SYNOPSIS

NAME OF SPONSOR/COMPANY: Janssen L.P.	INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER	(FOR NATIONAL AUTHORITY USE ONLY)
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Protocol No.: RIS-DEP-401

Title of Study: A double-blind, randomized, prospective trial to evaluate the efficacy and safety of adjunctive risperidone versus placebo in subjects with Major Depressive Disorder with suboptimal response to standard antidepressant therapy

Principal Investigator: H. Mikel Thomas, M.D. - [Contact]

Publication (Reference): Anand R, Gharabawi G, Greist J, Rapaport M, Sheehan D. Approach for assessing patients with Generalized Anxiety Disorder or Major Depression and Residual Symptoms. Presented at the American Psychiatric Association 159th Annual Meeting; May 20-25, 2006; Toronto, Canada. Gharabawi G, Canuso C, Pandina G, et al. A double-blind placebo-controlled study of risperidone augmentation for Major Depressive Disorder suboptimally responsive to antidepressant treatment. Presented at the Collegium Internationale Neuro-Psychopharmacologicum 25th Biennial Congress; July 9-13, 2006; Chicago, Illinois.

Study Initiation/Completion Dates: Study initiated on 19 October, 2004, study completed on 17 November, 2005

Phase of development: 3B

Objectives: The primary objective was to demonstrate the efficacy of adjunctive risperidone therapy added to standard antidepressant (SAD) pharmacotherapy over placebo in subjects with sub-optimally responding Major Depressive Disorder (MDD), as measured by the HAM-D. The secondary objectives were to evaluate the safety of adjunctive risperidone to SADs in subjects with suboptimal response to SADs; to evaluate the efficacy of adjunctive risperidone to SADs on symptoms of depression that are most troubling to subjects, as measured by the MTS; to evaluate subject functioning and quality of life, as assessed by the PGIS, CGI-S, SDS, and Q-LES-Q-SF.

Methodology: This was a six-week, double-blind, randomized, prospective, placebo-controlled, multi-site trial, of adjunctive risperidone with an open-label run-in of SAD therapy (i.e., SSRI, SRNI, or bupropion). Leading into this trial, subjects received SAD for at least four weeks at optimal dose. Those subjects who continued to demonstrate suboptimal response to the trial were randomized in a double-blind fashion, to receive either risperidone or placebo adjunctive to ongoing treatment with the SAD for 6 weeks. They were judged to exhibit a sub-optimal response to this therapy at double-blind baseline, as reflected by a CDS score of 20 or greater and CGI-S score of 4 or greater, and continued on this dose of SAD throughout adjunctive risperidone treatment. All subjects completing at least four weeks of double-blind treatment were offered four weeks of open-label adjunctive risperidone therapy with their SADs given at an optimal dose. It evaluated the efficacy and safety of up to and including 2 mg/day adjunctive risperidone versus adjunctive placebo in subjects undergoing standard treatment with antidepressant medication for MDD.

Number of Subjects (planned and analyzed): Approximately 332 subjects were planned to be randomized to either risperidone (n=166) or placebo (n=166) to a SAD. The total number of subjects randomized is 274; 141 subjects were assigned to risperidone treatment and 133 subjects were randomized to receive placebo.

Diagnosis and Main Criteria for Inclusion: *Open-label SAD Phase:* (i) subject had a diagnosis of MDD, single or recurrent episodes, as confirmed by appropriate completion of the Mini International Neuropsychiatric Interview criteria for Major Depressive Episode; (ii) subject was judged to be healthy based on physical examination and vital signs at baseline; (iii) subject was being treated with a single SAD therapy for a minimum of four weeks immediately prior to OL-SAD-BL; (iv) subject was judged by the clinician to have shown a suboptimal response to his/her current treatment, as reflected by a CGI-S score of 4 or greater.

Double-blind Adjunctive Treatment Phase: (i) subject continued to have a diagnosis of MDD, single or recurrent episodes; (ii) subject was compliant with medication; (iii) subject demonstrated significant depressive symptoms during the open-label SAD phase, as reflected by a CDS score of 20 or greater at the end of the open-label SAD phase; (iv) subject continued to demonstrate depressive symptoms, as reflected by a CGI-S score of 4 or greater at DB-BL.

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Test Product, Dose and Mode of Administration, Batch No.:

Risperidone 0.25 mg tablets p.o. qd: Batch No. – 03D18/F070, 04H24/F070

Risperidone 0.5 mg tablets p.o. qd: Batch No. – 03D25/F009, 04H27/F009

Risperidone 1 mg tablets p.o. qd: Batch No. – 03D28/F005, 04I01/F005

Risperidone 2 mg tablets p.o. qd: Batch No. – 03D29/F013

Reference Therapy, Dose and Mode of Administration, Batch No.:

Placebo tablets p.o. qd: Batch No. – 03D23/F007, 04J01/F007

Duration of Treatment: 4 weeks of open-label treatment with a SAD; 6 weeks (4 weeks minimal) of double-blind treatment with risperidone or placebo; optional 4 weeks of open-label treatment with risperidone

Criteria for Evaluation:

Efficacy: the primary efficacy parameter was the HAM-D, based on the change between double-blind baseline and double-blind Week 4 in the total score. The secondary efficacy rating scales used in this study were the MTS, CGI-S, PGIS, SDS, Q-LES-Q SF.

Safety: the safety assessments used in this study included monitoring and recording of all treatment-emergent adverse events and serious adverse events; performance of physical examination; and monitoring of vital signs, fasting blood glucose testing, and urine pregnancy test.

Statistical Methods: The primary efficacy measure was the change from baseline in the HAM-D total score at Week 4 (LOCF at Week 4) in the ITT population, using the ANCOVA model, which included treatment, stratum, (possibly pooled) site as factors, and baseline HAM-D total score as a covariate, and possibly the interaction terms of treatment with each of the other factors and covariates. The secondary analyses included the change from Day DB-1 in HAM-D score at each visit and at each endpoint using the ANCOVA model. Change from baseline and actual values, including pertinent subscales and items, were summarized descriptively with 95% confidence intervals being provided at each visit and at endpoint. Within-group differences were evaluated using one-sample t-tests. Categorical variables were evaluated with the CMH mean score statistic using modified ridit scores, stratified by stratum and (possibly pooled) site. Change from baseline and actual values for the PGIS, CGI-S, SDS, and Q-LES-Q SF, including pertinent subscales and items, were summarized descriptively with 95% confidence intervals being provided at each visit and at endpoints. Within-group differences were evaluated using one-sample t-tests, and between-group differences were analyzed using ANCOVA or ANOVA, as appropriate. Categorical variables were evaluated with the CMH mean score statistic using modified ridit scores, stratified by stratum and (possibly pooled) site. Change and percent change from baseline and actual values for the MTS total score and the score for each symptom were summarized descriptively with 95% confidence intervals being provided at each visit and at endpoint. Within-group differences were evaluated using one-sample t-tests, and between-group comparisons were analyzed using ANCOVA. Repeated measures analysis of variance models were used for the observed MTS total score. A transition table was provided to show the number and percent of subjects who identified the same MTS symptoms or different MTS symptoms among the four most severe at DB Week 4 as compared to baseline, and at DB Week 6 as compared to baseline and DB Week 4. The frequency counts of MTS scores for each symptom were also provided by treatment at each assessment. Correlations among the HAM-D, PGIS, CGI-S, SDS, Q-LES-Q-SF, and the MTS total score were assessed by calculating parametric and nonparametric measures of association. The proportion of subjects with a dose increase in SAD was compared between the treatment groups. Select secondary parameters were summarized by the type of SAD (SSRI vs. Non-SSRI). The statistical models were repeated without controlling for the SAD category.

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SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

Primary Efficacy:

There was no difference between treatment groups in baseline values for the HAM-D Total Score (risperidone: 24.2; placebo: 24.6). During the double-blind treatment period, the HAM-D Total Score decreased over time in both treatment groups (Week 4 - LOCF: risperidone: -8.5; placebo: -7.1; Week 6 - LOCF: risperidone: -10.0; placebo: -7.9); however, the mean reduction in score at Week 4 (LOCF - the primary efficacy endpoint) and at Week 6 (LOCF) in the risperidone-treated subjects was significantly ($p<0.05$) greater than in the placebo group. Statistically significant reductions in the risperidone-treated subjects were also noted at Weeks 1, 4 and 6 in the OC analysis. Statistically significant reductions in the risperidone-treated subjects were noted for scores on the anxiety/somatization, retardation, sleep disturbance and Maier-Philip severity subscales. Some of these significant differences were noted as early as Weeks 1 or 2; all were significant at Week 6 (OC and LOCF).

Secondary Efficacy:

Open-label Standard Antidepressant Phase

During the open-label period, the HAM-D total scores showed a minimal decline of 1.4 points from its baseline value of 23.9, indicating a slight improvement in the total population. Within the entire population, the subjects who responded to their standard antidepressant (SAD) medication (“responders”) improved by 6.4 points on average; however, less than 20% of all subjects were considered “responders.” Scores on the anxiety/somatization, retardation, sleep disturbance and Maier-Philip severity subscales of the HAM-D also improved in this responder population.

Double-blind Treatment Phase

Analyses of the individual items of the HAM-D scale indicated that all items improved significantly from baseline in both groups. Improvements were significantly greater in the risperidone group than in the placebo group for at least one time point, except for suicidal ideation, insomnia late, psychomotor retardation, loss of appetite, sexual interest and insight; statistically significantly differences between groups in favor of risperidone were noted most frequently at the Week 6 evaluation.

Analyses stratified by the type of SAD used (dichotomized into SSRI and non-SSRI) indicated that risperidone was associated with an average 1.5-point greater improvement over placebo in the non-SSRI sub-group at endpoint, while the mean difference from placebo was 2.5 points in the SSRI-treated subjects. Interestingly, while the difference between treatment groups in the SSRI sub-group was statistically significant ($p=0.004$), the difference in the non-SSRI sub-group was not ($p=0.283$). However, this may be due to the smaller sample size of the non-SSRI sub-group ($n=103$), compared with the SSRI sub-group ($n=155$).

Only the anxiety/somatization and retardation subscale scores were significantly better for risperidone, compared to placebo, in the non-SSRI sub-group, while these two subscales, as well as scores for sleep disturbance and Maier-Phillip severity, were significantly better for risperidone-treated subjects in the SSRI sub-group.

A repeated measures ANOVA indicated that the baseline severity (score) significantly ($p<0.001$) affected outcome on the HAM-D. The reduction in score in both treatment groups indicated a significant effect of time ($p<0.001$). In addition, a statistically significant treatment effect ($p=0.001$), and treatment by time interaction ($p=0.048$) were noted, with the maximum improvement in the risperidone group, compared to the placebo group, being noted at Week 6 ($p<0.001$).

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Secondary Efficacy (continued):

Subjects were classified as "responders" if their total score on the HAM-D was reduced by 50% or more at endpoint, compared to the double-blind baseline value. A statistically significant (p=0.017) difference in the proportion of subjects classified as "responders" was noted for risperidone (40.9%), compared to placebo (28.6%), at endpoint. This difference in responder rates was significant from Week 4 onwards. Similarly, the proportion of subjects meeting the "remitter" definition (HAM-D score ≤7), was significantly (p=0.016) higher in the risperidone group (19.7%), compared to the placebo group (9.5%), at endpoint. This difference in the proportion of "remitters" in the risperidone group, compared to the placebo group, was noted from Week 4 onwards. Analyses of responder and remitter rates by type of SAD indicated that there was no additional benefit of risperidone in the non-SSRI population; in contrast, the proportion of subjects receiving SSRIs who were rated as "responders" was significantly higher in the risperidone group (45.7%), compared with the placebo group (24.3%). An even greater difference between groups was observed for "remitters" (22.2% vs. 4.1%).

During the OL-FU period, an additional 4 weeks of treatment with risperidone was associated with an additional improvement of 3.7 points on the HAM-D total score in the risperidone group. In subjects who received placebo during the double-blind period, open-label treatment with risperidone for 4 weeks resulted in a 5.9-point improvement from the double-blind endpoint.

Results of the analysis of the CGI-S broadly supported the results for the HAM-D scale. The CGI-S scores were reduced by 1.3 points in the risperidone group and 0.9 points in the placebo group from the double-blind baseline to endpoint, a difference that was statistically significant (p=0.002). The difference between groups was significant from Week 4 onwards. At Weeks 4 and 6, the distribution of subjects by severity scores, was also significantly different in the two groups, i.e., a significantly higher proportion of subjects in the risperidone group had lower severity ratings, compared with placebo-treated subjects.

Analyses of the Most Troubling Symptoms (MTS) identified as the 4 most severe by the subjects indicated that, for all 8 symptoms, the proportion of subjects who reported each symptom among the most severe at the double-blind baseline was approximately similar in each group. Although the severity of the MTS Total Score, based on the 4 most severe symptoms, improved over time, the reduction in the risperidone group was significantly (p<0.001) better than in the placebo group at endpoint. This difference between groups in MTS Total Score was also significant at Week 1. Analysis of the MTS Total Global Score, which includes scores on all 8 symptoms, indicated significant (p=0.004) improvement in favor of risperidone at endpoint. These analyses were supported by the findings that the mean change in Percent from the Maximum Score, Three Most Troubling Symptoms and Two Most Troubling Symptoms for the MTS at endpoint was significantly (p<0.001) better in risperidone-treated subjects, than in those receiving placebo.

Analysis of the 8 individual symptoms of the MTS indicated significant differences at Week 6 (OC and LOCF) in favor of risperidone for sadness, tense or uptight, reduced sleep, trouble concentrating, reduced involvement and negative thoughts.

Analyses performed on the ratings of severity of the subject's Chief Complaint indicated that there was a statistically significantly greater reduction in the risperidone-treated subjects, compared to those receiving placebo, at endpoint (2.3 vs. 1.6; p=0.003). The proportion of subjects whose Chief Complaint was rated 'absent' or 'mild' was higher at baseline and throughout the double-blind period in the risperidone group, than in the placebo group, with the percentages being 33.3% and 20.0%, respectively, at endpoint. Statistically significant differences between groups in the distribution of categorical ratings of severity, indicating a milder severity of the Chief Complaint in risperidone-treated subjects, were noted at Weeks 4 and 6.

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Secondary Efficacy (continued):

Subjects who improved by at least 50% on the MTS Total Score were considered "responders". Analyses indicated that the proportion of subjects meeting the "responder" definition was significantly (p=0.035) higher in the risperidone group (27.8%), than in the placebo group (17.5%) at endpoint. This analysis was also performed for subjects treated with SSRIs or non-SSRIs, and the data indicated that, while no significant difference between treatment groups was noted in the non-SSRI sub-group, there was a significantly (p<0.05) higher proportion of subjects in the SSRI sub-group treated with risperidone at Week 3 (19.6% vs. 5.0%) and Week 6 (LOCF: 26.9% vs. 12.3%). Similar differences between the non-SSRI and SSRI sub-populations in response to risperidone were observed for other analyses of the MTS.

The change in the MTS total Scores correlated significantly with changes in the scores on the HAM-D, CGI-S, PGIS (actual value), Q-LES-Q SF and SDS. This suggests that the MTS is at least equally sensitive to change as the other measures, and appears to be measuring domains that overlap with these other measures used to assess this subject population.

The results for the PGIS indicated that treatment with risperidone was associated with a statistically significant (p=0.048) improvement, compared with placebo, at endpoint on this patient-rated global assessment of change. The distribution of ratings across categories of change showed that the ratings were significantly lower (i.e., indicating greater improvement) for risperidone-treated subjects at endpoint.

Ratings on the SDS indicated that risperidone-treated subjects showed a statistically significant (p<0.001) mean reduction in the total score (6.7 points), compared to placebo (3.5 points), at endpoint. This statistically significant (p<0.05) improvement was also noted in the work/school, social life, and family life/home responsibilities dimensions at endpoint for risperidone-treated subjects. Evaluation of the level of disruption in each of these dimensions indicated that a significantly higher proportion of subjects in the risperidone group experienced lesser disruption, compared to placebo-treated subjects, at endpoint for the social life and family life/home responsibilities dimensions.

Analyses of the data for the Q-LES-Q SF indicated that there was statistically significant (p=0.002) greater improvement in the total score for risperidone-treated subjects (13.1 points), compared to those receiving placebo (8.8 points), at endpoint; similar effects were noted for the Medication Satisfaction item (0.9 vs. 0.5 points) and the Overall Life Satisfaction item (0.9 vs. 0.5 points). Comparison of the distribution of ratings for the Medication Satisfaction and Overall Life Satisfaction items indicated that a significantly (p<0.01) higher proportion of risperidone-treated subjects reported more favorable ratings of satisfaction, compared with the placebo group, at endpoint for both items.

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SAFETY RESULTS:

Open-label Standard Antidepressant Phase

During this phase of the study, treatment with the current SAD was very well tolerated, as evidenced by the low incidence of dropouts due to AEs (2 subjects; 0.4%) and the low incidence of TEAEs (~16% of subjects). The most common TEAEs related to the gastrointestinal system (4.3% of subjects). The most commonly reported TEAE was vomiting (5 subjects; 1.1%). Six serious AEs occurred during this period, including lower abdominal pain, pancreatitis, pyrexia, cholecystitis, bronchitis and neurological symptoms.

During the OL-SAD phase, vital signs changed very little. Only a statistically significant mean increase in pulse of ~1 bpm was observed during this period, but this was not considered clinically relevant. There were 6 reports of clinically notable changes in vital signs, including 2 subjects who experienced changes of systolic or diastolic blood pressure; 4 subjects experienced an increased body weight (≥7%). No other safety evaluations were conducted during the OL-SAD period.

Double-blind Treatment Phase

During the double-blind period, treatment with risperidone in conjunction with a standard antidepressant was well tolerated, as indicated by the low rate of discontinuations due to AEs (5.8%) in the risperidone group (placebo = 2.3%). The events leading to discontinuation in the risperidone group included 4 occurrences of somnolence and one episode each of depression, insomnia and panic attack, while those in the placebo group included one event each of somnolence and suicide attempt.

The proportion of subjects who experienced at least one TEAE during the double-blind treatment period was higher in the placebo group (55%) than in the risperidone group (46%), with the overall incidence of severe events being less than 5% (risperidone – 2.9%; placebo – 4.6%). The incidence of TEAEs related to nervous system disorders, gastrointestinal system disorders, and infections and infestations was higher in the placebo group, while those classified as psychiatric disorders were higher in risperidone-treated subjects. Individual TEAEs reported more frequently in the risperidone group, compared to the placebo group, included dry mouth (5.1% vs. 0.8%), weight increased (4.4% vs. 1.5%), somnolence (5.1% vs. 1.5%) and insomnia (4.4% vs. 1.5%). Headache occurred more frequently in placebo-treated subjects (14.5% vs. 8.8%). The incidence of movement disorders reported as TEAEs was very low, with one case each of tremor and akathisia in the risperidone group, and one case each of dystonia and tremor in the placebo group.

During the double-blind period, statistically significant mean changes from baseline were noted in systolic blood pressure (decrease), diastolic blood pressure (decrease) and body weight (increase) in risperidone-treated subjects; this resulted in statistically significant differences between the two treatment groups in the changes from baseline in these three vital signs parameters. There is no clinical relevance for the mean changes in systolic blood pressure (decrease of 3.1 mmHg) and diastolic blood pressure (decrease of 1.9 mmHg), as there were no subjects in the risperidone group who experienced clinically notable changes. Risperidone-treated subjects gained on average 2.8 lbs in body weight at endpoint, compared to 0.3 lbs in the placebo group; the proportion of subjects who showed clinically notable weight gain (≥7%) was 6.1 % in the risperidone group, compared to 0% in the placebo group.

The incidence of abnormalities detected on the physical examination at baseline was similar in the two groups. Although abnormalities emerged during the double-blind treatment period, the distribution was similar in risperidone- and placebo-treated subjects, eg, general appearance (13.2 vs. 15.3%), eyes (13.2 vs. 9.0%), skin (11.4 vs. 11.7%) and musculoskeletal system (7.9 vs. 12.6%).

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CONCLUSION:

- A total of 463 patients with MDD, who had not responded adequately, received an additional 4 weeks of treatment with their current antidepressant and other psychopharmacological agents. Of these 463 patients enrolled in the open-label period, of which 460 had received prior treatment with psychotropic medication, over 70% were treated with SSRIs. Only 23 patients benefited substantially from this additional 4 weeks of treatment, while 274 subjects did not benefit [CGI-Severity of moderate or higher; Carroll Depression Scale (CDS) ≥20] from open-label antidepressant treatment and were randomized to risperidone (n=141) or placebo (n=133).
- The study population had a mean age of 46 years, and was predominantly female (71%) and Caucasian (78%). The depressive illness in the subjects was both chronic and severe, based on the fact that, on average, their first depressive episode occurred at the age of 29, the depressive illness had been present for ~16 years, and subjects had an average of 7 lifetime episodes of depression, with at least one episode in the last year. In addition, 92 subjects (20%) had been hospitalized at least once for depression, and 87 subjects had a lifetime history of attempted suicide. At the end of the open-label period, on average, the CGI-Severity was 4.5 (moderately ill to markedly ill), the baseline HAM-D total Score was 23.9, and the CDS was 26.7.
- The overall rate of discontinuation in the double-blind augmentation period was low in both the risperidone 21.3% and placebo 13.5% groups, with a low incidence of severe adverse events in both groups (<5%). Symptoms reported more frequently with risperidone were dry mouth, weight increase, somnolence and insomnia; the difference from placebo did not exceed 5% for any of these symptoms. Headache was more frequent in placebo-treated subjects (15%), compared with those receiving risperidone (9%). One subject each complained of tremor and akathisia during treatment with risperidone, while one patient each complained of dystonia and tremor during placebo treatment.
- No clinically meaningful differences were noted for vital signs, except risperidone-treated subjects gained more body weight (2.8 lbs.), compared to those receiving placebo (0.3 lbs.). Clinically notable weight gain was noted in 6.1% of risperidone-treated subjects, but not in any subjects in the placebo group.
- During double-blind treatment, the HAM-D total score declined by an average of 8.5 and 7.1 points in the risperidone and placebo groups, respectively at the primary endpoint (Week 4, LOCF); the corresponding numbers at Week 6 (LOCF) were 10.0 and 7.9. These differences were statistically significant ($p<0.05$). Significant benefit of risperidone treatment was also noted on the anxiety/somatization, retardation, sleep disturbance, and Maier-Phillip severity subscales of the HAM-D. Significantly ($p<0.05$) greater improvements in the risperidone group, compared to the placebo group, were also noted in the clinician's global assessment of disease severity (CGI-S) at the Week 4 and Week 6 evaluations.
- Analyses of the HAM-D data, stratified by use of SSRI vs. non-SSRI antidepressants, indicated that SSRI-treated subjects benefited more from risperidone augmentation (2.5-point difference vs. placebo), compared with non-SSRI-treated subjects (1.5-point difference vs. placebo). A statistically significant ($p=0.004$) difference vs. placebo was noted for the SSRI, but not the non-SSRI, group.
- A statistically significant difference in the proportion of "responders" (≥50% reduction on HAM-D at endpoint) and "remitters" (HAM-D ≤7) was noted for risperidone (40.9% and 19.7%, respectively), compared with placebo (28.6% and 9.5%, respectively). In patients receiving risperidone, the responder and remitter rates were substantially higher in SSRI-treated subjects, compared to those receiving non-SSRIs.

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CONCLUSION (cont'd):

- Analyses of the change in the severity of the Most Troubling Symptoms identified by the patient indicated that the mean change in the 4 highest ranked most troubling symptoms was significantly greater ($p<0.001$) in the risperidone-treated subjects, compared to the placebo group, at endpoint; this difference was also significant at Week 1. Analyses of the MTS Total Global Score, which sums the severity ratings of all 8 symptoms, indicated significant ($p=0.004$) improvement in favor of risperidone at endpoint. These analyses were supported by similar findings in mean change on the MTS percent from maximum score, Three Most Troubling Symptoms, and Two Most Troubling Symptoms at endpoint.
- The rating of severity of the subject's Chief Complaint improved significantly ($p=0.003$) more in risperidone-treated subjects (2.3), compared with placebo-treated subjects (1.6). Responder (≥50% reduction on MTS Total Score) analyses indicated a significantly ($p=0.035$) higher proportion in the risperidone group (27.8%), compared with the placebo group (17.5%) at endpoint. Similar to the HAM-D data, while there was a significant difference between risperidone and placebo in responder rates in the SSRI-treated sub-group, no significant difference was observed in the non-SSRI treated subjects.
- The Patient Global Improvement Scale (PGIS) ratings showed significantly ($p=0.048$) greater improvement in risperidone-treated subjects, compared with the placebo group; similar statistically significant ($p<0.001$) reductions were noted on the Sheehan Disability Scale (SDS) total score in favor of risperidone (6.7), compared with placebo (3.5). This benefit was also noted in the Work/School, Social Life, and Family Life/Home Responsibilities dimensions of the SDS at endpoint.
- Analyses of the subject-rated quality of life scale, the Q-LES-Q SF, showed statistically significant ($p=0.002$) benefit (increase in score) of risperidone (13.1), compared to placebo (8.8) at endpoint. Similar effects were noted for the Medication Satisfaction and Overall Life Satisfaction items.
- In summary, adjunctive treatment with risperidone at doses of 1-2 mg/day, was well tolerated, and showed a consistent pattern of benefit in improving depressive symptoms and associated impairment in this population of patients with MDD experiencing inadequate response to their current antidepressant therapy. These effects were noted on both clinician-rated measures of depressive symptoms and disease severity, as well as patient-rated assessments of symptom severity, global improvement, disability and quality of life.

Date of the report: [19 October 2006]