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Quality of Life Outcomes from a Randomized Clinical Trial Comparing Antimetabolites for Intermediate, Posterior, and Panuveitis

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Abstract

Purpose—To evaluate the changes in quality of life in noninfectious uveitis patients treated with two of the most commonly prescribed antimetabolite treatments.

Design—Secondary analysis of a multicenter, block-randomized, clinical trial (ClinicalTrials.gov NCT01232920).

Methods—Eighty patients at Aravind Eye Hospitals in Madurai and Coimbatore, India, with noninfectious intermediate, posterior, or panuveitis were randomized to receive oral methotrexate, 25 mg weekly, or oral mycophenolate mofetil, 1 g twice daily, and were followed up monthly for 6 months. Best-corrected visual acuity, IND-VFQ, and SF-36 were obtained at enrollment and at 6 months (or prior in the event of early treatment failure).

Results—IND-VFQ scores, on average, increased by 9.2 points from trial enrollment to 6 months (95% CI: 4.9, 13.5, P=0.0001). While the SF-36 physical component summary score did not significantly differ over the course of the trial, the mental component summary score decreased by 2.3 points (95% CI: −4.4, −0.1, P=0.04) and the vitality subscale decreased by 3.5 points (95% CI: −5.6, −1.4, P=0.001). Quality of life scores did not differ between treatment arms. Linear regression modeling showed a 3.2 point improvement in IND-VFQ score for every 5 letter improvement in visual acuity (95% CI: 1.9, 4.3; P<0.001).

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Conclusions—Although uveitis treatment was associated with increased vision and vision-related quality of life, patient-reported physical health did not change after 6 months of treatment, and, mental health decreased. Despite improved visual outcomes, uveitis patients receiving systemic immunosuppressive therapy may experience a deterioration in mental health-related quality of life.

INTRODUCTION

Quality of life has long been recognized as a key health indicator for the measurement of general and vision-related health outcomes, providing a more comprehensive understanding of the patient experience than traditional ophthalmologic benchmarks, such as visual acuity.[1–4] Visual impairment, particularly in a patient's most productive years, can lead to difficulty securing employment and reliance upon others for completing daily activities.[5] While eye conditions such as cataracts, glaucoma, and macular degeneration primarily affect older adults, uveitis affects people of all ages.[6] Uveitis can also be a chronic disease that requires ongoing immunosuppressive therapy, which may produce many negative systemic effects. Patient-reported quality of life, therefore, is an important health outcome for this population.

Various instruments have been used to measure general health-related (HRQoL) and vision-related (VRQoL) quality of life in uveitis patients, including the Medical Outcomes Study 36-item Short Form Survey (SF-36), EuroQol survey (EQ-5D), and adaptations of the National Eye Institute Visual Function Questionnaire (NEI-VFQ), such as the Indian Vision Function Questionnaire (IND-VFQ).[7–9] Previous studies have demonstrated that patients with uveitis have a lower quality of life compared to the general population[7,10–13] and, in some cases, a lower quality of life compared to patients with other eye conditions.[14,15] Studies on quality of life in patients with noninfectious uveitis requiring systemic immunosuppressant therapy, however, have been limited in number and have typically explored populations on heterogeneous medication regimens.

In a randomized clinical trial of noninfectious intermediate, posterior, and panuveitis patients in India, participants were randomized to receive one of two corticosteroid-sparing antimetabolite treatments: methotrexate or mycophenolate mofetil.[16] The primary outcome of the trial was measured as steroid-sparing control of inflammation in both eyes at 5 and 6 months. This secondary analysis of data from this trial is the first to compare quality of life measures in patients randomized to two of the most commonly used steroid-sparing treatments for noninfectious uveitis. We aim to evaluate the changes in quality of life with antimetabolite therapy and assess the impact of treatment arm, visual acuity, and control of inflammation on HRQoL and VRQoL outcomes.

METHODS

Study Design

The multicenter, block-randomized, comparative effectiveness trial (ClinicalTrials.gov: NCT01232920) enrolled patients with noninfectious uveitis at two uveitis clinics in Aravind Eye Hospitals located in Madurai and Coimbatore, India. The Institutional Review Boards at

the University of California, San Francisco and Aravind Eye Hospitals approved the study. All patients provided written informed consent. Eligible patients were 16 years old, had noninfectious anterior and intermediate, intermediate, posterior, or panuveitis that was active within the last 60 days in at least one eye, and met criteria for starting immunosuppressive therapy.

Participants were randomized to receive oral methotrexate, 25 mg weekly, or oral mycophenolate mofetil, 1 g twice daily, and were followed up monthly for 6 months. The dosing and administration of study medications were chosen to reflect current treatment practices.[17–20] Of note, the oral methotrexate dose chosen in this study was on the higher end of current accepted practice, while mycophenolate mofetil was not dosed at the maximum accepted dose of 1.5 g twice daily.[21] If patients experienced intolerable symptoms or non-serious adverse events, the maintenance dose could be reduced by two levels. The primary outcome, described below, was assessed by masked examiners.

Treatment Outcome

Treatment success was defined as achieving the following in both eyes at 5 and 6 months: 1) 0.5+ anterior chamber cells, 0.5+ vitreous cells, 0.5+ vitreous haze, and no active retinal or choroidal lesions 2) 10 mg of prednisone and 2 drops of prednisolone acetate 1% a day and 3) no declaration of treatment failure because of intolerability or safety. Further details regarding the methodology of the trial have been published previously.[16]

Quality of Life Measures

Patients completed two quality of life questionnaires, the Indian Vision Function Questionnaire (IND-VFQ) and the Medical Outcomes Study 36-Item Short Form Survey (SF-36v2), at enrollment and at 6 months (or at the time of treatment failure if before the 6-month visit). A clinical coordinator who was unmasked to each subject's treatment administered the questionnaires. Translation services at Aravind Eye Hospital, Madurai translated the SF-36 from English into Tamil and the Tamil version of the IND-VFQ was used. Treating physicians were not present during administration of the questionnaires.

The IND-VFQ is an adaptation of the NEI-VFQ, developed by researchers in India to be applicable in an Indian cultural context.[22,23] The IND-VFQ contains 33 questions divided into three scales: general functioning scale (21 questions, each with five response options), psychosocial impact scale (five questions, each with four response options), and visual symptoms scale (seven questions, each with four response options).[24] For each scale, a summary score was created by summing the response within the scale, dividing by the maximum possible score, and multiplying by 100 to obtain a scale of 0 (worst) to 100 (best). An overall composite score on a scale of 0–100 was calculated as the mean of the scores for the three categories. The Tamil version of the IND-VFQ has been validated for use in south Indian uveitis patients.[23]

The SF-36v2 contains 36 questions with items assessing the respondent's self-perception of their physical health and mental health.[25] The physical health component consists of the following domains: physical functioning, role limitations caused by physical health, bodily pain, and general health perceptions. The mental health component consists of the domains:

vitality (energy and fatigue), general mental health (psychological distress), role limitations because of emotional problems, and social functioning limitations because of emotional problems. Scores are on a 0–100 scale, with a lower score indicating more disability, and normalized to a US population. Scores for each of the eight domains and for the physical and mental component summary scores were calculated using QualityMetric Health Outcomes™ Scoring Software v4.5.[26] The Tamil translation was found to be reliable with acceptable internal consistency in a Malaysian population.[27] Normative values for the SF-36 in India are unknown.

Visual Acuity

The visual acuity measurement protocol in our study was adapted from the Age-Related Eye Disease Study.[28] Best corrected visual acuity (BCVA) was measured by masked examiners using a tumbling "E" chart at 4 meters to obtain a logarithm of the minimum angle of resolution (logMAR) value. If the patient was not able to see the chart at 4 meters, they were moved to a distance of 1 meter. If the patient could not read the chart at 1 meter, counting fingers was assessed at 1 meter, hand motion at 0.5 meters, and light perception at 0.5 meters. The logMAR scale was developed to standardize visual acuity measurement. Each line contains 5 letters and the size of letters in each row is decreased in a uniform, step-wise fashion so that each line represents 0.10 log unit. Low visual acuity states were recorded as follows: counting fingers (logMAR = 1.7), hand motion (1.8), light perception (1.9), and no light perception (2.0). BCVA from the better seeing uveitic eye was used in analysis.

Statistical Analysis

The Wilcoxon rank-sum test was used to compare IND-VFQ and SF-36 summary and subscale scores between groups. Non-parametric testing was used for these measures, as the distribution of scores was non-normal. Paired t-tests were used to estimate the average change in scores over time. The estimated difference in change scores between treatment arms and between treatment outcomes (success versus failure), controlling for drug, were analyzed using regression models. Association between IND-VFQ and SF-36 scores and visual acuity were assessed with Spearman rank correlation analysis. Linear regression models were used to estimate the relationship between change in quality of life scores and change in visual acuity (by number of ETDRS letters read) controlling for age, gender, occupation, and study drug. Statistical tests were all 2-sided, using $P<0.05$ as significant. Data were analyzed using Stata 13 (StataCorp LP, College Station, TX) and R (The R Project for Statistical Computing, Version 3.0.2, available at: http://www.r-project.org/).

RESULTS

Forty-one patients were randomized to methotrexate and 39 to mycophenolate mofetil. Of the 68 patients who completed the study, 67 (35 methotrexate, 32 mycophenolate mofetil) completed questionnaires both at enrollment and at 6 months, or at treatment failure if prior to 6 months. The demographics and baseline characteristics of the study population can be seen in Table 1 and are reported in further detail elsewhere.[16]

Vision-related Quality of Life

The IND-VFQ total composite score increased from baseline by an average of 9.2 points for all patients (95% CI: 4.9, 13.5; P=0.0001). All IND-VFQ subscale scores had a mean improvement over the course of the trial (Table 2). There was no statistically significant difference in the change in composite or subscale scores by drug (Table 3).

While patients with treatment success had, on average, a 5 point higher increase in VFQ composite score over time, this was not statistically significant (Table 4). The same held true for all VFQ subscales, which did not demonstrate statistically significant differences by treatment outcome. There were no differences in VFQ scores based on anatomic location (intermediate versus posterior or panuveitis). Most patients had bilateral disease and laterality did not have an effect on quality of life scores.

Over the course of the 6 months, the better seeing eye improved by 8.5 ETDRS letters (95% CI: 5.8, 13.1; P<0.001). IND-VFQ scores were correlated with BCVA (P=0.005, Spearman correlation coefficient=0.34). For every 5 letter increase in the better seeing eye, on average, the IND-VFQ composite score improved by 3.2 points (95% CI: 1.9, 4.3; P<0.001, R-squared=0.38) (Figure 1). Treatment assignment was not significantly associated with changes in BCVA.

Health-related Quality of Life

There was no significant change in physical HRQoL from baseline to 6 months, as assessed by the SF-36 physical component summary (PCS) score (average change: 0.5 points; 95% CI: −1.2, 2.2; P=0.58). There was, however, a 2.3 point decrease in the mental component summary (MCS) score over the course of the trial (95% CI: −4.4, −0.1; P=0.04).

Between treatment arms, patients taking methotrexate had a significantly lower PCS score at baseline (P=0.04) but there was no statistically significant change in PCS score by drug (Table 2) and no significant difference in PCS scores at 6 months (P=0.36). There was no difference in MCS scores between medications.

While the change in PCS score from baseline was not statistically different by treatment outcome, the change in general health subscale score of the PCS was, on average, 4.3 points higher for patients that met criteria for treatment success compared to those who did not (95% CI: 0.3, 8.2; P=0.04). There was no difference in MCS scores by treatment outcome.

Overall, the vitality score of the mental health component decreased by an average of 3.5 points (95% CI: −5.6, −1.4; P=0.001). While treatment failures exhibited a 3.4 point larger average decline in vitality domain scores compared to treatment successes, this difference was not statistically significant (95% CI: 0.7, −7.4; P=0.10). No other SF-36 subscale scores were significantly different over time, between drugs, or between treatment outcomes.

DISCUSSION

Patients in both treatment arms demonstrated a significant overall improvement in visual acuity and visual function, as assessed by the IND-VFQ. Primary outcome results from the

trial showed no significant difference between the two antimetabolite treatments in corticosteroid-sparing control of inflammation, time to corticosteroid-sparing control of inflammation, change in BCVA, or resolution of macular edema.[16] The findings in this secondary analysis are consistent with this outcome, demonstrating no difference in self-reported visual function between patients taking methotrexate and mycophenolate mofetil.

The increase in vision-related quality of life with both antimetabolite treatments is consistent with the increases seen when patients are started on other steroid-sparing immunosuppressive treatment, such as in the MUST trial and studies on biologic drugs.[9,29–31] Both patients who met criteria for treatment success and those who did not had overall improvements in visual function scores that did not significantly differ. An explanation for this finding is that patients who did not meet all criteria for treatment success may still have had improvements in inflammation, leading to increased VRQoL scores during the trial.

There was a significant association between IND-VFQ composite scores and BCVA, consistent with other studies.[32,33] Each 5-letter improvement in BCVA corresponded to a 3.2-point improvement in IND-VFQ composite score, a significant change, though thresholds for clinically meaningful change have not been defined in this instrument. This association is comparable to the relationship found between NEI-VFQ scores and BCVA in the Multicenter Uveitis Steroid Treatment (MUST) trial (3.65 points for every line increase in vision, compared to the 3.2 points per line seen in this study).[34] Although the association between vision-related quality of life and BCVA was statistically significant, the correlation was weak. Patients with uveitis may experience floaters and flashes that impair visual function, without decreasing visual acuity. Other measures of visual performance, such as color vision and glare, were not assessed and these factors could have also impacted patients' self-reported visual function.

The increase in VRQoL after antimetabolite treatment was not paralleled in the HRQoL, as measured by SF-36 scores. The physical component summary score did not significantly differ between baseline and 6 months of treatment. The mental health component summary score showed a mild decrease in scores over the course of the trial. Other studies on the effect of systemic treatment on health-related quality of life in uveitis patients have had mixed results. The MUST trial found no change, and even decreases in some measures of HRQoL, while the use of infliximab in patients with Behcet's disease was associated with a significant increase in HRQoL.[8,9]

In uveitis, the treatment of disease is complicated by a heavy side effect burden that may account for the lack of change, and even decreases, in HRQoL. Of the 41 patients in the methotrexate arm, 33 patients reported headache, nausea, diarrhea, fatigue, vomiting, or systemic infection. Of the 39 patients in the mycophenolate mofetil arm, 32 patients reported headache, fever, diarrhea, fatigue, or systemic infection, as reported previously.[16] Additionally, all patients were exposed to high doses of corticosteroids prior to enrollment and remained on corticosteroids, though tapered to a low dose, throughout the trial. Long-term corticosteroid use carries its own side effects, which may have prevented patients' overall quality of life from improving.[35,36] These non-vision effects of systemic uveitis

treatment may account for the lack of increase in HRQoL, despite treatment of ocular inflammation.

Some of these side effects may be reflected in the vitality domain of the SF-36, which assesses a patient's energy level or fatigue. Fatigue is a well-documented adverse effect of the medications used in this study.[16,37–39] It is also a symptom that patients find extremely distressing and can have a significant negative impact on quality of life.[40] Over the course of our trial, the vitality scores decreased by an average of 3.2 points for all patients.

Patients that achieved treatment success had a greater improvement in the general health subscale of the physical health component of the SF-36, compared to patients who were considered treatment failures. The general health domain of the SF-36 assesses patients' perceptions of their health state, how their health state compares to other people, and whether they expect their health to worsen. The decrease in general health score that occurred in patients that did not achieve corticosteroid-sparing control of uveitis may be due to the fact that some patients who failed treatment continued to have uveitis symptoms, while also experiencing the side effects of their medications, lowering their perceived health state from baseline. The perception of disease state may also have been impacted by the positive or negative reinforcement that patients received from clinical evaluators.

When interpreting results, it is important to take into consideration the clinical impact of a change, in addition to statistical significance. The concept of the minimum clinically important difference (MCID) has been developed to guide decisions regarding patient-reported outcome measures, given that a statistically significant change may not necessarily suggest a clinically important change.[41,42] For the SF-36, the MCID is generally defined as a 3–5 point difference in scores, though the MCID may vary across subscale scores.[43] The slight decrease in MCS score over the course of the trial does not reach this threshold, and may not represent a clinically significant decrease in mental health quality of life. The 3.5 point decrease in vitality score seen in this trial does meet the SF-36 threshold for MCID. However, literature regarding the vitality domain specifically has shown that the MCID can vary widely amongst health states and is generally set at a 5 point difference in scores.[44,45] So, while statistically significant, our results may not reflect a clinically meaningful decrease in the patient's vitality.

While the MCID of the general health subscale score has not been thoroughly studied, the 4.3 point difference found in this study between patients that achieved treatment success and those who failed meets the MCID threshold for the SF-36 and is within range of the general health perception MCID in other disease states.[46] The difference in scores between patients with treatment success and patients with treatment failure, therefore, may represent a clinical difference in quality of life. Patients that achieved corticosteroid-sparing control of uveitis experienced a greater improvement in perception of their general health than those who did not, bolstering the necessity of controlling ocular inflammation in uveitis patients.

This study is the first randomized trial to compare the effectiveness of two of the most commonly used antimetabolites for treating noninfectious uveitis. Strengths of this trial include its prospective, randomized design with standardized treatment regimens and

assessments. Limitations include power and generalizability. The small sample size, decided on for feasibility considerations, may have limited our power to detect changes in quality of life and differences in quality of life measures between groups. Another limitation of the study was that the patients enrolled had a variety of uveitis etiologies, as it was not feasible to enroll patients with a single diagnosis. Different uveitis etiologies and associated systemic conditions may have varying impacts on quality of life. The dosing of medications may have impacted our results. While methotrexate was dosed at the high end of accepted practice, mycophenolate mofetil was not and it is possible that differences in quality of life by treatment arm may have been observed if a higher dose had been used. Because the patients were enrolled from a single hospital system in India, our study may also be limited in its generalizability. Though there are no known differences in response to uveitis treatment by race, variant cultures may have different perceptions of quality of life and how it is affected by treatment. Socioeconomic factors may also have influenced patient-reported quality of life in this study.

This study was also limited by available instruments of quality of life assessment. While the IND-VFQ was developed for Indian patients, the SF-36 questionnaire was developed for a US population and may not adequately assess the general or mental health of Indian patients.[47] In addition, neither the IND-VFQ nor the SF-36 is tailored specifically to uveitis patients. These questionnaires may miss key components of the impact that noninfectious uveitis has on a patient's quality of life. These patients not only live with a complex disease, characterized by heterogeneous presentations, but also require long-term treatment that can have many systemic side effects. Their experience, therefore, may not be adequately captured by available measures. Developing and validating questionnaires for uveitis patients may be able to capture specific factors that affect visual function within this particular group and more accurately assess their quality of life and how it changes with treatment.

CONCLUSION

In this study, antimetabolite uveitis treatment was associated with significant increases in visual acuity and VRQoL. The decreases in patients' mental health functioning and vitality suggest that uveitis treatments can negatively affect patients' HRQoL. For uveitis patients that require immunosuppressive therapy, monitoring mental health function, in addition to visual outcomes, may be advisable because of the potential impact uveitis and its treatment has on health-related quality of life.

Acknowledgments

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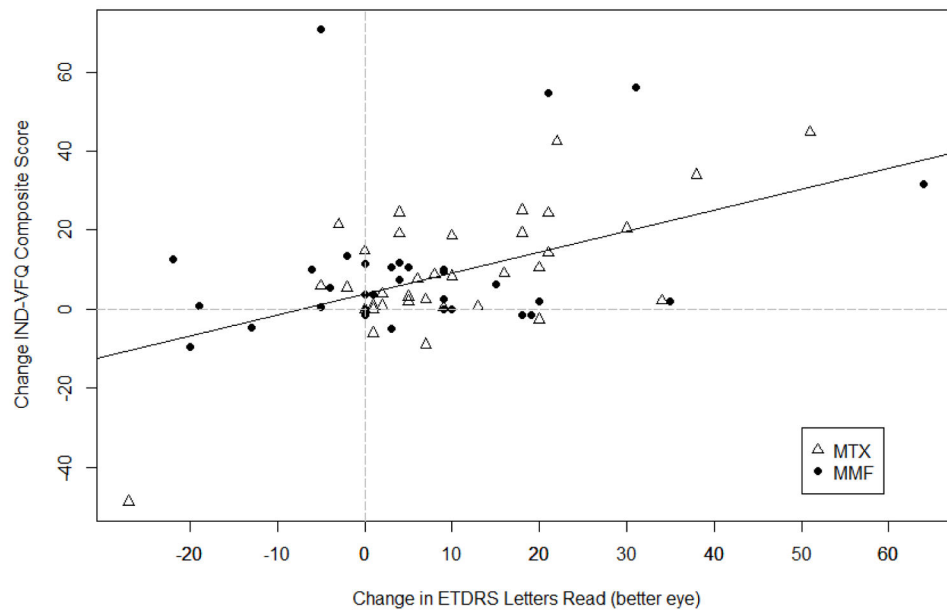**Figure 1.**
Scatterplot of change in visual acuity (letters read) and change in IND-VFQ composite score by treatment arm, with fitted regression line (R-squared=0.38, p<0.001).
Abbreviations used: MTX, methotrexate; MMF, mycophenolate mofetil

Table 1

Patient demographic and clinical characteristics at baseline

	Methotrexate N (%)	Mycophenolate Mofetil N (%)	P value
Age mean years (SD)	38.6 (10.3)	40.2 (14.2)	0.57
Female	26 (63%)	22 (56%)	0.65
Occupation			0.52
Agricultural Worker	4 (10%)	6 (15%)	
Non-agricultural worker	32 (78%)	27 (69%)	
Student	2 (5%)	4 (10%)	
Retired	0 (0%)	1 (3%)	
Unemployed	3 (7%)	1 (3%)	
Uveitis Diagnosis			0.09
Vogt-Koyanagi-Harada Disease	27 (66%)	16 (41%)	
Idiopathic	3 (7%)	4 (10%)	
Sympathetic Ophthalmia	4 (10%)	4 (10%)	
Pars Planitis	0 (0%)	6 (15%)	
Behcet's Disease	3 (7%)	3 (8%)	
Retinal Vasculitis	1 (2%)	1 (3%)	
Sarcoidosis	0 (0%)	2 (5%)	
Non-Granulomatous Panuveitis	2 (5%)	2 (5%)	
Serpiginous Choroiditis	0 (0%)	1 (3%)	
Granulomatous Panuveitis	1 (2%)	0 (0%)	
Laterality of Uveitis			0.05
Bilateral	37 (90%)	28 (72%)	
Anatomic Location[a]			0.02
Anterior and Intermediate/Intermediate	3 (7%)	11 (28%)	
Posterior/Panuveitis	38 (93%)	28 (72%)	

Abbreviations used: SD, standard deviation

[a]Anatomic location was assessed given all medical records available.

Table 2

Visual acuity and quality of life scores at baseline and 6 months

	Baseline		6 months[a]		P value[b]
	Median	IQR	Median	IQR	
Visual acuity[c]					
logMAR	0.25	(0.02 – 0.40)	0	(−0.080 – 0.1)	<0.001
Snellen equivalent	20/32	(20/21 – 20/50)	20/20	(20/16 – 20/25)	
IND-VFQ					
Composite Score	87.5	(73.4 – 94.6)	94.6	(87.1 – 99.6)	<0.001
General Functioning	94	(83.3 – 97.6)	97.6	(94.0 – 100.0)	<0.001
Psychosocial Impact	86.6	(66.7 – 100.0)	93.3	(59.9 – 100.0)	0.001
Visual Symptoms	76.1	(66.6 – 90.5)	90.5	(80.9 – 100.0)	<0.001
SF-36					
Physical Component Summary Score	53.2	(50.6 – 55.8)	55.2	(50.6 – 57.8)	0.58
Mental Component Summary Score	54.6	(49.4 – 58.6)	53.8	(44.9 – 57.5)	0.03

Abbreviations used: IQR, interquartile range; logMAR, logarithm of the minimum angle of resolution; IND-VFQ, Indian Vision Function Questionnaire; SF-36, Medical Outcomes Study 36-Item Short Form Survey

[a]Scores at 6 months or at treatment failure if before the 6-month visit

[b]P value from Wilcoxon signed-rank test

[c]Visual acuity of the better seeing uveitic eye

Table 3

IND-VFQ and SF-36 scores by treatment arm

	Methotrexate		Mycophenolate mofetil		Estimated Treatment Effect (MTX: MMF)		P value
	Median	IQR	Median	IQR	Mean	(95% CI)	
IND-VFQ							
Composite Score							
Baseline	87.8	(73.4, 94.0)	87.5	(76.0, 95.6)			
6 months[a]	94.4	(85.1, 99.0)	94.8	(87.4, 99.8)	−1.8	(−10.4, 6.8)	0.68
SF-36							
Physical Component Summary Score							
Baseline	52.1	(49.3, 55.0)	54.7	(52.2, 57.5)			
6 months[a]	56.2	(50.3, 59.1)	53.8	(51.1, 57.5)	2.8	(−0.5, 6.1)	0.10
Mental Component Summary Score							
Baseline	54.7	(50.9, 57.8)	53.8	(48.6, 57.8)			
6 months[a]	53.7	(44.9, 57.2)	54.5	(44.7, 57.8)	1.4	(−3.0, 5.7)	0.54

Abbreviations used: IND-VFQ, Indian Vision Function Questionnaire; SF-36, Medical Outcomes Study 36-Item Short Form Survey; MTX, methotrexate; MMF, mycophenolate mofetil; IQR, interquartile range; CI, confidence interval

[a]Scores at 6 months or at treatment failure if before the 6-month visit

Table 4

IND-VFQ and SF-36 scores by treatment outcome

	Treatment Success[a]		Treatment Failure		Estimated Difference		P value
	Median	IQR	Median	IQR	Mean	(95% CI)	
IND-VFQ							
Composite Score							
Baseline	87.5	(74.1,95.2)	87	(88.8, 100)			
6 months[b]	96	(70.4,93.1)	91.4	(79.9, 98.2)	5	(−3.8, 13.7)	0.26
SF-36							
Physical Component Summary Score							
Baseline	53.2	(51.4, 57.2)	53.6	(50.0, 55.4)			
6 months[b]	57.2	(53.6, 58.2)	52	(47.2, 55.7)	3	(−0.4, 6.3)	0.08
Mental Component Summary Score							
Baseline	55.6	(50.0, 59.5)	53.6	(49.0, 56.7)			
6 months[b]	53.9	(45.7, 57.8)	53.8	(42.2, 57.1)	0.5	(−3.7, 4.7)	0.80

Abbreviations used: IND-VFQ, Indian Vision Function Questionnaire; SF-36, Medical Outcomes Study 36-Item Short Form Survey; IQR, interquartile range; CI, confidence interval

[a] Treatment success defined as corticosteroid-sparing control of inflammation in both eyes at 5 and 6 months

[b] Scores at 6 months or at treatment failure if before the 6-month visit