On the use of Tecovirimat for MPXV infections: why does it not work?

Thomas Beneteau*[1]

[1]IAME - Université Paris Cité, INSERM – Hôpital Bichat - Claude Bernard – France

Résumé

In 2022, the mpox virus (MPXV) was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization following a global outbreak of clade IIb. In 2024, MPXV was again declared a PHEIC after a resurgence of clade Ib in Central Africa, particularly in the Democratic Republic of Congo. Tecovirimat, an antiviral targeting orthopoxviruses, was approved for smallpox treatment prior to the 2022 outbreak, based on animal efficacy data and safety studies in healthy individuals and was considered as the primary candidate for mpox treatment.
Following the 2022 outbreak, three clinical trials were launched to assess Tecovirimat's efficacy in humans. Early results from two studies showed the treatment was safe but did not reduce the time to lesions resolution nor shorten the duration of the viral presence in biological samples. These findings were unexpected, as Tecovirimat has demonstrated nanomolar *in vitro* efficacy against multiple MPXV clades, supported by studies in non-human primates and mice models.
In this study, we used a non-linear mixed effects modelling approach to assess the impact of delayed treatment initiation and suboptimal drug exposure on the time to viral clearance between treated and untreated participants. Our results suggests that, even with delayed treatment and/or under suboptimal dosage regimen, a significant difference in the time to viral clearance between treated and untreated individuals should be observed even 14 days after inclusion. More generally, our findings point to additional factors not captured by the current model that may contribute to the apparent lack of antiviral efficacy on the time to viral clearance observed in the clinical studies so far such as a poor diffusion of the drug to the targeted compartments or the emergence of tecovirimat-resistant MPXV strains.

*Intervenant