Indian J Hematol Blood Transfus (Oct-Dec 2022) 38(4):745–749
https://doi.org/10.1007/s12288-022-01528-y

SHORT COMMUNICATION

Short Research Communication Anti-Spike Antibody Response to COVISHIELD™ (SII-ChAdOx1 nCoV-19) Vaccine in Patients with B-Cell and Plasma Cell Malignancies and Hematopoietic Cell Transplantation Recipients

Madhu Chopra[1] · Arihant Jain[1] · Sanjeev Chhabra[2] · Shaweta Kaundal[1] · Charanpreet Singh[1] · Aditya Jandial[1] · Gaurav Prakash[1] · Alka Khadwal[1] · Chandan Das[1] · Mini P Singh[3] · Reena Das[2] · Pankaj Malhotra[1] · Deepesh P. Lad[1]

Received: 14 November 2021 / Accepted: 15 February 2022 / Published online: 3 March 2022

Abstract

Introduction There is limited data on the serologic antibody responses after the ChAdOx1 vaccine in patients with hematological malignancies and hematopoietic cell transplantation recipients. There is no data on the safety and efficacy of the Indian COVISHIELD™ vaccine in this population.

Methods This study reports the anti-S antibody response to the COVISHIELD™ vaccine in a prospective cohort of patients with B-cell and plasma cell malignancies and HCT recipients at a single center. The quantitative antibodies to the SARS-CoV-2 S protein receptor-binding domain in human plasma were determined by the validated Roche Elecsys Anti-SARS-CoV-2 S kit.

Results A total of 118 patients were included over the study period from April 2021 to August 2021. The seropositivity rate at baseline and after the first and second dose of the vaccine was 39%, 66%, and 79%, respectively ($p < 0.0001$). The seronegative cohort had a higher median age (65 vs. 60 years, $p = 0.03$), were more likely to be males (81% vs. 42%, $p = 0.009$), had a diagnosis of B-CLPD (100% vs. 42%, $p < 0.001$) and were more likely to be on ibrutinib therapy (56% vs. 15%, $p = 0.001$).

Conclusions This study confirms the safety and efficacy of the COVISHIELD™ vaccine in patients with hematological malignancies.

Keywords Ant-S antibody · COVISHIELD · B-CLPD · Myeloma · HCT

Introduction

The Oxford-AstraZeneca (ChAdOx1) nCoV- 19 Corona Virus vaccine is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Spike (S) glycoprotein, produced in genetically modified human embryonic kidney (HEK) 293 cells. It is manufactured in India by the Serum Institute and is available as COVISHIELD™. It was rolled out in India for people > 45 years of age and comorbidities from March 2021 and for > 18 years from May 2021. Despite no data on the safety or efficacy of a replication-deficient viral vector vaccine in immunocompromised patients, the vaccine was approved in this population wherever it was the only option considering the possible benefits over the risks of COVID-19. Most countries in the developed world resorted to mRNA vaccines

✉ Deepesh P. Lad
lad.deepesh@pgimer.edu.in

[1] Department of Clinical Hematology and Medical Oncology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

[2] Department of Hematology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

[3] Department of Virology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

in this population. The studies have uniformly shown that about ~ 50–80% of patients with hematological malignancies mount an immune response and have lower anti-S IgG titers [1–6]. The serologic antibody responses after the ChAdOx1 vaccine have also shown similar responses to the mRNA vaccines [7–10]. All studies have identified CLL, lymphoma, and myeloma patients receiving anti-B-cell therapies (BTK inhibitors, venetoclax, anti-CD20/CD38 antibodies) and HCT recipients to be associated with lesser immune responses.

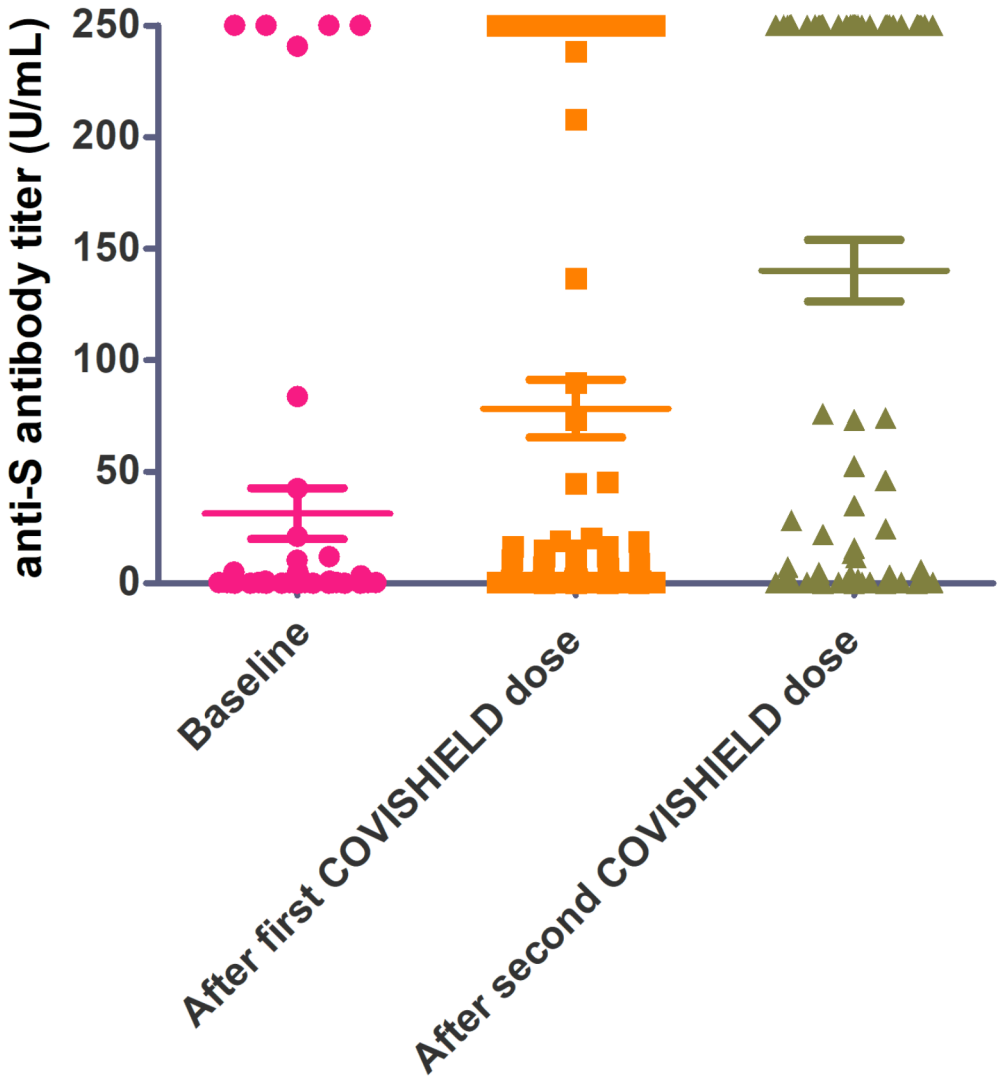

Fig. 1 Anti-S antibody titers at baseline and one month after first and second COVISHIELD dose in patients with B-cell and plasma cell malignancies and HCT recipients (Titers > 250 U/mL were capped at 250 for representation purposes as it is the upper limit of detection of the assay)

Methods

This study reports the anti-S antibody response to the COVISHIELD™ vaccine in a prospective cohort of patients with hematological malignancies at a single center. The institute ethics committee approved the study. Data on demographic variables (age, sex, cancer diagnosis), treatments, prior COVID-19, vaccine type and administration dates, and side effects of vaccination were collected. A total of 118 patients were included over the study period from April 2021 to August 2021 after informed consent. There were 63 patients with chronic lymphoproliferative disorders (chronic lymphocytic leukemia CLL, n = 48), plasma cell dyscrasia (n = 40), and post-hematopoietic cell transplantation (HCT, n = 15). As an institute policy we were advising COVID vaccination starting at 3 months post-HCT, preferably 6 months after rituximab-based therapy for B-CLPDs and anytime for plasma cell dyscrasias. Blood samples were collected at baseline and one month after the first and second doses of the vaccine. The antibodies to the SARS-CoV-2 S protein receptor-binding domain (RBD) in human plasma were determined by the Roche Elecsys Anti-SARS-CoV-2 S kit, as per the manufacturer's instructions. This immunoassay is validated for the in vitro quantitative determination of antibodies within the range of 0.40-250 U/mL. Analyte concentrations of < 0.80 U/mL were considered negative, while ≥ 0.80 U/mL were considered positive. The sensitivity and specificity of this assay are 98.8% and 99.9%, respectively. The positive agreement rate with the pseudo-neutralization assay is 92.3%.

Results

A total of 46 patient samples were available at baseline before any dose of the vaccine was administered. Out of these, 18 (39%) were already seropositive for anti-S. While five patients had titers > 250 U/ml at baseline, the titer of another seven patients increased to > 250 U/ml following subsequent vaccine doses. Only one patient had reported an unconfirmed COVID-like illness in this cohort. Of the 28 seronegative patients at baseline, 15 (54%) seroconverted after the first/ second vaccine dose. There were no differences in the diagnosis and treatments received by the seropositive or seronegative patients at baseline. Post the first vaccine, a total of 71 patient samples were available. The seropositivity rate in this cohort was 66%. Only three patients had reported prior confirmed COVID-19 in this cohort. Again, there were no differences in the diagnosis and treatments between the seropositive and negative cohorts. Post the second vaccine, a total of 76 patient samples were available for analysis. The seropositivity rate after the second vaccine dose was 79%. 68% of these had anti-S antibodies > 250 U/ml. The median anti-S antibody titers at baseline and after the first and second COVISHIELD doses were 0.4 (IQR 0.4-5), 11 (IQR 0.4–250), 250 (IQR 3.5–250), respectively ($p < 0.0001$) (Fig. 1). The seronegative cohort of 16 patients had a higher median age (65 vs. 60 years, $p = 0.03$), were more likely to be males (81% vs. 42%, $p = 0.009$), had a diagnosis of B-CLPD (100% vs. 42%, $p < 0.001$), more specifically CLL (88% vs. 32%, $p < 0.0001$) and were more likely to be on ibrutinib therapy (56% vs. 15%, $p = 0.001$). Patients with plasma cell dyscrasias on bortezomib or immunomodulatory therapy were all seropositive after the second vaccine. Only two patients in the seronegative and seropositive cohort reported having confirmed COVID-19 within a month after the second vaccination (Table I). The test was positive (90% had titers > 100 U/mL) in all ten health care workers who served as healthy controls and had received both doses of the vaccine 1–5 months before. The vaccine was well tolerated in the immunocompromised population. There were no serious adverse events reported in this study. The reporting of minor adverse events was not rigorous and hence nor reported in the study.

Discussion

This study highlights the high seroprevalence (~ 40%) even in the immunocompromised patients, in contrast to > 80% seroprevalence in the general population in recent regional serosurveys [11]. The seropositivity rate increased to ~ 80% after the second dose. Only CLPD patients on anti-B-cell therapies failed to mount an immune response despite the second dose of the vaccine. This is in concordance with previous studies [5–7]. The U.S. Food and Drug Administration (FDA) amended the emergency use authorization for the mRNA vaccines to allow a booster dose for immunocompromised patients based on higher immunogenicity [12]. A similar booster study showed seroconversion in 55% of the patients with B-cell malignancies [13]. Though similar data is not available for the ChAdOx1 vaccines, it is likely to be the same given similar overall responses with the two vaccines in the immunocompromised patients. The major limitation of this study is the lack of serial antibody levels in all patients and that the T-cell repertoire was not studied. However, patients with CLL have impaired T-cell function, the primary group of patients who did not mount a B-cell response to the vaccines [14]. This study aims to highlight the safety and efficacy of the COVISHIELD™ vaccine in patients with hematological malignancies. At the same time, we caution specific groups of patients that their protection against COVID-19 may still be suboptimal. It is essential to continue COVID-appropriate behavior and get

Table 1 PAnti-S antibody response to COVISHIELD™ vaccine as per patient, disease, and treatment characteristics

Characteristic	Baseline (pre-vaccination) N = 46		*p*	Post 1st vaccine dose N = 71		*p*	Post 2nd vaccine dose N = 75		*p*
	Seronegative	Seropositive		Seronegative	Seropositive		Seronegative	Seropositive	
N (%)	28 (61%)	18 (39%)		24 (34%)	47 (66%)		16 (21%)	59 (79%)	
Age	61 (53–68)	56 (50–69)	NS	61 (58–67)	60 (49–65)	NS	65 (61–71)	60 (53–66)	0.03
Female	6 (21%)	3 (17%)	NS	7 (29%)	16 (34%)	NS	3 (19%)	34 (58%)	0.009
Male	22 (79%)	15 (83%)		17 (71%)	31 (66%)		13 (81%)	25 (42%)	
Diagnosis	6 (21%)	3 (17%)	NS	4 (17%)	8 (17%)	NS	0	8 (14%)	NS
Post-HCT	16 (58%)	8 (44%)	NS	16 (66%)	20 (43%)	NS	16 (100%)	25 (42%)	<0.0001
B-CLPD	6 (21%)	7 (39%)	NS	4 (17%)	19 (40%)	NS	0	26 (44%)	0.002
Plasma cell dyscrasia									
Prior COVID	0	1 (6%)	NS	0	3 (6%)	NS	0	3 (5%)	NS
Current Rx	11 (39%)	7 (39%)	NS	11 (46%)	16 (34%)	NS	5 (31%)	21 (36%)	NS
Observation	7 (25%)	2 (11%)	NS	3 (12%)	5 (11%)	NS	9 (56%)	9 (15%)	0.001
Ibrutinib	2 (7%)	1 (6%)	NS	3 (12%)	4 (8%)	NS	1 (6%)	1 (2%)	NS
Rituximab +	7 (25%)	6 (33%)	NS	6 (25%)	17 (36%)	NS	0 (0%)	26 (44%)	0.007
Borte/IMid/dex	1 (4%)	2 (11%)	NS	1 (4%)	5 (11%)	NS	1 (6%)	2 (3%)	NS
Other IST									
Post-vaccination COVID	-	-	-	1 (4%)	0	NS	1 (6%)	1 (2%)	NS

NS: not significant, B-CLPD: B-cell chronic lymphoproliferative disorders, HCT: hematopoietic cell transplantation, Rituximab +: RCVP/RHOP/BR/R-chlorambucil, Borte/IMid/dex: bortezomib/ immunomodulator/ dexamethasone, IST: immunosuppressive therapy

the immediate family contacts vaccinated, as these patients' mortality rates remain high [15]. These patients may need additional booster doses pending approval by the government regulatory agencies.

Author Contributions AJ, PM, MPS, RD, and DPL conceived and planned the study. MC and SC analysed the lab data. AJ, PM ad DPL wrote the manuscript. All authors were involved in patient recruitment, reviewing and approving the final manuscript.

Funding none.

Declarations

Competing Interest The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval The study was cleared by the intuitional ethics committee.

Informed Consent Informed consent was obtained from all participants included in the study.

References

1. Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL (2021) Antibody response to SARS-CoV-2 vaccines in patients with hematologic malignancies. Cancer Cell 39(8):1031–1033
2. Chung DJ, Shah GL, Devlin SM, Ramanathan LV, Doddi S, Pessin MS et al (2021) Disease- and Therapy-Specific Impact on Humoral Immune Responses to COVID-19 Vaccination in Hematologic Malignancies. Blood Cancer Discov 2(6):568–576
3. Malard F, Gaugler B, Gozlan J, Bouquet L, Fofana D, Siblany L et al (2021) Weak immunogenicity of SARS-CoV-2 vaccine in patients with hematologic malignancies. Blood Cancer J 11(8):142
4. Dhakal B, Abedin S, Fenske T, Chhabra S, Ledeboer N, Hari P et al (2021) Response to SARS-CoV-2 vaccination in patients after hematopoietic cell transplantation and CAR T-cell therapy. Blood 138(14):1278–1281
5. Griffiths EA, Segal BH (2021) Immune responses to COVID-19 vaccines in patients with cancer: Promising results and a note of caution. Cancer Cell 39(8):1045–1047
6. Ghione P, Gu JJ, Attwood K, Torka P, Goel S, Sundaram S et al (2021) Impaired humoral responses to COVID-19 vaccination in patients with lymphoma receiving B-cell-directed therapies. Blood 138(9):811–814
7. Parry H, McIlroy G, Bruton R, Ali M, Stephens C, Damery S et al (2021) Antibody responses after first and second Covid-19 vaccination in patients with chronic lymphocytic leukaemia. Blood Cancer J 11(7):136
8. Lim SH, Campbell N, Johnson M, Joseph-Pietras D, Collins GP, O'Callaghan A et al (2021) Antibody Responses after SARS-CoV-2 Vaccination in Lymphoma. medRxiv. :2021.06.05.21258311
9. Terpos E, Gavriatopoulou M, Ntanasis-Stathopoulos I, Briasoulis A, Gumeni S, Malandrakis P et al (2021) The neutralizing antibody response post COVID-19 vaccination in patients with myeloma is highly dependent on the type of anti-myeloma treatment. Blood Cancer J 11(8):138
10. Easdale S, Shea R, Ellis L, Bazin J, Davis K, Dallas F et al (2021) Serologic Responses following a Single Dose of SARS-Cov-2 Vaccination in Allogeneic Stem Cell Transplantation Recipients. Transpl Cell Ther 27(10):880 e1- e4
11. Murhekar MV, Bhatnagar T, Thangaraj JWV, Saravanakumar V, Santhosh Kumar M, Selvaraju S et al (2021) Seroprevalence of IgG antibodies against SARS-CoV-2 among the general population and healthcare workers in India, June-July 2021: A population-based cross-sectional study. PLoS Med 18(12):e1003877
12. Hall VG, Ferreira VH, Ku T, Ierullo M, Majchrzak-Kita B, Chaparro C et al (2021) Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. N Eng J Med 385(13):1244–1246
13. Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL (2021) Anti-spike antibody response to SARS-CoV-2 booster vaccination in patients with B cell-derived hematologic malignancies. Cancer Cell 39(10):1297–1299
14. Lad D, Hoeppli R, Huang Q, Garcia R, Xu L, Toze C et al (2018) Regulatory T-cells drive immune dysfunction in CLL. Leuk Lymphoma 59(2):486–489
15. Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B et al (2020) Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood 136(25):2881–2892