Statistical Analysis Plan for Study M22-418

A Phase 3 Multicenter 24-Week Open-Label Study to Evaluate the Safety, Tolerability, and Efficacy of Atogepant When Added to OnabotulinumtoxinA (BOTOX) for the Preventive Treatment of Chronic Migraine

Version 2.0

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1.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical analyses for atogepant Study M22-418, A Phase 3, Multicenter, 24-Week, Open-Label Study to Evaluate the Safety, Tolerability, and Efficacy of Atogepant When Added to OnabotulinumtoxinA (BOTOX) for the Preventive Treatment of Chronic Migraine (CM).

The SAP will not be updated in case of administrative changes or amendments to the protocol unless the changes impact the analyses.

Unless noted otherwise, all analyses will be performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC 27513) or later.

2.0 Study Objectives and Design

2.1 Study Objectives

To evaluate the safety and tolerability of atogepant when added to BOTOX over 24 weeks in participants with CM.

To prospectively evaluate the responder rates and change from baseline in monthly migraine days when atogepant is added to BOTOX monotherapy in participants with CM.

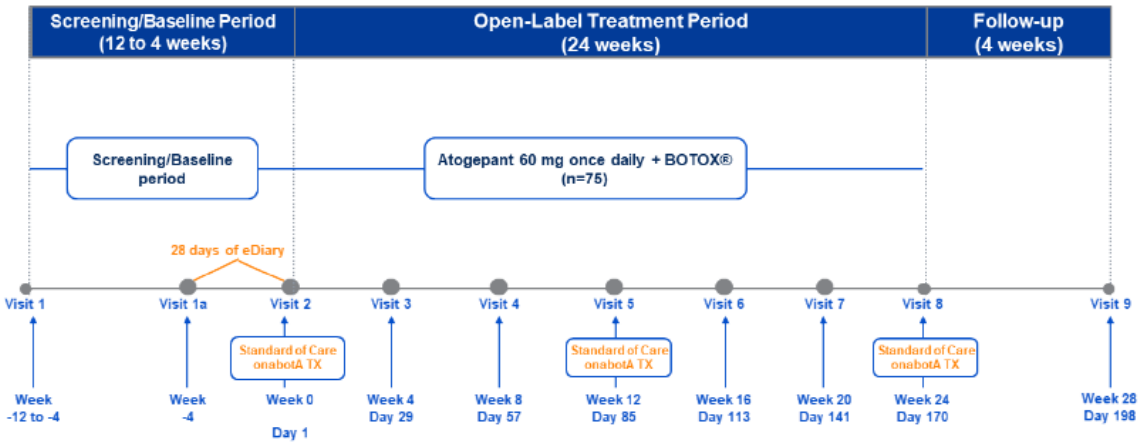
2.2 Study Design Overview

This is a 24-week, Phase 3, open-label, multicenter study to evaluate the safety and tolerability and explore efficacy of atogepant when added to BOTOX in participants with CM. This study will enroll approximately 75 participants from approximately 30 sites in the United States. Participants will receive once-daily atogepant 60 mg from Day 1 to Week 24, along with their concomitant, standard of care BOTOX. Concomitant BOTOX must be administered on Visits 2, 5, and 8.

The screening/baseline period is up to 12 weeks, which will include at least 28 days of eDiary collection of migraine days and headache days at the end of the screening/baseline period. The treatment period will include 7 scheduled clinic visits: Visit 1/Visit 1a

(Screening/Baseline), Visit 2 (Day 1), Visit 3 (Week 4), Visit 4 (Week 8), Visit 5 (Week 12), Visit 6 (Week 16), Visit 7 (Week 20), and Visit 8/Premature Discontinuation (Week 24). There will be a safety follow-up period of 4 weeks that includes 1 remote visit at Visit 9 (Week 28 or 4 weeks post-atogepant treatment for premature discontinuation). The Visit 9 (Follow-up) must be completed for all participants who take at least one dose of study intervention. The schematic of the study is shown in Figure 1.

Figure 1. Study Schematic



Note: Visits 1 and 1a may be on the same day based on timing of the previous and next BOTOX administrations. Visit 1a should occur approximately 28 days prior to the next scheduled BOTOX administration. Screening assessments should be performed at the study visits specified in Protocol Appendix D.

2.3 Treatment Assignment and Blinding

Approximately 75 participants will receive once-daily atogepant 60 mg from Day 1 to Week 24, along with their concomitant BOTOX (155 to 200 units, targeting approximately 50% of participants receiving 155 units). Concomitant BOTOX must be administered on Visits 2, 5, and 8.

2.4 Sample Size Determination

The study was powered empirically to include approximately 75 participants, as 60 participants with 6 months of exposure are required by payers to support the safety of the atogepant\BOTOX combination. An estimated early termination rate of 20% will allow for 60 participants to complete the 6-month study. 75 participants provide 95% probability to detect at least 1 occurrence of an adverse event (AE) with an incidence of ≥ 4%. The precision (half width of 95% confidence interval) of the estimate of change from baseline in mean monthly migraine days will be approximately 1.8 assuming an SD of 7.0 with an effective sample size of 60 participants.

3.0 Endpoints

3.1 Primary Endpoints

The primary objective of the study is to assess the safety endpoints (see Section 3.3).

3.2 Efficacy Endpoints

All efficacy endpoints are exploratory. The definitions of the efficacy measures based on the eDiary data can be found in Appendix B.

- Achievement of ≥ 25%, ≥ 30%, ≥ 50%, ≥ 75%, and 100% reduction in mean monthly migraine days across Weeks 1 to 12, Weeks 13 to 24, and at each 4-week interval
- Change from baseline in monthly migraine days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly headache days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly moderate or severe headache days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly cumulative hours of headache across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period

- Change from baseline in monthly acute medication use days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly headache free days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly complete migraine symptom-free days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly cardinal migraine symptom-free days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Achievement of ≥ 25%, ≥ 30%, ≥ 50%, ≥ 75%, and 100% reduction in mean monthly complete migraine symptom-free days across Weeks 1 to 12, Weeks 13 to 24, and at each 4-week interval
- Achievement of ≥ 25%, ≥ 30%, ≥ 50%, ≥ 75%, and 100% reduction in mean monthly cardinal migraine symptom-free days across Weeks 1 to 12, Weeks 13 to 24, and at each 4-week interval
- Change from baseline in monthly days with an individual non-headache symptom for each of the 5 most common non-headache symptoms (including difficulty with concentration and thinking clearly collected from AIM-D items 10 and 11) and cardinal individual non-headache symptoms across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period
- Change from baseline in monthly Performance of Daily Activities domain score of the AIM-D at each monthly period
- Change from baseline in monthly Physical Impairment domain score of the AIM-D at each monthly period
- Change from baseline in monthly AIM-D total score at each monthly period
- Change from baseline in monthly AIM-D Item 10 score at each monthly period
- Change from baseline in monthly AIM-D Item 11 score at each monthly period
- Change from baseline in the MSQ v2.1 Role Function-Preventive domain score at Weeks 4, 8, 12, 16, 20 and 24
- Change from baseline in the MSQ v2.1 Role Function-Restrictive domain score at Weeks 4, 8, 12, 16, 20 and 24

- Change from baseline in the MSQ v2.1 Emotional Function domain score at Weeks 4, 8, 12, 16, 20 and 24
- Change from baseline in Patient Health Questionnaire (PHQ-9) total score at Weeks 4, 8, 12, 16, 20 and 24
- Change from baseline in percent work time missed, percent impairment while working, percent overall impairment, and percent activity impairment due to migraine at Weeks 4, 8, 12, 16, 20 and 24 as assessed by the Work Productivity and Activity Impairment Questionnaire: Migraine v2.0 (WPAI: MIGRAINE)
- Participants reporting "satisfied" or "extremely satisfied" with study medication for migraine prevention at Weeks 4, 8, 12, 16, 20 and 24 on the Patient Satisfaction with Study Medication (PSSM)
- Participants assessed by Patient Global Impression of Change (PGIC) as "much better" or "very much better" at Weeks 4, 8, 12, 16, 20 and 24
- Change from baseline in Generalized Anxiety Disorder-7 (GAD-7) total score at Weeks 4, 8, 12, 16, 20 and 24
- Change from baseline in PROMIS v2.0 Cognitive Function Abilities Subset 6a score at Weeks 4, 8, 12, 16, 20 and 24

3.3 Safety Endpoints

Safety evaluation includes AE monitoring, serious adverse event (SAE) monitoring, AEs of special interest (AESI) monitoring, vital sign measurements, Columbia-Suicide Severity Rating Scale (C-SSRS) assessments, clinical laboratory testing (hematology, chemistry, and urinalysis), and electrocardiogram (ECG).

4.0 Analysis Populations

The following population sets will be used for the analyses.

The screened population will consist of all participants who signed informed consent and received a subject number.

The modified intention-to-treat (mITT) population includes all participants who receive at least 1 dose of atogepant study drug, have an evaluable baseline period of eDiary data, and have at least 1 evaluable postbaseline 4-week period (Weeks 1 to 4, 5 to 8, 9 to 12, 13 to 16, 17 to 20, or 21 to 24) of eDiary data during the open-label treatment period. The mITT population will be used for all efficacy analyses.

The safety population consists of all participants who received at least 1 dose of atogepant study drug. The safety population will be used for all safety analyses.

5.0 Participant Disposition

The total number of participants who were screened, screen failed (i.e., subjects who consented to participate in the study but were not enrolled) and treated will be summarized. A summary of participant accountability by investigator will be provided where the number of participants in each of the following categories will be tabulated:

- Participants enrolled in the study;
- Participants who screen failed;
- Participants who took at least one dose of study treatment;
- Participants who completed study treatment;
- Participants who prematurely discontinued study treatment;
- Participants in the mITT population.

The number and percentage of enrolled participants who completed study treatment and study will be summarized respectively.

6.0 Study Treatment Duration and Compliance

Duration of study drug (atogepant) will be summarized for safety population.

Duration of atogepant treatment is defined for each participant as last dose date minus first dose date + 1. Duration of atogepant treatment will be summarized by BOTOX dose group (≤ 155 units or >155 units) and overall for the safety population using the number

of participants treated, mean, standard deviation, median, Q1, Q3, minimum and maximum. In addition, the number and percentage of participants in each treatment duration of ≥ 1 day, ≥ 28 days, ≥ 56 days, ≥ 84 days, ≥ 90 days, ≥ 112 days, ≥ 140 days, and ≥ 168 days will be summarized.

The number and percentage of participants treated in each BOTOX treatment cycle (Visit 2, Visit 5, and Visit 8) will be summarized by BOTOX dose group (≤ 155 units or >155 units categorized at Visit 2) and overall.

Participant-years of atogepant, defined as exposure to the atogepant treatment in years, will be summarized for the safety population.

Treatment compliance for a specific period is defined as the number of atogepant study medications actually taken during that period divided by the number of study medications that should have been taken during the same period. Percent atogepant treatment compliance as well as the associated compliance categories (< 80%, 80% - 120%, > 120%) will be summarized in each period between 2 consecutive visits, as well as in the entire treatment period from the first dose of the open-label atogepant study drug actually taken to the last dose of open label atogepant study drug actually taken for the safety population.

7.0 Participant Characteristics

Categorical variables will be summarized with the number and percentage of participants; percentages will be calculated based on the number of non-missing observations. Continuous variables will be summarized with descriptive statistics (number of non-missing observations, mean and standard deviation, median, Q1, Q3, minimum and maximum).

7.1 Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized for the safety population and mITT population. Disease characteristics will be summarized for the safety population. Unless otherwise specified, baseline is defined as the last non-missing value prior to the first dose of atogepant.

Continuous demographic variables include age, weight, height, and body mass index (BMI).

Categorical demographic variables include:

- Sex
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- Race (White, Black or African American, Asian, American Indian or Alaska Native, and Native Hawaiian or Other Pacific Islander, Multiple)
- Age group (< 20, 20-29, 30-39, 40-49, 50-59, 60-69, ≥ 70 years)
- Age group (< 40 years, 40-64 years, ≥ 65 years)
- Nicotine user (current, former, never, unknown)
- Alcohol user (current, former, never, unknown)
- Actual BOTOX dose received at Visit 2.

Disease characteristics are contained in migraine headache history eCRF, including diagnosis, duration of migraine, duration of chronic migraine, average number of migraine or headache days per month in the last 1 year, duration of BOTOX administration, average number of BOTOX treatment cycles in the last 8 months. Migraine Disorder Duration and Chronic Migraine Disorder Duration will be determined from the earliest diagnosis date recorded as part of the migraine headache history as compared to the date of the subject's screening Visit 1. Duration of Botox Administration for Chronic Migraine will be determined from the date of first Botox administration for Chronic Migraine recorded as part of the migraine headache history as compared to the date of the subject's screening Visit 1.

7.2 Medical History and Prior and Concomitant Medications

Medical history and prior and concomitant medications will be summarized for the safety population.

Medical history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual version of the MedDRA coding dictionary will be noted in the statistical tables and clinical study report. The number and percentage of participants in each medical history category (by MedDRA system organ class (SOC) and preferred term (PT)) will be summarized. The SOC will be presented in alphabetical order, and the PTs will be presented in alphabetical order within each SOC. Participants reporting more than one condition/diagnosis will be counted only once in each row (SOC or PT).

Prior and concomitant medications will be summarized by generic names. Concomitant medication will be summarized for the open-label period and follow-up period. A prior medication is defined as any medication taken prior to the date of the first dose of study drug. A concomitant medication is defined as any medication that started prior to the date of the first dose of study drug and continued to be taken after the first dose of study drug or any medication that started on or after the date of the first dose of study drug, but not after the date of the last dose of study drug plus 30 days or Visit 9 which comes later. The number and percentage of participants taking medications will be summarized by generic drug name based on the World Health Organization (WHO) Drug Dictionary for both prior and concomitant medications. The number and percentage of participants taking prior preventive migraine medications will be summarized by generic name and class, and the number and percentage of participants taking prior acute headache medication will be summarized by generic name.

The dose of concomitant BOTOX medication injected will be summarized totaled across the head/neck injection areas and separately for each head/neck injection area. This will be done for each treatment cycle (Visit 2, Visit 5, and Visit 8) and totaled across injection cycles will be summarized by BOTOX dose groups (≤ 155 units or >155 units). The total

volume of concomitant BOTOX medication injected will be summarized by BOTOX dose groups.

7.3 Protocol Deviations

Protocol deviations include eligibility criteria violations, receipt of wrong treatment or incorrect dose of study treatment, development of withdrawal criteria without being withdrawn, and use of prohibited concomitant medications. A listing of participants with protocol deviations will be provided.

For each of the following protocol deviation categories and across all categories, the number and percentage of enrolled participants with at least one protocol deviation will be summarized:

- Participants entered into the study even though did not satisfy entry criteria;
- Participants developed withdrawal criteria during the study but was not withdrawn;
- Participants received wrong treatment or incorrect dose of study treatment;
- Participants took prohibited concomitant medication.

8.0 Handling of Potential Intercurrent Events for the Primary and Key Secondary Endpoints

The efficacy endpoints are exploratory, so no handling of intercurrent events for efficacy endpoints will be provided.

9.0 Efficacy Analyses

9.1 General Considerations

All analyses on efficacy variables will be performed in the mITT population, unless stated otherwise. For monthly endpoints, baseline is defined as assessments during the last 28 days of baseline period. For efficacy endpoints that are assessed at clinical visits,

baseline is defined as the last non-missing efficacy assessment before the first dose of atogepant.

9.2 Handling of Missing Data

Descriptive statistics for efficacy endpoints will be based on observed cases (OC) only. Missing data will be handled using mixed model for repeated measures (MMRM) without imputation for the efficacy analysis for continuous endpoints unless specified otherwise.

9.3 Efficacy Endpoints and Analyses

9.3.1 Efficacy Endpoints

The exploratory efficacy endpoints are listed in Section 3.2.

9.3.2 Main Analysis of Efficacy Endpoints

The migraine day responder status is defined as participants with at least 25%, 30%, 50%, 75%, and 100% reduction compared to baseline in mean monthly migraine days across Weeks 1 to 12, Weeks 13 to 24, and at each monthly period. They will be summarized using descriptive statistics. Achievement of ≥ 25%, ≥ 30%, ≥ 50%, ≥ 75%, and 100% reduction in mean monthly complete migraine symptom-free days and cardinal migraine symptom-free days will be analyzed in a similar way as migraine day responder status.

For endpoints collected from eDiary, change from baseline in monthly migraine days, headache days, moderate or severe headache days, cumulative hours of headache, acute medication use days, headache free days, complete migraine symptom-free days, cardinal migraine symptom-free days, days with individual non-headache symptom for each of the 5 most common and cardinal individual non-headache symptoms, Performance of Daily Activities domain score of the AIM-D, Physical Impairment domain score of the AIM-D, AIM-D total score, AIM-D Item 10 score, and AIM-D Item 11 score at each monthly period, they will be analyzed using a mixed-effect model for repeated measures (MMRM), including visit as a categorical fixed effect, and the baseline score, baseline-by-visit interaction as covariates. An unstructured covariance matrix will be used

to model the covariance of within-participant repeated measurements. The Kenward-Roger approximation[1] will be used to estimate the denominator degrees of freedom. The analysis will be performed based on all postbaseline monthly values using only the observed cases without imputation of missing values. The treatment effect across Weeks 1 to 12, Weeks 13-24 and at each monthly will be estimated by the least square (LS) Means, along with their SE and 95% confidence intervals, and the p-value.

For health outcome measures with a continuous response range change from baseline in the MSQ v2.1 Role Function-Preventive domain score, Role Function-Restrictive domain score and Emotional Function domain score, PHQ-9 total score, the percent work time missed, percent impairment while working, percent overall impairment, and percent activity impairment due to migraine as assessed by WPAI:MIGRAINE, GAD-7 total score, PROMIS v 2.0 Cognitive Function Abilities Subset 6a score at Weeks 4, 8, 12, 16, 20 and 24, they will be analyzed in a similar way as the above MMRM. The proportions of participants reporting "satisfied" or "extremely satisfied" and the proportions of participants with PGIC of "much better" or "very much better" at Weeks 4, 8, 12, 16, 20 and 24 will be summarized using descriptive statistics by visit.

10.0 Safety Analyses

10.1 General Considerations

Safety data will be summarized for the safety population. The safety parameters will include AEs, clinical laboratory tests (hematology, chemistry, and urinalysis), ECGs, vital signs, and the C-SSRS. For each safety parameter, the last non-missing safety assessment before the first dose of atogepant will be used as the baseline for all analyses of that safety parameter. Continuous variables will be summarized by number of participants and mean, SD, median, Q1, Q3, minimum, and maximum values. Categorical variables will be summarized by number and percentage of participants.

10.2 Adverse Events

Adverse events will be summarized and presented using primary MedDRA SOCs and PTs according to the version of the MedDRA coding dictionary used for the study at the time of database lock. The actual version of the MedDRA coding dictionary used will be noted in the AE tables and in the clinical study report. Specific adverse events will be counted once for each participant for calculating percentages, unless stated otherwise. In addition, if the same adverse event occurs multiple times within a participant, the highest severity and level of relationship to investigational product will be reported.

10.2.1 Treatment-Emergent Adverse Events

Treatment-emergent AEs (TEAEs) are defined as any AE with the onset that is after the first dose of study drug. Events when the onset date is the same as the study drug start date are assumed to be treatment-emergent. An AE that occurs more than 30 days after the last dose of open-label study treatment will not be counted as a TEAE. All TEAE will be summarized overall, as well as by primary MedDRA SOC and PT. The SOCs will be presented in alphabetical order, and the PTs will be presented in alphabetical order within each SOC.

The number and percentage of participants experiencing TEAEs will be summarized.

An AE will be considered a treatment-emergent serious AE (TESAE) if it is a TEAE that additionally meets any SAE criterion.

TEAEs that started after the date of last dose of study treatment will be considered as newly emergent.

10.2.2 Adverse Event Overview

An overview of AEs will be presented consisting of the number and percentage of participants experiencing at least one event for each of the following AE categories:

- Any TEAE

- Any TEAE related to study treatment according to the investigator
- Any severe TEAE
- Any TESAE
- Any TEAE leading to discontinuation of study treatment
- Any TEAE leading to death
- All deaths

10.2.3 Treatment-Emergent Adverse Events by SOC and/or PT

Treatment-emergent adverse events will be summarized by SOC and PT; by maximum relationship to study treatment as assessed by the investigator (e.g., reasonable possibility or no reasonable possibility) and SOC and PT; by maximum severity and SOC and PT; and by participant number and SOC and PT. Specific adverse events will be counted once for each participant for calculating percentages, unless stated otherwise. In addition, if the same adverse event occurs multiple times within a participant, the highest severity and level of relationship to investigational product will be reported.

The number and percentage of participants reporting newly emergent TEAEs will be summarized by system organ class and preferred term.

The incidence of common (≥ 2% of participants) TEAEs will be summarized by preferred term and sorted by decreasing frequency.

10.2.4 Deaths, Serious Adverse Events, and Adverse Events Leading to Study Treatment Discontinuation

Treatment-emergent serious adverse events and TEAEs leading to premature discontinuation of study treatment will be summarized by SOC and PT.

Tabular listings will be provided for all deaths, all SAEs, TESAEs, TEAEs leading to death, and TEAEs leading to premature discontinuation of study treatment.

10.2.5 Adverse Events of Special Interest

An adverse event of special interest (serious or nonserious) is one of scientific and medical concern specific to the sponsor's study intervention or program, which warrants ongoing monitoring and rapid communication by the investigator to the sponsor. Such an event might warrant further investigation in order to characterize and understand it.

Adverse Events of Special Interest (AESI) are defined in Appendix C.

The summaries of above are described in the corresponding SAP Section 10.3.

10.3 Analysis of Laboratory Data

Data collected from central laboratories, including additional laboratory testing due to an SAE, will be used in all analyses, except for Baseline where SAE-related laboratory assessments on or before the first dose of study drug will be excluded. The clinical laboratory tests defined in the protocol operations manual (e.g., hematology, clinical chemistry, and urinalysis) will be summarized.

Each laboratory variable will be summarized for all time points (starting with Baseline) with the number of non-missing observations, mean and standard deviation, median, Q1, Q3, minimum and maximum. Mean change from baseline to each applicable post-baseline visit will be summarized, with the number of observations, baseline mean, and visit mean. The change from baseline mean will be presented for the mean change from baseline. In addition, descriptive statistics for values and changes from the baseline values in conventional units at each assessment time point will be presented for selected clinical laboratory parameters listed in Appendix E. A description of reporting the lab values in conventional units in patient narratives (along with the standard reporting in SI units) is presented at the end of Appendix E.

Changes in laboratory parameters will be tabulated using shift tables categorized as low, normal, or high based on the normal ranges of the laboratory used for each sample. A shift table will be provided to summarize shifts from baseline to the final post-baseline value.

Laboratory abnormalities will be evaluated based on Potentially Clinically Significant (PCS) criteria (Appendix Table D-1). For each laboratory PCS criterion, the number and percentage of participants who have a laboratory value meeting the criteria will be summarized. Listings will be provided to summarize participant-level laboratory data for participants meeting PCS criteria.

In addition, ALT, AST, alkaline phosphatase, and total bilirubin will be categorized in Table D-2. The number and percentage of participants meeting each of the criteria for postbaseline hepatic laboratory abnormalities listed in Table D-2 will be summarized. The percentages will be calculated relative to the number of participants with at least 1 available postbaseline assessment. The numerator will be the total number of participants having at least 1 postbaseline value that meets the specific category during the study. A supportive listing will also be provided.

The number and percentage of participants with an adjudicated case (i.e., ALT $\geq 3 \times$ ULN and/or AST $\geq 3 \times$ ULN) will be summarized by relationship of ALT or AST elevation to study medication. The percentages will be calculated relative to the number of participants with at least 1 adjudicated case. The numerator will be the number of participants with at least 1 adjudicated case in the specific category of relationship. If a participant has more than 1 adjudicated case, he or she will be counted in the most relevant category of relationship.

Participants with an adjudicated case (i.e., ALT $\geq 3 \times$ ULN or AST $\geq 3 \times$ ULN) will be listed with their ALT and AST assessments, adjudication dates, relationship of ALT or AST elevation to study medication, and confounding factor(s). Additional listings will be provided for participants who meet ALT $\geq 3 \times$ ULN or AST $\geq 3 \times$ ULN and/or potential Hy's law and have one of the following categories: at least 1 abnormal liver biochemistry risk factor, at least 1 liver disease sign and symptom, at least 1 liver diagnostic test performed, consultation with a specialist for liver evaluation, liver lab tests performed, and drug screen performed, respectively.

A listing of possible Hy's Law cases, defined as those who meet all of the following conditions simultaneously, will be provided: ALT ≥ 3 × ULN or AST ≥ 3 × ULN that is associated with an increase in bilirubin ≥ 2 × ULN and alkaline phosphatase < 2 × ULN.

A listing of urine pregnancy test results will be provided for female participants of childbearing potential with at least one positive result.

10.4 Analysis of Vital Signs

Vital sign measurements of systolic and diastolic blood pressure, pulse rate, respiratory rate, body weight, and body temperature will be summarized.

Each vital sign variable will be summarized for all time points (starting with Baseline) with the number of non-missing observations, mean and standard deviation, median, Q1, Q3, minimum and maximum. Mean change from baseline to each applicable post-baseline visit will be summarized for each vital sign variable, with the number of observations, baseline mean, and visit mean. The change from baseline mean and standard error will be presented for the mean change from baseline.

Vital sign variables will be evaluated based on PCS criteria (Table D-3). For each vital sign PCS criterion, the number and percentage of participants who have a vital sign value meeting the criteria will be summarized. Listings will be provided to summarize participant-level vital sign data for participants meeting PCS criteria.

10.5 Other Safety Analyses

10.5.1 Electrocardiogram

Descriptive statistics for ECG parameters (i.e., heart rate, PR interval, QRS interval, RR interval, QT interval, and QTc interval) at baseline, postbaseline, and changes from baseline values at each postbaseline timepoint will be presented.

ECG parameter values are considered PCS if ECG values meet either the actual value or change from baseline PCS high criteria listed in Table D-4. The number and percentage of

participants with PCS postbaseline values and postbaseline values of clinical interest listed in Table D-5 will be tabulated. The number and percentage of participants with PCS postbaseline values will be summarized. The percentages will be calculated relative to the number of participants with an available non-PCS baseline value and at least 1 postbaseline assessment. The numerator will be the total number of participants with an available non-PCS baseline value and at least 1 PCS postbaseline ECG value during the study. A supportive listing of participants with PCS postbaseline values will be provided. A listing of all AEs for participants with PCS ECG values will also be provided.

A shift table from baseline to the end of open-label treatment period in the overall interpretation of the ECG will be presented for the following categories: normal and abnormal. A tabular display of participants with postbaseline clinically significant ECG abnormalities according to the investigator's overall interpretation will be provided.

10.5.2 Columbia-Suicide Severity Rating Scale

For C-SSRS, the number and percentage of participants with suicidal ideation or suicidal behavior as recorded on the C-SSRS will be summarized for the Safety Population. The distribution of responses for most severe suicidal ideation and most severe suicidal behavior in the participant's lifetime history, in the past 6 months, in the open-label treatment period, and in the follow-up period will also be presented. Supportive listings will be provided and will include the subject number, study center number, lifetime history, and postbaseline values. Intensity of suicidal ideation and suicidal behavior type will also be included in these listings.

11.0 Interim Analyses

No interim analysis of efficacy data will be performed.

12.0 Data Monitoring Committee

An independent DMC has been established to review unblinded safety data and summary reports, identify any safety issues and trends, and make recommendations to AbbVie,

including ongoing trial conduct or modifications to the trial, if emerging data show unexpected and clinically significant AEs of treatment.

Details of the DMC memberships, standard operational procedures for data monitoring/review, frequency of review, and other pertinent details have been provided in a separate DMC Charter.

13.0 Overall Type-I Error Control

No multiplicity adjustment for overall Type I error control is planned for this study.

14.0 COVID-19 Related Analyses

14.1 Efficacy Evaluation

For the endpoints are collected via eDiary, minimal disruption is expected for these endpoints because participants are expected to complete eDiary at home and submit the responses every day.

The health outcome measures will be collected using eTablet as electronic patient reported outcomes (ePRO) at site. To evaluate the missing rate for these efficacy endpoints, the number of participants who missed at least one visit due to COVID-19 will be summarized at each visit in the efficacy analysis population.

14.2 Safety and Other Evaluations

This section specifies analyses related to COVID-19 pandemic from the following aspects:

- Disposition
- Study visits and study procedures
- Treatment discontinuation related to COVID-19
- TEAEs related to COVID-19 infection
- COVID-19 status (COVID-19 testing results or contact with a COVID-19 positive person)

- COVID-19 vaccination

The safety population will be used for the planned COVID-19 related analyses.

The number of participants impacted by COVID-19 during the study will be summarized. The number of participants who missed at least one entire visit, had impacted in-person clinic visits, and had virtual visits due to COVID-19 will be summarized.

The number of participants with TEAEs related to COVID-19 infection will be provided. COVID-19 status, i.e., testing results or contact with a COVID-19 positive person, will be summarized.

The number and percentage of participants who received a COVID-19 vaccine will be tabulated by Anatomical Therapeutic Chemical (ATC) 4 class and preferred term (PT). The number and percentage of participants with TEAEs related to COVID-19 vaccine will be summarized.

Supporting listings for the described analyses above will be provided.

15.0 Version History

Table 1. SAP Version History Summary

Version	Date	Summary
1.0	14 Apr 2023	Initial version
2.0	08 May 2025	To align with Protocol v6.0: • Updated simple size and allowed BOTOX dose (Section 2.2, Section 2.3, Section 2.4). To clarify efficacy analyses: • Updated exploratory efficacy endpoints (Section 3.2) • Clarified the baseline for efficacy (Section 9.1). • Updated the analysis methods correspond to the changes in efficacy endpoints (Section 9.3.2) • Updated derivation method for eDiary data based endpoints (Appendix B). To align with the actual data collection: • Updated the section for subject disposition (Section 5.0). • Updated the BOTOX related treatment duration and compliance (Section 6.0) • Updated the section for participant characteristics (Section 7.1 and Section 7.2). • Reorganized the language for TEAEs (Section 10.2.1, Section 10.2.3 and Section 10.2.4). • Clarified the lab data will be included for analysis (Section 10.3). • Updated the scope of being presented in lab, vital signs, and ECG. (Section 10.3, Section 10.4 and Section 10.5.1) • Removed the summary analysis for the missed assessment due to COVID-19 by assessment category (Section 14.2) • Updated PCS for estimated glomerular filtration rate and ECG parameters (Appendix D). To align with the clinical updates: • Updated PCS for temperature, glucose and protein in urinalysis (Appendix D).

15.1 Changes to Planned Analyses in the Protocol

There are no changes to planned analyses described in protocol.

16.0 References

1. Kenward MG, Roger JH. Small sample inference for fixed effects from restricted maximum likelihood. Biometrics. 1997;53(3):983-97.

Appendix A. List of SAP Signatories

Name	Title	Role/Functional Area
[redacted]	[redacted]	Author
		Clinical Statistics
		Statistical Programming
		Scientific Monitor
		Medical Monitor

Appendix B. Derivation of Efficacy Endpoints Based on eDiary Data

Efficacy measures were defined as follow:

A migraine day is defined as any calendar day on which a headache occurs which meets Criteria A, B, and C OR meets Criteria D and E, as listed below, as per participant eDiary. Calendar days begin at midnight and last until 11:59 PM (23:59).

A. Headache has at least 2 of the following 4 characteristics:
   - Unilateral location
   - Pulsating quality
   - Moderate or severe pain intensity
   - Aggravated by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)

B. At least one of the following:
   - Nausea and/or vomiting
   - Photophobia and phonophobia
   - Typical aura (i.e., visual, sensory, or speech/language) accompanying or within 60 minutes before headache begins

C. Duration of headache lasting 2 hours or longer on a calendar day unless an acute, migraine-specific medication (i.e., triptan or ergot derivative) was used after the start of the headache, in which case no minimum duration will be specified.

OR

D. Any headache which fulfills 1 criterion from (1) and at least 1 criterion from (2) OR fulfills at least 2 criteria from (1) and no criteria from (2).
   1. Headache characteristics:
      - Unilateral location
      - Pulsating quality
      - Moderate or severe pain intensity

- Aggravated by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)

2. Symptoms:
   - Nausea and/or vomiting
   - Photophobia and phonophobia
   - Typical aura (i.e., visual, sensory, or speech/language) accompanying or within 60 minutes before headache begins

1. Duration of headache lasting 2 hours or longer on a calendar day unless an acute, migraine specific medication (i.e., triptan, ergot derivative, or ditan) was used after the start of the headache, in which case no minimum duration will be specified.

A headache day is defined as any calendar day on which headache pain lasting 2 hours or longer occurs unless an acute headache medication (e.g., ibuprofen, triptan) was used after the start of the headache, in which case no minimum duration will be specified. Note that antiemetics will not be counted as an acute headache medication for headache day identification. Calendar days begin at midnight and last until 11:59 PM (23:59).

An acute medication use day is defined as any day on which a participant reports, per eDiary, the intake of allowed medication(s) to treat an acute migraine. The allowed medications include the following categories of drugs: triptans, ergots, opioids, analgesics (including acetaminophen), NSAIDs (including aspirin), and antiemetics.

A moderate or severe headache day is defined as a headache day during which the maximum pain intensity is either moderate or severe. Headache day pain intensity is defined as the worst pain intensity on any headache day where headache pain intensity will be subjectively rated by the patient on a scale from mild to severe:

- Mild pain (1)
- Moderate pain (2)
- Severe pain (3)

Moderate/severe headache day is defined as a headache day during which the maximum pain severity is either moderate or severe. Severe headache day is defined as a headache day during which the maximum pain severity is severe.

If participants experience no headache in a day, then the corresponding pain intensity of that day will be set as missing.

A headache free day is defined as any calendar day on which does not meet the definition of a headache day.

A complete migraine symptom-free day is defined as any calendar day on which a participant reports, per eDiary, no headache and no experience of any of the following non-headache symptom(s): Nausea and/or Vomiting, Sensitivity to light, Sensitivity to sound, Dizziness, Neck pain, Tiredness, Mood change, Yawning, Thirst, Cravings, Urinary frequency, and other (Forehead/facial sweating, Abnormal shedding of tears, Nasal congestion, Eyelid swelling, and Runny nose).

A cardinal migraine symptom-free day is defined as any calendar day on which a participant reports, per eDiary, no headache and no experience of any of the following non-headache symptom(s): Nausea and/or Vomiting, Sensitivity to light, and Sensitivity to sound.

A day with an individual non-headache symptom for each of the 5 most common and cardinal individual non-headache symptoms is defined as any calendar day on which a participant reports, per eDiary, the each of the 5 most common individual non-headache symptoms. 5 most common individual non-headache symptoms are defined as the 5 most common individual non-headache symptoms reported by participants, per eDiary, during the baseline period. The monthly days with individual non-headache symptoms days (including difficulty with concentration and/or thinking clearly, see definition in SPP Section 4.2) during the baseline period will be summarized and sorted by decreasing mean. Other (Forehead/facial sweating, Abnormal shedding of tears, Nasal congestion, Eyelid swelling, and Runny nose) will be renamed as cranial autonomic symptoms. If the

cardinal symptoms (i.e., Nausea and/or Vomiting, Sensitivity to light, and Sensitivity to sound) are not included in the 5 most common individual non-headache symptoms, cardinal symptoms will be summarized individually as well. If difficulty with concentration and/or thinking clearly is included in the 5 most common individual non-headache symptoms, monthly days with individual non-headache symptom will only be summarized in the other 4 most common individual non-headache symptoms.

For analysis purposes, four weeks (28 days) will be considered as one month. On a daily basis during the 28 days of eDiary baseline period and throughout the open-label treatment period, participants are to record eDiary information on the duration of headache, headache specific characteristics and symptoms, the pain intensity, use of any acute headache pain medication, and non-headache symptoms. Daily headache diary data consists of data from "Today's Diary" completed on that day, "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary" completed on the following day. Participants are to report headache data in "Today's Diary" in the evening at any time from 19:00 to 23:59 and to complete "Yesterday's Additional Diary" on the following day to add the remaining headache data of previous evening until midnight. In case participants miss "Today's Diary," they can report the whole-day headache data in "24-Hour Recall of Yesterday's Diary" on the following day. In case participants miss "Yesterday's Additional Diary," headache data from "Today's Diary" alone will be used as daily headache diary data. If "Today's Diary," "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary" are all missing on one day, the daily headache diary data will be treated as missing.

Daily headache diary data will be merged from "Today's Diary," "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary" as following and will be used to derive migraine day and headache day.

- Daily headache total duration: summation of headache durations from "Today's Diary" and "Yesterday's Additional Diary"; or headache durations from "24-Hour Recall of Yesterday's Diary"

- Daily headache pain intensity: the worst pain intensity from "Today's Diary" "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary"
- Daily headache characteristics and symptoms: present if present in one of "Today's Diary," "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary"
- Daily acute headache medication usage: combination of acute headache medications usage from "Today's Diary" and "Yesterday's Additional Diary"; or acute headache medications usage from "24-Hour Recall of Yesterday's Diary"
- Daily non-headache symptoms: present if present in one of "Today's Diary" "24-Hour Recall of Yesterday's Diary" and "Yesterday's Additional Diary."

If a participant confirmed no headache in eDiary (Q1 in Today's Diary, Q2 in Yesterday's Additional Diary, or Q2 in 24-Hour Recall of Yesterday's Diary), then the participant will not answer subsequent questions related to headache symptoms, duration, and acute headache mediation use by design. Thus, the acute medication use for that diary ('Today,' '24-Hours Recall,' or 'Yesterday's Additional') will be treated as 'No' when deriving acute medication use day. However, the participants will continue to answer subsequent questions related to non-headache symptoms.

The monthly migraine days is defined the total number of recorded migraine days in the eDiary divided by the total number of days with eDiary records during each monthly period and multiplied by 28. For baseline, a minimum of 20 days' eDiary data during the 28 days of eDiary baseline period is required for the migraine days to be evaluable. For each postbaseline 4-week treatment period, a minimum of 14 days' eDiary data during that period is required for the migraine days to be evaluable. If a participant does not have at least 14 days of diary data for a monthly treatment period, the migraine days for that period will be considered as missing. Migraine days will be derived for each participant at baseline and for each postbaseline monthly treatment period (Weeks 1-4, 5-8, 9-12, 13-16, 17-20, 21-24). The same method to derive monthly migraine days will be used to derive monthly headache days, monthly moderate or severe headache days, monthly cumulative hours of headache, monthly acute medication use days, monthly headache free days,

monthly complete migraine symptom-free day, monthly cardinal migraine symptom-free day, monthly day with an individual non-headache symptom.

If a participant confirmed that acute medications were taken and entered medications in the eDiary, then the acute medication use day will be set to 'Yes.' If a participant reports 'Yes' to the intake of allowed medication(s) to treat an acute migraine but does not list any of them in the diary, then the acute medication use days will not be counted in this situation and vice versa.

Appendix C. Definition of Adverse Events of Special Interest

The following AESIs have been identified:

- Treatment-emergent elevated ALT or AST laboratory value ≥ 3 × ULN.
- Potential Hy's law cases: elevated ALT or AST laboratory value that is ≥ 3 × ULN and an elevated total bilirubin laboratory value that is ≥ 2 × ULN and, at the same time, an alkaline phosphatase laboratory value that is < 2 × ULN.

Appendix D. Potentially Clinically Significant Criteria for Safety Endpoints

The potentially clinically significant (PCS) criteria for clinical laboratory parameters are described in Table D-1, the criteria for hepatic laboratory abnormalities are described in Table D-2, the PCS criteria for vital sign findings are described in Table D-3, the PCS criteria for ECG parameters are described in Table D-4, and the Clinical Interest Criteria for ECG parameters are described in Table D-5.

Table D-1. Potentially Clinically Significant Criteria for Clinical Laboratory Parameters

Category	Parameter	SI Unit	PCS Criteria	
			PCS Low	PCS High
Chemistry	Albumin	g/L	< 0.8 × LLN	> 1.2 × ULN
	Alanine aminotransferase	U/L	—	≥ 3.0 × ULN
	Alkaline phosphatase	U/L	—	≥ 3.0 × ULN
	Aspartate aminotransferase	U/L	—	≥ 3.0 × ULN
	Bicarbonate	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Bilirubin, total	µmol/L	—	≥ 1.5 × ULN
	Blood urea nitrogen	mmol/L	—	> 1.5 × ULN
	Calcium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Chloride	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Cholesterol, total	mmol/L	—	> 1.6 × ULN
	Creatinine	µmol/L	—	> 1.5 × ULN
	Creatine kinase	U/L	—	> 2.0 × ULN
	Estimated glomerular filtration rate	mL/sec/1.73m^2	< 1	—
	Glucose, nonfasting	mmol/L	< 0.8 × LLN	> 2.0 × ULN
	Lactate dehydrogenase (LDH)	U/L	—	> 3.0 × ULN
	Phosphorus	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Potassium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Protein, total	g/L	< 0.9 × LLN	> 1.1 × ULN
	Sodium	mmol/L	< 0.9 × LLN	> 1.1 × ULN
	Triglycerides	mmol/L	—	> 2.0 × ULN
	Uric acid	µmol/L	—	> 1.2 × ULN

Category	Parameter	SI Unit	PCS Criteria	
			PCS Low	PCS High
Hematology	Basophils, absolute cell count	10^9/L	—	> 2.0 × ULN
	Eosinophils, absolute cell count	10^9/L	—	> 2.0 × ULN
	Hematocrit	Ratio	< 0.9 × LLN	> 1.1 × ULN
	Hemoglobin	g/L	< 0.9 × LLN	> 1.1 × ULN
	Lymphocytes, absolute cell count	10^9/L	< 0.7 × LLN	> 1.3 × ULN
	Monocytes, absolute cell count	10^9/L	< 0.5 × LLN	> 2.0 × ULN
	Neutrophils, absolute cell count	10^9/L	< 0.7 × LLN	> 1.3 × ULN
	Platelet count	10^9/L	< 0.5 × LLN	> 1.5 × ULN
	Red blood cell count	10^{12}/L	< 0.9 × LLN	> 1.1 × ULN
	White blood cell count	10^9/L	< 0.9 × LLN	> 1.5 × ULN
Urinalysis	pH	pH	< 0.9 × LLN	> 1.1 × ULN
	Glucose	mmol/L	—	At least 1+
	Protein	g/L	—	At least 1+
	Specific gravity	—	—	> 1.1 × ULN

LLN lower limit of normal value; ULN upper limit of normal value; normal value provided by laboratory;
SI Le Système International d'Unités (International System of Units)

Table D-2. Criteria for Hepatic Laboratory Abnormalities

Laboratory Parameter	Categories
ALT	≥ 1 × ULN
	≥ 1.5 × ULN
	≥ 2 × ULN
	≥ 3 × ULN
	≥ 5 × ULN
	≥ 10 × ULN
	≥ 20 × ULN
AST	≥ 1 × ULN
	≥ 1.5 × ULN
	≥ 2 × ULN
	≥ 3 × ULN
	≥ 5 × ULN
	≥ 10 × ULN
	≥ 20 × ULN
ALT or AST	≥ 1 × ULN
	≥ 1.5 × ULN
	≥ 2 × ULN
	≥ 3 × ULN
	≥ 5 × ULN
	≥ 10 × ULN
	≥ 20 × ULN
Bilirubin Total	≥ 1 × ULN
	≥ 1.5 × ULN
	≥ 2 × ULN
	≥ 3 × ULN
	≥ 5 × ULN
	≥ 10 × ULN
	≥ 20 × ULN

Laboratory Parameter	Categories
Alkaline Phosphatase	≥ 1 × ULN
	≥ 1.5 × ULN
	≥ 2 × ULN
	≥ 3 × ULN
	≥ 5 × ULN
	≥ 10 × ULN
	≥ 20 × ULN
Concurrent Elevations[a]	ALT or AST ≥ 3 × ULN and Bilirubin Total ≥ 1.5 × ULN
	ALT or AST ≥ 3 × ULN and Bilirubin Total ≥ 2 × ULN
Potential Hy's Law[a]	ALT or AST ≥ 3 × ULN and Bilirubin Total ≥ 2 × ULN and ALP < 2 × ULN

ALT alanine aminotransferase; AST aspartate aminotransferase; TBL total bilirubin; ALP alkaline phosphatase; ULN upper limit of normal (value provided by the laboratory)

a. Elevations are from the same day.

Note: A post baseline value must be more extreme than the baseline value to be considered a potentially clinically important finding.

Vital sign values will be considered PCS if they meet both the observed value criterion and the change from baseline value criterion, if both criteria are available, or meet either the observed value criterion or the change from baseline value criterion that is detailed in the following table.

Table D-3. Potentially Clinically Significant Criteria for Vital Signs

Parameter	Flag	Criteria	
		Observed Value	Change from Baseline
Siting systolic blood pressure, mm Hg	High	≥ 180	Increase of ≥ 20
	Low	≤ 90	Decrease of ≥ 20
Siting diastolic blood pressure, mm Hg	High	≥ 105	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15
Siting Pulse rate, bpm	High	≥ 120	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15
Weight, kg	High	—	Increase of ≥ 7%
	Low	—	Decrease of ≥ 7%

bpm beats per minute; kg kilogram; mmHg millimeters of mercury

ECG parameter values are considered PCS if ECG values meet either the actual value or change from baseline PCS high criteria listed in the following table.

Table D-4. Potentially Clinically Significant Criteria for ECG Parameters

Parameter	Unit	Actual Value	Change from Baseline
QRS interval	msec	≥ 150	—
PR interval	msec	≥ 250	—
QTcF	msec	> 500	Increase > 60

QTc QT interval corrected for heart rate; QTcF QT interval corrected for heart rate using the Fridericia formula.

To evaluate ECG postbaseline values of clinical interest, the number and percentage of participants will be tabulated, if ECG values meet either the actual value or change from baseline criteria listed in the following table.

Table D-5. Clinical Interest Criteria for ECG Parameters

Parameter	Unit	Actual Value
QTcF	msec	> 450, > 480, > 500
QTcF	msec	30 < Change from Baseline ≤ 60, Change from Baseline > 60

Participants will be counted only once for the most severe category. A supportive listing of participants with postbaseline QTcF increases > 30 msec will be provided, including the subject number, study center, and all QTc values (including changes from baseline). A listing of all AEs for participants with postbaseline QTcF increases > 30 msec will also be provided.

Appendix E. Laboratory Parameters in Conventional Unit

All clinical laboratory parameters will be reported in the International System (SI) units as standard practice. In addition, descriptive statistics for values and changes from baseline in conventional units at all assessed visits will be reported for selected laboratory parameters as listed in the following table.

Table E. List of Selected Parameters Reported in Conventional Unit

Number	Laboratory Parameter	Conventional Unit	Decimal Places
1	Alanine Aminotransferase (SGPT)	U/L	0
2	Albumin	g/dL	1
3	Alkaline Phosphatase	U/L	0
4	Aspartate Aminotransferase (SGOT)	U/L	0
5	Bilirubin, Direct (Conjugated)	mg/dL	1
6	Bilirubin, Indirect (Unconjugated)	mg/dL	1
7	Bilirubin, Total	mg/dL	1
8	Blood Urea Nitrogen	mg/dL	0
9	Calcium	mg/dL	1
10	Cholesterol, HDL	mg/dL	0
11	Cholesterol, LDL	mg/dL	0
12	Cholesterol, LDL direct and calculated (combined) *(This lab parameter could be the same as #11)*	mg/dL	0
13	Cholesterol, Total	mg/dL	0
14	Creatine Kinase	U/L	0
15	Creatinine	mg/dL	1
16	Glucose	mg/dL	0
17	Insulin	µIU/mL	1
18	Triglycerides	mg/dL	0
19	Uric Acid	mg/dL	1
20	Hemoglobin	g/dL	1

Appendix F. List of Abbreviations

Abbreviation/Term	Definition
AE	adverse event
AESI	adverse events of special interest
AIM-D	Activity Impairment in Migraine - Diary
ALP	alkaline phosphatase
ALT	alanine aminotransferase
BOTOX	OnabotulinumtoxinA
BP	blood pressure
CM	Chronic migraine
COVID-19	Coronavirus Disease – 2019
C-SSRS	Columbia–Suicide Severity Rating Scale
DMC	Data Monitoring Committee
ECG	electrocardiogram, electrocardiographic
eDiary	electronic diary
ePRO	electronic patient reported outcomes
GAD-7	Generalized Anxiety Disorder-7
IHS	International Headache Society
LLN	lower limit of normal value
LS	least squares
MedDRA	Medication Dictionary for Regulatory Activities
mITT	modified intent-to-treat
MMRM	mixed-effects model for repeated measures
MSQ v2.1	Migraine-Specific Quality of Life Questionnaire, version 2.1
NSAIDs	nonsteroidal anti-inflammatory drugs
PCS	potentially clinically significant
PGIC	Patient Global Impression of Change
PHQ-9	Patient Health Questionnaire-9
PROMIS	Patient-Reported Outcomes Measurement Information System
PSSM	Patient Satisfaction with Study Medications
PT	preferred term
Q1	first quartile (25th percentile of the data)
Q3	third quartile (75th percentile of the data)
QD	once daily

Abbreviation/Term	Definition
QTc	QT interval corrected for heart rate
QTcF	QT interval corrected for heart rate using the Fridericia formula ($QTcF = QT/(RR)^{1/3}$)
SAE	serious adverse event
SAP	statistical analysis plan
SI	Le Système International d'Unités (International System of Units)
SOC	standard of care
TBL	total bilirubin
TEAE	treatment-emergent adverse event
TESAE	treatment-emergent serious adverse event
ULN	upper limit of normal value
WHO	World Health Organization
WPAI:MIGRAINE	Work Productivity and Activity Impairment Questionnaire: Migraine v2.0

Document Approval

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