



DGI recommendations for COVID-19 pharmacotherapy

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Received: 18 August 2020 / Accepted: 21 August 2020
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German Society for Infectious Diseases (DGI) recommendations for COVID-19 pharmacotherapy
Last updated: 19.08.2020

<i>Mild-moderate disease</i>	No specific therapy recommended ^a	
Symptoms of a lower respiratory tract infection		
No oxygen support required		
<i>Severe disease</i>	Dexamethasone ^{b,c,d}	6 mg/day per OS or intravenous for up to 10 days
Oxygen support required (oxygen saturation \leq 94% on room air)	plus Remdesivir ^{e,f,g}	Day 1: 200 mg intravenous loading dose Day 2–5: 100 mg intravenous per day maintenance dose Duration: 5 days, consider extension to maximal 10 days ^h
	There are no clinical data on combination therapy with remdesivir and dexamethasone available	
<i>Critical disease</i>	Dexamethasone ^{b,i}	6 mg per day intravenous for up to 10 days
Hypoxic respiratory failure	plus	Day 1: 200 mg intravenous (loading dose)
Invasive/non-invasive ventilation	Remdesivir ^{e,j}	Day 2–5 (10): 100 mg intravenous per day (maintenance dose)
High-flow oxygen therapy		Duration: 5–10 days ^h
	There are no clinical data on combination therapy with remdesivir and dexamethasone available	

CI confidence interval

^aCurrent evidence supporting the use of remdesivir in patients with mild or moderate COVID-19 (no oxygen therapy required) [1] is insufficient

^bOff-label-use based upon preliminary results from the RECOVERY trial [2]

^cReduced 28-day-mortality by one-fifth in patients that require oxygen therapy (in this study oxygen saturation 92–94% on room air) without invasive ventilation [23.3% vs. 26.2%; rate ratio (RR) 0.82 (95% CI 0.72–0.94)] [2]

^dThe clinical benefit of dexamethasone demonstrated in the RECOVERY trial was plainest in patients being treated after 7 days from symptom onset [2]

^eConditional European authorization for patients with COVID-19 pneumonia (\geq 12 years, weighing \geq 40 kg) that require oxygen support and have an estimated glomerular filtration rate (eGFR) $>$ 30 ml/min [3]; When applied, close monitoring of biochemical markers for organ toxicity (in particular hepatotoxicity) is mandatory. Adverse events must be reported immediately to the Federal Institute for Drugs and Medical Devices (humanweb.pei.de) and the manufacturer Gilead Sciences. Remdesivir should be administered as intravenous infusion over 30–60 min [4]

^fThe clinical benefit of remdesivir has been demonstrated in the Adaptive COVID-19 Treatment Trial (ACTT-1 trial) irrespective of the duration of illness. The time from symptom onset to study enrollment was 6–12 days (median 9) [1]. Subgroup analyses of a previous trial showed a numerical reduction in time to recovery of median 5 days only in patients that were treated within 10 days after symptom onset [hazard ratio 1.52 (95% CI 0.95–2.43)] [5]. Results from a macaque model of SARS-CoV-2 infection also support the use of remdesivir in an early phase of disease [6]

Jakob J. Malin and Christoph D. Spinner took charge of developing the DGI Recommendations for COVID-19 Pharmacotherapy. Correspondence concerning these recommendations should be addressed to the secretary of the German Society for Infectious Diseases (DGI): vorstand@dgi-net.de.

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[§]A 10-day course of remdesivir decreased the time to recovery from COVID-19 in the ACTT-1 trial by 31%. This effect was most pronounced in patients that required oxygen therapy [relative risk reduction 1.47 (95% CI 1.17–1.84). The mortality at day 14 was reduced in patients receiving remdesivir [7.1% vs. 11.9%; hazard ratio 0.7 (95% CI 0.47–1.03, *p* value = 0.06)] [1]. In a meta-evaluation of the SIMPLE (GS-US-540-5773) trial and retrospective cohort data, remdesivir treatment was associated with a 62% reduction of the odds ratio for mortality in patients with severe COVID-19 [7]

^hComparing the efficacy of a 5-day versus a 10-day course of remdesivir in patients with severe COVID-19 (SIMPLE SEVERE trial) a 10-day course was not superior to a 5-day treatment [8]

ⁱReduced mortality at day 28 by one-third in patients with mechanical ventilation [29.3% vs 41.4%; rate ratio (RR) 0.64 (95% CI 0.72–0.94)] [2]

^jA clinical benefit of remdesivir for patients with critical COVID-19 is less well documented. In the subgroup of patients with invasive ventilation in the ACTT trial, no effect on the time to recovery was demonstrated [1]. The present recommendation is based on patients with severe COVID-19

Funding Open Access funding provided by Projekt DEAL.

Compliance with ethical standards

Conflict of interest JJM reports no conflicts of interest. CDS reports grants and personal fees from Gilead Sciences, during remdesivir studies. Personal fees from AbbVie, grants and personal fees from Janssen-Cilag, MSD, GSK/ViiV, Grants from Lilly and Selinexor, outside remdesivir studies.

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