Mpox : actualités nationales et internationales

Journées Thématiques Santé Sexuelle, Paris, mai 2025

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Conflicts of interets (5 years)

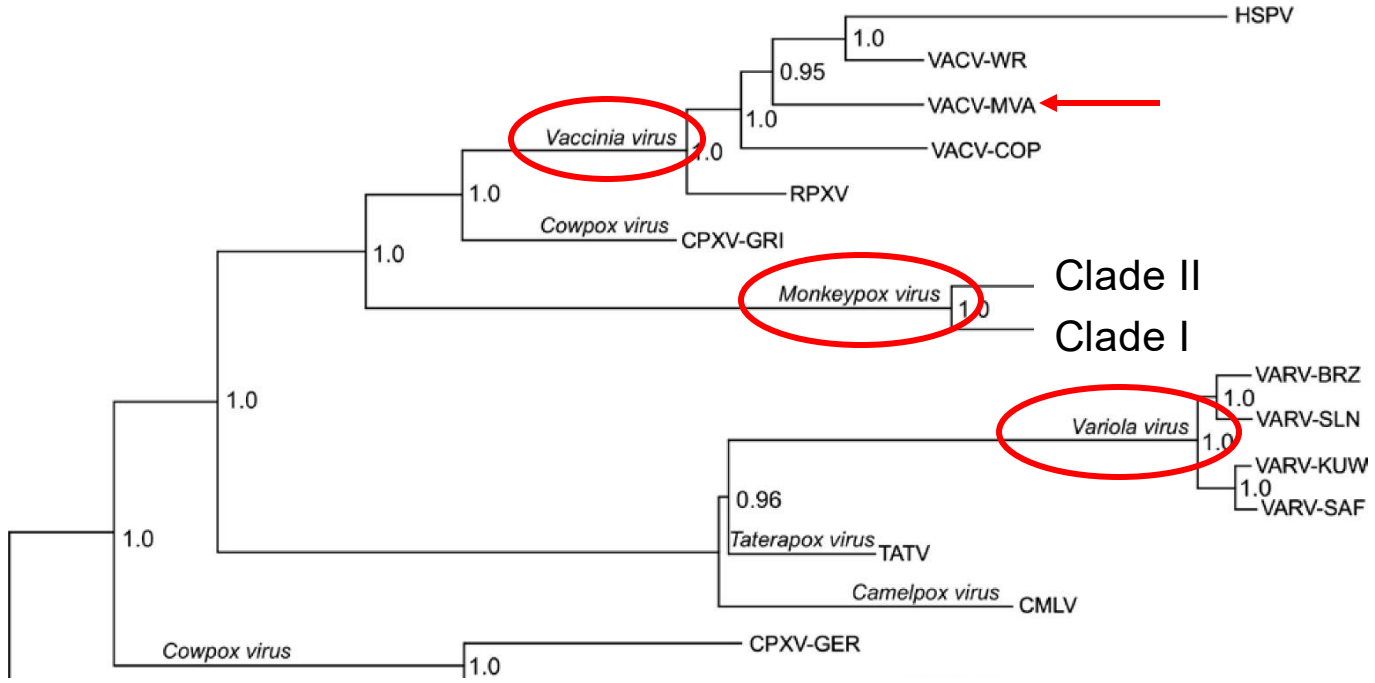
- French national mission of operational coordination for Epidemic and Biological Risk, Director
- ESCMID, Emerging Infections Subcommittee, Director

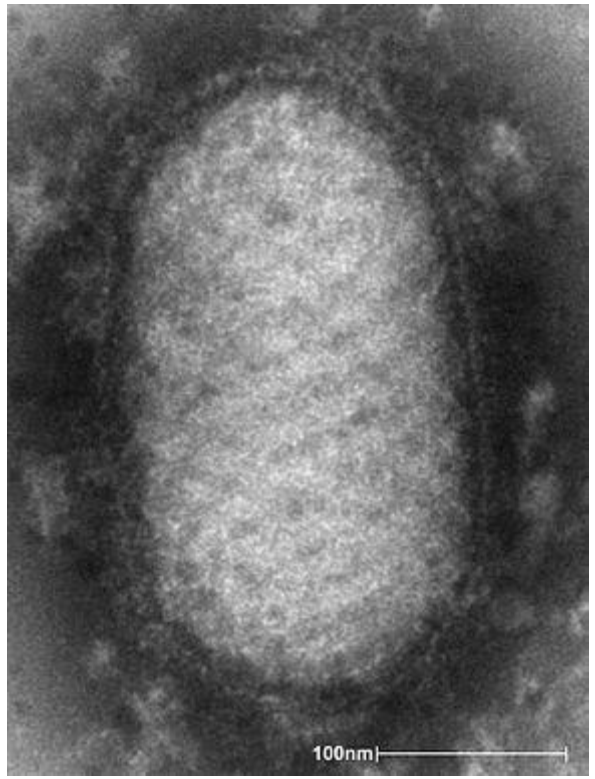
- COVARS (Committee for Monitoring and Anticipating Health Risks), advising the Health Ministry and the Higher Education and Research Ministry, member
- COVID advisor for the Ministry of Health

- Support for attending meetings and travels: MSD, Astrazeneca

Pox viruses

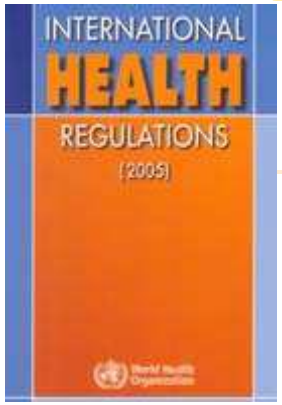
- *Poxviridae* > Orthopoxviridae
- Large double-stranded DNA, enveloped
- Have 2 forms : Mature virions and extracellular virions





Hendrikson, Viruses, 2010

Responsible of the 2 last PHEIC declarations in 2 years



(IHR 2005)

25 avr. 2009 — Pandemic flu A (H1N1) de 2009

5 mai 2014 — Poliomyelitis

8 août 2014 — Ebola virus disease

1 févr. 2016 — Zika Virus Disease

17 juil. 2019 — Ebola Virus Disease (RDC)

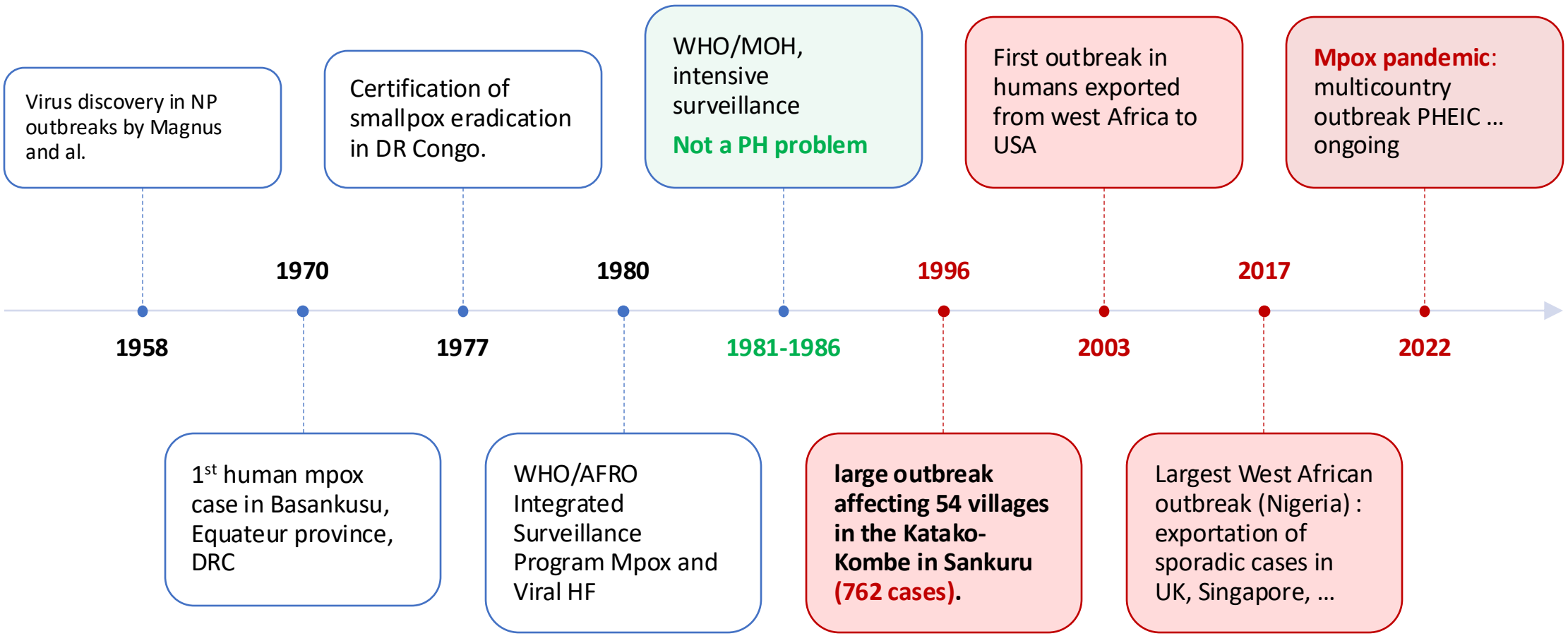
30 janv. 2020 — Covid-19 Pandemic

23 juil. 2022 — **Mpox pandemic**: multicountry outbreak PHEIC … ongoing

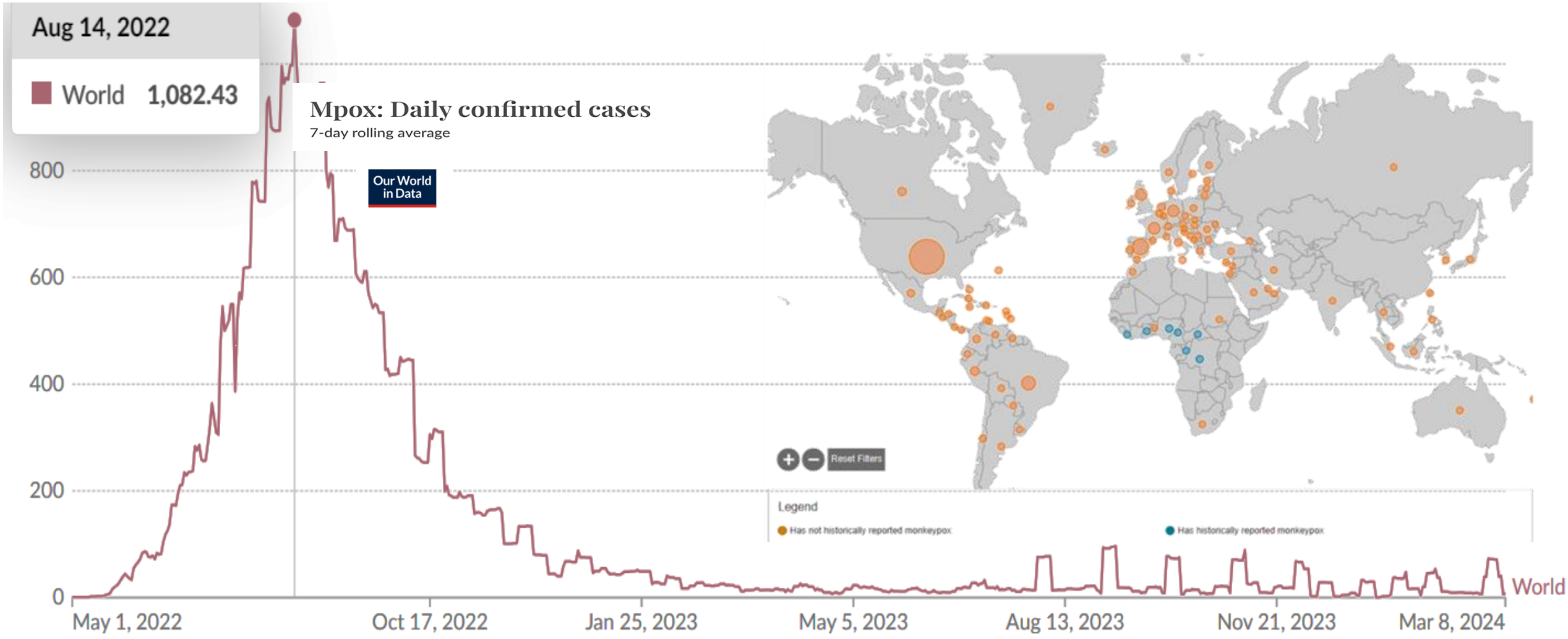
14 août 2024 — **Mpox resurgence in African region , clade Ib outbreak 2023- 2024** (RDC)

health Crisis → **Social, economical, political impacts…**

Historical reminder

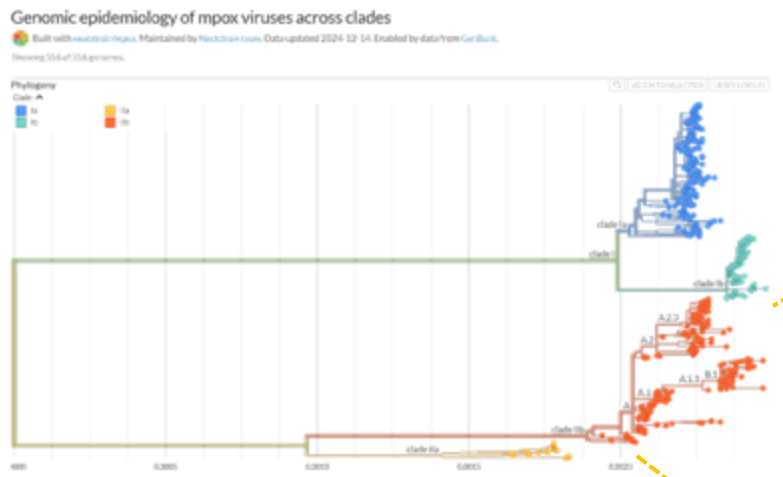


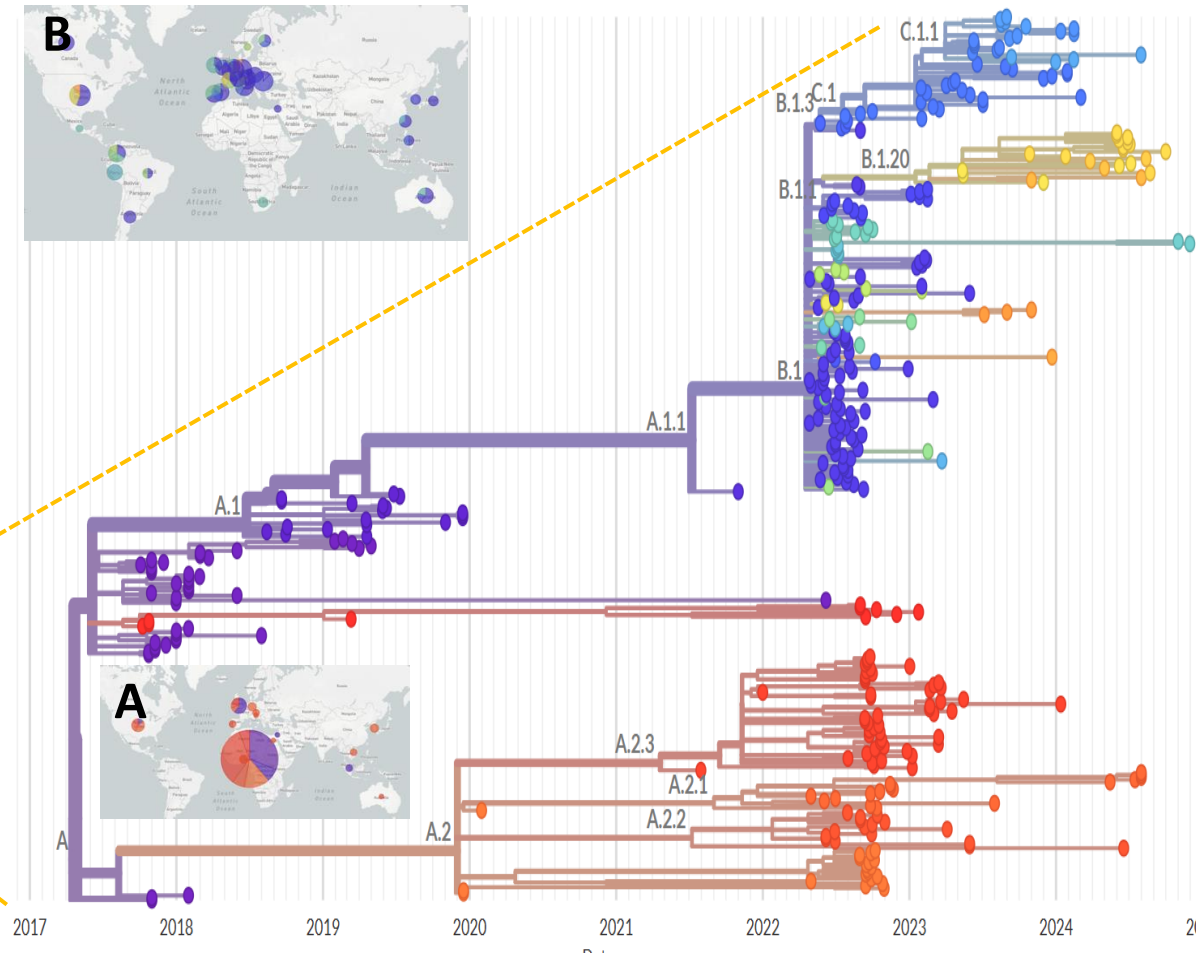
1st PHEIC in 2022 (rapidly controlled)

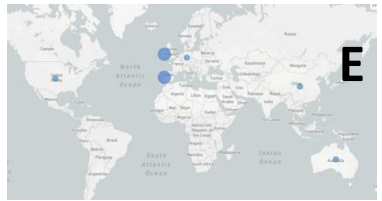


Especially clade IIb with 6 lineages described

- **High rate of APOBEC3 mutations**
- **Sustained H-H transmission marker**

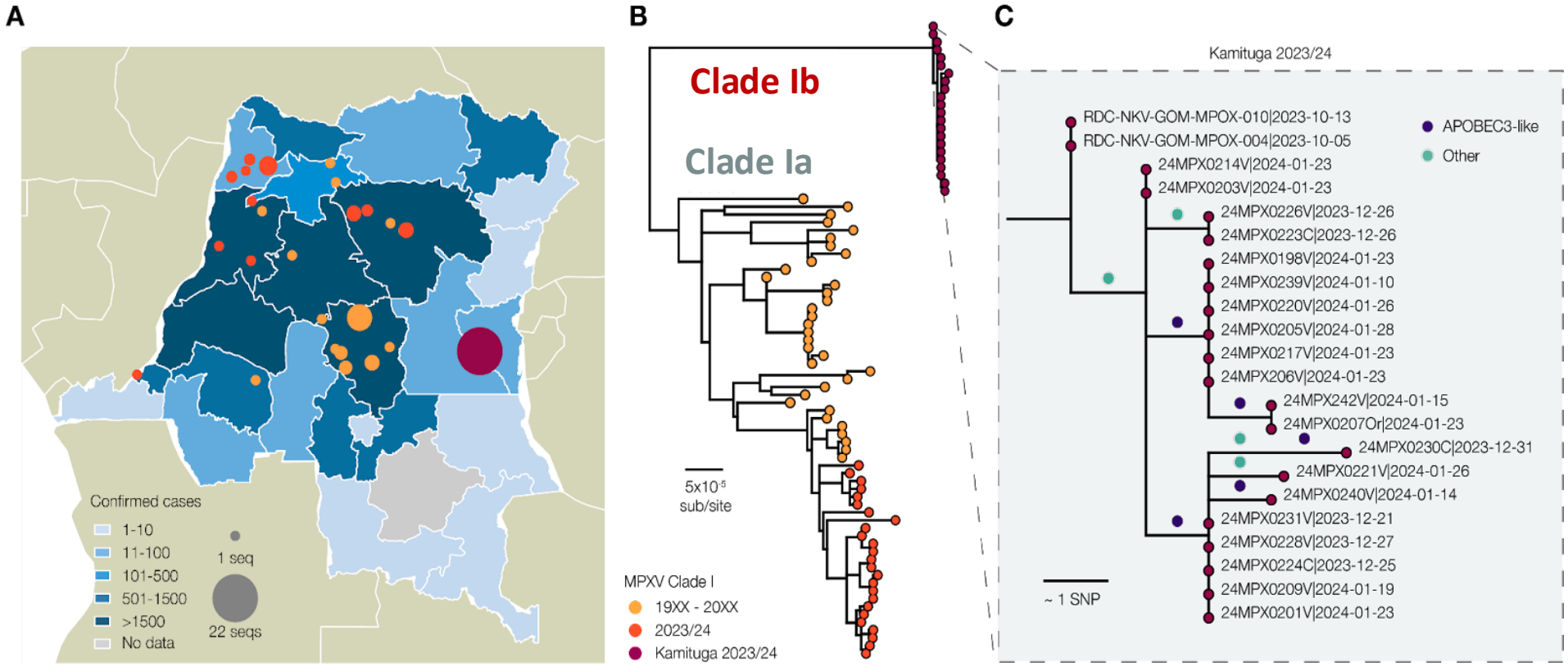


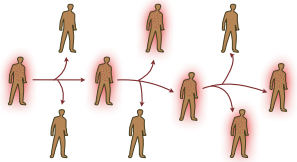




Brief Communication | Published: 13 June 2024

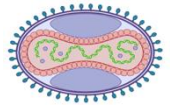
Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo





- *New sh2023a outbreak*
- *Sustained human-to-human transmission*
- *Low diversity*
- *Increased APOBEC3 mutation rate*
- *Challenges for diagnosis*

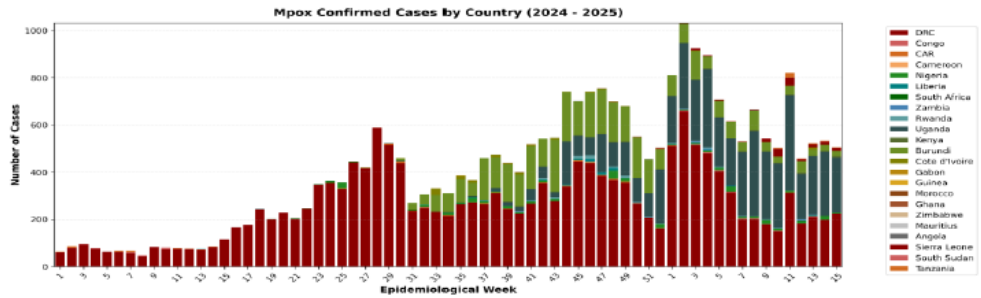
Clade Ia : high diversity

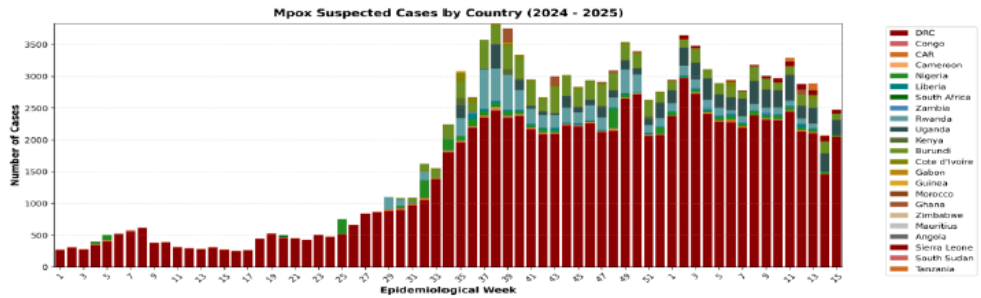


AfricaCDC
Centres for Disease Control and Prevention

WEEKLY SPECIAL PRESS BRIEFING No. 34

Mpox situation in Africa *(as of Epi Week 15, 2025)*





New cases in epi week 15

- New cases notified: **2479** vs **2074** in Epi W14 **(19.5%)** ↑
- New confirmed cases: **504** vs **534** Epi W14 **(5.6%)** ↓
- New deaths on suspected cases: **17** (CFR 0.68%) vs **4** in Epi W14
- Reporting coverage: **11/22** vs **12/22** Countries Epi W14
- **Malawi reports its first cases on April 16th**

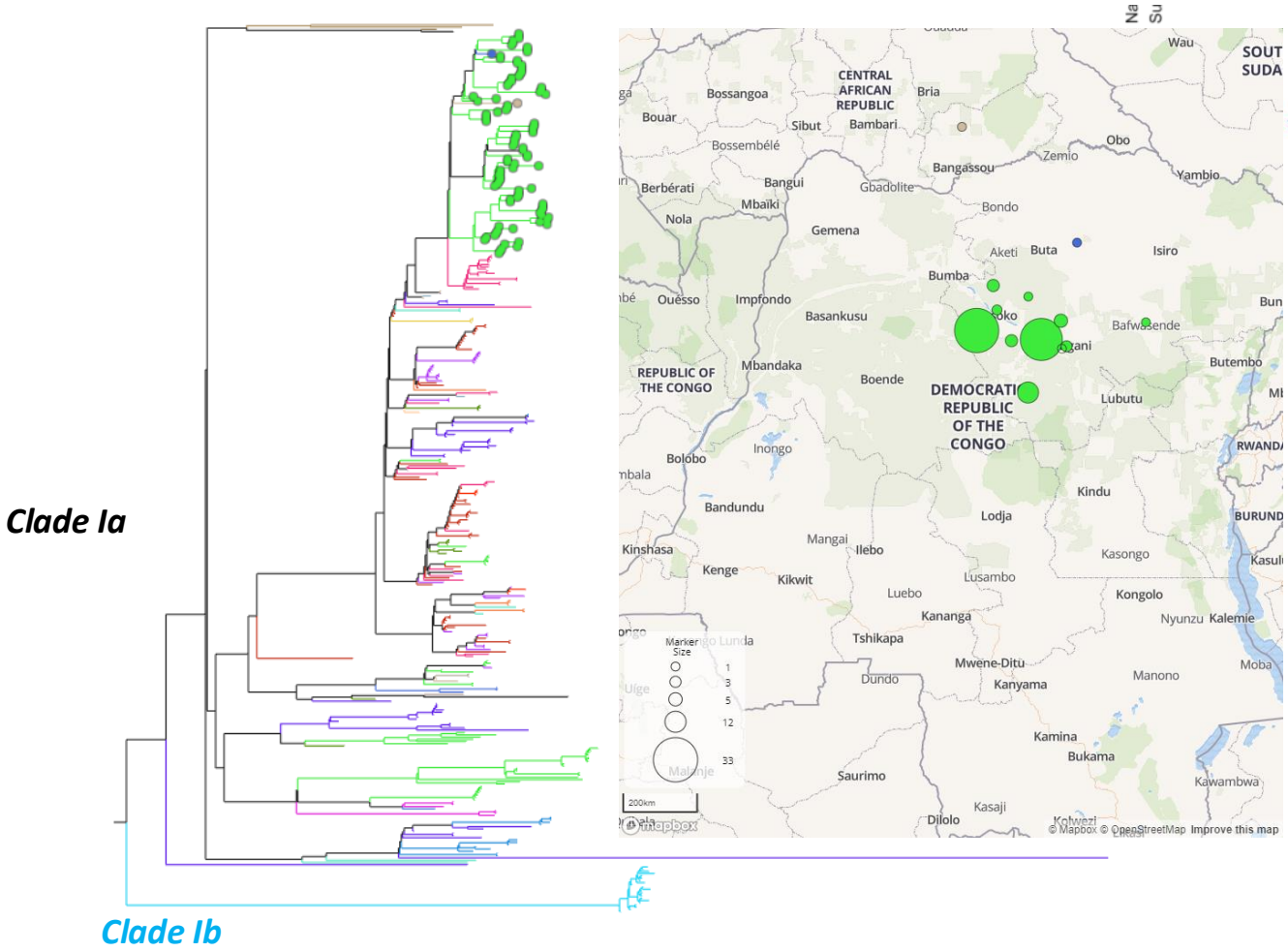
Indicator	2024	2025 (Week 14)
Suspected	77,838	44,503 (57% of cases in 2024)
Confirmed	17,907	10,095 (56.3% of cases in 2024)

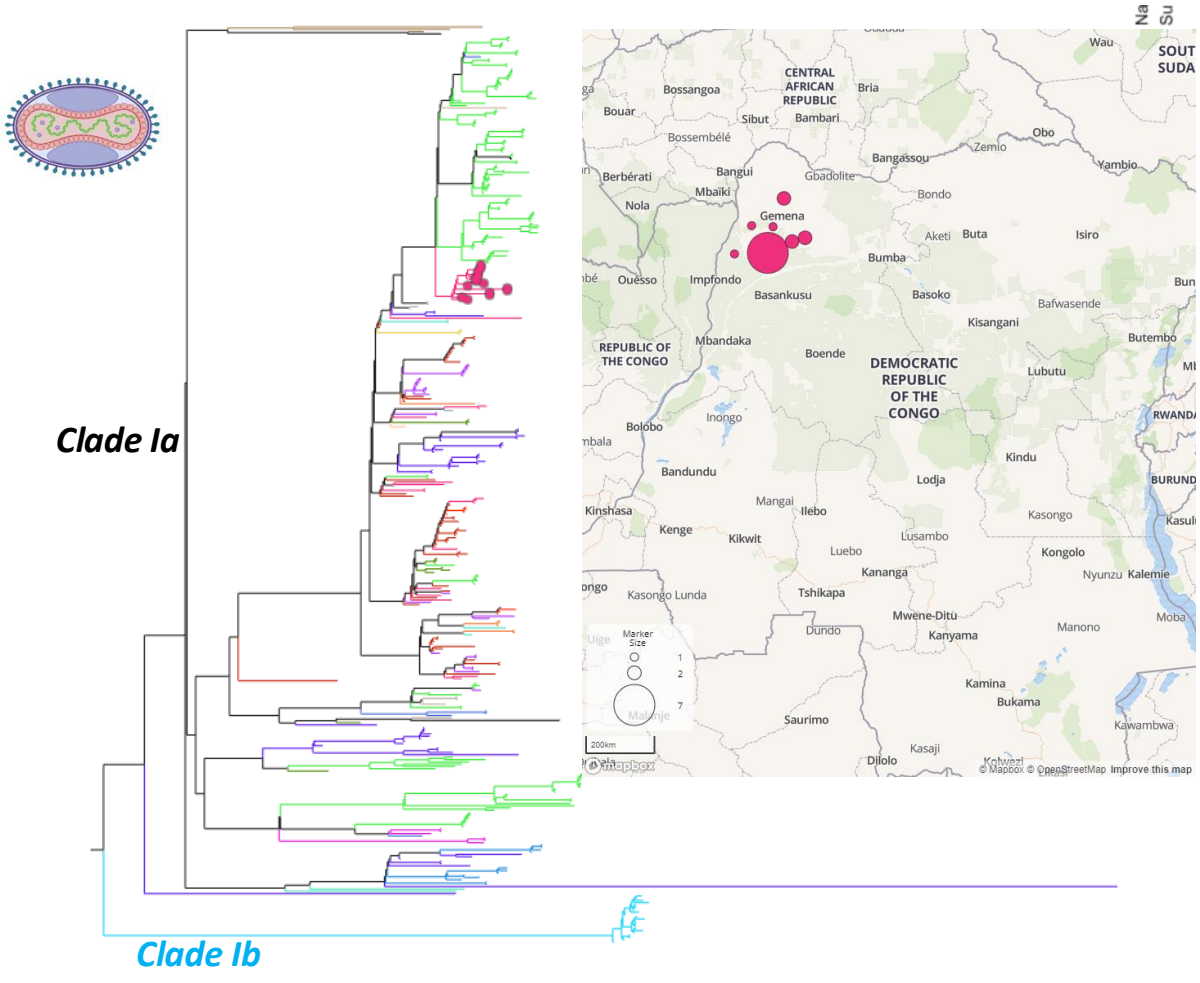
Cumulative 2024 - 2025

122,344	28,002	1730	167
Susp. Cases	Conf. Cases	(CFR: 1.4) Deaths Susp Cases	(CFR: 0.6) Deaths Conf. Cases

- 24 African countries reporting mpox between 2024-2025
- An observed average weekly decline in suspected (2487) and confirmed cases (310) in the last 6 weeks compared to PHECS
- Decline partly due to Burundi

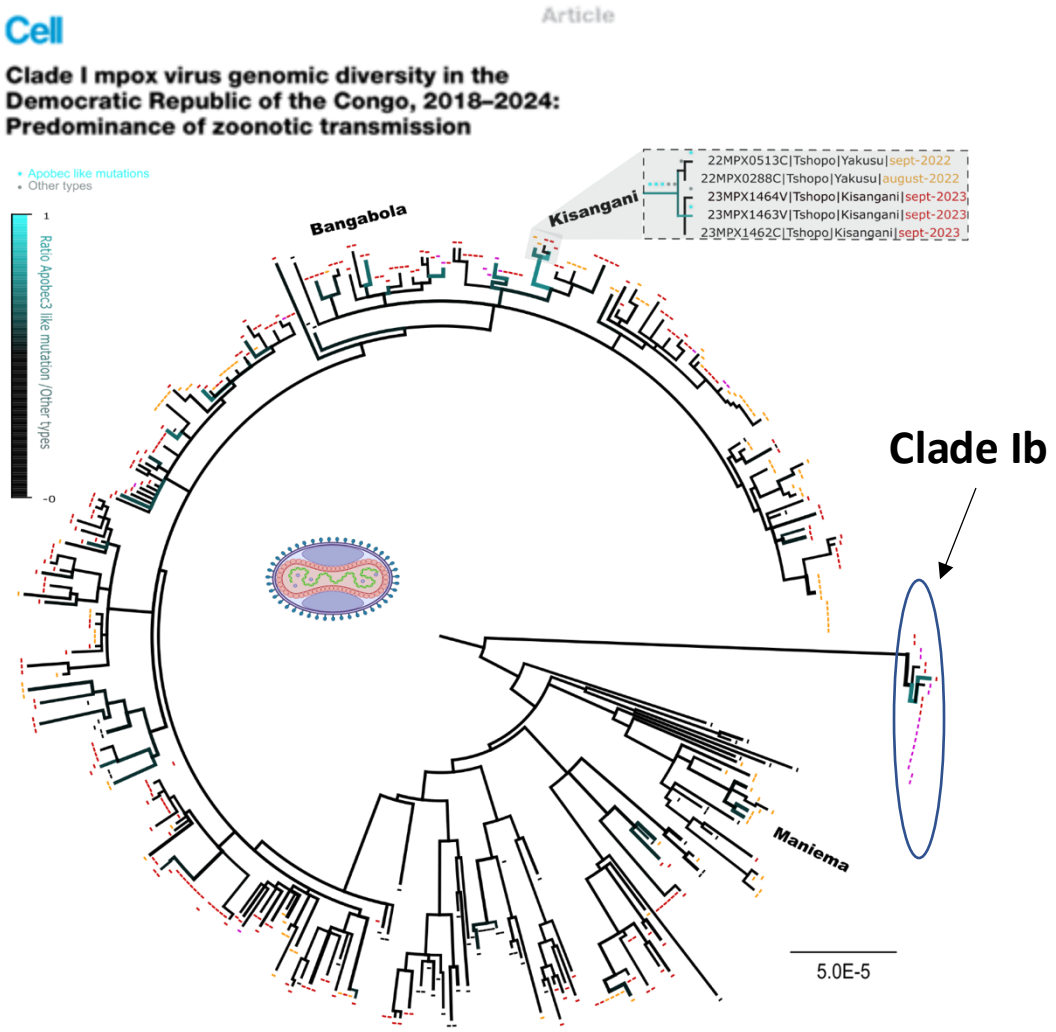
Examples of phylogeographic clusters

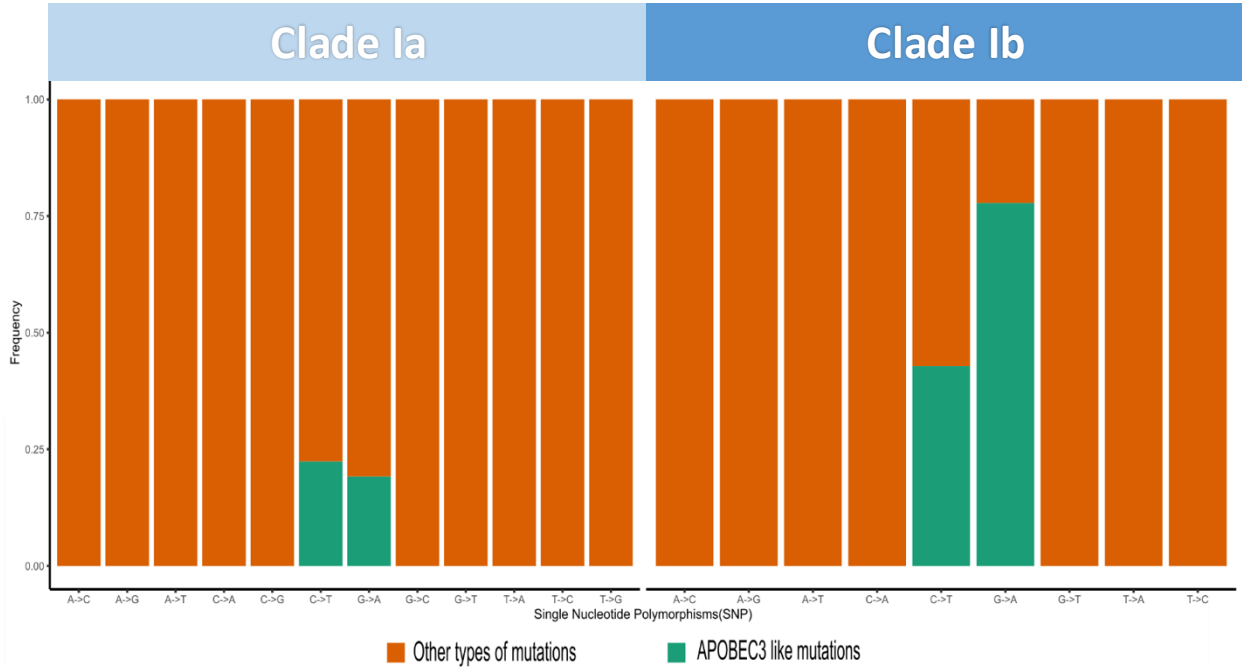




0.000078

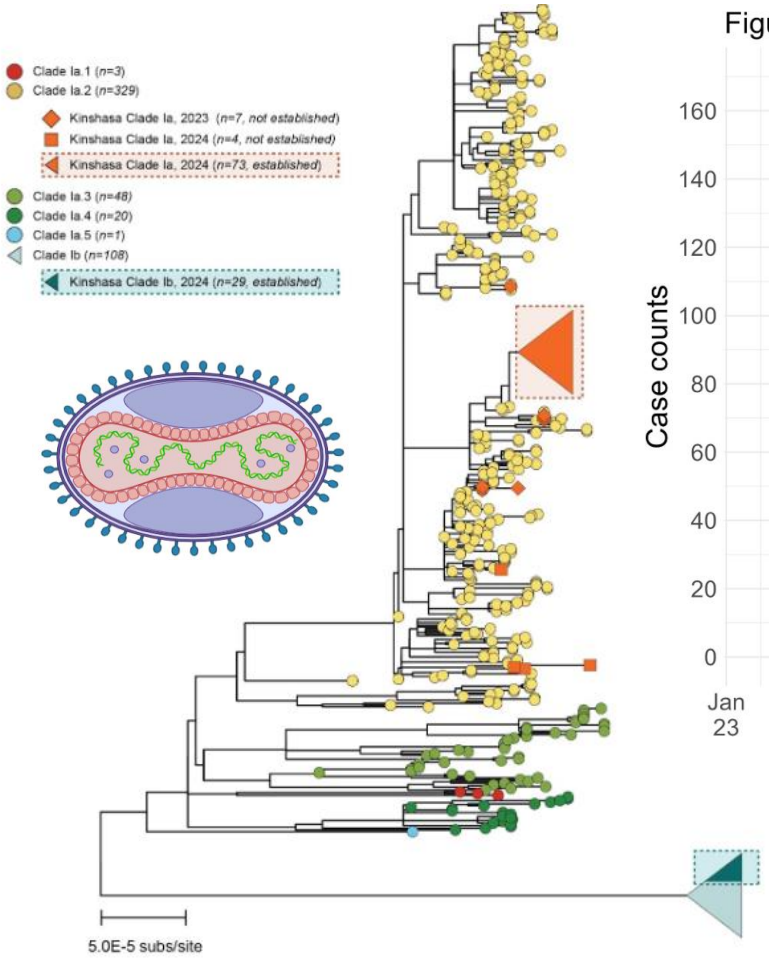
Predominance of zoonotic transmissions





- **Documented zoonotic transmission for clade Ia**
- **Different profile in clades Ia compared to clade Ib which has a high rate of type APOBEC3 mutations**

Kinshasa outbreaks



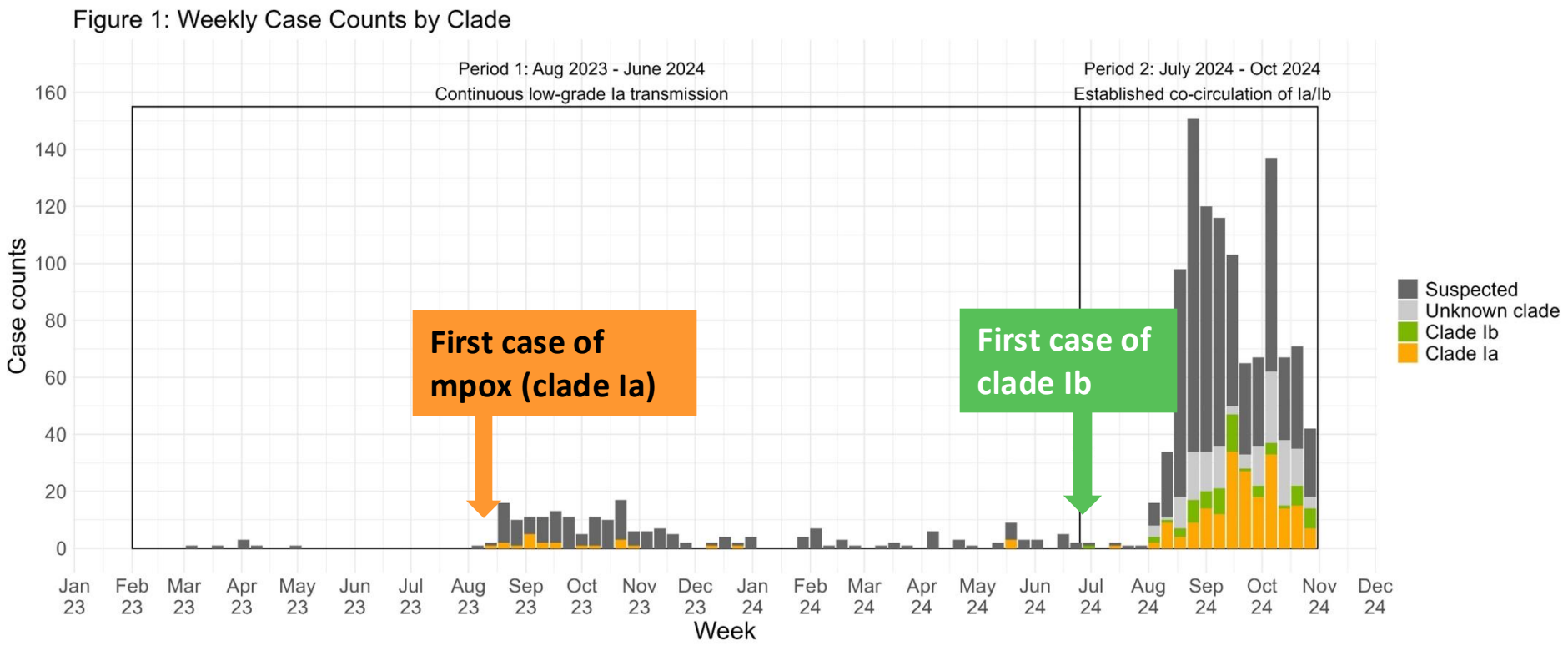
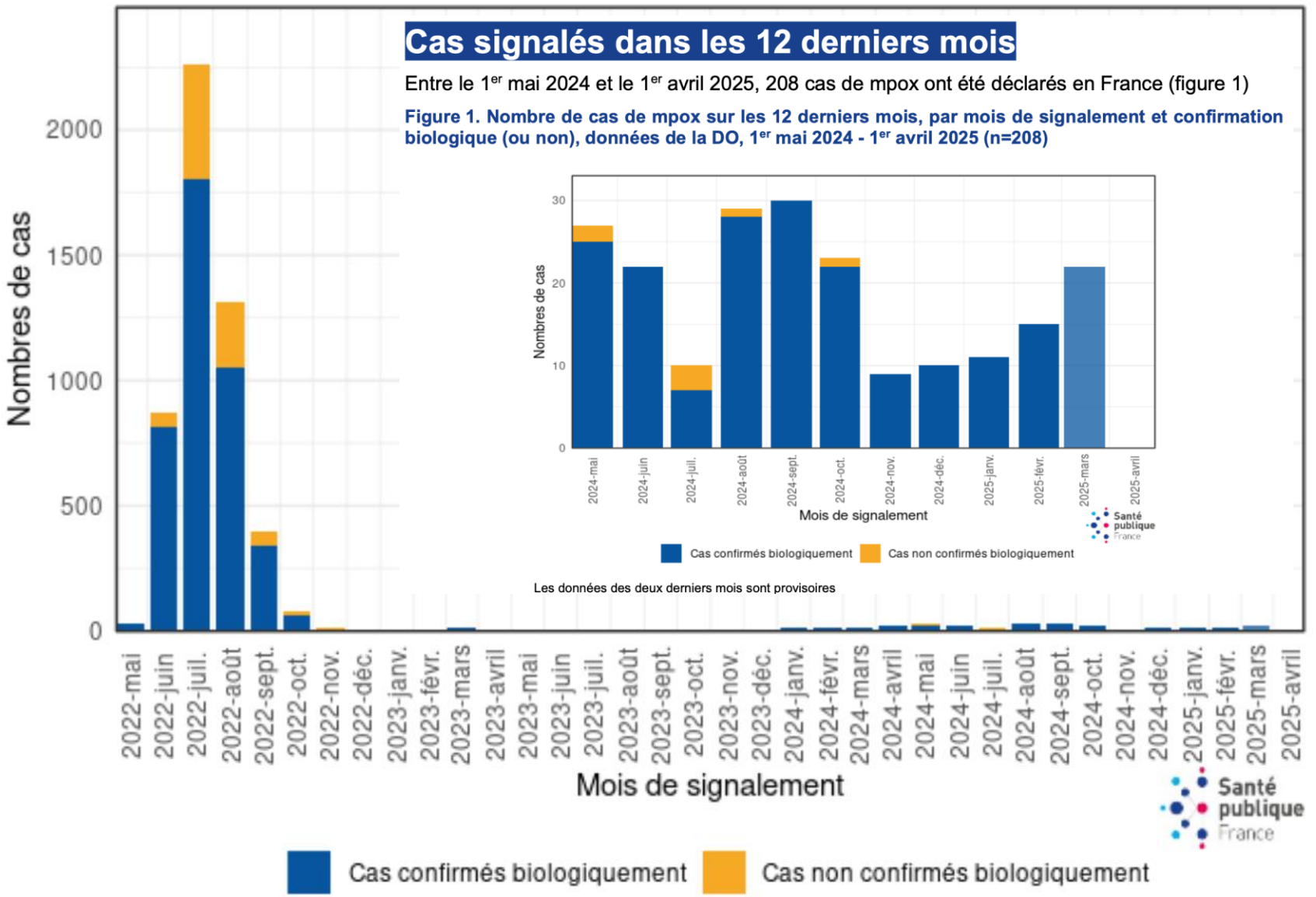
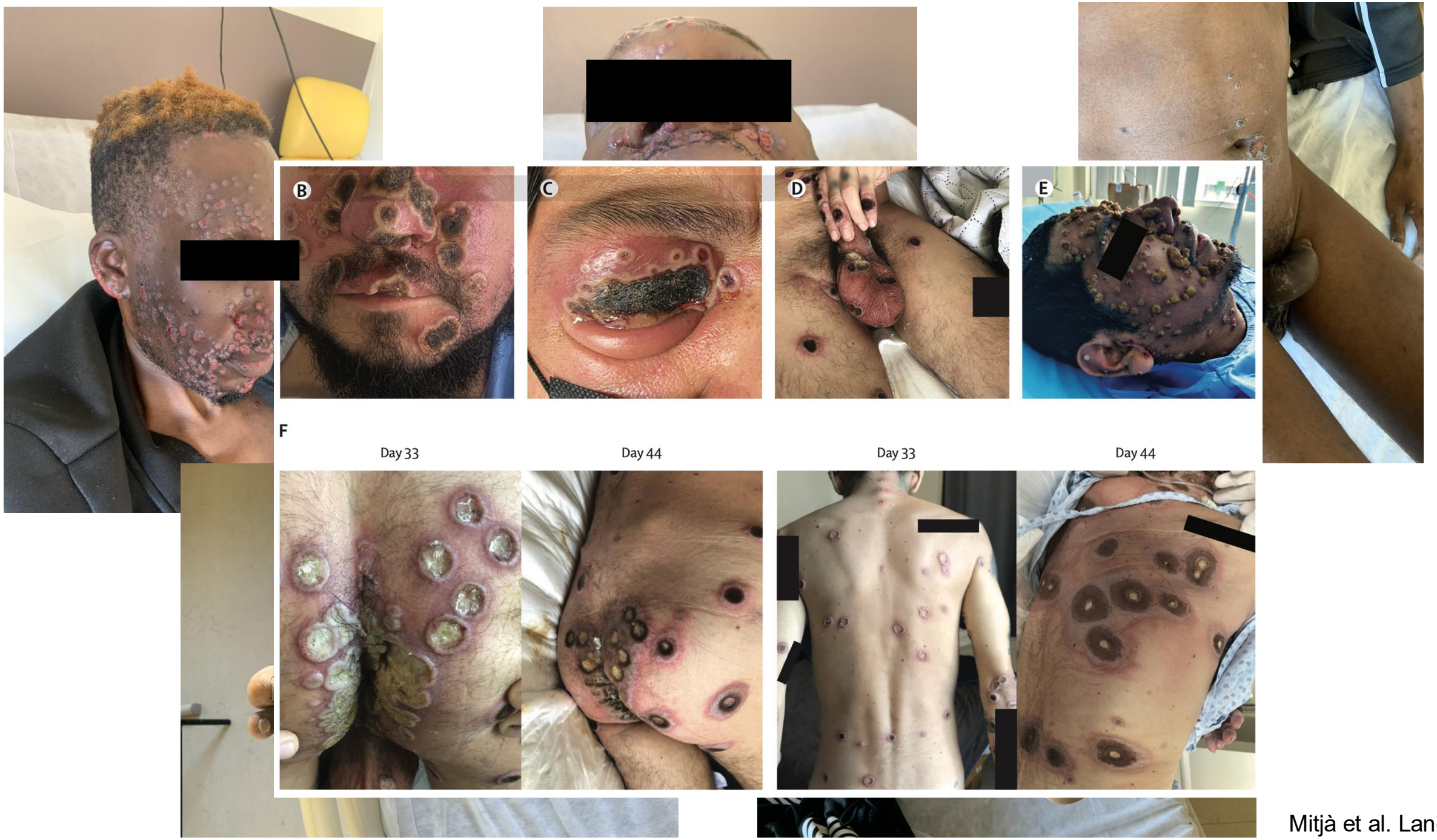
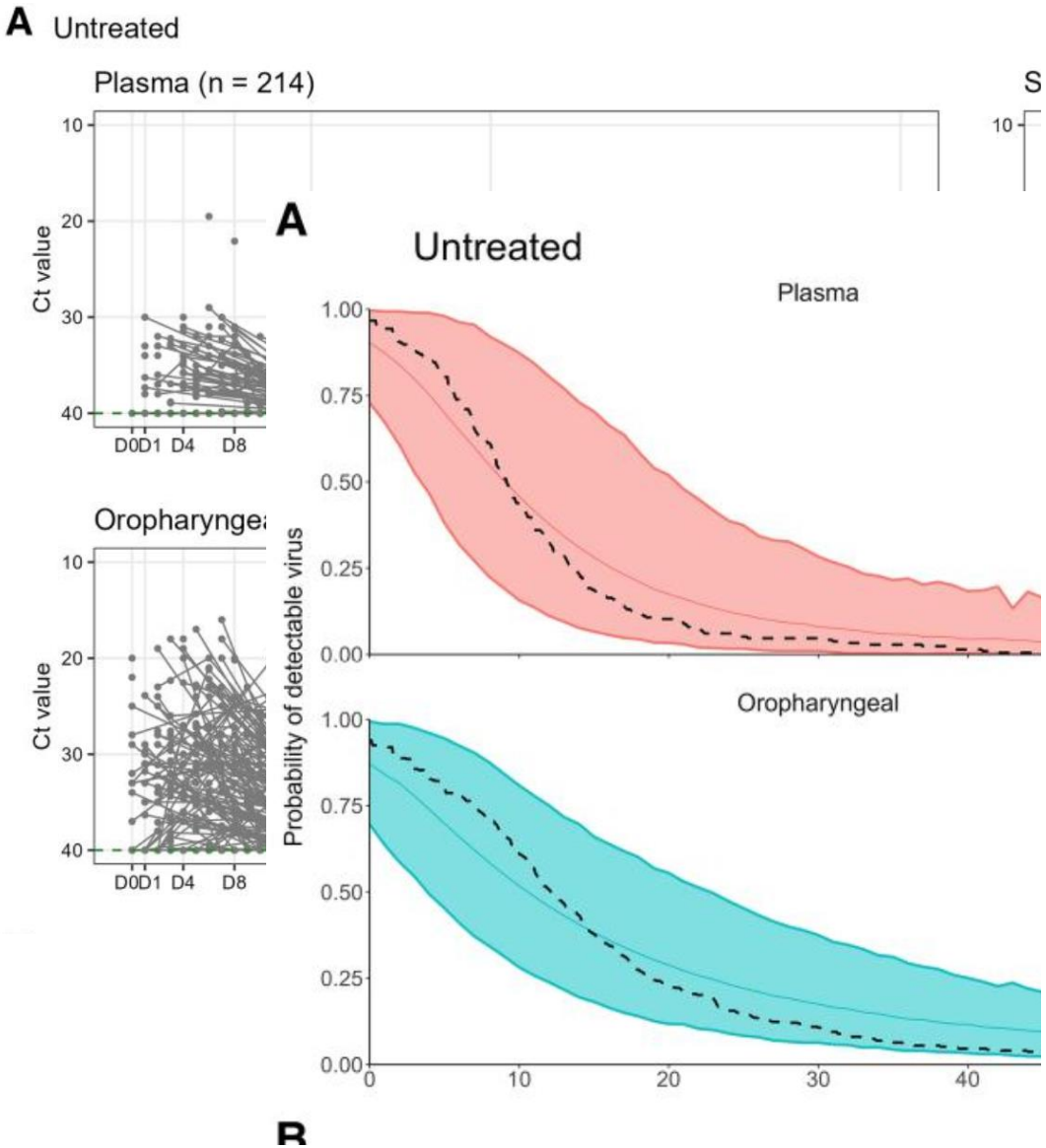


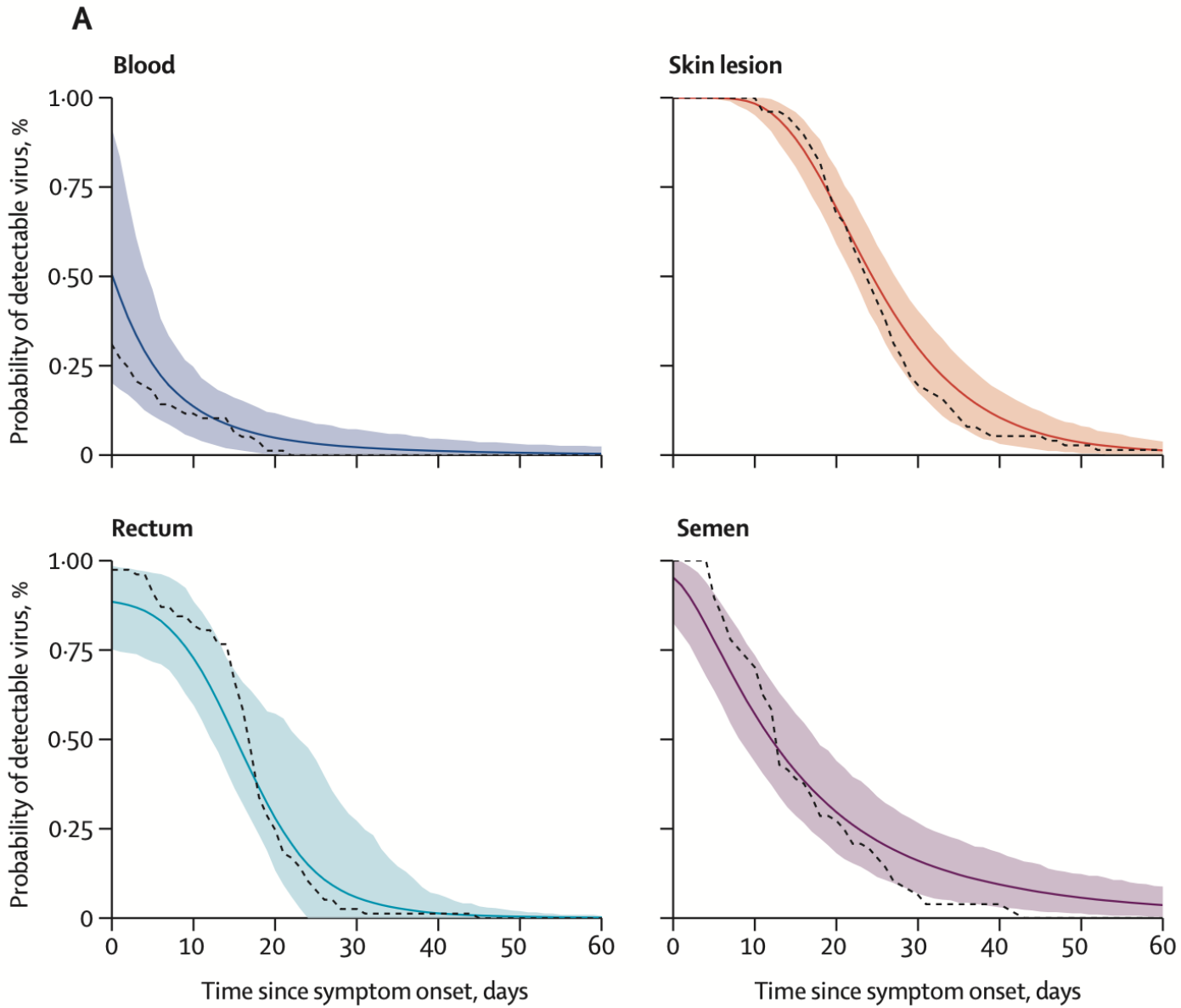
Figure 2. Nombre de cas de mpox par mois de signalement et confirmation biologique (ou non), données de la DO, mai 2022 - 1er avril (n=5 297)





Mitjà et al. Lancet 2023





Suñer et al. Lancet ID 2023

Table 5. Predicted Time to Undetectability (Cycle Threshold [Ct] ≥40) and Predicted Time to Ct ≥30 (From Simulations, in Days)

Sample Location	No.	Predicted Time to Undetectability (Ct ≥40), Mean (95% CI)			Predicted Time to Nonculturable Virus (Ct ≥30), Mean (95% CI)		
		50%	90%	95%	50%	90%	95%
Untreated							
Plasma	214	10 (4–21)	27 (13–57)	39 (17–60)	0 (0–5)	4 (0–36)	10 (0–39)
Skin	361	23 (13–38)	58 (33–60)	60 (42–60)	13 (4–28)	37 (16–60)	52 (22–60)
Oropharyngeal	347	11 (4–23)	44 (23–60)	60 (33–60)	2 (0–11)	19 (6–44)	31 (10–60)
Anal	180	15 (7–24)	34 (20–50)	44 (25–60)	9 (1–17)	23 (11–36)	30 (15–44)
Treated							
Plasma	28	15 (9–30)	44 (19–60)	60 (22–60)	4 (2–7)	13 (7–39)	20 (8–60)
Skin	46	44 (21–60)	60 (58–60)	60 (60–60)	22 (11–60)	60 (32–60)	60 (43–60)
Oropharyngeal	46	18 (12–31)	50 (28–60)	60 (35–60)	9 (4–21)	30 (15–59)	43 (19–60)
Anal	16	19 (10–60)	60 (31–60)	60 (39–60)	8 (4–25)	60 (18–60)	60 (24–60)

Abbreviation: CI, confidence interval; Ct, cycle threshold.

Pesonel et al. CID 2025

	Time to clearance in 50% of patients Days (95% CI)	Time to clearance in 90% of patients Days (95% CI)	Time to clearance in 95% of patients Days (95% CI)
Blood	1 (0–5)	13 (6–23)	20 (10–39)
Semen	13 (9–18)	39 (27–56)	53 (34–84)
Rectum	16 (13–23)	27 (21–38)	31 (23–42)
Oropharynx	16 (13–19)	34 (27–42)	42 (32–53)
Skin lesion	25 (23–28)	41 (34–47)	47 (38–56)

Suñer et al. Lancet ID 2023

Table. Screening for Sexually Transmitted Infections and MPXV Infection in 706 MSM Visiting the Sexual Health Clinic Between 5 June and 11 July 2022

Variable	MSM With No Symptoms of MPXV Infection	MSM With Symptoms Suggesting MPXV Infection
Total number of MSM visiting between 5 June and 11 July 2022	323	383
C trachomatis infections detected on anal swab, *n/N (%)*	32/323 (9.9)	Not tested
N gonorrhoeae infections detected on anal swab, *n/N (%)*	24/323 (7.4)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on anal swab, *n/N (%)*	8/323 (2.5)	Not tested
C trachomatis infections detected on first-void urine sample or urethral swab, *n/N (%)*	6/323 (1.9)	Not tested
N gonorrhoeae infections detected on first-void urine sample or urethral swab, *n/N (%)*	3/323 (0.9)	Not tested
C trachomatis and *N gonorrhoeae* co-infection detected on first-void urine sample or urethral swab, *n/N (%)*	1/323 (0.3)	Not tested
MPXV-positive test result, *n/N (%)*	13/200* (6.5)	271/383 (71)

C trachomatis = *Chlamydia trachomatis*; MPXV = monkeypox virus; MSM = men who have sex with men; *N gonorrhoeae* = *Neisseria gonorrhoeae*.
* All 200 of the asymptomatic participants who were tested for MPXV were negative for both *C trachomatis* and *N gonorrhoeae* on anal swab.

Ferre et al. Annals Intern Med 2022

Post-exposure use (PEP)

- Timing :
  - Historical study of smallpox, using a Delphi method

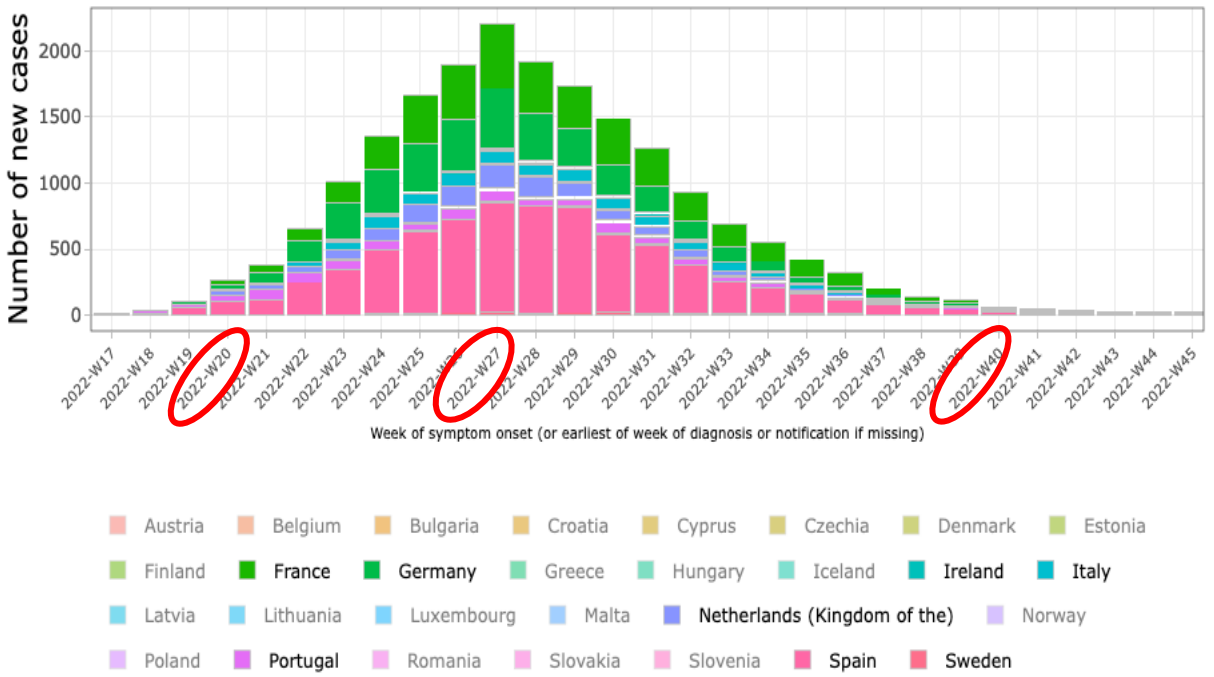
	0-6 h	6-24 h	1-3 days
Prevention	93%	90%	80%
Clinical change	80%	80%	75%

- Animal challenge in prairie dogs: 88% survival with vaccination on D1, and 38% on D3, compared with 25% in the control group.
- Use of Imvanex® in the United Kingdom
  - In 2018: 3 cases, 131/154 contacts vaccinated, 1 secondary case in 1 healthcare professional (at D6/7).
  - In 2019: 17/18 contacts vaccinated, no secondary cases, no AEs.

Massousi, 2003, JID ; Keckler, 2020, Vaccines ; Adler, 2019, LID

Mpox vaccination in 2022 in Europe

- Started in the end of May 2022
- Total of 27,180 cases from 46 countries
- Vaccination recommendations in France
  - 20/05: Post-exposure prophylaxis (PEP)
  - 07/07: Pre-exposure prophylaxis (PrEP)
  - 06/10: extension to women at risk



ECDC
Krug, Eurosurv, 2023

Vaccine effectiveness

- Systematic Review and meta-analyses
  - PEP : 79.51% (20.34%)
  - PrEP 1 dose: 95.60% (76.16%)
  - PrEP 2 doses: 87.97 (81.88%)

Review

Vaccine effectiveness of 3rd generation mpox vaccines against mpox and disease severity: A systematic review and meta-analysis

Lauren Pischel [a,*], Brett A. Martini [b], Natalle Yu [c], David Cacesse [b], Mahder Tracy [d], Kolambi Kharbanda [d], Noureen Ahmed [d], Kavin M. Patel [a], Alyssa A. Grimshaw [e], Amyn A. Malik [d], George Goshua [f,g], Saad B. Omer [d]

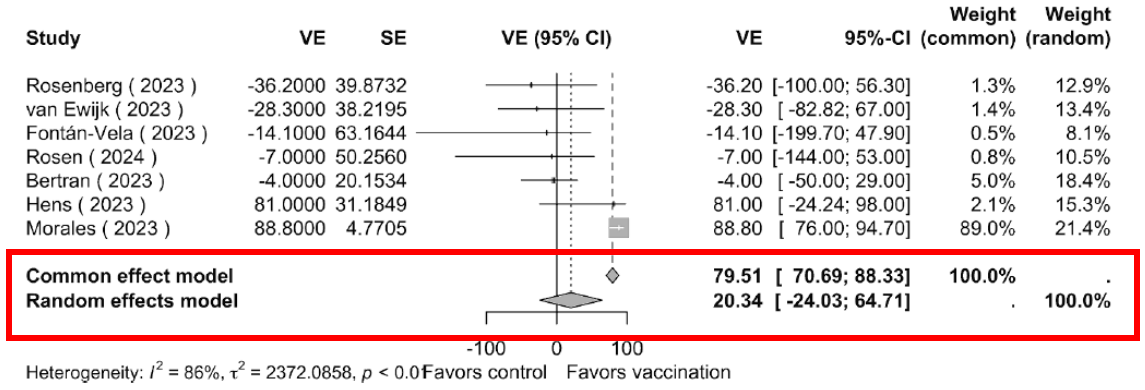


Fig. 4. Meta-analysis of PEP vaccine effectiveness for mpox.

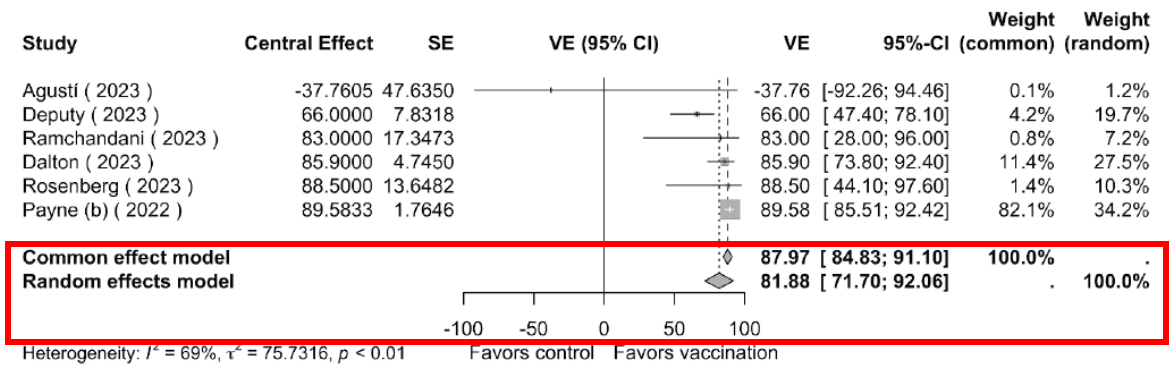
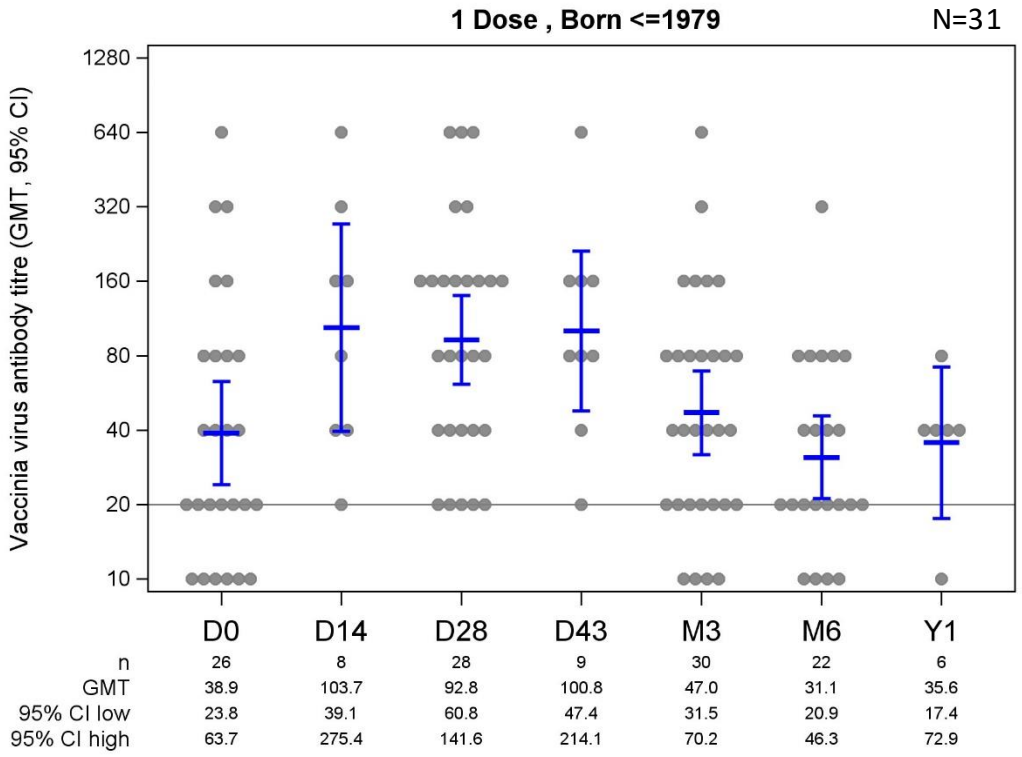
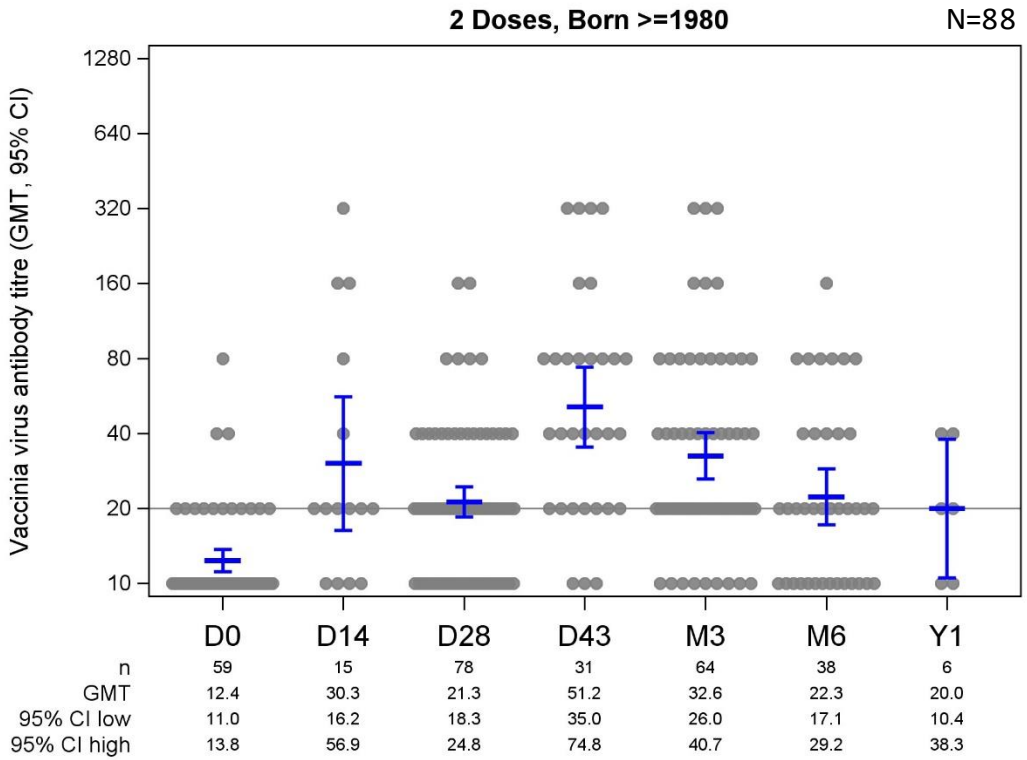


Fig. 3. Meta-analysis of 2 doses of MVA-BN vaccine effectiveness for mpox.

MVA-BN yields anamnestic response



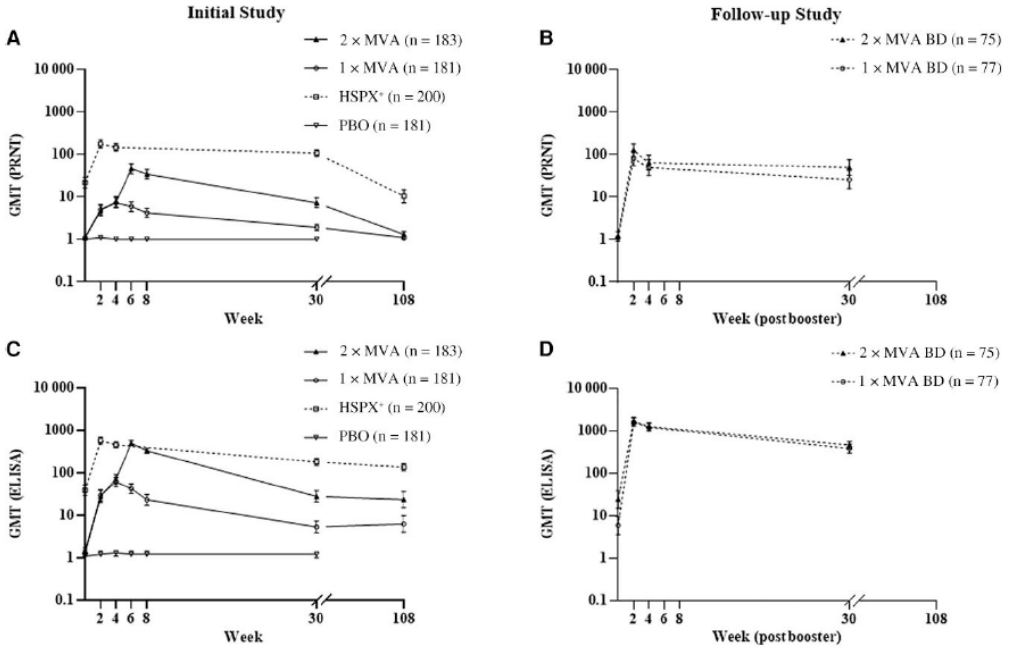


	D0	D14	D28	D43	M3	M6	Y1
Title>=20, n (%)	20 (77%)	8 (100%)	28 (100%)	9 (100%)	26 (87%)	18 (82%)	5 (83%)

	D0	D14	D28	D43	M3	M6	Y1
Title>=20, n (%)	14 (24%)	11 (73%)	55 (71%)	28 (90%)	55 (86%)	24 (63%)	4 (67%)

Luong Nguyen, ECCMID, 2024

A booster dose?



HAS HAUTE AUTORITÉ DE SANTÉ | Développer la qualité dans le champ sanitaire, social et médico-social

Avis n° 2024.0058/AC/SESPEV du 29 août 2024 du collège de la Haute Autorité de santé relatif à la stratégie de vaccination contre le mpox

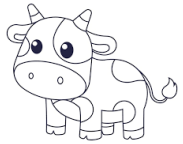
People eligible for vaccination	Vaccination schedule			
	Immunocompetent		Immunosuppressed	
	Vaccinated in childhood (before 1980)[a]	Not vaccinated in childhood (before 1980)	Vaccinated in childhood (before 1980)[a]	Not vaccinated in childhood (before 1980)
Never vaccinated with an MVA-BN vaccine	1 booster dose	2 doses	3 doses	3 doses
Having received a single dose MVA-BN vaccine	No	1 dose	2 doses	2 doses
With complete MVA-BN vaccination regimen	No	1 booster dose[b]	1 booster dose[b]	1 booster dose[b]
Having contracted mpox between 2022 and today	No	No	No	No

[a]A booster dose is recommended for people who received a smallpox vaccination before 1980; [b]The booster dose should be administered at a distance from the primary vaccination, i.e., in the current situation, around two years after the last dose.

Ilchman, JID, 2023

Smallpox vaccines & mpox prevention

- 3 generations of smallpox vaccines



All based on vaccinia virus

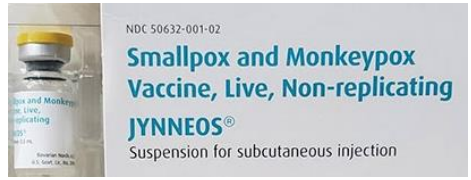
1st : live unattenuated *vaccinia* virus grown in the skin of live animals

2nd : live vaccinia virus grown in eggs or in cell culture

3rd : based on attenuated vaccinia viruses

→ Strains much less virulent = lesser side effects

MVA-BN = IMVANEX = Imvamune =JYNNEOS By Bavarian Nordic



Approved for mpox prevention

→ Safer for immunocompromised patients
→ As immunogenic as ACAM2000
→ Vaccination recommended for at risk population

sex workers
men having sex with men
people in mpox endemic areas
health workers

✓ Strong effectiveness against mpox : 66-86% after 2 doses

→ Protection persistence after vaccination ?
→ Effectiveness against Clade Ib ?

Deputy et al., 2023
Payne et al., 2022
Bertran et al., 2023
Wolff Sagy et al., 2023
Liu et al., 2024

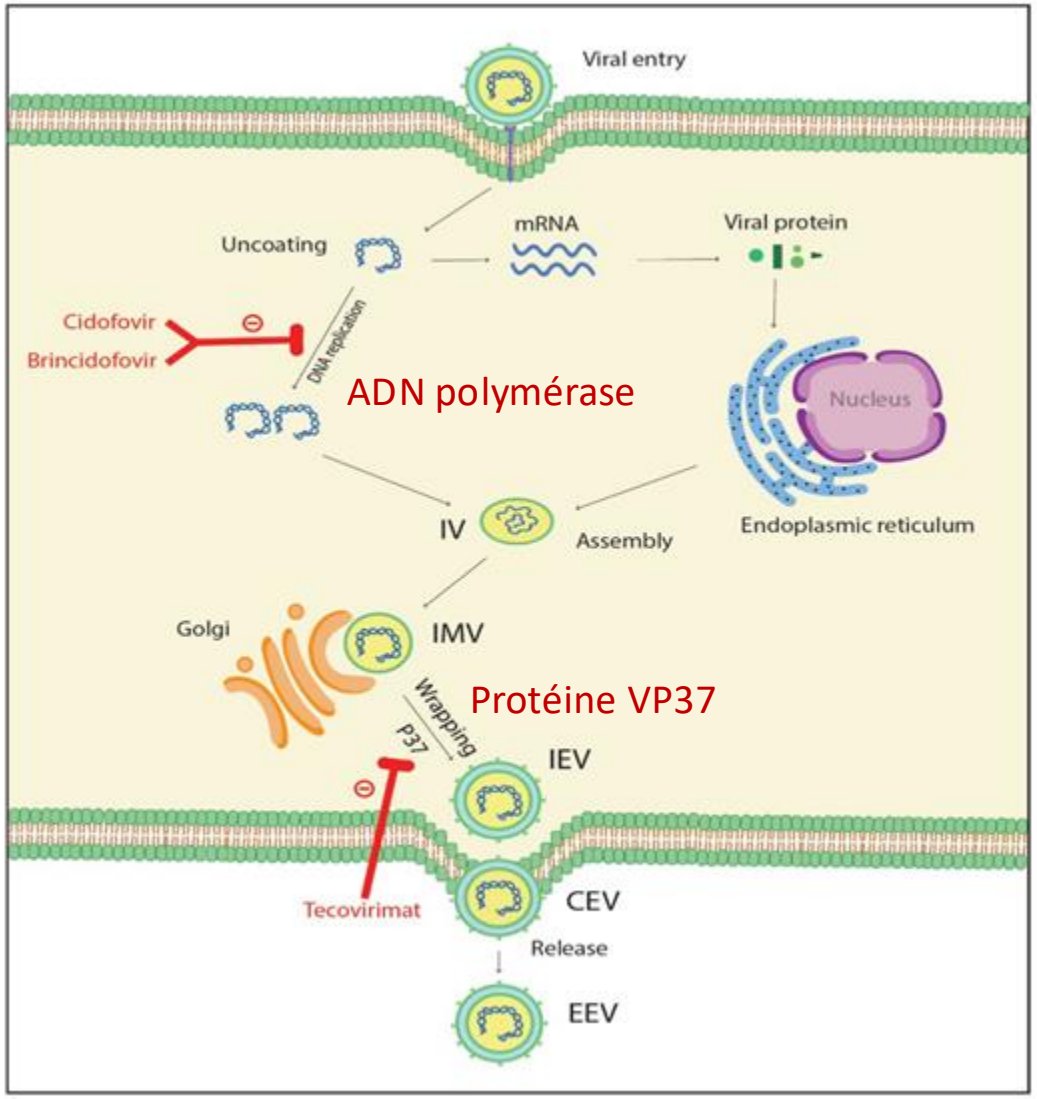
Antiviral molecule : tecovirimat (tpoxx)

- Several on going & recently terminated international randomized clinical studies to assess TPOXX efficacy

	The UNITY study ANRS NCT05597735	STOMP Study of Tecovirimat for Mpox NIAID NCT05534984	PALM NIAID NCT05559099
	N=460	**N=336**	**N=597**
Treatment timeline	Symptomatic mpox any duration	Symptomatic mpox <14d	Lab confirmed mpox > or <7d
Included patient age	<14y	Any age	64% <18y
Success	Time to complete lesion resolution	Time to active lesion resolution	Time to lesion resolution
Country	50% Brazil (&50% HIV)	USA	DRC
	Clade IIb	Clade IIb	Clade Ib
Conclusion	Waiting for results	Safe but ineffective	Safe but ineffective

- So far ineffective in patients ?
- Mainly tested in Clade IIb infected patients : what about Clade Ib ?

Brincidofovir, cidofovir – alternatives?



Pourkarim et al, Pharmacol Res Perspect. 2024;12:e01164.

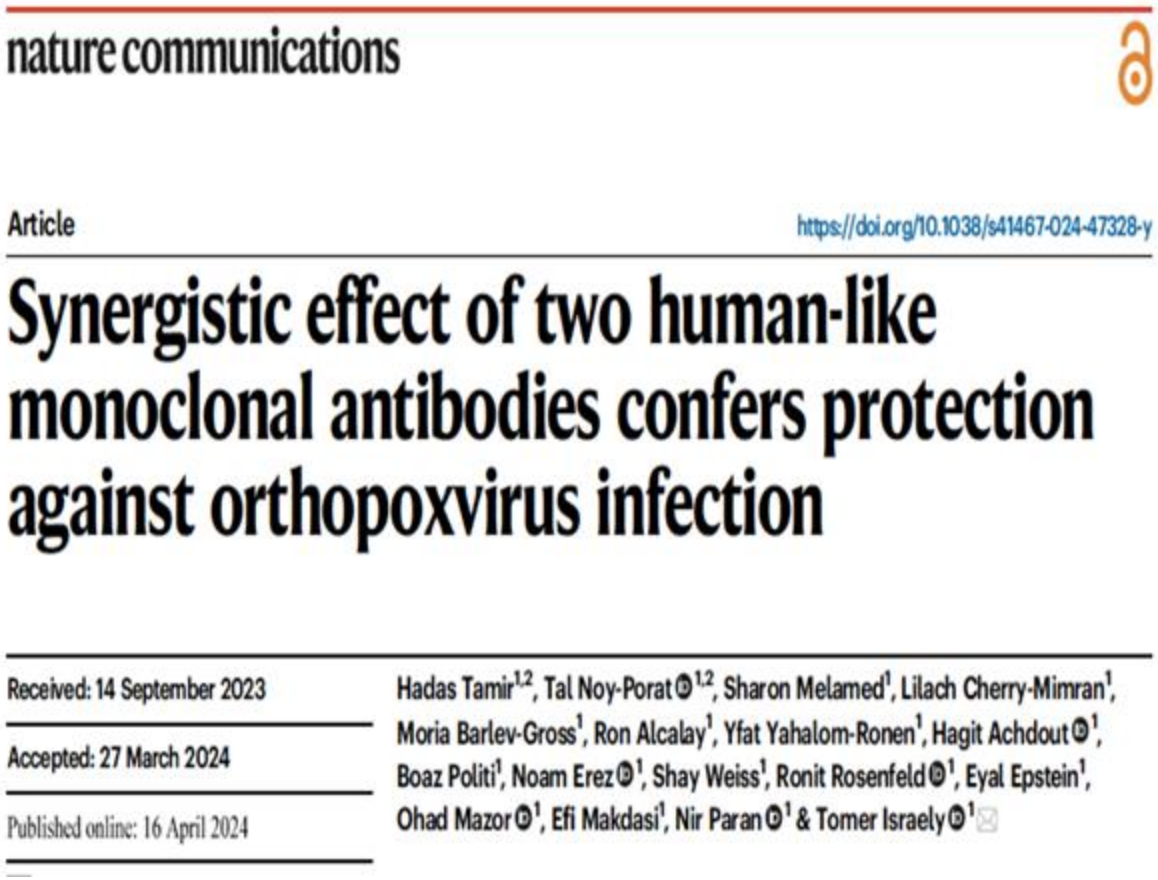
Brincidofovir
A prodrug of cidofovir, with better renal tolerance.FDA-approved in the USA, used for the treatment of smallpox.

Cidofovir (3rd line)
Nucleoside analogue, inhibits DNA synthesis.Efficacy in preventing clinical disease and mortality in primate models of infection.High renal or hematologic toxicity, as well as carcinogenic, teratogenic, and reprotoxic effects.

No efficacy data in humans for the treatment of Mpox infections.

Mpox mAbs – animal models

Tamir, H et al Nature Communications 2023



nature communications

Article

https://doi.org/10.1038/s41467-024-47328-y

Synergistic effect of two human-like monoclonal antibodies confers protection against orthopoxvirus infection

Received: 14 September 2023

Accepted: 27 March 2024

Published online: 16 April 2024

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Emerging Microbes & Infections
2024, VOL. 13, 2401931 (14 pages)
https://doi.org/10.1080/22221751.2024.2401931

Identification of mpox M1R and B6R monoclonal and bispecific antibodies that efficiently neutralize authentic mpox virus

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Monoclonal antibodies administered just after infection

Conclusion

- Transition épidémiologique profonde
- IST/HSH et IST « exotique »
- Transmission H/H >>> zoonotique
- Portage pauci-asymptomatique
- Présentation clinique dépendant du mode de transmission et du terrain
- Mortalité dépendant du clade et des conditions de PEC
- PEP et PREP
- Durabilité de l'immunité post vaccination et post-infection?
- Efficacité du técovirimat ? et suites?

Remerciements

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