Virologic and Immunologic Characteristics of Severe Mpox among Persons with Advanced HIV (VIRISMAP)

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Overview

Background

- **During the 2022 multinational mpox outbreak, most cases were among gay, bisexual, and other men who have sex with men (MSM).**
- **Severe illness and death from mpox has been observed among people with advanced HIV.**
- **Clinicians have observed worsening mpox manifestations among people with advanced HIV after initiation of antiretroviral therapy.**

Severe Mpox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR (cdc.gov)
Mpox in people with advanced HIV infection: a global case series - The Lancet

Background

- **The extent to which mpox pathology in people with advanced HIV is virally versus immunologically mediated, is unknown.**

- **Knowledge of mpox disease pathogenesis among people with advanced HIV can inform clinical care and prevent mpox-associated morbidity and mortality.**

Primary objective

Describe the relationship between the systemic immunologic response, and the persistence and replication competence of *Monkeypox virus* (MPXV) from lesions over the course of mpox illness among people with advanced HIV.

Secondary objectives

Among patients living with advanced HIV and severe mpox:

- **Describe associations between clinical outcomes and virologic and immunologic parameters.**
- **Survey for emergence of antiviral drug resistance among MPXV isolates collected over time during mpox illness among patients with advanced HIV.**
- **Characterize the effects of antivirals to treat mpox and/or HIV infection based on virologic and immunologic parameters.**
- **Assess persistence and replication competence of MPXV in novel specimen types (oropharynx and rectum) over the course of mpox illness.**

Study Design

Study overview

- **Design: prospective cohort study.**
- **Cohort: 100 participants aged at least 18 years with confirmed or probable mpox and HIV in the United States (including 15 outpatients and 85 inpatients).**
- **Study visits: conducted at pre-scheduled time points and at specific sentinel events.**

Study overview

- **Data collection: Clinical data and samples will be collected at each study visit.**
- **Laboratory testing: Analysis of viral and immunologic parameters will be conducted at CDC and NIH laboratories.**
- **Data analysis: descriptive.**
- **Timeline: 12 months of participant enrollment, 18 months total.**

Study team

- **CDC**
  - Poxvirus and Rabies Branch
    - **Nicolle Baird**, PhD
    - **Christina Hutson,** PhD, MS
    - **Taina Joseph**, MPH
    - **Faisal Minhaj,** PharmD, MPH
    - **Sathesh Panayampalli**, PhD
    - **Agam Rao,** MD
  - HIV Research Branch
    - **Jesse O'Shea,** MD
  - Infectious Diseases Pathology Branch
    - **Julu Bhatnagar**, PhD
    - **Sarah Reagan-Steiner,** MD, MPH
    - **Roosecelis Martines**, MD, PhD
    - **Julian Villalba**, MD
    - **Jana Ritter**, DVM
  - **Shama Cash-Goldwasser,** MD, MPH
- **NIH**
  - **Brian Epling,** MD
  - **Claire Deleage,** PhD
  - **Katy Saliba,** ScM, PhD
  - **Irini Sereti,** MD, MHS
- **Karius**
  - **Sarah Park**, MD
- **Consultant**
  - **Jason Zucker**, MD, Columbia University

Design: participant recruitment

Cohort recruitment:

- **Up to 15 outpatients will be recruited from a single pre-determined clinical site (Columbia University).**
- **Up to 85 inpatients will be recruited from participating clinical sites, and participants will be followed only while hospitalized.**

Design: participant recruitment

Eligibility Criteria for 85 inpatients:

- **Age ≥ 18 years.**
- **HIV infection and CD4 count < 200 cells/mL.**
- **Probable or confirmed mpox infection.**
  - **Does NOT need to be a new infection.**
- **Hospitalized while symptomatic from mpox.**
  - **For reasons other than infection prevention and control.**

Design: study visits

1. **Routine visits:**
   - **Enrollment.**
   - **Every four weeks while hospitalized.**
   - **Every week while in intensive care.**
   - **Resume two weeks after study visit.**

2. **Sentinel events:**
   - **Two weeks after antiretroviral therapy (ART) initiation.**
   - **One week after vaccinia immune globulin intravenous (VIGIV) administration.**
   - **Surgery under general anesthesia related to mpox-associated complications.**
   - **Admission to ICU from non-ICU.**
   - **Hospital discharge.**
   - **Death.**

Design: data and sample collection

At study visits:

- **Clinical data: current symptoms and physical exam findings.**

- **Laboratory samples:**
  - **Lesion swabs.**
  - **Mucosal swabs (e.g., oropharyngeal, rectal).**
  - **Blood samples.**

Design: data and sample collection

Tissue biopsy samples (antemortem) per clinical discretion:

- **Formalin-fixed, paraffin-embedded tissues.**
- **Fresh tissue.**
- **Autopsy tissue samples (if performed):**
  - **Formalin-fixed, paraffin-embedded tissues.**

At end of enrollment:

- **Medical chart abstraction reports.**
  - **Medications administered.**
  - **Results of routine laboratory tests.**

Design: laboratory analysis (swabs and blood samples)

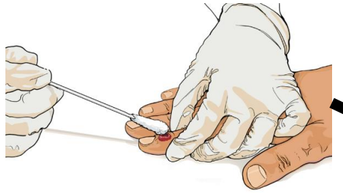
Sample Type	Test to be Performed	Processing Lab
Lesion swabs	PCR Viral culture Viral sequencing/resistance	CDC
Mucosal swabs	PCR Viral culture Viral sequencing/resistance	CDC
Blood/Serum	PCR Antibodies to *Orthopoxvirus* Viral culture Viral sequencing/resistance Immunoassays Cellular RNA analysis Microbial DNA detection	CDC NIH Karius

Design: laboratory analysis (tissue samples)

Sample Type	Test to be Performed	Processing Lab
Fresh tissue (ante-mortem)	PCR Viral culture Viral sequencing	CDC
FFPE tissue (ante-mortem)	IHC for *Orthopoxvirus* ISH for *Monkeypox virus* Immunostaining	CDC NIH
FFPE tissue (post-mortem)	IHC for *Orthopoxvirus* ISH for *Monkeypox virus* Immunostaining	CDC NIH

FFPE = formalin-fixed, paraffin-embedded; IHC = Immunohistochemistry (detects antigen); ISH = In-situ hybridization (detects DNA)

Design: data management and flow



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*Note: This does not necessarily represent submission of formalin-fixed, paraffin-embedded or fresh tissue specimens

Ethical considerations and approval

- **Institutional review board (IRB): CDC holds single IRB which may be used by collaborating sites via reliance agreement.**
  - **Sites may seek independent IRB determination, if desired.**
- **Informed consent: Specific methods of informed consent (e.g., written, electronic, etc.) will be provided per site institutional policies and preference.**
  - **Frequency and reasons for refusal will be documented.**

Ethical considerations and approval

- **Risks and benefits:**
  - **Risks: minimal, associated with blood draws.**
  - **Benefits: no direct benefits (no financial compensation).**
    - **Findings may inform the care of future patients.**
- **Clinical care is not modified by study participation and is at the discretion of the treating clinical team.**

Other collaborating site considerations

- Data analysis to satisfy study objectives: led by CDC and NIH.
  - These analyses should not preclude other case reports.
    - Open to data-sharing agreements if desired.

- Participation in other studies is allowed.

- Collaborators will be included in group authorship (VIRISMAP study team) on publications.

- State and/or local public health jurisdictions will be notified of participating sites in their jurisdiction.

Other collaborating site considerations

- **Blood, swabs, and viral culture testing will not be performed under CLIA, so results will not be returned to clinicians to inform patient care.**
- **Tissue biopsy samples will be collected per clinician (not study) discretion:**
  - **For FFPE biopsy or autopsy sample submission, sites will contact CDC with the participant ID in the body of the email.**
  - **Results of CDC testing on FFPE tissues will be reported back to clinicians.**
- **Results of MPXV-resistance testing will be reported back to public health jurisdictions to inform public health response efforts (as is currently done) but may not be used to inform patient care**

CLIA = Clinical laboratory Improvement Amendments

Resources provided by STUDY

- **IRB: CDC holds IRB determination.**
- **Forms: printed copies (informed consents, clinical data forms) provided.**
- **Sample collection: sample collection tubes provided.**
- **Sample shipping:**
  - **Specimen shipment will be covered, and the number of shipments will be minimized.**
  - **For FFPE, shipping will be coordinated with CDC.**

Resources provided by STUDY

- **Laboratory testing: costs associated with testing outside clinical site.**
- **Data collection and input: data from clinical forms and electronic medical record will be input to database by CDC.**
- **Resources to analyze, interpret, and publish study findings.**

Resources provided by SITE

- **Enrollment, including informed consent**
- **Clinical data collection: Performed by site staff and documented on paper forms at each study visit.**
- **Sample collection: blood samples and lesion swabs at each study visit.**
- **Sample preparation: at site lab, for shipping to NIH/CDC.**

Initiating collaboration

If you are interested in collaborating on VIRISMAP, please email poxvirus@cdc.gov.

We will then start working with you to set up the collaboration.

Collaboration may be initiated any time during the study, but we recommend getting set up as soon as possible so that your site is prepared to enroll eligible patients.

Website & Contact Information

- **Website with link to this presentation and written study description: https://www.cdc.gov/poxvirus/mpox/clinicians/treatment.html#MPOX-eval.**

- **Email for expression of interest or any questions: poxvirus@cdc.gov.**

Thank You!


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