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A randomized trial of adding a plano lens to atropine for amblyopia

Pediatric Eye Disease Investigator Group*

Abstract

Background—Some children have residual amblyopia after treatment with atropine eyedrops for amblyopia due to strabismus and/or anisometropia. We conducted a randomized clinical trial to evaluate the effectiveness of augmenting the effect of atropine by changing the lens over the fellow eye to plano in children with residual amblyopia.

Methods—A total of 73 children 3 to <8 years of age (mean, 5.8 years) with stable residual amblyopia (range, 20/32 to 20/160, mean 20/63⁺¹) were enrolled after at least 12 weeks of atropine treatment of the fellow eye. Participants were randomly assigned to continuing weekend atropine alone or wearing a plano lens over the fellow eye (while continuing atropine). The primary outcome was assessed at 10 weeks, and participants were followed until improvement ceased.

Results—At the 10-week primary outcome visit, amblyopic-eye visual acuity had improved an average of 1.1 lines with the plano lens and 0.6 lines with atropine only (difference adjusted for baseline visual acuity = + 0.5 line; 95% CI, −0.1 to +1.2). At the primary outcome or later visit when the best-measured visual acuity was observed, the mean amblyopic-eye improvement from baseline was 1.9 lines with the plano lens and 0.8 lines with atropine only.

Conclusions—When amblyopic-eye visual acuity stops improving with atropine treatment, there may be a small benefit to augmenting atropine therapy with a plano lens over the fellow eye. However, the effect was not statistically significant, and the large confidence interval raises the possibility of no benefit or a benefit larger than we observed. A larger study would be necessary to get a more precise estimate of the treatment effect.

Amblyopia is a common cause of visual impairment in children and young and middle-aged adults.^{1–4} Some clinicians prescribe atropine eyedrops to the (nonamblyopic) fellow eye, either as initial treatment or when a child will not comply with patching.^{5–9} In a previous

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*A complete listing of the Pediatric Eye Disease Investigator Group members participating in this study appears in e-Supplement 1, available at jaapos.org.

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study, daily and weekend atropine were found to be equally effective initial treatments for amblyopia.⁸ Although many children are successfully treated with atropine, some fail to attain normal visual acuity in the amblyopic eye.^{8–10} When improvement with initial atropine treatment ceases and amblyopia is still present, treatment options include continuing the same treatment, switching to another treatment, such as patching, and combining different treatment modalities. Most children with amblyopia have a hyperopic refractive error, and for these children another approach for subsequent therapy is to augment atropine with optical blur of the fellow eye by reducing the hyperopic correction or replacing it with a plano lens.^{6,7,9} We conducted a randomized trial to determine whether addition of a plano lens to atropine treatment for the fellow eye improves amblyopic-eye visual acuity in 3- to 8-year-old children with clinically stable residual amblyopia following prescribed initial treatment with at least 12 weeks of daily or weekend atropine.

Methods

This study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and conducted by the Pediatric Eye Disease Investigator Group (PEDIG). The protocol and Health Insurance Portability and Accountability Act–compliant informed consent forms were approved by institutional review boards, and a parent or guardian (hereinafter referred to as “parent”) of each study participant provided written informed consent. Oversight was provided by an independent data and safety monitoring committee. The study protocol is available on the PEDIG website (www.pedig.net) and is summarized below.

Synopsis of Study Design

Prior to being considered for the randomized trial, participants who had not completed at least 12 weeks of atropine with demonstrated stable visual acuity in the amblyopic eye were enrolled into a run-in phase and treated with weekend atropine 1% ophthalmic solution (one drop on Saturday and one on Sunday) and spectacles based upon a recent cycloplegic refraction, with follow-up every 6 weeks until the amblyopic-eye visual acuity no longer improved (<1 line improvement). Participants who had been using daily atropine were switched to weekend atropine at enrollment. Participants who had completed at least 12 weeks of atropine with documented visual acuity stability were eligible to be randomized at enrollment. The minimum amount of time in spectacles prior to randomization was 6 weeks, with the vast majority of participants undergoing optical treatment for at least 12 weeks. The spectacles could undercorrect the full cycloplegic hypermetropic correction by no more than +1.50 D spherical equivalent (SE), and any reduction in plus sphere was the same for both eyes. A complete list of spectacle correction requirements is found in Table A of e-Supplement 2, available at jaapos.org.

Major eligibility criteria for the randomized trial included: (1) age 3 to <8 years at enrollment; (2) treatment of amblyopia with prescribed weekend and/or daily atropine for at least 12 weeks, with no improvement in visual acuity (<1 line) at 2 consecutive visits at least 6 weeks apart (confirmed by retest), during which time there was no change in spectacle correction; (3) +1.50 D SE in the fellow eye; (4) best amblyopic-eye visual acuity of 20/40

to 20/160 inclusive, with an interocular difference (IOD) of ≥ 2 lines or an amblyopic-eye visual acuity of 20/32 with 3 lines of IOD; (5) the presence of strabismus and/or anisometropia meeting study-specific criteria (see e-Supplement 2, Table A); (6) fellow-eye visual acuity of 20/32 or better; and (7) compliance with atropine treatment based on investigator judgment.

Randomization and Treatment Protocols

Data were entered on the PEDIG website and participants were randomly assigned (using a permuted block design stratified by site and by weekend or daily atropine frequency at enrollment), with equal probability to either continue weekend atropine with best spectacle correction (the atropine-only group) or to weekend atropine augmented by spectacles with a plano lens over the fellow eye (the plano lens group).

All participants were provided atropine 1% eyedrops and instructed to instill 1 drop in the fellow eye each Saturday and Sunday morning. Those randomly assigned to the plano lens group received new spectacles, which were identical to the original prescription except that the fellow-eye lens had been changed to plano. The study provided nonprescription sunglasses or clip-on sunglasses for participants to wear in sunlight (if needed), and they were encouraged to wear a brimmed hat for daytime outdoor activities.

Testing Procedures and Follow-up

The primary study outcome was amblyopic-eye visual acuity 10 weeks after randomization, which was obtained by a study-certified tester who was masked to the participant's assigned treatment. Following the 10-week primary outcome examination, participants discontinued the randomized treatment and returned 2 weeks later for a 12-week visit to measure off-treatment fellow-eye visual acuity, ocular alignment, and stereoacuity. Participants whose 10-week amblyopic-eye visual acuity improved at least 1 line from randomization (based on the better of the test–retest visual acuity measurements) continued in the study with visits every 10 ± 1 weeks until there was no improvement in visual acuity of at least 1 line from the previous visit, confirmed by a retest.

At each visit, visual acuity was measured in each eye using the participant's best spectacle correction by a study-certified tester using the ATS-HOTV¹¹ protocol on the Electronic Visual Acuity Tester.¹² Ocular alignment was measured at distance and near with a simultaneous prism and cover test at randomization and each follow-up visit except for the 10-week examination. Stereoacuity was measured at the 12-week examination with the Randot Preschool Stereoacuity Test (Stereo Optical Co, Chicago, IL).

At the 12-week examination and subsequent visits, the fellow eye was retested if the visual acuity tested ≥ 1 line worse than at enrollment. If the better of the fellow eye test and retest visual acuity measurements was reduced by ≥ 2 lines, a cycloplegic refraction was performed. If a significant change in refraction was found such that the participant's glasses were not in compliance with the study spectacle guidelines (see e-Supplement 2, Table A), visual acuity was retested in trial frames with the new correction, and new spectacles were prescribed. Whether or not there was a change in cycloplegic refraction, any participant whose visual acuity was reduced by ≥ 2 lines returned for a visit 5 weeks later for a recheck

of the fellow-eye visual acuity, and subsequent treatment was at the investigator's discretion.

At each follow-up visit, investigators queried parents about adverse effects from treatment. An assessment of compliance with atropine and spectacle wear was based on discussions with the parent and by reviewing study calendars maintained by the parent, who recorded the frequency of atropine administration. Compliance was judged to be excellent (>75%), good (51%–75%), fair (26%–50%), or poor (<25%).

After 40 months of recruitment, less than half of the preplanned sample size ($n = 158$) had been randomized. Consequently, the study steering committee recommended stopping the study due to insufficient recruitment.

Statistical Methods

The primary outcome measure was the masked 10-week amblyopic-eye visual acuity. The sample size for the randomized trial was computed to be 158 participants in order to have 90% power with a type 1 error rate of 5% and no more than 5% loss to follow-up to reject a null hypothesis of no difference between groups, assuming a true treatment group difference in change in visual acuity from randomization to 10 weeks as small as 0.75 logarithm of minimum angle of resolution (logMAR) line, and a standard deviation of change of 1.4 logMAR lines (based on prior PEDIG studies^{8,9} using atropine for the treatment of amblyopia).

The primary analysis was a treatment group comparison of the masked 10-week amblyopic-eye visual acuity using an analysis of covariance (ANCOVA) model, adjusting for visual acuity at randomization. The primary analysis included data from 10-week visual acuity examinations completed between 8 and 15 weeks (inclusive) with no imputation for missing data. As an alternative approach, the primary analysis was repeated, adjusting for baseline covariates imbalanced between treatment groups by including them in the ANCOVA model.

Additional alternative analyses yielded similar treatment effects (data not shown) and consisted of the following: exclusion of 10-week visual acuity examinations outside the 10 ± 1 week protocol window ($n = 7$), exclusion of ineligible participants ($n = 3$), and multiple imputation of 10-week visual acuity measurements based on visual acuity scores at randomization for participants with missing 10-week scores ($n = 1$). If a visual acuity retest was performed, then the amblyopic-eye efficacy analyses were performed using the initial visual acuity, and the retest was used only to determine whether the participant continued in the study.

Secondary analyses compared the following: (1) the proportion of participants with ≥ 2 logMAR lines improvement in 10-week amblyopic-eye visual acuity from randomization using binomial regression, adjusting for visual acuity at randomization; (2) the proportion of participants who achieved 20/25 or better amblyopic-eye visual acuity at 10 weeks; and (3) mean amblyopic-eye visual acuity improvement and proportion of participants with ≥ 2 lines

improvement at the visit of best-outcome visual acuity (10-week primary outcome or a subsequent 10-week follow-up visit) from randomization.

For analysis of the fellow-eye visual acuity, we used the better of the initial test–retest visual acuity measurements (if a retest was indicated). A treatment group difference in fellow-eye visual acuity change at the 12-week exam was evaluated using an ANCOVA model, adjusting for the fellow-eye visual acuity at randomization. The distribution of 12-week Randot Preschool Stereoacuity scores was compared between treatment groups using a Wilcoxon rank sum test.

Analyses followed the intent-to-treat principle and were conducted using SAS version 9.3 (SAS Institute Inc, Cary, NC).

Results

Between November 2009 and August 2013, 73 participants from 20 sites were randomly assigned to either augmenting weekend atropine by changing the lens over the fellow eye to plano ($n = 33$) or continuing with weekend atropine with best spectacle correction ($n = 40$). At randomization, the average age of participants was 5.8 years and the average amblyopic-eye visual acuity was 0.48 logMAR ($20/63^{+1}$). Table 1 provides the baseline characteristics according to treatment group.

Visit Completion and Treatment

The 10-week primary outcome for the amblyopic eye and the 12-week outcome for the fellow eye were completed by all participants in both the plano lens group ($n = 33$) and in the atropine-only group ($n = 40$; Figure 1). One participant in the atropine-only group was excluded from the primary outcome analysis because the 10-week visual acuity examination was completed >15 weeks after randomization. The vision tester was masked to treatment group for 99% of 10-week examinations (100% in the plano lens group and 97% in the atropine-only group).

During the first 10 weeks after randomization, atropine compliance was judged to be excellent in 94% and good in 6% of participants randomized to the plano lens group and excellent in 95% and good in 5% of participants randomized to the atropine-only group (see e-Supplement 2, Table B). Spectacle compliance during the initial 10 weeks was deemed excellent in 91%, good in 3%, fair in 3%, and poor in 3% of participants in the plano lens group and excellent in 98% and good in 3% of participants in the atropine-only group.

Amblyopic-Eye Visual Acuity—Primary Analysis at 10 Weeks

At the 10-week primary outcome visit, amblyopic-eye visual acuity improved from randomization by an average of 1.1 lines in the plano lens group and 0.6 line in the atropine-only group (Table 2). The treatment group difference in mean visual acuity after 10 weeks, adjusting for visual acuity at randomization, was +0.5 line (2-sided 95% CI, -0.1 to $+1.2$ line; $P = 0.12$), favoring the plano lens group. Amblyopic-eye visual acuity met a prespecified secondary outcome of ≥ 2 lines improvement for 9 (27%) participants in the plano lens group and 8 (21%) participants in the atropine only group (difference, $+10\%$; 2-

sided 95% CI = -10% to +30%, $P = 0.33$). Visual acuity 20/25 was achieved by 18% and 10%, respectively.

Adjustment for treatment group imbalances in amblyopia cause (anisometropic, strabismic, or combined), weeks of atropine treatment prior to randomization (continuous), and fellow-eye refractive error at enrollment (continuous) yielded a similar treatment effect as the primary outcome analysis (mean difference = +0.5 line; 2-sided 95% CI = -0.2 to +1.2 line; $P = 0.15$). The mean visual acuity change at 10 weeks from randomization according to baseline factors is provided in Table C of e-Supplement 2.

Follow-up after the 10-week Primary Outcome

At the 10-week primary outcome evaluation, 26 (79%) participants in the plano lens group and 24 (60%) participants in the atropine-only group met the study criteria to continue their assigned treatment (amblyopic-eye visual acuity improved 1 line from randomization; Figure 1). Randomized treatment was continued for one additional study visit for 15 participants in the plano lens group and 19 participants in the atropine-only group, two visits for 6 and 4 participants, and three or more visits for 4 and 0 participants, respectively. Four participants in the plano lens group reported noncompliance with plano lens wear after the 12-week examination, but all 4 had worn the plano lens until at least the primary outcome examination.

The best visual acuity at the 10-week primary outcome or any subsequent 10-week follow-up visit improved by an average of 1.9 lines from randomization in the plano lens group and 0.8 line in the atropine-only group (Table D in e-Supplement 2). Twenty (61%) participants in the plano lens group and 11 (28%) in the atropine-only group improved 2 lines in amblyopic-eye visual acuity at the best outcome visit.

Of those whose best outcome visual acuity occurred after randomization, the time point of best amblyopic-eye visual acuity for participants in the plano lens group was the 10-week primary outcome examination for 14 (54%), 18 to <25 weeks for 6 (23%), and 25 weeks for 6 (23%) participants. The time point of best amblyopic-eye visual acuity for participants in the atropine-only group was the 10-week primary outcome examination for 16 (70%), 18 to <25 weeks for 6 (26%), and 25 weeks for 1 (4%) participant.

Adverse Events and Stereoacuity

The fellow-eye visual acuity tested 2 or more lines worse from randomization for no participants in the plano lens group at the 12-week (off-treatment) examination and for 1 participant in the atropine-only group, whose visual acuity was 20/20 on retesting in trial frames after refraction (e-Supplement 2, Table E). There was no difference between groups in mean fellow-eye visual acuity change since randomization at the 12-week examination (mean difference, +0.10 line; 2-sided 95% CI, -0.23 to +0.43; $P = 0.55$), adjusted for visual acuity at randomization. Two participants (1 in each treatment group) did not discontinue randomized treatment prior to the 12-week examination. There were 7 participants (6 in the plano lens group and 1 in the atropine-only group) who reported light sensitivity, and 1 participant in the atropine only group reported dry skin on the wrists. There were no

treatment group differences in the number of participants who developed new-onset strabismus or had an increase in a preexisting strabismus, and no participants developed diplopia (data not shown).

Randot Preschool Stereoacuity scores were similar between treatment groups at the 12-week examination for the overall cohort ($P = 0.23$) and when limited to participants with no history of strabismus ($P = 0.66$; e-Supplement 2, Table F).

Discussion

We studied the benefit of augmenting the effect of topical atropine by changing the lens over the fellow eye to plano for children 3 to 8 years of age with residual amblyopia whose visual acuity had stopped improving after using atropine for at least 12 weeks. We found that augmenting atropine with a plano lens resulted in an average of 0.5 line additional improvement (1.1 vs 0.6 line) 10 weeks after randomization compared with continuing atropine with best spectacle correction. However, due to the smaller-than-planned sample size, the study results are inconclusive as to whether there is no benefit or a small-to-moderate benefit of treatment. It was difficult to recruit participants for this study because our investigators were much more likely to prescribe patching than atropine as initial treatment for amblyopia and most participants who were enrolled in the run-in phase improved to the point that their amblyopic-eye visual acuity was too good to be eligible for randomization. When interpreting these results, it is important to consider both the point estimate and the 95% confidence interval. Our point estimate suggests a small benefit to adding a plano lens, but the large confidence interval is consistent with no benefit (lower limit of 95% CI = -0.1 line) or a larger benefit (upper limit of 95% CI = $+1.2$ lines).

Previous studies have measured improvement with atropine plus a plano lens, but no studies have randomized participants when amblyopic-eye visual acuity stops improving after initial treatment of daily or weekend atropine and a period of spectacle wear. In a previous PEDIG study, 55 participants who did not respond adequately to atropine alone were prescribed a plano lens for the fellow eye. Their mean improvement before the use of the plano lens was 1.0 line, compared with 1.6 lines after prescribing the plano lens.¹³ Another study evaluated atropine with or without a plano lens as *initial* treatment for amblyopia and enrolled children with no atropine treatment within the previous 6 months. That study found that initial treatment outcomes (after visual acuity stability with spectacles) showed no substantial advantage of atropine with a plano lens over atropine alone, although a slightly higher proportion of participants using a plano lens achieved amblyopic-eye visual acuity of 20/25 or better (40% vs 29%).⁹

In the current study, we observed continued improvement beyond the 10-week primary outcome examination in 12 participants (36%) in the plano lens group and 7 participants (18%) in the atropine only group. At the visit of best outcome visual acuity (10-week primary outcome or any subsequent 10-week examination), the difference between groups in amblyopic-eye visual acuity improvement (1.1 line) was greater than that found at the 10-week primary outcome examination (0.5 line). Nevertheless, the comparison of best outcome visual acuity is possibly biased because participants who did not improve 1 line

since randomization were not followed beyond the 10-week primary outcome examination. A comparison of best outcome visual acuity between treatment groups likely overestimates the true difference between groups because more participants were followed beyond 10 weeks in the plano lens group than in the atropine-only group, so this treatment group had more opportunity to show improvement. Therefore, we did not test for statistical significance of the difference between groups for this secondary outcome. Ideally, we would have followed all participants in both groups beyond 10 weeks, but this was not deemed to be feasible because it was unlikely that investigators and families would have been willing to continue atropine alone after using it for at least 22 weeks, with no improvement between 3 consecutive visits over 16 weeks.

Despite treatment with spectacles and atropine before and after randomization, most participants in both treatment groups had residual amblyopia at study completion. Only 14 participants (19%) achieved an amblyopic-eye visual acuity of 20/25 or better by study completion (e-Supplement 2, Table D). Nevertheless, this study was not designed to assess final visual acuity after an extended course of treatment, even though we followed participants at 10-week intervals until their visual acuity stopped improving by 1 line. It is likely that a longer duration of treatment would be necessary to achieve best possible visual acuity. In addition, our study population was a select cohort of children whose amblyopia had not resolved with spectacles and at least 12 weeks of atropine treatment. These children might have amblyopia that is particularly resistant to treatment, even when augmenting atropine with a plano lens.

Adding a plano lens to atropine in hyperopic children induces substantial blurring of the fellow eye, creating concern for reverse amblyopia. In a previous randomized trial of atropine with or without a plano lens as primary treatment of amblyopia, 2 children were treated for suspected reverse amblyopia.⁹ Kaye and colleagues¹⁴ found that 2 of 42 children treated with atropine plus a plano lens required treatment for reverse amblyopia. In the current study, no participant in the plano lens group experienced reverse amblyopia. However, we treated most study participants for a relatively short amount of time after randomization, so it is possible we would have observed more instances of reverse amblyopia if we had treated participants for longer periods of time.

In conclusion, when amblyopic-eye visual acuity stops improving in children who are treated with atropine in the fellow eye, our point estimate of a 0.5 line difference between groups suggests there may be a small benefit to adding a plano lens; however, it was not statistically significant. This treatment appears to be safe, and it may be a useful option for children who have difficulty wearing a patch and have stopped improving after a course of atropine alone. Whether atropine therapy is or is not augmented with a plano lens, some residual amblyopia remains in most cases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIG 1.

Flowchart showing study completion within each treatment group.

*One participant in the atropine only group did not complete the 10-week primary outcome examination within the analysis window (8–15 weeks after randomization) and therefore, the visual acuity examination was considered missed for the 10-week primary outcome analysis.

Table 1Baseline characteristics of all randomized participants according to treatment group^a

Characteristic	Atropine only (N = 40), n (%)	Atropine plus plano lens (N = 33), n (%)
Sex: female	22 (55)	19 (58)
Race/ethnicity		
White	33 (83)	29 (88)
African American	3 (8)	1 (3)
Hispanic	4 (10)	3 (9)
Age at randomization, years		
3 to <4	5 (13)	4 (12)
4 to <5	8 (20)	6 (18)
5 to <6	9 (23)	9 (27)
6 to <7	7 (18)	5 (15)
7 ^b	11 (28)	9 (27)
Mean $\pm$ SD	5.8 $\pm$ 1.5	5.8 $\pm$ 1.4
Duration of atropine treatment prior to randomization, weeks		
12 to <15	11 (28)	5 (15)
15 to <21	6 (15)	9 (27)
21 to <27	13 (33)	9 (27)
27 to 84	10 (25)	10 (30)
Mean $\pm$ SD	24.0 $\pm$ 11.2	26.4 $\pm$ 14.6
Cause of amblyopia		
Strabismus	9 (23)	13 (39)
Anisometropia	10 (25)	6 (18)
Strabismus and anisometropia	21 (53)	14 (42)
Distance VA in amblyopic eye at randomization		
20/160	2 (5)	1 (3)
20/125	2 (5)	2 (6)
20/100	5 (13)	1 (3)
20/80	2 (5)	6 (18)
20/63	9 (23)	8 (24)
20/50	7 (18)	8 (24)
20/40	11 (28)	6 (18)
20/32	2 (5)	1 (3)
LogMAR, mean $\pm$ SD [Snellen equivalent]	0.48 $\pm$ 0.19 [$\sim$ 20/63 ⁺¹]	0.48 $\pm$ 0.16 [$\sim$ 20/63 ⁺¹]
Distance VA in fellow eye at randomization		
20/32	5 (13)	6 (18)
20/25	13 (33)	9 (27)
20/20	16 (40)	13 (39)
20/16	6 (15)	5 (15)
LogMAR, mean $\pm$ SD [Snellen equivalent]	0.04 $\pm$ 0.09 [$\sim$ 20/20 ⁻²]	0.05 $\pm$ 0.10 [$\sim$ 20/20 ⁻²]
Interocular eye VA difference at randomization		

Characteristic	Atropine only (N = 40), n (%)	Atropine plus plano lens (N = 33), n (%)
LogMAR lines, mean $\pm$ SD	4.4 $\pm$ 1.8	4.4 $\pm$ 1.7
SE refractive error in amblyopic eye at enrollment, D		
0 to <+1.00	0 (0)	0 (0)
+1.00 to <+2.00	0 (0)	1 (3)
+2.00 to <+3.00	1 (3)	1 (3)
+3.00 to <+4.00	6 (15)	5 (15)
+4.00	33 (83)	26 (79)
Mean $\pm$ SD	5.73 $\pm$ 1.62	5.84 $\pm$ 1.89
SE refractive error in fellow eye at enrollment, D		
+1.50 to <+2.00	5 (13)	5 (15)
+2.00 to <+3.00	6 (15)	2 (6)
+3.00 to <+4.00	7 (18)	9 (27)
+4.00 D	22 (55)	17 (52)
Mean $\pm$ SD	3.95 $\pm$ 1.60	4.55 $\pm$ 2.28

D, diopter; *logMAR*, logarithm of the minimum angle of resolution; *SD*, standard deviation; *SE*, spherical equivalent; *VA*, visual acuity.

^aOf the 33 participants who were on atropine at enrollment, 3 had daily atropine administration (all randomized to the atropine-only group).

^bFour participants (2 in each group) were <8 years of age at time of enrollment into the run-in phase and 8 years old at time of randomization (8.0 and 8.1 in the atropine-only group, and 8.1 and 8.3 in the atropine-plus-plano-lens group).

Table 2

Amblyopic-eye visual acuity at 10-week primary outcome

	10-week Masked exam (8 to 15 weeks)	
	Atropine only (N = 39) n (%)	Atropine plus plano lens (N = 33) n (%)
Change in VA from randomization		
3 lines worse	0	0
2 lines worse	1 (3)	2 (6)
1 line worse	4 (10)	3 (9)
No change	14 (36)	6 (18)
1 line improved	12 (31)	13 (39)
2 lines improved	7 (18)	2 (6)
3 lines improved	1 (3)	7 (21)
Change in lines, mean $\pm$ SD	0.6 $\pm$ 1.1	1.1 $\pm$ 1.8
Distribution of VA		
20/200	0	1 (3)
20/160	2 (5)	0
20/125	1 (3)	2 (6)
20/100	4 (10)	0
20/80	5 (13)	4 (12)
20/63	3 (8)	4 (12)
20/50	6 (15)	6 (18)
20/40	11 (28)	4 (12)
20/32	3 (8)	6 (18)
20/25	3 (8)	5 (15)
20/20	1 (3)	1 (3)
20/16	0	0
LogMAR VA, mean $\pm$ SD [Snellen equivalent]	0.42 $\pm$ 0.22 [$\sim$ 20/50 ⁻¹]	0.37 $\pm$ 0.23 [$\sim$ 20/50 ⁺²]
Difference between treatment groups (2-sided 95% CI), logMAR lines [†]	+0.5 (−0.1 to +1.2)	
Interocular difference (lines) at 12-week exam		
0 line	3 (8)	2 (6)
1 line	2 (5)	2 (6)
2 lines	6 (15)	8 (24)
3 lines	6 (15)	8 (24)
4 lines	5 (13)	4 (12)
5 lines	5 (13)	5 (15)
6 lines	12 (31)	4 (12)
Mean lines $\pm$ SD	4.3 $\pm$ 2.6	3.3 $\pm$ 2.0

CI, confidence interval; logMAR, logarithm of the minimum angle of resolution; SD, standard deviation; VA, visual acuity.

One participant in the atropine only group did not complete the 10-week primary outcome exam within the analysis window (8–15 weeks after randomization) and is not included in the primary outcome analysis.

[†] Positive values favor the atropine plus plano lens group for the treatment comparison, adjusting for amblyopic-eye visual acuity at randomization.