



HAL
open science

The international Unity study for antivirals against mpox is a blueprint for future epidemics

Erica Telford, Beatriz Grinsztejn, Inge Christoffer Olsen, Nicolas Pulik, France Mentré, Skerdi Haviari, Maxime Hentzien, Olivier Ségéral, Miquel B Ekkelenkamp, Dimie Ogoina, et al.

► To cite this version:

Erica Telford, Beatriz Grinsztejn, Inge Christoffer Olsen, Nicolas Pulik, France Mentré, et al.. The international Unity study for antivirals against mpox is a blueprint for future epidemics. *Nature Medicine*, 2023, 29 (8), pp.1894 - 1895. 10.1038/s41591-023-02393-6 . hal-04735301

HAL Id: hal-04735301

<https://hal.science/hal-04735301v1>

Submitted on 14 Oct 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

The international Unity study for antivirals against mpox is a blueprint for future epidemics



In 2022, the world experienced an unprecedented outbreak of mpox (formerly called monkeypox). Most cases were reported among gay, bisexual and other men who have sex with men in Europe, the USA and Latin America^{1,2}. At the time of writing, the epidemic is under control in most countries where mpox was not previously endemic. Nevertheless, the disease remains endemic in Africa, and the potential for its re-emergence outside endemic Africa exists.

Current treatments for mpox were approved in Europe and USA based on animal efficacy and safety studies along with human pharmacokinetics and safety studies. However, these treatments have yet to be tested for efficacy in randomized clinical trials (RCTs). The 2022 global spread of this disease, which was previously neglected and restricted to few countries in Africa, is a wake-up call for international collaboration to confirm the efficacy of therapeutics for mpox through RCTs³.

The need for international collaboration to provide information on the efficacy and safety of drug treatments for mpox was affirmed following a World Health Organization (WHO) meeting last year of mpox experts, who emphasized the potential of well-coordinated international collaborations to enable timely and robust evidence generation with a wide applicability⁴.

WHO-supported international consultations among mpox experts organized in July 2022 led to the development of a global, inclusive core protocol for mpox-focused RCTs⁵. This protocol was derived from the PALM007 (NCT05559099) RCT protocol for the evaluation of treatments for human mpox in the Democratic Republic of Congo. The core protocol was developed to improve robustness in clinical efficacy assessment through the use of comparable endpoints.

The Unity study was based on the WHO core protocol (NCT05597735). Unity is a phase 3, multi-country, randomized, placebo-controlled, double-blinded clinical trial to assess the efficacy and safety of the antiviral tecovirimat (TPOXX, SIGA Technologies) in adults and adolescents with mpox. The primary objective is to assess clinical

efficacy, defined as the time to resolution of all visible lesions. Unity is conceived as a platform trial, enabling the evaluation of new therapeutic candidates as they become available. In March 2023, Unity initiated recruitment in the first two co-sponsor countries: Switzerland and Brazil.

The innovative feature of Unity is its governance model, which promotes inclusiveness and international collaboration. Each participating country or region sponsors and seeks funding for the study implemented in its territories, but all work together under global governance. A Trial Steering Committee and a Trial Coordination Team jointly oversee scientific and operational implementation. Importantly, a shared Data and Safety Monitoring Board analyzes data from all participating countries, which are integrated in a common database hosted at the Oslo University Hospital. Working groups are set up to collaboratively address matters such as data management and statistics, data sharing, pharmacovigilance and community engagement. All committees have an international component, and all co-sponsors are represented in the Trial Steering Committee. This study model supports the participation of countries that might lack resources or sufficient disease cases to individually produce conclusive evidence, while guaranteeing in-country data ownership and encouraging international collaboration to promptly obtain robust results.

To further reinforce international cooperation, Unity shares the Data and Safety Monitoring Board with two other clinical trials of tecovirimat against mpox, the European study EPOXI (European monkeyPOX randomized clinical trial), led by the European Clinical Research Alliance for Infectious Diseases (ECRAID), and the African study MOSA (MpOx Study Africa), led by the Pandemic preparedness platform for health and emerging infections response (PANTHER). EPOXI and MOSA are represented in the Unity Trial Steering Committee and Trial Coordination Team. Like Unity, these studies were designed based on the WHO core protocol, sharing the same intervention and primary endpoint⁵. This sets

the ground for data sharing between the trials, strengthening the value of data produced by each study. Furthermore, the collaborative nature of the study paves the way for potential data-based meta-analyses with other tecovirimat trials launched in 2022.

Unity has recently been accepted for funding by the European Commission to support its global coordination, as part of the framework of the MPX-RESPONSE project (101115188), led by ANRS|Emerging Infectious Diseases at Inserm in France. However, two important barriers in setting up such studies should be urgently addressed by the international community. First, European Commission funding mostly targets European countries, which hinders global collaboration. Funding for low- and middle-income countries should be promoted by international funding organizations and should be made available soon after an epidemic starts. Second, the time taken for regulatory procedures and authorizations are not well adapted to an emergency context, which hampers the prompt launch of clinical studies. Because of these delays, opportunities to rapidly gather data during the peak of a health crisis are missed, delaying potential benefits for patients. Upfront discussion with ethics committees and regulatory authorities should be planned as part of pandemic preparedness roadmaps to allow rapid clinical trial initiation.

In conclusion, Unity has the ambition to establish an innovative inclusive international framework and a model for platform trials that allow prompt and efficient evaluation of therapeutic candidates against mpox and other future infectious threats.

Erica Telford¹, Beatriz Grinsztejn², Inge Christoffer Olsen³, Nicolas Pulik¹, France Mentre^{4,5}, Skerdi Haviari⁴, Maxime Hentzien⁶, Olivier Ségéral⁶, Miquel B. Ekkelenkamp⁷, Dimie Ogoina⁸, Nathalie Strub-Wourgaft⁹, Alpha Diallo¹, Yazdan Yazdanpanah^{1,5,10} & Alexandra Calmy⁶✉

¹ANRS|Emerging Infectious Diseases/Inserm, Paris, France. ²Instituto Nacional de Infectologia Evandro Chagas, FIOCRUZ,

Correspondence

Rio de Janeiro, Brazil. ³Department of Research Support for Clinical Trials, Oslo University Hospital, Oslo, Norway. ⁴Département d'Épidémiologie, Biostatistique et Recherche Clinique, Hôpital Bichat, AP-HP, Paris, France. ⁵Université de Paris, IAME, Inserm, Paris, France. ⁶HIV/AIDS Unit, Infectious Diseases Division, Geneva University Hospitals, Geneva, Switzerland. ⁷Department of Medical Microbiology, University Medical Center Utrecht, Utrecht, The Netherlands. ⁸Infectious Diseases Unit,

Department of Internal Medicine, Niger Delta University/Niger Delta University Teaching Hospital, Bayelsa, Nigeria. ⁹PANTHER, Paris, France. ¹⁰Service de Maladies Infectieuses et Tropicales, Hôpital Bichat, AP-HP, Paris, France.

✉ e-mail: Alexandra.Calmy@hcuge.ch

Published online: 30 June 2023

References

1. Girometti, N. et al. *Lancet Infect. Dis.* **22**, 1321–1328 (2022).

- World Health Organization. https://worldhealthorg.shinyapps.io/mpx_global/ (accessed 5 February 2023).
- Tomori, O. & Ogoina, D. *Science* **377**, 1261–1263 (2022).
- World Health Organization. go.nature.com/3BWl8ji (2022).
- World Health Organization. go.nature.com/3N5Yvzj (2022).

Competing interests

M.H. received travel fees and/or honorary for lectures from Gilead Science, ViiV Healthcare, Mylan, MSD and Menarini in the past 3 years. Y.Y. has been a board member receiving consultancy fees from AbbVie, BMS, Gilead, MSD, J&J, Pfizer and ViiV Healthcare; all of these activities stopped in the past 4 years. All other authors declare no conflicts.