Published in final edited form as:

Am J Ophthalmol. 2014 May ; 157(5): 1048–1055. doi:10.1016/j.ajo.2014.01.020.

Epiretinal membranes in uveitic macular edema: Effect on vision and response to therapy

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Abstract

Purpose—To evaluate the effects of epiretinal membranes on the response of uveitic macular edema to therapy and on visual acuity outcomes.

Design—Retrospective case series.

Methods—104 eyes of 77 patients with uveitic macular edema were identified at a tertiary care center. Epiretinal membranes were diagnosed when identified by two investigators' grading of spectral-domain optical coherence tomography and scored for the presence or absence of surface wrinkling. Outcomes included best corrected visual acuity, central subfield thickness, and rates of macular edema improvement (>20% reduction in central subfield thickness) and resolution (reduction of central subfield thickness to <315 μ m) at 3 and 6 months follow-up.

Results—72 eyes of 59 patients had an epiretinal membrane on presentation. Eyes without epiretinal membranes and with epiretinal membranes without surface wrinkling were not

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Financial Disclosures: Brian Lehpamer: none; Erin Moshier: none; Patricia Pahk: none; Naomi Goldberg: none; Jessica Ackert: none; James Godbold: none; Douglas A. Jabs: Abbott Laboratories, Applied Genetic Technologies Corporation (AGTC), Alcon Laboratories, Corcept Therapeutics, Genentech, Inc., Genzyme Corporation, GlaxoSmithKline, Novartis Pharmaceutical Corp., Regeneron, and Santen Pharmaceuticals.

Contributions to Authors: Design of the study: (DAJ); Conduct of the study: (BL, PP, NG, JA, DAJ); Collection of the data (BL, PP); Management of the data: (BL); Analysis of the data (BL, EM, PP, DAJ); Interpretation of the data: (BL, EM, PP, DAJ); Preparation of the manuscript: (BL, PP, JG); Review of the manuscript (JG, PP, NG, JA, DAJ); Approval of the manuscript (BL, EM, PP, JG, JA, JG DAJ).

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significantly different at presentation or at 3 and 6 months follow-up. Conversely, eyes with an epiretinal membrane with retinal surface wrinkling had a greater proportion of eyes with 20/200 or worse visual acuity at presentation, and had worse mean acuities at 3 months (20/94 vs. 20/35 for eyes without an epiretinal membrane, $P=0.002$) and at 6 months follow-up (20/110 vs. 20/36 for eyes without an epiretinal membrane, $P=0.02$). At 6 months of follow-up the mean central subfield thicknesses were: eyes without an epiretinal membrane, $338 \pm 23 \mu\text{m}$; and eyes with an epiretinal membrane and surface wrinkling, $405 \pm 22 \mu\text{m}$ ($P=0.05$).

Conclusions—In eyes with epiretinal membranes and retinal surface wrinkling, uveitic macular edema had a poorer visual acuity response to medical therapy and thicker maculae at 6 months.

Uveitic macular edema is the most common cause of visual impairment in patients with uveitis and the most frequent structural complication of uveitis.^{1,2} Epiretinal membrane formation in association with uveitis and uveitic macular edema is a relatively common structural complication of the uveitis.^{3–6} The advent of Optical Coherence Tomography (OCT), and in particular, spectral-domain optical coherence tomography, has improved our ability to detect epiretinal membranes and describe their morphologic effects on the retina.^{7,8} Detrimental clinical effects of epiretinal membrane formation on uveitic macular edema have been described. Epiretinal membranes have been associated with worse visual acuity in uveitic macular edema patients 3 months after treatment with intravitreal triamcinolone acetonide,⁹ as well as a higher risk of failing medical therapy for uveitic macular edema.¹⁰ In one study, foveal involvement of the epiretinal membrane and focal attachment of the epiretinal membrane to the inner retinal surface were predictors of poor vision.⁶ The goal of our study was to characterize the effects of epiretinal membranes in uveitic macular edema on visual acuity, and on improvement and resolution of the edema.

Methods

A retrospective review of patients with uveitic macular edema seen at the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai from 2008 through 2011 was conducted. Prior to the initiation of the study, approval was obtained from the Institutional Review Board of the Medical School. A query of the billing records database cross-referencing cases of uveitis (ICD-9 codes 363.00 through 364.99) and macular edema (ICD-9 code 362.53) was performed in order to identify cases of uveitic macular edema. Additionally, all spectral-domain OCTs (Heidelberg Spectralis, Heidelberg Engineering, Vota, CA) of patients with diagnosis codes 363.00 through 364.99 were reviewed in order to ensure complete identification of uveitic macular edema cases. The data collection period spanned from September 2008, when spectral-domain OCT capability was obtained, until December 2011, and all patients meeting the criteria were included. All spectral-domain OCT measurements were performed on the Heidelberg Spectralis machine using volume scans and registration between scans. Macular edema was diagnosed based on spectral-domain OCT findings. Patients with choroidal neovascularization with associated retinal edema were excluded. Only de-identified, HIPPA-compliant data were entered into the data base for statistical analysis.

Data Collection and Outcome Measures

Uveitic macular edema patients were identified, and all OCTs of both eyes were reviewed, confirming the presence or absence of an epiretinal membrane, which was defined as a thin, smooth hyper-reflective layer between the neural retina and the vitreous (Figure 1).⁸ The first visit at which uveitic macular edema was identified (macular edema “presentation” or baseline visit) was used to categorize patients and eyes as either having or not having an epiretinal membrane. All available cross-sections of the macula at the baseline visit were scored independently by the same two investigators (B.L. and P.P.). At the end of this initial data collection phase, the investigators reviewed together any OCT on which there was initial disagreement regarding epiretinal membrane status and thereby reached a consensus interpretation for all OCTs.⁶ In many cases, the epiretinal membrane was attached at multiple focal points to the underlying internal limiting membrane, creating hyporeflexive spaces between the epiretinal membrane and internal limiting membrane, and producing numerous folds or wrinkles along the internal limiting membrane. Therefore, the epiretinal membranes were scored as either associated with retinal surface wrinkling or not associated with wrinkling by the same two investigators.^{8,11} Central subfield thickness, as recorded by the Spectralis OCT, and best-corrected visual acuity data were recorded at presentation, 3-months, and 6-months after presentation. Only the available data for each patient were used, and those patients who did not complete both a 3 and 6 month follow-up visit by the end of the data collection period were noted as having only partial follow-up. A central subfield retinal thickness of 315 μm or greater as calculated by the Spectralis OCT was used to identify macular edema.¹² The presence of cystoid spaces also was noted.

For the analysis of outcomes, resolution of macular edema was defined as a decrease in macular thickness to a normal level ($<315\mu\text{m}$). Improvement in edema was defined as achieving at least a 20% reduction in macular thickness or resolution of edema if a less than 20% decrease led to a macular thickness of less than 315 μm .¹³ LogMAR transformation was used to determine mean acuities and converted back to Snellen acuities for reporting purposes. Previously described logMAR equivalents for hand motion or count fingers acuities were used where necessary.¹⁴ In addition, the percentage of patients with acuities at traditional benchmark thresholds (20/200 or worse and 20/40 or better) were recorded at baseline, 3 months and 6 months. Months elapsed since the diagnosis of uveitis, patient gender, age, and race, presence or absence of subretinal fluid, treatment regimen (regional corticosteroids, oral corticosteroids, immunomodulatory therapy, or combination regional and oral corticosteroids), and anatomic location of uveitis (anterior, intermediate, anterior and intermediate, posterior, or panuveitis) also were noted and accounted for as potential confounders.¹⁵

Statistical Analysis

Eyes without an epiretinal membrane served as the control group for comparisons to 1) eyes with an epiretinal membrane without surface wrinkling and 2) eyes with an epiretinal membrane with surface wrinkling. Eyes with an epiretinal membrane without and with surface wrinkling also were also compared. Central subfield thickness and logMAR visual acuity were related to the presence or absence of the epiretinal membrane type using mixed Analysis of Variance (ANOVA) models, stratified by visit.¹⁶ The correlation between eyes

in the same patient was accounted for by these models. The binary outcomes of improvement and resolution of macular edema were related to presence or absence of an epiretinal membrane (without or with wrinkling) using log-binomial regression models. Similar to the mixed ANOVA models, this method accounts for the correlation between measurements taken from two eyes of the same patient. The parameters of these models were estimated using Generalized Estimating Equations methods.¹⁷ Patient characteristics on categorical and continuous variables were compared between epiretinal membrane groups using Chi square and Wilcoxon tests, respectively.¹⁸ SAS 9.2 (SAS Institute Inc., Cary, NC) was used to conduct all analyses. No correction was made for multiple comparisons, and all hypothesis testing was conducted at the 5% level. Since the median ages of patients with and without an epiretinal membrane were significantly different, all analyses of the impact of epiretinal membranes on outcomes were age-adjusted.

Results

Characteristics of the patient population

Table 1 outlines the general characteristics and demographics of the study population. 77 patients with uveitic macular edema were identified. There were 10 different uveitic diagnoses, the most frequent one of which was intermediate uveitis, non-pars planitis type, present in 26%. Of these 77 patients, 59 (76.6%) had an epiretinal membrane in at least one eye, and 18 (23.4%) did not have an epiretinal membrane in either eye. Patients with an eye with an epiretinal membrane either without (median, 55 years, $P=0.01$ vs. eyes without an epiretinal membrane) or with surface wrinkling (median, 63 years, $P=0.0005$ vs. eyes without an epiretinal membrane) were significantly older than those without an epiretinal membrane (median, 40.5 years). No other significant differences among the three groups in patient characteristics at presentation were identified.

Epiretinal membrane, macular thickness, and visual acuity at presentation

Table 2 details the pair-wise comparisons of eyes without an epiretinal membrane at presentation, with an epiretinal membrane without surface wrinkling at presentation, and with an epiretinal membrane and surface wrinkling at presentation. There were no significant differences in mean central subfield retinal thickness among the three groups; mean central subfield retinal thickness $\pm$ standard errors were: $420 \pm 25 \mu\text{m}$ for eyes without an epiretinal membrane; $401 \pm 21 \mu\text{m}$ for eyes with an epiretinal membrane without surface wrinkling ($P=0.55$ vs. eyes without an epiretinal membrane); and $442 \pm 24 \mu\text{m}$ for eyes with an epiretinal membrane with surface wrinkling ($P=0.52$ vs. eyes without an epiretinal membrane). Mean Snellen acuities were 20/59 for eyes without an epiretinal membrane; 20/64 for eyes with an epiretinal membrane without surface wrinkling ($P=0.37$ vs. eyes without an epiretinal membrane); and 20/109 for eyes with an epiretinal membrane and surface wrinkling ($P=0.61$ vs. eyes without an epiretinal membrane). However, the percentage of eyes with presenting visual acuities 20/200 or worse appeared to be greater among those with an epiretinal membrane with surface wrinkling than among those without an epiretinal membrane. The percentages of eyes with 20/200 or worse acuity at presentation were: eyes without an epiretinal membrane, 16%; eyes with an epiretinal membrane without surface wrinkling, 13% ($P=0.36$ vs. eyes without an epiretinal membrane); and eyes with an

epiretinal membrane with surface wrinkling, 38% ($P=0.02$ vs. eyes without an epiretinal membrane).

Epiretinal membrane and response to treatment

Patients with an epiretinal membrane and those without an epiretinal membrane underwent similar treatment regimens. Between the two groups, there was no significant difference in the percentage of patients receiving regional (periocular or intravitreal) corticosteroids (19% for those without an epiretinal membrane vs. 25% for those with an epiretinal membrane, $P=0.74$), oral corticosteroids (63% for those without an epiretinal membrane vs. 63% for those with an epiretinal membrane, $P=0.96$), immunosuppression (50% for those without an epiretinal membrane vs. 45% for those with an epiretinal membrane, $P=0.78$), or combination regional and oral corticosteroids (13% for those without an epiretinal membrane vs. 22% for those with an epiretinal membrane, $P=0.49$).

The response to therapy of eyes with uveitic macular edema is detailed in Table 3. At the 3-month follow-up visit, the mean central subfield retinal thickness $\pm$ the standard errors were: eyes without an epiretinal membrane, $360 \pm 15 \mu\text{m}$; eyes with an epiretinal membrane without surface wrinkling, $332 \pm 13 \mu\text{m}$ ($P=0.14$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling $392 \pm 16 \mu\text{m}$ ($P=0.15$ vs. eyes without an epiretinal membrane). At the 6-month follow-up visit, the mean central subfield retinal thickness $\pm$ the standard errors were: eyes without an epiretinal membrane, $338 \pm 23 \mu\text{m}$; eyes with an epiretinal membrane without surface wrinkling, $332 \pm 20 \mu\text{m}$ ($P=0.88$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling $405 \pm 22 \mu\text{m}$ ($P=0.05$ vs. eyes without an epiretinal membrane). Among eyes with an epiretinal membrane, at 3 and 6 months, eyes with wrinkling consistently had a thicker central subfield retinal thickness than eyes without wrinkling ($P=0.004$ and 0.02 , respectively). At 3 and 6 months follow-up, eyes with an epiretinal membrane and surface wrinkling consistently had worse visual acuities than the other groups. At 3 months, the mean Snellen visual acuities were: eyes without an epiretinal membrane, 20/35; eyes with an epiretinal membrane without surface wrinkling, 20/47 ($P=0.18$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling, 20/94 ($P=0.002$ vs. eyes without an epiretinal membrane and $P=0.01$ vs. eyes with an epiretinal membrane without surface wrinkling). At 6 months, the mean Snellen visual acuities were: eyes without an epiretinal membrane, 20/36; eyes with an epiretinal membrane without surface wrinkling, 20/46 ($P=0.55$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling, 20/110 ($P=0.02$ vs. eyes without an epiretinal membrane and $P=0.04$ vs. eyes with an epiretinal membrane without surface wrinkling). These differences in mean acuities are due in part to a greater percentage of eyes with acuities of 20/200 or worse at the 3- and 6-month follow-up visits. The percentages of eyes with 20/200 or worse acuity at the 3-month visit were: eyes without an epiretinal membrane, 4%; eyes with an epiretinal membrane without surface wrinkling, 9% ($P=0.35$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling, 37% ($P=0.02$ vs. eyes without an epiretinal membrane and $P=0.03$ vs. eyes with an epiretinal membrane without surface wrinkling). The percentages of eyes with 20/200 or worse acuity at the 6-month visit were: eyes without an epiretinal membrane, 5%; eyes with

an epiretinal membrane without surface wrinkling, 6% ($P=0.95$ vs. eyes without an epiretinal membrane); and eyes with an epiretinal membrane with surface wrinkling, 39% ($P=0.02$ vs. eyes without an epiretinal membrane and $P=0.06$ vs. eyes with an epiretinal membrane without surface wrinkling).

Discussion

Our data suggest that in patients with uveitic macular edema, the presence of an epiretinal membrane of sufficient severity to cause wrinkling of the retinal surface may limit the response to medical therapy, whereas the presence of a membrane without wrinkling may not. Indeed although the mean visual acuity for eyes without an epiretinal membrane and with an epiretinal membrane without surface wrinkling improved from 20/59 and 20/64, respectively to 20/35 and 20/47, respectively, at 3 months and to 20/36 and 20/46, respectively, at 6 months, the mean acuity among eyes with an epiretinal membrane and retinal surface wrinkling showed little improvement. The mean acuity among these eyes was 20/109 at presentation and 20/110 at 6 months. Similarly, the proportion of eyes with poor acuity (20/200 or worse) among those with an epiretinal membrane and retinal surface wrinkling was similar at presentation (38%) and at 6 months follow-up (39%).

Previous studies of epiretinal membranes and uveitic macular edema also have found that epiretinal membranes limit the response to therapy, as eyes with epiretinal membranes had significantly worse acuity at 3 months after intravitreal triamcinolone acetonide injection⁹ and were significantly more likely to fail medical therapy for uveitic macular edema.¹⁰ Our data, though limited by sample size, support this concept. In addition, the presence of preoperative epiretinal membrane in patients undergoing vitrectomy for complicated chronic endogenous or autoimmune uveitis was a predictor for postoperative reduction in the number of drugs required,¹⁹ suggesting that epiretinal membrane removal (or perhaps the vitrectomy itself) may reduce the long-term burden of therapy. A retrospective review of 80 eyes with epiretinal membrane and uveitis found that 50% of epiretinal membranes demonstrated a focal attachment pattern with underlying retinal surface corrugation,⁶ similar to the percentage of epiretinal membranes with retinal surface wrinkling in our group (44%). In both groups, retinal surface wrinkling was associated with worse visual acuity outcomes. In non-uveitic epiretinal membranes, pre-operative internal limiting membrane distortion and wrinkling likewise has been correlated with poor visual acuity outcome after epiretinal membrane surgery.²⁰

As with any retrospective review, caution is recommended when interpreting our data. Since our patient population was seen at a tertiary-care referral center, the results may not be generalizable to all patients with uveitic macular edema. Although we were able to eliminate selection bias by including all patients with uveitic macular edema evaluated since the adoption of spectral-domain OCT, we cannot exclude the possibility of referral bias. The identification of an epiretinal membrane is somewhat subjective even with specified definitions. Controversy exists regarding detection of an epiretinal membrane by spectral-domain OCT. Distinction between a globally attached epiretinal membrane and a hyperreflective inner retina or thickened posterior hyaloid can be difficult. Contraction of the epiretinal membrane causes tractional effects on the retina, resulting in “wrinkling” of

the retina, and making the diagnosis more evident.^{21,22} To address this issue, all OCTs were read by two observers, and an epiretinal membrane was diagnosed only if both observers agreed that one was present. In some cases, both graders identified a distinct layer above the retinal surface with hyporeflective areas of separation between the epiretinal membrane and the underlying retina (typically with mild focal retinal corrugation) on at least one scan, but in which there was not a substantial tangential tractional component caused by the epiretinal membrane. In this group the appearance of the epiretinal membrane itself was indistinguishable from that in eyes with retinal wrinkling, and so an “epiretinal membrane without retinal surface wrinkling” was diagnosed. Although not all may concur with this approach, we believed that it was important to evaluate its impact on macular edema, as aside from the wrinkling aspect, the appearance of the epiretinal membrane in the two situations was similar. Importantly, our data suggest that the appearance of an epiretinal membrane without wrinkling does not impact the response to medical therapy. Conversely, an epiretinal membrane sufficient to wrinkle the retina does appear to impact the results of medical therapy for the macular edema.

The numbers of eyes and patients were relatively small, limiting power to detect mild differences and introducing the possibility of type II error. Some analyses, such as the response of different uveitic diagnoses to treatment, were not possible due to the small sample size and the number of different diseases. The possibility of a type II error is evident in the 6-month data on improvement and resolution of macular edema, where risk ratios of 0.36 and 0.31, respectively, for improvement and resolution of macular edema in the group with an epiretinal membrane and surface wrinkling vs. the group without an ERM had broad 95% confidence intervals and were not significant at the conventional, 0.05, level ($P=0.12$ and 0.19 , respectively). Follow-up was incomplete, particularly at 6 months, which also is a potential source of unknown bias. However, despite the limited numbers, significant differences were detected between eyes with an epiretinal membrane and surface wrinkling and eyes without an epiretinal membrane in visual acuity measurements at 3 and 6 months and retinal thickness at 6 months. These results are consistent with the concept that in an eye with an epiretinal membrane and surface wrinkling, the response to medical therapy is limited. Although surgical intervention was not evaluated, these data suggest that, given the poor response to medical therapy, eyes with an epiretinal membrane and retinal wrinkling might be candidates for surgical removal of the epiretinal membrane, after there is control of the inflammation.

In conclusion, the presence of epiretinal membrane of sufficient severity to wrinkle the retinal surface in an eye with uveitic macular edema is associated with a poorer response to medical therapy.

Acknowledgments

Funding/Support: Supported in part by an unrestricted grant from Research to Prevent Blindness to the Department of Ophthalmology, Mount Sinai School of Medicine, New York, New York. Supported in part by award number UL1RR029887 from the National Center for Research Resources.

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Figure 1.
Optical coherence tomogram demonstrating presence of an epiretinal membrane, surface wrinkling, and macular edema.

Table 1

Characteristics of the Uveitic Macular Edema Study Population

Characteristic	All patients	No epiretinal membrane	Epiretinal membrane, no wrinkling	P-value*	Epiretinal membrane with wrinkling	P-value*	P-value [†]
Number patients	77	18	33		26		
Percent of population	100	23.3	55.9		44.1		
Age (years)							
Median	55	40.5	55	0.01	63	0.0005	0.09
Interquartile range	41–66	28–48	42–65		51–68		
Gender (%)							
Men	43	50	33	0.24	50	1.0000	0.20
Women	57	50	67		50		
Race (%)							
White, non-Hispanic	70	56	76	0.25	73	0.66	0.94
Hispanic	9	11	9		8		
African American	17	28	12		15		
Other	3	6	0		4		
Months since uveitis diagnosis							
Median	23	10.5	20	0.21	24	0.07	0.63
Interquartile range	5–56	3–36	4–84		7–60		
Anatomic type of uveitis							
Anterior	16	11	21	0.83	12	0.76	0.34
Intermediate	22	22	27		15		
Anterior & intermediate	23	28	24		19		
Posterior	22	17	15		35		
Panuveitis	17	22	12		19		
Macular edema							
Bilateral macular edema (%)	35	39	30	0.53	38	0.98	0.51
Patients with subretinal fluid in at least one eye (%)	40	61	36	0.09	31		0.65

* P-value comparing patients in group to those with uveitic macular edema without an epiretinal membrane.

[†] P-value comparing patients with uveitic macular edema, an epiretinal membrane, and surface wrinkling to those with an epiretinal membrane without surface wrinkling.

Table 2

Comparison among eyes with Uveitic Macular Edema without an Epiretinal Membrane, with an Epiretinal Membrane without Retinal Surface Wrinkling, and with an Epiretinal Membrane with Retinal Surface Wrinkling

Characteristic	Eyes without an epiretinal membrane	Eyes with an epiretinal membrane without wrinkling	Eyes with an epiretinal membrane and wrinkling	P-value*	Mean difference/risk ratio*	P-value*	Mean difference/risk ratio†	P-value†
Number eyes	32	38	34					
<i>Central subfield thickness (μm)</i>								
Mean	420	401	442	0.55	-18	0.52	41	0.19
Standard error	25	21	24		[-78, 42]		[-21, 103]	
<i>Cystoid spaces (%)</i>	44	63	56	0.25	1.34 [0.81–2.23]	0.66	0.84 [0.58, 1.22]	0.36
<i>Visual acuity</i>								
logMAR								
Mean	0.444	0.52	0.73	0.37	0.077	0.08	0.210	0.15
Standard error	0.116	0.10	0.11		[-0.215, 0.369]		[-0.079, 0.498]	
Mean Snellen acuity	20/59	20/64	20/109					
20/40 or better (%)	53	42	35	0.29	0.75 [0.45, 1.27]	0.20	0.88 [0.48, 1.62]	0.69
20/200 or worse (%)	16	13	38	0.36	1.88 [0.49, 7.25]	0.02	2.18 [0.99, 4.81]	0.06

* Numbers in brackets are 95% confidence intervals. P-values are for comparison between eyes in group to those with uveitic macular edema without an epiretinal membrane.

† P-values are for comparison between eyes with uveitic macular edema, an epiretinal membrane, and surface wrinkling to those with an epiretinal membrane without surface wrinkling.

Table 3

Response of Uveitic Macular Edema Eyes to Treatment for Eyes without an Epiretinal Membrane, Eyes with an Epiretinal Membrane without Retinal Surface Wrinkling, and Eyes with an Epiretinal Membrane and Retinal Surface Wrinkling

Outcome	Eyes without an epiretinal membrane		Eyes with an epiretinal membrane without wrinkling		Eyes with an epiretinal membrane with retinal wrinkling		Mean difference / risk ratio*		P-value*		Mean difference / risk ratio†		P-value†	
	Number	eyes	Number	eyes	Number	eyes	Mean difference / risk ratio*		P-value*		Mean difference / risk ratio†		P-value†	
<i>At 3 months follow-up</i>														
Number eyes	27		32		27									
<i>Central Subfield Thickness (μm)</i>														
Mean	360		332		392		-27		0.14		32		0.15	
Standard error	15		13		16		[-64, 9]				[19, 99]			
Improvement edema (%)	44		53		36		1.39 [0.79, 2.43]		0.25		1.00 [0.48, 2.08]		1.00	
Resolution edema (%)	33		37		24		1.42 [0.64, 3.16]		0.39		0.98 [0.39, 2.47]		0.97	
<i>Visual acuity</i>														
Mean logMar	0.23		0.35		0.66		0.12		0.32		0.43		0.002	
Standard error	0.09		0.08		0.09		[-0.119, 0.358]				[0.164, 0.695]			
Mean Snellen acuity	20/35		20/47		20/94									
20/40 or better (%)	81		59		44		0.80 [0.58, 1.11]		0.18		0.66 [0.42, 1.03]		0.06	
20/200 or worse (%)	4		9		37		2.69 [0.33, 21.77]		0.35		10.28 [1.56, 67.81]		0.02	
<i>At 6 months follow-up</i>														
Number eyes	19		18		17									
<i>Central Subfield Thickness (μm)</i>														
Mean	338		333		405		-5		0.88		67		0.05	
Standard error	23		20		22		[-68, 59]				[13, 131]			
Improvement edema (%)	53		56		29		0.72 [0.48, 1.09]		0.13		0.31 [0.07, 1.38]		0.12	
Resolution edema (%)	37		39		12		0.89 [0.34, 2.29]		0.80		0.31 [0.05, 1.79]		0.19	
<i>Visual acuity</i>														
Mean logMar	0.23		0.35		0.74		0.12 [-0.28, 0.51]		0.55		0.51 [0.09, 0.94]		0.02	
Standard error	0.14		0.13		0.14									
Mean Snellen acuity	20/36		20/46		20/110									
20/40 or better (%)	84		61		33		0.87 [0.56, 1.35]		0.54		0.49 [0.23, 1.04]		0.06	
														0.13

Outcome	Eyes without an epiretinal membrane		Eyes with an epiretinal membrane without wrinkling		Eyes with an epiretinal membrane with retinal wrinkling		Mean difference / risk ratio [*]		Mean difference / risk ratio [†]	
	5	6	1.07 [0.10, 11.13]	0.95	39	8.36 [1.41, 49.74]	0.02	7.79 [0.94, 64.75]	0.06	

* Numbers in brackets are 95% confidence intervals. P-values are for comparison between eyes in group to those without an epiretinal membrane.

[†] P-value for comparison between eyes with an epiretinal membrane with retinal surface wrinkling and those with an epiretinal membrane without retinal surface wrinkling.