Title: A Systematic Literature Review of Immunoglobulin Levels Among B-Cell–Depleting Therapies and Risk of Infections in Relapsing Multiple Sclerosis

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Background

Selectively targeting B-cell depletion with anti-CD20 monoclonal antibodies, including ofatumumab and ocrelizumab, has been proven highly effective at limiting disease activity in people with relapsing forms of multiple sclerosis (RMS). However, B-cell depletion may lead to decreased immunoglobulin (Ig) levels and, consequently, increased risk of infection.

Objectives

To explore the change in Ig levels for people with RMS taking ocrelizumab (OCR) or ofatumumab (OMB) and the relationship between Ig levels and infections.

Methods

A systematic literature review (SLR) was conducted to identify publications of trials and real-world evidence (RWE) studies on Ig levels over time for OCR and OMB for people with RMS through 10 Sept 2021. Searches were conducted in Embase, MEDLINE, Cochrane Library, trial registries, and recent conference abstracts. Data on study design, follow-up time, patient characteristics, Ig levels, and association with infections were extracted from included publications. A targeted literature review (TLR) was performed to consider the relationship between Ig levels and infection risk in trials and RWE for MS.

Results

Of 1,580 articles identified in the SLR, 30 reporting data on 11 trials and 5 RWE studies met the inclusion criteria. Trials (n=4) of OCR had 24-336 weeks of follow-up and reported a decrease in IgG levels, while RWE (n=5) had 52-78 weeks of follow-up and reported IgG to be stable or decrease only slightly; IgG levels were stable in trials (n=5) of OMB (104-168 weeks of follow-up), but no RWE studies were identified. In the same trials that reported IgG, IgM levels decreased over time for both OCR and OMB. Limited data suggested that IgA levels decreased with OCR and remained stable with OMB (n=2

trials). Among 16 studies (28 publications) included in the TLR, most found an association between decreased IgG levels and increased risk of infections. No evidence of a relationship between IgM levels and infections was found. Increased IgA levels were related to reduced infections (n=1 study).

Conclusion

Evidence suggests that decreasing IgG levels correspond to increased risk of infection. Among people treated with OCR, it appears that IgG levels may decrease over time. Interestingly, although OCR and OMB are in the same drug class, IgG levels appear to remain relatively stable over time among those treated with OMB. Additional research is needed to compare OCR and OMB, in particular longer-term RWE, and to identify people at risk of decreasing IgG levels.