South African National Department of Health
Brief Report of Rapid Review
Component: COVID-19

TITLE: REMDESIVIR FOR COVID-19: EVIDENCE REVIEW OF THE CLINICAL BENEFIT AND HARM

Date: 15 FEBRUARY 2022 *(sixth update of the initial 16 April 2020 rapid review report)*

Key findings

- We conducted a rapid review of available clinical evidence about use of remdesivir, with or without other medicines, for patients with COVID-19.
- We identified a systematic review including eleven RCTs (n=8137) which includes the latest trial data in an cohort of ambulatory patients (www.covid-nma.com).
- Remdesivir is likely to make little or no difference to all-cause mortality at 14 to 28 days, when initiated in hospitalised patients (RR 0.90 95% confidence interval (CI) 0.73 to 1.11, six trials, n = 7553, *moderate certainty evidence due to imprecision).*
- One study in ambulatory patients found a reduction in the composite end-point of hospitalisation and death at 28 days (RR 0.28 CI 0.1 to 0.74), although both treatment and placebo arms recorded no deaths by 28 days.
- Remdesivir is not associated with an increased risk of adverse events compared with placebo (RR 1.00 95% CI 0.91 to 1.11, 4 trials, n = 2752, *low certainty evidence* due to risk of bias in included trials and unexplained heterogeneity).
- We identified no reports of clinical trials with remdesivir specifically conducted in paediatric patients with COVID-19, but did note that the trial conducted in ambulatory patients included a small number of patients (n=8) aged between 12 and 18 years.

NEML MAC ON COVID-19 THERAPEUTICS RECOMMENDATION:

1. NON-HOSPITALISED PATIENTS

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option or to use the alternative **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
		X			

Recommendation: The NEML MAC on COVID-19 therapeutics suggests that remdesivir not be used for the treatment of non-hospitalised patients with COVID-19.

Rationale: Remdesivir reduced hospitalisation rates in a single trial that included unvaccinated patients only; the effects in vaccinated patients, or those with previous SARS-CoV-2 infection are unknown. In addition, the use of an intravenous treatment in ambulatory care settings remains impractical, access to the medicine is limited, and it remains expensive.

Level of Evidence: RCTs of low to moderate quality

2. HOSPITALISED PATIENTS:

Type of recommendation	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option or to use the alternative **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
		X			

Recommendation: The NEML MAC on COVID-19 therapeutics suggests that remdesivir not be used for the treatment of hospitalised patients with COVID-19.

Rationale: Remdesivir has not demonstrated a significant effect on pre-specified clinically important outcomes such as mortality or need for ventilation. In addition, access to the medicine is limited and it remains expensive.

Level of Evidence: RCTs of low to moderate quality

(Refer to appendix 4 and appendix 5 for the evidence to decision framework)

NEML MAC ON COVID-19 THERAPEUTICS: Marc Blockman, Karen Cohen, Renee De Waal, Andy Gray, Tamara Kredo, Gary Maartens, Jeremy Nel, Andy Parrish *(Chair),* Helen Rees, Gary Reubenson *(Vice-chair).*

Note: Due to the continuous emergence of new evidence, the rapid review will be updated if and when more relevant evidence becomes available. As of 3 February 2022, there are 44 clinical trials investigating the role of remdesivir (monotherapy or with standard of care) treatment of COVID-19 are registered on the International Clinical Trials Registry Platform https://www.who.int/clinical-trials-registry-platform

PROSPERO registration: CRD42021286710

BACKGROUND

SARS-CoV-2, like other coronaviruses, is an enveloped positive-stranded RNA virus. Remdesivir is an inhibitor of the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp), which is essential for viral replication. Remdesivir has broad-spectrum activity against members of several virus families, including filoviruses (e.g., Ebola) and coronaviruses (e.g., SARS-CoV and Middle East respiratory syndrome coronavirus [MERS-CoV]) and has shown prophylactic and therapeutic efficacy in nonclinical models of these coronaviruses.[1,2,3] Remdesivir has also demonstrated activity against SARS-CoV-2 *in vitro*.[2] The medicine has been granted regulatory approval for remdesivir as treatment for COVID-19 in a number of countries, including South Africa (SAHPRA registration number: 55/20.2.8/0458), and is recommended for treatment in a number of international protocols.[4]

RESEARCH QUESTION: Should remdesivir be used to treat hospitalised or non-hospitalised patients with confirmed COVID-19?

METHODS

We searched the Cochrane COVID-19 trials database and the Cochrane Library electronic databases on 25 January 2022 for RCTs and systematic reviews. PubMed was also searched for systematic reviews published since June 2021. Details of each search are provided in Appendix 1.

Additionally the living systematic review of RCTs on www.covid-nma.com was reviewed and results included.

Eligibility criteria for review

Population: Patients with confirmed SARS-CoV-2 infection; no restriction to age or co-morbidity.

Intervention: Remdesivir, either alone or in combination with other medicines. No restriction on dose, frequency, or timing with respect to onset of symptoms/severity of disease.

Comparators: Standard of care or placebo.

Outcomes: Mortality; progression to hospitalisation; duration of hospitalisation; progression to requiring oxygen; progression to ICU admission; progression to mechanical ventilation; duration of ICU stay; clinical improvement on an ordinal scale at chosen time points; and time to clinical improvement; adverse reactions and adverse events.

Study design: Systematic reviews of randomised controlled trials; individual randomised controlled trials.

RESULTS

Table 1 summarises the main characteristics and outcomes of the included studies.

From the Cochrane trials database, 62 references were identified. Of these, 27 were not trial results, whereas a further 17 references were not studies involving remdesivir. Eighteen references were evaluated, and a further 7 were excluded (2 were abstracts only, one was not an RCT, another was only a protocol, 1 was not a remdesivir trial, 1 was not placebo-controlled, and 1 was a pre-print of a publication which was included in full and another did not report on the outcomes of interest).

Thus eleven publications of RCTs were reviewed in full. Four newly identified individual RCTs publications were included since the previous rapid review update (December 2020). [5-8]

In addition, a single systematic review of remdesivir was identified in the COVID-NMA database. The updated Cochrane-supported living review[9] comparing remdesivir against placebo, included 9 trials, all of which have been considered individually in this review. This analysis has now also separated out into remdesivir versus standard of

care (any duration), in non-hospitalised and hospitalised patients, and remdesivir 10 days' versus remdesivir 5 days' treatment in hospitalised patients.

One of the studies excluded from this review (as patients in both arms received remdesivir), was a double-blind, randomised, placebo-controlled trial comparing baricitinib plus remdesivir compared to remdesivir alone in hospitalised adults (≥18 years) with Covid-19 (ACTT-2).[10] Patients who received combination treatment with baricitinib plus remdesivir recovered a median of 1 day faster than patients who received remdesivir and placebo (median, 7 days vs. 8 days; rate ratio for recovery, 1.16; 95% confidence interval [CI], 1.01 to 1.32; P = 0.03 by log-rank test stratified according to actual baseline severity).

Baricitinib, in combination with remdesivir, was initially given FDA emergency use authorisation for hospitalised adults and children aged ≥2 years with COVID-19 who require supplemental oxygen, invasive mechanical ventilation, or ECMO. However, advice for use in children appears to have been extrapolated from studies in adults, as data regarding remdesivir (and baricitinib) use in children with COVID-19 are extremely limited.

NON-HOSPITALISED PATIENTS

Remdesivir 3 days compared to standard of care/placebo for mild disease in patients at risk of disease progression (One study, n= 562).[8]

All-cause mortality at day 14 to day 28

- There were no deaths in the treatment or placebo group at 28 days

Progression to hospitalisation

- Measured as a composite endpoint: COVID-19–related hospitalisation or death from any cause by day 28:
- Remdesivir 2 (0.7%); Placebo 15 (5.3%); Hazard ratio 0.13 (95% CI 0.03 to 0.59)
- As there were no deaths in the two groups, the results are based on hospitalisation events only

Duration of hospitalisation

- Not reported

Proportion with negative SARS-CoV-2 PCR on nasopharyngeal swab

- Not reported

Time to negative SARS-CoV2 PCR on nasopharyngeal swab

- Not reported

Progression to ICU admission

- Not reported

Progression to mechanical ventilation

- Not reported

Duration of ICU stay

- Not reported

Adverse reactions and adverse events

- Remdesivir 42.3%; Placebo: 46.3% (RR = 0.9 CI 0.75 to 1.09)

HOSPITALISED PATIENTS

The COVID-NMA living review[9] pooled data from six trials[5,12,13,15,16,17] (n=7553) conducted in hospitalised patients, comparing either 5 or 10 days' treatment with remdesivir to standard of care/placebo.

All-cause mortality at day 14 to day 28

- **Remdesivir 10 and 5 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19 (six studies):**
  The included studies showed no statistically significant impact: Hazard ratio 0.91 (95% CI 0.74 to 1.11). Six RCTs, 7553 patients.
- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19 (two studies)**

The included studies showed no significant difference: RR 1.16 (95% CI 0.71 to 1.87). Two RCTs,[13,14] 798 patients.

Time to negative SARS-CoV2 PCR on nasopharyngeal swab

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  2 trials,[7,16] 1094 patients. Hazard ratio 1.04 (95% confidence interval 0.83 to 1.31)
- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19**
  Not reported.

Progression to ICU admission

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  Not reported.
- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19**
  Not reported.

Progression to mechanical ventilation

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  In the Solidarity Trial,[12] remdesivir did not reduce initiation of ventilation in those not already ventilated at randomisation (295/2743 versus 284/2708 for remdesivir versus control respectively).
- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19**
  Not reported.

WHO Progression score level 7 or above

The COVID-NMA living review[9] did not report on need for mechanical ventilation specifically, but did report the composite outcome of mechanical ventilation, additional organ support, or death (WHO Progression score level 7 or above) at Day 28.

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  Based on 5 RCTs[5,7,13,15,16] and 2834 participants, the rate was lower in the remdesivir group (135 per 1000) versus 180 per 1000 in standard of care (RR 0.75; 95% CI 0.62 to 0.89).
- **Remdesivir 5 days compared to 10 days Moderate/Severe/Critical COVID-19**
  RR 1.72 (95% CI 1.17 to 2.52), based on 2 RCTs[13,14] and 798 patients. 146 per 1000 patients in the 5-day group and 85 per 1000 patients in the 10-day group.

Duration of ICU stay

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  Not reported.
- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19**
  Not reported

Adverse reactions and adverse events

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  RR 1.00 (95% CI 0.91 to 1.11). Four RCTs,[7,13,15,16] 2752 patients
- **Remdesivir 5 days compared to 10 days for mild/moderate/severe/critical COVID-19**
  RR 1.27 (95% CI 1.11 to 1.44), two RCTs,[13,14] 798 patients.

Duration of hospitalisation

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**
  Wang et al[7] reported median duration of stay of 25 days (IQR 16 to 38) in the remdesivir group, and 24 (IQR 18 to 36) in the placebo group, but reported no significant difference in length of hospital stay. Spinner et al[13] did not quantify this endpoint but stated that there were no significant differences between the remdesivir and standard of care groups. Beigel et al[15,] and Pan et al[12] did not report.
- **Remdesivir 5 days compared to 10 days Moderate/Severe/Critical COVID-19**
  Not reported.

Proportion with negative SARS-CoV-2 PCR on nasopharyngeal swab

Hospitalised patients

- **Remdesivir 10 days compared to standard of care/placebo for mild/moderate/severe/critical COVID-19**

This was only reported in two[7,16] of the included RCTs as incidence of viral negative conversion by day 7: 219 per 1.000 for the standard care group and 215 per 1.000 in the remdesivir group (RR 1.02, 95% CI (0.83 to 1.25)).

- **Remdesivir 5 days compared to 10 days moderate/severe/critical COVID-19**
  Not reported.

CONCLUSION

Our rapid review included a high quality, up-to-date systematic review with five included trials. Remdesivir has not demonstrated a statistically significant effect on mortality or other clinically important benefits or harms in hospitalised patients. The relative balance of benefits to cost, feasibility and equity underpin the decision not to suggest remdesivir use in the South African public sector context for hospitalised or non-hospitalised patients. Thus far, only one RCT has investigated remdesivir in high-risk outpatients. Remdesivir reduced the risk of hospitalisation, but as there were no deaths in either arm, the trial did not demonstrate an effect on mortality.

Reviewers: Shelley McGee (Ophthalmological Society of South Africa), Renee De Waal (Centre for Infectious Disease Epidemiology and Research, University of Cape Town).

Declaration of interests: SM is employed by the Ophthalmological Society of South Africa (OSSA) that is sponsored by various pharmaceutical and device companies for CPD activities, exhibition at conferences and advertising in SAOJ; RdW has no interests to declare.

Acknowledgements: Trudy Leong from the National Department of Health, Essential Drugs Programme supported the review.

Table 1. Characteristics of included studies

CITATION	STUDY DESIGN	POPULATION (N)	TREATMENT	MAIN FINDINGS
Remdesivir versus standard of care/ Placebo				
• ***Non-hospitalised patients***				
Gottlieb et al 2022[8] Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients https://www.nejm.org/doi/10.1056/NEJMoa2116846?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed	Randomized, double-blind, placebo-controlled trial	Non-hospitalized unvaccinated patients (12 years and older) with Covid-19 Symptom onset within the previous 7 days AND and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions) Risk factors included hypertension, cardiovascular or cerebrovascular disease, diabetes mellitus, obesity (a body-mass index [BMI of ≥30), immune compromise, chronic mild or moderate kidney disease, chronic liver disease, chronic lung disease, current cancer, or sickle cell disease. Remdesivir = 279 Placebo = 283	Intravenous remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) OR Placebo	**Primary efficacy end point** Composite endpoint Covid-19–related hospitalization or death from any cause by day 28: Remdesivir 2 (0.7%); Placebo 15 (5.3%) Placebo Hazard ratio 0.13 (0.03 to 0.59) P= 0.008 By day 28 there were no deaths in either study group. Primary safety end point - any adverse event. Adverse events occurred in 42.3% of the patients in the remdesivir group and in 46.3% of those in the placebo group. Fewer patients in the remdesivir group than in the placebo group had serious adverse events (5 of 279 patients [1.8%] vs. 19 of 283 patients [6.7%]). **Secondary efficacy end points** Composite of Covid-19–related medically attended visits or death from any cause by days 14 and 28, Day 28 Remdesivir 4 (1.6%); Placebo 21 (8.3%); Hazard Ratio 0.19 (0.07 to 0.56) The primary efficacy end point was initially a composite of hospitalization for any cause or death from any cause by day 14 and was modified on January 14, 2021, in response to comments from the Food and Drug Administration; trial blinding was maintained.
• ***Hospitalised Patients***				
Ader et al 2021[7] Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial	Randomised controlled trial, Phase 3 open-label	Adult patients (≥18 years) admitted to hospital with laboratory confirmed SARS-CoV-2, and clinical evidence of hypoxaemic pneumonia or requiring oxygen supplementation.	Participants were randomly assigned (1:1:1:1:1) to receive standard of care alone or in combination with remdesivir, lopinavir–ritonavir, lopinavir–ritonavir and interferon beta-1a, or hydroxychloroquine.	Primary outcome was clinical status at day 15 measured by the WHO seven-point ordinal scale, assessed in the intention-to- treat population. There was no significant difference in the distribution of the seven-point ordinal scale at day 15 between the remdesivir and control groups. No significant difference was observed between the remdesivir and control groups in subgroup analyses according to age, sex, duration of symptoms before random assignment, disease severity, or country of randomisation.

CITATION	STUDY DESIGN	POPULATION (N)	TREATMENT	MAIN FINDINGS
Mahajan et al 2021[5] Clinical outcomes of using remdesivir in patients with moderate to severe COVID-19: A prospective randomised study	Prospective RCT	Hospitalised patients between 18 and 60 years age group and had SARS-CoV-2 infection confirmed by polymerase-chain-reaction assay within the last 4 days.	200 mg IV remdesivir on D1 and then 100mg IV on D2-10. Versus Standard of care	The clinical status was assessed from day 12 to day 24 on a 6-point ordinal scale.
Pan H et al 2020[12] Repurposed antiviral drugs for COVID-19 –interim WHO SOLIDARITY trial results Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results (nejm.org)	Randomised controlled trial, phase 3, open-label	Adults ≥18 years recently hospitalised, or already in hospital, with definite COVID19 (mild to severe) n=2743 remdesivir n=2708 controls	• Local standard of care alone, OR local standard of care plus one of • Remdesivir (daily infusion for 10 days) • Chloroquine or hydroxychloroquine (two oral loading doses, then orally twice daily for 10 days) • Lopinavir with Ritonavir (orally twice daily for 14 days) • Lopinavir with Ritonavir (ditto) plus Interferon (daily injection for 6 days).	Mortality: Remdesivir vs its control (pre-planned analysis) RR=0.95 (95% CI 0.81-1.11; P=0.50), At 28 Days, mortality was 12.7% in the control group versus 12.5% in the Remdesivir group Initiation of ventilation and time to discharge: Remdesivir did not reduce initiation of ventilation in those not already ventilated at randomisation (295/2743 versus 284/2708 for remdesivir versus control respectively). Time to discharge was not appreciably changed in the remdesivir group versus the control group.
Spinner et al 2020 [13] Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19 (9) A Randomized Clinical Trial https://jamanetwork.com/journals/jama/fullarticle/2769871	Randomised controlled trial, phase 3, open-label	Hospitalised patients ≥12 years. Oxygen saturation on room air >94%. US, Europe, Asia (105 hospitals) n=197: 10-day course n=199: 5-day course n=200: standard of care (SoC)	Remdesivir IV 200 mg on Day 1, followed by 100 mg daily. Patients could be discharged before completing the course. A minority of patients received concomitant medications that included steroids, hydroxychloroquine/chloroquine, lopinavir/ritonavir, tocilizumab, and azithromycin. Steroid use was: 10-day group: 29/193(15%) 5-day group: 33/191 (17%) SoC: 38/200 (19%)	Original primary endpoint was hospital discharge by Day 14. This was amended during the study to distribution of clinical status (on a 7-point ordinal scale from death to hospital discharge) by Day 11. All-cause mortality (by Day 28): 10-day group: 2% (95% CI 0.0 to 3.6, p=0.72 versus SoC); 5-day group: 1% (95% CI 0.0 to 2.6, p=0.43 versus SoC); SoC group: 2% (95% CI 0.1 to 4.1) Duration of hospitalisation: Not reported, but authors state that there were no significant differences between remdesivir and SoC Duration of ICU admission or ventilation: Not reported, but very few patients progressed to invasive ventilation. Adverse reactions: 10-day group: 59% (12% more than Soc, 95% CI 1.6 to 21.8, p=0.02); 5-day group: 51% (4.8% more than Soc, 95% CI -5.2 to 14.7, p=0.36); SoC: 47%.

CITATION	STUDY DESIGN	POPULATION (N)	TREATMENT	MAIN FINDINGS
				Most common AEs: nausea, diarrhoea, headache, hypokalaemia. Primary endpoint: Better clinical status (versus SoC): 10-day group: not significantly different (p=0.18); 5-day group: odds ratio 1.65 (95% CI 1.09 to 2.48)
Goldman et al 2020[14] Remdesivir for 5 or 10 Days in Patients with Severe Covid-19(4) https://www.nejm.org/doi/full/10.1056/NEJMoa2015301?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed	Randomised open label phase 3 trial	Hospitalised patients >12 years of age with confirmed SARS-CoV-2 infection; radiographic evidence of pulmonary infiltrates; and oxygen saturation ≤94% or receiving supplemental oxygen. n = 200: 5-day course n = 197: 10-day course	Remdesivir 200 mg on day 1, followed by remdesivir 100 mg once daily for the subsequent 4 or 9 days. Primary outcome: day 14 clinical status on a 7-point ordinal scale	By day 14, a clinical improvement of ≥2 points occurred in 64% of patients in the 5-day group and in 54% in the 10-day group. After adjustment for baseline clinical status, Day 14 clinical status was similar between the two groups (P = 0.14).
Beigel et al. 2020[15] Remdesivir for the Treatment of Covid-19 — Final Report (8)https://www.nejm.org/doi/full/10.1056/NEJMoa2007764?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed 60 trial sites and 13 subsites in the United States (45 sites), Denmark (8), the United Kingdom (5), Greece (4), Germany (3), Korea (2), Mexico (2), Spain (2), Japan (1), and Singapore (1).	Double-blind, multi-centre randomized, placebo-controlled trial	Adults hospitalised with Covid-19 with lower respiratory tract involvement. n= 541 remdesivir n= 522 placebo At time of treatment initiation: 89% had severe disease. 127 did not require oxygen 421 required oxygen but no ventilation 197 were receiving non-invasive ventilation 272 were receiving invasive ventilation	IV Remdesivir 200-mg on day 1 followed by 100mg on days 2-10 or until discharge/death. Other treatment were allowed if the hospital had included them in a written policy. Other treatment received (if any) wasn't reported. Follow up of 29 days. *Primary outcome:* Time to recovery, defined by either discharge from the hospital (with or without need for home oxygen) or hospitalisation for infection-control purposes only (i.e.no need for oxygen or treatment). *Key secondary outcomes:* • Mortality at days 14 and 28 • Difference in clinical status defined by 8-category scale at day 15 • Grade 3 and 4 adverse events • Serious adverse events	The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29 (hazard ratio, 0.73; 95% CI, 0.52 to 1.03). Serious adverse events were reported in 131 of the 532 patients who received remdesivir (24.6%) and in 163 of the 516 patients who received placebo (31.6%).
Wang et al (2020)[16] Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial ([7])	Double-blind, multi-centre randomised, placebo-controlled trial	Adults hospitalized with SARS-CoV-2 infection, with an interval from symptom onset to enrolment of ≤12 days, oxygen saturation of ≤94% or on room	IV Remdesivir 200-mg on day 1 followed by 100mg on days 2 -10	Recruitment was terminated early because of control of the epidemic in Wuhan (the intended sample size was ±450).

CITATION	STUDY DESIGN	POPULATION (N)	TREATMENT	MAIN FINDINGS
https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)31022-9.pdf 10 hospitals in China were involved		air or a ratio of arterial oxygen partial pressure to fractional inspired oxygen of ≤300 mm Hg Remdesivir group (n=158) Placebo group (n=78) *At time of treatment initiation:* 3 did not require oxygen 194 required oxygen but no ventilation 37 were receiving non-invasive ventilation 1 was receiving invasive ventilation	Patients were permitted concomitant use of lopinavir–ritonavir, interferons, and corticosteroids. *Primary outcome:* The primary endpoint was time to clinical improvement within 28 days. Clinical improvement was defined as a two-point reduction in patients' admission status on a six-point ordinal scale, or discharge from the hospital, whichever came first. *Secondary outcomes:* Proportions of patients in each category of the six-point scale at day 7, 14, and 28 after randomisation; all-cause mortality at day 28; frequency of invasive mechanical ventilation; duration of oxygen therapy; duration of hospital admission; and proportion of patients with nosocomial infection. *Safety outcomes* included treatment-emergent adverse events, serious adverse events, and premature discontinuations of study drug.	28-day mortality was similar between the two groups (22 [14%] died in the remdesivir group vs 10 (13%) in the placebo group; difference 1·1% [95% CI –8·1 to 10·3]). No significant differences were observed between the two groups in terms of length of mechanical ventilation, length of oxygen support, length of hospital stay, days from randomisation to discharge, days from randomisation to death and distribution of six-category scale at day 7, day 14, and day 28 . Adverse events were reported in 102 (66%) of 155 remdesivir recipients versus 50 (64%) of 78 placebo recipients. Remdesivir was stopped early due to adverse events in 18 (12%) patients versus 4 (5%) patients who stopped placebo early
The COVID-NMA initiative [9] Living review of remdesivir versus placebo https://covid-nma.com/	Meta-analysis of four studies against standard of care (Beigel et al 2020, Wang et al 2020 and Spinner et al and Pan et al 2020) as well as meta-analysis of 5 days versus 10 days of remdesivir (Goldman et al and Spinner et al)	As for RCTs	**Outpatients** IV Remdesivir 200mg on day 1 followed by 100mg on day 2 and 3 **Inpatients** IV Remdesivir 200-mg on day 1 followed by 100mg on days 2 -10 IV Remdesivir on day one followed by 100 mg on days 2 to 5	See Appendix 2

Table 2. Characteristics of planned and ongoing studies

Treatment (per arm)	n	Severity at enrollment	Sponsor/Funder	Reg. number	Full text link
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Standard of care	443	Moderate/severe/critical	Oslo University Hospital	EUCTR2020-000982-18-NO	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2020-000982-18
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Lopinavir + ritonavir vs (4) Lopinavir + ritonavir + interferon beta 1a vs (5) Standard of care	600	No restriction on type of patients	AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA VERONA	EUCTR2020-001366-11-IT	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2020-001366-11
(1) Interferon beta 1a vs (2) Acalabrutinib vs (3) Remdesivir vs (4) Artesunate vs (5) Imatinib vs (6) Infliximab vs (7) Standard of care	1000	Moderate/severe/critical	Vilnius University Hospital Santaros Klinikos	EUCTR2020-001366-11-LT	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001366-11/LT/
(1) Remdesivir vs (2) Standard of care	800	Severe	Gesundheit Nord gGmbH	EUCTR2020-001549-38-DE	https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001549-38/DE
(1) Artesunate vs (2) Imatinib vs (3) Infliximab vs (4) Standard of care	664	Moderate/severe/critical	University of Helsinki / CLUE Working Group	EUCTR2020-001784-88-FI	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2020-001784-88
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Lopinavir + ritonavir vs (4) Lopinavir + ritonavir + interferon vs (5) Standard of care	3000	Moderate/severe	Iranian Ministry of Health and Medical Education, Deputy of Research and Technology	IRCT20200405046953N1	http://en.irct.ir/trial/46930
(1) Chloroquine vs (2) Remdesivir vs (3) Lopinavir + ritonavir vs (4) Lopinavir + ritonavir + interferon beta vs (5) Standard of care	11266	Moderate/severe/critical	Multiple funders including the World Health Organization (Switzerland)	ISRCTN83971151	http://isrctn.com/ISRCTN83971151
(1) Remdesivir vs (2) Placebo	100	Severe	Ohmagari Norio	JPRN-jRCT2031190264	https://jrct.niph.go.jp/latest-detail/jRCT2031190264
(1) Remdesivir vs (2) Standard of care	1000	Moderate/severe/critical	WHO	LBCTR2020043495	http://lbctr.moph.gov.lb/LBCTR/Trials/Details/3498
(1) Remdesivir vs (2) Placebo	308	Mild	Capital Medical University	NCT04252664	https://clinicaltrials.gov/show/NCT04252664
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Lopinavir + ritonavir vs (4) Lopinavir + ritonavir + interferon beta 1a vs (5) Cilgavimab + tixagevimab vs (6) Standard of care	3100	Moderate/severe/critical	Institut National de la Santâ—Ž Et de la Recherche Mâ—Ždicale, France	NCT04315948	https://clinicaltrials.gov/show/NCT04315948
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Standard of care	700	Severe/critical	Oslo University Hospital	NCT04321616	https://ClinicalTrials.gov/show/NCT04321616
(1) Remdesivir vs (2) Interferon beta-1a vs (3) Standard of care	440	No restriction on type of patients	Sunnybrook Health Sciences Centre	NCT04330690	https://clinicaltrials.gov/show/NCT04330690
(1) Remdesivir vs (2) Standard of care	100	Mild	Tanta University	NCT04345419	https://clinicaltrials.gov/show/NCT04345419
(1) Renin-Angiotensin-System-Blockade vs (2) Non-RAS blocking antihypertensive agent vs (3) Rivaroxaban vs (4) Hydroxychloroquine vs (5) Lopinavir + ritonavir vs (6) Asunercept vs (7) Asunercept vs (8) Asunercept vs (9) Remdesivir vs (10) Pentaglobin vs (11) Placebo vs (12) Standard of care	500	No restriction on type of patients	Medical University of Vienna	NCT04351724	https://clinicaltrials.gov/show/NCT04351724
(1) Remdesivir vs (2) NA-831 vs (3) NA-831 + remdesivir vs (4) Placebo	48	Healthy volunteers	NeuroActiva, Inc.	NCT04480333	https://clinicaltrials.gov/show/NCT04480333
(1) Remdesivir vs (2) Remdesivir + dornase alfa vs (3) Remdesivir + atibuclimab vs (4) Remdesivir + celecoxib + famotidine vs (5) Remdesivir + narsoplimab vs (6) Remdesivir + aviptadil (vasoactive intestinal peptide) vs (7) Remdesivir + ciclosporin	1500	Critical	QuantumLeap Healthcare Collaborative	NCT04488081	https://clinicaltrials.gov/show/NCT04488081
(1) Bamlanivimab vs (2) Remdesivir vs (3) Sotrovimab vs (4) BRII-196 + BRII-198 vs (5) Cilgavimab + tixagevimab vs (6) Ensovibep vs (7) PF-07304814 vs (8) Standard of care	10000	Moderate/severe	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04501978	https://clinicaltrials.gov/show/NCT04501978
(1) Remdesivir vs (2) Remdesivir + risankizumab	200	Moderate/severe/critical	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04583956	https://clinicaltrials.gov/show/NCT04583956
(1) Remdesivir vs (2) Remdesivir + lenzilumab	200	Moderate/severe/critical	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04583969	https://clinicaltrials.gov/show/NCT04583969
(1) Remdesivir vs (2) Standard of care	60	Severe	Dr. Md. Alimur Reza	NCT04596839	https://clinicaltrials.gov/show/NCT04596839
(1) Remdesivir vs (2) Interferon beta 1a vs (3) Acalabrutinib vs (4) Standard of care	100	No restriction on type of patients	The University of The West Indies	NCT04647669	https://clinicaltrials.gov/show/NCT04647669
(1) Interferon beta 1b + remdesivir vs (2) Remdesivir	100	Severe/critical	The University of Hong Kong	NCT04647695	https://clinicaltrials.gov/show/NCT04647695

(1) Remdesivir + baricitinib vs (2) Remdesivir + tocilizumab	150	Severe/critical	M Abdur Rahim Medical College and Hospital	NCT04693026	https://clinicaltrials.gov/show/NCT04693026
(1) Favipiravir vs (2) Favipiravir + remdesivir	676	Mild/moderate	Nepal Health Research Council	NCT04694612	https://clinicaltrials.gov/show/NCT04694612
(1) Remdesivir vs (2) Remdesivir + camostat mesilate	1120	Moderate/severe	Daewoong Pharmaceutical Co. LTD.	NCT04713176	https://clinicaltrials.gov/show/NCT04713176
(1) Remdesivir vs (2) Placebo	1116	Moderate/severe	Gilead Sciences	NCT04745351	https://clinicaltrials.gov/show/NCT04745351
(1) Lopinavir + remdesivir + ritonavir + tocilizumab vs (2) Hydroxychloroquine + ivermectin + tocilizumab	150	Moderate/severe	October 6 University	NCT04779047	https://clinicaltrials.gov/show/NCT04779047
(1) Baricitinib vs (2) Remdesivir vs (3) Remdesivir + baricitinib vs (4) Standard of care	4000	Moderate/severe	ASST Fatebenefratelli Sacco	NCT04832880	https://clinicaltrials.gov/show/NCT04832880
(1) Remdesivir + aviptadil (vasoactive intestinal peptide) vs (2) Aviptadil (vasoactive intestinal peptide) vs (3) Remdesivir vs (4) Placebo	640	Critical	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04843761	https://clinicaltrials.gov/show/NCT04843761
(1) Remdesivir + ivermectin vs (2) Remdesivir	60	Moderate/severe	Assiut University	NCT04944082	https://clinicaltrials.gov/show/NCT04944082
(1) Remdesivir + baricitinib vs (2) Remdesivir + dexamethasone	382	Moderate/severe	Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders	NCT04970719	https://clinicaltrials.gov/show/NCT04970719
(1) Hydroxychloroquine vs (2) Remdesivir vs (3) Lopinavir + ritonavir vs (4) Lopinavir + ritonavir + interferon beta 1 vs (5) Standard of care	1000	Moderate/severe/critical	OMS	PER-010-20	https://www.ins.gob.pe/ensayosclinicos/rpec/recuperarECPBNuevoEN.asp?numec=010-20
(1) Danicopan + Remdesivir vs (2) Danicopan + Remdesivir vs (3) Placebo vs (4) Placebo	200	Moderate/severe	National Institute of Allergy and Infectious Diseases (NIAID)	NCT04988035	https://clinicaltrials.gov/show/NCT04988035
(1) Acalabrutinib vs (2) Hydroxychloroquine vs (3) Interferon beta 1a vs (4) Lopinavir + ritonavir + interferon beta 1a vs (5) Lopinavir + ritonavir vs (6) Remdesivir vs (7) Standard of care	1314	No restriction on type of patients	University of the Philippines	NCT05024006	https://clinicaltrials.gov/show/NCT05024006
(1) Remdesivir vs (2) Interferon beta 1a	100	Moderate/severe	Vice Chancellor for Research and Technology of Lorestan University of Medical Sciences	IRCT20200721048159N4	http://en.irct.ir/trial/57494
(1) Favipiravir vs (2) Ivermectin vs (3) Remdesivir vs (4) Casirivimab + imdevimab vs (5) Standard of care	750	Mild	University of Oxford	NCT05041907	https://clinicaltrials.gov/show/NCT05041907
(1) Efesovir vs (2) Remdesivir,62,Moderate/severe,"Scientific Center for Anti-infectious Drugs, Kazakhstan",NCT05060705,https://clinicaltrials.gov/show/NCT05060705					
(1) Remdesivir + tocilizumab vs (2) Remdesivir	60	Moderate/severe	Dr Swati Datta	CTRI/2020/12/029615	http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=49731
(1) Remdesivir vs (2) Standard of care	202	No restriction on type of patients	Clinical Urology and Epidemiology Working Group	NCT04978259	https://clinicaltrials.gov/show/NCT04978259
(1) Remdesivir vs (2) Remdesivir	120	Severe	Shahid Beheshti University of Medical Sciences	IRCT20151227025726N28	http://en.irct.ir/trial/58253
(1) Remdesivir vs (2) Placebo	100	Moderate/severe	Men's Health and Reproductive Health Research Center(MHRHRC)	IRCT20210709051824N1	http://en.irct.ir/trial/57516
(1) Remdesivir vs (2) Remdesivir + molnupiravir	60	Moderate	Shahid Beheshti University of Medical Sciences	IRCT20150107020592N31	http://en.irct.ir/trial/60926
(1) Ceftriaxone + levofloxacin + remdesivir vs (2) Remdesivir	90	Severe	Shahre-kord University of Medical Sciences	IRCT20210510051248N1	http://en.irct.ir/trial/60668

Appendix 1: Search strategy (25 January 2022)

Cochrane COVID-19 Study Register
15 studies with 62 references
Filters:
Journal Article
Report Results
Interventional
Treatment And Management
Randomised
Remdesivir
27 references not study results (protocols, descriptions)
17 References not applicable (not studies involving remdesivir)
18 References included

Pubmed

Filter: Systematic Review, meta-analysis; Date: 01/06/2021 to 30/01/2022
Remdesivir (Title / abstract)
25 Results

COVID-NMA Initiative
https://www.cochrane.org/news/cochrane-france-leads-collaborative-covid-19-living-evidence-project
https://covid-nma.com/living_data/index.php

Appendix 2: Summary of findings of the Cochrane Living Meta-analysis: Remdesivir vs Placebo for Mild/ Moderate/Severe COVID-19 (hospitalised patients)

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Remdesivir	SOC/placebo	Relative (95% CI)	Absolute (95% CI)	
Viral negative conversion D7											
12 (n=1053)	RCTs	serious[a]	not serious	not serious	serious[b]	none	219 per 1,000 (178 - 269)	215 per 1,000	**RR: 1.02** (0.83 - 1.25)	**4 more per 1000** (from 37 fewer to 54 more)	⊕⊕◯◯ Low
Clinical improvement D28											
4 (n=1772)	RCTs	serious[c]	not serious	not serious	serious[b]	none	729 per 1,000 (687 - 764)	701 per 1,000	**RR: 1.04** (0.98 - 1.09)	**28 more per 1000** (from 14 fewer to 63 more)	⊕⊕◯◯ Low
Clinical improvement D60											
Outcome not reported											
WHO progression score (level 7 or above) D28											
5 (n=2834)	RCTs	serious[c]	not serious	not serious	serious[b]	none	135 per 1,000 (112 - 161)	180 per 1,000	**RR: 0.75** (0.62 - 0.89)	**45 fewer per 1000** (from 69 fewer to 20 fewer)	⊕⊕◯◯ Low
WHO progression score (level 7 or above) D60											
Outcome not reported											
All-cause mortality D28											
6 n=7553	RCTs	not serious[d]	not serious	not serious	serious[e]	1 additional RCT identified, but no results were reported	101 per 1,000 (82 - 123)	111 per 1,000	**RR: 0.91** (0.74 - 1.11)	**10 fewer per 1000** (from 29 fewer to 12 more)	⊕⊕⊕◯ Moderate
All-cause mortality D60											
1 n=101	RCT	not serious	not serious	serious[f]	very serious[g]	1 additional RCT identified, but no results were reported	70 per 1,000 (17 - 296)	69 per 1,000	**RR: 1.01** (0.24 - 4.29)	**1 more per 1000** (from 52 fewer to 227 more)	⊕◯◯◯ Very low
Adverse events											
4 n=2752	RCTs	serious[a]	not serious	not serious	serious	none	572 per 1,000 (520 - 635)	572 per 1,000	**RR: 1.00** (0.91 - 1.11)	**0 fewer per 1000** (from 51 fewer to 63 more)	⊕⊕◯◯ Low
Serious adverse events											
4 n=2752	RCTs	serious[a]	not serious	not serious	very serious[h]	1 additional RCT identified, but no results were reported	218 per 1,000 (170 - 280)	270 per 1,000	**RR: 0.81** (0.63 - 1.04)	**51 fewer per 1000** (from 100 fewer to 11 more)	⊕⊕◯◯ Low

CI: Confidence interval; **RCT**: randomised controlled trial; **RR:** Risk ratio

Explanations

a: Risk of bias downgraded by 1 level: some concerns regarding deviation from intended intervention and selection of the reported results
b. Imprecision downgraded by 1 level: due to low number of participants
c. Risk of bias downgraded by 1 level: some concerns or high risk regarding adequate randomization, deviation from intended intervention, missing data, outcome measurement and selection of the reported results
d. Despite some concerns with adequate randomization, deviation from intended intervention, missing data and selection of the reported results, not downgraded for risk of bias because the studies with these concerns contributed only a small proportion of the data
e. Imprecision downgraded by 1 level: due to wide confidence interval consistent with the possibility for benefit and the possibility for no effect
f. Indirectness downgraded by 1 level: despite a multicentre design this is a single study from a single country, therefore results in this population might not be generalizable to other settings
g. Imprecision downgraded by 2 level: due to very wide confidence interval consistent with the possibility for benefit and the possibility for harm and low number of events
h. Wide confidence interval consistent with the possibility for benefit and the possibility for harm and low number of participants

Appendix 3: Forest plots for Cochrane Living Meta-analysis: Remdesivir 10 or 5 days vs Placebo for Moderate/Severe COVID-19

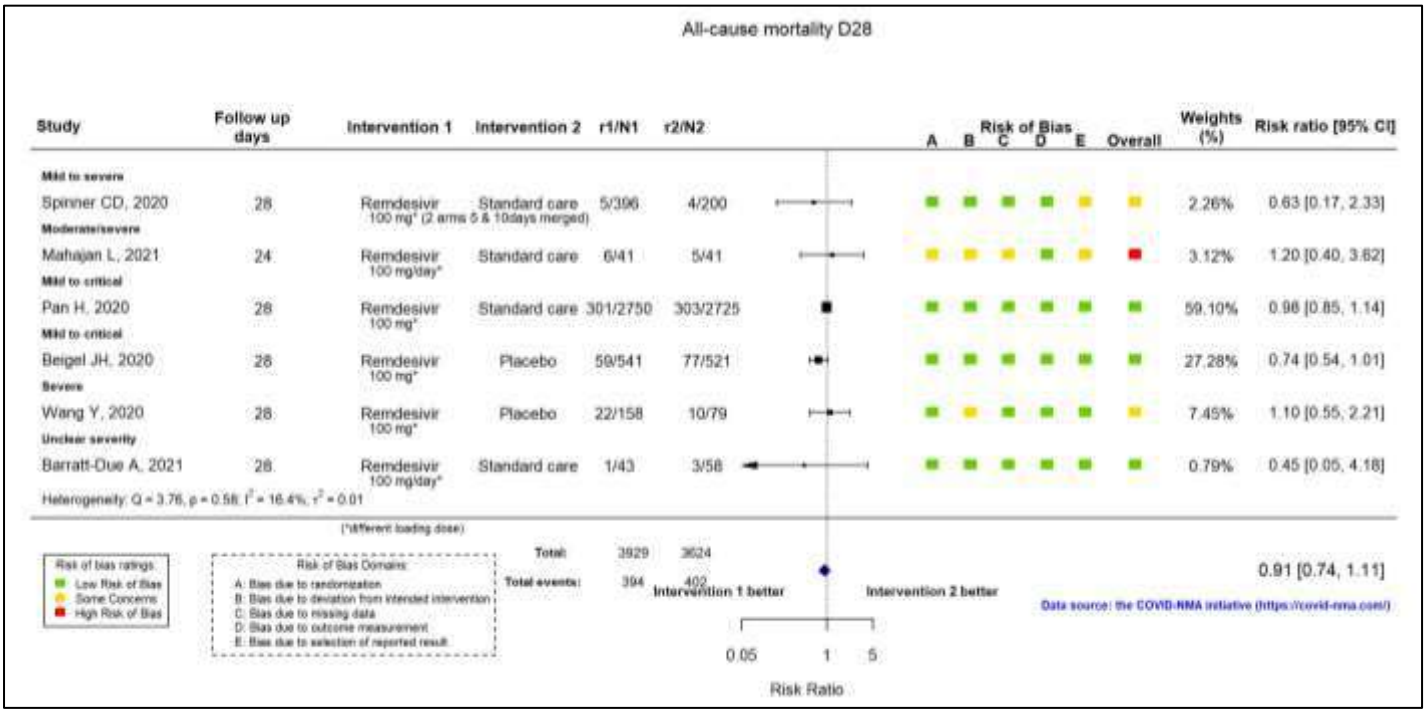

Figure 1: All-cause mortality, D28; Remdesivir 5 or 10 days versus standard of care

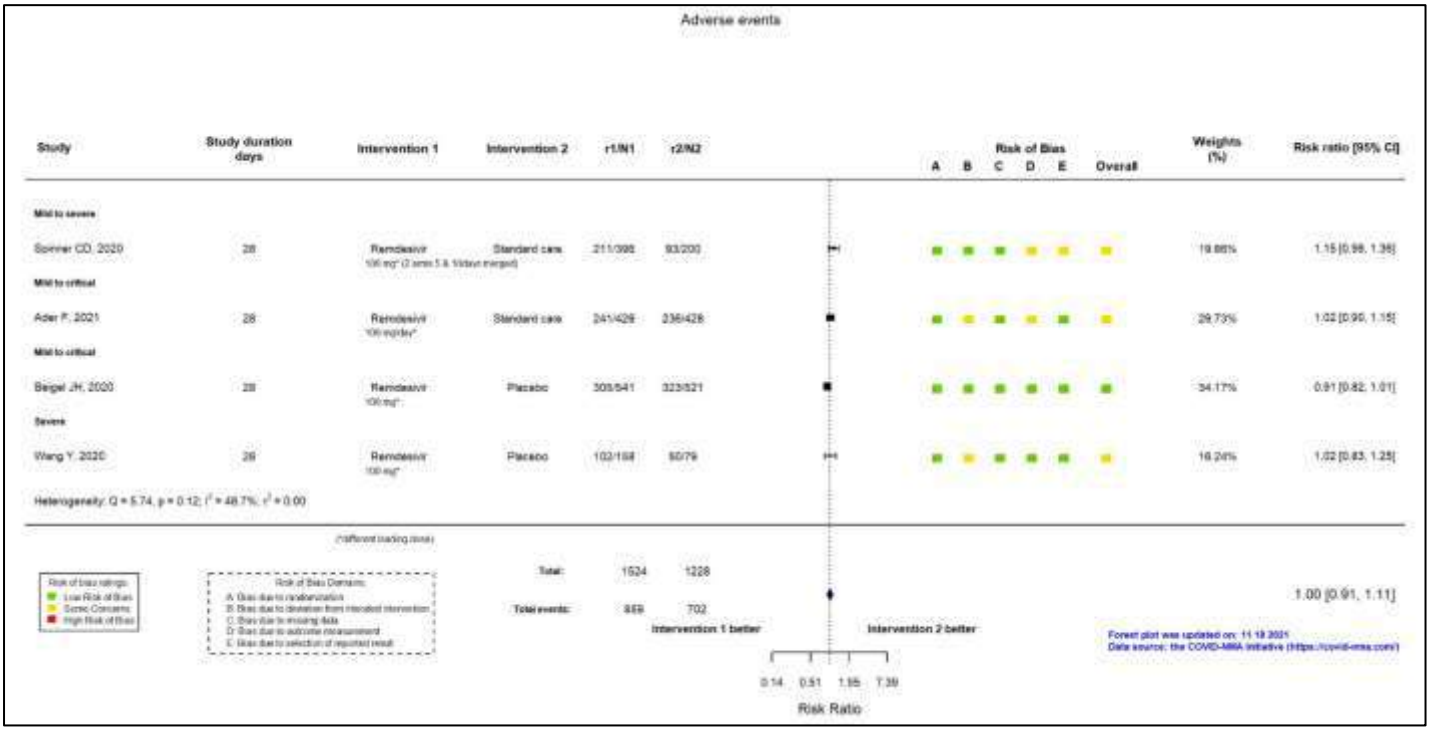

Figure 2: Adverse events

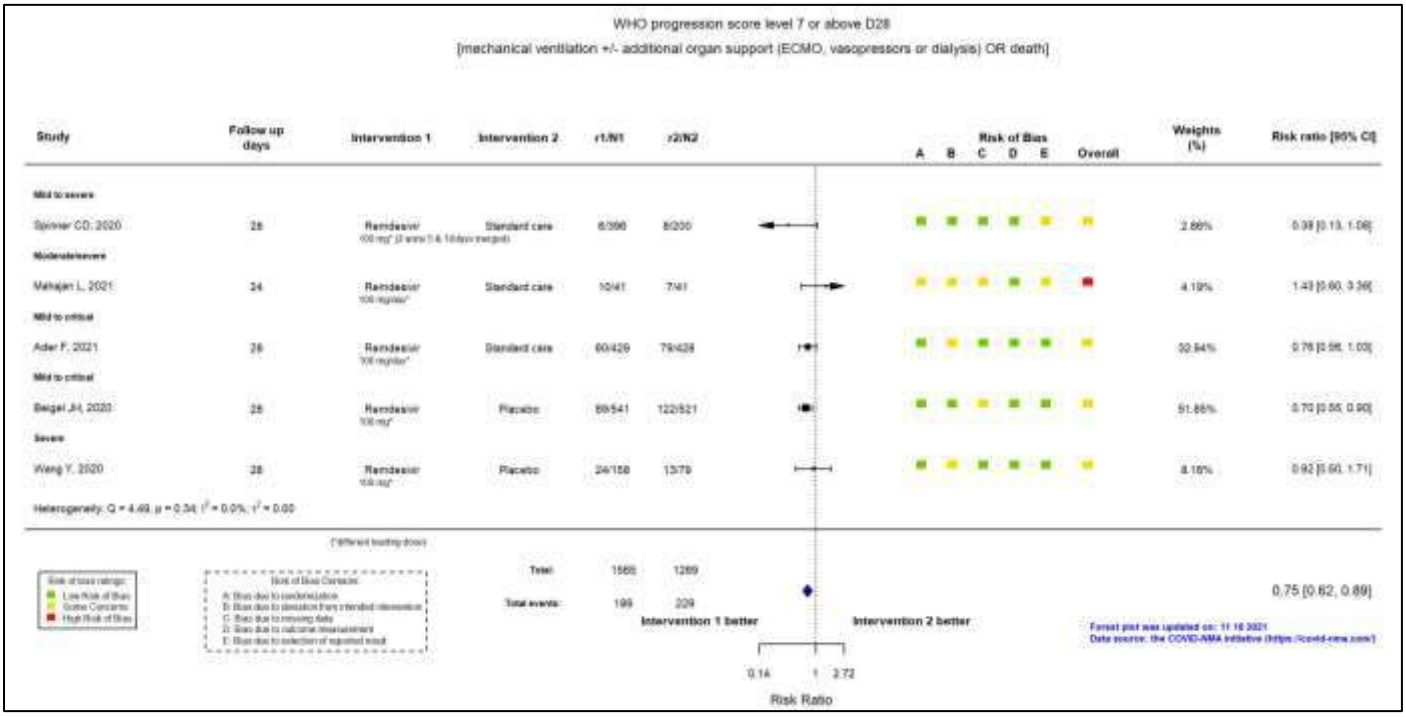

Figure 2: Progression to WHO progression level 7 and above D28

Appendix 4: Evidence to decision framework – Non-hospitalised patients

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE OF BENEFIT	**What is the certainty/quality of evidence?** High: [ ] Moderate: [X] Low: [ ] Very low: [ ] *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	Only one randomised trial has been published at this point and confidence intervals were relatively wide.
EVIDENCE OF BENEFIT	**What is the size of the effect for beneficial outcomes?** Large: [ ] Moderate: [x] Small: [ ] None: [ ]	All-cause mortality by D 28: no deaths in either of the groups. For the composite endpoint of hospitalisation and death, there was a significant difference based on hospitalisation, which is an important consideration. Remdesivir (0.7%); Placebo (5.3%) Hazard ratio 0.13 (0.03 to 0.59)
QUALITY OF EVIDENCE OF HARM	**What is the certainty/quality of evidence?** High: [ ] Moderate: [x] Low: [ ] Very low: [ ] *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	Adverse events were similar with remdesivir and placeboe.
EVIDENCE OF HARMS	**What is the size of the effect for harmful outcomes?** Large: [ ] Moderate: [ ] Small: [ ] None: [x]	There do not seem to be any additional harms associated with remedesivir compared with placebo.
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable harms?** Favours intervention: [x] Favours control: [ ] Intervention = Control *or* Uncertain: [ ]	
FEASABILITY	**Is implementation of this recommendation feasible?** Yes: [ ] No: [ ] Uncertain: [X]	The innovator product is now SAHPRA registered, but supply remains an issue. The fact that the regimen in ambulatory care was only 3 days of treatment may be appealing. One of the generic products has previously been accessed in terms of section 21.
RESOURCE USE	**How large are the resource requirements?** More intensive: [X] Less intensive: [ ] Uncertain: [ ]	**Price of medicines/treatment course:** **Medicine** | **Price (ZAR)*** Remdesivir, IV, 200 mg loading dose, followed by 100 mg per day for 2 days (4 x 100 vials) | ***3 days***: 4002.00 to 4301.04 *The original manufacturer has licensed a number of Indian generic firms to make generic versions, and has included South Africa in the list of countries to which such products can be exported. Private sector S21 prices for 6 x 100mg vials: • Cipla Medpro: R6451.50 • Hetero: R6003.00 • Mylan: R6016.80 **Additional resources:** Safety monitoring (liver function tests).
VALUES, PREFERENCES, ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the options?** Minor: [ ] Major: [ ] Uncertain: [X] **Is the option acceptable to key stakeholders?** Yes: [X] No: [ ] Uncertain: [ ]	Patients: No specific research surveying patients' value of this therapeutic agent is currently available. Healthcare workers are likely to consider the intervention to be acceptable.
EQUITY	**Would there be an impact on health inequity?** Yes: [ ] No: [ ] Uncertain: [X]	This would depend on the availability of the medicine across different sectors, and ability of outpatients to access intravenous therapy.

Appendix 5: Evidence to decision framework – Hospitalised patients

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE OF BENEFIT	**What is the certainty/quality of evidence?** High: ☐ Moderate: X Low: ☐ Very low: ☐ *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	Several randomised trials have been published at this point and results consistently demonstrate little to no benefit in hospitalised patients.
EVIDENCE OF BENEFIT	**What is the size of the effect for beneficial outcomes?** Large: ☐ Moderate: ☐ Small: ☐ None: X	All-cause mortality at D28 RR: 0.92 (95% CI 0.78 to 1.07) This lack of effect has been relatively consistently reported.
QUALITY OF EVIDENCE OF HARM	**What is the certainty/quality of evidence?** High: ☐ Moderate: ☐ Low: X Very low: ☐ *High quality: confident in the evidence* *Moderate quality: mostly confident, but further research may change the effect* *Low quality: some confidence, further research likely to change the effect* *Very low quality: findings indicate uncertain effect*	
EVIDENCE OF HARMS	**What is the size of the effect for harmful outcomes?** Large: ☐ Moderate: ☐ Small: ☐ None: x	There does not seem to be any additional harms versus placebo.
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable harms?** Favours intervention: ☐ Favours control: ☐ Intervention = Control *or* Uncertain: x	While there are no signals for added adverse effects, the clinical efficacy remains uncertain.
FEASABILITY	**Is implementation of this recommendation feasible?** Yes: ☐ No: ☐ Uncertain: X	The innovator product is now SAHPRA registered, but supply remains an issue.
RESOURCE USE	**How large are the resource requirements?** More intensive: X Less intensive: ☐ Uncertain: ☐	**Price of medicines/treatment course:** **Medicine** | **Price (ZAR)*** Remdesivir, IV, 200 mg loading dose, followed by 100 mg per day for 5-10 days (6 to 11 vials) | ***5 days***: 6003.00 to 6451.50 ***10 days***: 12006.00 to 12903 *The original manufacturer has licensed a number of Indian generic firms to make generic versions, and has included South Africa in the list of countries to which such products can be exported. Private sector S21 prices for 6 x Remdesivir 100mg vials include: • Cipla Medpro: R6451.50 • Hetero: R6003.00 • Mylan: R6016.80 **Additional resources:** Safety monitoring (liver function tests).
VALUES, PREFERENCES, ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the options?** Minor: ☐ Major: ☐ Uncertain: X **Is the option acceptable to key stakeholders?** Yes: X No: ☐ Uncertain: ☐	Patients: No specific research surveying patients' value of this therapeutic agent is currently available. Healthcare workers are likely to consider the intervention to be acceptable.
EQUITY	**Would there be an impact on health inequity?** Yes: X No: ☐ Uncertain: ☐	This would depend on the availability of the medicine through different sectors and the ability of hospitals to access the medicine. Currently, there are supply concerns.

Appendix 6: Updating of rapid report

Date	Signal	Rationale
9 December 2020	WHO SOLIDARITY RCT results printed in NEJM	The WHO SOLIDARITY RCT results reported in preprint format reported has recently been published peer-review format in the NEJM.
30 January 2022	Trial results in outpatients	Gottlieb et al published a positive trial in patients not hospitalised

Version	Date	Reviewer(s)	Recommendation and Rationale
First	16 April 2020	SM, RdW	Currently insufficient evidence to recommend remdesivir in treatment guidelines for COVID-19, except in a clinical trial setting.
Second	24 June 2020	SM, RdW	Remdesivir does not warrant preferential use over other alternative options. While evidence for the efficacy of remdesivir has improved it is still generally weak to moderate. The reduced time to improvement of severe disease may be desirable in the face of limited resources.
Third	29 September 2020	SM, RdW	Remdesivir does not warrant preferential use over other alternative options. While evidence for the efficacy of remdesivir has improved it is still generally weak to moderate. The reduced time to improvement of severe disease may be desirable in the face of limited resources.
Fourth	17 November 2020	SM, RdW	Remdesivir does not warrant preferential use over other alternative options. Remdesivir has not demonstrated a significant effect on mortality or need for ventilation.
Fifth	15 December 2020	SM, RdW	Remdesivir does not warrant preferential use over other alternative options. Remdesivir has not demonstrated a significant effect on mortality or need for ventilation.
Sixth	3 February 2022	SM, RdW	Remdesivir does not warrant preferential use over other alternative options. For hospitalised patients - remdesivir has not demonstrated a significant effect on mortality or need for ventilation. For non-hospitalised patients - remdesivir reduced hospitalisation rates in a single RCT, but the effects amongst the vaccinated or previously infected are unknown; intravenous administration for ambulatory care is not feasible; supply is limited and medicine is unaffordable.

For internal NDoH use:
WHO INN: Remdesivir
ATC: J05AB16
ICD10: U07.1/U07.2

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