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Effect of tecovirimat on MPXV DNA clearance in participants randomized in the ANRS 0576s UNITY trial

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Background

Unity is a phase III, randomized trial to assess tecovirimat for patients with Mpox disease in Brazil, Argentina and Switzerland. Tecovirimat did not shorten time to resolution of Mpox lesions (B. Grinsztejn et al. IAS 2025).

The objective of this substudy was to assess viral load decrease and time to undetectability of Mpox virus (MPXV) DNA.

Methods

- Mpox active lesions, oral and rectal swabs were collected at day 1 (D1), D8, D15, D22 and D29 after randomization.
- DNA was quantified using the NeuMoDX MPVX test (Qiagen, France) and a standard calibration curve (limit of detection 8.6 copies/mL). Resolved lesions were not swabbed and were imputed as negative PCR.
- The pre-specified secondary endpoint of overall time to undetectability (from merged samples) among patients with centralized positive baseline PCR (N=418) was presented using interval-censored Weibull parametric survival regression, adjusted for center, time from onset, and presence of complications.
- Exploratory viral loads by specimen sample were compared using the Mann-Whitney-Wilcoxon rank-sum test at each time point.
- We stratified by HIV status, CD4 count (< or > 500 cells/mm3) and presence of sexually transmitted infection (STI) at baseline (gonorrhea, syphilis and/or chlamydia).

Results

- In total, 5275 lesion, oral, and rectal swabs specimens from 442 participants were centrally analyzed.
- Main characteristics were presented in **Table 1**. The median (IQR) time from symptom onset to randomization was 9 (6;12) days.
- At baseline, the viral load was higher in lesions (7 (6.3-7.6) log10 copies/ml) compared to oral (3.4 (2.7-4.4)) and rectal (4.7 (2.9-7.3)) swabs.
- Time to overall MPXV DNA negativation (lesion and/or oral and/or rectal swabs) is shown among 418 participants with baseline positive PCR performed centrally (**Figure 1**). The median time to MPXV PCR negativation was 24.2 days (IQR 16.1-33.4) in the placebo group and 21.9 days (IQR 14.6–30.1) in the tecovirimat group (p=0,71).
- Subgroups analyses for time to PCR negativation was presented in **Figure 2**. There was no interaction between tecovirimat and analyzed subgroups

Table 1

	Overall, pITT (N= 446), N (%)	Tecovirimat (N=223), n (%)	Placebo (N=223), n (%)
Age, Median [IQR]	34 [29; 39]	34 [29 ;39]	33 [30 ;39]
Sex, Male n (%)	442 (99.1%)	220 (98.7%)	222 (99.6%)
STI	109/395 (27.6%)	45/196 (23%)	64/199 (32.2%)
People living with HIV	217/445 (48.7%)	105/223 (47.1%)	112/222 (50.5%)
On regular ART	210 (97.2%)	101 (96.2%)	109 (98.2%)
HIV RNA Viral Load < 50 copies/mL	185/216 (85.6%)	94/105 (89.5%)	91/111 (82%)
CD4+ cell count (cells/mm^3)			
>500	163 (75.5%)	76 (72.4%)	87 (78.4%)
200-500	36 (16.7%)	18 (17.1%)	18 (16.2%)
<200	17 (7.9%)	11 (10.5%)	6 (5.4%)
Time from symptom onset to randomization (median (IQR) days)	9 [6; 12]	9 [6 ;12]	9 [6 ;12]

Figure 1 : Time to MPXV PCR negativation on merged samples

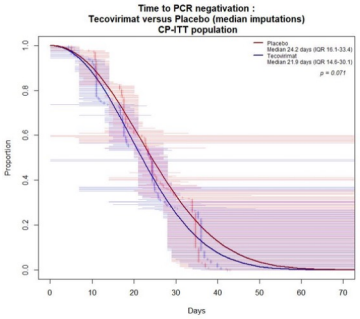
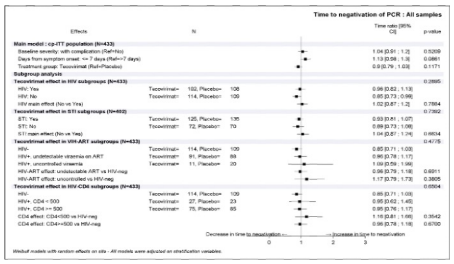


Figure 2 : Subgroups analysis for time to MPXV PCR negativation



- **Figure 3** presented MPXV viral load in each specimen : (A) skin-lesion, (B) oral and (C) rectal swabs among the 442 participants.
- Viral load were lower with tecovirimat than with placebo in oral swabs at D8 (p<0.001) and D15 (p=0.008), but not in skin-lesion or rectal swabs.
- In multivariate analyses (**Figure 4**), the nominally significant difference in oral swabs persisted at D8. The MPXV DNA copy number in the tecovirimat group was 0.11 times that in the placebo group (95% confidence interval [CI], 0.04 to 0.29). HIV infection with a CD4 count of less than 500 cells/mL was associated with a smaller decline in oral-swab viral load at D8 and D15 than HIV-negative status.

Figure 3A : Lesion-skin swabs

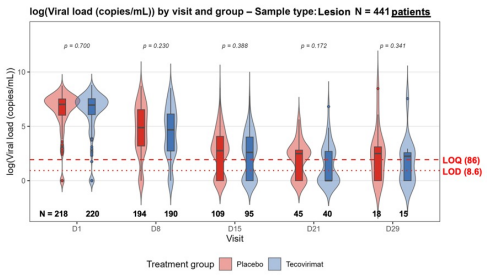


Figure 3C : Rectal swabs

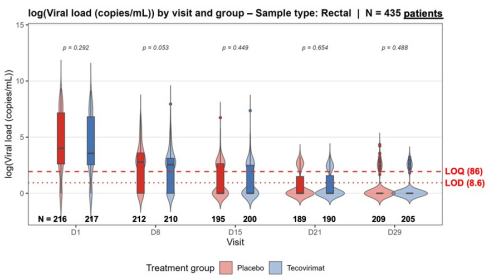


Figure 3B : Oral swabs

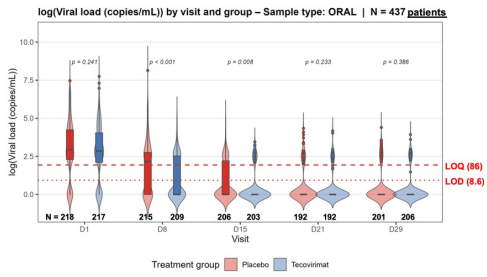
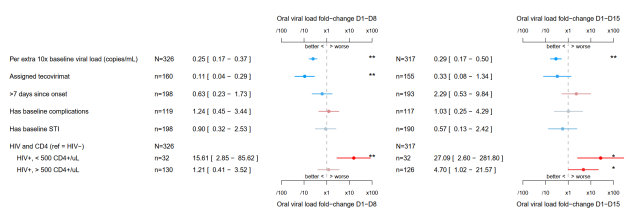


Figure 4 : Viral load fold change in oral swabs at D8 and D15



Conclusions

- Lesion swabs harbored the highest and most persistent viral loads, underscoring their importance for isolation recommendations.
- Tecovirimat did not reduce time to undetectability of MPXV DNA among patients with Mpox disease whatever the specimen type.
- Tecovirimat did lower MPXV viral loads in oral swabs at D8 and D15, which also showed an association with CD4+ counts. This compartment-specific pattern may reflect differences in drug penetration or local viral dynamics.

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