



Journal club

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tocilizumab treatment. However, clinicians in both primary and secondary care should be cognisant of the immunosuppressive nature of therapy and the potential for increased infections in patients treated with tocilizumab.

INTERIM RESULTS OF CHADOX1 NCOV-19 VACCINE (AZD1222): SAFE AND EFFECTIVE

The ChAdOx1 nCoV-19 (AZD1222) contains a replicant-deficient chimpanzee adenoviral vector (ChAdOx1), containing the SARS-CoV-2 structural surface glycoprotein antigen (spike protein: nCoV-19) gene. Data from 11 636 participants (5807 vaccine and 5829 placebo) across four trials were included in this interim primary efficacy analysis (Lancet 2020;297:99). All participants in the vaccine arm received two standard doses (SDs), except a subgroup of participants in the UK that received a low dose (LD) then an SD. Participants over 55 accounted for 12.2% of the total cohort with majority female (61%) and white (UK, 91%; Brazil, 67%). There were 30/5807 (0.5%) cases of COVID-19 in the vaccine arm and 101/5829 (1.7%) cases in the control arm with an overall efficacy of 70.4% (95.8% CI, 54.8% to 80.6%). Vaccine efficacy in participants who received SD/SD was 62.1% (95% CI, 41.0% to 75.7%), and in LD/SD was 90.0% (95% CI, 67.4% to 97.0%). Further work is required to understand reasons for increased efficacy in the LD/SD regimen. Age and time interval between vaccinations were potential confounding variables. All 10 participants hospitalised with COVID-19 after day 21 were in the control arm. The overall safety profile of the vaccine was good with <1% (vaccine, 79/1201 and placebo, 89/11724) serious adverse events in both groups. For safety reasons, older participants were vaccinated after the 18–55 cohort and hence only 5 cases of COVID-19 had occurred in participants older than 55 at data lock; therefore, vaccine efficacy in this age group could not be assessed. Duration of protection from ChAdOx1 nCoV-19 is yet to be determined but these data suggest excellent early efficacy.

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CONVALESCENT PLASMA TREATMENT OF SEVERE COVID-19: POTENTIAL BENEFIT BUT MANY UNANSWERED QUESTIONS

Virus-specific antibodies in convalescent plasma have demonstrated a therapeutic benefit in viral infections such as SARS and may offer similar potential in COVID-19 infection. Liu and colleagues (Nar Med 2020;26:1708) conducted a retrospective propensity score matched control study to evaluate the effectiveness of convalescent plasma therapy in 39 patients with severe or life-threatening COVID-19 within 14 days of symptom onset. The study used a 1:2 and 1:4 matching analysis with attempts to account for major confounders. The cohorts were broadly well matched on important factors with the exception of therapeutic anticoagulation. The 1:4 matched model showed significant survival benefit with convalescent plasma (HR, 0.34; 95% CI, 0.13 to 0.89; $p=0.027$). Convalescent plasma recipients who were not mechanically ventilated at the time of transfusion ($n=34$) were significantly less likely to die than their matched controls (HR, 0.23; 95% CI, 0.05 to 0.98; $p=0.046$). The study was unable to observe any impact on mechanically ventilated patients due to the small sample size ($n=4$). Subgroup analysis also suggested a benefit of convalescent plasma in those with less than a week of symptoms ($p=0.035$), and those receiving therapeutic anticoagulation ($p=0.018$). No correlation was observed between donor antibody neutralisation titres and convalescent plasma recipient outcomes. No serious adverse events were identified as directly related to convalescent plasma transfusion. While the study is supportive of convalescent plasma transfusion as an effective intervention for this group of patients with COVID-19, caution is needed due to the nature of the study design, which cannot account for unmeasured confounders and case selection bias further work with randomised data is needed.

RACIAL BIAS IN PULSE OXIMETRY MEASUREMENT: ALWAYS KNOW THE LIMITATIONS OF YOUR TEST

The use of pulse oximetry (SpO_2) to monitor patients and inform treatment decisions is almost ubiquitous in modern medicine. However, little is known about potential differences in accuracy between racial groups. Sjo-Jing *et al*'s (NEJM 2021;383:2477) report

paired SpO_2 and arterial (SaO_2) samples study in adult inpatients receiving supplemental oxygen from a single site, adjusted for age, sex and cardiovascular impairment, and wider unadjusted multicentre dataset. A total of 10 786 paired measurements were obtained from 1333 White patients and 276 Black patients in the single-centre cohort and 37 308 paired measurements were obtained from 7342 White patients and 1050 Black patients in the multicentre cohort. In the single-centre cohort, in patients who had an SpO_2 of 92%–96%, an SaO_2 of <88% was found in 88/749 Black patients (11.7%; 95% CI 8.5% to 16%) and in 99/2778 White patients (3.6%; 95% CI 2.7% to 4.7%). Results were similar in the multi-centre cohort. These data demonstrate an approximate three times higher risk of occult hypoxia in black patients when compared with white patients. Given the importance of pulse oximetry for medical decision-making, these findings could have major implications for medical management and escalation of care, especially during the current COVID-19 pandemic.

TOCILUZIMAB IN PATIENTS HOSPITALISED WITH COVID-19 PNEUMONIA: MORE OPTIONS IN THE ARMAMENTARIUM

Higher levels of interleukin-6 (IL-6) have been found in cases of severe COVID-19 with lower levels associated with mild disease. Tocilizumab, an IL-6 receptor monoclonal antibody, has been shown to potentially improve outcomes in patients with COVID-19 pneumonia in observational studies. Salama *et al* (NEJM 2021;384:20) present a global phase 3 randomised double blind placebo controlled trial, conducted to evaluate the safety and efficacy of tocilizumab in hospitalised patients with COVID-19 pneumonia not receiving mechanical or non-invasive ventilation. Primary outcome was progression to ventilatory support or death. The trial randomised 389 participants with 377 receiving treatment, more than 80% of participants were in a minority racial or ethnic group and more than 75% of patients had at least one comorbidity. Death or escalation to ventilatory support was lower in the tocilizumab group (12%; 95% CI, 8.5% to 16.9%) than the placebo group (19.3%; 95% CI, 13.3% to 27.4%) with a significant treatment effect (HR, 0.56, 95% CI, 0.33 to 0.97, $p=0.04$). Similar rates of antiviral and steroid therapy were reported in both groups with suggestion of greater benefit in patients with combined steroid and tocilizumab treatment. There was no difference in serious adverse events (tocilizumab, 15.2% and placebo, 19.7%). These results suggest that patients with moderate to severe COVID-19 benefit from

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