VIP Study

A prospective multi-site observational study of SARS-CoV-2 vaccination immunogenicity in patients with hematologic malignancy

Presentation to CITF:

Vaccine responses in people with compromised immune systems

March 8, 2023

Conflict of Interest

- C. Arianne Buchan
  - Nothing to disclose relevant to this talk
  - Previously honorariums for speaking engagements
    - Pfizer

Study Team

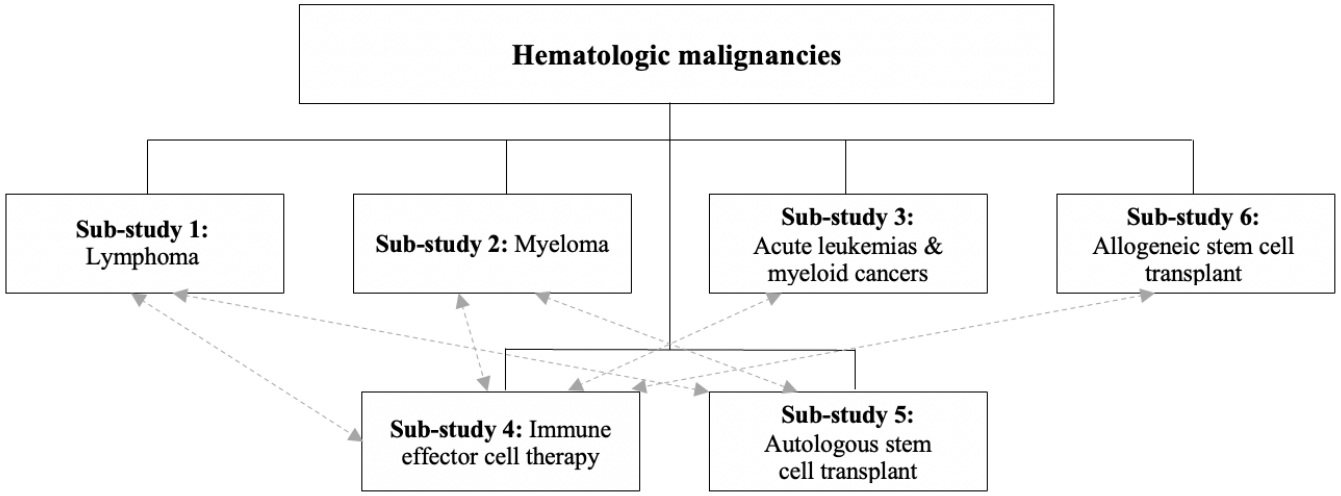
C. Arianne Buchan, MD MSc FRCPC — University of Ottawa / Ottawa Hospital Research Institute

- Co-PIs:
  - Sita Bhella, MD MEd FRCPC — University of Toronto / Princess Margaret Cancer Centre
  - Abi Vijenthira, MD SM FRCPC — University of Toronto / Princess Margaret Cancer Centre
  - Michael Sebag, MD PhD FRCPC — McGill University Health Centre
  - Peng Wang , MD PhD FRCPC — University of Alberta Hospital Cross Cancer Institute

- Lead study coordinator: Allison Wilkin, PhD

Study Overview

- Prospective observational multi-centre study
  - 12 sites recruiting nationally: 4 main hubs and 8 partner sites
- Study Population: Patients with hematologic malignancies (≥ 18y)
  - Six parallel sub-studies by diagnosis, will also include breakdown by treatment



Study Overview

- Web based platform: VIP (ohri.ca)
- “Do at home” mail-in Dried Blood Spot (DBS) Cards
- Baseline & follow-up questionnaires

- Optional Sub Study
  - Blood draws for neutralizing antibody and T-cell assays
  - Hybrid immunity extension

- Sample collection started August 2021 and finished January 31, 2023

- REB approval: OCREB within Ontario, local REB for centres outside Ontario

Humoral Immunity Results

- Partnered with Dr. Marc-Andre Langlois & his lab in Ottawa
- High throughput ELISA assay
  - IgG against nucleocapsid (N), spike (S) and receptor binding domain (RBD or R)
- Value or level measured in $mBAU/mm^2$
- Positive or negative antibody result
  - Lab threshold for positive anti-S $\geq$ ~6.9 $mBAU/mm^2$

Colwill, K. et al. (2022), A scalable serology solution for profiling humoral immune responses to SARS-CoV-2 infection and vaccination. Clin Transl Immunol, 11: e1380. https://doi.org/10.1002/cti2.1380

Recruitment

- Enrolled: 954 participants
  - 842 completed the study
  - 112 dropped out

- 63 participants enrolled in T-cell sub-study
- 156 participants enrolled in Hybrid Immunity study

ABSTRACT: COVID-19 vaccine immunogenicity surrounding fourth vaccine dose in patients with hematologic malignancies: A prospective real world observational multi-site Canadian study

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Preliminary Results

- We present data from 240 participants that had “paired” samples
  - 240 participants had results available both pre- and post-dose 4
  - 89 participants had results available post-dose 3, pre- and post-dose 4

Preliminary Results: Patient Population

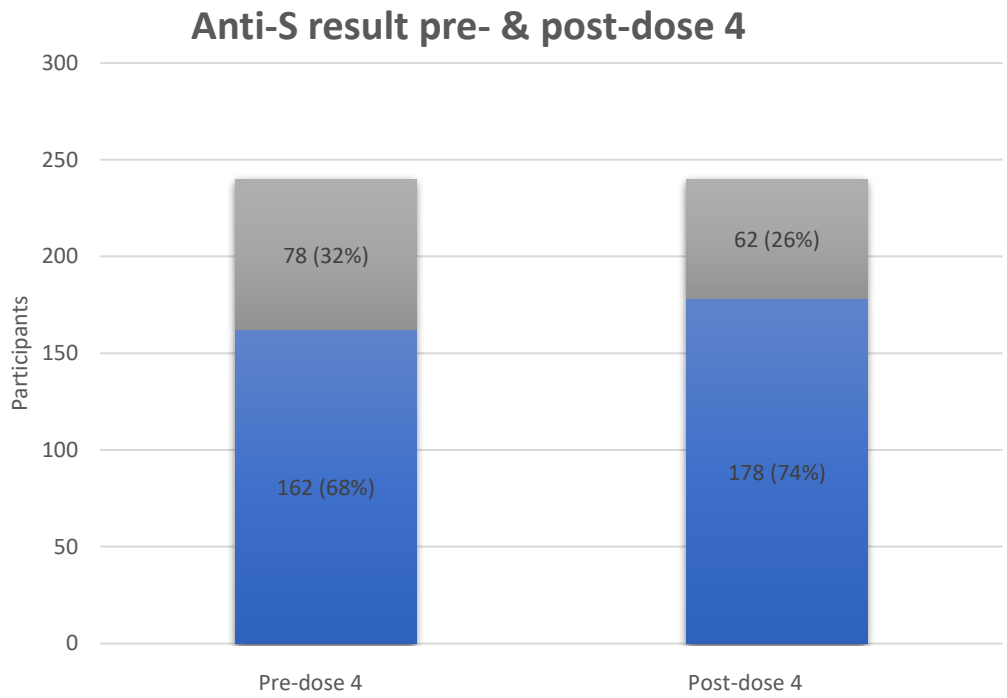
Disease Group	N = 240
Chronic lymphocytic leukemia (CLL)	25 (10.4%)
Lymphoma	81 (33.8%)
Myeloid or leukemia ALL (n=7), AML (n=14), MDS (n=7), MPN (n=14)	42 (17.5%)
Plasma Cell Disorders (PCD)	92 (38.3%)

Preliminary Results: Baseline characteristic highlights

Baseline characteristics	N = 240
Age (years)	66.5 [60-72.3]
Sex (male)	116 (49.0%)
Years Since Diagnosis	4 [1-10]
Treatment Status (n = 191)	
Never treated	17 (8.9%)
Currently on active treatment	117 (61.3%)
Post Treatment	57 (29.8%)
Missing data	49
Transplant Status (n = 212)	
No history of transplant	129 (60.9%)
History of allo-HCT	19 (9.0%)
History of auto-HCT	64 (30.2%)
Missing data	28
Exposure to Anti-CD20 Agents	
No history of exposure	116 (69.2%)
History of exposure	72 (30%)
Exposure in preceding 3 months (27)	
Unknown	2 (0.8%)

Preliminary Results: anti-S

Of the 240 participants with 4th dose data available:

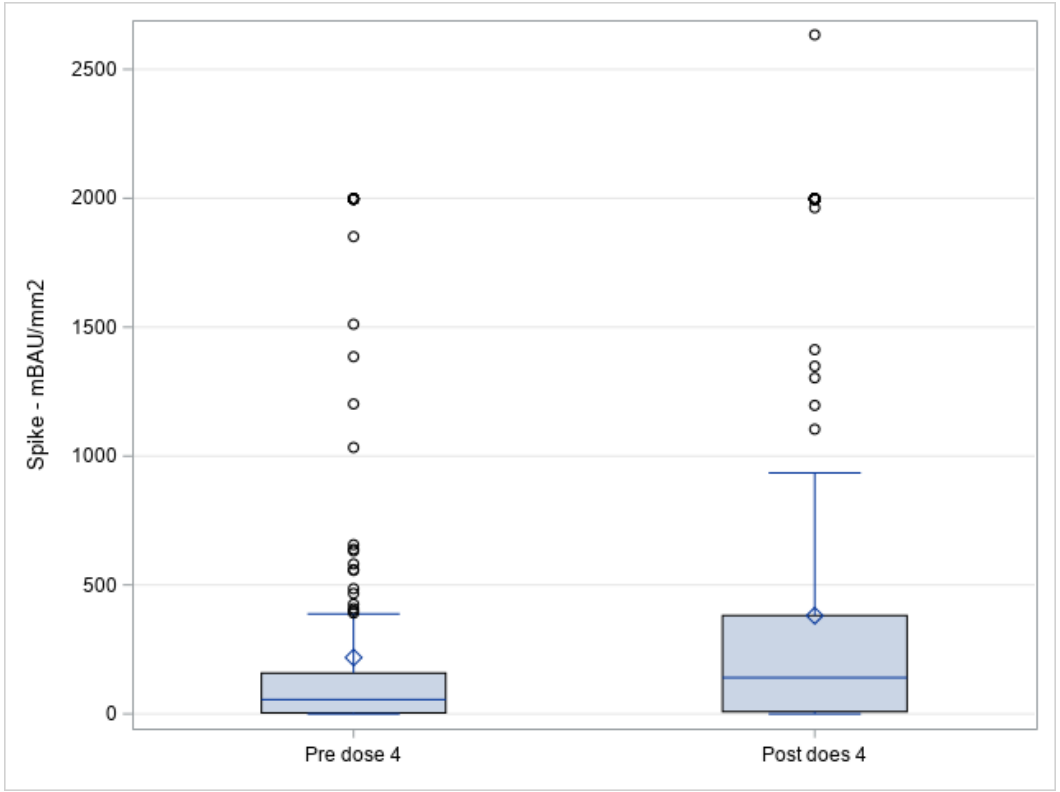


- 162 (68%) had a positive* result pre-dose 4 (median of 44 [18-73] days pre-dose)
- 178 (74%) had a positive* result post-dose 4 (median of 24 [22-27] days post-dose)

*Threshold for positive
S $\geq$ ~6.9 mBAU/mm^2

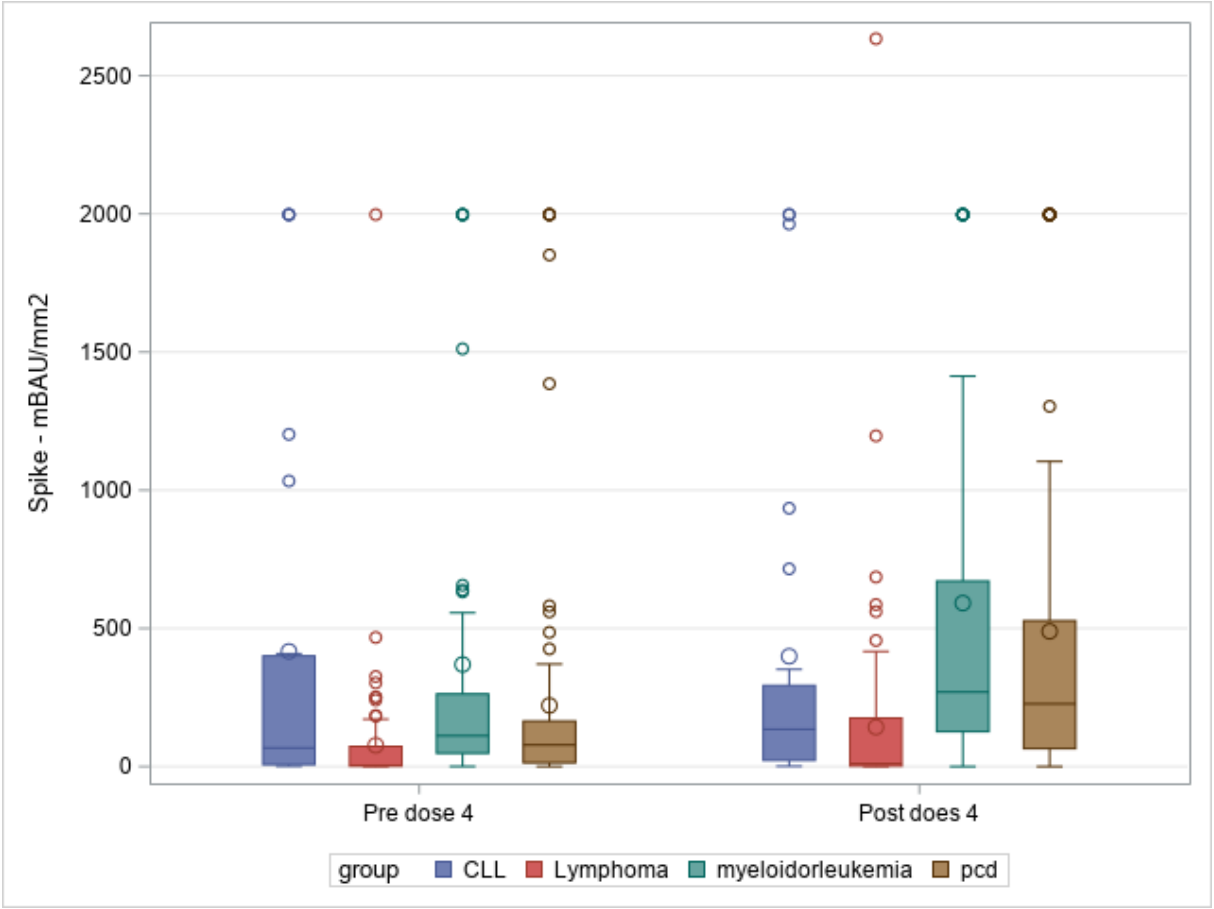
Preliminary Results: anti-S

Among the 240 participants with paired samples:



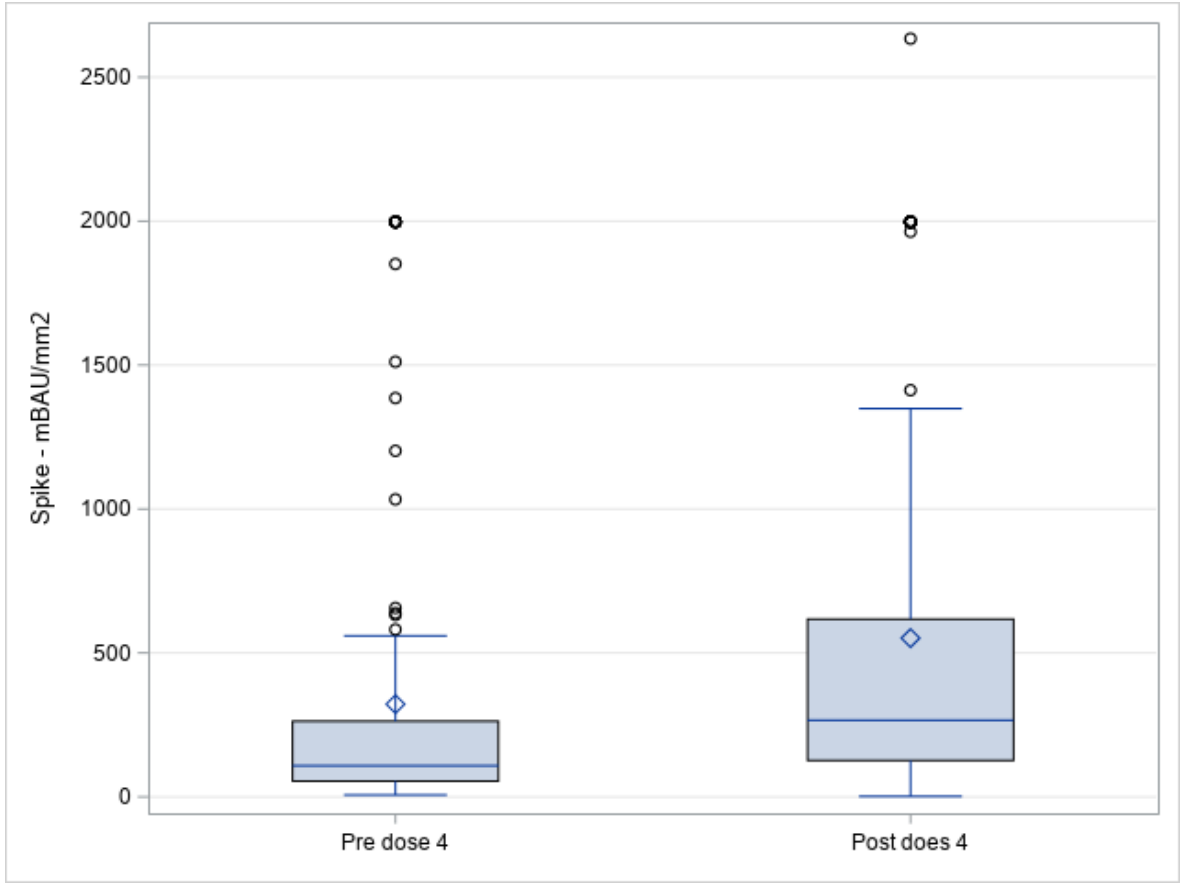
	Median anti-S [IQR]
Pre dose 4	55 [4-158] mBAU/mm^2
Post dose 4	140 [8-380] mBAU/mm^2

Preliminary Results: anti-S



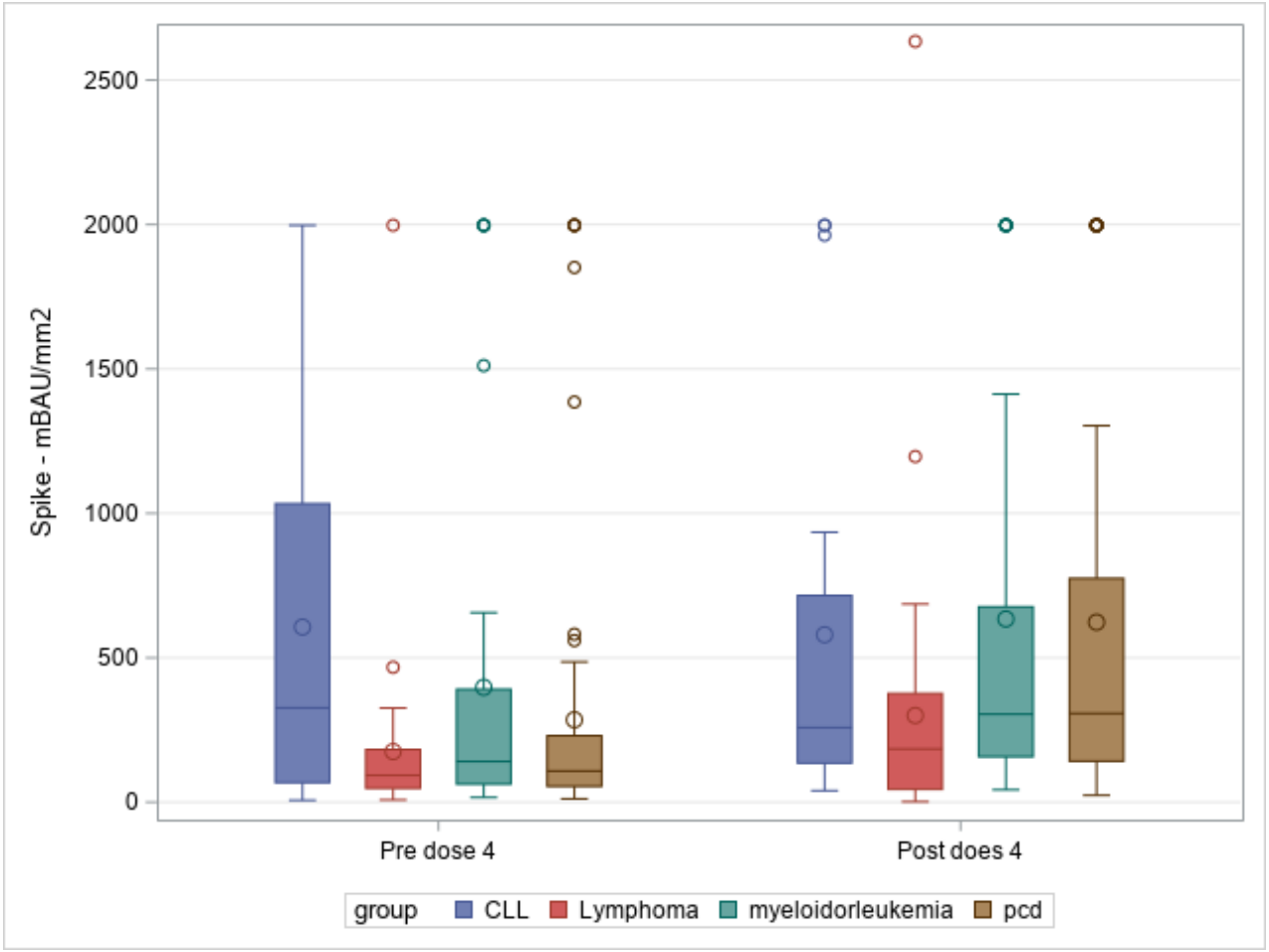
Preliminary Results: anti-S

Among the 162 participants with a positive anti-S result:



	Median anti-S [IQR]
Pre dose 4	108 [55-262] mBAU/mm^2
Post dose 4	251 [113-533] mBAU/mm^2

Preliminary Results: anti-S

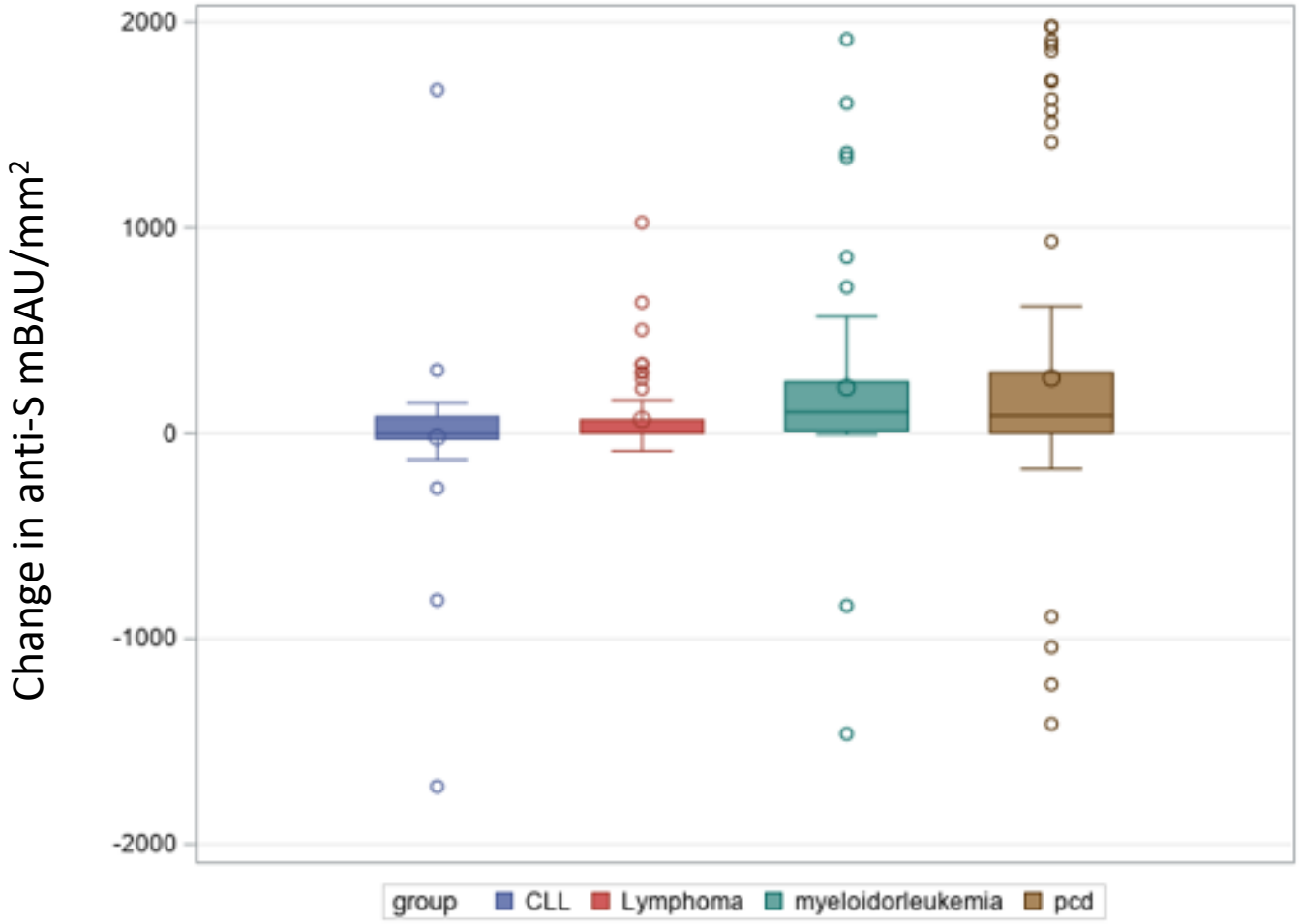


Preliminary Results: anti-S

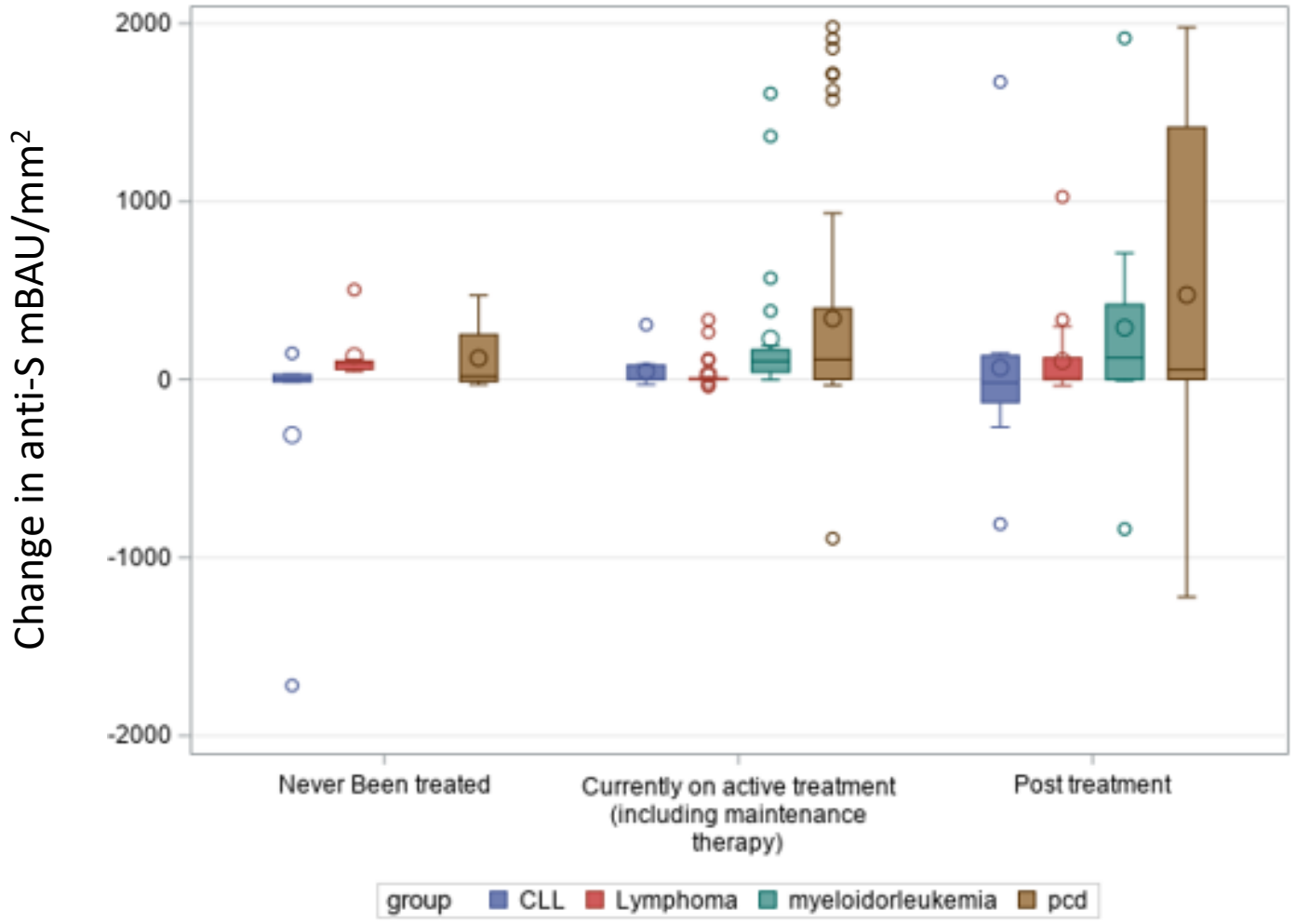
- Of 78 participants with negative result pre-dose 4
  - 20 (26%) had a positive* result post-dose 4

*Threshold for positive
S $\geq$ ~6.9 mBAU/mm^2

Change in anti-S pre- & post-dose 4

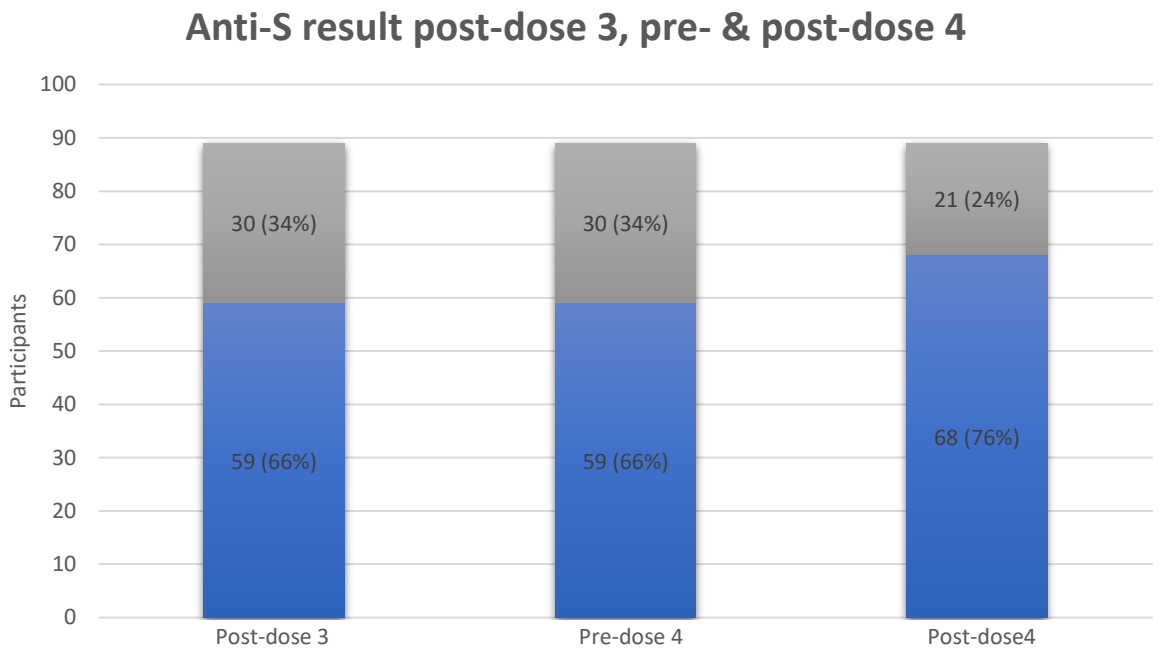


Change in anti-S pre- & post-dose 4: by treatment status



Preliminary Results: anti-S

Of the 89 participants with post-3rd and 4th data available:

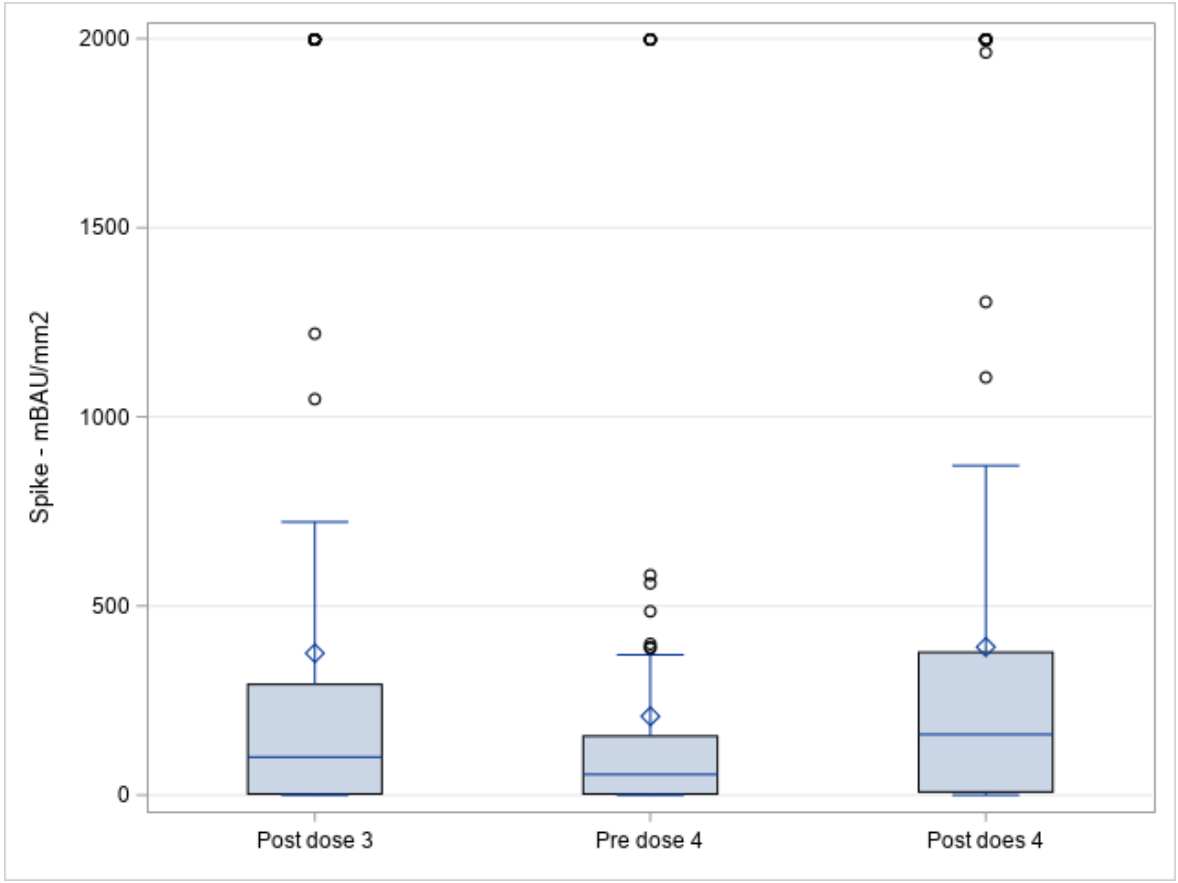


- 59 (66%) had positive* result post-dose 3 (median of 24 [19-30] days post-dose)
- 59 (66%) had positive* result pre-dose 4 (median of 44 [18-73] days pre-dose)
- 68 (76%) had positive* result post-dose 4 (median of 24 [22-27] days post-dose)

*Threshold for positive
S ≥ ~6.9 mBAU/mm^2

Preliminary Results: anti-S

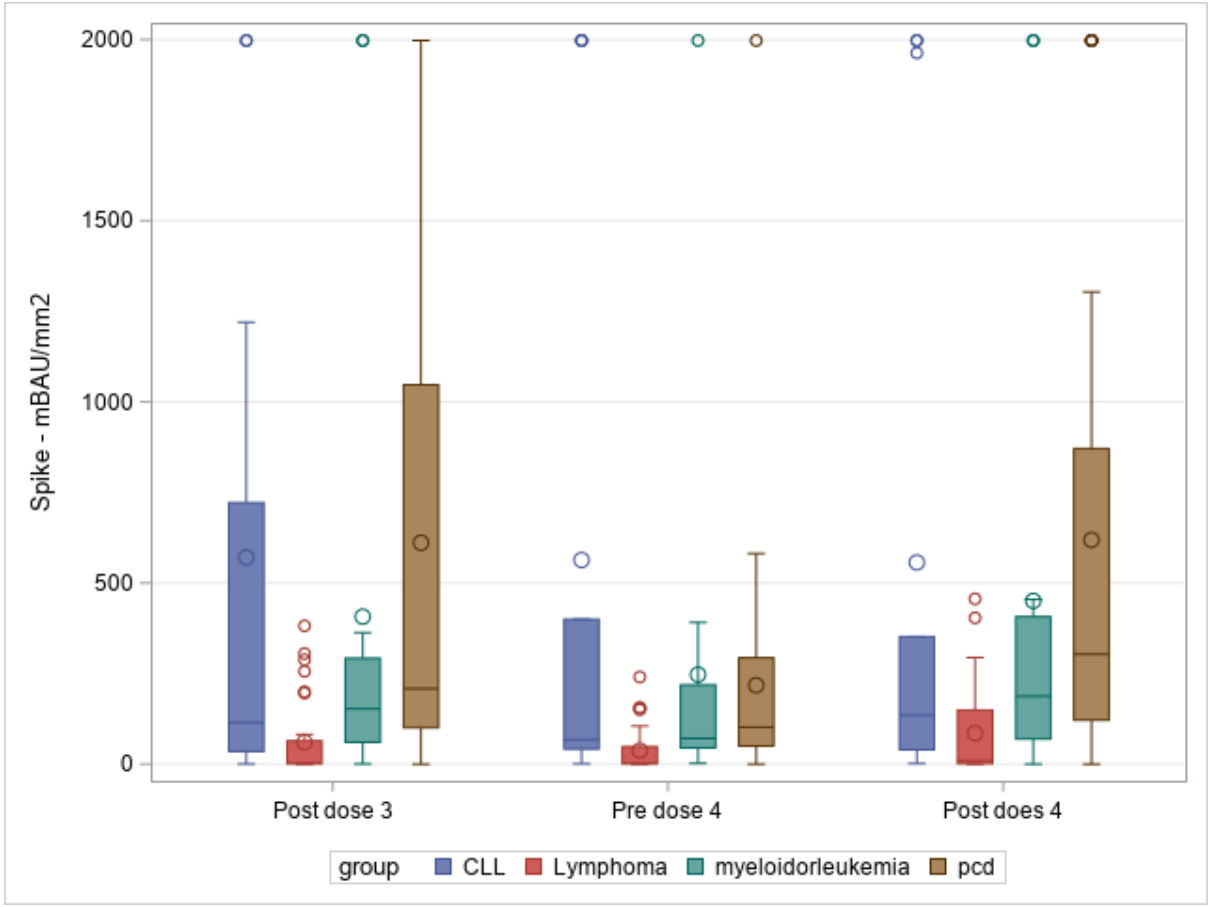
Among the 89 participants with a positive anti-S result:



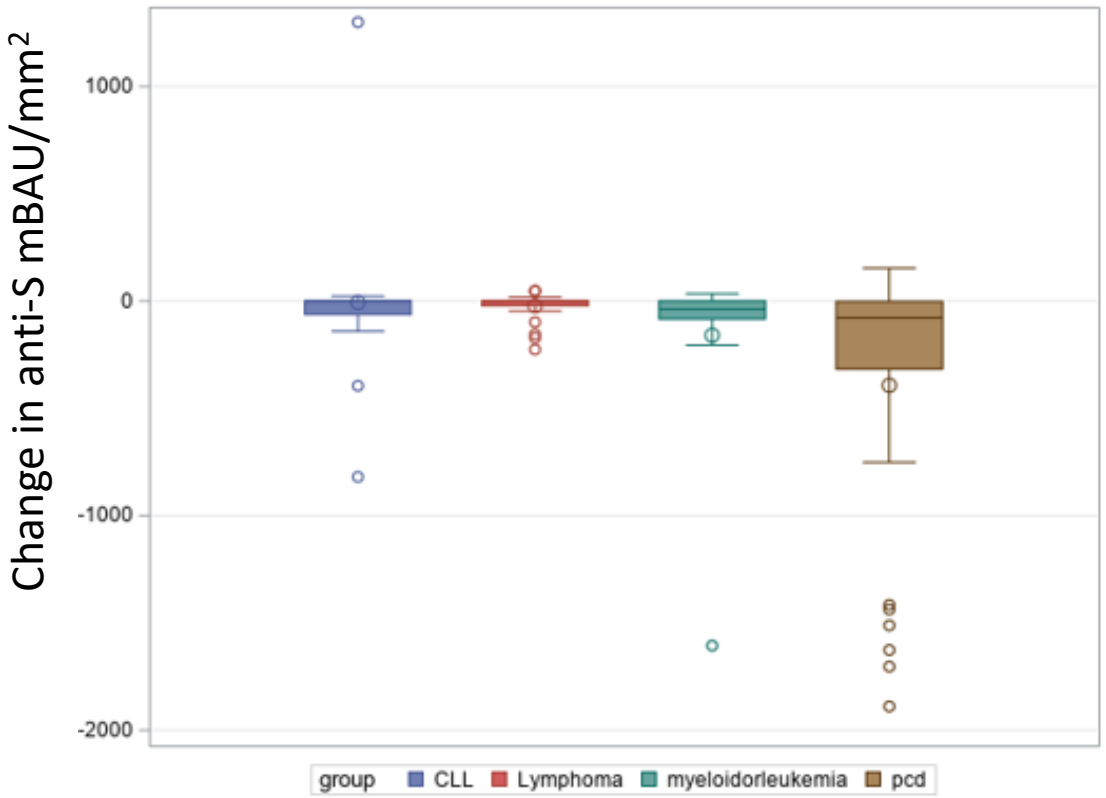
	Median Anti-S [IQR]
Post dose 3	114 [4-299] mBAU/mm^2
Pre dose 4	54 [3-156] mBAU/mm^2
Post dose 4	160 [8-377] mBAU/mm^2

Preliminary Results: anti-S

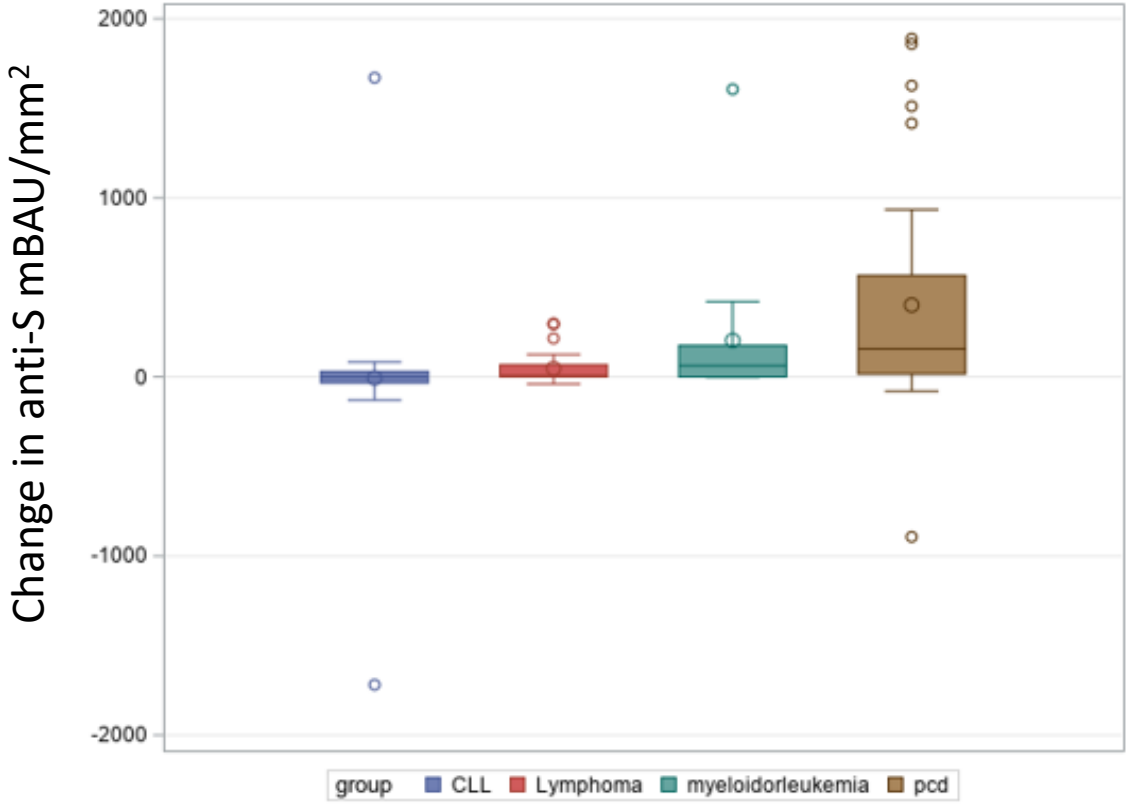
Among the 89 participants with a positive anti-S result:



Change in anti-S post-dose 3, pre- & post-dose 4



Change from post-dose 3 to pre-dose 4



Change from pre-dose 4 to post-dose 4

Preliminary Results: Anti-CD20 Exposure

- Anti-CD20 Exposure (linear regression results)
  - Anti-S antibody level post-dose 4 will be 94% less for those participants with a history of anti-CD20 exposure than those with no exposure, while controlling disease group, treatment status, history of allo/auto transplant and anti-N antibody value

- Anti-CD20 Exposure (logistic regression results)
  - The odds for participants with a history of anti-CD20 exposure of having a positive anti-S antibody level post dose-4 were 0.081 (95% CI 0.023-0.278) compared to those were not exposed to anti-CD20 while controlling for disease group and anti-N antibody

Preliminary Conclusions

- Humoral immune response (measured by anti-S levels) improved after fourth dose
  - 26% of participants with a negative anti-S level developed positive result post-dose 4
- Humoral immune response (measured by anti-S levels) decreased between post-3rd and pre-4th dose levels and increased again post-4th
- Participants exposed to anti-CD20 agent had lower odds of having positive anti-S antibody level post dose-4

Challenges & Limitations

- Lack of clear immune correlate of protection and clinical meaning of waning antibodies post-dose.
  - Further analysis on clinical outcomes, mainly incidence of infection, may provide more information
- Adaptation to changing vaccine recommendations & schedules
  - Multiple protocol amendments to ensure data capture on additional doses
  - Variability in timing of vaccine makes interpreting waning immunity challenging
- Delay in sample processing and lab results
  - Repeat analyses & analyses by disease group planned when more data available

Next Steps

- Currently addressing missing data and linking clinical/outcome data to lab data
- With further lab results, we will have more robust data set with which to repeat analyses per individual patient group

- Further & more detailed analyses planned include:
  - Neutralizing antibodies
  - T-cell immunity
  - 5^{th} and subsequent doses
  - Vaccine products (mRNA type, dose, bivalent)
  - Monoclonal antibodies (ie. Evusheld®)
  - Hybrid immunity

Thank you

CITF for support of this project

Lab Partners: Langlois & Crawley Labs

Co-Investigators across hub & partner sites

Research Coordinators & Assistants across the sites

VIP Participants

COVID-19 IMMUNITY TASK FORCE
GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

Public Health Agency of Canada

The Ottawa Hospital Research Institute | L'Hôpital d'Ottawa Institut de recherche

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab Michener Institute

UNIVERSITY OF ALBERTA

McGill University Health Centre

COVID-19 IMMUNITY TASK FORCE

Public Health Agency of Canada

The VIP study

COVID-19 Vaccine Immunogenicity in Patients with Hematologic Malignancies: A Prospective Real World Observational Multi-Site Canadian Study

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