LB6. Asymptomatic Infection and Duration of Viral Shedding in Symptomatic Breakthrough Infections in a Phase 3 Study of AZD1222 (ChAdOx1 nCoV-19)

Magdalena Sobieszczyk, MD, MPH[1]; Ann R. Falsey, MD[2]; Merlin L. Robb, M.D.[3]; Hong-Van Tieu, M.D, M.S.[4]; Julie McElrath, MD, PhD[5]; Lawrence Corey, MD[5]; Kathleen Neuzil, MD, MPH[6]; Tina Tong, M.S.[7]; Margaret Brewinski Isaacs, M.D, M.P.H[7]; Jill Maaske, M.D.[8]; Brett Jepson, n/a[9]; Stephanie Sproule, n/a[8]; Elizabeth Kelly, n/a[8]; [1]Columbia University Irving Medical Center, New York, NY; [2]University of Rochester, Rochester, New York; [3]Walter Reed Army Institute of Research, Silver Spring, MD, Silver Spring, Maryland; [4]Columbia University Irving Medical Center and New York-Presbyterian Hospital, New York, NY and Laboratory of Infectious Disease Prevention, Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY, New York, New York; [5]Fred Hutchinson Cancer Research Center, Seattle, WA; [6]University of Maryland School of Medicine, Baltimore, Maryland; [7]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, Bethesda, Maryland; [8]AstraZeneca Pharmaceuticals LP, Gaithersburg, MD, Gaithersburg, Maryland; [9]AstraZeneca Pharmaceuticals LP, Gaithersburg, MD and Cytel, Inc., Cambridge, MA, Bethesda, Maryland

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Background. SARS-CoV-2 vaccine efficacy (VE) against asymptomatic infection and impact on viral shedding during breakthrough infections have critical implications for pandemic control. AZD1222 (ChAdOx1 nCoV-19; 2 doses, 4 weeks apart) demonstrated VE of 74.0% (95% CI 65.3, 80.5) against the primary endpoint of symptomatic RT-PCR-confirmed COVID-19 and safety in a Phase 3, 2:1 randomized, placebo-controlled study in the US, Chile and Peru (n=32,451). Here we present exploratory analyses on asymptomatic infections determined by nucleocapsid (N) seroconversion and time to viral clearance in participants with symptomatic infections determined by N seroconversion (primary data cut, March 5, 2021).

Methods. N seroconversion was assessed at all scheduled and illness visits in the fully vaccinated analysis set (Table). In this analysis, symptomatic infections are defined as N seroconversion ≥ 15 days post second dose in participants who attended an illness visit with ≥ 1 qualifying COVID-19 symptom and had ≥ 1 positive RT-PCR result for SARS-CoV-2. Asymptomatic infections are defined as N seroconversion ≥ 15 days post second dose in participants who did not meet the criteria for symptomatic infections. In participants with symptomatic infections, viral shedding in saliva was assessed for 28 days and cumulative incidence of viral clearance was determined.

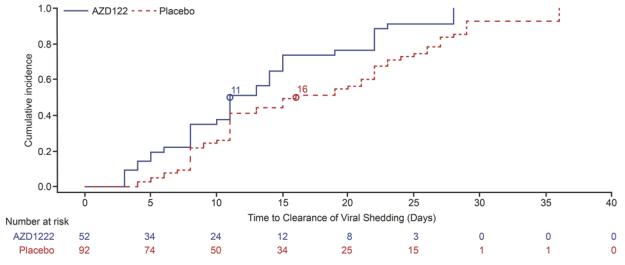
Table. AZD1222 VE against symptomatic and potentially asymptomatic SARS-CoV-2 infections as determined by N seroconversion

	All SARS-CoV-2 infections*		Symptomatic infections		Asymptomatic infections	
	AZD1222 (n=17662)	Placebo (n=8550)	AZD1222 (n=17662)	Placebo (n=8550)	AZD1222 (n=17662)	Placebo (n=8550)
Participants with Observed Events, n (%)	156 (0.88)	202 (2.36)	52 (0.29)	97 (1.13)	104 (0.59)	105 (1.23)
Total follow-up time (1,000 person-years)	2.03	0.94	2.03	0.94	2.03	0.94
Incidence rate (Cases per 1,000 person-years)	76.86	215.37	25.62	103.42	51.24	111.95
VE (95% CI)	**64.32** (56.05, 71.03)		**75.23** (65.33, 82.31)		**54.24** (39.99, 65.10)	
p-value	< 0.001		< 0.001		< 0.001	

*Assessed in the fully vaccinated analysis set, which comprised 26,212 participants (17,662 AZD1222, 8,550 placebo) who were baseline SARS-CoV-2 seronegative, received 2 doses of study intervention and remained on study ≥15 days post second dose without prior confirmed SARS-CoV-2 RT-PCR-positive infection. Participants were reminded weekly to monitor for COVID-19 symptoms and contact the clinic with qualifying symptoms.
CI, confidence interval; N, nucleocapsid; VE, vaccine efficacy

Results. Overall, 358 participants had SARS-CoV-2 infections as determined by N seroconversion (Table). Incidences per 1000 person-years of symptomatic infections were 25.62 for AZD1222 vs 103.42 for placebo (VE 75.23%; 95% CI 65.33, 82.31) and of asymptomatic infections were 51.24 vs 111.95 (VE 54.24%; 95% CI 39.99, 65.10) (Table). Sensitivity analyses for N seroconversion using the primary endpoint and CDC criteria for defining symptomatic/asymptomatic status were supportive. Median time to viral clearance in saliva in participants with symptomatic infections was 11 days (AZD1222, n=52) vs 16 days (placebo, n=92) (Figure).

Figure. Viral clearance in saliva samples in participants with symptomatic infections as determined by N seroconversion



Conclusion. AZD1222 resulted in lower yet meaningful VE against asymptomatic compared to symptomatic infections, as determined by N seroconversion, and shortened viral shedding in symptomatic SARS-CoV-2 breakthrough infections vs placebo, highlighting its potential contribution to reducing viral transmission.

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LB7. Ad26.COV2.S-Elicted Neutralizing Activities Against SARS-CoV-2 Variants of Concern in Phase 1/2a and Phase 3 Clinical Trials

Mathieu Le Gars, n/a[1]; Jerald Sadoff, MD[2]; Mandy Jongeneelen, n/a[1]; Dirk Heerwegh, n/a[3]; Georgi Shukarev, MD[4]; Carla Truyers, n/a[3]; Anne Marit de Groot, n/a[1]; Gert Scheper, n/a[1]; Jenny Hendriks, n/a[1]; Boerries Brandenburg, n/a[1]; Frank Struyf, n/a[3]; Johan Van Hoof, n/a[1]; Macaya Douoguih, MD, MPH[4]; Hanneke Schuitemaker, PhD[2]; [1]Janssen Vaccines and Prevention, Leiden, The Netherlands, Leiden, Zuid-Holland, Netherlands; [2]Janssen Infectious Diseases and Vaccines, Leiden, Zuid-Holland, The Netherlands, 2333, Leiden, Zuid-Holland, Netherlands; [3]Janssen Research and Development, Beerse, Belgium, Beerse, Antwerpen, Belgium; [4]Janssen Vaccines and Prevention, Leiden, Netherlands, Leiden, Zuid-Holland, Netherlands

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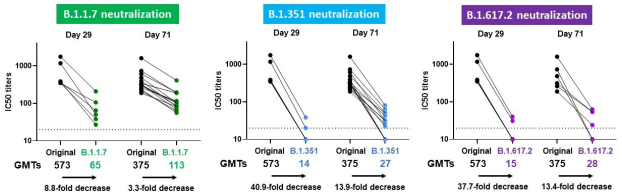
Background. In a Phase 3 trial, the Janssen COVID-19 vaccine, Ad26.COV2.S, showed robust efficacy against severe–critical COVID-19 in countries where different SARS-CoV-2 variants were circulating. We evaluated Ad26.COV2.S-elicited antibody neutralizing activity against variants of concern (VOC) B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta) in sera from participants in clinical trials following a single dose of Ad26.COV2.S.

Methods. Neutralizing activities of Ad26.COV2.S (given at a dose level of 5 x 10^{10} viral particles [vp]) against VOC were assessed by wild-type virus neutralizing (wtVNA) and pseudovirion neutralization (psVNA) assays in sera from participants in Phase 1/2a and Phase 3 clinical trials, respectively. Geometric mean titers (GMTs) were determined at Days 29 and 71 after vaccination.

Results. In serum samples from Phase 1/2a participants (n = 6), at Day 29 after 1 dose of Ad26.COV2.S, wtVNA titers against VOC were lower than for the original strain (GMT = 573), with GMT = 65, 14, and 15 for Alpha, Beta, and Delta, respectively, representing 8.8-, 40.9-, and 37.7-fold decreases. By Day 71 after vaccination (n = 14), fold differences between the original strain (GMT = 375) and VOC (GMT = 113, 27, and 28) were smaller (3.3-, 13.9-, and 13.4-fold) than at Day 29, suggestive of B-cell maturation (**Figure 1**). Day 71 titers against the Delta variant were maintained for at least 8 months following a single dose of Ad26.COV2.S (5 x 10^{10} vp). In serum samples from Phase 3 participants (n = 8), psVNA titers against VOC were lower than the original strain at Day 71 after vaccination, with the lowest titers observed for the Beta variant (3.6-fold decrease vs original strain). Smaller reductions in Nab titers for VOC were observed in the psVNA assay compared to wtVNA.

Figure 1. Neutralization of B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta) lineages in serum samples from participants who received Ad26.COV2.S. n = 6 samples at Day 29 and n = 14 (n = 14 for Alpha and Beta; n = 6 for Delta, comprising the same 6 participants at Day 29) samples at Day 71 after vaccination with a single dose of Ad26.COV2.S (5 x 10^10 vp dose level) were analyzed in wild-type virus neutralization assays against the SARS-CoV-2 Victoria strain (D614, black dots), the B.1.1.7 (Alpha; green dots) the B.1.351 (Beta; blue dots), and the B.1.617.2 (Delta; purple dots) lineages. Dots represent the IC50 (inhibitory concentration) titers per participant. Geometric mean titers (GMTs) and fold decrease in neutralizing activity between the original Victoria strain and each lineage are shown.



Conclusion. Ad26.COV2.S-elicited serum neutralizing activity against VOC showed an overall decrease in titers relative to the original strain that was largest for the Beta variant, even though vaccine efficacy against severe–critical COVID-19 was maintained in countries where these variants were circulating versus in countries where they were not circulating. Over time, titers against variants increased, suggesting B-cell affinity maturation leading to increasing coverage of VOC.

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LB8. Lower SARS-CoV-2 IgG and Pseudovirus Neutralization Titers Post-mRNA Vaccination among People Living with HIV

Matthew A. Spinelli, MD, MAS[1]; Michael J. Peluso, MD[1]; Kara Lynch, PhD[2]; Cassandra Yun, BA[3]; David V. Glidden, PhD[1]; Timothy J. Henrich, MD[1]; Steve Deeks, MD[3]; Monica Gandhi, MD, MPH[1]; [1]University of California, San Francisco, San Francisco, CA; [2]University of California San Francisco, San Francisco, California; [3]UCSF, San Francisco, California

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Background. Limited data are available on whether there are differences in the immune response to SARS-CoV-2 vaccination by HIV status or by mRNA vaccine type.

Methods. We saved residual outpatient laboratory samples of all previously mRNA-vaccinated individuals in the adult medicine clinics of a public hospital with a large outpatient HIV clinic during May 2021, and then excluded individuals with prior SARS-CoV-2 infection. We next 1:1 matched 100 PLWH to 100 outpatient HIV-negative adult medicine patients receiving care for chronic medical conditions on days since completion of second vaccination (minimum 10), sex, age +/-5 years, and the type of mRNA vaccine received. We defined a non-response as reciprocal pseudovirus neutralizing titer< 10 and anti-RBD IgG< 10 relative fluorescent units, and compared non-response by HIV status using mixed models.

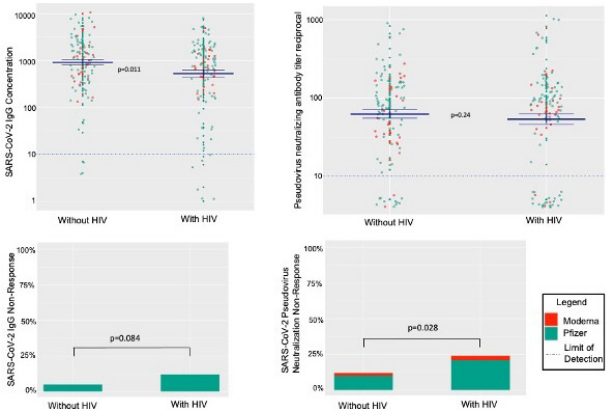
Results. In each matched group there were 13 women; 25 received the mRNA-1273 vaccine and 75 received the BNT162b2 vaccine; the median age was 59. The median time from second vaccination was 35 days (IQR: 20–63). Among PLWH, the median CD4+ T-cell count was 511 (IQR: 351–796) and 5 individuals had HIV RNA > 200.

We found 2.4-fold greater odds of pseudovirus neutralizing antibody non-response among PLWH compared to people without HIV (95% CI=1.1–5.4). Although few individuals in each group did not mount an IgG response (12 among PLWH vs. 5; p=0.08), continuous anti-RBD IgG concentrations were 43% lower among PLWH (95% CI=0.36–0.88).

Among PLWH, when adjusting for age, sex, and days post-vaccination, each 100-cell increase in CD4+T-cell count was associated with 22% higher neutralizing antibody titers (GMR 1.22; 95% CI=1.09–1.37). Unsuppressed HIV RNA >200 was associated with 89% lower neutralizing antibody titers (GMR 0.11; 95% CI=0.01–0.84). Receipt of the BNT162b2 vs. mRNA-1273 vaccine was associated with 77% lower neutralizing titers (GMR 0.23; 95% CI=0.08–0.65) among PLWH.

Post-mRNA Vaccination SARS-CoV-2 IgG Concentrations and Pseudovirus Neutralizing Titers by HIV Status and Vaccine

Conclusion. PLWH had lower than expected response to mRNA SARS-CoV-2 vaccines, with the highest non-response among those with low CD4+ counts, unsuppressed HIV RNA, and those who received the BNT162b2 vaccine. Immunization strategies to improve immune responses among PLWH should be studied, and may include booster vaccination or preference of the mRNA-1273 vaccine in this group.



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LB9. Longitudinal antibody dynamics in children infected with SARS-CoV-2 through 6 months post-infection

Lauren E. Gentles[1]; Leanne P. Kehoe, BA[2]; Katharine D. Crawford, PhD[3]; Kirsten Lacombe, RN, MSN[2]; Jane Dickerson, PhD[4]; Joanna H. Yuan, B.A.[2]; Susanna L. Schuler, BA[2]; Sankan Nyanseor, MPH[5]; Sharon Saydah, PhD[6]; Claire Midgley, PHD[7]; Kimberly Pringle, MD[6]; Jesse Bloom, PhD[1]; Janet A. Englund, MD[8]; [1]Fred Hutchinson Cancer Research Center, Seattle, WA; [2]Seattle Children's Hospital, Seattle, Washington; [3]University of Washington, Seattle, Washington; [4]Seattle Children's Hospital, Seattle, Washington; [5]U.S. Centers for Disease Control and Prevention, Atlanta, Georgia; [6]Centers for Disease Control and Prevention, Atlanta, Georgia; [7]CDC, Atlanta, Georgia; [8]Seattle Children's Hospital/Univ. of Washington, Seattle, Washington

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Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection elicits antibodies (Abs) that bind several viral proteins such as the spike entry protein and the abundant nucleocapsid (N) protein. We examined convalescent sera collected through 6 months (~24wks) post-SARS-CoV-2 infection in children to evaluate changes in neutralization potency and N-binding.

Methods. Outpatient, hospitalized, and community recruited volunteers < 18 years with COVID-19 were enrolled in a longitudinal study at Seattle Children's Hospital. Analysis includes symptomatic and asymptomatic children with laboratory-confirmed SARS-CoV-2 infection who provided blood samples at approximately 4wks (range: 2-18wks, IQR:4-8wks) and 24 wks (range: 23-35wks, IQR:25-27wks) after diagnosis. We measured neutralizing Ab using an in-house pseudoneutralization assay and anti-N binding Ab using the Abbott Architect assay.

Results. Of 32 children enrolled between April 2020 and January 2021, 27 had no underlying immunocompromised state and 25 of these 27 children had symptomatic disease. Ten of 27 had a > 2-fold decrease neutralization titers between 4 and 24wks (most were < 10-fold); 12 had < 2-fold change; and 5 had neutralization titers that increased > 2-fold over time (Fig. 1A). All but one of these 27 children had detectable neutralizing activity at 24wks. Anti-N Abs were assessed for 25 children at 4wks and 17 children at 24wks (data pending for 14 samples); all children with paired samples had a > 1.75-fold Abbott index reduction at 24wks, and 5 children had no detectable anti-N Abs by 24wks (Fig. 2A). An additional 5 children with symptomatic disease had complicating immunosuppression or multiple blood transfusions; 2 had decreasing neutralizing titers, 2 increased, and 1 had no change (Fig. 1B). Anti-N Abs were undetectable for one child by 24wks (data pending for 4 samples) (Fig. 2B). No participants received COVID-19 vaccine.