

NMH Antimicrobial Stewardship Review of Remdesivir Use Recommendations

Remdesivir is the only FDA-approved treatment of COVID-19 in hospitalized patients

Organization	Not hospitalized OR hospitalized but not requiring supp oxygen	Hospitalized & requiring supp oxygen (low-flow)	Hospitalized & requiring high-flow supp oxygen or noninvasive ventilation	Hospitalized & requiring invasive mechanical ventilation or ECMO
	Non-severe		Severe	Critical
IDSA	Recommend against RDV <i>(very low evidence)</i>	Recommend RDV 5 day treatment course <i>(mod evidence)</i>	Recommend RDV 5 day treatment course <i>(mod evidence)</i>	Recommend RDV up to 10 days [^] <i>(mod evidence)</i>
NIH	No recommendation <i>(insufficient evidence)</i> <i>Use should be guided by clinical judgment in high risk patients</i>	Recommend RDV 5 day treatment [^] <i>(controlled trial evidence)</i> OR RDV plus dexamethasone ^{‡*} (DEX) for up to 10 day treatment [^] <i>(expert opinion)</i>	Recommend DEX alone <i>(controlled trial evidence)</i> OR RDV plus DEX <i>(expert opinion)</i> <i>For patients receiving RDV who progress to high-flow sup O₂, NIMV, MV, or ECMO, RDV course should be completed</i>	Recommend DEX alone [#] <i>(controlled trial evidence)</i> <i>#Combination with DEX+RDV may be considered in patients recently intubated (expert opinion)</i>
WHO	Recommend against RDV <i>(weak recommendation)</i>		Recommend against RDV <i>(weak recommendation)</i>	
As of 12/3/2020	[^] or until hospital discharge	*DEX alone if RDV unavailable	[‡] For pts who require ↑ amount of sup O ₂	

- WHO weakly suggests not using remdesivir over supportive care in patients with COVID-19 of any severity due to evidence from the Solidarity trial citing no important effect on mortality, need for mechanical ventilation, nor time to clinical improvement, although the trial's primary endpoint only assessed mortality. **The WHO Guideline Development Group states that mortality is the most important outcome to patients.** Additionally, this conditional recommendation against remdesivir was supported by concerns for resources, feasibility, and equity for all countries included in the trial. **They did not take into consideration the potential impact of remdesivir on availability of hospital resources.** The panel concluded that most patients would not prefer IV RDV treatment given low certainty of evidence suggesting small beneficial effects, although some patients would opt for use due to the possibility of benefit.
- Outcomes from Clinical Trials:
 - **Solidarity** – Randomized, unblinded, comparator: Standard of Care
 - No substantial mortality benefit (28-day mortality RR 0.95, 95% CI 0.81-1.11)
 - Variation in standard of care & burden of COVID-19 disease across 30 low-, middle-, & high-income countries, which may not be reflective of all patient populations
 - Mortality is a finite endpoint that can be quickly assessed with high accuracy, but may not capture potential benefits of therapy including time to improvement nor reduced durations of hospitalization
 - **ACTT-1** – Randomized, blinded, comparator: Placebo
 - No mortality benefit (29-day mortality 11.4% v 15.2% with placebo, HR 0.73, 95% CI 0.52-1.03)
 - Shorter median time to recovery (10 days v 15 days)
 - Reduced time to hospital discharge (12 days v 17 days)
 - **Spinner et al** – Randomized, unblinded, comparator: Standard of Care
 - Improved clinical status at day 11 with RDV 5 day course v SOC (not shown with RDV 10 day course)
- **Summary:** Remdesivir use should be considered as early as possible in the COVID-19 disease process for hospitalized patients, particularly for those with increased risk factors for clinical deterioration, including requirement of supplemental oxygen, in hopes of reducing the risk of disease progression and accompanying complications, notably prolonged hospitalization. Based on randomized trial data, the use of remdesivir early in the course of care for patients with severe COVID-19 disease, may shorten illness duration as well reduce time to hospital discharge, freeing up valuable health care resources.

References:

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>.
2. Clinical management of COVID-19. World Health Organization. Available at <https://www.who.int/publications/i/item/clinical-management-of-covid-19>
3. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Infectious Diseases Society of America. Available at <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>
4. Harrington D et al. NEJM. 2020 Dec 2. DOI: 10.1056/NEJMe2034294