Early Use of Remdesivir

A Good Start

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At the time of the writing of this editorial, there have been over 600,000 deaths in the United States due to coronavirus disease 2019 (COVID-19), comparable to the number of deaths that occurred during the Spanish flu of 1918. In contrast to the pandemic of the last century, we have rapidly developed a vaccine and identified 3 effective treatments for hospitalized patients with COVID-19. The use of remdesivir, corticosteroids, and most recently tocilizumab are currently the established forms of therapy for the hospitalized patient with serious COVID-19 lower respiratory tract infection. The success in demonstrating the role of these therapies has been due to the outstanding scientific achievements in drug development and clinical trials and a strong collaborative approach by the scientific community.

The only antiviral that has been approved to date has been remdesivir, an intravenous nucleotide prodrug that binds to viral RNA-dependent RNA polymerase and inhibits viral replication. This drug that received an emergency use authorization was shown to be superior to placebo in shortening the time to recovery in hospitalized adults who had evidence of lower respiratory tract infection and required supplemental oxygenation. After a rigorous review of all the clinical trials data, the Food and Drug Administration gave full approval of the drug based on consideration of risk-benefit of this therapy. The original trial overseen by the National Institute of Allergy and Infectious Diseases (ACTT-1 clinical trials.gov number, NCT 04280705) demonstrated the efficacy of remdesivir. This trial had a median time of recovery of 5 days shorter for those receiving remdesivir compared with those who received placebo.[1] Although there was not a statistically significant mortality benefit, there was a trend toward reduced mortality for those who received remdesivir. Thus, the efficacy of this drug has been shown through rigorous scientific study. In addition, the drug has demonstrated an acceptable safety profile.

In this issue of the journal, Paranjape et al[2] demonstrated the effectiveness of remdesivir in a real-world situation evaluated in a network of hospitals in Georgia. For those patients who started therapy within 3 days of a positive test, their length of stay was shortened by 3.6 days, which was statistically significant. In addition, the need for mechanical ventilation and death rate was less for those who had remdesivir started within 3 days of onset of a positive COVID-19. These effects were influenced by oxygen supplementation as one might expect. Other variables could influence the outcome of the study as pointed out by the authors including the use of corticosteroids.

It is encouraging to see how the effectiveness of the drug was very similar to what one saw from the rigorous clinical trial demonstrating the efficacy of remdesivir. We have also learned that 5 days as compared with 10 days is sufficient for the duration of therapy with lower costs and lower potential adverse effects.[3] However, this is just the start in the management of this serious viral infection. Targeting the immune system with drugs such as tocilizumab and other immunomodulators will continue to be investigated and evolve.[4] In addition, we will have to address the issue of oral therapy for even earlier stages of disease and once other antivirals become available the potential role for combination therapy.

As one recalls the treatment of HIV early in the HIV epidemic, it took much longer for establishing a single drug that showed marginal effectiveness in the form of zidovudine alone and after nearly 40 years, we still do not have a vaccine. Thus, the accomplishments of scientific studies are remarkable, and the role of remdesivir as an effective agent is a good early start. However, more work will need to be performed as newer therapies are identified. The authors of this article are to be commended on their careful, critical analysis of the use of remdesivir, which clearly supports the role of remdesivir as an effective early therapy in the community setting outside of a rigorous clinical trial for the treatment of hospitalized patients with COVID-19. Remdesivir is efficacious and effective, and it is a good start in identifying the therapeutic armamentarium of antivirals against COVID-19.

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