Arzhang Cyrus Javan, MD, MPH, DTM&H
DAIDS/NIAID/NIH/HHS

ACTIV-2 Medical Officer
STOMP Medical Officer

A5418: A Randomized, Placebo-Controlled, Double-Blinded Trial of the Safety and Efficacy of Tecovirimat for the Treatment of Human Monkeypox Virus Disease

Study of Tecovirimat for Human Monkeypox Virus (STOMP)

https://www.stomptpoxx.org

STOMP
Study of Tecovirimat for Human Monkeypox Virus

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AIDS CLINICAL TRIALS GROUP

Why we need randomized, placebo-controlled clinical trials

- There are no controlled human efficacy data available for tecovirimat
- Tecovirimat has only been tested in a clinical trial setting in healthy human volunteers, without smallpox or mpox infection, to assess safety
- Primary outcome measure (time to clinical resolution of lesions) and key secondary outcomes (e.g. pain) are subjective endpoints; placebo control/blinding are critical for reducing bias
- Full approval and scale-up of treatment is challenging without controlled data
- If the drug doesn’t work, we are spending time and money that could be used to discover and test drugs that do
- Learn more about potential viral resistance to the drug

Timeline and current study status

- 1st protocol team meeting: 21JUL2022
- Submission to FDA/IRB: 11AUG2022
- **1st person/1st visit: 8SEP2022**
- 201 total participants enrolled; 190 in US and 11 ex-US
  - September: 11
  - October: 24
  - November: 27
- Of 201 enrolled, 121 are in Arms A/B and 80 in Arm C
- 57 sites activated in US
- 4 ex-US sites activated (Mexico, Japan, Brazil, Peru) + 10 pending

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IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Study Summary

Design and Sample size	Arms A/B - 2:1 Randomized, Blinded, Placebo-controlled (n=530) Arm C - Open label
Study Population	Symptomatic mpox infection
Design	Superiority
1^0 Outcome	Time to clinical resolution
Duration	57 days
Enrollment period	TBD
Agent	Weight based oral Tecovirimat (inhibitor of the orthopoxvirus VP37 envelope wrapping protein)

Hypothesis

- Tecovirimat will lead to faster clinical resolution of HMPXV disease compared to placebo.

1^0 Objective

- To compare time to clinical resolution between people with HMPXV randomized to tecovirimat or placebo.

and endpoint

- Clinical resolution is when all skin lesions are scabbed over, desquamated, or healed and all visible mucosal lesions healed

Step 1: daily self skin checks and photographs

Step 2: participant reports clinical resolution

Step 3: video visit to confirm clinical resolution

Step 4: confirmation at in person visit

Other Key Objectives

- To compare **pain scores** between randomized arms.
- To compare rates of **progression to severe HMPX disease** between randomized arms.
- To compare **clearance of HMPXV** between randomized arms in various compartments including blood, skin lesions, oropharynx, rectum, and genital secretions.
- To compare time to **complete lesion healing** between randomized arms.
- To compare **participant-reported outcomes** including adherence and EQ-5D-5L between randomized arms.
- To evaluate the **safety** of tecovirimat as compared to placebo.
- To describe time to lesion resolution, pain, clearance of HMPXV, time to complete lesion healing, participant-reported outcomes, and safety of tecovirimat in participants who receive **open-label tecovirimat**
- To determine the **steady-state tecovirimat $AUC_{0\text{-}12h}$ and C_{12}** in children less than 18 years of age.
- To evaluate the **safety profile of 14 days of tecovirimat in children** less than 18 years of age.
- To evaluate **resistance**

A5418 Population Eligibility (all arms)

- **Confirmed or presumptive** HMPXV disease
  - Laboratory confirmed HMPXV within 7 days
  - Presumptive diagnosis: Skin lesion(s), mucosal lesion(s) or proctitis consistent with a high probability of HMPXV in the opinion of the site investigator AND Sexual contact with 1 or more persons in the 21 days prior to symptom onset or close exposure to another person known to be infected with HMPXV.
- HMPXV illness of <14 days duration immediately prior to study entry
- At least one active (not yet scabbed) skin lesion, mouth lesion, or proctitis with or without visible ulcers.
- Non-pregnant people agree to contraception or abstinence
- Ability to provide informed consent; assent for children

A5418 Criteria for open-label tecovirimat in Arm C

- **Participants age <18 years** at the time of study entry
- Those with **severe HMPXV disease** defined as having one or more of the following conditions:
  - Suspected or confirmed ocular involvement
  - Facial lesions on the malar, nose, or eyelid region
  - Confluent facial lesions
  - Hospitalization due to HMPXV infection or its complications
  - Lesions that require surgical intervention including debridement, urinary catheterization or sigmoidoscopy, or lesions extending below the dermis
- **Severe immunosuppression** defined as:
  - HIV with CD4 <200 cells/mm^3 or plasma HIV-1 RNA >1000 copies/mL
  - Leukemia, Lymphoma, Generalized malignancy, etc.
  - *Other severe immunosuppression in the opinion of the site investigator*
- **Skin conditions** placing the person at higher risk for disseminated infection as defined as: Atopic dermatitis, Active exfoliative skin condition(s) such as eczema, burns, etc
- **Pregnancy or breastfeeding**
- Receipt of **potent inducers,** including rifampin, rifapentine, etc.
- Current or planned use of another investigational drug at any point during tecovirimat/placebo dosing that would be predicted to have a **significant drug-drug interaction** with tecovirimat therapeutics.

Therapeutic Landscape

- PALM 007 – NIAID Sponsored study
  - TPOXX in DRC
  - Clade I
- UNITY – Based off WHO Global Clinical Platform for Mpox
  - Brazil and Switzerland
- PLATINUM – Oxford University

Therapeutic Landscape

- Cidofovir
- Brincidofovir