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Early View

Original research article

Trimer IgG and Neutralising Antibody Response to COVID-19 mRNA Vaccination in Individuals with Sarcoidosis

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Title: Trimer IgG and Neutralizing Antibody Response to COVID-19 mRNA Vaccination in Individuals with Sarcoidosis

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Take home message: While subjects with sarcoidosis have a diminished quantitative antibody (anti-Trimer) response to the BNT162b2 mRNA COVID-19 vaccine, their functional neutralizing antibody response is comparable to controls indicating conferred immunity.

Plain Language Summary:

It is thought that patients with sarcoidosis have defects within their immune system that may affect their ability to adequately fight infection and respond to vaccination. Our study evaluated the antibody response to one one of the novel COVID-19 mRNA vaccines in individuals with and without sarcoidosis. We assessed the number of antibodies and their protective capacity and determined that the short and long term protection conferred by the vaccination are comparable between sarcoid and controls. The number of antibodies in individuals with sarcoidosis also did not strongly reflect the degree of protection offered by the vaccine.

ABSTRACT:

Background: Individuals with sarcoidosis are at higher risk for infection owing to underlying disease pathogenesis and need for immunosuppressive treatment. Current knowledge as to

how subjects with sarcoidosis respond to different forms of vaccination is limited. We examined quantitative and functional antibody response to COVID-19 vaccination in infection-naive subjects with and without sarcoidosis.
Methods: Our prospective cohort study recruited 14 subjects with biopsy-proven sarcoidosis and 27 age-gender matched controls who underwent a 2-shot series of the BNT162b2 mRNA vaccine at the University of Illinois at Chicago. Baseline, 4-week, and 6-month trimer spike protein IgG and neutralizing antibody (nAb) titers were assessed. Correlation and multivariate regression analysis was conducted.
Results: Sarcoidosis subjects had a significant increase in short term antibody production to a level comparable to controls, however IgG titers significantly declined back to baseline levels by 6 months. Corresponding neutralizing assays revealed robust nAb titers in sarcoidosis subjects that persisted at 6 months. A significant and strong correlation between IgG and nAb titers across all time points was observed in the control group. However within the sarcoidosis group, a significant but weak correlation between antibody levels was found. Overall, IgG levels were poor predictors of nAb titers at short or long term time points.
Conclusions: Sarcoidosis subjects exhibit nAb induced by the BNT162b2 mRNA SARS-CoV-2 vaccine at levels comparable to controls that persists at 6 months. Trimer IgG levels are poor predictors of nAb in subjects with sarcoidosis. Studies of further antibody immunoglobulins and subtypes warrant investigation.

INTRODUCTION:

Since the start of the COVID-19 pandemic, the development of effective treatments to diminish COVID-19 disease severity has been an international priority. Vaccines were developed at record speed and offer a life changing opportunity for disease mitigation and prevention. Initial studies demonstrated the mRNA-based COVID-19 vaccines, BNT162b2 and mRNA-1273, were efficacious in preventing up to 95% and 94.1% of COVID-19 disease in recipients, respectively [1, 2]. However, vaccine response in vulnerable populations remains ill defined.

Sarcoidosis is a multisystem disease of unknown etiology characterized by granulomatous inflammation and subsequent organ dysfunction. This inflammation is believed to stem from maladaptive immune responses, resulting from chronic immune stimulation with subsequent risk of lymphocyte anergy, exhaustion, and depletion [3-5]. Data supports sarcoidosis subjects as having increased risk of infection [6, 7], though the overall risk of SARS-CoV-2 is unclear [8]. Beyond immune susceptibility conferred by underlying disease pathology, nearly one-fourth of all sarcoidosis patients require treatment with immunosuppressive agents which further contributes to infectious risk [9]. Primary infection prevention with vaccination in this population is therefore of great importance.

Literature regarding how individuals with sarcoidosis respond to vaccines is limited and indicate varying responses. A study of tetanus vaccination in sarcoidosis patients found 50% had an insufficient increase in antibody titers regardless of sarcoid disease state, stage, or duration, and independent of treatment [10]. A separate study of a 3-dose series of the hepatitis B vaccine found that none of the 16 sarcoidosis subjects had detectable antibody levels at one month follow up [11]. In contrast, a study of the 2008-2009 trivalent influenza vaccine showed sarcoidosis and control subjects had a comparable serological response [12]. In addition, existing literature explores quantitative assessment of antibody response through measurement of immunoglobulin titers however these titers may not assure conferred protective immunity. While developed antibodies may target any viral epitope, neutralizing antibodies (nAb) bind to the virus in such a way that it inhibits cell entry and/or viral replication therefore blocking infection from propagating [13]. Post vaccination nAb assays provide insight into the functional protection allocated by the vaccine and to our knowledge there are no current studies evaluating nAb in sarcoidosis.

In regards to immunosuppression, data assessing the effect of immunosuppressive medication on vaccine efficacy in sarcoidosis is limited and recommendations are extrapolated from studies of other immune related disorders. Use of various immunosuppressive medications is associated with decreased antibody response to multiple types of vaccinations, including the mRNA COVID vaccines [14-17]. Regardless of a potential insufficient response, vaccination is strongly recommended in sarcoidosis to protect against various community acquired infections to include COVID-19 [18, 19].

We postulate that subjects with sarcoidosis will have a deficient immune response to COVID-19 vaccination. This study aims to characterize the antibody response to COVID-19 vaccination in subjects with and without sarcoidosis through quantitative assessment of binding antibodies and correlation to functional assessment of nAb. Our findings may direct vaccination guidelines, inform the need for further booster vaccines, and extrapolate further information about the immune dysregulation underlying sarcoidosis pathology.

METHODS:

Study population and sample acquisition

Study approval was obtained through the University of Illinois at Chicago (UIC) IRB Ethics Review Committee, Approval #2018-1038.

Subjects with biopsy-proven sarcoidosis, diagnosed in accordance with ATS/ERS/WASOG criteria [20], and who were undergoing vaccination with the BNT162b2 mRNA COVID-19 vaccination were recruited. All subjects were older than 18 years of age and receive their sarcoidosis care in the Bernie Mac Sarcoidosis Translational Advanced Research (STAR) Center at UIC. Demographic and clinical data was extracted from the electronic medical record and included sex, race, age, body mass index (BMI), sarcoidosis

organ involvement, as well as treatment with immunosuppressive therapy (systemic steroids and/or disease modifying anti-sarcoid drugs i.e. DMASDs). Peripheral lymphocyte counts in the preceding 6 month were also recorded. Age and gender matched self-reported-immunocompetent control subjects consisted of University of Illinois Hospital employees who were undergoing vaccination at UIC. Demographic and clinical data were collected using a questionnaire and included race, sex, age, height and weight, medication use, and existing medical problems. Any subject who self-reported a personal history of COVID-19 infection was excluded.

Blood samples were collected at baseline (just prior to 1st vaccine dose, timepoint V1D0), 4 weeks (i.e. 7 days after the booster dose, timepoint V2D7), and 6 months after the 1st vaccine dose (time point M6). Serum was extracted within two hours of sample collection and stored at -80°C.

Anti-Spike (Trimer) IgG Titer Quantification

The Human SARS-CoV-2 Spike Trimer IgG ELISA Kit from Invitrogen was used to quantitate serum IgG levels of each subject at each timepoint, per the manufacturer's protocol. All samples were diluted 1:100 and assayed in duplicate with a series of 2-fold serial dilutions (1:150,000 units/mL to 1:2,340 units/mL) of the standard control for relative quantification. Absorbance at 450 nm was quantified using a Spark® multimode microplate reader. Samples that produced signals greater than the upper limit of the standard curve were reassayed at 1:1000 dilution. IgG concentration was calculated by fitting 5-parameter logistic curves to the standard controls and reported as binding antibody units per milliliter (BAU/mL) The average concentration of duplicates was utilized for analysis. Inter-assay variability was addressed utilizing the ELISAtools package in R (version 4.0.4) which to account for batch-effect [21].

Antibody Neutralization Assays

Neutralization activity against SARS-2-CoV was measured in a single-round-of-infection assay using pseudotyped viruses [22]. Briefly, 293T ACE cells were infected with modified vesicular stomatitis virus (VSV), which lacks a gene vital for VSV replication and instead carries a firefly luciferase reporter gene that allows for chemiluminescence. The cells are also transfected with plasmids encoding full length SARS-CoV-2 spike (S) protein, which is a surface protein responsible for binding the host cell receptor, ACE2, to mediate viral entry during SARS-CoV-2 infection (SARS-CoV-2 Spike-pseudotyped lentiviral particle kit, BEI # NR-53816). The pseudotyped virus therefore contains the SARS-CoV-2 S protein to simulate viral entry, and VSV, which provides the structural genes for viral packaging without the ability to replicate. The 50% tissue culture infectious dose (TCID50) of the pseudotyped

virus, which indicates the amount of virus required to quash 50% of the inoculated cells, was calculated according to the Reed-Muench method.

Serial dilutions of each subject's serum were incubated for 1hr at 37 °C with 1000 TCID50/ mL of the pseudotyped virus (virus plus antibody) then added to monolayers of ACE2-overexpressing 293T cells in quadruplicate on a 96-well plate. Controls consisted of pseudotyped virus and 293T cells without added serum sample (virus-only). The plate was incubated for 65-72 hours in the cell culture incubator at 37 °C and 5% (vol/vol) CO2 after which 50 µL of luciferase substrate was added to stimulate chemiluminescence. The amount of chemiluminescence, determined by a plate reader, directly correlates with the amount of pseudotyped virus that has entered and "infected" the cells. The amount of nAbs, which inhibit viral entry into the 293T cell, is therefore inversely correlated with the chemiluminescence signal intensity. Neutralizing antibody titers are reported as the 50% inhibitory dilution (ID50), calculated using the Reed-Muench method, which refers to the dilution fold required to achieve 50% neutralization [22, 23]. The initial serum dilution was 1:25, therefore 25 is the cut off for antibody detection. Higher ID50 correlates to increased potency of nAb within the serum sample.

Statistical Analysis

Demographic data was tested for significance between groups utilizing the Mann-Whitney U (MWU) testing for nonparametric continuous data, or Fisher's exact test for categorical data, as appropriate. Statistical differences between groups of time from vaccination to sample collection were assessed using the student's T test. The primary outcome measures were absolute post vaccination Trimer IgG titers and nAb titers at both V2D7 and M6, as neither assay has a validated cut off indicating test positivity. Antibody titers for all time points were log transformed and z-scores were calculated to identify outliers (z score ≥2.5). Titers were tested for significance using the MWU test separately for each time point. Subgroup analysis was performed to assess the role of immunosuppressive therapy, with differences tested using the Kruskal-Wallis test with Dunn's post hoc test and Benjamini-Hochberg correction for multiple comparisons. Univariate correlation analysis was performed by calculating Pearson's coefficients for log transformed antibody titers. Multivariate regression models were then constructed separately for Trimer IgG and nAb to determine the relative effect of significant baseline variables on short term (V2D7) and long term (M6) results. P values <0.05 were considered significant. All analyses were performed in R version 4.0.4 (https://www.R-project.org/). Kruskal-Wallis and Dunn tests were implemented using the Dunn.test package. T testing, MWU, and Fisher's exact testing was implemented using the stats package. Pearsons coefficients were calculated using the corr.test function of the psych package.

RESULTS:

Demographics

Fourteen sarcoidosis subjects and 27 control subjects were recruited. Group characteristics are highlighted in **Table 1**. Nearly all subjects received the BNT162b2 mRNA COVID-19 vaccine and booster at the recommended time interval of 21 days (mean 21.15 days; st. dev 0.57, range 20-24 days). All subjects had blood samples collected just prior to the first vaccine dose administration (V1D0) and 7 days after the booster dose at time point V2D7 (mean 6.91 days; st. dev 0.28, range 6-7 days). All recruited subjects had available samples for Trimer IgG analysis at V1D0 and V2D7; of whom, 17 control samples and all 14 sarcoidosis samples were included in nAb analysis. Due to attrition, 22 control subjects and 11 sarcoidosis subjects were available for blood samples at the 6-month time point (mean 184.8 days from first vaccine, st dev 12.2, range 170-214 days) and included in Trimer IgG analysis at M6, of whom 11 control subjects and all 11 sarcoidosis subjects were included in nAb analysis.

The sarcoidosis group was comprised of 13 subjects with pulmonary manifestations and 6 with extrapulmonary involvement. Six subjects were not on any treatment and 8 were treated with immunosuppressive therapy. Specifics regarding sarcoidosis phenotypes and treatment regimens for each subject are described in **Table 2**. Absolute peripheral lymphocyte values were available for 12 sarcoidosis subjects and had a group median of 1.8 x 10^9 cells/liter. Four subjects had medication titration within this 6-month pre-vaccination time interval.

Anti-Spike Protein Trimer IgG Titer and Neutralizing Antibody Analysis

Trimer IgG titers for each group across all three time points are illustrated in **Figure 1**. There were no outliers detected at either time point. While sarcoidosis subjects had a higher median baseline IgG titer than the control group (*MWU p-val* <0.001), both groups demonstrated a significant increase in IgG titers at V2D7 compared to their respective baselines (sarcoidosis: *MWU p-val* <0.001; control: *MWU p-val* <0.001) with comparable titers at V2D7 between groups (*MWU p-val* =0.3680). IgG titers in both groups significantly decreased at the M6 time point from their respective V2D7 titers (sarcoidosis: *MWU p-val* <0.001; control: *MWU p-val* <0.001); however, M6 IgG titers in the sarcoidosis group fell to levels comparable to sarcoidosis V1D0 titers (*MWU p-val* =0.9786) and were significantly less than M6 control IgG titers (*MWU p-val* =0.0237). M6 IgG titers in the control group remained significantly higher than baseline values (*MWU p-val* <0.001). Overall, this trend indicates a robust initial IgG response in both groups that diminishes over time, returning to baseline in the sarcoidosis group and raising the concern for more transient antibody protection.

Functional nAb assays were performed to better determine protection conferred from vaccination. The ID50 for each group across all three time points (V1D0, V2D7, and M6) are illustrated in **Figure 2**. In contrast to significantly elevated IgG in the sarcoidosis group at baseline, there was no significant difference in ID50 between groups at the V1D0 time point (*MWU p-val* =0.5879). Both control and sarcoidosis groups had a significant increase in nAb titers from baseline to V2D7 suggesting robust nAb formation after 1st and 2nd vaccination doses (sarcoidosis: *MWU p-val* <0.001; controls: *MWU p-val* <0.001), similar to what was observed for IgG trends. However, median ID50 for both groups at M6 were not significantly changed from their respective V2D7 values (sarcoidosis: *MWU p-val* =0.2250; controls: *MWU p-val* =0.0894) and remained significantly higher than baseline (sarcoidosis: *MWU p-val* <0.001; controls: *MWU p-val* <0.001) suggesting persistent immunity. Finally, median ID50 for sarcoidosis subjects were comparable to those of controls at all time points (V1D0 *MWU p-val* =0.5879; V2D7 *MWU p-val* =0.5740; M6 *MWU p-val* =0.7409) indicating similar levels of nAb present.

Trends in IgG and nAb were further evaluated across sarcoidosis treatment groups (**Figure 3**). Pairwise comparisons using Dunn's test indicated sarcoidosis subjects on and off immunosuppression had comparable V2D7 IgG titers to controls (immunosuppression vs. control *BH adj p val* =0.3197, no treatment vs. control *BH adj p-val* =0.4514) as well as comparable nAb titers to controls (immunosuppression vs. control *BH adj p val* =0.4904, no treatment vs. control *BH adj p-val* =0.9333) indicating a robust initial antibody response regardless of immunosuppression. At M6, sarcoidosis subjects on immunosuppression had significantly decreased IgG titers compared to controls (*BH adj p-val* =0.0162), however nAb titers remained comparable (controls (*BH adj p-val* =0.3688) suggesting preserved protection.

Regression Analysis

Given variation in Trimer IgG and nAb trends, a univariate linear regression model was constructed to characterize the relationship between IgG and nAb titers across all time points. Correlation coefficients for control and sarcoidosis group are shown in **Figure 4**. IgG titers were significantly and directly associated with nAb titers in both groups, with a strong correlation for the control group (R =0.7715, *p-val* <0.001) and a weak correlation for sarcoidosis group (R =0.3905, *p-val* 0.0140). IgG titers in the sarcoidosis group were overall determined to be less predictive of nAb (R^2 =0.1525) than in the control group (R^2 =0.5952). With such low variance explained by IgG titers in the sarcoidosis group, a multivariate linear regression model was subsequently constructed to delineate which, if any, variables independently predict short term (V2D7) and long term (M6) nAb titers. Regression models for each outcome are shown in **Figure 5**. The overall regression was not statistically

significant for either group. Additional regression models for M6 for each group were constructed with the addition of V2D7 and M6 IgG titers, also with interdependencies accounted for, and yielded similar results. None of the additional independent variables were significantly predictive of nAb though analysis may be underpowered to detect significance.

INTERPRETATION:

We present a single center analysis of the quantitative and qualitative antibody response to vaccination with the BNT162b2 mRNA COVID-19 vaccine in infection naïve subjects with and without sarcoidosis. Our data indicates that sarcoidosis subjects mount a robust initial Trimer IgG antibody response to vaccination with subsequent quantitative decline by 6 months, driven by those on immunosuppression. Despite the decline in binding antibodies, sarcoidosis subjects develop and maintain functional immunity regardless of immunosuppressive treatment. With this discrepancy between IgG and nAb titers, it is not surprising that IgG antibodies weakly correlated with nAb and were not significantly predictive of nAb titers at any timepoint. While this study is of a single vaccine type, it sheds light on the clinical protection vaccination provides individuals with sarcoidosis despite IgG titers that may suggest otherwise.

The SARS-CoV-2 is an enveloped virus with numerous structural proteins vital for the viral life cycle. The S protein, which is composed a S1 subunit, S2 subunit, N-terminal domain, and receptor-binding domain (RBD), is responsible for viral entry into the host cell specifically through binding of the RBD. Antibodies to SARS-CoV-2 consist of IgM, IgG, and/or IgA antibodies and may target any subdomain of the S protein [24-27]. Upon viral binding to ACE2, conformational changes of surface glycoproteins result in the formation of an S protein trimer [28], which is the target of the IgG antibodies quantified in this study. Despite a wide array of antibodies produced, nAb confer protection by preventing viral entry, receptor mediated infection and infection propagation. Numerous studies support a strong correlation between various antibody titers and neutralization; however, the strength of correlation may vary with different tested antibody targets as well as with time from SARS-CoV-2 exposure [29-31]. Our findings reveal a strong correlation in controls between Trimeric anti-spike IgG levels and neutralization, which aligns with a similar study of this antibody type in healthy individuals after BNT162b2 vaccine [32]. The sarcoidosis group, however, had a weak correlation between IgG levels and neutralization which was otherwise not explained by group differences. Neutralization in this group is therefore likely explained by the presence of non-IgG antibodies or antibodies to other spike protein subdomains not measured in our study, though further analyses are needed to assess this.

Sarcoidosis is a T cell mediated disease characterized by local CD4+ T lymphocyte inflammation and peripheral lymphocyte depletion in severe or active disease, as well as anergy and exhaustion in progressive disease [4, 5, 33, 34]. Defects within humoral

immunity have also been described and include evidence of B cell hyperactivation, autoantibody production, decreased circulating memory B cells, as well as previously mentioned impaired serologic responses to Tetanus and Hepatitis vaccines [10, 11, 20, 35-38]. Despite these defects, vaccine induced development and persistence of neutralization antibodies in sarcoidosis subjects is a particularly important and reassuring finding. However, it is worth noting the median peripheral absolute lymphocyte count (1.8×10^9 cells/liter) in our cohort is greater than previously described thresholds of significant sarcoidosis-related lymphopenia [34]. This suggests lymphopenia is unlikely to be a significant disease manifestation in this cohort and therefore may explain the preserved nAb activity. Treatment was also uptitrated in four sarcoidosis individuals; despite this, neutralization was seemingly unaffected.

Limitations of this study include heterogeneity within the sarcoidosis group, limited sample size, and attrition rate at 6 months. Data regarding lymphocyte subsets in the sarcoidosis group were largely unavailable and may have allowed further interpretation of the immunity stimulated by vaccination if obtained concurrently. Only IgG antibody was quantified, and despite strong correlation to nAb among control subjects, further assessment of preserved immunity in sarcoidosis was limited. Future studies in the field should focus on inclusion of specific sarcoidosis phenotypes as well as direct assessment of cellular and humoral activity. Furthermore, baseline elevation of the Trimer IgG antibody in the sarcoidosis group raised the question of non-specific IgG binding from underlying hypergammagloulinemia [39] or prior community coronavirus exposure with cross reactivity [40]. Undiagnosed low-level exposure or infection in the sarcoidosis group is also considered as COVID-19 history was self-reported, though the similar levels of baseline neutralizing antibodies does not corroborate this. Lastly, only one mRNA COVID-19 vaccine was studied, thus conclusions should be cautiously applied to other COVID-19 vaccines.

Despite these limitations, we conclude that Trimer IgG levels in sarcoidosis subjects are poor predictors of nAb, which are an important mechanism in preventing infection While further analysis is needed to determine clinical outcomes from vaccination in this vulnerable population, particularly among those on immunosuppression, knowledge gained from our study suggests that vaccination may provide at least partial protection from COVID-19 infection in sarcoidosis. Additional studies of immune response stimulated by the BNT162b2 vaccine, which induces robust cellular and humoral immunity [41], may offer mechanistic insights into the pathogenesis of sarcoidosis.

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Table 1. Demographics of control and sarcoidosis groups			
	Control Subjects	**Subjects with Sarcoid**	*P-value*
Total Subjects, n	27	14	
Age, median (years)	53.0	60.5	*0.3355*
Sex, n **Female** **Male**	 10 17	 10 4	*0.7337*
Race, n **Black** **White** **Asian** **Other**	 2 18 1 6	 9 5 0 0	*0.0005*
Body Mass Index, median (kg/m^2)	26.1	31.84	*0.0319*
Days between Vaccine Dose, mean	21.3	20.9	*0.0793*
Days Between 1st Vaccine and V2D7, mean	6.9	6.9	*0.4939*
Days Between 1st Vaccine and M6, mean	180.9	192.6	*0.0575*
V2D7 = 7 days after vaccine dose 2 (4 weeks after 1st dose) M6 = month 6 time point			

Table 2. Clinical details regarding sarcoidosis chronicity, organ involvement, and treatment for each of the fourteen subjects in the sarcoidosis group.

Subject	**Years Since Diagnosis**	**Organ Involvement**	**Treatment**	**Prednisone Equivalent (mg)**	**Abs Lymphocyte (10^9 cells / L)**
1*	26	Pulmonary	Steroids, anti-metabolite, anti-TNF, IVIG	10	0.9
2	2	Lymph Node	Steroids, HCQ	7.5	1.2
3	13	Pulmonary, Ocular	Steroids, anti-metabolite	2.5	3.0
4	8	Pulmonary, Neurologic	Steroids	5	NA
5*	12	Pulmonary, Cardiac	None	0	1.2
6	24	Pulmonary	None	0	2.0
7	41	Pulmonary	None	0	1.7
8*	11	Pulmonary	Steroids, anti-TNF, IVIG	15	3.1
9	10	Pulmonary, Neurologic, Hepatic	Steroids, anti-metabolite, anti-TNF	10	1.6
10	6	Pulmonary	HCQ	0	1.7
11	8	Pulmonary	None	0	2.9
12	7	Pulmonary, Ocular	Anti-metabolite, anti-TNF	0	1.9
13	30	Pulmonary	None	0	NA
14	7	Pulmonary	None	0	2.0
*6 month time point not available					

REFERENCES

1. Baden, L.R., et al., *Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.* N Engl J Med, 2021. **384**(5): p. 403-416.
2. Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.* N Engl J Med, 2020. **383**(27): p. 2603-2615.
3. Ascoli, C., et al., *A Circulating MicroRNA Signature Serves as a Diagnostic and Prognostic Indicator in Sarcoidosis.* Am J Respir Cell Mol Biol, 2018. **58**(1): p. 40-54.
4. Sweiss, N.J., et al., *Significant CD4, CD8, and CD19 lymphopenia in peripheral blood of sarcoidosis patients correlates with severe disease manifestations.* PLoS One, 2010. **5**(2): p. e9088.
5. Hawkins, C., et al., *Local and Systemic CD4(+) T Cell Exhaustion Reverses with Clinical Resolution of Pulmonary Sarcoidosis.* J Immunol Res, 2017. **2017**: p. 3642832.
6. Dureault, A., et al., *Severe infections in sarcoidosis: Incidence, predictors and long-term outcome in a cohort of 585 patients.* Medicine (Baltimore), 2017. **96**(49): p. e8846.
7. Ungprasert, P., C.S. Crowson, and E.L. Matteson, *Sarcoidosis Increases Risk of Hospitalized Infection. A Population-based Study, 1976-2013.* Ann Am Thorac Soc, 2017. **14**(5): p. 676-681.
8. Baughman, R.P., et al., *Risk and outcome of COVID-19 infection in sarcoidosis patients: results of a self-reporting questionnaire.* Sarcoidosis Vasc Diffuse Lung Dis, 2020. **37**(4): p. e2020009.
9. Baughman, R.P., et al., *Sarcoidosis in America. Analysis Based on Health Care Use.* Ann Am Thorac Soc, 2016. **13**(8): p. 1244-52.
10. Seyhan, E.C., et al., *Results of tetanus vaccination in sarcoidosis.* Sarcoidosis Vasc Diffuse Lung Dis, 2012. **29**(1): p. 3-10.
11. Mert, A., et al., *Results of hepatitis B vaccination in sarcoidosis.* Respiration, 2000. **67**(5): p. 543-5.
12. Tavana, S., et al., *Influenza vaccination in patients with pulmonary sarcoidosis: efficacy and safety.* Influenza Other Respir Viruses, 2012. **6**(2): p. 136-41.
13. Payne, S. and C. Ebook Central Academic, *Viruses : from understanding to investigation*. First edition. ed. 2017, Boston, Massachusetts: Elsevier.
14. Friedman, M.A., J.R. Curtis, and K.L. Winthrop, *Impact of disease-modifying antirheumatic drugs on vaccine immunogenicity in patients with inflammatory rheumatic and musculoskeletal diseases.* Ann Rheum Dis, 2021. **80**(10): p. 1255-1265.
15. Mahil, S.K., et al., *The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: a cohort study.* Lancet Rheumatol, 2021. **3**(9): p. e627-e637.
16. Ruddy, J.A., et al., *High antibody response to two-dose SARS-CoV-2 messenger RNA vaccination in patients with rheumatic and musculoskeletal diseases.* Ann Rheum Dis, 2021. **80**(10): p. 1351-1352.
17. Subesinghe, S., et al., *A Systematic Review and Metaanalysis of Antirheumatic Drugs and Vaccine Immunogenicity in Rheumatoid Arthritis.* J Rheumatol, 2018. **45**(6): p. 733-744.
18. Manansala, M., et al., *COVID-19 and Sarcoidosis, Readiness for Vaccination: Challenges and Opportunities.* Front Med (Lausanne), 2021. **8**: p. 672028.
19. Syed, H., et al., *Infection prevention in sarcoidosis: proposal for vaccination and prophylactic therapy.* Sarcoidosis Vasc Diffuse Lung Dis, 2020. **37**(2): p. 87-98.
20. Hunninghake, G.W., et al., *ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders.* Sarcoidosis Vasc Diffuse Lung Dis, 1999. **16**(2): p. 149-73.
21. Feng, F., et al., *A computational solution to improve biomarker reproducibility during long-term projects.* PLoS One, 2019. **14**(4): p. e0209060.

22. Nie, J., et al., *Quantification of SARS-CoV-2 neutralizing antibody by a pseudotyped virus-based assay.* Nat Protoc, 2020. **15**(11): p. 3699-3715.
23. Ferrara, F. and N. Temperton, *Pseudotype Neutralization Assays: From Laboratory Bench to Data Analysis.* Methods Protoc, 2018. **1**(1).
24. Klingler, J., et al., *Role of IgM and IgA Antibodies in the Neutralization of SARS-CoV-2.* medRxiv, 2020.
25. Sterlin, D., et al., *IgA dominates the early neutralizing antibody response to SARS-CoV-2.* Sci Transl Med, 2021. **13**(577).
26. Ma, H., et al., *Serum IgA, IgM, and IgG responses in COVID-19.* Cell Mol Immunol, 2020. **17**(7): p. 773-775.
27. Salvagno, G.L., et al., *Anti-spike S1 IgA, anti-spike trimeric IgG, and anti-spike RBD IgG response after BNT162b2 COVID-19 mRNA vaccination in healthcare workers.* J Med Biochem, 2021. **40**(4): p. 327-334.
28. Walls, A.C., et al., *Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein.* Cell, 2020. **181**(2): p. 281-292 e6.
29. Mazzini, L., et al., *Comparative analyses of SARS-CoV-2 binding (IgG, IgM, IgA) and neutralizing antibodies from human serum samples.* J Immunol Methods, 2021. **489**: p. 112937.
30. Maeda, K., et al., *Neutralization of SARS-CoV-2 with IgG from COVID-19-convalescent plasma.* Sci Rep, 2021. **11**(1): p. 5563.
31. Volkova, L.D., *[Clinical value of the determination of isoenzymes of malate and lactate dehydrogenase in the urine in chronic kidney diseases in children].* Pediatriia, 1974. **0**(10): p. 71-3.
32. Matusali, G., et al., *Differential Dynamics of SARS-CoV-2 Binding and Functional Antibodies upon BNT162b2 Vaccine: A 6-Month Follow-Up.* Viruses, 2022. **14**(2).
33. Grunewald, J., et al., *Sarcoidosis.* Nat Rev Dis Primers, 2019. **5**(1): p. 45.
34. Vagts, C., et al., *Unsupervised Clustering Reveals Sarcoidosis Phenotypes Marked by a Reduction in Lymphocytes Relate to Increased Inflammatory Activity on 18FDG-PET/CT.* Front Med (Lausanne), 2021. **8**: p. 595077.
35. Hashemzadeh, K., et al., *Serum B cell activating factor (BAFF) and sarcoidosis activity.* Arch Rheumatol, 2021. **36**(1): p. 72-79.
36. Kudryavtsev, I., et al., *Imbalance in B cell and T Follicular Helper Cell Subsets in Pulmonary Sarcoidosis.* Sci Rep, 2020. **10**(1): p. 1059.
37. Musaelyan, A., et al., *Vimentin as antigenic target in autoimmunity: A comprehensive review.* Autoimmun Rev, 2018. **17**(9): p. 926-934.
38. Saussine, A., et al., *Active chronic sarcoidosis is characterized by increased transitional blood B cells, increased IL-10-producing regulatory B cells and high BAFF levels.* PLoS One, 2012. **7**(8): p. e43588.
39. Hunninghake, G.W. and R.G. Crystal, *Mechanisms of hypergammaglobulinemia in pulmonary sarcoidosis. Site of increased antibody production and role of T lymphocytes.* J Clin Invest, 1981. **67**(1): p. 86-92.
40. Hicks, J., et al., *Serologic Cross-Reactivity of SARS-CoV-2 with Endemic and Seasonal Betacoronaviruses.* Journal of Clinical Immunology, 2021. **41**(5): p. 906-913.
41. Fotin-Mleczek, M., et al., *Messenger RNA-based vaccines with dual activity induce balanced TLR-7 dependent adaptive immune responses and provide antitumor activity.* J Immunother, 2011. **34**(1): p. 1-15.

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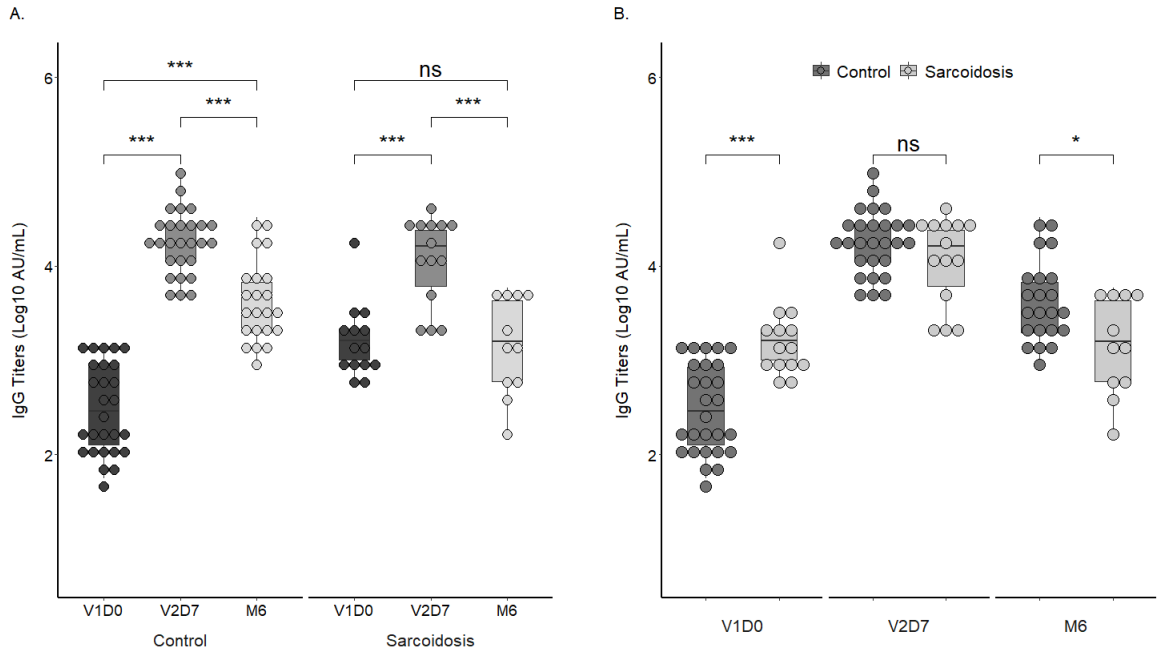
Figure 1. Trimer IgG titers for control and sarcoidosis groups are shown: (a) log transformed titers for comparison between time points for each group and (b) log transformed titers for comparison between groups at each time point. ns: p > 0.05; *: p <= 0.05; **: p <= 0.01; ***: p <= 0.001

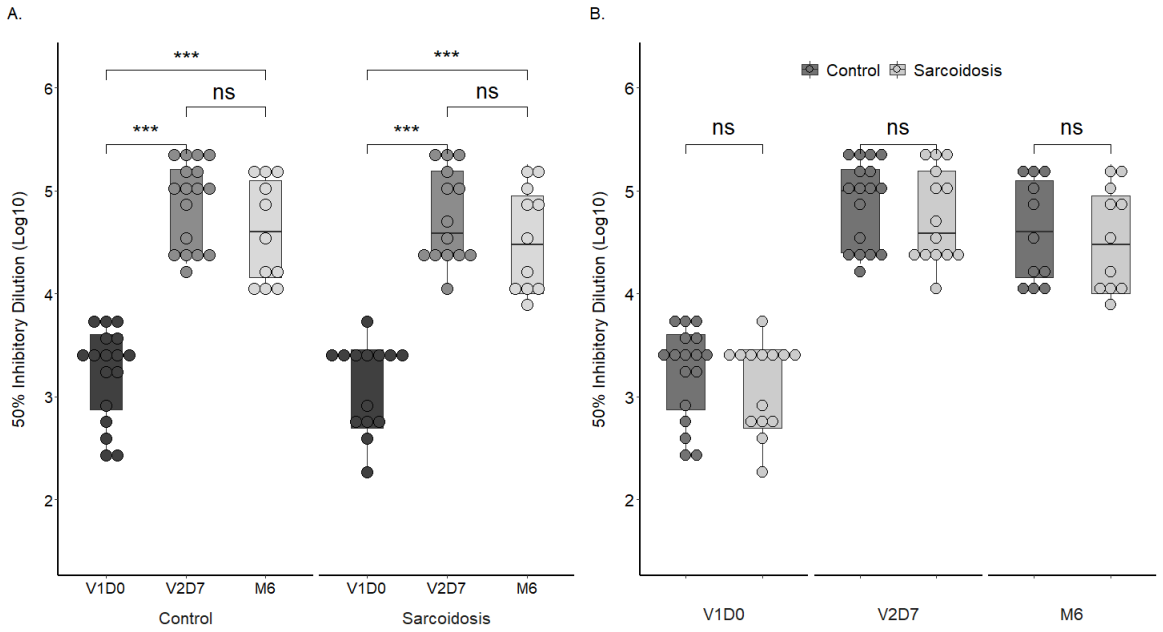
Figure 2. Neutralizing titers (50% Inhibitory Dilution) for control and sarcoidosis groups are shown: (a) log transformed titers for comparison between time points for each group and (b) log transformed titers for comparison between groups at each time point. ns: p > 0.05; *: p <= 0.05; **: p <= 0.01; ***: p <=0.001

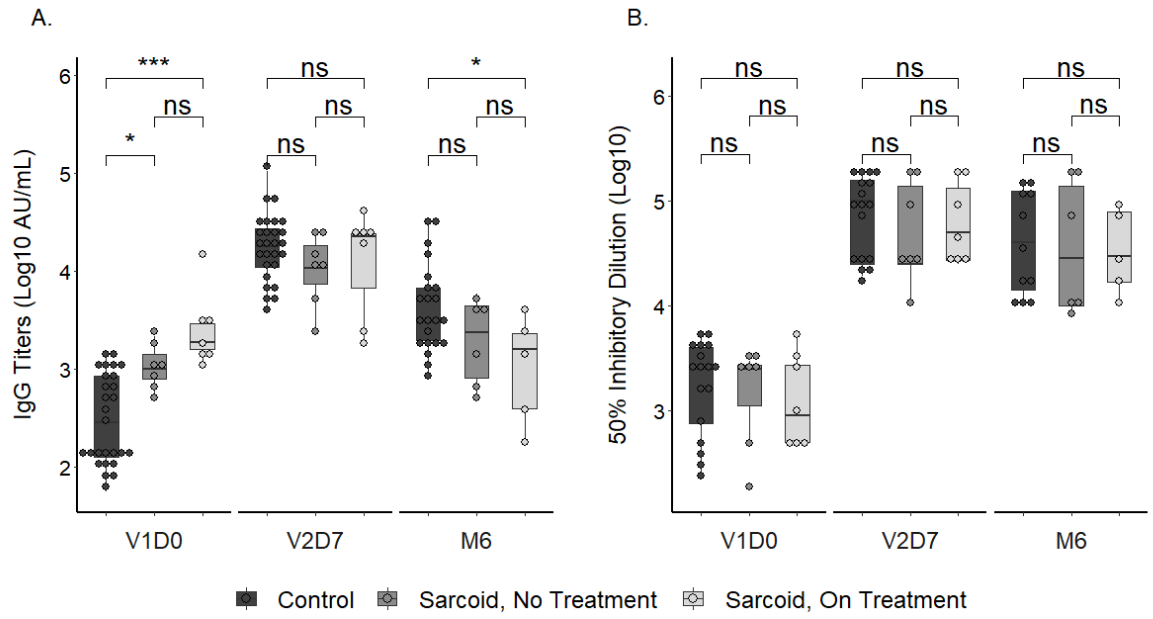
Figure 3. (a) log transformed trimer spike-protein IgG titers are shown. Sarcoidosis subjects not on treatment had significantly higher V1D0 titers than controls and comparable titers at V2D7. M6 IgG titers were significantly lower in the sarcoidosis group than controls. (b) log transformed neutralizing titers (50% inhibitory dilution). Values were comparable across all groups at each time point. ns: p > 0.05; *: p <=0.05; **: p <= 0.01; ***: p <= 0.001

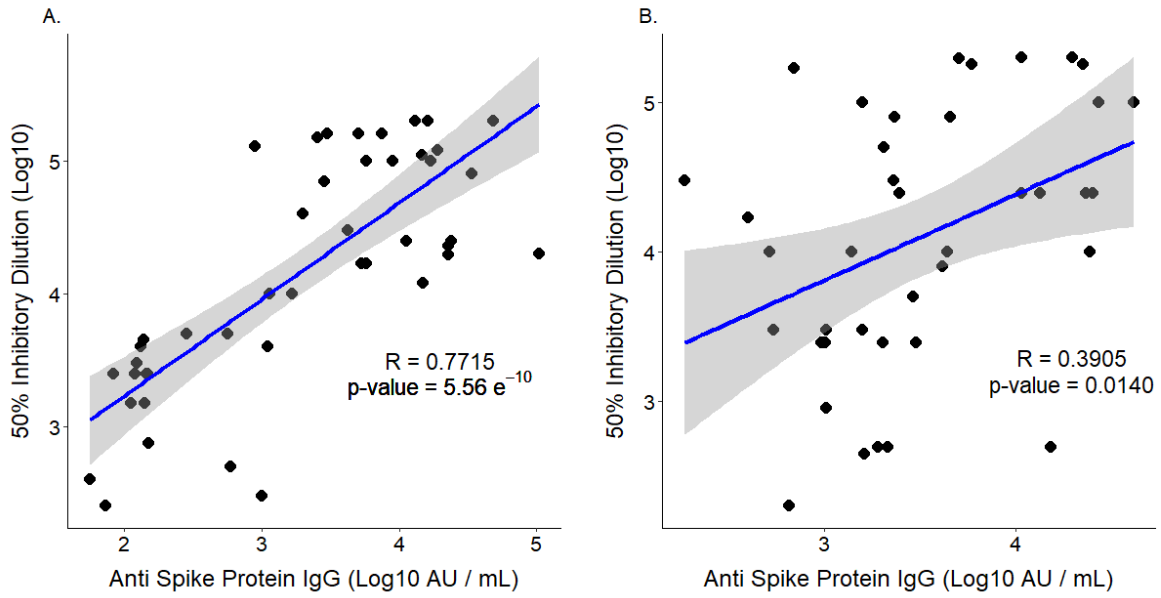
Figure 4. Univariate linear regression analysis illustrating the relationship between log transformed Trimer IgG titers and log transformed 50% inhibitory dilution across all time points. (a) Control group showing a significant and strong correlation, and (b) Sarcoidosis group showing a significant yet weak correlation.

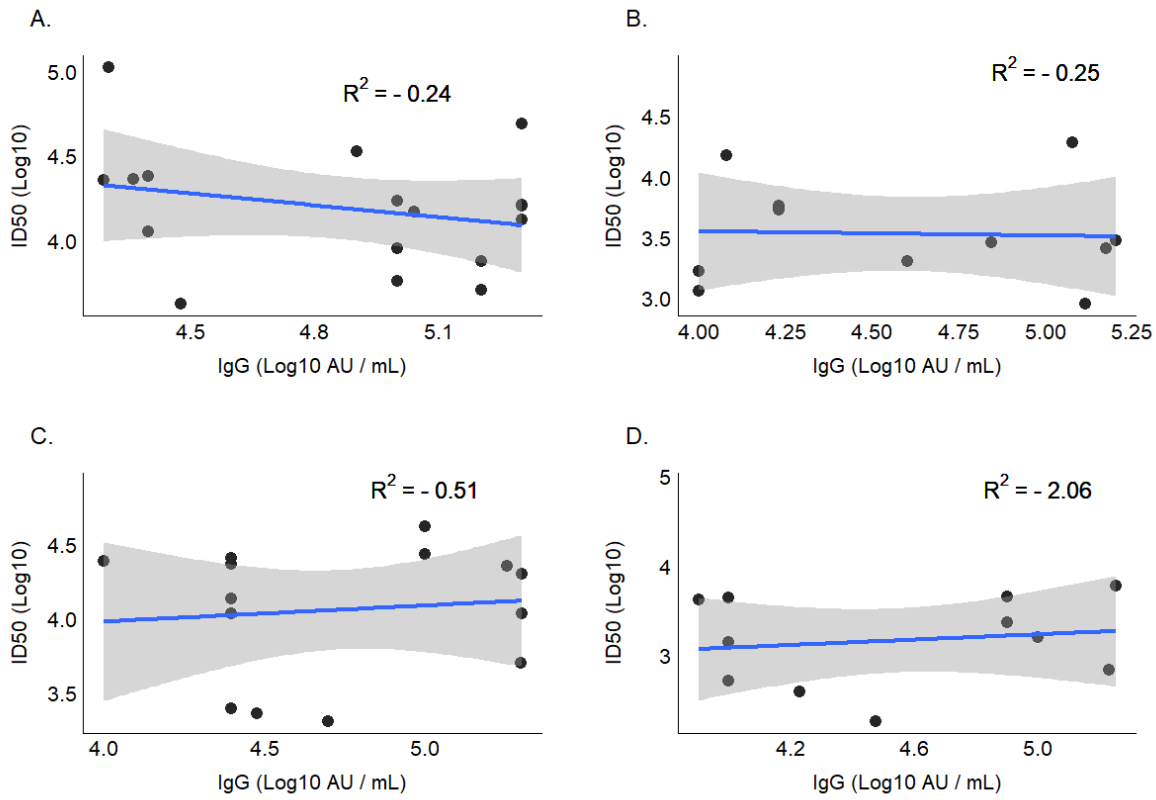
Figure 5. Multivariate regression analysis to assess independent predictors of 50% inhibitory dilution (ID50) for by group (top row: controls; bottom row: sarcoidosis) and outcome time points (left column: V2D7; right column: M6). Axes are log transformed. (a) V2D7 ID50 for control group. Model: Log10 V2D7 ID50 ~ Log10 V2D7 Trimer IgG * Log10 V1D0 Trimer IgG + Race + BMI. (b) M6 ID50 for the control group. Model: Log10 V2D7 ID50 ~ Log10 V2D7 Trimer IgG * Log10 V1D0 Trimer IgG + Log10 V2D7 Trimer IgG * Log10 M6 V2D7 IgG + Race + BMI. (c) V2D7 ID50 for the sarcoidosis group. Model: Log10 V2D7 ID50 ~ Log10 V2D7 Trimer IgG * Log10 V1D0 Trimer IgG + Race + BMI + Treatment Group. (d) M6 ID50 for the sarcoidosis group. Log10 V2D7 ID50 ~ Log10 V2D7 Trimer IgG * Log10 V1D0 Trimer IgG + Log10 V2D7 Trimer IgG *Log10 M6 V2D7 IgG + Race + BMI + Treatment Group. The overall regression was not statistically significant for either group at both time points.


A.
IgG Titers (Log10 AU/mL)
6
4
2
***
***
***
ns
***
***
V1D0
V2D7
M6
V1D0
V2D7
M6
Control
Sarcoidosis
B.
Control
Sarcoidosis
IgG Titers (Log10 AU/mL)
***
ns
*
V1D0
V2D7
M6


A.
B.
50% Inhibitory Dilution (Log10)
***
ns
***
***
ns
***
V1D0
V2D7
M6
Control
Sarcoidosis
Control
Sarcoidosis
ns
ns
ns


A.
B.
IgG Titers (Log10 AU/mL)
50% Inhibitory Dilution (Log10)
***
*
ns
*
V1D0
V2D7
M6
Control
Sarcoid, No Treatment
Sarcoid, On Treatment


A.
50% Inhibitory Dilution (Log10)
5
4
3
2
3
4
5
Anti Spike Protein IgG (Log10 AU / mL)
R = 0.7715
p-value = 5.56 e−10
B.
50% Inhibitory Dilution (Log10)
5
4
3
3
4
Anti Spike Protein IgG (Log10 AU / mL)
R = 0.3905
p-value = 0.0140


A.
R^2 = - 0.24
ID50 (Log10)
5.0
4.5
4.0
4.5
4.8
5.1
IgG (Log10 AU / mL)
B.
R^2 = - 0.25
ID50 (Log10)
4.5
4.0
3.5
3.0
4.00
4.25
4.50
4.75
5.00
5.25
IgG (Log10 AU / mL)
C.
R^2 = - 0.51
ID50 (Log10)
4.5
4.0
3.5
4.0
4.5
5.0
IgG (Log10 AU / mL)
D.
R^2 = - 2.06
ID50 (Log10)
5
4
3
4.2
4.6
5.0
IgG (Log10 AU / mL)

Subject	Group	TimePoint	Dilution	Abtiter	corr_conc	BAU	ID50	CovidHx	Tx
SX1_M6	SX	M6	NA	NA	NA	NA	NA	0	2
SX1_V1D0	SX	V1D0	0.001	576.6489	576648.9	1582.027	3000	0	2
SX1_V2D7	SX	V2D7	0.001	7244.442	7244442	19875.01	200000	0	2
SX2_M6	SX	M6	0.01	1439.52	143952	394.9299	17000	0	2
SX2_V1D0	SX	V1D0	0.001	590.7548	590754.8	1620.726	450	0	2
SX2_V2D7	SX	V2D7	0.001	9270.313	9270313	25432.96	25000	0	2
SX3_M6	SX	M6	0.01	670.6015	67060.15	183.9785	30000	0	2
SX3_V1D0	SX	V1D0	0.001	371.5519	371551.9	1019.347	900	0	2
SX3_V2D7	SX	V2D7	0.001	744.1444	744144.4	2041.548	50000	0	2
SX4_M6	SX	M6	0.01	5767.966	576796.6	1582.432	100000	0	2
SX4_V1D0	SX	V1D0	0.001	1092.065	1092065	2996.063	2500	0	2
SX4_V2D7	SX	V2D7	0.001	8241.955	8241955	22611.67	180000	0	2
SX5_M6	SX	M6	NA	NA	NA	NA	NA	0	1
SX5_V1D0	SX	V1D0	0.001	350.6806	350680.6	962.0867	2500	0	1
SX5_V2D7	SX	V2D7	0.001	4934.231	4934231	13536.99	25000	0	1
SX6_M6	SX	M6	0.01	2505.105	250510.5	687.2715	170000	0	1
SX6_V1D0	SX	V1D0	0.001	371.294	371294	1018.639	3000	0	1
SX6_V2D7	SX	V2D7	0.001	1846.998	1846998	5067.211	199000	0	1
SX7_M6	SX	M6	0.01	16592.6	1659260	4552.155	80000	0	1
SX7_V1D0	SX	V1D0	0.001	735.7285	735728.5	2018.46	2500	0	1
SX7_V2D7	SX	V2D7	0.001	9919.57	9919570	27214.18	100000	0	1
SX8_M6	SX	M6	NA	NA	NA	NA	NA	0	2
SX8_V1D0	SX	V1D0	0.001	690.8038	690803.8	1895.209	500	0	2
SX8_V2D7	SX	V2D7	0.001	840.3233	840323.3	2305.414	30000	0	2
SX9_M6	SX	M6	0.01	8501.915	850191.5	2332.487	80000	0	2
SX9_V1D0	SX	V1D0	0.001	1055.913	1055913	2896.881	5000	0	2
SX9_V2D7	SX	V2D7	0.001	15284.82	15284816	41933.65	100000	0	2
SX10_M6	SX	M6	0.01	15982.85	1598285	4384.869	10000	0	2
SX10_V1D0	SX	V1D0	0.001	5593.005	5593005	15344.32	500	0	2
SX10_V2D7	SX	V2D7	0.001	8553.846	8553846	23467.34	25000	0	2
SX11_M6	SX	M6	0.01	5044.475	504447.5	1383.944	10000	0	1
SX11_V1D0	SX	V1D0	0.001	784.1562	784156.2	2151.32	500	0	1
SX11_V2D7	SX	V2D7	0.001	902.4166	902416.6	2475.766	25000	0	1
SX12_M6	SX	M6	0.01	1870.233	187023.3	513.0954	10000	0	1
SX12_V1D0	SX	V1D0	0.001	195.8283	195828.3	537.252	3000	0	1
SX12_V2D7	SX	V2D7	0.001	3924.553	3924553	10766.95	25000	0	1
SX13_M6	SX	M6	0.01	21593.14	2159314	5924.044	180000	0	1
SX13_V1D0	SX	V1D0	0.001	364.8487	364848.7	1000.957	2500	0	1
SX13_V2D7	SX	V2D7	0.001	3930.949	3930949	10784.5	200000	0	1
SX14_M6	SX	M6	0.01	15077.64	1507764	4136.526	8000	0	1
SX14_V1D0	SX	V1D0	0.1	23815.89	238158.9	653.3853	200	0	1
SX14_V2D7	SX	V2D7	0.001	8920.111	8920111	24472.18	10000	0	1
C1_M6	Ctrl	M6	0.001	5476.513	5476513	15024.73	12000	0	0
C1_V1D0	Ctrl	V1D0	0.01	554.4652	55446.52	152.1167	750	0	0
C1_V2D7	Ctrl	V2D7	0.001	8275.197	8275197	22702.87	19500	0	0
C2_M6	Ctrl	M6	NA	NA	NA	NA	NA	0	0
C2_V1D0	Ctrl	V1D0	0.1	20671.55	206715.5	567.1207	5000	0	0
C2_V2D7	Ctrl	V2D7	0.001	2100.345	2100345	5762.264	100000	0	0
C3_M6	Ctrl	M6	0.001	11886.48	11886485	32610.38	NA	0	0
C3_V1D0	Ctrl	V1D0	0.001	312.8948	312894.8	858.4218	NA	0	0
C3_V2D7	Ctrl	V2D7	0.001	9512.933	9512933	26098.58	NA	0	0
C4_M6	Ctrl	M6	0.001	10920.45	10920449	29960.08	NA	0	0
C4_V1D0	Ctrl	V1D0	0.001	235.4378	235437.8	645.9198	NA	0	0
C4_V2D7	Ctrl	V2D7	0.001	11948.75	11948755	32781.22	NA	0	0
C5_M6	Ctrl	M6	0.001	1937.284	1937284	5314.909	17000	0	0
C5_V1D0	Ctrl	V1D0	0.001	215.3532	215353.2	590.8182	500	0	0
C5_V2D7	Ctrl	V2D7	0.001	4122.533	4122533	11310.11	25000	0	0

C6_M6	Ctrl	M6	0.001	326.2471	326247.1	895.0538	130000	0	0
C6_V1D0	Ctrl	V1D0	0.01	533.0884	53308.84	146.252	2500	0	0
C6_V2D7	Ctrl	V2D7	0.01	27302.62	2730262	7490.431	160000	0	0
C7_M6	Ctrl	M6	0.001	653.8231	653823.1	1793.753	NA	0	0
C7_V1D0	Ctrl	V1D0	0.001	560.7263	560726.3	1538.344	NA	0	0
C7_V2D7	Ctrl	V2D7	0.001	6503.375	6503375	17841.91	NA	0	0
C8_M6	Ctrl	M6	0.001	933.9069	933906.9	2562.159	150000	0	0
C8_V1D0	Ctrl	V1D0	0.1	4814.046	48140.46	132.0726	4000	0	0
C8_V2D7	Ctrl	V2D7	0.001	5870.198	5870198	16104.8	200000	0	0
C9_M6	Ctrl	M6	0.001	2345.422	2345422	6434.627	NA	0	0
C9_V1D0	Ctrl	V1D0	0.01	205.2038	20520.38	56.29735	400	0	0
C9_V2D7	Ctrl	V2D7	0.001	8718.115	8718115	23918.01	25000	0	0
C10_M6	Ctrl	M6	0.001	717.8541	717854.1	1969.421	NA	0	0
C10_V1D0	Ctrl	V1D0	0.001	307.7635	307763.5	844.3444	NA	0	0
C10_V2D7	Ctrl	V2D7	0.001	6582.793	6582793	18059.79	NA	0	0
C11_M6	Ctrl	M6	0.001	551.5962	551596.2	1513.296	NA	0	0
C11_V1D0	Ctrl	V1D0	0.001	466.2531	466253.1	1279.158	NA	0	0
C11_V2D7	Ctrl	V2D7	0.001	7330.561	7330561	20111.28	NA	0	0
C12_M6	Ctrl	M6	0.001	1130.913	1130913	3102.643	NA	0	0
C12_V1D0	Ctrl	V1D0	0.001	437.4686	437468.6	1200.188	NA	0	0
C12_V2D7	Ctrl	V2D7	0.001	10591.68	10591682	29058.11	NA	0	0
C13_M6	Ctrl	M6	0.001	6929.224	6929224	19010.22	120000	0	0
C13_V1D0	Ctrl	V1D0	0.01	504.971	50497.1	138.538	4500	0	0
C13_V2D7	Ctrl	V2D7	0.001	1860.506	1860506	5104.268	160000	0	0
C14_M6	Ctrl	M6	0.01	6097.287	609728.7	1672.781	10000	0	0
C14_V1D0	Ctrl	V1D0	0.01	437.7276	43772.76	120.0899	2500	0	0
C14_V2D7	Ctrl	V2D7	0.001	1531.563	1531563	4201.819	30000	0	0
C15_M6	Ctrl	M6	0.01	7268.259	726825.9	1994.035	40000	0	0
C15_V1D0	Ctrl	V1D0	0.01	545.0773	54507.73	149.5411	2500	0	0
C15_V2D7	Ctrl	V2D7	0.001	3252.516	3252516	8923.226	100000	0	0
C16_M6	Ctrl	M6	0.001	2168.454	2168454	5949.118	NA	0	0
C16_V1D0	Ctrl	V1D0	0.001	165.2604	165260.4	453.3892	NA	0	0
C16_V2D7	Ctrl	V2D7	0.001	22302.99	22302991	61187.9	NA	0	0
C17_M6	Ctrl	M6	0.001	3071.7	3071700	8427.16	NA	0	0
C17_V1D0	Ctrl	V1D0	0.01	1422.096	142209.6	390.1499	NA	0	0
C17_V2D7	Ctrl	V2D7	0.001	13282.13	13282127	36439.31	NA	0	0
C18_M6	Ctrl	M6	0.001	1096.852	1096852	3009.197	160000	0	0
C18_V1D0	Ctrl	V1D0	0.001	404.8597	404859.7	1110.726	4000	0	0
C18_V2D7	Ctrl	V2D7	0.001	5851.516	5851516	16053.54	200000	0	0
C19_M6	Ctrl	M6	0.001	419.8612	419861.2	1151.883	10000	0	0
C19_V1D0	Ctrl	V1D0	0.001	364.0755	364075.5	998.8354	300	0	0
C19_V2D7	Ctrl	V2D7	0.001	38115.78	38115775	104570	20000	0	0
C20_M6	Ctrl	M6	0.001	2512.198	2512198	6892.176	NA	0	0
C20_V1D0	Ctrl	V1D0	0.01	407.4451	40744.51	111.7819	1500	0	0
C20_V2D7	Ctrl	V2D7	0.001	5383.053	5383053	14768.32	110000	0	0
C21_M6	Ctrl	M6	0.001	1046.084	1046084	2869.915	70000	0	0
C21_V1D0	Ctrl	V1D0	0.01	517.9829	51798.29	142.1078	1500	0	0
C21_V2D7	Ctrl	V2D7	0.001	6179.124	6179124	16952.33	100000	0	0
C22_M6	Ctrl	M6	0.001	2113.636	2113636	5798.726	17000	0	0
C22_V1D0	Ctrl	V1D0	0.01	269.6152	26961.52	73.9685	250	0	0
C22_V2D7	Ctrl	V2D7	0.001	8374.243	8374243	22974.6	23000	0	0
C23_M6	Ctrl	M6	NA	NA	NA	NA	NA	0	0
C23_V1D0	Ctrl	V1D0	0.01	452.5026	45250.26	124.1434	3000	0	0
C23_V2D7	Ctrl	V2D7	0.001	17701.39	17701385	48563.47	200000	0	0
C24_M6	Ctrl	M6	0.01	10045.76	1004576	2756.037	NA	0	0
C24_V1D0	Ctrl	V1D0	0.01	346.0473	34604.73	94.93752	NA	0	0
C24_V2D7	Ctrl	V2D7	0.001	3902.59	3902590	10706.69	NA	0	0
C25_M6	Ctrl	M6	NA	NA	NA	NA	NA	0	0

C25_V1D0	Ctrl	V1D0		0.01	1048.209	104820.9	287.5745	5000	0	0
C25_V2D7	Ctrl	V2D7		0.001	4788.686	4788686	13137.68	200000	0	0
C26_M6	Ctrl	M6	NA		NA	NA	NA	NA	0	0
C26_V1D0	Ctrl	V1D0		0.01	306.994	30699.4	84.22333	2500	0	0
C26_V2D7	Ctrl	V2D7		0.001	12210.07	12210070	33498.13	80000	0	0
C27_M6	Ctrl	M6	NA		NA	NA	NA	NA	0	0
C27_V1D0	Ctrl	V1D0		0.001	433.8418	433841.8	1190.238	NA	0	0
C27_V2D7	Ctrl	V2D7		0.001	2787.18	2787180	7646.583	NA	0	0

Subject	Group	Age	Race	Hispanic	Sex	BMI	CovidHx	Days_Boos	Days_boos	Days_M6	Time_sarc	Pulm	Skin	Eye	Cardiac	Neuro	Liver	Tx_sum	Steroid	Antimetab	TNF	HCQ	IVIG	Prednisone	pre_med	post_med	lymph	Nabgroup	M6Nab
C1	Ctrl	36	W	0	M	21.79	0	21	7	183	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C2	Ctrl	50	AA	0	W	29.86	0	21	7	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C3	Ctrl	34	Other	0	M	31	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C4	Ctrl	40	W	0	W	19.6	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C5	Ctrl	66	W	0	W	22.5	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C6	Ctrl	59	W	0	M	25.84	0	21	7	188	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C7	Ctrl	41	W	0	W	25.1	0	21	7	185	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C8	Ctrl	77	W	0	M	27.94	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C9	Ctrl	58	W	0	M	24.41	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C10	Ctrl	45	W	0	W	24.4	0	24	7	178	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C11	Ctrl	46	Other	0	W	27.5	0	22	6	178	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C12	Ctrl	39	Other	0	W	24.5	0	22	6	178	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C13	Ctrl	65	W	1	W	20.98	0	22	7	177	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C14	Ctrl	51	Other	1	W	32.01	0	22	7	186	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C15	Ctrl	66	W	0	W	27.44	0	21	7	183	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C16	Ctrl	48	W	0	W	21.1	0	21	7	180	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C17	Ctrl	42	W	0	W	35	0	21	7	182	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C18	Ctrl	61	W	0	W	21.8	0	21	7	195	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C19	Ctrl	58	W	0	W	30.9	0	21	7	177	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C20	Ctrl	54	Other	1	M	29.53	0	21	7	176	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C21	Ctrl	62	AA	0	W	49.38	0	21	7	177	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C22	Ctrl	39	Asian	0	M	24.39	0	21	7	177	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	1
C23	Ctrl	53	W	1	W	31.64	0	21	7	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C24	Ctrl	67	W	0	M	29.84	0	21	7	170	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
C25	Ctrl	51	Other	0	M	26.5	0	21	7	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C26	Ctrl	71	W	0	M	23.92	0	21	7	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	1	0
C27	Ctrl	69	W	0	W	26.1	0	21	7	NA	NA	NA	NA	NA	NA	NA	NA	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	0
SX1	Sarc	65	W	0	M	29.22	0	21	7	NA	26	1	0	0	0	0	0	2	1	1	1	0	1	10	Increase	Decrease	s	0.9	1	0
SX2	Sarc	70	W	0	W	27.14	0	21	7	214	2	0	0	0	0	0	0	2	1	0	0	1	0	7.5	Increase	None		1.2	1	1
SX3	Sarc	67	W	0	M	37.21	0	21	7	212	13	1	0	1	0	0	0	2	1	1	0	0	0	2.5	None	Increase		3	1	1
SX4	Sarc	59	AA	0	M	29.62	0	21	7	211	8	1	0	0	0	1	0	2	1	0	0	0	0	5	None	None	NA		1	1
SX5	Sarc	61	W	0	W	44.84	0	21	7	NA	12	1	0	0	1	0	0	1	0	0	0	0	0	0	None	Increase		1.2	1	0
SX6	Sarc	67	AA	0	W	23.4	0	20	7	173	24	1	0	0	0	0	0	1	0	0	0	0	0	0	None	None		2	1	1
SX7	Sarc	68	AA	0	W	32.59	0	21	7	177	41	1	0	0	0	0	0	1	0	0	0	0	0	0	None	None		1.7	1	1
SX8	Sarc	60	W	0	M	22.24	0	21	6	NA	11	1	0	0	0	0	0	2	1	0	1	0	1	15	Increase	Increase		3.1	1	0
SX9	Sarc	52	AA	0	W	39.94	0	21	6	213	10	1	0	0	0	1	1	2	1	1	1	0	0	10	None	Increase		1.6	1	1
SX10	Sarc	36	AA	0	W	19.98	0	21	7	175	6	1	0	0	0	0	0	2	0	0	0	1	0	0	None	None		1.7	1	1
SX11	Sarc	39	AA	0	W	33.84	0	21	7	181	8	1	0	0	0	0	0	1	0	0	0	0	0	0	None	None		2.9	1	1
SX12	Sarc	25	AA	0	W	53.73	0	21	7	171	7	1	0	1	0	0	0	2	0	1	1	0	0	0	Increase	None		1.9	1	1
SX13	Sarc	60	AA	0	W	32.7	0	21	7	202	30	1	0	0	0	0	0	1	0	0	0	0	0	0	None	None	NA		1	1
SX14	Sarc	61	AA	0	W	31.09	0	21	7	190	7	1	0	0	0	0	0	1	0	0	0	0	0	0	None	None		2	1	1