Table 1. The OR of being above a given Ab threshold, regardless of the threshold. Ref. levels: mean age, no medication, no past SARS-CoV-2 inf., BNT162b2. Included in model but not shown: diagnosis, infrequently used medication (all non-signif.)

Weeks post full vacc.	4		12		24	
	OR (95% CI); p					
Age	**0.96** (0.94 – 0.97)	****	**0.98** (0.96 – 0.996)	*	0.98 (0.97 – 1.00)	
mRNA-1273 (vs BNT162b2)	**3.28** (2.34 – 4.61)	****	**3.96** (2.83 – 5.54)	****	**3.94** (2.93 – 5.50)	****
Past COVID inf. (vs none)	**7.56** (4.32 – 13.2)	****	**8.14** (4.78 – 13.86)	****	**11.65** (6.62 – 20.50)	****
csDMARD[†]	1.27 (0.67 – 2.41)		1.78 (0.94 – 3.35)		1.70 (0.86 – 3.36)	
TNFi[†]	**0.46** (0.28 – 0.71)	****	**0.30** (0.19 – 0.48)	****	**0.13** (0.081 – 0.22)	****
IL-1/6/17/23i[†]	0.97 (0.54 – 1.75)		1.04 (0.57 – 1.89)		0.89 (0.49 – 1.64)	
JAKi[†]	**0.38** (0.16 – 0.91)	*	**0.38** (0.16 – 0.91)	*	0.53 (0.22 – 1.28)	
RTX[†]	**0.078** (0.013 – 0.46)	**	**0.078** (0.015 – 0.42)	**	**0.16** (0.037 – 0.71)	*
ABA[†]	**0.14** (0.039 – 0.51)	**	**0.087** (0.022 – 0.35)	***	**0.068** (0.017 – 0.27)	***
Interactions[§] Age:vaccine[‡]	**1.04** (1.02 – 1.07)	**	1.02 (0.99 – 1.05)		**1.03** (1.0008 – 1.058)	*
csDMARD:combi	**0.12** (0.02 – 0.70)	*	**0.17** (0.029 – 0.95)	*	**0.11** (0.023 – 0.56)	**
TNFi:combi	**0.34** (0.20 – 0.59)	***	**0.37** (0.22 – 0.61)	***	**0.36** (0.21 – 0.62)	***
IL-1/6/17/23i:combi	**0.26** (0.09 – 0.78)	*	**0.25** (0.085 – 0.70)	**	**0.20** (0.071 – 0.58)	**
JAKi:combi	1.76 (0.33 – 9.44)		1.23 (0.32 – 4.70)		0.95 (0.25 – 3.65)	
RTX:combi	**0.11** (0.01 – 0.87)	*	**0.095** (0.012 – 0.73)	*	**0.085** (0.0091 – 0.79)	*
ABA:combi	1.75 (0.25 – 12.2)		0.74 (0.096 – 5.75)		0.51 (0.073 – 3.62)	

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; [†]Medication as monoth. vs no medication [‡]Interaction terms showing how OR of mRNA-1273 (vs BNT162b2) increases with age [§]Interaction terms with medications: medication in combination th. vs medication as monoth.
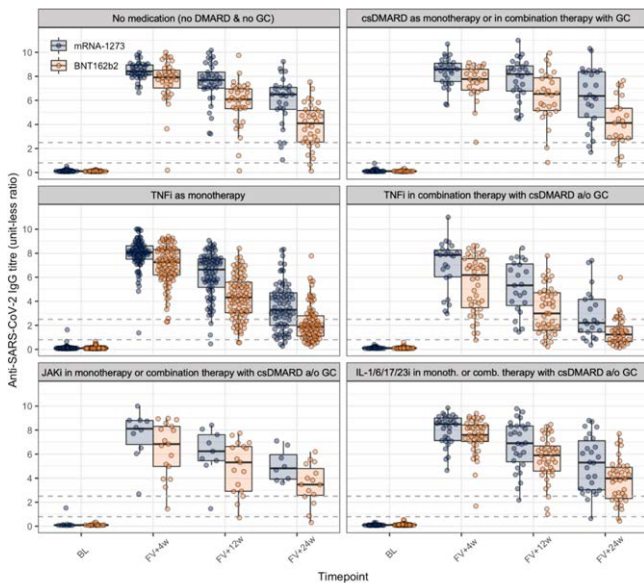

Figure 1. The variation with time of anti-S1 antibodies post mRNA COVID-19 vaccination in adult **SARS-CoV-2 naïve** IRD patients **as a function of medication** (in mono/combination therapy) **and vaccine**. Only medication groups corresponding to at least 10% of the study population are shown. Results are reported as a ratio (sample optical density / calibrator optical density). The dashed lines indicate the thresholds below (0.8) and above (2.5) which the results are considered negative and positive for the presence of anti-SARS-CoV2 IgG, respectively; samples with results in the zone between the two thresholds were considered indeterminate and were further tested with recombinant immunofluorescence. GC = glucocorticoids; csDMARD = conventional synthetic disease-modifying antirheumatic drug; TNFi = tumour necrosis factor inhibitor; JAKi = janus kinase inhibitor; IL-1/6/17/23i = interleukin inhibitors. BL = baseline (sample taken on day before or on day of first vaccination, before vaccination), FV+4w/12w/24w = 4/12/24 weeks post full vaccination. Boxplot whiskers extend to 1.5*IQR.

Conclusion: Compared to no medication, some immunomodulatory therapies resulted in markedly lower Ab levels at all timepoints. In IRD patients, a past SARS-CoV-2 infection resulted in strikingly increased immunogenicity, as did mRNA-1273 compared to BNT162b2.

DOI: 10.1136/annrheumdis-2022-eular.1796

OP0176	THE PERSISTENCE OF ANTI-SPIKE ANTIBODIES FOLLOWING TWO SARS-COV-2 VACCINES IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES USING IMMUNOSUPPRESSIVE THERAPY, COMPARED TO HEALTHY CONTROLS

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Background: Limited data is available regarding long-term effectiveness of SARS-CoV-2 vaccines in patients with immune-mediated inflammatory diseases (IMIDs) on immunosuppressive therapy. Whether the persistence of vaccine-induced humoral immunity against SARS-CoV-2 differs between this patient population and the general public is currently unknown.

Objectives: To compare the persistence of anti-Spike antibodies following two SARS-CoV-2 vaccine doses between IMID patients using immunosuppressive medication and healthy controls and identify predictors of antibody decline.

Methods: We included patients with inflammatory joint- and bowel diseases on immunosuppressive medication and healthy controls enrolled in the prospective observational Nor-vaC study. Serum samples were collected at two time points following two dose SARS-CoV-2 vaccination (first assessment within 6–48 days and second within 49–123 days). Sera were analysed for antibodies binding the receptor-binding domain (RBD) of the SARS-CoV-2 Spike protein. Anti-RBD <200 BAU /ml were defined as low levels. The estimated percent reduction in anti-RBD standardised to 30 days was calculated and factors associated with reduction were identified in multivariable regression models.

Results: A total of 1097 patients (400 rheumatoid arthritis, 189 psoriatic arthritis, 189 spondyloarthritis, 129 ulcerative colitis, 190 Crohn´s disease) (median age 54 years [IQR 43–64]; 56% women) and 133 controls (median age 45 years [IQR 35–56]; 83% women) provided blood samples within the defined intervals (median 19 days [IQR 15–24] and 97 days [86–105] after second vaccine dose). Antibody levels were significantly lower in patients compared to controls at both assessments, with median anti-RBD 1468 BAU/ml [IQR 500–5062] in patients and 5514 BAU/ml [2528–9580] in controls (p<0.0001) and 298 BAU/ml [IQR 79–500] in patients and 715 BAU/ml [28–2870] in controls (p<0.0001), at first and second assessment respectively. Figure 1 show antibody levels at both assessments after medication group. At the second assessment, anti-RBD antibody levels decreased below 200 BAU/ml in 452 (41%) patients and in 1 (0.8%) control (p<0.0001) (Table 1). The percentage change in anti-RBD levels were -86 % in patients and -77 % in controls (p<0.0001). The majority of patients using rituximab had low antibody levels at both assessments, Figure 1. In the multivariable regression analyses, patients had a greater decline in anti-RBD levels compared to controls β -3.7 (95% CI -6.0, -1.4) (p<0.001). Use of tumor necrosis factor inhibitors in mono- or combination therapy was associated with the greatest decline compared to controls, β -6.1 (95% CI -8.1, -4.1) and β -6.4 (-8.4, -4.2) respectively (p<0.001).

Conclusion: Within four months after the second vaccine dose, anti-Spike antibody levels declined considerably in both IMID patients and controls. Patients had lower antibody levels at the first assessment and a more pronounced decline compared to controls, and were consequently more likely to have low antibody levels four months after the second vaccine dose. Our results support that IMID patients lose humoral protection and need additional vaccine doses sooner than healthy individuals.

Figure 1. Level of anti-RBD antibodies at first and second assessment after medication group
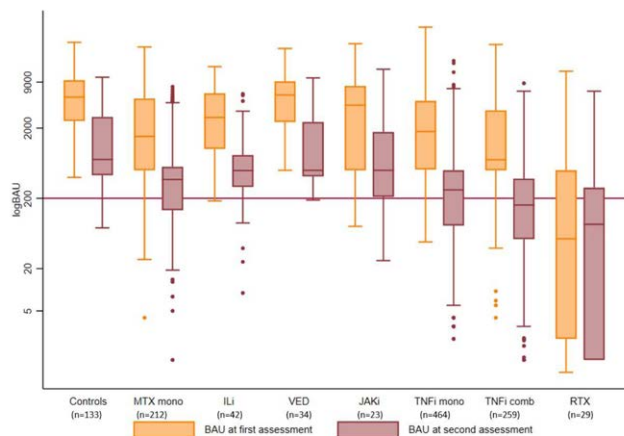
MTX mono: methotrexate monotherapy; ILI: Interleukin inhibitors including tocilizumab, ustekinumab, iksekizumab, risankizumab, secukinumab; VED: vedolizumab; JAKi: janus kinase inhibitor; TNFi mono: Tumor necrosis factor inhibitor in monotherapy; TNFi comb: Tumor necrosis factor inhibitor in combination with metabolite inhibitor(s) or vedolizumab; RTX: rituximab. All groups include patients using prednisolone in doses <10mg/day in combination with other medication. A cut-off at 200 BAU/ml is indicated.

Table 1. Serological response in patients and controls

Anti-RBD antibodies (BAU/ml)	Controls (n=133)		Patients (n=1097)	
	1st assessment	2nd assessment	1st assessment	2nd assessment
<5, n (%)	0	0	18 (1.6)	54 (5)
5-19, n (%)	0	0	4 (0.4)	60 (5)
20-199, n (%)	0	1 (1)	40 (4)	338 (31)
200-1999, n (%)	25 (19)	89 (67)	548 (50)	558 (51)
2000-8999, n (%)	71 (53)	40 (30)	398 (36)	82 (7.5)
≥ 9000, n (%)	37 (28)	3 (2)	89 (8)	5 (0.5)

1st assessment 6 - 48 days and 2nd assessment 49 -123 days after second vaccine dose.
BAU= Binding antibody Units

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IMMUNOGENICITY INDUCED BY TWO AND THREE DOSES OF THE BNT162B2 MRNA VACCINE IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES AND IMMUNOCOMPETENT CONTROLS: A LONGITUDINAL MULTI-CENTER STUDY

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Background: Data on the kinetics of the immune response to SARS-CoV-2 vaccination in patients with autoimmune inflammatory rheumatic diseases (AIIRD) are limited.

Objectives: To evaluate the kinetics of the immune response induced by two and three doses of the BNT162b2 mRNA vaccine in adult patients with AIIRD and immunocompetent controls.

Methods: A prospective multicenter study investigated the antibody response to the BNT162b2 vaccine by serial measurement of serum anti-SARS-CoV-2