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

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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.

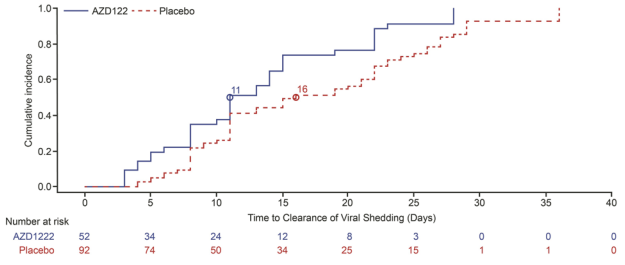
Table. AZD1222 VE against symptomatic and potentially asymptomatic SARS-CoV-2 infections as determined by N seroconversion

	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

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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.