

Title of the article: Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo

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(250 words)

Background: Mpox (clade I & II) incidence is rising globally, including in Queensland, where probable congenital infection recently occurred. Tecovirimat, an oral antiviral, is used in mpox based on animal efficacy and human safety data but clinical efficacy trials are lacking. This double-blind, randomised, placebo-controlled trial evaluated tecovirimat in patients with clade I mpox in the Democratic Republic of Congo. Patients weighing >3kg with ≥ 1 skin lesion and PCR-confirmed infection for were randomised 1:1 to 14 days of tecovirimat or placebo. The primary end point was time to lesion resolution. The study was powered (85%) to detect a 40% reduction in time to resolution with a 5% two-sided type-I error-rate.

Main Findings: Between 2022 – 2024, 597 patients were randomised (295 tecovirimat, 302 placebo) with balanced baseline characteristics. Median time to lesion resolution was 7 days with tecovirimat and 8 days with placebo (HR 1.13, 95%CI 0.97 – 1.31; $p=0.14$). Results were consistent between patients who began treatment before, or after 7 days of symptoms. Adverse events (72.9% vs 70.5%) and serious adverse events (5.1% vs 5.0%) were comparable in the treatment vs control arms. Notably, 35% of 60 measured drug levels were below the minimum effective concentration, but this did not correlate with outcomes.

Take home message: Tecovirimat was safe but did not shorten time to lesion resolution in clade I mpox in this robust randomised controlled trial. Alternative therapeutic agents need to be explored.

Quiz Club Questions:

Prepare 1-3 multiple choice questions, preferably 'A-type' single best of 5 alternatives A-E, with a brief explanation at the end, for the correct/incorrect answers.

1) Mpox is considered endemic in which regions, with which animal reservoir?

- A) Northern Africa; Camels
- B) South and east Africa; Monkeys
- C) Central and west Africa; Rodents
- D) Central America; Monkeys
- E) South America; Rodents

Correct answer: C

Explanation: The monkeypox virus (MPXV) is an orthopox virus within the same genus as variola virus (the causative agent of smallpox) and vaccinia virus (used in the smallpox vaccine). There are two distinct clades: Clade I historically in Central (and east) Africa (more virulent), and Clade 2 historically in Western Africa (less virulent). Each clade has sub-clades (a & b) with clade 1b less virulent than 1a. MPXV is a zoonotic infection with a reservoir in rodents, with humans and monkeys incidental hosts.

2. Which clade was responsible for the large global outbreak of mpox in 2022-2023

- A) Clade Ia
- B) Clade Ib
- C) Clade IIa
- D) Clade IIb
- E) Clade III

Correct answer: B

Explanation: There has been two major outbreaks of Mpox in the last few years. The first was a global outbreak in 2022-2023 of Clade IIb which spread from Africa to Europe, Americas and Australia. This largely affected the men who have sex with men (MSM) population with transmission predominantly through close sexual contact. A second outbreak of clade Ib predominantly affected central and east Africa (DRC, Uganda, Burundi, Kenya, Rwanda), with travel-associated spread outside of Africa. The clade Ib outbreak showed household as well as sexual transmission.

3. What clinical features make a diagnosis of varicella more likely than mpox?

- A) Firm, Umbilicated lesions
- B) Painful lesions
- C) Lymphadenopathy
- D) Lesions in different stages
- E) Lesions in the same stages

Correct answer: D

Explanation: Mpox has an incubation period of 5-13 days (range 4-21). Clinical features include a prodrome (fever, fatigue, headache, dysphagia, myalgia), followed by rash which occurs 2 days before to 4 days after the prodrome. The rash lasts 2-3 weeks and is characterised by 2-5mm macules progressing to papules, vesicles which then crust. The lesions are well circumscribed, deep seated, often umbilicated, synchronous, painful. The location is variable depending on the setting (eg. wide distribution but somewhat sparing trunk in endemic settings, to oral/genital lesions in the 2022 outbreak). Features which differentiate Mpox from varicella include: lymphadenopathy and the lesions which are all at the same stage (rather than polymorphous), umbilicated and painful, and more centrifugal (rather than centripetal).

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