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Immune response to SARS-CoV-2 mRNA booster vaccinations in relapsing multiple sclerosis patients treated with ofatumumab s.c.– Final results from the open-label multicenter KYRIOS trial

Tjalf Ziemssen¹, Eugen Schlegel², Veronika E. Winkelmann³, Lea Leist³, Tobias Bopp⁴

¹Department of Neurology, Center of Clinical Neuroscience, Carl Gustav Carus University Clinic, University Hospital of Dresden, Fetscherstr. 74, 01307, Dresden, Germany.

³Novartis Pharma GmbH, Roonstr. 25, D-90429 Nuernberg, Germany.

²Zentrum für neurologische Studien, 57076 Siegen, Deutschland

⁴Institute for Immunology, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany

Introduction

SARS-CoV-2 mRNA vaccines have been shown to efficiently protect healthy individuals against COVID-19, however only limited data is available for booster vaccination in Multiple Sclerosis (MS) patients with immunosuppressive treatment. This study was initiated 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 was a prospective, open-label, two-cohort study including 34 MS patients at 8 sites in Germany. Patients receive initial or first 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

Final analysis will show the complete primary and secondary endpoints of the KYRIOS study. T-cell response so far was not affected by ofatumumab treated after initial and first booster vaccination. Neutralizing antibodies increased in all patients as soon as week 1 after full vaccination, even though titers were lower compared to the control group. However neutralizing antibody response after booster vaccination was comparable in patients boosted before and during stable ofatumumab treatment, including patients who seroconverted during stable ofatumumab treatment. In this final analysis we will also show immune response data from patients receiving a second booster vaccination while on stable ofatumumab therapy. Data from the trial will be compared to findings from other SARS-CoV-2 vaccination studies in MS patients. This final analysis will confirm positive interim analysis data presented at ECTRIMS 2022.

Conclusions

KYRIOS data demonstrate that ofatumumab treated patients can mount specific immune responses towards SARS-CoV-2 mRNA vaccines regardless if initial or booster vaccination occur under stable ofatumumab treatment. 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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