TPOXX Is Safe but Did Not Improve Mpox Resolution or Pain

NIH study evaluated tecovirimat treatment in countries affected by global Clade II monkeypox outbreak.

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The antiviral drug tecovirimat did not reduce the time to lesion resolution or have an effect on pain among adults with mild to moderate Clade II mpox and a low risk of developing severe disease, according to an interim data analysis from the international clinical trial called the Study of Tecovirimat for Mpox (STOMP). There were no safety concerns associated with tecovirimat.

Considering these definitive findings, the study's Data Safety and Monitoring Board (DSMB) recommended stopping further enrollment of participants who were being randomized to tecovirimat or placebo. As the study sponsor, the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) accepted the DSMB's recommendation. Given the lack of an efficacy signal, NIAID also closed enrollment into an open-label study arm for participants with or at elevated risk of severe disease that was not designed to estimate the drug's efficacy.

"The initial STOMP findings provide valuable insight to inform Clade II mpox medical countermeasures and underscore the critical importance of conducting well-designed randomized clinical trials during infectious disease outbreaks," said NIAID Director Jeanne Marrazzo, MD, MPH. "Before 2022, no treatment candidate had been studied in people with mpox, and this trial is a critical step in our systematic evaluation of existing antivirals like tecovirimat while pursuing novel antivirals and antibody-based mpox therapeutics."

Mpox is caused by a virus that spreads mainly through close contact. Two types of the virus have been identified, referred to as Clades I and II, historically present in Central and West Africa, respectively. A Clade II subtype virus caused a global mpox outbreak in 2022 and the virus continues to circulate at low levels.

In 2024, a Clade I outbreak in Central and East African countries was declared a public health emergency of international concern by the World Health Organization. Travel-related cases of Clade I mpox have been reported internationally and the first reported case in the United States was diagnosed on November 15. In the United States, the risk of Clade I mpox to the public remains low. People with significantly compromised immune systems or certain preexisting skin

conditions, children, and individuals who are pregnant have an elevated risk of developing severe mpox.

Tecovirimat, also known as TPOXX, was initially approved by the Food and Drug Administration (FDA) to treat smallpox—a virus closely related to, but far more serious than, the virus that causes mpox—but the drug's safety and efficacy as an mpox treatment have not been established prior to this year.

The STOMP study began in September 2022 as part of the U.S. whole-of-government response to the Clade II mpox outbreak. The randomized international efficacy study enrolled participants who had been ill with mpox for less than 14 days in Argentina, Brazil, Japan, Mexico, Peru, Thailand and the United States, including Puerto Rico. Participants were randomized at a two-to-one ratio to receive tecovirimat or a placebo. Randomized participants and investigators were blinded, meaning they did not know who received tecovirimat or placebo. Children, pregnant people, and other participants with severe disease, certain skin conditions, or substantially suppressed immune systems were assigned to an open-label study arm, meaning they all received tecovirimat instead of being randomized. The STOMP study assessed all participants' safety and, in randomized arms, evaluated whether a 14-day course of tecovirimat reduced the time to clinical resolution of visible mpox lesions and improved other outcome measures like pain, compared to a placebo.

A planned interim analysis at 75% of the study's target enrollment showed there was no difference in the time to lesion resolution between participants treated with tecovirimat compared with those who received a placebo. Pain decreased similarly between participants treated with tecovirimat and those who received a placebo. At the DSMB's request, an additional assessment was performed and showed that there was a less than 1% chance that the study would show tecovirimat to be effective if it were to complete enrollment and follow-up, based on the study design and available data. At the time of analysis, reported adverse events were low and comparable between tecovirimat and placebo. By design, the open-label study arm did not assign participants to receive a placebo, so STOMP will not draw conclusions about the efficacy of tecovirimat in participants with, or at elevated risk for, severe Clade II mpox.

Further analyses of the study data are ongoing. Study participants are being notified of the findings and study clinicians will make individual clinical care plans with participants based on their disease severity and symptoms. The Centers for Disease Control and Prevention (CDC) holds an expanded access investigational new drug (EA-IND) protocol for mpox treatment outside of research settings. Eligible persons include those with severe immunocompromise, including people with advanced HIV, for whom the role of tecovirimat treatment has not been fully established through a clinical trial. Information on the tecovirimat EA-IND is on the CDC Web site.

"STOMP was a banner study for its speed of startup, inclusiveness, and collaboration across governments and public health authorities" said study chair Timothy Wilkin, MD, MPH, chief of the Division of Infectious Diseases and Global Public Health at the University of California, San Diego. "This study may serve as a model for outbreak response, delivering essential scientific evidence

while also enabling equitable treatment access.”

The STOMP findings are consistent with results reported earlier this year from a NIAID-cosponsored randomized controlled trial of tecovirimat among children and adults with clade I mpox in the Democratic Republic of the Congo.

The NIAID-sponsored study was implemented by the NIH-funded ACTG, a global clinical trials network focused on HIV and other infectious diseases. SIGA Technologies, Inc., based in New York, provided tecovirimat for the study. Throughout the study, NIAID and STOMP investigators collaborated closely with the CDC, FDA, other study country health authorities, teams conducting other studies of tecovirimat, and additional key partners in the mpox response. These consultations allowed research partners to arrive at efficient answers to scientific questions, balance evidence needs with compassionate use considerations, and to avail up-to-date information for clinicians treating clade II mpox globally. An additional study, UNITY, sponsored by ANRS Emerging Infectious Disease, is evaluating tecovirimat with a similar study design to STOMP in Argentina, Brazil and Switzerland. More information about the UNITY study can also be found on ClinicalTrials.gov using the identifier NCT05597735.

NIAID is supporting research to address evidence gaps on medical countermeasures for mpox and other health threats. These efforts include the Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness Network, the Antiviral Program for Pandemics, and the Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern, which collectively conduct discovery, basic and translational research to develop safe and effective vaccines, monoclonal antibodies, and antiviral medicines against virus families of pandemic potential.

For more information about STOMP, please visit ClinicalTrials.gov using the identifier NCT05534984.

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