relative benefit of vaccination. Less favourable outcomes among rituximab-treated warrant that this drug should be considered with extra care.

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T-CELL RESPONSE AFTER COVID-19 VACCINE IS NOT IMPAIRED BY EARLY RITUXIMAB TREATMENT OR BELIMUMAB IN SYSTEMIC AUTOIMMUNE DISORDERS

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Background: Patients with autoimmune systemic diseases have an increased risk to contract infections and develop severe complications; infections in turn can reactivated and worsen the disease itself in a vicious circle. Thus, vacci- nation is the main weapon to prevent infectious diseases and represents an important and safe instrument of care for rheumatic patients that needs to be further promoted. However, the immunosuppressive drugs used to treat rheu- matic diseases may impair response to vaccines, in particular those targeting B or T cells directly (1).

Objectives: The aim of this study is to evaluate the B and T-cell mediated immune response to mRNA vaccination in patients with systemic autoimmune diseases such as vasculitis or systemic connective tissue diseases, early or continuously treated with B-cell targeting therapies, rituximab (RTX) or beli- mumab (BEL), by comparing with controls and each other. Secondary we evaluated the in vitro effective neutralizing capacity in belimumab-exposed patients.

Methods: Twenty-eight consecutive patients under treatment with rituximab (RTX, n=11) or belimumab (BEL, n=17) and 13 age/sex matched controls (non-rheumatic healthcare personnel) were enrolled in the study. Nobody presented anti-SARS-CoV2 antibodies related to previous viral contact and all were always negative at the molecular swab monthly control. All patients and controls received mRNA vaccines and were tested three to four weeks after complete vaccination. All RTX patients started vaccination within 5 months from the last infusion, and all but one of them were B-cell depleted. Anti-SARS-CoV-2 RBD total antibodies were analysed by a diagnostic assay (Elecsys, Roche) while T-cell response was evaluated using the IGRA test (Euroimmun). A subgroup of BEL-patients was tested with pseudovirus neutralization assay.

Results: Detectable anti-SARS-CoV2 RBD antibodies were documented in 1/11 RTX patients versus 16/17 BEL patients (p<0.0001). The median concentration was significantly lower than that observed in controls (39.6 AU/ml vs 1133 AU/ ml, p<0.0001). A very low titer of anti-RBD antibodies were documented only in 1 out of 11 patients in the RTX subgroup (0.93 U/ml, positive if >0.79 U/ml) and the patient was the only one who showed an initial B-cell recovery (CD19+ B-cell 5 cells/microL). Anti-RBD antibodies were documented in 16 out of 17 patients in the BEL subgroup. The median anti-RBD antibody titer in patients receiving BEL was 243 [77.5–744.0] U/ml, and it was significantly lower compared to the controls (p=0.002).

The IGRA test was positive in 8/11 (72.7%) RTX patients vs 16/17 (94.1%) BEL patients (p=0.7), with interferon release comparable to control subjects (p=0.2).

Six patients with BEL were also stratified according to total antibodies (IgG+IgA+IgM) against-RBD into high responders (>800 AU/mL, n=3) and low responders (≥45 AU/mL, n=3) and tested with pseudovirus neutralization assay. Two thirds of low titer group of patients neutralized the Wuhan-Hu1 strain at medium-low titer (IC50 >102) but were almost ineffective in inhibiting the B.1.1.7 entry into target cells (IC50 >10). Regarding high responders, while two patients were able to inhibit both the strains at medium-high titer (approxi- mately IC50 >103 for Wuhan-Hu1 and B.1.1.7), one patient neutralized only the WT strain.

Conclusion: B-cell targeting therapies do not preclude SARS-CoV-2 vaccination since a cellular immune can raise even in the absence of circulating B cells. Most importantly, the immunogenicity of COVID-19 vaccination in SLE patients treated with belimumab is supported. However, patients showing the lowest humoral response to vaccine could remain at higher risk of infections, due to low neutralizing capacity.

REFERENCES:

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TYPE OF MRNA COVID-19 VACCINE AND TREATMENT INFLUENCE ANTIBODY KINETICS IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: Patients on immunomodulatory treatments mount an attenuated immune response following mRNA COVID-19 vaccination, yet long- term studies of vaccine-induced anti-SARS-CoV-2 antibody (Ab) kinetics are missing.

Objectives: In this prospective observational study, we mapped the humoral antibody response to mRNA COVID-19 vaccines up to 24 weeks post full vac- cination in patients with inflammatory rheumatic diseases (IRDs). We aimed to assess differences due to treatment, age, past SARS-CoV-2 infection, and vac- cine (BNT162b2 vs mRNA-1273).

Methods: Adult patients from the SCQM cohort who assented to an mRNA COVID-19 vaccine were recruited between 3/21 – 9/21. Participants answered questionnaires via an app and received kits for the self-collection of capillary blood samples at baseline, 4, 12, and 24 weeks post full vaccination. Samples were tested for IgG Ab against the S1 domain of the SARS-CoV-2 spike protein (anti-S1-IgG) using the EUROMIMUN ELISA. To examine differences in Ab titres arising from the defined parameters, while accounting for inter-assay variability, mixed effects continuous outcome logistic regression models were applied at each timepoint.

Results: Samples were obtained from 570 patients: 67% female, mean age 53 ± 12 years (SD 12 y) with 37% RA, 36% axSpA, 21% PsA, and 6% UA (undifferentiated arthritis), on no medication (no DMARDs & no glucocorticoids; 15%), csD- MARDS (10%), TNFi (48%), IL-1/6/17/23 (14%), JAKI (6%), rituximab (RTX; 4%), or abatacept (ABA; 2%) in mono/combination therapy at the first vaccination. 10% of patients had a past SARS-CoV-2 infection, 54% received BNT162b2, 46% mRNA-1273.

For any Ab threshold, the odds of having a higher Ab titre at 4, 12, and 24 weeks post full vaccination were 3.3 – 4 times higher with mRNA-1273 compared to BNT162b2 (Table 1, Figure 1). TNFi, JAKI, RTX, and ABA as monotherapy resulted in significantly lower Ab levels compared to no medication at almost all timepoints. In combination therapy, TNFi, IL-1/6/17/23, RTX, and csDMARDs led to consistently lower Ab titres at all timepoints compared to respective.