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The impact of ocrelizumab on health-related quality of life in individuals with multiple sclerosis

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Abstract

Background: Ocrelizumab is approved for the treatment of both relapsing and progressive multiple sclerosis (MS).

Objective: To examine the impact of ocrelizumab on health-related quality of life (HRQOL) in individuals with MS.

Methods: Ninety-eight individuals with relapsing and 32 with progressive MS were enrolled. Participants were administered a battery of patient-reported outcome (PRO) measures at their first ocrelizumab infusion, and infusions at 6 and 12 months. PRO measures included the Medical Outcomes Study SF-36 and Neuro-QoL.

Results: At baseline, participants had low mean scores across HRQOL domains. After 12 months, increases were observed on SF-36 Role-Physical, General Health, Vitality, Role-Emotional, Mental health and Mental Component Summary. On Neuro-QoL, improvements were seen in Positive Affect, Anxiety, Emotional and Behavioral Dyscontrol and Fatigue. Several demographic and clinical characteristics were associated with HRQOL at baseline. The strongest associations were between physical HRQOL measures and measures of MS disability. Associations between the longitudinal change in HRQOL scores and baseline demographic and clinical characteristics were mild.

Conclusions: We observed significant improvements across multiple mental HRQOL domains at 12 months in individuals treated with ocrelizumab. These findings support the use of HRQOL measures to provide a subjective measure of treatment impact that complements traditional outcomes.

Keywords: Multiple sclerosis, ocrelizumab, patient-reported outcome measures, health-related quality of life

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Introduction

Interferon beta-1b was approved by the Food and Drug Administration (FDA) for the treatment of multiple sclerosis (MS) in 1993.[1] Since then, the number of approved MS disease modifying therapies (DMTs) has grown to more than 15. These drugs were approved based on their ability to decrease relapse rates, reduce the number of new brain and spinal cord lesions and slow disability progression in individuals with MS.[1–7] In 2017, ocrelizumab, an anti-CD20 monoclonal antibody, was the first drug approved for the treatment of both relapsing and primary progressive forms of MS. In two identical, randomized controlled trials (RCTs), OPERA I and OPERA II,[8] participants with relapsing MS (RMS) were randomized to receive ocrelizumab or interferon beta-1a. In both trials, treatment with ocrelizumab significantly reduced the annualized relapse rate, mean number of gadolinium-enhancing lesions on MRI, and proportion of participants with 12-week and 24-week confimed disability progression. In ORATORIO,[9] a separate RCT for individuals with primary progressive MS (PPMS), participants were randomized 2:1 to receive ocrelizumab or placebo. Treatment with ocrelizumab

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was associated with lower rates of clinical and MRI progression.

In addition to the standard clinical outcome measures (i.e., relapse rate, new and/or enhancing lesions on MRI, confirmed disability progression) used to evaluate the efficacy of ocrelizumab, the phase III trials also included patient-reported outcome (PRO) measures. These measures were used to capture the participant's subjective experience of health status. OPERA I, OPERA II and ORATORIO gave participants the Medical Outcomes Study Short Form-36 (SF-36),[10] a generic health-related quality of life (HRQOL) questionnaire. The Physical Component Summary (PCS) of the SF-36 was selected as the secondary outcome measure. PCS is an aggregate of the eight scale scores derived from the SF-36. These scales include Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. In OPERA I, the mean change in SF-36 PCS in the ocrelizumab-treated participants did not differ from the mean change in the INFB-1a-treated group at 96 weeks. In OPERA II, the adjusted mean change was higher in the ocrelizumab than IFNB-1a-treated group at the end of the 96-week trial. There was no difference in the adjusted mean change in SF-36 PCS between ocrelizumab and placebo groups in the ORATORIO trial at 120 weeks. Although there are several advantages to relying on the physical summary scale rather than the eight scale scores of the SF-36 including smaller confidence intervals, smaller floor and ceiling effects and a smaller number of analyses required which avoids a reduction in statistical power,[11] the use of a single summary score did not allow for a detailed analysis of the effects of ocrelizumab on specific HRQOL domains that may be of particular interest to individuals with neurologic disease.[12]

In this study, we examined the impact of ocrelizumab on HRQOL in individuals with MS using both SF-36 and Neuro-QoL.[13] Neuro-QoL is a validated PRO developed as part of a National Institutes of Health-supported measurement system to assess HRQOL in patients with chronic neurological diseases. By including both SF-36 and Neuro-QoL, we were able to compare our findings with results from the phase III ocrelizumab clinical trials as well as examine HRQOL across a wide range of symptom-focused, domain-specific physical, mental and social outcomes of particular relevance to individuals with MS.

Methods

Participants

Patients at the Brigham Multiple Sclerosis Center in Boston, MA who were prescribed ocrelizumab by their treating physician as part of clinical care were eligible to participate in this study. Additional inclusion criteria included age 18–65 years and diagnosis of relapsing or progressive MS according to the revised McDonald criteria.[14] Patients with concomitant autoimmune or inflammatory diseases, ongoing treatment with other immunomodulatory medications, previous treatment with rituximab, methotrexate, cyclophosphamide, mitoxantrone, or mycophenolate mofetil in the last five years, previous treatment with alemtuzumab, pregnancy or lactation, active hepatitis B virus infection or hypersensitivity to ocrelizumab were excluded.

Recruitment letters were sent to all eligible patients prior to the start of ocrelizumab treatment. Interested individuals were asked to call a member of the research staff to learn about the study in more detail. After one week, if patients had not called study staff, study staff called them directly to discuss their interest in participating in the study. One hundred and thirty individuals contributed to this analysis, and their baseline characteristics including age, sex, disease duration, disability status, disease course, previous treatment and reason for treatment switching were extracted from the medical record. Baseline demographic and clinical features are provided in Table 1. This study was approved by the Partners Human Research Committee and all participants provided written informed consent.

Procedures

Participants in the study were administered a battery of PRO measures using iPads at their first ocrelizumab infusion (enrollment), and at their infusions at 6 and 12 months. In addition, participants provided blood samples for immunologic analyses that will be reported separately. PRO measures were accessed through REDCap. REDCap is a free, secure, web-based application for electronic collection and management of research and clinical data. It was developed by Vanderbilt University in collaboration with a multi-institutional consortium and is hosted by Partners HealthCare Research Computing, Enterprise Research Infrastructure & Services (ERIS). Data collection is customized for each study or clinical trial by the research team with guidance from ERIS REDCap administrators. The following PRO measures were included:

Table 1. Baseline demographic characteristics of study participants.

N	130
Female (N (%))	85 (65.4)
Age at visit (mean (SD))	46.7 (8.7)
Disease duration at visit (mean (SD))	14.4 (9.8)
EDSS (median (range))	2.5 (0, 8)
Disease category	
Relapsing MS (N (%))	98 (76%)
Secondary progressive (N (%))	24 (18%)
Primary progressive (N (%))	8 (6%)
Previous treatment	
Aubagio	10
Avonex	2
Betaseron	3
Cellcept	1
Copaxone	24
Cytoxan	1
Gilenya	25
IVIG	2
Plegridy	3
Rebif	3
Tecfidera	34
Tysabri	8
Untreated	14
Reason for switching treatment*	
Allergy	1
Disease progression	47
Financial issue	1
Finished protocol	1
MRI activity	14
Non-compliance	2
Patient intolerance	5
Patient preference	22
Pregnancy	4
Relapses	8
Side effects	16
First treatment	14
No information	12

*Subjects could have multiple reasons for switching treatment so the total number of reasons is greater than 130.

1. Medical Outcomes Study SF-36: The SF-36 is a generic, HRQOL questionnaire developed as part of the Medical Outcomes Study. It provides scores across 8 domains (Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, Mental Health) as well as two summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS).
2. Neuro-QoL: Neuro-QoL is a set of self-report measures developed through a collaborative, multisite research initiative sponsored by the National Institute of Neurological Disorders and Stroke to construct psychometrically-sound and clinically-relevant HRQOL tools for individuals with neurological conditions such as MS, stroke and Parkinson's disease. It covers 11 domains including Ability to Participate in Social Roles and Activities, Anxiety, Cognitive Function, Depression, Emotional and Behavioral

Table 2. Baseline statistics and longitudinal change for SF-36 measures.

	Baseline mean (SD)	Estimated change per year after initiation of ocrelizumab (estimate (95% CI); p-value)
Physical Functioning	38.4 (13.2); n = 101	0.6; 95% CI: −0.7, 1.8; p = 0.378
Role-Physical	37.3 (11.6); n = 100	**2.5; 95% CI: 0.2, 4.7; p = 0.033**
Bodily Pain	44.1 (11.6); n = 106	0.9; 95% CI: −0.8, 2.6; p = 0.292
General Health	38.7 (9.8); n = 104	**1.7; 95% CI: 0.1, 3.2; p = 0.035**
Vitality	39.3 (10.7); n = 105	**2.1; 95% CI: 0.5, 3.7; p = 0.011**
Social Functioning	44.2 (10.3); n = 104	0.5; 95% CI: −1.3, 2.3; p = 0.579
Role-Emotional	40.0 (11.7); n = 103	**3.9; 95% CI: 1.6, 6.2; p = 0.001**
Mental Health	46.8 (9.7); n = 105	1.5; 95% CI: −0.1, 3.1; p = 0.059
Physical Component Summary	37.7 (11.0); n = 89	1.0; 95% CI: −0.5, 2.5; p = 0.205
Mental Component Summary	45.1 (9.6); n = 89	**2.4; 95% CI: 0.5, 4.3; p = 0.013**

Bold values indicate statistically significant associations ($p < 0.05$).

Dyscontrol, Fatigue, Lower Extremity Function, Positive Affect and Well-Being, Satisfaction with Social Roles and Activities, Stigma and Upper Extremity Function. The computer adaptive testing (CAT) version of Neuro-QoL was used.

Statistical analysis

The baseline descriptive statistics were reported for each of the SF-36 and Neuro-QoL domains. The longitudinal change after initiation of ocrelizumab was estimated using a linear mixed model with study time as a fixed effect and a random intercept to account for correlation of observations within a participant. All available data from the three time points (enrollment, 6 months and 12 months) were included in the analysis. The estimate, 95% confidence interval and p-value for the coefficient of study time is reported.

In addition, the associations between five patient characteristics (sex, age, disease duration, EDSS score and disease category at baseline) and baseline SF-36 and Neuro-QoL scores were estimated using linear regression. The regression coefficient corresponds to the group difference in mean HRQOL score for sex and disease category, and the regression coefficient corresponds to the change in the mean HRQOL score for a one-unit increase in age, disease duration and EDSS score. Finally, the association between the five patient characteristics and longitudinal change in SF-36 and Neuro-QoL scores was estimated using a linear mixed model with fixed effects for study time, the characteristic of interest, and the interaction between study time and the characteristic of interest and a random intercept. The coefficient for the interaction was the focus of the analysis. All statistical analyses were completed in the statistical package R version 3.6.3 (www.r-project.org).

Results

The baseline summary SF-36 scores and longitudinal change are presented in Table 2. Participants had low mean scores across all SF-36 domains, indicating that patients initiating ocrelizumab had impairment in HRQOL. In terms of 1-year longitudinal change, increases were observed on Role-Physical, General Health, Vitality, Role-Emotional and MCS, largely the mental components of the SF-36.

The association between baseline demographic/clinical characteristics and SF-36 scores are provided in Supplementary Table 1. Age, EDSS and progressive disease category were each associated with several SF-36 domains, though the strongest associations were with the Physical Functioning subscale and PCS. The association between the longitudinal change in SF-36 scores and the baseline demographic/clinical characteristics are provided in Table 3. Progressive status at baseline was associated with greater increases in Role-Physical, Social Functioning, Role-Emotional and MCS; higher EDSS score at baseline was associated with greater increases in Role-Physical and Social Functioning.

The baseline summary statistics and longitudinal change in Neuro-QoL scores are presented in Table 4. As with the SF-36, impairment was observed on several scores at baseline. In terms of longitudinal change, improvements were observed on Positive Affect and Well-being, Anxiety, Emotional and Behavioral Dyscontrol and Fatigue. These domains are related to mental HRQOL which

Table 3. Association between baseline patient characteristics and longitudinal change in SF-36 measurements over one year.

	Female	Age at baseline (10 year increase)	Disease duration at baseline (10 year increase)	EDSS score at baseline	Progressive disease category at baseline
Physical Functioning	−0.5; 95% CI: −3.1, 2.0; p = 0.679	−1.1; 95% CI: −2.6, 0.4; p = 0.15	−0.2; 95% CI: −1.4, 1.0; p = 0.761	0.5; 95% CI: −0.2, 1.2; p = 0.155	0.4; 95% CI: −2.6, 3.3; p = 0.815
Role-Physical	−1.2; 95% CI: −5.9, 3.6; p = 0.63	2.1; 95% CI: −0.6, 4.8; p = 0.122	**2.3; 95% CI: 0.0, 4.5; p = 0.049**	**1.4; 95% CI: 0.2, 2.6; p = 0.025**	**6.4; 95% CI: 1.1, 11.8; p = 0.019**
Bodily Pain	−2.0; 95% CI: −5.5, 1.4; p = 0.249	1.2; 95% CI: −0.8, 3.2; p = 0.221	0.4; 95% CI: −1.3, 2.1; p = 0.64	0.3; 95% CI: −0.6, 1.2; p = 0.473	−1.1; 95% CI: −5.2, 3.0; p = 0.609
General Health	−1.0; 95% CI: −4.2, 2.3; p = 0.564	−0.3; 95% CI: −2.2, 1.6; p = 0.76	−0.1; 95% CI: −1.6, 1.5; p = 0.948	0.7; 95% CI: −0.1, 1.6; p = 0.096	1.0; 95% CI: −2.9, 4.8; p = 0.626
Vitality	1.0; 95% CI: −2.4, 4.4; p = 0.553	1.3; 95% CI: −0.7, 3.2; p = 0.199	1.0; 95% CI: −0.6, 2.6; p = 0.233	0.8; 95% CI: −0.0, 1.7; p = 0.061	1.8; 95% CI: −2.2, 5.8; p = 0.379
Social Functioning	0.5; 95% CI: −3.3, 4.3; p = 0.784	1.8; 95% CI: −0.4, 3.9; p = 0.103	1.1; 95% CI: −0.7, 2.9; p = 0.234	**1.1; 95% CI: 0.1, 2.0; p = 0.029**	**4.5; 95% CI: 0.1, 8.9; p = 0.045**
Role-Emotional	−2.4; 95% CI: −7.3, 2.4; p = 0.323	0.6; 95% CI: −2.2, 3.3; p = 0.688	1.1; 95% CI: −1.2, 3.4; p = 0.358	1.2; 95% CI: −0.0, 2.5; p = 0.053	**5.8; 95% CI: 0.1, 11.4; p = 0.045**
Mental Health	−0.2; 95% CI: −3.4, 3.1; p = 0.928	−1.2; 95% CI: −3.1, 0.7; p = 0.216	0.2; 95% CI: −1.4, 1.9; p = 0.759	0.3; 95% CI: −0.6, 1.2; p = 0.517	−0.9; 95% CI: −4.9, 3.1; p = 0.66
Physical Component Summary	−0.7; 95% CI: −3.8, 2.4; p = 0.653	1.4; 95% CI: −0.3, 3.2; p = 0.114	1.0; 95% CI: −0.5, 2.5; p = 0.186	0.6; 95% CI: −0.2, 1.4; p = 0.148	1.5; 95% CI: −2.2, 5.2; p = 0.415
Mental Component Summary	−0.8; 95% CI: −4.6, 3.1; p = 0.701	0.4; 95% CI: −1.9, 2.6; p = 0.751	0.9; 95% CI: −0.9, 2.8; p = 0.323	0.9; 95% CI: −0.1, 2.0; p = 0.076	**4.7; 95% CI: 0.1, 9.2; p = 0.044**

Bold values indicate statistically significant associations ($p < 0.05$).

Table 4. Baseline statistics and longitudinal change for Neuro-QoL.

	Baseline mean (SD)	Estimated change per year after initiation of ocrelizumab (estimate (95% CI); p-value)
Higher scores indicate better function		
Ability to Participate in Social Roles and Activities	48.9 (7.4); n = 126	−0.6; 95% CI: −1.6, 0.5; p = 0.277
Cognitive Function	44.5 (7.9); n = 116	0.6; 95% CI: −0.6, 1.8; p = 0.299
Lower Extremity Function	44.1 (9.6); n = 121	0.4; 95% CI: −0.6, 1.4; p = 0.421
Positive Affect and Well-being	53.2 (6.2); n = 117	**1.4; 95% CI: 0.3, 2.4; p = 0.011**
Satisfaction with Social Roles and Activities	45.9 (6.7); n = 117	0.1; 95% CI: −0.9, 1.2; p = 0.811
Upper Extremity Function	45.3 (9.0); n = 117	−0.9; 95% CI: −2.0, 0.3; p = 0.151
Lower scores indicate better function		
Anxiety	53.5 (7.3); n = 124	**−1.4; 95% CI: −2.5, −0.2; p = 0.018**
Depression	47.7 (5.7); n = 124	−0.1; 95% CI: −1.0, 0.8; p = 0.791
Emotional and Behavioral Dyscontrol	51.0 (8.7); n = 122	**−1.5; 95% CI: −2.8, −0.2; p = 0.026**
Fatigue	52.0 (8.1); n = 122	**−1.7; 95% CI: −2.8, −0.7; p = 0.001**
Stigma	50.9 (6.3); n = 119	−1.0; 95% CI: −2.0, 0.0; p = 0.051

Bold values indicate statistically significant associations ($p < 0.05$).

are consistent with the domains that showed improvement on the SF-36. For each of these Neuro-QoL domains, the observed increase was slightly more than 1 point per year.

As with the SF-36, participants with more advanced disease were observed to have worse HRQOL at baseline across several Neuro-QoL domains including Ability to Participate in Social Roles, Lower Extremity Function, Satisfaction with Social Roles and Activities, Upper Extremity Function and Stigma (Supplementary Table 2). There were limited associations between baseline clinical/demographic characteristics and longitudinal change across the Neuro-QoL domains (Table 5).

Discussion

We found that prior to starting treatment with ocrelizumab, individuals with MS demonstrated deficits in multiple domains on both generic and neurologic-disease specific measures of HRQOL. These findings are consistent with previous studies showing lower HRQOL in MS compared to the general population[15] and individuals with other neurologic diseases.[16] After 12 months of treatment with ocrelizumab, improvements in fatigue, anxiety and positive affect were observed. Interestingly, most of the observed changes were on the mental rather than the physical components of HRQOL. This suggests that improvements may not have been due to a reduction in physical disability alone. In addition, improvements were in domains that have proved to be difficult to address in MS. Fatigue, for example, is a commonly reported MS symptom that is associated with significant patient morbidity[17] including reduced worked productivity,[18] but is poorly measured in routine clinical visits. Improvements in fatigue were noted on both SF-36 (Vitality) and Neuro-QoL (Fatigue) and although this finding requires further validation, it may be important to consider when assessing the clinical impact of ocrelizumab.

In phase III clinical trials of ocrelizumab, the SF-36 PCS was used as a secondary outcome measure. In OPERA I and ORATORIO, there were no differences in the mean change on SF-36 PCS between ocrelizumab-treated participants and IFNB-1a-treated participants at the end of the trials. In OPERA II, the adjusted mean change was higher in the ocrelizumab than IFNB-1a-treated group at 96 weeks. Since ocrelizumab RCTs were designed and powered to detect differences in relapse rates and sustained disability progression, secondary outcomes may have been limited to one PRO, and changes in secondary outcomes may have failed to achieve statistical significance.[12] It is not clear why PCS was chosen over MCS in the ocrelizumab trials. Additional observational studies are required to assess the impact of ocrelizumab across a wider range of HRQOL

Table 5. Association between baseline patient characteristics and longitudinal change in Neuro-QoL measurements over one year.

	Female	Age at baseline (10 year increase)	Disease duration at baseline (10 year increase)	EDSS score at baseline	Progressive disease category at baseline
Higher scores indicate better function					
Ability to Participate in Social Roles and Activities	2.0; 95% CI: −0.1, 4.1; p = 0.057	0.4; 95% CI: −0.8, 1.5; p = 0.538	0.3; 95% CI: −0.7, 1.4; p = 0.55	0.5; 95% CI: −0.1, 1.0; p = 0.112	1.7; 95% CI: −0.8, 4.2; p = 0.176
Cognitive Function	0.6; 95% CI: −1.9, 3.1; p = 0.634	−0.2; 95% CI: −1.6, 1.2; p = 0.821	0.2; 95% CI: −1.0, 1.4; p = 0.717	0.4; 95% CI: −0.3, 1.1; p = 0.259	1.5; 95% CI: −1.5, 4.5; p = 0.336
Lower Extremity Function	−0.9; 95% CI: −2.9, 1.1; p = 0.381	−0.5; 95% CI: −1.6, 0.7; p = 0.425	0.6; 95% CI: −0.4, 1.6; p = 0.217	0.1; 95% CI: −0.4, 0.6; p = 0.74	0.0; 95% CI: −2.4, 2.4; p = 0.984
Positive Affect and Well-being	0.4; 95% CI: −1.9, 2.6; p = 0.751	−0.4; 95% CI: −1.6, 0.8; p = 0.53	0.3; 95% CI: −0.8, 1.4; p = 0.586	0.5; 95% CI: −0.1, 1.1; p = 0.076	−0.6; 95% CI: −3.2, 2.0; p = 0.659
Satisfaction with Social Roles and Activities	1.2; 95% CI: −1.1, 3.5; p = 0.295	−0.2; 95% CI: −1.4, 1.1; p = 0.77	0.7; 95% CI: −0.4, 1.7; p = 0.23	0.5; 95% CI: −0.1, 1.1; p = 0.129	1.7; 95% CI: −0.9, 4.4; p = 0.202
Upper Extremity Function	0.6; 95% CI: −1.8, 3.1; p = 0.612	−0.6; 95% CI: −1.9, 0.8; p = 0.401	−0.2; 95% CI: −1.4, 1.0; p = 0.72	0.4; 95% CI: −0.3, 1.0; p = 0.256	1; 95% CI: −1.9, 3.9; p = 0.483
Lower scores indicate better function					
Anxiety	−1.9; 95% CI: −4.2, 0.5; p = 0.122	−0.3; 95% CI: −1.6, 1.0; p = 0.613	**−1.3; 95% CI: −2.4, −0.1; p = 0.027**	−0.3; 95% CI: −1.0, 0.3; p = 0.28	−0.5; 95% CI: −3.3, 2.4; p = 0.752
Depression	1.1; 95% CI: −0.8, 3.1; p = 0.243	0.5; 95% CI: −0.6, 1.6; p = 0.355	−0.6; 95% CI: −1.5, 0.3; p = 0.217	0.2; 95% CI: −0.3, 0.7; p = 0.467	−0.3; 95% CI: −2.6, 2.0; p = 0.78
Emotional and Behavioral Dyscontrol	1.4; 95% CI: −1.4, 4.1; p = 0.338	−0.5; 95% CI: −2.0, 1.1; p = 0.529	−0.5; 95% CI: −1.8, 0.9; p = 0.49	−0.3; 95% CI: −1.0, 0.4; p = 0.435	−0.1; 95% CI: −3.4, 3.2; p = 0.939
Fatigue	−0.8; 95% CI: −3.0, 1.3; p = 0.451	−0.2; 95% CI: −1.4, 1.0; p = 0.783	−0.9; 95% CI: −1.9, 0.2; p = 0.101	−0.2; 95% CI: −0.8, 0.3; p = 0.428	−0.8; 95% CI: −3.4, 1.8; p = 0.535
Stigma	−0.4; 95% CI: −2.5, 1.7; p = 0.699	0.2; 95% CI: −0.9, 1.4; p = 0.706	−0.3; 95% CI: −1.3, 0.7; p = 0.544	−0.4; 95% CI: −0.9, 0.2; p = 0.184	0.1; 95% CI: −2.4, 2.5; p = 0.964

Bold value indicates statistically significant association ($p<0.05$).

domains. The evaluation of ocrelizumab under real-life as opposed to experimental conditions will also help to improve our understanding of the clinical impact of ocrelizumab.

Previous research has demonstrated the impact of DMTs on HRQOL in MS. In an RCT of oral teriflunomide that included SF-36 as an outcome measure, there was no between-group difference from baseline to last visit on the PCS, but there was a significant between-group difference from baseline to last visit on the MCS for participants receiving teriflunomide 14 mg compared to placebo.[19] The effects of dimethyl fumarate on HRQOL were evaluated in a secondary analysis of CONFIRM, an RCT comparing dimethyl fumarate 240 mg twice daily, dimethyl fumarate 240 mg three times daily and glatiramer acetate.[20] A higher proportion of participants in the active treatment arms had clinically significant change in both SF-36 PCS and SF-36 MCS at two years. These findings support the inclusion of HRQOL measures in the evaluation of DMTs to provide a subjective measure of treatment impact.

We found that several baseline demographic and clinical characteristics were associated with HRQOL at baseline, and the strongest associations were between physical HRQOL measures and measures of MS disability (EDSS and progressive disease). When we estimated the association between baseline features and longitudinal change in HRQOL measures, the associations were generally mild, especially when considering the large number of comparisons that were completed. The main differences showed that participants with progressive disease had greater increases on several mental scales of the SF-36 including Social Functioning, Role-Emotional and MCS. For individuals with primary progressive disease, access to the first FDA-approved therapy for the treatment of primary progressive MS may have resulted in an increase on mental HRQOL variables. For secondary progressive patients who have failed other DMTs, enthusiasm for ocrelizumab may have also played a role. Associations between increased disability and longitudinal change were not observed for Neuro-QoL.

This study has several limitations. First, this was a single arm observational study and not an RCT. RCTs are considered the gold standard for assessing the effectiveness of a DMT. Although single arm observational studies can provide valuable information regarding the clinical impact of DMTs because each patient is compared to him- or herself, they have been shown in some instances to overestimate treatment effects. This may be the explained by the placebo effect that occurs when an individual knowingly starts a new and more effective treatment.[21] Studies that include comparator DMTs are needed to strengthen the argument that the observed improvements in HRQOL were due to ocrelizumab. Second, the changes in HRQOL observed after initiation of ocrelizumab may have been driven in part by participants' experiences with prior treatments.[12] Unfortunately, given the large number of reasons provided for treatment switching and the small number of participants in each group, it was not possible to explore this question more fully. In addition, the small number of newly treated patients made it impossible to compare the impact of ocrelizumab on treatment-naïve compared to treatment-experienced participants. Future studies will be needed to understand the relationship between treatment initiation or switching and changes in HRQOL in MS. Third, this was a 12-month study. It is not known whether the improvements in HRQOL seen over 12 months would remain stable, and future studies should include longer follow-up periods. Fourth, although we observed statistically significant changes in HRQOL domains after 12 months of ocrelizumab therapy, the mean change from baseline remained small. Future work is required to determine the minimum difference required for an individual to experience meaningful change.[12]

In summary, we examined the impact of ocrelizumab on HRQOL in individuals with MS. There were significant improvements across multiple mental HRQOL domains at 12 months. The positive impact of ocrelizumab on fatigue may be particularly important to investigate in future studies given its prevalence among MS patients. Although Phase III trials continue to focus on traditional outcome measures including relapse rate, new MRI lesions and confirmed disability progression, the addition of HRQOL measures contributes to a fuller understanding of the impact of DMTs and may play an important role in clinical decision-making.

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Supplemental material

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