Tecovirimat Is Safe but Ineffective as Treatment for Clade II Mpox

TPOXX data from NIH-sponsored trial offer further evidence to help inform monkeypox treatment decisions.

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The antiviral drug tecovirimat (TPOXX) used without other antivirals did not reduce the time to clinical resolution of clade II mpox lesions or improve pain control among adults in an international clinical trial sponsored by the National Institutes of Health (NIH).

The trial enrollment was stopped in late 2024 when an interim analysis showed that tecovirimat monotherapy was ineffective in the study population. Detailed results were presented at the 2025 Conference on Retroviruses and Opportunistic Infections (CROI) in San Francisco.

“This study brought us a step forward in better understanding mpox disease and potential treatment strategies,” said Jeanne Marrazzo, MD, MPH, director of NIH’s National Institute of Allergy and Infectious Diseases (NIAID), which sponsored and funded the trial. “We are grateful to the study team and participants for their contributions to groundbreaking research on a disease that we still do not know enough about.”

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. A clade II virus subtype 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. Travel-related cases of clade I mpox have been reported in the United States, but the risk of clade I mpox to the U.S. population remains low. People with significantly compromised immune systems or certain preexisting skin conditions, children and pregnant women have an elevated risk of developing severe mpox.

The Study of Tecovirimat for Mpox (STOMP) began in September 2022 as part of the U.S. whole-of-government response to the clade II mpox outbreak. There are no mpox treatments approved in the United States. Based on animal studies, tecovirimat, also known as TPOXX, was approved by the Food and Drug Administration (FDA) to treat smallpox—a disease caused by a virus closely related to, but typically causing disease far more serious than, the virus that causes mpox. The drug had not been studied in people with mpox until the STOMP trial and a complementary study

called PALM007 in the Democratic Republic of the Congo. PALM007 reported findings in 2024 that were similar to the findings reported from STOMP.

STOMP was a randomized international efficacy study that enrolled participants who had been ill with mpox for fewer than 14 days in Argentina, Brazil, Japan, Mexico, Peru, Thailand and the United States, including Puerto Rico. Randomized study participants and trial investigators were blinded, meaning they did not know who received tecovirimat or placebo. Children, pregnant women, study participants with certain skin conditions or substantially suppressed immune systems, and participants who had severe mpox disease as defined in the study protocol were assigned to an open-label study arm, meaning they all received tecovirimat instead of being randomized.

The STOMP study assessed the safety of the drug among all study participants and, in randomized arms, evaluated whether a 14-day course of tecovirimat monotherapy reduced the time to clinical resolution of visible mpox lesions and improved other outcome measures like pain, compared to a placebo.

Randomized participants reported experiencing mpox symptoms for a median of eight days before study entry and had a median of nine mpox lesions. About a third of participants reported severe pain, selecting scores of 7-10 on an 11-point scale.

By day 29 following study entry, an estimated 83% of participants receiving tecovirimat had reached clinical resolution, compared to 84% who received a placebo, a non-significant difference. Among those reporting severe pain at baseline, improvements were similar between those who received tecovirimat and placebo, with average pain scores decreasing by 3.2 points for participants receiving tecovirimat and by 3.1 points among those receiving the placebo.

Participants' lesions were swabbed and tested for the presence of DNA from the virus that causes mpox throughout the study. At day eight, 48% of participants receiving tecovirimat had undetectable viral DNA compared to 37% of participants receiving the placebo. The difference between the two arms narrowed by day 15 (82% for those receiving tecovirimat versus 80% for those receiving the placebo) as mpox resolved. These differences were not statistically significant at either time point. Adverse event rates were similar between both of the randomized study arms.

A separate exploratory analysis of data collected in STOMP's open-label arm before the study had closed aimed to determine whether any factors were associated with faster mpox lesion resolution in participants with or at elevated risk of severe mpox. Faster clinical resolution was observed in participants who were younger in age or who did not have HIV or were living with HIV but virally suppressed on antiretroviral therapy; however, no association was significant when considering the duration of symptoms before study entry. The investigators noted that STOMP open-label participants had fewer lesions, but slower clinical resolution than reported from the PALM007 trial.

"Since the start of the clade II outbreak, clinicians treating mpox have had limited evidence to guide their practice, and STOMP provided definitive answers on the lack of clinical utility of tecovirimat monotherapy for the randomized population studied" said Timothy Wilkin, MD, MPH,

chief of the Division of Infectious Diseases and Global Public Health at the University of California, San Diego. “Taken together, these latest results also highlight that we still have yet to isolate which factors influence mpox disease progression and clinical resolution.”

The STOMP study was conducted 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. Study results also will be published in a scientific journal.

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

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