Three-Year Follow-up of a Randomized Trial Comparing Focal/Grid Photocoagulation and Intravitreal Triamcinolone for Diabetic Macular Edema

*Diabetic Retinopathy Clinical Research Network (DRCR.net)**

Objective: To report 3-year outcomes of patients who participated in a randomized trial evaluating 1-mg and 4-mg doses of preservative-free intravitreal triamcinolone compared with focal/grid photocoagulation for treatment of diabetic macular edema.

Methods: Eyes with diabetic macular edema and visual acuities of 20/40 to 20/320 were randomly assigned to focal/grid photocoagulation or 1 mg or 4 mg of triamcinolone. At the conclusion of the trial, 3-year follow-up data were available in 306 eyes.

Results: Between 2 years (time of the primary outcome) and 3 years, more eyes improved than worsened in all 3 treatment groups. Change in visual acuity letter score from baseline to 3 years was +5 in the laser group and 0 in each triamcinolone group. The cumulative probability of cataract surgery by 3 years was 31%, 46%, and 83% in the laser and 1-mg and 4-mg triamcinolone groups, respectively. Intraocular pressure increased by more than 10 mm Hg at any visit in 4%, 18%, and 33% of eyes, respectively.

Conclusions: Results in a subset of randomized subjects who completed the 3-year follow-up are consistent with previously published 2-year results and do not indicate a long-term benefit of intravitreal triamcinolone relative to focal/grid photocoagulation in patients with diabetic macular edema similar to those studied in this clinical trial. Most eyes receiving 4 mg of triamcinolone as given in this study are likely to require cataract surgery.

Trial Registration: clinicaltrials.gov Identifier: NCT00367133

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MACULAR EDEMA IS A FREquent manifestation of diabetic retinopathy and an important cause of impaired vision in individuals with diabetes.[1-3] The Diabetic Retinopathy Clinical Research Network (DRCR.net) conducted a trial in 840 eyes of 693 subjects to evaluate intravitreal triamcinolone (1- and 4-mg doses) compared with focal/grid photocoagulation for the treatment of diabetic macular edema (DME).[4] The study found that there was an initial beneficial effect of 4 mg of triamcinolone on retinal thickening and visual acuity at 4 months compared with a 1-mg dose or with focal/grid photocoagulation. However, the benefit diminished thereafter, and at 2 years, mean visual acuity was better in the laser group than in either of the other 2 groups (comparing the laser and 1-mg groups, $P=.02$; comparing the laser and 4-mg groups, $P=.002$). Optical coherence tomography (OCT) results paralleled the visual acuity results. Both triamcinolone doses, especially the 4-mg dose, were associated with an increased incidence of elevated intraocular pressure and cataract surgery.[4]

Although the primary trial outcome was assessed at 2 years, a substantial number of eyes had 3-year follow-up data at the time the trial was stopped. These data provide the opportunity to evaluate change in visual acuity and retinal thickening between 2 and 3 years and to determine whether the treatment group differences seen after 2 years of follow-up were sustained at 3 years.

METHODS

Details of the protocol have been published[4,5] and the protocol is available on the DRCR.net Web site (http://www.drcr.net). Herein, we will summarize key aspects of the protocol that are pertinent to this article.

SUMMARY OF PROTOCOL

Eligible subjects were aged at least 18 years, had type 1 or 2 diabetes, and had at least 1 eye that met the following criteria: (1) best-corrected electronic Early Treatment Diabetic Retinopathy Study visual acuity letter score between 73 (approximately 20/40) and 24 (approximately 20/320), (2) definite retinal thickening due to DME that involved the center of the macula (assessed

*Members of the Writing Committee are listed at the end of this article.
Group Information: A list of the DRCR.net investigators and staff participating in this protocol was published in *Ophthalmology*. 2008;115(9):1447-1449.

Table 1. Baseline Characteristics Comparing Completers and Noncompleters

Characteristic	Completers (n=306 Eyes)	Noncompleters[a]	
		With Potential to Complete (n=69 Eyes)	Without Potential to Complete[b] (n=465 Eyes)
Treatment group, No. (%)			
Laser	115 (38)	28 (41)	187 (40)
1 mg of triamcinolone	93 (30)	23 (33)	140 (30)
4 mg of triamcinolone	98 (32)	18 (26)	138 (30)
Gender, women, No. (%)	144 (47)	24 (35)	243 (52)
Age, median (IQR), y	63 (58-69)	63 (56-67)	64 (57-70)
Race, No. (%)			
White	235 (77)	46 (67)	331 (71)
Black/African American	32 (10)	5 (7)	42 (9)
Hispanic	23 (8)	16 (23)	67 (14)
Asian	9 (3)	1 (1)	10 (2)
American Indian/Alaskan native	4 (1)	0	2 (<1)
Native Hawaiian/other Pacific islander	0	0	2 (<1)
Multiracial	0	0	2 (<1)
Unknown/not reported	3 (1)	1 (1)	9 (2)
Type 2 diabetes, No. (%)	293 (96)	64 (93)	445 (96)
Duration of diabetes, median (IQR), y	15 (9-21)	14 (10-19)	16 (10-22)
Hemoglobin A_{1c}, median (IQR)	7.4 (6.7-8.4)	8.1 (6.8-9.8)	7.6 (6.8-8.6)
Prior panretinal scatter photocoagulation, No. (%)	57 (19)	9 (13)	69 (15)
Prior photocoagulation for DME, No. (%)	198 (65)	44 (64)	268 (58)
IOP, median (IQR), mm Hg	15 (14-18)	15 (13-17)	16 (14-18)
Phakic lens at clinical examination, No. (%)	255 (83)	52 (75)	355 (76)
Electronic ETDRS visual acuity, letter score, median (IQR), approximate Snellen equivalent	62 (54-67), 20/63	61 (53-66), 20/63	62 (53-68), 20/63
Central subfield thickness on OCT, median (IQR), μm	398 (330-500)	422 (350-486)	400 (318-502)
Retinal volume on OCT, median (IQR), mm^3	9.0 (8.0-10.4)	9.4 (8.4-10.3)	8.9 (7.8-10.3)
Retinopathy severity level, ETDRS severity scale, No. (%)			
Microaneurysms, mild/moderate NPDR	46 (16)	9 (13)	106 (24)
Moderately severe/severe NPDR	172 (59)	34 (50)	223 (50)
Mild/moderate/high-risk PDR	76 (26)	25 (37)	119 (27)

Abbreviations: DME, diabetic macular edema; ETDRS, Early Treatment Diabetic Retinopathy Study; IOP, intraocular pressure; IQR, interquartile range; NPDR, nonproliferative diabetic retinopathy; OCT, optical coherence tomography; PDR, proliferative diabetic retinopathy.

[a] Those who did not complete the 3-year follow-up.

[b] Includes 51 subjects who died and 331 subjects who were randomized less than 34 months from the study close-out (70 who withdrew or were lost to follow-up and 261 who were active at the time of study close-out).

to be the main cause of visual loss), and (3) an OCT-measured retinal thickness of 250 μm or greater in the central subfield using a Stratus OCT (Carl Zeiss Meditec, Dublin, California).

Each study eye was randomly assigned to 1 of the 3 treatment groups: (1) focal/grid photocoagulation (referred to as the laser group), (2) 1 mg of intravitreal triamcinolone, or (3) 4 mg of intravitreal triamcinolone. Subjects with 2 study eyes had 1 assigned to the laser group and the other to 1 of the triamcinolone groups. For the study, triamcinolone was prepared without preservatives (1 mg or 4 mg) in a prefilled syringe (Allergan Inc, Irvine, California; 4 mg of triamcinolone, TRIVARIS; Allergan Inc). The focal/grid photocoagulation technique was modified from the original Early Treatment Diabetic Retinopathy Study protocol as described previously and used in prior DRCR.net protocols.[6]

Follow-up visits occurred every 4 months. Testing at each visit included measurement of best-corrected visual acuity using an electronic procedure based on the Early Treatment Diabetic Retinopathy Study method[7] and measurement of retinal thickness with OCT. At each visit, study eyes were evaluated for retreatment according to previously published guidelines.[4]

Fifty-one subjects (with 28, 18, and 16 study eyes in the laser, 1-mg triamcinolone, and 4-mg triamcinolone treatment groups, respectively) died within 3 years of entering the study. Among the remaining eyes without 3 years of follow-up, 159, 122, and 122, respectively, were from subjects who were enrolled less than 34 months (the beginning of the time window for the 3-year visit) from the close-out date of the trial and therefore did not have the ability to complete the 3-year visit. Thus, there was the potential for 3-year follow-up in 143 (43%), 116 (45%), and 116 (46%) of the randomized eyes in the laser, 1-mg triamcinolone, and 4-mg triamcinolone treatment groups, respectively. Among eyes with the potential to have 3-year follow-up, 3-year follow-up was completed in 115 eyes (80%) in the laser group, 93 eyes (80%) in the 1-mg triamcinolone group, and 98 eyes (84%) in the 4-mg triamcinolone group (referred to as *completers*). Follow-up was incomplete for the other eyes owing to subject withdrawal or loss to follow-up (referred to as *noncompleters*).

STATISTICAL ANALYSIS

Visual acuity was the primary outcome measure, with OCT-measured central retinal thickness a secondary outcome. Results were tabulated to assess consistency with those reported at the 2-year follow-up primary outcome. When statistical analyses were performed, they paralleled those reported in the 2-year analysis.[4] In addition, the cumulative probability of a cataract extraction was calculated for each treatment group using the

Table 2. Change in VA From 2 to 3 Years Stratified by 2-Year VA[a]

Characteristic	2-Year VA ≥74 (≥20/32)			2-Year VA <74 (<20/32)		
		Triamcinolone			Triamcinolone	
	Laser (n=26)	1 mg (n=13)	4 mg (n=24)	Laser (n=89)	1 mg (n=80)	4 mg (n=74)
Change in VA from 2- to 3-y examination, letter score						
Mean (SD)	–2 (8)	0 (6)	–4 (7)	2 (13)	3 (15)	4 (21)
Median (IQR)	–2 (–5 to 5)	2 (–3 to 3)	–2 (–7 to 1)	3 (–2 to 9)	2 (–4 to 12)	3 (–4 to 13)
Distribution of change, No. (%)						
≥15 Letters better	0	0	0	10 (11)	15 (19)	17 (23)
10-14 Letters better	0	0	0	11 (12)	6 (8)	3 (4)
5-9 Letters better	7 (27)	2 (15)	1 (4)	15 (17)	8 (10)	13 (18)
No change, ±4 letters	11 (42)	9 (69)	13 (54)	37 (42)	33 (41)	23 (31)
5-9 Letters worse	5 (19)	1 (8)	6 (25)	8 (9)	10 (13)	7 (9)
10-14 Letters worse	2 (8)	0	1 (4)	3 (3)	2 (3)	0
≥15 Letters worse	1 (4)	1 (8)	3 (13)	5 (6)	6 (8)	11 (15)

Abbreviations: IQR, interquartile range; VA, visual acuity.

[a] Includes only eyes with VA measurements at 2 and 3 years. Visits occurring between 609 and 852 days from randomization were used as completed 2-year visits. Visits occurring between 1035 and 1156 days from randomization were used as completed 3-year visits. When more than 1 visit occurred in either of these windows, data from the visit closest to the target date were used.

Kaplan-Meier product-limit method. Pairwise comparisons were made using a proportional hazards model, adjusted for the factors used to stratify the randomization (baseline visual acuity and prior macular photocoagulation) and accounting for correlation within subjects who had 2 study eyes with a robust sandwich estimate of the covariance matrix.[8] For subjects who did not complete the 3-year visit, visual acuity scores from visits completed earlier were compared with those from subjects who did complete the 3-year visit in a repeated-measures regression model, adjusted for a treatment group by time interaction and factors used to stratify the randomization (baseline visual acuity and prior macular photocoagulation).

RESULTS

Completers and noncompleters differed by racial/ethnic distribution, with a higher proportion of completers being white and a higher proportion of noncompleters (who had the potential to complete the study before it was closed) being Hispanic (**Table 1**). In all 3 treatment groups, baseline visual acuity was similar in completers and noncompleters. However, visual acuity during follow-up on average was about 4 letters worse in noncompleters (who had the potential for 3-year follow-up) through their last completed visit compared with completers ($P=.01$). Visual acuity during follow-up appeared to be similar in completers and the noncompleters who did not have the potential for 3-year follow-up ($P=.15$).

Among the eyes with 3-year follow-up, the mean number of treatments during the 3 years of follow-up were 3.1 in the laser group, 4.2 in the 1-mg triamcinolone group, and 4.1 in the 4-mg triamcinolone group. There were no cases of endophthalmitis following any of the 1898 injections during the entire study. During the third year of follow-up, 20 eyes in the laser group (17%), 22 eyes in the 1-mg triamcinolone group (24%), and 28 eyes in the 4-mg triamcinolone group (29%) were treated once with the assigned treatment regimen; 8 (7%), 9 (10%), and 21 (21%), respectively, were treated twice, and 1 (1%), 8 (9%), and 4 (4%), respectively, were treated 3 times.

Among the 3-year completers, 7 in the laser group (6%) received 4 mg of triamcinolone at some point during follow-up; 21 in the 1-mg triamcinolone group (23%) received focal/grid photocoagulation; and 20 in the 4-mg triamcinolone group (20%) received focal/grid photocoagulation. Other treatments for DME (primarily vitrectomy, nonstudy triamcinolone [Kenalog; Bristol-Myers Squibb, New York, New York], and bevacizumab) were used in 15 eyes (13%), 16 eyes (17%), and 11 eyes (11%) in the laser, 1-mg triamcinolone, and 4-mg triamcinolone treatment groups, respectively.

EFFECT OF TREATMENT ON VISUAL ACUITY

Between 2 and 3 years of follow-up, visual acuity improved more often than it worsened in all 3 treatment groups. Among eyes with visual acuity worse than 20/32 at 2 years, about twice as many in each treatment group improved by 10 or more letters than those that worsened by 10 or more letters from 2 to 3 years (**Table 2**).

At 3 years, visual acuity outcomes slightly favored the laser group compared with the 2 triamcinolone groups (**Table 3**), with the differences between groups at 3 years of similar magnitude as those at 2 years (**Figure 1**). The mean change in the visual acuity letter score from baseline to 3 years was +5 in the laser group and 0 in the 2 triamcinolone groups (mean difference adjusted for baseline visual acuity and prior macular photocoagulation: laser vs 1 mg of triamcinolone = +5.6 [95% confidence interval (CI), +0.8 to +10.4]; laser vs 4 mg of triamcinolone = +4.7 [95% CI, 0.0 to +9.5]; and 1 mg vs 4 mg of triamcinolone = –0.8 [95% CI, –6.0 to +4.3]). Using multiple imputation to handle missing data for eyes without 3-year follow-up, mean change in the letter score was +2, 0, and –1, in the laser, 1-mg triamcinolone, and 4-mg triamcinolone groups, respectively, and using the last-observation-carried-forward method, mean change in the letter score was +1, –1, and –2. For subjects with 2 study eyes, the mean paired difference in the change in the vi-

Table 3. Change in VA and Retinal Thickness From Baseline to 3 Years[a]

Characteristic	Laser	Triamcinolone 1 mg	Triamcinolone 4 mg
Change in VA from baseline to 3 y, letter score[b]			
Mean (SD)	5 (17)	0 (16)	0 (21)
Median (IQR)	8 (–2 to 15)	2 (–11 to 9)	4 (–8 to 14)
Distribution of VA change, No. (%)			
≥15 Letters better	30 (26)	19 (20)	21 (21)
10-14 Letters better	21 (18)	4 (4)	16 (16)
5-9 Letters better	21 (18)	16 (17)	9 (9)
No change, ±4 letters	24 (21)	21 (23)	24 (24)
5-9 Letters worse	5 (4)	9 (10)	6 (6)
10-14 Letters worse	5 (4)	8 (9)	6 (6)
≥15 Letters worse	9 (8)	16 (17)	16 (16)
Central subfield thickness on OCT, μm[c]			
At 3 y, median (IQR)	211 (175-271)	269 (210-388)	248 (195-342)
Change from baseline			
Mean (SD)	–175 (149)	–124 (184)	–126 (159)
Median (IQR)	–158 (–273 to –75)	–103 (–248 to 4)	–114 (–224 to –50)
<250 μm at 3 y, No. (%)	75 (68)	37 (43)	45 (51)
Change in retinal volume on OCT from baseline, mm^3[d]			
Mean (SD)	–2.0 (1.7)	–1.6 (2.1)	–0.7 (1.8)
Median (IQR)	–1.6 (–2.6 to –0.7)	–1.1 (–3.0 to –0.3)	–0.9 (–1.9 to 0.1)

Abbreviations: IQR, interquartile range; OCT, optical coherence tomography; VA, visual acuity.
[a]Visual acuity results include only eyes with baseline and 3-year VA measurements, and OCT results include only eyes with baseline and 3-year OCT measurements. Visits occurring between 1035 and 1156 days from randomization were used as completed 3-year visits. When more than 1 visit occurred in this window, data from the visit closest to the 3-year target date were used.
[b]Laser, n=115; 1 mg of triamcinolone, n=93; 4 mg of triamcinolone, n=98.
[c]Laser, n=111; 1 mg of triamcinolone, n=87; 4 mg of triamcinolone, n=89.
[d]Laser, n=54; 1 mg of triamcinolone, n=53; 4 mg of triamcinolone, n=51.

sual acuity letter score at 3 years was +9.3 (95% CI, +2.1 to +16.4) for those in both the laser and the 1-mg triamcinolone groups (n=29) and +4.6 (95% CI, –6.2 to +15.5) for those in both the laser and the 4-mg triamcinolone groups (n=27); in each case, the laser group was favored.

Among the completers of the 3-year visit, 51 in the laser group (44%), 23 in the 1-mg group (25%), and 37 in the 4-mg group (38%) had improved visual acuities of 10 or more letters from baseline to 3 years and 14 (12%), 24 (26%), and 22 (22%), respectively, had worsening of 10 or more letters. In comparison, from baseline to 2 years among the completers of the 3-year visit, 33%, 18%, and 32%, respectively, improved and 12%, 29%, and 27%, respectively, worsened.

Results of treatment group comparisons were similar when limited to eyes that were either pseudophakic or had minimal lens changes by clinician assessment at 3 years. The mean change in the visual acuity letter score from baseline to 3 years was +5 in the laser group (n=79), +2 in the 1-mg triamcinolone group (n=61), and 0 in the 4-mg triamcinolone group (n=90).

EFFECT OF TREATMENT ON RETINAL THICKENING

Similar to the visual acuity results, more eyes in all 3 treatment groups had a decrease in OCT central subfield thickness (compared with an increase) from year 2 to year 3 (**Table 4**). At 3 years, central subfield thickness was less than 250 μm in 75 eyes (67%) in the laser group, 37 eyes (43%) in the 1-mg triamcinolone group, and 45 eyes (51%) in the 4-mg triamcinolone group (Table 3).

GLAUCOMA AND CATARACT

Four eyes in the 4-mg triamcinolone group had a procedure for glaucoma prior to the 2-year visit (1 had laser trabeculoplasty and 3 had glaucoma surgery), but there were no additional cases of glaucoma surgery in any treatment group during the third year of follow-up. At 3 years, mean intraocular pressure was 16 mm Hg (standard deviation [SD], 3 mm Hg) in the laser group, 17 mm Hg (SD, 3 mm Hg) in the 1-mg triamcinolone group, and 16 mm Hg (SD, 4 mm Hg) in the 4-mg triamcinolone group, with 6 eyes (5%), 14 eyes (15%), and 10 eyes (10%), respectively, having an intraocular pressure greater than 21 mm Hg. Intraocular pressure–lowering medications were being used in 3 eyes (3%), 2 eyes (2%), and 12 eyes (12%) in the laser, 1-mg triamcinolone, and 4-mg triamcinolone groups, respectively. Among completers of the 3-year visit, an intraocular pressure increase of more than 10 mm Hg occurred at any visit between baseline and 2 years in 4 eyes in the laser group (3%), 16 in the 1-mg triamcinolone group (17%), and 30 in the 4-mg triamcinolone group (31%) and at any visit between baseline and 3 years in 4%, 18%, and 33% of eyes, respectively.

Among phakic eyes at baseline, the 3-year cumulative probability of cataract surgery was 31% in the laser group, 46% in the 1-mg triamcinolone group, and 83% in the 4-mg triamcinolone group ($P<.001$, for all pairwise comparisons). Excluding eyes in the laser group that

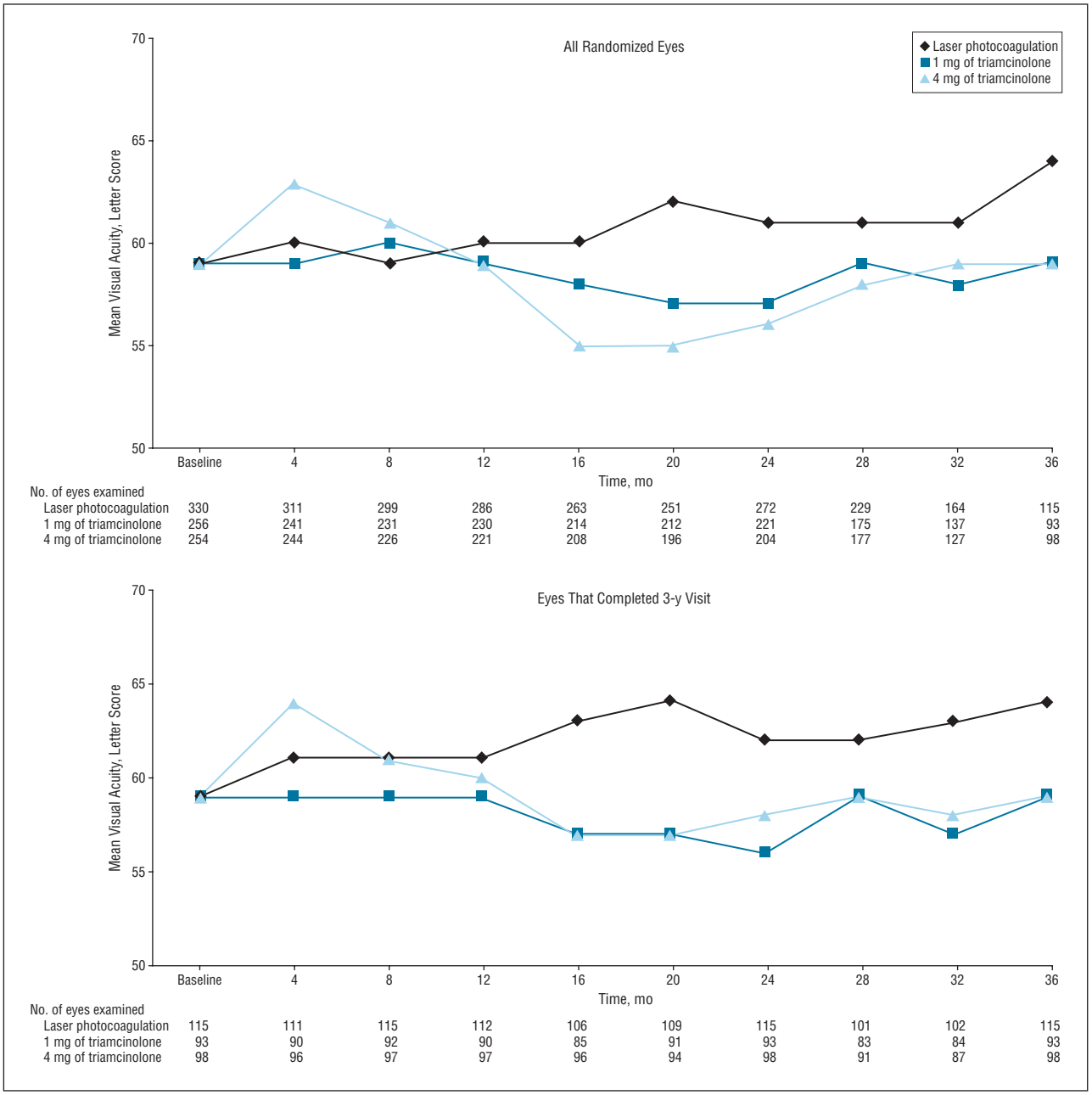

Figure 1. Mean visual acuity at each visit according to treatment group.

received triamcinolone, the cumulative probability was 27%. The timing of the cataract surgery is depicted in **Figure 2**.

COMMENT

In the subset of the originally randomized cohort with DME who completed a third year of follow-up, visual acuity improved more often than it worsened and residual macular edema tended to lessen. Treatment group differences seen at 2 years were in the same direction and of similar magnitude at 3 years, with a slight favor toward the laser group.

In the triamcinolone groups, intraocular pressure was generally in the normal range at 3 years, though a greater proportion of eyes in the 4-mg triamcinolone group were being treated with intraocular pressure–lowering medications. It is not known if the intraocular pressure in these eyes would be abnormally high if treatment were discontinued. Similar to the reported findings with corticosteroid implants,[9] most eyes treated with 4 mg of triamcinolone developed lens changes that required cataract surgery, with the 3-year cumulative probability estimated to be 83%.

An issue in interpreting these results is the completeness of follow-up. The cohort with 3-year follow-up was a subset (36%) of the total randomized cohort; a substantial number of subjects enrolled in the study less than 34 months (the open window for the 3-year visit) before the study close-out. Three-year follow-up was com-

Table 4. Change in Central Subfield Thickness From 2 to 3 Years Stratified by 2-Year Central Subfield Thickness[a]

Characteristic	No. (%)					
	2-y Central Subfield Thickness <250 µm			2-y Central Subfield Thickness ≥250 µm		
		Triamcinolone			Triamcinolone	
	Laser (n=61)	1 mg (n=27)	4 mg (n=31)	Laser (n=50)	1 mg (n=59)	4 mg (n=54)
<250 µm at 3 y	57 (93)	18 (67)	23 (74)	18 (36)	18 (31)	21 (39)
Change from 2- to 3-y visit, µm						
Mean (SD)	−3 (53)	12 (50)	27 (119)	−79 (115)	−44 (133)	−84 (164)
Median (IQR)	−10 (−26 to 3)	−2 (−26 to 41)	−3 (−24 to 30)	−77 (−155 to 2)	−45 (−91 to 32)	−53 (−145 to −7)
Decreased ≥10% and ≥25 µm	17 (28)	7 (26)	7 (23)	30 (60)	32 (54)	31 (57)
Decreased ≥20% and ≥50 µm	7 (7)	1 (4)	4 (13)	27 (54)	20 (34)	25 (46)
Increased ≥10% and ≥25 µm	5 (8)	9 (33)	8 (26)	8 (16)	14 (24)	10 (19)
Increased ≥20% and ≥50 µm	4 (7)	6 (22)	6 (19)	5 (10)	7 (12)	7 (13)

Abbreviation: IQR, interquartile range.

[a]Includes only eyes with optical coherence tomography measurements at 2 and 3 years. Visits occurring between 609 and 852 days from randomization were used as completed 2-year visits. Visits occurring between 1035 and 1156 days from randomization were used as completed 3-year visits. When more than 1 visit occurred in either of these windows, data from the visit closest to the target date were used.

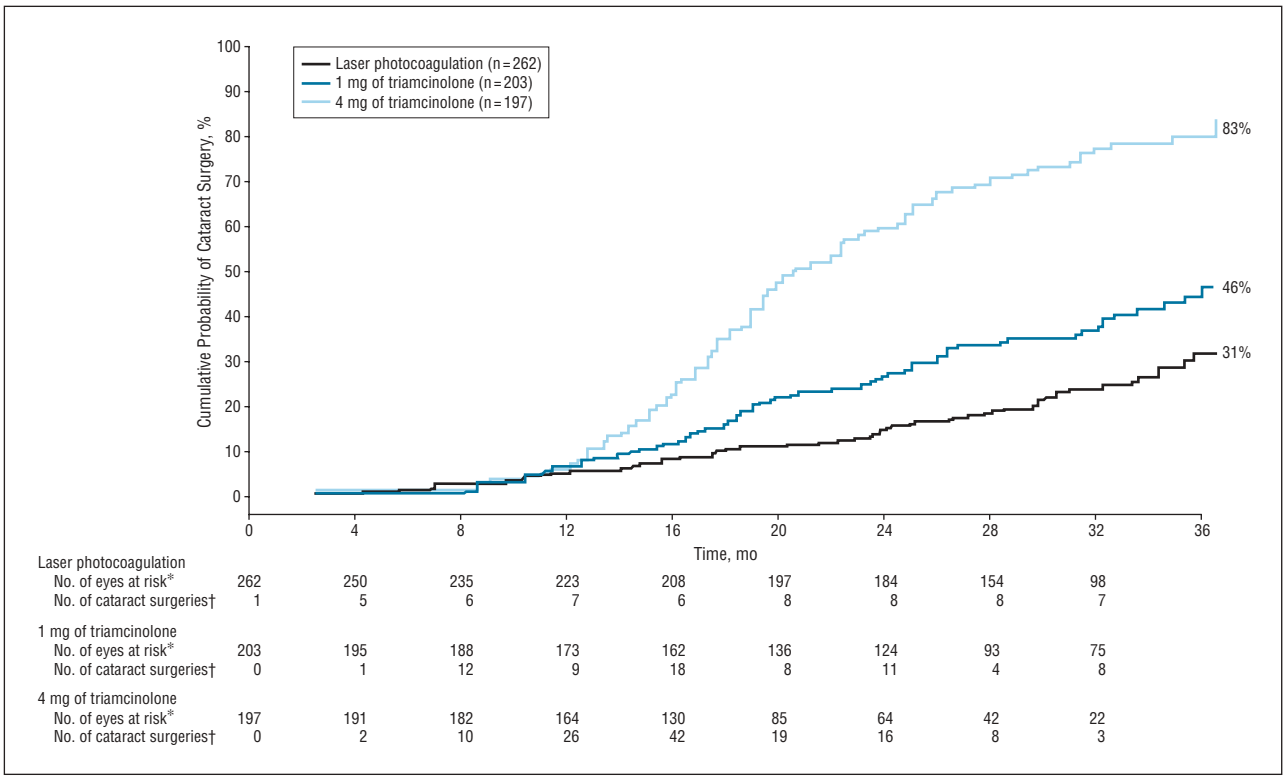

Figure 2. Cumulative probability of cataract surgery for all eyes that were phakic at baseline. *Number of eyes in follow-up at the start of the interval that had not previously had cataract surgery; †number of eyes having cataract surgery during the subsequent 4 months.

plete for only 80% of the subjects who did have the potential for 3 years of follow-up. However, the completion rate was similar among the 3 treatment groups. We evaluated the potential impact of incomplete follow-up on the results. It appears that the 3-year results likely slightly overestimate the amount of visual acuity improvement from baseline because visual acuity during follow-up tended to be slightly worse in those who did not complete the 3-year visit who had the potential (based on date of randomization) to do so compared with those who completed the 3-year visit. However, there was no indication that the treatment group comparisons were affected by the missing data. Analyses with imputation for missing data gave similar results to analyses of the completed 3-year examinations. In view of the smaller sample size than that which was present for the primary outcome analysis at 2 years, we emphasized determining whether the 3-year treatment group comparison results appeared to be consistent with the 2-year results rather than drawing conclusions based on statistical testing.

Our 3-year results, analyzed from a subset of the randomized subjects, are consistent with the previously published results after 2 years of follow-up. There was no long-term benefit of intravitreal triamcinolone relative to focal/grid photocoagulation for patients with DME receiving treatment as performed in this clinical trial. Rather, visual acuity outcomes slightly favored the laser group over either of the 2 triamcinolone groups. It appears that most eyes receiving this 4-mg triamcinolone preparation will require cataract surgery, though only a few will develop glaucoma that will require surgery.

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Financial Disclosure: A complete list of all DRCR.net investigator financial disclosures can be found at http://www.drcr.net. Dr Aiello has received compensation for travel and honoraria from and/or has served on the speakers' bureau for Allergan Inc; has consulted for and received compensation for travel and honoraria from and/or has served on the speakers' bureau for Eli Lilly; has consulted for Novartis; has stock ownership or options in Opko Health; has consulted for and received compensation for travel from Pfizer; and has served on the data monitoring board of a Thrombogenics study. Dr Bressler's work has been supported by research grants from Carl Zeiss, Genentech, Novartis, Emmes, Acucela, Notal Vision, Regeneron, Fovea Pharmaceuticals, Schering-Plough, Merck, Pfizer, Allergan Inc, Othera, Jerini, Bausch & Lomb; his spouse has consulted for Notal Vision, Genentech, Oxigene, Potentia, and Astra Zeneca; his spouse has received compensation for travel from Genentech; and his spouse has received honoraria from Pfizer. Dr Ferris is one of the inventors of a patent entitled "Nutritional supplement to treat macular degeneration" (No. 6,660,297), which was issued on December 9, 2003 and is owned by Bausch & Lomb. Dr Ferris has assigned his interest in the patent to the US government and receives government compensation. Dr Hartnett has consulted for Ophthalmic Research Associates. Dr Ip has consulted for Bausch & Lomb, Sirion Therapeutics, Genentech, and QLT; and his work has been supported by grants from Bausch & Lomb, Allergan Inc, and Neovista. Dr Kim's work has been supported by research grants from (OSI) Eyetech, Allergan Inc, Genentech, and Novartis; and she has consulted for Heidelberg.
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