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Green or Yellow Laser Treatment for Diabetic Macular Edema: Exploratory Assessment within the Diabetic Retinopathy Clinical Research Network

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Abstract

Purpose: Explore differences in green compared with yellow focal/grid laser treatment on functional and anatomic endpoints in eyes with diabetic macular edema.

Methods: Data from two randomized clinical trials were evaluated for differences in visual acuity (VA) and optical coherence tomography (OCT) parameters, eyes were assigned to sham injection+prompt laser, ranibizumab+prompt laser, or prompt laser only; among subgroups of eyes treated exclusively and electively with either green or yellow laser.

Results: In the sham injection+prompt laser group, the mean VA letter score change for eyes receiving green and yellow laser treatment, respectively, was $+2.4 \pm 14$ and $+5.1 \pm 13$ at the 52-week visit ($P = 0.06$), and $+2.4 \pm 15$ and $+6.0 \pm 13$ at the 104-week visit ($P = 0.13$), with no corresponding evidence of differences in OCT thickness. When comparing wavelength groups in the ranibizumab +prompt laser and prompt-laser only groups, meaningful differences in VA and OCT thickness were not detected at 1 or 2 years.

Conclusion: A trend towards improved vision outcome with yellow laser observed in one trial was not corroborated by anatomic outcomes or by the other trial. Without random assignment to different wavelengths controlling for bias and confounding, it is not possible to determine whether one wavelength is better than the other.

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*A published list of the Diabetic Retinopathy Clinical Research Network investigators and staff participating in this protocol can be found in *Ophthalmology* 2010;117:1064-1077.e35 with a current list available at www.drcr.net

Keywords

diabetic macular edema; laser photocoagulation; laser wavelength

Introduction

Focal/grid photocoagulation was the standard treatment for diabetic macular edema (DME) until the recent advent of anti-vascular endothelial growth factor therapy.^{1, 2} Intravitreal ranibizumab therapy with prompt or deferred (24 weeks) focal/grid laser treatment has been demonstrated to result in superior visual acuity outcomes as compared with sham injection plus focal/grid laser treatment, as have bevacizumab and aflibercept in smaller randomized clinical trials.³⁻⁶ However, new treatment paradigms are likely to continue to utilize photocoagulation in some circumstances. Initially, green laser was the predominant wavelength used for treating DME,¹ but advances in laser technology have led to a variety of available wavelengths that have been used in clinical studies or clinical practice.^{7, 8}

The effects of photocoagulation on a particular tissue depend on parameters related both to the laser itself and the target tissue. Pigments within target ocular tissues have differential absorption capacities for various wavelengths. The critical macular pigments that absorb light and their respective peak absorption spectra are xanthophylls (420-500 nm) within the neurosensory retina, melanin (400-1000 nm) within the retinal pigment epithelial cells and choroidal melanocytes, and hemoglobin (450 to 550 nm) within red blood cells contained within the retinal and choroidal vessels or within areas of extravasated blood.⁹ Both green (495-570 nm)¹⁰ and yellow (570-590 nm) wavelengths are absorbed by melanin and hemoglobin, which makes each wavelength suitable for use in photocoagulation of macular disorders. Blue and blue-green wavelengths were abandoned due to the inherent negative attributes of blue light absorption by the crystalline lens (attenuating laser delivery to the retina) and macular xanthophyll pigment absorption (enhancing destruction of the inner retinal layers).¹¹⁻¹³ Theoretically, longer monochromatic green, yellow, and red wavelengths provide successively better penetrance of the nuclear sclerotic lens and decreased absorption by xanthophylls.

Although relatively close in the spectral wavelength to green laser (argon, 514.5 nm; krypton, 530.9 nm; PASCAL and diode, 532 nm), yellow laser (krypton, 568 nm; dye and diode, 577 nm)¹⁴ may offer some theoretical advantages. The “slightly” longer wavelength of yellow laser results in less scatter by ocular structures (such as nuclear sclerotic lenses) and deeper penetration to vascular and pigmented structures than the green wavelength.^{15, 16} In keeping with this hypothesis, yellow laser has been shown to require less power on average than green laser to achieve similar retinal burns during retinal photocoagulation for diabetic retinopathy.¹⁷ Furthermore, data from animal studies suggest that yellow laser may be more effective in producing occlusion of retinal vessels in comparison to green laser.¹⁸ Despite the theoretical benefits of yellow laser, it is the green wavelength that is more commonly used in the Diabetic Retinopathy Clinical Research Network (DRCR.net) (unpublished data). This may be explained partially by the relatively similar action of the

two laser wavelengths, perceptions that clinical outcomes are the same, and a history of higher cost associated with lasers supplying yellow wavelengths.¹⁵

Studies reporting clinical differences between green and yellow laser wavelength as applied in posterior segment disorders are limited. Available observational¹⁹ or experimental²⁰ studies have included relatively small numbers of participants, and reported on few outcomes, mainly visual acuity and change in thickness of macular edema. In this article we explore the effect of green or yellow laser wavelengths on several functional and anatomic outcomes using data collected from participants in two large [DRCR.net](http://www.drcr.net) DME clinical trials.

Methods

Data utilized for this analysis were obtained during performance of two multi-center randomized trials conducted by the [DRCR.net](http://www.drcr.net). The Intravitreal Ranibizumab or Triamcinolone Acetonide in Combination with Laser Photocoagulation for Diabetic Macular Edema Trial (LRT-DME),² evaluated ranibizumab plus prompt or deferred (24 weeks) laser treatment or triamcinolone plus prompt laser treatment with laser treatment alone for center-involved DME that caused vision impairment. Data from the sham + prompt laser, and ranibizumab+prompt laser arms are included in the current study. Data from the ranibizumab + deferred laser group are not included because the majority of eyes in this group did not receive laser. Furthermore, data from the triamcinolone + prompt laser group are not reported due to the confounding effects of progressive cataract and cataract surgery on visual outcomes in this group. The second trial reviewed, a Randomized Trial Comparing Intravitreal Triamcinolone Acetonide and Laser Photocoagulation for Diabetic Macular Edema (IVT),²¹ evaluated the long term effects of intravitreal triamcinolone versus focal/grid laser photocoagulation for center-involved DME that caused vision impairment. Only data from the laser arm were included in the current study. Both study protocols are available at the [DRCR.net](http://www.drcr.net) website (www.drcr.net [accessed: August 28, 2012]). Key aspects of both protocols pertinent to this article are summarized below.

Major eligibility criteria for participation in the two trials included: 1) best-corrected Electronic-Early Treatment Diabetic Retinopathy Study²² (E-ETDRS Visual Acuity Test) visual acuity letter score 78 to 24 (Snellen visual acuity equivalent of 20/32-20/320) in the LRT-DME, and between 73 to 24 (Snellen equivalent of 20/40-20/320) in the IVT study, 2) definite retinal thickening from DME involving the fovea on clinical exam as the cause of vision loss, and 3) central subfield (CSF) thickness ≥ 250 μm on time domain optical coherence tomography (OCT) (Stratus OCT3, Carl Zeiss Meditec, Dublin, CA).

Focal/grid photocoagulation in both trials followed the [DRCR.net](http://www.drcr.net) procedures for treating DME. Details of the procedure, minimally modified from the ETDRS original technique of photocoagulation,¹ have been reported previously.²¹ Investigators were required to use green or yellow wavelength; however, the specific selection was at investigator discretion. The required spot size was 50 μm , although 60 μm was permitted when using a PASCAL laser²³ and 75 μm was permitted when using a diode laser. Direct (focal) treatment of all leaking microaneurysms within areas of retinal thickening, lying between 500 and 3000 μm from the fovea, and grid application to all remaining areas of retinal thickening, not

associated with microaneurysms within the same zone, was recommended. Retreatment with focal/grid laser in the LRT-DME study could occur as frequently as every 13 weeks provided that central-involved DME or edema threatening the fovea was present and as long as “complete” focal/grid laser had not already been given. Retreatment in the IVT study was given at each of the 16-week protocol visits, unless there was little or no edema involving the center of macula and there was an OCT CSF thickness of 225 μm or less, visual acuity letter score of 70 or higher (Snellen equivalent 20/25 or better), 50% or more reduction in OCT CSF thickness from last treatment, clinically significant adverse effect from last treatment, or there were no areas identified for which additional treatment was indicated. Stratus OCT 3 was used to calculate mean CSF thickness and retinal volume from fast macular scans at study entry and at all annual visits.

An eye was considered to have received only green or only yellow laser treatment if it had exclusively received that laser color at each treatment encounter (‘pure groups’). If an eye had received laser treatment with each of the wavelengths at different treatment sessions, it was classified as having received both green and yellow.

One-way analysis of covariance was used to compare change in E-ETDRS visual acuity letter scores, OCT-derived CSF retinal thickness, and retinal volume measurements from baseline to the 52-week (‘1-year’) and 104-week (‘2-year’) follow-up visits, in eyes that received only green wavelength with those that received only yellow wavelength, adjusting for the baseline value. Analyses also adjusted for potential confounding baseline factors, including age, level of hemoglobin A_{1c}, prior treatment for DME, level of diabetic retinopathy ascertained by reading center review of 7-field fundus photographs, and lens status (phakic or non-phakic). There were too few investigators who treated eyes in both the pure green group and the pure yellow group to adjust analyses for possible investigator effects. In the LRT-DME study, only 2 of 87 investigators managing eyes in the sham + prompt laser group and 0 of 65 investigators managing eyes in the ranibizumab + prompt laser group treated eyes in both wavelength groups. Similarly in the IVT-study, 89 investigators managed study eyes with only green laser, and 35 used only yellow laser in some eyes; however, only one investigator had patients in both groups. The reported *P* values for visual acuity change were obtained after the data were transformed to Van der Waerden normal scores. Poisson regression analysis was used to compare the number of laser treatments administered in the two ‘pure’ wavelength groups. All reported *P* values are two sided. All statistical analyses were conducted using SAS 9.3 (SAS Institution Inc., Cary, NC).

Results

LRT-DME Study

Prior to the change in treatment protocol that allowed all eyes to be treated with ranibizumab, of 284 eyes randomly assigned to the sham + prompt laser group, 268 (94%), and 210 (74%) eyes had available data on laser color and completed the one and two-year visits, respectively. Similarly, of 180 eyes assigned to the ranibizumab + prompt laser group, 165 (92%), and 156 (87%) eyes had available data from the 1 and 2 year visits, respectively (Table 1).

In the sham injection + prompt laser group, 66% and 62% of eyes received only green laser treatment through the first and second year visits, respectively, whereas 21% and 20% received only yellow laser through the first and second year visits. At study entry, the mean visual acuity letter score (Snellen equivalent) was 63 (20/63) $\pm$ 12 in the green group and 65 (20/50) $\pm$ 9 in the yellow group. The average improvement in visual acuity letter score from baseline to the 1 year visit in the green laser group was +2.4 $\pm$ 14 compared with +5.1 $\pm$ 13 in the yellow laser group (difference = -3.4 letters, 95% CI: -7.6 to +0.8, P = 0.06). At the 2 year visit, the difference in mean change in visual acuity with green compared to yellow was -3.5 letters (95% CI: -8.6 to +1.7, P = 0.13, Table 1).

The average baseline OCT CSF thickness and volume was 425 μ m and 9.0 mm³ in the green only group compared with 427 μ m and 9.2 mm³ for the yellow only group. Mean change from baseline in CSF and retinal volume appeared similar between the eyes that received green laser treatment compared with eyes that received yellow laser treatment, both at the 1 and 2 year visits (Table 1). Eyes that received green laser treatment only appear to have undergone fewer laser treatment sessions by the end of the second year (mean 3.4 $\pm$ 1.6) than those that received yellow laser exclusively (mean 4.0 $\pm$ 2.2) (Table 1, P = 0.06).

Among the eyes allocated to ranibizumab + prompt laser treatment, 72% received green laser only throughout two years of follow-up; 21% of eyes received yellow laser only throughout the first two years. In this cohort, baseline visual acuity measured four letters worse on average in the green only eyes as compared with yellow only eyes. A similar trend was noticed in the baseline CSF thickness where, on average, green only eyes were 20 μ m thicker than yellow only eyes. No major difference in baseline levels of retinal volume were identified between the eyes that received treatment purely with one wavelength vs. the other. A difference in change in visual acuity at either the 1 or 2 year visit was not identified when comparing the two laser wavelength groups in the ranibizumab + prompt laser arm (mean visual acuity changes from baseline for green only and yellow only laser groups were +8.2 $\pm$ 12 and +7.6 $\pm$ 9, respectively, (P = 0.86) at the 1-year visit, and +6.5 $\pm$ 14 and +7.5 $\pm$ 10 (P = 0.61) at the 2-year visit. Results also were similar for changes in CSF and retinal volume (Table 2). By the end of the second year of treatment, eyes managed exclusively with green laser received fewer treatment sessions (mean 2.6 $\pm$ 1.5) than those that received exclusively yellow laser (mean 3.4 $\pm$ 1.7) (P = 0.02).

In the green only laser group through the first year, 22% and 24% of the eyes in the sham + prompt laser and ranibizumab + prompt laser groups, respectively, received at least 1 session of PASCAL laser. Results were similar when the analyses were performed excluding eyes that had at least 1 PASCAL laser sitting.

IVT Study

For 330 eyes randomized to receive focal/grid laser photocoagulation in the IVT study, complete wavelength and outcome data were available for 287 (87%) and 272 (82%) for the 1 and 2-year visits, respectively (Table 2). The majority of eyes received green laser only through 1 year (68%) and 2 years (68%), with 25% and 21% receiving yellow laser only through 1 and 2 years, respectively. Baseline visual acuity and OCT parameters appeared similar between the green only and yellow only groups (Table 2). The mean change in visual

acuity letter score in the green only group at 1 year was $+0.8 \pm 16$ while that of the yellow only group was 0 ± 15 ($P = 0.70$). There was no difference between the laser wavelength groups in the mean change in OCT CSF thickness, mean change in OCT total retinal volume, or number of laser sessions through 1 and 2 years (Table 2). In the green only eyes, 1 and 6 eyes received at least one PASCAL session through 1 and 2 years respectively. Results appeared similar when these eyes were not included in the analysis.

Discussion

Although there may be theoretic reasons to believe that various laser wavelengths may offer unique advantages to manage macular disease, there is little information in human eyes to support this in regard to clinical outcomes. Only one study²⁰ randomly assigned 85 individuals with DME to the two competing wavelengths of green and yellow. At one year, vision improvement, defined as 2 or more lines of visual acuity improvement, was seen in 19% and 26% of eyes that received argon green and dye yellow respectively ($P > 0.05$). As the focus of this study may have been the evaluation of anatomic effects of the laser wavelengths on macular edema it is unclear whether there was sufficient statistical power to address the question of vision benefit with one wavelength or another. Reductions in macular edema were seen in about 70% of each group as assessed subjectively by slit-lamp exam and leakage on fluorescein angiography. This previous clinical observation is consistent with our result which is based on objective quantitative information provided by OCT imaging. In addition, in a retrospective case-control study¹⁹, no difference was identified in logMAR visual acuity outcomes at 6 months between eyes that received green and yellow laser. Given the paucity of clinical information comparing outcomes with green and yellow laser, the DRCR.net performed an exploratory analysis of functional and anatomic outcomes in DME eyes that were monitored prospectively while managed with laser alone ($\pm$ sham injection) or laser in conjunction with ranibizumab in two trials performed by the DRCR.net. The individual study protocols did not assign eyes randomly to a particular wavelength; rather, the choice to use green or yellow was at the discretion of the treating physician. Among the three intervention arms available for review, each with standardized measures of visual acuity, and OCT data to evaluate changes in retinal thickness, there were a total of 492 eyes and 160 eyes exclusively managed with green or yellow laser, respectively, with one year outcomes.

In only one of the three comparisons, the sham + prompt laser arm of the LRT-DME trial, was there a suggestion of a difference in change in visual acuity by the yellow laser wavelength. None of the results were judged to be different with great confidence, particularly since the trials were not designed to address this question and the trials did not incorporate random allocation to one wavelength or another. While effort was made to adjust the analyses for potential confounding variables that might affect the outcomes evaluated there are likely other confounding factors that may be unknown or unmeasured that may be influencing these results. As such, it is difficult or impossible to adjust for all potential confounding variables, including differences in the number of treatment sessions, laser spot size, and potential differences between treating ophthalmologists. Furthermore, there were no anatomical differences seen between green vs. yellow in all three intervention arms.

Current data suggest that it is unlikely that there are large clinical differences related to wavelength choice. In the present era of anti-VEGF agents and with other pharmaceutical products actively under investigation for the management of diabetic macular edema, it is unlikely that an adequately-sized randomized clinical trial of different wavelengths will be performed. Treating physicians likely will continue to select the laser wavelength that they have available and are comfortable using. The results of this exploratory analysis by the [DRCR.net](http://www.drcr.net) do not suggest that alterations to this practice are needed.

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Summary Statement

An exploratory assessment of visual acuity and OCT outcomes in eyes with diabetic macular edema, treated with green or yellow laser, did not show consistent differences favoring one wavelength over another. These results may be due to factors other than wavelength, especially considering that wavelength assignment was not randomly allocated.

Table 1

Visual Acuity And OCT Outcomes By Laser Wavelength In The LRT-DME Study

	Sham + Prompt Laser			Ranibizumab + Prompt Laser		
		Green	Yellow		Green	Yellow
Proportion of eyes with laser wavelength						
Through 1 year [†]	N = 268	178 (66%)	55 (21%)	N = 165	119 (72%)	34 (21%)
Through 2 years [†]	N = 210	131 (62%)	43 (20%)	N = 156	113 (72%)	32 (21%)
Visual Acuity (ETDRS letter score)						
<i>Baseline</i>						
N		178	55		119	34
Mean (SD) [Snellen Equivalent]		63 (12) [20/63]	65 (9) [20/50]		62 (13) [20/63]	66 (9) [20/50]
Median (Q1,Q3) [Snellen Equivalent]		66 (55,73) [20/50 (20/80, 20/40)]	65 (59,73) [20/50 (20/63,20/40)]		65 (53,73) [20/50 (20/100,20/40)]	67 (60,72) [20/50 (20/63,20/40)]
<i>Change from Baseline to 1 year</i>						
N		178	55		119	34
Mean (SD)		+2.4 (14)	+5.1 (13)		+8.2 (12)	+7.6 (9)
Median (Q1,Q3)		+4.5 (−3.0,+10.0)	+7.0 (+1.0,+12.0)		+9 (+2,+15)	+8 (+2,+12)
Difference in mean change from Yellow (95% CI) [P value] [*]		−3.4 (−7.6 to +0.8) [P=0.06]			−1.3 (−5.8 to +3.2) [P=0.86]	
<i>Change from Baseline to 2 year</i>						
N		131	43		113	32
Mean (SD)		+2.4 (15)	+6.0 (13)		+6.5 (14)	+7.5 (10)
Median (Q1,Q3)		+6.0 (−3.0,+11.0)	+8.0 (0,+15.0)		+8.0 (+2,+15)	+7.0 (+3,+13)
Difference in mean change from Yellow (95% CI) [P value] [*]		−3.5 (−8.6 to +1.7) [P=0.13]			−1.8 (−7.2 to +3.6) [P=0.61]	
OCT Central Subfield Thickness μm						
<i>Baseline</i>						
N		178	55		119	34
Mean (SD)		425 (139)	427 (123)		401 (126)	380 (132)
Median (Q1,Q3)		408 (307,503)	411 (322,535)		374 (312,461)	336 (264,480)
<i>Change from Baseline to 1 year</i>						
N		175	55		119	34
Mean (SD)		−108 (149)	−93 (145)		−137 (132)	−117 (119)
Median (Q1,Q3)		−82 (−194,−9)	−74 (−175,0)		−115 (−199,−53)	−107 (−210,−15)
Difference in mean change from Yellow (95% CI) [P value] [*]		−17 (−56 to +22) [P=0.39]			−22 (−73 to +29) [P=0.39]	
<i>Change from Baseline to 2 years</i>						
N		129	42		109	32
Mean (SD)		−135 (143)	−139 (145)		−147 (158)	−111 (138)

	Sham + Prompt Laser		Ranibizumab + Prompt Laser	
	Green	Yellow	Green	Yellow
Median (Q1,Q3)	-109 (-222,-34)	-138 (-245,-47)	-116 (-221,-62)	-73 (-183,-14)
Difference in mean change from Yellow (95% CI) [P value] [*]	+6.4 (-33 to 46) [P=0.75]		-23 (-60 to +13) [P=0.21]	
Retinal Volume mm³				
<i>Baseline</i> [‡]				
N	135	46	88	25
Mean (SD)	9.0 (1.7)	9.2 (1.7)	8.7 (1.7)	9.0 (1.9)
Median (Q1,Q3)	8.5 (7.7,9.7)	8.9 (7.8,10.0)	8.5 (7.5,9.7)	8.3 (7.7,10.4)
<i>Change from Baseline to 1 year</i>				
N	124	39	80	24
Mean (SD)	-1.0 (1.4)	-0.7 (1.1)	-1.4 (1.3)	-1.6 (1.8)
Median (Q1,Q3)	-0.6 (-1.7,-0.2)	-0.4 (-1.1,-0.1)	-1.2 (-2.1,-0.6)	-1.0 (-2.0,-0.6)
Difference in mean change from Yellow (95% CI) [P value] [*]	-0.3 (-0.7 to +0.1) [P=0.13]		-0.45 (-1.2 to +0.3) [P=0.24]	
<i>Change from Baseline to 2 years</i>				
N	92	33	71	20
Mean (SD)	-1.2 (1.2)	-1.2 (1.7)	-1.5 (1.4)	-1.6 (1.7)
Median (Q1,Q3)	-0.9 (-1.7,-0.5)	-1 (-1.7,-0.1)	-1.4 (-2.2,-0.6)	-1.0 (-2.6,-0.5)
Difference in mean change from Yellow (95% CI) [P value] [*]	-0.1 (-0.6 to +0.3) [P=0.52]		-0.4 (-0.9 to +0.1) [P=0.13]	
Laser Treatment Sessions				
<i>Laser Treatment through 1 year</i>				
Mean (SD)	2.7 (1.0)	2.9 (1.1)	2.1 (1.0)	2.5 (1.0)
Median (Q1,Q3)	3 (2,4)	3 (2,4)	2 (1,3)	3 (2,3)
P value [§]	0.42		0.26	
<i>Laser Treatment through 2 years</i>				
Mean (SD)	3.4 (1.6)	4.0 (2.2)	2.6 (1.5)	3.4 (1.7)
Median (Q1,Q3)	3 (2,4)	3 (2, 7)	2 (1,4)	3 (2,4)
P value [§]	0.06		0.02	

LRT-DME = Intravitreal Ranibizumab or Triamcinolone Acetonide in Combination with Laser Photocoagulation for Diabetic Macular Edema Trial; ETDRS = Early Treatment Diabetic Retinopathy Study; SD = Standard Deviation; OCT = Optical Coherence Tomography; CSF = Central Subfield

[‡] Counts of eyes that received *both* green and yellow laser at any point are as follows through 1 year and 2 years respectively: sham + prompt laser [35 (13%), 36 (17%)], ranibizumab + prompt laser (12 [7%], 11 [7%]).

^{*} Estimates of difference in means and P values from analysis of covariance model comparing the mean change of Green to Yellow, with adjustment for the following baseline factors: visual acuity in the vision analyses, and OCT CSF in the OCT central subfield thickness analyses, retinal volume in the retinal volume analysis and age, Hemoglobin A1c, history of DME treatment, diabetic retinopathy level, and lens status.

[‡] Cannot be graded in 43, 9 in green and yellow respectively in sham group; and in 31 and 9 in green and yellow respectively in ranibizumab group.

[§] P value from Poisson regression model.

Table 2

Visual Acuity and Optical Coherence Tomography Outcomes By Laser Wavelength In The IVT Study

		Laser	
		Green	Yellow
Proportion of eyes with laser wavelength			
Through 1 year [†]	N = 287	195 (68%)	71 (25%)
Through 2 years [†]	N = 272	185 (68%)	56 (21%)
Visual Acuity (ETDRS letter score)			
<i>Baseline</i>			
N		195	71
Mean (SD) [Snellen Equivalent]		59 (11) [20/63]	59 (10) [20/63]
Median (Q1,Q3) [Snellen Equivalent]		62 (54, 67) [20/63 (20/80-20/50)]	62 (53, 67) [20/63 (20/100, 20/50)]
<i>Change from Baseline to 1 year</i>			
N		194	71
Mean (SD)		+0.8 (16)	0.0 (15)
Median (Q1,Q3)		+3.0 (−6.0, +11.0)	+2.0 (−3.0, +9.0)
Difference in mean change from Yellow (95% CI) [P value] [*]		+0.5 (−4.5 to +5.4) [P=0.70]	
<i>Change from Baseline to 2 year</i>			
N		185	56
Mean (SD)		+1.5 (16)	+2.6 (20)
Median (Q1,Q3)		+4 (−6, +13)	+7 (−3, +13)
Difference in mean change from Yellow (95% CI) [P value] [*]		−2.3 (−7.7 to +3.0) [P=0.36]	
OCT Central Subfield Thickness			
<i>Baseline</i>			
N		194	71
Mean (SD)		421 (131)	418 (130)
Median (Q1,Q3)		402 (325, 490)	387 (323, 471)
<i>Change from Baseline to 1 year</i>			
N		188	70
Mean (SD)		−106 (145)	−89 (143)
Median (Q1,Q3)		−82 (−187, −14)	−109 (−157, −15)
Difference in mean change from Yellow (95% CI) [P value] [*]		−12 (−51 to +26) [P=0.52]	
<i>Change from Baseline to 2 years</i>			
N		178	54
Mean (SD)		−143 (150)	−133 (138)
Median (Q1,Q3)		−132 (−223, −50)	−127 (−201, −45)
Difference in mean change from Yellow (95% CI) [P value] [*]		+7.0 (−31 to +45) [P=0.71]	
Retinal Volume			

	Laser	
	Green	Yellow
<i>Baseline</i> [†]		
N	164	65
Mean (SD)	9.5 (2.0)	9.2 (1.9)
Median (Q1,Q3)	9.4 (7.9, 10.7)	8.5 (7.9, 10.0)
<i>Change from Baseline to 1 year</i>		
N	127	49
Mean (SD)	-1.0 (1.6)	-0.7 (1.2)
Median (Q1,Q3)	-0.6 (-1.8, -0.1)	-0.5 (-1.3, -0.1)
Difference in mean change from Yellow (95% CI) [P value] [*]	-0.1 (-0.7 to +0.4) [P = 0.63]	
<i>Change from Baseline to 2 years</i>		
N	102	43
Mean (SD)	-1.5 (1.7)	-1.2 (1.6)
Median (Q1,Q3)	-1.2 (-2.4, -0.4)	-0.7 (-1.8, -0.4)
Difference in mean change from Yellow (95% CI) [P value] [*]	+0.2 (-0.2 to +0.6) [P = 0.29]	
Laser Treatment		
<i>Laser Treatment through 1 year</i>		
Mean (SD)	2.1 (0.8)	2.1 (0.8)
Median (Q1,Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)
P value [§]	0.78	
<i>Laser Treatment through 2 years</i>		
Mean (SD)	2.9 (1.4)	2.7 (1.4)
Median (Q1,Q3)	3.0 (2.0, 4.0)	2.0 (1.5, 3.0)
P value [§]	0.34	

IVT = Randomized Trial Comparing Intravitreal Triamcinolone Acetonide and Laser Photocoagulation for Diabetic Macular Edema; ETDRS = Early Treatment Diabetic Retinopathy Study; SD = Standard Deviation; OCT = Optical Coherence Tomography; CSF = Central Subfield

[†] Counts of eyes that received *both* green and yellow laser (data not included) are as follows through 1 year and 2 years respectively: 21 (7%) and 31 (11%).

^{*} Estimates of difference in means and *P* values from analysis of covariance model comparing the mean change of Green to Yellow, with adjustment for the following baseline factors: visual acuity in the vision analyses, and OCT CSF in the OCT central subfield thickness analyses, retinal volume in the retinal volume analysis and age, Hemoglobin A1c, history of DME treatment, diabetic retinopathy level, and lens status.

[†] Cannot be graded in 31 and 6 in green and yellow group respectively.

[§] *P* value from Poisson regression model.