

Supplementary Table S1. Demographic and clinical characteristics of the study population with no previous exposure to SARS-CoV-2, stratified for response to the first dose of the BNT162b2 mRNA COVID-19 vaccine.

	All n=120 pts	Responders n=66	Non-responders n=54	p
Age, mean (SD), yrs	56.7 (14.0)	51.2 (13.4)	63.5 (11.6)	<0.001
Females, n. (%)	81 (67.5)	40 (60.6)	41 (75.9)	0.11
BMI, mean (SD)	26.09 (5.22)	25.59 (5.33)	26.69 (5.09)	0.30
Smoking, n. (%)	20 (16.7)	11 (16.7)	9 (16.6)	0.82
Hypertension, n. (%)	42 (35)	18 (27.3)	24 (44.4)	0.08
Obesity, n. (%)	24 (20)	13 (19.7)	11 (20.4)	0.89
CCI, mean (SD)	0.53 (0.88)	0.39 (0.82)	0.70 (0.92)	0.05
≥1 comorbidity*, n. (%)	42 (35)	16 (24.2)	26 (48.1)	0.01
Diagnosis, n. (%):				
RA	69 (57.5)	27 (40.9)	42 (77.8)	<0.001
PsA,	26 (21.7)	17 (25.8)	9 (16.7)	0.33
SpA	25 (20.8)	22 (18.3)	3 (5.6)	0.07
Disease duration, median (IQR), yrs	13.8 (8.0)	13.2 (8.7)	14.6 (7.0)	0.34
Active disease [§] , n. (%)	27 (22.5)	15 (22.7)	12 (22.2)	0.88
Glucocorticoids, n. (%)	47 (39.2)	20 (30.3)	27 (50)	0.04
Prednisone dose, mean (SD), mg/d	3.6 (1.8)	3.5 (1.3)	3.7 (2.1)	0.69
csDMARDs, n. (%)	67 (55.8)	26 (39.4)	41 (75.9)	<0.001
MTX	55 (45.8)	17 (25.8)	38 (70.4)	<0.001
SSZ	11 (9.2)	9 (13.6)	2 (3.7)	0.12
LFN	3 (2.5)	1 (1.5)	2 (3.7)	0.86
CYA	1 (0.8)	0 (0)	1 (1.9)	0.90
MTX dose, mean (SD), mg/wk	14.8 (5.3)	15.3 (5.7)	14.6 (5.2)	0.66
Days of MTX withholding, mean (SD)	16.3 (3.5)	15.9 (3.5)	16.6 (3.6)	0.57
Adherence to MTX withholding [^] , n. (%)	26 (47.3)	6 (35.3)	20 (52.6)	0.37
b/tsDMARDs, n. (%)	120 (100)	66 (100)	54 (100)	
TNFi	53 (44.2)	33 (50)	20 (37)	0.21
IL-6Ri	12 (10)	6 (9.1)	6 (11.1)	0.95
IL-17/IL-23i	16 (13.3)	14 (21.2)	2 (3.7)	0.01
CTLA4Ig	25 (20.8)	4 (6.1)	21 (38.9)	<0.001
JAKi	10 (8.3)	7 (10.6)	3 (5.6)	0.51
PDE4i	4 (3.3)	3 (4.5)	1 (1.9)	0.78
Days of b/tsDMARD withholding, mean (SD)	22 (13.8)	24.1 (15.9)	19.4 (10.2)	0.06
Adherence to b/tsDMARDs withholding [^] , n. (%)	80 (66.7)	47 (71.2)	33 (61.1)	0.33

b/ts = Biologic/Targeted Synthetic; BMI = Body Mass Index; CCI = Charlson Comorbidity Index; cs = Conventional Synthetic; CTLA4Ig = Cytotoxic T-lymphocyte Associated Protein-4 Immunoglobulin; CYA = Cyclosporine; DMARD = Disease Modifying Anti-Rheumatic Drug; IL-6Ri = Interleukin-6 Receptor Inhibitor; IL-17/IL-23i = Interleukin-17/Interleukin-23 Inhibitor; JAKi = Janus Kinase Inhibitor; LFN = Leflunomide; MTX = Methotrexate; PDE4i = Phosphodiesterase-4 inhibitor; RA = Rheumatoid Arthritis; PsA = Psoriatic Arthritis; SpA = Spondyloarthritis; SSZ = Sulphasalazine; TNFi = Tumor Necrosis Factor Inhibitor.

*among those listed in the Charlson Comorbidity Index

[§]above the threshold of low disease activity according to the appropriate composite index: DAS28 >3.2; DAPSA >14; ASDAS-PCR >2.1. DAS28 = Disease Activity Score on 28 joints; DAPSA = Disease Activity in Psoriatic Arthritis; ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score calculated with C-Reactive Protein.

[^]recommendations for timing of immunomodulatory therapies in relation to vaccination: (i) for all the bDMARDs and MTX, withholding of therapy in the 7 days before and after vaccination; (ii) for tsDMARDs, withholding of therapy from the day before until day 7 after vaccination; (iii) for glucocorticoids and csDMARDs other than MTX, no modifications.

Supplementary Table S2. Demographic and clinical factors associated with non-response to the first dose of the BNT162b2 mRNA COVID-19 vaccine. Univariable and multivariable analysis.

	All n=140			No previous COVID-19 n=120		
Univariable analysis						
	OR	95% CI	p	OR	95% CI	p
Age>55	6.30	2.86 to 13.91	<0.001	6.77	2.91 to 15.77	<0.001
Female gender	1.95	0.91 to 4.18	0.09	2.05	0.93 to 4.54	0.08
BMI	1.05	0.98 to 1.13	0.19	1.04	0.96 to 1.13	0.30
Smoking	1.07	0.41 to 2.82	0.89	1.09	0.40 to 3.03	0.86
CCI	1.35	0.93 to 1.95	0.11	1.52	0.98 to 2.36	0.06
≥1 comorbidity*	2.60	1.27 to 5.30	0.009	2.90	1.34 to 6.30	0.007
Previous COVID-19 [#]	0.06	0.01 to 0.50	0.009	--	--	--
Diagnosis						
RA	Reference			Reference		
PsA	0.42	0.17 to 1.03	0.06	0.34	0.13 to 0.87	0.02
SpA	0.11	0.03 to 0.40	<0.001	0.09	0.02 to 0.32	<0.001
Disease duration	1.03	0.99 to 1.08	0.16	1.02	0.98 to 1.07	0.34
Active disease [§]	1.27	0.39 to 4.17	0.69	1.07	0.30 to 3.79	0.92
Glucocorticoids	2.19	1.08 to 4.41	0.03	2.30	1.09 to 4.86	0.03
Prednisone dose	1.16	0.99 to 1.36	0.07	1.21	1.01 to 1.45	0.04
MTX	5.24	2.50 to 10.97	<0.001	6.85	3.07 to 15.29	<0.001
MTX dose	1.09	1.04 to 1.14	<0.001	1.10	1.05 to 1.16	<0.001
Days of MTX withholding	1.04	0.88 to 1.24	0.64	1.05	0.86 to 1.27	0.65
Adherence to MTX withholding [^]	1.20	0.37 to 3.92	0.76	1.98	0.49 to 7.94	0.34
b/tsDMARD						
TNFi	Reference			Reference		
IL-6Ri	1.39	0.43 to 4.55	0.58	1.60	0.45 to 5.65	0.47
IL17/IL-23i	0.22	0.05 to 1.04	0.06	0.23	0.05 to 1.11	0.07
CTLA4Ig	4.33	1.69 to 11.14	0.002	8.40	2.51 to 28.07	<0.001
JAKi	0.62	0.15 to 2.54	0.51	0.69	0.16 to 2.96	0.61
PDE4i	0.62	0.06 to 6.33	0.69	0.53	0.05 to 5.49	0.60
Days of b/tsDMARD withholding	0.97	0.94 to 1.00	0.06	0.97	0.94 to 0.99	0.04
Adherence to b/tsDMARDs withholding [^]	0.58	0.28 to 1.20	0.14	0.60	0.27 to 1.29	0.19
Multivariable analysis						
	OR	95% CI	p	OR	95% CI	p
Age>55	3.93	1.46 to 10.55	0.006	5.74	2.07 to 15.93	<0.001
Female gender	--	--	--	--	--	--
≥1 comorbidity*	--	--	--	--	--	--
Previous COVID-19 [#]	0.03	0.00 to 0.25	0.002			
RA	--	--	--	--	--	--
Glucocorticoids	2.69	1.04 to 5.89	0.04	3.17	1.18 to 7.09	0.03
MTX	7.46	2.88 to 19.33	<0.001	5.73	2.11 to 15.58	<0.001
b/tsDMARD						
anti-IL17/IL-23	0.20	0.04 to 1.27	0.10	0.21	0.04 to 1.21	0.08
CTLA4Ig	2.28	0.69 to 6.26	0.19	3.64	1.11 to 13.28	0.04
Days of b/tsDMARD withholding	--	--	--	--	--	--

b/ts = Biologic/Targeted Synthetic; BMI = Body Mass Index; CCI = Charlson Comorbidity Index; CTLA4Ig = Cytotoxic T-lymphocyte Associated Protein-4 Immunoglobulin; DMARD = Disease Modifying Anti-Rheumatic Drug; IL-6Ri = Interleukin-6 Receptor Inhibitor; IL-17/IL-23i = Interleukin-17/Interleukin-23 Inhibitor; JAKi = Janus Kinase Inhibitor; MTX = Methotrexate; PDE4i = Phosphodiesterase-4 inhibitor; RA = Rheumatoid Arthritis; PsA = Psoriatic Arthritis; SpA = Spondyloarthritis; TNFi = Tumor Necrosis Factor Inhibitor.

*among those listed in the Charlson Comorbidity Index

#based on patient-reported history of swab-confirmed SARS-CoV-2 infection and/or on pre-vaccine anti-S IgG levels >15 AU/mL (LIAISON[®] SARS-CoV-2 S1/S2 IgG; DiaSorin)

[§]above the threshold of low disease activity according to the appropriate composite index: DAS28 >3.2; DAPSA >14; ASDAS-PCR >2.1. DAS28 = Disease Activity Score on 28 joints; DAPSA = Disease Activity in Psoriatic Arthritis; ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score calculated with C-Reactive Protein.

[^]recommendations for timing of immunomodulatory therapies in relation to vaccination: (i) for all the bDMARDs and MTX, withholding of therapy in the 7 days before and after vaccination; (ii) for tsDMARDs, withholding of therapy from the day before until day 7 after vaccination; (iii) for glucocorticoids and csDMARDs other than MTX, no modifications.

Supplementary Table S3. Demographic and clinical factors associated with non-response to the first dose of the BNT162b2 mRNA COVID-19 vaccine in the subgroup of patients treated with tumor necrosis factor inhibitors. Univariable and multivariable analysis.

	All n=61			No previous COVID-19 n=53		
Univariable analysis						
	OR	95% CI	p	OR	95% CI	p
Age>55	7.23	2.01 to 25.96	0.002	8.08	1.95 to 33.40	0.004
Female gender	0.91	0.30 to 2.80	0.87	0.97	0.30 to 3.14	0.96
BMI	1.05	0.95 to 1.17	0.34	1.04	0.93 to 1.15	0.51
Smoking	0.32	0.04 to 2.87	0.31	0.33	0.04 to 3.05	0.33
CCI	1.57	0.83 to 2.95	0.16	1.48	0.75 to 2.90	0.26
≥1 comorbidity*	3.71	1.13 to 12.16	0.03	3.73	1.04 to 13.45	0.04
Previous COVID-19 [#]	0.27	0.03 to 2.37	0.24	--	--	--
Diagnosis						
RA	Reference			Reference		
PsA	0.71	0.17 to 3.03	0.65	0.67	0.15 to 3.04	0.60
SpA	0.20	0.05 to 0.83	0.03	0.18	0.04 to 0.78	0.02
Disease duration	1.06	0.99 to 1.12	0.07	1.06	0.99 to 1.13	0.10
Active disease [§]	1.06	0.08 to 13.52	0.96	0.81	0.06 to 10.48	0.87
Glucocorticoids	3.71	1.13 to 12.16	0.03	3.86	1.11 to 13.37	0.03
Prednisone dose	1.36	1.01 to 1.83	0.04	1.35	0.99 to 1.83	0.06
MTX	8.40	2.43 to 29.04	<0.001	7.14	1.97 to 25.94	0.003
MTX dose	1.12	1.04 to 1.21	0.002	1.11	1.03 to 1.20	0.006
Days of MTX withholding, mean (SD)	1.05	0.80 to 1.38	0.73	1.06	0.79 to 1.42	0.71
Adherence to MTX withholding [^]	0.90	0.13 to 6.08	0.91	1.50	0.17 to 13.23	0.72
Days of TNFi withholding, mean (SD)	0.98	0.94 to 1.03	0.41	0.97	0.93 to 1.02	0.26
Adherence to TNFi withholding [^]	1.10	0.37 to 3.29	0.87	1.11	0.35 to 3.49	0.86
Multivariable analysis						
	OR	95% CI	p	OR	95% CI	p
Age>55	6.86	1.02 to 46.19	0.04	11.38	1.64 to 78.80	0.01
≥1 comorbidity*	3.68	0.59 to 22.98	0.16	--	--	--
SpA	--	--	--	--	--	--
Disease duration	--	--	--	--	--	--
Glucocorticoids	7.66	1.29 to 45.61	0.03	6.44	1.16 to 35.71	0.03
MTX	23.26	3.37 to 160.42	0.001	14.94	2.34 to 95.30	0.004

BMI = Body Mass Index; CCI = Charlson Comorbidity Index; MTX = Methotrexate; RA = Rheumatoid Arthritis; PsA = Psoriatic Arthritis; SpA = Spondyloarthritis; TNFi = Tumor Necrosis Factor Inhibitor.

*among those listed in the Charlson Comorbidity Index

[#]based on patient-reported history of swab-confirmed SARS-CoV-2 infection and/or on pre-vaccine anti-S IgG levels >15 AU/mL (LIAISON[®] SARS-CoV-2 S1/S2 IgG; DiaSorin)

[§]above the threshold of low disease activity according to the appropriate composite index: DAS28 >3.2; DAPSA >14; ASDAS-PCR >2.1. DAS28 = Disease Activity Score on 28 joints; DAPSA = Disease Activity in Psoriatic Arthritis; ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score calculated with C-Reactive Protein.

[^]recommendations for timing of immunomodulatory therapies in relation to vaccination: (i) for all the bDMARDs and MTX, withholding of therapy in the 7 days before and after vaccination; (ii) for tsDMARDs,

withholding of therapy from the day before until day 7 after vaccination; (iii) for glucocorticoids and csDMARDs other than MTX, no modifications

Supplementary Table S4. Association of methotrexate and glucocorticoids with anti-S IgG levels in responders to the first dose of the BNT162b2 mRNA COVID-19 vaccine. Multivariable analysis.

	All n=85		No previous COVID-19 n=66	
	Stand β	p	Stand β	p
Age	--	--	--	--
Pre-vaccine anti-S IgG levels	0.56	<0.001	--	--
Prednisone dose	-0.17	0.04	-0.16	0.04
Methotrexate dose	-0.15	0.05	-0.18	0.04