Digital, Decentralized, and Democratized: New Approaches to (Long COVID) Research

The PaxLC Trial Team

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Yale School of Medicine
The PAX LC Trial

Principal Investigator
Dr. Harlan Krumholz

Study Design
A decentralized Phase 2, 1:1 randomized, double-blind, superiority, placebo-controlled study on non-hospitalized highly symptomatic adult participants with Long COVID.

Aim
To determine the efficacy, safety, and tolerability of 15 days of nirmatrelvir/ritonavir compared with placebo/ritonavir.

Rationale
A plausible mechanism for PASC is viral persistence. PAXLOVID, which includes nirmatrelvir (PF-07321332), an antiviral agent that targets the SARS CoV-2 3-chymotrypsin–like cysteine protease (Mpro: also referred to as 3CLpro or nsp5 protease), and ritonavir, a human immunodeficiency virus (HIV)-1 protease inhibitor and CYP3A inhibitor.

Outcomes
- Primary outcome is the PROMIS-29 Physical Health Summary Score at Day 28 (2 weeks after the end of the trial drug treatment).
- Secondary outcomes will include other health status measures.
- Exploratory outcomes: immunophenotyping to explore the effects of treatment on immune signatures and immune markers of response.

Number of Participants: 100
Four possible root causes of long COVID

- Viral reservoir
- Autoimmunity
- Tissue damage and dysfunctions
- Latent virus reactivation
Decentralized study design

Non-hospitalized symptomatic adult participants with PASC (WHO definition)

Preliminary consent

HIV, renal, liver function, TSH (thyroid), CBC counts, pregnancy tests (CLIA approved tests)

Screened PASC participants ($n=100$)

Randomization

Placebo / Ritonavir

(n=50)

Nirmatrelvir / Ritonavir

(n=50)

15 days 2 doses/day

Day 1 - Day 15

Day 1 - Day 15

Biospecimen Collection

Day 0

Day 14

Day 28

Pharmacokinetics analyses

No history of clinically significant hypersensitivity to the product
No known/suspected debilitating chronic conditions
HIV negative
Liver function normal
Renal function normal
TSH levels normal
Not Pregnant
Not breastfeeding
No neutropenia
Deep immune phenotyping
Disclosure

Harlan Krumholz is a co-founder of Hugo Health, a digital health company that enables people to gain agency over their health data and provide permissions for sharing. Hugo Health is being used in the PaxLC study.
This talk describes our strategies to implement digital, decentralized, and democratized approaches to multidisciplinary research.
Our approach seeks to address the deficiencies of traditional research studies, which can tend to be hierarchical, siloed, slow, expensive, and inconvenient.
We believe that research can improve by simultaneously leveraging *advances in technology and culture.*
Our studies must be **convenient, meaningful, respectful, efficient, rapid, and fair.**
The research optimization requires **partnership with participants**, including involvement in study design and workflow, data collection and analysis, and data and results sharing.

Participants should have access to investigators and the results of the studies.
So, we have developed an approach that is digital, decentralized, and democratized.
PaxLC Trial Goals

- Meet or exceed the standards of traditional trials
- Optimize rigor, access, convenience, efficiency, and speed
- Support meaningful participant partnership
PaxLC brings together many innovations.

- Online screening
- Digital medical record review
- e-Consent
- Home-delivery of medications
- Local clinical blood draws
- Home-based biospecimen collection
- Online diaries and surveys
- Digital medical record outcomes
- Participant-centricity, and return of results
Thank you.

harlan.krumholz@yale.edu