Background: The SARS-CoV-2 messenger RNA (mRNA) vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) have benefitted all countries amid the coronavirus disease 2019 (COVID-19) crisis. Whereas both of them have shown efficacy in preventing COVID-19 illness in healthy participants, there is a paucity of data about immunogenicity and safety of mRNA COVID-19 vaccines in patients with autoimmune, inflammatory rheumatic disease. Recent observational studies evaluated mainly BNT162b2, suggesting that glucocorticoids, immunosuppressants and biologic agents impair SARS-CoV-2 vaccine responses. However, difference in immune reactions and safety between BNT162b2 and mRNA-1273 have not been clarified in patients with inflammatory rheumatic diseases.

Objectives: To assess humoral and T cell immune responses and safety profiles after two doses of different mRNA vaccine against SARS-CoV-2; BNT162b2 and mRNA-1273.

Methods: We enrolled consecutive, previously uninfected patients with inflammatory rheumatic diseases receiving mRNA vaccine including BNT162b2 and mRNA-1273. Healthy participants receiving BNT162b2 were also recruited as control. Blood samples were obtained 31–37 days after the first and after 2–9 weeks after the second dose of vaccines. We measured titres of neutralizing antibodies against SARS-CoV-2 and calculated seroconversion rates to evaluate humoral responses. We also assessed T-Cell immunity responses by using interferon releasing assay against SARS-CoV-2 in a part of the patients. Answers to questionnaires about adverse reactions were obtained from participants.

Results: A total of 974 patients with inflammatory rheumatic diseases and healthy 630 control participants were enrolled. Among them, 796 patients received BNT162b2, 178 patients received mRNA-1273, and all control participants received BNT162b2. Seroconversion rates and neutralizing antibody titres 3 weeks after vaccination were significantly higher in patients with mRNA-1273 and healthy participants with BNT162b2 compared with patients with BNT162b2; seroconversion rates, 97.2% vs 95.9% vs 83.3%, p<0.001; titer of neutralizing antibodies, 29.4±33.9 IU/mL vs 23.9±14.2 IU/mL vs 10.6±16.5 IU/mL, p<0.001, respectively. Graphs 1A and 1B. Before front, The cell reaction against SARS-CoV-2 was similar in both groups, with mRNA-1273 and BNT162b2; interferon gamma levels for antigen 1, 1.24±2.1 IU/mL vs 0.8±2.5 IU/mL, p=0.23; and for antigen 2, 1.4±1.9 IU/mL vs 1.0±2.1 IU/mL, p=0.11, respectively. Regarding adrenal reaction of each mRNA vaccine, the frequency of systemic adverse reactions including fever and general fatigue are also significantly higher in patients with mRNA-1273 and healthy controls than patients with BNT162b2; fever, 48.0% vs 44.9% vs 10.2%, p<0.001; general fatigue, 70.4% vs 61.8% vs 31.2%, p<0.001, respectively. In longitudinal measurement, neutralizing antibody titres in patients with BNT162b2 were decreased more rapidly than those in healthy controls; 3.3±3.2 IU/mL in patients with BNT162b2 at 4 months and 3.2±4.7 IU/mL in healthy controls with BNT162b2 at 6 months. We identified age, glucocorticoid dose (prednisolone > 75mg), use of immunosuppressants including methotrexate, mycophenolate, cyclosporine, and tacrolimus are associated with rapid attenuation of humoral responses in patients with BNT162b2.

Conclusion: Our results demonstrated a significant higher humoral immunogenicity and frequency of systemic adverse reaction of the SARS-CoV-2 mRNA-1273 (Moderna) compared with the BNT162b2 (Pfizer-BioNTech) in inflammatory rheumatic disease patients. Glucocorticoid and immunosuppressive agents impaired induction and sustention of neutralizing antibody, and earlier third booster vaccination may be required within 4 months, especially for those receiving glucocorticoids.

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Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2022-eular.4091
A RANDOMIZED CLINICAL TRIAL OF 2-WEEK METHOTREXATE DISCONTINUATION IN RHEUMATOID ARTHRITIS PATIENTS VACCINATED WITH INACTIVATED SARS-COV-2 VACCINE

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Background: Patients with rheumatoid arthritis (RA) on methotrexate have reduced vaccine responses. Temporary discontinuation has improved immunogenicity of anti-influenza vaccine, but this strategy has not been evaluated in anti-SARS-Cov-2 vaccines.

Objectives: To evaluate the effect on immunogenicity and safety of 2-week methotrexate (MTX) discontinuation after each dose of the Sinovac-CoronaVac vaccine versus MTX maintenance in RA patients.

Methods: This was a single-center, prospective, randomized, investigator-blinded, intervention study (#NCT04754698, CoronavRheum), including adult RA patients (stable CDAI≤10, prednisone ≤7.5mg/day), randomized (1:1) to withdraw MTX (MTX-hold) for 2 weeks after each vaccine dose or maintain MTX (MTX-maintain), evaluated at D0, D28 and D69. Co-primary outcomes were anti-SARS-CoV-2 S1/S2 IgG seroconversion (SC) and neutralizing antibody (NAb) positivity at D69. Secondary outcomes were geometric mean titers (GMT) and flare rates. For immunogenicity analyses, we excluded patients with baseline positive IgG/NAb, and, for safety reasons, those who flared at D28 (CDAI>10) and did not withdraw MTX twice.

Results: Randomization included 138 patients with 9 exclusions (5 COVID-19, 4 protocol violations). Safety evaluation included 60 (MTX-hold) and 69 (MTX-maintain) patients. Further exclusions: 27 patients (13 (21.7%) vs. 14 (20.3%), p=0.848) with positive baseline IgG/NAb and 10 patients (21.3%) in MTX-hold with CDAI>10 at D28. At D69, MTX-hold (n=37) had a higher rate of seroconversion than MTX-maintain (n=55) group [29 (78.4%) vs 30 (54.5%), p=0.019], with parallel augmentation in GMT [34.2 (25.2-46.4) vs 16.8 (11.9-23.6), p=0.006]. No differences were observed for NAb positivity [23 (62.2%) vs 27 (49.1%), p=0.217]. At D28 flare, rates were comparable in both groups (CDAI, p=0.122; DAS28-CRP p=0.576), whereas CDAI>10 was more frequent in MTX-hold at D69 (p=0.024).

Conclusion: We provide novel data that 2-week MTX withdrawal after each Sinovac-CoronaVac vaccine dose improves anti-SARS-CoV-2 IgG response. The increased flare rates after second MTX withdrawal may be attributed to the short-term interval between vaccine doses. This strategy requires close surveillance and shared decision making due to the possibility of flares.

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Acknowledgements: This protocol is part of a larger study of immunosuppressed patients with ARD (Clinicatrails.gov#NCT04754698).

Disclosure of Interests: None declared.


LONG-TERM HUMORAL RESPONSE TO SARS-COV-2 VACCINATION IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASE


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Background: The first vaccine against SARS-CoV-2 was approved in December 2020. Immunogenicity of SARS-CoV2 vaccines in patients with immune-mediated inflammatory disease (IMID) have so far been evaluated in the 2-6 weeks following complete vaccination and risk groups for poor early vaccine response have been identified leading to specific vaccination recommendations. However, data on the long-term course and persistence of vaccine response in IMID patients, as well as the outcomes of the specific recommendations are lacking.

Objectives: To evaluate the long-term course of humoral response to SARS-CoV-2 vaccination in a large prospective cohort of IMID patients and non-IMID controls with a follow-up duration of up to 10 months after the first vaccine dose.

Methods: We have initiated a prospective dynamic cohort of patients and healthy controls in February 2020 to monitor immune response to SARS-CoV-2 and respiratory infections including COVID-19 (1). Participants who contributed data starting from the 4 weeks before their first vaccination onwards were included in this analysis. Antibodies against SARS-CoV-2 spike protein were quantified with an ELISA from Euroimmun (Lübeck, Germany) with an optical density cutoff of 0.8. We fitted linear mixed-effect models for log-transformed antibody levels using time splines with adjustment for age and sex. Marginal mean antibody levels with 95% confidence intervals (CI) were estimated at selected time points for IMID patients and controls with double vaccination. We descriptively analyzed the observed antibody levels over time in cohort participants receiving two vaccinations vs. three vaccinations.

Results: Among 5076 cohort participants, 3147 IMID patients and healthy controls (mean [SD] age 49 [16] yrs) provided 4756 samples for this analysis between December 2020 and 2021, with a median (IQR) 28 (14-31) weeks of follow-up after the first vaccination (Table 1). 2965 (94%) participants had received at least 2 and 223 (7%) participants had received three vaccine doses by the date of their latest sampling.