Comparison of Time to Clinically Meaningful Improvement in Neuro-QoL Domains in Patients Treated with Natalizumab Versus Ocrelizumab


Mellen Center for Multiple Sclerosis and Cellular Therapeutics; Clinical Core; Louis Ruizer Center for Brain Health, Las Vegas, NV, USA; Mellen Center for Multiple Sclerosis, Cleveland, OH, USA; Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Department of Neurology, University of Rochester Medical Center, Rochester, NY, USA; University Hospital Carl Gustav Carus, Dresden, Germany; Rigoni, Cambridge, MA, USA; at this time of study.

INTRODUCTION

• An understanding of change over repeated phases in physical, mental, and social health after initiation of multiple sclerosis (MS) disease-modifying therapies (DMTs) is important in optimizing treatment.
• Natalizumab and combination therapies are highly efficacious DMTs approved to treat relapsing-remitting and relapsing forms of MS, respectively [1, 2].
• In previous assessment of relapsing-remitting and relapsing forms of MS, patient self-assessed quality of life in Neuro-Qol (Neuro-QoL) domains following treatment [3, 4] observed in 1:2 Neuro-QoL, domain with natalizumab and in 1:2 of domains with natalizumab [4].
• Little is known about the time to improvement in quality of life (QoL) domains.

AIM

• To assess time to improvement in each Neuro-QoL domain for patients treated with natalizumab compared to that for those treated with ocrelizumab.

METHODS

Patient cohorts

• Eight DMTs are included in the MS Patient-Advancing Technology and Health Outcomes (MS PATHS) network as of July 2020, including treatments other than natalizumab or ocrelizumab while enrolled in the MS PATHS network, and that had at least one Neuro-QoL assessment in the prior 2 years.
• Patients with primary progressive MS, prior treatment with natalizumab or combination therapies, missing baseline covariates, no follow-up QoL assessments after baseline, and/or a baseline Neuro-QoL score ≤ 50 were excluded. Patients Determination of Disease Stages (PDSD) score, number of relapses in the prior year, Prior Risk (20): Risk of Average Mental Activity (MMAT) score, use of prior DMTs, use of opad medication, and the corresponding baseline Neuro-QoL score were also excluded.
• In addition, for each Neuro-QoL domain, a sensitivity analysis was conducted using a 2:1 matching of natalizumab and ocrelizumab patients.

Outcomes and analyses

• Trainers for 12 Neuro-QoL domains were obtained at routine visits through the MS PATHS network.
• Baseline characteristics were obtained at the last Neuro-QoL measurement of year prior to initiating treatment with natalizumab or ocrelizumab.
• Events were defined as a clinically meaningful improvement in T-score.
• Clinically meaningful improvement in T-score was defined as a change of 10 points or more in the baseline, previously identified as the threshold for minimally important differences in patient-reported quality of life in clinical practice.
• Event times were defined as the interval between the last visit before baseline assessment and the PDSD point improvement was measured.
• Times to clinically meaningful improvement in T-score were measured using Kaplan-Meier analysis.
• Times to clinically meaningful improvement in T-score were measured using Cox proportional hazards analysis, with events being “censored” for patients who remained in the study.

RESULTS

• There were 486 natalizumab and 632 ocrelizumab MS PATHS patients eligible for the analysis (Table 1).
• Baseline Neuro-QoL differences between treatment groups exhibited differences in baseline covariates (Table 2).
• Median (IQR) MS duration, 14.43 (14.00-15.87) years.
• Matched sample size: 244.
• Matched Neuro-QoL domains (Table 3).
• Time to clinically meaningful improvement in T-score was significantly shorter with natalizumab than with ocrelizumab in 1:2 PS matched patients (ever event ratio: 0.50, 95% CI: 0.33-0.74, P = 0.002).

Table 1. Baseline characteristics of MS PATHS patients treated with natalizumab or ocrelizumab.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Natalizumab (n=244)</th>
<th>Ocrelizumab (n=486)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.72 (1.54)</td>
<td>55.08 (1.17)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>139/105</td>
<td>239/147</td>
</tr>
<tr>
<td>MS duration</td>
<td>14.43 (2.84)</td>
<td>14.36 (2.83)</td>
</tr>
<tr>
<td>EDSS score</td>
<td>0.87 (0.92)</td>
<td>0.96 (1.03)</td>
</tr>
<tr>
<td>PDDS score</td>
<td>1.24 (1.54)</td>
<td>1.28 (1.52)</td>
</tr>
<tr>
<td>Point improved</td>
<td>1.38 (1.54)</td>
<td>1.26 (1.52)</td>
</tr>
<tr>
<td>SMD</td>
<td>0.063</td>
<td>0.040</td>
</tr>
<tr>
<td>CI</td>
<td>0.047</td>
<td>0.056</td>
</tr>
<tr>
<td>CStatistic</td>
<td>0.873</td>
<td>0.915</td>
</tr>
</tbody>
</table>

Table 2. Sensitivity analyses of 1:2 PS-matched natalizumab and ocrelizumab patients.

<table>
<thead>
<tr>
<th>Event time ratio (95% CI)</th>
<th>Natalizumab/Ocrelizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matched sample size</td>
<td>244</td>
</tr>
<tr>
<td>Time to clinically meaningful improvement in T-score</td>
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<tr>
<td>Event time ratio</td>
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<tr>
<td>Matched Neuro-QoL domains (Table 3)</td>
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</tr>
</tbody>
</table>

CONCLUSIONS

• This head-to-head comparison of MS PATHS patients demonstrated that natalizumab treatment can shorten the time to clinically meaningful improvement in the Neuro-QoL domain of Cognitive and Satisfaction with Social Roles and Activities compared with ocrelizumab treatment.
• While these PS-matched analyses controlled for potential confounding differences in baseline covariates, they have limitations that should be considered.
• While the PS-matched analyses control for potential confounding differences in baseline covariates, the impact of a new, unmeasured confounder on the results is limited by the similarity of these observations to the overall population of natalizumab patients, though the results are sensitive to any new unmeasured confounder.

These results may be informative for health care providers making decisions about the efficacy and treatment of their patients with MS.

BIBLIOGRAPHY

References:
[1] de Moor CM, Miller DM, Avila PH, Williams JR, Fitzgerald KC, Pang M, McGinley MP, Hyland M, Zarssemen T, Kooumlfka F. Mellen Center for Multiple Sclerosis and Cellular Therapeutics; Clinical Core; Louis Ruizer Center for Brain Health, Las Vegas, NV, USA; Mellen Center for Multiple Sclerosis, Cleveland, OH, USA; Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Department of Neurology, University of Rochester Medical Center, Rochester, NY, USA; University Hospital Carl Gustav Carus, Dresden, Germany; Rigoni, Cambridge, MA, USA; at this time of study.

DISCLOSURES

This work was supported by Bayer, Roche, Biogen, Genzyme, and Shire. Contribution: R. de Jager conceived the study; M. de Moor performed the analysis; both reviewed and edited the manuscript. M. de Moor had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Open access: This work was supported by the Clinical and Translational Science Collaborative of Cleveland, and received funding from the National Institutes of Health, National Library of Medicine, 2T32-ES019920-14, and F31-EB021054-01A1.

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Figure 1. (A) Event time ratios and (B) probability of clinically meaningful improvement in Cognitive Function, Satisfaction with Social Roles and Activities, Participation in Social Roles and Activities, and Positive Affect and Well-being in 2:1 Natalizumab heated. 0.040

Figure 2. Event ratios for Neuro-QoL domains in MS-matched natalizumab and ocrelizumab patients.

Table 3. Baseline covariates of PS-matched natalizumab and ocrelizumab patients.

Table 4. Baseline covariates of PS-matched natalizumab and ocrelizumab patients for the Sleep Disturbance Neuro-QoL domain.

Table 2. Study follow-up and assessments in 1:2 PS-matched natalizumab and ocrelizumab patients.

Figure 2. Event ratios for Neuro-QoL domains in MS-matched natalizumab and ocrelizumab patients.