

Tecovirimat Is Safe but Did Not Improve Clade I Mpox Resolution in DRC

The antiviral drug did not reduce duration of mpox lesions in the Democratic Republic of the Congo, where an outbreak is ongoing.

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The antiviral drug tecovirimat [TPOXX] did not reduce the duration of mpox [formerly monkeypox] lesions among children and adults with clade I mpox in the Democratic Republic of the Congo (DRC), based on an initial analysis of data from a randomized, placebo-controlled trial.

However, the study's 1.7% overall mortality among enrollees, regardless of whether they received the drug or not, was much lower than the mpox mortality of 3.6% or higher reported among all cases in the DRC. This shows that better outcomes among people with mpox can be achieved when they are hospitalized and provided high-quality supportive care.

The trial is sponsored by the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) and co-led through a government-to-government partnership with the DRC's Institut National de Recherche Biomédicale (INRB). Further analyses and detailed results will be released through scientific channels.

"These findings are disappointing, but they give us essential information and reinforce the need to identify other therapeutic candidates for mpox while we continue research on tecovirimat use in other populations with mpox," said NIAID Director Jeanne Marrazzo, MD, MPH. "We remain committed to developing safe and effective interventions, including treatments and vaccines, that can ease the devastating mpox burden in Central Africa and address the milder form of the virus that is circulating globally."

Mpox has occurred in West, Central and East Africa for decades, with the first human case identified in 1970. Two types of the virus that causes mpox have been identified. Clade I, studied in this trial, is endemic in Central Africa and can cause severe illness. Clade II, endemic in West Africa, tends to result in milder illness. A clade II subtype virus caused a global mpox outbreak in 2022. People with compromised immune systems, children, and people who are pregnant are especially vulnerable to severe mpox regardless of the virus clade.

Reports of clade I mpox are increasing in Central African countries, particularly in the DRC. A [recent report from the Centers for Disease Control and Prevention](#) (CDC) indicated that 67% of suspected DRC mpox cases and 78% of suspected mpox deaths have occurred in people aged 15 years and younger.

[Tecovirimat](#), also known as TPOXX, was initially developed and approved by the Food and Drug Administration to treat [smallpox](#) — a virus closely related to, but far more serious than, mpox—but the drug’s safety and efficacy as an mpox treatment have not been established. It is currently available for mpox treatment in the United States as part of a separate [NIAID-sponsored trial called STOMP](#) and through a CDC [expanded access Investigational New Drug \(EA-IND\)](#) request process. Tecovirimat is authorized in Europe and the United Kingdom for the treatment of smallpox, mpox, and other indications.

In October 2022, [NIAID and INRB launched the PALM007](#) trial to examine the safety and efficacy of tecovirimat for mpox treatment in adults and children. The study enrolled 597 people with laboratory-confirmed mpox at two sites in the DRC. Study participants were randomly assigned to receive tecovirimat or placebo and were admitted to a hospital for at least 14 days, where they were monitored closely for safety and resolution of mpox lesions. All participants received supportive care including nutrition, hydration, and treatment for secondary infections.

Tecovirimat was well-tolerated with no drug-related serious adverse events. Overall, mortality was lower, and lesions resolved faster than anticipated regardless of whether participants received tecovirimat or placebo.

Study participants are being notified of the initial results and offered the opportunity to participate in an ongoing extension study providing further supportive medical care. Additional analyses are planned to better understand outcomes observed in the study, including whether there were any significant differences in clinical outcomes by days of symptoms prior to enrollment, severity of clinical disease, participant characteristics, or the genetic variant of mpox being treated.

“This study delivered urgently needed evidence to guide the mpox response in Central Africa” said co-principal investigator Jean-Jacques Muyembe-Tamfum, MD, PhD, director-general of INRB and professor of microbiology at Kinshasa University Medical School in Kinshasa, DRC. “Although not what we had hoped for, the results show that study clinicians provided exceptional supportive care to all participants, which is a testament to the knowledge and skill that Congolese clinicians have acquired on managing mpox-related disease.”

“The PALM007 study demonstrated the importance and value of testing investigational mpox treatments through robust clinical trials in the DRC’s endemic setting,” said Lori Dodd, PhD, NIAID’s PALM project lead for the DRC. “We’ll continue to evaluate the trial data to determine whether additional studies of tecovirimat in patient subgroups are warranted.

The PALM007 trial is led by co-principal investigators Professor Muyembe-Tamfum and Placide Mbala, MD, PhD, operations manager of the PALM clinical research partnership, and head of the Epidemiology and Global Health Department and the Pathogen Genomic Laboratory at INRB.

NIAID's Veronique Nussenblatt, MD, and Olivier Tshiani, MD, of Leidos Biomedical Research were protocol co-chairs. The trial was implemented in Tunda (Maniema province) and Kole (Sankuru province) with support from Congolese staff, the Mitchell Group and the NIH's Frederick National Laboratory for Cancer Research. Collaborating institutions include the U.S. CDC, the Institute of Tropical Medicine Antwerp (ITM), the aid organization Alliance for International Medical Action (ALIMA) and the World Health Organization (WHO). The U.S. Embassy in the DRC and DRC-based U.S. CDC staff supported logistics and operations for shipments, travel and regional security. SIGA Technologies, Inc., based in New York, provided tecovirimat for the study.

The "Pamoja Tulinde Maisha" or "PALM" clinical research partnership was established in response to the 2018 Ebola outbreak in DRC. The collaboration has continued as a multilateral clinical research program composed of NIAID, the DRC Ministry of Health, INRB and INRB's partners.

NIAID and the INRB thank the extraordinary team of individuals who carried out this study in remote regions of the DRC, the members of the independent study Data and Safety Monitoring Board, and most importantly, the study participants and their families.

For more information about PALM007, please visit [ClinicalTrials.gov](https://clinicaltrials.gov/study/NCT05559099) using the study identifier [NCT05559099](https://clinicaltrials.gov/study/NCT05559099).

"Given the differences in populations affected by the two mpox clades, the types of clinical disease that are appearing and the ongoing spread of both clades, it's very important that we continue with the STOMP trial and other related studies, so that we can develop treatments that benefit all people with mpox," said Dr. Marrazzo.

The international [STOMP trial](https://clinicaltrials.gov/study/NCT05534984) is examining the safety and efficacy of tecovirimat against clade II mpox. For more information about the STOMP trial, please visit [ClinicalTrials.gov](https://clinicaltrials.gov/study/NCT05534984) using the study identifier [NCT05534984](https://clinicaltrials.gov/study/NCT05534984). 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](https://clinicaltrials.gov/study/NCT05597735) using the identifier [NCT05597735](https://clinicaltrials.gov/study/NCT05597735). Both studies will continue to enroll participants and work in close collaboration.

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