

THE STATE OF SOUTH CAROLINA
In The Supreme Court

APPEAL FROM SPARTANBURG COUNTY
Court of Common Pleas

Roger L. Couch, Circuit Court Judge

Case No. 2007-CP-42-1438

State of South Carolina ex. rel. Alan Wilson in his
capacity as Attorney General of the State of South
Carolina, ... Respondent,

v.

Ortho-McNeill-Janssen Pharmaceuticals, Inc., f/k/a
Janssen Pharmaceutica, Inc., and/or Janssen, L.P., and
Johnson & Johnson, Inc., ... Defendants.

Of whom Ortho-McNeill-Janssen Pharmaceuticals, Inc.
is Appellant.

RECORD ON APPEAL - VOLUME IX

**Nelson Mullins Riley
& Scarborough LLP**
C. Mitchell Brown
William C. Wood, Jr.
A. Mattison Bogan
Miles E. Coleman
Post Office Box 11070
Columbia, SC 29201
(803) 799-2000

**Richardson Plowden
& Robinson, P.A.**
Steven J. Pugh
Steven W. Hamm
Mason A. Summers
1900 Barnwell Street
Post Office Drawer 7788
Columbia, SC 29202
(803) 771-4400

**Drinker Biddle
& Reath LLP**
Edward M. Posner
Chanda A. Miller
One Logan Square
Suite 2000
Philadelphia, PA 19103
(215) 988-2700

Attorneys for Appellant

**Office of Attorney
General**
The Honorable Alan
Wilson
C. Havird Jones, Jr.
1000 Assembly Street
Room 519
Columbia, SC 29201
(803) 734-3656

Bailey Perrin Bailey
Fletcher V. Trammell
Robert W. Cowan
Elizabeth W. Dwyer
440 Louisiana, Ste 2100
Houston, TX 77002
(713) 425-7100

**Harrison White Smith &
Coggins, P.C.**
John B. White, Jr.
Donald C. Coggins, Jr.
178 West Main Street
Post Office Box 3547
Spartanburg, SC 29304
(864) 585-5100

Simmons Law Firm, LLC
John S. Simmons
1711 Pickens Street
Columbia, SC 29202
(803) 779-4600

Attorneys for Respondent

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VII. CERTIFICATE OF COUNSEL

RISPERDAL Milestones



- **Only 56 products have reached \$100 MM (US Sales) in first 12 months on the market!**

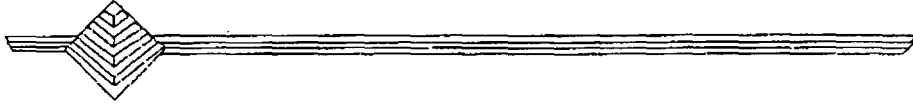
RISPERDAL did!

- **Only 11 products have achieved \$500 MM in annual sales after only 3 years on the market!**

RISPERDAL did!

Message and execution are the two critical pieces - one without the other will not lead to success.

RISPERDAL Milestones



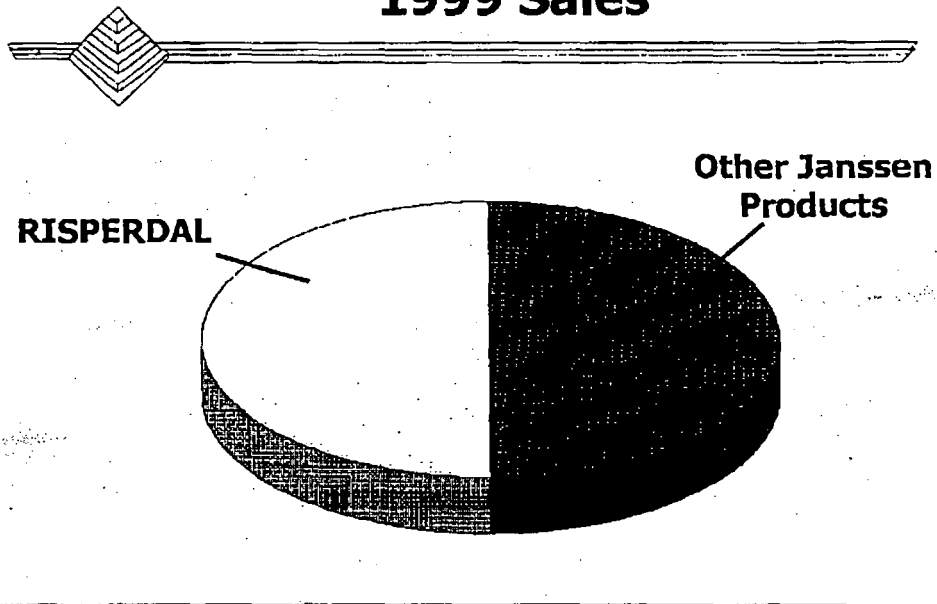
Only 11 products sold \$1 BB last year

RISPERDAL will...

CAN YOU MAKE IT HAPPEN?

Message and execution are the two critical pieces - one without the other will not lead to success.

Janssen Pharmaceutica 1999 Sales



We have also done analysis on opinion leader status based upon input from the MSL team. Currently, as you can see, the majority of the top 150 are positive towards RISPERDAL.

When you consider that about a year ago we would have had less than one third this number, this is a substantial improvement. Medical Business Development, the MSL team, and Professional Services have made significant strides in this area. However, there are about 80 more people to go.

Johnson & Johnson



- **"...Worldwide pharmaceutical sales increased 7.1%...This growth reflects the strong performance of RISPERDAL..."** 1997 J&J Annual Report
- **"J&J attributed the growth in worldwide pharmaceutical sales in the last quarter to RISPERDAL..."** 1998 J&J Q3 Report

Johnson & Johnson

Credo

**"We believe our first responsibility
is to the doctors, nurses, and
patients..."**

A Profile of Success: Ken Steele



- **Age 15 - Diagnosed with Paranoid Schizophrenia**
- **Next 30 Years - Homelessness & State Hospitals**
- **1994 - First Treatment with RISPERDAL**
- **Voices Stopped for First Time in 30 Years**

Message and execution are the two critical pieces - one without the other will not lead to success.

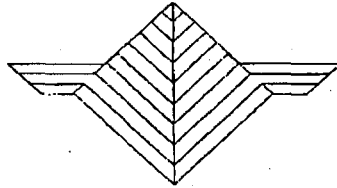
A Profile of Success: Ken Steele - Today



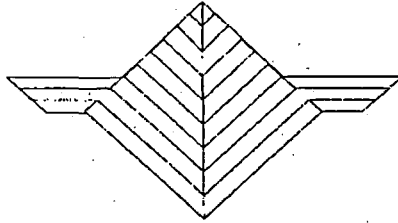
- **Appeared on front page of NY Times**
- **Publisher of New York City Voices**
- **Founder of NY Voter Empowerment Project**
- **Celebrated 4-Years of Being Voice-Free (5/99)...**

Message and execution are the two critical pieces - one without the other will not lead to success.

ALEX GORSKY
Vice President, Marketing



Janssen Pharmaceutica:



A Market Leader in CNS

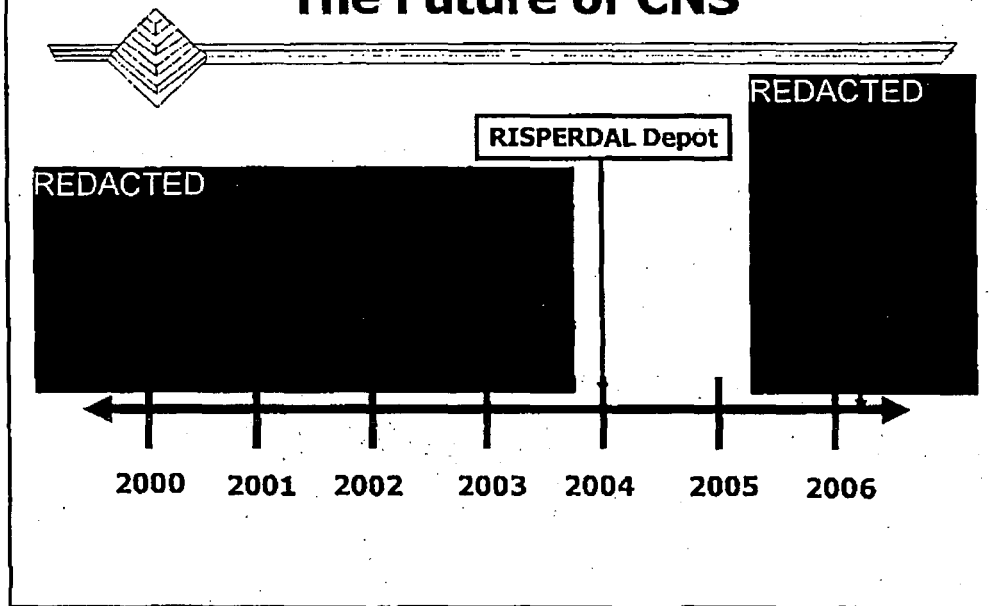
Janssen Pharmaceutica: The Future of CNS



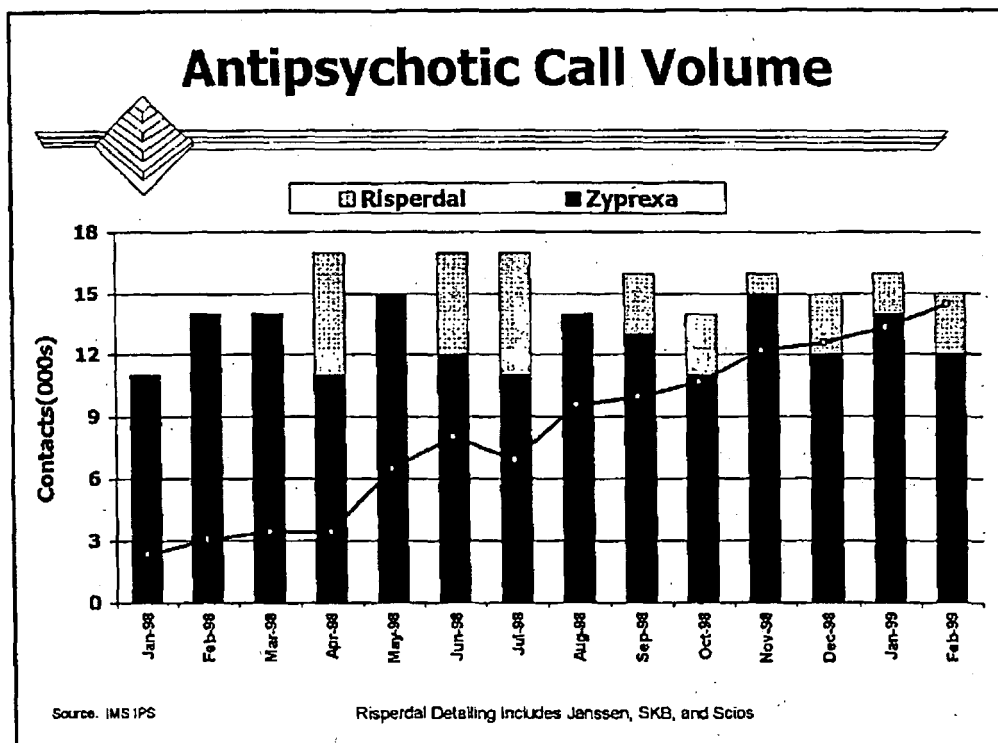
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- **RISPERDAL Depot(s)**

Message and execution are the two critical pieces - one without the other will not lead to success.

Janssen Pharmaceutica: The Future of CNS



Message and execution are the two critical pieces - one without the other will not lead to success.

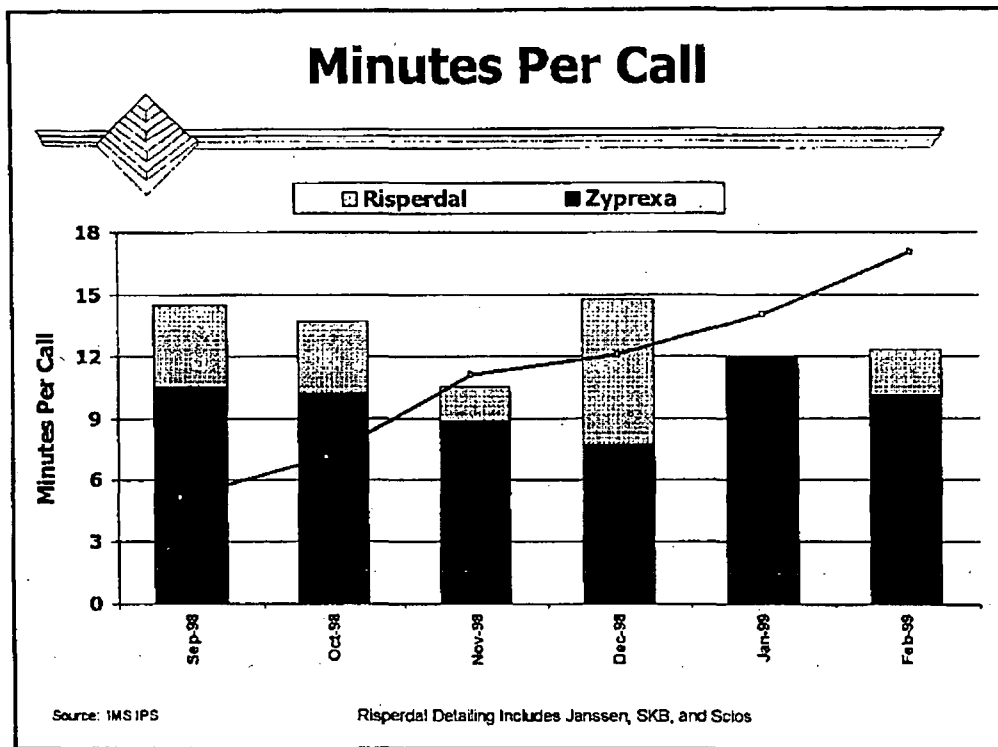


KEY POINTS

Currently, Zyprexa has high levels of detailing, higher than those of Risperdal.

RECOMMENDATIONS

Continue to monitor detailing levels.

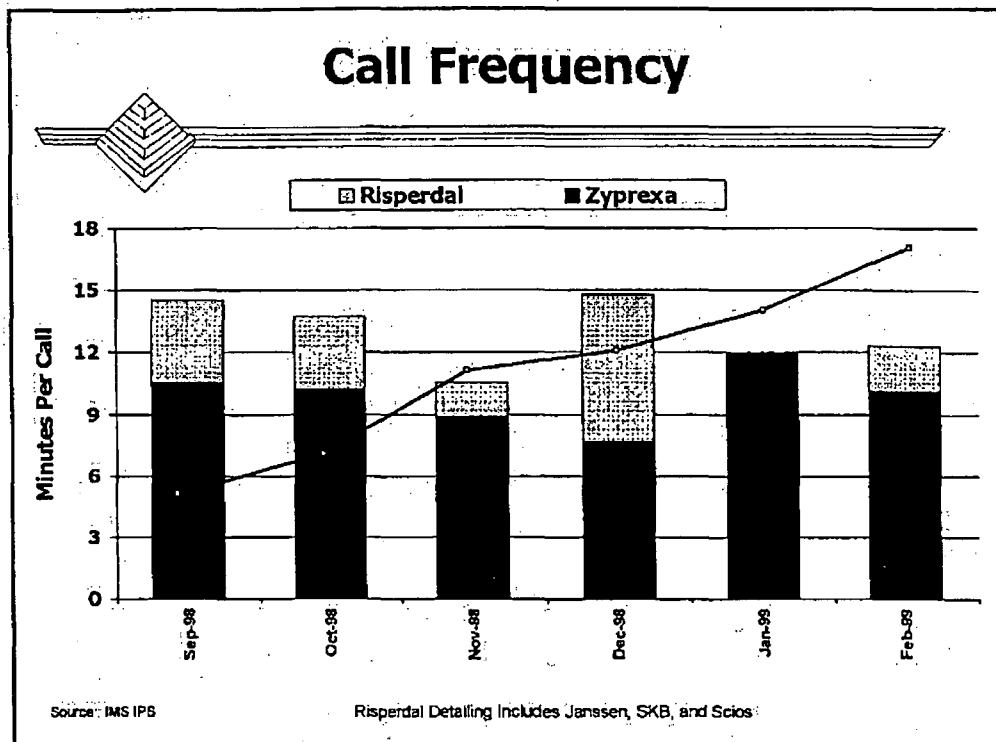


KEY POINTS

Currently, Zyprexa has high levels of detailing, higher than those of Risperdal.

RECOMMENDATIONS

Continue to monitor detailing levels.



KEY POINTS

Currently, Zyprexa has high levels of detailing, higher than those of Risperdal.

RECOMMENDATIONS

Continue to monitor detailing levels.

Message Consistency



- **Efficacy**
- **Weight Gain / Safety**
- **Dosing**

Message and execution are the two critical pieces - one without the other will not lead to success.

Home Office Support



- **Medical Meetings** **20,000 MDs**
- **Medical Ed Programs** **15,000 MDs**
- **Home Office Visitation** **300 Top MDs**

Message and execution are the two critical pieces - one without the other will not lead to success.

RISPERDAL Sales Forces

Partnership & Teamwork

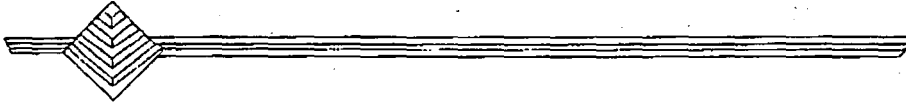
CNS-S
164

Scios
95

Eldercare
85

CNS-I
51

"Every Minute Counts!"

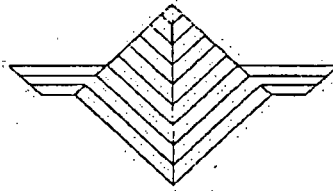


Our Strong Future in CNS...

**... Will Be Built With
RISPERDAL!**

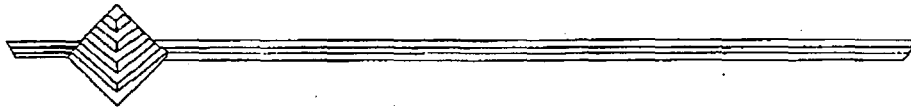
Message and execution are the two critical pieces - one without the other will not lead to success.

JANET VERGIS
Group Product Director, CNS



LUDWIG HANTSON
Franchise Director, CNS

Congratulations!!



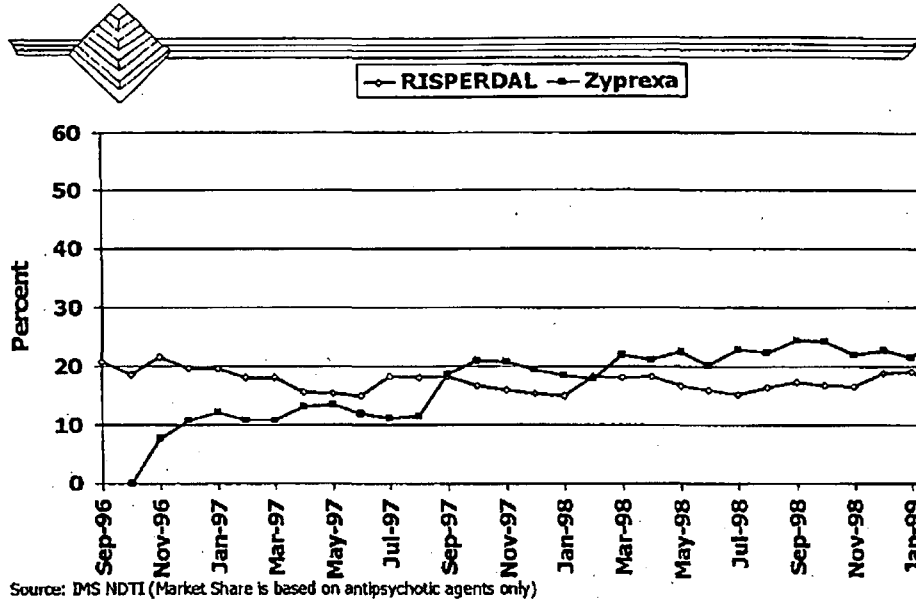
- **New High NRx Share 9-Months Running**
- **RISPERDAL Share Growth = Zyprexa Share Growth in 1999 (+1.1)**
- **Sales are up 39% over last year**
- **Sales are tracking to achieve \$____ in 1999**
- **RISPERDAL has been #1 for nearly 3 years!!**

Message and execution are the two critical pieces - one without the other will not lead to success.

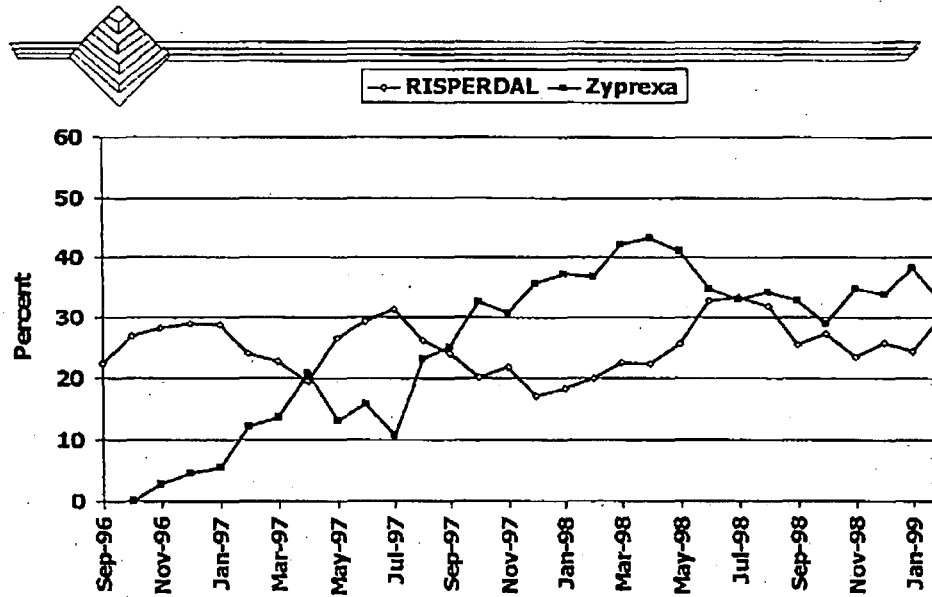
APA 1999 MARKET RESEARCH

Message and execution are the two critical pieces - one without the other will not lead to success.

Schizophrenia Market Share

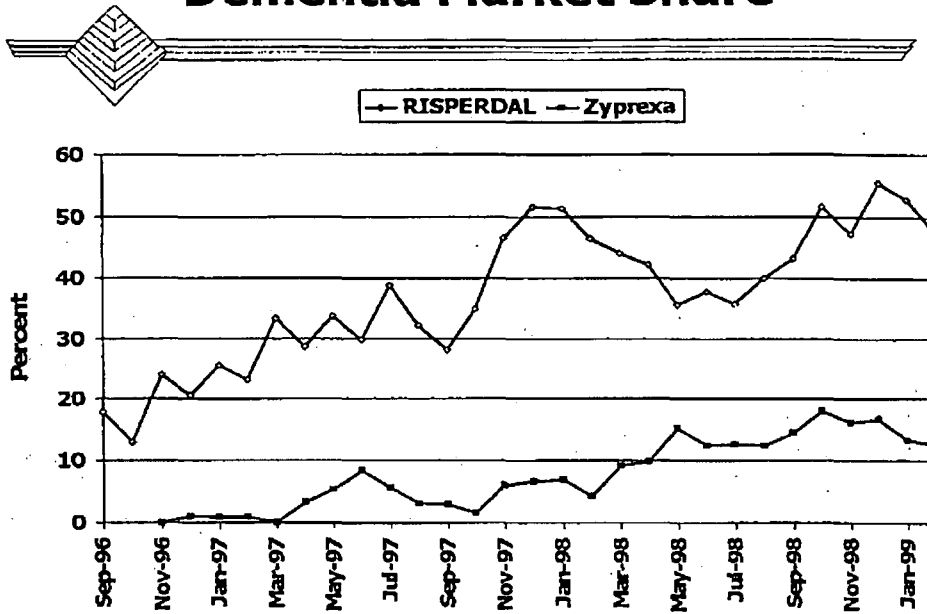


Bipolar Disorder Market Share

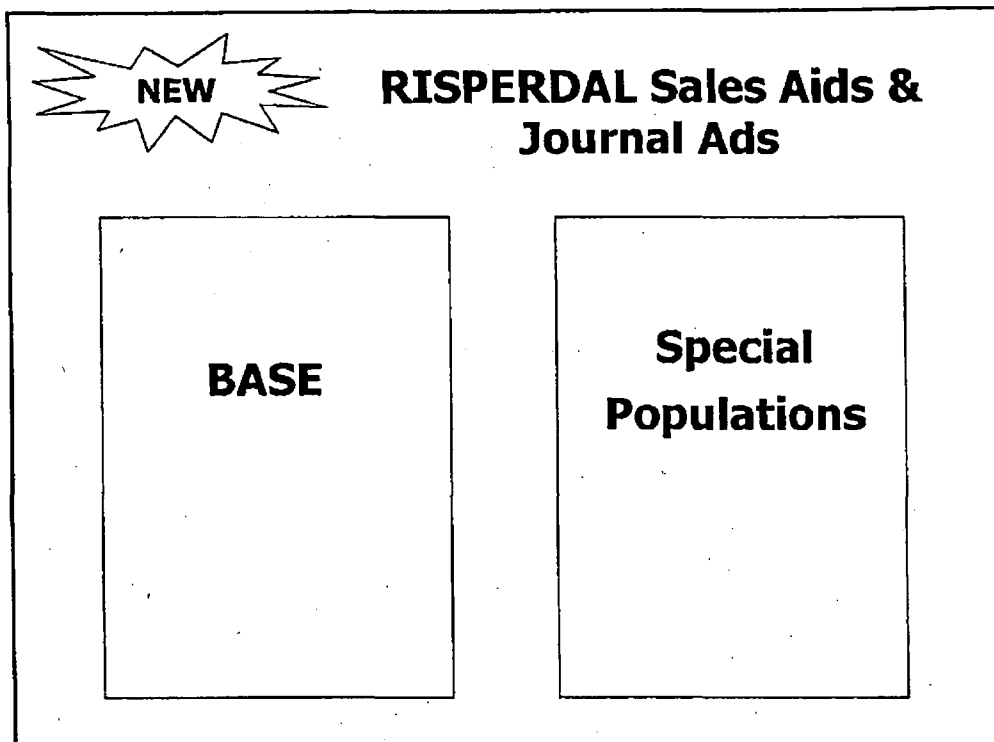


Source: IMS NDTI (Market Share is based on antipsychotic agents only)

Dementia Market Share

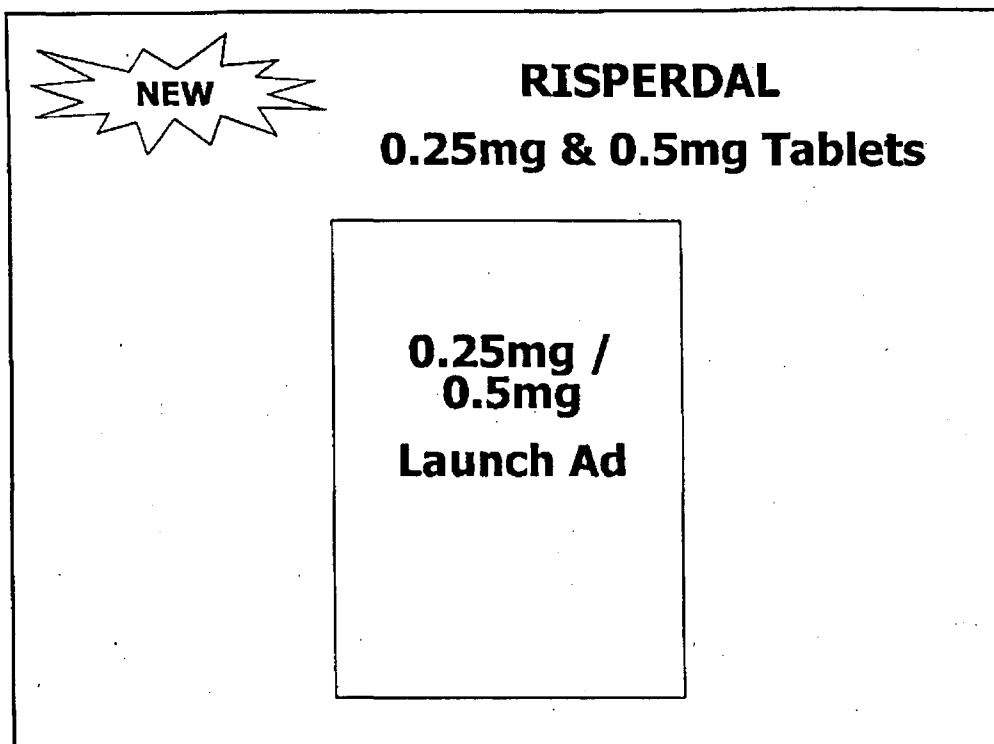


Source: IMS NDTI (Market Share is based on antipsychotic agents only)



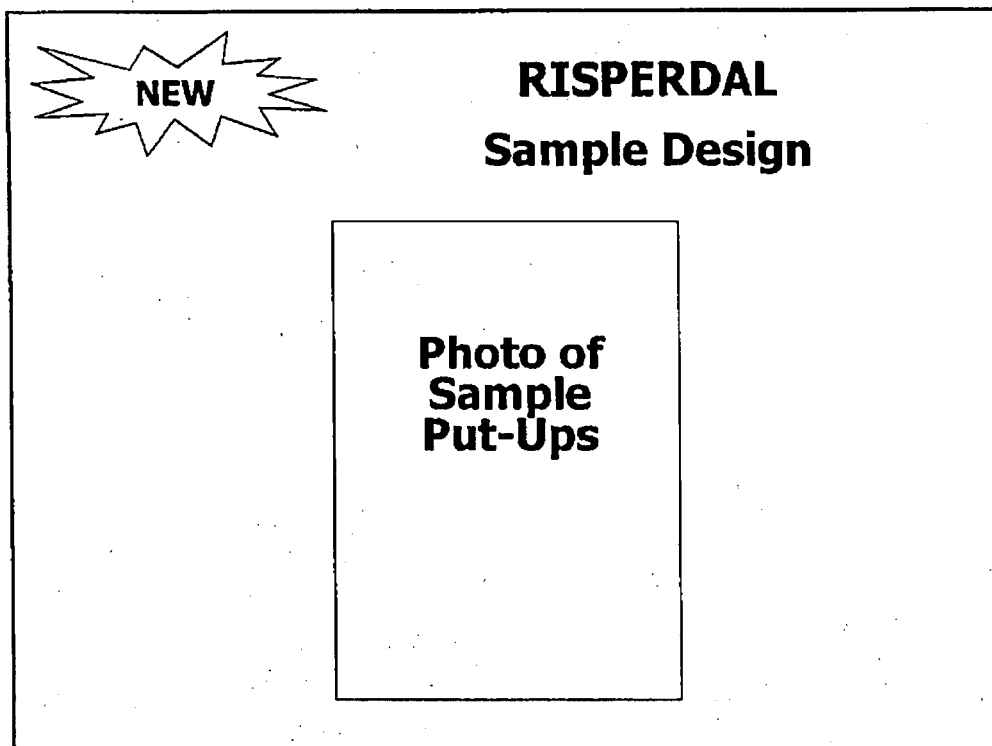
Tactics directed at the opinion leaders are aimed at enhancing our relationship, but more importantly ensuring their endorsement for RISPERDAL.

This year, there are a few new tactics such as Future Leaders and Visiting Professorships. In addition, we are continuing with many of the successful things we have done in the past, such as the CNS Summit and Regional Advisory Boards.



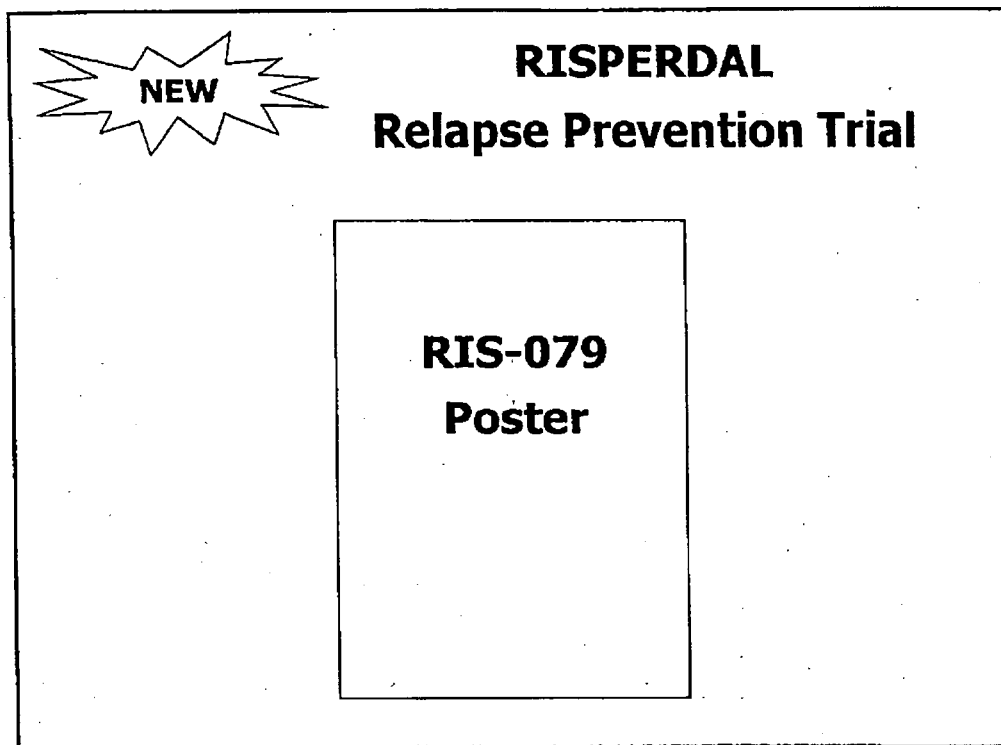
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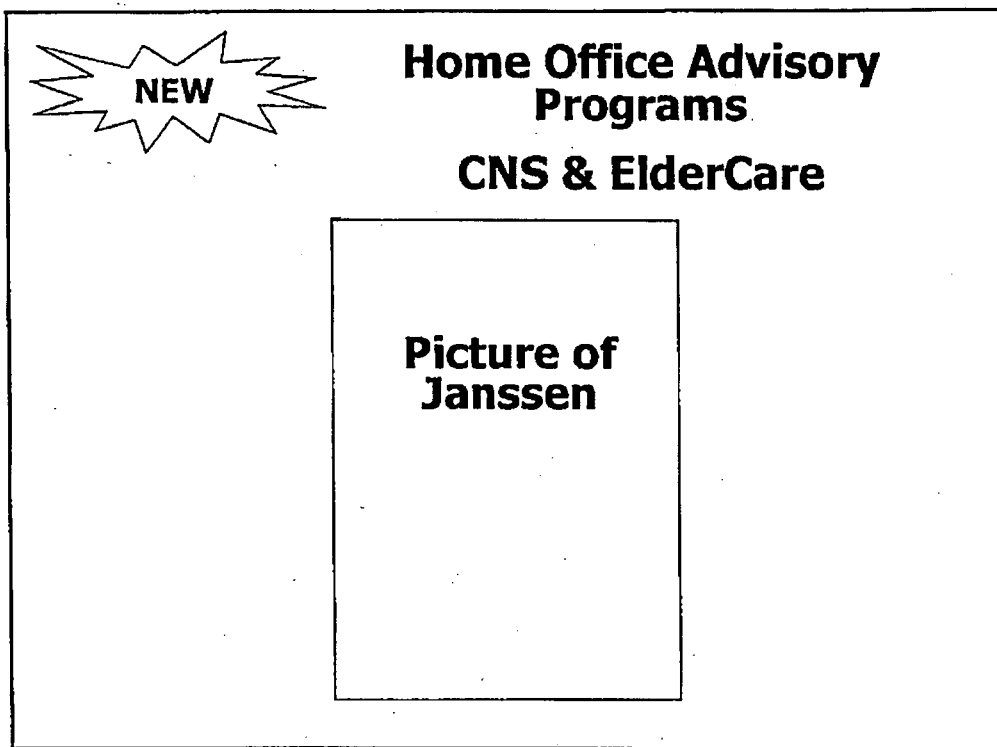
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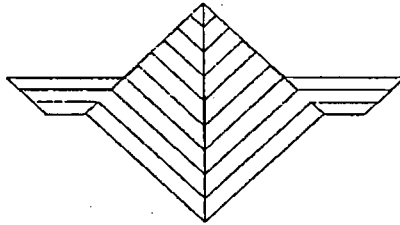
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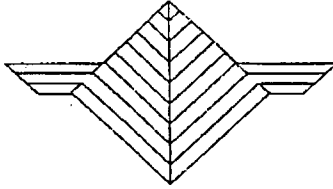
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RISPERDAL '99

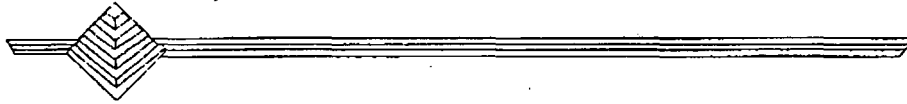


Make Every Minute Count!

MIKE WALSMAN
CNS National Sales Director



KEY POINTS

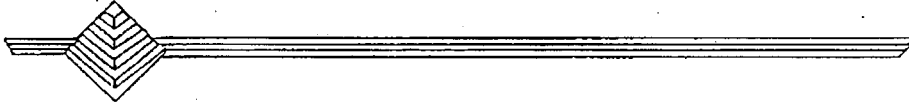


- Risperdal is #1!
- Importance of RISPERDAL!
- Janssen/J&J Commitment!
- Every minute counts-Preparation!

- Review the morning's key points

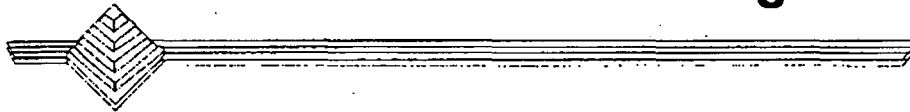
- Importance of Risperdal to Patients, Janssen, J&J
- David/Alex - Commitment to the success of RISPERDAL
- Every minute counts - preparation

HOUSEKEEPING NOTES



- Check Your Agenda!
- Be on Time!
- This Evening Function!
– 6:30pm

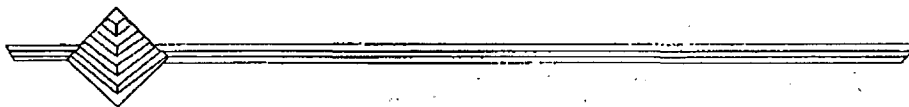
The RISPERDAL Challenge



"...Lilly not only scored all the points, but Janssen didn't even get a first down. They (Lilly) are going to bury them....It's a matter of time.."

K. Huer, SmithBarney, Dec. '96'

The RISPERDAL CHALLENGE



We woke up above ground today!

We're Still Here!

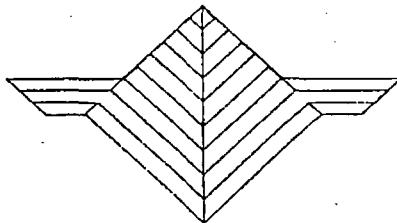
We're Still Growing!



WE'RE STILL #1!!

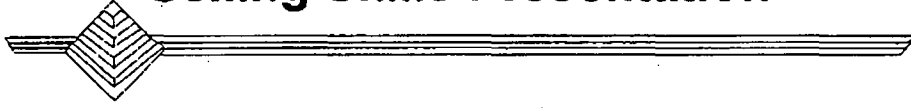
**WE'RE GOING TO
STAY #1!!!!!!**

RISPERDAL '99



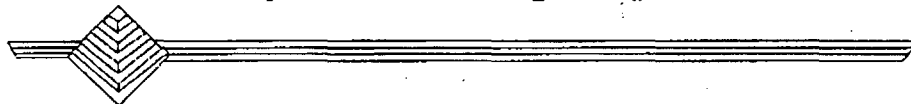
Make Every Minute Count!

Selling Skills Presentation



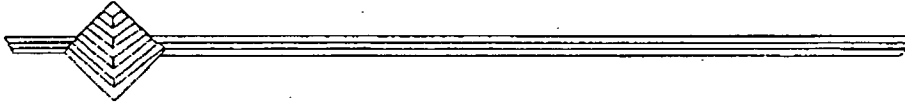
Tuesday June 8, 1999

Why A New Selling Program?



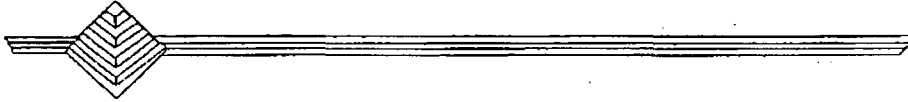
- Establish consistent selling platform for all representative/selling partners
- Establish a consistent selling language for all representatives
- Improve ability to fully engage physicians during sales calls

Why A New Selling Program?



- Provide well defined selling skills expectations:
 - Field Work Sessions
 - FCRs/Human Resources Review
- Enhance competitive selling capability

RISPERDAL NATIONAL TRAINING MEETING



TEAM DAY PRESENTATION

"Welcome to Team Day"



THE BEST OF THE BEST IN CNS

CNS - EC - SCIOS

TEAM DAY AGENDA



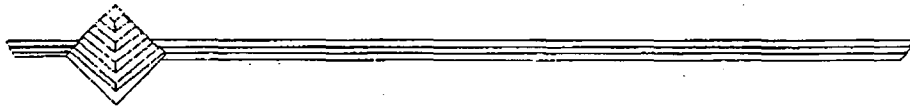
- Review Objectives
- Sales Direction
 - CNS
 - EC
 - SCIOS
- Breakout Session

Objectives



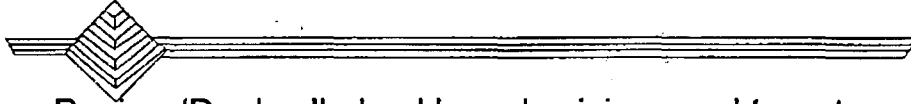
- Maximize 'Teamwork'
- Clarify Roles and Responsibilities
 - CNS - EC - SCIOS
- Understand Sales Direction for each Team
- Enhance Communication
- Maximize RISPERDAL® growth
- Follow up

General Guidelines



- Communication
- Big Picture

Breakout Session Co-Promotion Partners



- Review 'Dual called on' key physicians and target accounts
- Develop specific action plans to:
 - Enhance coverage
 - Improve and Exchange Communication
 - Leverage Resources i.e. CME, speaker programs etc.
 - Grow RISPERDAL® share - both - schizophrenia and special population
 - Follow up - Develop a plan - What-Where-When-How?

CNS SALES FORCE



3Q99 SALES DIRECTION

CNS SALES FORCE

3Q99 OBJECTIVES



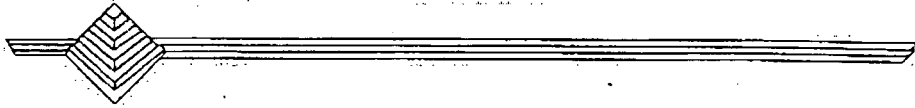
- GROW RISPERDAL Market Share!
- STOP the Growth of Zyprexa!
- REGAIN Market Share Leadership with Decile 8-9 Psychiatrists!
- OWN Schizophrenia Segment of Market!
- EXECUTE CNS Call Plan!

**1999 CNS SALES DIRECTION
3Q99 CALL PLAN**



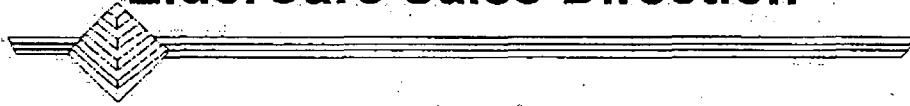
- 100% Reach on all target HVP physicians
 - S-Rep = Top 60 Physicians
 - I-Rep = Top 100 Physicians
- 90% 2X/mo Frequency on Decile 8-9 physicians
- Avoid Distractions - Maintain Focus!
- Maintain 2x/mo Hospital Call Activity!
- Partner with Scios to Maintain Decile 5-7 Call Activity!
- Effectively Utilize Resources!

RISPERDAL KEY COMMUNICATION POINTS



- Focus on ***EFFICACY*** FIRST!
- Emphasize **low weight gain!**
- Stress **appropriate dosing!**
- **Ask** for the BUSINESS!
 - Specific Patient Types

1999 3rd Cycle ElderCare Sales Direction



- **Target the Right Customers**
 - **Priority #1 - Prescribers**
 - Geriatric Psychiatrists/Consultant Psychiatrists
 - Medical Directors
 - Attending Physicians/Physician Extenders
 - **Priority #2 - Influencers**
 - Directors of Nursing
 - Facility Staff
 - Consultant Pharmacist

1999 3rd Cycle ElderCare Sales Direction

- **Achieve Frequency on Targeted Customers**

Goal: 6 Physicians and 2 Nursing Homes/Day

<u>Prescribers</u>	<u>Frequency</u>	<u>Goal</u>
Psychiatrists	3x per Qtr	90%
Medical Directors	3x per Qtr	90%
Attending Physicians	3x per Qtr	65%
Hospice	3x per Qtr	90%
<u>Influencers</u>		
Top 20 NH	3x per Qtr	80%
Bottom 20 NH	2x per Qtr	65%
Consult. Pharm.	As Needed	As Needed

1999 3rd Cycle ElderCare Sales Direction

- **Execute High Impact Sales Message**

- Consistent Core Message Delivery
- Tailored to Customer Need/Concern
- Execution of Multiple Product Presentations

- Risperdal - 50%

REDACTED

1999 3rd Cycle ElderCare Sales Direction

- Teamwork

LTC Manager

CNS

275

500 Blue & Gold

REDACTED

All Products

Risperdal

REDACTED

RISPERDAL TRAINING MEETING

THURSDAY CLOSING SESSION

'THE BEST OF THE BEST'



WELCOME BACK!

KEY OBJECTIVES



- ***GROW*** RISPERDAL SHARE!
- ***STOP*** THE GROWTH OF OLANZAPINE!

RISPERDAL CRITICAL SUCCESS FACTORS



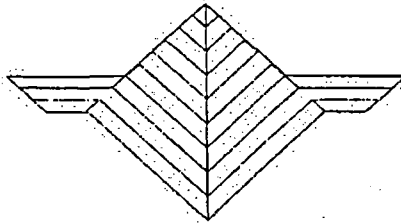
- Pride & Confidence
- Effective Use of New Sales Materials
- Successful Execution of Call Plans
- Effective Selling Skills
- Maximize Teamwork

**RISPERDAL
CRITICAL SUCCESS FACTORS**



'ASK FOR THE BUSINESS'

RISPERDAL '99



Make Every Minute Count!

RISPERDAL AWARDS BANQUET

Thursday June 10, 1999

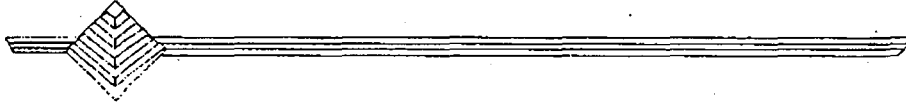
8:00pm

CNS 'SPRINT CONTEST' WINNERS



- Contest Period:
 - October 1998 - March 1999
- Top District per CNS Region (PI)
- Awards:
 - \$5,000 per District Manager
 - \$2,500 per District Members

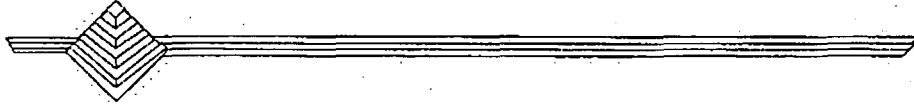
**CNS SPRINT CONTEST WINNER
EASTERN REGION**



NEW YORK DISTRICT

Janet Petrillo, DM

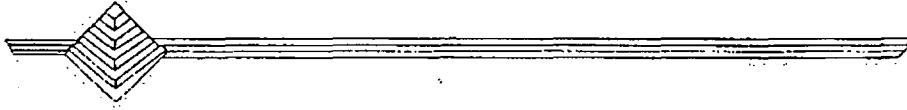
**CNS 'SPRINT CONTEST' WINNER
CNS CENTRAL REGION**



CHICAGO CNS DISTRICT

Jeff Hoover, DM

**CNS 'SPRINT CONTEST' WINNER
WESTERN REGION**



Los Angeles District

Jeff Doherty, DM

**RISPERDAL University Freshman Year
Minneapolis District**

Anthony Cartwright District Manager

Ben Breskovich

Elizabeth Bucholz

David Conforti

Lawrence Danger

Paula Dunnum

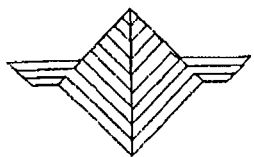
Susan Grogan

Rick Hansen

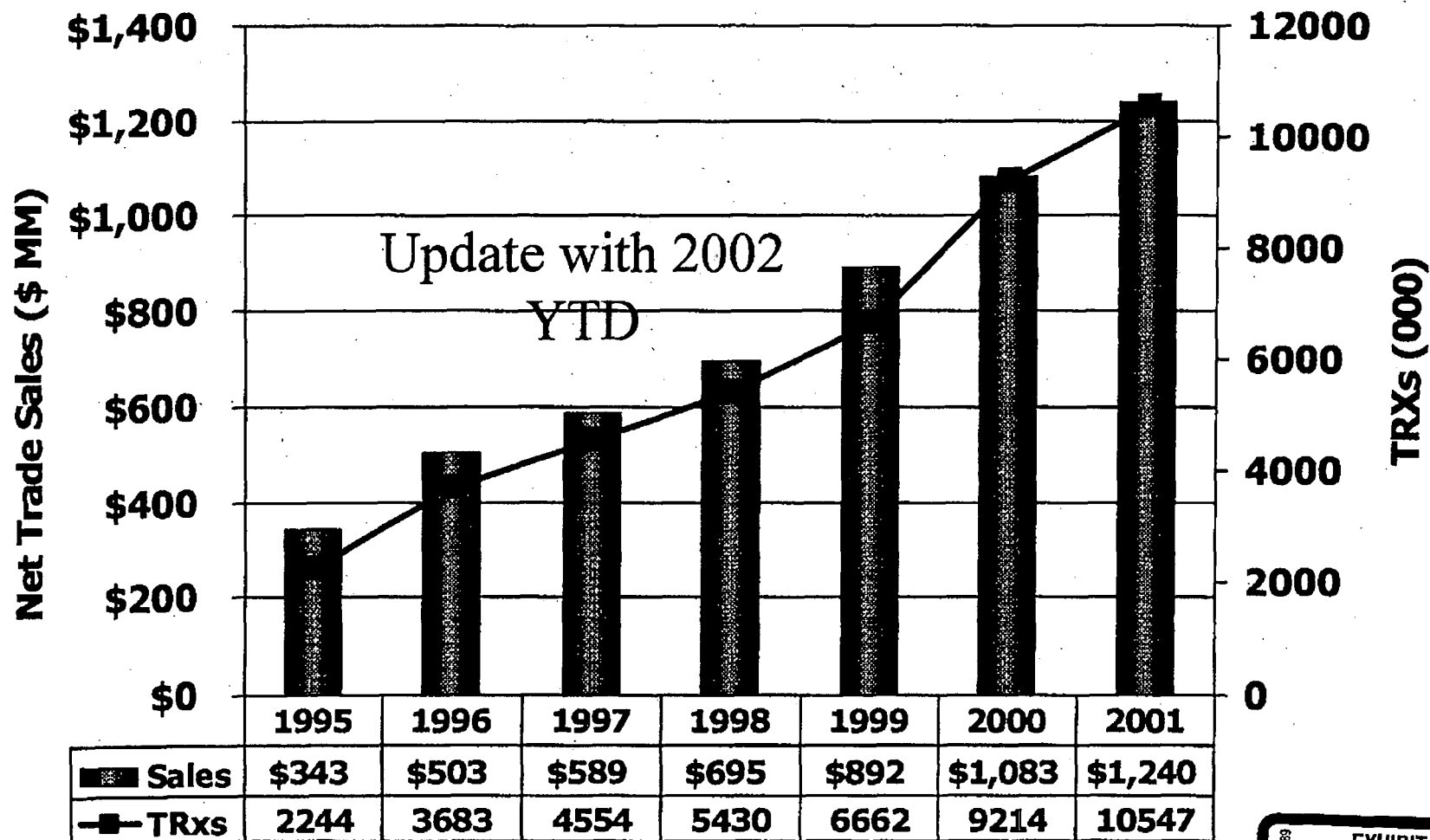
Sarah Kim

Lamont Roth

Saeed Siddiqui



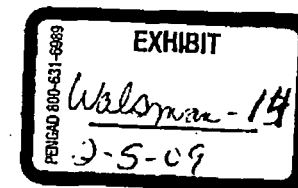
Risperdal Total Sales & TRxs 1995 - 2001



Subject to legal &
regulatory review

CAGR: Sales = 24%, TRxs = 29% 2002, \$1,425

Source: Internal NTS and IMS Health, NPA Plus



CONTAINS CONFIDENTIAL COMMERCIAL INFORMATION

RISP-EDPA000673353

From: Pruden, Gary [JANUS]
Sent: Sunday, October 05, 2003 11:40 PM
To: Mahmoud, Ramy [JANUS]; Vergis, Janet [PGSMUS]; Fabbri, David [JANUS]; Shaw, Christi [JANUS]; Rielly-Gauvin, Katherine [PGSM]
Subject: FW: Risperdal & Risperdal Consta Diabetes Labeling
Sensitivity: Confidential

FYI...updated discussion on Tuesday. (Post G.Neill conf call friday)

Gary

-----Original Message-----

From: Norton, David [JJCUS]
Sent: Sunday, October 05, 2003 12:49 PM
To: Weisman, Harlan [CNTUS]; Peterson, Per A [PRDUS]; Poon, Christine [JJCUS]
Cc: Neil, Garry [PRDUS]; Miller, Peter [JANUS]; Pruden, Gary [JANUS]
Subject: RE: Risperdal & Risperdal Consta Diabetes Labeling
Sensitivity: Confidential

All,

I agree with Harlan and have also talked about this with the folks at Janssen on Friday and everyone is in agreement.

From my perspective we need to achieve two key points or we should have the right to back away.

Those key points are:

1. Level the playing field with the an FDA Talk paper or something equivalent that captures all manufactures . AZ, Pfizer and BMS should not be able to use any new Risperdal Label to "bash us".
2. We need to get assurance of Risperdal Consta approval. This is clearly more difficult as Rusty will likely not go against a negative recommendation from one of the Reviewers. On this one we will need to walk a delicate line, but I would hate us to be in a position that we accept the label and the Bipolar indication only to get a non-approvable for Consta..... we would then loose on both accounts. We should remember that the agency has reneged in the past.

David

-----Original Message-----

From: Weisman, Harlan [PRDUS]
Sent: Saturday, October 04, 2003 8:53 PM
To: Peterson, Per A [PRDUS]; Poon, Christine [JJCUS]
Cc: Neil, Garry [PRDUS]; Norton, David [JJCUS]
Subject: RE: Risperdal & Risperdal Consta Diabetes Labeling
Sensitivity: Confidential

Garry and I have discussed this and I endorse his suggested approach.

Harlan

-----Original Message-----

From: Neil, Garry [PRDUS]
Sent: Saturday, October 04, 2003 2:21 PM
To: Peterson, Per A [PRDUS]; Poon, Christine [JJCUS]; Weisman, Harlan [PRDUS]
Subject: Risperdal & Risperdal Consta Diabetes Labeling
Importance: High
Sensitivity: Confidential

Per, Chris and Harlan:

We are continuing to negotiate the diabetes class label for Risperdal bipolar. Rusty Katz at FDA is not returning calls through regular channels so I asked Trish DeSantis to leverage her personal relationship with him and to call him yesterday. She learned that Rusty is digging in his heels on the need for class labeling on diabetes and that he is not willing to consider much modification to the label he offered us. He was annoyed by our attempt to substantially modify the class label to a precaution. This is an important public health issue in his mind and he intends to see that "everyone" gets this label, referring to our competitors at Lilly, BMS, Pfizer and AZ. He has not heard from any of the other companies except Lilly, who will accept the label "as is". It doesn't seem that the consensus conference organized by APA and ADA with industry, NIH and FDA participation (November) is not a very large blip on his radar screen and I don't think we can count on it to have too much impact in the end. His action date on Risperdal bipolar is Oct. 16 and Rusty never misses his dates. He indicated that he would very much like to "get Risperdal and Risperdal Consta off his desk". He suggested that we could send a fax with some "small tweaks" to the label and he would consider it.

He knows our main priority is Consta and let us know that he will not approve it until this is resolved. The Consta NDA is not on his desk yet (action date Oct. 29) but he hasn't heard anything from his staff that would indicate a problem. It seems that Bob Temple has continued to express an interest in the application and is following it. Taken together, these are good signs pointing to an approval - and this is as strong a signal as we can get right now. However we know we have a difficult toxicology reviewer on this package and approval is not assured, but based on what I know today I would say our chances are 80 - 90% for on time approval IF we can resolve the diabetes issue.

I asked Trish to make sure he understood that our competitors would try to disadvantage us in the marketplace if we change our label before at least some of them do. We pointed out that they were using the stroke labeling against us etc. He seemed somewhat sympathetic to the idea of a level playing field. He did say that given all the publicity around this he didn't view a DDL as necessary but if it was he would make certain it would come from everyone so that it couldn't be used for competitive advantage (perhaps an opening for us, see below). As you know whether or not FDA mandates a DDL, it is J&J policy to issue one every time we implement a new Warning.

We discussed this new information with Peter Miller, Gary Pruden, Scott Reines, Bob Delap, Jack Singer, Jack Grebb and Fred Grossman yesterday. We had a good and open discussion about what is and is not possible. Obviously our priority is to get Consta approved on time, but we want to minimize the chances that we will be in the marketplace with the class label before AZ, BMS and Pfizer but without Consta. We also want to limit the opportunity for our competitors to take unfair advantage of our situation. Rusty is swamped with work. If we send in a big data package to support the sort of label change we previously proposed it won't be well received and I am certain it will take months for him to review it. I doubt that we would prevail anyway. He views the diabetes as an important public health issue and would like to line up another company besides Lilly to accept the class label and help bring the others in line. With Lilly going out with class labeling it would be very difficult for him to back down. Consta is his main leverage with us and he knows it.

We formulated the following plan:

- 1) I asked the team to desist from calling and leaving voice mails for Rusty. This is obviously not having a positive impact. We have a lot of pending and future business with Rusty and I want to preserve a good working relationship.
- 2) I will ask Trish to call Rusty back next week to continue the "back channel" negotiations.
- 3) We will telegraph that we agree with his position and will take the class label almost as written for both Risperdal and Consta (one or two small tweaks) provided that we can be assured of a Consta approval. In order to do this we suggest that he issue an approvable letter on bipolar and send us the Consta label now or ASAP so we can see the diabetes warning in context and so we can have everything ready to go on the action date for Consta. We will indicate that we will then accept the same label for Risperdal. I don't believe he would be willing to delay his action letter on bipolar so we go straight to approval or that he could accelerate Consta, but we will see if the latter might be possible.
- 4) We offer to prepare a draft "talk letter" for FDA for their website discussing the class label in a neutral way that will not allow any company to take advantage. Gary Pruden has offered to send this to all 700,000 physicians in the US. We will explain that we believe this will level the playing field, force the other companies to get in line sooner and get the message out to physicians.

If we can achieve all or most of this I would recommend that we move forward. There are certainly no guarantees. I will let you know soonest after the next discussion with Rusty - I hope Monday or Tuesday.

Garry Neil
(908) 927-3637 (Office)
(908) 252-1798 (FAX)

Administrative Assistant: Loraine Koury (908) 927-3632

Johnson & Johnson Pharmaceutical Research & Development, L.L.C

Abbreviated Clinical Study Report

Risperidone versus Olanzapine in the Treatment of Schizophrenia - Extension Trial

Protocol RIS-USA-113; Phase 4

R064766 (risperidone)

COORDINATING INVESTIGATOR: Dr. R. Chengappa, MD, Western Psychiatric Institute and Clinic, Pittsburgh, PA 15213, U.S.A.

DATE STUDY INITIATED: 18 December 1997

DATE STUDY COMPLETED: 26 February 1999

Issue Date: 16 April 2009
Prepared by: Johnson & Johnson Pharmaceutical Research & Development, Division of Janssen-Cilag Ltd.
Document No.: EDMS-PSDB-9076477; 2.0

GCP Compliance: This study was conducted in compliance with Good Clinical Practice, including the archival of essential documents.

Confidentiality Statement

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OTHER DOCUMENTATION

Although recommended in the ICH guidelines, there is either no information available for the following or they do not apply to this study:

- Batch Numbers for Subjects Receiving More than One Batch of Study Drug
- Publications Based on the Study
- Other Key Documents Referred to in the Report
- Audit Certificates
- Interlaboratory Standardization Methods and Quality Assurance Procedures

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviations

ACS	anticholinergic symptoms
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
AST	aspartate aminotransferase
BMI	body mass index
B-QoLI	Brief Quality of Life Interview
CGI	Clinical Global Impression
CGI-C	Clinical Global Impression of Change
CPK	creatine phosphokinase
CRF	case report form
DAI	Drug Attitude Inventory
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
ECG	electrocardiogram
EPS	extrapyramidal symptoms
ESRS	Extrapyramidal Symptom Rating Scale
GCP	Good Clinical Practice
GGT	gamma-glutamyltransferase
HAMD	Hamilton Depression Scale
HbA1c	glycosylated hemoglobin
HDL	high-density lipoprotein
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ITT	intent-to-treat
IVRS	interactive voice response system
J&JPRD	Johnson & Johnson Pharmaceutical Research & Development (the sponsor)
LDL	low-density lipoprotein
M-SIP	Modified Sickness Impact Profile

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS (CONTINUED)

Abbreviations (Continued)

PANSS	Positive and Negative Syndrome Scale for Schizophrenia
PRSQ	Prolactin-Related Symptoms Questionnaire
SD	standard deviation
TSH	thyroid-stimulating hormone
U.S.	United States
VAS	Visual Analogue Scale
WHO-ART	World Health Organization Adverse Reaction Terminology

ETHICS

Independent Ethics Committee/Institutional Review Board

The study protocol was reviewed by an Independent Ethics Committee/Institutional Review Board (IEC/IRB).

Ethical Conduct of the Study

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Known instances of nonconformance were documented and are not considered to have had an impact on the overall conclusions of this study.

Subject Information and Consent

Subjects or their legally acceptable representatives provided their written consent to participate in the study after having been informed about the nature and purpose of the study, participation/termination conditions, and risks and benefits of treatment. Known instances of nonconformance were documented and are not considered to have impacted the overall conclusions of this study.

Personal data from subjects enrolled in this study was limited to those data necessary to investigate the efficacy, safety, quality, and utility of the investigational study drug(s) used in this study, and were collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. Additional information on the ethical conduct of this study is contained in the Ethical Aspects section of the protocol, which is appended to this report.

INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Coordinating Investigator:	Dr. R. Chengappa, M.D., Western Psychiatric Institute and Clinic, 3811 O'hara Street, Pittsburgh, PA 15213, U.S.A.
Sponsor's Responsible:	
Medical Officer:	Jaskaran Singh, M.D.*
Project Physician:	Martin Brecher, M.D. Stuart Kushner, M.D.*
Statisticians:	Keith Karcher, M.Sc.* Benjamin Lyons, Ph.D.
Medical Writer:	Wendy Shore, Ph.D.*
Central Clinical Laboratory:	SmithKline Beecham Clinical laboratories, 7600 Tyrone Avenue, Van Nuys, CA 91405, U.S.A.
Contract Research Organization and level of involvement:	IRI Trials Management Center, Route 22 East, P.O Box 999, Anandale, New Jersey, 08801-0999, U.S.A.

* Considered an author of this report

1. INTRODUCTION

Risperidone (RISPERDAL®) is a benzisoxazole derivative with potent combined serotonin 5HT_{2A} and dopamine D₂ receptor-blocking properties. Adrenergic α_1 and, to a lesser extent, histamine H₁ and adrenergic α_2 receptors are also antagonized by risperidone. In adults, there is clear evidence that risperidone is an effective antipsychotic, ameliorating positive, negative, and mood-related symptoms of schizophrenia and exhibiting a low rate of extrapyramidal symptoms (EPS) and other side effects. Risperidone has also been shown to effectively delay relapse during maintenance treatment in clinically stable patients. In the United States (U.S.), risperidone is approved for the treatment of schizophrenia in adolescents, ages 13 to 17, and for the short-term treatment of acute manic or mixed episodes of bipolar I disorder in children and adolescents ages 10 to 17.

Olanzapine (Zyprexa®) is a psychotropic agent that belongs to the thienobenzodiazepine class¹. Oral olanzapine is indicated for the treatment of schizophrenia, and acute mixed or manic episodes associated with bipolar I disorder. Olanzapine has strong affinity for the 5HT_{2A}, D₂, and α -adrenergic receptors. It is distinguished pharmacologically from risperidone by having strong affinity for the muscarinic receptors, a 20-fold stronger affinity than risperidone at the histamine H₁ receptor and weaker affinity at the α_2 adrenergic receptor. The pharmacological differences in the receptor-binding properties of these 2 antipsychotic agents may result in differences in efficacy and safety.

The purpose of this study was to compare the long-term (1 year) safety and efficacy of risperidone versus olanzapine in subjects with schizophrenia and schizoaffective disorders who had completed 8 weeks of treatment with risperidone or olanzapine in study RIS-USA-112.

2. OBJECTIVES

The objectives of the study were:

- To compare the safety, particularly the incidence of weight gain, of risperidone with olanzapine in subjects with schizophrenia and schizoaffective disorder treated for up to 44 weeks.
- To compare the efficacy of risperidone with olanzapine on the symptoms, quality of life, and satisfaction of subjects with schizophrenia and schizoaffective disorder over a 44-week period.

3. METHODS

3.1. Study Design

This was a randomized, double-blind, parallel-group, multicenter, comparative study of risperidone versus olanzapine in subjects with schizophrenia and schizoaffective disorder. Subjects who had completed study RIS-USA-112 in its entirety (i.e., 8 weeks) were eligible to enter this study. Subjects would continue on the study medication to which they had been assigned in study RIS-USA-112 (i.e., risperidone or olanzapine) for 44 weeks. The total length of both studies was 52 weeks (1 year). Safety and efficacy assessments were performed at Weeks 4, 8, 12, 28, and 44. Additional clinic visits were scheduled at Weeks 16, 20, 24, 32, 36 and 40.

Subjects with a diagnosis of schizophrenia or schizoaffective disorder (according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]) who had completed the preceding study RIS-USA-112 in its entirety (and who did not have a time lapse of more than 3 days since the completion of RIS-USA-112) and who continued to meet all of the inclusion criteria defined for RIS-USA-112 were eligible to enter this study. Subjects could be inpatients or outpatients;

Subjects remained in the same double-blind treatment arm they were randomly assigned to in the preceding study, and were treated with 1 of the following 2 treatments for 44 weeks:

- Treatment A: 1 to 3 risperidone 2-mg tablets (corresponding to 2 to 6 mg risperidone)
- Treatment B: 1 to 4 olanzapine 5-mg tablets (corresponding to 5 to 20 mg olanzapine)

The study medication was overencapsulated to maintain the blind. The capsules were identical in appearance, taste and smell, and were taken once daily preferably in the morning (around 08.00 h). The subject could receive the entire dose in the evening (around 20.00 h) to improve tolerability.

The dose was continued from study RIS-USA-112. If there was worsening of psychiatric symptoms, the dose could be increased by 1 capsule per week. The maximum permitted number of capsules per day remained 4 capsules per day. Dose decreases to a minimum of 1 capsule per day could occur at anytime.

Efficacy was evaluated by the Positive and Negative Symptom Scale (PANSS), Clinical Global Impression (CGI) and Clinical Global Impression of Change (CGI-C), the 21-item Hamilton Depression Scale (HAMD), Cognitive Functioning (i.e., Wisconsin Card Sorting Test; Trails A and B; Continuous Performance Test; California Verbal Learning Test; Visual Working Memory; Verbal Fluency

Examinations), Brief Quality of Life Interview (B-QoLI), Visual Analogue Scales for Sleep and drowsiness (VAS), and the Drug Attitude Inventory (DAI).

Safety assessment was based on reported adverse events, clinical laboratory tests, vital sign measurements, physical examinations, electrocardiogram (ECG) findings, body weight and Body Mass Index (BMI), waist/hip ratio, evaluation of the Extrapyramidal Symptom Rating Scale (ESRS), anticholinergic symptoms (ACS), prolactin-related symptoms questionnaire (PRSQ), and Modified Sickness Impact Profile (M-SIP).

Table 1 provides an overview of key procedures performed during the study.

Table 1: Time and Event Schedule

Visit ^b	Treatment Period											
	Entry ^a	2	3	4	5	6	7	8	9	10	11	12 ^e
Day	1	28	56	84	112	140	168	196	224	252	280	308
Week	0	4	8	12	16	20	24	28	32	36	40	44
Month	0	1	2	3	4	5	6	7	8	9	10	11
Informed consent	X											
Physical examination	X											X ^e
Vital signs	X	X	X	X				X				X ^e
ECG	X											X ^e
Laboratory tests	X	X ^c	X ^c	X ^c				X ^c				X ^d
Prolactin	X			X				X				X ^e
ESRS	X	X	X	X				X				X ^e
Body weight	X	X	X	X				X				X ^e
Waist/Hip ratio				X				X				X ^e
M-SIP	X			X				X				X
PRSQ	X			X				X				X
ACS	X	X	X	X				X				X
PANSS	X	X	X	X		X		X				X ^e
CGI/CGI-C ^f	X	X	X	X				X				X
HAM-D	X											X ^e
Cognitive tests	X			X				X				X
B-QoLI	X			X				X				X
VAS Quality of Sleep	X	X	X	X				X				X
VAS Daytime drowsiness	X	X	X	X								X
DAI	X			X				X				X
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X
Dispense medication	X	X	X	X	X	X	X	X	X	X	X	
Return medication		X	X	X	X	X	X	X	X	X	X	X

^a The evaluations from Week 8 of RIS-USA-112 were used for entry to RIS-USA-113.

^b Visits could be conducted within ± 3 days on either side of the scheduled assessment date.

^c Liver transaminases only (aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma-glutamyltransferase [GGT]).

^d Included cholesterol, lipid profile (high-density lipoprotein [HDL], low-density lipoprotein [LDL], triglycerides), thyroid panel (T₃, T₄, and thyroid-stimulating hormone [TSH]), glycosylated hemoglobin [HbA1c] and creatine phosphokinase (CPK).

^e Visit 12 and/or endpoint

^f Both the CGI and the CGI-C were evaluated at these visits. The CGI-C was compared to the severity of illness at the randomization visit of the preceding study (RIS-USA-112)

The main efficacy results and all safety results of the study are located in the main text of this report. Additional detailed summary tables are included as attachments in the Supporting Data Section located at the end of the text. Documentation regarding the conduct of the study is provided in Appendix 1. The study protocol is provided in Appendix 1.1. Sample case report form (CRF) pages and a sample informed consent form are located in Appendices 1.2 and 1.3, respectively. Institutional Review Board (IRB) information and investigator documentation is located in Appendix 1.4.1, and the signature of the sponsor's Responsible Medical Officer is provided in Appendix 1.5.

3.2. Statistical Methods

Sample size determinations were made based on the expected rates of increased body weight. The olanzapine package insert specified that 56% of subjects met the criterion

for having gained more than 7% of their baseline weight during long-term continuation therapy. A weight gain rate of 32% was assumed for subjects on long-term risperidone therapy (based on an integrated database of long-term risperidone clinical studies). Using an overall 2-tailed alpha level of 0.05 with 80% power and assuming the true rates of 32% versus 56% for the risperidone and olanzapine groups, 75 subjects per group were required. To also adjust for drop-outs (60%), the total number of subjects was increased to 376 (188 per group). This 60% drop-out rate included subjects who did not continue from RIS-USA-112 into this long-term extension study.

General

The analyses described below are based on the prespecified statistical analyses described in the protocol. Not all of the protocol-specified analyses are included in this abbreviated report, particularly for efficacy.

Twenty-nine investigators with fewer than 8 randomized and treated subjects were combined into 9 pooled sites with 8 to 21 subjects per site. The 12 sites that were not pooled included 8 to 19 subjects per site. In the statistical analyses, 'investigator' refers to pooled investigator.

Analysis sets

The intent-to-treat (ITT) analysis set was defined as all randomized subjects with at least 1 dose of study medication in RIS-USA-113.

Due to unspecified interactive voice response system (IVRS) errors, 9 subjects were assigned to a different treatment than they had received in study RIS-USA-112. This included 4 subjects in the RIS-USA-113 risperidone group who were randomized to olanzapine in RIS-USA-112 and 5 subjects in the RIS-USA-113 olanzapine group who were randomized to risperidone in RIS-USA-112. The term 'crossover subjects' is used to refer to these subjects in this report. Since analyses of change in study RIS-USA-113 were with respect to the baseline of RIS-USA-112, the primary analysis set for RIS-USA-113 was defined as the ITT analysis set excluding crossover subjects. All analyses having to do with change from baseline of RIS-USA-112 were based on this analysis set. For the primary parameter of percent of subjects with 7% or greater weight gain, an additional analysis on the ITT analysis set was performed.

For analyses of efficacy, 2 sites (#7 and #36) were excluded for non-compliance with Good Clinical Practice (GCP).

Analysis of safety

The primary parameter was the percent of subjects who gained at least 7% of their RIS-USA-112 baseline weight at any time during treatment in RIS-USA-113. The Cochran-Mantel-Haenszel test, stratifying for investigator was used to test for treatment differences in these rates. In addition to the analysis excluding crossover subjects, this analysis was also performed on the entire ITT analysis set.

The spontaneous adverse event rates (newly emergent in RIS-USA-113 or a worsening from baseline of RIS-USA-113) of EPS were also calculated. The following World Health Organization Adverse Reaction Terminology (WHO-ART) preferred terms were considered EPS: tremor, dystonia, hypokinesia, hypertonia, hyperkinesia, oculogyric crisis, ataxia, abnormal gait, involuntary muscle contractions, hyporeflexia, akathisia, and extrapyramidal disorders. A subject who reported at least 1 of these events at any time during the study was considered to have experienced EPS. The Cochran-Mantel-Haenszel test stratifying for investigator was used to test for treatment differences in these rates. This analysis was performed on the ITT analysis set. An additional analysis was performed on the percentage of RIS-USA-113 subjects with EPS adverse events emergent in either RIS-USA-112 or RIS-USA-113. This analysis was based on the ITT set excluding crossover subjects.

The incidence of new diabetes and hypertension onset was calculated. New onset of diabetes was defined as HbA1c increasing from less than 7% at baseline of RIS-USA-112 to 7% or greater at least once postbaseline in RIS-USA-112 or in RIS-USA-113. New onset of hypertension was defined as either institution of antihypertensive medication or new onset of diastolic blood pressure of at least 95 mmHg on 2 consecutive visits in either RIS-USA-112 or RIS-USA-113. The Cochran-Mantel-Haenszel test stratifying for investigator was used to test for treatment differences. For both parameters, the ITT analysis set excluding crossover subjects was used.

The ESRS total and subtotals (total Parkinsonism, Dystonia, Dyskinesia, CGI of severity of parkinsonism, CGI of severity of dystonia, CGI of severity of dyskinesia) was calculated. The change versus RIS-USA-112 baseline to each visit and endpoint during RIS-USA-113 was compared between treatments by means of an analysis of covariance (ANCOVA) model with treatment, investigator, and baseline ESRS score.

Vital signs (blood pressure, heart rate), body weight, and BMI were tabulated and analyzed descriptively. The change versus RIS-USA-112 baseline to each visit and endpoint during RIS-USA-113 was compared between treatments by means of an ANCOVA model with treatment, investigator, and baseline value.

Similar ANCOVA models with factors of treatment, investigator, and baseline value were used to compare treatment groups with respect to change from baseline for the following parameters:

- ACS total score and the ACS bowel function, urinary function, and vision subscales.
- M-SIP total score and the M-SIP sleep and rest, home management, social interaction, alertness behavior, communication, and recreation/relaxing subscales.
- The 'how bothered' and 'how much' totals for the chest-related, penile function (men only), and menstrual changes (women only) scales of the PRSQ.

Incidences of all adverse events were tabulated as the number of subjects who experienced at least 1 episode in RIS-USA-113 expressed as a percentage of the total number of subjects entered in the study per treatment group. Adverse events were also summarized by severity and by relationship to study medication. The incidence of severe adverse events and the incidence of adverse with an action taken of permanent stop were also summarized. Since the analysis of adverse events included only events emergent in RIS-USA-113, the analysis is based on the entire ITT analysis set.

For the clinical laboratory data, descriptive statistics and pre- versus posttreatment crosstabulations (with classes for below, within and above normal range) were generated for all tests performed. Baseline of RIS-USA-112 was used as the pretreatment value for all analyses of changes and shifts. Important abnormalities, as determined by the occurrence of pathological values, were tabulated. Pathological values are values that are outside the pathological limits. For most hematological and biochemical tests, pathological limits were defined by Lippert and Lehmann². For enzymes, the lower pathological limit was defined as zero, and the upper pathological limit as twice the upper normal limit. For leukocyte differential count, no pathological limits were defined. If a value was outside the pathological limits but not outside the normal limits for the particular laboratory, it was not considered pathological. Analyses of laboratory data were based on the ITT analysis set excluding crossover subjects.

Analysis of efficacy

For each of the continuous efficacy parameters with a baseline response (PANSS, HAM-D, CGI-Severity, cognitive tests, quality of sleep and daytime drowsiness, B-QOLI, and the DAI), the change from RIS-USA-112 baseline score at each RIS-USA-113 visit and at endpoint was analyzed using ANCOVA methods. The model included treatment, investigator, and baseline value. The number of subjects

experiencing clinical improvement, i.e., with a percentage decrease in total PANSS of at least 20% versus baseline was calculated. Comparisons were performed by means of the Cochran-Mantel-Haenszel row mean scores differ test, controlling for investigator. The distribution of CGI-C scores at each RIS-USA-113 visit was summarized and between-group comparisons were made using a Cochran-Mantel-Haenszel row mean scores differ test, controlling for investigator.

4. SUBJECT AND TREATMENT INFORMATION

The first study visit for subjects included in the analysis was on 18 December 1997 and the last study visit was on 26 February 1999.

The study was conducted at 41 centers in the U.S. (Attachment 1.1). A total of 267 enrolled subjects (n=126 on risperidone and n=141 on olanzapine) received at least 1 dose of study drug and were included in the ITT analysis set.

Nine subjects were assigned to a different treatment than they had received in study RIS-USA-112. This involved 4 subjects in the risperidone group and 5 subjects in the olanzapine group. The ITT analysis set excluding crossover subjects was thus comprised of 258 subjects (n=122 on risperidone and n=136 on olanzapine).

Subjects who discontinued from the study prematurely and the reasons for discontinuation are provided in Table 2. Overall, 55% of the subjects completed the study. The most common reasons for discontinuation were withdrawal of consent and adverse events, reported for 15% and 11% of subjects, respectively, with no relevant difference between treatment groups.

**Table 2: Subject Disposition and Discontinuation Reasons
(RIS-USA-113: ITT Analysis Set)**

Termination Type	RISPERIDONE (N=126)	OLANZAPINE (N=141)	Total (N=267)
Termination Reason	n (%)	n (%)	n (%)
Completed	65 (52)	83 (59)	148 (55)
Discontinued	61 (48)	58 (41)	119 (45)
Subject withdrew consent	20 (16)	21 (15)	41 (15)
Adverse event	14 (11)	15 (11)	29 (11)
Subject non-compliant	8 (6)	9 (6)	17 (6)
Subject lost to follow-up	7 (6)	4 (3)	11 (4)
Other	6 (5)	5 (4)	11 (4)
Insufficient response	4 (3)	3 (2)	7 (3)
Subject ineligible to continue the study	2 (2)	1 (1)	3 (1)

Note: Percentages calculated with the number of subjects in each group as denominator.
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Demographic characteristics at baseline are provided in Table 3. Subjects were 18 to 64 years of age (median 40 years). The majority of subjects were male (69%) and most were white (55%). The median weight of the study population was 83.5 kg. The

majority of subjects (61%) reported current nicotine use (Attachment 1.2); 18% reported current alcohol use (Attachment 1.3).

Table 3: Demographics
(RIS-USA-113: ITT Analysis Set)

	RISPERIDONE (N=126)	OLANZAPINE (N=141)	Total (N=267)
Age, years			
N	126	141	267
Mean (SD)	41.0 (10.50)	39.1 (10.92)	40.0 (10.75)
Median	40.0	39.0	40.0
Range	(20;64)	(18;62)	(18;64)
Sex, n (%)			
N	126	141	267
Female	37 (29)	47 (33)	84 (31)
Male	89 (71)	94 (67)	183 (69)
Race, n (%)			
N	126	141	267
Black	42 (33)	49 (35)	91 (34)
Caucasian	73 (58)	75 (53)	148 (55)
Hispanic	10 (8)	15 (11)	25 (9)
Oriental	0	1 (1)	1 (<1)
Other	1 (1)	1 (1)	2 (1)
Weight, kg			
N	126	139	265
Mean (SD)	83.0 (18.59)	84.3 (22.55)	83.7 (20.73)
Median	82.3	84.4	83.5
Range	(45;135)	(40;167)	(40;167)
Height, cm			
N	126	141	267
Mean (SD)	172.6 (8.76)	170.7 (10.59)	171.6 (9.79)
Median	172.7	170.2	172.7
Range	(147;196)	(147;196)	(147;196)

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The subjects' medical history is provided in Attachment 1.4, and psychiatric history is provided in Attachment 1.5. Overall, subjects had a diagnosis of schizophrenia (87%) or schizoaffective disorder (13%). Most subjects were outpatients (83%). There were no relevant differences between treatment groups.

Previous antipsychotic therapy (excluding depot neuroleptics) is provided in Attachment 1.6. Nearly all subjects (92% in the risperidone group and 89% in the olanzapine group) used antipsychotic medication before the start of the study, mostly risperidone and haloperidol. Seventeen percent (17%) of subjects in each treatment group used depot neuroleptics (haloperidol, fluphenazine) before the start of the study (Attachment 1.7).

The use of concomitant therapy is provided in Attachment 1.9. The most commonly used concomitant medication was lorazepam (used by 24% of subjects in the

risperidone group, and by 21% of subjects in the olanzapine group). Other frequently used medications were anticholinergics (benzotropine mesilate, used by 12% of subjects in the risperidone group, and by 9% of subjects in the olanzapine group) and analgesics (paracetamol, acetylsalicylic acid, and ibuprofen). No other concomitant therapy was used by more than 10% of subjects in either treatment group. The administration of lorazepam for treatment of agitation was allowed per protocol. Anticholinergic medication could be initiated at the investigator's discretion if EPS emerged or worsened during the study.

The proportion of subjects with protocol deviations was 33% (Attachment 1.10). The most commonly reported protocol deviations were intercurrent forbidden therapy (i.e., use of any disallowed medication [mostly lorazepam for more than 5 days]; 22%) and non-compliance (10%), with no noteworthy differences between treatment groups. Individual subjects with protocol deviations are listed in Attachment 1.11.

The combined extent of exposure in studies RIS-USA-112 and RIS-USA-113 is shown in Table 4. The median treatment duration in the risperidone group was 346.5 days, and 356.0 days in the olanzapine group. The median modal risperidone dose was 6 mg and the median modal olanzapine dose was 15 mg.

**Table 4: Extent of Exposure - Total Exposure Over RIS-USA-112 and RIS-USA-113
(RIS-USA-113: ITT Excluding Crossover Subjects Analysis Set)**

	RISPERIDONE	OLANZAPINE
Total Duration, Days		
N	122	136
Mean (SD)	271.7 (111.45)	286.4 (105.08)
Median	349.5	356.5
Range	(56;386)	(63;379)
Treatment Duration, Days		
N	122	136
Mean (SD)	265.7 (114.29)	277.5 (109.60)
Median	346.5	356.0
Range	(56;385)	(60;378)
Total Exposure (subject years)	88.8	103.3
Mean Dose (Including Days Off Drug)		
N	122	134
Mean (SD)	4.7 (1.18)	12.7 (4.49)
Median	4.7	12.4
Range	(2;6)	(4;20)
Mode Dose (Including Days Off Drug)		
N	122	136
Mean (SD)	4.9 (1.29)	13.6 (5.23)
Median	6.0	15.0
Range	(2;6)	(5;20)

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5. EFFICACY RESULTS

The results of the PANSS are provided in Attachment 2.1 and 2.2. A summary of the data is given in Tables 5 to 8.

The mean changes ($\pm$ standard deviation [SD]) from baseline to end point for the total PANSS score are presented in Table 5. Over time, the mean total PANSS scores decreased from baseline in both treatment groups, indicating improvement in the severity of psychotic symptoms. At end point, the mean change from baseline was numerically larger for subjects treated with olanzapine than for subjects treated with risperidone, but the difference was not statistically significant.

Table 5: Total PANSS - Change From Baseline to End Point
 (RIS-USA-113: ITT Excluding Crossover Subjects
 [Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Parameter: Total PANSS (non-imputed) Excluding sites 7 and 36		
	RISPERIDONE	OLANZAPINE
Baseline		
N	106	120
Mean (SD)	81.6 (11.80)	80.4 (13.07)
Median (Range)	81.0 (56;118)	78.0 (61;120)
End Point		
N	106	120
Mean (SD)	65.6 (19.46)	61.2 (16.99)
Median (Range)	62.0 (34;124)	59.0 (31;129)
Change from Baseline		
N	106	120
Mean (SD)	-16.0 (19.55)	-19.3 (18.47)
Median (Range)	-20.5 (-51;57)	-19.5 (-88;48)
P-value (minus RISPERIDONE) ^a		0.229
Difference of LS Means (SE)		-2.8 (2.32)
95% confidence interval		(-7.37;1.78)

^a Test for no difference between TREATMENT from ANCOVA model with factors TREATMENT, base, investigator (type III SS).
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The patterns in change from baseline for the positive and negative symptoms subscales were consistent with total PANSS, i.e., no statistically significant difference in the mean change from baseline to end point between treatment group (Tables 6 and 7).

Table 6: Positive Symptoms - Change From Baseline to End Point
(RIS-USA-113: ITT Excluding Crossover Subjects
[Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Parameter: Positive symptoms (non-imputed)			
Excluding sites 7 and 36			
	RISPERIDONE	OLANZAPINE	
Baseline			
N	106	120	
Mean (SD)	24.2 (5.55)	23.4 (5.89)	
Median (Range)	24.0 (11;39)	23.0 (11;43)	
End Point			
N	106	120	
Mean (SD)	18.3 (7.28)	17.5 (6.51)	
Median (Range)	17.0 (8;41)	16.0 (8;38)	
Change from Baseline			
N	106	120	
Mean (SD)	-5.9 (7.33)	-5.9 (6.58)	
Median (Range)	-6.0 (-21;18)	-6.0 (-33;14)	
P-value (minus RISPERIDONE) ^a		0.828	
Difference of LS Means (SE)		-0.2 (0.84)	
95% confidence interval		(-1.83;1.47)	

^a Test for no difference between TREATMENT from ANCOVA model with factors TREATMENT, base, investigator (type III SS).
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Table 7: Negative Symptoms - Change From Baseline to End Point
(RIS-USA-113: ITT Excluding Crossover Subjects
[Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Parameter: Negative symptoms (non-imputed)			
Excluding sites 7 and 36			
	RISPERIDONE	OLANZAPINE	
Baseline			
N	106	120	
Mean (SD)	21.7 (6.67)	21.2 (6.20)	
Median (Range)	21.0 (7;39)	21.0 (7;37)	
End Point			
N	106	120	
Mean (SD)	17.9 (6.79)	16.4 (6.33)	
Median (Range)	18.0 (7;37)	16.0 (7;37)	
Change from Baseline			
N	106	120	
Mean (SD)	-3.8 (6.50)	-4.8 (6.34)	
Median (Range)	-4.0 (-17;21)	-5.0 (-23;11)	
P-value (minus RISPERIDONE) ^a		0.324	
Difference of LS Means (SE)		-0.7 (0.74)	
95% confidence interval		(-2.19;0.73)	

^a Test for no difference between TREATMENT from ANCOVA model with factors TREATMENT, base, investigator (type III SS).
panss01c.rtf generated by parun.sas.

Clinical response was defined as a 20% or greater reduction in the total PANSS score from baseline. The percentages of subjects with a 20% or greater reduction from baseline in total PANSS score at end point are presented in Table 8. At end point, approximately 70% of subjects had a 20% or greater reduction in the PANSS total score from baseline. The percentage was not statistically significantly different between treatment groups.

Table 8: Percent of Subjects With $\geq 20\%$ Improvement in Total PANSS at End Point
(RIS-USA-113: ITT Excluding Crossover Subjects
[Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Excluding sites 7 and 36					
		RISPERIDONE		OLANZAPINE	Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
20% clinical improvement					
<u>Treatment</u>					
End Point					
No	33	31.1	33	27.5	0.656
Yes	73	68.9	87	72.5	
Total	106		120		

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.

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Investigators recorded their CGI of the subject's illness severity at each visit during the study and their CGI of the subject's improvement compared to the baseline of RIS-USA-112 at each postbaseline visit. The results of the CGI are provided in Attachment 2.3 and 2.4.

Table 9 presents the mean change (SD) from baseline to end point. Both groups showed a mean decrease in CGI score from baseline to end point, indicating global improvement in the severity of schizophrenic symptoms. The change was not statistically significantly different between treatment groups.

Table 9: Clinical Global Impression - Change From Baseline to End Point
 (RIS-USA-113: ITT Excluding Crossover Subjects
 [Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Parameter: Clinical global impression Excluding sites 7 and 36		
	RISPERIDONE	OLANZAPINE
Baseline		
N	109	124
Mean (SD)	4.3 (0.90)	4.1 (0.91)
Median (Range)	4.0 (2;6)	4.0 (2;7)
End Point		
N	109	124
Mean (SD)	3.6 (1.02)	3.3 (0.91)
Median (Range)	3.0 (2;6)	3.0 (2;6)
Change from Baseline		
N	109	124
Mean (SD)	-0.8 (0.99)	-0.8 (0.96)
Median (Range)	-1.0 (-3;2)	-1.0 (-3;1)
P-value (minus RISPERIDONE) ^a		0.135
Difference of LS Means (SE)		-0.2 (0.11)
95% confidence interval		(-0.39;0.05)

^a Test for no difference between TREATMENT from ANCOVA model with factors TREATMENT, base, investigator (type III SS).
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The distribution of CGI-C ratings over time is summarized in Table 10. At end point, much or very much improvement was recorded for more than 50% of the subjects, with no statistically significant difference between treatment groups.

Table 10: Clinical Global Impression Change at End Point
 (RIS-USA-113: ITT Excluding Crossover Subjects
 [Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Excluding sites 7 and 36							
	RISPERIDONE			OLANZAPINE			Pairwise Comparison OLANZAPINE Minus RISPERIDONE
	n	%	Cum.%	n	%	Cum.%	P-value ^a
Clinical global impression change							
<u>Treatment</u>							
End Point							
Very much improved	11	9.9	9.9	12	9.7	9.7	
Much improved	38	34.2	44.1	44	35.5	45.2	
Minimally improved	30	27.0	71.2	38	30.6	75.8	
Unchanged	9	8.1	79.3	19	15.3	91.1	
Minimally worse	13	11.7	91.0	8	6.5	97.6	
Much worse	10	9.0	100.0	3	2.4	100.0	
Total	111			124			0.174

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator
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Results from other efficacy parameters are provided in Attachments 2.5 (HAM-D), 2.6 (cognitive tests), 2.7 (VAS), 2.8 (B-QoLI), and 2.9 (DAI).

6. SAFETY RESULTS

All subjects who were treated and had at least 1 post-baseline assessment in RIS-USA-113 were included in the safety analysis. Baseline values were defined as the baseline value from RIS-USA-112, unless specified differently.

The primary parameter was the percent of patients who gained at least 7% of their baseline weight at any time during treatment (compared with the baseline of RIS-USA-112). The results from this analysis are described in Section 6.3.3.

6.1. Adverse Events

6.1.1. Summary of All Adverse Events

The incidence of all treatment-emergent adverse events (WHO-ART preferred terms) is provided in Attachment 3.1. The incidence of treatment-emergent adverse events by maximum severity is provided in Attachment 3.2 and the incidence of treatment-emergent adverse events by the investigator's assessment of relationship to study drug is provided in Attachment 3.3. Adverse events that occurred in at least 5% of subjects are included in Table 11.

The most common treatment-emergent adverse events (i.e., that occurred in at least 15% of subjects) in the risperidone treatment group were headache, rhinitis, agitation, and anxiety. The most common treatment-emergent adverse events in the olanzapine group were somnolence and headache. All other treatment-emergent adverse events were reported for less than 15% of subjects.

The overall incidence of treatment-emergent adverse events was similar in subjects treated with olanzapine (87%) and in subjects treated with risperidone (86%).

The following adverse events had a difference of at least 5% between the 2 groups (Table 11):

- Headache, rhinitis, hyperprolactinemia, paranoid reaction, dyspepsia, and hyperkinesia were reported more often for subjects treated with risperidone than for subjects treated with olanzapine.
- Somnolence, dizziness, back pain, and weight increase were reported more often for subjects treated with olanzapine than for subjects treated with risperidone.

There were 11 (6 risperidone, 5 olanzapine) reports coded as suicide attempt: 10 (6 risperidone, 4 olanzapine) of these were described as suicidal ideation, thoughts, or tendencies with no documentation or evidence of an actual suicide attempt. One olanzapine subject (30282) had a documented suicide attempt. On Day 82 of treatment, the subject experienced increased auditory hallucinations and attempted suicide by drinking insecticide, which caused severe convulsions. The

investigator considered the events to be not related to study medication. The event was treated with intravenous fluids and renal dialysis, and lorazepam 8 mg for the seizures. The subject recovered after 1 day. A narrative for this subject is provided in Attachment 3.6.

The incidence of suicide-related events was similar in both treatment groups.

Table 11: Incidence of Treatment-Emergent Adverse Events - $\geq 5\%$ in Either Group (RIS-USA-113)

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with adverse events	108 (86)	123 (87)
Psychiatric disorders	69 (55)	72 (51)
Agitation	19 (15)	16 (11)
Anxiety	19 (15)	15 (11)
Depression	15 (12)	18 (13)
Somnolence	14 (11)	29 (21)
Insomnia	12 (10)	20 (14)
Paranoid reaction	12 (10)	7 (5)
Psychosis	12 (10)	13 (9)
Hallucination	6 (5)	13 (9)
Suicide attempt	6 (5)	5 (4)
Central & peripheral nervous system disorders	53 (42)	49 (35)
Headache	29 (23)	21 (15)
Hyperkinesia	8 (6)	2 (1)
Hypertonia	7 (6)	7 (5)
Dizziness	5 (4)	13 (9)
Gastro-intestinal system disorders	47 (37)	44 (31)
Mouth dry	14 (11)	13 (9)
Saliva increased	10 (8)	6 (4)
Dyspepsia	9 (7)	1 (1)
Constipation	6 (5)	10 (7)
Diarrhea	2 (2)	7 (5)
Respiratory system disorders	35 (28)	30 (21)
Rhinitis	23 (18)	19 (13)
Coughing	7 (6)	5 (4)
Body as a whole - general disorders	30 (24)	38 (27)
Pain	10 (8)	7 (5)
Fatigue	7 (6)	5 (4)
Injury	7 (6)	7 (5)
Back pain	4 (3)	12 (9)
Metabolic and nutritional disorders	19 (15)	29 (21)
Weight increase	5 (4)	19 (13)
Endocrine disorders	15 (12)	3 (2)
Hyperprolactinemia	15 (12)	0
Musculo-skeletal system disorders	13 (10)	13 (9)
Myalgia	6 (5)	6 (4)
Vision disorders	8 (6)	11 (8)
Vision abnormal	7 (6)	9 (6)

Note: Incidence is based on the number of subjects experiencing at least 1 adverse event, not the number of events.

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The majority of adverse events were mild or moderate in severity (Attachment 3.2). Severe individual adverse events (preferred terms) reported for more than 1 subject included adverse events associated with the underlying psychiatric disorder (i.e., psychosis, suicide attempt, agitation, anxiety, depression, and hallucination).

Of the most frequently reported adverse events, the investigator considered most cases of somnolence to be at least possibly related to the study drug. Approximately half to one third of the reports of agitation, approximately one third to one fourth of the reports of anxiety and approximately one fifth of the reports of headache were considered at least possibly drug-related. Rhinitis was not considered to be treatment related (Attachment 3.3).

6.1.2. Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

6.1.2.1. Deaths

There were no deaths during the study.

6.1.2.2. Serious Adverse Events

The incidence of serious adverse events that occurred during treatment or within 30 days after treatment is summarized in Table 12. Serious adverse events were reported somewhat more often in risperidone-treated subjects (21%) than in olanzapine treated subjects (16%).

The serious adverse events reported by more than 2 subjects in either treatment group were psychosis, paranoid reaction, delusion, suicide attempt, depression, hallucination, agitation, and anxiety. The majority of these events appear to be related to the underlying psychiatric disorder. There were no clinically relevant differences between treatment groups.

**Table 12: Incidence of Treatment-Emergent Serious Adverse Events
(RIS-USA-113 ITT Analysis Set)**

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
	n (%)	n (%)
Total no. subjects with serious adverse events	26 (21)	23 (16)
Psychiatric disorders	21 (17)	19 (13)
Psychosis	10 (8)	11 (8)
Paranoid reaction	5 (4)	3 (2)
Delusion	4 (3)	1 (1)
Suicide attempt	4 (3)	4 (3)
Depression	2 (2)	3 (2)
Hallucination	2 (2)	3 (2)
Aggressive reaction	1 (1)	2 (1)
Agitation	1 (1)	4 (3)
Anorexia	1 (1)	0
Anxiety	1 (1)	3 (2)
Catatonic reaction	1 (1)	0
Confusion	1 (1)	2 (1)
Depression aggravated	1 (1)	1 (1)
Personality disorder	1 (1)	0
Thinking abnormal	1 (1)	1 (1)
Amnesia	0	1 (1)
Depersonalization	0	1 (1)
Drug abuse	0	2 (1)
Insomnia	0	2 (1)
Manic reaction	0	1 (1)
Nervousness	0	1 (1)
Schizophrenic reaction	0	1 (1)
Body as a whole - general disorders	5 (4)	4 (3)
Allergic reaction	1 (1)	0
Chest pain	1 (1)	1 (1)
Fever	1 (1)	0
Injury	1 (1)	0
Lab values abnormal	1 (1)	1 (1)
Crying abnormal	0	1 (1)
Therapeutic response increased	0	2 (1)
Central & peripheral nervous system disorders	3 (2)	5 (4)
Headache	2 (2)	1 (1)
Hypokinesia	1 (1)	0
Convulsions	0	1 (1)
Dizziness	0	1 (1)
Extrapyramidal disorder	0	1 (1)
Hypoesthesia	0	1 (1)
Myelitis	0	1 (1)
Tremor	0	1 (1)
Metabolic and nutritional disorders	3 (2)	0
Creatine phosphokinase increased	1 (1)	0
Hypokalemia	1 (1)	0
Weight decrease	1 (1)	0
Gastro-intestinal system disorders	2 (2)	0
Intestinal obstruction	1 (1)	0
Tooth disorder	1 (1)	0

Table continued on next page

Table 12: Incidence of Treatment-Emergent Serious Adverse Events (continued)
(RIS-USA-113 ITT Analysis Set)

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Heart rate and rhythm disorders	2 (2)	1 (1)
Arrhythmia	1 (1)	0
Tachycardia	1 (1)	0
Bradycardia	0	1 (1)
Resistance mechanism disorders	2 (2)	1 (1)
Infection	1 (1)	0
Infection viral	1 (1)	0
Infection bacterial	0	1 (1)
Cardiovascular disorders, general	1 (1)	1 (1)
Edema dependent	1 (1)	0
ECG abnormal	0	1 (1)
Endocrine disorders	1 (1)	0
Hyperprolactinemia	1 (1)	0
Neoplasm	1 (1)	0
Pulmonary carcinoma	1 (1)	0
Reproductive disorders, female	1 (1)	1 (1)
Amenorrhea	1 (1)	0
Pregnancy unintended	0	1 (1)
Respiratory system disorders	1 (1)	3 (2)
Dyspnea	1 (1)	0
Bronchitis	0	1 (1)
Coughing	0	1 (1)
Pulmonary congestion	0	1 (1)
Rhinitis	0	1 (1)
Upper respiratory tract infection	0	1 (1)
Secondary terms	1 (1)	1 (1)
Alcohol problem	1 (1)	0
Surgical intervention	0	1 (1)
Urinary system disorders	1 (1)	0
Hematuria	1 (1)	0
Urinary incontinence	1 (1)	0
Vision disorders	1 (1)	0
Lacrimation abnormal	1 (1)	0

Note: Incidence is based on the number of subjects experiencing at least one adverse event, not the number of events.

Note: Events with onset within 30 days of last dose of study medication are included.
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Narratives for serious adverse events are provided in Attachment 3.6.

6.1.2.3. Other Significant Adverse Events

There was a low rate of discontinuation due to adverse events from the study (11%; Table 13). Adverse events leading to permanent discontinuation reported by more than 2 subjects in either treatment group were psychosis and agitation. The majority of these events appear to be related to the underlying psychiatric disorder. There were no clinically relevant differences between treatment groups.

**Table 13: Incidence of Adverse Events With Action Taken of Permanent Stop
(RIS-USA-113 ITT Analysis Set)**

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with perm stop med	14 (11)	15 (11)
Psychiatric disorders	12 (10)	10 (7)
Psychosis	8 (6)	4 (3)
Paranoid reaction	2 (2)	1 (1)
Agitation	1 (1)	4 (3)
Anorexia	1 (1)	0
Delusion	1 (1)	0
Depression aggravated	1 (1)	0
Personality disorder	1 (1)	0
Suicide attempt	1 (1)	2 (1)
Aggressive reaction	0	2 (1)
Anxiety	0	1 (1)
Depression	0	1 (1)
Drug abuse	0	1 (1)
Emotional lability	0	1 (1)
Hallucination	0	2 (1)
Manic reaction	0	1 (1)
Metabolic and nutritional disorders	2 (2)	2 (1)
Weight decrease	1 (1)	0
Weight increase	1 (1)	2 (1)
Neoplasm	1 (1)	0
Pulmonary carcinoma	1 (1)	0
Body as a whole - general disorders	0	1 (1)
Lab values abnormal	0	1 (1)
Central & peripheral nervous system disorders	0	1 (1)
Dizziness	0	1 (1)
Liver and biliary system disorders	0	1 (1)
Hepatic function abnormal	0	1 (1)
Reproductive disorders, female	0	1 (1)
Pregnancy unintended	0	1 (1)

Note: Incidence is based on the number of subjects experiencing at least one adverse event, not the number of events.

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Narratives for subjects with adverse events leading to discontinuation are provided in Attachment 3.6.

6.1.2.4. Adverse Events of Interest

The percent of subjects with treatment-emergent EPS-related adverse events in RIS-USA-113 and in RIS-USA-112 or RIS-USA-113 are provided in Attachments 3.4 and 3.5.

EPS-related adverse events that first emerged or worsened after the start of study RIS-USA-113 were reported for 17.5% of risperidone-treated subjects and for 12.8% of subjects in the olanzapine group (Table 14). When all treatment-emergent EPS-related adverse events over both studies were taken into consideration, the percentages were 32.0% and 30.1%, respectively (Table 15). Neither of the treatment comparisons were statistically significant.

There were no cases of tardive dyskinesia.

Table 14: Percent of Subjects With Treatment-Emergent EPS-Related Adverse Events in RIS-USA-113 (RIS-USA-113 ITT Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
Extrapyramidal symptoms					
<u>Treatment</u>					
Overall					
No	104	82.5	123	87.2	
Yes	22	17.5	18	12.8	0.167
Total	126		141		

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator
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Table 15: Percent of Subjects With EPS-Related Adverse Events Emergent in RIS-USA-112 or RIS-USA-113 - Crossover Subjects Excluded (RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
Extrapyramidal symptoms					
<u>Treatment</u>					
Overall					
No	83	68.0	95	69.9	
Yes	39	32.0	41	30.1	0.555
Total	122		136		

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.
ac07.rtf generated by aeepsrun.sas.

6.2. Clinical Laboratory Evaluation

Laboratory values were assessed based on changes from baseline and treatment-emergent changes to values outside laboratory and pathologic limits. Data are provided in Attachment 4.1 through 4.9 (hematology and chemistry) and Attachment 4.10 (urinalysis). By protocol, all laboratory tests were to be performed after a 12-hour fast. Serum glucose was not collected.

For most parameters, there were no clinically notable mean changes in hematology and chemistry parameters from baseline to end point (Attachments 4.1 and 4.2). Results for liver enzymes, lipids, and prolactin are summarized in Table 16.

- Mean changes from baseline to end point in ALT and AST levels were small. Subjects treated with risperidone showed a small mean decrease from baseline in AST and ALT, whereas subjects treated with olanzapine showed a small mean increase from baseline, that was most pronounced for AST. Subjects in both

treatment groups showed a small mean increase from baseline to end point for GGT, which was somewhat larger for subjects in the olanzapine group than for risperidone-treated subjects. None of these mean changes were considered clinically relevant.

- Overall, mean changes from baseline to end point in triglycerides and cholesterol levels were small with larger differences in mean changes from baseline for olanzapine compared to risperidone.
- For prolactin, a mean increase of 26 ng/mL was observed in the risperidone treatment group compared with a mean decrease of -10 ng/mL in the olanzapine group. Prolactin is further discussed in Section 6.3.8. This increase is consistent with the known profile of risperidone.

**Table 16: Selected Laboratory Tests - Descriptive Statistics of Values and Change From Baseline to End Point - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects
[Restricted to Subjects With Visit End Point Data Only] Analysis Set)**

	RISPERIDONE			OLANZAPINE		
	N	Mean (SD)	Mean Change from Baseline (SD)	N	Mean (SD)	Mean Change from Baseline (SD)
AST (U/L)						
Baseline	122	19.57 (11.454)		134	20.06 (14.170)	
End point	122	19.04 (8.170)	-0.53 (9.705)	134	24.07 (24.142)	4.01 (25.418)
ALT (U/L)						
Baseline	122	25.47 (25.022)		134	26.87 (30.250)	
End point	122	24.46 (18.201)	-1.01 (21.798)	134	27.75 (23.539)	0.88 (31.037)
GGT (U/L)						
Baseline	122	44.07 (113.155)		134	37.26 (45.837)	
End point	122	47.03 (113.888)	2.97 (28.723)	134	44.07 (45.072)	6.81 (28.702)
Cholesterol (mmol/L)						
Baseline	122	5.16 (1.118)		134	5.11 (1.059)	
End point	122	5.15 (1.097)	-0.01 (0.775)	134	5.27 (1.074)	0.17 (0.866)
Triglycerides (mmol/L)						
Baseline	122	1.93 (1.603)		134	1.92 (1.099)	
End point	122	1.95 (1.568)	0.02 (1.228)	134	2.26 (1.795)	0.34 (1.518)
HDL (g/L)						
Baseline	122	0.50 (0.160)		133	0.51 (0.152)	
End point	122	0.52 (0.149)	0.02 (0.107)	133	0.50 (0.162)	-0.00 (0.122)
LDL (g/L)						
Baseline	116	1.18 (0.380)		127	1.14 (0.374)	
End point	116	1.17 (0.382)	-0.02 (0.268)	127	1.17 (0.341)	0.03 (0.298)
Prolactin (ng/mL)						
Baseline	108	19.30 (20.150)		120	25.52 (34.200)	
End point	108	44.97 (44.191)	25.68 (44.902)	120	15.08 (14.788)	-10.44 (30.935)

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Shift tables of liver enzyme, lipid, and prolactin values from baseline category (below, within, or above the laboratory limits) to the category at end point are provided in Table 17.

Table 17: Selected Laboratory Tests - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)

		Treatment Group and Evaluation at Baseline							
		RISPERIDONE				OLANZAPINE			
		LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
AST (U/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	117	3	120	0	122	3	125
	High	0	1	1	2	0	6	3	9
	Total	0	118	4	122	0	128	6	134
ALT (U/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	104	8	112	0	111	7	118
	High	0	6	4	10	0	10	6	16
	Total	0	110	12	122	0	121	13	134
GGT (U/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	101	5	106	0	102	4	106
	High	0	6	10	16	0	14	14	28
	Total	0	107	15	122	0	116	18	134
Cholesterol (mmol/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	53	19	72	0	52	13	65
	High	0	12	38	50	0	18	51	69
	Total	0	65	57	122	0	70	64	134
Triglycerides (mmol/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	81	15	96	0	77	11	88
	High	0	13	13	26	0	22	24	46
	Total	0	94	28	122	0	99	35	134
HDL (g/L)									
End point	Low	5	3	0	8	10	7	0	17
	Normal	13	101	0	114	6	110	0	116
	High	0	0	0	0	0	0	0	0
	Total	18	104	0	122	16	117	0	133
LDL (g/L)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	66	14	80	0	70	15	85
	High	0	14	22	36	0	17	25	42
	Total	0	80	36	116	0	87	40	127
Prolactin (ng/mL)									
End point	Low	0	0	0	0	0	0	0	0
	Normal	0	51	4	55	1	92	16	109
	High	0	34	19	53	0	4	7	11
	Total	0	85	23	108	1	96	23	120

lab07.rtf generated by lbrun.sas.

The percentages of subjects with liver enzyme, lipids, or prolactin values within pathological limits at baseline and outside pathological limits some time during RIS-USA-113 are summarized in Table 18.

**Table 18: Selected Laboratory Tests - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)**

Within Limits at Baseline	RISPERIDONE				OLANZAPINE			
	Total	PATHOLOGICAL LIMITS, n (%)			Total	PATHOLOGICAL LIMITS, n (%)		
	n	Below	Within	Above	n	Below	Within	Above
Cholesterol (mmol/L)	122	0	122 (100)	0	134	0	132 (99)	2 (1)
Triglycerides (mmol/L)	99	0	83 (84)	16 (16)	101	0	73 (72)	28 (28)
GGT (U/L)	119	0	115 (97)	4 (3)	127	0	122 (96)	5 (4)
AST (U/L)	121	0	120 (99)	1 (1)	132	0	126 (95)	6 (5)
ALT (U/L)	120	0	116 (97)	4 (3)	130	0	123 (95)	7 (5)

Note: Percentages of pathological limits sub-groups calculated with the number of subjects per within limits at baseline as denominator.

A subject may be in more than one category.

lab10.rtf generated by lbpath.sas.

Small numbers of subjects had changes in hematology or chemistry values from within normal limits at baseline to outside these limits at 1 or more postbaseline evaluation. Shifts from normal at baseline to outside these limits at end point for hepatic parameters and for lipids were somewhat more frequent in the olanzapine group than in the risperidone group, and more subjects in the olanzapine group had postbaseline elevations in triglycerides to above the pathologic limits. The most frequent changes from normal to above the pathological limits were noted for triglycerides (28% in the olanzapine group and 16% in the risperidone group).

Changes in prolactin (from normal at baseline to high at end point) were more frequent in the risperidone group. No pathological limits were defined for prolactin.

For most subjects, abnormal laboratory findings were not considered clinically important and were not reported as adverse events. Elevated prolactin levels were reported as adverse event for 15 subjects (12%) in the risperidone group, and for none of the olanzapine-treated subjects. For most other analytes, adverse events related to abnormal findings were each reported by 1 or 2 subjects.

6.3. Other Safety Observations

6.3.1. Vital Signs and Physical Findings

There were no clinically noteworthy changes from baseline in mean values for vital sign parameters (supine and standing pulse rate, systolic blood pressure, and diastolic blood pressure). Mean changes in supine and standing blood pressure and pulse rate measurements over time are displayed in Attachment 5.1.

New onset of hypertension was defined as either institution of antihypertensive medication or new onset of diastolic blood pressure of at least 95 mmHg on 2 consecutive visits during either USA-112 or USA-113. Results are provided in Attachment 5.2 and in Table 19. The percent of subjects with new onset hypertension was 12.6% in the risperidone group, and 10.8% in olanzapine-treated subjects. The difference was not statistically significant.

Table 19: Percent of Subjects With New Onset Hypertension in RIS-USA-112 or RIS-USA-113 - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
Onset of hypertension					
<u>Treatment</u>					
Overall					
No	104	87.4	116	89.2	
Yes	15	12.6	14	10.8	0.745
Total	119		130		

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.
vs03.rtf generated by vsrun2.sas.

Results from the physical examination at baseline and end point are provided in Attachments 1.8 and 5.3. For each body system, physical examination results were unchanged from baseline for the vast majority of subjects. Treatment-emergent abnormal findings on physical examinations were to be reported as adverse events (see Section 6.1).

6.3.2. Electrocardiograms

There were no clinically meaningful changes in the mean ECG parameters (HR, PR interval, QRS interval, QT interval, and QT interval corrected by Bazett) from baseline over time. Changes in the mean ECG parameters were similar for subjects in both treatment groups (Attachment 6.1 and 6.2).

6.3.3. Body Weight and Body Mass Index

The primary parameter of the study was the percent of subjects who gained at least 7% of their baseline weight at any time during treatment. Data are provided in Attachments 7.1, 7.2, and 7.3. A summary of the data is provided in Table 20 (crossover subjects excluded) and Table 21 (all subjects).

Table 20: Percent of Subjects With $\geq 7\%$ Weight Gain From Baseline of RIS-USA-112 - Crossover Subjects Excluded (RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
Weight increase $\geq 7\%$					
<u>Treatment</u>					
Overall					
No	63	53.4	59	44.7	
Yes	55	46.6	73	55.3	
Total	118		132		0.203

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.

vs01.rtf generated by vsrun.sas.

Table 21: Percent of Subjects With $\geq 7\%$ Weight Gain From Baseline of RIS-USA-112 - All Subjects (RIS-USA-113 ITT Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
Weight increase $\geq 7\%$					
<u>Treatment</u>					
Overall					
No	65	53.3	61	45.2	
Yes	57	46.7	74	54.8	
Total	122		135		0.189

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.

vs02.rtf generated by vsrun.sas.

The percentage of subjects who gained at least 7% of their RIS-USA-112 baseline weight at any time during treatment was higher in the olanzapine treatment group than in the risperidone group, but the effect was not statistically significant. Approximately 55% of olanzapine subjects gained at least 7% of their baseline weight during RIS-USA-113. This percentage is comparable to the percentage reported in the Zyprexa USPI (56%). The percentage observed for risperidone in this study (47%), is higher than what was assumed in sample size calculations for this study (32%). Therefore, while (in absolute terms) the percentage of subjects in the olanzapine group with a 7% or greater weight gain was 8% higher than the percentage in the risperidone group, the sample size was not large enough to detect this difference as statistically significant.

Mean body weight and mean BMI showed an increase from baseline to end point, with no statistically significant difference between treatment groups (Table 22 and Attachment 7.4).

Table 22: Body Weight and BMI - Change From Baseline to End Point - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects
[Restricted to Subjects With Visit End Point Data Only] Analysis Set)

Parameter: Weight, kg - excludes missing change		
	RISPERIDONE	OLANZAPINE
Baseline		
N	118	132
Mean (SD)	82.7 (17.94)	83.5 (20.90)
Median (Range)	81.9 (45;134)	83.3 (42;159)
End Point		
N	118	132
Mean (SD)	87.2 (18.88)	88.8 (22.16)
Median (Range)	86.2 (47;137)	87.1 (49;159)
Change from Baseline		
N	118	132
Mean (SD)	4.6 (7.24)	5.3 (9.09)
Median (Range)	4.6 (-29;23)	4.3 (-20;39)
P-value (minus RISPERIDONE) ^a		0.498
Difference of LS Means (SE)		0.7 (1.08)
95% confidence interval		(-1.40;2.87)
Parameter: Body Mass Index - excludes missing change		
Baseline		
N	118	132
Mean (SD)	28.3 (5.87)	29.0 (6.94)
Median (Range)	27.8 (18;46)	28.2 (17;57)
End Point		
N	118	132
Mean (SD)	29.8 (6.01)	30.8 (7.20)
Median (Range)	29.2 (19;48)	29.6 (19;57)
Change from Baseline		
N	118	132
Mean (SD)	1.5 (2.40)	1.8 (3.14)
Median (Range)	1.6 (-9;7)	1.6 (-6;11)
P-value (minus RISPERIDONE) ^a		0.391
Difference of LS Means (SE)		0.3 (0.36)
95% confidence interval		(-0.40;1.03)

^a Test for no difference between TREATMENT from ANCOVA model with factors TREATMENT, base, investigator (type III SS).

vs05a.rtf and vs05b.rtf generated by vsrun.sas.

Weight increase was more frequently reported as an adverse event for subjects in the olanzapine group (13%) than in the risperidone group (4%) (see Section 6.1).

6.3.4. Waist/Hip Ratio

Waist/hip ratio was not analyzed.

6.3.5. Assessment of Extrapyrimal Symptoms

The effect of treatment on EPS was evaluated using the ESRS and CGI. The ESRS total and subtotals are provided in Attachments 8.1 (ESRS) and 8.2 (CGI).

The mean baseline total ESRS was 5.4 in the olanzapine treatment group and 5.8 in the risperidone group. The mean improvement in total ESRS at end point was statistically significantly greater in the olanzapine treatment group (2.0) than in the risperidone group (0.7; $p=0.013$). This was primarily driven by the Parkinsonism ($p=0.036$) and dyskinesia ($p=0.037$) subscales.

CGI ratings of parkinsonism, dystonia, and dyskinesia at end point were very mild to absent for $\geq 88\%$ of subjects in both groups. Ratings tended to be less severe in the olanzapine group compared to the risperidone group, but differences were not statistically significant ($p \geq 0.073$).

EPS-related adverse events are discussed in Section 6.1.

6.3.6. Anti-Cholinergic Symptom Assessment

The effect of treatment on ACS is shown in Attachments 9.1 and 9.2.

Both treatment groups showed comparable mean decreases in total ACS scores, and in total scores for bowel function, urinary function, and vision from baseline to end point.

Subjects treated with risperidone had less symptoms of dry mouth than olanzapine-treated subjects, both at baseline and at end point. The difference at end point was statistically significant ($p=0.017$) in favor of risperidone, when 82% of risperidone subjects reported not having dry mouth symptoms compared to 69% of olanzapine subjects.

Dry mouth reported as adverse event is discussed in Section 6.1.1.

6.3.7. Prolactin-Related Symptom Questionnaire

Descriptive statistics for 'how bothered' and 'how much' scores from the PRSQ are provided in Attachment 10.1.

Despite more frequent and greater elevations of prolactin in the risperidone group (Sections 6.1.1 and 6.2), there were no clinically relevant or statistically significant differences between treatment groups in the PRSQ.

6.3.8. New Onset Diabetes

New onset of diabetes was defined as HbA1c increasing from less than 7% to 7% or higher. Results are provided in Attachment 11.1 and in Table 23. The percent of

subjects with new onset diabetes was low and comparable between treatment groups (3.3% and 3.0% in risperidone- and olanzapine-treated subjects, respectively).

Table 23: Percent of Subjects With HbA1c <7% at Baseline (RIS-USA-112) and ≥7% Postbaseline - Crossover Subjects Excluded
(RIS-USA-113 ITT Excluding Crossover Subjects Analysis Set)

	RISPERIDONE		OLANZAPINE		Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value ^a
	n	%	n	%	
HbA1c increase					
<u>Treatment</u>					
Overall					
No	117	96.7	130	97.0	
Yes	4	3.3	4	3.0	0.975
Total	121		134		

^a Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investigator.

lab01.rtf generated by lbrun2.sas.

6.3.9. Modified Sickness Impact Profile

Both treatment groups showed mean decreases from baseline to end point in total M-SIP scores, and for the different subscales (sleep and rest, home management, social interaction, alertness behavior, communication, and recreation/pastimes) (Attachment 12.1). Between-group differences favored risperidone by approximately 1 to 5 points on a 0 to 100 scale for each subscale. The between-group difference was marginally statistically significant for total M-SIP ($p=0.059$) and not statistically significant for any other subscale ($p\geq 0.139$).

Health and quality of life improved from baseline to end point in both treatment groups with no statistically significant differences between treatment groups ($p\geq 0.841$; Attachment 12.2). Present health was rated 'good' or 'very good' for 54% of risperidone subjects and 60% of olanzapine subjects at baseline and for 65% of risperidone subjects and 66% of olanzapine subjects at end point. Present quality of life was rated 'good' or 'very good' for 47% of risperidone subjects and 50% of olanzapine subjects at baseline and for 56% of risperidone subjects and 58% of olanzapine subjects at end point.

7. SUMMARY

- Approximately 55% of olanzapine treated subjects gained at least 7% of their baseline weight compared with 47% of risperidone treated subjects but this difference did not reach statistical significance. Weight increase reported as an adverse event was also more frequent for subjects in the olanzapine group (13%) than in the risperidone group (4%).
- Over time, the mean total PANSS scores decreased from baseline in both treatment groups, indicating improvement in the severity of psychotic symptoms.

There were no statistically significant differences between groups at end point. The patterns of change from baseline to end point for the positive and negative symptoms subscales were consistent with the changes in total PANSS.

- Both groups showed a mean decrease in CGI severity score from baseline to end point. The change was not statistically significantly different between treatment groups.
- The overall incidence of treatment-emergent adverse events was similar in subjects treated with olanzapine (87%) and risperidone (86%). Headache, rhinitis, hyperprolactinemia, paranoid reaction, dyspepsia, and hyperkinesia were reported more often for subjects treated with risperidone than for subjects treated with olanzapine. Somnolence, dizziness, back pain, and weight increase were reported more often for subjects treated with olanzapine than for subjects treated with risperidone.
- Most serious adverse events and adverse events leading to treatment discontinuation appeared to be related to the underlying psychiatric disorder. There were no clinically relevant differences between treatment groups. The incidence of suicide events was similar in both treatment groups.
- There were no statistically significant differences between treatment groups in the percentages of subjects with EPS-related adverse events.
- With respect to laboratory parameters, there were no clinically notable mean changes in hematology and chemistry parameters from baseline to end point in either treatment group. For prolactin, a mean increase of 26 ng/mL was observed in the risperidone group compared with a mean decrease of -10 ng/mL in the olanzapine group. Changes in prolactin levels (from normal at baseline to high at end point) were also more frequent in the risperidone group. These changes are consistent with the known pharmacological profile of risperidone (D₂ receptor blockade).
- The percent of subjects with new onset diabetes was low and comparable between treatment groups.
- There were no clinically noteworthy changes from baseline in mean values for vital sign parameters and there were no statistically significant differences between groups in the percentage of subjects with new onset of hypertension.
- There were no clinically meaningful changes in the mean ECG parameters from baseline over time in either treatment group.
- Improvements in health and quality of life (based on M-SIP and quality of life scales) were comparable for the 2 treatment groups.

8. CONCLUSION

Overall, after a 1-year period of treatment, there were no significant differences in efficacy between risperidone and olanzapine in a population of subjects with schizophrenia or schizoaffective disorder. Both drugs demonstrated continuing efficacy, both symptomatic and with respect to global functioning. Tolerability and safety were also comparable between the 2 treatment groups, with the exception that

there was a higher incidence of weight gain reported as an adverse event with olanzapine compared to risperidone (although no statistical difference in percent of subjects gaining more than 7% of body weight). As expected, there was a higher incidence of prolactin elevation in subjects treated with risperidone.

REFERENCES

1. Olanzapine U.S. Package Insert.
2. Lippert and Lehmann SI Units in medicine. Baltimore-Munich: Urban & Schwarzenberg, 1978

SUPPORTING DATA

The Supporting Data section is organized using a flexible numbering system that provides logical groups of data while minimizing the number of decimal levels. Numbering can start at any level (eg, 1 or 1.1 or 1.1.1) to provide the most efficient organization for a particular set of data. Levels that are omitted do not indicate missing data.

Attachment 1.1: Enrollment by Investigator

Page 1 of 2

25AUG2008 16:53
System Used: Arrow5.1 (U) /dmrun

JNJPRD--TRIAL RIS-USA-113

Table SUE01: Enrollment by Investigator

Analysis Set: Intent-to-treat

Main Invest.	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Baker R.	1 (1)	3 (2)	4 (1)
Berman I.	3 (2)	1 (1)	4 (1)
Brenner R.	4 (3)	4 (3)	8 (3)
Brown D.	2 (2)	4 (3)	6 (2)
Carman J.	2 (2)	0	2 (1)
Chengappa R.	1 (1)	2 (1)	3 (1)
Cohn C.	2 (2)	2 (1)	4 (1)
Csernansky J.	5 (4)	4 (3)	9 (3)
Daniel D.	2 (2)	2 (1)	4 (1)
Depriest M.	1 (1)	2 (1)	3 (1)
Feifel D.	3 (2)	3 (2)	6 (2)
Flaum M.	4 (3)	4 (3)	8 (3)
Gurklis J.	1 (1)	1 (1)	2 (1)
Howanitz E.	3 (2)	0	3 (1)
Josiassen R.	1 (1)	0	1 (<1)
Kanof P.	5 (4)	5 (4)	10 (4)
Knesevich M.	3 (2)	4 (3)	7 (3)
Kopelowicz A.	4 (3)	3 (2)	7 (3)
Lauriello J.	4 (3)	7 (5)	11 (4)
Lesem M.	1 (1)	2 (1)	3 (1)
Levinson D.	3 (2)	2 (1)	5 (2)
Logue E.	6 (5)	8 (6)	14 (5)
Love R.	1 (1)	0	1 (<1)
Manschreck T.	5 (4)	3 (2)	8 (3)
Mcevoy J.	1 (1)	3 (2)	4 (1)
Meltzer H.	2 (2)	7 (5)	9 (3)
Mendelowitz A.	4 (3)	2 (1)	6 (2)
Mihtar H.	4 (3)	3 (2)	7 (3)
Miller A.	4 (3)	9 (6)	13 (5)
Nakra R.	7 (6)	10 (7)	17 (6)
Pahl J.	8 (6)	9 (6)	17 (6)
Pandurangi A.	1 (1)	3 (2)	4 (1)
Plopper M.	4 (3)	3 (2)	7 (3)
Reddy N.	9 (7)	10 (7)	19 (7)
Roy-byrne P.	4 (3)	1 (1)	5 (2)
Stern R.	0	2 (1)	2 (1)
Strakowski S.	1 (1)	2 (1)	3 (1)

Note: Percentages calculated with the number of subjects in each group as denominator.

Attachment 1.1: Enrollment by Investigator

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System Used: Arrow5.1(U)/dmrun

JNJPRD--TRIAL RIS-USA-113

Table SUB01: Enrollment by Investigator (continued)

Analysis Set: Intent-to-treat

Main Invest.	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Swann A.	4 (3)	3 (2)	7 (3)
Targum S.	2 (2)	2 (1)	4 (1)
Van Kammen D.	2 (2)	2 (1)	4 (1)
Wirshing D.	2 (2)	4 (3)	6 (2)

See footnotes on the first page of the table.

Attachment 1.2: Nicotine Use

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25AUG2008 16:53
System Used: Arrow5.1 (U) /dmrun

JNJPRD--TRIAL RIS-USA-113

Table SUE05: Nicotine Use

Analysis Set: Intent-to-treat

Nicotine Use	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Nicotine Current User	81 (64)	82 (58)	163 (61)
Nicotine Non-user	45 (36)	59 (42)	104 (39)

Note: Percentages calculated with the number of subjects in each group as denominator.

Attachment 1.3: Alcohol Use

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25AUG2008 16:53
System Used: Arrow5.1(U)/dmrun

JNJPRD--TRIAL RIS-USA-113

Table SUE06: Alcohol Use

Analysis Set: Intent-to-treat

Alcohol Use	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Alcohol Current User	26 (21)	23 (16)	49 (18)
Alcohol Non-user	100 (79)	118 (84)	218 (82)

Note: Percentages calculated with the number of subjects in each group as denominator.

Attachment 1.4: Medical History

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System Used: Arrow5.1 (U) /mhrun

JNJPRD--TRIAL RIS-USA-113

Table SUE07: Medical History

Analysis Set: Intent-to-treat

* Hist./not active & curr. active: Different diseases possible within the same system.

Disease Body System Condition	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Allergic/immunologic	126 (100)	141 (100)	267 (100)
None	92 (73)	104 (74)	196 (73)
History and not active	8 (6)	14 (10)	22 (8)
Currently active	23 (18)	21 (15)	44 (16)
Hist./not active & curr. active	3 (2)	2 (1)	5 (2)
Cardiovascular	126 (100)	141 (100)	267 (100)
None	85 (67)	103 (77)	193 (72)
History and not active	14 (11)	12 (9)	26 (10)
Currently active	23 (18)	19 (13)	42 (16)
Hist./not active & curr. active	4 (3)	2 (1)	6 (2)
Dermatological	126 (100)	141 (100)	267 (100)
None	104 (83)	107 (76)	211 (79)
History and not active	7 (6)	13 (9)	20 (7)
Currently active	13 (10)	20 (14)	33 (12)
Hist./not active & curr. active	2 (2)	1 (1)	3 (1)
Ears, nose, throat	126 (100)	141 (100)	267 (100)
None	95 (75)	103 (73)	198 (74)
History and not active	10 (8)	19 (13)	29 (11)
Currently active	16 (13)	17 (12)	33 (12)
Hist./not active & curr. active	5 (4)	2 (1)	7 (3)
Endocrine	126 (100)	141 (100)	267 (100)
None	108 (86)	127 (90)	235 (88)
History and not active	5 (4)	2 (1)	7 (3)
Currently active	12 (10)	10 (7)	22 (8)
Hist./not active & curr. active	1 (1)	2 (1)	3 (1)
Eyes	126 (100)	140 (99)	266 (>99)
None	91 (72)	98 (70)	189 (71)
History and not active	9 (7)	3 (2)	12 (4)
Currently active	23 (18)	38 (27)	61 (23)
Hist./not active & curr. active	3 (2)	1 (1)	4 (1)

Note: Percentages calculated with the number of subjects in each group as denominator.

JNJPRD--TRIAL RIS-USA-113

Table SUB07: Medical History (continued)

Analysis Set: Intent-to-treat

* Hist./not active & curr. active: Different diseases possible within the same system.

Disease Body System Condition	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Gastrointestinal	126 (100)	141 (100)	267 (100)
None	82 (65)	106 (75)	188 (70)
History and not active	25 (20)	11 (8)	36 (13)
Currently active	14 (11)	22 (16)	36 (13)
Hist./not active & curr. active	5 (4)	2 (1)	7 (3)
Genito-urinary	126 (100)	141 (100)	267 (100)
None	85 (67)	108 (77)	193 (72)
History and not active	19 (15)	15 (11)	34 (13)
Currently active	19 (15)	14 (10)	33 (12)
Hist./not active & curr. active	3 (2)	4 (3)	7 (3)
Haematological	126 (100)	141 (100)	267 (100)
None	109 (87)	128 (91)	237 (89)
History and not active	9 (7)	5 (4)	14 (5)
Currently active	7 (6)	8 (6)	15 (6)
Hist./not active & curr. active	1 (1)	0	1 (<1)
Musculoskeletal	126 (100)	141 (100)	267 (100)
None	89 (71)	98 (70)	187 (70)
History and not active	17 (13)	24 (17)	41 (15)
Currently active	10 (8)	14 (10)	24 (9)
Hist./not active & curr. active	10 (8)	5 (4)	15 (6)
Neurological	126 (100)	141 (100)	267 (100)
None	96 (76)	115 (82)	211 (79)
History and not active	12 (10)	3 (2)	15 (6)
Currently active	15 (12)	21 (15)	36 (13)
Hist./not active & curr. active	3 (2)	2 (1)	5 (2)
Respiratory	126 (100)	141 (100)	267 (100)
None	90 (71)	120 (85)	210 (79)
History and not active	20 (16)	7 (5)	27 (10)
Currently active	15 (12)	12 (9)	27 (10)

See footnotes on the first page of the table.

Attachment 1.4: Medical History

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JNJPRD--TRIAL RIS-USA-113

Table SUB07: Medical History (continued)

Analysis Set: Intent-to-treat

* Hist./not active & curr. active: Different diseases possible within the same system.

Disease Body System Condition	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Respiratory (continued)			
Hist./not active & curr. active	1 (1)	2 (1)	3 (1)
Other	44 (35)	59 (42)	103 (39)
History and not active	24 (19)	28 (20)	52 (19)
Currently active	14 (11)	24 (17)	38 (14)
Hist./not active & curr. active	6 (5)	7 (5)	13 (5)

See footnotes on the first page of the table.

Attachment 1.5: Psychiatric History

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System Used: Arrow5.1 (U) /dmrun

JNJPRD--TRIAL RIS-USA-113

Table SUE04: Psychiatric History

Analysis Set: Intent-to-treat

	RISPERIDONE (N=126)	OLANZAPINE (N=141)	--- Total --- (N=267)
Diagnosis			
N	126	141	267
Category, n (%)			
Schizoaffective disorder	15 (12)	20 (14)	35 (13)
Schizophrenia	111 (88)	121 (86)	232 (87)
Family history of psychiatric illness			
N	126	141	267
Category, n (%)			
Yes	58 (46)	50 (35)	108 (40)
No	49 (39)	75 (53)	124 (46)
Unknown	19 (15)	16 (11)	35 (13)
Age at onset (years)			
N	123	139	262
Mean (SD)	24.8 (6.94)	23.6 (8.05)	24.2 (7.56)
Median	24.0	21.0	23.0
Range	(13;48)	(5;58)	(5;58)
Age at first hospitalization			
N	117	133	250
Mean (SD)	26.3 (8.39)	24.9 (9.06)	25.5 (8.76)
Median	26.0	23.0	24.0
Range	(0;56)	(0;58)	(0;58)
No. of hospitalizations			
N	121	138	259
Category, n (%)			
0	9 (7)	12 (9)	21 (8)
>0	112 (93)	126 (91)	238 (92)
Mean (SD)	5.5 (7.18)	4.6 (5.56)	5.0 (6.37)
Median	4.0	3.0	3.0
Range	(0;61)	(0;40)	(0;61)

Attachment 1.5: Psychiatric History

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JNJPRD--TRIAL RIS-USA-113

Table SUB04: Psychiatric History (continued)

Analysis Set: Intent-to-treat

	RISPERIDONE (N=126)	OLANZAPINE (N=141)	--- Total --- (N=267)
Current status of hospitalization			
N	126	141	267
Category, n (%)			
Yes	20 (16)	26 (18)	46 (17)
No	106 (84)	115 (82)	221 (83)

Attachment 1.6: Previous Antipsychotic Therapy - Other Neuroleptics

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System Used: Arrow5.1 (U) /ptrun

JNJPRD--TRIAL RIS-USA-113

Table SUB09: Previous Antipsychotic Therapy - Other Neuroleptics

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with prior other neuroleptic	116 (92)	125 (89)
Psycholeptics	112 (89)	121 (86)
Antipsychotics	37 (29)	32 (23)
Risperidone	36 (29)	44 (31)
Haloperidol	33 (26)	30 (21)
Fluphenazine hydrochloride	7 (6)	11 (8)
Tiotixene	7 (6)	8 (6)
Thioridazine hydrochloride	6 (5)	5 (4)
Lorazepam	5 (4)	3 (2)
Trifluoperazine hydrochloride	5 (4)	2 (1)
Perphenazine	4 (3)	6 (4)
Chlorpromazine	3 (2)	0
Chlorpromazine hydrochloride	3 (2)	1 (1)
Fluphenazine	2 (2)	3 (2)
Mesoridazine	2 (2)	1 (1)
Lithium	1 (1)	1 (1)
Lithium carbonate	1 (1)	0
Loxapine succinate	1 (1)	2 (1)
Thioridazine	1 (1)	1 (1)
Zolpidem tartrate	0	1 (1)
Anti-parkinson drugs	8 (6)	6 (4)
Benzatropine mesilate	7 (6)	4 (3)
Trihexyphenidyl hydrochloride	1 (1)	1 (1)
Trihexyphenidyl	0	1 (1)
All other therapeutic products	6 (5)	7 (5)
All other therapeutic products	6 (5)	7 (5)
Antiepileptics	2 (2)	2 (1)
Carbamazepine	1 (1)	1 (1)
Valproate semisodium	1 (1)	1 (1)

Note: Percentages calculated with the number of subjects in each group as denominator.
A subject can be taking more than one medication

Attachment 1.6: Previous Antipsychotic Therapy - Other Neuroleptics

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System Used: Arrow5.1(U)/ptrun

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Table SUE09: Previous Antipsychotic Therapy - Other Neuroleptics (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antihistamines for systemic use Diphenhydramine hydrochloride	1 (1) 1 (1)	0 0
Antipruritics, incl antihist, anesthet, etc. Diphenhydramine hydrochloride	1 (1) 1 (1)	0 0
Psychoanaleptics Trazodone	1 (1) 1 (1)	1 (1) 1 (1)

See footnotes on the first page of the table.

Attachment 1.7: Previous Antipsychotic Therapy - Depot Neuroleptics

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System Used: Arrow5.1(U)/ptrun

JNJPRD--TRIAL RIS-USA-113

Table SUB08: Previous Antipsychotic Therapy - Depot Neuroleptics

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with prior depot neuroleptic	21 (17)	24 (17)
Psycholeptics	21 (17)	24 (17)
Haloperidol decanoate	16 (13)	12 (9)
Fluphenazine decanoate	5 (4)	6 (4)
Fluphenazine hydrochloride	1 (1)	1 (1)
Haloperidol	0	5 (4)

Note: Percentages calculated with the number of subjects in each group as denominator.
A subject can be taking more than one medication

JNJPRD--TRIAL RIS-USA-113

Table SUE10: Physical Examination - Baseline of RIS-USA-113

Analysis Set: INTENT-TO-TREAT

PHYS. EXAM. BODY SYSTEM VALUE DESCRIPTION	RISPERIDONE (N=122) n (%)	OLANZAPINE (N=136) n (%)
TOTAL NO. SUBJECTS WITH EXAM	122 (100)	136 (100)
GENERAL APPEARANCE	122	136
ABNORMAL	18 (15)	23 (17)
NORMAL	104 (85)	113 (83)
SKIN	122	136
ABNORMAL	16 (13)	21 (15)
NORMAL	106 (87)	115 (85)
EYES	122	136
ABNORMAL	15 (12)	12 (9)
NORMAL	107 (88)	124 (91)
EARS, NOSE, THROAT	122	136
ABNORMAL	14 (11)	19 (14)
NORMAL	108 (89)	117 (86)
HEAD AND NECK	122	136
ABNORMAL	3 (2)	3 (2)
NORMAL	119 (98)	133 (98)
HEART	122	136
ABNORMAL	6 (5)	3 (2)
NORMAL	116 (95)	133 (98)
CHEST AND LUNGS	122	136
ABNORMAL	7 (6)	5 (4)
NORMAL	115 (94)	131 (96)
BREASTS	112	122
ABNORMAL	7 (6)	3 (2)
NORMAL	105 (94)	119 (98)
ABDOMEN	122	136
ABNORMAL	9 (7)	14 (10)

Note: Percentages calculated with the number of subjects per phys. exam. body system as denominator.

JNJPRD--TRIAL RIS-USA-113

Table SUB10: Physical Examination - Baseline of RIS-USA-113 (continued)

Analysis Set: INTENT-TO-TREAT

PHYS. EXAM. BODY SYSTEM VALUE DESCRIPTION	RISPERIDONE (N=122) n (%)	OLANZAPINE (N=136) n (%)
ABDOMEN (continued)		
NORMAL	113 (93)	122 (90)
EXTREMITIES	122	136
ABNORMAL	5 (4)	7 (5)
NORMAL	117 (96)	129 (95)
BACK	122	136
ABNORMAL	1 (1)	1 (1)
NORMAL	121 (99)	135 (99)
LYMPH NODES	121	136
ABNORMAL	1 (1)	0
NORMAL	120 (99)	136 (100)
PERIPHERAL PULSES	122	135
NORMAL	122 (100)	135 (100)
MUSCULOSKELETAL	122	136
ABNORMAL	6 (5)	5 (4)
NORMAL	116 (95)	131 (96)
NEUROLOGICAL	122	136
ABNORMAL	8 (7)	9 (7)
NORMAL	114 (93)	127 (93)
OTHER	7	8
ABNORMAL	7 (100)	8 (100)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with concomitant medication	105 (83)	109 (77)
Psycholeptics	45 (36)	45 (32)
Lorazepam	30 (24)	30 (21)
Chloral hydrate	8 (6)	6 (4)
Flurazepam	4 (3)	6 (4)
Olanzapine	4 (3)	2 (1)
Risperidone	4 (3)	4 (3)
Flurazepam hydrochloride	3 (2)	7 (5)
Haloperidol	2 (2)	2 (1)
Chlorpromazine hydrochloride	1 (1)	0
Flupentixol dihydrochloride	1 (1)	0
Hydroxyzine	1 (1)	0
Loxapine succinate	1 (1)	0
Oxazepam	1 (1)	1 (1)
Seroquel	1 (1)	1 (1)
Thioridazine hydrochloride	1 (1)	0
Tiotixene	1 (1)	0
Chlordiazepoxide hydrochloride	0	1 (1)
Fluphenazine decanoate	0	1 (1)
Fluphenazine hydrochloride	0	1 (1)
Hydroxyzine embonate	0	1 (1)
Prochlorperazine edisylate	0	1 (1)
Temazepam	0	6 (4)
Valerian root	0	1 (1)
Zolpidem tartrate	0	3 (2)
Analgesics	41 (33)	48 (34)
Paracetamol	24 (19)	28 (20)
Acetylsalicylic acid	18 (14)	13 (9)
Excedrin	2 (2)	2 (1)
Vicodin	2 (2)	1 (1)
Clonidine	1 (1)	0
Co-tylenol	1 (1)	2 (1)
Excedrin p.m.	1 (1)	0
Other analgesics and antipyretics	1 (1)	0

Note: Percentages calculated with the number of subjects in each group as denominator.
A subject can be taking more than one medication

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)

Analgesics (continued)		
Salsalate	1 (1)	0
Thomapyrin n	1 (1)	0
Tylenol no 3	1 (1)	0
Tylenol pm	1 (1)	0
Albyl med kodein	0	1 (1)
Alka-seltzer	0	1 (1)
Alka-seltzer plus	0	1 (1)
Cold capsules	0	1 (1)
Medinite	0	1 (1)
Panadeine co	0	2 (1)
Pethidine hydrochloride	0	1 (1)
Sumatriptan	0	1 (1)
Theraflu	0	1 (1)
Tylox	0	1 (1)
Vincent's tablets	0	1 (1)
Antiinflammatory and antirheumatic products	26 (21)	17 (12)
Ibuprofen	18 (14)	14 (10)
Naproxen	3 (2)	2 (1)
Naproxen sodium	3 (2)	0
Diclofenac sodium	1 (1)	0
Ketorolac tromethamine	1 (1)	1 (1)
Morniflumate	1 (1)	0
Penicillamine and similar agents	1 (1)	0
Nabumetone	0	1 (1)
Topical products for joint and muscular pain	25 (20)	15 (11)
Ibuprofen	18 (14)	14 (10)
Naproxen	3 (2)	2 (1)
Naproxen sodium	3 (2)	0
Diclofenac sodium	1 (1)	0
Topical products for joint and muscular pain	1 (1)	0
Other gynecologicals	23 (18)	15 (11)
Ibuprofen	18 (14)	14 (10)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

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Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Other gynecologicals (continued)		
Naproxen	3 (2)	2 (1)
Naproxen sodium	3 (2)	0
Antacids, drugs for treatm.of pept.ulc.and flatul.		
Maalox	22 (17)	12 (9)
Famotidine	7 (6)	1 (1)
Magnesium hydroxide	6 (5)	1 (1)
Cimetidine	4 (3)	2 (1)
Tums	3 (2)	3 (2)
Omeprazole	3 (2)	4 (3)
Lansoprazole	2 (2)	0
Mynta	1 (1)	1 (1)
Nizatidine	1 (1)	1 (1)
Ranitidine	1 (1)	0
Calcium carbonate	0	1 (1)
Stomatological preparations		
Acetylsalicylic acid	22 (17)	23 (16)
Chlorhexidine gluconate	18 (14)	13 (9)
Clotrimazole	2 (2)	0
Epinephrine	1 (1)	4 (3)
Triamcinolone	1 (1)	0
Triamcinolone acetonide	1 (1)	1 (1)
Hydrocortisone	1 (1)	0
Metronidazole	0	2 (1)
Miconazole nitrate	0	2 (1)
Tetracycline	0	1 (1)
Antibacterials for systemic use		
Amoxicillin	19 (15)	18 (13)
Bactrim	4 (3)	1 (1)
Ciprofloxacin hydrochloride	3 (2)	3 (2)
Antibiotics	3 (2)	1 (1)
Cefalexin monohydrate	2 (2)	0
Erythromycin	2 (2)	2 (1)
	2 (2)	0

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antibacterials for systemic use (continued)		
Phenoxymethylpenicillin potassium	2 (2)	1 (1)
Azithromycin	1 (1)	3 (2)
Cefalexin	1 (1)	1 (1)
Cefprozil	1 (1)	0
Cefuroxime axetil	1 (1)	2 (1)
Ciprofloxacin	1 (1)	0
Clarithromycin	1 (1)	0
Clavulin	1 (1)	0
Sultamicillin	1 (1)	0
Tobramycin	1 (1)	0
Cefotetan disodium	0	1 (1)
Clindamycin phosphate	0	1 (1)
Metronidazole	0	2 (1)
Ofloxacin	0	1 (1)
Penicillin nos	0	2 (1)
Polymyxin b sulfate	0	1 (1)
Steroid antibacterials	0	1 (1)
Sulfamethoxazole	0	1 (1)
Tetracycline	0	2 (1)
Antithrombotic agents	19 (15)	13 (9)
Acetylsalicylic acid	18 (14)	13 (9)
Warfarin sodium	1 (1)	0
Ophthalmicologics	18 (14)	16 (11)
Ciprofloxacin hydrochloride	3 (2)	1 (1)
Antibiotics	2 (2)	0
Chlorhexidine gluconate	2 (2)	0
Erythromycin	2 (2)	0
Ciprofloxacin	1 (1)	0
Clonidine	1 (1)	0
Cocaine	1 (1)	2 (1)
Conjunctin	1 (1)	0
Diclofenac sodium	1 (1)	0
Dorzolamide hydrochloride	1 (1)	0

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Ophthalmologicals (continued)		
Epinephrine	1 (1)	0
Ketorolac tromethamine	1 (1)	1 (1)
Polysporin drops	1 (1)	0
Procaine hydrochloride	1 (1)	0
Timolol	1 (1)	0
Timolol maleate	1 (1)	0
Tobramycin	1 (1)	0
Triamcinolone	1 (1)	1 (1)
Triamcinolone acetoneide	1 (1)	0
Artificial tears	0	2 (1)
Betaxolol hydrochloride	0	1 (1)
Cortisone	0	1 (1)
Hydrocortisone	0	2 (1)
Latanoprost	0	1 (1)
Maxitrol	0	1 (1)
Ofloxacin	0	1 (1)
Polymyxin b sulfate	0	1 (1)
Tetracycline	0	2 (1)
Anti-parkinson drugs	17 (13)	14 (10)
Benzatropine mesilate	15 (12)	13 (9)
Trihexyphenidyl hydrochloride	2 (2)	0
Trihexyphenidyl	0	1 (1)
Psychoanaleptics	16 (13)	12 (9)
Sertraline hydrochloride	8 (6)	1 (1)
Amfebutamone hydrochloride	5 (4)	2 (1)
Fluoxetine hydrochloride	3 (2)	4 (3)
Cannabis	1 (1)	0
Fluvoxamine	1 (1)	0
Nefazodone hydrochloride	1 (1)	0
Paroxetine	1 (1)	1 (1)
Paroxetine hydrochloride	1 (1)	2 (1)
Amitriptyline	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Psychoanaleptics (continued)		
Desipramine	0	1 (1)
Vitamins	15 (12)	17 (12)
Multivitamins	9 (7)	8 (6)
Tocopherol	5 (4)	3 (2)
Ascorbic acid	3 (2)	4 (3)
Multivitamins w/minerals	1 (1)	0
Pyridoxine hydrochloride	1 (1)	2 (1)
Thiamine	1 (1)	3 (2)
Vitamidyne a and d	1 (1)	0
Becosym forte	0	1 (1)
Cod-liver oil	0	1 (1)
Pyridoxine	0	1 (1)
Theragran-m	0	1 (1)
Vitamin b	0	1 (1)
Antihistamines for systemic use	13 (10)	7 (5)
Diphenhydramine hydrochloride	6 (5)	4 (3)
Loratadine	3 (2)	2 (1)
Cetirizine hydrochloride	2 (2)	0
Chlorphenamine maleate	1 (1)	0
Diphenhydramine	1 (1)	1 (1)
Promethazine hydrochloride	1 (1)	0
Cough and cold preparations	12 (10)	13 (9)
Guaifenesin	7 (6)	6 (4)
Cough syrup	2 (2)	0
Hydrocodone	2 (2)	2 (1)
Tussin dm	1 (1)	0
Antitussives and expectorants, combinations	0	1 (1)
Cough and cold preparations	0	2 (1)
Robitussin-dm	0	3 (2)
Triaminic-dm	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Drugs used in diabetes	12 (10)	5 (4)
Glipizide	5 (4)	4 (3)
Metformin hydrochloride	4 (3)	1 (1)
Glibenclamide	3 (2)	0
Insulin	2 (2)	1 (1)
Human mixtard	1 (1)	0
Insulin injection, isophane	1 (1)	0
Metformin	1 (1)	0
Oral antidiabetics	1 (1)	0
Tolazamide	1 (1)	0
Humulin 70/30	0	1 (1)
Anti-asthmatics	11 (9)	3 (2)
Salbutamol	5 (4)	2 (1)
Beclometasone dipropionate	2 (2)	0
Ipratropium bromide	2 (2)	1 (1)
Beclometasone	1 (1)	0
Bronkaid	1 (1)	0
Combiivent	1 (1)	0
Epinephrine	1 (1)	0
Isoprenaline hydrochloride	1 (1)	0
Theophylline	1 (1)	1 (1)
Antipruritics, incl antihist, anesthet, etc.	10 (8)	6 (4)
Diphenhydramine hydrochloride	6 (5)	4 (3)
Anbesol	1 (1)	0
Caladryl	1 (1)	0
Diphenhydramine	1 (1)	1 (1)
Flex-all 454	1 (1)	0
Promethazine hydrochloride	1 (1)	0
Anaesthetics for topical use	0	1 (1)
Calcium channel blockers	10 (8)	7 (5)
Nifedipine	6 (5)	2 (1)
Amlodipine	1 (1)	0
Diltiazem hydrochloride	1 (1)	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Calcium channel blockers (continued)		
Isradipine	1 (1)	0
Verapamil	1 (1)	1 (1)
Amlodipine besilate	0	3 (2)
Nasal preparations	10 (8)	7 (5)
Dimetapp	3 (2)	0
Beclometasone dipropionate	2 (2)	0
Ipratropium bromide	2 (2)	1 (1)
Beclometasone	1 (1)	0
Pseudoephedrine	1 (1)	0
Pseudoephedrine hydrochloride	1 (1)	1 (1)
Tavist-d	1 (1)	0
Contac 700	0	1 (1)
Nasal decongestants for topical use	0	1 (1)
Nasal preparations	0	1 (1)
Phenylpropanolamine	0	1 (1)
Wick sinex	0	1 (1)
Beta blocking agents	9 (7)	10 (7)
Atenolol	3 (2)	5 (4)
Propranolol hydrochloride	2 (2)	1 (1)
Bisect	1 (1)	1 (1)
Labetalol hydrochloride	1 (1)	0
Nadolol	1 (1)	0
Propranolol	1 (1)	2 (1)
Timolol	1 (1)	0
Timolol maleate	1 (1)	0
Betaxolol hydrochloride	0	1 (1)
Antidiarr.,intest. antiinfl./antiinfect. agents	7 (6)	8 (6)
Antibiotics	2 (2)	0
Hydrocortisone valerate	1 (1)	1 (1)
Loperamide	1 (1)	0
Loperamide hydrochloride	1 (1)	2 (1)
Nystatin	1 (1)	0

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antidiarr.,intest. antiinfl./antiinfect. agents (continued)		
Prednisone	1 (1)	1 (1)
Bismuth subsalicylate	0	1 (1)
Hydrocortisone	0	2 (1)
Miconazole nitrate	0	1 (1)
Polymyxin b sulfate	0	1 (1)
Sex hormones and modulators of the genital system		
Estrogens	7 (6)	8 (6)
Estrogens conjugated	2 (2)	0
Medroxyprogesterone acetate	2 (2)	3 (2)
Estropipate	1 (1)	3 (2)
Ethinylestradiol	1 (1)	0
Progesterone	1 (1)	0
Provette /generic/	1 (1)	0
Cilest	0	1 (1)
Estradiol	0	1 (1)
Eugynon	0	1 (1)
Marvelon	0	1 (1)
Oral contraceptive nos	0	1 (1)
Urologicals		
Magnesium hydroxide	7 (6)	4 (3)
Phenazopyridine hydrochloride	4 (3)	2 (1)
Methenamine hippurate	2 (2)	0
Oxybutynin	1 (1)	0
Finasteride	1 (1)	1 (1)
Phenazopyridine	0	1 (1)
Corticosteroids, dermatological preparations		
Beclometasone dipropionate	6 (5)	4 (3)
Beclometasone	2 (2)	0
Hydrocortisone valerate	1 (1)	0
Triamcinolone	1 (1)	1 (1)
Triamcinolone acetonide	1 (1)	1 (1)
Hydrocortisone	0	0
		2 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUB12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Corticosteroids, dermatological preparations (continued)		
Methylprednisolone	0	1 (1)
Diuretics	6 (5)	5 (4)
Hydrochlorothiazide	3 (2)	2 (1)
Furosemide	2 (2)	2 (1)
Theophylline	1 (1)	1 (1)
Torsemide	0	1 (1)
Endocrine therapy	6 (5)	4 (3)
Estrogens	2 (2)	0
Estrogens conjugated	2 (2)	3 (2)
Medroxyprogesterone acetate	2 (2)	3 (2)
Ethinylestradiol	1 (1)	0
Estradiol	0	1 (1)
Throat preparations	6 (5)	2 (1)
Antibiotics	2 (2)	0
Chlorhexidine gluconate	2 (2)	0
Cocaine	1 (1)	2 (1)
Throat preparations	1 (1)	0
Agents acting on the renin-angiotensin system	5 (4)	6 (4)
Lisinopril	3 (2)	1 (1)
Enalapril maleate	1 (1)	2 (1)
Prinzide	1 (1)	1 (1)
Benazepril	0	1 (1)
Valsartan	0	1 (1)
Antifungals for dermatological use	5 (4)	6 (4)
Antifungals for topical use	1 (1)	0
Clotrimazole	1 (1)	4 (3)
Lotrisone	1 (1)	0
Nystatin	1 (1)	0
Tolnaftate	1 (1)	1 (1)
Ketoconazole	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antifungals for dermatological use (continued)		
Miconazole nitrate	0	1 (1)
Laxatives	5 (4)	12 (9)
Bisacodyl	2 (2)	2 (1)
Docusate sodium	2 (2)	5 (4)
Peri-colace	1 (1)	1 (1)
Yellow phenolphthalein	1 (1)	1 (1)
Coloxyl with danthron	0	1 (1)
Docusate calcium	0	1 (1)
Laxative nos	0	1 (1)
Psyllium hydrophilic mucilloid	0	4 (3)
Plasma substitutes and perfusion solutions	5 (4)	2 (1)
Chlorhexidine gluconate	2 (2)	0
Cetylpyridinium chloride	1 (1)	0
Magnesium citrate	1 (1)	0
Potassium chloride	1 (1)	1 (1)
Electrolyte solutions	0	1 (1)
Parenteral	0	1 (1)
Vaccines	5 (4)	3 (2)
Influenza virus vaccine polyvalent	5 (4)	3 (2)
Pneumococcal vaccine	1 (1)	0
Antianemic preparations	4 (3)	5 (4)
Ferrous sulfate	3 (2)	0
Folate sodium	1 (1)	1 (1)
Cyanocobalamin	0	1 (1)
Folic acid	0	2 (1)
Iron	0	1 (1)
Antibiotics and chemother. for dermatological use	4 (3)	4 (3)
Bacitracin	3 (2)	0
Antibiotics	2 (2)	0
Galenic /polymyxin b/neomycin/bacitracin	1 (1)	0

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUB12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antibiotics and chemother. for dermatological use (continued)		
Metronidazole	0	2 (1)
Tetracycline	0	2 (1)
Antihypertensives		
Terazosin hydrochloride	4 (3)	4 (3)
Clonidine	3 (2)	1 (1)
Doxazosin mesilate	1 (1)	0
Antihypertensives	1 (1)	1 (1)
Doxazosin	0	1 (1)
Antiseptics and disinfectants		
Chlorhexidine gluconate	4 (3)	0
Cetylpyridinium chloride	2 (2)	0
Noxzema	1 (1)	0
Corticosteroids for systemic use		
Hydrocortisone valerate	4 (3)	6 (4)
Prednisone	1 (1)	1 (1)
Triamcinolone	1 (1)	1 (1)
Triamcinolone acetonide	1 (1)	0
Cortisone	0	1 (1)
Hydrocortisone	0	2 (1)
Methylprednisolone	0	1 (1)
Emollients and protectives		
Ammonium lactate	4 (3)	1 (1)
Neutrogena soap	3 (2)	0
Betacarctene	1 (1)	0
	0	1 (1)
Otologicals		
Chlorhexidine gluconate	4 (3)	8 (6)
Cocaine	2 (2)	0
Urea hydrogen peroxide	1 (1)	2 (1)
Hydrocortisone	1 (1)	0
Otosporin	0	2 (1)
	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUB12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Otologicals (continued)		
Polymyxin b sulfate	0	1 (1)
Tetracycline	0	2 (1)
Serum lipid reducing agents	4 (3)	5 (4)
Simvastatin	2 (2)	1 (1)
Cholesterol- and triglyceride reducers	1 (1)	1 (1)
Pravastatin sodium	1 (1)	0
Gemfibrozil	0	3 (2)
Anti-acne preparations	3 (2)	2 (1)
Erythromycin	2 (2)	0
Tretinoin	1 (1)	0
Clindamycin phosphate	0	1 (1)
Methylprednisolone	0	1 (1)
Antispas. and anticholinergic agents and propulsiv	3 (2)	1 (1)
Benztropine	2 (2)	0
Hyoscyamine sulfate	1 (1)	0
Metoclopramide	1 (1)	0
Dicycloverine hydrochloride	0	1 (1)
Cardiac therapy	3 (2)	1 (1)
Glyceryl trinitrate	2 (2)	1 (1)
Isoprenaline hydrochloride	1 (1)	0
Gynecological antiinfectives and antiseptics	3 (2)	9 (6)
Antibiotics	2 (2)	0
Clotrimazole	1 (1)	4 (3)
Nystatin	1 (1)	0
Clindamycin phosphate	0	1 (1)
Ketoconazole	0	1 (1)
Metronidazole	0	2 (1)
Miconazole nitrate	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1 (U) /ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUB12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Medicated dressings	3 (2)	0
Chlorhexidine gluconate	2 (2)	0
Cetylpyridinium chloride	1 (1)	0
Mineral supplements	3 (2)	4 (3)
Magnesium citrate	1 (1)	0
Potassium chloride	1 (1)	1 (1)
Zinc	1 (1)	0
Calcium	0	2 (1)
Calcium carbonate	0	1 (1)
Anesthetics	2 (2)	2 (1)
Cocaine	1 (1)	2 (1)
Procaine hydrochloride	1 (1)	0
Antiepileptics	2 (2)	3 (2)
Clonazepam	2 (2)	2 (1)
Valproate semisodium	0	1 (1)
Antineoplastic agents	2 (2)	0
Methotrexate	1 (1)	0
Tretinoin	1 (1)	0
Ophthalmological and otological preparations	2 (2)	3 (2)
Chlorhexidine gluconate	2 (2)	0
Polymyxin b sulfate	0	1 (1)
Tetracycline	0	2 (1)
Other nervous system drugs	2 (2)	2 (1)
Nicotine	2 (2)	2 (1)
Bethanechol	0	1 (1)
All other therapeutic products	1 (1)	3 (2)
Herbal preparation	1 (1)	1 (1)
Garlic	0	1 (1)
Naltrexone	0	1 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1(U)/ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUE12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
All other therapeutic products (continued)		
Yohimbine	0	1 (1)
Antihemorrhagics	1 (1)	0
Epinephrine	1 (1)	0
Antimycobacterials	1 (1)	1 (1)
Isoniazid	1 (1)	1 (1)
Diagnostic agents	1 (1)	1 (1)
Tuberculin ppd	1 (1)	1 (1)
Digestives, incl enzymes	1 (1)	0
Alpha-d-galactosidase	1 (1)	0
General nutrients	1 (1)	2 (1)
Protein supplements	1 (1)	0
Ensure	0	1 (1)
Fat/carbohydrates/proteins/minerals/vitamins,	0	1 (1)
Other dermatological preparations	1 (1)	0
Other dermatological preparations	1 (1)	0
Vasoprotectives	1 (1)	2 (1)
Procaine hydrochloride	1 (1)	0
Hydrocortisone	0	2 (1)
Antimycotics for systemic use	0	3 (2)
Itraconazole	0	1 (1)
Ketoconazole	0	1 (1)
Miconazole nitrate	0	1 (1)
Antiprotzoals	0	2 (1)
Metronidazole	0	2 (1)

See footnotes on the first page of the table.

Attachment 1.9: Concomitant Therapy

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System Used: Arrow5.1 (U) /ctrun

JNJPRD--TRIAL RIS-USA-113

Table SUB12: Concomitant Therapy (continued)

Analysis Set: Intent-to-treat

ATC Class WHO Generic Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Antivirals for systemic use Valaciclovir	0 0	1 (1) 1 (1)
Muscle relaxants Carisoprodol Methocarbamol	0 0 0	2 (1) 1 (1) 1 (1)
Peripheral vasodilators Ginkgo biloba	0 0	1 (1) 1 (1)
Thyroid therapy Levothyroxine sodium	0 0	2 (1) 2 (1)

See footnotes on the first page of the table.

Attachment 1.10: Protocol Deviations - Summary

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System Used: Arrow5.1(U)/dvrn

JNJPRD--TRIAL RIS-USA-113

Table SUB13: Protocol Deviations

Analysis Set: Intent-to-treat

Deviation	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)	Total (N=267) n (%)
Total no. subjects with deviation	46 (37)	43 (30)	89 (33)
Intercurrent therapy	29 (23)	30 (21)	59 (22)
Intercurrent forbidden therapy	29 (23)	30 (21)	59 (22)
Treatment deviation	16 (13)	12 (9)	28 (10)
Non-compliance	14 (11)	12 (9)	26 (10)
Wrong dose	2 (2)	1 (1)	3 (1)
Insufficient data	6 (5)	4 (3)	10 (4)
No efficacy data	6 (5)	4 (3)	10 (4)
Selection criteria not met	3 (2)	5 (4)	8 (3)
Abnormal lab values	0	4 (3)	4 (1)
Selection criteria not met	3 (2)	1 (1)	4 (1)

Note: Percentages calculated with the number of subjects in each group as denominator.

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

JNJPRD--TRIAL RIS-USA-113

Listing LSUB01: Protocol Deviations

RANDOMISATION GROUP: RISPERIDONE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30009	DANIEL D.	INSUFFICIENT DATA INTERCURRENT THERAPY INTERCURRENT THERAPY	NO EFFICACY DATA INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	NO VISITS DONE KLONOPIN PRE-TRIAL - ONGOING TOOK RISPERIDONE (4/24/98-ONGOING)
A30018	TARGUM S.	TREATMENT DEVIATION	WRONG DOSE	SUBJECT TOOK GREATER THAN 4 CAPS/DAY
A30032	CHENGAPPA R.	INTERCURRENT THERAPY TREATMENT DEVIATION TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE NON-COMPLIANCE	TOOK LORAZEPAM >5 DAYS NON-RESEARCH PSYCH. INSISTED ON INFO. SUBJECT NON-COMPLIANT
A30035	MCEVOY J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK ANTIPSYCHOTICS (PRIOR-ONGOING)
A30041	ROY-BYRNE P.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENADRYL 6/15/98 - 6/24/98 FOR AKATHISIA - NO ESRs
A30044	ROY-BYRNE P.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK OLANZAPINE (7/15/98-8/26/98)
A30058	MANSCHRECK T.	TREATMENT DEVIATION	NON-COMPLIANCE	SUBJECT OPENED CAPSULE AND SAW ENCLOSED MEDICINE
A30060	CSERNANSKY J.	TREATMENT DEVIATION	NON-COMPLIANCE	FINAL ASSESSMENT NOT PERFORMED
A30065	LOGUE E.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK ANTIPSYCHOTICS (PRIOR-11/3/97)
A30073	PLOPPER M.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK SEROQUEL 3/13/98-ONGOING, TOOK STUDY MEDS UNTIL 3/15/98
A30079	PLOPPER M.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	PAXIL 5/27/98-6/3/98 FOR DEPRESSION - NO HAM-D
A30084	KOPELOWICZ A.	INSUFFICIENT DATA	NO EFFICACY DATA	NO VISITS COMPLETED
A30098	PAHL J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK HYDROXYZINE (4/3/98-4/17/98)
A30100	PAHL J.	TREATMENT DEVIATION	NON-COMPLIANCE	FINAL SAFETY EXAM NOT PERFORMED
A30103	PAHL J.	INTERCURRENT THERAPY TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE	TOOK METHYLENEDIOXYAMPHETAMINE (3/25/98) PT. EXTREMELY NON-COMPLIANT
A30125	VAN KAMMEN D.	SELECTION CRITERIA NOT MET	SELECTION CRITERIA NOS NOT MET	EXCLUSION CRITERIA #4 NOT MET

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dvlist

JNJPRD--TRIAL RIS-USA-113

Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: RISPERIDONE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30125	VAN KAMMEN D.	TREATMENT DEVIATION	NON-COMPLIANCE	ENVELOPE OPENED BY PRINCIPLE INVESTIGATOR-IRI NOTIFIED
A30126	GURKLIS J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	FLUVOXAMINE 6/27/98 - 7/16/98 FOR DEPRESSION - NO HAM-D
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	PAROXETINE 5/27/98 - 6/26/98 FOR DEPRESSION - NO HAM-D
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
A30129	MENDELOWITZ A.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	WELLBUTIN (10/17/98 - ONGOING) FOR DEPRESSION - NO HAM-D
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	ZOLOFT (2/5/98 - 10/7/98) FOR DEPRESSION - NO HAM-D
A30130	MENDELOWITZ A.	TREATMENT DEVIATION	NON-COMPLIANCE	TOOK MORE THAN 4 TABS
A30131	MENDELOWITZ A.	INSUFFICIENT DATA	NO EFFICACY DATA	NO VISITS DONE
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
A30132	MENDELOWITZ A.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	COGENTIN 5/28/98-6/8/98 FOR EPS - NO ESRS
		INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
		TREATMENT DEVIATION	WRONG DOSE	SUBJECT TOOK GREATER THAN 4 CAPS/DAY
A30153	BRENNER R.	SELECTION CRITERIA NOT MET	SELECTION CRITERIA NOS NOT MET	EXCLUSION CRITERIA #4 NOT MET
A30161	CARMAN J.	TREATMENT DEVIATION	NON-COMPLIANCE	SUBJECT NON-COMPLIANT
A30170	CSERNANSKY J.	TREATMENT DEVIATION	NON-COMPLIANCE	DUE TO 4 DAY GAP IN TREATMENT
A30173	CSERNANSKY J.	TREATMENT DEVIATION	NON-COMPLIANCE	SUBJECT WANTED TO KNOW CONTENTS OF CAPSULES
A30178	BROWN D.	TREATMENT DEVIATION	NON-COMPLIANCE	SUBJECT NON-COMPLIANT
A30179	BROWN D.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

JNJPRD--TRIAL RIS-USA-113

Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: RISPERIDONE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30196	MIHTAR H.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK OLANZAPINE (7/14/98-ONGOING)
A30222	PAHL J.	TREATMENT DEVIATION	NON-COMPLIANCE	EXTRA DOSES TAKEN
A30224	PAHL J.	TREATMENT DEVIATION	NON-COMPLIANCE	FINAL VISIT NOT DONE
A30226	BAKER R.	INTERCURRENT THERAPY INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	COGENTIN 4/4/98-6/6/98 FOR EPS - NO ESRS TOOK LORAZEPAM >5 DAYS TOOK OLANZAPINE (7/23/98-ONGOING)
A30235	FEIFEL D.	INSUFFICIENT DATA	NO EFFICACY DATA	LOST TO FOLLOW-UP - NO VISITS DONE
A30236	FEIFEL D.	INSUFFICIENT DATA INTERCURRENT THERAPY	NO EFFICACY DATA INTERCURRENT FORBIDDEN THERAPY	PATIENT WITHDREW CONSENT - NO VISITS DONE TOOK MARIJUANA (2/3/98-ONGOING)
A30248	LAURIELLO J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENADRYL 8/8/98-8/11/98 FOR WASP STING - NO ESRS
A30249	HOWANITZ E.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
A30275	KNESEVICH M.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LOXAPINE SUCCINATE (8/5/98-ONGOING)
A30283	PANDURANGI A.	INTERCURRENT THERAPY TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE	TOOK RISPERIDONE (6/2/98) BLIND OPENED BY MISTAKE
A30289	BERMAN I.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	CLONAZEPAM PRE-TRIAL - ONGOING FOR ANXIETY
A30297	LAURIELLO J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	ARTANE (10/17/98-11/16/98) FOR STIFFNESS - NO ESRS
A30327	SWANN A.	INSUFFICIENT DATA	NO EFFICACY DATA	PATIENT LOST TO FOLLOW-UP - NO VISITS DONE
A30333	MANSCHRECK T.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	BENADRYL 4/8/98-6/9/98 FOR INSOMNIA - NO ESRS TOOK RISPERIDONE (6/9/98-ONGOING)
A30335	MANSCHRECK T.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	WELLBUTIN (6/1/98 - ONGOING) FOR DEPRESSION - NO HAM-D

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dvlist

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Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: RISPERIDONE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30371	LAURIELLO J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	LORAZEPAM FOR INSOMNIA
A30375	LOGUE E.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK CHLORPROMAZINE HYDROCHLORIDE
A30378	LOGUE E.	SELECTION CRITERIA NOT MET	SELECTION CRITERIA NOS NOT MET	EXCLUSION CRITERIA #4 NOT MET
A30395	NAKRA R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK RISPERIDONE (8/24/98-8/25/98)

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

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Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: OLANZAPINE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30001	MELTZER H.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	TOOK HYDROXYZINE (PRIOR-1/12/98) TOOK VALPROATE SEMISODIUM (PRIOR-12/26/97)
A30003	MELTZER H.	TREATMENT DEVIATION	NON-COMPLIANCE	SUBJECT W/D - NON-COMPLIANCE
A30006	MELTZER H.	INSUFFICIENT DATA INTERCURRENT THERAPY INTERCURRENT THERAPY INTERCURRENT THERAPY	NO EFFICACY DATA INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	NO VISITS DONE PROPRANOLOL FOR TREMOR, NO ESRS DONE, MED WAS ADMIN PRE-TRIAL TOOK LITHIUM CARBONATE (PRIOR-12/16/97) TOOK PROMETHAZINE (PRIOR-1/11/98)
A30008	MELTZER H.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	OXAZEPAM (12/18/98-ONG) FOR AGITATION
A30010	DANIEL D.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK RISPERIDONE (5/8/98-ONGOING)
A30011	DANIEL D.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	OVERDOSE OF STUDY MEDICATION - 20 CAPS TOOK RISPERIDONE (5/22/98-ONGOING)
A30031	CHENGAPPA R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENADRYL 7/4/98 FOR INSECT BITE R CHEEK - NO ESRS
A30033	MCEVOY J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	PROZAC 4/28/98-5/28/98 FOR DEPRESSION - NO HAM-D
A30034	MCEVOY J.	TREATMENT DEVIATION	NON-COMPLIANCE	SITE CANNOT DETERMINE IF PATIENT TOOK STUDY MED CONSISTENTLY
A30036	MCEVOY J.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	LIBRIUM 7/7/98 - 8/10/98 TOOK LORAZEPAM >5 DAYS
A30067	LOGUE E.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	AMBIEN PRE-TRIAL - ONGOING FOR INSOMNIA
A30070	LOGUE E.	INTERCURRENT THERAPY SELECTION CRITERIA NOT MET TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY SELECTION CRITERIA NOS NOT MET NON-COMPLIANCE	TOOK RISPERIDONE (9/23/98-ONGOING) EXCLUSION CRITERIA #4 NOT MET PATIENT NON-COMPLIANT WITH STUDY MED
A30074	PLOPPER M.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	COGENTIN (3/20/98-12/23/98) FOR EPS - NO ESRS PROZAC (4/8/98-ONG) FOR DEPRESSION - NO HAM-D

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

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Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: OLANZAPINE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30101	PAHL J.	INTERCURRENT THERAPY TREATMENT DEVIATION TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE WRONG DOSE	BENADRYL (PRE-TRIAL - ONGOING) FOR INSOMNIA TOOK MORE THAN 4 TABS SUBJECT TOOK GREATER THAN 4 CAPS/DAY
A30118	WIRSHING D.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TEMAZEPAM (PRIOR-ONG) FOR INSOMNIA
A30121	GURKLIS J.	TREATMENT DEVIATION	NON-COMPLIANCE	NON-COMPLIANT 4/22/98 - 4/26/98
A30149	COHN C.	INSUFFICIENT DATA	NO EFFICACY DATA	NO VISITS DONE
A30155	BRENNER R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK RISPERIDONE (1/26/99-ONGOING)
A30157	BRENNER R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENADRYL 2/21/98-2/27/98 - NO ESRS
A30169	CSERNANSKY J.	TREATMENT DEVIATION	NON-COMPLIANCE	DR. POSENER REQUESTED VIA URSULA AFTER-CARE TREATMENT
A30223	PAHL J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
A30227	BAKER R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENADRYL 4/30/98-5/6/98 FOR COLD - NO ESRS
A30228	BAKER R.	INTERCURRENT THERAPY TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE	TOOK ANTIPSYCHOTICS (5/4/98-ONGOING) CAPS RANDOMLY TAKEN
A30237	FEIFEL D.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	PAROXETINE 6/10/98-10/28/98 FOR DEPRESSION - NO HAM-D
A30238	FEIFEL D.	INSUFFICIENT DATA	NO EFFICACY DATA	PATIENT WITHDREW CONSENT - NO VISITS DONE
A30242	LAURIELLO J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	TOOK LORAZEPAM >5 DAYS
A30243	LAURIELLO J.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	RESTORIL (3/12/98 - 3/12/98) FOR PANIC ATTACK
A30247	LAURIELLO J.	TREATMENT DEVIATION	NON-COMPLIANCE	PT. TOOK STUDY MEDS INTERMITTENTLY
A30268	KANOF P.	TREATMENT DEVIATION	NON-COMPLIANCE	DID NOT COMPLY WITH DOSING

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

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Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: OLANZAPINE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30272	KANOF P.	INTERCURRENT THERAPY INTERCURRENT THERAPY SELECTION CRITERIA NOT MET	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY ABNORMAL LAB VALUES	PROZAC (3/25/98 - ONGOING) FOR DEPRESSION - NO HAM-D PROZAC 3/25/98-4/1/98 FOR DEPRESSION - NO HAM-D TRIGLYCERIDES 842 INCREASED
A30276	KNESEVICH M.	INSUFFICIENT DATA	NO EFFICACY DATA	ONLY LABS/VITALS DONE
A30281	PANDURANGI A.	INTERCURRENT THERAPY INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	BENZTROPINE 11/29/98-12/7/98 FOR STIFF GAIT - NO ESRS TEMAZEPAM (11/28/98-11/30/98) FOR INSOMNIA TOOK LORAZEPAM >5 DAYS
A30282	PANDURANGI A.	INTERCURRENT THERAPY INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	CLONAZEPAM (PRIOR-4/16/98) FOR PSYCHOSIS TEMAZEPAM 6/16/98-11/6/98) FOR SLEEPLESSNESS VALIUM (5/21/98-6/1/98) FOR ANXIETY
A30284	PANDURANGI A.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	RESTORIL (11/20/98-12/18/98) FOR INSOMNIA
A30317	REDDY N.	TREATMENT DEVIATION	NON-COMPLIANCE	NON-COMPLIANT
A30338	MILLER A.	INTERCURRENT THERAPY INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY	PAXIL 1/23/98-3/20/98 FOR DEPRESSION - NO HAM-D TOOK PAXIL FROM 1/23/98-3/20/98-ONGOING, HAM-D DONE ON 5/1/98
A30352	DEPRIEST M.	SELECTION CRITERIA NOT MET	ABNORMAL LAB VALUES	CREATININE PHOSPHOKINASE 21200 INCREASED
A30376	LOGUE E.	SELECTION CRITERIA NOT MET	ABNORMAL LAB VALUES	TRIGLYCERIDES 873 INCREASED
A30380	MILLER A.	INTERCURRENT THERAPY TREATMENT DEVIATION	INTERCURRENT FORBIDDEN THERAPY NON-COMPLIANCE	TOOK LORAZEPAM >5 DAYS SUBJECT NON-COMPLIANT PT MISSED DOSES
A30393	NAKRA R.	INTERCURRENT THERAPY INTERCURRENT THERAPY SELECTION CRITERIA NOT MET	INTERCURRENT FORBIDDEN THERAPY INTERCURRENT FORBIDDEN THERAPY ABNORMAL LAB VALUES	AMITRIPTYLINE (8/6/98 - 9/17/98) FOR INSOMNIA TOOK AMITRIPTYLINE (8/6/98-9/17/98) TRIGLYCERIDES 852 INCREASED
A30396	NAKRA R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	ZOLOFT (8/11/98 - ONGOING) FOR DEPRESSION - NO HAM-D

Attachment 1.11: Protocol Deviations - Listing

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System Used: Arrow5.1/dv1st

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Listing LSUB01: Protocol Deviations (continued)

RANDOMISATION GROUP: OLANZAPINE

CRF ID.	MAIN INVEST.	DEVIATION	DEVIATION	DEVIATION (SPECIF.)
A30396	NAKRA R.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	ZOLOFT 8/11/98-9/17/98 FOR DEPRESSION - NO HAM-D
A30397	NAKRA R.	TREATMENT DEVIATION	NON-COMPLIANCE	PATIENT ADMITTED TO MISSING DOSES AND THROWING AWAY TABLETS
A30399	KNESEVICH M.	INTERCURRENT THERAPY	INTERCURRENT FORBIDDEN THERAPY	BENZTROPINE (8/19/98-9/16/98) FOR HYPERSALIVATION - NO ESRs

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE							
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	Overall P-value(a)	investpl P-value(a)	base P-value(a)
TOTAL PANSS (NON-IMPUTED)													
TREATMENT													
BASELINE	106	81.6	11.80			120	80.4	13.07			0.218	<0.001	
WEEK 8/STUDY ENTRY	103	63.4	15.34	-17.9	16.41	116	63.8	14.33	-16.7	16.73	0.133	<0.001	<0.001
WEEK 12/WEEK 4	97	62.3	15.08	-18.5	15.21	117	61.4	14.54	-18.5	16.80	0.773	0.047	<0.001
WEEK 16/WEEK 8	94	63.8	17.29	-16.6	17.25	109	59.3	12.31	-20.8	15.73	0.166	0.008	<0.001
WEEK 20/WEEK 12	87	64.7	19.35	-15.9	18.19	104	58.0	12.57	-22.2	16.50	0.082	0.001	<0.001
WEEK 28/WEEK 20	69	60.7	14.08	-20.6	13.46	82	58.8	13.24	-21.5	15.26	0.775	0.108	<0.001
WEEK 36/WEEK 28	72	61.4	14.33	-19.6	14.92	79	58.0	13.09	-20.7	17.33	0.509	0.532	<0.001
WEEK 52/WEEK 44	53	61.1	14.70	-20.3	13.57	67	56.3	13.31	-22.0	17.95	0.688	0.108	<0.001
END POINT	106	65.6	19.46	-16.0	19.55	120	61.2	16.99	-19.3	18.47	0.229	0.026	<0.001
POSITIVE SYMPTOMS (NON-IMPUTED)													
TREATMENT													
BASELINE	106	24.2	5.55			120	23.4	5.89			0.101	0.135	
WEEK 8/STUDY ENTRY	104	17.9	6.26	-6.3	6.33	116	18.2	6.18	-5.2	6.31	0.109	0.010	<0.001
WEEK 12/WEEK 4	98	17.7	5.63	-6.4	5.72	117	17.5	6.12	-5.8	6.07	0.340	0.018	<0.001
WEEK 16/WEEK 8	94	18.3	6.18	-5.6	6.37	110	16.8	5.28	-6.3	5.78	0.314	0.127	<0.001
WEEK 20/WEEK 12	87	18.6	6.95	-5.3	6.78	104	16.3	5.47	-6.6	5.97	0.169	0.064	<0.001
WEEK 28/WEEK 20	69	16.9	5.11	-7.4	5.58	82	16.5	6.18	-6.2	5.82	0.188	0.028	<0.001
WEEK 36/WEEK 28	72	17.4	5.64	-6.6	5.48	79	16.3	5.49	-6.3	6.53	0.867	0.470	<0.001
WEEK 52/WEEK 44	53	16.7	5.01	-7.0	5.06	67	15.5	5.39	-6.8	6.08	0.895	0.253	<0.001
END POINT	106	18.3	7.28	-5.9	7.33	120	17.5	6.51	-5.9	6.58	0.828	0.024	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)
TOTAL PANSS (NON-IMPUTED)		
TREATMENT		
BASELINE	-2.0	(-5.12; 1.17)
WEEK 8/STUDY ENTRY	2.8	(-0.86; 6.48)
WEEK 12/WEEK 4	0.6	(-3.27; 4.39)
WEEK 16/WEEK 8	-2.8	(-6.67; 1.15)
WEEK 20/WEEK 12	-3.8	(-8.13; 0.49)
WEEK 28/WEEK 20	0.6	(-3.58; 4.80)
WEEK 36/WEEK 28	-1.6	(-6.19; 3.09)
WEEK 52/WEEK 44	-1.0	(-6.20; 4.11)
END POINT	-2.8	(-7.37; 1.78)
POSITIVE SYMPTOMS (NON-IMPUTED)		
TREATMENT		
BASELINE	-1.3	(-2.78; 0.25)
WEEK 8/STUDY ENTRY	1.2	(-0.27; 2.67)
WEEK 12/WEEK 4	0.7	(-0.72; 2.07)
WEEK 16/WEEK 8	-0.7	(-2.21; 0.72)
WEEK 20/WEEK 12	-1.1	(-2.79; 0.49)
WEEK 28/WEEK 20	1.1	(-0.54; 2.70)
WEEK 36/WEEK 28	-0.1	(-1.89; 1.59)
WEEK 52/WEEK 44	-0.1	(-1.92; 1.68)
END POINT	-0.2	(-1.83; 1.47)

See footnotes on the first page of the table.

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

See footnotes on the first page of the table.

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)

NEGATIVE SYMPTOMS (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.3	(-1.97; 1.43)
WEEK 8/STUDY ENTRY	1.0	(-0.32; 2.34)
WEEK 12/WEEK 4	0.6	(-0.81; 1.93)
WEEK 16/WEEK 8	-0.4	(-1.89; 1.00)
WEEK 20/WEEK 12	-0.6	(-2.08; 0.86)
WEEK 28/WEEK 20	-0.2	(-1.84; 1.41)
WEEK 36/WEEK 28	0.1	(-1.70; 1.85)
WEEK 52/WEEK 44	-0.0	(-1.81; 1.80)
END POINT	-0.7	(-2.19; 0.73)
DISORGANIZED THOUGHTS (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.8	(-2.17; 0.47)
WEEK 8/STUDY ENTRY	-0.3	(-1.32; 0.66)
WEEK 12/WEEK 4	-0.8	(-1.80; 0.28)
WEEK 16/WEEK 8	-1.4	(-2.56; -0.30)
WEEK 20/WEEK 12	-1.1	(-2.24; -0.03)
WEEK 28/WEEK 20	-0.7	(-1.83; 0.43)
WEEK 36/WEEK 28	-0.7	(-1.93; 0.51)
WEEK 52/WEEK 44	-1.1	(-2.55; 0.35)
END POINT	-1.4	(-2.65; -0.15)

See footnotes on the first page of the table.

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE							
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	Overall P-value(a)	investpl P-value(a)	base P-value(a)
ANXIETY/DEPRESSION (NON-IMPUTED)													
TREATMENT													
BASELINE	106	10.3	3.36			120	10.7	3.35			0.372	0.005	
WEEK 8/STUDY ENTRY	104	7.7	3.11	-2.6	3.40	116	8.3	3.28	-2.4	3.34	0.066	0.004	<0.001
WEEK 12/WEEK 4	98	7.7	3.23	-2.4	3.34	118	7.8	3.01	-2.8	3.36	0.992	0.539	<0.001
WEEK 16/WEEK 8	94	7.5	3.11	-2.6	3.33	110	7.3	2.45	-3.4	3.43	0.582	0.079	<0.001
WEEK 20/WEEK 12	87	7.7	3.47	-2.3	3.91	105	7.3	2.36	-3.3	3.63	0.464	0.038	<0.001
WEEK 28/WEEK 20	69	7.2	3.19	-2.7	3.59	82	7.2	2.82	-3.0	3.53	0.673	0.093	<0.001
WEEK 36/WEEK 28	72	7.5	3.53	-2.4	3.67	79	7.1	2.41	-3.1	3.49	0.397	0.817	<0.001
WEEK 52/WEEK 44	54	7.5	3.21	-2.5	3.46	67	7.0	2.66	-3.1	3.80	0.718	0.351	<0.001
END POINT	106	8.4	3.59	-1.9	3.98	120	7.9	3.38	-2.8	3.94	0.199	0.021	<0.001
UNCONTROLLED HOSTILITY/EXCITEMENT (NON-IMP)													
TREATMENT													
BASELINE	106	7.2	2.95			120	7.4	2.63			0.959	0.025	
WEEK 8/STUDY ENTRY	104	5.4	1.76	-1.8	2.71	116	5.6	2.18	-1.8	2.63	0.345	0.778	<0.001
WEEK 12/WEEK 4	98	5.4	1.69	-1.8	2.78	117	5.7	2.29	-1.7	2.85	0.235	0.225	<0.001
WEEK 16/WEEK 8	94	5.5	1.81	-1.6	2.86	110	5.5	2.01	-1.9	2.77	0.579	0.039	<0.001
WEEK 20/WEEK 12	87	6.0	2.80	-1.2	2.94	105	5.3	1.74	-2.0	2.61	0.171	0.047	<0.001
WEEK 28/WEEK 20	69	5.4	1.97	-1.9	2.41	82	5.4	1.51	-1.9	2.57	0.754	0.473	<0.001
WEEK 36/WEEK 28	72	5.4	2.13	-1.9	2.86	79	5.2	1.75	-1.9	2.36	0.784	0.895	<0.001
WEEK 52/WEEK 44	54	5.4	2.14	-2.2	2.94	67	5.1	1.89	-1.8	2.81	0.895	0.354	<0.001
END POINT	106	5.9	2.84	-1.3	3.17	120	5.9	2.52	-1.5	3.32	0.969	0.119	<0.001

See footnotes on the first page of the table.

Attachment 2.1: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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28AUG2008 17:45
System Used: Arrow5.1(U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS01: Positive and Negative Syndrome Scale - Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)
ANXIETY/DEPRESSION (NON-IMPUTED)		
TREATMENT		
BASELINE	0.4	(-0.47; 1.25)
WEEK 8/STUDY ENTRY	0.7	(-0.05; 1.43)
WEEK 12/WEEK 4	0.0	(-0.77; 0.78)
WEEK 16/WEEK 8	-0.2	(-0.92; 0.52)
WEEK 20/WEEK 12	-0.3	(-1.12; 0.51)
WEEK 28/WEEK 20	0.2	(-0.73; 1.13)
WEEK 36/WEEK 28	-0.4	(-1.41; 0.56)
WEEK 52/WEEK 44	-0.2	(-1.27; 0.88)
END POINT	-0.6	(-1.42; 0.30)
UNCONTROLLED HOSTILITY/EXCITEMENT (NON-IMP)		
TREATMENT		
BASELINE	0.0	(-0.71; 0.74)
WEEK 8/STUDY ENTRY	0.2	(-0.26; 0.75)
WEEK 12/WEEK 4	0.3	(-0.21; 0.84)
WEEK 16/WEEK 8	0.1	(-0.36; 0.65)
WEEK 20/WEEK 12	-0.4	(-1.02; 0.18)
WEEK 28/WEEK 20	0.1	(-0.45; 0.62)
WEEK 36/WEEK 28	-0.1	(-0.72; 0.55)
WEEK 52/WEEK 44	0.1	(-0.70; 0.80)
END POINT	0.0	(-0.66; 0.69)

See footnotes on the first page of the table.

Attachment 2.2: Percent of Subjects with $\geq 20\%$ Improvement in Total PANSS - Crossover Subjects Excluded

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28AUG2008 17:45
System Used: Arrow5.1(U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS02: Percent of Subjects with $\geq 20\%$ Improvement in Total PANSS - Crossover Subjects ExcludedAnalysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	- RISPERIDONE -		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
20% CLINICAL IMPROVEMENT						
~~						
TREATMENT						
WEEK 8/STUDY ENTRY						
NO	26	25.2	35	30.2		
YES	77	74.8	81	69.8		
Total	103		116		(-0.07; 0.17)	0.124
WEEK 12/WEEK 4						
NO	29	29.9	32	27.4		
YES	68	70.1	85	72.6		
Total	97		117		(-0.15; 0.10)	0.892
WEEK 16/WEEK 8						
NO	24	25.5	21	19.3		
YES	70	74.5	88	80.7		
Total	94		109		(-0.18; 0.05)	0.635
WEEK 20/WEEK 12						
NO	24	27.6	22	21.2		
YES	63	72.4	82	78.8		
Total	87		104		(-0.19; 0.06)	0.735

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp1.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having higher scores; RR: p-value ≤ 0.05 .
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having higher scores; OO: p-value ≤ 0.05 .

Attachment 2.2: Percent of Subjects with $\geq 20\%$ Improvement in Total PANSS - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/parun

JNJPRD--TRIAL RIS-USA-113

Table EFF.PANSS02: Percent of Subjects with $\geq 20\%$ Improvement in Total PANSS - Crossover Subjects Excluded (continued)Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	- RISPERIDONE -		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
20% CLINICAL IMPROVEMENT						
TREATMENT						
WEEK 28/WEEK 20						
NO	13	18.8	18	22.0		
YES	56	81.2	64	78.0		
Total	69		82		(-0.10; 0.16)	0.237
WEEK 36/WEEK 28						
NO	20	27.8	14	17.7		
YES	52	72.2	65	82.3		
Total	72		79		(-0.23; 0.03)	0.235
WEEK 52/WEEK 44						
NO	13	24.5	14	20.9		
YES	40	75.5	53	79.1		
Total	53		67		(-0.19; 0.11)	0.912
END POINT						
NO	33	31.1	33	27.5		
YES	73	68.9	87	72.5		
Total	106		120		(-0.16; 0.08)	0.656

See footnotes on the first page of the table.

Attachment 2.3: Clinical Global Impression - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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29AUG2003 17:00
System Used: Arrow5.1(U)/cgirun

JNJPRD--TRIAL RIS-USA-113

Table EFF.CGI01: Clinical Global Impression - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE		N	Mean	SD	CHANGE FROM TREATMENT BASE				
				Mean	SD				Mean	SD			
CLINICAL GLOBAL IMPRESSION													
TREATMENT													
BASLINE	109	4.3	0.90			124	4.1	0.91			0.036	<0.001	
WEEK 8/STUDY ENTRY	107	3.5	1.00	-0.9	0.89	121	3.4	0.99	-0.8	0.84	0.793	<0.001	<0.001
WEEK 12/WEEK 4	101	3.4	0.96	-0.9	0.90	120	3.2	1.00	-0.9	1.03	0.577	0.002	<0.001
WEEK 16/WEEK 8	97	3.5	0.96	-0.7	0.93	113	3.2	0.89	-0.9	0.96	0.049	<0.001	<0.001
WEEK 20/WEEK 12	89	3.5	1.02	-0.7	0.93	107	3.2	0.88	-1.0	0.95	0.026	0.008	<0.001
WEEK 36/WEEK 28	74	3.4	0.93	-0.8	0.88	81	3.2	0.81	-0.9	0.94	0.334	0.015	<0.001
WEEK 52/WEEK 44	56	3.3	0.91	-0.8	0.88	67	3.2	0.81	-0.9	0.98	0.407	0.140	<0.001
END POINT	109	3.6	1.02	-0.8	0.99	124	3.3	0.91	-0.8	0.96	0.135	0.004	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.3: Clinical Global Impression - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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29AUG2008 17:00
System Used: Arrow5.1(U)/cgirun

JNJPRD--TRIAL RIS-USA-113

Table EFF.CGI01: Clinical Global Impression - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus ----- RISPERIDONE -----	
	L.S.Mean	95% CI(a)

CLINICAL GLOBAL IMPRESSION		

TREATMENT		
BASELINE	-0.2	(-0.46; -0.02)
WEEK 8/STUDY ENTRY	0.0	(-0.18; 0.23)
WEEK 12/WEEK 4	-0.1	(-0.29; 0.16)
WEEK 16/WEEK 8	-0.2	(-0.44; -0.00)
WEEK 20/WEEK 12	-0.3	(-0.50; -0.03)
WEEK 36/WEEK 28	-0.1	(-0.37; 0.13)
WEEK 52/WEEK 44	-0.1	(-0.42; 0.17)
END POINT	-0.2	(-0.39; 0.05)

See footnotes on the first page of the table.

Attachment 2.4: Clinical Global Impression Change - Crossover Subjects Excluded

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29AUG2008 17:00
System Used: Arrow5.1(U)/cgirun

JNJPRD--TRIAL RIS-USA-113

Table EFF.CG102: Clinical Global Impression Change - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

-- RISPERIDONE --				--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE --- P-value (a)
n	%	Cum.%		n	%	Cum.%	
CLINICAL GLOBAL IMPRESSION CHANGE							
~~							
TREATMENT							
WEEK 8/STUDY ENTRY							
VERY MUCH IMPROVED	9	8.3	8.3	6	6.6	6.6	
MUCH IMPROVED	42	38.5	46.8	43	35.5	42.1	
MINIMALLY IMPROVED	37	33.9	80.7	47	38.8	81.0	
UNCHANGED	19	17.4	98.2	17	14.0	95.0	
MINIMALLY WORSE	2	1.8	100.0	6	5.0	100.0	
MUCH WORSE	0	0.0	100.0	0	0.0	100.0	
-----				-----			
Total	109			121			0.259
WEEK 12/WEEK 4							
VERY MUCH IMPROVED	10	9.8	9.8	13	10.8	10.8	
MUCH IMPROVED	41	40.2	50.0	48	40.0	50.8	
MINIMALLY IMPROVED	24	23.5	73.5	37	30.8	81.7	
UNCHANGED	19	18.6	92.2	17	14.2	95.8	
MINIMALLY WORSE	7	6.9	99.0	4	3.3	99.2	
MUCH WORSE	1	1.0	100.0	1	0.8	100.0	
-----				-----			
Total	102			120			0.520

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investpl.
 R: two-sided p-value <= 0.10 with RISPERIDONE having lower scores; RR: p-value <= 0.05.
 O: two-sided p-value <= 0.10 with OLANZAPINE having lower scores; OO: p-value <= 0.05.

Attachment 2.4: Clinical Global Impression Change - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /cgirun

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Table EFF.CGI02: Clinical Global Impression Change - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

-- RISPERIDONE --				--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE --- P-value(a)
n	%	Cum.%		n	%	Cum.%	
CLINICAL GLOBAL IMPRESSION CHANGE							
~~							
TREATMENT							
WEEK 16/WEEK 8							
VERY MUCH IMPROVED	9	9.2	9.2	10	8.8	8.8	
MUCH IMPROVED	35	35.7	44.9	52	46.0	54.9	
MINIMALLY IMPROVED	28	28.6	73.5	26	23.0	77.9	
UNCHANGED	14	14.3	87.8	19	16.8	94.7	
MINIMALLY WORSE	8	8.2	95.9	5	4.4	99.1	
MUCH WORSE	4	4.1	100.0	1	0.9	100.0	
-----				-----			
Total	98			113			0.327
WEEK 20/WEEK 12							
VERY MUCH IMPROVED	8	8.9	8.9	16	15.1	15.1	
MUCH IMPROVED	31	34.4	43.3	47	44.3	59.4	
MINIMALLY IMPROVED	29	32.2	75.6	25	23.6	83.0	
UNCHANGED	11	12.2	87.8	14	13.2	96.2	
MINIMALLY WORSE	6	6.7	94.4	4	3.8	100.0	
MUCH WORSE	5	5.6	100.0	0	0.0	100.0	
-----				-----			
Total	90			106			0.027 00
WEEK 36/WEEK 28							
VERY MUCH IMPROVED	5	6.8	6.8	9	11.1	11.1	
MUCH IMPROVED	29	39.2	45.9	37	45.7	56.8	
MINIMALLY IMPROVED	17	23.0	68.9	16	19.8	76.5	
UNCHANGED	14	18.9	87.8	13	16.0	92.6	
MINIMALLY WORSE	7	9.5	97.3	5	6.2	98.8	
MUCH WORSE	2	2.7	100.0	1	1.2	100.0	
-----				-----			
Total	74			81			0.142

See footnotes on the first page of the table.

Attachment 2.4: Clinical Global Impression Change - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/cgirun

JNJPRD--TRIAL RIS-USA-113

Table EFF.CGI02: Clinical Global Impression Change - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

							Pairwise Comparison	
							OLANZAPINE	
							Minus	
-- RISPERIDONE --							RISPERIDONE	
n % Cum.%							P-value (a)	
-----							-----	
CLINICAL GLOBAL IMPRESSION CHANGE								

TREATMENT								
WEEK 52/WEEK 44								
VERY MUCH IMPROVED	6	10.7	10.7	10	14.9	14.9		
MUCH IMPROVED	18	32.1	42.9	23	34.3	49.3		
MINIMALLY IMPROVED	20	35.7	78.6	22	32.8	82.1		
UNCHANGED	7	12.5	91.1	10	14.9	97.0		
MINIMALLY WORSE	3	5.4	96.4	2	3.0	100.0		
MUCH WORSE	2	3.6	100.0	0	0.0	100.0		

Total	56			67			0.151	
END POINT								
VERY MUCH IMPROVED	11	9.9	9.9	12	9.7	9.7		
MUCH IMPROVED	38	34.2	44.1	44	35.5	45.2		
MINIMALLY IMPROVED	30	27.0	71.2	38	30.6	75.8		
UNCHANGED	9	8.1	79.3	19	15.3	91.1		
MINIMALLY WORSE	13	11.7	91.0	8	6.5	97.6		
MUCH WORSE	10	9.0	100.0	3	2.4	100.0		

Total	111			124			0.174	

See footnotes on the first page of the table.

Attachment 2.5: Hamilton Depression Scale - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 1 of 2

29AUG2008 17:02
System Used: Arrow5.1(U)/hamdrun

JNJPRD--TRIAL RIS-USA-113

Table EFF.HAMD01: Hamilton Depression Scale - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
TOTAL HAM-D (NON-IMPUTED)													
TREATMENT													
BASELINE	110	12.3	7.80			121	13.0	7.85			0.770	<0.001	
WEEK 8/STUDY ENTRY	107	7.1	5.84	-5.2	6.84	117	8.2	6.18	-4.8	6.24	0.103	0.047	<0.001
WEEK 52/WEEK 44	56	7.5	5.89	-4.1	6.67	67	6.7	5.17	-5.7	6.16	0.396	0.120	<0.001
END POINT	110	9.0	7.46	-3.3	8.56	121	8.2	6.51	-4.9	7.96	0.256	0.421	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.5: Hamilton Depression Scale - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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29AUG2008 17:02
System Used: Arrow5.1(U)/hamdrun

JNJPRD--TRIAL RIS-USA-113

Table EFF.HAMD01: Hamilton Depression Scale - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus ----- RISPERIDONE -----	
	L.S.Mean	95% CI (a)

TOTAL HAM-D (NON-IMPUTED)		

TREATMENT		
BASELINE	0.3	(-1.57; 2.11)
WEEK 8/STUDY ENTRY	1.1	(-0.22; 2.36)
WEEK 52/WEEK 44	-0.8	(-2.50; 1.00)
END POINT	-1.0	(-2.69; 0.72)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 1 of 14

29AUG2008 17:02
System Used: Arrow5.1 (U) /cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
 Cognitive Assessment Tests: CPT
 Excluding sites 7 and 36

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
D' TOTAL													
TREATMENT													
BASELINE	100	0.6	0.57			115	0.7	0.62			0.586	0.067	
WEEK 8/STUDY ENTRY	97	0.7	0.75	-0.1	0.74	109	0.9	0.79	0.2	0.55	0.024	0.180	<0.001
WEEK 20/WEEK 12	77	0.7	0.97	0.1	0.79	98	0.8	0.74	0.2	0.72	0.224	0.383	0.001
WEEK 36/WEEK 28	61	0.9	0.98	0.3	0.76	72	1.0	0.86	0.3	0.69	0.919	0.678	0.312
WEEK 52/WEEK 44	48	0.8	0.97	0.2	0.80	61	0.7	1.11	0.1	1.20	0.934	0.086	0.002
END POINT	100	0.8	0.88	0.2	0.71	115	0.8	1.00	0.1	1.00	0.938	0.009	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
 Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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29AUG2008 17:02
System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: CPT
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)
D' TOTAL		
TREATMENT		
BASELINE	0.0	(-0.12; 0.21)
WEEK 8/STUDY ENTRY	0.2	(0.03; 0.38)
WEEK 20/WEEK 12	0.1	(-0.09; 0.38)
WEEK 36/WEEK 28	-0.0	(-0.29; 0.27)
WEEK 52/WEEK 44	-0.0	(-0.43; 0.40)
END POINT	0.0	(-0.22; 0.24)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 3 of 14

29AUG2008 17:02
System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: CVLT
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE							
	N	Mean	SD	CHANGE FROM TREATMENT BASE		N	Mean	SD	CHANGE FROM TREATMENT BASE		Overall P-value (a)	investpl P-value (a)	base P-value (a)
				Mean	SD				Mean	SD			
LEARNING TRIAL 1													
TREATMENT													
BASELINE	109	4.6	2.07			120	4.7	2.14			0.940	0.064	
WEEK 8/STUDY ENTRY	106	5.9	2.37	1.3	1.93	114	5.8	2.17	1.1	2.06	0.246	0.392	<0.001
WEEK 20/WEEK 12	87	6.3	2.32	1.7	2.24	102	6.3	2.29	1.5	2.33	0.433	0.491	<0.001
WEEK 36/WEEK 28	66	6.9	2.27	2.5	2.05	76	6.5	2.56	1.9	2.47	0.190	0.578	<0.001
WEEK 52/WEEK 44	55	6.5	2.48	2.1	2.19	65	7.1	2.83	2.4	2.59	0.176	0.120	<0.001
END POINT	109	6.5	2.59	1.9	2.21	120	6.8	2.64	2.1	2.52	0.460	0.398	<0.001
LEARNING TRIALS 1 TO 5													
TREATMENT													
BASELINE	109	34.4	13.13			120	35.5	12.68			0.693	0.055	
WEEK 8/STUDY ENTRY	106	39.2	13.63	4.9	7.83	114	38.8	13.87	2.9	11.71	0.217	0.469	<0.001
WEEK 20/WEEK 12	87	39.1	12.88	5.1	10.26	102	40.4	13.10	5.0	9.92	0.883	0.490	<0.001
WEEK 36/WEEK 28	66	40.6	13.55	7.9	9.57	76	42.3	14.42	7.4	10.77	0.767	0.394	0.006
WEEK 52/WEEK 44	55	40.3	13.08	7.5	9.11	65	43.9	14.17	8.6	13.21	0.121	0.010	<0.001
END POINT	109	39.8	13.78	5.4	9.87	120	42.2	14.59	6.8	12.62	0.310	0.221	<0.001
LONG-DELAY FREE RECALL													
TREATMENT													
BASELINE	109	6.7	3.85			120	7.1	3.32			0.437	0.295	
WEEK 8/STUDY ENTRY	105	7.7	3.72	1.0	2.87	114	7.9	3.54	0.8	3.04	0.705	0.952	<0.001
WEEK 20/WEEK 12	87	8.0	3.62	1.5	2.92	102	8.2	3.61	1.1	2.90	0.692	0.394	<0.001
WEEK 36/WEEK 28	66	8.1	3.84	1.8	3.56	76	9.0	3.79	1.8	3.24	0.542	0.133	<0.001
WEEK 52/WEEK 44	55	8.3	3.48	1.9	2.91	65	9.5	3.71	2.1	3.29	0.304	0.089	<0.001
END POINT	109	8.3	3.73	1.6	3.02	120	8.8	3.96	1.8	3.24	0.793	0.268	<0.001

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: CVLT
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI (a)
LEARNING TRIAL 1		
~~		
TREATMENT		
BASELINE	0.0	(-0.53; 0.57)
WEEK 8/STUDY ENTRY	-0.3	(-0.80; 0.21)
WEEK 20/WEEK 12	-0.2	(-0.86; 0.37)
WEEK 36/WEEK 28	-0.5	(-1.26; 0.25)
WEEK 52/WEEK 44	0.6	(-0.27; 1.48)
END POINT	0.2	(-0.37; 0.82)
LEARNING TRIALS 1 TO 5		
~~		
TREATMENT		
BASELINE	0.7	(-2.69; 4.02)
WEEK 8/STUDY ENTRY	-1.6	(-4.25; 0.97)
WEEK 20/WEEK 12	0.2	(-2.62; 3.04)
WEEK 36/WEEK 28	0.5	(-3.00; 4.06)
WEEK 52/WEEK 44	3.1	(-0.84; 7.07)
END POINT	1.5	(-1.38; 4.32)
LONG-DELAY FREE RECALL		
~~		
TREATMENT		
BASELINE	0.4	(-0.57; 1.32)
WEEK 8/STUDY ENTRY	-0.1	(-0.91; 0.62)
WEEK 20/WEEK 12	-0.2	(-0.99; 0.66)
WEEK 36/WEEK 28	0.3	(-0.77; 1.45)
WEEK 52/WEEK 44	0.6	(-0.54; 1.72)
END POINT	0.1	(-0.68; 0.88)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
 Cognitive Assessment Tests: CVLT
 Excluding sites 7 and 36

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE		N	Mean	SD	CHANGE FROM TREATMENT BASE				
				Mean	SD				Mean	SD			
RECOGNITION DISCRIMINABILITY													

TREATMENT													
BASELINE	108	84.9	12.03			119	84.8	11.60			0.799	0.018	
WEEK 8/STUDY ENTRY	103	84.9	12.26	0.2	10.61	113	85.5	13.19	0.6	11.62	0.765	0.653	<0.001
WEEK 20/WEEK 12	85	85.5	13.93	1.0	11.79	102	86.7	11.51	2.2	11.78	0.606	0.052	<0.001
WEEK 36/WEEK 28	65	84.8	13.23	0.7	12.14	76	88.0	10.63	4.0	10.98	0.059	0.650	<0.001
WEEK 52/WEEK 44	54	85.6	11.69	0.6	10.54	65	90.7	10.05	6.2	10.65	0.001	0.214	<0.001
END POINT	108	86.3	11.61	1.4	9.87	119	88.9	10.74	4.0	11.06	0.082	0.045	<0.001

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Cognitive Assessment Tests: CVLT

Excluding sites 7 and 36

	OLANZAPINE	
	Minus	
	----- RISPERIDONE -----	
	L.S.Mean	95% CI (a)

RECOGNITION DISCRIMINABILITY		

TREATMENT		
BASELINE	0.4	(-2.65; 3.44)
WEEK 8/STUDY ENTRY	0.4	(-2.42; 3.29)
WEEK 20/WEEK 12	0.8	(-2.30; 3.93)
WEEK 36/WEEK 28	3.6	(-0.14; 7.27)
WEEK 52/WEEK 44	5.8	(2.27; 9.29)
END POINT	2.1	(-0.27; 4.46)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: SWMT
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SE			
DIFFERENCE BTWN TOTALS AT 5 AND 15 SEC													
~~													
TREATMENT													
BASELINE	98	1.8	5.02			114	3.4	6.60			0.077	0.020	
WEEK 8/STUDY ENTRY	94	1.5	4.86	-0.4	7.07	109	2.9	5.21	-0.6	7.17	0.112	0.259	<0.001
WEEK 20/WEEK 12	75	1.3	4.44	-0.1	6.95	98	2.1	4.97	-1.2	7.43	0.530	0.951	<0.001
WEEK 36/WEEK 28	60	1.7	4.32	0.3	6.22	72	2.2	6.14	-0.7	8.42	0.693	0.778	<0.001
WEEK 52/WEEK 44	50	0.8	4.43	-1.0	7.22	63	2.2	5.25	-0.4	8.30	0.140	0.750	<0.001
END POINT	98	1.7	5.57	-0.1	6.34	114	2.1	4.63	-1.3	8.12	0.702	0.607	<0.001

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: SWMT
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI (a)
DIFFERENCE BTWN TOTALS AT 5 AND 15 SEC		
TREATMENT		
BASELINE	1.4	(-0.16; 3.00)
WEEK 8/STUDY ENTRY	1.1	(-0.27; 2.55)
WEEK 20/WEEK 12	0.5	(-1.06; 2.05)
WEEK 36/WEEK 28	0.4	(-1.64; 2.46)
WEEK 52/WEEK 44	1.5	(-0.51; 3.55)
END POINT	0.3	(-1.14; 1.69)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
 Cognitive Assessment Tests: TRAIL MAKING TEST A AND B
 Excluding sites 7 and 36

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investpl P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
PART B													
TREATMENT													
BASELINE	107	142.8	79.83			118	132.2	71.92			0.436	0.117	
WEEK 8/STUDY ENTRY	103	134.9	75.68	-5.7	45.53	113	122.3	71.30	-9.5	53.96	0.412	0.159	<0.001
WEEK 20/WEEK 12	85	133.8	77.60	-12.0	66.89	100	116.8	76.71	-12.1	59.69	0.690	0.152	<0.001
WEEK 36/WEEK 28	66	131.2	82.45	-13.3	62.00	73	111.9	76.97	-11.5	64.45	0.707	0.031	<0.001
WEEK 52/WEEK 44	53	118.8	77.50	-25.5	61.95	64	116.5	82.99	-5.5	67.57	0.163	<0.001	<0.001
END POINT	107	127.8	81.48	-15.0	58.08	118	122.3	81.72	-9.9	63.48	0.746	<0.001	<0.001

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: TRAIL MAKING TEST A AND B
Excluding sites 7 and 36

	OLANZAPINE Minus ----- RISPERIDONE -----	
	L.S.Mean	95% CI (a)

PART B		

TREATMENT		
BASELINE	-7.9	(-27.81; 12.04)
WEEK 8/STUDY ENTRY	-5.3	(-17.91; 7.38)
WEEK 20/WEEK 12	-3.5	(-20.91; 13.87)
WEEK 36/WEEK 28	-3.9	(-24.42; 16.62)
WEEK 52/WEEK 44	14.6	(-5.98; 35.10)
END POINT	2.3	(-11.41; 15.91)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: VFE
Excluding sites 7 and 36

	RISPERIDONE						OLANZAPINE								
	N	Mean	SD	CHANGE FROM TREATMENT BASE		N	Mean	SD	CHANGE FROM TREATMENT BASE		Overall P-value (a)	investpl P-value (a)	base P-value (a)		
				Mean	SD				Mean	SD					
CATEGORY FLUENCY - TOTAL SCORE															
TREATMENT															
BASELINE	110	33.4	10.91			122	32.6	10.54			0.686	<0.001			
WEEK 8/STUDY ENTRY	107	32.9	10.48	-0.6	8.71	116	33.8	10.92	1.3	6.67	0.094	0.083	<0.001		
WEEK 20/WEEK 12	89	33.4	11.13	0.5	8.97	104	33.4	10.10	0.1	7.43	0.933	0.371	<0.001		
WEEK 36/WEEK 28	69	33.1	9.92	0.4	8.44	77	33.9	10.87	0.6	7.97	0.659	0.515	<0.001		
WEEK 52/WEEK 44	55	36.6	10.01	3.1	9.95	66	35.6	9.69	2.6	7.87	0.880	0.252	<0.001		
END POINT	110	33.8	10.98	0.4	9.39	122	34.3	10.91	1.7	8.19	0.283	0.258	<0.001		
LETTER FLUENCY - TOTAL SCORE															
TREATMENT															
BASELINE	109	26.5	12.00			121	27.7	12.31			0.400	0.050			
WEEK 8/STUDY ENTRY	106	27.1	11.82	0.7	7.96	115	28.6	12.34	1.0	7.85	0.429	0.100	<0.001		
WEEK 20/WEEK 12	88	25.6	12.27	0.3	9.26	103	29.2	12.69	1.0	8.01	0.164	0.391	<0.001		
WEEK 36/WEEK 28	69	27.2	11.79	2.6	8.43	77	29.9	13.48	1.1	9.12	0.860	0.178	<0.001		
WEEK 52/WEEK 44	54	28.5	11.56	2.9	10.95	66	30.0	11.19	2.0	9.45	0.958	0.160	<0.001		
END POINT	109	27.1	11.11	0.6	9.96	121	29.2	11.34	1.5	8.52	0.080	0.203	<0.001		
SUM OF CATEGORY AND LETTER TOTALS															
TREATMENT															
BASELINE	108	59.8	20.72			121	60.5	20.49			0.656	0.012			
WEEK 8/STUDY ENTRY	105	60.0	19.99	0.3	13.58	115	62.5	21.14	2.3	12.11	0.152	0.138	<0.001		
WEEK 20/WEEK 12	87	58.9	21.29	0.9	15.08	103	62.7	21.26	1.0	13.46	0.505	0.739	<0.001		
WEEK 36/WEEK 28	69	60.3	19.90	3.1	13.91	77	63.8	22.55	1.7	14.98	0.918	0.466	<0.001		
WEEK 52/WEEK 44	54	64.7	18.21	6.0	17.89	66	65.7	19.31	4.6	14.40	0.940	0.174	<0.001		
END POINT	108	60.7	19.44	1.0	16.41	121	63.5	20.68	3.1	13.53	0.114	0.538	<0.001		

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: VFE
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI (a)
CATEGORY FLUENCY - TOTAL SCORE		
TREATMENT		
BASELINE	-0.5	(-3.19; 2.10)
WEEK 8/STUDY ENTRY	1.6	(-0.28; 3.53)
WEEK 20/WEEK 12	-0.1	(-2.29; 2.10)
WEEK 36/WEEK 28	0.6	(-2.05; 3.23)
WEEK 52/WEEK 44	-0.2	(-3.15; 2.70)
END POINT	1.2	(-0.97; 3.29)
LETTER FLUENCY - TOTAL SCORE		
TREATMENT		
BASELINE	1.3	(-1.81; 4.50)
WEEK 8/STUDY ENTRY	0.8	(-1.19; 2.78)
WEEK 20/WEEK 12	1.7	(-0.72; 4.20)
WEEK 36/WEEK 28	-0.3	(-3.19; 2.66)
WEEK 52/WEEK 44	0.1	(-3.34; 3.52)
END POINT	1.9	(-0.23; 4.06)
SUM OF CATEGORY AND LETTER TOTALS		
TREATMENT		
BASELINE	1.2	(-4.09; 6.48)
WEEK 8/STUDY ENTRY	2.4	(-0.83; 5.66)
WEEK 20/WEEK 12	1.4	(-2.73; 5.53)
WEEK 36/WEEK 28	0.3	(-4.65; 5.16)
WEEK 52/WEEK 44	-0.2	(-5.65; 5.23)
END POINT	3.0	(-0.71; 6.65)

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: WCST
Excluding sites 7 and 36

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investp1 P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
CATEGORIES													
TREATMENT													
BASELINE	105	2.8	2.40			119	2.9	2.26			0.687	0.026	
WEEK 8/STUDY ENTRY	101	3.2	2.50	0.4	1.67	112	3.1	2.42	0.1	1.64	0.363	0.041	<0.001
WEEK 20/WEEK 12	81	2.9	2.46	0.2	1.67	101	3.2	2.28	0.2	1.84	0.868	0.041	<0.001
WEEK 36/WEEK 28	65	3.1	2.57	0.4	1.60	73	3.4	2.38	0.3	1.84	0.693	0.282	<0.001
WEEK 52/WEEK 44	54	3.2	2.58	0.4	1.56	65	3.3	2.48	0.2	1.81	0.991	0.246	0.003
END POINT	105	3.2	2.56	0.4	1.56	119	3.3	2.43	0.4	1.94	0.880	0.108	<0.001

See footnotes on the first page of the table.

Attachment 2.6: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/cogrun

JNJPRD--TRIAL RIS-USA-113

Table COG01: Cognitive Assessments - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Cognitive Assessment Tests: WCST
Excluding sites 7 and 36

	OLANZAPINE Minus ----- RISPERIDONE -----	
	L.S.Mean	95% CI(a)

CATEGORIES		

TREATMENT		
BASELINE	0.1	(-0.48; 0.73)
WEEK 8/STUDY ENTRY	-0.2	(-0.62; 0.23)
WEEK 20/WEEK 12	0.0	(-0.45; 0.54)
WEEK 36/WEEK 28	0.1	(-0.48; 0.72)
WEEK 52/WEEK 44	-0.0	(-0.65; 0.64)
END POINT	0.0	(-0.42; 0.48)

See footnotes on the first page of the table.

Attachment 2.7: Visual Analogue Scale (0-100) for Sleep and Drowsiness - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/vasrun

JNJPRD--TRIAL RIS-USA-113

Table VAS01: Visual Analogue Scale (0-100) for Sleep and Drowsiness - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	RISPERIDONE					OLANZAPINE					Overall P-value(a)	investpl P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
QUALITY OF SLEEP													
~~													
TREATMENT													
BASELINE	110	63.3	28.09			124	64.3	29.32			0.821	0.014	
WEEK 8/STUDY ENTRY	106	71.8	24.05	8.0	26.76	120	71.7	27.13	6.9	30.88	0.999	0.830	<0.001
WEEK 12/WEEK 4	102	72.6	25.39	9.5	28.52	120	72.8	27.03	7.4	30.13	0.831	0.600	<0.001
WEEK 16/WEEK 8	97	72.0	26.38	9.6	31.36	112	78.0	21.55	11.9	28.59	0.136	0.362	<0.001
WEEK 20/WEEK 12	88	70.2	27.09	7.6	28.93	106	72.9	26.34	5.9	32.21	0.744	0.867	<0.001
WEEK 36/WEEK 28	74	72.1	26.70	7.8	27.42	81	74.6	23.56	4.7	30.65	0.903	0.198	<0.001
WEEK 52/WEEK 44	55	72.4	27.33	6.9	27.76	67	74.8	27.78	5.3	26.14	0.676	0.211	<0.001
END POINT	110	68.5	29.99	5.3	30.81	124	68.7	28.95	4.4	32.65	0.963	0.545	<0.001
DAYTIME DROWSINESS													
~~													
TREATMENT													
BASELINE	110	37.5	33.39			124	39.1	30.27			0.629	0.977	
WEEK 8/STUDY ENTRY	106	29.2	28.01	-7.8	36.05	120	36.3	28.63	-3.1	34.20	0.060	0.067	<0.001
WEEK 12/WEEK 4	102	25.7	24.62	-11.5	38.97	120	32.0	28.62	-7.0	30.13	0.109	0.313	<0.001
WEEK 16/WEEK 8	97	29.3	26.52	-9.1	37.06	112	32.6	28.97	-7.3	31.00	0.314	0.011	<0.001
WEEK 20/WEEK 12	88	32.4	28.31	-5.3	35.50	106	33.9	29.83	-5.2	32.15	0.921	0.818	<0.001
WEEK 36/WEEK 28	74	27.7	27.94	-11.4	33.94	81	37.6	30.31	-2.0	33.47	0.011	0.518	<0.001
WEEK 52/WEEK 44	55	25.2	26.52	-12.8	34.35	67	31.5	31.20	-6.7	29.24	0.181	0.545	<0.001
END POINT	110	30.5	28.54	-7.0	35.06	124	35.8	30.71	-3.3	33.87	0.095	0.198	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.7: Visual Analogue Scale (0-100) for Sleep and Drowsiness - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/vasrun

JNJPRD--TRIAL RIS-USA-113

Table VAS01: Visual Analogue Scale (0-100) for Sleep and Drowsiness - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded
(continued)Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Excluding sites 7 and 36

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)
QUALITY OF SLEEP		
TREATMENT		
BASELINE	0.8	(-6.46; 8.13)
WEEK 8/STUDY ENTRY	-0.0	(-6.31; 6.30)
WEEK 12/WEEK 4	-0.7	(-7.19; 5.79)
WEEK 16/WEEK 8	4.7	(-1.51; 11.01)
WEEK 20/WEEK 12	1.2	(-6.19; 8.56)
WEEK 36/WEEK 28	-0.5	(-8.21; 7.26)
WEEK 52/WEEK 44	1.9	(-7.08; 10.87)
END POINT	-0.2	(-7.30; 6.96)
DAYTIME DROWSINESS		
TREATMENT		
BASELINE	2.1	(-6.46; 10.66)
WEEK 8/STUDY ENTRY	6.8	(-0.29; 13.83)
WEEK 12/WEEK 4	5.6	(-1.26; 12.48)
WEEK 16/WEEK 8	3.6	(-3.41; 10.58)
WEEK 20/WEEK 12	0.4	(-7.59; 8.40)
WEEK 36/WEEK 28	11.9	(2.80; 20.91)
WEEK 52/WEEK 44	6.9	(-3.27; 17.12)
END POINT	6.1	(-1.07; 13.30)

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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29AUG2008 16:22
System Used: Arrow5.1(U)/bqolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

FROM P21 SECTION A17, B18, C19, D19, E19, F19, G19, H19, I19, J19, K19, L19, M19, N19, O19, P19, Q19, R19, S19, T19, U19, V19, W19, X19, Y19, Z19, AA19, AB19, AC19, AD19, AE19, AF19, AG19, AH19, AI19, AJ19, AK19, AL19, AM19, AN19, AO19, AP19, AQ19, AR19, AS19, AT19, AU19, AV19, AW19, AX19, AY19, AZ19, BA19, BB19, BC19, BD19, BE19, BF19, BG19, BH19, BI19, BJ19, BK19, BL19, BM19, BN19, BO19, BP19, BQ19, BR19, BS19, BT19, BU19, BV19, BW19, BX19, BY19, BZ19, CA19, CB19, CC19, CD19, CE19, CF19, CG19, CH19, CI19, CJ19, CK19, CL19, CM19, CN19, CO19, CP19, CQ19, CR19, CS19, CT19, CU19, CV19, CW19, CX19, CY19, CZ19, DA19, DB19, DC19, DD19, DE19, DF19, DG19, DH19, DI19, DJ19, DK19, DL19, DM19, DN19, DO19, DP19, DQ19, DR19, DS19, DT19, DU19, DV19, DW19, DX19, DY19, DZ19, EA19, EB19, EC19, ED19, EE19, EF19, EG19, EH19, EI19, EJ19, EK19, EL19, EM19, EN19, EO19, EP19, EQ19, ER19, ES19, ET19, EU19, EV19, EW19, EX19, EY19, EZ19, FA19, FB19, FC19, FD19, FE19, FF19, FG19, FH19, FI19, FJ19, FK19, FL19, FM19, FN19, FO19, FP19, FQ19, FR19, FS19, FT19, FU19, FV19, FW19, FX19, FY19, FZ19, GA19, GB19, GC19, GD19, GE19, GF19, GG19, GH19, GI19, GJ19, GK19, GL19, GM19, GN19, GO19, GP19, GQ19, GR19, GS19, GT19, GU19, GV19, GW19, GX19, GY19, GZ19, HA19, HB19, HC19, HD19, HE19, HF19, HG19, HH19, HI19, HJ19, HK19, HL19, HM19, HN19, HO19, HP19, HQ19, HR19, HS19, HT19, HU19, HV19, HW19, HX19, HY19, HZ19, IA19, IB19, IC19, ID19, IE19, IF19, IG19, IH19, II19, IJ19, IK19, IL19, IM19, IN19, IO19, IP19, IQ19, IR19, IS19, IT19, IU19, IV19, IW19, IX19, IY19, IZ19, JA19, JB19, JC19, JD19, JE19, JF19, JG19, JH19, JI19, JJ19, JK19, JL19, JM19, JN19, JO19, JP19, JQ19, JR19, JS19, JT19, JU19, JV19, JW19, JX19, JY19, JZ19, KA19, KB19, KC19, KD19, KE19, KF19, KG19, KH19, KI19, KJ19, KK19, KL19, KM19, KN19, KO19, KP19, KQ19, KR19, KS19, KT19, KU19, KV19, KW19, KX19, KY19, KZ19, LA19, LB19, LC19, LD19, LE19, LF19, LG19, LH19, LI19, LJ19, LK19, LL19, LM19, LN19, LO19, LP19, LQ19, LR19, LS19, LT19, LU19, LV19, LW19, LX19, LY19, LZ19, MA19, MB19, MC19, MD19, ME19, MF19, MG19, MH19, MI19, MJ19, MK19, ML19, MM19, MN19, MO19, MP19, MQ19, MR19, MS19, MT19, MU19, MV19, MW19, MX19, MY19, MZ19, NA19, NB19, NC19, ND19, NE19, NF19, NG19, NH19, NI19, NJ19, NK19, NL19, NM19, NO19, NP19, NQ19, NR19, NS19, NT19, NU19, NV19, NW19, NX19, NY19, NZ19, OA19, OB19, OC19, OD19, OE19, OF19, OG19, OH19, OI19, OJ19, OK19, OL19, OM19, ON19, OO19, OP19, OQ19, OR19, OS19, OT19, OU19, OV19, OW19, OX19, OY19, OZ19, PA19, PB19, PC19, PD19, PE19, PF19, PG19, PH19, PI19, PJ19, PK19, PL19, PM19, PN19, PO19, PP19, PQ19, PR19, PS19, PT19, PU19, PV19, PW19, PX19, PY19, PZ19, QA19, QB19, QC19, QD19, QE19, QF19, QG19, QH19, QI19, QJ19, QK19, QL19, QM19, QN19, QO19, QP19, QQ19, QR19, QS19, QT19, QU19, QV19, QW19, QX19, QY19, QZ19, RA19, RB19, RC19, RD19, RE19, RF19, RG19, RH19, RI19, RJ19, RK19, RL19, RM19, RN19, RO19, RP19, RQ19, RR19, RS19, RT19, RU19, RV19, RW19, RX19, RY19, RZ19, SA19, SB19, SC19, SD19, SE19, SF19, SG19, SH19, SI19, SJ19, SK19, SL19, SM19, SN19, SO19, SP19, SQ19, SR19, SS19, ST19, SU19, SV19, SW19, SX19, SY19, SZ19, TA19, TB19, TC19, TD19, TE19, TF19, TG19, TH19, TI19, TJ19, TK19, TL19, TM19, TN19, TO19, TP19, TQ19, TR19, TS19, TT19, TU19, TV19, TW19, TX19, TY19, TZ19, UA19, UB19, UC19, UD19, UE19, UF19, UG19, UH19, UI19, UJ19, UK19, UL19, UM19, UN19, UO19, UP19, UQ19, UR19, US19, UT19, UV19, UW19, UX19, UY19, UZ19, VA19, VB19, VC19, VD19, VE19, VF19, VG19, VH19, VI19, VJ19, VK19, VL19, VM19, VN19, VO19, VP19, VQ19, VR19, VS19, VT19, VU19, VV19, VW19, VX19, VY19, VZ19, WA19, WB19, WC19, WD19, WE19, WF19, WG19, WH19, WI19, WJ19, WK19, WL19, WM19, WN19, WO19, WP19, WQ19, WR19, WS19, WT19, WU19, WV19, WW19, WX19, WY19, WZ19, XA19, XB19, XC19, XD19, XE19, XF19, XG19, XH19, XI19, XJ19, XK19, XL19, XM19, XN19, XO19, XP19, XQ19, XR19, XS19, XT19, XU19, XV19, XW19, XX19, XY19, XZ19, YA19, YB19, YC19, YD19, YE19, YF19, YG19, YH19, YI19, YJ19, YK19, YL19, YM19, YN19, YO19, YP19, YQ19, YR19, YS19, YT19, YU19, YV19, YW19, YX19, YY19, YZ19, ZA19, ZB19, ZC19, ZD19, ZE19, ZF19, ZG19, ZH19, ZI19, ZJ19, ZK19, ZL19, ZM19, ZN19, ZO19, ZP19, ZQ19, ZR19, ZS19, ZT19, ZU19, ZV19, ZW19, ZX19, ZY19, ZZ19, AA20, AB20, AC20, AD20, AE20, AF20, AG20, AH20, AI20, AJ20, AK20, AL20, AM20, AN20, AO20, AP20, AQ20, AR20, AS20, AT20, AU20, AV20, AW20, AX20, AY20, AZ20, BA20, BB20, BC20, BD20, BE20, BF20, BG20, BH20, BI20, BJ20, BK20, BL20, BM20, BN20, BO20, BP20, BQ20, BR20, BS20, BT20, BU20, BV20, BW20, BX20, BY20, BZ20, CA20, CB20, CC20, CD20, CE20, CF20, CG20, CH20, CI20, CJ20, CK20, CL20, CM20, CN20, CO20, CP20, CQ20, CR20, CS20, CT20, CU20, CV20, CW20, CX20, CY20, CZ20, DA20, DB20, DC20, DD20, DE20, DF20, DG20, DH20, DI20, DJ20, DK20, DL20, DM20, DN20, DO20, DP20, DQ20, DR20, DS20, DT20, DU20, DV20, DW20, DX20, DY20, DZ20, EA20, EB20, EC20, ED20, EE20, EF20, EG20, EH20, EI20, EJ20, EK20, EL20, EM20, EN20, EO20, EP20, EQ20, ER20, ES20, ET20, EU20, EV20, EW20, EX20, EY20, EZ20, FA20, FB20, FC20, FD20, FE20, FF20, FG20, FH20, FI20, FJ20, FK20, FL20, FM20, FN20, FO20, FP20, FQ20, FR20, FS20, FT20, FU20, FV20, FW20, FX20, FY20, FZ20, GA20, GB20, GC20, GD20, GE20, GF20, GG20, GH20, GI20, GJ20, GK20, GL20, GM20, GN20, GO20, GP20, GQ20, GR20, GS20, GT20, GU20, GV20, GW20, GX20, GY20, GZ20, HA20, HB20, HC20, HD20, HE20, HF20, HG20, HH20, HI20, HJ20, HK20, HL20, HM20, HN20, HO20, HP20, HQ20, HR20, HS20, HT20, HU20, HV20, HW20, HX20, HY20, HZ20, IA20, IB20, IC20, ID20, IE20, IF20, IG20, IH20, II20, IJ20, IK20, IL20, IM20, IN20, IO20, IP20, IQ20, IR20, IS20, IT20, IU20, IV20, IW20, IX20, IY20, IZ20, JA20, JB20, JC20, JD20, JE20, JF20, JG20, JH20, JI20, JJ20, JK20, JL20, JM20, JN20, JO20, JP20, JQ20, JR20, JS20, JT20, JU20, JV20, JW20, JX20, JY20, JZ20, KA20, KB20, KC20, KD20, KE20, KF20, KG20, KH20, KI20, KJ20, KK20, KL20, KM20, KN20, KO20, KP20, KQ20, KR20, KS20, KT20, KU20, KV20, KW20, KX20, KY20, KZ20, LA20, LB20, LC20, LD20, LE20, LF20, LG20, LH20, LI20, LJ20, LK20, LL20, LM20, LN20, LO20, LP20, LQ20, LR20, LS20, LT20, LU20, LV20, LW20, LX20, LY20, LZ20, MA20, MB20, MC20, MD20, ME20, MF20, MG20, MH20, MI20, MJ20, MK20, ML20, MM20, MN20, MO20, MP20, MQ20, MR20, MS20, MT20, MU20, MV20, MW20, MX20, MY20, MZ20, NA20, NB20, NC20, ND20, NE20, NF20, NG20, NH20, NI20, NJ20, NK20, NL20, NM20, NO20, NP20, NQ20, NR20, NS20, NT20, NU20, NV20, NW20, NX20, NY20, NZ20, OA20, OB20, OC20, OD20, OE20, OF20, OG20, OH20, OI20, OJ20, OK20, OL20, OM20, ON20, OO20, OP20, OQ20, OR20, OS20, OT20, OU20, OV20, OW20, OX20, OY20, OZ20, PA20, PB20, PC20, PD20, PE20, PF20, PG20, PH20, PI20, PJ20, PK20, PL20, PM20, PN20, PO20, PP20, PQ20, PR20, PS20, PT20, PU20, PV20, PW20, PX20, PY20, PZ20, QA20, QB20, QC20, QD20, QE20, QF20, QG20, QH20, QI20, QJ20, QK20, QL20, QM20, QN20, QO20, QP20, QQ20, QR20, QS20, QT20, QU20, QV20, QW20, QX20, QY20, QZ20, RA20, RB20, RC20, RD20, RE20, RF20, RG20, RH20, RI20, RJ20, RK20, RL20, RM20, RN20, RO20, RP20, RQ20, RR20, RS20, RT20, RU20, RV20, RW20, RX20, RY20, RZ20, SA20, SB20, SC20, SD20, SE20, SF20, SG20, SH20, SI20, SJ20, SK20, SL20, SM20, SN20, SO20, SP20, SQ20, SR20, SS20, ST20, SU20, SV20, SW20, SX20, SY20, SZ20, TA20, TB20, TC20, TD20, TE20, TF20, TG20, TH20, TI20, TJ20, TK20, TL20, TM20, TN20, TO20, TP20, TQ20, TR20, TS20, TT20, TU20, TV20, TW20, TX20, TY20, TZ20, UA20, UB20, UC20, UD20, UE20, UF20, UG20, UH20, UI20, UJ20, UK20, UL20, UM20, UN20, UO20, UP20, UQ20, UR20, US20, UT20, UV20, UW20, UX20, UY20, UZ20, VA20, VB20, VC20, VD20, VE20, VF20, VG20, VH20, VI20, VJ20, VK20, VL20, VM20, VN20, VO20, VP20, VQ20, VR20, VS20, VT20, VU20, VV20, VW20, VX20, VY20, VZ20, WA20, WB20, WC20, WD20, WE20, WF20, WG20, WH20, WI20, WJ20, WK20, WL20, WM20, WN20, WO20, WP20, WQ20, WR20, WS20, WT20, WU20, WV20, WW20, WX20, WY20, WZ20, XA20, XB20, XC20, XD20, XE20, XF20, XG20, XH20, XI20, XJ20, XK20, XL20, XM20, XN20, XO20, XP20, XQ20, XR20, XS20, XT20, XU20, XV20, XW20, XX20, XY20, XZ20, YA20, YB20, YC20, YD20, YE20, YF20, YG20, YH20, YI20, YJ20, YK20, YL20, YM20, YN20, YO20, YP20, YQ20, YR20, YS20, YT20, YU20, YV20, YW20, YX20, YY20, YZ20, ZA20, ZB20, ZC20, ZD20, ZE20, ZF20, ZG20, ZH20, ZI20, ZJ20, ZK20, ZL20, ZM20, ZN20, ZO20, ZP20, ZQ20, ZR20, ZS20, ZT20, ZU20, ZV20, ZW20, ZX20, ZY20, ZZ20																RISPERIDONE						OLANZAPINE						Overall P-value (a)	investpl P-value (a)	base P-value (a)
																CHANGE FROM TREATMENT BASE		CHANGE FROM TREATMENT BASE												
																N	Mean	SD	Mean	SD	N	Mean	SD	Mean	SD					
D-T SCALE (SECTION A) (NON-IMPUTED)																														
TREATMENT																														
BASELINE																109	4.6	1.62			124	4.4	1.49			0.420	0.083			
WEEK 8/STUDY ENTRY																106	4.8	1.43	0.3	1.44	120	4.8	1.45	0.4	1.63	0.875	0.393	<0.001		
WEEK 20/WEEK 12																88	4.6	1.59	-0.1	1.76	105	5.0	1.35	0.5	1.55	0.022	0.042	<0.001		
WEEK 36/WEEK 28																74	4.8	1.46	0.1	1.43	81	4.9	1.32	0.4	1.37	0.255	0.142	<0.001		
WEEK 52/WEEK 44																55	4.7	1.66	0.0	1.89	67	5.0	1.21	0.4	1.38	0.219	0.388	<0.001		
END POINT																109	4.6	1.60	0.1	1.77	124	4.7	1.53	0.3	1.66	0.509	0.077	<0.001		
D-T SCALE (SECTION B) (NON-IMPUTED)																														
TREATMENT																														
BASELINE																108	13.5	4.30			124	14.1	3.89			0.226	0.329			
WEEK 8/STUDY ENTRY																105	14.3	4.07	0.6	3.76	120	14.3	4.09	0.3	3.63	0.497	0.527	<0.001		
WEEK 20/WEEK 12																87	14.4	3.54	0.9	3.99	105	14.6	3.41	0.3	3.55	0.754	0.763	<0.001		
WEEK 36/WEEK 28																73	14.4	3.87	0.9	4.04	81	15.1	3.51	1.0	3.84	0.431	0.229	<0.001		
WEEK 52/WEEK 44																55	14.4	4.09	1.4	4.42	67	15.1	2.94	0.7	3.05	0.876	0.868	<0.001		
END POINT																108	14.2	3.94	0.7	4.44	124	14.5	3.42	0.4	3.47	0.916	0.663	<0.001		

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investpl (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bgolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

OLANZAPINE

Minus

----- RISPERIDONE -----

L.S.Mean 95% CI(a)

D-T SCALE (SECTION A) (NON-IMPUTED)

TREATMENT

BASELINE	-0.2	(-0.57; 0.24)
WEEK 8/STUDY ENTRY	0.0	(-0.31; 0.37)
WEEK 20/WEEK 12	0.5	(0.07; 0.84)
WEEK 36/WEEK 28	0.2	(-0.16; 0.62)
WEEK 52/WEEK 44	0.3	(-0.20; 0.84)
END POINT	0.1	(-0.25; 0.50)

D-T SCALE (SECTION B) (NON-IMPUTED)

TREATMENT

BASELINE	0.7	(-0.41; 1.74)
WEEK 8/STUDY ENTRY	-0.3	(-1.20; 0.59)
WEEK 20/WEEK 12	-0.1	(-1.04; 0.75)
WEEK 36/WEEK 28	0.4	(-0.64; 1.50)
WEEK 52/WEEK 44	-0.1	(-1.33; 1.13)
END POINT	-0.0	(-0.91; 0.81)

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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29AUG2008 16:22
System Used: Arrow5.1(U)/bqolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Cross over Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investpt1 P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE		N	Mean	SD	CHANGE FROM TREATMENT BASE				
D-T SCALE (SECTION C) (NON-IMPUTED)													
TREATMENT				Mean	SD				Mean	SD			
BASELINE	109	18.3	4.82			124	18.7	4.92			0.702	0.022	
WEEK 8/STUDY ENTRY	105	18.9	4.94	0.6	3.88	119	19.1	5.03	0.4	4.78	0.762	0.677	<0.001
WEEK 20/WEEK 12	87	19.5	4.61	1.1	3.96	105	20.3	3.98	1.4	4.90	0.329	0.223	<0.001
WEEK 36/WEEK 28	73	18.9	4.56	0.5	4.37	81	20.1	4.06	1.3	4.57	0.083	0.289	<0.001
WEEK 52/WEEK 44	54	19.1	5.04	0.9	4.24	67	20.5	4.10	1.1	4.10	0.614	0.889	<0.001
END POINT	109	18.7	5.23	0.4	4.19	124	19.4	4.49	0.7	4.71	0.441	0.090	<0.001
D-T SCALE (SECTION D) (NON-IMPUTED)													
TREATMENT													
BASELINE	104	9.7	2.65			122	9.8	2.71			0.883	0.667	
WEEK 8/STUDY ENTRY	100	10.3	2.53	0.6	2.24	116	10.2	2.83	0.3	2.80	0.683	0.976	<0.001
WEEK 20/WEEK 12	84	9.9	2.72	-0.0	2.33	103	10.3	2.76	0.4	2.61	0.217	0.855	<0.001
WEEK 36/WEEK 28	70	10.1	2.59	0.2	2.72	79	10.4	2.54	0.4	2.65	0.242	0.236	<0.001
WEEK 52/WEEK 44	52	9.8	3.06	0.2	3.48	65	10.4	2.50	0.2	2.29	0.435	0.738	<0.001
END POINT	104	10.0	2.84	0.3	2.86	122	10.0	2.98	0.1	2.68	0.964	0.229	<0.001
D-T SCALE (SECTION E) (NON-IMPUTED)													
TREATMENT													
BASELINE	105	14.5	3.69			121	13.7	3.59			0.146	0.057	
WEEK 8/STUDY ENTRY	100	14.5	3.54	0.0	3.43	115	14.2	3.93	0.6	4.47	0.862	0.008	<0.001
WEEK 20/WEEK 12	84	14.5	3.76	-0.1	4.12	104	14.8	3.05	1.2	4.12	0.188	0.675	<0.001
WEEK 36/WEEK 28	71	13.9	3.56	-0.7	4.11	80	14.8	3.19	1.4	4.06	0.008	0.137	<0.001
WEEK 52/WEEK 44	53	14.2	3.88	-0.2	4.00	66	14.8	3.14	1.0	3.99	0.063	0.037	<0.001
END POINT	105	14.1	3.71	-0.4	3.97	121	14.4	3.31	0.7	4.25	0.273	0.011	<0.001

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bgolrun

JNJPRD--TRIAL RIS-USA-113

Table BQCL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

OLANZAPINE

Minus

----- RISPERIDONE -----

L.S.Mean 95% CI(a)

D-T SCALE (SECTION C) (NON-IMPUTED)

TREATMENT

BASELINE	0.2	(-1.00; 1.49)
WEEK 8/STUDY ENTRY	-0.2	(-1.25; 0.92)
WEEK 20/WEEK 12	0.5	(-0.55; 1.62)
WEEK 36/WEEK 28	1.1	(-0.15; 2.32)
WEEK 52/WEEK 44	0.4	(-1.13; 1.90)
END POINT	0.4	(-0.63; 1.43)

D-T SCALE (SECTION D) (NON-IMPUTED)

TREATMENT

BASELINE	0.1	(-0.67; 0.78)
WEEK 8/STUDY ENTRY	-0.1	(-0.77; 0.51)
WEEK 20/WEEK 12	0.4	(-0.25; 1.12)
WEEK 36/WEEK 28	0.5	(-0.31; 1.22)
WEEK 52/WEEK 44	0.4	(-0.62; 1.42)
END POINT	-0.0	(-0.68; 0.65)

D-T SCALE (SECTION E) (NON-IMPUTED)

TREATMENT

BASELINE	-0.7	(-1.66; 0.25)
WEEK 8/STUDY ENTRY	-0.1	(-0.99; 0.83)
WEEK 20/WEEK 12	0.7	(-0.32; 1.62)
WEEK 36/WEEK 28	1.4	(0.37; 2.49)
WEEK 52/WEEK 44	1.2	(-0.06; 2.37)
END POINT	0.5	(-0.38; 1.33)

See footnotes on the first page of the table.

R. 4094

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JURIS 03529025

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bgolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

RISPERIDONE														OLANZAPINE																
CHANGE FROM TREATMENT BASE														CHANGE FROM TREATMENT BASE														Overall P-value (a)	investp1 P-value (a)	base P-value (a)
		N	Mean	SD	Mean	SD			N	Mean	SD	Mean	SD																	
D-T SCALE (SECTION F) (NON-IMPUTED)																														
TREATMENT																														
BASELINE																		109	10.9	4.97			123	11.1	5.09		0.614	0.546		
WEEK 8/STUDY ENTRY																		106	11.3	4.42	0.3	3.99	118	11.6	5.01	0.6	4.94	0.939	0.220	<0.001
WEEK 20/WEEK 12																		88	11.4	4.33	0.7	4.11	104	12.5	4.22	1.3	4.62	0.323	0.450	<0.001
WEEK 36/WEEK 28																		74	11.8	4.07	1.3	4.64	81	12.3	4.60	0.7	5.13	0.739	0.780	<0.001
WEEK 52/WEEK 44																		55	11.5	4.63	1.3	5.03	67	12.7	4.73	0.9	4.94	0.590	0.875	<0.001
END POINT																		109	11.4	4.56	0.5	4.50	123	11.8	4.72	0.7	5.20	0.765	0.392	<0.001
D-T SCALE (SECTION G) (NON-IMPUTED)																														
TREATMENT																														
BASELINE																		19	16.2	3.32			12	15.5	2.28		0.217	0.270		
WEEK 8/STUDY ENTRY																		18	14.5	4.23	-1.4	3.73	8	14.6	2.88	-0.5	2.27	0.213	0.656	0.871
WEEK 20/WEEK 12																		13	14.6	3.23	-0.7	2.90	9	15.0	3.08	-1.0	2.96	0.535	0.900	0.832
WEEK 36/WEEK 28																		14	13.7	3.38	-1.9	3.32	8	13.1	4.49	-2.4	4.31	0.260	0.459	0.573
WEEK 52/WEEK 44																		10	15.3	3.56	-0.8	2.86	6	16.0	3.03	0.2	3.25	0.861	0.768	0.520
END POINT																		19	14.2	4.52	-2.0	4.18	12	13.8	3.91	-1.8	3.28	0.405	0.410	0.954
D-T SCALE (SECTION H) (NON-IMPUTED)																														
TREATMENT																														
BASELINE																		108	14.8	3.90			122	14.7	4.04		0.848	0.936		
WEEK 8/STUDY ENTRY																		104	15.4	3.49	0.4	3.37	118	14.7	3.98	0.0	4.05	0.134	0.005	<0.001
WEEK 20/WEEK 12																		88	15.4	3.50	0.4	3.62	103	14.8	3.81	0.2	4.18	0.387	0.199	<0.001
WEEK 36/WEEK 28																		73	15.2	3.52	0.2	4.14	79	15.1	3.54	0.3	4.33	0.913	0.811	<0.001
WEEK 52/WEEK 44																		55	14.4	4.05	-0.5	4.51	65	15.3	3.30	0.5	4.13	0.170	0.904	<0.001
END POINT																		108	14.9	3.91	0.1	4.27	122	14.9	3.87	0.2	4.29	0.889	0.111	<0.001

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bqolrun

JNJPRD--TRIAL RIS-USA-113

Table BQCL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

	OLANZAPINE	Minus	RISPERIDONE
	L.S.Mean	95% CI (a)	

D-T SCALE (SECTION F) (NON-IMPUTED)

TREATMENT		
BASELINE	0.3	(-0.99; 1.67)
WEEK 8/STUDY ENTRY	0.0	(-1.00; 1.08)
WEEK 20/WEEK 12	0.5	(-0.53; 1.59)
WEEK 36/WEEK 28	0.2	(-1.12; 1.57)
WEEK 52/WEEK 44	0.5	(-1.21; 2.12)
END POINT	0.2	(-0.91; 1.23)

D-T SCALE (SECTION G) (NON-IMPUTED)

TREATMENT		
BASELINE	-1.7	(-4.57; 1.13)
WEEK 8/STUDY ENTRY	2.9	(-1.97; 7.82)
WEEK 20/WEEK 12	1.5	(-3.86; 6.79)
WEEK 36/WEEK 28	3.1	(-2.83; 8.94)
WEEK 52/WEEK 44	0.6	(-7.93; 9.07)
END POINT	1.6	(-2.46; 5.75)

D-T SCALE (SECTION H) (NON-IMPUTED)

TREATMENT		
BASELINE	-0.1	(-1.18; 0.97)
WEEK 8/STUDY ENTRY	-0.6	(-1.46; 0.20)
WEEK 20/WEEK 12	-0.4	(-1.35; 0.53)
WEEK 36/WEEK 28	0.1	(-1.09; 1.22)
WEEK 52/WEEK 44	1.0	(-0.42; 2.37)
END POINT	0.1	(-0.86; 1.00)

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bgolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1															
----- RISPERIDONE -----															
CHANGE FROM															
TREATMENT BASE															
Mean SD															
N Mean SD															
----- OLANZAPINE -----															
CHANGE FROM															
TREATMENT BASE															
Mean SD															
Overall investpt base															
P-value(a) P-value(a) P-value(a)															

D-T SCALE (SECTION I) (NON-IMPUTED)															

TREATMENT															
BASELINE															
109	13.9	3.50				123	13.6	3.71				0.243	0.033		
106	14.7	3.31	0.7	2.76		120	14.6	3.52	1.1	3.61		0.794	0.556	<0.001	
88	14.4	3.68	0.2	3.20		105	14.5	3.64	0.7	3.89		0.503	0.707	<0.001	
74	14.0	3.53	-0.2	3.12		80	14.8	3.22	1.1	3.02		0.007	0.936	<0.001	
55	14.4	4.12	0.3	3.46		67	14.8	3.46	0.7	3.27		0.427	0.931	<0.001	
109	14.0	3.88	0.2	3.40		123	14.3	3.73	0.8	3.80		0.240	0.773	<0.001	

D-T SCALE (SECTION J) (NON-IMPUTED)															

TREATMENT															
BASELINE															
109	4.7	1.61				124	4.7	1.61				0.861	0.406		
106	5.0	1.30	0.3	1.28		120	4.9	1.49	0.2	1.32		0.349	0.690	<0.001	
88	4.9	1.51	0.2	1.63		104	5.0	1.31	0.3	1.49		0.948	0.037	<0.001	
74	4.8	1.44	0.1	1.25		80	5.1	1.42	0.3	1.33		0.271	0.310	<0.001	
55	4.7	1.62	0.1	1.67		67	5.0	1.35	0.1	1.28		0.629	0.526	<0.001	
109	4.7	1.61	0.1	1.63		124	4.9	1.46	0.2	1.41		0.435	0.201	<0.001	

See footnotes on the first page of the table.

Attachment 2.8: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/bqolrun

JNJPRD--TRIAL RIS-USA-113

Table BQOL01: Brief Quality of Life Interview - Delighted-Terrible Scale Item Totals by Section - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Excluding sites 7 and 36

D-T Scale: 1 (TERRIBLE) TO 7 (DELIGHTED)

Items per section: A:1; B:3; C:4; D:2; E:3; F:3; G:3; H:3; I:3; J:1

OLANZAPINE

Minus

----- RISPERIDONE -----

L.S.Mean 95% CI (a)

D-T SCALE (SECTION I) (NON-IMPUTED)

TREATMENT

BASELINE	-0.6	(-1.48; 0.38)
WEEK 8/STUDY ENTRY	0.1	(-0.66; 0.86)
WEEK 20/WEEK 12	0.3	(-0.62; 1.26)
WEEK 36/WEEK 28	1.3	(0.35; 2.20)
WEEK 52/WEEK 44	0.5	(-0.74; 1.73)
END POINT	0.5	(-0.35; 1.39)

D-T SCALE (SECTION J) (NON-IMPUTED)

TREATMENT

BASELINE	-0.0	(-0.46; 0.39)
WEEK 8/STUDY ENTRY	-0.1	(-0.43; 0.15)
WEEK 20/WEEK 12	0.0	(-0.34; 0.37)
WEEK 36/WEEK 28	0.2	(-0.16; 0.57)
WEEK 52/WEEK 44	0.1	(-0.37; 0.61)
END POINT	0.1	(-0.20; 0.47)

See footnotes on the first page of the table.

Attachment 2.9: Drug Attitude Inventory Total Score - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Page 1 of 1

29AUG2008 16:18
System Used: Arrow5.1(U)/dairun

JNJPRD--TRIAL RIS-USA-113

Table DAI01: Drug Attitude Inventory Total Score - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
 Excluding sites 7 and 36
 Scale: 1 TO 10; HIGHER SCORES ARE BETTER

OLANZAPINE Minus RISPERIDONE									
--- RISPERIDONE ---			--- OLANZAPINE ---			Overall P-value (a)	investpl P-value (a)	----- RISPERIDONE -----	
N	Mean	SD	N	Mean	SD			L.S.Mean	95% CI (a)
DAI TOTAL (NON-IMPUTED)									
TREATMENT									
WEEK 8/STUDY ENTRY	95	7.8	1.95	111	7.7	1.96	0.635	0.220	-0.1 (-0.68; 0.41)
WEEK 20/WEEK 12	88	7.6	1.96	104	7.7	2.08	0.926	0.010	0.0 (-0.54; 0.60)
WEEK 36/WEEK 28	73	7.8	1.99	81	7.7	2.13	0.908	0.231	-0.0 (-0.72; 0.64)
WEEK 52/WEEK 44	55	7.8	1.82	67	7.9	1.94	0.408	0.183	0.3 (-0.41; 1.01)
END POINT	100	7.4	1.93	119	7.5	2.27	0.696	0.013	0.1 (-0.45; 0.67)

(a) Test for no difference between TREATMENT from ANOVA model with factor(s) TREATMENT, investpl (type III SS).

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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28AUG2008 09:31
System Used: Arrow5.1 (U) / aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Total no. subjects with adverse events	108 (86)	123 (87)
Psychiatric disorders	69 (55)	72 (51)
Agitation	19 (15)	16 (11)
Anxiety	19 (15)	15 (11)
Depression	15 (12)	18 (13)
Somnolence	14 (11)	29 (21)
Insomnia	12 (10)	20 (14)
Paranoid reaction	12 (10)	7 (5)
Psychosis	12 (10)	13 (9)
Hallucination	6 (5)	13 (9)
Suicide attempt	6 (5)	5 (4)
Delusion	4 (3)	4 (3)
Apathy	3 (2)	0
Confusion	3 (2)	2 (1)
Impotence	3 (2)	0
Aggressive reaction	2 (2)	2 (1)
Anorexia	2 (2)	2 (1)
Nervousness	2 (2)	3 (2)
Thinking abnormal	2 (2)	2 (1)
Catatonic reaction	1 (1)	0
Depression aggravated	1 (1)	2 (1)
Dreaming abnormal	1 (1)	1 (1)
Personality disorder	1 (1)	0
Schizophrenic reaction	1 (1)	1 (1)
Sleep disorder	1 (1)	1 (1)
Amnesia	0	1 (1)
Depersonalization	0	1 (1)
Drug abuse	0	3 (2)
Emotional lability	0	2 (1)
Libido decreased	0	1 (1)
Manic reaction	0	2 (1)
Neurosis	0	1 (1)
Centr & periph nervous system disorders	53 (42)	49 (35)
Headache	29 (23)	21 (15)
Hyperkinesia	8 (6)	2 (1)

Note: Incidence is based on the number of subjects experiencing at least one adverse event, not the number of events.

R. 4100

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JURIS 03629031

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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28AUG2008 09:31
System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Centr & periph nervous system disorders (continued)		
Hypertonia	7 (6)	7 (5)
Dizziness	5 (4)	13 (9)
Hypokinesia	5 (4)	1 (1)
Tremor	3 (2)	5 (4)
Dyskinesia	2 (2)	3 (2)
Dystonia	2 (2)	1 (1)
Extrapyramidal disorder	2 (2)	2 (1)
Speech disorder	2 (2)	0
Bradykinesia	1 (1)	0
Cramps legs	1 (1)	0
Dementia	1 (1)	0
Hypoaesthesia	1 (1)	2 (1)
Migraine	1 (1)	2 (1)
Muscle contractions involuntary	1 (1)	0
Convulsions	0	1 (1)
Myelitis	0	1 (1)
Paralysis	0	1 (1)
Reflexes abnormal	0	1 (1)
Vertigo	0	1 (1)
Gastro-intestinal system disorders		
Mouth dry	47 (37)	44 (31)
Saliva increased	14 (11)	13 (9)
Dyspepsia	10 (8)	6 (4)
Constipation	9 (7)	1 (1)
Nausea	6 (5)	10 (7)
Abdominal pain	5 (4)	6 (4)
Tooth ache	4 (3)	3 (2)
Vomiting	4 (3)	3 (2)
Flatulence	4 (3)	4 (3)
Tooth disorder	3 (2)	0
Diarrhoea	3 (2)	3 (2)
Gastric ulcer	2 (2)	7 (5)
Gastroesophageal reflux	1 (1)	0
Intestinal obstruction	1 (1)	0

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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28AUG2008 09:31
System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Gastro-intestinal system disorders (continued)		
Teeth-grinding	1 (1)	0
Tenesmus	1 (1)	0
Gastro-intestinal disorder nos	0	1 (1)
Gingivitis	0	2 (1)
Rectal disorder	0	1 (1)
Respiratory system disorders		
Rhinitis	35 (28)	30 (21)
Coughing	23 (18)	19 (13)
Pharyngitis	7 (6)	5 (4)
Sinusitis	4 (3)	5 (4)
Dyspnoea	4 (3)	0
Pulmonary congestion	2 (2)	1 (1)
Upper resp tract infection	2 (2)	1 (1)
Bronchitis	2 (2)	3 (2)
Bronchospasm	1 (1)	2 (1)
Chronic obstruct airways disease	1 (1)	1 (1)
Pneumonia	1 (1)	0
Stridor	1 (1)	1 (1)
Laryngitis	0	0
Body as a whole - general disorders		
Pain	30 (24)	38 (27)
Fatigue	10 (8)	7 (5)
Injury	7 (6)	5 (4)
Back pain	7 (6)	7 (5)
Chest pain	4 (3)	12 (9)
Lab values abnormal	3 (2)	1 (1)
Fever	3 (2)	2 (1)
Oedema peripheral	2 (2)	1 (1)
Allergic reaction	2 (2)	1 (1)
Allergy	1 (1)	0
Asthenia	1 (1)	2 (1)
Leg pain	1 (1)	1 (1)
Oedema	1 (1)	1 (1)

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Body as a whole - general disorders (continued)		
Carpal tunnel syndrome	0	1 (1)
Condition aggravated	0	1 (1)
Crying abnormal	0	1 (1)
Hot flushes	0	1 (1)
Rigors	0	1 (1)
Therapeutic response increased	0	2 (1)
Metabolic and nutritional disorders		
Weight increase	19 (15)	29 (21)
Creatine phosphokinase increased	5 (4)	19 (13)
Weight decrease	3 (2)	4 (3)
Hypercholesterolaemia	3 (2)	1 (1)
Hyperglycaemia	2 (2)	1 (1)
Dehydration	2 (2)	1 (1)
Glycosuria	1 (1)	0
Hypokalaemia	1 (1)	0
Lactose intolerance	1 (1)	0
Obesity	1 (1)	0
Hypertriglyceridaemia	0	3 (2)
Xerophthalmia	0	1 (1)
Endocrine disorders		
Hyperprolactinaemia	15 (12)	3 (2)
Breast pain male	15 (12)	0
Gynaecomastia	1 (1)	0
Thyroid disorder	0	1 (1)
Skin and appendages disorders		
Dermatitis fungal	0	2 (1)
Acne	3 (2)	1 (1)
Nail disorder	2 (2)	2 (1)
Rash	2 (2)	2 (1)
Rash erythematous	2 (2)	6 (4)
Bullous eruption	2 (2)	0
Dermatitis contact	1 (1)	0

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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System Used: Arrow5.1 (U) / aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Skin and appendages disorders (continued)		
Eczema	1 (1)	1 (1)
Folliculitis	1 (1)	0
Seborrhoea	1 (1)	0
Skin ulceration	1 (1)	1 (1)
Sweating increased	1 (1)	0
Dermatitis	0	1 (1)
Photosensitivity reaction	0	1 (1)
Pruritus genital	0	1 (1)
Psoriasis	0	1 (1)
Skin striae	0	1 (1)
Musculo-skeletal system disorders		
Myalgia	13 (10)	13 (9)
Arthralgia	6 (5)	6 (4)
Arthritis	4 (3)	2 (1)
Arthrosis	1 (1)	1 (1)
Bursitis	1 (1)	0
Muscle weakness	1 (1)	0
Skeletal pain	1 (1)	3 (2)
Torticollis	0	2 (1)
Resistance mechanism disorders		
Infection	11 (9)	7 (5)
Infection viral	5 (4)	2 (1)
Infection fungal	5 (4)	1 (1)
Infection bacterial	1 (1)	0
Herpes simplex	0	1 (1)
Herpes zoster	0	1 (1)
Infection bacterial	0	2 (1)
Urinary system disorders		
Urinary incontinence	11 (9)	11 (8)
Urinary tract infection	4 (3)	4 (3)
Urinary retention	3 (2)	4 (3)
Dysuria	2 (2)	1 (1)
Haematuria	1 (1)	1 (1)
	1 (1)	0

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Urinary system disorders (continued)		
Micturition disorder	1 (1)	0
Micturition frequency	1 (1)	2 (1)
Urine abnormal	1 (1)	0
Cystitis	0	1 (1)
Nocturia	0	1 (1)
Renal calculus	0	1 (1)
Reproductive disorders, female	9 (7)	4 (3)
Menstrual disorder	4 (3)	0
Amenorrhoea	2 (2)	1 (1)
Lactation nonpuerperal	1 (1)	0
Menopausal symptoms	1 (1)	0
Menorrhagia	1 (1)	0
Uterine disorder nos	1 (1)	0
Vaginal haemorrhage	1 (1)	0
Breast pain female	0	1 (1)
Pregnancy unintended	0	1 (1)
Vaginitis	0	1 (1)
Cardiovascular disorders, general	8 (6)	8 (6)
Hypertension	3 (2)	4 (3)
ECG abnormal	1 (1)	3 (2)
Hypertension aggravated	1 (1)	0
Hypotension	1 (1)	0
Hypotension postural	1 (1)	0
Oedema dependent	1 (1)	0
ECG abnormal specific	0	1 (1)
Heart disorder	0	1 (1)
Vision disorders	8 (6)	11 (8)
Vision abnormal	7 (6)	9 (6)
Lacrimation abnormal	2 (2)	0
Eye abnormality	0	1 (1)
Mydriasis	0	1 (1)

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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System Used: Arrow5.1 (U) / aerun

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Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Heart rate and rhythm disorders	6 (5)	7 (5)
Tachycardia	4 (3)	4 (3)
Arrhythmia	1 (1)	1 (1)
Palpitation	1 (1)	1 (1)
Bradycardia	0	1 (1)
Neoplasm	4 (3)	0
Skin hypertrophy	2 (2)	0
Pulmonary carcinoma	1 (1)	0
Thrombocythaemia	1 (1)	0
Secondary terms	4 (3)	4 (3)
Surgical intervention	2 (2)	2 (1)
Alcohol problem	1 (1)	1 (1)
Burn	1 (1)	0
Fall	0	1 (1)
White cell and RES disorders	4 (3)	1 (1)
Granulocytopenia	2 (2)	0
Leukocytosis	1 (1)	0
Lymphadenopathy cervical	1 (1)	0
Lymphadenopathy	0	1 (1)
Hearing and vestibular disorders	3 (2)	4 (3)
Ear ache	1 (1)	3 (2)
Ear disorder nos	1 (1)	0
Tinnitus	1 (1)	1 (1)
Liver and biliary system disorders	3 (2)	6 (4)
Gamma-gt increased	2 (2)	2 (1)
Liver fatty	1 (1)	0
Hepatic enzymes increased	0	1 (1)
Hepatic function abnormal	0	1 (1)
Hepatitis viral	0	1 (1)
SGPT increased	0	3 (2)

See footnotes on the first page of the table.

Attachment 3.1: Incidence of Treatment-Emergent Adverse Events

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Table AE01: Incidence of Treatment-Emergent Adverse Events (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126) n (%)	OLANZAPINE (N=141) n (%)
Reproductive disorders, male	3 (2)	3 (2)
Sexual function abnormal	2 (2)	1 (1)
Prostatic disorder	1 (1)	1 (1)
Penis disorder	0	1 (1)
Platelet,bleeding & clotting disorders	2 (2)	3 (2)
Coagulation disorder	1 (1)	0
Thrombocytopenia	1 (1)	2 (1)
Epistaxis	0	1 (1)
Red blood cell disorders	1 (1)	2 (1)
Anaemia	1 (1)	2 (1)
Special senses other,, disorders	1 (1)	0
Parosmia	1 (1)	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1 (U) / aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)					OLANZAPINE (N=141)				
	Total n (%)	NS	Mild	Mod	Sev	Total n (%)	NS	Mild	Mod	Sev
Total no. subjects with adverse events	108 (86)					123 (87)				
Psychiatric disorders	69 (55)	0	27	27	15	72 (51)	0	30	29	13
Agitation	19 (15)	0	11	6	2	16 (11)	0	4	10	2
Anxiety	19 (15)	0	11	6	2	15 (11)	0	10	3	2
Depression	15 (12)	0	5	6	4	18 (13)	0	5	11	2
Somnolence	14 (11)	0	12	2	0	29 (21)	0	21	8	0
Insomnia	12 (10)	0	8	4	0	20 (14)	0	11	9	0
Paranoid reaction	12 (10)	0	7	4	1	7 (5)	0	5	2	0
Psychosis	12 (10)	0	1	5	6	13 (9)	0	2	6	5
Hallucination	6 (5)	0	1	4	1	13 (9)	0	7	5	1
Suicide attempt	6 (5)	0	1	3	2	5 (4)	0	0	4	1
Delusion	4 (3)	0	1	3	0	4 (3)	0	2	1	1
Apathy	3 (2)	0	2	1	0	0	0	0	0	0
Confusion	3 (2)	0	1	1	1	2 (1)	0	0	1	1
Impotence	3 (2)	0	1	1	1	0	0	0	0	0
Aggressive reaction	2 (2)	0	1	0	1	2 (1)	0	0	1	1
Anorexia	2 (2)	0	0	2	0	2 (1)	1	1	0	0
Nervousness	2 (2)	0	1	1	0	3 (2)	0	0	3	0
Thinking abnormal	2 (2)	0	2	0	0	2 (1)	0	1	0	1
Catatonic reaction	1 (1)	0	0	0	1	0	0	0	0	0
Depression aggravated	1 (1)	0	0	0	1	2 (1)	0	1	1	0
Dreaming abnormal	1 (1)	0	0	1	0	1 (1)	0	1	0	0
Personality disorder	1 (1)	0	0	0	1	0	0	0	0	0
Schizophrenic reaction	1 (1)	0	1	0	0	1 (1)	0	0	1	0
Sleep disorder	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Amnesia	0	0	0	0	0	1 (1)	0	0	0	1
Depersonalization	0	0	0	0	0	1 (1)	0	0	1	0
Drug abuse	0	0	0	0	0	3 (2)	0	1	1	1
Emotional lability	0	0	0	0	0	2 (1)	0	2	0	0
Libido decreased	0	0	0	0	0	1 (1)	0	0	1	0
Manic reaction	0	0	0	0	0	2 (1)	0	1	0	1
Neurosis	0	0	0	0	0	1 (1)	0	1	0	0

Note: Incidence is based on the number of subjects, not the number of events. The subject's event with worst severity is used.
 <a> Severity: NS=Not Specified; MILD=Mild; MOD=Moderate; SEV=Severe.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1(U)/aerun

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Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

		RISPERIDONE (N=126)					OLANZAPINE (N=141)				
		--- SEVERITY<a> ---					--- SEVERITY<a> ---				
Adverse Event System Organ Class	Total	Ns	Mild	Mod	Sev	Total	Ns	Mild	Mod	Sev	
Adverse Event Preferred Term	n (%)					n (%)					
Centr & periph nervous system disorders	53 (42)	1	34	15	3	49 (35)	0	38	9	2	
Headache	29 (23)	1	21	6	1	21 (15)	0	17	3	1	
Hyperkinesia	8 (6)	0	5	3	0	2 (1)	0	2	0	0	
Hypertonia	7 (6)	0	5	1	1	7 (5)	0	7	0	0	
Dizziness	5 (4)	0	5	0	0	13 (9)	0	10	3	0	
Hypokinesia	5 (4)	0	3	1	1	1 (1)	0	1	0	0	
Tremor	3 (2)	0	3	0	0	5 (4)	0	4	1	0	
Dyskinesia	2 (2)	0	1	1	0	3 (2)	0	3	0	0	
Dystonia	2 (2)	0	1	1	0	1 (1)	0	1	0	0	
Extrapyramidal disorder	2 (2)	0	2	0	0	2 (1)	0	1	1	0	
Speech disorder	2 (2)	0	2	0	0	0	0	0	0	0	
Bradykinesia	1 (1)	0	1	0	0	0	0	0	0	0	
Cramps legs	1 (1)	0	1	0	0	0	0	0	0	0	
Dementia	1 (1)	0	0	1	0	0	0	0	0	0	
Hypoaesthesia	1 (1)	0	1	0	0	2 (1)	0	1	1	0	
Migraine	1 (1)	0	0	1	0	2 (1)	0	1	1	0	
Muscle contractions involuntary	1 (1)	0	1	0	0	0	0	0	0	0	
Convulsions	0	0	0	0	0	1 (1)	0	0	0	1	
Myelitis	0	0	0	0	0	1 (1)	1	0	0	0	
Paralysis	0	0	0	0	0	1 (1)	0	1	0	0	
Reflexes abnormal	0	0	0	0	0	1 (1)	0	1	0	0	
Vertigo	0	0	0	0	0	1 (1)	0	1	0	0	
Gastro-intestinal system disorders	47 (37)	2	30	12	3	44 (31)	1	34	9	0	
Mouth dry	14 (11)	1	13	0	0	13 (9)	1	11	1	0	
Saliva increased	10 (8)	0	10	0	0	6 (4)	0	6	0	0	
Dyspepsia	9 (7)	1	4	3	1	1 (1)	0	1	0	0	
Constipation	6 (5)	1	3	2	0	10 (7)	1	7	2	0	
Nausea	5 (4)	0	3	2	0	6 (4)	0	3	3	0	
Abdominal pain	4 (3)	0	2	2	0	3 (2)	0	3	0	0	
Tooth ache	4 (3)	0	2	1	1	3 (2)	0	0	3	0	
Vomiting	4 (3)	1	3	0	0	4 (3)	0	2	2	0	
Flatulence	3 (2)	0	1	2	0	0	0	0	0	0	
Tooth disorder	3 (2)	0	2	1	0	3 (2)	1	1	1	0	
Diarrhoea	2 (2)	0	1	1	0	7 (5)	0	5	2	0	

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1(U)/aerun

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Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	----- RISPERIDONE ----- (N=126)					----- OLANZAPINE ----- (N=141)				
	Total n (%)	--- SEVERITY<a> --- Ns Mild Mod Sev				Total n (%)	--- SEVERITY<a> --- Ns Mild Mod Sev			
Gastro-intestinal system disorders (continued)										
Gastric ulcer	1 (1)	0	0	1	0	0	0	0	0	0
Gastroesophageal reflux	1 (1)	0	0	1	0	0	0	0	0	0
Intestinal obstruction	1 (1)	0	0	0	1	0	0	0	0	0
Teeth-grinding	1 (1)	0	1	0	0	0	0	0	0	0
Tenesmus	1 (1)	0	1	0	0	0	0	0	0	0
Gastro-intestinal disorder nos	0	0	0	0	0	1 (1)	0	1	0	0
Gingivitis	0	0	0	0	0	2 (1)	0	2	0	0
Rectal disorder	0	0	0	0	0	1 (1)	0	1	0	0
Respiratory system disorders	35 (28)	0	25	10	0	30 (21)	0	24	6	0
Rhinitis	23 (18)	0	19	4	0	19 (13)	0	15	4	0
Coughing	7 (6)	0	6	1	0	5 (4)	0	5	0	0
Pharyngitis	4 (3)	0	4	0	0	5 (4)	0	5	0	0
Sinusitis	4 (3)	0	2	2	0	0	0	0	0	0
Dyspnoea	2 (2)	0	0	2	0	1 (1)	0	1	0	0
Pulmonary congestion	2 (2)	0	1	1	0	1 (1)	0	1	0	0
Upper resp tract infection	2 (2)	0	2	0	0	3 (2)	0	1	2	0
Bronchitis	1 (1)	0	0	1	0	2 (1)	0	2	0	0
Bronchospasm	1 (1)	0	0	1	0	1 (1)	0	1	0	0
Chronic obstruct airways disease	1 (1)	0	1	0	0	0	0	0	0	0
Pneumonia	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Stridor	1 (1)	0	1	0	0	0	0	0	0	0
Laryngitis	0	0	0	0	0	1 (1)	0	1	0	0
Body as a whole - general disorders	30 (24)	1	12	15	2	38 (27)	0	21	15	2
Pain	10 (8)	0	8	1	1	7 (5)	0	4	2	1
Fatigue	7 (6)	0	4	3	0	5 (4)	0	2	3	0
Injury	7 (6)	0	4	2	1	7 (5)	0	4	3	0
Back pain	4 (3)	0	2	2	0	12 (9)	0	8	4	0
Chest pain	3 (2)	0	2	1	0	1 (1)	0	1	0	0
Lab values abnormal	3 (2)	0	1	2	0	2 (1)	0	1	1	0
Fever	2 (2)	1	0	1	0	1 (1)	0	1	0	0
Oedema peripheral	2 (2)	0	2	0	0	1 (1)	0	0	1	0
Allergic reaction	1 (1)	0	0	0	1	0	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)				Total n (%)	OLANZAPINE (N=141)			
		--- SEVERITY<a> ---					--- SEVERITY<a> ---			
		Ns	Mild	Mod	Sev		Ns	Mild	Mod	Sev
Body as a whole - general disorders (continued)										
Allergy	1 (1)	0	0	1	0	2 (1)	0	2	0	0
Asthenia	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Leg pain	1 (1)	0	0	1	0	1 (1)	0	1	0	0
Oedema	1 (1)	0	0	1	0	1 (1)	0	1	0	0
Carpal tunnel syndrome	0	0	0	0	0	1 (1)	0	1	0	0
Condition aggravated	0	0	0	0	0	1 (1)	0	0	1	0
Crying abnormal	0	0	0	0	0	1 (1)	0	0	1	0
Hot flushes	0	0	0	0	0	1 (1)	0	1	0	0
Rigors	0	0	0	0	0	1 (1)	0	1	0	0
Therapeutic response increased	0	0	0	0	0	2 (1)	0	0	1	1
Metabolic and nutritional disorders										
Weight increase	19 (15)	1	11	6	1	29 (21)	0	18	11	0
Creatine phosphokinase increased	5 (4)	0	5	0	0	19 (13)	0	10	9	0
Weight decrease	3 (2)	1	0	1	1	4 (3)	0	2	2	0
Hypercholesterolaemia	3 (2)	0	1	2	0	1 (1)	0	1	0	0
Hyperglycaemia	2 (2)	0	1	1	0	1 (1)	0	1	0	0
Dehydration	2 (2)	0	2	0	0	1 (1)	0	1	0	0
Glycosuria	1 (1)	0	0	1	0	0	0	0	0	0
Hypokalaemia	1 (1)	0	1	0	0	0	0	0	0	0
Lactose intolerance	1 (1)	0	0	1	0	0	0	0	0	0
Obesity	1 (1)	0	1	0	0	0	0	0	0	0
Hypertriglyceridaemia	0	0	0	0	0	3 (2)	0	3	0	0
Xerophthalmia	0	0	0	0	0	1 (1)	0	1	0	0
Endocrine disorders										
Hyperprolactinaemia	15 (12)	1	7	7	0	3 (2)	0	1	2	0
Breast pain male	15 (12)	1	7	7	0	0	0	0	0	0
Gynaecomastia	1 (1)	0	1	0	0	0	0	0	0	0
Thyroid disorder	0	0	0	0	0	1 (1)	0	0	1	0
	0	0	0	0	0	2 (1)	0	1	1	0
Skin and appendages disorders										
Dermatitis fungal	15 (12)	0	12	3	0	17 (12)	0	14	3	0
Acne	3 (2)	0	2	1	0	1 (1)	0	1	0	0
	2 (2)	0	2	0	0	2 (1)	0	1	1	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)					OLANZAPINE (N=141)				
	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev
Skin and appendages disorders (continued)										
Nail disorder	2 (2)	0	2	0	0	2 (1)	0	1	1	0
Rash	2 (2)	0	2	0	0	6 (4)	0	6	0	0
Rash erythematous	2 (2)	0	1	1	0	0	0	0	0	0
Bullous eruption	1 (1)	0	1	0	0	0	0	0	0	0
Dermatitis contact	1 (1)	0	1	0	0	0	0	0	0	0
Eczema	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Folliculitis	1 (1)	0	1	0	0	0	0	0	0	0
Seborrhoea	1 (1)	0	1	0	0	0	0	0	0	0
Skin ulceration	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Sweating increased	1 (1)	0	0	1	0	0	0	0	0	0
Dermatitis	0	0	0	0	0	1 (1)	0	1	0	0
Photosensitivity reaction	0	0	0	0	0	1 (1)	0	1	0	0
Pruritus genital	0	0	0	0	0	1 (1)	0	1	0	0
Psoriasis	0	0	0	0	0	1 (1)	0	0	1	0
Skin striae	0	0	0	0	0	1 (1)	0	1	0	0
Musculo-skeletal system disorders										
Myalgia	13 (10)	1	8	4	0	13 (9)	0	10	3	0
Arthralgia	6 (5)	0	6	0	0	6 (4)	0	6	0	0
Arthritis	4 (3)	1	1	2	0	2 (1)	0	0	2	0
Arthrosis	1 (1)	0	0	1	0	1 (1)	0	0	1	0
Bursitis	1 (1)	0	1	0	0	0	0	0	0	0
Muscle weakness	1 (1)	0	1	0	0	0	0	0	0	0
Skeletal pain	1 (1)	0	1	0	0	3 (2)	0	3	0	0
Torticollis	0	0	0	0	0	2 (1)	0	2	0	0
Resistance mechanism disorders										
Infection	11 (9)	0	5	6	0	7 (5)	0	5	2	0
Infection viral	5 (4)	0	3	2	0	2 (1)	0	1	1	0
Infection fungal	5 (4)	0	2	3	0	1 (1)	0	1	0	0
Herpes simplex	1 (1)	0	0	1	0	0	0	0	0	0
Herpes zoster	0	0	0	0	0	1 (1)	0	1	0	0
Infection bacterial	0	0	0	0	0	2 (1)	0	2	0	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)					OLANZAPINE (N=141)				
	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev
Urinary system disorders	11 (9)	0	7	4	0	11 (8)	0	7	3	1
Urinary incontinence	4 (3)	0	3	1	0	4 (3)	0	3	1	0
Urinary tract infection	3 (2)	0	2	1	0	4 (3)	0	1	3	0
Urinary retention	2 (2)	0	2	0	0	1 (1)	0	1	0	0
Dysuria	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Haematuria	1 (1)	0	1	0	0	0	0	0	0	0
Micturition disorder	1 (1)	0	0	1	0	0	0	0	0	0
Micturition frequency	1 (1)	0	1	0	0	2 (1)	0	2	0	0
Urine abnormal	1 (1)	0	0	1	0	0	0	0	0	0
Cystitis	0	0	0	0	0	1 (1)	0	0	0	1
Nocturia	0	0	0	0	0	1 (1)	0	1	0	0
Renal calculus	0	0	0	0	0	1 (1)	0	0	1	0
Reproductive disorders, female	9 (7)	0	6	1	2	4 (3)	0	3	0	1
Menstrual disorder	4 (3)	0	3	1	0	0	0	0	0	0
Amenorrhoea	2 (2)	0	1	0	1	1 (1)	0	1	0	0
Lactation nonpuerperal	1 (1)	0	1	0	0	0	0	0	0	0
Menopausal symptoms	1 (1)	0	1	0	0	0	0	0	0	0
Menorrhagia	1 (1)	0	0	0	1	0	0	0	0	0
Uterine disorder nos	1 (1)	0	0	1	0	0	0	0	0	0
Vaginal haemorrhage	1 (1)	0	1	0	0	0	0	0	0	0
Breast pain female	0	0	0	0	0	1 (1)	0	1	0	0
Pregnancy unintended	0	0	0	0	0	1 (1)	0	0	0	1
Vaginitis	0	0	0	0	0	1 (1)	0	1	0	0
Cardiovascular disorders, general	8 (6)	0	4	4	0	8 (6)	0	4	4	0
Hypertension	3 (2)	0	1	2	0	4 (3)	0	2	2	0
ECG abnormal	1 (1)	0	1	0	0	3 (2)	0	2	1	0
Hypertension aggravated	1 (1)	0	0	1	0	0	0	0	0	0
Hypotension	1 (1)	0	0	1	0	0	0	0	0	0
Hypotension postural	1 (1)	0	1	0	0	0	0	0	0	0
Oedema dependent	1 (1)	0	1	0	0	0	0	0	0	0
ECG abnormal specific	0	0	0	0	0	1 (1)	0	0	1	0
Heart disorder	0	0	0	0	0	1 (1)	0	0	1	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)				Total n (%)	OLANZAPINE (N=141)			
		---	SEVERITY<a>	---	---		---	SEVERITY<a>	---	---
		Ns	Mild	Mod	Sev		Ns	Mild	Mod	Sev
Vision disorders	8 (6)	0	5	2	1	11 (8)	1	9	1	0
Vision abnormal	7 (6)	0	5	2	0	9 (6)	0	9	0	0
Lacrimation abnormal	2 (2)	0	1	0	1	0	0	0	0	0
Eye abnormality	0	0	0	0	0	1 (1)	0	0	1	0
Mydriasis	0	0	0	0	0	1 (1)	1	0	0	0
Heart rate and rhythm disorders	6 (5)	1	3	2	0	7 (5)	0	5	2	0
Tachycardia	4 (3)	1	2	1	0	4 (3)	0	3	1	0
Arrhythmia	1 (1)	0	0	1	0	1 (1)	0	0	1	0
Palpitation	1 (1)	0	1	0	0	1 (1)	0	1	0	0
Bradycardia	0	0	0	0	0	1 (1)	0	1	0	0
Neoplasm	4 (3)	0	2	1	1	0	0	0	0	0
Skin hypertrophy	2 (2)	0	1	1	0	0	0	0	0	0
Pulmonary carcinoma	1 (1)	0	0	0	1	0	0	0	0	0
Thrombocythaemia	1 (1)	0	1	0	0	0	0	0	0	0
Secondary terms	4 (3)	0	0	4	0	4 (3)	0	1	3	0
Surgical intervention	2 (2)	0	0	2	0	2 (1)	0	1	1	0
Alcohol problem	1 (1)	0	0	1	0	1 (1)	0	0	1	0
Burn	1 (1)	0	0	1	0	0	0	0	0	0
Fall	0	0	0	0	0	1 (1)	0	0	1	0
White cell and RES disorders	4 (3)	0	2	2	0	1 (1)	0	1	0	0
Granulocytopenia	2 (2)	0	0	2	0	0	0	0	0	0
Leukocytosis	1 (1)	0	1	0	0	0	0	0	0	0
Lymphadenopathy cervical	1 (1)	0	1	0	0	0	0	0	0	0
Lymphadenopathy	0	0	0	0	0	1 (1)	0	1	0	0
Hearing and vestibular disorders	3 (2)	0	3	0	0	4 (3)	0	3	1	0
Ear ache	1 (1)	0	1	0	0	3 (2)	0	2	1	0
Ear disorder nos	1 (1)	0	1	0	0	0	0	0	0	0
Tinnitus	1 (1)	0	1	0	0	1 (1)	0	1	0	0

See footnotes on the first page of the table.

Attachment 3.2: Incidence of Treatment-Emergent Adverse Events by Severity

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE02: Incidence of Treatment-Emergent Adverse Events by Severity (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	----- RISPERIDONE ----- (N=126)					----- OLANZAPINE ----- (N=141)				
	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev	Total n (%)	--- SEVERITY<a> --- Ns	Mild	Mod	Sev
Liver and biliary system disorders	3 (2)	0	0	3	0	6 (4)	0	4	2	0
Gamma-gt increased	2 (2)	0	0	2	0	2 (1)	0	2	0	0
Liver fatty	1 (1)	0	0	1	0	0	0	0	0	0
Hepatic enzymes increased	0	0	0	0	0	1 (1)	0	0	1	0
Hepatic function abnormal	0	0	0	0	0	1 (1)	0	1	0	0
Hepatitis viral	0	0	0	0	0	1 (1)	0	1	0	0
SGPT increased	0	0	0	0	0	3 (2)	0	2	1	0
Reproductive disorders, male	3 (2)	0	0	3	0	3 (2)	0	1	2	0
Sexual function abnormal	2 (2)	0	0	2	0	1 (1)	0	0	1	0
Prostatic disorder	1 (1)	0	0	1	0	1 (1)	0	0	1	0
Penis disorder	0	0	0	0	0	1 (1)	0	1	0	0
Platelet,bleeding & clotting disorders	2 (2)	0	1	1	0	3 (2)	0	3	0	0
Coagulation disorder	1 (1)	0	1	0	0	0	0	0	0	0
Thrombocytopenia	1 (1)	0	0	1	0	2 (1)	0	2	0	0
Epistaxis	0	0	0	0	0	1 (1)	0	1	0	0
Red blood cell disorders	1 (1)	0	0	1	0	2 (1)	0	2	0	0
Anaemia	1 (1)	0	0	1	0	2 (1)	0	2	0	0
Special senses other, disorders	1 (1)	0	1	0	0	0	0	0	0	0
Parosmia	1 (1)	0	1	0	0	0	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)						Total n (%)	OLANZAPINE (N=141)					
		Ns	None	Dful	Poss	Prob	Vlik		Ns	None	Dful	Poss	Prob	Vlik
Total no. subjects with adverse events	108 (86)							123 (87)						
Psychiatric disorders	69 (55)	0	17	11	36	5	0	72 (51)	1	13	15	36	5	2
Agitation	19 (15)	0	6	3	10	0	0	16 (11)	0	6	4	5	1	0
Anxiety	19 (15)	0	10	4	5	0	0	15 (11)	0	4	6	5	0	0
Depression	15 (12)	0	3	4	8	0	0	18 (13)	1	6	5	6	0	0
Somnolence	14 (11)	0	1	2	9	2	0	29 (21)	0	2	4	18	3	2
Insomnia	12 (10)	0	5	2	5	0	0	20 (14)	0	11	2	7	0	0
Paranoid reaction	12 (10)	0	2	3	7	0	0	7 (5)	0	3	0	4	0	0
Psychosis	12 (10)	0	5	4	2	1	0	13 (9)	0	7	2	4	0	0
Hallucination	6 (5)	0	2	1	3	0	0	13 (9)	0	2	5	6	0	0
Suicide attempt	6 (5)	0	1	3	2	0	0	5 (4)	0	1	1	3	0	0
Delusion	4 (3)	0	2	1	1	0	0	4 (3)	0	0	2	2	0	0
Apathy	3 (2)	0	1	0	2	0	0	0	0	0	0	0	0	0
Confusion	3 (2)	0	0	1	1	1	0	2 (1)	0	1	0	1	0	0
Impotence	3 (2)	0	0	0	3	0	0	0	0	0	0	0	0	0
Aggressive reaction	2 (2)	0	1	0	1	0	0	2 (1)	0	0	1	1	0	0
Anorexia	2 (2)	0	0	2	0	0	0	2 (1)	1	0	1	0	0	0
Nervousness	2 (2)	0	0	0	1	1	0	3 (2)	0	2	0	1	0	0
Thinking abnormal	2 (2)	0	2	0	0	0	0	2 (1)	0	2	0	0	0	0
Catatonic reaction	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Depression aggravated	1 (1)	0	0	0	1	0	0	2 (1)	0	0	2	0	0	0
Dreaming abnormal	1 (1)	0	0	0	1	0	0	1 (1)	0	0	0	1	0	0
Personality disorder	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Schizophrenic reaction	1 (1)	0	0	0	1	0	0	1 (1)	0	0	1	0	0	0
Sleep disorder	1 (1)	0	0	1	0	0	0	1 (1)	0	1	0	0	0	0
Amnesia	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Depersonalization	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Drug abuse	0	0	0	0	0	0	0	3 (2)	0	2	1	0	0	0
Emotional lability	0	0	0	0	0	0	0	2 (1)	0	1	0	0	1	0
Libido decreased	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Manic reaction	0	0	0	0	0	0	0	2 (1)	0	0	0	1	1	0
Neurosis	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0

Note: Incidence is based on the number of subjects, not the number of events. The subject's event with worst relation to trial medication is used.
 <a> Relation to Trial Medication: NS= Not Specified; NONE=None; DFUL=Doubtful; POSS=Possible; PROB=Probable; VLIK=Very Likely.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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28AUG2008 09:31
System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)						Total n (%)	OLANZAPINE (N=141)					
		Ns	None	Dful	Poss	Prob	Vlik		Ns	None	Dful	Poss	Prob	Vlik
Centr & periph nervous system disorders	53 (42)	0	17	12	17	3	4	49 (35)	0	13	6	25	3	2
Headache	29 (23)	0	14	9	6	0	0	21 (15)	0	12	5	4	0	0
Hyperkinesia	8 (6)	0	0	0	6	1	1	2 (1)	0	0	0	1	1	0
Hypertonia	7 (6)	0	1	0	6	0	0	7 (5)	0	1	1	5	0	0
Dizziness	5 (4)	0	1	2	1	1	0	13 (9)	0	1	1	9	1	1
Hypokinesia	5 (4)	0	1	1	1	0	2	1 (1)	0	0	0	1	0	0
Tremor	3 (2)	0	0	0	1	2	0	5 (4)	0	0	0	3	0	2
Dyskinesia	2 (2)	0	0	0	2	0	0	3 (2)	0	0	0	2	1	0
Dystonia	2 (2)	0	0	0	1	0	1	1 (1)	0	0	0	0	1	0
Extrapyramidal disorder	2 (2)	0	0	0	0	1	1	2 (1)	0	0	0	2	0	0
Speech disorder	2 (2)	0	1	0	1	0	0	0	0	0	0	0	0	0
Bradykinesia	1 (1)	0	0	0	0	1	0	0	0	0	0	0	0	0
Cramps legs	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Dementia	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Hypoaesthesia	1 (1)	0	1	0	0	0	0	2 (1)	0	0	2	0	0	0
Migraine	1 (1)	0	1	0	0	0	0	2 (1)	0	1	0	1	0	0
Muscle contractions involuntary	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Convulsions	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Myelitis	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Paralysis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Reflexes abnormal	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Vertigo	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Gastro-intestinal system disorders	47 (37)	1	15	5	21	4	1	44 (31)	0	21	5	15	3	0
Mouth dry	14 (11)	0	0	1	11	2	0	13 (9)	0	2	1	9	1	0
Saliva increased	10 (8)	0	1	1	5	2	1	6 (4)	0	2	0	2	2	0
Dyspepsia	9 (7)	0	4	4	1	0	0	1 (1)	0	0	1	0	0	0
Constipation	6 (5)	1	2	1	2	0	0	10 (7)	0	5	1	4	0	0
Nausea	5 (4)	0	3	1	1	0	0	6 (4)	0	3	2	1	0	0
Abdominal pain	4 (3)	0	2	2	0	0	0	3 (2)	0	2	0	1	0	0
Tooth ache	4 (3)	0	3	1	0	0	0	3 (2)	0	3	0	0	0	0
Vomiting	4 (3)	0	2	1	1	0	0	4 (3)	0	3	1	0	0	0
Flatulence	3 (2)	0	1	0	2	0	0	0	0	0	0	0	0	0
Tooth disorder	3 (2)	0	3	0	0	0	0	3 (2)	0	3	0	0	0	0
Diarrhoea	2 (2)	0	0	2	0	0	0	7 (5)	0	6	1	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)							OLANZAPINE (N=141)						
	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik
Gastro-intestinal system disorders (continued)														
Gastric ulcer	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Gastroesophageal reflux	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Intestinal obstruction	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Teeth-grinding	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Tenesmus	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Gastro-intestinal disorder nos	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Gingivitis	0	0	0	0	0	0	0	2 (1)	0	2	0	0	0	0
Rectal disorder	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Respiratory system disorders														
Rhinitis	35 (28)	0	26	9	0	0	0	30 (21)	0	27	3	0	0	0
Coughing	23 (18)	0	16	7	0	0	0	19 (13)	0	17	2	0	0	0
Pharyngitis	7 (6)	0	5	2	0	0	0	5 (4)	0	5	0	0	0	0
Sinusitis	4 (3)	0	3	1	0	0	0	5 (4)	0	4	1	0	0	0
Dyspnoea	4 (3)	0	3	1	0	0	0	0	0	0	0	0	0	0
Pulmonary congestion	2 (2)	0	1	1	0	0	0	1 (1)	0	1	0	0	0	0
Upper resp tract infection	2 (2)	0	1	1	0	0	0	1 (1)	0	1	0	0	0	0
Bronchitis	2 (2)	0	2	0	0	0	0	3 (2)	0	3	0	0	0	0
Bronchospasm	1 (1)	0	1	0	0	0	0	2 (1)	0	2	0	0	0	0
Chronic obstruct airways disease	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Pneumonia	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Stridor	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Laryngitis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Body as a whole - general disorders														
Pain	30 (24)	0	16	10	3	1	0	38 (27)	0	25	4	8	1	0
Fatigue	10 (8)	0	7	2	1	0	0	7 (5)	0	6	1	0	0	0
Injury	7 (6)	0	2	2	2	1	0	5 (4)	0	0	2	2	1	0
Back pain	7 (6)	0	6	1	0	0	0	7 (5)	0	7	0	0	0	0
Chest pain	4 (3)	0	4	0	0	0	0	12 (9)	0	9	2	1	0	0
Lab values abnormal	3 (2)	0	1	2	0	0	0	1 (1)	0	0	0	1	0	0
Fever	3 (2)	0	1	2	0	0	0	2 (1)	0	0	0	2	0	0
Oedema peripheral	2 (2)	0	0	2	0	0	0	1 (1)	0	1	0	0	0	0
Allergic reaction	2 (2)	0	2	0	0	0	0	1 (1)	0	0	0	1	0	0
	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1 (U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

		RISPERIDONE (N=126)						OLANZAPINE (N=141)						
		RELATION<a>						RELATION<a>						
Adverse Event System Organ Class	Total	Ns	None	Dful	Poss	Prob	Vlik	Total	Ns	None	Dful	Poss	Prob	Vlik
Adverse Event Preferred Term	n (%)							n (%)						
Body as a whole - general disorders (continued)														
Allergy	1 (1)	0	1	0	0	0	0	2 (1)	0	2	0	0	0	0
Asthenia	1 (1)	0	0	1	0	0	0	1 (1)	0	0	0	1	0	0
Leg pain	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Oedema	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Carpal tunnel syndrome	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Condition aggravated	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Crying abnormal	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Hot flushes	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Rigors	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Therapeutic response increased	0	0	0	0	0	0	0	2 (1)	0	2	0	0	0	0
Metabolic and nutritional disorders														
Weight increase	5 (15)	1	6	5	5	0	2	29 (21)	0	4	1	13	6	5
Creatine phosphokinase increased	3 (2)	0	0	1	2	0	0	4 (3)	0	1	1	2	0	0
Weight decrease	3 (2)	1	0	2	0	0	0	1 (1)	0	0	0	1	0	0
Hypercholesterolaemia	2 (2)	0	1	1	0	0	0	1 (1)	0	1	0	0	0	0
Hyperglycaemia	2 (2)	0	2	0	0	0	0	1 (1)	0	0	0	1	0	0
Dehydration	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Glycosuria	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Hypokalaemia	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Lactose intolerance	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Obesity	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Hypertriglyceridaemia	0	0	0	0	0	0	0	3 (2)	0	1	1	1	0	0
Xerophthalmia	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Endocrine disorders														
Hyperprolactinaemia	15 (12)	0	0	1	3	6	5	3 (2)	0	0	1	2	0	0
Breast pain male	1 (1)	0	0	0	0	0	1	0	0	0	0	0	0	0
Gynaecomastia	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Thyroid disorder	0	0	0	0	0	0	0	2 (1)	0	0	1	1	0	0
Skin and appendages disorders														
Dermatitis fungal	3 (2)	0	3	0	0	0	0	1 (1)	0	1	0	0	0	0
Acne	2 (2)	0	2	0	0	0	0	2 (1)	0	1	1	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)							OLANZAPINE (N=141)						
	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik
Skin and appendages disorders (continued)														
Nail disorder	2 (2)	0	2	0	0	0	0	2 (1)	0	2	0	0	0	0
Rash	2 (2)	0	2	0	0	0	0	6 (4)	0	6	0	0	0	0
Rash erythematous	2 (2)	0	1	1	0	0	0	0	0	0	0	0	0	0
Bullous eruption	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Dermatitis contact	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Eczema	1 (1)	0	0	1	0	0	0	1 (1)	0	0	1	0	0	0
Folliculitis	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Seborrhoea	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Skin ulceration	1 (1)	0	0	1	0	0	0	1 (1)	0	1	0	0	0	0
Sweating increased	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Dermatitis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Photosensitivity reaction	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Pruritus genital	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Psoriasis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Skin striae	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Musculo-skeletal system disorders														
Myalgia	6 (5)	0	2	1	3	0	0	6 (4)	0	3	1	2	0	0
Arthralgia	4 (3)	0	3	1	0	0	0	2 (1)	0	2	0	0	0	0
Arthritis	1 (1)	0	1	0	0	0	0	1 (1)	0	0	1	0	0	0
Arthrosis	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Bursitis	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Muscle weakness	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Skeletal pain	1 (1)	0	1	0	0	0	0	3 (2)	0	2	0	1	0	0
Torticollis	0	0	0	0	0	0	0	2 (1)	0	0	1	0	1	0
Resistance mechanism disorders														
Infection	5 (4)	0	3	2	0	0	0	2 (1)	0	2	0	0	0	0
Infection viral	5 (4)	0	3	2	0	0	0	1 (1)	0	1	0	0	0	0
Infection fungal	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Herpes simplex	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Herpes zoster	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Infection bacterial	0	0	0	0	0	0	0	2 (1)	0	2	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1 (U) / aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)						Total n (%)	OLANZAPINE (N=141)					
		Ns	None	Dful	Poss	Prob	Vlik		Ns	None	Dful	Poss	Prob	Vlik
Urinary system disorders	11 (9)	0	6	1	4	0	0	11 (8)	0	6	2	3	0	0
Urinary incontinence	4 (3)	0	2	0	2	0	0	4 (3)	0	2	1	1	0	0
Urinary tract infection	3 (2)	0	3	0	0	0	0	4 (3)	0	3	1	0	0	0
Urinary retention	2 (2)	0	1	0	1	0	0	1 (1)	0	1	0	0	0	0
Dysuria	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Haematuria	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Micturition disorder	1 (1)	0	0	0	1	0	0	0	0	0	0	0	0	0
Micturition frequency	1 (1)	0	0	0	1	0	0	2 (1)	0	1	0	1	0	0
Urine abnormal	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Cystitis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Nocturia	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Renal calculus	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Reproductive disorders, female	9 (7)	0	2	2	3	2	0	4 (3)	0	2	0	2	0	0
Menstrual disorder	4 (3)	0	1	0	3	0	0	0	0	0	0	0	0	0
Amenorrhoea	2 (2)	0	0	0	1	1	0	1 (1)	0	0	0	1	0	0
Lactation nonpuerperal	1 (1)	0	0	0	0	1	0	0	0	0	0	0	0	0
Menopausal symptoms	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Menorrhagia	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Uterine disorder nos	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Vaginal haemorrhage	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Breast pain female	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Pregnancy unintended	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Vaginitis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Cardiovascular disorders, general	8 (6)	0	2	3	2	1	0	8 (6)	0	3	1	4	0	0
Hypertension	3 (2)	0	1	1	1	0	0	4 (3)	0	3	0	1	0	0
ECG abnormal	1 (1)	0	0	0	1	0	0	3 (2)	0	0	1	2	0	0
Hypertension aggravated	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Hypotension	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Hypotension postural	1 (1)	0	0	0	0	1	0	0	0	0	0	0	0	0
Oedema dependent	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
ECG abnormal specific	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Heart disorder	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	RISPERIDONE (N=126)							OLANZAPINE (N=141)						
	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik	Total n (%)	Ns	None	Dful	Poss	Prob	Vlik
Vision disorders	8 (6)	0	3	0	4	1	0	11 (8)	0	1	3	6	1	0
Vision abnormal	7 (6)	0	3	0	3	1	0	9 (6)	0	1	1	6	1	0
Lacrimation abnormal	2 (2)	0	0	1	1	0	0	0	0	0	0	0	0	0
Eye abnormality	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Mydriasis	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Heart rate and rhythm disorders	6 (5)	0	1	2	3	0	0	7 (5)	0	2	2	3	0	0
Tachycardia	4 (3)	0	1	1	2	0	0	4 (3)	0	1	1	2	0	0
Arrhythmia	1 (1)	0	0	1	0	0	0	1 (1)	0	0	0	1	0	0
Palpitation	1 (1)	0	0	0	1	0	0	1 (1)	0	1	0	0	0	0
Bradycardia	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Neoplasm	4 (3)	0	3	1	0	0	0	0	0	0	0	0	0	0
Skin hypertrophy	2 (2)	0	1	1	0	0	0	0	0	0	0	0	0	0
Pulmonary carcinoma	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Thrombocythaemia	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Secondary terms	4 (3)	0	4	0	0	0	0	4 (3)	0	3	1	0	0	0
Surgical intervention	2 (2)	0	2	0	0	0	0	2 (1)	0	2	0	0	0	0
Alcohol problem	1 (1)	0	1	0	0	0	0	1 (1)	0	1	0	0	0	0
Burn	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Fall	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
White cell and RES disorders	4 (3)	0	3	1	0	0	0	1 (1)	0	0	1	0	0	0
Granulocytopenia	2 (2)	0	1	1	0	0	0	0	0	0	0	0	0	0
Leukocytosis	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Lymphadenopathy cervical	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Lymphadenopathy	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Hearing and vestibular disorders	3 (2)	0	2	1	0	0	0	4 (3)	0	4	0	0	0	0
Ear ache	1 (1)	0	1	0	0	0	0	3 (2)	0	3	0	0	0	0
Ear disorder nos	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Tinnitus	1 (1)	0	0	1	0	0	0	1 (1)	0	1	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.3: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug

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System Used: Arrow5.1(U)/aerun

JNJPRD--TRIAL RIS-USA-113

Table AE03: Incidence of Treatment-Emergent Adverse Events by Relationship To Study Drug (continued)

Analysis Set: Intent-to-treat

Adverse Event System Organ Class Adverse Event Preferred Term	Total n (%)	RISPERIDONE (N=126)						Total n (%)	OLANZAPINE (N=141)					
		RELATION<a>							RELATION<a>					
		Ns	None	Dful	Poss	Prob	Vlik		Ns	None	Dful	Poss	Prob	Vlik
Liver and biliary system disorders	3 (2)	0	0	2	1	0	0	6 (4)	0	1	2	3	0	0
Gamma-gt increased	2 (2)	0	0	1	1	0	0	2 (1)	0	1	1	0	0	0
Liver fatty	1 (1)	0	0	1	0	0	0	0	0	0	0	0	0	0
Hepatic enzymes increased	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Hepatic function abnormal	0	0	0	0	0	0	0	1 (1)	0	0	0	1	0	0
Hepatitis viral	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
SGPT increased	0	0	0	0	0	0	0	3 (2)	0	0	1	2	0	0
Reproductive disorders, male	3 (2)	0	2	1	0	0	0	3 (2)	0	0	3	0	0	0
Sexual function abnormal	2 (2)	0	1	1	0	0	0	1 (1)	0	0	1	0	0	0
Prostatic disorder	1 (1)	0	1	0	0	0	0	1 (1)	0	0	1	0	0	0
Penis disorder	0	0	0	0	0	0	0	1 (1)	0	0	1	0	0	0
Platelet,bleeding & clotting disorders	2 (2)	0	2	0	0	0	0	3 (2)	0	1	1	1	0	0
Coagulation disorder	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Thrombocytopenia	1 (1)	0	1	0	0	0	0	2 (1)	0	0	1	1	0	0
Epistaxis	0	0	0	0	0	0	0	1 (1)	0	1	0	0	0	0
Red blood cell disorders	1 (1)	0	0	1	0	0	0	2 (1)	0	1	1	0	0	0
Anaemia	1 (1)	0	0	1	0	0	0	2 (1)	0	1	1	0	0	0
Special senses other, disorders	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0
Parosmia	1 (1)	0	1	0	0	0	0	0	0	0	0	0	0	0

See footnotes on the first page of the table.

Attachment 3.4: Percent of Subjects With Treatment-Emergent EPS-Related Adverse Events in RIS-USA-113

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System Used: Arrow5.1(U)/aeepsrun

JNJPRD--TRIAL RIS-USA-113

Table AE06: Percent of Subjects with Treatment-Emergent EPS-Related Adverse Events in RIS-USA-113

Analysis Set: Intent-to-treat

	-- RISPERIDONE --		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
Extrapyramidal symptoms						
Treatment						
Overall						
No	104	82.5	123	87.2		
Yes	22	17.5	18	12.8		
Total	126		141		(-0.04; 0.13)	0.167

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05.
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05.

Attachment 3.5: Percent of Subjects With EPS-Related Adverse Events Emergent in RIS-USA-112 or RIS-USA-113 - Crossover Subjects Excluded

Page 1 of 1

28AUG2008 17:21
System Used: Arrow5.1(U)/aeeprun

JNJPRD--TRIAL RIS-USA-113

Table AE07: Percent of Subjects with EPS-Related Adverse Events Emergent in RIS-USA-112 or RIS-USA-113 - Crossover Subjects Excluded

Analysis Set: ITT Excluding Crossover Subjects

	-- RISPERIDONE --		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
Extrapyramidal symptoms						
Treatment						
Overall						
No	83	68.0	95	69.9		
Yes	39	32.0	41	30.1		
Total	122		136		(-0.09; 0.13)	0.555

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05 .
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05 .

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

RIS-USA-113

**Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events**

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

Narratives were written for all serious adverse events and for all adverse events leading to discontinuation that occurred during study RIS-USA-113.

Narratives were written based upon information in the clinical database. Additional information, when applicable, was obtained from other source documents including CIOMS reports. Within the narrative text, the preferred term for the adverse event(s) is provided in the bolded text at the beginning of the narrative; quotation marks are used for the first use of any adverse event verbatim term within the narrative.

The subject cross-reference table is a list of all subjects for whom narratives have been provided. The events included are all serious adverse events and treatment-emergent adverse events leading to discontinuation. Narratives are arranged by serious adverse event or discontinuations due to adverse event for all subjects within the relevant treatment groups.

Only 1 narrative text is provided for each subject and is shown under the first applicable heading in the following hierarchy: (1) serious adverse events, and (2) adverse events leading to discontinuation. The cross-reference table, grouped by treatment, shows whether a subject had events in any of those categories, and provides a text link to the narrative for any subject with such event(s).

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Table NR.01: Subjects by Narrative Category
JNJPRD--TRIAL RIS-USA-113

Treatment Group Subject ID Number	----- Narrative Criteria -----		
	Death	DC due to AE leading to Discontinuation	Serious AE Emerged in RIS-USA-113
Total Number of Narratives	55		
Total Number of Subjects	0	29	49
OLANZAPINE			
A30001			X
A30010			X
A30011		X	X
A30033		X	X
A30036		X	X
A30051		X	X
A30075		X	X
A30086			X
A30113			X
A30121			X
A30137		X	
A30149		X	X
A30158		X	
A30169		X	X
A30175		X	
A30195		X	X
A30200		X	
A30228		X	X
A30234			X
A30242			X
A30268			X
A30269			X
A30272			X
A30281		X	X
A30282			X
A30334			X
A30412			X
A30415		X	
RISPERIDONE			
A30009		X	X
A30012		X	
A30044			X
A30050			X
A30060			X
A30098		X	X
A30115		X	X

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

A30122	X
A30129	X

Table NR.01: Subjects by Narrative Category
JNJPRD--TRIAL RIS-USA-113

Treatment Group Subject ID Number	----- Narrative Criteria -----		
	Death	DC due to AE leading to Discontinuation	Serious AE Emerged in RIS-USA-113
Total Number of Narratives	55		
Total Number of Subjects	0	29	49
RISPERIDONE			
A30132		X	X
A30146		X	X
A30154			X
A30170			X
A30176			X
A30187		X	X
A30192			X
A30194		X	X
A30196		X	X
A30226		X	X
A30246		X	X
A30249		X	X
A30267			X
A30275		X	X
A30283			X
A30333		X	X
A30335			X
A30395			X

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**Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events**

Subject Narratives for Serious Adverse Events

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30001 (A30009 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30001 (serious adverse events: agitation and psychosis): This 40-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 17. His first psychiatric hospitalization was at age 19. The number of previous psychiatric hospitalizations was unknown. There was no family history of psychiatric illness. Previous bipolar medications included risperidone 7 mg bid, which was discontinued at the start of study RIS-USA-112. *Concomitant medication was hydrochlorothiazide 50 mg/day (source: CIOMS).* The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	16
	15	41
USA-113	15	17
	0	11
	15	1
	20	72
	0	16

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Agitation ^b	N	48	15	Recovered	None	Moderate	Doubtful	Y
Agitation	Y	75	69	Recovered	Temporary stop	Severe	Doubtful	Y
Psychosis ^c	Y	75	69	Recovered	None	Severe	Doubtful	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: exacerbation of agitation

^c Investigator verbatim: increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	85	Moderate	-
USA-113	57	Week 8/study entry	-	Moderate	Minimally improved
	85	Week 12/week 4	52	Moderate	Much improved
	114	Week 16/week 8	43	Moderate	Much improved
	143	Week 20/week 12	52	Moderate	Minimally improved

On Day 75, the subject experienced agitation and psychosis (investigator verbatim: increased psychosis), and was hospitalized 2 days later. Both events were of severe intensity. The investigator considered the events to be doubtfully related to the study medication *but to the stress caused by the death of the subject's stepfather*. Treatment with study medication was temporarily discontinued for 11 days from Day 75 onward. *She was treated with olanzapine*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
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1 tablet/day and with quinapril 10 mg/day. (source: CIOMS). The event subsided 69 days later and the subject was discharged from the hospital on Day 143. The subject stopped taking study medication on Day 159 and was discontinued from the study due to withdrawal of consent on Day 174. [Manufacturer's Control No. JAUSA32146]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30010 (A30014 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30010 (serious adverse event: psychosis): This 49-year-old Caucasian female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 25. Her first psychiatric hospitalization was at age 25. The number of previous psychiatric hospitalizations was 7. There was no family history of psychiatric illness. Previous bipolar medications included tiotixene 10 mg/day, which was discontinued at the start of study RIS-USA-112. Concomitant medication was lorazepam (1 mg/day) for anxiety/agitation. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	6
	15	53
USA-113	15	9
	0	5

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Tremor	N	8	66	Not recovered	None	Mild	Possible	N
Anxiety	N	59	15	Not recovered	None	Moderate	None	N
Agitation	N	59	15	Not recovered	None	Moderate	None	N
Psychosis ^b	Y	70	8	Recovered	None	Severe	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: Increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	83	Marked	-
USA-113	59	Week 8/study entry	54	Mild	Much improved
	73	Week 12/week 4	75	Moderate	Minimally improved

Time interval	Days in phase	Total ESRS	Parkinsonism total score	Dystonia total score	Dyskinesia total score	CGI-dyskinesia	CGI-parkinsonism	CGI-dystonia	Stage of parkinsonism
Baseline	0	0	0	0	0	Absent	Absent	Absent	Absent
Week 8/study entry	59	0	0	0	0	Absent	Absent	Absent	Absent
Week 12/week 4	73	0	0	0	0	Absent	Absent	Absent	Absent

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Subject A30010 stopped taking olanzapine on Day 68. On Day 70, the subject experienced psychosis (investigator verbatim: increased psychosis). *She reported to the emergency room and was hospitalized. Urine drug screen was positive for cocaine and benzodiazepines. (source: CIOMS).* The investigator considered the event to be severe and not related to study medication. The subject was treated with risperidone 3 mg bid and lorazepam 2 mg/6 h PRN. The subject recovered after 8 days. The subject was discontinued from the study on Day 73. [Manufacturer's Control No. JAUSA32817]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30011 (A30017 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30011 (serious adverse events: psychosis and therapeutic response increased): This 40-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 21. Her first psychiatric hospitalization was at age 21. The number of previous psychiatric hospitalizations was 22. The family history of psychiatric illness was unknown. Previous bipolar medications included Zyprexa (olanzapine, 10 mg/day), which was discontinued before the start of study RIS-USA-112. Concomitant medication was lorazepam (2 mg/day) for agitation. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	56
USA-113	10	22
	0	17
	100	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	80	7	Recovered	Permanent stop	Moderate	None	Y
Therapeutic response increased ^c	Y	96	3	Recovered	None	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator's verbatim: Increased psychosis

^c Investigator's verbatim: Overdose of study meds

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	81	Moderate	-
USA-113	56	Week 8/study entry	54	Mild	Much improved
	85	Week 12/week 4	129	-	-

On Day 78 the subject stopped taking study medication. On Day 80, the subject experienced psychosis (investigator verbatim: increased psychosis) and was hospitalized. The event was of moderate intensity. The investigator considered the event to be not related to the study medication. The subject was discontinued from the study, and received treatment with risperidone 3 mg bid and lorazepam (doses between 2 and 6 mg/day). The event lasted 7 days. She was discharged on Day 88. Her psychosis had not completely cleared by then, she was still hearing some voices and responding to internal stimuli, but she was no longer suicidal or homicidal and she felt that she could take care of herself at home and (source: CIOMS).

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 96 the subject *ingested 20 tablets of study medication* (serious adverse event: therapeutic response increased, investigator verbatim: overdose of study meds) *and was admitted to the hospital for observation*. The investigator considered this serious adverse event to be moderate and not related to study medication. The subject recovered after 3 days (*source: CIOMS*). [Manufacturer's Control No. JAUSA32972 and JAUSA33340]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30033 (A30042 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30033 (serious adverse events: aggressive reaction, agitation, anxiety, depression, extrapyramidal disorder, hallucination, paranoid reaction, psychosis, suicide attempt): This 40-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 38. Her first psychiatric hospitalization was at age 40. There were no previous psychiatric hospitalizations. Previous bipolar medications were not present or unknown. The family history of psychiatric illness was unknown. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	13
	0	1
	15	14
	20	31
USA-113	20	144
	0	1
	20	3
	15	9
	0	2

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged In USA-113	Start Day ^a	AE Duration (Days)	Outcome	Action Taken	Severity	Investigator-Assigned Relationship	SAE Y/N
Anxiety	Y	190	20	Recovered	None	Severe	Possible	Y
Agitation	Y	203	7	Recovered	None	Moderate	Possible	Y
Extrapyramidal disorder	Y	203	1	Recovered	None	Moderate	Possible	Y
Hallucination	Y	203	7	Recovered	Dosage Reduced	Moderate	Possible	Y
Psychosis	Y	203	7	Recovered	None	Moderate	Possible	Y
Depression	Y	204	27	Recovered	Dosage Reduced	Moderate	Possible	Y
Hallucination	Y	217	14	Recovered	Permanent stop	Moderate	Possible	Y
Paranoid reaction	Y	217	14	Recovered	Permanent stop	Moderate	Possible	Y
Aggressive reaction	Y	218	13	Recovered	Permanent stop	Moderate	Possible	Y
Agitation	Y	218	13	Recovered	Permanent stop	Moderate	Possible	Y
Suicide attempt	Y	218	13	Recovered	Permanent stop	Moderate	Possible	Y

^aDay = Day in study from the start of USA-112

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	64	Moderate	-
USA-113	61	Week 8/study entry	56	Mild	Much improved
	89	Week 12/week 4	52	Very mild	Much improved
	117	Week 16/week 8	54	Very mild	Much improved
	146	Week 20/week 12	62	Mild	Much improved
	219	Week 32/week 24	70	Moderate	Minimally worse

Time Interval	Days in Phase	Total ESRS	Parkinsonism Total score	Dystonia Total score	Dyskinesia Total score	CGI-Dyskinesia	CGI-Parkinsonism	CGI-Dystonia	Stage of Parkinsonism
Baseline	0	0	0	0	0	Absent	Absent	Absent	Absent
Week 8/study entry	61	1	1	0	0	Absent	Borderline	Absent	Absent
Week 12/week 4	89	0	0	0	0	Absent	Absent	Absent	Absent
Week 16/week 8	117	1	1	0	0	Absent	Borderline	Absent	Absent
Week 20/week 12	146	3	3	0	0	Absent	Very mild	Absent	Stage I
Week 28/week 20	205	4	4	0	0	Absent	Borderline	Absent	Absent
Week 32/week 24	219	4	4	0	0	Absent	Mild	Absent	Stage I

On Day 190 the subject experienced anxiety of severe intensity. *She was hearing voices, and experienced restlessness, and was hospitalized. She was discharged 6 days later, and the anxiety resolved after 20 days.* On Day 204 the subject was rehospitalized due to the serious adverse events agitation, extrapyramidal disorder, hallucination, and psychosis that had started on Day 203. On Day 217, the subject experienced hallucination and paranoid reaction, and on Day 218, the subject experienced aggressive reaction (investigator verbatim: homicidal ideation), agitation, and attempted suicide (investigator verbatim: suicidal ideation). All events were considered to be of moderate intensity. The investigator considered the events to be possibly related to the study medication, more specifically *that fluoxetine had interacted with the antipsychotic. During the hospitalization her condition improved. She was discharged on Day 210 (source: CIOMS).* Treatment with study medication was discontinued and the subject was discontinued from the study on Day 219. [Manufacturer's Control No. JAUSA32994 and JAUSA33153]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30036 (A30456 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30036 (serious adverse events: agitation, dizziness, hallucination, psychosis): This 18-year-old Hispanic male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 17. His first psychiatric hospitalization was at age 18. There was 1 previous psychiatric hospitalization. The family history of psychiatric illness was unknown. Previous bipolar medication included haloperidol 2-5 mg/day, which was discontinued at the start of study RIS-USA-112.

The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	5
	15	9
	0	1
	10	6
	10	7
	15	29
USA-113	15	29
	20	104

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged In USA-113</i>	<i>Start Day^a</i>	<i>AE Duration (Days)</i>	<i>Outcome</i>	<i>Action Taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE Y/N</i>
Agitation ^b	Y	149	4	Recovered	None	Moderate	Doubtful	N
Agitation ^c	Y	186	5	Recovered	None	Mild	Doubtful	N
Agitation ^d	Y	186	16	Recovered	Permanent stop	Severe	Doubtful	Y
Dizziness	Y	186	16	Recovered	Permanent stop	Moderate	Doubtful	Y
Hallucination ^e	Y	186	16	Recovered	Permanent stop	Moderate	Doubtful	Y
Psychosis	Y	186	16	Recovered	Permanent stop	Moderate	Doubtful	Y
Tremor	Y	190	1	Recovered	None	Mild	Possible	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: panic attack

^c Investigator verbatim: panic reaction

^d Investigator verbatim: restlessness

^e Investigator verbatim: auditory and visual hallucinations

Assessment Scores

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	1	Baseline	110	Extremely severe	-
USA-113	57	Week 8/study entry	51	Mild	Very much improved
	86	Week 12/week 4	84	Marked	Minimally improved
	114	Week 16/week 8	69	Moderate	Minimally improved
	142	Week 20/week 12	71	Moderate	Much improved
	190	Week 28/week 20	70	Moderate	Much improved

<i>Time Interval</i>	<i>Days in Phase</i>	<i>Total ESRS</i>	<i>Parkinsonism Total score</i>	<i>Dystonia Total score</i>	<i>Dyskinesia Total score</i>	<i>CGI-Dyskinesia</i>	<i>CGI-Parkinsonism</i>	<i>CGI-Dystonia</i>	<i>Stage of Parkinsonism</i>
Baseline	1	2	2	0	0	Absent	Very mild	Absent	Stage I
Week 8/study entry	57	1	1	0	0	Absent	Very mild	Absent	Absent
Week 12/week 4	86	6	6	0	0	Absent	Mild	Absent	Absent
Week 16/week 8	114	16	13	0	3	Borderline	Mild	Absent	Absent
Week 20/week 12	142	6	6	0	0	Absent	Very mild	Absent	Absent
Week 28/week 20	190	2	2	0	0	Absent	Borderline	Absent	Absent

On Day 149 the subject experienced agitation (investigator verbatim: panic attack) and then again on Day 186 (agitation, investigator verbatim: panic reaction). On the second occasion, the subjects also experienced agitation (investigator verbatim: restlessness), dizziness, hallucination (investigator verbatim: auditory and visual hallucinations), and psychosis and was hospitalized. The events dizziness, hallucination, and psychosis were considered to be of moderate intensity, the event restlessness was severe. The investigator considered all events to be doubtfully related to the study medication. The event restlessness was treated with lorazepam 2 mg bid from Day 188 onward. The subject recovered 16 days later. The subject was discontinued from the study due to these serious adverse events on Day 190. [Manufacturer's Control No. JAUSA34146]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30051 (A30065 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30051 (serious adverse event: pregnancy): This 27-year-old Black female subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 19. Her first psychiatric hospitalization was at age 22. She had one previous psychiatric hospitalization. There was a family history of psychiatric illness. Previous bipolar medication included haloperidol 2 mg/8 h PRN, which was discontinued at the start of study RIS-USA-112. The subject's medical history included 3 abortions and one miscarriage. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)		Dose (mg)	Duration (days)
USA-RIS-112	10	5	USA-RIS-113	10	14
	0	1		0	1
	10	1		10	2
	15	3		5	1
	0	1		10	2
	10	15		0	2
	0	1		10	2
	10	5		0	1
	0	1		10	4
	10	2		0	1
	0	1		10	2
	10	3		0	1
	0	1		10	2
	10	13		0	2
USA-RIS-113	10	5		10	4
	0	2		0	2
	10	1		10	5
	0	1		0	3
	10	2		10	11
	0	2		0	1
	10	5		5	2
	0	1		0	1

The relevant adverse event is shown in the table below:

Adverse Event Details								
MedDRA Preferred Term	Emerged In USA-113	Start Day ^a	AE Duration (Days)	Outcome	Action Taken	Severity	Investigator-Assigned Relationship	SAE Y/N
Pregnancy unintended	Y	140	1	Not recovered	Permanent stop	Severe	Not related	Y

^a Day = Day in study from the start of USA-112

On Day 140, the subject presented with an unintended pregnancy. The investigator considered the event to be not related to study medication. The subject was discontinued from the study the same day. *The study coordinator was unsuccessful in contacting the subject, as subject had moved and was lost to follow-up. The associate spoke with subject's mother and*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

learned that the subject had experienced a miscarriage late in OCT 1998 (day unknown)
(source: CIOMS). approximately 3 months after the date of the study discontinuation.
[Manufacturer's Control No. JAUSA33661]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30075 (A30094 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30075 (serious adverse event: drug abuse): This 39-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 22. Her first psychiatric hospitalization was at age 22. The number of previous psychiatric hospitalizations was 5. There was a family history of psychiatric illness. Previous bipolar medications included fluphenazine hydrochloride (10 mg/day) and olanzapine (10 mg/day), which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	14
	15	41
USA-113	15	130
	0	8
	15	55
	0	4

The relevant adverse events are shown in the table below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day *	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Drug abuse	Y	184	13	Recovered	Temporary stop	Severe	None	Y
Drug abuse	Y	226	11	Recovered	Permanent stop	Severe	None	Y

* Day = Day in study from the start of USA-112

On Day 184, the subject had a relapse of drug abuse and used cocaine for 13 days. The investigator considered the event to be severe in intensity and not related to the study medication. Study medication was temporarily stopped. *She was admitted to a detoxification center and study medication was resumed on Day 193 (source: CIOMS).* On Day 226, the subject had another relapse of drug abuse and used cocaine for 11 days. The investigator considered the event to be severe in intensity and not related to the study medication. Study medication was temporarily stopped *and she was readmitted to a detoxification center and recovered (source: CIOMS).* Study medication was resumed (date unknown) and then permanently discontinued on Day 248. The subject was discontinued from the study on Day 252. [Manufacturer's Control No. JAUSA34065 and JAUSA34691]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30086 (A30108 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30086 (serious adverse event: confusion): This 27-year-old Hispanic male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 15. This was his first psychiatric hospitalization. There was no family history of psychiatric illness. Previous bipolar medications included fluphenazine hydrochloride (2.5 mg/day) and risperidone (1 mg/day), which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	60
USA-113	10	20
	0	1
	10	283
	0	1

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Confusion	Y	80	2	Recovered	Temporary stop	Moderate	None	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	63	Moderate	-
USA-113	57	Week 8/study entry	60	Moderate	Minimally improved
	86	Week 12/week 4	66	Moderate	Unchanged
	114	Week 16/week 8	57	Moderate	Unchanged
	148	Week 20/week 12	64	Moderate	Minimally improved
	196	Week 28/week 20	53		-
	255	Week 36/week 28	67	Moderate	Minimally worse
	365	Week 52/week 44	60	Moderate	Unchanged

On Day 80, the subject experienced confusion *after an argument with his mother (source: CIOMS)* and was hospitalized. The investigator considered the event to be moderate in intensity and not related to the study medication. The subject recovered the next day, and completed the study on Day 365. [Manufacturer's Control No. JAUSA32671]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30113 (A30142 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30113 (serious adverse events: insomnia, anxiety, paranoid reaction): This 36-year-old Hispanic male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 26. His first psychiatric hospitalization was at age 26. The number of previous psychiatric hospitalizations was 20. There was a family history of psychiatric illness. Previous bipolar medications included risperidone 8 mg/day, which was discontinued at the start of study RIS-USA-112. Concomitant medication was tocopherol 800 IU bid for tardive dyskinesia. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	56
USA-113	15	142
	10	170
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Insomnia	Y	154	9	Recovered	None	Mild	None	Y
Anxiety	Y	157	6	Recovered	None	Mild	None	Y
Paranoid reaction	Y	157	6	Recovered	None	Mild	None	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	62	Moderate	-
USA-113	57	Week 8/study entry	51	Moderate	Minimally improved
	85	Week 12/week 4	47	Moderate	Minimally improved
	113	Week 16/week 8	41	Mild	Much improved
	141	Week 20/week 12	50	Moderate	Minimally worse
	196	Week 28/week 20	43	-	-
	257	Week 36/week 28	37	Moderate	Much improved
	369	Week 52/week 44	40	Mild	Very much improved

On Day 154, the subject experienced insomnia. The investigator considered the event to be mild and to be not related to study medication *but to stress about a pending social security benefits hearing. He was hospitalized for observation (source: CIOMS)*, and was treated with temazepam 30 mg/day PRN. The duration of the event was 9 days and the subject recovered. On Day 157, the subject experienced anxiety and paranoid reaction. The investigator considered the events to be mild and to be not related to study medication. The duration of the event was 6 days. The subject completed the study on Day 369. [Manufacturer's Control No. JAUSA32463]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30121 (A30157 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30121 (serious adverse events: schizophrenic reaction, depression aggravated, suicidal attempt): This 51-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 22. His first psychiatric hospitalization was at age 22. The number of previous psychiatric hospitalizations was 12. There was a family history of psychiatric illness. Previous bipolar medications included haloperidol (150 mg/4 weeks, and 4-10 mg/day), which was discontinued before the start of study RIS-USA-112. Concomitant medication was flurazepam hydrochloride 15 mg/day PRN for insomnia, atenolol 25 mg/day for hypertension, and cimetidine 400 mg/day for heartburn.

The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	7
	15	21
	20	27
USA-113	20	28
	15	28
	20	42
	0	5
	20	60
	0	131

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Drug abuse	Y	152	8	Recovered	None	Moderate	Doubtful	N
Schizophrenic reaction	Y	154	24	Recovered	None	Moderate	Doubtful	Y
Depression aggravated	Y	159	19	Recovered	None	Moderate	Doubtful	Y
Suicidal attempt	Y	159	19	Recovered	None	Moderate	Doubtful	Y

^aDay = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	85	Marked	-
USA-113	56	Week 8/study entry	63	Moderate	Minimally improved
	84	Week 12/week 4	60	Mild	Minimally improved
	112	Week 16/week 8	60	Mild	Much improved
	140	Week 20/week 12	55	Very mild	Much improved
	196	Week 28/week 20	55	-	-
	349	Week 48/week 40	81	Moderate	Minimally improved

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 159, the subject experienced depression aggravated and suicidal attempt, and was hospitalized. *The subject had left his structured living arrangement approximately 1 month earlier and started to drink alcohol. He began living in his car. He became non compliant with his study medication on Day 154 for 5 days while continuing to drink alcohol. The subject presented at the hospital in a relapsed state. Treatment with the study medication was restarted at hospitalization (source: CIOMS).* He was discontinued from the study on Day 349 due to non-compliance. [Manufacturer's Control No. JAUSA32558]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30149 (A30186 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30149 (serious adverse events: aggressive reaction and anxiety): This 33-year-old Black female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 16. Her first psychiatric hospitalization was at age 21. The number of previous psychiatric hospitalizations was 10. There was a family history of psychiatric illness. Previous bipolar medications included thioridazine 100 mg/day, which was discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	7
	15	7
	20	43
USA-113	20	3
	0	6

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Aggressive reaction	Y	61	6	Not recovered	Permanent stop	Severe	Doubtful	Y
Anxiety	Y	61	6	Not recovered	Permanent stop	Severe	Doubtful	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	85	Moderate	-
USA-113	57	Week 8/study entry	80	Moderate	Minimally improved

On Day 61, the subject experienced aggressive reaction and anxiety and was hospitalized. The investigator considered the events to be severe and doubtfully related to the study medication. Study medication was discontinued on Day 61. The subject was discontinued permanently from the study on Day 66. *The subject recovered without sequelae (source: CIOMS).* [Manufacturer's Control No. JAUSA32194]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30169 (A30219 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30169 (serious adverse events: lab values abnormal): This 33-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 24. His first psychiatric hospitalization was at age 24. The number of previous psychiatric hospitalizations was 7. There was a family history of psychiatric illness. Previous bipolar medications included fluphenazine decanoate (37.5 mg/day) and haloperidol (dosage unknown), which were discontinued before the start of study RIS-USA-112. Concomitant medications were pyridoxine 50 mg/day and isoniazid 300 mg/day for stabilization of tuberculosis and loratidine PRN for sinusitis. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	7
	15	36
	20	14
USA-113	20	14
	0	10

The relevant adverse events and the laboratory values are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Rhinitis	N	44	18	Recovered	None	Mild	Doubtful	N
Lab value abnormal ^b	Y	58	91	Recovered	Permanent stop	Moderate	Possible	Y
Chest pain	Y	72	1	Recovered	None	Mild	Possible	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: Dec white blood count

Laboratory details			
Test	Test date	Result/unit	Normal low range
White blood cell count	22-JAN-1998; baseline	4.2 giga/L	3.8-10.8 giga/L
	24-MAR-1998; Day 58	2.8 giga/L	
	27-MAR-1998; Day 61	2.7 giga/L	
	31-MAR-1998; Day 65	3.1 giga/L	
	07-APR-1998; Day 72	3.0 giga/L	
Neutrophils	22-JAN-1998; baseline	2.42 giga/L	1.80-8.00 giga/L; 1500-7800 giga/L
	24-MAR-1998; Day 58	1.44 giga/L	
	27-MAR-1998; Day 61	1002 giga/L	
	31-MAR-1998; Day 65	1119 giga/L	
	18-MAY-1998	1400 giga/L	

Source: CIOMS

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 58, the subject developed neutropenia (investigator verbatim: decreased white blood count). The white blood count (WBC) value was 2.8 giga/L (clinically significant lower range 3.8 giga/L). The investigator considered the event to be moderate in intensity and possibly related to the study medication. On Day 72, the subject was hospitalized and study medication *and isoniazid* were stopped. The subject was discontinued from the study on Day 81. *During his admission the subject was asymptomatic. His absolute neutrophil count gradually recovered. He was discharged to a boarding home on quetiapine (source: CIOMS).* [Manufacturer's Control No. JAUSA32447]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30195 (A30248 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30195 (serious adverse event: psychosis): This 48-year-old Caucasian male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 26. His first psychiatric hospitalization was at age 26. The number of previous psychiatric hospitalizations was 4. There was no family history of psychiatric illness. Previous bipolar medications included thioridazine hydrochloride 150 mg/day and 25 mg PRN, fluphenazine decanoate 50 mg/2 weeks, and fluphenazine hydrochloride 10 mg/day, which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	20
	15	35
USA-113	15	56
	20	91
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	112	29	Recovered	Dosage reduced	Mild	None	N
Psychosis ^b	Y	202	2	Not recovered	Permanent stop	Severe	Possible	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	92	Mild	-
USA-113	56	Week 8/study entry	68	Mild	Much improved
	84	Week 12/week 4	63	Mild	Minimally improved
	112	Week 16/week 8	70	Marked	Much worse
	140	Week 20/week 12	62	Moderate	Much improved

On Day 112, the subject experienced psychosis (investigator verbatim: increased psychosis). The investigator considered the event to be mild and not related to the study medication. The study medication dosage was adjusted from 15 to 20 mg/day. The subject recovered after 29 days. On Day 202, the subject again experienced psychosis (investigator verbatim: increased psychosis) and was hospitalized. The investigator considered the event to be severe and possibly related to the study medication. The study medication was stopped on Day 203 and the subject was discontinued from the study. [Manufacturer's Control No. JAUSA34558]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30228 (A30286 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30228 (serious adverse events: agitation, manic reaction): This 39-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 15. Her first psychiatric hospitalization was at age 18. The number of previous psychiatric hospitalizations was 5. There was a family history of psychiatric illness. Previous bipolar medications included risperidone 9 mg/day and tiotixene 5 mg/day, which were discontinued before the start of study RIS-USA-112. Concomitant medication was lorazepam 1 mg PRN for agitation. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	20
	15	22
	20	15
USA-113	20	10
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Agitation	Y	64	19	Recovered	Permanent stop	Moderate	Possible	Y
Manic reaction	Y	64	19	Recovered	Permanent stop	Severe	Probable	Y

^aDay = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	75	Marked	-
USA-113	57	Week 8/study entry	64	Moderate	Minimally improved
	68	Week 12/week 4	71	Marked	Minimally worse

On Day 64, the subject was hospitalized due to agitation and manic reaction. The investigator considered the manic reaction to be severe in intensity and probably related to the study medication, and the agitation to be moderate in intensity and possibly related to the study medication. The subject was discontinued from the study on Day 68. Upon admission, the subject was treated first with olanzapine and lithium, and then later changed to risperidone and lithium with improvement in mental status. The subject was discharged from the hospital 2 weeks later (source: CIOMS) [Manufacturer's Control No. JAUSA32819]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30234 (A30295 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30234 (serious adverse event: hypoaesthesia): This 33-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 17. His first psychiatric hospitalization was at age 27. The number of previous psychiatric hospitalizations was 8. There was no family history of psychiatric illness. Previous bipolar medications included fluphenazine (5 mg/AM, 20 mg/QHS and 5 mg/AM, 10 mg/QHS), which was discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	10
	0	4
	15	7
	15	44
USA-113	15	113

The relevant adverse events are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Hypoaesthesia ^b	Y	135	3	Recovered	None	Moderate	Doubtful	Y
Myelitis	Y	135	3	Recovered	-	-	Doubtful	-

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: numbness in left extremity

On Day 135, the subject presented with hypoaesthesia (investigator verbatim: numbness in left extremity). The investigator considered the event to be moderate in intensity and doubtfully related to the study medication. *The subject was examined in the emergency room and was hospitalized for tests. The symptom resolved spontaneously the same day. A work-up indicated no serious process occurred, rather a possible myelitis or flexitis (benign) (source: CIOMS).* The subject got lost to follow up and was discontinued from the study on Day 178. [Manufacturer's Control No. JAUSA33536]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30242 (A30302 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30242 (serious adverse events: paranoid reaction, nervousness, insomnia, and psychosis): This 43-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 15. His first psychiatric hospitalization was at age 15. The number of previous psychiatric hospitalizations was 27. There was no family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 200 mg/4 weeks and haloperidol 20 mg/day, which were discontinued before the start of study RIS-USA-112. Concomitant medication was flurazepam hydrochloride 15 mg PRN for insomnia. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	3
	15	55
USA-113	15	111
	20	196

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Paranoid reaction	Y	170	6	Recovered	Dosage reduced*	Moderate	None	Y
Nervousness	Y	170	6	Recovered	Dosage reduced	Moderate	None	Y
Insomnia	Y	170	6	Recovered	Dosage reduced	Moderate	None	Y
Psychosis	Y	350	16	Recovered	None	Moderate	Possible	Y

* Dose was actually increased

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: numbness in left extremity

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	78	Moderate	-
USA-113	58	Week 8/study entry	58	Mild	Much improved
	86	Week 12/week 4	40	Very mild	Much improved
	114	Week 16/week 8	54	Mild	Much improved
	142	Week 20/week 12	45	Mild	Much improved
	196	Week 28/week 20	47	-	-
	252	Week 36/week 28	44	Very mild	Much improved
	365	Week 52/week 44	55	Mild	Minimally worse

On Day 170, the subject was hospitalized due to paranoid reaction, nervousness, and insomnia. The investigator considered the events to be moderate in intensity and not related

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

to the study medication. The events were treated with lorazepam 1 mg/day PRN and the study medication was increased from 15 to 20 mg/day. The subject recovered after 6 days.

On Day 350, the subject was admitted *voluntarily to the mental health center (source: CIOMS)* due to psychosis. The investigator considered the event to be moderate in intensity and possibly related to the study medication. The event had subsided after 16 days, when the subject completed the study on Day 365. [Manufacturer's Control Nos. JAUSA33002 and JAUSA35376]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30268 (A30335 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30268 (serious adverse event: psychosis): This 31-year-old Hispanic male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 25. His first psychiatric hospitalization was at age 31. The number of previous psychiatric hospitalizations was 1. There was no family history of psychiatric illness. Previous bipolar medications included fluphenazine decanoate 25 mg/2 weeks, fluphenazine hydrochloride 5 mg/day, and risperidone 6 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	55
USA-113	10	140
	0	57

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	Y	142	111	Not recovered	None	Moderate	Doubtful	N
Psychosis ^b	Y	225	3	Recovered	None	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: hospitalization due to increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	67	Mild	-
USA-113	56	Week 8/study entry	55	Very mild	Much improved
	85	Week 12/week 4	53	Very mild	Much improved
	113	Week 16/week 8	45	Very mild	Very much improved
	141	Week 20/week 12	76	Mild	Minimally worse

The subject had stopped taking study medication on Day 195. One month later, on Day 225, the subject was hospitalized due to psychosis (investigator verbatim: hospitalization due to increased psychosis). The investigator considered the event to be moderate and to be not related to study medication. The subject was treated with fluphenazine decanoate IM 5 mg/2 weeks. *He was discharged home following symptom resolution on Day 228 (source: CIOMS).* The subject was discontinued from the study on Day 252 due to non-compliance. [Manufacturer's Control No. JAUSA33801]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30269 (A30338 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30269 (serious adverse event: psychosis): This 49-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: disorganized). The subject's age at onset was 21. His first psychiatric hospitalization was at age 21. The number of previous psychiatric hospitalizations was 7. There was no family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 100 mg/2 weeks and haloperidol 5 mg/day, which were discontinued at the start of study RIS-USA-112. Concomitant medications were lorazepam 1-4 mg/day (4 days/week maximum) for agitation, cimetidine 400 mg bid PRN for gastrointestinal reflux disease, and atenolol 100 mg/day and hydrochlorothiazide 25 mg/day for hypertension. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	6
	15	7
	20	42
USA-113	20	45
	0	4
	20	5
	0	3
	20	23
	0	1
	20	1
	0	2

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	113	20	Recovered	None	Severe	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: increased psychosis due to non-compliance.

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	97	Marked	-
USA-113	56	Week 8/study entry	98	Marked	Unchanged
	84	Week 12/week 4	89	Marked	Minimally improved
	120	Week 16/week 8	100	Marked	Minimally worse
	139	Week 20/week 12	93	Moderate	Minimally improved

On Day 113, the subject was hospitalized due to severe psychosis (investigator verbatim: increased psychosis due to non-compliance). *The subject had done well for a period (nos) until he became non-compliant with the study medication, and then his condition aggravated.*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

Upon hospitalization, study medication was restarted and the subject showed improvement of symptoms after 10 days. The subject was discharged 20 days later and treatment with study medication continued (source: CIOMS). The subject was discontinued from the study on Day 139 due to withdrawal of consent. [Manufacturer's Control No. JAUSA32461]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30272 (A30465 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30272 (serious adverse events: depression, psychosis, suicide attempt): This 45-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 19. His first psychiatric hospitalization was at age 19. The number of previous psychiatric hospitalizations was 8. There was no family history of psychiatric illness. Previous bipolar medications included perphenazine 16-24 mg/day and tiotixene 10 mg bid, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	6
	15	7
	20	49
USA-113	20	95
	0	1
	20	17
	0	1
	20	19
	0	1
	20	4
	0	3
	20	163
	0	11

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	Y	71	16	Recovered	None	Severe	Doubtful	Y
Psychosis	Y	71	16	Recovered	None	Moderate	Possible	Y
Suicide attempt ^b	Y	71	36	Recovered	None	Moderate	Possible	Y
Therapeutic response increased ^c	Y	195	2	Recovered	None	Severe	None	Y
Suicide attempt ^b	Y	195	2	Recovered	None	Moderate	None	Y
Psychosis	Y	195	2	Recovered	None	Moderate	Possible	Y
Suicide attempt ^d	Y	371	7	Recovered	None	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: suicidal tendency

^c Investigator verbatim: overdose chloral hydrate

^d Investigator verbatim: suicidal ideation, hospitalized

Assessment Scores

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	92	Marked	-
USA-113	62	Week 8/study entry	103	Marked	Minimally worse
	90	Week 12/week 4	68	Moderate	Much improved
	115	Week 16/week 8	63	Moderate	Much improved
	146	Week 20/week 12	63	Moderate	Much improved
	196	Week 28/week 20	80	-	-
	259	Week 36/week 28	65	Moderate	Much improved
	367	Week 52/week 44	91	Moderate	Minimally improved

The subject experienced intermittent episodes of depression throughout study RIS-USA-112 and RIS-USA-113. The depressions were treated with fluoxetine hydrochloride 20 mg/day. On Day 71, while on treatment with fluoxetine, the subject was hospitalized due to psychosis, depression and suicide attempt. *The subject admitted lapsing into illicit drug and alcohol abuse. The admitting psychiatrist attributed the events as possibly due to illicit drug use and the initiation of fluoxetine. Fluoxetine was discontinued, the study medication was continued and the subject remained hospitalized for observation. The subject recovered after 16 days, and was discharged on study medication (source: CIOMS).* [Manufacturer's Control No. JAUSA32259]

On Day 195, the subject was rehospitalized due to psychosis, suicide attempt (investigator verbatim: suicidal tendency), and therapeutic response increased (investigator verbatim: overdose chloral hydrate). *The subject had become upset over being denied disability benefits and had a 1-day lapse with alcohol, cocaine and marijuana, and overdosed on an unknown amount of chloral hydrate in an attempt to go to sleep. In the hospital he was lavaged and given activated charcoal. The study medication continued. The subject recovered after 2 days and was discharged (source: CIOMS).* [Manufacturer's Control No. JAUSA34015]

On Day 367, the subject had stopped taking study medication and began therapy with olanzapine 20 mg at bedtime. On Day 371, the subject was rehospitalized due to a suicide attempt (investigator verbatim: suicidal ideation, hospitalized). The subject completed the study on Day 377. The subject had recovered by then. *(source: CIOMS).* [Manufacturer's Control No. JAUSA36072]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30281 (A30352 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30281 (serious adverse event: psychosis): This 37-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 23. His first psychiatric hospitalization was at age 23. The number of previous psychiatric hospitalizations was 5. There was no family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 200 mg/4 weeks and haloperidol 10 mg bid, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	8
	5	1
	10	5
	15	6
	20	35
USA-113	20	73
	0	1
	20	191
	0	2
	10	1
	20	7
	0	4

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day *	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Confusion	Y	127	7	Recovered	None	Severe	None	Y
Amnesia	Y	127	4	Recovered	None	Severe	None	Y
Crying abnormal	Y	127	4	Recovered	None	Moderate	None	N
Psychosis	Y	127	4	Recovered	Dose reduced	Severe	None	Y
Thinking abnormal	Y	127	4	Recovered	Dose reduced	Severe	None	Y
Delusion	Y	136	7	Recovered	None	Moderate	Possible	Y
Confusion	Y	136	7	Recovered	None	Moderate	Possible	Y
Anxiety	Y	139	3	Recovered	None	Mild	None	N
Agitation	Y	214	5	Recovered	None	Moderate	None	N
Anxiety	Y	214	5	Recovered	None	Moderate	None	N
Delusion	Y	244	4	Recovered	None	Moderate	None	Y
Confusion	Y	244	4	Recovered	None	Moderate	None	Y
Psychosis	Y	320	15	Not recovered	Permanent stop	Moderate	None	Y
Delusion	Y	320	15	Not recovered	None	Severe	None	Y

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Confusion	Y	320	15	Not recovered	None	Moderate	None	Y
Agitation	Y	321	14	Not recovered	None	Mild	None	N

^aDay = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	84	Moderate	-
USA-113	56	Week 8/study entry	46	Mild	Much improved
	84	Week 12/week 4	-	Mild	Much improved
	112	Week 16/week 8	53	Mild	Much improved
	141	Week 20/week 12	58	Moderate	Minimally worse
	196	Week 28/week 20	61	-	-
	249	Week 36/week 28	51	Mild	Minimally improved
	333	Week 48/week 40	60	Moderate	Minimally worse

On Day 127, the subject was hospitalized due to confusion, amnesia, abnormal crying, psychosis and abnormal thinking. The investigator considered the events to be severe in intensity and not related to the study medication. Study medication was temporarily discontinued (Day 129), and the subject was treated with haloperidol (5 mg bid), valproate semisodium (250 mg tid) and desipramine (75 mg/day).

On Day 136, the subject was rehospitalized due to delusion and confusion. The events were moderate in intensity and the investigator considered the events to be possibly related to the study medication. The subject improved in 6 days, and the subject was discharged from the hospital.

On Day 244, the subject was rehospitalized for 2 days (source: CIOMS) due to delusion and confusion. The investigator considered the events to be moderate in intensity and not related to the study medication.

On Day 320, the subject was rehospitalized due to psychosis, delusion, confusion, and agitation. The investigator considered all events to be not related to the study medication. *The subject had a history of short psychotic episodes several times a year (source: CIOMS).* The subject received treatment with lorazepam (2 mg/6h PRN), temazepam (15 mg/day), diphenhydramine (25-50 mg/day) and chloral hydrate (500 mg/day). The study medication was temporarily discontinued on Days 321 and 322 and permanently discontinued on Day 330. The subject discontinued from the study on Day 334 *secondary to lack of improvement.* [Manufacturer's Control Nos. JAUSA33177, JAUSA35389, and JAUSA34590]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30282 (A30353 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30282 (serious adverse events: suicide attempt, convulsions, hallucination, depersonalization, tremor): This 42-year-old Black male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 33. His first psychiatric hospitalization was at age 39. The number of previous psychiatric hospitalizations was 1. There was no family history of psychiatric illness. Previous bipolar medications were not present or unknown. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	10
	15	8
	20	47
USA-113	15	16
	0	6
	15	13
	20	146
	-	17
	0	14

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Suicide attempt	Y	82	1	Recovered	Temporary stop	Moderate	None	Y
Convulsions ^b	Y	82	1	Recovered	Temporary stop	Severe	None	Y
Hallucination ^c	Y	82	21	Recovered	None	Moderate	None	Y
Hallucination	Y	103	11	Recovered	None	Severe	None	Y
Depersonalization	Y	103	11	Recovered	None	Moderate	Possible	Y
Tremor	Y	103	11	Recovered	None	Moderate	Possible	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: seizures secondary to boric acid ingestion

^c Investigator verbatim: increased auditory hallucinations hospitalized from 5/1/98-6/1/98

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	-6	Baseline	85	Moderate	-
USA-113	100	Week 16/week 8	78	Moderate	Minimally worse
	128	Week 20/week 12	61	Mild	-
	156	Week 24/week 16	70	Mild	Much improved
	196	Week 28/week 20	56	-	-
	277	Week 40/week 32	52	Mild	Minimally improved

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 82, the subject experienced hallucinations and attempted suicide by drinking insecticide (boric acid), which caused severe convulsions. *He was brought to the emergency room by his roommate.* He was treated with IV fluids 3.175 L/day and renal dialysis, and with haloperidol (dose unknown), chloral hydrate 500 mg and clonazepam 1 mg/day. *While in the emergency room he experienced a left focal seizure, which was treated with IV lorazepam 8 mg. The seizure resolved, but he was hospitalized for observation (source: CIOMS).* The investigator considered the events to be not related to study medication. Study medication was temporarily discontinued.

After 21 days when the subject was still hospitalized (Day 103), the hallucinations worsened again. This event was considered to be severe and not related to treatment by the investigator. The subject also experienced depersonalization and tremor. These events were considered to be moderate and possibly related to treatment by the investigator. After 11 days the events subsided and the subject was discharged from the hospital (after 1 month). Concomitant medication was flurazepam hydrochloride 30 mg/day PRN for 12 days for insomnia. [Manufacturer's Control No. JAUSA32818]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30334 (A30414 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30334 (serious adverse event: depression): This 50-year-old Caucasian female subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 49. Her first psychiatric hospitalization was at age 44. The number of previous psychiatric hospitalizations was 1. There was a family history of psychiatric illness. Previous bipolar medications included thioridazine hydrochloride 300 mg/day, which was discontinued at the start of study RIS-USA-112. Concomitant medications were levothyroxin sodium 125 mcg/day for Graves' Disease and simvastatin 1 tablet/day for hypercholesterolemia. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	38
	15	6
	20	14
USA-113	20	320
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	N	45	46	Recovered	None	Severe	Possible	Y
Suicide attempt ^b	N	45	47	Recovered	None	Severe	Possible	Y
Depression	Y	91	29	Recovered	None	Moderate	Doubtful	Y
Depression	Y	203	29	Recovered	None	Moderate	None	N
Depression	Y	315	36	Recovered	None	Moderate	Possible	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: suicidal ideation

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	84	Moderate	-
USA-113	59	Week 8/study entry	72	Moderate	Minimally worse
	91	Week 12/week 4	75	Moderate	Unchanged
	119	Week 16/week 8	78	Moderate	Minimally improved
	147	Week 20/week 12	63	Moderate	Much improved
	259	Week 36/week 28	64	Moderate	Much improved
	379	Day 379	47	Mild	Much improved

On Day 91, the subject experienced depression. The investigator considered the event to be moderate and to be doubtfully related to study medication. Treatment was started with amfebutamone hydrochloride 100 mg bid/tid. The subject recovered after 29 days. The subject had had several episodes of depression in study RIS-USA-112. On Day 203 and Day

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

315, the subject again experienced an episode of depression. Treatment with amfebutamone hydrochloride 100 mg bid/tid was continued. The subject completed the study on Day 379.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30412 (A30513 in RIS-USA-112)
Country: United States of America
Treatment Group: Olanzapine

Subject A30412 (serious adverse event: surgical intervention): This 45-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 15. Her first psychiatric hospitalization was at age 15. The number of previous psychiatric hospitalizations was 3. There was no family history of psychiatric illness. Previous bipolar medications included risperidone 6 mg/day, which was discontinued before the start of study RIS-USA-112.

The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	55
USA-113	10	319
	0	1

The relevant adverse events are shown in the table below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Surgical intervention ^b	Y	319	1	Recovered	None	Mild	None	Y
Surgical intervention ^c	Y	319	1	Recovered	None	Mild	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: hysterectomy

^c Investigator verbatim: hiatal hernia

On Day 319, the subject underwent hysterectomy and surgical treatment of a hiatal hernia. The investigator considered the event to be mild and not related to treatment. Concomitant medications were cefotetan disodium (1 g IV) and cefalexin monohydrate (500 mg qid) as prophylaxis for postoperative infection, metronidazole (500 mg bid) as postoperative antibiotic, tylox, pethidine hydrochloride, hydroxyzine embonate, and vicodin PRN for postoperative pain, and prochlorperazine edisylate (10 mg IM PRN) for nausea and bisacodyl (1 tab/day) for concomitant nausea and constipation respectively. The subject recovered and completed the study after 375 days. [Manufacturer's Control No. JAUSA35646]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30009 (A30012 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30009 (serious adverse event: psychosis): This 41-year-old Caucasian female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 21. Her first psychiatric hospitalization was at age 21. Her number of previous psychiatric hospitalizations was 20. The subject had a family history of psychiatric illness. Previous bipolar medications included 'other neuroleptics' (blinded study medication), which was discontinued before the start of study RIS-USA-112. Ongoing medications that had started before the start of the study included clonazepam 1 mg/day PRN for anxiety and fluoxetine hydrochloride 20 mg/day for depression.

The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	57
USA-113	4	21

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	N	-	51 ^c	Not recovered	None	Mild	None	N
Psychosis ^b	Y	78	4	Recovered	Permanent stop	Severe	None	Y
Alcohol problem ^c	Y	78	4	Recovered	None	Moderate	None	N
Suicide attempt ^d	Y	78	4	Recovered	None	Mild	None	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: Increasing psychosis

^c Investigator verbatim: Alcohol intoxication

^d Investigator verbatim: Suicidal

^e AE duration in the study

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	89	Moderate	-
USA-113	57	Week 8/study entry	-	Mild	Much improved

On Day 78 (RIS-USA-113), the subject was admitted to the psychiatric unit with the serious adverse event psychosis of severe intensity (investigator verbatim: increased psychosis), alcohol problem (investigator verbatim: alcohol intoxication), and suicide attempt (investigator verbatim: suicidal). The investigator considered the events to be not related to the study medication. The subject was discontinued from the study and was treated with

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

risperidone 1 mg bid and lorazepam 2 mg/6 h PRN. *The subject stabilized and was discharged on Day 81 (source: CIOMS). [Manufacturer's Control No. JAUSA32565]*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events

RIS-USA-113

CRF ID: A30044 (A30057 in RIS-USA-112)

Country: United States of America

Treatment Group: Risperidone (crossover subject)

Subject A30044 (serious adverse event: hospitalization): This 32-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 27. His first psychiatric hospitalization was at age 30. There was one previous psychiatric hospitalization. The subject did not have a family history of psychiatric illness. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	28
	15	27
USA-113	6	24
	6	30
	4	11
	0	62

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Somnolence	Y	83	38	Recovered	Dosage reduced	Mild	Possible	N
Thinking abnormal ^b	Y	124	45	Recovered	None	Mild	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: court ordered hospitalization (evaluate completely to stand trial)

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	83	Moderate	-
USA-113	56	Week 8/study entry	78	Moderate	Minimally improved
	82	Week 12/week 4	81	Moderate	Minimally improved
	110	Week 16/week 8	83	Moderate	Minimally improved

On Day 120 the subject stopped taking study medication. Four days later, on Day 124, the subject was hospitalized because of a court-ordered hospitalization, for a complete evaluation of the subject if he was able to stand trial. During this period the subject was treated with olanzapine 5-20 mg/day for psychosis, and (for 2 days) with oxazepam 15 mg/day for anxiety. Study medication was not resumed after discharge 45 days later. The subject was discontinued from the study on Day 182.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30050 (A30063 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30050 (serious adverse event: delusion, hallucination, paranoid reaction, psychosis, and suicide attempt): This 40-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 19. His first psychiatric hospitalization was at age 19. His number of previous psychiatric hospitalizations was 7. The subject did not have a family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 200 mg/4 weeks, which was discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	13
	6	42
USA-113	6	117
	0	1
	6	190
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

<i>Adverse event details</i>								
<i>MedDRA preferred term</i>	<i>Emerged in RIS-USA-113</i>	<i>Start day^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-assigned relationship</i>	<i>SAE (Y/N)</i>
Delusion	Y	173	7	Recovered	None	Moderate	Doubtful	Y
Hallucination	Y	173	7	Recovered	None	Moderate	Doubtful	Y
Paranoid reaction	Y	173	7	Recovered	None	Moderate	Doubtful	Y
Psychosis	Y	173	7	Recovered	None	Moderate	Doubtful	Y
Suicide attempt	Y	173	7	Recovered	None	Moderate	Doubtful	Y

^a Day = Day in study from the start of USA-112

<i>Assessment Scores</i>					
<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	1	Baseline	81	Marked	-
USA-113	56	Week 8/study entry	42	Moderate	Minimally improved
	87	Week 12/week 4	47	Moderate	Minimally improved
	111	Week 16/week 8	47	Moderate	Minimally improved
	140	Week 20/week 12	48	Moderate	Minimally improved
	196	Week 28/week 20	43	-	-
	252	Week 36/week 28	49	Moderate	Minimally improved
	364	Week 52/week 44	48	Moderate	Minimally improved

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Discontinuations Due to Adverse Events

On Day 173, the subject reported the serious adverse events delusion, hallucination, paranoid reaction, psychosis, and suicide attempt. Severity was moderate and the investigator considered the events to be doubtfully related to treatment. The subject was hospitalized for these events. The subject was treated with lorazepam. The subject completed the study on Day 364. [Manufacturer's Control No. JAUSA33557]

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30060 (A30217 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30060 (serious adverse event: catatonic reaction, paranoid reaction and hypokinesia): This 36-year-old Black female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 33. Her first psychiatric hospitalization was at age 33. Her number of previous psychiatric hospitalizations was 3. The family history of psychiatric illness was unknown. Previous bipolar medications included haloperidol decanoate 2.5 mL/day and risperidone 2 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	57
USA-113	2	55
	0	36

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Catatonic reaction	Y	112	37	Not recovered	None	Severe	Possible	Y
Paranoid reaction	Y	112	37	Not recovered	None	Severe	Possible	Y
Hypokinesia	Y	112	37	Not recovered	None	Severe	Possible	Y

^aDay = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	56	Mild	-
USA-113	57	Week 8/study entry	97	Mild	Unchanged
	85	Week 12/week 4	54	Mild	Unchanged
	112	Week 16/week 8	113	Moderate	Much worse

Time interval	Days in phase	Total ESRS	Parkinsonism total score	Dystonia total score	Dyskinesia total score	CGI-dyskinesia	CGI-parkinsonism	CGI-dystonia	Stage of parkinsonism
Baseline	1	4	2	0	2	Mild	Very mild	Absent	Stage I
Week 8/study entry	57	1	1	0	0	Absent	Absent	Absent	Absent
Week 12/week 4	85	1	1	0	0	Absent	Absent	Absent	Absent
Week 16/week 8	112	0	0	0	0	Absent	Absent	Absent	Absent

On Day 112, the subject experienced catatonic reaction, paranoid reaction, and hypokinesia and was hospitalized. The events were considered to be of severe intensity. The investigator

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

considered the events to be possibly related to treatment. The subject was discontinued from the study on Day 148 due to non-compliance. The subject had not yet recovered at that time. [Manufacturer's Control No. JAUSA32821]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30098 (A30436 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30098 (serious adverse events: delusion and headache): This 38-year-old Black female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 24. Her first psychiatric hospitalization was at age 24. Her number of previous psychiatric hospitalizations was 12. The subject had no family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate (300 mg IM/month), which was discontinued at the start of study RIS-USA-112. Concomitant medication was yellow phenolphthalein 1/day PRN for constipation. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	7
	6	42
USA-113	6	39
	0	5
	6	29

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged in USA-113</i>	<i>Start Day ^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE (Y/N)</i>
Headache	Y	128	2	Recovered	None	Severe	None	Y
Delusion	Y	128	2	Recovered	Permanent stop	Moderate	None	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	1	Baseline	99	Severe	-
USA-113	56	Week 8/study entry	101	Severe	Unchanged
	100	Week 16/week 8	108	Severe	Much worse
	129	Week 20/week 12	124	Severe	Much worse

On Day 128 the subject experienced delusion and headache. The intensity of the headache was severe, the intensity of delusion was moderate. The investigator considered the events to be not related to treatment. The subject recovered after 2 days. The subject was discontinued from the study on Day 129.

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Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30115 (A30145 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30115 (serious adverse event: pulmonary carcinoma): This 61-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 28. His first psychiatric hospitalization was at age 28. His number of previous psychiatric hospitalizations was 5. The subject had no family history of psychiatric illness. Previous bipolar medications included tiotixene 10 mg/day, which was discontinued before the start of study RIS-USA-112.

The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	42
	2	14
USA-113	2	227

The relevant adverse event is shown in the table below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged in USA-113</i>	<i>Start Day^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE (Y/N)</i>
Pulmonary carcinoma ^b	Y	283	1 ^c	Not recovered	Permanent stop	Severe	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: Hospitalization for lung mass (squamous cell carcinoma)

^c AE duration in the study

On Day 283, the subject experienced pulmonary carcinoma (investigator verbatim: hospitalization for lung mass [squamous cell carcinoma]). The event was of severe intensity. The investigator considered the event to be not related to the study medication. The subject was discontinued from the study on Day 283. [Manufacturer's Control No. JAUSA35052]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30122 (A30152 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30122 (serious adverse event: tooth disorder): This 52-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 28. His first psychiatric hospitalization was at age 28. His number of previous psychiatric hospitalizations was 4. The family history of psychiatric illness was unknown. Previous bipolar medications included haloperidol decanoate (150 mg/month) and haloperidol (10 mg/day), which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	7
	6	43
USA-113	6	320
	0	8

The relevant adverse event is shown in the table below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Tooth disorder ^b	Y	139	23	Recovered	None	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: dental abscess (hospitalized)

On Day 139, the subject experienced tooth disorder (investigator verbatim: dental abscess) and was hospitalized. The event was considered to be of moderate intensity and not related to treatment. The event was treated with amoxicillin 1500 mg STAT, 500 mg tid, 500 mg bid, 500 mg/day subsequently) and chlorhexidine gluconate 30 cc/day. The subject completed the study on Day 385. [Manufacturer's Control No. JAUSA32973]

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Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30129 (A30163 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30129 (serious adverse events: depression, hallucination, suicide attempt):
This 40-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 25. His first psychiatric hospitalization was at age 25. His number of previous psychiatric hospitalizations was 2. There was a family history of psychiatric illness. Previous bipolar medications included olanzapine 10 mg/day and chlorpromazine (50-400 mg/day), which were discontinued at the start of study RIS-USA-112.

The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)		Dose (mg)	Duration (days)
USA-112	4	13	USA-113	4	10
	0	1	cont'd	0	1
	4	4		4	3
	0	2		0	1
	6	5		4	2
	0	2		0	1
	6	9		4	4
	6	21		6	9
USA-113	6	5		0	1
	6	51		6	11
	4	11		0	1
	0	1		6	131
	4	14		0	1
	0	2		6	48
	4	5		0	1
	0	1			

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Depression	Y	87	106	Recovered	None	Moderate	Possible	N
Depression ^b	Y	193	67	Recovered	None	Severe	Doubtful	Y
Suicide attempt ^b	Y	193	67	Recovered	None	Severe	Doubtful	Y
Hallucination	Y	193	67	Recovered	None	Severe	None	Y
Anxiety	Y	207	52	Recovered	None	Moderate	Possible	N
Depression	Y	314	60	Not recovered	None	Moderate	Possible	N

^a Day = Day in study from the start of USA-112

^b With hospitalization

Assessment Scores

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	1	Baseline	76	Moderate	-
USA-113	59	Week 8/study entry	72	Moderate	Much improved
	87	Week 12/week 4	68	Moderate	Much improved
	115	Week 16/week 8	76	Moderate	Much improved
	141	Week 20/week 12	76	Moderate	Minimally improved
	196	Week 28/week 20	66	-	-
	255	Week 36/week 28	87	Moderate	Much improved
	373	Week 52/week 44	78	Moderate	Much improved

On Day 193, the subject was hospitalized for the serious adverse events depression, hallucination and suicide attempt. The adverse events were considered to be of severe intensity. The investigator considered the events to be doubtfully or not related to treatment, *and due to increased stress at home with the family (source: CIOMS)*. The depression and suicidal feelings were treated with sertraline hydrochloride 200-225 mg/day. The subject recovered after 67 days and was discharged from the hospital. The subject completed the study on Day 372. [Manufacturer's Control No. JAUSA32971]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30132 (A30167 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30132 (serious adverse event: depression aggravated): This 36-year-old Caucasian male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 27. His first psychiatric hospitalization was at age 28. His number of previous psychiatric hospitalizations was 7. The subject had no family history of psychiatric illness. Previous bipolar medications included perphenazine (8 mg bid), which was discontinued at the start of study RIS-USA-112. Concomitant medications were sertraline hydrochloride 50 mg/day and amfebutamone hydrochloride 150 mg/day for depression. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	16
	2	4
	4	5
	6	5
	10	1
	6	11
	6	15
USA-113	6	83
	6	3
	6	2
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	N	52	93	Recovered	None	Moderate	Possible	N
Depression aggravated	Y	145	2 ^b	Not recovered	Permanent stop	Severe	Possible	Y

^a Day = Day in study from the start of USA-112

^b Days in the study

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	76	Moderate	-
USA-113	55	Week 8/study entry	60	Mild	Much improved
	86	Week 12/week 4	60	Mild	Much improved
	118	Week 16/week 8	53	Mild	Very much improved
	141	Week 20/week 12	56	Mild	Very much improved
	146	Week 20/week 12	52	Moderate	Minimally worse

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Discontinuations Due to Adverse Events

On Day 52, the subject experienced moderate depression. The event was treated with sertraline hydrochloride 50 mg/day and amfebutamone hydrochloride 150 mg/day. On Day 145, the depression aggravated and became severe. The investigator considered the depression to be possibly related to treatment. The subject was discontinued from the study on Day 146, *was started on other antipsychotic medication, improved and was discharged.* [Manufacturer's Control No. JAUSA33348]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30146 (A30182 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30146 (serious adverse event: psychosis): This 30-year-old Caucasian female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 20. Her first psychiatric hospitalization was at age 18. Her number of previous psychiatric hospitalizations was 6. The subject had no family history of psychiatric illness. Previous bipolar medications included lorazepam 0.5 mg PRN and thioridazine hydrochloride 200 mg/day, which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	14
	6	7
	6	39
USA-113	6	123
	0	1

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	183	4	Recovered	Permanent stop	Severe	Doubtful	Y

^aDay = Day in study from the start of USA-112

^bInvestigator verbatim: Increase of psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	106	Moderate	-
USA-113	60	Week 8/study entry	72	Mild	Minimally improved
	87	Week 12/week 4	69	Mild	Minimally improved
	116	Week 16/week 8	68	Mild	Minimally improved
	144	Week 20/week 12	60	Mild	Unchanged
	184	Week 28/week 20	-	Moderate	Minimally worse

On Day 183, the subject experienced psychosis (investigator verbatim: increase of psychosis) and was hospitalized. The intensity of the event was severe. The investigator considered the event to be doubtfully related to treatment. The event was treated with thioridazine hydrochloride 200 mg/day. The subject recovered after 4 days. *The subject's urine drug screen was positive for THC, and she acknowledged that she had been using other drugs as well. She has a history of substance abuse in the past. The investigators attributed this episode and exacerbation of psychosis to her substance abuse.* Treatment was permanently

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

stopped due to this serious adverse event on Day 184. *The subject was discharged on Day 187 in fair condition (source: CIOMS).* [Manufacturer's Control No. JAUSA32567]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30154 (A30192 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30154 (serious adverse event: delusion): This 60-year-old Black female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 35. Her first psychiatric hospitalization was at age 35. Her number of previous psychiatric hospitalizations was 3. There was no family history of psychiatric illness. Previous bipolar medications included haloperidol 3 mg/day, which was discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	42
	0	1
	4	15
USA-113	4	65
	6	188
	0	14
	2	39
	0	2

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Agitation	Y	123	3	Recovered	Dosage reduced	Mild	Possible	N
Agitation	Y	305	4	Recovered	None	Mild	Possible	N
Delusion ^b	Y	311	15	Recovered	Temporary stop	Mild	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: delusions d/t neurosis - hospitalization

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	91	Moderate	-
USA-113	58	Week 8/study entry	65	Mild	Minimally improved
	87	Week 12/week 4	59	Mild	Unchanged
	115	Week 16/week 8	69	Mild	Unchanged
	143	Week 20/week 12	68	Mild	Unchanged
	196	Week 28/week 20	66	-	-
	254	Week 36/week 28	68	Mild	Unchanged
	364	Week 52/week 44	65	Mild	Unchanged

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 311, the subject was hospitalized with delusion (investigator verbatim: delusions d/t neurosis - hospitalization). The event was considered to be of mild intensity and not related to treatment. The study medication was temporarily stopped and the subject was treated with sertraline hydrochloride 50 mg bid (indication verbatim: somatic delusion secondary to depressive neurosis). After 15 days the subject recovered and continued study medication. Previously in the study the subject had experienced 2 episodes of agitation, on Day 123 with a duration of 3 days and on Day 305 with a duration of 4 days. The events were considered to be of mild intensity. In the first episode the dose was reduced, in the second episode the event was treated with lorazepam 2 mg/day. The subject completed the study on Day 366. [Manufacturer's Control No. JAUSA35473]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30170 (A30220 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30170 (serious adverse events: depression, lacrimation abnormal, and suicide attempt): This 26-year-old Caucasian male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 24. His first psychiatric hospitalization was at age 24. His number of previous psychiatric hospitalizations was 2. The family history of psychiatric illness was unknown. Previous bipolar medications included Zyprexa (olanzapine) 10 mg/day and valproate semisodium 250 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	49
USA-113	6	126
	6	181
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Suicide attempt ^b	Y	161	6	Recovered	None	Severe	Possible	Y
Lacrimation abnormal	Y	161	23	Recovered	None	Severe	Possible	Y
Depression	Y	161	27	Recovered	None	Severe	Possible	Y
Suicide attempt ^c	Y	194	171	Recovered	None	Mild	Possible	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: suicidal thoughts

^c Investigator verbatim: intermittent suicidal ideation

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	79	Mild	-
USA-113	53	Week 8/study entry	76	Mild	Unchanged
	78	Week 12/week 4	42	Mild	Unchanged
	111	Week 16/week 8	64	Mild	Unchanged
	131	Week 20/week 12	40	Very mild	Unchanged
	196	Week 28/week 20	73	-	-
	250	Week 36/week 28	54	Mild	Unchanged
	364	Week 52/week 44	51	Mild	Unchanged

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 161, the subject was hospitalized due to depression and suicide attempt (investigator verbatim: suicidal thoughts). The subject also had lacrimation abnormal. The investigator considered the events of severe intensity and to be possibly related to treatment. The subject recovered from the depression after 27 days. The suicidal thoughts subsided after 6 days, although suicidal ideation was reported again intermittently from Day 194 until study completion. The investigator considered the latter to be not serious, mild, and possibly related to treatment. The subject completed the study on Day 364. [Manufacturer's Control No. JAUSA33757]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30176 (A30218 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30176 (serious adverse event: agitation): This 26-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 26. His first psychiatric hospitalization was at age 26. His number of previous psychiatric hospitalizations was 2. The subject did not have a family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 150-200 mg (frequency unknown), olanzapine 10-15 mg/day, and risperidone 1-5 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	7
	6	43
USA-113	6	98

The relevant adverse event and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Agitation ^b	Y	155	1	Not recovered	None	Severe	Possible	Y

^aDay = Day in study from the start of USA-112

^bInvestigator verbatim: increased agitation

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	84	Mild	-
USA-113	57	Week 8/study entry	79	Mild	Unchanged
	85	Week 12/week 4	76	Mild	Unchanged
	113	Week 16/week 8	78	Mild	Unchanged
	141	Week 20/week 12	97	Mild	Minimally worse
	155	Week 24/week 16	123	Moderate	Minimally worse

On Day 155, the subject was hospitalized due to agitation (investigator verbatim: increased agitation). *He became unresponsive to the medication and became very agitated (source: CIOMS).* The intensity was severe and the investigator considered the event to be possibly related to treatment. The subject was discontinued from the study on Day 155 due to insufficient response. [Manufacturer's Control No. JAUSA33539]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30187 (A30233 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30187 (serious adverse event: psychosis): This 33-year-old Black female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 33. She had not been previously hospitalized. The subject had no family history of psychiatric illness. Previous bipolar medications included Zyprexa (olanzapine) 5-10 mg/day and risperidone 1 mg once, which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	58
USA-113	4	28
	2	30
	4	168
	6	16
	0	3

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	297	7	Not recovered	Permanent stop	Severe	Doubtful	Y
Agitation	Y	297	7	Not recovered	Permanent stop	Severe	Doubtful	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: severe psychotic exacerbation, increased psychotic delusion, hospitalized

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	92	Marked	-
USA-113	59	Week 8/study entry	48	Very mild	Very much improved
	87	Week 12/week 4	53	Mild	Much improved
	115	Week 16/week 8	52	Very mild	Much improved
	143	Week 20/week 12	81	Mild	Much improved
	196	Week 28/week 20	65	-	-
	250	Week 36/week 28	59	Mild	Much improved

On Day 297, the subject was hospitalized due to psychosis (investigator verbatim: severe psychotic exacerbation, increased psychotic delusion, hospitalized) and agitation. Intensity was severe and the investigator considered the events to be doubtfully related to treatment. *A number of attempts were made to have her take an additional tablet daily, but the subject refused. Her condition worsened and she refused all medication.* On Day 303, the subject was discontinued from the study. *She recovered approximately 5 weeks later (source: CIOMS).* [Manufacturer's Control No. JAUSA34819]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30192 (A30238 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30192 (serious adverse event: infection): This 49-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 39. His first psychiatric hospitalization was at age 49. His number of previous psychiatric hospitalizations was 1. The subject had a family history of psychiatric illness. Previous bipolar medications included olanzapine 10-15 mg/day, which was discontinued at the start of study RIS-USA-112. Concomitant medication was metformin hydrochloride 500 mg tid for diabetes mellitus Type II, during the study changed to glibenclamide 5 mg bid and discontinued on Day 216. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	21
	6	38
USA-113	6	53
	4	244
	0	1

The relevant adverse events are shown in the table below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Infection ^b	Y	132	40	Recovered	None	Mild	Doubtful	N
Infection ^c	Y	216	5	Recovered	None	Moderate	None	Y
Skin ulceration ^d	Y	221	137	Not recovered	None	Mild	Doubtful	N
Infection ^e	Y	307	3	Recovered	None	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: Skin infection L foot

^c Investigator verbatim: I. foot inf. d/t diabetes, (hospitalized) I. 2nd & 3rd toe cellulitis

^d Investigator verbatim: Left foot unhealed, ulcerated foot wound

^e Investigator verbatim: L foot infection d/t diabetes hospitalized cellulitis/left foot ulcer

On Day 132, the subject experienced infection (investigator verbatim: skin infection left foot). The event was treated with cefalexin 500 mg bid for 10 days. The subject recovered after 40 days. On Day 216, the subject experienced another infection on the left foot (cellulitis 2nd and 3rd toe, due to diabetes) which required hospitalization. The event was treated with sultamicillin IV (3 g in normal saline/6 h) for 4 days. The wound became ulcerated on Day 221. The event was treated with clavulin 875 mg bid for 7 days, and continuously with a zinc wrapping, but the subject did not recover. On Day 307, the subject was hospitalized again for the ulcerated left foot. The event was treated with sultamicillin IV (3 g in normal saline/6 h) for 3 days and subsequently with clavulin 875 mg bid for 10 days. The subject recovered after 3 days. The subject completed the study after 357 days. *The*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

investigator related the events to the underlying condition of diabetes (source: CIOMS).
[Manufacturer's Control Nos. JAUSA34690 and JAUSA35755]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30194 (A30249 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30194 (serious adverse event: psychosis): This 36-year-old Caucasian male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 31. His first psychiatric hospitalization was at age 31. His number of previous psychiatric hospitalizations was 10. The subject had a family history of psychiatric illness. Previous bipolar medications included risperidone (4 mg/day), which was discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	57
USA-113	4	187
	0	4

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	244	5	Not recovered	Permanent stop	Moderate	None	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: increased psychosis due to cocaine

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-113	58	Week 8/study entry	45	Mild	Minimally improved
	86	Week 12/week 4	41	Moderate	Minimally worse
	112	Week 16/week 8	47	Mild	Much improved
	135	Week 20/week 12	46	Mild	Much improved

On Day 244, the subject was hospitalized due to psychosis (investigator verbatim: increased psychosis due to cocaine). The subject had taken cocaine and crystal methamphetamine (source: CIOMS) since 10 days. The severity of the event was moderate. The investigator considered the event to be related to the crystal methamphetamine use (source: CIOMS). Study medication was stopped on Day 244 and the subject was discontinued from the study on Day 248. [Manufacturer's Control No. JAUSA35289]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30196 (A30246 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30196 (serious adverse event: psychosis): This 46-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 22. His first psychiatric hospitalization was at age 29. His number of previous psychiatric hospitalizations was 61. The subject had no family history of psychiatric illness. Previous bipolar medications included lithium 300 mg bid, thioridazine hydrochloride 300 mg/day, tiotixene 10 mg tid, fluphenazine hydrochloride 10 mg tid, and fluphenazine decanoate 37.5 mg/2 weeks, which were discontinued at the start of study RIS-USA-112.

The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	12
	6	26
	0	9
	6	4
USA-113	6	79
	0	14

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Psychosis ^b	Y	138	14	Not recovered	Permanent stop	Moderate	Doubtful	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: increased psychosis

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	98	Severe	-
USA-113	54	Week 8/study entry	101	Marked	Unchanged
	84	Week 12/week 4	86	Moderate	Minimally improved
	112	Week 16/week 8	86	Moderate	Unchanged
	138	Week 20/week 12	87	Severe	Unchanged

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 138, the subject was hospitalized due to psychosis (investigator verbatim: increased psychosis). The severity of the event was moderate. The investigator considered the event to be doubtfully related to treatment. Study medication was stopped on Day 138, and the subject was permanently discontinued from the study 14 days later (on Day 151). The subject had not yet recovered by that time and the subject was started on diphenhydramine hydrochloride 50 mg/day and olanzapine 20 mg/day. [Manufacturer's Control No. JAUSA33410]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30226 (A30283 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30226 (serious adverse event: psychosis): This 49-year-old Black female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 21. Her first psychiatric hospitalization was at age 25. Her number of previous psychiatric hospitalizations was 6. The subject had a family history of psychiatric illness. Previous bipolar medications included haloperidol 5 mg bid, which was discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	9
	6	6
	6	42
USA-113	6	91
	6	8
	6	42
	0	4

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged in USA-113</i>	<i>Start Day^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE (Y/N)</i>
Tremor	Y	86	117	Not recovered	None	Mild	Probable	N
Extrapyramidal disorder	Y	86	117	Not recovered	None	Mild	Probable	N
Bradykinesia	Y	86	117	Not recovered	None	Mild	Probable	N
Hyperkinesia	Y	86	117	Not recovered	None	Mild	Probable	N
Nervousness	Y	154	4	Recovered	None	Mild	Probable	N
Psychosis	Y	198	5	Not recovered	Permanent stop	Moderate	Possible	Y
Agitation	Y	198	5	Not recovered	None	Moderate	Possible	N
Fever	Y	198	40	Recovered	-	-	Doubtful	-
Tachycardia	Y	198	2	Recovered	-	-	Possible	-
Hyperprolactinaemia	Y	198	5	-	-	-	Possible	-
Creatine phosphokinase increased	Y	199	4	-	-	-	Possible	-

^aDay = Day in study from the start of USA-112

Assessment Scores

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	1	Baseline	86	Marked	-
USA-113	57	Week 8/study entry	57	Moderate	Much improved
	86	Week 12/week 4	57	Moderate	Much improved
	114	Week 16/week 8	59	Moderate	Much improved
	142	Week 20/week 12	58	Moderate	Much improved
	199	Week 28/week 20	75	Marked	Minimally improved

<i>Time interval</i>	<i>Days in phase</i>	<i>Total ESRS</i>	<i>Parkinsonism total score</i>	<i>Dystonia total score</i>	<i>Dyskinesia total score</i>	<i>CGI-dyskinesia</i>	<i>CGI-parkinsonism</i>	<i>CGI-dystonia</i>	<i>Stage of parkinsonism</i>
Week 8/study entry	57	10	8	0	2	Absent	Borderline	Absent	Absent
Week 12/week 4	86	16	13	0	3	Borderline	Moderate	Absent	Stage III
Week 16/week 8	114	9	9	0	0	Absent	Very mild	Absent	Stage II
Week 20/week 12	142	19	13	0	6	Mild	Mild	Absent	Stage II
Week 24/week 16	156	10	8	0	2	Borderline	Mild	Absent	Stage II
Week 28/week 20	199	7	5	0	2	Borderline	Borderline	Absent	Absent

On Day 198, the subject was hospitalized due to psychosis and agitation. Severity was moderate and the investigator considered the events to be possibly related to treatment. Study medication was discontinued and the subject was discontinued from the study on Day 202. She was treated with olanzapine 10 mg/day for the first 3 days and then with 20 mg/day. *Later, olanzapine was discontinued, and she was started on risperidone and lithium and the symptoms improved. She was discharged in stable condition to her home app. 1 month after discontinuation (source: CIOMS).*[Manufacturer's Control No. JAUSA33891]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30246 (A30308 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30246 (serious adverse event: anxiety, personality disorder, paranoid reaction, anorexia, weight decrease): This 48-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 27. He had not been previously hospitalized. The family history of psychiatric illness was unknown. Previous bipolar medications were unknown or not present. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	62
USA-113	4	28
	0	11
	4	2
	0	2

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Anxiety	Y	80	26	Not recovered	Dosage reduced	Severe	None	Y
Depression	Y	85	5	Recovered	None	Mild	Doubtful	N
Personality disorder ^b	Y	102	4	Not recovered	Permanent stop	Severe	None	Y
Paranoid reaction	Y	102	23	Recovered	Permanent stop	Moderate	Doubtful	Y
Anorexia	Y	102	23	Recovered	Permanent stop	Moderate	Doubtful	Y
Weight decrease	Y	102	23	Recovered	Permanent stop	Moderate	Doubtful	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: hospitalized, condition aggravated d/t grave passive neglect

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	-	Marked	-
USA-113	63	Week 8/study entry	79	Marked	Minimally improved
	91	Week 12/week 4	84	Moderate	Minimally worse
	105	Week 16/week 8	91	Marked	Much worse

The subject was hospitalized due to severe anxiety that started on Day 80, and mild depression that started on Day 85. The investigator considered the events to be not or doubtfully related to treatment. *The subject was started on sertraline 50-100 mg/day and was discharged in stable condition 9 days later (on Day 90). (source: CIOMS).*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

From Day 90 to Day 101 the subject did not take study medication. On Day 102, the subject was hospitalized due to personality disorder (investigator verbatim: hospitalized, condition aggravated due to grave passive neglect). The intensity of the event was severe and the investigator considered the event to be not related to treatment. The subject also reported paranoid reaction, anorexia, and weight decrease and was discontinued from the study on Day 105. Nineteen (19) days after discontinuation, the paranoid reaction, anorexia, and weight decrease had subsided. The subject had not yet recovered from the personality disorder. The anxiety that started on Day 80 was also ongoing. [Manufacturer's Control No. JAUSA32834 and JAUSA32974]

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30249 (A30311 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30249 (serious adverse events: delusion and paranoid reaction): This 59-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 29. His first psychiatric hospitalization was at age 29. His number of previous psychiatric hospitalizations was 8. The subject had no family history of psychiatric illness. Previous bipolar medications included olanzapine 10 mg/day and tiotixene 50 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	7
	6	44
USA-113	6	68
	0	2

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Paranoid reaction	Y	107	23	Recovered	Permanent stop	Moderate	Possible	Y
Delusion	Y	107	23	Recovered	None	Moderate	Possible	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	62	Marked	-
USA-113	58	Week 8/study entry	76	Moderate	Much improved
	84	Week 12/week 4	71	Moderate	Much improved
	115	Week 16/week 8	72	Moderate	Minimally improved
	129	Week 20/week 12	77	Moderate	Minimally worse

On Day 107, the subject was hospitalized due to delusion and paranoid reaction. The investigator considered the intensity of the events as moderate and as possibly related to treatment. The events were treated with lorazepam 1-2 mg/day (indication verbatim: agitation). The subject recovered after 23 days. Study medication was stopped on Day 126 and the subject was discontinued from the study on Day 128. [Manufacturer's Control No. JAUSA32970]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30267 (A30334 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30267 (serious adverse event: injury): This 45-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 20. His first psychiatric hospitalization was at age 20. His number of previous psychiatric hospitalizations was 25. There was no family history of psychiatric illness. Previous bipolar medications included haloperidol decanoate 250 mg/2 weeks, haloperidol 10 mg bid, and risperidone 3-6 mg/day, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	7
	6	25
	6	24
USA-113	6	125
	0	1
	6	182

The relevant adverse events are shown in the table below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Injury ^b	Y	181	32	Recovered	Temporary stop	Severe	None	Y
Pain ^c	Y	181	45	Recovered	None	Severe	None	N

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: fractured hip (right)

^c Investigator verbatim: hip pain secondary to fracture

On Day 181, the subject was hospitalized for surgery caused by a motor cycle accident (investigator verbatim: fractured hip (right)). The event was considered to be of severe intensity and not related to treatment. Study medication was temporarily discontinued (Day 182) and resumed the next day. The pain was treated with ibuprofen 600 mg bid, paracetamol 650 mg/4 h PRN, and vicodin 1-2 caps/4-6 h PRN. The subject recovered after 32 days and the pain subsided after 45 days. The subject completed the study on Day 364. [Manufacturer's Control No. JAUSA32968]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30275 (A30342 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30275 (serious adverse event: psychosis): This 29-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 27. His first psychiatric hospitalization was at age 27. His number of previous psychiatric hospitalizations was 1. The subject had a family history of psychiatric illness. Previous bipolar medications included 'other therapeutic products (blinded study medication' and Zyprexa (olanzapine, 5 mg/day), which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	3
	2	33
	0	2
USA-113	2	19
	2	194
	0	10

The relevant adverse event and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator- Assigned Relationship	SAE (Y/N)
Psychosis	Y	252	10	Recovered	Permanent stop	Severe	None	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	72	Marked	-
USA-113	57	Week 8/study entry	54	Moderate	Minimally improved
	85	Week 12/week 4	53	Moderate	Minimally improved
	113	Week 16/week 8	48	Moderate	Minimally improved
	141	Week 20/week 12	56	Moderate	Unchanged
	196	Week 28/week 20	54	-	-
	252	Week 36/week 28	67	Moderate	Minimally worse

On Day 252, the subject experienced psychosis (investigator verbatim: exacerbation of psychosis). The investigator considered the event to be of severe intensity and not related to the study medication. The event lasted 10 days and the subject recovered. Study medication was discontinued and the subject was treated with loxapine succinate 5 mg/day for psychosis and with benzotropeine 4 mg/day for prevention of EPS. The subject was discontinued from the study on Day 261.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30283 (A30355 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30283 (serious adverse event: paranoid reaction): This 26-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 26. His first psychiatric hospitalization was at age 26. His number of previous psychiatric hospitalizations was 1. The subject did not have a family history of psychiatric illness. Previous bipolar medications included risperidone 2 mg/day, which was discontinued at the start of study RIS-USA-112. Concomitant medication was benztropine mesilate 2 mg/day for mild parkinsonism symptoms. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	4
	2	4
	4	51
USA-113	4	21
	0	2
	4	27

The relevant adverse event and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Paranoid reaction	Y	81	5	Recovered	None	Mild	None	Y

^aDay = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	83	Moderate	-
USA-113	60	Week 8/study entry	48	Very mild	Much improved
	88	Week 12/week 4	41	Mild	-
	109	Week 16/week 8	60	Mild	Minimally improved

On Day 81, the subject was hospitalized due to paranoid reaction. Severity was mild and the investigator considered the event to be not related to treatment. *His condition improved and study medication continued uninterrupted. His worsening condition may have been caused by non-compliance (source: CIOMS).* The subject was withdrawn from the study on Day 109 due to ineligibility to continue the study. [Manufacturer's Control No. JAUSA33285]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30333 (A30413 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30333 (serious adverse events: aggressive reaction, confusion, chest pain, dyspnoea, psychosis, suicide attempt): This 44-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 24. His first psychiatric hospitalization was at age 24. His number of previous psychiatric hospitalizations was unknown. The subject had a family history of psychiatric illness. Previous bipolar medications included risperidone 9-12 mg/day, which was discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	45
	0	1
	2	9
USA-113	2	7
	4	26
	6	23
	6	35
	0	5

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Psychosis	Y	62	36	Recovered	Dosage reduced	Moderate	Probable	Y
Aggressive reaction	Y	113	6	Recovered	Dosage reduced	Severe	Possible	Y
Confusion	Y	113	6	Recovered	Dosage reduced	Severe	Possible	Y
Psychosis	Y	113	6	Recovered	Dosage reduced	Severe	Possible	Y
Psychosis	Y	124	28	Not recovered	Permanent stop	Moderate	Doubtful	Y
Suicide attempt	Y	124	28	Not recovered	Permanent stop	Moderate	Possible	Y
Dyspnoea	Y	136	16	Not recovered	None	Moderate	Doubtful	Y
Chest pain	Y	136	16	Not recovered	None	Moderate	Doubtful	N
Chest pain	Y	161	3	Recovered	None	-	Doubtful	Y

^aDay = Day in study from the start of USA-112

Assessment Scores

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	1	Baseline	62	Moderate	-
USA-113	58	Week 8/study entry	72	Moderate	Minimally improved
	85	Week 12/week 4	101	Moderate	Minimally worse
	112	Week 16/week 8	105	Severe	Much worse
	140	Week 20/week 12	116	Severe	Much worse

On Day 62, the subject experienced psychosis. Severity was moderate and the investigator considered the event to be probably related to treatment. Study medication was increased from 2 to 4 mg/day the next day and 4 weeks later to 6 mg/day. The subject recovered 36 days later.

On Day 113, the subject was hospitalized due to aggressive reaction, confusion, and psychosis. Intensity was severe and the investigator considered the events to be possibly related to treatment. *The study medication was increased from 3 tablets to 4 tablets daily 1 day prior to admission. The subject was discharged from the inpatient unit due to remission of symptom of psychosis on Day 118 (source: CIOMS).*

On Day 124, the subject was rehospitalized due to psychosis and suicide attempt. Severity was moderate and the investigator considered the psychosis to be doubtfully related and the suicide attempt to be possibly related to treatment. *He was prescribed risperidone 7 mg daily and amfebutamone sr 300 mg daily which were eventually discontinued on Day 151 because the investigator did not feel the drug was an effective type antipsychotic for this subject. The subject remained hospitalized. Clozapine was initiated and titrated to 125 mg daily. Although he was medication compliant he had not stabilized (source: CIOMS).*

While still in the hospital (Day 136), the subject was seen in the emergency room due to dyspnoea and chest pain. Intensity was moderate and the investigator considered the events to be doubtfully related to treatment. The events were treated with glyceryl nitrate (0.4 mg/5h PRN), azithromycin (250-500 mg/day) and ipratropium bromide 2 puffs tid.

On Day 161, 10 days after discontinuation from the study, the subject was rehospitalized to further treat his cardiac problems. *His ECG from Day 146 suggested cardiac wall changes (nos). The investigator assessed the chest wall pain as probably not related to study drug because of a family history of cardiac problems (source: CIOMS). The final diagnosis was arrhythmia (nos). (source: CIOMS) [Manufacturer's Control No. JAUSA32937].*

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30335 (A30418 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30335 (serious adverse event: allergic reaction): This 46-year-old Caucasian male subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 20. His first psychiatric hospitalization was at age 35. His number of previous psychiatric hospitalizations was 4. The subject had a family history of psychiatric illness. Previous bipolar medications included risperidone 4 mg/day, which was discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	55
USA-113	2	56
	4	28
	6	230
	0	1

The relevant adverse event is shown in the table below:

Adverse event details								
MedDRA preferred term	Emerged in RIS-USA-113	Start day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-assigned relationship	SAE (Y/N)
Allergic reaction ^b	Y	186	8	Recovered	None	Severe	Doubtful	Y

^a Day = Day in study from the start of USA-112

^b Investigator verbatim: hives all over body, allergic rxn – ER visit

On Day 186, the subject was treated in the emergency room for an allergic reaction (investigator verbatim: hives all over body, allergic rxn – ER visit). The intensity was severe and the investigator considered the event to be doubtfully related to treatment. The event was treated with diphenhydramine hydrochloride 50 mg/6 h for 6 days and prednisone (20 mg bid for 2 days 10 mg bid for the next 2 days). Study medication continued uninterrupted. The subject recovered after 8 days. The subject completed the study after 370 days. [Manufacturer's Control No. JRFUSA1999001894]

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Serious Adverse Events
RIS-USA-113
CRF ID: A30395 (A30494 in RIS-USA-112)
Country: United States of America
Treatment Group: Risperidone

Subject A30395 (serious adverse events: psychosis and intestinal obstruction): This 57-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 25. His first psychiatric hospitalization was at age 32. His number of previous psychiatric hospitalizations was 6. There was no family history of psychiatric illness. Previous bipolar medications included risperidone 1-2 mg bid and thioridazine hydrochloride 100 mg/day, which were discontinued at the start of study RIS-USA-112. Concomitant medication was glipizide 10 mg/day for diabetes mellitus. The subject completed 8-week treatment with risperidone in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	4	6
	6	7
	6	48
USA-113	6	24
	0	1
	6	108
	0	7

The relevant adverse events and assessment scores are shown in the tables below:

Adverse event details								
<i>MedDRA preferred term</i>	<i>Emerged in RIS-USA-113</i>	<i>Start day^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-assigned relationship</i>	<i>SAE (Y/N)</i>
Depression	Y	126	14	Recovered	None	Moderate	None	N
Depression	Y	139	36	Recovered	None	Severe	None	N
Depression	Y	174	28	Not recovered	None	Moderate	None	N
Psychosis	Y	193	9	Not recovered	None	Severe	None	Y
Intestinal obstruction	Y	214	10	Recovered	None	Severe	None	Y

^a Day = Day in study from the start of USA-112

Assessment Scores					
<i>Study</i>	<i>Days in study</i>	<i>Time interval</i>	<i>Total PANSS</i>	<i>CGI</i>	<i>CGI change</i>
USA-112	0	Baseline	86	Marked	-
USA-113	61	Week 8/study entry	56	Mild	Very much improved
	89	Week 12/week 4	57	Mild	Very much improved
	120	Week 16/week 8	55	Mild	Very much improved
	146	Week 20/week 12	70	Moderate	Minimally improved

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 193, the subject was hospitalized due to psychosis. The event was considered to be of severe intensity and not related to treatment. Study medication was discontinued and the subject was treated with risperidone and *trihexyphenidyl* (source: *CIOMS*). Study medication was not resumed and the subject was discontinued from the study on Day 201.

On Day 214, 2 weeks post study, the subject was hospitalized due to intestinal obstruction. The event was considered to be of severe intensity and not related to treatment. *A bowel resection was performed* (source: *CIOMS*) and the subject recovered after 10 days. [Manufacturer's Control No. JAUSA34294 and JRFUSA1999001896]

**Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events**

Subject Narratives for Adverse Events Leading to Discontinuation

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Adverse Events leading to Discontinuation

RIS-USA-113

CRF ID: A30137 (A30171 in RIS-USA-112)

Country: United States of America

Treatment Group: Olanzapine

Subject A30137 (adverse events leading to discontinuation: depression and suicide attempt): This 48-year-old Black male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 23. His first psychiatric hospitalization was at age 23. The number of previous psychiatric hospitalizations was 3. There was no family history of psychiatric illness. Previous bipolar medications included perphenazine (16 mg bid) and olanzapine (20 mg/day), which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	58
USA-113	10	43
	15	14

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Depression	Y	82	26	Recovered	None	Mild	Possible	N
Hallucination	Y	89	14	Recovered	Dosage reduced	Mild	Possible	N
Depression	Y	108	8	Not recovered	Permanent stop	Severe	Possible	N
Suicide attempt	Y	108	8	Not recovered	Permanent stop	Severe	Possible	N

^a Day = Day in study from the start of USA-112.

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	71	Moderate	-
USA-113	58	Week 8/study entry	56	Moderate	Minimally improved
	87	Week 12/week 4	60	Moderate	Minimally improved
	115	Week 16/week 8	63	Mild	Minimally improved

On Day 82, the subject experienced depression, and on Day 89 hallucination. The investigator considered the events to be mild in intensity and possibly related to the study medication. On Day 108, the subject experienced depression and suicide attempt. The investigator considered the events to be severe in intensity and possibly related to the study medication. The subject was permanently discontinued from the study on Day 115.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Adverse Events leading to Discontinuation

RIS-USA-113

CRF ID: A30158 (A30198 in RIS-USA-112)

Country: United States of America

Treatment Group: Olanzapine

Subject A30158 (adverse events leading to discontinuation: emotional lability and agitation): This 51-year-old Caucasian female subject had a primary diagnosis of schizophrenia (type: undifferentiated). The subject's age at onset was 17. Her first psychiatric hospitalization was at age 17. The number of previous psychiatric hospitalizations was 6. There was no family history of psychiatric illness. Previous bipolar medications included Zyprexa (olanzapine, 25 mg/day), which was discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	11
	15	5
	20	42
USA-113	20	51

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Agitation	N	19	51	Recovered	None	Mild	Probable	N
Emotional lability	Y	90	20	Not recovered	Permanent stop	Mild	Probable	N
Agitation	Y	102	8	Not recovered	Permanent stop	Mild	Probable	N

^a Day = Day in study from the start of USA-112

Assessment Scores					
Study	Days in study	Time interval	Total PANSS	CGI	CGI change
USA-112	0	Baseline	78	Moderate	-
USA-113	56	Week 8/study entry	87	Moderate	Minimally worse
	87	Week 12/week 4	80	Moderate	Minimally improved
	108	Week 16/week 8	91	Moderate	Minimally worse

On Day 90, the subject experienced emotional lability, and on Day 102 agitation. The investigator considered the events to be mild in intensity and probably related to the study medication. On Day 109, the study medication was stopped and the subject was discontinued from the study due to these events.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Adverse Events leading to Discontinuation
RIS-USA-113

CRF ID: A30175 (A30216 in RIS-USA-112)

Country: United States of America

Treatment Group: Olanzapine

Subject A30175 (adverse event leading to discontinuation: hepatic abnormal function): This 33-year-old Caucasian male subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 28. His first psychiatric hospitalization was at age 28. The number of previous psychiatric hospitalizations was 6. There was a family history of psychiatric illness. Previous bipolar medications included olanzapine 10-15 mg/day, haloperidol 5 mg/4h PRN, and risperidone 8 mg/day, which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	57
USA-113	10	168
	0	8

The relevant adverse events and laboratory values are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
SGTP increased	Y	114	120	Recovered	None	Mild	Possible	N
Hepatic abnormal function	Y	217	17	Recovered	Permanent stop	Mild	Possible	N

^a Day = Day in study from the start of USA-112

Laboratory values				
Study	Days in study	Time interval	ASAT (SGOT) ^b U/L	ALAT (SGTP) ^c U/L
USA-112	-3	Baseline	34	74 A
	0	Baseline	33	63 A
USA-113	58	Week 8/study entry	44 A	80 A
	86	Week 12/week 4	47 A	78 A
	114	Week 16/week 8	43 A	64 A
	127	Week 20/week 12	45 A	71 A
	140	Week 20/week 12	37	56 A
	233	Week 32/week 24	25	36

^b Reference range SGOT: 0-42 U/L

^c Reference range SGTP: 0-48 U/L

A= above reference range

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and
Discontinuations Due to Adverse Events

On Day 114, the investigator reported the adverse event ALAT increased (64 U/L). The investigator considered the event to be mild in intensity and possibly related to the study medication. ALAT had been high since baseline (63 U/L). Upon entry of RIS-USA-113 (Day 58) ALAT was 80 U/L and on Day 86, 78 U/L. On Day 217, the investigator reported the adverse event hepatic function abnormal. On Day 225 the study medication was stopped. The subject was permanently discontinued from the study on Day 233.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Adverse Events leading to Discontinuation

RIS-USA-113

CRF ID: A30200 (A30242 in RIS-USA-112)

Country: United States of America

Treatment Group: Olanzapine

Subject A30200 (adverse event leading to discontinuation: weight increase): This 49-year-old Caucasian female subject had a primary diagnosis of schizophrenia (type: paranoid). The subject's age at onset was 23. Her first psychiatric hospitalization was at age 23. The number of previous psychiatric hospitalizations was 5. There was no family history of psychiatric illness. Previous bipolar medications included risperidone 3 mg bid, which was discontinued before the start of study RIS-USA-112. Concomitant medications were conjugated estrogens 0.3 mg/day and medroxyprogesterone acetate 2 mg/day (last 10 days of the month) as hormonal replacement, famotidine 20 mg/day for a hiatus hernia, itraconazole 100 mg bid for a fungal infection, and zolpidem tartrate 3 mg/day PRN for sleeping. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	15
	15	7
	20	34
USA-113	20	100
	0	55

The relevant adverse event and assessment values are shown in the tables below:

Adverse Event Details								
MedDRA Preferred Term	Emerged in USA-113	Start Day ^a	AE duration (days)	Outcome	Action taken	Severity	Investigator-Assigned Relationship	SAE (Y/N)
Weight increase	Y	141	29	Recovered	Permanent stop	Mild	Probable	N

^a Day = Day in study from the start of USA-112

Time interval	Study day	Weight (kg)
Baseline	1	59
Week 8/study entry	57	60
Week 12/week 4	85	63
Week 16/week 8	112	63
Week 20/week 12	141	64
Week 32/week 24	211	64

On Day 141, the subject experienced weight increase. The investigator considered the event to be mild in intensity and probably related to the study medication. The study medication was discontinued 2 weeks after the start of the event. The subject recovered 29 days after start of the event. The subject was permanently discontinued from the study on Day 211, 55 days after stopping study medication.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

Narratives for Adverse Events leading to Discontinuation

RIS-USA-113

CRF ID: A30415 (A30517 in RIS-USA-112)

Country: United States of America

Treatment Group: Olanzapine

Subject A30415 (adverse event leading to discontinuation: weight increase): This 26-year-old Black female subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 21. She had not been previously hospitalized. There was no family history of psychiatric illness. Previous bipolar medications included fluphenazine hydrochloride 50 mg/2 weeks and trihexyphenidyl hydrochloride 1 mg bid, which were discontinued before the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with olanzapine in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	63
USA-113	10	112
	0	1

The relevant adverse event and assessment values are shown in the tables below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged in USA-113</i>	<i>Start Day^a</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE (Y/N)</i>
Weight increase	Y	64	113	Not recovered	Permanent stop	Moderate	Very likely	N

^aDay = Day in study from the start of USA-112

Time interval	Study day	Weight (kg)	BMI (kg/m ²)
Baseline	1	100	35
Week 12/week 4	92	115	40
Week 16/week 8	117	116	41
Week 20/week 12	145	120	42
Week 24/week 16	176	123	43

On Day 64, at the entry of study RIS-USA-113, the adverse event weight increase was reported. The investigator considered the event to be moderate in intensity and to be very likely related to the study medication. The subject continued the study for 113 days but did not recover. The subject was discontinued permanently on Day 176.

Attachment 3.6: Subject Narratives for Deaths, Serious Adverse Events, and Discontinuations Due to Adverse Events

**Narratives for Adverse Events leading to Discontinuation
RIS-USA-113**

CRF ID: A30012 (A30018 in RIS-USA-112)

Country: United States of America

Treatment Group: Risperidone (crossover subject)

Subject A30012 (adverse event leading to discontinuation: weight increase): This 50-year-old Caucasian female subject had a primary diagnosis of schizoaffective disorder. The subject's age at onset was 43. Her first psychiatric hospitalization was at age 40. The number of previous psychiatric hospitalizations was 2. There was a family history of psychiatric illness. Previous bipolar medications included lithium carbonate 300 mg bid and tiotixene 5 mg tid, which were discontinued at the start of study RIS-USA-112. The subject completed 8-week treatment with olanzapine in study RIS-USA-112, and continued treatment with risperidone in study RIS-USA-113 according to the following schedule:

	Dose (mg)	Duration (days)
USA-112	10	60
USA-113	4	121
	0	1

The relevant adverse events and assessment scores are shown in the tables below:

Adverse Event Details								
<i>MedDRA Preferred Term</i>	<i>Emerged in USA-113</i>	<i>Start Day *</i>	<i>AE duration (days)</i>	<i>Outcome</i>	<i>Action taken</i>	<i>Severity</i>	<i>Investigator-Assigned Relationship</i>	<i>SAE (Y/N)</i>
Weight increase	N	7	176	Not recovered	Permanent stop	Severe	Probable	N

* Day = Day in study from the start of USA-112

On Day 7 (RIS-USA-112), the subject experienced weight increase. The event was considered to be severe and probably related to study medication. The adverse event did not subside. The subject continued to take study medication until Day 181. The subject was discontinued from the study on Day 182.

Time point	Body weight (kg)
Baseline	118
Week 8/Study Entry	133
Week 12/Week 4	136
Week 16/Week 8	133
Week 20/Week 12	133
Week 24/Week 16	133

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Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAE02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														

CALCIUM (mmol/l)														

RISPERIDONE														
TREATMENT														
BASELINE	122	2.44	0.105	2.43	2.2	2.8								
WEEK 8/STUDY ENTRY	119	2.42	0.090	2.42	2.2	2.6	2.44	119	-0.03	0.009	0.104	-0.02	-0.4	0.2
WEEK 52/WEEK 44	59	2.36	0.102	2.35	2.1	2.7	2.44	59	-0.08	0.013	0.101	-0.07	-0.4	0.1
END POINT	122	2.38	0.103	2.37	2.1	2.7	2.44	122	-0.06	0.010	0.109	-0.07	-0.4	0.2
OLANZAPINE														
TREATMENT														
BASELINE	134	2.44	0.098	2.42	2.2	2.7								
WEEK 8/STUDY ENTRY	128	2.42	0.083	2.42	2.2	2.6	2.43	128	-0.02	0.008	0.089	-0.02	-0.2	0.2
WEEK 52/WEEK 44	70	2.37	0.098	2.37	2.1	2.5	2.43	70	-0.06	0.010	0.082	-0.07	-0.2	0.1
END POINT	134	2.39	0.101	2.40	2.1	2.7	2.44	134	-0.05	0.009	0.099	-0.05	-0.4	0.2
CHLORIDE (mmol/l)														

RISPERIDONE														
TREATMENT														
BASELINE	122	105.02	3.063	105.00	93.0	112.0								
WEEK 8/STUDY ENTRY	119	105.28	3.273	106.00	93.0	112.0	105.05	119	0.23	0.287	3.126	0.00	-7.0	12.0
WEEK 52/WEEK 44	59	104.90	2.721	105.00	96.0	110.0	105.47	59	-0.58	0.379	2.914	-1.00	-6.0	7.0
END POINT	122	104.89	3.204	105.00	93.0	112.0	105.02	122	-0.14	0.288	3.181	0.00	-7.0	9.0
OLANZAPINE														
TREATMENT														
BASELINE	134	105.43	2.663	106.00	96.0	111.0								
WEEK 8/STUDY ENTRY	128	105.83	2.469	106.00	97.0	111.0	105.49	128	0.34	0.250	2.829	0.00	-6.0	13.0
WEEK 52/WEEK 44	70	104.73	2.745	105.00	96.0	110.0	105.27	70	-0.54	0.414	3.463	-1.00	-11.0	10.0
END POINT	134	105.22	2.747	106.00	96.0	112.0	105.43	134	-0.21	0.266	3.076	0.00	-11.0	10.0
POTASSIUM (mmol/l)														

RISPERIDONE														
TREATMENT														
BASELINE	122	4.34	0.516	4.30	3.3	8.5								

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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Table LAE02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
POTASSIUM (mmol/l)														
RISPERIDONE														
TREATMENT														
WEEK 8/STUDY ENTRY	119	4.26	0.298	4.20	3.6	5.2	4.33	119	-0.07	0.050	0.551	0.00	-4.3	0.9
WEEK 52/WEEK 44	59	4.26	0.284	4.30	3.5	5.2	4.33	59	-0.07	0.048	0.367	-0.10	-1.1	0.9
END POINT	122	4.28	0.319	4.30	3.4	5.2	4.34	122	-0.06	0.051	0.566	0.00	-4.6	0.9
OLANZAPINE														
TREATMENT														
BASELINE	134	4.34	0.418	4.30	3.5	6.7								
WEEK 8/STUDY ENTRY	128	4.29	0.258	4.30	3.6	5.1	4.34	128	-0.05	0.037	0.418	0.00	-2.2	0.7
WEEK 52/WEEK 44	70	4.23	0.279	4.30	3.7	4.9	4.26	70	-0.03	0.041	0.346	0.00	-1.1	0.7
END POINT	134	4.26	0.316	4.30	3.6	5.1	4.34	134	-0.09	0.035	0.410	0.00	-2.2	0.7
SODIUM (mmol/l)														
RISPERIDONE														
TREATMENT														
BASELINE	122	140.56	2.568	141.00	129.0	146.0								
WEEK 8/STUDY ENTRY	119	140.49	2.783	141.00	132.0	148.0	140.57	119	-0.08	0.296	3.225	0.00	-6.0	13.0
WEEK 52/WEEK 44	59	140.61	2.371	141.00	135.0	145.0	140.97	59	-0.36	0.338	2.598	-1.00	-9.0	5.0
END POINT	122	140.53	2.632	141.00	130.0	145.0	140.56	122	-0.02	0.294	3.249	0.00	-12.0	11.0
OLANZAPINE														
TREATMENT														
BASELINE	134	140.56	2.677	141.00	129.0	146.0								
WEEK 8/STUDY ENTRY	128	140.78	2.436	141.00	133.0	146.0	140.56	128	0.22	0.272	3.079	0.00	-7.0	14.0
WEEK 52/WEEK 44	70	140.70	2.661	141.00	131.0	145.0	140.41	70	0.29	0.393	3.284	0.00	-5.0	10.0
END POINT	134	140.76	2.622	141.00	131.0	147.0	140.56	134	0.20	0.253	2.930	0.00	-5.0	10.0
TOTAL PROTEIN (g/l)														
RISPERIDONE														
TREATMENT														
BASELINE	122	75.06	5.069	75.00	60.0	88.0								
WEEK 8/STUDY ENTRY	119	73.37	4.517	73.00	62.0	83.0	75.13	119	-1.76	0.419	4.568	-2.00	-15.0	9.0

Risperidone: Clinical Study Report RIS-USA-113

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
TOTAL PROTEIN (g/l)														
RISPERIDONE														
TREATMENT														
WEEK 52/WEEK 44	59	71.61	4.698	71.00	62.0	84.0	74.47	59	-2.86	0.582	4.470	-2.00	-16.0	8.0
END POINT	122	72.32	4.785	72.00	62.0	84.0	75.06	122	-2.74	0.446	4.926	-2.00	-16.0	8.0
OLANZAPINE														
TREATMENT														
BASELINE	134	74.51	4.941	75.00	59.0	88.0								
WEEK 8/STUDY ENTRY	128	74.34	4.838	74.00	58.0	88.0	74.40	128	-0.05	0.405	4.584	0.00	-10.0	13.0
WEEK 52/WEEK 44	70	73.64	5.053	74.00	57.0	85.0	74.27	70	-0.63	0.601	5.025	-1.00	-10.0	12.0
END POINT	134	73.61	4.888	74.00	57.0	88.0	74.51	134	-0.90	0.438	5.073	-1.00	-10.0	21.0
BLOOD UREA NITROGEN (mmol/l)														
RISPERIDONE														
TREATMENT														
BASELINE	122	4.11	1.489	3.93	1.4	10.4								
WEEK 8/STUDY ENTRY	119	4.10	1.265	3.93	1.4	9.3	4.06	119	0.04	0.107	1.165	0.00	-5.0	2.9
WEEK 52/WEEK 44	59	4.05	1.180	3.93	2.1	7.9	4.18	59	-0.13	0.185	1.419	0.00	-5.4	2.1
END POINT	122	4.07	1.247	3.93	1.8	9.3	4.11	122	-0.03	0.125	1.381	0.00	-6.1	3.2
OLANZAPINE														
TREATMENT														
BASELINE	134	4.33	1.584	3.93	1.8	9.3								
WEEK 8/STUDY ENTRY	128	4.20	1.300	4.28	1.4	8.9	4.36	128	-0.16	0.119	1.349	0.00	-4.6	3.6
WEEK 52/WEEK 44	70	3.84	1.082	3.75	1.1	7.5	4.16	70	-0.33	0.158	1.322	-0.36	-3.6	2.5
END POINT	134	3.95	1.134	3.93	1.1	7.5	4.33	134	-0.39	0.112	1.293	-0.36	-4.3	2.5
URIC ACID (umol/l)														
RISPERIDONE														
TREATMENT														
BASELINE	122	287.45	87.027	285.50	101.1	541.3								
WEEK 8/STUDY ENTRY	119	285.05	79.171	279.56	71.4	529.4	289.40	119	-4.35	4.949	53.988	-11.90	-142.8	178.4
WEEK 52/WEEK 44	59	299.52	92.402	303.35	83.3	535.3	294.78	59	4.74	6.902	53.014	0.00	-160.6	178.4

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
URIC ACID (umol/l)														
RISPERIDONE TREATMENT END POINT	122	291.31	83.277	291.45	83.3	535.3	287.45	122	3.85	4.685	51.746	0.00	-160.6	178.4
OLANZAPINE														
TREATMENT BASELINE	134	295.71	90.107	288.48	124.9	630.5								
WEEK 8/STUDY ENTRY	128	315.62	85.734	303.35	148.7	594.8	298.65	128	16.96	4.876	55.165	14.87	-101.1	178.4
WEEK 52/WEEK 44	70	323.15	91.385	309.30	178.4	565.1	302.07	70	21.07	7.695	64.379	14.87	-148.7	148.7
END POINT	134	312.76	91.099	297.40	148.7	571.0	295.71	134	17.05	5.274	61.050	11.90	-148.7	148.7
CREATININE (umol/l)														
RISPERIDONE TREATMENT BASELINE	122	90.57	15.388	88.40	61.9	132.6								
WEEK 8/STUDY ENTRY	119	90.85	15.351	88.40	53.0	123.8	90.78	119	0.07	1.237	13.495	0.00	-53.0	26.5
WEEK 52/WEEK 44	59	93.94	15.822	97.24	61.9	132.6	93.79	59	0.15	1.592	12.228	0.00	-17.7	26.5
END POINT	122	92.31	15.668	92.82	53.0	132.6	90.57	122	1.74	1.172	12.940	0.00	-53.0	26.5
OLANZAPINE														
TREATMENT BASELINE	134	91.24	16.426	88.40	53.0	150.3								
WEEK 8/STUDY ENTRY	128	91.09	17.026	88.40	53.0	141.4	91.58	128	-0.48	1.429	16.164	0.00	-53.0	44.2
WEEK 52/WEEK 44	70	90.55	16.100	88.40	53.0	123.8	89.16	70	1.39	1.665	13.927	0.00	-61.9	26.5
END POINT	134	91.37	16.438	88.40	53.0	150.3	91.24	134	0.13	1.263	14.624	0.00	-61.9	35.4
CHOLESTEROL (mmol/l)														
RISPERIDONE TREATMENT BASELINE	122	5.16	1.118	5.07	2.9	8.2								
WEEK 8/STUDY ENTRY	119	5.12	1.059	5.02	2.8	8.2	5.16	119	-0.04	0.066	0.725	-0.03	-1.7	3.3
WEEK 52/WEEK 44	59	5.32	1.087	5.15	3.2	8.1	5.23	59	0.08	0.108	0.828	0.08	-1.8	1.8

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	change from baseline usa-112						
								N	Mean	SE	SD	Med	Min	Max
CHOLESTEROL (mmol/l)														
~~														
RISPERIDONE														
TREATMENT														
END POINT	122	5.15	1.097	5.04	3.1	8.2	5.16	122	-0.01	0.070	0.775	0.03	-1.8	2.9
OLANZAPINE														
TREATMENT														
BASELINE	134	5.11	1.059	5.04	2.7	8.2								
WEEK 8/STUDY ENTRY	128	5.49	1.013	5.38	3.4	8.7	5.12	128	0.37	0.067	0.758	0.30	-1.2	2.6
WEEK 52/WEEK 44	70	5.27	1.171	5.11	2.2	8.8	5.08	70	0.19	0.106	0.888	0.14	-1.9	2.5
END POINT	134	5.27	1.074	5.22	2.2	8.8	5.11	134	0.17	0.075	0.866	0.13	-2.0	2.5
TRIGLYCERIDES (mmol/l)														
~~														
RISPERIDONE														
TREATMENT														
BASELINE	122	1.93	1.603	1.57	0.4	12.4								
WEEK 8/STUDY ENTRY	119	1.67	1.306	1.33	0.4	9.3	1.94	119	-0.27	0.091	0.988	-0.15	-4.9	2.2
WEEK 52/WEEK 44	59	1.79	1.141	1.37	0.5	6.8	1.74	59	0.05	0.145	1.116	-0.01	-2.9	4.6
END POINT	122	1.95	1.568	1.49	0.4	9.3	1.93	122	0.02	0.111	1.228	-0.01	-4.0	4.6
OLANZAPINE														
TREATMENT														
BASELINE	134	1.92	1.099	1.70	0.5	6.0								
WEEK 8/STUDY ENTRY	128	2.12	1.196	1.82	0.5	6.1	1.94	128	0.18	0.095	1.080	0.14	-2.4	3.8
WEEK 52/WEEK 44	70	2.52	2.137	1.89	0.4	10.0	2.07	70	0.45	0.215	1.796	-0.05	-2.4	7.5
END POINT	134	2.26	1.795	1.69	0.4	10.0	1.92	134	0.34	0.131	1.518	-0.02	-2.5	7.5
HDL (g/l)														
~~														
RISPERIDONE														
TREATMENT														
BASELINE	122	0.50	0.160	0.47	0.3	1.1								
WEEK 8/STUDY ENTRY	119	0.50	0.146	0.50	0.2	1.0	0.50	119	0.01	0.007	0.080	0.00	-0.2	0.2
WEEK 52/WEEK 44	59	0.52	0.146	0.49	0.3	1.0	0.48	59	0.04	0.014	0.105	0.03	-0.3	0.3

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
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Table LAE02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
HDL (g/l)														
RISPERIDONE														
TREATMENT														
END POINT	122	0.52	0.149	0.50	0.3	1.0	0.50	122	0.02	0.010	0.107	0.02	-0.5	0.3
OLANZAPINE														
TREATMENT														
BASELINE	133	0.51	0.152	0.48	0.2	1.0								
WEEK 8/STUDY ENTRY	126	0.51	0.158	0.47	0.2	1.0	0.51	126	0.00	0.009	0.099	0.00	-0.4	0.4
WEEK 52/WEEK 44	69	0.47	0.144	0.46	0.2	0.9	0.47	69	0.01	0.013	0.111	0.00	-0.3	0.5
END POINT	133	0.50	0.162	0.47	0.2	1.2	0.51	133	-0.00	0.011	0.122	-0.01	-0.4	0.5
LDL (g/l)														
RISPERIDONE														
TREATMENT														
BASELINE	116	1.18	0.380	1.15	0.5	2.3								
WEEK 8/STUDY ENTRY	112	1.21	0.382	1.16	0.5	2.4	1.19	112	0.02	0.022	0.229	-0.01	-0.4	0.9
WEEK 52/WEEK 44	57	1.22	0.378	1.20	0.6	2.2	1.24	57	-0.02	0.040	0.304	0.00	-0.8	0.5
END POINT	116	1.17	0.382	1.11	0.5	2.4	1.18	116	-0.02	0.025	0.268	-0.01	-0.8	0.7
OLANZAPINE														
TREATMENT														
BASELINE	127	1.14	0.374	1.10	0.3	2.2								
WEEK 8/STUDY ENTRY	117	1.23	0.346	1.26	0.4	2.3	1.12	117	0.12	0.023	0.253	0.13	-0.6	0.9
WEEK 52/WEEK 44	60	1.15	0.373	1.14	0.3	1.9	1.14	60	0.01	0.039	0.300	0.01	-0.6	0.8
END POINT	127	1.17	0.341	1.17	0.3	1.9	1.14	127	0.03	0.026	0.298	0.02	-0.6	0.8
TOTAL BILIRUBIN (umol/l)														
RISPERIDONE														
TREATMENT														
BASELINE	122	10.32	3.665	8.55	5.1	23.9								
WEEK 8/STUDY ENTRY	119	9.44	3.505	8.55	5.1	27.4	10.42	119	-0.98	0.281	3.065	-1.71	-10.3	12.0
WEEK 52/WEEK 44	59	10.12	3.258	8.55	5.1	23.9	10.52	59	-0.41	0.438	3.366	0.00	-8.6	8.6

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
TOTAL BILIRUBIN (umol/l)														
RISPERIDONE TREATMENT END POINT	122	9.69	3.375	8.55	5.1	25.7	10.32	122	-0.63	0.307	3.393	0.00	-10.3	10.3
OLANZAPINE TREATMENT BASELINE	134	10.08	3.402	8.55	1.7	27.4	10.05	128	-0.20	0.303	3.424	0.00	-15.4	10.3
WEEK 8/STUDY ENTRY	128	9.85	3.123	9.41	5.1	22.2	10.05	128	-0.20	0.303	3.424	0.00	-15.4	10.3
WEEK 52/WEEK 44	70	11.07	5.074	10.26	1.7	42.8	10.19	70	0.88	0.600	5.024	1.71	-13.7	29.1
END POINT	134	10.59	4.243	10.26	1.7	42.8	10.08	134	0.51	0.373	4.313	0.00	-13.7	29.1
ALKALINE PHOSPHATASE (U/L)														
RISPERIDONE TREATMENT BASELINE	122	80.22	29.375	76.50	37.0	267.0	80.08	119	-2.92	1.154	12.592	-1.00	-80.0	35.0
WEEK 8/STUDY ENTRY	119	77.17	26.692	73.00	36.0	278.0	80.08	119	-2.92	1.154	12.592	-1.00	-80.0	35.0
WEEK 52/WEEK 44	59	77.41	23.493	74.00	45.0	164.0	75.59	59	1.81	2.186	16.789	-2.00	-24.0	66.0
END POINT	122	80.19	29.098	74.00	43.0	243.0	80.22	122	-0.03	1.432	15.822	-1.50	-64.0	66.0
OLANZAPINE TREATMENT BASELINE	134	80.43	25.657	76.00	38.0	214.0	80.44	128	3.48	1.021	11.553	3.00	-25.0	40.0
WEEK 8/STUDY ENTRY	128	83.92	28.180	80.00	34.0	254.0	80.44	128	3.48	1.021	11.553	3.00	-25.0	40.0
WEEK 52/WEEK 44	70	89.94	23.402	86.00	49.0	150.0	84.07	70	5.87	2.167	18.127	4.00	-31.0	65.0
END POINT	134	87.07	30.166	82.00	34.0	254.0	80.43	134	6.64	1.464	16.942	4.00	-34.0	65.0
GGT (U/L)														
RISPERIDONE TREATMENT BASELINE	122	44.07	113.155	22.50	4.0	1173.0	44.53	120	-2.94	1.969	21.568	-2.00	-124.0	155.0
WEEK 8/STUDY ENTRY	120	41.58	125.333	21.00	6.0	1328.0	44.53	120	-2.94	1.969	21.568	-2.00	-124.0	155.0
WEEK 12/WEEK 4	112	42.62	125.165	20.00	4.0	1234.0	44.76	112	-2.14	2.151	22.765	-2.00	-146.0	86.0
WEEK 16/WEEK 8	104	45.31	146.397	20.00	5.0	1392.0	46.27	104	-0.96	3.409	34.765	-1.50	-175.0	219.0

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
GGT (U/L)														
RISPERIDONE														
TREATMENT														
WEEK 20/WEEK 12	96	43.52	153.688	20.00	5.0	1518.0	44.09	96	-0.57	4.337	42.493	-2.00	-195.0	345.0
WEEK 36/WEEK 28	77	45.95	128.403	26.00	9.0	1142.0	46.83	77	-0.88	3.198	28.059	1.00	-204.0	88.0
WEEK 52/WEEK 44	59	33.95	22.850	28.00	7.0	108.0	29.00	59	4.95	2.102	16.146	3.00	-41.0	52.0
END POINT	122	47.03	113.888	26.50	7.0	1133.0	44.07	122	2.97	2.600	28.723	1.00	-202.0	145.0
OLANZAPINE														
TREATMENT														
BASELINE	134	37.26	45.837	25.00	2.0	337.0								
WEEK 8/STUDY ENTRY	129	39.97	41.627	29.00	5.0	282.0	38.12	129	1.84	1.680	19.086	2.00	-74.0	99.0
WEEK 12/WEEK 4	127	39.20	47.672	26.00	5.0	344.0	37.29	127	1.91	1.810	20.398	2.00	-91.0	126.0
WEEK 16/WEEK 8	118	41.34	62.595	24.00	3.0	514.0	37.01	118	4.33	2.910	31.612	1.00	-78.0	214.0
WEEK 20/WEEK 12	115	40.27	48.755	27.00	4.0	381.0	37.03	115	3.24	2.386	25.584	3.00	-100.0	169.0
WEEK 36/WEEK 28	84	40.39	32.467	33.00	4.0	164.0	32.73	84	7.67	2.362	21.649	3.00	-46.0	76.0
WEEK 52/WEEK 44	70	47.11	40.473	32.50	6.0	198.0	34.83	70	12.29	3.875	32.418	5.00	-70.0	164.0
END POINT	134	44.07	45.072	28.00	4.0	259.0	37.26	134	6.81	2.479	28.702	3.00	-78.0	164.0
LACTATE DEHYDROGENASE (U/L)														
RISPERIDONE														
TREATMENT														
BASELINE	122	149.91	29.702	145.00	94.0	250.0								
WEEK 8/STUDY ENTRY	119	149.64	32.570	144.00	91.0	276.0	150.03	119	-0.39	2.541	27.724	-1.00	-104.0	118.0
WEEK 52/WEEK 44	59	140.19	23.867	140.00	100.0	221.0	145.36	59	-5.17	2.759	21.192	-9.00	-70.0	64.0
END POINT	122	148.80	32.293	144.50	96.0	276.0	149.91	122	-1.11	2.387	26.362	-4.50	-103.0	94.0
OLANZAPINE														
TREATMENT														
BASELINE	134	144.56	39.725	141.00	63.0	408.0								
WEEK 8/STUDY ENTRY	128	150.34	31.832	147.50	76.0	254.0	143.76	128	6.59	3.498	39.570	14.00	-259.0	79.0
WEEK 52/WEEK 44	70	148.81	61.755	140.50	80.0	590.0	141.33	70	7.49	8.672	72.552	6.50	-301.0	481.0
END POINT	134	151.69	51.026	143.50	77.0	590.0	144.56	134	7.13	5.075	58.744	7.00	-301.0	481.0

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
AST (U/L)														
RISPERIDONE														
TREATMENT														
BASELINE	122	19.57	11.454	17.00	9.0	100.0								
WEEK 8/STUDY ENTRY	120	18.00	9.350	15.00	7.0	65.0	19.62	120	-1.62	0.741	8.116	-2.00	-47.0	27.0
WEEK 12/WEEK 4	112	18.70	9.067	16.50	5.0	73.0	19.67	112	-0.97	1.139	12.056	0.00	-61.0	55.0
WEEK 16/WEEK 8	104	18.84	11.904	16.00	6.0	100.0	19.67	104	-0.84	0.715	7.294	-1.00	-32.0	28.0
WEEK 20/WEEK 12	96	18.63	11.839	16.00	8.0	94.0	19.83	96	-1.21	0.968	9.480	-1.00	-42.0	32.0
WEEK 36/WEEK 28	77	19.48	10.309	17.00	7.0	70.0	18.44	77	1.04	0.799	7.014	0.00	-19.0	29.0
WEEK 52/WEEK 44	59	18.86	7.058	17.00	10.0	48.0	18.51	59	0.36	1.334	10.243	1.00	-62.0	27.0
END POINT	122	19.04	8.170	17.00	10.0	58.0	19.57	122	-0.53	0.879	9.705	0.00	-62.0	27.0
OLANZAPINE														
TREATMENT														
BASELINE	134	20.06	14.170	16.00	8.0	106.0								
WEEK 8/STUDY ENTRY	129	22.64	13.708	18.00	8.0	92.0	20.26	129	2.37	1.027	11.670	2.00	-62.0	49.0
WEEK 12/WEEK 4	128	22.30	15.513	18.00	9.0	103.0	20.02	128	2.29	1.201	13.583	1.50	-67.0	72.0
WEEK 16/WEEK 8	118	21.87	16.660	18.00	7.0	138.0	20.55	118	1.32	1.395	15.157	2.00	-71.0	104.0
WEEK 20/WEEK 12	115	22.83	16.401	18.00	8.0	132.0	20.57	115	2.25	1.293	13.870	1.00	-46.0	98.0
WEEK 36/WEEK 28	84	22.98	15.302	19.00	10.0	113.0	18.54	84	4.44	1.682	15.413	3.00	-71.0	94.0
WEEK 52/WEEK 44	70	24.43	27.932	19.50	9.0	234.0	18.64	70	5.79	3.520	29.447	2.50	-74.0	226.0
END POINT	134	24.07	24.142	18.50	9.0	234.0	20.06	134	4.01	2.196	25.418	1.50	-74.0	226.0
ALT (U/L)														
RISPERIDONE														
TREATMENT														
BASELINE	122	25.47	25.022	18.00	1.0	182.0								
WEEK 8/STUDY ENTRY	120	22.10	18.708	17.00	4.0	131.0	25.54	120	-3.44	1.413	15.479	-1.00	-112.0	44.0
WEEK 12/WEEK 4	112	24.10	22.837	17.50	3.0	186.0	25.63	112	-1.53	2.123	22.467	-1.00	-117.0	142.0
WEEK 16/WEEK 8	104	24.47	25.256	17.00	5.0	158.0	25.64	104	-1.17	1.401	14.282	-1.00	-39.0	62.0
WEEK 20/WEEK 12	96	25.36	33.963	16.50	5.0	287.0	26.61	96	-1.25	2.193	21.488	-2.00	-90.0	116.0
WEEK 36/WEEK 28	77	24.91	23.315	18.00	4.0	151.0	24.45	77	0.45	1.567	13.748	0.00	-35.0	73.0
WEEK 52/WEEK 44	59	23.93	16.663	19.00	6.0	93.0	23.76	59	0.17	3.173	24.371	2.00	-153.0	62.0
END POINT	122	24.46	18.201	19.00	5.0	97.0	25.47	122	-1.01	1.974	21.798	0.00	-153.0	67.0

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Table LAE02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
ALT (U/L)														
OLANZAPINE														
TREATMENT														
BASELINE	134	26.87	30.250	20.00	5.0	239.0								
WEEK 8/STUDY ENTRY	129	31.71	29.885	24.00	5.0	200.0	27.40	129	4.31	2.599	29.519	3.00	-184.0	185.0
WEEK 12/WEEK 4	127	29.35	24.509	23.00	6.0	140.0	27.24	127	2.12	2.294	25.857	4.00	-202.0	86.0
WEEK 16/WEEK 8	118	29.19	27.226	21.00	3.0	181.0	28.25	118	0.95	2.694	29.262	2.00	-217.0	127.0
WEEK 20/WEEK 12	115	29.23	25.356	21.00	5.0	172.0	28.05	115	1.18	2.578	27.650	2.00	-190.0	118.0
WEEK 36/WEEK 28	84	28.93	21.008	21.00	6.0	99.0	25.54	84	3.39	3.316	30.389	4.00	-218.0	74.0
WEEK 52/WEEK 44	70	27.99	20.737	21.50	6.0	108.0	25.63	70	2.36	4.081	34.148	2.00	-221.0	86.0
END POINT	134	27.75	23.539	20.00	6.0	176.0	26.87	134	0.88	2.681	31.037	1.00	-221.0	122.0
CPK (U/L)														
RISPERIDONE														
TREATMENT														
BASELINE	122	126.91	106.519	93.50	20.0	663.0								
WEEK 8/STUDY ENTRY	119	155.11	244.869	107.00	17.0	2610.0	128.41	119	26.70	21.116	230.347	6.00	-412.0	2348.0
WEEK 52/WEEK 44	59	150.86	116.552	110.00	23.0	504.0	119.24	59	31.63	10.236	78.625	17.00	-160.0	300.0
END POINT	122	148.65	125.411	120.50	17.0	972.0	126.91	122	21.74	9.137	100.919	13.50	-477.0	574.0
OLANZAPINE														
TREATMENT														
BASELINE	134	119.51	109.416	91.00	26.0	1016.0								
WEEK 8/STUDY ENTRY	128	139.30	150.905	99.00	32.0	1512.0	119.70	128	19.60	12.692	143.599	4.00	-855.0	1065.0
WEEK 52/WEEK 44	70	446.69	2519.789	112.50	26.0	21200.0	107.40	70	339.29	301.733	2524.479	12.50	-323.0	21135.0
END POINT	134	313.04	1825.733	108.50	26.0	21200.0	119.51	134	193.52	158.039	1829.438	12.00	-852.0	21135.0
PROLACTIN (ng/ml)														
RISPERIDONE														
TREATMENT														
BASELINE	108	19.30	20.150	12.00	2.0	112.0								
WEEK 8/STUDY ENTRY	104	51.13	41.918	40.50	4.0	200.0	19.57	104	31.56	3.904	39.810	21.50	-21.0	191.0
WEEK 52/WEEK 44	52	45.85	32.151	37.50	6.0	160.0	21.52	52	24.33	4.850	34.973	14.50	-39.0	157.0

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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
PROLACTIN (ng/ml)														
RISPERIDONE														
TREATMENT														
END POINT	108	44.97	44.191	34.00	2.0	282.0	19.30	108	25.68	4.321	44.902	14.00	-87.0	274.0
OLANZAPINE														
TREATMENT														
BASELINE	120	25.52	34.200	13.00	2.0	221.0								
WEEK 8/STUDY ENTRY	112	13.77	13.583	10.00	2.0	105.0	24.33	112	-10.56	2.856	30.228	-2.50	-175.0	56.0
WEEK 52/WEEK 44	64	12.80	12.261	10.00	2.0	82.0	24.98	64	-12.19	4.175	33.400	-2.50	-139.0	39.0
END POINT	120	15.08	14.788	10.00	2.0	82.0	25.52	120	-10.44	2.824	30.935	-3.00	-139.0	63.0
FREE THYROXINE (INDEX)														
RISPERIDONE														
TREATMENT														
BASELINE	121	2.26	0.446	2.30	1.2	3.7								
WEEK 8/STUDY ENTRY	118	2.26	0.401	2.20	1.5	3.4	2.26	118	-0.00	0.038	0.410	0.00	-1.2	1.1
WEEK 52/WEEK 44	57	2.34	0.373	2.30	1.7	3.3	2.30	57	0.03	0.046	0.350	0.00	-0.8	0.8
END POINT	121	2.29	0.385	2.30	1.4	3.3	2.26	121	0.03	0.035	0.390	0.00	-1.1	1.0
OLANZAPINE														
TREATMENT														
BASELINE	133	2.25	0.488	2.20	1.3	5.4								
WEEK 8/STUDY ENTRY	127	2.09	0.431	2.10	1.2	4.0	2.25	127	-0.16	0.049	0.550	-0.10	-4.0	1.1
WEEK 52/WEEK 44	69	2.41	0.523	2.40	1.4	4.2	2.22	69	0.19	0.055	0.461	0.20	-1.0	2.1
END POINT	133	2.31	0.535	2.30	1.2	4.6	2.25	133	0.06	0.041	0.470	0.10	-1.0	2.1
T3 UPTAKE (%)														
RISPERIDONE														
TREATMENT														
BASELINE	121	28.62	3.946	29.00	18.0	38.0								
WEEK 8/STUDY ENTRY	118	28.57	3.598	29.00	18.0	35.0	28.74	118	-0.17	0.267	2.904	0.00	-7.0	8.0
WEEK 52/WEEK 44	57	28.37	3.953	28.00	19.0	37.0	29.88	57	-1.51	0.430	3.247	-2.00	-9.0	7.0

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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System Used: Arrow5.1/lbrun

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Table LAE02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
T3 UPTAKE (%)														
~~														
RISPERIDONE														
TREATMENT														
END POINT	121	27.83	4.065	28.00	17.0	37.0	28.62	121	-0.79	0.291	3.199	-1.00	-10.0	7.0
OLANZAPINE														
TREATMENT														
BASLINE	133	29.17	4.520	29.00	18.0	43.0								
WEEK 8/STUDY ENTRY	127	28.01	4.441	28.00	17.0	39.0	29.20	127	-1.20	0.257	2.898	-1.00	-10.0	7.0
WEEK 52/WEEK 44	69	28.19	4.824	29.00	16.0	38.0	29.13	69	-0.94	0.408	3.391	-1.00	-12.0	9.0
END POINT	133	27.98	4.796	28.00	16.0	42.0	29.17	133	-1.19	0.272	3.131	-1.00	-12.0	9.0
THYROXINE (nmol/L)														
~~														
RISPERIDONE														
TREATMENT														
BASLINE	121	103.08	23.073	101.67	55.3	175.0								
WEEK 8/STUDY ENTRY	118	103.08	21.044	101.67	63.1	193.1	102.83	118	0.25	1.363	14.801	1.93	-45.0	37.3
WEEK 52/WEEK 44	57	107.27	17.514	104.25	79.8	160.9	100.39	57	6.89	1.892	14.283	7.72	-37.3	43.8
END POINT	121	107.62	20.694	104.25	63.1	193.1	103.08	121	4.54	1.586	17.441	3.86	-43.8	75.9
OLANZAPINE														
TREATMENT														
BASLINE	133	101.08	24.757	97.81	45.0	204.6								
WEEK 8/STUDY ENTRY	127	97.50	22.124	95.24	46.3	158.3	101.02	127	-3.53	1.699	19.149	-2.57	-127.4	39.9
WEEK 52/WEEK 44	69	111.63	21.526	109.40	74.6	187.9	99.96	69	11.68	2.444	20.298	10.30	-45.0	69.5
END POINT	133	107.56	23.212	105.53	51.5	187.9	101.08	133	6.47	1.662	19.173	6.44	-45.0	69.5
TSH (U/L)														
~~														
RISPERIDONE														
TREATMENT														
BASLINE	121	1588.43	1008.480	1300.00	200.0	6000.0								
WEEK 8/STUDY ENTRY	118	1492.37	775.827	1300.00	300.0	4400.0	1578.81	118	-86.44	75.299	817.952	0.00	-3800.0	1700.0
WEEK 52/WEEK 44	57	1636.84	1016.758	1400.00	400.0	6000.0	1552.63	57	84.21	120.483	909.629	100.00	-2800.0	4100.0

Attachment 4.1: Clinical Chemistry - Descriptive Statistics of Values and Change From Baseline - Crossover
Subjects Excluded

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Table LAB02: Clinical Chemistry - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	change from baseline usa-112						
								N	Mean	SE	SD	Med	Min	Max
TSH (U/L)														
RISPERIDONE TREATMENT END POINT	121	1592.56	923.866	1400.00	400.0	6000.0	1588.43	121	4.13	80.232	882.553	100.00	-2800.0	4100.0
OLANZAPINE TREATMENT BASELINE	133	1841.35	1162.164	1500.00	100.0	7100.0								
WEEK 8/STUDY ENTRY	126	2195.24	2560.152	1700.00	100.0	26100.0	1863.49	126	331.75	226.127	2538.272	50.00	-3600.0	26000.0
WEEK 52/WEEK 44	68	2022.06	1172.934	1850.00	500.0	8300.0	1919.12	68	102.94	131.563	1084.899	100.00	-2600.0	4300.0
END POINT	133	1903.76	1344.991	1500.00	200.0	8300.0	1841.35	133	62.41	104.825	1208.906	0.00	-3800.0	5400.0

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAB03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														

HAEMOGLOBIN (g/l)														

RISPERIDONE														
TREATMENT														
BASELINE	120	144.83	15.898	146.00	90.0	181.0								
WEEK 8/STUDY ENTRY	115	143.63	14.831	145.00	86.0	178.0	145.31	115	-1.68	0.763	8.181	-2.00	-18.0	20.0
WEEK 52/WEEK 44	57	145.42	13.068	145.00	102.0	168.0	146.67	57	-1.25	1.259	9.502	-1.00	-22.0	21.0
END POINT	120	143.08	14.565	143.00	86.0	170.0	144.83	120	-1.75	0.807	8.843	-3.00	-22.0	21.0

OLANZAPINE														
TREATMENT														
BASELINE	133	145.95	14.993	147.00	107.0	177.0								
WEEK 8/STUDY ENTRY	125	146.55	15.698	149.00	102.0	178.0	145.73	125	0.82	0.705	7.878	2.00	-23.0	17.0
WEEK 52/WEEK 44	68	148.94	17.400	150.00	88.0	178.0	146.65	68	2.29	1.185	9.769	3.00	-31.0	20.0
END POINT	133	147.32	16.156	149.00	88.0	178.0	145.95	133	1.37	0.824	9.504	2.00	-35.0	20.0

HAEMOGLOBIN A1C (%)														

RISPERIDONE														
TREATMENT														
BASELINE	121	5.99	1.120	5.70	4.7	10.8								
WEEK 8/STUDY ENTRY	116	6.05	1.436	5.70	4.7	12.3	5.99	116	0.06	0.048	0.517	0.00	-0.8	3.1
WEEK 52/WEEK 44	57	6.04	1.061	5.80	4.8	11.2	6.00	57	0.04	0.092	0.698	0.10	-3.7	2.0
END POINT	121	6.04	1.213	5.80	4.8	12.1	5.99	121	0.05	0.063	0.697	0.10	-3.7	2.7

OLANZAPINE														
TREATMENT														
BASELINE	134	5.78	1.188	5.60	3.9	16.2								
WEEK 8/STUDY ENTRY	127	5.75	1.180	5.50	4.0	13.2	5.79	127	-0.03	0.043	0.488	-0.10	-3.0	2.1
WEEK 52/WEEK 44	71	5.88	1.206	5.70	4.1	13.7	5.73	71	0.15	0.094	0.794	0.00	-1.3	5.0
END POINT	134	5.88	1.330	5.60	4.1	13.7	5.78	134	0.10	0.062	0.718	0.10	-3.0	5.0

HAEMATOCRIT (vol-%)														

RISPERIDONE														
TREATMENT														
BASELINE	120	42.84	4.529	43.35	29.6	52.4								

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAB03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	change from baseline usa-112						
								N	Mean	SE	SD	Med	Min	Max
HAEMATOCRIT (vol-%)														
~~														
RISPERIDONE														
TREATMENT														
WEEK 8/STUDY ENTRY	115	42.24	4.067	42.70	28.7	52.9	42.97	115	-0.73	0.252	2.699	-0.90	-7.0	6.1
WEEK 52/WEEK 44	57	42.92	3.842	42.70	30.4	49.6	43.19	57	-0.26	0.378	2.856	-0.50	-5.4	6.5
END POINT	120	42.26	4.119	42.25	29.8	52.5	42.84	120	-0.58	0.256	2.801	-0.85	-7.0	7.4
OLANZAPINE														
TREATMENT														
BASELINE	133	43.12	4.099	43.40	32.4	51.7								
WEEK 8/STUDY ENTRY	125	43.13	4.169	43.80	32.3	51.4	43.02	125	0.11	0.226	2.523	-0.10	-7.5	5.9
WEEK 52/WEEK 44	68	44.12	4.953	44.60	29.3	54.2	43.15	68	0.97	0.406	3.348	0.85	-8.1	9.1
END POINT	133	43.59	4.537	44.10	29.3	54.2	43.12	133	0.47	0.280	3.225	0.60	-11.9	9.1
RED BLOOD CELL COUNT (tera/l)														
~~														
RISPERIDONE														
TREATMENT														
BASELINE	120	4.78	0.570	4.80	3.6	6.7								
WEEK 8/STUDY ENTRY	115	4.76	0.479	4.80	3.6	6.2	4.80	115	-0.04	0.029	0.307	0.00	-0.9	0.7
WEEK 52/WEEK 44	57	4.79	0.544	4.80	3.4	6.5	4.81	57	-0.02	0.040	0.301	0.00	-0.7	0.8
END POINT	120	4.74	0.517	4.75	3.4	6.5	4.78	120	-0.05	0.029	0.314	-0.10	-0.8	0.8
OLANZAPINE														
TREATMENT														
BASELINE	133	4.82	0.460	4.80	3.8	6.2								
WEEK 8/STUDY ENTRY	125	4.83	0.446	4.80	3.7	5.9	4.80	125	0.03	0.023	0.260	0.00	-0.8	0.6
WEEK 52/WEEK 44	68	4.91	0.435	4.95	4.0	5.8	4.83	68	0.09	0.039	0.321	0.15	-0.5	0.9
END POINT	133	4.88	0.455	4.90	3.7	5.9	4.82	133	0.06	0.027	0.314	0.10	-1.3	0.9
WBC (giga/l)														
~~														
RISPERIDONE														
TREATMENT														
BASELINE	120	7.46	2.392	7.00	3.1	16.3								
WEEK 8/STUDY ENTRY	115	7.32	2.467	7.10	2.5	16.9	7.50	115	-0.18	0.161	1.729	-0.20	-5.1	6.9

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAE03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
WBC (giga/l)														
RISPERIDONE														
TREATMENT														
WEEK 52/WEEK 44	57	6.99	2.115	6.60	2.8	12.6	7.48	57	-0.48	0.237	1.792	-0.60	-6.3	2.7
END POINT	120	7.15	2.384	6.70	2.8	16.1	7.46	120	-0.31	0.168	1.836	-0.30	-6.3	4.7
OLANZAPINE														
TREATMENT														
BASELINE	133	7.83	2.668	7.20	3.9	20.5								
WEEK 8/STUDY ENTRY	125	7.55	2.651	7.00	2.8	22.1	7.82	125	-0.28	0.187	2.092	-0.10	-6.4	11.6
WEEK 52/WEEK 44	68	8.05	2.925	7.40	2.9	17.0	8.19	68	-0.14	0.225	1.853	-0.05	-4.8	4.0
END POINT	133	7.65	2.578	7.20	2.8	17.0	7.83	133	-0.18	0.152	1.748	-0.20	-4.8	4.0
SEGMENTED NEUTROPHILS (%)														
RISPERIDONE														
TREATMENT														
BASELINE	121	60.93	11.152	61.00	20.0	84.5								
WEEK 8/STUDY ENTRY	117	60.95	9.857	61.80	40.0	82.7	61.21	117	-0.26	0.733	7.930	-0.60	-21.0	31.0
WEEK 52/WEEK 44	58	60.94	9.038	60.05	37.8	77.1	60.88	58	0.06	1.231	9.375	-0.10	-16.4	20.4
END POINT	121	60.99	9.667	60.20	33.2	81.5	60.93	121	0.06	0.843	9.271	-0.30	-21.0	31.0
OLANZAPINE														
TREATMENT														
BASELINE	135	61.17	10.150	63.00	32.3	81.8								
WEEK 8/STUDY ENTRY	127	59.54	9.758	60.30	19.9	79.2	61.23	127	-1.68	0.810	9.129	-1.80	-25.1	19.1
WEEK 52/WEEK 44	71	62.05	9.538	64.00	42.2	79.3	62.05	71	0.00	1.089	9.179	-0.90	-18.9	30.0
END POINT	135	60.82	9.297	61.10	35.1	79.3	61.17	135	-0.35	0.785	9.116	-1.00	-19.5	30.0
NEUTROPHILS (giga/l)														
RISPERIDONE														
TREATMENT														
BASELINE	120	4.65	2.055	4.25	1.3	12.1								
WEEK 8/STUDY ENTRY	115	4.58	2.038	4.12	1.2	13.4	4.71	115	-0.13	0.149	1.597	-0.08	-5.5	7.3
WEEK 52/WEEK 44	57	4.34	1.713	4.16	1.3	9.6	4.65	57	-0.31	0.209	1.575	-0.14	-5.1	2.9

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAE03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
NEUTROPHILS (giga/l)														
RISPERIDONE TREATMENT END POINT	120	4.46	1.949	4.13	1.3	11.8	4.65	120	-0.19	0.148	1.626	-0.02	-5.5	3.6
OLANZAPINE TREATMENT BASELINE	133	4.89	2.145	4.42	1.4	14.8	4.88	124	-0.30	0.171	1.908	-0.27	-7.7	10.8
WEEK 8/STUDY ENTRY	124	4.59	2.110	3.97	1.0	17.4	5.25	68	-0.13	0.204	1.681	0.17	-4.6	3.1
WEEK 52/WEEK 44	68	5.12	2.379	4.54	1.3	13.2	4.89	133	-0.15	0.138	1.586	-0.08	-4.6	3.1
END POINT	133	4.75	2.075	4.31	1.3	13.2								
LYMPHOCYTES (%)														
RISPERIDONE TREATMENT BASELINE	121	29.25	9.441	29.00	9.7	71.0	28.91	117	0.35	0.616	6.665	0.40	-23.0	17.7
WEEK 8/STUDY ENTRY	117	29.26	8.506	28.00	12.1	50.0	29.29	58	-0.60	0.976	7.433	0.45	-18.7	13.4
WEEK 52/WEEK 44	58	28.69	6.993	28.75	14.5	46.3	29.25	121	-0.51	0.689	7.584	0.40	-23.0	15.5
END POINT	121	28.74	8.203	27.90	10.3	52.5								
OLANZAPINE TREATMENT BASELINE	135	29.32	9.032	28.40	13.0	55.0	29.35	127	1.45	0.739	8.331	1.30	-19.1	23.7
WEEK 8/STUDY ENTRY	127	30.80	8.438	30.40	13.2	56.8	28.65	71	0.43	0.970	8.173	0.90	-34.0	21.8
WEEK 52/WEEK 44	71	29.08	8.823	28.10	14.9	50.0	29.32	135	0.65	0.711	8.263	0.60	-34.0	23.7
END POINT	135	29.97	8.552	29.20	13.8	52.1								
MONOCYTES (%)														
RISPERIDONE TREATMENT BASELINE	121	6.03	2.500	5.60	0.0	15.0	6.04	117	-0.02	0.195	2.114	0.10	-6.9	5.2
WEEK 8/STUDY ENTRY	117	6.02	2.130	5.80	1.4	13.0	5.88	58	0.49	0.304	2.318	0.25	-4.9	7.6
WEEK 52/WEEK 44	58	6.37	2.584	6.05	0.4	13.1								
END POINT														

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAE03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
MONOCYTES (%)														
RISPERIDONE														
TREATMENT														
END POINT	121	6.53	2.561	6.20	0.4	13.1	6.03	121	0.50	0.214	2.350	0.40	-5.0	8.6
OLANZAPINE														
TREATMENT														
BASLINE	135	6.05	2.356	5.90	0.1	12.5								
WEEK 8/STUDY ENTRY	127	6.13	2.493	6.00	0.0	16.0	6.05	127	0.09	0.235	2.648	0.30	-9.8	11.1
WEEK 52/WEEK 44	71	5.62	2.525	5.60	1.0	15.0	5.66	71	-0.04	0.299	2.517	-0.20	-7.0	6.2
END POINT	135	5.89	2.461	5.90	0.0	15.0	6.05	135	-0.16	0.224	2.597	0.00	-9.8	6.2
EOSINOPHILS (%)														
RISPERIDONE														
TREATMENT														
BASLINE	121	3.15	1.946	2.70	0.0	9.0								
WEEK 8/STUDY ENTRY	117	3.23	2.014	3.00	0.0	13.9	3.19	117	0.04	0.191	2.071	0.10	-7.5	6.3
WEEK 52/WEEK 44	58	3.45	2.116	2.75	0.5	9.1	3.32	58	0.14	0.289	2.198	0.05	-5.5	7.1
END POINT	121	3.22	1.913	2.90	0.5	9.1	3.15	121	0.07	0.189	2.079	0.10	-5.5	7.1
OLANZAPINE														
TREATMENT														
BASLINE	135	2.99	1.845	2.60	0.3	9.0								
WEEK 8/STUDY ENTRY	127	3.08	2.032	2.60	0.0	10.3	2.89	127	0.18	0.159	1.790	0.20	-5.3	5.2
WEEK 52/WEEK 44	71	2.69	1.853	2.20	0.2	10.0	3.13	71	-0.44	0.268	2.257	-0.20	-7.0	4.8
END POINT	135	2.83	1.941	2.50	0.0	10.0	2.99	135	-0.15	0.172	1.996	-0.10	-7.0	4.8
BASOPHILS (%)														
RISPERIDONE														
TREATMENT														
BASLINE	121	0.61	0.464	0.60	0.0	2.2								
WEEK 8/STUDY ENTRY	117	0.44	0.332	0.40	0.0	1.3	0.62	117	-0.18	0.051	0.555	-0.10	-1.8	1.0
WEEK 52/WEEK 44	58	0.57	0.484	0.50	0.0	3.3	0.65	58	-0.08	0.084	0.637	0.00	-1.6	2.7

Attachment 4.2: Haematology - Descriptive Statistics of Values and Change From Baseline - Crossover Subjects Excluded

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Table LAE03: Haematology - Descriptive Statistics of Values and Change from Baseline - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	N	Mean	SD	Med	Min	Max	Base Mean	N	Mean	SE	SD	Med	Min	Max
----- change from baseline usa-112 -----														
BASOPHILS (%)														
RISPERIDONE														
TREATMENT														
END POINT	121	0.49	0.410	0.40	0.0	3.3	0.61	121	-0.12	0.054	0.597	-0.10	-1.6	2.7
OLANZAPINE														
TREATMENT														
BASLINE	135	0.54	0.391	0.50	0.0	2.2								
WEEK 8/STUDY ENTRY	127	0.47	0.337	0.40	0.0	2.0	0.54	127	-0.07	0.043	0.481	0.00	-1.7	1.3
WEEK 52/WEEK 44	71	0.52	0.400	0.50	0.0	1.7	0.57	71	-0.04	0.065	0.546	0.00	-1.4	1.1
END POINT	135	0.50	0.346	0.50	0.0	1.7	0.54	135	-0.05	0.044	0.506	0.00	-1.4	1.1
PLATELET COUNT (giga/l)														
RISPERIDONE														
TREATMENT														
BASLINE	120	218.46	59.373	212.00	86.0	388.0								
WEEK 8/STUDY ENTRY	115	217.47	61.845	212.00	52.0	393.0	219.88	115	-2.41	2.522	27.043	-1.00	-92.0	97.0
WEEK 52/WEEK 44	57	217.63	48.687	216.00	80.0	375.0	216.93	57	0.70	3.943	29.772	0.00	-84.0	69.0
END POINT	120	214.69	55.634	211.50	80.0	393.0	218.46	120	-3.77	2.769	30.333	-2.50	-84.0	81.0
OLANZAPINE														
TREATMENT														
BASLINE	133	226.19	55.943	221.00	100.0	431.0								
WEEK 8/STUDY ENTRY	125	231.68	61.995	221.00	70.0	461.0	227.04	125	4.64	3.212	35.912	5.00	-161.0	134.0
WEEK 52/WEEK 44	68	240.22	68.780	248.00	39.0	382.0	233.44	68	6.78	5.880	48.491	14.00	-183.0	135.0
END POINT	133	234.95	66.990	217.00	39.0	437.0	226.19	133	8.77	3.534	40.753	14.00	-183.0	135.0

Attachment 4.3: Selected Laboratory Tests - Descriptive Statistics of Values and Change From Baseline to End Point - Crossover Subjects Excluded

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Table LAE04: Selected Laboratory Tests - Descriptive Statistics of Values and Change from Baseline to End Point - Crossover Subjects Excluded

Analysis Set: Itt Excluding Crossover Subjects (Restricted to Subjects with Visit End Point Data Only)

	N	Mean (SD)	Mean Change from Baseline (SD)

Cholesterol (mmol/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	5.16 (1.118)	
End point	122	5.15 (1.097)	-0.01 (0.775)
OLANZAPINE			
Treatment			
Baseline	134	5.11 (1.059)	
End point	134	5.27 (1.074)	0.17 (0.866)
Triglycerides (mmol/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	1.93 (1.603)	
End point	122	1.95 (1.568)	0.02 (1.228)
OLANZAPINE			
Treatment			
Baseline	134	1.92 (1.099)	
End point	134	2.26 (1.795)	0.34 (1.518)
Hdl (g/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	0.50 (0.160)	
End point	122	0.52 (0.149)	0.02 (0.107)
OLANZAPINE			
Treatment			
Baseline	133	0.51 (0.152)	
End point	133	0.50 (0.162)	-0.00 (0.122)

Attachment 4.3: Selected Laboratory Tests - Descriptive Statistics of Values and Change From Baseline to End Point - Crossover Subjects Excluded

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Table LAP04: Selected Laboratory Tests - Descriptive Statistics of Values and Change from Baseline to End Point - Crossover Subjects Excluded (continued)

Analysis Set: Itt Excluding Crossover Subjects (Restricted to Subjects with Visit End Point Data Only)

	N	Mean (SD)	Mean Change from Baseline (SD)

Ldl (g/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	116	1.18 (0.380)	
End point	116	1.17 (0.382)	-0.02 (0.268)
OLANZAPINE			
Treatment			
Baseline	127	1.14 (0.374)	
End point	127	1.17 (0.341)	0.03 (0.298)
~~			
GGT (U/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	44.07 (113.155)	
End point	122	47.03 (113.888)	2.97 (28.723)
OLANZAPINE			
Treatment			
Baseline	134	37.26 (45.837)	
End point	134	44.07 (45.072)	6.81 (28.702)
~~			
AST (U/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	19.57 (11.454)	
End point	122	19.04 (8.170)	-0.53 (9.705)
OLANZAPINE			
Treatment			
Baseline	134	20.06 (14.170)	
End point	134	24.07 (24.142)	4.01 (25.418)

Attachment 4.3: Selected Laboratory Tests - Descriptive Statistics of Values and Change From Baseline to End Point - Crossover Subjects Excluded

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Table LAB04: Selected Laboratory Tests - Descriptive Statistics of Values and Change from Baseline to End Point - Crossover Subjects Excluded (continued)

Analysis Set: Itt Excluding Crossover Subjects (Restricted to Subjects with Visit End Point Data Only)

	N	Mean (SD)	Mean Change from Baseline (SD)
-----	-----	-----	-----
ALT (U/L)			
~~			
RISPERIDONE			
Treatment			
Baseline	122	25.47 (25.022)	
End point	122	24.46 (18.201)	-1.01 (21.798)
OLANZAPINE			
Treatment			
Baseline	134	26.87 (30.250)	
End point	134	27.75 (23.539)	0.88 (31.037)
Prolactin (ng/ml)			
~~			
RISPERIDONE			
Treatment			
Baseline	108	19.30 (20.150)	
End point	108	44.97 (44.191)	25.68 (44.902)
OLANZAPINE			
Treatment			
Baseline	120	25.52 (34.200)	
End point	120	15.08 (14.788)	-10.44 (30.935)

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

CALCIUM (mmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	110	5	115	0	119	8	127
HIGH	0	1	3	4	0	0	1	1

Total	0	111	8	119	0	119	9	128

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	54	4	58	0	66	4	70
HIGH	0	0	1	1	0	0	0	0

Total	0	54	5	59	0	66	4	70

END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	112	6	118	0	122	9	131
HIGH	0	2	2	4	0	2	1	3

Total	0	114	8	122	0	124	10	134

CHLORIDE (mmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	1	0	1	0	0	0	0
NORMAL	1	95	6	102	0	104	8	112
HIGH	0	13	3	16	0	10	6	16

Total	1	109	9	119	0	114	14	128

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
CHLORIDE (mmol/l)								
TREATMENT								
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	53	2	55	0	63	5	68
HIGH	0	2	2	4	0	2	0	2
Total	0	55	4	59	0	65	5	70
END POINT								
LOW	0	1	0	1	0	0	0	0
NORMAL	1	102	4	107	0	115	12	127
HIGH	0	9	5	14	0	5	2	7
Total	1	112	9	122	0	120	14	134
POTASSIUM (mmol/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	2	115	2	119	0	125	3	128
HIGH	0	0	0	0	0	0	0	0
Total	2	115	2	119	0	125	3	128
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	58	1	59	0	69	1	70
HIGH	0	0	0	0	0	0	0	0
Total	0	58	1	59	0	69	1	70

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

		Treatment Group and Evaluation at Baseline							
		RISPERIDONE				OLANZAPINE			
		LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

POTASSIUM (mmol/l)									

TREATMENT									
END POINT									
LOW		0	1	0	1	0	0	0	0
NORMAL		2	117	2	121	0	131	3	134
HIGH		0	0	0	0	0	0	0	0

Total		2	118	2	122	0	131	3	134

SODIUM (mmol/l)									

TREATMENT									
WEEK 8/STUDY ENTRY									
LOW		1	4	0	5	1	1	0	2
NORMAL		2	110	0	112	4	122	0	126
HIGH		0	2	0	2	0	0	0	0

Total		3	116	0	119	5	123	0	128

WEEK 52/WEEK 44									
LOW		0	0	0	0	1	1	0	2
NORMAL		1	58	0	59	3	65	0	68
HIGH		0	0	0	0	0	0	0	0

Total		1	58	0	59	4	66	0	70

END POINT									
LOW		0	3	0	3	2	1	0	3
NORMAL		3	116	0	119	3	126	0	129
HIGH		0	0	0	0	0	2	0	2

Total		3	119	0	122	5	129	0	134

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

TOTAL PROTEIN (g/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	1	0	1
NORMAL	0	115	4	119	1	123	2	126
HIGH	0	0	0	0	0	0	1	1

Total	0	115	4	119	1	124	3	128

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	1	0	1
NORMAL	0	57	2	59	0	69	0	69
HIGH	0	0	0	0	0	0	0	0

Total	0	57	2	59	0	70	0	70

END POINT								
LOW	0	0	0	0	0	1	0	1
NORMAL	0	118	4	122	1	129	2	132
HIGH	0	0	0	0	0	0	1	1

Total	0	118	4	122	1	130	3	134

BLOOD UREA NITROGEN (mmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	3	4	0	7	4	5	0	9
NORMAL	9	101	1	111	6	112	1	119
HIGH	0	1	0	1	0	0	0	0

Total	12	106	1	119	10	117	1	128

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

		Treatment Group and Evaluation at Baseline									
		RISPERIDONE			Total	OLANZAPINE			Total		
		LOW	NORMAL	HIGH		LOW	NORMAL	HIGH			

BLOOD UREA NITROGEN (mmol/l)											

TREATMENT											
WEEK 52/WEEK 44											
LOW		0	1	0	1	2	4	0	6		
NORMAL		7	51	0	58	5	59	0	64		
HIGH		0	0	0	0	0	0	0	0		
Total		7	52	0	59	7	63	0	70		

END POINT											
LOW		2	4	0	6	3	7	0	10		
NORMAL		10	104	1	115	8	115	1	124		
HIGH		0	1	0	1	0	0	0	0		
Total		12	109	1	122	11	122	1	134		

URIC ACID (umol/l)											

TREATMENT											
WEEK 8/STUDY ENTRY											
LOW		12	8	0	20	6	3	0	9		
NORMAL		5	93	0	98	7	109	1	117		
HIGH		0	0	1	1	0	1	1	2		
Total		17	101	1	119	13	113	2	128		

WEEK 52/WEEK 44											
LOW		7	2	0	9	4	1	0	5		
NORMAL		3	44	0	47	5	58	0	63		
HIGH		0	2	1	3	0	1	1	2		
Total		10	48	1	59	9	60	1	70		

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
URIC ACID (umol/l)								
TREATMENT								
END POINT								
LOW	9	5	14		8	3	11	
NORMAL	9	96	105		7	112	119	
HIGH	0	2	3		0	2	4	
Total	18	103	122		15	117	134	
CREATININE (umol/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	1	1		1	0	1	
NORMAL	0	116	118		1	119	124	
HIGH	0	0	0		0	3	3	
Total	0	117	119		2	122	128	
WEEK 52/WEEK 44								
LOW	0	0	0		1	0	1	
NORMAL	0	57	58		1	68	69	
HIGH	0	0	1		0	0	0	
Total	0	57	59		2	68	70	
END POINT								
LOW	0	1	1		1	0	1	
NORMAL	0	119	120		1	126	131	
HIGH	0	0	1		0	2	2	
Total	0	120	122		2	128	134	

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Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

CHOLESTEROL (mmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	53	14	67	0	44	7	51
HIGH	0	10	42	52	0	23	54	77

Total	0	63	56	119	0	67	61	128

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	23	7	30	0	29	7	36
HIGH	0	9	20	29	0	10	24	34

Total	0	32	27	59	0	39	31	70

END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	53	19	72	0	52	13	65
HIGH	0	12	38	50	0	18	51	69

Total	0	65	57	122	0	70	64	134

TRIGLYCERIDES (mmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	83	15	98	0	76	9	85
HIGH	0	8	13	21	0	18	25	43

Total	0	91	28	119	0	94	34	128

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		OLANZAPINE					
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
TRIGLYCERIDES (mmol/l)								
TREATMENT								
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	43	6	49	0	38	5	43
HIGH	0	5	5	10	0	13	14	27
Total	0	48	11	59	0	51	19	70
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	81	15	96	0	77	11	88
HIGH	0	13	13	26	0	22	24	46
Total	0	94	28	122	0	99	35	134
HDL (g/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	8	6	0	14	8	4	0	12
NORMAL	10	95	0	105	7	107	0	114
HIGH	0	0	0	0	0	0	0	0
Total	18	101	0	119	15	111	0	126
WEEK 52/WEEK 44								
LOW	2	1	0	3	7	4	0	11
NORMAL	6	50	0	56	4	54	0	58
HIGH	0	0	0	0	0	0	0	0
Total	8	51	0	59	11	58	0	69

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

HDL (g/l)								

TREATMENT								
END POINT								
LOW	5	3	0	8	10	7	0	17
NORMAL	13	101	0	114	6	110	0	116
HIGH	0	0	0	0	0	0	0	0

Total	18	104	0	122	16	117	0	133

LDL (g/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	66	5	71	0	62	9	71
HIGH	0	11	30	41	0	20	26	46

Total	0	77	35	112	0	82	35	117

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	26	8	34	0	34	8	42
HIGH	0	11	12	23	0	7	11	18

Total	0	37	20	57	0	41	19	60

END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	66	14	80	0	70	15	85
HIGH	0	14	22	36	0	17	25	42

Total	0	80	36	116	0	87	40	127

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		OLANZAPINE		RISPERIDONE		OLANZAPINE	
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
TOTAL BILIRUBIN (umol/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	117	0	117	0	127	1	128
HIGH	0	1	1	2	0	0	0	0
Total	0	118	1	119	0	127	1	128
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	58	0	58	0	68	1	69
HIGH	0	1	0	1	0	1	0	1
Total	0	59	0	59	0	69	1	70
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	120	0	120	0	132	1	133
HIGH	0	1	1	2	0	1	0	1
Total	0	121	1	122	0	133	1	134
ALKALINE PHOSPHATASE (U/L)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	116	1	117	0	121	1	122
HIGH	0	0	2	2	0	2	4	6
Total	0	116	3	119	0	123	5	128

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAP05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

ALKALINE PHOSPHATASE (U/L)								

TREATMENT								
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	54	1	55	0	64	2	66
HIGH	0	4	0	4	0	3	1	4

Total	0	58	1	59	0	67	3	70
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	113	2	115	0	126	2	128
HIGH	0	5	2	7	0	3	3	6

Total	0	118	4	122	0	129	5	134
GGT (U/L)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	104	5	109	0	104	3	107
HIGH	0	1	10	11	0	7	15	22

Total	0	105	15	120	0	111	18	129
WEEK 12/WEEK 4								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	97	4	101	0	104	5	109
HIGH	0	3	8	11	0	6	12	18

Total	0	100	12	112	0	110	17	127

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
GGT (U/L)								
TREATMENT								
WEEK 16/WEEK 8								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	91	5	96	0	97	4	101
HIGH	0	1	7	8	0	6	11	17
Total	0	92	12	104	0	103	15	118
WEEK 20/WEEK 12								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	82	3	85	0	94	4	98
HIGH	0	3	8	11	0	6	11	17
Total	0	85	11	96	0	100	15	115
WEEK 36/WEEK 28								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	66	3	69	0	65	2	67
HIGH	0	3	5	8	0	10	7	17
Total	0	69	8	77	0	75	9	84
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	50	2	52	0	49	2	51
HIGH	0	4	3	7	0	11	8	19
Total	0	54	5	59	0	60	10	70

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

Treatment Group and Evaluation at Baseline								
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
GGT (U/L)								
TREATMENT								
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	101	5	106	0	102	4	106
HIGH	0	6	10	16	0	14	14	28
Total	0	107	15	122	0	116	18	134
LACTATE DEHYDROGENASE (U/L)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	118	0	118	0	125	2	127
HIGH	0	1	0	1	0	1	0	1
Total	0	119	0	119	0	126	2	128
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	59	0	59	0	68	1	69
HIGH	0	0	0	0	0	1	0	1
Total	0	59	0	59	0	69	1	70
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	121	0	121	0	130	2	132
HIGH	0	1	0	1	0	2	0	2
Total	0	122	0	122	0	132	2	134

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
AST (U/L)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	115	2	117	0	118	2	120
HIGH	0	1	2	3	0	5	4	9
Total	0	116	4	120	0	123	6	129
WEEK 12/WEEK 4								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	106	3	109	0	115	2	117
HIGH	0	3	0	3	0	7	4	11
Total	0	109	3	112	0	122	6	128
WEEK 16/WEEK 8								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	100	1	101	0	108	3	111
HIGH	0	1	2	3	0	4	3	7
Total	0	101	3	104	0	112	6	118
WEEK 20/WEEK 12								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	90	1	91	0	103	2	105
HIGH	0	3	2	5	0	6	4	10
Total	0	93	3	96	0	109	6	115

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

		Treatment Group and Evaluation at Baseline							
		RISPERIDONE				OLANZAPINE			
		LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

AST (U/L)									

TREATMENT									
WEEK 36/WEEK 28									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	74	1	75	0	78	2	80
HIGH		0	1	1	2	0	3	1	4

Total		0	75	2	77	0	81	3	84

WEEK 52/WEEK 44									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	57	1	58	0	65	1	66
HIGH		0	1	0	1	0	3	1	4

Total		0	58	1	59	0	68	2	70

END POINT									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	117	3	120	0	122	3	125
HIGH		0	1	1	2	0	6	3	9

Total		0	118	4	122	0	128	6	134

ALT (U/L)									

TREATMENT									
WEEK 8/STUDY ENTRY									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	105	5	110	0	108	4	112
HIGH		0	3	7	10	0	8	9	17

Total		0	108	12	120	0	116	13	129

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
ALT (U/L)								
TREATMENT								
WEEK 12/WEEK 4								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	96	5	101	0	107	4	111
HIGH	0	5	6	11	0	7	9	16
Total	0	101	11	112	0	114	13	127
WEEK 16/WEEK 8								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	91	6	97	0	98	5	103
HIGH	0	2	5	7	0	7	8	15
Total	0	93	11	104	0	105	13	118
WEEK 20/WEEK 12								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	84	5	89	0	97	3	100
HIGH	0	2	5	7	0	6	9	15
Total	0	86	10	96	0	103	12	115
WEEK 36/WEEK 28								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	68	2	70	0	66	4	70
HIGH	0	2	5	7	0	11	3	14
Total	0	70	7	77	0	77	7	84

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

		Treatment Group and Evaluation at Baseline							
		RISPERIDONE				OLANZAPINE			
		LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

ALT (U/L)									

TREATMENT									
WEEK 52/WEEK 44									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	53	3	56	0	57	4	61
HIGH		0	2	1	3	0	8	1	9
Total		0	55	4	59	0	65	5	70

END POINT									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	104	8	112	0	111	7	118
HIGH		0	6	4	10	0	10	6	16
Total		0	110	12	122	0	121	13	134

CPK (U/L)									

TREATMENT									
WEEK 8/STUDY ENTRY									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	94	6	100	0	105	5	110
HIGH		0	10	9	19	0	12	6	18
Total		0	104	15	119	0	117	11	128

WEEK 52/WEEK 44									
LOW		0	0	0	0	0	0	0	0
NORMAL		0	46	1	47	0	58	1	59
HIGH		0	7	5	12	0	8	3	11
Total		0	53	6	59	0	66	4	70

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
CPK (U/L)								
TREATMENT								
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	93	7	100	0	109	3	112
HIGH	0	14	8	22	0	14	8	22
Total	0	107	15	122	0	123	11	134
PROLACTIN (ng/ml)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	43	4	47	1	85	16	102
HIGH	0	38	19	57	0	4	6	10
Total	0	81	23	104	1	89	22	112
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	20	1	21	1	49	10	60
HIGH	0	18	13	31	0	1	3	4
Total	0	38	14	52	1	50	13	64
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	51	4	55	1	92	16	109
HIGH	0	34	19	53	0	4	7	11
Total	0	85	23	108	1	96	23	120

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAP05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

FREE THYROXINE (INDEX)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	2	0	2
NORMAL	3	115	0	118	1	122	1	124
HIGH	0	0	0	0	0	1	0	1

Total	3	115	0	118	1	125	1	127

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	57	0	57	1	66	0	67
HIGH	0	0	0	0	0	2	0	2

Total	0	57	0	57	1	68	0	69

END POINT								
LOW	0	0	0	0	0	1	0	1
NORMAL	3	118	0	121	1	128	0	129
HIGH	0	0	0	0	0	2	1	3

Total	3	118	0	121	1	131	1	133

T3 UPTAKE (%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	3	1	0	4	7	4	0	11
NORMAL	4	106	4	114	0	105	5	110
HIGH	0	0	0	0	0	3	3	6

Total	7	107	4	118	7	112	8	127

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

T3 UPTAKE (%)								

TREATMENT								
WEEK 52/WEEK 44								
LOW	0	3	0	3	2	3	0	5
NORMAL	1	49	3	53	0	57	4	61
HIGH	0	1	0	1	0	2	1	3

Total	1	53	3	57	2	62	5	69

END POINT								
LOW	4	4	0	8	7	4	0	11
NORMAL	4	103	4	111	0	112	5	117
HIGH	0	2	0	2	0	2	3	5

Total	8	109	4	121	7	118	8	133

THYROXINE (nmol/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	1	1	0	2
NORMAL	3	110	3	116	1	121	3	125
HIGH	0	1	1	2	0	0	0	0

Total	3	111	4	118	2	122	3	127

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	55	2	57	0	66	1	67
HIGH	0	0	0	0	0	2	0	2

Total	0	55	2	57	0	68	1	69

Attachment 4.4: Clinical Chemistry - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAB05: Clinical Chemistry - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

Treatment Group and Evaluation at Baseline								
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

THYROXINE (nmol/l)								
TREATMENT								
END POINT								
LOW	0	0	0	0	1	0	0	1
NORMAL	3	113	3	119	1	125	2	128
HIGH	0	1	1	2	0	3	1	4
Total	3	114	4	121	2	128	3	133

TSH (U/L)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	1	0	1	2	0	0	2
NORMAL	3	113	1	117	0	117	2	119
HIGH	0	0	0	0	1	4	0	5
Total	3	114	1	118	3	121	2	126

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	3	53	0	56	1	64	1	66
HIGH	0	1	0	1	0	2	0	2
Total	3	54	0	57	1	66	1	68

END POINT								
LOW	0	0	0	0	1	1	0	2
NORMAL	3	116	1	120	2	123	1	126
HIGH	0	1	0	1	0	4	1	5
Total	3	117	1	121	3	128	2	133

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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System Used: Arrow5.1/lbrun

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Table LAE06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

HAEMOGLOBIN (g/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	11	6	0	17	8	4	0	12
NORMAL	5	89	3	97	10	95	3	108
HIGH	0	1	0	1	0	4	1	5

Total	16	96	3	115	18	103	4	125

WEEK 52/WEEK 44								
LOW	3	4	0	7	5	2	0	7
NORMAL	5	44	1	50	6	50	1	57
HIGH	0	0	0	0	0	4	0	4

Total	8	48	1	57	11	56	1	68

END POINT								
LOW	10	10	0	20	8	4	0	12
NORMAL	7	90	3	100	12	100	2	114
HIGH	0	0	0	0	0	5	2	7

Total	17	100	3	120	20	109	4	133

HAEMOGLOBIN A1C (%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	97	2	99	0	111	3	114
HIGH	0	3	14	17	0	3	10	13

Total	0	100	16	116	0	114	13	127

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAB06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total	OLANZAPINE		Total		
	LOW	NORMAL		HIGH	LOW			NORMAL

HAEMOGLOBIN A1C (%)								

TREATMENT								
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	
NORMAL	0	43	3	0	61	1	62	
HIGH	0	6	5	0	4	5	9	

Total	0	49	8	0	65	6	71	

END POINT								
LOW	0	0	0	0	0	0	0	
NORMAL	0	96	3	0	114	2	116	
HIGH	0	8	14	0	7	11	18	

Total	0	104	17	0	121	13	134	

HAEMATOCRIT (vol-%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	11	9	0	7	5	0	12	
NORMAL	8	81	5	9	94	4	107	
HIGH	0	1	0	0	5	1	6	

Total	19	91	5	16	104	5	125	

WEEK 52/WEEK 44								
LOW	3	5	0	4	3	0	7	
NORMAL	6	41	2	7	46	1	54	
HIGH	0	0	0	0	6	1	7	

Total	9	46	2	11	55	2	68	

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAE06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		OLANZAPINE		RISPERIDONE		OLANZAPINE	
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total
HAEMATOCRIT (vol-%)								
TREATMENT								
END POINT								
LOW	8	11	0	19	7	5	0	12
NORMAL	12	83	5	100	11	97	4	112
HIGH	0	1	0	1	0	7	2	9
Total	20	95	5	120	18	109	6	133
RED BLOOD CELL COUNT (tera/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	5	4	0	9	1	2	0	3
NORMAL	9	90	4	103	6	111	2	119
HIGH	0	0	3	3	0	2	1	3
Total	14	94	7	115	7	115	3	125
WEEK 52/WEEK 44								
LOW	3	2	0	5	2	1	0	3
NORMAL	5	43	1	49	5	56	2	63
HIGH	0	0	3	3	0	2	0	2
Total	8	45	4	57	7	59	2	68
END POINT								
LOW	8	6	0	14	2	2	0	4
NORMAL	7	91	4	102	5	115	4	124
HIGH	0	1	3	4	0	4	1	5
Total	15	98	7	120	7	121	5	133

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAE06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE		Total		OLANZAPINE		Total	
	LOW	NORMAL			LOW	NORMAL		
WBC (giga/l)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	2	3	5		0	2	2	
NORMAL	1	94	99		0	102	7	109
HIGH	0	6	11		0	5	9	14
Total	3	103	115		0	109	16	125
WEEK 52/WEEK 44								
LOW	0	3	3		0	1	0	1
NORMAL	1	47	52		0	53	6	59
HIGH	0	2	2		0	1	7	8
Total	1	52	57		0	55	13	68
END POINT								
LOW	1	3	4		0	2	0	2
NORMAL	3	101	108		0	110	8	118
HIGH	0	3	8		0	4	9	13
Total	4	107	120		0	116	17	133
SEGMENTED NEUTROPHILS (%)								
TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0		0	2	0	2
NORMAL	1	102	109		5	108	6	119
HIGH	0	4	8		0	5	1	6
Total	1	106	117		5	115	7	127

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAE06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

SEGMENTED NEUTROPHILS (%)								

TREATMENT								
WEEK 52/WEEK 44								
LOW	0	1	0	1	0	0	0	0
NORMAL	0	49	4	53	4	57	4	65
HIGH	0	4	0	4	0	5	1	6

Total	0	54	4	58	4	62	5	71

END POINT								
LOW	1	1	0	2	0	2	0	2
NORMAL	1	102	8	111	5	115	5	125
HIGH	0	6	2	8	0	6	2	8

Total	2	109	10	121	5	123	7	135

NEUTROPHILS (giga/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	1	3	0	4	1	2	0	3
NORMAL	2	97	5	104	1	105	10	116
HIGH	0	3	4	7	0	3	2	5

Total	3	103	9	115	2	110	12	124

WEEK 52/WEEK 44								
LOW	0	2	0	2	1	0	0	1
NORMAL	0	48	4	52	0	56	6	62
HIGH	0	2	1	3	0	0	5	5

Total	0	52	5	57	1	56	11	68

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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System Used: Arrow5.1/lbrun

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Table LAB06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

		Treatment Group and Evaluation at Baseline							
		RISPERIDONE		Total	OLANZAPINE		Total		
		LOW	NORMAL		HIGH	LOW		NORMAL	HIGH

NEUTROPHILS (giga/l)									

TREATMENT									
END POINT									
LOW		1	2	3	1	1	0	2	
NORMAL		2	104	112	1	116	8	125	
HIGH		0	2	5	0	1	5	6	

Total		3	108	120	2	118	13	133	

LYMPHOCYTES (%)									

TREATMENT									
WEEK 8/STUDY ENTRY									
LOW		1	5	6	1	5	0	6	
NORMAL		4	103	109	3	105	7	115	
HIGH		0	2	2	0	5	1	6	

Total		5	110	117	4	115	8	127	

WEEK 52/WEEK 44									
LOW		1	1	2	0	4	1	5	
NORMAL		0	55	55	3	57	2	62	
HIGH		0	1	1	0	2	2	4	

Total		1	57	58	3	63	5	71	

END POINT									
LOW		2	2	4	1	5	1	7	
NORMAL		3	108	113	3	114	5	122	
HIGH		0	3	4	0	4	2	6	

Total		5	113	121	4	123	8	135	

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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System Used: Arrow5.1/lbrun

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Table LAB06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE			Total	OLANZAPINE			Total
	LOW	NORMAL	HIGH		LOW	NORMAL	HIGH	

MONOCYTES (%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	114	2	116	0	124	1	125
HIGH	0	1	0	1	0	2	0	2

Total	0	115	2	117	0	126	1	127

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	56	1	57	0	70	0	70
HIGH	0	0	1	1	0	1	0	1

Total	0	56	2	58	0	71	0	71

END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	118	1	119	0	133	1	134
HIGH	0	1	1	2	0	1	0	1

Total	0	119	2	121	0	134	1	135

EOSINOPHILS (%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	107	6	113	0	116	4	120
HIGH	0	2	2	4	0	5	2	7

Total	0	109	8	117	0	121	6	127

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAB06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

EOSINOPHILS (%)								

TREATMENT								
WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	50	4	54	0	64	5	69
HIGH	0	3	1	4	0	2	0	2

Total	0	53	5	58	0	66	5	71

END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	109	7	116	0	123	6	129
HIGH	0	4	1	5	0	4	2	6

Total	0	113	8	121	0	127	8	135

BASOPHILS (%)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	115	2	117	0	126	1	127
HIGH	0	0	0	0	0	0	0	0

Total	0	115	2	117	0	126	1	127

WEEK 52/WEEK 44								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	56	1	57	0	70	1	71
HIGH	0	1	0	1	0	0	0	0

Total	0	57	1	58	0	70	1	71

Attachment 4.5: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

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Table LAB06: Hematology - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	Treatment Group and Evaluation at Baseline							
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

BASOPHILS (%)								

TREATMENT								
END POINT								
LOW	0	0	0	0	0	0	0	0
NORMAL	0	118	2	120	0	134	1	135
HIGH	0	1	0	1	0	0	0	0

Total	0	119	2	121	0	134	1	135

PLATELET COUNT (giga/l)								

TREATMENT								
WEEK 8/STUDY ENTRY								
LOW	5	3	0	8	2	1	0	3
NORMAL	0	107	0	107	0	120	1	121
HIGH	0	0	0	0	0	1	0	1

Total	5	110	0	115	2	122	1	125

WEEK 52/WEEK 44								
LOW	1	0	0	1	1	3	0	4
NORMAL	0	56	0	56	0	64	0	64
HIGH	0	0	0	0	0	0	0	0

Total	1	56	0	57	1	67	0	68

END POINT								
LOW	4	1	0	5	3	3	0	6
NORMAL	1	114	0	115	0	126	0	126
HIGH	0	0	0	0	0	0	1	1

Total	5	115	0	120	3	129	1	133

Attachment 4.6: Selected Laboratory Tests - Crosstabulation of Baseline Versus End Point Values - Crossover Subjects Excluded

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Table LAE07: Selected Laboratory Tests - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded

Analysis Set: Itt Excluding Crossover Subjects

Treatment Group and Evaluation at Baseline								
	RISPERIDONE					OLANZAPINE		
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

Cholesterol (mmol/L)								

Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	53	19	72	0	52	13	65
High	0	12	38	50	0	18	51	69
	-----				-----			
Total	0	65	57	122	0	70	64	134

Triglycerides (mmol/L)								

Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	81	15	96	0	77	11	88
High	0	13	13	26	0	22	24	46
	-----				-----			
Total	0	94	28	122	0	99	35	134

Hdl (g/L)								

Treatment								
End point								
Low	5	3	0	8	10	7	0	17
Normal	13	101	0	114	6	110	0	116
High	0	0	0	0	0	0	0	0
	-----				-----			
Total	18	104	0	122	16	117	0	133

Attachment 4.6: Selected Laboratory Tests - Crosstabulation of Baseline Versus End Point Values - Crossover
Subjects Excluded

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Table LAE07: Selected Laboratory Tests - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: Itt Excluding Crossover Subjects

Treatment Group and Evaluation at Baseline								
	RISPERIDONE				OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

Ldl (g/L)								
Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	66	14	80	0	70	15	85
High	0	14	22	36	0	17	25	42

Total	0	80	36	116	0	87	40	127

GGT (U/L)								
Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	101	5	106	0	102	4	106
High	0	6	10	16	0	14	14	28

Total	0	107	15	122	0	116	18	134

AST (U/L)								
Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	117	3	120	0	122	3	125
High	0	1	1	2	0	6	3	9

Total	0	118	4	122	0	128	6	134

Attachment 4.6: Selected Laboratory Tests - Crosstabulation of Baseline Versus End Point Values - Crossover
Subjects Excluded

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Table LAB07: Selected Laboratory Tests - Crosstabulation of Baseline versus End Point Values - Crossover Subjects Excluded (continued)

Analysis Set: Itt Excluding Crossover Subjects

Treatment Group and Evaluation at Baseline								
RISPERIDONE					OLANZAPINE			
	LOW	NORMAL	HIGH	Total	LOW	NORMAL	HIGH	Total

ALT (U/L)								

Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	104	8	112	0	111	7	118
High	0	6	4	10	0	10	6	16

Total	0	110	12	122	0	121	13	134

Prolactin (ng/ml)								

Treatment								
End point								
Low	0	0	0	0	0	0	0	0
Normal	0	51	4	55	1	92	16	109
High	0	34	19	53	0	4	7	11

Total	0	85	23	108	1	96	23	120

Attachment 4.7: Clinical Chemistry - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

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Table LAE08: Clinical Chemistry - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

WITHIN LIMITS AT BASELINE	RISPERIDONE			OLANZAPINE		
	Total n	PATHOLOGICAL LIMITS, BELOW WITHIN ABOVE	n (%)	Total n	PATHOLOGICAL LIMITS, BELOW WITHIN ABOVE	n (%)
CALCIUM (mmol/l)	122	0	122 (100)	0	134 (100)	0
CHLORIDE (mmol/l)	120	1 (1)	116 (97)	3 (3)	134	1 (1) 131 (98) 2 (1)
POTASSIUM (mmol/l)	121	0	121 (100)	0	132	0 132 (100) 0
SODIUM (mmol/l)	122	0	122 (100)	0	134	0 134 (100) 0
TOTAL PROTEIN (g/l)	121	0	121 (100)	0	131	2 (2) 129 (98) 0
BLOOD UREA NITROGEN (mmol/l)	120	1 (1)	117 (98)	2 (2)	133	4 (3) 129 (97) 0
URIC ACID (umol/l)	122	1 (1)	121 (99)	0	132	0 132 (100) 0
CREATININE (umol/l)	122	0	122 (100)	0	134	0 134 (100) 0
CHOLESTEROL (mmol/l)	122	0	122 (100)	0	134	0 132 (99) 2 (1)
TRIGLYCERIDES (mmol/l)	99	0	93 (84)	16 (16)	101	0 73 (72) 28 (28)
TOTAL BILIRUBIN (umol/l)	122	0	120 (98)	2 (2)	133	0 132 (99) 1 (1)
ALKALINE PHOSPHATASE (U/L)	121	0	121 (100)	0	134	0 133 (99) 1 (1)
GGT (U/L)	119	0	115 (97)	4 (3)	127	0 122 (96) 5 (4)
LACTATE DEHYDROGENASE (U/L)	122	0	122 (100)	0	134	0 133 (99) 1 (1)
AST (U/L)	121	0	120 (99)	1 (1)	132	0 126 (95) 6 (5)
ALT (U/L)	120	0	116 (97)	4 (3)	130	0 123 (95) 7 (5)
CPK (U/L)	118	0	115 (97)	3 (3)	133	0 124 (93) 9 (7)
FREE THYROXINE (INDEX)	118	0	118 (100)	0	132	2 (2) 130 (98) 0
THYROXINE (nmol/l)	117	0	115 (98)	2 (2)	130	0 128 (98) 2 (2)

Note: Percentages of pathological limits sub-groups calculated with the number of subjects per within limits at baseline as denominator.
A subject may be in more than one category.

Attachment 4.8: Hematology - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

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Table LAB09: Hematology - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

WITHIN LIMITS AT BASELINE	RISPERIDONE				OLANZAPINE			
	Total n	PATHOLOGICAL LIMITS, n (%)			Total n	PATHOLOGICAL LIMITS, n (%)		
		BELOW	WITHIN	ABOVE		BELOW	WITHIN	ABOVE
HAEMOGLOBIN (g/l)	116	2 (2)	114 (98)	0	130	3 (2)	127 (98)	0
HAEMATOCRIT (vol-%)	113	3 (3)	110 (97)	0	130	5 (4)	125 (96)	0
RED BLOOD CELL COUNT (tera/l)	118	1 (1)	116 (98)	1 (1)	133	0	133 (100)	0
WBC (giga/l)	112	1 (1)	103 (92)	8 (7)	118	0	113 (96)	5 (4)
PLATELET COUNT (giga/l)	115	3 (3)	112 (97)	0	129	4 (3)	124 (96)	1 (1)

Note: Percentages of pathological limits sub-groups calculated with the number of subjects per within limits at baseline as denominator.
A subject may be in more than one category.

Attachment 4.9: Selected Laboratory Tests - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

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Table LAE10: Selected Laboratory Tests - Percent of Subjects Within Pathological Limits at Baseline and Outside Post-Baseline - Crossover Subjects Excluded

Analysis Set: Itt Excluding Crossover Subjects

Within Limits at Baseline	RISPERIDONE				OLANZAPINE			
	Total	-- PATHOLOGICAL LIMITS, n (%) --			Total	-- PATHOLOGICAL LIMITS, n (%) --		
	n	Below	Within	Above	n	Below	Within	Above
Cholesterol (mmol/L)	122	0	122 (100)	0	134	0	132 (99)	2 (1)
Triglycerides (mmol/L)	99	0	83 (84)	16 (16)	101	0	73 (72)	28 (28)
GGT (U/L)	119	0	115 (97)	4 (3)	127	0	122 (96)	5 (4)
AST (U/L)	121	0	120 (99)	1 (1)	132	0	126 (95)	6 (5)
ALT (U/L)	120	0	116 (97)	4 (3)	130	0	123 (95)	7 (5)

Note: Percentages of pathological limits sub-groups calculated with the number of subjects per within limits at baseline as denominator.
A subject may be in more than one category.

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Table LAE11: Urinalysis - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%

URINE GLUCOSE						

TREATMENT						
BASELINE						
NEGATIVE	107	92.2	92.2	127	96.2	96.2
TRACE OR 1/10 G/	1	0.9	93.1	0	0.0	96.2
1+ OR 1/4 G/DL (	1	0.9	94.0	1	0.8	97.0
2+ OR 1/2 G/DL (	1	0.9	94.8	1	0.8	97.7
3+ OR 1 G/DL (%)	6	5.2	100.0	3	2.3	100.0

Total	116			132		
END POINT						
NEGATIVE	107	90.7	90.7	130	95.6	95.6
TRACE OR 1/10 G/	1	0.8	91.5	0	0.0	95.6
1+ OR 1/4 G/DL (	2	1.7	93.2	1	0.7	96.3
2+ OR 1/2 G/DL (	2	1.7	94.9	0	0.0	96.3
3+ OR 1 G/DL (%)	6	5.1	100.0	5	3.7	100.0

Total	118			136		
URINE OCCULT BLOOD						

TREATMENT						
BASELINE						
NEGATIVE	109	94.0	94.0	122	92.4	92.4
TRACE	4	3.4	97.4	4	3.0	95.5
1+	2	1.7	99.1	2	1.5	97.0
2+	1	0.9	100.0	2	1.5	98.5
3+	0	0.0	100.0	2	1.5	100.0

Total	116			132		

Attachment 4.10: Urinalysis - Crossover Subjects Excluded

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Table LAE11: Urinalysis - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%
URINE OCCULT BLOOD						
TREATMENT						
END POINT						
NEGATIVE	107	90.7	90.7	125	91.9	91.9
TRACE	3	2.5	93.2	4	2.9	94.9
1+	6	5.1	98.3	3	2.2	97.1
2+	2	1.7	100.0	0	0.0	97.1
3+	0	0.0	100.0	4	2.9	100.0
Total	118			136		
URINE PROTEIN						
TREATMENT						
BASELINE						
NEGATIVE	111	95.7	95.7	129	97.7	97.7
TRACE	2	1.7	97.4	2	1.5	99.2
1+	2	1.7	99.1	0	0.0	99.2
2+	1	0.9	100.0	0	0.0	99.2
3+	0	0.0	100.0	1	0.8	100.0
Total	116			132		
END POINT						
NEGATIVE	113	95.8	95.8	132	97.1	97.1
TRACE	4	3.4	99.2	3	2.2	99.3
1+	1	0.8	100.0	1	0.7	100.0
2+	0	0.0	100.0	0	0.0	100.0
3+	0	0.0	100.0	0	0.0	100.0
Total	118			136		

Attachment 4.10: Urinalysis - Crossover Subjects Excluded

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Table LAE11: Urinalysis - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%

URINE RBC						

TREATMENT						
BASELINE						
NONE SEEN	109	94.0	94.0	123	93.2	93.2
0-1	1	0.9	94.8	0	0.0	93.2
1-3	1	0.9	95.7	2	1.5	94.7
3-5	2	1.7	97.4	3	2.3	97.0
5-10	1	0.9	98.3	3	2.3	99.2
10-15	1	0.9	99.1	0	0.0	99.2
15-25	1	0.9	100.0	0	0.0	99.2
25-50	0	0.0	100.0	1	0.8	100.0
50-100	0	0.0	100.0	0	0.0	100.0

Total	116			132		

END POINT						
NONE SEEN	105	89.0	89.0	128	94.1	94.1
0-1	2	1.7	90.7	0	0.0	94.1
1-3	4	3.4	94.1	1	0.7	94.9
3-5	4	3.4	97.5	4	2.9	97.8
5-10	2	1.7	99.2	0	0.0	97.8
10-15	0	0.0	99.2	0	0.0	97.8
15-25	1	0.8	100.0	0	0.0	97.8
25-50	0	0.0	100.0	2	1.5	99.3
50-100	0	0.0	100.0	1	0.7	100.0

Total	118			136		

Attachment 4.10: Urinalysis - Crossover Subjects Excluded

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Table LAE11: Urinalysis - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%

URINE WBC						

TREATMENT						
BASELINE						
NONE SEEN	20	17.2	17.2	30	22.7	22.7
0-1	55	47.4	64.7	63	47.7	70.5
1-3	25	21.6	86.2	27	20.5	90.9
3-5	8	6.9	93.1	4	3.0	93.9
5-10	3	2.6	95.7	4	3.0	97.0
10-15	2	1.7	97.4	2	1.5	98.5
15-25	1	0.9	98.3	0	0.0	98.5
25-50	1	0.9	99.1	1	0.8	99.2
50-100	1	0.9	100.0	1	0.8	100.0
INNUMERABLE	0	0.0	100.0	0	0.0	100.0

Total	116			132		

END POINT						
NONE SEEN	23	19.5	19.5	20	14.7	14.7
0-1	67	56.8	76.3	80	58.8	73.5
1-3	19	16.1	92.4	22	16.2	89.7
3-5	1	0.8	93.2	9	6.6	96.3
5-10	3	2.5	95.8	3	2.2	98.5
10-15	1	0.8	96.6	1	0.7	99.3
15-25	1	0.8	97.5	0	0.0	99.3
25-50	2	1.7	99.2	1	0.7	100.0
50-100	0	0.0	99.2	0	0.0	100.0
INNUMERABLE	1	0.8	100.0	0	0.0	100.0

Total	118			136		

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 1 of 6

28AUG2003 10:06
System Used: Arrow5.1 (U)/vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
SUPINE PULSE, 1/MIN.													
~~													
TREATMENT													
BASELINE	116	78.3	11.94			126	76.6	10.39			0.284	0.045	
WEEK 8/STUDY ENTRY	114	77.9	12.15	-0.1	12.86	122	78.2	11.81	1.7	10.94	0.273	0.025	<0.001
WEEK 12/WEEK 4	108	79.1	12.08	1.1	15.36	122	79.5	11.81	2.9	12.48	0.658	0.666	<0.001
WEEK 16/WEEK 8	100	77.7	10.99	-0.6	12.59	115	79.7	11.76	3.5	13.31	0.042	0.129	<0.001
WEEK 20/WEEK 12	91	78.4	10.29	1.2	12.64	107	79.2	12.18	3.3	13.03	0.399	0.054	<0.001
WEEK 36/WEEK 28	74	78.2	11.67	0.9	11.77	82	77.9	11.29	2.6	11.96	0.659	0.561	<0.001
WEEK 52/WEEK 44	55	78.6	12.44	1.7	13.42	68	79.9	13.10	4.4	14.03	0.570	0.247	<0.001
END POINT	116	78.3	12.19	0.1	13.58	126	79.4	12.53	2.8	13.25	0.420	0.482	<0.001
~~													
STANDING PULSE, 1/MIN.													
~~													
TREATMENT													
BASELINE	116	85.0	12.22			126	82.7	12.12			0.194	<0.001	
WEEK 8/STUDY ENTRY	113	85.1	15.77	0.3	13.46	122	85.1	13.74	2.6	13.35	0.402	0.005	<0.001
WEEK 12/WEEK 4	107	86.1	13.21	1.2	14.35	123	87.0	12.08	4.5	14.00	0.420	0.573	<0.001
WEEK 16/WEEK 8	99	86.3	14.06	1.2	14.28	115	84.9	13.07	2.4	13.67	0.857	0.009	<0.001
WEEK 20/WEEK 12	90	86.9	12.26	2.4	13.54	107	84.3	12.88	2.2	14.75	0.221	0.030	<0.001
WEEK 36/WEEK 28	74	85.8	13.57	1.4	12.88	82	84.6	12.47	3.1	13.64	0.944	0.120	<0.001
WEEK 52/WEEK 44	53	86.5	13.53	2.3	14.44	68	86.7	13.39	5.1	14.48	0.862	0.193	<0.001
END POINT	116	86.3	14.64	1.3	14.39	126	85.0	12.69	2.3	14.45	0.484	0.084	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 2 of 6

28AUG2008 10:08
System Used: Arrow5.1(U)/vstrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)

SUPINE PULSE, 1/MIN.		
~~		
TREATMENT		
BASELINE	-1.5	(-4.34; 1.28)
WEEK 8/STUDY ENTRY	1.5	(-1.20; 4.21)
WEEK 12/WEEK 4	0.7	(-2.38; 3.76)
WEEK 16/WEEK 8	3.0	(0.11; 5.99)
WEEK 20/WEEK 12	1.3	(-1.74; 4.35)
WEEK 36/WEEK 28	0.8	(-2.74; 4.31)
WEEK 52/WEEK 44	1.3	(-3.25; 5.88)
END POINT	1.2	(-1.77; 4.24)
STANDING PULSE, 1/MIN.		
~~		
TREATMENT		
BASELINE	-1.9	(-4.86; 0.99)
WEEK 8/STUDY ENTRY	1.4	(-1.83; 4.55)
WEEK 12/WEEK 4	1.3	(-1.87; 4.46)
WEEK 16/WEEK 8	-0.3	(-3.57; 2.98)
WEEK 20/WEEK 12	-2.1	(-5.45; 1.27)
WEEK 36/WEEK 28	0.1	(-3.74; 4.01)
WEEK 52/WEEK 44	-0.4	(-5.26; 4.41)
END POINT	-1.1	(-4.36; 2.07)

See footnotes on the first page of the table.

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 3 of 6

28AUG2003 10:08
System Used: Arrow5.1 (U) /vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
SUPINE SYSTOLIC BP, MMHG													
TREATMENT													
BASLINE	116	122.6	15.14			126	122.0	13.79			0.626	0.024	
WEEK 8/STUDY ENTRY	114	121.3	12.47	-1.6	13.88	122	124.3	13.83	2.4	12.90	0.031	0.090	<0.001
WEEK 12/WEEK 4	108	118.7	13.54	-3.5	14.95	122	125.1	16.81	3.4	15.35	<0.001	0.831	<0.001
WEEK 16/WEEK 8	100	118.3	13.65	-3.7	15.52	115	123.8	15.10	2.1	15.45	0.005	0.861	<0.001
WEEK 20/WEEK 12	91	119.8	13.44	-3.0	14.26	107	124.2	14.38	3.1	14.72	0.006	0.714	<0.001
WEEK 36/WEEK 28	74	122.4	16.89	-1.2	17.90	82	123.7	16.18	2.8	15.18	0.313	0.997	<0.001
WEEK 52/WEEK 44	55	123.3	14.95	0.6	18.67	68	126.1	13.56	4.8	13.63	0.347	0.179	<0.001
END POINT	116	122.3	15.35	-0.3	16.81	126	125.4	16.71	3.4	15.25	0.137	0.314	<0.001
STANDING SYSTOLIC BP, MMHG													
TREATMENT													
BASLINE	116	119.3	14.76			126	121.8	14.76			0.154	0.001	
WEEK 8/STUDY ENTRY	114	119.3	13.82	-0.0	15.92	122	122.3	14.77	0.5	14.07	0.426	0.036	<0.001
WEEK 12/WEEK 4	108	120.1	12.16	0.9	14.80	123	124.7	17.65	3.1	15.61	0.090	0.376	<0.001
WEEK 16/WEEK 8	99	117.5	14.50	-2.1	16.22	115	124.3	17.12	2.9	17.23	0.005	0.817	<0.001
WEEK 20/WEEK 12	90	121.0	17.21	0.5	17.70	107	122.2	14.73	1.3	16.01	0.653	0.511	<0.001
WEEK 36/WEEK 28	74	120.8	16.11	0.2	18.36	82	124.1	16.00	2.5	14.96	0.327	0.547	<0.001
WEEK 52/WEEK 44	54	123.1	14.26	3.0	18.02	68	127.7	14.70	6.4	16.95	0.461	0.170	<0.001
END POINT	116	121.7	15.44	2.4	16.96	126	126.3	17.67	4.5	18.16	0.169	0.064	<0.001

See footnotes on the first page of the table.

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 4 of 6

28AUG2008 10:08
System Used: Arrow5.1(U)/vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)

SUPINE SYSTOLIC BP, MMHG		

TREATMENT		
BASELINE	-0.9	(-4.52; 2.72)
WEEK 8/STUDY ENTRY	3.2	(0.30; 6.08)
WEEK 12/WEEK 4	6.2	(2.57; 9.81)
WEEK 16/WEEK 8	5.3	(1.64; 8.94)
WEEK 20/WEEK 12	5.0	(1.45; 8.58)
WEEK 36/WEEK 28	2.7	(-2.53; 7.83)
WEEK 52/WEEK 44	2.4	(-2.59; 7.31)
END POINT	2.8	(-0.90; 6.49)
STANDING SYSTOLIC BP, MMHG		

TREATMENT		
BASELINE	2.6	(-0.99; 6.24)
WEEK 8/STUDY ENTRY	1.3	(-1.93; 4.56)
WEEK 12/WEEK 4	3.1	(-0.48; 6.63)
WEEK 16/WEEK 8	5.9	(1.80; 9.99)
WEEK 20/WEEK 12	1.0	(-3.25; 5.18)
WEEK 36/WEEK 28	2.4	(-2.48; 7.38)
WEEK 52/WEEK 44	1.9	(-3.27; 7.15)
END POINT	2.7	(-1.17; 6.67)

See footnotes on the first page of the table.

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 5 of 6

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System Used: Arrow5.1(U)/vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
SUPINE DIASTOLIC BP, MMHG													
~~													
TREATMENT													
BASELINE	116	77.7	9.22			126	77.4	9.29			0.712	<0.001	
WEEK 8/STUDY ENTRY	114	75.6	9.56	-2.3	10.63	122	79.4	8.91	1.7	9.12	0.002	0.002	<0.001
WEEK 12/WEEK 4	108	75.5	9.85	-2.0	10.06	122	79.6	9.61	2.3	9.40	<0.001	0.879	<0.001
WEEK 16/WEEK 8	100	75.2	9.74	-2.0	10.78	115	79.8	9.41	2.4	10.21	<0.001	0.060	<0.001
WEEK 20/WEEK 12	91	75.5	9.53	-2.0	10.45	107	80.0	8.40	3.2	8.91	<0.001	0.333	<0.001
WEEK 36/WEEK 28	74	76.6	9.84	-1.5	10.44	82	79.6	10.19	3.0	9.28	0.035	0.139	<0.001
WEEK 52/WEEK 44	55	79.2	10.20	1.5	11.06	68	78.5	9.01	1.2	10.17	0.646	0.013	<0.001
END POINT	116	77.5	9.88	-0.2	10.64	126	78.8	9.19	1.4	11.17	0.274	0.028	<0.001
STANDING DIASTOLIC BP, MMHG													
~~													
TREATMENT													
BASELINE	116	78.6	10.14			126	80.4	9.89			0.082	<0.001	
WEEK 8/STUDY ENTRY	114	77.0	8.77	-1.7	12.45	122	80.8	9.41	0.3	9.60	0.019	0.024	<0.001
WEEK 12/WEEK 4	108	77.2	10.64	-1.2	13.25	123	80.8	10.32	0.6	10.29	0.047	0.141	<0.001
WEEK 16/WEEK 8	99	77.4	9.73	-1.1	13.17	115	80.4	10.01	0.2	10.78	0.058	0.023	<0.001
WEEK 20/WEEK 12	90	78.6	10.46	-0.8	13.32	107	81.0	10.26	1.1	11.48	0.090	0.038	<0.001
WEEK 36/WEEK 28	74	78.1	10.86	-1.3	14.00	82	81.2	10.35	1.6	10.40	0.097	<0.001	<0.001
WEEK 52/WEEK 44	54	81.4	11.05	1.3	14.99	68	80.4	9.28	-0.0	12.05	0.614	0.016	<0.001
END POINT	116	80.0	10.92	1.4	12.97	126	80.2	10.24	-0.2	12.44	0.821	<0.001	<0.001

See footnotes on the first page of the table.

Attachment 5.1: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

Page 6 of 6

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System Used: Arrow5.1 (U) /vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS04: Pulse and Blood Pressure - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus ----- RISPERIDONE ----- L.S.Mean 95% CI(a)	

SUPINE DIASTOLIC BP, MMHG		

TREATMENT		
BASELINE	-0.4	(-2.68; 1.84)
WEEK 8/STUDY ENTRY	3.3	(1.19; 5.37)
WEEK 12/WEEK 4	4.1	(1.75; 6.37)
WEEK 16/WEEK 8	4.5	(2.15; 6.87)
WEEK 20/WEEK 12	4.8	(2.44; 7.09)
WEEK 36/WEEK 28	3.1	(0.22; 6.01)
WEEK 52/WEEK 44	-0.7	(-3.91; 2.44)
END POINT	1.3	(-1.00; 3.53)
STANDING DIASTOLIC BP, MMHG		

TREATMENT		
BASELINE	2.1	(-0.28; 4.54)
WEEK 8/STUDY ENTRY	2.7	(0.45; 4.87)
WEEK 12/WEEK 4	2.6	(0.03; 5.21)
WEEK 16/WEEK 8	2.5	(-0.09; 5.00)
WEEK 20/WEEK 12	2.4	(-0.38; 5.22)
WEEK 36/WEEK 28	2.6	(-0.48; 5.65)
WEEK 52/WEEK 44	-0.9	(-4.53; 2.69)
END POINT	-0.3	(-2.81; 2.23)

See footnotes on the first page of the table.

Risperidone: Clinical Study Report RIS-USA-113

Attachment 5.2: Percent of Subjects With New Antihypertensive Co-Med or 2 Consecutive Visits With DBP>95 in RIS-USA-112 or RIS-USA-113 - Crossover Subjects Excluded

Page 1 of 1

28AUG2008 17:46
System Used: Arrow5.1(U)/vsrun2

JNJPRD--TRIAL RIS-USA-113

Table VS03: Percent of Subjects with New Antihypertensive Co-Med or 2 Consecutive Visits with DBP>95 in RIS-USA-112 or RIS-USA-113
- Crossover Subjects Excluded

Analysis Set: ITT Excluding Crossover Subjects

				Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
-- RISPERIDONE --		-- OLANZAPINE --		95% CI	P-value (a)
n	%	n	%		
Onset of hypertension					
~~					
Treatment					
Overall					
No	104	87.4	116	89.2	
Yes	15	12.6	14	10.8	
Total	119		130	(-0.06; 0.10)	0.745

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
R: two-sided p-value <= 0.10 with RISPERIDONE having lower scores; RR: p-value <= 0.05.
O: two-sided p-value <= 0.10 with OLANZAPINE having lower scores; OO: p-value <= 0.05.

Attachment 5.3: Physical Examination at End Point - Crossover Subjects Excluded

Page 1 of 2

25AUG2008 16:56
System Used: Arrow5.1(U)/perun

JNJPRD--TRIAL RIS-USA-113

Table PE02: Physical Examination at End Point - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

PHYS. EXAM. BODY SYSTEM VALUE DESCRIPTION	RISPERIDONE (N=122) n (%)	OLANZAPINE (N=136) n (%)
TOTAL NO. SUBJECTS WITH EXAM	122 (100)	136 (100)
GENERAL APPEARANCE	122	136
ABNORMAL	23 (19)	24 (18)
NORMAL	99 (81)	112 (82)
SKIN	122	136
ABNORMAL	20 (16)	24 (18)
NORMAL	102 (84)	112 (82)
EYES	122	136
ABNORMAL	12 (10)	9 (7)
NORMAL	110 (90)	127 (93)
EARS, NOSE, THROAT	122	136
ABNORMAL	13 (11)	11 (8)
NORMAL	109 (89)	125 (92)
HEAD AND NECK	122	136
ABNORMAL	4 (3)	2 (1)
NORMAL	118 (97)	134 (99)
HEART	122	136
ABNORMAL	8 (7)	4 (3)
NORMAL	114 (93)	132 (97)
CHEST AND LUNGS	122	136
ABNORMAL	10 (8)	6 (4)
NORMAL	112 (92)	130 (96)
BREASTS	115	128
ABNORMAL	8 (7)	4 (3)
NORMAL	107 (93)	124 (97)
ABDOMEN	122	136
ABNORMAL	11 (9)	16 (12)

Note: Percentages calculated with the number of subjects per phys. exam. body system as denominator.

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Attachment 5.3: Physical Examination at End Point - Crossover Subjects Excluded

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25AUG2003 16:58
System Used: Arrow5.1 (U) /perun

JNJPRD--TRIAL RIS-USA-113

Table PE02: Physical Examination at End Point - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

PHYS. EXAM. BODY SYSTEM VALUE DESCRIPTION	RISPERIDONE (N=122) n (%)	OLANZAPINE (N=136) n (%)
ABDOMEN (continued)		
NORMAL	111 (91)	120 (88)
EXTREMITIES	122	136
ABNORMAL	9 (7)	8 (6)
NORMAL	113 (93)	128 (94)
BACK	122	136
ABNORMAL	1 (1)	2 (1)
NORMAL	121 (99)	134 (99)
LYMPH NODES	121	136
ABNORMAL	1 (1)	1 (1)
NORMAL	120 (99)	135 (99)
PERIPHERAL PULSES	122	135
ABNORMAL	0	1 (1)
NORMAL	122 (100)	134 (99)
MUSCULOSKELETAL	122	136
ABNORMAL	5 (4)	3 (2)
NORMAL	117 (96)	133 (98)
NEUROLOGICAL	122	136
ABNORMAL	3 (2)	4 (3)
NORMAL	119 (98)	132 (97)
OTHER	9	10
ABNORMAL	9 (100)	10 (100)

See footnotes on the first page of the table.

Attachment 6.1: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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28AUG2008 10:53
System Used: Arrow5.1(U)/ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG01: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value(a)	investp P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT SCORE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT SCORE Mean	SD			
QTC INTERVAL (ms)													
~~													
TREATMENT													
SCREENING	117	412.8	32.14			136	409.8	24.97			0.418	<0.001	
WEEK 8/STUDY ENTRY	114	410.9	29.49	-1.5	29.08	128	410.3	23.11	0.2	21.05	0.811	0.080	<0.001
WEEK 52/WEEK 44	56	414.3	43.09	1.8	37.13	73	412.1	30.45	1.9	23.33	0.751	<0.001	<0.001
END POINT	117	409.0	46.56	-3.8	43.20	136	411.7	27.70	2.0	22.82	0.713	<0.001	<0.001
QT INTERVAL (ms)													
~~													
TREATMENT													
SCREENING	117	374.0	36.07			136	375.1	32.11			0.653	<0.001	
WEEK 8/STUDY ENTRY	114	374.7	32.16	1.0	33.07	128	375.0	32.46	-1.1	35.55	0.812	0.154	<0.001
WEEK 52/WEEK 44	56	376.9	34.81	-0.4	35.00	73	370.6	32.37	-2.2	32.38	0.537	0.662	<0.001
END POINT	117	371.8	40.24	-2.1	37.23	136	372.7	31.72	-2.4	32.95	0.998	0.057	<0.001
HEART RATE (1/min)													
~~													
TREATMENT													
SCREENING	117	76.4	14.01			136	75.1	13.32			0.301	0.002	
WEEK 8/STUDY ENTRY	114	75.1	13.51	-1.4	13.00	127	75.7	14.83	0.8	12.71	0.379	0.833	<0.001
WEEK 52/WEEK 44	56	77.6	16.42	2.0	15.36	73	77.2	14.29	1.3	13.08	0.739	0.608	0.003
END POINT	117	77.3	15.48	0.9	14.16	136	76.8	14.44	1.7	13.70	0.873	0.613	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at SCREENING is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT SCREENING.

Attachment 6.1: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Page 2 of 4

28AUG2008 10:53
System Used: Arrow5.1(U)/ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG01: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

OLANZAPINE Minus RISPERIDONE		
	L.S.Mean	95% CI(a)

QTC INTERVAL (ms)		

TREATMENT		
SCREENING	-2.7	(-9.29; 3.87)
WEEK 8/STUDY ENTRY	0.7	(-4.77; 6.08)
WEEK 52/WEEK 44	-1.5	(-10.70; 7.74)
END POINT	1.2	(-5.12; 7.47)
QT INTERVAL (ms)		

TREATMENT		
SCREENING	1.8	(-6.21; 9.88)
WEEK 8/STUDY ENTRY	-0.9	(-8.23; 6.45)
WEEK 52/WEEK 44	-3.5	(-14.71; 7.70)
END POINT	-0.0	(-7.72; 7.70)
HEART RATE (1/min)		

TREATMENT		
SCREENING	-1.7	(-5.03; 1.56)
WEEK 8/STUDY ENTRY	1.4	(-1.70; 4.46)
WEEK 52/WEEK 44	-0.8	(-5.83; 4.15)
END POINT	0.3	(-2.97; 3.50)

See footnotes on the first page of the table.

Attachment 6.1: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG01: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value(a)	investp P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT SCORE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT SCORE Mean	SD			
----- QRS WIDTH (ms) -----													
TREATMENT													
SCREENING	117	86.7	16.13			136	87.8	14.53			0.725	<0.001	
WEEK 8/STUDY ENTRY	114	87.9	15.30	1.2	11.02	128	87.4	14.37	-0.1	7.83	0.272	0.392	<0.001
WEEK 52/WEEK 44	56	102.3	78.59	14.5	81.45	73	89.7	19.52	1.8	15.49	0.274	0.101	0.158
END POINT	117	94.0	55.59	7.3	56.98	136	88.4	17.72	0.6	12.20	0.370	0.304	0.081
----- PR INTERVAL (ms) -----													
TREATMENT													
SCREENING	117	153.9	21.18			136	154.6	24.32			0.972	0.040	
WEEK 8/STUDY ENTRY	114	153.7	20.43	-0.2	11.49	128	154.7	24.19	-0.1	14.55	0.920	0.640	<0.001
WEEK 52/WEEK 44	55	152.1	24.35	-2.3	14.92	73	150.8	19.02	-6.1	15.18	0.132	0.834	<0.001
END POINT	117	153.7	23.62	-0.2	14.38	136	152.1	21.31	-2.4	15.60	0.200	0.646	<0.001

See footnotes on the first page of the table.

Attachment 6.1: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG01: Electrocardiogram - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

OLANZAPINE Minus RISPERIDONE		
	L.S. Mean	95% CI(a)
QRS WIDTH (ms)		
TREATMENT		
SCREENING	0.6	(-2.94; 4.23)
WEEK 8/STUDY ENTRY	-1.3	(-3.60; 1.02)
WEEK 52/WEEK 44	-10.7	(-30.04; 8.62)
END POINT	-4.5	(-14.37; 5.36)
PR INTERVAL (ms)		
TREATMENT		
SCREENING	0.1	(-5.55; 5.75)
WEEK 8/STUDY ENTRY	-0.2	(-3.41; 3.08)
WEEK 52/WEEK 44	-3.8	(-8.72; 1.16)
END POINT	-2.3	(-5.91; 1.25)

See footnotes on the first page of the table.

Attachment 6.2: Electrocardiogram Clinical Interpretation - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG02: Electrocardiogram Clinical Interpretation - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%

ECG WITHIN NORMAL LIMITS						

TREATMENT						
SCREENING						
NO	1	0.9	0.9	3	2.2	2.2
YES	116	99.1	100.0	133	97.8	100.0

Total	117			136		

WEEK 8/STUDY ENTRY						
NO	12	10.3	10.3	10	7.9	7.9
YES	104	89.7	100.0	117	92.1	100.0

Total	116			127		

WEEK 52/WEEK 44						
NO	17	29.8	29.8	14	19.2	19.2
YES	40	70.2	100.0	59	80.8	100.0

Total	57			73		

END POINT						
NO	25	21.0	21.0	27	19.9	19.9
YES	94	79.0	100.0	109	80.1	100.0

Total	119			136		

CLIN. RELEVANT CHANGES						

TREATMENT						
WEEK 8/STUDY ENTRY						
NO	111	100.0	100.0	125	100.0	100.0

Total	111			125		

Attachment 6.2: Electrocardiogram Clinical Interpretation - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/ecgrun

JNJPRD--TRIAL RIS-USA-113

Table ECG02: Electrocardiogram Clinical Interpretation - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---		
	n	%	Cum.%	n	%	Cum.%

CLIN. RELEVANT CHANGES						

TREATMENT						
WEEK 52/WEEK 44						
NO	57	100.0	100.0	71	100.0	100.0

Total	57			71		

END POINT						
NO	119	100.0	100.0	133	100.0	100.0

Total	119			133		

Attachment 7.1: Percent of Subjects with Weight Increase $\geq 7\%$ by Time Point - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS06: Percent of Subjects with Weight Increase $\geq 7\%$ by Time Point - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	- RISPERIDONE -		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
WEIGHT INCREASE $\geq 7\%$						
TREATMENT						
WEEK 8/STUDY ENTRY						
NO	97	85.8	92	72.4		
YES	16	14.2	35	27.6		
Total	113		127		(-0.23; -0.03)	0.011 RR
WEEK 12/WEEK 4						
NO	84	78.5	77	59.7		
YES	23	21.5	52	40.3		
Total	107		129		(-0.30; -0.07)	0.003 RR
WEEK 16/WEEK 8						
NO	77	76.2	71	59.7		
YES	24	23.8	48	40.3		
Total	101		119		(-0.29; -0.04)	0.011 RR
WEEK 20/WEEK 12						
NO	67	72.0	60	53.6		
YES	26	28.0	52	46.4		
Total	93		112		(-0.31; -0.05)	0.009 RR
WEEK 36/WEEK 28						
NO	48	65.8	46	54.1		
YES	25	34.2	39	45.9		

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05 .
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05 .

Attachment 7.1: Percent of Subjects with Weight Increase $\geq 7\%$ by Time Point - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS06: Percent of Subjects with Weight Increase $\geq 7\%$ by Time Point - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS

	- RISPERIDONE -		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
WEIGHT INCREASE $\geq 7\%$						
~~						
TREATMENT						
WEEK 36/WEEK 28						
Total	73		85		(-0.27; 0.04)	0.185
WEEK 52/WEEK 44						
NO	25	44.6	40	57.1		
YES	31	55.4	30	42.9		
Total	56		70		(-0.05; 0.30)	0.070 0
END POINT						
NO	68	57.6	76	57.6		
YES	50	42.4	56	42.4		
Total	118		132		(-0.12; 0.12)	0.904

See footnotes on the first page of the table.

Attachment 7.2: Percent of Subjects With $\geq 7\%$ Weight Gain From Baseline of RIS-USA-112 - Crossover Subjects Excluded

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28AUG2003 10:06
System Used: Arrow5.1 (U) /vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS01: Percent of Subjects with $\geq 7\%$ Weight Gain from Baseline of RIS-USA-112 - Crossover Subjects Excluded

Analysis Set: ITT Excluding Crossover Subjects

	-- RISPERIDONE --		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
Weight increase $\geq 7\%$						
Treatment						
Overall						
No	63	53.4	59	44.7		
Yes	55	46.6	73	55.3		
Total	118		132		(-0.21; 0.04)	0.203

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05 .
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05 .

Attachment 7.3: Percent of Subjects With $\geq 7\%$ Weight Gain From Baseline of RIS-USA-112 - All Subjects

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28AUG2008 10:06
System Used: Arrow5.1 (U) / vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS02: Percent of Subjects with $\geq 7\%$ Weight Gain from Baseline of RIS-USA-112 - All Subjects

Analysis Set: Intent-to-treat

	-- RISPERIDONE --		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
Weight increase $\geq 7\%$						
Treatment						
Overall						
No	65	53.3	61	45.2		
Yes	57	46.7	74	54.8		
Total	122		135		(-0.20; 0.04)	0.189

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05 .
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05 .

Attachment 7.4: Weight and Body Mass Index - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /vsrun

JNJPRD--TRIAL RIS-USA-113

Table VS05: Weight and Body Mass Index - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value(a)	investp P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
WEIGHT, KG													
~~													
TREATMENT													
BASELINE	118	82.7	17.94			132	83.5	20.90			0.783	0.026	
WEEK 8/STUDY ENTRY	113	84.9	18.03	2.0	3.45	127	87.7	21.31	3.8	4.70	<0.001	0.154	0.220
WEEK 12/WEEK 4	107	85.5	18.38	2.4	4.68	129	87.3	20.75	4.3	5.71	0.007	0.596	0.709
WEEK 16/WEEK 8	101	85.4	19.20	2.8	5.10	119	88.6	20.48	4.9	6.63	0.011	0.354	0.427
WEEK 20/WEEK 12	93	87.4	18.27	2.8	6.42	112	89.2	21.24	5.7	6.98	0.005	0.862	0.749
WEEK 36/WEEK 28	73	88.9	18.17	3.7	6.86	85	90.0	23.07	6.4	8.47	0.045	0.974	0.953
WEEK 52/WEEK 44	56	89.4	18.15	6.2	7.84	70	90.0	22.91	6.0	9.86	0.676	0.835	0.636
END POINT	118	87.2	18.88	4.6	7.24	132	88.8	22.16	5.3	9.09	0.498	0.937	0.496
~~													
BODY MASS INDEX													
~~													
TREATMENT													
BASELINE	118	28.3	5.87			132	29.0	6.94			0.428	0.084	
WEEK 8/STUDY ENTRY	113	29.1	5.78	0.7	1.14	127	30.4	6.97	1.3	1.58	<0.001	0.059	0.006
WEEK 12/WEEK 4	107	29.2	5.92	0.8	1.57	129	30.3	6.63	1.5	1.95	0.004	0.400	0.107
WEEK 16/WEEK 8	101	29.1	6.14	0.9	1.69	119	30.5	6.45	1.6	2.24	0.007	0.195	0.034
WEEK 20/WEEK 12	93	29.7	6.02	0.9	2.12	112	30.7	6.82	2.0	2.34	0.004	0.667	0.115
WEEK 36/WEEK 28	73	30.1	6.17	1.2	2.25	85	31.1	7.42	2.2	2.88	0.039	0.973	0.555
WEEK 52/WEEK 44	56	30.2	6.23	2.1	2.57	70	31.4	7.60	2.0	3.35	0.755	0.787	0.315
END POINT	118	29.8	6.01	1.5	2.40	132	30.8	7.20	1.8	3.14	0.391	0.850	0.074

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 7.4: Weight and Body Mass Index - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /vsrun

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Table VS05: Weight and Body Mass Index - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value(a)	investp P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
WEIGHT, KG													
~~													
TREATMENT													
BASELINE	118	82.7	17.94			132	83.5	20.90			0.783	0.026	
WEEK 8/STUDY ENTRY	113	84.9	18.03	2.0	3.45	127	87.7	21.31	3.8	4.70	<0.001	0.154	0.220
WEEK 12/WEEK 4	107	85.5	18.38	2.4	4.68	129	87.3	20.75	4.3	5.71	0.007	0.596	0.709
WEEK 16/WEEK 8	101	85.4	19.20	2.8	5.10	119	88.6	20.48	4.9	6.63	0.011	0.354	0.427
WEEK 20/WEEK 12	93	87.4	18.27	2.8	6.42	112	89.2	21.24	5.7	6.98	0.005	0.862	0.749
WEEK 36/WEEK 28	73	88.9	18.17	3.7	6.86	85	90.0	23.07	6.4	8.47	0.045	0.974	0.953
WEEK 52/WEEK 44	56	89.4	18.15	6.2	7.84	70	90.0	22.91	6.0	9.86	0.676	0.835	0.636
END POINT	118	87.2	18.88	4.6	7.24	132	88.8	22.16	5.3	9.09	0.498	0.937	0.496
~~													
BODY MASS INDEX													
~~													
TREATMENT													
BASELINE	118	28.3	5.87			132	29.0	6.94			0.428	0.084	
WEEK 8/STUDY ENTRY	113	29.1	5.78	0.7	1.14	127	30.4	6.97	1.3	1.58	<0.001	0.059	0.006
WEEK 12/WEEK 4	107	29.2	5.92	0.8	1.57	129	30.3	6.63	1.5	1.95	0.004	0.400	0.107
WEEK 16/WEEK 8	101	29.1	6.14	0.9	1.69	119	30.5	6.45	1.6	2.24	0.007	0.195	0.034
WEEK 20/WEEK 12	93	29.7	6.02	0.9	2.12	112	30.7	6.82	2.0	2.34	0.004	0.667	0.115
WEEK 36/WEEK 28	73	30.1	6.17	1.2	2.25	85	31.1	7.42	2.2	2.88	0.039	0.973	0.555
WEEK 52/WEEK 44	56	30.2	6.23	2.1	2.57	70	31.4	7.60	2.0	3.35	0.755	0.787	0.315
END POINT	118	29.8	6.01	1.5	2.40	132	30.8	7.20	1.8	3.14	0.391	0.850	0.074

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 8.1: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS01: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
TOTAL ESRS (NON-IMPURED)													
TREATMENT													
BASELINE	115	5.8	5.93			132	5.4	6.23			0.688	<0.001	
WEEK 8/STUDY ENTRY	113	4.4	5.13	-1.4	4.97	128	3.5	4.12	-2.0	4.58	0.188	0.081	<0.001
WEEK 12/WEEK 4	113	4.2	4.85	-1.6	5.25	131	3.1	3.64	-2.2	5.52	0.143	0.007	<0.001
WEEK 16/WEEK 8	107	4.4	5.10	-1.4	5.46	122	2.7	3.75	-2.7	5.67	0.008	0.008	<0.001
WEEK 20/WEEK 12	95	4.8	5.22	-0.8	5.09	116	3.2	3.82	-2.1	5.36	0.030	0.015	<0.001
WEEK 36/WEEK 28	78	5.0	5.84	-0.7	6.11	87	3.6	4.58	-1.6	5.05	0.278	<0.001	<0.001
WEEK 52/WEEK 44	59	5.5	5.81	0.4	5.25	72	3.5	4.61	-2.1	5.80	0.075	0.001	<0.001
END POINT	115	5.1	5.77	-0.7	6.04	132	3.4	4.08	-2.0	5.73	0.013	0.001	<0.001
PARKINSONISM TOTAL SCORE (NON-IMPURED)													
TREATMENT													
BASELINE	115	4.0	3.80			132	3.8	4.20			0.778	<0.001	
WEEK 8/STUDY ENTRY	113	3.1	3.55	-0.9	3.41	128	2.6	3.16	-1.2	3.45	0.505	0.052	<0.001
WEEK 12/WEEK 4	113	2.9	3.41	-1.1	3.83	131	2.4	2.79	-1.3	3.72	0.475	0.038	<0.001
WEEK 16/WEEK 8	107	3.0	3.32	-0.9	3.77	122	2.1	2.86	-1.7	4.17	0.041	0.034	<0.001
WEEK 20/WEEK 12	95	3.1	3.29	-0.8	3.62	116	2.5	2.93	-1.4	4.11	0.385	0.001	<0.001
WEEK 36/WEEK 28	78	3.3	3.71	-0.5	3.86	87	2.6	3.23	-1.3	4.25	0.474	0.002	<0.001
WEEK 52/WEEK 44	59	3.5	3.82	-0.1	3.77	72	2.7	3.28	-1.3	4.12	0.361	0.010	<0.001
END POINT	115	3.4	3.90	-0.5	4.04	132	2.4	3.03	-1.3	4.17	0.036	0.027	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 8.1: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1(U)/esrun

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Table ESRS01: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI (a)

TOTAL ESRS (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.2	(-1.47; 0.97)
WEEK 8/STUDY ENTRY	-0.6	(-1.51; 0.30)
WEEK 12/WEEK 4	-0.7	(-1.59; 0.23)
WEEK 16/WEEK 8	-1.4	(-2.36; -0.36)
WEEK 20/WEEK 12	-1.2	(-2.23; -0.12)
WEEK 36/WEEK 28	-0.7	(-2.04; 0.59)
WEEK 52/WEEK 44	-1.4	(-2.88; 0.14)
END POINT	-1.4	(-2.44; -0.29)
PARKINSONISM TOTAL SCORE (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.1	(-0.94; 0.71)
WEEK 8/STUDY ENTRY	-0.2	(-0.92; 0.45)
WEEK 12/WEEK 4	-0.3	(-0.95; 0.44)
WEEK 16/WEEK 8	-0.8	(-1.51; -0.03)
WEEK 20/WEEK 12	-0.3	(-1.08; 0.42)
WEEK 36/WEEK 28	-0.3	(-1.30; 0.61)
WEEK 52/WEEK 44	-0.5	(-1.61; 0.59)
END POINT	-0.8	(-1.63; -0.06)

See footnotes on the first page of the table.

Attachment 8.1: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1 (U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS01: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
DYSTONIA TOTAL SCORE (NON-IMPUTED)													
TREATMENT													
BASELINE	115	0.2	0.59			132	0.1	0.43			0.139	<0.001	
WEEK 8/STUDY ENTRY	113	0.1	0.57	-0.1	0.51	128	0.0	0.25	-0.1	0.44	0.222	0.737	<0.001
WEEK 12/WEEK 4	113	0.0	0.31	-0.1	0.50	132	0.0	0.09	-0.1	0.44	0.503	0.386	<0.001
WEEK 16/WEEK 8	107	0.1	0.55	-0.1	0.62	122	0.0	0.31	-0.0	0.54	0.795	0.279	<0.001
WEEK 20/WEEK 12	95	0.1	0.55	-0.1	0.72	116	0.1	0.30	-0.0	0.53	0.941	0.606	<0.001
WEEK 36/WEEK 28	78	0.2	0.73	-0.0	0.81	87	0.1	0.59	0.1	0.68	0.701	0.086	<0.001
WEEK 52/WEEK 44	59	0.2	0.52	-0.1	0.69	72	0.1	0.60	0.0	0.74	0.491	0.229	<0.001
END POINT	115	0.1	0.55	-0.1	0.63	132	0.1	0.45	-0.0	0.63	0.671	0.266	<0.001
DYSKINESIA TOTAL SCORE (NON-IMPUTED)													
TREATMENT													
BASELINE	115	1.7	2.89			132	1.5	3.10			0.911	<0.001	
WEEK 8/STUDY ENTRY	113	1.2	2.64	-0.5	2.76	128	0.9	1.94	-0.7	2.20	0.204	0.510	<0.001
WEEK 12/WEEK 4	113	1.3	2.42	-0.4	2.57	132	0.7	1.77	-0.8	2.88	0.069	0.011	<0.001
WEEK 16/WEEK 8	107	1.3	2.57	-0.4	2.83	122	0.6	1.43	-0.9	2.63	0.014	0.102	<0.001
WEEK 20/WEEK 12	95	1.7	2.73	0.1	2.68	116	0.7	1.64	-0.6	2.52	0.001	0.091	<0.001
WEEK 36/WEEK 28	78	1.5	2.71	-0.2	3.05	87	0.9	2.20	-0.3	2.21	0.226	0.009	<0.001
WEEK 52/WEEK 44	59	1.9	2.90	0.5	2.13	72	0.8	1.67	-0.8	2.80	0.010	0.004	<0.001
END POINT	115	1.5	2.70	-0.1	2.83	132	0.9	1.82	-0.6	2.75	0.037	<0.001	<0.001

See footnotes on the first page of the table.

Attachment 8.1: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover
Subjects Excluded

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System Used: Arrow5.1 (U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS01: Total ESRS and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus RISPERIDONE	
	L.S.Mean	95% CI(a)

DYSTONIA TOTAL SCORE (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.1	(-0.21; 0.03)
WEEK 8/STUDY ENTRY	-0.1	(-0.16; 0.04)
WEEK 12/WEEK 4	-0.0	(-0.07; 0.04)
WEEK 16/WEEK 8	-0.0	(-0.13; 0.10)
WEEK 20/WEEK 12	-0.0	(-0.13; 0.12)
WEEK 36/WEEK 28	0.0	(-0.16; 0.24)
WEEK 52/WEEK 44	0.1	(-0.13; 0.28)
END POINT	-0.0	(-0.15; 0.10)

DYSKINESIA TOTAL SCORE (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.0	(-0.72; 0.64)
WEEK 8/STUDY ENTRY	-0.3	(-0.79; 0.17)
WEEK 12/WEEK 4	-0.4	(-0.88; 0.03)
WEEK 16/WEEK 8	-0.6	(-1.06; -0.12)
WEEK 20/WEEK 12	-0.9	(-1.41; -0.35)
WEEK 36/WEEK 28	-0.4	(-1.07; 0.25)
WEEK 52/WEEK 44	-0.9	(-1.55; -0.21)
END POINT	-0.5	(-0.99; -0.03)

See footnotes on the first page of the table.

Risperidone: Clinical Study Report RIS-USA-113

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)
	n	%	Cum.%	n	%	Cum.%	
CGI - PARKINSONISM							
TREATMENT							
BASELINE							
ABSENT	62	53.9	53.9	70	53.0	53.0	
BORDERLINE	26	22.6	76.5	35	26.5	79.5	
VERY MILD	16	13.9	90.4	9	6.8	86.4	
MILD	8	7.0	97.4	11	8.3	94.7	
MODERATE	3	2.6	100.0	3	2.3	97.0	
MODERATELY SEVERE	0	0.0	100.0	4	3.0	100.0	
Total	115			132			0.361
WEEK 8/STUDY ENTRY							
ABSENT	60	52.6	52.6	74	57.8	57.8	
BORDERLINE	28	24.6	77.2	31	24.2	82.0	
VERY MILD	13	11.4	88.6	14	10.9	93.0	
MILD	9	7.9	96.5	5	3.9	96.9	
MODERATE	4	3.5	100.0	4	3.1	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
Total	114			128			0.542

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
R: two-sided p-value <= 0.10 with RISPERIDONE having lower scores; RR: p-value <= 0.05.
O: two-sided p-value <= 0.10 with OLANZAPINE having lower scores; OO: p-value <= 0.05.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR502: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value(a)
	n	%	Cum.%	n	%	Cum.%	
CGI - PARKINSONISM							
TREATMENT							
WEEK 12/WEEK 4							
ABSENT	63	55.3	55.3	86	65.2	65.2	
BORDERLINE	30	26.3	81.6	25	18.9	84.1	
VERY MILD	13	11.4	93.0	12	9.1	93.2	
MILD	3	2.6	95.6	4	3.0	96.2	
MODERATE	5	4.4	100.0	5	3.8	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
Total	114			132			0.639
WEEK 16/WEEK 8							
ABSENT	60	55.6	55.6	80	65.6	65.6	
BORDERLINE	23	21.3	76.9	26	21.3	86.9	
VERY MILD	11	10.2	87.0	11	9.0	95.9	
MILD	10	9.3	96.3	3	2.5	98.4	
MODERATE	4	3.7	100.0	2	1.6	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
Total	108			122			0.056 0
WEEK 20/WEEK 12							
ABSENT	50	52.1	52.1	73	62.9	62.9	
BORDERLINE	24	25.0	77.1	23	19.8	82.8	
VERY MILD	11	11.5	88.5	13	11.2	94.0	
MILD	7	7.3	95.8	3	2.6	96.6	
MODERATE	4	4.2	100.0	4	3.4	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
Total	96			116			0.410

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value(a)
	n	%	Cum.%	n	%	Cum.%	
CGI - PARKINSONISM							
TREATMENT							
WEEK 36/WEEK 28							
ABSENT	48	61.5	61.5	60	69.0	69.0	
BORDERLINE	14	17.9	79.5	12	13.8	82.8	
VERY MILD	6	7.7	87.2	7	8.0	90.8	
MILD	8	10.3	97.4	6	6.9	97.7	
MODERATE	2	2.6	100.0	2	2.3	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
Total	78			87			0.952
WEEK 52/WEEK 44							
ABSENT	35	59.3	59.3	48	66.7	66.7	
BORDERLINE	10	16.9	76.3	14	19.4	86.1	
VERY MILD	6	10.2	86.4	5	6.9	93.1	
MILD	5	8.5	94.9	2	2.8	95.8	
MODERATE	2	3.4	98.3	3	4.2	100.0	
MODERATELY SEVERE	1	1.7	100.0	0	0.0	100.0	
Total	59			72			0.328
END POINT							
ABSENT	70	60.3	60.3	91	68.9	68.9	
BORDERLINE	16	13.8	74.1	24	18.2	87.1	
VERY MILD	16	13.8	87.9	9	6.8	93.9	
MILD	9	7.8	95.7	4	3.0	97.0	
MODERATE	4	3.4	99.1	4	3.0	100.0	
MODERATELY SEVERE	1	0.9	100.0	0	0.0	100.0	
Total	116			132			0.073 0

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table EPRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	Pairwise Comparison					
	-- RISPERIDONE --			OLANZAPINE		
	n	%	Cum.%	n	%	Cum.%
	-----			-----		
	n			n		
	%			%		
	Cum.%			Cum.%		
	-----			-----		
	P-value (a)			P-value (a)		
	-----			-----		
CGI - DYSTONIA						
~~						
TREATMENT						
BASELINE						
ABSENT	102	88.7	88.7	125	94.7	94.7
BORDERLINE	8	7.0	95.7	5	3.8	98.5
VERY MILD	3	2.6	98.3	0	0.0	98.5
MILD	1	0.9	99.1	2	1.5	100.0
MODERATE	1	0.9	100.0	0	0.0	100.0

Total	115			132		
WEEK 8/STUDY ENTRY						
ABSENT	110	96.5	96.5	126	98.4	98.4
BORDERLINE	1	0.9	97.4	0	0.0	98.4
VERY MILD	0	0.0	97.4	1	0.8	99.2
MILD	2	1.8	99.1	1	0.8	100.0
MODERATE	1	0.9	100.0	0	0.0	100.0

Total	114			128		
WEEK 12/WEEK 4						
ABSENT	111	97.4	97.4	129	97.7	97.7
BORDERLINE	2	1.8	99.1	2	1.5	99.2
VERY MILD	0	0.0	99.1	1	0.8	100.0
MILD	1	0.9	100.0	0	0.0	100.0
MODERATE	0	0.0	100.0	0	0.0	100.0

Total	114			132		

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value(a)
	n	%	Cum.%	n	%	Cum.%	
CGI - DYSTONIA							
TREATMENT							
WEEK 16/WEEK 8							
ABSENT	104	96.3	96.3	119	97.5	97.5	
BORDERLINE	1	0.9	97.2	2	1.6	99.2	
VERY MILD	1	0.9	98.1	1	0.8	100.0	
MILD	0	0.0	98.1	0	0.0	100.0	
MODERATE	2	1.9	100.0	0	0.0	100.0	
Total	108			122			0.266
WEEK 20/WEEK 12							
ABSENT	92	95.8	95.8	114	98.3	98.3	
BORDERLINE	2	2.1	97.9	2	1.7	100.0	
VERY MILD	0	0.0	97.9	0	0.0	100.0	
MILD	0	0.0	97.9	0	0.0	100.0	
MODERATE	2	2.1	100.0	0	0.0	100.0	
Total	96			116			0.251
WEEK 36/WEEK 28							
ABSENT	71	91.0	91.0	83	95.4	95.4	
BORDERLINE	1	1.3	92.3	1	1.1	96.6	
VERY MILD	4	5.1	97.4	1	1.1	97.7	
MILD	1	1.3	98.7	1	1.1	98.9	
MODERATE	1	1.3	100.0	1	1.1	100.0	
Total	78			87			0.739

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

							Pairwise Comparison
							OLANZAPINE
							Minus
-- RISPERIDONE --			--- OLANZAPINE ---			--- RISPERIDONE ---	
n	%	Cum.%	n	%	Cum.%	P-value (a)	

CGI - DYSTONIA							
~~							
TREATMENT							
WEEK 52/WEEK 44							
ABSENT	53	89.8	89.8	68	94.4	94.4	
BORDERLINE	3	5.1	94.9	2	2.8	97.2	
VERY MILD	2	3.4	98.3	0	0.0	97.2	
MILD	0	0.0	98.3	1	1.4	98.6	
MODERATE	1	1.7	100.0	1	1.4	100.0	

Total	59			72		0.724	
END POINT							
ABSENT	107	92.2	92.2	128	97.0	97.0	
BORDERLINE	3	2.6	94.8	2	1.5	98.5	
VERY MILD	4	3.4	98.3	0	0.0	98.5	
MILD	0	0.0	98.3	1	0.8	99.2	
MODERATE	2	1.7	100.0	1	0.8	100.0	

Total	116			132		0.239	

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)
	n	%	Cum.%	n	%	Cum.%	
CGI - DYSKINESIA							
TREATMENT							
BASELINE							
ABSENT	73	63.5	63.5	93	70.5	70.5	
BORDERLINE	13	11.3	74.8	12	9.1	79.5	
VERY MILD	11	9.6	84.3	10	7.6	87.1	
MILD	10	8.7	93.0	10	7.6	94.7	
MODERATE	7	6.1	99.1	4	3.0	97.7	
MODERATELY SEVERE	1	0.9	100.0	2	1.5	99.2	
MARKED	0	0.0	100.0	1	0.8	100.0	
Total	115			132			0.550
WEEK 8/STUDY ENTRY							
ABSENT	83	72.8	72.8	98	76.6	76.6	
BORDERLINE	12	10.5	83.3	14	10.9	87.5	
VERY MILD	8	7.0	90.4	7	5.5	93.0	
MILD	6	5.3	95.6	8	6.3	99.2	
MODERATE	5	4.4	100.0	1	0.8	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
MARKED	0	0.0	100.0	0	0.0	100.0	
Total	114			128			0.433

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Pairwise Comparison									
OLANZAPINE									
Minus									
RISPERIDONE									
P-value (a)									
-- RISPERIDONE --				--- OLANZAPINE ---					
n % Cum.%				n % Cum.%					

CGI - DYSKINESIA									
~~									
TREATMENT									
WEEK 12/WEEK 4									
ABSENT		82	71.9	71.9	101	76.5	76.5		
BORDERLINE		12	10.5	82.5	16	12.1	88.6		
VERY MILD		11	9.6	92.1	8	6.1	94.7		
MILD		4	3.5	95.6	6	4.5	99.2		
MODERATE		5	4.4	100.0	1	0.8	100.0		
MODERATELY SEVERE		0	0.0	100.0	0	0.0	100.0		
MARKED		0	0.0	100.0	0	0.0	100.0		

Total		114			132			0.308	
WEEK 16/WEEK 8									
ABSENT		80	74.1	74.1	98	80.3	80.3		
BORDERLINE		7	6.5	80.6	15	12.3	92.6		
VERY MILD		14	13.0	93.5	6	4.9	97.5		
MILD		2	1.9	95.4	2	1.6	99.2		
MODERATE		5	4.6	100.0	1	0.8	100.0		
MODERATELY SEVERE		0	0.0	100.0	0	0.0	100.0		
MARKED		0	0.0	100.0	0	0.0	100.0		

Total		108			122			0.062 0	

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

							Pairwise Comparison	
							OLANZAPINE	
							Minus	
-- RISPERIDONE --							--- RISPERIDONE ---	
n % Cum.%							P-value (a)	
-----							-----	
CGI - DYSKINESIA								
~~								
TREATMENT								
WEEK 20/WEEK 12								
ABSENT	66	68.8	68.8	94	81.0	81.0		
BORDERLINE	8	8.3	77.1	10	8.6	89.7		
VERY MILD	11	11.5	88.5	7	6.0	95.7		
MILD	7	7.3	95.8	4	3.4	99.1		
MODERATE	4	4.2	100.0	1	0.9	100.0		
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0		
MARKED	0	0.0	100.0	0	0.0	100.0		

Total	96				116	0.014 00		
WEEK 36/WEEK 28								
ABSENT	55	70.5	70.5	73	83.9	83.9		
BORDERLINE	6	7.7	78.2	6	6.9	90.8		
VERY MILD	7	9.0	87.2	3	3.4	94.3		
MILD	8	10.3	97.4	4	4.6	98.9		
MODERATE	2	2.6	100.0	1	1.1	100.0		
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0		
MARKED	0	0.0	100.0	0	0.0	100.0		

Total	78				87	0.103		

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Pairwise Comparison							
OLANZAPINE							
Minus							
--- RISPERIDONE ---							
P-value (a)							

	-- RISPERIDONE --			--- OLANZAPINE ---			
	n	%	Cum.%	n	%	Cum.%	

CGI - DYSKINESIA							

TREATMENT							
WEEK 52/WEEK 44							
ABSENT	35	59.3	59.3	58	80.6	80.6	
BORDERLINE	9	15.3	74.6	7	9.7	90.3	
VERY MILD	6	10.2	84.7	4	5.6	95.8	
MILD	7	11.9	96.6	2	2.8	98.6	
MODERATE	2	3.4	100.0	1	1.4	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
MARKED	0	0.0	100.0	0	0.0	100.0	

Total	59			72			0.017 00

END POINT							
ABSENT	77	66.4	66.4	102	77.3	77.3	
BORDERLINE	16	13.8	80.2	13	9.8	87.1	
VERY MILD	11	9.5	89.7	9	6.8	93.9	
MILD	8	6.9	96.6	7	5.3	99.2	
MODERATE	4	3.4	100.0	1	0.8	100.0	
MODERATELY SEVERE	0	0.0	100.0	0	0.0	100.0	
MARKED	0	0.0	100.0	0	0.0	100.0	

Total	116			132			0.099 0

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)
	n	%	Cum.%	n	%	Cum.%	
STAGE OF PARKINSONISM							
TREATMENT							
BASELINE							
ABSENT	75	65.2	65.2	96	72.7	72.7	
STAGE I	18	15.7	80.9	17	12.9	85.6	
STAGE II	18	15.7	96.5	13	9.8	95.5	
STAGE III	4	3.5	100.0	6	4.5	100.0	
-----				-----			
Total	115			132			0.380
WEEK 8/STUDY ENTRY							
ABSENT	81	71.1	71.1	101	78.9	78.9	
STAGE I	12	10.5	81.6	16	12.5	91.4	
STAGE II	20	17.5	99.1	7	5.5	96.9	
STAGE III	1	0.9	100.0	4	3.1	100.0	
-----				-----			
Total	114			128			0.337
WEEK 12/WEEK 4							
ABSENT	83	72.8	72.8	107	81.1	81.1	
STAGE I	16	14.0	86.8	15	11.4	92.4	
STAGE II	10	8.8	95.6	7	5.3	97.7	
STAGE III	5	4.4	100.0	3	2.3	100.0	
-----				-----			
Total	114			132			0.245

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/esrun

JNJPRD--TRIAL RIS-USA-113

Table ESRS02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			-- OLANZAPINE --			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)
	n	%	Cum.%	n	%	Cum.%	

STAGE OF PARKINSONISM							
~~							
TREATMENT							
WEEK 16/WEEK 8							
ABSENT	76	70.4	70.4	106	86.9	86.9	
STAGE I	15	13.9	84.3	11	9.0	95.9	
STAGE II	16	14.8	99.1	2	1.6	97.5	
STAGE III	1	0.9	100.0	3	2.5	100.0	
-----				-----			
Total	108			122			0.008 00
WEEK 20/WEEK 12							
ABSENT	65	67.7	67.7	88	75.9	75.9	
STAGE I	15	15.6	83.3	19	16.4	92.2	
STAGE II	14	14.6	97.9	6	5.2	97.4	
STAGE III	2	2.1	100.0	3	2.6	100.0	
-----				-----			
Total	96			116			0.432
WEEK 36/WEEK 28							
ABSENT	56	71.8	71.8	69	79.3	79.3	
STAGE I	12	15.4	87.2	7	8.0	87.4	
STAGE II	9	11.5	98.7	10	11.5	98.9	
STAGE III	1	1.3	100.0	1	1.1	100.0	
-----				-----			
Total	78			87			0.563

See footnotes on the first page of the table.

Attachment 8.2: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /esrun

JNJPRD--TRIAL RIS-USA-113

Table ESR02: Clinical Global Impression and Stage of Parkinsonism - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value(a)
	n	%	Cum.%	n	%	Cum.%	
STAGE OF PARKINSONISM							
~~							
TREATMENT							
WEEK 52/WEEK 44							
ABSENT	41	69.5	69.5	60	83.3	83.3	
STAGE I	12	20.3	89.8	7	9.7	93.1	
STAGE II	5	8.5	98.3	3	4.2	97.2	
STAGE III	1	1.7	100.0	2	2.8	100.0	
-----				-----			
Total	59			72			0.375
END POINT							
ABSENT	82	70.7	70.7	110	83.3	83.3	
STAGE I	22	19.0	89.7	15	11.4	94.7	
STAGE II	10	8.6	98.3	5	3.8	98.5	
STAGE III	2	1.7	100.0	2	1.5	100.0	
-----				-----			
Total	116			132			0.105

See footnotes on the first page of the table.

Attachment 9.1: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS01: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
ACS TOTAL (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	120	4.2	5.56			136	4.0	5.52			0.908	0.467	
WEEK 8/STUDY ENTRY	118	2.1	3.37	-2.2	5.31	132	2.5	4.26	-1.3	4.56	0.291	0.440	<0.001
WEEK 12/WEEK 4	110	2.0	3.77	-2.5	5.66	130	2.0	3.48	-1.6	4.64	0.659	0.410	<0.001
WEEK 16/WEEK 8	105	1.9	3.92	-2.5	6.36	119	1.9	3.55	-1.8	4.70	0.796	0.216	<0.001
WEEK 20/WEEK 12	92	1.8	3.17	-2.7	5.78	115	2.3	3.71	-1.5	5.17	0.156	0.242	<0.001
WEEK 36/WEEK 28	77	2.9	5.25	-1.7	6.25	86	2.5	3.85	-1.6	5.31	0.592	0.085	<0.001
WEEK 52/WEEK 44	57	2.2	3.79	-2.7	6.21	71	2.4	4.61	-1.2	4.84	0.372	0.302	<0.001
END POINT	120	2.4	4.10	-1.9	6.01	136	2.6	4.68	-1.4	5.20	0.452	0.005	<0.001
BOWEL FUNCTION TOTAL (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	120	0.9	1.99			136	0.8	2.17			0.927	0.141	
WEEK 8/STUDY ENTRY	118	0.5	1.71	-0.4	2.11	132	0.2	1.13	-0.6	1.78	0.107	0.962	<0.001
WEEK 12/WEEK 4	111	0.4	1.30	-0.5	1.88	131	0.1	0.50	-0.6	1.94	0.013	0.197	<0.001
WEEK 16/WEEK 8	105	0.6	1.77	-0.4	2.33	119	0.2	0.99	-0.6	2.14	0.110	0.698	<0.001
WEEK 20/WEEK 12	93	0.4	1.42	-0.6	1.77	115	0.3	0.99	-0.5	2.37	0.719	0.294	<0.001
WEEK 36/WEEK 28	77	0.4	1.38	-0.5	1.49	86	0.3	1.22	-0.7	2.41	0.389	0.019	<0.001
WEEK 52/WEEK 44	57	0.4	1.59	-0.5	2.08	71	0.5	1.76	-0.5	2.80	0.660	0.518	<0.001
END POINT	120	0.5	1.52	-0.4	2.16	136	0.5	1.63	-0.4	2.30	0.937	0.076	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 9.1: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS01: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)

ACS TOTAL (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.1	(-1.47; 1.31)
WEEK 8/STUDY ENTRY	0.5	(-0.40; 1.33)
WEEK 12/WEEK 4	0.2	(-0.67; 1.06)
WEEK 16/WEEK 8	0.1	(-0.82; 1.07)
WEEK 20/WEEK 12	0.7	(-0.26; 1.62)
WEEK 36/WEEK 28	-0.4	(-1.72; 0.98)
WEEK 52/WEEK 44	0.7	(-0.80; 2.12)
END POINT	0.4	(-0.61; 1.36)
BOWEL FUNCTION TOTAL (NON-IMPUTED)		

TREATMENT		
BASELINE	0.0	(-0.49; 0.54)
WEEK 8/STUDY ENTRY	-0.3	(-0.62; 0.06)
WEEK 12/WEEK 4	-0.3	(-0.52; -0.06)
WEEK 16/WEEK 8	-0.3	(-0.68; 0.07)
WEEK 20/WEEK 12	-0.1	(-0.39; 0.27)
WEEK 36/WEEK 28	-0.2	(-0.52; 0.21)
WEEK 52/WEEK 44	0.1	(-0.48; 0.76)
END POINT	-0.0	(-0.39; 0.36)

See footnotes on the first page of the table.

Attachment 9.1: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/acsrun

JNJPRD--TRIAL RIS-USA-113

Table ACS01: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	RISPERIDONE					OLANZAPINE					Overall P-value(a)	investp P-value(a)	base P-value(a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
URINARY FUNCTION TOTAL (NON-IMPUTED)													
TREATMENT													
BASELINE	121	1.0	2.30			136	0.4	1.22			0.021	0.161	
WEEK 8/STUDY ENTRY	119	0.4	1.26	-0.6	2.04	132	0.3	1.04	-0.2	1.21	0.817	0.262	<0.001
WEEK 12/WEEK 4	112	0.6	1.72	-0.5	2.56	131	0.2	0.85	-0.1	1.03	0.195	0.672	<0.001
WEEK 16/WEEK 8	106	0.4	1.30	-0.7	2.75	119	0.3	0.98	-0.1	1.16	0.652	0.286	<0.001
WEEK 20/WEEK 12	93	0.3	1.07	-0.8	2.57	115	0.4	1.21	0.1	1.30	0.246	0.298	<0.001
WEEK 36/WEEK 28	78	0.7	2.52	-0.5	3.43	86	0.3	0.94	-0.1	1.01	0.398	0.712	<0.001
WEEK 52/WEEK 44	58	0.3	0.93	-1.1	3.02	72	0.3	1.01	-0.0	1.05	0.858	0.675	<0.001
END POINT	121	0.3	1.19	-0.7	2.54	136	0.3	1.19	-0.1	1.30	0.416	0.003	<0.001
VISION TOTAL (NON-IMPUTED)													
TREATMENT													
BASELINE	121	1.6	2.96			136	1.8	3.18			0.496	0.857	
WEEK 8/STUDY ENTRY	119	0.8	1.74	-0.9	3.16	132	1.3	2.71	-0.5	2.66	0.123	0.490	<0.001
WEEK 12/WEEK 4	113	0.8	1.95	-0.9	3.20	131	1.0	2.57	-0.7	2.85	0.413	0.365	<0.001
WEEK 16/WEEK 8	106	0.6	1.81	-1.0	3.00	119	0.8	2.10	-1.1	2.95	0.742	0.324	<0.001
WEEK 20/WEEK 12	94	0.7	1.98	-1.0	3.24	115	0.9	2.24	-0.9	3.06	0.432	0.086	<0.001
WEEK 36/WEEK 28	78	1.3	3.01	-0.5	3.24	86	1.2	2.35	-0.7	3.04	0.622	0.463	<0.001
WEEK 52/WEEK 44	58	1.1	2.32	-0.9	3.16	72	1.0	2.39	-0.6	2.77	0.874	0.299	<0.001
END POINT	121	1.2	2.40	-0.4	3.23	136	1.1	2.61	-0.8	3.27	0.682	0.695	<0.001

See footnotes on the first page of the table.

Attachment 9.1: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS01: Anticholinergic Symptom Assessment Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	OLANZAPINE Minus ----- RISPERIDONE -----	
	L.S.Mean	95% CI (a)

URINARY FUNCTION TOTAL (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.5	(-0.97; -0.08)
WEEK 8/STUDY ENTRY	-0.0	(-0.29; 0.23)
WEEK 12/WEEK 4	-0.2	(-0.56; 0.11)
WEEK 16/WEEK 8	-0.1	(-0.38; 0.24)
WEEK 20/WEEK 12	0.2	(-0.14; 0.53)
WEEK 36/WEEK 28	-0.3	(-0.89; 0.36)
WEEK 52/WEEK 44	0.0	(-0.35; 0.42)
END POINT	0.1	(-0.17; 0.40)
VISION TOTAL (NON-IMPUTED)		

TREATMENT		
BASELINE	0.3	(-0.51; 1.05)
WEEK 8/STUDY ENTRY	0.4	(-0.11; 0.95)
WEEK 12/WEEK 4	0.2	(-0.32; 0.77)
WEEK 16/WEEK 8	0.1	(-0.42; 0.59)
WEEK 20/WEEK 12	0.2	(-0.34; 0.79)
WEEK 36/WEEK 28	-0.2	(-1.01; 0.60)
WEEK 52/WEEK 44	0.1	(-0.73; 0.85)
END POINT	-0.1	(-0.72; 0.47)

See footnotes on the first page of the table.

Attachment 9.2: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS02: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Symptom Score: 0 (DID NOT HAVE), 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED)

-- RISPERIDONE --				--- OLANZAPINE ---			Pairwise Comparison	
							OLANZAPINE	
							Minus	
							RISPERIDONE	
							P-value (a)	
-----				-----			-----	
DRY MOUTH (NON-IMPUTED)								
~~								
TREATMENT								
BASELINE								
0	85	70.2	70.2	89	65.4	65.4		
1	6	5.0	75.2	11	8.1	73.5		
2	16	13.2	88.4	16	11.8	85.3		
3	8	6.6	95.0	10	7.4	92.6		
4	3	2.5	97.5	8	5.9	98.5		
5	3	2.5	100.0	2	1.5	100.0		
-----				-----				
Total	121			136			0.389	
WEEK 8/STUDY ENTRY								
0	99	82.5	82.5	91	68.9	68.9		
1	6	5.0	87.5	13	9.8	78.8		
2	8	6.7	94.2	10	7.6	86.4		
3	5	4.2	98.3	9	6.8	93.2		
4	2	1.7	100.0	5	3.8	97.0		
5	0	0.0	100.0	4	3.0	100.0		
-----				-----				
Total	120			132			0.022	RR

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value ≤ 0.10 with RISPERIDONE having lower scores; RR: p-value ≤ 0.05.
 O: two-sided p-value ≤ 0.10 with OLANZAPINE having lower scores; OO: p-value ≤ 0.05.

Attachment 9.2: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded

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29AUG2003 16:16
System Used: Arrow5.1(U)/acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS02: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Symptom Score: 0 (DID NOT HAVE), 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED)

-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)	
n	%	Cum.%	n	%	Cum.%		

DRY MOUTH (NON-IMPUTED)							

TREATMENT							
WEEK 12/WEEK 4							
0	98	86.0	86.0	88	67.7	67.7	
1	5	4.4	90.4	17	13.1	80.8	
2	8	7.0	97.4	13	10.0	90.8	
3	3	2.6	100.0	9	6.9	97.7	
4	0	0.0	100.0	3	2.3	100.0	
5	0	0.0	100.0	0	0.0	100.0	

Total	114			130			0.003 RR
WEEK 16/WEEK 8							
0	85	79.4	79.4	80	67.2	67.2	
1	10	9.3	88.8	12	10.1	77.3	
2	7	6.5	95.3	16	13.4	90.8	
3	4	3.7	99.1	7	5.9	96.6	
4	0	0.0	99.1	2	1.7	98.3	
5	1	0.9	100.0	2	1.7	100.0	

Total	107			119			0.027 RR
WEEK 20/WEEK 12							
0	78	82.1	82.1	78	67.8	67.8	
1	7	7.4	89.5	15	13.0	80.9	
2	6	6.3	95.8	11	9.6	90.4	
3	2	2.1	97.9	5	4.3	94.8	
4	2	2.1	100.0	6	5.2	100.0	
5	0	0.0	100.0	0	0.0	100.0	

Total	95			115			0.092 R

See footnotes on the first page of the table.

Attachment 9.2: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /acsrn

JNJPRD--TRIAL RIS-USA-113

Table ACS02: Anticholinergic Symptom Assessment Dry Mouth Item - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
Symptom Score: 0 (DID NOT HAVE), 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED)

				Pairwise Comparison			
				OLANZAPINE			
				Minus			
				RISPERIDONE			
				P-value(a)			

See footnotes on the first page of the table.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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29AUG2008 16:26
System Used: Arrow5.1 (U) /prsrn

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW BOTHERED

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED; HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
TOTAL CHEST SYMPTOMS (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	119	0.5	1.45			131	0.4	1.13			0.439	0.068	
WEEK 8/STUDY ENTRY	113	0.3	0.94	-0.2	1.22	125	0.3	1.03	-0.1	1.11	0.800	0.274	<0.001
WEEK 20/WEEK 12	92	0.3	1.05	-0.2	1.54	110	0.1	0.44	-0.3	1.31	0.048	0.699	<0.001
WEEK 36/WEEK 28	75	0.3	1.16	-0.1	1.63	83	0.7	1.93	0.4	2.11	0.146	<0.001	<0.001
WEEK 52/WEEK 44	57	0.5	1.85	-0.1	1.63	69	0.3	1.09	0.0	1.30	0.753	0.088	<0.001
END POINT	119	0.3	1.33	-0.2	1.39	131	0.3	1.06	-0.1	1.56	0.629	0.108	<0.001
TOTAL PENILE FUNCTION (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	85	1.5	3.88			92	1.9	3.26			0.403	0.648	
WEEK 8/STUDY ENTRY	84	1.5	3.60	0.2	4.99	89	1.1	2.41	-0.9	3.08	0.318	0.061	<0.001
WEEK 20/WEEK 12	69	1.5	4.08	-0.3	4.80	79	1.1	3.11	-0.7	3.55	0.584	0.131	<0.001
WEEK 36/WEEK 28	57	1.8	3.76	0.0	5.19	60	0.8	2.86	-1.1	3.11	0.361	0.324	<0.001
WEEK 52/WEEK 44	43	2.1	4.04	0.2	6.16	51	0.8	2.43	-1.2	3.44	0.053	0.131	<0.001
END POINT	85	1.8	3.51	0.2	5.06	92	1.0	2.91	-0.9	3.85	0.244	0.052	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT-BASELINE.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) / prsrun

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW BOTHERED

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED; HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)
TOTAL CHEST SYMPTOMS (NON-IMPUTED)		
TREATMENT		
BASELINE	-0.1	(-0.45; 0.20)
WEEK 8/STUDY ENTRY	0.0	(-0.19; 0.25)
WEEK 20/WEEK 12	-0.2	(-0.45; -0.00)
WEEK 36/WEEK 28	0.4	(-0.12; 0.83)
WEEK 52/WEEK 44	0.1	(-0.41; 0.56)
END POINT	0.1	(-0.22; 0.36)
TOTAL PENILE FUNCTION (NON-IMPUTED)		
TREATMENT		
BASELINE	0.5	(-0.64; 1.58)
WEEK 8/STUDY ENTRY	-0.5	(-1.39; 0.46)
WEEK 20/WEEK 12	-0.3	(-1.46; 0.83)
WEEK 36/WEEK 28	-0.6	(-1.85; 0.68)
WEEK 52/WEEK 44	-1.4	(-2.82; 0.02)
END POINT	-0.6	(-1.51; 0.39)

See footnotes on the first page of the table.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/prsrn

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW BOTHERED

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED); HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	----- RISPERIDONE -----					----- OLANZAPINE -----					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
TOTAL MENSTRUAL CHANGES (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	32	1.5	3.41			40	1.1	2.72			0.983	0.245	
WEEK 8/STUDY ENTRY	29	0.7	1.45	-1.0	2.92	35	0.5	1.17	-0.5	3.00	0.318	0.079	<0.001
WEEK 20/WEEK 12	19	0.6	1.30	-1.0	3.80	32	1.0	2.43	-0.4	3.65	0.791	0.386	<0.001
WEEK 36/WEEK 28	17	2.1	4.18	-0.3	3.42	24	0.7	1.20	-0.3	1.96	0.469	0.554	0.013
WEEK 52/WEEK 44	12	1.1	1.62	-1.9	4.52	18	0.7	1.57	-0.2	2.37	0.524	0.821	<0.001
END POINT	32	0.9	1.86	-0.6	3.11	40	0.5	1.24	-0.7	2.94	0.330	0.002	<0.001

See footnotes on the first page of the table.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/prsrn

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW BOTHERED

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED; HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)
TOTAL MENSTRUAL CHANGES (NON-IMPUTED)		

TREATMENT		
BASELINE	-0.0	(-1.53; 1.50)
WEEK 8/STUDY ENTRY	-0.3	(-0.97; 0.32)
WEEK 20/WEEK 12	0.2	(-1.14; 1.48)
WEEK 36/WEEK 28	-0.7	(-2.52; 1.20)
WEEK 52/WEEK 44	0.6	(-1.33; 2.48)
END POINT	-0.3	(-0.94; 0.32)

See footnotes on the first page of the table.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /prsrn

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW MUCH

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED; HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
TOTAL CHEST SYMPTOMS (NON-IMPUTED)													
TREATMENT													
BASELINE	120	0.6	1.45			134	0.5	1.43			0.807	0.049	
WEEK 8/STUDY ENTRY	117	0.4	1.22	-0.2	1.51	129	0.4	1.39	-0.1	1.40	0.747	0.048	<0.001
WEEK 20/WEEK 12	93	0.4	1.36	-0.1	1.72	113	0.1	0.63	-0.4	1.58	0.040	0.295	<0.001
WEEK 36/WEEK 28	77	0.3	1.11	-0.0	1.23	86	0.8	2.00	0.4	2.36	0.053	0.009	<0.001
WEEK 52/WEEK 44	57	0.5	1.89	-0.0	1.64	72	0.4	1.33	-0.1	1.61	0.779	0.093	<0.001
END POINT	120	0.3	1.34	-0.3	1.56	134	0.4	1.26	-0.1	1.72	0.244	0.263	<0.001
TOTAL PENILE FUNCTION (NON-IMPUTED)													
TREATMENT													
BASELINE	84	1.5	3.53			91	2.8	4.82			0.048	0.359	
WEEK 8/STUDY ENTRY	83	2.1	4.92	0.8	5.96	88	1.6	3.72	-1.1	4.26	0.186	0.009	<0.001
WEEK 20/WEEK 12	69	1.6	3.91	-0.2	4.62	78	1.5	3.21	-1.4	5.60	0.651	0.423	<0.001
WEEK 36/WEEK 28	57	2.0	3.72	0.4	4.75	60	1.3	3.62	-1.5	5.73	0.460	0.119	<0.001
WEEK 52/WEEK 44	43	2.6	4.47	0.8	5.92	51	1.1	3.06	-1.7	5.67	0.044	0.234	<0.001
END POINT	84	2.1	3.74	0.6	4.93	91	1.4	3.26	-1.4	5.56	0.296	0.268	<0.001
TOTAL MENSTRUAL CHANGES (NON-IMPUTED)													
TREATMENT													
BASELINE	33	1.8	3.74			43	1.8	3.24			0.615	0.194	
WEEK 8/STUDY ENTRY	31	1.3	3.04	-0.6	2.81	39	0.7	1.58	-0.6	2.69	0.103	0.214	<0.001
WEEK 20/WEEK 12	21	0.9	1.87	-1.1	4.44	33	0.9	2.41	-1.1	3.29	0.722	0.581	<0.001
WEEK 36/WEEK 28	18	2.2	4.84	-0.6	5.20	25	2.2	4.11	0.7	4.48	0.311	0.161	<0.001
WEEK 52/WEEK 44	12	1.6	2.23	-0.8	4.69	19	1.3	3.64	-0.2	4.86	0.770	0.395	<0.001
END POINT	33	1.4	3.04	-0.5	4.08	43	0.8	2.58	-1.0	4.35	0.558	0.001	<0.001

See footnotes on the first page of the table.

Attachment 10.1: Prolactin-Related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) / prsrn

JNJPRD--TRIAL RIS-USA-113

Table PRSQ01: Prolactin-related Symptom Questionnaire - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Parameter Type: HOW MUCH

Scales: HOW BOTHERED: 1 (NOT AT ALL BOTHERED) TO 5 (EXTREMELY BOTHERED; HOW MUCH: 0 (DID NOT HAVE), 1 (HARDLY ANY) TO 5 (VERY MUCH)

	OLANZAPINE Minus RISPERIDONE	
	L.S. Mean	95% CI (a)
TOTAL CHEST SYMPTOMS (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	-0.0	(-0.40; 0.31)
WEEK 8/STUDY ENTRY	-0.0	(-0.35; 0.25)
WEEK 20/WEEK 12	-0.3	(-0.59; -0.01)
WEEK 36/WEEK 28	0.5	(-0.01; 0.98)
WEEK 52/WEEK 44	0.1	(-0.45; 0.60)
END POINT	0.2	(-0.13; 0.50)
TOTAL PENILE FUNCTION (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	1.3	(0.01; 2.63)
WEEK 8/STUDY ENTRY	-0.9	(-2.14; 0.42)
WEEK 20/WEEK 12	-0.3	(-1.50; 0.94)
WEEK 36/WEEK 28	-0.5	(-1.94; 0.88)
WEEK 52/WEEK 44	-1.7	(-3.41; -0.05)
END POINT	-0.6	(-1.66; 0.51)
TOTAL MENSTRUAL CHANGES (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	0.4	(-1.24; 2.08)
WEEK 8/STUDY ENTRY	-0.9	(-1.93; 0.18)
WEEK 20/WEEK 12	-0.2	(-1.57; 1.10)
WEEK 36/WEEK 28	1.4	(-1.44; 4.32)
WEEK 52/WEEK 44	-0.4	(-3.64; 2.76)
END POINT	-0.3	(-1.50; 0.82)

See footnotes on the first page of the table.

Attachment 11.1: Percent of Subjects With HGB A1c <7% at Baseline (RIS-USA-112) and >=7% Postbaseline - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /lbrun2

JNJPRD--TRIAL RIS-USA-113

Table LAE01: Percent of Subjects with HGB A1c <7% at Baseline (RIS-USA-112) and >=7% Postbaseline - Crossover Subjects Excluded

Analysis Set: ITT Excluding Crossover Subjects

	-- RISPERIDONE --		-- OLANZAPINE --		Pairwise Comparison OLANZAPINE Minus RISPERIDONE	
	n	%	n	%	95% CI	P-value(a)
Hgb a1c increase						
Treatment						
Overall						
No	117	96.7	130	97.0		
Yes	4	3.3	4	3.0		
Total	121		134		(-0.04; 0.05)	0.975

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.
 R: two-sided p-value <= 0.10 with RISPERIDONE having lower scores; RR: p-value <= 0.05.
 O: two-sided p-value <= 0.10 with OLANZAPINE having lower scores; OO: p-value <= 0.05.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/msrun

JNJPRD--TRIAL RIS-USA-113

Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

	RISPERIDONE					OLANZAPINE							
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	Overall P-value (a)	investp P-value (a)	base P-value (a)
TOTAL MSIP (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	112	34.5	18.82			120	35.3	22.56			0.966	0.023	
WEEK 8/STUDY ENTRY	104	23.6	17.63	-10.5	17.25	111	26.2	22.27	-8.9	18.98	0.136	0.229	<0.001
WEEK 20/WEEK 12	87	25.2	18.86	-8.4	20.85	96	23.6	23.01	-10.1	19.34	0.846	0.361	<0.001
WEEK 36/WEEK 28	73	24.5	18.90	-8.1	17.21	72	23.3	23.86	-10.9	25.22	0.814	0.024	<0.001
WEEK 52/WEEK 44	54	22.9	19.18	-10.0	18.36	64	23.7	23.00	-8.7	20.95	0.374	0.340	<0.001
END POINT	112	25.0	19.20	-9.5	18.65	120	28.8	25.80	-6.4	22.33	0.059	0.122	<0.001
SLEEP AND REST (NON-IMPUTED)													
~~													
TREATMENT													
BASELINE	120	33.2	28.87			136	34.4	29.64			0.805	0.248	
WEEK 8/STUDY ENTRY	115	23.8	26.20	-9.1	27.27	130	27.9	28.21	-6.5	30.15	0.143	0.477	<0.001
WEEK 20/WEEK 12	93	27.8	27.76	-5.2	32.50	115	24.8	29.56	-10.3	31.99	0.421	0.869	<0.001
WEEK 36/WEEK 28	78	29.6	27.91	-3.1	31.77	85	27.5	29.01	-9.6	29.42	0.422	0.662	<0.001
WEEK 52/WEEK 44	59	28.1	27.47	-5.8	39.44	72	26.4	28.62	-7.1	27.94	0.679	0.497	<0.001
END POINT	120	25.8	26.35	-7.4	31.90	136	29.9	29.04	-4.5	30.05	0.177	0.591	<0.001

(a) Test for no difference between TREATMENT from ANCOVA model with factor(s) TREATMENT,base,investp (type III SS).
Analysis at BASELINE is based on value, whereas at other times analysis is based upon CHANGE FROM TREATMENT BASELINE.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and
Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1 (U) /msrun

JNJPRD--TRIAL RIS-USA-113

Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded
(continued)Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

OLANZAPINE		
Minus		
----- RISPERIDONE -----		
	L.S.Mean	95% CI(a)

TOTAL MSIP (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	-0.1	(-5.44; 5.22)
WEEK 8/STUDY ENTRY	3.3	(-1.06; 7.74)
WEEK 20/WEEK 12	-0.5	(-5.90; 4.84)
WEEK 36/WEEK 28	0.8	(-5.55; 7.36)
WEEK 52/WEEK 44	3.1	(-3.81; 10.05)
END POINT	4.8	(-0.18; 9.71)
SLEEP AND REST (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	0.9	(-6.37; 8.19)
WEEK 8/STUDY ENTRY	4.6	(-1.56; 10.74)
WEEK 20/WEEK 12	-3.1	(-10.82; 4.54)
WEEK 36/WEEK 28	-3.4	(-11.74; 4.94)
WEEK 52/WEEK 44	-2.0	(-11.81; 7.72)
END POINT	4.4	(-2.00; 10.77)

See footnotes on the first page of the table.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/msrun

JNJPRD--TRIAL RIS-USA-113

Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

	RISPERIDONE					OLANZAPINE							
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	Overall P-value(a)	investp P-value(a)	base P-value(a)
HOME MANAGEMENT (NON-IMPURED)													
TREATMENT													
BASELINE	117	34.5	26.06			134	35.7	29.75			0.775	0.587	
WEEK 8/STUDY ENTRY	114	25.7	24.58	-8.6	31.72	128	27.5	28.56	-8.6	27.64	0.457	0.553	<0.001
WEEK 20/WEEK 12	93	26.4	24.85	-8.8	33.45	112	20.4	25.62	-13.1	27.99	0.093	0.879	<0.001
WEEK 36/WEEK 28	78	27.0	27.44	-8.5	30.84	84	23.5	26.21	-11.8	36.57	0.549	0.194	<0.001
WEEK 52/WEEK 44	57	27.5	25.58	-8.0	33.34	71	21.2	24.24	-12.0	28.49	0.281	0.247	<0.001
END POINT	117	26.1	25.18	-8.4	32.27	134	27.0	29.52	-8.7	31.48	0.532	0.094	<0.001
SOCIAL INTERACTION (NON-IMPURED)													
TREATMENT													
BASELINE	113	32.8	21.09			122	33.1	24.33			0.919	0.027	
WEEK 8/STUDY ENTRY	107	22.3	18.24	-9.8	19.35	115	25.0	23.12	-7.9	23.42	0.231	0.459	<0.001
WEEK 20/WEEK 12	89	24.4	21.44	-5.9	23.74	97	23.0	23.63	-8.0	21.69	0.737	0.327	<0.001
WEEK 36/WEEK 28	74	21.3	19.24	-7.9	20.75	74	21.6	23.59	-10.3	26.92	0.648	0.011	<0.001
WEEK 52/WEEK 44	54	19.8	18.41	-9.1	18.96	65	20.8	23.02	-9.0	24.20	0.504	0.173	<0.001
END POINT	113	23.2	18.98	-9.6	21.78	122	26.2	26.38	-6.9	24.00	0.139	0.060	<0.001
ALERTNESS BEHAVIOR (NON-IMPURED)													
TREATMENT													
BASELINE	119	34.9	30.25			134	42.5	32.57			0.065	0.013	
WEEK 8/STUDY ENTRY	116	23.1	27.26	-11.0	27.51	128	27.9	31.76	-14.3	27.51	0.487	0.049	<0.001
WEEK 20/WEEK 12	94	24.9	28.32	-10.9	29.73	113	26.2	31.38	-14.2	27.47	0.941	0.165	<0.001
WEEK 36/WEEK 28	78	24.0	26.33	-8.9	27.57	85	25.6	32.03	-13.9	33.23	0.679	0.001	<0.001
WEEK 52/WEEK 44	58	21.5	26.01	-11.5	28.38	72	26.8	31.39	-10.8	33.09	0.183	0.565	<0.001
END POINT	119	25.3	29.17	-9.5	28.04	134	32.3	35.38	-10.1	35.01	0.209	0.141	<0.001

See footnotes on the first page of the table.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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System Used: Arrow5.1(U)/msrun

JNJPRD--TRIAL RIS-USA-113

Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

OLANZAPINE		
Minus		
----- RISPERIDONE -----		
	L.S.Mean	95% CI (a)
HOME MANAGEMENT (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	1.0	(-6.12; 8.20)
WEEK 8/STUDY ENTRY	2.4	(-3.94; 8.72)
WEEK 20/WEEK 12	-5.9	(-12.84; 0.99)
WEEK 36/WEEK 28	-2.5	(-10.03; 5.78)
WEEK 52/WEEK 44	-4.7	(-13.28; 3.89)
END POINT	2.1	(-4.41; 8.52)
SOCIAL INTERACTION (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	-0.3	(-6.11; 5.51)
WEEK 8/STUDY ENTRY	3.0	(-1.92; 7.88)
WEEK 20/WEEK 12	-1.0	(-6.95; 4.92)
WEEK 36/WEEK 28	1.5	(-4.98; 7.98)
WEEK 52/WEEK 44	2.4	(-4.69; 9.48)
END POINT	3.9	(-1.27; 9.32)
ALERTNESS BEHAVIOR (NON-IMPUTED)		
~~		
TREATMENT		
BASELINE	7.2	(-0.45; 14.89)
WEEK 8/STUDY ENTRY	2.1	(-3.90; 8.17)
WEEK 20/WEEK 12	-0.3	(-7.13; 6.61)
WEEK 36/WEEK 28	1.6	(-6.05; 9.27)
WEEK 52/WEEK 44	6.5	(-3.10; 16.02)
END POINT	4.5	(-2.55; 11.56)

See footnotes on the first page of the table.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

All scales range from 0 (no dysfunction) to 100 (maximum dysfunction)													
	RISPERIDONE					OLANZAPINE					Overall P-value (a)	investp P-value (a)	base P-value (a)
	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD	N	Mean	SD	CHANGE FROM TREATMENT BASE Mean	SD			
COMMUNICATION (NON-IMPUTED)													
TREATMENT													
BASELINE	119	26.5	22.48			136	29.6	28.58			0.354	0.003	
WEEK 8/STUDY ENTRY	116	16.8	21.18	-8.7	23.25	130	21.5	26.92	-8.6	23.21	0.211	0.143	<0.001
WEEK 20/WEEK 12	94	19.4	20.66	-6.6	25.92	114	21.8	27.64	-7.0	24.81	0.689	0.285	<0.001
WEEK 36/WEEK 28	78	19.6	25.56	-5.4	24.79	84	20.2	27.23	-8.9	27.69	0.883	0.442	<0.001
WEEK 52/WEEK 44	58	18.4	22.85	-7.9	24.32	72	21.9	29.08	-5.7	28.81	0.242	0.539	<0.001
END POINT	119	20.2	23.44	-6.3	23.72	136	24.0	30.20	-5.6	28.56	0.238	0.043	<0.001
RECREATION/PASTIMES (NON-IMPUTED)													
TREATMENT													
BASELINE	117	48.5	32.85			136	46.0	34.23			0.430	0.039	
WEEK 8/STUDY ENTRY	114	31.8	29.01	-15.8	34.67	131	35.0	31.57	-11.4	34.79	0.260	0.136	<0.001
WEEK 20/WEEK 12	92	34.7	31.53	-12.3	36.41	114	29.0	29.65	-16.2	38.28	0.284	0.446	<0.001
WEEK 36/WEEK 28	76	33.0	33.08	-10.4	28.49	86	33.3	32.07	-12.0	37.03	0.651	0.385	<0.001
WEEK 52/WEEK 44	58	30.8	31.36	-12.4	31.13	71	34.8	32.05	-9.7	35.61	0.678	0.013	<0.001
END POINT	117	36.5	33.29	-11.9	34.79	136	35.8	31.97	-10.2	33.50	0.743	0.017	<0.001

See footnotes on the first page of the table.

Attachment 12.1: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded

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Table MSIP01: Modified Sickness Impact Profile Total Score and Subscales - Descriptive Statistics and Between-Group Comparisons - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)
All scales range from 0 (NO DYSFUNCTION) TO 100 (MAXIMUM DYSFUNCTION)

	OLANZAPINE		
	Minus		
	----- RISPERIDONE -----		
	L.S.	Mean	95% CI (a)

COMMUNICATION (NON-IMPUTED)			

TREATMENT			
BASELINE	2.9		(-3.29; 9.16)
WEEK 8/STUDY ENTRY	3.2		(-1.85; 8.34)
WEEK 20/WEEK 12	1.2		(-4.84; 7.32)
WEEK 36/WEEK 28	0.6		(-6.97; 8.10)
WEEK 52/WEEK 44	5.2		(-3.57; 13.97)
END POINT	3.5		(-2.31; 9.25)
RECREATION/PASTIMES (NON-IMPUTED)			

TREATMENT			
BASELINE	-3.3		(-11.58; 4.95)
WEEK 8/STUDY ENTRY	4.0		(-3.00; 11.05)
WEEK 20/WEEK 12	-4.5		(-12.75; 3.76)
WEEK 36/WEEK 28	2.1		(-7.12; 11.35)
WEEK 52/WEEK 44	2.1		(-7.72; 11.83)
END POINT	1.2		(-5.88; 8.23)

See footnotes on the first page of the table.

Attachment 12.2: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded

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Table MSIP02: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Pairwise Comparison						
-- RISPERIDONE --			--- OLANZAPINE ---			OLANZAPINE
n	%	Cum.%	n	%	Cum.%	Minus
						RISPERIDONE, ---
						P-value (a)

PRESENT HEALTH						
~~						
TREATMENT						
BASELINE						
VERY GOOD	22	18.3	18.3	25	18.4	18.4
GOOD	43	35.8	54.2	57	41.9	60.3
FAIR	47	39.2	93.3	45	33.1	93.4
POOR	7	5.8	99.2	7	5.1	98.5
VERY POOR	1	0.8	100.0	2	1.5	100.0
-----	-----		-----			
Total	120		136			0.705
~~						
WEEK 8/STUDY ENTRY						
VERY GOOD	24	20.2	20.2	29	22.1	22.1
GOOD	61	51.3	71.4	66	50.4	72.5
FAIR	33	27.7	99.2	32	24.4	96.9
POOR	1	0.8	100.0	3	2.3	99.2
VERY POOR	0	0.0	100.0	1	0.8	100.0
-----	-----		-----			
Total	119		131			0.947
~~						
WEEK 20/WEEK 12						
VERY GOOD	24	25.3	25.3	21	18.3	18.3
GOOD	35	36.8	62.1	45	39.1	57.4
FAIR	32	33.7	95.8	39	33.9	91.3
POOR	4	4.2	100.0	7	6.1	97.4
VERY POOR	0	0.0	100.0	3	2.6	100.0
-----	-----		-----			
Total	95		115			0.103

(a) Pairwise comparison: Generalized Cochran-Mantel-Haenszel test for row mean scores differ controlling for investp.

R: two-sided p-value <= 0.10 with RISPERIDONE having lower scores; RR: p-value <= 0.05.

O: two-sided p-value <= 0.10 with OLANZAPINE having lower scores; OO: p-value <= 0.05.

Attachment 12.2: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded

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Table MSIP02: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

	-- RISPERIDONE --			--- OLANZAPINE ---			Pairwise Comparison OLANZAPINE Minus RISPERIDONE P-value (a)
	n	%	Cum.%	n	%	Cum.%	
PRESENT HEALTH							
TREATMENT							
WEEK 36/WEEK 28							
VERY GOOD	10	12.8	12.8	22	25.6	25.6	
GOOD	42	53.8	66.7	40	46.5	72.1	
FAIR	22	28.2	94.9	21	24.4	96.5	
POOR	3	3.8	98.7	3	3.5	100.0	
VERY POOR	1	1.3	100.0	0	0.0	100.0	
Total	78			86			0.107
WEEK 52/WEEK 44							
VERY GOOD	9	15.3	15.3	16	22.2	22.2	
GOOD	25	42.4	57.6	34	47.2	69.4	
FAIR	21	35.6	93.2	19	26.4	95.8	
POOR	4	6.8	100.0	3	4.2	100.0	
VERY POOR	0	0.0	100.0	0	0.0	100.0	
Total	59			72			0.316
END POINT							
VERY GOOD	20	16.4	16.4	26	19.1	19.1	
GOOD	59	48.4	64.8	64	47.1	66.2	
FAIR	36	29.5	94.3	34	25.0	91.2	
POOR	6	4.9	99.2	11	8.1	99.3	
VERY POOR	1	0.8	100.0	1	0.7	100.0	
Total	122			136			0.925

See footnotes on the first page of the table.

Attachment 12.2: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded

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Table MSIP02: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Pairwise Comparison						
-- RISPERIDONE --			-- OLANZAPINE --			-- RISPERIDONE --
n	%	Cum.%	n	%	Cum.%	Minus P-value (a)

PRESENT QUALITY OF LIFE						

TREATMENT						
BASELINE						
VERY GOOD	22	18.3	18.3	13	9.6	9.6
GOOD	34	28.3	46.7	55	40.7	50.4
FAIR	44	36.7	83.3	44	32.6	83.0
POOR	16	13.3	96.7	16	11.9	94.8
VERY POOR	4	3.3	100.0	7	5.2	100.0

Total	120		135			0.510
WEEK 8/STUDY ENTRY						
VERY GOOD	15	12.6	12.6	15	11.5	11.5
GOOD	53	44.5	57.1	55	42.0	53.4
FAIR	39	32.8	89.9	42	32.1	85.5
POOR	12	10.1	100.0	13	9.9	95.4
VERY POOR	0	0.0	100.0	6	4.6	100.0

Total	119		131			0.271
WEEK 20/WEEK 12						
VERY GOOD	15	15.8	15.8	25	21.9	21.9
GOOD	37	38.9	54.7	41	36.0	57.9
FAIR	32	33.7	88.4	39	34.2	92.1
POOR	11	11.6	100.0	6	5.3	97.4
VERY POOR	0	0.0	100.0	3	2.6	100.0

Total	95		114			0.561

See footnotes on the first page of the table.

Attachment 12.2: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded

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Table MSIP02: Modified Sickness Impact Profile Present Health and Quality of Life Items - Crossover Subjects Excluded (continued)

Analysis Set: ITT EXCLUDING CROSSOVER SUBJECTS (RESTRICTED TO SUBJECTS WITH VISIT END POINT DATA ONLY)

Pairwise Comparison							
-- RISPERIDONE --				OLANZAPINE			
				Minus			
				RISPERIDONE			
				P-value(a)			

PRESENT QUALITY OF LIFE							

TREATMENT							
WEEK 36/WEEK 28							
VERY GOOD	12	15.4	15.4	11	12.8	12.8	
GOOD	35	44.9	60.3	41	47.7	60.5	
FAIR	24	30.8	91.0	25	29.1	89.5	
POOR	6	7.7	98.7	9	10.5	100.0	
VERY POOR	1	1.3	100.0	0	0.0	100.0	
-----				-----			
Total	78			86			0.956
WEEK 52/WEEK 44							
VERY GOOD	8	13.6	13.6	15	20.8	20.8	
GOOD	25	42.4	55.9	30	41.7	62.5	
FAIR	19	32.2	88.1	24	33.3	95.8	
POOR	7	11.9	100.0	3	4.2	100.0	
VERY POOR	0	0.0	100.0	0	0.0	100.0	
-----				-----			
Total	59			72			0.378
END POINT							
VERY GOOD	16	13.1	13.1	21	15.4	15.4	
GOOD	51	41.8	54.9	58	42.6	58.1	
FAIR	38	31.1	86.1	40	29.4	87.5	
POOR	16	13.1	99.2	13	9.6	97.1	
VERY POOR	1	0.8	100.0	4	2.9	100.0	
-----				-----			
Total	122			136			0.841

See footnotes on the first page of the table.

APPENDICES

APPENDIX 1
STUDY INFORMATION

Appendix 1.1

Study Protocol Including Amendments

The Local Sponsors (if any) for this study are listed on the following page

Legal Entity Considered as the Sponsor

for Investigational Sites Located In:

Johnson & Johnson
Pharmaceutical Research & Development, L.L.C.
920 US Route 202
Raritan, NJ 08869-0602
USA

United States

JANSSEN RESEARCH FOUNDATION		
International Clinical Research & Development		
CLINICAL TRIAL PROTOCOL		
Final version date: 31-Mar-97	Drug number: R064766	
Trial number: RIS-USA-113	Clinical Phase: IIIb	
Title:	Risperidone vs. olanzapine in the treatment of schizophrenia	
Summary:	A multicenter, randomized, double blind, parallel group trial comparing the safety and efficacy of risperidone and olanzapine in the treatment of psychosis in patients with schizophrenia and schizoaffective disorder. The trial duration is 44 weeks.	
Trial Location:	USA	
Sponsor:	Janssen Research Foundation 1125 Trenton-Harbourton Road Titusville, NJ 08560	
Trial Coordinator:	Martin Brecher, MD Janssen Research Foundation 1125 Trenton-Harbourton Road Titusville, NJ 08560	
Approvals:		
Investigator:	 (name, title)	 (date)
Development Project Leader: Janssen Research Foundation	 (date)	
Clinical Development Director: Janssen Research Foundation	 (date)	
This protocol contains confidential information that should only be disclosed to those persons responsible for execution and organization of the trial and on condition that all such persons agree not to further disseminate it.		

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PART I: CLINICAL TRIAL PROTOCOL

1. INTRODUCTION

For the past 40 years antagonists at the D_2 dopamine receptor have been widely prescribed for the symptoms of psychosis. Most D_2 blockers also cause significant extrapyramidal symptoms (EPS)(1) which reduce both clinical efficacy and compliance (2). These compounds are also associated with tardive dyskinesia which is irreversible in some cases (3). Clozapine, a weak D_2 blocker, causes very little EPS and may be more efficacious than other neuroleptics, but its use is restricted because of the risk of agranulocytosis (4). In the past decade research on the pharmacotherapy of schizophrenia has focused on discovering a "clozapine without the risk of agranulocytosis".

Since its introduction into clinical practice in 1994 risperidone, a substituted benzisoxazole, has become established as a first line treatment for psychosis (5). The widespread acceptance of risperidone is based on its efficacy against positive and negative symptoms of schizophrenia, rapid titration schedule and onset of action, low incidence of EPS and a benign side effect profile (6, 7). These attributes are in large measure attributable to risperidone's potent and partially specific pharmacological activity. It is a highly potent $5HT_{2A}$ antagonist (K_i 0.16 nm) and a potent D_2 (K_i 3.13 nm), α_1 -adrenergic (K_i 0.81 nm) and α_2 -adrenergic (K_i 7.54 nm) antagonist (8).

Olanzapine, a thienobenzodiazepine structurally related to clozapine (9), has recently been approved for the treatment of psychosis. This compound also has strong affinity for the $5HT_{2A}$ (K_i 4 nm), D_2 (K_i 11 nm) and α -adrenergic (K_i 19 nm) receptors (8). Olanzapine is distinguished pharmacologically from risperidone by having strong affinity for the muscarinic M_1 - M_5 receptors ($K_i \leq 25$ nm with K_i for M_1 1.9 nm), 20 fold stronger affinity than risperidone at the histamine H_1 receptor and weaker affinity at the α_2 adrenergic receptor (K_i 230 nm) (8). The difference in muscarinic potency may result in different rates of extrapyramidal symptoms, tardive dyskinesia, gastrointestinal side effects, bladder dysfunction and memory impairment. Alpha-2 adrenergic antagonism may contribute to the antipsychotic response (10) which would represent a relative advantage for risperidone. The higher affinity of olanzapine for the histamine H_1 receptor may account for the sedation seen with olanzapine. Olanzapine's relatively greater potency at $5HT_{2C}$ receptors versus $5HT_{2A}$ receptors compared to risperidone may account for the larger weight gain compared to risperidone (8, 11).

Despite its relatively potent α_1 adrenergic antagonism risperidone can be titrated to its maximally effective dose (6 mg/day) in 3 days (6). Olanzapine dosing starts at 10 mg/day, and subsequent dose increases must be at 7 day intervals (12). The purpose of this trial is to compare the long term safety and efficacy of risperidone versus olanzapine in patients with schizophrenia and schizoaffective disorders.

2. TRIAL OBJECTIVES

The objectives of the trial are :

1. To compare the safety, particularly the incidence of weight gain, of risperidone versus olanzapine in patients with schizophrenia and schizoaffective disorder treated for 44 weeks.
2. To compare the efficacy of risperidone versus olanzapine on the symptoms, quality of life, and satisfaction of patients with schizophrenia and schizoaffective disorder over a 44 week period.

3. SUBJECTS AND METHODS

3.A. Trial design

3.A.1. OVERVIEW

This trial is a randomized, double blind parallel group, multicenter comparison of risperidone and olanzapine for 44 weeks. Subjects can be either inpatients or outpatients. Subjects who have completed the preceding trial (RIS-USA-112) in its entirety are eligible to enter this study. Subjects will continue on the drug (either risperidone or olanzapine) to which they had been assigned in the preceding trial. Safety and efficacy assessments will be performed at Weeks 4, 8, 12, 28, and 44. The subjects will be scheduled for clinic visits at Weeks 16, 20, 24, 32, 36 and 40.

3.B. Subjects

3.B.1. TRIAL SAMPLE

Subjects who have completed the preceding trial (RIS-USA-112) are eligible to participate in this trial.

3.B.2. INCLUSION CRITERIA

1. Subjects who continue to meet all of the inclusion criteria defined for RIS-USA-112 are eligible for this trial with the exception of age (subjects who were 64 years old upon entry to RIS-USA-112 may enter this study if they had turned 65 during the preceding study)
2. Subjects are to have completed the preceding study, RIS-USA-112, in its entirety;
3. Diagnosis of schizophrenia or schizoaffective disorder (DSM-IV);
4. Inpatients or outpatients;
5. Subject and/or legal guardian or representative has signed the informed consent form;

3.B.3. EXCLUSION CRITERIA

Subjects meeting one or more of the following criteria cannot be selected:

1. Subjects who have experienced a hypersensitivity reaction or suspected hypersensitivity reaction to the trial medication administered in RIS-USA-112.
2. Subjects experiencing extrapyramidal symptoms (EPS) not adequately controlled with medication.
3. The subject did not complete RIS-USA-112.
4. A time lapse of more than 3 days since the completion of RIS-USA-112

In addition, the following exclusion criteria, as listed in RIS-USA-112 still apply:

5. A DSM IV Axis I diagnosis other than schizophrenia or schizoaffective disorder (subjects with concurrent post-traumatic stress disorder which does not account for the subject's psychotic symptoms, in the opinion of the investigator, can be enrolled);
6. DSM IV diagnosis of substance abuse or dependence within 3 months prior to selection (nicotine and caffeine dependence are not exclusionary);
7. Documented disease of the central nervous system including but not limited to stroke, tumor, Parkinson's Disease, Alzheimer's Disease, Huntington's Disease, seizure disorder requiring anti-convulsants, history of brain trauma resulting in documented cognitive impairment, chronic infection, neurosyphilis;
8. Hepatic, renal or gastrointestinal disease of sufficient degree to interfere with the excretion, absorption and/or metabolism of trial medication. Subjects with clinical signs of liver disease should be excluded from the study;
9. Acute (e.g. infection), unstable (e.g. labile hypertension, unstable angina), significant or untreated medical illness; patients with diastolic blood pressure ≥ 95 mm Hg at screening should be treated and stabilized before randomization;
10. Patients with clinical signs of liver disease, should be excluded;
11. Subjects with narrow angle glaucoma, chronic urinary retention and/or clinically significant prostatic hypertrophy, paralytic ileus or related conditions, which in the opinion of the investigator may be exacerbated by the anticholinergic effects of olanzapine;
12. Pregnant or breast-feeding females;
13. Female subjects of childbearing potential without adequate contraception. Adequate contraception includes: abstinence, oral contraceptives, intrauterine devices, barrier (diaphragm or condom) plus spermicide, NorplantTM or Depo ProveraTM. A negative pregnancy test is required at entry;
14. Use of disallowed concomitant therapy (see section 3.C.3.);

15. Treatment with antidepressants within 28 days prior to screen;
16. History of treatment with clozapine for more than 4 consecutive weeks ;
17. Treatment with clozapine within 28 days prior to screen;
18. Participation in an investigational drug trial in the 28 days prior to the screening visit;
19. History of severe drug allergy or hypersensitivity;
20. Known sensitivity to risperidone or olanzapine;
21. Subjects known to be unresponsive to either risperidone or olanzapine in the opinion of the investigator;
22. History of neuroleptic malignant syndrome;

3.B.4. WITHDRAWAL CRITERIA

Subjects may be withdrawn from the trial if:

1. A serious adverse event occurs;
2. The investigator considers it, for safety reasons, in the best interest of the subject that he/she be withdrawn;
3. The subject develops clinical signs of liver disease;
4. The randomization code is broken;
5. Subjects must be withdrawn from the trial if they withdraw their consent.

The date and the reason for discontinuation must be noted on the Case Report Form (CRF). All subjects prematurely discontinuing the trial must be seen for a final evaluation and the Trial Termination Form will be completed.

3.C. Trial plan

3.C.1. FLOW CHART

The flow chart showing trial phases and timing of treatment and assessments is given on the next page.

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	Entry ¹	Treatment period											
Visit ²	1	2	3	4	5	6	7	8	9	10	11	12 ³	
Day	1	28	56	84	112	140	168	196	224	252	280	308	
Week	0	4	8	12	16	20	24	28	32	36	40	44	
Month	0	1	2	3	4	5	6	7	8	9	10	11	
Informed consent	X												
Physical examination	X											X ⁵	
Vital signs	X	X	X	X				X				X ⁵	
ECG	X											X ⁵	
Lab	X ⁴	X ³	X ³	X ³				X ³				X ⁴	
Prolactin	X							X				X ⁵	
Body weight	X	X	X	X				X				X ⁵	
Waist/Hip Ratio				X				X				X ⁵	
PANSS	X	X	X	X				X				X ⁵	
HAMD	X											X ⁵	
ESRS	X	X	X	X				X				X ⁵	
CGI/CGI-C ⁶	X	X	X	X				X				X	
Cognitive tests	X			X				X				X	
Quality of sleep	X	X	X	X				X				X	
Daytime drowsiness	X	X	X	X				X				X	
ACS	X	X	X	X				X				X	
PRAEQ	X			X				X				X	
Modified SIP	X			X				X				X	
QOLI-S	X			X				X				X	
DAI	X			X				X				X	
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	
Dispense medication	X	X	X	X	X	X	X	X	X	X	X	X	
Return medication	X	X	X	X	X	X	X	X	X	X	X	X	

1. The evaluations from Week 8 of RIS-USA-112 will be used for entry to RIS-USA-113

2. Visits may be conducted within ± 3 days on either side of the scheduled assessment date.

3. Liver transaminases only (AST, ALT and GGT).

4. Includes cholesterol, lipid profile (HDL, LDL, triglycerides), thyroid panel (T₃, T₄ and TSH), HbA1c and CPK.

5. Visit 12 and/or endpoint

6. Both the CGI and the CGI-C will be evaluated at every visit. The CGI-C will be compared to the severity of illness at the randomization visit of the preceding trial (RIS-USA-112)

Clinical Trial Protocol (Final version, 31-mar-97 Janssen Research Foundation)

3.C.2. TREATMENT**3.C.2.a. Drugs, formulations and strengths**

The trial medication will be provided by the Janssen Research Foundation (JRF). The double blind treatment will consist of capsules which will be identical in appearance, taste and smell, and which will contain risperidone 2 mg or olanzapine 5 mg.

3.C.2.b. Dosages

Administration is done once daily in the morning (around 08.00 h). The subject may receive the entire dose in the evening (around 20.00 h) to improve tolerability. The chosen time of dosing should, if possible, remain constant throughout the trial.

The dosing schedule is given in the following chart:

	No. of Caps/ Day	Dose of Risperidone	Dose of Olanzapine
Days 1-308	1-4	2mg (1 x2mg) or 4mg(2x2mg) or 6mg(3x2mg) or 6mg(3x2mg) and 1x placebo	5mg(1x5mg) or 10mg(2x5mg) or 15mg(3x5mg) or 20mg(4x5mg)

Medication will be supplied in blistercards that allow flexible dosage.

The dose should be continued from the preceding study, RIS-USA-112. If there is an increase in symptoms, the dose may be increased by one capsule per week. The maximum permitted number of capsules per day remains 4 capsules per day. If the dose is increased to 4 capsules/day, the investigator should document in the patient's chart the clinical basis for the dose increase. Dose decreases to one capsule per day may occur at anytime. The reasons for the decrease in dosage should also be reflected in the subject's chart.

3.C.2.c. Subject Numbers

Subjects who participate in this trial will remain in the same treatment arm they were assigned to in the preceding study (RIS-USA-112). Investigators will contact the central number and provide information to the vendor designated by Janssen on the following :

- 1) The subject's birth date;
- 2) The subject's medication number in RIS-USA-112

The randomization center will ensure that the subjects are randomized to the same treatment arm as in the preceding study.

3.C.3. CONCOMITANT THERAPY

All medications (prescription or over-the-counter medications) continued at the start of the trial or started during the trial and different from the trial medication, must be documented on the Concomitant Therapy Form of the CRF

The following medications are not allowed during the study:

- Antipsychotic medication other than the trial medication;
- Mood stabilizers including lithium and anticonvulsants;

Other concomitant psychotropic medications may be given under the following circumstance:

1. If extrapyramidal symptoms emerge or worsen during the double blind period the investigator should perform an additional ESRS examination. Following completion of the ESRS, the investigator may either initiate anticholinergic medication or reduce the study medication dose. At each subsequent scheduled visit the investigator should determine whether continuation of anticholinergic medication is necessary.
2. During the study, propranolol may be initiated for akathisia, following administration of the ESRS.
3. If the subject experiences agitation during the trial lorazepam may be administered on 4 days in any 7 day period at a maximum dose of 4 mg/day. Lorazepam may not be given for insomnia.

4. No other sedative, anxiolytic or other psychoactive drug may be administered during the trial. If medication for sleep needs to be initiated during the study, it should be flurazepam or chloral hydrate.
5. Antidepressants may be initiated during the study, following the administration of a HAM-D.

For any concomitant therapy given as a treatment for a new condition or a worsening of an existing condition, the condition must be documented on the Adverse Event Form of the CRF.

3.C.4. SUPPLY AND BLINDING

The investigator will be provided with a sealed envelope for each subject, containing coded details of the treatment in the double-blind period. This code should be broken only in case of an emergency where the further treatment of the subject is dependent on the trial medication he or she has been receiving. The date and time of the code breaking as well as the reason for it must be documented on the Code Breaking Form in the CRF. In addition, the reason must be documented on the Adverse Event Form of the CRF. The trial monitor should be notified immediately if the code is broken the subject must be withdrawn from the trial and must be followed up if appropriate.

All envelopes, whether opened or sealed, will be collected at the end of the trial.

3.C.5. DRUG ACCOUNTABILITY

The investigator, his/her designee or a hospital pharmacist must maintain an adequate record of the receipt and distribution of all trial supplies using the Drug Dispensing Form and Drug Return Form. These forms must be available for inspection at any time.

Assessments

3.C.6. EFFICACY

The effect of trial medication will be evaluated as follows:

3.C.6.a. Positive and Negative Symptom Scale (PANSS)

Subjects will be interviewed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point) using the Structured Clinical Interview - Positive and Negative Symptom Scale (SCI-PANSS) (15, 16, 17). The PANSS will provide a total score, a positive symptom scale score, a negative symptom score and a general psychopathology score.

3.C.6.b. Clinical Global Impression (CGI) and Clinical Global Impression of Change (CGI-C)

Subjects will be rated for both overall severity of illness (CGI) and the change in severity (CGI-C) at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). The

change in severity will be compared to the subject's condition at randomization (visit 2) of the preceding study (RIS-USA-112)(18).

3.C.6.c. Cognitive Functioning

The following tests will be performed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8 and 12/end-point):

- Wisconsin Card Sorting Test;
- Trails A and B;
- Continuous Performance Test;
- California Verbal Learning Test;
- Visual Working Memory;
- Verbal Fluency Examinations;

3.C.6.d. Visual Analogue Scales for Sleep and drowsiness (VAS)

The subjects will be asked to fill in visual analogue scales (VAS) for quality of sleep and daytime drowsiness at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point).

3.C.6.e. Hamilton Depression Scale (HAMD) 21 Item

Subjects will be rated for depressive symptoms using the 21 item Hamilton Depression Scale (HAMD) (19). Assessments will be done at study entry and at week 44 (visit 1 and 12/endpoint).

3.C.6.f. Drug Attitude Inventory (DAI)

The Drug Attitude Inventory (DAI) (20) is a brief, self-administered 10-item scale to assess the subject's satisfaction with antipsychotic drug therapy. The DAI will be completed at study entry and at weeks 12, 28 and 44 (Visits 1, 4, 8 and 12/endpoint).

3.C.6.g. Quality of Life Interview, short version (QoLI-S)

The shortened version of Quality of Life interview (QOLI-S) (21, 22), a validated survey for chronic mental illness, will be performed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8, and 12/endpoint). The QOLI includes objective (e.g., quantity of leisure activities) and subjective (e.g., satisfaction with leisure activities) scales for the following areas: living situation, family relations, social relations, leisure, work, finances, safety, health, and religion.

3.C.6.h. Modified Sickness Impact Profile (M-SIP)

The Modified Sickness Impact Profile (M-SIP) (23, 24) will be assessed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8, and 12/endpoint). The M-SIP measures overall function within the following six areas: social interaction, alertness behavior, communication, sleep and rest, home management, and recreation and pastimes.

3.C.7. SAFETY

3.C.7.a. Adverse events

See Adverse events (Part II - §)

3.C.7.b. Extrapyramidal Symptom Rating Scale (ESRS)

The Extrapyramidal Symptom Rating Scale (ESRS) (28) will be performed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). It will also be performed before the institution of anticholinergic medication or propranolol for emergent EPS.

3.C.7.c. Body weight and Body Mass Index (BMI)

Body weight will be measured at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). The same standard scale should be used throughout the trial. Patients should be lightly clothed, wear similar clothing at each visit, and be weighed without shoes. Body Mass Index (BMI) will be calculated as weight in kilograms over height in meters² (kg/m²).

3.C.7.d. Waist/Hip Ratio

Waist/hip ratio: the circumference of the waist and hips will be measured using a standard tape measure. Waist/hip ratio is an indirect measure of intra-abdominal fat. This measurement will be taken at weeks 12, 28 and 44 (visits 4, 8 and 12/endpoint).

3.C.7.e. Anticholinergic Symptoms (ACS)

An anticholinergic symptom survey, developed specifically for this study, will be assessed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/endpoint). The survey questions patients to report on manifestations of the following: dry mouth, blurred vision, constipation, and urinary retention. A positive response will be followed by a query as to how bothersome the symptom is on a 4 point scale.

3.C.7.f. Prolactin Related Adverse Event Questionnaire (PRAEQ)

A short questionnaire documenting the presence of menstrual disturbance, galactorrhea, erectile dysfunction, ejaculatory dysfunction and gynecomastia. It will be administered at study entry and at weeks 28 and 44 (visits 1, 8 and 12/endpoint). A positive response will be followed by a query as to how bothersome the symptom is on a 4 point scale.

3.C.7.g. Clinical laboratory tests

Blood and urine samples will be analyzed by a central laboratory. Samples will be collected and the sample tubes labeled following the method described in the Users Manual provided by the central laboratory.

The lab report must be reviewed by the investigator and any clinically relevant changes occurring during the trial must be recorded on the AE Form of the CRF.

Blood samples for biochemistry and hematology and random urine samples for urinalysis will be taken at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point).

Liver transaminases only will be determined at weeks 4, 8, 12 and 28 (visits 2, 3, 4, and 8). Full CBCs, U/As and chemistry panels will be performed at study entry and at week 44 (visits 1 and 12/endpoint).

Subjects with serum transaminase levels (AST, ALT, GGT) > 3X the upper limit of normal, either upon study entry or during the study, should have the transaminases performed weekly until:

- 1) the levels fall below 3X ULN,
- 2) the subject completes the study and is clinically asymptomatic,
- 3) the subject develops clinical signs of liver disease, in which case the subject must be discontinued from the study.

If, in the opinion of the investigator, the subject's liver transaminases stabilize at a level >3X ULN and the subject does not have signs of liver disease, the transaminases may be followed every 2 weeks.

The following analyses will be done and reported:

3.C.7.g.1. Hematology

Hemoglobin, Hemoglobin A1C, hematocrit, RBC, WBC, white differential blood cell count (neutrophils, lymphocytes, monocytes, eosinophils, basophils), platelet count. These evaluations will be done at study entry and week 44 only (visits 1 and 12/end point).

3.C.7.g.2. Biochemistry

Total protein, alkaline phosphatase, AST, ALT, gamma GT, LDH, cholesterol, lipid profile (HDL, LDL, triglycerides), thyroid panel (T3, T4, TSH), total bilirubin, urea, uric acid, creatinine, sodium, potassium, chloride, calcium, CPK and prolactin. Prolactin levels will be done at study entry and at weeks 28 and 44 only (visits 8 and 12/endpoint). The full panel will be done at study entry and week 44 only (visits 1 and 12/end point). Transaminase levels will be done at weeks 4, 8 12 and 28 (visits 2, 3, 4, and 8).

The entry and endpoint labs should be performed following a 12-hour fast, with the time since last food consumption recorded.

3.C.7.g.3. Urinalysis

Urinalysis for protein, glucose, occult blood will be performed by dipstick at screen, randomization (if necessary) and at endpoint. If results are abnormal, microscopic examination for WBC, RBC, and casts will be performed.

3.C.7.h. Vital signs and physical examination

At study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point), systolic and diastolic blood pressure must be measured both in the supine (after 5 minutes rest) and standing positions. Supine blood pressure should be measured twice with the average rounded to the nearest integer and entered in the CRF. Pulse must also be recorded.

Physical exams will be done at study entry and at week 44 (visits and 12/endpoint). All abnormalities should be recorded in the CRF. Changes for the worse which are judged clinically significant by the investigator should also be recorded as adverse events.

3.C.7.i. Electrocardiogram (ECG)

An electrocardiogram (ECG) must be recorded at study entry and at week 44 (visits 1, and 12/endpoint). The investigator must indicate in the CRF whether the ECG is within normal limits.

3.D. Statistics

3.D.1. SAMPLE SIZE CALCULATION

Sample size determinations were made based on the expected rates of increased body weight. The Zyprexa package insert specifies that 56% of patients met the criterion for having gained greater than 7% of their baseline weight during long-term continuation therapy. A weight gain rate of 32% is assumed for patients on long-term Risperdal therapy (based on an integrated database of long-term Risperdal trials). Using an overall two-tailed alpha level of 0.05 with 80% power and assuming the true rates of 32% vs. 56% for the risperidone and olanzapine groups, 75 patients per group will be required. To also adjust for drop-outs (60%), the total number of patients will be increased to 376 (188 per group). This 60% drop-out rate includes patients who do not continue from RIS-USA-112 into this long-term extension trial.

3.D.2. STATISTICAL ANALYSIS

The statistical analysis will be performed by the Janssen Research Foundation. Statistical tests will be performed at the 5% two-tailed significance level (unless specified differently). In case of non-normality or heteroscedasticity appropriate transformations (e.g.: logarithm) will be applied. Alternatively, parametric tests will be replaced by non-parametric tests (e.g. Mann-Whitney-U, Van Elteren test).

3.D.2.a. Safety

All patients who had at least one dose of study medication in RIS-USA-113 will be included in the safety analysis. Baseline values will be defined as the baseline value from RIS-USA-112 unless specified differently.

The primary parameter is the percent of patients who gain at least 7% of their baseline weight at any time during treatment. The Cochran-Mantel-Haenszel test, stratifying for investigator will be used to test for treatment differences in these rates. The spontaneous adverse event rates (newly emergent or a worsening from baseline) of extrapyramidal symptoms will also be calculated. The following WHO preferred terms will be considered extrapyramidal symptoms: tremor, dystonia, hypokinesia, hypertonia, hyperkinesia, oculogyric crisis, ataxia, abnormal gait, involuntary muscle contractions, hyporeflexia, akathisia, and extrapyramidal disorders. A patient who reports at least one of these events at any time during the trial will be considered to have experienced extrapyramidal symptoms. The Cochran-Mantel-Haenszel test, stratifying for investigator and baseline ESRS strata will be used to test for treatment differences in these rates. Additionally, adverse event rates will be calculated for patients who were experiencing extrapyramidal symptoms at the time of their discontinuation or completion of the trial and separately for those patients who completed the trial at 44 weeks. The incidence of new diabetes and hypertension onset will be calculated. New onset of diabetes will be defined as HbA1c increasing from <7% to ≥7%. New onset of hypertension will be defined as either institution of antihypertensive medication or new onset of diastolic blood pressure of ≥95 Hg on two consecutive visits. The primary analysis will include information on all patients randomized into RIS-USA-112 i.e., rates will be calculated for the entire 52 weeks of exposure. A secondary analysis will include information only from those patients who continued into RIS-USA-113.

The Extrapyramidal Symptom Rating Scale (ESRS) total and subtotals (total Parkinsonism, Dystonia, Dyskinesia, Questionnaire, CGI of severity of parkinsonism, CGI of severity of dystonia, CGI of severity of dyskinesia) will be calculated. The change versus baseline to each visit, endpoint, and to the maximum during double-blind treatment will be compared between treatments by means of an analysis of covariance model with treatment, investigator, baseline ESRS score, and the treatment-by-covariate interaction terms included in the model. If the interaction terms are not significant at the 0.1 level, the treatment effects will be tested by means of the reduced model (without the interaction terms). The number of patients taking anti-parkinsonism medication will be compared by means of the Cochran-Mantel-Haenszel test for general association, controlling for investigator and baseline ESRS strata.

Vital Signs (blood pressure, heart rate), body weight, BMI, and waist/hip ratio will be tabulated and analyzed descriptively. Inter-group changes will be performed by means of an ANOVA model with factors of treatment, investigator and baseline BMI strata (for body weight, BMI, waist/hip ratios only).

Additionally, an ANCOVA model with factors of treatment, investigator, and baseline value will be used to compare treatment group differences in the mean change from baseline for the anti-cholinergic symptom assessment (ACS), the modified sickness impact profile (M-SIP), and the prolactin-related adverse event questionnaire (PRAEQ).

Within group comparisons will be performed using the paired t-test or the Wilcoxon sign rank test.

3.D.2.a.1. Adverse events

Incidences of all AEs will be tabulated as the number of patients who experienced at least one episode expressed as a percentage of the total number of subjects entered in the trial per treatment group. The combined adverse event rate of extrapyramidal symptoms will also be calculated as described in 3.D.2.a.

3.D.2.a.2. Clinical laboratory tests

For the clinical laboratory data, descriptive statistics and pre versus post treatment cross-tabulations (with classes for below, within and above normal range) will be generated for all tests performed. Important abnormalities, as determined by the occurrence of pathological values, will be tabulated. Pathological values are values that are outside the pathological limits. For most hematological and biochemical tests, pathological limits are defined by Lippert and Lehmann (SI Units in medicine. Baltimore-Munich: Urban & Schwarzenberg, 1978). For enzymes, the lower pathological limit is defined as zero, and the upper pathological limit as twice the upper normal limit. For leukocyte differential count, no pathological limits are defined. If a value is outside the pathological limits but not outside the normal limits for the particular laboratory, it is not considered pathological. The type of important abnormality depends on the time of occurrence of the pathological value, i.e., before (reference value of the parameter), during or after treatment (e.g., non-pathological before, pathological during treatment).

3.D.2.b. Analysis of efficacy parameters

The main analysis will be an intent to treat analysis containing all patients who were treated and have at least one post-baseline assessment. Additionally an on-protocol analysis may be performed. The primary timepoint is endpoint. The primary analysis will use the baseline from the RIS-USA-112 trial at the time of randomization. A secondary analysis will also be performed using the baseline from the RIS-USA-113 study (endpoint from the RIS-USA-112).

For each of the continuous efficacy parameters with a baseline response (PANSS, HAMD, CGI, cognitive tests, quality of sleep and daytime drowsiness, QOLI-S, and the DAI), the change from baseline score at each visit and at endpoint will be analyzed using analysis of

covariance methods. The model will include treatment, investigator, baseline value, and the treatment-by covariate interaction terms. If the interaction terms are not significant at the 0.1 level, the treatment effects will be tested by means of the reduced model (without the interaction terms). The number of patients experiencing clinical improvement, i.e. with a percentage decrease in total PANSS of at least 20% versus baseline will be calculated. Comparisons will be performed by means of the Cochran-Mantel-Haenszel test for general association, controlling for the baseline PANSS strata.

The time to relapse controlling for investigator will also be calculated using standard survival analysis methods including product-limit estimators, logrank tests, and proportional hazard regression models. Categorical data such as one-year relapse rates will be analyzed using the Cochran-Mantel-Haenszel test, controlling for investigator. Relapse will be defined as psychiatric hospitalization for a subject living in the community.

In addition, methods for repeated measures will be used. These methods compare treatment groups over time rather than at each visit. The baseline values may be used as covariates in these analyses to adjust for baseline differences between treatment groups.

3.D.2.c. Subgroup Analyses

A subgroup analysis will be performed based on the average daily dose of study medication received. Patients who received an average dose of less than 4 mg of risperidone will be analyzed separately from those who received greater than or equal to 4 mg. Likewise, patients who received less than 12.5 mg of olanzapine will be analyzed separately from those who received greater than or equal to 12.5 mg.

Also, if the size of the study permits, other relevant demographic or baseline value-defined subgroups will be examined for unusually large or small responses, e.g., comparison of effects by age, sex, and race.

3.D.3. ADMINISTRATIVE INTERIM ANALYSIS

One administrative interim analysis may be performed with a spending function of 0.001. The analysis will be performed only on the basis of blinded groupings (Group A, B, ...). The overall results will be made available to Janssen Research Foundation management at the level of Head, Clinical Research/Medical Development and above. The results of an administrative interim analysis will be documented in the clinical research report. Included in the documentation will be the names of Janssen management who viewed the results. If any of the Janssen reviewers also had access to the true treatment code, that will also be documented.

The results will not be disseminated to those involved in the day-to-day management of the trial. As a result of the administrative interim analysis, the trial will not be terminated early to claim superiority of one treatment group, the study protocol will not be altered due to the interim results, nor will any exploratory or subpopulations analyses be performed.

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5. ADDENDA

ADDENDUM I: SUBJECT INFORMATION LETTER AND INFORMED CONSENT FORM

Introduction and purpose of the trial

You are being asked to participate as one of approximately 376 patients in a medical research trial with two drugs called risperidone and olanzapine. This study is being conducted in up 40 centers.

Risperidone is a drug which is effective in the treatment of your disorder. It has been registered in more than 30 countries, has been administered to more than 800 000 patients world-wide and is well tolerated.

Olanzapine is a new drug for the treatment of your disorder. It has recently been registered in several countries, including the USA, England and several other European countries. It has been administered to approximately 3 000 subjects participating in medical research trials.

The safety and efficacy of risperidone and olanzapine in the treatment of your disorder will be studied.

Treatment

You will receive either risperidone or olanzapine. The starting doses will be 2 mg of risperidone and 10 mg of olanzapine. This dose may be increased up to a maximum of 8 mg of risperidone and 20 mg of olanzapine. Your doctor will evaluate your response to treatment and adjust the dose accordingly.

Procedures during the trial

The trial lasts 44 weeks (11 months). If you agree to take part, it is important that you will go to your doctor's office for 12 scheduled visits. These visits will occur once every 4 weeks. These visits may be two hours long. The evaluations from your last visit of the study you just completed will be used at the first visit of this study. During the rest of these visits specific assessments to evaluate the efficacy and safety of the treatment will be performed. At the start and end of treatment you will undergo a full medical examination. ECG (Electrocardiogram) will be done before start of treatment. This examination studies exactly how your heart is functioning. Blood and urine samples for routine laboratory tests will be taken up to 6 times during the trial. the amount of blood taken each time will be approximately 10ml (2 tablespoons).

Please remember to bring with you all unused medication as well as all empty medication containers to each visit.

If your symptoms worsen at any time between visits or you experience any unwanted effects, you should contact your doctor as soon as possible.

For this trial to be successful, it is important that you fully co-operate with the doctor and follow his/her instructions precisely. You should not take any other

medication, either on prescription or from the pharmacy or supermarket unless it has been approved by the doctor.

Pregnancy

If you are a female of childbearing potential (have not had a tubal ligation or hysterectomy), you must not be pregnant or a nursing mother during this trial. If you are sexually active, you will be required to take precautions to avoid the possibility of becoming pregnant. Abstinence, the use of oral contraceptives, intrauterine devices, barrier method (diaphragm or condom) plus spermicide, Norplant TM or Depo Provera TM are acceptable methods of birth control. You must notify your doctor immediately if you do become pregnant during the trial and he/she will then evaluate your condition and decide whether you should discontinue the study drug or not. As with all other medications, there is always a risk to the subject, embryo or fetus.

Early termination

Participation in this trial is voluntary. Your refusal to participate or decision to withdraw at any time during the trial will not involve any penalty or loss of benefits to which you are otherwise entitled. The doctor may decide that it is in your best interest to stop or Janssen Research Foundation, the sponsor of this trial, may also stop your participation. You may be enrolled in this trial prior to your doctor receiving the results of your first tests. If the results of any of these tests show that you fulfill one or more of the exclusion criteria, you will become ineligible and will be withdrawn from the trial. If you discontinue the trial early, you will be asked to return all your trial medication, and have the end-point evaluations done.

Benefits and risks

Possible benefits of participating in this trial may include improvement of your condition and relief of symptoms. Also, your condition may be monitored more closely than usual. In addition, new information may be learned that would be helpful in developing new therapies for other subjects with similar illnesses. It is possible, however, that no therapeutic or other direct benefits may result during or following completion of this trial.

All therapies have the potential to cause some side effects or other reactions. The side effects reported on risperidone and olanzapine are to some extent similar, although they may differ in degree and frequency. The following reactions may occur: drowsiness, tiredness, sleeplessness, agitation, anxiety, headache, concentration difficulties, blurred vision, dizziness, indigestion, nausea, vomiting, abdominal pain, difficult stools, sexual potency disorders, some loss of urine, blocked nose, skin rash. In some cases, the blood pressure may fall slightly in the early stages of treatment, resulting in dizziness, but this will usually pass off automatically. You may put on a bit of weight during the treatment and minor motor disorders may occur such as trembling, slight muscle stiffness and restlessness in the legs. The latter symptoms are usually not dangerous and will disappear after the doctor has reduced the dose or administered an additional drug.

On olanzapine treatment transient, asymptomatic elevations of liver enzymes have been reported, especially in early treatment.

Although rare and harmless, swelling of the ankles may occur. Hypersensitivity to risperidone or olanzapine are rare. It can be recognized by for instance, skin rash, itching, shortness of breath or swollen face. Please contact your doctor if any of these occur. Very rarely, a state of confusion, reduced consciousness, high fever or pronounced muscle stiffness might occur. If this should happen, please notify your doctor. In extremely rare cases, generally as a result of several factors together including extreme heat or cold, marked changes in body temperature occur. You must notify the doctor if this happens. The treatment in this trial is relatively short, but during long-term treatment twitching of the tongue, face and mouth or jaws may occur. Please inform the doctor if this happens. After prolonged use, women may suffer from lactation and menstruation disturbances, while in some cases men may develop breasts to a very slight degree. There may be some side effects which are not yet known.

The risks observed for drawing blood are minor. Some local pain, bruising, swelling, soreness and discoloration has been observed.

You will be informed of any new findings that may develop during the trial as this may relate to your willingness to continue to participate in the trial. You will be asked to report any possible side effects to the doctor at any time during the trial. Any severe or unusual reactions or research-related injuries should be reported as soon as possible to

.....(investigator's name) at (phone).

Alternative treatments

There are other medications currently available on the market for treating your condition. Your doctor will discuss these and other alternatives with you in the event that you choose to be treated with them rather than participate in this research trial.

Confidentiality

All records and documents pertaining to your participation in this trial will be held strictly confidential and your name will not be reported in any publications resulting from this trial. All records and documents will be reviewed by the sponsor (the Janssen Research Foundation) or representatives from the sponsor and may be reviewed by the Food and Drug Administration (FDA), and/or registration authorities in the European Community countries.

Before signing this consent form, you are free to ask your doctor about any aspect of this trial that are not clear to you. You will be given a copy of this consent form.

Compensation

There will be no costs involved for you for participation in this trial. All costs for the required visits, examinations, laboratory procedures and supply of medication

are provided by the Janssen Research Foundation, Inc. In the event an illness or injury is directly attributable to the use of the research drug, the cost of emergency care will be provided by Janssen Research Foundation, Inc.. Financial compensation for such things as disability or discomfort due to injury, transportation costs, etc., is not available. Any medical expenses due to self-inflicted injury are your responsibility.

PART II: PROCEDURES

6. ADVERSE EVENTS

6.A. Definitions

6.A.1. ADVERSE EVENT (AE)

Any undesirable experience occurring to a subject, during a clinical trial, whether or not considered related to the investigational product(s) should be considered as an adverse event.

6.A.2. SERIOUS ADVERSE EVENT

A serious adverse event is an adverse event that is fatal; life-threatening; significantly, persistently or permanently disabling; requiring intervention to prevent permanent impairment or damage; requiring in-patient hospitalization or prolongation of hospitalization. In addition, congenital anomaly, occurrence of malignancy or clinical injuries resulting from overdose are always considered a serious adverse event.

If there is any doubt by the investigator or clinical trial monitor about whether an event meets the definition of a serious adverse event as stated above, the event must be reported as a serious adverse event.

6.A.3. UNEXPECTED ADVERSE EVENT

An unexpected adverse event is an event not previously reported (in nature, severity or incidence), i.e. not included in the current Investigator's Brochure or in the International Product Information Document, or local package insert.

6.A.4. LIFE-THREATENING

Life-threatening means that the patient was, in view of the investigator, at immediate risk of death from the reaction as it occurred (i.e. it does not include a reaction that, had it occurred in a more serious form, might have caused death).

6.A.5. ASSOCIATED WITH THE USE OF THE DRUG

An adverse event is considered associated with the use of the drug when the causality assessment is certain or probable/likely.

6.B. Reporting of adverse events

All adverse events occurring during clinical trials have to be reported on the Adverse Event Form of the CRF from the D of the first visit recorded in the CRF

till the D of the last visit of the subject in the trial. The investigator must provide information on symptoms, time of onset and subsidence, severity, drug-relatedness, action taken with reference to the trial drug and subject outcome.

Clinically relevant changes in laboratory parameters, ECG, vital signs and body weight as well as intercurrent illnesses are considered adverse events and should be recorded on the Adverse Event Form of the CRF.

All serious adverse events must be reported by the investigator within 1 working D of his or her becoming aware of them to one of the Janssen Research Foundation (JRF) contact persons mentioned below. Serious adverse events occurring after the trial but within a period of 30 Ds after the last intake and spontaneously reported by the investigator will be handled by JRF as serious adverse events occurring during clinical trials.

Trial monitor:

NAME/ADDRESS/PHONE/FAX

Local Trial Coordinator:

NAME/ADDRESS/PHONE/FAX

The first report of a serious adverse event may be made by telephone or facsimile (FAX).

This report of a serious adverse event by telephone must always be confirmed by a written, more detailed report. For this purpose, the JRF contact person will provide the investigator with a Serious Adverse Event and Pregnancy Reporting Form for Clinical Trials, to be completed and signed by the latter.

Pregnancies occurring during a clinical trial must be reported as soon as possible using the same Serious Adverse Event and Pregnancy Reporting Form for Clinical Trials. The outcome of the pregnancy must also be reported to the JRF.

The JRF will assume responsibility for appropriate reporting of adverse events to the authorities. The JRF will also report all serious adverse events that are unexpected and associated with the use of the drug to the investigators. It is the investigator's responsibility to report the adverse events which are classified by the JRF as serious, unexpected and associated with the use of the drug to the Ethics Committee which has approved the protocol unless otherwise required and documented by the Ethics Committee.

If the subjects are not under 24-hour supervision of the investigator or his/her staff (out-patients, volunteers), they (or their designee, if appropriate) must be provided with a "trial card" indicating the name of the investigational product, the trial number, the investigator's name and a 24-hour emergency contact number.

7. TRIAL CLOSURE CONSIDERATIONS

The JRF reserves the right to close the investigational site or terminate the trial at any time.

Reasons for such action include, but are not limited to:

1. Safety concerns;
2. Sufficient data suggesting lack of efficacy;
3. Inadequate recruitment of subjects by the investigator;
4. The required number of subjects for the trial has been recruited;
5. Failure of the investigator to comply with the protocol, JRF procedures or Good Clinical Practice (GCP) guidelines.

8. TRIAL MATERIALS

8.A. Investigational drugs

The investigator acknowledges that the drug supplies are investigational and as such must be handled strictly in accordance with the protocol and the container label. Supplies must be retained in a safe, secure location and stored under the appropriate conditions as specified on delivery. Supplies should be dispensed under the supervision of the investigator or the assistant investigator, or by a hospital pharmacist.

It is the investigator's responsibility to ensure that subjects or those held to be responsible for subjects, return their medication. Returned supplies must not be dispensed again, even to the same subject. Unused medication and medication returned by the subject must be available for verification by the trial monitor.

8.B. Trial documents

The following documents must be provided to the Janssen Research Foundation:
a signed protocol and Trial Agreement;

the curriculum vitae of the investigator and all persons listed on the Trial Agreement;

1. a copy of the dated and signed approval notice from the ethics committee, clearly identifying the trial by title and number;
2. the names of the current members or composition of the ethics committee and their position in the health-care institution or their credentials;
3. a copy of the subject information and informed consent form approved by the ethics committee or institutional review board;
4. evidence of laboratory certification and institutional accreditation, if applicable;

5. a list of reference ranges and appropriate units for all laboratory tests to be performed at the institution, if applicable.

8.C. Case report forms

CRFs are provided for each subject. All forms must be filled in legibly in durable black ball-point pen.

All data relating to the trial must be recorded on CRFs prepared by the JRF. These CRFs are to be completed at the time of the subject's visit, with the exception of results of tests performed outside the investigator's office, so that they always reflect the latest observations on the subjects participating in the trial. Every effort should be made to ensure that all efficacy evaluations are completed by the same individual who made the initial baseline determinations. The investigator must verify that all data entries in the CRFs are accurate and correct. If certain information is not done, not available or not applicable, the investigator must enter "N.D." or "N.A.V." or "N.A.P.", respectively in the appropriate space.

During monitoring visits, the monitor will review the CRF, evaluate them for completeness and give back the forms with missing information and/or errors to the investigator for correction. All entries, corrections and alterations are to be made by the responsible investigator or his/her designee. Corrections must be made in such a way that the original entry is not obscured. Correction fluid must NOT be used. The correct data must be inserted, dated and initialed by the investigator or his/her designee.

A CRF must be completed and in the case of a CRF printed on No Carbon Required (NCR) paper, the original must be returned to the JRF. One copy is to be retained in the archives of the sponsor from the country in which the trial is performed. A second copy will be provided for the investigator's convenience.

8.D. Subject identification register

In order to permit easy identification of the individual subject during and after the trial, the Investigator is responsible for keeping an up-dated "Subject Identification Register".

This document will be reviewed by the monitor for completeness. However, in order to ensure subject confidentiality, no copy will be made.

8.E. Archiving

The investigator shall arrange for the retention of the Subject Identification Register for at least fifteen years after the Final Trial Report has been signed. All other documentation relating to this trial (source documents, informed consent forms, approvals) shall be kept for the maximum period of time permitted by the hospital, institution or private practice.

Under no circumstance shall the investigator re-locate or dispose of any trial documents before having obtained the Janssen Research Foundation's written approval.

If it becomes necessary for the JRF or the appropriate Regulatory Authority to review any documentation relating to this trial, the investigator must permit, with the approval of the subject, access to such reports.

Any difficulty in storing original documents must be discussed with the monitor prior to the initiation of the trial.

9. REPORTING AND PUBLICATION

Trial conduct and results will be described in a Clinical Trial Report, prepared according to the existing Standard Operating Procedures.

Publication of the results by the investigator must be subject to mutual agreement between the investigator and the JRF. Manuscripts and abstracts should be sent to the JRF at least one month prior to submission for publication or presentation.

10. ETHICS

10.A. Ethics Committee or institutional review board (IRB)

This trial will be undertaken only after full approval of the protocol and addenda has been obtained from the local Ethics Committee and a copy of the approval has been received by the JRF.

The Ethics Committee must be informed of all subsequent protocol amendments proposed by either the investigator or the JRF and should be asked for its opinion if a re-evaluation of the ethical aspects of the trial appears to be called for.

Reports on, and reviews of, the trial and its progress will be submitted to Ethics Committees or IRB by the investigator at intervals stipulated in their guidelines.

10.B. Declaration of Helsinki

This trial will be conducted in accordance with the current version of the Declaration of Helsinki.

10.C. Subject information and informed consent

Prior to entry in the trial, the investigator must explain to potential subjects or their legal representatives the aims, methods, reasonably anticipated benefits and potential hazards of the trial and any discomfort it may entail. Subjects will be informed that they are free not to participate in the trial and that they may withdraw consent to participate at any time. They will be told which alternative treatments are available if they refuse to take part and that such refusal will not prejudice future

treatment. Finally, they will be told that their records may be examined by competent authorities and authorized persons but that personal information will be treated as strictly confidential and will not be publicly available. Subjects must be given the opportunity to ask questions. After this explanation and before entry to the trial, consent should be appropriately recorded by means of either the subject's or his/her legal representative's dated signature or the signature of an independent witness who certifies the subject's consent in writing.

If neither signed informed consent nor witnessed verbal consent can be obtained, the reason must be documented by the investigator.

11. REGULATORY APPROVAL

This trial must be submitted to the Regulatory Authority for approval under the requirement/scheme. The trial will only be undertaken following receipt by the JRF of (written) approval from the Regulatory Authority.

12. INDEMNITY INSURANCE

For subjects treated according to the protocol, injury possibly arising from the test treatment is covered by the Janssen product liability insurance.

13. MONITORING

The trial will be monitored according to the current JRF Standard Operating Procedure (SOP) for the Monitoring of Clinical Trials.

The trial monitor will meet with the investigator and all staff involved in the trial shortly before the trial starts to review the procedures to be followed in conducting it and recording the findings in the CRF. During the trial, the investigator shall permit the trial monitor to verify the progress of the trial on site as frequently as necessary. The investigator shall make the CRF available, provide missing or corrected data and sign the CRFs. Key data transcribed onto the CRFs, such as the subject's sex, date of birth, assessment dates, test results etc, will be reviewed against source documents. Personal information will be treated as strictly confidential and will not be publicly available. The CRF must be amended, after any inconsistencies found at this review have been resolved.

14. INSPECTION OF THE TRIAL

This trial may be reviewed by an independent QA department and/or regulatory authorities. This implies that auditors/inspectors will have the right to inspect the trial center(s) at any time during and/or after completion of the trial and will have access to source documents, including the subject's file. By participating in this trial, investigators agree to this requirement.

Measures will be undertaken to protect subject data handed over by the investigator to the JRF and to inspections against disclosure to unauthorized third parties and subject confidentiality will be maintained at all times.

JANSSEN RESEARCH FOUNDATION		
International Clinical Research & Development		
CLINICAL TRIAL PROTOCOL		
Final version date: 19-Jun-97	Drug number: R064766	
Trial number: RIS-USA-113	Clinical Phase: IV	
Title:	Risperidone vs. olanzapine in the treatment of schizophrenia	
Summary:	A multicenter, randomized, double blind, parallel group trial comparing the safety and efficacy of risperidone and olanzapine in the treatment of psychosis in patients with schizophrenia and schizoaffective disorder. The trial duration is 44 weeks.	
Trial Location:	USA	
Sponsor:	Janssen Research Foundation 1125 Trenton-Harbourton Road Titusville, NJ 08560	
Trial Coordinator:	Martin Brecher, MD Janssen Research Foundation 1125 Trenton-Harbourton Road Titusville, NJ 08560	
Approvals:	March 5, 1997 #030597005	
Investigator:	 (name, title)	 (date)
Development Project Leader: Janssen Research Foundation	 (date)	
Clinical Development Director: Janssen Research Foundation	 (date)	
This protocol contains confidential information that should only be disclosed to those persons responsible for execution and organization of the trial and on condition that all such persons agree not to further disseminate it.		

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PART I: CLINICAL TRIAL PROTOCOL

1. INTRODUCTION

For the past 40 years antagonists at the D₂ dopamine receptor have been widely prescribed for the symptoms of psychosis. Most D₂ blockers also cause significant extrapyramidal symptoms (EPS)(1) which reduce both clinical efficacy and compliance (2). These compounds are also associated with tardive dyskinesia which is irreversible in some cases (3). Clozapine, a weak D₂ blocker, causes very little EPS and may be more efficacious than other neuroleptics, but its use is restricted because of the risk of agranulocytosis (4). In the past decade research on the pharmacotherapy of schizophrenia has focused on discovering a "clozapine without the risk of agranulocytosis".

Since its introduction into clinical practice in 1994 risperidone, a substituted benzisoxazole, has become established as a first line treatment for psychosis (5). The widespread acceptance of risperidone is based on its efficacy against positive and negative symptoms of schizophrenia, rapid titration schedule and onset of action, low incidence of EPS and a benign side effect profile (6, 7). These attributes are in large measure attributable to risperidone's potent and partially specific pharmacological activity. It is a highly potent 5HT_{2A} antagonist (K_i 0.16 nm) and a potent D₂ (K_i 3.13 nm), α_1 -adrenergic (K_i 0.81 nm) and α_2 -adrenergic (K_i 7.54 nm) antagonist (8).

Olanzapine, a thienobenzodiazepine structurally related to clozapine (9), has recently been approved for the treatment of psychosis. This compound also has strong affinity for the 5HT_{2A} (K_i 4 nm), D₂ (K_i 11 nm) and α -adrenergic (K_i 19 nm) receptors (8). Olanzapine is distinguished pharmacologically from risperidone by having strong affinity for the muscarinic M₁-M₅ receptors (K_i $\leq$ 25 nm with K_i for M₁ 1.9 nm), 20 fold stronger affinity than risperidone at the histamine H₁ receptor and weaker affinity at the α_2 adrenergic receptor (K_i 230 nm) (8). The difference in muscarinic potency may result in different rates of extrapyramidal symptoms, tardive dyskinesia, gastrointestinal side effects, bladder dysfunction and memory impairment. Alpha-2 adrenergic antagonism may contribute to the antipsychotic response (10) which would represent a relative advantage for risperidone. The higher affinity of olanzapine for the histamine H₁ receptor may account for the sedation seen with olanzapine. Olanzapine's relatively greater potency at 5HT_{2C} receptors versus 5HT_{2A} receptors compared to risperidone may account for the larger weight gain compared to risperidone (8, 11).

Despite its relatively potent α_1 adrenergic antagonism risperidone can be titrated to its maximally effective dose (6 mg/day) in 3 days (6). Olanzapine dosing starts at 10 mg/day, and subsequent dose increases must be at 7 day intervals (12). The purpose of this trial is to compare the long term safety and efficacy of risperidone versus olanzapine in patients with schizophrenia and schizoaffective disorders.

2. TRIAL OBJECTIVES

The objectives of the trial are :

1. To compare the safety, particularly the incidence of weight gain, of risperidone versus olanzapine in patients with schizophrenia and schizoaffective disorder treated for 44 weeks.
2. To compare the efficacy of risperidone versus olanzapine on the symptoms, quality of life, and satisfaction of patients with schizophrenia and schizoaffective disorder over a 44 week period.

3. SUBJECTS AND METHODS

3.A. Trial design

3.A.1. OVERVIEW

This trial is a randomized, double blind parallel group, multicenter comparison of risperidone and olanzapine for 44 weeks. Subjects can be either inpatients or outpatients. Subjects who have completed the preceding trial (RIS-USA-112) in its entirety are eligible to enter this study. Subjects will continue on the drug (either risperidone or olanzapine) to which they had been assigned in the preceding trial. Safety and efficacy assessments will be performed at Weeks 4, 8, 12, 28, and 44. The subjects will be scheduled for clinic visits at Weeks 16, 20, 24, 32, 36 and 40.

3.B. Subjects

3.B.1. TRIAL SAMPLE

Subjects who have completed the preceding trial (RIS-USA-112) are eligible to participate in this trial.

3.B.2. INCLUSION CRITERIA

1. Subjects who continue to meet all of the inclusion criteria defined for RIS-USA-112 are eligible for this trial with the exception of age (subjects who were 64 years old upon entry to RIS-USA-112 may enter this study if they had turned 65 during the preceding study)
2. Subjects are to have completed the preceding study, RIS-USA-112, in its entirety;
3. Diagnosis of schizophrenia or schizoaffective disorder (DSM-IV);
4. Inpatients or outpatients;
5. Subject and/or legal guardian or representative has signed the informed consent form;

3.B.3. EXCLUSION CRITERIA

Subjects meeting one or more of the following criteria cannot be selected:

1. Subjects who have experienced a hypersensitivity reaction or suspected hypersensitivity reaction to the trial medication administered in RIS-USA-112.
2. Subjects experiencing extrapyramidal symptoms (EPS) not adequately controlled with medication.
3. The subject did not complete RIS-USA-112.
4. A time lapse of more than 3 days since the completion of RIS-USA-112

In addition, the following exclusion criteria, as listed in RIS-USA-112 still apply:

5. A DSM IV Axis I diagnosis other than schizophrenia or schizoaffective disorder (subjects with concurrent post-traumatic stress disorder which does not account for the subject's psychotic symptoms, in the opinion of the investigator, can be enrolled);
6. DSM IV diagnosis of substance abuse or dependence within 3 months prior to selection (nicotine and caffeine dependence are not exclusionary);
7. Documented disease of the central nervous system including but not limited to stroke, tumor, Parkinson's Disease, Alzheimer's Disease, Huntington's Disease, seizure disorder requiring anti-convulsants, history of brain trauma resulting in documented cognitive impairment, chronic infection, neurosyphilis;
8. Hepatic, renal or gastrointestinal disease of sufficient degree to interfere with the excretion, absorption and/or metabolism of trial medication. Subjects with clinical signs of liver disease should be excluded from the study;
9. Acute (e.g. infection), unstable (e.g. labile hypertension, unstable angina), significant or untreated medical illness; patients with diastolic blood pressure $\geq$ 95 mm Hg at screening should be treated and stabilized before randomization;
10. Patients with clinical signs of liver disease, should be excluded;
11. Subjects with narrow angle glaucoma, chronic urinary retention and/or clinically significant prostatic hypertrophy, paralytic ileus or related conditions, which in the opinion of the investigator may be exacerbated by the anticholinergic effects of olanzapine;
12. Pregnant or breast-feeding females;
13. Female subjects of childbearing potential without adequate contraception. Adequate contraception includes: abstinence, oral contraceptives, intrauterine devices, barrier (diaphragm or condom) plus spermicide, NorplantTM or Depo ProveraTM. A negative pregnancy test is required at entry;
14. Use of disallowed concomitant therapy (see section 3.C.3.);

15. Treatment with antidepressants within 28 days prior to screen;
16. History of treatment with clozapine for more than 4 consecutive weeks;
17. Treatment with clozapine within 28 days prior to screen;
18. Participation in an investigational drug trial in the 28 days prior to the screening visit;
19. History of severe drug allergy or hypersensitivity;
20. Known sensitivity to risperidone or olanzapine;
21. Subjects known to be unresponsive to either risperidone or olanzapine in the opinion of the investigator;
22. History of neuroleptic malignant syndrome;

3.B.4. WITHDRAWAL CRITERIA

Subjects may be withdrawn from the trial if:

1. A serious adverse event occurs;
2. The investigator considers it, for safety reasons, in the best interest of the subject that he/she be withdrawn;
3. The subject develops clinical signs of liver disease;
4. The randomization code is broken;
5. Subjects must be withdrawn from the trial if they withdraw their consent.

The date and the reason for discontinuation must be noted on the Case Report Form (CRF). All subjects prematurely discontinuing the trial must be seen for a final evaluation and the Trial Termination Form will be completed.

3.C. Trial plan

3.C.1. FLOW CHART

The flow chart showing trial phases and timing of treatment and assessments is given on the next page.

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	Entry ¹	Treatment period										
Visit ²	1	2	3	4	5	6	7	8	9	10	11	12 ³
Day	1	28	56	84	112	140	168	196	224	252	280	308
Week	0	4	8	12	16	20	24	28	32	36	40	44
Month	0	1	2	3	4	5	6	7	8	9	10	11
Informed consent	X											
Physical examination	X											X ⁵
Vital signs	X	X	X	X				X				X ⁵
ECG	X											X ⁵
Lab	X ⁴	X ³	X ³	X ³				X ³				X ⁴
Prolactin	X							X				X ⁵
Body weight	X	X	X	X				X				X ⁵
Waist/Hip Ratio				X				X				X ⁵
HAMD	X											X ⁵
ESRS	X	X	X	X				X				X ⁵
PANSS	X	X	X	X		X		X				X ⁵
CGI/CGI-C ⁶	X	X	X	X				X				X
Cognitive tests	X			X				X				X
Modified SIP	X			X				X				X
B-QOLI	X			X				X				X
PRAEQ	X			X				X				X
Quality of sleep	X	X	X	X				X				X
Daytime drowsiness	X	X	X	X				X				X
ACS	X	X	X	X				X				X
DAI	X			X				X				X
Concomitant therapy	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X
Dispense medication	X	X	X	X	X	X	X	X	X	X	X	
Return medication		X	X	X	X	X	X	X	X	X	X	X

1. The evaluations from Week 8 of RIS-USA-112 will be used for entry to RIS-USA-113

2. Visits may be conducted within ± 3 days on either side of the scheduled assessment date.

3. Liver transaminases only (AST, ALT and GGT).

4. Includes cholesterol, lipid profile (HDL, LDL, triglycerides), thyroid panel (T₃, T₄ and TSH), HbA1c and CPK.

5. Visit 12 and/or endpoint

6. Both the CGI and the CGI-C will be evaluated at every visit. The CGI-C will be compared to the severity of illness at the randomization visit of the preceding trial (RIS-USA-112)

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3.C.2. TREATMENT**3.C.2.a. Drugs, formulations and strengths**

The trial medication will be provided by the Janssen Research Foundation (JRF). The double blind treatment will consist of capsules which will be identical in appearance, taste and smell, and which will contain risperidone 2 mg or olanzapine 5 mg.

3.C.2.b. Dosages

Administration is done once daily in the morning (around 08.00 h). The subject may receive the entire dose in the evening (around 20.00 h) to improve tolerability. The chosen time of dosing should, if possible, remain constant throughout the trial.

The dosing schedule is given in the following chart:

	No. of Caps/ Day	Dose of Risperidone	Dose of Olanzapine
Days 1-308	1-4	2mg (1 x 2mg) or 4mg (2x2mg) or 6mg (3x2mg) or 6mg (3x2mg) and 1x placebo	5mg (1x5mg) or 10mg (2x5mg) or 15mg (3x5mg) or 20mg (4x5mg)

Medication will be supplied in blistercards that allow flexible dosage.

The dose should be continued from the preceding study, RIS-USA-112. If there is an increase in symptoms, the dose may be increased by one capsule per week. The maximum permitted number of capsules per day remains 4 capsules per day. If the dose is increased to 4 capsules/day, the investigator should document in the patient's chart the clinical basis for the dose increase. Dose decreases to one capsule per day may occur at anytime. The reasons for the decrease in dosage should also be reflected in the subject's chart.

3.C.2.c. Subject Numbers

Subjects who participate in this trial will remain in the same treatment arm they were assigned to in the preceding study (RIS-USA-112). Investigators will contact the central number and provide information to the vendor designated by Janssen on the following :

- 1) The subject's birth date;
- 2) The subject's medication number in RIS-USA-112

The randomization center will ensure that the subjects are randomized to the same treatment arm as in the preceding study.

3.C.3. CONCOMITANT THERAPY

All medications (prescription or over-the-counter medications) continued at the start of the trial or started during the trial and different from the trial medication, must be documented on the Concomitant Therapy Form of the CRF

The following medications are not allowed during the study:

- Antipsychotic medication other than the trial medication;
- Mood stabilizers including lithium and anticonvulsants;

Other concomitant psychotropic medications may be given under the following circumstance:

1. If extrapyramidal symptoms emerge or worsen during the double blind period the investigator should perform an additional ESRS examination. Following completion of the ESRS, the investigator may either initiate anticholinergic medication or reduce the study medication dose. At each subsequent scheduled visit the investigator should determine whether continuation of anticholinergic medication is necessary;
2. During the study, propranolol may be initiated for akathisia, following administration of the ESRS.
3. If the subject experiences agitation during the trial lorazepam may be administered on 4 days in any 7 day period at a maximum dose of 4 mg/day. Lorazepam may not be given for insomnia.

4. No other sedative, anxiolytic or other psychoactive drug may be administered during the trial. If medication for sleep needs to be initiated during the study, it should be flurazepam or chloral hydrate.
5. Antidepressants may be initiated during the study, following the administration of a HAMD.

For any concomitant therapy given as a treatment for a new condition or a worsening of an existing condition, the condition must be documented on the Adverse Event Form of the CRF.

3.C.4. SUPPLY AND BLINDING

The investigator will be provided with a sealed envelope for each subject, containing coded details of the treatment in the double-blind period. This code should be broken only in case of an emergency where the further treatment of the subject is dependent on the trial medication he or she has been receiving. The date and time of the code breaking as well as the reason for it must be documented on the Code Breaking Form in the CRF. In addition, the reason must be documented on the Adverse Event Form of the CRF. The trial monitor should be notified immediately. If the code is broken the subject must be withdrawn from the trial and must be followed up if appropriate.

All envelopes, whether opened or sealed, will be collected at the end of the trial.

3.C.5. DRUG ACCOUNTABILITY

The investigator, his/her designee or a hospital pharmacist must maintain an adequate record of the receipt and distribution of all trial supplies using the Drug Dispensing Form and Drug Return Form. These forms must be available for inspection at any time.

Assessments

3.C.6. EFFICACY

The effect of trial medication will be evaluated as follows:

3.C.6.a. Positive and Negative Symptom Scale (PANSS)

Subjects will be interviewed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point) using the Structured Clinical Interview - Positive and Negative Symptom Scale (SCI-PANSS) (15, 16, 17). The PANSS will provide a total score, a positive symptom scale score, a negative symptom score and a general psychopathology score.

3.C.6.b. Clinical Global Impression (CGI) and Clinical Global Impression of Change (CGI-C)

Subjects will be rated for both overall severity of illness (CGI) and the change in severity (CGI-C) at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). The change in severity will be compared to the subject's condition at randomization (visit 2) of the preceding study (RIS-USA-112)(18).

3.C.6.c. Cognitive Functioning

The following tests will be performed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8 and 12/end-point):

- Wisconsin Card Sorting Test;
- Trails A and B;
- Continuous Performance Test;
- California Verbal Learning Test;
- Visual Working Memory;
- Verbal Fluency Examinations;

3.C.6.d. Visual Analogue Scales for Sleep and drowsiness (VAS)

The subjects will be asked to fill in visual analogue scales (VAS) for quality of sleep and daytime drowsiness at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point).

3.C.6.e. Hamilton Depression Scale (HAMD) 21 item

Subjects will be rated for depressive symptoms using the 21 item Hamilton Depression Scale (HAMD) (19). Assessments will be done at study entry and at week 44 (visit 1 and 12/endpoint).

3.C.6.f. Drug Attitude Inventory (DAI)

The Drug Attitude Inventory (DAI) (20) is a brief, self-administered 10-item scale to assess the subject's satisfaction with antipsychotic drug therapy. The DAI will be completed at study entry and at weeks 12, 28 and 44 (Visits 1, 4, 8 and 12/endpoint).

3.C.6.g. Quality of Life Interview, short version (QoLI-S)

The shortened version of Quality of Life interview (QOLI-S) (21, 22), a validated survey for chronic mental illness, will be performed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8, and 12/endpoint). The QOLI includes objective (e.g., quantity of leisure activities) and subjective (e.g., satisfaction with leisure activities) scales for the following areas: living situation, family relations, social relations, leisure, work, finances, safety, health, and religion.

3.C.6.h. Modified Sickness Impact Profile (M-SIP)

The Modified Sickness Impact Profile (M-SIP) (23, 24) will be assessed at study entry and at weeks 12, 28, and 44 (visits 1, 4, 8, and 12/endpoint). The M-SIP measures overall function within the following six areas: social interaction, alertness behavior, communication, sleep and rest, home management, and recreation and pastimes.

3.C.7. SAFETY

3.C.7.a. Adverse events

See Adverse events (Part II - §)

3.C.7.b. Extrapyramidal Symptom Rating Scale (ESRS)

The Extrapyramidal Symptom Rating Scale (ESRS) (28) will be performed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). It will also be performed before the institution of anticholinergic medication or propranolol for emergent EPS.

3.C.7.c. Body weight and Body Mass Index (BMI)

Body weight will be measured at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point). The same standard scale should be used throughout the trial. Patients should be lightly clothed, wear similar clothing at each visit, and be weighed without shoes. Body Mass Index (BMI) will be calculated as weight in kilograms over height in meters² (kg/m²).

3.C.7.d. Waist/Hip Ratio

Waist/hip ratio: the circumference of the waist and hips will be measured using a standard tape measure. Waist/hip ratio is an indirect measure of intra-abdominal fat. This measurement will be taken at weeks 12, 28 and 44 (visits 4, 8 and 12/endpoint).

3.C.7.e. Anticholinergic Symptoms (ACS)

An anticholinergic symptom survey, developed specifically for this study, will be assessed at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/endpoint). The survey questions patients to report on manifestations of the following: dry mouth, blurred vision, constipation, and urinary retention. A positive response will be followed by a query as to how bothersome the symptom is on a 4 point scale.

3.C.7.f. Prolactin Related Adverse Event Questionnaire (PRAEQ)

A short questionnaire documenting the presence of menstrual disturbance, galactorrhea, erectile dysfunction, ejaculatory dysfunction and gynecomastia. It will be administered at study entry and at weeks 28 and 44 (visits 1, 8 and 12/endpoint). A positive response will be followed by a query as to how bothersome the symptom is on a 4 point scale.

3.C.7.g. Clinical laboratory tests

Blood and urine samples will be analyzed by a central laboratory. Samples will be collected and the sample tubes labeled following the method described in the Users Manual provided by the central laboratory.

The lab report must be reviewed by the investigator and any clinically relevant changes occurring during the trial must be recorded on the AE Form of the CRF.

Blood samples for biochemistry and hematology and random urine samples for urinalysis will be taken at study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/endpoint).

Liver transaminases only will be determined at weeks 4, 8, 12 and 28 (visits 2, 3, 4, and 8). Full CBCs, U/A's and chemistry panels will be performed at study entry and at week 44 (visits 1 and 12/endpoint).

Subjects with serum transaminase levels (AST, ALT, GGT) > 3X the upper limit of normal, either upon study entry or during the study, should have the transaminases performed weekly until:

- 1) the levels fall below 3X ULN,
- 2) the subject completes the study and is clinically asymptomatic,
- 3) the subject develops clinical signs of liver disease, in which case the subject must be discontinued from the study.

If, in the opinion of the investigator, the subject's liver transaminases stabilize at a level >3X ULN and the subject does not have signs of liver disease, the transaminases may be followed every 2 weeks.

The following analyses will be done and reported:

3.C.7.g.1. Hematology

Hemoglobin, Hemoglobin A1C, hematocrit, RBC, WBC, white differential blood cell count (neutrophils, lymphocytes, monocytes, eosinophils, basophils), platelet count. These evaluations will be done at study entry and week 44 only (visits 1 and 12/endpoint).

3.C.7.g.2. Biochemistry

Total protein, alkaline phosphatase, AST, ALT, gamma GT, LDH, cholesterol, lipid profile (HDL, LDL, triglycerides), thyroid panel (T3, T4, TSH), total bilirubin, urea, uric acid, creatinine, sodium, potassium, chloride, calcium, CPK and prolactin. Prolactin levels will be done at study entry and at weeks 28 and 44 only (visits 8 and 12/endpoint). The full panel will be done at study entry and week 44 only (visits 1 and 12/end point). Transaminase levels will be done at weeks 4, 8, 12 and 28 (visits 2, 3, 4, and 8).

The entry and endpoint labs should be performed following a 12-hour fast, with the time since last food consumption recorded.

3.C.7.g.3. Urinalysis

Urinalysis for protein, glucose, occult blood will be performed by dipstick at screen, randomization (if necessary) and at endpoint. If results are abnormal, microscopic examination for WBC, RBC, and casts will be performed.

3.C.7.h. Vital signs and physical examination

At study entry and at weeks 4, 8, 12, 28, and 44 (visits 1-4, 8 and 12/end-point), systolic and diastolic blood pressure must be measured both in the supine (after 5 minutes rest) and standing positions. Supine blood pressure should be measured twice with the average rounded to the nearest integer and entered in the CRF. Pulse must also be recorded.

Physical exams will be done at study entry and at week 44 (visits 1 and 12/endpoint). All abnormalities should be recorded in the CRF. Changes for the worse which are judged clinically significant by the investigator should also be recorded as adverse events.

3.C.7.i. Electrocardiogram (ECG)

An electrocardiogram (ECG) must be recorded at study entry and at week 44 (visits 1, and 12/endpoint). The investigator must indicate in the CRF whether the ECG is within normal limits.

3.D. Statistics

3.D.1. SAMPLE SIZE CALCULATION

Sample size determinations were made based on the expected rates of increased body weight. The Zyprexa package insert specifies that 56% of patients met the criterion for having gained greater than 7% of their baseline weight during long-term continuation therapy. A weight gain rate of 32% is assumed for patients on long-term Risperdal therapy (based on an integrated database of long-term Risperdal trials). Using an overall two-tailed

alpha level of 0.05 with 80% power and assuming the true rates of 32% vs. 56% for the risperidone and olanzapine groups, 75 patients per group will be required. To also adjust for drop-outs (60%), the total number of patients will be increased to 376 (188 per group). This 60% drop-out rate includes patients who do not continue from RIS-USA-112 into this long-term extension trial.

3.D.2. STATISTICAL ANALYSIS

The statistical analysis will be performed by the Janssen Research Foundation. Statistical tests will be performed at the 5% two-tailed significance level (unless specified differently). In case of non-normality or heteroscedasticity appropriate transformations (e.g.: logarithm) will be applied. Alternatively, parametric tests will be replaced by non-parametric tests (e.g. Mann-Whitney-U, Van Elteren test).

3.D.2.a. Safety

All patients who had at least one dose of study medication in RIS-USA-113 will be included in the safety analysis. Baseline values will be defined as the baseline value from RIS-USA-112 unless specified differently.

The primary parameter is the percent of patients who gain at least 7% of their baseline weight at any time during treatment. The Cochran-Mantel-Haenszel test, stratifying for investigator will be used to test for treatment differences in these rates. The spontaneous adverse event rates (newly emergent or a worsening from baseline) of extrapyramidal symptoms will also be calculated. The following WHO preferred terms will be considered extrapyramidal symptoms: tremor, dystonia, hypokinesia, hypertonia, hyperkinesia, oculogyric crisis, ataxia, abnormal gait, involuntary muscle contractions, hyporeflexia, akathisia, and extrapyramidal disorders. A patient who reports at least one of these events at any time during the trial will be considered to have experienced extrapyramidal symptoms. The Cochran-Mantel-Haenszel test, stratifying for investigator and baseline ESRS strata will be used to test for treatment differences in these rates. Additionally, adverse event rates will be calculated for patients who were experiencing extrapyramidal symptoms at the time of their discontinuation or completion of the trial and separately for those patients who completed the trial at 44 weeks. The incidence of new diabetes and hypertension onset will be calculated. New onset of diabetes will be defined as HbA1c increasing from <7% to ≥7%. New onset of hypertension will be defined as either institution of antihypertensive medication or new onset of diastolic blood pressure of ≥95 Hg on two consecutive visits. The primary analysis will include information on all patients randomized into RIS-USA-112 i.e., rates will be calculated for the entire 52 weeks of exposure. A secondary analysis will include information only from those patients who continued into RIS-USA-113.

The Extrapyramidal Symptom Rating Scale (ESRS) total and subtotals (total Parkinsonism, Dystonia, Dyskinesia, Questionnaire, CGI of severity of parkinsonism, CGI of severity of dystonia, CGI of severity of dyskinesia) will be calculated. The change versus baseline to each visit, endpoint, and to the maximum during double-blind treatment will be

compared between treatments by means of an analysis of covariance model with treatment, investigator, baseline ESRS score, and the treatment-by-covariate interaction terms included in the model. If the interaction terms are not significant at the 0.1 level, the treatment effects will be tested by means of the reduced model (without the interaction terms). The number of patients taking anti-parkinsonism medication will be compared by means of the Cochran-Mantel-Haenszel test for general association, controlling for investigator and baseline ESRS strata.

Vital Signs (blood pressure, heart rate), body weight, BMI, and waist/hip ratio will be tabulated and analyzed descriptively. Inter-group changes will be performed by means of an ANOVA model with factors of treatment, investigator and baseline BMI strata (for body weight, BMI, waist/hip ratios only).

Additionally, an ANCOVA model with factors of treatment, investigator, and baseline value will be used to compare treatment group differences in the mean change from baseline for the anti-cholinergic symptom assessment (ACS), the modified sickness impact profile (M-SIP), and the prolactin-related adverse event questionnaire (PRAEQ).

Within group comparisons will be performed using the paired t-test or the Wilcoxon sign rank test.

3.D.2.a.1. Adverse events

Incidences of all AEs will be tabulated as the number of patients who experienced at least one episode expressed as a percentage of the total number of subjects entered in the trial per treatment group. The combined adverse event rate of extrapyramidal symptoms will also be calculated as described in 3.D.2.a.

3.D.2.a.2. Clinical laboratory tests

For the clinical laboratory data, descriptive statistics and pre versus post treatment cross-tabulations (with classes for below, within and above normal range) will be generated for all tests performed. Important abnormalities, as determined by the occurrence of pathological values, will be tabulated. Pathological values are values that are outside the pathological limits. For most hematological and biochemical tests, pathological limits are defined by Lippert and Lehmann (SI Units in medicine. Baltimore-Munich: Urban & Schwarzenberg, 1978). For enzymes, the lower pathological limit is defined as zero, and the upper pathological limit as twice the upper normal limit. For leukocyte differential count, no pathological limits are defined. If a value is outside the pathological limits but not outside the normal limits for the particular laboratory, it is not considered pathological. The type of important abnormality depends on the time of occurrence of the pathological value, i.e.,

before (reference value of the parameter), during or after treatment (e.g., non-pathological before, pathological during treatment).

3.D.2.b. Analysis of efficacy parameters

The main analysis will be an intent to treat analysis containing all patients who were treated and have at least one post-baseline assessment. Additionally an on-protocol analysis may be performed. The primary timepoint is endpoint. The primary analysis will use the baseline from the RIS-USA-112 trial at the time of randomization. A secondary analysis will also be performed using the baseline from the RIS-USA-113 study (endpoint from the RIS-USA-112).

For each of the continuous efficacy parameters with a baseline response (PANSS, HAM-D, CGI, cognitive tests, quality of sleep and daytime drowsiness, QOLI-S, and the DAI), the change from baseline score at each visit and at endpoint will be analyzed using analysis of covariance methods. The model will include treatment, investigator, baseline value, and the treatment-by covariate interaction terms. If the interaction terms are not significant at the 0.1 level, the treatment effects will be tested by means of the reduced model (without the interaction terms). The number of patients experiencing clinical improvement, i.e. with a percentage decrease in total PANSS of at least 20% versus baseline will be calculated. Comparisons will be performed by means of the Cochran-Mantel-Haenszel test for general association, controlling for the baseline PANSS strata.

The time to relapse controlling for investigator will also be calculated using standard survival analysis methods including product-limit estimators, logrank tests, and proportional hazard regression models. Categorical data such as one-year relapse rates will be analyzed using the Cochran-Mantel-Haenszel test, controlling for investigator. Relapse will be defined as psychiatric hospitalization for a subject living in the community.

In addition, methods for repeated measures will be used. These methods compare treatment groups over time rather than at each visit. The baseline values may be used as covariates in these analyses to adjust for baseline differences between treatment groups.

3.D.2.c. Subgroup Analyses

A subgroup analysis will be performed based on the average daily dose of study medication received. Patients who received an average dose of less than 4 mg of risperidone will be analyzed separately from those who received greater than or equal to 4 mg. Likewise, patients who received less than 12.5 mg of olanzapine will be analyzed separately from those who received greater than or equal to 12.5 mg.

Also, if the size of the study permits, other relevant demographic or baseline value-defined subgroups will be examined for unusually large or small responses, e.g., comparison of effects by age, sex, and race.

3.D.3. ADMINISTRATIVE INTERIM ANALYSIS

One administrative interim analysis may be performed with a spending function of 0.001. The analysis will be performed only on the basis of blinded groupings (Group A, B, ...). The overall results will be made available to Janssen Research Foundation management at the level of Head, Clinical Research/Medical Development and above. The results of an administrative interim analysis will be documented in the clinical research report. Included in the documentation will be the names of Janssen management who viewed the results. If any of the Janssen reviewers also had access to the true treatment code, that will also be documented.

The results will not be disseminated to those involved in the day-to-day management of the trial. As a result of the administrative interim analysis, the trial will not be terminated early to claim superiority of one treatment group, the study protocol will not be altered due to the interim results, nor will any exploratory or subpopulations analyses be performed.

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5. ADDENDA

ADDENDUM I: SUBJECT INFORMATION LETTER AND INFORMED CONSENT FORM

Introduction and purpose of the trial

You are being asked to participate as one of approximately 376 patients in a medical research trial with two drugs called risperidone and olanzapine. This study is being conducted in up 40 centers.

Risperidone is a drug which is effective in the treatment of your disorder. It has been registered in more than 30 countries, has been administered to more than 800 000 patients world-wide and is well tolerated.

Olanzapine is a new drug for the treatment of your disorder. It has recently been registered in several countries, including the USA, England and several other European countries. It has been administered to approximately 3 000 subjects participating in medical research trials.

The safety and efficacy of risperidone and olanzapine in the treatment of your disorder will be studied.

Treatment

You will receive either risperidone or olanzapine. The starting doses will be 2 mg of risperidone and 10 mg of olanzapine. This dose may be increased up to a maximum of 8 mg of risperidone and 20 mg of olanzapine. Your doctor will evaluate your response to treatment and adjust the dose accordingly.

Procedures during the trial

The trial lasts 44 weeks (11 months). If you agree to take part, it is important that you will go to your doctor's office for 12 scheduled visits. These visits will occur once every 4 weeks. These visits may be two hours long. The evaluations from your last visit of the study you just completed will be used at the first visit of this study. During the rest of these visits specific assessments to evaluate the efficacy and safety of the treatment will be performed. At the start and end of treatment you will undergo a full medical examination. ECG (Electrocardiogram) will be done before start of treatment. This examination studies exactly how your heart is functioning. Blood and urine samples for routine laboratory tests will be taken up to 6 times during the trial. the amount of blood taken each time will be approximately 10ml (2 tablespoons).

Please remember to bring with you all unused medication as well as all empty medication containers to each visit.

If your symptoms worsen at any time between visits or you experience any unwanted effects, you should contact your doctor as soon as possible.

For this trial to be successful, it is important that you fully co-operate with the doctor and follow his/her instructions precisely. You should not take any other medication, either on prescription or from the pharmacy or supermarket unless it has been approved by the doctor.

Pregnancy

If you are a female of childbearing potential (have not had a tubal ligation or hysterectomy), you must not be pregnant or a nursing mother during this trial. If you are sexually active, you will be required to take precautions to avoid the possibility of becoming pregnant. Abstinence, the use of oral contraceptives, intrauterine devices, barrier method (diaphragm or condom) plus spermicide, Norplant™ or Depo Provera™ are acceptable methods of birth control. You must notify your doctor immediately if you do become pregnant during the trial and he/she will then evaluate your condition and decide whether you should discontinue the study drug or not. As with all other medications, there is always a risk to the subject, embryo or fetus.

Early termination

Participation in this trial is voluntary. Your refusal to participate or decision to withdraw at any time during the trial will not involve any penalty or loss of benefits to which you are otherwise entitled. The doctor may decide that it is in your best interest to stop or Janssen Research Foundation, the sponsor of this trial, may also stop your participation. You may be enrolled in this trial prior to you doctor receiving the results of your first tests. If the results of any of these tests show that you fulfill one or more of the exclusion criteria, you will become ineligible and will be withdrawn from the trial. If you discontinue the trial early, you will be asked to return all your trial medication, and have the end-point evaluations done.

Benefits and risks

Possible benefits of participating in this trial may include improvement of your condition and relief of symptoms. Also, your condition may be monitored more closely than usual. In addition, new information may be learned that would be helpful in developing new therapies for other subjects with similar illnesses. It is possible, however, that no therapeutic or other direct benefits may result during or following completion of this trial.

All therapies have the potential to cause some side effects or other reactions. The side effects reported on risperidone and olanzapine are to some extent similar, although they may differ in degree and frequency. The following reactions may occur: drowsiness, tiredness, sleeplessness, agitation, anxiety, headache, concentration difficulties, blurred vision, dizziness, indigestion, nausea, vomiting, abdominal pain, difficult stools, sexual potency disorders, some loss of urine, blocked nose, skin rash. In some cases, the blood pressure may fall slightly in the early stages of treatment, resulting in dizziness, but this will usually pass off automatically. You may put on a bit of weight during the treatment and minor motor disorders may occur such as trembling, slight muscle stiffness and

restlessness in the legs. The latter symptoms are usually not dangerous and will disappear after the doctor has reduced the dose or administered an additional drug. On olanzapine treatment transient, asymptomatic elevations of liver enzymes have been reported, especially in early treatment.

Although rare and harmless, swelling of the ankles may occur. Hypersensitivity to risperidone or olanzapine are rare. It can be recognized by for instance, skin rash, itching, shortness of breath or swollen face. Please contact your doctor if any of these occur. Very rarely, a state of confusion, reduced consciousness, high fever or pronounced muscle stiffness might occur. If this should happen, please notify your doctor. In extremely rare cases, generally as a result of several factors together including extreme heat or cold, marked changes in body temperature occur. You must notify the doctor if this happens. The treatment in this trial is relatively short, but during long-term treatment twitching of the tongue, face and mouth or jaws may occur. Please inform the doctor if this happens. After prolonged use, women may suffer from lactation and menstruation disturbances, while in some cases men may develop breasts to a very slight degree. There may be some side effects which are not yet known.

The risks observed for drawing blood are minor. Some local pain, bruising, swelling, soreness and discoloration has been observed.

You will be informed of any new findings that may develop during the trial as this may relate to your willingness to continue to participate in the trial. You will be asked to report any possible side effects to the doctor at any time during the trial. Any severe or unusual reactions or research-related injuries should be reported as soon as possible to

.....(investigator's name) at (phone).

Alternative treatments

There are other medications currently available on the market for treating your condition. Your doctor will discuss these and other alternatives with you in the event that you choose to be treated with them rather than participate in this research trial.

Confidentiality

All records and documents pertaining to your participation in this trial will be held strictly confidential and your name will not be reported in any publications resulting from this trial. All records and documents will be reviewed by the sponsor (the Janssen Research Foundation) or representatives from the sponsor and may be reviewed by the Food and Drug Administration (FDA), and/or registration authorities in the European Community countries.

Before signing this consent form, you are free to ask your doctor about any aspect of this trial that are not clear to you. You will be given a copy of this consent form.

Compensation

There will be no costs involved for you for participation in this trial. All costs for the required visits, examinations, laboratory procedures and supply of medication are provided by the Janssen Research Foundation, Inc. In the event an illness or injury is directly attributable to the use of the research drug, the cost of emergency care will be provided by Janssen Research Foundation, Inc.. Financial compensation for such things as disability or discomfort due to injury, transportation costs, etc., is not available. Any medical expenses due to self-inflicted injury are your responsibility.

Subject's statement

I (print name) have fully reviewed and understand the contents and nature of the above text describing this trial. I have had the opportunity to have all my questions answered about this trial and understand that there are alternative treatments available. I understand that side-effects, complications and injury may occur as a result of this trial and I have been assured that appropriate medical care will be available. In the event an illness or injury is directly attributable to the use of the research drug, the costs of emergency care will be provided by Janssen Research Foundation. I understand that I will be free to withdraw from the trial at any time without having to give any reason for withdrawal. I know my decision will not affect my future medical care. I give my permission to have the sponsor, or their representatives, and the FDA and/or registration authorities of the European Countries review my medical records in connection with this trial. I will be given a copy of this form to take with me. My signature below indicates that I have voluntarily agreed to participate in this trial and hereby give my consent:

..... /...../.....
Subject's Name - Printed Date

..... /...../.....
Subject's / Legal Guardian's Signature Date

..... /...../.....
Investigator's Signature Date

..... /...../.....
Investigator's Name - Printed Date

..... /...../.....
Witness' Signature Date

PART II: PROCEDURES

6. ADVERSE EVENTS

6.A. Definitions

6.A.1. ADVERSE EVENT (AE)

Any undesirable experience occurring to a subject, during a clinical trial, whether or not considered related to the investigational product(s) should be considered as an adverse event.

6.A.2. SERIOUS ADVERSE EVENT

A serious adverse event is an adverse event that is fatal; life-threatening; significantly, persistently or permanently disabling; requiring intervention to prevent permanent impairment or damage; requiring in-patient hospitalization or prolongation of hospitalization. In addition, congenital anomaly, occurrence of malignancy or clinical injuries resulting from overdose are always considered a serious adverse event.

If there is any doubt by the investigator or clinical trial monitor about whether an event meets the definition of a serious adverse event as stated above, the event must be reported as a serious adverse event.

6.A.3. UNEXPECTED ADVERSE EVENT

An unexpected adverse event is an event not previously reported (in nature, severity or incidence), i.e. not included in the current Investigator's Brochure or in the International Product Information Document, or local package insert.

6.A.4. LIFE-THREATENING

Life-threatening means that the patient was, in view of the investigator, at immediate risk of death from the reaction as it occurred (i.e. it does not include a reaction that, had it occurred in a more serious form, might have caused death).

6.A.5. ASSOCIATED WITH THE USE OF THE DRUG

An adverse event is considered associated with the use of the drug when the causality assessment is certain or probable/likely.

6.B. Reporting of adverse events

All adverse events occurring during clinical trials have to be reported on the Adverse Event Form of the CRF from the D of the first visit recorded in the CRF till the D of the last visit of the subject in the trial. The investigator must provide information on symptoms, time of onset and subsidence, severity, drug-relatedness, action taken with reference to the trial drug and subject outcome.

Clinically relevant changes in laboratory parameters, ECG, vital signs and body weight as well as intercurrent illnesses are considered adverse events and should be recorded on the Adverse Event Form of the CRF.

All serious adverse events must be reported by the investigator within 1 working D of his or her becoming aware of them to one of the Janssen Research Foundation (JRF) contact persons mentioned below. Serious adverse events occurring after the trial but within a period of 30 Ds after the last intake and spontaneously reported by the investigator will be handled by JRF as serious adverse events occurring during clinical trials.

Trial monitor:

NAME/ADDRESS/PHONE/FAX

Local Trial Coordinator:

NAME/ADDRESS/PHONE/FAX

The first report of a serious adverse event may be made by telephone or facsimile (FAX).

This report of a serious adverse event by telephone must always be confirmed by a written, more detailed report. For this purpose, the JRF contact person will provide the investigator with a Serious Adverse Event and Pregnancy Reporting Form for Clinical Trials, to be completed and signed by the latter.

Pregnancies occurring during a clinical trial must be reported as soon as possible using the same Serious Adverse Event and Pregnancy Reporting Form for Clinical Trials. The outcome of the pregnancy must also be reported to the JRF.

The JRF will assume responsibility for appropriate reporting of adverse events to the authorities. The JRF will also report all serious adverse events that are unexpected and associated with the use of the drug to the investigators. It is the investigator's responsibility to report the adverse events which are classified by the JRF as serious, unexpected and associated with the use of the drug to the Ethics