Serum Immunoglobulin Levels and Infections in Relapsing Multiple Sclerosis

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INTRODUCTION

Patients with MS are at an increased risk of infections compared with the general population. As immunoglobulins (Ig) play a major role in immunoprotection, serum IgM/IgG levels below the lower-limit-of-normal (<LLN) have been attributed to an increased risk of infections in MS patients receiving disease-modifying therapies, particularly B-cell-depleting therapies.

OBJECTIVE

Evaluate the association between serum IgM and IgG levels and risk of infections in relapsing MS (RMS). We report results from the Phase 3 ASCLEPIOS I/II trials, which led to US-FDA-approval of ofatumumab for RMS.

METHODS

Eligible patients with serum IgM/IgG≥LLN at screening were treated with monthly-subcutaneous ofatumumab 20mg (n=946) or once-daily oral teriflunomide 14mg (n=936) for up to 30 months(m). Serum IgM/IgG levels were monitored at baseline, Week (W)4, W12, and every 12 weeks thereafter. Proportion of patients with IgM/IgG<LLN and the association of IgM/IgG levels with incidence of infections occurred up to 1m prior and 1m after any decrease in IgM/IgG<LLN were analysed and compared with the IgM/IgG≥LLN group.

RESULTS

Mean IgM levels were reduced from baseline in both treatment groups, but remained well within the reference ranges. No decline in mean IgG levels was observed at the end-of-study; a transient reduction was observed until W36, which recovered thereafter in both treatment groups. Proportion of ofatumumab-treated patients with ≥1 infection (IgM/IgG<LLN vs IgM/IgG≥LLN) during a drop in IgM was 31.1% versus 51.5% and in IgG was 27.6% versus 50.6%. Common infections were nasopharyngitis, upper respiratory tract and urinary tract

infections; majority were non-serious and mild-to-moderate in severity that were resolved while continuing ofatumumab treatment. No opportunistic infections were reported.

CONCLUSIONS

There was no association between a decrease in immunoglobulin levels and incidence of infections observed in ofatumumab-treated RMS patients. More information, especially longer follow-up, is needed to understand the association of risk of infections with IgM/IgG<LLN.

Disclosures: