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# Nirmatrelvir/Ritonavir Compared With Placebo/Ritonavir for Long COVID: A Comment

*To the Editor,*

We would like to comment on "The PAX LC Trial: A Decentralized, Phase 2, Randomized, Double-blind Study of Nirmatrelvir/Ritonavir Compared with Placebo/Ritonavir for Long COVID."[1] In order to determine if nirmatrelvir/ritonavir is more effective, safe, and tolerable than placebo/ritonavir for treating long-term COVID-19 in adult volunteers living in the 48 contiguous US states, the PAX LC trial is a Phase 2 clinical investigation. One hundred people with severe symptoms are involved in the trial, which is run as a randomized, double-blind, placebo-controlled investigation. Patient groups, cultural ambassadors, and social media platforms are some of the recruitment strategies used. A platform that facilitates data collection from electronic health records is used to analyze medical information. The research medicine is supplied straight to participants' homes, and they must complete daily digital diaries and have blood drawn for eligibility and safety evaluations at or near their residences.

The inclusion of many outcome measures, including the PROMIS-29 Physical Health Summary Score and other secondary endpoints, to evaluate the effect of the medication on prolonged COVID symptoms is a major strength of the PAX LC trial. In order to find biomarkers and treatment responders, the trial also uses immunophenotyping. This could be useful in figuring out the underlying causes of long-term COVID and customized treatment plans. The trial's dependence on participant-mediated data collection from electronic health records, which could result in bias and poor data quality, is one of its possible drawbacks. Furthermore, the limited generalizability of the study results could be attributed to the small sample size of only 100 participants.

Future plans for the PAX LC study may involve stepping up recruitment efforts to boost participant diversity and sample size in order to solve these shortcomings. Further safety monitoring procedures and the use of a more capable data-collecting technology that connects directly with electronic health records could also improve the study's trustworthiness. Additionally, evaluating the sustainability of treatment effects by long-term follow-up assessments and investigating the possibilities of combination medicines or other treatment modalities may offer important new perspectives on the management of long-term COVID-19 infections. All things considered, the PAX LC trial holds great promise for advancing our knowledge of and ability to treat long-term COVID-19 patients. However, in order to maximize the study's results and consequences, further adjustments and enhancements could be required.

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## Reference

1. Krumholz HM, Sawano M, Bhattacharjee B, et al. The PAX LC trial: a decentralized, phase 2, randomized, double-blind study of nirmatrelvir/ritonavir compared with placebo/ritonavir for long COVID. *Am J Med* 2024. https://doi.org/10.1016/j.amjmed.2024.04.030. Online ahead of print.

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