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Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial

Six-Year Results of Primary Selective Laser Trabeculoplasty versus Eye Drops for the Treatment of Glaucoma and Ocular Hypertension

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Purpose: The Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial has shown selective laser trabeculoplasty (SLT) to be clinically and cost-effective as a primary treatment of open-angle glaucoma (OAG) and ocular hypertension (OHT) at 3 years. This article reports health-related quality of life (HRQoL) and clinical effectiveness of initial treatment with SLT compared with intraocular pressure (IOP)-lowering eye drops after 6 years of treatment.

Design: Prospective, multicenter randomized controlled trial.

Participants: Treatment-naive eyes with OAG or OHT initially treated with SLT or IOP-lowering drops.

Methods: Patients were allocated randomly to initial SLT or eye drops. After the initial 3 years of the trial, patients in the SLT arm were permitted a third SLT if necessary; patients in the drops arm were allowed SLT as a treatment switch or escalation. This study is registered at controlled-trials.com (identifier, ISRCTN32038223).

Main Outcome Measures: The primary outcome was HRQoL at 6 years; secondary outcomes were clinical effectiveness and adverse events.

Results: Of the 692 patients completing 3 years in the LiGHT Trial, 633 patients (91.5%) entered the extension, and 524 patients completed 6 years in the trial (82.8% of those entering the extension phase). At 6 years, no significant differences were found for the EuroQol EQ-5D 5 Levels, Glaucoma Utility Index, and Glaucoma Quality of Life-15 ($P > 0.05$ for all). The SLT arm showed better Glaucoma Symptom Scale scores than the drops arm (83.6 ± 18.1 vs. 81.3 ± 17.3, respectively). Of eyes in the SLT arm, 69.8% remained at or less than the target IOP without the need for medical or surgical treatment. More eyes in the drops arm exhibited disease progression (26.8% vs. 19.6%, respectively; $P = 0.006$). Trabeculectomy was required in 32 eyes in the drops arm compared with 13 eyes in the SLT arm ($P < 0.001$); more cataract surgeries occurred in the drops arm (95 compared with 57 eyes; $P = 0.03$). No serious laser-related adverse events occurred.

Conclusions: Selective laser trabeculoplasty is a safe treatment for OAG and OHT, providing better long-term disease control than initial drop therapy, with reduced need for incisional glaucoma and cataract surgery over 6 years. *Ophthalmology 2023;130:139-151 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

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Selective laser trabeculoplasty (SLT) was endorsed by the United States Food and Drug Administration for the treatment of glaucoma in 2001. Since then, SLT increasingly has been adopted as an alternative to intraocular pressure (IOP)-lowering eye drops, but until recently, data on its efficacy as a sole treatment were scarce.[1,2] Recent studies have compared SLT with monotherapy, which does not reflect routine clinical practice in which IOP is treated to target. As a result, a Cochrane systematic review called for more research into the efficacy of SLT compared with contemporary medication regimens.[3]

The Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial is a multicenter randomized controlled trial comparing initial treatment with SLT with initial treatment with IOP-lowering eye drops for treatment-naïve patients with OAG or OHT, assessing health-related quality of life (HRQoL), cost-effectiveness, and clinical efficacy after 3

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years.[4] In 2019, the LiGHT Trial reported that initial treatment of ocular hypertension (OHT) or open-angle glaucoma (OAG) with SLT is more cost-effective than initial treatment with contemporary IOP-lowering eye drops after 3 years, while also providing drop freedom to 74.2% of patients, a reduced number of glaucoma surgeries, and very low rates of adverse events.[5] After the publication of our 3-year results, international guidelines on the treatment of glaucoma have been updated; the European Glaucoma Society[6] and the American Academy of Ophthalmology[7] now list SLT as initial treatment for OAG and OHT alongside medications, and the United Kingdom National Institute for Health and Care Excellence (NICE)[8] recommends SLT be used as a first-line treatment.

Glaucoma is a long-term condition requiring life-long treatment; average life expectancy at initial diagnosis of glaucoma is 9 to 13 years,[9] and mean life expectancy after trabeculectomy is 7.5 years.[10] Although we reported previously that initial treatment with SLT offered freedom from drops to nearly 75% of LiGHT Trial participants for at least 3 years, longer-term IOP control after initial SLT and additional SLT could prolong drops freedom further and could reduce the requirement for intense medical or surgical treatment over a patient's lifetime. Such potential may also be invaluable for the management of OAG and OHT internationally, after coronavirus disease 2019 pandemic-related delays in monitoring and treatment and consequent greater number of glaucoma emergencies and patient anxiety.[11–13]

After 3 years of treatment and monitoring, the LiGHT Trial was extended to a total of 6 years of monitoring. We report HRQoL and clinical effectiveness of initial treatment with SLT compared with initial IOP-lowering eye drops after 6 years of protocolized treatment to predefined eye-specific IOP targets.[4] The cost-effectiveness analysis and data on crossover outcomes will be presented separately.

Methods

Recruitment

Details of the LiGHT Trial design have been described previously.[4,5] Patients with a new diagnosis of previously untreated OAG or OHT in 1 or both eyes who qualify for treatment according to United Kingdom NICE guidelines were identified at 6 hospitals across the United Kingdom between October 10, 2012, and October 27, 2014. For patients with a diagnosis of OAG, mean deviation visual field (VF) loss was not worse than −12 dB in the better eye or −15 dB in the worse eye, and corresponding damage to the optic nerve was present. Patients were 18 years of age or older and were able to read and understand English. Visual acuity was 6/36 or better in the treated eye(s); eyes with no previous intraocular surgery, except uncomplicated phacoemulsification at least 1 year before randomization, were eligible. Patients were excluded if they had contraindications to SLT (e.g., unable to sit at the slit-lamp–mounted laser, history of uveitis, inadequate view of trabecular meshwork), were unable to use eye drops, had symptomatic cataract, were under active treatment for another ophthalmic condition, or a combination thereof.

Randomization

Patients were randomized (month 0) using a web-based system (www.sealedenvelope.com) and were assigned randomly to receive either primary therapy with IOP-lowering eye drops or SLT, followed by IOP-lowering eye drops if required. Stratification factors in the randomization were diagnosis and treatment center, with random block sizes (of 4, 6, or 8). All measurements influencing treatment escalation decisions (VF, optic disc imaging, and IOP) were made by masked observers; clinicians and patients were unmasked to treatment allocation.

Disease Definition, Deterioration, and Target Intraocular Pressure

Disease definition and treatment initiation followed the NICE thresholds at the time[14]; this was incorporated into a real-time web-based clinical decision-support software, which was based on optic disc analysis using Heidelberg Retina Tomography (Heidelberg Engineering), automated VF assessment with the Humphrey Field Analyzer Mark II Swedish interactive threshold algorithm standard 24-2 (Carl Zeiss Meditec), and IOP measurements (Goldmann applanation tonometry with daily calibration verification). Disease category and severity were specified at baseline using predefined objective severity criteria from the Canadian Target IOP Workshop[15] with additional central VF loss criteria according to Mills et al.[16]

Eye-specific target IOP and patient monitoring intervals were based on the Canadian Target IOP Workshop,[15] according to the disease severity stratification (OHT and mild, moderate, or severe OAG). The eye-specific target IOP was determined from a single untreated baseline (month 0) IOP measurement: eyes with OHT had a target IOP at least 20% reduced from baseline or less than 25 mmHg (whichever was lower), eyes with mild OAG had a target IOP at least 20% reduced from baseline or less than 21 mmHg (whichever was lower), eyes with moderate OAG had a target IOP at least 30% reduced from baseline or less than 18 mmHg (whichever was lower), and eyes with advanced OAG had a target IOP at least 30% reduced from baseline or less than 18 mmHg (whichever was lower).[4,17]

Deterioration of glaucoma, that is, disease progression, or conversion of OHT to OAG was derived from the decision support software and required verification by a consultant ophthalmologist. Evidence of deterioration was stratified to strong or less strong based on glaucoma progression analysis or Heidelberg Retina Tomography rim area as described previously.[4] Treatment escalation followed international guidelines of the European Glaucoma Society,[18] the American Academy of Ophthalmology Preferred Practice Patterns,[19] and the South-East Asia Glaucoma Interest Group.[20] Treatment was escalated when (1) IOP was more than the target IOP by more than 4 mmHg at a single visit, (2) evidence of deterioration regardless of IOP was strong, and (3) IOP was more than the target by less than 4 mmHg in the presence of evidence of progression.

Target IOP was reduced by 20% if deterioration was identified despite the measured IOP being at or less than the initially set target IOP. Intraocular pressure was revised upward if an eye was $\geq$ 2 mmHg and $<$ 4 mmHg more than the target IOP for 2 consecutive visits while demonstrating disease stability as assessed by Heidelberg Retina Tomography, VF, with a minimum of 4 VF examinations according to the Early Manifest Glaucoma Trial,[21] and by a decision support software. In these patients, treatment escalation was not attempted, but the target IOP was adjusted to the mean of the last 3 visits over which deterioration had not occurred.[4] If fewer than 4 VF examinations had been carried out,

additional visits were required to confirm stability before the target was relaxed.

Selective Laser Trabeculoplasty Arm

Selective laser trabeculoplasty was delivered according to a predefined protocol at 360° of the trabecular meshwork with 100 nonoverlapping shots (25 per quadrant; energy, 0.3−1.4 mJ, according to a prespecified protocol).[4,17] For the first 36 months (3 years) of the trial, 1 additional SLT retreatment was allowed (total of 2 SLT treatments), and thereafter, the next escalation was medical treatment. After the first 3 years, patients were permitted a third SLT treatment; the next escalation was medical treatment. Significant complications of laser treatment (e.g., severe uveitis, IOP spike of more than 15 mmHg) or other new medical conditions (e.g., uveitis, angle closure, etc.) prohibited repetition of SLT.

Eye Drops Arm

Single-drug eye drops were prescribed initially after randomization for patients in the drops arm and for patients whose IOP remained uncontrolled after SLT. Different or additional eye drops were prescribed in the event of a treatment switch (e.g., adverse reaction) or treatment escalation (e.g., IOP above target). Drug classes for first-line, second-line, or third-line treatment were defined according to NICE[14] and the European Glaucoma Society guidance[18]: first line, prostaglandin analogs; second line, β-blockers; and third or fourth line, topical carbonic anhydrase inhibitors or α-agonists. Fixed combination drops were allowed; systemic carbonic anhydrase inhibitors were permitted only as a temporary measure while awaiting surgery and were not considered a treatment escalation for the purposes of the analysis.

Procedures

For the first 36 months (3 years) of the trial, patients initially randomized to receive IOP-lowering eye drops were not permitted SLT; failure to control IOP or OAG with eye drops resulted in surgical treatment (trabeculectomy). After the first 3 years, patients were allowed a crossover, whereby they could opt to undergo SLT as a treatment switch, that is, to reduce medication load, or as a treatment escalation, that is, to avoid increasing medication load or to delay surgery.

The primary outcome measure was HRQoL measured using the EuroQol 5 Dimensions 5 Levels (EQ-5D) utility scores. Utility scores were calculated from patient-reported health states using the EQ-5D descriptive system and value set for England.[22] The secondary outcomes were glaucoma-specific treatment-related quality of life using the Glaucoma Utility Index (GUI),[23] patient-reported disease and treatment-related symptoms using the Glaucoma Symptom Scale (GSS),[24] patient-reported visual function using the Glaucoma Quality of Life-15 (GQL-15), and clinical effectiveness and safety of the treatment arms. Adverse events were classified and reported according to local standard operating procedures and good clinical practice guidelines.[25]

Statistical Analysis

The statistical analysis plan is described in detail elsewhere.[26] In summary, the primary outcome was analyzed using linear regression with terms for randomization group, baseline EQ-5D score, stratification factors (diagnosis and center), baseline IOP, and number of eyes affected at baseline. The unit of analysis was the patient. If both of a patient's eyes were included in the study, baseline severity and IOP were based on the worse eye, where the worst eye was defined using VF mean deviation at baseline. Several sensitivity analyses were performed to verify the results of this primary analysis (details provided in Appendix 1, available at www.aaojournal.org). In addition, mixed-effects models were used to analyze the EQ-5D measurements recorded at all time points to investigate possible changes in treatment effect over the 72 months (using interaction terms between the randomization group and time) and to estimate the average treatment effect over the 72-month follow-up period. The secondary outcomes were analyzed using similar regression methods to those described here. All analyses were performed on an intention-to-treat basis with participants analyzed according to the group to which they were randomized. Kaplan−Meier plots were used to summarize disease progression and time to glaucoma surgery and phacoemulsification, and the log-rank test was used to compare these outcomes. Eyes were compared with respect to visits at target and number of clinical visits using mixed-effects logistic regression and Poisson regression models, respectively. Eyes also were compared with respect to the remaining measurement of pathway effectiveness and visual function variables using the *t* test for numerical outcomes and the chi-square test (or Fisher exact test when numbers were small) for categorical outcomes. The chi-square test and Fisher exact test also were used to compare the number of reported adverse and serious adverse events. All analyses were performed in Stata software version 17 (StataCorp LLC).

The study was conducted in accordance with good clinical practice guidelines and adhered to the tenets of the Declaration of Helsinki. Ethical approval was granted by local boards. All patients provided written informed consent before participation. An independent data and safety monitoring committee was appointed by the independent trial steering committee, to whom adverse events were reported according to standard operating procedures for the duration of the trial. The LiGHT Trial is registered at www.controlled-trials.com (identifier, ISRCTN32038223), and the protocol can be accessed at https://www.journalslibrary.nihr.ac.uk/programmes/hta/0910440/#/.

Results

Baseline Data

Of the 692 patients who completed 3 years of the LiGHT Trial, 633 patients (91.5%) entered the 3-year extension (from 36 to 72 months); 313 patients (547 treated eyes) initially received SLT, and 320 patients (549 eyes) initially commenced treatment with IOP-lowering eye drops (Fig 1). Eighty-six protocol violations or deviations occurred; 30 took place during the first 3 years, and 56 took place during the extension (36 to 72 months), the latter relating to the coronavirus disease 2019 pandemic. Of the 59 patients not continuing into the extension, 29 came from a single center that chose not to continue in the study (Appendix 2, available at www.aaojournal.org). A total of 524 patients completed the trial extension (82.8% of those entering the extension phase, 73% of those initially randomized).

Presented results refer to the sample of patients who entered the LiGHT Trial extension (36 to 72 months); this sample was representative of the original trial participants and maintained the balance of the allocation groups achieved by randomization. Baseline (month 0) patient and eye characteristics of the patients who participated in the extension phase were similar between the two groups (Table 1; Appendix 2); 493 patients (77.9%) had a diagnosis of OAG in at least 1 eye, and 140 patients (22.1%) had a diagnosis of OHT. The treatment groups showed similar average EQ-5D, GUI, and GQL-15 scores at baseline (month 0; Table 2); the medication group showed slightly higher average GSS scores at baseline, similar to the original trial data.[5] At 36

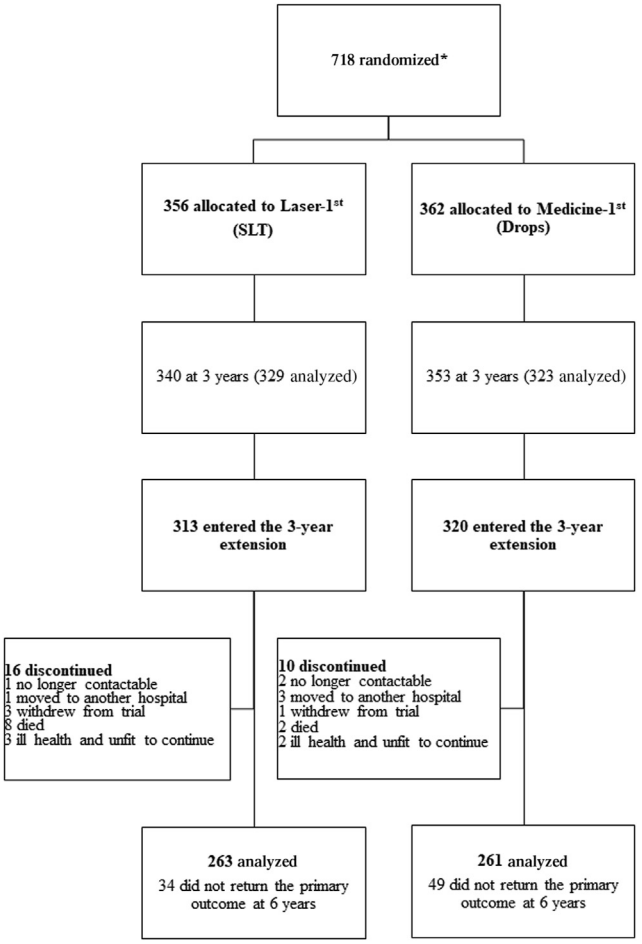


Figure 1. Consolidated Standards of Reporting Trials flowchart for the Laser in Glaucoma and Ocular Hypertension Trial. *Two patients initially were randomized twice because of an information technology failure in which the initial randomization was not visible, and subsequently, a second randomization was carried out. One of these patients initially was randomized to medication but subsequently was randomized to and underwent selective laser trabeculoplasty (SLT). The other initially was randomized to SLT but subsequently was randomized to and underwent medication. These patients are included in the diagram according to the second randomizations.

months (start of the extension), the two groups showed average EQ-5D, GUI, GSS, and GQL-15 scores that continued to be similar to the scores recorded in the first 3 years of the trial.[5]

Of the 320 patients allocated to medication, 112 patients (176 eyes; 35% of patients) decided to undergo SLT immediately or shortly after the end of the 3-year monitoring period. Of those, 70 patients (115 eyes) underwent SLT as a treatment switch, that is, to reduce medication load, and 29 patients (35 eyes) underwent SLT as a treatment escalation because of uncontrolled IOP, disease progression, or both. Thirteen patients (26 eyes) underwent SLT as a treatment escalation in one eye and as a treatment switch in the other eye. Of the 112 patients who underwent SLT after 36 months, 94 patients (83.9%) completed the trial extension to 72 months.

Health-Related Quality of Life

The mean values for the HRQoL questionnaires across the 72 months of the trial are shown in in Figure 2. Based on an intention-to-treat analysis, no significant difference in HRQoL was found between the two treatments at 72 months for the EQ-5D, GUI, and GQL-15 scores (Table 3); the eye drops group showed a mean ± standard deviation EQ-5D score of 0.89 ± 0.14, compared with 0.90 ± 0.14 in the SLT group (adjusted mean difference [selective laser trabeculoplasty minus eye drops], 0.01; 95% confidence interval [CI], −0.01 to 0.04; $P = 0.18$). These results were confirmed in sensitivity analyses (results not shown; see Appendix 1). The mean ± standard deviation GUI score at 72 months in the SLT group was 0.90 ± 0.14 compared with 0.88 ± 0.13 for the eye drops group (adjusted mean difference, 0.01; 95% CI, −0.01 to 0.03). Mean GQL-15 scores also were similar between the two groups (20.80 for the SLT group and 20.57 eye drops group; adjusted mean difference, −0.13; 95% CI, −1.57 to 1.31). For the GSS, the medication group showed worse scores at 72 months with a mean ± standard deviation score of 81.3 ± 17.3 compared with 83.6 ± 18.1 for the SLT group (adjusted mean difference, 3.3; 95% CI, 0.54−6.0); however, this was the only time point at which a notable difference was observed. Repeated measures analysis for the secondary HRQoL outcomes (GUI, GSS, and GQL-15 scores) showed comparable outcomes between the two groups over the course of the trial (Appendix 3, available at www.aaojournal.org). When excluding the eyes that underwent SLT after the 36-month time point (n = 176), mean scores for all HRQoL questionnaires were similar between the two groups (Table 3).

Measurements of Treatment Effectiveness and Visual Function

At 72 months, 537 patients (267 patients in the drops arm and 270 patients in the SLT arm) and 930 eyes (460 eyes in the drops arm and 470 eyes in the SLT arm) were available for analysis of clinical outcomes (Table 4). Overall, 94.2% of eyes initially treated with SLT were at target at 72 months, and target IOP was achieved at 92.8% of visits, compared with 94.7% of eyes and 93.2% of visits for eyes initially treated with medication. Fewer eyes initially treated with SLT demonstrated progression from OHT to OAG or deterioration of OAG compared with eyes initially treated with eye drops (19.6% vs. 26.8%, respectively; $P = 0.006$; Table 4; Fig 3).

Drop-free IOP control at 72 months, obtained without incisional surgery, was achieved in 69.8% of eyes initially treated with SLT compared with 18.0% of eyes initially treated with IOP-lowering eye drops. Of the eyes initially treated with SLT and being drop and surgery free at 6 years, 90% of eyes (295 eyes) needed up to 2 SLT treatments in total. Of the eyes initially treated with eye drops and being drop free at 72 months, 79.5% of eyes (66 eyes) had switched to SLT, and 20.5% underwent either cataract surgery alone or cataract surgery and SLT. At 72 months, 61.2% of eyes initially treated with eye drops were using 1 or 2 medications compared with 18.5% of eyes initially treated with SLT.

Target IOP was revised in 85 eyes initially treated with SLT and in 89 eyes initially treated with IOP-lowering eye drops. Target IOP was revised downward on 50 occasions in eyes initially treated with SLT and on 65 occasions in eyes initially treated with IOP-lowering eye drops and upward on 40 and 31 occasions, respectively. Eyes initially treated with SLT needed fewer trabeculectomies (13 eyes [2.4%]) compared with eyes initially treated with eye drops (32 eyes [5.8%]; Table 4; Fig 4; $P < 0.001$) and fewer phacoemulsifications (57 compared with 95, respectively; $P = 0.03$; Table 4; Fig 5). Of the 32 eyes that needed a trabeculectomy during trial's 6-year duration, 11 eyes initially treated with drops underwent a trabeculectomy during the first 3 years of the trial; none of the eyes initially treated with SLT required a trabeculectomy during the initial 3 years of the trial. During the extension of the trial, that is, from 3 to 6 years,

Table 1. Baseline (Month 0) Patient Characteristics of Those Participating in the Extension

Characteristic	Drops Group (n = 320)	Selective Laser Trabeculoplasty Group (n = 313)
Age, yrs	63.2 ± 11.4	63.1 ± 12.0
Sex		
Male	170 (53.1)	178 (56.9)
Female	150 (46.9)	135 (43.1)
Diagnosis		
OHT	69 (21.6)	71 (22.7)
OAG	251 (78.4)	242 (77.3)
Race or ethnic origin		
Asian	26 (8.1)	23 (7.3)
Black	57 (17.8)	67 (21.4)
White	231 (72.2)	211 (67.4)
Other	6 (1.9)	12 (3.8)
Family history of glaucoma in first-degree relative*		
Yes	94 (29.4)	100 (32.1)
No	226 (70.6)	212 (67.9)

OAG = open-angle glaucoma; OHT = ocular hypertension.
Data are presented as mean ± standard deviation or number (%). No evidence was found that the patient characteristics were significantly different between arms (all $P > 0.05$).
*One value was missing.

minimally invasive glaucoma surgery was performed in 11 eyes of 6 patients initially treated with IOP-lowering eye drops (all were angle procedures; no minimally invasive glaucoma surgery was performed in eyes initially randomized to SLT). This may have resulted in fewer trabeculectomy surgeries in the drops arm but is not expected to have affected the reported statistical and clinical differences in incisional glaucoma surgery between the treatment arms.

Eyes initially treated with SLT showed higher IOP at 72 months compared with eyes initially treated with IOP-lowering eye drops (16.3 mmHg vs. 15.4 mmHg, respectively; $P < 0.001$); however, VF mean deviation loss and visual acuity at 72 months were similar between the two groups (−4.0 dB vs. −3.9 dB and 0.1 vs. 0.1, respectively; $P > 0.05$ for both; Table 4; Appendix 4, available at www.aaojournal.org). Patients initially treated with SLT needed a total of 5175 visits over 72 months, and patients initially treated with eye drops needed 4970 visits. Excluding the 2-week visits after laser treatment resulted in 4678 visits for the SLT group compared with 4852 visits for the eye drops group.

Safety

No sight-threatening complications of SLT and no clinically identifiable corneal changes occurred throughout the trial (Table 5). A total of 274 transient SLT-related adverse events were reported, including 10 incidents of a rise in IOP (1.0% of all SLT treatments, with only 1 eye requiring treatment). More ocular adverse events were reported in the group initially treated with IOP-lowering eye drops (1470 ocular adverse events were reported by 271 patients) compared with the group initially treated with SLT (897 ocular adverse events by 224 patients; Table 5). Serious adverse events were similar overall between the two groups (180 events in 110 patients initially treated with eye drops and 209 events in 107 patients initially treated with SLT), with pulmonary and cardiac events being balanced between the two groups (Table 5).

Discussion

In 2019, the LiGHT Trial reported that initial treatment with SLT provided eyes with newly diagnosed OHT and OAG with predominantly drop-free IOP control (78.2% of eyes after 3 years) and a reduced need for glaucoma and cataract surgery, compared with initial treatment with IOP-lowering eye drops.[5] Data from this 3-year trial also indicated that eyes initially treated with SLT may demonstrate less frequent progression to more advanced stages of glaucoma, and a further VF analysis indicated that more eyes initially treated with topical medical therapy undergo rapid VF progression compared with eyes initially treated with SLT.[27]

The LiGHT Trial was extended to a total of 6 years to provide longer-term, pragmatic treatment outcome data. Patients within 5 United Kingdom settings who were treated

Table 2. Baseline Questionnaire Scores

Questionnaire	Drops Group (n = 320)	Selective Laser Trabeculoplasty Group (n = 313)	Difference (95% Confidence Interval)
EQ-5D*	0.92 ± 0.11	0.92 ± 0.13	0.00 (−0.02 to 0.02)
GUI*	0.89 ± 0.11	0.89 ± 0.11	0.00 (−0.02 to 0.01)
GSS*	83.3 ± 16.3	81.3 ± 17.0	−2.1 (−4.7 to 0.5)
Symptom subscale	81.4 ± 18.7	79.2 ± 19.9	−2.2 (−5.3 to 0.8)
Function subscale	86.3 ± 17.1	84.5 ± 17.7	−1.8 (−4.6 to 0.9)
GQL-15†	18.5 ± 5.4	18.8 ± 6.4	0.3 (−0.6 to 1.2)
Central subscale	2.5 ± 0.9	2.5 ± 1.0	0.1 (−0.1 to 0.2)
Peripheral subscale	8.3 ± 2.8	8.5 ± 3.3	0.2 (−0.3 to 0.6)
Dark subscale	7.8 ± 2.7	7.9 ± 2.9	0.0 (−0.4 to 0.5)
Outdoor subscale	1.1 ± 0.4	1.1 ± 0.4	0.0 (−0.1 to 0.0)

EQ-5D = EuroQol 5 Dimensions 5 Levels; GQL-15 = Glaucoma Quality of Life-15; GSS = Glaucoma Symptom Scale; GUI = Glaucoma Utility Index.
Data are presented as mean ± standard deviation, unless otherwise indicated. One value was missing for GUI (drops group), 6 values were missing for GSS (4 in the drops group, 2 in the selective laser trabeculoplasty group), and 1 value was missing for GLQ-15 (drops group).
*Higher scores indicate better health-related quality of life.
†Higher scores indicate worse health-related quality of life.

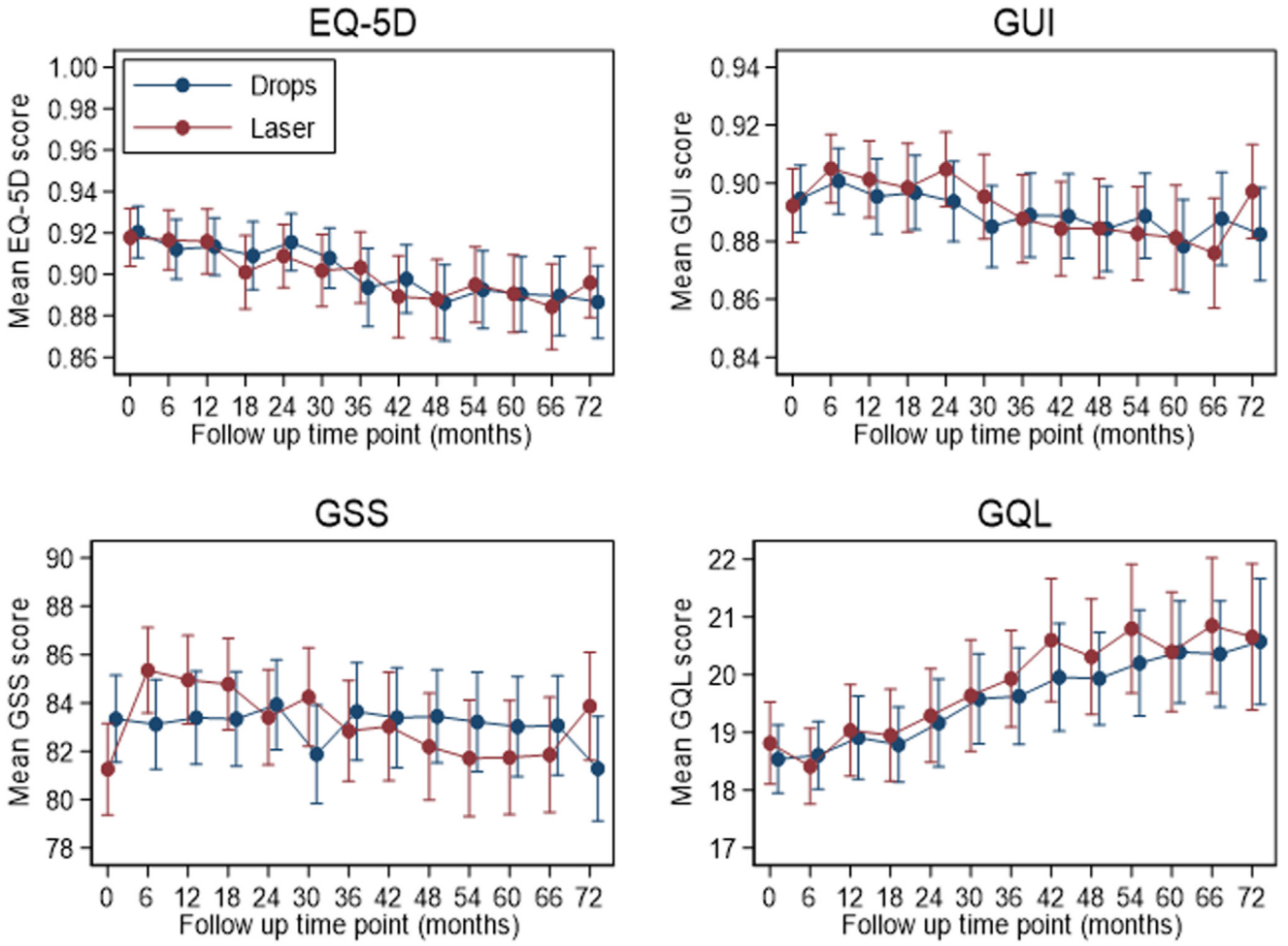


Figure 2. Graphs showing the mean EuroQol 5 Dimensions 5 Levels (EQ-5D), Glaucoma Utility Index (GUI), Glaucoma Symptom Scale (GSS), and Glaucoma Quality of Life-15(GQL-15) scores at each time point across 72 months based on all available data for patients who participated in the extension study. Time point 0 refers to before treatment. For the GSS, higher scores indicate better health-related quality of life. For the GQL-15, higher scores indicate worse health-related quality of life. Error bars indicate ± 2 standards errors.

initially with IOP-lowering eye drops were permitted to undergo SLT to reduce medication load, to avoid increasing medication load, or to delay surgery. Patients initially treated with SLT were allowed to undergo a third and final SLT before escalating to IOP-lowering eye drops. Data after 6 years of treatment indicate statistically significant lower rates of disease progression and reduced need for glaucoma and cataract surgery for eyes initially treated with SLT. Drop-free IOP control and safety of SLT as a first-line treatment for OHT and OAG are confirmed after 6 years of careful, protocolized monitoring and treatment.

Selective laser trabeculoplasty allowed successful drop-free IOP control in nearly 70% of the eyes after 6 years of treatment. This is reduced only slightly from 78% of eyes not needing topical therapy at 3 years and is an important outcome for long-term glaucoma and OHT management; of the initial SLT eyes that were free of drops, 90% underwent only 1 or 2 SLT treatments. Intraocular pressure-lowering eye drops come with sometimes significant adverse effects, affecting trabeculectomy outcomes; increasing expenditure for health care systems, patients, or both[28,29]; and often leading to nonadherence.[30] Freedom from drops was achieved in nearly one fifth of eyes initially treated with eye drops, predominantly by switching to SLT alone (79.5%) or after undergoing SLT, cataract surgery, or both (20.5%).

The LiGHT Trial reports 70% of eyes being drop free after 6 years of treatment, whereby IOP had to be reduced by a minimum of 20% from pretreatment IOP (and at least by 30% for moderate and severe OAG) and to < 25 mmHg for OHT, to < 21 mmHg for mild OAG, to < 18 mmHg for moderate OAG, and to < 15 mmHg for severe OAG.[4,15] Absolute IOP reduction has been reported elsewhere[31]; reporting absolute IOP reduction at 6 years has limited usefulness because no washout was performed and a proportion of eyes were receiving IOP-lowering topical medical treatment. Success rates for SLT have been published using various definitions.[1,32] A large United States-based retrospective study clearly indicated that reported success rates are influenced heavily by disease severity and

Table 3. Primary and Secondary Analysis: EuroQol 5 Dimensions 5 Levels, Glaucoma Utility Index, Glaucoma Symptom Scale, and Glaucoma Quality of Life-15 Scores at 72 Months for the Intention-to-Treat and Per-Protocol Analysis

	Drops Group (n = 320)		Selective Laser Trabeculoplasty Group (n = 313)		Adjusted Mean Difference (95% Confidence Interval)*	P Value
	No.	*Mean ± SD*	*No.*	*Mean ± SD*		
Intention to treat						
EQ-5D†	261	0.89 ± 0.14	263	0.90 ± 0.14	0.01 (−0.01 to 0.04)	0.18
GUI†	255	0.88 ± 0.13	257	0.90 ± 0.13	0.01 (−0.01 to 0.03)	
GSS†	247	81.29 ± 17.33	244	83.62 ± 18.06	3.27 (0.54 to 6.00)	
GQL-15‡	208	20.57 ± 8.01	203	20.80 ± 9.40	−0.13 (−1.57 to 1.31)	
Per original protocol§						
EQ-5D†	167	0.89 ± 0.14	263	0.90 ± 0.14	0.01 (−0.01 to 0.04)	
GUI†	163	0.89 ± 0.13	257	0.90 ± 0.13	0.01 (−0.02 to 0.03)	
GSS†	162	82.11 ± 16.76	244	83.62 ± 18.06	2.68 (−0.45 to 5.81)	
GQL-15‡	130	20.59 ± 8.44	203	20.80 ± 9.40	0.22 (−1.50 to 1.94)	

EQ-5D = EuroQol 5 Dimensions 5 Levels; GQL-15 = Glaucoma Quality of Life-15; GSS = Glaucoma Symptom Scale; GUI = Glaucoma Utility Index; SD = standard deviation.
*Estimated from linear regression model adjusting for baseline EQ-5D score, severity of glaucoma, site, and baseline intraocular pressure.
†Higher scores indicate better health-related quality of life.
‡Higher scores indicate worse health-related quality of life.
§Patients initially treated with eye drops who switched to selective laser trabeculoplasty were removed.

comorbidities of the included populations, concluding that SLT can be an effective means of prolonging medication-free IOP control,[33] but lower SLT success rates have been reported for less carefully selected eyes already receiving medication.[34]

The LiGHT Trial used eye-specific target IOPs that could be revised in the absence of evident deterioration[4]; this has been suggested potentially to drive the reported outcomes.[35] The European Glaucoma Society guidelines recommend clinicians consider upward revision of target pressure in patients with stable IOP when the initial target has not been reached.[36] In the LiGHT Trial, target IOP was reassessed using decision support software and was applied to both treatment arms, according to predetermined criteria,[37] when VF and disc imaging analysis provided evidence of disease stability accounting for intervisit IOP measurement variation.[38] A risk-dependent upper limit was set at which surgery may be offered even in the absence of progressive glaucomatous optic neuropathy. Herein, we report the number of upward and downward IOP revisions that are comparable between the two treatment arms and therefore are unlikely to affect the reported outcomes.

The LiGHT Trial has monitored patients carefully and objectively in a pragmatic manner across 5 National Health Service centers, retaining more than 80% of participants after 6 years of treatment. Data reported by the LiGHT Trial are an accurate representation of realistic and complete glaucoma management for eyes with newly diagnosed, previously untreated OHT or OAG; these data have supported the update of the American, European, and United Kingdom NICE glaucoma management guidelines.[6–8] The LiGHT Trial population consisted of a large proportion of eyes with OHT and mild OAG for which IOP reduction targets are less stringent than those for more advanced disease. Eyes with advanced OAG often will require more intense treatment, whereas initial intervention may differ from that recommended for early disease.[39]

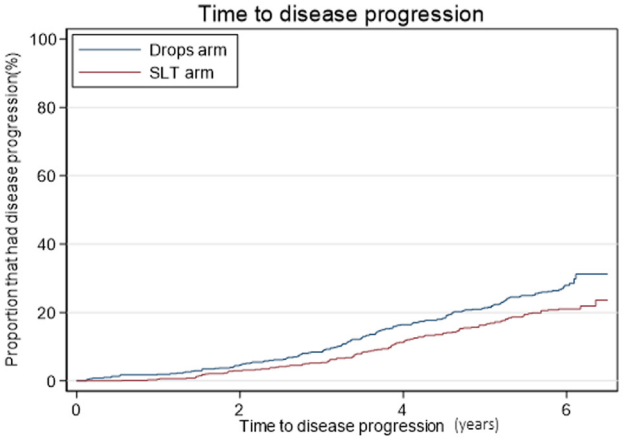
Adding to the evidence from the LiGHT Trial, the Glaucoma Intensive Treatment Study[40] has reported favorably on the use of SLT as an adjunctive therapy for patients with OAG over 3 years, and the West Indies Glaucoma Laser Study reported that SLT monotherapy safely provided 78% of Afro-Caribbean eyes with at least 20% IOP reduction for 12 months.[41] Selective laser trabeculoplasty also was shown recently to be an ideal therapeutic approach in situations in which frequent monitoring visits and treatment changes are difficult.[42] With 90% of the drop-free eyes initially treated with SLT needing a maximum of 2 SLT treatments over 6 years and 55.5% requiring only a single SLT treatment, great potential exists for treating patients with SLT in such situations.

Data published previously have indicated that initial treatment with SLT may delay progression of OHT and OAG; data from the first 3 years of treatment indicated a 2% difference in eyes progressing, and VF analysis suggests more eyes initially treated with IOP-lowering eye drops undergo rapid VF progression compared with eyes first treated with SLT.[5,27] After 6 years of treatment, eyes initially treated with SLT demonstrated reduced objectively defined progression compared with IOP-lowering eye drops; this was achieved despite eyes initially treated with IOP-lowering eye drops achieving lower IOP at 6 years, possibly suggesting other protective roles of SLT. Differences in progression between the two treatment arms also influence the rates of incisional glaucoma surgery. Eyes initially treated with SLT needed fewer trabeculectomies, supporting original trial data.[5] For the first 3 years after initial treatment, no trabeculectomies were needed in eyes receiving initial SLT, whereas at 6 years, almost 3 times fewer eyes initially treated with

Table 4. Measurement of Pathway Effectiveness and Visual Function for Eyes at 72 Months (± 6 Months)

Variable	Drops Group	Selective Laser Trabeculoplasty Group	P Value
Control of disease during the 72 mos of the trial			
Visits with eyes at target (cumulative)	93.2%	92.8%	0.88
Eyes at target IOP at 72 mos	429(94.7)	437 (94.2)	0.73
OHT	118 (94.4)	134 (96.3)	0.51
Mild OAG	239 (96.4)	227 (93.0)	0.01
Moderate OAG	48 (88.9)	45 (95.7)	0.28
Severe OAG	24 (92.3)	31 (91.2)	1.00
Treatment escalations	477	543	0.47
Disease progression*	147 (26.8)	107 (19.6)	0.01
OHT to OAG conversion	22	15	0.55
OAG progression	125	92	0.01
Algorithm-defined VF progression (OAG)	100	73	
Algorithm-defined ON progression (OAG)	9	12	
Algorithm-defined VF and ON progression (OAG)	16	7	
Ocular surgeries during the 72 mos of the trial†			
Trabeculectomy at 72 mos	32 (5.8)	13 (2.4)	< 0.001
Trabeculectomy at 36 mos	11	0	
Trabeculectomy revision	2 (0.4)	0	0.50
Phacoemulsification‡	95 (17.3)	57 (10.4)	0.03
Treatment intensity at 72 mos			
Drop freedom for eyes at target IOP (% of all eyes reaching 6 yrs)			
No medications	106 (23.0)	338 (71.9)	< 0.001
No medications, no trabeculectomy	83 (18.0)	328 (69.8)	< 0.001
SLT only	66	295	
Phacoemulsification, no SLT	10	0	
Phacoemulsification and SLT	7	33	
No. of medications per eye at target IOP			
1	196 (42.6)	56 (11.9)	< 0.001
2	87 (18.9)	31 (6.6)	
3	37 (8.0%)	11 (2.3)	
4	3 (0.7%)	1 (0.2)	
No. of SLT treatments per eye			
1	164 (29.9)	343 (62.7)	—
2	10 (1.8)	169 (30.9)	—
3	2 (0.4)	32 (5.9)	—
4§	0 (0.0)	3 (0.5)	—
No. of SLT treatments per eye, for eyes with no medication and no trabeculectomy			
1	65 (78.3)	182 (55.5)	—
2	6 (7.2)	113 (34.5)	—
3	2 (2.4)	31 (9.5)	—
4§	0	2 (0.6)	—
IOP target revisions‖	96 (89 eyes)	90 (85 eyes)	0.76
Upward IOP target revisions	31	40	—
Downward IOP target revisions	65	50	—
Clinical outcomes at 72 mos			
Visual acuity (logMAR)	0.1 (0.2)	0.1 (0.2)	0.24
IOP	15.4 (3.9)	16.3 (4.0)	< 0.001
MD	−3.9 (4.4)	−4.0 (4.5)	0.80
Clinic visits			
Total no. of clinic visits	4970	5175	0.13
No. of visits excluding the 2-wk IOP check	4852	4678	0.49

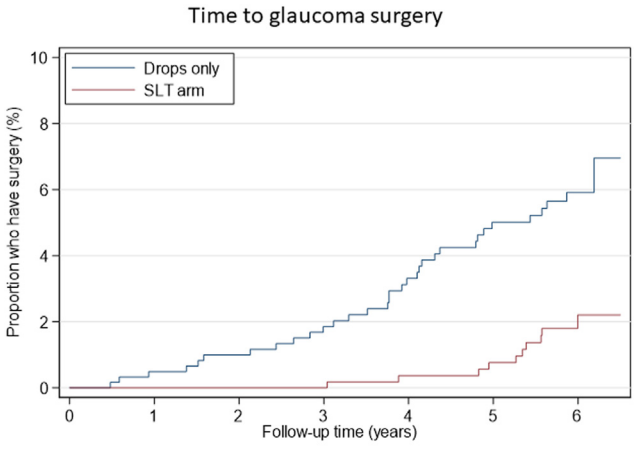
IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; MD = mean deviation; OAG = open-angle glaucoma; OHT = ocular hypertension; ON = optic nerve; SLT = selective laser trabeculoplasty; VF = visual field; — = not applicable.
Data are presented as number (%) unless otherwise indicated. Diagnosis indicates diagnosis at baseline.
*Conversion of OHT to OAG required a sign of progression derived from the decision support software and verification by a consultant ophthalmologist; OAG progression OAG required a sign of progression derived from the decision support software; and 4 eyes with OHT received a single OAG diagnosis during the trial, and these were assumed to be errors. See Figure 3 for a full statistical comparison. An analysis of progression by disease severity is available in Appendix 4.
†See Figures 4 and 5 for a full statistical comparison.
‡Minimally invasive glaucoma surgery combined phacoemulsification was performed in 11 eyes of 6 patients initially treated with IOP-lowering eye drops during the extension of the trial.
§Protocol deviation: 3 eyes of 2 patients.
‖Target IOP was reassessed when VF and sequential disc imaging provided evidence of disease stability; IOP was revised after a decision support software recommendation, according to preset criteria.[21]



Number of patients at risk / years	0	2	4	6*
Drops arm	361	335	282	235
SLT arm	355	339	287	243

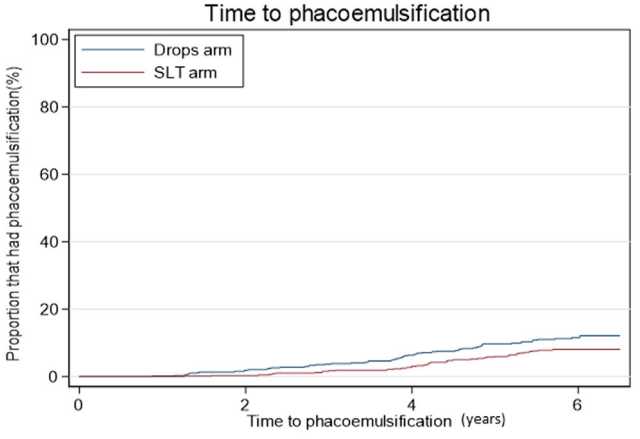
Figure 3. Failure plot indicating time of disease progression from baseline by treatment arm ($P < 0.006$, log-rank test) based on intention-to-treat analysis (the unit of analysis is the eye) for all randomized patients. The number at risk at 6 years includes the patients whose last visit was ± 6 months. SLT = selective laser trabeculoplasty.

SLT need a trabeculectomy, compared with eyes initially treated with IOP-lowering eye drops. Excess surgeries in eyes initially treated with eye drops might have led to the slightly lower IOP at 72 months, compared with eyes initially treated with SLT. These data have significant implications for patients and health care systems. Trabeculectomy is performed on average 10 years after initial



Number of patients at risk / years	0	1	2	3	4	5	6*
Drops arm	361	352	342	334	307	291	266
SLT arm	355	351	345	328	304	287	270

Figure 4. Failure plot indicating time to glaucoma surgery from baseline by treatment arm ($P < 0.001$, log-rank test) based on intention-to-treat analysis (y-axis on a scale of 0–10%; the unit of analyses is the eye). The number at risk at 6 years includes the patients whose last visit was ± 6 months. SLT = selective laser trabeculoplasty.



Number of patients at risk / years	0	2	4	6*
Drops arm	353	331	287	240
SLT arm	351	340	296	256

Figure 5. Failure plot indicating time to phacoemulsification from baseline by treatment arm ($P < 0.03$, log-rank test) based on intention-to-treat analysis (the unit of analyses is the eye). The number at risk at 6 years includes the patients whose last visit was ± 6 months.

diagnosis, and average life expectancy after glaucoma diagnosis is 9 to 13 years[9,43,44]; SLT can delay and potentially obviate the need for glaucoma surgery for a proportion of patients.

Selective laser trabeculoplasty also leads to a reduced need for cataract surgery; at least 50% more eyes initially treated with eye drops needed cataract surgery during the 6-year course of the LiGHT Trial compared with eyes initially treated with SLT, supporting evidence from the Early Manifest Glaucoma Trial on a greater need for surgical cataract removal in eyes treated with IOP-lowering eye drops.[45]

Selective laser trabeculoplasty seems comparable with medical IOP-lowering treatment in terms of HRQoL. For the first 3 years of the LiGHT Trial, generic and disease-specific HRQoL tools indicated that patients using drops experienced comparable HRQoL to those who received initial SLT, and these findings are supported further by the LiGHT Trial extension to 6 years. The single time point when SLT seemed to lead to better GSS scores was 72 months and is unlikely to have clinical significance. Selective laser trabeculoplasty also has been compared with timolol monotherapy using the World Health Organization Prevention of Blindness and Deafness 20-item Visual Functioning Questionnaire (PBD-VF20) vision-related quality-of-life instrument, which also revealed comparable results between the two treatment methods.[42] Recently, the sensitivity of existing quality-of-life tools to capture changes and their suitability as primary outcomes in clinical trials have been questioned.[46]

The safety profile of SLT remains very good, with no sight-threatening complications. Intraocular pressure rose > 5 mmHg from IOP before treatment in only 1% of treated eyes, and of these, only 1 eye needed treatment. Other adverse events were comparable between the two groups.

Table 5. Adverse Events

Events	Total (n = 633)		Drops Group (n = 320)		SLT Group (n = 313)		P Value
Adverse events							
Total no. of events	3647		2069		1578		
Total no. (%) of patients reporting	557 (88.0)		286 (89.4)		271 (86.6)		0.33
	No. of Events	No. of Patients (%)	No. of Events	No. of Patients (%)	No. of Events	No. of Patients (%)	
Ocular	2367	495 (78.2)	1470	271 (84.7)	897	224 (71.6)	< 0.001
Aesthetic side effects of medication*	195	71 (11.2)	164	57 (17.8)	31	14 (4.5)	< 0.001
Ophthalmic allergic reactions†	81	48 (7.6)	54	27 (8.4)	27	21 (6.7)	0.41
Reactivation of herpes simplex keratitis	2	2 (0.3)	1	1 (0.3)	1	1 (0.3)	1.00
Uveitis	17	10 (1.6)	7	5 (1.6)	10	5 (1.6)	0.97
Vision changes	43	38 (6.0)	26	22 (6.9)	17	16 (5.1)	0.35
Other‡	2029	484 (76.5)	1218	262 (81.9)	811	222 (70.9)	0.001
Systemic§	1006	287 (45.3)	544	154 (48.1)	462	133 (42.5)	0.16
Pulmonary problems‖	86	41 (6.5)	44	23 (7.2)	42	18 (5.8)	0.46
Cardiac events	27	19 (3.0)	11	10 (3.1)	16	9 (2.9)	0.85
Drug-related events¶	345	89 (14.1)	202	59 (18.4)	143	30 (9.6)	0.001
Other#	548	237 (37.4)	287	121 (37.8)	261	116 (37.1)	0.85
		% of SLT Treatments		% of SLT Treatments		% of SLT Treatments	
SLT related	274	28.0	55	28.9	219	27.8	0.74
Inflammation after SLT	3	0.3	1	0.5	2	0.3	0.48
IOP spike after SLT**	10	1.0	4	2.1	6	0.8	0.11
Other transient events††	241	24.6	50	26.3	191	24.2	0.55
AE during SLT procedure‡‡	20	2.0	0	0	20	2.5	0.02
Serious adverse events							
Total no. of events	389		180		209		
Total no. of patients reporting	217		110		107		0.003
		No. of Patients (%)		No. of Patients (%)		No. of Patients (%)	
Ocular§§	433	34 (5.4)	18	15 (4.7)	255	19 (6.0)	0.6
Pulmonary problems‖‖	10	10 (1.6)	4	4 (1.2)	6	6 (1.9)	0.50
Cerebrovascular accidents	7	7 (1.1)	5	5 (1.6)	2	2 (0.6)	0.45
Cardiac events	29	26 (4.1)	15	14 (4·4)	14	12 (3.8)	0.73
Cancer	44	38 (6.0)	14	12 (3.8)	30	26 (8.3)	0.02
Death	25	25 (3.9)	10	10 (3.1)	15	15 (4.8)	0.28
Other systemic	231	193 (30.5)	114	77 (24.1)	117	79 (25.2)	0.73

AE = adverse event; IOP = intraocular pressure; SLT = selective laser trabeculoplasty.
*Includes excessive lash growth, periocular pigmentation, and change in iris color.
†Includes periocular skin rash.
‡Includes ocular irritation, discomfort, dry eye, retinal hemorrhages, flashes, floater, conjunctivitis, blepharitis, vascular occlusions, diabetic retinopathy, and macular pathologic features.
§Not requiring hospitalization.
‖Includes asthma, shortness of breath, and reduced exercise tolerance.
¶Includes impotence, depression, somnolence or tiredness, nightmares, taste disturbance, and generalized skin rash.
#Unrelated events, such as headaches, pain, falls, etc.
**IOP spike defined as > 5 mmHg; 2 eyes had an IOP rise of > 10 mmHg, 1 eye was monitored and received no treatment, and 1 eye received treatment.
††Includes discomfort, transient blurred vision, transient photophobia, and hyperemia.
‡‡Includes discomfort, variation in the number of laser shots, and angle visualization issues.
§§Excludes cataract and glaucoma surgery; includes central retinal artery occlusion, choroidal neovascularization, epiretinal membrane, angle closure, anterior chamber surgery, corneal pathologic features, orbital cellulitis, retinal detachment, trauma, and any treatment required for these pathologic features.
‖‖Requiring hospitalization.

Selective laser trabeculoplasty has been shown to be a safe alternative to eye drops in areas where advanced glaucoma is more common and where treatment resources and access to these are limited.[42] The proven safety of SLT in such areas can transform glaucoma treatment rapidly and prevent sight loss.

Conclusions

After 6 years of treatment and monitoring, SLT safely offers IOP control without the need for medical or surgical treatment in more than 70% of eyes with OHT and OAG, while also demonstrating reduced progression rates and a reduced need for glaucoma and cataract surgery. Selective laser trabeculoplasty now is the recommended first-line treatment for OAG and OHT by the United Kingdom NICE[8] and is listed as a first-line treatment in the European Union and the United States, alongside IOP-lowering eye drops.

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HUMAN SUBJECTS: Human subjects were included in this study. The study was conducted in accordance with good clinical practice guidelines (GCP) and adhered to the tenets of the Declaration of Helsinki. Ethical approval was granted by local boards (the City Road and Hampstead Research and Ethics Committee [former Moorfields and Whittington Research Ethics Committee then East London and The City Research Ethics Committee 1, reference 12/LO/0940]; and by the local boards of the participating centres [Moorfields Eye Hospital NHS Foundation Trust, Moorfields at St George's University Hospital, Moorfields at Northwick Park Hospital, Royal Victoria Hospital Belfast, Guys and St Thomas' Hospital, Hinchingbrooke Hospital, Norfolk and Norwich University Hospital, York Hospital]). All patients provided written informed consent before participation.

No animal subjects were included in this study.

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Analysis and interpretation: Gazzard, Konstantakopoulou, Garway-Heath, Adeleke, Vickerstaff, Ambler, Hunter, Bunce, Nathwani, Barton

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Obtained funding: N/A

Overall responsibility: Gazzard, Konstantakopoulou, Garway-Heath, Adeleke, Vickerstaff, Ambler, Hunter, Bunce, Nathwani, Barton

Abbreviations and Acronyms:
CI = confidence interval; **EQ-5D** = EuroQol 5 Dimensions 5 Levels; **GQL-15** = Glaucoma Quality of Life-15; **GSS** = Glaucoma Symptom Scale; **GUI** = Glaucoma Utility Index; **HRQoL** = health-related quality of life; **IOP** = intraocular pressure; **LiGHT** = Laser in Glaucoma and Ocular Hypertension; **NICE** = National Institute for Health and Care Excellence; **OAG** = open-angle glaucoma; **OHT** = ocular hypertension; **ON** = optic nerve; **PBD-VF20** = Prevention of Blindness and Deafness 20-item Visual Functioning Questionnaire; **SLT** = selective laser trabeculoplasty; **VF** = visual field.

Keywords:
Glaucoma progression, Ocular hypertension, Open-angle glaucoma, Selective laser trabeculoplasty.

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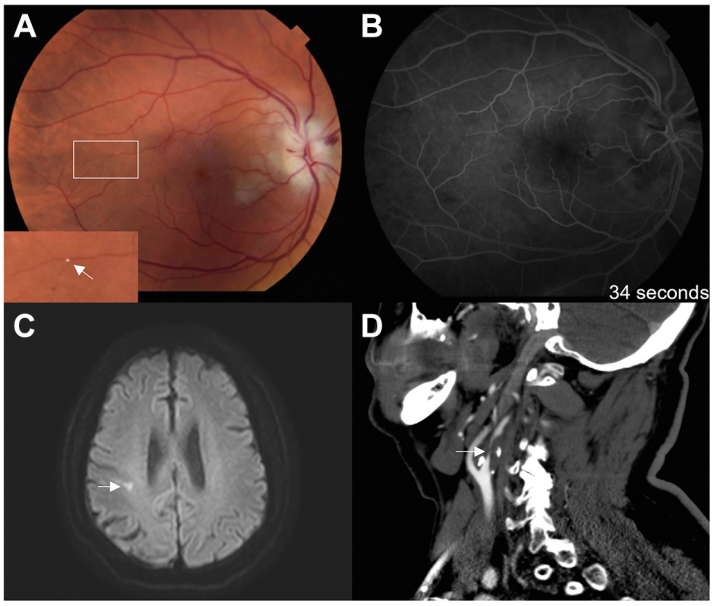
Pictures & Perspectives



Severe Unilateral Vision Loss in a 77-Year-Old Man

A 77-year-old man with mild headache and sudden vision loss (no light perception) in his right eye was referred for giant cell arteritis (GCA). Fundoscopy revealed chalky white optic disc edema, focal retinal edema, and 2 Hollenhorst plaques (HHP) in the distal arcades (Fig **A**). Choroidal filling was delayed (Fig **B**). Erythrocyte sedimentation rate was 12 mm/hr; C-reactive protein was 5.02 mg/dl (normal ≤5.00 mg/dl). Neuroimaging demonstrated subclinical infarcts (Fig **C**) and near complete right internal carotid artery occlusion (Fig **D**). Bilateral temporal artery biopsies were negative. When ophthalmic artery occlusion is suspected, the presence of HHP suggests a thromboembolic source rather than GCA (Magnified version of Fig **A**-**D** is available online at www.aaojournal.org).

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