

Antibody development and disease severity of COVID-19 in non-immunized patients with rheumatic immune-mediated inflammatory diseases: data from a prospective cohort study

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Appendix

Table S1. The development of rheumatic disease activity over time in patients with rheumatoid arthritis and ankylosing spondylitis.

	RAPID-3 score in patients with rheumatoid arthritis			BASDAI score in patients with ankylosing spondylitis		
April – July, 2020	n = 1073	9.7	(6.0)	n = 624	3.7	(2.0)
August – December, 2020	n = 1016	9.4	(6.0)	n = 593	3.6	(2.0)
January – March, 2021	n = 1115	11.4	(5.6)	n = 658	4.3	(1.9)

Data are number of responses in each time-window (n), and mean (SD). RAPID-3 = routine assessment of patient index data 3, BASDAI = bath ankylosing spondylitis disease activity index

Table S2. Logistic and linear mixed model analyses comparing seropositivity rates and IgG antibody titres of different treatment groups.

	Seropositivity			IgG antibody titer			
	OR	95% CI	P value	Beta	Ratio	95% CI	P value
No treatment with csDMARDs*	1.00	N.A.		0.00	1.00	N.A.	
Treatment with any csDMARD	0.99	(0.44 – 2.45)	0.99	0.24	1.27	(0.66 – 2.42)	0.47
Methotrexate	0.98	(0.43 – 2.24)	0.96	0.38	1.47	(0.74 – 2.90)	0.27
No treatment with bDMARD*				0.00	1.00	N.A.	
Treatment with any bDMARD	0.38	(0.18 – 0.82)	0.014	-0.38	0.68	(0.36 – 1.28)	0.23
TNF inhibitor	0.48	(0.21 – 0.11)	0.085	-0.57	0.56	(0.29 – 1.11)	0.098
B-cell targeting therapy	0.10	(0.010 – 1.08)	0.058	-0.21	0.81	(0.043 – 15.3)	0.89
No treatment with prednisone*				0.00	1.00	N.A.	
Prednisone	0.58	(0.21 – 1.60)	0.29	-1.02	0.36	(0.040 – 3.22)	0.33

Seropositivity data are adjusted odds ratios with 95% CI's in parentheses, and p values. IgG antibody titer data are adjusted β 's, back-transformed betas (ratios) with corresponding 95% CI's in parentheses, and p-values. All odds ratios and β 's are adjusted for age, sex, COVID-19 related hospitalization, time since COVID-19 disease onset and concomitant treatment with other immunosuppressive drugs. csDMARDs = conventional synthetic disease modifying anti-rheumatic drugs, TNF = tumor necrosis factor. *Reference group. † Below the Benjamini threshold.

Table S3. Development of SARS-CoV-2 antibodies over time stratified for treatment groups.		
	No. seroconversion (%)	Median IgG titer (IQR)
< 3 months after disease onset of COVID-19		
Healthy controls	27/33 (82)	12.9 (8.0 – 41.1)
All Patients	76/84 (91)	24.1 (9.5 – 71.3)
No immunosuppressive therapy	21/23 (91)	17.9 (9.8 – 40.9)
Treatment with any csDMARD	43/49 (88)	27.6 (7.4 – 91.6)
Methotrexate	33/38 (87)	24.2 (5.4 – 88.3)
Treatment with any biological	24/28 (86)	24.2 (5.4 – 68.9)
TNF-inhibitor	20/24 (83)	44.9 (5.4 – 43.8)
B-cell inhibitor	1/1 (100)	300 N.A.
Prednisone	7/8 (88)	18.0 (2.7 – 107.0)
3 – 6 months after disease onset of COVID-19		
Healthy controls	22/25 (88)	8.9 (3.1 – 24.6)
All Patients	70/83 (84)	18.4 (5.1 – 44.5)
No immunosuppressive therapy	15/19 (79)	20.4 (11.6 – 46.3)
Treatment with any csDMARD	36/39 (92)	21.3 (5.0 – 52.1)
Methotrexate	28/31 (90)	25.8 (5.1 – 70.1)
Treatment with any biological	25/34 (73)	10.3 (4.3 – 41.4)
TNF-inhibitor	22/28 (78)	11.3 (4.3 – 39.9)
B-cell inhibitor	2/2 (100)	120.6 -
Prednisone	7/11 (64)	67.4 (22.0 – 183.5)
>6 months after disease onset of COVID-19		
Healthy controls	52/60 (87)	7.1 (1.6 – 12.4)
All Patients	120/156 (77)	8.2 (1.9 – 16.9)
No immunosuppressive therapy	25/28 (90)	6.6 (3.7 – 13.6)
Treatment with any csDMARD	62/87 (71)	8.5 (2.1 – 17.5)
Methotrexate	50/70 (71)	8.3 (1.8 – 17.5)
Treatment with any biological	50/72 (69)	13.3 (0.4 – 14.4)
TNF-inhibitor	41/55 (75)	1.8 (0.3 – 9.3)
B-cell inhibitor*	2/7 (29)	-
Prednisone	15/22 (68)	6.4 (0.2 – 24.1)

Data are mean (SD), median (IQR), or n (%). Patients could contribute to data on multiple time-points. Quantification of IgG titers could not be performed in 14 (4%) of 367 samples due to a shortage of serum volume.

Table S4. Treatment alternations during follow-up in IMID patients receiving immunosuppressive agents.	
	Patients N = 2728
Treatment alteration during follow-up (yes) – no. (%)	848 (30)
Reason of change – no. (%)	N = 815
COVID-19 infection	53 (7)
Other infection	58 (7)
Adverse events	252 (31)
Failure	252 (31)
Other	376 (46)
Type of change – no. (%)	N = 695
Temporary discontinuation	176
Dose adjustment	342
Switch to alternative therapy (permanent)	156
Initiation of additional drug	73
Other	43

Data are n (%). IMID = immune-mediated inflammatory disease. Change in medication use since baseline was evaluated; 2728 of 3080 patients completed a follow-up questionnaire in which this information was assessed. Type of change was only assessed in questionnaires distributed since January, 2021. Patients could alter their medication more than once during follow-up, and therefore contribute to multiple types and reasons of change.