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2 **Tecovirimat for Monkeypox in Central African**
 3 **Republic under Expanded Access**

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For print edition:

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31 **To the Editor:** We report on the protocolized use of tecovirimat (SIGA
 32 Technologies), an antiviral drug with activity against orthopoxviruses (including
 33 monkeypox and smallpox),¹ under an expanded access program for all patients
 34 with monkeypox virus (MPXV) disease in Mbaïki, Central African Republic,
 35 between December 2021 and February 2022.² Included in the study were 14
 36 patients in whom MPXV infection had been diagnosed. All 14 patients tested
 37 positive for MPXV on at least one admission sample; of these patients, 12 had
 38 positive results on a real-time polymerase-chain-reaction (PCR) assay with
 39 a mean cycle threshold of 32 (range, 21 to 42); 12 were also positive on an
 40 MPXV CL3 assay that was specific for clade I (see the Methods section in the
 41 Supplementary Appendix, available with the full text of this letter at NEJM.org).
 42 Data regarding the patients' clinical signs and symptoms were recorded daily

1 throughout treatment and at follow-up visits (Table S2 in the Supplementary
 2 Appendix). Blood or lesion samples were obtained on admission, throughout
 3 treatment, and on day 28 to assess MPXV status. Ethics-committee approval
 4 was obtained from the University of Oxford and the University of Bangui
 5 before enrollment began. All the patients provided written informed consent to
 6 participate in the study.

7 The median age of the patients was 23 years (range, 4 to 38), 71% were
 8 female, and the median time from symptom onset to the initiation of treatment
 9 was 21 days (range, 5 to 45) (Table 1 and Table S3). At the time of admission, all
 10 14 patients presented with muscle pain, headache, lymphadenopathy, and lesions
 11 that are characteristic of MPXV infection; of these patients, 11 had more than
 12 100 lesions. Active lesions were reported in 10 patients.

13 All the patients received a 14-day course of oral tecovirimat (600 mg twice
 14 daily in adults; doses for children according to weight category are detailed
 15 in the Supplementary Appendix). A total of 13 patients completed the 28-day
 16 follow-up.

17 MPXV was detected in at least one sample in 7 of 14 patients by day 4, in
 18 1 of 10 patients by day 8, in 1 of 8 patients by day 14, in 1 of 2 patients by
 19 day 21, and in 1 patient by day 28. By day 14, a total of 12 of 14 patients had
 20 been discharged with no active lesions; of the remaining 2 patients, 1 was
 21 discharged on day 21 with negative results on a PCR assay, and 1 remained
 22 positive on day 28. By the final study visit, 12 of 13 patients were PCR-negative
 23 and had recovered; scarring was visible in 9 patients. The median time from
 24 the initiation of treatment until the absence of active lesions was 5 days (Fig.
 25 S4). Two serious adverse events were reported: life-threatening anemia during
 26 treatment in an HIV-positive patient and an unexplained death after discharge;
 27 neither event was considered to be related to the study treatment.

28 Data collected through this study have increased our knowledge of the use of
 29 tecovirimat in a country in which clade I MPXV is endemic and 106 confirmed
 30 cases were recorded between 2010 and September 2022, with 11 deaths (10.4%)
 31 (Table S5). This program has also piloted a community outreach program and
 32 sustainable community-based surveillance system and increased clinical research
 33 capacity in the Central African Republic.

Version of record

34 This is the *New England Journal of Medicine* version of record, which includes all *Journal* editing and
 35 enhancements. The Author Final Manuscript, which is the author's version after external peer review
 36 and before publication in the *Journal*, is available under a CC BY license at XX.

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 42 expanded access program.

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43 Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

References

1. TPOXX (tecovirimat) investigator's brochure. New York: SIGA Technologies, 2021 (brochure).
2. ISRCTN Registry. Expanded access protocol for the use of tecovirimat for the treatment of monkeypox infection. 2022 (<https://www.isrctn.com/ISRCTN43307947>).

Table 1. Characteristics of the 14 Patients at Baseline and Outcomes.

Characteristic or Outcome	Value
Demographic data	
Ratio of males to females	4:10
Median age (range) — yr	23 (4–38)
Medical history — no./total no. (%)	
Malaria	11/13 (85)
Human immunodeficiency virus infection	1/3 (33)
Presentation	
Median interval from symptom onset to initiation of treatment (range) — days	21 (5–45)
Signs and symptoms — no./total no. (%)	
Body temperature >38°C	9/14 (64)
Lesions	14/14 (100)
Active	10/14 (71)
>100	11/14 (79)
Outcome — no./total no. (%)	
Completed full course of treatment	14/14 (100)
Positivity for monkeypox virus	
Day 4	7/14 (50)
Day 8	1/10 (10)
Day 14	1/8 (12)
Day 21	1/2 (50)
Final visit	1/13 (8)
Median interval from initiation of treatment to absence of active lesions (range) — days	5 (0–28)
Status on day 28 — no./total no. (%)	
Recovered without sequelae	4/13 (31)
Recovered with sequelae	9/13 (69)
Had ≥1 serious adverse event	2/14 (14)

Queries

q1. AU: Is the support statement OK as slightly revised per style?