LONG-TERM SAFETY/EFFICACY STUDY REPORT

STUDY TITLE: An Open-Label, Long-Term Evaluation of Sertraline in Children and Adolescents With Obsessive Compulsive Disorder or Depression

PROTOCOL NO: 91CK21-0550

INVESTIGATORS AND STUDY LOCATIONS:

[redacted]

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* [redacted]

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STUDY DATES: June 19, 1992 – April 7, 1994

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LONG-TERM SAFETY/EFFICACY STUDY SYNOPSIS

Study Title: An Open-Label, Long-Term Evaluation of Sertraline in Children and Adolescents with Obsessive Compulsive Disorder or Depression

Protocol No.: 91CK21-0550

Investigator: [See preceding list]

Study Location: [See preceding list]

Study Objective: To evaluate the long-term safety and efficacy of sertraline in children and adolescents ages 6-18 years with obsessive compulsive disorder (OCD) or depression who completed Protocol 90CK21-0525 (Study 525), a 51-day multiple dose pharmacokinetic trial of sertraline.

Study Population: Study participants were 43 psychiatric patients who met DSM-III-R criteria for either depression (n = 32) or OCD (n = 10) or both (n = 1). Twenty-five patients were female; 18 were male. Thirty-five patients were white, 5 were black, and 3 had other ethnic backgrounds. The age (mean ± SD) for all patients was 13.3 ± 2.5 years. The patients were divided into two age-stratified groups (ages 6-12 years and ages 13-18 years). The 16 patients in the 6 -12 year group (mean age ± SD, 10.7 ± 1.4 years) had a mean body weight of 97.9 ± 35.0 lb, and the 27 patients in the 13-18 year group (mean age ± SD, 14.9 ± 1.4 years) had a mean body weight of 128.4 ± 41.4 lb. Their overall mean weight was 117.0 ± 41.5 lb. All patients were in good health as determined by their medical histories, physical exams, and clinical laboratory tests. At endpoint, the mean maximum dose of sertraline was 153, 159, and 157 mg/day in the 6-12 year group, in the 13-18 year group, and in patients overall, respectively. The mean duration of treatment was 149.9, 110.0, and 124.8 days in the 6-12 year group, in the 13-18 year group, and in patients overall, respectively.

Dosage Form: Sertraline was administered as 25 and/or 50 mg capsules. The 50 mg capsules were used for upward titration; the 25 mg capsules were to be used if downward titration was indicated by limiting adverse experiences.

Study Design: This was a 24-week open-label study of sertraline. The initial dose was 50 mg/day and patients were to be titrated up in 50 mg increments to a maximum of 200 mg/day based upon clinical response, with a minimum of one week at each dose level prior to an increase. After baseline, visits took place at the end of Weeks 1, 2, 4, 6, 8, 12, 16, 20, and 24.

For patients with OCD, the following rating scales were completed by the investigator:

1. Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)
2. National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH)
3. CGI Severity of Illness
4. CGI Improvement

CY-BOCS, NIMH, and CGI Severity and Improvement data were collected by the investigator at the Study 550 baseline and at all subsequent treatment visits. The CGI Improvement rating question asked how much the patient had changed since the beginning of Study 525.

Patients with depression were evaluated at the same time points as for the OCD patients by the following:

1. CGI Severity of Illness
2. CGI Improvement

Blood was drawn for measurement of plasma concentrations of sertraline and N-desmethylsertraline at the end of Weeks 1, 4, 8, 12, and 24 (the baseline blood draw was Day 51 of Study 525). Safety was assessed by adverse experiences, clinical laboratory tests, physical examination, blood pressure and pulse rate, body weight, and electrocardiograms (ECGs) at various time points throughout the study.

Data Analysis: In the efficacy analysis, mean changes from both the Study 525 and Study 550 baselines were displayed by study week and endpoint. The mean changes for OCD patients were evaluated using a Wilcoxon test for the CY-BOCS, NIMH, CGI Severity, and CGI Improvement scales. The mean changes for depression patients, and all patients combined, were evaluated using a t-test for the CGI Severity and CGI Improvement scales. (CGI Improvement was analyzed for changes only from the 550 baseline.) Patients with a baseline score and at least one follow-up measure were included in the analyses. Analyses for each study week each included only the available data at that study week. Values were assigned to study weeks using the actual number of days relative to baseline and were excluded from the by-weeks analysis if the actual day was more than ±7 days from the target day for study weeks 1, 2, 4, 6 and 8 or if the actual day was more than ±14 days from the target day for study weeks 12, 16, 20 and 24. The endpoint analysis included the last post-baseline value for each patient.

Mean sertraline and N-desmethylsertraline plasma concentrations were analyzed by gender and age group; a two-way analysis of variance model provided p-values by age, gender, and age-by-gender interaction. The values were normalized to a 200 mg dose and averaged over study weeks 1 through 24. Values were assigned to study weeks using actual number of days relative to baseline. The values were

additionally normalized by both dose and body weight, and then averaged over study weeks 1 through 24. Mean plasma concentrations were also calculated for the last concentration values for patients receiving 200 mg/day, including means of values normalized to body weight at baseline. In addition, the concentration-efficacy relationship was explored using CGI Improvement and Severity as efficacy parameters for the group of depressed patients and the group of all patients. The NIMH scale and CY-BOCS were additionally examined for the group of patients with OCD. A correlation between change from the Study 525 baseline for each efficacy measure and sertraline concentration at the last concentration-efficacy pair was calculated and tested for significance.

Safety data were summarized and patients were evaluated to determine if they had clinically significant findings during the study.

Efficacy Results: At endpoint in Study 550, there was statistically significant improvement in CY-BOCS for OCD patients from both the Study 525 and Study 550 baselines (p=0.001 and p=0.029, respectively). The mean changes in CY-BOCS were -19.3 units (74% decrease) from the Study 525 baseline of 26.1, and -6.6 units (49% decrease) from the Study 550 baseline of 13.5. The endpoint NIMH evaluation of OCD patients in Study 550 also showed statistically significant improvement from both the Study 525 baseline and the Study 550 baseline (p=0.001 and p=0.010, respectively). The mean changes in NIMH were -6.8 units (68% decrease) from the Study 525 baseline value of 10.0 and -2.8 units (47% decrease) from the Study 550 baseline value of 6.0. In OCD patients, CGI Severity showed a statistically significant decrease in severity from the Study 525 baseline (p=0.001) to the endpoint in Study 550; no significant change was seen for CGI Improvement. In depression patients, CGI Severity at endpoint in Study 550, showed statistically significant decreases from both the Study 525 and 550 baselines (p=0.001 and p=0.002, respectively); CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline (p=0.011). In all patients combined, the evaluation of CGI Severity showed, at endpoint in Study 550, statistically significant decreases in severity from both the Study 525 and 550 baselines (p=0.001); CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline (p=0.001) to endpoint.

Plasma Concentration Results: There was no statistically significant difference for mean sertraline or N-desmethylsertraline plasma concentrations by age or gender whether dose normalized (to the 200-mg dose) or dose and body weight normalized. There were no statistically significant plasma concentration-effect relationships in patients with OCD and/or depression for any efficacy variable.

Safety Results: For newly emergent adverse experiences in Study 550, the incidence in the 6-12 year old group, the 13-18 year old group, and in patients overall was 56% (9/16), 59% (16/27), and 58% (25/43), respectively. For adverse

experiences in Study 550, including those continuing from Study 525, the incidence in the 6-12 year old group, the 13-18 year old group, and in patients overall was 81% (13/16), 70% (19/27), and 74% (32/43), respectively. The incidence in males and females in Study 550 were 72% (13/18) and 76% (19/25), respectively. Three patients were discontinued because of adverse experiences: Patient [redacted] due to nervousness, Patient [redacted]) due to exacerbated suicidal ideation and homicidal ideation, and Patient [redacted]) due to the requirement for Demerol, which was excluded by the protocol as well as because of the injury [redacted] sustained in a [redacted] Two patients had serious adverse events: Patient [redacted]) was hospitalized due to a fractured vertebra sustained in a motor vehicle accident; Patient [redacted]) had exacerbated suicidal ideation and homicidal ideation which led to hospitalization.

Twenty-one patients (49%) had a total of 26 clinically significant laboratory abnormalities with onset during Study 550 (low hematocrit levels in 15 patients and low hemoglobin levels in 2 patients, low albumin levels in 4 patients, high random glucose levels in 3 patients, and high eosinophil levels in 2 patients). None were serious or required discontinuation. Note that the threshold levels used for determining clinically significant abnormalities in these children and adolescents were those mandated by FDA (as adopted in sertraline Safety Update II for NDA [redacted]) for sertraline studies in adults, whose hemoglobin/hematocrit is normally higher than pediatric levels. During Studies 525 and 550, with the Study 525 baseline as reference, 24 patients (56%) had a total of 35 clinically significant laboratory abnormalities.

During Study 550, with the Study 550 baseline as reference, 7 patients (16%) had a total of 18 clinically significant changes in blood pressure (BP) or heart rate. During Studies 525 and 550, with the Study 525 baseline as reference, 17 patients (40%) had a total of 40 clinically significant changes in BP or heart rate. None were serious or required discontinuation of treatment. The majority of the clinically significant changes were decreases in systolic or diastolic BP. Note that the threshold values for determining clinically significant blood pressures in Studies 525 and 550 were those adopted for adults in sertraline Safety Update II for NDA [redacted] In pediatric subjects, systolic and diastolic BP are lower than adult norms.

Clinically significant increases in body weight (≥7%) from the Study 550 baseline were seen in 75% (12/16) of patients in the 6-12 year group, 26% (7/27) of patients in the 13-18 year group, and 44% (19/43) of all patients. From the Study 525 baseline to the final measurement in Study 550, increases ≥7% in body weight were seen in 75% (12/16) of patients in the 6-12 year group, 33% (9/27) of patients in the 13-18 year group, and 49% (21/43) of all patients; and decreases ≥7% in body weight were seen in 13% (2/16) of patients in the 6-12 year group, 4% (1/27) of patients in the 13-18

year group, and 7% (3/43) of all patients. There were no clinically significant changes in ECGs.

Summary/Conclusions

1. For OCD patients at endpoint in Study 550, there was statistically significant improvement in OCD as measured by the CY-BOCS and NIMH rating scales from both the Study 525 and Study 550 baselines. In OCD patients, CGI Severity showed a statistically significant decrease in severity from the Study 525 baseline to the endpoint in Study 550; no significant change was seen for CGI Improvement. In depression patients and in all patients combined, CGI Severity at endpoint in Study 550 showed statistically significant decreases from both the Study 525 and 550 baselines; CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline.

2. There was no statistically significant difference for mean sertraline or N-desmethylsertraline plasma concentrations by age group (6-12 and 13-18 years) or gender whether dose normalized (to the 200-mg dose) or dose and body weight normalized.

3. There were no statistically significant plasma concentration-effect relationships in patients with OCD and/or depression for any efficacy variable.

4. The most common (≥ 10%) treatment-emergent adverse experiences overall in this study were insomnia, somnolence, and headache, which are also commonly seen in adult patients. Three patients (7%) discontinued due to adverse experiences. Clinically significant laboratory abnormalities were largely limited to low hematocrit levels based upon normally higher adult reference values. Clinically significant vital sign abnormalities were largely limited to decreased systolic or diastolic blood pressure also partially attributable to higher adult reference values. The mean changes from baseline in laboratory values and vital signs were not considered clinically important. There were no unusual or unexpected changes in body weight and no clinically significant ECG abnormalities. Overall, the safety profile in Study 550 was generally similar to Study 525, the tolerance and pharmacokinetic study that preceded Study 550. The adverse experience profiles seen in both 6-12 year old and 13-17 year old patients were similar to those previously reported in the Zoloft package labeling for adults.

5. In conclusion, based on the above results, sertraline was shown to be safe and effective when administered for a long term (24 weeks) at a dose of 50 to 200 mg/day to children and adolescents 6-18 years old who were diagnosed with OCD and/or depression.

1. STUDY OBJECTIVE

The objective of this study was to evaluate the long-term safety and efficacy of sertraline in children and adolescents 6-18 years of age with OCD or depression who completed Protocol 90CK21-0525 (Study 525), a 51-day multiple dose pharmacokinetic trial of sertraline.

2. STUDY DESIGN

This multicenter study, Protocol 91CK21-0550 (Study 550), was a 24-week open trial of sertraline in children and adolescents (6-12 and 13-18 years of age) with OCD or depression. The study was designed so that sertraline would be titrated, beginning at 50 mg/day in all patients, to 200 mg/day based on individual clinical response. Dosage increases were to be in 50-mg increments, with a minimum of one week at each dose level prior to the increase.

In Study 525, in which sertraline was administered in a forced upward titration from 50 to 200 mg/day, the last dosing day was Day 42; the last study measurements and blood collections were performed on Day 51. Between Days 42 and 51, the investigator made the decision (subject to approval of the Pfizer Project Physician) whether to offer the patient admission to Study 550. Study 550 began on the evening of Day 51 of Study 525.

The protocols for both Studies 525 and 550 were originally designed to include a maximum of 24 patients at three sites, with the intent that all patients who completed Study 525 would be considered for enrollment in Study 550. The protocol for Study 525 was then amended to allow 56 patients to participate at up to seven sites. The protocol for Study 550 was not amended; however, all eligible patients from Study 525 were enrolled in Study 550 for consistency with the purpose of the protocol.

2.1 Subjects

Male and female outpatients 6-18 years of age who completed Study 525 were eligible for inclusion in Study 550. Baseline laboratory values were to be normal, or abnormalities were to be clinically insignificant. Females of child-bearing potential were to have a negative serum beta-hCG pregnancy test.

The exclusion criteria were specified in the protocol as follows:

- Patients who were pregnant or nursing women; if a patient became pregnant [redacted] was to be discontinued immediately and followed appropriately.

- Women of childbearing potential who were sexually active and not using a contraceptive method judged by the investigator to be effective.

- Patients who planned to be blood donors while they were participating in the study. (Patients were to be instructed not to act as blood donors for one month after completing the study.)

- Patients requiring concomitant therapy with a psychotropic drug of any kind (with the exception of chloral hydrate), any drug with a psychotropic component (Donnatal, Librax, an antihistamine other than Seldane, etc.), or any drug other than those permitted by the protocol. (See "Drugs Allowed and Drugs Not Allowed as Concomitant Medications" in the protocol, Appendix III.)

- Patients were instructed not to take MAOIs for 2 weeks after completing the study.

The protocol and Informed Consent Form were reviewed and approved by the Institutional Review Boards of the participating clinical centers. The patients' agreement to participate in the study was required. In addition, since all patients were minors, the parent or legal guardian of each patient was required to understand the procedures and risks and benefits of participating in the study, be willing to insure that each patient would abide by protocol requirements, and give written informed consent for the patient's participation in the study.

2.2 Drug Administration

Patients who qualified for participation in this trial were instructed to take study medication once daily, with the evening meal. The initial dose was given as one capsule of 50 mg at the Study 550 baseline (the end of Day 51 of Study 525, 9 days after discontinuation of dosing in that study).

Patients were titrated up in 50 mg increments from the initial dose to a maximum of four capsules of 50 mg sertraline (200 mg sertraline). Titration was based on each individual patient's clinical response, with a minimum of one week at each dose level before an incremental dose was given. Study medication was provided on five-column blister cards (one card for each week) with the 50 mg capsules contained in the first four columns.

Dosing could be decreased by 25 mg at any time if limiting adverse experiences emerged. The fifth column of the blister cards contained 25 mg capsules that were to be used if downward titration was indicated. Medication provided in each blister pack was sufficient for 9 days of drug administration. Patients were asked to abstain from alcohol during the study.

2.3 Efficacy Assessments

The psychiatric rating scales used by the investigator to evaluate efficacy were: the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS),[1] the National

Institute of Mental Health Global Obsessive Compulsive Scale (NIMH),[2] the Clinical Global Impression (CGI) of Severity of Illness Scale and the CGI Improvement Scale.[3] These data were collected at the Study 550 baseline and all subsequent visits (the end of Weeks 1, 2, 4, 6, 8, 12, 16, 20, and 24).

CY-BOCS, NIMH, and CGI Severity and Improvement Scales were used to evaluate patients with OCD. CGI Severity and Improvement Scales were used to evaluate patients with depression.

A brief description of each rating scale is provided below:

- CY-BOCS: This scale consists of ten items, each scored from 0 to 4. The initial five items measure obsessions, and the remaining five items measure compulsions. Thus, the CY-BOCS total score ranges from 0 to 40.

- NIMH: This scale ranges from 1 to 15, rated as follows: 1 to 3, minimal within range of normal; 4 to 6, subclinical obsessive compulsive behavior; 7 to 9, clinical obsessive compulsive behavior; 10 to 12, severe obsessive compulsive behavior; and 13 to 15, very severe obsessive compulsive behavior.

- CGI Severity: This scale ranges from 1 (normal, not at all ill) to 7 (among the most extremely ill).

- CGI Improvement: This scale ranges from 1 (very much improved) to 7 (very much worse). (The CGI Improvement question asked how much the patient had changed compared to the beginning of Study 525.)

2.4 Plasma Concentration Assessments

Blood samples for plasma sertraline and N-desmethylsertraline levels were to be drawn at baseline (Day 51 of Study 525 for blood samples) and immediately after the rating scales were administered at the end of Weeks 1, 4, 8, 12, and 24. Sampling times were to be 12-22 hours after the previous evening dose. Data were statistically evaluated for all patients, by gender and age group, and summarized by patients who received 200 mg/day, by gender and age group. In addition, the concentration-effect relationship was analyzed using CY-BOCS, NIMH, the CGI Improvement scale, and the CGI Severity scale for the OCD population and the CGI Improvement and Severity scales for both patients with depression and all patients combined.

2.5 Safety Assessments

2.5.1 Adverse Experiences

All volunteered or observed adverse experiences were recorded on the case report form, specifying the date of onset, duration, severity, the investigator's assessment of its relationship to the test medication, action taken, and outcome. In tabulating safety results, all reported adverse experiences were included regardless of their severity or relationship to study drug. The adverse experiences were categorized by WHO dictionary preferred terminology. In computing the incidence for an individual adverse experience, a patient reporting more than one episode of the same complaint, even of differing severity, was counted once and the highest level of severity used.

At the discretion of the investigator, a patient could be dropped from the study or the dosage decreased at any time due to adverse experiences (or insufficient treatment response). Any patient dropped from the study due to an adverse experience was to be followed until the adverse experience resolved.

The investigator was instructed to report any serious adverse event immediately to the Pfizer Project Physician. Telephone numbers were provided to the investigator so that the Project Physician could be called both during and outside working hours.

A serious adverse event is defined as an event that is fatal, is life-threatening or potentially life-threatening, results in permanent disability, requires hospitalization or prolongation of a hospital stay, involves cancer or a congenital anomaly, is the result of a drug overdose, or suggests a significant hazard to the patient.

Any additional adverse experience that the investigator considered significant was also to be reported immediately to the Pfizer Project Physician.

2.5.2 Clinical Laboratory Tests

At baseline and at the end of Weeks 1, 4, 8, 12, and 24, the following tests were to be performed: hematology (CBC with platelet count), blood chemistries (including liver function tests), and urinalysis. A serum beta-hCG pregnancy test was to be performed for women of child-bearing potential at the Study 550 baseline and at the end of Weeks 4, 8, 12, and 24.

2.5.3 Vital Signs/Weight/Electrocardiograms/Physical Examinations

Blood pressure and pulse rate were measured at baseline, at the end of Weeks 1, 2, 4, 6, 8, 12, 16, 20, and 24, and at any time a patient complained of symptoms potentially indicating orthostatic hypotension. Measurements were to be taken after the patient had been supine for 5 minutes and after the patient had been standing for

2 minutes. Body weight was recorded at baseline and at the end of Weeks 1, 2, 4, 6, 8, 12, 16, 20, and 24. Body height was recorded at baseline and at Week 24. A 12-lead ECG was taken at baseline and at the end of Weeks 1, 4, 8, and 24. Physical examinations were performed at baseline and at Week 24. (If a patient discontinued prematurely, all evaluations scheduled for Week 24 were performed at the time of discontinuation.)

2.5.4 Concomitant Medications and Concurrent Illnesses

Concomitant medications were recorded on the case report form specifying the drug name, total daily dose, start date, end date, and indication. Concurrent illnesses were recorded specifying the name of the illness, the onset date, and the resolution date.

3. DOSAGE FORM

The 25 and 50 mg sertraline capsules administered in this study were manufactured and supplied by Pfizer Pharmaceuticals. The 25 mg capsules were identified by Formulation Identification (FID) [redacted] The 50 mg capsules were identified by [redacted] and [redacted] Information about the formulation is presented in Appendix III.

4. DATA ANALYSIS

A p-value of ≤ 0.05 was considered statistically significant.

4.1 Efficacy Analysis

Mean changes from both the Study 525 and Study 550 baselines were analyzed by study week and endpoint. The mean changes for OCD patients were evaluated using a Wilcoxon test for the CY-BOCS, NIMH, CGI Severity, and CGI Improvement scales. The mean changes for the depression patients, and all patients combined, were evaluated using a t-test for the CGI Severity and CGI Improvement scales. (CGI Improvement was analyzed for changes only from the 550 baseline.) The analysis was done using SAS PROC UNIVARIATE.

Patients with a baseline score and at least one follow-up measure were included in the analyses. Analyses for each study week include only the available data at that study week. Values were assigned to study weeks using the actual number of days relative to baseline and were excluded from the by-weeks analysis if the actual day was more than ± 7 days from the target day for study weeks 1, 2, 4, 6 and 8 or if the actual day was more than ± 14 days from the target day for study weeks 12, 16, 20 and 24. The endpoint analysis includes the last post-baseline value for each patient.

Baseline and endpoint means for all efficacy variables were also summarized by age group: 6 to 12 and 13 to 18 years.

4.2 Plasma Concentration Analysis

Mean sertraline and N-desmethylsertraline plasma concentrations were analyzed by gender and age group; a two-way analysis of variance model provided p-values by age, gender, and age-by-gender interaction. The values were normalized to a 200 mg dose and averaged over study weeks 1 through 24. Values were assigned to study weeks using the actual number of days relative to baseline. The values were additionally normalized by both dose and body weight, i.e. (200/dose) X (body weight at a particular visit/mean body weight for all patients at study baseline), and then averaged over study weeks 1 through 24. Dose values were selected using the actual number of days relative to baseline. The dose taken on the evening before blood sampling was reported as "not taken" if the dose was reported as zero on the study medication page of the case report form and was reported as "unknown" if the dosing information was not available. Body weight values were assigned to study weeks using the actual number of days relative to baseline. If a body weight value was not available, then the value from the previous study visit or from study 550 baseline was used. The analysis of variance was performed using SAS PROC GLM.

Mean plasma concentrations were also calculated for the last concentration values for patients receiving 200 mg/day, including means of values normalized to body weight at baseline.

To insure that plasma concentrations were a reasonable approximation of steady state values, a concentration value was excluded from analysis if any of the following were true: if the dose prior to plasma collection was missed, if 2 of the 3 preceding doses were missed, if 4 of the 7 preceding doses were missed, if either sertraline or desmethylsertraline were below the quantitation limit, or if the ratio of N-desmethylsertraline to sertraline was 5.0 or greater. Because of its longer half-life, N-desmethylsertraline/sertraline typically exceeds 5.0 only when sertraline dosing has been discontinued for several dosing intervals. Usual N-desmethylsertraline/sertraline ratios are between 1 and 2 at steady state.

In addition, the concentration-efficacy relationship was explored using CGI Improvement and Severity as efficacy parameters for the group of depressed patients and the group of all patients. The NIMH scale and CY-BOCS were additionally examined for the group of patients having OCD. A correlation between change from the Study 525 baseline for each efficacy measure and sertraline concentration at the last concentration-efficacy pair was calculated and tested for significance. The analysis was performed using SAS PROC CORR.

4.3 Safety Analysis

4.3.1 Adverse Experiences

The incidence and severity of adverse experiences were summarized separately and combined for the 6-12 and 13-18 year age groups. The incidence of adverse experiences was also summarized by gender. Serious adverse events (defined in Section 2.5.1) were reported.

4.3.2 Clinical Laboratory Tests

The incidence of clinically significant laboratory abnormalities was summarized by age groups 6-12 and 13-18 years, and the age groups combined, during both Study 550 and Studies 525 and 550 combined. The criteria for clinically significant laboratory abnormalities are identical to those for adults adopted in sertraline Safety Update II for NDA [redacted]

4.3.3 Vital Signs/Weight/Electrocardiograms/Physical Examinations

During Study 550, vital signs were to be measured with the patient in supine and standing positions, while during Study 525, vital signs had been measured with the patient in a sitting position. Therefore, in Study 550, the determination of change in supine and standing measurements from the Study 525 baseline used Study 525 baseline sitting values.

The incidence of clinically significant abnormalities in vital signs (summarized by age groups 6 to 12 and 13 to 18 years, and the age groups combined) was based on changes from the Study 550 baseline and on changes from the Study 525 baseline. Clinically significant vital sign abnormalities were defined by the following criteria (which applies to sitting, supine, and standing positions):

Systolic blood pressure:

- ≥ 180 mmHg plus an increase from baseline ≥ 20 mmHg or
- ≤ 90 mmHg plus a decrease from baseline ≥ 20 mmHg

Diastolic blood pressure:

- ≥ 105 mmHg plus an increase from baseline ≥ 15 mmHg or
- ≤ 50 mmHg plus a decrease from baseline ≥ 15 mmHg

Heart rate:

- ≥ 120 beats/min plus an increase from baseline ≥ 15 beats/min or
- ≤ 50 beats/min plus a decrease from baseline ≥ 15 beats/min

Nine patients had vital signs measured while in the sitting position at the Study 550 baseline and in the supine and standing positions during the rest of the study (see Section 5.6.3). These patients were included in the data evaluation; their baseline sitting values were used as baseline supine and standing values.

Mean changes in vital sign parameters and body weight, from both the Study 525 and Study 550 baselines to the Study 550 final values, were summarized by age groups 6-12 and 13-18 years, and the age groups combined. The incidence of patients with clinically significant changes (increase or decrease of ≥7%) in body weight during Study 550 and Studies 525 and 550 combined was also summarized by age groups 6-12 and 13-18 years, and the age groups combined.

The incidence of patients with changes in ECGs (normal to abnormal and abnormal to normal) was presented for all patients in both Study 550 and Studies 525 and 550 combined. The incidence of clinically significant ECGs was also calculated for all patients in both Study 550 and Studies 525 and 550 combined.

Changes in physical examination from baseline for Study 550 were reported.

4.3.4 Concomitant Medications and Concurrent Illnesses

Concomitant medications were summarized as follows: at entry into Study 550, at entry into Study 525, during Study 550, and during Studies 525 and 550. Concurrent illnesses were summarized as follows: present at the Study 550 baseline, present at the Study 525 baseline, occurring during Study 550, or occurring during Studies 525 or 550.

5. RESULTS AND DISCUSSION

5.1 Patient Disposition and Characteristics

The distribution of patients is presented in Table 1 by study site and age group. Fifty-three patients completed Study 525 at six study sites and 43 entered Study 550 at four study sites. There were 16 and 27 patients, respectively, in the 6-12 year and 13-18 year groups enrolled in Study 550. Note that two 12-year-old patients reached their 13th birthday during Study 525 and were assigned to the 13-18 year group in Study 550 (Patient [redacted], and Patient [redacted]). All 43 patients were included in the safety and efficacy analyses.

The patient characteristics of sex, race, age, weight, and major diagnosis are summarized overall and by age groups 6-12 years and 13-18 years in Table 2; data by individual patient are presented in Appendix II, Table 3. (There were no patients who were 18 years old at the time of enrollment into Study 550.) The data for sex, race and major diagnosis were obtained from study 525 baseline. The data for age and weight were determined at study 550 baseline. Twenty-five females (8, 6-12 year group; 17, 13-18 year group) and 18 males (8, 6-12 years; 10, 13-18 year group) participated in the study. There were 35 white patients (13, 6-12 year group; 22, 13-18 year group), 5 black patients (1, 6-12 years; 4, 13-18 years); and 3 designated as "other" (2, 6-12 year group; 1, 13-18 year group). The mean age overall was 13.3 years (10.7 years, 6-12 year group; 14.9 years, 13-18 year group). The mean weight overall was 117.0 lb (97.9 lb, 6-12 year group; 128.4 lb; 13-18 year group).

Depression was diagnosed in 32 patients (13, 6-12 year group; 19, 13-18 year group), OCD was diagnosed in 10 patients (2, 6-12 year group; 8, 13-18 year group), and both were diagnosed in 1 patient (Patient [redacted], 6-12 year group).

5.2 Study Drug Administration

The mean duration of treatment in this study, presented in Table 3, was 124.8 days overall, and 149.9 and 110.0 days in the 6-12 and 13-18 year age groups, respectively. The mean maximum daily dose is summarized in Table 5 by study week and endpoint. Overall, the mean maximum dose at endpoint was 157 mg (153 mg for the 6-12 year old group and 159 mg for the 13-18 year old group.

Fifteen patients were at the 200 mg dose level at endpoint. One of these patients, Patient [redacted] took 225 mg for one day 42 days after starting sertraline treatment. [redacted] dosage never exceeded 200 mg/day for the remaining 124 days during which [redacted] participated in the study. The investigator did not explain why the patient took the extra 25 mg capsule. (Note that blister cards with the 50 mg sertraline capsules also contained a 25 mg capsule for each day to allow for a decreased dose.)

Two patients were at 225 mg/day at endpoint: Beginning 86 days after sertraline treatment was initiated, Patient [redacted], increased [redacted] dosage to 225 mg/day for 30 days. [redacted] took no more than 200 mg/day for the next 26 days, but again increased [redacted] dosage to 225 mg/day for the following 30 days (and then forgot to take the final study dose). Patient [redacted], at the same study site, increased [redacted] dosage 114 days after the start of sertraline treatment to 225 mg/day for 21 days. [redacted] was then was lost to follow-up. Both patients had increased dosage without permission. (Therapy by patient is presented in Appendix II, Table 4.)

5.3 Study Discontinuations

As shown in Table 4.1, 21 (49%) of 43 patients withdrew from treatment during Study 550. Discontinuations in the 6-12 and 13-18 year age groups were 38% (6/16) and 56% (15/27), respectively. The overall causes of withdrawal from treatment were: lost to follow-up, 10 (23%); other, 8 (19%), and adverse experience, 3 (7%). A list of study discontinuations by patient is presented in Table 4.2.

Three patients (7%), all in the depression group, were withdrawn from treatment because of adverse experiences: Patient [redacted] reported nervousness, Patient [redacted] had exacerbated suicidal ideation and homicidal ideation, and Patient [redacted] was discontinued during in-hospital treatment for a burst fracture of the second lumbar vertebrae. Discontinuation for Patient [redacted] was due to both the injury sustained [redacted] and to the requirement for medication excluded by the study protocol. Note that the exacerbated suicidal ideation and homicidal ideation in Patient [redacted] and the injury in Patient [redacted] are serious adverse events.) See Section 5.6.1 for detailed narratives on these three patients.

5.4 Efficacy

5.4.1 CY-BOCS

CY-BOCS was evaluated in OCD patients only. At endpoint in Study 550, there was statistically significant improvement in CY-BOCS from both the Study 525 and Study 550 baselines ($p<0.001$ and $p=0.029$, respectively). The mean changes were -19.3 units (74% decrease) from the Study 525 baseline of 26.1, and -6.6 units (49% decrease) from the Study 550 baseline of 13.5. The by-week evaluation demonstrated statistically significant improvement from the Study 525 baseline at all Study 550 CY-BOCS assessments ($p<0.01$). The improvement was maintained and somewhat enhanced in the 24 weeks of Study 550 as measured by CY-BOCS and NIMH Scales. (See Tables 6 and 7.1.1 and Figure 1 for CY-BOCS data for patients overall. See Appendix II, Table 1 for individual patient data for all efficacy parameters.)

5.4.2 NIMH

NIMH was also evaluated in OCD patients only. The endpoint evaluation in Study 550 showed statistically significant improvement from both the Study 525 and Study 550 baselines ($p=0.001$ and $p=0.010$, respectively). The mean changes were -6.8 units (68% decrease) from the Study 525 baseline value of 10.0 and -2.8 units (47% decrease) from the Study 550 baseline value of 6.0. The by-week evaluation showed statistically significant improvement from the Study 525 baseline at all Study 550

NIMH assessments ($p<0.05$); significant improvement from the 550 baseline was reported at Weeks 6, 8, 12, 16, 20, and 24 ($p<0.05$). (See Tables 6 and 7.1.2 and Figure 2.)

5.4.3 CGI Severity and CGI Improvement

OCD Patients

At the Study 550 endpoint, the mean decrease in severity for OCD patients from the Study 525 baseline was statistically significant ($p=0.001$). In the by-week analysis, there were statistically significant decreases in severity from the Study 525 baseline at all CGI Severity assessments. There were no statistically significant mean changes from the Study 550 baseline to the endpoint or to any study week for CGI Severity. (See Tables 6 and 7.1.3 and Figure 3.) The mean absolute values for CGI Severity for OCD patients in the 6-12 year-old group were 4.3, 3.0, and 1.0 at the Study 525 baseline, Study 550 baseline, and Study 550 endpoint, respectively. In the 13-18 year old group, the corresponding mean absolute values were 5.4, 3.3, and 2.6. (See Table 8.)

For CGI improvement in all OCD patients, the mean change from the Study 550 baseline to endpoint was not statistically significant. The by-week evaluation showed statistically significant improvement at Weeks 12 and 16 ($p<0.05$). (See Tables 6 and 7.1.4. Also see Figure 4. Note that Table 7.1.4 presents mean change values by visit week while Figure 4 presents mean absolute values by visit week.) The mean absolute values for CGI improvement for OCD patients in the 6-12 year old group were 1.7 and 1.0 at the Study 550 baseline and endpoint, respectively. In the 13-18 year old group, the corresponding mean absolute values were 2.9 and 1.8, respectively. (See Table 8.) Note: There are no Study 525 baseline means for CGI Improvement.

Depression Patients

At the Study 550 endpoint for depression patients, the mean decreases in severity from both the Study 525 and 550 baselines were statistically significant ($p=0.001$ and 0.002, respectively). The by-week evaluation showed statistically significant decreases in severity from the Study 525 baseline at all CGI Severity assessments ($p=0.001$); significant decreases in severity from the Study 550 baseline were reported at Weeks 4, 6, 8, 12, 16, and 20 ($p<0.05$).). (See Tables 6 and 7.2.1 and Figure 3.) The mean absolute values for CGI Severity for depression patients in the 6-12 year old group were 4.9, 2.4, and 1.9 at the Study 525 baseline, Study 550 baseline, and Study 550 endpoint, respectively, for depression patients. The corresponding mean absolute values in the 13-18 year old group were 4.7, 3.0, and 2.1, respectively. (See Table 8.)

The mean change in CGI Improvement from the Study 550 baseline to the Study 550 endpoint was statistically significant (p=0.011). The by-week evaluation of CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline at Weeks 2, 4, 6, 8, 12, 16, 20, and 24 (p<0.05). (See Tables 6 and 7.2.2. Also see Figure 4. Note that Table 7.2.2 presents mean change values by visit week while Figure 4 presents mean absolute values by visit week.) The mean absolute values for CGI improvement in the 6-12 year old group were 2.4 and 1.6 at the Study 550 baseline and endpoint, respectively. The corresponding mean absolute values in the 13-18 year old group were 2.8 and 2.1, respectively. (See Table 8.)

All Patients

The endpoint evaluation of CGI Severity in Study 550 showed statistically significant mean decreases in severity from both the Study 525 and 550 baselines (p<0.001). The by-week evaluation showed statistically significant decreases in severity from the Study 525 baseline at all CGI Severity assessments (p=0.001); there were also statistically significant decreases in severity from the Study 550 baseline at Weeks 2, 4, 6, 8, 12, 16, 20, and 24 (p<0.05). (See Tables 6 and 7.3.1 and Figure 3.)

The endpoint evaluation of CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline (p=0.001). The by-week evaluation demonstrated statistically significant improvement at Weeks 2, 4, 6, 8, 12, 16, 20, and 24 (p<0.005). (See Tables 6 and 7.3.2. Also see Figure 4. Note that Table 7.3.2 presents mean change values by visit week while Figure 4 presents mean absolute values by visit week.)

5.5 Plasma Concentrations

Mean sertraline and N-desmethylsertraline concentrations are summarized in Table 9 for all patients contributing plasma samples. Investigators were requested to collect plasma samples 12-22 hours after the last dose; however, actual collection times were not recorded and time after dosing could not be calculated. Because there was considerable variation in dose levels (see Table 1 in Appendix 1), concentrations were dose-normalized in the preparation of summary statistics (Table 9). In addition, to facilitate comparisons with values in the core study (Study 525) in which steady state values were only assessed at 200 mg/day, values for those patients receiving 200 mg/day in the present study are separately summarized in Table 10. Because some variation in pharmacokinetic parameters with body weight was seen in Study 525, concentration values in Tables 9 and 10 are also presented after further normalizing the dose-normalized concentration values by each patient's baseline body weight. Table 11 presents correlation results for key efficacy parameters and sertraline plasma concentrations. Supplementary tables and listings of plasma

concentration information are provided in Appendix 1, Tables 4 (concentration data excluded from analysis), 5 (normalized concentrations by individual), and 6 (concentrations in patients who discontinued due to adverse events), and in Appendix 2, Table 2 (non-normalized individual concentrations).

In addition to tabular presentations, mean dose-normalized concentrations of sertraline and desmethylsertraline are presented in Figures 5 and 6, respectively, plotted against patient body weights to allow visual estimation of trends in change in concentration with body weight. Figures 7-14 present changes in efficacy measures from baseline plotted against sertraline concentrations to help assess possible concentration-response relationships. (Since desmethylsertraline contributes less than 10% of the overall serotonin reuptake blockade at concentrations seen at steady state following sertraline dosing, it is considered clinically inactive and was not included in the analysis of efficacy-concentration relationships.)

Of the 43 patients in this study (Table 1, Appendix 1), 40 contributed plasma concentration values to the summary listed in Table 9. There are 3 patients who do not appear in Table 9: Patient [redacted] (3 samples) and Patients [redacted] and [redacted] from [redacted] (1 sample each). Each of these was excluded according to the compliance criteria shown in Section 4.2. Mean sertraline concentration values (normalized to a 200 mg/day dose) were 85.0 ng/ml (n=8) for 6-12 year old females, 79.3 ng/ml (n=8) for 6-12 year old males, 70.5 ng/ml (n=16) for 13-18 year old females, and 76.3 ng/ml (n=8) for 13-18 year old males (Table 9). As p values in Table 9 indicate, there were no significant age or gender effects or age by gender interactions observed in the dose-normalized sertraline values.

Seventeen patients were receiving 200 mg/day (see Table 2 in Appendix 2) when plasma samples were collected, and 16 contributed plasma concentration values to the summary listed in Table 10. One patient (No. [redacted]) was excluded according to compliance criteria shown in Section 4.2. Among those receiving 200 mg/day, there appears to be a difference in sertraline concentrations between males and females 6-12 years old (females 34.9 ng/ml, n=2, and males 147 ng/ml, n=2; Table 10), but the small number does not allow any conclusion to be drawn. The absence of the same trend in the larger group in Table 9 suggests that the difference is an artifact of the small subject number. An inspection of dose-normalized concentrations vs body weight in Figures 5 and 6 suggest a tendency toward lower concentrations occurring with higher body weights, which is reflected in the negative (though not statistically significant) correlations of weight and concentration (shown in Figures 5 and 6: r=-0.22 for sertraline and -0.24 for N-desmethylsertraline). Analysis of the dose and body weight normalized concentration data in Table 9 also did not reveal any significant differences according to age or gender.

It is of interest to compare values obtained in the present study with those obtained in the core pediatric pharmacokinetic study (Study 525). Since Tmax in the core study (see the Study 525 report, Table 23) was 8.4 hr for subjects who had their last dose at 200mg, the 12-22 hr postdose collection time requested for this study corresponds to an approximation of Cmin or slightly higher. The overall mean ± SD sertraline dose-normalized concentration in the present study was 76.3 ± 39.2 ng/ml; n=40 (Table 9). Overall mean ± SD value for patients who were receiving 200 mg/day sertraline was 96.2 ± 57.2 ng/ml; n=16 (Table 10). By comparison, in Study 525, Cmin was 88.2 ± 44.9 ng/ml (n=47) at 200 mg/day (day 42 of the study). Thus, values in the two studies are consistent. A comparison with adult values is also of interest. Study 88CE21-0371/0372 [OCD indication, filed to NDA [redacted] on May 14, 1995]) evaluated the efficacy of fixed sertraline doses of 50, 100 and 200 mg/day in OCD patients 18 years and older; drug concentrations 10-24 hrs postdose were also measured. Sertraline concentrations in the 200 mg/day group were 85.3 ± 30.9 ng/ml (n=31), which is closely comparable to values observed in the present study.

Possible concentration-effect relationships were investigated by correlating sertraline concentrations with CGI Severity and Improvement for depressed patients, and CGI Severity, CYBOCS, and NIMH scale for OCD patients (Table 11, Figures 7-14). For all patients, the correlation coefficients for the change from the Study 525 baseline and the sertraline concentration at the last concentration-effect pair ranged from 0.032 to -0.335; none reached statistical significance. This is similar to findings in adult phase III studies which included plasma monitoring: in each case, significant relationships between concentration and efficacy were not seen unless placebo-treated patients were included in the correlation (refer to Studies 90CE0514 and 90CE21-0529 [panic indication, filed to NDA [redacted] on Dec. 20, 1995] and Study 88CE21-0371/0372). These findings suggest that, while sertraline has superior efficacy compared to placebo, there is no consistent relationship of sertraline plasma concentrations and therapeutic response within the clinical dosage range.

5.6 Safety

5.6.1 Adverse Experiences

Incidence of Adverse Experiences

The incidence of adverse experiences newly emergent in Study 550 is presented in Table 12.1. The most common adverse experiences (≥10%) overall were insomnia, 16% (7/43); somnolence, 12% (5/43), and headache (5/43). In the 6-12 year old group, in addition to insomnia and headache, the most common adverse experiences (≥10%) were nervousness, hyperkinesia, nausea, and coughing. In the 13-18 year age group, the most common (≥10%) were insomnia and somnolence. Two serious newly emergent adverse events (5%) occurred in Study 550 (suicidal ideation, a

serious adverse experience in Patient [redacted], and lumbar vertebral fracture in Patient [redacted]; see reports below).

The incidence of adverse experiences in Study 550 including those continuing from Study 525 is presented in Table 12.2. The most common adverse experiences (≥10%) overall were insomnia, 28% (12/43); headache, 26% (11/43); and somnolence, 14% (6/43). In the 6-12 year old group, in addition to headache and insomnia, the most common adverse experiences (≥10%) were nervousness, nausea, anorexia, coughing, and hyperkinesia. In the 13-18 year old group, in addition to insomnia, somnolence, and headache, the most common (≥10%) was agitation.

The incidence of adverse experiences that occurred during Studies 525 and 550 is presented in Table 12.3. The most common adverse experiences (≥10%) overall were headache, 40% (17/43); insomnia, 37% (16/43); nausea, 33% (14/43); somnolence, 28% (12/43); dyspepsia, 23% (10/43); anorexia, 16% (7/43); diarrhea, 14% (6/43); and dizziness and agitation, 12% (5/43) each. In the 6-12 year old group, the most common adverse experiences (≥10%) were insomnia, headache, nausea, anorexia, dyspepsia, diarrhea, somnolence, abdominal pain, vomiting, hyperkinesia, agitation, nervousness, back pain, and coughing. In the 13-18 year old group, the most common were headache, somnolence, nausea, insomnia, dyspepsia, dizziness, diarrhea, agitation, and anorexia.

Table 13 presents the incidence of adverse experiences in all patients in Study 550 by gender. The incidence in males and females were 72% (13/18) and 76% (19/25), respectively. Among males, the most common adverse experiences (≥10%) were: insomnia, 33% (6/18); headache, 22% (4/18); and somnolence, agitation, nervousness, dizziness, back pain, and anorexia, 11% (2/18) each. Among females, the most common adverse experiences (≥10%) were: headache, 28% (7/25); insomnia, 24% (6/25); somnolence, 16% (4/25); and dyspepsia, 12% (3/25).

(See Appendix II, Table 5, for individual patient data.)

Discontinuations Due to Adverse Experiences

Three sertraline patients (7%) were discontinued due to adverse experiences and are described in detail below.

Patient [redacted]
Nervousness

This [redacted] was treated with sertraline for 156 days in Study 550. [redacted] was permanently discontinued at the 200 mg/day dosage level 2 weeks prior to the final study week because of mild nervousness.

Patient [redacted]
Exacerbated Suicidal Ideation and Homicidal Ideation

This [redacted] patient was admitted to an inpatient psychiatric unit due to severe exacerbated suicidal ideation and homicidal ideation on day nine of sertraline treatment. The patient received up to 100 mg/day of sertraline during [redacted] participation in Study 550. [redacted] was discontinued from the study three days after [redacted] hospital admission. On the following day, [redacted] was inadvertently given one dose of sertraline. Three days later family therapy was initiated and [redacted] was started on bupropion 50 mg/day. The patient was discharged on day 12 of [redacted] hospitalization. At that time, [redacted] was on a bupropion dosage of 100 mg bid with instructions to further increase the dosage 2 days later to 150 mg bid.

The patient had a history of two suicide attempts within the year prior to study entry and a history of treatment with fluoxetine and nortriptyline.

Patient [redacted]
Lumbar Vertebral Fracture

This [redacted] patient received sertraline for 95 days in Study 550, at which time [redacted]. The accident occurred when [redacted] was on the 200 mg/day dosage level. After 1 day of hospitalization, [redacted] was discontinued from the study because [redacted] required Demerol, which was excluded by the protocol, as well as because of the injury. After 5 days of hospitalization, [redacted] underwent anterior spinal fusion. [redacted] was discharged after 13 days of hospitalization. (On the day of hospital discharge and on the following day, [redacted] mistakenly took sertraline at a dosage of 200 mg/day.)

Serious Adverse Events

Two patients (5%) had serious adverse events during this study and are described above.

Patient [redacted]
Exacerbated Suicidal Ideation and Homicidal Ideation

This patient was discontinued because of [redacted] serious adverse event, and is described in detail above.

Patient [redacted]
Lumbar Vertebral Fracture

This patient was discontinued because of [redacted] serious adverse event and because [redacted] was required to take medication excluded by the protocol. This is described in detail above.

5.6.2 Clinical Laboratory Test Results

Twenty-one patients (49%) had a total of 26 clinically significant laboratory abnormalities with onset during Study 550: low hematocrit levels in 15 patients, low hemoglobin levels in 2 patients, low albumin levels in 4 patients, high random glucose levels in 3 patients, and high eosinophil levels in 2 patients. For low hematocrit in the 6-12 year old and 13-18 year old groups, the incidence of clinically significant abnormalities were 63% (10/16) and 19% (5/27), respectively. See Tables 14.1 (incidence of clinically significant laboratory abnormalities by age group and test), 15.1.1 (list of clinically significant laboratory abnormalities by test and patient), and 15.2.1 (list of clinically significant laboratory abnormalities by patient and test).

Twenty-four patients (56%) had a total of 35 clinically significant laboratory abnormalities that occurred during Study 525 and 550: low hematocrit levels in 19 patients and low hemoglobin levels in 3 patients, high random glucose levels in 6 patients, low albumin levels in 4 patients, and high eosinophil levels in 3 patients. The incidence of clinically significant abnormalities for low hematocrit in the 6-12 year old and 13-18 year old groups were 63% (10/16) and 33% (9/27), respectively. See Tables 14.2 (incidence of clinically significant laboratory abnormalities by age group and test), 15.1.2 (list of clinically significant laboratory abnormalities by test and patient), and 15.2.2 (list of clinically significant laboratory abnormalities by patient and test).

Most of these laboratory values were no longer at clinically significant levels at endpoint. None of the patients were discontinued due to laboratory abnormalities and none of the mean changes from baseline were considered clinically significant. (Mean changes from the Study 550 baseline to the final values in Study 550 are shown in Table 16.1. Mean changes from the Study 525 baseline to the final values in Study 550 are shown in Table 16.2. See Appendix II, Table 6.1, for criteria for normal ranges and Appendix II, Table 6.2, for individual patient data; both Appendix Tables 6.1 and 6.2 include criteria for laboratory abnormalities. The columns in Table 6.2 of Appendix II list the study during which the laboratory values were collected as well as the study day relative to the start of study 525.)

Note that the threshold levels provided for determining clinically significant abnormalities in these children and adolescents were those adopted for adults in sertraline Safety Update II for NDA [redacted]. The normal ranges for hemoglobin and hematocrit are generally higher for adult patients than for pediatric patients.

5.6.3 Vital Signs

Criteria for clinically significant changes in vital signs are provided in Section 4.3.3 of this report. All clinically significant changes are based on comparisons with the Study 525 or Study 550 baseline vital signs. In evaluating these data, it should be noted that—from Study 550 baseline on—vital signs were to be measured with the patient in supine and standing positions, while during Study 525, vital signs were measured with the patient in the sitting position. Therefore, the determination of clinically significant changes in supine and standing measurements (and of mean changes) in Study 550 from the Study 525 baseline actually used Study 525 baseline sitting values.

In addition, 9 patients (: Patients . Patients) had vital signs measured in the sitting position at the Study 550 baseline and vital signs measured in the supine and standing position during the rest of the study. Those patients were included in the data evaluation of Study 550; their baseline sitting values were used as baseline supine and standing values.

It should be noted that the threshold values for determining clinically significant blood pressures in Studies 525 and 550 were those adopted for adults in sertraline Safety Update II for NDA . In pediatric subjects, systolic and diastolic blood pressures are lower than adult norms. This was a contributing factor to the changes noted here.

Seven patients had a total of 18 clinically significant changes in blood pressure (BP) or heart rate (HR) with onset during Study 550 (6 patients had decreases in supine diastolic blood pressure, 5 patients had decreases in standing diastolic BP, 2 patients had an increase in standing HR, 2 patients had a decrease in supine HR, 1 patient had an increase in standing systolic BP, 1 patient had an increase in supine HR, and 1 patient had a decrease in supine HR. All but four significant changes resolved by the end of study participation. Three of the seven patients with clinically significant changes were in the 6-12 year age group; 4 patients were in the 13-18 year age group. (See Table 17.1 for the incidence of clinically significant changes in vital signs with onset during Study 550, Table 18.1.1 for a list by parameter, and Table 18.2.1 for a list by patient. All individual patient vital sign data are presented in Appendix II, Table 7.)

During Studies 525 and 550, with the Study 525 baseline as reference, 17 patients had a total of 40 clinically significant changes in BP or HR (9 patients had decreases in sitting systolic BP, 4 patients had decreases in sitting diastolic BP, 6 patients had decreases in standing systolic BP, 5 patients had decreases in standing diastolic BP, 3 patients had increases in standing heart rate, 5 patients had decreases in supine systolic BP, 6 patients had decreases in supine diastolic BP, 1 patient had a increase in supine heart rate, and 1 patient had a decrease in supine heart rate). All but 8

significant changes had resolved by the end of study participation. Six of 17 patients with clinically significant changes were in the 6-12 year age group; 11 patients were in the 13-18 year age group. (See Table 17.2 for the incidence of clinically significant changes in vital signs during Studies 525 or 550, Table 18.1.2 for a list by parameter, and Table 18.2.2 for a list by patient.)

See Table 19.1 for mean changes from the Study 550 baseline to the final value and Table 19.2 for mean changes from the Study 525 baseline to the final value of Study 550. In general, these changes were small and not clinically important.

5.6.4 Body Weight

There were mean increases in body weight from the Study 550 baseline to the final measurement of 9.1 lb, 4.6 lb, and 6.3 lb, respectively, in the 6-12 year group, 13-18 year group, and in all patients (Table 19.1). In Study 550, increases ≥7% in body weight were seen in 75% (12/16) of patients in the 6-12 year group, 26% (7/27) of patients in the 13-18 year group, and 44% (19/43) of all patients (Tables 20.1 and 20.2). There were no patients with decreases ≥7% in body weight with the Study 550 baseline as reference. (All body weight data by individual patient are presented in Appendix II, Table 7.)

There were mean increases in body weight from the Study 525 baseline to the final measurement in Study 550 of 9.4 lb, 6.1 lb, and 7.3 lb, respectively, in the 6-12 year group, 13-18 year group, and all patients (Table 19.2). Increases ≥7% in body weight were seen in 75% (12/16) of patients in the 6-12 year group, 33% (9/27) of patients in the 13-18 year group, and 49% (21/43) of all patients. The ≥7% weight gain in 75% of patients in the 6-12 year old group can be attributed to normal expected growth over a 6-month period of study participation. Decreases ≥7% in body weight were seen in 13% (2/16) of patients in the 6-12 year group, 4% (1/27) of patients in the 13-18 year group, and 7% (3/43) of all patients (Tables 21.1 and 21.2).

5.6.5 Electrocardiograms

As shown in Table 22.1, 14% (6/43) of patients in Study 550 had a normal ECG at the Study 550 baseline and at least one or more abnormal ECGs at subsequent visits. (However, 5 of these 6 patients reverted to normal while continuing in the study; for the sixth patient, the abnormality appeared at the last study visit.) Five percent (2/43) of patients went from abnormal to normal. As shown in Table 22.2, 12% (5/43) of patients enrolled in Study 550 had a normal ECG at the Study 525 baseline and at least one or more abnormal ECGs at subsequent visits during Studies 525 and 550; 7% (3/43) of patients went from abnormal to normal. (ECG data by individual patient are presented in Appendix II, Table 8.)

None of the changes from either baseline in ECGs were considered clinically significant (Tables 23.1 and 23.2).

5.6.6 Concomitant Medications

At entry to Study 550, 26% (11/43) of patients had been taking one or more concomitant medications; the most common were: terfenadine, 3 patients; and multivitamins, 2 patients (Table 24.1).

During Study 550, 74% (32/43) of patients took one or more concomitant medications; the most common were: ibuprofen, 9 patients; acetaminophen, 8 patients; amoxicillin, 6 patients; pseudoephedrine HCl, 5 patients; multivitamins and terfenadine, 4 patients each (Table 25.1 and Appendix II, Table 9.2).

(For concomitant medications at entry to Study 525, see Table 24.2 and Appendix II, Table 9.1. For concomitant medications during Studies 525 and 550, see Table 25.2 and Appendix II, Table 10.)

5.6.7 Concurrent Illnesses

At entry into Study 550, 40% (17/43) of patients had one or more concurrent illnesses; the most common were hay fever, 7 patients; headache, 4 patients; asthma, 3 patients; and acne, 2 patients (Table 26.1 and Appendix II, Table 11.1).

During Study 550, 58% (25/43) of patients developed one or more concurrent illnesses; the most common were: upper respiratory infection, 10 patients; influenza, 7 patients; sore throat, 3 patients; and allergies unspecified and strep throat, 2 patients each (Table 27.1 and Appendix II, Table 12).

(For concurrent illnesses at entry to Study 525, see Table 26.2 and Appendix II, Table 11.2. For concurrent illnesses present occurring during Studies 525 or 550, see Table 27.2 and Appendix II, Table 12.)

6. SUMMARY/CONCLUSIONS

1. The objective of this 24-week open label study was to evaluate the long-term safety and efficacy of sertraline beginning at 50 mg/day and titrated up to a maximum of 200 mg/day as clinically indicated.

2. The safety and efficacy population consisted of 43 patients from 6 to 18 years of age who had a diagnosis of OCD or depression according to DSM-III-R and who had previously completed Study 525, a 51-day multiple dose pharmacokinetic trial of sertraline. Depression was diagnosed in 32 patients, OCD in 10 patients, and both OCD and depression in 1 patient. At endpoint, the mean maximum dose was

153, 159, and 157 mg/day in the 6-12 year group, in the 13-18 year group, and in patients overall. The mean duration of treatment was 149.9, 110.0, and 124.8 days in the 6-12 year group, in the 13-18 year group, and in patients overall, respectively.

3. For OCD patients at endpoint in Study 550, there was statistically significant improvement in OCD as measured by the CY-BOCS and NIMH rating scales from both the Study 525 and Study 550 baselines. In OCD patients, CGI Severity showed a statistically significant decrease in severity from the Study 525 baseline to the endpoint in Study 550; no significant change was seen for CGI Improvement. In depression patients, CGI Severity at endpoint in Study 550 showed statistically significant decreases from both the Study 525 and 550 baselines; CGI Improvement demonstrated statistically significant improvement from the Study 550 baseline. The same results pertained to all patients combined.

4. There was no statistically significant difference for mean sertraline or N-desmethylsertraline plasma concentrations by age group (6-12 and 13-18 years) or gender whether dose normalized (to the 200-mg dose) or dose and body weight normalized.

5. There were no statistically significant plasma concentration-effect relationships in patients with OCD and/or depression for any efficacy variable.

6. The most common (≥ 10%) treatment-emergent adverse experiences overall in this study were insomnia, somnolence, and headache, which are also commonly seen in adult patients. Three patients (7%) discontinued due to adverse experiences. Clinically significant laboratory abnormalities were largely limited to low hematocrit levels based upon normally higher adult reference values. Clinically significant vital sign abnormalities were largely limited to decreased systolic or diastolic blood pressure based upon normally higher adult references values. The mean changes from baseline in laboratory values and vital signs were not considered clinically important. There were no unusual or unexpected changes in body weight and no clinically significant ECG abnormalities. Overall, the safety profile in Study 550 was generally similar to Study 525, the tolerance and pharmacokinetic study that preceded Study 550. The adverse experience profiles seen in both 6-12 year old and 13-17 year old patients were similar to those previously reported in the Zoloft package labeling for adults.

7. In conclusion, based on the above results, sertraline was shown to be safe and effective when administered for a long term (24 weeks) at a dose of 50 to 200 mg/day to children and adolescents 6-18 years old who were diagnosed with OCD and/or depression.

REFERENCES

1. [redacted]

TABLES

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 1: DISTRIBUTION OF RANDOMIZED PATIENTS BY SITE AND AGE GROUP

	AGE GROUP								
	6-12 YEARS			13-18 YEARS			TOTAL		
SITE	COMPLETED STUDY 525	ENTERED STUDY 550	COMPLETED STUDY 550	COMPLETED STUDY 525	ENTERED STUDY 550	COMPLETED STUDY 550	COMPLETED STUDY 525	ENTERED STUDY 550	COMPLETED STUDY 550
[redacted]	3	2	2	6	4	4	9	6	6
	4	3	1	12	11	4	16	14	5
	1	0	0	1	0	0	2	0	0
	0	0	0	1	0	0	1	0	0
	9	8	6	10	9	3	19	17	9
	3	3	1	3	3	1	6	6	2
TOTAL	20	16	10	33	27	12	53	43	22

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 2: SUMMARY OF PATIENT CHARACTERISTICS

		AGE GROUP		
		6-12 YEARS	13-18 YEARS	TOTAL
SEX:	FEMALE	8	17	25
	MALE	8	10	18
	TOTAL	16	27	43
RACE:	WHITE	13	22	35
	BLACK	1	4	5
	OTHER	2	1	3
	TOTAL	16	27	43
AGE(YEARS):	MEAN	10.7	14.9	13.3
	STANDARD DEV.	1.4	1.4	2.5
	MINIMUM	7	13	7
	MAXIMUM	12	17	17
	N	16	27	43
WEIGHT(LBS.):	MEAN	97.9	128.4	117.0
	STANDARD DEV.	35.0	41.4	41.5
	MINIMUM	70.0	76.0	70.0
	MAXIMUM	187.5	297.0	297.0
	N	16	27	43
MAJOR DIAGNOSIS	OCD	2	8	10
	DEPRESSION	13	19	32
	OCD AND DEPRESSION	1	0	1
	TOTAL	16	27	43

RACE, SEX AND DIAGNOSIS DETERMINED AT STUDY 525 BASELINE. AGE AND WEIGHT DETERMINED AT STUDY 550 BASELINE.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 3: DURATION OF THERAPY (DAYS)

	AGE: 6 - 12	AGE:13 - 18	TOTAL
NUMBER OF PATIENTS	16	27	43
DURATION CATEGORY (DAYS)			
1- 28	0	5	5
29- 56	0	4	4
57- 84	2	1	3
85-112	1	2	3
113-140	0	2	2
141-168	8	5	13
>=169	5	8	13
MEAN DURATION (DAYS)	149.9	110.0	124.8
RANGE (DAYS)	57 -202	1 -217	1 -217

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 4.1: SUMMARY OF REASONS FOR DISCONTINUATION

	NUMBER OF PATIENTS		
REASON FOR DISCONTINUATION	AGE 6-12	AGE 13-18	TOTAL
TOTAL NO. OF PATIENTS	16	27	43
NO. OF PATIENTS DISCONTINUED	6	15	21
LOST TO FOLLOW-UP	2	8	10
OTHER	3	5	8
ADVERSE EXPERIENCE	1	2	3

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 4.2: REASON FOR DISCONTINUATION - PATIENT LISTING

GRANT	PATIENT	SEX	AGE (YRS)	DOSE AT TIME OF WITHDRAWAL (MG/DAY)	DURATION OF THERAPY(DAYS)	REASON
[redacted]				50	149	LOST TO FOLLOW-UP
				150	76	OTHER
				200	58	LOST TO FOLLOW-UP
				200	44	LOST TO FOLLOW-UP
				200	29	LOST TO FOLLOW-UP
				225	135	LOST TO FOLLOW-UP
				100	28	LOST TO FOLLOW-UP
				150	90	LOST TO FOLLOW-UP
				100	13	ADVERSE EXPERIENCE
				100	57	OTHER
				200	154	ADVERSE EXPERIENCE
				175	142	OTHER
				150	29	LOST TO FOLLOW-UP
				150	32	LOST TO FOLLOW-UP
				50	10	OTHER
				50	1	OTHER
				150	139	OTHER

[redacted] [redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 4.2: REASON FOR DISCONTINUATION - PATIENT LISTING

GRANT	PATIENT	SEX	AGE (YRS)	DOSE AT TIME OF WITHDRAWAL (MG/DAY)	DURATION OF THERAPY(DAYS)	REASON
[redacted]				200	157	LOST TO FOLLOW-UP
				150	107	OTHER
				200	108	ADVERSE EXPERIENCE
				50	22	OTHER

[redacted] [redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 5: MEAN MAXIMUM DOSE BY STUDY WEEK AND AT ENDPOINT

	AGE GROUP								
	6-12 YEARS			13-18 YEARS			OVERALL		
STUDY WEEK	N	DOSE(MG) MEAN	STD	N	DOSE(MG) MEAN	STD	N	DOSE(MG) MEAN	STD
1	16	56	17.1	27	63	22.3	43	60	20.6
2	16	103	22.1	26	102	17.2	42	102	19.0
3-4	16	159	41.7	24	165	34.5	40	163	37.1
5-6	16	161	47.4	22	194	51.1	38	180	51.7
7-8	16	150	44.7	19	191	19.0	35	172	38.7
9-12	16	147	46.4	18	183	22.7	34	166	39.8
13-16	14	157	43.2	17	181	25.8	31	170	36.2
17-20	13	158	53.4	15	180	28.7	28	170	42.7
21-24	13	158	53.4	13	175	33.9	26	166	44.7
>24	5	170	27.4	8	181	39.5	13	177	34.6
ENDPOINT	16	153	49.9	27	159	49.1	43	157	48.9

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 6: SUMMARY OF EFFICACY VARIABLES AT BASELINE

		------ STUDY 0525 ------			------ STUDY 0550 ------		
VARIABLE	GROUP	N	MEAN	SD	N	MEAN	SD
CY-BOCS	OCD	11	26.09	4.66	11	13.45	9.52
NIMH OC SCALE	OCD	11	10.00	1.84	11	6.00	3.29
CGI SEVERITY	OCD	11	5.09	1.14	11	3.18	1.33
	DEPRESSION	32(1)	4.78	0.71	33	2.76	1.03
	ALL PATIENTS	42(1,2)	4.86	0.84	43(2)	2.88	1.12
CGI IMPROVEMENT(3)	OCD				11	2.55	1.29
	DEPRESSION				33	2.61	1.06
	ALL PATIENTS				43(2)	2.63	1.09

1. PATIENT [redacted] IS MISSING STUDY 0525 BASELINE CGI SEVERITY.

2. NUMBERS OF PATIENTS IN OCD AND DEPRESSION GROUPS DO NOT ADD TO THIS TOTAL BECAUSE PATIENT [redacted] IS INCLUDED IN BOTH GROUPS.

3. BASELINE CGI IMPROVEMENT FOR STUDY 0550 IS LAST MEASURE FROM STUDY 0525.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.1.1: SUMMARY OF CY-BOCS IN OCD PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0525 BASELINE N	MEAN	SD	P-VALUE**	CHANGE FROM STUDY 0550 BASELINE N	MEAN	SD	P-VALUE**
0*	11	-12.64	10.61	0.002				
1	11	-13.64	11.25	0.002	11	-1.00	3.55	0.267
2	11	-12.82	9.64	0.001	11	-0.18	5.72	0.703
4	11	-13.73	8.66	0.001	11	-1.09	5.63	0.351
6	9	-16.11	8.59	0.003	9	-4.56	6.54	0.078
8	9	-17.44	11.74	0.003	9	-3.78	7.38	0.218
12	10	-17.60	8.60	0.002	10	-4.50	7.98	0.105
16	8	-17.63	7.60	0.007	8	-6.25	7.91	0.156
20	10	-18.40	7.81	0.002	10	-5.30	8.64	0.070
24	9	-18.78	6.46	0.003	9	-4.44	8.53	0.210
ENDPOINT	11	-19.27	7.11	0.001	11	-6.64	7.83	0.029

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* STUDY WEEK 0 = STUDY 0550 BASELINE(DAY 51 OF STUDY 0525).

** FROM WILCOXON TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.1.2: SUMMARY OF NIMH OC SCALE IN OCD PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0525 BASELINE N	MEAN	SD	P-VALUE**	CHANGE FROM STUDY 0550 BASELINE N	MEAN	SD	P-VALUE**
0*	11	-4.00	3.69	0.003				
1	11	-4.45	3.75	0.003	11	-0.45	1.13	0.375
2	11	-4.27	3.90	0.005	11	-0.27	1.95	0.625
4	11	-4.55	3.88	0.002	11	-0.55	1.81	0.328
6	9	-5.44	4.19	0.011	9	-1.78	1.86	0.031
8	9	-5.78	4.35	0.011	9	-1.89	2.09	0.031
12	10	-6.20	3.22	0.002	10	-2.40	2.46	0.023
16	8	-6.38	2.92	0.007	8	-2.63	2.20	0.031
20	10	-6.40	3.06	0.002	10	-2.60	2.72	0.031
24	9	-6.78	2.64	0.003	9	-2.56	2.74	0.046
ENDPOINT	11	-6.82	2.27	0.001	11	-2.82	2.68	0.010

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* STUDY WEEK 0 = STUDY 0550 BASELINE(DAY 51 OF STUDY 0525).

** FROM WILCOXON TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.1.3: SUMMARY OF CGI SEVERITY IN OCD PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0525 BASELINE N	MEAN	SD	P-VALUE**	CHANGE FROM STUDY 0550 BASELINE N	MEAN	SD	P-VALUE**
0*	11	-1.91	1.76	0.003				
1	11	-2.27	1.95	0.007	11	-0.36	0.92	0.359
2	11	-2.09	1.81	0.003	11	-0.18	1.25	0.812
4	11	-2.00	1.73	0.002	11	-0.09	1.22	1.000
6	9	-2.11	1.83	0.007	9	-0.44	1.24	0.500
8	9	-2.44	1.88	0.007	9	-0.56	1.24	0.375
12	10	-2.70	1.57	0.002	10	-0.90	1.29	0.093
16	8	-2.63	1.69	0.007	8	-0.88	0.99	0.062
20	10	-2.50	1.58	0.002	10	-0.70	1.64	0.281
24	9	-2.78	1.56	0.003	9	-0.78	1.64	0.250
ENDPOINT	11	-2.91	1.45	0.001	11	-1.00	1.61	0.093

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* STUDY WEEK 0 = STUDY 0550 BASELINE(DAY 51 OF STUDY 0525).

** FROM WILCOXON TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.1.4: SUMMARY OF CGI IMPROVEMENT IN OCD PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0550 BASELINE* N	MEAN	SD	P-VALUE**
1	11	-0.45	0.93	0.250
2	11	-0.45	1.29	0.500
4	11	-0.45	1.44	0.500
6	9	-0.78	1.30	0.125
8	9	-0.89	1.27	0.062
12	10	-1.20	1.23	0.015
16	7	-1.14	0.69	0.031
20	10	-0.70	1.89	0.242
24	9	-0.89	1.45	0.156
ENDPOINT	11	-1.00	1.48	0.078

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* STUDY 0550 BASELINE IS DAY 51 OF STUDY 0525.

** FROM WILCOXON TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.2.1: SUMMARY OF CGI SEVERITY IN DEPRESSION PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0525 BASELINE N	MEAN	SD	P-VALUE**	CHANGE FROM STUDY 0550 BASELINE N	MEAN	SD	P-VALUE**
0*	32(1)	-2.00	1.30	0.001				
1	32	-1.97	1.12	0.001	32(2)	0.03	1.06	0.868
2	28	-2.32	0.98	0.001	29	-0.41	1.18	0.069
4	29	-2.66	0.97	0.001	29	-0.62	1.15	0.006
6	25	-2.92	1.00	0.001	25	-0.84	1.14	0.001
8	25	-2.92	1.15	0.001	25	-0.80	1.22	0.003
12	22	-3.00	1.11	0.001	22	-0.91	1.31	0.003
16	19	-2.95	1.03	0.001	19	-0.84	1.07	0.002
20	19	-2.95	1.27	0.001	19	-0.84	1.34	0.013
24	14	-2.71	1.20	0.001	14	-0.64	1.22	0.069
ENDPOINT	32	-2.78	1.41	0.001	33	-0.76	1.35	0.002

---

1. PATIENT [redacted] IS MISSING STUDY 0525 BASELINE CGI SEVERITY.

2. PATIENT [redacted] IS NOT INCLUDED IN STUDY WEEK 1 ANALYSIS SINCE THE FIRST VISIT OCCURRED TWO WEEKS AFTER THE BASELINE VISIT.

* STUDY WEEK 0 = STUDY 0550 BASELINE(DAY 51 OF STUDY 0525).

** FROM T-TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.2.2: SUMMARY OF CGI IMPROVEMENT IN DEPRESSION PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0550 BASELINE* N	MEAN	SD	P-VALUE**
1	32(1)	-0.06	1.32	0.790
2	29	-0.66	1.14	0.004
4	29	-0.69	1.34	0.009
6	25	-0.76	1.30	0.007
8	25	-0.84	1.25	0.002
12	22	-1.09	1.15	0.001
16	19	-1.11	1.24	0.001
20	19	-0.95	1.27	0.004
24	14	-1.00	1.36	0.016
ENDPOINT	33	-0.70	1.49	0.011

1. PATIENT [redacted] IS NOT INCLUDED IN STUDY WEEK 1 ANALYSIS SINCE THE FIRST VISIT OCCURRED TWO WEEKS AFTER THE BASELINE VISIT.

* STUDY 0550 BASELINE IS DAY 51 OF STUDY 0525.

** FROM T-TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.3.1: SUMMARY OF CGI SEVERITY IN ALL PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0525 BASELINE N	MEAN	SD	P-VALUE**	CHANGE FROM STUDY 0550 BASELINE N	MEAN	SD	P-VALUE**
0*	42(1)	-1.95	1.41	0.001				
1	42	-2.00	1.34	0.001	42(2)	-0.05	1.03	0.767
2	38	-2.29	1.25	0.001	39	-0.41	1.14	0.030
4	39	-2.51	1.23	0.001	39	-0.54	1.12	0.004
6	34	-2.71	1.29	0.001	34	-0.74	1.16	0.001
8	33	-2.76	1.37	0.001	33	-0.73	1.23	0.001
12	31	-2.94	1.26	0.001	31	-0.97	1.25	0.001
16	27	-2.85	1.23	0.001	27	-0.85	1.03	0.001
20	28	-2.82	1.39	0.001	28	-0.86	1.41	0.003
24	22	-2.73	1.35	0.001	22	-0.73	1.39	0.022
ENDPOINT	42	-2.76	1.43	0.001	43	-0.79	1.46	0.001

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1. PATIENT [redacted] IS MISSING STUDY 0525 BASELINE CGI SEVERITY.

2. PATIENT [redacted] IS NOT INCLUDED IN STUDY WEEK 1 ANALYSIS SINCE THE FIRST VISIT OCCURRED TWO WEEKS AFTER THE BASELINE VISIT.

* STUDY WEEK 0 = STUDY 0550 BASELINE(DAY 51 OF STUDY 0525).

** FROM T-TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 7.3.2: SUMMARY OF CGI IMPROVEMENT IN ALL PATIENTS BY STUDY WEEK

STUDY WEEK	CHANGE FROM STUDY 0550 BASELINE* N	MEAN	SD	P-VALUE**
1	42(1)	-0.17	1.25	0.391
2	39	-0.64	1.16	0.001
4	39	-0.69	1.30	0.002
6	34	-0.76	1.28	0.001
8	33	-0.88	1.24	0.001
12	31	-1.16	1.16	0.001
16	26	-1.12	1.11	0.001
20	28	-0.93	1.46	0.002
24	22	-1.00	1.38	0.002
ENDPOINT	43	-0.79	1.49	0.001

1. PATIENT [redacted] IS NOT INCLUDED IN STUDY WEEK 1 ANALYSIS SINCE THE FIRST VISIT OCCURRED TWO WEEKS AFTER THE BASELINE VISIT.

* STUDY 0550 BASELINE IS DAY 51 OF STUDY 0525.

** FROM T-TEST.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 8: SUMMARY OF EFFICACY VARIABLES BY AGE GROUP

AGE GROUP	DIAGNOSIS GROUP	VARIABLE	N	MEAN SD 525 BASELINE		MEAN SD 550 BASELINE		MEAN SD 550 ENDPOINT	
AGE 6-12	OCD	CY-BOCS	3	27.00	6.08	13.67	5.86	2.67	2.31
		NIMH OC SCALE	3	8.67	0.58	5.33	1.15	1.33	0.58
		CGI SEVERITY	3	4.33	0.58	3.00	1.00	1.00	0.00
		CGI IMPROVEMENT	3	-		1.67	0.58	1.00	0.00
	DEPRESSION	CGI SEVERITY	14	4.86	0.77	2.43	0.76	1.93	0.92
		CGI IMPROVEMENT	14	-		2.36	0.74	1.64	0.74
	ALL PATIENTS	CGI SEVERITY	16(1)	4.75	0.77	2.56	0.81	1.81	0.91
		CGI IMPROVEMENT	16(1)	-		2.31	0.70	1.56	0.73
AGE 13-18	OCD	CY-BOCS	8	25.75	4.46	13.38	10.94	8.38	7.82
		NIMH OC SCALE	8	10.50	1.93	6.25	3.85	3.88	2.70
		CGI SEVERITY	8	5.38	1.19	3.25	1.49	2.63	1.51
		CGI IMPROVEMENT	8	-		2.88	1.36	1.75	0.71
	DEPRESSION	CGI SEVERITY	19	4.72	0.67	3.00	1.15	2.05	1.13
		CGI IMPROVEMENT	19	-		2.79	1.23	2.11	1.33
	ALL PATIENTS	CGI SEVERITY	27	4.92	0.89	3.07	1.24	2.22	1.25
		CGI IMPROVEMENT	27	-		2.81	1.24	2.00	1.18

1. NUMBERS OF PATIENTS IN OCD AND DEPRESSION GROUPS DO NOT ADD TO THIS TOTAL BECAUSE PATIENT [redacted] IS INCLUDED IN BOTH GROUPS.

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 9: MEAN NORMALIZED PLASMA CONCENTRATIONS BY AGE GROUP AND GENDER

		MEAN SD							P-VALUE***		
		6-12 YEARS			13-18 YEARS						AGE BY GENDER
DRUG	UNITS	FEMALES	MALES	OVERALL	FEMALES	MALES	OVERALL	OVERALL	AGE	GENDER	INTERACTION
SERTRALINE											
	NG/ML *	85.043.2 (N=8)	79.341.1 (N=8)	82.240.8 (N=16)	70.538.9 (N=16)	76.339.6 (N=8)	72.438.4 (N=24)	76.339.2 (N=40)	0.514	0.998	0.669
	NG/ML **	81.033.3 (N=8)	55.427.6 (N=8)	68.232.4 (N=16)	70.040.0 (N=16)	83.346.5 (N=8)	74.441.8 (N=24)	71.938.0 (N=40)	0.507	0.628	0.132
DESMETHYL											
	NG/ML *	16090.1 (N=8)	13459.7 (N=8)	14775.1 (N=16)	10949.8 (N=16)	12063.8 (N=8)	11353.6 (N=24)	12664.5 (N=40)	0.132	0.703	0.390
	NG/ML **	15573.6 (N=8)	94.941.8 (N=8)	12565.7 (N=16)	10850.2 (N=16)	12971.6 (N=8)	11557.5 (N=24)	11960.3 (N=40)	0.732	0.319	0.042

* CONCENTRATION VALUE FOR EACH PATIENT WAS OBTAINED BY DOSE NORMALIZING((200/DOSE)*CONCENTRATION) AND AVERAGING OVER STUDY WEEKS 1 TO 24.

** CONCENTRATION VALUE FOR EACH PATIENT WAS OBTAINED BY DOSE AND BODYWEIGHT NORMALIZING ((200/DOSE)*(BODYWEIGHT AT A VISIT/MEAN BODYWEIGHT FOR ALL PATIENTS AT STUDY 550 BASELINE)*CONCENTRATION) AND AVERAGING OVER STUDY WEEKS 1 TO 24.

*** FROM TWO-WAY ANALYSIS OF VARIANCE MODEL.

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 10: MEAN PLASMA CONCENTRATIONS IN PATIENTS RECEIVING 200 MG/DAY SERTRALINE

		MEAN SD						
		6-12 YEARS			13-18 YEARS			
DRUG	UNITS	FEMALES	MALES	OVERALL	FEMALES	MALES	OVERALL	OVERALL
SERTRALINE								
	NG/ML *	34.99.26 (N=2)	14744.5 (N=2)	90.769.6 (N=4)	89.344.1 (N=6)	10769.0 (N=6)	98.056.0 (N=12)	96.257.2 (N=16)
	NG/ML **	41.89.92 (N=2)	99.032.6 (N=2)	70.438.4 (N=4)	92.348.5 (N=6)	11361.9 (N=6)	10354.1 (N=12)	94.651.5 (N=16)
DESMETHYL								
	NG/ML *	63.10.460 (N=2)	1559.19 (N=2)	10953.1 (N=4)	12337.2 (N=6)	13470.7 (N=6)	12954.2 (N=12)	12452.8 (N=16)
	NG/ML **	81.040.0 (N=2)	1048.99 (N=2)	92.527.1 (N=4)	12844.8 (N=6)	14675.3 (N=6)	13759.8 (N=12)	12656.3 (N=16)

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* CONCENTRATION VALUE FOR EACH PATIENT IS LAST VALUE AT 200 MG DOSE.

** CONCENTRATIONS VALUE FOR EACH PATIENT IS LAST VALUE AT 200 MG DOSE NORMALIZED BY BODYWEIGHT
((BODYWEIGHT AT A VISIT/MEAN BODYWEIGHT FOR ALL PATIENTS AT STUDY 550 BASELINE)*CONCENTRATION)

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 11: SUMMARY OF SERTRALINE CONCENTRATION-EFFECT RELATIONSHIP(1)

GROUP	PARAMETER(2)	N	CORRELATION COEFFICIENT	P-VALUE
OCD				
	CY-BOCS	11	-0.065	0.849
	NIMH OC SCALE	11	0.032	0.924
	CGI SEVERITY	11	0.025	0.941
	CGI IMPROVEMENT	11	-0.051	0.882
DEPRESSION				
	CGI SEVERITY	32(3)	-0.335	0.061
	CGI IMPROVEMENT	33	-0.144	0.423
ALL PATIENTS				
	CGI SEVERITY	42(3)	-0.279	0.073
	CGI IMPROVEMENT	43	-0.152	0.330

1. AT LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR(BOTH SERTRALINE CONCENTRATION AND EFFICACY PARAMETER NOT MISSING) IN STUDY 0550.

2. CHANGE FROM 0525 BASELINE FOR CY-BOCS, NIMH SCORE AND CGI SEVERITY.

3. PATIENT [redacted] IS MISSING 0525 BASELINE CGI SEVERITY.

[redacted]

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.1: INCIDENCE AND SEVERITY OF NEWLY EMERGENT ADVERSE EXPERIENCES DURING STUDY 550

ADVERSE EXPERIENCE	ALL PATIENTS PATIENT INCIDENCE NO. PTS. (%)	ALL PATIENTS --SEVERITY- MID	MOD	SEV	6 - 12 YEARS PATIENT INCIDENCE NO. PTS. (%)	6 - 12 YEARS --SEVERITY- MID	MOD	SEV	13 - 18 YEARS PATIENT INCIDENCE NO. PTS. (%)	13 - 18 YEARS --SEVERITY- MID	MOD	SEV
TOTAL NO. PATIENTS	43				16				27			
NO. OF PTS. WITH ADVERSE EXPERIENCE	25 (58.1%)				9 (56.3%)				16 (59.3%)			
NO. OF PTS. DISCONTINUED DUE TO ADV. EXP.	3 (7.0%)				1 (6.3%)				2 (7.4%)			
PSYCHIATRIC DISORDERS												
INSOMNIA	7 (16.3%)	3	4	0	2 (12.5%)	2	0	0	5 (18.5%)	1	4	0
SOMNOLENCE	5 (11.6%)	4	1	0	1 (6.3%)	1	0	0	4 (14.8%)	3	1	0
NERVOUSNESS	3 (7.0%)	2	1	0	2 (12.5%)	2	0	0	1 (3.7%)	0	1	0
AGITATION	2 (4.7%)	1	1	0	0 (0.0%)	0	0	0	2 (7.4%)	1	1	0
SUICIDE IDEATION	1 (2.3%)	0	0	1	0 (0.0%)	0	0	0	1 (3.7%)	0	0	1
CENTR & PERIPH NERV SYST DISORDERS												
HEADACHE	5 (11.6%)	4	1	0	3 (18.8%)	3	0	0	2 (7.4%)	1	1	0
HYPERKINESIA	3 (7.0%)	1	2	0	2 (12.5%)	0	2	0	1 (3.7%)	1	0	0
DIZZINESS	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
TREMOR	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
GASTRO-INTESTINAL DISORDERS												
DYSPEPSIA	3 (7.0%)	2	1	0	1 (6.3%)	0	1	0	2 (7.4%)	2	0	0
NAUSEA	2 (4.7%)	2	0	0	2 (12.5%)	2	0	0	0 (0.0%)	0	0	0
ABDOMINAL PAIN	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
VOMITING	1 (2.3%)	0	1	0	1 (6.3%)	0	1	0	0 (0.0%)	0	0	0
BODY AS A WHOLE - GENERAL DISORDERS												
CHEST PAIN	2 (4.7%)	0	2	0	1 (6.3%)	0	1	0	1 (3.7%)	0	1	0
ASTHENIA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
BACK PAIN	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
HOT FLUSHES	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
RESPIRATORY SYSTEM DISORDERS												
COUGHING	2 (4.7%)	2	0	0	2 (12.5%)	2	0	0	0 (0.0%)	0	0	0

-- (CONTINUED) --

EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.1: INCIDENCE AND SEVERITY OF NEWLY EMERGENT ADVERSE EXPERIENCES DURING STUDY 550

	ALL PATIENTS				6 - 12 YEARS				13 - 18 YEARS			
ADVERSE EXPERIENCE	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV
EPISTAXIS	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
AUTONOMIC NERVOUS SYSTEM DISORDERS												
ANOREXIA	2 (4.7%)	2	0	0	1 (6.3%)	1	0	0	1 (3.7%)	1	0	0
HEART RATE AND RHYTHM DISORDERS												
PALPITATION	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
REPRODUCTIVE DISORDERS, FEMALE												
DYSMENORRHEA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
APPLICATION SITE DISORDERS												
SKIN NODULE	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
OTHER ADVERSE EVENTS												
INJURY ACCIDENTAL	1 (2.3%)	0	0	1	0 (0.0%)	0	0	0	1 (3.7%)	0	0	1

---- (END) ----

EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

[redacted]

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.2: INCIDENCE AND SEVERITY OF ADVERSE EXPERIENCES DURING STUDY 550[a]

ADVERSE EXPERIENCE	ALL PATIENTS: PATIENT INCIDENCE NO. PTS. (%)	ALL PATIENTS: SEVERITY MID	ALL PATIENTS: SEVERITY MOD	ALL PATIENTS: SEVERITY SEV	6 - 12 YEARS: PATIENT INCIDENCE NO. PTS. (%)	6 - 12 YEARS: SEVERITY MID	6 - 12 YEARS: SEVERITY MOD	6 - 12 YEARS: SEVERITY SEV	13 - 18 YEARS: PATIENT INCIDENCE NO. PTS. (%)	13 - 18 YEARS: SEVERITY MID	13 - 18 YEARS: SEVERITY MOD	13 - 18 YEARS: SEVERITY SEV
TOTAL NO. PATIENTS	43				16				27			
NO. OF PTS. WITH ADVERSE EXPERIENCE	32 (74.4%)				13 (81.3%)				19 (70.4%)			
NO. OF PTS. DISCONTINUED DUE TO ADV. EXP.	3 (7.0%)				1 (6.3%)				2 (7.4%)			
PSYCHIATRIC DISORDERS												
INSOMNIA	12 (27.9%)	7	5	0	5 (31.3%)	4	1	0	7 (25.9%)	3	4	0
SOMNOLENCE	6 (14.0%)	5	1	0	1 (6.3%)	1	0	0	5 (18.5%)	4	1	0
AGITATION	4 (9.3%)	1	3	0	1 (6.3%)	0	1	0	3 (11.1%)	1	2	0
NERVOUSNESS	3 (7.0%)	2	1	0	2 (12.5%)	2	0	0	1 (3.7%)	0	1	0
AGGRESSIVE REACTION	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
SUICIDE IDEATION	1 (2.3%)	0	0	1	0 (0.0%)	0	0	0	1 (3.7%)	0	0	1
CENTR & PERIPH NERV SYST DISORDERS												
HEADACHE	11 (25.6%)	10	1	0	7 (43.8%)	7	0	0	4 (14.8%)	3	1	0
DIZZINESS	3 (7.0%)	2	1	0	1 (6.3%)	1	0	0	2 (7.4%)	1	1	0
HYPERKINESIA	3 (7.0%)	1	2	0	2 (12.5%)	0	2	0	1 (3.7%)	1	0	0
TREMOR	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
GASTRO-INTESTINAL DISORDERS												
DYSPEPSIA	3 (7.0%)	2	1	0	1 (6.3%)	0	1	0	2 (7.4%)	2	0	0
NAUSEA	3 (7.0%)	3	0	0	2 (12.5%)	2	0	0	1 (3.7%)	1	0	0
ABDOMINAL PAIN	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
VOMITING	1 (2.3%)	0	1	0	1 (6.3%)	0	1	0	0 (0.0%)	0	0	0
BODY AS A WHOLE - GENERAL DISORDERS												
BACK PAIN	2 (4.7%)	1	1	0	1 (6.3%)	1	0	0	1 (3.7%)	0	1	0
CHEST PAIN	2 (4.7%)	0	2	0	1 (6.3%)	0	1	0	1 (3.7%)	0	1	0
ASTHENIA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
HOT FLUSHES	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0

-- (CONTINUED) --

[a]INCLUDED EVENTS WHICH WERE ONGOING FROM 525
EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

[redacted]

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.2: INCIDENCE AND SEVERITY OF ADVERSE EXPERIENCES DURING STUDY 550[a]

	ALL PATIENTS				6 - 12 YEARS				13 - 18 YEARS			
ADVERSE EXPERIENCE	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV
AUTONOMIC NERVOUS SYSTEM DISORDERS												
ANOREXIA	4 (9.3%)	4	0	0	3 (18.8%)	3	0	0	1 (3.7%)	1	0	0
RESPIRATORY SYSTEM DISORDERS												
COUGHING	2 (4.7%)	2	0	0	2 (12.5%)	2	0	0	0 (0.0%)	0	0	0
EPISTAXIS	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
HEART RATE AND RHYTHM DISORDERS												
PALPITATION	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
REPRODUCTIVE DISORDERS, FEMALE												
DYSMENORRHEA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
APPLICATION SITE DISORDERS												
SKIN NODULE	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
OTHER ADVERSE EVENTS												
INJURY ACCIDENTAL	1 (2.3%)	0	0	1	0 (0.0%)	0	0	0	1 (3.7%)	0	0	1

---- (END) ----

[a]INCLUDED EVENTS WHICH WERE ONGOING FROM 525
EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.3: INCIDENCE AND SEVERITY OF ADVERSE EXPERIENCES DURING STUDY 525 AND 550

ADVERSE EXPERIENCE	ALL PATIENTS: PATIENT INCIDENCE NO. PTS. (%)	ALL PATIENTS: SEVERITY MID	MOD	SEV	6 - 12 YEARS: PATIENT INCIDENCE NO. PTS. (%)	6 - 12 YEARS: SEVERITY MID	MOD	SEV	13 - 18 YEARS: PATIENT INCIDENCE NO. PTS. (%)	13 - 18 YEARS: SEVERITY MID	MOD	SEV
TOTAL NO. PATIENTS	43				16				27			
NO. OF PTS. WITH ADVERSE EXPERIENCE	39 (90.7%)				14 (87.5%)				25 (92.6%)			
NO. OF PTS. DISCONTINUED DUE TO ADV. EXP.	3 (7.0%)				1 (6.3%)				2 (7.4%)			
GASTRO-INTESTINAL DISORDERS												
NAUSEA	14 (32.6%)	12	2	0	6 (37.5%)	6	0	0	8 (29.6%)	6	2	0
DYSPEPSIA	10 (23.3%)	8	2	0	5 (31.3%)	3	2	0	5 (18.5%)	5	0	0
DIARRHEA	6 (14.0%)	3	3	0	3 (18.8%)	2	1	0	3 (11.1%)	1	2	0
ABDOMINAL PAIN	3 (7.0%)	3	0	0	2 (12.5%)	2	0	0	1 (3.7%)	1	0	0
VOMITING	3 (7.0%)	1	2	0	2 (12.5%)	1	1	0	1 (3.7%)	0	1	0
CONSTIPATION	2 (4.7%)	2	0	0	0 (0.0%)	0	0	0	2 (7.4%)	2	0	0
CENTR & PERIPH NERV SYST DISORDERS												
HEADACHE	17 (39.5%)	16	1	0	8 (50.0%)	8	0	0	9 (33.3%)	8	1	0
DIZZINESS	5 (11.6%)	4	1	0	1 (6.3%)	1	0	0	4 (14.8%)	3	1	0
HYPERKINESIA	4 (9.3%)	1	3	0	2 (12.5%)	0	2	0	2 (7.4%)	1	1	0
HYPOESTHESIA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
TREMOR	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
PSYCHIATRIC DISORDERS												
INSOMNIA	16 (37.2%)	11	5	0	8 (50.0%)	7	1	0	8 (29.6%)	4	4	0
SOMNOLENCE	12 (27.9%)	10	2	0	3 (18.8%)	3	0	0	9 (33.3%)	7	2	0
AGITATION	5 (11.6%)	1	4	0	2 (12.5%)	0	2	0	3 (11.1%)	1	2	0
NERVOUSNESS	3 (7.0%)	2	1	0	2 (12.5%)	2	0	0	1 (3.7%)	0	1	0
SUICIDE IDEATION	2 (4.7%)	0	1	1	0 (0.0%)	0	0	0	2 (7.4%)	0	1	1
AGGRESSIVE REACTION	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
CONCENTRATION IMPAIRED	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
THINKING ABNORMAL	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
BODY AS A WHOLE - GENERAL DISORDERS												
BACK PAIN	3 (7.0%)	2	1	0	2 (12.5%)	2	0	0	1 (3.7%)	0	1	0

-- (CONTINUED) --

EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.3: INCIDENCE AND SEVERITY OF ADVERSE EXPERIENCES DURING STUDY 525 AND 550

ADVERSE EXPERIENCE	ALL PATIENTS: PATIENT INCIDENCE NO. PTS. (%)	ALL PATIENTS: SEVERITY MID	MOD	SEV	6 - 12 YEARS: PATIENT INCIDENCE NO. PTS. (%)	6 - 12 YEARS: SEVERITY MID	MOD	SEV	13 - 18 YEARS: PATIENT INCIDENCE NO. PTS. (%)	13 - 18 YEARS: SEVERITY MID	MOD	SEV
CHEST PAIN	3 (7.0%)	0	3	0	1 (6.3%)	0	1	0	2 (7.4%)	0	2	0
ASTHENIA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
FATIGUE	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
HOT FLUSHES	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
MALAISE	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
PAIN	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
AUTONOMIC NERVOUS SYSTEM DISORDERS												
ANOREXIA	7 (16.3%)	6	1	0	4 (25.0%)	4	0	0	3 (11.1%)	2	1	0
SYNCOPE	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
RESPIRATORY SYSTEM DISORDERS												
COUGHING	2 (4.7%)	2	0	0	2 (12.5%)	2	0	0	0 (0.0%)	0	0	0
EPISTAXIS	2 (4.7%)	1	0	1	1 (6.3%)	1	0	0	1 (3.7%)	0	0	1
DYSPNEA	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
RESPIRATORY DISORDER	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
APPLICATION SITE DISORDERS												
INJECTION SITE INFLAMMATION	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
INJECTION SITE PAIN	1 (2.3%)	0	1	0	1 (6.3%)	0	1	0	0 (0.0%)	0	0	0
SKIN NODULE	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
SKIN AND APPENDAGES DISORDERS												
SWEATING INCREASED	1 (2.3%)	0	1	0	0 (0.0%)	0	0	0	1 (3.7%)	0	1	0
MUSCULO-SKELETAL SYSTEM DISORDERS												
MYALGIA	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
VISION DISORDERS												
VISION ABNORMAL	1 (2.3%)	0	1	0	1 (6.3%)	0	1	0	0 (0.0%)	0	0	0

-- (CONTINUED) --

EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

[redacted]

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 12.3: INCIDENCE AND SEVERITY OF ADVERSE EXPERIENCES DURING STUDY 525 AND 550

	ALL PATIENTS				6 - 12 YEARS				13 - 18 YEARS			
ADVERSE EXPERIENCE	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV	PATIENT INCIDENCE NO. PTS. (%)	SEVERITY- MID	MOD	SEV
HEARING AND VESTIBULAR DISORDERS												
TINNITUS	1 (2.3%)	1	0	0	1 (6.3%)	1	0	0	0 (0.0%)	0	0	0
HEART RATE AND RHYTHM DISORDERS												
PALPITATION	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
URINARY SYSTEM DISORDERS												
POLYURIA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
REPRODUCTIVE DISORDERS, FEMALE												
DYSMENORRHEA	1 (2.3%)	1	0	0	0 (0.0%)	0	0	0	1 (3.7%)	1	0	0
OTHER ADVERSE EVENTS												
INJURY ACCIDENTAL	1 (2.3%)	0	0	1	0 (0.0%)	0	0	0	1 (3.7%)	0	0	1

---- (END) ----

EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT, THE MOST SEVERE OCCURRENCE IS SHOWN.

PROTOCOL: 91CK21-0550
STUDY : AN OPEN-LABEL LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 13: INCIDENCE OF ADVERSE EXPERIENCES DURING STUDY 550[a] BY GENDER

ADVERSE EXPERIENCE	MALE NO. PTS. (%)	FEMALE NO. PTS. (%)	TOTAL NO. PTS. (%)
TOTAL NO. PATIENTS	18	25	43
NO. OF PTS. WITH ADVERSE EXPERIENCE	13 (72.2%)	19 (76.0%)	32 (74.4%)
NO. OF PTS. DISCONTINUED DUE TO ADV. EXP.	1 (5.6%)	2 (8.0%)	3 (7.0%)
PSYCHIATRIC DISORDERS			
INSOMNIA	6 (33.3%)	6 (24.0%)	12 (27.9%)
SOMNOLENCE	2 (11.1%)	4 (16.0%)	6 (14.0%)
AGITATION	2 (11.1%)	2 (8.0%)	4 (9.3%)
NERVOUSNESS	2 (11.1%)	1 (4.0%)	3 (7.0%)
AGGRESSIVE REACTION	0 (0.0%)	1 (4.0%)	1 (2.3%)
SUICIDE IDEATION	0 (0.0%)	1 (4.0%)	1 (2.3%)
CENTR & PERIPH NERV SYST DISORDERS			
HEADACHE	4 (22.2%)	7 (28.0%)	11 (25.6%)
DIZZINESS	2 (11.1%)	1 (4.0%)	3 (7.0%)
HYPERKINESIA	1 (5.6%)	2 (8.0%)	3 (7.0%)
TREMOR	0 (0.0%)	1 (4.0%)	1 (2.3%)
GASTRO-INTESTINAL DISORDERS			
DYSPEPSIA	0 (0.0%)	3 (12.0%)	3 (7.0%)
NAUSEA	1 (5.6%)	2 (8.0%)	3 (7.0%)
ABDOMINAL PAIN	0 (0.0%)	1 (4.0%)	1 (2.3%)
VOMITING	0 (0.0%)	1 (4.0%)	1 (2.3%)
BODY AS A WHOLE - GENERAL DISORDERS			
BACK PAIN	2 (11.1%)	0 (0.0%)	2 (4.7%)
CHEST PAIN	1 (5.6%)	1 (4.0%)	2 (4.7%)
ASTHENIA	1 (5.6%)	0 (0.0%)	1 (2.3%)
HOT FLUSHES	1 (5.6%)	0 (0.0%)	1 (2.3%)
AUTONOMIC NERVOUS SYSTEM DISORDERS			
ANOREXIA	2 (11.1%)	2 (8.0%)	4 (9.3%)

-- (CONTINUED) --

[a]INCLUDED EVENTS WHICH WERE ONGOING FROM 525
EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT.

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TABLE 13: INCIDENCE OF ADVERSE EXPERIENCES DURING STUDY 550[a] BY GENDER

ADVERSE EXPERIENCE	MALE NO. PTS. (%)	FEMALE NO. PTS. (%)	TOTAL NO. PTS. (%)
RESPIRATORY SYSTEM DISORDERS			
COUGHING	1 (5.6%)	1 (4.0%)	2 (4.7%)
EPISTAXIS	1 (5.6%)	0 (0.0%)	1 (2.3%)
HEART RATE AND RHYTHM DISORDERS			
PALPITATION	0 (0.0%)	1 (4.0%)	1 (2.3%)
REPRODUCTIVE DISORDERS, FEMALE			
DYSMENORRHEA	0 (0.0%)	1 (4.0%)	1 (2.3%)
APPLICATION SITE DISORDERS			
SKIN NODULE	1 (5.6%)	0 (0.0%)	1 (2.3%)
OTHER ADVERSE EVENTS			
INJURY ACCIDENTAL	0 (0.0%)	1 (4.0%)	1 (2.3%)

---- (END) ----

[a]INCLUDED EVENTS WHICH WERE ONGOING FROM 525
EACH ADVERSE EXPERIENCE WAS TABULATED ONCE PER PATIENT REGARDLESS OF THE NUMBER OF TIMES IT WAS REPORTED BY THAT PATIENT.

[redacted]

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TABLE 14.1 : INCIDENCE OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES WITH ONSET DURING STUDY 550

				AGE 6 - 12			AGE 13 - 18			TOTAL		
LABORATORY PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM-ALITY	NUMBER TESTED	NUMBER ABNORMAL	AND %	NUMBER TESTED	NUMBER ABNORMAL	AND %	NUMBER TESTED	NUMBER ABNORMAL	AND %
HEMATOLOGY												
WBC (WHITE BLOOD COUNT)	<= 2.8, >= 16	X10E3/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
EOSINOPHILS	>= 10	%	HIGH	16	1	6.3%	27	1	3.7%	43	2	4.7%
NEUTROPHILS	<= 15	%	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
RBC (RED BLOOD CELLS)	<= 3, >= 6	X10E6/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
PLATELETS	<= 75, >= 700	X10E3/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
HGB(HEMOGLOBIN)	<= 9.5(F) 11.5(M)	G/DL	LOW	16	2	12.5%	27	0	0.0%	43	2	4.7%
HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	16	10	62.5%	27	5	18.5%	43	15	34.9%
URINALYSIS												
PROTEIN:URINE	>= 2	UNITS	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
GLUCOSE:URINE	>= 2	UNITS	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
LIVER FUNCTION TESTS												
T/PROTEIN	<= 4.5, >= 9	G/DL	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	16	1	6.3%	27	3	11.1%	43	4	9.3%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
T/BILIRUBIN	>= 2	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
ALK PHOSPHATASE	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
SGOT UNITS	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
SGPT UNITS	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
RENAL FUNCTION TESTS												
BUN	>= 30	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
CREATININE	>= 2	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
URIC ACID	>= 8.5(F) 10.5(M)	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
OTHER												
CHOLESTEROL	>= 330	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
RANDOM GLUCOSE	>= 140	MG/DL	HIGH	16	2	12.5%	27	1	3.7%	43	3	7.0%

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TABLE 14.2 : INCIDENCE OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES DURING STUDIES 525 AND 550

				AGE 6 - 12			AGE 13 - 18			TOTAL		
LABORATORY PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM-ALITY	NUMBER TESTED	NUMBER ABNORMAL	AND %	NUMBER TESTED	NUMBER ABNORMAL	AND %	NUMBER TESTED	NUMBER ABNORMAL	AND %
HEMATOLOGY												
WBC (WHITE BLOOD COUNT)	<= 2.8, >= 16	X10E3/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
EOSINOPHILS	>= 10	%	HIGH	16	2	12.5%	27	1	3.7%	43	3	7.0%
NEUTROPHILS	<= 15	%	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
RBC (RED BLOOD CELLS)	<= 3, >= 6	X10E6/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
PLATELETS	<= 75, >= 700	X10E3/MM3	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
HGB(HEMOGLOBIN)	<= 9.5(F) 11.5(M)	G/DL	LOW	16	3	18.8%	27	0	0.0%	43	3	7.0%
HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	16	10	62.5%	27	9	33.3%	43	19	44.2%
URINALYSIS												
PROTEIN:URINE	>= 2	UNITS	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
GLUCOSE:URINE	>= 2	UNITS	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
LIVER FUNCTION TESTS												
T/PROTEIN	<= 4.5, >= 9	G/DL	LOW	16	0	0.0%	27	0	0.0%	43	0	0.0%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	16	1	6.3%	27	3	11.1%	43	4	9.3%
			HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
T/BILIRUBIN	>= 2	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
ALK PHOSPHATASE	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
SGOT UNITS	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
SGPT UNITS	>= 3.0 X ULN	U/L	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
RENAL FUNCTION TESTS												
BUN	>= 30	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
CREATININE	>= 2	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
URIC ACID	>= 8.5(F) 10.5(M)	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
OTHER												
CHOLESTEROL	>= 330	MG/DL	HIGH	16	0	0.0%	27	0	0.0%	43	0	0.0%
RANDOM GLUCOSE	>= 140	MG/DL	HIGH	16	2	12.5%	27	4	14.8%	43	6	14.0%

[redacted]

PROTOCOL : 91CK21-0550
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TABLE 15.1.1 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES WITH ONSET DURING STUDY 550 : BY TEST.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				9	EOSINOPHILS	>= 10	%	HIGH	8.0	11.7	7.2
				58				HIGH	8.4	14.7	10.7
				8	HGB(HEMOGLOBIN)	<= 9.5(F) 11.5(M)	G/DL	LOW	11.4	11.1	11.4
				84				LOW	13.3	11.4	12.6
				4	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	32.0	30.0	38.0
				25				LOW	37.0	36.0	38.0
				24				LOW	31.0	29.0	32.0
				56				LOW	33.0	32.0	33.0
				9				LOW	39.0	37.0	40.0
				31				LOW	37.0	36.0	42.0
				86				LOW	42.0	37.0	37.0
				28				LOW	38.0	36.0	37.0
				9				LOW		37.0	42.0
				9				LOW	33.0	35.0	39.0
				58				LOW		36.0	42.0
				9				LOW	34.0	29.0	35.0
				90				LOW	37.0	36.0	36.0
				8				LOW	34.0	32.0	32.0
				84				LOW	38.0	34.0	38.0
				56	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.8	3.5	3.6
				29				LOW	3.9	3.5	3.6
				29				LOW	3.8	3.0	3.9
				18				LOW	3.3	3.4	3.4
				60	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	74.0	140.0	85.0
				58				HIGH	79.0	140.0	79.0
				3				HIGH	107.0	167.0	103.0

* DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

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TABLE 15.1.2 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES DURING STUDIES 525 AND 550 : BY TEST.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				61	EOSINOPHILS	>= 10	%	HIGH	5.0	11.7	7.2
				108				HIGH	5.4	14.7	10.7
				14				HIGH	6.5	10.9	3.0
				15	HGB(HEMOGLOBIN)	<= 9.5(F) 11.5(M)	G/DL	LOW	13.0	11.5	12.9
				59				LOW	11.3	11.1	11.4
				132				LOW	13.3	11.4	12.6
				54	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	39.0	30.0	38.0
				14				LOW	36.0	32.0	38.0
				74				LOW	38.0	29.0	32.0
				14				LOW	36.0	29.0	33.0
				21				LOW	34.0	33.0	40.0
				14				LOW	42.0	30.0	43.0
				82				LOW	39.0	36.0	42.0
				137				LOW	40.0	37.0	37.0
				14				LOW		36.0	40.0
				78				LOW	38.0	36.0	37.0
				59				LOW	44.0	37.0	42.0
				21				LOW	40.0	33.0	39.0
				108				LOW	41.0	36.0	42.0
				60				LOW	35.0	29.0	35.0
				51				LOW	35.0	32.0	37.0
				140				LOW	37.0	36.0	36.0
				59				LOW	32.0	32.0	32.0
				132				LOW	38.0	34.0	38.0
				14				LOW	40.0	35.0	38.0
				108	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	4.0	3.5	3.6
				80				LOW	3.8	3.5	3.6
				79				LOW	4.2	3.0	3.9

* DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

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TABLE 15.1.2 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES DURING STUDIES 525 AND 550 : BY TEST.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				52	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.4	3.3	3.4
				14	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	93.0	144.0	111.0
				112				HIGH	86.0	140.0	85.0
				109				HIGH	116.0	140.0	79.0
				15				HIGH	80.0	155.0	93.0
				51				HIGH	96.0	167.0	103.0
				14				HIGH	75.0	147.0	87.0

* DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

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TABLE 15.2.1 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES WITH ONSET DURING STUDY 550 : BY PATIENT.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				4	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	32.0	30.0	38.0
				25	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	37.0	36.0	38.0
				24	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	31.0	29.0	32.0
				60	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	74.0	140.0	85.0
				56	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	33.0	32.0	33.0
				56	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.8	3.5	3.6
				9	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	39.0	37.0	40.0
				29	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.9	3.5	3.6
				9	EOSINOPHILS	>= 10	%	HIGH	8.0	11.7	7.2
				31	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	37.0	36.0	42.0
				58	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	79.0	140.0	79.0
				86	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	42.0	37.0	37.0
				29	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.8	3.0	3.9
				28	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	38.0	36.0	37.0
				58	EOSINOPHILS	>= 10	%	HIGH	8.4	14.7	10.7
				9	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW		37.0	42.0
				9	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	33.0	35.0	39.0

* DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
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TABLE 15.2.1 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES WITH ONSET DURING STUDY 550 : BY PATIENT.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				58	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW		36.0	42.0
				9	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	34.0	29.0	35.0
				18	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.3	3.4	3.4
				90	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	37.0	36.0	36.0
				8	HGB(HEMOGLOBIN)	<= 9.5(F)	11.5(M) G/DL	LOW	11.4	11.1	11.4
				8	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	34.0	32.0	32.0
				3	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	107.0	167.0	103.0
				84	HGB(HEMOGLOBIN)	<= 9.5(F)	11.5(M) G/DL	LOW	13.3	11.4	12.6
				84	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	38.0	34.0	38.0

* DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

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TABLE 15.2.2 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES DURING STUDIES 525 AND 550 : BY PATIENT.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				54	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	39.0	30.0	38.0
				14	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	36.0	32.0	38.0
				14	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	93.0	144.0	111.0
				74	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	38.0	29.0	32.0
				112	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	86.0	140.0	85.0
				14	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	36.0	29.0	33.0
				108	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	4.0	3.5	3.6
				21	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	34.0	33.0	40.0
				80	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.8	3.5	3.6
				14	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	42.0	30.0	43.0
				61	EOSINOPHILS	>= 10	%	HIGH	5.0	11.7	7.2
				82	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	39.0	36.0	42.0
				109	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	116.0	140.0	79.0
				137	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	40.0	37.0	37.0
				14	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW		36.0	40.0
				79	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	4.2	3.0	3.9
				78	HCT(HEMATOCRIT)	<= 32(F) 37(M)	%	LOW	38.0	36.0	37.0
				108	EOSINOPHILS	>= 10	%	HIGH	5.4	14.7	10.7

* DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

PROTOCOL : 91CK21-0550
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TABLE 15.2.2 : LIST OF CLINICALLY SIGNIFICANT LABORATORY ABNORMALITIES DURING STUDIES 525 AND 550 : BY PATIENT.

SITE	PATIENT	AGE**	SEX	DAY* OF MOST ABNORMAL VALUE	PARAMETER	CRITERIA FOR ABNORMALITY		ABNORM -ALITY	BASE -LINE	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				59	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	44.0	37.0	42.0
				15	HGB(HEMOGLOBIN)	<= 9.5(F)	11.5(M) G/DL	LOW	13.0	11.5	12.9
				21	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	40.0	33.0	39.0
				108	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	41.0	36.0	42.0
				60	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	35.0	29.0	35.0
				15	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	80.0	155.0	93.0
				52	ALBUMIN	<= 3.5, >= 6.5	G/DL	LOW	3.4	3.3	3.4
				51	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	35.0	32.0	37.0
				14	EOSINOPHILS	>= 10	%	HIGH	6.5	10.9	3.0
				140	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	37.0	36.0	36.0
				59	HGB(HEMOGLOBIN)	<= 9.5(F)	11.5(M) G/DL	LOW	11.3	11.1	11.4
				59	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	32.0	32.0	32.0
				51	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	96.0	167.0	103.0
				132	HGB(HEMOGLOBIN)	<= 9.5(F)	11.5(M) G/DL	LOW	13.3	11.4	12.6
				132	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	38.0	34.0	38.0
				14	HCT(HEMATOCRIT)	<= 32(F)	37(M) %	LOW	40.0	35.0	38.0
				14	RANDOM GLUCOSE	>= 140	MG/DL	HIGH	75.0	147.0	87.0

* DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT.
** AGE AT ENTRY INTO STUDY 550

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 16.1 : LABORATORY TEST CHANGE FROM 550 BASELINE TO FINAL VALUE.

	AGE 6-12				AGE 13-18				TOTAL			
		BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE	
LABORATORY TEST	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.
HEMATOLOGY												
WBC (WHITE BLOOD COUNT)	16	7.62	-0.25	1.48	27	6.37	-0.08	1.82	43	6.84	-0.14	1.68
EOSINOPHILS	16	3.27	-0.64	2.13	27	2.10	-0.07	1.35	43	2.54	-0.28	1.68
NEUTROPHILS	16	53.32	1.21	5.15	27	56.79	0.56	8.14	43	55.50	0.80	7.11
RBC (RED BLOOD CELLS)	16	4.43	0.28	0.27	27	4.49	0.29	0.33	43	4.47	0.28	0.31
PLATELETS	16	309.31	-12.00	46.66	27	297.89	-2.56	56.82	43	302.14	-6.07	52.89
HGB(HEMOGLOBIN)	16	12.36	0.55	0.78	27	12.96	0.47	0.94	43	12.74	0.50	0.88
HCT(HEMATOCRIT)	12	36.25	0.58	2.84	27	38.48	1.19	2.88	39	37.79	1.00	2.85
LIVER FUNCTION TESTS												
T/PROTEIN	16	6.93	0.35	0.44	26	7.08	0.15	0.45	42	7.02	0.23	0.45
ALBUMIN	16	4.16	-0.04	0.23	26	4.12	0.10	0.28	42	4.13	0.04	0.27
T/BILIRUBIN	16	0.34	0.04	0.15	26	0.47	0.00	0.24	42	0.42	0.02	0.21
ALK PHOSPHATASE	16	231.94	-8.31	26.87	26	173.00	-13.12	30.66	42	195.45	-11.29	29.03
SGOT UNITS	16	23.25	-0.19	4.37	26	19.88	0.81	12.96	42	21.17	0.43	10.47
SGPT UNITS	16	17.56	-2.63	6.83	26	15.31	-1.88	14.32	42	16.17	-2.17	11.93
RENAL FUNCTION TESTS												
BUN	16	14.69	-1.50	4.18	26	11.69	-0.19	3.20	42	12.83	-0.69	3.61
CREATININE	16	0.80	0.04	0.17	26	0.89	0.05	0.13	42	0.86	0.05	0.14
URIC ACID	16	3.66	-0.08	0.94	26	4.77	-0.36	0.91	42	4.35	-0.25	0.92
OTHER												
CHOLESTEROL	16	178.94	-4.06	42.88	26	166.69	-1.19	29.17	42	171.36	-2.29	34.55
RANDOM GLUCOSE	16	87.50	-0.94	16.70	26	91.00	-8.12	19.75	42	89.67	-5.38	18.77

* TOTAL NUMBER OF PATIENTS FOR WHOM EACH LABORATORY TEST'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
NOTE1: CHANGE FROM BASELINE TO FINAL VALUE WAS CALCULATED FOR EACH PATIENT AND THE MEANS OF THESE CHANGES DETERMINED.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 16.2 : LABORATORY TEST CHANGE FROM 525 BASELINE TO 550 FINAL VALUE.

	AGE 6-12				AGE 13-18				TOTAL			
		BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE	
LABORATORY TEST	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.
HEMATOLOGY												
WBC (WHITE BLOOD COUNT)	16	7.05	0.33	2.27	26	6.20	0.19	1.34	42	6.53	0.24	1.73
EOSINOPHILS	16	3.21	-0.58	2.44	26	1.98	0.05	1.71	42	2.45	-0.19	2.01
NEUTROPHILS	16	52.12	2.41	11.41	26	57.97	-0.17	9.94	42	55.74	0.82	10.46
RBC (RED BLOOD CELLS)	16	4.64	0.07	0.24	26	4.73	0.06	0.34	42	4.70	0.06	0.30
PLATELETS	16	294.19	3.13	36.07	26	287.38	9.96	34.88	42	289.98	7.36	35.06
HGB(HEMOGLOBIN)	16	13.05	-0.14	0.51	26	13.53	-0.13	0.83	42	13.35	-0.13	0.71
HCT(HEMATOCRIT)	16	38.31	-0.06	3.09	26	39.58	0.08	3.27	42	39.10	0.02	3.17
LIVER FUNCTION TESTS												
T/PROTEIN	16	7.13	0.15	0.38	27	7.17	0.09	0.41	43	7.16	0.11	0.39
ALBUMIN	16	4.15	-0.04	0.28	27	4.22	0.00	0.22	43	4.20	-0.01	0.24
T/BILIRUBIN	16	0.41	-0.02	0.22	27	0.61	-0.12	0.21	43	0.54	-0.08	0.21
ALK PHOSPHATASE	16	225.75	-2.13	35.40	27	165.81	-9.26	31.23	43	188.12	-6.60	32.61
SGOT UNITS	16	23.44	-0.38	3.16	27	18.04	2.93	12.39	43	20.05	1.70	10.06
SGPT UNITS	16	15.06	-0.13	4.67	27	12.78	0.63	7.55	43	13.63	0.35	6.58
RENAL FUNCTION TESTS												
BUN	16	13.06	0.13	2.50	27	11.30	0.11	4.85	43	11.95	0.12	4.10
CREATININE	16	0.78	0.06	0.13	27	0.91	0.04	0.07	43	0.86	0.05	0.10
URIC ACID	16	4.26	-0.69	0.73	27	4.75	-0.31	0.81	43	4.57	-0.45	0.79
OTHER												
CHOLESTEROL	16	157.88	17.00	28.87	27	157.26	9.19	18.43	43	157.49	12.09	22.86
RANDOM GLUCOSE	16	95.81	-9.25	20.03	27	88.85	-5.89	21.40	43	91.44	-7.14	20.72

* TOTAL NUMBER OF PATIENTS FOR WHOM EACH LABORATORY TEST'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
NOTE1: CHANGE FROM BASELINE TO FINAL VALUE WAS CALCULATED FOR EACH PATIENT AND THE MEANS OF THESE CHANGES DETERMINED.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 17.1 : INCIDENCE OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS WITH ONSET DURING STUDY 550.

			AGE 6-12		AGE 13-18		TOTAL	
PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**
STANDING SYSTOLIC BP	>=180 MMHG	INCREASE >=20	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 90 MMHG	DECREASE >=20	16	1 6.2%	27	0 0.0%	43	1 2.3%
STANDING DIASTOLIC BP	>=105 MMHG	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 MMHG	DECREASE >=15	16	3 18.7%	27	2 7.4%	43	5 11.6%
STANDING HEART RATE	>=120 BPM	INCREASE >=15	16	0 0.0%	27	2 7.4%	43	2 4.6%
	<= 50 BPM	DECREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
SUPINE SYSTOLIC BP	>=180 MMHG	INCREASE >=20	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 90 MMHG	DECREASE >=20	16	2 12.5%	27	0 0.0%	43	2 4.6%
SUPINE DIASTOLIC BP	>=105 MMHG	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 MMHG	DECREASE >=15	16	3 18.7%	27	3 11.1%	43	6 13.9%
SUPINE HEART RATE	>=120 BPM	INCREASE >=15	16	0 0.0%	27	1 3.7%	43	1 2.3%
	<= 50 BPM	DECREASE >=15	16	0 0.0%	27	1 3.7%	43	1 2.3%

* TOTAL NUMBER OF PATIENTS FOR WHOM EACH VITAL SIGN'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME. BASELINE IS FIRST READING IN STUDY 550. FOR SOME PATIENTS, SITTING VALUES OBTAINED AT THE LAST VISIT IN STUDY 525 WERE USED AS BASELINE.

** NUMBER AND % OF PATIENTS FOR WHOM ONE OR MORE FOLLOW UP VALUE MEETS THE CRITERION.

NOTE: IN ORDER TO BE IDENTIFIED, A VALUE MUST MEET THE CRITERION VALUE AND ALSO REPRESENT A CHANGE OF AT LEAST THE MAGNITUDE NOTED IN THE CHANGE COLUMN.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 17.2 : INCIDENCE OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS DURING STUDIES 525 AND 550.

			AGE 6-12		AGE 13-18		TOTAL	
PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**	NUMBER TESTED*	NUMBER AND % W/ SPECIFIED CHANGE**
SITTING SYSTOLIC BP	>=180 MMHG	INCREASE >=20	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 90 MMHG	DECREASE >=20	16	2 12.5%	27	7 25.9%	43	9 20.9%
SITTING DIASTOLIC BP	>=105 MMHG	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 MMHG	DECREASE >=15	16	3 18.7%	27	1 3.7%	43	4 9.3%
SITTING HEART RATE	>=120 BPM	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 BPM	DECREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
STANDING SYSTOLIC BP	>=180 MMHG	INCREASE >=20	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 90 MMHG	DECREASE >=20	16	4 25.0%	27	2 7.4%	43	6 13.9%
STANDING DIASTOLIC BP	>=105 MMHG	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 MMHG	DECREASE >=15	16	2 12.5%	27	3 11.1%	43	5 11.6%
STANDING HEART RATE	>=120 BPM	INCREASE >=15	16	0 0.0%	27	3 11.1%	43	3 6.9%
	<= 50 BPM	DECREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
SUPINE SYSTOLIC BP	>=180 MMHG	INCREASE >=20	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 90 MMHG	DECREASE >=20	16	2 12.5%	27	3 11.1%	43	5 11.6%
SUPINE DIASTOLIC BP	>=105 MMHG	INCREASE >=15	16	0 0.0%	27	0 0.0%	43	0 0.0%
	<= 50 MMHG	DECREASE >=15	16	3 18.7%	27	3 11.1%	43	6 13.9%
SUPINE HEART RATE	>=120 BPM	INCREASE >=15	16	0 0.0%	27	1 3.7%	43	1 2.3%
	<= 50 BPM	DECREASE >=15	16	0 0.0%	27	1 3.7%	43	1 2.3%

* TOTAL NUMBER OF PATIENTS FOR WHOM EACH VITAL SIGN'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE OBTAINED IN THE SITTING POSITION ONLY.
** NUMBER AND % OF PATIENTS FOR WHOM ONE OR MORE FOLLOW UP VALUE MEETS THE CRITERION.

NOTE: IN ORDER TO BE IDENTIFIED, A VALUE MUST MEET THE CRITERION VALUE AND ALSO REPRESENT A CHANGE OF AT LEAST
THE MAGNITUDE NOTED IN THE CHANGE COLUMN.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.1.1 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS WITH ONSET DURING STUDY 550: BY PARAMETER.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				173	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	116	80	80
				5	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	70
				86	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	72	50	68
				142	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	50	60
				105	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	74	40	80
				116	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	42	42
				88	STANDING HEART RATE	>=120 BPM	INCREASE >=15	78	124	92
				17	STANDING HEART RATE	>=120 BPM	INCREASE >=15	80	120	104
				86	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	102	80	100
				142	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	86	89
				5	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	72
				86	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	40	60
				86	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	48	68
				14	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	78
				87	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	40	74
				112	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	43	43
				53	SUPINE HEART RATE	>=120 BPM	INCREASE >=15	80	120	92
				112	SUPINE HEART RATE	<=50 BPM	DECREASE >=15	80	48	48

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
(1) BASELINE IS FIRST READING IN STUDY 550. FOR SOME PATIENTS, SITTING VALUES OBTAINED AT THE LAST VISIT IN STUDY 525 WERE USED AS BASELINE.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.1.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS DURING STUDIES 525 AND 550: BY PARAMETER.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				51 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	90
				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	84	100
				42	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	106
				28	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	90	104
				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	96
				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	110
				43	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	108
				52 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	88	88
				49 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	82
				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	76	38	56
				8	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	60
				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	42	54
				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	48	68
				51 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	110
				55 (5)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	90	120
				160 (109)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	90
				223 (173)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	100	80	80
				52 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	90	108
				49 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	100
				55 (5)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	70
				155 (105)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	40	80
				109 (59)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	47	72
				167 (116)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	78	42	42
				179 (131)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	49	58

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE OBTAINED IN THE SITTING POSITION ONLY.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.1.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS DURING STUDIES 525 AND 550: BY PARAMETER.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL	MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				138	(88)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	76	124	92
				67	(17)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	88	120	104
				138	(88)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	80	121	89
				51	(1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	98
				81	(30)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	102
				95	(44)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	120
				52	(1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	88	106
				49	(1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	93
				55	(5)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	72
				136	(86)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	40	60
				64	(14)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	50	78
				138	(87)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	78	40	74
				179	(131)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	46	62
				160	(112)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	43	43
				103	(53)	SUPINE HEART RATE	>=120 BPM	INCREASE >=15	88	120	92
				160	(112)	SUPINE HEART RATE	<=50 BPM	DECREASE >=15	68	48	48

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE OBTAINED IN THE SITTING POSITION ONLY.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.2.1: LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS WITH ONSET DURING STUDY 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				88	STANDING HEART RATE	>=120 BPM	INCREASE >=15	78	124	92
				5	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	70
				5	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	72
				17	STANDING HEART RATE	>=120 BPM	INCREASE >=15	80	120	104
				53	SUPINE HEART RATE	>=120 BPM	INCREASE >=15	80	120	92
				86	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	72	50	68
				86	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	102	80	100
				86	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	40	60
				86	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	48	68
				142	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	50	60
				142	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	86	89
				173	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	116	80	80
				14	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	78
				105	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	74	40	80
				87	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	40	74
				116	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	42	42
				112	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	43	43
				112	SUPINE HEART RATE	<=50 BPM	DECREASE >=15	80	48	48

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
(1) BASELINE IS FIRST READING IN STUDY 550. FOR SOME PATIENTS, SITTING VALUES OBTAINED AT THE LAST VISIT IN STUDY 525 WERE USED AS BASELINE.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.2.2: LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS DURING STUDIES 525 AND 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	76	38	56
				51 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	90
				51 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	110
				51 (1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	118	90	98
				138 (88)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	76	124	92
				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	84	100
				55 (5)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	90	120
				55 (5)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	70
				55 (5)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	50	72
				67 (17)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	88	120	104
				103 (53)	SUPINE HEART RATE	>=120 BPM	INCREASE >=15	88	120	92
				8	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	68	50	60
				160 (109)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	90
				42	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	106
				28	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	112	90	104
				136 (86)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	60	40	60
				223 (173)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	100	80	80
				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	96
				81 (30)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	102

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE OBTAINED IN THE SITTING POSITION ONLY.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 18.2.2: LIST OF CLINICALLY SIGNIFICANT CHANGES IN VITAL SIGNS DURING STUDIES 525 AND 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	PARAMETER	CRITERION VALUE	CHANGE RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				8	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	110
				43	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	108
				95 (44)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	110	90	120
				64 (14)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	50	78
				155 (105)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	66	40	80
				109 (59)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	47	72
				52 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	88	88
				52 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	90	108
				52 (1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	120	88	106
				138 (87)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	78	40	74
				167 (116)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	78	42	42
				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	42	54
				49 (1)	SITTING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	82
				49 (1)	STANDING SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	100
				49 (1)	SUPINE SYSTOLIC BP	<=90 MMHG	DECREASE >=20	108	82	93
				179 (131)	STANDING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	49	58
				179 (131)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	64	46	62
				138 (88)	STANDING HEART RATE	>=120 BPM	INCREASE >=15	80	121	89
				28	SITTING DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	48	68
				160 (112)	SUPINE DIASTOLIC BP	<=50 MMHG	DECREASE >=15	70	43	43
				160 (112)	SUPINE HEART RATE	<=50 BPM	DECREASE >=15	68	48	48

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE OBTAINED IN THE SITTING POSITION ONLY.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 19.1: VITAL SIGNS AND BODY WEIGHT CHANGE FROM 550 BASELINE TO FINAL VALUE.

	AGE 6-12				AGE 13-18				TOTAL			
		BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE	
VITAL SIGN	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.
STANDING SYSTOLIC BP MMHG	16	102.25	-0.50	14.72	27	108.04	1.81	11.04	43	105.88	0.95	12.41
STANDING DIASTOLIC BP MMHG	16	63.00	5.13	10.81	27	71.33	0.85	11.02	43	68.23	2.44	11.01
STANDING HEART RATE BPM	16	81.25	-9.44	10.82	27	77.74	-2.11	14.16	43	79.05	-4.84	13.37
SUPINE SYSTOLIC BP MMHG	16	104.75	-0.44	14.50	27	108.07	2.26	10.85	43	106.84	1.26	12.23
SUPINE DIASTOLIC BP MMHG	16	62.13	6.38	9.10	27	67.04	1.07	9.87	43	65.21	3.05	9.83
SUPINE HEART RATE BPM	16	78.38	-8.56	9.15	27	74.67	-6.11	12.85	43	76.05	-7.02	11.56
BODY WEIGHT LB.	16	97.94	9.09	5.72	27	128.37	4.57	7.61	43	117.05	6.26	7.24

* TOTAL NUMBER OF PATIENTS FOR WHOM EACH VITAL SIGN'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
BASELINE IS FIRST READING IN STUDY 550. FOR SOME PATIENTS, SITTING VALUES OBTAINED AT THE LAST VISIT
IN STUDY 525 WERE USED AS BASELINE FOR STANDING AND SUPINE BLOOD PRESSURE AND HEART RATE MEASUREMENTS.
NOTE: CHANGE FROM BASELINE TO FINAL VALUE WAS CALCULATED FOR EACH PATIENT AND THE MEANS OF THESE CHANGES DETERMINED.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 19.2: VITAL SIGNS AND BODY WEIGHT CHANGE FROM 525 BASELINE TO 550 FINAL VALUE.

	AGE 6-12				AGE 13-18				TOTAL			
		BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE			BASE	CHANGE FROM BASE	
VITAL SIGN	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.	N*	MEAN	MEAN	S.D.
STANDING SYSTOLIC BP MMHG	16	103.19	-1.44	12.69	27	107.63	2.22	14.89	43	105.98	0.86	14.07
STANDING DIASTOLIC BP MMHG	16	64.88	3.25	12.37	27	67.11	5.07	10.75	43	66.28	4.40	11.27
STANDING HEART RATE BPM	16	73.38	-1.56	14.50	27	75.00	0.63	11.02	43	74.40	-0.19	12.31
SUPINE SYSTOLIC BP MMHG	16	103.19	1.13	12.50	27	107.63	2.70	14.23	43	105.98	2.12	13.48
SUPINE DIASTOLIC BP MMHG	16	64.88	3.63	6.66	27	67.11	1.00	11.30	43	66.28	1.98	9.83
SUPINE HEART RATE BPM	16	73.38	-3.56	15.13	27	75.00	-6.44	10.64	43	74.40	-5.37	12.40
BODY WEIGHT LB.	16	97.66	9.38	7.74	27	126.82	6.13	10.47	43	115.97	7.33	9.58

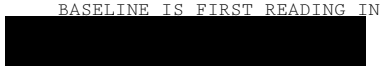
* TOTAL NUMBER OF PATIENTS FOR WHOM EACH VITAL SIGN'S ASSESSMENT WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
ALL CALCULATIONS USE STUDY 525 BASELINE READINGS, WHICH WERE ONLY OBTAINED IN THE SITTING POSITION FOR
BLOOD PRESSURE AND HEART RATE.
NOTE: CHANGE FROM BASELINE TO FINAL VALUE WAS CALCULATED FOR EACH PATIENT AND THE MEANS OF THESE CHANGES DETERMINED.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 20.1 : INCIDENCE OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT WITH ONSET DURING STUDY 550.

CHANGE	AGE 6-12 NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE	AGE 13-18 NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE	TOTAL NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE
	(N=16)*	(N=27)*	(N=43)*
INCREASE (>=7% ABOVE BASELINE)	12 75.0%	7 25.9%	19 44.1%
DECREASE (>=7% BELOW BASELINE)	0 0.0%	0 0.0%	0 0.0%

* TOTAL NUMBER OF PATIENTS FOR WHOM BODY WEIGHT DATA WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
BASELINE IS FIRST READING IN STUDY 550.



PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 20.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT (LB.) WITH ONSET DURING STUDY 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	CHANGE (>=7%) RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				53	INCREASE	93	99	98
				135	INCREASE	83	91	91
				172	INCREASE	109	135	135
				136	INCREASE	95	106	99
				176	INCREASE	188	201	201
				113	INCREASE	79	95	95
				109	INCREASE	92	101	101
				113	INCREASE	116	136	131
				90	INCREASE	165	187	187
				167	INCREASE	70	77	77
				144	INCREASE	90	100	98
				170	INCREASE	179	206	206
				142	INCREASE	99	110	108
				173	INCREASE	80	88	88

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
(1) BASELINE IS FIRST READING IN STUDY 550.

[redacted]

PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 20.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT (LB.) WITH ONSET DURING STUDY 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	CHANGE (>=7%) RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				186	INCREASE	83	92	92
				159	INCREASE	76	84	84
				185	INCREASE	98	108	108
				116	INCREASE	73	81	81
				203	INCREASE	75	82	82

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT.
(1) BASELINE IS FIRST READING IN STUDY 550.

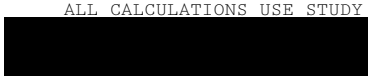
[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 21.1 : INCIDENCE OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT DURING STUDIES 525 AND 550.

CHANGE	AGE 6-12 NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE	AGE 13-18 NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE	TOTAL NUMBER AND % OF PATIENTS WITH SPECIFIED CHANGE
	(N=16)*	(N=27)*	(N=43)*
INCREASE (>=7% ABOVE BASELINE)	12 75.0%	9 33.3%	21 48.8%
DECREASE (>=7% BELOW BASELINE)	2 12.5%	1 3.7%	3 6.9%

* TOTAL NUMBER OF PATIENTS FOR WHOM BODY WEIGHT DATA WAS AVAILABLE AT BASELINE AND AT LEAST ONE FOLLOW UP TIME.
ALL CALCULATIONS USE STUDY 525 BASELINE READINGS.



PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 21.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT (LB.) DURING STUDIES 525 AND 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	CHANGE (>=7%) RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				103 (53)	INCREASE	92	99	98
				186 (135)	INCREASE	82	91	91
				222 (172)	INCREASE	98	135	135
				186 (136)	INCREASE	94	106	99
				228 (176)	INCREASE	178	201	201
				165 (113)	INCREASE	84	95	95
				160 (109)	INCREASE	89	101	101
				271 (218)	INCREASE	98	112	112
				59 (8)	DECREASE	147	135	140
				164 (113)	INCREASE	115	136	131
				187 (136)	INCREASE	141	151	151
				140 (90)	INCREASE	152	187	187
				234 (184)	INCREASE	116	124	124
				42	DECREASE	78	69	77

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS.

[redacted]

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STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 21.2 : LIST OF CLINICALLY SIGNIFICANT CHANGES IN BODY WEIGHT (LB.) DURING STUDIES 525 AND 550: BY PATIENT.

SITE	PATIENT	SEX	AGE*	DAY** OF MOST ABNORMAL VALUE	CHANGE (>=7%) RELATIVE TO BASELINE	BASELINE VALUE(1)	MOST ABNORMAL VALUE	FINAL VALUE
[redacted]				50 (1)	DECREASE	100	90	98
				108 (58)	INCREASE	94	103	103
				220 (170)	INCREASE	177	206	206
				192 (142)	INCREASE	95	110	108
				223 (173)	INCREASE	81	88	88
				237 (186)	INCREASE	86	92	92
				235 (185)	INCREASE	94	108	108
				180 (130)	INCREASE	78	84	84
				167 (116)	INCREASE	72	81	81
				251 (203)	INCREASE	72	82	82

* AGE AT ENTRY INTO STUDY 550
** DAY IS RELATIVE TO FIRST DAY OF STUDY 525 TREATMENT. (DAY) IS RELATIVE TO FIRST DAY OF STUDY 550 TREATMENT
(1) ALL CALCULATIONS USE STUDY 525 BASELINE READINGS.

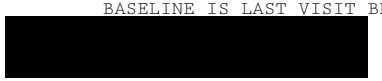
[redacted]

PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 22.1: INCIDENCE OF CHANGES FROM BASELINE IN ECG DURING STUDY 550.

BASELINE/SUBSEQUENT VISIT(S)*	NUMBER OF PATIENTS (%)
	(N=43)
NORMAL /NORMAL	35 (81.4%)
NORMAL /ABNORMAL	6 (14.0%)
ABNORMAL/NORMAL	2 (4.7%)
ABNORMAL/ABNORMAL	0 (0.0%)

* INCIDENCES FOR ALL SUBSEQUENT VISITS WERE SUMMARIZED. THE DESIGNATION "ABNORMAL" INDICATES ONE OR MORE ABNORMAL ECG'S FOLLOWING BASELINE.
NOTE: PATIENT REQUIRED A BASELINE ECG AND AT LEAST ONE ADDITIONAL ECG IN ORDER TO BE INCLUDED IN THE SUMMARY. BASELINE IS LAST VISIT BEFORE STUDY 550 TREATMENT.

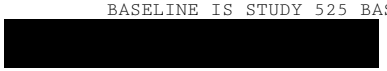


PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 22.2: INCIDENCE OF CHANGES FROM BASELINE IN ECG DURING STUDIES 525 AND 550.

BASELINE/SUBSEQUENT VISIT(S)*	NUMBER OF PATIENTS (%)	
	(N=43)	
NORMAL /NORMAL	32	(74.4%)
NORMAL /ABNORMAL	5	(11.6%)
ABNORMAL/NORMAL	3	(7.0%)
ABNORMAL/ABNORMAL	3	(7.0%)

* INCIDENCES FOR ALL SUBSEQUENT VISITS WERE SUMMARIZED. THE DESIGNATION "ABNORMAL" INDICATES ONE OR MORE ABNORMAL ECG'S FOLLOWING BASELINE.
NOTE: PATIENT REQUIRED A BASELINE ECG AND AT LEAST ONE ADDITIONAL ECG IN ORDER TO BE INCLUDED IN THE SUMMARY. BASELINE IS STUDY 525 BASELINE ECG.



PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 23.1: INCIDENCE OF CLINICALLY SIGNIFICANT ABNORMALITIES IN ECG'S DURING STUDY 550

	NUMBER OF PATIENTS (%)
	(N=43)
CLINICALLY SIGNIFICANT ABNORMALITIES*	0 (0.0%)

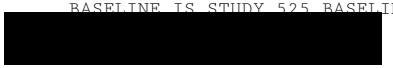
* INCIDENCES FOR ALL SUBSEQUENT VISITS WERE SUMMARIZED. THE DESIGNATION "CLINICALLY SIGNIFICANT ABNORMALITIES" INDICATES A CLINICALLY SIGNIFICANT ABNORMALITY IN ONE OR MORE ECG'S FOLLOWING BASELINE.
PATIENT REQUIRED A BASELINE ECG AND AT LEAST ONE ADDITIONAL ECG IN ORDER TO BE INCLUDED IN THE SUMMARY.
BASELINE IS LAST VISIT BEFORE STUDY 550 TREATMENT.

PROTOCOL : 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 23.2: INCIDENCE OF CLINICALLY SIGNIFICANT ABNORMALITIES IN ECG'S DURING STUDIES 525 AND 550

	NUMBER OF PATIENTS (%)
	(N=43)
CLINICALLY SIGNIFICANT ABNORMALITIES*	0 (0.0%)

* INCIDENCES FOR ALL SUBSEQUENT VISITS WERE SUMMARIZED. THE DESIGNATION "CLINICALLY SIGNIFICANT ABNORMALITIES" INDICATES A CLINICALLY SIGNIFICANT ABNORMALITY IN ONE OR MORE ECG'S FOLLOWING BASELINE.
PATIENT REQUIRED A BASELINE ECG AND AT LEAST ONE ADDITIONAL ECG IN ORDER TO BE INCLUDED IN THE SUMMARY.
BASELINE IS STUDY 525 BASELINE ECG.



PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 24.1 : CONCOMITANT MEDICATIONS AT ENTRY INTO STUDY 550.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
SELDANE (TERFENADINE)	3
MULTIVITAMINS (UNSPECIFIED)	2
ACETAMINOPHEN	1
APPETITE SUPPRESSANT	1
ASPIRIN	1
BENZAC-GEL	1
SEPTRA DS	1
SUPRAX (CEFIXIME)	1
TETRACYCLINE HYDROCHLORIDE	1
VENTOLIN	1
VENTOLIN INHALER	1
TOTAL NUMBER OF PATIENTS WITH CONCOMITANT MEDICATIONS *	11 (25.6%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE MEDICATION.

* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
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TABLE 24.2 : CONCOMITANT MEDICATIONS AT ENTRY INTO STUDY 525.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
ACETAMINOPHEN	2
MULTIVITAMINS (UNSPECIFIED)	2
SELDANE (TERFENADINE)	2
SEPTRA DS	2
ALLERGY SHOT(UNSPECIFIED)	1
AMOXICILLIN	1
APPETITE SUPPRESSANT	1
BECONASE AQ NASAL SPRAY	1
BENZAC-GEL	1
FIBERALL	1
IBUPROFEN	1
TETRACYCLINE HYDROCHLORIDE	1
TOTAL NUMBER OF PATIENTS WITH CONCOMITANT MEDICATIONS *	11 (25.6%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE MEDICATION.

* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 25.1 : CONCOMITANT MEDICATIONS TAKEN DURING STUDY 550.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
IBUPROFEN	9
ACETAMINOPHEN	8
AMOXICILLIN	6
PSEUDOEPHEDRINE HYDROCHLORIDE	5
MULTIVITAMINS (UNSPECIFIED)	4
SELDANE (TERFENADINE)	4
CHLORAL HYDRATE	2
ANAPROX-DS	1
ANTIBIOTIC(UNSPECIFIED)	1
ANTIBIOTIC-PCE	1
APPETITE SUPPRESSANT	1
ASPIRIN	1
BECONASE AQ NASAL SPRAY	1
BECONASE INHALER	1
BENADRYL D	1
BENZAC-GEL	1
BUFFERIN	1
CEFACLOR(CECLOR)	1
CEFZIL	1
CEPHALEXIN (KEFLEX)	1
CHLORASEPTIC SPRAY	1
DIPHENHYDRAMINE	1
DONNAGEL	1
ENTEX	1
HUMIBID L.A.	1
MAALOX	1
MEPERIDINE HYDROCHLORIDE	1
PEPTO-BISMOL	1
PHENYLPROPANOLAMINE	1
PREMSYN PMS	1
SEPTRA DS	1
SUPRAX (CEFIXIME)	1
TETRACYCLINE HYDROCHLORIDE	1

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 25.1 : CONCOMITANT MEDICATIONS TAKEN DURING STUDY 550.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
TUMS	1
TYLENOL COLD & FLU	1
VANCENASE AQ SPRAY	1
VENTOLIN	1
VENTOLIN INHALER	1
VISINE	1
TOTAL NUMBER OF PATIENTS WITH CONCOMITANT MEDICATIONS *	32 (74.4%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE MEDICATION.

* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

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STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 25.2 : CONCOMITANT MEDICATIONS TAKEN DURING STUDIES 525 AND 550.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
ACETAMINOPHEN	20
IBUPROFEN	14
AMOXICILLIN	9
PSEUDOEPHEDRINE HYDROCHLORIDE	6
SELDANE (TERFENADINE)	5
MULTIVITAMINS (UNSPECIFIED)	4
CHLORAL HYDRATE	3
CHLORASEPTIC SPRAY	3
DIPHENHYDRAMINE	3
SEPTRA DS	3
ASPIRIN	2
BECONASE AQ NASAL SPRAY	2
ERYTHROMYCIN	2
PEPTO-BISMOL	2
PROCAINE HCL (NOVOCAIN)	2
THROAT LOZENGERS	2
ACTIFED	1
AFRIN NASAL SPRAY	1
ALBUTEROL INHALER (PROVENTIL INHALER}	1
ALLERGY SHOT(UNSPECIFIED)	1
ANAPROX-DS	1
ANTIBIOTIC(UNSPECIFIED)	1
ANTIBIOTIC-PCE	1
APPETITE SUPPRESSANT	1
BECONASE INHALER	1
BENADRYL D	1
BENZAC-GEL	1
BUFFERIN	1
CEFACLOR(CECLOR)	1
CEFZIL	1
CEPHALEXIN (KEFLEX)	1
CHLORASEPTIC LOZENGES	1
CLOTRIMAZOLE	1

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 25.2 : CONCOMITANT MEDICATIONS TAKEN DURING STUDIES 525 AND 550.

CONCOMITANT MEDICATION	NUMBER OF PATIENTS (N= 43)
DONNAGEL	1
ENTEX	1
EX-LAX	1
FIBERALL	1
HUMIBID L.A.	1
LORAZEPAM	1
MAALOX	1
MEPERIDINE HYDROCHLORIDE	1
MYLANTA	1
NASAL SPRAY UNSPECIFIED	1
NEOSPORIN OINTMENT	1
NYQUIL	1
PEN V K	1
PHENYLPROPANOLAMINE	1
PREMSYN PMS	1
SUPRAX (CEFIXIME)	1
TETRACYCLINE HYDROCHLORIDE	1
TRETINOIN	1
TUMS	1
TYLENOL COLD & FLU	1
VANCENASE AQ SPRAY	1
VENTOLIN	1
VENTOLIN INHALER	1
VISINE	1
TOTAL NUMBER OF PATIENTS WITH CONCOMITANT MEDICATIONS *	40 (93.0%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE MEDICATION.

* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

[redacted]

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STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 26.1 : INCIDENCE OF ILLNESSES PRESENT AT STUDY 550 BASELINE.

CONCURRENT ILLNESSES	NUMBER OF PATIENTS (N=43)
HAYFEVER	7
HEADACHE	4
ASTHMA	3
ACNE	2
ALLERGIES UNSPECIFIED	1
STREP THROAT	1
COLD SORES	1
ANEMIA	1
CERVICAL LESION	1
UPPER RESPIRATORY INFECTION	1
INFLUENZA	1
ALLERGIC ASTHMA	1
CONSTIPATION	1
ECZEMA	1
EPISTAXIS	1
PALPITATIONS	1
COUGH	1
STOMACH ACHE	1
TOTAL NUMBER OF PATIENTS WITH CONCURRENT ILLNESSES *	17 (39.5%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE ILLNESS.
* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

[redacted]

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 26.2 : INCIDENCE OF ILLNESSES PRESENT AT STUDY 525 BASELINE.

CONCURRENT ILLNESSES	NUMBER OF PATIENTS (N=43)
HAYFEVER	5
HEADACHE	4
ACNE	3
ASTHMA	2
SEASONAL ALLERGIES	1
COLD SORES	1
RINGWORM	1
YEAST INFECTION	1
VAGINAL YEAST INFECTION	1
EAR INFECTION	1
UPPER RESPIRATORY INFECTION	1
ALLERGY TO POLLEN,MOLD	1
CONSTIPATION	1
ECZEMA	1
EPISTAXIS	1
PALPITATIONS	1
COUGH	1
STOMACH ACHE	1
TAILBONE INJURY	1
TOTAL NUMBER OF PATIENTS WITH CONCURRENT ILLNESSES *	17 (39.5%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE ILLNESS.
* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 27.1 : INCIDENCE OF ILLNESSES OCCURRING DURING STUDY 550.

INTERCURRENT ILLNESSES	NUMBER OF PATIENTS (N=43)
UPPER RESPIRATORY INFECTION	10
INFLUENZA	7
SORE THROAT	3
ALLERGIES UNSPECIFIED	2
STREP THROAT	2
STOMACH VIRUS	1
ANEMIA	1
EYE IRRITATION	1
REDNESS OF EYE	1
EAR INFECTION	1
UPPER RESPIRATORY CONGESTION	1
BILATERAL MAXILLARY SINUSITIS	1
SINUS INFECTION	1
TOOTHACHE	1
PAROTID MASS	1
DYSMENORRHEA	1
PREMENSTRUAL SYNDROME	1
POISON OAK	1
PSORIASIS	1
HIVES	1
BODY PAIN	1
CHEST PAIN	1
GAS	1
ARM LACERATION	1
TOTAL NUMBER OF PATIENTS WITH INTERCURRENT ILLNESSES *	25 (58.1%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE ILLNESS.
* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 27.2 : INCIDENCE OF ILLNESSES PRESENT AT STUDY 525 BASELINE OR OCCURRING DURING STUDIES 525 OR 550.

CONCURRENT ILLNESSES	NUMBER OF PATIENTS (N=43)
UPPER RESPIRATORY INFECTION	16
SORE THROAT	9
INFLUENZA	8
HEADACHE	8
HAYFEVER	7
STREP THROAT	4
ALLERGIES UNSPECIFIED	3
EAR INFECTION	3
ASTHMA	3
ACNE	3
RINGWORM	2
ANEMIA	2
TOOTHACHE	2
PAIN,DENTAL	2
GASTRIC UPSET	2
URINARY TRACT INFECTION	2
COUGH	2
STOMACH ACHE	2
SEASONAL ALLERGIES	1
TEETH BANDS	1
COLD SORES	1
STOMACH VIRUS	1
YEAST INFECTION	1
VAGINAL YEAST INFECTION	1
CERVICAL LESION	1
EYE IRRITATION	1
REDNESS OF EYE	1
OTITIS MEDIA	1
EARACHE	1
UPPER RESPIRATORY CONGESTION	1
PHARYNGITIS	1
BILATERAL MAXILLARY SINUSITIS	1
SINUS INFECTION	1
ALLERGY TO POLLEN,MOLD	1
ALLERGIC ASTHMA	1

PROTOCOL : 91CK21-0550
STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

TABLE 27.2 : INCIDENCE OF ILLNESSES PRESENT AT STUDY 525 BASELINE OR OCCURRING DURING STUDIES 525 OR 550.

CONCURRENT ILLNESSES	NUMBER OF PATIENTS (N=43)
PAROTID MASS	1
STOMACH UPSET	1
CONSTIPATION	1
DIARRHEA	1
DYSMENORRHEA	1
PREMENSTRUAL SYNDROME	1
POISON OAK	1
ECZEMA	1
PSORIASIS	1
HIVES	1
LIGHTHEADEDNESS	1
BODY PAIN	1
EPISTAXIS	1
PALPITATIONS	1
CHEST PAIN	1
GAS	1
ARM LACERATION	1
TAILBONE INJURY	1
PAIN AT INJECTION SITE	1
TOTAL NUMBER OF PATIENTS WITH CONCURRENT ILLNESSES *	36 (83.7%)

PATIENTS MAY BE INCLUDED IN MORE THAN ONE ILLNESS.
* EACH PATIENT IS COUNTED ONLY ONCE ON THIS LINE.

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STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION.

TABLE 28.1 : INCIDENCE OF CHANGES FROM BASELINE IN PHYSICAL EXAM DURING STUDY 550.

BASELINE/FINAL VISIT	NUMBER OF PATIENTS (%)
	(N=43)
CHANGE	3(7.0)

NOTE: BASELINE IS FIRST VISIT OF STUDY 550.

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STUDY : AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS
WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION.

TABLE 28.2 : CHANGES FROM BASELINE IN PHYSICAL EXAM DURING STUDY 550 - PATIENT LISTING.

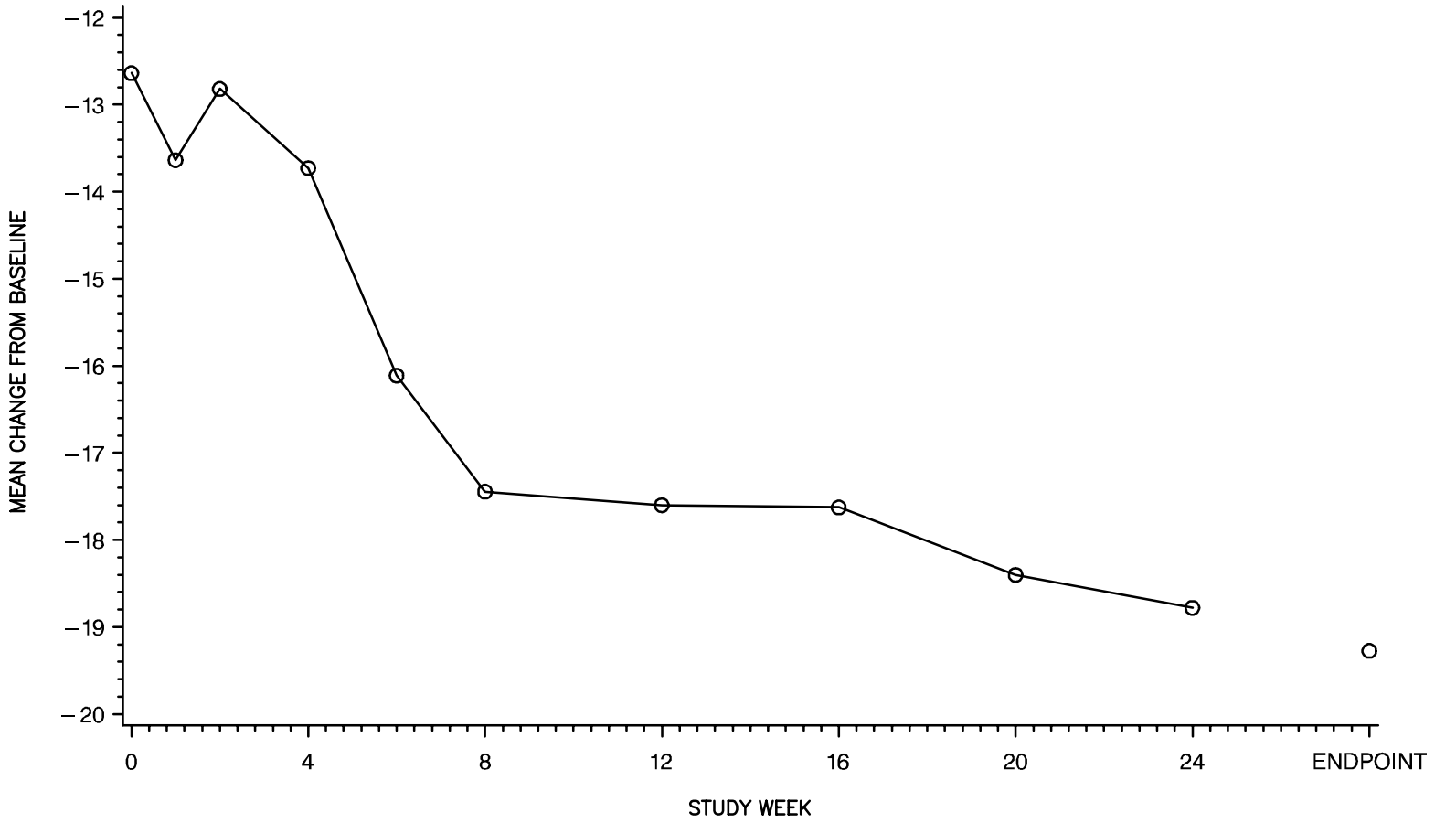
GRANT	PATIENT	SEX	AGE (YRS)	DURATION OF THERAPY (DAYS)	SITE	BASELINE COMMENT	FINAL COMMENT
[redacted]				172	GENERAL APPEARANCE	ACNE	ACNE CLEARED
					EARS	SLIGHTLY CONTRACTED L TYMPANIC MEMBRANE	EARS NORMAL
				173	SKIN		PSORIASIS R ANKLE, R&L ELBOW
				22	EXTREMITIES		[redacted]

[redacted]

FIGURES

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 1. CHANGE IN CY-BOCS FROM STUDY 0525 BASELINE IN OCD PATIENTS
(STUDY WEEK 0 IS STUDY 0550 BASELINE)

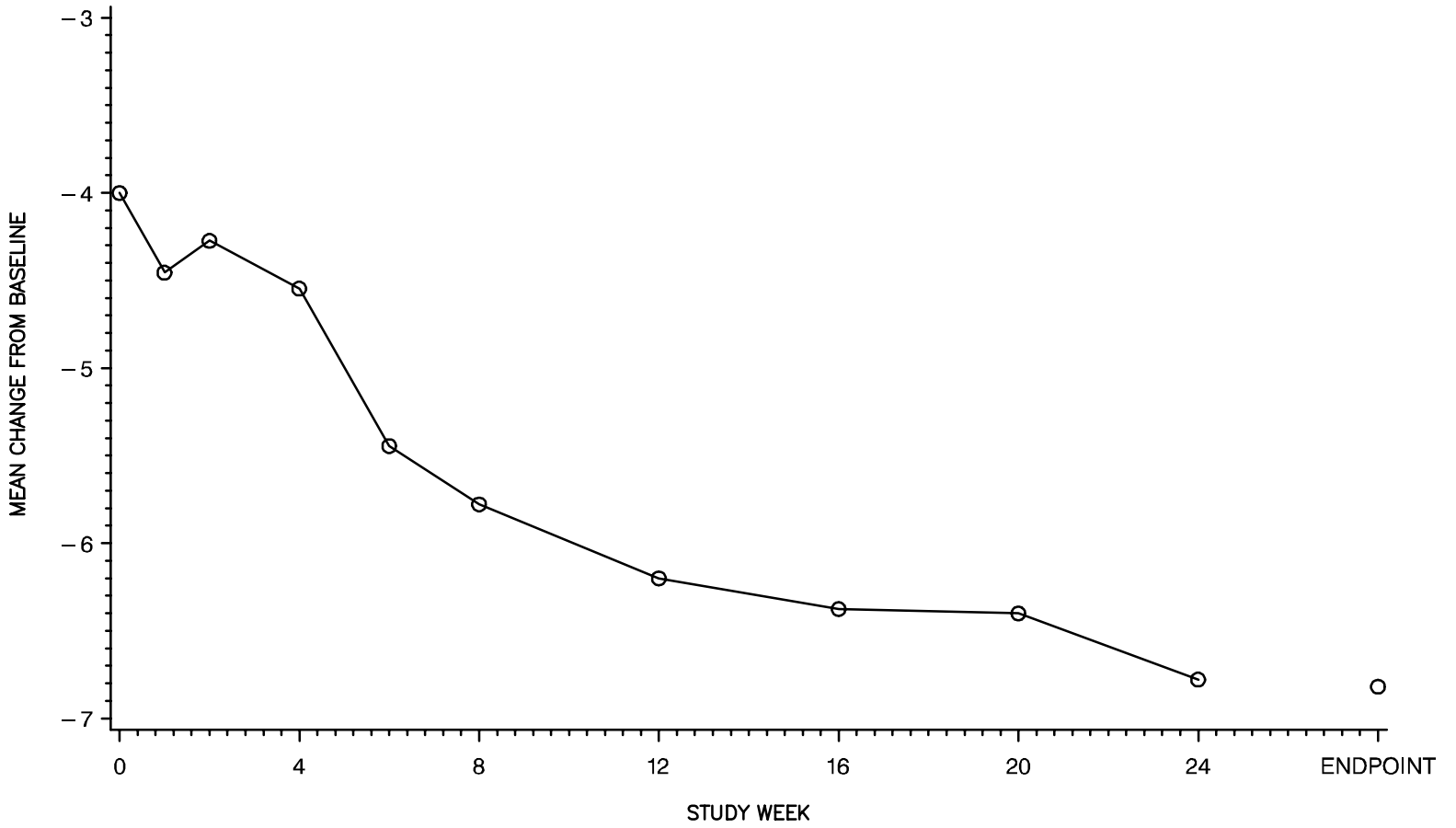


[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 2. CHANGE IN NIMH OC SCALE FROM STUDY 0525 BASELINE IN OCD PATIENTS (STUDY WEEK 0 IS STUDY 0550 BASELINE)



[redacted]

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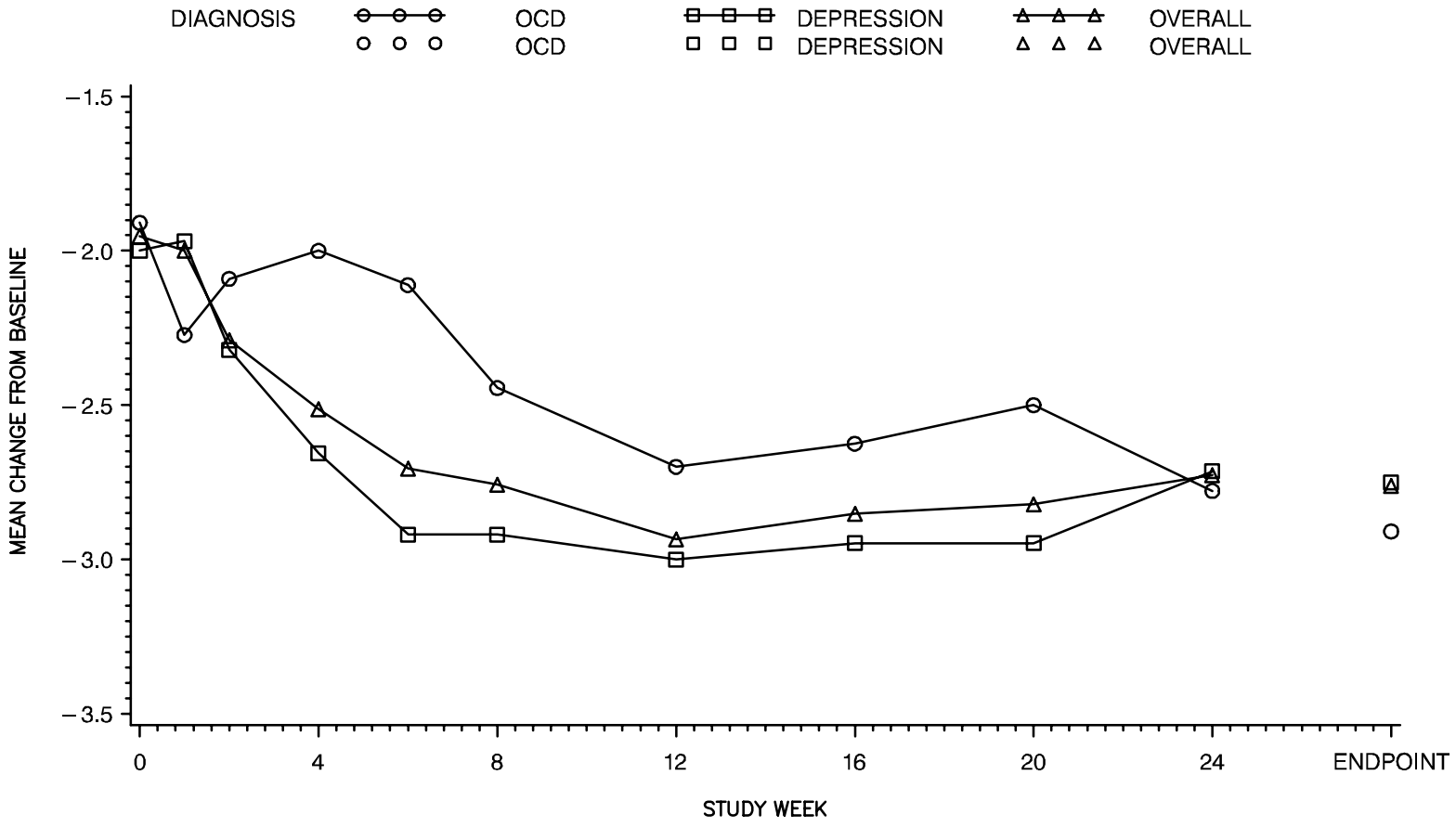
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 3. CHANGE IN CGI SEVERITY FROM STUDY 0525 BASELINE
(STUDY WEEK 0 IS STUDY 0550 BASELINE)

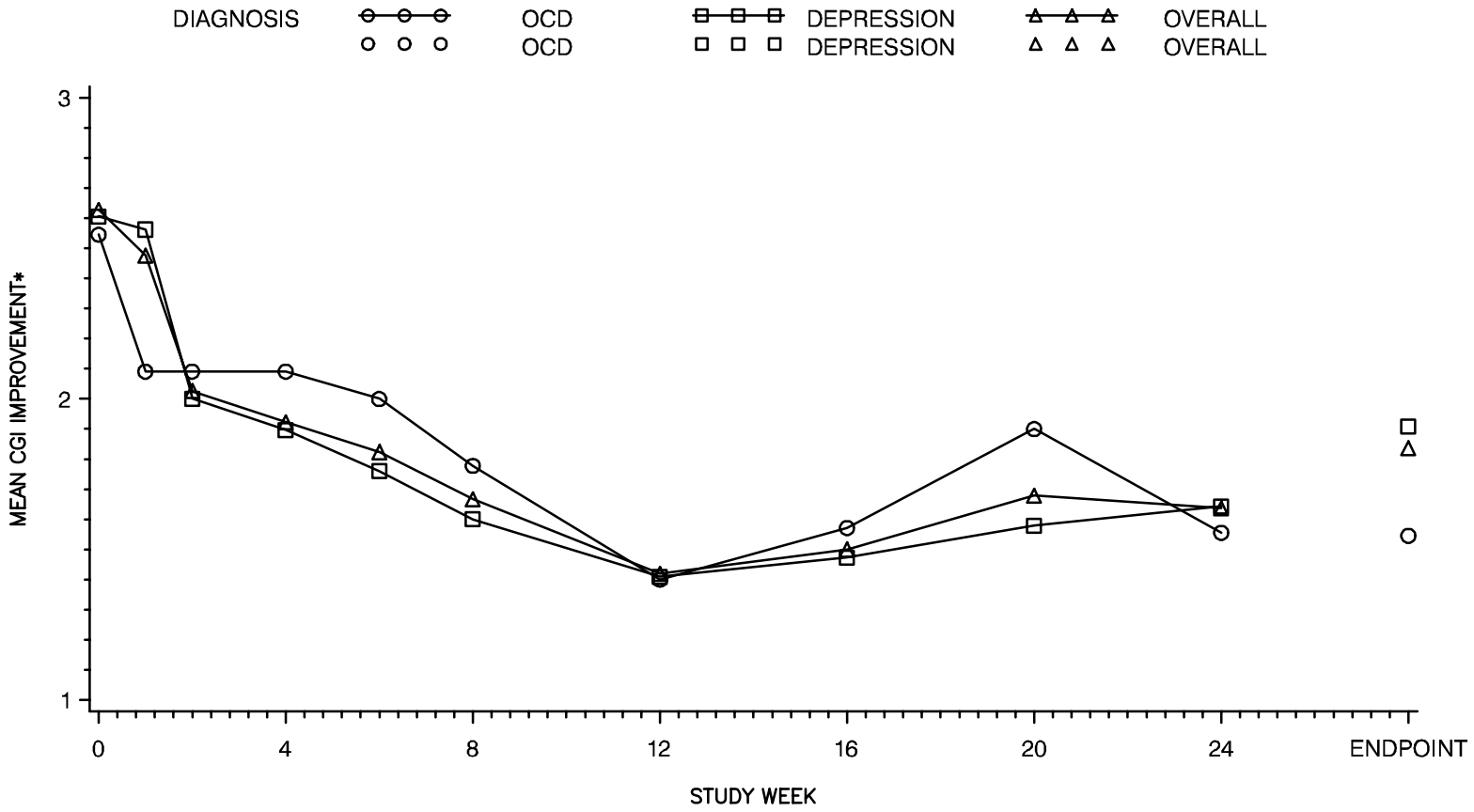


[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 4. CGI IMPROVEMENT RELATIVE TO START OF 0525 STUDY
(STUDY WEEK 0 IS STUDY 0550 BASELINE)



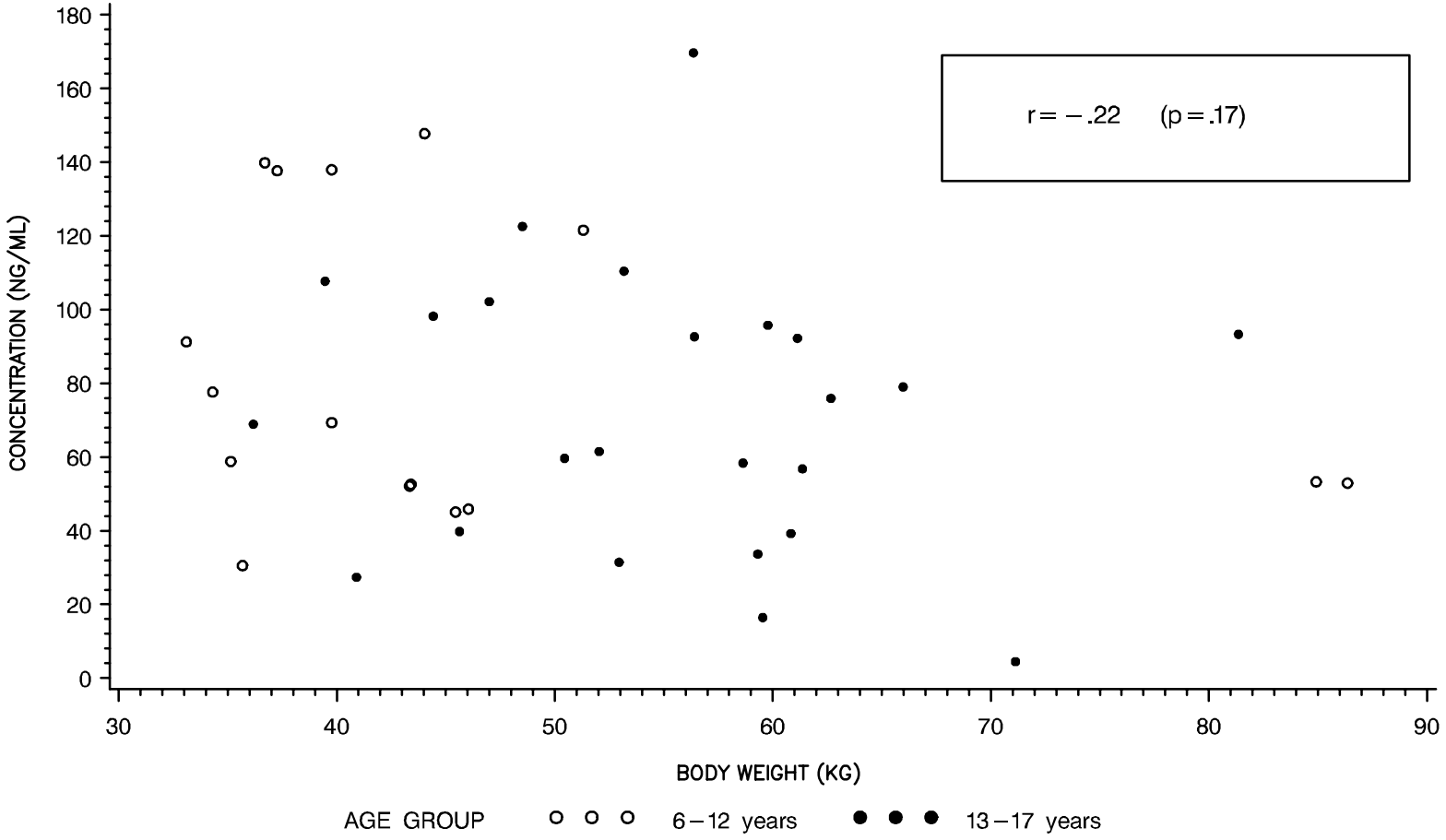
* 1 = VERY MUCH IMPROVED, 2 = MUCH IMPROVED, 3 = MINIMALLY IMPROVED.

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 5. MEAN DOSE NORMALIZED SERTRALINE PLASMA CONCENTRATIONS* VERSUS BODYWEIGHT** FOR PROTOCOL 550



* CONCENTRATION VALUE FOR EACH PATIENT WAS OBTAINED BY DOSE NORMALIZING((200/DOSE)*CONCENTRATION) AND AVERAGING OVER STUDY WEEKS 1 TO 24.

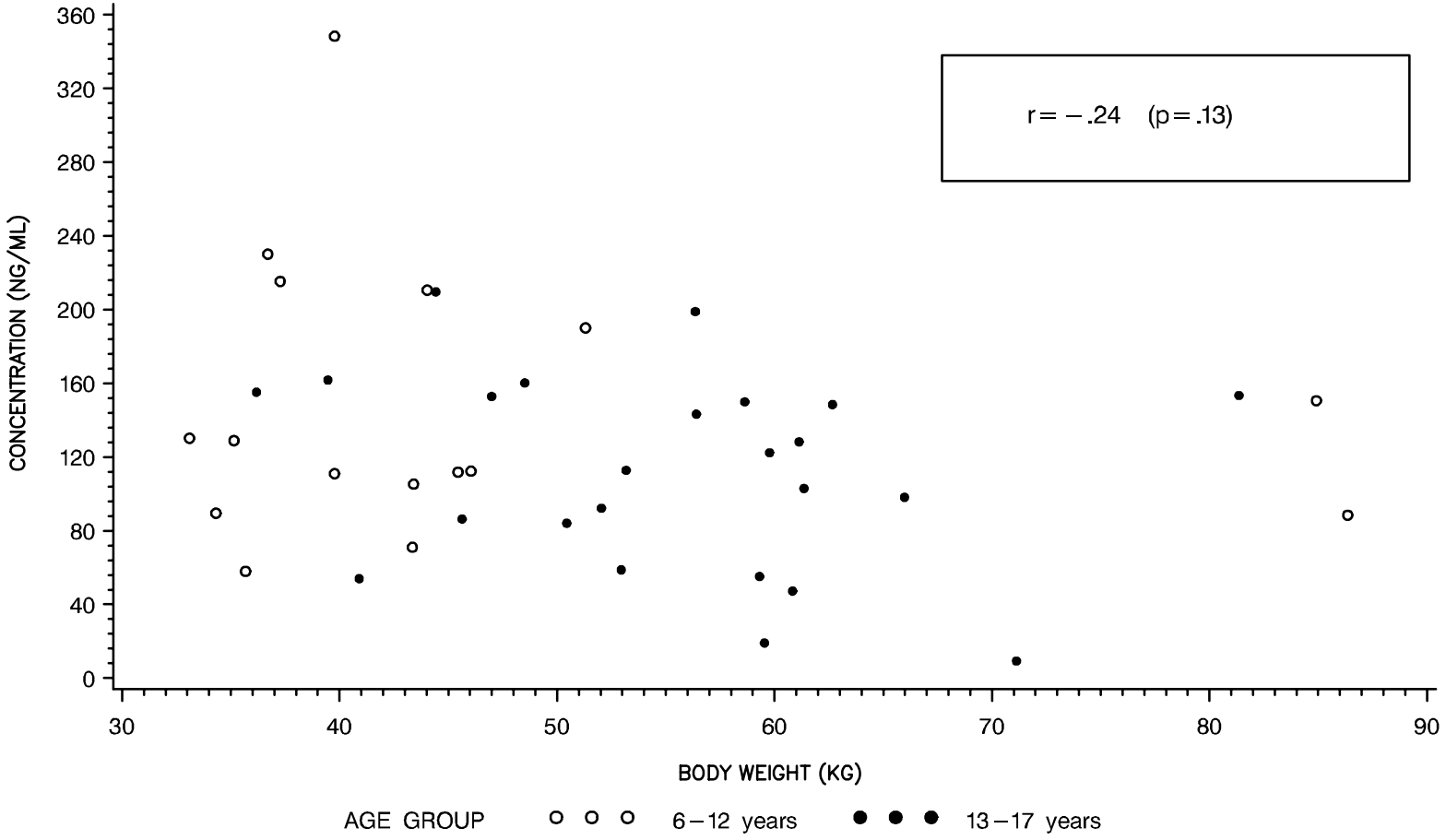
** MEAN BODYWEIGHT FOR EACH PATIENT OVER STUDY WEEKS 1 TO 24.

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 6. MEAN SERTRALINE DOSE NORMALIZED DESMETHYLSERTRALINE PLASMA CONCENTRATIONS* VERSUS BODYWEIGHT** FOR PROTOCOL 550



* CONCENTRATION VALUE FOR EACH PATIENT WAS OBTAINED BY DOSE NORMALIZING((200/DOSE)*CONCENTRATION) AND AVERAGING OVER STUDY WEEKS 1 TO 24.

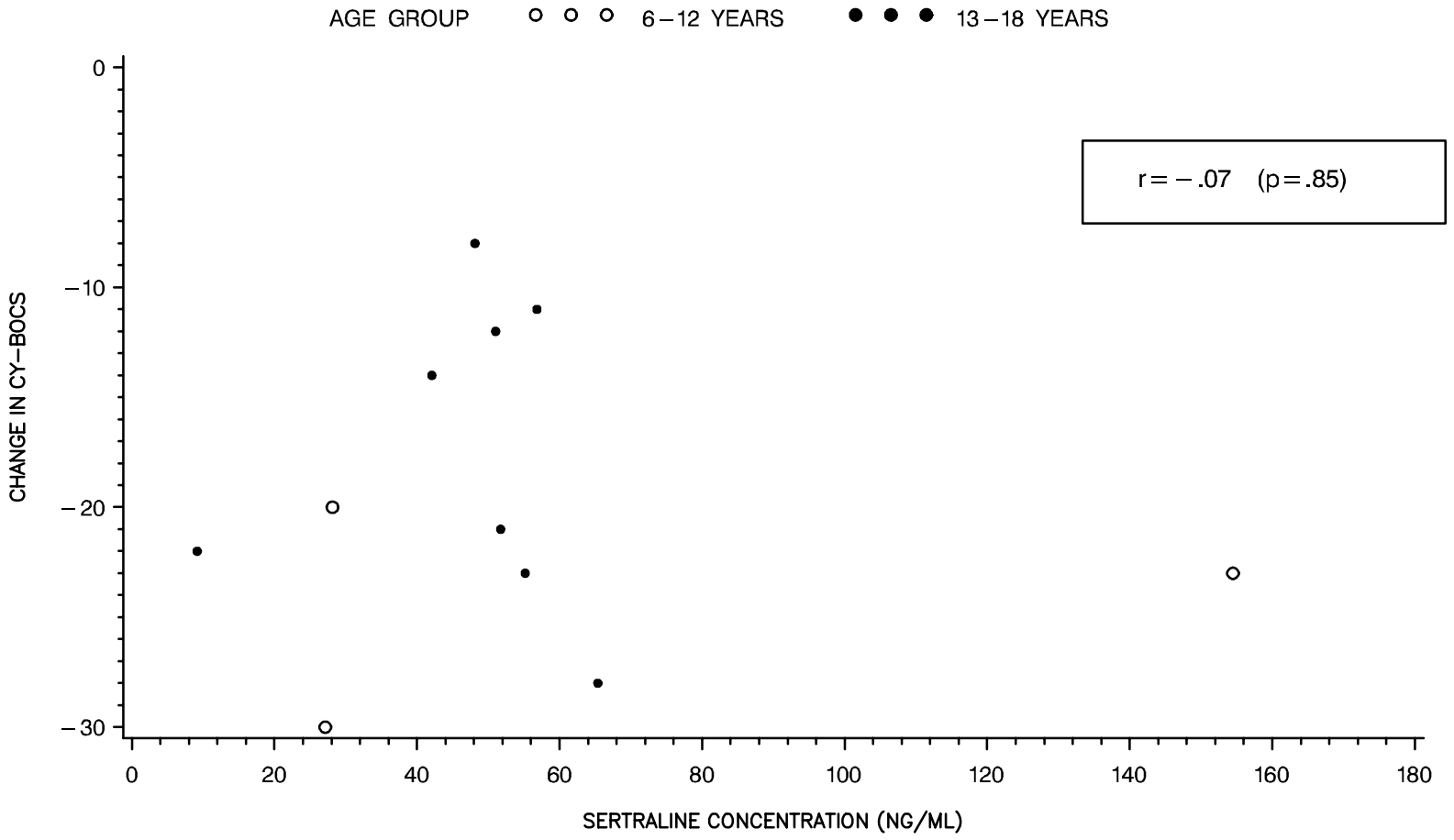
** MEAN BODYWEIGHT FOR EACH PATIENT OVER STUDY WEEKS 1 TO 24.

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 7. CHANGE IN CY-BOCS FROM STUDY 0525 BASELINE VERSUS SERTRALINE CONCENTRATION IN OCD PATIENTS



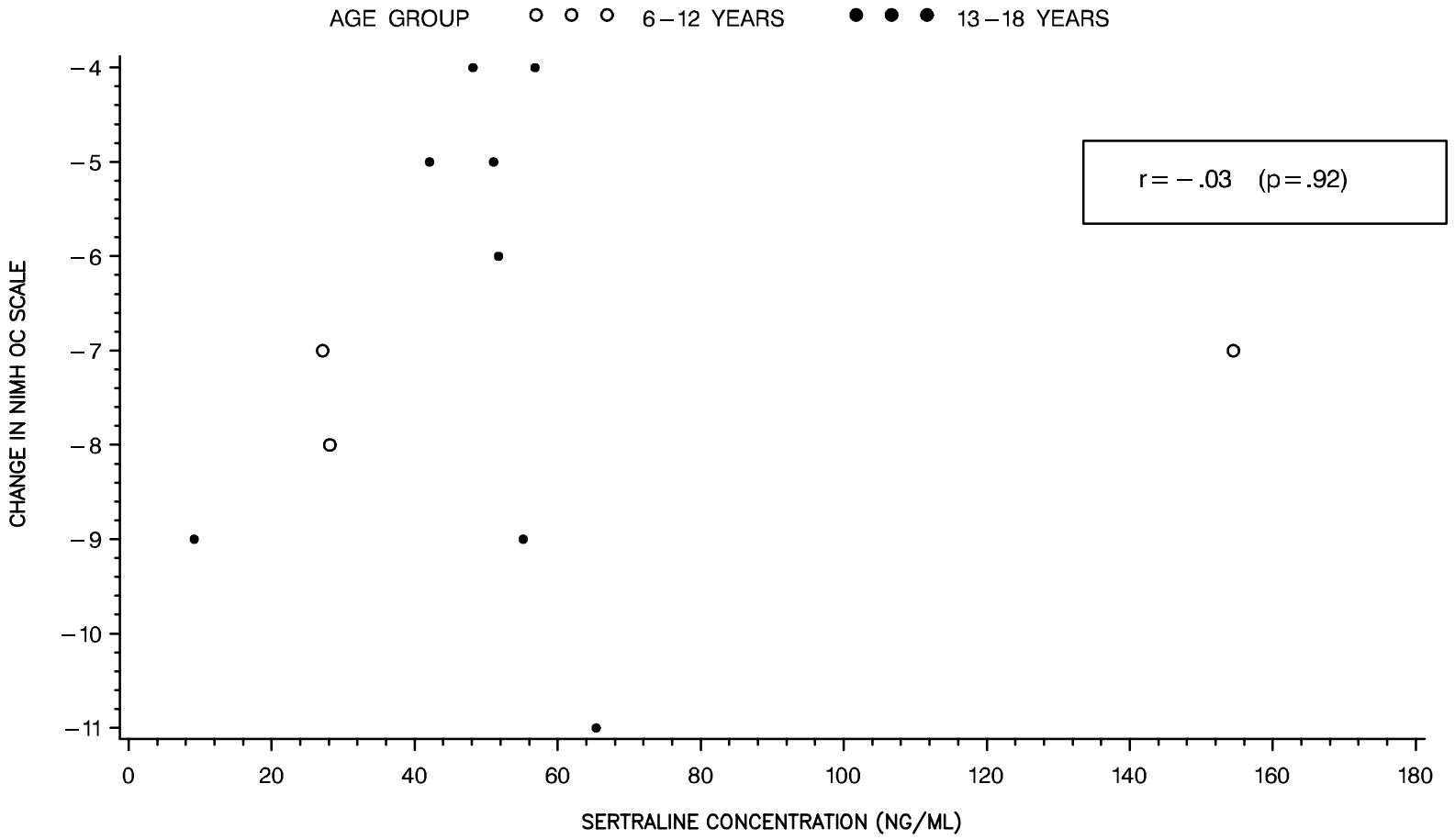
NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 8. CHANGE IN NIMH OC SCALE FROM STUDY 0525 BASELINE VERSUS SERTRALINE CONCENTRATION IN OCD PATIENTS



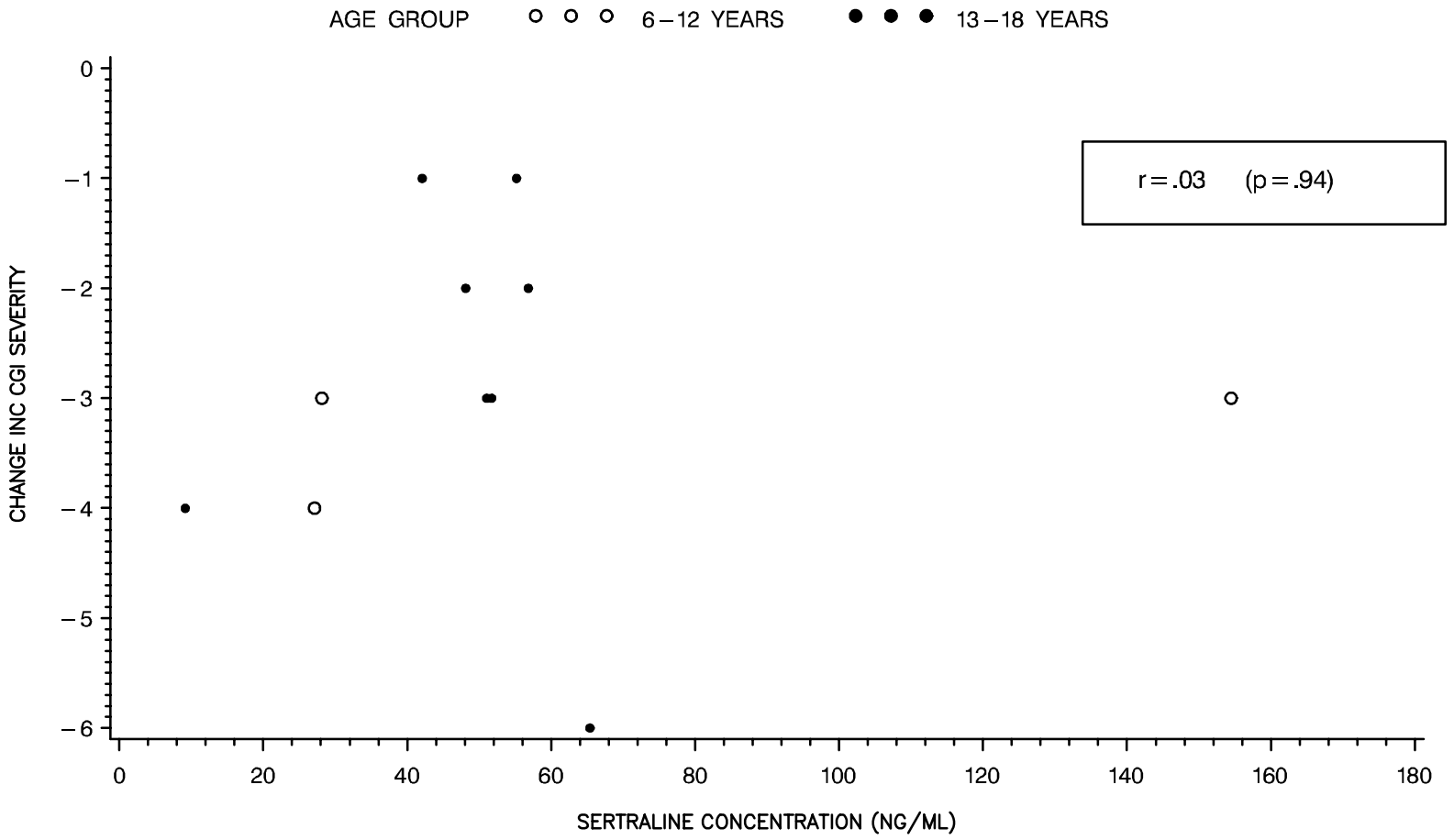
NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 9. CHANGE IN CGI SEVERITY FROM STUDY 0525 BASELINE VERSUS SERTRALINE CONCENTRATION IN OCD PATIENTS

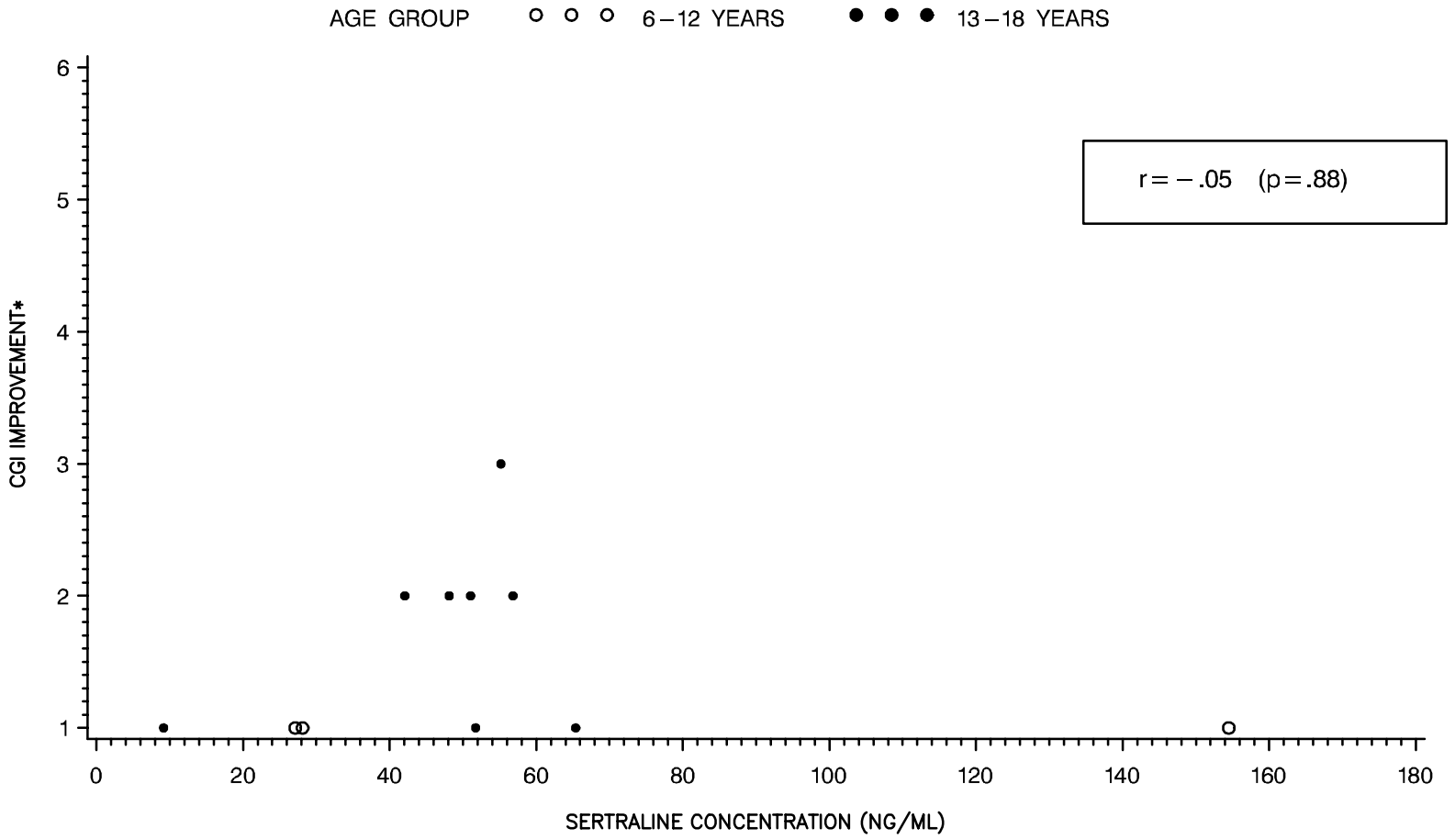


NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 10. CGI IMPROVEMENT VERSUS SERTRALINE CONCENTRATION IN OCD PATIENTS



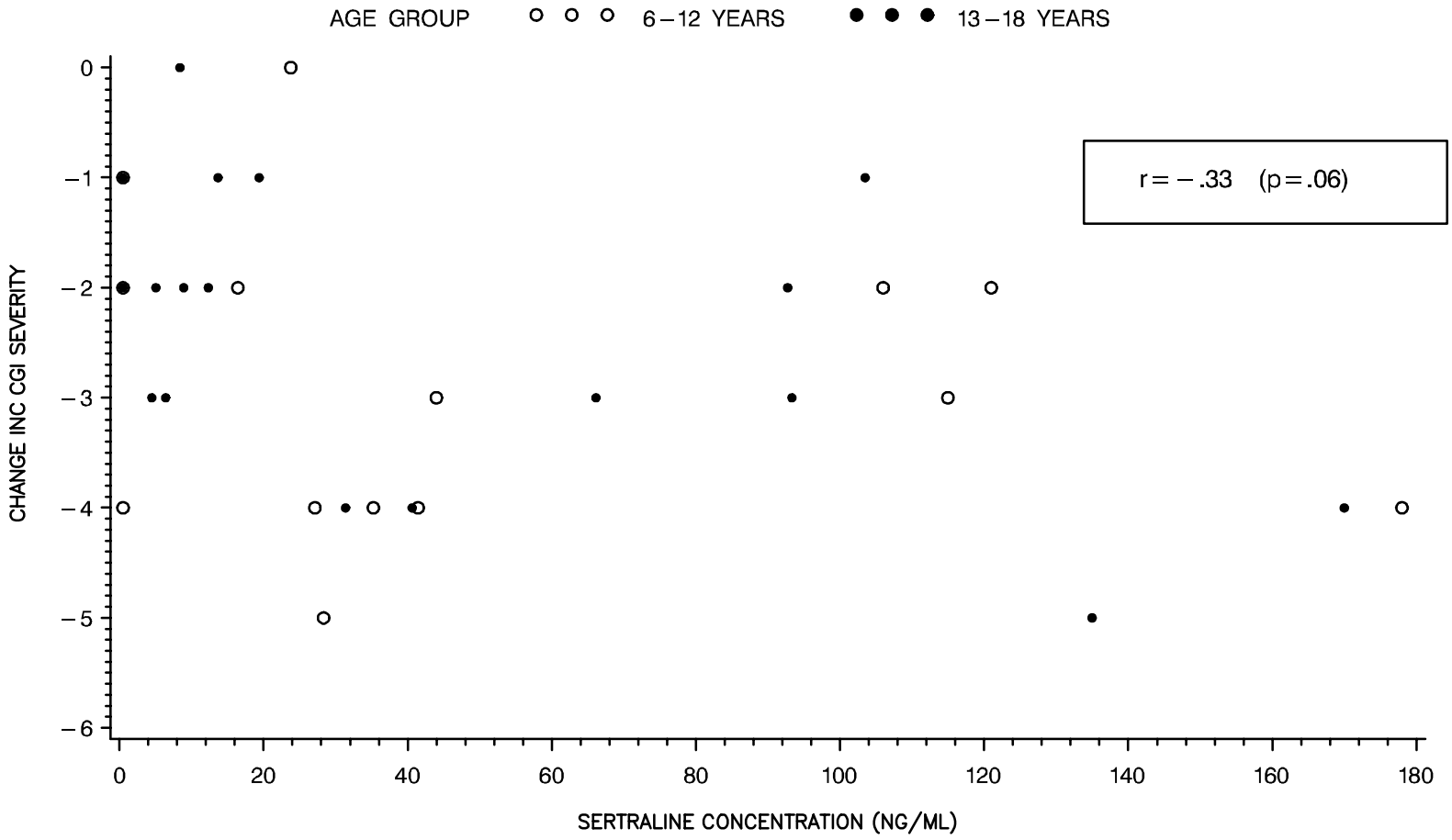
* 1 = VERY MUCH IMPROVED, 2 = MUCH IMPROVED, 3 = MINIMALLY IMPROVED, 4 = NO CHANGE, 5 = MINIMALLY WORSE, 6 = MUCH WORSE, 7=VERY MUCH WORSE.
NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 11. CHANGE IN CGI SEVERITY FROM STUDY 0525 BASELINE VERSUS SERTRALINE CONCENTRATION IN DEPRESSION PATIENTS

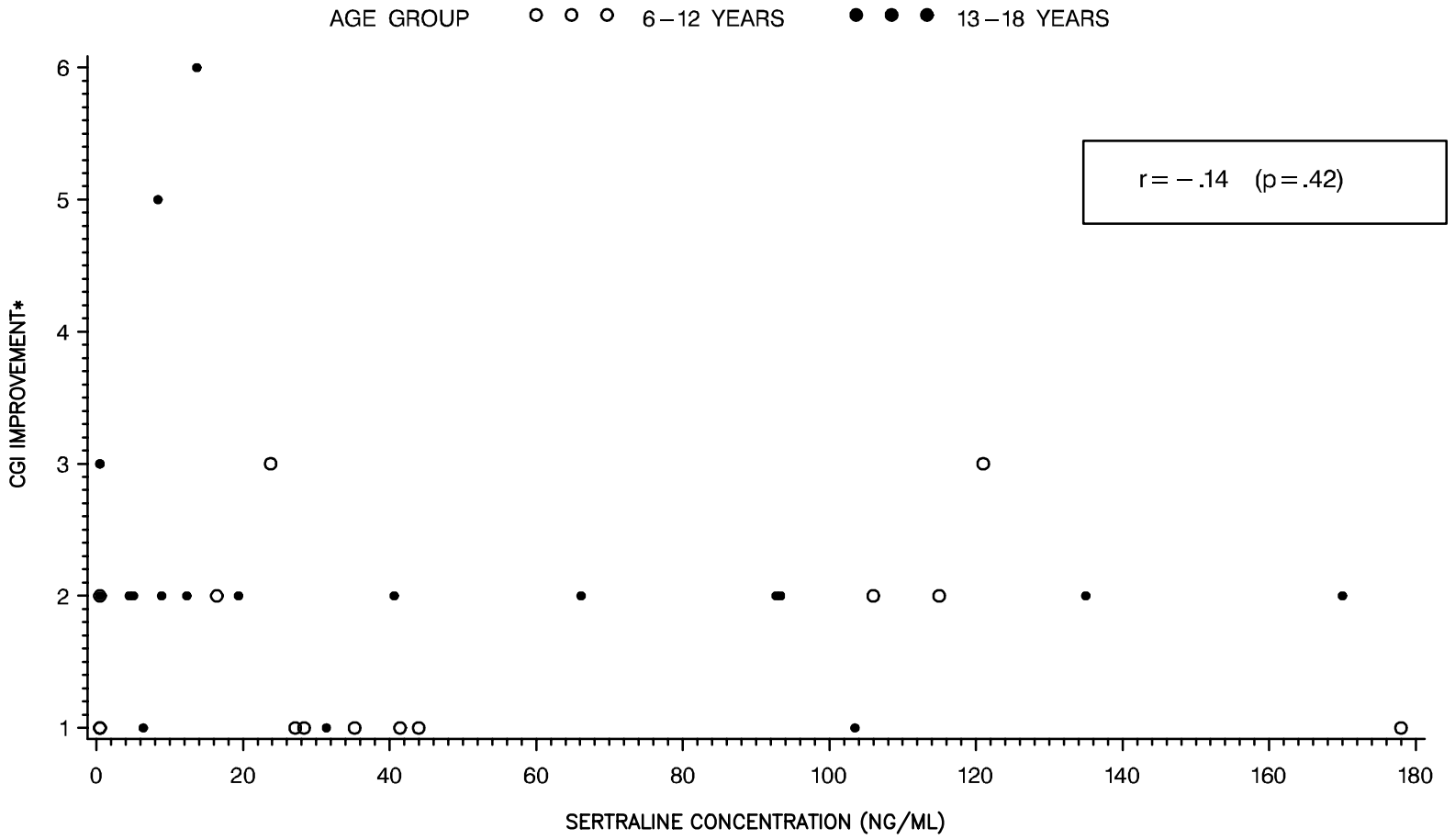


NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 12. CGI IMPROVEMENT VERSUS SERTRALINE CONCENTRATION IN DEPRESSION PATIENTS



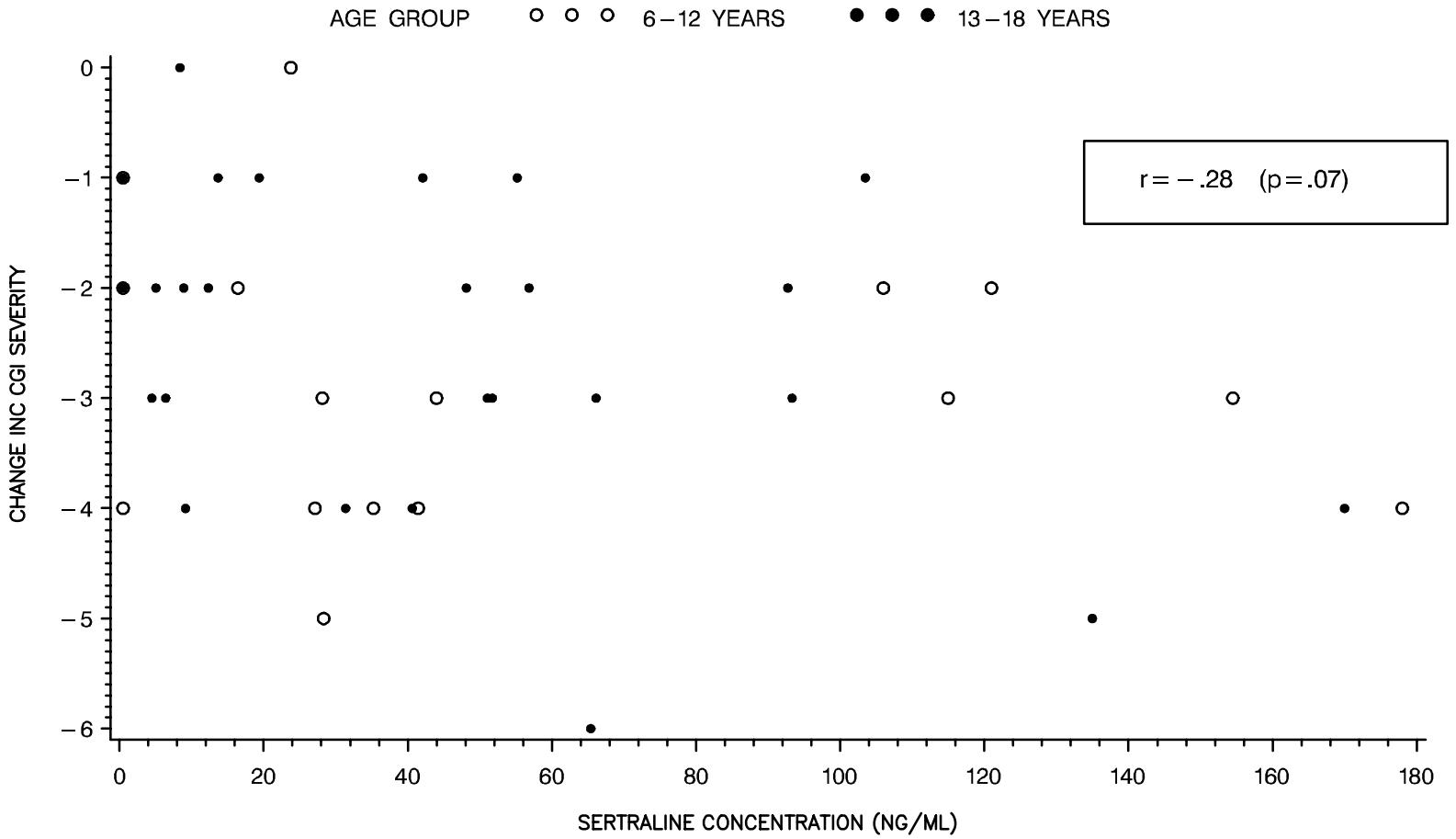
* 1= VERY MUCH IMPROVED, 2 = MUCH IMPROVED, 3 = MINIMALLY IMPROVED, 4 = NO CHANGE, 5 = MINIMALLY WORSE, 6 = MUCH WORSE, 7=VERY MUCH WORSE.
NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550

STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 13. CHANGE IN CGI SEVERITY FROM STUDY 0525 BASELINE VERSUS SERTRALINE CONCENTRATION IN ALL PATIENTS

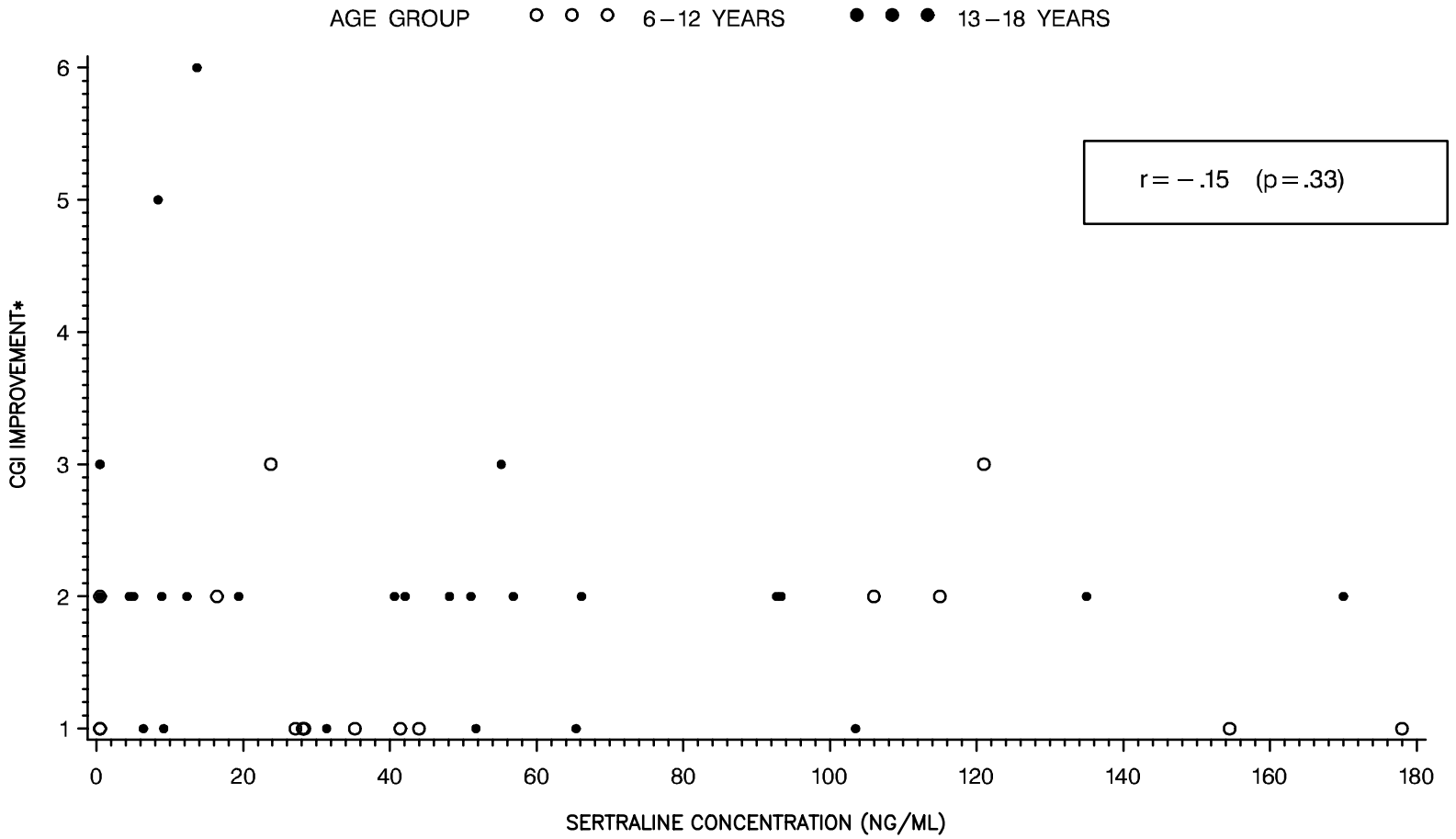


NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]

PROTOCOL: 91CK21-0550
STUDY: AN OPEN-LABEL, LONG-TERM EVALUATION OF SERTRALINE IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER OR DEPRESSION

FIGURE 14. CGI IMPROVEMENT VERSUS SERTRALINE CONCENTRATION IN ALL PATIENTS



* 1= VERY MUCH IMPROVED, 2 = MUCH IMPROVED, 3 = MINIMALLY IMPROVED, 4 = NO CHANGE, 5 = MINIMALLY WORSE, 6 = MUCH WORSE, 7=VERY MUCH WORSE.
NOTE: LAST AVAILABLE SERTRALINE CONCENTRATION-EFFECT PAIR IN STUDY 0550 FOR EACH PATIENT

[redacted]