Extended Course of Paxlovid May Help Some Patients With Long COVID

Key Takeaways

- 1. Long COVID affects approximately 7% of US adults, with symptoms persisting beyond 12 weeks post-infection.
- 2. Nirmatrelvir/ritonavir therapy showed varied efficacy in a case series, with only 5 of 13 patients experiencing sustained improvement.
- 3. The study underscores the complexity of long COVID and the need for research to identify responsive patient subgroups.
- 4. Future trials should explore patient phenotyping and the potential benefits of extended antiviral treatment courses.

Some patients treated with prolonged courses of oral nirmatrelvir/ritonavir experienced long COVID symptom improvements, while others reported little to no changes in their symptoms.

Extended courses of oral nirmatrelvir and ritonavir combination therapy (Paxlovid; Pfizer) may have meaningful clinical benefits for some patients with post-COVID syndrome, also known as long COVID; however, not everyone with the condition benefits from extended therapy.^{1,2}



Paxlovid may provide benefits to some patients with long COVID.

Patients with long COVID, a chronic condition associated with SARS-CoV-2 infection the virus that causes COVID-19—experience symptoms that persist for more than 12 weeks following an acute infection. The illness can last weeks, months, or years following a bout with COVID-19; anyone who has had a COVID-19 infection can experience long COVID, and data suggest that approximately 7% of US adults have reported having long COVID.^{1,3} The combination of nirmatrelvir/ritonavir can reduce viral activity, symptom intensity, and fatalities for patients with acute COVID-19. Previous case series, including one conducted by Peluso et al, have suggested marginal symptomatic improvement in patients with long COVID who completed a 5-day course of nirmatrelvir/ritonavir, with the investigator group recommending further systematic trials.⁴

In the current case series, the experiences of 13 individuals with long COVID who were treated with 5-day-or-longer courses of nirmatrelvir/ritonavir are described in detail. Notably, the individuals contracted the condition from different SARS-CoV-2 strains and were administered nirmatrelvir/ritonavir at different lengths of time since the initial infection. The investigators discuss these factors as a strength of the trial, noting how the population reflects the diversity of individuals with long COVID.¹

Despite those strengths, the patients demonstrated varying clinical manifestations of long COVID and differing impacts of antiviral therapy on their symptoms, as only 5 of the 13 patients experienced sustained clinical improvement. Other patients had temporary relief of their symptoms, while some reported no improvements. Most of the patients took nirmatrelvir/ritonavir for a 15-day course.¹

Two cases stick out as examples of both the therapeutic potential of nirmatrelvir/ritonavir. A 56-year-old man who had been dealing with fatigue, photosensitivity, brain fog, elevated heart rate, and joint pain for 2 years following his infection reported an improvement in both his physical and cognitive symptoms after a 15-day course. However, one woman, a 45-year-old who developed long COVID in January 2022 and experienced fatigue, chest pain, and weight loss for months following her infection, reported no effects on her symptoms after a 15-day course of nirmatrelvir/ritonavir the month after a 5-day course gave her a partial reprieve.²

"If we've learned one thing over the last 4 years, it's that long COVID is complex, and figuring out why some people benefit so remarkably from antiviral treatment while others don't is one of the most important questions for the field," Michael Peluso, MD, infectious disease researcher, said in a corresponding news release. "We are going to need to embrace that complexity to get answers for the millions of people suffering from this condition."²

Future research considerations were discussed by the investigators to better assess antiviral treatment in patients with long COVID. Noting the heterogeneity regarding different endotypes of long COVID, they recommended future clinical trials to phenotype patients who exhibit a benefit to antiviral treatment, even if the signal is lost in a larger group. In addition, they postulate on the therapeutic potential of longer courses of

nirmatrelvir/ritonavir, as some patients in the case series only experienced improvement after 10 or more days receiving treatment.¹

"We are about 5 years into the pandemic, and there are not yet any federally approved treatments for long COVID," first author on the study Alison Cohen, PhD, MPH, said in the news release. "This is not a silver bullet, but it may help a lot of people in a meaningful way."²

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