Long-Term Care Updates

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Safety and Effectiveness of Paxlovid for Long COVID

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Introduction

Postacute sequelae of SARS-CoV-2 infection (PASC), also known as long COVID or post-COVID-19 condition, refers to a range of persistent or new symptoms that emerge during or after acute COVID-19 infection. Symptoms of long COVID are wide ranging but generally include physical symptoms (e.g., fatigue, dyspnea, muscle pain, loss of smell), psychological symptoms (e.g., anxiety, depression), and cognitive symptoms (e.g., "brain fog" – poor memory, difficulty concentrating). Various definitions of long COVID have been proposed by the Centers for Disease Control and Prevention (CDC); National Academies of Sciences, Engineering, and Medicine (NASEM); and World Health Organization (WHO). The CDC suggests that long COVID is present if recovery from acute COVID-19 infection does not occur after the 4-week acute phase, while WHO and NASEM suggest that symptoms persistent 3 months after the acute illness are consistent with long COVID.[1] While long COVID affects millions of individuals, no pharmacotherapeutic interventions have been approved for this condition; treatment generally involves supportive care, focusing on the most concerning symptoms on a patient-specific basis.[2]

Nirmatrelvir/ritonavir (Paxlovid) is a SARS-CoV-2 main protease (nirmatrelvir) and HIV-1 protease inhibitor and CYP3A inhibitor (ritonavir) FDA-approved for the treatment of mild-to-moderate COVID-19 in adults at high risk for progression to severe COVID-19.[3] Given anecdotal evidence of symptom improvement in patients with long COVID treated with Paxlovid for COVID-19 reinfection, there has been interest in its use for the treatment of long COVID.[4]

This newsletter will review evidence addressing the safety and efficacy of Paxlovid for the treatment of long COVID.

Novel Drug Approvals (August 2024)

Brand	Generic	Indication	Mechanism of Action	Dosage Form
Lazcluze	Lazertinib	Non-small cell lung cancer	Kinase inhibitor	Oral tablets
Livdelzi	Seladelpar	Primary biliary cholangitis	PPAR-delta agonist	Oral capsules
Nemluvio	Nemolizumab-ilto	Prurigo nodularis	IL-31 antagonist	Injection (subcutaneous)
Niktimvo	Axatilimab-csfr	Chronic graft-versus-host disease	CSF-1R blocking antibody	Injection (intravenous)
Voranigo	Vorasidenib	Grade 2 astrocytoma or oligodendroglioma	IDH1 and IDH2 inhibitor	Oral tablets
Yorvipath	Palopegteriparatide	Hypoparathyroidism	PTH analog (PTH(1-34))	Injection (subcutaneous)

Clinical Evidence

In June of 2024, Geng and colleagues published results of the Selective Trial of Paxlovid for PASC (STOP-PASC). This double-blind, randomized, controlled trial aimed to evaluate the safety and efficacy of a 15-day course of Paxlovid in adult outpatients with long COVID. All participants had a confirmed COVID-19 infection, with symptoms persisting for more than 90 days. To be included, patients had to self-report at least 2 moderate or severe core symptoms (e.g., fatigue, brain fog, body aches, cardiovascular symptoms, dyspnea, and/or gastrointestinal symptoms). Patients who received a COVID-19 vaccine within 28 days of randomization were excluded. Study participants were randomized in a 2:1 ratio to receive Paxlovid or placebo plus ritonavir twice daily for 15 days, with outcomes assessed up until 15 weeks after randomization. A total of 155 patients were randomized, and baseline characteristics were similar between groups. The average duration of long COVID symptoms was around 9 months. All patients reported fatigue, and 95% reported brain fog at baseline. Only one patient in each group had not received the initial COVID-19 vaccination series.[4]

At both the 10- and 15-week follow-ups, Paxlovid did not significantly improve pooled symptom severity or individual symptom severity when compared with placebo plus ritonavir. While Paxlovid was generally well tolerated, more patients reported dysgeusia (62% vs. 8%) and diarrhea (43% vs. 36%) when compared with placebo. The researchers concluded that, while the 15-day course of Paxlovid was generally safe in a mostly vaccinated cohort of patients with long COVID, it did not lead to an improvement in select symptoms of long COVID. This study was limited by enrollment of patients from a single academic medical center, which impacts the generalizability of the findings, and a smaller sample size than was planned due to early enrollment closure, which impacts the statistical power of the study.[4]

While the STOP-PASC trial is the first published clinical trial addressing the safety and efficacy of Paxlovid for long COVID, other studies are ongoing. Researchers at Yale University are conducting a decentralized, double-blind, randomized controlled trial (PAX LC trial) in around 100 adult outpatients with long-COVID [NCT05668091]. Similar to STOP-PASC, this study is also evaluating a 15-day course of Paxlovid as compared to placebo plus ritonavir. However, these researchers are enrolling patients from across the U.S.[5] Additionally, researchers at Karolinska Institute in Sweden are conducting a double-blind, randomized controlled trial evaluating a 15-day course of Paxlovid as compared to placebo plus ritonavir in around 400 adult outpatients with long COVID [NCT05823896].[6]

Prior to publication of the STOP-PASC trial, evidence concerning the use of Paxlovid for long COVID was limited to case reports and case series. Across all cases, the duration of Paxlovid therapy ranged from 5-15 days, and outcomes were mixed. While a few patients reported sustained resolution of long COVID symptoms, many patients reported initial improvement/resolution followed by symptom recurrence shortly after the end of therapy.[7-9]

FDA Safety Alerts

9/12/2024
FDA adds warning about rare occurrence of serious liver injury with use of Veozah (fezolinetant) for hot flashes due to menopause.

Stop medicine if signs and symptoms of liver injury occur

Learn more about this Drug Safety Communication HERE.

Conclusion

The jury is still out with respect to the safety and efficacy of Paxlovid for the treatment of long COVID. The STOP-PASC trial suggests that, while safe, Paxlovid does not seem to improve symptoms associated with long COVID to a statistically or clinically significant degree. Results of ongoing clinical trials in this area will provide a clearer picture of Paxlovid's role, if any, in the treatment of long COVID.

References

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