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Supplemental Table 1 Categorization of IMID treatments

Treatment Disease	Inflammatory Bowel Disease	Multiple Sclerosis	Rheumatoid Arthritis and SARDs
Corticosteroids (N=37)	Methylprednisolone Prednisolone) Prednisone Budesonide Hydrocortisone	Methylprednisolone Prednisolone Prednisone	Methylprednisolone) Prednisolone Prednisone Triamcinolone Cortisone
Anti-inflammatory or Immunomodulatory therapies (N=77)	5-ASA Sulfasalazine	Glatiramer acetate interferon-beta 1a interferon-beta 1b dimethyl fumarate Teriflunomide Peg interferon-beta	Sulfasalazine sodium aurothiomalate auranofin aurothioglucose Penicillamine Hydroxychloroquine (
Traditional immunosuppressive therapies (N=78)	Azathioprine Methotrexate 6-mercaptopurine Cyclosporine Tacrolimus	Azathioprine Methotrexate) Mitoxantrone Cyclophosphamide	Azathioprine methotrexate Cyclophosphamide Cyclosporine Leflunomide Mycophenolate Tacrolimus
Novel therapies/ Biologics¹ (N=98)	Infliximab adalimumab Golimumab Ustekinumab Vedolizumab Tofacitinib	Natalizumab Fingolimod ² Alemtuzumab Cladribine Ocrelizumab	Infliximab) Adalimumab Etanercept Anakinra Rituximab ³ Abatacept ³ Tocilizumab Tofacitinib Golimumab Certolizumab Upadacitinib Baricitinib Belimumab Sekukinumab Ustekinumab

¹ Anti-TNF N= 51, B cell depletion N=21, Past B cell depletion N=9, Other therapy N=27 (ustekinumab n=6, vedolizumab n=6, tofacitinib n=4, tocilizumab n=2, fingolimod n=2, alemtuzumab n=1, natalizumab n=1, upadacitinib n=1)

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Supplemental Table 2 Seroconversion rates based on vaccine mixture between first and second vaccinations

RBD= receptor binding domain; BNT= BNT162b2

Homologous (any) versus heterologous (any) vaccine combination and seroconversion 1 month post V2 anti-Spike χ^2 7.8 $p < 0.01$; antiRBD χ^2 6.8 $p < 0.01$; 1 month post V3 anti-Spike χ^2 0.5 $p = \text{NS}$; anti RBD χ^2 0.2 $p = \text{NS}$

	1month post V2 Anti-Spike seroconverted n/N (%)	1month post V2 Anti-RBD seroconverted n/N (%)	1month post V3 Anti-Spike seroconverted n/N (%)	1month post V3 Anti-RBD seroconverted n/N (%)
Homologous	137/158 (86.7)	139/158 (88.0)	130/140 (92.9)	132/140 (94.3)
ChAdOX1-ChAdOX1	4/6 (66.7)	4/6 (66.7)	5/6 (83.3)	5/6 (83.3)
BNT-BNT	120/139 (84.3)	122/139 (87.8)	112/121 (92.6)	113/121 (93.4)
mRNA 1273-mRNA1273	13/13 (100)	13/13 (100)	13/13 (100.0)	13/13 (100.0)
Heterologous	69/70 (98.6)	69/70 (98.6)	64/65 (98.5)	64/65 (98.5)
ChAdOX1-BNT	30/31 (96.8)	30/31 (96.8)	27/28 (96.4)	27/28 (96.4)
ChAdOX1-mRNA1273	25/25 (100)	25/25 (100)	24/24 (100.0)	24/24 (100.0)
BNT-mRNA1273	14/14 (100)	14/14 (100)	13/13 (100.0)	13/13 (100.0)

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Supplemental Table 3 Clinical features of IMIDs not seroconverting after 2 vaccinations

IMID = immune mediated inflammatory disease; IA= inflammatory arthritis; SARDs= Systemic autoimmune rheumatic disease; MS= multiple sclerosis; IBD= inflammatory bowel disease M=male; F=female

IMID	Sex	Age baseline	Medication	vaccine combination
IA	M	82	Prednisone	BNT-BNT
IA	F	77	Methotrexate + rituximab	BNT-BNT
IA	F	76	tocilizumab	BNT-BNT
IA	F	70	methotrexate + anti-TNF	BNT-BNT
IA	F	61	mycophenolate	BNT-BNT
SARDs	F	66	rituximab + prednisone	BNT-BNT
SARDs	F	60	mycophenolate	ChAdOX1-ChAdOX1
SARDs	F	31	rituximab + prednisone	BNT-BNT
SARDs	F	72	mycophenolate	BNT-BNT
SARDs	F	71	mycophenolate	BNT-BNT
SARDs	F	69	mycophenolate + IV Immune globulin	BNT-BNT
SARDs	F	69	azathioprine + past rituximab	BNT-BNT
MS	F	56	ocrelizumab	ChAdOX1-BNT
MS	M	57	ocrelizumab	BNT-BNT
MS	F	74	none	BNT-BNT
MS	F	36	ocrelizumab	BNT-BNT
MS	F	48	fingolimod	BNT-BNT
MS	F	81	none	BNT-BNT
MS	F	34	ocrelizumab	BNT-BNT
IBD	F	31	anti-TNF + prednisone	ChAdOX1-ChAdOX1

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Supplemental table 4: Clinical characteristics of anti-nucleocapsid seropositive participants

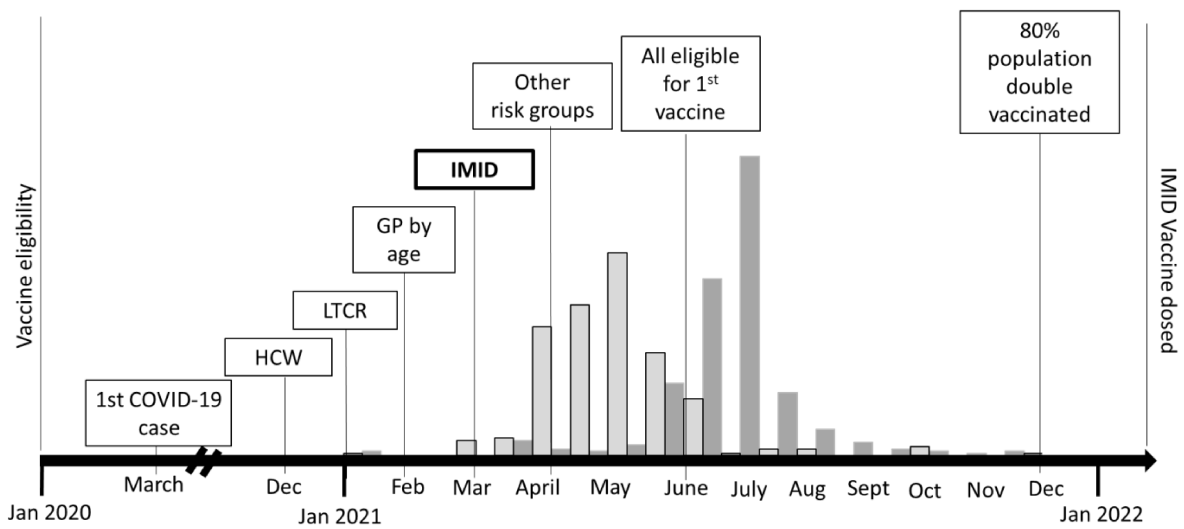
IMID	Age (years)	First visit tested positive	Preceding visit with serology	Anti-RBD titer at preceding visit ¹	Anti-S1 titer at preceding visit ²	First and second vaccine	Last vaccine prior to infection	IMID treatment
IA	63	1moV4	1moV3	76752	11941	v/mRNA	mRNA1273	JAKi
IA	63	1moV3	3moV1	NA	NA	mRNA/mRNA	mRNA1273	HDQ;MTX
IA	65	3moV4	3moV2	1547	1505	mRNA/mRNA	BNT	HDQ
IA	69	1moV4	1moV3	1365	1526	mRNA/mRNA	mRNA1273	HDQ aTNF
IA	53	1moV3	3moV2	923	178	mRNA/mRNA	BNT	HDQ, MTX
IA	68	1moV4	1moV3	4680	3403	mRNA/mRNA	BNT	aTNF. Pred
IA	49	1moV1	NA	NA	NA	mRNA/mRNA	BNT	HDQ MTX
IA	62	1moV1	NA	NA	NA	mRNA/mRNA	BNT	HDQ
SARDs	61	1moV4	1moV3	2756	2825	v/v	BNT	HDQ
SARDs	60	1moV3	3moV2	867	556	mRNA/mRNA	BNT	HDQ
SARDs	62	1moV4	1moV3	17969	12938	mRNA/mRNA	BNT	MTX
SARDs	44	1moV3	3moV2	172	254	mRNA/mRNA	BNT	MTX
SARDs	64	1moV4	3moV2	74	96	v/mRNA	BNT	Ritux
SARDs	38	1moV4	1moV3	3734	4104	v/mRNA	mRNA1273	AZA
SARDs	39	3moV2	NA	NA	NA	v/mRNA	mRNA1273	AZA
SARDs	30	1moV4	NA	NA	NA	mRNA/mRNA	BNT	aTNF
MS	53	1moV2	NA	NA	NA	v/mRNA	mRNA1273	GLA
MS	75	1moV1	NA	NA	NA	mRNA/mRNA	BNT	None
MS	56	1moV3	3moV3	2304	2811	v/mRNA	mRNA1273	INF
IBD	50	1moV2	NA	NA	NA	mRNA/mRNA	BNT	VED
IBD	67	1moV4	3moV2	591	584	mRNA/mRNA	mRNA1273	VED
IBD	30	1moV4	1moV3	1339	1464	mRNA/mRNA	BNT	UST
IBD	20	1moV4	1moV3	6221	6375	mRNA/mRNA	BNT	aTNF
IBD	64	1moV3	3moV2	497	536	v/mRNA	mRNA1273	5-ASA
IBD	45	1moV3	3moV2	Neg	neg	mRNA/mRNA	BNT	aTNF

IMID = immune mediated inflammatory disease; IA= inflammatory arthritis; SARDs= Systemic autoimmune rheumatic disease; MS= multiple sclerosis; IBD= inflammatory bowel disease; NA not available (no prior visit with serology data). 1moV1 = 1 month post first vaccine, 1moV2 = 1 month post second vaccine; 3moV2 = 3 months post second vaccine; 1moV3 = 1 month post third vaccine; 1moV4 = 1 month post fourth vaccine

¹ anti-Receptor Binding Domain BAU/ml; median (interquartile range) for all samples 1moV2 1686.8 (2199.44); 3moV2 555.8 (809.3); 1moV3 4280.3(6380.6)

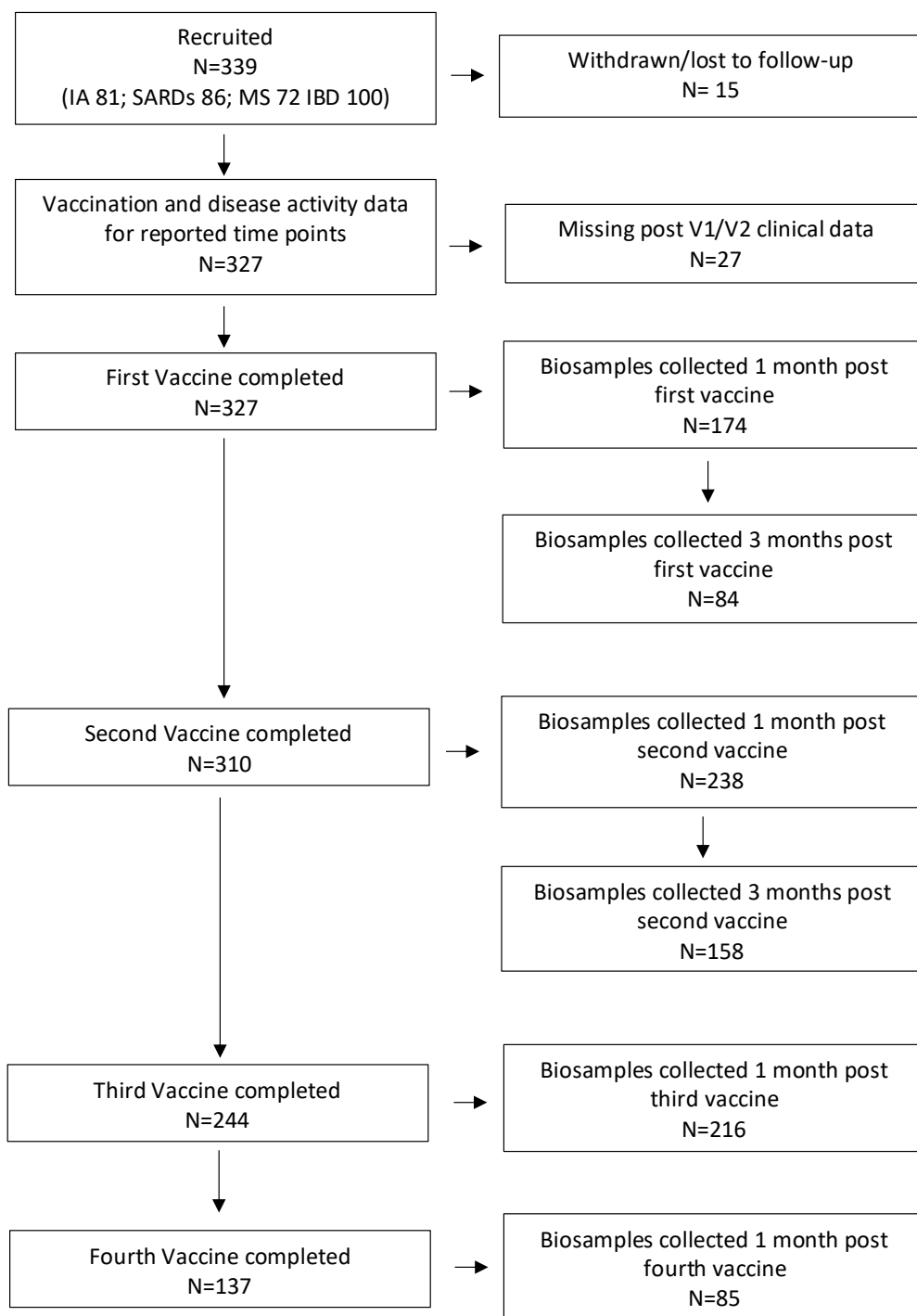
² anti-Spike BAU/ml; median values for all samples 1moV2 1835 (2448); 3moV2 629.1 (883.4); 1moV3 4280.3(6380.6)

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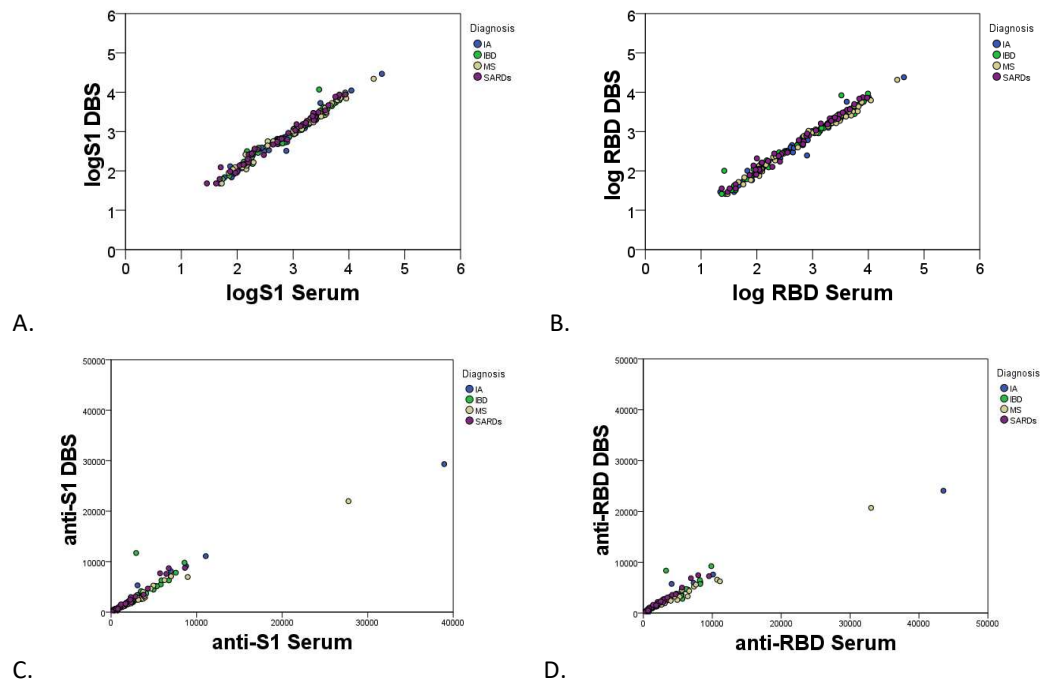


Supplemental Figure 1 Covid-19 vaccination timeline

HCW= health care workers; LTCR= long term care residents, GP= general population, IMiD=immune mediated inflammatory disease; Bars indicate time when study participants (IMiDs) received vaccine. Light grey bars indicate time of first vaccine (V1); dark grey bars indicate time of second vaccine (V2).

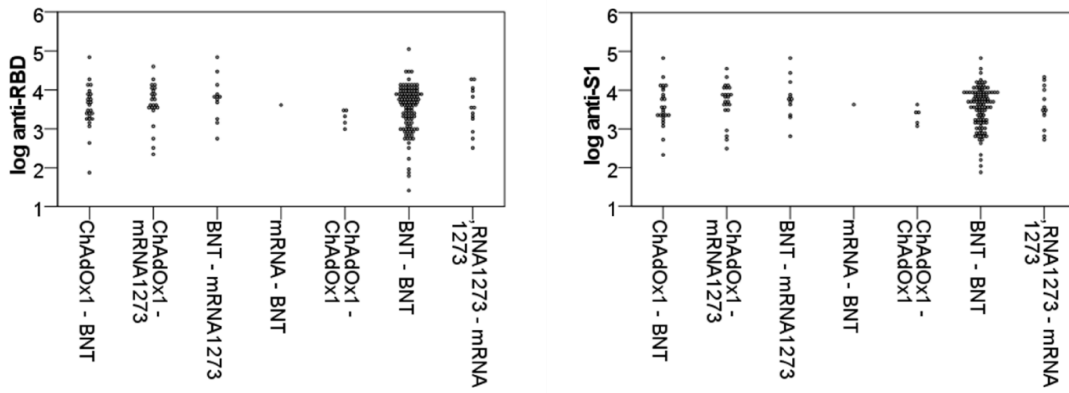
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Supplemental Figure 2 Recruitment and sample acquisition chart

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Supplemental Figure 3 Correlation between assays performed using serum and dried blood spot samples. A. \log Anti-S1 B \log anti-RBD, C. anti-S1 BAU/ml D anti RBD BAU/ml (Kendalls tau b correlation co-efficient anti-S1 BAU/ml= 0.92; anti-RBD BAU/ml=0.93)

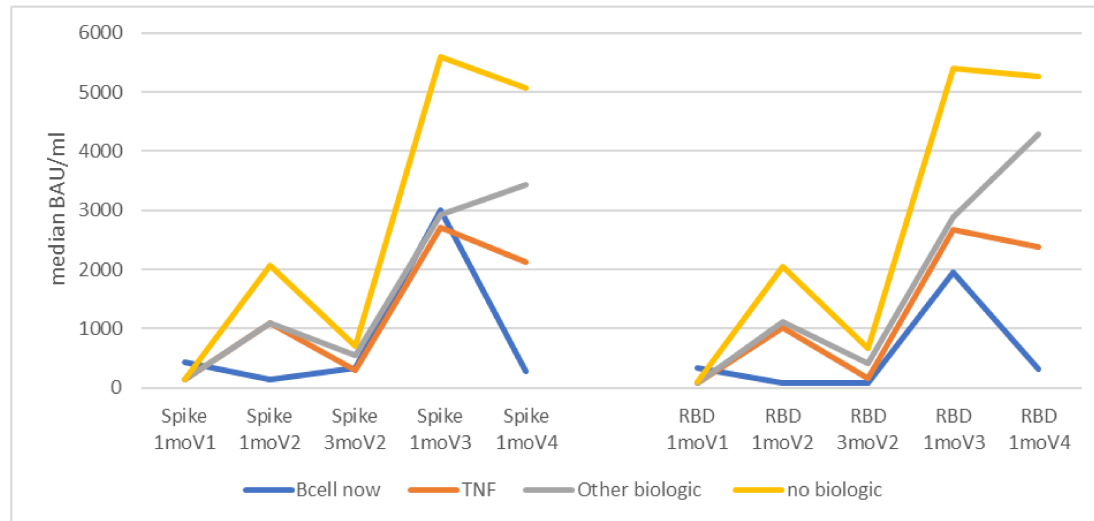
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Supplemental Figure 4 Anti-SARS-CoV2 titers 1 month post third vaccine based on first and second vaccine mixture.

RBD= Receptor binding domain; S1= Spike 1. All comparisons p=NS

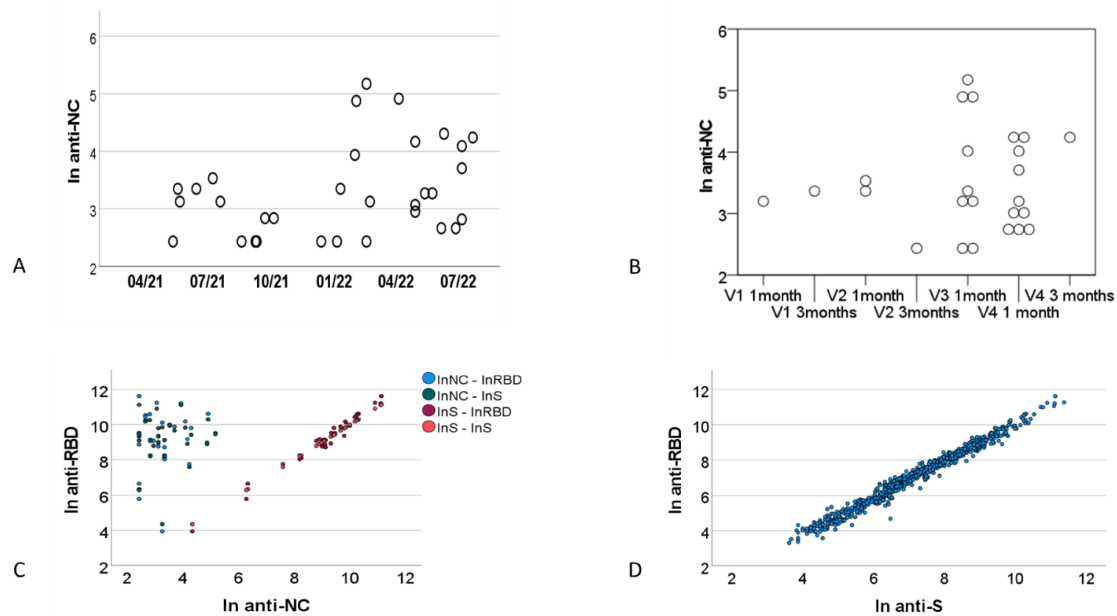
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	B cell targeting now	anti-TNF	other biologic	no biologic	B cell targeting past
N 1moV1	2	14	8	77	2
N 1moV2	5	37	16	152	4
N 3moV2	5	34	20	154	5
N 1moV3	8	34	19	140	5
N 1moV4	5	18	11	46	5

Supplemental Figure 5 Median titers of anti-Spike and anti-RBD for individuals on different biologic categories and number participants in each treatment category for each visit.

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Supplemental Figure 6 Anti-Nucleocapsid antibody levels and correlations with Anti-Spike and Anti-Receptor Binding Domain antibodies

- A. Anti-NC titer by Calendar month/year B. Anti-NC titer by Study visit C. Correlation of anti-NC anti RBD and anti-S1 titers in samples seropositive for anti-NC D. Correlation of anti-RBD and anti-S1 titers in all seropositive samples.

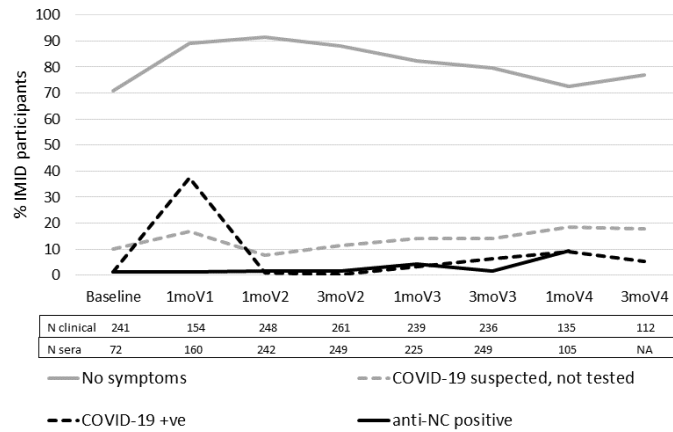
NC = nucleocapsid S = Spike; RBD = receptor binding domain; ln = natural log. V1 = vaccine 1; V2 = vaccine 2; V3 = vaccine 3; V4= vaccine 4. Values are natural log transformed BAU/ml.

Spearman correlation coefficient anti-NC with anti-S1 = 0.06 ($p=NS$); anti-NC with anti-RBD = 0.03 ($p=NS$); anti-S with anti-RBD 0.96 $p<0.001$. Figure 3 Disease activity before and after each vaccine

A Inflammatory arthritis B Systemic autoimmune rheumatic disease C Inflammatory bowel disease D Multiple Sclerosis

RAPID-3 Routine Assessment of Patient Index Data 3; SLAQ Systemic lupus activity questionnaire IBDSI-SF Inflammatory bowel disease symptom inventory – short form; EDSS Expanded disability status scale. V1 vaccine one; V2 vaccine two; V3 vaccine 3; V4 vaccine 4; mo = month(s).

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Supplemental Figure 7 COVID-19 infection

Grey line = no COVID-19 symptoms reported; Dashed grey line = COVID-19 suspected but not tested; dashed black line = COVID-19 infection confirmed by community based testing (rapid detection or polymerase chain reaction test); solid black line = proportion anti-nucleocapsid seropositive.

V1 vaccine one; V2 vaccine two; V3 vaccine 3; V4 vaccine 4; mo = month(s); N = number