**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 74.9% (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 ill 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-diary with ≥2 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 infection, viral shedding in saliva was assessed for 28 days and cumulative incidence of viral clearance was determined.

**Results.** Overall, 358 participants had SARS-CoV-2 infections as determined by N seroconversion (Table). Incidences per 1000 person-years of symptomatic and asymptomatic infections were 25.6% for AZD1222 vs 103.4% 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 with symptomatic infections was 11 days (AZD1222, n=52) vs 16 days (placebo, n=92) (Figure).

**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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Conclusion. Ad26.COV2.S-elicted 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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LB9. Longitudinal antibody dynamics in children infected with SARS-CoV-2 through 6 months post-infection

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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 neutralizing and N-binding Abs.

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 pseudonutralization 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 neutralizing 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 compulsive 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.