A randomized, placebo-controlled trial of the safety and efficacy of Tecovirimat for the treatment of patients with Monkeypox virus disease

PALM007

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Disclosures

I have no financial interest or relationships to disclose.
History of PALM

- The PALM program was initiated in 2018 as part of NIAID DCR’s emergency research response to the 2018 Ebola outbreak in Eastern Democratic Republic of Congo (DRC).

- A government-to-government agreement was established between NIAID and the DRC Ministry of Public Health (MoH) to initiate research collaboration.

- The outcome of this collaboration is a multilateral clinical research program composed of NIAID, the National Institute of Biomedical Research (INRB)/MoH and INRB’s partners.
Study rationale

- Human MPX cases have been increasing in sub-Saharan Africa
- Cessation of routine smallpox vaccination resulted in the emergence of susceptible populations to other Orthopoxviruses.
- No approved treatments for MPX in areas with greatest burden of disease
- Tecovirimat (ST-246®), developed by SIGA Technologies
  - FDA 2018 (smallpox), EMA 2022 (smallpox, monkeypox)
  - No randomized controlled clinical trial has evaluated the efficacy of tecovirimat for treatment of human MPX.
Primary and Secondary Objectives

Primary:
To evaluate the clinical efficacy, as assessed by time to lesion resolution, of Tecovirimat (+SOC) compared placebo (+SOC) for patients with Monkeypox disease.

Secondary:
1) To evaluate the virologic efficacy, as assessed by time to resolution of viremia, of tecovirimat relative to placebo for patients with monkeypox.

2) To evaluate the clinical efficacy of tecovirimat (+SOC) versus placebo (+SOC) in patients with monkeypox as assessed by mortality, clinical severity, and duration of symptoms.

3) To evaluate the safety of tecovirimat relative to placebo for patients with monkeypox
Exploratory Objectives

Clinical
➢ To evaluate the frequency and characteristics of persistent lesions.
➢ To develop a baseline disease severity metric for monkeypox.
➢ To assess the effect of HIV infection on monkeypox clinical outcomes and treatment effect.

Viral
➢ To evaluate viral persistence in skin lesions and in the oropharynx.
➢ To assess genomic variability in monkeypox virus isolated from participants based on geographic and clinical differences.
➢ To assess if viral resistance develops due to selective pressure by treatment.

Serologic
➢ To evaluate the impact of anti-OPXV antibodies on the course of disease and the clinical efficacy of tecovirimat.
➢ To evaluate the trajectory of monkeypox IgM and IgG during infection.

Epidemiologic
➢ To evaluate exposure history of confirmed monkeypox cases and to identify risk factors for monkeypox infection.
Study sites and subjects

➢ Study sites:

➢ Study subjects:

➢ Symptomatic patients admitted to the study site health facilities with a laboratory-confirmed monkeypox infection will be enrolled as long as they meet inclusion criteria.
Eligibility criteria

Inclusion Criteria:

➢ + Monkeypox PCR from blood, oropharynx or skin lesion within 48 hours of screening.
➢ Any illness duration if at least one active, not yet scabbed, lesion is present.
➢ ≥3kg
➢ Agree to use of effective contraception.
➢ Willingness to follow all study procedures
➢ Written informed consent provided by the patient, legal representative, or culturally acceptable representative.

Exclusion Criteria:

➢ Current or planned use of a meglitinide (repaglinide, nateglinide)
➢ Planned use of midazolam while on study drug
➢ Severe anemia, defined as HGB <7g/dL
➢ Inability to safely swallow oral medications
➢ Current/planned use of other investigational drug
➢ Patients who, in the judgement of the investigator, will be at significantly increased risk as a result of participation in the study
Inclusion
MPXV PCR+
Any age
≥ 3kg
≥ 1 active lesion

Exclusion
Severe anemia
Use of a meglitinide /midazolam
Inability to swallow

Evaluations
Lesion counts in assessment region *daily until fully resolved*, then full body lesion assessment *(yes/no) until fully resolved*
Clinical assessments *daily until discharge.*
MPX blood PCR *daily until negative x2 separated by 24 hours*
MPX skin and oropharyngeal swab *daily for 7 days then every other day until discharge.*
Lab tests *every other day until discharge.*
Blood for storage *day 1, 14, 28, 58*
AE/SAE monitoring *daily until discharge.*

Primary endpoint: lesion resolution (scabbing or desquamation stage) up to 28 days after randomization.

Primary hypothesis: treatment with tecovirimat will increase the time to resolution of monkeypox lesions relative to placebo.
Acknowledgements