

## CORE PROTOCOL

### **An international adaptive multi-country randomized, placebo-controlled, double-blinded trial of the safety and efficacy of treatments for patients with monkeypox virus disease**

#### **Why a CORE protocol?**

Soon after the multi-country outbreak of Monkeypox was declared, [in June 2-3, 2022](#), the international scientific community met to identify the knowledge gaps and research priorities. Experts concluded that given that antiviral data come just from animal models, with remaining uncertainties about their efficacy, especially against monkeypox, randomized trials with standard of care control can be done, are needed, and are ethical.

Following the declaration of the ongoing multi-country monkeypox outbreak as a [Public Health Emergency of International Concern](#), researchers and stakeholders around the world, in collaboration with WHO R&D Blueprint for epidemics, are working to enhance the implementation of the outbreak response actions and to coordinate the implementation of research priorities as [an important component of the response](#).

A core protocol for an international adaptive multi-country randomized, placebo-controlled, double-blinded trial of the safety and efficacy of treatments for patients with monkeypox virus disease has been developed.

It aims to facilitate the participation of clinical researchers, countries' research institutions or regional networks who are interested in contributing to generate the missing data and in reducing the uncertainties regarding treatments for monkeypox.

Assessing common main objectives as defined by the core protocol, enrolling homogenous population, and standardizing data collection tools and agreeing on an analysis for main outcomes through such a protocol could rapidly accelerate generation of robust evidence on the efficacy and safety of one or more treatments for monkeypox and reduce the uncertainty of such estimates.

Particular countries or groups of centres may want to collaborate in assessing additional endpoints or to include further measurements or observations to address questions that are locally relevant (add-on trials). There is an option for countries or regions to complement the core protocol and include such add-on studies, with additional independent data collection and sub-analyses.

#### **Who has contributed to the development of this CORE protocol?**

This CORE protocol is a result of deliberations from several individual experts and from various expert groups including: the WHO R&D Blueprint expert group on clinical trials and statistical methods experts, WHO Clinical Expert Group which comprised the monkeypox guidelines development group, regulatory experts consulted via the WHO Access to Medicines and Health Products Division, members of the WHO expert group for the Target Product Profile for monkeypox therapeutics and many more.

Importantly, this protocol also benefits from the inputs from over 500 experts who attended the first and [second consultations on this topic](#) in June and July 2022. These consultations were organized by the National Institute for Biological Research (INRB) from the DRC, the ANRS | Emerging Infectious Disease, and US NIAID/NIH in collaboration with the WHO R&D Blueprint for epidemics.

The protocol writing group would like to thank the INRB and its partners in particular US NIAID/NIH for providing access to their protocol for randomized evaluation of treatments for human monkeypox (the PALM 007 RCT protocol) which served as the initial basis for this protocol.

### **How can I express interest if my institution would like to participate?**

Each site interested in participating can enroll patients in this international trial and implement the core protocol.

This will require commitment to assess the main objectives as defined by the core protocol, enrolling homogenous population (common inclusion criteria), and evaluating the same interventions with the same primary and secondary endpoints. This adaptive design will allow future flexibility in testing several treatments.

If you and your institution are interested in joining this international trial, please send an email message to the following address: [clinicaltrialmonkeypox@anrs.fr](mailto:clinicaltrialmonkeypox@anrs.fr)

Clearly indicate the country, where you are located, the name of your institution, your name and institutional affiliation, your previous experience in randomised clinical trials and, state whether you are already treating patients with monkeypox.

The global trial team will contact you shortly to discuss some of the requirements and the next steps.