STATISTICAL ANALYSIS PLAN

NCT03649477

Protocol Number	LV-101-3-01
Trial Phase	Phase 3
Protocol Title	Phase 3, Randomized, Double-Blind, Placebo-Controlled, 8-week Clinical Study to Assess the Efficacy, Safety, and Tolerability, of Intranasal Carbetocin (LV-101) in Prader Willi Syndrome (PWS) with Long Term Follow-Up: CARE-PWS
Protocol Version	Version 3.0, Amendment 4, 19 June 2019
Compound Name or Number	Intranasal Carbetocin (LV-101)
Indication	Prader-Willi Syndrome
Sponsor	Levo Therapeutics, Inc. 5215 Old Orchard Road Skokie, IL 60077 USA
Document Type	Statistical Analysis Plan
Prepared by	Brent A. Blumenstein, PhD Trial Architecture Consulting [redacted]
Version Number (Release Date)	v. 1.1 (08 July 2020)

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Phase 3, Randomized, Double-Blind, Placebo-Controlled, 8-week Clinical Study to Assess the Efficacy, Safety, and Tolerability, of Intranasal Carbetocin (LV-101) in Prader Willi Syndrome (PWS) with Long Term Follow-Up: CARE-PWS

AUTHOR

Brent A. Blumenstein, PhD
Lead Biostatistician
Trial Architecture Consulting

Date

APPROVAL SIGNATURES

Davis C. Ryman, MD, PhD
Vice President, Clinical Development
Levo Therapeutics, Inc.

Date

Jay Cormier, JD, PhD
Senior Vice President
Levo Therapeutics, Inc.

Date

Sara Cotter
Chief Executive Officer
Levo Therapeutics, Inc.

Date

REVISION HISTORY

Version	Date	Summary of Revision(s)
1.0	18 June 2020	New Document
1.1	08 July 2020	An addition to the analyses of global impression of change scales was made to include a proportional odds cumulative logit model. This addition is reflected in Sections 6.3 and 6.4. [redacted]

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation/Term	Definition
[redacted]	[redacted]
[redacted]	[redacted]
AE	Adverse Event
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
ATC	Anatomic Therapeutic Chemical
AUC	Area Under the Concentration-time Curve
C_{max}	Maximum Concentration
CGI-C	Clinical Global Impression – Change
CGI-S	Clinical Global Impression – Severity
cLDA	Constrained Longitudinal Data Analysis
COVID-19	Coronavirus Disease 2019
CY-BOCS	Children's Yale Brown Obsessive Compulsive Scale
ECG	Electrocardiogram
EoP	End-of-Period
EoS	End-of-Study
ET	Early Termination
FAS	Full Analysis Set
[redacted]	[redacted]
[redacted]	[redacted]
HQ-CT	Hyperphagia Questionnaire for Clinical Trials
IP	Investigational Product
IWRS	Interactive Web Response System
LS Mean	Least Square Mean
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed Model Repeated Measures
[redacted]	[redacted]
[redacted]	[redacted]
PADQ	PWS Anxiety and Distress Behaviors Questionnaire
PAS	Primary Analysis Set

Abbreviation/Term	Definition
[redacted]	[redacted]
PT	Preferred Term
PWS	Prader-Willi syndrome
SAE	Serious Adverse Event
SD	Standard deviation
SE	Standard Error
SOC	System Organ Class
SOP	Standard Operating Procedures
[redacted]	[redacted]
T_{max}	Time to Maximum Concentration
TEAE	Treatment Emergent Adverse Event
TLF	Tables, Listings, and Figures
WHODrug Global	World Health Organization Drug Global

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1 STUDY OVERVIEW

Prader-Willi syndrome (PWS) is a rare, serious, and life-threatening neurodevelopmental disorder that is caused by a defect on chromosome 15. In healthy individuals, several relevant genes in the 15q11-13 locus are expressed only from the paternal allele. The corresponding maternal allele is silenced (or "imprinted"), resulting in a complete reliance on the copy inherited from the father. When an individual lacks expression of these paternal genes, he/she develops PWS.

It is essential that the user of this document also be familiar with the contents of the CARE-PWS study protocol. The protocol is the designated place where background, operational, and procedural details necessary for the understanding of this trial can be found.

This is a randomized and double-blind phase 3 study to assess the efficacy, safety, and tolerability of intranasal carbetocin (LV-101) in patients with PWS. Clinical study drug (carbetocin and placebo vials) will be blinded at the study level, ensuring the blind of the sponsor, patient, caregiver, and study site. While approximately 175 patients were originally intended to be enrolled, due to the Coronavirus Disease 2019 (COVID-19) pandemic, 130 patients were randomized to receive 9.6 mg LV-101 or 3.2 mg LV-101 or placebo (1:1:1) during the placebo-controlled period. Efficacy will be assessed using both caregiver-reported and clinician-reported outcome measures as listed in Appendix B.

The initial 8-week, placebo-controlled period is the primary focus of the efficacy analyses. After the 8-week double-blind, placebo-controlled period, there will be a long-term follow-up period of 56 weeks during which all patients will receive active treatment with LV-101. The study provides for optional continued safety data collection during an extension period after Week 64 with possible switch of carbetocin dose depending on the outcome of the primary efficacy analyses.

2 STUDY OBJECTIVES AND ENDPOINTS

Objectives and endpoints for the study are summarized in Table 1. The primary efficacy estimand is the arm- and visit-specific mean of the changes from Baseline to the visit for the arm, and the analyses of this estimand will be performed in the context of a statistical model of repeated measures on the same patient.

The efficacy objectives are primarily focused on analyses of data from the 8-week placebo-controlled period. Objectives for data collected after Week 64 are focused on descriptive analyses of long-term safety events.

Table 1. Study Protocol Objectives and Endpoints

Objectives	Endpoints
Primary	
• To assess the efficacy of 9.6 mg/dose LV-101 3 times per day versus placebo on PWS behavioral symptoms	• Change in HQ-CT total score from Baseline to Week 8 • Change in CY-BOCS Severity Rating total score from Baseline to Week 8
Secondary	
• To assess the efficacy of 3.2 mg/dose LV-101 3 times per day versus placebo on PWS behavioral symptoms	• Change in HQ-CT total score from Baseline to Week 8 • Change in CY-BOCS Severity Rating total score from Baseline to Week 8
• To assess the treatment effect of LV-101 versus placebo on a broader range of maladaptive behavioral symptoms, first assessing 9.6 mg/dose LV-101 then assessing 3.2 mg/dose LV-101	• Change in PADQ score from Baseline to Week 8 • CGI-C score at Week 8
• To further characterize the treatment effect of LV-101 versus placebo on hyperphagia-related behavioral symptoms (as assessed by the caregiver), looking specifically at factors that may be less impacted by environmental controls (i.e., food security), first assessing 9.6 mg/dose LV-101 then assessing 3.2 mg/dose LV-101	• Change in score of a subset of HQ-CT items (Questions 1, 2, 5, 6, 8, 9) from Baseline to Week 8 • Change in score of Question 9 of HQ-CT from Baseline to Week 8
Safety	
• To assess the safety and tolerability of LV-101	• Frequency, severity, and seriousness of adverse events during the study • Clinically significant changes in physical examinations, laboratory assessments, electrocardiograms, and vital signs during the study

[redacted]

The study contains three distinct periods: the placebo-controlled period (Baseline through the Week 8 visit), the long-term follow-up period (from the Week 8 visit to the Week 64 visit), and the extension period (following the Week 64 visit). Analyses of efficacy and safety will be conducted for the placebo-controlled period, and descriptive statistics will be provided for efficacy and safety data collected in the long-term follow-up and extension periods. The statistical objectives and methodology for the evaluation of study data are described in more detail below.

3 STUDY DESIGN

3.1 Sample Size and Randomization

The study was originally designed to enroll approximately 175 patients. [redacted]

The results from the Phase 2 study of LV-101 served as the basis for powering this phase 3 study. The primary endpoint in the phase 2 study was HPWSQ-R, an 11-item questionnaire that was subsequently revised and validated, resulting in a 9-item questionnaire now called HQ-CT. These nine questions are a subset of the larger HPWSQ-R questionnaire. [redacted]

As a result, the subset of questions contained in the HQ-CT (9 vs. 11 questions) were used as the basis for power calculations [redacted], along with the CY-BOCS results from the Phase 2 study [redacted]

To account for a possible diminution of effect from Phase 2 to Phase 3, the mean differences in both the HQ-CT and CY-BOCS were reduced by [redacted] while maintaining the same standard deviations for the purposes of powering the study [redacted] A variety of statistical models were then applied (e.g., ANCOVA, simple t-test). Based on these models, the study was designed to have at least 90% power to detect a treatment arm difference in HQ-CT total score change from Baseline to Week 8 and at least 99% power to detect a treatment arm difference in CY-BOCS total score change from Baseline to Week 8.

Due to the COVID-19 pandemic, however, the sample size will be reduced to 130 patients.

Patients will be randomized (1:1:2:2) to one of four planned treatment arms:

a. Placebo during the 8-week controlled period followed by 9.6 mg/dose LV-101 after the 8-week placebo-controlled period

b. Placebo during the 8-week controlled period followed by 3.2 mg/dose LV-101 after the 8-week placebo-controlled period

c. 9.6 mg/dose LV-101 throughout the study

d. 3.2 mg/dose LV-101 throughout the study

Because there is no study intervention difference between the two placebo arms during the placebo-controlled period, the data from these arms will be pooled in all analyses focused on the

outcome from the placebo-controlled period, thereby creating a single placebo arm for all such analyses.

Patients will be randomized on the day prior to the Baseline visit (with Baseline visit representing Day 1, the first dose day) using an Interactive Web Response System (IWRS). The IWRS will provide a patient number and a unit number to be dispensed. This randomization is performed prior to the Baseline visit to allow for refrigerated thawing of investigational product vials prior to initiation of study intervention. The pharmacist will not know the identity of the intervention in the vials moved from freezing to refrigeration. Therefore, this randomization prior to the Baseline visit does not unblind any clinical site worker (i.e., pharmacist, Investigator), caregiver, or patient.

During the long-term follow-up and extension periods, all patients will receive LV-101. Patients randomized to initially receive placebo in the placebo-controlled period will receive intranasal carbetocin at either 9.6 mg/dose or 3.2 mg/dose in the long-term follow-up and extension periods according to the identity of the placebo arm to which randomized. Patients randomized to 9.6 mg/dose or 3.2 mg/dose LV-101 in the placebo-controlled period will continue on that same dose throughout the long-term follow-up and extension periods.

[redacted]

3.2 Data Monitoring Committee

The Data Monitoring Committee (DMC) is an independent multidisciplinary group consisting of clinicians and a biostatistician that, collectively, has experience in the management of subjects with Prader-Willi syndrome and in the conduct and monitoring of randomized clinical trials with interim analyses, and will act as an independent group to evaluate data to assure patient safety and study integrity. The objectives, roles, and responsibilities of the DMC and the format and frequency of the DMC meetings are documented in the DMC Charter.

The DMC will review all adverse events that are deemed severe, serious, or IP-related, as well as clinically significant vital signs, ECGs, and laboratory test results. The committee may also review specific study conduct related items, such as protocol deviations, in order to determine if these deviations are critical to the evaluation of safety during the clinical trial.

3.3 Primary Analysis

The primary analyses will be performed after all patients randomized for the placebo-controlled period have completed the Week 8 site visit assessments or have withdrawn from the study prior to completing the Week 8 visit. Following completion of the Week 8 visit by the last patient, all data through Week 8 in the database will be locked, and treatment assignments will be unblinded for the purpose of analyses of study endpoints. Unblinded information will not be disclosed to Investigators, caregivers, or patients.

The list of tables that will be generated for the locked data are specified in Appendix C. Additional tables and listings will be generated at the time of interim lock that may include data that is not yet locked (i.e., data in the long-term follow-up period). Those tables and listings are specified in Appendix D.

4 GENERAL METHODS

4.1 Presentation of Data

The data from the placebo-controlled period will be summarized separately from the long-term follow-up and extension periods. The data from the long-term follow-up period may be summarized together with the data from the extension period.

Data with qualifiers (e.g., "<") will be listed with the qualifier but summarized without the qualifier. Patient data listings will include data collected for all patients. Listings will be sorted by treatment arm, site, patient number, nominal visit, date and time (as applicable), unless otherwise indicated.

Categorical analyses will be summarized using counts and percentages. Percentages will be based on the number of patients in the analysis set for whom there are non-missing data, unless otherwise specified. Continuous variables, including change from Baseline, will be summarized using descriptive statistics [n, mean, standard deviation (SD), minimum, Q1, median, Q3, maximum]. For modeling results, least square (LS) means and standard errors (SEs) will be presented.

All statistical comparisons will be performed using two-sided tests at an $\alpha = 0.05$ significance level, unless specifically stated otherwise. P-values will be presented to four decimal places. P-values < 0.0001 will be presented as "< 0.0001."

All analyses will be performed using SAS v 9.3 or higher (SAS Institute, Inc, Cary, North Carolina, USA). Validation and quality control of the tables, listings, and figures (TLFs) will follow the appropriate Innovative Analytics standard operating procedures (SOPs).

4.2 Arms

There are four treatment arms, as indicated by the randomization scheme in Section 3.1. Treatment arm designations are defined separately for each study period, according to the following table.

Table 2. Treatment Arms by Period

Randomization Arm Planned Treatment	Placebo-Controlled Period Arm Designation	Long-Term Follow-Up and Extension Period Arm Designation	Long-Term Follow-Up and Extension Period Pooled Arm Designation
Placebo to 9.6 mg/dose	Pooled placebo	Placebo to 9.6 mg/dose	Pooled 9.6 mg/dose
Placebo to 3.2 mg/dose	Pooled placebo	Placebo to 3.2 mg/dose	Pooled 3.2 mg/dose
9.6 mg/dose	9.6 mg/dose	9.6 mg/dose	Pooled 9.6 mg/dose
3.2 mg/dose	3.2 mg/dose	3.2 mg/dose	Pooled 3.2 mg/dose

4.3 Study Day

The day of first IP administration is defined as Day 1. All other study days will be labeled relative to Day 1. Thus, study day for a particular event date on or after Day 1 is calculated as: *(Date of event – Date of first IP administration + 1)*. An event that occurs prior to Day 1 is calculated as: *(Date of event – Date of IP administration)*. Day 0 will not be used.

The duration of AE events will be calculated as *(Event end date – Event start date + 1)*.

4.4 Definition of Baseline, End-of-Period, and End-of-Study Values

The Baseline value for each patient is the value obtained during the Baseline visit, unless otherwise indicated.

For the primary analyses, the End-of-Period (EoP) value per patient is the last post-Baseline value during the placebo-controlled period. For the long-term analyses, the End-of-Study (EoS) value per patient is the last post-Baseline value, which may be relative to the EoP value for the placebo controlled period (for example, time to first AE of placebo patients starting long-term follow-up).

4.5 Scheduled and Unscheduled Visits

For the purposes of statistical analyses, the nominal visit designations as assigned by the investigator will be used.

4.6 Handling of Dropouts or Missing Data

Patient-level listings will present data as reported. Missing or partially missing dates that are required for date-dependent definitions (e.g., treatment-emergent adverse events, concomitant medications) will be assumed to be the most conservative date possible.

For the efficacy endpoints, no imputation will be performed, and, as described further in Section 6.1, the mixed model repeated measures (MMRM) analysis will use all available data to estimate the mean treatment effect.

An adverse event (AE) with a completely missing start date will be considered treatment-emergent; similarly, an AE that started the same month and year as IP administration but with missing start day will be considered treatment-emergent.

AEs with missing seriousness will be counted as “serious” in tables and missing in listings; likewise, AEs with missing severity will be counted as “severe” in tables and missing in listings and AEs with missing relatedness to the IP will be counted as “possibly related” and missing in listings.

Medical history with missing stop dates will be considered ongoing. Medications with missing stop dates will be considered in concurrent use during the study and will be counted in the summary table of concomitant medications.

4.7 Invalid Questionnaire Data

For the study, Levo and qualified consultants have engaged with designated raters and Investigators to train such individuals on the proper administration of all observer-reported and clinician-rated outcome measures used in the study. Despite these best efforts, it is possible that the administration of such measures may be improperly conducted or that circumstances beyond the control of the study site may cause the collected data to be invalid.

Any CY-BOCS, HQ-CT, PADQ, or other efficacy measures judged to be invalid in the opinion of the designated rater or Investigator prior to database lock will not be included in the efficacy analyses. The following criteria indicates that the time point is suspect and may be considered invalid:

- A scale or questionnaire is administered improperly (e.g., due to inadequate administration).
- An unexpected or unforeseen circumstance limits the ability of the respondent (caregiver) or designated rater to focus properly on completing the assessment or otherwise calls into question the reliability of the data collected.

Any instances of questionnaire invalidity will be appropriately documented prior to unblinding of study data and will be deemed missing from all efficacy analyses.

[redacted]

4.9 Analysis Sets

Final decisions regarding assignment of patients to the Safety and Per-Protocol Analysis Sets will be made during the Data Review Committee (DRC) meeting and documented in the DRC report prior to database lock and unblinding for the primary efficacy and final analyses. The DRC will be comprised, at a minimum, of Levo representatives and the Lead Statistician from Innovative Analytics (IA).

A summary of the number and percentage of patients in each analysis set will be provided. A listing of patient assignment into each analysis set will also be displayed.

4.9.1 Full Analysis Set

The Full Analysis Set (FAS) includes all patients who are both randomized and dosed. Patients will be analyzed according to the arm to which they are randomized. The FAS will be used in lieu of an Intent-to-Treat Set as a result of the logistical requirement in the CARE-PWS study to randomize patients in advance of their Baseline visit (in order to thaw frozen LV-101) – prior to

confirmation that they indeed meet entry criteria. This results in patients that are "randomized but not dosed" when they do not meet entry criteria at Baseline.

The justification for the use of the FAS in lieu of a traditional Intent-to-Treat is based on the fact that the FAS will be free of bias because no unblinding occurs as a result of randomization and therefore not initiating study intervention cannot be related to assigned arm. The use of the FAS with the specified justification is consistent with ICH E9, "Statistical Principles for Clinical Trials."

4.9.2 Primary Analysis Set

The Primary Analysis Set (PAS) is a subset of the FAS that includes all patients with at least one post-Baseline visit (i.e., Week 2 or Week 8) completed prior to March 1, 2020 and excludes all efficacy data collected on or after March 1, 2020. Patients who withdrew from the study prior to March 1, 2020 will be included even if no post-Baseline visits are recorded. Patients will be analyzed according to the arm to which they are randomized.

The PAS will be used as the definitive analysis for all alpha-controlled analyses (analyses associated with primary and secondary objectives).

Sensitivity analyses will be conducted that include all data in the FAS.

4.9.3 Per-Protocol Analysis Set

The Per-Protocol Analysis Set (PPS) includes patients in the PAS who have no protocol deviations during the placebo-controlled period that could significantly impact the completeness, accuracy, and/or reliability of the trial data. Identification of all patients and measures to be included in the PPS analyses will be determined before the database lock and unblinding for the interim analysis.

The PPS will be used as an additional sensitivity analysis for the efficacy endpoints. PPS patients will be analyzed according to the arm to which they are randomized.

4.9.3.1 Important Protocol Deviations Leading to Exclusion from the PPS Analysis

Only those deviations considered to have a major effect on efficacy will lead to complete exclusion of a patient from the PPS. For the purposes of this study, the following criteria have been identified as protocol deviations potentially warranting exclusion from the PPS, as it is considered that the occurrences of any of these criteria might have an important influence on the primary efficacy endpoint. Other deviations not specifically identified here may result in exclusion from the PPS analysis and will be identified prior to final database lock and unblinding.

Table 3. Important Protocol Deviations Leading to Exclusion from PPS

Type	Deviation	Method of Identification
Missing Data	Primary efficacy questionnaires incomplete or absent for the Basline, Week 2, or Week 8 visit	Programmatic
Visit Out of Window	Week 8 study visit is greater than two weeks from the scheduled visit date (visit date ± 2 weeks)	Programmatic
Concomitant Medications	Patient is administered an exclusionary concomitant medication or dosing change that may, in the determination of the Sponsor, alter efficacy of the investigational product during the placebo-controlled period	Manual
Study Drug Compliance	Patient misses greater than 20% of doses of investigational product during the placebo-controlled period of the study	Manual
Study Drug Compliance	Incorrect study drug or incorrect dose administered during the placebo-controlled period of the study	Manual
Patient Eligibility	Patient is inappropriately entered into the study or is later found to have violated an inclusion or exclusion criteria which may affect study efficacy measures	Manual

4.9.4 Safety Analysis Set

The Safety Analysis Set includes all patients who receive at least 1 dose of IP. Patients will be analyzed according to the treatment actually received. All safety analyses will be based on the Safety Analysis Set.

5 STUDY DESCRIPTORS

The study descriptors to be listed and summarized are described below. The FAS and PAS will be used for the listings and summaries, unless otherwise stated, as some of the summaries may also be prepared for other analysis sets, such as the PPS analysis set, defined in Section 4.9. All summaries will be presented by treatment arm and overall (i.e., all LV-101 patients), unless otherwise stated.

5.1 Eligibility and Informed Consent

Eligibility and informed consent parameters will be listed for all screened patients and will include date of informed consent/assent, protocol version at study entry, Screening and Baseline eligibility criteria, and randomization date.

The number and percentage of patients meeting all Screening and Baseline eligibility criteria and the number and percentage of patients with screen failure will be summarized. Reason for screen failure (as applicable) will be summarized for all screened patients.

5.2 Missed Visits and Assessments

A patient listing of missed visits will be presented.

5.3 Protocol Deviations

The number and percentage of patients with a protocol deviation will be displayed by protocol deviation category. Protocol deviations will be listed and tabulated for the placebo-controlled, long-term follow-up, and extension periods. Protocol deviations due to COVID-19, such as remote visits and missed assessments due to remote visits, will be listed.

5.4 Demographics and Baseline Characteristics

Demographic and Baseline characteristics will be listed and summarized for both the placebo-controlled and long-term follow-up periods by treatment arm and overall (as applicable). The demographic characteristics will consist of age, sex, genetic subtype of PWS, ethnicity, race, and prior use of oxytocin and carbetocin. A patient's age in years is calculated using the date of informed consent/assent, birth month, and birth year using the following formula:

$$\text{Age} = \text{INT}\left[\frac{[(\text{year(ICDATE)}*12 + \text{month(ICDATE)}] - [\text{year(BIRTH)}*12 + \text{month(BIRTH)}]}{12}\right]$$

where ICDATE = Informed Consent Date.

Baseline characteristics to be summarized include Baseline PWS nutritional phase, Baseline weight (expressed in kilograms where 2.2 pounds are equal to 1 kilogram), calculated Baseline BMI (using Baseline weight and screening height), calculated Baseline weight z-scores, and Baseline growth hormone use (receiving or not). Baseline values, as defined in Section 4.4, will be used for these Baseline characteristics.

5.5 General Medical History

General medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) coding system (Version 23.0) and will be listed and summarized for the placebo-controlled and long-term follow-up periods. The summary will be presented by MedDRA System Organ Class (SOC) and Preferred Term (PT). At each level of patient summarization, a patient will be counted only once within that level.

5.6 Pre-Treatment and Concomitant Medications

Prescription, over-the-counter, and alternative medication use will be coded to drug class, preferred drug name, and generic/trade drug name using the World Health Organization Drug Global dictionary (WHODrug Global) version September 1, 2018.

Medications that were stopped before the start of the initial IP administration will be considered "pre-treatment." All other medications will be considered "concomitant."

Pre-treatment medications will be presented separately from concomitant medications. Pre-treatment medications will be summarized and listed. Concomitant medications will be summarized and listed for the placebo-controlled, long-term follow-up, and extension periods.

For frequency tables, medications will be summarized by WHODrug Global Anatomic Therapeutic Chemical (ATC) Level 2 and Preferred Term. At each level of patient summarization, patients who reported one or more medications within that level are only counted once for that level.

5.7 IP Administration

Details of IP administration will be listed for the Safety Analysis Set and will include for each visit: the kit number, date of first and last dose dispensed from the kit, number of missed doses, and number of unrecorded doses for the placebo-controlled, long-term follow-up, and extension periods.

5.7.1 Treatment Duration

Overall treatment duration in days will be calculated using the following formula:

Overall treatment duration = last IP administration date – first IP administration date + 1

Summary statistics for overall treatment duration (days) will be presented by treatment arm and overall (as applicable) for the placebo-controlled, long-term follow-up, and extension periods. A frequency table of treatment duration will also be presented for the following duration categories:

- ≤ 56 days
- > 56 and < 120 days
- ≥ 120 and < 180 days
- ≥ 180 and < 270 days
- ≥ 270 and < 360 days
- ≥ 360 days

5.7.2 IP Compliance

IP compliance for each patient will be calculated using the following formula:

$$\text{IP Compliance (\%)} = \frac{\text{Number of doses administered during the period}}{\text{Number of planned doses during the period}} \times 100$$

The number of doses administered will be calculated based on the number of days between visits (multiplied by 3 planned doses per day) less the number of missed doses and number of unrecorded doses, accounting for instances where less than three doses are planned to be administered on the first day of each study period (i.e., if the Baseline or Week 8 visit occurs at the lunchtime dose).

Where necessary to account for dose type, dose types are defined as follows.

Dose Type	Dose Time Interval
Pre-breakfast	06:00 – 10:29
Pre-lunch	10:30 – 15:59

Dose Type	Dose Time Interval
Pre-dinner	16:00 – 20:00
Query for data entry error	20:01 – 05:59

IP compliance will be summarized by treatment arm for each visit in the placebo-controlled and long-term follow-up periods, as well as overall for each study period. A frequency table will also be presented by treatment arm, which will include the number of patients who received at least 1 dose, the total number of doses administered, the number of patients who missed at least one dose, the total number of missed doses, the number of patients with at least 1 missing data dose, and the total number of missing data doses.

5.8 Patient Study Progress

A listing of patient study progress will be presented, displaying the following dates by patient: Screening, informed consent, randomization, first IP administration, last IP administration, and study visits. The number of patients that completed each study visit will be summarized.

5.9 Patient Disposition

Patient disposition will be listed and summarized for all screened patients. The following will be summarized:

- the number of patients randomized;
- the number of patients who received IP;
- the number of patients who completed Week 8 of the study;
- the number of patients who discontinued from the study prior to Week 8 and the primary reason for discontinuation;
- the number of patients who discontinued from the study after Week 8 but prior to Week 64 and the primary reason for discontinuation;
- the number of patients still active in the study, if any;
- the number of patients who completed Week 64;
- the number of patients who chose to continue in the extention period; and
- the number of patients who discontinued from the study during the extention period.

6 PRIMARY EFFICACY ANALYSES

Listings and summaries of the efficacy parameters will be presented for the Primary Analysis Set (PAS), unless indicated otherwise. Efficacy parameters are described below, and unless otherwise indicated, all efficacy analyses will use study site as a covariate, where low enrolling sites will be pooled. Low enrolling sites are defined as sites that did not enroll at least one subject in each of the three placebo-controlled treatment arms. Therefore, site pooling may differ for each analysis set.

6.1 Primary Efficacy Endpoints

As discussed during Levo's [redacted] meeting with FDA, there are two primary efficacy endpoints in this study focusing specifically on the 9.6 mg/dose LV-101 versus placebo:

1. the HQ-CT total score change from Baseline to Week 8

and

2. the CY-BOCS total score change from Baseline to Week 8.

[redacted]

In accordance with FDA's draft guidance, "Multiple Endpoints in Clinical Trials, Guidance for Industry," and as agreed to with FDA during the [redacted] meeting, these primary efficacy endpoints will be evaluated using the Hochberg multi-step, step-up procedure (Hochberg, 1988; Huang and Hsu, 2007) at an overall 2-sided 0.05 level of significance. The hypotheses to be tested are as follows:

$$\text{HQ-CT: } H_o: \mu_H - \mu_P = 0 \; vs. \; H_a: \mu_H - \mu_P \neq 0$$

$$\text{CY-BOCS: } H_o: \mu_H - \mu_P = 0 \; vs. \; H_a: \mu_H - \mu_P \neq 0$$

Where H_o is the null hypothesis, H_a is the alternative hypothesis, and μ_H and μ_P are the population mean changes from Baseline to Week 8 in 9.6 mg/dose LV-101 and placebo-treated patients, respectively. Change from Baseline is defined as the Week 8 value minus the Baseline value for each patient.

The overall Type I error probability is specified to be two-sided 0.05 (overall two-sided alpha). Protection for the overall two-sided alpha against multiplicity across the two primary outcomes will be implemented using the Hochberg procedure. If the largest of the two-sided p-values is ≤ 0.05 (the specified level of significance), then both comparisons will be identified as having met statistical criterion. If the largest of the two-sided p-values is > 0.05, but the smallest of the two-sided p-values for the two comparisons is ≤ 0.025 (half the specified level of significance), then the associated comparison with the smaller p-value will be identified as having met statistical criterion. If neither of the two-sided p-values for the two primary comparisons is ≤ 0.025 (= 0.05/2), then neither of the primary objectives will be identified as having met statistical criterion.

The process for the Hochberg multi-step procedure is illustrated in Figure 1.

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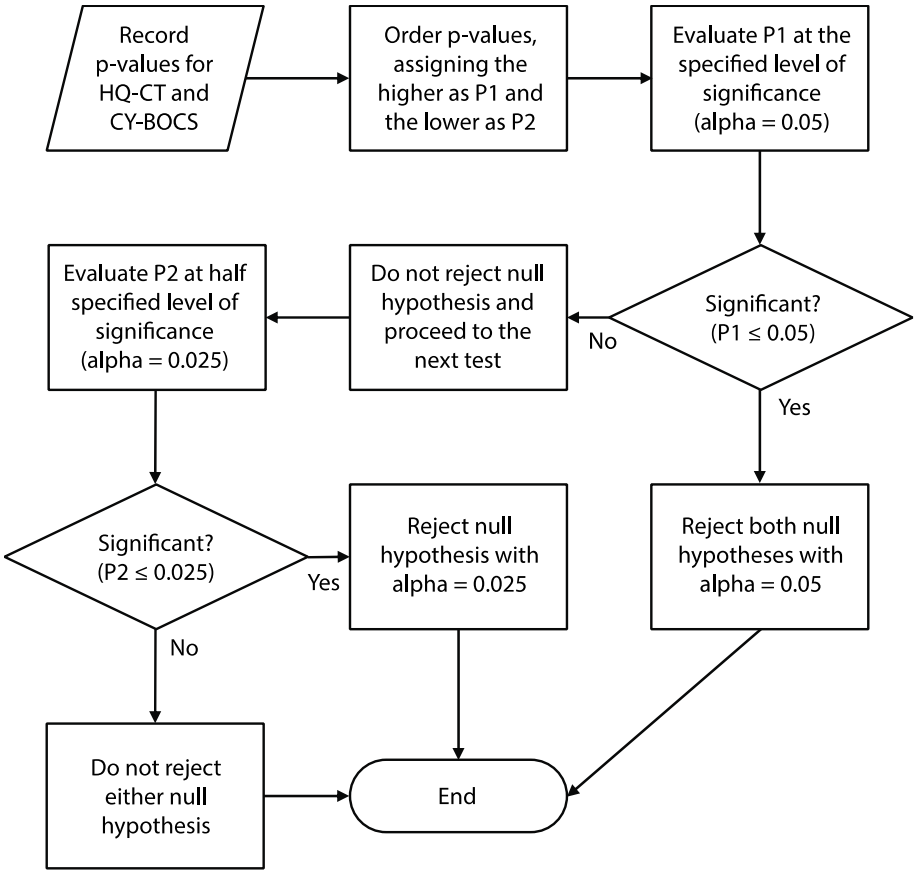
Figure 1. Process for Hochberg multi-step, step-up procedure



6.1.1 Sensitivity Analyses

The primary efficacy analyses will be repeated using the FAS replacing the PAS, then using the PPS replacing the PAS.

The primary efficacy analyses will also be repeated by replacing the primary model with an MMRM where Baseline values are not included as dependent variables but instead are used as an additional covariate. This analysis will then be repeated using the FAS replacing the PAS. [redacted]

[redacted]

[redacted]

An effect modifier analysis will be used to assess departures from homogeneity of effect across subsets defined by Baseline attributes. Baseline attributes may include, but are not limited to gender, age (tertiles), gender by age (tertiles), [redacted] and site. Low-enrolling sites, as defined in Section 6, will be pooled. The effect modifier analysis will first be performed for the PAS, then subsequently for the FAS.

The sensitivity of the primary analysis to missing data may be evaluated using multiple imputation on the PAS and FAS. These planned multiple imputation sensitivity analyses may use the pattern mixture methodology to impute with 500 replicates. Two imputations are planned:

1. replace experimental arm missing data with random sampling from non-missing experimental arm data and replace missing control arm missing data with random sampling from non-missing control arm data

and

2. replace experimental arm missing data with random sampling from non-missing control arm data and replace missing control arm missing data with random sampling from non-missing experimental arm data.

Additional multiple imputations will be done if deemed beneficial, based on data-driven results, when it is obvious that such data-driven analyses challenge the original analyses planned. The motivation will be to illustrate the nature and extent of imputations necessary to challenge favorable outcomes by nearly reversing or reversing to an unfavorable outcome.

Sensitivity analyses will be performed removing study visit data where either the caregiver or clinician rater differ from the caregiver or clinician rater during the Baseline visit.

6.2 Secondary Efficacy Endpoints

If at least one of the two primary efficacy endpoints meet statistical significance using the Hochberg procedure, the secondary endpoints will then be tested for the PAS. [redacted]

[redacted]

The first secondary efficacy evaluation will repeat the primary efficacy Hochberg procedure, using the 3.2 mg/dose LV-101 (instead of 9.6 mg/dose LV-101). Specifically, this is an analysis of HQ-CT total score change from Baseline to Week 8 and the CY-BOCS total score change from Baseline to Week 8, for the 3.2 mg/dose LV-101 arm versus placebo, using the same Hochberg procedure as described in Section 6.1 and the appropriate level of significance remaining from the primary analyses. This first secondary efficacy analysis will act as a gatekeeper to subsequent secondary evaluations.

If the first secondary evaluation fails (i.e., neither HQ-CT nor CY-BOCS meet significance using the Hochberg approach for the 3.2 mg/dose), all subsequent analyses will become descriptive.

Otherwise, if the first secondary evaluation succeeds (i.e., either HQ-CT or CY-BOCS meet significance using the Hochberg approach for the 3.2 mg/dose), then a fixed-sequence test procedure will be performed to assess the following additional secondary efficacy endpoints in the order specified (hierarchical alpha protection).

- PADQ total score change from Baseline to Week 8
- CGI-C score through Week 8
- HQ-CT total score for Questions 1, 2, 5, 6, 8, and 9 change from Baseline to Week 8
- HQ-CT score for Question 9 change from Baseline to Week 8

The previously described cLDA analysis will be performed when appropriate, with the comparison of 9.6 mg/dose LV-101 versus placebo tested first for each endpoint sequentially, followed by 3.2 mg/dose LV-101 versus placebo. For the analysis of CGI-C, the secondary MMRM model will be used instead of the cLDA model, with the Baseline CGI-S as the covariate.

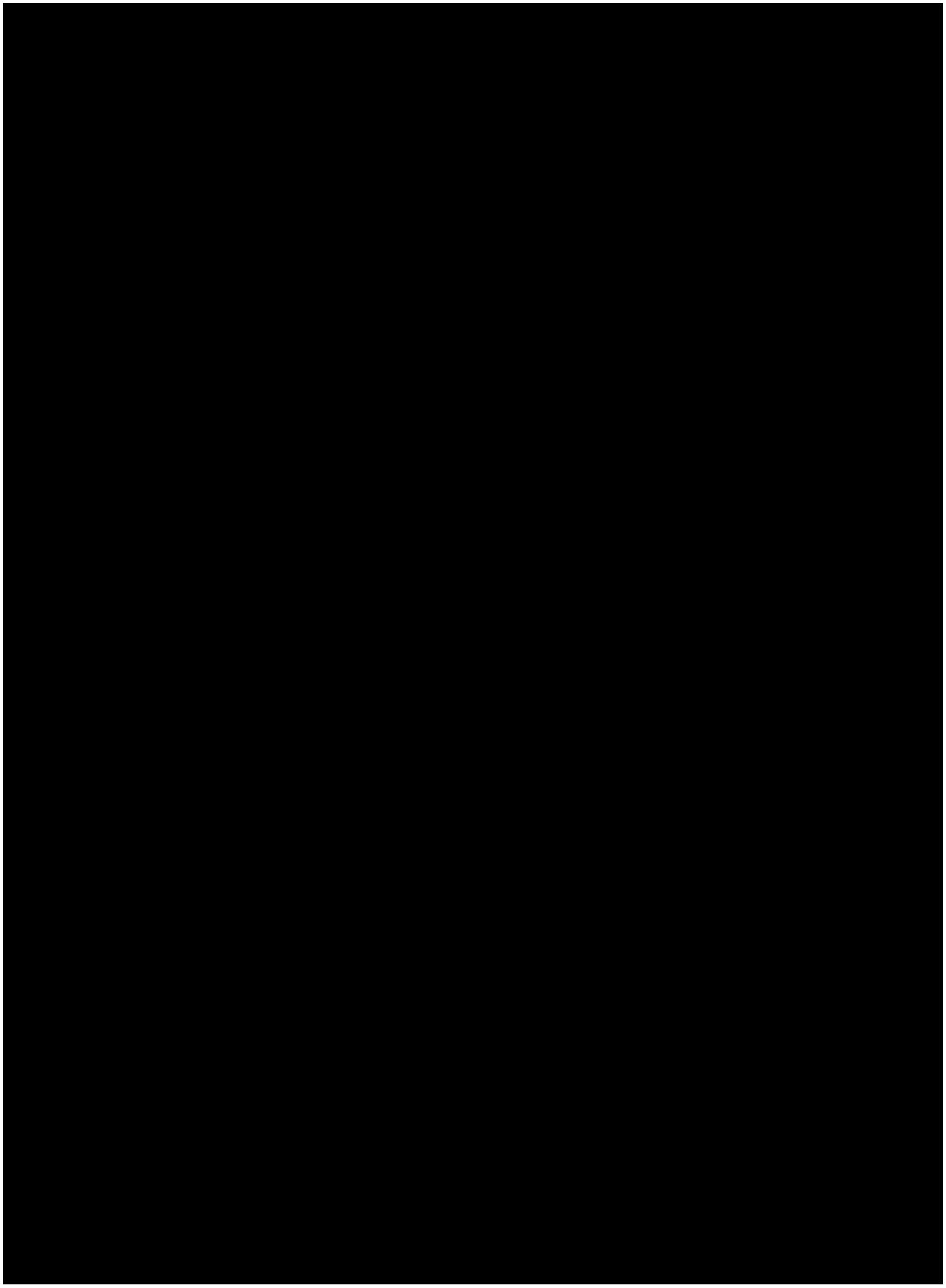
Once one test fails to meet significance, then all subsequent statistical tests will provide only nominal p-values; all subsequent analyses will be considered descriptive.

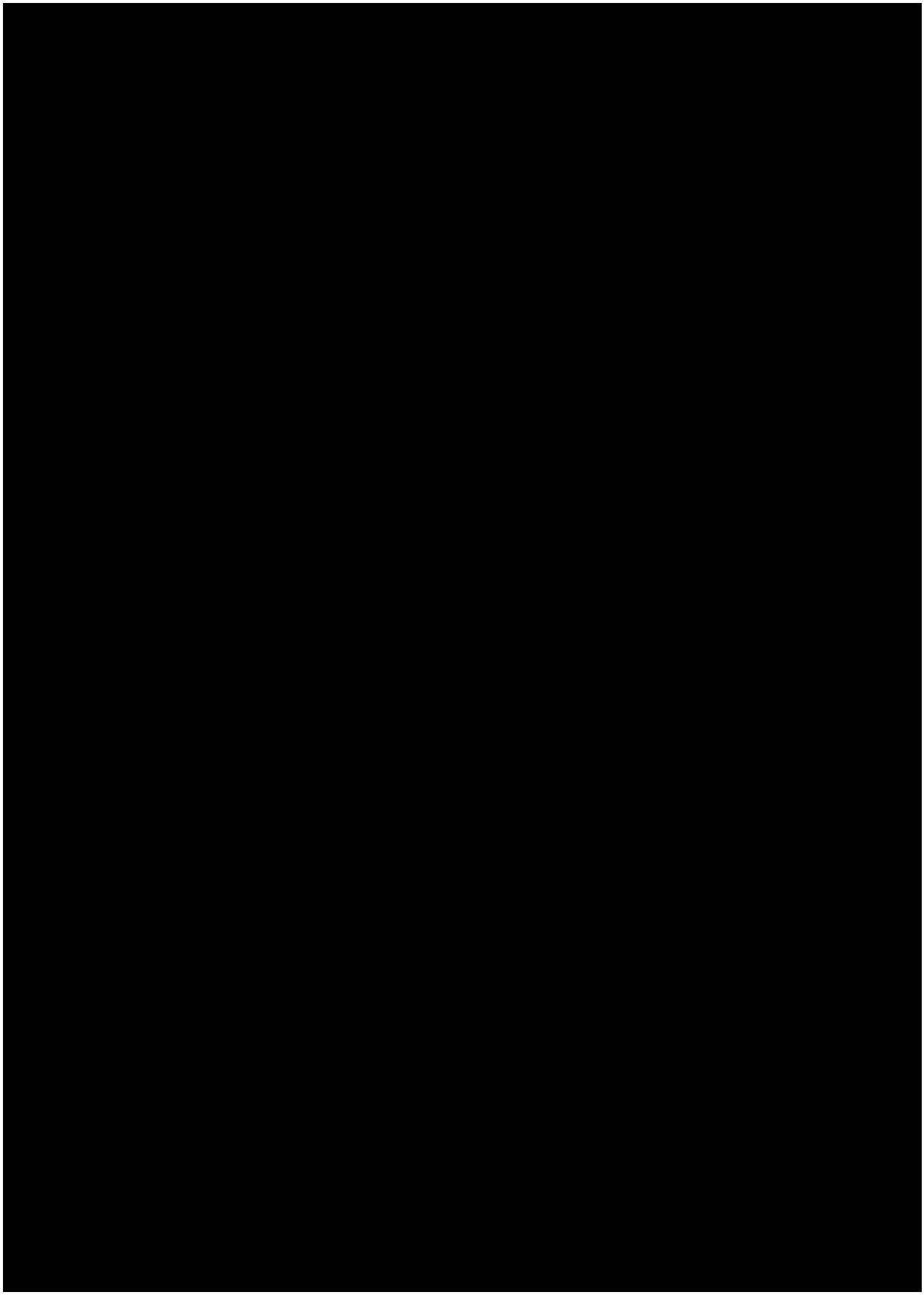
6.2.1 Sensitivity Analyses

The secondary efficacy analyses will be repeated using the FAS replacing the PAS, then the PPS replacing the PAS.

The secondary sensitivity analysis will also repeat the primary sensitivity analyses as described in Section 6.1.1, instead using the 3.2 mg/dose LV-101 (vs. 9.6 mg/dose LV-101), including the application of the secondary MMRM model for both the PAS and FAS.

Effect modifier analyses will be performed on the first two secondary endpoints (i.e., HQ-CT total score change from Baseline to Week 8 and the CY-BOCS total score change from Baseline to Week 8, for the 3.2 mg/dose LV-101 arm versus placebo) for the PAS and FAS.





[redacted]

7 EFFICACY ASSESSMENTS DURING THE LONG-TERM FOLLOW-UP PERIOD

Listings and tables for the efficacy assessments during the long-term follow-up period will be presented for the PAS and FAS, unless indicated otherwise. All presentations of change in values will be presented as change from Baseline and change from Week 8.

7.1.1 PWS Nutritional Phase

Observed values will be listed. A frequency table will be presented by treatment arm and overall.

7.1.2 Hyperphagia Questionnaire for Clinical Trials (HQ-CT)

Observed values will be listed.

Observed totals of the individual raw scores, changes from the placebo-controlled period Baseline total scores, and changes from Week 8 total scores will be summarized by treatment arm and overall for Weeks 10, 16, 28, 40, 52, 64, and at EoS.

Observed totals for each subset and changes of the prospectively identified HQ-CT subsets (Questions 1, 2, 5, 6, 8, and 9, and Question 9 alone) will also be summarized by treatment arm and overall for Weeks 10, 16, 28, 40, 52, 64, and at EoS.

7.1.3 Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS)

Results of the clinician-completed symptom checklists will be listed. Observed values, changes from the placebo-controlled period Baseline values, and changes from Week 8 values will be summarized by treatment arm and overall for Weeks 10, 16, 28, 40, 52, 64, and at EoS. These summaries will be presented for total scores, obsessions severity subscores, and compulsions severity subscores.

7.1.4 PWS Anxiety and Distress Behaviors Questionnaire (PADQ)

Results of the caregiver-completed questionnaire will be listed. PADQ total scores are calculated as the sum of the first 14 items of the questionnaire. Observed values, changes from the placebo-controlled Baseline values, and changes from Week 8 values will be summarized by treatment arm and overall for Weeks 10, 16, 28, 40, 52, 64, and at EoS.

7.1.5 Clinical Global Impression – Severity (CGI-S) and Clinical Global Impression – Change (CGI-C)

Clinician global impressions of the current severity of illness and changes in severity of illness will be listed. Observed values for CGI-S and CGI-C will be summarized by treatment arm and overall for Weeks 10, 16, 28, 40, 52, 64, and at EoS.

8 SAFETY ANALYSES

Listings and tables of the safety parameters will be presented for the Safety Analysis Set, with separate tables for the placebo-controlled, long-term follow-up, and extension periods. The data from the long-term follow-up period may be summarized together with the data from the extension period, where applicable. Note that the study remains blinded with respect to carbetocin dose even after the placebo-controlled period and therefore between-arm comparisons are free of confounding with the exception of the loss due to study departures and deviations related to intervention used. Safety parameters are described below.

All presentations of change in values for the long-term follow-up period will be presented as change from Baseline and change from Week 8. For the purposes of Baseline and Week 8 values for safety and laboratory assessments, the values will be the values obtained on the date of the Baseline and Week 8 visit, or, if missing, the last non-missing value prior to the visit (the last observation will be carried forward).

8.1 Adverse Events (AEs)

Adverse events will be coded using MedDRA Version 23.0.

For the placebo-controlled period, summaries will include AEs with a start date from the start date of the first dose of IP in the placebo-controlled period to the patient's last placebo-controlled period visit, but summaries will exclude any events with a start date that is on or after the start date of the first dose of IP in the long-term follow-up period.

Combined long-term follow-up/extension period summaries will include events with a start date from the start date of the first dose of IP in the long-term follow-up period to study termination.

8.1.1 Pre-Treatment Serious Adverse Events (SAEs)

Pre-treatment SAEs are defined as any SAE that started before the patient's first exposure to the IP in the placebo-controlled period. An SAE that is ongoing at the time of initial IP exposure

and subsequently worsens after IP exposure is considered treatment-emergent and will be recorded as a separate SAE. Pre-treatment SAEs will be listed only.

8.1.2 Treatment-Emergent AEs

The following AEs are defined as treatment-emergent AEs (TEAEs).

- AEs that begin or worsen after the first administration of investigational product
- AEs with a completely missing start date or AEs with missing start day that started the same month and year as investigational product administration

Patient listings of all treatment-emergent adverse events as reported will be presented.

An overall summary table will be presented by treatment arm for all TEAEs, TEAEs by maximum severity, TEAEs by greatest degree of relationship to IP, serious TEAEs, TEAEs leading to drug interruption, TEAEs leading to study discontinuation, and deaths.

Serious TEAEs, deaths, and TEAEs that resulted in study discontinuation will be listed and summarized.

[redacted]

All adverse event tables will include summaries by MedDRA System Organ Class and Preferred Term, with patients who have the same adverse event more than once counted only once for that event and with patients who have more than one adverse event within a System Organ Class counted only once in that System Organ Class. The numbers and percentages of patients reporting an event will be presented in these summaries.

8.2 Pregnancy Reporting

If observed, pregnancy related information from a female patient or a male participant's female partner who becomes pregnant while the male participant is in the study will be listed.

8.3 Intranasal Spray Pump Incidents (Including Malfunctions)

All medical device incidents or malfunctions of the device that resulted in an incident will be listed. Incidents reported by the site and by the sponsor will be listed separately.

8.4 Clinical Safety Laboratory Assessments

Clinical safety laboratory assessments will be summarized separately for the placebo-controlled period and the long-term follow-up period. Laboratory assessments are not performed in the extension period.

8.4.1 Hematology, Coagulation, D-dimer, Chemistry, and Urinalysis

- Hematology: Platelet count, red blood cell count, hemoglobin, hematocrit, white blood cell count with differential (neutrophils, lymphocytes, monocytes, eosinophils, and basophils)

- Coagulation: Prothrombin time, activated partial thromboplastin time, thrombin time, fibrinogen
- D-dimer (during placebo-controlled period only)
- Chemistry: Calcium, chloride, sodium, potassium, glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total and direct bilirubin (reflex to direct), creatinine, blood urea nitrogen, total protein, alkaline phosphatase, and albumin
- Urinalysis: specific gravity, pH, glucose, protein, blood, urobilinogen by dipstick, and microscopic examination (if blood or protein is abnormal)

For hematology, coagulation, D-dimer, chemistry, and urinalysis quantitative tests, summary statistics will be presented for the observed values at each visit. Summary statistics will also be presented for the change from Baseline values to each post-Baseline visit, including EoP/EoS.

The shift from Baseline to EoP/EoS (as applicable) will also be presented for the hematology, coagulation, D-dimer, and chemistry panel parameters with results classified as low (L), Normal (N), and high (H) according to the laboratory-supplied normal ranges. A summary of shift to low and high will be presented for each parameter, displaying the number of patients whose values shifted as a percentage of the number of patients at risk for shifting, defined as follows:

- The patients at risk for shifting to high are those with normal or low values at Baseline.
- The patients at risk for shifting to low are those with normal or high values at Baseline.

For all tests, results will be displayed in patient listings, with those values falling outside the laboratory reference range flagged. Laboratory reference ranges will be provided by the laboratory site(s) and included in an appendix of the clinical study report.

8.4.2 Pregnancy Testing

Urine pregnancy tests performed on females of childbearing potential will be listed.

8.5 Physical Examination

Physical examination results will be listed and summarized for both the placebo-controlled and long-term follow-up periods. Physical examinations are not performed in the extension period. Observed status (e.g., normal, abnormal-not clinically significant, abnormal-clinically significant, not done) will be summarized for each body system by visit.

Observed status of Tanner staging (e.g., Stage 1 – Stage 5) will also be summarized.

8.6 Nasal Assessment

Nasal assessment results will be listed and summarized for both the placebo-controlled and long-term follow-up periods. Nasal assessments are not performed in the extension period. Observed protocol-specified grades (e.g., Grade 0, Grade 1A, Grade 1B, Grade 2, Grade 3 and Grade 4) by visit will be summarized.

8.7 Vital Signs and Weight

Vital signs include systolic and diastolic blood pressure, pulse, respiration rate, and body temperature. Observed values of vital signs, height, weight, and BMI will be displayed in patient listings. BMI scores, weight Z-scores, and BMI Z-scores will be calculated, where applicable, and listed. Observed values and changes from Baseline (for all parameters except height) will be summarized at each post-Baseline visit, including EoP/EoS separately for the placebo-controlled and long-term follow-up periods. Vital signs are not collected in the extension period.

8.8 12-Lead Electrocardiograms

Overall interpretation of 12-lead Electrocardiograms (ECGs) will be listed and summarized separately for the placebo-controlled and long-term follow-up period. A summary of shift to normal, abnormal (not clinically significant), and abnormal (clinically significant) will be presented for each parameter, displaying the number of patients whose values shifted as a percentage of the number of patients at risk for shifting, defined as follows:

- The patients at risk for shifting to abnormal are those with normal values at Baseline.
- The patients at risk for shifting to normal are those with abnormal values at Baseline.

[redacted]

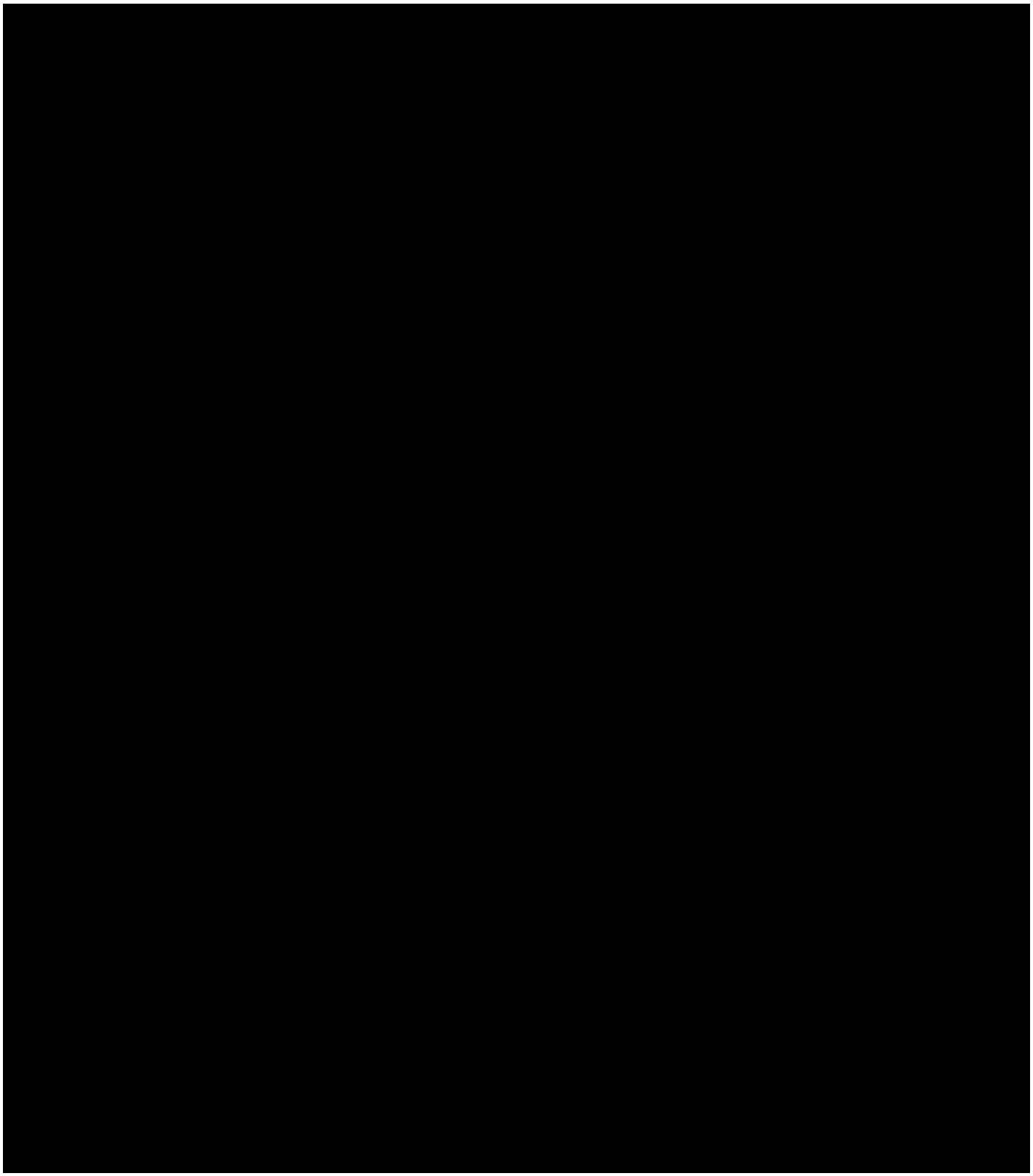
10 DEVIATIONS FROM STATISTICAL METHODS IN THE PROTOCOL

There were no changes to the conduct of the study since the last protocol amendment. Analyses planned but not performed and the rationales for the changes are as follows.

<Deviations to be added later if necessary>

11 REFERENCES

[redacted]



APPENDIX B: SCHEDULE OF ASSESSMENTS

The schedule of assessments for the placebo-controlled period is provided in Table 4, the schedule of assessments for the long-term follow-up period is provided in Table 5, and the schedule of assessments for the extension period is provided in Table 8. The schedule of assessments for questionnaires is provided in Table 6 for the placebo-controlled period and in Table 7 for the long-term follow-up period.

Table 4. Schedule of Assessments for the Placebo-Controlled Period

Procedure	Screening (14 to 28 days prior to Baseline)	Baseline Site Visit	Week 2 Site Visit (±2 days)	Week 8 Site Visit (±2 days)
Informed consent/assent	X			
Inclusion and exclusion criteria	X	X		
Demography	X			
Medical history	X	X		
Physical examination	X	X	X	X
Nasal assessment	X	X	X	X
Vital signs (including weight)	X	X	X	X
Height	X			
Pregnancy test[a]	X	X	X	X
Laboratory assessments (chemistry, hematology, coagulation, urinalysis)	X	X	X	X
12-lead electrocardiogram	X	X		X
Randomization, if patient qualifies		X		X[b]
Training on investigational product administration		X		
Study drug dosing		X	ongoing	ongoing
Adverse event review		X	X	X
Serious adverse event review	X	X	X	X
Concomitant medication review (including all supplements)	X	X	X	X
Caregiver training on clinical outcomes assessments	X	X		
Structured interview, including clinical outcomes assessments by caregiver and clinician[c]	X	X	X	X
Plasma collection for pharmacokinetics			X[d]	
Archive blood/plasma samples[e]		X	X	X

[a] Pregnancy testing will be conducted only for females of childbearing potential, as judged by the Investigator.

[b] At Week 8, patients who were randomized to placebo in the placebo-controlled period will be randomized (1:1) to 9.6 mg/dose intranasal carbetocin (LV-101) 3 times per day before meals or 3.2 mg/dose intranasal carbetocin (LV-101) 3 times per day before meals.

[c] See Table 6. Appropriate training and procedures will be instituted (including structured interviews) to ensure familiarity with the instruments, administer instruments consistently (reducing measurement error), and enable honest feedback.

[d] Obtain blood sample at 25 to 35 minutes after observed dosing of study drug.

[e] Archive samples may be tested for immunogenicity (presence and characterization of anti-drug antibodies), genetic testing (including genome sequencing) and biochemical analyses of hormones or other analytes of relevance to Prader-Willi syndrome.

Table 5. Schedule of Assessments for the Long-Term Follow-Up Period

Procedure	Week 10 (±2 Days)	Week 16 (±1 Week)	Week 28 (±1 Week)	Week 40 (±1 Week)	Week 52 (±1 Week)	Week 64 (±1 Week)	Early Term (if required)
Physical examination	X	X	X	X	X	X	X
Nasal assessment	X	X	X	X	X	X	X
Vital signs (including weight)	X	X	X	X	X	X	X
Height						X	X
Pregnancy test[a]	X	X	X	X	X	X	X
Laboratory assessments (chemistry, hematology, urinalysis)	X	X	X	X	X	X	X
12-lead electrocardiogram		X				X	X
Study drug dosing	ongoing	ongoing	ongoing	ongoing	ongoing	X	
Adverse event review	X	X	X	X	X	X	X
Serious adverse event review	X	X	X	X	X	X	X
Concomitant medication review (including all supplements)	X	X	X	X	X	X	X
Structured interview, including clinical outcomes assessments by caregiver and clinician[b]	X	X	X	X	X	X	X
[redacted]							
Archive blood/plasma samples[d]	X	X	X	X	X	X	X

[redacted]

[a] Pregnancy testing will be conducted only for females of childbearing potential, as judged by the Investigator.

[b] See Table 7. Appropriate training and procedures will be instituted (including structured interviews) to ensure familiarity with the instruments, administer instruments consistently (reducing measurement error), and enable honest feedback.

[c] Obtain at 5 to 10 minutes, 25 to 35 minutes, 1.5 hours ±15 minutes, and 2.5 hours ±15 minutes after observed dosing.

[d] Archive samples may be tested for immunogenicity (presence and characterization of anti-drug antibodies), genetic testing (including genome sequencing) and biochemical analyses of hormones or other analytes of relevance to Prader-Willi syndrome.

Table 6. Schedule for the Questionnaires During the Placebo-Controlled Period

Instrument	Screening (14 to 28 days prior to Baseline)	Baseline Site Visit	Week 2 Site Visit (±2 days)	Week 8 Site Visit (±2 days)
PWS Nutritional Phase Assessment	X	X		
[redacted]				
Hyperphagia Questionnaire for Clinical Trials (HQ-CT)	X	X	X	X
[redacted]				
Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS)	X	X	X	X
[redacted]				
PWS Anxiety and Distress Behaviors Questionnaire (PADQ)	X	X	X	X
[redacted]				
Clinical Global Impression	X[a]	X[a]	X[a]	X[a]
[redacted]				

A = anxiety; CGI = clinical global impression; CareGI = caregiver global impression; H = hyperphagia;
OC = obsessive-compulsive; PWS = Prader Willi Syndrome

[a] Screening and Baseline assessments will include only Severity. Post-Baseline assessments will include Severity and Change.

Table 7. Schedule for the Questionnaires During the Long-Term Follow-Up Period

Instrument	Week 10 (±2 Days)	Week 16 (±1 Week)	Week 28 (±1 Week)	Week 40 (±1 Week)	Week 52 (±1 Week)	Week 64 (±1 Week)	Early Term (if required)
PWS Nutritional Phase Assessment						X	X
[redacted]							
Hyperphagia Questionnaire for Clinical Trials (HQ-CT)	X	X	X	X	X	X	X
[redacted]							
Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS)	X	X	X	X	X	X	X
[redacted]							
PWS Anxiety and Distress Behaviors Questionnaire (PADQ)	X	X	X	X	X	X	X
[redacted]							
Clinical Global Impression	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]
[redacted]							

A = anxiety; CGI = clinical global impression; CareGI = caregiver global impression; H = hyperphagia;
OC = obsessive-compulsive; PWS = Prader Willi Syndrome; Term = termination

[a] Screening and Baseline assessments will include only Severity. Post-Baseline assessments will include Severity and Change.

Table 8. Schedule of Assessments for the Extension Period

Procedure	Week 64[b] (±1 Week)	Quarterly (±3 Weeks)	End of Study (EOS)/ Early Term (ET)
Physical examination	X		X
Nasal assessment	X		X
Vital signs (including weight)	X		X
Height	X		X
Pregnancy test[a]	X		X
Laboratory assessments (chemistry, hematology, urinalysis)	X		X
12-lead electrocardiogram	X		
Study drug dosing	ongoing	ongoing	
Extension period ICF/assent	X		
Extension period Enrollment	X		
Safety Phone call		X	
Adverse event review	X	X	X
Serious adverse event review	X	X	X
Concomitant medication review (including all supplements)	X	X	X
Structured interview, including clinical outcomes assessments by caregiver and clinician[b]	X		
[redacted]			
Archive blood/plasma samples[d]	X		

[redacted]

[a] Pregnancy testing will be conducted only for females of childbearing potential, as judged by the Investigator.

[b] Week 64 Visit of long-term follow-up period will serve as first visit of extension period

APPENDIX C: LIST OF TABLES FOR THE PLACEBO-CONTROLLED PERIOD

The statistical tables will appear in Section 14 of the clinical study report. The statistical tables, therefore, have a prefix of "14."

14.1 Demographic Data Summary Tables

14.1A Demographic Data Summary Tables for the Placebo-Controlled Period

Table 14.1A.1: Patient Eligibility by Treatment Arm

Table 14.1A.2: Patient Disposition by Treatment Arm

Table 14.1A.3.1: Patient Study Visit Occurrence by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.1A.3.2: Patient Study Visit Occurrence by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.1A.4.1: Important Protocol Deviations by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.1A.4.2: Important Protocol Deviations by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.1A.5: Analysis Sets by Treatment Arm – Placebo-Controlled Period

Table 14.1A.6.1: Summary of Demographic and Baseline Characteristics by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.1A.6.2: Summary of Demographic and Baseline Characteristics by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.1A.7.1: Medical History by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.1A.7.2: Medical History by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.1A.8.1: Pre-Treatment Medications by Treatment Arm (Primary Analysis Set)

Table 14.1A.8.2: Pre-Treatment Medications by Treatment Arm (Full Analysis Set)

Table 14.1A.9.1: Concomitant Medications by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.1A.9.2: Concomitant Medications by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.1A.10: Summary of Treatment Duration by Treatment Arm – Placebo-Controlled Period

Table 14.1A.12: Frequency Table of Study Drug Compliance by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.1A.13: Frequency Table of Administered Doses by Treatment Arm – Placebo-Controlled Period

14.2 Efficacy Data Summary Tables

14.2A Efficacy Data Summary Tables for the Placebo-Controlled Period

14.2A.1 Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Summary Tables

Table 14.2A.1.1.1: Summary of Observed Values and Change from Baseline in HQ-CT Total Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.1.2: Summary of Observed Values and Change from Baseline in HQ-CT Total Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.2.1: HQ-CT Total Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.2.2: HQ-CT Total Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.2.3: HQ-CT Total Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Per-Protocol Analysis Set)

Table 14.2A.1.3.1: HQ-CT Total Score – Repeated Measures Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.3.2: HQ-CT Total Score – Repeated Measures Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.4.1: HQ-CT Total Score by Gender – Effect Modifier Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.4.2: HQ-CT Total Score by Age Tertile – Effect Modifier Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.4.3: HQ-CT Total Score by Gender and Age Tertile– Effect Modifier Analysis – Placebo-Controlled Period (Primary Analysis Set)

[redacted]

Table 14.2A.1.4.5: HQ-CT Total Score by Site – Effect Modifier Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.5.1: HQ-CT Total Score by Gender – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.5.2: HQ-CT Total Score by Age Tertile – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.5.3: HQ-CT Total Score by Gender and Age Tertile– Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

[redacted]

Table 14.2A.1.5.5: HQ-CT Total Score by Site – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.6.1: Summary of Observed Values and Change from Baseline in Total Score of a Subset of HQ-CT by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.6.2: Summary of Observed Values and Change from Baseline in Total Score of a Subset of HQ-CT by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.7.1: Total Score of a Subset of HQ-CT – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.7.2: Total Score of a Subset of HQ-CT – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.7.3: Total Score of a Subset of HQ-CT – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Per-Protocol Analysis Set)

Table 14.2A.1.8.1: Total Score of a Subset of HQ-CT – Repeated Measures Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.8.2: Total Score of a Subset of HQ-CT – Repeated Measures Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.9.1: Summary of Observed Values and Change from Baseline in HQ-CT Question 9 Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.9.2: Summary of Observed Values and Change from Baseline in HQ-CT Question 9 Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.1.10.1: HQ-CT Question 9 Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.1.10.2: HQ-CT Question 9 Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

14.2A.2 Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Summary Tables

[redacted]

Table 14.2A.2.5.1: CY-BOCS Severity Rating Total Score by Gender – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.5.2: CY-BOCS Severity Rating Total Score by Age Tertile – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.5.3: CY-BOCS Severity Rating Total Score by Gender and Age Tertile – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

[redacted]

Table 14.2A.2.5.5: CY-BOCS Severity Rating Total Score by Site – Effect Modifier Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.6.1: Summary of Observed Values and Change from Baseline in CY-BOCS Obsessions Severity Rating Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.2.6.2: Summary of Observed Values and Change from Baseline in CY-BOCS Obsessions Severity Rating Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.7.1: CY-BOCS Obsessions Severity Rating Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.2.7.2: CY-BOCS Obsessions Severity Rating Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.8.1: Summary of Observed Values and Change from Baseline in CY-BOCS Compulsions Severity Rating Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.2.8.2: Summary of Observed Values and Change from Baseline in CY-BOCS Compulsions Severity Rating Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.2.9.1: CY-BOCS Compulsions Severity Rating Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.2.9.2: CY-BOCS Compulsions Severity Rating Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

14.2A.3 PWS Anxiety and Distress Behaviors Questionnaire (PADQ) Summary Tables

Table 14.2A.3.1.1: Summary of Observed Values and Change from Baseline in PADQ Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.3.1.2: Summary of Observed Values and Change from Baseline in PADQ Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.3.2.1: PADQ Score – Constrained Longitudinal Data Analysis– Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.3.2.2: PADQ Score – Constrained Longitudinal Data Analysis– Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.3.2.3: PADQ Score – Constrained Longitudinal Data Analysis– Placebo-Controlled Period (Per-Protocol Analysis Set)

Table 14.2A.3.3.1: PADQ Score – Repeated Measures Analysis– Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.3.3.2: PADQ Score – Repeated Measures Analysis– Placebo-Controlled Period (Full Analysis Set)

14.2A.4 Overall PWS Clinical Global Impression (CGI) Summary Tables

Table 14.2A.4.1.1: Summary of Observed Values and Change from Baseline in CGI-S Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.4.1.2: Summary of Observed Values and Change from Baseline in CGI-S Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.4.2.1: CGI-S Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.4.2.2: CGI-S Score – Constrained Longitudinal Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.4.3.1: Summary of Observed CGI-C Score by Treatment Arm – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.4.3.2: Summary of Observed CGI-C Score by Treatment Arm – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.4.4.1: CGI-C Score – Repeated Measures Analysis – Placebo-Controlled Period (Primary Analysis Set)

Table 14.2A.4.4.2: CGI-C Score – Repeated Measures Data Analysis – Placebo-Controlled Period (Full Analysis Set)

Table 14.2A.4.4.3: CGI-C Score – Repeated Measures Data Analysis – Placebo-Controlled Period (Per-Protocol Analysis Set)

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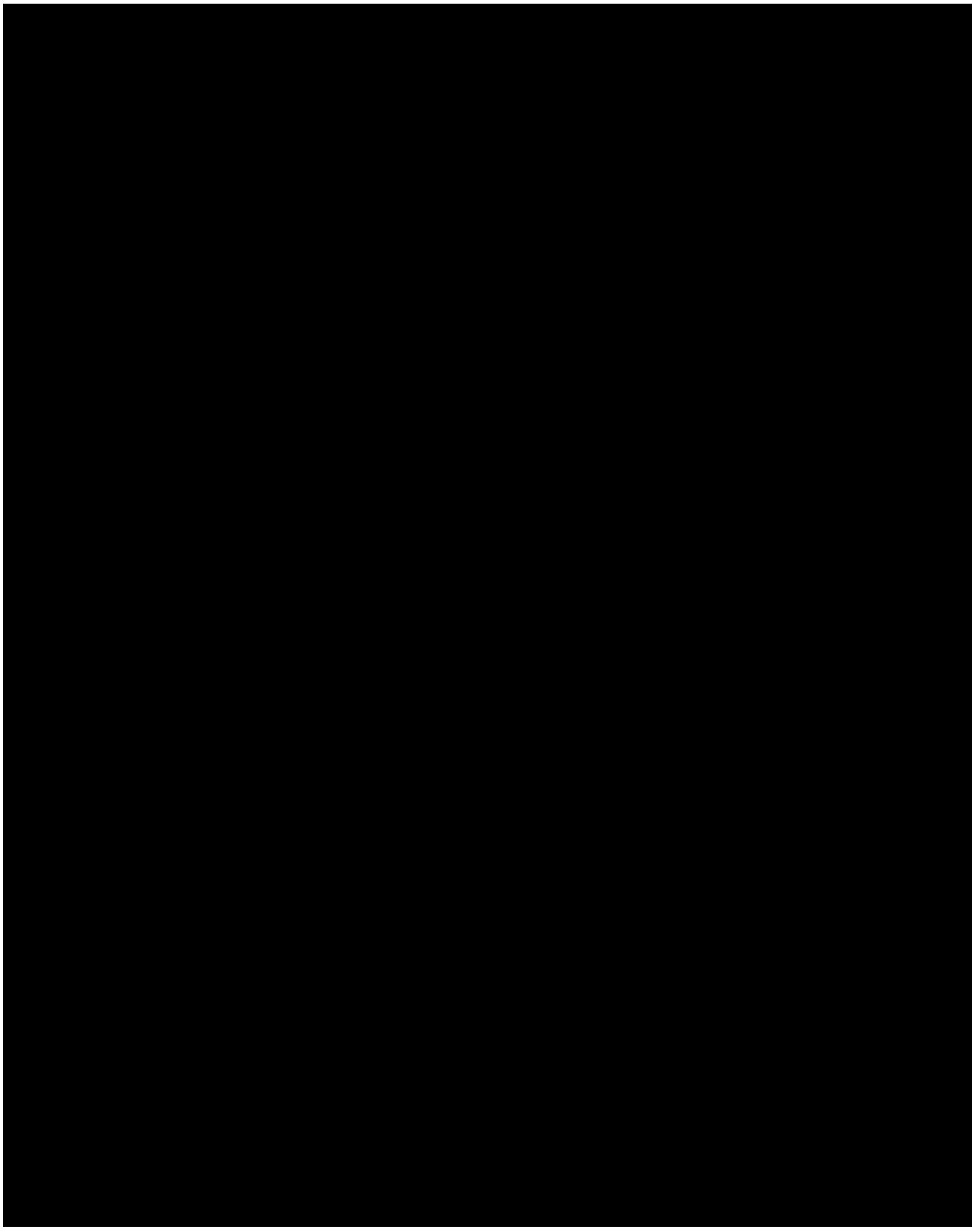

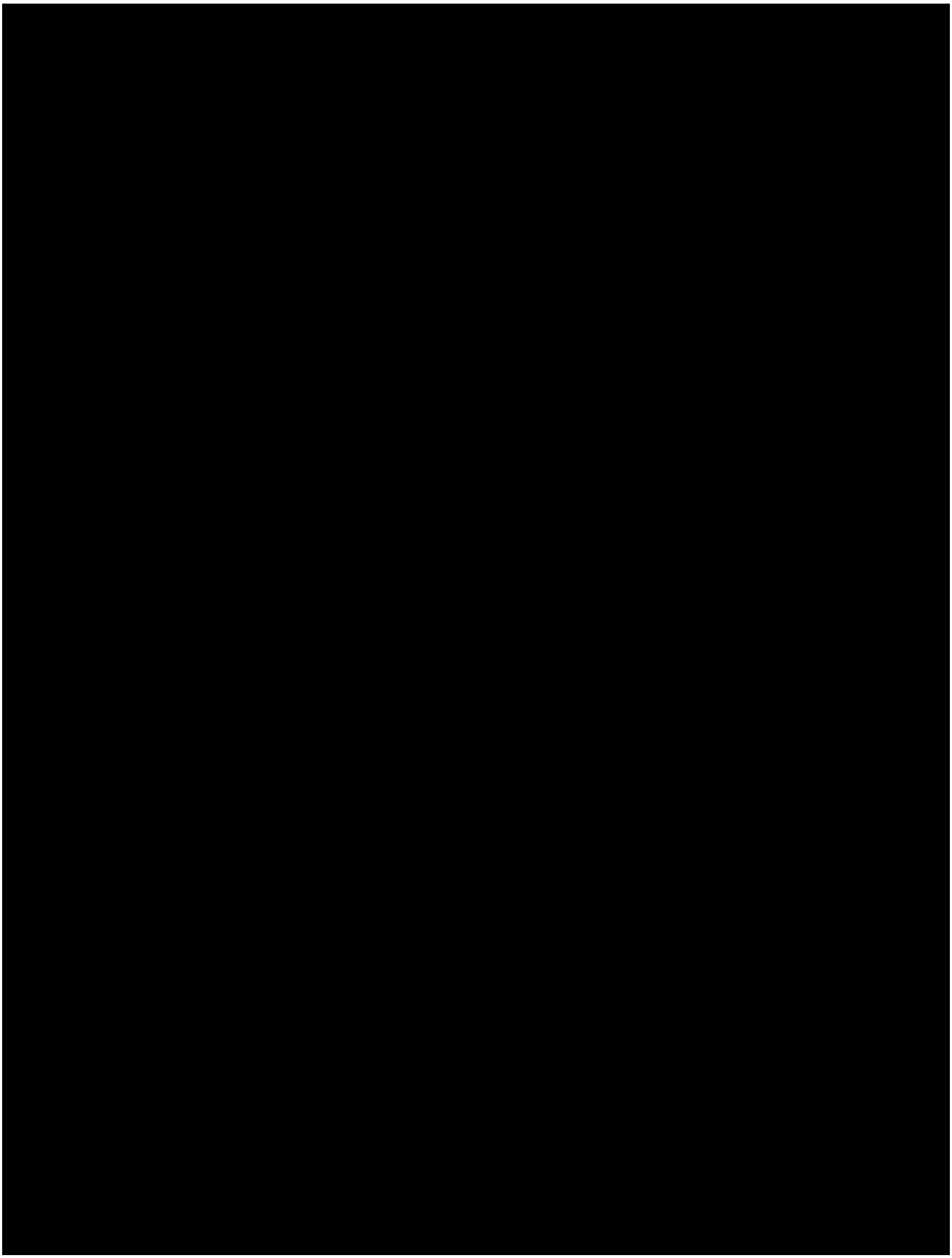

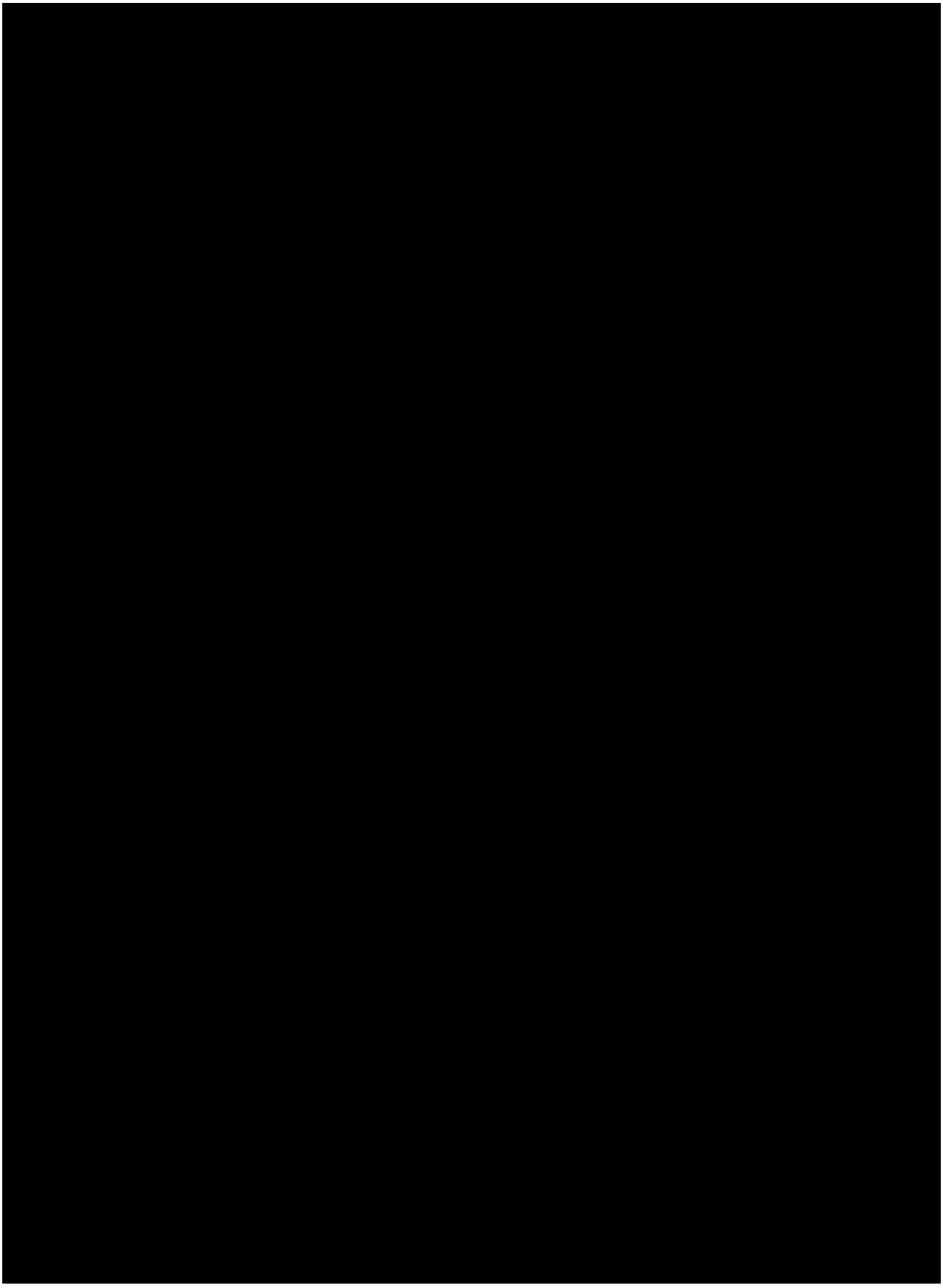

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14.3 Safety Data Summary Tables

14.3A Safety Data Summary Tables During the Placebo-Controlled Period

14.3A.1 Displays of Adverse Events During the Placebo-Controlled Period

Table 14.3A.1.1: Overall Summary Table of Treatment-Emergent Adverse Events – Placebo-Controlled Period

Table 14.3A.1.2: Frequency Table of Treatment-Emergent Adverse Events by SOC, PT, and Treatment Arm – Placebo-Controlled Period

Table 14.3A.1.3: Frequency Table of Treatment-Emergent Adverse Events Leading to Study Drug Interruption by SOC, PT, and Treatment Arm – Placebo-Controlled Period

Table 14.3A.1.4: Frequency Table of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by SOC, PT, and Treatment Arm – Placebo-Controlled Period

Table 14.3A.1.5: Frequency Table of Treatment-Emergent Adverse Events by SOC, PT, Maximum Severity, and Treatment Arm – Placebo-Controlled Period

Table 14.3A.1.6: Frequency Table of Treatment-Emergent Adverse Events Possibly Related to Study Drug by SOC, PT, and Treatment Arm – Placebo-Controlled Period

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14.3A.2 Deaths and Serious Adverse Events During the Placebo-Controlled Period

Table 14.3A.2.1: Frequency Table of Treatment-Emergent Serious Adverse Events by SOC, PT, and Treatment Arm – Placebo-Controlled Period

Table 14.3A.2.2: Frequency Table of Treatment-Emergent Serious Adverse Events Possibly Related to Study Drug by SOC, PT, and Treatment Arm – Placebo-Controlled Period

14.3A.4 Laboratory Data During the Placebo-Controlled Period

Table 14.3A.4.1: Summary of Hematology Results by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.2: Shift Table of Hematology Results by Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.3: Summary of Serum Chemistry Results by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.4: Shift Table of Serum Chemistry Results by Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.5: Summary of Urinalysis Results by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.6: Summary of Coagulation Results by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.7: Shift Table of Coagulation Results by Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.9: Frequency Table of ECG Global Assessments by Visit and Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.10: Shift Table of ECG Results by Treatment Arm – Placebo-Controlled Period

Table 14.3A.4.11: Summary of Vital Sign Parameter by Visit and Treatment Arm – Placebo-Controlled Period

APPENDIX D: LIST OF TABLES AND LISTINGS FOR THE LONG-TERM FOLLOW-UP PERIOD

The statistical tables will appear in Section 14 of the clinical study report. The statistical tables, therefore, have a prefix of "14."

14.1 Demographic Data Summary Tables

14.1B Demographic Data Summary Tables for the Long-Term Follow-Up Period

Table 14.1B.3.1: Patient Study Visit Occurrence by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.1B.3.2: Patient Study Visit Occurrence by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.1B.4.1: Important Protocol Deviations by Treatment Arm – Long-Term Follow-Up and Extension Periods (Primary Analysis Set)

Table 14.1B.4.2: Important Protocol Deviations by Treatment Arm – Long-Term Follow-Up and Extension Periods (Full Analysis Set)

Table 14.1B.5: Analysis Sets by Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.1B.6.1: Summary of Demographic and Baseline Characteristics by Treatment Arm – Long-Term Follow-Up and Extension Periods (Primary Analysis Set)

Table 14.1B.6.2: Summary of Demographic and Baseline Characteristics by Treatment Arm – Long-Term Follow-Up and Extension Periods (Full Analysis Set)

Table 14.1B.7.1: Medical History by Treatment Arm – Long-Term Follow-Up and Extension Periods (Primary Analysis Set)

Table 14.1B.7.2: Medical History by Treatment Arm – Long-Term Follow-Up and Extension Periods (Full Analysis Set)

Table 14.1B.9.1: Concomitant Medications by Treatment Arm – Long-Term Follow-Up and Extension Periods (Primary Analysis Set)

Table 14.1B.9.2: Concomitant Medications by Treatment Arm – Long-Term Follow-Up and Extension Periods (Full Analysis Set)

Table 14.1B.10: Summary of Treatment Duration by Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.1B.11: Frequency Table of Treatment Duration by Treatment Arm

Table 14.1B.12: Frequency Table of Study Drug Compliance by Visit and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.1B.13: Frequency Table of Administered Doses by Treatment Arm – Long-Term Follow-Up and Extension Periods

14.2 Efficacy Data Summary Tables

14.2B Efficacy Data Summary Tables for the Long-Term Follow-Up Period

14.2B.1 Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Summary Tables

Table 14.2B.1.1.1: Summary of Observed Values and Change from Baseline in HQ-CT Total Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.1.1.2: Summary of Observed Values and Change from Baseline in HQ-CT Total Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.2B.1.6.1: Summary of Observed Values and Change from Baseline in Total Score of a Subset of HQ-CT by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.1.6.2: Summary of Observed Values and Change from Baseline in Total Score of a Subset of HQ-CT by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.2B.1.9.1: Summary of Observed Values and Change from Baseline in HQ-CT Question 9 Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.1.9.2: Summary of Observed Values and Change from Baseline in HQ-CT Question 9 Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

14.2B.2 Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Summary Tables

Table 14.2B.2.1.1: Summary of Observed Values and Change from Baseline in CY-BOCS Severity Rating Total Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.2.1.2: Summary of Observed Values and Change from Baseline in CY-BOCS Severity Rating Total Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.2B.2.6.1: Summary of Observed Values and Change from Baseline in CY-BOCS Obsessions Severity Rating Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.2.6.2: Summary of Observed Values and Change from Baseline in CY-BOCS Obsessions Severity Rating Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.2B.2.8.1: Summary of Observed Values and Change from Baseline in CY-BOCS Compulsions Severity Rating Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.2.8.2: Summary of Observed Values and Change from Baseline in CY-BOCS Compulsions Severity Rating Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

14.2B.3 PWS Anxiety and Distress Behaviors Questionnaire (PADQ) Summary Tables

Table 14.2B.3.1.1: Summary of Observed Values and Change from Baseline in PADQ Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.3.1.2: Summary of Observed Values and Change from Baseline in PADQ Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

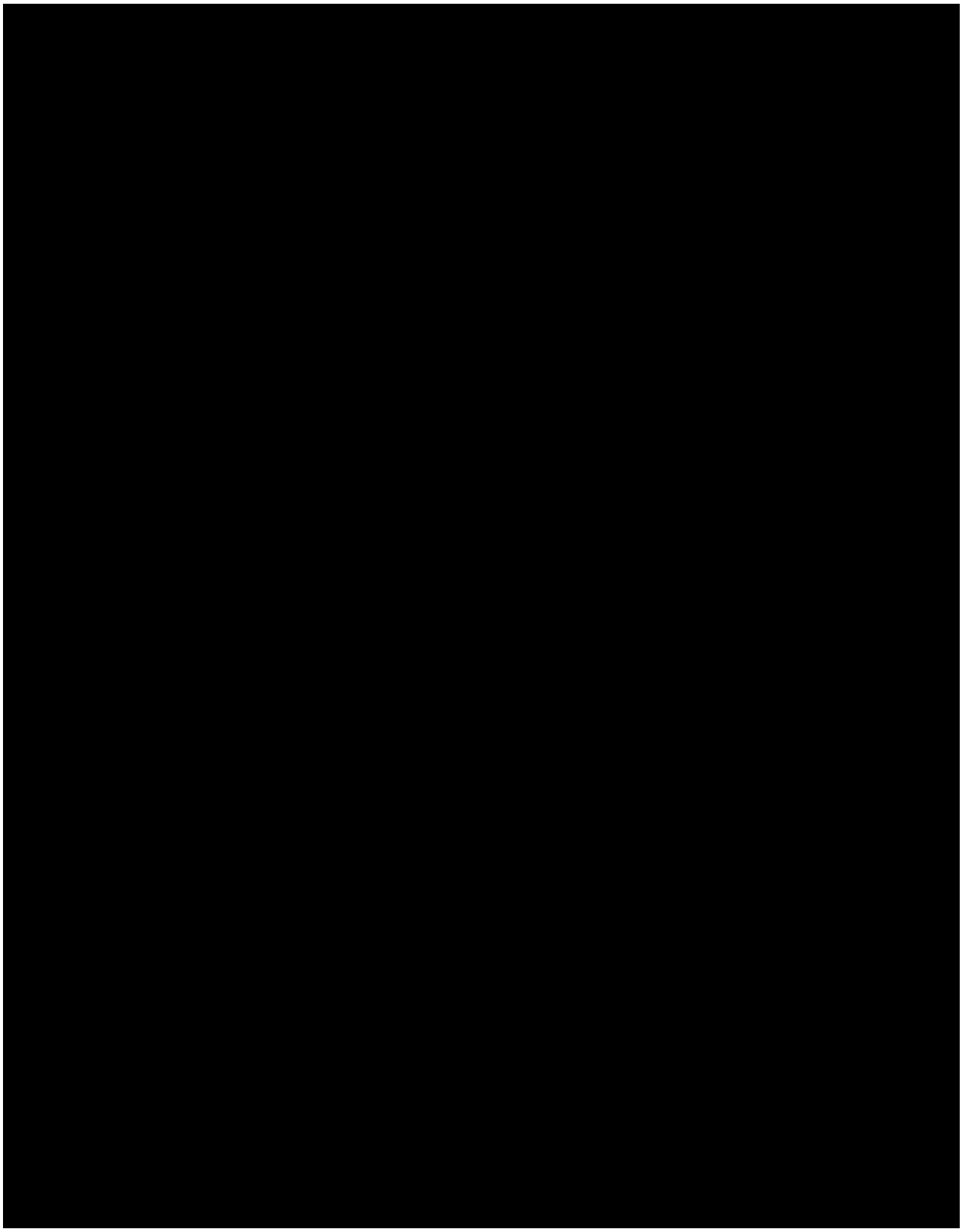
14.2B.4 Overall PWS Clinical Global Impression (CGI) Summary Tables

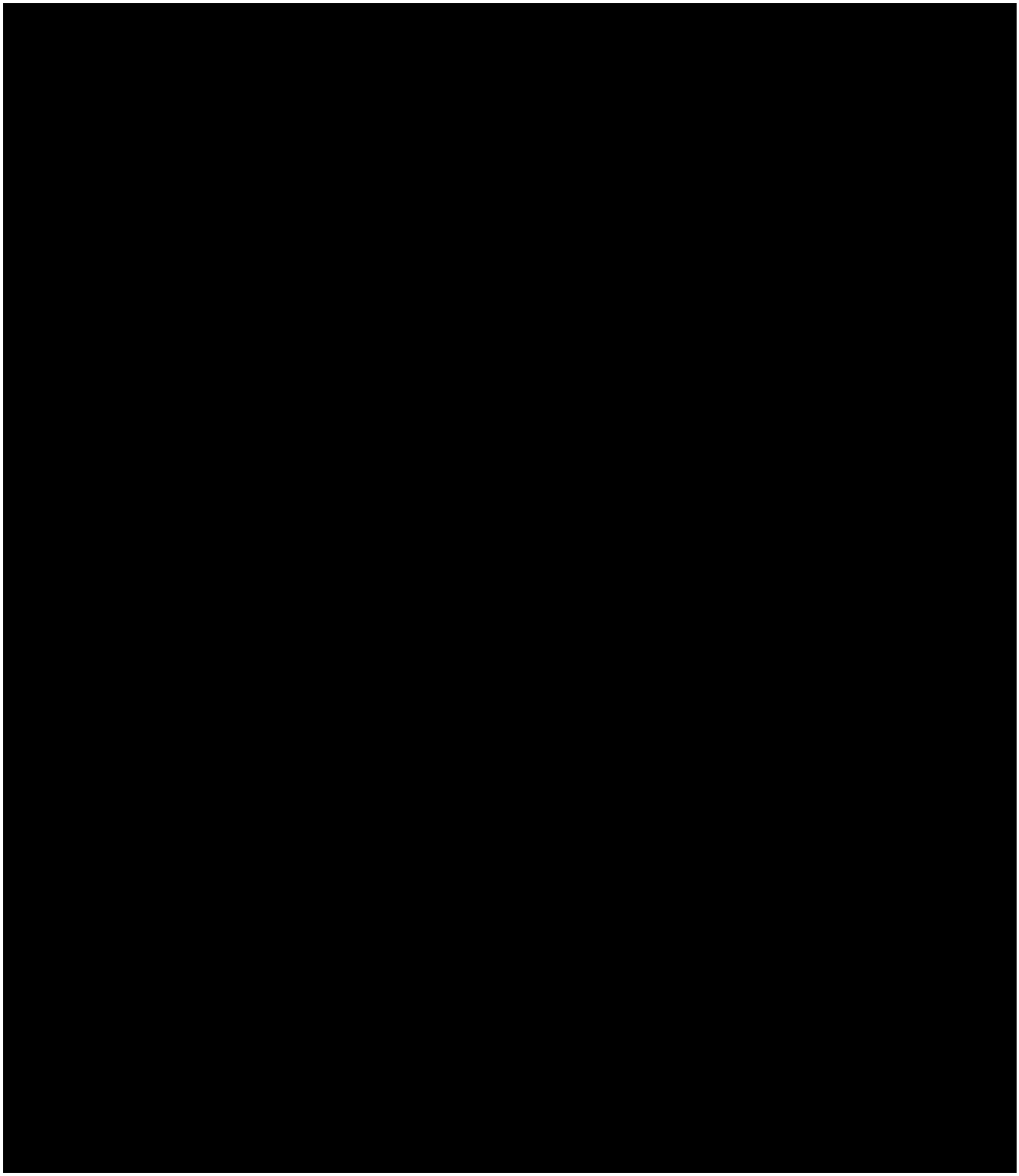
Table 14.2B.4.1.1: Summary of Observed Values and Change from Baseline in CGI-S Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.4.1.2: Summary of Observed Values and Change from Baseline in CGI-S Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)

Table 14.2B.4.3.1: Summary of Observed CGI-C Score by Treatment Arm – Long-Term Follow-Up Period (Primary Analysis Set)

Table 14.2B.4.3.2: Summary of Observed CGI-C Score by Treatment Arm – Long-Term Follow-Up Period (Full Analysis Set)





14.2B.9 Other Efficacy Summary Tables

Table 14.2B.9.1.1: PWS Nutritional Phase by Treatment Arm (Primary Analysis Set)

Table 14.2B.9.1.2: PWS Nutritional Phase by Treatment Arm (Full Analysis Set)

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14.3 Safety Data Summary Tables

14.3B Safety Data Summary Tables During the Long-Term Follow-Up Period

14.3B.1 Displays of Adverse Events During the Long-Term Follow-Up Period

Table 14.3B.1.1: Overall Summary Table of Treatment-Emergent Adverse Events – Long-Term Follow-Up and Extension Periods

Table 14.3B.1.2: Frequency Table of Treatment-Emergent Adverse Events by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.3B.1.3: Frequency Table of Treatment-Emergent Adverse Events Leading to Study Drug Interruption by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.3B.1.4: Frequency Table of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.3B.1.5: Frequency Table of Treatment-Emergent Adverse Events by SOC, PT, Maximum Severity, and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.3B.1.6: Frequency Table of Treatment-Emergent Adverse Events Possibly Related to Study Drug by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

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14.3B.2 Deaths and Serious Adverse Events During the Long-Term Follow-Up Period

Table 14.3B.2.1: Frequency Table of Treatment-Emergent Serious Adverse Events by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

Table 14.3B.2.2: Frequency Table of Treatment-Emergent Serious Adverse Events Possibly Related to Study Drug by SOC, PT, and Treatment Arm – Long-Term Follow-Up and Extension Periods

14.3B.4 Laboratory Data During the Long-Term Follow-Up Period

Table 14.3B.4.1: Summary of Hematology Results by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.2: Shift Table of Hematology Results by Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.3: Summary of Serum Chemistry Results by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.4: Shift Table of Serum Chemistry Results by Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.5: Summary of Urinalysis Results by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.6: Summary of Coagulation Results by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.7: Shift Table of Coagulation Results by Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.8: Frequency Table of Tanner Staging by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.9: Frequency Table of ECG Global Assessments by Visit and Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.10: Shift Table of ECG Results by Treatment Arm – Long-Term Follow-Up Period

Table 14.3B.4.11: Summary of Vital Sign Parameter by Visit and Treatment Arm – Long-Term Follow-Up Period

APPENDIX E: LIST OF PATIENT LISTINGS

The patient listings will appear in Appendix 16.2 of the clinical study report. The patient listings, therefore, have a prefix of "16.2."

16.2.1 Discontinued Patients

Listing 16.2.1.1: Informed Consent and Protocol Version

Listing 16.2.1.2: Patient Disposition and Reasons for Discontinuation from Study

16.2.2 Protocol Deviations

Listing 16.2.2.1: Important Protocol Deviations by Patient

Listing 16.2.2.2: Protocol Deviations – Remote Visits Due to COVID-19 by Patient

Listing 16.2.2.3: Missed Assessments for Remote Visits Due to COVID-19 by Patient

Listing 16.2.2.4: Missed Visits by Patient

Listing 16.2.2.5: Study Visit Occurrence by Patient

Listing 16.2.2.6: Analysis Sets by Patient

16.2.3 Patients Excluded from the Efficacy Analysis

Listing 16.2.3.1: Data Points Excluded from the Primary Analysis Set

Listing 16.2.3.2: Patients Excluded from the Per-Protocol Analysis Set

16.2.4 Demographic and Baseline Characteristics

Listing 16.2.4.1: Demographic and Baseline Characteristics by Patient

Listing 16.2.4.2: Medical History by Patient

Listing 16.2.4.3: Substance Use by Patient

Listing 16.2.4.4: Prior Oxytocin or Carbetocin Use by Patient

Listing 16.2.4.5: Pre-Treatment Medications by Patient (Part 1)

Listing 16.2.4.6: Pre-Treatment Medications by Patient (Part 2)

Listing 16.2.4.7: Concomitant Medications by Patient (Part 1)

Listing 16.2.4.8: Concomitant Medications by Patient (Part 2)

Listing 16.2.4.9: Pre-Treatment Treatments and Procedures by Patient

Listing 16.2.4.10: Concomitant Treatments and Procedures by Patient

16.2.5 Compliance and/or Drug Concentration Data

Listing 16.2.5.1: Study Drug Dispensation by Patient

Listing 16.2.5.2: Study Drug Administration by Patient

Listing 16.2.5.3: Missed and Missing Doses by Patient

16.2.6 Individual Efficacy Response Data

Listing 16.2.6.1.1: Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Scores by Patient (Part 1)

Listing 16.2.6.1.2: Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Scores by Patient (Part 2)

Listing 16.2.6.1.3: Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Scores by Patient (Part 3)

Listing 16.2.6.2.1: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Obsessions – Contamination, Aggressive, Sexual, and Hoarding / Saving Obsessions by Patient

Listing 16.2.6.2.2: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Obsessions – Magical/Superstitious, Somatic, Religious, and Miscellaneous Obsessions by Patient

Listing 16.2.6.2.3: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Obsessions – Target Symptoms by Patient

Listing 16.2.6.2.4: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Compulsions – Washing / Cleaning, Checking, Repeating, and Counting Compulsions by Patient

Listing 16.2.6.2.5: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Compulsions – Ordering / Arranging, Hoarding / Saving, and Excessive Games / Superstitious Compulsions by Patient

Listing 16.2.6.2.6: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Compulsions – Rituals Involving Other Persons and Miscellaneous Compulsions by Patient

Listing 16.2.6.2.7: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Compulsions – Target Symptoms by Patient

Listing 16.2.6.2.8: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Obsessions Severity Ratings by Patient

Listing 16.2.6.2.9: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Compulsions Severity Ratings by Patient

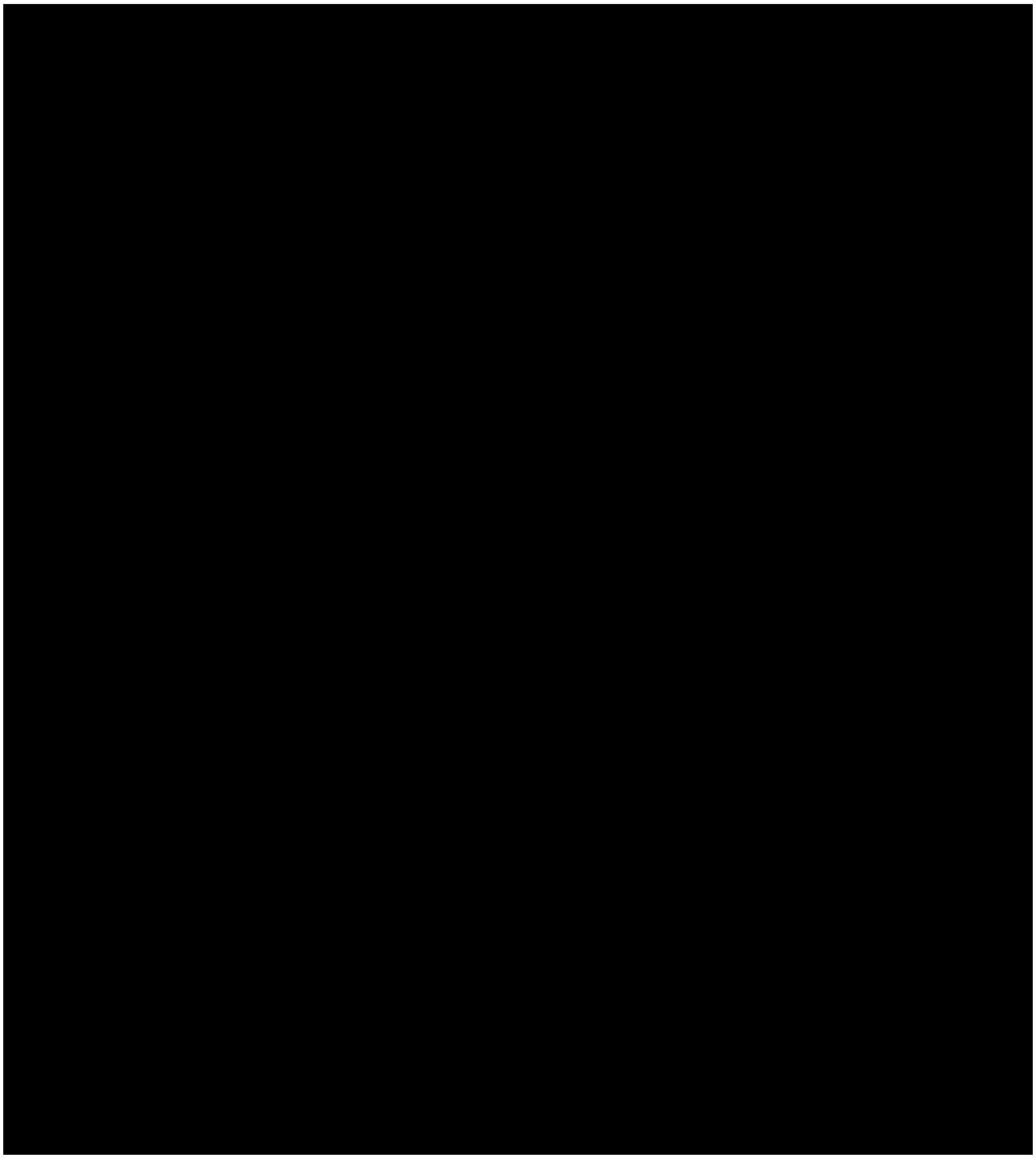
Listing 16.2.6.2.10: Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) Subtotals and Total Scores by Patient

Listing 16.2.6.3.1: PWS Anxiety and Distress Behaviors Questionnaire (PADQ) Scores by Patient (Part 1)

Listing 16.2.6.3.2: PWS Anxiety and Distress Behaviors Questionnaire (PADQ) Scores by Patient (Part 2)

Listing 16.2.6.3.3: PWS Anxiety and Distress Behaviors Questionnaire (PADQ) Scores by Patient (Part 3)

Listing 16.2.6.4: Clinical Global Impressions of Severity and Change by Patient



Listing 16.2.6.12: PWS Nutritional Phase by Patient

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16.2.7 Adverse Event Data

Listing 16.2.7.1: Treatment-Emergent Adverse Events by Patient (Part 1)

Listing 16.2.7.2: Treatment-Emergent Adverse Events by Patient (Part 2)

Listing 16.2.7.3: Treatment-Emergent Adverse Events Possibly Related to Study Drug by Patient (Part 1)

Listing 16.2.7.4: Treatment-Emergent Adverse Events Possibly Related to Study Drug by Patient (Part 2)

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Listing 16.2.7.7: Pre-Treatment Serious Adverse Events by Patient (Part 1)

Listing 16.2.7.8: Pre-Treatment Serious Adverse Events by Patient (Part 2)

Listing 16.2.7.9: Pre-Treatment Serious Adverse Events by Patient (Part 3)

Listing 16.2.7.10: Treatment-Emergent Serious Adverse Events by Patient (Part 1)

Listing 16.2.7.11: Treatment-Emergent Serious Adverse Events by Patient (Part 2)

Listing 16.2.7.12: Treatment-Emergent Serious Adverse Events by Patient (Part 3)

Listing 16.2.7.13: Treatment-Emergent Adverse Events Leading to Study Drug Interruption by Patient (Part 1)

Listing 16.2.7.14: Treatment-Emergent Adverse Events Leading to Study Drug Interruption by Patient (Part 2)

Listing 16.2.7.15: Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by Patient (Part 1)

Listing 16.2.7.16: Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by Patient (Part 2)

Listing 16.2.7.17: Treatment-Emergent Serious Adverse Events Leading to Death (Part 1)

Listing 16.2.7.18: Treatment-Emergent Serious Adverse Events Leading to Death (Part 2)

Listing 16.2.7.19: Treatment-Emergent Serious Adverse Events Leading to Death (Part 3)

Listing 16.2.7.20: Investigator Narratives of Adverse Events

Listing 16.2.7.21: Investigator Narratives of CY-BOCS Results

16.2.8 Listing of Individual Laboratory Measurements

Listing 16.2.8.1: Hematology Results by Patient

Listing 16.2.8.2: Serum Chemistry Results by Patient

Listing 16.2.8.3: Urinalysis Results by Patient

Listing 16.2.8.4: Coagulation Results by Patient

Listing 16.2.8.5: Physical Exam Results by Patient

Listing 16.2.8.6: Tanner Staging by Patient

Listing 16.2.8.7: Nasal Assessment Results by Patient

Listing 16.2.8.8: ECG Results by Patient

Listing 16.2.8.9: Vital Sign Results by Patient

Listing 16.2.8.10: Urine Pregnancy Test Results by Patient

16.2.9 Other Data Listings

Listing 16.2.9.1: Intranasal Spray Pump Incidents Reported by Site

Listing 16.2.9.2: Intranasal Spray Pump Incidents Reported by Sponsor (Part 1)

Listing 16.2.9.3: Intranasal Spray Pump Incidents Reported by Sponsor (Part 2)