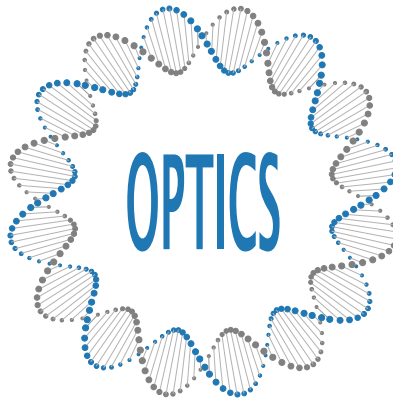


OPTICS Trial

Administrative Information

Trial registration: NCT05286203

Protocol Version: Version 2.5, Updated 2022-04-22



**Ocular Pathogen and Transcriptome Investigation using Comprehensive Sequencing
(OPTICS)**

Manual of Operations of Procedures

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Abbreviations

OPTICS: Ocular Pathogen and Transcriptome Investigation using Comprehensive Sequencing

MDS: Metagenomic Deep Sequencing

DSMC: Data and Safety Monitoring Committee

UCSF: University of California, San Francisco

Chapter 1: Overview

1.1 Summary and Overview

We propose to conduct a randomized clinical trial to compare the diagnostic strategies of providing metagenomic deep sequencing (MDS) in addition to traditional diagnostics versus traditional diagnostics only for intraocular infections. Patients with presumed infectious uveitis or patients in which the clinicians need to rule out infections will be randomized into one of two arms: (1) MDS and traditional diagnostics or (2) traditional diagnostics only. The primary outcome for the trial will be the belief that the patient had received the appropriate antimicrobial therapy, as determined by a panel of multidisciplinary experts, 4 weeks after randomization. Secondary outcomes include clinical improvements at the end of the study, the provider's belief of that it's infectious, the belief that the patient had received the appropriate immunosuppression, improvements in quality of life for patients and clinicians, and identifying host and non-host genomic markers that may be important to patient care.

1.2 Background

Diagnostic tests for ocular inflammation are inadequate.(1, 2) The majority of uveitis is "idiopathic." Although timely and accurate diagnosis is critical for improving visual outcomes, a definitive diagnosis can be challenging and failure to identify an infectious pathogen can have serious consequences. Cultures are insensitive.(3) Molecular diagnostics have better sensitivity than cultures for pathogen detection, but they are candidate-based; this requires clinicians to order individual tests for each suspected etiology.(2) Numerous bacteria, fungi, parasites, viruses, and non-infectious etiologies (e.g. autoimmune), may be potential causes of ocular inflammation, forcing clinicians to prioritize testing. If clinicians do not suspect a particular infectious etiology, then they may not even test for it further delaying a diagnosis. These limitations not only delay targeted therapy, but also hamper public health surveillance of emerging infections, and impede research into new potential treatments.

Unbiased testing with next-generation sequencing may improve patient care. Innovations in the past decade, such as metagenomic deep sequencing (MDS) approaches, allow for rapid identification of all pathogens in any clinical sample.(4, 5) Even when no pathogen was identified on MDS, this information afforded physicians the confidence needed to transition to immunosuppression to treat active inflammation. Laboratories in the US and Europe are actively pursuing MDS-equivalent assays for various tissue types. Therefore, it is important that clinicians have evidence-based data to determine if and when these assays may provide benefit to their patients.

Most diagnostic technologies are not assessed to determine if their application improves patient care. A test may be technologically advanced, accurate, and yet may influence neither therapy nor patient outcome.(6) While MDS can identify any pathogen (i.e. DNA and RNA virus, bacteria, parasites, and fungi) using minute amounts of tissue, its usefulness has not been tested for patients with presumed ocular infections. Establishing patient benefit requires a randomized controlled trial (RCT) in which a test is compared against alternative tests.

Chapter 2: Objective

The overall objectives of this study are to rigorously determine if MDS changes treatment, clinical diagnosis and improves clinical outcomes for patients with ocular infections.

Chapter 3: Hypothesis and Specific Aims

3.1 Hypothesis

We hypothesize that providers with access to MDS early in the study will have improved clinical decision making and provide the correct treatment based on pathogen detected as reflected by their treatment decision.

We hypothesize that patients with access to MDS early in the study will have improved clinical outcomes (decreased inflammation and/or improved vision) compared to patients with access to traditional testing only.

We hypothesize that host gene analysis will accurately discriminate between categories of infection (viral versus bacterial versus fungal versus non-infectious) and that non-host gene analysis will identify resistance, allowing for precision care and prompt transition to appropriate therapy.

3.2 Specific Aims

Specific Aim 1: To determine if metagenomic deep sequencing (MDS) will improve treatment for patients with presumed ocular infections in a multicenter, evaluator-masked, randomized controlled trial.

Specific Aim 2: To determine if metagenomic deep sequencing (MDS) will alter clinical outcomes for patients with presumed ocular infections.

Specific Aim 3: To determine the performance of MDS compared to conventional diagnostics

Specific Aim 4: To determine the quality-of-life impact on patients.

Chapter 4: Trial Design

The OPTICS Trial is a randomized control trial evaluating the impact of metagenomic deep sequencing (MDS) of ocular samples in suspected infectious ocular inflammatory disease syndromes on the clinical diagnosis and pathogen detection.

4.1 Screening/Eligibility

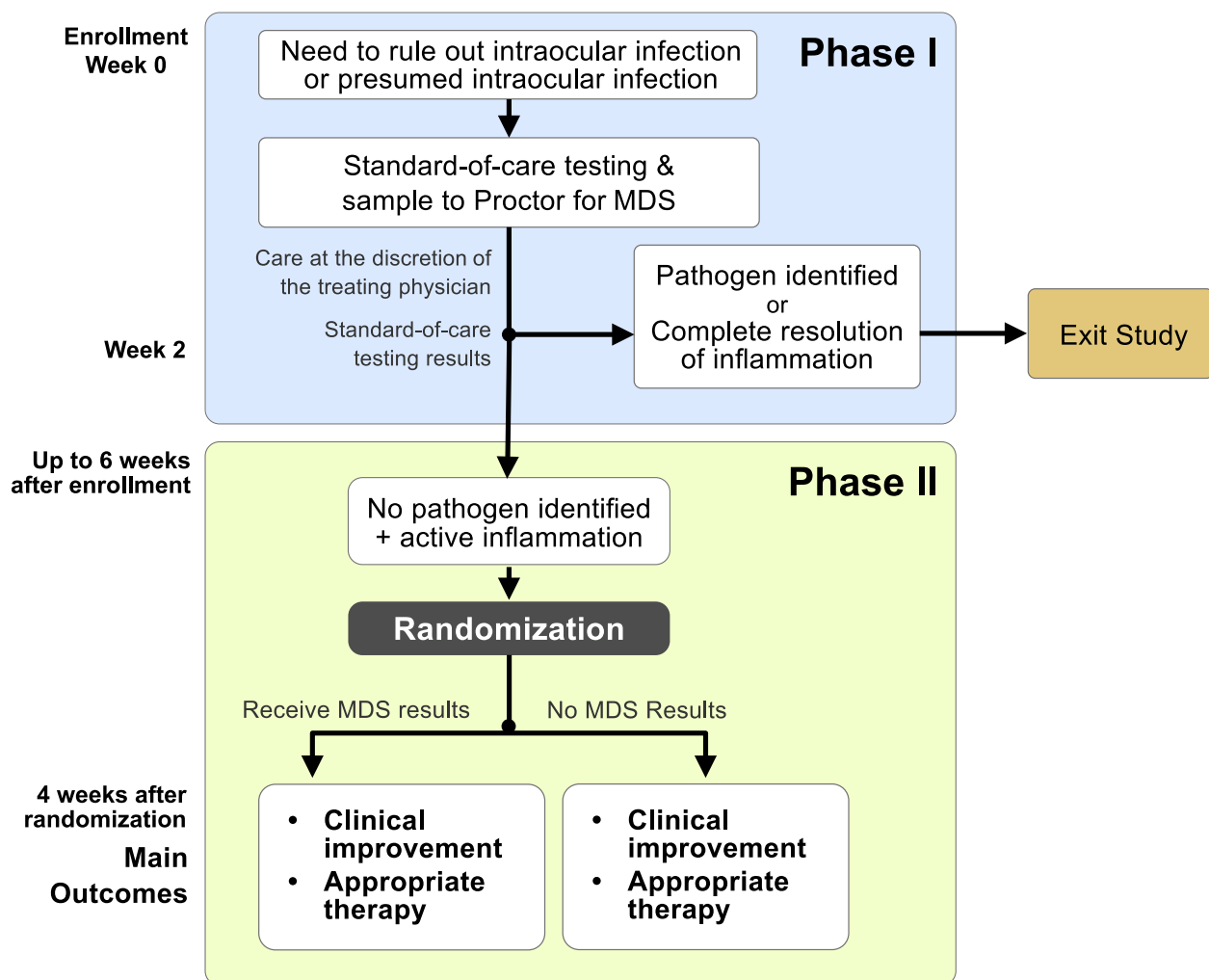
This trial involves 2 phases that requires distinct inclusion criteria. At baseline (Phase I), patients 18 years of age and older with presumed infectious uveitis or patients in which the clinicians need to rule out infections and requiring a biopsy are included. At week 3-6 (Phase II), based on MDS result availability, enrolled patients with no pathogen identified by traditional diagnostics and with persistent inflammation will be randomized to receiving MDS results at either at randomization (Phase II) or at the end of the study.

4.2 Randomization

This trial will be stratified by center. The randomization will be conducted in R. We propose to use permuted block randomization within centers, with blocks of size 4 and 6 (with proportions 0.8 and 0.2), respectively. Each center will be provided with consecutive unique IDs, and randomization assignments (Disclose and Standard). Each is provided one at a time upon subject enrollment. Randomization will be conducted at a central site by an analyst under the supervision of Dr. Ben Arnold using previously prescribed protocols.

Randomization Units. The randomization unit for this trial will be the patient.

4.3 Study at a Glance



4.4 Interventions

Patients without a pathogen identified by traditional diagnostics will be randomized into one of two diagnostic groups: (1) get MDS results or (2) do not get MDS results. Patients in either randomization arm may proceed with additional available diagnostics as deemed necessary by their treating physician.

4.5 Main Outcomes

Clinical outcome. The proportion of patients with clinical improvement at the final visit.

Process outcome. The proportion of patients receiving the appropriate antimicrobial therapy.

Other Outcomes

1. Impact on providers
 - a. Certainty of belief (credible interval for infectious vs. non-infectious) at randomization and at the final visit.
 - b. The impact of MDS on the providers by evaluating quality of life as measured by the WHOQOL-BREF at randomization and the final visit.
2. Impact on patients
 - a. The impact of MDS on the patients by evaluating quality of life as measured by NEI-VFQ at the randomization and at the final visit (4 weeks after randomization).
3. Latent class analysis to estimate the sensitivity and specificity of MDS to detect an unobserved gold standard compared to traditional tests for presumed ocular infections.
4. Identify host and non-host genomic markers

4.6 Sample Size

We assumed that 40 patients will enter Phase II of the trial and will be randomized and up to 10% loss to follow-up over the 4-week follow-up period (36 patients completing the trial). With equal allocation (1:1) and 18 patients per group, the trial will have 80% power to detect a 44% improvement in control of inflammation (from 40% improvement in standard of care to 84% improvement in the MDS group).

To detect a 20% improvement in control of inflammation (from 40% to 60%) with 80% power, the trial would need 194 patients to complete Phase II (97 per group). Assuming 10% loss to follow-up, that would require enrollment of approximately 110 patients per group, or 220 total.

4.7 Masking

An evaluator, previously not involved in the patient care and is masked to the patient's randomization arm, will be assessing the patient at the final study.

4.8 Study Period

Each participant will be in the study for a range of 7-10 weeks based on the timing of the MDS results being available for randomization.

4.9 Study Timeline

Timepoint	Activity
Day 0	• Eligibility Screening • Informed Consent • Study Enrollment • Ocular sample collected (left over fluid) • Baseline Physician Questionnaire • NEI VFQ (Patient Survey) • Baseline Ocular Exam and History • Optos and OCT
Week 2	• Ocular Exam • Laboratory Results Form • Treatment Form • Optos and OCT
Randomization (Week 3-6)	• MDS Results Available • Randomization • NEI-VFQ (Patient Survey) • WHOQOF-BREF (Provider Survey) • Physician Questionnaire • Ocular Exam Form • Optos and OCT • Laboratory Results Form • Treatment Course Form
Final visit (4 weeks after randomization)	• NEI VFQ (Patient Survey) • WHOQOF-BREF (Provider Survey) • Physician Questionnaire • Ocular Exam (Masked Examiner) Form (Main Outcome) • Optos and OCT • Laboratory Results Form • Treatment Course Form
Independent Expert Panel Meetings (only review data after patients have completed the study)	• Receive clinical information up to randomization visit without MDS results: a) Probability of Infection Form b) Appropriate Antimicrobial Assessment Form

	c) Appropriate Immunosuppression Assessment Form d) Probability of Infection • Receive clinical information for all visits with MDS results: a) Appropriate Antimicrobial Assessment Form (Main Outcome) b) Appropriate Immunosuppression Assessment Form c) Probability of Infection
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Chapter 5 Study Eligibility

Inclusion Criteria:

1. Presumed infectious anterior uveitis, or intermediate uveitis, or posterior uveitis, or panuveitis
2. Presumed post-operative endophthalmitis
3. Unilateral or bilateral
4. 18 years and older

Exclusion Criteria:

1. Insufficient specimen for MDS (e.g., < 50 uL intraocular fluid)
2. Age < 18 years of age
3. Pregnancy
4. Unable to consent

Chapter 6 Study Methods

6.1 Recruitment

Patient Recruitment: Patients will be identified by study investigators as they present to clinical sites for evaluation and management of uveitis. Patients will be enrolled by treating physician.

6.2 Enrollment

Patients will be enrolled at outpatient clinical sites.

6.3 Informed Consent

The consent process will occur in person in the study investigators clinic. The consenting process will occur in the patient's room in a private location. The study investigator will conduct the informed consent discussion in a manner so that the patient understands the study procedures and goals of the study. This will give the potential study subject time to ask any questions directly to the study investigator and consider all options in terms of participation and alternatives to participation. Written informed consent will be obtained for all subjects.

6.4 Baseline Assessment

Once a participant is determined eligible for the study and informed consent has been signed the patient will proceed with standard of care testing and removal of intraocular fluid. Leftover fluid will be kept for the study. At the baseline visit the treating physician will complete a survey and clinical exam and history form. Optos and OCT imaging will be obtained on this visit and at all subsequent visits. The patient will complete the NEI-VFQ form. See Appendix for all forms.

6.5 Week 2 Assessment

On this visit, the physician will review previously ordered diagnostic test results. If a pathogen is identified that is consistent with the patient's clinical findings, then the patient will exit the study. Also, if inflammation is resolved, then the patient will exit the study. However, if no pathogen is identified on conventional diagnostics and inflammation is still persistent, then the patient is scheduled to proceed to randomization. On this visit, the provider will complete the Ocular Exam and the Laboratory Results Forms. Imaging will be obtained. See Appendix for all forms.

6.6 Randomization (Week 3-6) Assessment

In order to proceed with randomization, the patient's clinical exam must meet the inclusion criteria. The exclusion criteria also are listed below.

Inclusion criteria: Active inflammation in at least one eye defined by the presence of any of the following according to the SUN criteria and the NEI vitreous haze grading scale:

≥ 1+ anterior chamber cells and/or
≥ 1+ vitreous haze and/or
active retinal or choroidal inflammation and/or
Macular edema

Exclusion criteria:

1. Pathogen identified that was consistent with clinical findings
2. Complete resolution of inflammation
3. NLP vision

The timing of this randomization visit will be dependent on when the MDS results will be available given the timing of sample receipt, sample processing, and sample sequencing. When the MDS results are available, the physician treating the patient will be randomized to receive MDS or not receive the MDS results at this visit. The physician will complete the Physician Questionnaire Form, Clinical Ocular Exam form, Treatment Course form, and WHOQOL-BREF form. The patient will complete the NEI-VFQ questionnaire. If the patient is randomized to receive MDS results on this visit, then the physician will complete **another** Physician Questionnaire Form prior to receiving the MDS results. Therefore, the physician treating with patient with MDS results will complete 2 Physician Questionnaire forms, and the physician

treating the patient without MDS results will complete 1 Physician Questionnaire form. See Appendix for all forms.

6.7 Final visit (4 weeks after randomization) Assessment

This will be the last study visit for the participant. A masked clinical exam will take place and the masked examiner will complete the clinical Ocular Exam form. The treating physician will complete the Physician Questionnaire form, Treatment and Laboratory form, the WHOQOL-BREF form, and the Ocular Exam Form. OCT and Optos will be obtained. The patient will complete the NEI-VFQ form. For patients were randomized to the no MDS arm, the physicians treating them will receive the MDS results after the study ends. Please see Appendix for all forms.

6.8 Independent Expert Panel

An independent expert panel, all of whom have not been involved in patient care, will be presented with multiple sets of data for each patient. They will be asked to make assessments based on the data presented. These meetings will be taken throughout the duration of the study.

For all patients who have enrolled in Phase II and completed the study, their clinical course will be assessed by the expert panel. Data will be shown, and assessment will be made as followed:

- a) The panel will receive all clinical information from the enrollment, week 2, and the randomization visits **without** MDS results. They will be asked:
 - i) To make an assessment on the probability of infection. This will be on a scale from 0-100% without 0% being not infectious, 50% being unsure, and 100% infectious.
Please also see form in Appendix.
- b) The panel will receive all clinical information from the enrollment, week 2, and the randomization, and the final visits **with** MDS results. Only treatment at the final visit will be disclosed. They will be asked:
 - i) To make an assessment if the appropriate antimicrobial assessment was provided
 - ii) To make an assessment if the appropriate immunosuppression was provided
 - iii) To make an assessment on the probability of infection

Chapter 7 Sample Collection

Intraocular samples will be obtained from either an anterior chamber paracentesis or vitreous tap and contained in a syringe. The physician performing the procedure will be wearing gloves and transfer 50 microliters to a small tube containing DNA/RNA Shield (Zymo Research). The top will be sealed, and the unique patient identifier will be placed on the specimen tube. Specimens will be placed in a small biohazard bag and placed in a -20C until sample processing. Samples from outside of UCSF will be shipped overnight to UCSF at 490 Illinois Street, Floor 2 (Proctor Foundation/ Ralph and Sophie Heintz Lab), San Francisco, CA 94158, for sample processing.

Chapter 8 Laboratory Procedures

Sample Analysis. Samples from all patients enrolled will be processed for MDS (RNA-seq and DNA-seq). RNA-seq host sequencing reads will be evaluated for differential host transcript expression between infectious types. DNA-seq non-host (bacteria and viruses) sequencing reads will be evaluated for the presence antibacterial and antiviral resistance genes.

Laboratory Methods. Samples will be processed by a trained laboratory technician. DNA and RNA will be extracted using the Quick-DNA/RNA Microprep Plus Kit according to manufacturer's recommendations. For DNA-seq sequencing library preparation, 5 µL of extracted DNA is used to prepare DNA libraries using the New England Biolabs' (NEB) NEBNext Ultra II DNA Library Prep Kit for Illumina (<https://www.neb.com/-/media/nebus/files/manuals/manuale7103-e7645.pdf?rev=339d6c65a9314c9e988851a9d671fd9a&hash=2AF765847CD54F1B7464205F7920A50F>) and then amplified with 16 PCR cycles. Library size and concentration are determined using the High Sensitivity DNA Chips (Agilent Technologies) and the Qubit® DNA HS Assay Kit (ThermoFisher Scientific), respectively. For RNA-seq sequencing library preparation, 5 µL of extracted RNA is used to prepare RNA libraries using the NEBNext Ultra II RNA Library Prep Kit for Illumina (<https://www.neb.com/protocols/2017/03/04/protocol-for-use-with-purified-mrna-or-rna-depleted-rna-and-nebnext-ultra-ii-rna-library-prep-ki>) and then amplified with 20 PCR cycles. Library size selection, pooling, and sequencing are performed as DNA-seq. All libraries will be sequenced using an Illumina sequencing platform (MiSeq, HiSeq, or NovaSeq) using 150-nucleotide (nt) paired-end sequencing.(7, 8)

Bioinformatics. The Ralph & Sophie Heintz laboratory has customized all components of these pipelines for efficient analyses. All paired-end reads were subjected to three rounds of human sequencing read removal. In an initial removal step, all paired-end reads were aligned to the human reference genome 38 (hg38) and the Pan troglodytes genome (panTro4, 2011, UCSC), using the to a Reference (STAR) aligner (v2.5.4b).(9) Unaligned reads were quality filtered using PriceSeqFilter (v1.2) with the “-rnf 90” and “-rqf 85 0.98” settings.(10) Reads that were at least 95% identical were compressed by cd-hit-dup (cd-hit v4.7). Furthermore, read pairs with a compression score less than 0.45 using the Lempel-Ziv-Welch algorithm were discarded because of low complexity.(11) Another round of human reads removal was performed using the very-sensitive-local mode of Bowtie2 (v2.3.4.1) with the same hg38 and panTro4 reference genomes described above. Lastly, the remaining reads were subject to taxonomic classification using the Centrifuge Taxonomic Classifier engine (v.1.0.3-beta), using an index created from the NCBI nucleotide non-redundant sequences (3/3/2018).(12) The pre-specified criteria for positive pathogen are 1) it is known to be a human pathogen and represented the most abundant reads after background (no template control) subtraction or 2) two or more unique reads covering separate regions in the HSV, VZV, or CMV genomes.(7)

Transcriptome analysis. Following quality filtering with PRICESeqFilter, transcripts obtained from RNA-seq will be aligned to the ENSEMBL GRCh38 human genome built using HISAT2 and filtered to include only protein-coding genes. Gene count data will be analyzed using DESeq2.

Antibacterial and antiviral resistance gene analyses. Non-host reads will be aligned to the MEGARes reference antimicrobial database using BWA with default settings. Only antibiotic

resistance determinants (ARDs) with gene fraction of >80% were identified as present in the sample and included for further analyses. Each identified ARD was classified at the class and gene level using Resistome Analyzer (<https://github.com/cdeanj/resistomeanalyzer>).⁽¹³⁾ For antiviral resistance analysis, we will evaluate CMV antiviral resistance as previously described.⁽⁸⁾

Chapter 9 Statistical Methods

9.1 Proportion of patients with clinical improvement

The outcome Y_i is a binary outcome that indicates whether patient i showed clinical improvement, assessed 4 weeks after randomization. Assignment to inclusion of MDS information in patient care, A_i , will be equal to 1 in the MDS group and 0 if they are in the standard of care group. We will estimate the proportion of patients in each group who had clinical improvement and will estimate the difference in proportions and 95% confidence interval using a generalized linear model with binomial error, identity link, and indicator variables for k clinical sites (used to stratify the randomization), $I(S_i=k)$, where S_i is the site for patient:

$$P(Y_i | A_i, S_i) = \alpha + \beta A_i + \sum_k \gamma_k I(S_i=k).$$

The P-value for differences between groups will be the test that the difference in proportions is different from zero $\beta \neq 0$.

In the main outcome analyses and all other comparisons between randomized groups proposed below, since randomization is stratified by clinical center inclusion of indicator variables for center, $\sum_k \gamma_k I(S_i=k)$, is appropriate (14,15). However, given the small size of the trial and the potentially small number of patients enrolled at each clinical center, it is possible that including indicator variables for center will result in too much stratification in the analysis. In this event, we will exclude those variables, which will make the analysis conservative with respect to the size of the standard errors and width of the 95% confidence intervals (14,15).

Given the small size of the trial we do not propose any pre-specified subgroup analyses for the main outcomes or additional outcomes.

9.2 Proportion of patients that received appropriate antimicrobial therapy

The analysis of the proportion of patients that receive appropriate antimicrobial therapy will proceed identically to the analysis of patients with clinical improvement.

9.3 Provider certainty of belief that the patient has an infection

Bayesian credible intervals will be elicited from participating providers using procedures we have used in the past (16). Change in credible intervals over time will be calculated by computing the area of the difference between two curves. The prespecified analysis will be conducted using the two-sample Wilcoxon test (rank sum test) on these changes.

9.4 Patient quality of life

Patient quality of life as measured by the NEI-VFQ instrument will be measured in concert with each patient enrolled at the time of randomization and again at 4 weeks after randomization. The outcome Y_i is continuous outcome of quality of life measured for patient i 4 weeks after randomization $Y_i(0)$ is their corresponding measure at baseline. We will estimate the difference between groups in quality of life and its 95% confidence interval using linear regression that includes an indicator for group assignment, A_i , and the patient's baseline quality of life measure:

$$E(Y_i | A_i, S_i, Y_i(0)) = \alpha + \beta A_i + \sum_k \gamma_k I(S_i = k) + \delta Y_i(0)$$

The P -value for differences between groups will be the test that the difference in means, adjusted for baseline quality of life, is different from zero $\hat{\beta} \neq 0$.

9.5 Performance of MDS compared to conventional diagnostics

For Aim 3, testing will be divided into 3 categories: (1) MDS (RNA-seq and DNA-seq), (2) traditional diagnostics (HSV-, VZV-, CMV-, Toxoplasma gondii-PCR, 16S PCR, 23- and ITS-PCR, cultures, stains, and serology), and (3) clinical diagnosis at presentation (any combination of testing or clinical evaluation that can be done at the physician's clinic that help forms the clinician's belief).

The 3 diagnostic categories will be evaluated for their performances on identifying whether the patient has (a) an infectious vs non-infectious etiology, (b) a bacterial vs fungal vs viral vs parasitic infection, and (c) has a specific infection such as P. acnes, VZV, etc...

The sensitivity and specificity of these diagnostics and the latent gold standard prevalence will be estimated using latent class analysis (LCA). Uncertainty will be estimated using bootstraps percentile 95% confidence intervals (1,000 simulations). If estimates do not vary from unity under resampling, then the Poisson approximation will be reported for the lower confidence bound. For the analysis of class and specific organism, only diagnoses with more than 10 patients will be considered. We propose to use the R package poLCA v.1.4 or higher (17).

9.6 Host and non-host genomic markers

The analysis of host and non-host genomic markers is strictly exploratory and hypothesis-generating and will be identified as such in all reporting.

In brief, we propose to systematically compare the relative abundances of individual transcripts between groups at the species levels by negative binomial Wald test using a Benjamini-Hochberg False Discovery Rate (FDR) correction for multiple comparisons. The transcript count data will be pre-filtered, so that only genes that were represented in 25% or greater in the dataset will be used. Differentially abundant transcripts with $FDR < 0.05$ and a 2-fold change will be considered as notable.

Chapter 10 Adverse Event Monitoring and Safety Assessment

10.1 Adverse Events

Adverse events are minimal in this study given that the intraocular fluid is left over specimen from an intraocular procedure (anterior paracentesis and posterior chamber (i.e., vitreous) tap) to remove fluid from the eye as deemed necessary for standard of care.

There is an increased risk to the participant when performing the anterior paracentesis and posterior chamber (i.e., vitreous) tap. While these procedures are a routine part of ophthalmologist diagnostic procedures, particularly in clinics with uveitis and vitreoretinal emphasis, there are some risks of adverse events that can occur while performing the procedure and after the procedure. Adverse ocular events related to an anterior chamber paracentesis and vitreous tap include corneal scar, cataract (lens opacity), infection (endophthalmitis), hyphema (blood/bleeding), hypotony (low eye pressure), shallow anterior chamber, vitreous collapse, suprachoroidal hemorrhage, and vision loss.

Specific safety steps have been taken to minimize the risks associated with the above-mentioned procedures. For infection control precautions the procedures have been reviewed by the collaborators in this study. To decrease the risk of infection, the procedure protocol calls for betadine to be applied to the eye pre-procedure and antibiotic drops will be administered post procedure. A post procedure exam will be performed with intraocular pressure to ensure no immediate adverse events occurred. Treatment will be administered at the office visit if an adverse event is detected.

10.2 Adverse Event Monitoring

Adverse events will be monitored at each clinic visit. Patients are aware that they may contact the treating physicians if they have concerning signs and symptoms such as worsening redness, decreased vision, and worsening eye pain.

10.3 Serious Adverse Events

Any serious adverse events (SAE) will be reported to the study team.

An SAE is defined as any adverse event that :

- Results in death
- Results in no light perception (NLP)
- Requires inpatient hospitalization
- Changes the risk/benefit ratio of the study

Or that is considered to be:

- An important medical event

Serious adverse events will be reported to the Data and Safety Monitoring Board and the Institutional Review Board at the University of California, San Francisco. Any event deemed to be definitely, probably, or possibly related and is serious or unexpected will be reported to the IRB within 5 working days. Death and life-threatening events will be reported as soon as possible.

Chapter 11 Protection of Human Subjects

The research team will obtain formal ethical approval prior to the study start. Informed written consent will be collected from all participants. If, at any time, a participant wishes to withdraw from the study, they will be free to do so.

A Data and Safety Monitoring Committee (DSMC) will be empaneled, to include at least three members, and to include the following expertise: (a) expertise in ocular infection and inflammation, (b) biostatistics, (c) bioethics, (d) representation from the USA and participating countries. The DSMC responsibilities include monitoring study progress (recruitment, retention) and data quality as well as the safety of patients. The DSMC will approve their charter on their first meeting. This DSMC will meet yearly. See details below.

11.1 Institutional Review Board Approval

UCSF's Committee on Human Research will review the study protocol for ethical approval.

11.2 Informed Consent

All participants will sign an informed consent form. Young adults and children under 18 years of age, who cannot give consent by law, will not be included in the study. Participants will be able to ask the research team questions about the study procedures and withdraw from the study at any time. Open ended questions will be asked to ascertain comprehension of the consent discussion such as: Why we're asking you to be as part of this study?, What are alternatives to participation?, Are there any benefits to your care for participation?, and What are the risks to participation?

11.3 Risk and Benefits of Study Procedures

There are minimal risks to the participant during this trial as outlined in Chapter 10. Adverse effects will be monitored. The patient may withdraw from the study at any time.

Chapter 12 Data Collection, Management, and Security

The project will be continuously monitored by the supervisory team, which will consist of members from the UCSF F.I. Proctor Foundation. This section discusses how the data are collected, entered the database, stored, and transferred to the Data Coordinating Center under the supervision of Dr. Ben Arnold.

12.1 Scope of the Data

Data will be collected at each study visit which includes the baseline visit, week-2, randomization visit (week 3-6), and final visit (4 weeks after randomization). Data to be collected includes demographic information, ocular clinical exam, diagnostics studies, quality of life of the patients and the providers, and treatment at specified time points. Additional patient and physician surveys will be completed.

12.2 Data Storage, Management, and Security

Data will be recorded electronically using REDCap. Data will be stored in a secure directory on Box, which maintains HIPAA-level compliance and encryption for UCSF accounts (details here: <https://it.ucsf.edu/services/ucsf-box/additional/how-does-box-protect-your-data>). Rapid transfer of electronically captured data will allow nearly real-time monitoring of activity at the study site. All handheld devices and data entry coordinating centers will be password protected, and all changes in data will be noted, including the date of the change, and the person who made the change. All information collected will adhere to HIPAA compliance rules.

12.3 Electronic Data Collection Forms

All forms for this study will be created electronically on REDCap. These forms will be tested by the UCSF investigators prior to using them for the study. All REDCap forms are electronic and should be completed in their online version. Paper copies will be available to be downloaded, printed, and completed by hand, if necessary, but electronic data entry is preferred. Study personnel should communicate any clarifications or updates to the study forms to all participants.

12.4 Data Entry

Once the study coordinator has reviewed the completed REDCap forms, they will submit the electronic forms to the REDCap database. The data manager at the Coordinating Center will review the data for accuracy and completion.

12.5 Data Transfer

The Coordinating Center will access the data through a secure, online REDCap database system. The database manager will download the data sets and conduct checks for completeness and validity. Any queries generated will be communicated by secure encrypted email to the study coordinator for resolution.

12.6 Data Entry Errors

The data manager at the CC will assess study data using an automated program in REDCap (with a goal of completing within 2 days of data entry), searching for missing and contradicting data fields. Wherever there is a mismatch, an error file is generated with relevant data such as the form, field name, and data for which discrepancy is found. The data manager will then contact the study coordinator to verify the forms. Discrepancies and missing values will be assessed by the data manager, and resolved by queries sent to the study coordinator and appropriate observers (e.g., clinician). A logfile will preserve the date and time of any changes, together with who entered the changes.

12.7 Data Consistency and Validity

Through range checks, the data entry software helps prevent inconsistencies or invalid data. The database program will check for the following errors: (1) improper entry of the patient ID based

on the checksum, (2) data fields that are out of range, (3) inconsistent or illogical entries, (4) incompleteness, and (5) numerical values that are far outside the range of those previously entered. The software will create an error file with relevant data such as the form identification, field names and the data. Automated checks will be made to ensure consistency and that each variable in the analysis set has in-range values (protecting against negative ages, spelling errors in categorical factors, and similar errors). The data manager will contact the study coordinator about any errors to resolve the inconsistencies.

12.8 Data Preparation and Cleaning

Datasets for analysis will be produced in comma separated values (.csv) files containing a single header line whose variable names match the REDCap database. Each analysis set will be in the form of a rectangular table in which each column corresponds to a single variable and each row to an observation. All missing values will be coded explicitly using the string “NA” (as used in the R software). Codes for categorical variables (such as 1 for male, and 2 for female) will be avoided in favor of self-documenting character strings or factor variables (such as Male, Female).

A detailed codebook will be prepared, containing for each variable, (a) the form from which the variable derived, (b) the text of the question, (c) all possible values for the variable, and (d) summary statistics for the variable. Note that all codes and character strings that represent categorical factors will be clearly defined in the codebook. Units for each continuous variable will be unambiguously indicated for each variable. Each release of the analysis set will be accompanied by the corresponding version of the codebook. Version numbering with dates will be strictly observed.

12.9 Monitoring

We will maintain a record of changes to the REDCap database. Database errors include (a) missing information, (b) erroneous information, and (c) errors arising from difficulties with the electronic forms themselves. Weekly quality assurance reports will summarize the number of each of these. Most importantly, we will closely monitor the time between the study visit date and submission of the electronic forms to REDCap to ensure that this time is less than 3 days. If entry times exceed 5 days, then this will trigger a response, which may include investigation and/or reassignment.

12.10 Data Storage and Security

Electronic forms will be completed on an encrypted electronic device, requiring a passcode to unlock the device and additional separate login credentials to access the REDCap forms. Copies of the electronic forms will not be stored on the device itself but rather within the secured REDCap database.

All electronic storage will be subjected to standard security procedures in compliance with established enterprise information security standards. Each computer will be hardware-firewalled and will not be accessible outside the Local Area Network. Hard-disk encryption will be used for

each machine, and the machine will not be accessible without a network account and password. Only study-specific personnel will have password access to the encrypted Box directory. Accounts will be immediately deactivated for data entry or other personnel who leave the study.

Chapter 13 Data and Safety Monitoring Committee Charter

A Data and Safety Monitoring Committee (DSMC) will be empaneled, to include at least three members, and to include the following expertise: (a) expertise in ocular infection and inflammation, (b) biostatistics, (c) bioethics, (d) representation from the USA and participating countries. The DSMC responsibilities include monitoring study progress (recruitment, retention) and data quality as well as the safety of patients. The DSMC will approve their charter on their first meeting.

Interim reports for the DSMC will be prepared by the data analytic team. These reports will include (a) recruitment overall, and by study site, (b) compliance, and (c) retention. The reports will also list study outcomes and all adverse outcomes, including deaths. The DSMC will determine the database closure dates for each report in advance; archival copies of the a) main database and (b) study analysis file as they exist at the time of each report will be maintained.

All reports will be sent using secure email to the members of the DSMC at least one week prior to each meeting.

Each printed (hard copy) interim report will be labeled clearly as confidential, bound so that the contents are not visible from the outside, and labeled with the name of each person authorized to receive it. Reports will be kept in possession of the primary biostatistician and research data analyst and only delivered in person or by encrypted email; reports not delivered due to absences are to be shredded. In addition, redacted versions of the interim reports will be prepared which contain no masked study information, and which are suitable for restricted distribution to other personnel on an as-needed basis. All hard copies will be destroyed at the end of each meeting, except for a copy to be kept in a locked file cabinet accessible only to the research data analyst.

We anticipate that the DSMC will review reports with the study arms distinguished. The DSMC will choose whether we will (a) provide labels for Disclose and Standard at all times to all members, or (b) label arms randomly as A or B (with the option of unmasking/unblinding at any time).

The incidence of deviations from the inclusion and exclusion criteria will be summarized using counts and percentages, and the treatment groups compared for the overall frequency of deviations using the Fisher's exact test. Similar deviations will be grouped into general categories of deviations for a more condensed summary. A listing of deviations by participant will also be produced. Any major deviations from the protocol will be listed and/or summarized, including, but not limited to, participants who never received diagnostic testing, were subsequently found to be ineligible for the study, never returned for a follow-up visit.

The number and percentage of randomized participants receiving the study diagnostic intervention and permanently discontinuing the study interventions will be summarized. A

summary of study participants randomized by site will also be provided. Randomization groups will be compared for the proportion and reason for study intervention discontinuation using Fisher's Exact test. A summary of participant status at the end of the study period will also be generated with categories including lost to follow-up.

Safety. Adverse events will be reported within 24 hours to the medical monitor. The medical monitor will make a determination of relatedness to the study intervention. Adverse event narratives will always be reported to the DSMC, with the reporting format and timing to be decided at the first meeting.

We will tabulate and report adverse events in manuscripts and publications, by study arm. Statistical comparisons between arms will be reported internally at the discretion of the investigators and the DSMC, but we do not propose to report such comparisons in research communications. Trials are often underpowered with respect to such comparisons, and failure to find statistical evidence of a difference may be misleadingly reassuring. Additional information is provided below.

The trial may be terminated for reasons of harm at the judgment of the DSMC. Several endpoints will be examined, including serious adverse events as described in the protocol. While the analysis would consider maldistribution of predictive factors such as age, it is recognized that ethical considerations require careful considerations of statistical tests as well as qualitative judgments in the light of experience. Any additional analyses required by the DSMC will be reported as needed.

Efficacy. A single interim analysis conducted at alpha of 0.001 will be conducted. Specifically, the interim analysis will be conducted when ocular outcome data are available for the first half of patients. The final analysis would be conducted at alpha 0.049.

Chapter 14 References

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Chapter 15 Appendix

Informed Consent

Eligibility and Screening

Eligibility and Screening Phase 2

Baseline Demographics

Baseline Ophthalmology

Visual Acuity Form

Clinical Eye Exam (Baseline, Week 2, Randomization, Final visits)

Imaging Form (Baseline, Week 2, Randomization, Final visits)

Physician Survey

Standard of Care Investigation Form (Week 2, Randomization and Final visits)

Treatment Form (Baseline, Week 2, Randomization and Final Visits)

Patient Dropout

Research Sample Lab

Adverse Event Checklist

Protocol Deviation

WHOQOF-BREF (Physician Survey)

NEI-VFQ (Patient Survey)

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN RESEARCH

Study Title: Ocular Pathogen and Transcriptome Investigation using Comprehensive Sequencing (OPTICS)

Research Project Director:	Thuy Doan M.D. PhD, Associate Professor of Ophthalmology. 490 Illinois Street, Floor 2 San Francisco, CA 94143 Phone: (415) 476-6939; e-mail: thuy.doan@ucsf.edu
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This is a research study. Your study doctor(s), Dr. Thuy Doan, Dr. Jessica Shantha, Dr. Nisha Acharya, and Dr. John Gonzales from the UCSF Department of Ophthalmology and the Proctor Foundation will explain the research to you.

STUDY SUMMARY

We are asking you to consider taking part in a research study being done by Dr. Thuy Doan at UCSF.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study: This is a study to determine if metagenomic deep sequencing (MDS) can be useful for detecting infections in the eye and the impact this test might have on your diagnosis and clinical care such as treatment. Metagenomic deep sequencing is a test that can detect all types of infections including viruses, bacteria, and parasites in one sample. Standard testing can only detect one infection at a time, but MDS has the ability to look for all types of infections at the same time. To find out if having MDS results are better we will either give you the standard of care testing with or without the MDS results. Depending on your study designation you may not receive MDS results until the end of the study.

Study Procedures: If you choose to be in the study, left over fluid from your intraocular procedure will be kept and undergo MDS. Your care team will receive the MDS results either at 3-6 weeks or at your last study visit.

Potential Risks:

- Risk is minimal in this study since eye fluid is being taken as left over from your standard of care procedures and testing.
- Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health.

- To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

We'll tell you about the other risks later in this consent form.

Possible Benefits: You may benefit from participating in this study, but this cannot be guaranteed. A benefit from being in this study includes using an innovative new technology to potentially help aid with the diagnosis of your ocular condition.

Your Other Options: You do not have to participate in this study. Your other choices may include:

- Getting treatment or care for your condition without being in a study.
- Using already approved standard of care testing.

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

Sponsor: Research to Prevent Blindness

DETAILED STUDY INFORMATION

Why is this research being done?

This is a study to determine if metagenomic deep sequencing (MDS) can be useful for detecting infections in the eye and the impact this test might have on your diagnosis and clinical care such as treatment. Metagenomic deep sequencing is a test that can detect all types of infections (i.e. a bacterium, virus, or other parasite) in one sample. Standard testing can only detect one infection at a time, but MDS has the ability to look for all types of infections at the same time. To find out if having MDS results are better we will either give you the standard of care testing with or without the MDS results. Depending on your study designation you may not receive MDS results until the end of the study.

Who pays for this study?

Research to Prevent Blindness

How many people will take part in this research?

About 254 people will take part in this study at UCSF.

What will happen if I take part in this research study?

If you agree to take part in this study, the following will happen:

After all routine tests required for your care are finished, instead of discarding your leftover specimens you are giving us permission to use any extra fluid for this research study. We will be testing for infectious agents in addition to antimicrobial resistance markers in your eye as a result of your uveitis (eye inflammation: eye redness, light sensitivity, floaters, blurry vision) as well as looking at genetic information. At this time, metagenomic deep sequencing, or the

interrogation of the genetic information in ocular samples, is not standard of care or approved by the Federal Drug Administration.

The sample you give us to use for this study will be stored with your identifying information in the Francis I. Proctor Foundation's Heintz Laboratory at 490 Illinois St. Floor 2, San Francisco, CA 94158 United States. Testing will be done using metagenomics deep sequencing in the Heintz Laboratory.

Your medical record will also be reviewed. We will collect and save information from your medical record, including things like your name, date of birth, diagnosis, treatments and the results of laboratory tests. Clinical photography such as eye photographs collected as part of your regular care will also be reviewed for research purposes only. Using this information, we will be able to determine whether deep sequencing tests are accurate and cost-effective, to compare them to other clinical tests, and to evaluate the impact of the tests on your clinical diagnosis and patient outcomes. Researchers will continue to gather additional information from your medical record indefinitely.

Once the deep sequencing tests are performed, we would like permission to store and use the leftover sample for other experiments in the lab. You may agree to this or not under the "optional research" section of this document. If you wish to not take part in the bio banking of your left-over specimen you can still participate in the study, but your sample will not be used for additional research studies.

For randomized studies: You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in any group.

- If you are in group 1 your physician will receive the results from the MDS results and will use that information to guide further diagnostic and treatment decisions that is left up to the treating physician.
- If you are in group 2 your physician will NOT receive the results from the MDS analysis until the end of the study period. During the study, standard of care testing and information to guide further diagnostic and treatment decisions that is left up to the treating physician. The physician will receive the results at the final study visit. It is possible that the eye inflammation (uveitis) will still be active and the physician may decide to use the MDS results to make treatment changes.

You will also be asked to complete a vision related quality of life survey that includes 25 questions (NEI VFQ) about the impact of your eye condition on your life and functioning at your baseline, 3-6 weeks, and a final visit at 7-10 weeks. We will also request that you take a fundus photo and optical coherence tomography photo (OCT) at each visit to document exam findings. These photos do not add any additional risk and cause harm to you. You may notice a flash a light few a seconds. Otherwise no other side effects will be noted from the photos.

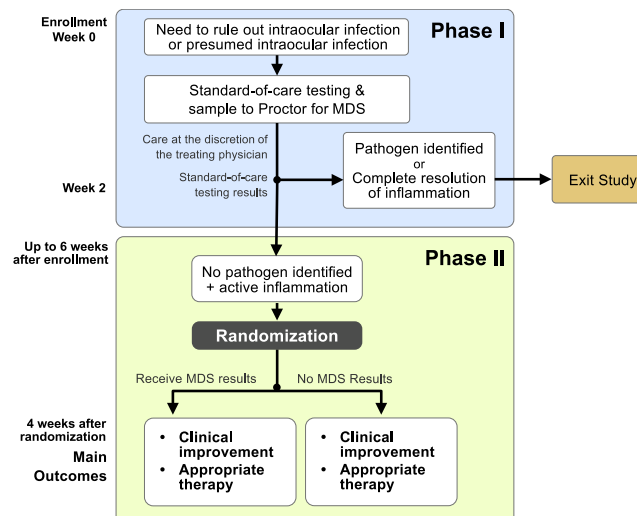
Study visits will be prespecified which include an initial visit, a visit at 3-6 weeks, and a final visit at 7-10 weeks. An eye exam will be performed at each visit.

Study Chart

Timepoint	Activity
Day 0	Eligibility Screening Informed Consent Study Enrollment Ocular sample collected (left over fluid) Baseline Eye Exam NEI VFQ (Patient Survey) Eye Imaging (Fundus Photography, Optical Coherence Tomography)
Week 2	Ocular Exam Eye Imaging (Fundus Photography, Optical Coherence Tomography) Laboratory Results Form Treatment Form
Week 3-6	MDS Results Completed Randomization NEI VFQ (Patient Survey) Ocular Exam Eye Imaging (Fundus Photography, Optical Coherence Tomography) Laboratory Results Form Treatment Form WHOQOF-BREF (Provider Survey)
Week 7-10 (4 weeks after randomization)	NEI VFQ (Patient Survey) Ocular Exam (Masked Examiner) Eye Imaging (Fundus Photography, Optical Coherence Tomography) Laboratory Results Form Treatment Form WHOQOF-BREF (Provider Survey)

Study Location: UCSF Mission Bay, Wayne and Gladys Valley Center for Vision

Study Plan:



How long will I be in the study?

You will be in the study for up to 10 weeks. However, researchers will continue to use your information and specimens indefinitely or until you decide that you no longer want the researchers to use your information and specimens.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to withdraw from the study.

If you decide later that you do not want your specimen and information to be used for this research, you can notify the investigator in writing at 490 Illinois St. Floor 2, San Francisco, CA 94158 United States, and we will destroy any remaining identifiable sample and information if it is no longer needed for your care. However, if any research has already been done using portions of your specimens or information, the data will be kept and analyzed as part of this study.

What will happen if I agree to donate my specimens?

If you agree to let researchers collect and store your specimens for future research, the following will happen:

- After all routine tests required for your care are finished, instead of discarding your leftover specimens we will save them in what is called a “tissue bank” used for future studies. We also will collect and save information from your medical record, including things like your name, medical record number, date of birth, including results of diagnostic tests, diagnoses, and treatments. Genetic information taken from the specimens (also known as genotype data) and the medical record data (also known as phenotype data) may be shared broadly in coded form but identifying information will not be shared.
- We may give your specimens and certain medical information about you (for example, diagnosis) to other scientists or companies not at UCSF, including to a government health research database, but we will not give them your name, address, phone number, or any other information that would identify you. Reports about any research will not be given to you or your doctor.
- Sometimes specimens are used for genetic research (about diseases that are passed on in families). Even if we use the specimen for genetic research, we will not put the results in your medical record. The research will not change the care you receive. Your specimen and any information about you will be kept until it is used up or destroyed. It may be used to develop new drugs, tests, treatments or products. In some instances, these may have potential commercial value. Your personal health information cannot be used for additional research without additional approval from either you or a review committee.
- Your specimens will be kept and will remain in the repository created within this study. The specimens will be kept indefinitely. If you decide later that you do not want your specimens and information to be used for future research, you can notify the investigator in writing at 490 Illinois Street, Floor 2 San Francisco, CA 94143, and we will destroy any

remaining identifiable specimens and information if they are no longer needed for your care. However, if any research has already been done using portions of your specimens, the data will be kept and analyzed as part of those research studies.

What risks are involved with donating specimens for research?

Confidentiality: Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Representatives of the University of California and the U.S. Food and Drug Administration may also see information about you for the purpose of monitoring or managing the conduct of this study.

There is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk. Although your name will not be with the sample, it will have other facts about you such as age, sex, and date of birth. These facts are important because they will help us learn if the factors that caused the uveitis to occur or get worse are the same or different based on these facts. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

Potential risks that may occur if you participate in this study include:

The risk is minimal in this study given that the eye fluid is left over specimen from an intraocular procedure to remove fluid from the eye as deemed necessary for standard of care.

There is an increased risk to the participant when performing a procedure to remove fluid from the eye. This procedure would be part of the standard of care at this time, so the risks would be what is normally experienced as standard of care. While these procedures are a routine part of ophthalmologist diagnostic procedures, there are some risk of adverse events that can occur while performing the procedure and after the procedure. Adverse ocular events related removal of eye fluid include the following: include corneal scar (scratch on the outer surface/ layer of the eye), cataract (lens clouding), infection (eye redness and eye pain), hyphema (blood/bleeding), hypotony (low eye pressure), and vision loss.

Specific safety steps have been taken to minimize the risks associated with the above-mentioned procedures. For infection control precautions the procedures have been reviewed by the collaborators in this study. To decrease the risk of infection, the procedure protocol calls for betadine to be applied to the eye pre-procedure and antibiotic drops will be administered post procedure. A post procedure exam will be performed with intraocular pressure to ensure no immediate adverse events occurred. Treatment will be administered at the office visit if an adverse event is detected.

Eye photos such as the OCT and fundus photos do not add any additional risk and cause no harm to you, your eyes, or your vision. You may notice a flash a light few a seconds. Otherwise, no other side effects will be noted from the photos.

Randomization risks: You will be assigned to an intervention arm to receive MDS results by chance.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Thuy Doan, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at (415) 476-6939.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, or the Research to Prevent Blindness depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

Are there benefits to taking part in the study?

There are benefits from being in this study that include using an innovative technology to potentially help aid with the diagnosis of your ocular condition. As a reminder, this is chosen at random to receive the results.

Participating in this study and releasing your clinical information will help us assess the accuracy and potential impact of MDS in diagnosing pathogens. This information may also be helpful in making these tests more widely available to the general community in the future.

What other choices do I have if I do not take part in this study?

If you choose not to enroll into the study no left-over fluid will be sent to UCSF for additional testing with MDS. Your specimens will be sent to the clinical laboratory for pathological or microbiological analysis as part of standard of care. Not enrolling into OPTICS will not impact your clinical care.

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study as stated above. Specimens and information gathered during this research study will be used for this study; the specimens and information will not be shared with other researchers unless you agree to this under the “optional research” section of this document.

Genetic Testing: Researchers will use your specimens to look at all of your DNA (this is called “whole genome sequencing”). DNA contains information that determines things like eye color, height, or disease risk that are passed on from parent to child.

Research results: There may be times when researchers using your information and/or specimens may learn new information. The researchers may or may not share these results with you, depending on several factors.

Commercial Use: If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the Research to Prevent Blindness
- Representatives of the University of California
-

Are there any costs to me for taking part in this study?

Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for the standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer.

If you have questions about what costs you will be responsible for, please talk with the study investigator before deciding to enroll in the study. Depending on the type of study, some of your costs could be substantial.

Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk with the study researcher about any questions, concerns or complaints you have about this study. Contact the study researcher, Dr. Thuy Doan, at (415)476-6939 or by email at

thuy.doan@ucsf.edu or Dr. Jessica Shantha at (415) 502-7923 or by email at Jessica.shantha@ucsf.edu.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

Consent

Please read each sentence below and think about your choice. After reading each sentence, put your initials in the "Yes" or "No" box. If you have any questions about this study, please talk to the study doctor or nurse. No matter what you decide to do, it will not affect your care.

1. My **identifiable** specimens and associated data may be kept for use in research to learn about, prevent, or treat ocular inflammation or ocular infections.

YES	NO
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2. My **identifiable** specimens and associated data may be kept for use in research to *learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease)*.

YES	NO
-----	----

3. Someone may contact me in the future to ask me to take part in more research.

YES	NO
-----	----

If you decline to participate in the bio-banking aspect of this study then you can still participate in this study.

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Subject's Signature for Consent
------	---------------------------------

Date	Person Obtaining Consent
------	--------------------------

Date	Witness – Only required if the participant is a non-English speaker or is legally blind/non reader
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Eligibility and Screening

Patient ID:

OPTICS Eligibility and Screening Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

GENERAL INFORMATION

Visit Date: (MM-DD-YYYY)

(MM-DD-YYYY)

A. INCLUSION CRITERIA

1. Is the patient at least 18 years of age?

☐ Yes
☐ No

2. Is the patient able to give consent?

☐ Yes
☐ No

3. Does the patient have a presumed infectious uveitis or endophthalmitis?

☐ Yes
☐ No

If "YES" all of questions 1-3, the patient may be eligible for OPTICS. Advance to next section.

NOTE: If "NO" was answered for ANY of questions 1-3, the patient is ineligible for participation in OPTICS.

B. EXCLUSION CRITERIA

4. Insufficient specimen for MDS (e.g. < 50 uL intraocular fluid)?

☐ Yes
☐ No

If patient answered "YES" to question 4, then the participant is not eligible for enrollment based on exclusion criteria.

D. DECISION TO ENROLL

5. Does the patient meet ALL of the inclusion criteria (Questions 1 through 3)?	☐ Yes ☐ No
6. Does the patient meet ANY of the exclusion criteria (Questions 4)?	☐ Yes ☐ No
7. Will the patient be enrolled in the study?	☐ Yes ☐ No

Administrative Information

Clinic Coordinator's/Ophthalmologist's initials:	
Please enter any additional comments, feedback, or issues:	
(For urgent matters, please email jessica.shantha@ucsf.edu)	
END TIME (HIDDEN):	

Eligibility and Screening Phase 2

Patient ID:

OPTICS Eligibility and Screening Form Phase 2 - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

GENERAL INFORMATION

Visit Date: (MM-DD-YYYY)

(MM-DD-YYYY)

A. INCLUSION CRITERIA

1. Is there active inflammation? (Any one criteria below)

☐ Yes
☐ No

a. $\geq$ 1+ anterior chamber cell and/or

b. $\geq$ 1+ vitreous haze and/or

c. Active retinal or choroidal inflammation and/or

d. Macular edema

If "YES" to question 1, the patient may be eligible for OPTICS PHASE 2. Advance to next section.

NOTE: If "NO" was answered for questions 1, the patient is ineligible for participation in OPTICS PHASE 2.

B. EXCLUSION CRITERIA

2. Has a pathogen been identified that is consistent with the clinical findings?

☐ Yes
☐ No

3. Is there complete resolution of inflammation?

☐ Yes
☐ No

4. Does the patient have no light perception vision?

☐ Yes
☐ No

If "YES" to any question 2-4, the patient may NOT be eligible for OPTICS PHASE 2. Advance to next section.

D. DECISION TO ENROLL

5. Does the patient meet the inclusion criteria
(Question 1)?

☐ Yes
☐ No
6. Does the patient meet ANY of the exclusion criteria
(Questions 2-4)?

☐ Yes
☐ No
7. Will the patient be enrolled into Phase 2?

☐ Yes
☐ No

Administrative Information

Clinic Coordinator's/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Baseline Demographics

Patient ID:

OPTICS Baseline Demographics Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

Visit Date (MM-DD-YYYY):

(MM-DD-YYYY)

BASELINE DEMOGRAPHICS

Patient's date of birth (MM-DD-YYYY):

(MM-DD-YYYY)

Sex:

- ☐ Male
☐ Female
☐ Other

If "Other", please specify:

Race (check all that apply):

- ☐ Asian
☐ African American, African, or Afro-Caribbean
☐ Middle Eastern/North African
☐ Indigenous Australian
☐ Native American, American Indian, or Alaska Native
☐ Native Hawaiian or other Pacific Islander
☐ Caucasian
☐ Prefer not to answer
☐ Other (specify)

If "Other", please (specify):

Ethnicity:

- ☐ Hispanic, Latino, or Spanish origin
☐ Not of Hispanic, Latino, or Spanish origin
☐ Prefer not to answer
☐ Other (specify)

If "Other", please specify:

LIFESTYLE

Smoking Status (including e-cigarettes):

- ☐ Current smoker
☐ Past smoker
☐ Never smoked

Average number of e-cigarette cartridges, cigarettes,
or cigars smoked per day (when smoking):

How many years did/have they smoke(d)?

Number of alcoholic drinks per week?

- ☐ 0
☐ 1-2
☐ 3-5
☐ 6+

Patient's height (numeric value only):

Units for height:

- ☐ Inches
☐ Centimeters

Patient's weight:

Units for weight:

- ☐ Pounds
☐ Kilograms

Is there anything else related to demographics that
you would like to report not collected on this form?

- ☐ Yes
☐ No

If yes, please describe other demographic information
here:

ADMINISTRATIVE INFORMATIONClinic Coordinator's initials/Ophthalmologist's
initials:

Please enter any additional comments, feedback, or
issues:

(For urgent matters, please email
jason.richards@ucsf.edu)

END TIME (HIDDEN):

Baseline Ophthalmology

Patient ID:

OPTICS Baseline Ophthalmology Form - V1.0

Patient ID:

Last Name:

START TIME (HIDDEN):

General Information

Visit Date (MM-DD-YYYY)

(MM-DD-YYYY)**Anatomical classification based on entire uveitis history**

	Right Eye	Left Eye	Both	Neither
Anterior	☐	☐	☐	☐
Intermediate	☐	☐	☐	☐
Anterior and Intermediate	☐	☐	☐	☐
Posterior	☐	☐	☐	☐
Panuveitis	☐	☐	☐	☐
Other (specify)	☐	☐	☐	☐

If other for the RIGHT eye, please specify:

If other for the LEFT eye, please specify:

Identify if any of the following procedures have ever been performed:

	Right Eye	Left Eye	Both	Neither
Vitrectomy	☐	☐	☐	☐
Peripheral iridotomy	☐	☐	☐	☐
Cataract surgery/extraction	☐	☐	☐	☐
Intravitreal injection	☐	☐	☐	☐
Glaucoma surgery (Specify type below)	☐	☐	☐	☐

Other (Specify type below)

☐☐☐☐

If other ocular procedure was performed in their RIGHT eye, please specify:

If other ocular procedure was performed in their LEFT eye, please specify:

If patient had glaucoma surgery in their RIGHT eye, please specify what type:

- ☐ Goniotomy
☐ Laser
☐ Minimally Invasive Glaucoma Surgery (MIGS)
☐ Trabeculectomy
☐ Tube

If patient had glaucoma surgery in their LEFT eye, please specify what type:

- ☐ Goniotomy
☐ Laser
☐ Minimally Invasive Glaucoma Surgery (MIGS)
☐ Trabeculectomy
☐ Tube

Have any of the following conditions ever occurred?

	Right Eye	Left Eye	Both	Neither
Epiretinal membrane	☐	☐	☐	☐
Macular edema	☐	☐	☐	☐
Optic nerve edema	☐	☐	☐	☐
Ocular hypertension	☐	☐	☐	☐
Glaucoma	☐	☐	☐	☐
Cataract	☐	☐	☐	☐
Ruptured globe	☐	☐	☐	☐
Vitreous hemorrhage	☐	☐	☐	☐
Endophthalmitis	☐	☐	☐	☐
Choroidal neovascularization	☐	☐	☐	☐
Retinal detachment	☐	☐	☐	☐
Retinal neovascularization	☐	☐	☐	☐
Other, specify	☐	☐	☐	☐

If other for the RIGHT eye, please specify:

If other for the LEFT eye, please specify:

Is there anything that you would like to report that is not collected on this form?

- ☐ Yes
☐ No

If yes, please specify:

Administrative Information

Clinic Coordinator's/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Visual Acuity

Patient ID:

OPTICS Visual Acuity Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

General Information

Visit Date (MM-DD-YYYY)

(MM-DD-YYYY)

Visit

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other, specify:

If other, please specify

RIGHT Eye Visual Acuity

Which type of chart did you use for the patient's
RIGHT eye?

- ☐ Snellen
☐ Tumbling E
☐ Other (specify):

Specify other method used:

Please select right eye visual acuity:

- ☐ 20/20
☐ 20/25
☐ 20/30
☐ 20/40
☐ 20/50
☐ 20/60
☐ 20/70
☐ 20/80
☐ 20/100
☐ 20/150
☐ 20/200
☐ 20/400
☐ Other

5. Was low vision testing performed for patient's right eye? ☐ Done ☐ Not done

Section II: RIGHT Eye Low Vision Testing

NOTE: Only complete Section II if the patient's visual acuity is not measurable for the right eye.

6. If visual acuity is not measurable for the RIGHT eye, please conduct the count fingers (CF) test: ☐ Pass ☐ Fail

7. If patient fails the count fingers test for the RIGHT eye, please conduct the hand motion (HM) test: ☐ Pass ☐ Fail

8. If patient fails the hand motion test for the RIGHT eye, please conduct the light perception (LP) test: ☐ Pass ☐ Fail

LEFT Eye Visual Acuity

12.a Which type of chart did you use for the patient's left eye? ☐ Snellen ☐ Tumbling E ☐ Other (specify):

12.ii Specify other method used: _____

Please select left eye visual acuity: ☐ 20/20 ☐ 20/25 ☐ 20/30 ☐ 20/40 ☐ 20/50 ☐ 20/60 ☐ 20/70 ☐ 20/80 ☐ 20/100 ☐ 20/150 ☐ 20/200 ☐ 20/400 ☐ Other

13. Was low vision testing performed for patient's right eye? ☐ Done ☐ Not done

Section IV: LEFT Eye Low Vision Testing

NOTE: Only complete Section V if the patient's visual acuity is not measurable for the left eye.

14. If visual acuity is not measurable for the LEFT eye, please conduct the count fingers (CF) test: ☐ Pass ☐ Fail

15. If patient fails the count fingers test for the LEFT eye, please conduct the hand motion (HM) test: ☐ Pass ☐ Fail

16. If patient fails the hand motion test for the LEFT eye, please conduct the light perception (LP) test:

☐ Pass

☐ Fail

Section V: Administrative Information

Clinic Coordinator's initials/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Clinical Eye Exam

Patient ID:

OPTICS Clinical Eye Exam Form - V1.0

Patient ID:

Last Name:

START TIME (HIDDEN):

General Information

Visit Date (MM-DD-YYYY)

(MM-DD-YYYY)

Visit

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other, specify:

Other:

Has the participant received a COVID vaccination since their last visit?

- ☐ No
☐ Yes

Which COVID vaccination did the participant receive?

- ☐ None
☐ Moderna
☐ Pfizer
☐ Johnson and Johnson

Date of most recent COVID-19 vaccination

Which eye(s) were examined?

- ☐ Right eye
☐ Left eye
☐ Both eyes

If only the RIGHT eye was examined, specify reason:

- ☐ a. Left eye eviscerated or enucleated
☐ b. Artificial left eye/eye not present
☐ c. Severe phthisis; left eye present but cannot examine

If only the LEFT eye was examined, specify reason:

- ☐ a. Right eye eviscerated or enucleated
☐ b. Artificial right eye/eye not present
☐ c. Severe phthisis; right eye present but cannot examine

SECTION I: Eye Examination**Are there any pupil abnormalities?**

	None	Relative afferent pupillary defect	Transillumination defect	Other abnormality, specify:	Cannot assess pupillary function (specify why below)
RIGHT eye	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐

If other pupil abnormality for the RIGHT eye, please specify: _____

Specify why pupillary function cannot be assessed for the RIGHT eye:

- ☐ Corneal opacity
☐ Extensive posterior synechiae
☐ Other reason cannot assess (specify)

If cannot assess RIGHT eye pupillary function for another reason, please specify: _____

If other pupil abnormality for the LEFT eye, please specify: _____

Specify why pupillary function cannot be assessed for the LEFT eye:

- ☐ Corneal opacity
☐ Extensive posterior synechiae
☐ Other reason cannot assess (specify)

If cannot assess LEFT eye pupillary function for another reason, please specify: _____

Intraocular Pressure

RIGHT eye intraocular pressure (mmHg) _____

LEFT eye intraocular pressure (mmHg) _____

How was intraocular pressure measured?

	Goldmann Applanation Tonometer	Tonopen	iCare	Pneumotonometer	Not done (explain why):
RIGHT eye method of capture (if examined)	☐	☐	☐	☐	☐
LEFT eye method of capture (if examined)	☐	☐	☐	☐	☐

If intraocular pressure was not done on the RIGHT eye, please specify why: _____

If intraocular pressure was not done on the LEFT eye,
please specify why _____

Does the eye have any conjunctival/scleral abnormalities? (Check all that apply)

	None	Conjunctivitis	Scleritis	Episcleritis	Scleral thinning	Other, specify:	Cannot assess (explain why):
RIGHT eye	☐	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐	☐

If a different conjunctival/scleral abnormality was found on the RIGHT eye, please specify what: _____

If the presence of conjunctival/scleral abnormalities could not be assessed on the RIGHT eye, please specify why: _____

If a different conjunctival/scleral abnormality was found on the LEFT eye, please specify what: _____

If the presence of conjunctival/scleral abnormalities could not be assessed on the LEFT eye, please specify why: _____

Are any of the following present on the cornea? (Check all that apply)

	None	Corneal scar	Corneal edema	Active keratitis	Other, specify:	Cannot assess (explain why):
RIGHT eye	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐

If another corneal condition was found in the RIGHT eye, please specify what: _____

If the cornea in the RIGHT eye could not be assessed, please specify why: _____

If another corneal condition was found in the LEFT eye, please specify what: _____

If the cornea in the LEFT eye could not be assessed, please specify why: _____

Check for keratic precipitates on the corneal endothelium. Are any found?

	Yes--Active keratic precipitates	Yes--Inactive keratic precipitates	No	Cannot assess (explain why):
RIGHT eye	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐

If there are active keratic precipitates on the RIGHT eye, are they granulomatous?

- ☐ Granulomatous
☐ Non-granulomatous

If unable to assess for keratic precipitates for the RIGHT eye, please specify why:

If there are active keratic precipitates on the LEFT eye, are they granulomatous?

- ☐ Granulomatous
☐ Non-granulomatous

If unable to assess for keratic precipitates for the LEFT eye, please specify why:

Check for any iris abnormalities. Were any found? (Check all that apply)

	None	Posterior synechiae	Iris atrophy	Iridocorneal touch	Other, specify:	Cannot assess (explain why)
RIGHT eye	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐

If there is posterior synechiae in the RIGHT eye, please specify how many degrees (0-360):

If another iris abnormality was found in the RIGHT eye, please specify what:

If the iris was not able to be assessed for abnormalities in the RIGHT eye, please specify why:

If there is posterior synechiae in the LEFT eye, please specify how many degrees (0-360):

If another iris abnormality was found in the LEFT eye, please specify what:

If the iris was not able to be assessed for abnormalities in the LEFT eye, please specify why:

Indicate the aqueous inflammatory cell level in the anterior chamber visible in a 1 mm height narrow slit beam.

Cell levels:

0: < 1 cell

0.5+: 1 to 5 cells

1+: 6 to 15 cells

2+: 16 to 25 cells

3+: 26 to 50 cells

4+: greater than 50 cells

	0	0.5+	1+	2+	3+	4+	Cannot assess (specify why):
RIGHT eye	☐	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐	☐

If unable to assess for aqueous inflammatory cells in the RIGHT eye, please specify why: _____

If unable to assess for aqueous inflammatory cells in the LEFT eye, please specify why: _____

Specify the aqueous flare level in the anterior chamber.

Flare levels:

0: absent

1+: faint, barely detectable

2+: moderate iris/lens detail clear

3+: marked, iris/lens details hazy

4+: intense, fixed coagulated aqueous humor, considerable fibrin present

	0	1+	2+	3+	4+	Cannot assess (specify why):
RIGHT eye	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐

If unable to assess for aqueous flare in the RIGHT eye anterior chamber, please specify why: _____

If unable to assess for aqueous flare in the LEFT eye anterior chamber, please specify why: _____

Assess for hypopyon. Is hypopyon present?

	Yes, there is hypopyon	No hypopyon
RIGHT eye	☐	☐
LEFT eye	☐	☐

If hypopyon is present in the RIGHT eye, indicate the severity (in millimeters)

_____ (mm)

If hypopyon is present in the LEFT eye, indicate the severity (in millimeters)

_____ (mm)

Lens abnormality (check all that apply)

Please check all lens abnormalities that apply for the RIGHT eye:

- ☐ None
- ☐ Trivial opacities
- ☐ Posterior subcapsular
- ☐ Cortical changes
- ☐ Nuclear sclerosis
- ☐ Mature cataract
- ☐ Significant enough opacity to affect assessment of the back of the eye
- ☐ Pseudophakic
- ☐ Aphakic
- ☐ Other, specify: _____
- ☐ Cannot assess (specify why): _____

If there is another type of lens abnormality for the RIGHT eye, please specify: _____

If unable to assess for any lens abnormalities for the RIGHT eye, please specify why:

- ☐ Posterior synechiae
- ☐ Other, specify: _____

If unable to assess for lens abnormalities for the RIGHT eye for other reasons than posterior synechiae, please specify why: _____

Please check all lens abnormalities that apply for the LEFT eye:

- ☐ None
- ☐ Trivial opacities
- ☐ Posterior subcapsular
- ☐ Cortical changes
- ☐ Nuclear sclerosis
- ☐ Mature cataract
- ☐ Significant enough opacity to affect assessment of the back of the eye
- ☐ Pseudophakic
- ☐ Aphakic
- ☐ Other, specify: _____
- ☐ Cannot assess (specify why): _____

If there is another type of lens abnormality for the LEFT eye, please specify: _____

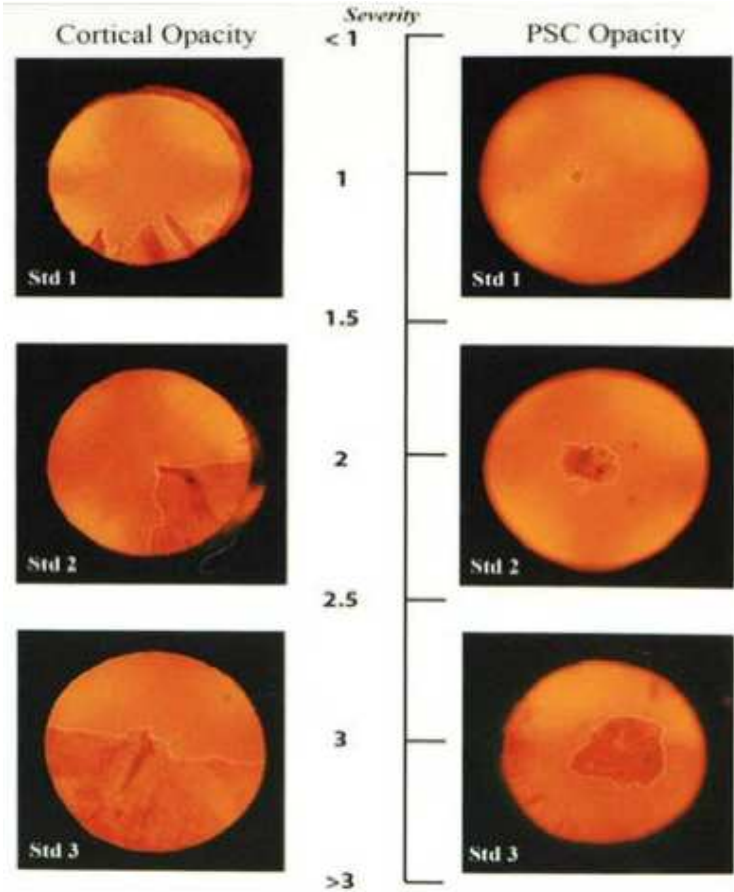
If unable to assess for any lens abnormalities for the LEFT eye, please specify why:

- ☐ Posterior synechiae
- ☐ Other, specify: _____

If unable to assess for lens abnormalities for the LEFT eye for other reasons than posterior synechiae, please specify why: _____

Age-Related Eye Disease Study (AREDS) Clinical Lens Grading System.

Please use the slit lamp and compare the view to the attached image for all parts of this question.



Posterior subcapsular opacities (PSC)

RIGHT eye:

☐ 0
 ☐ < 1
 ☐ 1
 ☐ 1.5
 ☐ 2
 ☐ 2.5
 ☐ 3
 ☐ > 3
 ☐ Cannot grade
 ☐ N/A

LEFT eye:

☐ 0
 ☐ < 1
 ☐ 1
 ☐ 1.5
 ☐ 2
 ☐ 2.5
 ☐ 3
 ☐ > 3
 ☐ Cannot grade
 ☐ N/A

Cortical opacities (CO)

RIGHT eye:

- ☐ 0
☐ < 1
☐ 1
☐ 1.5
☐ 2
☐ 2.5
☐ 3
☐ > 3
☐ Cannot grade
☐ N/A

LEFT eye:

- ☐ 0
☐ < 1
☐ 1
☐ 1.5
☐ 2
☐ 2.5
☐ 3
☐ > 3
☐ Cannot grade
☐ N/A

Indicate the level of anterior vitreous cells seen in the 1 x 0.5mm beam (consider only cells in clear lacunae)

Anterior vitreous cell levels:**0: no cells present****0.5+: 1 to 5 cells****1+: 6 to 10 cells****2+: 11 to 20 cells****3+: 21 to 50 cells****4+: greater than 50 cells**

	0	0.5+	1+	2+	3+	4+	Cannot assess (specify why):
RIGHT eye	☐	☐	☐	☐	☐	☐	☐
LEFT eye	☐	☐	☐	☐	☐	☐	☐

RIGHT eye

☐

0.5+

☐

1+

☐

2+

☐

3+

☐

4+

☐

Cannot assess (specify why):

☐

LEFT eye

☐

0.5+

☐

1+

☐

2+

☐

3+

☐

4+

☐☐

If unable to assess the anterior vitreous cells in the RIGHT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Other, specify:

If unable to assess the anterior vitreous cells in the RIGHT eye for reasons other than posterior synechiae or dense cataracts, please specify why:

If unable to assess the anterior vitreous cells in the LEFT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Other, specify:

If unable to assess the anterior vitreous cells in the LEFT eye for reasons other than posterior synechiae or dense cataracts, please specify why: _____

SECTION II: Ophthalmoscopy

Are there any other vitreous abnormalities?

	None	Other, specify:	Cannot assess (specify why)
RIGHT eye	☐	☐	☐
LEFT eye	☐	☐	☐

If any other vitreous abnormalities are found in the RIGHT eye that aren't noted elsewhere, please indicate them here: _____

If unable to assess for other vitreous abnormalities in the RIGHT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Other, specify: _____

If unable to assess for other vitreous abnormalities in the RIGHT eye for other reasons, please specify why: _____

If any other vitreous abnormalities are found in the LEFT eye that aren't noted elsewhere, please indicate them here: _____

If unable to assess for other vitreous abnormalities in the LEFT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Other, specify: _____

If unable to assess for other vitreous abnormalities in the LEFT eye for other reasons, please specify why: _____

For the question below, please use the indirect ophthalmoscope and compare the view using the NEI Nussenblatt Scale below:

NEI Nussenblatt Scale for Vitreous Haze

Grade	Description
0	Clear
0.5+	Slight blurring of optic disc margin Normal striations and reflex of nerve fiber layer cannot be visualized
1+	Opacities without obscuration of retinal details
2+	Few opacities resulting in mild blurring of details of optic nerve and retinal vessels
3+	Optic nerve head and retinal vessels significantly blurred but still visible
4+	Dense opacity obscuring optic nerve head



NEI Nussenblatt Scale (see NEI vitreous haze grading poster)

	0	0.5+	1+	2+	3+	4+
RIGHT eye:	☐	☐	☐	☐	☐	☐
LEFT eye:	☐	☐	☐	☐	☐	☐

Were you able to grade vitreous haze accurately?

In some instances, dense cataract, vitreous hemorrhage, or extensive posterior synechiae may influence your grading.

	Yes	No
RIGHT eye:	☐	☐
LEFT eye:	☐	☐

Can the fundus be seen?

	Yes	Partial view	No (specify why):
RIGHT eye:	☐	☐	☐
LEFT eye:	☐	☐	☐

If the fundus cannot be seen in the RIGHT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the fundus cannot be seen in the RIGHT eye for a different reason than those listed above, please specify why it cannot be seen here:

If the fundus cannot be seen in the LEFT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the fundus cannot be seen in the LEFT eye for a different reason than those listed above, please specify why it cannot be seen here:

Optic nerve edema

	Present	Absent	Cannot assess (specify why):
RIGHT eye:	☐	☐	☐
LEFT eye:	☐	☐	☐

If the presence of optic nerve edema cannot be assessed in the RIGHT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the presence of optic nerve edema cannot be assessed in the RIGHT eye for a different reason than listed above, please specify why it cannot be seen here:

If the presence of optic nerve edema cannot be assessed in the LEFT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the presence of optic nerve edema cannot be assessed in the LEFT eye for a different reason than listed above, please specify why it cannot be seen here:

Cup-to-Disc (C/D) ratio

RIGHT eye Cup-to-Disc (C/D) ratio:

Note: if cannot assess the C/D ratio, please enter "99"

_____ (Right Eye)

If the Cup-to-Disc (C/D) ratio cannot be assessed in the RIGHT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the Cup-to-Disc (C/D) ratio cannot be assessed in the RIGHT eye for a different reason than listed above, please specify why it cannot be seen here:

LEFT eye Cup-to-Disc (C/D) ratio:

Note: If cannot assess the C/D ratio, please enter "99"

_____ (Left Eye)

If the Cup-to-Disc (C/D) ratio cannot be assessed in the LEFT eye, please specify why:

- ☐ Posterior synechiae
☐ Dense cataract
☐ Vitreous opacity
☐ Other, specify:

If the Cup-to-Disc (C/D) ratio cannot be assessed in the LEFT eye for a different reason than listed above, please specify why it cannot be seen here:

Are any retinal choroidal abnormalities present?

	Present (if so, specify):	Absent
RIGHT eye:	☐	☐
LEFT eye:	☐	☐

If any retinal choroidal abnormalities are present in the RIGHT eye, please specify what abnormalities are present here:

If any retinal choroidal abnormalities are present in the LEFT eye, please specify what abnormalities are present here:

Location of current inflammation

In the RIGHT eye, please specify the location of current inflammation based on the parts of the eye you can assess:
(Check one for each eye)
Do not include Cystoid Macular Edema (CME)

- ☐ Anterior: Mostly anterior chamber ($\geq 1+$ AC cell)
- ☐ Anterior + Intermediate: Anterior chamber AND vitreous/pars plana
- ☐ Posterior: Retinal/choroidal involvement
- ☐ Panuveitis: Anterior chamber AND retinal/choroidal involvement
- ☐ Uveitis not currently active: (i.e., grade $\leq 0.5+$ for anterior chamber cells and vitreous haze and no active retinal/choroidal lesions)
- ☐ Never had uveitis
- ☐ Unable to determine

In the LEFT eye, please specify the location of current inflammation based on the parts of the eye you can assess:
(Check one for each eye)
Do not include Cystoid Macular Edema (CME)

- ☐ Anterior: Mostly anterior chamber ($\geq 1+$ AC cell)
- ☐ Anterior + Intermediate: Anterior chamber AND vitreous/pars plana
- ☐ Posterior: Retinal/choroidal involvement
- ☐ Panuveitis: Anterior chamber AND retinal/choroidal involvement
- ☐ Uveitis not currently active: (i.e., grade $\leq 0.5+$ for anterior chamber cells and vitreous haze and no active retinal/choroidal lesions)
- ☐ Never had uveitis
- ☐ Unable to determine

Administrative Information

Clinic Coordinator's initials/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Imaging Form

Patient ID:

OPTICS IMAGING Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

Visit date (MM-DD-YYYY)

((MM-DD-YYYY))

Visit:

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other (specify):

If "Other" please specify:

Fundus Photos

Fundus Photo Machine Right and Left Eye

- ☐ Optos
☐ Zeiss Clarus
☐ Other, (specify):

If "Other" please specify:

Fundus Photo Right Eye

Is the fundus photo in the right eye normal?

- ☐ Yes
☐ No
☐ Not Done

If not done, reason:

Fundus Photo Right Eye Findings

	Present	Absent
Vitreous Haze	☐	☐
Disc Edema	☐	☐
Vasculitis	☐	☐
Retinitis	☐	☐
Chorioretinal Scar	☐	☐
Other, (specify):	☐	☐

If "Other" please specify:

Fundus Photo Left Eye

Is the fundus photo in the left eye normal?

☐ Yes
☐ No
☐ Not Done

If not done, reason:

Fundus Photo Left Eye Findings

	Present	Absent
Vitreous Haze	☐	☐
Disc Edema	☐	☐
Vasculitis	☐	☐
Retinitis	☐	☐
Chorioretinal Scar	☐	☐
Other, (specify):	☐	☐

If "Other" please specify:

Fundus Photo Right Eye Upload

Fundus Photo Left Eye Upload

OCT**OCT Right Eye**

OCT Machine Right Eye:

☐ Heidelberg Spectralis
☐ Zeiss Cirrus
☐ Other
☐ Not done

If "Other", please specify:

If "Not done", reason:

RIGHT EYE central subfield thickness:

($\pm$ 95 μ m)

OCT Findings Right Eye

	Present	Absent
Subretinal Fluid	☐	☐
Cystoid Spaces	☐	☐
Epiretinal Membrane	☐	☐
Other (specify):	☐	☐

If "Other", please specify:

OCT Left Eye

OCT Machine Left Eye:

☐ Heidelberg Spectralis
☐ Zeiss Cirrus
☐ Other, specify:
☐ Not done

If other, please specify:

If "Not done", reason:

LEFT EYE central subfield thickness:

($\pm$ 95 μ m)

OCT Findings Left Eye

	Present	Absent
Subretinal Fluid	☐	☐
Cystoid Spaces	☐	☐
Epiretinal Membrane	☐	☐
Other (specify):	☐	☐

If "Other", please specify:

14.a OCT Upload Right Eye

14.b OCT Upload Left Eye

Other Imaging

Other Imaging Right Eye

- ☐ None
- ☐ B-Scan
- ☐ Fundus autofluorescence
- ☐ Fluorescein angiography
- ☐ Indocyanine green angiography
- ☐ Other

If "Other" please specify:

Right Eye Image Upload

Right Eye Image Upload

Right Eye Image Upload

Right Eye Image Upload

Right Eye Image Upload

Other Imaging Left Eye

- ☐ None
- ☐ B-Scan
- ☐ Fundus autofluorescence
- ☐ Fluorescein angiography
- ☐ Indocyanine green angiography
- ☐ Other

If "Other" please specify:

Left Eye Image Upload

Left Eye Image Upload

Left Eye Image Upload

Left Eye Image Upload

Left Eye Image Upload

Administrative information

Clinic Coordinator's initials/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email
jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Physician Survey

Patient ID:

OPTICS Physician Survey - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

Visit Date (MM-DD-YYYY):

(MM-DD-YYYY)

Visit

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other, specify:

If "other", please specify:

Provider Information

1. Provider Name (Last Name, First Name):

Physician Survey

1. What do you believe as the TRUE likelihood that this patient has an infection?

0% Non-Infectious 50% Unsure 100% Infectious

(Place a mark on the scale above)

2. What specific pathogen(s) are you most suspicious for if any?

3. How certain are you of your leading diagnosis?

0% Uncertain 50% Unsure 100% Certain

(Place a mark on the scale above)

4. Additional comments?

Do you believe this patient has an infection?

- ☐ Yes
☐ No

Did you receive MDS results?

☐ Yes
☐ No

We would like to access the impact of MDS results on your clinical diagnostic reasoning. Please indicate if you agree with the following statements. The MDS results:

	YES	NO
1. Helped to identify a diagnosis that we had not previously considered	☐	☐
2. Increased clinical confidence in certain diagnoses on our differential	☐	☐
3. Helped to rule out infectious etiologies on our differential	☐	☐
4. Did not provide any additional information to refine our differential	☐	☐
5. Provided information that was difficult to interpret so increased diagnostic uncertainty	☐	☐

We would like to assess the impact of the MDS assay on your clinical management. Please indicate whether the results of the MDS assay have increased, decreased, or not affected the likelihood of the following management decisions:

	Increased	Decreased	Not Affected
1. Order additional laboratory testing for infectious etiologies	☐	☐	☐
2. Order additional laboratory testing for non-infectious etiologies	☐	☐	☐
3. Order additional invasive diagnostic procedures	☐	☐	☐
4. Narrowing/discontinuing empiric treatment for infection	☐	☐	☐
5. Start target treatment for infection	☐	☐	☐
6. Start treatment for autoimmune or other non-infectious etiologies	☐	☐	☐

Administrative Information

Clinic Coordinator's initials/Ophthalmologist's initials: _____

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu) _____

END TIME (HIDDEN): _____

Standard of Care Investigation Form

Patient ID:

OPTICS Investigation Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

General Information

Visit:

- ☐ Baseline
- ☐ Week 2
- ☐ Randomization (MDS result or no MDS result)
- ☐ Final Follow Up (4 weeks after randomization)
- ☐ Other, specify:

If "Other", please specify:

Blood Work

Was bloodwork performed?

- ☐ Yes
- ☐ No

Date of blood draw (MM-DD-YYYY)?

(MM-DD-YYYY)

Type of TB testing?

- ☐ QuantiFERON Gold
- ☐ T.SPOT
- ☐ PPD
- ☐ Not performed

Results of most recent TB test (must be from within a year or at baseline)

- ☐ Positive
- ☐ Negative
- ☐ Indeterminate

Syphilis Antibody Testing?

- ☐ Yes
- ☐ No

Syphilis Antibody Result?

- ☐ Positive
- ☐ Negative

RPR testing?

- ☐ Yes
- ☐ No

RPR Result (Titer)?

Chest X-Ray

Was a chest X-ray performed?

- ☐ Yes
☐ No

What were the results of the chest X-ray?

- ☐ Normal
☐ Abnormal

If "Abnormal" please specify findings:

Intraocular Fluid

Date of intraocular fluid aquisition (MM-DD-YYYY)?

What type of procedure was performed?

- ☐ Anterior Chamber Paracentesis
☐ Vitreous Tap
☐ Pars Plana Vitrectomy
☐ None
☐ Chorioretinal Biopsy
☐ Other (specify):

If "Other" please specify:

What eye was the procedure performed on?

- ☐ Right Eye
☐ Left Eye

PCR Testing

Was PCR testing performed?

- ☐ Yes
☐ No

What PCR testing was sent?

- ☐ HSV
☐ VZV
☐ CMV
☐ Toxoplasmosis
☐ Other (specify):

If "Other", please specify:

Are PCR results available?

- ☐ Yes
☐ No

Date PCR test results were available (MM-DD-YYYY)?

HSV result?

- ☐ Positive
☐ Negative

VZV result? ☐ Positive
☐ Negative

CMV result? ☐ Positive
☐ Negative

Toxoplasmosis result? ☐ Positive
☐ Negative

Other Result?

Cultures

Were cultures sent? ☐ Yes
☐ No

What cultures were tested? ☐ Blood agar culture
☐ Potato flake culture
☐ Thioglycolate
☐ Other (specify):

If "Other", please specify:

Are culture results available? ☐ Yes
☐ No

Blood agar culture result? ☐ Positive
☐ No growth to date

Potato flake culture result? ☐ Positive
☐ No growth to date

Thioglycolate result? ☐ Positive
☐ No growth to date

Other culture result? ☐ Positive
☐ No growth to date

Cytopathology

Was cytopathology sent on tissue? ☐ Yes
☐ No

What tissue source?

Is the result available? ☐ Yes
☐ No

Date cytopathology results were available (MM-DD-YYYY)?

Cytopathology results:

Other Laboratory Investigations

Complete Blood Count

☐ Normal
☐ Abnormal
☐ Results not available
☐ Test not performed

What is the abnormal findings?

Comprehensive Metabolic Panel

☐ Normal
☐ Abnormal
☐ Results not available
☐ Test not performed

What is the abnormal findings?

Other Investigations

Other Investigations?

☐ Yes
☐ No

Other test name?

Is the other test result available?

☐ Yes
☐ No

Other test results?

Other Investigations?

☐ Yes
☐ No

Other test name?

Is the other test result available?

☐ Yes
☐ No

Other test results?

Please list any additional investigations and results:

Administrative Information:

Clinic Coordinator's initials/Ophthalmologist's initials: _____

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu) _____

END TIME (HIDDEN): _____

Treatment

Patient ID:

OPTICS Treatment Form V1.0

Patient ID:

Patient Last Name

Visit

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other, specify:

If "Other", please specify

Treatment Intravitreal Injection(s)

Was an anti-infective intravitreal injection administered in the RIGHT EYE?

- ☐ Yes
☐ No

Was an anti-infective intravitreal injection administered in the LEFT EYE?

- ☐ Yes
☐ No

Date of administration (MM/DD/YYYY)

(MM-DD-YYYY)

Intravitreal Injection (s)
What treatment was administered in the RIGHT EYE?
(Mark all that apply)

- ☐ Foscarnet
☐ Ganciclovir
☐ Clindamycin
☐ Vancomycin
☐ Ceftazidime
☐ Voriconazole
☐ Amphotericin B
☐ Other, specify:

If "Other", please specify

Intravitreal Injection (s)
What treatment was administered in the LEFT EYE?
(Mark all that apply)

- ☐ Foscarnet
☐ Ganciclovir
☐ Clindamycin
☐ Vancomycin
☐ Ceftazidime
☐ Voriconazole
☐ Amphotericin B
☐ Other, specify:

If "Other", please specify

Was a corticosteroid injection given in the RIGHT EYE?

- ☐ Yes
☐ No

Was a corticosteroid injection given in the LEFT EYE?

- ☐ Yes
☐ No

Corticosteroid injection
What treatment was administered in the RIGHT EYE?

- ☐ Subtenons Kenalog
☐ Subconjunctival Kenalog
☐ Intravitreal Dexamethasone
☐ Intravitreal Triamcinolone
☐ Dexamethasone Intravitreal Implant (Ozurdex)
☐ Fluocinolone acetonide Intravitreal Implant (Yutiq)

Corticosteroid injection
What treatment was administered in the LEFT EYE?

- ☐ Subtenons Kenalog
☐ Subconjunctival Kenalog
☐ Intravitreal Dexamethasone
☐ Intravitreal Triamcinolone
☐ Dexamethasone Intravitreal Implant (Ozurdex)
☐ Fluocinolone acetonide Intravitreal Implant (Yutiq)

Systemic Medication

Was systemic medication given?

- ☐ Yes
☐ No

Was an anti-infective medication given?

- ☐ Yes
☐ No

Systemic Medication
What therapy was given?
(Mark all that apply)

- ☐ Oral Valacyclovir
☐ Oral Acyclovir
☐ Oral Valganciclovir
☐ Intravenous Acyclovir
☐ Intravenous Ganciclovir
☐ Intravenous Foscarnet
☐ Oral Clindamycin
☐ Oral Azithromycin
☐ Other, specify:

If "Other", please specify (route, medication)

Was a systemic corticosteroid given?

- ☐ Yes
☐ No

Corticosteroid
What medication was administered?
(Mark all that apply)

- ☐ Oral Prednisone
☐ Intravenous SoluMedrol

Dose and Frequency

Topical Treatment

Were topical drop(s) prescribed?

- ☐ Yes
☐ No

Were topical corticosteroid(s) given for the RIGHT EYE?

- ☐ Yes
☐ No

Were topical corticosteroid(s) given for the LEFT EYE?

- ☐ Yes
☐ No

Corticosteroid RIGHT EYE
What medication was prescribed?
(Mark all that apply)

- ☐ Prednisolone acetate 1%
☐ Difluprednate
☐ Lotemax
☐ Fluorometholone
☐ Other, specify:

If "Other", please specify

Corticosteroid LEFT EYE
What medication was prescribed?
(Mark all that apply)

- ☐ Prednisolone acetate 1%
☐ Difluprednate
☐ Lotemax
☐ Fluorometholone
☐ Other, specify:

If "Other", please specify

Were ocular hypotensive(s) given for the RIGHT EYE?

- ☐ Yes
☐ No

Ocular Hypotensive(s) RIGHT EYE
What medication(s) was prescribed?
(Mark all that apply)

- ☐ Dorzolamide
☐ Brimonidine
☐ Timolol
☐ Prostaglandin analogue
☐ Dorzolamide/Timolol
☐ Brimonidine/Timolol
☐ Diamox
☐ Other, specify:

If "Other", please specify

Were ocular hypotensive(s) given for the LEFT EYE?

- ☐ Yes
☐ No

Ocular Hypotensive(s) LEFT EYE
What medication(s) was prescribed?
(Mark all that apply)

- ☐ Dorzolamide
☐ Brimonidine
☐ Timolol
☐ Prostaglandin analogue
☐ Dorzolamide/Timolol
☐ Brimonidine/Timolol
☐ Diamox
☐ Other, specify:

If "Other", please specify

Was a cycloplegic drop given for the RIGHT EYE?

☐ Yes
☐ No

Was a cycloplegic drop given for the LEFT EYE?

☐ Yes
☐ No

What other topical medications were adminsterted to the RIGHT EYE that have not been captured?
Please list medication(s)

What other topical medications were adminsterted to the LEFT EYE that have not been captured?
Please list medication(s)

Administrative Information

Clinic Coordinator's initials/Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email
jessica.shantha@ucsf.edu)

Patient Dropout

Patient ID:

OPTICS Patient Dropout Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

Visit Date

(MM-DD-YYYY)

Visit:

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other (specify):

If "Other", please specify:

1. Reason for dropout:

- ☐ Patient moved and is unable to return
☐ Patient is no longer willing to participate in the study
☐ Death of the patient
☐ Other reason (specify):

1.a. Other (specify):

2. Comments:

Administrative Information:

Clinic Coordinator's initials:

Investigator's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email
jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Research Sample Lab

Patient ID:

OPTICS Research Sample Lab Form - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

General Information

Date of introcular fluid collection (MM-DD-YYYY):

((MM-DD-YYYY))

Introcular Fluid Sample

Is the collection tube for the sample labeled?

- ☐ Yes
☐ No
☐ N/A

Barcode label number:

Date the sample was sent to F.I. Proctor Foundation
(MM/DD/YYYY):

Administrative Information

Technician initials:

Please enter any additional comments, feedback, or
issues:

(For urgent matters, please email
jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Adverse Event Checklist

Patient ID:

OPTICS Adverse Event Checklist - V1.0

Patient ID:

Patient Last Name:

START TIME (HIDDEN):

General Information

Visit Date (MM-DD-YYYY)

(MM-DD-YYYY)

Visit:

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other (specify):

Other (specify):

Ocular Adverse Event

Did the patient have an ocular adverse event?

- ☐ Yes
☐ No

Eye involved?

- ☐ Right Eye
☐ Left Eye

What type of adverse event did the patient have?
(choose all that apply)

- ☐ Hyphema
☐ Hypotony
☐ Ocular hypertension
☐ Wound leak
☐ Corneal ulcer
☐ Endophthalmitis
☐ Vitreous hemorrhage
☐ Cataract
☐ Anterior capsule violation
☐ Retinal detachment
☐ Other (specify)

Other (specify):

Please rate the relatedness of the AE to the ocular procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocular procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

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4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Please rate the relatedness of the AE to the ocualr procedure performed:

- ☐ 1. Certain
☐ 2. Probable
☐ 3. Possible
☐ 4. Unlikely

1. Certain - The AE occurs in a plausible temporal relationship with the procedure and cannot be explained by concurrent disease or other drugs.

2. Probable - The AE occurs in a reasonable time sequence with the procedure and unlikely to be explained by concurrent disease or other drugs.

3. Possible - The AE occurs in a reasonable time sequence with the procedure but could be explained by concurrent disease or other drugs.

4. Unlikely - The AE occurs in a temporal relationship with the procedure that makes a causal relationship improbable and concurrent disease and/or other drugs provide plausible explanations.

Treatment

Was a treatment adminisitered?

- ☐ Yes
☐ No

Treatment, please specify:

Treatment, please specify:

Treatment, please specify:

Systemic Adverse Event

Did the patient have a systemic adverse event?

- ☐ Yes
☐ No

2. What type of complication did the patient have? (choose all that apply)

- ☐ Allergic reaction
☐ Other (specify)

Allergic reaction to what medication?

If "Other", please specify:

Please specify the type of : Allergic reaction

☐ None

☐ Non-serious: Pruritis without rash or erythema or localized urticaria, or diffuse maculopapular rash, or dry desquamation.

☐ Serious: Generalized urticaria, angioedema or worse, vesiculation, moist desquamation, ulceration up to and including: exfoliative dermatitis; mucous membrane involvement; or Stevens-Johnson Syndrome, or erythema multiforme, or necrosis requiring surgery.

Treatment

Was a treatment adminisitered?

☐ Yes

☐ No

Treatment, please specify:

Treatment, please specify:

Treatment, please specify:

Administrative Information:

Clinic Coordinator's initials:

Ophthalmologist's initials:

Please enter any additional comments, feedback, or issues:

(For urgent matters, please email jessica.shantha@ucsf.edu)

END TIME (HIDDEN):

Protocol Deviation

Patient ID:

OPTICS Protocol Deviation Form - V1.0

Patient ID:

Patient Last Name

START TIME (HIDDEN):

Visit Date

(DD-MM-YYYY)

Visit

- ☐ Baseline
☐ Week 2
☐ Randomization (MDS result or no MDS result)
☐ Final Follow Up (4 weeks after randomization)
☐ Other, specify:

Other (specify):

Description of the Protocol Deviation:

Description of the protocol deviation: (please specify)

- ☐ Patient missed follow up appointment per study protocol
☐ Final visit clinical exam was not performed by a masked examiner
☐ Other specify:

If "Other", please (specify):

3. Date of the protocol deviation:

(MM-DD-YYYY)

4. Explanation of the protocol deviation:

Administrative Information:

Clinic Coordinator's initials: _____

Investigator's initials: _____

Please enter any additional comments, feedback, or issues: _____

(For urgent matters, please email
jessica.shantha@ucsf.edu) _____

END TIME (HIDDEN): _____

WHOQOL-BREF

Please complete the survey below.

Thank you for your Participation!

WHOQOL-BREF

Physician Name (Last Name, First Name):

Patient ID:

Survey Consent

We are conducting a research study using metagenomic deep sequencing and traditional diagnostics in the diagnosis of ocular infectious diseases. As part of the study, we would like to learn more about the quality of life in the physicians caring for these complex patients. If you agree to be a part of this study, we will ask you to complete an online survey, the World Health Organization Quality of Life BREF survey which ask questions pertaining to physical health, psychological health, social relationships, and environment. There will be no direct benefit to you for participating in this study, but what we learn from it may provide insight into the quality of life of physicians which can be used for future research studies.

We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- University of California
- Research to Prevent Blindness

Being in this study is optional. If you choose to participate, you can tell me if you want to stop being in the study at any time.

If you have questions about the survey or study, please contact Jessica Shantha at Jessica.shantha@ucsf.edu.

If you would like to participate and give consent please mark below (Yes: agreeing to participate, No: agreeing not to participate).

Thank you.

☐ Yes ☐ No

What is your gender?

- ☐ Female
☐ Male

What is your Date of Birth (MM-DD-YY)?

(MM-DD-YYYY)

Date that the survey was completed (MM-DD-YY)?

(MM-DD-YYYY)

What is the highest education you received?

- ☐ None at all
☐ Primary school
☐ Secondary school
☐ Tertiary

What is your marital status?

- ☐ Single
☐ Married
☐ Living as married
☐ Separated
☐ Divorced
☐ Widowed

Are you currently ill?

- ☐ Yes
☐ No

If something is wrong with your health who do you think it is (illness/problem)?

Instructions:

This assessment asks how you feel about your quality of life, health, or other areas of your life.

Please answer all the questions. If you are unsure about which response to give to a question, please choose the one that appears most appropriate. This can often be your first response.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life in the last two weeks.

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

How would you rate your quality of life?

- ☐ Very poor
- ☐ Poor
- ☐ Neither poor nor good
- ☐ Good
- ☐ Very good

How satisfied are you with your health?

- ☐ Very dissatisfied
- ☐ Dissatisfied
- ☐ Neither satisfied nor dissatisfied
- ☐ Satisfied
- ☐ Very satisfied

The following questions ask about how much you have experienced certain things in the last two weeks.

1: Not at all
2: A little
3: A moderate amount
4: Very much
5: An extreme amount

	1	2	3	4	5
To what extent do you feel that physical pain prevents you from doing what you need to do?	☐	☐	☐	☐	☐
How much do you need any medical treatment to function in your daily life?	☐	☐	☐	☐	☐
How much do you enjoy life?	☐	☐	☐	☐	☐
To what extent do you feel your life to be meaningful?	☐	☐	☐	☐	☐

The following questions ask about how much you have experienced certain things in the last two weeks.

1: Not at all

2: A little

3: A moderate amount

4: Very much

5: Extremely

	1	2	3	4	5
How well are you able to concentrate?	☐	☐	☐	☐	☐
How safe do you feel in your daily life?	☐	☐	☐	☐	☐
How healthy is your physical environment?	☐	☐	☐	☐	☐

The following questions ask about how completely you experience or were able to do certain things in the last two weeks.

1: Not at all

2: A little

3: Moderately

4: Mostly

5: Completely

	1	2	3	4	5
Do you have enough energy for everyday life?	☐	☐	☐	☐	☐
Are you able to accept your bodily appearance?	☐	☐	☐	☐	☐
Have you enough money to meet your needs?	☐	☐	☐	☐	☐
How available to you is the information that you need in your day-to-day life?	☐	☐	☐	☐	☐
To what extent do you have the opportunity for leisure activities?	☐	☐	☐	☐	☐

How well are you able to get around?

☐ Very poor
☐ Poor
☐ Neither
☐ Good
☐ Very good

The following questions ask you to say how good or satisfied you have felt about various aspects of your life over the last two weeks.

1: Very dissatisfied

2: Dissatisfied

3: Neither satisfied nor dissatisfied

4: Satisfied

5: Very satisfied

	1	2	3	4	5
How satisfied are you with your sleep?	☐	☐	☐	☐	☐
How satisfied are you with your ability to perform your daily living activities?	☐	☐	☐	☐	☐
How satisfied are you with your capacity for work?	☐	☐	☐	☐	☐
How satisfied are you with yourself?	☐	☐	☐	☐	☐
How satisfied are you with your personal relationships?	☐	☐	☐	☐	☐
How satisfied are you with your sex life?	☐	☐	☐	☐	☐
How satisfied are you with the support you get from your friends?	☐	☐	☐	☐	☐
How satisfied are you with the conditions of your living place?	☐	☐	☐	☐	☐
How satisfied are you with your access to health services?	☐	☐	☐	☐	☐
How satisfied are you with your transport?	☐	☐	☐	☐	☐

The following question refers to how often you have felt or experienced certain things in the last two weeks.

How often do you have negative feelings such as blue mood, despair, anxiety, depression?

☐ Never ☐ Seldom ☐ Quite often ☐ Very often ☐ Always

Did someone help you fill out this form?

☐ Yes ☐ No

Time completed survey

NEI-VFQ

Thank you for your participation in the OPTICS Study. Please complete the survey below.

Thank you!

NEI Vision Function Questionnaire

Instructions:
Please choose the response that best describes your situation.
Please answer all the questions as if you were wearing your glasses or contact lenses (if any).
Please take as much time as you need to answer each question. All your answers are confidential. In order for this survey to improve our knowledge about vision problems and how they affect your quality of life, your answers must be as accurate as possible.
Remember, if you wear glasses or contact lenses for a particular activity, please answer all of the following questions as though you were wearing them.

THANK YOU!!!!!!

Patient ID: _____

Patient Name (Last name, first name): _____

Date (MM-DD-YY): _____
(MM-DD-YYYY)

How did you complete the survey?
☐ Completed online by self
☐ Someone read the questions and responses
☐ Other (please specify)

If "Other" please specify: _____

Part-1 General Health and Vision

At the present time, would you say your eyesight using both eyes (with glasses or contact lenses, if you wear them) is excellent, good, fair, poor, or very poor or are you completely blind (choose one):

- ☐ 1 Excellent
- ☐ 2 Good
- ☐ 3 Fair
- ☐ 4 Poor
- ☐ 5 Very poor
- ☐ 6 Completely Blind

How much of the time do you worry about your eyesight (choose one):

- ☐ 1 None of the time
- ☐ 2 A little of the time
- ☐ 3 Some of the time
- ☐ 4 Most of the time
- ☐ 5 All of the time

How much pain or discomfort have you had in and around your eyes (for example, burning, itching or aching)? Would you say it is (choose one):

- ☐ 1 None
- ☐ 2 Mild
- ☐ 3 Moderate
- ☐ 4 Severe
- ☐ 5 Very severe

Part-2 Difficulty with Activities

The next questions are about how much difficulty, if any, you have doing certain activities wearing your glasses or contact lenses, if you use them for that activity. (choose one answer for each item)

1: No difficulty at all

2: A little difficulty

3: Moderate difficulty

4: Extreme difficulty

5: Stopped doing this because of your eyesight

6: Stopped doing this for other reasons or not interested in doing this

	1	2	3	4	5	6
How much difficulty do you have reading ordinary print in newspapers?	☐	☐	☐	☐	☐	☐
How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have finding something on a crowded shelf?	☐	☐	☐	☐	☐	☐
How much difficulty do you have reading street signs or the names of stores?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have going down steps, stairs, or curbs in dim light or at night?	☐	☐	☐	☐	☐	☐

Part-2 Difficulty with Activities

The next questions are about how much difficulty, if any, you have doing certain activities wearing your glasses or contact lenses, if you use them for that activity. (choose one answer for each item)

1: No difficulty at all

2: A little difficulty

3: Moderate difficulty

4: Extreme difficulty

5: Stopped doing this because of your eyesight

6: Stopped doing this for other reasons or not interested in doing this

	1	2	3	4	5	6
Because of your eyesight, how much difficulty do you have noticing objects off to the side while you are walking along?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have seeing how people react to things you say?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have picking out and matching your own clothes?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have visiting with people in their homes, at parties, or in restaurants?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events?	☐	☐	☐	☐	☐	☐

Are you currently driving?

- ☐ Yes
☐ No

If No, have you never driven a car or have you given up driving (choose one):

- ☐ Never drove
☐ Gave up

IF YOU GAVE UP DRIVING: Was that mainly because of your eyesight, mainly for some other reason, or because of both eyesight and other reasons? (choose one):

- ☐ Mainly eyesight (1)
☐ Mainly other reason (2)
☐ Both eye sight and other reason (3)

IF CURRENTLY DRIVING: How much difficulty do you have driving during the daytime in familiar places? Would you say you have (choose one):

- ☐ No difficulty at all (1)
- ☐ A little difficulty (2)
- ☐ Moderate difficulty (3)
- ☐ Extreme difficulty (4)

Part-2 Difficulty with Activities

Please answer the below questions using the following options

1: No difficulty at all

2: A little difficulty

3: Moderate difficulty

4: Extreme difficulty

5: Stopped doing this because of your eyesight

6: Stopped doing this for other reasons or not interested in doing this

	1	2	3	4	5	6
How much difficulty do you have driving at night?	☐	☐	☐	☐	☐	☐
How much difficulty do you have driving in difficult conditions, such as in bad weather, during rush hour, on the freeway, or in the city traffic?	☐	☐	☐	☐	☐	☐

Part 3- Responses to Vision Problems

The next questions are about how things you do may be affected by your vision.

For each one, I'd like you to tell me if this is true for all, most, some, a little, or none of the time. (choose one answer for each item)

1: All of the time

2: Most of the time

3: Some of the time

4: A little of the time

5: None of the time

	1	2	3	4	5
Do you accomplish less than you would like because of your vision?	☐	☐	☐	☐	☐
Are you limited in how long you can work or do other activities because of your vision?	☐	☐	☐	☐	☐
How much does pain or discomfort in or around your eyes, for example, burning, itching or aching, keep you from doing what you'd like to be doing?	☐	☐	☐	☐	☐

Part 3- Responses to Vision Problems

For each of the following statements, please tell me if it is definitely true, mostly true, mostly false, or definitely false for you, or you are not sure. (choose one answer for each item)

1: Definitely true

2: Mostly true

3: Not sure

4: Mostly false

5: Definitely false

	1	2	3	4	5
I stay home most of the time because of my eyesight:	☐	☐	☐	☐	☐
I feel frustrated a lot of the time because of my eyesight:	☐	☐	☐	☐	☐
I have much less control over what I do, because of my eyesight:	☐	☐	☐	☐	☐
Because of my eyesight, I have to rely too much on what other people tell me:	☐	☐	☐	☐	☐
I need a lot of help from others because of my eyesight:	☐	☐	☐	☐	☐
I worry about doing things that will embarrass myself or others, because of my eyesight:	☐	☐	☐	☐	☐

Part 4: Additional Questions**GENERAL HEALTH**

How would you rate your overall health, on a scale where zero is as bad as death and 10 is best possible health:

☐ 0 Worst ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Best

GENERAL VISION

How would you rate your eyesight now (with glasses or contact lens on, if you wear them), on a scale from 0 to 10, here zero means the worst possible eyesight, as bad or worse than being blind, and 10 means the best possible eyesight:

☐ 0 Worst ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Best

Near Vision

For each of the following statements, please choose the response that matches your difficulty level (choose one)

1: No difficulty at all

2: A little difficulty

3: Moderate difficulty

4: Extreme difficulty

5: Stopped doing this because of your eyesight

6: Stopped doing this for other reasons or not interested in doing this

	1	2	3	4	5	6
Wearing glasses, how much difficulty do you have reading the small print in a telephone book, on a medicine bottle, or on legal forms?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have figuring out whether bills you receive are accurate?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have doing things like shaving, styling your hair, or putting on makeup?	☐	☐	☐	☐	☐	☐

Distance Vision and Social Functioning

For each of the following statements, please choose the response that matches your difficulty level (choose one)

1: No difficulty at all

2: A little difficulty

3: Moderate difficulty

4: Extreme difficulty

5: Stopped doing this because of your eyesight

6: Stopped doing this for other reasons or not interested in doing this

	1	2	3	4	5	6
Because of your eyesight, how much difficulty do you have recognizing people you know from across the room?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have taking part in active sports or other outdoor activities that you enjoy (like golf, bowling, jogging, or walking)	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have seeing and enjoying programs on TV?	☐	☐	☐	☐	☐	☐
Because of your eyesight, how much difficulty do you have entertaining friends and family in your home?	☐	☐	☐	☐	☐	☐

Role Limitations

The next questions are about things you may do because of your vision. For each item, I'd like you to tell me if this is true for you all, most, some, a little or none of the time. (choose one answer for each item)

1: All of the time**2: Most of the time****3: Some of the time****4: A little of the time****5: None of the time**

	1	2	3	4	5
Do you have more help from others because of your vision?	☐	☐	☐	☐	☐
Are you limited in the kinds of things you can do because of your vision?	☐	☐	☐	☐	☐

Well-Being/Distress and Dependency

The next questions are about how you deal with your vision. For each of the following statements, please tell me if it is definitely true, mostly true, mostly false, or definitely false for you or you are not sure. (choose one answer for each item)

1: Definitely true**2: Mostly true****3: Not sure****4: Mostly false****5: Definitely false**

	1	2	3	4	5
I am often irritable because of my eyesight:	☐	☐	☐	☐	☐
I don't go out of my home alone, because of my eyesight:	☐	☐	☐	☐	☐