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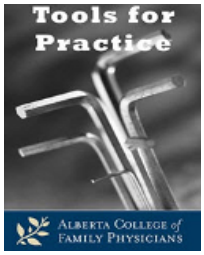
COVID-19 Rapid Reviews

Along with regular Tools for Practice, the PEER team will be writing rapid reviews to address COVID-19 topics relevant for primary care. The evidence is changing rapidly and it is possible that as you read this, new evidence will already be available. We will try our best to stay in front and keep you up-to-date during these challenging times.



Antivirals for COVID-19

Clinical Question: Do treatments such as remdesivir or other anti-virals change patient outcomes in COVID-19 patients?

Bottom Line: To date, published RCTs have not demonstrated benefit of treating COVID-19 patients with remdesivir, lopinavir-ritonavir or oseltamivir. There are signals of potential benefits from one interim analysis of remdesivir and non-statistically different results, but more research is needed. Full publication of studies and ongoing trials will help to answer this question.

Evidence:

- Focusing on randomized, controlled trials (RCTs) as cohort studies of treatments can be misleading.
    - Currently >300 RCTs evaluating different COVID-19 treatments underway.[1]
- Remdesivir:
    - Industry supported, double-blind, placebo-controlled trial of 237 admitted (non-ventilated) patients with confirmed COVID-19, oxygen saturation ≤94% and radiographic pneumonia in Wuhan, China.[2] Patients were ~66 years old, and received concomitant antibiotics (~90%), steroids (~70%), or anti-virals (18%).
        - Outcomes:
            - 28-day mortality: 14% versus 13% (placebo): no difference.
            - Duration of mechanical ventilation (days): 7 versus 15.5 (placebo): not statistically different.
            - Time to clinical improvement: 21 versus 23 days (placebo) not statistically different.

            - Adverse events leading to medication discontinuation: 12% versus 5% (placebo), number needed to harm=15.
        - Limitations:
            - Study ended early (sample size not achieved) due to "outbreak being controlled in Wuhan".
            - Baseline imbalances suggest inadequate allocation concealment.
    - Double-blind, placebo-controlled trial of remdesivir. Information from clinical trial registry[3] and interim results available via media release;[4] 1063 hospitalized patients, oxygen saturation ≤94% and radiographic pneumonia.
        - Median time to recovery: 11 days versus 15 days (placebo), statistically different.
        - Mortality (unknown time frame): 8% versus 11.6% (placebo), not statistically different.
    - Another pharmaceutical company press release reported similar outcomes between 5 and 10 days of remdesivir but did not report whether treatment improved outcomes compared to no remdesivir.[5]
    - Other RCTs ongoing.[6-8]
- Lopinavir-Ritonavir (Kaletra®):
    - Open-label RCT of 199 admitted COVID-19 positive patients with Sp02 <94% in Wuhan, China.[9] Patients randomized to lopinavir-ritonavir for 14 days or usual care. Patients were ~58 years and 60% were men.
        - Outcomes:
            - 28-day mortality: 19% lopinavir-ritonavir, 25% usual care: not statistically different.
            - Time to clinical improvement: no difference: 15 versus 16 days.
            - Length of ICU stay shorter: 6 versus 11 days (control), not quite statistically different.
            - Adverse events leading to medication discontinuation: 14%.
        - Limitations: enrollment suspended when remdesivir became available for clinical trials.
- Oseltamivir:
    - No RCTs in COVID-19 or other coronaviral infections.[10]

Context:

- Remdesivir is currently only available in Canada through clinical trials.[11]
- Guidelines do not recommend any COVID-19 specific antiviral treatments.[12,13]

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Disclosures:

Authors do not have any conflicts of interest to declare.

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