Should remdesivir be used for COVID-19?

This write-up summarises a rapid evidence review of remdesivir as a potential treatment for patients with COVID-19. The information may be revised as new evidence emerges.

Background

Remdesivir is a novel nucleotide analog prodrug (broad spectrum antiviral). It was developed by Gilead Sciences as a treatment for Ebola and Marburg virus infections, though it has subsequently shown reasonable antiviral activity against more distantly related viruses including MERS-coronavirus. Possible activity against other coronaviruses including COVID-19 infection is predicted. Remdesivir is not currently approved to treat any condition by any regulatory agencies, including the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA).

Clinical evidence

Published evidence for remdesivir to treat COVID-19 infection is limited and concludes that remdesivir requires further investigation:

- A case report described a patient in the USA diagnosed and admitted to hospital with COVID-19. On day 6 of hospitalisation the patient required supplemental oxygen and on the evening of day 7 intravenous infusion of remdesivir was started. On day 8 the patient’s condition improved and supplemental oxygen was discontinued. During hospitalisation the patient also received other medicines such as vancomycin and cefepime.

- Review articles identified remdesivir as one of several possible treatments for COVID-19. Lu (2020) stated that remdesivir “may be the best potential drug for the treatment of [COVID-19]” given the drug had completed the clinical program for Ebola virus infection with relatively complete safety and pharmacokinetics data in humans.

A number of trials have been registered and are in planning or active recruitment with data anticipated to mature in the near future.

Table 1: Ongoing or planned studies for remdesivir in patients with COVID-19

<table>
<thead>
<tr>
<th>Study identifier</th>
<th>Study Design</th>
<th>Intervention</th>
<th>Comparator(s)</th>
<th>Date of primary completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT04257656</td>
<td>DB, SC*, phIII, RCT</td>
<td>remdesivir</td>
<td>placebo</td>
<td>May 2020</td>
</tr>
<tr>
<td>NCT04252664</td>
<td>DB, SC*, phIII, RCT</td>
<td>remdesivir</td>
<td>placebo</td>
<td>April 2020</td>
</tr>
<tr>
<td>NCT04292899</td>
<td>MC†, OL, phIII, RCT</td>
<td>remdesivir</td>
<td>standard of care</td>
<td>May 2020</td>
</tr>
<tr>
<td>NCT04292730</td>
<td>MC†, OL, phIII, RCT</td>
<td>remdesivir</td>
<td>standard of care</td>
<td>May 2020</td>
</tr>
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<td>NCT04280705</td>
<td>DB, MC†, phIII, RCT</td>
<td>remdesivir</td>
<td>placebo</td>
<td>April 2020</td>
</tr>
<tr>
<td>NCT04315948</td>
<td>MC, OL, phIII, RCT</td>
<td>remdesivir, lopinavir/ritonavir, lopinavir/ritonavir + interferon β-1A</td>
<td>standard of care</td>
<td>March 2023</td>
</tr>
</tbody>
</table>

Abbreviations: DB, double blind; MC, multicenter; OL, open label; phIII, phase III; RCT, randomised controlled trial; SC, single centre.
* China; † Study has sites in Singapore; ‡ France

In addition, the World Health Organization (WHO) has also recently announced that it will be conducting a large, global trial (SOLIDARITY) on the four most promising therapies identified to date to treat COVID-19: remdesivir; chloroquine and hydroxychloroquine; ritonavir/lopinavir; and ritonavir/lopinavir + interferon beta. The following countries are currently included in the trial: Argentina, Bahrain, Canada, France, Iran, Norway, South Africa, Spain, Switzerland and Thailand. More countries are likely to be included over time. The trial completion date has not been released yet.
Recommendations from professional bodies

WHO has yet to recommend any specific antiviral medicine to prevent or treat COVID-19. This view is also shared locally by the Singapore National Centre for Infectious Disease (NCID).16,17 Interim clinical guidance from the Centers for Disease Control and Prevention (CDC, USA) on the management of coronavirus identifies remdesivir as an investigational therapeutic. Remdesivir has been administered via compassionate use to some patients with COVID-19 in the USA and trials are underway; however, the CDC notes that there is no available data from RCTs in humans to support recommending any investigational therapeutics at this time.18 The seventh edition of the China National Health Commission (NHC) clinical guidance for COVID-19 diagnosis and treatment does not specifically refer to remdesivir.19

Conclusion

Given the current lack of existing evidence, no firm scientific conclusion can be made on the efficacy and safety of remdesivir to treat COVID-19 infection. However, several large, global clinical trials (some of which have sites in Singapore) are likely to report results in the months ahead and the findings of these will determine whether remdesivir should be used more widely in this setting.

References

1. Agostini ML, Andres EL, Denison MR et al., (2018) Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease MBio Mar-Apr 9(2)