Reference of the Week

  
  Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials - ScienceDirect pdf

Premise/Methods: 1. The UK’s decision to delay the booster dose of AstraZeneca-Oxford (AZO) vaccine in order to provide more initial doses was controversial: would the delay from ≤6 weeks to 12 weeks compromise efficacy? 2. This report incorporates 4 AZO studies: 2 in the UK; 1 in Brazil; and 1 in South Africa. 3. Primary outcome: symptomatic COVID-19 and a positive nucleic acid amplification test occurring 21 days after the first dose or 14 days after the second dose. 4. Anti-spike IgG antibody and neutralizing antibody studies were performed.

Findings: 1. 17,178 participants across 4 studies were included in the primary analysis. 2. Symptomatic COVID-19 occurred in 84 of 8,597 in the AZO group, and 248 of 8,581 in the control group. 3. Vaccine efficacy against COVID-19 requiring hospitalization was 100% (0 in the AZO group and 15 cases in the control group). 4. Participants aged 18–55 years who received a second standard vaccine more than 12 weeks after the first had antibody titres more than two-fold higher than those who received the second dose within 6 weeks of their initial vaccination. 5. Vaccine efficacy after the second dose was higher in those with a longer prime-boost interval, reaching 81.3% in those with a dosing interval of 12 weeks or more versus 55.1% in those with an interval of less than 6 weeks.

Other References:


Premise/Methods: 1. ACE2 is the cell entry receptor for SARS-CoV-2 and is upregulated by interferon during COVID-19 as determined from bronchoalveolar lavage fluid cells. 2. Plasma ACE2 concentration and metabolites of the renin angiotensin system (RAS) were measured and stratified according to disease severity. 3. Levels were compared to critically ill subjects with influenza pneumonia. 4. This study assesses plasma ACE2 in patients with COVID-19 of variable severity over the time course of their disease, in comparison with a retrospective cohort of influenza patients.

Findings: 1. Levels of ACE2 and RAS were determined in 126 patients with SARS-CoV-2 and 27 patients with influenza and significant differences included: age in severe COVID vs influenza – 68 (n=32) vs 58 (n=27); hypertension in severe COVID vs influenza – 64% (n=20) vs 9.1% (n=2); and when comparing severe vs non-severe COVID-19 differences include –CRP, Creat, IL-6, hospital days, and mortality. 2. ACE2 and RAS levels increased over time particularly in severe COVID-19 patients. 3. ACE2 in

Figure. Plotting anti-SARS-CoV-2 spike IgG against vaccine efficacy for each dose interval showed evidence of a potential relationship between binding antibody and vaccine protection, as well as between neutralisation antibody and vaccine efficacy, suggesting potential correlates of protection
influenza patients were significantly lower compared to severe COVID-19 patients. 4. Therapy with corticosteroids, anti-viral meds, or tocilizumab did not have an effect on ACE2 levels.

**Figure.** Comparison of ACE2 levels in severe and non-severe COVID-19 over time.

- Firestone MJ. First Identified Cases of SARS-CoV-2 Variant B.1.1.7 in Minnesota – December 2020-January 2021. MMWR. Early Release. 02.17.2021. [Link](https://www.cdc.gov/mmwr/volumes/70/wr/mm7008e1.htm?s_cid=mm7008e1_w)

**Findings:** 1. On January 9, 2021, the Minnesota Department of Health (MDH) announced the identification of the SARS-CoV-2 variant of concern (VOC) B.1.1.7 in specimens from five persons; on January 25, MDH announced the identification of this variant in specimens from three additional persons. 2. Of the first 8 people identified with this variant, 6 reported recent travel (3 international, 3 domestic). 3. Identification of this variant in Minnesota, a variant that epidemiologic and genomic evidence suggests has increased transmissibility, highlights the importance of mitigation measures such as mask use, physical distancing, avoiding crowds and poorly ventilated indoor spaces, isolation of persons with diagnosed COVID-19, quarantine of close contacts of persons with COVID-19, and adherence to CDC travel guidance to slow transmission. 4. Modeling data suggest that B.1.1.7 could become the predominant variant in the United States in March 2021.


**Premise/Methods:** 1. In vaccine trials, enrollment should target populations at greatest risk for infection, serious morbidity, or mortality. 2. When people with diverse backgrounds are not adequately represented, treatments shown to be effective in trials may not be generalizale to or effective for all populations and lack of trust and vaccine hesitancy may emerge when exclusion occurs during the trials. 3. Cross-sectional study of vaccine trials from 07/01/2011 to 06/30/2020 were assessed for demographic data.

**Findings:** 1. 230 US-based clinical trials with a total of 219 555 participants. 2. In large phase 3 trials in which Black or African American and other minority research participants in both adult and pediatric vaccine trials were often underrepresented. 3. Adults 65 years or older were less frequently enrolled in trials than expected according to their representation in the US.
population based on census data. 4. Surprisingly, data revealed that female adults were overrepresented in trials of all phases. We might posit that females maybe easier to approach, more likely to enroll, access healthcare more often than men, or publicity regarding gender disparity in trials may be having an effect.


Premise/Methods: 1. CDC recommends 10 day quarantine without testing or a 7 day quarantine with testing. 2. Incubation period of SARS-CoV-2 is 4-5 days in adults and 6-7 days in children: most infected children should test positive by day 9. 3. This study assesses test positivity rates among student contacts. Findings: 1. Of the 388 student contacts in high school who were tested, 32 (8.2%) were positive for SARSCoV-2 infection on days 9 to 14 compared with 8 (1.8%) of 451 student contacts in elementary and middle school who tested positive. 2. From 08/01-11/30/2020, 2189 contacts were quarantined: Of the 839 student contacts tested on days 9 to 14, 40 (4.8%) were positive for SARS-CoV-2 infection. 3. Clearly, loss of instructional time can be safely reduced with a 9 day quarantine and test strategy versus a 14 day quarantine strategy alone.

SEE THE ARTICLE CABINET ON THE S: DRIVE, “COVID-19 ARTICLE RESOURCE CABINET” FOR CHILDREN’S FULL COLLECTION