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The role of clinical trials in a multi-omics discovery pipeline for SUD treatments.

This talk describes our prior work with the St. PETER HIV trial which was designed to re-purpose Varenicline and Cytisine for hazardous alcohol consumption among people with HIV who were heavy drinkers, current smokers, and use opioids. We will also present an ongoing trial of GLP-1 receptor agonists for the reduction of alcohol consumption, cigarette smoking, systemic inflammation, and CVD risk among people with HIV. Each of these trials provides a framework for how FDA approved medications can be re-purposed for substance use disorders.

Building on this framework and the complementary talks in our symposium, we will describe how integrating multi-omic data with trial emulation in large electronic health system datasets informs a new drug repurposing effort in individuals with methamphetamine use disorder. We then show how this strategy directly shapes the design and execution of a randomized, placebo-controlled Phase 2 pilot trial advancing a mechanistically prioritized, FDA-approved candidate. The trial employs a double-masked, parallel-group design with 24 weeks of follow-up, including 12 weeks of active treatment with twice-weekly visits, yielding 24 repeated primary outcome measurements. Randomization is stratified by sex, age, and baseline methamphetamine use severity, and all analyses follow an intention-to-treat framework. The primary endpoint is urine-confirmed methamphetamine abstinence, analyzed using generalized estimating equations to account for within-subject correlation across repeated measures. Secondary endpoints include reduction in craving measured by visual analogue scale and continuous abstinence during prespecified windows.

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