Published in final edited form as:

Ocul Immunol Inflamm. 2012 June ; 20(3): 171–181. doi:10.3109/09273948.2012.658467.

The impact of macular oedema on visual function in intermediate, posterior and panuveitis

SRJ Taylor^{1,2}, SL Lightman^{2,3}, EA Sugar⁴, GJ Jaffe⁵, WR Freeman⁶, MM Altaweel⁷, I Kozak⁸, JT Holbrook⁹, DA Jabs¹⁰, and JH Kempen¹¹ for the Multicentre Uveitis Steroid Treatment (MUST) Trial Research Group

¹Division of Immunology & Inflammation, Imperial College London, London, UK

²Royal Surrey County Hospital NHS Foundation Trust, Guildford, UK

³UCL Institute of Ophthalmology, London, UK

⁴Departments of Epidemiology and Biostatistics, Bloomberg School of Public Health, Division of Oncology Biostatistics, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA

⁵Duke Eye Centre, Durham, NC, USA

⁶University of California San Diego, Jacobs Retina Centre, CA, USA

⁷Department of Ophthalmology, the University of Wisconsin, Madison WI, USA

⁸University of California San Diego, CA, USA

⁹Department of Epidemiology and Center for Clinical Trials, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

¹⁰Departments of Ophthalmology and Medicine, the Mount Sinai School of Medicine, New York, NY, USA and Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

¹¹Scheie Eye Institute, Centre for Preventive Ophthalmology and Biostatistics, and Centre for Clinical Epidemiology and Biostatistics, Departments of Ophthalmology and Biostatistics & Epidemiology, University of Pennsylvania School of Medicine, USA

Keywords

Cystoid macular oedema; uveitis; cataract; vitrectomy; OCT; visual acuity; visual field

Introduction

Uveitis encompasses approximately 30 inflammatory disorders characterized by intraocular inflammation, and is a major cause of visual loss in people of working age.^{1,2} Uveitis involving the posterior segment more commonly affects vision than anterior uveitis, and macular oedema is the most common mechanism of visual loss.^{1,3,4} The advent of optical

Corresponding author: Simon R J Taylor, PhD, FRCOphth. Division of Immunology & Inflammation, Imperial College London, Hammersmith Hospital, Du Cane Road, London W12 0NN. Tel: +44 207 566 2266. Fax: +44 207 251 9350. s.r.taylor@ucl.ac.uk.
Reprint Requests: Douglas A. Jabs, MD, MBA; MUST Trial Chairman's Office; One Gustave L. Levy Place; Box 1183; New York, NY, USA.

Conflict of interest: On file with the MUST Coordinating Centre, The Johns Hopkins University Bloomberg School of Public Health

Off label use of drugs: Not applicable.

coherence tomography (OCT) has enabled quantitative assessment of macular thickening and qualitative assessment of macular cysts.⁵ More complex parameters can be calculated from OCT data, and have been proposed as potential outcomes in studying macular oedema in non-uveitic conditions,⁶ but macular thickening and the presence of macular cysts are the manifestations of macular oedema most accessible to clinicians, and are easily characterized using widely-available time-domain or spectral-domain OCT.

Nevertheless, the impact of these macular characteristics on visual acuity remains unclear. Previous studies have looked at the relationship between OCT findings and visual function, but have been limited by small sample sizes and retrospectively ascertained outcomes, and their results have proved inconsistent.^{5,7–11} Similarly, although the presence of cystoid macular oedema has been reported to have an effect on the central visual field when measured by microperimetry,¹² its effect and the effects of isolated macular thickening and isolated cysts on the standard perimetric assessments performed in most clinics are unknown.

One of the main limitations in evaluating these relationships is that a large cohort of patients is needed, all evaluated using common visual function and OCT imaging protocols. The Multicentre Uveitis Steroid Treatment (MUST) Trial provides such a resource, having recruited 255 patients with 479 eyes affected by non-infectious intermediate, posterior or panuveitis. OCT images, visual acuity and Humphrey visual field were obtained at the same visit following standardised protocols.¹³ Here, we use these to evaluate the relationship between alternative macular oedema phenotypes and best-corrected visual acuity or visual field sensitivity.

Methods

Data for this analysis come from baseline visits in the Multicentre Uveitis Steroid Treatment (MUST) Trial, a randomized, parallel treatment clinical trial comparing fluocinolone acetonide implant therapy^{14,15} vs. systemic therapy¹⁶ for active or recently active (within 60 days) non-infectious intermediate, posterior or panuveitis. Patients were enrolled at 23 centres in the United States, the United Kingdom and Australia, with the approval of all governing institutional review boards. In all enrolled patients, systemic immunosuppressive therapy was considered necessary to control uveitis; patients were randomized to receive implants or systemic therapy post-enrolment. A detailed description of the study methods previously has been published.¹³ Demographic, behavioural, and clinical characteristics (including duration of uveitis, type of uveitis, laterality of involvement with uveitis, current grading of the activity of uveitis consistent with Standardization of Uveitis Nomenclature-endorsed methods,¹⁷ and the presence of ocular co-morbidities such as glaucoma and prior surgeries) were collected at baseline. In addition, as part of the baseline visit, patients simultaneously had several visual function and imaging studies performed.

Best-corrected visual acuity was measured by certified study examiners, using standard logarithmic (ETDRS) visual acuity charts under standardized lighting conditions.^{18,19} Visual acuity was scored by the number of standard letters read; in this system, reading of 85 letters corresponds to 20/20 visual acuity, 70 letters corresponds to 20/40, and 35 letters corresponds to 20/200. Humphrey 24-2 SITA-fast visual field testing with appropriate refractive correction in place also was performed, from which the mean deviation provided the primary result studied in this analysis. An introductory practice run was conducted before visual field testing, and abnormal test results were repeated in order to prevent “first try” effects from interfering with results. Both visual acuity and visual field testing were done with the pupil undilated. Implementation of the visual function protocols was

supervised by a Visual Function Quality Assurance Committee, which conducted annual site visits to ensure proper protocol administration at the clinical sites.

Imaging of macular oedema

To document the ocular abnormalities of uveitis and its complications, MUST Trial clinical centres obtained fundus photographs, fluorescein angiograms, optical coherence tomography (OCT) scans, and lens photographs using standardized protocols generated by the Reading Centre at the University of Wisconsin, Madison. The presence versus absence of macular oedema in this report was determined by OCT using the Stratus time domain OCT machine (Carl Zeiss Meditec, Dublin, CA; software version 4.0) with an axial resolution of 12 microns, a system which accurately and reproducibly detects macular thickening and macular cysts.^{9,20} Images were obtained through a dilated pupil, and images with quality scan index 6 and higher were saved and graded at the Reading Centre according to standardized protocols.

Macular thickness was measured at the centre point²¹, and OCT features consistent with macular oedema, including central macular thickening and cystoid spaces in the central macula (alone or in combination), were graded in terms of presence and extent.¹³ Diffuse macular oedema was defined as the presence of retinal thickening greater than or equal to 240 μm at the centre point, without cystoid spaces. Eyes with retinal thickness less than 240 μm and cystoid spaces were defined as having cystoid spaces alone (Figure 1). Cystoid macular oedema was defined as the presence of both retinal thickening greater than or equal to 240 μm at the centre point and cystoid spaces.²² Epiretinal membrane diagnoses are based upon a consensus grading of OCT images and Colour Fundus Photographs, whereby suggestive features on either modality were required to substantiate clinical assessment.

Imaging quality and reproducibility of grading were enforced throughout the period of data acquisition via regular quality control exercises and systematic evaluation of the data stream for unexpected variations; corrective feedback was provided if needed. Of the 479 enrolled eyes, 53 had missing baseline OCT data or had images that were considered ungradeable, leaving 426 eyes to be included in the analysis.

Statistical Methods

Patient, ocular and imaging characteristics at randomization were summarized for eyes with uveitis, stratified by macular oedema category (no macular oedema, retinal thickening alone, cystoid spaces alone, or cystoid macular oedema), based on data collected as of December 2010 from baseline visits (conducted between 6 December 2005 and 9 December 2008). Comparisons of characteristics between strata were made using linear, logistic or proportional odds logistic regression models for continuous, binary and ordinal covariates, respectively.²³ The association between visual acuity and specific risk factors was assessed using linear regression models. No visually significant vascular occlusions were seen in the study patients, and capillary loss was excluded from the analysis as 47% of the data was missing and only 11 cases were observed among the remaining eyes.

The assessment of visual field sensitivity was categorized by mean deviation (> -3 , -3 to -6 and < -6), and proportional odds logistic regression was used to evaluate the effects of macular oedema morphology and other risk factors. The associations between each outcome variable (visual acuity and mean deviation) and specific risk factors of interest were modelled for each risk factor separately and for all risk factors simultaneously to adjust for potential confounding. Generalized estimating equations were used for all regression models to adjust for within-person between eye correlation.²³ Analyses were performed using SAS (SAS/STAT User's Guide, Version 9.2, Cary, NC: SAS Institute) and R (The R Project for

Statistical Computing, Version 2.11.1, <http://www.r-project.org/>) statistical packages. Missing data were accommodated via multiple imputation.²⁴

Results

Baseline characteristics (Table 1)

Macular oedema and retinal cysts were common in the 426 eyes with active or recently active (within 60 days) non-infectious intermediate, posterior, or panuveitis for whom OCT information on macular oedema was available. At baseline, approximately 13% of patients had cystoid spaces alone, 10% had diffuse macular thickening alone, and 25% had cystoid macular oedema. Patients whose eyes had macular thickening (with or without cysts) were significantly older than those without ($P<0.01$), but there were no other demographic associations with macular oedema. Uveitic eyes with macular oedema of any type were more likely to have developed cataract or to have had cataract surgery ($P<0.01$). Eyes with macular thickening were more likely to have epiretinal membranes ($P<0.01$) and eyes with cystoid macular oedema more often had active uveitis ($P<0.01$) and vitreous haze ($P<0.01$).

Baseline visual acuity and visual field data (Table 2)

Macular oedema was significantly associated with poorer baseline visual acuity, regardless of its morphology ($P<0.01$). The least deficit in visual acuity was observed in those eyes with cystoid spaces alone (−5 letters), with larger deficits in eyes with retinal thickening only (−13 letters) and in those with both cysts and macular thickening (cystoid macular oedema; −19 letters). Eyes with cystoid macular oedema had, on average, visual acuity nearly 4 lines worse than those without macular oedema. Furthermore, the proportion of eyes with visual impairment (VA worse than 20/40) and severe visual impairment (VA of 20/200 or worse) was doubled in eyes with cystoid macular oedema compared to those without (70.1% vs. 30.6% among eyes with visual impairment and 13.1% vs. 7.8% among eyes with severe visual impairment, respectively).

Macular oedema also was associated with reduced overall visual field sensitivity, as reflected by Humphrey mean deviation scores. Although eyes with uveitis but no macular oedema had lower visual field sensitivity than the normative range, the median mean deviation being −4.4 dB, eyes with the morphologic characteristics of macular oedema had an even worse field sensitivity ($P=0.03$). In contrast to the pattern for visual acuity, the extent of depression of visual field sensitivity was similar for eyes with cystoid spaces (−5.2 dB), retinal thickening (−5.5 dB), and cystoid macular oedema (−5.4 dB).

Risk factors for reduced visual acuity (Table 3)

Multivariate analyses were performed in order to determine whether cystoid spaces and increased retinal thickness were independently associated with visual acuity after controlling for other potentially confounding variables. After adjusting for characteristics potentially confounding the effects of macular oedema, retinal thickness greater than or equal to 240 μm was significantly associated with worse vision, on average 8.8 letters worse (95% confidence interval (CI) −14.0 to −3.6; $P<0.01$). The presence of cystoid spaces was not significantly associated with lower visual acuity after adjusting for retinal thickness and other potential confounders (−4.2 letters; 95% CI −9.9 to +1.4; $P=0.14$).

Several other variables were significantly associated with worse visual acuity: visual acuity decreased by 1.8 letters for every decade of disease duration ($P=0.02$); cataract ($P<0.01$) or previous cataract surgery ($P=0.03$), chorioretinal lesions ($P<0.01$), and non-white race ($P<0.01$) were each associated with visual acuities of more than 6 letters worse than their comparison groups. Vitrectomy was associated with a visual acuity 9 letters worse ($P=0.03$).

Risk factors for reduced visual field sensitivity (Table 4)

Multivariate analyses were performed to determine the effect of the morphology of macular oedema on visual field impairment, after adjusting for potential cofounders. The increase in risk was quantified as the odds ratio for greater impairment, and the greatest impacts on visual field sensitivity was observed in eyes from patients of non-white ethnicity (Odds Ratio (OR) 3.2; $P<0.01$) and eyes with chorioretinal lesions, prior cataract surgery or cataract (OR 3.4, 1.8 and 2.4, respectively). After adjusting for potential cofounders, having cysts and/or retinal thickening was associated with an OR of 1.7 of having greater visual field impairment ($P<0.01$). In sensitivity analyses, adjusted models examining cysts and retinal thickening separately produced similar findings (results not shown).

Discussion

This study analysed patients with active or recently active intermediate, posterior or panuveitis of a severity for which systemic corticosteroid therapy or fluocinolone acetonide implant therapy were considered to be indicated. Both macular thickening and macular cysts were found to be highly prevalent and indicative of visual field impairment; macular thickening was also found to be associated with a clinically important degree of visual acuity impairment of 13 letters (2.6 lines).

The effect of macular thickening on visual acuity was greater than that of macular cysts: macular cysts were associated with a five letter (one line) reduction in visual acuity which was relatively small and not statistically significant after adjusting for central macular thickening. In addition, while eyes with both macular thickening and cysts (i.e. cystoid macular oedema) had the greatest degree of visual acuity impairment, this was not significantly greater than the additive effect of macular thickening and cysts (test for interaction, $P=0.43$). Thus macular thickening is the better predictor of diminished visual acuity and may be a suitable outcome in clinical trials evaluating uveitic macular oedema as well as a more relevant parameter to follow in its clinical management.

These results also provide corroborative, more precise evidence that macular oedema is a key contributor to impairment of visual function in uveitis.^{2,3,5,7-9,25,26} In addition to its effects on distance visual acuity, macular oedema was also associated with a clinically important degree of impairment of visual field sensitivity. This is consistent with previous reports that macular oedema can reduce central light sensitivity in uveitis^{12,27} and can affect the central visual field in other retinal diseases,²⁸⁻³¹ having a major impact on reading vision.²⁷ Significantly, however, our results demonstrate that the visual field as a whole is affected to a degree that can be measured using widely-available automated visual field testing. This suggests that OCT imaging may be useful in evaluating patients with raised intraocular pressure and apparently progressive loss of visual field sensitivity in order to exclude interval development of macular oedema (rather than glaucoma) as an underlying cause. Further, given our observation that uveitis of the nature studied in the MUST Trial is itself associated with reduced visual field sensitivity, this should be taken into account when evaluating patients with uveitis and raised intraocular pressure for evidence of glaucomatous optic neuropathy, even in the absence of cysts or macular thickening.

Macular oedema was also more prevalent among eyes with active uveitis and eyes with cataract or which had undergone cataract surgery. These observations are not surprising: macular oedema can be a consequence of uveitis activity, which also is known to cause cataract; cataract surgery is well-known to cause macular oedema in some cases; and hypotony can result from glaucoma surgery and lead to macular oedema. Each of these may also reflect a higher degree of disease severity and damage to the eye. Macular oedema was also more common with increasing age, consistent with the results of one prior study,³²

perhaps reflecting either increasing physiological impairment in clearing retinal oedema or a higher burden of ocular co-morbidity not otherwise adjusted for in the analysis. Other patient characteristics were not associated significantly with ME, including ethnicity, smoking, presence of systemic disease, prior glaucoma surgery and previous vitrectomy. Smoking has been reported to be associated with an increased risk of macular oedema in patients with intermediate uveitis,^{33,34} but the majority of patients in this study had posterior or panuveitis, possibly accounting for the discrepancy.

Strengths of this study include a large sample size sufficient to detect differences between strata of macular oedema of clinical importance, and prospective ascertainment of the primary outcomes of best-corrected ETDRS visual acuity and Humphrey mean deviation using widely accepted methods suitable for clinical trials. Macular oedema status was classified using prospective standardized imaging and grading of cases following a strict protocol, with vigorous quality control measures. While spectral domain OCT — which provides better resolution of fine retinal details — has become available since the MUST Trial was initiated, Stratus OCT remains effective for identifying substantial cystic changes in the retina and retinal thickening, the two chief items of interest in evaluating macular oedema.

Limitations include the fact that this is a group of patients with relatively severe disease; individuals with less severe disease may have had less visual field impairment in the absence of macular oedema than observed here. This study also uses best-corrected ETDRS distance acuity as its primary endpoint, and it may be that this measures macular function inadequately when compared to, for example, functional measures of reading vision.²⁷ However, these considerations do not invalidate the importance of the observations that individuals with severe disease commonly do have impairment of visual field sensitivity, that macular oedema is associated with substantially worse visual acuity and visual field sensitivity, and that macular thickening is more predictive of deficits in visual acuity than the presence of macular cysts. Since our study also lacks information regarding cases of anterior uveitis, these results may not be applicable to that subset of cases. Although the study was reasonably large, only 56 were observed to have macular cysts without retinal thickening. After adjusting for macular thickening and other factors, no statistically significant decrement in visual acuity with this set of eyes was observed, but it is possible that cysts without oedema worsen visual function somewhat, to a lesser degree below the threshold we were able to detect; further data would be needed to evaluate that possibility.

In summary, macular thickening in patients with intermediate, posterior and panuveitis is associated with substantial, clinically-important visual dysfunction, both in terms of visual acuity and visual field sensitivity. Macular cysts without thickening are not as clearly associated with visual dysfunction. The combination of macular thickening and macular cysts was not substantially more predictive of impairment of visual acuity or visual field sensitivity than macular thickening alone. The visual acuity results suggest that central macular thickening may be a suitable outcome for use in clinical trials and is an important parameter in the clinical management of macular oedema. Furthermore, the potential presence of uveitis, macular cysts or macular thickening should be borne in mind when evaluating visual field loss for glaucomatous changes. Given the importance of macular oedema as a mechanism of visual impairment in uveitis, our results suggest that macular oedema itself is an important endpoint to study in the treatment of uveitis, something that has not been a major feature of recent clinical trials in this area.

Acknowledgments

Financial support: Supported by cooperative agreements from the National Eye Institute to the Mount Sinai School of Medicine (U10 EY 014655), The Johns Hopkins University Bloomberg School of Public Health (U10 EY 014660), and the University of Wisconsin, Madison, School of Medicine (U10 EY 014656).

MUST Grant Support: The project described was supported by cooperative agreements from the National Eye Institute to Mount Sinai School of Medicine (U10 EY 014655), The Johns Hopkins University Bloomberg School of Public Health (U10 EY 014660), and the University of Wisconsin, Madison, School of Medicine (U10 EY 014656). SRJT was supported by the UK National Institute of Health Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the US National Eye Institute, the US National Institutes of Health or the UK National Institute of Health Research. Additional support was provided by Bausch & Lomb, Inc, Rochester, NY.

References

1. Durrani OM, Meads CA, Murray PI. Uveitis: a potentially blinding disease. *Ophthalmologica*. Jul-Aug;2004 218(4):223–236. [PubMed: 15258410]
2. Rothova A, Suttrop-van Schulten MS, Frits Treffers W, Kijlstra A. Causes and frequency of blindness in patients with intraocular inflammatory disease. *Br J Ophthalmol*. Apr; 1996 80(4):332–336. [PubMed: 8703885]
3. Durrani OM, Tehrani NN, Marr JE, Moradi P, Stavrou P, Murray PI. Degree, duration, and causes of visual loss in uveitis. *Br J Ophthalmol*. Sep; 2004 88(9):1159–1162. [PubMed: 15317708]
4. Nussenblatt RB. The natural history of uveitis. *Int Ophthalmol*. Oct; 1990 14(5–6):303–308. [PubMed: 2249907]
5. Sivaprasad S, Ikeji F, Xing W, Lightman S. Tomographic assessment of therapeutic response to uveitic macular oedema. *Clin Experiment Ophthalmol*. Nov; 2007 35(8):719–723. [PubMed: 17997774]
6. Alasil T, Keane PA, Updike JF, et al. Relationship between optical coherence tomography retinal parameters and visual acuity in diabetic macular edema. *Ophthalmology*. Dec; 2010 117(12):2379–2386. [PubMed: 20561684]
7. Brar M, Yuson R, Kozak I, et al. Correlation between morphologic features on spectral-domain optical coherence tomography and angiographic leakage patterns in macular edema. *Retina*. Mar; 2010 30(3):383–389. [PubMed: 20216291]
8. Markomichelakis NN, Halkiadakis I, Pantelia E, et al. Course of macular edema in uveitis under medical treatment. *Ocul Immunol Inflamm*. Mar-Apr;2007 15(2):71–79. [PubMed: 17558831]
9. Markomichelakis NN, Halkiadakis I, Pantelia E, et al. Patterns of macular edema in patients with uveitis: qualitative and quantitative assessment using optical coherence tomography. *Ophthalmology*. May; 2004 111(5):946–953. [PubMed: 15121373]
10. Shukla D, Behera UC, Chakraborty S, Mahalakshmi R, Prasad NM. Serous macular detachment as a predictor of resolution of macular edema with intravitreal triamcinolone injection. *Ophthalmic Surg Lasers Imaging*. Mar-Apr;2009 40(2):115–119. [PubMed: 19320299]
11. Tran TH, de Smet MD, Bodaghi B, Fardeau C, Cassoux N, Lehoang P. Uveitic macular oedema: correlation between optical coherence tomography patterns with visual acuity and fluorescein angiography. *Br J Ophthalmol*. Jul; 2008 92(7):922–927. [PubMed: 18577643]
12. Kiss CG, Barisani-Asenbauer T, Simader C, Maca S, Schmidt-Erfurth U. Central visual field impairment during and following cystoid macular oedema. *Br J Ophthalmol*. Jan; 2008 92(1):84–88. [PubMed: 17591669]
13. Kempen JH, Altaweel MM, Holbrook JT, Jabs DA, Sugar EA. The multicenter uveitis steroid treatment trial: rationale, design, and baseline characteristics. *Am J Ophthalmol*. Apr; 2010 149(4):550–561. e510. [PubMed: 20097325]
14. Callanan DG, Jaffe GJ, Martin DF, Pearson PA, Comstock TL. Treatment of posterior uveitis with a fluocinolone acetonide implant: three-year clinical trial results. *Arch Ophthalmol*. Sep; 2008 126(9):1191–1201. [PubMed: 18779477]

15. Jaffe GJ, Martin D, Callanan D, Pearson PA, Levy B, Comstock T. Fluocinolone acetonide implant (Retisert) for noninfectious posterior uveitis: thirty-four-week results of a multicenter randomized clinical study. *Ophthalmology*. Jun; 2006 113(6):1020–1027. [PubMed: 16690128]
16. Jabs DA, Rosenbaum JT, Foster CS, et al. Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. *Am J Ophthalmol*. Oct; 2000 130(4):492–513. [PubMed: 11024423]
17. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. Sep; 2005 140(3): 509–516. [PubMed: 16196117]
18. Ferris FL 3rd, Kassoff A, Bresnick GH, Bailey I. New visual acuity charts for clinical research. *Am J Ophthalmol*. Jul; 1982 94(1):91–96. [PubMed: 7091289]
19. Ferris FL 3rd, Sperduto RD. Standardized illumination for visual acuity testing in clinical research. *Am J Ophthalmol*. Jul; 1982 94(1):97–98. [PubMed: 7091290]
20. Antcliff RJ, Stanford MR, Chauhan DS, et al. Comparison between optical coherence tomography and fundus fluorescein angiography for the detection of cystoid macular edema in patients with uveitis. *Ophthalmology*. Mar; 2000 107(3):593–599. [PubMed: 10711901]
21. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study research group. *Arch Ophthalmol*. Dec; 1985 103(12):1796–1806. [PubMed: 2866759]
22. Kempen JH, Altaweel MM, Holbrook JT, Jabs DA, Sugar EA. The multicenter uveitis steroid treatment trial: rationale, design, and baseline characteristics. *Am J Ophthalmol*. Apr; 149(4):550–561. e510. [PubMed: 20097325]
23. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. Mar; 1986 42(1):121–130. [PubMed: 3719049]
24. Little, RJ.; Rubin, DB. Statistical Analysis with Missing Data. In: Hoboken, NJ., editor. Statistical Analysis with Missing Data. J. Wiley & Sons Inc; 2002. p. 85-87.
25. Lardenoye CW, van Kooij B, Rothova A. Impact of macular edema on visual acuity in uveitis. *Ophthalmology*. Aug; 2006 113(8):1446–1449. [PubMed: 16877081]
26. de Smet MD, Taylor SR, Bodaghi B, et al. Understanding uveitis: the impact of research on visual outcomes. *Prog Retin Eye Res*. Nov; 2011 30(6):452–470. [PubMed: 21807112]
27. Kiss CG, Barisani-Asenbauer T, Maca S, Richter-Mueksch S, Radner W. Reading performance of patients with uveitis-associated cystoid macular edema. *Am J Ophthalmol*. Oct; 2006 142(4):620–624. [PubMed: 17011854]
28. Charbel Issa P, Helb HM, Holz FG, Scholl HP. Correlation of macular function with retinal thickness in nonproliferative type 2 idiopathic macular telangiectasia. *Am J Ophthalmol*. Jan; 2008 145(1):169–175. [PubMed: 17981256]
29. Jivrajka RV, Kim JK, Fink W, Sadun AA, Sebag J. Quantitative analysis of central visual field defects in macular edema using three-dimensional computer-automated threshold Amsler grid testing. *Graefes Arch Clin Exp Ophthalmol*. Feb; 2009 247(2):165–170. [PubMed: 18958487]
30. Okada K, Yamamoto S, Mizunoya S, Hoshino A, Arai M, Takatsuna Y. Correlation of retinal sensitivity measured with fundus-related microperimetry to visual acuity and retinal thickness in eyes with diabetic macular edema. *Eye (Lond)*. Jul; 2006 20(7):805–809. [PubMed: 16021181]
31. Vujosevic S, Midena E, Pilotto E, Radin PP, Chiesa L, Cavarzeran F. Diabetic macular edema: correlation between microperimetry and optical coherence tomography findings. *Invest Ophthalmol Vis Sci*. Jul; 2006 47(7):3044–3051. [PubMed: 16799051]
32. van Kooij B, Probst K, Fijnheer R, Roest M, de Loos W, Rothova A. Risk factors for cystoid macular oedema in patients with uveitis. *Eye (Lond)*. Feb; 2008 22(2):256–260. [PubMed: 17024221]
33. Lin P, Loh AR, Margolis TP, Acharya NR. Cigarette smoking as a risk factor for uveitis. *Ophthalmology*. Mar; 2010 117(3):585–590. [PubMed: 20036011]
34. Thorne JE, Daniel E, Jabs DA, Kedhar SR, Peters GB, Dunn JP. Smoking as a risk factor for cystoid macular edema complicating intermediate uveitis. *Am J Ophthalmol*. May; 2008 145(5): 841–846. [PubMed: 18321467]

MUST Credit Roster, Key Personnel (MUST certified), 2005 – 2010 (30 July 2010)

Participating Clinical Centres

Duke University, Durham, NC: Glenn J. Jaffe, MD (Director); Michael Cusick, MD; Justis Ehlers. *Former Members:* Claxton Baer, MD; Sai Chavala, MD; Pouya Dayani, MD; Muge Kesen, MD Alex Melamud, MD; Jawad A. Qureshi, MD; Robert F. See, MD; Cindy Skalak; Adrienne Williams Scott; Robert K. Shuler, MD.

Emory University, Atlanta, GA: Sunil Srivastava, MD (Director); Alicides Fernandes, MD. *Former Members:* Deborah Gibbs, COMT; Daniel F. Martin, MD.

Johns Hopkins University, Baltimore, MD: James P. Dunn, MD (Director); Ellen Arnold, BS; Jeff Boring, COA; Diane M. Brown, MSN, RN; Alison G. Livingston, BSN, RN; Kisten Nolan, BSN, MPH, RN; Terry Reed, COA. *Former Members:* Marie-Lynn Belair, MD; Stephen G. Bolton, CRNP; Joseph B. Brodine; Lisa M. Brune, BSN, RN; Anat Galor, MD; Adam Jacobowitz, MD; Meera Kapoor; Sanjay Kedhar, MD; Henry A. Leder, MD; Yavette Morton; George B. Peters, MD, MBA; Priscilla Soto; Ricardo Stevenson, MD; Michelle Tarver-Carr, MD, PhD; Yue Wang, MD; Stephen Kim, MD.

Massachusetts Eye Research and Surgery Institute, Cambridge, MA: C. Stephen Foster, MD (Director); Angelica Contero; Linda Bruner; Kayleigh Fitzpatrick; David M. Hinkle, MD; Jyothir Johnson; Danielle Marvell; Jennifer Pinto. *Former Members:* Sarah Acevedo, MD; Fahd Anzaar, MD; Tom Cesca; Karina Q. Lebron, MD; Chandra Morgan; Nita Patel, MSW; Janet Sprague; Taygan Yilmaz.

National Eye Institute, Bethesda, MD: H. Nida Sen, MD, MHSc (Director); Denise Cunningham, CRA; Chloe Gottlieb, MD; Darryl Hayes, COA; Dessie Koutsandreas, BS, COA; Nupura Krishnadev, MD; Annal D. Meleth, MD; Richard Mercer, COT; Robert B. Nussenblatt, MD; Patti R. Sherry, BSN; Gregory L. Short, COMT; Alana Temple, BSN. *Former Members:* Allison Bamji, RN; Hanna Coleman, MD; Geetani Ali Davuluri, MD; Lisa Faia, MD; Guy V. Jirawuthiworavong, MD; Julie C. Lew, MD; Dominic Obiyor, BSN; Cheryl H. Perry, BSN; Natalia Potapova, MD; Eric Weichel, MD; Keith J. Wroblewski, MD; Steven Yeh, MD.

New York Eye & Ear Infirmary, New York, NY: Paul A. Laskany, MD (Director); Jason Badamo; Jenny Gallardo; Monica Lorenzo-Laskany, MD; Robert Masini; Susan Morell; Ann Nour; Meredith Sanchez; Kate Steinberg. *Former Members:* Kenneth M. Boyd; Jacek Jarczyński; Mirjana McGrosky.

Royal Victorian Eye & Ear Hospital, East Melbourne, Australia: Richard J. Stawell (Director); Lisa Breayley; Julie Ewing; Carly D'Sylva; Lauren Hodgson; Ignatios Koukouras; Lyndell Lim; Cecilia Ling; Rachel McIntosh; Andrew Newton; Richard Smallwood; Ehud Zamir. *Former Members:* Nicola Hunt; Lisa Jones; Suzanne Williams.

Rush University Medical Centre, Chicago, IL: Pauline T. Merrill, MD (Director); Pam Hulvey; Elaine Kernbauer; Scott Toennessen; Denise L. Voskuil-Marre, BS. *Former Members:* Bruce Gaines; Christina Giannoulis; Heena S. Khan, BA; Sarah J. Levine.

Texas Retina Associates, Dallas, TX: Robert C. Wang, MD (Director); Hank Aguado; Sally Arceneaux; Kimberly Cummings; Gary E. Fish, MD; Keith Gray; Nick Hesse; Susie Howden; Diana Jaramillo; Michael Mackens; Karin Mutz; Brenda Sanchez. *Former Members:* Jean Arnwine; David Callanan, MD.

United Kingdom Institute of Ophthalmology, London, UK: Susan Lightman, PhD, FRCOphth (Director); Simon R.J. Taylor, PhD, FRCOphth; Jiten Morarji. *Former Members:* Kate Edwards, Timothy Stubbs, Hamish Towler, Rebecca Tronnberg.

University of California at Los Angeles, Los Angeles, CA: Gary N. Holland, MD (Director); Robert D. Almazan, COA; Jose Castellanos, COT; Jean Pierre Hubschman, MD; Ann K. Johiro, NP; Michael A. Kapamajian, MD; Ralph D. Levinson, MD; Susan S. Ransome, MD. *Former Members:* Christine R. Gonzales, MD; Anurag Gupta, MD; Peter J. Kappel, MD.

University of California at San Diego, San Diego, CA: William R. Freeman, MD (Director); Denine E. Cochran, COT, CCRC; Igor Kozak, MD; Vivian Nguyen; Stephen F. Oster, MD; Debbie Powell, BBA. *Former Members:* Tom Clark, BSc, CRA; Joshua Hedaya, MD; Tiara Kemper; Jacqueline M. LeMoine; Megan E. Loughran, BA; Luzandra Magana; Francesca Mojana, MD; Victoria Morrison, MD.

University of California at San Francisco, San Francisco, CA: Todd P. Margolis, MD (Director); Nisha Acharya, MD; David Clay; Claire M. Khouri, BA; Mary Lew, BA; Jay Stewart, MD; Ira G. Wong, MD. *Former Members:* Salena Lee, BA, OD.

University of Illinois at Chicago, Chicago, IL: Debra A. Goldstein, MD (Director); Marcia Niec; Misel Ramirez; Howard H. Tessler, MD. *Former Members:* Catherine E. Crooke; Dimitry Pyatetsky, MD.

University of Miami, Miami, FL: Janet L. Davis, MD (Director); Thomas Albini, MD; Aura Pacini; David A. Pinto. *Former Members:* Daniela Castaño; Macy Ho; Jaclyn L. Kovach, MD; Susan Pineda; Richard C-S Lin, MD; Jackie K-D Nguyen, MD; Kimberly E. Stepien, MD; Claudia Teran.

University of Michigan, Ann Arbor, MI: Susan G. Elner, MD (Director); Rebecca Brown, COA; Linda Fournier, COA; Julie R. Gothrup, COA; Richard Hackel; Moella Hesselgrave, COA; Robert Prusak; Stephen J. Saxe, MD. *Former Members:* Melissa Bergeron, COA; Reneé Blosser, COMT; Carrie Chrisman-McClure; Deanna Sizemore, COA.

University of Pennsylvania, Philadelphia, PA: John H. Kempen, MD, PhD (Director); Jim Berger; Joan DuPont; Sheri Grand; Dawn McCall; Albert M. Maguire, MD; Laurel Weeny; Daniel Will, MD; Wei Xu. *Former Members:* Tim Hopkins, MD; Monique McRay.

University of South Florida, Tampa, FL: Peter Reed Pavan, MD (Director); JoAnn Leto; Lori Mayor; Kim McDonald; Scott E. Pautler, MD; Wyatt Saxon; Judy Soto. *Former Members:* Maria Ortiz; Dee Dee Szalay.

University of Southern California, Los Angeles, CA: Amani Fawzi, MD; (Director); Lupe Cisneros, COA; Elizabeth Corona; Jackie Douglass; Dean Elliott, MD; Margaret Padilla Narsing A. Rao, MD. *Former Members:* Alexia Aguirre; Lawrence Chong, MD; Rahul Khurana, MD; Jennifer Lim, MD; Rachel Mead; Sylvia Ramos; Julie H. Tsai, MD.

University of Utah, Salt Lake City, UT: Albert Vitale, MD (Director); Paul S. Bernstein, MD, PhD; Bonnie Carlstrom, COA; James Gilman, CRA; Sandra Hanseen, COA; Paula Morris, CRA; Diana Ramirez; Kimberley Wegner, BS, CRC.

Virginia Eye Consultants, Norfolk, VA: John D. Sheppard, MD, MMSc (Director); Brianne Anthony; Lisa Franklin; Krista Hamelin; Stephen V. Scoper, MD; Jeanette Fernandez, COMT; Lisa Felix-Kent, COA; Rebecca Marx. *Former Members:* Nancy

Crawford; Rebecca De La Garza; R. Denise Cole; Jen Martin; Gregory Schultz, DD; Joseph Webb, BS Pamela Yeager.

Vitreoretinal Consultants, Houston, TX: Rosa Y. Kim, MD (Director); Matthew S. Benz, MD; David M. Brown, MD; Eric Chen, MD; Richard H. Fish, MD; Shayla Hay; Jame Major, MD, PhD; Laura Shawver; Tien P. Wong, MD.

Washington University, St. Louis, MO: P. Kumar Rao, MD (Director); Rhonda Weeks. *Former Members:* Rajendra S. Apte, MD; Kevin J. Blinder, MD; Pam Light; Gaurav K. Shah, MD; Russell VanGelder, MD, PhD.

Committees

Executive Committee: Douglas A. Jabs, MD, MBA (Chair); Michael M. Altaweel, MD; Janet T. Holbrook, PhD; John H. Kempen, MD, PhD; Natalie Kurinij, PhD.

Steering Committee: Douglas A. Jabs, MD, MBA (Chair); Robert D. Almanzor, COA; Michael M. Altaweel; Diane Brown; James P. Dunn, MD; James Gilman; Janet T. Holbrook, PhD; Gary N. Holland, MD; John H. Kempen, MD, PhD; Rosa Y. Kim, MD; Natalie Kurinij, PhD; Nancy Prusakowski, MS; Jennifer Thorne, MD. *Former Members:* Stephen G. Bolton, RN, BSN; Lisa M. Brune, RN, BSN; Tom Clark, CRA; Larry Hubbard, MAT; Daniel F. Martin, MD; Robert B. Nussenblatt, MD;.

Data, Safety and Monitoring Committee: Janet Wittes, PhD (Chair); William E. Barlow, PhD; Marc Hochberg, MD; Janet T. Holbrook, PhD; Douglas A. Jabs, MD, MBA; Natalie Kurinij, PhD; Alice T. Lyon, MD; Michael M. Altaweel, MD; Alan G. Palestine, MD; Lee S. Simon, MD; Harmon Smith, PhD. *Former Members:* James T. Rosenbaum, MD.

Surgical Quality Assurance Committee: John H. Kempen, MD, PhD (Chair); James P. Dunn, MD; Glenn J. Jaffe, MD. *Former Members:* Daniel F. Martin, MD.

Medical Therapy Quality Assurance Committee: Jennifer E. Thorne, MD; PhD (Chair); Nisha Acharya, MD; Douglas A. Jabs, MD, MBA; John H. Kempen, MD, PhD; Paul A. Latkany, MD; Robert B. Nussenblatt, MD; Albert Vitale, MD. *Former Members:* Russell VanGelder, MD, PhD.

Visual Function Quality Assurance Committee: Robert D. Almanzor, COA (Chair); Judith Alexander, BA, CCRP; Jeffrey A. Boring, COA; Deborah Gibbs, COMT; Salena Lee, OD, FAAO; Jennifer E. Thorne, MD, PhD (Advisor). *Former Members:* Wai Ping Ng, BS.

Glaucoma Committee: David Friedman, MD (Chair); Anna Adler, MS; Alyce Burke, MPH; Janet T. Holbrook, PhD; Joanne Katz, ScD; John H. Kempen, MD, PhD; Nancy Prusakowski, MS; Susan Reed; Jennifer E. Thorne, MD, PhD. *Former Members:* Nicholas Cohen; Sanjukta Modak, MS; Wai Ping Ng, BS.

Statistical Analysis Committee: Elizabeth Sugar, PhD (Chair); Lea Drye, PhD; Kevin Frick, PhD; Janet T. Holbrook, PhD; JoAnn Katz, ScD; Thomas Louis, PhD; Mark L. Van Natta, MHS. *Former Members:* Sanjukta Modak, MS; David Shade, JD.

Resource Centres

Chairman's Office: Mount Sinai School of Medicine, New York, NY: Douglas A. Jabs, MD, MBA (Study Chairman); Yasmin Hilal, MHS; Melissa A. Nieves, BA; Karen Pascual, MBA; Jill S. Slutsky, MPA. *Former Members:* Maria Stevens, CM; Colby Glomp

University of Pennsylvania, Philadelphia, PA: John H. Kempen, MD, PhD (Study Vice-Chairman).

Coordinating Centre, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD: Janet Holbrook, PhD, MPH (Director); Anna Adler, MS; Judith Alexander; Jeff Boring; Alyce Burke, MPH; Karen Collins; John Dodge; Lea Drye, PhD; Cathleen Ewing; Kevin Frick, PhD; David Friedman, MD, PhD; Rosetta Jackson; Joanne Katz, ScD; Andrea Lears; Hope Livingston; Thomas Louis, PhD; Curtis Meinert, PhD; Jill Meinert; Vinnette Morrison; Deborah Nowakowski; Nancy Prusakowski, MS; Dave Shade, JD; Rochelle Smith; Karen Steuernagle; Elizabeth Sugar, PhD; Jennifer Thorne, MD, PhD; James Tonascia, PhD; Mark Van Natta, MHS; Richard Zheng. *Former Members:* Paul Chen; Nicholas Cohen, MS; Sanjukta Modak, MS; Wai Ping Ng; Weijiang Shen; Charles Shiflett; Ada Tieman, MBA.

Fundus Photograph Reading Centre, University of Wisconsin, Madison, WI: Michael M. Altaweel, MD; Wendy K. Benz, PhD; Geoffrey Chambers, MS; Debra J. Christianson, BS; Amitha Domalpally, MD; Jacquelyn Freund, MS; Vonnice Gama; Sapna Gangaputra, M.D., MPH; Kathleen E. Glander, BBA; Anne Goulding, BA; Jeffrey M. Joyce, MS; Christina N. Kruse, BA; Dawn J. Myers, BS; Susan Reed, BS; James L. Reimers, BA; Amy Remm, BS; Ruth A. Susman, BS; Dennis Thayer; Erika Treichel, DVM; Kelly J. Warren, RN, BS, MSES; Sheila M. Watson, BS, DVM; James K. White, BME; Tara Wilhelmson, BS. *Former Members:* Margaret A. Fleischli, AB, DVM; Dennis Hafford; Susan E. Harris, MS; Larry D. Hubbard, MAT; Kristine A. Johnson; Lauren Nagle; Gwyn E. Padden-Lechten, BS; Alyson Pohlman, BA; Peggy Sivesind; Mary K. Webster, BS; Grace Zhang, BA.

National Eye Institute, Bethesda, MD: Natalie Kurinij, PhD.

Figure 1. Representative OCT images obtained from the trial

OCT images indicating: cystoid spaces without retinal thickening (central macular thickness < 240 μm; left panel), diffuse macular thickening with central macular thickness > 240 μm, but no cyst formation (middle panel), and cystoid macular oedema with both cystoid spaces and central macular thickness > 240 μm (right panel).

Table 1

Baseline demographic and disease characteristics for cases of uveitis enrolled in the MUST trial, stratified by macular oedema (ME) status.

Characteristics	No ME (N = 221)	Cystoid spaces (N = 56)	Diffuse ME (N = 42)	Cystoid ME (N = 107)	P-value
Age at enrolment (years)					
Median (25th to 75th %-tile)	44.8 (31.7 to 52.7)	45.0 (35.0 to 54.6)	53.3 (38.6 to 62.6)	54.9 (49.9 to 65.4)	< 0.01
Duration of uveitis (years)					
Median (25th to 75th %-tile)	3.4 (1.0 to 6.9)	3.0 (0.8 to 8.0)	4.9 (1.0 to 8.7)	4.0 (1.3 to 9.8)	0.21 ^a
Missing			2 (4.8%)	4 (3.7%)	
Gender: N(%)					
Male	24.0% (53/221)	25.0% (14/56)	33.3% (14/42)	23.4% (25/107)	0.72
Female	76.0% (168/221)	75.0% (42/56)	66.7% (28/42)	76.6% (82/107)	
Race/ethnicity: N(%)					
White	52.0% (115/221)	58.9% (33/56)	71.4% (30/42)	56.1% (60/107)	0.06 ^b
Non-white	48% (106/221)	41.1% (23/56)	28.6% (12/42)	43.9% (47/107)	
Hispanic	14.5% (32/221)	16.1% (9/56)	2.4% (1/42)	14.0% (15/107)	
Black	28.1% (62/221)	21.4% (12/56)	19.0% (8/42)	24.3% (26/107)	
Other	5.4% (12/223)	3.6% (2/56)	7.1% (3/42)	5.6% (6/107)	
Smoking status: N(%)					
Never	47.1% (104/221)	46.4% (26/56)	52.4% (22/42)	40.2% (43/107)	0.90
Former	20.4% (45/221)	23.2% (13/56)	19.0% (8/42)	32.7% (35/107)	
Current	32.6% (72/221)	30.4% (17/56)	28.6% (12/42)	27.1% (29/107)	
Any systemic inflammatory disease: N(%)					
No	72.0% (157/218)	74.5% (41/55)	78.6% (33/42)	74.8% (80/107)	0.80
Yes	28.0% (61/218)	25.5% (14/55)	21.4% (9/42)	25.2% (27/107)	
Missing	1.4% (3/221)	1.8% (1/56)			
Uveitis at baseline: N(%)					
Unilateral	3.6% (8/221)	0% (0/0)	9.5% (4/42)	11.2% (12/107)	n/a
Bilateral	96.4% (213/221)	100% (56/56)	90.5% (38/42)	88.8% (95/107)	
Type of uveitis: N(%)					
Posterior or panuveitis	62.9% (139/221)	73.2% (41/56)	64.3% (27/42)	57.0% (61/107)	0.27
Intermediate	37.1% (82/221)	26.8% (15/56)	35.7% (15/42)	43.0% (46/107)	

Characteristics	No ME (N = 221)	Cystoid spaces (N = 56)	Diffuse ME (N = 42)	Cystoid ME (N = 107)	P-value
Active uveitis: N(%)^c					
No	28.2% (62/220)	21.8% (12/55)	26.2% (11/42)	8.4% (9/107)	< 0.01
Yes	71.8% (158/220)	78.2% (43/55)	73.8% (31/42)	91.6% (98/107)	
Missing	0.5% (1/221)	1.8% (1/56)			
Lens status: N(%)					
Phakic without cataract	33.9% (75/221)	21.4% (12/56)	7.1% (3/42)	14.0% (15/107)	< 0.01
Cataract	29.4% (65/221)	37.5% (21/56)	40.5% (17/42)	29.9% (32/107)	
Pseudophakic or aphakic	36.7% (81/221)	41.1% (23/56)	52.4% (22/42)	56.1% (60/107)	
History of glaucoma: N(%)					
No	90.5% (200/221)	92.9% (52/56)	88.1% (37/42)	94.4% (101/107)	0.87
Yes	9.5% (21/221)	7.1% (4/56)	11.9% (5/42)	5.6% (6/107)	
Prior filtration surgery: N(%)					
No	93.2% (204/219)	96.4% (53/55)	95.1% (39/41)	93.5% (100/107)	0.43
Yes	6.8% (15/219)	3.6% (2/55)	4.9% (2/41)	6.5% (7/107)	
Missing	0.9% (2/221)	1.8% (1/56)	2.4% (1/42)		
Vitreous haze: N(%)					
0	37.4% (80/214)	38.2% (21/55)	31.0% (13/42)	19.0% (20/105)	< 0.01
1+	62.6% (134/214)	61.8% (34/55)	69.0% (29/42)	81% (85/105)	
Missing	3.2% (7/221)	1.8% (1/56)		1.9% (2/107)	
Prior vitrectomy: N(%)					
No	92.8% (205/221)	94.6% (53/56)	83.3% (35/42)	88.8% (95/107)	0.37
Yes	7.2% (16/221)	5.4% (3/56)	16.7% (7/42)	11.2% (12/107)	
Epiretinal membrane: N(%)^d					
No	83.2% (183/220)	90.9% (50/55)	61.5% (24/39)	61.9% (65/105)	< 0.01
Yes	16.8% (37/220)	9.1% (5/55)	38.5% (15/39)	38.1% (40/105)	
Missing	0.5% (1/221)	1.8% (1/56)	7.1% (3/42)	1.9% (2/107)	
Chorioretinal lesions: N(%)					
No	51.8% (99/191)	43.8% (21/48)	45.5% (15/13)	57.1% (52/91)	0.91
Yes	48.2 (92/191)	56.3% (27/48)	54.5% (18/33)	42.9% (39/91)	
Missing	13.6% (30/221)	14.3% (8/56)	21.4% (9/42)	15% (16/107)	

MUST Trial, Multicenter Uveitis Steroid Treatment Trial; ME, Macular oedema; P-values were generated using generalized estimating equations (GEE) to adjust for the between eye correlation for individuals with bilateral uveitis;

^a Log transformation was used to compare duration of uveitis among macular oedema categories due to skewness;

^b P-value based upon comparison of white versus non-white individuals;

^c Note that the inclusion criteria included eyes with active or recently active (within 60 days) non-infectious intermediate, posterior, or panuveitis, so enrolled eyes could have inactive uveitis at baseline and one or both enrolled eyes of patients with bilateral disease could have inactive uveitis at baseline;

^d Epiretinal membrane diagnoses are based upon a consensus grading of OCT images and Colour Fundus Photographs.

Table 2

Baseline visual acuity and visual field automated perimetry for eyes with uveitis enrolled in the MUST* trial stratified by macular oedema status.

Outcome	No ME [†] (N = 221)	Cystoid spaces (N = 56)	Diffuse ME [†] (N = 42)	Cystoid ME [†] (N = 107)	P-value [‡]
Visual Acuity (Standard letters)					
Median (25th to 75th %tile)	79.1 (63.1 to 85.1)	74.1 (57.1 to 80.1)	66.1 (40.1 to 75.1)	60.1 (46.1 to 71.1)	< 0.01
Missing	2 (0.9%)	1 (1.8%)			
20/40 or better	69.4% (152/219)	54.5% (30/55)	38.1% (16/42)	29.9% (32/107)	< 0.01
20/100 or worse	11.0% (24/219)	18.2% (10/55)	31.0% (13/42)	33.6% (36/107)	< 0.01
20/200 or worse	7.8% (17/219)	10.9% (6/55)	21.4% (9/42)	13.1% (14/107)	0.14
Visual field automated perimetry (Mean deviation)					
Median (25th to 75th %tile), dB	-4.4 (-7.3 to -2.4)	-5.2 (-11.6 to -2.8)	-5.5 (-11.1 to -3.3)	-5.4 (-9.2 to -3.4)	0.03
Missing	2 (0.9%)		2 (4.8%)	4 (3.7%)	
Mild impairment (> -3 dB)	32.4% (71/219)	26.8% (15/56)	20.0% (8/40)	18.4% (19/103)	0.03
Moderate impairment (-3 dB to -6 dB)	34.7% (76/219)	30.4% (17/56)	35.0% (14/40)	34.0% (35/103)	
Severe impairment (< -6 dB)	32.9% (72/219)	42.9% (24/56)	45.0% (18/40)	47.6% (49/103)	
Missing	0.9% (2/221)		4.8% (2/42)	3.7% (4/107)	

MUST Trial, Multicenter Uveitis Steroid Treatment Trial; ME, Macular oedema. P-values were generated using generalized estimating equations (GEE) to adjust for between eye correlation for individuals with bilateral disease.

Table 3

Change in visual acuity associated with clinical characteristics of macular edema and potential confounders.

Characteristics	Unadjusted		Adjusted	
	Estimated change, standard letters (95% CI)	P-value	Estimated change, standard letters (95% CI)	P-value
Cystoid spaces	-10.7 (-15.5 to -5.9)	<0.01	-4.2 (-9.9 to 1.4)	0.14
Retinal thickness 240	-14.2 (-18.5 to -9.8)	<0.01	-8.8 (-14.0 to -3.6)	<0.01
Age (per 10 years)	-3.8 (-5.4 to -2.2)	<0.01	-1.8 (-3.4 to -0.2)	0.02
Cataract	-11.3 (-16.6 to -6.0)	<0.01	-6.9 (-11.9 to -1.8)	<0.01
Aphakic/pseudophakic	-18.7 (-23.9 to -13.5)	<0.01	-6.1 (-11.7 to -0.5)	0.03
Vitreous haze 1+	-6.2 (-11.1 to -1.4)	0.01	-3.2 (-7.8 to 1.4)	0.16
Active uveitis	-4.9 (-10.4 to 0.7)	0.08	0.04 (-5.3 to 5.4)	0.99
Race/ethnicity: non-white	-4.9 (-9.9 to 0.2)	0.06	-6.2 (-10.6 to -1.8)	<0.01
Time since uveitis diagnosis (per year)	-1.0 (-1.4 to -0.6)	<0.01	-0.7 (-1.2 to -0.3)	<0.01
Prior vitrectomy	-16.0 (-25.0 to -6.9)	<0.01	-9.4 (-17.8 to -1.1)	0.03
Chorioretinal lesions	-8.2 (-13.3 to -3.2)	<0.01	-7.1 (-11.7 to -2.5)	<0.01

The following factors were not found to be significantly associated with visual acuity: gender (P=0.55), smoking (P=0.63), a history of systemic disease (P=0.93) or glaucoma (P=0.24), the presence of an epiretinal membrane (P=0.12).

Table 4

Risk of greater impairment in visual field mean deviation associated with clinical characteristics of macular oedema and potential confounders.

Characteristics	Unadjusted		Adjusted	
	OR of greater impairment (95% CI)	P value	OR of greater impairment (95% CI)	P value
Retinal thickness 240	1.81 (1.26 to 2.58)	< 0.01	1.85 (1.20 to 2.84)	< 0.01
Age (per 10 years)	1.71 (1.07 to 2.73)	0.01	1.13 (0.96 to 1.32)	0.12
Cataract	1.71 (1.07 to 2.73)	0.02	1.82 (1.09 to 3.03)	0.02
Aphakic/pseudophakic	3.12 (1.99 to 4.89)	< 0.01	2.41 (1.40 to 4.15)	< 0.01
Active uveitis	1.03 (0.67 to 1.59)	0.89	0.96 (0.60 to 1.54)	0.88
Race/Ethnicity: Non-white	2.90 (2.00 to 4.19)	< 0.01	3.10 (2.03 to 4.72)	< 0.01
Time since uveitis diagnosis (per year)	1.03 (0.99 to 1.06)	0.06	1.00 (0.90 to 1.03)	0.92
Individual diagnosed with posterior/panuveitis	1.96 (1.35 to 2.82)	< 0.01	1.37 (0.90 to 2.08)	0.14
Chorioretinal lesions	3.65 (2.43 to 5.47)	< 0.01	3.42 (2.19 to 5.32)	< 0.01

OR, Odds Ratio. Vitreous haze (p = 0.66), gender (p = 0.94), smoking (p = 0.89), systemic disease (p = 0.88), prior vitrectomy (p = 0.67), epiretinal membrane (p = 0.73), and history of glaucoma (p = 0.21) were not significantly associated with greater impairment in mean deviation. Cystoid spaces were not significantly associated with greater impairment in mean deviation after adjusting for the other variables in the model (adjusted OR: 1.21, 95% CI: 0.76 to 1.91, p = 0.41).