The Vaccine Immunogenicity and Safety in ImmunoDeficient patients (VISID) study: Immunological responses of patients with primary and secondary immunodeficiencies to SARS-CoV-2 BNT162b2 and mRNA-1273 vaccines, and breakthrough infections in Canada.

Unninayar D[1], Chapdelaine H[2], Falcone E[2], Vinh D[3], Top K[4], Derfalvi B[4], Decaluwe H[5] , Pham-Huy A[6], Upton J[7] , Betschel S[8], Rubin T[9] , Suresh S[10], Wright N[11], Sadarangani M[12], Palma A[13], Lacuesta G[4], Murguia-Favela L[11] , Oldford S[4], Langlois M[14], Barrett L[4] , Cowan J[15]

[1]The Ottawa Hospital, Medicine, ON, [2]Montreal Clinical Research Institute, QC, [3]McGill University Health Centre, QC, [4]Dalhousie University, Medicine, NS, [5]CHU Ste Justine, Centre de Recherche, QC, [6]Children's Hospital of Eastern Ontario, ON, [7]The Hospital for Sick Children, University of Toronto, Department of Pediatrics, ON, [8]Unity Health Toronto, Clinical Immunology and Allergy, ON, [9]University of Manitoba, Medicine, MB, [10]University of Alberta, Medicine, AB, [11]Alberta Children's Hospital, AB, [12] BC Children's Hospital, BC, [13]IWK Health Centre/Dalhousie University,Pediatrics; Division of Immunology, NS, [14]University of Ottawa, Faculty of Medicine, ON, [15]Ottawa Hospital Research Institute, Infectious Diseases, ON, Canada

Introduction

Adults and children with inborn or acquired immunodeficiency (ID) are at increased risk of severe SARS-CoV-2 infection. SARS-CoV2 BNT162b2 and mRNA-1273 mRNA vaccines are the most effective vaccines in inducing immunity against SARS-CoV2 in healthy participants. People with immunodeficiency were excluded from trials that informed Health Canada's approval of the mRNA COVID-19 vaccines, and therefore **data on vaccine safety and effectiveness in this population is limited.**

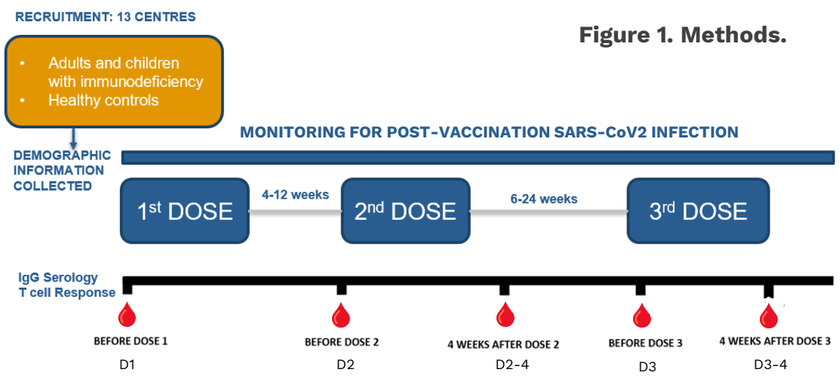
Objectives

- Determine SARS-CoV2 specific humoral and cellular immune responses to COVID-19 vaccination in people with immunodeficiency compared to healthy controls.
- Measure the frequency of post-vaccine SARS-CoV2 infection.

Methods

The VISID study is a nationwide multicentre prospective study conducted to assess vaccine immunogenicity and breakthrough infections in ID. Blood was collected from participants pre-vaccination and 4 weeks post-vaccination. Humoral response was measured by anti-S IgG titers using ELISA as well as neutralization titers at 50% inhibitory dilution (ID50) against the original and Omicron strains. T-cell responses were measured by IFN-γ-ELISpot. Post-vaccination COVID-19 infections were captured

Figure 1. Methods.



Results

172 adults (133 primary ID, 4 secondary ID, 35 controls) and 106 children (80 primary ID, 5 secondary ID, 21 controls) were recruited.

Table 1. Anti-Spike (S) Seroconversion Rates.

	Proportion of participants with IgG seroconversion (%)					
	Pediatric			Adult		
	Anti S IgG	Anti R IgG	Anti N IgG	Anti S IgG	Anti R IgG	Anti N IgG
Healthy						
Before Dose 1	1/6 (16.67)	0/6 (0.00)	2/6 (33.33)	1/8 (12.50)	0/8 (0.00)	0/8 (0.00)
Before Dose 2	4/4 (100.00)	2/4 (50.00)	0/4 (0.00)	8/8 (100.00)	7/8 (87.50)	0/8 (0.00)
4 weeks after Dose 2	1/1 (100.00)	1/1 (100.00)	0/1 (0.00)	7/7 (100.00)	7/7 (100.00)	0/7 (0.00)
24 weeks after Dose 2	1/1 (100.00)	1/1 (100.00)	1/1 (100.00)	4/4 (100.00)	3/4 (75.00)	2/4 (50.00)
Before Dose 3	2/2 (100.00)	2/2 (100.00)	1/2 (50.00)	6/6 (100.00)	6/6 (100.00)	2/6 (33.33)
4 weeks after Dose 3	1/1 (100.00)	1/1 (100.00)	0/1 (0.00)	-	-	-
Immunodeficient						
Before Dose 1	8/26 (30.77)	4/26 (15.38)	6/26 (23.08)	3/12 (25.00)	2/12 (16.67)	2/12 (16.67)
Before Dose 2	23/28 (82.14)	15/28 (31.25)	9/28 (32.14)	9/13 (69.23)	8/13 (61.54)	0/13 (0.00)
4 weeks after Dose 2	1/1 (100.00)	1/1 (100.00)	0/1 (0.00)	19/24 (79.17)	16/24 (66.67)	1/24 (4.17)
24 weeks after Dose 2	4/4 (100.00)	4/4 (100.00)	2/4 (50.00)	7/7 (100.00)	7/7 (100.00)	1/7 (14.29)
48 weeks after Dose 2	-	-	-	2/2 (100.00)	2/2 (100.00)	1/2 (50.00)
Before Dose 3	23/25 (92.00)	21/25 (84.00)	8/25 (32.00)	38/46 (82.61)	37/46 (80.43)	7/46 (15.22)
4 weeks after Dose 3	3/3 (100.00)	3/3 (100.00)	1/3 (33.33)	62/67 (92.54)	59/67 (88.06)	11/67 (16.42)

Figure 2. Humoral and T-cell responses post-vaccination.

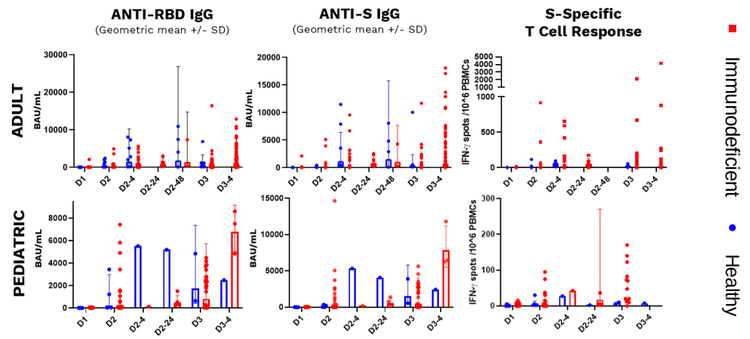
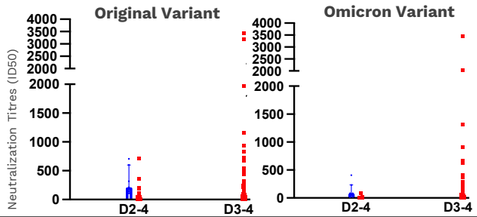


Figure 3. Neutralization antibody response in adult participants.



Among adult participants, the neutralization (ID50) titres were higher in healthy controls after dose 2 compared to ID for both the original strain (p=0.003) and omicron variant (p=0.0004).

Figure 4. Humoral and cellular immune responses in adults with immunodeficiency after Dose 3 by interval between Dose 2 and 3.

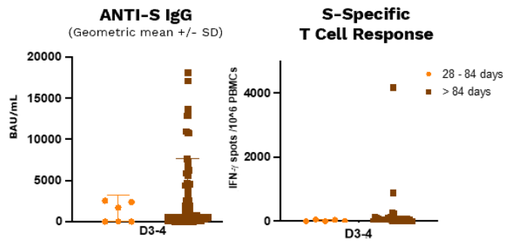


Figure 5. Rates of post-vaccination SARS-CoV2 infection*.

	Adult		Pediatric	
	Healthy	Immunodeficient	Healthy	Immunodeficient
Timing of SARS-CoV2 Infection				
Before Dose 1	12	2	4	3
After Dose 1	0	1	0	6
After Dose 2	7	13	2	31
After Dose 3	7	37	4	25
After Dose 4	1	25	0	1
Total Post-Dose Infections (%)	15/35 (42.86)	76/135 (56.3)	6/21 (28.57)	63/85 (74.11)

*Two adult and one pediatric ID participants were hospitalized.

Conclusions

- Adult ID participants mount serological and T-cell responses post-dose 3 comparable to healthy controls post-dose 2.
- Pediatric ID participants may have a higher humoral immune response than adults.
- >84 days between dose 2 and 3 vaccination may result in a higher serological and cellular responses to vaccination in adults with ID.

References

1. Covid-19 Daily Epidemiology update. Canada.ca. https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html. Published May 28, 2021. Accessed April 20, 2022.

2. Fung M, Babik JM. COVID-19 in immunocompromised hosts: what we know so far. *Clin Infect Dis* 2021; 72:340–50.

3. Shields AM, Burns SO, Savic S, Richter AG; UK PIN COVID-19 Consortium. COVID-19 in patients with primary and secondary immunodeficiency: The United Kingdom experience. J Allergy Clin Immunol. 2021 Mar;147(3):870-875.e1. doi: 10.1016/j.jaci.2020.12.620. Epub 2020 Dec 15. PMID: 33338534; PMCID: PMC7737531.

THE VISID COVID-19 VACCINE IMMUNOGENICITY & SAFETY IN IMMUNODEFICIENT PATIENTS STUDY

OTTAWA METHODS CENTRE

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