Characterisation of the immune system after ocrelizumab treatment in MS

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INTRODUCTION: B cell depletion by the anti-CD20 antibody ocrelizumab (OCR) is a highly effective treatment for RRMS and PPMS. This study aimed to investigate the phenotypic changes of the immune system after OCR treatment in RRMS and PPMS patients over time.

METHODS: Peripheral blood mononuclear cells (PBMC) were collected of 18 RRMS and 22 PPMS patients before, 6 months (m) and 12m after OCR initiation. Clinical characteristics at baseline were for RRMS and PPMS patients on average, respectively: age – 42/48 years, sex – 61/41% female, EDSS score – 3/5 and disease duration – 9.6/5.2 years. In-depth immunological phenotyping was done by flow cytometry. B cells, T cells, monocytes, dendritic cells (DC) and natural killer (NK) cells were analysed.

RESULTS: For all patients, the frequency of $CD20^+$ B cells was reduced after 6 (0.8%) and 12m (0.6%) of OCR compared to baseline (12.0%). The frequency of naive (IgD^+CD27^-) B cells was reduced, whereas transitional ($CD24^{++}CD38^{++}$), double negative (IgD^-CD27^-) and class-switched memory (IgD^-CD27^+) B cells were increased after 6 and 12m of OCR. For both RRMS and PPMS patients, $CD3^+CD20^+$ T cells completely disappeared after 6 and 12m of OCR treatment, whereas the frequency of $CD4^+$, $CD8^+$ and regulatory T cells was not affected. No differences were observed in the frequency of inflammatory monocytes ($CD14^+CD16^+$), plasmacytoid and myeloid DC ($CD123^+CD11c^-$,$CD123^-CD11c^+$/$CD123^-CD11c^-$) after 6 and 12m of OCR. The number of $CD20^+$ NK cells ($CD56^{dim}CD16^+$/$CD56^{high}CD16^-$) was reduced after 6 and 12m of OCR. For all immune cell subsets, no significant difference between 6 and 12m was observed.

CONCLUSION: Besides depletion of $CD20^+$ B, T and NK cells, OCR treatment induced changes in the distribution of B cell subsets in both RRMS and PPMS patients. Understanding

the effect of OCR on the distribution of immune cell subsets in MS will contribute to unravelling their role in MS pathology.