Introduction

• Lower serum immunoglobulin (Ig) levels are generally associated with infections; reduced Ig levels is known to occur with anti-CD20 treatment in multiple sclerosis (MS) patients and have been linked to an increased risk of infection.7

• In the ofatumumab ASCLEPIOS Phase 3 trials, the rate of serious infections was low, and no association was observed between decreased Ig levels and the risk of serious infections for up to 96 weeks.8

Objective

• To assess the effect of ofatumumab on serum IgG/IgM levels over ~3.5 years (168 weeks) and evaluate the risk of serious infections associated with a decrease in IgG/IgM during the core (ASCLEPIOS III; APLIOS or APOLOTS) and open-label extension (ALITHIOS) studies.

Methods

Study Design and Assessments

• Serum IgG/IgM levels were monitored during the core and open-label extension study periods.

• Change in IgG/IgM levels from baseline to 168 weeks was analysed in the overall, long-term (continuous ofatumumab in core+extension) and switch (teriflunomide core/ofatumumab extension) groups.

• Mean IgG/IgM levels were analysed by baseline quartiles in the long-term treatment group.

• Proportion of patients with IgG/IgM less than lower limit of normal (<LLN) at any time during the post-baseline visits was assessed.

• Association of serious infections reported for patients in conjunction with low IgG/IgM levels <LLN during 1 month prior to any detection of the drop in the levels were analysed and compared with serious infections reported in patients who maintained normal Ig levels (2LLN).

Results

• As of 29 Jan 2021, median time at risk (treatment-emergent period of a patient in the study) was 21.0 (range 0 to 51.8) months in the overall and 35.5 months in long-term group; total 4238.5 patient-years.

• Change in IgG/IgM levels was analysed in the overall (N=1699), long-term (N=1292) and switch (N=677) groups.

Change in IgG levels over 3.5 years

• The mean serum IgG remained stable with up to 3.5 years of ofatumumab treatment (Figure 1A).

• Ofatumumab was associated with a transient drop in IgG levels through Week 48, which completely recovered and was maintained at later time points.

• Patients did not show any decline after switching from teriflunomide and followed the same trajectory as long-term group.

• Treatment interruptions and discontinuations were observed in 0.1% and 0.2% of patients respectively.

Change in IgM levels over 3.5 years

• Average IgM levels remained well within the reference ranges over time (Figure 1B).

• Most of the reduction from baseline in IgM levels was observed at Week 48 (absolute mean, 0.93 g/L; % change, −31.8%), which stabilised thereafter (Week 108: absolute mean, 0.71 g/L; % change, +46%).

• Treatment interruptions and discontinuations were observed in 9.1% and 3.3% of patients respectively.

IgG/IgM levels by baseline quartiles in the long-term group

• IgG levels remained similar to the baseline values in all quartiles throughout the treatment period (Figure 2A).

• IgM levels decreased over time; the mean values remained above LLN with the least reduction observed for the lowest quartile group, IgM <0.45 g/L (<LLN).

• The mean serum IgG remained stable with up to 3.5 years (168 weeks) and evaluate the risk of serious infections associated with a decrease in IgG/IgM during the core (ASCLEPIOS III; APLIOS or APOLOTS) and open-label extension (ALITHIOS) studies.

Table 1. Patients with ≥1 serious infection within 1 month prior/after any detection of drop in IgG/IgM <LLN

<table>
<thead>
<tr>
<th>Group</th>
<th>% of patients with ≥1 serious infection</th>
<th>% of patients with ≥1 serious infection (%)</th>
<th>% of patients with ≥1 serious infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>7.02</td>
<td>2.8</td>
<td>0.19</td>
</tr>
<tr>
<td>IgM</td>
<td>0.14</td>
<td>0.7</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Conclusions

• Mean IgM levels remained stable in patients treated with ofatumumab for up to 3.5 years.

• A great majority (96.7%) of patients in both groups had IgM levels observed, which was more pronounced in the first year than in the subsequent period.

• The overall incidence of serious infections was low, and no association was observed between decreased IgM levels and the risk of serious infections.

• Results from this analysis, up to 3.5 years of ofatumumab treatment, are consistent with 96-week ASCLEPIOS study data.

References


Acknowledgments

Medical writing support was provided by Sreelatha Komatireddy and Sreelatha Komatireddy (PhD) and Numbers Knowledge (Reade, EMD Serono, Biogen, Roche Pharma AG, GlaxoSmithKline GmbH, Sanofi-Genzyme, Pfizer, Novartis Pharma, B.V., Roche, Novartis Pharma B.V., Biogen, and Genzyme). The authors had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis. The corresponding author had final responsibility for the decision to submit for publication.

Poster presented at ECTRIMS 2021 congress

Effect of Ofatumumab on Serum Immunoglobulin Levels and Infection Risk in Patients With Relapsing Multiple Sclerosis Over 3.5 Years

Heinz Wiendl1, Jérôme de Seze2, Amit Bar-Or3, Jorge Correale4, Anne H. Cross5, Ludwig Kappos6, Krzysztof Selmaj7,8,

1University of Muenster, Muenster, Germany; 2University Hospital of Strasbourg, Strasbourg, France; 3Center for Neuroimmunology and Experimental Therapeutics and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States; 4Institute for Neurological Research Dr. Raul Carrea, Buenos Aires, Argentina; 5Department of Neurology, Washington University School of Medicine, Saint Louis, MO, United States; 6Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB) and MS Center, Departments of Head, Spine and Neuromedicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital and University of Basel, Basel, Switzerland; 7Center for Neurology, Lodz, Poland; 8University of Warmia & Mazury, Olsztyn, Poland; 9Public Health and Preventive Medicine, Division of Infectious Diseases, Dr. António Frota Neto University Hospital, Rio de Janeiro, RJ, Brazil; 10Department of Neuroimmunology, Innsbruck Medical University, Innsbruck, Austria; 11Novartis, Geneva, Switzerland; 12University Federico II of Naples, Italy; 13Novartis Healthcare Pvt Ltd, Hyderabad, India; 14Novartis Pharma AG, Basel, Switzerland; 15Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; 16UCSF Weill Institute for Neurosciences, University of California, San Francisco, CA, United States.