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 & Objective

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.

Objective/Aim: To assess cytokine producing monocyte, B cell and NK cell responses in MS patients on high efficacy immunotherapies like fingolimod and ocrelizumab and healthy controls (HC) who received 2 doses of SARS-CoV-2 mRNA vaccine.

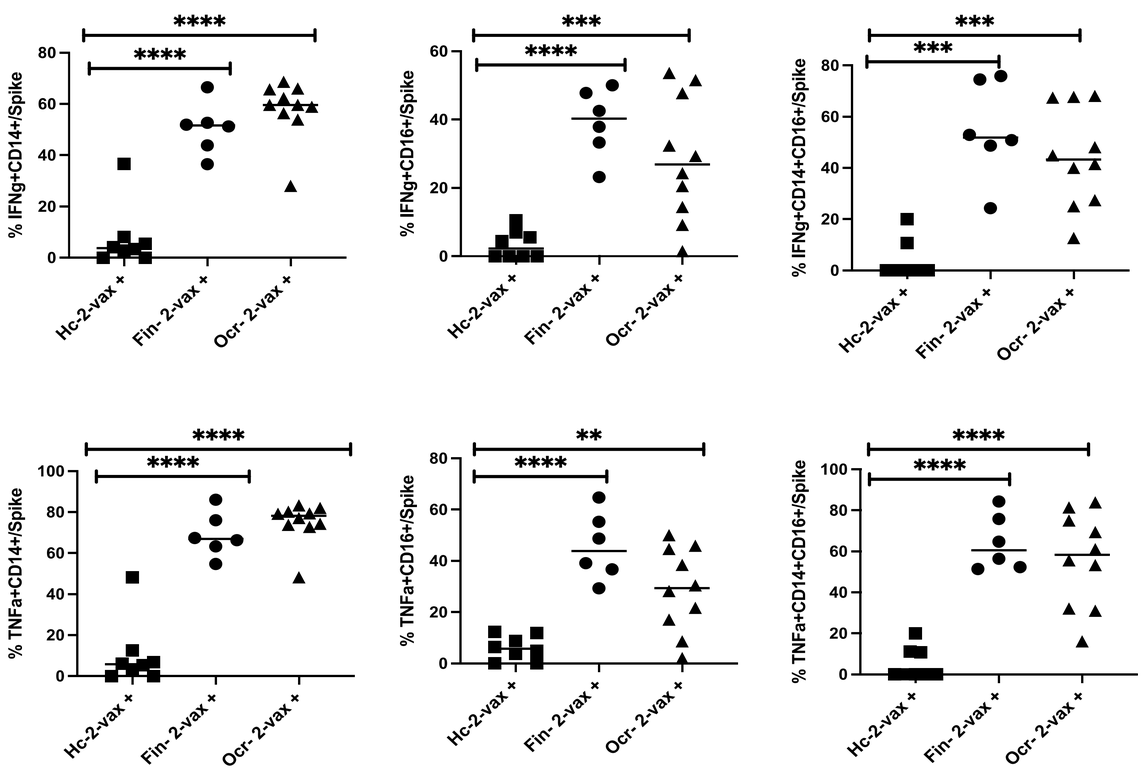
Methods

This is a sub study of 16 MS patients out of the total 177 enrolled in the Brigham MS COVID vaccine immunology study, aged 18-65, on fingolimod (FIN n=6) and ocrelizumab (OCR n=10) for at least 3 months prior to 1st SARS-CoV-2 mRNA vaccine dose (BNT162b2 by Pfizer or mRNA-1273 by Moderna) and a cohort of HC (n=8). Blood samples were collected after 2 doses of SARS-CoV-2 mRNA vaccine. Cells were stimulated with a pool of lyophilized peptides covering the immunodominant sequence domain of the spike glycoprotein-SARS-CoV-2 Prot_S at a concentration of 4 μg/ml for 18 hours. Unstimulated cells containing only media were used as exvivo. IFNγ and TNFα response was examined in monocytes, B cells and NK cells in patients with MS and HC upon stimulation with SARS-CoV-2 Prot_S peptide and exvivo by flow cytometry.

Results

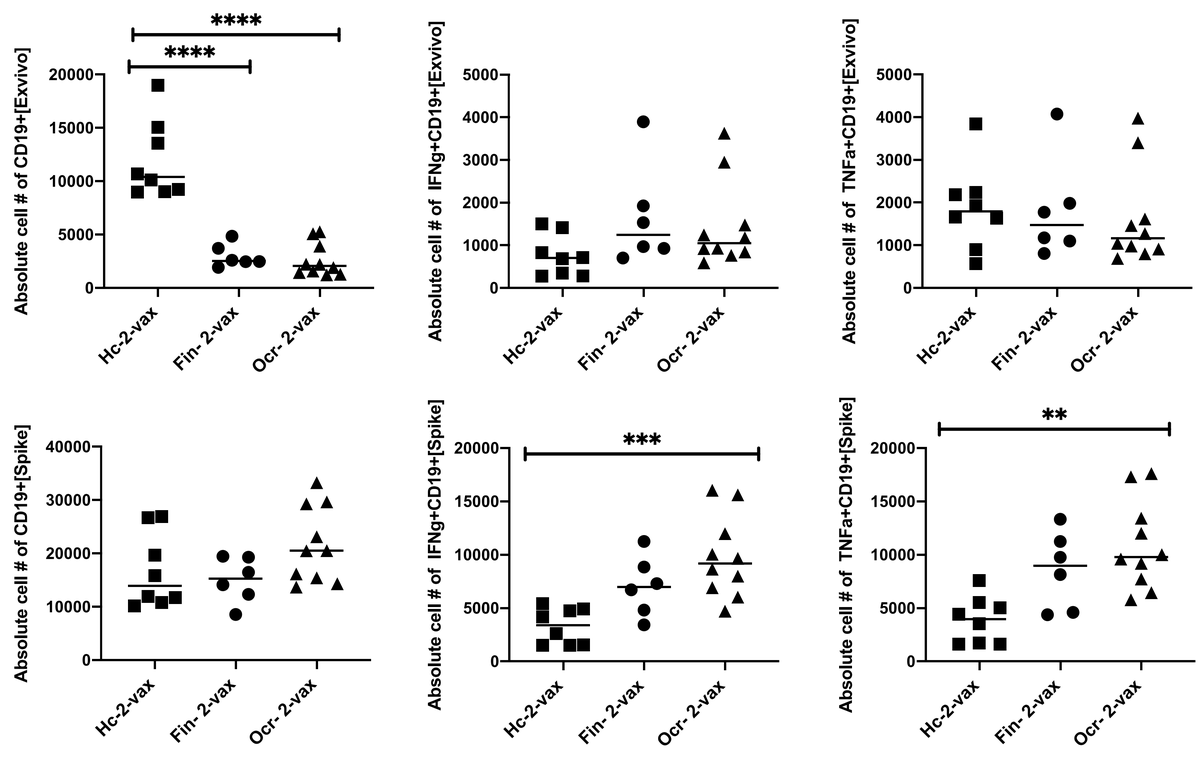
Result 1: Increased percentage of SARS-CoV-2 peptide reactive IFNγ and TNFα producing monocytes in MS patients compared to healthy controls

- There was a significant increase in the percentage of SARS-CoV-2 Prot_S reactive IFNγ and TNFα producing CD14+, CD16+ and CD14+/CD16+ monocytes in the FIN and OCR groups as compared to HC.



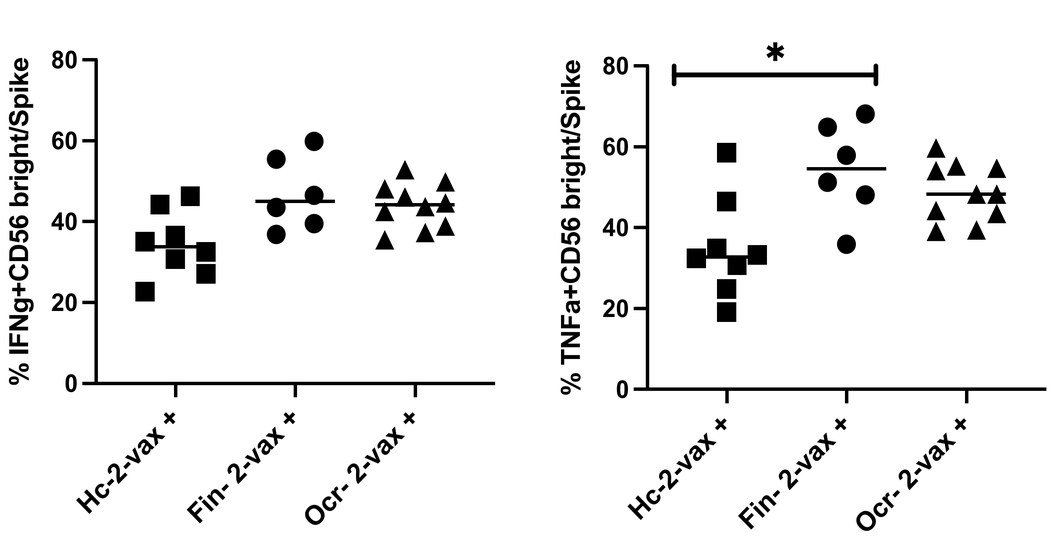
Result 2: Increased absolute cell number of SARS-CoV-2 peptide reactive IFNγ and TNFα producing CD19+ B cells in ocrelizumab group compared to healthy controls

- There was a significant increase in the absolute cell number of the total CD19+ cells in HC as compared to FIN and OCR groups exvivo, however the absolute cell number in the FIN and OCR groups increased after SARS-CoV-2 Prot_S peptide stimulation as compared to HC.
- There was a significant increase in the absolute cell number of SARS-CoV-2 Prot_S reactive IFNγ and TNFα producing CD19+ B cells in the OCR group as compared to HC.



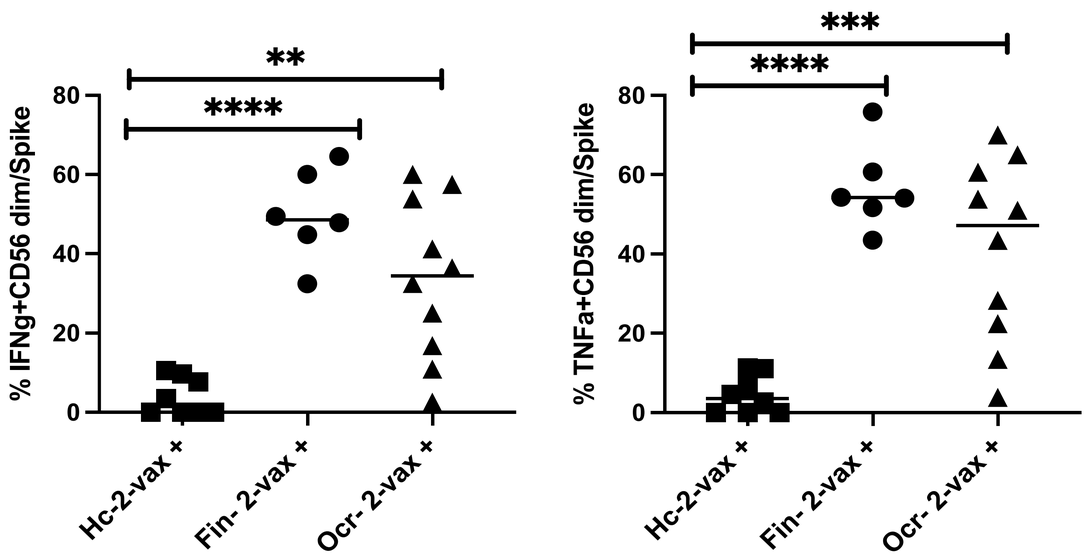
Result 3: Increased percentage of SARS-CoV-2 peptide reactive TNFα producing CD56^{bright} NK cells in fingolimod patients compared to healthy controls

- There was a significant increase in the percentage of SARS-CoV-2 Prot_S reactive TNFα producing CD56^{bright} NK cells in the FIN group as compared to HC, however IFNγ producing CD56^{bright} NK cells demonstrated a trend of being increased in MS patients as compared to HC but did not reach significance.



Result 4: Increased percentage of SARS-CoV-2 peptide reactive IFNγ and TNFα producing CD56^{dim} NK cells in MS patients compared to healthy controls

- There was a significant increase in the percentage of SARS-CoV-2 Prot_S reactive IFNγ and TNFα producing CD56^{dim} NK cells in the FIN and OCR group as compared to HC.



Conclusion

Multiple sclerosis patients on fingolimod and ocrelizumab have increased cytokine producing monocyte, NK cell and B cell responses as compared to healthy controls after SARS-CoV-2 mRNA vaccination. Further work is needed to correlate these responses with COVID disease outcomes.

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