Treatment of COVID-19 with remdesivir

Summary:
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] Trials suggest that IV administration of remdesivir may shorten the time to recovery from COVID-19 and may reduce mortality. It has few adverse effects.

Discussion:
Results are available for 5 randomized trials that have evaluated remdesivir 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.[2] Patients were treated with 10 days of IV 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- to 10-day treatment with IV remdesivir.[3] Adult patients with pneumonia, oxygen saturation ≤94% on room air, or requiring supplemental oxygen and a confirmed presence of SARS-CoV-2 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) was a large, multicentre, randomized, placebo-controlled trial that enrolled hospitalized patients positive for SARS-CoV-2 with oxygen saturation ≤94% on room air or requiring supplemental oxygen, mechanical ventilation, or other invasive support. Patients (n=1062) with evidence of lower respiratory tract involvement received up to 10 days of IV remdesivir or placebo. Preliminary data suggested a reduced time to recovery with remdesivir.[4] When follow-up was completed, the median time to recovery, defined according to an 8-point scale, was 10 days with remdesivir compared to 15 days with placebo (rate ratio for recovery, 1.29; 95% CI, 1.12 to 1.49; P<0.001).[5] All-cause mortality at day 29 was reduced in the remdesivir group (11.4% vs. 15.2%), but the difference was not statistically significant. The frequency of adverse effects was comparable in both groups.

In another similar multicentre, open-label trial using remdesivir, patients (n=584) with moderate COVID-19 pneumonia (pulmonary infiltrates, oxygen saturation >94% on room air) were randomized to 5 or 10 days of remdesivir or standard care.[6] 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 of treatment. 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.

Preliminary results from the World Health Organization (WHO) Solidarity trial evaluated 10 days of remdesivir (n=2743) or standard care (n=2708) in hospitalized patients with diagnosed COVID-19.[7] The primary outcome was in-hospital mortality, and secondary endpoints were initiation of ventilation and duration of hospitalization. There were no statistically significant differences in death, ventilation initiation or time to discharge.

In Canada, remdesivir is approved with conditions for use in COVID-19 patients who have severe pneumonia and require supplemental oxygen.[8] Public Health Agency of Canada guidance endorsed by the Canadian Critical Care Society and the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada) states that use of remdesivir may be considered for COVID-19 infection, preferably as part of a randomized clinical trial.[9] The Ontario COVID-19 Antimicrobial Therapy Guideline Standing Committee suggests the preferred use of remdesivir is in clinical studies, although it may be considered in moderately ill, hospitalized patients,[10] while the WHO and the BC COVID-19 Therapeutics Committee recommend using remdesivir only in clinical trials at this time.[11,12]

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