Statistical Analysis Plan

for

Evaluation of Oral Minocycline in the Treatment of Geographic Atrophy Associated with Age-Related Macular Degeneration (GA)

15-EI-0202

NCT02564978

Version 4.0

March 21, 2023

Prepared by [redacted]

Original Author Signature:

Reviewer Signature:

Principal Investigator Signature:

[redacted]

Restricted

TABLE OF CONTENTS

TABLE OF CONTENTS (CONTINUED)

TABLE OF TABLES

TABLE OF LISTINGS

TABLE OF FIGURES

VERSION HISTORY

Version/Date	Changes
1.0/20DEC2018	***Initial Document***
2.0/20AUG2020	***Sections 3.1 and 3.3:*** Updated to specify that 45 participants will be enrolled; ***Section 4.3:*** Added per-protocol population 3; ***Section 4.6***: Provided clarification on p-value thresholds for one-sided tests in addition to two-sided tests; ***Sections 5.0, 6.1, 6.2, 7.1, 7.1.2, 7.1.3:*** Indicated that information will be presented by site; ***Section 5.0:*** Updated to present participants who withdraw from IP separately, if sufficient data are present; ***Section 7.1:*** Updated per NIH Intramural Research Program Policy 801 and separated summaries for participant-specific and non-participant-specific protocol deviations; ***Sections 7.1.2 and 7.1.3:*** Removed waiver language previously included in protocol; ***Section 8.0:*** Removed redundant term in model for primary outcome analysis; ***Sections 9.1 and 11.0:*** Added analyses based on Student's paired t-test for GA area expansion rates based on FAF as secondary and exploratory analyses, respectively; ***Section 10.0:*** Added sensitivity analysis based on per-protocol population 3; ***Section 12.1:*** Updated "E-ETDRS letters" to "letter score"; ***Section 13.4:*** Added thresholds for clinical significance for IOP of >10 mmHg change from baseline and >30 mmHg; ***Section 17.0:*** Made applicable corresponding updates described above to mock shells.
3.0/04OCT2022	***Title page:*** Added ClinicalTrials.gov identifier and placeholder for PI's signature ***Sections 2.0:*** Updated to specify that DIRRL will grade OCT images as well; ***Section 3.1:*** Updated to clarify that participants recruited at the beginning of the study may complete the study as early as Month 45 at the discretion of the investigator. ***Section 3.4.3:*** Updated to point to later sections that provide additional details. ***Section 4.3:*** Updated to further clarify/define the analysis populations. ***Section 10.0:*** Updated to further clarify/define the method for calculating the rate of missingness. ***Section 11.0:*** Updated to further clarify/define the exploratory analyses to be performed. ***Section 13.7***: Added information regarding descriptive summary of graded OCT parameters; ***Section 17.0:*** Edited the summary of age as a continuous parameter from Table 2 to remove participants whose age is > 89 (ages > 89 are considered Protected Health Information (PHI) and are masked prior to transfer of data to the Coordinating Center); added Table 26 corresponding to graded OCT parameters; updated numbering of other relevant tables; updated formatting and footnotes of select tables for increased clarity ***Section 18.0:*** Added section to indicate the presentations to be included in the primary outcome analysis report.
4.0/21MAR2023	***Section 3.4.2:*** Removed "changes in macular sensitivity on microperimetry" as a secondary study outcome as this was made an exploratory study outcome through Amendment M of the protocol. ***Section 9.6:*** Removed this section as macular sensitivity was made an exploratory study outcome. ***Section 17.0:*** Revised Table 14 to remove presentation of statistics pertaining to non-qualifying fellow eyes. Removed Table 15 and Listing 7 as macular sensitivity was made an exploratory study outcome. Revised Table 1 and Figure 1 to more clearly depict participants who complete or discontinue the study at or after Month 45.

LIST OF ABBREVIATIONS

AE	Adverse Event
AF	Autofluorescence
AMD	Age-Related Macular Degeneration
AREDS	Age-Related Eye Disease Study
BCVA	Best-Corrected Visual Acuity
BEH	Bristol Eye Hospital
CFH	Complement Factor H
CFP	Color Fundus Photos
CI	Confidence Interval
CNV	Choroidal Neovascularization
COVID-19	Coronavirus Disease 2019
DDAF	Definitely Decreased Autofluorescence
DIRRL	Doheny Image Reading & Research Lab
EDC	Electronic Data Capture
EMR	Electronic Medical Record
ETDRS	Early Treatment Diabetic Retinopathy Study
EVA	Electronic Visual Acuity
FAF	Fundus Autofluorescence
GA	Geographic Atrophy
IAF	Increased Autofluorescence
IOP	Intraocular Pressure
IP	Investigational Product
LLVA	Low Luminance Visual Acuity
logMAR	Logarithm of the Minimum Angle of Resolution
MCAR	Missing Completely at Random
MI	Multiple Imputation
MPS DA	Macular Photocoagulation Study Disk Area
NEI	National Eye Institute
OCT	Optical Coherence Tomography
PHI	Protected Health Information
PT	Preferred Term
QDAF	Questionably Decreased Autofluorescence
RPE	Retinal Pigment Epithelial
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SD	Standard Deviation
SNP	Single Nucleotide Polymorphism
SOC	System Organ Class
Std Err	Standard Error
VA	Visual Acuity
VEGF	Vascular Endothelial Growth Factor
YAG	Yttrium Aluminum Garnet

1.0 INTRODUCTION

This statistical analysis plan provides proposed analyses for the study "Evaluation of Oral Minocycline in the Treatment of Geographic Atrophy Associated with Age-Related Macular Degeneration (GA)." This document contains 17 sections: (1) background of the study, (2) data sources for analyses, (3) an overview of the study design, (4) statistical considerations, (5) participant disposition, (6) participant characteristics, (7) participant compliance, (8) statistical analyses for primary outcome, (9) statistical analyses for secondary outcomes, (10) sensitivity analyses, (11) exploratory analyses, (12) review of ocular safety outcomes, (13) review of other safety outcomes, (14) rationale for any deviations from this statistical analysis plan, (15) quality assurance plans, (16) references and (17) proposed data tables, figures and listings. Any deviation from this statistical plan, not outlined in Section 14.0, will be described and justified in protocol amendments and/or in the final study report, as appropriate.

1.1 Age-related Macular Degeneration (AMD)

AMD is the leading cause of late onset visual impairment and legal blindness in people 65 years of age or older in the United States (1, 2). The World Health Organization has placed AMD as the third leading cause of blindness worldwide. The phrase "age-related" is associated with macular degeneration because data show that the risk of developing AMD dramatically increases after age 60. It is estimated that 13 million people in the United States, age 40 and older, have signs and symptoms of macular degeneration. Based on population demographics and current prevalence data, the number of individuals affected with AMD will double in the year 2020.

AMD is a disease of the macula, the central area within the posterior retina that helps produce sharp, central vision. Central vision is required for seeing objects clearly and for common daily activities essential for independent living such as reading, writing, sewing and driving. While the pathogenesis of AMD remains unknown, several lines of evidence have indicated the role of inflammation. Complement factor H (CFH) is a major regulatory factor in the complement cascade. Several groups have identified single nucleotide polymorphisms (SNPs) in the CFH gene that are associated with AMD. A single copy of the risk-associated haplotype increases the risk of AMD by two- to four-fold, whereas those with a dual copy may increase their lifetime risk by five- to seven-fold (3-7). Macrophages are known to have an important role in the initiation and

maintenance of the immune response, including the regulation of complement activation. Previous studies have shown that patients with AMD were more likely to have circulating, activated macrophages (which produce high amounts of proinflammatory cytokines) compared to controls without AMD (8).

1.2 Treatment of Age-related Macular Degeneration

Treatment of AMD has mostly focused on therapy for neovascular AMD. These have included classic laser photocoagulation, photodynamic therapy (verteporfin, Visudyne®) and anti-vascular endothelial growth factor (VEGF) pegylated aptamer (pegaptanib sodium, Macugen®), an anti-VEGF monoclonal antibodies ranibizumab (Lucentis®) and aflibercept.

In October 2001, the results of the Age-Related Eye Disease Study (AREDS), a multi-center, randomized, controlled clinical trial of high-dose vitamins C and E, beta carotene and zinc supplements demonstrated a 25% reduction in the risk of progression to late AMD (9). However, this effect appears to be limited to reducing risk for progressing to neovascular AMD and does not influence the risk for progression to geographic atrophy (GA) (unpublished data).

There are currently no available treatments or therapies for GA that have demonstrated efficacy in either preventing the onset, slowing the progression of disease, or improving vision of affected patients.

1.3 Geographic Atrophy

Atrophic AMD or GA is characterized by an absence of neovascular changes and the gradual progression of atrophic changes in the macula on the level of outer retina and the retinal pigment epithelial (RPE) cell layer, resulting in progressive central vision loss. Over time, this progresses to result in serious impairment of central vision and often legal blindness. Wet or exudative AMD can also arise in the context of GA. Both GA involving the center of the macula and wet AMD are considered forms of late AMD.

One of the most common signs in early or intermediate AMD is drusen, which is typically seen in people over the age of 60. Drusen are usually seen clinically as whitish-yellow irregularities under the retina. Large drusen have been shown to contain immunoglobulins, activated microglia and fragments of activated complement factors (10-12), which may be a source of chronic inflammatory stimulus in the aging retina. In the absence of findings consistent with late AMD, intermediate AMD is typically defined as the presence of large (>125µm) macular drusen and/or pigmentary (hypopigmentary or hyperpigmentary) changes, while early AMD is typically defined as the presence of macular drusen <125µm in size.

2.0 DATA SOURCE

All data analyzed will come from one of two sources. Data received from the National Eye Institute (NEI) will be collected via their electronic data capture system (EMR), which will then be uploaded on a daily basis to the Coordinating Center's database, Advantage EDC. Data received from the Bristol Eye Hospital (BEH) and Doheny Image Reading and Research Lab (DIRRL) will be collected directly through Advantage EDC.

It is expected that the data received from DIRRL will only contain data concerning the grading of participants' Color Fundus and Fundus Autofluorescence (FAF) photos at all visits and Optical Coherence Tomography (OCT) images at baseline, Month 9 and Month 33, while the data received from NEI and BEH will contain all other participant data.

3.0 GENERAL REVIEW OF STUDY DESIGN

3.1 Study Design

The GA study is a multi-center, prospective, single-arm, Phase II study to evaluate minocycline as a potential treatment to decrease the rate of worsening of GA associated with AMD. Up to 45 participants will be enrolled and will undergo a nine month run-in phase prior to receiving investigational product (IP). During this run-in phase, participants will have a total of four pre-treatment visits at baseline and Months 3, 6 and 9. Following the run-in phase, beginning at Month 9, participants will receive an oral dose of 100 mg of minocycline twice daily for 36 months and will return to the clinic at Months 12, 15, 21, 27, 33, 39, and 45 for follow-up assessments. The study is designed with a common termination date, meaning it will not terminate

until the last recruited participant has completed the Month 45 visit. Therefore, participants enrolled at the beginning of the study could receive additional months of IP beyond the scheduled 36-months and will continue to be followed every six months until the common termination date. However, participants may complete participation in the study as early as Month 45, at the discretion of the investigator. Although participants may withdraw from IP during the study, all participants will be asked to return for all visits through their study termination visit.

3.2 Study Objective

The study objective is to investigate the safety and possible efficacy of oral minocycline for slowing down the worsening of GA associated with AMD.

3.3 Study Population

Up to forty five (45) participants, aged 55 years or older, with unilateral or bilateral GA associated with atrophic AMD will be enrolled in this study. Approximately 20-25 participants will be enrolled at NEI, and approximately 20-25 participants will be enrolled at BEH to reach the target sample size of 45 participants. Participants who withdraw or are lost to follow-up before the Month 33 visit (i.e., before completing 24 months on treatment) may be replaced by new enrollments up to 30 participants at NEI and 30 participants at BEH.

3.3.1 Participant Eligibility Criteria

To be eligible, participants must meet all of the inclusion criteria, when applicable, and none of the exclusion criteria.

3.3.1.1 Inclusion Criteria

1. Participant must be 55 years of age or older.
2. Participant (or legal guardian) must understand and sign the protocol's informed consent document.
3. Participant must have evidence of early or intermediate AMD as defined by characteristic presence of drusen and/or pigmentary changes.
4. Participant must be able to swallow capsules.

5. Participant must have normal renal function and liver function or have mild abnormalities not above grade 1 as defined by the Common Terminology Criteria for Adverse Events v4.0.
6. Participant must agree to minimize exposure to sunlight or artificial ultraviolet rays and to wear protective clothing, sunglasses and sunscreen (minimum sun protection factor of 15) when out in the sun.
7. Any female participant of childbearing potential must have a negative pregnancy test at screening and be willing to undergo pregnancy tests throughout the study.
8. Any female participant of childbearing potential and any male participant able to father children must have (or have a partner who has) had a hysterectomy or vasectomy, be completely abstinent from intercourse or must agree to practice two acceptable methods of contraception throughout the course of the study and for at least one week after IP discontinuation.

3.3.1.2 Exclusion Criteria

1. Participant is actively receiving study therapy in another investigational study.
2. Any female participant of childbearing potential who is pregnant, breast-feeding or planning to become pregnant during the study.
3. Participant is expected to be unable to comply with study procedures or follow-up visits.
4. Participant is on ocular or systemic medications known to be toxic to the lens, retina or optic nerve (e.g., ethambutol, chloroquine, or hydroxychloroquine).
5. Participant has a condition that would preclude participation in the study (e.g., unstable medical status including blood pressure and glycemic control) by interfering with the participant's ability to engage in the required protocol evaluation and testing and/or comply with study visits.
6. Participant has a history of chronic renal failure requiring dialysis or kidney transplant.
7. Participant has a history of chronic hepatitis or liver failure.
8. Participant has a history of thyroid cancer.

9. Participant has an allergy or hypersensitivity to minocycline or any drug in the tetracycline family.
10. Participant is currently taking minocycline or another tetracycline medication.
11. Participant is taking any medication that could adversely interact with minocycline such as methoxyflurane.
12. Participant has a prior history of idiopathic intracranial hypertension.

3.3.2 Study Eye Eligibility Criteria

The participant must have at least one eye meeting all inclusion criteria and none of the exclusion criteria listed below.

3.3.2.1 Study Eye Inclusion Criteria

1. The study eye must have greater than ½ disc area (approximately 1 mm^2) of GA compatible with dry AMD. GA is defined as one or more well-defined and often circular patches of partial or complete depigmentation of the RPE, typically with exposure of underlying choroidal blood vessels. Even if much of the RPE appears to be preserved and large choroidal vessels are not visible, a round patch of RPE partial depigmentation may be classified as early GA. The GA in the study eye must be able to be photographed in their entirety, and it must not be contiguous with any areas of peripapillary atrophy, which can complicate area measurements.
2. The total area of GA lesions combined should be less than 7.0 MPS disc areas (DA) (17.78 mm^2) as evident on FAF imaging.
3. The visual acuity of the study eye should be >19 E-ETDRS letters (i.e., 20/400 or better).
4. The study eye must have clarity of ocular media and degree of pupil dilation sufficient to permit adequate fundus photographs.

3.3.2.2 Study Eye Exclusion Criteria

1. Current evidence of choroidal neovascularization (CNV) as determined by the treating physician or a history of treatments for CNV.
2. Evidence of retinal atrophy due to causes other than atrophic AMD.
3. Current evidence or history of ocular disorders in the study eye that in the opinion of the investigator confounds study outcome measures, including (but not limited to):
    a. Non-proliferative diabetic retinopathy involving 10 or more hemorrhages or microaneurysms, or active proliferative diabetic retinopathy
    b. Branch or central retinal vein or artery occlusion
    c. Macular hole
    d. Pathologic myopia
    e. Uveitis
    f. Pseudovitelliform maculopathy
4. History of vitreoretinal surgery.
5. Need for ocular surgery during the course of the study.
6. Recent history of lens removal (< 3 months) or Yttrium Aluminum Garnet (YAG) laser capsulotomy (< 1 month).

3.3.2.3 Choice of Study Eye in Cases of Bilateral Disease

If both eyes meet the study eye eligibility criteria described above, the eye with the better best-corrected visual acuity (BCVA) will be chosen as the study eye. If both eyes are of equal visual acuity (VA), the study eye will be assigned by the enrolling investigator. For participants with two qualifying eyes, the fellow (non-study) eye will be noted as a “qualifying fellow eye” and anatomical data from it will be analyzed as part of the secondary outcome measures.

3.4 Outcomes

3.4.1 Primary Study Outcome

The primary outcome is the difference in the rates of GA area expansion in the study eye between the run-in phase of the study and following IP initiation. GA area determination will be based on digital grading of FAF images by an external Reading Center. Specifically, the primary outcome will be the difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9).

3.4.2 Secondary Study Outcomes

Exploratory secondary outcomes will examine the difference in the rates of outcome measure progression in the study eye between the run-in phase of the study and following IP initiation. Measures obtained from qualifying fellow eyes will also be analyzed separately and together with study eyes as secondary outcomes.

Specifically, the secondary outcome measures include difference in rates of progression from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9) in (a) study eyes alone, (b) qualifying fellow eyes alone and (c) study and qualifying fellow eyes together in the following:

1. GA area expansion based on FAF images by an external Reading Center using a different statistical approach compared to primary outcome
2. GA area expansion based on digital grading of color fundus images by an external Reading Center
3. changes in BCVA
4. changes in low luminance visual acuity (LLVA)
5. changes in central retinal thickness on OCT and

3.4.3 Safety Outcomes

Ocular safety outcomes include:

1. Changes in VA
2. Ocular surface changes
3. Intraocular inflammation and
4. Any other ocular changes not consistent with the natural progression of GA

Additional details regarding ocular safety outcomes are provided in Section 12.1 and Section 12.2.

Other safety outcomes include:

- Frequency, type, severity and assessed relatedness to IP of Adverse Events (AEs)
- Number of participants withdrawn from IP due to vision loss, AEs and treatment failures

4.0 STATISTICAL CONSIDERATIONS

4.1 Sample Size Calculation

The accrual goal is to enroll 45 participants, approximately 20 at NEI and 25 at BEH. Up to 15 additional participants may be enrolled to replace those participants who withdraw prior to their Month 33 visit. This sample size was determined for the primary analysis of the difference in rate of change in square-root transformed GA area in the study eye between IP start visit to 24 months of treatment and initial study visit to IP start visit. A two-sided paired t-test at an alpha level of 0.05, comparing square-root transformed rates of change in GA between 24 months of treatment and the run-in phase was employed.

A rate of 1.52 mm^2/year is assumed for the run-in phase in the current study, based on the median GA expansion rates suggested in the literature (13). For data that are skewed, the square-root of the mean is not equal to the mean of the square-root transformed data. However, since a quantile of strictly positive data is invariant to transformation (e.g., the square-root of a given quantile of the original observations is equal to that quantile of the transformed observations), and for symmetric data mean and median are equal, the square-root of the median progression rate ($\sqrt{1.52}$ mm^2/year = 1.23 mm/year) is used to approximate the assumed mean progression rate for

the square-root transformed run-in phase. The treatment phase is assumed to have a 25% reduction in the GA growth rate, equivalent to a 13% reduction of the square-root transformed rate, implying a mean progression rate of 1.07 mm/year for the square-root transformed GA growth rate during the treatment phase. A standard deviation of 0.30 mm/year was obtained from previous NEI GA protocols exploratory analyses data and was assumed for the GA growth rate during the run-in phase. Given the strictly positive nature of GA enlargement, a reduction in mean progression rate during the treatment phase necessitates a smaller standard deviation. However, on the square-root scale, the difference in standard deviations between the run-in and treatment phases is negligible for the proposed 25% reduction in means, and a standard deviation of 0.30 was also assumed for the square-root transformed GA growth rate during the treatment phase. Since this is a single arm study utilizing each participant as their own control, measurements will be highly correlated between the run-in and treatment phases. A correlation of 0.8 was used to account for the high dependence in measurements between the run-in and treatment phases. Based on these square-root transformed mean and standard deviation estimates, a sample size of at least 17 participants is required to obtain at least 90% power to detect a difference in progression rates if the true square-root transformed progression rates are 1.23 mm/year during the run-in phase and 1.07 mm/year during the treatment phase of 24 months, with an 80% within-in participant correlation. Since the study population consists of older adults, loss to follow-up due to various reasons is expected and needs to be taken into account for an accurate sample size. Therfore, the target sample size for this study is 45 participants, with a provision to enroll up to an additional 15 participants to replace those participants who withdraw prior to their Month 33 visit. Approximately 12 months will be necessary to accrue these participants.

Sunness, et al. (14), (13) state that a sample size of 306 is necessary to detect a treatment effect of 25% when examining the effect of a new systemic treatment on GA growth rate in individuals (14). One of the factors that resulted in the reduction of sample size from the Sunness suggestion is the use of FAF instead of color fundus photos (CFP) to grade GA. FAF appears to be more precise (i.e., lower within-patient SD) than CFP. For example, the coefficient of variation for the square-root transformed FAF data is 2.5, while the coefficient of variation for the CFP data summarized in Sunness is 1.3. Further, the current study design utilizes each participant as their own control, significantly decreasing within-participant variability and the need for a large sample size.

4.2 Sample Size Re-estimation

After the first 15 participants have reached their Month 9 visit, the study dropout rate will be assessed and a sample size re-estimation may be performed to ensure at least 17 participants complete Month 33 visit.

The current drop-out rate will be determined as:

$$\frac{\textit{Number of participants who withdraw from the study}}{\textit{Number of participants enrolled in the study}}$$

Sample size will be re-estimated as follows:

$$\frac{\textit{Minimum number of participants required}}{\textit{1-Current drop-out rate}}$$

If the re-estimated sample size is more than 60 participants (planned target sample size of 45 + provision to enroll 15 additional participants to replace those participants who withdraw prior to their Month 33 visit), then the sample size *may be* revised to accommodate the increased drop-out rate observed after discussion between the Principal Investigator and Coordinating Center.

4.3 Analysis Populations

The following analysis populations will be considered for this study:

Enrolled population: Includes all participants enrolled in the study, regardless of compliance, follow-up or treatment received. Participant disposition, characteristics, compliance, primary outcome analysis, and summaries of pre-treatment AEs will be based on this population.

Safety population: Includes all participants who received at least one dose of the study drug. Summaries of ocular and other safety outcomes will be based on this population.

Per-protocol population 1: Includes those participants who completed treatment through Month 33 without any missing observations for the assessment and eye(s) being summarized. Sensitivity analysis will be performed using this population.

Per-protocol population 2: Includes those participants who completed at least three follow-up visits during the treatment phase and did not discontinue treatment prior to the completion of at least three follow-up visits. For participants included in this population, all visits subsequent to treatment discontinuation will be excluded from analyses. Summaries of secondary outcomes will be based on this population. Sensitivity analysis will also be performed using this population.

Per-protocol population 3: Includes all participants in the enrolled population except those who initiated treatment during the Month 9 visit out of window. Sensitivity analysis will be performed using this population.

4.4 Study Phases

The study is divided into two phases:

1. Run-in phase: Defined as the time from Baseline through Month 9 before participants receive the first dose of IP.
2. Treatment Phase: Defined as the time from Month 9 after participants receive the first dose of IP through early withdrawal from study or study completion. Participants who received at least one dose of IP but withdrew from IP early, will be considered to be in the treatment phase until withdrawal from or completion of study. Therefore, all participants who are followed during the treatment phase, regardless of whether they discontinued IP, will be included in the corresponding analysis, unless otherwise specified.

4.5 Descriptive Statistics

For continuous parameters, descriptive statistics will include number of observations, mean, standard deviation, median, minimum and maximum. For categorical parameters, frequency and percentage of participants will be summarized.

4.6 Statistical Tests and Adjustments for Multiple Comparisons

Results of statistical analyses are considered significant if the p-value from the statistical test is < 0.05 for two-sided tests or <0.025 for one-sided tests. Results will be considered moderately significant if the p-value from the statistical test is < 0.10 for two-sided tests or <0.05 for one-sided tests.

Since all analyses in this study are considered exploratory, no adjustments for multiple comparisons will be made.

4.7 Handling Duplicate Assessments

The assessments at each visit may be completed over multiple days. If assessments are performed more than once at a given visit, the results of the most recent assessment will be considered in the analysis. For example, if the Month 3 visit is completed over multiple days and an assessment was performed on more than one day as part of Month 3 assessment, then the results of the most recent Month 3 visit will be included in the analyses.

4.8 Software for Analyses

Statistical analyses will be performed using SAS version 9.4 or higher or R v3.3.1 or higher. All tables, listings and figures presented in the analysis will be created using either SAS v9.4 or Rv3.3.1 or higher.

5.0 PARTICIPANT DISPOSITION

Overall participant disposition including the number and percentage of participants enrolled, completed the run-in phase, initiated and completed the treatment phase, and discontinued study early will be summarized by site. Reasons for study discontinuation will also be summarized (Table 1). If sufficient data are present, reasons for treatment discontinuation will be summarized. The number and percentage of participants who withdraw from IP due to safety, including due to vision loss in a manner inconsistent with the natural history of GA (manually identified based on investigator's comments for those particpiants with reason for withdrawal from IP indicated as "safety withdrawal") and AEs (reason for withdrawal from IP indicated as "safety withdrawal" for the occurrence of AEs assessed as being related to study IP that preclude further administration of IP), and treatment failure (reason for withdrawal from IP indicated as "lack of efficacy") will be included. These tables will be based on the enrolled population.

Participant flow as outlined in Figure 1 will also be presented.

6.0 PARTICIPANT CHARACTERISTICS

These presentations will be based on the enrolled population.

6.1 Participant Demographics

Demographic characteristics including baseline age, sex, race and ethnicity will be summarized by site as outlined in Table 2 and listed as in Listing 1. The listing will also include the registration date and will indicate the eye determined to be the study eye and whether the participants' fellow eye is a qualifying fellow eye.

6.2 Medical and Ocular History

The total number and percentage of participants with a history of medical and ocular conditions and ocular procedures will be summarized. History of ocular conditions and procedures will also be summarized by eye (study eye, qualifying fellow eye and non-qualifying fellow eye) (Table 3). Separate summaries will be included for each site. Medical and ocular history will also be listed; the listing will include date of diagnosis and/or time since diagnosis at baseline for select conditions and procedures.

7.0 PARTICIPANT COMPLIANCE

These presentations will be based on the enrolled population.

7.1 Protocol Deviations and Unanticipated Problems

The total number of protocol deviations and unanticipated problems and the number and percentage of participants with deviations and unanticipated problems will be summarized by site and overall.

Effective July 1, 2019, with the implementation of NIH Intramural Research Program Policy 801, protocol deviations and unanticipated problems are classified by the Investigator as major or minor at the time of data entry (as opposed to serious or not serious), and seriousness of major deviations, and unanticipated problems is determined after review by the NIH Institutional Review Board (IRB). The number of events per participant and the type (minor, serious, not serious, or pending determination by IRB) and outcome of events will also be summarized. Separate summaries will be included for participant-specific and non-participant specific protocol deviations (Table 4 and Table 5, respectively). Listings of participant-specific and non-participant-specific protocol deviations and unanticipated problems will be presented.

7.1.1 IP Compliance Deviations

This table will present the expected number of doses, number of doses missed and compliance rates cumulatively and between visits for each participant (Table 6). For each participant, the number of expected doses overall and between visits will be calculated as follows:

$$N_{\text{Doses expected (cumulative)}} = (Date_{\text{Early IP/study withdrawal or study completion}} - Date_{\text{IP first taken}}) * 2$$

$$N_{\text{Doses expected (between visits)}} = (Date_{\text{Current visit}} - Date_{\text{Previous visit IP start}}) * 2$$

If participants took IP on the date they withdrew from the study or completed the study, the number of expected doses overall and between the last visit and the previous visit will be calculated as follows:

$$N_{\text{Doses expected (cumulative)}} = (Date_{\text{Early IP/study withdrawal or study completion}} - Date_{\text{IP first taken}} + 1) * 2$$

$$N_{\text{Doses expected (between visits)}} = (Date_{\text{Current visit}} - Date_{\text{Previous visit IP start}} + 1) * 2$$

$Date_{\text{IP first taken}}$ is the date participant first started taking the pills. If this date is missing, then the date of the visit when IP was first dispensed (i.e, Month 9 visit) to the participant will be used; however, if the IP was mailed to the participant instead, then the date when the mail was sent will be used. Similarly, $Date_{\text{Previous visit IP start}}$ is the date participant started taking the pills following the previous visit. If this date is missing, then the date of the previous visit when IP was dispensed to the participant will be used; however, if the IP was mailed to the participant instead, then the date when the mail was sent will be used.

The sites will report number of pills returned at each study visit. Number of doses taken and missed will be calculated for each participant for each timeframe as:

$$N_{\text{Doses taken}} = N_{\text{Pills dispensed}} - N_{\text{Pills returned}}$$

$$N_{\text{Doses missed}} = N_{\text{Doses expected}} - N_{\text{Doses taken}}$$

Negative values will indicate participants who took excess IP.

Compliance rate for each timeframe will be calculated as:

$$Compliance\ rate = (N_{Doses\ taken}/N_{Doses\ expected})*100$$

Participants with compliance rates between visits less than 50% will be flagged in this table.

7.1.2 Study Procedure Deviations

This table will present the number of procedures not completed, the expected number of procedures completed, and the percentage of procedures missed a) for each participant considering all procedures together, b) cumulatively for all participants by procedure and c) cumulatively for all participants considering all procedures (Table 7). Statistics will be presented for each site and overall. Number of procedures not completed is defined when the site reports a missed procedure or when the protocol monitors note missed procedures at a site, and will be presented as a sum. Expected number of procedures is defined based on the study flowsheet included in the protocol, and will also be presented as a sum. Percentage of procedures missed will be calculated as follows:

$$(N_{procedures\ not\ completed} / N_{expected\ procedures\ completed})*100$$

7.1.3 Visit Schedule Deviations

This table will present the number of expected visits, number of missed study visits, the percentage of missed study visits, the number of out of window visits, and the percentage of out of window visits cumulatively and by participant (Table 8). Statistics will be presented for each site and overall. Number of expected, missed and out of window study visits will be calculated from the study flowsheet and will all be presented as sums. The percentage of missed study visits will be calculated as:

$$(N_{visits\ missed} / N_{expected\ visits})*100$$

Similarily, the percentage of out of window study visits will be calculated as:

$$(N_{visits\ out\ of\ window} / N_{expected\ visits})*100$$

7.2 Premature Treatment and Study Withdrawals

Participants who withdrew from treatment and study early will be summarized as outlined in Section 5.0 and will be listed separately along with reason(s) for withdrawal. Participants who discontinue IP early due to vision loss in a manner inconsistent with the natural history of GA, AEs and treatment failure will be included in the listing (see Section 5.0 for identification of such participants).

8.0 PRIMARY OUTCOMES ANALYSIS

GA area, based on digital grading of FAF imaging, will be assessed at all study visits in study and qualifying fellow eyes.

The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using FAF, in study eyes will be assessed by fitting a linear spline regression model with a fixed knot at Month 9.

The model will be fit using the MIXED procedure in SAS 9.4 or higher using GA area as the outcome that's appropriately transformed to satisfy the linear trend assumption as follows:

$$\text{Model 1: } \hat{Y}_t = \hat{\beta}_0 + \hat{\beta}_1 * \text{Time}_t + + \hat{\beta}_2 * (\text{Time}_t - t^*) + b_t + \varepsilon_t$$

Where:

$\hat{Y}_t$ = Estimate of mean of appropriately transformed GA area at Month t

t = Time in months from baseline

t* = Month when treatment started or month corresponding to the knot (i.e.,Month 9)

$\hat{\beta}_0$ = Estimate of mean of appropriately transformed GA area at baseline

$\hat{\beta}_1$ = Estimate of rate of change in appropriately transformed GA area during the run-in phase

$\hat{\beta}_2$ = Estimate of difference in rates of change in mean of appropriately transformed GA area between the treatment phase and run-in phase (i.e, β_2 is applicable only to time points after the knot [Month 9])

b_t =Within-subject correlation

ε_t = Random variability not explained by the model at Month t, which is assumed to be normally distributed and independent across participants and time.

Note that $\hat{\beta}_1 + \hat{\beta}_2$ = Estimate of rate of change in appropriately transformed GA area during the treatment phase

Square-root transformation of the GA area will be used in the model. If the square-root transformation does not achieve a sufficiently symmetric distribution, Box-Cox or logarithm transformations may be used.

The analysis will only include measurements from study eyes, will treat missing observations as missing completely at random (MCAR) and will be based on the enrolled population as outlined in Table 9. Table 9 also includes information described in Sections 10.0 and 11.0. Information will also be presented by participant (Listing 2).

If the estimate of β_2 is < 0 and the corresponding p-value is < 0.025, then the treatment is indicated to have slowed the rate of progression of GA

9.0 SECONDARY OUTCOMES ANALYSIS

The analysis of secondary outcomes will be considered exploratory in nature and will be based on per-protocol population 2, unless otherwise specified.

9.1 Area of GA based on Fundus Autofluorescence (FAF)

The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using FAF, will be assessed using Student's paired t-test for:

1. Study eyes alone
2. Qualifying fellow eyes alone
3. Study eyes and qualifying fellow eyes together

as shown in Table 10. This analysis will use appropriately transformed GA area, the enrolled population, and treat missing observations as MCAR. Rate of appropriately transformed GA area expansion will be calculated as follows for each participant:

Rate of appropriately transformed GA area expansion during run-in phase (mm/year) = (Appropriately transformed GA Area$_{\text{Month 9}}$ – Appropriately transformed GA Area$_{\text{Baseline}}$)/((Date $_{\text{Month 9}}$ – Date$_{\text{Baseline}}$)/365.25)

Rate of appropriately transformed GA area expansion during treatment phase (mm/year) = (Appropriately transformed GA Area$_{\text{Month 33}}$ – Appropriately transformed GA Area$_{\text{Month 9}}$)/((Date $_{\text{Month 33}}$ – Date$_{\text{Month 9}}$)/365.25)

The following hypotheses will be evaluated using the TTEST SAS procedure:

$$H_0: \Delta_{\text{Run-in phase}} = \Delta_{\text{Treatment phase}}$$

$$H_A: \Delta_{\text{Run-in phase}} \neq \Delta_{\text{Treatment phase}}$$

Where:

$\Delta_{\text{Run-in phase}}$ = Mean rate of appropriately transformed GA area expansion during the run-in phase

$\Delta_{\text{Treatment phase}}$ = Mean rate of appropriately transformed GA area expansion during the treatment phase.

9.2 Area of GA based on Color Fundus Photos (CFP)

GA area, based on CFP, will be assessed at all study visits in study and qualifying fellow eyes.

The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using CFP, will be assessed by fitting a linear spline regression model with a fixed knot at Month 9, similar to Model 1, in study eyes alone, qualifying fellow eyes alone and study and qualifying fellow eyes together (Table 11, Listing 3). Table 11 also includes information as outlined in Section 11.0). The outcome of the model will be GA area, that's appropriately transformed to satisfy the linear trend assumption. The analysis will treat missing observations as missing completely at random (MCAR).

9.3 Best-Corrected Visual Acuity (BCVA)

Visual acuity measures for each eye will be obtained using an electronic visual acuity (EVA) algorithm.

Mean rate of change in BCVA during the treatment phase will be compared to the mean rate of change in BCVA during the run-in phase using Student's paired t-test for

1. Study eyes alone
2. Qualifying fellow eyes alone
3. Study eyes and qualifying fellow eyes together

as shown in Table 12. Rate of change in BCVA during run-in and treatment phases as well as change in these rates between the phases will be presented as in Listing 4. Rate of change in BCVA will be calculated as follows for each participant:

Rate of change in BCVA during run-in phase (BCVA letters/month) = (BCVA letter score$_{\text{Month 9}}$ – BCVA letter score$_{\text{Baseline}}$)/((Date $_{\text{Month 9}}$ – Date$_{\text{Baseline}}$)/30.4)

Rate of change in BCVA during treatment phase (BCVA letters/month) = (BCVA letter score$_{\text{Month 33}}$ – BCVA letter score$_{\text{Month 9}}$)/((Date $_{\text{Month 33}}$ – Date$_{\text{Month 9}}$)/30.4)

Mean rate of change during the treatment phase will be assessed at Month 33 compared to Month 9. The following hypotheses will be evaluated using the TTEST SAS procedure:

$$H_0: \Delta_{\text{Run-in phase}} = \Delta_{\text{Treatment phase}}$$

$$H_A: \Delta_{\text{Run-in phase}} \neq \Delta_{\text{Treatment phase}}$$

Where:

$\Delta_{\text{Run-in phase}}$ = Mean rate of change in BCVA during the run-in phase

$\Delta_{\text{Treatment phase}}$ = Mean rate of change in BCVA during the treatment phase.

9.4 Low Luminance Visual Acuity (LLVA)

LLVA will be evaluated in a similar manner as BCVA (Table 13, Listing 5).

9.5 Central Retinal Thickness

Central retinal thickness, as measured on OCT, will be evaluated in a similar manner as BCVA (Table 14, Listing 6).

10.0 SENSITIVITY ANALYSES

Sensitivity analysis will be performed by assessing the difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using FAF, in study eyes by fitting a linear spline regression model with a fixed knot at Month 9, similar to Model 1, as follows:

1. Using enrolled population and multiple imputation (MI) for missing observations if >10% of the overall observations for the assessment and eye(s) being analyzed are missing. Observations are considered missing if for a given assessment and eye at a given visit, the participant has not previously terminated from the study, the visit is not missing, and the data for the given assessment and eye are not available. The rate of missingness, for all subjects (i=1, … n) will be calculated for a given outcome as follows:

$$\frac{\sum_{i=1}^{n} \#\ missing\ observations_i}{\sum_{i=1}^{n} \#\ visits\ prior\ to\ study\ completion/early\ termination_i * \#\ eyes\ _i} * 100$$

   Under the assumption that the transformation of the rates of change in GA area are normally distributed, the missing rates from the run-in and treatment phases will be predicted from each participant's observed area of GA and scheduled visits and joint relationships with other variables (e.g., participant's age, visual acuities, OCT measurements, etc.);

2. Using per-protocol population 1;
3. Using per-protocol population 2 and treating missing observations as MCAR;
4. Using per-protocol population 3 and treating missing observations as MCAR;

as outlined in Table 9 (note: Table 9 also includes information as described in Sections 8.0 and 11.0).

11.0 EXPLORATORY ANALYSES

Exploratory analyses supplement the primary and secondary outcome analyses.

The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using FAF, will be assessed by fitting a linear spline regression model with a fixed knot at Month 9, similar to Model 1, in:

1) qualifying fellow eyes alone and/or
2) study and qualifying fellow eyes together

as outlined in Table 9.

Further, the analysis may be repeated by determining the rate of change in appropriately transformed GA area during the treatment phase at other time points relative to Month 9 in study eyes alone, qualifying fellow eyes alone, and study and qualifying fellow eyes together. The association of IP compliance and drop-outs with treatment effect at Months 12, 15 and 21 may also be evaluated by adding IP compliance rates and/or drop-out rates to the model. Any lag in treatment effect may be assesed by adding another knot to the model. If there is sufficient data, the effect of rate of change in appropriately transformed GA area during the run-in phase on treatment response (i.e., rate of change in appropriately transformed GA area during the treatment phase) may be assessed. Further, appropriately transformed GA area will be plotted against time.

The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using FAF, will also be assessed using Student's paired t-test for study eyes alone, qualifying fellow eyes alone and/or study and qualifying fellow eyes together:

1) Using enrolled population and MI for missing observations if >10% of the observations are missing, similar to sensitivity analysis described in Section 10.0 above;
2) Using per-protocol population 1;
3) Using per-protocol population 2 and treating missing observations as MCAR;

as outlined in Table 10.The difference in the rate of GA area expansion from IP start visit (Month 9) to 24 months of treatment (Month 33) compared to initial study visit (Month 0) to IP start visit (Month 9), as determined using CFP, may be assessed by fitting a linear spline regression model with a fixed knot at Month 9, similar to Model 1, for (a) study eyes alone, qualifying fellow eyes

alone, and study and qualifying fellow eyes together, (b) enrolled population, per-protocol population 1 and/or per-protocol population 2, and/or (c) treating missing observerations as MCAR and/or using MI (Table 11).

Mean change in BCVA during the treatment phase may be compared to the mean change in BCVA during the run-in phase using Student's paired t-test for non-qualifying fellow eyes. A similar anlaysis may be performed for central retinal thickness. Further, mean change in BCVA during the treatment phase at time points other than Month 33 relative to Month 9 may be compared to the mean change in BCVA during the run-in phase using Student's paired t-test for study eyes alone, qualifying fellow eyes alone, study and qualifying fellow eyes together, and/or non-qualifying fellow eyes alone. A similar analysis may be performed for LLVA (except in non-qualifying fellow eyes) and central retinal thickness (except in non-qualifying fellow eyes) (Table 12 through Table 14).

The number of participants with a 3-line (15-letter) worsening in BCVA during the treatment phase will be compared with the number of participants with a worsening during the run-in phase using a Chi-square test. If any of the expected cell counts is < 5, then Fisher's exact test will be used (Table 12).

Other exploratory analyses may be performed as appropriate.

12.0 OCULAR SAFETY OUTCOMES

These presentations will be based on the safety population. All relevant information will be listed; data for all enrolled participants will be included in the listings. Outcome measurements or relevant change in outcome measurements may be plotted against time.

12.1 Best-Corrected Visual Acuity (BCVA)

Visual acuity is assessed at baseline and all follow-up visits in both eyes.

Total letters read at each visit and change from baseline at each follow-up visit will be presented by eye (study eye, qualifying fellow eye, study eye and qualifying fellow eyes together, non-qualifying fellow eye) (Table 15).

Change from baseline of 15 letter score or more is considered clinically significant and participants experiencing a loss of >30 letter score from baseline may be withdrawn from the study at investigator's discretion. Therefore, frequency and percentage of participants with change from baseline of >=15 letter score and loss of >30 letter score at each follow-up visit from baseline will be summarized.

12.2 Ocular Surface Changes and Inflammation

Participants are monitored for ocular surface changes and inflammation starting at Month 9 in both eyes. Ocular surface changes are defined as any changes to the ocular surface that are clinically apparent on slit lamp examination and/or newly symptomatic, i.e., representing a change from IP initiation at Month 9 that is clinically meaningful in the judgment of the investigator. For example, this could include a clinically meaningful new finding of, or worsening in, punctate keratopathy, infectious or inflammatory keratitis, or corneal scarring. Intraocular inflammation could include the presence of clinically meaningful anterior chamber inflammatory activity (haze, cells, and/or keratic precipitates), vitreous activity (haze and/or cells), and/or signs of posterior uveitis or retinal vasculitis. The number and percentage of participants with ocular surface changes and inflammation at each visit will be summarized by eye (study eye, qualifying fellow eye, study eye and qualifying fellow eyes together, non-qualifying fellow eye) (Table 16).

13.0 OTHER SAFETY OUTCOMES

These presentations will be based on the safety population, unless otherwise specified. All relevant information will be listed; data for all enrolled participants will be included in the listings. Outcome measurements or relevant change in outcome measurements may be plotted against time.

13.1 Adverse Events (AEs)

All treatment-emergent AEs reported will be summarized. Treatment-emergent AEs are those events occuring at the time of or after administration of first dose of study drug. Total number and percentage of participants with AEs and number of AEs will be summarized by severity of the AE, ocular specification (ocular vs. systemic) and relatedness to the IP (Table 17). AEs will also be summarized by system organ class (SOC) and preferred term (PT) (Table 18).

If sufficient data are present, summaries similar to Table 17 and Table 18 will be generated for all serious adverse events (SAEs) and pre-treatment AEs (i.e, AEs occuring during run-in phase), and summaries similar to Table 18 will be presented for natual progressions of the disease. Summaries of pre-treatment AEs will be based on the enrolled population.

All AEs, treatment-emergent or otherwise, will be listed.

13.2 Withdrawal from IP Due to Vision Loss, Adverse Events, and Treatment Failure

Participants who discontinue IP due to vision loss, AEs and treatment failure will be summarized in Table 1 and will be listed as outlined in Section 7.2 (see Section 5.0 for identification of such participants).

13.3 Low-Luminance Visual Acuity (LLVA)

LLVA is assessed at baseline and all follow-up visits except Months 6 and 12. The assessment will be performed only on study and qualifying fellow eyes. However, at investigator's discretion, the assessment may also be performed on the non-qualifying fellow eye.

Total letters read at each visit and change from baseline at each follow-up visit will be presented by eye (study eye, qualifying fellow eye, and study eye and qualifying fellow eyes together) (Table 19). Assessments performed on the non-qualifying fellow eyes will be included in listings.

13.4 Intraocular Pressure (IOP)

IOP is assessed at baseline and all follow-up visits in both eyes. IOP measurements at each visit and change from baseline at each follow-up visit will be summarized by eye (study eye, qualifying fellow eye, study eye and qualifying fellow eyes together, and non-qualifying fellow eye) (Table 20). Number of participants with IOP > 30 mmHg or change from baseline in IOP of > 10 mmHg will be included in the summary in Table 20 and the individual occurrences will be highlighted in the listing.

13.5 FAF Assessments

FAF image data are collected at all study visits in both eyes. The number and percentage of participants with decreased and increased autofluorescence (AF), various locations of definite decreased AF (DDAF), various junctional AF patterns (along with subcategories of diffused

junctional AF pattern) and significant medical findings at baseline and Months 9 and 33 will be summarized (Table 21). Participants whose images were obtained but could not be graded will be included in the denominators; participants for whom the assessment is not applicable or not evaluated will be excluded in the denominators.

In addition, total areas of definite, questionable, and definite + questionable decreased and increased AF as well as distance from foveal center to the nearest point on the retina not showing DDAF, questionably decreased autofluorescence (QDAF) or increased autofluorescence (IAF) at baseline and Months 9 and 33 will be summarized. Change from baseline at Month 9 and change from Month 9 at Month 33 will be included. If correction factor was used, then scaled measurements will be used in the table (Table 22).

Summaries may be presented for other visits as well.

13.6 CFP Assessments

CFP data are collected at all study visits in both eyes. The number and percentage of participants with macular GA, evidence of CNV and other features such as RPE hyperplasia/pigmentation and RPE depigmentation will be summarized at baseline and Months 9 and 33 (Table 23). Participants whose images were obtained but could not be graded will be included in the denominators; participants for whom the assessment is not applicable or not evaluated will be excluded from the denominators.

In addition, location of macular GA, total area of macular GA and distance from foveal center to nearest uninvolved retina at baseline and Months 9 and 33 will be summarized. Change from baseline at Month 9 and change from Month 9 at Month 33 will be included for total area of macular GA and distance from foveal center to nearest uninvolved retina. If correction factor was used, then scaled measurements will be used in the table (Table 24).

Summaries may be presented for other visits as well.

13.7 OCT Assessments

OCT data are collected at all study visits in both eyes, however, graded results from an external Reading Center are available only for baseline, Month 9 and Month 33. Central retinal thickness and linear GA enlargement on horizontal and vertical scans as measured on OCT at baseline,

Month 9 and Month 33 will be summarized. Change from baseline at Month 9 and change from Month 9 at Month 33 will be included (Table 25).

13.8 Physical Examination, Thyroid Palpation, Intracranial Hypertension, CNV and Optic Nerve Swelling

Participants are assessed for CNV at all visits and for intracranial hypertension and optic nerve swelling at all visits starting at Month 9. Physical examination is performed at baseline and thyroid palpation at all visits except Months 3, 6 and 12.

The number and percentage of participants with clinically significant physical examination and thyroid palpation findings, intracranial hypertension, CNV and optic nerve swelling will be summarized as outlined in Table 26.

13.9 Laboratory Assessments

Acute care panel, hepatic panel, complete blood count and thyroid function tests will be performed at baseline, Month 9, Month 15 and all visits thereafter.

Frequency and percentage of participants reporting laboratory abnormalities at baseline will be summarized with shift from baseline to each follow-up visit (Table 27).

13.10 Other Safety Outcomes

Exploratory analyses and/or descriptive summary statistics of other OCT parameters, microperimetry (including macular sensitivity measured using microperimetry) and other assessments will be presented as appropriate.

14.0 Rationale For Any Deviation From Pre-Specified Analysis Plan

Depending on the nature of the data, certain outcomes may be presented differently than outlined in this analysis plan. Tables and figures will be presented only when adequate amount of data are available. Data for some outcomes may not be available to the Coordinating Center at every visit. Because of this, these outcomes may not be presented until after study closure.

15.0 QUALITY ASSURANCE PLANS

To ensure accurate, reliable study results, two statisicians will seperately analyze and compare the primary study outcome. All SAS code used to generate primary and secondary outcomes will undergo a code audit by an independent project statistician. All protocol tables, figures, listings, and reports will also undergo review by a secondary statistician. Documentation of these audits will be kept on file at the Coordinating Center.

16.0 REFERENCES

1. Klein R, Klein BE, Jensen SC, Meuer SM. The five-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology. 1997;104(1):7-21.

2. Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy. The Beaver Dam Eye Study. Ophthalmology. 1992;99(6):933-43.

3. Edwards AO, Ritter R, 3rd, Abel KJ, Manning A, Panhuysen C, Farrer LA. Complement factor H polymorphism and age-related macular degeneration. Science. 2005;308(5720):421-4.

4. Hageman GS, Anderson DH, Johnson LV, Hancox LS, Taiber AJ, Hardisty LI, et al. A common haplotype in the complement regulatory gene factor H (HF1/CFH) predisposes individuals to age-related macular degeneration. Proc Natl Acad Sci U S A. 2005;102(20):7227-32.

5. Haines JL, Hauser MA, Schmidt S, Scott WK, Olson LM, Gallins P, et al. Complement factor H variant increases the risk of age-related macular degeneration. Science. 2005;308(5720):419-21.

6. Klein RJ, Zeiss C, Chew EY, Tsai JY, Sackler RS, Haynes C, et al. Complement factor H polymorphism in age-related macular degeneration. Science. 2005;308(5720):385-9.

7. Tuo J, Ning B, Bojanowski CM, Lin ZN, Ross RJ, Reed GF, et al. Synergic effect of polymorphisms in ERCC6 5' flanking region and complement factor H on age-related macular degeneration predisposition. Proc Natl Acad Sci U S A. 2006;103(24):9256-61.

8. Cousins SW, Espinosa-Heidmann DG, Csaky KG. Monocyte activation in patients with age-related macular degeneration: a biomarker of risk for choroidal neovascularization? Arch Ophthalmol. 2004;122(7):1013-8.

9. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol. 2001;119(10):1417-36.

10. Anderson DH, Mullins RF, Hageman GS, Johnson LV. A role for local inflammation in the formation of drusen in the aging eye. Am J Ophthalmol. 2002;134(3):411-31.

11. Johnson LV, Leitner WP, Staples MK, Anderson DH. Complement activation and inflammatory processes in Drusen formation and age related macular degeneration. Exp Eye Res. 2001;73(6):887-96.

12. Rodrigues EB. Inflammation in dry age-related macular degeneration. Ophthalmologica. 2007;221(3):143-52.

13. Holz FG, Bindewald-Wittich A, Fleckenstein M, Dreyhaupt J, Scholl HP, Schmitz-Valckenberg S. Progression of geographic atrophy and impact of fundus autofluorescence patterns in age-related macular degeneration. Am J Ophthalmol. 2007;143(3):463-72.

14. Sunness JS, Margalit E, Srikumaran D, Applegate CA, Tian Y, Perry D, et al. The long-term natural history of geographic atrophy from age-related macular degeneration: enlargement of atrophy and implications for interventional clinical trials. Ophthalmology. 2007;114(2):271-7.

17.0 MOCK SHELLS

TABLES

Table 1. Participant Disposition

Disposition	BEH (N=X) N (%)[a]	NEI (N=X) N (%)[a]	Total (N=X) N (%)[a]
Enrolled	**x (x)**	**x (x)**	**x (x)**
Run-in Phase (Baseline - Month 9)			
Discontinued study during run-in phase	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)
Insufficient therapeutic response	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Completed run-in phase	**x (x)**	**x (x)**	**x (x)**
Treatment Phase			
Month 9 – Month 33[b]			
Initiated treatment at Month 9	**x (x)**	**x (x)**	**x (x)**
Discontinued study prior to Month 33	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)
Insufficient therapeutic response	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Completed Month 33 visit	**x (x)**	**x (x)**	**x (x)**
Month 33-Month 45[c]			
Discontinued study after Month 33 and prior to Month 45	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)
Insufficient therapeutic response	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)

Table 1. Participant Disposition (continued)

Disposition	BEH (N=X) N (%)[a]	NEI (N=X) N (%)[a]	Total (N=X) N (%)[a]
Participant request/refusal	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Completed Month 45 visit	**x (x)**	**x (x)**	**x (x)**
Month 45-Month 57[c]			
Discontinued study after Month 45 and prior to Month 57	**x (x)**	**x (x)**	**x (x)**
AE/intercurrent illness	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)
Insufficient therapeutic response	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Completed Month 57 visit	**x (x)**	**x (x)**	**x (x)**
Completed study at or after Month 57 per-protocol	x (x)	x (x)	x (x)
Discontinued study at or after Month 57	x (x)	x (x)	x (x)
AE/intercurrent illness	x (x)	x (x)	x (x)
Death	x (x)	x (x)	x (x)
Insufficient therapeutic response	x (x)	x (x)	x (x)
Lost to follow-up	x (x)	x (x)	x (x)
Participant request/refusal	x (x)	x (x)	x (x)
Early study closure	x (x)	x (x)	x (x)
Protocol deviation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)

[a] Column header count and denominators are the number of participants in the enrolled population. Percentages are rounded to the nearest whole number.

[b] Primary outcome is assessed at Month 33.

[c] Minimum required follow-up is through Month 45. Common termination date is reached when the last recruited participant completes the study through Month 45. Prior to protocol Amendment L (Institutional Review Board approved on March 17, 2022), additional follow-up beyond Month 45 may be completed for those participants enrolled at the beginning of the study and continue on study until the common termination date. As of protocol Amendment L, participants could complete the study per-protocol prior to the common termination date and as early as Month 45 at the discretion of the Principal Investigator.

Table 2. Summary of Demographic Characteristics

Demographic Characteristics	BEH (N=X)[a]	NEI (N=X)[a]	Total (N=X)[a]
Gender, N (%)			
Male	x (x)	x (x)	x (x)
Female	x (x)	x (x)	x (x)
Age Category (years) at Baseline, N (%)			
55-60	x (x)	x (x)	x (x)
61-65	x (x)	x (x)	x (x)
66-70	x (x)	x (x)	x (x)
71-75	x (x)	x (x)	x (x)
76-80	x (x)	x (x)	x (x)
>80	x (x)	x (x)	x (x)
Age (years) at Baseline[b]			
N	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x
Range (Min, Max)	x, x	x, x	x, x
Ethnicity, N (%)			
Hispanic or Latino	x (x)	x (x)	x (x)
Not Hispanic or Latino	x (x)	x (x)	x (x)
Unknown	x (x)	x (x)	x (x)
Race, N (%)			
American Indian or Alaskan Native	x (x)	x (x)	x (x)
Asian	x (x)	x (x)	x (x)
Black	x (x)	x (x)	x (x)
Hawaiian or Pacific Islander	x (x)	x (x)	x (x)
White	x (x)	x (x)	x (x)
Multiple Race	x (x)	x (x)	x (x)
Unknown	x (x)	x (x)	x (x)

[a]Column header count and denominators are the number of participants in the enrolled population at the respective sites and overall. Percentages are rounded to the nearest whole number.
[b]Participants over the age of 89 (N=X at BEH, N=X at NEI, and N=X total) are excluded as ages over 89 are Protected Health Information (PHI).

Table 3. Medical and Ocular History

Conditions/Procedures	Study Eye (N=X) N (%)[a]	Fellow Eye		Total Participants (N=X) N (%)[a,d]
		Qualifying (N=X) N (%)[b]	Non-Qualifying (N=X) N (%)[c]	
Any Medical Condition				x (x)
Dizzy spells				x (x)
Hypertension				x (x)
Controlled				x (x)
Uncontrolled				x (x)
…				x (x)
Any Ocular Condition	x (x)	x (x)	x (x)	x (x)
Diabetic retinopathy	x (x)	x (x)	x (x)	x (x)
Uveitis	x (x)	x (x)	x (x)	x (x)
…	x (x)	x (x)	x (x)	x (x)
Any Ocular Procedure	x (x)	x (x)	x (x)	x (x)
Cataract surgery	x (x)	x (x)	x (x)	x (x)
YAG	x (x)	x (x)	x (x)	x (x)
…	x (x)	x (x)	x (x)	x (x)

Percentages are rounded to the nearest whole number.

[a]Column header count and denominators are the number of participants in the enrolled population at all sites.

[b]Column header count and denominators are number of participants in the enrolled population at all sites with qualifying fellow eye.

[c]Column header count and denominators are number of participants in the enrolled population at all sites with non-qualifying fellow eye.

[d]If a participant reported an ocular condition or procedure in both eyes, the participant will be counted only once in this column.

Table 4. Summary of Participant-Specific Protocol Deviations and Unanticipated Problems

	Number of Participants with Events			Number of Events		
	BEH (N=X) N (%)[a]	NEI (N=X) N (%)[a]	Total (N=X) N (%)[a]	BEH	NEI	Total
All events	x (x)	x (x)	x (x)	xx	xx	xx
Protocol deviations	x (x)	x (x)	x (x)	xx	xx	xx
Unanticipated problems	x (x)	x (x)	x (x)	xx	xx	xx
Type						
Minor	x (x)	x (x)	x (x)	xx	xx	xx
Not Serious	x (x)	x (x)	x (x)	xx	xx	xx
Serious	x (x)	x (x)	x (x)	xx	xx	xx
Pending Determination	x (x)	x (x)	x (x)	xx	xx	xx
Outcome						
Participant follow-up continues	x (x)	x (x)	x (x)	xx	xx	xx
Participant follow-up terminated	x (x)	x (x)	x (x)	xx	xx	xx
Investigational product remains stable	x (x)	x (x)	x (x)	xx	xx	xx
Investigational product returned or discarded	x (x)	x (x)	x (x)	xx	xx	xx
Other	x (x%)	x (x%)	x (x%)	xx	xx	xx

Prior to July 1, 2019, Investigators classified deviations and unanticipated problems as serious or not serious. Effective July 1 2019, Investigators classify deviations and unanticipated problems as minor or major and IRB classifies the major deviations and unanticipated problems as serious or not serious. Pending determination category corresponds to those major deviations or unanticipated problems that the IRB is yet to classify as serious or not serious.

[a]Column header count and denominators are the total number of participants enrolled at each site and overall. Percentages are rounded to the nearest whole number.

Table 5. Summary of Non-Participant Specific Protocol Deviations and Unanticipated Problems

	Number of Events		
	BEH	**NEI**	**Total**
All events	xx	xx	xx
Protocol deviations	xx	xx	xx
Unanticipated problems	xx	xx	xx
Type			
Minor	xx	xx	xx
Not Serious	xx	xx	xx
Serious	xx	xx	xx
Determination Pending	xx	xx	xx
Outcome			
Participant follow-up continues	xx	xx	xx
Participant follow-up terminated	xx	xx	xx
Investigational product remains stable	xx	xx	xx
Investigational product returned or discarded	xx	xx	xx
Other	xx	xx	xx

Prior to July 1, 2019, Investigators classified deviations and unanticipated problems as serious or not serious. Effective July 1 2019, Investigators classify deviations and unanticipated problems as minor or major and IRB classifies the major deviations and unanticipated problems as serious or not serious. Pending determination category corresponds to those major deviations or unanticipated problems that the IRB is yet to classify as serious or not serious.

Table 6. IP Compliance

Site	Participant ID	Visit	Number of Days on IP	Expected Number of Doses Taken	Number of Doses Taken	Number of Doses Missed	Compliance Rate[a]
BEH	BEH001	Month 9 to Month 12	xx	xx	xx	Xx	x.x
		Month 12 to Month 15	xx	xx	xx	xx	x.x
		Month 15 to Month 21	xx	xx	xx	xx	x.x
		…	xx	xx	xx	xx	x.x
		…	xx	xx	xx	xx	x.x
		Total	xx	xx	xx	xx	x.x
	BEH002	Month 9 to Month 12	xx	xx	xx	xx	x.x
		Month 12 to Month 15	xx	xx	xx	xx	x.x
		Month 15 to Month 21	xx	xx	xx	xx	x.x
		…	xx	xx	xx	xx	x.x
		…	xx	xx	xx	xx	x.x
	…	…	…	…	…	…	…
NEI	NEI001	…	…	…	…	…	…
		…	…	…	…	…	…
		Total	xx	xx	xx	xx	x.x

[a] Green highlighted cells indicate that the IP compliance rate is <50% between visits for a participant. Yellow highlighted cells (i.e., in "Total" rows) correspond to overall compliance rate <50%. Percentages are rounded to the nearest tenth.

Table 7. Missed Study Procedures

	BEH			NEI			Total		
	Expected[a]	Missed[b]	Percentage Missed[c]	Expected[a]	Missed[b]	Percentage Missed[c]	Expected[a]	Missed[b]	Percentage Missed[c]
By Participant									
BEH									
BEH001	xxx	xxx	xx.x						
BEH002	xxx	xxx	xx.x						
…	…	…	…						
NEI									
NEI001				xxx	xxx	xx.x			
NEI002				xxx	xxx	xx.x			
…				…	…	…			
By Procedure									
Acute Care Panel	xxx	xxx	xx.x	xxx	xxx	xx.x	xxx	xxx	xx.x
Adverse Event Assessment	xxx	xxx	xx.x	xxx	xxx	xx.x	xxx	xxx	xx.x
…	…	…	…	…	…	…	…	…	…
Total	xxx	xxx	xx.x	xxx	xxx	xx.x	xxx	xxx	xx.x

[a] The expected number of procedures is defined based on the study flowsheet included in the protocol.
[b] Procedures not completed are defined when the site reports a missed procedure or when the protocol monitors note missed procedures at a site visit.
[c] Percentages are rounded to the nearest tenth.

Table 8. Missed and Out of Window Study Visits

Site	Participant ID	Number of Expected Study Visits	Missed Study Visits			Out of Window Study Visits		
			Number	Percentage	Visits	Number	Percentage	Visits
BEH	BEH001	xx	xx	xx		xx	x.x	xx
	BEH002	xx	xx	xx	xxx	xx	x.x	xx
	…	xx	xx	xx		xx	x.x	xx
	Total	**xx**	**xx**	**xx**		**xx**	**x.x**	**xx**
NEI	NEI001	xx	xx	xx		xx	x.x	xx
	NEI002	xx	xx	xx	xxx	xx	x.x	xx
	…	xx	xx	xx		xx	x.x	xx
	Total	**xx**	**xx**	**xx**		**xx**	**x.x**	**xx**
All	**Total**	**xx**	**xx**	**xx**		**xx**	**x.x**	**xx**

Table 9. Analysis of Primary Outcome of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images and Corresponding Sensitivity and Exploratory Analyses

	Study Eye			Qualifying Fellow Eye			Study Eye + Qualifying Fellow Eye		
Population Used, Assumption	**Coefficient**	**SE**	**p-value**	**Coefficient**	**SE**	**p-value**	**Coefficient**	**SE**	**p-value**
Enrolled population, MCAR									
GA progression rate during run-in phase	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Difference in GA progression rate between run-in and treatment phases	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Enrolled population, MI									
GA progression rate during run-in phase	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Difference in GA progression rate between run-in and treatment phases	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Per-protocol population 1									
GA progression rate during run-in phase	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Difference in GA progression rate between run-in and treatment phases	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Per-protocol population 2, MCAR									
GA progression rate during run-in phase	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Difference in GA progression rate between run-in and treatment phases	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Per-protocol population 3, MCAR									
GA progression rate during run-in phase	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Difference in GA progression rate between run-in and treatment phases	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Abbreviations: SE - standard error, MCAR - missing completely at random, MI - multiple imputation

All analyses are based on appropriately transformed GA area.

Change in appropriately transformed GA area during run-in phase is assessed from Baseline to Month 9 and during treatment phase is assessed from Month 9 to Month 33.

Cells highlighted in green correspond to the primary outcome analysis; cells highlighted in yellow correspond to sensitivity analyses and the remaining correspond to exploratory analyses.

Table 10. Analysis of Secondary Outcome of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images and Corresponding Exploratory Analyses

	Study Eye		Qualifying Fellow Eye		Study Eye + Qualifying Fellow Eye	
Population Used, Assumption	**Mean (95% CI)**	**p-value**	**Mean (95% CI)**	**p-value**	**Mean (95% CI)**	**p-value**
Enrolled population, MCAR						
Difference in GA progression rate between run-in and treatment phases	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx
Enrolled population, MI						
Difference in GA progression rate between run-in and treatment phases	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx
Per-protocol population 1						
Difference in GA progression rate between run-in and treatment phases	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx
Per-protocol population 2, MCAR						
Difference in GA progression rate between run-in and treatment phases	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx	x.xx (x.xx, x.xx)	x.xx

Abbreviations: MCAR - missing completely at random, MI - multiple imputation

All analyses are based on appropriately transformed GA area.

Mean (95% CI) and two-sided p-value from Student's paired t-test conducted at type I error rate of 5%.

Cells highlighted in yellow correspond to secondary analyses and the remaining correspond to exploratory analyses.

Table 11. Analysis of Secondary Outcome of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using CFP and Corresponding Exploratory Analyses

This table will be similar to Table 9 and may not include all analyses outlined in Table 9.

Table 12. Analysis of Secondary Outcome of Change in BCVA

Eye	Statistic	Rate of Change during Run-in Phase Month 9 – Baseline	Rate of Change during Treatment Phase Month 33 – Month 9
Study Eye	N	x	x
	Mean (SD)	x.x (x.x)	x.x (x.x)
	Difference (95% CI)[a]		x.x (x.x, x.x)
	p-value[b]		x.xx
	Participants with 3-line worsening, N (%)	x (x)	x (x)
	p-value[3]		x.xx
Qualifying Fellow Eye	N	x	x
	Mean (SD)	x.x (x.x)	x.x (x.x)
	Difference (95% CI)[a]		x.x (x.x, x.x)
	p-value[b]	…	x.xx
	Participants with 3-line worsening, N(%)	x (x%)	x (x)
	p-value[c]		x.xx
Study Eye and Qualifying Fellow Eye	…	…	…
	…	…	…
Non-Qualifying Fellow Eye	…	…	…
	…	…	…

[a]Difference between mean rate of change during treatment phase vs. mean rate of change during run-in phase.

[a]p-value from Student's paired t-test corresponding to the difference in mean rate of change during the treatment phase vs. run-in phase.

[b]p-value from Chi-squared test or Fisher's exact test corresponding to the difference in proportions of participants with 3-line worsening between the treatment phase and run-in phase.

Table 13. Analysis of Secondary Outcome of Change in LLVA

This table will be similar to Table 12. This table will not include statistics for non-qualifying fellow eye and proportions of participants.

Table 14. Analysis of Secondary Outcome of Change in Central Retinal Thickness on OCT

This table will be similar to Table 12. This table will not include statistics for non-qualifying fellow eye and proportions of participants.

Table 15. Summary of BCVA Total Letters Read Over Time

	BCVA Total Letters Read				Change from Baseline			
Visit	**Study Eye**	**Qualifying Fellow Eye**	**Study Eye + Qualifying Fellow Eye**	**Non-Qualifying Fellow Eye**	**Study Eye**	**Qualifying Fellow Eye**	**Study Eye + Qualifying Fellow Eye**	**Non-Qualifying Fellow Eye**
Baseline								
N	x	x	x	x				
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)				
Median	x	x	x	x				
Range (Min, Max)	x, x	x, x	x, x	x, x				
Month 3								
N	x	x	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
Gain of >=15 letters, N (%)[a]					x (x)	x (x)	x (x)	x (x)
Loss of 15 to 30 letters, N (%)[a]					x (x)	x (x)	x (x)	x (x)
Loss of >30 letters, N (%)[a]					x (x)	x (x)	x (x)	x (x)
Month X								
…								
…								
…								
Month 57								
…								

[a]Denominators are the number of applicable eyes in the safety population with data at the given visit for the given eye(s).

Table 16. Summary of Ocular Surface Changes and Inflammation Over Time

	Ocular Surface Changes				Inflammation			
Visit	Study Eye n/N (%)	Qualifying Fellow Eye n/N (%)	Study Eye + Qualifying Fellow Eye n/N (%)	Non-Qualifying Fellow Eye n/N (%)	Study Eye n/N (%)	Qualifying Fellow Eye n/N (%)	Study Eye + Qualifying Fellow Eye n/N (%)	Non-Qualifying Fellow Eye n/N (%)
At least once during the study	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 9	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 12	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 15	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
…	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
…	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 57	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)

Denominators are the number of applicable eyes for participants in the safety population with data at the given visit for the given eye(s).

Table 17. Summary of Treatment-Emergent Adverse Events

	Participants with Events N (%)[a]	Number of Events N
All AEs	x (x)	x
Serious Adverse Events	x (x)	x
Severity		
Mild	x (x)	x
Moderate	x (x)	x
Severe	x (x)	x
Life-threatening	x (x)	x
Death	x (x)	x
Ocular Specification		
Non-ocular	x (x)	x
Study Eye	x (x)	x
Qualifying Fellow Eye	x (x)	x
Fellow Eye	x (x)	x
Relation to IP		
Related	x (x)	x
Not Related	x (x)	x

[a]Denominators are the number of participants in the safety population. Percentages are rounded to the nearest whole number.

Table 18. Summary of Treatment-Emergent Adverse Events by System Organ Class (SOC) and Preferred Term (PT)

MedDRA System Organ Class/Preferred Term[a,b]	Participants with Events N (%)[c]	Number of Events N
Total	x (x)	x
SOC1	x (x)	x
PT1	x (x)	x
PT2	x (x)	x
SOC2	x (x)	x
PT1	x (x)	x
PT2	x (x)	x
…	x (x)	x
…	x (x)	x

[a] MedDRA version XX.X.

[b] SOCs are presented in descending order of number of events reported; PTs within each SOC are also presented in descending order of number of events reported.

[c] Denominators are the number of participants in the safety population. Percentages are rounded to the nearest whole number.

Table 19. Summary of LLVA Total Letters Read Over Time

This table will be similar to Table 16. Rows corresponding to number and percentage of participants experiencing a change of 15 letters or more or loss of >30 letters from baseline as well as statistics for non-qualifying fellow eye will be excluded.

Table 20. Summary of IOP Over Time

This table will be similar to Table 16. Rows corresponding to number and percentage of participants experiencing change from baseline in letters read will be excluded. A row summarizing number and percentage of participants with IOP > 30 mmHg or an increase an increase from baseline of > 10mmHg will be added to the table.

Table 21. Summary of FAF Assessments at Baseline and Months 9 and 33

Visit	Study Eye n/N (%)	Qualifying Fellow Eye n/N (%)	Study Eye + Qualifying Fellow Eye n/N (%)
Baseline			
Decreased AF present			
No	x/X (x)	x/X (x)	x/X (x)
Yes	x/X (x)	x/X (x)	x/X (x)
Questionable	x/X (x)	x/X (x)	x/X (x)
Location of definite decreased AF			
Not subfoveal	x/X (x)	x/X (x)	x/X (x)
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)
Subfoveal	x/X (x)	x/X (x)	x/X (x)
Increased AF present			
No	x/X (x)	x/X (x)	x/X (x)
Yes	x /X (x)	x/X (x)	x/X (x)
Questionable	x/X (x)	x/X (x)	x/X (x)
Junctional AF pattern			
None	x/X (x)	x/X (x)	x/X (x)
Focal	x/X (x)	x/X (x)	x/X (x)
Banded	x/X (x)	x/X (x)	x/X (x)
Patchy	x/X (x)	x/X (x)	x/X (x)
Diffuse	x/X (x)	x/X (x)	x/X (x)
Fine granular	x/X (x)	x/X (x)	x/X (x)
Branching	x/X (x)	x/X (x)	x/X (x)
Trickling	x/X (x)	x/X (x)	x/X (x)
Reticular	x/X (x)	x/X (x)	x/X (x)
Fine granular with punctuated spots	x/X (x)	x/X (x)	x/X (x)
Significant medical findings	x/X (x)	x/X (x)	x/X (x)
Month 9			
Decreased AF present			
No	x/X (x)	x/X (x)	x/X (x)
Yes	x/X (x)	x/X (x)	x/X (x)
Questionable	x/X (x)	x/X (x)	x/X (x)
Location of definite decreased AF			
Not subfoveal	x/X (x)	x/X (x)	x/X (x)
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)
Subfoveal	x/X (x)	x/X (x)	x/X (x)
Increased AF present			
No	x/X (x)	x/X (x)	x/X (x)
Yes	x/X (x)	x/X (x)	x/X (x)
Questionable	x/X (x)	x/X (x)	x/X (x)

Table 21. Summary of FAF Assessments at Baseline and Months 9 and 33 (continued)

Visit	Study Eye n/N (%)	Qualifying Fellow Eye n/N (%)	Study Eye + Qualifying Fellow Eye n/N (%)
Junctional AF pattern			
None	x/X (x)	x/X (x)	x/X (x)
Focal	x/X (x)	x/X (x)	x/X (x)
Banded	x/X (x)	x/X (x)	x/X (x)
Patchy	x/X (x)	x/X (x)	x/X (x)
Diffuse	x/X (x)	x/X (x)	x/X (x)
Fine granular	x/X (x)	x/X (x)	x/X (x)
Branching	x/X (x)	x/X (x)	x/X (x)
Trickling	x/X (x)	x/X (x)	x/X (x)
Reticular	x/X (x)	x/X (x)	x/X (x)
Fine granular with punctuated spots	x/X (x)	x/X (x)	x/X (x)
Significant medical findings	x/X (x)	x/X (x)	x/X (x)
Month 33			
…			
…			
…			

Denominators are the number of applicable eyes for participants in the safety population with data at the given visit for the given eye(s). Participant eyes for which the FAF images could not be graded are included in the denominators. Participant eyes for which the assessment was not applicable or were not evaluated are excluded from this table.

Table 22. Summary of Total Areas of Decreased and Increased AF and Scaled Distance from Foveal Center as Assessed by FAF at Baseline and Months 9 and 33

	FAF Assessments			Change[a]		
Visit	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye
Baseline						
Total area of decreased AF (definite + questionable) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Total area of decreased AF (definite) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Total area of decreased AF (questionable) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Total area of increased AF (definite + questionable) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Total area of increased AF (definite) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			

Table 22. Summary of Total Areas of Decreased and Increased AF and Scaled Distance from Foveal Center as Assessed by FAF at Baseline and Months 9 and 33 (continued)

	FAF Assessments			Change[a]		
Visit	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye
Total area of increased AF (questionable) (mm^2)						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Distance from foveal center to nearest point on retina not showing DDAF[b], QDAF[c] or IAF[d] (mm)[b]						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Month 9						
Total area of decreased AF (definite + questionable) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Total area of decreased AF (definite) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Total area of decreased AF (questionable) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x

Table 22. Summary of Total Areas of Decreased and Increased AF and Scaled Distance from Foveal Center as Assessed by FAF at Baseline and Months 9 and 33 (continued)

	FAF Assessments			Change[a]		
Visit	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye
Total area of increased AF (definite + questionable) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Total area of increased AF (definite) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Total area of increased AF (questionable) (mm^2)						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Distance from foveal center to nearest point on retina not showing DDAF[b], QDAF[c] or IAF[d] (mm)[e]						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Month 33						
…						
…						
…						

[a]Change is calculated from baseline at Month 9 and from Month 9 at Month 33.

[b] DDAF – definite decreased autofluorescence

[c] QDAF – questionable decreased autofluorescence

[d] IAF – increased autofluorescence

[e]If linear measurement correction factor was used, then scaled values are used in the analysis.

Table 23. Summary of CFP Assessments at Baseline and Months 9 and 33

Visit/Parameter	Study Eye			Qualifying Fellow Eye			Study Eye + Qualifying Fellow Eye		
	No N (%)	Yes N (%)	Questionable N (%)	No N (%)	Yes N (%)	Questionable N (%)	No N (%)	Yes N (%)	Questionable N (%)
Baseline									
Geographic Atrophy									
Macular GA present	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
All sites of macular GA visible within the field of view of Field 2 fundus photos	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
CNV									
Evidence of CNV	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Hemorrhage	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Lipid	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Fluid	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Subretinal fibrosis	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Fibrosis subfoveal	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other CNV evidence	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other Features									
RPE hyperplasia/ pigment	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
RPE depigmentation	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Pattern dystrophy	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Pseudovitelliform lesion	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Vitreomacular traction (ERM, MH, other)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Evidence of laser or photodynamic therapy to the macula	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other disease likely to confound study outcome	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 23. Summary of CFP Assessments at Baseline and Months 9 and 33 (continued)

Visit/Parameter	Study Eye			Qualifying Fellow Eye			Study Eye + Qualifying Fellow Eye		
	No N (%)	Yes N (%)	Questionable N (%)	No N (%)	Yes N (%)	Questionable N (%)	No N (%)	Yes N (%)	Questionable N (%)
Other disease or finding unlikely to confound study outcome	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Significant medical finding	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Month 9									
…									
…									
Month 33									
…									
…									

Denominators are the number of applicable eyes for participants in the safety population with data at the given visit for the given eye(s). Participant eyes for which the CFP images could not be graded are included in the denominators. Participant eyes for which the assessment was not applicable or were not evaluated are excluded from this table.

Table 24. Summary of Macular GA and CNV as Assessed by CFP at Baseline and Months 9 and 33

	CFP Assessments			Change[a]		
Visit	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye	Study Eye	Qualifying Fellow Eye	Study Eye + Qualifying Fellow Eye
Baseline						
Macular GA location, n/N (%)[b]						
Not subfoveal	x/X (x)	x/X (x)	x/X (x)			
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)			
Subfoveal	x/X (x)	x/X (x)	x/X (x)			
Total area of macular GA (mm^2)[c]						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
Distance from foveal center to nearest uninvolved retina (mm)[c]						
N	x	x	x			
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)			
Median	x	x	x			
Range (Min, Max)	x, x	x, x	x, x			
CNV location in relation to fovea, n/N (%)[b]						
Not subfoveal	x/X (x)	x/X (x)	x/X (x)			
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)			
Subfoveal	x/X (x)	x/X (x)	x/X (x)			
Month 9						
Macular GA location, n/N (%)[b]						
Not subfoveal	x/N (x)	x/X (x)	x/X (x)			
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)			
Subfoveal	x/X (x)	x/X (x)	x/X (x)			
Total area of macular GA (mm^2)[c]						
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
Distance from foveal center to nearest uninvolved retina (mm)[c]						

Table 24. Summary of Macular GA and CNV as Assessed by CFP at Baseline and Months 9 and 33 (continued)

	CFP Assessments			Change[a]		
Visit	**Study Eye**	**Qualifying Fellow Eye**	**Study Eye + Qualifying Fellow Eye**	**Study Eye**	**Qualifying Fellow Eye**	**Study Eye + Qualifying Fellow Eye**
N	x	x	x	x	x	x
Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
Median	x	x	x	x	x	x
Range (Min, Max)	x, x	x, x	x, x	x, x	x, x	x, x
CNV location in relation to fovea, n/N (%)[b]						
Not subfoveal	x/X (x)	x/X (x)	x/X (x)			
Probably subfoveal	x/X (x)	x/X (x)	x/X (x)			
Subfoveal	x/X (x)	x/X (x)	x/X (x)			
Month 33						
…						
…						
…						

[a]Change is calculated from Baseline at Month 9 and from Month 9 at Month 33.

[b]Denominators are the number of applicable eyes for participants in the safety population with data at the given visit for the given eye(s). Percentages are rounded to the nearest whole number. Participant eyes for which the CFP images could not be graded are included in the denominators. Participant eyes for which the assessment was not applicable or were not evaluated are excluded from this table.
[c]If correction factor was used, then scaled values are used in the analysis.

Table 25. Summary of OCT Parameters Over Time

This table will be similar to Table 16. Rows corresponding to number and percentage of participants experiencing a change of 15 letters or more or loss of >30 letters from baseline as well as statistics for non-qualifying fellow eye will be excluded.

Table 26. Results of Physical Examination, Thyroid Palpation, Intracranial Hypertension, CNV and Optic Nerve Swelling Assessments Over Time

	Significant Findings			CNV				Optic Nerve Swelling			
Visit	Physical Examination n/N (%)[a]	Thyroid Palpation n/N (%)[a]	Signs of Intracranial Hypertension n/N (%)[a]	Study Eye n/N (%)[b]	Qualifying Fellow Eye n/N (%)[b]	Study Eye + Qualifying Fellow Eye n/N (%)[b]	Non-Qualifying Fellow Eye n/N (%)[b]	Study Eye n/N (%)[b]	Qualifying Fellow Eye n/N (%)[b]	Study Eye + Qualifying Fellow Eye n/N (%)[b]	Non-Qualifying Fellow Eye n/N (%)[b]
Baseline	x/X (x)	x/X (x)									
At least once during a follow-up visit		x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 9		x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 12			x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
…		x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
…		x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)
Month 57		x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)	x/X (x)

[a]Denominators are the number of participants in the safety population with data at the given visit.

[b]Denominators are the number of applicable eyes for participants in the safety population with data at the given visit for the given eye(s)

Table 27. Summary of Laboratory Assessments Over Time

Visit	Participants with Laboratory Assessments Done N[a]	Abnormal Laboratory Assessments N (%)[b]	Any Change from Baseline N (%)[b]	Clinically Significant Change from Baseline N (%)[b]
Baseline	x	x (x)		
Month 9	x		x (x)	x (x)
Month 15	x		x (x)	x (x)
Month 21	x		x (x)	x (x)
...	x		x (x)	x (x)
…	x		x (x)	x (x)
	x		x (x)	x (x)
Month 57	x		x (x)	x (x)

[a]Participants in the safety population with laboratory assessment data at the given visit.

[b]Denominators are the number of participants in the safety population with laboratory assessment data at the given visit. Percentages are rounded to the nearest whole number.

Listings

Listing 1. Demographic Information by Participant

Site	Participant ID	Registration Date	Study Eye*	Age	Gender	Race	Ethnicity
BEH	BEH001	mm/dd/yy	xx*	xx	xxx	xxx	xxx
	BEH002	mm/dd/yy	xx	xx	xxx	xxx	xxx
	…	mm/dd/yy	xx*	xx	xxx	xxx	xxx
NEI	NEI001	mm/dd/yy	xx*	xx	xxx	xxx	xxx
	…	mm/dd/yy	xx	xx	xxx	xxx	xxx

*Participant with qualifying fellow eye are indicated by an asterisk (*)

Listing 2. Rate of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images (Study Eye)

Site	Participant ID	Appropriately Transformed GA Area			Rate of Change in Appropriately Transformed GA Area		
		Baseline	Month 9	Month 33	During Run-in Phase: Month 9-Baseline	During Treatment Phase: Month 33-Month 9	Between Treatment and Run-in Phases
BEH	BEH001	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	BEH002	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	…	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
NEI	NEI001	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	…	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Listing 3. Rate of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using CFP

Site	Participant ID	Eye	Appropriately Transformed GA Area			Rate of Change in Appropriately Transformed GA Area		
			Baseline	Month 9	Month 33	During Run-in Phase: Month 9-Baseline	During Treatment Phase: Month 33-Month 9	Between Treatment and Run-in Phases
BEH	BEH001	Study eye	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Qualifying fellow eye	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Both	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	BEH002	Study eye	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Qualifying fellow eye	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Both	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
NEI	NEI001	…	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	…	…	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Listing 4. Rate of Change in BCVA During Run-in and Treatment Phases

This listing will be similar to Listing 3. Participants with 3-line worsening during either phase will be highlighted.

Listing 5. Rate of Change in LLVA During Run-in and Treatment Phases

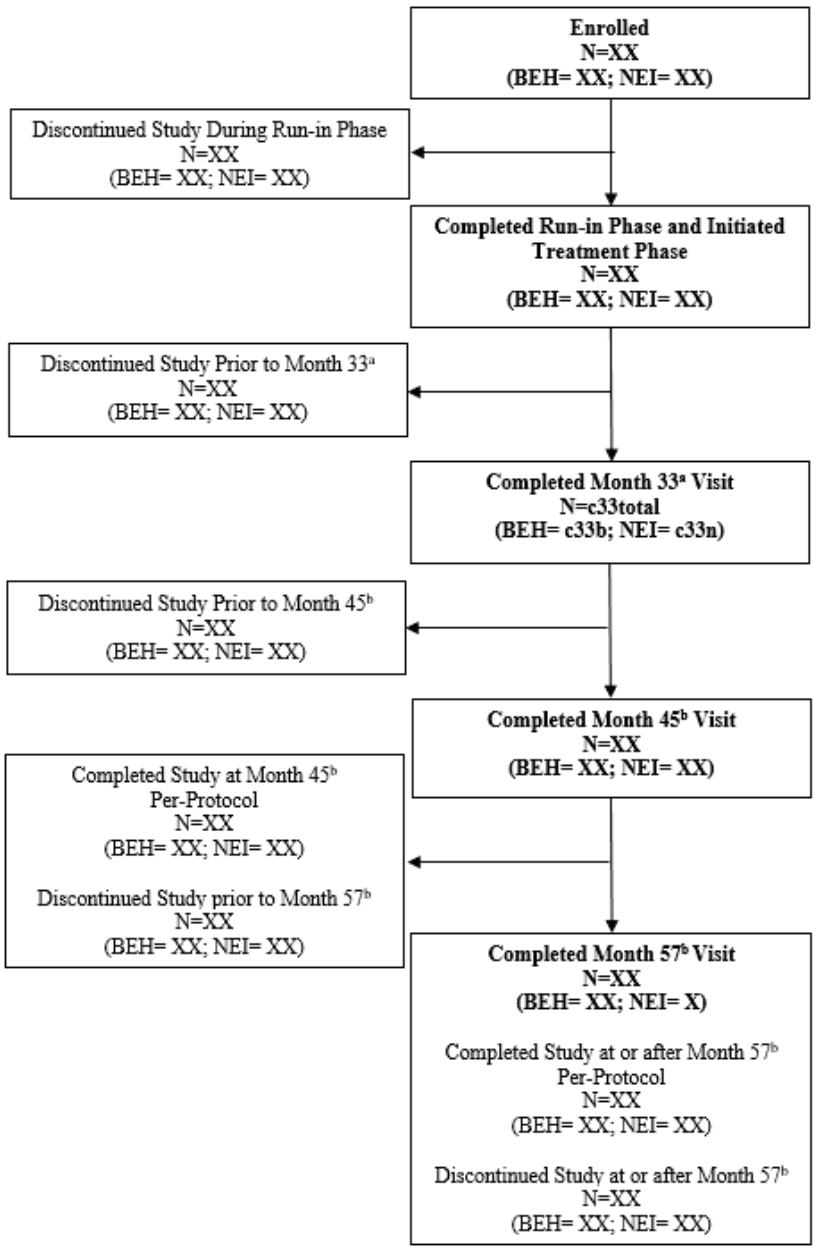
This listing will be similar to Listing 3.

Listing 6. Rate of Change in Central Retinal Thickness on OCT During Run-in and Treatment Phases

This listing will be similar to Listing 3.

Figures

Figure 1. Consort Diagram of Participant Disposition



[a] Primary outcome is assessed at Month 33.

[b] Minimum required follow-up is through Month 45. Common termination date is reached when the last enrolled participant completes the study through Month 45. Prior to Amendment L (Institutional Review Board approved on March 17, 2022), additional follow-up beyond Month 45 may be completed for those participants enrolled at the beginning of the study and continue on study until the common termination date. As of Amendment L, participants could complete the study per-protocol prior to the common termination date and as early as Month 45 at the discretion of the Principal Investigator.

18.0 PRIMARY OUTCOME ANALYSIS PRESENTATIONS

The primary outcome analysis report, to be completed after the final participant has completed their primary outcome visit (Month 33), will include all presentations included in the DSMC meeting immediately preceding the primary outcome analysis DSMC meeting as well as the SAP TFLs included in Table 28. Modifications to be made to TFLs prior to being included in the primary outcome analysis report, where applicable, are also outlined in Table 28.

Table 28. SAP-Specific Tables, Figures, and Listings (TFLs) to be Included in Primary Outcome Analysis Report

SAP TFL Number	SAP TFL Title	Modifications
Table 9[a]	Analysis of Primary Outcome of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images	Will include analyses for the study eye related to the enrolled population under the MCAR assumption.
Table 10[a]	Analysis of Secondary Outcomes of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images	Will include analyses for the study eye related to the enrolled population under the MCAR assumption.
Table 11[a]	Analysis of Secondary Outcome of Difference in Rates of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using CFP Images	Will include analyses for the study eye related to the enrolled population under the MCAR assumption.
Table 12	Analysis of Secondary Outcome of Change in BCVA	
Table 13	Analysis of Secondary Outcome of Change in LLVA	
Table 14	Analysis of Secondary Outcome of Change in Central Retinal Thickness on OCT	
Listing 2	Rate of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using FAF Images (Study Eye)	
Listing 3	Rate of Change in Appropriately Transformed GA Area During Run-in and Treatment Phases as Determined Using CFP	
Listing 4	Rate of Change in BCVA During Run-in and Treatment Phases	
Listing 5	Rate of Change in LLVA During Run-in and Treatment Phases	
Listing 6	Rate of Change in Central Retinal Thickness on OCT During Run-in and Treatment Phases	

[a]SAP TFL title modified for accuracy based on content of TFL to be included in primary outcome analysis report