Appendix

Key protocol of LiGHT China Trial

a. Eligibility criteria，operational definition of OAG & OHT：

We have used the NICE recommended thresholds for initiating treatment1, with stringent diagnostic definitions of disease (OAG or OHT) for entry into the study. Uniocular patients are eligible.

1.1 Diagnosis of OAG

Open Angle Glaucoma is defined as an open drainage angle with no secondary causes (such as trauma)：

(1) and reproducible glaucomatous visual field (VF) defects as tested by the SITA Standard white-on-white 24-2 algorithm on the Humphrey Visual Field Analyser (HVF) (i.e. reproducible defect, in at least, of two or more contiguous points with $P < 0.01$ loss or greater, or three or more contiguous points with $P<0.05$ loss or greater, or abnormal Glaucoma Hemifield Test, GHT);

(2) or GON with localised absence of the neuro-retinal rim or, cup disc ratio of 0.7 or more, or asymmetry of cup disc ratio of 0.2 or more in similar sized eyes / optic discs.

And deemed to require treatment in the opinion of glaucoma specialist.

Subjects with pseudo-exfoliation are eligible，subjects who have undergone less than 4 weeks of medical treatment from their primary care ophthalmologists as a temporising control measure (with medications other than prostaglandins) will be permitted to enter the study, but will be required to undergo a 4-week washout period to establish their baseline IOP. Subjects with GON and IOP in the normal range are eligible. ‘Phasing’ (diurnal IOP pressure measurements) will be performed at the discretion of the treating clinician and if performed the maximum IOP recorded will be used as that day’s measurement.

1.2 Diagnosis of OHT

OHT with IOP above 21mmHg and requiring treatment as per NICE Guidelines. NICE OHT guidelines treat 4 categories of OHT on the basis of central corneal

thickness (CCT) and age (the rest are monitored for 3-5 years).

b. Criteria for treatment escalation decisions

Treatment will be escalated under the following circumstances:

1. "Strong Evidence" of progression (as defined below) irrespective of IOP.
2. IOP above Target by more than a certain threshold at a single visit (irrespective of evidence for progression)
3. IOP above Target by less than threshold plus "Less Strong Evidence" for progression. If the IOP is above Target by less than threshold with no evidence for progression, then the 'Treatment Target IOP' will be re-evaluated. More detail of the indications for treatment escalation and 'Treatment Target IOP' re-evaluation, to deal with specific clinical scenarios, is given in the full version protocol of the trial.

c. Method and unit of randomization（eyes/patients）

Randomization will be carried out according to a trial specific SOP. Online randomization (with blocking with random block sizes) will be used to randomize at the level of the patient and be stratified by diagnosis (OHT/OAG). The primary analysis will adjust for the stratification factor used in randomization. Participants will be randomized to medication or SLT group in equal proportion using a web-based randomization service provided by a specialist company to achieve full allocation concealment (www.sealedenvelope.co.uk). 'Sealed Envelope' will also hold the randomization list. A backup telephone service will be available. The incremental escalation of treatment flow-chat displays the procedure of the trial (**Figure A**).

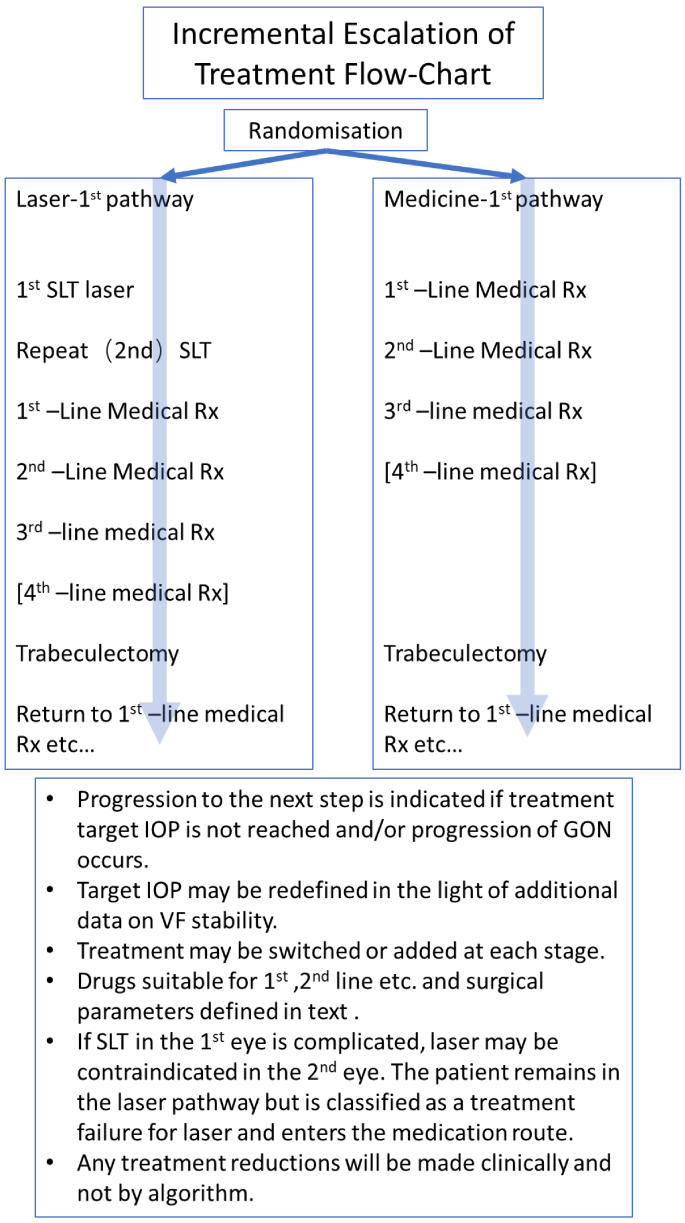

Figure A. Incremental escalation of treatment flow-chat.

d. Outcome measures

1. The primary outcome measure is Health Related Quality of Life(HRQL).

2. The secondary outcome measures including:

2.1 Treatment Pathway Cost and Cost-Effectiveness

2.2 Glaucoma-specific treatment-related quality of life: Glaucoma Utility Index (GUI)

2.3 Patient Reported Visual Function: VF-14

2.4 Other secondary outcomes：Patient Reported Disease and Treatment Related Symptoms: Glaucoma Symptom Scale83 (GSS), Patient Reported Visual Function: Glaucoma Quality of Life - 1510 (GQL-15), Objective measures of pathway effectiveness and visual function, Objective measures of the safety profiles of each pathway.

e. Specific statement as to whether participants signed a consent document should be included.

Informed consent was obtained from all individual participants included in the study. And all patients will be given a Patient Information Leaflet (PIL) and a copy of the Informed Consent. The original signed form will be retained at the study site. Vulnerable groups who would have difficulty in giving informed consent will not form part of this study. Patients who are unable to read Chinese but are able to retain and understand oral information about the study will be permitted to enter the study with an independent witness to counter-sign the consent form.

f. Method for assessment of ocular and systemic conditions

The baseline assessments will be done once the patient has been entered into the trial and before their first treatment. These will be the same as the screening assessment (slit-lamp examination, automated visual field test, HRT disc imaging, and KOWA simultaneous stereo digital disc photography) with the addition of self-completed baseline questionnaires (EQ5-D Glaucoma Utility Index (GUI), Glaucoma Symptom Scale (GSS), Glaucoma Quality of Life - 15 (GQL-15; a visual function measure) and Visual Function 14 (VF-14; a Chinese-validated function measure).

All patients will undergo a comprehensive medical history inquiry to find out if they had any history of other systemic diseases. The subjects will be tested for blood pressure and blood sugar to determine whether they had hypertension, diabetes,

asthma, angina, cardiac arrhythmia, ischaemic heart disease, migraines, cerebrovascular accident/stroke, peripheral vasospastic symptoms or blood loss/transfusion.

Full version of protocol is available via the link as following:

https://www.moorfields.nhs.uk/sites/default/files/LiGHT%20Trial%20Protocol%203.0%20-%2020-5-2015_3.pdf