ICU
MANAGEMENT & PRACTICE

Nirmatrelvir-Ritonavir for Long-COVID

In a recent clinical trial, a 15-day course of nirmatrelvir-ritonavir targeting SARS-CoV-2 was found to be safe as an extended-duration treatment. However, it did not alleviate specific symptoms of long COVID. These findings are published in JAMA Internal Medicine.

The combination of nirmatrelvir-ritonavir is approved by the FDA for treating acute COVID-19 in newly infected adults, with mild or moderate symptoms, and at high risk of complications due to age or predisposing conditions. A five-day regimen has been shown to reduce the likelihood of hospitalisation and death by over 85%.

The STOP-PASC trial (Selective Trial of Paxlovid for Post-Acute Sequelae of COVID) is the first randomised, controlled, double-blinded phase 2 trial of nirmatrelvir-ritonavir for long COVID. While improved therapies for acute COVID now exist, there are no FDA-approved treatments for long COVID. An estimated 10% to 20% of people infected with SARS-CoV-2 develop long COVID. The estimate is imprecise because the definition of long COVID is ambiguous, with more than 200 symptoms attributed to the syndrome. These symptoms overlap with other conditions, complicating diagnosis. Long COVID may encompass different diseases triggered by acute COVID, each with distinct mechanisms and treatment needs.

Potential causes of long COVID include virus-induced changes in gut bacteria, residual inflammation, COVID-induced autoimmunity, and the reactivation of other dormant viruses.

The trial enrolled 155 participants who had tested positive for SARS-CoV-2. Only two had been vaccinated. The median age was 43, with about two-thirds between 34 and 54 years old.

On average, participants had been initially infected more than 16 months before enrolling. Each reported moderate to severe cases of at least two of six common long-COVID symptoms: fatigue, brain fog, shortness of breath, body aches, and cardiovascular or gastrointestinal symptoms.

Study participants were randomised 2:1 to receive nirmatrelvir, 300 mg, with ritonavir, 100 mg, or placebo with ritonavir, 100 mg, taken orally twice daily for 15 days and followed up until 15 weeks from randomisation.

While the trial did not demonstrate that nirmatrelvir-ritonavir reduced long COVID symptoms, it confirmed the safety of a 15-day course.

At the 10-week mark, there was no statistically significant difference between the two groups in reducing the severity of the six core symptoms or in various secondary outcomes like blood pressure, heart rates, and the one-minute “sit and stand” test.

The 15-day regimen was safe. There was one serious, possibly trial-related adverse event (hepatitis) among the placebo recipients, while three serious adverse events (blood loss anaemia, forearm fracture, and melanoma) in nirmatrelvir-ritonavir recipients were unrelated to the drug treatment.

The researchers note that the lack of a clinical response in the trial doesn't rule out nirmatrelvir-ritonavir's potential to reduce long-COVID symptoms in some individuals. Both the intervention and placebo groups' overall symptoms improved over the study. This might indicate that long-COVID symptoms generally subside over time, or it could reflect a placebo effect from the extra attention and hope for relief.

Results from various tests and wearables measurements taken during the trial may help determine whether some participants benefited more from nirmatrelvir-ritonavir and how to identify them for future treatment or trials.

Source: JAMA
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