Accurate Modeling of Clinical Trials to Guide Antiviral Development

Business Opportunity

Sponsored research

Technology Type

Quantitative Systems Pharmacology

State of Development

Several validated models developed

Esmaeili, S., Owens, K., Wagoner, J., Polyak, S. J., White, J. M., & Schiffer, J. T. (2024). A unifying model to explain frequent SARS-CoV-2 rebound after nirmatrelvir treatment and limited prophylactic efficacy. Nature Communications, 15(1), 5478.

Investigator

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Brief Description

A mathematical framework to optimize antiviral drug selection, dosing, and clinical trial design.

Technology Overview

While notable for enormous successes, clinical development of antiviral therapies lacks efficiency. The most salient example is the discovery and deployment of safe and effective antiviral drugs for SARS-CoV-2 which took nearly two years versus the one-year for vaccines. The blockbuster drug Paxlovid demonstrated unprecedented success in trials, leading to a 90% reduction in hospitalization and death. However, real world use of the drug was severely limited by frequent viral and symptomatic rebound, an outcome which could have been predicted in advance and prevented with alternate dosing strategies.

Dr. Schiffer's group at the Fred Hutchinson Cancer Center has developed a clinical trial simulation / quantitative systems pharmacology approach that can be applied throughout the drug development process, from pre-clinical testing in animal models to early and late phase human trials. This approach can rapidly identify drugs that do and do not have efficacy with relatively few trial participants. Upon identification of antiviral agents with high therapeutic potential, the models can then be used to select 1) optimal dose, 2) treatment duration, 3) timing of treatment and 4) trial endpoints.

A key concept of the clinical trial simulation approach is that drug PK and PD models are necessary but insufficient to predict trial outcomes. A detailed and accurate viral dynamic model capturing the timing and intensity of immune responses against infection is also critical, because antiviral drugs work in synergy with these immune responses. Each human viral pathogen requires its own viral dynamic model. The Schiffer group has deep experience developing these highly specialized models for a wide range of viruses including HIV, hepatitis B, SARS-CoV-2, influenza, Ebola, dengue, HSV-1 and 2, EBV, HHV8 and CMV, and is equipped to perform clinical trial simulation for all relevant viruses.

Applications

- Modeling pre-clinical treatment in animal models, human phase 1, 2 & 3 data, and for post licensure assessment of drug treatment in diverse study populations, including immunocompromised hosts.
- Optimal selection of drug, dose, treatment duration, timing of treatment initiation, combination treatments and trial endpoints

Advantages

- More effective, less expensive and faster clinical trials with antiviral drugs
- Bespoke mechanistic models built using model-informed data collected during preclinical and clinical development; high data granularity increases confidence in prediction.
- Applicable to neutralizing antibodies, CAR T cells, in vivo gene editing technologies, etc.