The United Kingdom Glaucoma Treatment Study: A Multicenter, Randomized, Double-masked, Placebo-controlled Trial

Baseline Characteristics

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Objective: The United Kingdom Glaucoma Treatment Study (UKGTS) tests the hypothesis that treatment with a topical prostaglandin analog, compared with placebo, reduces the frequency of visual field (VF) deterioration events in patients with open-angle glaucoma (OAG) by 50% over a 2-year period. Additional goals are to evaluate study power with novel clinical trial outcomes: (1) VF deterioration velocity and (2) VF and quantitative imaging measurements modeled as joint outcomes.

Design: The UKGTS is a randomized, double-masked, placebo-controlled, multicenter treatment trial for OAG.

Participants: A total of 516 patients with newly diagnosed (previously untreated) OAG were prospectively recruited at 10 UK centers between 2007 and 2010.

Methods: Eligible patients were randomly assigned to treatment with latanoprost 0.005% or placebo. The observation period was 2 years, with subjects monitored by VF testing, quantitative imaging, optic disc photography, and tonometry at 11 visits.

Main Outcome Measures: The primary outcome measure is time to VF deterioration within 24 months. Secondary outcomes include the deterioration velocity of VF and quantitative imaging measures.

Results: The main source of referrals was optometrists (88%). A total of 777 subjects were assessed for eligibility, and 261 were excluded because they did not meet the inclusion criteria or declined to participate. The mean age of the 516 participants was 66 years, and 52.9% were male; 90.1% of the participants were white, and approximately one third (32.2%) reported a family history of glaucoma. A total of 777 eyes were eligible at initial assessment. Both eyes were eligible for 265 participants. Mean (standard deviation) intraocular pressure (IOP) at baseline for the eyes with better versus worse mean deviation (MD) was 18.9 (4.1) and 19.9 (4.7) mmHg, respectively ($P = 0.0053$). Some 56.1% of all eligible eyes had IOP <20 mmHg at baseline. The median (interquartile range) VF MD for all eligible eyes was −2.9 dB (−1.6 to −4.8 dB).

Conclusions: This is the first randomized, placebo-controlled trial to evaluate the efficacy of medical treatment in reducing VF deterioration in OAG. The baseline characteristics for eligible patients and eyes from this cohort are presented and compared with those of previous trials. The baseline characteristics are similar to those of the largely population-based Early Manifest Glaucoma Trial. The early stage of the glaucoma and relatively low IOP at diagnosis suggest remarkably sensitive case findings by community optometrists in the United Kingdom.

Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references. *Ophthalmology 2013;120:2540-2545*

**Group members available online in Appendix 1 (http://aaojournal.org).*

Primary open-angle glaucoma (OAG) is the most common cause of irreversible blindness worldwide and remains the second leading cause of blind registrations in the United Kingdom.[1] At present, increased intraocular pressure (IOP) is the only known modifiable risk factor for glaucoma, and the main goal of medical and surgical treatment for glaucoma is to reduce IOP. To date, IOP-lowering treatment studies in OAG have compared a treatment with no treatment[2–4] or an active control,[5,6] but not with a placebo.[7] The United Kingdom Glaucoma Treatment Study (UKGTS) is the first randomized, double-masked, placebo-controlled clinical trial for the medical treatment of OAG to assess the impact of treatment with a prostaglandin analog on visual field (VF) preservation.

The design and methodology of the UKGTS have been described in detail elsewhere.[8] Briefly, 516 eligible patients

ISSN 0161-6420/13/$ - see front matter
http://dx.doi.org/10.1016/j.ophtha.2013.07.054

were prospectively recruited in 10 UK centers and randomized in a 1:1 ratio to receive latanoprost 0.005% or placebo once in the evening in both eyes for 24 months or until reaching an end point. Unlike the Early Manifest Glaucoma Trial (EMGT), in which patients with early OAG were randomized to argon laser trabeculoplasty plus betaxolol (n = 129) or no immediate treatment (n = 126) and followed up for a median of 6 years,[9] the UKGTS was designed to detect changes in VF outcomes while having the shortest observation period of all OAG therapeutic trials with a VF outcome to date. The UKGTS was also designed to assess novel data analysis methods, which may further reduce the trial duration or sample size required by future studies seeking to identify treatment effects; these design features are related to VF test frequency and interval, selected to maximize the accuracy of estimates of the VF deterioration velocity,[10] and to the inclusion of frequent quantitative imaging of optic nerve head and retinal nerve fiber layer structure. Data were collected over 11 visits. The primary outcome measure in the UKGTS was time to VF deterioration within 24 months, and secondary outcomes included the deterioration velocity of VF and quantitative imaging measures. Thus, the UKGTS is the first medical treatment trial in OAG designed to enable the assessment of whether the inclusion of structural measures as joint outcomes increases statistical power to identify treatment effects and risk factors. Additional objectives of the UKGTS were to establish whether initial observation, rather than immediate treatment, is feasible for selected patients and to evaluate the association of VF loss with measures of quality of life. The aim of this article is to report and discuss the baseline characteristics of the UKGTS cohort.

Methods

The detailed UKGTS protocol has been described previously.[8] A total of 516 patients with newly detected, previously untreated OAG (including primary OAG, normal-tension glaucoma, and pseudoexfoliation glaucoma) in either eye were included. Eligible eyes were characterized by glaucomatous VF defects with corresponding damage to the optic nerve head (cup-to-disc ratio $\geq$0.7, focal narrowing of the neural rim, or both) and with open angles on gonioscopy, in the absence of a nonglaucomatous retinal or neurologic condition that could account for the VF loss. Patients were required to be 18 years of age or older, with a Snellen visual acuity of $\geq$20/40 and a VF mean deviation (MD) of 2 post-screening VFs differing by no more than 3 dB, for an MD of better than $-$6.0 dB, or by no more than 4 dB, for an MD worse than $-$6.0 dB. Patients with moderately advanced VF loss ($<-$16 dB) or a threat to fixation in either eye were excluded. Additional exclusion criteria included IOP >35 mmHg on 2 consecutive occasions in either eye or mean baseline IOP $\geq$30 mmHg; inability to perform reliable VF testing; and cataractous lens gradings of more than N1, C2, or P1 according to Lens Opacities Classification System III grading.

Baseline IOP data represent the mean of the Goldmann applanation tonometry (GAT) IOP at 2 visits before group allocation (screening and training visits). The IOP was measured by experienced staff in the screening clinic and according to the trial Standard Operating Procedures at the training visit. The VF tests were performed with the Humphrey Field Analyzer (HFA) Mark II (or II-i) (Carl Zeiss Meditec, Dublin, CA) and the Swedish interactive threshold algorithm standard 24-2 program.[8] For the baseline VF data, the mean of the 2 baseline VFs (after-allocation) performed at visit 1 was used; for the 32 patients who failed to attend visit 1, the mean of the 2 screening VFs is presented. Where the HFA software excluded a baseline VF because of learning effects or high false-positive rates, the mean of the baselines selected by the HFA software is presented. The baseline spherical equivalent (SE) calculation (algebraic sum of the value of the sphere and half of the value of the cylinder) was based on the refractive error recorded in the case report form from an autorefractor or spectacle focimetry. Where neither of these was recorded (n = 86 eligible eyes), the trial lens correction used to perform the VFs was used to estimate the SE, based on the age of the patient. The measurement of blood pressure and anthropometric measures (body mass index [BMI], waist circumference, waist-to-hip ratio), and the evaluation of history of hypertension, general arteriosclerosis (stroke, angina, and intermittent claudication), vasospasm, migraine, and Raynaud's phenomenon were undertaken during the first study visit after treatment allocation. All iris features, including color, transillumination, and thickness, were determined clinically. Data on ethnicity, family history, and education were obtained by self-report.

In this study, baseline characteristics were evaluated by patient and eye. For eye-based baseline data, 2 approaches were taken: (1) analysis of all eligible eyes and (2) "worse" eye analysis to compare the baseline characteristics between the eyes with worse and better MD.

Statistical Analyses

Summary measures for continuous variables have been presented in the baseline tables as mean and standard deviation (SD) for normally distributed measures and as median and interquartile range (IQR) for data that are not normally distributed. Frequencies (numbers) and percentages were used for categoric variables. A 2-sample *t* test was used to compare the means of continuous variables, and a chi-square test was used for categoric variables. An unpaired *t* test was used to compare the mean IOP between the eligible eyes with worse MD and better MD in all study participants. An unpaired test was used, despite paired data in 50% of cases, for simplicity and because results were highly significant despite ignoring nonindependence. STATA software (version 11; StataCorp LP, College Station, TX) was used for data analysis.

Results

Source of Referrals

The main source of referrals in the UKGTS was optometrists (88%), whereas only a small percentage of patients were referred from their general practitioner (3%) or a hospital (8%).

Participant Flow

Of 777 subjects assessed for eligibility, 261 were excluded because they did not meet the inclusion criteria or declined to participate (Fig 1, available at http://aaojournal.org); 66.4% of the patients screened took part in the UKGTS. The 516 eligible patients were randomized to latanoprost or placebo.

Baseline Patient Characteristics

The 11 initial participating centers across the United Kingdom with the corresponding patient cohorts are presented in Table 1 (available at http://aaojournal.org). Approximately 70% of the

participants were recruited and followed up in 1 of the following 4 centers: Moorfields Eye Hospital, Norfolk and Norwich University Hospital, Birmingham Heartlands and Solihull Hospital, and Hinchingbrooke Hospital.

The 516 participants had a mean (SD) age of 66 (11) years. The age distribution of all randomized patients at baseline is shown in Figure 2 (available at http://aaojournal.org). There were slightly more male patients in our cohort (52.9%). Approximately one third (32.2%) had a family history of glaucoma. The majority in our cohort was white (90.1%). A total of 28 participants (5.4%) had a history of myocardial infarction, 54 participants (10.5%) had a history of diabetes mellitus, 31 participants (6%) had obstructive pulmonary disease, and 65 participants (12.6%) had concomitant neurologic disease (Parkinson's, Alzheimer's, multiple sclerosis, or deafness). Use of systemic antihypertensive medications was noted in 207 patients (40.1%), use of corticosteroids (including inhalers) was noted in 45 patients (8.7%), use of statins was noted in 140 patients (27.1%), and use of other medications was noted in 304 patients (58.9%).

The baseline characteristics for the UKGTS participants attending at least 1 post-allocation visit (n = 484) are summarized in Table 2 (available at http://aaojournal.org). The median (IQR) BMI, calculated as the weight in kilograms divided by the height in meters squared, in our cohort was 26.9 (23.9−30.1). The median (IQR) waist-to-hip ratio, calculated as the ratio of the circumference of the waist in centimeters to that of the hips, was 0.91 (0.84−0.96). History of hypertension, defined as systolic blood pressure >160 mmHg or diastolic blood pressure >95 mmHg or antihypertensive treatment history,[3] was noted in 279 patients (57.8%). History of general arteriosclerosis (stroke, angina, or intermittent claudication) was found in 38 patients (7.9%), whereas evidence of vasospasm, migraine, or Raynaud's phenomenon was reported for 229 patients (47.4%).

Baseline Characteristics for All Eligible Eyes (n = 777)

The number of right and left eyes meeting the study eligibility criteria at baseline was almost equal, whereas both eyes met eligibility criteria in just more than half (51.8%) of the subjects (Table 3, available at http://aaojournal.org). In more detail, 265 patients had both eyes eligible, 117 had only the right eye and 130 had only the left eye, whereas 4 participants were recruited without having an eligible eye and represented protocol violations. Approximately one third of the eligible eyes (32.7%) had a myopic refractive error (SE <−1 diopter [D]), and approximately one quarter (24.4%) were hypermetropic (SE >1 D). The majority of patients (97.2%) had a best-corrected visual acuity (BCVA) of ≥0.67. The mean (SD) axial length was 24.1 (1.3) mm.

Among the UKGTS eligible eyes, the median (IQR) for the mean MD (average of the 2 baseline VFs for each eye) of the better and worse eyes was −2.0 dB (−1.2 to −3.3) and −3.5 dB (−2.1 to −5.9), respectively. The median (IQR) for the mean MD of all eligible eyes was −2.9 dB (−1.6 to −4.8). In the case of the right eyes, the mean difference (95% confidence interval) between the 2 baseline VFs was 0.16 dB (0.04−0.28), with the first VF having slightly higher sensitivity than the second. In the left eyes, which were tested after the right eyes, this difference was slightly larger at 0.31 dB (0.20−0.42) (see Appendix 2, available at http://aaojournal.org, for agreement plots and explanation). The mean (SD) GAT IOP for all eligible eyes was 19.5 (4.5) mmHg. Some 87% of eligible eyes had a baseline IOP of <25 mmHg, and 56.1% of eligible eyes had a baseline IOP of <20 mmHg. For the 4 participants who were recruited without having an eligible eye, the mean age was 56 years, and the mean baseline GAT IOP and VF MD of all eyes were 20.4 mmHg and −0.62 dB, respectively.

Any iridotrabecular contact was noted in approximately one tenth of all eligible eyes (9.5%), whereas peripheral anterior synechiae (0.6%) and a posterior embryotoxon of any grade (1.5%) were rare in our cohort. The majority of cases had "wide" open angles, with only 3.3% having a Van Herick grade of less than 25%. Significant trabecular pigmentation was uncommon (2.8%), with the majority of eligible eyes (78.1%) having no or very mild pigmentation. Likewise, a Krukenberg spindle of any grade and mid-peripheral iris transillumination were found in only 2.1% of the UKGTS-eligible eyes. The most common iris color was blue (46.7%), followed by light brown (15.0%) and hazel (14.7%). Eligible eyes with any degree of pseudoexfoliation (0.5%) and iris sphincter transillumination (0.8%) were rare in this UK cohort.

Protocol violations were noted in 1 eye with BCVA <0.5, in 1 eye with baseline MD <−16 dB, in 19 eyes with nuclear cataract score >1, and 1 eye with cortical cataract score >2.

Eyes with Better versus Worse Mean Deviation

The baseline characteristics of the eyes with better versus worse MD in the UKGTS (n = 516) are presented in Table 4 (available at http://aaojournal.org). Right eyes were more likely to have a better MD at baseline (60.5%) ($P < 0.0001$). The mean (SD) IOP at baseline was lower in the eyes with better MD (18.9 [4.1] mmHg) than in the eyes with worse MD (19.9 [4.7] mmHg) ($P = 0.0053$). More than half of the eyes with better MD (59.7%) and worse MD (53.1%) presented with an IOP of less than 20 mmHg at baseline. Axial length and central corneal thickness (CCT) were similar between the eyes with better MD and the eyes with worse MD, whereas pseudoexfoliation was rare in both groups.

Discussion

Evidence to date for the beneficial effect of IOP-lowering treatment in OAG with established VF loss comes from a number of sources, particularly the Collaborative Normal Tension Glaucoma Study,[4] the EMGT,[3] the Collaborative Initial Glaucoma Treatment Study (CIGTS),[5] and the Advanced Glaucoma Intervention Study (AGIS).[6] The first 2 of these trials were unmasked and compared treatment with no treatment using an objective VF primary outcome measure; the CIGTS compared medical and surgical interventions, whereas the AGIS compared 2 surgical management strategies. The UKGTS is the first randomized, double-masked, placebo-controlled trial to assess the impact of medical IOP lowering (with a prostaglandin analog) on VF preservation.

The primary source of referrals in the UKGTS was community optometrists (88%), representing standard case detection in the United Kingdom. This is in contrast with the EMGT, in which the majority of subjects (85%) were recruited by actively screening 70% of the local population fulfilling the age criteria for eligibility. Recruitment from clinical centers (6.6%) and practitioners (8.6%) in the EMGT represented the minority of cases, similar to the UKGTS, in which only 8% of the study patients were referred from a hospital and 3% were referred from their general practitioner.

More than half of the UKGTS patients had both eyes eligible, unlike the EMGT, in which only 24% of cases were bilateral. A refractive error more myopic than −1 D at

baseline was found in 32.7% of our cohort and was more common than in the EMGT (13%). Hypermetropia of more than 1 D was over-represented in the EMGT cohort (57%) compared with the UKGTS cohort (24.4%). As expected for a clinical trial recruiting newly diagnosed OAG cases, and given the eligibility criteria, the BCVA was ≥0.67 in the majority of our cohort (97.2%), similar to that of the EMGT (99%). The mean axial length in the UKGTS (24.1 mm) was slightly longer than the average reported for a British population in the European Prospective Investigation of Cancer (EPIC)-Norfolk study (23.8 mm in men, 23.3 mm in women),[11] thus reflecting the higher percentage of axial myopia in our cohort. A possible explanation for the difference is the referral source (optometry), with myopes being more used to visiting optometry for refractive error correction than emmetropes or low hypermetropes, who may be more likely to buy off-the-shelf reading glasses.

The median (IQR) MD for all UKGTS-eligible eyes was −2.9 dB (−1.6 to −4.8); this represents earlier disease than in the EMGT (MD of −4.7 dB)[3] and the CIGTS (MD of −5.5 dB)[12] cohorts, whereas the AGIS (MD of −10.5 dB)[13] and Collaborative Normal-Tension Glaucoma Study (CNTGS) (MD of −8 dB)[4] included subjects with more advanced glaucomatous damage at baseline. The IOP distribution in the UKGTS showed that 86.9% of eligible eyes had a baseline IOP <25 mmHg, which is in line with the EMGT (80%). The mean (SD) IOP at baseline was 19.5 (4.5) mmHg, lower than in the EMGT (20.7 [4.1] mmHg). As expected, the UKGTS mean IOP was higher than the one recorded at baseline in studies focusing on normal tension glaucoma, such as the CNTGS (16.1 [2.3] mmHg for the controls and 16.9 [2.1] mmHg for the treated group). The early stage of glaucoma and relatively low IOP at diagnosis suggest remarkably sensitive case findings by community optometrists in the United Kingdom.

The majority of eligible eyes had wide open angles (≥40%) on Van Herick grading (74.4%), similar to the EMGT (82%). Significant trabecular pigmentation was relatively uncommon in both the UKGTS (2.8%) and EMGT (6%) cohorts. Pseudoexfoliation was rare in the UKGTS cohort (0.5%), unlike in the EMGT or CIGTS, in which it was noted in 8% of eligible eyes and 4.8% of enrolled patients, respectively. However, unlike the EMGT and the other major glaucoma clinical trials, the UKGTS is the first to report detailed baseline phenotypic data and to include the Krukenberg spindle grade, embryotoxon grade, presence of any iridotrabecular contact, iris thickness, iris color, and iris transillumination.

The mean age of the participants was 66 years and was almost identical to the mean age of participants in the CNTGS[4] and similar to the mean age of 68.1 years in the EMGT.[3] Both sexes were almost equally represented in our cohort, as opposed to the EMGT, in which participants were predominantly female (66%). Family history of glaucoma was relatively common in our study, with approximately one third of the participants reporting a first-degree relative with the disease; this was almost identical to the family history rate reported in the CIGTS,[5] but higher than in the EMGT,[4] in which a positive family history was noted in only one fifth of the participants. With regard to education, approximately half of the UKGTS participants did not pursue education beyond the age of 16 years, whereas in the AGIS approximately three quarters (71.3%) of the subjects had not been to any college or graduate school. The majority of UKGTS participants were white, similar to the Swedish cohort described in the EMGT. Unlike the CIGTS and AGIS, in which a substantial proportion of the study groups (38% and 56%, respectively) were black, only 5.2% of the UKGTS participants were black, the second most common ethnicity in our cohort.

Hypertension (defined as in the EMGT to allow for comparisons) at baseline was more common in our cohort (57.8%) than in the EMGT (38%) and the AGIS (50%), in which hypertension was determined only by self-report. The mean systolic and diastolic blood pressures in the UKGTS (136 [20] and 81 [11] mmHg, respectively) were lower compared with those in the EMGT (148.0 [18.8] and 85.7 [10.3] mmHg, respectively). This is likely explained by the fact that more than one third of our participants were taking antihypertensive medications, compared with only 24% in the EMGT. Statins (widely prescribed in the United Kingdom at present) were taken by more than one quarter of the UKGTS patients. The median BMI was 26.9 in our cohort, suggesting that the majority of patients were overweight (BMI >25), in line with the latest Health Survey for England, showing that in 2009 61.3% of adults in England were overweight. Similar to the BMI results, waist circumference, thought to assess the proportion of body fat located intra-abdominally as opposed to subcutaneously and to better reflect cardiovascular risk,[14] was also found to be higher in the UKGTS cohort (median 98 cm) compared with the recommended limits (<94 cm for men and <80 cm for women). The median waist-to-hip ratio, considered a more efficient predictor of mortality in older people than waist circumference or BMI,[15] was 0.91 in our cohort, suggesting that the majority of UKGTS patients had abdominal obesity (defined as a waist-to-hip ratio >0.90 for men and >0.85 for women by the World Health Organization).[16]

History of myocardial infarction was similar in the UKGTS (5.4%) and EMGT (6%) cohorts, whereas diabetes mellitus was more frequent in the UKGTS (10.5%) than in the EMGT (4%) cohort, but less frequent when compared with the AGIS cohort (20%). Obstructive pulmonary disease also was more frequent in our study population (8%) compared with the EMGT (1%). General arteriosclerosis (defined more broadly than in the EMGT to include stroke, angina, or intermittent claudication) was noted in more patients (7.9%) in the UKGTS than in the EMGT (5%). Moreover, approximately half of our participants reported a history suggestive of peripheral vasospasm, migraine, or Raynaud's phenomenon, whereas these conditions were encountered in only 19% of cases in the EMGT. In the UKGTS, recognized standardized protocols were used to elicit a history of these conditions, such as the Rose questionnaire for angina and intermittent claudication,[17] the International Headache Society diagnostic criteria for migraine,[18] and protocols derived from well-established definitions for vasospasm and Raynaud's.[19]

Left eyes were slightly more likely to be associated with a worse MD at baseline in our cohort. Fatigue may have contributed to this difference because left eyes were tested after the right eyes; however, Poinoosawmy et al[20] identified that left eyes more often had worse VF loss than right eyes in normal-tension glaucoma but not in high-tension glaucoma.[20] The mean IOP at baseline was 1 mmHg lower in the eyes with better MD (18.9 [4] mmHg) compared with the eyes with worse MD (19.9 [4.7] mmHg), as expected by the link between increased IOP and glaucoma, although other studies have suggested only a poor correlation between IOP and VF damage.[21,22] Just more than half of the eyes with better MD and eyes with worse MD demonstrated an IOP <20 mmHg at baseline, largely in line with the EMGT, in which 46% of eligible eyes fell below this same IOP threshold. The mean CCT in our cohort was consistent with the mean CCT reported in epidemiologic studies[23] and meta-analyses.[24]

In conclusion, the UKGTS is the first randomized, placebo-controlled trial to evaluate the efficacy of medical treatment in reducing VF deterioration in OAG. The outcome will provide evidence for the efficacy of the most widely prescribed class of IOP-reducing medication (prostaglandin analogs) in preserving VF in patients with glaucoma; it will also allow the quantification of risk factors for deterioration, enabling more precise risk profiling of patients and the development of patient management protocols. Some groups of patients were under-represented in our cohort, such as those with high IOP (>30 mmHg) or pseudoexfoliation and black subjects. However, the study will provide useful information on the effectiveness of IOP-lowering treatment in the majority of patients with OAG. The protocols for VF and imaging frequency and interval, together with new data analysis methods, may enable the measurement of deterioration behavior in clinical practice over a shorter period than is possible at present.[25]

References

1. Bunce C, Xing W, Wormald R. Causes of blind and partial sight certifications in England and Wales: April 2007-March 2008. Eye (Lond) 2010;24:1692–9.
2. Holmin C, Thorburn W, Krakau CE. Treatment versus no treatment in chronic open angle glaucoma. Acta Ophthalmol (Copenh) 1988;66:170–3.
3. Leske MC, Heijl A, Hyman L, Bengtsson B. Early Manifest Glaucoma Trial Group. Early Manifest Glaucoma Trial: design and baseline data. Ophthalmology 1999;106:2144–53.
4. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Am J Ophthalmol 1998;126:487–97.
5. Musch DC, Lichter PR, Guire KE, Standardi CL, CIGTS Study Group. The Collaborative Initial Glaucoma Treatment Study: study design, methods, and baseline characteristics of enrolled patients. Ophthalmology 1999;106:653–62.
6. Advanced Glaucoma Intervention Study. 2. Visual field test scoring and reliability. Ophthalmology 1994;101:1445–55.
7. Vass C, Hirn C, Sycha T, et al. Medical interventions for primary open angle glaucoma and ocular hypertension. Cochrane Database Syst Rev 2007;(4):CD003167.
8. Garway-Heath DF, Lascaratos G, Bunce C, et al. United Kingdom Glaucoma Treatment Study Investigators. The United Kingdom Glaucoma Treatment Study: a multicenter, randomized, placebo-controlled clinical trial: design and methodology. Ophthalmology 2013;120:68–76.
9. Heijl A, Leske MC, Bengtsson B, et al. Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120:1268–79.
10. Crabb DP, Garway-Heath DF. Intervals between visual field tests when monitoring the glaucomatous patient: wait-and-see approach. Invest Ophthalmol Vis Sci 2012;53:2770–6.
11. Foster PJ, Broadway DC, Hayat S, et al. Refractive error, axial length and anterior chamber depth of the eye in British adults: the EPIC-Norfolk Eye Study. Br J Ophthalmol 2010;94:827–30.
12. Gillespie BW, Musch DC, Guire KE, et al; CIGTS Study Group. The Collaborative Initial Glaucoma Treatment Study: baseline visual field and test-retest variability. Invest Ophthalmol Vis Sci 2003;44:2613–20.
13. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 3. Baseline characteristics of black and white patients. Ophthalmology 1998;105:1137–45.
14. Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. BMJ 1995;311:158–61.
15. Price GM, Uauy R, Breeze E, et al. Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. Am J Clin Nutr 2006;84:449–60.
16. World Health Organization. Waist circumference and waist−hip ratio: report of a WHO expert consultation, Geneva, 8−11 December 2008. Available at: http://whqlibdoc.who.int/publications/2011/9789241501491_eng.pdf. Accessed July 23, 2013.
17. Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. Br J Prev Soc Med 1977;31:42–8.
18. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 1988;8(Suppl):1–96.
19. Flammer J, Pache M, Resink T. Vasospasm, its role in the pathogenesis of diseases with particular reference to the eye. Prog Retin Eye Res 2001;20:319–49.
20. Poinoosawmy D, Fontana L, Wu JX, et al. Frequency of asymmetric visual field defects in normal-tension and high-tension glaucoma. Ophthalmology 1998;105:988–91.
21. Greenfield DS, Liebmann JM, Ritch R, Krupin T. Low-Pressure Glaucoma Study Group. Visual field and intraocular pressure asymmetry in the Low-Pressure Glaucoma Treatment Study. Ophthalmology 2007;114:460–5.
22. Orgül S, Flammer J. Interocular visual-field and intraocular-pressure asymmetries in normal-tension-glaucoma. Eur J Ophthalmol 1994;4:199–201.
23. Wolfs RC, Klaver CC, Vingerling JR, et al. Distribution of central corneal thickness and its association with intraocular pressure: the Rotterdam Study. Am J Ophthalmol 1997;123:767–72.
24. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. Surv Ophthalmol 2000;44:367–408.
25. Chauhan BC, Garway-Heath DF, Goñi FJ, et al. Practical recommendations for measuring rates of visual field change in glaucoma. Br J Ophthalmol 2008;92:569–73.

Footnotes and Financial Disclosures

Originally received: March 19, 2013.
Final revision: July 31, 2013.
Accepted: July 31, 2013.
Available online: October 14, 2013. Manuscript no. 2013-437.

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Financial Disclosure(s):
The author(s) have made the following disclosure(s): G.L.: Allergan (meeting expenses), Pfizer (unrestricted grant), Heidelberg Engineering (equipment loan), Carl Zeiss Meditec (equipment loan), Optovue (equipment loan). D.F.G-H.: Carl Zeiss Meditec (equipment loan), Allergan (consultancy, grant, lectures, educational presentations), Bausch & Lomb (consultancy, lectures), GSK (consultancy), Pfizer (unrestricted grant), Heidelberg Engineering (equipment loan), OptoVue (equipment loan), Alcon (consultancy), Merck (consultancy, lectures), Alimera (consultancy), Forsight (consultancy), Quark (consultancy). R.B.: none. C.B.: Pfizer (unrestricted grant), Heidelberg Engineering (equipment loan), Carl Zeiss Meditec (equipment loan), Optovue (equipment loan). W.X.: none. D.P.C.: Allergan (grant, lectures), MSD (grant, lectures), Pfizer (unrestricted grant). R.A.R.: none. A.S.: none.

Funding: The trial was funded by an unrestricted Investigator-Initiated Research Grant from Pfizer, Inc. The research was also supported by the National Institute for Health Research Biomedical Research Centre based at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology. The views expressed are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health. Equipment loans were made by Heidelberg Engineering GhbH, Carl Zeiss Meditec Inc., and Optovue Inc. The trial sponsor was Moorfields Eye Hospital NHS Foundation Trust. The funding organizations had no role in the design or conduct of this research. Trial registration: ISRCTN96423140.

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