

**Title:**

**Innate and B cell responses in MS patients on Fingolimod and Ocrelizumab following 2 doses of SARS-CoV-2 mRNA vaccine**

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**Introduction:** There is limited knowledge about different innate and B cell responses specifically in immunosuppressed patients with multiple sclerosis (MS) who receive 2 doses of SARS-CoV-2 mRNA vaccine.

**Objectives & Aims:** To assess cytokine producing monocyte, NK cell and B cell responses in MS patients on high efficacy immunotherapies and healthy controls (HC) who received 2 doses of SARS-CoV-2 mRNA vaccine.

**Methods:** This is a study of patients with MS, aged 18-65, on fingolimod (FIN n=6) and ocrelizumab (OCR n=10) for at least 3 months prior to 1<sup>st</sup> mRNA SARS-CoV-2 vaccine dose (BNT162b2 or mRNA-1273) and a cohort of HC (n=8). Blood samples were collected after 2 doses of mRNA vaccine. IFN $\gamma$  and TNF $\alpha$  producing monocyte, NK cell and B cell responses were examined in patients with MS and HC upon stimulation with SARS-CoV-2 Prot\_S peptide by flow cytometry.

**Results:** There was a significant increase in the percentage of SARS-CoV-2 Prot\_S reactive IFN $\gamma$  and TNF $\alpha$  producing CD14+, CD16+ and CD14+/CD16+ monocytes in the FIN and OCR group as compared to HC. There was a significant increase in the percentage of SARS-CoV-2 Prot\_S reactive TNF $\alpha$  producing CD56<sup>bright</sup> NK cells in the FIN and OCR group as compared to HC. There was a significant increase in the percentage of SARS-CoV-2 Prot\_S reactive IFN $\gamma$  and TNF $\alpha$  producing CD56<sup>dim</sup> NK cells in the FIN and OCR group as compared to HC. There was a significant increase in the percentage of SARS-CoV-2 Prot\_S reactive IFN $\gamma$  and TNF $\alpha$  producing CD19+ B cells in the FIN and OCR group as compared to HC.

**Conclusions:** MS patients on fingolimod and ocrelizumab have increased cytokine producing monocyte, NK cell and B cell responses as compared to HCs after SARS-CoV-2 mRNA vaccination.

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