Research team successfully tests new antifungal therapy for fungal meningitis

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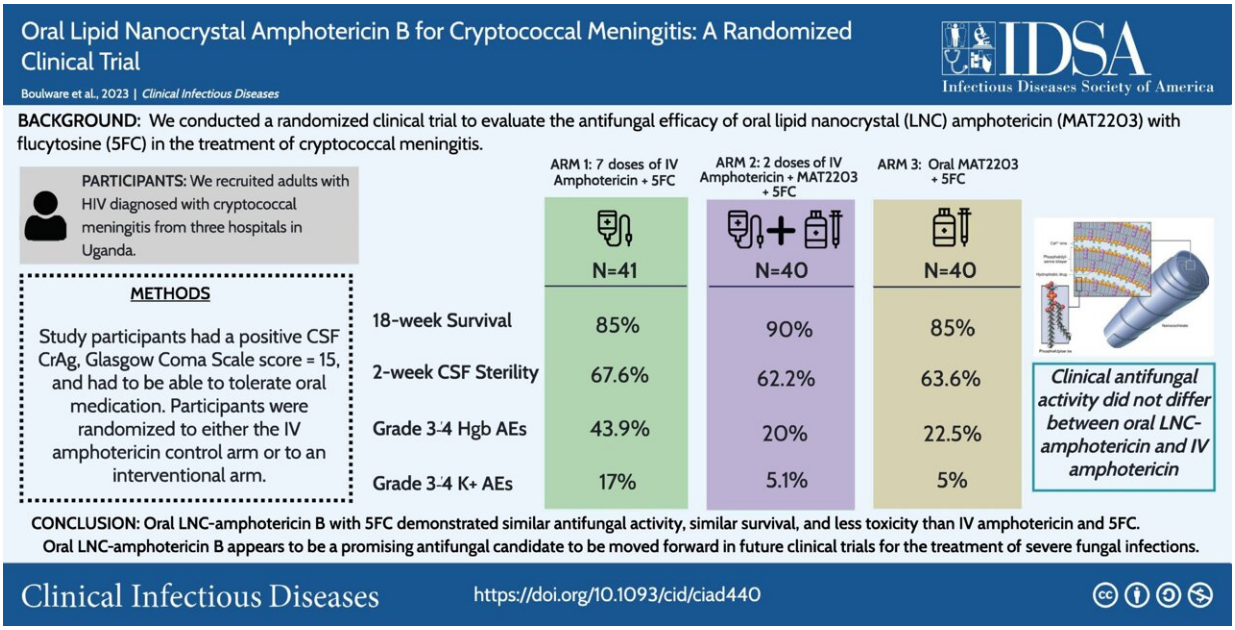

Graphical Abstract. Credit: *Clinical Infectious Diseases* (2023). DOI: 10.1093/cid/ciad440

A team of University of Minnesota Medical School researchers successfully tested a new antifungal therapy to treat fungal meningitis. The trial results were published in *Clinical Infectious Diseases*.

The research team tested a new oral formulation of the antifungal medication amphotericin among people who had HIV and cryptococcal

meningitis—a common fungal infection around the brain. Cryptococcal meningitis is the most common cause of central nervous system infection in people living with HIV worldwide. Conventional amphotericin B can only be administered directly into veins and is highly toxic. The new lipid nanocrystal formulation—which was tested in the EnACT trial—can be taken orally and is non-toxic.

"An orally administered amphotericin that is effective against nearly all fungus and non-toxic sounds like the holy grail of antifungal medicines. While further clinical trials are needed in other fungal conditions, the EnACT trial establishes proof of concept for the safe and effective treatment of invasive fungal infections," said David Boulware, MD, MPH, an infectious disease physician and professor at the University of Minnesota Medical School and M Health Fairview. Dr. Boulware is also the senior investigator of the EnACT trial.

In this randomized trial, 141 HIV-positive people with cryptococcal meningitis received the oral amphotericin combined with oral flucytosine. This combination was found to be promising for cryptococcal meningitis in regard to antifungal activity, similar survival and less toxicity in comparison to intravenous amphotericin B.

Statistically fewer lab abnormalities occurred with the six weeks of LNC-enabled oral amphotericin B compared to one week of intravenous amphotericin B. In the group given two IV loading doses then the experimental oral amphotericin formulation, 90% of participants survived >4 months compared to 85% who received one week of standard intravenous amphotericin.

"With the rising incidence of life-threatening fungal infections, our currently available conventional methods are limited by rising rates of drug resistance and toxicities," said Mahsa Abassi, DO, assistant professor at the U of M Medical School and co-investigator on the trial.

"The development of new antifungal regimens that are orally available, less toxic, and can treat highly resistant fungal infections is crucial."

The trial was conducted in partnership with researchers from the U of M's Medical School, School of Public Health, the Infectious Diseases Institute of Makerere University in Uganda and Matinas BioPharma, a clinical-stage biopharmaceutical company.

"We are very pleased that the important EnACT data are being shared with the clinical and scientific community at large through publication in this peer-reviewed journal," said Theresa Matkovits, Ph.D., and Chief Development Officer of Matinas.

"The results from EnACT in cryptococcal meningitis and our experience with patients enrolled in our ongoing Compassionate/Expanded Use Access Program support our belief that MAT2203 has the potential to become an important part of the regimen for treatment of invasive fungal infections, including in the highest-need patients who require longer-term treatment and have limited or no treatment options."

"The publication of the EnACT data in *Clinical Infectious Diseases* is yet another milestone for our development program. We would like to thank all the EnACT participants, our dedicated investigators, and the entire clinical study team in Uganda for their commitment to this important clinical trial."

More information: David R. Boulware et al, Oral Lipid Nanocrystal Amphotericin B for Cryptococcal Meningitis: a Phase II Randomized Trial, *Clinical Infectious Diseases* (2023). DOI: 10.1093/cid/ciad440

Provided by University of Minnesota Medical School