Letters

RESEARCH LETTER

Compassionate Use of Tecovirimat for the Treatment of Monkeypox Infection

Monkeypox is a zoonotic orthopoxvirus in the same genus as variola (the causative agent of smallpox).[1] A recent global outbreak has led to more than more than 39 000 cases reported as of August 18, 2022.[2] Monkeypox is typically self-limited with symptoms generally lasting between 2 and 4 weeks in prior outbreaks. Hospitalization was required in 13% of patients in a recent study, suggesting the need for effective therapy.[3]

Tecovirimat is an antiviral that inhibits p37, a protein involved in release of enveloped virus, dissemination, and viral virulence.[4] In vitro testing has shown activity against both smallpox and monkeypox, and tecovirimat appears to have a favorable clinical safety profile based on the experience of healthy volunteers.[4,5] We assessed adverse events and clinical resolution of systemic symptoms and lesions in an uncontrolled cohort study of patients with monkeypox who were treated with tecovirimat on a compassionate use basis.[6]

Methods | Patients were eligible for tecovirimat treatment following laboratory confirmation of orthopoxvirus infection from skin lesions by polymerase chain reaction. Outpatients referred to UC Davis primarily through the Sacramento County Department of Public Health between June 3, 2022, and August 13, 2022, and who had disseminated disease or lesions in sensitive areas including the face or genital region were offered treatment. Oral treatment with tecovirimat for adult patients was weight-based, administered every 8 or 12 hours, and was taken within 30 minutes of a meal containing moderate to high fat content for improved bioavailability. The duration of therapy was 14 days but could be extended depending on the clinical status of the patient. Clinical data were collected at initial in-person evaluation for treatment and by in-person or telephone interview on day 7 and day 21 following initiation of therapy. All patients provided written informed consent. This protocol was approved by the UC Davis Institutional Review Board.

Results | As of August 13, 2022, 25 patients with confirmed monkeypox infection had completed a course of tecovirimat therapy (**Table**). All patients were self-reported male and the median age was 40.7 years (range, 26-76). Nine patients had HIV, 1 patient had received the smallpox vaccine more than 25 years prior, and 4 received 1 dose of JYNNEOS vaccination after symptom onset. At the time of treatment, systemic symptoms, lesions, or both were present for a mean of 12 days (range, 6-24). Systemic symptoms included fever in 19 patients (76%), headache in 8 (32%), fatigue in 7 (28%), sore throat in 5 (20%), chills in 5 (20%), backache in 3 (12%), myalgia in 2 (8%), nausea in 1 (4%), and diarrhea in 1 (4%). Almost all patients (23 [92%]) had genital and/or perianal lesions, and 13 (52%) had fewer than 10 lesions over their entire body. All patients had pain associated with lesions.

One patient received 21 days of therapy while the remainder were treated for 14 days. Complete resolution of lesions was reported in 10 patients (40%) on day 7 of therapy, while 23 (92%) had resolution of lesions and pain by day 21. Treatment with tecovirimat was generally well tolerated with no patient discontinuing therapy. The most frequently reported adverse events on day 7 of therapy included the following: fatigue in 7 patients (28%), headache in 5 (20%), nausea in 4 (16%), itching in 2 (8%), and diarrhea in 2 (8%) (Table).

Discussion | In this preliminary study, oral tecovirimat was well tolerated by all patients with monkeypox infection, with minimal adverse effects. However, adverse effects could not always be differentiated from symptoms related to the infection. No control group was included, limiting conclusions of antiviral efficacy pertaining to duration of symptoms or severity. Time from symptom onset to presentation was variable among patients, and conclusions related to antiviral use vs natural evolution of disease should be made with caution.

Limited clinical data exist on the use of tecovirimat for monkeypox infection. In one case report, no new lesions followed 24 hours of therapy and no adverse effects occurred by treatment completion at 14 days.[1]

Limitations of the study include the small number of patients, lack of a control group, and selection bias. Additional large-scale studies are needed to elucidate antiviral efficacy, dosing, and adverse events.

Angel N. Desai, MD, MPH
George R. Thompson III, MD
Sonja M. Neumeister, MPH
Anna M. Arutyunova, BS
Katelyn Trigg, MPH
Stuart H. Cohen, MD

Author Affiliations: Division of Infectious Diseases, University of California Davis Medical Center, Sacramento, California.

Accepted for Publication: August 17, 2022.

Published Online: August 22, 2022. doi:10.1001/jama.2022.15336

Corresponding Author: Angel Desai, MD, MPH, Division of Infectious Diseases, University of California Davis Medical Center, 4150 V St, Sacramento, CA 95816 (andesai@ucdavis.edu).

Author Contributions: Drs Desai and Thompson had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Desai, Thompson, Cohen.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Desai, Thompson, Neumeister, Arutyunova.
Critical revision of the manuscript for important intellectual content: Desai, Thompson, Trigg, Cohen.
Statistical analysis: Thompson.
Administrative, technical, or material support: Thompson, Neumeister, Arutyunova, Trigg, Cohen.
Supervision: Thompson, Trigg, Cohen

Table. Clinical Characteristics of Patients With Monkeypox Infection Treated With Tecovirimat

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Smallpox vaccination history	Unk	Unk	No	No	No	No	No	Unk	Unk	Unk	Unk	No	No	No	Unk	No	Unk	Jynneos	Jynneos	No	Jynneos	Remote	No	Jynneos	Unk
HIV,[a] hepatitis B, hepatitis C status	HIV	None	None	None	None	HIV	HIV	HIV	None	HIV	HIV	None	HIV	None	None	HIV	None	None	None	None	None	None	None	None	HIV
Systemic symptoms	None	Fever, backache, fatigue	Nausea, chills, myalgias	Fever	Fatigue	Fever, fatigue	Fever, backache, headache, diarrhea, chills	None	Malaise, fever	Fever	Fever, sore throat, itching, fatigue	Fever, headache	Fever, headache	Headache, shoulder and neck pain	Headache, hoarseness	Fever, fatigue, headache, constipation, sore throat	Fever, headache, nausea, fatigue	Fever, myalgia, headache, sore throat	Fever, chills, urethritis	Fever	Fever, sore throat, back pain	Fever, sore throat	Fever, chills, night sweats	Fever, chills, fatigue, painful bowel movements	Fever
Lymphadenopathy	None	None	None	None	Inguinal	Inguinal and neck	None	None	Neck and inguinal	Cervical	Neck and inguinal	Right inguinal	None	None	Inguinal	Inguinal	None	Inguinal	None	Inguinal	Cervical, inguinal	Cervical	None	Inguinal	None
No. of lesions	10-100	<10	<10	10-100	<10	10-100	10-100	<10	10-100	10-100	10-100	10-100	>100	10-100	<10	<10	10-100	<10	<10	<10	<10	<10	<10	10-100	<10
Genital lesions	Perianal	Perianal	Genital	Genital	Genital	Perianal	Perianal	Genital	Genital	No	Genital	No	Perianal and genital	Genital	Genital	Perianal	Genital	Genital	Perianal	Genital	Perianal and genital	Genital	Genital	Genital	Perianal
Distribution of other lesions	Chest, eyelid, right hand, right knee, shoulder	Face, neck, arms		Scalp, face, forearms, hands, chest, back, legs, buttocks		Face, abdomen, groin, back, legs	Neck, arms, head, legs, abdomen, back		Face, back, arms, hands	Entire body	Throat, chest, arm, abdomen, hand, buttocks	Scalp, face, neck, abdomen, arms, back	Entire body	Arms, scalp		Arm, chest, face	Chest, back	Face, arm, chest	Arm, thigh	Chest	Wrist, chest	Arms, legs	Chest, back, arm, shin	Head, arms, legs, foot	Chest, back, arms, legs
Symptom onset to tecovirimat initiation, d	24	17	6	8	15	6	9	16	10	12	9	14	10	16	7	7	6	12	12	7	19	14	13	10	22
Days of tecovirimat therapy	14	14	14	14	14	14	14	14	21[b]	14	14	14	14[b]	14	14	14	14	14	14	14	14	14	14	14	14
7-Day self-reported outcomes[c]	Rec	Rec	Rec	No new lesions	No new lesions	No new lesions	Rec	No new lesions	New lesions	No new lesions	No new lesions	No new lesions	No new lesions	No new lesions	Rec	No new lesions	Rec	No new lesions	Rec	No new lesions	No new lesions	Rec	No new lesions	Rec	Rec
21-Day self-reported outcomes[c]	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	New lesions	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	No new lesions	Rec	Rec	Rec	Rec	Rec
Adverse effects at day 7	Backache, fatigue	None	None	None	Headache, nausea	None	Hand burning, weak nails	None	Fatigue, nausea, itching, headache	Fatigue	Fatigue, itching	None	None	Nausea, headache	None	Fatigue	None	Headache, diarrhea	None	None	Fatigue	Headache	Fatigue, nausea	Dry skin	Diarrhea

Abbreviation: unk, unknown.

[a] Patients with HIV were receiving antiretroviral therapy and confirmed or reported to be virologically suppressed.

[b] Dose increased on day 10 (patient 9) and day 7 (patient 13) due to delayed clinical response and borderline weight-based dosing.

[c] Recovered (rec): all lesions self-reported as crusted or fallen off; new lesions: development of new lesions; no new lesions: no new lesions reported but not yet recovered.

Conflict of Interest Disclosures: None reported.

Disclaimer: Dr Desai is an Associate Editor for *JAMA Network Open*. She had no role in the review of this submission or the decision to accept for publication.

Additional Contributions: We thank Olivia Kasirye, MD, Sacramento County Department of Public Health, and surrounding counties and health departments for their assistance in rapid diagnosis and treatment of our patients. Dr Kasiyre received no compensation.

1. Adler H, Gould S, Hine P, et al; NHS England High Consequence Infectious Diseases (Airborne) Network. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis*. 2022;22(8):1153-1162. doi:10.1016/S1473-3099(22)00228-6

2. CDC. 2022 Monkeypox outbreak global map. July 27, 2022. Accessed July 28, 2022. https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html

3. Thornhill JP, Barkati S, Walmsley S, et al; SHARE-net Clinical Group. Monkeypox virus infection in humans across 16 countries—April-June 2022. *N Engl J Med*. Published online July 21, 2022. doi:10.1056/NEJMoa2207323

4. Yang G, Pevear DC, Davies MH, et al. An orally bioavailable antipoxvirus compound (ST-246) inhibits extracellular virus formation and protects mice from lethal orthopoxvirus challenge. *J Virol*. 2005;79(20):13139-13149. doi:10.1128/JVI.79.20.13139-13149.2005

5. Grosenbach DW, Honeychurch K, Rose EA, et al. Oral tecovirimat for the treatment of smallpox. *N Engl J Med*. 2018;379(1):44-53. doi:10.1056/NEJMoa1705688

6. CDC. Information for healthcare providers on obtaining and using TPOXX (tecovirimat) for treatment of monkeypox. August 9, 2022. Accessed August 15, 2022. https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html