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 405-201-00014

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. 405-201-00014
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Statistical Analysis Plan

Version: Final

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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 405-201-00014. 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.

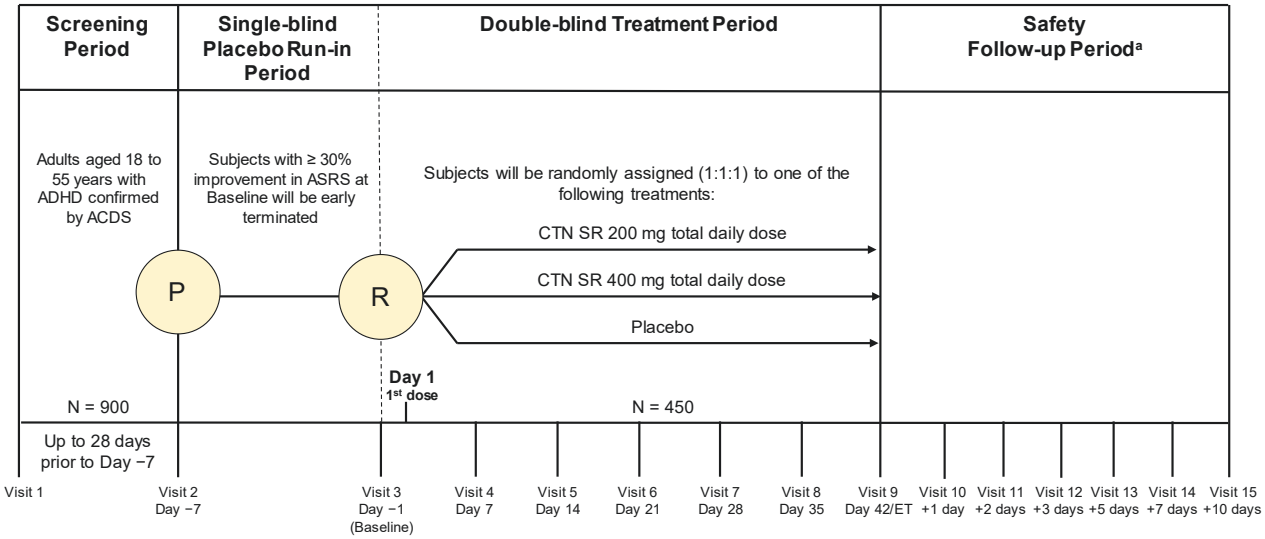

Figure 3-1 Trial Design Schematic

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. Missing data 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 Other Sensitivity Analyses

The following analyses will be performed to evaluate of the sensitivity of the results due to the impact of COVID-19.

1. A MMRM analysis (the same model for the primary efficacy analysis) based on the pre-COVID Efficacy Sample using all OC data set during the double-blind treatment

period . The pre-COVID Efficacy Sample comprises those subjects in the Efficacy Sample who completed or discontinued from the study before March 13, 2020, the National Emergency Announcement on COVID-19[11].

2. A MMRM analysis (the same model for the primary efficacy analysis) based on the Efficacy Sample using pre-COVID data set. The pre-COVID data set consists of actual observations recorded at each visit during the double-blind treatment period before March 13, 2020, the National Emergency Announcement on COVID-19[11].
3. A MMRM analysis (the same model for the primary efficacy analysis) based on the non-COVID Efficacy Sample using all OC data set during the double-blind treatment period. The non-COVID Efficacy Sample comprises those subjects in the Efficacy Sample who had no COVID-19 related PDs.
4. A MMRM analysis (the same model for the primary efficacy analysis) based on the Efficacy Sample using non-COVID data set. The non-COVID data set consists of actual observations recorded at each visit during the non-COVID treatment period which represents the time period where subjects did not have any COVID-19 related PDs during the double-blind treatment period. For each subject, the non-COVID treatment period starts from randomization and ends on the Day 42/ET date or the date before the first COVID-19 related PD (if present), whichever occurs earlier.
5. A MMRM analysis (the same model for the primary efficacy analysis) based on the Efficacy Sample excluding the assessments performed remotely.

8.1.3.4 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].

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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.

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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.

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

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.

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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.

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

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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.

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

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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: $QTcN=QT/(RR)^{0.37}$

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.

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Categorical Change Criteria in QT/QTc Parameters		
Classification	**Category**	**Criteria**
	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 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.

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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.

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.

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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]

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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

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(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.

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.

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-5.2.1.3 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, UN (Pre-COVID Efficacy Sample)

CT-5.2.1.4 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, UN – Pre-COVID Data Set (Efficacy Sample)

CT-5.2.1.5 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, UN (Non-COVID Efficacy Sample)

CT-5.2.1.6 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 – Non-COVID Data Set (Efficacy Sample)

CT-5.2.1.7 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 – Excluding Remote Assessments (Efficacy 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)

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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)

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)

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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)

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)

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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)

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)

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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)

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)

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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)

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)

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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)

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)

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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)

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)

SAP 405-201-00014

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[redacted]	Clinical Approval	26-May-2020 18:40:37
[redacted]	Biostatistics Approval	26-May-2020 19:20:14

CENTANAFADINE 1 OF 5
PROTOCOL 405-201-00014

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	140	2.15	-0.75	140	2.19	-0.72	141	2.18	-0.44	EB-1020 200mg VS PLACEBO	-0.32	0.0059	-0.33
										EB-1020 400mg VS PLACEBO	-0.29	0.0149	-0.29
FIDGET OR SQUIRM WITH YOUR HANDS OR FEET	140	2.21	-0.50	140	2.28	-0.51	141	2.18	-0.50	EB-1020 200mg VS PLACEBO	-0.00	0.9973	-0.00
										EB-1020 400mg VS PLACEBO	-0.01	0.9113	-0.01
DIFFICULTY KEEPING YOUR ATTENTION	140	2.57	-0.78	140	2.54	-0.73	141	2.54	-0.49	EB-1020 200mg VS PLACEBO	-0.29	0.0113	-0.30
										EB-1020 400mg VS PLACEBO	-0.24	0.0450	-0.24
LEAVE YOUR SEAT	140	1.72	-0.59	140	1.78	-0.65	141	1.64	-0.50	EB-1020 200mg VS PLACEBO	-0.09	0.4319	-0.09
										EB-1020 400mg VS PLACEBO	-0.15	0.1936	-0.16
DIFFICULTY CONCENTRATING ON	140	2.29	-0.80	140	2.30	-0.75	141	2.29	-0.50	EB-1020 200mg VS PLACEBO	-0.30	0.0104	-0.31

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.25	0.0356	-0.25
FEEL RESTLESS OR FIDGETY	140	1.93	-0.44	140	2.15	-0.62	141	2.06	-0.41	EB-1020 200mg VS PLACEBO	-0.04	0.7284	-0.04
										EB-1020 400mg VS PLACEBO	-0.22	0.0486	-0.24
TROUBLE WRAPPING UP THE FINAL DETAILS	140	2.40	-0.67	140	2.44	-0.73	141	2.55	-0.47	EB-1020 200mg VS PLACEBO	-0.20	0.0649	-0.22
										EB-1020 400mg VS PLACEBO	-0.26	0.0202	-0.28
DIFFICULTY UNWINDING AND RELAXING	140	1.87	-0.44	140	1.91	-0.41	141	1.80	-0.34	EB-1020 200mg VS PLACEBO	-0.09	0.4355	-0.09
										EB-1020 400mg VS PLACEBO	-0.06	0.5941	-0.06
DIFFICULTY GETTING THINGS IN ORDER	140	2.36	-0.74	140	2.54	-0.84	141	2.53	-0.62	EB-1020 200mg VS PLACEBO	-0.13	0.2832	-0.13
										EB-1020 400mg VS PLACEBO	-0.22	0.0627	-0.22

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 3 OF 5
PROTOCOL 405-201-00014

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	140	1.79	-0.49	140	1.92	-0.61	141	1.75	-0.46	EB-1020 200mg VS PLACEBO	-0.02	0.8394	-0.02
										EB-1020 400mg VS PLACEBO	-0.14	0.2203	-0.15
AVOID OR DELAY GETTING STARTED	140	2.51	-0.67	140	2.52	-0.59	141	2.50	-0.44	EB-1020 200mg VS PLACEBO	-0.23	0.0473	-0.24
										EB-1020 400mg VS PLACEBO	-0.15	0.2113	-0.15
TALKING TOO MUCH	140	1.71	-0.61	140	1.85	-0.68	141	1.71	-0.47	EB-1020 200mg VS PLACEBO	-0.14	0.1981	-0.15
										EB-1020 400mg VS PLACEBO	-0.21	0.0668	-0.22
MISPLACE OR HAVE DIFFICULTY FINDING	140	2.20	-0.77	140	2.21	-0.78	141	2.12	-0.41	EB-1020 200mg VS PLACEBO	-0.35	0.0022	-0.37
										EB-1020 400mg VS PLACEBO	-0.37	0.0017	-0.38
FINISHING THE SENTENCES OF THE PEOPLE	140	1.90	-0.84	140	1.92	-0.77	141	1.80	-0.42	EB-1020 200mg VS PLACEBO	-0.42	0.0002	-0.45

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 4 OF 5
PROTOCOL 405-201-00014

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	-0.35	0.0025	-0.36
BEING DISTRACTED BY ACTIVITY OR NOISE	140	2.39	-0.75	140	2.47	-0.60	141	2.53	-0.35	EB-1020 200mg VS PLACEBO	-0.41	0.0001	-0.46
										EB-1020 400mg VS PLACEBO	-0.25	0.0191	-0.28
DIFFICULTY WAITING YOUR TURN	140	1.87	-0.74	140	1.91	-0.77	141	1.79	-0.48	EB-1020 200mg VS PLACEBO	-0.26	0.0176	-0.28
										EB-1020 400mg VS PLACEBO	-0.29	0.0100	-0.31
PROBLEMS REMEMBERING	140	2.01	-0.81	140	2.11	-0.67	141	2.11	-0.44	EB-1020 200mg VS PLACEBO	-0.37	0.0026	-0.36
										EB-1020 400mg VS PLACEBO	-0.23	0.0648	-0.22
INTERRUPT OTHERS WHEN THEY ARE BUSY	140	1.71	-0.71	140	1.73	-0.82	141	1.57	-0.43	EB-1020 200mg VS PLACEBO	-0.29	0.0068	-0.32
										EB-1020 400mg VS PLACEBO	-0.39	0.0004	-0.43

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.1 FINAL

CENTANAFADINE 5 OF 5
PROTOCOL 405-201-00014

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)	140	37.59	-12.1	140	38.76	-12.5	141	37.65	-8.07	EB-1020 200mg VS PLACEBO	-4.01	0.0021	-0.37
										EB-1020 400mg VS PLACEBO	-4.42	0.0009	-0.40

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

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PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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 405-201-00014

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	124	2.85	-0.67	114	2.73	-0.57	130	2.95	-0.29	EB-1020 200mg VS PLACEBO	-0.38	0.0015	-0.40
										EB-1020 400mg VS PLACEBO	-0.29	0.0213	-0.30
ASRS-DIFFICULTY GETTING THINGS IN ORDER	124	2.81	-0.72	114	2.90	-0.62	130	3.00	-0.30	EB-1020 200mg VS PLACEBO	-0.42	0.0008	-0.43
										EB-1020 400mg VS PLACEBO	-0.33	0.0100	-0.33
ASRS-PROBLEM REMEMBERING APPTS/OBLIGATNS	124	2.56	-0.82	114	2.67	-0.70	130	2.72	-0.42	EB-1020 200mg VS PLACEBO	-0.40	0.0022	-0.39
										EB-1020 400mg VS PLACEBO	-0.28	0.0330	-0.27
ASRS-AVOID/DELAY GETTNG STARTD ON THGHTS	124	3.06	-0.63	114	3.22	-0.72	130	3.19	-0.40	EB-1020 200mg VS PLACEBO	-0.22	0.0685	-0.23
										EB-1020 400mg VS PLACEBO	-0.32	0.0128	-0.32

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

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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	124	3.01	-0.59	114	2.99	-0.56	130	3.00	-0.47	EB-1020 200mg VS PLACEBO	-0.12	0.3314	-0.12
										EB-1020 400mg VS PLACEBO	-0.09	0.4849	-0.09
ASRS-FEEL OVERLY ACTIVE TO DO THINGS	124	2.56	-0.52	114	2.56	-0.56	130	2.55	-0.46	EB-1020 200mg VS PLACEBO	-0.07	0.6162	-0.06
										EB-1020 400mg VS PLACEBO	-0.10	0.4410	-0.10
ASRS-MAKE CARELESS MISTAKES	124	2.69	-0.73	114	2.76	-0.79	130	2.81	-0.40	EB-1020 200mg VS PLACEBO	-0.33	0.0104	-0.32
										EB-1020 400mg VS PLACEBO	-0.39	0.0034	-0.38
ASRS-DIFFICULTY KEEPING ATTENTION	124	3.18	-0.84	114	3.28	-0.75	130	3.38	-0.37	EB-1020 200mg VS PLACEBO	-0.46	0.0004	-0.45
										EB-1020 400mg VS PLACEBO	-0.38	0.0042	-0.37
ASRS-DIFFICULTY KEEPING CONCENTRATION	124	2.76	-0.81	114	2.89	-0.79	130	2.96	-0.30	EB-1020 200mg VS PLACEBO	-0.50	0.0000	-0.52

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 3 OF 5
PROTOCOL 405-201-00014

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	-0.49	0.0001	-0.50
ASRS-MISPLACE/DIFFICULTY FINDING THINGS	124	2.74	-0.83	114	3.00	-0.85	130	2.90	-0.40	EB-1020 200mg VS PLACEBO	-0.42	0.0009	-0.42
										EB-1020 400mg VS PLACEBO	-0.44	0.0007	-0.44
ASRS-DISTRACTED BY ACTIVITY OR NOISE	124	3.10	-0.73	114	3.09	-0.61	130	3.15	-0.27	EB-1020 200mg VS PLACEBO	-0.47	0.0001	-0.48
										EB-1020 400mg VS PLACEBO	-0.35	0.0061	-0.35
ASRS-LEAVE SEAT IN MEETNGS/ORDR SITUATNS	124	1.95	-0.59	114	2.10	-0.76	130	1.90	-0.32	EB-1020 200mg VS PLACEBO	-0.26	0.0347	-0.27
										EB-1020 400mg VS PLACEBO	-0.44	0.0008	-0.44
ASRS-FEELING RESTLESS OR FIDGETY	124	2.92	-0.65	114	2.89	-0.70	130	2.89	-0.46	EB-1020 200mg VS PLACEBO	-0.19	0.1224	-0.19
										EB-1020 400mg VS PLACEBO	-0.24	0.0623	-0.24

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 4 OF 5
PROTOCOL 405-201-00014

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	124	2.56	-0.57	114	2.61	-0.61	130	2.64	-0.42	EB-1020 200mg VS PLACEBO	-0.15	0.2810	-0.14
										EB-1020 400mg VS PLACEBO	-0.19	0.1729	-0.18
ASRS-FIND YOURSELF TALKING TOO MUCH	124	2.52	-0.75	114	2.61	-0.70	130	2.58	-0.45	EB-1020 200mg VS PLACEBO	-0.31	0.0119	-0.32
										EB-1020 400mg VS PLACEBO	-0.26	0.0408	-0.26
ASRS-FINISH SENTENCES OF PEOPLE	124	2.62	-0.87	114	2.65	-0.86	130	2.68	-0.54	EB-1020 200mg VS PLACEBO	-0.33	0.0103	-0.32
										EB-1020 400mg VS PLACEBO	-0.32	0.0165	-0.31
ASRS-DIFFCULTY WAITING YOUR TURN	124	2.30	-0.72	114	2.55	-0.74	130	2.42	-0.45	EB-1020 200mg VS PLACEBO	-0.26	0.0433	-0.25
										EB-1020 400mg VS PLACEBO	-0.28	0.0355	-0.27
ASRS-INTERRUPT OTHERS WHEN THEY ARE BUSY	124	2.21	-0.67	114	2.33	-0.83	130	2.47	-0.54	EB-1020 200mg VS PLACEBO	-0.13	0.2921	-0.13

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

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OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-1.2 FINAL

CENTANAFADINE 5 OF 5
PROTOCOL 405-201-00014

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	-0.28	0.0211	-0.30
ASRS TOTAL SCORE OF 18 ITEMS (DERIVED)	124	48.39	-12.2	114	49.83	-12.6	130	50.21	-7.28	EB-1020 200mg VS PLACEBO	-4.91	0.0016	-0.40
										EB-1020 400mg VS PLACEBO	-5.33	0.0009	-0.43

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

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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	39	[redacted]

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

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

The Mixed Procedure

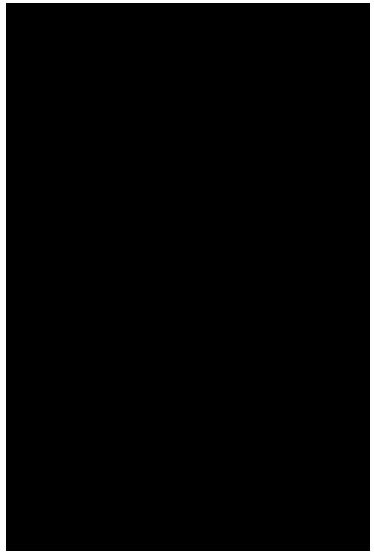
Class Level Information

Class	Levels	Values
SUBJID	421	[redacted]

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

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

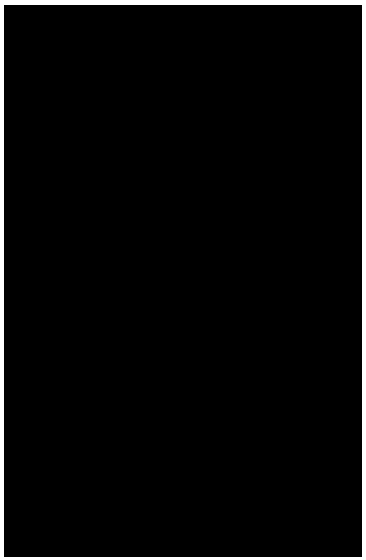
The Mixed Procedure



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

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

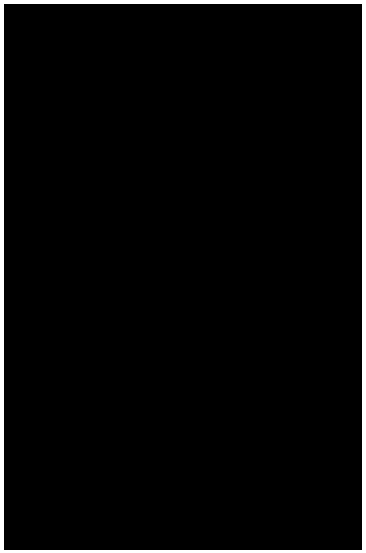
The Mixed Procedure



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

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

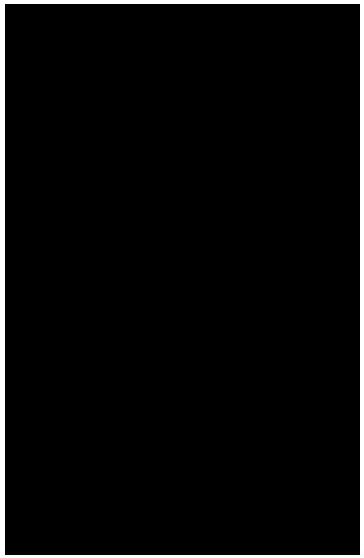
The Mixed Procedure



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

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

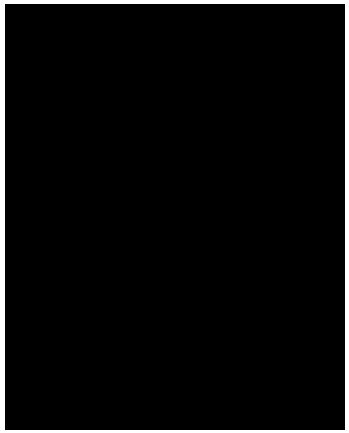
The Mixed Procedure



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

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

The Mixed Procedure



SEX 2 F M

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

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

The Mixed Procedure

Dimensions

Covariance Parameters	21
Columns in X	129
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2227
Number of Observations Used	2227
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	15728.87827870	
1	2	13520.41397294	0.00033945
2	1	13518.67561888	0.00000469
3	1	13518.65293347	0.00000000

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

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

The Mixed Procedure

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	43.3236
UN(2,1)	SUBJID	38.2897
UN(2,2)	SUBJID	70.3806
UN(3,1)	SUBJID	37.4535
UN(3,2)	SUBJID	60.2826
UN(3,3)	SUBJID	81.6833
UN(4,1)	SUBJID	38.9483
UN(4,2)	SUBJID	59.0458
UN(4,3)	SUBJID	73.8743
UN(4,4)	SUBJID	89.8024
UN(5,1)	SUBJID	38.5482
UN(5,2)	SUBJID	60.6062
UN(5,3)	SUBJID	72.6270
UN(5,4)	SUBJID	82.3083
UN(5,5)	SUBJID	97.7229
UN(6,1)	SUBJID	37.9468
UN(6,2)	SUBJID	60.5956
UN(6,3)	SUBJID	74.6496

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(6,4)	SUBJID	84.5321
UN(6,5)	SUBJID	91.9940
UN(6,6)	SUBJID	109.35

Fit Statistics

-2 Res Log Likelihood	13518.7
AIC (Smaller is Better)	13560.7
AICC (Smaller is Better)	13561.1
BIC (Smaller is Better)	13645.5

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2210.23	<.0001

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

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

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
POOLCNTR	38	377	2.08	0.0003
AVISITN	5	348	1.04	0.3931
TRTPN	2	375	10.16	<.0001
AVISITN*TRTPN	10	518	1.60	0.1019
SEX	1	389	0.50	0.4820
AVISITN*SEX	5	346	1.55	0.1739
TRTPN*SEX	2	391	1.17	0.3101
AVISITN*TRTPN*SEX	10	518	0.43	0.9331
BASE*AVISITN	6	376	1.86	0.0859

Coefficients for 1 vs. 3 BY SEX AT DAY 42

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

FILE: stat2a.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat2.sas
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]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					

FILE: stat2a.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat2.sas
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]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
AVISITN			7		

FILE: stat2a.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat2.sas
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
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	
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	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			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		
AVISITN*SEX		F	35		
AVISITN*SEX		M	35		

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	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	
AVISITN*TRTPN*SEX		M	14	2	
AVISITN*TRTPN*SEX		F	14	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*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	
AVISITN*TRTPN*SEX		F	35	3	
AVISITN*TRTPN*SEX		M	35	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*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					

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					
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POOLCNTR					
POOLCNTR					
POOLCNTR					

FILE: stat2a.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
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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]				
POOLCNTR					
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	

FILE: stat2a.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat2.sas
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
AVISITN*TRTPN			21	3	
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		

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		M	28		
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	

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	14	2	
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	

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	35	2	
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	0.2939	2.6567	383	0.11	0.9120
2 vs. 3 BY SEX AT DAY 42	-2.4115	2.6901	387	-0.90	0.3706

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	-5.4027	0.8667	378	-6.23	<.0001	0.05	-7.1068	-3.6986
AVISITN*TRTPN*SEX	M	7	1	-6.9479	0.8409	383	-8.26	<.0001	0.05	-8.6013	-5.2946
AVISITN*TRTPN*SEX	F	7	2	-7.1868	0.8594	376	-8.36	<.0001	0.05	-8.8767	-5.4969
AVISITN*TRTPN*SEX	M	7	2	-5.0335	0.8496	379	-5.92	<.0001	0.05	-6.7041	-3.3629
AVISITN*TRTPN*SEX	F	7	3	-3.7852	0.8669	378	-4.37	<.0001	0.05	-5.4897	-2.0807
AVISITN*TRTPN*SEX	M	7	3	-4.6461	0.8279	378	-5.61	<.0001	0.05	-6.2739	-3.0183
AVISITN*TRTPN*SEX	F	14	1	-7.8481	1.0852	397	-7.23	<.0001	0.05	-9.9815	-5.7147
AVISITN*TRTPN*SEX	M	14	1	-10.2218	1.0454	386	-9.78	<.0001	0.05	-12.2771	-8.1665
AVISITN*TRTPN*SEX	F	14	2	-9.4956	1.1164	412	-8.51	<.0001	0.05	-11.6901	-7.3010
AVISITN*TRTPN*SEX	M	14	2	-8.6092	1.0577	399	-8.14	<.0001	0.05	-10.6885	-6.5298

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	-5.3059	1.0908	381	-4.86	<.0001	0.05	-7.4506	-3.1612
AVISITN*TRTPN*SEX	M	14	3	-5.5124	1.0340	407	-5.33	<.0001	0.05	-7.5451	-3.4797
AVISITN*TRTPN*SEX	F	21	1	-10.5355	1.1670	394	-9.03	<.0001	0.05	-12.8298	-8.2411
AVISITN*TRTPN*SEX	M	21	1	-11.0775	1.1325	393	-9.78	<.0001	0.05	-13.3040	-8.8510
AVISITN*TRTPN*SEX	F	21	2	-12.3262	1.2227	419	-10.08	<.0001	0.05	-14.7295	-9.9229
AVISITN*TRTPN*SEX	M	21	2	-10.3736	1.1476	408	-9.04	<.0001	0.05	-12.6295	-8.1176
AVISITN*TRTPN*SEX	F	21	3	-6.9788	1.1675	374	-5.98	<.0001	0.05	-9.2745	-4.6830
AVISITN*TRTPN*SEX	M	21	3	-6.6063	1.1096	403	-5.95	<.0001	0.05	-8.7877	-4.4249
AVISITN*TRTPN*SEX	F	28	1	-10.4794	1.2327	400	-8.50	<.0001	0.05	-12.9028	-8.0561
AVISITN*TRTPN*SEX	M	28	1	-11.4879	1.1864	390	-9.68	<.0001	0.05	-13.8205	-9.1553
AVISITN*TRTPN*SEX	F	28	2	-12.7682	1.2871	416	-9.92	<.0001	0.05	-15.2983	-10.2381
AVISITN*TRTPN*SEX	M	28	2	-10.4550	1.2036	406	-8.69	<.0001	0.05	-12.8211	-8.0890
AVISITN*TRTPN*SEX	F	28	3	-7.5212	1.2256	373	-6.14	<.0001	0.05	-9.9311	-5.1113
AVISITN*TRTPN*SEX	M	28	3	-6.6440	1.1591	399	-5.73	<.0001	0.05	-8.9227	-4.3652
AVISITN*TRTPN*SEX	F	35	1	-11.4369	1.2920	398	-8.85	<.0001	0.05	-13.9769	-8.8969
AVISITN*TRTPN*SEX	M	35	1	-11.7373	1.2478	391	-9.41	<.0001	0.05	-14.1904	-9.2842
AVISITN*TRTPN*SEX	F	35	2	-14.6552	1.3521	409	-10.84	<.0001	0.05	-17.3132	-11.9971
AVISITN*TRTPN*SEX	M	35	2	-11.6595	1.2727	414	-9.16	<.0001	0.05	-14.1614	-9.1577
AVISITN*TRTPN*SEX	F	35	3	-8.5420	1.2828	371	-6.66	<.0001	0.05	-11.0644	-6.0196

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	-7.1620	1.2125	396	-5.91	<.0001	0.05	-9.5458	-4.7783
AVISITN*TRTPN*SEX	F	42	1	-12.3096	1.3743	401	-8.96	<.0001	0.05	-15.0112	-9.6079
AVISITN*TRTPN*SEX	M	42	1	-11.8471	1.3215	389	-8.96	<.0001	0.05	-14.4454	-9.2489
AVISITN*TRTPN*SEX	F	42	2	-14.1591	1.4448	408	-9.80	<.0001	0.05	-16.9992	-11.3190
AVISITN*TRTPN*SEX	M	42	2	-10.9912	1.3502	412	-8.14	<.0001	0.05	-13.6453	-8.3372
AVISITN*TRTPN*SEX	F	42	3	-8.4423	1.3593	370	-6.21	<.0001	0.05	-11.1152	-5.7695
AVISITN*TRTPN*SEX	M	42	3	-7.6860	1.2832	394	-5.99	<.0001	0.05	-10.2088	-5.1632

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	39	[redacted]

FILE: stat2b.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
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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

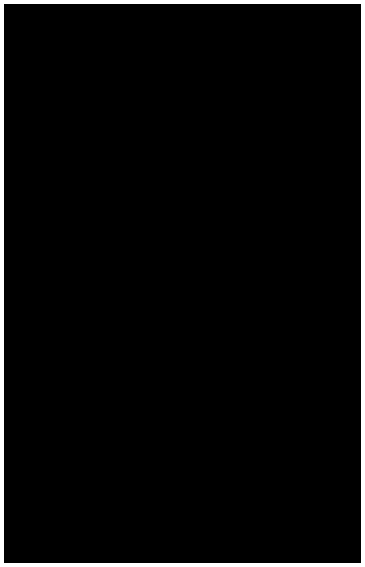
Class Level Information

Class	Levels	Values
SUBJID	421	[redacted]

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

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

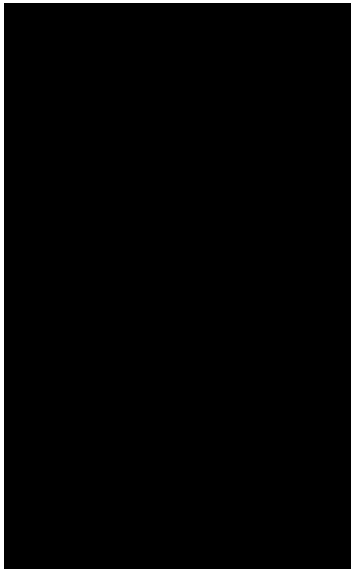
The Mixed Procedure



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

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

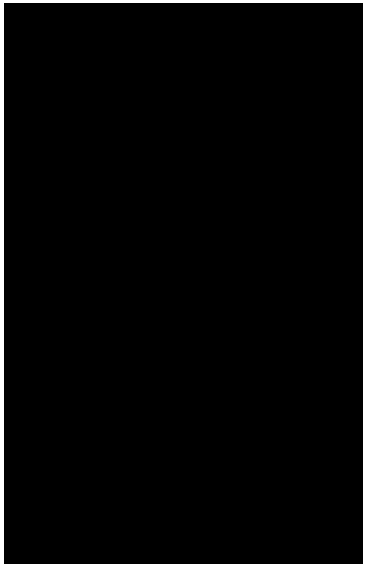
The Mixed Procedure



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

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

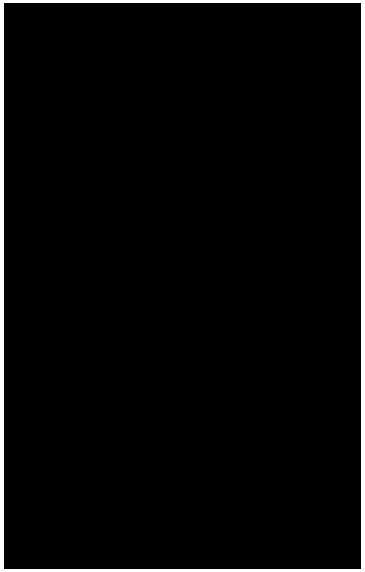
The Mixed Procedure



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

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

The Mixed Procedure

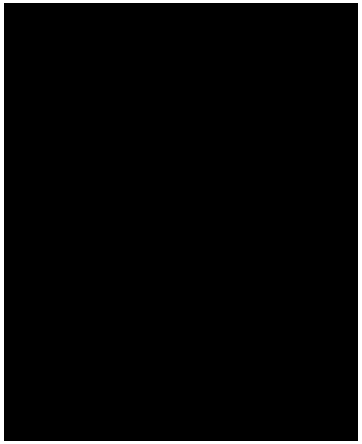


FILE: stat2b.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat2.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-3.2 FINAL

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

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

The Mixed Procedure



RACEGRP 2 All Other Races White

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

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

The Mixed Procedure

Dimensions

Covariance Parameters	21
Columns in X	129
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2227
Number of Observations Used	2227
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	15704.36373766	
1	2	13498.26971465	0.00024380
2	1	13497.03266047	0.00000273
3	1	13497.01951942	0.00000000

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

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

The Mixed Procedure

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	43.3078
UN(2,1)	SUBJID	37.9417
UN(2,2)	SUBJID	69.5782
UN(3,1)	SUBJID	36.8986
UN(3,2)	SUBJID	59.1553
UN(3,3)	SUBJID	80.0027
UN(4,1)	SUBJID	38.6686
UN(4,2)	SUBJID	58.2307
UN(4,3)	SUBJID	72.5007
UN(4,4)	SUBJID	88.6310
UN(5,1)	SUBJID	38.3557
UN(5,2)	SUBJID	59.4955
UN(5,3)	SUBJID	71.0718
UN(5,4)	SUBJID	81.0660
UN(5,5)	SUBJID	96.3614
UN(6,1)	SUBJID	37.6519
UN(6,2)	SUBJID	59.1146
UN(6,3)	SUBJID	72.6172

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(6,4)	SUBJID	82.6569
UN(6,5)	SUBJID	90.2016
UN(6,6)	SUBJID	106.64

Fit Statistics

-2 Res Log Likelihood	13497.0
AIC (Smaller is Better)	13539.0
AICC (Smaller is Better)	13539.5
BIC (Smaller is Better)	13623.9

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2207.34	<.0001

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

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

The Mixed Procedure

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
POOLCNTR	38	377	2.15	0.0002
AVISITN	5	352	1.25	0.2856
TRTPN	2	389	9.82	<.0001
AVISITN*TRTPN	10	527	2.05	0.0272
RACEGRP	1	414	8.58	0.0036
AVISITN*RACEGRP	5	353	2.06	0.0695
TRTPN*RACEGRP	2	394	0.85	0.4284
AVISIT*TRTPN*RACEGRP	10	526	1.21	0.2828
BASE*AVISITN	6	380	2.09	0.0534

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

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

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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

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					
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POOLCNTR					

FILE: stat2b.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
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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

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					
AVISITN			7		

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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

Coefficients for 1 vs. 3 BY RACEGRP AT DAY 42

Effect	Pooled Center Number	RACEGRP	Analysis Visit (N)	Planned Treatment (N)	Row1
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	
AVISITN*TRTPN			28	1	
AVISITN*TRTPN			28	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
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		
AVISITN*RACEGRP		All Other Races	35		
AVISITN*RACEGRP		White	35		

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	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	
AVISIT*TRTPN*RACEGRP		White	14	2	
AVISIT*TRTPN*RACEGRP		All Other Races	14	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 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	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	
AVISIT*TRTPN*RACEGRP		All Other Races	35	3	
AVISIT*TRTPN*RACEGRP		White	35	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 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	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	[redacted]				
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
POOLCNTR					
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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

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					
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POOLCNTR					

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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

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					
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	

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			21	3	
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		

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		White	28		
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	

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	14	2	
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	

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	35	2	
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	-1.8375	3.1294	385	-0.59	0.5574
2 vs. 3 BY RACEGRP AT DAY 42	-1.0598	3.3731	395	-0.31	0.7535

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	-7.0994	1.2575	381	-5.65	<.0001	0.05	-9.5720	-4.6268
AVISIT*TRTPN*RACEGRP	White	7	1	-5.9784	0.6928	382	-8.63	<.0001	0.05	-7.3405	-4.6163
AVISIT*TRTPN*RACEGRP	All Other Races	7	2	-9.0250	1.3770	376	-6.55	<.0001	0.05	-11.7327	-6.3173
AVISIT*TRTPN*RACEGRP	White	7	2	-5.4838	0.6732	378	-8.15	<.0001	0.05	-6.8075	-4.1602
AVISIT*TRTPN*RACEGRP	All Other Races	7	3	-4.0554	1.2955	376	-3.13	0.0019	0.05	-6.6028	-1.5080
AVISIT*TRTPN*RACEGRP	White	7	3	-4.3810	0.6867	378	-6.38	<.0001	0.05	-5.7311	-3.0309
AVISIT*TRTPN*RACEGRP	All Other Races	14	1	-11.5844	1.5470	394	-7.49	<.0001	0.05	-14.6259	-8.5429
AVISIT*TRTPN*RACEGRP	White	14	1	-8.3630	0.8593	397	-9.73	<.0001	0.05	-10.0523	-6.6737
AVISIT*TRTPN*RACEGRP	All Other Races	14	2	-12.1861	1.7791	416	-6.85	<.0001	0.05	-15.6834	-8.6889
AVISIT*TRTPN*RACEGRP	White	14	2	-8.4720	0.8445	407	-10.03	<.0001	0.05	-10.1321	-6.8120

FILE: stat2b.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	All Other Races	14	3	-4.3684	1.6060	390	-2.72	0.0068	0.05	-7.5259	-1.2109
AVISIT*TRTPN*RACEGRP	White	14	3	-5.7832	0.8529	406	-6.78	<.0001	0.05	-7.4599	-4.1064
AVISIT*TRTPN*RACEGRP	All Other Races	21	1	-13.4900	1.6638	398	-8.11	<.0001	0.05	-16.7608	-10.2191
AVISIT*TRTPN*RACEGRP	White	21	1	-10.0518	0.9235	400	-10.88	<.0001	0.05	-11.8674	-8.2363
AVISIT*TRTPN*RACEGRP	All Other Races	21	2	-15.6552	1.9656	433	-7.96	<.0001	0.05	-19.5185	-11.7918
AVISIT*TRTPN*RACEGRP	White	21	2	-10.4459	0.9123	409	-11.45	<.0001	0.05	-12.2393	-8.6525
AVISIT*TRTPN*RACEGRP	All Other Races	21	3	-8.2352	1.7156	389	-4.80	<.0001	0.05	-11.6083	-4.8622
AVISIT*TRTPN*RACEGRP	White	21	3	-6.4527	0.9087	398	-7.10	<.0001	0.05	-8.2391	-4.6662
AVISIT*TRTPN*RACEGRP	All Other Races	28	1	-13.8665	1.7467	394	-7.94	<.0001	0.05	-17.3004	-10.4326
AVISIT*TRTPN*RACEGRP	White	28	1	-10.1758	0.9760	404	-10.43	<.0001	0.05	-12.0944	-8.2572
AVISIT*TRTPN*RACEGRP	All Other Races	28	2	-14.8643	2.0891	437	-7.12	<.0001	0.05	-18.9702	-10.7584
AVISIT*TRTPN*RACEGRP	White	28	2	-10.8890	0.9603	407	-11.34	<.0001	0.05	-12.7767	-9.0013
AVISIT*TRTPN*RACEGRP	All Other Races	28	3	-8.8032	1.8058	391	-4.87	<.0001	0.05	-12.3536	-5.2529
AVISIT*TRTPN*RACEGRP	White	28	3	-6.6365	0.9533	395	-6.96	<.0001	0.05	-8.5106	-4.7624
AVISIT*TRTPN*RACEGRP	All Other Races	35	1	-14.0585	1.8441	403	-7.62	<.0001	0.05	-17.6837	-10.4333
AVISIT*TRTPN*RACEGRP	White	35	1	-10.8714	1.0221	400	-10.64	<.0001	0.05	-12.8808	-8.8621
AVISIT*TRTPN*RACEGRP	All Other Races	35	2	-18.2432	2.2321	447	-8.17	<.0001	0.05	-22.6299	-13.8565
AVISIT*TRTPN*RACEGRP	White	35	2	-12.0993	1.0101	407	-11.98	<.0001	0.05	-14.0849	-10.1137
AVISIT*TRTPN*RACEGRP	All Other Races	35	3	-9.4821	1.8927	392	-5.01	<.0001	0.05	-13.2032	-5.7609

FILE: stat2b.lis, RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-7.4198	0.9957	392	-7.45	<.0001	0.05	-9.3775	-5.4622
AVISIT*TRTPN*RACEGRP	All Other Races	42	1	-16.2801	1.9359	397	-8.41	<.0001	0.05	-20.0860	-12.4743
AVISIT*TRTPN*RACEGRP	White	42	1	-10.8032	1.0812	402	-9.99	<.0001	0.05	-12.9286	-8.6777
AVISIT*TRTPN*RACEGRP	All Other Races	42	2	-16.4160	2.3407	424	-7.01	<.0001	0.05	-21.0168	-11.8152
AVISIT*TRTPN*RACEGRP	White	42	2	-11.7167	1.0708	409	-10.94	<.0001	0.05	-13.8216	-9.6118
AVISIT*TRTPN*RACEGRP	All Other Races	42	3	-10.9567	1.9920	390	-5.50	<.0001	0.05	-14.8731	-7.0403
AVISIT*TRTPN*RACEGRP	White	42	3	-7.3172	1.0483	390	-6.98	<.0001	0.05	-9.3781	-5.2562

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	39	[redacted]

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

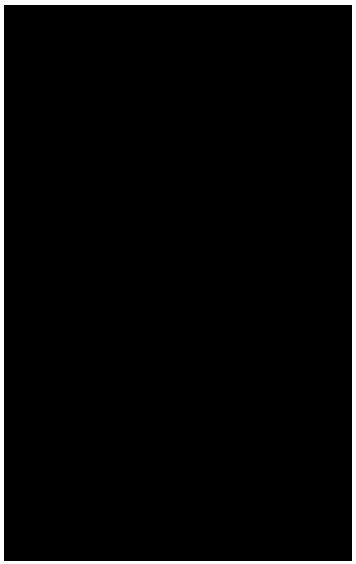
Class Level Information

Class	Levels	Values
SUBJID	421	[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

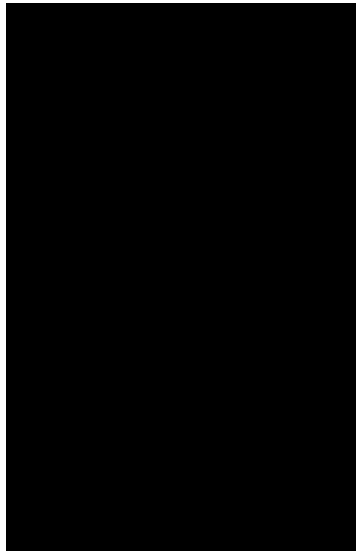
[redacted]

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

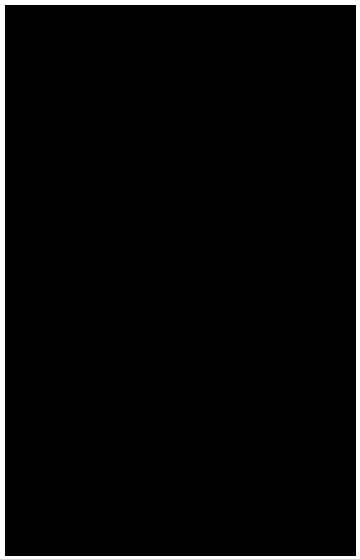


SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

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

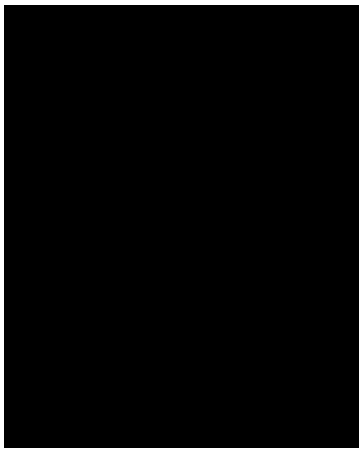


SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.1 FINAL

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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	73
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2227
Number of Observations Used	2227
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	15800.38727426	
1	2	13568.79752107	0.00031679
2	1	13567.17482444	0.00000418
3	1	13567.15460435	0.00000000

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	SUBJID	43.6133
UN(2,1)	SUBJID	38.4610
UN(2,2)	SUBJID	70.3656
UN(3,1)	SUBJID	37.5232
UN(3,2)	SUBJID	59.9507
UN(3,3)	SUBJID	81.2761
UN(4,1)	SUBJID	39.2740
UN(4,2)	SUBJID	59.0315
UN(4,3)	SUBJID	73.7748
UN(4,4)	SUBJID	89.8567
UN(5,1)	SUBJID	38.9775
UN(5,2)	SUBJID	60.4118
UN(5,3)	SUBJID	72.5077
UN(5,4)	SUBJID	82.3971
UN(5,5)	SUBJID	97.7856
UN(6,1)	SUBJID	38.2789
UN(6,2)	SUBJID	60.0226
UN(6,3)	SUBJID	74.3151

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	84.3266
UN(6,5)	SUBJID	91.8307
UN(6,6)	SUBJID	108.84

Fit Statistics

-2 Res Log Likelihood	13567.2
AIC (Smaller is Better)	13609.2
AICC (Smaller is Better)	13609.6
BIC (Smaller is Better)	13694.0

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2233.23	<.0001

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				1.1270	4.7691	581	0.24	0.8133
AVISITN		7		0.5954	2.6832	341	0.22	0.8245
AVISITN		14		-1.3583	2.4093	363	-0.56	0.5733
AVISITN		21		0.8510	2.0449	353	0.42	0.6775
AVISITN		28		-1.3535	1.7676	346	-0.77	0.4444
AVISITN		35		-0.6029	1.5610	337	-0.39	0.6996
AVISITN		42		0				
TRTPN			1	-4.0055	1.2937	368	-3.10	0.0021
TRTPN			2	-4.4192	1.3220	378	-3.34	0.0009
TRTPN			3	0				
AVISITN*TRTPN		7	1	2.0743	1.0975	335	1.89	0.0596
AVISITN*TRTPN		7	2	2.6082	1.1265	339	2.32	0.0212
AVISITN*TRTPN		7	3	0				
AVISITN*TRTPN		14	1	0.3557	0.9813	357	0.36	0.7172
AVISITN*TRTPN		14	2	0.7686	1.0094	356	0.76	0.4469
AVISITN*TRTPN		14	3	0				
AVISITN*TRTPN		21	1	-0.01500	0.8285	348	-0.02	0.9856
AVISITN*TRTPN		21	2	-0.07966	0.8542	350	-0.09	0.9258
AVISITN*TRTPN		21	3	0				

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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|
AVISITN*TRTPN		28	1	0.06611	0.7137	344	0.09	0.9263
AVISITN*TRTPN		28	2	-0.05910	0.7352	343	-0.08	0.9360
AVISITN*TRTPN		28	3	0				
AVISITN*TRTPN		35	1	0.2307	0.6270	335	0.37	0.7131
AVISITN*TRTPN		35	2	-0.8321	0.6479	335	-1.28	0.1999
AVISITN*TRTPN		35	3	0				
AVISITN*TRTPN		42	1	0				
AVISITN*TRTPN		42	2	0				
AVISITN*TRTPN		42	3	0				
POOLCNTR	[redacted]			1.7152	3.7658	428	0.46	0.6490
POOLCNTR				-5.1572	5.2435	403	-0.98	0.3259
POOLCNTR				1.6504	3.6560	432	0.45	0.6519
POOLCNTR				0.5885	4.4348	413	0.13	0.8945
POOLCNTR				-3.9263	4.4129	414	-0.89	0.3741
POOLCNTR				1.2240	3.7770	428	0.32	0.7460
POOLCNTR				0.8833	3.7274	429	0.24	0.8128
POOLCNTR				-2.1241	4.2789	416	-0.50	0.6199
POOLCNTR				1.9882	5.1695	403	0.38	0.7007
POOLCNTR				-3.3736	3.8277	426	-0.88	0.3786

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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]			-2.6399	4.1913	418	-0.63	0.5291
POOLCNTR				-9.4424	5.1658	404	-1.83	0.0683
POOLCNTR				-3.1314	4.3052	416	-0.73	0.4674
POOLCNTR				3.6852	4.0316	425	0.91	0.3612
POOLCNTR				-1.5147	4.0615	421	-0.37	0.7094
POOLCNTR				-0.7002	4.5899	411	-0.15	0.8788
POOLCNTR				-3.9140	4.1883	418	-0.93	0.3506
POOLCNTR				2.1512	4.8016	408	0.45	0.6544
POOLCNTR				-2.5698	4.8033	408	-0.54	0.5929
POOLCNTR				0.4082	3.9332	424	0.10	0.9174
POOLCNTR				-2.0848	4.1288	419	-0.50	0.6139
POOLCNTR				9.2093	4.8043	408	1.92	0.0560
POOLCNTR				3.0940	3.9314	423	0.79	0.4317
POOLCNTR				-3.5346	3.9635	422	-0.89	0.3730
POOLCNTR				-2.2842	4.1174	419	-0.55	0.5793
POOLCNTR				6.8249	4.3486	415	1.57	0.1173
POOLCNTR				-5.2814	4.4034	414	-1.20	0.2311
POOLCNTR				-2.7571	4.2019	417	-0.66	0.5121
POOLCNTR				2.0058	3.6634	432	0.55	0.5843

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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]			3.0549	3.6512	431	0.84	0.4032
POOLCNTR				-2.0401	4.5650	411	-0.45	0.6552
POOLCNTR				1.7734	4.5671	411	0.39	0.6980
POOLCNTR				-4.4210	3.9066	427	-1.13	0.2584
POOLCNTR				0.6462	4.4087	414	0.15	0.8835
POOLCNTR				-0.5512	3.8270	427	-0.14	0.8855
POOLCNTR				-1.6096	5.1715	403	-0.31	0.7558
POOLCNTR				-3.2196	4.4113	414	-0.73	0.4659
POOLCNTR				-3.8034	4.4030	413	-0.86	0.3882
POOLCNTR				0				
BASE*AVISITN		7		-0.1387	0.05917	381	-2.34	0.0196
BASE*AVISITN		14		-0.1179	0.07108	437	-1.66	0.0979
BASE*AVISITN		21		-0.2124	0.07568	436	-2.81	0.0052
BASE*AVISITN		28		-0.1613	0.07907	439	-2.04	0.0419
BASE*AVISITN		35		-0.2010	0.08284	444	-2.43	0.0156
BASE*AVISITN		42		-0.2232	0.08730	443	-2.56	0.0109

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	353	1.23	0.2932
TRTPN	2	379	10.09	<.0001
AVISITN*TRTPN	10	524	1.66	0.0881
POOLCNTR	38	380	2.12	0.0002
BASE*AVISITN	6	382	2.15	0.0468

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-1.9312	0.7960	381	-2.43	0.0157	0.05	-3.4963	-0.3661
DAY7 2 vs 3	-1.8111	0.7992	379	-2.27	0.0240	0.05	-3.3825	-0.2396
DAY14 1 vs 3	-3.6498	1.0171	373	-3.59	0.0004	0.05	-5.6498	-1.6497
DAY14 2 vs 3	-3.6506	1.0304	381	-3.54	0.0004	0.05	-5.6766	-1.6246
DAY21 1 vs 3	-4.0205	1.0982	369	-3.66	0.0003	0.05	-6.1801	-1.8609
DAY21 2 vs 3	-4.4989	1.1183	380	-4.02	<.0001	0.05	-6.6978	-2.2999
DAY28 1 vs 3	-3.9394	1.1597	369	-3.40	0.0008	0.05	-6.2198	-1.6589
DAY28 2 vs 3	-4.4783	1.1797	378	-3.80	0.0002	0.05	-6.7980	-2.1586

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-3.7747	1.2192	368	-3.10	0.0021	0.05	-6.1721	-1.3774
DAY35 2 vs 3	-5.2513	1.2437	378	-4.22	<.0001	0.05	-7.6968	-2.8058
DAY42 1 vs 3	-4.0055	1.2937	368	-3.10	0.0021	0.05	-6.5494	-1.4615
DAY42 2 vs 3	-4.4192	1.3220	378	-3.34	0.0009	0.05	-7.0186	-1.8198

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	-6.2099	0.6181	385	-10.05	<.0001	0.05	-7.4251	-4.9947
AVISITN*TRTPN	7	2	-6.0897	0.6199	381	-9.82	<.0001	0.05	-7.3085	-4.8709
AVISITN*TRTPN	7	3	-4.2786	0.6120	381	-6.99	<.0001	0.05	-5.4820	-3.0753
AVISITN*TRTPN	14	1	-9.0936	0.7625	402	-11.93	<.0001	0.05	-10.5925	-7.5947
AVISITN*TRTPN	14	2	-9.0945	0.7770	415	-11.70	<.0001	0.05	-10.6218	-7.5672
AVISITN*TRTPN	14	3	-5.4438	0.7599	405	-7.16	<.0001	0.05	-6.9376	-3.9501
AVISITN*TRTPN	21	1	-10.8348	0.8200	407	-13.21	<.0001	0.05	-12.4468	-9.2228
AVISITN*TRTPN	21	2	-11.3132	0.8431	423	-13.42	<.0001	0.05	-12.9703	-9.6560

SOURCE: MMRMOUT; TABLE: stat1aa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-6.8143	0.8114	399	-8.40	<.0001	0.05	-8.4095	-5.2191
AVISITN*TRTPN	28	1	-11.0222	0.8636	409	-12.76	<.0001	0.05	-12.7198	-9.3245
AVISITN*TRTPN	28	2	-11.5611	0.8869	422	-13.04	<.0001	0.05	-13.3044	-9.8179
AVISITN*TRTPN	28	3	-7.0828	0.8508	396	-8.33	<.0001	0.05	-8.7554	-5.4102
AVISITN*TRTPN	35	1	-11.6110	0.9058	407	-12.82	<.0001	0.05	-13.3916	-9.8304
AVISITN*TRTPN	35	2	-13.0876	0.9345	423	-14.00	<.0001	0.05	-14.9245	-11.2507
AVISITN*TRTPN	35	3	-7.8362	0.8895	394	-8.81	<.0001	0.05	-9.5850	-6.0875
AVISITN*TRTPN	42	1	-12.0791	0.9584	409	-12.60	<.0001	0.05	-13.9632	-10.1951
AVISITN*TRTPN	42	2	-12.4928	0.9915	422	-12.60	<.0001	0.05	-14.4418	-10.5439
AVISITN*TRTPN	42	3	-8.0736	0.9387	393	-8.60	<.0001	0.05	-9.9192	-6.2281

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	380	3.70	0.0257
AVISITN*TRTPN	14	2	378	8.52	0.0002
AVISITN*TRTPN	21	2	377	10.00	<.0001
AVISITN*TRTPN	28	2	377	8.80	0.0002
AVISITN*TRTPN	35	2	377	9.66	<.0001
AVISITN*TRTPN	42	2	377	7.04	0.0010

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	39	[redacted]

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

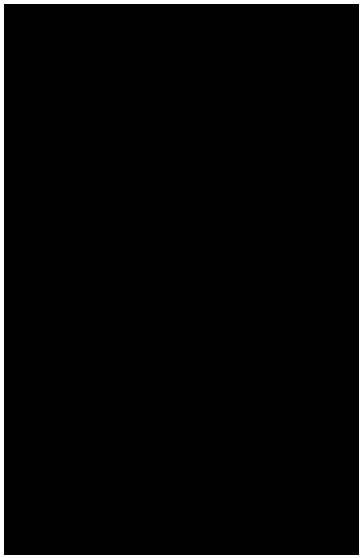
Class Level Information

Class	Levels	Values
SUBJID	421	[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

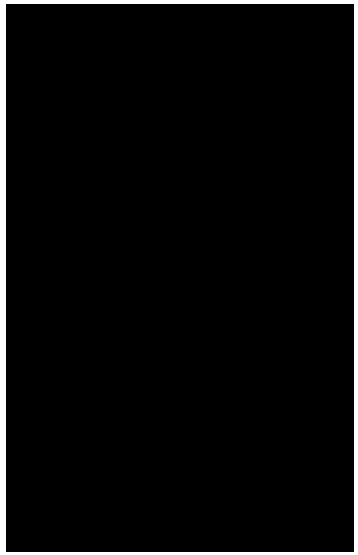


SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

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

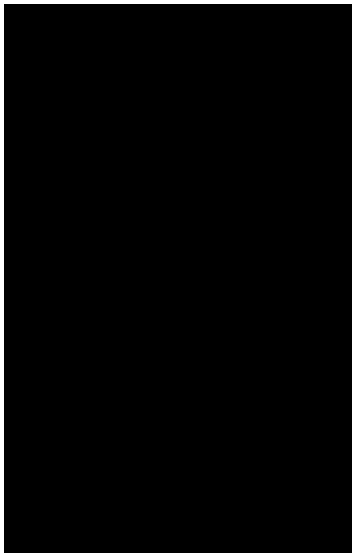


SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

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

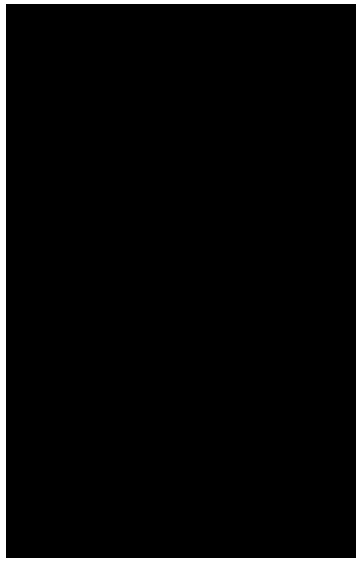


SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.1.2 FINAL

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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	73
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2227
Number of Observations Used	2227
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	15800.38727426	
1	2	13568.79752107	0.00031679
2	1	13567.17482444	0.00000418
3	1	13567.15460435	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	43.6133
UN(2,1)	SUBJID	38.4610
UN(2,2)	SUBJID	70.3656
UN(3,1)	SUBJID	37.5232
UN(3,2)	SUBJID	59.9507
UN(3,3)	SUBJID	81.2761
UN(4,1)	SUBJID	39.2740
UN(4,2)	SUBJID	59.0315
UN(4,3)	SUBJID	73.7748
UN(4,4)	SUBJID	89.8567
UN(5,1)	SUBJID	38.9775
UN(5,2)	SUBJID	60.4118
UN(5,3)	SUBJID	72.5077
UN(5,4)	SUBJID	82.3971
UN(5,5)	SUBJID	97.7856
UN(6,1)	SUBJID	38.2789
UN(6,2)	SUBJID	60.0226
UN(6,3)	SUBJID	74.3151

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	84.3266
UN(6,5)	SUBJID	91.8307
UN(6,6)	SUBJID	108.84

Fit Statistics

-2 Res Log Likelihood	13567.2
AIC (Smaller is Better)	13609.2
AICC (Smaller is Better)	13609.6
BIC (Smaller is Better)	13694.0

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	2233.23	<.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	357	1.25	0.2860
TRTPN	2	379	10.10	<.0001
AVISITN*TRTPN	10	356	1.68	0.0835
POOLCNTR	38	380	2.18	0.0001
BASE*AVISITN	6	378	2.19	0.0430

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-1.9312	0.7958	381	-2.43	0.0157	0.05	-3.4959	-0.3665
DAY7 2 vs 3	-1.8111	0.7989	379	-2.27	0.0240	0.05	-3.3820	-0.2401
DAY14 1 vs 3	-3.6498	1.0169	373	-3.59	0.0004	0.05	-5.6493	-1.6502
DAY14 2 vs 3	-3.6506	1.0301	381	-3.54	0.0004	0.05	-5.6760	-1.6253
DAY21 1 vs 3	-4.0205	1.0980	369	-3.66	0.0003	0.05	-6.1796	-1.8614
DAY21 2 vs 3	-4.4989	1.1179	380	-4.02	<.0001	0.05	-6.6970	-2.3008
DAY28 1 vs 3	-3.9394	1.1594	369	-3.40	0.0008	0.05	-6.2192	-1.6596
DAY28 2 vs 3	-4.4783	1.1792	378	-3.80	0.0002	0.05	-6.7970	-2.1596

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-3.7747	1.2186	368	-3.10	0.0021	0.05	-6.1711	-1.3784
DAY35 2 vs 3	-5.2513	1.2430	378	-4.22	<.0001	0.05	-7.6953	-2.8074
DAY42 1 vs 3	-4.0055	1.2930	368	-3.10	0.0021	0.05	-6.5480	-1.4630
DAY42 2 vs 3	-4.4192	1.3210	378	-3.35	0.0009	0.05	-7.0167	-1.8217

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	-6.2099	0.6166	385	-10.07	<.0001	0.05	-7.4223	-4.9975
AVISITN*TRTPN	7	2	-6.0897	0.6184	381	-9.85	<.0001	0.05	-7.3056	-4.8738
AVISITN*TRTPN	7	3	-4.2786	0.6107	381	-7.01	<.0001	0.05	-5.4793	-3.0780
AVISITN*TRTPN	14	1	-9.0936	0.7613	402	-11.95	<.0001	0.05	-10.5902	-7.5971
AVISITN*TRTPN	14	2	-9.0945	0.7757	415	-11.72	<.0001	0.05	-10.6193	-7.5697
AVISITN*TRTPN	14	3	-5.4438	0.7587	405	-7.18	<.0001	0.05	-6.9353	-3.9524
AVISITN*TRTPN	21	1	-10.8348	0.8189	407	-13.23	<.0001	0.05	-12.4445	-9.2251
AVISITN*TRTPN	21	2	-11.3132	0.8418	423	-13.44	<.0001	0.05	-12.9677	-9.6586

SOURCE: MMRMOUT; TABLE: stat1ab.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-6.8143	0.8103	399	-8.41	<.0001	0.05	-8.4073	-5.2213
AVISITN*TRTPN	28	1	-11.0222	0.8624	409	-12.78	<.0001	0.05	-12.7175	-9.3269
AVISITN*TRTPN	28	2	-11.5611	0.8855	422	-13.06	<.0001	0.05	-13.3017	-9.8205
AVISITN*TRTPN	28	3	-7.0828	0.8497	396	-8.34	<.0001	0.05	-8.7533	-5.4124
AVISITN*TRTPN	35	1	-11.6110	0.9044	407	-12.84	<.0001	0.05	-13.3890	-9.8330
AVISITN*TRTPN	35	2	-13.0876	0.9329	423	-14.03	<.0001	0.05	-14.9214	-11.2538
AVISITN*TRTPN	35	3	-7.8362	0.8884	394	-8.82	<.0001	0.05	-9.5828	-6.0897
AVISITN*TRTPN	42	1	-12.0791	0.9570	409	-12.62	<.0001	0.05	-13.9603	-10.1979
AVISITN*TRTPN	42	2	-12.4928	0.9898	422	-12.62	<.0001	0.05	-14.4384	-10.5473
AVISITN*TRTPN	42	3	-8.0736	0.9375	393	-8.61	<.0001	0.05	-9.9168	-6.2304

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	380	3.70	0.0257
AVISITN*TRTPN	14	2	378	8.52	0.0002
AVISITN*TRTPN	21	2	377	10.01	<.0001
AVISITN*TRTPN	28	2	377	8.80	0.0002
AVISITN*TRTPN	35	2	377	9.67	<.0001
AVISITN*TRTPN	42	2	377	7.05	0.0010

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	39	[redacted]

Number of Observations Read 421
Number of Observations Used 421

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	41	8805.99497	214.78037	2.07	0.0002
Error	379	39250.45633	103.56321		
Corrected Total	420	48056.45131			

R-Square	Coeff Var	Root MSE	CHG Mean
0.183243	-105.7081	10.17660	-9.627078

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	1454.328052	727.164026	7.02	0.0010
POOLCNTR	38	6862.153762	180.582994	1.74	0.0053
BASE	1	280.694601	280.694601	2.71	0.1005

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.7071429	10.8359224	37.5857143	6.75041775
2	140	-11.0571429	10.7125768	38.7642857	6.95578090
3	141	-7.1347518	10.1624096	37.6453901	6.34837972

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-11.6211087	0.9465643	<.0001	1
2	-11.7874384	0.9518103	<.0001	2
3	-7.7408197	0.9407099	<.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		0.8926	0.0016
2	0.8926		0.0011
3	0.0016	0.0011	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-11.621109	-13.482284	-9.759933
2	-11.787438	-13.658929	-9.915948

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-7.740820	-9.590484	-5.891156

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.166330	-2.253380	2.586039
1	3	-3.880289	-6.279048	-1.481530
2	3	-4.046619	-6.461174	-1.632064

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

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-3.88028896	1.21997068	-3.18	0.0016
2 vs 3	-4.04661870	1.22800435	-3.30	0.0011

SOURCE: GLMOUT; TABLE: stat1b.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	421
Number of Observations Used	421

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	1943.84121	647.94707	5.86	0.0006
Error	417	46112.61010	110.58180		
Corrected Total	420	48056.45131			

R-Square	Coeff Var	Root MSE	CHG Mean
0.040449	-109.2314	10.51579	-9.627078

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	1249.405044	624.702522	5.65	0.0038
BASE	1	618.365333	618.365333	5.59	0.0185

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.7071429	10.8359224	37.5857143	6.75041775
2	140	-11.0571429	10.7125768	38.7642857	6.95578090
3	141	-7.1347518	10.1624096	37.6453901	6.34837972

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-10.7820438	0.8893105	<.0001	1
2	-10.9177347	0.8906994	<.0001	2
3	-7.1988014	0.8860032	<.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		0.9143	0.0045
2	0.9143		0.0033
3	0.0045	0.0033	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-10.782044	-12.530134	-9.033954
2	-10.917735	-12.668555	-9.166914

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-7.198801	-8.940391	-5.457212

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.135691	-2.341328	2.612710
1	3	-3.583242	-6.049479	-1.117006
2	3	-3.718933	-6.190945	-1.246921

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

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-3.58324241	1.25465498	-2.86	0.0045
2 vs 3	-3.71893327	1.25759322	-2.96	0.0033

SOURCE: GLMOUT; TABLE: stat1c.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	39	[redacted]

Number of Observations Read	421
Number of Observations Used	421

SOURCE: GLMCNTR; TABLE: stat1d.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	117	17215.30877	147.13939	1.45	0.0067
Error	303	30841.14254	101.78595		
Corrected Total	420	48056.45131			

R-Square	Coeff Var	Root MSE	CHG Mean
0.358231	-104.7971	10.08890	-9.627078

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	475.234975	237.617487	2.33	0.0986
POOLCNTR	38	6881.047923	181.080208	1.78	0.0046
TRTPN*POOLCNTR	76	8409.313799	110.648866	1.09	0.3087
BASE	1	246.568428	246.568428	2.42	0.1207

SOURCE: GLMCNTR; TABLE: stat1d.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.4 FINAL

CENTANAFADINE 1 OF 4
PROTOCOL 405-201-00014

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	140	-11.6 (0.95)	140	-11.8 (0.95)	141	-7.74 (0.94)	CTN SR 200MG VS. PLACEBO	-3.88 (-6.28, -1.48)
							CTN SR 400MG VS. PLACEBO	-4.05 (-6.46, -1.63)
[redacted]	8	-5.26 (3.63)	6	-10.1 (4.15)	7	-5.83 (3.85)	CTN SR 200MG VS. PLACEBO	0.57 (-9.71, 10.85)
							CTN SR 400MG VS. PLACEBO	-4.23 (-15.3, 6.82)
	1	-48.7 (10.2)	1	-8.22 (10.2)	1	-32.6 (10.2)	CTN SR 200MG VS. PLACEBO	-16.2 (-44.2, 11.92)
							CTN SR 400MG VS. PLACEBO	24.35 (-3.73, 52.44)
	11	-9.62 (3.06)	13	-9.01 (2.81)	12	-6.45 (2.91)	CTN SR 200MG VS. PLACEBO	-3.18 (-11.5, 5.13)
							CTN SR 400MG VS. PLACEBO	-2.57 (-10.5, 5.39)
	2	-12.6 (7.24)	1	-2.74 (10.2)	3	-7.95 (5.82)	CTN SR 200MG VS. PLACEBO	-4.62 (-22.9, 13.66)
							CTN SR 400MG VS. PLACEBO	5.21 (-17.9, 28.30)
	2	-17.5 (7.14)	2	-30.1 (7.24)	2	-2.90 (7.14)	CTN SR 200MG VS. PLACEBO	-14.6 (-34.5, 5.27)
							CTN SR 400MG VS. PLACEBO	-27.2 (-47.2, -7.09)
	7	-13.7 (3.84)	8	-9.60 (3.58)	6	-1.71 (4.13)	CTN SR 200MG VS. PLACEBO	-12.0 (-23.0, -0.93)
							CTN SR 400MG VS. PLACEBO	-7.89 (-18.6, 2.84)
	8	-6.71 (3.57)	8	-11.4 (3.57)	8	-7.37 (3.60)	CTN SR 200MG VS. PLACEBO	0.66 (-9.33, 10.65)
							CTN SR 400MG VS. PLACEBO	-4.05 (-14.1, 5.95)
	3	-8.54 (5.84)	2	-7.61 (7.16)	2	-2.89 (7.16)	CTN SR 200MG VS. PLACEBO	-5.65 (-23.8, 12.48)
							CTN SR 400MG VS. PLACEBO	-4.72 (-24.7, 15.26)
	1	-18.5 (10.1)	1	6.32 (10.1)	1	-4.45 (10.1)	CTN SR 200MG VS. PLACEBO	-14.1 (-42.2, 14.12)
							CTN SR 400MG VS. PLACEBO	10.78 (-17.4, 38.94)
	5	-16.8 (4.52)	6	-9.67 (4.12)	6	-11.4 (4.12)	CTN SR 200MG VS. PLACEBO	-5.37 (-17.4, 6.67)
							CTN SR 400MG VS. PLACEBO	1.75 (-9.72, 13.21)
	3	-13.7 (5.87)	3	-11.1 (5.89)	2	-3.10 (7.14)	CTN SR 200MG VS. PLACEBO	-10.6 (-28.9, 7.57)
							CTN SR 400MG VS. PLACEBO	-7.97 (-26.2, 10.30)

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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]	1	-1.84 (10.1)	1	-19.7 (10.1)	1	-18.7 (10.1)	CTN SR 200MG VS. PLACEBO	16.84 (-11.2, 44.92)
							CTN SR 400MG VS. PLACEBO	-1.00 (-29.1, 27.08)
	2	-25.0 (7.14)	2	-15.6 (7.19)	3	-1.25 (5.84)	CTN SR 200MG VS. PLACEBO	-23.8 (-41.9, -5.64)
							CTN SR 400MG VS. PLACEBO	-14.4 (-32.5, 3.76)
	3	-10.5 (5.85)	4	-8.93 (5.05)	4	-5.67 (5.04)	CTN SR 200MG VS. PLACEBO	-4.80 (-20.0, 10.39)
							CTN SR 400MG VS. PLACEBO	-3.26 (-17.3, 10.78)
	3	-10.4 (5.84)	4	-11.4 (5.04)	3	-6.21 (5.83)	CTN SR 200MG VS. PLACEBO	-4.19 (-20.4, 12.05)
							CTN SR 400MG VS. PLACEBO	-5.20 (-20.4, 9.96)
	2	-1.69 (7.15)	1	-17.7 (10.1)	2	-29.9 (7.15)	CTN SR 200MG VS. PLACEBO	28.16 (8.31, 48.02)
							CTN SR 400MG VS. PLACEBO	12.15 (-12.2, 36.47)
	3	-16.3 (5.83)	2	-7.29 (7.18)	3	-10.2 (5.83)	CTN SR 200MG VS. PLACEBO	-6.14 (-22.4, 10.10)
							CTN SR 400MG VS. PLACEBO	2.89 (-15.4, 21.15)
	1	0.55 (10.1)	2	-7.98 (7.14)	1	-9.32 (10.1)	CTN SR 200MG VS. PLACEBO	9.87 (-18.2, 37.98)
							CTN SR 400MG VS. PLACEBO	1.34 (-23.0, 25.65)
	1	-10.6 (10.1)	2	-4.48 (7.14)	1	-20.1 (10.1)	CTN SR 200MG VS. PLACEBO	9.52 (-18.6, 37.60)
							CTN SR 400MG VS. PLACEBO	15.65 (-8.68, 39.97)
	5	-11.2 (4.54)	5	-10.6 (4.53)	4	1.78 (5.17)	CTN SR 200MG VS. PLACEBO	-13.0 (-26.4, 0.38)
							CTN SR 400MG VS. PLACEBO	-12.3 (-25.7, 1.06)
	3	-14.6 (5.88)	3	-14.9 (5.91)	3	-12.1 (5.87)	CTN SR 200MG VS. PLACEBO	-2.49 (-18.7, 13.72)
							CTN SR 400MG VS. PLACEBO	-2.76 (-19.0, 13.46)
	2	-3.18 (7.14)	1	-13.3 (10.1)	1	6.39 (10.1)	CTN SR 200MG VS. PLACEBO	-9.56 (-34.0, 14.87)
							CTN SR 400MG VS. PLACEBO	-19.7 (-47.8, 8.40)
	4	-14.2 (5.08)	5	-4.19 (4.53)	4	-2.45 (5.05)	CTN SR 200MG VS. PLACEBO	-11.7 (-25.8, 2.34)
							CTN SR 400MG VS. PLACEBO	-1.73 (-15.1, 11.62)

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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 405-201-00014

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]	3	-10.2 (5.90)	5	-14.2 (4.52)	4	-17.8 (5.05)	CTN SR 200MG VS. PLACEBO	7.58 (-7.74, 22.91)
							CTN SR 400MG VS. PLACEBO	3.54 (-9.81, 16.88)
	3	-10.8 (5.85)	3	-14.5 (5.83)	3	-2.23 (5.83)	CTN SR 200MG VS. PLACEBO	-8.58 (-24.8, 7.67)
							CTN SR 400MG VS. PLACEBO	-12.2 (-28.4, 3.98)
	2	2.03 (7.20)	3	3.22 (5.95)	2	-2.39 (7.21)	CTN SR 200MG VS. PLACEBO	4.42 (-15.4, 24.27)
							CTN SR 400MG VS. PLACEBO	5.60 (-12.5, 23.73)
	2	-13.9 (7.14)	2	-19.0 (7.19)	2	-20.2 (7.13)	CTN SR 200MG VS. PLACEBO	6.23 (-13.6, 26.10)
							CTN SR 400MG VS. PLACEBO	1.21 (-18.7, 21.13)
	2	-13.0 (7.19)	3	-7.01 (5.89)	3	-11.3 (5.88)	CTN SR 200MG VS. PLACEBO	-1.66 (-19.8, 16.46)
							CTN SR 400MG VS. PLACEBO	4.28 (-11.9, 20.49)
	12	-9.45 (2.91)	10	-14.6 (3.19)	11	-0.87 (3.05)	CTN SR 200MG VS. PLACEBO	-8.58 (-16.9, -0.29)
							CTN SR 400MG VS. PLACEBO	-13.7 (-22.4, -5.01)
	12	-5.08 (2.91)	11	-7.96 (3.04)	12	-5.60 (2.91)	CTN SR 200MG VS. PLACEBO	0.52 (-7.59, 8.62)
							CTN SR 400MG VS. PLACEBO	-2.37 (-10.7, 5.93)
	2	-10.7 (7.15)	1	-0.39 (10.1)	2	-10.1 (7.14)	CTN SR 200MG VS. PLACEBO	-0.66 (-20.5, 19.19)
							CTN SR 400MG VS. PLACEBO	9.68 (-14.8, 34.15)
	2	-17.0 (7.19)	1	-0.29 (10.1)	2	-0.69 (7.15)	CTN SR 200MG VS. PLACEBO	-16.3 (-36.3, 3.80)
							CTN SR 400MG VS. PLACEBO	0.40 (-24.1, 24.86)
	5	-15.9 (4.52)	5	-26.3 (4.59)	5	-12.3 (4.55)	CTN SR 200MG VS. PLACEBO	-3.55 (-16.1, 9.03)
							CTN SR 400MG VS. PLACEBO	-14.0 (-26.5, -1.41)
	2	0.08 (7.13)	3	-8.71 (5.83)	1	-13.6 (10.1)	CTN SR 200MG VS. PLACEBO	13.69 (-10.7, 38.10)
							CTN SR 400MG VS. PLACEBO	4.90 (-18.1, 27.88)
	6	-16.2 (4.12)	5	-13.8 (4.52)	6	-5.68 (4.13)	CTN SR 200MG VS. PLACEBO	-10.5 (-22.0, 0.93)
							CTN SR 400MG VS. PLACEBO	-8.17 (-20.2, 3.90)

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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 405-201-00014

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]	1	-6.32 (10.1)	1	-15.6 (10.1)	1	-1.48 (10.1)	CTN SR 200MG VS. PLACEBO	-4.84 (-32.9, 23.24)
							CTN SR 400MG VS. PLACEBO	-14.1 (-42.2, 13.98)
	3	-7.77 (5.83)	1	-27.8 (10.1)	2	-14.0 (7.14)	CTN SR 200MG VS. PLACEBO	6.24 (-11.9, 24.38)
							CTN SR 400MG VS. PLACEBO	-13.8 (-38.1, 10.50)
	1	-25.6 (10.1)	2	-13.8 (7.14)	3	-16.8 (5.84)	CTN SR 200MG VS. PLACEBO	-8.86 (-31.8, 14.09)
							CTN SR 400MG VS. PLACEBO	2.93 (-15.2, 21.06)
	1	-18.5 (10.1)	1	3.16 (10.1)	2	-9.65 (7.15)	CTN SR 200MG VS. PLACEBO	-8.84 (-33.2, 15.48)
							CTN SR 400MG VS. PLACEBO	12.81 (-11.5, 37.14)

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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 405-201-00014

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	2	-18.00	2	-32.00	2	-2.50	-15.50	-29.50
	USA	2	-3.50	1	-12.00	1	8.00	-11.50	-20.00
	USA	2	-25.50	2	-17.00	3	-2.00	-23.50	-15.00
	USA	5	-16.20	5	-27.60	5	-13.20	-3.00	-14.40
	USA	12	-9.33	10	-14.70	11	-0.64	-8.70	-14.06
	USA	3	-7.67	1	-28.00	2	-14.50	6.83	-13.50
	USA	1	-6.00	1	-14.00	1	-1.00	-5.00	-13.00
	USA	3	-10.00	3	-14.67	3	-2.33	-7.67	-12.33
	USA	5	-12.00	5	-11.20	4	0.00	-12.00	-11.20
	USA	6	-16.00	5	-14.20	6	-5.17	-10.83	-9.03
	USA	7	-14.43	8	-10.00	6	-2.17	-12.26	-7.83
	USA	3	-8.00	2	-8.50	2	-2.00	-6.00	-6.50
	USA	3	-12.67	3	-9.67	2	-3.50	-9.17	-6.17
	USA	3	-11.00	4	-11.50	3	-6.00	-5.00	-5.50
	USA	8	-6.88	8	-11.63	8	-6.63	-0.25	-5.00
	USA	8	-4.25	6	-9.33	7	-5.00	0.75	-4.33
	USA	3	-11.33	4	-9.25	4	-5.75	-5.58	-3.50
	USA	11	-10.09	13	-9.46	12	-6.50	-3.59	-2.96
	USA	4	-13.25	5	-4.80	4	-2.25	-11.00	-2.55
	USA	3	-13.33	3	-13.33	3	-11.00	-2.33	-2.33
	USA	12	-5.08	11	-7.82	12	-5.67	0.58	-2.15
	USA	1	-2.00	1	-20.00	1	-19.00	17.00	-1.00

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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 405-201-00014

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	2.00	2	-7.50	1	-9.00	11.00	1.50
	USA	5	-16.40	6	-9.83	6	-11.50	-4.90	1.67
	USA	2	-14.50	2	-17.50	2	-20.00	5.50	2.50
	USA	2	-15.50	1	1.00	2	-1.50	-14.00	2.50
	USA	1	-24.00	2	-13.50	3	-16.00	-8.00	2.50
	USA	2	-14.50	1	-5.00	3	-8.00	-6.50	3.00
	USA	2	0.00	3	-8.33	1	-12.00	12.00	3.67
	USA	3	-8.67	5	-13.80	4	-18.00	9.33	4.20
	USA	2	-11.50	3	-5.67	3	-10.00	-1.50	4.33
	USA	3	-16.00	2	-6.00	3	-10.67	-5.33	4.67
	USA	2	0.50	3	1.33	2	-4.00	4.50	5.33
	USA	2	-10.00	1	-2.00	2	-9.50	-0.50	7.50
	USA	1	-19.00	1	6.00	1	-3.00	-16.00	9.00
	USA	2	-2.50	1	-19.00	2	-30.50	28.00	11.50
	USA	1	-18.00	1	3.00	2	-9.00	-9.00	12.00
	USA	1	-9.00	2	-4.00	1	-19.00	10.00	15.00
	USA	1	-51.00	1	-10.00	1	-35.00	-16.00	25.00

[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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/center.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.5.2 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
1	137	-5.3431	7.5542	0.6454	-27.0000	12.0000
3	139	-3.5612	6.6693	0.5657	-31.0000	10.0000
Diff (1-2)		-1.7819	7.1223	0.8574		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-5.3431	-6.6194	-4.0668	7.5542	6.7532	8.5724
3		-3.5612	-4.6797	-2.4426	6.6693	5.9667	7.5609
Diff (1-2)	Pooled	-1.7819	-3.4699	-0.0939	7.1223	6.5726	7.7730
Diff (1-2)	Satterthwaite	-1.7819	-3.4716	-0.0922			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	274	-2.08	0.0386
Satterthwaite	Unequal	268.85	-2.08	0.0388

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	136	138	1.28	0.1458

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-8.1429	9.6018	0.8115	-48.0000	10.0000
3	141	-4.6879	7.7994	0.6568	-38.0000	8.0000
Diff (1-2)		-3.4549	8.7440	1.0432		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-8.1429	-9.7473	-6.5384	9.6018	8.5936	10.8803
3		-4.6879	-5.9865	-3.3894	7.7994	6.9830	8.8336
Diff (1-2)	Pooled	-3.4549	-5.5085	-1.4013	8.7440	8.0747	9.5351
Diff (1-2)	Satterthwaite	-3.4549	-5.5105	-1.3994			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.31	0.0010
Satterthwaite	Unequal	267	-3.31	0.0011

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.52	0.0146

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-9.5857	10.1450	0.8574	-45.0000	10.0000
3	141	-5.8582	8.7436	0.7363	-40.0000	11.0000
Diff (1-2)		-3.7276	9.4678	1.1296		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-9.5857	-11.2810	-7.8905	10.1450	9.0797	11.4957
3		-5.8582	-7.3140	-4.4024	8.7436	7.8284	9.9031
Diff (1-2)	Pooled	-3.7276	-5.9512	-1.5039	9.4678	8.7431	10.3244
Diff (1-2)	Satterthwaite	-3.7276	-5.9526	-1.5025			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.30	0.0011
Satterthwaite	Unequal	272.48	-3.30	0.0011

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.35	0.0801

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-9.8000	10.4587	0.8839	-44.0000	13.0000
3	141	-6.2553	8.9836	0.7566	-37.0000	13.0000
Diff (1-2)		-3.5447	9.7465	1.1629		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-9.8000	-11.5477	-8.0523	10.4587	9.3605	11.8512
3		-6.2553	-7.7511	-4.7596	8.9836	8.0433	10.1749
Diff (1-2)	Pooled	-3.5447	-5.8338	-1.2556	9.7465	9.0005	10.6283
Diff (1-2)	Satterthwaite	-3.5447	-5.8353	-1.2541			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.05	0.0025
Satterthwaite	Unequal	272.21	-3.05	0.0025

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.36	0.0735

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.2929	10.6376	0.8990	-51.0000	11.0000
3	141	-6.9716	9.5086	0.8008	-37.0000	12.0000
Diff (1-2)		-3.3212	10.0869	1.2035		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.2929	-12.0704	-8.5153	10.6376	9.5206	12.0539
3		-6.9716	-8.5548	-5.3885	9.5086	8.5133	10.7695
Diff (1-2)	Pooled	-3.3212	-5.6903	-0.9522	10.0869	9.3149	10.9995
Diff (1-2)	Satterthwaite	-3.3212	-5.6914	-0.9511			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-2.76	0.0062
Satterthwaite	Unequal	275.12	-2.76	0.0062

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.25	0.1862

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.7071	10.8359	0.9158	-51.0000	11.0000
3	141	-7.1348	10.1624	0.8558	-39.0000	12.0000
Diff (1-2)		-3.5724	10.5034	1.2532		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.7071	-12.5178	-8.8964	10.8359	9.6981	12.2787
3		-7.1348	-8.8268	-5.4427	10.1624	9.0987	11.5100
Diff (1-2)	Pooled	-3.5724	-6.0392	-1.1055	10.5034	9.6995	11.4537
Diff (1-2)	Satterthwaite	-3.5724	-6.0399	-1.1049			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-2.85	0.0047
Satterthwaite	Unequal	277.59	-2.85	0.0047

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.14	0.4493

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	-5.4460	6.6389	0.5631	-24.0000	9.0000
3	139	-3.5612	6.6693	0.5657	-31.0000	10.0000
Diff (1-2)		-1.8849	6.6541	0.7982		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-5.4460	-6.5595	-4.3326	6.6389	5.9395	7.5264
3		-3.5612	-4.6797	-2.4426	6.6693	5.9667	7.5609
Diff (1-2)	Pooled	-1.8849	-3.4562	-0.3136	6.6541	6.1423	7.2597
Diff (1-2)	Satterthwaite	-1.8849	-3.4562	-0.3136			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	276	-2.36	0.0189
Satterthwaite	Unequal	275.99	-2.36	0.0189

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	138	138	1.01	0.9572

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-8.1143	8.1850	0.6918	-35.0000	12.0000
3	141	-4.6879	7.7994	0.6568	-38.0000	8.0000
Diff (1-2)		-3.4263	7.9938	0.9537		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-8.1143	-9.4820	-6.7466	8.1850	7.3255	9.2748
3		-4.6879	-5.9865	-3.3894	7.7994	6.9830	8.8336
Diff (1-2)	Pooled	-3.4263	-5.3038	-1.5489	7.9938	7.3820	8.7171
Diff (1-2)	Satterthwaite	-3.4263	-5.3041	-1.5485			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.59	0.0004
Satterthwaite	Unequal	278.15	-3.59	0.0004

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.10	0.5693

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.1071	9.2088	0.7783	-34.0000	17.0000
3	141	-5.8582	8.7436	0.7363	-40.0000	11.0000
Diff (1-2)		-4.2490	8.9784	1.0712		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.1071	-11.6459	-8.5683	9.2088	8.2418	10.4349
3		-5.8582	-7.3140	-4.4024	8.7436	7.8284	9.9031
Diff (1-2)	Pooled	-4.2490	-6.3577	-2.1403	8.9784	8.2912	9.7907
Diff (1-2)	Satterthwaite	-4.2490	-6.3581	-2.1399			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.97	<.0001
Satterthwaite	Unequal	278.03	-3.97	<.0001

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.11	0.5411

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-10.2714	9.6387	0.8146	-42.0000	7.0000
3	141	-6.2553	8.9836	0.7566	-37.0000	13.0000
Diff (1-2)		-4.0161	9.3157	1.1115		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.2714	-11.8821	-8.6608	9.6387	8.6266	10.9220
3		-6.2553	-7.7511	-4.7596	8.9836	8.0433	10.1749
Diff (1-2)	Pooled	-4.0161	-6.2040	-1.8282	9.3157	8.6028	10.1586
Diff (1-2)	Satterthwaite	-4.0161	-6.2046	-1.8276			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.61	0.0004
Satterthwaite	Unequal	277.34	-3.61	0.0004

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.15	0.4067

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-11.4000	10.1689	0.8594	-40.0000	10.0000
3	141	-6.9716	9.5086	0.8008	-37.0000	12.0000
Diff (1-2)		-4.4284	9.8431	1.1744		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-11.4000	-13.0992	-9.7008	10.1689	9.1011	11.5229
3		-6.9716	-8.5548	-5.3885	9.5086	8.5133	10.7695
Diff (1-2)	Pooled	-4.4284	-6.7402	-2.1166	9.8431	9.0898	10.7337
Diff (1-2)	Satterthwaite	-4.4284	-6.7408	-2.1160			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.77	0.0002
Satterthwaite	Unequal	277.47	-3.77	0.0002

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.14	0.4286

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-11.0571	10.7126	0.9054	-41.0000	11.0000
3	141	-7.1348	10.1624	0.8558	-39.0000	12.0000
Diff (1-2)		-3.9224	10.4401	1.2456		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-11.0571	-12.8472	-9.2670	10.7126	9.5877	12.1389
3		-7.1348	-8.8268	-5.4427	10.1624	9.0987	11.5100
Diff (1-2)	Pooled	-3.9224	-6.3744	-1.4704	10.4401	9.6411	11.3847
Diff (1-2)	Satterthwaite	-3.9224	-6.3749	-1.4699			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	279	-3.15	0.0018
Satterthwaite	Unequal	278.01	-3.15	0.0018

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	139	140	1.11	0.5341

SOURCE: TTESTLOCF; TABLE: stat1h.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.6 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)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
1	137	-5.3431	7.5542	0.6454	-27.0000	12.0000
3	139	-3.5612	6.6693	0.5657	-31.0000	10.0000
Diff (1-2)		-1.7819	7.1223	0.8574		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-5.3431	-6.6194	-4.0668	7.5542	6.7532	8.5724
3		-3.5612	-4.6797	-2.4426	6.6693	5.9667	7.5609
Diff (1-2)	Pooled	-1.7819	-3.4699	-0.0939	7.1223	6.5726	7.7730
Diff (1-2)	Satterthwaite	-1.7819	-3.4716	-0.0922			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	274	-2.08	0.0386
Satterthwaite	Unequal	268.85	-2.08	0.0388

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	136	138	1.28	0.1458

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	132	-8.5606	9.7042	0.8446	-48.0000	10.0000
3	132	-4.8561	7.9070	0.6882	-38.0000	8.0000
Diff (1-2)		-3.7045	8.8514	1.0895		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-8.5606	-10.2315	-6.8897	9.7042	8.6579	11.0404
3		-4.8561	-6.2175	-3.4946	7.9070	7.0545	8.9958
Diff (1-2)	Pooled	-3.7045	-5.8499	-1.5592	8.8514	8.1540	9.6801
Diff (1-2)	Satterthwaite	-3.7045	-5.8503	-1.5588			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	262	-3.40	0.0008
Satterthwaite	Unequal	251.73	-3.40	0.0008

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	131	131	1.51	0.0197

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	127	-9.9685	10.4501	0.9273	-45.0000	10.0000
3	132	-5.9924	8.8925	0.7740	-40.0000	11.0000
Diff (1-2)		-3.9761	9.6875	1.2041		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-9.9685	-11.8036	-8.1334	10.4501	9.3038	11.9212
3		-5.9924	-7.5236	-4.4613	8.8925	7.9337	10.1169
Diff (1-2)	Pooled	-3.9761	-6.3473	-1.6049	9.6875	8.9175	10.6042
Diff (1-2)	Satterthwaite	-3.9761	-6.3551	-1.5971			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	257	-3.30	0.0011
Satterthwaite	Unequal	247.28	-3.29	0.0011

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	126	131	1.38	0.0680

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	122	-10.0492	10.4580	0.9468	-44.0000	13.0000
3	130	-6.4462	9.1313	0.8009	-37.0000	13.0000
Diff (1-2)		-3.6030	9.7959	1.2348		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.0492	-11.9237	-8.1747	10.4580	9.2900	11.9645
3		-6.4462	-8.0307	-4.8616	9.1313	8.1400	10.3996
Diff (1-2)	Pooled	-3.6030	-6.0349	-1.1711	9.7959	9.0073	10.7369
Diff (1-2)	Satterthwaite	-3.6030	-6.0459	-1.1602			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	250	-2.92	0.0038
Satterthwaite	Unequal	240.57	-2.91	0.0040

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	121	129	1.31	0.1299

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	115	-10.1391	10.5945	0.9879	-51.0000	11.0000
3	125	-7.1840	9.3657	0.8377	-37.0000	12.0000
Diff (1-2)		-2.9551	9.9732	1.2887		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.1391	-12.0962	-8.1820	10.5945	9.3797	12.1737
3		-7.1840	-8.8420	-5.5260	9.3657	8.3310	10.6962
Diff (1-2)	Pooled	-2.9551	-5.4938	-0.4165	9.9732	9.1521	10.9574
Diff (1-2)	Satterthwaite	-2.9551	-5.5074	-0.4029			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	238	-2.29	0.0227
Satterthwaite	Unequal	228.34	-2.28	0.0234

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	114	124	1.28	0.1789

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	113	-10.5841	10.5117	0.9889	-40.0000	11.0000
3	123	-7.3008	10.1658	0.9166	-39.0000	12.0000
Diff (1-2)		-3.2833	10.3328	1.3464		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1		-10.5841	-12.5434	-8.6248	10.5117	9.2969	12.0944
3		-7.3008	-9.1153	-5.4863	10.1658	9.0346	11.6234
Diff (1-2)	Pooled	-3.2833	-5.9359	-0.6306	10.3328	9.4754	11.3621
Diff (1-2)	Satterthwaite	-3.2833	-5.9399	-0.6266			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	234	-2.44	0.0155
Satterthwaite	Unequal	230.76	-2.44	0.0156

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	112	122	1.07	0.7162

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)

TRTPN	N	Mean	Std Dev	Std Err	Minimum	Maximum
2	139	-5.4460	6.6389	0.5631	-24.0000	9.0000
3	139	-3.5612	6.6693	0.5657	-31.0000	10.0000
Diff (1-2)		-1.8849	6.6541	0.7982		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-5.4460	-6.5595	-4.3326	6.6389	5.9395	7.5264
3		-3.5612	-4.6797	-2.4426	6.6693	5.9667	7.5609
Diff (1-2)	Pooled	-1.8849	-3.4562	-0.3136	6.6541	6.1423	7.2597
Diff (1-2)	Satterthwaite	-1.8849	-3.4562	-0.3136			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	276	-2.36	0.0189
Satterthwaite	Unequal	275.99	-2.36	0.0189

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	138	138	1.01	0.9572

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	125	-8.0880	8.3396	0.7459	-35.0000	12.0000
3	132	-4.8561	7.9070	0.6882	-38.0000	8.0000
Diff (1-2)		-3.2319	8.1202	1.0134		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-8.0880	-9.5644	-6.6116	8.3396	7.4182	9.5243
3		-4.8561	-6.2175	-3.4946	7.9070	7.0545	8.9958
Diff (1-2)	Pooled	-3.2319	-5.2277	-1.2362	8.1202	7.4725	8.8919
Diff (1-2)	Satterthwaite	-3.2319	-5.2307	-1.2332			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	255	-3.19	0.0016
Satterthwaite	Unequal	252.07	-3.18	0.0016

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	124	131	1.11	0.5473

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	116	-10.5690	9.5555	0.8872	-34.0000	17.0000
3	132	-5.9924	8.8925	0.7740	-40.0000	11.0000
Diff (1-2)		-4.5765	9.2084	1.1719		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.5690	-12.3264	-8.8116	9.5555	8.4641	10.9727
3		-5.9924	-7.5236	-4.4613	8.8925	7.9337	10.1169
Diff (1-2)	Pooled	-4.5765	-6.8848	-2.2683	9.2084	8.4616	10.1008
Diff (1-2)	Satterthwaite	-4.5765	-6.8960	-2.2571			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	246	-3.91	0.0001
Satterthwaite	Unequal	236.43	-3.89	0.0001

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	115	131	1.15	0.4242

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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
2	114	-10.4298	10.0344	0.9398	-42.0000	7.0000
3	130	-6.4462	9.1313	0.8009	-37.0000	13.0000
Diff (1-2)		-3.9837	9.5636	1.2271		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-10.4298	-12.2918	-8.5679	10.0344	8.8794	11.5377
3		-6.4462	-8.0307	-4.8616	9.1313	8.1400	10.3996
Diff (1-2)	Pooled	-3.9837	-6.4009	-1.5664	9.5636	8.7822	10.4989
Diff (1-2)	Satterthwaite	-3.9837	-6.4165	-1.5508			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	242	-3.25	0.0013
Satterthwaite	Unequal	230.32	-3.23	0.0014

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	113	129	1.21	0.2991

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	104	-12.0577	10.7666	1.0557	-40.0000	10.0000
3	125	-7.1840	9.3657	0.8377	-37.0000	12.0000
Diff (1-2)		-4.8737	10.0256	1.3306		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-12.0577	-14.1515	-9.9639	10.7666	9.4757	12.4678
3		-7.1840	-8.8420	-5.5260	9.3657	8.3310	10.6962
Diff (1-2)	Pooled	-4.8737	-7.4957	-2.2517	10.0256	9.1821	11.0411
Diff (1-2)	Satterthwaite	-4.8737	-7.5308	-2.2166			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	227	-3.66	0.0003
Satterthwaite	Unequal	205.77	-3.62	0.0004

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	103	124	1.32	0.1375

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	102	-11.5490	11.6293	1.1515	-41.0000	11.0000
3	123	-7.3008	10.1658	0.9166	-39.0000	12.0000
Diff (1-2)		-4.2482	10.8531	1.4534		

TRTPN	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2		-11.5490	-13.8332	-9.2648	11.6293	10.2229	13.4878
3		-7.3008	-9.1153	-5.4863	10.1658	9.0346	11.6234
Diff (1-2)	Pooled	-4.2482	-7.1124	-1.3840	10.8531	9.9325	11.9632
Diff (1-2)	Satterthwaite	-4.2482	-7.1502	-1.3463			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	223	-2.92	0.0038
Satterthwaite	Unequal	202.31	-2.89	0.0043

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	101	122	1.31	0.1554

SOURCE: TTESTOC; TABLE: stat1i.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	0.4550	0.5000
2	Row Mean Scores Differ	2	4.9054	0.0861

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	6.1912	0.0128
2	Row Mean Scores Differ	2	14.3978	0.0007

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	7.3934	0.0065
2	Row Mean Scores Differ	2	17.6867	0.0001

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

CENTANAFADINE 4 OF 6
PROTOCOL 405-201-00014

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	6.0289	0.0141
2	Row Mean Scores Differ	2	14.5765	0.0007

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.8 FINAL

CENTANAFADINE 5 OF 6
PROTOCOL 405-201-00014

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	3.2902	0.0697
2	Row Mean Scores Differ	2	11.9563	0.0025

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[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=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	2.7238	0.0989
2	Row Mean Scores Differ	2	10.7158	0.0047

---

[1] WILCOXON TEST STRATIFIED BY (POOLED) CENTER.

SOURCE: NPAR; TABLE: stat1j.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	338	Sum Weights	338
Mean	0.21994106	Sum Observations	74.3400787
Std Deviation	10.206485	Variance	104.172337
Skewness	-0.4662637	Kurtosis	-0.2816581
Uncorrected SS	35122.428	Corrected SS	35106.0776
Coeff Variation	4640.5546	Std Error Mean	0.5551596

Basic Statistical Measures

Location		Variability	
Mean	0.219941	Std Deviation	10.20649
Median	2.116541	Variance	104.17234
Mode	7.859023	Range	51.41794
		Interquartile Range	14.95136

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.396176	Pr > |t|	0.6922
Sign	M	21	Pr >= |M|	0.0256
Signed Rank	S	1936.5	Pr >= |S|	0.2821

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

Quantiles (Definition 5)

Level	Quantile
100% Max	21.91943
99%	20.45404
95%	14.85949
90%	12.11174
75% Q3	7.82680
50% Median	2.11654
25% Q1	-7.12456
10%	-14.10923
5%	-18.33244
1%	-27.07807
0% Min	-29.49851

Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-29.4985	961	19.4617	1608
-27.6116	257	20.4540	298
-27.3096	1412	20.7976	1491
-27.0781	401	21.6142	973

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

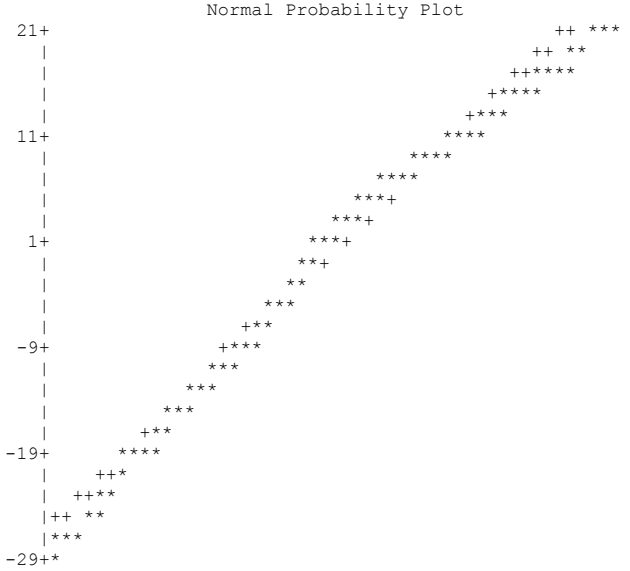
Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-25.9557	1117	21.9194	1066

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

Stem	Leaf	#	Boxplot
20	5869	4	
18	95	2	
16	023709	6	
14	003899946	9	
12	01245678891238	14	
10	11123799911225888	17	
8	00115566678990012222234566789	29	
6	000122233455667800012345677788889999	35	+-----+
4	233446779901223344555777 88	26	| |
2	00222334577888990111244456899	29	*-----*
0	0144555668880035779	19	| + |
-0	87544421098873331100	20	| |
-2	7322098543222110	16	| |
-4	87532119976544210	17	| |
-6	87765317766431000	17	+-----+
-8	9772110096541	13	|
-10	986321007766554300	18	|
-12	9866421986520	13	|
-14	95287544431	11	|
-16	65510	5	|
-18	00966533	8	|
-20	3	1	|
-22	932	3	|
-24	1	1	|
-26	6310	4	|
-28	5	1	|



SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	338	Sum Weights	338
Mean	0.02186339	Sum Observations	7.38982701
Std Deviation	1.00255899	Variance	1.00512453
Skewness	-0.4654092	Kurtosis	-0.2701205
Uncorrected SS	338.888534	Corrected SS	338.726967
Coeff Variation	4585.55983	Std Error Mean	0.05453202

Basic Statistical Measures

Location		Variability	
Mean	0.021863	Std Deviation	1.00256
Median	0.204955	Variance	1.00512
Mode	0.760366	Range	5.13076
		Interquartile Range	1.45333

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.400928	Pr > |t|	0.6887
Sign	M	21	Pr >= |M|	0.0256
Signed Rank	S	1930.5	Pr >= |S|	0.2836

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

Quantiles (Definition 5)

Level	Quantile
100% Max	2.170595
99%	1.980822
95%	1.444907
90%	1.182725
75% Q3	0.762961
50% Median	0.204955
25% Q1	-0.690365
10%	-1.369158
5%	-1.794783
1%	-2.635345
0% Min	-2.960170

Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-2.96017	961	1.88413	1608
-2.72302	1412	1.98082	298
-2.68489	257	2.07185	1491
-2.63534	401	2.14336	1066

SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

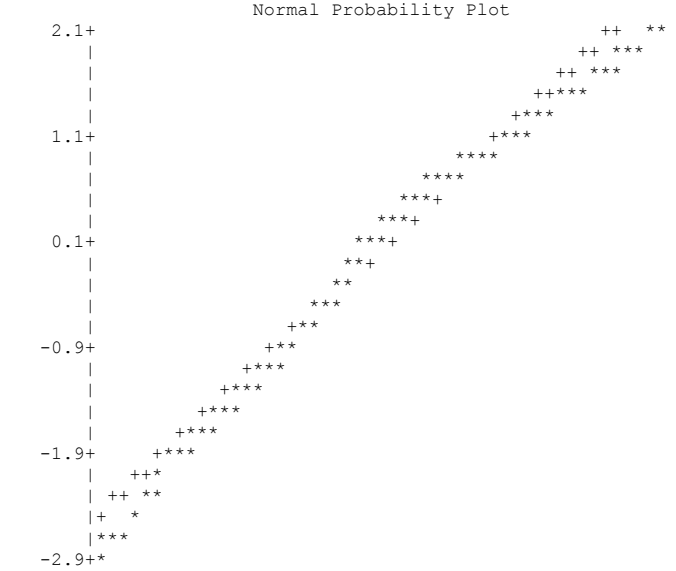
Extreme Observations

------Lowest-----		-----Highest-----	
Value	Obs	Value	Obs
-2.54132	1117	2.17059	973

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
20	747	3	
18	488	3	
16	35884	5	
14	224456938	9	
12	113355688346	12	
10	0122778889923566789	19	
8	012344556888880013334466679	28	
6	00111223455788890013556666666677888	34	+-----+
4	012223566799011222333455567999	30	| |
2	00122234577788899000233446 78	28	*-----*
0	0144455667880035678	19	| + |
-0	987444411988863331100	21	| |
-2	9621109854221110	16	| |
-4	9886642200887554330	19	| |
-6	975555397654220	15	+-----+
-8	86644309877331	14	
-10	98442108777332200	17	
-12	87765322877310	14	
-14	76509743310	11	
-16	98101	5	
-18	9985420	7	
-20	6	1	
-22	532	3	
-24	4	1	
-26	284	3	
-28	6	1	0



SOURCE: MMRMDX1; TABLE: stat1k.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)

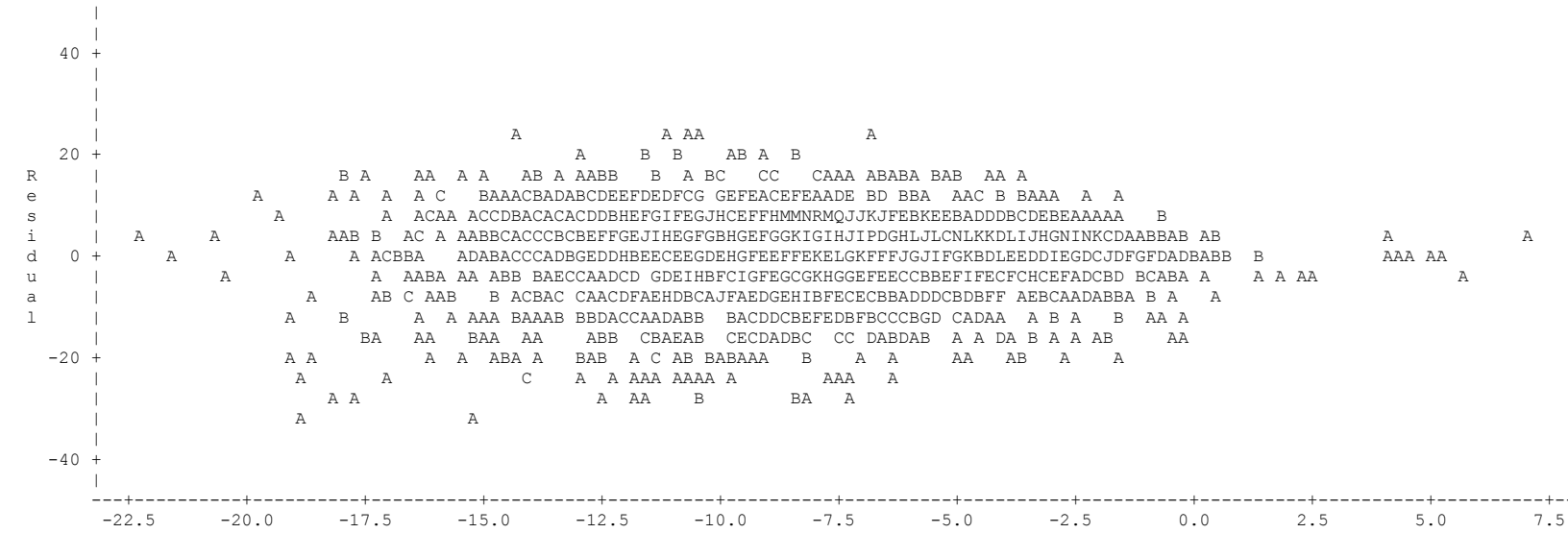
The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)
AVISITN = 42
AVISIT = DAY 42

```
    ----+----+----+----+----+----+----                                  +----+----+----+----+----+----+----+----+----+----+
Multiply Stem.Leaf by 10**-1                                            -2        -1         0        +1        +2
```

CENTANAFADINE 11 OF 11
PROTOCOL 405-201-00014

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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	39	[redacted]

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

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

The Mixed Procedure

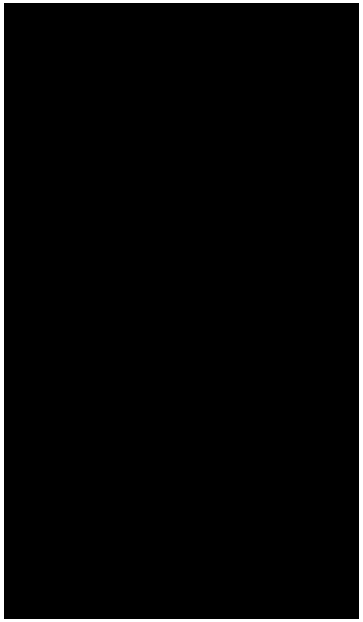
Class Level Information

Class	Levels	Values
SUBJID	421	[redacted]

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

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

The Mixed Procedure

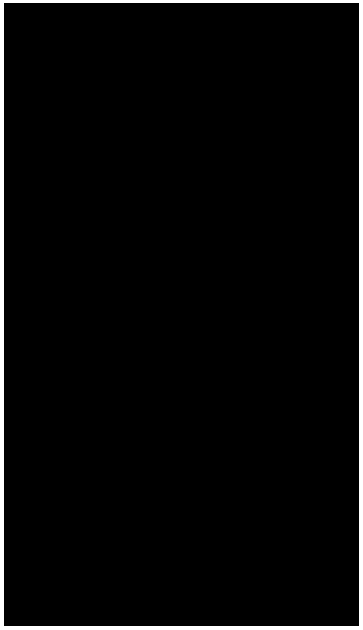


SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

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

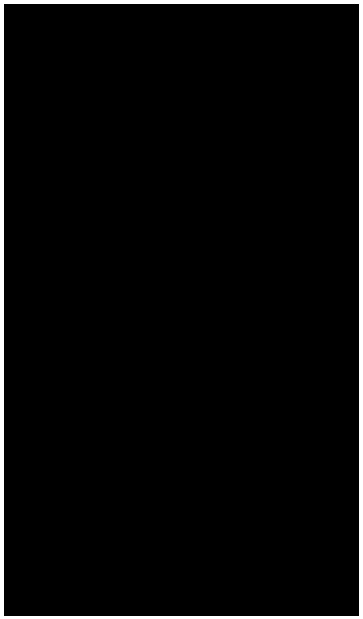
The Mixed Procedure



STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

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

The Mixed Procedure

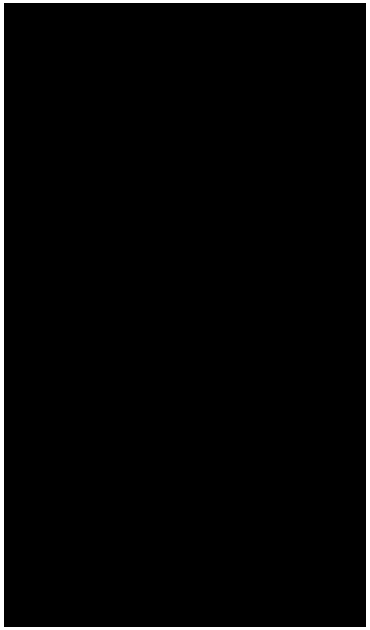


SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-4.10 FINAL

STAT-4.10
Proc Mixed Output Using Heterogeneous Variance Structure for Treatment Groups
(Efficacy Sample)

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

The Mixed Procedure



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	73
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2227
Number of Observations Used	2227
Number of Observations Not Used	0

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	15800.38727426	
1	4	13478.73670114	0.00213540
2	1	13467.00275618	0.00024731
3	1	13465.70016597	0.00001037
4	1	13465.64921223	0.00000003
5	1	13465.64904810	0.00000000

Convergence criteria met.

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4
1	36.9737	26.0068	31.4785	33.3871
2	26.0068	59.7634	55.9805	56.6731
3	31.4785	55.9805	78.9073	73.4766
4	33.3871	56.6731	73.4766	94.5512

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
1	1.0000	0.5533	0.5828	0.5647
2	0.5533	1.0000	0.8152	0.7539
3	0.5828	0.8152	1.0000	0.8507
4	0.5647	0.7539	0.8507	1.0000

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	48.7945	45.9963	44.9550	46.9027	44.0988	44.7419
2	45.9963	92.0313	77.3240	75.1467	71.7701	69.6304
3	44.9550	77.3240	93.5276	87.1175	77.8069	80.6325
4	46.9027	75.1467	87.1175	101.83	91.1218	92.2892
5	44.0988	71.7701	77.8069	91.1218	101.52	89.0164
6	44.7419	69.6304	80.6325	92.2892	89.0164	109.05

Estimated R Matrix for SUBJID [redacted]

Row	Col1	Col2	Col3	Col4	Col5	Col6
1	45.3296	42.2715	36.0407	39.1670	40.8245	39.9697
2	42.2715	58.5296	46.1505	46.4824	51.7087	50.9898

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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
3	36.0407	46.1505	71.3771	62.2249	65.8373	69.3392
4	39.1670	46.4824	62.2249	75.8237	70.2194	74.6922
5	40.8245	51.7087	65.8373	70.2194	84.4321	83.9356
6	39.9697	50.9898	69.3392	74.6922	83.9356	97.8853

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
UN(1,1)	SUBJID	TRTPN 1	48.7945
UN(2,1)	SUBJID	TRTPN 1	45.9963
UN(2,2)	SUBJID	TRTPN 1	92.0313
UN(3,1)	SUBJID	TRTPN 1	44.9550
UN(3,2)	SUBJID	TRTPN 1	77.3240
UN(3,3)	SUBJID	TRTPN 1	93.5276
UN(4,1)	SUBJID	TRTPN 1	46.9027
UN(4,2)	SUBJID	TRTPN 1	75.1467
UN(4,3)	SUBJID	TRTPN 1	87.1175
UN(4,4)	SUBJID	TRTPN 1	101.83
UN(5,1)	SUBJID	TRTPN 1	44.0988
UN(5,2)	SUBJID	TRTPN 1	71.7701
UN(5,3)	SUBJID	TRTPN 1	77.8069
UN(5,4)	SUBJID	TRTPN 1	91.1218

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(5,5)	SUBJID	TRTPN 1	101.52
UN(6,1)	SUBJID	TRTPN 1	44.7419
UN(6,2)	SUBJID	TRTPN 1	69.6304
UN(6,3)	SUBJID	TRTPN 1	80.6325
UN(6,4)	SUBJID	TRTPN 1	92.2892
UN(6,5)	SUBJID	TRTPN 1	89.0164
UN(6,6)	SUBJID	TRTPN 1	109.05
UN(1,1)	SUBJID	TRTPN 2	36.9737
UN(2,1)	SUBJID	TRTPN 2	26.0068
UN(2,2)	SUBJID	TRTPN 2	59.7634
UN(3,1)	SUBJID	TRTPN 2	31.4785
UN(3,2)	SUBJID	TRTPN 2	55.9805
UN(3,3)	SUBJID	TRTPN 2	78.9073
UN(4,1)	SUBJID	TRTPN 2	33.3871
UN(4,2)	SUBJID	TRTPN 2	56.6731
UN(4,3)	SUBJID	TRTPN 2	73.4766
UN(4,4)	SUBJID	TRTPN 2	94.5512
UN(5,1)	SUBJID	TRTPN 2	32.3181
UN(5,2)	SUBJID	TRTPN 2	56.3760
UN(5,3)	SUBJID	TRTPN 2	72.7477
UN(5,4)	SUBJID	TRTPN 2	86.8002
UN(5,5)	SUBJID	TRTPN 2	107.38
UN(6,1)	SUBJID	TRTPN 2	30.4643
UN(6,2)	SUBJID	TRTPN 2	56.8611

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(6,3)	SUBJID	TRTPN 2	70.9567
UN(6,4)	SUBJID	TRTPN 2	85.9523
UN(6,5)	SUBJID	TRTPN 2	101.05
UN(6,6)	SUBJID	TRTPN 2	117.94
UN(1,1)	SUBJID	TRTPN 3	45.3296
UN(2,1)	SUBJID	TRTPN 3	42.2715
UN(2,2)	SUBJID	TRTPN 3	58.5296
UN(3,1)	SUBJID	TRTPN 3	36.0407
UN(3,2)	SUBJID	TRTPN 3	46.1505
UN(3,3)	SUBJID	TRTPN 3	71.3771
UN(4,1)	SUBJID	TRTPN 3	39.1670
UN(4,2)	SUBJID	TRTPN 3	46.4824
UN(4,3)	SUBJID	TRTPN 3	62.2249
UN(4,4)	SUBJID	TRTPN 3	75.8237
UN(5,1)	SUBJID	TRTPN 3	40.8245
UN(5,2)	SUBJID	TRTPN 3	51.7087
UN(5,3)	SUBJID	TRTPN 3	65.8373
UN(5,4)	SUBJID	TRTPN 3	70.2194
UN(5,5)	SUBJID	TRTPN 3	84.4321
UN(6,1)	SUBJID	TRTPN 3	39.9697
UN(6,2)	SUBJID	TRTPN 3	50.9898
UN(6,3)	SUBJID	TRTPN 3	69.3392
UN(6,4)	SUBJID	TRTPN 3	74.6922
UN(6,5)	SUBJID	TRTPN 3	83.9356

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(6,6)	SUBJID	TRTPN 3	97.8853

Fit Statistics

-2 Res Log Likelihood	13465.6
AIC (Smaller is Better)	13591.6
AICC (Smaller is Better)	13595.5
BIC (Smaller is Better)	13846.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
62	2334.74	<.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				2.2570	4.8279	484	0.47	0.6404
AVISITN		7		0.1158	2.6468	338	0.04	0.9651
AVISITN		14		-1.0804	2.4063	361	-0.45	0.6537
AVISITN		21		1.3469	2.0492	336	0.66	0.5115
AVISITN		28		-1.3671	1.7371	334	-0.79	0.4318
AVISITN		35		-1.2228	1.5148	307	-0.81	0.4202
AVISITN		42		0				
TRTPN			1	-3.9849	1.2601	249	-3.16	0.0018
TRTPN			2	-4.4036	1.3262	243	-3.32	0.0010
TRTPN			3	0				
AVISITN*TRTPN		7	1	2.0812	1.0252	214	2.03	0.0436
AVISITN*TRTPN		7	2	2.5703	1.1536	220	2.23	0.0269
AVISITN*TRTPN		7	3	0				
AVISITN*TRTPN		14	1	0.3743	0.9708	239	0.39	0.7002
AVISITN*TRTPN		14	2	0.8059	1.0165	221	0.79	0.4288
AVISITN*TRTPN		14	3	0				
AVISITN*TRTPN		21	1	-0.03336	0.7740	225	-0.04	0.9657
AVISITN*TRTPN		21	2	-0.05933	0.8789	200	-0.07	0.9462
AVISITN*TRTPN		21	3	0				
AVISITN*TRTPN		28	1	0.04623	0.6580	232	0.07	0.9440
AVISITN*TRTPN		28	2	-0.08429	0.7725	199	-0.11	0.9132
AVISITN*TRTPN		28	3	0				

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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|
AVISITN*TRTPN		35	1	0.2367	0.6395	189	0.37	0.7117
AVISITN*TRTPN		35	2	-0.9126	0.5964	187	-1.53	0.1276
AVISITN*TRTPN		35	3	0				
AVISITN*TRTPN		42	1	0				
AVISITN*TRTPN		42	2	0				
AVISITN*TRTPN		42	3	0				
POOLCNTR	[redacted]			0.8283	3.8363	321	0.22	0.8292
POOLCNTR				-6.1914	5.3240	366	-1.16	0.2456
POOLCNTR				1.0964	3.7183	309	0.29	0.7683
POOLCNTR				-1.6031	4.5459	325	-0.35	0.7246
POOLCNTR				-4.5469	4.4902	349	-1.01	0.3119
POOLCNTR				0.4501	3.8364	321	0.12	0.9067
POOLCNTR				-0.1036	3.7924	316	-0.03	0.9782
POOLCNTR				-3.2912	4.3656	360	-0.75	0.4514
POOLCNTR				1.9748	5.2591	363	0.38	0.7075
POOLCNTR				-4.1388	3.8918	320	-1.06	0.2884
POOLCNTR				-3.1507	4.2517	350	-0.74	0.4592
POOLCNTR				-10.6697	5.2445	363	-2.03	0.0426
POOLCNTR				-4.3208	4.3847	332	-0.99	0.3251
POOLCNTR				2.8042	4.0999	331	0.68	0.4945
POOLCNTR				-2.4878	4.1211	333	-0.60	0.5465
POOLCNTR				-3.2434	4.7088	355	-0.69	0.4914

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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]			-4.6400	4.2765	342	-1.08	0.2787
POOLCNTR				0.3984	4.8159	338	0.08	0.9341
POOLCNTR				-1.9005	4.8163	339	-0.39	0.6934
POOLCNTR				-1.4595	3.9964	336	-0.37	0.7152
POOLCNTR				-4.0268	4.1976	338	-0.96	0.3381
POOLCNTR				8.7760	4.9299	391	1.78	0.0758
POOLCNTR				2.1905	3.9947	328	0.55	0.5838
POOLCNTR				-5.0765	4.0162	322	-1.26	0.2071
POOLCNTR				-3.2253	4.1899	338	-0.77	0.4420
POOLCNTR				5.7015	4.3994	342	1.30	0.1959
POOLCNTR				-7.0249	4.4804	348	-1.57	0.1178
POOLCNTR				-4.1895	4.2580	328	-0.98	0.3259
POOLCNTR				1.1537	3.7287	314	0.31	0.7572
POOLCNTR				2.2150	3.7161	311	0.60	0.5516
POOLCNTR				-2.3843	4.6802	355	-0.51	0.6108
POOLCNTR				1.3772	4.6860	354	0.29	0.7690
POOLCNTR				-5.2391	3.9702	332	-1.32	0.1879
POOLCNTR				-0.5364	4.4506	351	-0.12	0.9041
POOLCNTR				-1.5627	3.8965	323	-0.40	0.6886
POOLCNTR				-3.9649	5.2626	363	-0.75	0.4517
POOLCNTR				-5.0626	4.5384	368	-1.12	0.2654
POOLCNTR				-4.3025	4.4648	310	-0.96	0.3360

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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]			0				
BASE*AVISITN		7		-0.1300	0.06016	371	-2.16	0.0313
BASE*AVISITN		14		-0.1294	0.07004	408	-1.85	0.0655
BASE*AVISITN		21		-0.2303	0.07607	431	-3.03	0.0026
BASE*AVISITN		28		-0.1649	0.08037	436	-2.05	0.0408
BASE*AVISITN		35		-0.1882	0.08325	439	-2.26	0.0243
BASE*AVISITN		42		-0.2273	0.08808	441	-2.58	0.0102

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
AVISITN	5	347	1.35	0.2432
TRTPN	2	247	10.64	<.0001
AVISITN*TRTPN	10	288	1.85	0.0523
POOLCNTR	38	361	2.24	<.0001
BASE*AVISITN	6	372	2.28	0.0359

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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

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	-6.2343	0.6492	143	-9.60	<.0001	0.05	-7.5175	-4.9510
AVISITN*TRTPN	7	2	-6.1638	0.5830	159	-10.57	<.0001	0.05	-7.3153	-5.0123
AVISITN*TRTPN	7	3	-4.3306	0.6230	146	-6.95	<.0001	0.05	-5.5618	-3.0994
AVISITN*TRTPN	14	1	-9.1119	0.8613	144	-10.58	<.0001	0.05	-10.8143	-7.4095
AVISITN*TRTPN	14	2	-9.0991	0.7308	140	-12.45	<.0001	0.05	-10.5441	-7.6541
AVISITN*TRTPN	14	3	-5.5013	0.6996	153	-7.86	<.0001	0.05	-6.8835	-4.1192
AVISITN*TRTPN	21	1	-10.9137	0.8728	148	-12.50	<.0001	0.05	-12.6385	-9.1890
AVISITN*TRTPN	21	2	-11.3585	0.8343	140	-13.61	<.0001	0.05	-13.0079	-9.7090
AVISITN*TRTPN	21	3	-6.8955	0.7677	143	-8.98	<.0001	0.05	-8.4130	-5.3780
AVISITN*TRTPN	28	1	-11.0717	0.9127	144	-12.13	<.0001	0.05	-12.8758	-9.2676
AVISITN*TRTPN	28	2	-11.6209	0.9119	136	-12.74	<.0001	0.05	-13.4243	-9.8176
AVISITN*TRTPN	28	3	-7.1331	0.7890	146	-9.04	<.0001	0.05	-8.6924	-5.5737
AVISITN*TRTPN	35	1	-11.6202	0.9220	138	-12.60	<.0001	0.05	-13.4433	-9.7972
AVISITN*TRTPN	35	2	-13.1883	0.9849	137	-13.39	<.0001	0.05	-15.1358	-11.2407
AVISITN*TRTPN	35	3	-7.8720	0.8310	144	-9.47	<.0001	0.05	-9.5146	-6.2295
AVISITN*TRTPN	42	1	-12.1124	0.9593	140	-12.63	<.0001	0.05	-14.0089	-10.2158
AVISITN*TRTPN	42	2	-12.5311	1.0402	135	-12.05	<.0001	0.05	-14.5884	-10.4738
AVISITN*TRTPN	42	3	-8.1275	0.8928	142	-9.10	<.0001	0.05	-9.8925	-6.3625

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	1	7	2	-0.07041	0.7962	240	-0.09	0.9296	0.05	-1.6389	1.4980
AVISITN*TRTPN	7	1	7	3	-1.9037	0.8264	248	-2.30	0.0221	0.05	-3.5313	-0.2761
AVISITN*TRTPN	7	1	14	1	2.8777	0.6083	130	4.73	<.0001	0.05	1.6742	4.0812
AVISITN*TRTPN	7	1	14	2	2.8648	0.9105	235	3.15	0.0019	0.05	1.0711	4.6586
AVISITN*TRTPN	7	1	14	3	-0.7329	0.8853	251	-0.83	0.4086	0.05	-2.4765	1.0107
AVISITN*TRTPN	7	1	21	1	4.6795	0.6357	125	7.36	<.0001	0.05	3.4213	5.9376
AVISITN*TRTPN	7	1	21	2	5.1242	0.9953	223	5.15	<.0001	0.05	3.1629	7.0855
AVISITN*TRTPN	7	1	21	3	0.6613	0.9401	234	0.70	0.4825	0.05	-1.1909	2.5134
AVISITN*TRTPN	7	1	28	1	4.8374	0.6689	107	7.23	<.0001	0.05	3.5114	6.1635
AVISITN*TRTPN	7	1	28	2	5.3867	1.0612	209	5.08	<.0001	0.05	3.2946	7.4788
AVISITN*TRTPN	7	1	28	3	0.8988	0.9577	232	0.94	0.3489	0.05	-0.9880	2.7856
AVISITN*TRTPN	7	1	35	1	5.3860	0.7106	103	7.58	<.0001	0.05	3.9767	6.7953
AVISITN*TRTPN	7	1	35	2	6.9540	1.1245	205	6.18	<.0001	0.05	4.7370	9.1711
AVISITN*TRTPN	7	1	35	3	1.6378	0.9925	229	1.65	0.1003	0.05	-0.3178	3.5934
AVISITN*TRTPN	7	1	42	1	5.8781	0.7520	100	7.82	<.0001	0.05	4.3862	7.3700
AVISITN*TRTPN	7	1	42	2	6.2968	1.1733	197	5.37	<.0001	0.05	3.9829	8.6107
AVISITN*TRTPN	7	1	42	3	1.8932	1.0448	220	1.81	0.0713	0.05	-0.1659	3.9523
AVISITN*TRTPN	7	2	7	3	-1.8333	0.7769	236	-2.36	0.0191	0.05	-3.3638	-0.3028
AVISITN*TRTPN	7	2	14	1	2.9481	0.9769	217	3.02	0.0029	0.05	1.0226	4.8736
AVISITN*TRTPN	7	2	14	2	2.9352	0.5957	124	4.93	<.0001	0.05	1.7563	4.1142
AVISITN*TRTPN	7	2	14	3	-0.6625	0.8392	237	-0.79	0.4306	0.05	-2.3157	0.9907
AVISITN*TRTPN	7	2	21	1	4.7499	0.9872	222	4.81	<.0001	0.05	2.8045	6.6953

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	5.1946	0.6623	127	7.84	<.0001	0.05	3.8840	6.5052
AVISITN*TRTPN	7	2	21	3	0.7317	0.8968	222	0.82	0.4154	0.05	-1.0357	2.4990
AVISITN*TRTPN	7	2	28	1	4.9078	1.0227	212	4.80	<.0001	0.05	2.8918	6.9238
AVISITN*TRTPN	7	2	28	2	5.4571	0.7394	123	7.38	<.0001	0.05	3.9936	6.9207
AVISITN*TRTPN	7	2	28	3	0.9692	0.9152	226	1.06	0.2907	0.05	-0.8343	2.7727
AVISITN*TRTPN	7	2	35	1	5.4564	1.0312	202	5.29	<.0001	0.05	3.4231	7.4897
AVISITN*TRTPN	7	2	35	2	7.0244	0.8369	117	8.39	<.0001	0.05	5.3670	8.6819
AVISITN*TRTPN	7	2	35	3	1.7082	0.9516	218	1.80	0.0740	0.05	-0.1674	3.5838
AVISITN*TRTPN	7	2	42	1	5.9485	1.0645	201	5.59	<.0001	0.05	3.8495	8.0475
AVISITN*TRTPN	7	2	42	2	6.3673	0.9160	116	6.95	<.0001	0.05	4.5531	8.1814
AVISITN*TRTPN	7	2	42	3	1.9637	1.0060	208	1.95	0.0523	0.05	-0.01970	3.9470
AVISITN*TRTPN	7	3	14	1	4.7814	1.0016	225	4.77	<.0001	0.05	2.8076	6.7551
AVISITN*TRTPN	7	3	14	2	4.7685	0.8936	227	5.34	<.0001	0.05	3.0077	6.5293
AVISITN*TRTPN	7	3	14	3	1.1708	0.3843	131	3.05	0.0028	0.05	0.4106	1.9310
AVISITN*TRTPN	7	3	21	1	6.5832	1.0115	226	6.51	<.0001	0.05	4.5899	8.5764
AVISITN*TRTPN	7	3	21	2	7.0279	0.9799	219	7.17	<.0001	0.05	5.0966	8.9592
AVISITN*TRTPN	7	3	21	3	2.5650	0.5796	122	4.43	<.0001	0.05	1.4176	3.7124
AVISITN*TRTPN	7	3	28	1	6.7411	1.0463	218	6.44	<.0001	0.05	4.6790	8.8032
AVISITN*TRTPN	7	3	28	2	7.2904	1.0468	207	6.96	<.0001	0.05	5.2266	9.3542
AVISITN*TRTPN	7	3	28	3	2.8025	0.5700	132	4.92	<.0001	0.05	1.6749	3.9301
AVISITN*TRTPN	7	3	35	1	7.2897	1.0544	212	6.91	<.0001	0.05	5.2111	9.3682
AVISITN*TRTPN	7	3	35	2	8.8577	1.1109	201	7.97	<.0001	0.05	6.6671	11.0483

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	3.5415	0.6078	121	5.83	<.0001	0.05	2.3383	4.7447
AVISITN*TRTPN	7	3	42	1	7.7818	1.0871	208	7.16	<.0001	0.05	5.6387	9.9249
AVISITN*TRTPN	7	3	42	2	8.2005	1.1603	193	7.07	<.0001	0.05	5.9120	10.4891
AVISITN*TRTPN	7	3	42	3	3.7969	0.6986	121	5.44	<.0001	0.05	2.4139	5.1800
AVISITN*TRTPN	14	1	14	2	-0.01284	1.0728	241	-0.01	0.9905	0.05	-2.1262	2.1005
AVISITN*TRTPN	14	1	14	3	-3.6106	1.0505	244	-3.44	0.0007	0.05	-5.6798	-1.5414
AVISITN*TRTPN	14	1	21	1	1.8018	0.4983	124	3.62	0.0004	0.05	0.8156	2.7880
AVISITN*TRTPN	14	1	21	2	2.2465	1.1457	246	1.96	0.0510	0.05	-0.01000	4.5031
AVISITN*TRTPN	14	1	21	3	-2.2164	1.0971	248	-2.02	0.0444	0.05	-4.3773	-0.05549
AVISITN*TRTPN	14	1	28	1	1.9598	0.5937	126	3.30	0.0013	0.05	0.7848	3.1347
AVISITN*TRTPN	14	1	28	2	2.5090	1.2033	242	2.09	0.0381	0.05	0.1387	4.8793
AVISITN*TRTPN	14	1	28	3	-1.9789	1.1122	246	-1.78	0.0764	0.05	-4.1696	0.2119
AVISITN*TRTPN	14	1	35	1	2.5083	0.6469	124	3.88	0.0002	0.05	1.2279	3.7887
AVISITN*TRTPN	14	1	35	2	4.0764	1.2595	241	3.24	0.0014	0.05	1.5953	6.5574
AVISITN*TRTPN	14	1	35	3	-1.2399	1.1423	252	-1.09	0.2788	0.05	-3.4897	1.0099
AVISITN*TRTPN	14	1	42	1	3.0004	0.7209	123	4.16	<.0001	0.05	1.5735	4.4274
AVISITN*TRTPN	14	1	42	2	3.4192	1.3033	235	2.62	0.0093	0.05	0.8516	5.9868
AVISITN*TRTPN	14	1	42	3	-0.9844	1.1881	252	-0.83	0.4081	0.05	-3.3243	1.3554
AVISITN*TRTPN	14	2	14	3	-3.5977	0.9490	240	-3.79	0.0002	0.05	-5.4672	-1.7283
AVISITN*TRTPN	14	2	21	1	1.8147	1.0821	244	1.68	0.0948	0.05	-0.3168	3.9461
AVISITN*TRTPN	14	2	21	2	2.2594	0.4852	117	4.66	<.0001	0.05	1.2985	3.2202
AVISITN*TRTPN	14	2	21	3	-2.2036	1.0001	237	-2.20	0.0285	0.05	-4.1737	-0.2334

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	1.9726	1.1146	237	1.77	0.0780	0.05	-0.2231	4.1683
AVISITN*TRTPN	14	2	28	2	2.5219	0.6012	117	4.19	<.0001	0.05	1.3313	3.7125
AVISITN*TRTPN	14	2	28	3	-1.9660	1.0166	246	-1.93	0.0543	0.05	-3.9684	0.03631
AVISITN*TRTPN	14	2	35	1	2.5211	1.1224	230	2.25	0.0256	0.05	0.3096	4.7327
AVISITN*TRTPN	14	2	35	2	4.0892	0.7094	112	5.76	<.0001	0.05	2.6836	5.4949
AVISITN*TRTPN	14	2	35	3	-1.2270	1.0495	241	-1.17	0.2435	0.05	-3.2945	0.8404
AVISITN*TRTPN	14	2	42	1	3.0133	1.1531	228	2.61	0.0096	0.05	0.7411	5.2855
AVISITN*TRTPN	14	2	42	2	3.4320	0.7779	110	4.41	<.0001	0.05	1.8903	4.9737
AVISITN*TRTPN	14	2	42	3	-0.9716	1.0991	236	-0.88	0.3776	0.05	-3.1369	1.1937
AVISITN*TRTPN	14	3	21	1	5.4124	1.0600	245	5.11	<.0001	0.05	3.3245	7.5003
AVISITN*TRTPN	14	3	21	2	5.8571	1.0305	236	5.68	<.0001	0.05	3.8269	7.8873
AVISITN*TRTPN	14	3	21	3	1.3942	0.5352	124	2.61	0.0103	0.05	0.3349	2.4535
AVISITN*TRTPN	14	3	28	1	5.5703	1.0932	237	5.10	<.0001	0.05	3.4167	7.7240
AVISITN*TRTPN	14	3	28	2	6.1196	1.0943	225	5.59	<.0001	0.05	3.9632	8.2760
AVISITN*TRTPN	14	3	28	3	1.6317	0.5625	130	2.90	0.0044	0.05	0.5189	2.7446
AVISITN*TRTPN	14	3	35	1	6.1189	1.1010	230	5.56	<.0001	0.05	3.9495	8.2882
AVISITN*TRTPN	14	3	35	2	7.6869	1.1558	218	6.65	<.0001	0.05	5.4090	9.9649
AVISITN*TRTPN	14	3	35	3	2.3707	0.5550	119	4.27	<.0001	0.05	1.2717	3.4697
AVISITN*TRTPN	14	3	42	1	6.6110	1.1323	226	5.84	<.0001	0.05	4.3799	8.8421
AVISITN*TRTPN	14	3	42	2	7.0298	1.2033	210	5.84	<.0001	0.05	4.6576	9.4019
AVISITN*TRTPN	14	3	42	3	2.6262	0.6518	120	4.03	<.0001	0.05	1.3357	3.9166
AVISITN*TRTPN	21	1	21	2	0.4447	1.1553	250	0.38	0.7006	0.05	-1.8307	2.7201

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-4.0182	1.1060	249	-3.63	0.0003	0.05	-6.1964	-1.8400
AVISITN*TRTPN	21	1	28	1	0.1579	0.4168	121	0.38	0.7054	0.05	-0.6672	0.9831
AVISITN*TRTPN	21	1	28	2	0.7072	1.2123	246	0.58	0.5602	0.05	-1.6806	3.0950
AVISITN*TRTPN	21	1	28	3	-3.7807	1.1210	249	-3.37	0.0009	0.05	-5.9886	-1.5728
AVISITN*TRTPN	21	1	35	1	0.7065	0.5769	114	1.22	0.2232	0.05	-0.4362	1.8492
AVISITN*TRTPN	21	1	35	2	2.2745	1.2680	245	1.79	0.0741	0.05	-0.2230	4.7721
AVISITN*TRTPN	21	1	35	3	-3.0417	1.1509	253	-2.64	0.0087	0.05	-5.3083	-0.7751
AVISITN*TRTPN	21	1	42	1	1.1986	0.5977	115	2.01	0.0473	0.05	0.01472	2.3825
AVISITN*TRTPN	21	1	42	2	1.6174	1.3116	239	1.23	0.2187	0.05	-0.9664	4.2011
AVISITN*TRTPN	21	1	42	3	-2.7862	1.1963	253	-2.33	0.0206	0.05	-5.1422	-0.4303
AVISITN*TRTPN	21	2	21	3	-4.4629	1.0784	244	-4.14	<.0001	0.05	-6.5872	-2.3387
AVISITN*TRTPN	21	2	28	1	-0.2868	1.1855	247	-0.24	0.8091	0.05	-2.6218	2.0482
AVISITN*TRTPN	21	2	28	2	0.2625	0.4862	114	0.54	0.5903	0.05	-0.7006	1.2256
AVISITN*TRTPN	21	2	28	3	-4.2254	1.0936	251	-3.86	0.0001	0.05	-6.3792	-2.0716
AVISITN*TRTPN	21	2	35	1	0.2618	1.1929	242	0.22	0.8265	0.05	-2.0880	2.6115
AVISITN*TRTPN	21	2	35	2	1.8298	0.6210	112	2.95	0.0039	0.05	0.5995	3.0602
AVISITN*TRTPN	21	2	35	3	-3.4864	1.1242	250	-3.10	0.0021	0.05	-5.7006	-1.2723
AVISITN*TRTPN	21	2	42	1	0.7539	1.2219	242	0.62	0.5378	0.05	-1.6529	3.1607
AVISITN*TRTPN	21	2	42	2	1.1726	0.7252	110	1.62	0.1087	0.05	-0.2645	2.6098
AVISITN*TRTPN	21	2	42	3	-3.2310	1.1706	250	-2.76	0.0062	0.05	-5.5365	-0.9254
AVISITN*TRTPN	21	3	28	1	4.1762	1.1379	246	3.67	0.0003	0.05	1.9348	6.4175
AVISITN*TRTPN	21	3	28	2	4.7254	1.1393	234	4.15	<.0001	0.05	2.4808	6.9701

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	0.2375	0.4197	124	0.57	0.5725	0.05	-0.5932	1.0683
AVISITN*TRTPN	21	3	35	1	4.7247	1.1454	239	4.12	<.0001	0.05	2.4683	6.9811
AVISITN*TRTPN	21	3	35	2	6.2928	1.1985	231	5.25	<.0001	0.05	3.9314	8.6541
AVISITN*TRTPN	21	3	35	3	0.9765	0.4363	125	2.24	0.0270	0.05	0.1131	1.8399
AVISITN*TRTPN	21	3	42	1	5.2168	1.1755	237	4.44	<.0001	0.05	2.9011	7.5326
AVISITN*TRTPN	21	3	42	2	5.6356	1.2444	223	4.53	<.0001	0.05	3.1832	8.0880
AVISITN*TRTPN	21	3	42	3	1.2320	0.4938	124	2.49	0.0139	0.05	0.2546	2.2093
AVISITN*TRTPN	28	1	28	2	0.5493	1.2420	246	0.44	0.6587	0.05	-1.8971	2.9956
AVISITN*TRTPN	28	1	28	3	-3.9386	1.1523	245	-3.42	0.0007	0.05	-6.2082	-1.6690
AVISITN*TRTPN	28	1	35	1	0.5486	0.4314	115	1.27	0.2061	0.05	-0.3059	1.4030
AVISITN*TRTPN	28	1	35	2	2.1166	1.2961	246	1.63	0.1037	0.05	-0.4363	4.6695
AVISITN*TRTPN	28	1	35	3	-3.1996	1.1814	251	-2.71	0.0072	0.05	-5.5264	-0.8728
AVISITN*TRTPN	28	1	42	1	1.0407	0.4870	114	2.14	0.0347	0.05	0.07594	2.0054
AVISITN*TRTPN	28	1	42	2	1.4594	1.3388	242	1.09	0.2768	0.05	-1.1778	4.0967
AVISITN*TRTPN	28	1	42	3	-2.9442	1.2257	253	-2.40	0.0170	0.05	-5.3581	-0.5303
AVISITN*TRTPN	28	2	28	3	-4.4879	1.1541	240	-3.89	0.0001	0.05	-6.7614	-2.2144
AVISITN*TRTPN	28	2	35	1	-0.00071	1.2487	244	-0.00	0.9995	0.05	-2.4604	2.4590
AVISITN*TRTPN	28	2	35	2	1.5673	0.5233	106	3.00	0.0034	0.05	0.5299	2.6047
AVISITN*TRTPN	28	2	35	3	-3.7489	1.1831	243	-3.17	0.0017	0.05	-6.0794	-1.4184
AVISITN*TRTPN	28	2	42	1	0.4914	1.2765	245	0.38	0.7006	0.05	-2.0229	3.0057
AVISITN*TRTPN	28	2	42	2	0.9101	0.6303	107	1.44	0.1516	0.05	-0.3393	2.1596
AVISITN*TRTPN	28	2	42	3	-3.4934	1.2273	247	-2.85	0.0048	0.05	-5.9108	-1.0761

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	4.4872	1.1598	240	3.87	0.0001	0.05	2.2026	6.7718
AVISITN*TRTPN	28	3	35	2	6.0552	1.2125	237	4.99	<.0001	0.05	3.6666	8.4439
AVISITN*TRTPN	28	3	35	3	0.7390	0.3985	123	1.85	0.0661	0.05	-0.04985	1.5278
AVISITN*TRTPN	28	3	42	1	4.9793	1.1895	239	4.19	<.0001	0.05	2.6361	7.3225
AVISITN*TRTPN	28	3	42	2	5.3980	1.2579	229	4.29	<.0001	0.05	2.9194	7.8766
AVISITN*TRTPN	28	3	42	3	0.9944	0.4443	125	2.24	0.0270	0.05	0.1151	1.8738
AVISITN*TRTPN	35	1	35	2	1.5681	1.3037	244	1.20	0.2302	0.05	-1.0000	4.1361
AVISITN*TRTPN	35	1	35	3	-3.7482	1.1884	246	-3.15	0.0018	0.05	-6.0888	-1.4075
AVISITN*TRTPN	35	1	42	1	0.4921	0.5403	111	0.91	0.3644	0.05	-0.5785	1.5628
AVISITN*TRTPN	35	1	42	2	0.9109	1.3458	239	0.68	0.4992	0.05	-1.7403	3.5620
AVISITN*TRTPN	35	1	42	3	-3.4927	1.2325	249	-2.83	0.0050	0.05	-5.9203	-1.0652
AVISITN*TRTPN	35	2	35	3	-5.3162	1.2406	241	-4.29	<.0001	0.05	-7.7601	-2.8724
AVISITN*TRTPN	35	2	42	1	-1.0759	1.3301	247	-0.81	0.4193	0.05	-3.6956	1.5438
AVISITN*TRTPN	35	2	42	2	-0.6572	0.4852	99.7	-1.35	0.1786	0.05	-1.6198	0.3054
AVISITN*TRTPN	35	2	42	3	-5.0608	1.2827	247	-3.95	0.0001	0.05	-7.5871	-2.5344
AVISITN*TRTPN	35	3	42	1	4.2403	1.2175	244	3.48	0.0006	0.05	1.8421	6.6385
AVISITN*TRTPN	35	3	42	2	4.6591	1.2849	235	3.63	0.0004	0.05	2.1277	7.1905
AVISITN*TRTPN	35	3	42	3	0.2555	0.3442	121	0.74	0.4594	0.05	-0.4260	0.9369
AVISITN*TRTPN	42	1	42	2	0.4187	1.3727	245	0.31	0.7606	0.05	-2.2850	3.1225
AVISITN*TRTPN	42	1	42	3	-3.9849	1.2601	249	-3.16	0.0018	0.05	-6.4667	-1.5030
AVISITN*TRTPN	42	2	42	3	-4.4036	1.3262	243	-3.32	0.0010	0.05	-7.0159	-1.7913

SOURCE: MMRMDX2; TABLE: stat11.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	243	3.60	0.0289
AVISITN*TRTPN	14	2	246	9.18	0.0001
AVISITN*TRTPN	21	2	248	10.57	<.0001
AVISITN*TRTPN	28	2	246	9.47	0.0001
AVISITN*TRTPN	35	2	246	10.24	<.0001
AVISITN*TRTPN	42	2	247	7.30	0.0008

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	39	[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

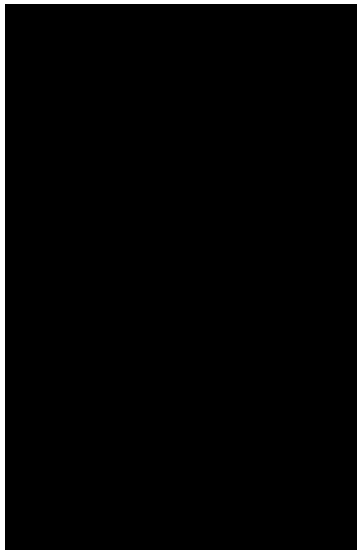
Class Level Information

Class	Levels	Values
SUBJID	421	[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

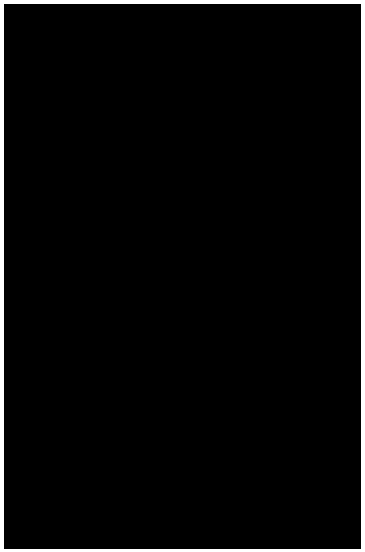


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

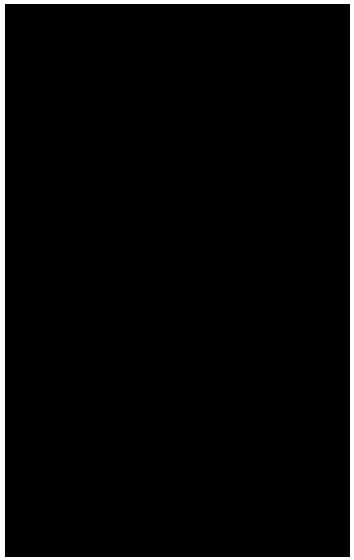


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

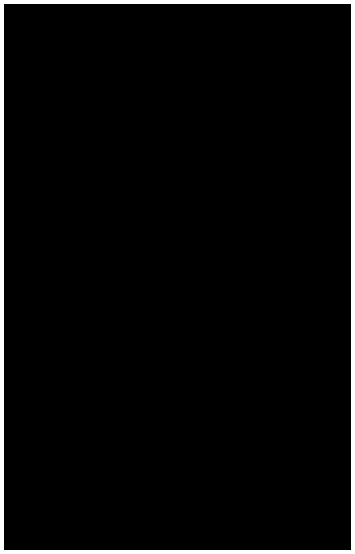


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

STAT-5.1
Proc Mixed Output for Change from Baseline in CGI-S Scale, MMRM (UN)
(Efficacy Sample)

---------- Parameter Code=CGI0201 ----------

The Mixed Procedure

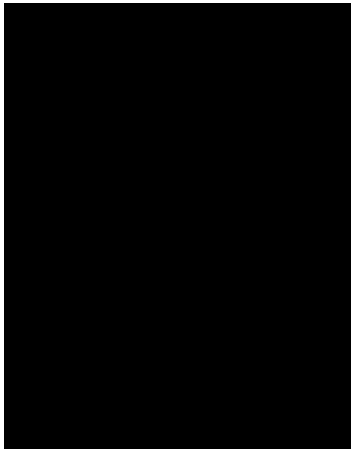


SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 FINAL

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: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	73
Columns in Z	0
Subjects	421
Max Obs per Subject	6

Number of Observations

Number of Observations Read	2220
Number of Observations Used	2220
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	5534.17561525	
1	2	3687.88676445	0.00358545
2	1	3687.36668372	0.00001709
3	1	3687.36429296	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	0.3911
UN(2,1)	SUBJID	0.2991
UN(2,2)	SUBJID	0.6117
UN(3,1)	SUBJID	0.3110
UN(3,2)	SUBJID	0.5237
UN(3,3)	SUBJID	0.7431
UN(4,1)	SUBJID	0.2804
UN(4,2)	SUBJID	0.5001
UN(4,3)	SUBJID	0.5893
UN(4,4)	SUBJID	0.7650
UN(5,1)	SUBJID	0.3206
UN(5,2)	SUBJID	0.5243
UN(5,3)	SUBJID	0.6146
UN(5,4)	SUBJID	0.6923
UN(5,5)	SUBJID	0.9120
UN(6,1)	SUBJID	0.2947
UN(6,2)	SUBJID	0.5097
UN(6,3)	SUBJID	0.5999

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	0.7026
UN(6,5)	SUBJID	0.8049
UN(6,6)	SUBJID	0.9541

Fit Statistics

-2 Res Log Likelihood	3687.4
AIC (Smaller is Better)	3729.4
AICC (Smaller is Better)	3729.8
BIC (Smaller is Better)	3814.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
20	1846.81	<.0001

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	352	0.16	0.9771
TRTPN	2	377	4.07	0.0179
AVISITN*TRTPN	10	522	1.44	0.1591
POOLCNTR	38	379	1.62	0.0135
BASE*AVISITN	6	378	6.13	<.0001

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > |t|	Alpha	Lower	Upper
DAY7 1 vs 3	-0.05184	0.07546	381	-0.69	0.4925	0.05	-0.2002	0.09652
DAY7 2 vs 3	-0.03062	0.07587	379	-0.40	0.6868	0.05	-0.1798	0.1186
DAY14 1 vs 3	-0.1951	0.09505	376	-2.05	0.0408	0.05	-0.3820	-0.00824
DAY14 2 vs 3	-0.1611	0.09681	384	-1.66	0.0968	0.05	-0.3515	0.02920
DAY21 1 vs 3	-0.2313	0.1053	367	-2.20	0.0286	0.05	-0.4383	-0.02432
DAY21 2 vs 3	-0.2400	0.1076	376	-2.23	0.0262	0.05	-0.4515	-0.02852
DAY28 1 vs 3	-0.2650	0.1076	364	-2.46	0.0142	0.05	-0.4766	-0.05345
DAY28 2 vs 3	-0.2665	0.1099	371	-2.42	0.0158	0.05	-0.4827	-0.05034

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.2626	0.1183	364	-2.22	0.0271	0.05	-0.4952	-0.02991
DAY35 2 vs 3	-0.3555	0.1212	373	-2.93	0.0036	0.05	-0.5938	-0.1173
DAY42 1 vs 3	-0.3287	0.1219	365	-2.70	0.0073	0.05	-0.5684	-0.08902
DAY42 2 vs 3	-0.2820	0.1249	372	-2.26	0.0245	0.05	-0.5276	-0.03644

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	-0.4635	0.05831	389	-7.95	<.0001	0.05	-0.5781	-0.3488
AVISITN*TRTPN	7	2	-0.4422	0.05866	386	-7.54	<.0001	0.05	-0.5576	-0.3269
AVISITN*TRTPN	7	3	-0.4116	0.05774	385	-7.13	<.0001	0.05	-0.5251	-0.2981
AVISITN*TRTPN	14	1	-0.7240	0.07107	405	-10.19	<.0001	0.05	-0.8637	-0.5843
AVISITN*TRTPN	14	2	-0.6900	0.07311	420	-9.44	<.0001	0.05	-0.8337	-0.5463
AVISITN*TRTPN	14	3	-0.5289	0.07093	407	-7.46	<.0001	0.05	-0.6683	-0.3894
AVISITN*TRTPN	21	1	-0.8550	0.07830	405	-10.92	<.0001	0.05	-1.0089	-0.7010
AVISITN*TRTPN	21	2	-0.8637	0.08093	419	-10.67	<.0001	0.05	-1.0227	-0.7046

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.6236	0.07749	396	-8.05	<.0001	0.05	-0.7760	-0.4713
AVISITN*TRTPN	28	1	-0.9048	0.08001	403	-11.31	<.0001	0.05	-1.0621	-0.7475
AVISITN*TRTPN	28	2	-0.9063	0.08273	413	-10.96	<.0001	0.05	-1.0689	-0.7437
AVISITN*TRTPN	28	3	-0.6398	0.07895	392	-8.10	<.0001	0.05	-0.7950	-0.4846
AVISITN*TRTPN	35	1	-0.9406	0.08760	403	-10.74	<.0001	0.05	-1.1128	-0.7684
AVISITN*TRTPN	35	2	-1.0336	0.09091	418	-11.37	<.0001	0.05	-1.2123	-0.8549
AVISITN*TRTPN	35	3	-0.6781	0.08597	389	-7.89	<.0001	0.05	-0.8471	-0.5090
AVISITN*TRTPN	42	1	-1.0402	0.09021	406	-11.53	<.0001	0.05	-1.2176	-0.8629
AVISITN*TRTPN	42	2	-0.9935	0.09365	415	-10.61	<.0001	0.05	-1.1776	-0.8095
AVISITN*TRTPN	42	3	-0.7115	0.08826	388	-8.06	<.0001	0.05	-0.8851	-0.5380

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	380	0.24	0.7878
AVISITN*TRTPN	14	2	381	2.39	0.0931
AVISITN*TRTPN	21	2	374	3.30	0.0379
AVISITN*TRTPN	28	2	370	4.03	0.0186
AVISITN*TRTPN	35	2	372	4.73	0.0094
AVISITN*TRTPN	42	2	372	4.24	0.0150

SOURCE: MMRMOUT; TABLE: stat1cgisa.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.1 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

Class Level Information

Class	Levels	Values
TRTPN	3	1 2 3
POOLCNTR	39	[redacted]

Number of Observations Read 421
Number of Observations Used 421

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	41	75.2669725	1.8357798	1.97	0.0006
Error	379	352.9087994	0.9311578		
Corrected Total	420	428.1757720			

R-Square	Coeff Var	Root MSE	CHG Mean
0.175785	-118.7866	0.964965	-0.812352

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	6.97064551	3.48532275	3.74	0.0246
POOLCNTR	38	46.93646590	1.23517016	1.33	0.0997
BASE	1	17.18753428	17.18753428	18.46	<.0001

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-0.92142857	1.10634441	4.55714286	0.56608498
2	140	-0.89285714	0.97225118	4.65714286	0.54668956
3	141	-0.62411348	0.92225660	4.52482270	0.55525490

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.99635472	0.08963644	<.0001	1
2	-0.93139660	0.09048002	<.0001	2
3	-0.69523223	0.08917989	<.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		0.5780	0.0096
2	0.5780		0.0437
3	0.0096	0.0437	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-0.996355	-1.172602	-0.820108
2	-0.931397	-1.109302	-0.753491

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.695232	-0.870582	-0.519883

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.064958	-0.294343	0.164427
1	3	-0.301122	-0.528624	-0.073621
2	3	-0.236164	-0.465593	-0.006735

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

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.30112249	0.11570382	-2.60	0.0096
2 vs 3	-0.23616436	0.11668402	-2.02	0.0437

SOURCE: GLMOUT; TABLE: stat1cgisb.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	421
Number of Observations Used	421

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	28.3305066	9.4435022	9.85	<.0001
Error	417	399.8452653	0.9588615		
Corrected Total	420	428.1757720			

R-Square	Coeff Var	Root MSE	CHG Mean
0.066166	-120.5408	0.979215	-0.812352

Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRTPN	2	6.17656237	3.08828118	3.22	0.0409
BASE	1	20.76132028	20.76132028	21.65	<.0001

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	140	-0.92142857	1.10634441	4.55714286	0.56608498
2	140	-0.89285714	0.97225118	4.65714286	0.54668956
3	141	-0.62411348	0.92225660	4.52482270	0.55525490

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.93041807	0.08278130	<.0001	1
2	-0.86176789	0.08302801	<.0001	2
3	-0.64605649	0.08259948	<.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		0.5589	0.0154
2	0.5589		0.0668
3	0.0154	0.0668	

TRTPN	CHG LSMEAN	95% Confidence Limits	
1	-0.930418	-1.093139	-0.767697
2	-0.861768	-1.024973	-0.698562

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.646056	-0.808420	-0.483693

Least Squares Means for Effect TRTPN

i	j	Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.068650	-0.299331	0.162031
1	3	-0.284362	-0.514078	-0.054646
2	3	-0.215711	-0.446452	0.015030

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

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	-0.28436158	0.11686401	-2.43	0.0154
2 vs 3	-0.21571140	0.11738543	-1.84	0.0668

SOURCE: GLMOUT; TABLE: stat1cgisc.lis; RUN: 31AUG2020 08:32; ANALYSIS DATASET CREATED: 16JUN2020 08:14
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/STAT/Program.dev/DOC_STAT/stat1.sas
OPDC, NEW DRUG APPLICATION, IND # 119,361 CENTANAFADINE STAT-5.3 FINAL

CENTANAFADINE 1 OF 1
PROTOCOL 405-201-00014

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
40520100014	DAY 7	RESID	Shapiro-Wilk	0.9618	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9619	<0.0001
	DAY 14	RESID	Shapiro-Wilk	0.9742	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9729	<0.0001
	DAY 21	RESID	Shapiro-Wilk	0.9755	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9754	<0.0001
	DAY 28	RESID	Shapiro-Wilk	0.9780	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9785	<0.0001
	DAY 35	RESID	Shapiro-Wilk	0.9772	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9776	<0.0001
	DAY 42	RESID	Shapiro-Wilk	0.9767	<0.0001
		STUDENTRESID	Shapiro-Wilk	0.9772	<0.0001

FILE: normality_ba.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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	415	Sum Weights	415
Mean	0.00590733	Sum Observations	2.45154156
Std Deviation	6.29621838	Variance	39.6423659
Skewness	-0.7622497	Kurtosis	1.20879183
Uncorrected SS	16411.9539	Corrected SS	16411.9395
Coeff Variation	106583.167	Std Error Mean	0.3090692

Basic Statistical Measures

Location		Variability	
Mean	0.005907	Std Deviation	6.29622
Median	0.890327	Variance	39.64237
Mode	2.147650	Range	41.51301
		Interquartile Range	6.74509

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=7 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.019113	Pr > |t|	0.9848
Sign	M	31.5	Pr >= |M|	0.0023
Signed Rank	S	4203	Pr >= |S|	0.0856

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.961785	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.084284	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.900816	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	5.031644	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	17.902786
99%	11.786668
95%	8.673196
90%	6.633776
75% Q3	3.932496
50% Median	0.890327
25% Q1	-2.812590
10%	-8.383850
5%	-12.326090
1%	-17.376429
0% Min	-23.610226

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
-23.6102	40520100014-[redacted]	253	11.7867	40520100014-[redacted]	24
-23.5381	40520100014-[redacted]	267	12.5707	40520100014-[redacted]	44
-20.6914	40520100014-[redacted]	395	14.6909	40520100014-[redacted]	36
-18.3791	40520100014-[redacted]	48	15.9070	40520100014-[redacted]	281
-17.3764	40520100014-[redacted]	381	17.9028	40520100014-[redacted]	186

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	415	Sum Weights	415
Mean	0.00076876	Sum Observations	0.31903492
Std Deviation	1.01663979	Variance	1.03355646
Skewness	-0.7470648	Kurtosis	1.26177724
Uncorrected SS	427.892621	Corrected SS	427.892376
Coeff Variation	132244.305	Std Error Mean	0.04990488

Basic Statistical Measures

Location		Variability	
Mean	0.000769	Std Deviation	1.01664
Median	0.138127	Variance	1.03356
Mode	0.330816	Range	6.97281
		Interquartile Range	1.04756

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=7 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.015404	Pr > |t|	0.9877
Sign	M	31.5	Pr >= |M|	0.0023
Signed Rank	S	4190	Pr >= |S|	0.0866

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.961929	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.086473	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.912147	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	5.104489	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	3.049245
99%	1.938606
95%	1.444558
90%	1.079590
75% Q3	0.613816
50% Median	0.138127
25% Q1	-0.433740
10%	-1.322380
5%	-2.093381
1%	-2.777724
0% Min	-3.923569

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
-3.92357	40520100014-[redacted]	267	1.93861	40520100014-[redacted]	328
-3.74529	40520100014-[redacted]	253	2.19553	40520100014-[redacted]	24
-3.23957	40520100014-[redacted]	395	2.26410	40520100014-[redacted]	36
-2.83208	40520100014-[redacted]	48	2.64914	40520100014-[redacted]	281
-2.77772	40520100014-[redacted]	414	3.04925	40520100014-[redacted]	186

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	389	Sum Weights	389
Mean	-0.0478972	Sum Observations	-18.632024
Std Deviation	8.10987026	Variance	65.7699957
Skewness	-0.6462853	Kurtosis	0.96373179
Uncorrected SS	25519.6508	Corrected SS	25518.7583
Coeff Variation	-16931.814	Std Error Mean	0.41118674

Basic Statistical Measures

Location		Variability	
Mean	-0.04790	Std Deviation	8.10987
Median	1.17581	Variance	65.77000
Mode	5.07029	Range	55.06309
		Interquartile Range	10.14964

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=14 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.11649	Pr > |t|	0.9073
Sign	M	25.5	Pr >= |M|	0.0111
Signed Rank	S	2399.5	Pr >= |S|	0.2801

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.974232	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.075075	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.543451	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.960271	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	22.23178
99%	16.59354
95%	11.12111
90%	9.36192
75% Q3	5.23846
50% Median	1.17581
25% Q1	-4.91118
10%	-10.67147
5%	-15.17154
1%	-23.34365
0% Min	-32.83131

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
-32.8313	40520100014-[redacted]	437	16.5927	40520100014-[redacted]	451
-29.4798	40520100014-[redacted]	665	16.5935	40520100014-[redacted]	459
-25.1439	40520100014-[redacted]	796	17.5325	40520100014-[redacted]	470
-23.3436	40520100014-[redacted]	651	17.8254	40520100014-[redacted]	589
-22.7128	40520100014-[redacted]	482	22.2318	40520100014-[redacted]	678

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	389	Sum Weights	389
Mean	-0.0058977	Sum Observations	-2.2942086
Std Deviation	1.00702053	Variance	1.01409034
Skewness	-0.6687682	Kurtosis	1.22213191
Uncorrected SS	393.480582	Corrected SS	393.467052
Coeff Variation	-17074.776	Std Error Mean	0.05105797

Basic Statistical Measures

Location		Variability	
Mean	-0.00590	Std Deviation	1.00702
Median	0.14300	Variance	1.01409
Mode	0.61175	Range	7.23960
		Interquartile Range	1.23899

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=14 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	-0.11551	Pr > |t|	0.9081
Sign	M	25.5	Pr >= |M|	0.0111
Signed Rank	S	2371.5	Pr >= |S|	0.2858

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.972919	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.075857	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.550481	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.96986	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	2.814987
99%	2.126709
95%	1.349592
90%	1.156538
75% Q3	0.635037
50% Median	0.142997
25% Q1	-0.603950
10%	-1.376566
5%	-1.830571
1%	-2.869759
0% Min	-4.424614

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
-4.42461	40520100014-[redacted]	437	2.00259	40520100014-[redacted]	459
-3.72916	40520100014-[redacted]	665	2.12671	40520100014-[redacted]	470
-3.07149	40520100014-[redacted]	796	2.13944	40520100014-[redacted]	558
-2.86976	40520100014-[redacted]	482	2.28195	40520100014-[redacted]	589
-2.86776	40520100014-[redacted]	651	2.81499	40520100014-[redacted]	678

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	375	Sum Weights	375
Mean	0.04424235	Sum Observations	16.5908809
Std Deviation	8.77628273	Variance	77.0231386
Skewness	-0.5795826	Kurtosis	0.26916873
Uncorrected SS	28807.3879	Corrected SS	28806.6538
Coeff Variation	19836.8372	Std Error Mean	0.45320529

Basic Statistical Measures

Location		Variability	
Mean	0.04424	Std Deviation	8.77628
Median	0.97708	Variance	77.02314
Mode	-4.26252	Range	53.44257
		Interquartile Range	12.23517

Note: The mode displayed is the smallest of 3 modes with a count of 2.

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.097621	Pr > |t|	0.9223
Sign	M	14.5	Pr >= |M|	0.1481
Signed Rank	S	2381	Pr >= |S|	0.2575

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.975477	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.067214	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.379476	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.479975	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	23.818333
99%	15.303207
95%	12.320121
90%	10.028486
75% Q3	6.741001
50% Median	0.977085
25% Q1	-5.494165
10%	-11.975058
5%	-16.506856
1%	-25.986745
0% Min	-29.624234

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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
-29.6242	40520100014-[redacted]	1043	14.0883	40520100014-[redacted]	1081
-26.7808	40520100014-[redacted]	966	15.3032	40520100014-[redacted]	921
-26.7543	40520100014-[redacted]	825	17.2591	40520100014-[redacted]	1076
-25.9867	40520100014-[redacted]	848	20.5261	40520100014-[redacted]	1056
-23.7829	40520100014-[redacted]	832	23.8183	40520100014-[redacted]	856

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	375	Sum Weights	375
Mean	0.00487939	Sum Observations	1.82977148
Std Deviation	1.00562938	Variance	1.01129045
Skewness	-0.5952846	Kurtosis	0.35653957
Uncorrected SS	378.231556	Corrected SS	378.222628
Coeff Variation	20609.7331	Std Error Mean	0.05193048

Basic Statistical Measures

Location		Variability	
Mean	0.00488	Std Deviation	1.00563
Median	0.11437	Variance	1.01129
Mode	-0.47879	Range	6.14534
		Interquartile Range	1.39912

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	0.09396	Pr > |t|	0.9252
Sign	M	14.5	Pr >= |M|	0.1481
Signed Rank	S	2414	Pr >= |S|	0.2510

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.97535	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.067951	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.375553	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.435138	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	2.685261
99%	1.737520
95%	1.409697
90%	1.150881
75% Q3	0.773889
50% Median	0.114367
25% Q1	-0.625233
10%	-1.363214
5%	-1.907909
1%	-2.928031
0% Min	-3.460083

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
-3.46008	40520100014-[redacted]	1043	1.72616	40520100014-[redacted]	914
-3.30052	40520100014-[redacted]	825	1.73752	40520100014-[redacted]	921
-3.15665	40520100014-[redacted]	966	1.93699	40520100014-[redacted]	1076
-2.92803	40520100014-[redacted]	848	2.39535	40520100014-[redacted]	1056
-2.67885	40520100014-[redacted]	868	2.68526	40520100014-[redacted]	856

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	366	Sum Weights	366
Mean	0.10619435	Sum Observations	38.8671306
Std Deviation	9.24929929	Variance	85.5495374
Skewness	-0.504134	Kurtosis	-0.0661248
Uncorrected SS	31229.7086	Corrected SS	31225.5812
Coeff Variation	8709.78509	Std Error Mean	0.48346862

Basic Statistical Measures

Location		Variability	
Mean	0.106194	Std Deviation	9.24930
Median	1.270199	Variance	85.54954
Mode	6.917760	Range	50.29097
		Interquartile Range	12.74462

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.219651	Pr > |t|	0.8263
Sign	M	24	Pr >= |M|	0.0139
Signed Rank	S	2320.5	Pr >= |S|	0.2525

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.977981	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.069596	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.475034	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.720452	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	23.67290
99%	17.88792
95%	13.05207
90%	10.51949
75% Q3	7.10617
50% Median	1.27020
25% Q1	-5.63845
10%	-12.94030
5%	-16.83098
1%	-24.63841
0% Min	-26.61808

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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
-26.6181	40520100014-[redacted]	1408	17.6443	40520100014-[redacted]	1440
-26.2893	40520100014-[redacted]	1199	17.8879	40520100014-[redacted]	1350
-24.9814	40520100014-[redacted]	1242	18.4836	40520100014-[redacted]	1213
-24.6384	40520100014-[redacted]	1245	20.7367	40520100014-[redacted]	1421
-24.6213	40520100014-[redacted]	1334	23.6729	40520100014-[redacted]	1336

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	366	Sum Weights	366
Mean	0.010984	Sum Observations	4.02014573
Std Deviation	1.00683954	Variance	1.01372586
Skewness	-0.5138819	Kurtosis	0.01054228
Uncorrected SS	370.054095	Corrected SS	370.009937
Coeff Variation	9166.41575	Std Error Mean	0.05262835

Basic Statistical Measures

Location		Variability	
Mean	0.010984	Std Deviation	1.00684
Median	0.140686	Variance	1.01373
Mode	0.737348	Range	5.69482
		Interquartile Range	1.37277

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.208709	Pr > |t|	0.8348
Sign	M	24	Pr >= |M|	0.0139
Signed Rank	S	2326.5	Pr >= |S|	0.2513

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.978466	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.069808	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.472312	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.687998	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	2.640998
99%	1.970411
95%	1.401831
90%	1.157699
75% Q3	0.763652
50% Median	0.140686
25% Q1	-0.609115
10%	-1.386098
5%	-1.825071
1%	-2.744377
0% Min	-3.053825

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
-3.05383	40520100014-[redacted]	1199	1.88200	40520100014-[redacted]	1440
-2.94301	40520100014-[redacted]	1408	1.97041	40520100014-[redacted]	1213
-2.77174	40520100014-[redacted]	1242	2.02350	40520100014-[redacted]	1350
-2.74438	40520100014-[redacted]	1334	2.29077	40520100014-[redacted]	1421
-2.64333	40520100014-[redacted]	1245	2.64100	40520100014-[redacted]	1336

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	344	Sum Weights	344
Mean	0.22073119	Sum Observations	75.9315287
Std Deviation	9.61866843	Variance	92.5187824
Skewness	-0.4952975	Kurtosis	-0.1237985
Uncorrected SS	31750.7028	Corrected SS	31733.9424
Coeff Variation	4357.63905	Std Error Mean	0.51860385

Basic Statistical Measures

Location		Variability	
Mean	0.220731	Std Deviation	9.61867
Median	1.701746	Variance	92.51878
Mode	7.432365	Range	54.67437
		Interquartile Range	14.33341

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=35 ----------

The UNIVARIATE Procedure
Variable: RESID (Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.425626	Pr > |t|	0.6706
Sign	M	16	Pr >= |M|	0.0945
Signed Rank	S	2217	Pr >= |S|	0.2302

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.977242	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.067652	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.438875	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.629038	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	22.53512
99%	18.03788
95%	13.41618
90%	11.23166
75% Q3	7.76020
50% Median	1.70175
25% Q1	-6.57321
10%	-13.76659
5%	-16.80512
1%	-23.07843
0% Min	-32.13925

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
-32.1393	40520100014-[redacted]	1562	17.1124	40520100014-[redacted]	1590
-28.7832	40520100014-[redacted]	1691	18.0379	40520100014-[redacted]	1575
-24.7266	40520100014-[redacted]	1606	21.5556	40520100014-[redacted]	1707
-23.0784	40520100014-[redacted]	1569	22.1875	40520100014-[redacted]	1693
-21.5722	40520100014-[redacted]	1663	22.5351	40520100014-[redacted]	1775

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	344	Sum Weights	344
Mean	0.02322776	Sum Observations	7.99034796
Std Deviation	1.00148516	Variance	1.00297252
Skewness	-0.5068561	Kurtosis	-0.0234398
Uncorrected SS	344.205173	Corrected SS	344.019575
Coeff Variation	4311.58814	Std Error Mean	0.05399646

Basic Statistical Measures

Location		Variability	
Mean	0.023228	Std Deviation	1.00149
Median	0.176296	Variance	1.00297
Mode	0.759057	Range	5.93096
		Interquartile Range	1.49444

FILE: normalitybc.lis, RUN: 31AUG2020 08:32
PROGRAM: /opt/sas/Data/DAP/EB1020/P40520100014/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)=35 ----------

The UNIVARIATE Procedure
Variable: STUDENTRESID (Studentized Residual)

Tests for Location: Mu0=0

Test	-Statistic-		-----p Value------	
Student's t	t	0.430172	Pr > |t|	0.6673
Sign	M	16	Pr >= |M|	0.0945
Signed Rank	S	2252	Pr >= |S|	0.2230

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.977591	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.069272	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.428574	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.550366	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	2.378000
99%	1.842423
95%	1.414009
90%	1.195080
75% Q3	0.813832
50% Median	0.176296
25% Q1	-0.680604
10%	-1.427671
5%	-1.744891
1%	-2.358551
0% Min	-3.552963

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
-3.55296	40520100014-[redacted]	1562	1.74930	40520100014-[redacted]	1590
-3.06229	40520100014-[redacted]	1691	1.84242	40520100014-[redacted]	1575
-2.54111	40520100014-[redacted]	1606	2.22747	40520100014-[redacted]	1707
-2.35855	40520100014-[redacted]	1569	2.36251	40520100014-[redacted]	1693
-2.26636	40520100014-[redacted]	1663	2.37800	40520100014-[redacted]	1775

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	338	Sum Weights	338
Mean	0.21994106	Sum Observations	74.3400787
Std Deviation	10.206485	Variance	104.172337
Skewness	-0.4662637	Kurtosis	-0.2816581
Uncorrected SS	35122.428	Corrected SS	35106.0776
Coeff Variation	4640.5546	Std Error Mean	0.5551596

Basic Statistical Measures

Location		Variability	
Mean	0.219941	Std Deviation	10.20649
Median	2.116541	Variance	104.17234
Mode	7.859023	Range	51.41794
		Interquartile Range	14.95136

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	0.396176	Pr > |t|	0.6922
Sign	M	21	Pr >= |M|	0.0256
Signed Rank	S	1936.5	Pr >= |S|	0.2821

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.976668	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.076295	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.500683	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.723085	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	21.91943
99%	20.45404
95%	14.85949
90%	12.11174
75% Q3	7.82680
50% Median	2.11654
25% Q1	-7.12456
10%	-14.10923
5%	-18.33244
1%	-27.07807
0% Min	-29.49851

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
-29.4985	40520100014-[redacted]	2031	19.4617	40520100014-[redacted]	2128
-27.6116	40520100014-[redacted]	1928	20.4540	40520100014-[redacted]	1934
-27.3096	40520100014-[redacted]	2099	20.7976	40520100014-[redacted]	2111
-27.0781	40520100014-[redacted]	1950	21.6142	40520100014-[redacted]	2033
-25.9557	40520100014-[redacted]	2054	21.9194	40520100014-[redacted]	2046

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	338	Sum Weights	338
Mean	0.02186339	Sum Observations	7.38982701
Std Deviation	1.00255899	Variance	1.00512453
Skewness	-0.4654092	Kurtosis	-0.2701205
Uncorrected SS	338.888534	Corrected SS	338.726967
Coeff Variation	4585.55983	Std Error Mean	0.05453202

Basic Statistical Measures

Location		Variability	
Mean	0.021863	Std Deviation	1.00256
Median	0.204955	Variance	1.00512
Mode	0.760366	Range	5.13076
		Interquartile Range	1.45333

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	0.400928	Pr > |t|	0.6887
Sign	M	21	Pr >= |M|	0.0256
Signed Rank	S	1930.5	Pr >= |S|	0.2836

Tests for Normality

Test	--Statistic---		-----p Value------	
Shapiro-Wilk	W	0.977218	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.075766	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.494181	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	2.68251	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	2.170595
99%	1.980822
95%	1.444907
90%	1.182725
75% Q3	0.762961
50% Median	0.204955
25% Q1	-0.690365
10%	-1.369158
5%	-1.794783
1%	-2.635345
0% Min	-2.960170

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
-2.96017	40520100014-[redacted]	2031	1.88413	40520100014-[redacted]	2128
-2.72302	40520100014-[redacted]	2099	1.98082	40520100014-[redacted]	1934
-2.68489	40520100014-[redacted]	1928	2.07185	40520100014-[redacted]	2111
-2.63534	40520100014-[redacted]	1950	2.14336	40520100014-[redacted]	2046
-2.54132	40520100014-[redacted]	2054	2.17059	40520100014-[redacted]	2033

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SIGNATURE PAGE

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Document Version: 3.0

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[redacted]	Safety Approval	22-Sep-2020 14:15:24
[redacted]	Biostatistics Approval	22-Sep-2020 00:48:53
[redacted]	Clinical Programming Approval	22-Sep-2020 16:17:04
[redacted]	Clinical Approval	23-Sep-2020 00:10:52