Correspondence on 'Immunogenicity and safety of anti-SARS-CoV-2 mRNA vaccines in patients with chronic inflammatory conditions and immunosuppressive therapy in a monocentric cohort'

We read with interest the work by Geisen and colleagues[1] on the efficacy and safety of anti-SARS-CoV-2 mRNA vaccine in patients with rheumatic diseases. While substantial data on the efficacy and safety of SARS-CoV-2 vaccination have been created during the last months, it is currently unclear whether the vaccination is efficacious and safe in patients with autoinflammatory diseases (AIDs). These patients present with exacerbated innate immune responses associated with enhanced production of interleukin (IL)-1.[2]

Testing the immune response to SARS-CoV-2 vaccination in patients with AIDs is of interest, as IL-1 has been involved in the pathogenesis of COVID-19; thus, IL-1 expression is massively increased in patients with severe COVID-19.[3–5] Furthermore, COVID-19 has shown to trigger an increased inflammatory disease activity in patients with AIDs.[6 7] In addition, IL-1 inhibition has been applied in the treatment of COVID-19 and while initial uncontrolled studies revealed promising results,[8] a randomised controlled trial showed no improvement of COVID-19 on IL-1 blockade.[9] While current data suggest the immune response to SARS-CoV-2 vaccination may be reduced in certain diseases, such as rheumatoid arthritis,[10] and certain treatments such as methotrexate,[11] such data cannot be applied to AID or to IL-1 inhibitors as the underlying pathophysiology is fundamentally different. Hence, we aimed to investigate SARS-CoV-2 vaccination responses in patients with AIDs treated with IL-1 inhibitors and compared them with healthy controls (HCs).

Ten patients with AIDs, four with adult-onset Still's disease, three with familial Mediterranean fever (FMF) and each one with gout, systemic AID and tumour necrosis factor receptor-associated periodical syndrome were investigated (online supplemental table 1). Their mean age was 33±10 years, eight were women and two men. All patients with AIDs were treated with

IL-1 inhibitors, eight with canakinumab and two with anakinra, administered regularly and at standard dosages of 150 mg/300 mg every 4 weeks and 100 mg/day, respectively. Two patients with FMF were additionally treated with 1 mg colchicine. None of the patients received glucocorticoids. In addition, 10 HCs were examined. All patients with AIDs and HCs received the BNT162b2 vaccine (Pfizer/BioNTech). None of the patients with AIDs and HCs did have COVID-19 before, nor did they have a positive anti-SARS-CoV-2 antibody test before vaccination.

IgG antibodies against the S1 domain of the spike protein of SARS-CoV-2 were tested by CE-certified ELISA (Euroimmun, Lübeck, Germany).[12] To assess neutralisation activity of antibodies, a CE-certified SARS-CoV-2 surrogate virus neutralisation assay (cPASS, Medac, Wedel, Germany) was used. A cut-off of 30% inhibition was considered as positive, according to the manufacturer's instructions.[13] We compared binary response status of antibody levels and neutralising activity using Fisher's exact test. ODs and per cent neutralising activity of the antibodies were compared using Mann-Whitney U tests. Two-sided p values were considered significant when <0.05. Analyses were performed using the open-source R software V.4.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

Nine out of 10 patients with AIDs and all HCs developed SARS-CoV-2-specific IgG antibodies (OD >0.8 units). The time course of the antibody response in patients and controls was very similar (figure 1A). SARS-CoV-2-specific IgG antibodies were even higher in patients with AIDs than in HCs (figure 1B). Respective median (IQR) ODs were 7.0 (6.6 to 7.4) in HCs and 8.4 (7.3 to 8.9) in patients with AIDs (p=0.00.19, Wilcoxon rank-sum test). The neutralising activity of receptor-binding domain binding to ACE2 was 96.4% (95.4% to 97.2%) in HCs and 95.3% (87.2% to 96.2%) in patients with AIDs, respectively (p=0.21, Wilcoxon rank-sum test). Vaccination was tolerated well in all patients and controls.

These data show good responses to SARS-CoV-2 vaccination in patients with AIDs treated with IL-1 inhibitors. They support previous anecdotal reports that IL-1 inhibitors may not impair the immune response in the context of COVID-19.[14] Importantly, both IgG levels as well as neutralising capacity of the anti-SARS-CoV-2 antibodies were comparable in patients with AIDs
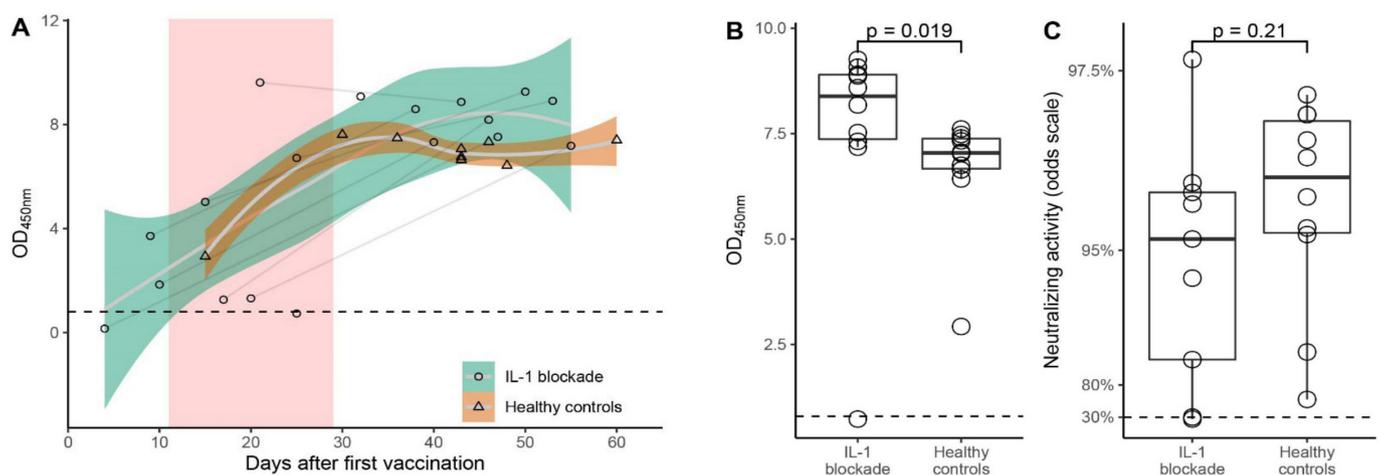

Figure 1 (A) Time course of anti-SARS-CoV-2 antibody response in patients with autoinflammatory disease receiving interleukin (IL)-1 blockade and healthy controls. Horizontal dashed line indicates the cut-off at OD 0.8. Shaded area represents the period during which second vaccine dose was administered. Dots connected by lines indicate antibody measurements from the same participants after the first and second vaccine dose. (B) Optical densities after the second vaccination, horizontal dashed line indicates the OD cut-off of 0.8. P value by Wilcoxon rank-sum test. (C) Neutralising activity of the antibodies after second vaccination. Horizontal dashed line indicates the cut-off at 30%. P value by Wilcoxon rank-sum test.

and HCs. Only one patient with gout and chronic renal failure undergoing haemodialysis did not respond to SARS-CoV-2 vaccination. The data also showed that there is no overshooting inflammatory response to SARS-CoV-2 vaccination in patients with AID. Taken together, these data support the current American College of Rheumatology guidelines for SARS-CoV-2 vaccination in patients with rheumatic diseases, including AIDs.[15]

In summary, SARS-CoV-2 vaccination in patients with AIDs receiving IL-1 inhibition is efficacious and well tolerated.

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