

New clinical trial to test Paxlovid's effectiveness against long COVID

April 7 2023, by Isabella Backman



Paxlovid. Credit: [Kches16414/Wikimedia Commons](#), [CC BY-SA](#)

Millions of people worldwide are suffering from often debilitating symptoms of long COVID that can persist weeks, months, or even years following an acute infection. But researchers are still in the dark on the mechanisms underlying and how to treat the mysterious post-viral syndrome. A new clinical trial using the oral antiviral Paxlovid will provide urgently needed insights for COVID long-haulers and their providers.

Since the pandemic's onset, Harlan Krumholz, MD, Harold H. Hines, Jr. Professor of Medicine (Cardiology) and professor in the Institute for Social and Policy Studies, of investigative medicine, and of [public health](#) ([health policy](#)) and Akiko Iwasaki, Ph.D., Sterling Professor of Immunobiology and professor of dermatology, of molecular, cellular & [developmental biology](#), and of epidemiology ([infectious diseases](#)) have been leaders in unraveling the mysteries of long COVID and advocating for those who are suffering.

Through their clinical trial, they plan to combine their expertise in the clinic and lab to understand the biological mechanisms that occur throughout the course of receiving Paxlovid. The trial will be held through a unique decentralized format designed to boost accessibility for its participants.

Krumholz and Iwasaki hope their findings will generate clinical insights on potential markers for diagnostic testing and targets for future interventions. Because studies on long COVID are still scarce, finding answers for long-haulers is crucial. "We need to get out there and start testing things for this group that basically has nothing available to them" says Krumholz. "And by pairing expert biological investigation with

expert clinical investigation, we're opening the door for an entirely different approach to how we're going to do this research and the kind of progress we can make."

Viral persistence is one of several long COVID hypotheses

Krumholz and Iwasaki believe that the manifestation of long COVID may have different pathologies in different patients. Iwasaki was one of the first to propose that long COVID may be the result of the acute SARS-CoV-2 infection reactivating a latent virus, disturbing the microbiome, causing damage that results in downstream inflammation, triggering hyperreactivity of the immune system that fails to shut off post-infection, or, relevant to their trial, that the virus may be stubbornly persisting in some individuals.

"We think that some people never really get rid of the virus, so it continues to cause mischief over time, creating lingering symptoms," says Krumholz. Because of the varying pathologies, some patients may respond more strongly to one treatment than to others.

"We are not expecting everyone to respond, but we should be able to find out who improves from Paxlovid and what their immune signatures are, so we can get better insights into the disease pathogenesis and identify people who are likely to benefit by taking this drug," Iwasaki says.

Although researchers don't know which hypothesis or combination of hypotheses is the true culprit, Krumholz says there is no time to waste as patients continue to suffer. "We've been feeling that we can't really wait until we have a full understanding of the mechanisms," he says. "But one way to gain a better understanding may be to test some strategies that are

specific to one particular theory."

Furthermore, he continues, it will be important to pair these studies with sub-studies that characterize the immune responses of the subjects. That way, if some patients benefit but not others, researchers may be able to identify markers that indicate which individuals may respond best to a certain treatment.

The new clinical trial was inspired by the viral persistence theory, which says that in some individuals, long COVID symptoms may be caused by a lingering virus. Prior research has shown that Paxlovid has antiviral activity against SARS-CoV-2 when used acutely. Therefore, Krumholz and Iwasaki wondered if prescribing patients with the antiviral medication for a longer period may benefit those who are still suffering after the acute infection. By joining forces with Iwasaki, he hopes to identify which participants show the greatest benefit, as well as the underlying immunological changes that occur as they receive the antiviral drug.

Long COVID trial has a novel, accessible design

The randomized trial will involve prescribing symptomatic long haulers with Paxlovid for 15 days, as well as taking blood samples before, during, and after taking the drug for assessing immune responses to the drug. But participation in clinical trials can be burdensome. For many patients, especially those who earn hourly wages, traveling to a study site can interfere with their ability to make ends meet. The study's innovative, decentralized design addresses this obstacle and makes it easier than ever for patients to join. "Through our decentralized trial design, we're going straight to people. We're saying, if you've got this condition, you don't have to come to us. We can come to you," says Krumholz.

Krumholz is a co-founder of Hugo Health, a company that gives patients agency over their health data. Since its launch, it has fostered a community of long COVID patients looking to take part in studies. "It's creating a means through which we can enroll people really rapidly and offer a participant-centric approach," he says. Through the platform, participants can give permission for their data to be used and fill out questionnaires from their mobile devices or computers. Furthermore, individuals will be able to receive blood draws in their own homes and have the drug delivered to their doorstep.

"We're making it so that they can fully participate from home," he says. "We're not only trying to push our long COVID knowledge forward, but also we hope to demonstrate how we can change the way this research is done so that we can test hypotheses much more rapidly, less expensively, and much faster than we would otherwise."

"I am so excited that we are able to offer this patient-centric decentralized trial design to study the impact of Paxlovid on long COVID," Iwasaki adds. "This was only made possible because of Professor Krumholz's deep experience and his perseverance in getting all our ducks in a row."

Another novel aspect of the study is Krumholz's and Iwasaki's unique partnership. Three years ago, no one was a specialist in long COVID. The pandemic forced researchers from different fields who weren't naturally working together to team up. "It required people, no matter what they were doing, to stand up and say that they were willing to try," says Krumholz. "We're creating a study that's truly leveraging my expertise on the best clinical research practices with Professor Iwasaki's expertise on the best laboratory research practices to produce the best insights at a fast pace."

New avenues of understanding for long COVID and

beyond

The team hopes that its study will not only help those struggling with long COVID, but also provide a greater understanding of other post-infectious syndromes. "Infectious triggers are responsible for a whole lot of downstream suffering among people," says Krumholz. "This study will help us begin to understand this phenomenon diagnostically and start identifying targets to help relieve the widespread suffering."

"There are a number of other similar post-acute infection syndromes that happen after many different virus infections and some bacteria and parasitic infections," says Iwasaki. "The fact that the downstream consequences, including myalgic encephalomyelitis, are so similar to each other makes us believe that once we figure out one of these syndromes, we can apply a similar insight into other post-acute phase diseases."

Patients with long COVID and other post-[acute infection](#) syndromes frequently report feeling unbelieved and dismissed by the health care system. "The more we can begin to demonstrate biological correlates, the better we can anchor these as legitimate conditions," says Krumholz. "There's no question in our minds that these are real, but patients often have a hard time with a health care system that doesn't know what to do with them."

Krumholz and Iwasaki are looking forward to working alongside patients as they seek answers to alleviating their suffering.

"For people who join us, they'll be truly a part of something that's important," says Krumholz. "We will treat the people who join as part of the team. We want to make sure they know what is going on and learn the results as soon as we know them. And we want this to become the norm for how research is conducted."

"Throughout this pandemic, we have already learned a great deal about long COVID from patients and advocates," says Iwasaki. "We are about to learn something incredible from patients through our trial. I feel very fortunate to be working as partners in my journey with patients to find a viable therapy against this devastating disease."

Provided by Yale University

Citation: New clinical trial to test Paxlovid's effectiveness against long COVID (2023, April 7) retrieved 11 July 2024 from <https://medicalxpress.com/news/2023-04-clinical-trial-paxlovid-effectiveness-covid.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.