Treatment of COVID-19 with remdesivir

Remdesivir is an antiviral drug developed by Gilead Sciences, Inc. for the treatment of Ebola virus infection. It is known to have activity in vitro and in animal models against other viruses including SARS-CoV and MERS-CoV.[1]

Early in the coronavirus pandemic, remdesivir was used to treat a small, nonrandomized group of hospitalized COVID-19 patients.[2] Thirty-five patients with SARS-CoV-2 pneumonia in an Italian hospital were given 10 days of intravenous remdesivir. At the 28-day follow-up, the clinical condition of 88% of these patients had improved. Another paper describes the status of patients using remdesivir as part of a compassionate-use program.[3] The patients involved were hospitalized for severe COVID-19. Most patients received a 10-day treatment; at the 28-day follow-up, 84% of the 61 patients showed clinical improvement.

Full or partial results are available for 4 randomized trials using remdesivir. In all trials, the dose of remdesivir used was 200 mg on day 1 followed by 100 mg daily. The first published trial selected patients with laboratory-confirmed SARS-CoV-2, pneumonia and oxygen saturation ≤94% on room air.[4] Patients were treated with 10 days of intravenous remdesivir or placebo and assessed for 28 days. No overall clinical improvement, based on a 6-point ordinal scale, was seen in the treated patients compared to the control group. The study was stopped early after only 237 patients had been enrolled, since the infection rate in the recruiting area declined.

An open-label, randomized, multicentre trial enrolled 397 patients and compared 5-day treatment to 10-day treatment with intravenous remdesivir.[5] Adult patients with pneumonia, oxygen saturation ≤94% on room air, or requiring supplemental oxygen and confirmed presence of the virus were enrolled. The patients' clinical status on a 7-point ordinal scale was assessed at 14 days. After adjusting for baseline differences, the proportion of patients who showed clinical improvement was similar in both groups (64% vs. 54%).

The Adaptive COVID-19 Treatment Trial (ACTT) is a large, multicentre, randomized, placebo-controlled trial enrolling hospitalized patients positive for SARS-CoV-2 with oxygen saturation ≤94% on room air, or requiring supplemental oxygen, mechanical ventilation or other invasive support. Preliminary data describing remdesivir treatment versus placebo have been published.[6] Patients (n=1059) with evidence of lower respiratory tract involvement received up to 10 days of intravenous remdesivir or placebo. The time to recovery, defined according to an 8-point scale, was 11 days with remdesivir compared to 15 days with placebo (rate ratio for recovery, 1.32; 95% CI, 1.12 to 1.55; P<0.001). The frequency of reported adverse effects was comparable in both groups.

Another similar multicentre trial using remdesivir has completed enrolment, and results have been published.[7] In this open-label trial, patients (n=596) with moderate COVID-19 pneumonia (pulmonary infiltrates, oxygen saturation >94% on room air) were randomized to 5 or 10 days of treatment or standard care. Patients were assessed at day 11 using a 7-point ordinal scale. Compared to standard care, there was no significant difference in clinical status in patients receiving 10 days' treatment. However, clinical status was improved in the 5-day group, but the difference is of uncertain clinical significance. Nausea, hypokalemia and headache were more common in patients receiving remdesivir.

Although not conclusive, the trials suggest remdesivir has few adverse effects and that intravenous administration may shorten the time to recovery by a few days. Full publication of results of the ongoing trials is needed to confirm the effectiveness of remdesivir.

In some countries (European Union, Japan, UK, US), remdesivir has been given expedited approval based on existing data. In Canada, remdesivir was previously available only through the Special Access Program, but has recently been approved with conditions for use in COVID-19 patients who have severe pneumonia and require supplemental oxygen.[8] Current Public Health Agency of Canada guidance on the management of COVID-19 infection, endorsed by the Canadian Critical Care Society and the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada), state that use of remdesivir may be considered, but preferably as part of a randomized clinical trial.[9]

CPhA supports all efforts made by Health Canada to assess the efficacy of the drug in treating COVID-19.

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