

Original Article



# Comparison of Antibody and T Cell Responses Induced by Single Doses of ChAdOx1 nCoV-19 and BNT162b2 Vaccines

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## ABSTRACT

There are limited data directly comparing humoral and T cell responses to the ChAdOx1 nCoV-19 and BNT162b2 vaccines. We compared Ab and T cell responses after first doses of ChAdOx1 nCoV-19 vs. BNT162b2 vaccines. We enrolled healthcare workers who received ChAdOx1 nCoV-19 or BNT162b2 vaccine in Seoul, Korea. Anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) S1 protein-specific IgG Abs (S1-IgG), neutralizing Abs (NT Abs), and SARS-CoV-2-specific T cell response were evaluated before vaccination and at 1-wk intervals for 3 wks after vaccination. A total of 76 persons, comprising 40 injected with the ChAdOx1 vaccine and 36 injected with the BNT162b2 vaccine, participated in this study. At 3 wks after vaccination, the mean levels ( $\pm$ SD) of S1-IgG and NT Abs in the BNT162b2 participants were significantly higher than in the ChAdOx1 participants (S1-IgG,  $14.03 \pm 7.20$  vs.  $6.28 \pm 8.87$ ,  $p < 0.0001$ ; NT Ab,  $183.1 \pm 155.6$  vs.  $116.6 \pm 116.2$ ,  $p = 0.035$ ), respectively. However, the mean values of the T cell responses in the 2 groups were comparable after 2 wks. The humoral immune response after the 1st dose of BNT162b2 developed faster and was stronger than after the 1st dose of ChAdOx1. However, the T cell responses to BNT162b2 and ChAdOx1 were similar.

**Keywords:** Immunogenicity; Antibody response; T cell response; ChAdOx1 nCoV-19 vaccine; BNT162b2 vaccine

## INTRODUCTION

The worldwide coronavirus disease 2019 (COVID-19) pandemic persists in 2021, and vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to end the pandemic have been rapidly developed. The ChAdOx1 nCoV-19 vaccine (Oxford-AstraZeneca [AZ]; Cambridge, UK) consists of the replication-deficient adenovirus vector ChAdOx1 encoding the full-length spike protein (structural surface glycoprotein) of SARS-CoV-2 (1). The BNT162b2 vaccine is an mRNA-based vaccine that is a cof formulation of a lipid nanoparticle

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## Conflict of Interest

The authors declare no potential conflicts of interest.

## Abbreviations

AZ, Oxford-AstraZeneca; CAR, coxsackie adenovirus receptor; COVID-19, coronavirus disease 2019; HCW, healthcare worker; LNP, lipid nanoparticle; NT Ab, neutralizing antibody; PF, Pfizer-BioNTech; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SFC, spot-forming cells; SMD, standardized mean difference; S1-IgG, SARS-CoV-2 S1 protein-specific IgG antibody; S1-IgM, SARS-CoV-2 S1 protein-specific IgM antibody.

## Author Contributions

Conceptualization: Kim SH; Data curation: Kim JY, Bae S, Park S, Kwon JS, Lim SY, Park JY, Cha HH, Lee N, Heo J, Shum D, Jee Y, Kim SH; Formal analysis: Kim JY, Bae S, Park S, Kwon JS, Lim SY, Park JY, Cha HH, Lee HJ, Lee N, Heo J, Shum D, Jee Y; Funding acquisition: Jee Y, Kim SH; Investigation: Kim JY, Bae S, Park S, Kwon JS, Lim SY, Park JY, Cha HH, Seo MH, Lee HJ, Jee Y, Kim SH; Methodology: Kim JY, Bae S, Park S, Kwon JS, Lim SY, Park JY, Cha HH, Lee N, Heo J, Shum D, Kim SH; Project administration: Kim JY, Bae S, Kwon JS, Seo MH, Lee HJ, Kim SH; Supervision: Jee Y, Kim SH; Validation: Kim JY, Bae S, Kwon JS, Lee HJ, Kim SH; Visualization: Kim JY, Bae S, Park S, Kwon JS, Cha HH; Writing - original draft: Kim JY, Bae S, Kwon JS, Kim SH; Writing - review & editing: Kim JY, Bae S, Park S, Kwon JS, Lim SY, Park JY, Cha HH, Seo MH, Lee HJ, Lee N, Heo J, Shum D, Jee Y, Kim SH.

(LNP) vehicle with nucleoside-modified RNA encoding the SARS-CoV-2 full-length spike (2,3). These 2 vaccines have been used world-wide against SARS-CoV-2 infection.

Previously, separate studies have reported on the immunogenicity of the ChAdOx1 nCoV-19 and BNT162b2 vaccines (1,3-7), but comparisons of the immunogenicity across studies are difficult, because the studies assessed different Abs or the same type of Abs but using different assays. Several previous review articles compared the immunogenicity of the COVID-19 vaccines using a meta-analysis methodology (8-10). McDonald et al. (8) reported that mRNA vaccines such as mRNA-1273 (Moderna; Cambridge, MA, USA) or BNT162b2 elicited the highest IgG Ab responses compared to other platforms and ChAdOx1 nCoV-19 might produce the highest T cell responses. In the comparison of COVID-19 vaccine phase 1/2 clinical trials, neutralizing Ab (NT Ab) titers of ChAdOx1 nCoV-19 and BNT162b2 were 218.0 and 361.0 (age 18–55) (9). Meanwhile, Rogliani et al. (10) compared NT Abs of the COVID-19 vaccines with standardized mean difference (SMD) analysis, and estimated that ChAdOx1 nCoV-19 produces higher NT Abs (SMD=2.11) than BNT162b2 (SMD=1.64).

At present, data directly comparing the humoral and T cell responses to the 2 vaccines are still limited. This study compared the immune responses induced by first doses of the ChAdOx1 nCoV-19 and BNT162b2 vaccines in Korean healthcare workers (HCWs).

## MATERIALS AND METHODS

### Study participants and collection of specimens

A nationwide vaccination program against COVID-19 is currently ongoing in South Korea. This study enrolled HCWs who received the ChAdOx1 nCoV-19 vaccine (AZ) or the BNT162b2 vaccine (Pfizer-BioNTech [PF]; Pfizer, New York, NY, USA and BioNTech, Mainz, Germany) at a tertiary care hospital in Seoul, South Korea, between March 5th and March 25th, 2021. In accord with the policy of the Korean government, the BNT162b2 vaccine was assigned to high-risk HCWs in direct contact with COVID-19 patients, and the ChAdOx1 vaccine was assigned to those involved in general patient care. All participants agreed to peripheral blood sampling, and blood sampling was carried out once before vaccination, for baseline serology, and once per week for 3 wks after vaccination. The study was reviewed and approved by the Institutional Review Board (IRB) of Asan Medical Center (IRB No. 2021-0170).

### Measurement of Ab responses

SARS-CoV-2 S1-specific IgG and IgM Ab titers were measured using an in-house-developed ELISA, details of which were described in a previous report (11). The data are presented as relative OD values based on a 1:100 dilution factor at 450 nm. To determine cut-off values for the ELISA, the mean and SD of the OD obtained with negative control plasma not exposed to SARS-CoV-2 were measured, and cut-off values were defined as mean OD plus 3-fold the SD value; the value was 0.4 for IgG, as reported previously (12,13).

We also measured plasma levels of NT Abs using a microneutralization assay. Briefly, a 100 tissue culture infective dose 50 (100 TCID<sub>50</sub>) of SARS-CoV-2 (βCoV/Korea/KCDC/2020 NCCP43326) was mixed with an equal volume of diluted plasma specimen, incubated at 37°C for 30 min, and added to Vero cells. After 96 h, the cytopathic effect of SARS-CoV-2 on the infected cells was measured. Neutralization Ab titer was calculated as the reciprocal of the highest dilution of test plasma giving 50% neutralization (ID<sub>50</sub>).

### Measurement of T cell responses

An IFN- $\gamma$  ELISPOT assay was performed to measure the SARS-CoV-2-specific T cell response from PBMCs isolated from blood samples of the participants. T cells were stimulated with overlapping peptides of SARS-CoV-2 spike protein (Miltenyi Biotec, Bergisch Gladbach, Germany) and numbers of spot-forming cells (SFC) per  $5.0 \times 10^5$  PBMCs were counted with an automated ELISPOT reader (AID iSPOT; Autoimmun Diagnostika GmbH, Strassberg, Germany). This threshold was established by taking into account: the mean SFC from 5 SARS-CoV-2-unexposed individuals was 10.

### Statistical analysis

Statistical analyses were performed with SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA), and graphs were plotted with GraphPad Prism 8 (GraphPad software, Inc., San Diego, CA, USA). Depending on the normality of the data, we used the  $\chi^2$  test or Fisher's exact test to analyze categorical variables, and Student's *t*-test or the Mann-Whitney *U* test for continuous variables. All tests of significance were 2-tailed, and *p*-values  $<0.05$  were considered statistically significant.

## RESULTS

### Baseline characteristics of the study participants

A total of 76 HCWs were enrolled in this study; 40 (53%) were vaccinated with AZ and 36 (47%) with PF. None of them had had a previous infection with SARS-CoV-2. The baseline characteristics of the participants are shown in **Table 1**. Median age was higher in the AZ participants (40 vs. 32,  $p < 0.0001$ ). After the first dose of vaccine, local and systemic reactogenicities were significantly higher in the AZ participants than the PF participants (local, 5 vs. 3,  $p = 0.014$ ; systemic, 12 vs. 4.5,  $p = 0.002$ ).

### IgG and IgM Ab responses

SARS-CoV-2 S1 protein-specific IgG Ab (S1-IgG) and IgM Ab (S1-IgM) titers were measured in the plasmas of 75 (AZ,  $n = 39$ ; PF,  $n = 36$ ) participants at baseline, 73 (AZ,  $n = 37$ ; PF,  $n = 36$ ) at 1 wk after vaccination, 71 (AZ,  $n = 38$ ; PF,  $n = 33$ ) at 2 wks after vaccination, and 75 (AZ,  $n = 40$ ; PF,  $n = 35$ ) at 3 wks after vaccination.

**Table 1.** Baseline characteristics of the study participants

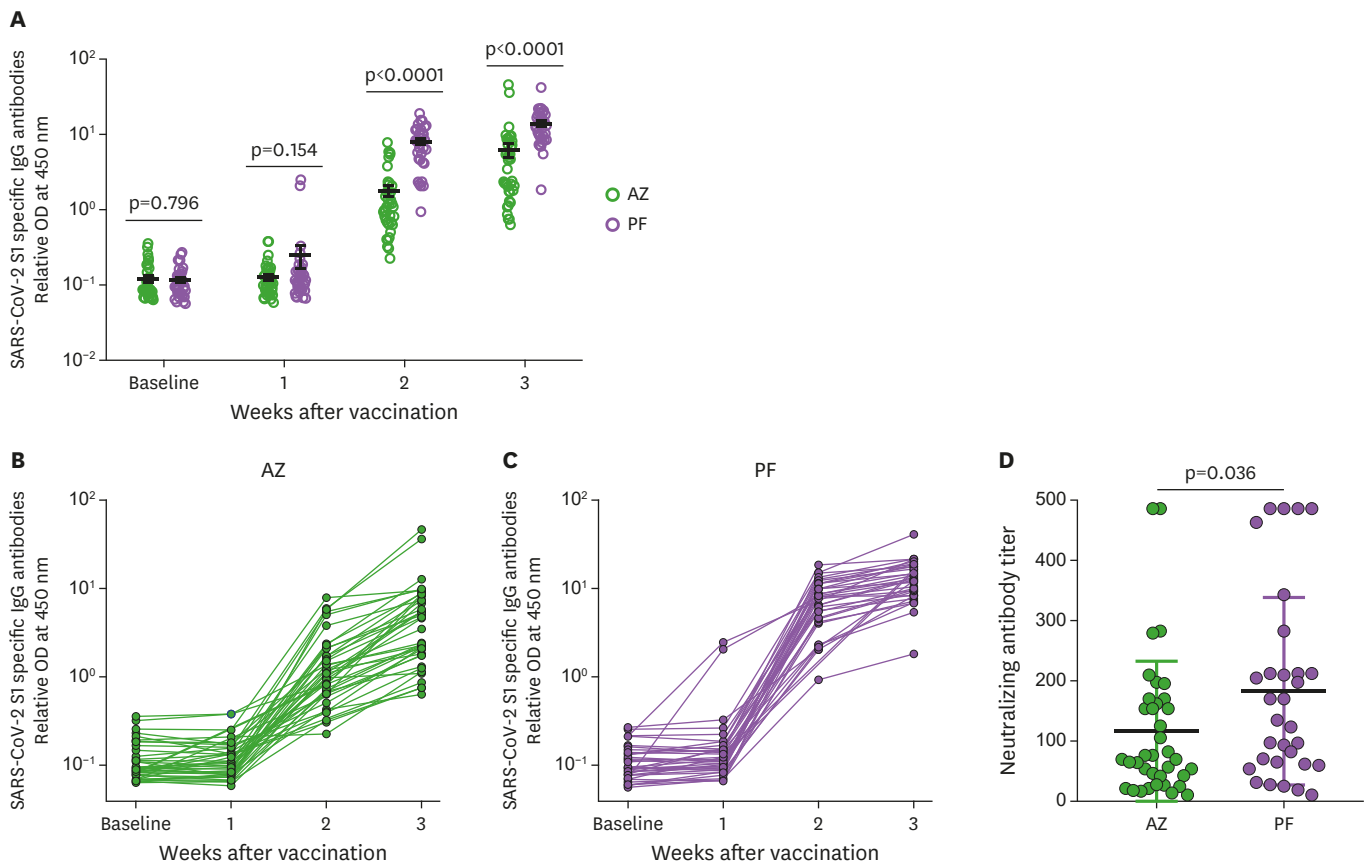
Variables	ChAdOx1 ( $n = 40$ )	BNT162b2 ( $n = 36$ )	Total ( $n = 76$ )	<i>p</i> -value
Age (yr)	40 (33–46)	32 (26–36)	35 (29–43)	$<0.0001$
Age group				$<0.0001$
20s	4 (10)	16 (44)	20 (26)	
30s	14 (35)	15 (42)	29 (38)	
40s	17 (43)	4 (11)	21 (28)	
50s	4 (10)	1 (2.8)	5 (7)	
60s	1 (3)	0 (0)	1 (1)	
Sex				1.000
Male	16 (40)	14 (39)	30 (40)	
Female	24 (60)	22 (61)	46 (61)	
Reactogenicity				
Local reaction	5 (2–9)	3 (0.25–5)	3 (2–7)	0.014
Systemic reaction	12 (4–22)	4.5 (0–13)	7.5 (1–15)	0.002
Total reaction	18 (7–30)	8 (1.3–17)	12 (4–23)	0.002

Values are presented as median (interquartile range) or number (%).

All the participants gave negative values of S1-IgG (cut-off=0.4) at baseline. At 1 wk after vaccination, none of the AZ participants gave positive S1-IgG responses, whereas 2 of the PF participants (2/36, 5.6%) gave positive values (2.51 and 2.09) for S1-IgG. Titers of S1-IgG increased continuously in both sets of participants from baseline to 3 wks after vaccination, but their levels were significantly different (**Fig. 1A**). At 2 wks and 3 wks after vaccination, mean levels ( $\pm$ SD) of S1-IgG were  $1.78 \pm 1.84$  and  $6.28 \pm 8.87$  in the AZ participants and  $8.10 \pm 4.55$  and  $14.03 \pm 7.20$  in the PF participants (at 2 wks,  $p < 0.0001$ ; at 3 wks,  $p < 0.0001$ ). At 3 wks after vaccination, all the participants in both groups had levels of S1-IgG above the cut-off value, but the levels in 4 of the AZ participants (4/40, 10%) were borderline (0.4–1.0).

As shown in **Fig. 1B and C**, S1-IgG levels in the AZ participants increased gradually between 1 and 3 wks, while Ab rose steeply between 1 wk and 2 wks in the PF participants; the slopes of the mean values of S1-IgG between 1 wk and 2 wks were 1.66 and 7.85, respectively, and the slopes between 2 wks and 3 wks were 4.50 and 5.93, respectively, in AZ and PF participants.

At baseline, 2 specimens gave borderline levels (0.4–1.0) of S1-IgM over the cut-off value (0.4). Titers of S1-IgM increased continuously from baseline to 3 wks after vaccination in both sets of participants, but the levels in the 2 groups were significantly different at 2 wks ( $p = 0.0006$ ) and 3 wks ( $p = 0.0002$ ) after vaccination (**Supplementary Fig. 1**).



**Figure 1.** Ab responses after single dose vaccination with the ChAdOx1 nCoV-19 and BNT162b2 vaccines. (A) Comparison of S1-IgG titers induced by ChAdOx1 nCoV-19 (AZ) and BNT162b2 (PF) vaccines from baseline to 3 wks after first vaccination. (B) Kinetics of S1-IgG titers induced by ChAdOx1 nCoV-19 vaccine (AZ) from baseline to 3 wks after vaccination. (C) Kinetics of S1-IgG titers induced by BNT162b2 vaccine (PF) from baseline to 3 wks after vaccination. (D) Comparison of NT Ab titers at 3 wks after vaccination with ChAdOx1 nCoV-19 (AZ) and BNT162b2 (PF) vaccines.

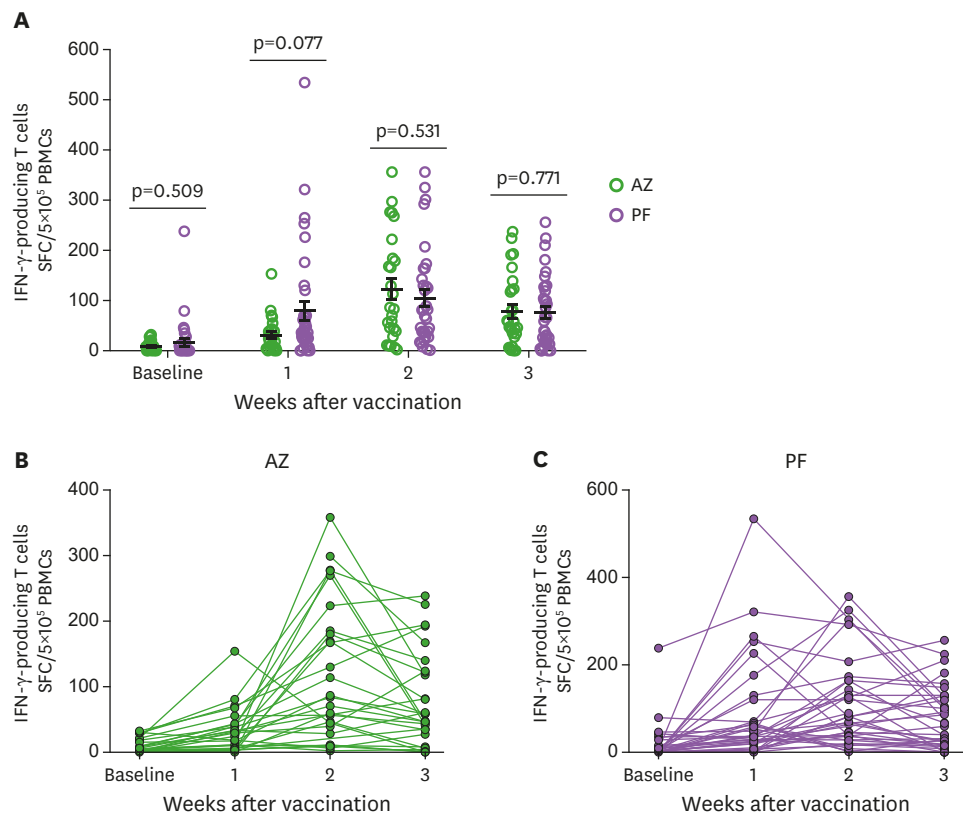
### Virus NT Ab response

SARS-CoV-2 virus NT Ab titers were measured in the plasmas of 68 (AZ, n=37; PF, n=31) participants in a Bio Safety Level-3 laboratory at Institut Pasteur Korea (Seongnam, Korea). At 3 wks after vaccination, the NT Ab titers were significantly higher in the PF participants than the AZ participants ( $183.1 \pm 155.6$  vs.  $116.6 \pm 116.2$ ,  $p=0.035$ ; **Fig. 1D**). The NT Ab titer was significantly correlated with the S1-IgG titer (Pearson  $r=0.463$ ,  $p<0.0001$ ; **Supplementary Fig. 2**).

### Cell-mediated immune response

SARS-CoV-2 spike protein-specific IFN- $\gamma$ -producing T cell responses were measured in the PBMC of 63 (AZ, n=27; PF, n=36) participants at baseline, 62 (AZ, n=26; PF, n=36) participants at 1 wk after vaccination, 59 (AZ, n=26; PF, n=33) at 2 wks after vaccination, and 63 (AZ, n=28; PF, n=35) at 3 wks after vaccination.

At baseline before vaccination, 8 of 27 (29.6%) AZ participants and 10 of 36 (27.8%) PF participants gave T cell responses over the cut-off value (10 SFC/ $5 \times 10^5$  PBMCs). The IFN- $\gamma$ -producing T cell responses peaked at 2 wks after vaccination in both (**Fig. 2A**). At 1 wk after vaccination, the mean value ( $\pm$ SD) of the T cell response in the PF participants showed a (non-significant) trend to being higher than in the AZ participants (AZ,  $30.37 \pm 34.04$ ; PF,  $79.33 \pm 112.93$ ;  $p=0.077$ ). At 2 and 3 wks after vaccination, the mean values of the T cell response in the 2 groups were similar (at 2 wks; AZ,  $122.08 \pm 106.25$ ; PF,  $104.39 \pm 97.79$ ;  $p=0.531$ ; at 3 wks; AZ,  $77.91 \pm 70.98$ ; PF,  $75.24 \pm 70.76$ ;  $p=0.771$ ).



**Figure 2.** Cell-mediated immune responses after single dose vaccination with ChAdOx1 nCoV-19 and BNT162b2 vaccines. (A) Comparison of IFN- $\gamma$ -producing T cell responses from baseline to 3 wks after first vaccination between ChAdOx1 nCoV-19 (AZ) and BNT162b2 (PF) vaccines. (B) Kinetics of IFN- $\gamma$ -producing T cell responses induced by ChAdOx1 nCoV-19 vaccine (AZ) from baseline to 3 wks after vaccination. (C) Kinetics of IFN- $\gamma$ -producing T cell responses induced by BNT162b2 vaccine (PF) from baseline to 3 wks after vaccination.



The slopes of the mean values of the T cell responses in the AZ participants were 21.48 between baseline and 1 wk, and 91.71 between 1 wk and 2 wks. The slopes in the PF participants were 63.03 between baseline and 1 wk, and 25.06 between 1 wk and 2 wks (**Fig. 2B and C**). Therefore, the AZ vaccine induced the strongest T cell response between 1 wk and 2 wks after vaccination, whereas the PF vaccine seemed to already elicit a strong T cell response by 1 wk after vaccination.

## DISCUSSION

Currently, several paper has reported a comparative analysis of the reactogenicity and immunogenicity of COVID-19 vaccines, but that analysis used systematic review and meta-analysis methodology (8-10); few publications have directly compared the immunogenicity of the adenovirus vector-based vaccine and the mRNA-based vaccine against COVID-19. We investigated the detailed kinetics of Ab and cell-mediated responses induced by a 1st vaccination with the adenovirus vector-based ChAdOx1 nCoV-19 vaccine (AZ) and the mRNA-based BNT162b2 vaccine (PF) in a relatively homogeneous young population. The 1st dose of the BNT162b2 vaccine elicited a more rapid and higher Ab response than that of the ChAdOx1 nCoV-19 vaccine. There was also a trend for the IFN- $\gamma$ -producing T cell response to be more rapidly induced by the BNT162b2 vaccine, but the mean values for the 2 vaccines were similar after 2 wks. The IgG and IgM Ab responses to the 2 vaccines increased continuously for 3 wks after vaccination, while the IFN- $\gamma$ -producing T cell responses peaked after 2 wks.

One of main outcomes of this study was that the BNT162b2 vaccine induced faster immune responses than the ChAdOx1 nCoV-19 vaccine. The BNT162b2 vaccine induced Ab and T cell responses 1 wk sooner than the ChAdOx1 nCoV-19 vaccine. In randomized clinical trials, the ChAdOx1 nCoV-19 vaccine induced SARS-CoV-2 spike-specific IgG Ab by 4 wks after the first dose (1,14), while the BNT162b2 vaccine elicited spike IgG Ab by 3 wks after vaccination, at which point a second dose of BNT162b2 vaccine was delivered (3). The rapid immune responses to the BNT162b2 vaccine may be explained by the different nature of the 2 vaccines. After injection, the adenovirus vector-based vaccine infects coxsackie adenovirus receptor (CAR) positive cells (15). The various types of cells, such as epithelial cells, endothelial cells, myoblasts and hepatocytes, express CAR on cell surface and the knob domain of adenovirus capsid structure utilizes CAR as primary receptor for cell entry (16,17). Then, the SARS spike protein is produced from the hybrid adenovirus genome and provokes humoral and cellular immune responses (15). The mRNA-based BNT162b2 vaccine is encapsulated by LNPs and enters cells by membrane-derived endocytic pathways (18), and induces spike protein production. LNPs have been shown to be efficient mRNA delivery vehicles, allowing rapid uptake and protein expression in host cells (19,20). In earlier work, unmodified mRNA induced protein expression 12–24 h after injection of an mRNA-based vaccine (21).

Unlike S1 protein-specific IgG Ab responses, 18 of 63 (28.6%) participants yielded positive SARS-CoV-2 S protein-specific T cell responses prior to vaccination in this study. This result is consistent with previous reports that the CD4<sup>+</sup> T cells of 17%–44% of non-exposed humans gave positive SARS-CoV-2-specific responses (22,23). Mateus et al. (22) reported that preexisting memory T cells might cross-react with SARS-CoV-2 spike protein due to comparable affinity for the common cold HCoV-OC43, HCoV-229E, HCoV-NL63 and HCoV-HKU1.

A previous meta-analysis predicted, based on IFN- $\gamma$  ELISPOT responses, that the ChAdOx1 nCoV-19 vaccine would give stronger T cell responses than other vaccine platforms apart from mRNA platforms (8). However, that study did not include T cell responses to mRNA-based vaccine platforms. In the present work we found that the peak value of IFN- $\gamma$ -producing T cell responses to BNT162b2 was comparable with that to ChAdOx1 nCoV-19.

This study has 2 main limitations: the relatively small number of enrolled participants and the absence of measurements of diverse T cell cytokines. In addition, the HCWs were not randomly assigned to BNT162b2 vs. ChAdOx1 nCoV-19, rather the assignment followed government vaccine policy; therefore the median age of participants receiving BNT162b2 was lower than that of participants receiving ChAdOx1 nCoV-19. A previous study in which about half of the participants exceeded 80 years of age reported that Ab responses to BNT162b2 decreased with age (5). Hence, some might argue that the stronger Ab response in the BNT162b2 group could be due to the difference in age distribution between 2 groups. However, age was not significantly associated with Ab response to either vaccine in our cohort. In this study, most participants in both groups (87% in ChAdOx1 nCoV-19 group and 97% in BNT162b2 group) were homogeneously young (between 20s and 40s). As shown in **Supplementary Fig. 3**, the S1-IgG was significantly higher in each age groups between 20s and 40s of BNT162b2 vaccinees compared to ChAdOx1 nCoV-19 vaccinees. The NT Ab titers were also higher in each age groups of BNT162b2 vaccinees, even though some age groups were not significantly different. Thus, age difference did not substantially affect our main findings. Finally, we did not investigate the underlying mechanisms in depth for different Ab response between 2 vaccines. One possible explanation may be due to the differences in the spike protein conformations between no proline mutation in ChAdOx1 and 2 proline mutations in BNT162b2 that elicit Ab responses against various portions of the spike protein, especially receptor binding domain. Another explanation may be due to the different platforms between adenovirus vector-based and mRNA-based protein synthesis. Further studies are needed on this area.

Despite these limitations, our study provides valuable data on the differences in kinetics of the humoral and cell-mediated immune responses between the adenovirus vector-based ChAdOx1 nCoV-19 vaccine and the mRNA-based BNT162b2 vaccine. The Ab responses induced by the BNT162b2 vaccine (PF) were more rapid and stronger than those induced by the ChAdOx1 nCoV-19 vaccine (AZ). The IFN- $\gamma$ -producing T cell responses induced by the BNT162b2 vaccine were also faster than those induced by the ChAdOx1 nCoV-19 vaccine, but the maximum T cell responses were similar for the 2 vaccines. Further research is needed comparing immune responses to a boosting vaccination and the persistence of immune responses.

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## SUPPLEMENTARY MATERIALS

### Supplementary Figure 1

Comparison of S1-IgM titers induced by ChAdOx1 nCoV 19 (AZ) and BNT162b2 (PF) vaccines from baseline to 3 wks after first vaccination.

[Click here to view](#)

### Supplementary Figure 2

Correlation between SARS-CoV-2 virus NT Ab titer and S1-IgG titer.

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### Supplementary Figure 3

Comparisons of immune responses, S1-IgG, SARS-CoV-2 virus NT Ab, and IFN- $\gamma$ -producing T cell responses between ChAdOx1 nCoV-19 (AZ) and BNT162b2 (PF) vaccines in accordance with the age groups.

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## REFERENCES

1. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, Belij-Rammerstorfer S, Bellamy D, Bibi S, Bittaye M, Clutterbuck EA, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet* 2020;396:467-478.  
[PUBMED](#) | [CROSSREF](#)
2. Pardi N, Tuyishime S, Muramatsu H, Kariko K, Mui BL, Tam YK, Madden TD, Hope MJ, Weissman D. Expression kinetics of nucleoside-modified mRNA delivered in lipid nanoparticles to mice by various routes. *J Control Release* 2015;217:345-351.  
[PUBMED](#) | [CROSSREF](#)
3. Walsh EE, Frenck RW Jr, Falsey AR, Kitchin N, Absalon J, Gurtman A, Lockhart S, Neuzil K, Mulligan MJ, Bailey R, et al. Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates. *N Engl J Med* 2020;383:2439-2450.  
[PUBMED](#) | [CROSSREF](#)
4. Kalimuddin S, Tham CYL, Qui M, de Alwis R, Sim JXY, Lim JME, Tan HC, Syenina A, Zhang SL, Le Bert N, et al. Early T cell and binding antibody responses are associated with COVID-19 RNA vaccine efficacy onset. *Med (N Y)* 2021;2:682-688.e4.  
[PUBMED](#) | [CROSSREF](#)
5. Müller L, André M, Moskorz W, Drexler I, Walotka L, Grothmann R, Ptak J, Hillebrandt J, Ritchie A, Rabl D, et al. Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination. *Clin Infect Dis* 2021;ciab381.  
[PUBMED](#) | [CROSSREF](#)
6. Krammer F, Srivastava K, Alshammary H, Amoako AA, Awawda MH, Beach KF, Bermúdez-González MC, Bielak DA, Carreño JM, Chernet RL, et al. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. *N Engl J Med* 2021;384:1372-1374.  
[PUBMED](#) | [CROSSREF](#)
7. van Doremalen N, Lambe T, Spencer A, Belij-Rammerstorfer S, Purushotham JN, Port JR, Avanzato VA, Bushmaker T, Flaxman A, Ulaszewska M, et al. ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques. *Nature* 2020;586:578-582.  
[PUBMED](#) | [CROSSREF](#)
8. McDonald I, Murray SM, Reynolds CJ, Altmann DM, Boyton RJ. Comparative systematic review and meta-analysis of reactogenicity, immunogenicity and efficacy of vaccines against SARS-CoV-2. *NPJ Vaccines* 2021;6:74.  
[PUBMED](#) | [CROSSREF](#)



9. Giurgea LT, Memoli MJ. Navigating the quagmire: comparison and interpretation of COVID-19 vaccine phase 1/2 clinical trials. *Vaccines (Basel)* 2020;8:746.  
[PUBMED](#) | [CROSSREF](#)
10. Rogliani P, Chetta A, Cazzola M, Calzetta L. SARS-CoV-2 neutralizing antibodies: a network meta-analysis across vaccines. *Vaccines (Basel)* 2021;9:227.  
[PUBMED](#) | [CROSSREF](#)
11. Kim JY, Kwon JS, Bae S, Cha HH, Lim JS, Kim MC, Chung JW, Park SY, Lee MJ, Kim BN, et al. SARS-CoV-2-specific antibody and T cell response kinetics according to symptom severity. *Am J Trop Med Hyg* 2021;tpmd201594.  
[PUBMED](#) | [CROSSREF](#)
12. Classen DC, Morningstar JM, Shanley JD. Detection of antibody to murine cytomegalovirus by enzyme-linked immunosorbent and indirect immunofluorescence assays. *J Clin Microbiol* 1987;25:600-604.  
[PUBMED](#) | [CROSSREF](#)
13. Lardeux F, Torrico G, Aliaga C. Calculation of the ELISA's cut-off based on the change-point analysis method for detection of *Trypanosoma cruzi* infection in Bolivian dogs in the absence of controls. *Mem Inst Oswaldo Cruz* 2016;111:501-504.  
[PUBMED](#) | [CROSSREF](#)
14. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, Voysey M, Aley PK, Angus B, Babbage G, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021;396:1979-1993.  
[PUBMED](#) | [CROSSREF](#)
15. Hasanpourghadi M, Novikov M, Ertl HC. COVID-19 vaccines based on adenovirus vectors. *Trends Biochem Sci* 2021;46:429-430.  
[PUBMED](#) | [CROSSREF](#)
16. Tomko RP, Xu R, Philipson L. HCAR and MCAR: the human and mouse cellular receptors for subgroup C adenoviruses and group B coxsackieviruses. *Proc Natl Acad Sci U S A* 1997;94:3352-3356.  
[PUBMED](#) | [CROSSREF](#)
17. Bergelson JM, Krithivas A, Celi L, Droguett G, Horwitz MS, Wickham T, Crowell RL, Finberg RW The murine CAR homolog is a receptor for coxsackie B viruses and adenoviruses. *J Virol* 1998;72:415-419.  
[PUBMED](#) | [CROSSREF](#)
18. Gilleron J, Querbes W, Zeigerer A, Borodovsky A, Marsico G, Schubert U, Manygoats K, Seifert S, Andree C, Stöter M, et al. Image-based analysis of lipid nanoparticle-mediated siRNA delivery, intracellular trafficking and endosomal escape. *Nat Biotechnol* 2013;31:638-646.  
[PUBMED](#) | [CROSSREF](#)
19. Maruggi G, Zhang C, Li J, Ulmer JB, Yu D. mRNA as a transformative technology for vaccine development to control infectious diseases. *Mol Ther* 2019;27:757-772.  
[PUBMED](#) | [CROSSREF](#)
20. Ulmer JB, Geall AJ. Recent innovations in mRNA vaccines. *Curr Opin Immunol* 2016;41:18-22.  
[PUBMED](#) | [CROSSREF](#)
21. Vogel AB, Lambert L, Kinnear E, Busse D, Erbar S, Reuter KC, Wicke L, Perkovic M, Beissert T, Haas H, et al. Self-amplifying RNA vaccines give equivalent protection against influenza to mRNA vaccines but at much lower doses. *Mol Ther* 2018;26:446-455.  
[PUBMED](#) | [CROSSREF](#)
22. Mateus J, Grifoni A, Tarke A, Sidney J, Ramirez SI, Dan JM, Burger ZC, Rawlings SA, Smith DM, Phillips E, et al. Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. *Science* 2020;370:89-94.  
[PUBMED](#) | [CROSSREF](#)
23. Schmidt KG, Nganou-Makamdop K, Tenbusch M, El Kenz B, Maier C, Lapuente D, Überla K, Spriewald B, Bergmann S, Harrer EG, et al. SARS-CoV-2-seronegative subjects target CTL epitopes in the SARS-CoV-2 nucleoprotein cross-reactive to common cold coronaviruses. *Front Immunol* 2021;12:627568.  
[PUBMED](#) | [CROSSREF](#)