disease 2019 (Covid-19) pandemic, have eliminated performance of preabortion ultrasonography.[4] Early data do not suggest an increased incidence of ectopic pregnancy detected after abortion with the use of no-touch protocols.[5] However, clinicians must maintain a high index of suspicion for ectopic pregnancy in persons presenting with suggestive symptoms, in particular in persons without confirmation of an intrauterine pregnancy before abortion.

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Drug Sensitivity of Currently Circulating Mpox Viruses

TO THE EDITOR: As of November 10, 2022, the ongoing global monkeypox (recently renamed mpox) outbreak has resulted in 79,231 cases in 110 countries and 49 deaths, according to the Centers for Disease Control and Prevention. Approximately 10% of patients with mpox are hospitalized.[1]

Tecovirimat (ST-246), cidofovir, and brincidofovir (CMX001) are the antiviral agents currently used for the treatment of mpox.[2] The currently circulating mpox viruses (MPXVs) have genomic alterations that were not observed previously and appear to affect virus biology, as indicated by the clinical and epidemiologic features seen with the viruses in the current outbreak, which are different from those seen in previous mpox outbreaks.[2-5] These alterations may also affect virus sensitivity to antiviral drugs.

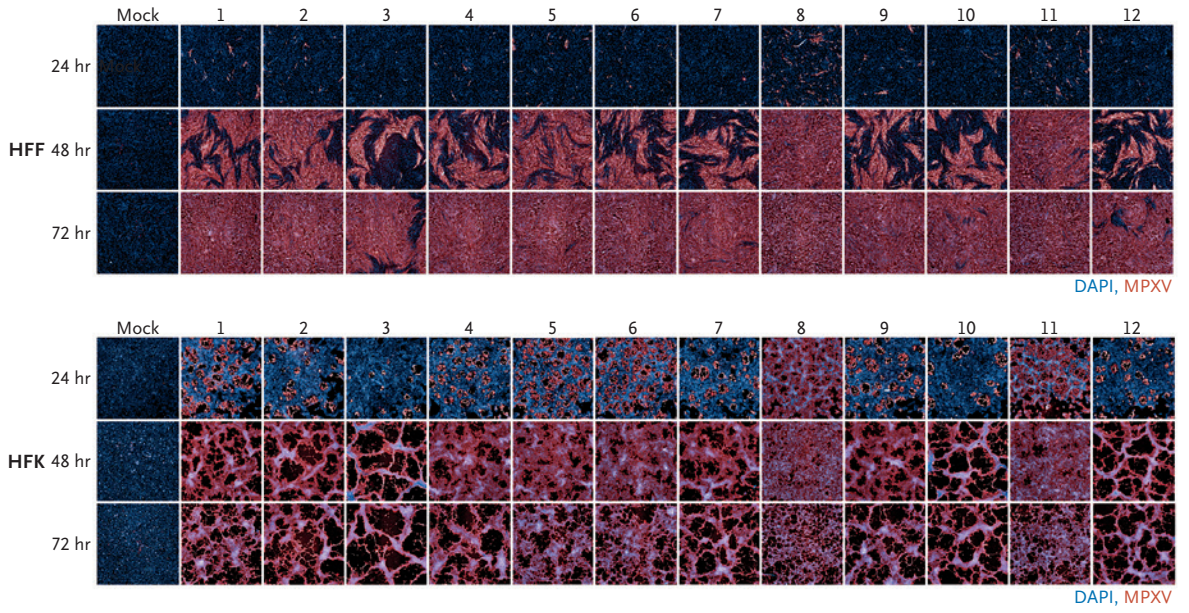
We obtained MPXV isolates from 12 patients, who had no known relationship to one another, during the current outbreak to assess virus sensitivity to tecovirimat, cidofovir, and brincidofovir in commonly used cell-line models and primary cultures of pathologically relevant cell types (human foreskin fibroblasts [HFF] and human foreskin keratinocytes [HFK]) (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). All isolates reacted with primers that detect clade II (West African clade) and had mutational profiles that closely resembled that of a reference genome from the current worldwide outbreak (ON563414.2) (Figs. S1 and S2 and Table S2), results that are consistent with previous findings.[2,3,5] However, the isolates and ON563414.2 harbored mutations in the viral DNA polymerase (gp57, the target of cidofovir and brincidofovir) and in F13L (gp45, the target of tecovirimat) that were not present in a reference genome (MT903344.1) before the current outbreak. These mutations have arisen without known selective pressure from antiviral medications.

All isolates replicated in both HFF and HFK cells, as indicated by immunofluorescence staining for orthopoxvirus (Fig. 1A and Fig. S3) and the detection of virus DNA in cell supernatants (Fig. S4). Pronounced cytopathogenic effects were seen in HFK cells but not in HFF cells.

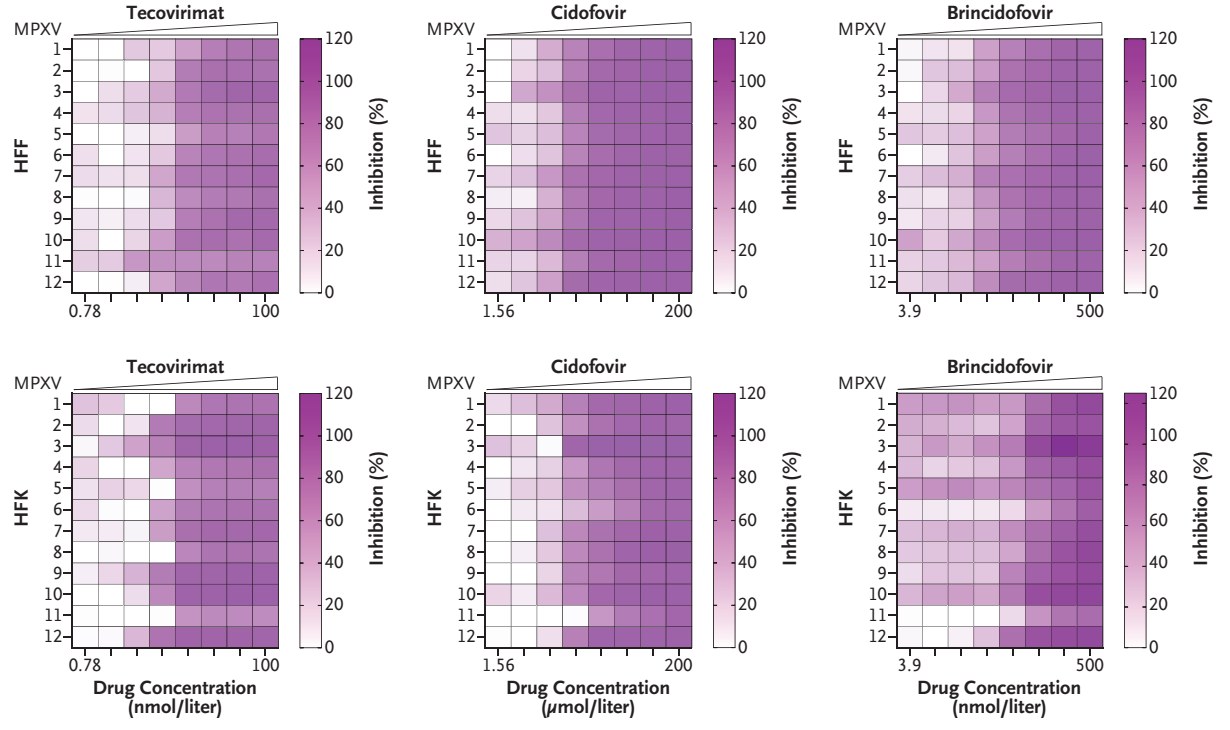
Tecovirimat, cidofovir, and brincidofovir inhibited MPXV infection in a dose-dependent manner (Fig. 1B). The 50% inhibitory concentration (IC_{50}) of the drugs ranged from 4 to 20 nmol for tecovirimat, from 5 to 32 μmol for cidofovir, and from 9 to 152 nmol for brincidofovir. IC_{50} values determined in continuous cell lines differed substantially from those in primary cultures, in particular for cidofovir and brincidofovir (Fig. S5 and Table S3), findings that stress the importance of physiologically relevant models.

The IC_{50} values for tecovirimat, cidofovir, and brincidofovir (4000 nmol, 80 μmol, and 600 nmol, respectively) are within the range of therapeutic

A Immunofluorescence Staining



B Inhibitory Activity of Antiviral Drugs



MPXV	1		2		3		4		5		6		7		8		9		10		11		12	
IC_{50}	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Tecovirimat (nmol) HFF	16.6	4.0	10.4	1.3	7.8	2.1	8.8	2.9	21.0	0.9	12.3	0.8	8.7	1.6	14.2	0.9	10.2	2.4	6.8	0.8	9.2	2.3	11.9	1.7
Tecovirimat (nmol) HFK	14.3	2.1	5.3	1.2	3.7	0.4	11.6	3.6	19.7	1.4	9.6	1.2	7.2	0.7	12.3	0.3	4.0	0.9	5.8	0.4	32.0	5.6	4.2	0.4
Cidofovir (μmol) HFF	9.2	1.3	9.1	0.6	5.4	1.0	9.1	0.3	8.8	1.0	10.1	0.8	5.7	0.5	8.4	0.4	6.8	1.5	3.6	0.2	8.5	0.9	6.2	0.5
Cidofovir (μmol) HFK	7.4	1.6	12.2	2.0	8.6	4.4	13.6	1.7	12.9	1.7	28.4	3.2	11.0	1.1	11.2	0.1	12.2	1.0	8.6	3.3	32.4	3.0	10.8	1.5
Brincidofovir (nmol) HFF	41.3	0.3	28.9	3.8	21.9	8.8	32.6	3.3	30.6	16.1	37.8	5.4	18.4	3.9	29.7	3.2	36.4	8.0	16.9	4.6	31.9	4.3	22.6	0.9
Brincidofovir (nmol) HFK	14.3	9.3	38.8	15.9	14.6	2.6	48.9	6.8	11.5	1.4	148.4	13.2	32.9	5.8	48.9	7.8	44.6	15.8	18.6	9.8	151.2	7.3	44.2	11.0

Figure 1 (facing page). Infection of Primary Human Cells with Mpox Virus (MPXV) Isolates Obtained from Patients during the Current Outbreak and Sensitivity to Antiviral Drugs.

Primary human foreskin fibroblasts (HFF) and human foreskin keratinocytes (HFK) were infected with MPXV isolates obtained from 12 patients with MPXV infection (multiplicity of infection, 0.01), and immunofluorescence staining was performed at 24 hours, 48 hours, and 72 hours after infection (Panel A). Cell nuclei were stained with 4′,6-diamidine-2-phenylindole (DAPI). Dose–response curves and 50% inhibitory concentrations (IC_{50}) were determined at 72 hours after infection (Panel B).

concentrations in plasma (Table S4). The highest plasma concentration of tecovirimat after one dose was 200 to 1000 times as high as the IC_{50} values for the agent. The plasma concentrations of brincidofovir were 3.9 to 67.0 times as high as the IC_{50} values, and the plasma concentrations of cidofovir were 2.5 to 16.0 times as high as the IC_{50} values. Our data indicate that the currently circulating MPXVs are likely to remain sensitive to the available antiviral drugs.

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Disparities According to Genetic Ancestry in the Use of Precision Oncology Assays

TO THE EDITOR: Modern oncology care relies on the assessment of tumor genomic profiles. Although it is known that there are racial and ethnic disparities in cancer outcomes, evidence regarding disparities in access to this increasingly important step in cancer diagnosis and treatment is lacking.[1] We examined the use of next-generation sequencing assays according to genetic ancestry of patients in a large cancer genomics database.

We retrospectively analyzed solid-tumor and liquid-biopsy specimens submitted to a national