Effect of Subcutaneous Ofatumumab on Lymphocyte Subsets in Patients with RMS: Analysis from the APLIOS Study

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INTRODUCTION

Ofatumumab, the first fully human anti-CD20 monoclonal antibody, binds to two distinct non-continuous regions of CD20, resulting in potent B-cell depletion and reduced B- and T-cell interactions. Ofatumumab demonstrated superior efficacy versus teriflunomide in the Phase 3 ASCLEPIOS I/II trials in RMS; its effect on B- and T-cell subsets warrants further investigation.

We evaluated the effect of ofatumumab 20 mg subcutaneous (s.c.) dosing regimen on B- and T-cell subsets in relapsing multiple sclerosis (RMS) patients.

METHODS

APLIOS was a 12-week, open-label, Phase 2 bioequivalence study. Patients received ofatumumab 20 mg (0.4 mL) s.c. loading doses on Days 1, 7, and 14, and maintenance doses every 4 weeks from Week 4 via a prefilled syringe or an autoinjector pen (SensoReady®). Changes in B- and T-cell subsets were analysed longitudinally in blood samples using fluorescence-activated cell sorting.

RESULTS

Ofatumumab treatment showed rapid and sustained depletion in total B-cells (CD19+CD45+) measured on Day 4 until Day 84 versus baseline. The median total B-cell levels decreased to =<5 cells/µL by Day 7 through Day 14 of the loading regimen and was maintained until the study end. An effective depletion of memory B-cells (CD19+CD45+CD27+) along with decrease in naïve B-cells (CD19+CD45+IgD+CD27-CD38^{dim}) was observed. Interestingly, a specific subset of T-cells (CD20+CD3+CD8+ T-cells), well-known to exhibit an activated phenotype, were also rapidly depleted, consistent with the previous findings from a primate study. By contrast, CD3+ T-cells were largely unaffected.

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CONCLUSIONS

Ofatumumab 20 mg s.c. led to rapid and sustained depletion of both CD20+ B- and CD20+ T-cells in RMS patients.

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