Supplementary Table 1. Pre-clinical studies of tecovirimat against monkeypox

Author	Year	Study design	Dosage	Subject	Clinical sign outcome	Adverse effect
O'Laughlin et al.[28]	2022	Cross-sectional	No data	549 people, 0-65 years old; median age 36.5	The median interval to subjective improvement was 3 days.	Non-serious adverse effects were reported in 3.5% of patients.
Adler et al.[7]	2022	Retrospective observational	Tecovirimat 600 mg (oral) twice daily for 14 days	Woman, 30s years old	No new lesions developed after 24 hours of tecovirimat therapy.	None
Matias et al.[24]	2022	Case series	Tecovirimat 600 mg (oral) twice daily for 14 days	Case 1 (man, 20s years old) Case 2 (man, 20s years old man with HIV on ARV) Case 3 (man, 40s years old)	Case 1 The resolution of the majority of the lesions was reported on day 14. Case 2 Tonsillar edema and odynophagia improved slowly after initiation of tecovirimat. All skin lesions had crusted at an outpatient visit on day 9. Case 3 Near-complete resolution of the rash was reported in outpatient follow-up on day 7.	Case 1 Mild nonfocal headache associated with the first dose was reported. Case 2 1-2 loose bowel movements a few hours after each dose. Case 3 No side effects were reported.
Pastula et al.[27]	2022	Case series	Case 1 Oral tecovirimat began immediately after the onset of neurologic symptoms. Case 2 Oral tecovirimat was started via nasogastric tube 2 days after neurologic symptom onset but quickly transitioned to IV tecovirimat over concerns for potential absorption issues.	2 Men, 30s years old homosexual, diagnosed with encephalomyelitis associated with MPXV	Case 1 Skin lesions were resolved over 3 weeks. He was discharged to outpatient rehabilitation therapy and was ambulatory with an assistive walking device at 1 month follow-up. Case 2 Skin lesions were resolved over 5 weeks. Patient was discharged to acute inpatient rehabilitation, ambulating with an assistive walking device.	None
Hernandez et al.[25]	2022	Case report	Tecovirimat 600 mg (oral) twice daily for 14 days	Human (man, 37 years old, HIV)	The skin lesions healed rapidly. At follow-up one month later, areas of hyperpigmentation were reported at the sites of the healed lesions.	None
Ajmera et al.[26]	2022	Case report	Tecovirimat 200 mg (oral) twice daily for 3 weeks	Human (Man, 26 years old, homosexual, on HIV PrEP)	The patient's symptoms started to improve on day 5 of hospitalization or day 3.	No data

HIV: human immunodeficiency virus ; ARV: antiretroviral drug ; MPXV: monkeypox virus; PrEP: pre-exposure prophylaxis

Supplementary Table 2. Pre-clinical studies of tecovirimat against monkeypox

Author	Year	Study design	Tecovirimat Dosage	Subject	Viral		Outcome	
					Viral strains	Viral Dosage	Viral load	Clinical sign
Warner et al.[16]	2022	In vivo and in vitro	30 mg/kg or 100 mg/kg (nares route) once daily for five days	CAST/EiJ mice (n=16)	In vivo MXPV/ SP2833 (Canada) and MPXV/V79–1-005 (Zaire) In vitro MXPV/ SP2833 (Canada)	10^4 or 10^6 PFU	Significantly reduced viral titers in the lungs, with mean titers around 10^4 TCID50/g [greater than a 1000-fold decrease ($p<0.05$)] **EC 50** MXPV/ SP2833 → 0.006 ± 0.0002 μM MPXV/V79–1-005 → 0.008 ± 0.0024 μM **EC 90** MXPV/ SP2833 → 0.012 ± 0.0010 μM MPXV/V79–1-005 → 0.0145 ± 0.0138 μM	Despite seeing some weight loss, none of the animals infected with MPXV/SP2833 succumbed to disease by the study's end point on day 21 p.i..
Russo et al.[22]	2020	In vivo	10 mg/kg tecovirimat (oral route) for 14 days (interval 24 ± 2 h) + ACAM2000	*Cynomolgus macaques, Indian rhesus macaques* (n=16)	MPXV (Zaire 79 strain V79-I-005)	$1.65x10^7$ and $5.4x10^7$ PFU	The observed viral loads in the ACAM2000 + tecovirimat group peak higher than observed in the other studies.	12 of 13 treated animals survived following lethal MPXV challenge. Clinical signs of disease (lesion count) were elevated in tecovirimat treated animals ($p<0.05$).
Sergeev et al.[20]	2016	In vivo	30 or 60 μg/g (intranasal route) once daily 1 day before MPXV infection and further for 7 days p.i..	ICR mice (n=24)	MPXV/V79–1-005 (Congo)	2.4 or 3.4 lg PFU	The number of infected mice treated with ST-246 and NIOCH-14 and challenged with 10 LID50 of MPXV was significantly lower than in the control.	No data
Berhanu et al.[21]	2015	In vivo	10 mg/kg daily (oral route) for 14 days	Cynomolgus monkeys (n=32)	MPXV Zaire-79	5×10^7 PFU	The maximum viral load was significantly reduced as assessed by number of MPXV genome copies in the blood ($P < 0.0001$).	Reduced body pox lesion count ($P < 0.01$).
Sergeev et al.[23]	2017	In vivo	40 mg/kg (oral route) once daily (1 day before challenge with MPXV and further for 7 days p.i.)	Ground squirrels (*Marmota bobak*) (n=4)	MPXV strain V79-1-005 (Congo Basin MPVX)	3.7 log10 PFU	A significant decrease in the pathogen concentration.	No death was reported. No signs of the disease were recorded in experimental group.
Smith et al.[18]	2011	In vivo	30 mg/kg (oral route) daily for 14 days	Prairie dogs (*Cynomys ludovicianus)* (n=16)	MPXV strain ROC-2003-358 (Congo)	3.8×10^5 PFU	Viable virus and viral DNA were undetected in animals that began treatment on 0 or 3 days.	No death was reported. None of the animals presented visible symptoms, including rash development.
Huggins et al.[19]	2009	In vivo	300 mg/kg (oral route) once daily for 14 days	Cynomolgus monkeys (n=8)	MPX Zaire '79 strain	5×10^7 PFU	Viral load was reduced by almost 5 logs. No lesions were observed in drug-treated group.	No death was reported. No lesions were observed in either drug-treated group.

Author	Year	Study design	Tecovirimat Dosage	Subject	Viral		Outcome	
					Viral strains	Viral Dosage	Viral load	Clinical sign
Jordan et al.[17]	2009	In vivo	3 mg/kg, 10 mg/kg, 30 mg/kg, and 100 mg/kg orally once per day for 14 days	Cynomolgus monkeys (*Macaca fascicularis*) (n=15)	MPVX strain Zaire 79 (V79-I-005)	5×10^7 PFU	Significantly fewer poxvirus viral load was reported ($P < 0.001$).	Significantly fewer poxvirus lesions were observed ($P < 0.001$).
Smith et al.[15]	2009	In Vitro	-	African green monkey kidney cells (BSC-40 cells)	MPXV strains V78-I-3945 (Benin), V81-I-179 (Ivory Coast), V77-I-823 (Zaire), V1979-I-005 (Zaire), 2003-RCG-358 (Republic of Congo), 2003-USA-039 (United States), and V70-I-266 (Sierra Leone)	No data	**EC 50** V78-I-3945 0.023 ± 0.0026 µM V81-I-179 0.032 ± 0.0061 µM 2003-USA-039 0.036 ± 0.0045 µM V77-I-823 0.030 ± 0.0114 µM V1979-I-005 0.039± 0.0016 µM **Plaque size** The plaque sizes of MPXV was effectively reduced (between 0.05 and 0.015 µM). **Comet tail formation** ST-246 that substantially reduced EEV particle production and release and comet tail formation by MPXV strains tested was between 0.05 and 0.015 µM .	No data

MPXV: monkeypox virus ; PFU: plaque forming units; EC 50: 50% effective concentration ; EC 90: 90% effective concentration ; p.i.: post infection; EEV:extracellular enveloped virion