IRB PROTOCOL

Sponsor / Study Title:	**The Effectiveness of DSLT in Asian Normal Tension Glaucoma Patients**
Protocol #	**NTG_DSLT-001**
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Background:

Normal-tension glaucoma (NTG) is a form of open-angle glaucoma characterized by glaucomatous optic neuropathy in patients with intraocular pressure (IOP) measurements consistently lower than 21 mmHg[1] and has been shown to account for the majority of primary open-angle glaucoma (POAG) in the

population older than 40 years in Asian countries.[2] Lowering IOP remains the only proven intervention to delay progression, and even modest reductions can be beneficial in NTG.[3] Selective laser trabeculoplasty (SLT) has demonstrated efficacy and safety in lowering IOP in primary open-angle glaucoma and ocular hypertension, but its role in NTG is recently emerging and less clearly established. Recent studies suggest that SLT can achieve clinically meaningful IOP reductions and decrease IOP variability in NTG patients, potentially slowing disease progression.[4,5] SLT may also be an effective and safe treatment option for NTG, as either a first-line or second-line treatment.[6] Studies looking at long term outcomes found that SLT achieved a ~22% IOP reduction with a 41% decrease in medication use, but absolute success without medications declined from 61% at 6 months to 11% at 24 months, with many eyes requiring retreatment.[7]

Direct selective laser trabeculoplasty (DSLT) is an emerging variant of SLT that delivers laser energy without the need for a contact lens—making it a non-contact and potentially more patient-friendly procedure. However, in the GLAURious study that compares the efficacy of DSLT and SLT, NTG patients were excluded from the study and data on DSLT's effectiveness or safety specifically in NTG patients has not yet been reported in the peer-reviewed literature.[8]

Unmet Medical Need:

DSLT offers potential procedural advantages in open angle glaucoma and ocular hypertension but lacks evidence specific to NTG in current studies.

Study Objective

The objective of the study is to evaluate the safety and efficacy of direct selective laser trabeculoplasty (DSLT) in normal tension glaucoma (NTG) in Asian patient populations. Studies have indicated that NTG has higher prevalence in Asian populations.[10]

Study Hypothesis:

It is hypothesized that the use of DSLT leads to the reduction of medication and IOP in Asian NTG patients.

Study Design

The study is a 12-month prospective, single arm, single center interventional study evaluating the safety and efficacy of DSLT in NTG patients.

Study Cohort

The study cohort will consist of approximately 40 Asian eyes with NTG of all severities on 1-3 glaucoma medications.

Study Sample Size & Justification

The sample size determination is based on the requirement that data from 30 eyes will provide sufficient information to evaluate the clinical performance of the treatment in this single-arm study. To account for an anticipated rate of screen failures and subject discontinuations of 20-25%, the total planned enrollment is up to 40 eyes

Anticipated Study Duration

The study duration will be approximately thirty months

Study Endpoints

Primary Endpoint:

- 12 months absolute washed out IOP (and IOP reduction) compared to washed out IOP at baseline

Secondary Endpoints:

- # of medication reduction at 11 months
- Proportion of patients that are medication free at 11 months
- Proportion of patients achieving ≥ 10%, 15%, and 20% IOP reduction at 12 months
- Rate of secondary surgical intervention (SSI) at 12 months

Exploratory Endpoints:

- Visual field and nerve stability as defined by change in visual field mean deviation and optical coherence tomography of the retinal nerve fiber layer (OCT RNFL) thickness at 12 months compared to baseline

Study Methodology

- **Screening/Baseline Visit 1:** Patients with NTG (glaucomatous optic neuropathy in patients with IOP measurements consistently lower than 21 mmHg) on 1-3 glaucoma medications will be screened, enrolled, and receive informed consent. If patients qualify to take part in this study, they will undergo:
    - Completed dilated fundus exam (DFE), Humphrey visual field 24-2 test (HVF 24-2), optical coherence tomography of the retinal nerve fiber layer (OCT RNFL), and central corneal thickness (CCT) within inclusion range
    - Patients using glaucoma medications will undergo washout period of 6 weeks
    - Washed out IOP must be <= 21mmHg, both eyes are eligible to enroll
    - Will restart patients back on meds (if any) for safety reasons (i.e. faster progression)

- **Visit 2:** Procedure Visit

- Patient will undergo DSLT (standard 1.8mJ, 120 shots, 360degrees)
- 1 drop tetracaine & brimonidine pre-procedure in treatment eye
- IOP check 5 mins and 1- 2 hours post-procedure
- As standard of care, IOP spikes and inflammation are treated at the discretion of the investigator
- One medication to be removed post-procedure
- Step down approach of medication removal for patient safety
- i.e. from 2 to 1 medication or 1 medication to no medication

- **Visit 3:** 1-month post-procedure (+/- 1 week)
  - IOP check
  - If IOP reduces ≥10% from baseline screening medicated IOP then another medication is removed
  - Meds are reintroduced if IOP increases >10% from medicated baseline screening IOP

- **Visit 4 and 5:** 4 month and 8-month post- procedure (+/- 1 month)
  - As standard of practice, patients are seen every 3-4 months
  - IOP check

- **Visit 6:** 11 months- post-procedure (+/- 1month)
  - IOP check, not standard visit but prepare patient to do washout of medications (6 weeks)

- **Visit 7:** 12-13 months post-procedure
  - Washed-out IOP check
  - HVF 24-2, OCT, gonioscopy (check for PAS)

- Adverse event rates (IOP spike >6mmHg and inflammation) and SSI will also be collected

Inclusion & Exclusion Criteria

Inclusion Criteria:

- Asian descent
- NTG diagnosis: glaucomatous optic neuropathy in patients with IOP measurements consistently lower than 21 mmHg
- Mean deviation (MD) of the visual field between 0 to -12dB
    - No significant central vision loss within 5 degrees within 5th percentile
- Age ≥20 years
- NTG patients who are medically controlled on 1-3 medications and safe to wash out or IOP is still insufficient from medications and safe to washout
- Shaffer grade II or more on 3 of the 4 quadrants
- Central corneal thickness (CCT) 450–600µm
- All participants are able to provide written informed consent before participation

Exclusion Criteria:

- Angle closure glaucoma or narrow angle status post laser peripheral iridotomy (LPI), or any other open angle glaucoma excluding NTG
- History of SLT within last 2 years
- History intraocular surgery including refractive surgery, except for history of cataract surgery that has been greater than 1 year
- Patients anticipating cataract surgery during the study follow-up period
- Unable to have DSLT procedure due to pre-limbal findings
- Any presence of relevant ocular diseases including retinal disease with no confirmed cure

Study Visit Assessments

	Screening/ Baseline	**Visit 2 Procedure**	**Visit 3 1M -F/U**	**Visit 4&5 4&8 M F/U**	**Visit 6 11M F/U**	**Visit 7 12.5M F/U**
Demographics Consent	X					

Medication	X	X	X	X	X	X
CCT	X					
Gonio	X					X
IOP	X (washed out)	X	X	X	X	X (washed out)
DSLT		X				

STUDY PRODUCT INFORMATION

See Appendix for DFU

Adverse Event Assessment

Adverse event assessments will be per Principal Investigator discretion

Statistical Analysis

Descriptive statistics will be prepared for all study timepoints. For continuous variables, summaries will include the sample size, mean, standard deviation, median, minimum, and maximum. For categorical variables, summaries will report the number and percentage of eyes in each category. Analyses will include all eyes that complete the study.

A planned sub-analysis will be conducted on the subset of patients with a prior history of selective laser trabeculoplasty (SLT) to assess whether treatment outcomes differed from those without prior SLT.

Study Milestones & Timelines

Milestones	Estimated Timelines
Contracting	November 2025
IRB Approval	December 2025
First Patient, First Visit (FPFV) date or Data Collection start date	February 2026
Last Patient, Last Visit (LPLV) date or Data Analysis start date	January 2028
Final Clinical Study Report (CSR)	March 2028

Procedures for Recording and Reporting

All AEs will be documented on the Adverse Event case report form (CRF) and collected on a routine basis at monitoring visits. Procedure-related postoperative conditions that are normal consequences of ocular procedure and not clinically relevant will only be reported as adverse events at the discretion of the Sponsor-Investigator.

In addition, the Sponsor-Investigator must document all SAEs with details including the date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. All available information must be submitted to the study monitor immediately (ie, within 24 hours of the Sponsor-Investigator's knowledge of the event).

The Sponsor-Investigator is responsible for reporting all adverse events, including product deficiencies, quality complaints, malfunctions, and events of special Interest to the investigational product's manufacturer, Alcon; irrespective of causality within 24 hours following first notification of the event. All subsequent follow-up information about the event should also be provided to Alcon. Sponsor-Investigator will send initial, and follow-up reports directly to the Alcon QA Medical Complaints team at **MSUS.safety@alcon.com** using the appropriate forms.

The Sponsor-Investigator must also report all SAEs according to the requirements of regulatory authorities or IRB/IEC.

Follow-Up of Safety Information

The Sponsor-Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study. Any additional data from these follow-up procedures must be documented appropriately.

DATA REVIEW AND HANDLING

Completion of Study Records

All study data must be recorded directly on the approved study forms, which will serve as both the source documents and the case report forms for this Investigator-Initiated Trial (IIT). Data must be complete, accurate, and legible. Any discrepancies or missing information should be explained in the final report.

At a minimum, study records must include the following information for each subject:

- Subject identification (name, sex)
- Documentation of subject eligibility
- Date of informed consent and a copy of the signed consent form

- Dates of study visits
- Documentation that protocol-specific procedures were performed
- Results of study assessments, as required by the protocol
- Documentation of adverse events (AEs) and other safety parameters (as applicable)
- Records of medical history and use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation (if applicable)

The Principal Investigator is responsible for reviewing and certifying the accuracy and completeness of the study records.

Subject identifiers must not be recorded beyond the subject number, demographic information, and/or other permitted study identifiers. Deviations from this protocol, regulatory requirements, and Good Clinical Practice (GCP) must be documented in the study records. An explanation for each deviation should be included, and any corrective and preventive actions must be documented by the Investigator.

ADMINISTRATIVE PROCEDURES

Regulatory and Ethical Compliance

This clinical study will be conducted in compliance with the protocol, current Good Clinical Practices, including the International Conference on Harmonization (ICH) Guidelines, and with the Declaration of Helsinki. In addition, all applicable local, state, and federal requirements relevant to the use of investigational products in the countries involved will be adhered to. The Sponsor-Investigator will ensure that all personnel involved in the conduct of the clinical study are qualified to perform their assigned duties through relevant education, training, and experience.

The Sponsor-Investigator assures that the key design elements of this protocol will be registered on www.clinicaltrials.gov as required by current regulations. In addition, the results of this study will be made publicly available on www.clinicaltrials.gov regardless of the outcome as required by current regulations as applicable.

Informed Consent Procedures

Voluntary informed consent will be obtained from every subject (and/or legal representative, as applicable) prior to the initiation of any screening or other clinical study-related procedures. The Sponsor-Investigator must have a defined process for obtaining consent. Specifically, the Sponsor-Investigator, or designee, will explain the clinical study to each potential subject, and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided with an opportunity to ask questions of the Sponsor-Investigator, and if required by local regulation, other qualified personnel. The Sponsor-Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws

and will provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the clinical study, along with any known risks and potential benefits associated with the investigational product, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the clinical study and will be provided with contact information for the appropriate individuals should questions or concerns arise during the clinical study. The subject also will be told that their records may be accessed by appropriate authorities and personnel. The Sponsor-Investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

References

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