UPDATE ALERTS

Update Alert 2: Remdesivir for Adults With COVID-19

This is the fourth update for our living, rapid review on remdesivir for adults with COVID-19 (1). Our first update, which included studies published through 7 December 2020, led to a major update (2). Our second update found no new evidence (3). Our third update included 1 new, small randomized controlled study with high risk of bias that did not change our original conclusions (4). This fourth quarterly update, done using the same search strategies as the original review (1), identified 650 citations between 11 May and 9 August 2021. One newly published add-on substudy of the World Health Organization (WHO) Solidarity trial, the Norwegian (NOR) Solidarity trial, was eligible for inclusion (**Supplement Figure**) (5).

The last update included 6 trials of remdesivir for any disease severity (**Supplement Table 1**). On the basis of the results of 4 trials, a 10-day course of remdesivir probably results in little to no difference in mortality but probably reduces serious adverse events and may reduce time to recovery in hospitalized patients (6–9) (**Supplement Table**s 2 and **3**). Two trials found that a 10-day course was not more effective than a 5-day course for moderate and severe disease (9,10).

In this update, we include results from NOR Solidarity, a small add-on substudy of WHO Solidarity (5) (**Supplement Table**s 1, **2**, and **4** to **8**). This randomized controlled trial compared a 10-day course of remdesivir (n = 42) to standard care (n = 57) in patients hospitalized with any severity of laboratory-confirmed SARS-CoV-2 infection at 23 Norwegian hospitals. All patients included in NOR Solidarity were also included in WHO Solidarity, results of which have been previously published and included in our major update. The primary goal of NOR Solidarity was to evaluate the effect of remdesivir on viral clearance as assessed by SARS-CoV-2 polymerase chain reaction in oropharyngeal specimens. In this study, compared with standard care, remdesivir did not alter viral clearance, with results not varying by symptom duration; results were consistent with findings in a previously included study (**Supplement Table 6**) (7). Although NOR Solidarity was not designed or adequately powered to address clinical outcomes, the authors provided additional substudy-specific clinical outcomes not previously reported by WHO Solidarity. The results showed that patients receiving remdesivir, compared with standard care, did not differ with regards to 28-day mortality (2.4% vs. 5.3%) or 60-day mortality (7.1% vs. 5.3%), with an estimated marginal risk difference of 1.9 percentage points (95% CI, −7.8 to 11.6 percentage points) at day 60. Admission to the intensive care unit during hospitalization (19.0% vs. 19.3%; estimated marginal risk difference, −0.3 percentage points [CI, −15.9 to 15.4 percentage points]) and time to receipt of mechanical ventilation (hazard ratio, 1.3 [CI, 0.5 to 3.4]) also did not differ between the remdesivir and standard care groups. There was also no difference in serious adverse effects between the 2 groups (**Supplement Table 7**). Because WHO Solidarity had previously reported results for all patients included in NOR Solidarity, we did not assess evidence certainty for this substudy or update our prior meta-analyses (which included all patients from WHO Solidarity). Furthermore, most of the additionally reported outcomes in NOR Solidarity did not meet our a priori–defined critical or important outcomes (1).

Hence, our original conclusions about certainty and strength of evidence of remdesivir for adults with COVID-19 remain unchanged (**Supplement Table**s 2 and **3**).

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