Clinical Study Protocol

A Prospective, Single-Arm Study Evaluating Crosslinked Hyaluronate Canalicular Gel for the Treatment of Dry Eye Disease in Patients Undergoing Refractive Cataract Surgery

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Sponsor:	Vance Thompson Vision
Sponsor Location:	Vance Thompson Vision 3101 West 57th Street Sioux Falls, SD, 57108
Study Name:	**The LaReCa Study**
Study Phase:	Investigator-Sponsored Trial

Clinical Study Protocol Synopsis

Title: A Prospective, Single-Arm Study Evaluating Crosslinked Hyaluronate Canalicular Gel for the Treatment of Dry Eye Disease in Patients Undergoing Refractive Cataract Surgery

Principal Investigator: Kayla Karpuk, OD / Vance Thompson, MD

Sponsor Location: Vance Thompson Vision
3101 West 57th Street
Sioux Falls, SD, 57108

Study Name: Crosslinked Hyaluronate Canalicular Gel: A Benefit Study

Objective: To determine patient reported outcomes of hyaluronate crosslinked canalicular gel placed in patients undergoing refractive cataract surgery

Background: Dry eye disease (DED) is a prevalent condition among patients presenting for cataract surgery, with nearly 50% exhibiting signs of DED, even if asymptomatic. [1] As a result, DED is often undiagnosed and underreported in patients undergoing cataract surgery.[1] This pre-existing condition can be exacerbated by the surgical procedure itself, leading to increased ocular surface irritation, fluctuating vision, and overall discomfort after surgery.[2] Consequently, despite achieving an improvement in vision from the cataract removal, patients may report dissatisfaction due to these persistent DED symptoms, highlighting a critical gap in aligning surgical success with patient-reported outcomes.[2,3]

The cataract surgery process, involving corneal incisions and abundant use of perioperative medications, can disrupt tear film stability and worsen DED.[1] Therefore, perioperative identification and management of DED is essential to optimize the visual and refractive outcome of the surgery. Addressing ocular surface health prior to surgery contributes to improved accuracy of biometric measurements, which are critical for intraocular lens (IOL) power calculations and achieving desired refractive targets.[3,4] Proactive management helps stabilize and prepare the ocular surface, potentially reducing postoperative complications and ensuring that patient expectations are more closely met.[4]

Fortunately, the dry eye treatment landscape continues to evolve which enables more individualized care for patients. Recently, a cross-linked hyaluronic acid canalicular gel (Lacrifill®) was introduced, which represents a novel, alternative solution for lacrimal occlusion. This treatment works by occluding the tear drainage system, thereby increasing the retention of natural tears, improving tear film stability, and reducing ocular surface irritation.[5] Proactive use of the canalicular gel could lead to more reliable pre-operative measurements, better visual outcomes, and increased post-operative comfort, which is particularly important for

patients receiving advanced technology IOLs.[5] Improvements in both signs and symptoms of DED have been reported using lacrimal occlusion, suggesting it could play a valuable role in optimizing the cataract surgery experience.[6]

Study Design: Prospective, single-site, single-arm study enrolling 60 patients who have elected advanced IOL implantation at the time of cataract surgery and have a diagnosis of dry eye disease. The study will consist of 5 study visits, over a 3-5 month time period. Patients will receive bilateral lacrimal occlusion of crosslinked hyaluronate canalicular gel pre-operatively

The primary endpoint will be the change from baseline to 3- month visit in non-invasive tear break up time (NITBUT) in primary eyes as measured by a non-invasive, automated ocular surface analyzer. Additional endpoints measured will be the change from baseline in the visual analog score and OSDI. The effect of pre-operative lacrimal occlusion on accuracy of preoperative biometry/keratometry measurements will be evaluated as well as residual refractive error at 30 and 90 days post-operative.

Subject Population: 60 subjects, who have elected bilateral refractive cataract surgery will be enrolled.

Materials and Methods

- Informed consent will be obtained prior to collection of any study specific data.
- Each subjects' demographics, medical and ocular history will be reviewed.
- Inclusion and exclusion criteria will be reviewed for each subject.
- Subjects will be asked to report satisfaction using the visual Analog Score (VAS) and dry eye symptoms using the Ocular Surface Disease Index (OSDI)
- Subjects' monocular and binocular uncorrected distance visual acuity (UDVA) will be obtained on an ETDRS chart at a distance of 4 meters
- A manifest refraction will be performed on each subject.
- Monocular and binocular best corrected distance visual acuity (BCDVA) will be obtained on an ETDRS chart at a distance of 20 feet in photopic lighting conditions.
- Biometry measurements will be obtained.
- Objective tear meniscus height will be measured.
- Objective non-invasive tear break up time will be measured.
- The subjects' eyes will be thoroughly examined at the slit lamp.
- Bilateral canalicular occlusion with cross-linked hyaluronate will be performed prior to cataract surgery
- Patients will undergo standard of care cataract post-operative visit testing and procedures

Inclusion criteria:

1. Be willing and able to understand and sign the informed consent form (ICF)
2. Men or non-pregnant women age 22 or older
3. Clear intraocular media other than cataract
4. Diagnosis of dry eye disease (OSDI score ≥ 13)
5. Non-invasive Tear break up time ≤ 10 seconds in at least one eye
6. Willing and able to comply with all study related visits and procedures
7. In the opinion of the investigator, patients who are appropriate for advanced technology lens implants

Exclusion criteria:

1. History of punctal cautery
2. Lacrimal anatomy (e.g., nasolacrimal duct obstruction) that per investigator suggests that the patient would not be a good candidate for lacrimal occlusion or patients for whom lacrimal occlusion would increase risk

Procedures

Subjects will be recruited from the site's current patient population who have been scheduled for refractive cataract surgery and have a concomitant diagnosis of dry eye disease. Enrollment and informed consent will be administered by study coordinators. Data will be collected by investigators and study coordinators as follows.

Visit 0 (7 to 45 days prior to surgery):

- Informed consent will be obtained prior to collection of any study-specific data.
- Potential subjects' demographics, medical and ocular history, and concomitant medications will be reviewed.
- Inclusion and exclusion criteria will be reviewed for each subject.
- Ocular Surface Disease Index (OSDI) will be obtained
- Visual Analog Score will be obtained

- Pre-operative biometry measurements will be obtained
- Non-invasive tear break up time (NITBUT) will be obtained
- Automated tear meniscus (TMH) will be obtained
- Best-corrected distance visual acuity (BCDVA) will be obtained using the ETDRS
- Slit Lamp Exam
- NaFl staining will be measured (NEI grading scale)
- If both eyes qualify for the study, the primary eye will be the eye with the smaller NITBUT. If the NITBUT is the same in both eyes, the primary eye will be the right eye.
- Lacrimal occlusion of the inferior canaliculi of both eyes will be performed

Visit 1A/B (operative day[s]):

- Repeated biometry measurements obtained on each eye
- VAS
- Patients may undergo sequential bilateral surgery per site standard of care
- Adverse events will be collected

Visit 2 (1-2 days post-op):

- UCDVA as measured by ETDRS
- Slit lamp exam
- Corneal fluorescein staining
- Intraocular pressure measured by standard of care
- Adverse events will be collected

Visit 3 (7 days post cataract surgery +/- 2 days)

- OSDI
- VAS
- NITBUT
- TMH
- Manifest refraction
- UCDVA/BCDVA measured by ETDRS
- Slit lamp exam
- Corneal fluorescein staining
- Intraocular pressure measured by standard of care
- Adverse events will be collected

Visit 4 (30 days post cataract surgery +/- 7 days)

- OSDI
- VAS
- NITBUT
- TMH
- Manifest refraction
- UCDVA/BCDVA measured by ETDRS
- Slit lamp exam
- Corneal fluorescein staining
- Intraocular pressure measured by standard of care
- Dilated fundus exam
- Adverse events will be collected

Visit 5 (90 days post cataract surgery +/- 14 days)

- OSDI
- VAS
- NITBUT
- TMH
- Manifest refraction
- UCDVA/BCDVA measured by ETDRS
- Slit lamp exam
- Corneal fluorescein staining
- Intraocular pressure measured by standard of care
- Adverse events will be collected

Data Analysis and Data Monitoring

Data will be captured by the principal investigators, sub-investigators and study coordinators. Data will be documented on source documents and subjects will be identified by subject numbers.

Data analysis will occur on an excel spreadsheet or in R statistical software with subjects identified by subject number. The Excel spreadsheet or R scripts will be on computer(s) that are password protected.

Baseline demographic and ocular characteristics will be quantified using descriptive statistics. Statistical analysis will be completed on all primary and secondary endpoints. A primary analysis will be conducted upon completion of the 3-month study period with an interim analysis of the first 30 patients to complete all visits.

The planned sample size is 60 eyes of 60 patients, with the primary eye selected as the eye with lower NITBUT at screening. Sample size was calculated to provide 80% power to detect a meaningful change of 0.8 seconds or greater from baseline to 3-months in NITBUT.

Secondary analyses will include fellow eyes and all (primary + fellow) eyes.

Data Storage and Confidentiality

Private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The research sponsor
- People who work with the research sponsor
- The Institutional Review Board (IRB) that reviewed this research

We may publish the results of this research. However, we will keep all names and other identifying information confidential.

We protect all information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

Sources documents will be placed in a binder and stored in locked cabinets.
This trial will be conducted in compliance with the protocol, GCP, and applicable regulatory requirement(s).

The participation for this trial is voluntary and subjects may stop or withdraw during the one-time examination at their discretion.

The principal investigator will report to the IRB any changes in research activity, serious adverse events, and completion of the study.

Sources

1. Trattler WB, Majmudar PA, Donnenfeld ED, et al. The Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) study: the effect of dry eye. *Clin Ophthalmol*. 2017;11:1423-1430.
2. De Gregorio C, Nunziata S, Spelta S, Lauretti P, Barone V, Surico PL, Mori T, Coassin M, Di Zazzo A. Unhappy 20/20: A New Challenge for Cataract Surgery. *Journal of Clinical Medicine*. 2025; 14(5):1408
3. Epitropoulos, A. T., et al. Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning. *J Cataract Refract Surg*. 2013;39(9):1352-1358.
4. Lai, E. C., & STArr, C. E. (2014). Managing dry eye disease in cataract patients. *Cataract & Refractive Surgery Today*, *14*(1), 53-55.
5. Fezza, J. P. (2018). Cross-linked hyaluronic acid gel occlusive device for the treatment of dry eye syndrome. *Clinical Ophthalmology*, 2277-2283.
6. Packer, M., Lindstrom, R., Thompson, V., Parekh, J. G., Gupta, P., Nijm, L. M., & Donnenfeld, E. (2022). The Effectiveness and Safety of a Novel Crosslinked Hyaluronate Canalicular Gel Occlusive Device for Dry Eye. *Journal of Cataract & Refractive Surgery*, 10-1097.