Is remdesivir important in clinical practice as a treatment of COVID-19? A study based on meta-analysis data

To the editor Remdesivir and dexamethasone are the only registered drugs nowadays for coronavirus disease 2019 (COVID-19) and also recommended in our country as the routine treatment.[1] Recent shortage in remdesivir in Polish hospitals generated discussion about the real impact of remdesivir on hospitalized patients with COVID-19, and new World Health Organization opinions on remdesivir issued in November 2020 added even more doubts.[2] In September 2020, a new study by Spinner et al[2] has been published with conclusions that among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared with standard care at 11 days after initiation of treatment. Patients randomized to a 5-day course of remdesivir had a statistically significant difference in clinical status compared with standard care, but the difference was of uncertain clinical importance.

We read the article by Spinner et al[2] with great interest. It is an important study in terms of efforts to combat the COVID-19 pandemic. As the authors point out, hospitalized patients with moderate COVID-19 treated by 5-day therapy with remdesivir had a statistically significant better clinical status compared with those with standard care.

Remdesivir, known also as GS-5734, is an adenosine analogue prodrug, which has inhibitory effects on RNA-viruses. Its therapeutic effect was first demonstrated by suppressing viral replication in Ebola-infected rhesus monkeys.[3] Remdesivir showed also a broad-spectrum antiviral activity with potent in vitro efficacy against multiple genetically unrelated RNA viruses similar to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)[4]; therefore, remdesivir has become the first approved COVID-19 therapy to alter the course of coronavirus-induced lung disease. The commonly recommended daily dose is 200 mg.

In recent months, many studies have concluded that the effectiveness of antiviral drugs in the fight against coronaviruses, especially SARS-CoV-2, is limited. However, the results varied among those studies. Therefore, we conducted the present meta-analysis to summarize the efficacy and safety of remdesivir as a treatment of COVID-19. A detailed procedure for performing the meta-analysis is provided in Supplementary material.

Three studies including 1883 patients[2,5,6] investigated the use of remdesivir as compared with placebo. A meta-analysis showed a statistically significant shortening of time to recovery (mean values in days [MD], –4.70; 95% CI, –4.80 to –4.60; P <0.001), duration of intensive mechanical ventilation (MD, –6.00; 95% CI, –2.60 to –5.36; P <0.001), and duration of oxygen support (MD, –1.80; 95% CI, –2.60 to –1.00; P <0.001) in the remdesivir group compared with the placebo group. However, while the incidence of all adverse events tended to be higher in the remdesivir group (58%) compared to the placebo group (51.4%; P = 0.07), serious adverse events were observed more frequently in the placebo group than in the remdesivir group (13.4% vs 7.4%; P = 0.02).

The analysis of 2 studies (n = 781) which focused on the duration of remdesivir therapy (5 and 10 days, respectively)[2,7] showed lower mortality with shorter duration of remdesivir treatment (4.3% vs 5.9%; P = 0.30), and the need for mechanical ventilation or extracorporeal membrane oxygenation (4.1% vs 8.7%; P = 0.007). Using 5-day therapy versus 10-day therapy was also associated with a numerical reduction in adverse events (61.1% vs 66.2%, P = 0.13) and a statistically significant decrease in serious adverse events rate (13% vs 20%; P = 0.005). A detailed list of adverse events in the analyzed studies is available in Supplementary material.

In view of the above data, among patients with moderate COVID-19, it is worth considering the use of 5-day remdesivir therapy, which, in the light of the above data, is the most

effective method with the lowest risk of serious adverse events. The drug should be therefore widely distributed among COVID-19 hospitals in Poland.

SUPPLEMENTARY MATERIAL

Supplementary material is available with the article at www.mp.pl/paim.

ARTICLE INFORMATION

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