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Timing of Remdesivir for COVID-19

Remdesivir (*Veklury* – Gilead), an investigational antiviral drug administered by IV infusion, is now available through an FDA Emergency Use Authorization (EUA) for treatment of COVID-19 in all hospitalized patients. An earlier EUA limited use of the drug to patients hospitalized with severe disease.[1]

MECHANISM OF ACTION — Remdesivir is a nucleotide prodrug of an adenosine analog that inhibits viral replication by binding to RNA-dependent RNA polymerase. It is active against SARS-CoV-2 and some other coronaviruses *in vitro* and in animal models.

CLINICAL STUDIES — In one clinical trial in 1062 patients who were hospitalized with COVID-19 and had evidence of lower respiratory tract infection (85% were classified as having severe disease), recovery time was shorter with remdesivir than with placebo (median 10 vs 15 days), a statistically significant difference. Kaplan-Meier estimates of mortality were 11.4% with remdesivir and 15.2% with placebo by day 29 (hazard ratio 0.73; 95% CI 0.52 to 1.03).[2]

A clinical trial in 584 patients hospitalized with moderate COVID-19 (pneumonia, but not requiring supplemental oxygen) compared treatment with remdesivir for 5 or 10 days to standard care. The 5-day treatment achieved statistical superiority in clinical status compared to standard care, but the 10-day treatment did not. Mortality rates were similar in all 3 groups.[3]

SARS-CoV-2 REPLICATION — According to the CDC, in patients with mild to moderate COVID-19, replication-competent virus has not been recovered after 10 days following symptom onset. Recovery of replication-competent virus between 10 and 20 days after symptom onset has been documented in some patients with severe COVID-19.[4]

TIMING — In other viral infections, early use of an effective antiviral drug (e.g., within 48 hours of symptom onset with oseltamivir in patients with influenza) is associated with improved clinical outcomes. In the first clinical trial, the median number of days between symptom onset and randomization was 9; the benefit of remdesivir was larger when given earlier in the illness.[2] The median time from symptom onset to treatment in the second trial was 8 days.[3]

CONCLUSION — In a large clinical trial, use of IV remdesivir shortened the time to recovery in hospitalized patients with COVID-19 who had evidence of lower respiratory infection. Whether earlier use of remdesivir, when viral replication is most active and disease-related complications have not yet occurred, would improve outcomes remains to be established. A phase 3 trial of IV remdesivir in outpatients with early COVID-19 is underway and an inhaled nebulized formulation of remdesivir is in development. ■

1. COVID-19 update: FDA broadens emergency use authorization for Veklury (remdesivir) to include all hospitalized patients for treatment of COVID-19. FDA 2020 August 28. Available at: https://bit.ly/3hUs7fO. Accessed October 8, 2020.
2. JH Beigel et al. Remdesivir for the treatment of COVID-19 - final report. N Engl J Med 2020 October 8 (epub).
3. CD Spinner et al. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. JAMA 2020; 324:1048.
4. CDC. Duration of isolation and precautions for adults with COVID-19. Available at: www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html. Accessed October 8, 2020.

Additional Content Available Online

Table: Treatments Considered for COVID-19
http://medicalletter.org/downloads/1595e_table.pdf

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