

## BET 1: THE ROLE OF REMDESIVIR IN COVID-19 INFECTION

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### ABSTRACT

A short-cut review of the available medical literature was carried out to establish whether remdesivir was an effective treatment for patients with confirmed COVID-19 infection. After abstract review, five papers were found to answer this clinical question using the detailed search strategy. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these papers are tabulated. It is concluded that despite some recent promising studies, further well-designed and larger trials are needed to answer this specific question.

### CLINICAL SCENARIO

A 55-year-old man presents to your ED with shortness of breath and fever for a few days. A nasopharyngeal swab confirms a COVID-19 infection. As an evidence-based doctor, you have been pretty active at following emerging potential treatments and wonder if treatment with remdesivir would improve your patient's clinical course.

### THREE-PART QUESTION

In [adult patients with confirmed COVID-19 infection] does treatment with [remdesivir] improve [clinical outcome]?

### SEARCH STRATEGY

OVID MEDLINE 1946 to June 19 2020

[Coronavirus.exp OR coronavirus.mp OR COVID-19.mp OR sars-cov-2.mp OR SARS\$.mp OR coroa\$.mp] AND [remdesivir.mp OR GS-5734.mp]

Search limited to English language and humans

75 Papers found of which three were deemed relevant

Embase 1996 to 2020 week 25

[Coronavirus.mp OR coronavirinae.exp OR COVID-19.mp OR SARS coronavirus.exp OR sars-cov-2.mp OR corona\$.mp OR SARS\$.mp] AND [remdesivir.mp OR remdesivir.exp OR GS-5734.mp]

Search limited to English Language and humans

422 papers found of which five were deemed relevant

Table 1 below summarises the relevant included studies after duplicates were excluded.

### DISCUSSION

Although several approved drugs have shown some antiviral activity against SARS-CoV-2 in in vitro settings, there are no antiviral therapies of proven benefit in treating patients infected with this emerging infection. Remdesivir is an adenosine prodrug that inhibits all human and animal coronaviruses in vitro so it was felt it would show some promising results in human trials.

This is a rapidly evolving picture with ongoing clinical trials at time of publication.

Several smaller trials<sup>1-3</sup> have been published to date, but two larger trials

### Clinical bottom line

Further larger-scale and well-designed clinical trials are needed to establish the exact role of remdesivir in the treatment of COVID-19 infections.

however merit further attention and scrutiny.

Wang *et al*<sup>4</sup> were unable to demonstrate any statistically significant clinical benefits for remdesivir but failed to complete full recruitment as set out at start of the trial due to the end of the outbreak. At the time of review and publication, we only had access to the preliminary report for the trial by Beigel *et al*,<sup>5</sup> the largest trial to date. The authors' conclusions were that remdesivir was of benefit for in-patients requiring supplemental oxygen but also cautioned that in view of the high mortality rate despite its use, remdesivir was unlikely to be sufficient alone.

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**Competing interests** None declared.



Table 1 Relevant papers

Author, date, country	Patient group	Study type	Outcomes measured	Results found	Study weaknesses
S Antinori <i>et al.</i> , Italy <sup>1</sup> 2020	35 patients over 18 years of age with confirmed COVID-19 infection requiring mechanical ventilation or had SpO <sub>2</sub> ≤94% on room air or national early warning score of ≥4 18 patients were recruited in the intensive care unit and 17 in the infectious disease ward Patients were allowed to continue their other treatments (including hydroxychloroquine) but had to discontinue other antivirals 37% discontinued the intervention because of side effects	Open-label prospective study	Hospitalisation status as primary outcome Side effects as secondary outcomes	At day 28, 82.3% of patients on the infectious disease ward were discharged and 5.9% had died 33.3% were discharged from intensive care and 44.4% had died with 16.7% still mechanically ventilated Hepatotoxicity in 42.8% as most common side effect	Presence of confounding factors No control group Open-label compassionate single-centre trial Small size cohort
J Grein <i>et al.</i> , 2020 <sup>2</sup>	53 patients with confirmed COVID-19 infection with SpO <sub>2</sub> ≤94% or who received oxygen support received at least one dose of remdesivir as intervention	Multicentre prospective study	Improvement in oxygen support, hospital discharge and adverse events	At day 28, the cumulative incidence of improvement was 84% (95% CI 70 to 99) Overall mortality was 0.56 per 100 hospitalisations (95% CI 0.14 to 0.97) 23% of patients developed severe adverse events	No clearly pre-defined endpoints Open-label compassionate trial Small size cohort No control group Short duration of follow-up
J Goldman <i>et al.</i> , USA 2020 <sup>3</sup>	Patients with COVID-19 infection with SpO <sub>2</sub> ≤94% or receiving supplemental oxygen therapy and radiological evidence of pneumonia 200 patients received remdesivir for 5 days and 197 for 10 days Patients requiring ventilatory support at baseline were excluded	Randomised, open-label multicentre trial	Clinical status at day 14 based on an ordinal scale Adverse events as secondary outcomes	After adjustment for clinical status, both patient groups had similar outcome at day 14 (p=0.14) 70% of patients in the 5-day group experienced adverse events vs 74% in the 10-day group	No placebo control group Results cannot be extrapolated to critically ill patients
J Beigel <i>et al.</i> , 2020 <sup>4</sup>	1063 patients with COVID-19 infection and confirmed lower respiratory tract involvement 541 randomised to remdesivir and 522 to placebo Patients were allowed to receive other supportive treatments	Multicentre double-blind, randomised placebo-controlled trial	Time to recovery Serious adverse events	The intervention group had a shorter recovery time (median days 11 vs 15 in the placebo group) Rate ratio 1.32 (95% CI 1.12 to 1.55, p<0.001) Mortality in the intervention group was 7.1% vs 11.9% HR 0.70 (95% CI 0.47 to 1.04) Serious adverse events occurred in 21.1% in the intervention group vs 27% in the placebo one	Potential confounders Unclear what was defined as lower respiratory involvement Full statistical analysis still ongoing (preliminary report)
Wang <i>et al.</i> , China 2020 <sup>5</sup>	237 patients with COVID-19 pneumonia confirmed with imaging with SpO <sub>2</sub> ≤94% or PaO <sub>2</sub> /FIO <sub>2</sub> ≤300 mm Hg 158 assigned to intervention and 79 to placebo (2:1 randomisation) Patients allowed concomitant use of anti-retrovirals, corticosteroids and interferons	Multicentre double-blind, randomised placebo-controlled trial	Clinical improvement Adverse events	Intervention was not found to be linked to improvement (median 21 days vs 23 in placebo) HR 1.23 (95% CI 0.87 to 1.75) 28-day mortality 14% vs 13%, difference 1.1% (95% CI -8.1 to 10.3) 66% patients in the intervention group displayed adverse events vs 64% in the control group	Potential confounders Intervention seems to have been started relatively late Underpowered as the study was terminated early

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