Tecovirimat

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Conflict of interest

- None

Monkeypox treatments

- Mostly mild disease
- Supportive care
  - Intravenous hydration
- Antivirals
  - Tecovirimat
  - Cidofovir
  - Brincidofovir

Tecovirimat

- Treatment of choice
- Inhibitor of orthopoxvirus surface protein VP37
  - required for the formation of infectious virus particle
  - essential for dissemination

Efficacy

- Animal studies

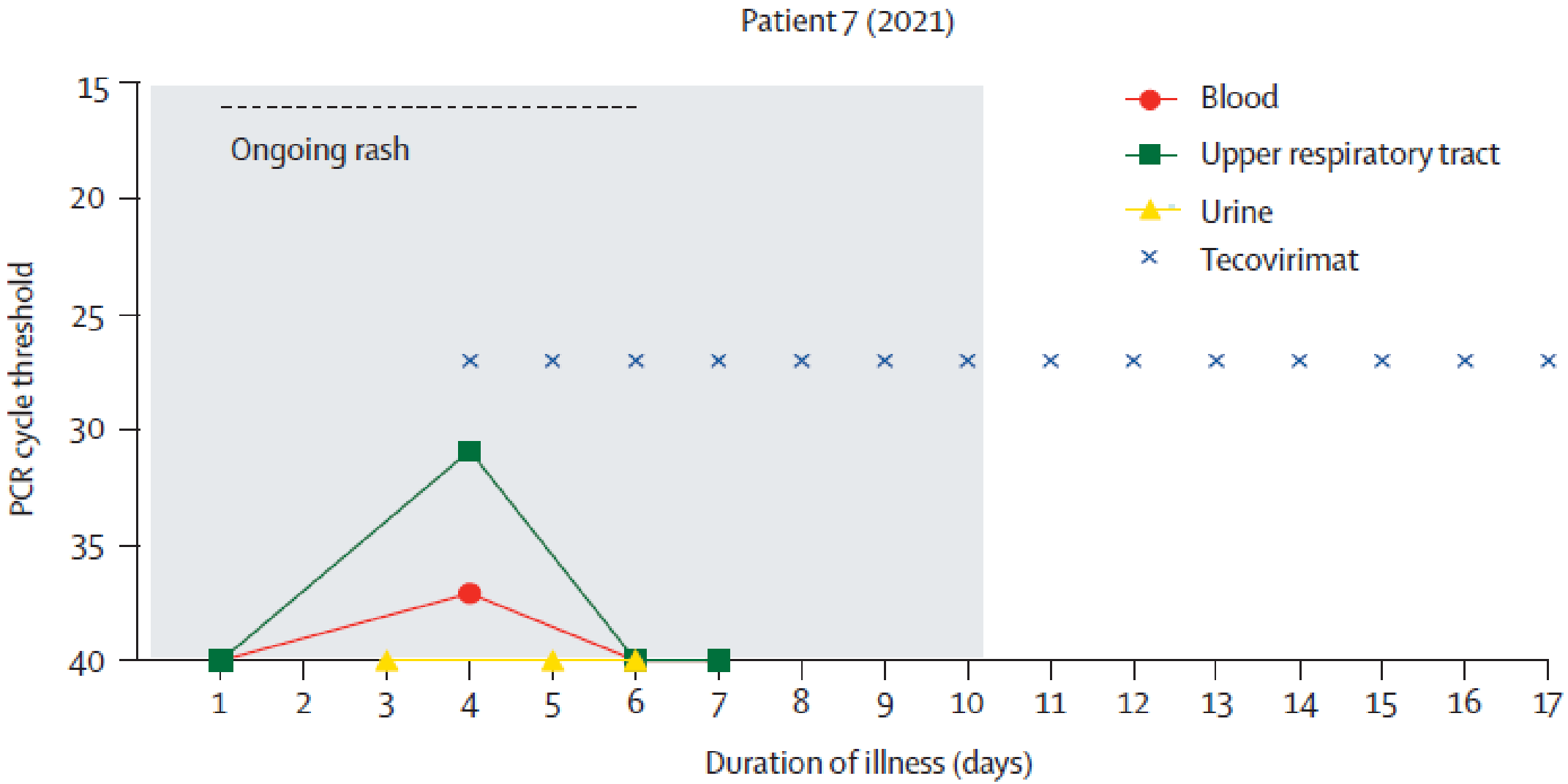
Table 4: Survival Rates in Tecovirimat Treatment Studies in Cynomolgus Macaques and NZW Rabbits Exhibiting Clinical Signs of Orthopoxvirus Disease

	Treatment Initiation[a]	Survival Percentage (No. survived/n)		p-value[b]	Survival Rate Difference[c] (95% CI)[d]
		Placebo	Tecovirimat		
Cynomolgus Macaques					
Study 1	Day 4	0% (0/7)	80% (4/5)	0.0038	80% (20.8%, 99.5%)
Study 2	Day 4	0% (0/6)	100% (6/6)	0.0002	100% (47.1%, 100%)
Study 3	Day 4	0% (0/3)	83% (5/6)	0.0151	83% (7.5%, 99.6%)
	Day 5		83% (5/6)	0.0151	83% (7.5%, 99.6%)
	Day 6		50% (3/6)	0.1231	50% (-28.3%, 90.2%)

Clinical features and management of human monkeypox: a retrospective observational study in the UK

Hugh Adler, Susan Gould, Paul Hine, Luke B Snell, Waison Wong, Catherine F Houlihan, Jane C Osborne, Tommy Rampling, Mike BJ Beadsworth, Christopher JA Duncan, Jake Dunning, Tom E Fletcher, Ewan R Hunter, Michael Jacobs, Saye H Khoo, William Newsholme, David Porter, Robert J Porter, Libuše Ratcliffe, Matthias L Schmid, Malcolm G Semple, Anne J Tunbridge, Tom Wingfield, Nicholas M Price* on behalf of the NHS England High Consequence Infectious Diseases (Airborne) Network†*

- Retrospective
- N=7
  - 3 no antiviral
  - 3 brincidofovir
    - All discontinued (hepatic toxicities)
  - 1 tecovirimat


Patient 7 (2021)
Ongoing rash
Blood
Upper respiratory tract
Urine
Tecovirimat
PCR cycle threshold
15
20
25
30
35
40
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
Duration of illness (days)

Side effects

- Expanded safety trial
  - 360 human volunteers
  - adverse effect profile similar to that of placebo
- Well tolerated
  - 12% headaches
  - 10% nausea

Tecovirimat dosing

- 13 à 25 kg: 200 mg BID x 14d
- 25 à 40 kg: 400 mg BID x 14d
- 40 à 120 kg: 600 mg BID x 14d
- ≥120 kg: 600 mg TID x 14d

Drug interactions

- Substrate
  - UGT1A1, UGT1A4
- Inhibitor (weak)
  - CYP2C19
  - CYP2C8
- Inductor (weak)
  - CYP3A4

Availability

- National Emergency Strategic Stockpile (NESS)
  - Special Access Program
- Provide report to PHAC, Health Canada's Special Access Program and SIGA
  - Results of the use of the Drug
  - Serious and/or unexpected adverse drug reactions

Tecovirimat use in Québec

- As of June 22nd
  - 184 cases
  - 11 patients treated (6%)
    - 5 HIV pos
    - 41 yo (29-63)
    - None received smallpox vaccine
    - 50% bacterial infection

Clinical justifications for tecovirimat

- 5 severe head and neck
  - 5 odynophagia
  - 1 conjunctivitis
  - 1 trismus
  - 1 peritonsilar abscess
- 4 highly symptomatic genital and/or anorectal lesions
  - 3 urinary retention
  - 1 rectal
- 2 aimed to reduce shedding within family

Outcomes

- Initiation
  - Average on day 12th of Sx (7 to 23)
- Outcomes (preliminary)
  - No ICU
  - No surgery
  - All noted improvement within few days
    - 1 case laryngeal swelling improved markedly x 24h
- Well tolerated
  - No significant adverse event

Discussion

- 5 to 10% required treatment
  - Most head and neck infections
- Limitations
  - No highly immunocompromised (all with CD4 >200)
  - No pregnancy
  - No pediatrics
  - High rate of bacterial co-infections

Conclusion

- Majority self-limited disease
- Tecovirimat
  - Well tolerated
  - May accelerate recovery
- Tecovirimat should be considered
  - Severe / disseminated disease
  - Severe head and neck
  - Severe genital or rectal
- ID referral if high risk of complications
  - Significant immunodeficiency
  - Pediatrics
  - Pregnancy

Questions?

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