Statistical Analysis Plan

for

A Pilot Study to Investigate Ustekinumab (STELARA®) for the Treatment of Active Sight-Threatening Uveitis

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VERSION HISTORY

Version/Date	Changes
1.0/30JAN2020	***Initial Document***
2.0/10NOV2020	***Sections 3.4.3:*** Updated other safety outcomes to clarify that laboratory assessments will include clinically significant changes from baseline and physical exams will include significant findings as well as vital signs; ***Section 4.2:*** Specified that additional ophthalmic assessments will be presented for the safety population; ***Section 6.2:*** Indicated that eligible eyes will be determined based on eye-specific inclusion criteria and presented by participant in a listing. ***Section 7.1:*** Updated per NIH Intramural Research Program Policy 801 and indicated that protocol deviations and unanticipated problems will be summarized by cohort and overall; ***Section 7.1.1, 7.1.2, 10.4:*** Indicated that information will be presented by cohort and overall; ***Section 9.0:*** Clarified that participants will be considered treatment responders if all eligible eyes met the definition for treatment response. ***Section 9.0, 10.0, and 11.0:*** Clarified that listings will include data from all enrolled participants. ***Section 9.0 and 10.2:*** Indicated that information will be presented for each eye. ***Section 10.1:*** Added boxplots presenting distribution of best-corrected visual acuity in each cohort at each visit ***Section 10.5:*** Added boxplots presenting distribution of central retinal thickness in each cohort at each visit ***Section 10.6:*** Added table summarizing number of participants experiencing quiescence ***Section 13.0:*** Indicated that additional ophthalmic assessments will be summarized by cohort and overall and based on the safety population ***Section 14.3:*** Specified that reported medications will be included in listing of physical examination findings ***Section 14.4:*** Added summaries for blood pressure and temperature and indicated that height and weight will also be included in vital signs listing ***Section 14.5:*** Indicated that responses to the vaccine reminder question from each visit will be presented by participant in a listing. ***Section 14.6:*** Indicated that additional safety presentations will include presentations for primary, secondary, and safety outcomes for all participants who received at least one dose of ustekinumab. ***Section 18.0:*** Made applicable corresponding updates described above to mock shells.

LIST OF ABBREVIATIONS

≥	Greater Than or Equal To
AC	Anterior chamber
BCVA	Best-corrected visual acuity
CBC	Complete blood count
CC	Clinical Center
CD	Crohn's Disease
EAU	Experimental autoimmune uveitis
ETDRS	Early Treatment Diabetic Retinopathy Study
EVA	Electronic visual acuity
FA	Fluorescein angiography
FDA	Food and Drug Administration
HIV	Human Immunodeficiency virus
IFN	Interferon gamma
IL	Interlukein
IOP	Intraocular pressure
IRB	Institutional Review Board
IV	Intravenous
mL	Milliliter
MTX	Methotrexate
NEI	National Eye Institute
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NLM	National Library of Medicine
NSAIDS	Nonsteroidal anti-inflammatory drugs
OCT	Optical coherence tomography
PPD	Purified protein derivative
PI	Principal Investigator
RCT	Randomized clinical trial
SAE	Serious Adverse Event
SC	Subcutaneous
SOP	Standard operating procedure
SUN	Standard of Uveitis Nomenclature
TB	Tuberculosis
TNF-alpha	Tumor necrosis factor alpha
VEGF	Vascular endothelial growth factor

1.0 INTRODUCTION

This statistical analysis plan (SAP) provides the proposed analyses for the protocol "A Pilot Study to Investigate Ustekinumab (STELARA®) for the Treatment of Active Sight-Threatening Uveitis" (STAR). This document has 18 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) treatment administration, (9) statistical analysis for primary outcome, (10) statistical analyses for secondary outcomes, (11) analysis of safety outcomes, (12) exploratory analyses, (13) additional ophthalmic assessments, (14) other safety assessments, (15) rationale for any deviations from this SAP, (16) quality assurance plans, (17) references, and (18) mock shells for proposed tables, figures, and listings. This document is based on version 10.0 of this protocol dated September 18, 2019. Any deviation from this SAP, not outlined in Section 15.0, will be described and justified in protocol amendments and/or in the final study report, as appropriate.

1.1 Uveitis

Uveitis, an inflammatory condition that affects the uvea (iris, ciliary body and choroid) and adjacent structures of the eyes, is an important cause of visual loss in both adults and children. A recent study in Northern California suggests that the incidence and prevalence of uveitis is three times what was previously thought, at 52/100,000 and 115/100,000 respectively.[1,2] It is believed that approximately 100,000 American citizens currently require the use of systemic corticosteroids or other immunosuppressive agents as treatment for ocular inflammation. It is particularly common to use immunosuppressive or immunomodulatory therapy for the treatment of posterior segment uveitis (intermediate, posterior or panuveitis), which are considered to be more likely to be sight threatening.[3] Management and prevention of the iatrogenic complications of immunosuppressive therapy accounts for most of the medical resources devoted to these individuals.[2]

Uveitis is a predominantly T-cell mediated immune disease, and drugs like cyclosporine targeted primarily at T-cells have demonstrated efficacy.[4] The dominant role of T-cells in the pathogenesis of uveitis is also observed in the experimental animal models of uveitis. Both Th1 and Th17 pathways are believed to drive inflammation in uveitis.[4] IL-12 and IL-23 are crucial parts of Th1 and Th17 pathways which have been implicated in autoimmune disorders including uveitis. IL-12, a heterodimer of p40 and p35 subunits, induces $CD4^+$ differentiation into Th1 cells which

produce interferon (IFN)-gamma and mediates cellular immunity. IL-23, also a heterodimer with p40 and p19 subunits, induces naïve CD4 cells to differentiate into Th17 cells which produce IL-17, IL-6 and tumor necrosis factor alpha (TNF-alpha) and similarly mediate cellular immunity. In addition, IL-12 and IL-23 each play an important role in the expression of experimental model of uveitis (EAU).[4,5] Anti-IL-12 administration in experimental uveitis models not only prevented the development of disease and pathogenic Th1 cells, but also induced suppressive Th2 cells.[6] Keino et. al. showed that oral administration of a potent IL-12/IL-23 inhibitor abrogated inflammation in an EAU both in afferent and efferent phases of the disease. They also found that IL-12/23 inhibitor administration also reduced the expansion of IL-17 producing cells.[7] Ustekinumab, by targeting the p40 subunit shared by both IL-12 and IL-23, offers a novel mechanism of action; it prevents IL-12/23 interaction with their receptors and blocks signaling through the IL-12β1 receptor, cell differentiation and cytokine production. IL-12 is also believed to be responsible for CD4+ cells escaping suppressor effects of regulatory T-cells (Tregs).[8] It is possible that IL-12/23 blockage may, in addition to inhibiting Th1 and Th17, also help expand regulatory T-cells through multiple mechanisms.

1.2 Ustekinumab

Ustekinumab is a human IL-12 and -23 antagonist and is currently approved by the FDA for the treatment of adult patients (18 years or older) with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Ustekinumab is administered by subcutaneous (SC) injection. For patients weighing ≤100 kg (220 lbs), the recommended dose is 45 mg initially and four weeks later, followed by 45 mg every 12 weeks. For patients weighing >100 kg (220 lbs), the recommended dose is 90 mg initially and four weeks later, followed by 90 mg every 12 weeks.

More recently, STELARA® is approved for moderate to severely active Crohn's disease. STELARA® is used for induction in intravenous (IV) infusion form at doses up to 520 mg/infusion (4 vials) for one infusion (at 6 mg/kg/infusion), followed by a single, SC 90 mg dose eight weeks after, and, for maintenance, a SC 90 mg dose every eight weeks thereafter.

Thousands of patients world-wide are treated for autoimmune disorders with various types of immunosuppressive and cytotoxic agents. Less toxic, more specific, or targeted immunosuppressive modalities are constantly being sought. Attempts to decrease morbidity, or reduce the dose of more toxic immunosuppressive drugs, or reduce the frequency or severity of

episodes of recurrence are clearly all important goals. Although previous clinical trials have not generated specific evidence, the involvement of IL-23 and IL-12 in the pathophysiology of uveitis and other autoimmune diseases known to be associated with uveitis and the clinical evidence from autoimmune diseases where ustekinumab has been used successfully suggests that ustekinumab could be a potential treatment for uveitis.[9]

2.0 DATA SOURCE

Data will be received from the National Eye Institute (NEI) via their electronic data capture system (EMR), which will then be uploaded on a daily basis to the Coordinating Center's database.

3.0 GENERAL REVIEW OF STUDY DESIGN

3.1 Study Design

The STAR study is a prospective, non-randomized, uncontrolled, single-center, two-arm pilot study to evaluate ustekinumab as a possible treatment for active intermediate uveitis, posterior uveitis or panuveitis. The first cohort will receive a 90 mg SC injection of ustekinumab at Baseline, Week 4 and Week 8. The second cohort will receive an initial high, weight-based dose of ustekinumab via IV infusion at the baseline visit, followed by a single, 90 mg SC injection of ustekinumab at Week 8. In second cohort participants who demonstrate allergic reaction to the first IV dose, the second dose can also be administered as IV infusion with pre-infusion desensitization instead of an SC injection as it allows better control on the rate of drug administration.

In both cohorts, participants will continue in the study for a total of 28 weeks, with follow-up visits monthly until Week 16 and a final safety visit at Week 28. Participants who experience recurrence (or those that are non-responders) by Week 16 can receive standard of care. Participants may continue to receive ustekinumab through Week 8 unless there is a medical contraindication (e.g., severe infection or severe allergic reaction). Participants will be instructed to contact the study investigators and return to the clinic as soon as possible for evaluation upon experiencing any symptoms of flare-up. Such symptoms include blurred vision, decreased visual acuity, floaters, pain, redness, irritation or photophobia.

3.2 Study Objective

The study objective is to investigate the safety, tolerability and potential efficacy of ustekinumab as a possible treatment for active intermediate uveitis, posterior uveitis or panuveitis.

3.3 Study Population

The first cohort will consist of five participants with active intermediate uveitis, posterior uveitis or panuveitis who meet the eligibility criteria. The second cohort will include up to four participants with active intermediate uveitis, posterior uveitis or panuveitis who meet the eligibility criteria. Up to eleven participants may be enrolled, as up to two additional participants may be accrued in the second cohort to account for participants who withdraw from the study prior to Week 16.

3.3.1 Participant Eligibility Criteria

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

3.3.1.1 Inclusion Criteria

1. Participant has the ability to understand and sign the informed consent document.
2. Participant is 18 years of age or older.
3. Participant has negative purified protein derivative (PPD) or quantiferon testing done within three months prior to enrollment or had latent tuberculosis (TB) but has completed prophylactic anti-TB treatment.
4. Participant has active intermediate uveitis, posterior uveitis or panuveitis in at least one eye requiring systemic therapy. Active disease is defined as:
    - +1 or more vitreous haze (according to Standardization of Uveitis Nomenclature (SUN) criteria[10]) AND/OR
    - Active chorioretinitis or leakage on fluorescein angiography (FA) (that is in more than one quadrant) that requires treatment.
5. Participant has visual acuity in at least one eye of 20/400 or better.
6. Participant is willing and able to comply with the study procedures.

7. Female participants of childbearing potential must not be pregnant or breast-feeding, have a negative pregnancy test at screening and must be willing to undergo pregnancy testing throughout the study.
8. Both female participants of childbearing potential and male participants able to father a child must have (or have a partner who has) had a hysterectomy or vasectomy, be completely abstinent from intercourse or must agree to practice two effective methods of contraception throughout the course of the study and for six weeks after the last investigational product injection. Acceptable methods of contraception for this study include:
    - hormonal contraception (i.e., birth control pills, injected hormones, dermal patch or vaginal ring),
    - intrauterine device,
    - barrier methods (diaphragm, condom) with spermicide, or
    - surgical sterilization (tubal ligation).

3.3.1.2 Exclusion Criteria

1. Participant has a significant active infection (an infection requiring treatment as determined by the medical team), including active TB or human immunodeficiency virus (HIV).
2. Participant received a live vaccination within the past six weeks.
3. Participant is expected to receive a live vaccination at any time during the study.
4. Participant received the Bacillus Calmette-Guérin (BCG) vaccine within the past year.
5. Participant is expected to receive the BCG vaccine at any time during the study or up to one year after discontinuing ustekinumab.
6. Participant has a history of cancer (other than a non-melanoma skin cancer) diagnosed within the past five years.
7. Participant has received intraocular (or periocular) steroid or anti-vascular endothelial growth factor (VEGF) injections within the last six weeks.
8. Participant received rituximab within the last six months or another biologic agent (e.g., infliximab, daclizumab, adalimumab) within the last two months.
9. Participant has received alkylating agents (e.g., cyclophosphamide, chlorambucil) within the last nine months.
10. Participant has a known hypersensitivity to ustekinumab or any of its components.

3.3.1.3 Choice of Study Eye

Since this is a systemic treatment, a study eye selection does not apply. Any eye meeting the eligibility criteria will be considered in the primary outcome. All eyes will be considered in the remaining outcomes.

3.4 Outcomes

3.4.1 Primary Study Outcome

The primary outcome for each cohort is the number of participants who experience a treatment response by Week 16.

3.4.2 Secondary Study Outcomes

The secondary outcomes include the following, as relevant to baseline:

- Mean and median change in visual acuity via electronic visual acuity (EVA) at all follow-up visits;
- Number of participants who experience a recurrence;
- Mean and median number of days following the baseline injection until first recurrence (of the participants who recur);
- Presence or extent of macular edema as determined by optical coherence tomography (OCT) and FA at all follow-up visits;
- Amount of retino-vascular leakage as measured by FA at all follow-up visits;
- Changes in retinal thickening as measured by OCT at all follow-up visits;
- Length of time to quiescence;
- Ability to taper concomitant immunosuppressive medications.

3.4.3 Safety Outcomes

Protocol-specified safety outcomes include:

- Number and severity of systemic and ocular toxicities and adverse events (AEs);
- Proportion of participants with loss of ≥15 letters at any follow-up visit;
- Number of participants experiencing a clinically significant increase in elevated intraocular pressure (IOP) at any follow-up visit. A change ≥10 mmHg as compared with baseline is considered a clinically significant increase.

3.4.4 Exploratory Outcomes

Participant serum and lymphocytes will be analyzed for soluble cytokines, exosomes, and intracellular immune markers as well as RNA-Seq before and after therapy at regular time points. Lymphocyte proliferation prior to and following treatment will be assessed. The changes in epigenetic modification following treatment will be addressed.

4.0 STATISTICAL CONSIDERATIONS

4.1 Sample Size Calculation

The accrual goal is five participants in the first cohort and four participants in the second cohort, for a total of nine participants. Up to two additional participants may be accrued in the second cohort to account for participants who withdraw from the study prior to Week 16. No formal sample size calculation was conducted, since this pilot study will not attempt to definitively determine the safety or efficacy of this treatment.

4.2 Analysis Population

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, and compliance will be based on this population.

Primary Analysis population: Includes all enrolled participants who received at least one dose of ustekinumab and completed the Week 16 visit. The primary, secondary, and safety analyses will be based on this population.

Safety population: Includes all enrolled participants who receive at least one dose of ustekinumab. The additional ophthalmic assessments and safety parameters described in Sections 13.0 and 14.0 will be based on this population.

4.3 Descriptive Statistics

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

4.4 Handling Duplicate Assessments

The assessments at each visit may be completed over multiple days. If participants completed assessments at both scheduled and supplementary visits, the assessments from the scheduled visit will be considered in the analysis and tabular summaries. However, if an assessment is completed only at supplementary visits, then the assessment from the most recent supplementary visit will be included in the analysis and tabular summaries. Results of all assessments, including those performed during supplementary visits, will be included in the listings.

4.5 Handling of Missing Values

In general, missing observations will be excluded from analyses.

4.6 Software for Analyses

Statistical analyses will be performed using SAS v9.4 or higher or R v3.6.1 or higher. All tables, listings and figures presented in the analysis will be created using either SAS v9.4 or Rv3.6.1 or higher.

5.0 PARTICIPANT DISPOSITION

Participant disposition including the number of participants enrolled, received treatment at each visit, discontinued treatment early, terminated the study early, and completed the study will be summarized for each cohort and overall as in Table 1. A consort diagram showing participant flow will be included as in Figure 1. Reasons for treatment and study discontinuation will also be summarized in Table 1 and listed by participant (see Section 7.2). These presentations will be based on the enrolled population.

6.0 PARTICIPANT CHARACTERISTICS

These presentations will be based on the enrolled population.

6.1 Participant Demographics

Demographic data including baseline age, gender, race and ethnicity will be summarized by cohort and overall (Table 2) and presented by participant.

6.2 Determination of Eligible Eyes

Since this is a systemic treatment, a study eye selection does not apply. Any eye meeting the eligibility criteria will be considered in the outcomes. Eye eligibility will be determined based on the eye-specific items in the inclusion criteria. An eye must meet the criteria defined below to be eligible.

- The eligible eye has active intermediate uveitis, posterior uveitis or panuveitis in at least one eye requiring systemic therapy. Active disease is defined as:
  - +1 or more vitreous haze (according to Standardization of Uveitis Nomenclature (SUN) criteria[10]) AND/OR
  - Active chorioretinitis or leakage on fluorescein angiography (FA) (that is in more than one quadrant) that requires treatment.
- The eligible eye has visual acuity of 20/400 or better.

Eligible eyes will be presented by participant in a listing.

Only eligible eyes will be considered in the primary outcome analysis. All eyes, regardless of eligibility, will be considered in the remaining presentations.

6.3 Medical, Medication, and Ocular History

History of medical and ophthalmic conditions and procedures and medication history will be summarized by cohort and overall (Tables 3 and 4) and presented by participant.

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 cohort and overall as in Table 5.

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 type (minor, serious, not serious, or pending determination by IRB) and outcome of events will also be summarized (Table 5). Listings of participant-specific and non-participant-specific protocol deviations and unanticipated problems will be presented.

7.1.1 Study Procedure Deviations

Table 6 presents the expected number of procedures, and number and percentage of procedures missed by participant, cohort, procedure, and cumulatively across all participants. Number of procedures missed is defined when a 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 and will also be presented as a sum. Percentage of procedures missed will be calculated as follows:

$$\%_{\text{procedures missed}} = (N_{\text{procedures missed}} / N_{\text{expected procedures}}) * 100$$

7.1.2 Visit Schedule Deviations

The number of expected visits, number and percentage of missed visits, and number and percentage of out-of-window visits will be summarized by participant, cohort, and cumulatively across all participants as in Table 7. The percentage of missed and out of window study visits will be calculated as follows:

$$\%_{\text{missed visits}} = (N_{\text{missed visits}} / N_{\text{expected visits}}) * 100$$

$$\%_{\text{out of window visits}} = (N_{\text{out of window visits}} / N_{\text{expected visits}}) * 100$$

7.2 Premature Treatment and Study Withdrawals

Participants who withdrew from treatment and study early will be summarized as in Table 1 and listed separately along with reasons(s) for withdrawal.

8.0 INVESTIGATIONAL PRODUCT (IP) ADMINISTRATION

Details of ustekinumab administration will be presented by participant. The listings will include date of visit and associated visit number, location of injection or start/end time of infusion (as applicable), whether treatment was not administered or stopped before completion for any reason, and any complications experienced.

9.0 PRIMARY OUTCOME ANALYSIS

The analysis of primary outcome will be exploratory and descriptive; no formal hypothesis testing will be performed. These presentations will be based on the primary analysis population; data from all enrolled participants will be included in the corresponding listings.

Treatment response is defined in the protocol as (all of the below for both/eligible eyes):

- No active inflammatory chorioretinal lesion and/or absent or decreased retinal vascular leakage
- ≤ 0.5+ anterior chamber (AC) cells (SUN criteria)
- ≤ 0.5+ vitreous haze (VH; NEI/SUN criteria)

A participant is considered a treatment responder if all eligible eyes met the definition for treatment response.

The definition of treatment response referencing the variables as specified in the case report forms will be as follows:

At least one of the following criteria in each eligible eye:

- No active inflammatory chorioretinal lesions
- Absent retinal vascular lesion
- Decreased retinal vascular lesions

AND all of the following criteria in each eligible eye:

- AC cells graded as 0, 0.5, or Trace
- VH graded as Clear or Trace

Table 8 summarizes the number and percentage of participants who achieved the treatment response criteria in each all eligible eyes at each visit and cumulatively by Week 16, by cohort and overall.

Treatment response by specific criteria and overall will be presented by participant as in Listing 1.

10.0 SECONDARY OUTCOMES ANALYSIS

These presentations will be based on the primary analysis population; data from all enrolled participants will be included in the corresponding listings.

10.1 Best-Corrected Visual Acuity (BCVA)

BCVA with manifest refraction is assessed at baseline and all follow-up visits in both/eligible eyes. Total letters read and change from baseline in total letters read will be summarized by cohort and overall as in Table 9 and presented by participant as in Listing 2. Boxplots showing distribution of change from baseline in BCVA at each visit will be presented as in Figure 2. Frequency and percentage of participants presenting with a loss of ≥ 15 letters from baseline at each follow-up visit will be included in Table 9.

10.2 Recurrence of Uveitis

The criteria for recurrence of uveitis will be evaluated at all follow-up visits.
Recurrence is defined in the protocol as presence of one of the following four parameters in at least one eye:

1. New active inflammatory chorioretinal lesion and/or retinal vascular leakage.
2. A 2+ increase in AC cells relative to baseline (SUN criteria). This is represented by a change of Grade 0 to Grade 2+; or Grade 0.5+ to Grade 3+.
3. A 2-step increase in vitreous haze relative to baseline (NEI/SUN criteria). This is represented by a change of Grade 0 to Grade 2+; or Grade 0.5+ to Grade 3+.
4. Worsening of BCVA by ≥ 15 letters (ETDRS) relative to baseline.

The definition of recurrence referencing the variables in the case report forms will be as follows:

At least one of the following criteria in **at least one eye**:

- New/increased active inflammatory chorioretinal lesion

- New/increased retinal vascular lesion
- One of the following changes in AC cell grading compared to baseline: 0 to 2+, 0.5 to 3+, 1 to 3+, 2 to 4
- One of the following changes in VH grading compared to baseline: 0 to 2+, T to 3+, 1 to 3+, 2 to 4.
- Worsening of BCVA by ≥ 15 letters relative to baseline

Table 10 will summarize the number of participants who experience recurrence of uveitis in each eye at each visit by cohort and overall. Number of days until first recurrence will be summarized for each eye and cumulatively by cohort and overall as in Table 11 and specific recurrence criteria and days until first recurrence will be presented by participant (Listing 3).

10.3 Macular Edema

Presence or extent of macular edema will be analyzed by researchers at the NEI.

10.4 Retino-vascular leakage

Number and percentage of participants experiencing presence and increase of active inflammatory retinal vascular lesions will be summarized by cohort and overall as in Table 12 and presented by participant as in Listing 4.

10.5 Changes in Retinal Thickening

Central retinal thickness at each visit and changes from baseline in central retinal thickness will be summarized by cohort and overall as in Table 13 and presented by participant as in Listing 5. Boxplots showing distribution of change from baseline in central retinal thickness at each visit will be presented as in Figure 3.

10.6 Length of Time to Quiescence

Quiescence will be defined as the absence of active disease.

Active disease is defined in the protocol as:

- +1 or more VH (according to SUN criteria[10]); and/or
- Active chorioretinitis or leakage on FA (that is in more than one quadrant) that requires treatment.

The definition of quiescence, referencing the variables in the case report forms, will be as follows: **All** of the following in the specified eye:

- VH grading of 0 (Clear) or T (Trace)
- Absence of active chorioretinitis
- Absence of leakage on FA (that is more than one quadrant) that requires treatment

Length of time to quiescence in each eye will be summarized by cohort and overall as in Table 14. Number of participants experiencing quiescence in each eye will be summarized by cohort and overall as in Table 15. Quiescence criteria in each eye and time until quiescence will be presented by participant as in Listing 6.

10.7 Ability to Taper Concomitant Immunosuppressive Medications

Tapering of concomitant immunosuppressive medications, including medication name, starting dose, steroid indication, and the target and actual dates and doses of the tapering will be presented by participant as in Listing 7.

11.0 SAFETY OUTCOMES

These presentations will be based on the primary analysis population; data from all enrolled participants will be included in the corresponding listings.

11.1 Adverse Events (AEs)

Table 16 will summarize total number and percentage of participants with AEs by severity of the AE, ocular specification (ocular vs. systemic) and relation to IP. A summary of AEs by Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) and preferred term (PT) will be presented as in Table 17. Additional details for all reported AEs will be presented by participant, with serious adverse events (SAEs) highlighted in red. If sufficient data are present, summaries similar to Table 16 and 17 will be generated for SAEs. Events corresponding to natural progression of the disease will be listed by participant. If sufficient data are present, summaries similar to Tables 16 and 17 will be presented for these events.

11.2 Loss of ≥ 15 Letters

The proportion of participants with loss of ≥ 15 total letters read will be included in the BCVA summary in Table 9 and the individual occurrences will be highlighted in the listing.

11.3 Intraocular Pressure (IOP)

IOP is assessed at baseline and all follow-up visits in both eyes. IOP will be summarized for each eye by cohort and overall as in Table 18 and presented by participant in a listing. A change ≥ 10 mmHg relative to baseline is considered a clinically significant increase in IOP. Number of participants experiencing this change will be included in the summary in Table 18 and the individual occurrences will be highlighted in the listing.

12.0 EXPLORATORY OUTCOMES

Exploratory outcomes will be analyzed by researchers at the NEI.

13.0 ADDITIONAL OPHTHALMIC ASSESSMENTS

The following additional ophthalmic assessments are conducted at each visit and will be presented by participant and summarized by cohort and overall as in Tables 19-23. These presentations will be based on the safety population.

- Anterior Chamber Cells
- Anterior Chamber Flare
- Vitreous Cells
- Vitreous Haze
- Active Chorioretinitis and Chorioretinal Lesions
- FA Leakage in More Than One Quadrant (requiring treatment)

14.0 OTHER SAFETY ASSESSMENTS

These presentations will be based on the safety population.

14.1 Withdrawal from IP due to Vision Loss, Adverse Events, and Treatment Failure

Participants who discontinue IP due to vision loss (manually identified based on investigator's comments for those participants with reason for withdrawal from IP indicated as "safety withdrawal"), 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 summarized in Table 1 and will be listed as outlined in Section 7.2.

14.2 Laboratory Assessments

Laboratory assessments including complete blood count (CBC) with differential, acute care, mineral and hepatic panels, and urinalysis are collected at baseline, Week 4, Week 8, and Week 28.

Abnormal lab results, as well as clinically significant changes from baseline, will be presented by participant for each visit. Frequency and percentage of participants reporting laboratory abnormalities at baseline and changes from baseline will be summarized at each follow-up visit in Table 24.

14.3 Physical Examination

Physical examinations are conducted at baseline, Week 4, Week 8, and Week 28. Notable physical exam findings, as well as clinically significant changes from baseline and reported medications, will be presented by participant for each visit. Frequency and percentage of participants reporting significant physical exam findings at each visit will be summarized as in Table 25.

14.4 Vital Signs

Vital signs are recorded at baseline and all follow-up visits. Blood pressure and temperature at each visit and change from baseline at each follow-up visit will be summarized by cohort and overall (Tables 26 and 27) and presented by participant. Height and weight at each visit will also be included in the listing.

14.5 Vaccine Reminders

At each visit, the site staff filling out the case report form will be asked if the participant was reminded to avoid live vaccines while on ustekinumab and reminded about the risks of exposure to household members who receive a live vaccine. Responses to this question will be presented by participant in a listing.

14.6 Additional Safety Presentations

In the event that one or more participants discontinue therapy prior to reaching Week 16, the presentations for primary, secondary, and safety outcomes will be repeated for the safety

population, in a similar manner as described in Sections 9.0-11.0. These presentations will be similar to Tables 8-18.

15.0 Rationale for any Deviations 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 an adequate amount of data is available. Data for some outcomes may not be available to the Coordinating Center at every visit. Because of this, some outcomes may not be presented until after study closure.

16.0 Quality Assurance Plans

To ensure accurate, reliable study results, 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.

17.0 REFERENCES

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18.0 MOCK SHELLS

TABLES

Table 1. Participant Disposition

Disposition	Cohort 1 N (%)[1]	Cohort 2 N (%)[1]	Overall N (%)[1]
Enrolled	**x**	**x**	**x**
Received at least one dose of IP (Safety Population)	**x (x)**	**x (x)**	**x (x)**
Received IP at Week 0	x (x)	x (x)	x (x)
Received IP at Week 4	x (x)	N/A	x (x)
Received IP at Week 8	x (x)	x (x)	x (x)
Discontinued IP Early	**x (x)**	**x (x)**	**x (x)**
Reason for Discontinuation[2]			
Participant non-compliance	x (x)	x (x)	x (x)
Therapy unavailable	x (x)	x (x)	x (x)
Safety withdrawal	x (x)	x (x)	x (x)
Lack of efficacy	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Terminated Early from the Study	**x (x)**	**x (x)**	**x (x)**
Reason for Termination[3]			
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/violation	x (x)	x (x)	x (x)
Other	x (x)	x (x)	x (x)
Completed Study through Week 16 (Primary Analysis Population)	**x (x)**	**x (x)**	**x (x)**
Completed Study through Week 28	**x (x)**	**x (x)**	**x (x)**

[1]Denominators are the number of participants in the enrolled population in the respective cohort or overall, unless otherwise specified. Percentages are rounded to the nearest whole number.
[2]Denominators are the number of participants who discontinued IP early.
[3]Denominators are the number of participants who terminated early from the study.

Table 2. Summary of Participant Demographics

Demographic Characteristics	Cohort 1 (N=X)[1]	Cohort 2 (N=X)[1]	Overall (N=X)[1]
Gender, N (%)			
Male	x (x)	x (x)	x (x)
Female	x (x)	x (x)	x (x)
Age Category (years) at Baseline, N (%)			
18-25	x (x)	x (x)	x (x)
26-30	x (x)	x (x)	x (x)
31-35	x (x)	x (x)	x (x)
36-40	x (x)	x (x)	x (x)
41-45	x (x)	x (x)	x (x)
46-50	x (x)	x (x)	x (x)
51-55	x (x)	x (x)	x (x)
56-60	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			
N	x	x	x
Mean (SD)	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)

[1]Column header counts and denominators are the number of participants in the enrolled population in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 3. Medical and Medication History

Conditions	Cohort 1 (N=X) N (%)[1]	Cohort 2 (N=X) N (%)[1]	Overall (N=X) N (%)[1]
Any Medical Condition	x (x)	x (x)	x (x)
CVA/TIA			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
MI			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Hypertension			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Hypercholesterolemia			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Renal failure			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Diabetes			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Autoimmune disease			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Cancer			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Active infection			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
PPD			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Live vaccine within the last three months			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
BCG vaccine within the last year			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Expected to receive BCG vaccine			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Any Medication History	x (x)	x (x)	x (x)
Rituximab within the last year			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Other biologic (infliximab, daclizumab, adalimumab) within past six months			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)
Alkylating agent (cyclophosphamide, chlorambucil) within the last year			
Yes	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)

[1]Column header count and denominators are the number of participants in the enrolled population in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 4. Ocular History

Conditions/Procedures	Cohort 1 OD (N=X) N (%)[1]	Cohort 1 OS (N=X) N (%)[1]	Cohort 1 Total (N=X) N (%)[1,2]	Cohort 2 OD (N=X) N (%)[1]	Cohort 2 OS (N=X) N (%)[1]	Cohort 2 Total (N=X) N (%)[1,2]	Overall OD (N=X) N (%)[1]	Overall OS (N=X) N (%)[1]	Overall Total (N=X) N (%)[1,2]
Any Ocular Disease	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Uveitis									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Other									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	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)	x (x)	x (x)	x (x)	x (x)	x (x)
Intraocular steroid injection[3]									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Periocular steroid injection[3]									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Intravitreal anti-VEGF[3]									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Cataract surgery									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Glaucoma surgery									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
Vitrectomy									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

Table 4. Ocular History (continued)

Conditions/Procedures	Cohort 1 OD (N=X) N (%)[1]	Cohort 1 OS (N=X) N (%)[1]	Cohort 1 Total (N=X) N (%)[1,2]	Cohort 2 OD (N=X) N (%)[1]	Cohort 2 OS (N=X) N (%)[1]	Cohort 2 Total (N=X) N (%)[1,2]	Overall OD (N=X) N (%)[1]	Overall OS (N=X) N (%)[1]	Overall Total (N=X) N (%)[1,2]
Other Procedure									
Yes	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)
No	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)

[1]Column header counts and denominators are the number of participants in the enrolled population, in the respective cohort or overall. Percentages are rounded to the nearest whole number.
[2]Participants who reported an ocular condition or procedure in both eyes are counted only once in this column.
[3]Within the last three months.

Table 5. Protocol Deviations and Unanticipated Problems

	Participant-Specific						Non-Participant Specific	Total
	Number of Events			Number of Participants with Events N (%)[1]			Number of Events	Number of Events
	Cohort1	Cohort 2	Overall	Cohort 1 (N=X)	Cohort 2 (N=X)	Overall (N=X)		
All events[2]	x	x	x	x (x)	x (x)	x (x)	x	x
Protocol deviations	x	x	x	x (x)	x (x)	x (x)	x	x
Unanticipated problems	x	x	x	x (x)	x (x)	x (x)	x	x
Type[3]								
Minor	x	x	x	x (x)	x (x)	x (x)	x	x
Serious	x	x	x	x (x)	x (x)	x (x)	x	x
Not serious	x	x	x	x (x)	x (x)	x (x)	x	x
Determination Pending	x	x	x	x (x)	x (x)	x (x)	x	x
Outcome								
Participant follow-up continues	x	x	x	x (x)	x (x)	x (x)	x	x
Participant follow-up terminated	x	x	x	x (x)	x (x)	x (x)	x	x
Investigational product remains stable	x	x	x	x (x)	x (x)	x (x)	x	x
Investigational product returned or discarded	x	x	x	x (x)	x (x)	x (x)	x	x
Other	x	x	x	x (x)	x (x)	x (x)	x	x

[1]Column header count and denominators are the total number of participants in the enrolled population, in the respective cohort or overall. Percentages are rounded to the nearest whole number.
[2]Events that are both protocol deviations and unanticipated problems are included in both rows.
[3]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 the IRB classifies the major deviations and unanticipated problems as serious or not serious. Determination pending category corresponds to those major deviations or unanticipated problems that the IRB is yet to classify as serious or not serious.

Table 6. Study Procedure Deviations

Cohort	Participant ID	Number of Expected Procedures[1]	Number of Missed Procedures[2]	Percentage (%) of Missed Procedures[3]
1	**By participant**			
	NEI001	x	x	xx.x
	NEI002	x	x	xx.x
	…	x	x	xx.x
	Overall	**x**	**x**	**xx.x**
2	NEI006	x	x	xx.x
	NEI007	x	x	xx.x
	…	x	x	xx.x
	Overall	**x**	**x**	**xx.x**
NA	**By procedure**			
	Adverse Event Assessment	x	x	xx.x
	BCVA (EVA)	x	x	xx.x
	…	x	x	xx.x
NA	**Overall Total**	**x**	**x**	**xx.x**

[1]The number of expected procedures is defined based on the study flowsheet included in the protocol.
[2]Missed procedures are defined when the site reports a missed procedure or when the protocol monitors note missed procedures at a site visit.
[3]Percentages are rounded to the nearest tenth.

Table 7. Visit Schedule Deviations

Cohort	Participant ID	Number of Expected Visits	Number of Missed Visits	Percentage of Missed Visits[1]	Number of Out of Window Visits	Percentage of Out of Window Visits[1]	Visits Missed or Out of Window
1	NEI001	x	x	xx.x	x	xx.x	xxx, xxx
	NEI002	x	x	xx.x	x	xx.x	xxx, xxx
	…	x	x	xx.x	x	xx.x	xxx, xxx
	Overall	**x**	**x**	**xx.x**	**x**	**xx.x**	
2	NEI006	x	x	xx.x	x	xx.x	xxx, xxx
	…	x	x	xx.x	x	xx.x	xxx, xxx
	Overall	**x**	**x**	**xx.x**	**x**	**xx.x**	
NA	**Total**	**x**	**x**	xx.x	**x**	**xx.x**	

[1]Percentages are rounded to the nearest tenth.

Table 8. Primary Outcome Analysis of Treatment Response

	Cohort 1 n/N (%)[1]			Cohort 2 n/N (%)[1]			Overall n/N (%)[1]		
Visit	OD	OS	Total[2]	OD	OS	Total[2]	OD	OS	Total[2]
Week 4	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)
Week 8	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)
Week 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)
Week 16	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)
Total by Week 16	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)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall, considering only eligible eyes. Percentages are rounded to the nearest whole number.
[2]Only participants meeting treatment response criteria in all eligible eyes are counted as a treatment responder in this column. Highlighted cells correspond to primary outcome analysis.

Table 9. BCVA Total Letters Read over Time

	Cohort 1				Cohort 2				Overall			
	BCVA Total Letters Read		Change from Baseline		BCVA Total Letters Read		Change from Baseline		BCVA Total Letters Read		Change from Baseline	
Visit	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Baseline												
N	x	x			x	x			x	x		
Mean (SD)	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)		
…												
Week 28												
N	x	x	x	x	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)
Median	x	x	x	x	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)	(x, x)	(x, x)	(x, x)	(x, x)
>=15 letter loss, N (%)[1]			x (x)	x (x)			x (x)	x (x)			x (x)	x (x)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 10. Recurrence of Uveitis

Visit	Cohort 1 n/N (%)[1]			Cohort 2 n/N (%)[1]			Overall n/N (%)[1]		
	OD	OS	Total[2]	OD	OS	Total[2]	OD	OS	Total[2]
Week 4	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)
Week 8	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)
Week 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)
Week 16	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)
Total by Week 16	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)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.
[2]Participants who experienced recurrence in both eyes are counted only once in this column.

Table 11. Length of Time Until First Recurrence of Uveitis (Days)

	Cohort 1			Cohort 2			Overall		
	OD	OS	Total	OD	OS	Total	OD	OS	Total
N[1]	x	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)
Median	x	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)	(x, x)

[1]Number of participants in the primary analysis population who experienced recurrence of uveitis following the baseline injection or infusion, in the respective cohort or overall.

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Table 12. Retino-Vascular Leakage Over Time

	Retinovascular Lesions Present n/N (%)[1]						New /Increased Lesions n/N (%)[1]						Decreased Lesions n/N (%)[1]					
Visit	**Cohort 1**		**Cohort 2**		**Overall**		**Cohort 1**		**Cohort 2**		**Overall**		**Cohort 1**		**Cohort 2**		**Overall**	
	OD	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Week 4	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)
Week 8	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)
Week 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)
Week 16	/xx (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)
Week 28	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)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 13. Central Retinal Thickness over Time

	Cohort 1				Cohort 2				Overall			
	Central Retinal Thickness (µm)		Change from Baseline (µm)		Central Retinal Thickness (µm)		Change from Baseline (µm)		Central Retinal Thickness (µm)		Change from Baseline (µm)	
Visit	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Baseline												
N	x	x			x	x			x	x		
Mean (SD)	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)		
…												
Week 28	x	x	x	x	x	x	x	x	x	x	x	x
N	x	x	x	x	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)
Median	x	x	x	x	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)	(x, x)	(x, x)	(x, x)	(x, x)

Table 14. Length of Time to Quiescence (Days)

	Cohort 1			Cohort 2			Overall		
	OD	**OS**	**Total**	**OD**	**OS**	**Total**	**OD**	**OS**	**Total**
N[1]	x	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)
Median	x	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)	(x, x)

[1]Number of participants in the primary analysis population who experienced quiescence following the baseline injection or infusion, in the respective cohort or overall.

Table 15. Quiescence

	Cohort 1 n/N (%)[1]			Cohort 2 n/N (%)[1]			Overall n/N (%)[1]		
Visit	OD	OS	Total[2]	OD	OS	Total[2]	OD	OS	Total[2]
Week 4	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)
Week 8	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)
Week 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)
Week 16	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)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.
[2]Participants experiencing quiescence in both eyes are counted only once in this column.

Table 16. Summary of Adverse Events

	Participants with Events N (%)[1]			Number of Events N		
	Cohort 1	**Cohort 2**	**Overall**	**Cohort 1**	**Cohort 2**	**Overall**
All AEs	x (x)	x (x)	x (x)	x	x	x
Serious Adverse Events	x (x)	x (x)	x (x)	x	x	x
Severity[2]						
Mild	x (x)	x (x)	x (x)	x	x	x
Moderate	x (x)	x (x)	x (x)	x	x	x
Severe	x (x)	x (x)	x (x)	x	x	x
Life-threatening	x (x)	x (x)	x (x)	x	x	x
Death	x (x)	x (x)	x (x)	x	x	x
Ocular Specification[2]						
Non-ocular	x (x)	x (x)	x (x)	x	x	x
OD	x (x)	x (x)	x (x)	x	x	x
OS	x (x)	x (x)	x (x)	x	x	x
Relation to IP[2]						
Related	x (x)	x (x)	x (x)	x	x	x
Not Related	x (x)	x (x)	x (x)	x	x	x
Outcome[2]						
Resolved	x (x)	x (x)	x (x)	x	x	x
Resolved with sequelae	x (x)	x (x)	x (x)	x	x	x
Ongoing	x (x)	x (x)	x (x)	x	x	x
Death	x (x)	x (x)	x (x)	x	x	x
Resolved by convention	x (x)	x (x)	x (x)	x	x	x

[1]Denominators are the number of participants in the primary analysis population in the respective cohort or overall. Percentages are rounded to the nearest whole number.
[2]Participants may be counted in more than one category.

Table 17. AEs by System Organ Class (SOC) and Preferred Term (PT)

System Organ Class/ Preferred Term	Participants with Events N (%)[1]			Number of Events N		
	Cohort 1	Cohort 2	Overall	Cohort 1	Cohort 2	Overall
SOC1	x (x)	x (x)	x (x)	x	x	x
PT1	x (x)	x (x)	x (x)	x	x	x
PT2	x (x)	x (x)	x (x)	x	x	x
SOC2	x (x)	x (x)	x (x)	x	x	x
PT1	x (x)	x (x)	x (x)	x	x	x
PT2	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

[1]Denominators are the number of participants in the primary analysis population in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 18. IOP over Time

	Cohort 1				Cohort 2				Overall			
	IOP (mmHg)		Change from Baseline (mmHg)		IOP (mmHg)		Change from Baseline (mmHg)		IOP (mmHg)		Change from Baseline (mmHg)	
Visit	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Baseline												
N	x	x			x	x			x	x		
Mean (SD)	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)		
…												
Week 28												
N	x	x	x	x	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)
Median	x	x	x	x	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)	(x, x)	(x, x)	(x, x)	(x, x)
≥10 mmHg increase, N (%)[1]			x (x)	x (x)			x (x)	x (x)			x (x)	x (x)

[1]Denominators are the number of participants in the primary analysis population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 19. Anterior Chamber Cells

	Cohort 1 n/N (%)[1]		Cohort 2 n/N (%)[1]		Overall n/N (%)[1]	
Grade	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Grade 0 (no cells seen)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x(x)	x/x (x)	x/x (x)
0.5 or Trace (1-5 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 1 (6-15 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 2 (16-25 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 3 (26-50 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 4 (>50 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cannot grade or Not Done						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 20. Anterior Chamber Flare

	Cohort 1 n/N (%)[1]		Cohort 2 n/N (%)[1]		Overall n/N (%)[1]	
Grade	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Absent						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Faint, barely detectable						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Moderate, iris/lens details clear						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Marked, iris/lens details hazy						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Intense, fixed coagulated aqueuous humour, fibrin present						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cannot grade or Not Done						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 21. Vitreous Cells

	Cohort 1 n/N (%)[1]		Cohort 2 n/N (%)[1]		Overall n/N (%)[1]	
Grade	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Grade 0 (0-1 cell)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Trace (2-20 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 1 (21-50 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 2 (51-100 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 3 (101-250 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Grade 4 (>250 cells)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cannot grade or Not Done						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 22. Summary of Vitreous Haze

	Cohort 1 n/N (%)[1]		Cohort 2 n/N (%)[1]		Overall n/N (%)[1]	
Grade	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Clear						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Trace						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Few opacities, mild blurring						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Significant blurring, but still visible						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Optic nerve visible, no vessels seen						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Dense opacity obscures optic nerve head						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Cannot grade or Not Done						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 23. Chorioretinal Assessments and FA Leakage

	Cohort 1 n/N (%)[1]		Cohort 2 n/N (%)[1]		Overall n/N (%)[1]	
Grade	**OD**	**OS**	**OD**	**OS**	**OD**	**OS**
Presence of Active Chorioretinitis						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
FA Leakage In More than One Quadrant (Needs Treatment)						
Baseline	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Active Inflammatory Chorioretinal Lesions						
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
New/Increased Chorioretinal Lesions						
Week 4	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)
Week 28	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 24. Laboratory Assessments

	Abnormal Findings n/N (%)[1]			Any Change from Baseline n/N (%)[1]			Clinically Significant Change from Baseline n/N (%)[1]		
Visit	**Cohort 1**	**Cohort 2**	**Overall**	**Cohort 1**	**Cohort 2**	**Overall**	**Cohort 1**	**Cohort 2**	**Overall**
Baseline	x/x (x)	x/x (x)	x/x (x)						
Week 4				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)
Week 28				x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 25. Significant Physical Exam Findings

Visit	**Cohort 1 n/N (%)[1]**	**Cohort 2 n/N (%)[1]**	**Overall n/N (%)[1]**
Baseline	x/x (x)	x/x (x)	x/x (x)
Week 4	x/x (x)	x/x (x)	x/x (x)
…	x/x (x)	x/x (x)	x/x (x)
Week 28	x/x (x)	x/x (x)	x/x (x)

[1]Denominators are the number of participants in the safety population who completed the indicated visit, in the respective cohort or overall. Percentages are rounded to the nearest whole number.

Table 26. Blood Pressure

	Cohort 1				Cohort 2				Overall			
	Systolic		Diastolic		Systolic		Diastolic		Systolic		Diastolic	
Visit	Value (mmHg)	Δ (mmHg)	Value (mmHg)	Δ (mmHg)	Value (mmHg)	Δ (mmHg)	Value (mmHg)	Δ(mmHg)	Value (mmHg)	Δ (mmHg)	Value (mmHg)	Δ (mmHg)
Baseline												
N	x		x		x		x		x		x	
Mean (SD)	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)	
…												
Week 28												
N	x	x	x	x	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)
Median	x	x	x	x	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)	(x, x)	(x, x)	(x, x)	(x, x)

Δ indicates change from baseline.

Table 27. Temperature

	Cohort 1		Cohort 2		Overall	
Visit	**Value (°C)**	**Δ (°C)**	**Value (°C)**	**Δ (°C)**	**Value (°C)**	**Δ (°C)**
Baseline						
N	x		x		x	
Mean (SD)	x (x)		x (x)		x (x)	
Median	x		x		x	
Range (Min, Max)	(x, x)		(x, x)		(x, x)	
…						
Week 28						
N	x	x	x	x	x	x
Mean (SD)	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)

Δ indicates change from baseline.

LISTINGS

Listing 1. Treatment Response Criteria

Cohort	Participant ID	Visit	No Lesion[1]		Absent/Decreased Leakage[2]		AC Cells[3]		Vitreous Haze[4]	
			OD	OS	OD	OS	OD	OS	OD	OS
1	NEI001	Week 4	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		Week 8	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		Week 12	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		Week 16	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		Week 28	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
	…	Week 4	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		…	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
2	NEIxxx	Week 4	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
		…	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

[1]No active inflammatory chorioretinal lesion.
[2]Absent or decreased retinal vascular leakage.
[3]Less than or equal to 0.5+ anterior chamber (AC) cells.
[4] Less than or equal to 0.5+ vitreous haze.
Treatment responses are highlighted in green if occurring only in OD, blue if occurring only in OS, and yellow if in both eyes.

Listing 2. BCVA Total Letters Read Over Time

			BCVA Total Letters Read		Change from Baseline[1]	
Cohort	**Participant ID**	**Visit**	**OD**	**OS**	**OD**	**OS**
1	**NEI001**	Baseline	x	x		
		Week 4	x	x	x	x
		Week 8	x	x	x	x
		Week 12	x	x	x	x
		Week 16	x	x	x	x
		Week 28	x	x	x	x
	…	Baseline	x	x		
		…	x	x	x	x
2	**NEIxxx**	Baseline	x	x		
		…	x	x	x	x

[1]Yellow highlight indicates loss of ≥ 15 letters from baseline.

Listing 3. Recurrence of Uveitis

			Recurrence Criteria										
			New Lesion[1]		New Leakage[2]		AC Cells[3]		Vitreous Haze[4]		BCVA Change[5]		
Cohort	Participant ID	Visit	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS	Time (Days)[6]
1	**NEI001**	Week 4	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		Week 8	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		Week 12	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		Week 16	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		Week 28	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
	…		Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		…	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
2	**NEIxxx**	Week 4	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx
		…	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	Yes /No	xxx

[1]New active inflammatory chorioretinal lesion.
[2]New retinal vascular leakage.
[3]A 2+ increase in AC cells relative to baseline.
[4]A 2-step increase in vitreous haze relative to baseline.
[5]Worsening of BCVA by greater than or equal to 15 letters relative to baseline.
[6]Length of time until recurrence of uveitis relative to baseline.
Recurrences are highlighted in green if occurring only in OD, blue if occurring only in OS, and yellow if in both eyes.

Listing 4. Retino-Vascular Leakage

Cohort	Participant ID	Visit Number	Retinovascular Lesions Present		New/Increased Lesions		Decreased Lesions	
			OD	OS	OD	OS	OD	OS
1	**NEI001**	Week 4	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Week 8	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Week 12	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Week 16	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		Week 28	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
	NEI002	Week 4	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		…	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
2	**NEIxxx**	Week 4	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
		…	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No

Listing 5. Central Retinal Thickness on OCT Over Time

Cohort	Participant ID	Visit	Central Retinal Thickness (µm)		Change from Baseline (µm)	
			OD	OS	OD	OS
1	**NEI001**	Baseline	x	x		
		Week 4	x	x	x	x
		Week 8	x	x	x	x
		Week 12	x	x	x	x
		Week 16	x	x	x	x
		Week 28	x	x	x	x
	NEI002	Baseline	x	x		
		…	x	x	x	x
2	**NEIxxx**	Baseline	x	x		
		…	x	x	x	x

Listing 6. Quiescence

			Quiescence Criteria						
			Vitreous Haze[1]		No Chorioretinitis[2]		No Leakage[3]		
Cohort	Participant ID	Visit Number	OD	OS	OD	OS	OD	OS	Time (Days)[4]
1	NEI001	Week 4	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
		Week 8	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
		Week 12	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
		Week 16	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
		Week 28	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
	…	…	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
2	NEIxxx	Week 4	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx
		…	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxx

[1]Less than 1 vitreous haze.
[2]Absence of active chorioretinitis.
[3]Absence of leakage on FA.
[4]Length of time until quiescence relative to baseline.
Quiescence events are highlighted in green if occurring only in OD, blue if occurring only in OS, and yellow if in both eyes.

Listing 7. Steroid Tapering

Cohort	Participant ID	Medication Name	Starting Dose	Steroid Indication	Target Date	Target Dose	Actual Date[1]	Actual Dose[2]
1	**NEIxxx**	xxxxxxxx	xx mg	xxxxxxxxxx	xx/xx/xx	xx mg	xx/xx/xx	xx mg
					xx/xx/xx	xx mg	xx/xx/xx	xx mg
					xx/xx/xx	xx mg	xx/xx/xx	xx mg
					…	…	…	…
2	**NEIxxx**				xx/xx/xx	xx mg	xx/xx/xx	xx mg
					…	…	…	…

[2] Actual date only shown if different from target date.
[2] Actual dose only shown if different from target dose.

FIGURES

Figure 1. Study Disposition

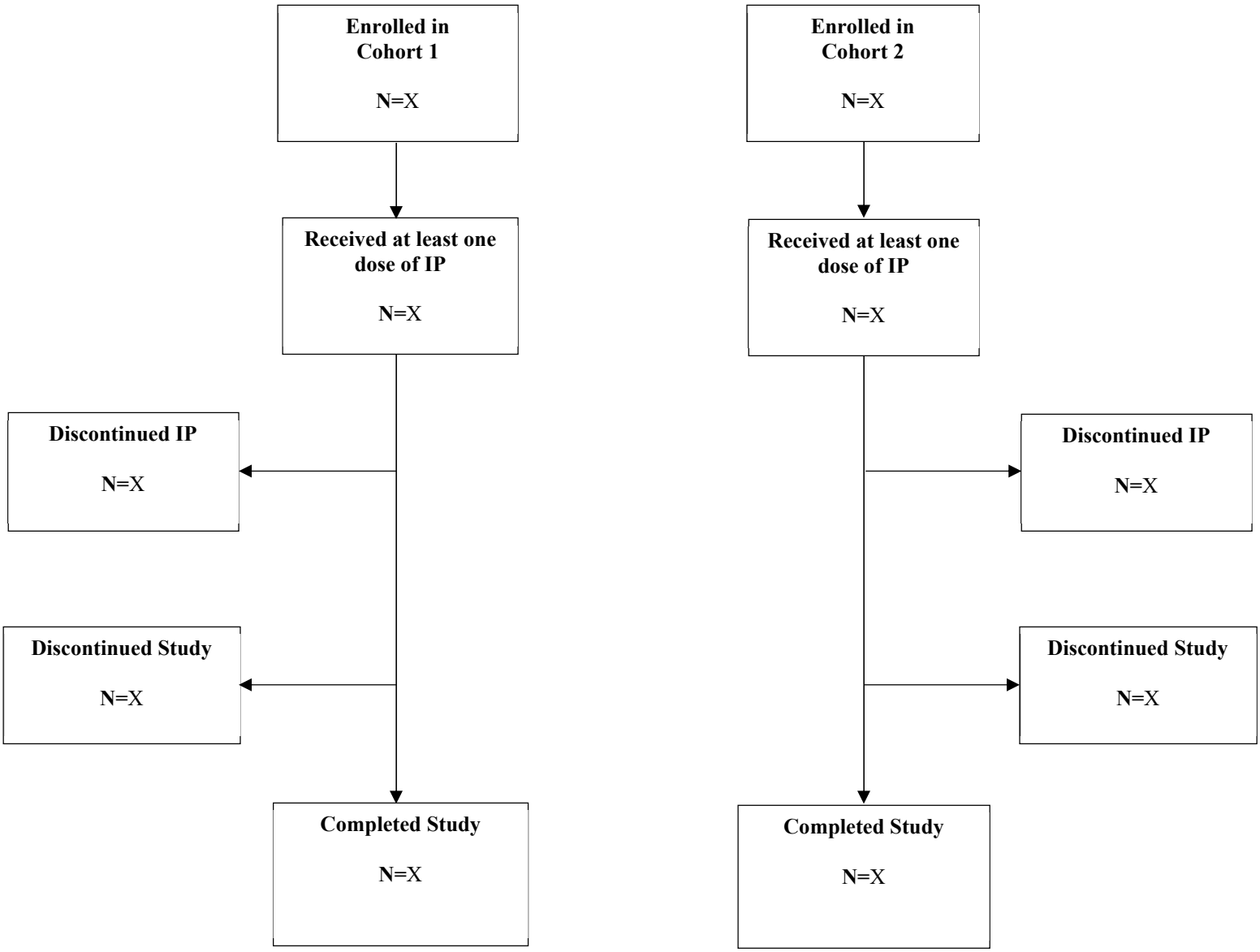
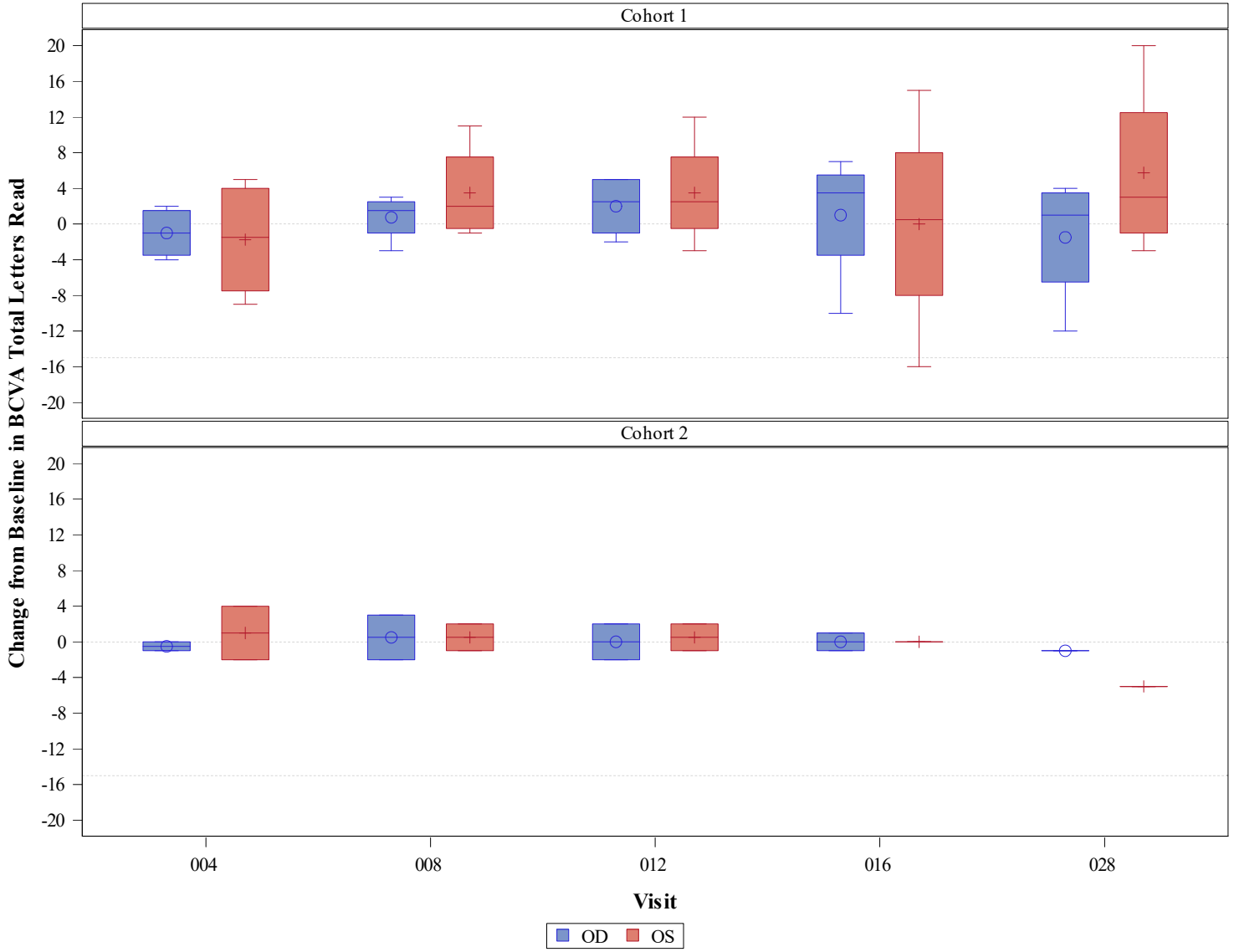


Figure 2. BCVA Total Letters Read Over Time



Reference line corresponds to loss of 15 letters compared to baseline.

Figure 3. Central Retinal Thickness Over Time

Figure 3 will be similar to Figure 2 and will present boxplots of central retinal thickness at each visit for each cohort.