Antibody response to four doses of SARS-CoV-2 vaccine in rare autoimmune rheumatic diseases: an observational study

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Abstract

Background: Antibody response to COVID-19 vaccines are reduced among immunocompromised patients but are not well-quantified among people with rare disease. We conducted an observational study to evaluate the antibody responses to the booster SARS-CoV-2 vaccine in people with rare autoimmune rheumatic diseases (RAIRD).

Methods: Blood samples were collected after second, before third, after third and after fourth vaccine doses. Anti-spike and anti-nucleocapsid antibody levels were measured using an in-house ELISA assay. Logistic regression models were built to determine the predictors for non-response. Results were compared to age and sex matched healthy controls (HC).

Results: 43 people with RAIRD were included, with a median age of 56 years. Anti-spike seropositivity increased from 42.9% after second dose to 51.2% after third dose and 65.6% after fourth dose. Median anti-spike antibody levels increased from 33.6 (IQR 7.8-724.5) post-second dose to 239.4 (IQR 35.8-1051.1) BAU after the booster dose (third dose, or fourth dose if eligible). 22.2% of participants who had sufficient antibody levels post-second dose had insufficient levels after the booster. 34.9% of participants had lower antibodies after the booster than the lowest HC had after the second dose. Rituximab in the six months prior to booster (p=0.02) and non-white ethnicity (p=0.04) was associated with non-response. There was a dose-response relationship between timing of rituximab and generation of sufficient antibodies (p=0.03).

Conclusions: Although the booster dose increased anti-spike IgG and seropositivity rates, some people with RAIRD, particularly those on rituximab, had insufficient antibody levels despite 3-4 doses.

Lay summary

Why was this research done?

People living with rare autoimmune rheumatic illnesses like vasculitis, lupus, myositis and scleroderma may have a weakened immune system due to their illness or its treatment. They may not respond to COVID-19 vaccinations as well as healthy people.

How was this research done?

43 people with a rare autoimmune rheumatic illness took part (30 had vasculitis, 8 SLE & 5 myositis). We used a questionnaire to collect health information including diagnosis, treatments, age, sex, ethnic origin and details about Covid-19 vaccination and infection.

We collected blood samples after the first "booster" vaccine – which was the third or fourth Covid-19 vaccine. We looked for anti-spike antibodies in the blood samples (a sign of response to the vaccine).

What did we find?

We used the lowest level of antibodies produced by a group of healthy people to define having "enough" antibodies.

- 65% of people living with a rare autoimmune disease made "enough" antibodies after their first booster dose of vaccine.

- More vaccines increased the chance of having protective antibodies: "enough" antibodies were found in 43% of people after their second dose, 51% after their third dose and 66% after their fourth dose.

- Having a drug called rituximab in the 12 months before vaccination and being from a non-white ethnic background reduced the chance of producing "enough" antibodies.

Keywords: rare autoimmune rheumatic diseases, SARS-CoV-2, vaccination, antibody, rituximab

Key messages

- Despite additional doses, individuals with RAIRD had lower antibodies than lowest healthy control.

- Antibodies diminish over time and rituximab treatment in the 6 months prior to the booster and non-white ethnicity was a predictor of poor response.

- Individual risk assessments in all ICPs on rituximab should be conducted and additional strategies will be necessary to provide protection.

Background

COVID-19 vaccination programmes have been effective at reducing the severity of COVID-19 infection [1, 2], however it remains important for future pandemic planning to better understand the immune response to vaccination of people who are immunocompromised, for whom vaccination may be less effective.

Among immunosuppressed groups, people with the rare autoimmune rheumatic diseases (RAIRD): vasculitis, lupus, scleroderma and myositis, are at greater risk of COVID-19 infection and associated mortality compared to both the general population and those with other types of inflammatory rheumatic diseases [3–7]. They are also more likely to have a weakened response to vaccination compared to healthy individuals of a similar age and sex [8–11]. In addition, those with rare diseases are also harder to recruit to research and there is less evidence available on their vaccine antibody responses than for people with more common diseases.

The aim of this study was to conduct a prospective cohort study to evaluate antibody responses to third and fourth SARS-CoV-2 vaccination in people with rare autoimmune rheumatic diseases.

Methods

Study design and participants

People aged 18 years or older with a diagnosis of RAIRD (vasculitis, systemic lupus erythematosus, myositis and scleroderma) were recruited from outpatient rheumatology and renal clinics in Nottingham University Hospitals NHS Trust from March to December 2021. People were not eligible if they were less than 18 years of age, ineligible to receive a SARS-CoV-2 vaccination, unable to provide blood samples, unable to travel to the hospital for study visits, unable to consent or had low English proficiency. All participants provided written informed consent and completed a questionnaire on demographic and clinical information.

All participants received SARS-CoV-2 vaccination as part of the UK vaccination programme. They received two primary doses 3 to 12 weeks apart [12] plus a booster dose six months later [13], or three primary doses plus a booster dose six months later if they were immunocompromised [14].

Patients and members of the public were involved at all stages of the study design and conduct. The study proposal was peer reviewed by people with vasculitis and other RAIRD and their feedback was incorporated into the study design. Findings will be disseminated to patients and the public through the Vasculitis UK website and newsletters.

Ethical approval

The study was approved by the West Midlands - Black Country Research Ethics Committee (REC reference: 21/WM/0097).

Sample collection

Whole blood samples were collected at five time points during the study period: (1) prior to the second SARS-CoV-2 vaccination dose, (2) four weeks (or three months if unable to attend sooner) after the second dose, (3) one to two weeks prior to the third dose (which was given approximately six months after the second dose in most people), (4) four to six weeks after the third dose and (5) two weeks after the fourth dose in the immunocompromised group. All samples were collected in accordance with national regulations and requirements.

Serological measurements

Heparinized whole blood was centrifuged at 300g for eight minutes to separate the plasma. Plasma was tested for nucleocapsid and spike specific antibodies in two separate ELISAs. Briefly, 384 well Maxisorp (NUNC) assay plates were coated with 20µL per well of 1µgmL-1 of either Wuhan strain SARS-CoV-2 full-length spike protein or Wuhan strain SARS-CoV-2 nucleocapsid protein. Plates were sealed with foil film and incubated overnight at 4°C. Plates were then washed 3 times with PBS with 0.05% Tween 20 (PBS-T) using a Biochrom ASYS Atlantis plate washing robot with 16-channel head. Wells were immediately filled with 100µL of blocking solution and 0.01% EDTA and blocked overnight at 4°C. Plates were washed a further 3 times and serum samples were diluted to 1:200. SARS-CoV-2 antibody positive and negative serum controls were obtained from the National Institute of Biological Standards and Controls (NIBSC, UK). Each assay contained a 12-point standard dilution of NIBSC 20/162 calibration standard diluted two-fold from 1:200, two negative controls from the NIBSC assay verification panel, and the NIBSC QC standard (20/764) all also diluted at 1:200. 20µL of gamma chain-specific anti-human IgG HRP conjugate (Sigma, A0170) was added per well at a 1:30,000 dilution. This was further incubated for 30

minutes and subject to a final three washes. 40µL of ultra-TMB (ThermoFisher, cat. 34028)) was added per well and incubated for 20 minutes, then the reaction stopped by the addition of 40µL of 2N H2SO4 was added to each well and absorbance read at 450 and 600nm using an EPOCH microplate reader (BioTek, UK). Data were presented as a conversion of delta OD (450nm-600nm) into BAU (binding antibody units). All assays were performed on Opentrons OT-2 liquid handling robots.

Statistical analysis

We performed a complete case analysis on all participants who provided samples after the third and/or fourth dose using 5% as the significance level. Missing data were assumed to be missing at random and no imputations were performed. Descriptive statistics were used to identify any differences in demographics and clinical characteristics. In the immunogenicity analysis we compared anti-spike protein IgG responses after the second dose, prior to third dose, after the third dose and after the fourth dose. No analysis was conducted on anti-nucleocapsid responses. We also calculated the percentage change for each participant at three time points (1) after third dose compared to after the second dose, (2) after fourth dose compared to after the third dose (3) after booster compared to after the second dose. A detectable response was defined as IgG spike protein antibody level above 10 binding antibody units (BAU), and a sufficient response ("responder") was defined as IgG level above the lowest HC after 2 doses of vaccine (>80.585 BAU). Due to the large variation in antibody responses, absolute levels have been summarised as median and interquartile ranges. Fishers exact test (appropriate due to cell counts <5) was used to determine the predictors for non-response after two and booster doses and logistic regression models were built adjusted for age, sex and rituximab treatment as a priori confounders, as these have previously been suggested to influence antibody levels [15–17]. Variables that were statistically significant in the univariate analysis were incorporated as additional confounding factors. All statistical analyses were performed using Stata version 14, Prism and Microsoft Excel.

Study outcomes

The primary outcome was to assess the antibody response following the booster dose (defined as third dose, or fourth dose if eligible for third primary dose due to immunosuppressive treatment) given routinely in the UK SARS-CoV-2 vaccination programme.

Results

Among 102 RAIRD patients identified, 52 were enrolled into the study of whom 43 provided a blood sample after their third and/or fourth dose and are included in this analysis (Figure 1). 32 people were eligible for a third primary dose and 11 were not. The median age of the cohort was 56.0 years (IQR 47.0-64.0) (Table 1). The majority of participants were female (67%) and of white ethnicity (88%). Diagnosis was ANCA-associated vasculitis in 24 participants (56%), SLE in eight (19%), another type of systemic vasculitis in six (14%) and myositis in five (12%). Most of the cohort had a history of treatment with rituximab (n=35, 81%). The median intervals between rituximab infusion and third dose and fourth dose were 251.0 (IQR 145.0-421.0) days and 121.5 (IQR 54.0-481.0) days respectively. 18 (42%) participants were taking steroids and 14 (33%) participants were taking oral immunosuppressants other than steroids or rituximab. The median interval between the date of third dose and fourth dose and sample collection were similar (31.0 days vs 30.5 days). During the study, 8 (19%) participants self-reported COVID-19 infection and 32 (74%) had a rise in their nucleocapsid antibodies suggesting COVID infection. It is noteworthy that natural COVID-19 infection will also increase spike antibody levels. All participants survived their infection. We did not collect data on COVID treatment. We excluded four participants from the analysis as they had immunoglobulin therapy during the study. Their median age was 33.0 years (IQR 28.7-36.2), three were female, all were of white ethnicity. Three had a diagnosis of ANCA-associated vasculitis and previous rituximab treatment and one had a diagnosis of SLE. Their anti-spike IgG concentration measured at 4 timepoints ranged from to 2.6 BAU to 288.5 BAU.

Table 1. Baseline characteristics of RAIRD participants

	RAIRD (n=43)
Age, years	
Median	56.0 (47.0-64.0)
18-49	14 (32%)
50-64	20 (47%)
≥65	9 (21%)
Sex	
Female	29 (67%)
Male	14 (33%)
Ethnicity	
White	38 (88%)
Non-white	5 (12%)
Diagnosis	
ANCA-associated vasculitis	24 (56%)

SLE	8 (19%)
Other systemic vasculitis[†]	6 (14%)
Myositis	5 (12%)
Current immunosuppression	
Steroids	18 (42%)
Other oral immunosuppressant[‡]	14 (33%)
Rituximab timing	
Before second dose, days (n=32)	198.5 (165.0-502.0)
Between second and third dose, days (n=27)	251.0 (145.0-421.0)
Between third and fourth dose, days (n=22)	121.5 (54.0-481.0)
Rituximab ever	35 (81%)
Vaccine	
Oxford-AstraZeneca	22 (51%)
Pfizer-BioNTech	21 (49%)
Interval between dose and sample, days	
After second (n=42)	35.5 (range 11.0-96.0)
Before third (n=33)	8.0 (range 1.0-72.0)
After third (n=41)	31.0 (range 12.0-51.0)
After fourth (n=32)	30.5 (range 12.0-74.0)

Data are median (IQR) or n (%)
[†]Other systemic vasculitis included giant cell arteritis and relapsing polychondritis
[‡]Other oral immunosuppressants included Methotrexate, Mycophenolate and Hydroxychloroquine

An increasing proportion of people with RAIRD developed sufficient antibody responses after each of second dose, third dose and fourth dose (42.9%, 51.2% and 65.6% respectively) as shown in Table 2. However, after the booster dose (defined as third dose, or fourth dose if eligible for third primary dose due to immunosuppressive treatment), 34.9% of people with RAIRD still had lower antibodies than the lowest healthy control did after the second dose. Antibody levels waned over time, and having antibodies after the second dose did not guarantee having them after the third dose or fourth dose; of the 18 people who had sufficient antibodies after the second dose, 4/18 (22.2%) did not after their booster (Figure 2). 13 (54%) of the non-responders to the second dose mounted a sufficient IgG response after the booster dose, whereas 11 (46%) did not respond to the second dose or the booster dose (Table S1). Additionally, antibody levels were significantly lower in individuals who had had rituximab, both after the second dose and the booster dose (Figure S2). Non-responders to the fourth dose were more likely to be female, of non-white ethnicity, have myositis and have received rituximab in the six months prior to their fourth dose. Oral immunosuppression did not have a significant effect on response to the fourth dose (Table S3).

Table 2. Antibody responses

	n (%)	SARS-CoV-2 anti-spike protein IgG concentration, BAU
After the second dose (n=42)		33.6 (7.8-724.5)
Responder	18 (42.9%)	783.2 (386.1-1050.0)
Non-responder	24 (57.1%)	9.2 (0.5-18.7)
Before the third dose (n=34)		7.8 (3.3-55.2)
After the third dose (n=41)		111.0 (16.8-529.4)
Responder	21 (51.2%)	529.4 (206.0-885.4)
Non-responder	20 (48.8%)	14.7 (0.3-45.0)
Percentage change (after third vs after second dose)	+2.3%	
After the fourth dose if eligible (n=32)		249.5 (34.3-920.0)
Responder	21 (65.6%)	695.5 (259.5-2042.8)
Non-responder	11 (34.4%)	3.4 (0-39.5)
Percentage change (after fourth vs after third dose)	+1.2%	
After booster dose (either 3rd or 4th vaccine depending on eligibility) (n=43)		239.4 (35.8-1051.1)
Responder	28 (65.1%)	784.0 (249.5-1737.8)
Non-responder	15 (34.9%)	12.6 (0-39.5)
Percentage change (after booster vs after second dose)	+6.1%	

Data are median (IQR). BAU=Binding antibody units
*Responder was defined as IgG above the lowest healthy control (>80.585 BAU)

The median anti-spike IgG concentration after the second dose was 33.6 BAU (IQR 5.5-724.5), which increased to 111.0 BAU (IQR 16.8-529.4) after the third dose and 249.5 BAU (IQR 34.3-920.0) after the fourth dose, a fold change of 2.3% and 1.2% respectively. 58% of RAIRD participants had IgG levels below the lowest healthy control after the second dose (median IgG 8.1 BAU), which reduced to 34% after the fourth dose (median IgG 3.4 BAU). The median anti-spike IgG concentration after the booster dose was 239.4 BAU, which represented a 6.1% increase from the median IgG concentration after the second dose (Table 2).

We have previously published the antibody responses to the first and second doses, as part of a more detailed study including cellular responses [18]. As the cohort differs slightly in this study, as not every patient gave a blood sample at every time point, we have repeated the post-second dose analysis, which can be found in the supplementary data (Table S4). The findings were in line with the previous paper.

Following the booster dose, non-white ethnicity and treatment with rituximab were significantly associated with non-response to vaccination on univariable testing using Fisher's exact test. There was a dose-response relationship with sufficient antibodies to the booster dose found in 8/8 (100%) of those who had never had rituximab, 8/10 (80.0%) who had last had rituximab more than 12 months ago, 6/11 (54.5%) who had rituximab 6-12 months ago, and 6/14 (42.9%) who had rituximab in the last 6 months. On multivariable regression analysis

including age and sex as a priori confounders, and ethnicity and timing of Rituximab (<6 months, 6-12 months or >12months/never), only timing of Rituximab remained significantly associated with response to vaccination after the booster dose (Table 3).

Table 3. Predictors of response after the SARS-CoV-2 booster vaccine.

	Responder (n=28)	Non-responder (n=15)	Fisher's exact test P value	Multivariate logistic regression OR (95% CI)	P value
Age, years (for each additional year)				0.99 (0.94-1.05)	0.76
18-49	7 (50.0%)	7 (50.0%)	0.32		
50-64	15 (75.0%)	5 (25.0%)			
≥65	6 (66.7%)	3 (33.3%)			
Sex			0.31		
Female	17 (58.6%)	12 (41.4%)		1 (reference)	
Male	11 (78.6%)	3 (21.4%)		0.36 (0.07-1.86)	0.22
Ethnicity			0.043*		
White	25 (65.8%)	13 (34.2%)		1 (reference)	
Non-white	3 (60.0%)	2 (40.0%)		8.46 (0.44-163.26)	0.16
Diagnosis			0.27		
ANCA-associated vasculitis	14 (58.3%)	10 (41.7%)			
SLE	5 (62.5%)	3 (37.5%)			
Other systemic vasculitis	6 (100.0%)	0			
Myositis	3 (60.0%)	2 (40.0%)			
Current oral immunosuppression	10 (71.4%)	4 (28.6%)	0.74		
Rituximab timing			0.027*		
<6 months	6 (42.9%)	8 (57.1%)		9.70 (1.37-68.82)	p-trend
6-12 months	6 (54.5%)	5 (45.5%)		6.92 (0.94-50.62)	0.03
>12 months	8 (80.0%)	2 (20.0%)		1 (reference)	
Never	8 (100.0%)	0		1 (reference)	

Data are n (%)
*Statistically significant p value

Discussion

We present data on antibody response following three and four doses of SARS-CoV-2 vaccines in people with RAIRD in the UK. There was an increase in the proportion of people responding to vaccination after each subsequent dose. However, 35% of participants were still non-responders after the booster – which we defined as having lower antibodies than the lowest healthy control after the second dose. Antibody levels wane over time, and we found having antibodies after the second dose did not guarantee having them after the third or fourth dose (22% of people who responded to the second dose did not respond to their booster dose). We observed that having

had rituximab, and the timing of rituximab treatment was significantly associated with reduced response to both the second and booster dose, but no other factors were statistically significant in this small study.

It is difficult to study vaccine responses in people with rare diseases, because it is difficult to recruit enough people. Each study of people with RAIRD such as vasculitis, SLE and myositis includes typically fewer than 50 people. This means each study is under-powered to report all clinically significant associations with vaccine response. One important aspect of publication of this and other studies in rare groups is enabling future pooled analyses of the findings which will enable more granular risk stratification by demographics, disease and treatment groups.

Our most statistically significant finding was the detrimental impact of rituximab on antibody response to SARS-CoV-2 vaccines, which corroborates the findings of other studies [8, 10, 17, 19]. We demonstrated that antibody responses were significantly diminished in people receiving rituximab and we found a dose-response relationship between the timing of rituximab prior to vaccine administration. People who had received rituximab in the six months prior to their booster dose were most at risk of non-response. A study on people with ANCA-associated vasculitis also found that cumulative dose and administration of rituximab in the six months prior to vaccination were important predictors of poor antibody response following the first vaccine. Vaccine administration more than six months after last rituximab was associated with a seven-fold increase in the odds of seroconversion, in line with our findings. Interestingly, they identified that CD19 count was the strongest predictor of seroconversion [20]. However, as data on reconstitution of B cells is not routinely collected in clinical practice in the UK, we were not able to identify the effect of this in our study. A blunted immune response which persists for up to 6 months after rituximab treatment has also been found in studies on other vaccines, such as Haemophilus influenza B, pneumococcus and hepatitis B [21]. More recently, an open-label trial on rituximab treated patients found that the proportion of participants who seroconverted increased from 33% to 58% following the fourth dose of COVID-19 vaccine. However, this study had a small number of RAIRD patients and did not look at the effects of rituximab timing on antibody response [22].

Our study also brings to light new findings about the relationship between ethnicity and response to vaccination. We observed that individuals from a non-white ethnic background were less likely to mount an antibody response despite additional booster doses than their white counterparts. However, this association was not sustained after

adjustment for age and sex. Although several studies have shown that individuals from a minority ethnic background have a higher risk of SARS-CoV-2 infection and mortality [23, 24], less evidence is available on ethnic differences in immunogenicity. A small association was observed in the OCTAVE study where patients of Asian ethnicity had a slightly higher odds of adequate serological response after two doses compared to White ethnicity [25]. However, the study was not adequately powered for a subset analysis on ethnicity, only included a small number of patients with RAIRD and did not assess if responses were sustained after booster doses. Further research from pooled data may help clarify if there are true ethnic differences in immunogenicity.

Our findings highlight the need for continued caution among people with RAIRD with the emergence of new strains of SARS-CoV-2. Seven (16.3%) participants had no measurable antibodies after a booster dose, and 15 (34.9%) had lower antibody levels than healthy controls after two doses. For individuals requiring maintenance rituximab, shared decision making and risk assessments should be conducted by clinicians to review the timing of rituximab in relation to future vaccinations, for example timing Rituximab infusions ≥2 weeks after vaccination if clinically reasonable.

Strengths and Limitations

The strengths of this study include the broad inclusion criteria, and adjustment for age and sex in our analyses as potential confounders. This study has several limitations including small sample size resulting in wide 95% confidence intervals for some of the analyses and lack of data on the cellular response and reconstitution of B cells. Although we did not measure neutralising antibodies, spike antibodies have been shown to correlate well with neutralising antibody levels [26] and we think are therefore a reasonable surrogate.

Conclusions

This study reports COVID antibody responses after 3 or 4 vaccines among 43 people with rare autoimmune rheumatic diseases. Our most significant finding was the detrimental impact of rituximab on antibody response to SARS-CoV-2 vaccines, which corroborates the findings of other studies. We also found that non-white ethnicity was a predictor of non-response but this was not sustained after adjustment. Publication will make the results

available for future meta-analyses which may identify associations that individual studies of rare diseases are underpowered to find.

Declarations

Ethics approval

The study was approved by the West Midlands - Black Country Research Ethics Committee (REC reference: 21/WM/0097).

Consent for publication

Not applicable.

Availability of data and materials

Due to the nature of the research and ethical restrictions, the data are not publicly available. Please contact the corresponding author should you wish to access the data.

Competing interests

FAP and PCL are recipients of an investigator-led research award from Vifor pharma for another project unrelated to COVID-19 or vaccination. None of the other authors have any competing interests.

Authors' contributions

The study was conceived by LF, FAP and PCL. LG did the entire data analysis and wrote up the final manuscript. FAP also contributed to the data analysis. MC, AF, SP, MJP and MR were involved in recruitment of participants and data collection. NG, GH, DT, HJ and PT contributed to the antibody analysis. All authors contributed to the manuscript.

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Figures
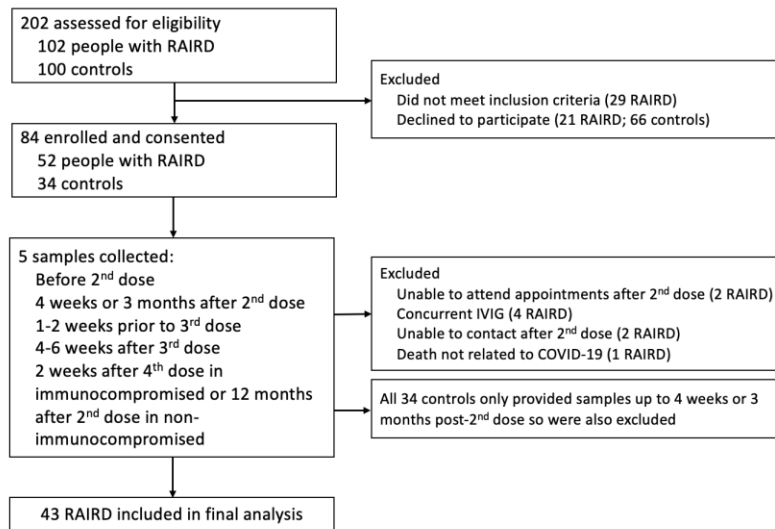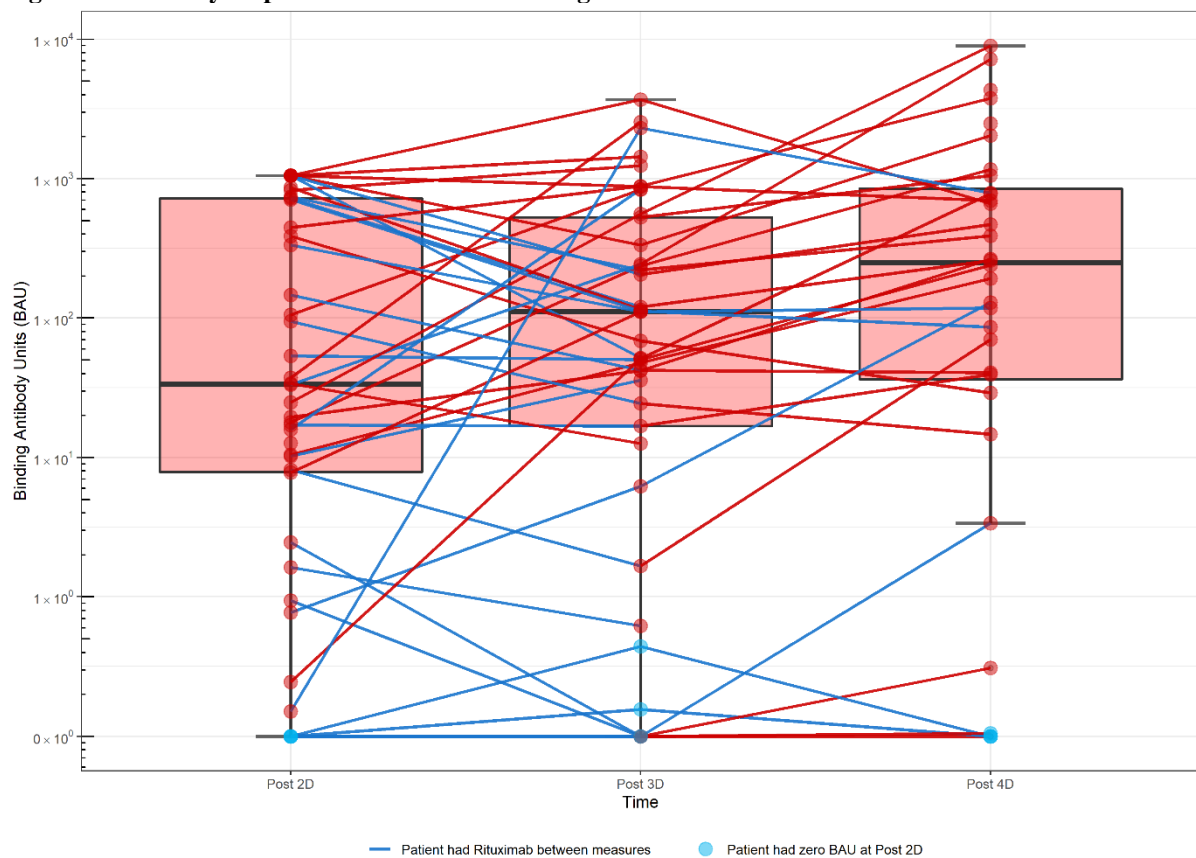**Figure 1. Participant journey through the study**

Figure 2: Antibody responses and rituximab timing for each dose of SARS-CoV-2 vaccine

Supplementary material

Table S1. Antibody responses after two doses and booster dose

		Responder after booster dose	
Responder after two doses		Responder*	Non-responder
	Responder*	14 (77.8%)	4 (22.2%)
	Non-responder	13 (54.2%)	11 (45.8%)

*Responder was defined as IgG above the lowest healthy control (>80.585 BAU)

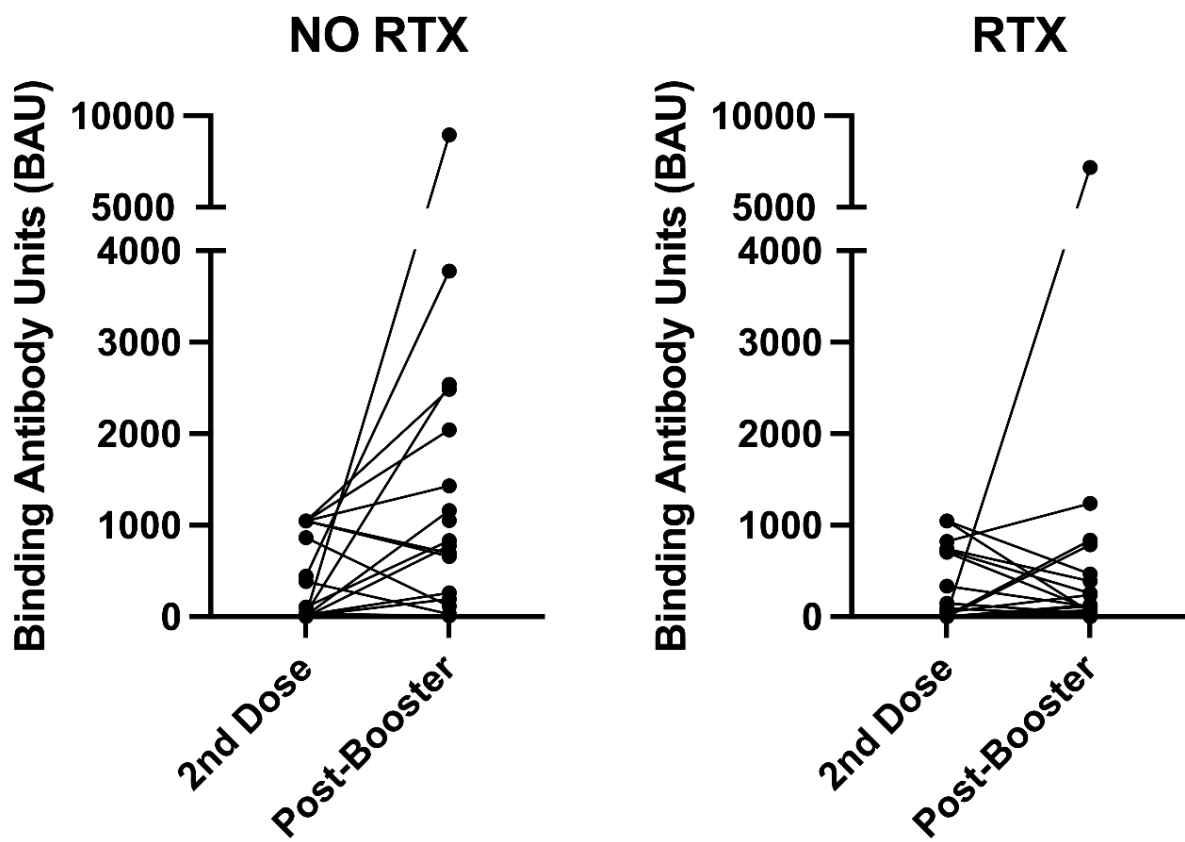**Figure S2. Antibody responses after second and booster dose**

Table S3. Characteristics of RAIRD participants who received the fourth dose of SARS-CoV-2 vaccination

	Responder (n=21)	Non-responder (n=11)
Age, years		
18-49	5 (55.6%)	4 (44.4%)
50-64	12 (75.0%)	4 (25.0%)
≥65	4 (57.1%)	3 (42.9%)
Sex		
Female	13 (56.5%)	10 (43.5%)
Male	8 (88.9%)	1 (11.1%)
Ethnicity		
White	20 (71.4%)	8 (28.6%)
Non-white	1 (25.0%)	3 (75.0%)
Diagnosis		
ANCA-associated vasculitis	10 (62.5%)	6 (37.5%)
SLE	5 (62.5%)	3 (37.5%)
Other systemic vasculitis	5 (100.0%)	0
Myositis	1 (33.3%)	2 (66.7%)
Current immunosuppression		
Steroids	10 (71.4%)	4 (28.6%)
Other oral immunosuppressant	8 (66.7%)	4 (33.3%)
Rituximab timing		
<6 months	4 (40.0%)	6 (60.0%)
6-12 months	6 (60.0%)	4 (40.0%)
>12 months or never	5 (83.3%)	1 (16.7%)

Data are n (%).
*Responder was defined as IgG above the lowest healthy control (>80.585 BAU)

Table S4. Predictors of response after two doses of SARS-CoV-2 vaccine.

	Responder (n=18)	Non-responder (n=24)	Fisher's exact test P value	Multivariate logistic regression OR (95% CI)	P value
Age, years (for each additional year)				1.01 (0.96-1.07)	0.65
18-49	7 (50.0%)	7 (50.0%)	0.79		
50-64	7 (36.8%)	12 (63.2%)			
≥65	4 (44.4%)	5 (55.6%)			
Sex			0.74		
Female	13 (46.4%)	15 (53.6%)		1 (reference)	
Male	5 (35.7%)	9 (64.3%)		2.32 (0.43-12.50)	0.33
Ethnicity			0.28		
White	17 (46.0%)	20 (54.0%)			
Non-white	1 (20.0%)	4 (80.0%)			
Diagnosis			0.20		
ANCA-associated vasculitis	11 (45.8%)	13 (54.2%)			
SLE	4 (50.0%)	4 (50.0%)			
Other systemic vasculitis	3 (60.0%)	2 (40.0%)			
Myositis	0	5 (100.0%)			
Current oral immunosuppression	5 (38.5%)	8 (61.5%)	0.75		
Rituximab timing			0.001*		
<6 months	1 (8.3%)	11 (91.7%)		36.18 (3.19-410.38)	0.004*
6-12 months	2 (22.2%)	7 (77.8%)		7.80 (1.17-52.10)	0.034*
>12 months	9 (81.8%)	2 (18.2%)		1 (reference)	
Never	6 (60.0%)	4 (40.0%)		1 (reference)	

Data are n (%)
*Statistically significant p value