Remdesivir for patients with COVID-19

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1 Remdesivir is an antiviral drug with activity against an array of RNA viruses

Remdesivir is an intravenous inhibitor of the viral RNA-dependent RNA polymerase with in vitro and in vivo activity against Middle East respiratory syndrome coronavirus, severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and SARS-CoV-2. In Canada, it is authorized and available through Health Canada for patients (\geq 12 yr of age and weighing \geq 40 kg) with coronavirus disease 2019 (COVID-19) who require oxygen.

2 Remdesivir has been tested as a treatment for COVID-19 in 2 large clinical trials

There are 4 published randomized controlled trials (RCTs) that evaluated remdesivir for treatment of COVID-19.^{1,2,4,5} The 2 largest were the Adaptive Covid-19 Treatment Trial (ACTT-1), a placebo-controlled RCT involving 1062 patients,¹ and Solidarity, an open-label RCT that compared treatment with remdesivir to standard of care in 6838 patients.⁵

Remdesivir may reduce recovery time but does not reduce mortality

The ACTT-1 found that median time to clinical improvement was shortened from 15 to 10 days, with the greatest improvement seen in patients requiring low-flow oxygen. The trial did not find a difference in mortality (hazard ratio 0.73, 95% confidence interval [CI] 0.52–1.03), although it was not powered to do so.¹ Solidarity failed to show a mortality benefit (rate ratio 0.95, 95% CI 0.81–1.11) and also did not show a benefit in the prespecified secondary outcomes of ventilation or time to discharge.⁵

4 Remdesvir does not help critically ill patients

Subgroup analyses from ACTT-1 and Solidarity showed that remdesivir conferred no benefit in patients who were intubated or on extracorporeal membrane oxygenation. ^{1,5} Although less certain, there did not appear to be significant benefit for patients on high-flow oxygen. ^{1,5}

5 Data for adverse events are limited but include hepatotoxicity and hypersensitivity reactions

Patients with elevated levels of liver enzymes or a glomerular filtration rate less than 30 mL/min were excluded from the published trials. ^{1,2,4,5} Drug-induced liver injuries have been reported, ⁶ and anaphylaxis and infusion-related reactions can occur. ¹

References

- Beigel JH, Tomashek KM, Dodd LE, et al.; ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19: final report. N Engl J Med 2020;383:1813-26.
- Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020;395:1569-78.
- Update on remdesivir: continued monitoring. Ottawa: Health Canada; modified 2020 Nov. 26. Available: www.canada.ca/en/ health-canada/services/drugs-health-products/covid19-industry/ drugs-vaccines-treatments/remdesivir-update.html (accessed 2020 Dec. 8).
- Spinner CD, Gottlieb RL, Criner GJ, et al.; GS-US-540-5774 Investigators. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. *JAMA* 2020;324:1048-57.
- WHO Solidarity Trial Consortium; Pan H, Peto R, Henao-Restrepo A-M, et al. Repurposed antiviral drugs for COVID-19: interim WHO Solidarity Trial results. N Engl J Med 2020 Dec. 2 [Epub ahead of print]. doi: 10.1056/NEJMoa2023184.
- Carothers C, Birrer K, Vo M. Acetylcysteine for the treatment of suspected remdesivir-associated acute liver failure in COVID-19: a case series. *Pharmacotherapy* 2020;40:1166-71.

Competing interests: Peter Wu is a member of and Andrew Morris chairs the Ontario COVID-19 Clinical Practice Guideline working group, a volunteer provincial working group aimed at providing consensus-based, evidence-informed treatment guidelines for COVID-19. No other competing interests were declared.

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