Official Title: **A Phase 3, Randomized, Double-blind, Multicenter, Placebo-controlled, Parallel-group Trial Evaluating the Efficacy, Safety, and Tolerability of Centanafadine Sustained-release Tablets in Adults With Attention-deficit/Hyperactivity Disorder**

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SAP 405-201-00013

Otsuka Pharmaceutical Development & Commercialization, Inc.

Investigational Medicinal Product

Centanafadine (EB-1020)

A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Evaluation the Efficacy, Safety and Tolerability of Centanafadine Sustained-release in Adults with Attention-deficit/Hyperactivity Disorder

Protocol No. 405-201-00013
IND No. 119,361

Statistical Analysis Plan

Version: Final

Date: April 27, 2020

CONFIDENTIAL – PROPRIETARY INFORMATION

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1 Introduction

This statistical analysis plan (SAP) documents the statistical methodology and data analysis algorithms and conventions to be applied for statistical analysis and reporting of efficacy and safety data of study 405-201-00013. All amendments to the protocol are taken into consideration in developing this SAP.

2 Study Objectives

Primary: To confirm the efficacy of centanafadine SR tablets administered BID (200 mg or 400 mg TDDs) compared to placebo in the treatment of adults with ADHD

Secondary: To confirm the safety and tolerability of centanafadine SR tablets administered BID (200 mg or 400 mg TDDs) compared to placebo in the treatment of adults with ADHD

3 Study Design

This trial is a phase 3, randomized, double-blind, multicenter, placebo-controlled, parallel-group trial to confirm the efficacy, safety, and tolerability of centanafadine SR (200 mg TDD or 400 mg TDD) compared to placebo for the treatment of adults with ADHD. The trial population will include male and female subjects 18 to 55 years of age (inclusive) with a current diagnosis of ADHD as confirmed by the Adult ADHD Clinical Diagnostic Scale (ACDS) Version 1.2 at screening.

The trial will have 4 periods: (1) screening and washout; (2) 1 week single-blind placebo run-in; (3) 6-week double blind treatment; and (4) 7-day follow-up period (follow-up telephone calls at 1, 3, and 5 days after the last dose of IMP, and in-clinic visits 2 and 7 days after the last dose of IMP) for subjects who complete the trial, and decide to enroll in Trial 405-201-00015. For subjects who terminate early, decide to not enroll in Trial 405-201-00015, or who are not eligible to enroll in Trial 405-201-00015, they will be required to participate in the 7-day follow-up period as well as participate in an additional follow-up telephone call 10 days after the last dose of IMP. Subjects randomized to receive a TDD of 200 mg centanafadine SR will start at their target dose at the start of the double-blind treatment period. Subjects randomized to receive a TDD of 400 mg centanafadine SR will start the double-blind treatment period at the TDD of 200 mg centanafadine SR for 7 days, before they are escalated to their target TDD of 400 mg for a total of approximately 42 days of treatment. Subjects will be required to visit the site up to 12 times over the trial. See Figure 3-1 for a schematic of the trial design.

Subjects who complete both the 6-week double-blind treatment period and the 7-day safety follow-up period (follow-up telephone calls at 1, 3, and 5 days after the last dose of IMP, and in-clinic visits 2 and 7 days after the last dose of IMP), and refrain from using prohibited

medications after the IMP is stopped may be eligible to enroll into Trial 405-201-00015, which is a 12-month, observational, open-label trial to evaluate the long-term safety and tolerability of subjects with ADHD who previously participated in Trials 405-201-00013 or 405-201-00014. Subjects who terminate early, decide to not enroll in Trial 405-201-00015, or who are not eligible to enroll in Trial 405-201-00015, will be required to participate in the 7-day follow-up period as well as participate in an additional follow-up telephone call 10 days after the last dose of IMP. For subjects who early terminate or decline participation in the open-label trial, they will be instructed to refrain from utilizing prohibited concomitant medications, including ADHD treatments, until after the follow-up telephone call 10 days after the last dose of IMP.

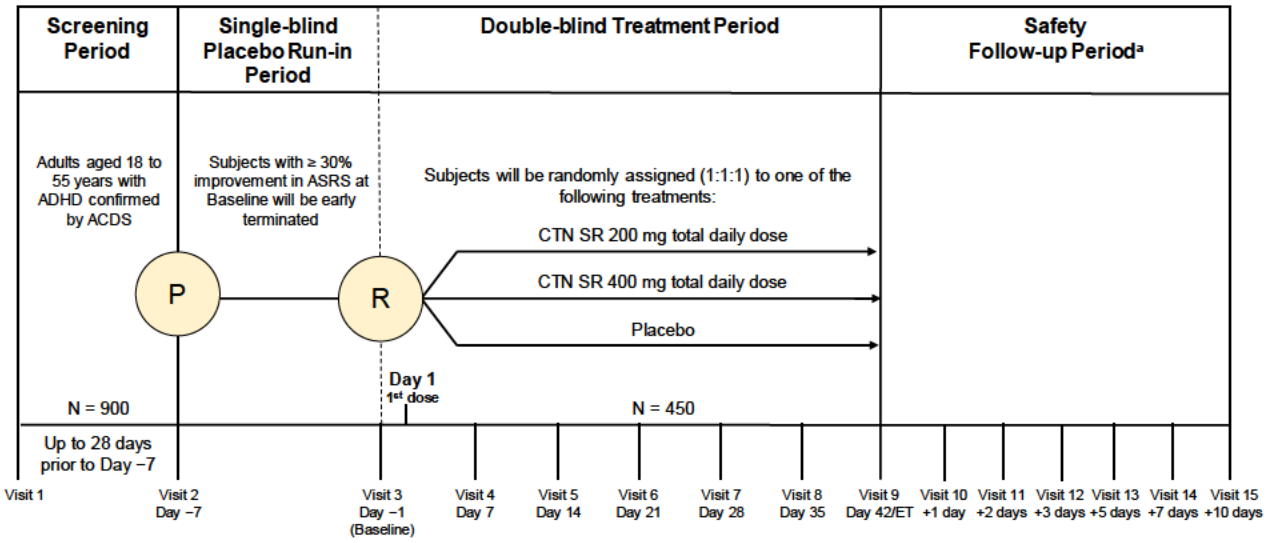

Figure 3-1 Trial Design Schematic

ASRS = Adult ADHD Self Report Scale; CTN SR = centanafadine sustained release; ET = early termination; P = placebo administration; R = randomization.

[a]All subjects will be required to participate in the 7-day follow-up period (follow-up telephone calls at 1, 3, and 5 days after the last dose of IMP, and in-clinic follow-up visits at 2 and 7 days after the last dose of IMP). Subjects who terminate early, decide to not enroll in Trial 405-201-00015, or who are not eligible to enroll in Trial 405-201-00015, will be required to participate in an additional follow-up telephone call 10 days after the last dose of IMP.

During the trial, administration of the investigational medicinal product (IMP) will be double-blinded. In other words, neither the investigator nor the subject will have knowledge of the treatment assignment (e.g., centanafadine SR 200 mg, 400 mg, or placebo). Treatment assignments will be based on a computer-generated randomization code provided by the Otsuka Pharmaceutical Development & Commercialization, Inc (OPDC) Biometrics Department. Sponsor personnel, including those involved in monitoring, data management, and data analysis, will not have access to the treatment code during the trial. The bioanalytical

laboratory will also be sent the randomization code. The randomization will be stratified by trial site and designed to allocate subjects in a 1:1:1 ratio to centanafadine SR 200 mg/day or 400 mg/day or placebo.

4 Sample Size and Power Justification

The primary efficacy endpoint is the change from baseline at Day 42 in Adult ADHD Investigator Symptom Rating Scale (AISRS) total score. The trial will compare the placebo arm to the centanafadine dose arms, randomized at a ratio of 1:1:1, with an overall alpha of 0.05 for the primary endpoint.

Based on the results from Phase 2 centanafadine trials, it is reasonable to expect a treatment effect of 5 points with a standard deviation (SD) of 12.5 in the mean change from baseline to Day 42 on AISRS total score. The planned sample size of 405 evaluable subjects (135 in each treatment arm) will yield at least 90% power to detect the treatment effects at a 2-tailed significance level of 0.05.

A sufficient number of subjects will be enrolled and randomized to achieve approximately 405 evaluable subjects in the Double-blind Treatment Phase (i.e., subjects with an AISRS total score at baseline and at least 1 subsequent AISRS total score in the Double-blind Treatment Phase). After allowance of 10% non-evaluable subjects in the Double-blind Treatment Phase, the total number of subjects to be randomized is 450 (150 in each treatment arm). In order to ensure 405 evaluable subjects, the number of non-evaluable subjects will be monitored in a blinded manner on an ongoing basis During the trial. The power and sample size were obtained using the PASS 14 (2015) statistical computing software.

5 Data Sets for Analysis and Missing Data

5.1 Data Sets for Analysis

The following analysis samples are defined for this trial:

Enrolled Sample: comprises all subjects who signed an informed consent form (ICF) for the trial and enrolled into the single-blind placebo run-in period.

Randomized Sample: comprises all subjects who were randomized in the double-blind treatment period. Subjects are considered randomized when they are assigned a treatment group by eSource at the end of single-blind placebo run-in period. A subject receiving IMP outside of the eSource will not be considered randomized, but safety will be reported.

Safety Sample: comprises those randomized subjects in the double-blind treatment period who received at least one dose of double-blind IMP as indicated on the dosing record. Subjects will only be excluded from this population if there is documented evidence (i.e., drug

dispensed = drug returned or no IMP dispensed) that the subject did not take IMP. If a subject is dispensed IMP and is lost to follow up, he/she will be considered exposed.

Efficacy Sample: the Full Analysis Set (FAS) comprises all subjects in the Safety Sample who have a baseline value and at least one valid post-randomization efficacy evaluation for AISRS total score in the double-blind treatment period.

Per Protocol (PP) Sample: comprises those subjects in the Efficacy Sample who complete at least the first 2 weeks of double-blind medication ((last day of IMP - first day of IMP + 1) ≥ 14 days) and have at least one post baseline AISRS measurement on or after Day 14 visit during the double-blind treatment period without major protocol violations deemed to compromise the assessment of efficacy. These major protocol violations will be any of the followings:

1. Subjects who were not at least 80% or were more than 120% compliant with double-blind IMP or missed 7 or more consecutive days of dosing immediately prior to the Day 42/ET AISRS measurement date during the double-blind treatment period based on subject-reported (eCRF) compliance data
2. Subjects who reported concomitant medication use that will impact the primary efficacy endpoint
3. Subjects who had major protocol deviation as represented on the protocol deviation eCRF page that will impact the primary efficacy endpoint
4. Subjects who took the wrong study treatment

The core dataset for all efficacy analyses is the FAS, which is created based on the intent-to-treat (ITT) principle. However, as will be described below, in order to handle missing data and restrictions imposed by different types of analyses (e.g., change from baseline analysis), other datasets derived from the FAS dataset will be used for the efficacy analyses.

5.2 Handling of Missing Data

The mixed-effect model repeated measure (MMRM) assumes data are missing at random (MAR), which is a reasonable assumption in longitudinal clinical trials in MDD[1]. However, the possibility of "missing not at random" (MNAR) data can never be ruled out. As sensitivity analyses, selection model[2], pattern-mixture model[3,4,5,6], and/or shared parameter model[7] will be used to explore data missing mechanisms of MNAR and investigate the response profile of dropout patients by last dropout reason under MNAR mechanism for the following 3 scenarios: 1) Dropout reasons due to either AE or LOE as MNAR, 2) Dropout reasons due to either AE or LOE or subject withdrew consent as MNAR, 3) All dropouts as MNAR using

both 1) Delta adjustment imputation method which is to departure from MAR assumption by progressively increasing the delta until conclusion from the primary analysis is overturned, and 2) Placebo based imputation methods in which missing data for both placebo and drug group are imputed based on the imputation model derived from placebo data. If drug improved outcomes prior to dropout, this benefit is carried into subsequent imputed values, but will diminish over time in accordance with the correlation structure. Details are provided in Section 8.1.3 Sensitivity Analysis.

The observed-cases (OC) data set will consist of actual observations recorded at each visit during the double-blind treatment period and no missing data will be imputed. MMRM, Wu-Bailey, and pattern-mixture model will be performed on the OC dataset.

The last-observation-carried-forward (LOCF) data set will include data recorded at a scheduled double-blind treatment period visit or, if no observation is recorded at that visit, data carried forward from the previous scheduled double-blind treatment period visit. Baseline data (e.g., the last visit of the single-blind placebo run-in period) will not be carried forward to impute missing values for the LOCF data set. The analysis of covariance (ANCOVA) analysis will be performed for the change from baseline to the end of the double-blind treatment period (Day 42, LOCF) in AISRS total score as sensitivity analysis. The ANCOVA_LOCF model includes treatment and study center as main effects, and baseline value as a covariate.

ANCOVA analysis with OC data will also be conducted on change from baseline for AISRS total score, as well as all continuous change from baseline efficacy endpoints.

For Clinical Global Impression (CGI) Change from Baseline and categorical response/remission variables, OC analyses will be performed in addition to LOCF analyses. Study center will not be included in the models for OC analyses.

6 Study Conduct

6.1 Subject Disposition, Completion Rate and Reasons for Discontinuation

Subject disposition will be summarized for the Randomized Sample by treatment group, and by center.

Subject completion rate and reasons for discontinuation will be summarized for the Randomized Sample by treatment group for the double-blind treatment period.

6.2 Treatment Compliance

For each subject, compliance in taking IMP is calculated by dividing the number of tablets taken by the total number of tablets the patients were scheduled to take during the double-blind

treatment period. Compliance is calculated on double-blind IMP for the double-blind treatment period. For lost-to-follow up patients, the last IMP end date record will be used as the treatment end date.

Summary of Treatment compliance will be provided based on both eCRF data and AiCure captured data, respectively.

6.3 Protocol Deviation

Protocol deviations are summarized by center and type of deviation for randomized subjects by treatment group. Listing of protocol deviation will list the treatment phases during which the deviations occurred. In addition, protocol deviations affected by the COVID-19 will be summarized. Listing of subjects with protocol deviations affected by the COVID-19 will also be provided.

7 Baseline Characteristics

7.1 Baseline Definition

Baseline for the single-blind placebo run-in period refers to last available measurement prior to the start of administration of placebo in the single-blind placebo run-in period.

For analyses of the double-blind treatment period data, the baseline is defined as the last available measurement prior to the first dose of double-blind Investigational Medicinal Product (IMP) in the double-blind treatment period.

7.2 Demographic Characteristics

For the Randomized Sample, demographic characteristics will be summarized by treatment group. Age, race, ethnicity, height, weight, waist circumference, and body mass index (BMI) will be tabulated by gender and overall using the baseline assessments for the single-blind placebo run-in period.

Mean, range and standard deviation will be used to describe continuous variables such as age. Frequency distributions will be tabulated for categorical variables such as race.

7.3 Medical and Psychiatric History

A summary of medical and psychiatric history will be presented for the Randomized Sample by treatment group and overall.

A summary of the Adult ADHD Clinical Diagnostic Scale (ACDS) at screening will also be presented for the Randomized Sample (by treatment group and overall). The number and

percentage of patients with each response to items A23-A41 from Section A (Childhood ADHD Symptoms Summary), B22-B39 from Section B (Adult ADHD Symptoms Summary), and C1-C5 will be presented.

7.4 Neuropsychiatric Diagnosis

A summary of MINI International Neuropsychiatric Interview (M.I.N.I.) will be presented for the Randomized Sample by treatment group and overall. Summarized will be the number and percentage of patients who meet each diagnosis criteria, and number and percentage of patients with each primary diagnosis.

7.5 Baseline Psychiatric Evaluation

For the Randomized Sample, baseline for the single-blind placebo run-in period and baseline for the double-blind treatment period psychiatric scale evaluation will be summarized by treatment group and overall. The mean, median, range and standard deviation will be used to summarize the assessments of: AISRS total score, ASRS and CGI - Severity of Illness Score (CGI-S).

8 Efficacy Analysis

All efficacy analyses pertaining to the double-blind treatment period will be performed on the Efficacy Sample, and patients will be included in the treatment group as randomized.

For analysis of the double-blind treatment period data, the baseline for the double-blind treatment period defined in Section 7.1 will be used. Statistical comparisons are based on 2-sided, 0.05 significance levels.

8.1 Primary Efficacy Endpoint

The primary efficacy endpoint is the change from the baseline of the double-blind treatment period to Day 42 in AISRS total score.

8.1.1 Primary Efficacy Analysis

The objective of the primary efficacy analysis is to compare the efficacy between centanafadine (SR 200 mg TDD or SR 400 mg TDD) and placebo.

The primary estimand defining the treatment effect of interest in the trial uses the hypothetical strategy specified in the draft ICH E9 (R1) Addendum. The objective of the primary analysis is to evaluate the efficacy of centanafadine SR 400mg TDD in adult subjects with ADHD

versus placebo. The estimand, or target of estimation, following the hypothetical strategy is the pharmacological effect seen, had no withdrawals occurred. This hypothetical estimand is justifiable in this case, since the focus is on the pharmacological effect of the drug additional to non-specific effects. Subjects who withdraw from a symptomatic IMP treatment either could have lost their treatment effect, had the subjects not taken any other symptomatic medication after withdrawal, or could have their treatment effect been masked, had the subjects taken other symptomatic medication after withdrawal. This means that any observations taken after subjects stop IMP will most likely not contribute relevant information about the pharmacological effect of the drug. Due to this strategy, the last collected efficacy assessment after premature trial discontinuation will be done only once at the ET Visit. Every effort will be made to complete all of the ET evaluations prior to administering any additional medications for the treatment of ADHD or other prohibited medications. In the case of terminal or lost to follow-up events, no ET evaluations would be expected, and only scheduled assessments performed before such an event has occurred.

The primary estimand for this trial is defined by the following components:

- Target Population: Efficacy Sample
- Endpoint: Change from baseline to Day 42 in the AISRS total score
- Intercurrent Events: Premature treatment discontinuation
- Measure of Intervention Effect: Difference in endpoint means between centanafadine (SR 200 mg TDD or SR 400 mg TDD) and placebo.

In this hypothetical strategy, the event of withdrawing IMP is considered missing at random (MAR), and the primary endpoint of the trial could be considered as a combination of the responses of on-treatment completers at Day 42 and the imputation of the endpoint to Day 42 following the trend in each treatment group using the MMRM method for subjects who withdraw IMP during the trial. All data collected during the trial treatment period will be used for statistical analysis. For the primary efficacy analysis, the treatment effect will be estimated using the MMRM method described below. Under the MAR assumption, MMRM provides an unbiased estimate of treatment effect for the treatment period. Analyses with missing values imputed by multiple imputation under MNAR and other methods will be performed as sensitivity analyses. The primary analysis will be performed on Efficacy Sample which includes all randomized subjects who took at least 1 dose of IMP in the double-blind treatment period and who have both a baseline for the double-blind treatment period and at least one post-randomization AISRS total score during the double-blind treatment period. The primary efficacy analysis will be performed by fitting a MMRM analysis with an unstructured (UN) variance covariance structure in which the change from baseline for the double-blind

treatment period in AISRS total score at the scheduled double-blind treatment period visits will be the dependent variable based on the OC data set. The model will include fixed class effect terms for treatment, study center, visit day, and an interaction term of treatment by visit day. The model will also include the interaction term of baseline values for the double-blind treatment period of AISRS Total score by visit day as covariates. The primary comparison between centanafadine (400 mg TDD group or 200 mg TDD group) and placebo at Day 42 in the double-blind treatment period will be estimated as the difference between Least Squares (LS) means utilizing the computing software SAS procedure PROC MIXED.

In case there is a convergence problem with MMRM model with the unstructured (UN) variance covariance matrix, the following structures other than unstructured will be used in order of 1) heterogeneous toeplitz (TOEPH), 2) heterogeneous autoregressive of order 1 (ARH1), and 3) heterogeneous compound symmetry (CSH) and the first (co)variance structure converging to the best fit will be used as the primary analysis. If a structured covariance has to be used, the empirical "sandwich" estimator of the standard error of the fixed effects parameters will be used in order to deal with possible model misspecification of the covariance matrix.

Small centers will be defined as centers that do not have at least one evaluable subject (evaluable with regard to the primary efficacy variable) in each treatment arm in the double-blind treatment period. All small centers will be pooled to form "pseudo centers" for the purpose of analysis according to the following algorithm. Small centers will be ordered from the largest to the smallest based on the number of evaluable subjects (i.e., subjects who have baseline and at least one post-baseline value for the primary endpoint in the double-blind treatment period). The process will start by pooling the largest of the small centers with the smallest of the small centers until a non-small center is formed. This process will be repeated using the centers left out of the previous pass. In case of ties in center size, the center with the smallest center code will be selected. If any centers are left out at the end of this process, they will be pooled with the smallest pseudo centers, or if no pseudo centers exist, they will be pooled with the smallest non-small center.

8.1.2 Technical Computation Details for Primary Efficacy Analysis

The SAS code for the PROC MIXED procedure to carry out the above MMRM analysis with an unstructured variance covariance structure is illustrated as follows:

```
proc mixed;
    class treatment center visit subjid;
   model change=treatment center visit treatment*visit baseline*visit  / s cl
ddfm=kenwardroger;
   repeated visit /type=un subject=subjid r rcorr;
```

```
   lsmeans treatment*visit / pdiff cl alpha=0.05 slice=visit;
run;
```

where baseline is the last AISRS Total score prior to the first dose of double-blind IMP in the double-blind treatment period.

8.1.3 Sensitivity Analyses

8.1.3.1 Sensitivity Analyses for Missing at Random (MAR) Assumption

Traditionally the dropout mechanisms are divided into three types (Little, 1995): (1) Missing Completely at Random (MCAR), in which the probability of dropout doesn't depend on the observed data and the missing data; (2) Missing at Random (MAR), in which the probability of dropout depends on the observed data, and (3) Missing Not at Random (MNAR), where the probability of dropout depends on the missing data and possibly the observed data.

Most of MNAR methods (Diggle P, Kenward MG, 1994) have treated all observations with dropout as if they fall within the same dropout type. In practice, we would find that different dropout reasons may be related to the outcomes in different ways, for example, detailed dropout reasons for this study are: adverse events (AE), lack of efficacy (LOE), lost to follow-up, protocol deviation, sponsor discontinued study, subject met (protocol specified) withdrawal criteria, subject was withdrawn from participation by the investigator, and subject withdrew consent to participate. Dropout due to an AE and LOE may lead to MNAR dropout. Subject withdrew consent may also lead to MNAR dropout. However, it is debatable whether a dropout caused by subjects withdrew consent is MAR or MNAR. Except AE, LOE, and subject withdrew consent, all the other dropout reasons may be assumed as either MCAR or MAR dropout. Dropout due to COVID-19 will also be assumed as MAR.

As sensitivity analyses for missing at random (MAR) assumption, analyses for missing not at random (MNAR) will be carried out. Pattern Mixture Models (PMM) based on Multiple Imputation (MI) with mixed missing data mechanisms will be used to investigate the response profile of dropout patients by last dropout reason under MNAR mechanism for the following three scenarios:

1) Dropout reasons due to either AE or LOE as MNAR
2) Dropout reasons due to either AE or LOE or subject withdrew consent as MNAR
3) All dropouts as MNAR

Delta Adjustment Imputation Methods

This MNAR sensitivity analysis is to departure from MAR assumption by progressively increasing the delta until conclusion from the primary analysis is overturned. The delta is 0%, 10%, 20%, 30%, ..., 100% of the expected treatment difference of 5 points and/or the observed

treatment difference between centanafadine and Placebo from the primary analysis of MMRM model until conclusion of the primary analysis is overturned. When delta=0 it is MAR. When delta > 0 it is MNAR.

1) Using Monte Carlo Markov Chain (MCMC) methodology from PROC MI to impute the intermittent missing data to a monotone missing pattern;
2) Using a standard MAR-based multiple imputation approach from PROC MI to impute the monotone missingness data
3) For patients in the treated group and with a dropout reason of AE or LOE or subject withdrew consent, a delta will be added for all the values after the dropout time.
4) Using MMRM model in the primary analysis to analyze the completed data using PROC MIXED on the multiple imputed data
5) Obtaining the overall results using PROC MIANALYZE.

Placebo Based Imputation Methods

Similar to "Standard" multiple imputations, except parameters for imputation model obtained from only the placebo (control) group. Missing data for both placebo and drug group are imputed based on the imputation model derived from placebo data. If drug improved outcomes prior to dropout, this benefit is carried into subsequent imputed values, but will diminish over time in accordance with the correlation structure.

In addition, model based MNAR methods such as the shared parameter model (Wu and Baily, 1989) and random coefficient pattern mixture model (Hedeker D, Gibbons RD, 1997) will be also performed.

LOCF and OC Analyses

Change from baseline of the double-blind treatment period for the AISRS total score will be evaluated using ANCOVA with baseline of the double-blind treatment period value as covariate and treatment and, in LOCF analyses, study center as main effects. For the OC analyses, study center will not be included in the model.

8.1.3.2 Per Protocol Analyses

Per Protocol analysis will be performed using the Per Protocol Sample.

8.1.3.3 Sensitivity Analyses for Violation of Normality Assumption

The primary endpoint MMRM analysis is a maximum likelihood method that relies on normality assumption. Residual analyses will be carried out to examine model assumption.

In the case of gross violations of the normality assumptions, nonparametric van Elteren test[8] (van Elteren, 1960) will be performed to compare treatment effect at Week 14 on both LOCF

dataset and Multiple Imputation (MI) data. The van Elteren test is a generalized CMH procedure useful for stratified continuous data in non-normal setting. It belongs to a general family of Mantel-Haenszel mean score tests. The test is performed via SAS procedure PROC FREQ, by including CMH2 and SCORES=MODRIDIT options in the TABLE statement. The stratification factor is trial center.

In addition, other methods that are robust to distributional assumption will also be performed to provide different views on the primary efficacy result, these include generalized estimating equations (GEE), weighted GEE (WGEE), and MI-robust regression[9].

For MI-van Elteren test and MI-robust regression, imputation datasets will be generated with SAS MI procedure, each dataset will be analyzed, then an overall estimate is derived with SAS MIANALYZE procedure.

8.1.4 Subgroup Analyses

Subgroup analyses of change from baseline of the double-blind treatment period in AISRS total score to every scheduled visit in the double-blind treatment period will be performed by the following factors:

- Sex (Based on the biological status)
- Race (White and All Other Races)

All subgroup analyses will be conducted using the same MMRM analysis as for the primary efficacy analysis except that the fixed class effect term for trial center will not be included in the model.

Interaction effects of treatment-by-subgroup will be assessed at Day 42 for the subgroups identified in the previous paragraph. MMRM analyses will be performed by adding addition of terms for subgroup-by-day and treatment-by-subgroup-by-day. These treatment-by-subgroup interaction analyses will be presented in statistical documentation.

8.2 Key Secondary Efficacy Endpoint

The key secondary efficacy endpoint is the change from baseline of the double-blind treatment period to Day 42 using the CGI-S. This key secondary efficacy endpoint will be analyzed by fitting the same MMRM model described in the primary analysis.

To control the overall experiment-wise type I error at 0.05 level, A fixed sequence testing approach will be applied. The statistical test will be performed in the following order:

1) Change from baseline to Day 42 in the double-blind treatment period in AISRS total score between centanafadine 400 mg TDD and placebo;

2) Change from baseline to Day 42 in the double-blind treatment period in AISRS total score between centanafadine 200 mg TDD and placebo;
3) Change from baseline to Day 42 in CGI-S score between centanafadine 400 mg TDD and placebo;
4) Change from baseline to Day 42 in CGI-S score between centanafadine 200 mg TDD and placebo.

The testing procedure will stop at the first comparison where the p-value is ≥ 0.05. None of the subsequent comparisons will be performed.

8.3 Other Efficacy Endpoints

Other efficacy analyses are listed below. All other efficacy variables will be evaluated at a nominal 0.05 level (2-sided) without adjusting for multiplicity.

1) Change from baseline in AISRS total score for every scheduled visit during the double-blind treatment period other than the Day 42 visit;
2) Change from baseline for the Inattentive subscale and Hyperactive-Impulsive subscale of the AISRS for scheduled visits during the double-blind treatment period, separately at every visit
3) Change from baseline in CGI-S for every scheduled visit during the double-blind treatment period other than the Day 42 visit
4) CGI Change from Baseline will be collected at each scheduled visit
5) Percentage of responders at each post-baseline visit during the double-blind treatment period, where a responder is defined as a subject with a CGI Change from Baseline score of 1 or 2 OR a ≥ 30% improvement in ADHD symptoms compared with baseline as measured by the AISRS total score
6) Response rate at each post-baseline visit during the double-blind treatment period, where response is defined as
    a) a CGI Change from Baseline score of 1 or 2 OR a ≥ 20% improvement in ADHD symptoms compared with baseline as measured by the AISRS total score.
    b) a CGI Change from Baseline score of 1 or 2 OR a ≥ 40% improvement in ADHD symptoms compared with baseline as measured by the AISRS total score.
7) Remission rate for every scheduled visit during the double-blind treatment period, where remission is defined as AISRS total score ≤ 18.

Variable (1) through variable (3) will be evaluated using the same MMRM model described in the primary analysis. Variable (4) will be evaluated by the Cochran Mantel Haenszel (CMH) Row Mean Score Differ Test controlling, in LOCF analysis, for trial center. Variable (5) through variable (7) will be evaluated by the CMH General Association Test controlling, in LOCF analysis, for study center. An OC analysis will also be conducted for variables (4)

through (7) but will not control for trial center. Separate summary and statistical test for response rate based only on the AISRS improvement and only on the CGI Change from Baseline score will be presented for (5) and (6).

8.4 Exploratory Efficacy Endpoints

The exploratory efficacy endpoints are listed below. The exploratory efficacy endpoints, when applicable, will be evaluated at a nominal 0.05 level (2-sided) without adjusting for multiplicity.

1) Change from baseline for Question 1 (Global Quality of Life) and Questions 9Aa – 9Ai and 9Ba – 9Bi (Impact of Symptoms) of AIM-A at scheduled visits during the double-blind treatment period, separately at every visit

2) Proportion of subjects in each response for the following questions of AIM-A at scheduled visits during the double-blind treatment period, separately at every visit

    a. Questions 2-4 (Global Quality of Life)

    b. Questions 5a-5j (Living with ADHD)

    c. Questions 6a-6k (General Well-Being)

    d. Questions 7a-7j (Work, Home and School Performance and Daily Functioning)

    e. Questions 8a-8h (Relationships and Communication)

    f. Economic impact (5 items)

    g. Questions 17-23 (Demographics/Medication Status)

3) Change from baseline in the total score of (18 item) ADHD Symptoms score of the ASRS and subscale scores for ASRS at scheduled visits during the double-blind treatment period, separately at every visit

Variables (1) and (3) will be evaluated using the same MMRM model described in the primary analysis. Variable (2) will be summarized by descriptive statistics and no statistical comparisons between centanafadine and placebo will be performed.

8.5 Exploratory Analysis

Exploratory efficacy analyses will be presented in Statistical Documentation.

Treatment-by-center interaction will be assessed at Day 42 by including the treatment-by-center-by-visit interaction in the model. Results for study centers will be displayed from largest center to smallest center.

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Line Item score will be performed for AISRS and ASRS on Change from baseline of the double-blind treatment period to Day 42 using the MMRM model for AISRS and ASRS, where Cohen's D Effect Size[10] is the difference between the two means divided by their standard deviation [as defined by Cohen's D and reviewed on pages 4-6 from the Sage book "Effect Size for ANOVA Designs" (Vol 129) by Cortina and Nouri]. For MMRM (using SAS PROC MIXED), or ANCOVA (Using SAS PROC GLM), LSMean difference of treatment effects for the between centanafadine and placebo groups, and the standard error of the difference (Stderr) will be obtained with an Estimate statement. Let n_1 and n_2 denote the respective sample sizes of the two groups to compare, Effect Size = d = ($LSMean_1$ – $LSMean_2$) / σ, where $\sigma = \frac{\text{Stderr}}{\sqrt{\frac{1}{n_1}+\frac{1}{n_2}}}$.

9 Safety Analysis

Standard safety variables to be analyzed include AEs, clinical laboratory tests, vital signs, electrocardiograms (ECGs), body weight, waist circumference, and BMI. In addition, data from the following safety scales will be evaluated: C-SSRS and Study Medication Withdrawal Questionnaire (SMWQ).

Analyses of the double-blind treatment period safety data will be performed on the Safety Sample unless indicated otherwise.

The Safety Sample will also be analyzed for the single-blind placebo lead-in period safety data, as applicable, by treatment groups the subjects eventually being assigned in the double-blind treatment period.

9.1 Adverse Events

All adverse events (AEs) will be coded by system organ class (SOC) and Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term (PT). The incidence of the following events will be summarized:

a) Treatment-emergent AEs (TEAEs)

b) TEAEs by severity

c) TEAEs potentially causally related to the IMP

d) TEAEs with an outcome of death

e) Serious TEAEs

f) TEAEs leading to discontinuation of the IMP

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g) Treatment-emergent Adverse Events of Special Interest (AESI)

h) Abuse-related TEAEs and TEAEs involving MHIs (Medication handling irregularities)

AEs will be classified by Primary SOC and PT according to the MedDRA. AEs that are gender-specific, e.g., ovarian cancer, will have their incidence rates evaluated for the specific gender.

Incidence of TEAEs will be summarized by double-blind treatment group for the double-blind treatment period. Incidence of TEAEs by SOC and MedDRA PT will be summarized for sex and race.

Adverse Events of Special Interest

Newly acquired skin eruptions that are non-traumatic will be considered AESIs. These may include but are not limited to eruptions such as skin rashes, skin irritations, skin reactions, or acneiform lesions. This does not include localized contact irritation at ECG lead sites due to application or removal of lead adhesive.

Refer to the separate rash workup plan for complete details, including reporting forms, and extra measures that must be performed to characterize any skin AESI of a newly acquired skin eruption that is non-traumatic. The trial site will have a local designated dermatologist available for immediate consultation during the trial for these AESIs.

9.1.1 Adverse Events in the Double-Blind Treatment Period

TEAEs in the double-blind treatment period are defined as AEs with an onset date on or after the start of double-blind treatment. In more detail, TEAEs are all adverse events which started after start of double-blind IMP; or if the event was continuous from end of the single-blind placebo run-in period and was worsening, serious, study drug related, or resulted in death, discontinuation, interruption or reduction of study therapy. Adverse Events occurring up to 30 days after the last day of double-blind dosing will be included in the summary tables.
The incidence of AEs in the double-blind treatment period will be tabulated by treatment group and overall using the Safety Sample. Incidence of TEAE during the double-blind treatment period of at least 5% in either centanafadine group and also greater than placebo by SOC and MedDRA PT will be provided.
Unless otherwise specified, in general, analysis of safety data will be performed on observed case and for last visit.

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9.1.2 Adverse Events in the Single-blind Placebo Run-in Period

Adverse Events in the single-blind placebo run-in period will be summarized for patients in the Safety Sample. AEs occurring up to 30 days after the last day of IMP in this period, but prior to the start of the double-blind treatment period, will be included in these summary tables. The incidence of adverse events in the single-blind placebo run-in period will be tabulated by the double-blind treatment patients receive in the double-blind treatment period.

9.2 Clinical Laboratory Tests

Summary statistics for routine clinical laboratory measurements will be provided. For The double-blind treatment period laboratory tests, change from baseline for the double-blind treatment period will be summarized by treatment group. Potentially clinically relevant results in laboratory tests will also be summarized.

9.2.1 Clinical Laboratory Tests in Double-Blind Treatment Period

Potentially clinically relevant laboratory measurement test results in the double-blind treatment period will be identified for the Safety Sample and will be summarized by treatment group and listed. Criteria for identifying laboratory values of potential clinical relevance are provided in Appendix 2.

9.2.2 Drug Induced Liver Injury (DILI)

Total bilirubin level should be checked for any subject with increased ALT or AST levels ≥ three times the upper normal limits (ULN) or baseline.

- Reporting all DILI as SAE to the FDA based on Hy's Law:
  - AST or ALT ≥ 3 x ULN or baseline and
  - T_Bili ≥ 2 x ULN or baseline

A separate incidence table will be provided for DILI cases, and the corresponding listing will be provided for Safety Sample during the double-blind treatment period and the single-blind placebo run-in period.

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9.2.3 Clinical Laboratory Tests in the Single-blind Placebo Run-in Period

Potentially clinically relevant laboratory measurement test results in the Single-blind Placebo Run-in Period will be summarized for the Safety Sample by treatment group and overall as well as listed by subject and by laboratory test.

9.3 Vital Signs

Summary statistics for vital signs will be provided. For the double-blind treatment period vital signs, change from baseline for the double-blind treatment period will be summarized for the Safety Sample by treatment group. Potentially clinically relevant results in vital signs will also be summarized. Similar summaries will be provided for the Safety Sample during the Single-blind Placebo Run-in Period.

9.3.1 Vital Signs in the Double-Blind Treatment Period

Potentially clinically relevant vital signs measurements identified in the double-blind treatment period for the Safety Sample will be summarized by treatment group. Criteria for identifying vital signs of potential clinical relevance are provided in Appendix 1. All potentially clinically relevant events or changes will be listed and included in summary tables.

9.3.2 Vital Signs in the Single-blind Placebo Run-in Period

Potentially clinically relevant vital signs measurements identified in the Single-blind Placebo Run-in Period for the Safety Sample will be summarized by treatment group.

9.4 Electrocardiogram (ECG) Data

Summary statistics and incidence of potentially clinically relevant changes will be provided for ECG parameters.

For the analysis of QT and QTc, data from three consecutive complexes (representing three consecutive heart beats) will be measured to determine average values. The following QT corrections will be used for reporting purposes in the clinical study report:

1) QTcB is the length of the QT interval corrected for heart rate by the Bazett formula: $QTcB=QT/(RR)^{0.5}$ and
2) QTcF is the length of the QT interval corrected for heart rate by the Fridericia formula: $QTcF=QT/(RR)^{0.33}$
3) QTcN is the length of the QT interval corrected for heart rate by the FDA Neuropharm Division formula: $QTcN=QT/(RR)^{0.37}$

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9.4.1 ECG Data in the Double-Blind Treatment Period

Potentially clinically relevant changes in the 12-lead ECG identified in the double-blind treatment period for the Safety Sample will be listed and summarized by treatment group. Criteria for identifying ECG measurements of potential clinical relevance are provided in Appendix 3.

Categorical changes in ECG parameters during the double-blind treatment period will be summarized based on the following criteria:

Categorical Change Criteria in QT/QTc Parameters		
Classification	**Category**	**Criteria**
QT	New Onset (> 450 Msec)	New onset (>450 msec) in QT means a subject who attains a value > 450 msec during treatment period but not at baseline.
QTc *	New Onset (> 450 Msec)	New onset (> 450 msec) in QTc means a subject who attains a value > 450 msec during treatment period but not at baseline.
	New Onset (> 450 Msec) And > 10% Increase	New onset (> 450 msec) and > 10% increase in QTc means a subject who attains a value > 450 msec and > 10% increase during treatment period but not at baseline
	New Onset (> 500 Msec)	New onset (> 500 msec) in QTc means a subject who attains a value > 500 msec during treatment period but not at baseline.
	Increase 30 - 60 Msec	Increase from baseline value > 30 and ≤ 60 msec in QTc
	Increase > 60 Msec	Increase from baseline value > 60 msec in QTc

* QTc categorical change criteria apply to QTcB, QTcF and QTcN.

9.4.2 ECG Data in the Single-blind Placebo Run-in Period

Potentially clinically relevant changes in the 12-lead ECG identified in the Single-blind Placebo Run-in Period for the Safety Sample will be listed and summarized by treatment group.

9.5 Physical Examinations

By-patient listings will be provided for physical examination.

9.5.1 Body Weight, Waist Circumference and Body Mass Index (BMI)

Analyses of body weight, waist circumference and BMI will be performed for the Safety Sample. The mean change from baseline of the double-blind treatment period to Day 42 (OC) and last visit in the double-blind treatment period in body weight will be tabulated and analyzed using ANCOVA. The ANCOVA models for both the OC and last visit analyses will

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include the baseline of the double-blind treatment period body weight and the treatment group.

Percentages of patients showing significant weight gain (≥ 7 % increase in weight), as well as percentages of patients showing significant weight loss (≥ 7 % decrease in weight) baseline of the double-blind treatment period to Day 42 (OC and LOCF) will be analyzed using Cochran-Mantel-Haenszel (CMH) General Association Test.

Body mass index is defined as weight in kilograms divided by the square of height in meters.

9.6 Suicidality Data

Suicidality will be monitored during the study using the C-SSRS and will be summarized as number and percentage of subjects reporting any suicidal behavior, ideation, behavior by type (4 types), ideation by type (5 types) and treatment emergent suicidal behavior and ideation. Summary will be provided for the single-blind placebo run-in period and the double-blind treatment period for the Safety Sample.

Suicidality is defined as report of at least one occurrence of any type of suicidal ideation or at least one occurrence of any type of suicidal behavior during assessment period (count each person only once).

Treatment emergent suicidal behavior and ideation is summarized by four types: Emergence of suicidal ideation, Emergence of serious suicidal ideation, Worsening of suicidal ideation, Emergence of suicidal behavior.

Emergence of suicidal behavior/ideation is defined as report of any type of suicidal behavior/ideation during treatment when there was no baseline suicidal behavior/ideation.

Emergence of serious suicidal ideation is defined as observation of suicidal ideation severity rating of 4 or 5 during treatment when there was no baseline suicidal ideation.

Worsening of suicidal ideation is defined as a suicidal ideation severity rating that is more severe than it was at baseline.

For the double-blind treatment period analyses, the last available measurement prior to the first dose of double-blind IMP is being used as “Baseline”.

9.7 SMWQ

Medication withdrawal symptoms assessed by SMWQ total scores at the scheduled visits during the double-blind treatment period and follow-up period will be summarized for the Safety Sample by treatment group and overall. The number of patients, mean, median, range and standard deviation will be presented.

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9.8 Medication Handling Irregularities (MHIs) and Events Subject to Additional Monitoring (ESAMs)

MHIs and ESAMs will be summarized for the Safety Sample by treatment group and overall. By-patient listings will be provided.

9.9 Concomitant Medications

Number and proportion of patients taking concomitant medications prior to the single-blind placebo run-in period, during the single-blind placebo run-in period, during the double-blind treatment period, and after study therapy are tabulated by drug classification using the World Health Organization (WHO) drug dictionary. For the double-blind treatment period Randomized Sample, data will be presented by treatment group and overall.

9.10 Extent of Exposure

The start date of double-blind IMP - centanafadine or placebo - will be the first day of double-blind dosing. The number and percentage of subjects who receive double-blind IMP, will be presented by week and by treatment group. Each dosing week will be based on the actual week; i.e., Day 1-7 in Week 1, Day 8-14 in Week 2, etc. This summary will be performed on the Safety Sample.

The mean daily dosage will be summarized by week and treatment group using descriptive statistics. The mean daily dosage per subject per week will be determined for each week of the study. This will be calculated by dividing the sum of individual total doses by the number of days in the week interval. The summary will contain for each treatment group the number of patients receiving double-blind IMP, and the mean and range of the mean daily dose for each week.

10 Conventions

10.1 Study Visit Windows

Study visit windows will be used to map visits using study day intervals. This visit window convention applies to tables and listings for all efficacy and safety scales (AISRS, CGI-S, AIM-A, ASRS and CGI Change from Baseline). This derived study window variable will be named as DAY and will be footnoted. In listings it will be listed along with the eCRF study visit.

Table 10-1 shows classifications for study day intervals in the double-blind treatment period. The variable “target day” is defined using the number of days since the start of double-blind

dosing in the double-blind treatment period. The first day of double-blind dosing is defined as "Day 1".

If more than one observation falls within a particular study day interval, then the last observation within that interval is used. Evaluations occurring more than three days after the last double-blind dosing date and evaluations occurring during the follow-up period will not be mapped into study visit windows and will be excluded from the double-blind treatment period analysis.

Table 10-1: Study Day and Visit Windows in the Double-Blind Treatment Period

Day	Target Day [a]	Study Day Interval [a]
7	7	2-10
14	14	11-17
21	21	18-24
28	28	25-31
35	35	32-38
42	42	39-49 [b]

[a] Relative to the first day of double-blind IMP in the double-blind treatment period.

[b] Evaluations occurring more than three days after the last double-blind dosing date and evaluations occurring during the follow-up period will be excluded from the double-blind treatment period analyses.

10.2 Pooling of small centers

Primary efficacy analysis will be performed on the Efficacy Sample which comprises those subjects in the Randomized Sample who have a baseline value for the double-blind treatment period and at least one post-randomization value for AISRS total score in the double-blind treatment period. Small centers will be defined as centers that do not have at least one evaluable subject (evaluable with regard to the primary efficacy variable) in each treatment arm in the double-blind treatment period. All small centers will be pooled to form "pseudo centers" for the purpose of analysis according to the following algorithm. Small centers will be ordered from the largest to the smallest based on the number of evaluable subjects (i.e., subjects who have a baseline value for the double-blind treatment period value and at least one post-randomization value for AISRS total score in the double-blind treatment period). The process will start by pooling the largest of the small centers with the smallest of the small centers until a non-small center is formed. This process will be repeated using the centers left out of the previous pass. In case of ties in center size, the center with the smallest center code will be selected. If any centers are left out at the end of this process, they will be pooled with

the smallest pseudo centers, or if no pseudo centers exist, they will be pooled with the smallest non-small center.

10.3 Scales: Rules for Scoring and Handling of Missing Data

10.3.1 Adult ADHD Investigator Symptom Rating Scale (AISRS)

The AISRS is utilized as the primary efficacy assessment of a subject's level of ADHD symptoms. It is a modified version of the ADHD Rating Scale that reflects the impact and severity of ADHD among adults and will be administered at each scheduled visit in the screening period, the single-blind placebo run-in period, the double-blind treatment period, and at 2 and 7 days after the last dose of IMP in the follow-up period. It is a clinician-administered scale that measures the 18 symptoms of adult ADHD using a Likert scale: 0 (none); 1 (mild); 2 (moderate); and 3 (severe) and uses a semi-structured interview methodology with suggested prompts for each item to improve interrater reliability. The scale's 18 items directly correspond to the 18 DSM-5 symptoms of ADHD where 9 inattentive items alternate with 9 hyperactive impulsive items. The maximum total score for the scale is 54 points, with 27 points for each subscale. The total score is the sum of both the Inattentive and Hyperactive Impulsive subscales.

The AISRS inattentive subscale score and hyperactive-impulsive subscale score, as well as the AISRS total score is set to be missing if more than one item of a subscale is missing for inattentive subscale or hyperactive-impulsive subscale, separately. If one item is missing for a given subscale (inattentive or hyperactive-impulsive), then the subscale score is derived as the mean of scores from the 8 non-missing items multiplied by 9. All imputed scores are rounded to the first decimal place. The 9 inattentive items consist of the 9 odd numbered items and the 9 hyperactive impulsive items consist of the 9 even numbered items.

10.3.2 Clinical Global Impression Severity of Illness Scale – Modified for Attention-Deficit Hyperactivity Disorder

The CGI-S modified is an observer-rated scale that will be used to measure symptom severity. To perform this assessment, the investigator or rater will respond to the following question: "Considering your total clinical experience with adult ADHD, how mentally ill is the patient at this time?" Response choices include: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; and 7 = among the most extremely ill patients. CGI-S is assessed at each scheduled visit in the double-blind treatment period.

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10.3.3 Clinical Global Impression Change from Baseline

The CGI Change from Baseline is an observer-rated scale that will be used to measure the subject's total improvement compared to before trial drug treatment was initiated. The rater or investigator will rate the subject's total improvement relative to baseline. Response choices include: 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse. CGI Change from Baseline is assessed at each scheduled visit in the double-blind treatment period except for the Day -1 visit.

10.3.4 Attention-Deficit Hyperactivity Disorder Impact Module – Adult (AIM-A)

The AIM-A is a subject self-report questionnaire which assesses quality of life in adults with ADHD. The questionnaire has 4 global quality of life items, 5 economic impact items, and 5 multi-item scales that assess the following key concepts: Living with ADHD, General Well-Being, Work, Home and School Performance and Daily Functioning. Additionally, Relationships and Communication, and Impact of Symptoms are also included.

10.3.5 Adult ADHD Self Report Scale (ASRS)

The ASRS is a self-report questionnaire developed by the WHO. The subject will answer 18 questions about the frequency of recent ADHD symptoms that are consistent with the DSM-IV criteria. The ASRS is assessed at the scheduled visits during the screening period, the single-blind placebo run-in period, and at Days -1, 28 and 42/ET during the double-blind treatment period.

The total score of (18 item) ADHD Symptoms score of the ASRS is set to be missing if more than one item of a subscale is missing for inattentive subscale or hyperactive-impulsive subscale, separately. If one item is missing for a given subscale (inattentive or hyperactive-impulsive), then the subscale score is derived as the mean of scores from the 8 non-missing items multiplied by 9. All imputed scores are rounded to the first decimal place. The 9 inattentive items consist of items 1-4 and 7-11 and the 9 hyperactive impulsive items consist of items 5-6 and 12-18.

10.3.6 Study Medication Withdrawal Questionnaire (SMWQ)

The SMWQ is a questionnaire to assess withdrawal symptoms. The SMWQ is a modification of the Amphetamine Withdrawal Questionnaire in which the terms "amphetamines and methamphetamine" are replaced with the term "the study medication." The SMWQ is assessed at Day 35 and Day 42/ET in the double-blind treatment period and at 1, 2, 3, 5, 7, and 10 days after the last dose of IMP in the follow-up period.

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10.3.7 Columbia-Suicide Severity Rating Scale (C-SSRS)

Suicidality will be monitored during the trial using the C-SSRS. The C-SSRS is a semi-structured interview that captures the occurrence, severity, and frequency of suicide-related thoughts and behaviors during the assessment period. The interview includes definitions and suggested questions to solicit the type of information needed to determine if a suicide-related thought or behavior has occurred. The interview and rating for the C-SSRS must be completed by a licensed clinician who has been successfully trained to rate this scale by the sponsor or a designee and is medically responsible for the subject. Documentation of trial training should be maintained in the investigational site's files.

The C-SSRS has a "Screening/Baseline" version, which will be completed at screening and a "Since Last Visit" version that will be completed at all other visits (including the ET visit, if applicable). There are a maximum of 19 items to be completed: 7 required, 10 potential additional items if there is a positive response to a required item, and 2 items for suicide/suicide behavior present during the interview. The C-SSRS uses dichotomous scales (i.e., yes or no), Likert scales, and text or narrative to further describe the thoughts or behaviors.

The C-SSRS is assessed at each scheduled visit in the screening period, the single-blind placebo run-in period, the double-blind treatment period, and at 2 and 7 days after the last dose of IMP in the follow-up period.

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12 Potential Clinical Relevance Criteria from Protocol

Appendix 1 Criteria for Identifying Vital Signs of Potential Clinical Relevance

Variable	Criterion Value[a]	Change Relative to Baseline[a]
Heart Rate[b]	> 100 bpm < 50 bpm	≥ 10 bpm increase ≥ 10 bpm decrease
Systolic Blood Pressure[b]	≥ 140 mmHg < 90 mmHg	≥ 20 mmHg increase ≥ 20 mmHg decrease
Diastolic Blood Pressure[b]	≥ 90 mmHg < 60 mmHg	≥ 10 mmHg increase ≥ 10 mmHg decrease
Orthostatic Hypotension	≥ 30 mmHg decrease in systolic blood pressure or a ≥ 20 mmHg in diastolic blood pressure after at least 3 minutes of standing compared to the previous supine blood pressure.	Not Applicable (baseline status not considered)
Orthostatic Tachycardia	≥ 25 bpm increase in heart rate from supine to standing	Not Applicable (baseline status not considered)
Weight	-	≥ 7% increase ≥ 7% decrease

[a] In order to be identified as potentially clinically relevant, an on-treatment value must meet the "Criterion Value" and also represent a change from the subject's baseline value of at least the magnitude shown in the "Change Relative to Baseline" column.

[b] As defined in "Supplementary Suggestions for Preparing an Integrated Summary of Safety Information in an Original NDA Submission and for Organizing Information in Periodic Safety Updates," FDA Division of Neuropharmacological Drug Products draft (2/27/87).

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Appendix 2 Criteria for Identifying Laboratory Values of Potential Clinical Relevance

Laboratory Tests	Criteria
Chemistry	
AST (SGOT)	≥ 3 x upper limit of normal (ULN)
ALT (SGPT)	≥ 3 x ULN
Alkaline phosphatase	≥ 3 x ULN
BUN	≥ 30 mg/dL
Creatinine	≥ 2.0 mg/dL
Uric Acid	
Men	≥ 10.5 mg/dL
Women	≥ 8.5 mg/dL
Bilirubin (total)	≥ 2.0 mg/dL
Creatine Phosphokinase (CPK)	> 3 x ULN
Hematology	
Hematocrit	
Men	≤ 37 % and decrease of ≥ 3 percentage points from Baseline
Women	≤ 32 % and decrease of ≥ 3 percentage points from Baseline
Hemoglobin	
Men	≤ 11.5 g/dL
Women	≤ 9.5 g/dL
White blood count	≤ 2,800/ mm^3 or ≥ 16,000/ mm^3
Eosinophils	≥ 10%
Neutrophils	≤ 15%
Absolute neutrophil count	≤ 1,500/ mm^3
Platelet count	≤ 75,000/ mm^3 or ≥ 700,000/ mm^3
Urinalysis	
Protein	Increase of ≥ 2 units
Glucose	Increase of ≥ 2 units
Additional Criteria	
Chloride	≤ 90 mEq/L or ≥ 118 mEq/L
Potassium	≤ 2.5 mEq/L or ≥ 6.5 mEq/L
Sodium	≤ 126 mEq/L or ≥ 156 mEq/L
Calcium	≤ 8.2 mg/dL or ≥ 12 mg/dL
Glucose	
Fasting	≥ 100 mg/dL
Non-Fasting	≥ 200 mg/dL
Total Cholesterol, Fasting	≥ 240 mg/dL
LDL Cholesterol, Fasting	≥ 160 mg/dL
HDL Cholesterol, Fasting	
Men	< 40 mg/dL
Women	< 50 mg/dL
Triglycerides, Fasting	≥ 150 mg/dL

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Appendix 3 Criteria for Identifying ECG Measurements of Potential Clinical Relevance

Variable	Criterion Value[a]	Change Relative to Baseline[a]
Rate		
Tachycardia	≥ 120 bpm	increase of ≥ 15 bpm
Bradycardia	≤ 50 bpm	decrease of ≥ 15 bpm
Rhythm		
Sinus tachycardia[b]	≥ 120 bpm	increase of ≥ 15 bpm
Sinus bradycardia[c]	≤ 50 bpm	decrease of ≥ 15 bpm
Supraventricular premature beat	all	not present → present
Ventricular premature beat	all	not present → present
Supraventricular tachycardia	all	not present → present
Ventricular tachycardia	all	not present → present
Atrial fibrillation	all	not present → present
Atrial flutter	all	not present → present
Conduction		
1° atrioventricular block	PR ≥ 200 msec	increase of ≥ 50 msec
2° atrioventricular block	all	not present → present
3° atrioventricular block	all	not present → present
Left bundle-branch block	all	not present → present
Right bundle-branch block	all	not present → present
Pre-excitation syndrome	all	not present → present
Other intraventricular conduction block[d]	QRS ≥ 120 msec	increase of ≥ 20 msec
Infarction		
Acute or subacute	all	not present → present
Old	all	not present → present ≥ 12 weeks post study entry
ST/T Morphological		
Myocardial Ischemia	all	not present → present
Symmetrical T-wave inversion	all	not present → present
Increase in QTc	QTcF > 450 msec (men) QTcF > 470 msec (women)	

[a] In order to be identified as potentially clinically relevant, an on-treatment value must meet the "Criterion Value" and also represent a change from the subject's baseline value of at least the magnitude shown in the "Change Relative to Baseline" column.

[b] No current diagnosis of supraventricular tachycardia, ventricular tachycardia, atrial fibrillation, atrial flutter, or other rhythm abnormality.

[c] No current diagnosis of atrial fibrillation, atrial flutter, or other rhythm abnormality.

[d] No current diagnosis of left bundle branch block or right bundle branch block.

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13 Proposed List of Summary Tables

CT-1.1 Subject Disposition

CT-1.2 Subject Disposition by Center

CT-1.3 Subject Completion Rates by Week During the Double-Blind Treatment Period (Randomized Sample)

CT-1.4.1 Subject Enrollment by Country (Randomized Sample)

CT-1.4.2 Subject Enrollment by Country by Age Group (Randomized Sample)

CT-2 Reasons for Discontinuation in the Double-Blind Treatment Period (Randomized Sample)

CT-3.1 Demographic Characteristics (Randomized Sample)

CT-3.2.1 Medical History (Randomized Sample)

CT-3.2.2 Psychiatric History (Randomized Sample)

CT-3.2.3 Summary of Adult ADHD Clinical Diagnostic Scale (ACDS) (Randomized Sample)

CT-3.3 MINI International Neuropsychiatric Interview (M.I.N.I.) (Randomized Sample)

CT-3.4.1 Baseline Psychiatric Scale Evaluations for the Single-Blind Placebo Run-in Period (Randomized Sample)

CT-3.4.2 Baseline Psychiatric Scale Evaluations for the Double-Blind Treatment Period (Randomized Sample)

CT-4.1 Concomitant Medications: Medications Taken Prior to Start of Double-Blind Treatment (Safety Sample)

CT-4.2 Concomitant Medications: Medications Taken During the Double-Blind Treatment Period (Safety Sample)

CT-4.3 Concomitant Medications: Medications Taken Post Study Period (Safety Sample)

CT-5.1 Summary of Efficacy Results at Day 42 in the Double-Blind Treatment Period (Efficacy Sample)

CT-5.2.1.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, UN (Efficacy Sample)

CT-5.2.1.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, UN (Per Protocol Sample)

CT-5.2.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, TOEPH Empirical (Efficacy Sample)

CT-5.2.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, ARH1 Empirical (Efficacy Sample)

CT-5.2.4 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, CSH Empirical (Efficacy Sample)

CT-5.2.5 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - MMRM, DDFM=SATTERTHWAITE (Efficacy Sample)

CT-5.2.6.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - LOCF (Efficacy Sample)

CT-5.2.6.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - OC (Efficacy Sample)

CT-5.2.7 Summary of Mean Change from Baseline to End of the Single-Blind Run-in Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score – OC (Efficacy Sample)

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CT-5.2.8 Summary of Mean Change from Baseline to End of the Follow-up Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score – OC (Efficacy Sample)

CT-5.3.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in AISRS Inattentive Subscale - MMRM, UN (Efficacy Sample)

CT-5.3.2 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in AISRS Inattentive Subscale - LOCF (Efficacy Sample)

CT-5.3.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day AISRS Inattentive Subscale - OC (Efficacy Sample)

CT-5.3.4 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in AISRS Inattentive Subscale - OC (Efficacy Sample)

CT-5.3.5 Summary of Mean Change from Baseline to End of the Follow-up Period in AISRS Inattentive Subscale - OC (Efficacy Sample)

CT-5.3.6 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in AISRS Hyperactive-Impulsive Subscale - MMRM, UN (Efficacy Sample)

CT-5.3.7 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in AISRS Hyperactive-Impulsive Subscale - LOCF (Efficacy Sample)

CT-5.3.8 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day AISRS Hyperactive-Impulsive Subscale - OC (Efficacy Sample)

CT-5.3.9 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in AISRS Hyperactive-Impulsive Subscale - OC (Efficacy Sample)

CT-5.3.10 Summary of Mean Change from Baseline to End of the Follow-up Period in AISRS Hyperactive-Impulsive Subscale - OC (Efficacy Sample)

CT-5.4.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Clinical Global Impression - Severity of Illness Modified for ADHD (CGI-S) Scale - MMRM, UN (Efficacy Sample)

CT-5.4.2 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Clinical Global Impression - Severity of Illness Modified for ADHD (CGI-S) Scale - LOCF (Efficacy Sample)

CT-5.4.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Clinical Global Impression - Severity of Illness Modified for ADHD (CGI-S) Scale - OC (Efficacy Sample)

CT-5.5.1 Summary of Mean Clinical Global Impression Change from Baseline Scale by Study Day in the Double-Blind Treatment Period - LOCF (Efficacy Sample)

CT-5.5.2 Summary of Mean Clinical Global Impression Improvement Change from Baseline Scale by Study Day in the Double-Blind Treatment Period - OC (Efficacy Sample)

CT-5.6.1 Summary of Proportion of Responders to Treatment During the Double-Blind Treatment Period Relative to the End of the Single-Blind Run-in Period - LOCF (Efficacy Sample)

CT-5.6.2 Summary of Proportion of Responders to Treatment During the Double-Blind Treatment Period Relative to the End of the Single-Blind Run-in Period - OC (Efficacy Sample)

CT-5.6.3 Summary of Proportion of Subjects with an Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score or a CGI Change from Baseline Response During the Double-Blind Treatment Period - LOCF (Efficacy Sample)

CT-5.6.4 Summary of Proportion of Subjects with an Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score or a CGI Change from Baseline Response During the Double-Blind Treatment Period - OC (Efficacy Sample)

CT-5.6.5 Summary of Proportion of Subjects with an Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score Remission During the Double-Blind Treatment Period - LOCF (Efficacy Sample)

CT-5.6.6 Summary of Proportion of Subjects with an Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score Remission During the Double-Blind Treatment Period - OC (Efficacy Sample)

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CT-5.7.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Attention-Deficit Hyperactivity Disorder Impact Module - Adult (AIM-A) Scale - MMRM, UN (Efficacy Sample)

CT-5.7.2 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Attention-Deficit Hyperactivity Disorder Impact Module - Adult (AIM-A) Scale - LOCF (Efficacy Sample)

CT-5.7.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Attention-Deficit Hyperactivity Disorder Impact Module - Adult (AIM-A) Scale - OC (Efficacy Sample)

CT-5.7.4 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in Attention-Deficit Hyperactivity Disorder Impact Module - Adult (AIM-A) Scale - OC (Efficacy Sample)

CT-5.7.5 Summary of Proportion of Subjects in Each Category During the Single-Blind Run-in Period and Double-Blind Treatment Period by Study Day in in Attention-Deficit Hyperactivity Disorder Impact Module - Adult (AIM-A) Scale - OC (Efficacy Sample)

CT-5.8.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Self Report Scale (ASRS) Scale - MMRM, UN (Efficacy Sample)

CT-5.8.2 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Self Report Scale (ASRS) Scale - LOCF (Efficacy Sample)

CT-5.8.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Self Report Scale (ASRS) Scale - OC (Efficacy Sample)

CT-5.8.4 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in Adult ADHD Self Report Scale (ASRS) Scale - OC (Efficacy Sample)

CT-5.9.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Inattentive Subscale - MMRM, UN (Efficacy Sample)

CT-5.9.2 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Inattentive Subscale - LOCF (Efficacy Sample)

CT-5.9.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Inattentive Subscale - OC (Efficacy Sample)

CT-5.9.4 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in ASRS Inattentive Subscale - OC (Efficacy Sample)

CT-5.9.5 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Hyperactive-Impulsive Subscale - MMRM, UN (Efficacy Sample)

CT-5.9.6 Summary of Mean Change Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Hyperactive-Impulsive Subscale - LOCF (Efficacy Sample)

CT-5.9.7 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in ASRS Hyperactive-Impulsive Subscale - OC (Efficacy Sample)

CT-5.9.8 Summary of Mean Change from Baseline to End of Single-Blind Placebo Run-in Period in ASRS Hyperactive-Impulsive Subscale - OC (Efficacy Sample)

CT-5.10.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score – MI, VAN ELTEREN TEST (Efficacy Sample)

CT-5.10.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - GEE (Efficacy Sample)

CT-5.10.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score - WGEE (Efficacy Sample)

CT-5.11.1 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in AISRS Total Score Assume All Dropouts as MNAR (Efficacy Sample)

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CT-5.11.2 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in AISRS Total Score Assume All Dropouts as MNAR (Efficacy Sample)

CT-5.11.3 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in AISRS Total Score Dropout due to AE or LOE or Withdrew Consent as MNAR (Efficacy Sample)

CT-5.11.4 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in AISRS Total Score Dropout due to AE or LOE or Withdrew Consent as MNAR (Efficacy Sample)

CT-5.11.5 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in AISRS Total Score Dropouts due to AE or Lack of Efficacy (LOE) as MNAR (Efficacy Sample)

CT-5.11.6 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in AISRS Total Score Dropouts due to AE or Lack of Efficacy (LOE) as MNAR (Efficacy Sample)

CT-5.11.7 Sensitivity Analysis of MNAR using Placebo Based Imputation in AISRS Total Score (Efficacy Sample)

CT-5.11.8 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in CGI-S Score Assume All Dropouts as MNAR (Efficacy Sample)

CT-5.11.9 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in CGI-S Score Assume All Dropouts as MNAR (Efficacy Sample)

CT-5.11.10 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in CGI-S Score Dropout due to AE or LOE or Withdrew Consent as MNAR (Efficacy Sample)

CT-5.11.11 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in CGI-S Score Dropout due to AE or LOE or Withdrew Consent as MNAR (Efficacy Sample)

CT-5.11.12 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 1) in SDS Mean Score Dropouts due to AE or Lack of Efficacy (LOE) as MNAR (Efficacy Sample)

CT-5.11.13 Sensitivity Analysis of MNAR using Pattern Mixture Model with Multiple Imputation (Delta Method 2) in CGI-S Score Dropouts due to AE or Lack of Efficacy (LOE) as MNAR (Efficacy Sample)

CT-5.11.14 Sensitivity Analysis of MNAR using Placebo Based Imputation in CGI-S Score (Efficacy Sample)

CT-5.11.15 Sensitivity Analysis of MNAR Using Model Based Methods: Shared Parameter Model and Random Coefficient Pattern Mixture Model –OC (Efficacy Sample)

CT-6.1.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS)Total Score in the Subgroup of Females - MMRM (Efficacy Sample)

CT-6.1.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score in the Subgroup of Males - MMRM (Efficacy Sample)

CT-6.2.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score in the Subgroup of Whites - MMRM (Efficacy Sample)

CT-6.2.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Adult ADHD Investigator Symptom Rating Scale (AISRS) Total Score in the Subgroup of All Other Races - MMRM (Efficacy Sample)

CT-7.1 Extent of Exposure to Study Medication During the Double-Blind Treatment Period (Safety Sample)

CT-7.2 Number and Percentage of Subjects Receiving Study Medication and Mean and Range of Average Daily Dose in the Double-Blind Treatment Period (Safety Sample)

CT-8.1.1 Adverse Events During the Double-Blind Treatment Period (All Causalities) (Safety Sample)

CT-8.1.2 Adverse Events During the Single-Blind Placebo Run-in Period (All Causalities) (Safety Sample)

CT-8.2.1.1 Incidence of TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.2 Incidence of TEAEs During the Double-Blind Treatment Period by System Organ Class, MedDRA Preferred Term and Severity (Safety Sample)

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CT-8.2.1.3 Incidence of TEAE During the Double-Blind Treatment Period of at Least 5% in Any Centanafadine Group and Greater Than Placebo by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.4 Incidence of TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term, by Sex (Safety Sample)

CT-8.2.1.5 Incidence of TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term, by Race (Safety Sample)

CT-8.2.1.6 Incidence of Non-Serious TEAEs During the Double-Blind Treatment Period of at Least 5% in Any Centanafadine Group and Greater Than Placebo by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.7 Incidence of TEAE During the Double-Blind Treatment Period of at Least 2% in Any Centanafadine Group and Greater Than Placebo by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.8 Incidence and Occurrence (Number of Events) of Serious TEAEs by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.9 Incidence and Occurrence (Number of Events) of Potentially Drug-Related Serious TEAEs by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.1.10 Incidence and Occurrence (Number of Events) of Non-Serious TEAEs by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.2.2 Incidence of AEs During the Single-Blind Placebo Run-in Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.3.1 Incidence of Potentially Drug-Related TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.3.2 Incidence of Potentially Drug-Related TEAEs During the Double-Blind Treatment Period by System Organ Class, MedDRA Preferred Term and Severity (Safety Sample)

CT-8.4.1.1 Incidence of Deaths Due to TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.4.1.2 Incidence of Deaths Due to TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term and Severity (Safety Sample)

CT-8.4.2 Incidence of Deaths Due to AEs During the Single-Blind Placebo Run-in Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.5.1.1 Incidence of Serious TEAEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.5.1.2 Incidence of Serious TEAEs During the Double-Blind Treatment Period by System Organ Class, MedDRA Preferred Term and Severity (Safety Sample)

CT-8.5.2.1 Incidence of Serious AEs During the Single-Blind Placebo Run-in Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.6.1 Incidence of TEAEs Resulting in Discontinuation of Study Medication During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.6.2 Incidence of TEAEs Resulting in Discontinuation of Study Medication During the Double-Blind Treatment Period by System Organ Class, MedDRA Preferred Term and Severity (Safety Sample)

CT-8.7.1 Incidence of Treatment-Emergent Adverse Events of Special Interests (AESIs) During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-8.7.2 Incidence of Treatment-Emergent Adverse Events of Special Interests (AESIs) During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term and Severity (Safety Sample)

CT-8.7.3 Listing of Treatment-Emergent Adverse Events of Special Interests (AESIs) During the Double-Blind Treatment Period (Safety Sample)

CT-8.8.1 Incidence of Treatment-Emergent Abuse Potential-Related Adverse Events During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

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CT-8.8.2 Incidence of Treatment-Emergent Abuse Potential-Related Adverse Events During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term and Severity (Safety Sample)

CT-8.8.3 Listing of Treatment-Emergent Abuse Potential-Related Adverse Events During the Double-Blind Treatment Period (Safety Sample)

CT-9.1.1 Listing of Deaths During the Double-Blind Treatment Period

CT-9.1.2 Listing of Deaths During the Single-Blind Placebo Run-in Period

CT-9.2.1 Listing of Serious Adverse Events During the Double-Blind Treatment Period

CT-9.2.2 Listing of Serious Adverse Events During the Single-Blind Placebo Run-in Period

CT-9.3 Listing of Discontinuations of Study Medication Due to Adverse Events During the Double-Blind Treatment Period

CT-9.4 Listing of Adverse Events for Subjects Discontinued from Study Due to Adverse Events During the Double-Blind Treatment Period

CT-10.1 Criteria for Laboratory Test Values with Potential Clinical Relevance

CT-10.2.1.1 Listing of Laboratory Test Values with Potential Clinical Relevance During the Double-Blind Treatment Period by Subject (Safety Sample)

CT-10.2.1.2 Listing of Laboratory Test Values with Potential Clinical Relevance During the Double-Blind Treatment Period by Test (Safety Sample)

CT-10.2.2 Incidence of Laboratory Test Values with Potential Clinical Relevance During the Double-Blind Treatment Period (Safety Sample)

CT-10.2.3.1 Mean Change from Baseline of the Double-Blind Treatment Period in Clinical Laboratory Test Results - Serum Chemistry (Safety Sample)

CT-10.2.3.2 Mean Change from Baseline of the Double-Blind Treatment Period in Clinical Laboratory Test Results - Hematology (Safety Sample)

CT-10.2.3.3 Mean Change from Baseline of the Double-Blind Treatment Period in Clinical Laboratory Test Results - Urinalysis (Safety Sample)

CT-10.3.1.1 Listing of Laboratory Test Values with Potential Clinical Relevance During the Single-Blind Placebo Run-in Period by Subject (Safety Sample)

CT-10.3.1.2 Listing of Laboratory Test Values with Potential Clinical Relevance During the Single-Blind Placebo Run-in Period by Test (Safety Sample)

CT-10.3.2 Incidence of Laboratory Test Values with Potential Clinical Relevance During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-10.3.3.1 Mean Change from Baseline of the Single-Blind Placebo Run-in Period in Clinical Laboratory Test Results During the Single-Blind Placebo Run-in Period - Serum Chemistry (Safety Sample)

CT-10.3.3.2 Mean Change from Baseline of the Single-Blind Placebo Run-in Period in Clinical Laboratory Test Results During the Single-Blind Placebo Run-in Period - Hematology (Safety Sample)

CT-10.3.3.3 Mean Change from Baseline of the Single-Blind Placebo Run-in Period in Clinical Laboratory Test Results During the Single-Blind Placebo Run-in Period - Urinalysis (Safety Sample)

CT-10.4.1 Incidence of Potentially Liver Injury Related Laboratory Test Abnormalities During the Double-Blind Treatment Period (Safety Sample)

CT-10.4.2 Incidence of Potentially Liver Injury Related Laboratory Test Abnormalities During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-10.5.1 Listing of Potentially Liver Injury Related Laboratory Test Abnormalities During the Double-Blind Treatment Period (Safety Sample)

CT-10.5.2 Listing of Potentially Liver Injury Related Laboratory Test Abnormalities During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-11.1 Criteria for Potentially Clinically Relevant Abnormalities in Vital Signs

CT-11.2.1 Listing of Potentially Clinically Relevant Abnormalities in Vital Signs During the Double-Blind Treatment Period (Safety Sample)

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CT-11.2.2 Incidence of Potentially Clinically Relevant Abnormalities in Vital Signs During the Double-Blind Treatment Period (Safety Sample)

CT-11.2.3 Mean Change from Baseline of the Double-Blind Treatment Period in Vital Signs During the Double-Blind Treatment Period (Safety Sample)

CT-11.3.1 Listing of Potentially Clinically Relevant Abnormalities in Vital Signs During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-11.3.2 Incidence of Potentially Clinically Relevant Abnormalities in Vital Signs During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-11.3.3 Mean Change from Baseline of the Single-Blind Placebo Run-in Period in Vital Signs During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-12.1 Criteria for Potentially Clinically Relevant Abnormalities in ECG Evaluations

CT-12.2.1 Listing of Potentially Clinically Relevant Abnormalities in ECG Evaluations During the Double-Blind Treatment Period (Safety Sample)

CT-12.2.2 Incidence of Potentially Clinically Relevant Changes in ECG Evaluations During the Double-Blind Treatment Period (Safety Sample)

CT-12.2.3 Mean Change from Baseline of the Double-Blind Treatment Period in Electrocardiogram Results During the Double-Blind Treatment Period (Safety Sample)

CT-12.3.1 Listing of Categorical Changes in QT/QTc During the Double-Blind Treatment Period (Safety Sample)

CT-12.3.2 Incidence of Categorical Changes in QT/QTc During the Double-Blind Treatment Period (Safety Sample)

CT-12.4.1 Listing of Potentially Clinically Relevant Abnormalities in ECG Evaluations During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-12.4.2 Incidence of Potentially Clinically Relevant Changes in ECG Evaluations During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-12.4.3 Mean Change from Baseline of the Single-Blind Placebo Run-in Period in Electrocardiogram Results During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-12.5.1 Listing of Categorical Changes in QT/QTc During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-12.5.2 Incidence of Categorical Changes in QT/QTc During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-13.1.1 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Body Weight (kg) (Safety Sample)

CT-13.1.2 Summary of Proportion of Patients with Potentially Clinically Relevant Weight Gain or Weight Loss During the Double-Blind Treatment Period (Safety Sample)

CT-13.2 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in Waist Circumference (cm) (Safety Sample)

CT-13.3 Summary of Mean Change from Baseline of the Double-Blind Treatment Period to the Double-Blind Treatment Period by Study Day in BMI (kg/m2) (Safety Sample)

CT-14.1.1 Columbia-Suicide Severity Rating Scale(C-SSRS) During the Double-Blind Treatment Period, Suicidality (Safety Sample)

CT-14.1.2 Columbia-Suicide Severity Rating Scale(C-SSRS) During the Double-Blind Treatment Period, Suicidal Behavior by Type (Safety Sample)

CT-14.1.3 Columbia-Suicide Severity Rating Scale(C-SSRS) During the Double-Blind Treatment Period, Suicidal Ideation by Type (Safety Sample)

CT-14.1.4 Columbia-Suicide Severity Rating Scale(C-SSRS) During the Double-Blind Treatment Period, Treatment Emergent Suicidal Behavior and Ideation (Safety Sample)

CT-14.1.5 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Suicidal Ideation During the Double-Blind Treatment Period (Safety Sample)

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CT-14.1.6 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Suicidal Behavior During the Double-Blind Treatment Period (Safety Sample)

CT-14.1.7 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Serious Suicidal Ideation During the Double-Blind Treatment Period (Safety Sample)

CT-14.1.8 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Worsening Suicidal Ideation During the Double-Blind Treatment Period (Safety Sample)

CT-14.2.1 Columbia-Suicide Severity Rating Scale (C-SSRS) During the Single-Blind Placebo Run-in Period, Suicidality (Safety Sample)

CT-14.2.2 Columbia-Suicide Severity Rating Scale (C-SSRS) During the Single-Blind Placebo Run-in Period, Suicidal Behavior by Type (Safety Sample)

CT-14.2.3 Columbia-Suicide Severity Rating Scale (C-SSRS) During the Single-Blind Placebo Run-in Period, Suicidal Ideation by Type (Safety Sample)

CT-14.2.4 Columbia-Suicide Severity Rating Scale (C-SSRS) During the Single-Blind Placebo Run-in Period, Treatment Emergent Suicidal Behavior and Ideation (Safety Sample)

CT-14.2.5 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Suicidal Ideation During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-14.2.6 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Suicidal Behavior During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-14.2.7 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Treatment Emergent Serious Suicidal Ideation During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-14.2.8 Columbia-Suicide Severity Rating Scale (C-SSRS) – Listing of Worsening Suicidal Ideation During the Single-Blind Placebo Run-in Period (Safety Sample)

CT-15 Summary of Mean Study Medication Withdrawal Questionnaire (SMWQ) Total Score During the Double-Blind Treatment Period and Follow-up Period by Study Day (Safety Sample)

CT-16 Summary of Medication Handling Irregularity (Safety Sample)

CT-17.1 Summary of ESAMs Reported as Abuse Potential AEs During the Double-Blind Treatment Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-17.2 Summary of Non-Adverse Events Reported as Findings (ESAM) During the Double-Blind Treatment Period (Safety Sample)

CT-17.3 Summary of ESAMs Reported as Abuse Potential AEs During the Single-Blind Placebo Run-in Period by System Organ Class and MedDRA Preferred Term (Safety Sample)

CT-17.4 Summary of Non-Adverse Events Reported as Findings (ESAM) During the Single-Blind Placebo Run-in Period (Safety Sample)

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STAT-1.1
Adjusted Mean Change from Baseline in AISRS Line Items at Day 42 - MMRM
(Efficacy Sample)

AISRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
MAKE CARELESS MISTAKES	147	2.23	-0.61	147	2.17	-0.61	144	2.27	-0.32	EB-1020 200mg VS PLACEBO	-0.29	0.0080	-0.31
										EB-1020 400mg VS PLACEBO	-0.29	0.0064	-0.32
FIDGET OR SQUIRM WITH YOUR HANDS OR FEET	147	2.37	-0.49	147	2.33	-0.50	144	2.28	-0.23	EB-1020 200mg VS PLACEBO	-0.26	0.0120	-0.30
										EB-1020 400mg VS PLACEBO	-0.27	0.0084	-0.31
DIFFICULTY KEEPING YOUR ATTENTION	147	2.74	-0.76	147	2.67	-0.69	144	2.58	-0.40	EB-1020 200mg VS PLACEBO	-0.36	0.0014	-0.38
										EB-1020 400mg VS PLACEBO	-0.28	0.0094	-0.31
LEAVE YOUR SEAT	147	1.77	-0.56	147	1.79	-0.62	144	1.78	-0.46	EB-1020 200mg VS PLACEBO	-0.10	0.3832	-0.10
										EB-1020 400mg VS PLACEBO	-0.16	0.1456	-0.17
DIFFICULTY CONCENTRATING ON	147	2.37	-0.80	147	2.42	-0.60	144	2.41	-0.48	EB-1020 200mg VS PLACEBO	-0.32	0.0033	-0.35

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itema.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

STAT-1.1
Adjusted Mean Change from Baseline in AISRS Line Items at Day 42 - MMRM
(Efficacy Sample)

AISRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
DIFFICULTY CONCENTRATING ON										EB-1020 400mg VS PLACEBO	-0.12	0.2531	-0.13
FEEL RESTLESS OR FIDGETY	147	2.18	-0.47	147	2.20	-0.54	144	2.10	-0.36	EB-1020 200mg VS PLACEBO	-0.10	0.3769	-0.10
										EB-1020 400mg VS PLACEBO	-0.18	0.1134	-0.19
TROUBLE WRAPPING UP THE FINAL DETAILS	147	2.58	-0.69	147	2.52	-0.54	144	2.51	-0.35	EB-1020 200mg VS PLACEBO	-0.34	0.0040	-0.34
										EB-1020 400mg VS PLACEBO	-0.19	0.1020	-0.19
DIFFICULTY UNWINDING AND RELAXING	147	1.84	-0.47	147	1.96	-0.40	144	1.86	-0.39	EB-1020 200mg VS PLACEBO	-0.08	0.4738	-0.08
										EB-1020 400mg VS PLACEBO	-0.02	0.8874	-0.02
DIFFICULTY GETTING THINGS IN ORDER	147	2.50	-0.60	147	2.49	-0.64	144	2.47	-0.38	EB-1020 200mg VS PLACEBO	-0.21	0.0691	-0.21
										EB-1020 400mg VS PLACEBO	-0.26	0.0256	-0.26

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itema.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

STAT-1.1
Adjusted Mean Change from Baseline in AISRS Line Items at Day 42 - MMRM
(Efficacy Sample)

AISRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
OVERLY ACTIVE AND COMPELLED TO DO THINGS	147	2.05	-0.55	147	2.08	-0.55	144	1.93	-0.38	EB-1020 200mg VS PLACEBO	-0.17	0.1608	-0.16
										EB-1020 400mg VS PLACEBO	-0.17	0.1541	-0.17
AVOID OR DELAY GETTING STARTED	147	2.63	-0.71	147	2.52	-0.55	144	2.65	-0.45	EB-1020 200mg VS PLACEBO	-0.26	0.0348	-0.25
										EB-1020 400mg VS PLACEBO	-0.10	0.3848	-0.10
TALKING TOO MUCH	147	1.89	-0.62	147	1.75	-0.50	144	1.80	-0.34	EB-1020 200mg VS PLACEBO	-0.27	0.0148	-0.29
										EB-1020 400mg VS PLACEBO	-0.15	0.1649	-0.16
MISPLACE OR HAVE DIFFICULTY FINDING	147	2.23	-0.54	147	2.16	-0.49	144	2.35	-0.47	EB-1020 200mg VS PLACEBO	-0.07	0.5480	-0.07
										EB-1020 400mg VS PLACEBO	-0.02	0.8648	-0.02
FINISHING THE SENTENCES OF THE PEOPLE	147	1.89	-0.64	147	1.93	-0.65	144	2.00	-0.53	EB-1020 200mg VS PLACEBO	-0.11	0.3294	-0.11

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itema.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 4 OF 5
PROTOCOL 405-201-00013

STAT-1.1
Adjusted Mean Change from Baseline in AISRS Line Items at Day 42 - MMRM
(Efficacy Sample)

AISRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
FINISHING THE SENTENCES OF THE PEOPLE										EB-1020 400mg VS PLACEBO	-0.12	0.2683	-0.13
BEING DISTRACTED BY ACTIVITY OR NOISE	147	2.59	-0.56	147	2.58	-0.55	144	2.59	-0.30	EB-1020 200mg VS PLACEBO	-0.26	0.0229	-0.27
										EB-1020 400mg VS PLACEBO	-0.24	0.0311	-0.25
DIFFICULTY WAITING YOUR TURN	147	1.91	-0.39	147	1.99	-0.55	144	1.88	-0.39	EB-1020 200mg VS PLACEBO	-0.01	0.9533	-0.01
										EB-1020 400mg VS PLACEBO	-0.16	0.1284	-0.18
PROBLEMS REMEMBERING	147	2.13	-0.54	147	2.18	-0.77	144	2.26	-0.63	EB-1020 200mg VS PLACEBO	0.09	0.4350	0.09
										EB-1020 400mg VS PLACEBO	-0.14	0.2301	-0.14
INTERRUPT OTHERS WHEN THEY ARE BUSY	147	1.69	-0.62	147	1.82	-0.58	144	1.80	-0.54	EB-1020 200mg VS PLACEBO	-0.08	0.4580	-0.09
										EB-1020 400mg VS PLACEBO	-0.04	0.7183	-0.04

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itema.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 5 OF 5
PROTOCOL 405-201-00013

STAT-1.1
Adjusted Mean Change from Baseline in AISRS Line Items at Day 42 - MMRM
(Efficacy Sample)

AISRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
AISRS TOTAL SCORE (DERIVED)	147	39.60	-10.1	147	39.56	-9.73	144	39.53	-6.98	EB-1020 200mg VS PLACEBO	-3.15	0.0193	-0.28
										EB-1020 400mg VS PLACEBO	-2.74	0.0392	-0.24

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itema.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 1 OF 5
PROTOCOL 405-201-00013

STAT-1.2
Adjusted Mean Change from Baseline in ASRS Line Items at Day 42 - MMRM
(Efficacy Sample)

ASRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
ASRS-TROUBLE TO WRAP DETAILS OF PROJECT	118	3.10	-0.55	127	3.05	-0.57	131	2.97	-0.26	EB-1020 200mg VS PLACEBO	-0.29	0.0210	-0.29
										EB-1020 400mg VS PLACEBO	-0.31	0.0129	-0.31
ASRS-DIFFICULTY GETTING THINGS IN ORDER	118	3.25	-0.59	127	3.08	-0.66	131	3.03	-0.38	EB-1020 200mg VS PLACEBO	-0.22	0.0855	-0.22
										EB-1020 400mg VS PLACEBO	-0.28	0.0196	-0.29
ASRS-PROBLEM REMEMBERING APPTS/OBLIGATNS	118	2.86	-0.62	127	2.80	-0.78	131	2.79	-0.41	EB-1020 200mg VS PLACEBO	-0.21	0.1187	-0.20
										EB-1020 400mg VS PLACEBO	-0.37	0.0050	-0.35
ASRS-AVOID/DELAY GETTNG STARTD ON THGHTS	118	3.36	-0.66	127	3.31	-0.66	131	3.31	-0.36	EB-1020 200mg VS PLACEBO	-0.30	0.0188	-0.30
										EB-1020 400mg VS PLACEBO	-0.30	0.0159	-0.30

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itemb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

STAT-1.2
Adjusted Mean Change from Baseline in ASRS Line Items at Day 42 - MMRM
(Efficacy Sample)

ASRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
ASRS-FIDGET/SQUIRM WITH HANDS/FEET	118	3.11	-0.56	127	3.18	-0.56	131	3.10	-0.31	EB-1020 200mg VS PLACEBO	-0.26	0.0490	-0.25
										EB-1020 400mg VS PLACEBO	-0.25	0.0497	-0.25
ASRS-FEEL OVERLY ACTIVE TO DO THINGS	118	2.58	-0.56	127	2.76	-0.72	131	2.66	-0.35	EB-1020 200mg VS PLACEBO	-0.20	0.1266	-0.19
										EB-1020 400mg VS PLACEBO	-0.37	0.0047	-0.35
ASRS-MAKE CARELESS MISTAKES	118	2.98	-0.65	127	2.72	-0.67	131	2.97	-0.38	EB-1020 200mg VS PLACEBO	-0.26	0.0357	-0.27
										EB-1020 400mg VS PLACEBO	-0.29	0.0216	-0.29
ASRS-DIFFICULTY KEEPING ATTENTION	118	3.45	-0.61	127	3.36	-0.66	131	3.32	-0.37	EB-1020 200mg VS PLACEBO	-0.24	0.0717	-0.23
										EB-1020 400mg VS PLACEBO	-0.29	0.0235	-0.28
ASRS-DIFFICULTY KEEPING CONCENTRATION	118	3.02	-0.80	127	3.09	-0.80	131	3.12	-0.47	EB-1020 200mg VS PLACEBO	-0.33	0.0129	-0.32

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itemb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 3 OF 5
PROTOCOL 405-201-00013

STAT-1.2
Adjusted Mean Change from Baseline in ASRS Line Items at Day 42 - MMRM
(Efficacy Sample)

ASRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
ASRS-DIFFICULTY KEEPING CONCENTRATION										EB-1020 400mg VS PLACEBO	-0.33	0.0107	-0.32
ASRS-MISPLACE/DIFFICULTY FINDING THINGS	118	3.05	-0.63	127	2.98	-0.69	131	3.07	-0.50	EB-1020 200mg VS PLACEBO	-0.13	0.3334	-0.12
										EB-1020 400mg VS PLACEBO	-0.19	0.1470	-0.18
ASRS-DISTRACTED BY ACTIVITY OR NOISE	118	3.25	-0.63	127	3.28	-0.61	131	3.30	-0.28	EB-1020 200mg VS PLACEBO	-0.35	0.0130	-0.32
										EB-1020 400mg VS PLACEBO	-0.32	0.0184	-0.29
ASRS-LEAVE SEAT IN MEETNGS/ORDR SITUATNS	118	2.26	-0.59	127	2.14	-0.70	131	2.02	-0.32	EB-1020 200mg VS PLACEBO	-0.27	0.0307	-0.28
										EB-1020 400mg VS PLACEBO	-0.39	0.0015	-0.40
ASRS-FEELING RESTLESS OR FIDGETY	118	2.97	-0.56	127	3.02	-0.68	131	2.98	-0.34	EB-1020 200mg VS PLACEBO	-0.22	0.0909	-0.22
										EB-1020 400mg VS PLACEBO	-0.34	0.0093	-0.33

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itemb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 4 OF 5
PROTOCOL 405-201-00013

STAT-1.2
Adjusted Mean Change from Baseline in ASRS Line Items at Day 42 - MMRM
(Efficacy Sample)

ASRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
ASRS-DIFF UNWINDING AND RELAXING	118	2.60	-0.55	127	2.91	-0.55	131	2.76	-0.32	EB-1020 200mg VS PLACEBO	-0.23	0.0946	-0.21
										EB-1020 400mg VS PLACEBO	-0.23	0.0835	-0.22
ASRS-FIND YOURSELF TALKING TOO MUCH	118	2.64	-0.70	127	2.59	-0.68	131	2.66	-0.38	EB-1020 200mg VS PLACEBO	-0.32	0.0170	-0.30
										EB-1020 400mg VS PLACEBO	-0.29	0.0251	-0.28
ASRS-FINISH SENTENCES OF PEOPLE	118	2.70	-0.78	127	2.66	-0.78	131	2.73	-0.50	EB-1020 200mg VS PLACEBO	-0.28	0.0417	-0.26
										EB-1020 400mg VS PLACEBO	-0.28	0.0405	-0.26
ASRS-DIFFCULTY WAITING YOUR TURN	118	2.57	-0.60	127	2.65	-0.82	131	2.44	-0.40	EB-1020 200mg VS PLACEBO	-0.20	0.1576	-0.18
										EB-1020 400mg VS PLACEBO	-0.42	0.0028	-0.38
ASRS-INTERRUPT OTHERS WHEN THEY ARE BUSY	118	2.46	-0.82	127	2.48	-0.81	131	2.46	-0.62	EB-1020 200mg VS PLACEBO	-0.20	0.1216	-0.20

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itemb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 5 OF 5
PROTOCOL 405-201-00013

STAT-1.2
Adjusted Mean Change from Baseline in ASRS Line Items at Day 42 - MMRM
(Efficacy Sample)

ASRS Line Items	CTN SR 200MG N	CTN SR 200MG MEAN Base	CTN SR 200MG LSMean Change[1]	CTN SR 400MG N	CTN SR 400MG MEAN Base	CTN SR 400MG LSMean Change[1]	PLACEBO N	PLACEBO MEAN Base	PLACEBO LSMean Change[1]	TREATMENT COMPARISON	ESTIMATED TREATMENT EFFECT [1]	P-VALUE[1]	COHEN's D EFFECT SIZE
ASRS-INTERRUPT OTHERS WHEN THEY ARE BUSY										EB-1020 400mg VS PLACEBO	-0.19	0.1325	-0.19
ASRS TOTAL SCORE OF 18 ITEMS (DERIVED)	118	52.22	-11.3	127	52.06	-12.0	131	51.67	-6.70	EB-1020 200mg VS PLACEBO	-4.60	0.0062	-0.35
										EB-1020 400mg VS PLACEBO	-5.28	0.0014	-0.40

[1] MIXED MODEL REPEATED MEASURES METHOD WITH MODEL TERMS: TREATMENT, (POOLED) STUDY CENTER, VISIT, TREATMENT BY VISIT AND BASELINE BY VISIT INTERACTIO

FILE: aisrs_itemb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/aisrs_item.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

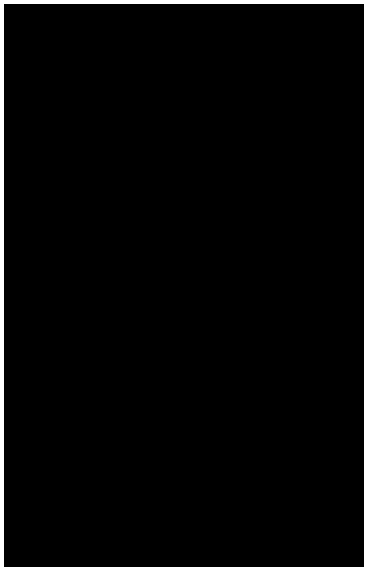
Class Level Information

Class	Levels	Values
SUBJID	438	[redacted]

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

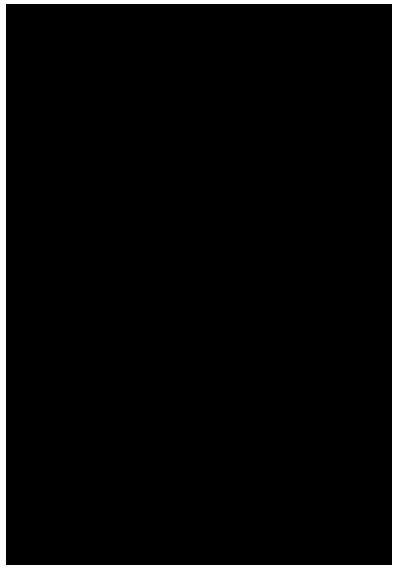
The Mixed Procedure



STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

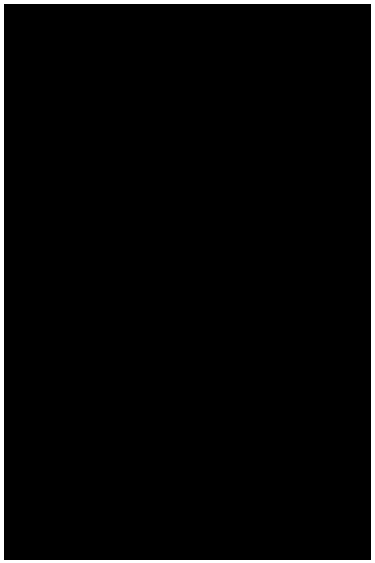
The Mixed Procedure



STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

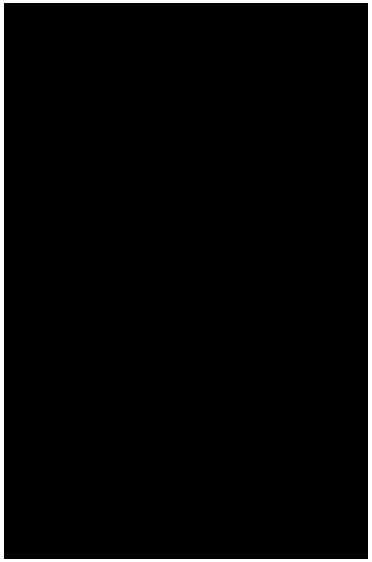
The Mixed Procedure



STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

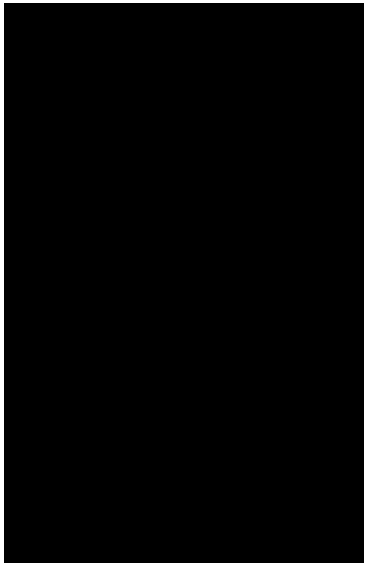
The Mixed Procedure



STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Class Level Information

Class	Levels	Values
SEX	2	F M

Dimensions

Covariance Parameters	21
Columns in X	128
Columns in Z	0
Subjects	438
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2292
Number of Observations Used	2292
Number of Observations Not Used	0

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16471.93771301	
1	2	14206.06433817	0.00014910
2	1	14205.26506836	0.00000141
3	1	14205.25788280	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	52.3976
UN(2,1)	SUBJID	40.2284
UN(2,2)	SUBJID	72.6755
UN(3,1)	SUBJID	38.1964
UN(3,2)	SUBJID	62.4528
UN(3,3)	SUBJID	81.8612
UN(4,1)	SUBJID	37.6894
UN(4,2)	SUBJID	63.0768

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(4,3)	SUBJID	77.7325
UN(4,4)	SUBJID	105.92
UN(5,1)	SUBJID	38.4856
UN(5,2)	SUBJID	63.7432
UN(5,3)	SUBJID	81.2609
UN(5,4)	SUBJID	96.6536
UN(5,5)	SUBJID	111.49
UN(6,1)	SUBJID	38.7755
UN(6,2)	SUBJID	64.7203
UN(6,3)	SUBJID	79.0855
UN(6,4)	SUBJID	96.9247
UN(6,5)	SUBJID	99.9728
UN(6,6)	SUBJID	118.03

Fit Statistics

-2 Res Log Likelihood	14205.3
AIC (Smaller is Better)	14247.3
AICC (Smaller is Better)	14247.7
BIC (Smaller is Better)	14333.0

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2266.68	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
POOLCNTR	37	393	2.24	<.0001
AVISITN	5	377	2.31	0.0434
TRTPN	2	396	3.03	0.0495
AVISITN*TRTPN	10	558	1.63	0.0954
SEX	1	412	0.02	0.8821
AVISITN*SEX	5	376	1.58	0.1649
TRTPN*SEX	2	408	0.17	0.8404
AVISITN*TRTPN*SEX	10	558	0.54	0.8603
BASE*AVISITN	6	402	2.38	0.0287

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
Intercept					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
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POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.1 FINAL

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
AVISITN			7		
AVISITN			14		
AVISITN			21		
AVISITN			28		
AVISITN			35		
AVISITN			42		
TRTPN				1	
TRTPN				2	
TRTPN				3	
AVISITN*TRTPN			7	1	
AVISITN*TRTPN			7	2	
AVISITN*TRTPN			7	3	
AVISITN*TRTPN			14	1	
AVISITN*TRTPN			14	2	
AVISITN*TRTPN			14	3	
AVISITN*TRTPN			21	1	
AVISITN*TRTPN			21	2	
AVISITN*TRTPN			21	3	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	2	
AVISITN*TRTPN			28	3	
AVISITN*TRTPN			35	1	
AVISITN*TRTPN			35	2	
AVISITN*TRTPN			35	3	
AVISITN*TRTPN			42	1	
AVISITN*TRTPN			42	2	
AVISITN*TRTPN			42	3	
SEX		F			
SEX		M			
AVISITN*SEX		F	7		
AVISITN*SEX		M	7		
AVISITN*SEX		F	14		
AVISITN*SEX		M	14		
AVISITN*SEX		F	21		
AVISITN*SEX		M	21		
AVISITN*SEX		F	28		
AVISITN*SEX		M	28		

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*SEX		F	35		
AVISITN*SEX		M	35		
AVISITN*SEX		F	42		
AVISITN*SEX		M	42		
TRTPN*SEX		F		1	1
TRTPN*SEX		M		1	-1
TRTPN*SEX		F		2	
TRTPN*SEX		M		2	
TRTPN*SEX		F		3	-1
TRTPN*SEX		M		3	1
AVISITN*TRTPN*SEX		F	7	1	
AVISITN*TRTPN*SEX		M	7	1	
AVISITN*TRTPN*SEX		F	7	2	
AVISITN*TRTPN*SEX		M	7	2	
AVISITN*TRTPN*SEX		F	7	3	
AVISITN*TRTPN*SEX		M	7	3	
AVISITN*TRTPN*SEX		F	14	1	
AVISITN*TRTPN*SEX		M	14	1	
AVISITN*TRTPN*SEX		F	14	2	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN*SEX		M	14	2	
AVISITN*TRTPN*SEX		F	14	3	
AVISITN*TRTPN*SEX		M	14	3	
AVISITN*TRTPN*SEX		F	21	1	
AVISITN*TRTPN*SEX		M	21	1	
AVISITN*TRTPN*SEX		F	21	2	
AVISITN*TRTPN*SEX		M	21	2	
AVISITN*TRTPN*SEX		F	21	3	
AVISITN*TRTPN*SEX		M	21	3	
AVISITN*TRTPN*SEX		F	28	1	
AVISITN*TRTPN*SEX		M	28	1	
AVISITN*TRTPN*SEX		F	28	2	
AVISITN*TRTPN*SEX		M	28	2	
AVISITN*TRTPN*SEX		F	28	3	
AVISITN*TRTPN*SEX		M	28	3	
AVISITN*TRTPN*SEX		F	35	1	
AVISITN*TRTPN*SEX		M	35	1	
AVISITN*TRTPN*SEX		F	35	2	
AVISITN*TRTPN*SEX		M	35	2	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN*SEX		F	35	3	
AVISITN*TRTPN*SEX		M	35	3	
AVISITN*TRTPN*SEX		F	42	1	1
AVISITN*TRTPN*SEX		M	42	1	-1
AVISITN*TRTPN*SEX		F	42	2	
AVISITN*TRTPN*SEX		M	42	2	
AVISITN*TRTPN*SEX		F	42	3	-1
AVISITN*TRTPN*SEX		M	42	3	1
BASE*AVISITN			7		
BASE*AVISITN			14		
BASE*AVISITN			21		
BASE*AVISITN			28		
BASE*AVISITN			35		
BASE*AVISITN			42		

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
Intercept					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.1 FINAL

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
AVISITN			7		
AVISITN			14		
AVISITN			21		
AVISITN			28		
AVISITN			35		
AVISITN			42		
TRTPN				1	
TRTPN				2	
TRTPN				3	
AVISITN*TRTPN			7	1	
AVISITN*TRTPN			7	2	
AVISITN*TRTPN			7	3	
AVISITN*TRTPN			14	1	
AVISITN*TRTPN			14	2	
AVISITN*TRTPN			14	3	
AVISITN*TRTPN			21	1	
AVISITN*TRTPN			21	2	
AVISITN*TRTPN			21	3	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	2	
AVISITN*TRTPN			28	3	
AVISITN*TRTPN			35	1	
AVISITN*TRTPN			35	2	
AVISITN*TRTPN			35	3	
AVISITN*TRTPN			42	1	
AVISITN*TRTPN			42	2	
AVISITN*TRTPN			42	3	
SEX		F			
SEX		M			
AVISITN*SEX		F	7		
AVISITN*SEX		M	7		
AVISITN*SEX		F	14		
AVISITN*SEX		M	14		
AVISITN*SEX		F	21		
AVISITN*SEX		M	21		
AVISITN*SEX		F	28		
AVISITN*SEX		M	28		

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*SEX		F	35		
AVISITN*SEX		M	35		
AVISITN*SEX		F	42		
AVISITN*SEX		M	42		
TRTPN*SEX		F		1	
TRTPN*SEX		M		1	
TRTPN*SEX		F		2	1
TRTPN*SEX		M		2	-1
TRTPN*SEX		F		3	-1
TRTPN*SEX		M		3	1
AVISITN*TRTPN*SEX		F	7	1	
AVISITN*TRTPN*SEX		M	7	1	
AVISITN*TRTPN*SEX		F	7	2	
AVISITN*TRTPN*SEX		M	7	2	
AVISITN*TRTPN*SEX		F	7	3	
AVISITN*TRTPN*SEX		M	7	3	
AVISITN*TRTPN*SEX		F	14	1	
AVISITN*TRTPN*SEX		M	14	1	
AVISITN*TRTPN*SEX		F	14	2	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN*SEX		M	14	2	
AVISITN*TRTPN*SEX		F	14	3	
AVISITN*TRTPN*SEX		M	14	3	
AVISITN*TRTPN*SEX		F	21	1	
AVISITN*TRTPN*SEX		M	21	1	
AVISITN*TRTPN*SEX		F	21	2	
AVISITN*TRTPN*SEX		M	21	2	
AVISITN*TRTPN*SEX		F	21	3	
AVISITN*TRTPN*SEX		M	21	3	
AVISITN*TRTPN*SEX		F	28	1	
AVISITN*TRTPN*SEX		M	28	1	
AVISITN*TRTPN*SEX		F	28	2	
AVISITN*TRTPN*SEX		M	28	2	
AVISITN*TRTPN*SEX		F	28	3	
AVISITN*TRTPN*SEX		M	28	3	
AVISITN*TRTPN*SEX		F	35	1	
AVISITN*TRTPN*SEX		M	35	1	
AVISITN*TRTPN*SEX		F	35	2	
AVISITN*TRTPN*SEX		M	35	2	

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY SEX AT DAY 42

Effect	Pooled Center Number	Sex	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN*SEX		F	35	3	
AVISITN*TRTPN*SEX		M	35	3	
AVISITN*TRTPN*SEX		F	42	1	
AVISITN*TRTPN*SEX		M	42	1	
AVISITN*TRTPN*SEX		F	42	2	1
AVISITN*TRTPN*SEX		M	42	2	-1
AVISITN*TRTPN*SEX		F	42	3	-1
AVISITN*TRTPN*SEX		M	42	3	1
BASE*AVISITN			7		
BASE*AVISITN			14		
BASE*AVISITN			21		
BASE*AVISITN			28		
BASE*AVISITN			35		
BASE*AVISITN			42		

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|
1 vs. 3 BY SEX AT DAY 42	0.008634	2.7164	405	0.00	0.9975
2 vs. 3 BY SEX AT DAY 42	1.0223	2.7042	403	0.38	0.7056

Least Squares Means

Effect	Sex	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN*SEX	F	7	1	-5.5125	0.9145	398	-6.03	<.0001	0.05	-7.3104	-3.7146
AVISITN*TRTPN*SEX	M	7	1	-5.4466	0.9030	402	-6.03	<.0001	0.05	-7.2219	-3.6713
AVISITN*TRTPN*SEX	F	7	2	-3.7780	0.9336	400	-4.05	<.0001	0.05	-5.6133	-1.9427
AVISITN*TRTPN*SEX	M	7	2	-4.3169	0.9075	402	-4.76	<.0001	0.05	-6.1010	-2.5329
AVISITN*TRTPN*SEX	F	7	3	-5.2355	0.9157	396	-5.72	<.0001	0.05	-7.0357	-3.4352
AVISITN*TRTPN*SEX	M	7	3	-3.0663	0.9328	400	-3.29	0.0011	0.05	-4.9001	-1.2324
AVISITN*TRTPN*SEX	F	14	1	-7.9530	1.0866	431	-7.32	<.0001	0.05	-10.0887	-5.8173
AVISITN*TRTPN*SEX	M	14	1	-6.9443	1.0453	415	-6.64	<.0001	0.05	-8.9991	-4.8895
AVISITN*TRTPN*SEX	F	14	2	-6.6749	1.0980	431	-6.08	<.0001	0.05	-8.8330	-4.5169
AVISITN*TRTPN*SEX	M	14	2	-6.7586	1.0477	416	-6.45	<.0001	0.05	-8.8180	-4.6993

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	Sex	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN*SEX	F	14	3	-7.0864	1.0693	422	-6.63	<.0001	0.05	-9.1883	-4.9846
AVISITN*TRTPN*SEX	M	14	3	-5.8234	1.0854	422	-5.37	<.0001	0.05	-7.9569	-3.6899
AVISITN*TRTPN*SEX	F	21	1	-8.8044	1.1479	418	-7.67	<.0001	0.05	-11.0608	-6.5480
AVISITN*TRTPN*SEX	M	21	1	-8.1444	1.1330	432	-7.19	<.0001	0.05	-10.3713	-5.9176
AVISITN*TRTPN*SEX	F	21	2	-8.2616	1.1716	434	-7.05	<.0001	0.05	-10.5644	-5.9589
AVISITN*TRTPN*SEX	M	21	2	-8.3214	1.1086	410	-7.51	<.0001	0.05	-10.5007	-6.1422
AVISITN*TRTPN*SEX	F	21	3	-6.5243	1.1292	415	-5.78	<.0001	0.05	-8.7439	-4.3047
AVISITN*TRTPN*SEX	M	21	3	-6.5280	1.1518	416	-5.67	<.0001	0.05	-8.7920	-4.2640
AVISITN*TRTPN*SEX	F	28	1	-9.7129	1.3221	429	-7.35	<.0001	0.05	-12.3114	-7.1143
AVISITN*TRTPN*SEX	M	28	1	-9.5818	1.2976	433	-7.38	<.0001	0.05	-12.1321	-7.0315
AVISITN*TRTPN*SEX	F	28	2	-8.5617	1.3340	435	-6.42	<.0001	0.05	-11.1835	-5.9398
AVISITN*TRTPN*SEX	M	28	2	-10.5997	1.2679	423	-8.36	<.0001	0.05	-13.0919	-8.1075
AVISITN*TRTPN*SEX	F	28	3	-5.7966	1.2745	413	-4.55	<.0001	0.05	-8.3020	-3.2913
AVISITN*TRTPN*SEX	M	28	3	-6.8225	1.3154	423	-5.19	<.0001	0.05	-9.4081	-4.2369
AVISITN*TRTPN*SEX	F	35	1	-10.3738	1.3557	421	-7.65	<.0001	0.05	-13.0386	-7.7090
AVISITN*TRTPN*SEX	M	35	1	-10.1739	1.3368	429	-7.61	<.0001	0.05	-12.8014	-7.5463
AVISITN*TRTPN*SEX	F	35	2	-10.6335	1.3813	440	-7.70	<.0001	0.05	-13.3484	-7.9187
AVISITN*TRTPN*SEX	M	35	2	-10.7772	1.3026	417	-8.27	<.0001	0.05	-13.3378	-8.2166
AVISITN*TRTPN*SEX	F	35	3	-7.3509	1.3131	412	-5.60	<.0001	0.05	-9.9321	-4.7697

STAT-3.1
MMRM Output for Test on Treatment by Sex Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	Sex	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN*SEX	M	35	3	-7.0325	1.3507	417	-5.21	<.0001	0.05	-9.6875	-4.3774
AVISITN*TRTPN*SEX	F	42	1	-10.3674	1.4025	421	-7.39	<.0001	0.05	-13.1242	-7.6106
AVISITN*TRTPN*SEX	M	42	1	-9.9078	1.3872	433	-7.14	<.0001	0.05	-12.6343	-7.1814
AVISITN*TRTPN*SEX	F	42	2	-9.4500	1.4201	434	-6.65	<.0001	0.05	-12.2411	-6.6589
AVISITN*TRTPN*SEX	M	42	2	-10.0041	1.3380	410	-7.48	<.0001	0.05	-12.6344	-7.3738
AVISITN*TRTPN*SEX	F	42	3	-7.2141	1.3547	411	-5.33	<.0001	0.05	-9.8771	-4.5510
AVISITN*TRTPN*SEX	M	42	3	-6.7459	1.3983	419	-4.82	<.0001	0.05	-9.4945	-3.9972

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

FILE: stat2b.lis, RUN: 18JUN2020 10:01; ANALYSIS DATASET CREATED: 11JUN2020 07:28
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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.2 FINAL

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

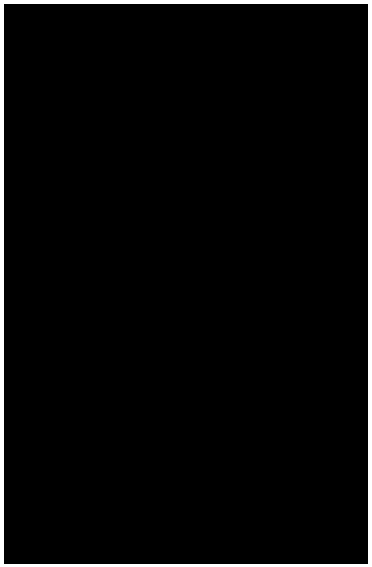
Class Level Information

Class	Levels	Values
SUBJID	438	[redacted]

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

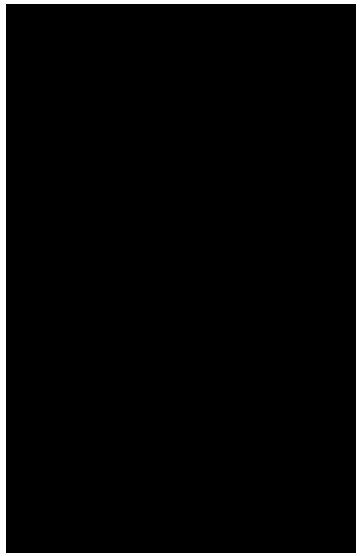
The Mixed Procedure



STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



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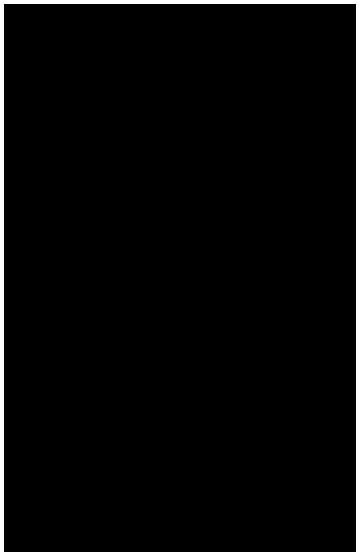
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.2 FINAL

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

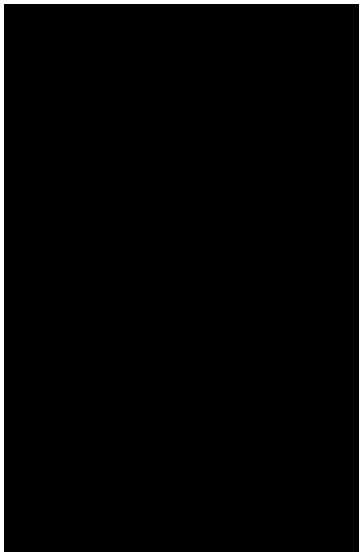
The Mixed Procedure



STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

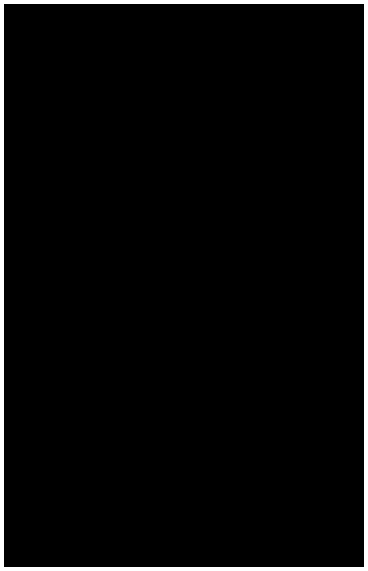
The Mixed Procedure



STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Class Level Information

Class	Levels	Values
RACEGRP	2	All Other Races White

Dimensions

Covariance Parameters	21
Columns in X	128
Columns in Z	0
Subjects	438
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2292
Number of Observations Used	2292
Number of Observations Not Used	0

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16457.56446856	
1	2	14194.15343914	0.00015243
2	1	14193.34064068	0.00000121
3	1	14193.33447925	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	52.6274
UN(2,1)	SUBJID	40.2457
UN(2,2)	SUBJID	72.4424
UN(3,1)	SUBJID	37.9044
UN(3,2)	SUBJID	62.1116
UN(3,3)	SUBJID	81.4367
UN(4,1)	SUBJID	37.1824
UN(4,2)	SUBJID	62.6074

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(4,3)	SUBJID	77.2494
UN(4,4)	SUBJID	105.45
UN(5,1)	SUBJID	38.0335
UN(5,2)	SUBJID	63.1832
UN(5,3)	SUBJID	80.6593
UN(5,4)	SUBJID	95.9188
UN(5,5)	SUBJID	110.56
UN(6,1)	SUBJID	38.5893
UN(6,2)	SUBJID	64.3249
UN(6,3)	SUBJID	78.5308
UN(6,4)	SUBJID	96.2386
UN(6,5)	SUBJID	99.4627
UN(6,6)	SUBJID	117.27

Fit Statistics

-2 Res Log Likelihood	14193.3
AIC (Smaller is Better)	14235.3
AICC (Smaller is Better)	14235.8
BIC (Smaller is Better)	14321.1

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2264.23	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
POOLCNTR	37	393	2.25	<.0001
AVISITN	5	377	1.96	0.0837
TRTPN	2	402	2.69	0.0690
AVISITN*TRTPN	10	559	1.68	0.0821
RACEGRP	1	415	1.14	0.2857
AVISITN*RACEGRP	5	376	1.25	0.2836
TRTPN*RACEGRP	2	410	0.44	0.6436
AVISIT*TRTPN*RACEGRP	10	559	1.01	0.4349
BASE*AVISITN	6	402	2.39	0.0280

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
Intercept	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
AVISITN			7		
AVISITN			14		
AVISITN			21		
AVISITN			28		
AVISITN			35		
AVISITN			42		
TRTPN				1	
TRTPN				2	
TRTPN				3	
AVISITN*TRTPN			7	1	
AVISITN*TRTPN			7	2	
AVISITN*TRTPN			7	3	
AVISITN*TRTPN			14	1	
AVISITN*TRTPN			14	2	
AVISITN*TRTPN			14	3	
AVISITN*TRTPN			21	1	
AVISITN*TRTPN			21	2	
AVISITN*TRTPN			21	3	

FILE: stat2b.lis, RUN: 18JUN2020 10:01; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat2.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.2 FINAL

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	2	
AVISITN*TRTPN			28	3	
AVISITN*TRTPN			35	1	
AVISITN*TRTPN			35	2	
AVISITN*TRTPN			35	3	
AVISITN*TRTPN			42	1	
AVISITN*TRTPN			42	2	
AVISITN*TRTPN			42	3	
RACEGRP		All Other Races			
RACEGRP		White			
AVISITN*RACEGRP		All Other Races	7		
AVISITN*RACEGRP		White	7		
AVISITN*RACEGRP		All Other Races	14		
AVISITN*RACEGRP		White	14		
AVISITN*RACEGRP		All Other Races	21		
AVISITN*RACEGRP		White	21		
AVISITN*RACEGRP		All Other Races	28		
AVISITN*RACEGRP		White	28		

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*RACEGRP		All Other Races	35		
AVISITN*RACEGRP		White	35		
AVISITN*RACEGRP		All Other Races	42		
AVISITN*RACEGRP		White	42		
TRTPN*RACEGRP		All Other Races		1	1
TRTPN*RACEGRP		White		1	-1
TRTPN*RACEGRP		All Other Races		2	
TRTPN*RACEGRP		White		2	
TRTPN*RACEGRP		All Other Races		3	-1
TRTPN*RACEGRP		White		3	1
AVISIT*TRTPN*RACEGRP		All Other Races	7	1	
AVISIT*TRTPN*RACEGRP		White	7	1	
AVISIT*TRTPN*RACEGRP		All Other Races	7	2	
AVISIT*TRTPN*RACEGRP		White	7	2	
AVISIT*TRTPN*RACEGRP		All Other Races	7	3	
AVISIT*TRTPN*RACEGRP		White	7	3	
AVISIT*TRTPN*RACEGRP		All Other Races	14	1	
AVISIT*TRTPN*RACEGRP		White	14	1	
AVISIT*TRTPN*RACEGRP		All Other Races	14	2	

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISIT*TRTPN*RACEGRP		White	14	2	
AVISIT*TRTPN*RACEGRP		All Other Races	14	3	
AVISIT*TRTPN*RACEGRP		White	14	3	
AVISIT*TRTPN*RACEGRP		All Other Races	21	1	
AVISIT*TRTPN*RACEGRP		White	21	1	
AVISIT*TRTPN*RACEGRP		All Other Races	21	2	
AVISIT*TRTPN*RACEGRP		White	21	2	
AVISIT*TRTPN*RACEGRP		All Other Races	21	3	
AVISIT*TRTPN*RACEGRP		White	21	3	
AVISIT*TRTPN*RACEGRP		All Other Races	28	1	
AVISIT*TRTPN*RACEGRP		White	28	1	
AVISIT*TRTPN*RACEGRP		All Other Races	28	2	
AVISIT*TRTPN*RACEGRP		White	28	2	
AVISIT*TRTPN*RACEGRP		All Other Races	28	3	
AVISIT*TRTPN*RACEGRP		White	28	3	
AVISIT*TRTPN*RACEGRP		All Other Races	35	1	
AVISIT*TRTPN*RACEGRP		White	35	1	
AVISIT*TRTPN*RACEGRP		All Other Races	35	2	
AVISIT*TRTPN*RACEGRP		White	35	2	

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISIT*TRTPN*RACEGRP		All Other Races	35	3	
AVISIT*TRTPN*RACEGRP		White	35	3	
AVISIT*TRTPN*RACEGRP		All Other Races	42	1	1
AVISIT*TRTPN*RACEGRP		White	42	1	-1
AVISIT*TRTPN*RACEGRP		All Other Races	42	2	
AVISIT*TRTPN*RACEGRP		White	42	2	
AVISIT*TRTPN*RACEGRP		All Other Races	42	3	-1
AVISIT*TRTPN*RACEGRP		White	42	3	1
BASE*AVISITN			7		
BASE*AVISITN			14		
BASE*AVISITN			21		
BASE*AVISITN			28		
BASE*AVISITN			35		
BASE*AVISITN			42		

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
Intercept					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
POOLCNTR	[redacted]				
AVISITN			7		
AVISITN			14		
AVISITN			21		
AVISITN			28		
AVISITN			35		
AVISITN			42		
TRTPN				1	
TRTPN				2	
TRTPN				3	
AVISITN*TRTPN			7	1	
AVISITN*TRTPN			7	2	
AVISITN*TRTPN			7	3	
AVISITN*TRTPN			14	1	
AVISITN*TRTPN			14	2	
AVISITN*TRTPN			14	3	
AVISITN*TRTPN			21	1	
AVISITN*TRTPN			21	2	
AVISITN*TRTPN			21	3	

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	2	
AVISITN*TRTPN			28	3	
AVISITN*TRTPN			35	1	
AVISITN*TRTPN			35	2	
AVISITN*TRTPN			35	3	
AVISITN*TRTPN			42	1	
AVISITN*TRTPN			42	2	
AVISITN*TRTPN			42	3	
RACEGRP		All Other Races			
RACEGRP		White			
AVISITN*RACEGRP		All Other Races	7		
AVISITN*RACEGRP		White	7		
AVISITN*RACEGRP		All Other Races	14		
AVISITN*RACEGRP		White	14		
AVISITN*RACEGRP		All Other Races	21		
AVISITN*RACEGRP		White	21		
AVISITN*RACEGRP		All Other Races	28		
AVISITN*RACEGRP		White	28		

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISITN*RACEGRP		All Other Races	35		
AVISITN*RACEGRP		White	35		
AVISITN*RACEGRP		All Other Races	42		
AVISITN*RACEGRP		White	42		
TRTPN*RACEGRP		All Other Races		1	
TRTPN*RACEGRP		White		1	
TRTPN*RACEGRP		All Other Races		2	1
TRTPN*RACEGRP		White		2	-1
TRTPN*RACEGRP		All Other Races		3	-1
TRTPN*RACEGRP		White		3	1
AVISIT*TRTPN*RACEGRP		All Other Races	7	1	
AVISIT*TRTPN*RACEGRP		White	7	1	
AVISIT*TRTPN*RACEGRP		All Other Races	7	2	
AVISIT*TRTPN*RACEGRP		White	7	2	
AVISIT*TRTPN*RACEGRP		All Other Races	7	3	
AVISIT*TRTPN*RACEGRP		White	7	3	
AVISIT*TRTPN*RACEGRP		All Other Races	14	1	
AVISIT*TRTPN*RACEGRP		White	14	1	
AVISIT*TRTPN*RACEGRP		All Other Races	14	2	

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISIT*TRTPN*RACEGRP		White	14	2	
AVISIT*TRTPN*RACEGRP		All Other Races	14	3	
AVISIT*TRTPN*RACEGRP		White	14	3	
AVISIT*TRTPN*RACEGRP		All Other Races	21	1	
AVISIT*TRTPN*RACEGRP		White	21	1	
AVISIT*TRTPN*RACEGRP		All Other Races	21	2	
AVISIT*TRTPN*RACEGRP		White	21	2	
AVISIT*TRTPN*RACEGRP		All Other Races	21	3	
AVISIT*TRTPN*RACEGRP		White	21	3	
AVISIT*TRTPN*RACEGRP		All Other Races	28	1	
AVISIT*TRTPN*RACEGRP		White	28	1	
AVISIT*TRTPN*RACEGRP		All Other Races	28	2	
AVISIT*TRTPN*RACEGRP		White	28	2	
AVISIT*TRTPN*RACEGRP		All Other Races	28	3	
AVISIT*TRTPN*RACEGRP		White	28	3	
AVISIT*TRTPN*RACEGRP		All Other Races	35	1	
AVISIT*TRTPN*RACEGRP		White	35	1	
AVISIT*TRTPN*RACEGRP		All Other Races	35	2	
AVISIT*TRTPN*RACEGRP		White	35	2	

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Coefficients for 2 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
AVISIT*TRTPN*RACEGRP		All Other Races	35	3	
AVISIT*TRTPN*RACEGRP		White	35	3	
AVISIT*TRTPN*RACEGRP		All Other Races	42	1	
AVISIT*TRTPN*RACEGRP		White	42	1	
AVISIT*TRTPN*RACEGRP		All Other Races	42	2	1
AVISIT*TRTPN*RACEGRP		White	42	2	-1
AVISIT*TRTPN*RACEGRP		All Other Races	42	3	-1
AVISIT*TRTPN*RACEGRP		White	42	3	1
BASE*AVISITN			7		
BASE*AVISITN			14		
BASE*AVISITN			21		
BASE*AVISITN			28		
BASE*AVISITN			35		
BASE*AVISITN			42		

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|
1 vs. 3 BY RACEGRP AT DAY 42	-4.2107	3.6531	413	-1.15	0.2497
2 vs. 3 BY RACEGRP AT DAY 42	-4.6414	3.5664	405	-1.30	0.1939

Least Squares Means

Effect	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISIT*TRTPN*RACEGRP	All Other Races	7	1	-5.4070	1.4741	402	-3.67	0.0003	0.05	-8.3049	-2.5092
AVISIT*TRTPN*RACEGRP	White	7	1	-5.5130	0.7191	401	-7.67	<.0001	0.05	-6.9267	-4.0993
AVISIT*TRTPN*RACEGRP	All Other Races	7	2	-5.5362	1.4286	409	-3.88	0.0001	0.05	-8.3446	-2.7278
AVISIT*TRTPN*RACEGRP	White	7	2	-3.6971	0.7401	399	-5.00	<.0001	0.05	-5.1521	-2.2421
AVISIT*TRTPN*RACEGRP	All Other Races	7	3	-4.4167	1.6472	402	-2.68	0.0076	0.05	-7.6548	-1.1786
AVISIT*TRTPN*RACEGRP	White	7	3	-4.1607	0.7267	399	-5.73	<.0001	0.05	-5.5893	-2.7320
AVISIT*TRTPN*RACEGRP	All Other Races	14	1	-9.1406	1.7282	425	-5.29	<.0001	0.05	-12.5375	-5.7437
AVISIT*TRTPN*RACEGRP	White	14	1	-7.0447	0.8377	421	-8.41	<.0001	0.05	-8.6913	-5.3981
AVISIT*TRTPN*RACEGRP	All Other Races	14	2	-7.7555	1.6612	425	-4.67	<.0001	0.05	-11.0208	-4.4903
AVISIT*TRTPN*RACEGRP	White	14	2	-6.4603	0.8573	427	-7.54	<.0001	0.05	-8.1453	-4.7753

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISIT*TRTPN*RACEGRP	All Other Races	14	3	-6.8926	1.8839	401	-3.66	0.0003	0.05	-10.5961	-3.1891
AVISIT*TRTPN*RACEGRP	White	14	3	-6.4045	0.8426	433	-7.60	<.0001	0.05	-8.0607	-4.7484
AVISIT*TRTPN*RACEGRP	All Other Races	21	1	-9.1324	1.8815	447	-4.85	<.0001	0.05	-12.8302	-5.4346
AVISIT*TRTPN*RACEGRP	White	21	1	-8.3083	0.8926	424	-9.31	<.0001	0.05	-10.0626	-6.5539
AVISIT*TRTPN*RACEGRP	All Other Races	21	2	-9.6889	1.7502	409	-5.54	<.0001	0.05	-13.1294	-6.2483
AVISIT*TRTPN*RACEGRP	White	21	2	-7.9419	0.9105	430	-8.72	<.0001	0.05	-9.7315	-6.1523
AVISIT*TRTPN*RACEGRP	All Other Races	21	3	-6.4777	2.0044	400	-3.23	0.0013	0.05	-10.4181	-2.5374
AVISIT*TRTPN*RACEGRP	White	21	3	-6.5518	0.8889	429	-7.37	<.0001	0.05	-8.2989	-4.8047
AVISIT*TRTPN*RACEGRP	All Other Races	28	1	-11.3582	2.1608	444	-5.26	<.0001	0.05	-15.6049	-7.1116
AVISIT*TRTPN*RACEGRP	White	28	1	-9.2681	1.0250	433	-9.04	<.0001	0.05	-11.2826	-7.2535
AVISIT*TRTPN*RACEGRP	All Other Races	28	2	-12.7159	1.9930	408	-6.38	<.0001	0.05	-16.6337	-8.7982
AVISIT*TRTPN*RACEGRP	White	28	2	-8.7879	1.0386	442	-8.46	<.0001	0.05	-10.8291	-6.7467
AVISIT*TRTPN*RACEGRP	All Other Races	28	3	-5.5914	2.3069	414	-2.42	0.0158	0.05	-10.1261	-1.0567
AVISIT*TRTPN*RACEGRP	White	28	3	-6.4036	1.0037	428	-6.38	<.0001	0.05	-8.3764	-4.4308
AVISIT*TRTPN*RACEGRP	All Other Races	35	1	-11.5318	2.2200	440	-5.19	<.0001	0.05	-15.8948	-7.1687
AVISIT*TRTPN*RACEGRP	White	35	1	-9.9860	1.0509	427	-9.50	<.0001	0.05	-12.0515	-7.9204
AVISIT*TRTPN*RACEGRP	All Other Races	35	2	-13.1394	2.0655	417	-6.36	<.0001	0.05	-17.1995	-9.0793
AVISIT*TRTPN*RACEGRP	White	35	2	-10.0665	1.0666	439	-9.44	<.0001	0.05	-12.1627	-7.9703
AVISIT*TRTPN*RACEGRP	All Other Races	35	3	-8.4240	2.3575	405	-3.57	0.0004	0.05	-13.0585	-3.7896

FILE: stat2b.lis, RUN: 18JUN2020 10:01; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat2.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.2 FINAL

STAT-3.2
MMRM Output for Test on Treatment by Race Interaction at Day 42
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISIT*TRTPN*RACEGRP	White	35	3	-6.9780	1.0307	426	-6.77	<.0001	0.05	-9.0039	-4.9521
AVISIT*TRTPN*RACEGRP	All Other Races	42	1	-11.5976	2.2803	430	-5.09	<.0001	0.05	-16.0795	-7.1158
AVISIT*TRTPN*RACEGRP	White	42	1	-9.8108	1.0918	431	-8.99	<.0001	0.05	-11.9568	-7.6648
AVISIT*TRTPN*RACEGRP	All Other Races	42	2	-11.4938	2.1175	406	-5.43	<.0001	0.05	-15.6564	-7.3313
AVISIT*TRTPN*RACEGRP	White	42	2	-9.2764	1.0974	433	-8.45	<.0001	0.05	-11.4333	-7.1195
AVISIT*TRTPN*RACEGRP	All Other Races	42	3	-4.9221	2.4639	416	-2.00	0.0464	0.05	-9.7653	-0.07897
AVISIT*TRTPN*RACEGRP	White	42	3	-7.3460	1.0634	424	-6.91	<.0001	0.05	-9.4363	-5.2558

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

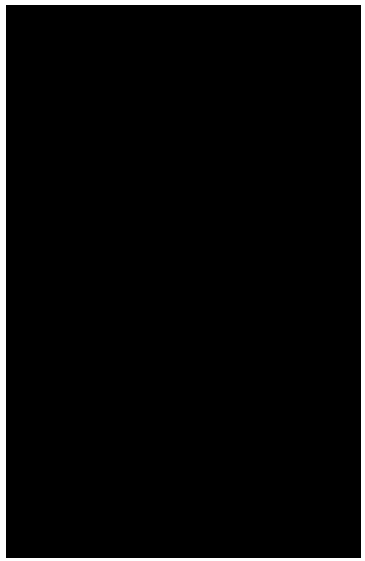
Class Level Information

Class	Levels	Values
SUBJID	438	[redacted]

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

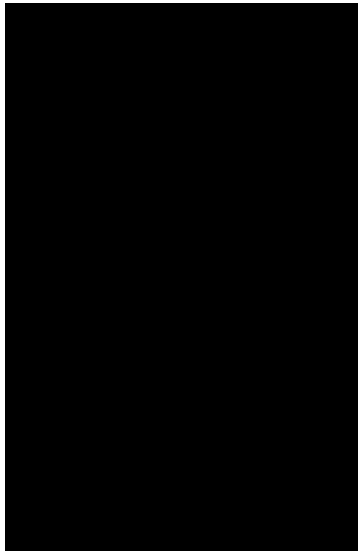


SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

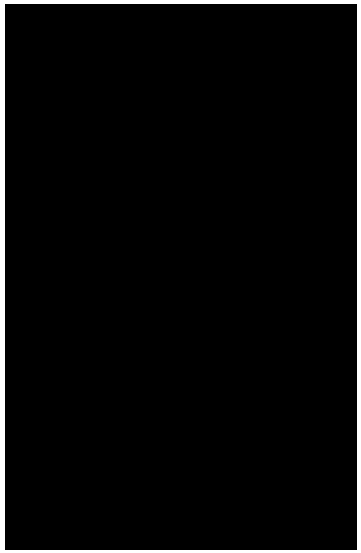


SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

[redacted]

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

[redacted]

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Dimensions

Covariance Parameters	21
Columns in X	72
Columns in Z	0
Subjects	438
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2292
Number of Observations Used	2292
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16529.25629156	
1	2	14254.41720522	0.00013099
2	1	14253.71654441	0.00000106
3	1	14253.71110309	0.00000000

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	52.4121
UN(2,1)	SUBJID	40.1625
UN(2,2)	SUBJID	72.3841
UN(3,1)	SUBJID	37.8797
UN(3,2)	SUBJID	62.0385
UN(3,3)	SUBJID	81.2283
UN(4,1)	SUBJID	37.2709
UN(4,2)	SUBJID	62.5977
UN(4,3)	SUBJID	77.1568
UN(4,4)	SUBJID	105.57
UN(5,1)	SUBJID	38.1278
UN(5,2)	SUBJID	63.2146
UN(5,3)	SUBJID	80.4768
UN(5,4)	SUBJID	95.8339
UN(5,5)	SUBJID	110.37
UN(6,1)	SUBJID	38.5259
UN(6,2)	SUBJID	64.2868
UN(6,3)	SUBJID	78.4374

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(6,4)	SUBJID	96.1387
UN(6,5)	SUBJID	99.0726
UN(6,6)	SUBJID	117.05

Fit Statistics

-2 Res Log Likelihood	14253.7
AIC (Smaller is Better)	14295.7
AICC (Smaller is Better)	14296.1
BIC (Smaller is Better)	14381.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2275.55	<.0001

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept				0.4831	4.8082	567	0.10	0.9200
AVISITN		7		-0.7357	2.9385	398	-0.25	0.8024
AVISITN		14		-0.8075	2.4473	388	-0.33	0.7416
AVISITN		21		-2.8674	2.0446	361	-1.40	0.1616
AVISITN		28		2.9224	1.7765	345	1.64	0.1009
AVISITN		35		0.5711	1.7576	352	0.32	0.7454
AVISITN		42		0				
TRTPN			1	-3.1497	1.3407	400	-2.35	0.0193
TRTPN			2	-2.7448	1.3267	392	-2.07	0.0392
TRTPN			3	0				
AVISITN*TRTPN		7	1	1.8448	1.2086	398	1.53	0.1277
AVISITN*TRTPN		7	2	2.8699	1.1928	393	2.41	0.0166
AVISITN*TRTPN		7	3	0				
AVISITN*TRTPN		14	1	2.1849	1.0072	387	2.17	0.0307
AVISITN*TRTPN		14	2	2.4905	0.9856	382	2.53	0.0119
AVISITN*TRTPN		14	3	0				
AVISITN*TRTPN		21	1	1.2025	0.8417	362	1.43	0.1540
AVISITN*TRTPN		21	2	0.9723	0.8240	360	1.18	0.2388
AVISITN*TRTPN		21	3	0				

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

Parameter Code=AISRSTOT

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
AVISITN*TRTPN		28	1	-0.2340	0.7283	342	-0.32	0.7481
AVISITN*TRTPN		28	2	-0.6011	0.7150	343	-0.84	0.4011
AVISITN*TRTPN		28	3	0				
AVISITN*TRTPN		35	1	0.07206	0.7186	348	0.10	0.9202
AVISITN*TRTPN		35	2	-0.7607	0.7085	349	-1.07	0.2837
AVISITN*TRTPN		35	3	0				
AVISITN*TRTPN		42	1	0				
AVISITN*TRTPN		42	2	0				
AVISITN*TRTPN		42	3	0				
POOLCNTR	[redacted]			-1.5781	3.9342	391	-0.40	0.6885
POOLCNTR				-1.0310	3.8358	391	-0.27	0.7882
POOLCNTR				-2.1594	3.9655	391	-0.54	0.5864
POOLCNTR				-1.5289	3.7488	393	-0.41	0.6836
POOLCNTR				-1.5067	3.8012	392	-0.40	0.6920
POOLCNTR				-2.4888	4.2744	391	-0.58	0.5607
POOLCNTR				-8.3662	4.3446	393	-1.93	0.0549
POOLCNTR				-6.3243	5.3927	393	-1.17	0.2416
POOLCNTR				-5.4404	3.9685	392	-1.37	0.1712
POOLCNTR				-1.9497	4.7926	406	-0.41	0.6844

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

Parameter Code=AISRSTOT

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
POOLCNTR	[redacted]			-3.3328	3.7186	392	-0.90	0.3707
POOLCNTR				-5.6893	4.1349	391	-1.38	0.1696
POOLCNTR				0.8859	4.2071	397	0.21	0.8333
POOLCNTR				-3.4584	4.1907	393	-0.83	0.4097
POOLCNTR				-2.1719	4.2744	391	-0.51	0.6117
POOLCNTR				-3.4300	4.7326	392	-0.72	0.4690
POOLCNTR				-3.1079	3.9681	391	-0.78	0.4340
POOLCNTR				-4.5105	4.3481	391	-1.04	0.3002
POOLCNTR				-0.4554	5.3811	393	-0.08	0.9326
POOLCNTR				-1.5914	4.4306	394	-0.36	0.7197
POOLCNTR				-5.6339	5.0120	390	-1.12	0.2617
POOLCNTR				0.2294	4.7268	391	0.05	0.9613
POOLCNTR				-1.1086	4.7948	392	-0.23	0.8173
POOLCNTR				-3.8392	4.5625	394	-0.84	0.4006
POOLCNTR				-1.8688	3.8721	393	-0.48	0.6296
POOLCNTR				-4.7987	4.2584	393	-1.13	0.2605
POOLCNTR				-4.5967	4.1713	391	-1.10	0.2712
POOLCNTR				-4.0969	4.7405	397	-0.86	0.3880
POOLCNTR				-12.4605	3.8212	392	-3.26	0.0012

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

Parameter Code=AISRSTOT

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
POOLCNTR	[redacted]			2.2378	5.3865	390	0.42	0.6780
POOLCNTR				3.2557	4.5695	390	0.71	0.4766
POOLCNTR				-2.8411	4.9870	390	-0.57	0.5692
POOLCNTR				-2.4274	5.0523	397	-0.48	0.6312
POOLCNTR				-1.0008	3.9085	391	-0.26	0.7980
POOLCNTR				-5.1075	3.8314	391	-1.33	0.1833
POOLCNTR				-1.5870	4.9866	392	-0.32	0.7505
POOLCNTR				-1.6255	4.9908	392	-0.33	0.7448
POOLCNTR				0				
BASE*AVISITN		7		-0.02833	0.06074	406	-0.47	0.6411
BASE*AVISITN		14		-0.08413	0.06890	455	-1.22	0.2227
BASE*AVISITN		21		-0.03354	0.07241	456	-0.46	0.6434
BASE*AVISITN		28		-0.1732	0.08145	469	-2.13	0.0340
BASE*AVISITN		35		-0.1373	0.08324	466	-1.65	0.0998
BASE*AVISITN		42		-0.1177	0.08570	465	-1.37	0.1704

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	380	2.06	0.0694
TRTPN	2	400	3.05	0.0482
AVISITN*TRTPN	10	563	1.68	0.0815
POOLCNTR	37	396	2.25	<.0001
BASE*AVISITN	6	405	2.18	0.0443

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-1.3049	0.8584	396	-1.52	0.1292	0.05	-2.9924	0.3826
DAY7 2 vs 3	0.1251	0.8581	396	0.15	0.8841	0.05	-1.5618	1.8121
DAY14 1 vs 3	-0.9648	1.0193	403	-0.95	0.3444	0.05	-2.9686	1.0390
DAY14 2 vs 3	-0.2542	1.0168	400	-0.25	0.8027	0.05	-2.2531	1.7446
DAY21 1 vs 3	-1.9472	1.0892	398	-1.79	0.0746	0.05	-4.0885	0.1941
DAY21 2 vs 3	-1.7725	1.0824	391	-1.64	0.1023	0.05	-3.9006	0.3556
DAY28 1 vs 3	-3.3837	1.2590	401	-2.69	0.0075	0.05	-5.8587	-0.9087
DAY28 2 vs 3	-3.3458	1.2483	395	-2.68	0.0077	0.05	-5.8000	-0.8917

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY35 1 vs 3	-3.0776	1.2921	398	-2.38	0.0177	0.05	-5.6178	-0.5375
DAY35 2 vs 3	-3.5055	1.2838	394	-2.73	0.0066	0.05	-6.0294	-0.9816
DAY42 1 vs 3	-3.1497	1.3407	400	-2.35	0.0193	0.05	-5.7855	-0.5139
DAY42 2 vs 3	-2.7448	1.3267	392	-2.07	0.0392	0.05	-5.3532	-0.1364

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	1	-5.4832	0.6575	405	-8.34	<.0001	0.05	-6.7757	-4.1907
AVISITN*TRTPN	7	2	-4.0531	0.6710	406	-6.04	<.0001	0.05	-5.3721	-2.7341
AVISITN*TRTPN	7	3	-4.1783	0.6708	402	-6.23	<.0001	0.05	-5.4970	-2.8596
AVISITN*TRTPN	14	1	-7.4261	0.7642	431	-9.72	<.0001	0.05	-8.9281	-5.9242
AVISITN*TRTPN	14	2	-6.7156	0.7740	436	-8.68	<.0001	0.05	-8.2368	-5.1943
AVISITN*TRTPN	14	3	-6.4613	0.7759	437	-8.33	<.0001	0.05	-7.9862	-4.9364
AVISITN*TRTPN	21	1	-8.4638	0.8150	436	-10.39	<.0001	0.05	-10.0655	-6.8620
AVISITN*TRTPN	21	2	-8.2891	0.8186	436	-10.13	<.0001	0.05	-9.8980	-6.6801

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	21	3	-6.5166	0.8184	435	-7.96	<.0001	0.05	-8.1251	-4.9080
AVISITN*TRTPN	28	1	-9.6450	0.9350	444	-10.32	<.0001	0.05	-11.4825	-7.8075
AVISITN*TRTPN	28	2	-9.6071	0.9317	446	-10.31	<.0001	0.05	-11.4382	-7.7761
AVISITN*TRTPN	28	3	-6.2613	0.9266	437	-6.76	<.0001	0.05	-8.0825	-4.4401
AVISITN*TRTPN	35	1	-10.2665	0.9572	438	-10.73	<.0001	0.05	-12.1478	-8.3852
AVISITN*TRTPN	35	2	-10.6944	0.9567	446	-11.18	<.0001	0.05	-12.5746	-8.8143
AVISITN*TRTPN	35	3	-7.1889	0.9493	434	-7.57	<.0001	0.05	-9.0547	-5.3231
AVISITN*TRTPN	42	1	-10.1321	0.9918	440	-10.22	<.0001	0.05	-12.0814	-8.1829
AVISITN*TRTPN	42	2	-9.7272	0.9830	439	-9.89	<.0001	0.05	-11.6593	-7.7951
AVISITN*TRTPN	42	3	-6.9824	0.9807	436	-7.12	<.0001	0.05	-8.9099	-5.0549

STAT-4.1.1
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=KENWARDROGER
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Tests of Effect Slices

Effect	Analysis Visit (N)	Num DF	Den DF	F Value	Pr > F
AVISITN*TRTPN	7	2	397	1.71	0.1821
AVISITN*TRTPN	14	2	402	0.48	0.6181
AVISITN*TRTPN	21	2	397	1.97	0.1409
AVISITN*TRTPN	28	2	400	4.82	0.0085
AVISITN*TRTPN	35	2	399	4.44	0.0124
AVISITN*TRTPN	42	2	398	3.30	0.0377

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Satterthwaite

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

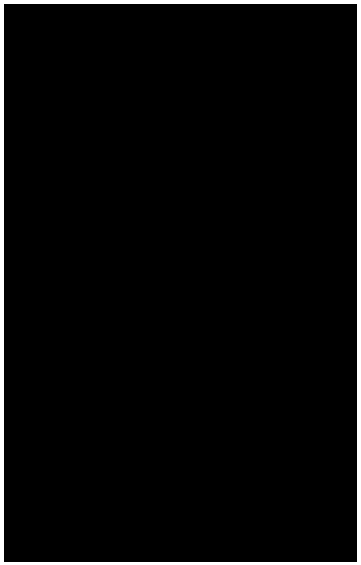
Class Level Information

Class	Levels	Values
SUBJID	438	[redacted]

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

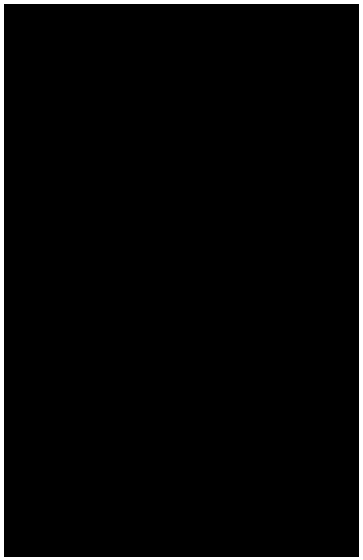


SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

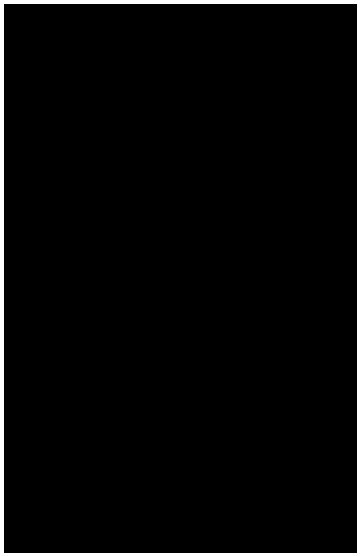


SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

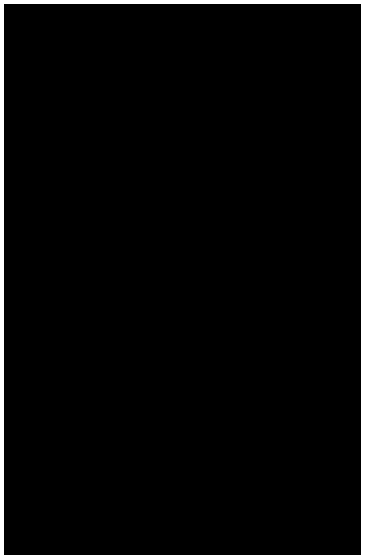
[redacted]

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Dimensions

Covariance Parameters	21
Columns in X	72
Columns in Z	0
Subjects	438
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2292
Number of Observations Used	2292
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16529.25629156	
1	2	14254.41720522	0.00013099
2	1	14253.71654441	0.00000106
3	1	14253.71110309	0.00000000

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	52.4121
UN(2,1)	SUBJID	40.1625
UN(2,2)	SUBJID	72.3841
UN(3,1)	SUBJID	37.8797
UN(3,2)	SUBJID	62.0385
UN(3,3)	SUBJID	81.2283
UN(4,1)	SUBJID	37.2709
UN(4,2)	SUBJID	62.5977
UN(4,3)	SUBJID	77.1568
UN(4,4)	SUBJID	105.57
UN(5,1)	SUBJID	38.1278
UN(5,2)	SUBJID	63.2146
UN(5,3)	SUBJID	80.4768
UN(5,4)	SUBJID	95.8339
UN(5,5)	SUBJID	110.37
UN(6,1)	SUBJID	38.5259
UN(6,2)	SUBJID	64.2868
UN(6,3)	SUBJID	78.4374

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(6,4)	SUBJID	96.1387
UN(6,5)	SUBJID	99.0726
UN(6,6)	SUBJID	117.05

Fit Statistics

-2 Res Log Likelihood	14253.7
AIC (Smaller is Better)	14295.7
AICC (Smaller is Better)	14296.1
BIC (Smaller is Better)	14381.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2275.55	<.0001

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	384	2.09	0.0662
TRTPN	2	400	3.06	0.0482
AVISITN*TRTPN	10	396	1.71	0.0774
POOLCNTR	37	396	2.31	<.0001
BASE*AVISITN	6	404	2.21	0.0415

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-1.3049	0.8582	396	-1.52	0.1291	0.05	-2.9920	0.3822
DAY7 2 vs 3	0.1251	0.8578	396	0.15	0.8841	0.05	-1.5614	1.8116
DAY14 1 vs 3	-0.9648	1.0190	403	-0.95	0.3443	0.05	-2.9680	1.0384
DAY14 2 vs 3	-0.2542	1.0165	400	-0.25	0.8026	0.05	-2.2526	1.7442
DAY21 1 vs 3	-1.9472	1.0889	398	-1.79	0.0745	0.05	-4.0879	0.1935
DAY21 2 vs 3	-1.7725	1.0822	391	-1.64	0.1022	0.05	-3.9001	0.3551
DAY28 1 vs 3	-3.3837	1.2584	401	-2.69	0.0075	0.05	-5.8576	-0.9098
DAY28 2 vs 3	-3.3458	1.2478	395	-2.68	0.0076	0.05	-5.7990	-0.8927

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY35 1 vs 3	-3.0776	1.2914	398	-2.38	0.0176	0.05	-5.6164	-0.5389
DAY35 2 vs 3	-3.5055	1.2831	394	-2.73	0.0066	0.05	-6.0281	-0.9829
DAY42 1 vs 3	-3.1497	1.3398	400	-2.35	0.0192	0.05	-5.7836	-0.5158
DAY42 2 vs 3	-2.7448	1.3259	392	-2.07	0.0391	0.05	-5.3516	-0.1379

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	1	-5.4832	0.6561	405	-8.36	<.0001	0.05	-6.7731	-4.1934
AVISITN*TRTPN	7	2	-4.0531	0.6693	406	-6.06	<.0001	0.05	-5.3688	-2.7374
AVISITN*TRTPN	7	3	-4.1783	0.6693	402	-6.24	<.0001	0.05	-5.4940	-2.8626
AVISITN*TRTPN	14	1	-7.4261	0.7629	431	-9.73	<.0001	0.05	-8.9256	-5.9266
AVISITN*TRTPN	14	2	-6.7156	0.7725	436	-8.69	<.0001	0.05	-8.2339	-5.1972
AVISITN*TRTPN	14	3	-6.4613	0.7745	437	-8.34	<.0001	0.05	-7.9835	-4.9392
AVISITN*TRTPN	21	1	-8.4638	0.8137	436	-10.40	<.0001	0.05	-10.0631	-6.8645
AVISITN*TRTPN	21	2	-8.2891	0.8172	436	-10.14	<.0001	0.05	-9.8952	-6.6829

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	21	3	-6.5166	0.8171	435	-7.98	<.0001	0.05	-8.1225	-4.9107
AVISITN*TRTPN	28	1	-9.6450	0.9336	444	-10.33	<.0001	0.05	-11.4799	-7.8102
AVISITN*TRTPN	28	2	-9.6071	0.9302	446	-10.33	<.0001	0.05	-11.4353	-7.7790
AVISITN*TRTPN	28	3	-6.2613	0.9253	437	-6.77	<.0001	0.05	-8.0799	-4.4427
AVISITN*TRTPN	35	1	-10.2665	0.9558	438	-10.74	<.0001	0.05	-12.1451	-8.3880
AVISITN*TRTPN	35	2	-10.6944	0.9551	446	-11.20	<.0001	0.05	-12.5714	-8.8175
AVISITN*TRTPN	35	3	-7.1889	0.9479	434	-7.58	<.0001	0.05	-9.0520	-5.3258
AVISITN*TRTPN	42	1	-10.1321	0.9902	440	-10.23	<.0001	0.05	-12.0783	-8.1860
AVISITN*TRTPN	42	2	-9.7272	0.9815	439	-9.91	<.0001	0.05	-11.6561	-7.7983
AVISITN*TRTPN	42	3	-6.9824	0.9792	436	-7.13	<.0001	0.05	-8.9069	-5.0579

STAT-4.1.2
Proc Mixed Output for Change from Baseline in AISRS Total Score, MMRM (UN), DDFM=SATTERTHWAITE
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Tests of Effect Slices

Effect	Analysis Visit (N)	Num DF	Den DF	F Value	Pr > F
AVISITN*TRTPN	7	2	397	1.71	0.1819
AVISITN*TRTPN	14	2	402	0.48	0.6179
AVISITN*TRTPN	21	2	397	1.97	0.1407
AVISITN*TRTPN	28	2	400	4.83	0.0085
AVISITN*TRTPN	35	2	399	4.44	0.0124
AVISITN*TRTPN	42	2	398	3.31	0.0376

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

Number of Observations Read 438
Number of Observations Used 438

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

Parameter Code=AISRSTOT Analysis Visit (N)=42

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	40	7613.60524	190.34013	1.72	0.0053
Error	397	43878.35138	110.52481		
Corrected Total	437	51491.95662			

R-Square	Coeff Var	Root MSE	CHG Mean
0.147860	-115.4357	10.51308	-9.107306

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	612.642653	306.321327	2.77	0.0638
POOLCNTR	37	5773.449566	156.039177	1.41	0.0603
BASE	1	231.354002	231.354002	2.09	0.1487

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

--- Parameter Code=AISRSTOT Analysis Visit (N)=42 ---

The GLM Procedure

Level of TRTPN	N	CHG Mean	CHG Std Dev	BASE Mean	BASE Std Dev
1	147	-9.97278912	11.8933305	39.5986395	6.69354613
2	147	-9.85714286	10.3632649	39.5646259	6.81664766
3	144	-7.45833333	10.0959557	39.5347222	7.19840036

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	Standard Error	Pr > |t|	LSMEAN Number
1	-10.0466880	0.9524391	<.0001	1
2	-9.5942969	0.9741456	<.0001	2
3	-7.3212133	0.9759953	<.0001	3

Least Squares Means for effect TRTPN
Pr > |t| for H0: LSMean(i)=LSMean(j)

Dependent Variable: CHG

i/j	1	2	3
1		0.7141	0.0284
2	0.7141		0.0674
3	0.0284	0.0674	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-10.046688	-11.919143	-8.174233
2	-9.594297	-11.509426	-7.679168

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	95% Confidence Limits	
3	-7.321213	-9.239979	-5.402448

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.452391	-2.877963	1.973180
1	3	-2.725475	-5.161161	-0.289788
2	3	-2.273084	-4.709885	0.163718

NOTE: To ensure overall protection level, only probabilities associated with pre-planned comparisons should be used.

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.2
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Parameter	Estimate	Standard Error	t Value	Pr > |t|
1 vs 3	-2.72547476	1.23893152	-2.20	0.0284
2 vs 3	-2.27308361	1.23949880	-1.83	0.0674

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.2 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3

Number of Observations Read	438
Number of Observations Used	438

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	1840.15567	613.38522	5.36	0.0012
Error	434	49651.80095	114.40507		
Corrected Total	437	51491.95662			

R-Square	Coeff Var	Root MSE	CHG Mean
0.035737	-117.4445	10.69603	-9.107306

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	578.702364	289.351182	2.53	0.0809
BASE	1	1255.840210	1255.840210	10.98	0.0010

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Level of TRTPN	N	CHG Mean	CHG Std Dev	BASE Mean	BASE Std Dev
1	147	-9.97278912	11.8933305	39.5986395	6.69354613
2	147	-9.85714286	10.3632649	39.5646259	6.81664766
3	144	-7.45833333	10.0959557	39.5347222	7.19840036

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	Standard Error	Pr > |t|	LSMEAN Number
1	-9.96480823	0.88219703	<.0001	1
2	-9.85753273	0.88219375	<.0001	2
3	-7.46608250	0.89133895	<.0001	3

Least Squares Means for effect TRTPN
Pr > |t| for H0: LSMean(i)=LSMean(j)

Dependent Variable: CHG

i/j	1	2	3
1		0.9315	0.0469
2	0.9315		0.0572
3	0.0469	0.0572	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-9.964808	-11.698718	-8.230898
2	-9.857533	-11.591436	-8.123629

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	95% Confidence Limits	
3	-7.466082	-9.217960	-5.714205

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.107275	-2.559390	2.344839
1	3	-2.498726	-4.963591	-0.033860
2	3	-2.391450	-4.856302	0.073402

NOTE: To ensure overall protection level, only probabilities associated with pre-planned comparisons should be used.

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.3
Proc GLM Output for Change from Baseline to Day 42 in AISRS Total Score, OC
(Efficacy Sample)

--- Parameter Code=AISRSTOT Analysis Visit (N)=42 ---

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Parameter	Estimate	Standard Error	t Value	Pr > |t|
1 vs 3	-2.49872573	1.25410047	-1.99	0.0469
2 vs 3	-2.39145023	1.25409345	-1.91	0.0572

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.3 FINAL

STAT-4.4
Proc GLM Output for Treatment by Center Interaction at Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Parameter Code=AISRSTOT Analysis Visit (N)=42 ----------

The GLM Procedure

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

Number of Observations Read	438
Number of Observations Used	438

SOURCE: GLMCNTR; TABLE: stat1d.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.4 FINAL

STAT-4.4
Proc GLM Output for Treatment by Center Interaction at Day 42 in AISRS Total Score, LOCF
(Efficacy Sample)

Parameter Code=AISRSTOT Analysis Visit (N)=42

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	114	17280.04047	151.57930	1.43	0.0080
Error	323	34211.91615	105.91925		
Corrected Total	437	51491.95662			

R-Square	Coeff Var	Root MSE	CHG Mean
0.335587	-113.0050	10.29171	-9.107306

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	316.610526	158.305263	1.49	0.2259
POOLCNTR	37	5824.724354	157.424983	1.49	0.0390
TRTPN*POOLCNTR	74	9666.435233	130.627503	1.23	0.1128
BASE	1	244.872536	244.872536	2.31	0.1294

SOURCE: GLMCNTR; TABLE: stat1d.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.4 FINAL

CENTANAFADINE 1 OF 4
PROTOCOL 405-201-00013

STAT-4.5.1
Summary of Mean Change at Day 42 from Baseline in AISRS Total Score
By Center - LOCF (Efficacy Sample)

	AISRS TOTAL SCORE							
	CTN SR 200MG		CTN SR 400MG		PLACEBO			
CENTER	N	LS MEAN (SE)	N	LS MEAN (SE)	N	LS MEAN (SE)	TREATMENT COMPARISON	LS MEAN DIFFERENCE[1]
OVERALL	147	-10.0 (0.95)	147	-9.59 (0.97)	144	-7.32 (0.98)	CTN SR 200MG VS. PLACEBO	-2.73 (-5.16, -0.29)
							CTN SR 400MG VS. PLACEBO	-2.27 (-4.71, 0.16)
[redacted]	5	-3.34 (4.60)	6	-18.0 (4.20)	6	-0.29 (4.20)	CTN SR 200MG VS. PLACEBO	-3.04 (-15.3, 9.22)
							CTN SR 400MG VS. PLACEBO	-17.7 (-29.4, -6.05)
	7	-7.96 (3.89)	8	-1.67 (3.64)	8	-5.76 (3.65)	CTN SR 200MG VS. PLACEBO	-2.21 (-12.7, 8.30)
							CTN SR 400MG VS. PLACEBO	4.09 (-6.04, 14.22)
	5	-12.9 (4.62)	5	-12.1 (4.66)	5	-11.3 (4.61)	CTN SR 200MG VS. PLACEBO	-1.66 (-14.5, 11.15)
							CTN SR 400MG VS. PLACEBO	-0.78 (-13.6, 12.05)
	11	-14.3 (3.10)	11	-3.96 (3.10)	10	-7.22 (3.31)	CTN SR 200MG VS. PLACEBO	-7.07 (-16.0, 1.84)
							CTN SR 400MG VS. PLACEBO	3.26 (-5.68, 12.19)
	9	-8.67 (3.44)	8	-12.9 (3.65)	8	-5.21 (3.65)	CTN SR 200MG VS. PLACEBO	-3.46 (-13.3, 6.38)
							CTN SR 400MG VS. PLACEBO	-7.64 (-17.8, 2.48)
	3	-11.5 (5.94)	3	-16.1 (5.94)	3	-11.3 (6.01)	CTN SR 200MG VS. PLACEBO	-0.20 (-16.8, 16.40)
							CTN SR 400MG VS. PLACEBO	-4.82 (-21.4, 11.78)
	3	-9.84 (5.95)	2	-14.0 (7.28)	3	-3.36 (5.95)	CTN SR 200MG VS. PLACEBO	-6.47 (-23.0, 10.06)
							CTN SR 400MG VS. PLACEBO	-10.6 (-29.1, 7.84)
	1	3.06 (10.3)	1	-23.4 (10.3)	1	-28.4 (10.3)	CTN SR 200MG VS. PLACEBO	31.43 (2.79, 60.07)
							CTN SR 400MG VS. PLACEBO	5.01 (-23.7, 33.67)
	5	-1.45 (4.61)	5	-15.0 (4.62)	6	-11.7 (4.20)	CTN SR 200MG VS. PLACEBO	10.27 (-1.99, 22.54)
							CTN SR 400MG VS. PLACEBO	-3.24 (-15.5, 9.04)
	2	-10.2 (7.29)	1	-11.2 (10.3)	2	-9.52 (7.31)	CTN SR 200MG VS. PLACEBO	-0.64 (-20.9, 19.61)
							CTN SR 400MG VS. PLACEBO	-1.72 (-26.5, 23.08)
	13	-6.23 (2.86)	13	-11.4 (2.85)	12	-2.49 (2.97)	CTN SR 200MG VS. PLACEBO	-3.74 (-11.8, 4.37)
							CTN SR 400MG VS. PLACEBO	-8.92 (-17.0, -0.82)

[1] OVERALL TREATMENT DIFFERENCE IS DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT AND BASELINE VALUE AS COVARIATE; BY CENTER DIFFERENCES ARE DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT, TREATMENT BY CENTER INTERACTION, AND BASELINE VALUE AS COVARIATE.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centera.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.1 FINAL

STAT-4.5.1
Summary of Mean Change at Day 42 from Baseline in AISRS Total Score
By Center - LOCF (Efficacy Sample)

	AISRS TOTAL SCORE							
	CTN SR 200MG		CTN SR 400MG		PLACEBO			
CENTER	N	LS MEAN (SE)	N	LS MEAN (SE)	N	LS MEAN (SE)	TREATMENT COMPARISON	LS MEAN DIFFERENCE[1]
[redacted]	4	-9.58 (5.15)	4	-8.41 (5.15)	3	-11.5 (5.97)	CTN SR 200MG VS. PLACEBO	1.87 (-13.6, 17.36)
							CTN SR 400MG VS. PLACEBO	3.05 (-12.5, 18.60)
	4	-9.37 (5.15)	2	-8.00 (7.31)	4	-0.58 (5.15)	CTN SR 200MG VS. PLACEBO	-8.79 (-23.1, 5.54)
							CTN SR 400MG VS. PLACEBO	-7.42 (-25.0, 10.15)
	4	-11.1 (5.15)	3	-12.6 (5.95)	3	-0.13 (5.94)	CTN SR 200MG VS. PLACEBO	-11.0 (-26.4, 4.51)
							CTN SR 400MG VS. PLACEBO	-12.5 (-29.1, 4.01)
	3	0.78 (5.95)	3	-12.8 (5.99)	3	-2.84 (5.94)	CTN SR 200MG VS. PLACEBO	3.62 (-12.9, 20.16)
							CTN SR 400MG VS. PLACEBO	-9.99 (-26.6, 6.59)
	2	-16.7 (7.32)	2	-2.53 (7.40)	1	-0.23 (10.3)	CTN SR 200MG VS. PLACEBO	-16.5 (-41.3, 8.32)
							CTN SR 400MG VS. PLACEBO	-2.31 (-27.2, 22.60)
	5	-4.09 (4.61)	6	-14.0 (4.25)	4	-9.65 (5.15)	CTN SR 200MG VS. PLACEBO	5.57 (-8.02, 19.16)
							CTN SR 400MG VS. PLACEBO	-4.37 (-17.5, 8.75)
	3	-7.50 (5.97)	2	-8.00 (7.28)	3	-16.5 (5.94)	CTN SR 200MG VS. PLACEBO	8.96 (-7.59, 25.51)
							CTN SR 400MG VS. PLACEBO	8.46 (-10.0, 26.94)
	1	2.20 (10.3)	1	-21.1 (10.3)	1	-1.51 (10.3)	CTN SR 200MG VS. PLACEBO	3.71 (-24.9, 32.35)
							CTN SR 400MG VS. PLACEBO	-19.6 (-48.2, 9.07)
	2	-7.22 (7.28)	2	-18.1 (7.29)	3	-17.8 (5.94)	CTN SR 200MG VS. PLACEBO	10.62 (-7.87, 29.12)
							CTN SR 400MG VS. PLACEBO	-0.24 (-18.7, 18.25)
	2	-29.1 (7.30)	1	0.50 (10.3)	1	-3.51 (10.3)	CTN SR 200MG VS. PLACEBO	-25.6 (-50.5, -0.77)
							CTN SR 400MG VS. PLACEBO	4.01 (-24.7, 32.67)
	2	-7.87 (7.28)	1	5.06 (10.3)	2	0.77 (7.28)	CTN SR 200MG VS. PLACEBO	-8.64 (-28.9, 11.60)
							CTN SR 400MG VS. PLACEBO	4.29 (-20.5, 29.09)
	2	-0.78 (7.37)	2	-8.14 (7.33)	1	-1.66 (10.3)	CTN SR 200MG VS. PLACEBO	0.88 (-24.1, 25.87)
							CTN SR 400MG VS. PLACEBO	-6.48 (-31.4, 18.46)

[1] OVERALL TREATMENT DIFFERENCE IS DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT AND BASELINE VALUE AS COVARIATE; BY CENTER DIFFERENCES ARE DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT, TREATMENT BY CENTER INTERACTION, AND BASELINE VALUE AS COVARIATE.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centera.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.1 FINAL

CENTANAFADINE 3 OF 4
PROTOCOL 405-201-00013

STAT-4.5.1
Summary of Mean Change at Day 42 from Baseline in AISRS Total Score
By Center - LOCF (Efficacy Sample)

	AISRS TOTAL SCORE							
	CTN SR 200MG		CTN SR 400MG		PLACEBO			
CENTER	N	LS MEAN (SE)	N	LS MEAN (SE)	N	LS MEAN (SE)	TREATMENT COMPARISON	LS MEAN DIFFERENCE[1]
[redacted]	2	-20.1 (7.29)	2	-12.2 (7.28)	2	1.85 (7.28)	CTN SR 200MG VS. PLACEBO	-21.9 (-42.2, -1.68)
							CTN SR 400MG VS. PLACEBO	-14.0 (-34.2, 6.25)
	7	-14.7 (3.91)	8	-5.20 (3.65)	7	-6.89 (3.90)	CTN SR 200MG VS. PLACEBO	-7.81 (-18.6, 3.01)
							CTN SR 400MG VS. PLACEBO	1.69 (-8.79, 12.17)
	3	-19.3 (5.96)	4	-11.7 (5.15)	2	-6.87 (7.28)	CTN SR 200MG VS. PLACEBO	-12.4 (-31.0, 6.09)
							CTN SR 400MG VS. PLACEBO	-4.85 (-22.4, 12.69)
	3	-11.0 (5.98)	4	-7.26 (5.15)	3	-15.9 (5.96)	CTN SR 200MG VS. PLACEBO	4.95 (-11.6, 21.49)
							CTN SR 400MG VS. PLACEBO	8.69 (-6.80, 24.17)
	1	-15.5 (10.3)	2	-11.0 (7.34)	2	-15.2 (7.32)	CTN SR 200MG VS. PLACEBO	-0.28 (-25.1, 24.54)
							CTN SR 400MG VS. PLACEBO	4.28 (-16.0, 24.53)
	9	-26.4 (3.52)	13	-14.5 (2.95)	12	-14.1 (3.10)	CTN SR 200MG VS. PLACEBO	-12.3 (-21.2, -3.37)
							CTN SR 400MG VS. PLACEBO	-0.42 (-8.53, 7.69)
	1	-5.95 (10.3)	1	-2.53 (10.3)	1	4.62 (10.3)	CTN SR 200MG VS. PLACEBO	-10.6 (-39.2, 18.07)
							CTN SR 400MG VS. PLACEBO	-7.14 (-35.8, 21.49)
	2	-1.93 (7.31)	2	2.70 (7.30)	2	-1.58 (7.28)	CTN SR 200MG VS. PLACEBO	-0.35 (-20.6, 19.91)
							CTN SR 400MG VS. PLACEBO	4.27 (-16.0, 24.58)
	1	-10.1 (10.3)	2	-15.2 (7.28)	1	-10.2 (10.3)	CTN SR 200MG VS. PLACEBO	0.16 (-28.5, 28.83)
							CTN SR 400MG VS. PLACEBO	-4.99 (-29.8, 19.84)
	2	-21.0 (7.28)	1	-2.64 (10.3)	1	-0.78 (10.3)	CTN SR 200MG VS. PLACEBO	-20.2 (-45.0, 4.59)
							CTN SR 400MG VS. PLACEBO	-1.86 (-30.5, 26.78)
	6	-4.42 (4.22)	6	-3.87 (4.20)	6	-8.94 (4.20)	CTN SR 200MG VS. PLACEBO	4.52 (-7.22, 16.25)
							CTN SR 400MG VS. PLACEBO	5.07 (-6.62, 16.76)
	7	-2.82 (3.89)	7	-9.31 (3.92)	8	-8.44 (3.66)	CTN SR 200MG VS. PLACEBO	5.63 (-4.86, 16.11)
							CTN SR 400MG VS. PLACEBO	-0.87 (-11.4, 9.61)

[1] OVERALL TREATMENT DIFFERENCE IS DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT AND BASELINE VALUE AS COVARIATE; BY CENTER DIFFERENCES ARE DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT, TREATMENT BY CENTER INTERACTION, AND BASELINE VALUE AS COVARIATE.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centera.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.1 FINAL

CENTANAFADINE 4 OF 4
PROTOCOL 405-201-00013

STAT-4.5.1
Summary of Mean Change at Day 42 from Baseline in AISRS Total Score
By Center - LOCF (Efficacy Sample)

	AISRS TOTAL SCORE							
	CTN SR 200MG		CTN SR 400MG		PLACEBO			
CENTER	N	LS MEAN (SE)	N	LS MEAN (SE)	N	LS MEAN (SE)	TREATMENT COMPARISON	LS MEAN DIFFERENCE[1]
[redacted]	2	1.21 (7.28)	1	-14.2 (10.3)	1	-12.9 (10.3)	CTN SR 200MG VS. PLACEBO	14.16 (-10.7, 39.00)
							CTN SR 400MG VS. PLACEBO	-1.29 (-29.9, 27.35)
	2	-12.5 (7.29)	1	-1.36 (10.3)	1	-10.5 (10.3)	CTN SR 200MG VS. PLACEBO	-2.01 (-26.8, 22.82)
							CTN SR 400MG VS. PLACEBO	9.14 (-19.5, 37.78)
	1	-23.9 (10.3)	1	-1.23 (10.3)	2	-6.52 (7.31)	CTN SR 200MG VS. PLACEBO	-17.4 (-42.2, 7.37)
							CTN SR 400MG VS. PLACEBO	5.29 (-19.5, 30.11)

[1] OVERALL TREATMENT DIFFERENCE IS DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT AND BASELINE VALUE AS COVARIATE; BY CENTER DIFFERENCES ARE DERIVED USING ANCOVA MODEL, WITH TREATMENT AND CENTER AS MAIN EFFECT, TREATMENT BY CENTER INTERACTION, AND BASELINE VALUE AS COVARIATE.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centera.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.1 FINAL

CENTANAFADINE 1 OF 2
PROTOCOL 405-201-00013

STAT-4.5.2
Differences in Unadjusted Mean Changes of AISRS Total Score at Day 42 Among Treatment Groups
By Center - LOCF (Efficacy Sample)

CENTER	COUNTRY	CTN SR 200M N	CTN SR 200M MEAN[1]	CTN SR 400MG N	CTN SR 400MG MEAN[1]	PLACEBO N	PLACEBO MEAN[1]	CTN SR 200MG VS. PLACEBO DIFF[2]	CTN SR 400MG VS. PLACEBO DIFF[2]
[redacted]	USA	1	3.00	1	-21.00	1	-1.00	4.00	-20.00
	USA	5	-3.40	6	-18.00	6	-0.50	-2.90	-17.50
	USA	2	-19.50	2	-12.00	2	2.00	-21.50	-14.00
	USA	4	-11.00	3	-13.00	3	-0.33	-10.67	-12.67
	USA	3	0.33	3	-14.00	3	-3.00	3.33	-11.00
	USA	3	-10.33	2	-14.00	3	-3.67	-6.67	-10.33
	USA	13	-6.08	13	-11.38	12	-2.33	-3.74	-9.05
	USA	2	-2.50	2	-9.50	1	-1.00	-1.50	-8.50
	USA	4	-9.00	2	-9.00	4	-0.75	-8.25	-8.25
	USA	9	-8.22	8	-12.38	8	-4.75	-3.47	-7.63
	USA	1	-5.00	1	-1.00	1	6.00	-11.00	-7.00
	USA	1	-10.00	2	-15.00	1	-9.00	-1.00	-6.00
	USA	3	-20.00	4	-11.75	2	-6.50	-13.50	-5.25
	USA	5	-1.80	5	-15.60	6	-11.83	10.03	-3.77
	USA	3	-11.67	3	-16.33	3	-12.67	1.00	-3.67
	USA	5	-3.60	6	-13.00	4	-9.50	5.90	-3.50
	USA	2	-21.50	1	-4.00	1	-2.00	-19.50	-2.00
	USA	2	-9.50	1	-10.00	2	-8.50	-1.00	-1.50
	USA	2	1.00	1	-13.00	1	-12.00	13.00	-1.00
	USA	7	-2.57	7	-8.57	8	-7.88	5.30	-0.70
	USA	2	-15.50	2	-0.50	1	0.00	-15.50	-0.50
	USA	5	-12.40	5	-11.00	5	-10.80	-1.60	-0.20

[1] MEAN CHANGE FROM BASELINE AT DAY 42 (LOCF).
[2] DIFFERENCE IN MEAN CHANGES AT DAY 42 BETWEEN TWO TREATMENT GROUPS.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centerb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.2 FINAL

CENTANAFADINE 2 OF 2
PROTOCOL 405-201-00013

STAT-4.5.2
Differences in Unadjusted Mean Changes of AISRS Total Score at Day 42 Among Treatment Groups
By Center - LOCF (Efficacy Sample)

CENTER	COUNTRY	CTN SR 200M N	CTN SR 200M MEAN[1]	CTN SR 400MG N	CTN SR 400MG MEAN[1]	PLACEBO N	PLACEBO MEAN[1]	CTN SR 200MG VS. PLACEBO DIFF[2]	CTN SR 400MG VS. PLACEBO DIFF[2]
[redacted]	USA	9	-27.56	13	-15.62	12	-15.42	-12.14	-0.20
	USA	2	-7.50	2	-17.50	3	-17.67	10.17	0.17
	USA	7	-15.29	8	-5.63	7	-7.29	-8.00	1.66
	USA	11	-14.18	11	-4.00	10	-6.30	-7.88	2.30
	USA	2	-30.00	1	0.00	1	-3.00	-27.00	3.00
	USA	1	3.00	1	-24.00	1	-28.00	31.00	4.00
	USA	2	-7.50	1	5.00	2	1.00	-8.50	4.00
	USA	4	-9.75	4	-8.00	3	-12.33	2.58	4.33
	USA	7	-7.71	8	-1.75	8	-6.13	-1.59	4.38
	USA	1	-15.00	2	-9.50	2	-14.00	-1.00	4.50
	USA	1	-23.00	1	-1.00	2	-5.50	-17.50	4.50
	USA	6	-3.83	6	-4.00	6	-9.17	5.33	5.17
	USA	2	-3.00	2	3.50	2	-2.00	-1.00	5.50
	USA	3	-10.00	4	-7.25	3	-15.33	5.33	8.08
	USA	3	-8.33	2	-8.50	3	-16.67	8.33	8.17
	USA	2	-12.00	1	-2.00	1	-11.00	-1.00	9.00

[1] MEAN CHANGE FROM BASELINE AT DAY 42 (LOCF).
[2] DIFFERENCE IN MEAN CHANGES AT DAY 42 BETWEEN TWO TREATMENT GROUPS.
NOTE: FOR ANALYSIS PURPOSE, SMALL CENTERS ARE POOLED TOGETHER.

FILE: centerb.lis, RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.2 FINAL

CENTANAFADINE 1 OF 24
PROTOCOL 405-201-00013

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	143	-5.9580	8.6959	0.7272	-40.0000	8.0000
3	142	-4.8169	7.2284	0.6066	-32.0000	7.0000
Diff (1-2)		-1.1411	7.9985	0.9476		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-5.9580	-7.3955	-4.5205	8.6959	7.7914	9.8398
3		-4.8169	-6.0161	-3.6177	7.2284	6.4742	8.1831
Diff (1-2)	Pooled	-1.1411	-3.0063	0.7241	7.9985	7.3903	8.7165
Diff (1-2)	Satterthwaite	-1.1411	-3.0054	0.7231			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	283	-1.20	0.2295
Satterthwaite	Unequal	274.51	-1.21	0.2292

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	142	141	1.45	0.0287

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	147	-7.7823	9.5684	0.7892	-41.0000	7.0000
3	144	-6.9167	8.7909	0.7326	-36.0000	8.0000
Diff (1-2)		-0.8656	9.1919	1.0777		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-7.7823	-9.3420	-6.2226	9.5684	8.5855	10.8076
3		-6.9167	-8.3647	-5.4686	8.7909	7.8794	9.9427
Diff (1-2)	Pooled	-0.8656	-2.9869	1.2556	9.1919	8.4998	10.0078
Diff (1-2)	Satterthwaite	-0.8656	-2.9850	1.2537			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-0.80	0.4225
Satterthwaite	Unequal	287.82	-0.80	0.4221

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.18	0.3099

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=21 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	147	-8.5714	9.5530	0.7879	-40.0000	7.0000
3	144	-6.9792	8.8929	0.7411	-39.0000	7.0000
Diff (1-2)		-1.5923	9.2323	1.0825		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-8.5714	-10.1286	-7.0142	9.5530	8.5717	10.7901
3		-6.9792	-8.4440	-5.5143	8.8929	7.9708	10.0581
Diff (1-2)	Pooled	-1.5923	-3.7228	0.5383	9.2323	8.5371	10.0517
Diff (1-2)	Satterthwaite	-1.5923	-3.7212	0.5367			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-1.47	0.1424
Satterthwaite	Unequal	288.25	-1.47	0.1421

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=21 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.15	0.3909

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	147	-9.5578	11.2318	0.9264	-47.0000	8.0000
3	144	-6.8611	9.5972	0.7998	-50.0000	10.0000
Diff (1-2)		-2.6967	10.4550	1.2258		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-9.5578	-11.3887	-7.7270	11.2318	10.0780	12.6863
3		-6.8611	-8.4420	-5.2802	9.5972	8.6021	10.8547
Diff (1-2)	Pooled	-2.6967	-5.1094	-0.2840	10.4550	9.6677	11.3829
Diff (1-2)	Satterthwaite	-2.6967	-5.1057	-0.2877			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-2.20	0.0286
Satterthwaite	Unequal	283.79	-2.20	0.0284

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.37	0.0599

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	147	-10.0816	11.1358	0.9185	-46.0000	7.0000
3	144	-7.5694	10.1545	0.8462	-41.0000	11.0000
Diff (1-2)		-2.5122	10.6616	1.2501		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.0816	-11.8968	-8.2664	11.1358	9.9919	12.5779
3		-7.5694	-9.2421	-5.8967	10.1545	9.1016	11.4850
Diff (1-2)	Pooled	-2.5122	-4.9725	-0.0518	10.6616	9.8587	11.6079
Diff (1-2)	Satterthwaite	-2.5122	-4.9703	-0.0541			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-2.01	0.0454
Satterthwaite	Unequal	287.53	-2.01	0.0452

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=35 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.20	0.2691

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	147	-9.9728	11.8933	0.9809	-47.0000	7.0000
3	144	-7.4583	10.0960	0.8413	-50.0000	9.0000
Diff (1-2)		-2.5145	11.0406	1.2945		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-9.9728	-11.9115	-8.0341	11.8933	10.6716	13.4335
3		-7.4583	-9.1214	-5.7953	10.0960	9.0492	11.4188
Diff (1-2)	Pooled	-2.5145	-5.0623	0.0334	11.0406	10.2092	12.0205
Diff (1-2)	Satterthwaite	-2.5145	-5.0582	0.0293			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-1.94	0.0531
Satterthwaite	Unequal	283.29	-1.95	0.0527

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.39	0.0500

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	144	-4.7569	7.1088	0.5924	-29.0000	11.0000
3	142	-4.8169	7.2284	0.6066	-32.0000	7.0000
Diff (1-2)		0.0600	7.1684	0.8478		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-4.7569	-5.9279	-3.5860	7.1088	6.3717	8.0402
3		-4.8169	-6.0161	-3.6177	7.2284	6.4742	8.1831
Diff (1-2)	Pooled	0.0600	-1.6088	1.7287	7.1684	6.6243	7.8108
Diff (1-2)	Satterthwaite	0.0600	-1.6090	1.7289			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	284	0.07	0.9437
Satterthwaite	Unequal	283.73	0.07	0.9437

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=7 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	141	143	1.03	0.8423

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	147	-7.2245	8.6395	0.7126	-42.0000	11.0000
3	144	-6.9167	8.7909	0.7326	-36.0000	8.0000
Diff (1-2)		-0.3078	8.7147	1.0218		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-7.2245	-8.6328	-5.8162	8.6395	7.7520	9.7583
3		-6.9167	-8.3647	-5.4686	8.7909	7.8794	9.9427
Diff (1-2)	Pooled	-0.3078	-2.3189	1.7033	8.7147	8.0585	9.4882
Diff (1-2)	Satterthwaite	-0.3078	-2.3193	1.7036			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-0.30	0.7634
Satterthwaite	Unequal	288.58	-0.30	0.7635

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	143	146	1.04	0.8344

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	147	-8.6871	9.4643	0.7806	-41.0000	10.0000
3	144	-6.9792	8.8929	0.7411	-39.0000	7.0000
Diff (1-2)		-1.7079	9.1860	1.0770		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-8.6871	-10.2298	-7.1443	9.4643	8.4920	10.6899
3		-6.9792	-8.4440	-5.5143	8.8929	7.9708	10.0581
Diff (1-2)	Pooled	-1.7079	-3.8277	0.4119	9.1860	8.4943	10.0013
Diff (1-2)	Satterthwaite	-1.7079	-3.8264	0.4106			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-1.59	0.1139
Satterthwaite	Unequal	288.5	-1.59	0.1137

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=21 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.13	0.4555

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	147	-9.7143	10.6179	0.8757	-41.0000	10.0000
3	144	-6.8611	9.5972	0.7998	-50.0000	10.0000
Diff (1-2)		-2.8532	10.1257	1.1872		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-9.7143	-11.4451	-7.9835	10.6179	9.5272	11.9929
3		-6.8611	-8.4420	-5.2802	9.5972	8.6021	10.8547
Diff (1-2)	Pooled	-2.8532	-5.1899	-0.5165	10.1257	9.3632	11.0244
Diff (1-2)	Satterthwaite	-2.8532	-5.1875	-0.5188			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-2.40	0.0169
Satterthwaite	Unequal	287.16	-2.41	0.0168

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.22	0.2260

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	147	-10.6327	11.0094	0.9080	-43.0000	10.0000
3	144	-7.5694	10.1545	0.8462	-41.0000	11.0000
Diff (1-2)		-3.0632	10.5950	1.2422		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.6327	-12.4273	-8.8381	11.0094	9.8784	12.4351
3		-7.5694	-9.2421	-5.8967	10.1545	9.1016	11.4850
Diff (1-2)	Pooled	-3.0632	-5.5082	-0.6182	10.5950	9.7972	11.5354
Diff (1-2)	Satterthwaite	-3.0632	-5.5062	-0.6202			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-2.47	0.0142
Satterthwaite	Unequal	287.96	-2.47	0.0142

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.18	0.3328

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	147	-9.8571	10.3633	0.8547	-38.0000	10.0000
3	144	-7.4583	10.0960	0.8413	-50.0000	9.0000
Diff (1-2)		-2.3988	10.2319	1.1997		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-9.8571	-11.5464	-8.1679	10.3633	9.2987	11.7053
3		-7.4583	-9.1214	-5.7953	10.0960	9.0492	11.4188
Diff (1-2)	Pooled	-2.3988	-4.7600	-0.0376	10.2319	9.4614	11.1400
Diff (1-2)	Satterthwaite	-2.3988	-4.7594	-0.0383			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	289	-2.00	0.0465
Satterthwaite	Unequal	288.99	-2.00	0.0464

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

STAT-4.6
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

--- Analysis Visit (N)=42 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	146	143	1.05	0.7543

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 FINAL

CENTANAFADINE 1 OF 24
PROTOCOL 405-201-00013

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	143	-5.9580	8.6959	0.7272	-40.0000	8.0000
3	142	-4.8169	7.2284	0.6066	-32.0000	7.0000
Diff (1-2)		-1.1411	7.9985	0.9476		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-5.9580	-7.3955	-4.5205	8.6959	7.7914	9.8398
3		-4.8169	-6.0161	-3.6177	7.2284	6.4742	8.1831
Diff (1-2)	Pooled	-1.1411	-3.0063	0.7241	7.9985	7.3903	8.7165
Diff (1-2)	Satterthwaite	-1.1411	-3.0054	0.7231			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	283	-1.20	0.2295
Satterthwaite	Unequal	274.51	-1.21	0.2292

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	142	141	1.45	0.0287

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=14 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	133	-7.9699	9.5932	0.8318	-41.0000	7.0000
3	136	-7.0588	8.9648	0.7687	-36.0000	8.0000
Diff (1-2)		-0.9111	9.2808	1.1318		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-7.9699	-9.6154	-6.3245	9.5932	8.5624	10.9084
3		-7.0588	-8.5791	-5.5385	8.9648	8.0111	10.1782
Diff (1-2)	Pooled	-0.9111	-3.1395	1.3173	9.2808	8.5559	10.1408
Diff (1-2)	Satterthwaite	-0.9111	-3.1412	1.3190			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	267	-0.81	0.4215
Satterthwaite	Unequal	264.86	-0.80	0.4219

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=14 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	132	135	1.15	0.4343

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	124	-8.8871	9.8346	0.8832	-40.0000	4.0000
3	134	-7.2910	9.1255	0.7883	-39.0000	7.0000
Diff (1-2)		-1.5961	9.4728	1.1804		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-8.8871	-10.6353	-7.1389	9.8346	8.7442	11.2381
3		-7.2910	-8.8503	-5.7318	9.1255	8.1483	10.3713
Diff (1-2)	Pooled	-1.5961	-3.9206	0.7285	9.4728	8.7186	10.3711
Diff (1-2)	Satterthwaite	-1.5961	-3.9276	0.7355			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	256	-1.35	0.1775
Satterthwaite	Unequal	250.2	-1.35	0.1788

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	123	133	1.16	0.3970

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=28 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	117	-10.4444	11.9391	1.1038	-47.0000	8.0000
3	129	-7.2093	10.0122	0.8815	-50.0000	10.0000
Diff (1-2)		-3.2351	10.9706	1.4006		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.4444	-12.6306	-8.2583	11.9391	10.5806	13.7010
3		-7.2093	-8.9536	-5.4650	10.0122	8.9216	11.4091
Diff (1-2)	Pooled	-3.2351	-5.9939	-0.4764	10.9706	10.0776	12.0386
Diff (1-2)	Satterthwaite	-3.2351	-6.0186	-0.4517			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	244	-2.31	0.0217
Satterthwaite	Unequal	227.35	-2.29	0.0229

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	116	128	1.42	0.0522

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	113	-10.8761	11.7975	1.1098	-46.0000	6.0000
3	122	-8.1721	10.4405	0.9452	-41.0000	11.0000
Diff (1-2)		-2.7040	11.1135	1.4510		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.8761	-13.0751	-8.6771	11.7975	10.4342	13.5739
3		-8.1721	-10.0435	-6.3008	10.4405	9.2744	11.9445
Diff (1-2)	Pooled	-2.7040	-5.5627	0.1548	11.1135	10.1895	12.2231
Diff (1-2)	Satterthwaite	-2.7040	-5.5767	0.1688			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	233	-1.86	0.0636
Satterthwaite	Unequal	224.22	-1.85	0.0649

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=35 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	112	121	1.28	0.1875

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=42 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	109	-10.8349	12.9332	1.2388	-47.0000	7.0000
3	119	-7.7815	10.5358	0.9658	-50.0000	9.0000
Diff (1-2)		-3.0533	11.7427	1.5569		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.8349	-13.2903	-8.3794	12.9332	11.4145	14.9218
3		-7.7815	-9.6941	-5.8689	10.5358	9.3460	12.0755
Diff (1-2)	Pooled	-3.0533	-6.1212	0.0145	11.7427	10.7527	12.9350
Diff (1-2)	Satterthwaite	-3.0533	-6.1500	0.0433			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	226	-1.96	0.0511
Satterthwaite	Unequal	208.64	-1.94	0.0533

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=42 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	108	118	1.51	0.0297

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	144	-4.7569	7.1088	0.5924	-29.0000	11.0000
3	142	-4.8169	7.2284	0.6066	-32.0000	7.0000
Diff (1-2)		0.0600	7.1684	0.8478		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-4.7569	-5.9279	-3.5860	7.1088	6.3717	8.0402
3		-4.8169	-6.0161	-3.6177	7.2284	6.4742	8.1831
Diff (1-2)	Pooled	0.0600	-1.6088	1.7287	7.1684	6.6243	7.8108
Diff (1-2)	Satterthwaite	0.0600	-1.6090	1.7289			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	284	0.07	0.9437
Satterthwaite	Unequal	283.73	0.07	0.9437

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	141	143	1.03	0.8423

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	137	-7.5985	8.7737	0.7496	-42.0000	11.0000
3	136	-7.0588	8.9648	0.7687	-36.0000	8.0000
Diff (1-2)		-0.5397	8.8694	1.0736		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-7.5985	-9.0809	-6.1162	8.7737	7.8434	9.9563
3		-7.0588	-8.5791	-5.5385	8.9648	8.0111	10.1782
Diff (1-2)	Pooled	-0.5397	-2.6534	1.5740	8.8694	8.1814	9.6847
Diff (1-2)	Satterthwaite	-0.5397	-2.6536	1.5741			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	271	-0.50	0.6156
Satterthwaite	Unequal	270.77	-0.50	0.6156

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=14 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	135	136	1.04	0.8022

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=21 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	133	-9.0902	9.5691	0.8297	-41.0000	10.0000
3	134	-7.2910	9.1255	0.7883	-39.0000	7.0000
Diff (1-2)		-1.7992	9.3491	1.1443		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-9.0902	-10.7315	-7.4489	9.5691	8.5409	10.8810
3		-7.2910	-8.8503	-5.7318	9.1255	8.1483	10.3713
Diff (1-2)	Pooled	-1.7992	-4.0523	0.4539	9.3491	8.6164	10.2191
Diff (1-2)	Satterthwaite	-1.7992	-4.0527	0.4544			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	265	-1.57	0.1171
Satterthwaite	Unequal	264.2	-1.57	0.1171

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=21 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	132	133	1.10	0.5855

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=28 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	124	-10.6452	10.9092	0.9797	-41.0000	10.0000
3	129	-7.2093	10.0122	0.8815	-50.0000	10.0000
Diff (1-2)		-3.4359	10.4614	1.3157		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.6452	-12.5844	-8.7059	10.9092	9.6997	12.4662
3		-7.2093	-8.9536	-5.4650	10.0122	8.9216	11.4091
Diff (1-2)	Pooled	-3.4359	-6.0270	-0.8447	10.4614	9.6208	11.4642
Diff (1-2)	Satterthwaite	-3.4359	-6.0316	-0.8401			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	251	-2.61	0.0096
Satterthwaite	Unequal	247.13	-2.61	0.0097

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	123	128	1.19	0.3369

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	114	-12.0263	11.1993	1.0489	-43.0000	10.0000
3	122	-8.1721	10.4405	0.9452	-41.0000	11.0000
Diff (1-2)		-3.8542	10.8136	1.4086		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-12.0263	-14.1044	-9.9482	11.1993	9.9101	12.8770
3		-8.1721	-10.0435	-6.3008	10.4405	9.2744	11.9445
Diff (1-2)	Pooled	-3.8542	-6.6294	-1.0790	10.8136	9.9163	11.8907
Diff (1-2)	Satterthwaite	-3.8542	-6.6363	-1.0721			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	234	-2.74	0.0067
Satterthwaite	Unequal	229.63	-2.73	0.0068

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

--- Analysis Visit (N)=35 ---

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	113	121	1.15	0.4477

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	119	-10.8908	10.6276	0.9742	-38.0000	10.0000
3	119	-7.7815	10.5358	0.9658	-50.0000	9.0000
Diff (1-2)		-3.1092	10.5818	1.3718		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.8908	-12.8200	-8.9615	10.6276	9.4274	12.1807
3		-7.7815	-9.6941	-5.8689	10.5358	9.3460	12.0755
Diff (1-2)	Pooled	-3.1092	-5.8118	-0.4066	10.5818	9.7072	11.6310
Diff (1-2)	Satterthwaite	-3.1092	-5.8118	-0.4066			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	236	-2.27	0.0243
Satterthwaite	Unequal	235.98	-2.27	0.0243

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.7
Unadjusted Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, OC
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The TTEST Procedure

Variable: CHG (Change from Baseline)

Equality of Variances

Method	Num DF	Den DF	F Value	Pr > F
Folded F	118	118	1.02	0.9251

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.7 FINAL

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	1.0718	0.3005
2	Row Mean Scores Differ	2	1.7562	0.4156

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	0.7626	0.3825
2	Row Mean Scores Differ	2	1.6961	0.4283

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	1.0930	0.2958
2	Row Mean Scores Differ	2	1.6783	0.4321

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	3.4385	0.0637
2	Row Mean Scores Differ	2	5.1565	0.0759

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

CENTANAFADINE 5 OF 6
PROTOCOL 405-201-00013

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	3.8708	0.0491
2	Row Mean Scores Differ	2	6.2158	0.0447

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

CENTANAFADINE 6 OF 6
PROTOCOL 405-201-00013

STAT-4.8
Non-Parametric Stratified by Center Analysis of Mean Change from Baseline to Double Blind Tretmnet Period by Study Day in AISRS Total Score, LOCF
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The FREQ Procedure

Summary Statistics for TRTP by CHG
Controlling for POOLCNTR

Cochran-Mantel-Haenszel Statistics (Based on Rank Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	3.0224	0.0821
2	Row Mean Scores Differ	2	3.9747	0.1371

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: RESID (Residual)
AVISITN = 42
AVISIT = DAY 42

Moments

N	347	Sum Weights	347
Mean	-0.3635827	Sum Observations	-126.16319
Std Deviation	10.8189753	Variance	117.050226
Skewness	-0.8029258	Kurtosis	0.15184193
Uncorrected SS	40545.2491	Corrected SS	40499.3783
Coeff Variation	-2975.6575	Std Error Mean	0.58079302

Basic Statistical Measures

Location		Variability	
Mean	-0.36358	Std Deviation	10.81898
Median	1.86002	Variance	117.05023
Mode	0.60473	Range	53.83629
		Interquartile Range	14.88131

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: RESID (Residual)
AVISITN = 42
AVISIT = DAY 42

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.62601	Pr > |t|	0.5317
Sign	M	28.5	Pr >= |M|	0.0026
Signed Rank	S	1596	Pr >= |S|	0.3942

Quantiles (Definition 5)

Level	Quantile
100% Max	19.94892
99%	17.59826
95%	13.42180
90%	11.14587
75% Q3	7.91676
50% Median	1.86002
25% Q1	-6.96455
10%	-15.95262
5%	-21.57855
1%	-31.78702
0% Min	-33.88736

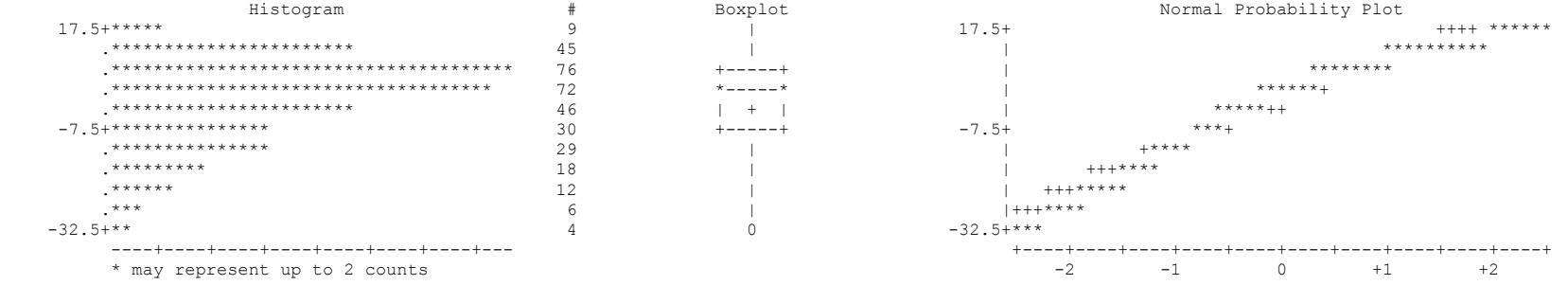
SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.9 FINAL

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: RESID (Residual)
AVISITN = 42
AVISIT = DAY 42

Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-33.8874	1677	16.6970	714
-33.3787	1554	17.5983	1295
-33.1571	411	18.8332	2204
-31.7870	1798	19.4803	2243
-28.1267	1406	19.9489	1355



SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.9 FINAL

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

Moments

N	347	Sum Weights	347
Mean	-0.0353861	Sum Observations	-12.278976
Std Deviation	1.02339086	Variance	1.04732886
Skewness	-0.8014075	Kurtosis	0.14366209
Uncorrected SS	362.810289	Corrected SS	362.375784
Coeff Variation	-2892.0705	Std Error Mean	0.0549385

Basic Statistical Measures

Location		Variability	
Mean	-0.03539	Std Deviation	1.02339
Median	0.17390	Variance	1.04733
Mode	0.05664	Range	5.12952
		Interquartile Range	1.41016

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.6441	Pr > |t|	0.5199
Sign	M	28.5	Pr >= |M|	0.0026
Signed Rank	S	1567	Pr >= |S|	0.4028

Quantiles (Definition 5)

Level	Quantile
100% Max	1.902521
99%	1.671961
95%	1.269575
90%	1.049981
75% Q3	0.749161
50% Median	0.173896
25% Q1	-0.660998
10%	-1.496158
5%	-2.066916
1%	-2.976287
0% Min	-3.227003

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

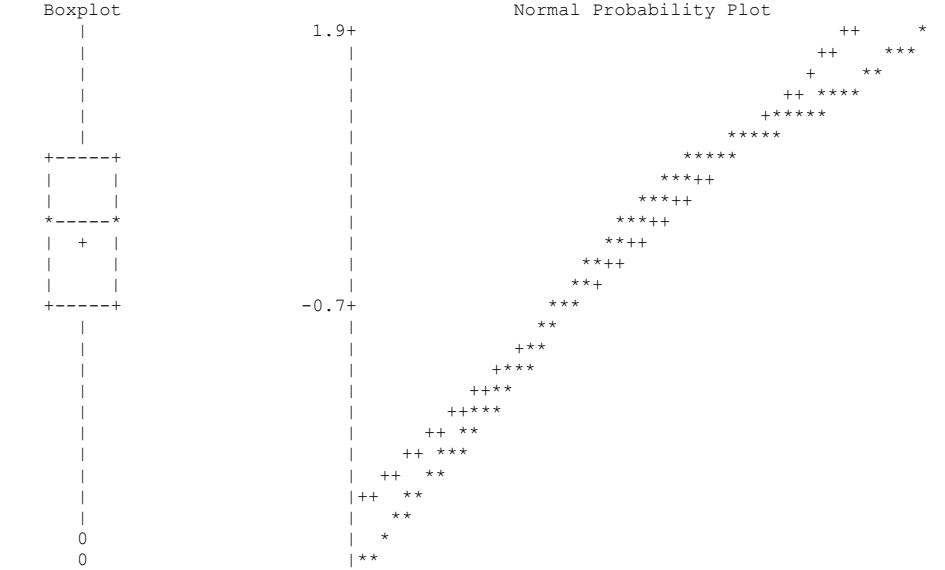
Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-3.22700	1677	1.65677	1295
-3.14078	1554	1.67196	714
-3.10521	411	1.76566	2204
-2.97629	1798	1.82508	2243
-2.70089	1406	1.90252	1355

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

Stem	Leaf	#	Boxplot
18	30	2	
16	677	3	
14	5711	4	
12	16777700777	11	
10	00011123555667711666789	23	
8	000012566777889000112344555555666778	36	
6	00011222333445566778899112222355556788	38	
4	11112234458888911146689	24	
2	013455667788899904455566678888	31	
0	11122334566667790012244556779	30	
-0	9753329887665443322	19	
-2	977654111998877631	18	
-4	99855427665543000	17	
-6	88652998765321	14	
-8	86541766431	11	
-10	8755332865333	13	
-12	76407765541	11	
-14	3007666310	10	
-16	985100642	9	
-18	977	3	
-20	4418720	7	
-22	7865	4	
-24	105	3	
-26	03	2	
-28	8	1	
-30	41	2	



SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.9 FINAL

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

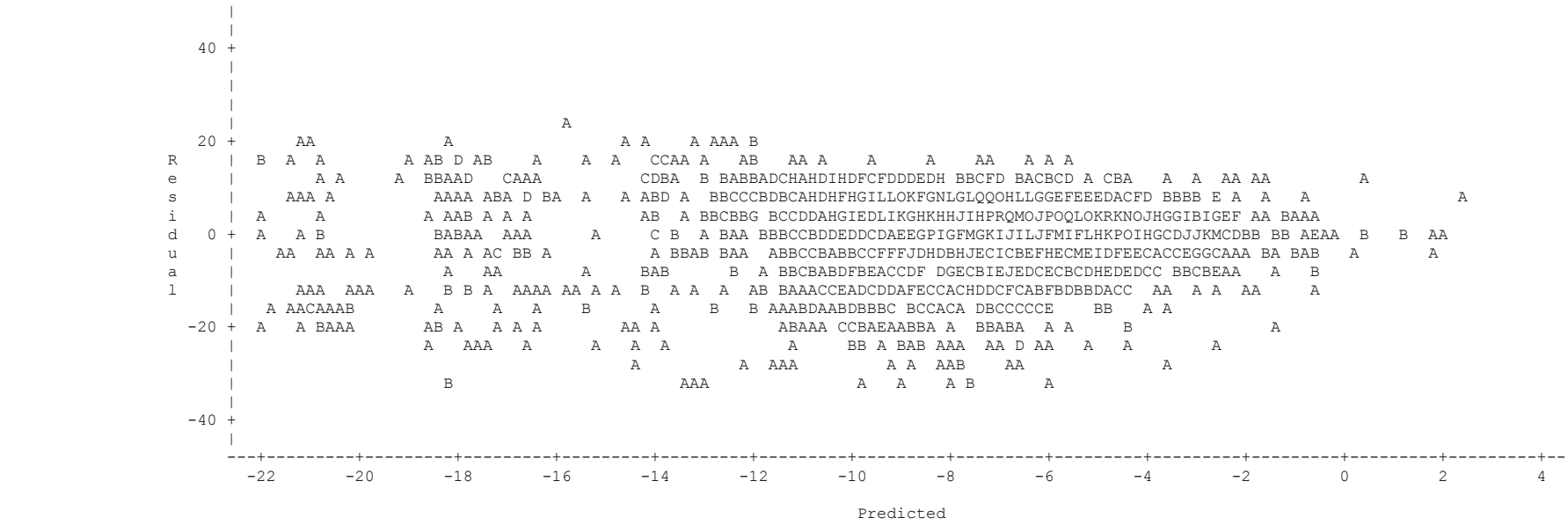
```
      -32 3                                    1               0                  -3.3+*
          ----+----+----+----+----+----+----+---                                      +----+----+----+----+----+----+----+----+----+----+
      Multiply Stem.Leaf by 10**-1                                                        -2        -1         0        +1        +2
```

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.9 FINAL

CENTANAFADINE 9 OF 9
PROTOCOL 405-201-00013

STAT-4.9
Residual at Day 42 from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

Plot of RESID*PRED. Legend: A = 1 obs, B = 2 obs, etc.



SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.9 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Group Effect	TRTPN
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Class Level Information

Class	Levels	Values
SUBJID	438	[redacted]

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

[redacted]

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

[redacted]

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

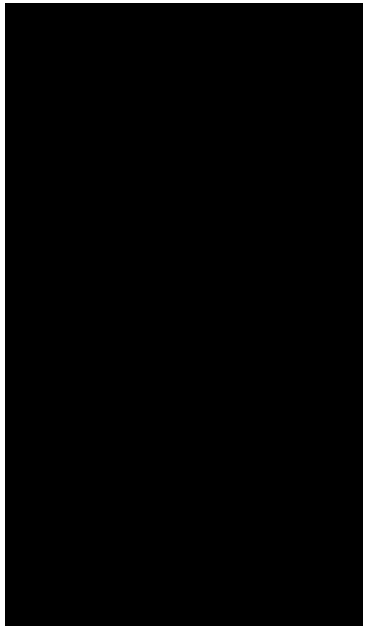
[redacted]

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure



SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

[redacted]

Dimensions

Covariance Parameters	63
Columns in X	72
Columns in Z	0
Subjects	438
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2292
Number of Observations Used	2292
Number of Observations Not Used	0

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	16529.25629156	
1	2	14188.42661779	0.00057908
2	1	14185.23002848	0.00001628
3	1	14185.14601175	0.00000002
4	1	14185.14589278	0.00000000

Convergence criteria met.

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	46.0381	41.1715	36.7487	32.9053	36.5459	38.5770
2	41.1715	72.3189	63.2366	57.9165	61.0600	61.5916
3	36.7487	63.2366	85.0775	79.2283	82.7270	77.0389
4	32.9053	57.9165	79.2283	109.98	96.5075	92.0782
5	36.5459	61.0600	82.7270	96.5075	108.06	90.3451
6	38.5770	61.5916	77.0389	92.0782	90.3451	107.13

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimated R Correlation Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	1.0000	0.7135	0.5872	0.4624	0.5182	0.5493
2	0.7135	1.0000	0.8062	0.6494	0.6907	0.6997
3	0.5872	0.8062	1.0000	0.8191	0.8628	0.8069
4	0.4624	0.6494	0.8191	1.0000	0.8853	0.8483
5	0.5182	0.6907	0.8628	0.8853	1.0000	0.8397
6	0.5493	0.6997	0.8069	0.8483	0.8397	1.0000

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	65.6662	44.0115	46.3127	47.7634	47.6829	43.0330
2	44.0115	78.8090	65.0532	70.3450	71.8874	74.0759
3	46.3127	65.0532	84.1997	82.8999	84.5571	87.9428
4	47.7634	70.3450	82.8999	117.91	107.76	115.71
5	47.6829	71.8874	84.5571	107.76	118.69	119.10
6	43.0330	74.0759	87.9428	115.71	119.10	146.06

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	46.3693	34.8314	31.0449	30.9025	30.4290	32.7595
2	34.8314	65.0980	57.0928	58.3247	56.0968	55.8943
3	31.0449	57.0928	73.8230	68.5633	73.5792	69.9148
4	30.9025	58.3247	68.5633	88.3257	83.0181	81.2208
5	30.4290	56.0968	73.5792	83.0181	104.07	88.0138
6	32.7595	55.8943	69.9148	81.2208	88.0138	99.0964

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
UN(1,1)	SUBJID	TRTPN 1	65.6662
UN(2,1)	SUBJID	TRTPN 1	44.0115
UN(2,2)	SUBJID	TRTPN 1	78.8090
UN(3,1)	SUBJID	TRTPN 1	46.3127
UN(3,2)	SUBJID	TRTPN 1	65.0532
UN(3,3)	SUBJID	TRTPN 1	84.1997
UN(4,1)	SUBJID	TRTPN 1	47.7634
UN(4,2)	SUBJID	TRTPN 1	70.3450
UN(4,3)	SUBJID	TRTPN 1	82.8999
UN(4,4)	SUBJID	TRTPN 1	117.91
UN(5,1)	SUBJID	TRTPN 1	47.6829
UN(5,2)	SUBJID	TRTPN 1	71.8874

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
UN(5,3)	SUBJID	TRTPN 1	84.5571
UN(5,4)	SUBJID	TRTPN 1	107.76
UN(5,5)	SUBJID	TRTPN 1	118.69
UN(6,1)	SUBJID	TRTPN 1	43.0330
UN(6,2)	SUBJID	TRTPN 1	74.0759
UN(6,3)	SUBJID	TRTPN 1	87.9428
UN(6,4)	SUBJID	TRTPN 1	115.71
UN(6,5)	SUBJID	TRTPN 1	119.10
UN(6,6)	SUBJID	TRTPN 1	146.06
UN(1,1)	SUBJID	TRTPN 2	46.0381
UN(2,1)	SUBJID	TRTPN 2	41.1715
UN(2,2)	SUBJID	TRTPN 2	72.3189
UN(3,1)	SUBJID	TRTPN 2	36.7487
UN(3,2)	SUBJID	TRTPN 2	63.2366
UN(3,3)	SUBJID	TRTPN 2	85.0775
UN(4,1)	SUBJID	TRTPN 2	32.9053
UN(4,2)	SUBJID	TRTPN 2	57.9165
UN(4,3)	SUBJID	TRTPN 2	79.2283
UN(4,4)	SUBJID	TRTPN 2	109.98
UN(5,1)	SUBJID	TRTPN 2	36.5459
UN(5,2)	SUBJID	TRTPN 2	61.0600
UN(5,3)	SUBJID	TRTPN 2	82.7270
UN(5,4)	SUBJID	TRTPN 2	96.5075
UN(5,5)	SUBJID	TRTPN 2	108.06

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
UN(6,1)	SUBJID	TRTPN 2	38.5770
UN(6,2)	SUBJID	TRTPN 2	61.5916
UN(6,3)	SUBJID	TRTPN 2	77.0389
UN(6,4)	SUBJID	TRTPN 2	92.0782
UN(6,5)	SUBJID	TRTPN 2	90.3451
UN(6,6)	SUBJID	TRTPN 2	107.13
UN(1,1)	SUBJID	TRTPN 3	46.3693
UN(2,1)	SUBJID	TRTPN 3	34.8314
UN(2,2)	SUBJID	TRTPN 3	65.0980
UN(3,1)	SUBJID	TRTPN 3	31.0449
UN(3,2)	SUBJID	TRTPN 3	57.0928
UN(3,3)	SUBJID	TRTPN 3	73.8230
UN(4,1)	SUBJID	TRTPN 3	30.9025
UN(4,2)	SUBJID	TRTPN 3	58.3247
UN(4,3)	SUBJID	TRTPN 3	68.5633
UN(4,4)	SUBJID	TRTPN 3	88.3257
UN(5,1)	SUBJID	TRTPN 3	30.4290
UN(5,2)	SUBJID	TRTPN 3	56.0968
UN(5,3)	SUBJID	TRTPN 3	73.5792
UN(5,4)	SUBJID	TRTPN 3	83.0181
UN(5,5)	SUBJID	TRTPN 3	104.07
UN(6,1)	SUBJID	TRTPN 3	32.7595
UN(6,2)	SUBJID	TRTPN 3	55.8943
UN(6,3)	SUBJID	TRTPN 3	69.9148

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
UN(6,4)	SUBJID	TRTPN 3	81.2208
UN(6,5)	SUBJID	TRTPN 3	88.0138
UN(6,6)	SUBJID	TRTPN 3	99.0964

Fit Statistics

-2 Res Log Likelihood	14185.1
AIC (Smaller is Better)	14311.1
AICC (Smaller is Better)	14314.9
BIC (Smaller is Better)	14568.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
62	2344.11	<.0001

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept				0.4124	4.8142	479	0.09	0.9318
AVISITN		7		-0.8831	2.8978	372	-0.30	0.7607
AVISITN		14		-0.7454	2.4446	354	-0.30	0.7606
AVISITN		21		-2.9398	2.0177	326	-1.46	0.1461
AVISITN		28		2.5080	1.7494	323	1.43	0.1526
AVISITN		35		0.3320	1.7659	337	0.19	0.8510
AVISITN		42		0				
TRTPN			1	-3.0330	1.3769	249	-2.20	0.0285
TRTPN			2	-2.7565	1.2456	260	-2.21	0.0278
TRTPN			3	0				
AVISITN*TRTPN		7	1	1.7304	1.2761	241	1.36	0.1764
AVISITN*TRTPN		7	2	2.8863	1.0986	274	2.63	0.0091
AVISITN*TRTPN		7	3	0				
AVISITN*TRTPN		14	1	2.0397	1.0425	235	1.96	0.0516
AVISITN*TRTPN		14	2	2.4871	0.9315	261	2.67	0.0081
AVISITN*TRTPN		14	3	0				
AVISITN*TRTPN		21	1	1.0810	0.8683	218	1.24	0.2145
AVISITN*TRTPN		21	2	0.9914	0.7662	241	1.29	0.1969
AVISITN*TRTPN		21	3	0				
AVISITN*TRTPN		28	1	-0.3136	0.7115	221	-0.44	0.6598
AVISITN*TRTPN		28	2	-0.5811	0.6981	233	-0.83	0.4061
AVISITN*TRTPN		28	3	0				

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
AVISITN*TRTPN		35	1	-0.02212	0.6892	228	-0.03	0.9744
AVISITN*TRTPN		35	2	-0.7416	0.7276	234	-1.02	0.3091
AVISITN*TRTPN		35	3	0				
AVISITN*TRTPN		42	1	0				
AVISITN*TRTPN		42	2	0				
AVISITN*TRTPN		42	3	0				
POOLCNTR	[redacted]			-1.3093	3.9540	335	-0.33	0.7408
POOLCNTR				-0.7279	3.8546	333	-0.19	0.8503
POOLCNTR				-1.6459	3.9898	337	-0.41	0.6802
POOLCNTR				-1.6408	3.7641	330	-0.44	0.6632
POOLCNTR				-1.6465	3.8229	333	-0.43	0.6670
POOLCNTR				-2.4145	4.3086	350	-0.56	0.5756
POOLCNTR				-6.6124	4.3891	343	-1.51	0.1328
POOLCNTR				-7.0649	5.4521	366	-1.30	0.1959
POOLCNTR				-5.7267	3.9888	333	-1.44	0.1520
POOLCNTR				-2.2694	4.8320	342	-0.47	0.6389
POOLCNTR				-3.1596	3.7355	330	-0.85	0.3983
POOLCNTR				-6.0142	4.1721	353	-1.44	0.1503
POOLCNTR				0.8807	4.2539	340	0.21	0.8361
POOLCNTR				-3.8300	4.2304	355	-0.91	0.3659
POOLCNTR				-2.5117	4.3115	345	-0.58	0.5606
POOLCNTR				-2.7422	4.8000	380	-0.57	0.5681

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
POOLCNTR	[redacted]			-2.6550	3.9942	344	-0.66	0.5067
POOLCNTR				-5.0193	4.3859	342	-1.14	0.2533
POOLCNTR				0.07424	5.4356	368	0.01	0.9891
POOLCNTR				-2.1018	4.4549	338	-0.47	0.6374
POOLCNTR				-4.1304	5.1284	376	-0.81	0.4211
POOLCNTR				0.3290	4.7835	343	0.07	0.9452
POOLCNTR				-1.2695	4.8590	375	-0.26	0.7940
POOLCNTR				-3.0686	4.5967	355	-0.67	0.5048
POOLCNTR				-2.1150	3.8922	338	-0.54	0.5872
POOLCNTR				-4.1346	4.2846	359	-0.96	0.3352
POOLCNTR				-4.7395	4.1998	347	-1.13	0.2599
POOLCNTR				-4.0008	4.7432	345	-0.84	0.3995
POOLCNTR				-11.9023	3.8364	333	-3.10	0.0021
POOLCNTR				2.1419	5.4591	363	0.39	0.6950
POOLCNTR				3.1038	4.6133	353	0.67	0.5015
POOLCNTR				-2.8280	5.0206	357	-0.56	0.5736
POOLCNTR				-2.0196	5.1661	388	-0.39	0.6961
POOLCNTR				-1.0234	3.9312	338	-0.26	0.7948
POOLCNTR				-5.1194	3.8469	331	-1.33	0.1842
POOLCNTR				-1.7274	5.0914	377	-0.34	0.7346
POOLCNTR				-1.2967	5.0881	378	-0.25	0.7990
POOLCNTR				0				

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Solution for Fixed Effects

Effect	Pooled Center Number	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|
BASE*AVISITN		7		-0.02539	0.06167	394	-0.41	0.6808
BASE*AVISITN		14		-0.08601	0.07029	442	-1.22	0.2217
BASE*AVISITN		21		-0.03257	0.07393	445	-0.44	0.6597
BASE*AVISITN		28		-0.1639	0.08209	447	-2.00	0.0465
BASE*AVISITN		35		-0.1325	0.08419	458	-1.57	0.1163
BASE*AVISITN		42		-0.1191	0.08648	447	-1.38	0.1690

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	369	1.80	0.1124
TRTPN	2	259	3.15	0.0444
AVISITN*TRTPN	10	316	1.70	0.0795
POOLCNTR	37	387	2.00	0.0007
BASE*AVISITN	6	392	1.99	0.0662

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	1	-5.4621	0.7260	152	-7.52	<.0001	0.05	-6.8964	-4.0278
AVISITN*TRTPN	7	2	-4.0298	0.6402	174	-6.29	<.0001	0.05	-5.2934	-2.7661
AVISITN*TRTPN	7	3	-4.1595	0.6417	166	-6.48	<.0001	0.05	-5.4263	-2.8926
AVISITN*TRTPN	14	1	-7.4177	0.7968	154	-9.31	<.0001	0.05	-8.9917	-5.8437
AVISITN*TRTPN	14	2	-6.6938	0.7750	166	-8.64	<.0001	0.05	-8.2239	-5.1637
AVISITN*TRTPN	14	3	-6.4243	0.7445	165	-8.63	<.0001	0.05	-7.8943	-4.9544
AVISITN*TRTPN	21	1	-8.4528	0.8292	144	-10.19	<.0001	0.05	-10.0918	-6.8137
AVISITN*TRTPN	21	2	-8.2660	0.8380	158	-9.86	<.0001	0.05	-9.9212	-6.6108
AVISITN*TRTPN	21	3	-6.5008	0.7887	165	-8.24	<.0001	0.05	-8.0580	-4.9436
AVISITN*TRTPN	28	1	-9.6039	0.9837	145	-9.76	<.0001	0.05	-11.5482	-7.6596
AVISITN*TRTPN	28	2	-9.5949	0.9555	153	-10.04	<.0001	0.05	-11.4827	-7.7071
AVISITN*TRTPN	28	3	-6.2572	0.8577	160	-7.30	<.0001	0.05	-7.9511	-4.5634
AVISITN*TRTPN	35	1	-10.2433	0.9879	145	-10.37	<.0001	0.05	-12.1959	-8.2908
AVISITN*TRTPN	35	2	-10.6864	0.9502	152	-11.25	<.0001	0.05	-12.5638	-8.8090
AVISITN*TRTPN	35	3	-7.1882	0.9300	159	-7.73	<.0001	0.05	-9.0250	-5.3515
AVISITN*TRTPN	42	1	-10.0246	1.1034	141	-9.09	<.0001	0.05	-12.2058	-7.8433
AVISITN*TRTPN	42	2	-9.7481	0.9464	155	-10.30	<.0001	0.05	-11.6176	-7.8787
AVISITN*TRTPN	42	3	-6.9916	0.9122	159	-7.66	<.0001	0.05	-8.7932	-5.1899

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	1	7	2	-1.4324	0.8834	249	-1.62	0.1062	0.05	-3.1723	0.3075
AVISITN*TRTPN	7	1	7	3	-1.3027	0.8872	253	-1.47	0.1433	0.05	-3.0499	0.4446
AVISITN*TRTPN	7	1	14	1	1.9555	0.6484	129	3.02	0.0031	0.05	0.6726	3.2385
AVISITN*TRTPN	7	1	14	2	1.2316	0.9852	263	1.25	0.2124	0.05	-0.7083	3.1716
AVISITN*TRTPN	7	1	14	3	0.9622	0.9628	263	1.00	0.3186	0.05	-0.9337	2.8580
AVISITN*TRTPN	7	1	21	1	2.9906	0.6630	136	4.51	<.0001	0.05	1.6796	4.3017
AVISITN*TRTPN	7	1	21	2	2.8038	1.0353	258	2.71	0.0072	0.05	0.7650	4.8426
AVISITN*TRTPN	7	1	21	3	1.0387	0.9969	266	1.04	0.2984	0.05	-0.9242	3.0015
AVISITN*TRTPN	7	1	28	1	4.1417	0.8366	125	4.95	<.0001	0.05	2.4860	5.7975
AVISITN*TRTPN	7	1	28	2	4.1328	1.1322	242	3.65	0.0003	0.05	1.9026	6.3630
AVISITN*TRTPN	7	1	28	3	0.7951	1.0524	262	0.76	0.4506	0.05	-1.2771	2.8673
AVISITN*TRTPN	7	1	35	1	4.7812	0.8422	126	5.68	<.0001	0.05	3.1144	6.4480
AVISITN*TRTPN	7	1	35	2	5.2243	1.1280	240	4.63	<.0001	0.05	3.0022	7.4463
AVISITN*TRTPN	7	1	35	3	1.7261	1.1120	255	1.55	0.1219	0.05	-0.4638	3.9160
AVISITN*TRTPN	7	1	42	1	4.5625	1.0080	124	4.53	<.0001	0.05	2.5674	6.5575
AVISITN*TRTPN	7	1	42	2	4.2860	1.1248	243	3.81	0.0002	0.05	2.0703	6.5017
AVISITN*TRTPN	7	1	42	3	1.5294	1.0974	255	1.39	0.1646	0.05	-0.6317	3.6905
AVISITN*TRTPN	7	2	7	3	0.1297	0.8064	260	0.16	0.8723	0.05	-1.4582	1.7177
AVISITN*TRTPN	7	2	14	1	3.3879	0.9433	247	3.59	0.0004	0.05	1.5300	5.2459
AVISITN*TRTPN	7	2	14	2	2.6640	0.5142	139	5.18	<.0001	0.05	1.6473	3.6807
AVISITN*TRTPN	7	2	14	3	2.3946	0.8886	255	2.69	0.0075	0.05	0.6447	4.1445
AVISITN*TRTPN	7	2	21	1	4.4230	0.9707	233	4.56	<.0001	0.05	2.5105	6.3355

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	2	21	2	4.2362	0.6527	138	6.49	<.0001	0.05	2.9457	5.5267
AVISITN*TRTPN	7	2	21	3	2.4711	0.9253	248	2.67	0.0081	0.05	0.6486	4.2936
AVISITN*TRTPN	7	2	28	1	5.5741	1.1055	214	5.04	<.0001	0.05	3.3950	7.7532
AVISITN*TRTPN	7	2	28	2	5.5651	0.8296	133	6.71	<.0001	0.05	3.9243	7.2060
AVISITN*TRTPN	7	2	28	3	2.2275	0.9848	232	2.26	0.0246	0.05	0.2872	4.1678
AVISITN*TRTPN	7	2	35	1	6.2136	1.1092	214	5.60	<.0001	0.05	4.0273	8.3998
AVISITN*TRTPN	7	2	35	2	6.6566	0.7932	130	8.39	<.0001	0.05	5.0873	8.2260
AVISITN*TRTPN	7	2	35	3	3.1585	1.0483	227	3.01	0.0029	0.05	1.0928	5.2241
AVISITN*TRTPN	7	2	42	1	5.9948	1.2133	198	4.94	<.0001	0.05	3.6023	8.3874
AVISITN*TRTPN	7	2	42	2	5.7184	0.7711	134	7.42	<.0001	0.05	4.1932	7.2435
AVISITN*TRTPN	7	2	42	3	2.9618	1.0328	226	2.87	0.0045	0.05	0.9267	4.9970
AVISITN*TRTPN	7	3	14	1	3.2582	0.9468	250	3.44	0.0007	0.05	1.3935	5.1229
AVISITN*TRTPN	7	3	14	2	2.5343	0.9168	245	2.76	0.0061	0.05	0.7286	4.3400
AVISITN*TRTPN	7	3	14	3	2.2649	0.5534	139	4.09	<.0001	0.05	1.1708	3.3589
AVISITN*TRTPN	7	3	21	1	4.2933	0.9741	231	4.41	<.0001	0.05	2.3741	6.2125
AVISITN*TRTPN	7	3	21	2	4.1065	0.9705	231	4.23	<.0001	0.05	2.1944	6.0186
AVISITN*TRTPN	7	3	21	3	2.3413	0.6524	140	3.59	0.0005	0.05	1.0515	3.6311
AVISITN*TRTPN	7	3	28	1	5.4444	1.1085	215	4.91	<.0001	0.05	3.2595	7.6293
AVISITN*TRTPN	7	3	28	2	5.4354	1.0732	214	5.06	<.0001	0.05	3.3200	7.5508
AVISITN*TRTPN	7	3	28	3	2.0978	0.7357	142	2.85	0.0050	0.05	0.6435	3.5521
AVISITN*TRTPN	7	3	35	1	6.0839	1.1121	215	5.47	<.0001	0.05	3.8918	8.2760
AVISITN*TRTPN	7	3	35	2	6.5269	1.0688	214	6.11	<.0001	0.05	4.4202	8.6336

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	3	35	3	3.0287	0.8227	140	3.68	0.0003	0.05	1.4022	4.6552
AVISITN*TRTPN	7	3	42	1	5.8651	1.2160	198	4.82	<.0001	0.05	3.4673	8.2630
AVISITN*TRTPN	7	3	42	2	5.5886	1.0654	221	5.25	<.0001	0.05	3.4889	7.6884
AVISITN*TRTPN	7	3	42	3	2.8321	0.7825	140	3.62	0.0004	0.05	1.2850	4.3792
AVISITN*TRTPN	14	1	14	2	-0.7239	1.0393	273	-0.70	0.4867	0.05	-2.7701	1.3222
AVISITN*TRTPN	14	1	14	3	-0.9933	1.0181	261	-0.98	0.3301	0.05	-2.9980	1.0113
AVISITN*TRTPN	14	1	21	1	1.0351	0.5228	121	1.98	0.0500	0.05	0.000165	2.0701
AVISITN*TRTPN	14	1	21	2	0.8483	1.0869	271	0.78	0.4358	0.05	-1.2916	2.9882
AVISITN*TRTPN	14	1	21	3	-0.9169	1.0504	265	-0.87	0.3835	0.05	-2.9850	1.1513
AVISITN*TRTPN	14	1	28	1	2.1862	0.6913	123	3.16	0.0020	0.05	0.8179	3.5545
AVISITN*TRTPN	14	1	28	2	2.1772	1.1796	259	1.85	0.0661	0.05	-0.1455	4.5000
AVISITN*TRTPN	14	1	28	3	-1.1604	1.1031	267	-1.05	0.2938	0.05	-3.3324	1.0115
AVISITN*TRTPN	14	1	35	1	2.8257	0.6812	124	4.15	<.0001	0.05	1.4775	4.1738
AVISITN*TRTPN	14	1	35	2	3.2687	1.1755	256	2.78	0.0058	0.05	0.9538	5.5837
AVISITN*TRTPN	14	1	35	3	-0.2295	1.1602	265	-0.20	0.8434	0.05	-2.5137	2.0548
AVISITN*TRTPN	14	1	42	1	2.6069	0.8200	121	3.18	0.0019	0.05	0.9836	4.2302
AVISITN*TRTPN	14	1	42	2	2.3305	1.1725	260	1.99	0.0479	0.05	0.02168	4.6392
AVISITN*TRTPN	14	1	42	3	-0.4261	1.1462	266	-0.37	0.7104	0.05	-2.6828	1.8306
AVISITN*TRTPN	14	2	14	3	-0.2694	0.9898	261	-0.27	0.7857	0.05	-2.2183	1.6795
AVISITN*TRTPN	14	2	21	1	1.7590	1.0642	265	1.65	0.0995	0.05	-0.3364	3.8545
AVISITN*TRTPN	14	2	21	2	1.5722	0.4849	133	3.24	0.0015	0.05	0.6131	2.5313
AVISITN*TRTPN	14	2	21	3	-0.1929	1.0229	262	-0.19	0.8505	0.05	-2.2071	1.8212

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	14	2	28	1	2.9101	1.1885	251	2.45	0.0150	0.05	0.5695	5.2508
AVISITN*TRTPN	14	2	28	2	2.9011	0.7202	131	4.03	<.0001	0.05	1.4764	4.3259
AVISITN*TRTPN	14	2	28	3	-0.4365	1.0770	256	-0.41	0.6856	0.05	-2.5574	1.6844
AVISITN*TRTPN	14	2	35	1	3.5496	1.1919	249	2.98	0.0032	0.05	1.2022	5.8970
AVISITN*TRTPN	14	2	35	2	3.9926	0.6830	132	5.85	<.0001	0.05	2.6415	5.3438
AVISITN*TRTPN	14	2	35	3	0.4945	1.1353	251	0.44	0.6636	0.05	-1.7415	2.7304
AVISITN*TRTPN	14	2	42	1	3.3308	1.2893	232	2.58	0.0104	0.05	0.7906	5.8711
AVISITN*TRTPN	14	2	42	2	3.0544	0.6732	131	4.54	<.0001	0.05	1.7227	4.3861
AVISITN*TRTPN	14	2	42	3	0.2978	1.1211	251	0.27	0.7907	0.05	-1.9101	2.5057
AVISITN*TRTPN	14	3	21	1	2.0285	1.0435	246	1.94	0.0530	0.05	-0.02684	4.0838
AVISITN*TRTPN	14	3	21	2	1.8416	1.0397	252	1.77	0.0777	0.05	-0.2060	3.8892
AVISITN*TRTPN	14	3	21	3	0.07648	0.4315	135	0.18	0.8596	0.05	-0.7769	0.9299
AVISITN*TRTPN	14	3	28	1	3.1795	1.1699	236	2.72	0.0071	0.05	0.8747	5.4844
AVISITN*TRTPN	14	3	28	2	3.1706	1.1362	239	2.79	0.0057	0.05	0.9323	5.4088
AVISITN*TRTPN	14	3	28	3	-0.1671	0.5311	135	-0.31	0.7536	0.05	-1.2175	0.8833
AVISITN*TRTPN	14	3	35	1	3.8190	1.1734	236	3.25	0.0013	0.05	1.5074	6.1306
AVISITN*TRTPN	14	3	35	2	4.2621	1.1320	238	3.76	0.0002	0.05	2.0320	6.4921
AVISITN*TRTPN	14	3	35	3	0.7639	0.6655	135	1.15	0.2530	0.05	-0.5522	2.0799
AVISITN*TRTPN	14	3	42	1	3.6003	1.2722	219	2.83	0.0051	0.05	1.0929	6.1076
AVISITN*TRTPN	14	3	42	2	3.3238	1.1289	246	2.94	0.0035	0.05	1.1003	5.5473
AVISITN*TRTPN	14	3	42	3	0.5672	0.6438	130	0.88	0.3799	0.05	-0.7064	1.8409
AVISITN*TRTPN	21	1	21	2	-0.1868	1.1108	266	-0.17	0.8666	0.05	-2.3740	2.0003

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	21	1	21	3	-1.9520	1.0750	255	-1.82	0.0706	0.05	-4.0690	0.1651
AVISITN*TRTPN	21	1	28	1	1.1511	0.5594	117	2.06	0.0418	0.05	0.04332	2.2589
AVISITN*TRTPN	21	1	28	2	1.1421	1.2016	261	0.95	0.3427	0.05	-1.2240	3.5082
AVISITN*TRTPN	21	1	28	3	-2.1955	1.1266	259	-1.95	0.0524	0.05	-4.4141	0.02302
AVISITN*TRTPN	21	1	35	1	1.7906	0.5443	116	3.29	0.0013	0.05	0.7125	2.8687
AVISITN*TRTPN	21	1	35	2	2.2336	1.1977	257	1.86	0.0633	0.05	-0.1249	4.5921
AVISITN*TRTPN	21	1	35	3	-1.2646	1.1825	260	-1.07	0.2859	0.05	-3.5931	1.0640
AVISITN*TRTPN	21	1	42	1	1.5718	0.6948	117	2.26	0.0255	0.05	0.1959	2.9478
AVISITN*TRTPN	21	1	42	2	1.2953	1.1947	261	1.08	0.2792	0.05	-1.0571	3.6478
AVISITN*TRTPN	21	1	42	3	-1.4612	1.1688	259	-1.25	0.2124	0.05	-3.7628	0.8404
AVISITN*TRTPN	21	2	21	3	-1.7652	1.0712	256	-1.65	0.1006	0.05	-3.8748	0.3444
AVISITN*TRTPN	21	2	28	1	1.3379	1.2304	259	1.09	0.2779	0.05	-1.0849	3.7607
AVISITN*TRTPN	21	2	28	2	1.3289	0.5423	125	2.45	0.0156	0.05	0.2557	2.4021
AVISITN*TRTPN	21	2	28	3	-2.0087	1.1231	257	-1.79	0.0749	0.05	-4.2203	0.2029
AVISITN*TRTPN	21	2	35	1	1.9774	1.2336	257	1.60	0.1102	0.05	-0.4519	4.4067
AVISITN*TRTPN	21	2	35	2	2.4204	0.4860	122	4.98	<.0001	0.05	1.4583	3.3826
AVISITN*TRTPN	21	2	35	3	-1.0778	1.1791	254	-0.91	0.3616	0.05	-3.3998	1.2443
AVISITN*TRTPN	21	2	42	1	1.7586	1.3280	243	1.32	0.1867	0.05	-0.8572	4.3745
AVISITN*TRTPN	21	2	42	2	1.4822	0.5617	123	2.64	0.0094	0.05	0.3702	2.5941
AVISITN*TRTPN	21	2	42	3	-1.2744	1.1654	254	-1.09	0.2752	0.05	-3.5694	1.0206
AVISITN*TRTPN	21	3	28	1	3.1031	1.1982	247	2.59	0.0102	0.05	0.7431	5.4630
AVISITN*TRTPN	21	3	28	2	3.0941	1.1652	246	2.66	0.0084	0.05	0.7991	5.3891

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	21	3	28	3	-0.2436	0.4409	129	-0.55	0.5816	0.05	-1.1158	0.6287
AVISITN*TRTPN	21	3	35	1	3.7425	1.2015	247	3.11	0.0021	0.05	1.3760	6.1091
AVISITN*TRTPN	21	3	35	2	4.1856	1.1611	246	3.60	0.0004	0.05	1.8987	6.4725
AVISITN*TRTPN	21	3	35	3	0.6874	0.4989	125	1.38	0.1707	0.05	-0.2999	1.6747
AVISITN*TRTPN	21	3	42	1	3.5238	1.2982	229	2.71	0.0071	0.05	0.9658	6.0817
AVISITN*TRTPN	21	3	42	2	3.2473	1.1580	252	2.80	0.0054	0.05	0.9667	5.5279
AVISITN*TRTPN	21	3	42	3	0.4908	0.5209	118	0.94	0.3481	0.05	-0.5408	1.5223
AVISITN*TRTPN	28	1	28	2	-0.00898	1.3130	269	-0.01	0.9945	0.05	-2.5940	2.5760
AVISITN*TRTPN	28	1	28	3	-3.3466	1.2447	256	-2.69	0.0076	0.05	-5.7977	-0.8955
AVISITN*TRTPN	28	1	35	1	0.6395	0.4336	113	1.47	0.1430	0.05	-0.2195	1.4985
AVISITN*TRTPN	28	1	35	2	1.0825	1.3093	266	0.83	0.4091	0.05	-1.4955	3.6605
AVISITN*TRTPN	28	1	35	3	-2.4157	1.2955	265	-1.86	0.0633	0.05	-4.9664	0.1351
AVISITN*TRTPN	28	1	42	1	0.4207	0.5447	112	0.77	0.4416	0.05	-0.6586	1.5001
AVISITN*TRTPN	28	1	42	2	0.1442	1.3066	267	0.11	0.9122	0.05	-2.4283	2.7168
AVISITN*TRTPN	28	1	42	3	-2.6123	1.2830	261	-2.04	0.0427	0.05	-5.1386	-0.08601
AVISITN*TRTPN	28	2	28	3	-3.3376	1.2130	252	-2.75	0.0064	0.05	-5.7265	-0.9488
AVISITN*TRTPN	28	2	35	1	0.6485	1.3160	268	0.49	0.6226	0.05	-1.9426	3.2395
AVISITN*TRTPN	28	2	35	2	1.0915	0.4672	117	2.34	0.0212	0.05	0.1662	2.0168
AVISITN*TRTPN	28	2	35	3	-2.4067	1.2650	256	-1.90	0.0582	0.05	-4.8978	0.08446
AVISITN*TRTPN	28	2	42	1	0.4297	1.4049	260	0.31	0.7600	0.05	-2.3367	3.1961
AVISITN*TRTPN	28	2	42	2	0.1532	0.5269	120	0.29	0.7717	0.05	-0.8901	1.1966
AVISITN*TRTPN	28	2	42	3	-2.6033	1.2522	255	-2.08	0.0386	0.05	-5.0693	-0.1373

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Differences of Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	28	3	35	1	3.9861	1.2479	256	3.19	0.0016	0.05	1.5286	6.4436
AVISITN*TRTPN	28	3	35	2	4.4291	1.2091	256	3.66	0.0003	0.05	2.0482	6.8101
AVISITN*TRTPN	28	3	35	3	0.9310	0.4637	127	2.01	0.0468	0.05	0.01342	1.8485
AVISITN*TRTPN	28	3	42	1	3.7673	1.3413	241	2.81	0.0054	0.05	1.1252	6.4095
AVISITN*TRTPN	28	3	42	2	3.4909	1.2061	259	2.89	0.0041	0.05	1.1159	5.8659
AVISITN*TRTPN	28	3	42	3	0.7343	0.4577	117	1.60	0.1113	0.05	-0.1721	1.6408
AVISITN*TRTPN	35	1	35	2	0.4430	1.3124	264	0.34	0.7359	0.05	-2.1410	3.0271
AVISITN*TRTPN	35	1	35	3	-3.0551	1.2986	265	-2.35	0.0194	0.05	-5.6120	-0.4983
AVISITN*TRTPN	35	1	42	1	-0.2188	0.4942	109	-0.44	0.6589	0.05	-1.1982	0.7607
AVISITN*TRTPN	35	1	42	2	-0.4952	1.3097	266	-0.38	0.7056	0.05	-3.0739	2.0834
AVISITN*TRTPN	35	1	42	3	-3.2518	1.2861	261	-2.53	0.0121	0.05	-5.7843	-0.7193
AVISITN*TRTPN	35	2	35	3	-3.4982	1.2613	258	-2.77	0.0059	0.05	-5.9819	-1.0145
AVISITN*TRTPN	35	2	42	1	-0.6618	1.4015	256	-0.47	0.6372	0.05	-3.4217	2.0981
AVISITN*TRTPN	35	2	42	2	-0.9383	0.5462	119	-1.72	0.0884	0.05	-2.0198	0.1432
AVISITN*TRTPN	35	2	42	3	-3.6948	1.2485	258	-2.96	0.0034	0.05	-6.1533	-1.2363
AVISITN*TRTPN	35	3	42	1	2.8364	1.3886	253	2.04	0.0421	0.05	0.1018	5.5710
AVISITN*TRTPN	35	3	42	2	2.5599	1.2584	261	2.03	0.0429	0.05	0.08197	5.0379
AVISITN*TRTPN	35	3	42	3	-0.1966	0.4806	120	-0.41	0.6832	0.05	-1.1482	0.7549
AVISITN*TRTPN	42	1	42	2	-0.2765	1.3989	258	-0.20	0.8435	0.05	-3.0313	2.4783
AVISITN*TRTPN	42	1	42	3	-3.0330	1.3769	249	-2.20	0.0285	0.05	-5.7448	-0.3212
AVISITN*TRTPN	42	2	42	3	-2.7565	1.2456	260	-2.21	0.0278	0.05	-5.2094	-0.3037

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

---------- Parameter Code=AISRSTOT ----------

The Mixed Procedure

Tests of Effect Slices

Effect	Analysis Visit (N)	Num DF	Den DF	F Value	Pr > F
AVISITN*TRTPN	7	2	257	1.52	0.2216
AVISITN*TRTPN	14	2	265	0.50	0.6098
AVISITN*TRTPN	21	2	259	2.06	0.1301
AVISITN*TRTPN	28	2	261	5.16	0.0063
AVISITN*TRTPN	35	2	262	4.53	0.0117
AVISITN*TRTPN	42	2	260	3.39	0.0352

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Model Information

Data Set	WORK.INDATA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	SUBJID
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
AVISITN	6	7 14 21 28 35 42
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

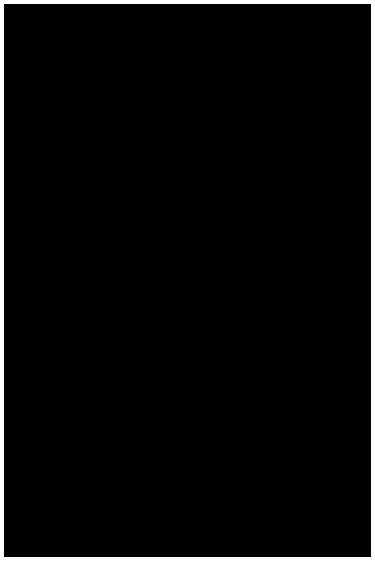
Class Level Information

Class	Levels	Values
SUBJID	437	[redacted]

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

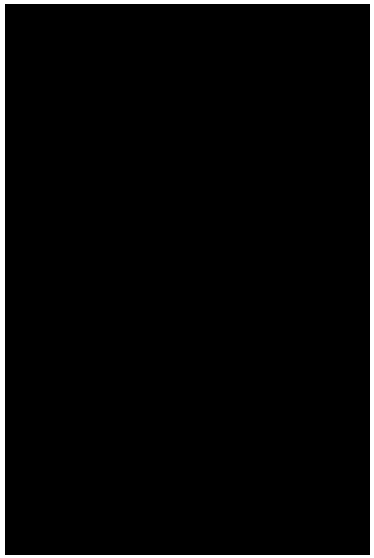


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

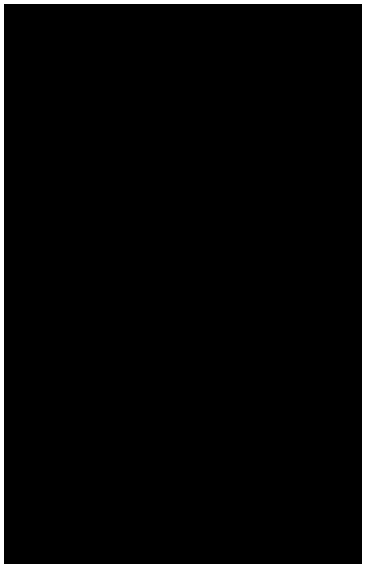


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

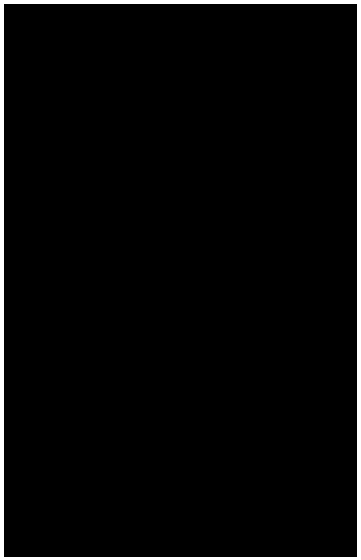


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure



SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

[redacted]

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Dimensions

Covariance Parameters	21
Columns in X	72
Columns in Z	0
Subjects	437
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2288
Number of Observations Used	2288
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	5394.49812760	
1	2	3445.02451748	0.00188171
2	1	3444.38818261	0.00001015
3	1	3444.38487436	0.00000000

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	0.3229
UN(2,1)	SUBJID	0.2034
UN(2,2)	SUBJID	0.4814
UN(3,1)	SUBJID	0.1871
UN(3,2)	SUBJID	0.4119
UN(3,3)	SUBJID	0.6159
UN(4,1)	SUBJID	0.1907
UN(4,2)	SUBJID	0.3954
UN(4,3)	SUBJID	0.5303
UN(4,4)	SUBJID	0.6979
UN(5,1)	SUBJID	0.1737
UN(5,2)	SUBJID	0.4163
UN(5,3)	SUBJID	0.5399
UN(5,4)	SUBJID	0.5865
UN(5,5)	SUBJID	0.7044
UN(6,1)	SUBJID	0.2284
UN(6,2)	SUBJID	0.4456
UN(6,3)	SUBJID	0.5853

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(6,4)	SUBJID	0.6539
UN(6,5)	SUBJID	0.6649
UN(6,6)	SUBJID	0.8820

Fit Statistics

-2 Res Log Likelihood	3444.4
AIC (Smaller is Better)	3486.4
AICC (Smaller is Better)	3486.8
BIC (Smaller is Better)	3572.1

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	1950.11	<.0001

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	380	2.29	0.0451
TRTPN	2	400	2.66	0.0710
AVISITN*TRTPN	10	562	1.94	0.0377
POOLCNTR	37	395	1.39	0.0694
BASE*AVISITN	6	423	4.40	0.0003

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-0.07467	0.06756	397	-1.11	0.2697	0.05	-0.2075	0.05815
DAY7 2 vs 3	-0.01014	0.06743	397	-0.15	0.8805	0.05	-0.1427	0.1224
DAY14 1 vs 3	-0.04254	0.08369	401	-0.51	0.6115	0.05	-0.2071	0.1220
DAY14 2 vs 3	-0.04226	0.08328	398	-0.51	0.6121	0.05	-0.2060	0.1215
DAY21 1 vs 3	-0.1321	0.09557	392	-1.38	0.1678	0.05	-0.3200	0.05583
DAY21 2 vs 3	-0.1574	0.09468	385	-1.66	0.0971	0.05	-0.3436	0.02870
DAY28 1 vs 3	-0.1752	0.1030	403	-1.70	0.0898	0.05	-0.3778	0.02735
DAY28 2 vs 3	-0.2175	0.1019	396	-2.13	0.0334	0.05	-0.4178	-0.01719

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY35 1 vs 3	-0.1864	0.1039	401	-1.79	0.0736	0.05	-0.3907	0.01789
DAY35 2 vs 3	-0.3316	0.1032	398	-3.21	0.0014	0.05	-0.5345	-0.1288
DAY42 1 vs 3	-0.2664	0.1169	407	-2.28	0.0232	0.05	-0.4963	-0.03659
DAY42 2 vs 3	-0.2789	0.1155	399	-2.42	0.0162	0.05	-0.5059	-0.05194

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	7	1	-0.3156	0.05150	409	-6.13	<.0001	0.05	-0.4169	-0.2144
AVISITN*TRTPN	7	2	-0.2511	0.05228	413	-4.80	<.0001	0.05	-0.3539	-0.1483
AVISITN*TRTPN	7	3	-0.2410	0.05226	411	-4.61	<.0001	0.05	-0.3437	-0.1383
AVISITN*TRTPN	14	1	-0.4574	0.06241	434	-7.33	<.0001	0.05	-0.5801	-0.3348
AVISITN*TRTPN	14	2	-0.4571	0.06273	440	-7.29	<.0001	0.05	-0.5804	-0.3339
AVISITN*TRTPN	14	3	-0.4149	0.06281	439	-6.61	<.0001	0.05	-0.5383	-0.2914
AVISITN*TRTPN	21	1	-0.5918	0.07085	432	-8.35	<.0001	0.05	-0.7311	-0.4526
AVISITN*TRTPN	21	2	-0.6172	0.07042	432	-8.76	<.0001	0.05	-0.7556	-0.4788

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

Parameter Code=CGI0201

The Mixed Procedure

Least Squares Means

Effect	Analysis Visit (N)	Planned Treatment (N)	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
AVISITN*TRTPN	21	3	-0.4598	0.07038	430	-6.53	<.0001	0.05	-0.5981	-0.3214
AVISITN*TRTPN	28	1	-0.6662	0.07633	445	-8.73	<.0001	0.05	-0.8162	-0.5162
AVISITN*TRTPN	28	2	-0.7085	0.07549	445	-9.38	<.0001	0.05	-0.8569	-0.5601
AVISITN*TRTPN	28	3	-0.4910	0.07503	437	-6.54	<.0001	0.05	-0.6385	-0.3435
AVISITN*TRTPN	35	1	-0.6877	0.07674	439	-8.96	<.0001	0.05	-0.8385	-0.5369
AVISITN*TRTPN	35	2	-0.8330	0.07652	449	-10.89	<.0001	0.05	-0.9833	-0.6826
AVISITN*TRTPN	35	3	-0.5013	0.07580	435	-6.61	<.0001	0.05	-0.6503	-0.3523
AVISITN*TRTPN	42	1	-0.7818	0.08592	443	-9.10	<.0001	0.05	-0.9507	-0.6130
AVISITN*TRTPN	42	2	-0.7943	0.08453	440	-9.40	<.0001	0.05	-0.9605	-0.6282
AVISITN*TRTPN	42	3	-0.5154	0.08437	438	-6.11	<.0001	0.05	-0.6812	-0.3496

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

Tests of Effect Slices

Effect	Analysis Visit (N)	Num DF	Den DF	F Value	Pr > F
AVISITN*TRTPN	7	2	397	0.72	0.4872
AVISITN*TRTPN	14	2	400	0.17	0.8421
AVISITN*TRTPN	21	2	390	1.59	0.2056
AVISITN*TRTPN	28	2	402	2.56	0.0788
AVISITN*TRTPN	35	2	402	5.19	0.0059
AVISITN*TRTPN	42	2	405	3.70	0.0257

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3
POOLCNTR	38	[redacted]

Number of Observations Read 437
Number of Observations Used 437

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	40	46.6607952	1.1665199	1.38	0.0659
Error	396	333.8884039	0.8431525		
Corrected Total	436	380.5491991			

R-Square	Coeff Var	Root MSE	CHG Mean
0.122614	-136.9515	0.918233	-0.670481

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	4.37202022	2.18601011	2.59	0.0761
POOLCNTR	37	31.85599793	0.86097292	1.02	0.4390
BASE	1	9.96617520	9.96617520	11.82	0.0006

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Level of TRTPN	N	CHG Mean	CHG Std Dev	BASE Mean	BASE Std Dev
1	146	-0.71917808	1.02212187	4.47945205	0.60136830
2	147	-0.76190476	0.94603233	4.53061224	0.60029813
3	144	-0.52777778	0.81028739	4.51388889	0.55452507

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	Standard Error	Pr > |t|	LSMEAN Number
1	-0.71916295	0.08370474	<.0001	1
2	-0.72793134	0.08502853	<.0001	2
3	-0.50965777	0.08513983	<.0001	3

Least Squares Means for effect TRTPN
Pr > |t| for H0: LSMean(i)=LSMean(j)

Dependent Variable: CHG

i/j	1	2	3
1		0.9353	0.0543
2	0.9353		0.0445
3	0.0543	0.0445	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-0.719163	-0.883724	-0.554602
2	-0.727931	-0.895095	-0.560768

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	95% Confidence Limits	
3	-0.509658	-0.677040	-0.342275

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.008768	-0.203504	0.221040
1	3	-0.209505	-0.422864	0.003854
2	3	-0.218274	-0.431132	-0.005415

NOTE: To ensure overall protection level, only probabilities associated with pre-planned comparisons should be used.

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.2
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, LOCF
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Parameter	Estimate	Standard Error	t Value	Pr > |t|
1 vs 3	-0.20950519	0.10852592	-1.93	0.0543
2 vs 3	-0.21827357	0.10827131	-2.02	0.0445

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.2 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3

Number of Observations Read	437
Number of Observations Used	437

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	14.8047973	4.9349324	5.84	0.0006
Error	433	365.7444018	0.8446753		
Corrected Total	436	380.5491991			

R-Square	Coeff Var	Root MSE	CHG Mean
0.038904	-137.0751	0.919062	-0.670481

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	4.53162949	2.26581475	2.68	0.0695
BASE	1	10.29745513	10.29745513	12.19	0.0005

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

Parameter Code=CGI0201 Analysis Visit (N)=42

The GLM Procedure

Level of TRTPN	N	CHG Mean	CHG Std Dev	BASE Mean	BASE Std Dev
1	146	-0.71917808	1.02212187	4.47945205	0.60136830
2	147	-0.76190476	0.94603233	4.53061224	0.60029813
3	144	-0.52777778	0.81028739	4.51388889	0.55452507

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	Standard Error	Pr > |t|	LSMEAN Number
1	-0.72668484	0.07609251	<.0001	1
2	-0.75596312	0.07582207	<.0001	2
3	-0.52623218	0.07658979	<.0001	3

Least Squares Means for effect TRTPN
Pr > |t| for H0: LSMean(i)=LSMean(j)

Dependent Variable: CHG

i/j	1	2	3
1		0.7854	0.0641
2	0.7854		0.0336
3	0.0641	0.0336	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-0.726685	-0.876241	-0.577128
2	-0.755963	-0.904988	-0.606938

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure
Least Squares Means

TRTPN	CHG LSMEAN	95% Confidence Limits	
3	-0.526232	-0.676766	-0.375698

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.029278	-0.181918	0.240475
1	3	-0.200453	-0.412667	0.011762
2	3	-0.229731	-0.441540	-0.017922

NOTE: To ensure overall protection level, only probabilities associated with pre-planned comparisons should be used.

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

STAT-5.3
Proc GLM Output for Change from Baseline to Day 42 in CGI-S Scale, OC
(Efficacy Sample)

---------- Parameter Code=CGI0201 Analysis Visit (N)=42 ----------

The GLM Procedure

Dependent Variable: CHG Change from Baseline

Parameter	Estimate	Standard Error	t Value	Pr > |t|
1 vs 3	-0.20045266	0.10797208	-1.86	0.0641
2 vs 3	-0.22973094	0.10776584	-2.13	0.0336

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 18JUN2020 10:00; ANALYSIS DATASET CREATED: 11JUN2020 07:28
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

CENTANAFADINE 1 OF 1
PROTOCOL 405-201-00013

STAT-6.1.1

Shapiro-Wilk Test for Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model (Efficacy Sample)

PROTOCOL	Day	TEST VARIABLE	GOODNESS OF FIT TEST	GOODNESS OF FIT TEST STATISTICS	Pvalue
40520100013	DAY 7	RESID	Shapiro-Wilk	0.9505	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9512	<0.0001
	DAY 14	RESID	Shapiro-Wilk	0.9461	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9474	<0.0001
	DAY 21	RESID	Shapiro-Wilk	0.9557	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9575	<0.0001
	DAY 28	RESID	Shapiro-Wilk	0.9600	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9604	<0.0001
	DAY 35	RESID	Shapiro-Wilk	0.9643	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9645	<0.0001
	DAY 42	RESID	Shapiro-Wilk	0.9468	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9468	<0.0001

FILE: normality_ba.lis, RUN: 18JUN2020 10:00
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/normality_b.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-6.1.1 FINAL

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	429	Sum Weights	429
Mean	-0.0358232	Sum Observations	-15.368154
Std Deviation	6.92317198	Variance	47.9303103
Skewness	-0.8989502	Kurtosis	1.59121128
Uncorrected SS	20514.7234	Corrected SS	20514.1728
Coeff Variation	-19325.943	Std Error Mean	0.33425389

Basic Statistical Measures

Location		Variability	
Mean	-0.03582	Std Deviation	6.92317
Median	1.02764	Variance	47.93031
Mode	-5.95541	Range	44.54954
		Interquartile Range	7.44768

Note: The mode displayed is the smallest of 2 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.10717	Pr > |t|	0.9147
Sign	M	30.5	Pr >= |M|	0.0037
Signed Rank	S	4507.5	Pr >= |S|	0.0794

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.950477	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.096707	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.114552	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	6.25502	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	18.12976
99%	14.28640
95%	9.63500
90%	7.03550
75% Q3	4.19872
50% Median	1.02764
25% Q1	-3.24896
10%	-9.50864
5%	-13.14533
1%	-22.53575
0% Min	-26.41979

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-26.4198	40520100013-[redacted]	31	14.2864	40520100013-[redacted]	253
-25.0595	40520100013-[redacted]	241	14.5137	40520100013-[redacted]	127
-24.7070	40520100013-[redacted]	345	15.9196	40520100013-[redacted]	344
-23.8012	40520100013-[redacted]	126	17.4347	40520100013-[redacted]	336
-22.5358	40520100013-[redacted]	215	18.1298	40520100013-[redacted]	348

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	429	Sum Weights	429
Mean	-0.0055696	Sum Observations	-2.3893447
Std Deviation	0.99907873	Variance	0.99815832
Skewness	-0.8889627	Kurtosis	1.51349761
Uncorrected SS	427.225068	Corrected SS	427.21176
Coeff Variation	-17938.172	Std Error Mean	0.04823598

Basic Statistical Measures

Location		Variability	
Mean	-0.00557	Std Deviation	0.99908
Median	0.14511	Variance	0.99816
Mode	-0.84411	Range	6.28819
		Interquartile Range	1.08259

Note: The mode displayed is the smallest of 2 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.11547	Pr > |t|	0.9081
Sign	M	30.5	Pr >= |M|	0.0037
Signed Rank	S	4427.5	Pr >= |S|	0.0849

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.951168	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.096496	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.109796	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	6.205792	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	2.547354
99%	2.106636
95%	1.406654
90%	1.041059
75% Q3	0.623263
50% Median	0.145113
25% Q1	-0.459331
10%	-1.394934
5%	-1.925385
1%	-3.293143
0% Min	-3.740832

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=7 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.74083	40520100013-[redacted]	31	2.10664	40520100013-[redacted]	253
-3.59734	40520100013-[redacted]	241	2.14602	40520100013-[redacted]	127
-3.51327	40520100013-[redacted]	126	2.23609	40520100013-[redacted]	344
-3.47412	40520100013-[redacted]	345	2.45134	40520100013-[redacted]	336
-3.29314	40520100013-[redacted]	215	2.54735	40520100013-[redacted]	348

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	406	Sum Weights	406
Mean	-0.0512213	Sum Observations	-20.795843
Std Deviation	8.29126377	Variance	68.745055
Skewness	-0.918599	Kurtosis	0.87158088
Uncorrected SS	27842.8125	Corrected SS	27841.7473
Coeff Variation	-16187.144	Std Error Mean	0.41148851

Basic Statistical Measures

Location		Variability	
Mean	-0.05122	Std Deviation	8.29126
Median	1.44518	Variance	68.74505
Mode	-4.28518	Range	45.92221
		Interquartile Range	10.09103

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.12448	Pr > |t|	0.9010
Sign	M	33	Pr >= |M|	0.0012
Signed Rank	S	4233.5	Pr >= |S|	0.0735

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.946146	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.091654	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.123579	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	6.515695	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	18.12438
99%	15.31626
95%	10.82306
90%	8.96116
75% Q3	5.77732
50% Median	1.44518
25% Q1	-4.31372
10%	-11.65152
5%	-16.87371
1%	-25.37928
0% Min	-27.79784

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-27.7978	40520100013-[redacted]	729	15.3163	40520100013-[redacted]	630
-26.3480	40520100013-[redacted]	701	15.4412	40520100013-[redacted]	549
-26.1345	40520100013-[redacted]	586	15.9561	40520100013-[redacted]	747
-25.7353	40520100013-[redacted]	459	17.3297	40520100013-[redacted]	748
-25.3793	40520100013-[redacted]	664	18.1244	40520100013-[redacted]	746

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	406	Sum Weights	406
Mean	-0.0056236	Sum Observations	-2.283187
Std Deviation	1.0070444	Variance	1.01413842
Skewness	-0.9021239	Kurtosis	0.83485956
Uncorrected SS	410.738899	Corrected SS	410.726059
Coeff Variation	-17907.426	Std Error Mean	0.04997877

Basic Statistical Measures

Location		Variability	
Mean	-0.00562	Std Deviation	1.00704
Median	0.17363	Variance	1.01414
Mode	-0.51324	Range	5.55938
		Interquartile Range	1.22582

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.11252	Pr > |t|	0.9105
Sign	M	33	Pr >= |M|	0.0012
Signed Rank	S	4183.5	Pr >= |S|	0.0770

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.947415	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.091557	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.124298	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	6.464081	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	2.162711
99%	1.902737
95%	1.310225
90%	1.083757
75% Q3	0.706394
50% Median	0.173632
25% Q1	-0.519422
10%	-1.416902
5%	-2.033019
1%	-3.115779
0% Min	-3.396667

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=14 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.39667	40520100013-[redacted]	729	1.90274	40520100013-[redacted]	747
-3.16989	40520100013-[redacted]	701	1.90542	40520100013-[redacted]	549
-3.12956	40520100013-[redacted]	664	2.01127	40520100013-[redacted]	554
-3.11745	40520100013-[redacted]	547	2.06617	40520100013-[redacted]	748
-3.11578	40520100013-[redacted]	586	2.16271	40520100013-[redacted]	746

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	391	Sum Weights	391
Mean	-0.1603789	Sum Observations	-62.708169
Std Deviation	8.75757561	Variance	76.6951306
Skewness	-0.7967468	Kurtosis	0.37509191
Uncorrected SS	29921.158	Corrected SS	29911.101
Coeff Variation	-5460.5518	Std Error Mean	0.44288964

Basic Statistical Measures

Location		Variability	
Mean	-0.16038	Std Deviation	8.75758
Median	1.40218	Variance	76.69513
Mode	-4.23564	Range	49.66442
		Interquartile Range	11.21801

Note: The mode displayed is the smallest of 3 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.36212	Pr > |t|	0.7175
Sign	M	24.5	Pr >= |M|	0.0151
Signed Rank	S	2593	Pr >= |S|	0.2467

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.95566	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.082594	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.827025	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	5.002996	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	17.73069
99%	14.32811
95%	11.25169
90%	9.52209
75% Q3	6.20743
50% Median	1.40218
25% Q1	-5.01058
10%	-12.76245
5%	-17.32377
1%	-23.46337
0% Min	-31.93373

FILE: normalitybc.lis, RUN: 18JUN2020 10:00
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/normality.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-6.1.2 FINAL

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-31.9337	40520100013-[redacted]	988	14.1209	40520100013-[redacted]	1020
-30.9690	40520100013-[redacted]	1101	14.3281	40520100013-[redacted]	1146
-24.7107	40520100013-[redacted]	1129	14.3988	40520100013-[redacted]	1192
-23.4634	40520100013-[redacted]	865	15.9977	40520100013-[redacted]	958
-22.6585	40520100013-[redacted]	952	17.7307	40520100013-[redacted]	955

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	391	Sum Weights	391
Mean	-0.0173302	Sum Observations	-6.7761143
Std Deviation	1.0026023	Variance	1.00521137
Skewness	-0.7767798	Kurtosis	0.33565986
Uncorrected SS	392.149864	Corrected SS	392.032433
Coeff Variation	-5785.2846	Std Error Mean	0.05070378

Basic Statistical Measures

Location		Variability	
Mean	-0.01733	Std Deviation	1.00260
Median	0.15766	Variance	1.00521
Mode	-0.47523	Range	5.64738
		Interquartile Range	1.29404

Note: The mode displayed is the smallest of 3 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.34179	Pr > |t|	0.7327
Sign	M	24.5	Pr >= |M|	0.0151
Signed Rank	S	2567	Pr >= |S|	0.2515

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.957454	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.082316	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.809936	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	4.874627	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	2.056753
99%	1.617161
95%	1.320311
90%	1.079049
75% Q3	0.709824
50% Median	0.157662
25% Q1	-0.584218
10%	-1.446331
5%	-2.015562
1%	-2.649605
0% Min	-3.590625

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=21 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.59062	40520100013-[redacted]	988	1.61159	40520100013-[redacted]	1146
-3.51155	40520100013-[redacted]	1101	1.61716	40520100013-[redacted]	1020
-2.83912	40520100013-[redacted]	1129	1.63078	40520100013-[redacted]	1192
-2.64961	40520100013-[redacted]	865	1.99613	40520100013-[redacted]	958
-2.63088	40520100013-[redacted]	952	2.05675	40520100013-[redacted]	955

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	370	Sum Weights	370
Mean	-0.4073769	Sum Observations	-150.72947
Std Deviation	10.1669831	Variance	103.367545
Skewness	-0.7010249	Kurtosis	0.12558616
Uncorrected SS	38204.0278	Corrected SS	38142.6241
Coeff Variation	-2495.7189	Std Error Mean	0.52855628

Basic Statistical Measures

Location		Variability	
Mean	-0.40738	Std Deviation	10.16698
Median	1.71750	Variance	103.36754
Mode	7.54797	Range	54.45127
		Interquartile Range	14.48720

Note: The mode displayed is the smallest of 2 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.77074	Pr > |t|	0.4414
Sign	M	25	Pr >= |M|	0.0108
Signed Rank	S	1007.5	Pr >= |S|	0.6252

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.959992	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.090634	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.856785	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	4.871079	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	20.54164
99%	18.23384
95%	12.28388
90%	10.47477
75% Q3	7.54797
50% Median	1.71750
25% Q1	-6.93923
10%	-14.81352
5%	-20.55486
1%	-29.58661
0% Min	-33.90962

FILE: normalitybc.lis, RUN: 18JUN2020 10:00
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/normality.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-6.1.2 FINAL

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-33.9096	40520100013-[redacted]	1498	18.2304	40520100013-[redacted]	1344
-31.7656	40520100013-[redacted]	1517	18.2338	40520100013-[redacted]	1519
-31.3573	40520100013-[redacted]	1478	19.0985	40520100013-[redacted]	1518
-29.5866	40520100013-[redacted]	1372	20.0136	40520100013-[redacted]	1589
-28.0541	40520100013-[redacted]	1504	20.5416	40520100013-[redacted]	1341

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	370	Sum Weights	370
Mean	-0.040986	Sum Observations	-15.164837
Std Deviation	1.01442638	Variance	1.02906089
Skewness	-0.6955724	Kurtosis	0.11422617
Uncorrected SS	380.345015	Corrected SS	379.723468
Coeff Variation	-2475.053	Std Error Mean	0.05273752

Basic Statistical Measures

Location		Variability	
Mean	-0.04099	Std Deviation	1.01443
Median	0.16987	Variance	1.02906
Mode	0.74219	Range	5.47903
		Interquartile Range	1.45931

Note: The mode displayed is the smallest of 2 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.77717	Pr > |t|	0.4376
Sign	M	25	Pr >= |M|	0.0108
Signed Rank	S	976.5	Pr >= |S|	0.6359

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.96038	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.09143	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.859455	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	4.871	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	2.070287
99%	1.881686
95%	1.228575
90%	1.053543
75% Q3	0.747789
50% Median	0.169875
25% Q1	-0.711522
10%	-1.471843
5%	-2.092184
1%	-2.912932
0% Min	-3.408746

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=28 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.40875	40520100013-[redacted]	1498	1.79657	40520100013-[redacted]	1519
-3.13286	40520100013-[redacted]	1517	1.88169	40520100013-[redacted]	1518
-3.10958	40520100013-[redacted]	1478	1.93934	40520100013-[redacted]	1344
-2.91293	40520100013-[redacted]	1372	1.97622	40520100013-[redacted]	1589
-2.80668	40520100013-[redacted]	1504	2.07029	40520100013-[redacted]	1341

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	349	Sum Weights	349
Mean	-0.4303981	Sum Observations	-150.20894
Std Deviation	10.4068682	Variance	108.302907
Skewness	-0.5781918	Kurtosis	-0.263225
Uncorrected SS	37754.0612	Corrected SS	37689.4115
Coeff Variation	-2417.9632	Std Error Mean	0.55706689

Basic Statistical Measures

Location		Variability	
Mean	-0.43040	Std Deviation	10.40687
Median	1.66772	Variance	108.30291
Mode	-6.91304	Range	55.34813
		Interquartile Range	14.82125

Note: The mode displayed is the smallest of 5 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.77261	Pr > |t|	0.4403
Sign	M	15.5	Pr >= |M|	0.1082
Signed Rank	S	345.5	Pr >= |S|	0.8550

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.964262	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.092832	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.74979	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	4.328771	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	22.75938
99%	17.91271
95%	12.68687
90%	10.84392
75% Q3	7.40753
50% Median	1.66772
25% Q1	-7.41372
10%	-15.22456
5%	-20.06777
1%	-26.48683
0% Min	-32.58874

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-32.5887	40520100013-[redacted]	1852	17.4072	40520100013-[redacted]	1877
-31.9099	40520100013-[redacted]	1833	17.9127	40520100013-[redacted]	1872
-26.7640	40520100013-[redacted]	1731	17.9954	40520100013-[redacted]	1891
-26.4868	40520100013-[redacted]	1694	18.6219	40520100013-[redacted]	1938
-26.1038	40520100013-[redacted]	1857	22.7594	40520100013-[redacted]	1702

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	349	Sum Weights	349
Mean	-0.0428873	Sum Observations	-14.967661
Std Deviation	1.0147428	Variance	1.02970295
Skewness	-0.5766127	Kurtosis	-0.2605306
Uncorrected SS	358.978549	Corrected SS	358.336627
Coeff Variation	-2366.0694	Std Error Mean	0.05431794

Basic Statistical Measures

Location		Variability	
Mean	-0.04289	Std Deviation	1.01474
Median	0.16924	Variance	1.02970
Mode	-0.67533	Range	5.44081
		Interquartile Range	1.43320

Note: The mode displayed is the smallest of 5 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.78956	Pr > |t|	0.4303
Sign	M	15.5	Pr >= |M|	0.1082
Signed Rank	S	313.5	Pr >= |S|	0.8683

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.964473	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.092875	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.750058	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	4.316386	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=35 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	2.240482
99%	1.731891
95%	1.229753
90%	1.062172
75% Q3	0.718334
50% Median	0.169236
25% Q1	-0.714868
10%	-1.501925
5%	-1.944037
1%	-2.576562
0% Min	-3.200330

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

--- Analysis Visit (N)=35 ---

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.20033	40520100013-[redacted]	1852	1.72589	40520100013 [redacted]	1872
-3.09371	40520100013-[redacted]	1833	1.73189	40520100013 [redacted]	1891
-2.60303	40520100013-[redacted]	1694	1.74498	40520100013 [redacted]	1705
-2.57656	40520100013-[redacted]	1731	1.79761	40520100013 [redacted]	1938
-2.55159	40520100013-[redacted]	1857	2.24048	40520100013 [redacted]	1702

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Moments

N	347	Sum Weights	347
Mean	-0.3635827	Sum Observations	-126.16319
Std Deviation	10.8189753	Variance	117.050226
Skewness	-0.8029258	Kurtosis	0.15184193
Uncorrected SS	40545.2491	Corrected SS	40499.3783
Coeff Variation	-2975.6575	Std Error Mean	0.58079302

Basic Statistical Measures

Location		Variability	
Mean	-0.36358	Std Deviation	10.81898
Median	1.86002	Variance	117.05023
Mode	0.60473	Range	53.83629
		Interquartile Range	14.88131

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.62601	Pr > |t|	0.5317
Sign	M	28.5	Pr >= |M|	0.0026
Signed Rank	S	1596	Pr >= |S|	0.3942

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.946801	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.099018	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.011224	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	5.883925	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	19.94892
99%	17.59826
95%	13.42180
90%	11.14587
75% Q3	7.91676
50% Median	1.86002
25% Q1	-6.96455
10%	-15.95262
5%	-21.57855
1%	-31.78702
0% Min	-33.88736

FILE: normalitybc.lis, RUN: 18JUN2020 10:00
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100013/STAT/Program.dev/DOC_STAT/normality.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-6.1.2 FINAL

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-33.8874	40520100013-[redacted]	2201	16.6970	40520100013-[redacted]	2053
-33.3787	40520100013-[redacted]	2183	17.5983	40520100013-[redacted]	2144
-33.1571	40520100013-[redacted]	2007	18.8332	40520100013-[redacted]	2278
-31.7870	40520100013-[redacted]	2218	19.4803	40520100013-[redacted]	2284
-28.1267	40520100013-[redacted]	2160	19.9489	40520100013-[redacted]	2153

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Moments

N	347	Sum Weights	347
Mean	-0.0353861	Sum Observations	-12.278976
Std Deviation	1.02339086	Variance	1.04732886
Skewness	-0.8014075	Kurtosis	0.14366209
Uncorrected SS	362.810289	Corrected SS	362.375784
Coeff Variation	-2892.0705	Std Error Mean	0.0549385

Basic Statistical Measures

Location		Variability	
Mean	-0.03539	Std Deviation	1.02339
Median	0.17390	Variance	1.04733
Mode	0.05664	Range	5.12952
		Interquartile Range	1.41016

Note: The mode displayed is the smallest of 4 modes with a count of 2.

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.6441	Pr > |t|	0.5199
Sign	M	28.5	Pr >= |M|	0.0026
Signed Rank	S	1567	Pr >= |S|	0.4028

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.946825	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.099802	Pr > D	<0.0100
Cramer-von Mises	W-Sq	1.019493	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	5.928715	Pr > A-Sq	<0.0050

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

---------- Analysis Visit (N)=42 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Quantiles (Definition 5)

Level	Quantile
100% Max	1.902521
99%	1.671961
95%	1.269575
90%	1.049981
75% Q3	0.749161
50% Median	0.173896
25% Q1	-0.660998
10%	-1.496158
5%	-2.066916
1%	-2.976287
0% Min	-3.227003

STAT-6.1.2
Residual by Week from Proc Mixed for Change from Baseline in AISRS Total Score, Primary Efficacy Analysis Model
(Efficacy Sample)

--- Analysis Visit (N)=42 ---

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Extreme Observations

Lowest			Highest		
Value	USUBJID	Obs	Value	USUBJID	Obs
-3.22700	40520100013-[redacted]	2201	1.65677	40520100013-[redacted]	2144
-3.14078	40520100013-[redacted]	2183	1.67196	40520100013-[redacted]	2053
-3.10521	40520100013-[redacted]	2007	1.76566	40520100013-[redacted]	2278
-2.97629	40520100013-[redacted]	2218	1.82508	40520100013-[redacted]	2284
-2.70089	40520100013-[redacted]	2160	1.90252	40520100013-[redacted]	2153

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[redacted]	Biostatistics Approval	28-Jul-2020 15:44:56
[redacted]	Clinical Programming Approval	28-Jul-2020 14:13:56
[redacted]	Clinical Approval	03-Aug-2020 18:34:55