SUPPLEMENTARY METHODS

Supplementary data S1: patient diagnosis

Diagnosis of GCA was based on presence of symptoms and signs consistent with GCA plus a positive temporal artery biopsy (TAB) and/or positive proof of vasculitis with an imaging test (FDG-PET/CT, ultrasound). In the majority of PMR patients, diagnosis was based on a positive FDG PET-CT scan showing inflammation in the shoulders and hips, or if unavailable, patients fulfilled the 2012 ACR/EULAR criteria for PMR.

Supplementary data S2: Multiplex immune assay (MIA)

To measure concentrations of SARS-CoV-2 Spike-specific IgG serum antibodies, we performed a human multiplex immunoassay (MIA), based on Luminex technology, as was described before. (1,2,3) Briefly, for each antigen (SARS-CoV-2 monomeric Spike S1 (40591-V08H) and nucleoprotein (N) (40588-V08B)), fluorescently labeled microspheres (Bio-Rad Laboratories, Hercules, USA) were activated in 50 mM 2-(N-morpholino)ethanesulfonic acid (MES, pH 5.5). The antigens were diluted (0.2 mg/mL) in phosphate-buffered saline (PBS, pH 7.4) and 5ug of antigens/ 75ul activated beads were added. Antigens were incubated with beads for 2 hours at room temperature (RT). Serum samples (25ul) were prepared in 1:400 and 1:8000 dilutions in SM01 buffer (Surmodics) plus 2% fetal calf serum. Each serum dilution was incubated with antigen-coated beads for 45 minutes at RT (in the dark). Then, beads were washed (in PBS) followed by 30 minutes incubation with phycoerythrin-conjugated goat anti-human IgG. LX200 or FM3D (Luminex) was used for acquiring samples. Mean fluorescence intensity (MFI) was converted to arbitrary units (AU/mL). The conversion method was described in previous studies. (3) Finally, IgG concentrations to SARS-CoV-2 Spike S1 were expressed in binding antibody units (BAU/mL) using the NIBSC 20/136 WHO standard (3).

Supplementary data S3: PBMC isolation and ELIspot assay

PBMCs were isolated and for all patients that had both a pre- and post-vaccination visit at both visits. PBMCs were isolated from fresh heparinized blood using Ficoll Paque density gradient media (Sigma Aldrich) and SepMate isolation tubes (Stemcell). After isolation and washing steps, PBMCs were dissolved in freezing medium containing 10% fetal calf serum (FCS) and 10% dimethylsulfoxide (DMSO) in RPMI, and were stored in vials, containing 10^6 cells each, in liquid nitrogen until use.

MultiScreen® HTS IP filter plates (Millipore) activated with 35% ethanol were coated with anti-human IFNγ antibody (1-D1K, Mabtech; 5 µg/mL) and incubated overnight at 4 °C. Next, plates were blocked with X-VIVO (Lonza) medium containing 2% human AB serum (HS; Sigma) and incubated for at least 1 hour at 37°C and 5% CO2. PBMCs were thawed, and dissolved in 4 °C IMDM (Gibco) medium containing 10% FCS and DNase I (Sigma-Aldrich). They were then centrifuged for 7 minutes at 375 g, and washed two times. Cells were counted using the Countess Automated Cell Counter (Thermofisher) and were checked for viability. PBMCs were brought to a concentration of $4x10^6$ live cells/mL and rested for 1 hour at 37 °C and 5% CO2.

SARS-CoV-2 Spike1 and Spike2 peptide pools (JPT Peptide Technologies) consisting 15-mer peptides overlapping 11 amino acids covering the sequence of the viral protein (of 0.5 µg/mL for each peptide) served to stimulate the PBMCs. The dilutions were performed in X-VIVO containing 2% human serum, and all stimulations were performed in triplicate. PHA (Remel Europe Ltd; 4 µg/mL) served as a positive control whereas DMSO 0.4% served as negative control. PBMCs (2×10^5) were seeded per well and cultured for 19-24 hours at 37 °C and 5% CO2.

The assay was continued the next day with washing of the plates with PBS containing 0.05% Tween 20. Anti-human biotinylated IFNγ antibody (7-B6-1, Mabtech; 1:1000) in 0.05% Poly-HRP buffer (ThermoFisher) diluted in PBS was added for 1.5 hours. After washing, streptavidin poly-HRP (Sanquin; 1:6000) in 0·05% Poly-HRP buffer was added for 1 hour. Finally, after new washing steps, filtered TMB substrate (Mabtech) was added to visualize the spots.

Spot forming cells (SFC) were quantified with the AID ELISpot/Fluorospot reader and expressed as SFCs/10^6 PBMCs. For each stimulation, the average of the DMSO negative control was subtracted. The total Spike-specific SFC was defined by summing up the SFCs both the S1 and S2 peptide pools. An antigen-specific response was defined as at least a 2-fold increase in the number of spots from pre- to post-vaccination and ≥50 IFNγ producing spot-forming cells (SFC) per 10^6 PBMCs post-vaccination (4). Samples were repeated when the positive control PHA was too low.

Supplementary data S4: regression analyses

The influence of predicting variables on post-vaccination anti-Spike antibody tiers was assessed with a linear regression analysis. The probability of F for removal was 0.10. Anti-Spike SARS-CoV-2 concentrations were used as the dependent variable. Predicting variables were: age (years); vaccine type (0 = ChAdOx1, 1 = BNT162b2); anti-N seropositive, prednisolone dose >10 mg, methotrexate use, leflunomide use, tocilizumab use (0 = no, 1 = yes). R squared (R2) was reported. Anti-Spike SARS-CoV-2 concentrations were not normally distributed, and were therefore transformed by square root. Normality of residuals was tested by histograms and P-P plots. Linearity and homoscedasticity was tested by scatter plots and P-P plots. Multicollinearity was excluded by Pearson correlation coefficient <0.7, variance inflation factor (VIF) <10, tolerance statistics >0.2 and Collinearity Diagnostics.

The influence of predicting variables on response/non-response in the ELIspot assay was analysed by a binary logistic regression analysis. The probability of F for removal was 0.10. Predicting variables were: age in years; vaccine type: 0 = ChAdOx1, 1 = BNT162b2; anti-COV19N seropositive, prednisolone dose > 10 mg, methotrexate use, leflunomide use, tocilizumab use: 0 = no, 1 = yes. Nagelkerke R2 and the model Chi Square ($\chi 2$) were reported. Linearity was examined by the Box-Tidwell Transformation Test. Multicollinearity was examined as mentioned for multiple linear regression. P values <0.05 were considered statistically significant.

Supplementary references:

1) van Gageldonk PG, van Schaijk FG, van der Klis FR, Berbers GA. Development and validation of a multiplex immunoassay for the simultaneous determination of serum antibodies to Bordetella pertussis, diphtheria and tetanus. J Immunol Methods. 2008 Jun 1;335(1-2):79-89. doi: 10.1016/j.jim.2008.02.018. Epub 2008 Mar 26. PMID: 18407287.
2) den Hartog G, Vos ERA, van den Hoogen LL, et al. Persistence of antibodies to SARS-CoV-2 in relation to symptoms in a nationwide prospective study [published online ahead of print, 2021 Feb 24]. *Clin Infect Dis*. 2021;ciab172. doi:10.1093/cid/ciab172
3) den Hartog G, Schepp RM, Kuijer M, et al. SARS-CoV-2-Specific Antibody Detection for Seroepidemiology: A Multiplex Analysis Approach Accounting for Accurate Seroprevalence. *J Infect Dis*. 2020;222(9):1452-1461. doi:10.1093/infdis/jiaa479
4) Oosting SF, van der Veldt, Astrid AM, GeurtsvanKessel CH, Fehrmann RS, van Binnendijk RS, Dingemans AC, et al. mRNA-1273 COVID-19 vaccination in patients receiving chemotherapy, immunotherapy, or chemoimmunotherapy for solid tumours: a prospective, multicentre, non-inferiority trial. The Lancet Oncology 2021.

SUPPLEMENTARY DATA

	Total	GCA	PMR
Lab at pre-vaccination; mean (SD)			
n	66	38	28
CRP (mg/L)	5.2 (7.1)	5.7 (7.3)	4.6 (6.7)
ESR (mm/hr)	16.3 (13.3)	18.4 (15.0)	13.5 (9.7)
Hb (mmol/L)	8.3 (0.85)	8.0 (0.76)	8.7 (0.84)
Leukocytes (10^9/mL)	7.86 (2.8)	8.13 (3.0)	7.50 (2.5)
Neutrophils (10^9/mL)	5.77 (2.8)	5.96 (3.0)	5.52 (2.6)
Monocytes (10^9/mL)	0.55 (0.22)	0.53 (0.24)	0.58 (0.18)
Lymphocytes (10^9/mL)	1.39 (0.63)	1.48 (0.76)	1.29 (0.38)
T cells (10^9/mL)	1.02 (0.53)	1.10 (0.61)	0.90 (0.36)
CD4+ T cells (10^9/mL)	0.72 (0.39)	0.81 (0.45)	0.59 (0.22)
CD8+ T cells (10^9/mL)	0.28 (0.19)	0.28 (0.18)	0.28 (0.20)
B cells (10^9/mL)	0.14 (0.09)	0.13 (0.10)	0.14 (0.08)
Lab at post-vaccination mean (SD)			
n	78	45	33
CRP (mg/L)	4.8 (5.4)	4.9 (6.8)	4.7 (4.2)
ESR (mm/hr)	15.3 (9.9)	15.7 (9.7)	14.7 (10)
Hb (mmol/L)	8.3 (0.83)	8.1 (0.75)	8.5 (0.88)
Leukocytes (10^9/mL)	7.39 (2.5)	7.45 (2.6)	7.30 (2.4)
Neutrophils (10^9/mL)	5.11 (2.1)	4.98 (2.0)	5.28 (2.3)
Monocytes (10^9/mL)	0.59 (0.21)	0.59 (0.23)	0.59 (0.18)
Lymphocytes (10^9/mL)	1.35 (0.49)	1.42 (0.52)	1.25 (0.43)
T cells (10^9/mL)	1.07 (0.53)	1.17 (0.60)	0.94 (0.38)
CD4+ T cells (10^9/mL)	0.74 (0.39)	0.81 (0.44)	0.64 (0.27)
CD8+ T cells (10^9/mL)	0.29 (0.19)	0.31 (0.20)	0.26 (0.18)
B cells (10^9/mL)	0.14 (0.09)	0.14 (0.08)	0.13 (0.10)

Supplementary table S1. Standard laboratory measurements at the pre- and post-vaccination visits. CRP, ESR, Hb and the leukocyte diff were determined by the XN-9000 (Sysmex, Kobe, Japan) as part of standard care. Lymphocyte subsets were determined by the BD (San Jose, CA, USA) MultiTest TruCount method. GCA: giant cell arteritis, PMR: polymyalgia rheumatica, CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; Hb= hemoglobin

Dependent variable	Predicting variable	Final model, Odds ratio (95% CI)	*p* value
Responder by Elispot	Age	-	
	Vaccine type	-	
	Anti-COV19N seropositive	-	
	Prednisolone dose > 10 mg	0.246 (0.053-1.154) [a]	0.075
	Methotrexate use	-	
	Leflunomide use	-	
	Tocilizumab use	-	

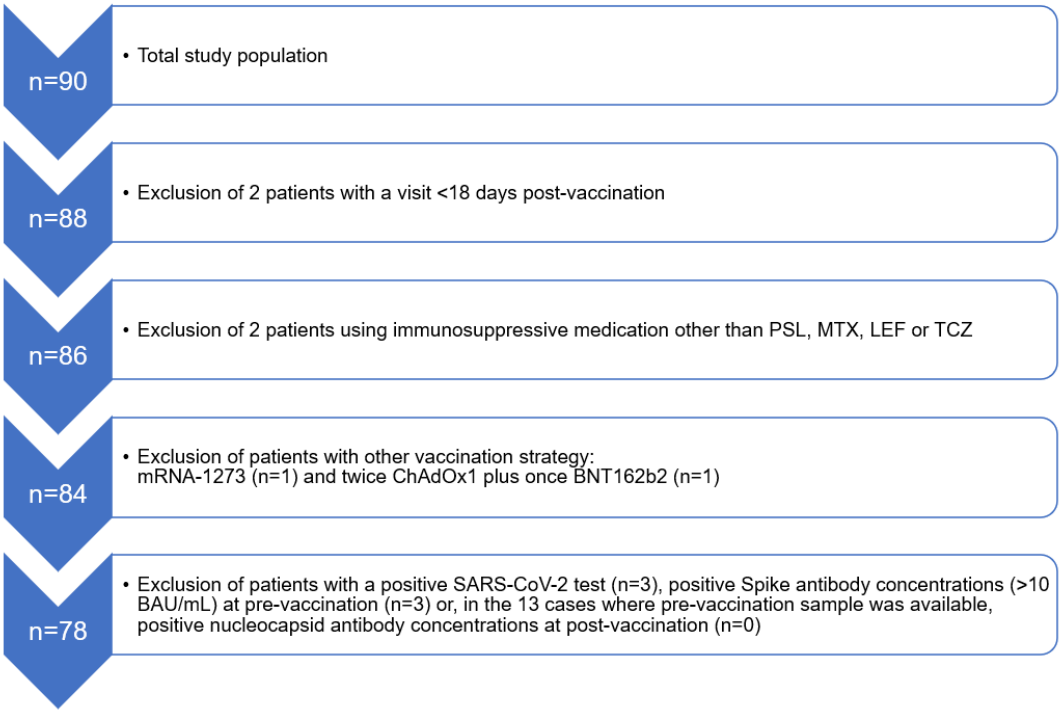
Supplementary table S2. Binary logistic regression analysis for responders/non-responders in the ELIspot assay. Data are shown for patients with GCA and/or PMR (n=63). Binary logistic regression analysis was performed with backward exclusion of predicting variables. The probability of F for removal was 0.10. Results of the final model are shown. Age in years. Vaccine type: 0 = ChAdOx1, 1 = BNT162b2. Anti-nucleocapsid seropositive, prednisolone dose > 10 mg, methotrexate use, leflunomide use, tocilizumab use: 0 = no, 1 = yes. (-) Variable removed due to backward exclusion. [a] Nagelkerke R^2 = 0.071. Model Chi square = 3.290, p = 0.070.

Group	N	Specific SFC counts* (median)	p-value
All	63	85	
BNT162b2	55	92	0.76
ChAdOx1	8	82	
GCA	36	78	0.55
PMR	27	125	
MTX	22	82	0.47
No MTX	41	85	
>10 mg PSL	8	22	0.09
≤10 mg or no PSL	55	98	
PSL	30	64	0.13
No PSL	33	102	

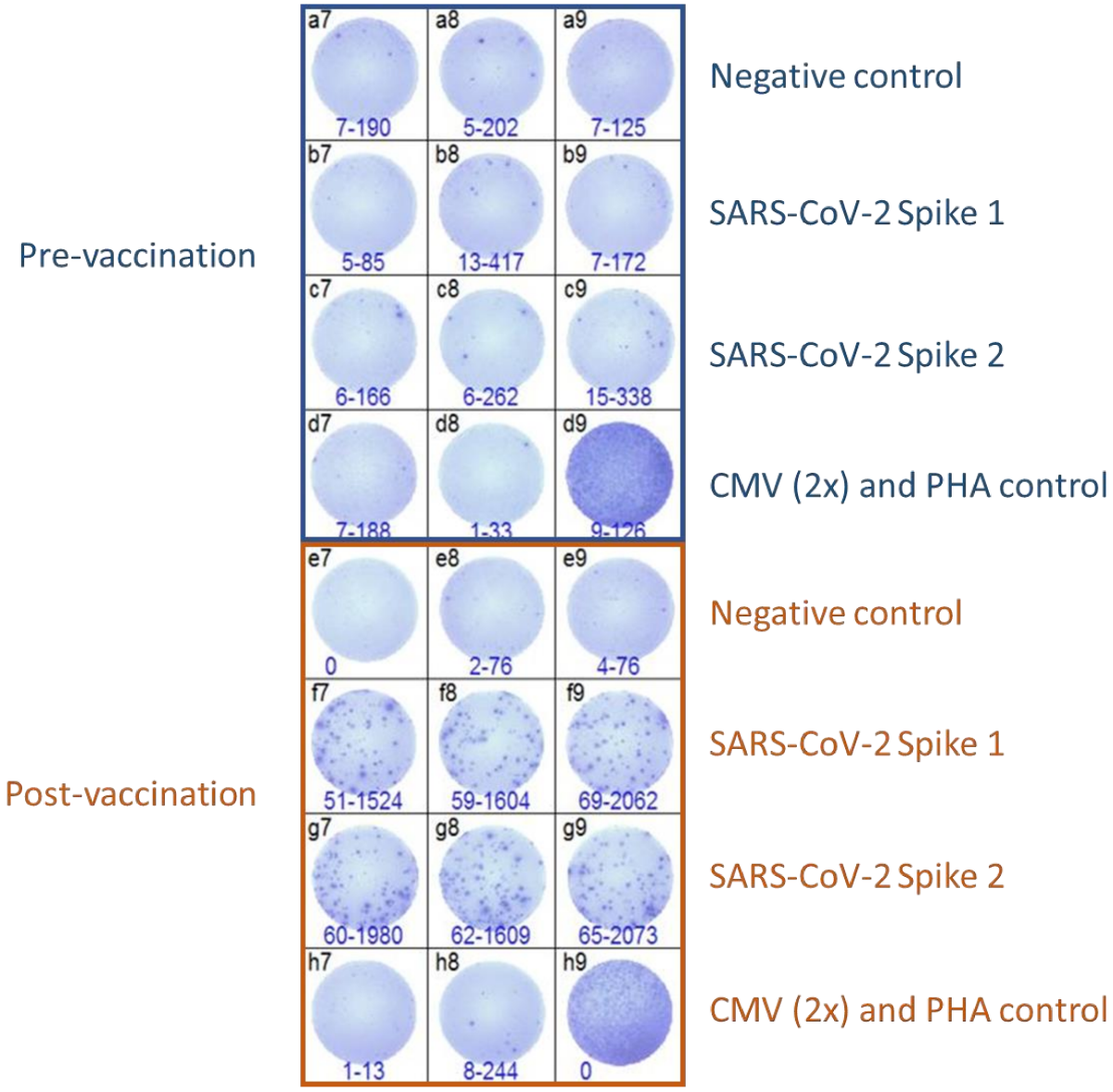
Supplementary table S3. Specific SFCs in the ELIspot assay. *Specific SFC counts were calculated by subtracting the SFC counts of the pre-vaccination sample from the counts of the post-vaccination sample. Statistical testing for differences in specific SFC counts with the Mann Whitney U test. *:SFC counts per 10^6 cells. SFC: spot-forming cell, MTX: methotrexate, PSL: prednisolone, GCA: giant cell arteritis, PMR: polymyalgia rheumatica.*

	Total	**GCA**	**PMR**
Pre-vaccination, n	66	38	28
Post-vaccination, n	78	45	33
Pre-vaccination, remission/active	50/16	27/11	23/5
Post-vaccination, remission/active	63/15	34/11	29/4
Pre-vaccination, minor relapse, n	6	4	2
Post-vaccination, minor relapse	4	4	0
Pre-vaccination, refractory disease	10	7	3
Post-vaccination, refractory disease	11	7	4
Pre-vaccination, CRP, mg/L (mean (SD))	5.2 (7.1)	5.7 (7.3)	4.6 (6.8)
Post-vaccination, CRP, mg/L (mean (SD))	4.8 (5.4)	4.9 (6.1)	4.7 (4.2)
Pre-vaccination, ESR, mm/hr (mean (SD))	16.3 (13.3)	18.4 (15.0)	13.5 (9.7)
Post-vaccination, ESR, mm/hr (mean (SD))	15.3 (9.9)	15.7 (9.7)	14.7 (10.0)

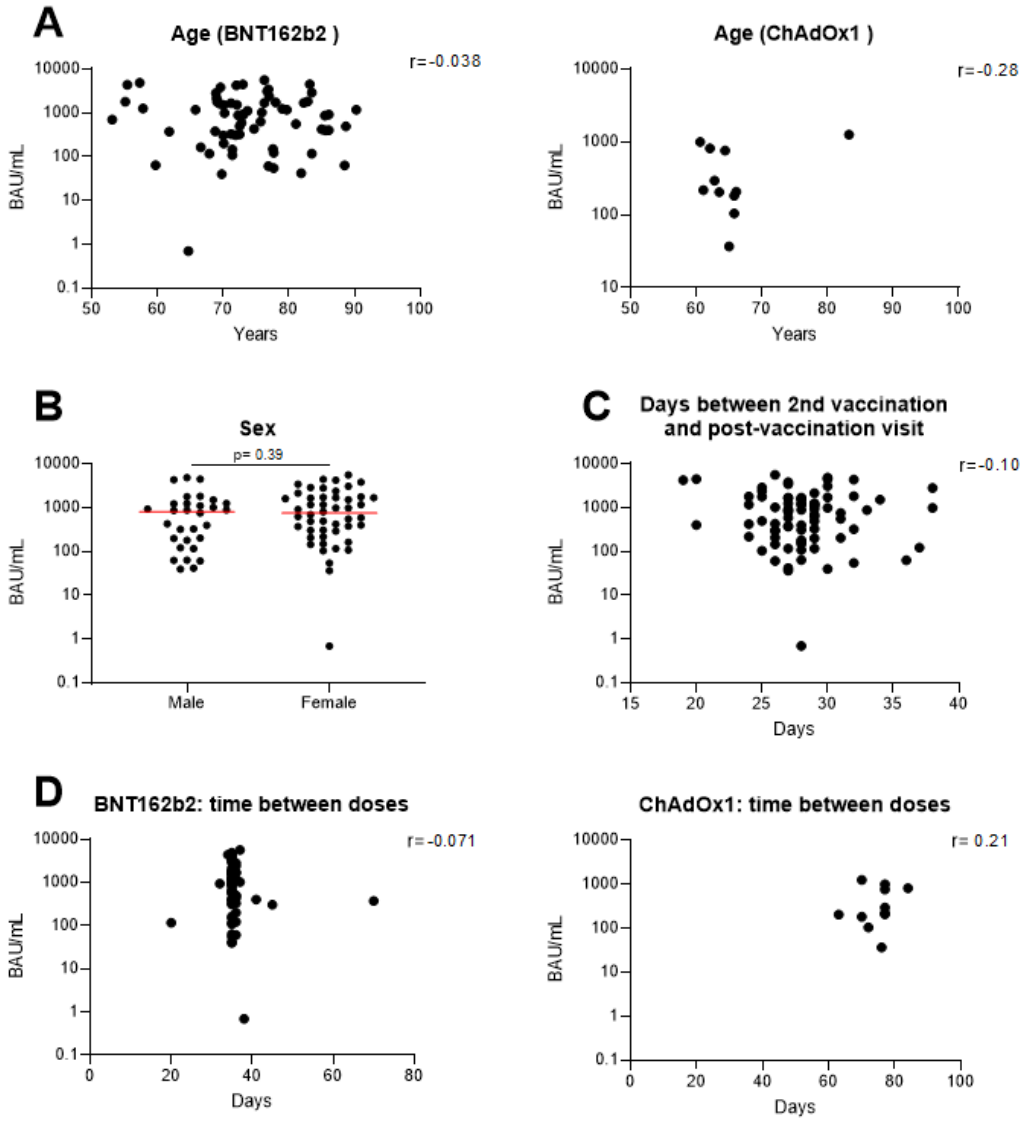
Supplementary table S4. Disease activity and acute-phase markers at the pre- and post-vaccination visits. Active disease was defined as the presence of symptoms attributable to active GCA/PMR, otherwise patients were considered to be in remission. GCA: giant cell arteritis, PMR: polymyalgia rheumatica, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SD: standard deviation.



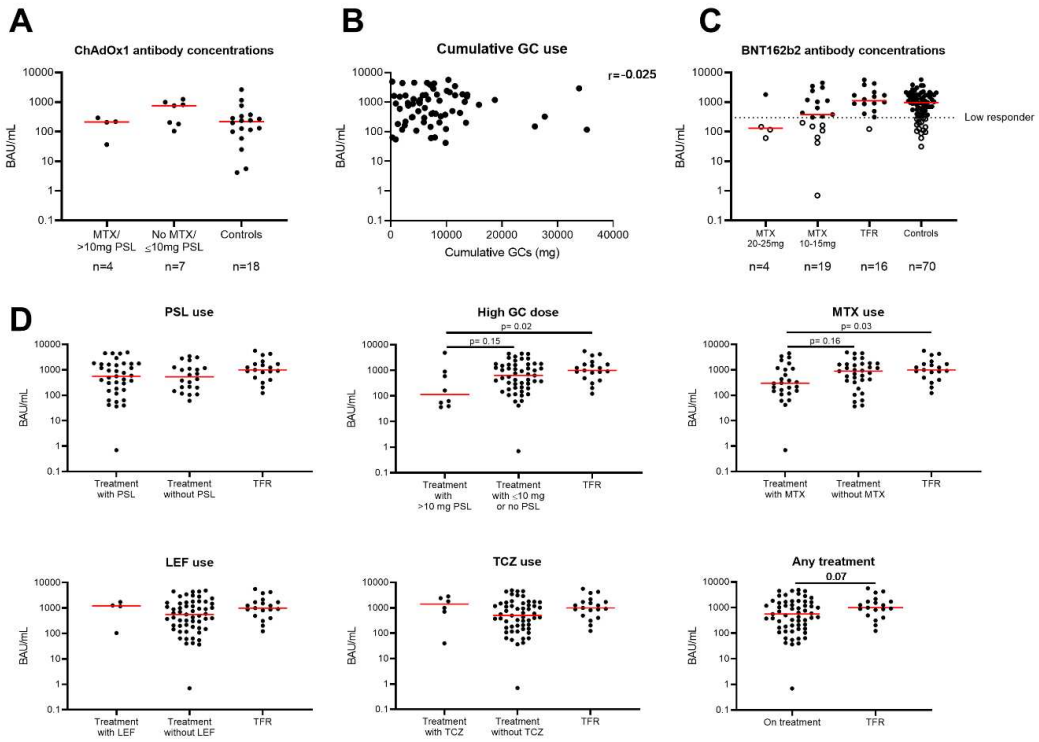
Supplementary figure S1: Flow diagram for GCA/PMR patients included in the main analysis for determination of antibody concentrations. GCA: giant cell arteritis, PMR: polymyalgia rheumatic, PSL: prednisolone, MTX: methotrexate, LEF: leflunomide, TCZ: tocilizumab, BAU: binding antibody units



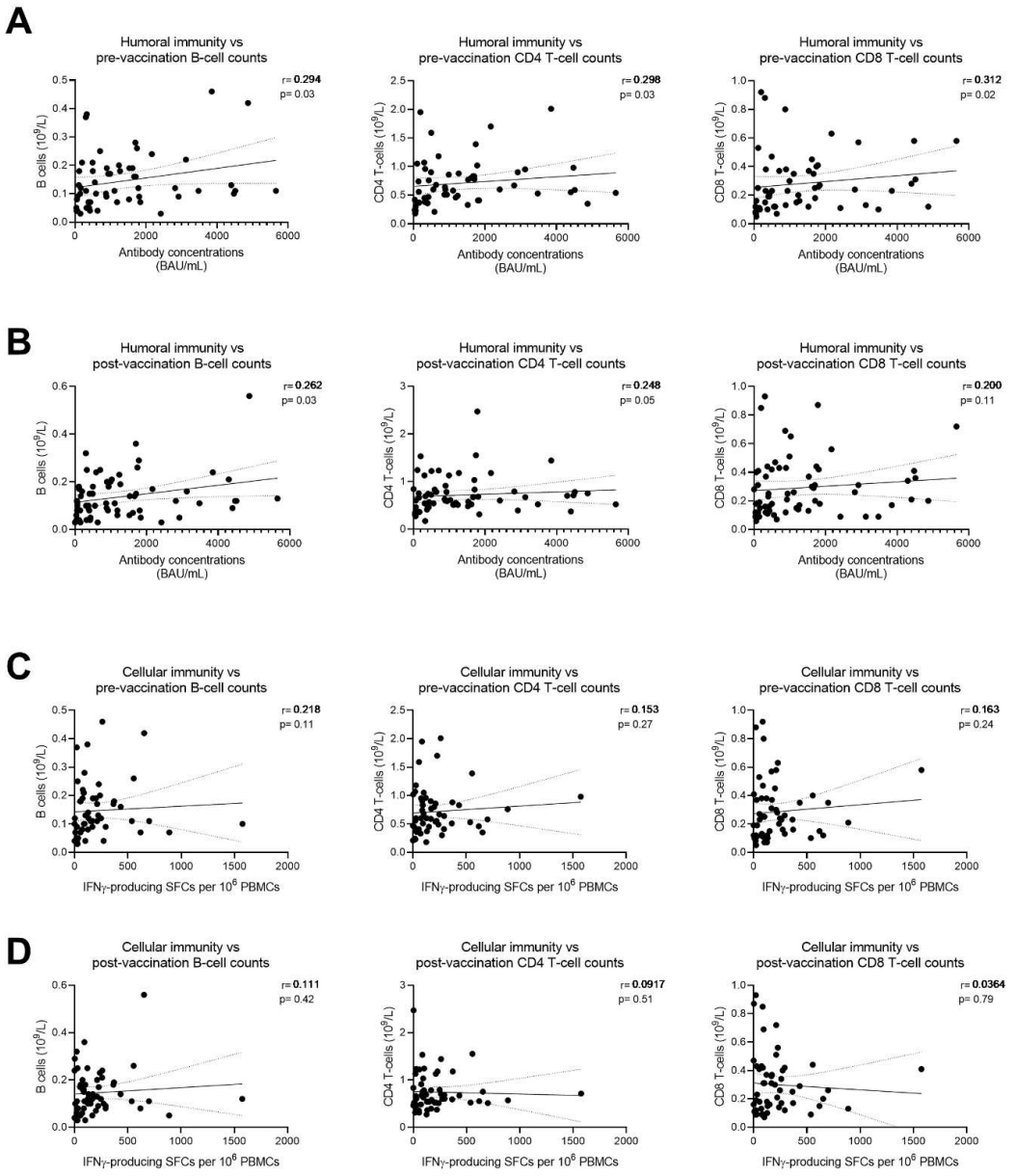
Supplementary figure S2. Layout of the ELIspot assay. Pre- and post-vaccination samples of each patient are measured in the same plate. Experimental conditions are performed in triplicate. The first number under each well indicate the SFC counts per $2x10^5$ cells. Average SFC counts in the Spike 1 and Spike 2 conditions are added up. To get the specific SFC count, the negative control SFC count is then subtracted. CMV: cytomegalovirus, PHA: Phytohemagglutinin, SFC: spot-forming cell.



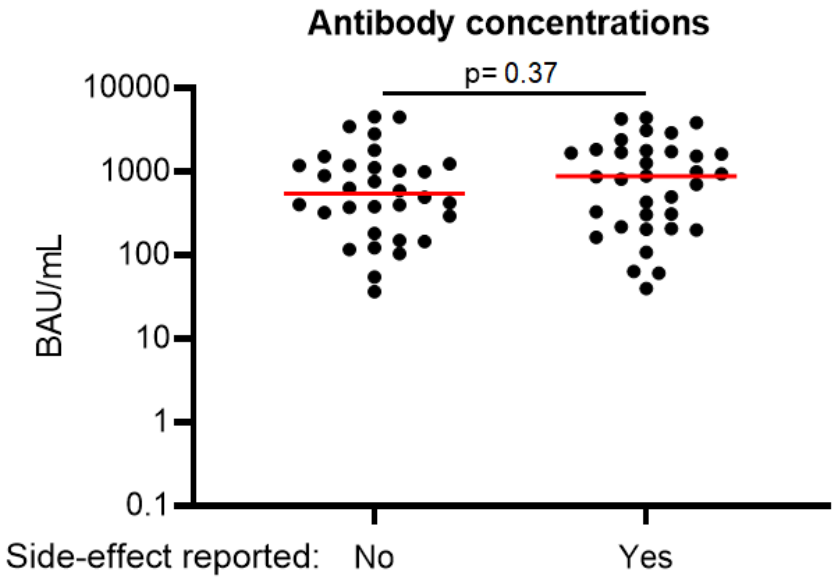
Supplementary figure S3. Influence of potential confounders on antibody concentrations in GCA/PMR patients. In **A**, we show that antibody concentrations are not correlated with age, when plotted separately for each vaccine. **B** shows that that antibody concentrations do not differ between male (n=30) and female (n=48) patients. **C** shows that antibody concentrations did not correlate with the time between second vaccination and the post-vaccination visit (ranging from 19 to 38 days). Finally, in **D** we show that the time between first and second vaccination has no effect on antibody concentrations, when plotted separately for each vaccine. Data are expressed in BAU (binding antibody units). Group differences are compared using the Mann Whitney U test and correlations with Spearman's rank coefficient.



Supplementary figure S4. Effects of treatment on SARS-CoV-2 antibody concentrations in GCA/PMR. A: shown are antibody concentrations in patients and controls after vaccination with ChAdOx1. The GCA/PMR patient population has been divided based on the use of MTX and/or a high PSL dose (>10mg/day) at the time of the first vaccination. **B** shows that cumulative GC dose, recorded since disease diagnosis, does not correlate with antibody concentrations (n=68). **C** shows antibody concentrations in patients and controls vaccinated with BNT162b2, split in groups based on MTX dosing. The difference between 10-15 mg and 20-25 mg MTX was not significant. In **D** antibody concentrations are shown for each type of immunosuppressive medication, including all types of treatment together. GC include prednisolone and methylprednisolone. GC= glucocorticoid; BAU= binding antibody units; PSL=prednisolone, MTX= methotrexate; LEF= leflunomide; TCZ= tocilizumab; TFR= treatment-free remission



Supplementary figure S5. Associations between counts of circulating B-cells, CD4 T-cells and CD8 T-cells with measures of humoral and cellular immunity. Counts at pre-vaccination (**A**) and post-vaccination (**B**) were correlated with antibody concentrations. Cellular immunity, expressed as spot forming cell (SFC) counts, was also associated with total counts of circulating B-cells and T-cells at the pre-vaccination (**C**) and post-vaccination (**D**) visit. Correlations were analysed by Spearman's rank coefficient. Shown in each plot is the simple linear regression line with the 95% confidence interval.



Supplementary figure S6: Spike antibody concentrations did not differ between patients that did not (n=32) and did (n=34) report any side-effects following the first or second vaccination.
BAU: binding antibody units.