COVID-19 Evidence Digest 12/24/20

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The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Moderna COVID-19 Vaccine (MMWR)

Bottom Line: The Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Moderna COVID-19 vaccine in persons aged ≥18 years for the prevention of COVID-19.

Details: On December 18, 2020, the FDA issued an Emergency Use Authorization (EUA) for the Moderna COVID-19 vaccine. The Advisory Committee on Immunization Practices (ACIP) performed a systematic review of available data, and used the GRADE approach to assess the certainty of evidence for outcomes related to the vaccine, rated on a scale of 1 (high certainty) to 4 (very low certainty). The evidence for the Moderna COVID-19 vaccine was primarily informed by one large, randomized, double-blind, placebo-controlled Phase III clinical trial that enrolled approximately 30,000 participants aged 18–95 years (median = 52 years). From the GRADE evidence assessment, the level of certainty for the benefits of the Moderna COVID-19 vaccine was type 1 (high certainty) for the prevention of symptomatic COVID-19. Evidence was type 2 (moderate certainty) for the estimate of prevention of COVID-19–associated hospitalization and type 4 (very low certainty) for the estimates of prevention of asymptomatic COVID-19 infection and all-cause death. Systemic adverse reactions were more commonly reported after the second dose than after the first dose and were more frequent and severe in persons aged 18–64 years than in those aged ≥65 years. Most local and systemic adverse reactions occurred within the first 1–2 days after vaccine receipt and resolved in a median of 2–3 days. The frequency of serious adverse events observed was low in both the vaccine (1.0%) and placebo (1.0%) recipients and without meaningful imbalances between the two groups. Evidence was type 2 (moderate certainty) for the estimate of serious adverse events and type 1 (high certainty) for the estimate of reactogenicity. ACIP determined that COVID-19 is a major public health problem and that use of the Moderna COVID-19 vaccine is a reasonable and efficient allocation of resources.

Key Takeaways:

- ACIP performed a systematic review of available data on the Moderna COVID-19 vaccine, and determined that use of the vaccine in persons aged ≥18 years is a reasonable and efficient allocation of resources.
- Systemic adverse reactions were more commonly reported after the second dose of vaccine, and mostly occurred 1-2 days after vaccination and resolving after 2-3 days.
- Advancing health equity will require efforts to identify and reduce access-related barriers to vaccination, as well as engagement with groups who experience disproportionate COVID-19–related morbidity and mortality.

REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19 (NEJM)

Bottom Line: In this ongoing, double-blind, phase 1-3 trial of non-hospitalized patients with COVID-19, the REGN-COV2 antibody cocktail reduced viral load through day 7.

Details: This is an interim analysis of an ongoing, double-blind, phase 1-3 trial of non-hospitalized patients with COVID-19. It investigates a combined cocktail (REGN-COV2) of two human neutralizing monoclonal antibodies against severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) spike protein. Patients (n=275) were randomly assigned (1:1:1) to receive placebo (n=93), 2.4 g of REGN-COV2 (n=92), or 8.0 g of REGN-COV2 (n=90). Patients were eligible for randomization, if they tested positive of COVID-19 within the previous 72 hours. Main end points included 1) time-weighted average change in viral load from baseline day 1 through day 7 and 2) percent of patients with one or more COVID-19 related medical visit through day 29. The least-square mean difference (combined RegN-COV2 vs placebo) doses in the time-weighted average change in viral load from day 1 through day 7 was -0.56 log10 copies per milliliters (95% CI -1.02 to -0.11) and -0.41 log10 copies per milliliter (95% CI -0.71 to -0.10) among patients who were serum antibody-negative at baseline, and the full study population, respectively. A total of 6% of the placebo group and 3% of the combined REGN-COV2 dose group had one or more COVID-19 related medical visit (difference, -3 percentage points; 95% CI, −16 to 9). A larger difference was seen among the patients who were serum antibody-negative at baseline, however the difference was not statistically significant (6% REGN-COV2 dose group vs 15% placebo, 9 percentage points; 95% CI, −29 to 11). Percentage of patients with infusion-related or adverse reactions was similar in the treatment and control groups.

Key Takeaways:

- In this ongoing, double-blind, phase 1-3 trial of non-hospitalized patients with COVID-19, the REGN-COV2 antibody cocktail reduced viral load through day 7.
- There was no statistically significant difference in the clinical outcome, that is, the percentage of patients reporting at least one medically attended visit through day 29 in the combined REGN-COV2 group compared to the placebo group.
- The percentage of patients with infusion-related or adverse reactions was similar in the treatment and control groups.

Safety and Immunogenicity of SARS- CoV-2 mRNA-1273 Vaccine in Older adults (NEJM)
Bottom Line: The Moderna mRNA-1273 vaccine is likely to be as safe and effective in older adults (56+) as it is in younger adults (18-55).

Details: The phase 1 trial of Moderna's mRNA-1273 vaccine was expanded to include adults over 55 to determine safety and immune response. The results were stratified by age: 56-70 and 71+. Doses of 25 ug or 100 ug were used (the current approved dose is 100 ug) with a schedule of 2 shots 28 days apart. There were 10 patients in each age/dose group (total 40 patients). No serious adverse events were reported through nearly 2 months of follow up. Solicited adverse events included headache, fatigue, myalgia (muscle pain), chills, pain or redness at the injection site. These adverse events were more severe and more common after the second dose of the vaccine and tended to occur the day of vaccination or the day after and to resolve quickly. Binding and neutralizing antibody levels were highest in the patients receiving the 100 ug dose and were higher than in unvaccinated patients who had recovered from COVID-19. Binding and neutralizing antibody levels were similar among 56-70 and 71 + year olds as compared to 18- 55 year olds. Strong T cell (CD4 helper Th1) response was noted to the 100 ug dose in 56-70 and 71 + year olds.

Key Takeaways: In a small sample of patients the Moderna mRNA-1273 vaccine was well tolerated and lead to a robust antibody and T cell immune response. The antibody levels in 56-

70 and 71 + year old patients receiving the 100 ug dose of the vaccine were comparable to the antibody response in younger patients.

Racial Bias in Pulse Oximetry Measurement (NEJM)

Bottom Line: Among Black patients, pulse oximetry may not be an accurate measure of oxygen levels in the blood when administering oxygen and may increase the risk of hypoxemia.

Details: Supplemental oxygen is often used as a medical therapy and the amount administered is usually determined by a pulse oximetry (measures oxygen levels in a patient). However, its use has been questioned since the technology was not originally tested in a racial diverse population. Thus, this study examined racial differences in oxygen saturation in two cohorts: adult inpatients receiving supplemental oxygen and patients at intensive care units (ICUs). Participants included 1,609 inpatients adults (1,333 White and 276 Black) receiving supplemental oxygen and 8,392 adults (7,342 White and 1,050 Black) in ICUs. The study included measures of pulse oximetry (non-invasive way of indirectly measuring oxygen levels in the blood) and arterial oxygen saturation in arterial blood gas (an invasive method which directly measures oxygen and carbon dioxide levels in the blood) for measures of oxygen saturation. The main outcome measure was occult hypoxemia, which is when arterial oxygen saturation is less than 88% but pulse oximetry oxygen saturation is between 92% and 96%. Among the inpatient cohort, the rates of occult hypoxia was significantly higher among Blacks compared to Whites (11.7% vs. 3.6%, respectively). Similar results were found in the ICU cohort (17% among Blacks vs. 6.2% among Whites). The study notes that not all Black patients in the cohorts had occult hypoxemia. However, the use of pulse oximetry to determine oxygen level and amount of oxygen to be administered, may be increasing Black patients' risk of hypoxemia. The discrepancy in oxygen saturation measurements among Blacks need to be taken into consideration when providing oxygen to ensure they are getting the right amount

Key Takeaways:

- Pulse oximetry is not as accurate as arterial blood gas measurements in determining oxygen levels in the blood, particularly among Black patients.
- Pulse oximetry was originally developed in populations that were not racially diverse and thus may be contributing to racial bias in pulse oximetry measurements
- Pulse oximetry should be paired with other clinical and patient data to determine proper supplemental oxygen levels, to decrease risk of hypoxia among Black patients.

Severe Covid-19 (NEJM)

A COVID-19 case vignette, highlighting the clinical problem, symptom timeline, current evidence supporting possible treatment strategies (e.g. respiratory management, endotracheal intubation, ventilator management, therapies and supportive care) and the author's clinical recommendation. A review of formal guidelines are also included where they exist.