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Lopinavir-Ritonavir Is Not Effective against COVID-19

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Update to Chapter 194: Common Viral Respiratory Infections

The ongoing pandemic of COVID-19, the disease caused by infection with the coronavirus SARS-CoV-2, has resulted in a frantic search for effective treatments. Although there have been anecdotal reports suggesting that various regimens might have some efficacy, there still lacks any definitive evidence for a drug that is effective against SARS-CoV-2 infection. The HIV-1 protease inhibitor lopinavir has in vitro activity against SARS-CoV, the coronavirus that caused the emergence of severe acute respiratory syndrome (SARS) in 2003, and SARS-CoV-2. Moreover, an earlier clinical study suggested that patients with SARS had a modest improvement when treated with lopinavir-ritonavir. (Ritonavir increases the plasma half-life of lopinavir.) Given these findings, there was interest in determining whether lopinavir-ritonavir is clinically effective against COVID-19.

Cao and colleagues (2020) performed an open-label, randomized, controlled study at a single hospital in Wuhan, China, the original epicenter for the COVID-19 outbreak. A total of 199 adults with confirmed SARS-CoV-2 infection, an oxygen saturation ≤94% (or a ratio of the partial pressure of oxygen to the fraction of inspired oxygen of ≤300 mmHg), and radiographic evidence of pneumonia were randomized to standard care or standard care plus lopinavir-ritonavir (400 mg–100 mg) twice daily for 14 days. There was no difference in the time to clinical improvement (median, 16 days in each group), although a modified intention-to-treat analysis demonstrated that treatment with lopinavir-ritonavir led to faster clinical improvement by 1 day (median, 15 days in the lopinavir-ritonavir group vs 16 days in the standard care group; hazard ratio, 1.39; 95% confidence interval [CI], 1.00–1.91). The viral RNA loads over time, duration of oxygen therapy, and duration of hospitalization were all similar between both groups. Patients in the lopinavir-ritonavir group had a lower point estimate for 28-day mortality that was not statistically different from the standard care group (19.2% vs 25.0%; difference, –5.8 percentage points; 95% CI, –17.3 to 5.7).

Perspective: Although the main findings of this study were disappointing in that lopinavir-ritonavir was not effective against COVID-19, this study demonstrates that—even in the setting of outbreaks—it is feasible to conduct well-done, randomized studies, the results of which are critical to guide management for patients throughout the world. It is noteworthy that this study was initiated within days of the identification of SARS-CoV-2, enrolled more patients within ~2 weeks than their target enrollment, and disseminated results within ~6 weeks of enrolling their final patient. As this pandemic continues to rapidly grow and spread across the globe, this study serves as a useful reminder that we need to continue to insist on high-quality trials for management of patients with COVID-19 rather than on anecdotal data or “hunches.”

Reference

Cao B et al: A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med, 2020 [Epub ahead of print].