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Tracking the immune response to SARS-CoV-2 mRNA vaccines in ofatumumab treated RMS patients in a multicenter study (KYRIOS trial)

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Introduction: Recently developed SARS-CoV-2 mRNA vaccines have been shown to efficiently protect healthy individuals against COVID-19 and contribute greatly towards fighting the COVID-19 pandemic.
Aims: As only limited data is available for Multiple Sclerosis (MS) patients with immunosuppressive treatment, this study aims to understand the impact of ofatumumab treatment on the development of cellular and humoral immune responses to initial and booster SARS-CoV-2 mRNA vaccines.
Methods: KYRIOS is a prospective, open-label, two-cohort study including 34 MS patients at 8 sites in Germany. Patients receive initial or booster SARS-CoV-2 mRNA vaccination either before (cohort 1) or at least 4 weeks after starting ofatumumab treatment (cohort 2). As primary endpoint, the impact of ofatumumab treatment on development of SARS-CoV-2 reactive T-cells will be evaluated. Additionally, neutralizing antibodies will be assessed, and the immune responses will be monitored and phenotypically described for up to 18 months.
Results: Interim analysis will show the complete primary endpoint results of the KYRIOS study. All patients vaccinated during continuous ofatumumab treatment (5/5) developed an immune response as soon as one week after initial vaccination cycle. While the extent of T-cell response was not affected in ofatumumab treated patients, neutralizing antibodies titers were lower compared to the control group. After the first booster vaccine, the majority of ofatumumab patients (n=15) showed an increase in neutralizing antibodies to a comparable extend as the control group (n=8). Data show that seroconversion during continuous ofatumumab treatment is possible. In general, this analysis confirms first positive interim analysis data presented at AAN 2022.
Conclusions: KYRIOS data demonstrate that ofatumumab treated patients can mount specific immune responses towards SARS-CoV-2 mRNA vaccines. The presented data further emphasize the importance of considering both, humoral and cellular immune response, for interpretation of vaccine efficacy and the importance of booster vaccines in immunocompromised patients.
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