
สมาคมโรคเอดส์แห่งประเทศไทย
Thai AIDS Society
TAS
21 st
HIV/AIDS
WORKSHOP
2022

TRC EIDCC
Thai Red Cross Emerging Infectious Diseases Clinical Center

21st HIV/AIDS WORKSHOP 2022

Updates IAS/CROI 2022

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Disclosures

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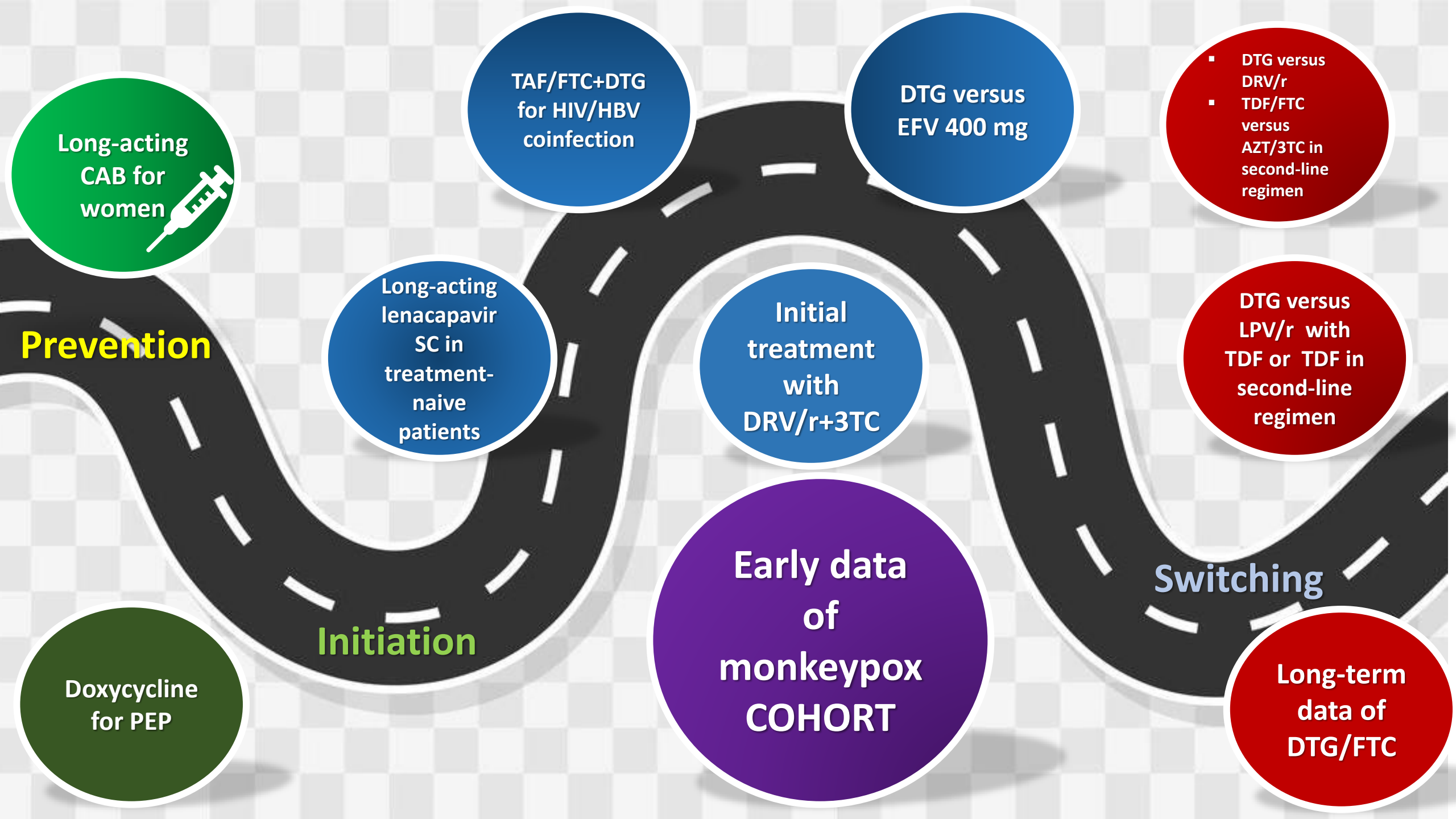
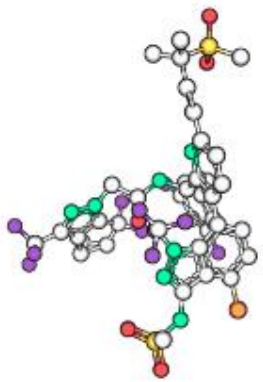
- **Non-CME/CE services: Gilead Sciences, BMS, Merck, Siam Pharmaceutical, ViiV, Hetero laboratory and Mylan, Abbott**
- **Advisory board: BMS, GSK, ViiV Healthcare, Celltrion, Pfizer and MSD**

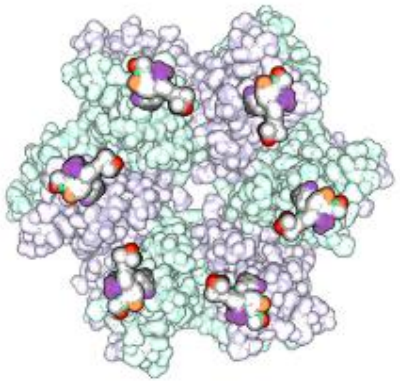

Long-acting CAB for women
TAF/FTC+DTG for HIV/HBV coinfection
DTG versus EFV 400 mg
DTG versus DRV/r
TDF/FTC versus AZT/3TC in second-line regimen
Prevention
Long-acting lenacapavir SC in treatment-naive patients
Initial treatment with DRV/r+3TC
DTG versus LPV/r with TDF or TDF in second-line regimen
Switching
Initiation
Doxycycline for PEP
Early data of monkeypox COHORT
Long-term data of DTG/FTC

Initial regimen

- New long-acting ART agent: efficacy and safety
- What combination?
- Two-drug regimen is durable?
- Option for specific populations: co-infections

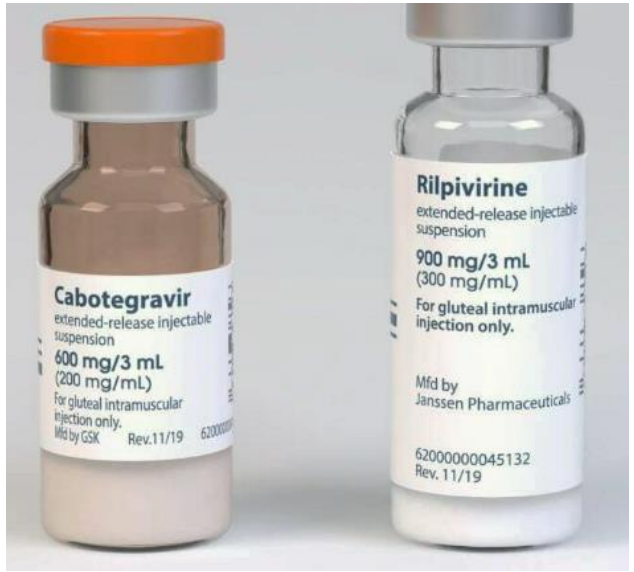


GS-6207
Gilead Sciences



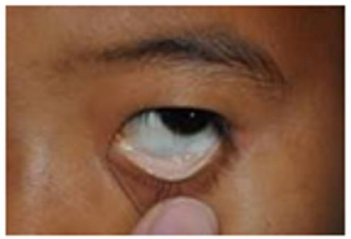
clinical
HIV capsid inhibitor

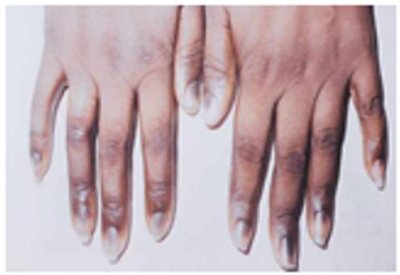
twice-a-year
dosing

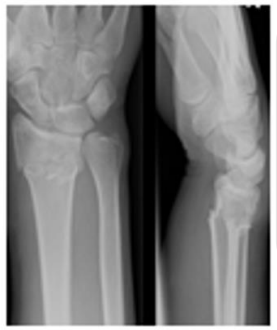


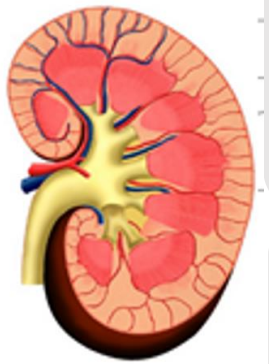
Two-Drug Regimens

Monotherapy → Dual therapy → Triple therapy → **Dual therapy** → Injectable ART → Implantable ART









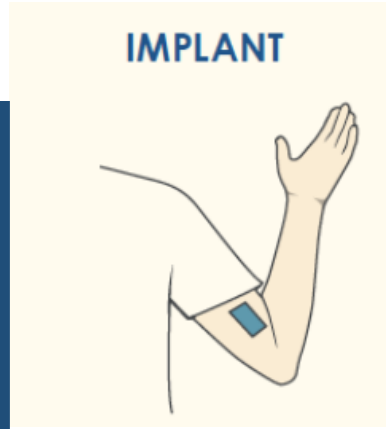
Integrase inhibitors
- **DTG**
- **BIC**
- RAL
- EVG/c

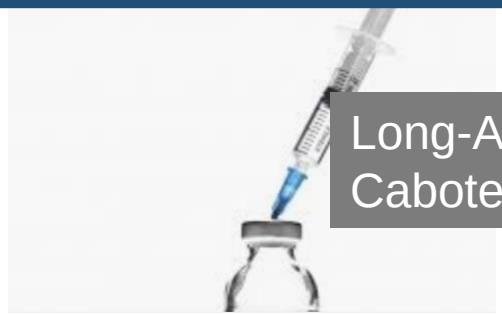
NRTI
- **TDF TAF**
- ABC
- 3TC FTC
- AZT

NNRTI: EFV, RPV
PI: **DRV**, ATV,LPV

Initial therapy:
- DTG+3TC

Maintenance:
- DTG+3TC
- DTG+RPV
- CAB+RPV



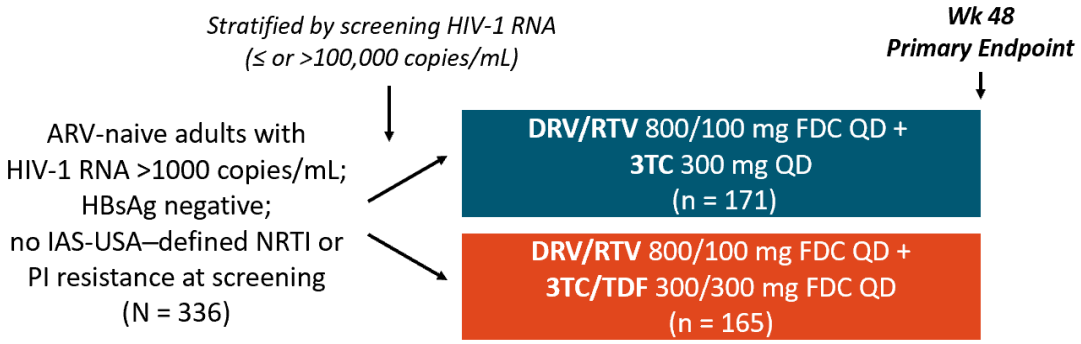


Long-Acting Injectable ART
Cabotegravir, Rilpivirine

DRV/R+3TC for initial regimen

AIDS 2022
29 July – 2 August

- Multicenter, randomized, open-label phase IV trial



- **Primary endpoint:** HIV-1 RNA <50 copies/mL (ITT-E) at 48 wk by FDA snapshot
  - 80% power to detect 12% margin
- **Secondary endpoints:** safety

Characteristic	DRV/RTV + 3TC (n = 171)	DRV/RTV + 3TC/TDF (n = 165)
Median age, yr (IQR)	29 (24-36)	30 (26-36)
Male, n (%)	156 (91)	146 (88)
Hispanic/Latinx, n (%)	118 (69)	102 (62)
MSM risk behavior, n (%)	130 (76)	118 (72)
CDC disease stage, n (%)		
▪ A	159 (93)	156 (95)
▪ B	10 (6)	9 (6)
▪ C	1 (0.6)	0 (0)
Median HIV-1 RNA, log_{10} copies/mL (IQR)	4.6 (4.1-5.1)	4.5 (4.1-5.0)
▪ HIV-1 RNA >100,000 copies/mL, n (%)	45 (26)	31 (19)
Median CD4+ cell count, cells/mm^3 (IQR)	414 (300-586)	417 (300-607)
▪ ≤200 cells/mm^3, n (%)	15 (9)	11 (7)

Outcome	DRV/RTV + 3TC (n = 171)	DRV/RTV + 3TC/TDF (n = 165)	Difference, % (95% CI)	*P* Value
HIV-1 RNA <50 copies/mL (ITT-E), n (n = 336)	91	93	-2.1 (-7.0 to 2.9)	<.01
▪ >100,000 copies/mL, n (n = 76)	87	90	-3.7 (-15.7 to 8.4)	.13
HIV-1 RNA <50 copies/mL (PP), n (n = 313)	98	99	-0.6 (-2.9 to 1.7)	<.01
Confirmed VF (ITT-E),* n	4	3		
▪ Baseline HIV-1 RNA >500,000 copies/mL	2	1	--	--
▪ Baseline CD4+ cell count <200 cells/mm^3	3	0		
Never suppressed (ITT-E), n	3	2	--	--
Median HIV-1 RNA at VF (ITT-E), copies/mL (IQR)	58 (50-250)	136 (68-39,914)		
▪ Amplified resistance test	2	1	--	--
▪ Treatment-emergent resistance	0	0		
Median CD4+ cell count increase vs baseline, cells/mm^3	275.31	238.14	--	.442

- **ART initiation with generic FDC DRV/RTV + 3TC noninferior to generic FDC DRV/RTV + 3TC/TDF at 48 wk in treatment-naive patients HIV-1 RNA <50 copies/mL: 91% vs 93% (difference -2.1%; 95% CI: -7.0 to 2.9; P <.01)**
- *Noninferiority margin not met for subgroup of patients with baseline HIV-1 RNA >100,000 copies/mL (n = 76) HIV-1 RNA <50 copies/mL: 87% vs 90% (difference -3.7%; 95% CI: -15.7 to 8.4; P = .13)*

DTG+FTC versus three-drug regimen: data at 144 weeks

- Randomized, open-label, multicenter phase III trial

Virologically suppressed adults with HIV (HIV-1 RNA <50 c/mL for ≥24 wk) on standard combination ART; no INSTI resistance; no HBV* (N = 187)

Wk 48

- Switch to DTG + FTC with SM (n = 45)
- Switch to DTG + FTC with PCM (n = 48)
- Maintain baseline ART with SM (n = 47)
- Maintain baseline ART with PCM (n = 47)

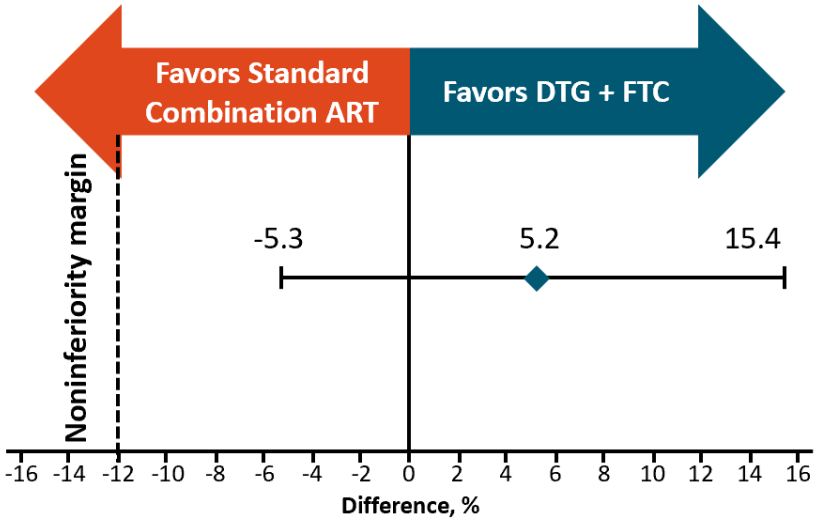
Therapy and monitoring at patient and physician discretion

Wk 144

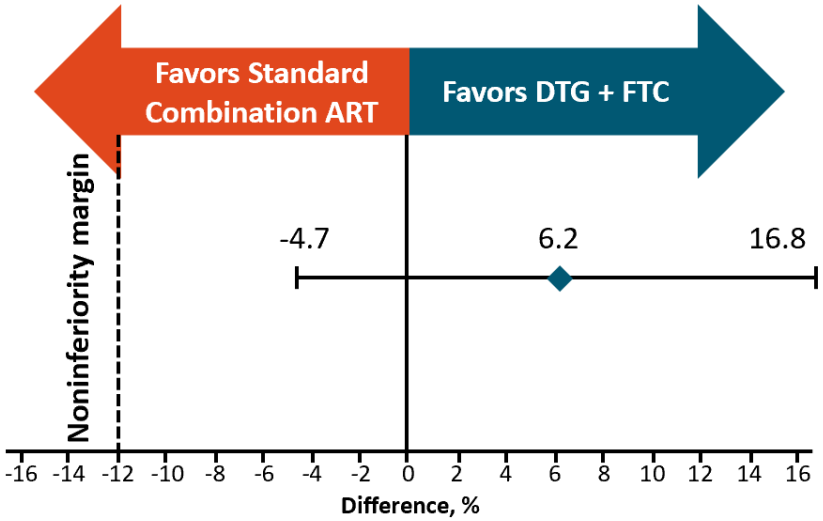
SIMPL'HIV Wk 48 results showed noninferiority of switching from standard combination ART to DTG + FTC vs continued standard combination ART in virologically suppressed PWH

*Excluded if previous ART change due to suboptimal virologic response (M184V accepted); CrCl <50 mL/min; transaminase elevation >2.5 ULN.

HIV-1 RNA <100 c/mL Through Wk 144



HIV-1 RNA <50 c/mL at Wk 144



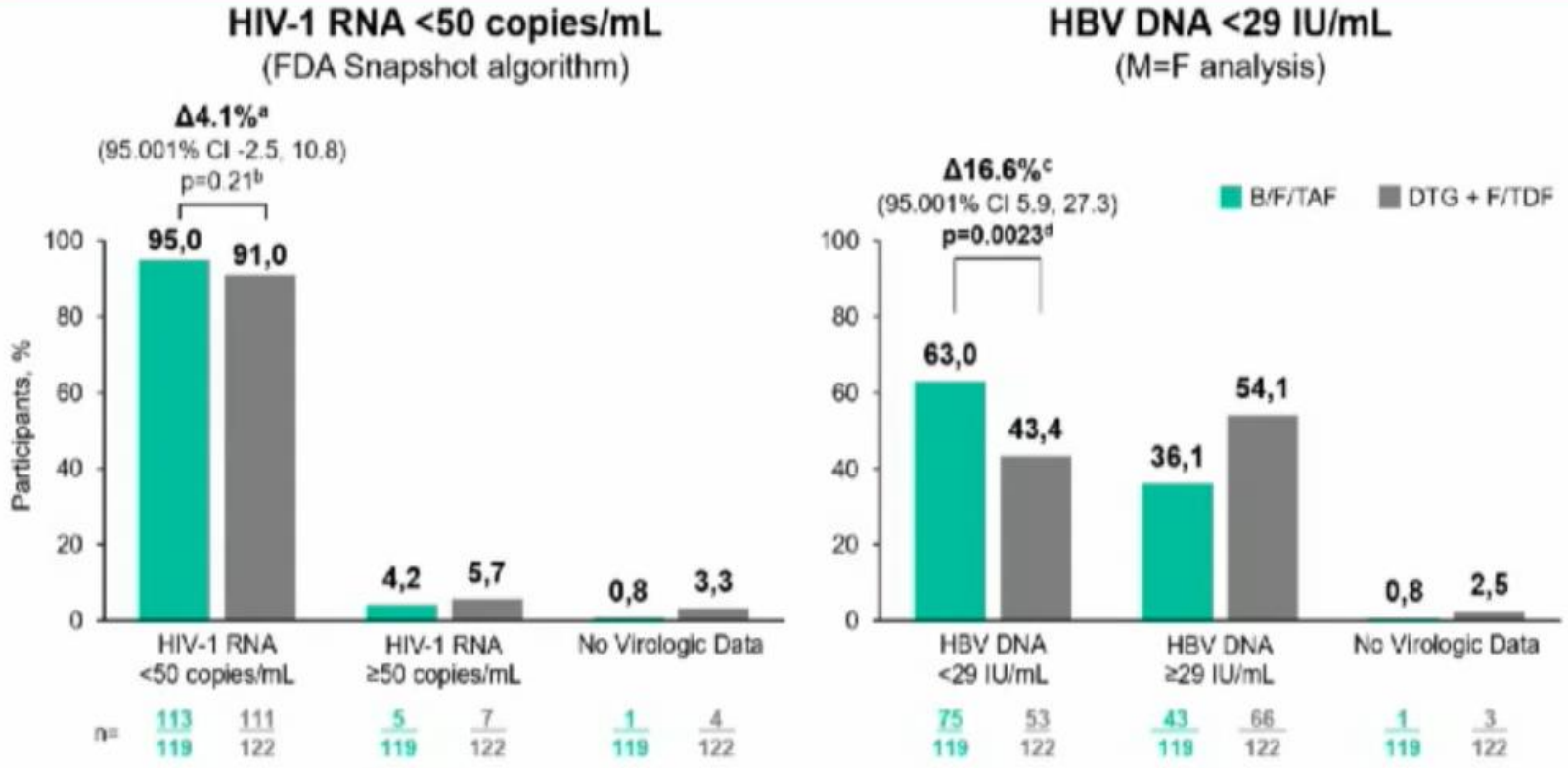
- Switching from standard combination ART to DTG + FTC was noninferior to continuing standard combination ART in virologically suppressed adults at Wk 144
- Quality of life was similar in both groups
- Weight changes from baseline were not clinically significant

Marinosci. AIDS 2022. Abstr OAB0302.

TAF/FTC/BIC versus TDF/FTC+DTG in HIV/HBV coinfection

Virologic Outcomes at Week 48: Co-primary Endpoints

AIDS 2022
29 July – 2 August



- Mean CD4 change from baseline, cells/μL (95% CI): B/F/TAF +200 (175, 226), DTG + F/TDF +175 (152, 198)

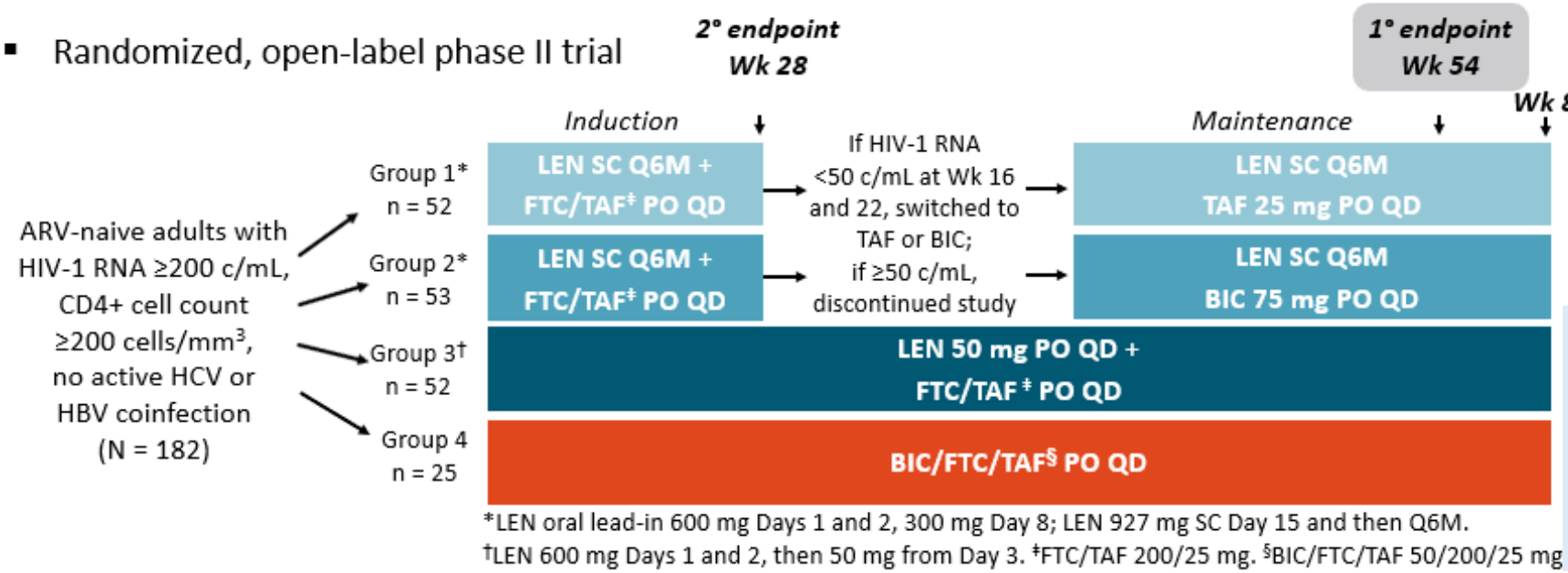
Adults with HIV-1/HBV coinfection were randomized 1:1 to initiate blinded treatment with B/F/TAF or DTG+F/TDF (with placebo). Primary endpoints were proportion of participants with HIV-1 RNA <50 copies/mL (FDA Snapshot) and plasma HBV DNA <29 IU/mL (missing=failure) at Week 48

In adults with HIV-1/HBV-coinfection starting antiviral therapy, both B/F/TAF and DTG+F/TDF had high HIV-1 suppression at year 1, with B/F/TAF resulting in superior HBV DNA suppression and significantly more HBeAg seroconversion. Safety findings were similar between groups.

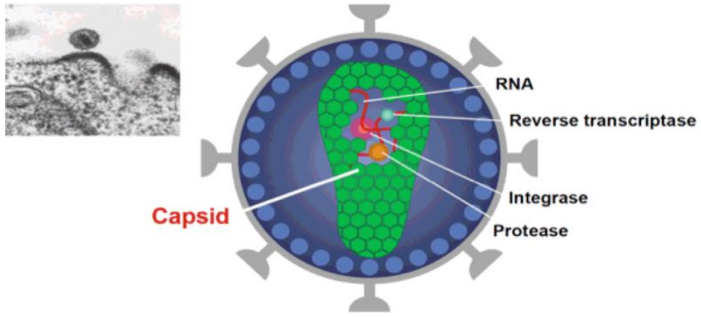
Abstract#12565

Long-Acting Subcutaneous Lenacapavir in Treatment-Naive Patients

- Randomized, open-label phase II trial



*LEN oral lead-in 600 mg Days 1 and 2, 300 mg Day 8; LEN 927 mg SC Day 15 and then Q6M.
†LEN 600 mg Days 1 and 2, then 50 mg from Day 3. ‡FTC/TAF 200/25 mg. §BIC/FTC/TAF 50/200/25 mg



- Primary outcome: proportion with HIV-1 RNA <50 c/mL at Wk 54
- Secondary outcomes: proportion with HIV-1 RNA <50 c/mL at Wk 28, 38, and 80; change from baseline in log10 HIV-1 RNA and CD4+ cell count at Wk 28, 38, 54, and 80

Virologic Outcome, %	LEN SC + FTC/TAF → TAF (n = 52)	LEN SC + FTC/TAF → BIC (n = 53)	LEN PO + FTC/TAF (n = 52)	BIC/FTC/TAF (n = 25)
FDA snapshot analysis (ITT)				
▪ HIV-1 RNA <50 c/mL	**90**	**85**	**85**	**92**
▪ HIV-1 RNA ≥50 c/mL	4*	4*†	6‡	0
▪ No data	6	11	10	8
FDA snapshot analysis among patients virologically suppressed at Wk 28				
▪ HIV-1 RNA <50 c/mL	94	92	90	92
▪ HIV-1 RNA ≥ 50 c/mL	4	0	6	0
▪ No data	2	8	4	8

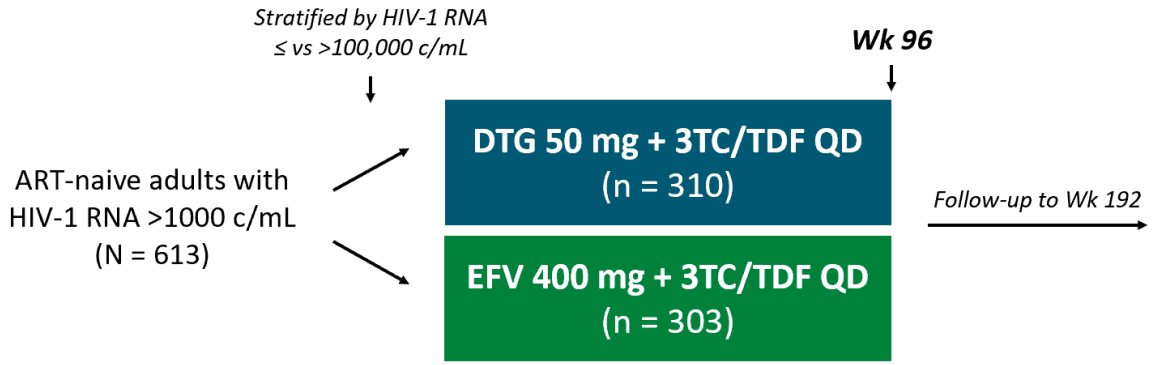
After 2-wk oral lead-in followed by induction with 6-mo LEN SC + daily FTC/TAF PO, maintenance treatment with 6-mo SC + daily TAF or BIC PO associated with high rates of virologic suppression through Wk 54 in treatment-naive patients

- **LEN SC + FTC/TAF PO → LEN SC + TAF PO: 90%**
- **LEN SC + FTC/TAF PO → LEN SC + BIC PO: 85%**
- **LEN PO + FTC/TAF PO: 85%**
- **BIC/FTC/TAF PO: 92%**

Gupta. CROI 2022. Abstr 138

DTG versus EFV 400 mg

- Multicenter, randomized, open-label phase III trial at 3 sites in Yaoundé, Cameroon
- Primary endpoint: HIV-1 RNA <50 c/mL at Wk 48 by FDA Snapshot in ITT population (noninferiority margin: 10%)



Response at Wk 192, %	DTG 50 mg + 3TC/TDF (n = 310)	EFV 400 mg + 3TC/TDF (n = 303)	Difference, % (95% CI)	*P* Value
HIV-1 RNA <50 c/mL	69.0	61.7	7.3 (-0.2 to 14.8)	.057
▪ In patients with HIV-1 RNA >100,000 c/mL at baseline	66.7	54.0	12.7 (3.2-22.1)	NR

- Patients with HIV-1 RNA >100,000 c/mL at baseline:
  - Had impaired virologic suppression vs patients with baseline HIV-1 RNA ≤100,000 c/mL (64% vs 87%) at Wk 192
  - Achieved faster virologic suppression with DTG vs EFV (66% vs 62%) by Wk 48
- Patients with HIV-1 RNA <100,000 c/mL on EFV had less durable virologic suppression (84% at Wk 48 and 77% at Wk 192)

- Both DTG + 3TC/TDF and low-dose (400 mg) EFV + 3TC/TDF effective and safe for treatment-naive PWH
  - Higher rates of virologic suppression with DTG vs EFV over time, particularly for those with high viral loads at baseline
  - Less durable virologic suppression for patients with baseline HIV-1 RNA >100,000 c/mL on EFV
- Significantly more weight gain with DTG + 3TC/TDF vs EFV (400 mg) + 3TC/TDF, particularly among women

Mpoudi-Etame. AIDS 2022. Abstr OAB0304.

Prevention of HIV and STIs

- New long-acting ART agent: efficacy and safety
- What about prevention of other STIs?

Doxycycline for PEP

AIDS 2022
29 July – 2 August

- Randomized, open-label study conducted at HIV and STI clinics in San Francisco and Seattle

PWH cohort: MSM and TGW with HIV* (Planned n = 390)

PrEP cohort: MSM and TGW receiving HIV PrEP* (Planned n = 390)

2:1

2:1

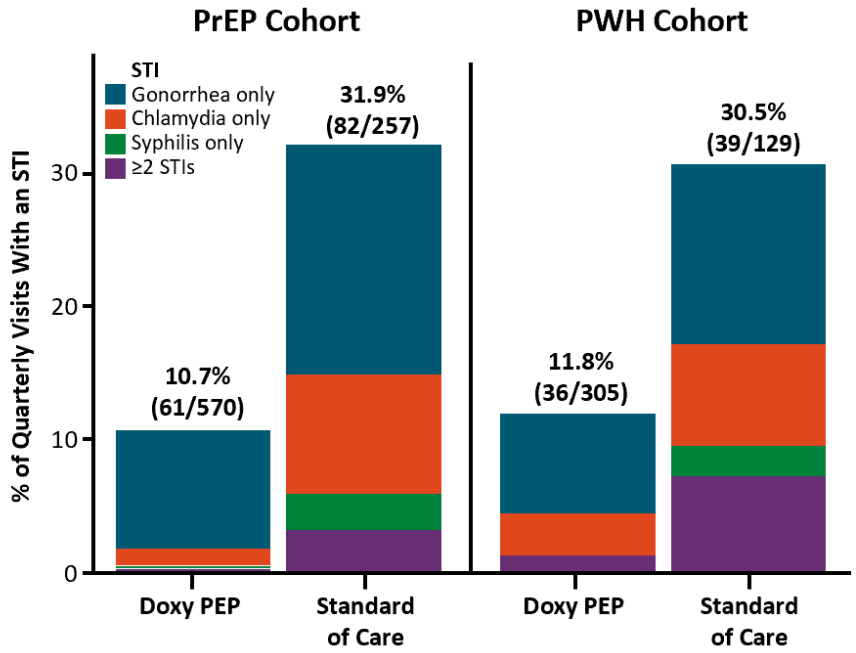
Doxycycline 200 mg PEP†
Within 72 hr of condomless sexual contact

No PEP
(standard of care)

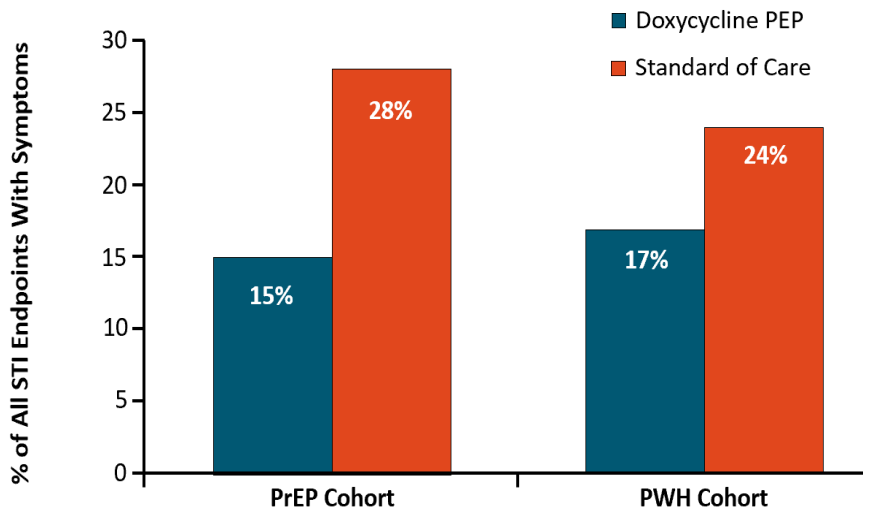
Doxycycline 200 mg PEP†
Within 72 hr of condomless sexual contact

No PEP
(standard of care)

→ *Quarterly STI testing for gonorrhea, chlamydia, and syphilis at 0, 3, 6, 9, and 12 mo post intervention*



- Doxycycline PEP taken within 72 hr of condomless sex reduced STI incidence in MSM and TGW
  - Reduced by 62% in PWH cohort and 66% in PrEP cohort per quarter
  - Incidence of gonorrhea, chlamydia, and syphilis each reduced substantially
- Doxycycline PEP was well tolerated and associated with high adherence (by self-report) and few discontinuations

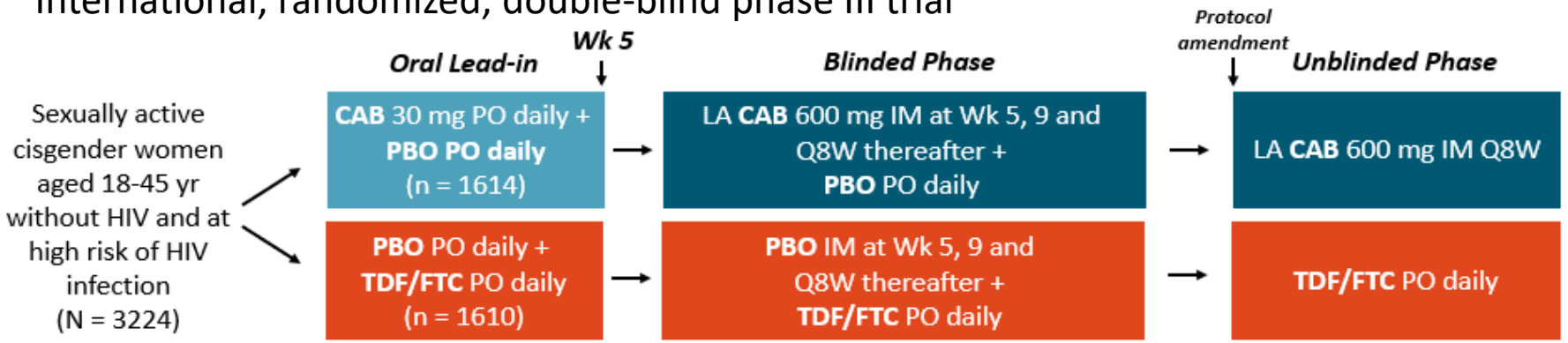


Luetkemeyer. AIDS 2022. Abstr OALBX0103.

Long-acting injectable CAB for women

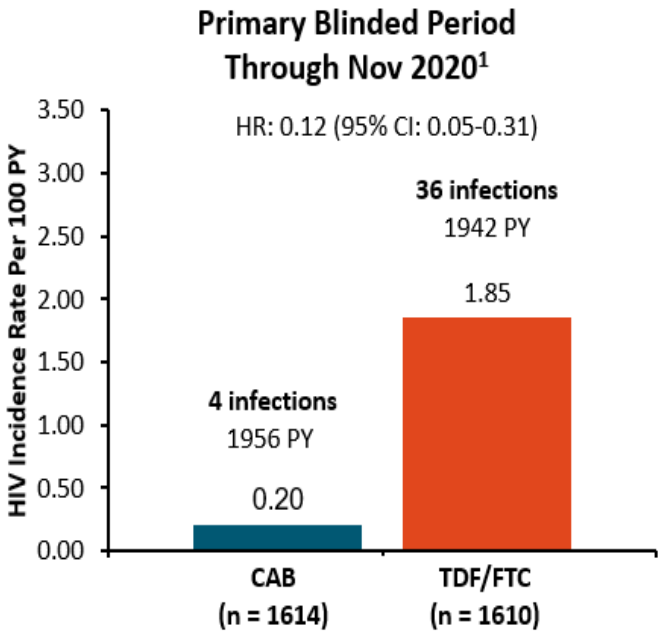
AIDS 2022
29 July – 2 August

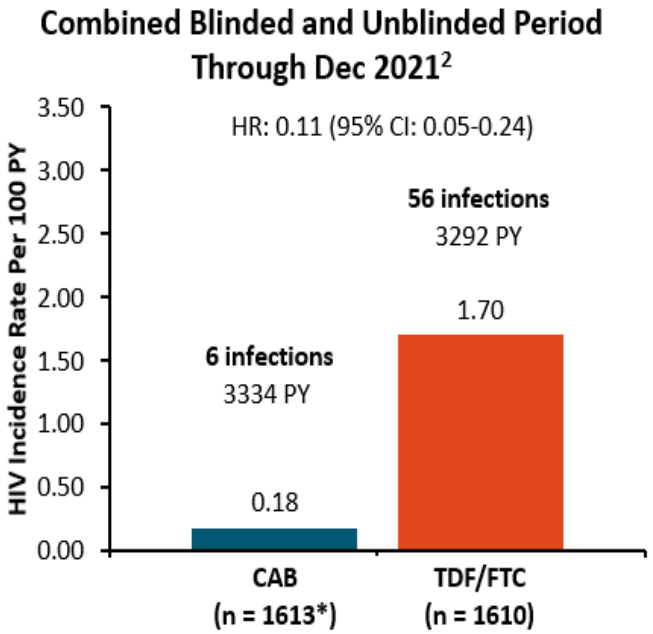
International, randomized, double-blind phase III trial



Current analysis: incident HIV infections during 12-mo period following unblinding (11/5/2020 - 11/5/2021, detected through 12/31/2021); grade ≥2 AEs, ISRs, pregnancy incidence/outcomes during 12-mo unblinded phase; cumulative HIV incidence for primary blinded and 12-mo unblinded follow-up

- Primary endpoints (blinded study): incident HIV infections (ITT), grade ≥2 AEs1



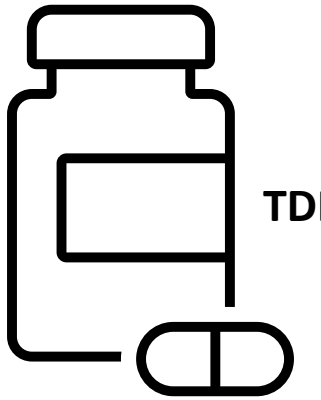


- During 12-mo unblinded phase, LA CAB maintained **superiority** over daily oral TDF/FTC for HIV PrEP in cisgender women
  - HIV incidence reduced by 89% with CAB vs TDF/FTC
  - Safety profile consistent with previous data; no new safety signals observed
- Incident infections during unblinded period were associated with CAB nonadherence
- No on-injection breakthrough infections occurred
- Incidence of pregnancy increased between blinded and unblinded period (1.3 vs 3.2 per 100 PY)
- No congenital anomalies resulted in either study group

Delany-Moretlwe. AIDS 2022. Abstr OALBX0107.

Search for optimal second-line ART after NNRTI failure in DTG era

- Genotypic-guided or NO?
- DTG versus PI?
- Recycling NRTI or continuing NRTI despite failure? : AZT/3TC versus TDF/3TC

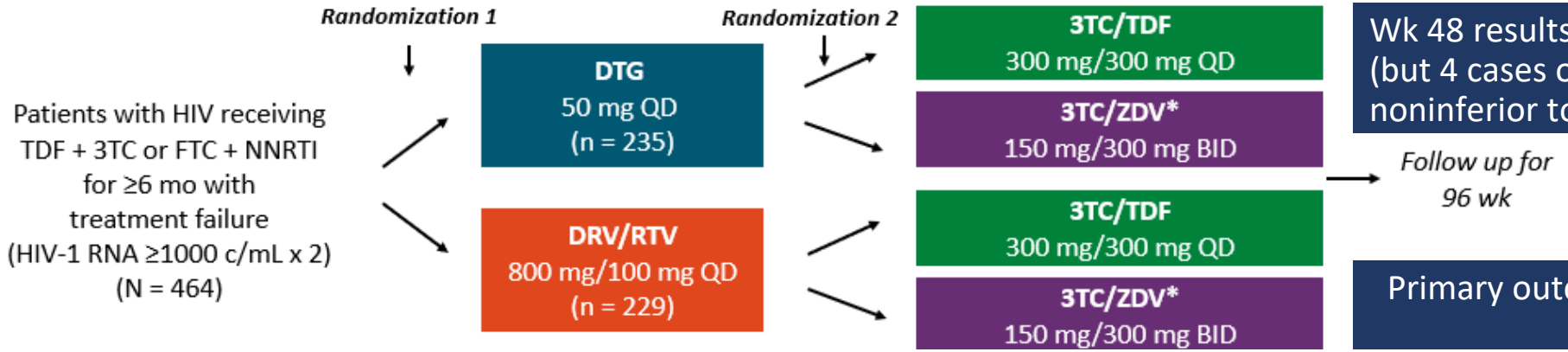


TDF/FTC/EFV failure

DTG+PI
AZT/3TC+DTG
AZT/3TC+PI
TDF/FTC+DTG

DTG vs DRV/RTV and TDF vs ZDV for Second-line Therapy

- Multicenter, 2 x 2 randomized, open-label, noninferiority phase III trial



Wk 48 results: DTG was noninferior to DRV/RTV (but 4 cases of DTG resistance); 3TC/TDF was noninferior to 3TC/ZDV

Primary outcome: HIV-1 RNA <400 c/mL at Wk 96 by FDA snapshot

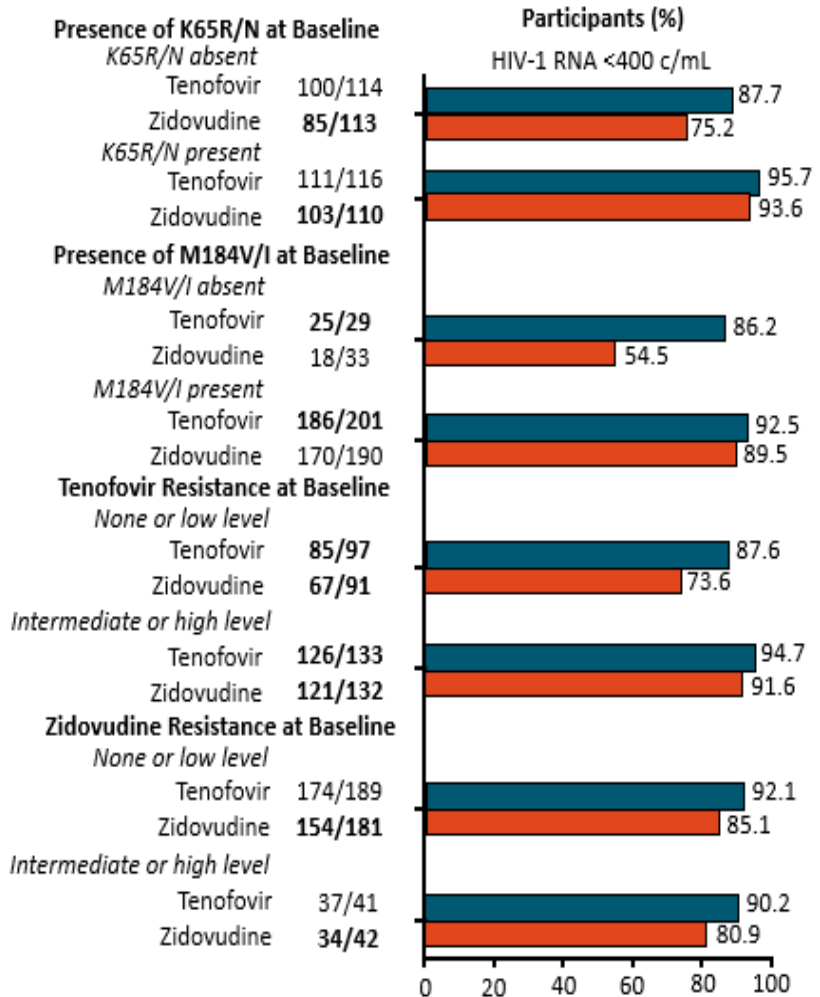
Outcome	DTG (n = 235)	DRV/RTV (n = 229)	P	3TC/TDF (n = 233)	3TC/ZDV (n = 231)	P
HIV-1 RNA level in ITT, n (%)						
▪ <400 c/mL	211 (89.8)	199 (86.9)	.332	214 (91.8)	196 (84.8)	.019
▪ ≥400 c/mL	20 (8.5)	25 (10.9)	--	13 (5.6)	32 (13.9)	--
▪ No virologic data	4 (1.7)	5 (2.2)	--	6 (2.6)	3 (1.3)	--
• Withdrew: AE/death	3 (1.3)	5 (2.2)		6 (2.6)	2 (0.9)	
• Withdrew: other reason	1 (0.4)	0		0	1 (0.4)	
HIV-1 RNA <1000 c/mL, n (%)	213 (90.6)	203 (88.6)	.481	216 (92.7)	200 (86.6)	.03
HIV-1 RNA <50 c/mL, n (%)	189 (80.4)	172 (75.1)	.168	188 (80.7)	173 (74.9)	.133
Confirmed HIV-1 RNA rebound ≥1000 c/mL (ITT), n (%)	20 (8.5)	26 (11.3)	.306	13 (5.6)	33 (14.3)	.002
Confirmed HIV-1 RNA rebound ≥1000 c/mL with ≥1 major RM to DTG or DRV, n	7 (all DTG)	0	--	2 (all DTG)	5 (all DTG)	--

Paton. CROI 2022. Abstr 137. Paton. NEJM. 2021;385:330. NCT03988452.

- **DTG + 2 NRTIs was noninferior to DRV/RTV + 2 NRTIs in patients who experienced failure of NNRTI-based initial regimen**
- **DTG + 2 NRTIs can be used as second-line ART, even if NRTIs are predicted to have no activity**

Characteristic	DTG (n = 235)	DRV/RTV (n = 226)	3TC/TDF (n = 233)	3TC/ZDV (n = 231)
Median time on first-line ART, yr (IQR)	3.6 (1.4-6.3)	3.7 (1.7-5.9)	3.7 (1.6-6.1)	3.7 (1.7-6.4)
Previously received ZDV, n (%)	14 (6.0)	14 (6.1)	15 (6.4)	13 (5.6)
Baseline resistance, n/N (%)				
▪ K65R/N*	120/228 (52.6)	106/225 (47.1)	116/230 (50.4)	110/223 (49.3)
▪ M184V/I	196/228 (86.0)	195/225 (86.7)	201/230 (87.4)	190/223 (85.2)
▪ Intermediate- or high-level resistance by Stanford algorithm to, n/N (%)				
– Tenofovir	139/228 (61.0)	126/225 (56.0)	133/230 (57.8)	132/223 (59.2)
– ZDV	45/228 (19.7)	38/225 (16.9)	41/230 (17.8)	42/223 (18.8)
– 3TC	213/228 (93.4)	203/225 (90.2)	213/230 (92.6)	203/223 (91.0)

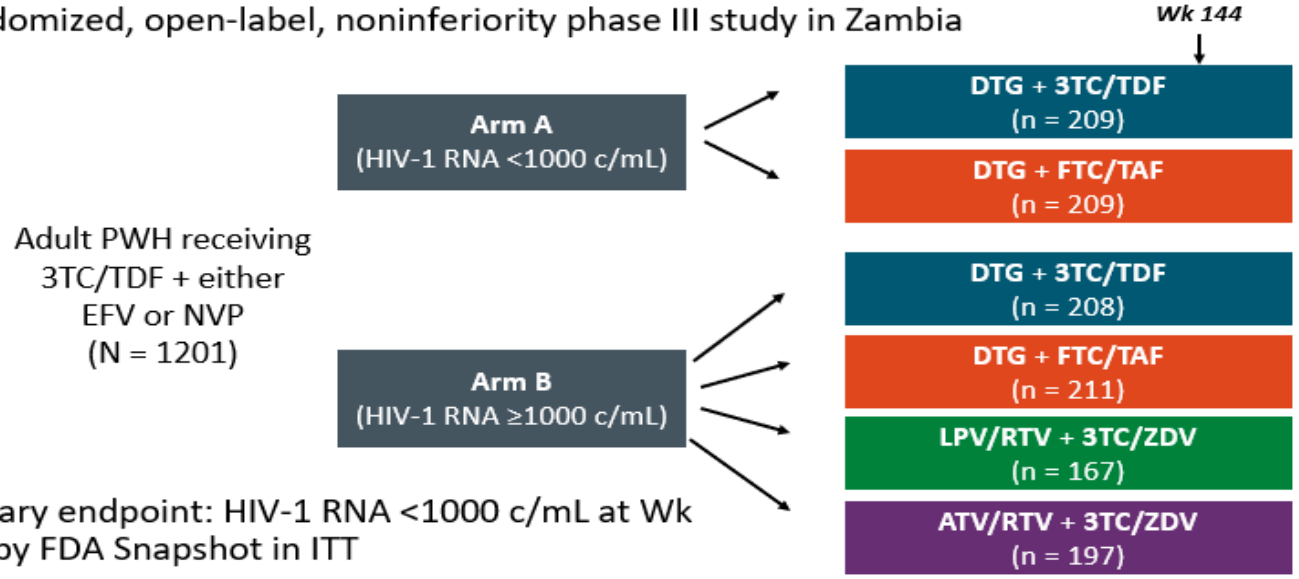
*K65R: n = 223; K65N: n = 3.



Paton. CROI 2022. Abstr 137. Paton. NEJM. 2021;385:330. NCT03988452.

DTG vs PI (LPV/R or ATV/R) and TDF vs TAF for Second-line Therapy

- Randomized, open-label, noninferiority phase III study in Zambia



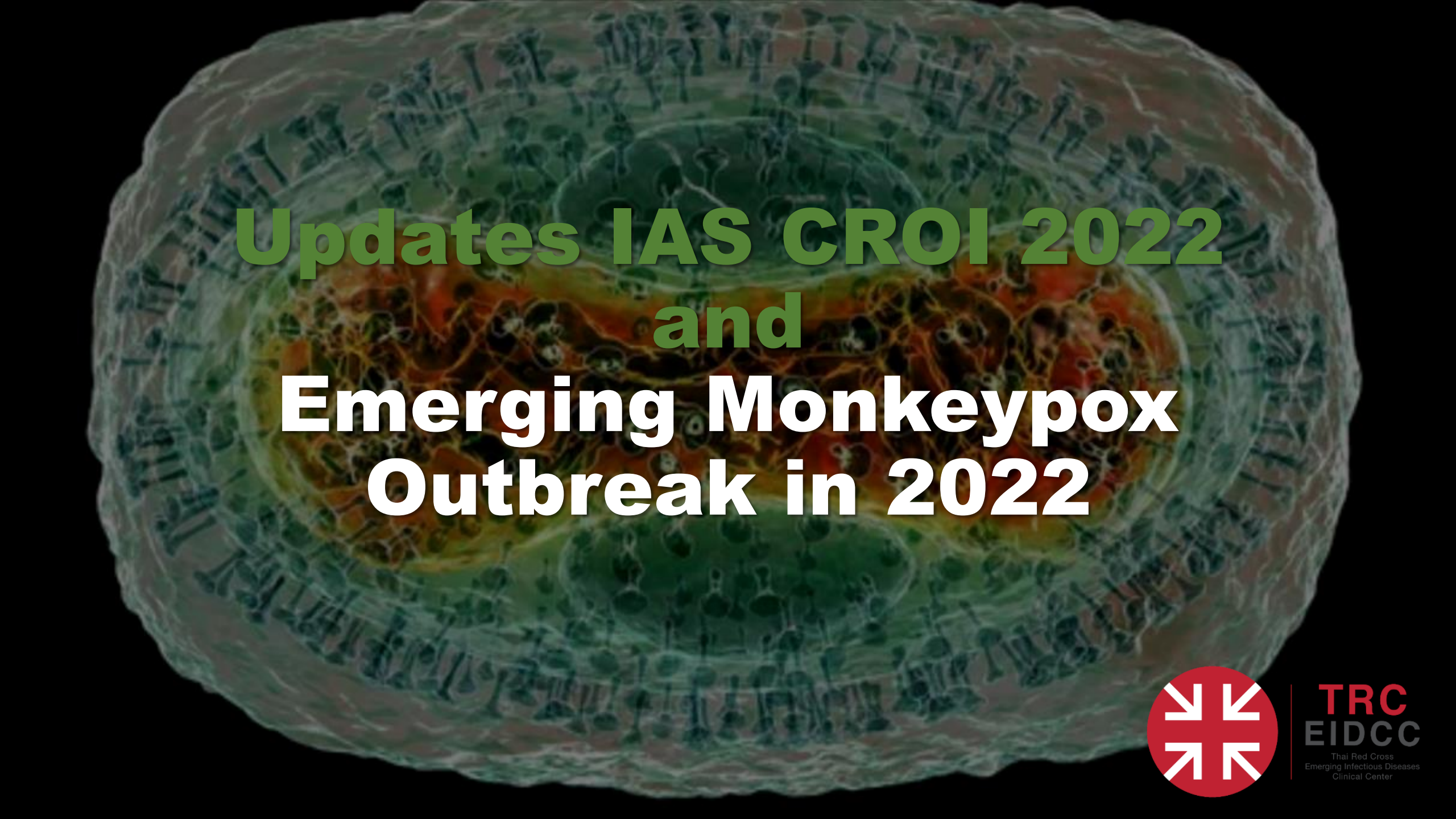
- Primary endpoint: HIV-1 RNA <1000 c/mL at Wk 144 by FDA Snapshot in ITT
- Current analysis presents results at Wk 48

Change in Weight From Baseline, kg	HIV-1 RNA <1000 c/mL		HIV-1 RNA ≥1000 c/mL			
	DTG + 3TC/TDF (n = 209)	DTG + FTC/TAF (n = 209)	DTG + 3TC/TDF (n = 208)	DTG + FTC/TAF (n = 211)	LPV/RTV + 3TC/ZDV (n = 167)	ATV/RTV + 3TC/ZDV (n = 197)
Wk 48						
▪ Overall	2.8	1.1	5	5.4	2	2.8
▪ Women	NR	NR	3.1	5.7	2.8	2.6
▪ Men	NR	NR	4.6	3.4	2.1	3.2

HIV-1 RNA Result at Wk 48, %	HIV-1 RNA <1000 c/mL		HIV-1 RNA ≥1000 c/mL			
	DTG + 3TC/TDF (n = 209)	DTG + FTC/TAF (n = 209)	DTG + 3TC/TDF (n = 208)	DTG + FTC/TAF (n = 211)	LPV/RTV + 3TC/ZDV (n = 167)	ATV/RTV + 3TC/ZDV (n = 197)
ITT						
▪ <1000 c/mL	88	85	83	86	69	81
▪ <50 c/mL	80	74	72	80	56	70
Per-protocol (FDA snapshot)						
▪ <1000 c/mL	98	98	93	95	83	90
▪ <50 c/mL	90	86	82	88	68	78

- DTG + 3TC/TDF noninferior to DTG + FTC/TAF regardless of baseline HIV-1 RNA <1000 c/mL and ≥1000 c/mL
- DTG + 3TC/TDF and DTG + FTC/TAF superior to combined PI/RTV arm
- Higher weight gain for women receiving DTG and TAF vs PI-based regimens or TDF
- Investigators conclude these results support switch to TDF (TAF)/XTC + DTG from first-line NNRTI-based regimens

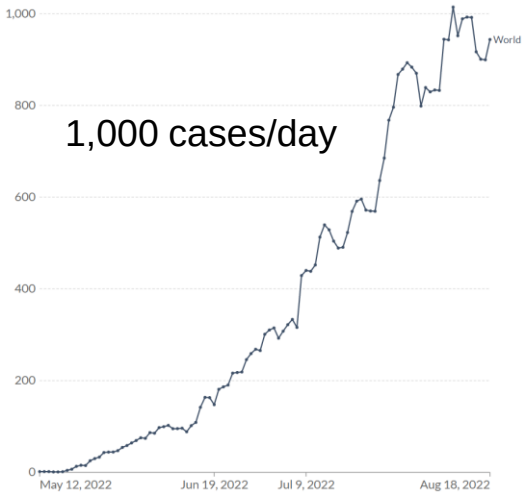
Mulenga. CROI 2022. Abstr 135.



Updates IAS CROI 2022 and Emerging Monkeypox Outbreak in 2022

TRC EIDCC
Thai Red Cross Emerging Infectious Diseases Clinical Center

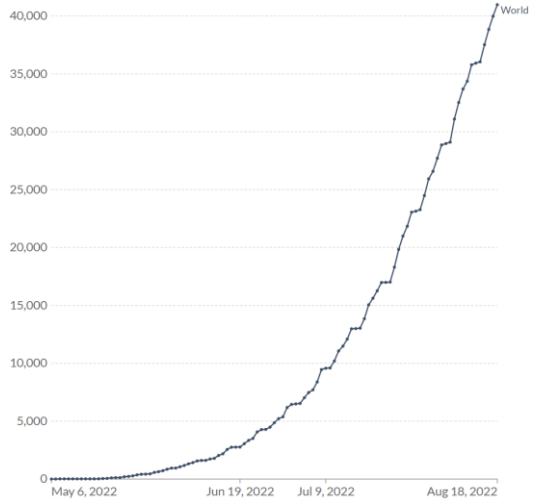
Monkeypox



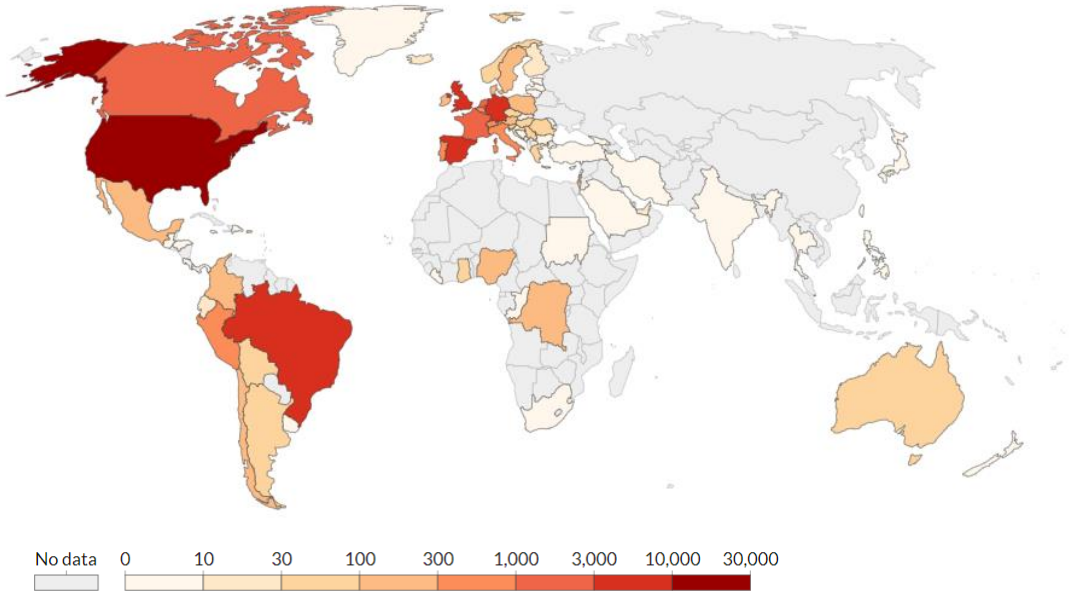
1,000 cases/day

Cases/day

40,000+

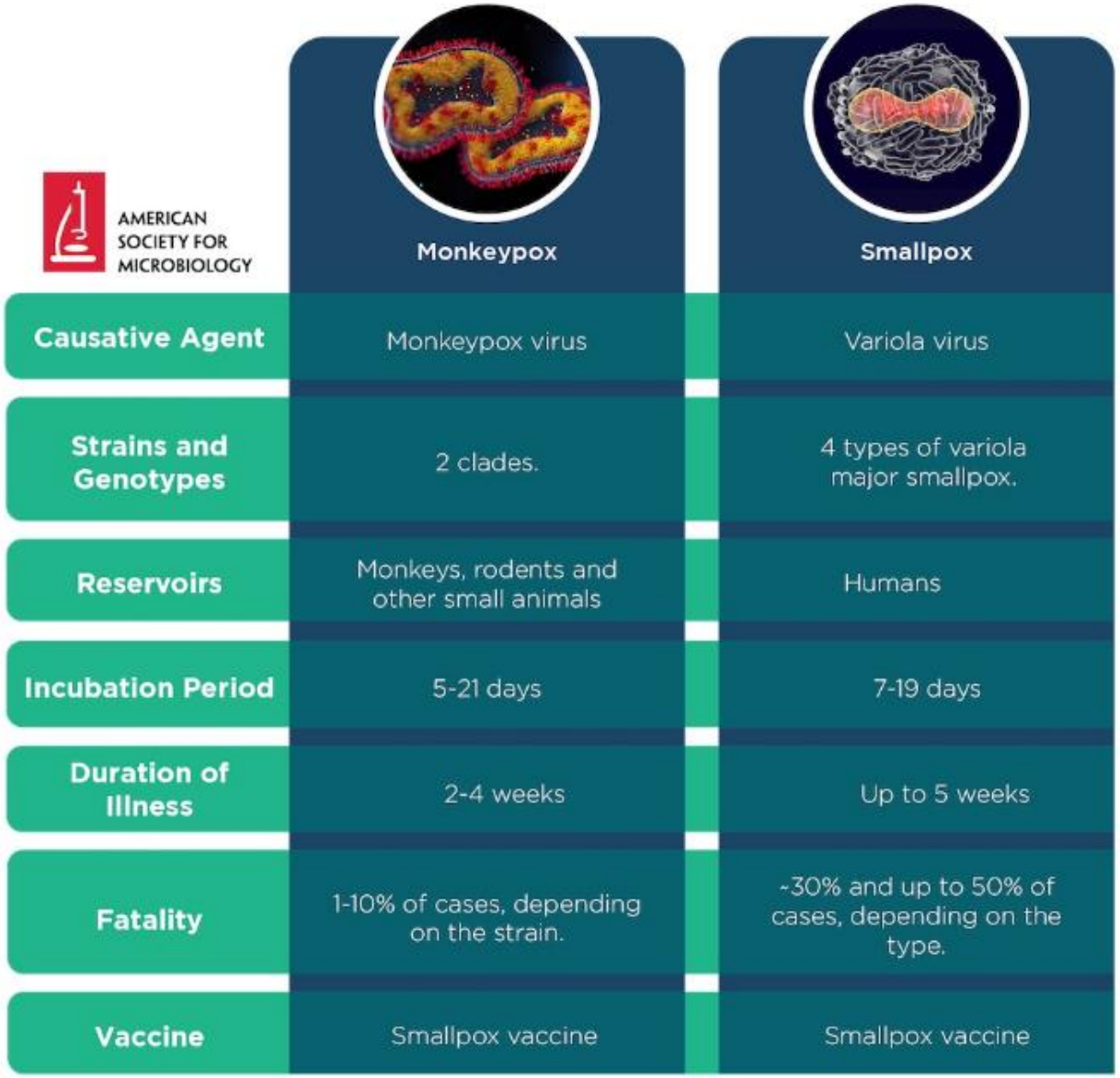


Cumulative confirmed cases



WHO chief declares monkeypox an international emergency after expert panel fails to reach consensus

Narrow majority on Emergency Committee voted against ringing WHO's loudest alarm bell



1. https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html
2. https://www.who.int/news-room/fact-sheets/detail/monkeypox
3. https://www.fda.gov/vaccines-blood-biologics/vaccines/smallpox

- **Orthopoxviruses** are a group of large, complex, double-stranded DNA viruses that replicate in the cytoplasm of the host cell
- **Vaccinia (smallpox vaccine), variola (smallpox), monkeypox**, cowpox, and several newly discovered orthopoxvirus species are known to cause human disease
- **Orthopoxvirus infections** can cause a spectrum of febrile rash illnesses in humans, ranging from fairly benign, localized skin infections to severe systemic infections.
- **Orthopoxviruses induce cross-reactive antibodies** that protect against infection from other orthopoxvirus species

Endemic areas of monkeypox

MPX RISK FACTORS FOR CHILDREN

- Trapping.
- Hunting
- Handling.
- Dead rodents found in the forest are source of food

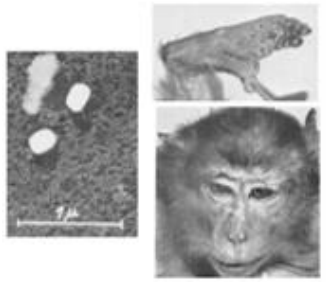
Squirrels are particularly the source of MPX in young children in rural areas in DRC.

Gambian Rats

Monkeypox epidemiology, surveillance, and laboratory capacity in DRC.
By Muyembe-Tamfum, MD, PhD

MONKEYPOX Central African Republic
By Emmanuel Nakouné-Yandoko

Historical overview



Monkeypox First described - *in Asian monkeys In Copenhagen –*

First *human* mpx case Zaire/DRC

Intensified Surveillance

Dramatic increase in reported cases, esp in DRC ,… also Nigeria …. and importations

Now !

1960 1970 1980 1990 2000 2010 2020

Global Smallpox eradication Programme

Last smallpox case in Equateur Zaire

Vaccination stopped (Zaire)

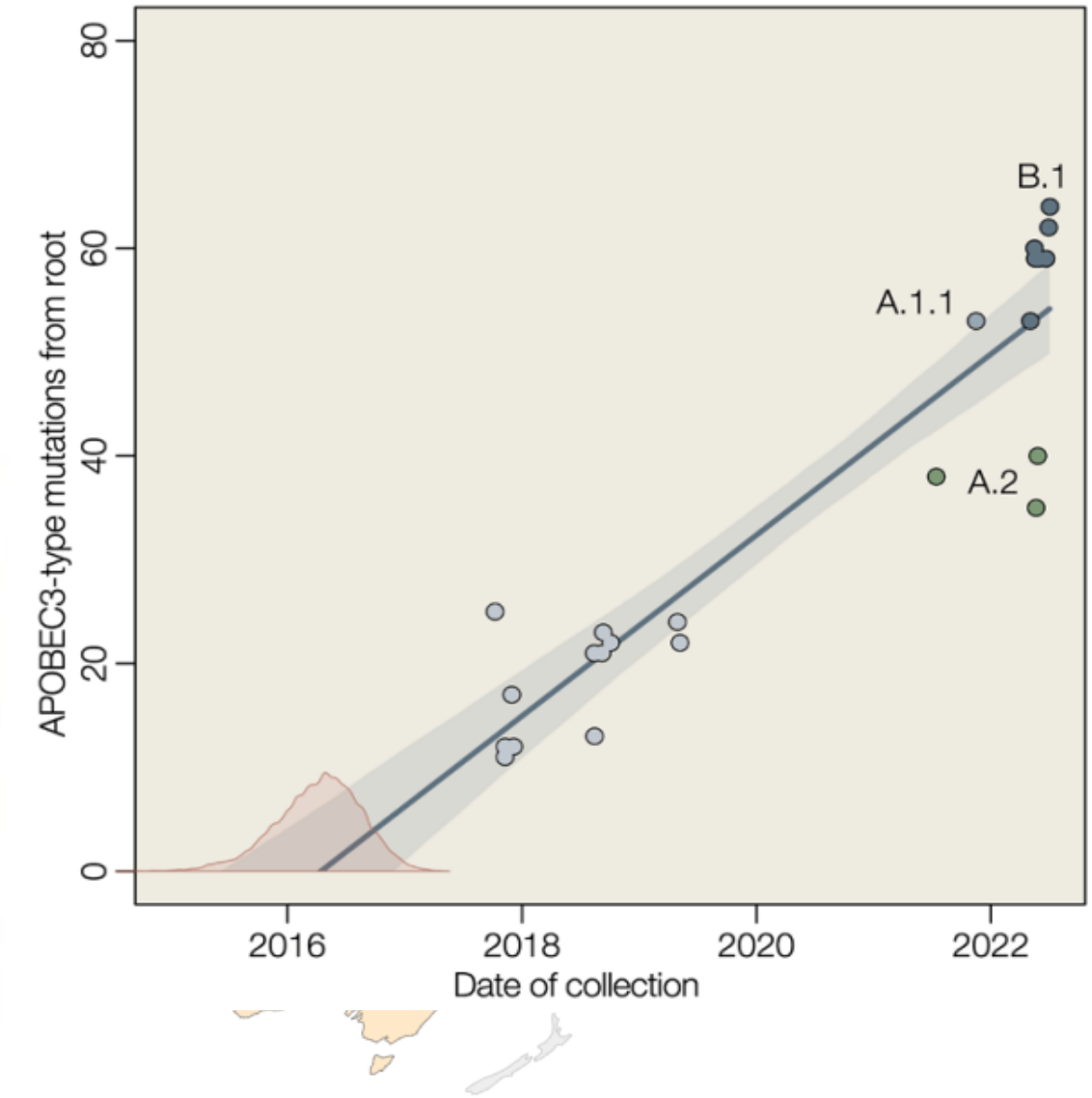
Increasing susceptibility ….

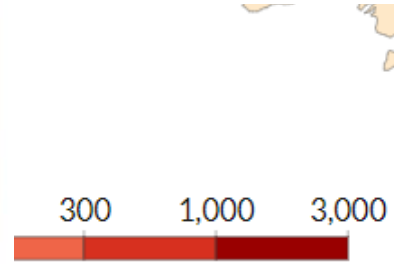
Monkeypox": Historical overview By Paul Fine

Monkeypox in Africa: the science the world ignored

African researchers have been warning about monkeypox outbreaks for years. As vaccines are deployed globally, they worry they will be left behind.

Max Kozlov



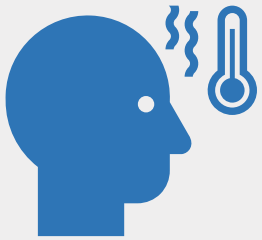


Clinical course of Monkeypox (pre 2022 outbreak)

Exposure

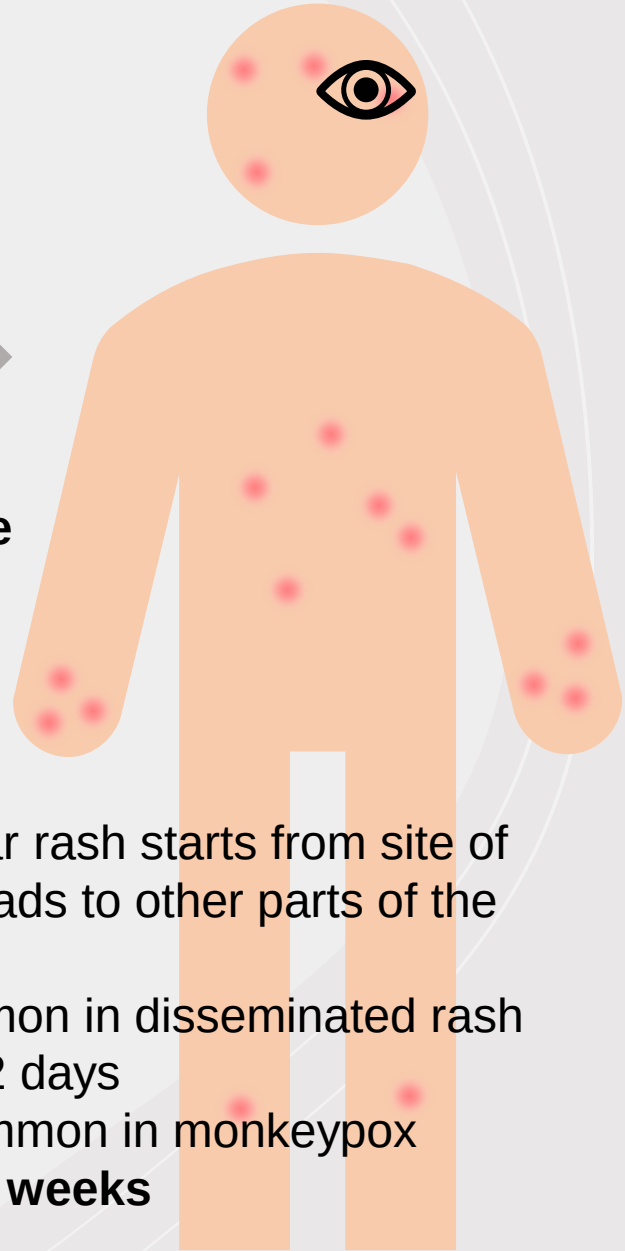
6-13 days

Incubation period
(5-21 days)



3 days

Fever, myalgia, headache

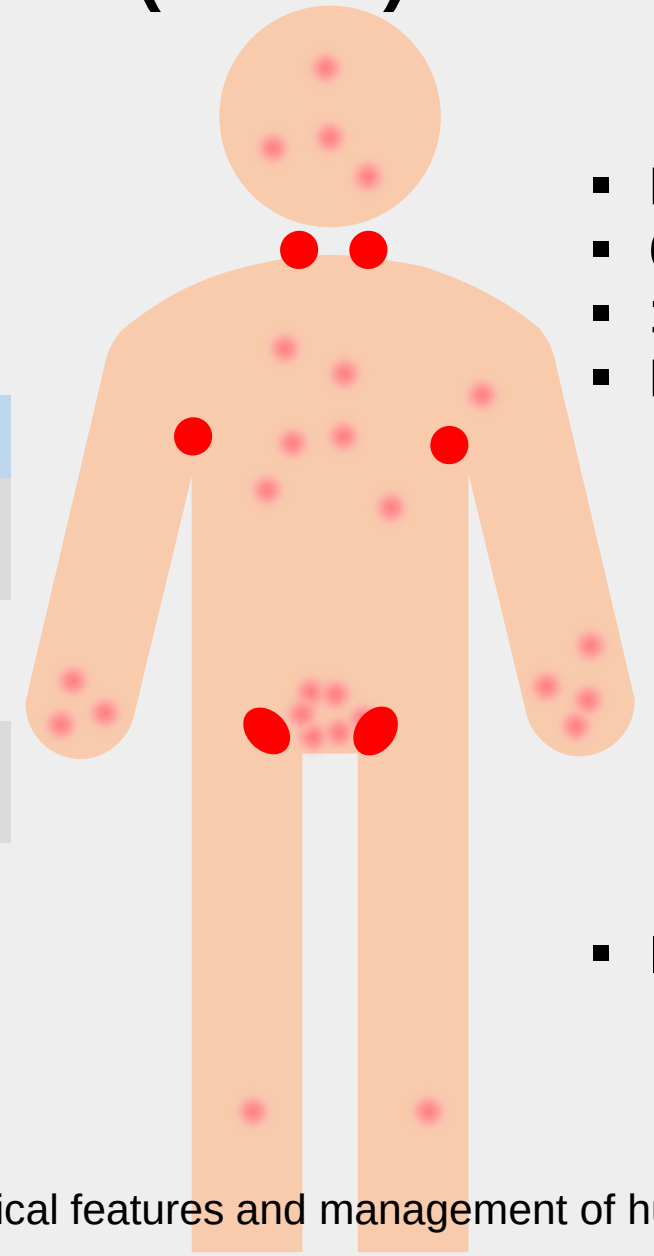


- **Centrifugal** maculopapular rash starts from site of primary infection and spreads to other parts of the body
- Palms and soles are common in disseminated rash
- Lesions progress within 12 days
- **Lymphadenopathy** is common in monkeypox
- **Duration of illness is 2-4 weeks**

Clinical features of 2022 monkeypox outbreak (N=104): US Cohort

Coinfection (UK cohort N=54)	
Any STIs	25% (GC or CT or both)
Chancre-like lesion at penis	26%
Preexisting HIV infection	24%

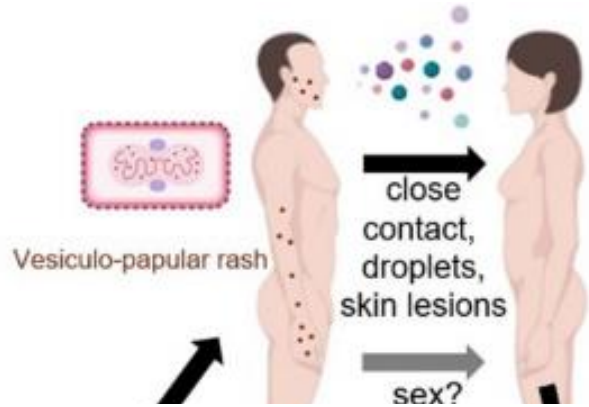
** HIV patients are likely to have STI coinfection and skin lesion more than 3 sites



- **Mainly occurs in MSM**
- **60% had no fever**
- **1% URI symptoms**
- **Rash**
  - **Characteristics**
    - **71% ulcerative (umbilicated) lesions**
    - **7% vesicles**
    - **1% pustule/papules**
  - **Distribution of rash:**
    - **51% Genital lesions**
    - **17% Oral lesion**
- **Inguinal and cervical lymphadenopathy**

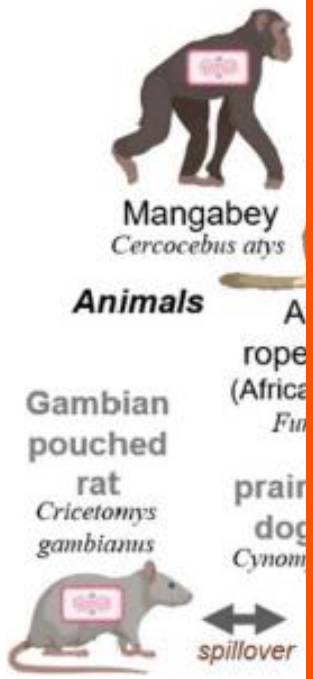
Clinical features and management of human monkeypox: US cohort 2022, MMWR June 2022

What do we know about route of transmission?



- respiratory – large droplets
- broken skin
- mucous membranes or mucosa
- direct contact with body fluids or lesion materials
- contaminated bedding or blankets
- prolonged face-to-face contact, and probably sex

Secondary attack rates among unvaccinated household members to be about 8%



Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding

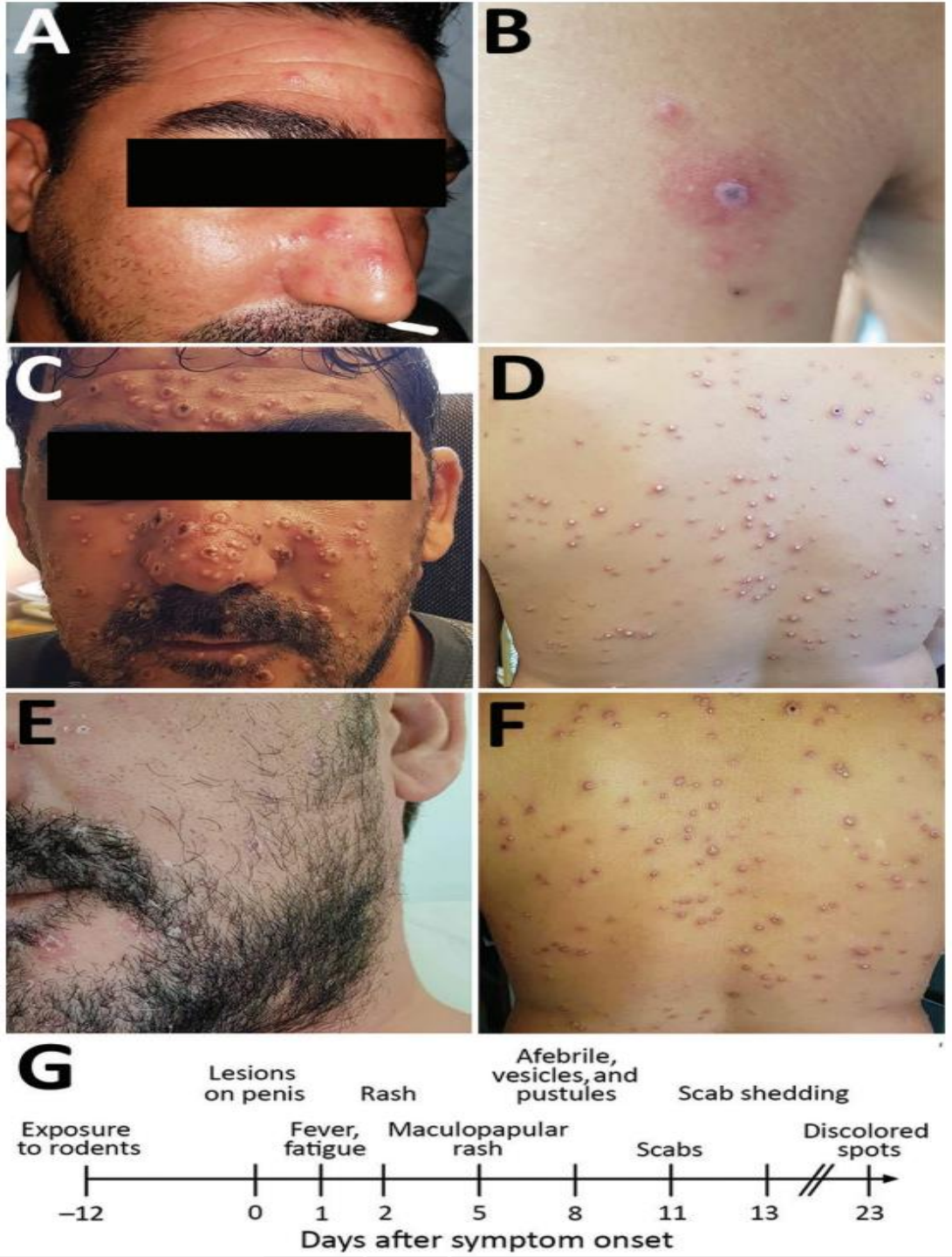
P1267-1269, SEPTEMBER 01, 2022
THE LANCET Infectious Diseases

	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 13	Day 14	Day 15	Day 16	Day 17	Day 19
Plasma	NA	NA	NA	Positive (34·5)	NA	Negative	NA	Negative	NA	Negative	Negative	Negative	Negative
Urine	NA	NA	Negative	NA	Negative	NA	Negative	Negative	NA	Negative	NA	NA	Negative
Semen	Positive (28·0)	Positive (29·3)	Positive (27·8)	NA	NA	NA	NA	NA	Positive (34·3)	Positive (35·6)	NA	Positive (38·7)	Positive (40·6)
Rash or skin lesion	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Negative

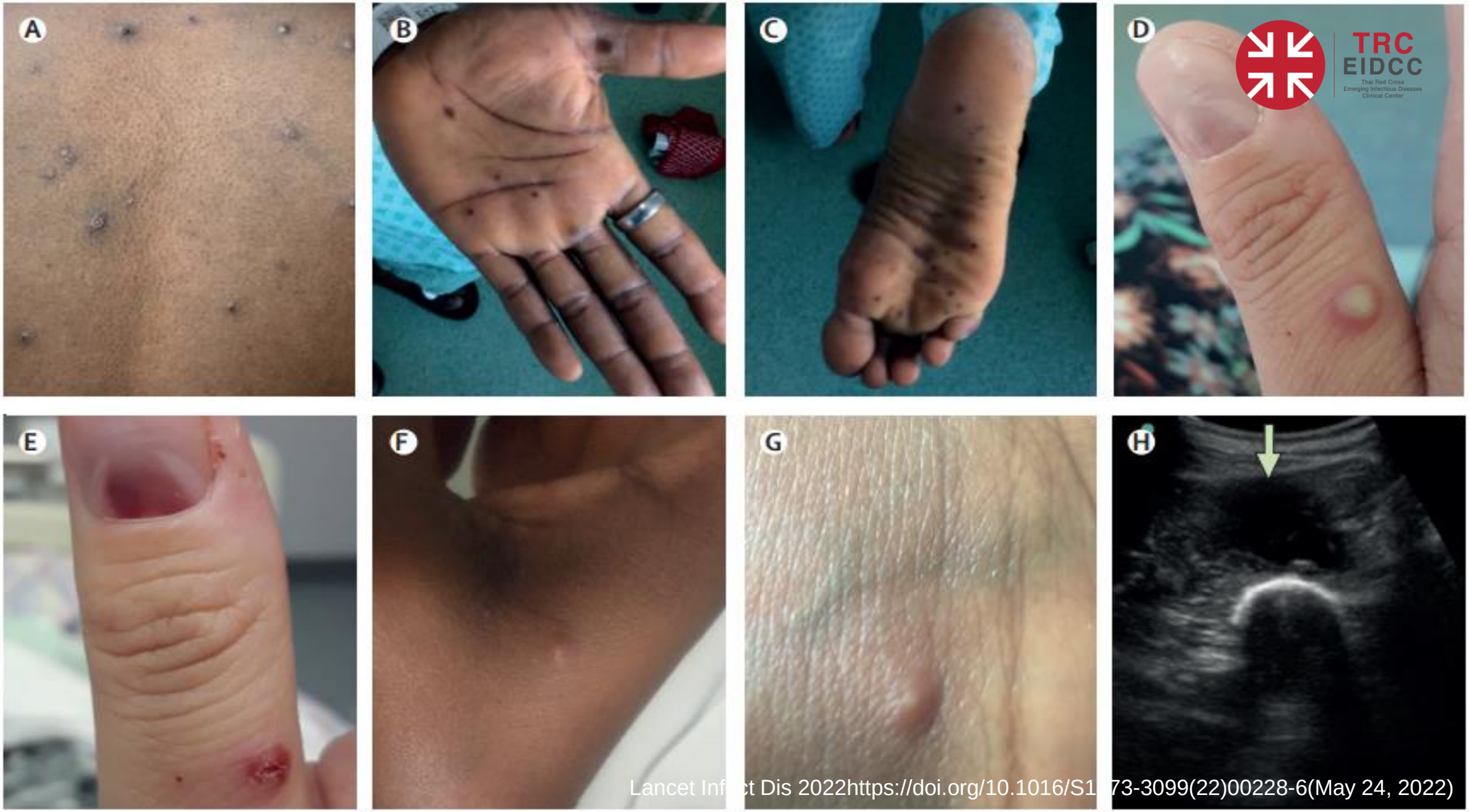
Quantification cycle values are indicated in brackets after positive results. The cutoff cycle threshold is 45, thresholds of 42 or higher are retested for confirmation. Negative indicates no detection of monkeypox virus DNA or absence of rash or skin lesions. Positive indicates detection of monkeypox virus DNA or presence of rash or skin lesions. NA=not available.

Table: **Timeline of monkeypox virus DNA detection in plasma, urine, and semen samples with increasing days from symptom onset**

Stage	Stage Duration	Characteristics
Enanthem		• The first lesions to develop are on the tongue and in the mouth.
Macules	1–2 days	• Following the enanthem, a macular rash appears on the skin, starting on the face and spreading to the arms and legs and then to the hands and feet, including the palms and soles. • The rash typically spreads to all parts of the body within 24 hours becoming most concentrated on the face, arms, and legs (centrifugal distribution).
Papules	1–2 days	• By the third day of rash, lesions have progressed from macular (flat) to papular (raised).
Vesicles	1–2 days	• By the fourth to fifth day, lesions have become vesicular (raised and filled with clear fluid).
Pustules	5–7 days	• By the sixth to seventh day, lesions have become pustular (filled with opaque fluid) – sharply raised, usually round, and firm to the touch (deep seated). • Lesions will develop a depression in the center (umbilication). • The pustules will remain for approximately 5 to 7 days before beginning to crust.
Scabs	7–14 days	• By the end of the second week, pustules have crusted and scabbed over. • Scabs will remain for about a week before beginning to fall off.



https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html



Lancet Inf ct Dis 2022https://doi.org/10.1016/S1 73-3099(22)00228-6(May 24, 2022)

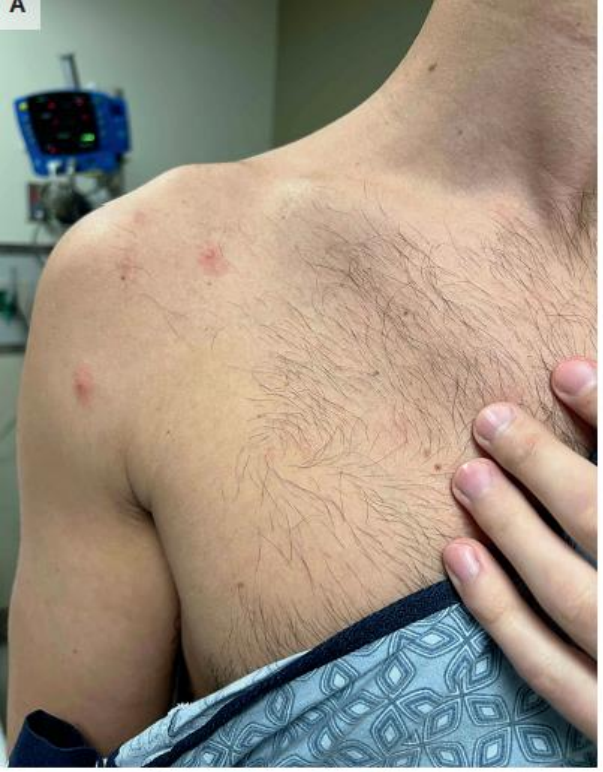
Clinical features and management of human monkeypox: US cohort 2022

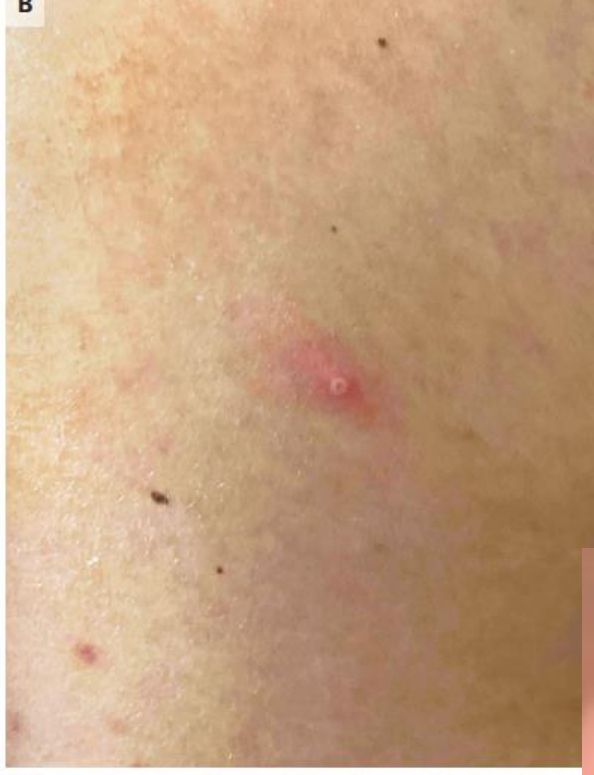
Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 71
June 3, 2022

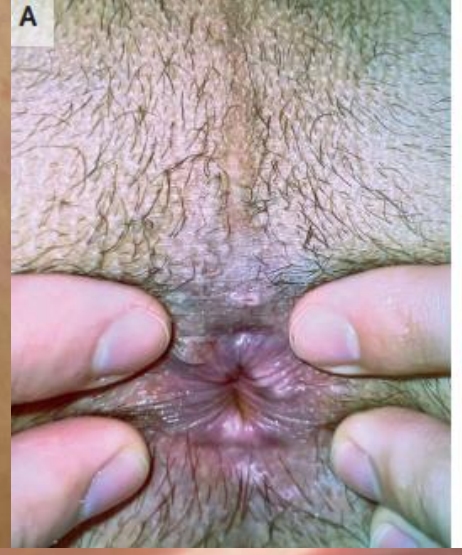
The rash associated with monkeypox involves firm, deep-seated, and well-circumscribed vesicles or pustules, which might umbilicate or become confluent. Lesions progress over time to scabs.

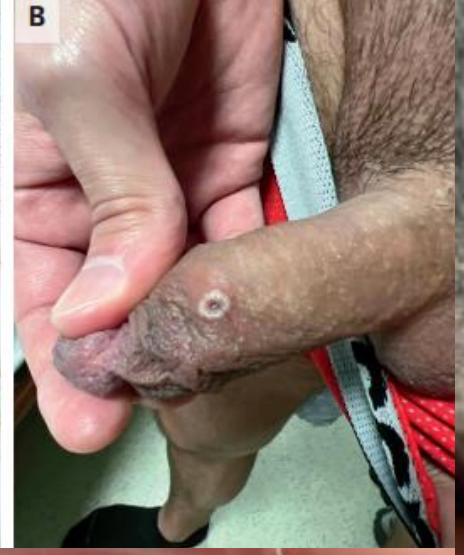
- **N=17 (16= MSM)**
- Age 40 (28-61)
- Some cases presented at STI clinic due to genital lesions
- 12/17 had prodromal symptoms; fatigue, fever and headache
- 6/17 had rash started at perianal or genital area

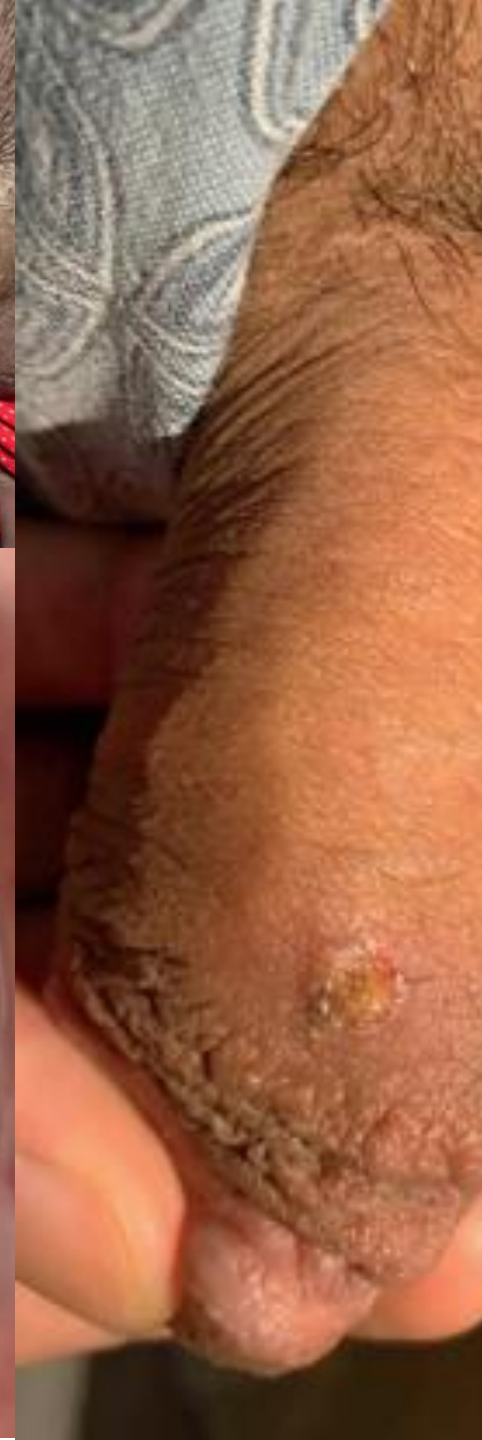
Characteristic	No. (%) At illness onset	Prodromal period†	At any point in illness
Signs and symptoms§ during illness			
Rash	5 (29)	NA	17 (100)
Fatigue or malaise	3 (18)	13 (76)	13 (76)
Chills	0 (—)	4 (24)	12 (71)
Lymphadenopathy	0 (—)	1 (6)	9 (53)
Inguinal	0 (—)	0 (—)	6 (35)
Cervical¶	0 (—)	1 (6)	3 (18)
Headache	2 (12)	5 (29)	8 (47)
Fever	6 (35)	5 (29)	7 (41)
Body ache	1 (6)	2 (12)	6 (35)
Sore throat or cough	2 (12)	3 (18)	5 (29)
Sweat	1 (6)	2 (12)	4 (24)
Other	3 (18)	4 (24)	13 (76)
Rash locations§			
Arm	4 (24)	NA	9 (53)
Trunk	1 (6)	NA	9 (53)
Leg	0 (—)	NA	8 (47)
Face	2 (12)	NA	7 (41)
Hand	1 (6)	NA	6 (35)
Perianal	5 (29)	NA	6 (35)
Oral	0 (—)	NA	5 (29)
Neck	1 (6)	NA	5 (29)
Genital (penis or vagina)	4 (24)	NA	4 (24)
Feet	1 (6)	NA	4 (24)

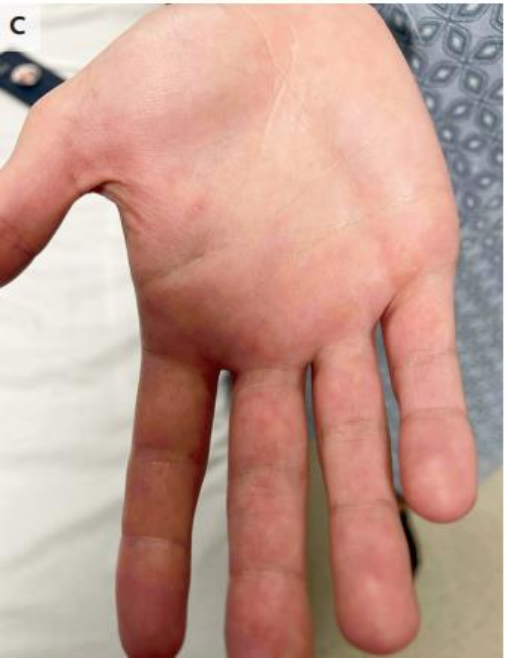






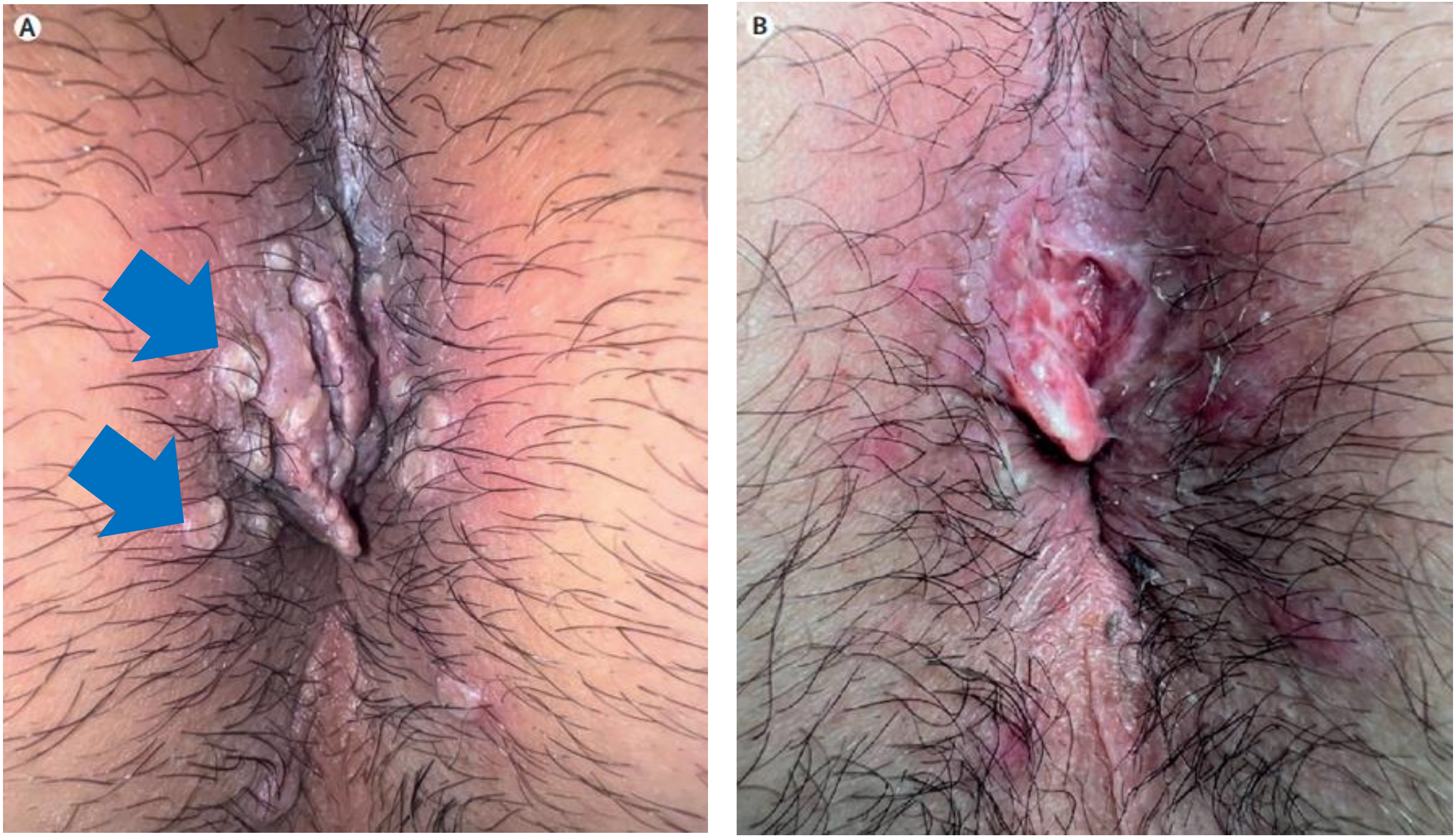




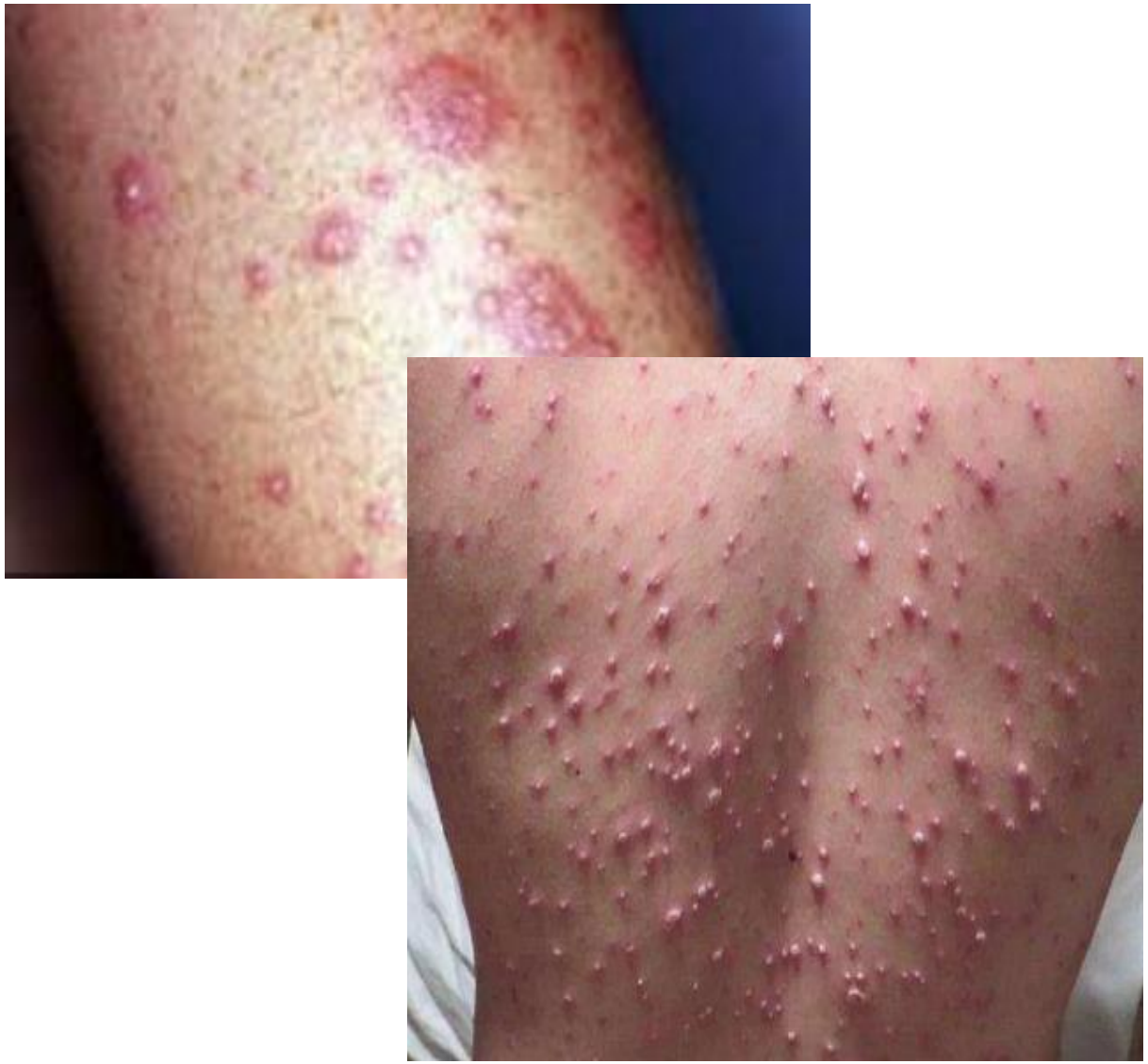


Case 24-2022: A 31-Year-Old Man with Perianal and Penile Ulcers, Rectal Pain, and Rash

US CDC

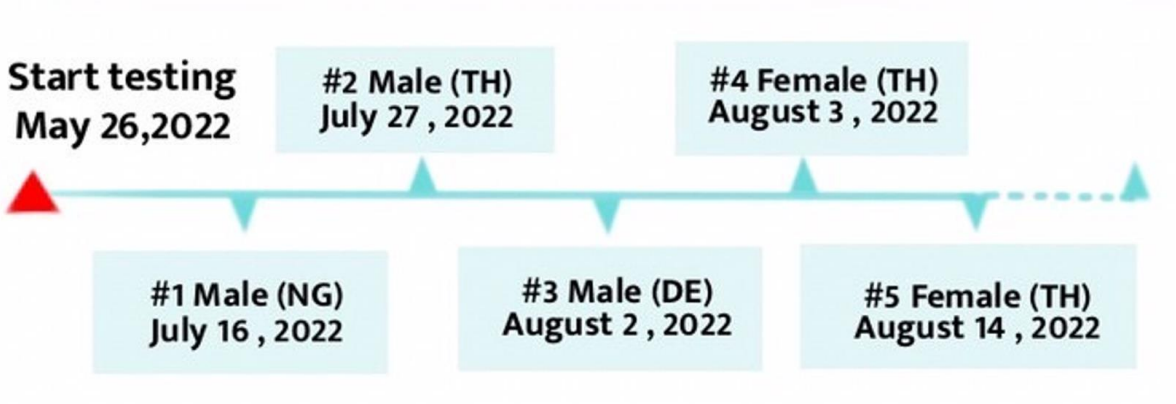

A
B

Differential Diagnosis of Febrile Vesicular Pustular Rash Illnesses That May Be Confused With Smallpox



DISEASE	CLUES
Varicella	Most common in children younger than 10 years; children do not usually have a viral prodrome
Disseminated herpes zoster	Immunocompromised or elderly persons; rash looks like varicella, usually begins or erupts in dermatomal pattern
Impetigo *(Streptococcus pyogenes, Staphylococcus aureus)*	Honey-colored crusted plaques with bullae are classic but may begin as vesicles
Drug eruptions	Exposure to medications
Erythema multiforme minor	Target or bull's-eye lesions; often follows systemic viral infections such as herpes simplex virus; may include palms and soles
Erythema multiforme (including Stevens-Johnson syndrome)	Involves conjunctivae and mucous membranes
Enteroviral infections (especially hand-foot-and-mouth disease)	Seasonal—summer and fall
Disseminated herpes simplex virus	Similar to varicella
Scabies and insect bites	Pruritus; patient not febrile
Molluscum contagiosum	May disseminate in immunosuppressed individuals
Generalized vaccinia	History of vaccination with smallpox vaccine or contact with vaccinated individual
Monkeypox	Travel to endemic area; animal exposure

Monkeypox cases in Thailand



ผู้ป่วยไทยทั้งหมดได้รับการตรวจยืนยันทางห้องปฏิบัติการณ์ที่ TRC EID Clinical Center

Sex	Age	Country	Nationality
Male	27	Nigeria	Nigerian
Male	47	Thailand	Thai
Male	25	Germany	Deutsch
Female	22	Thailand	Thai
Female	24	Dubai	Thai

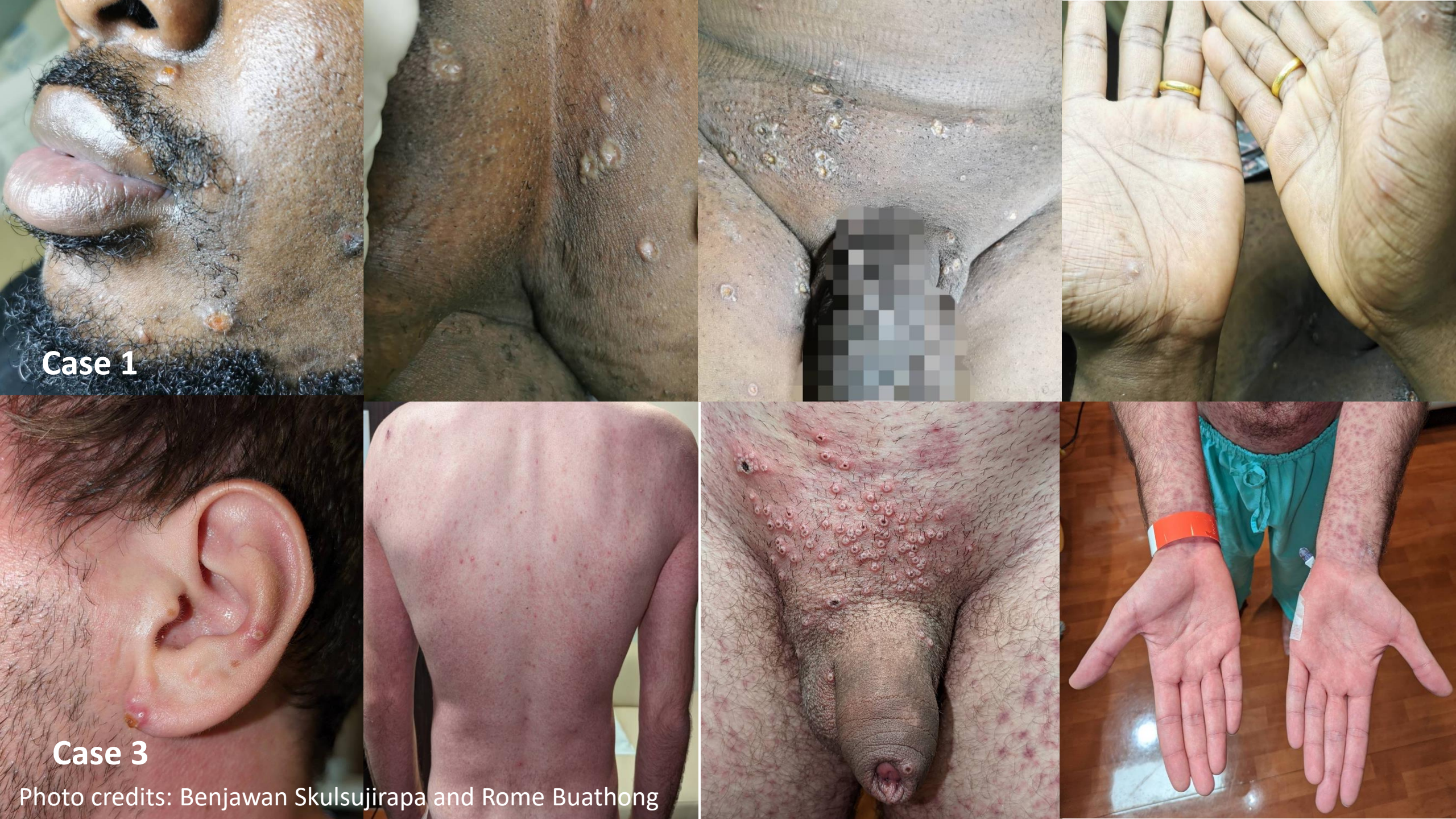
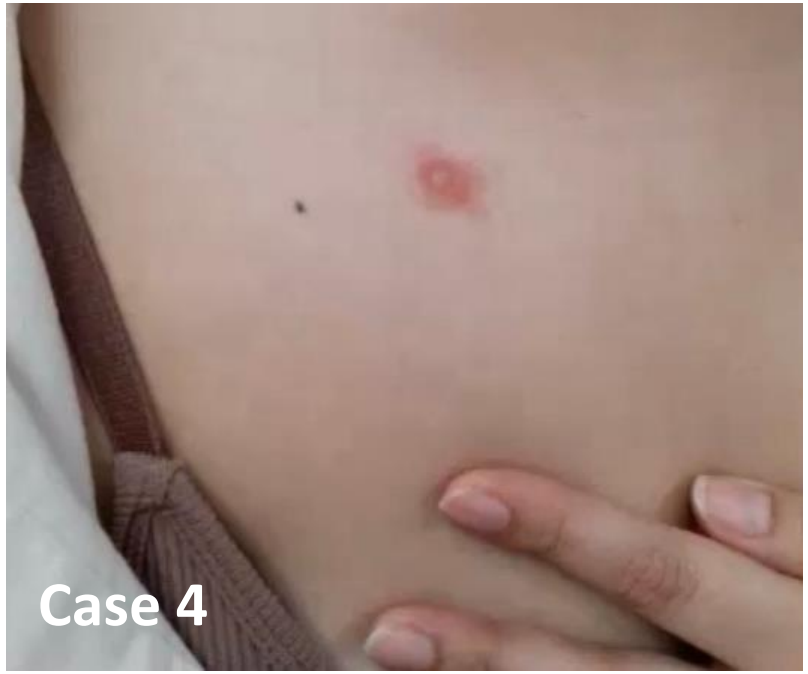
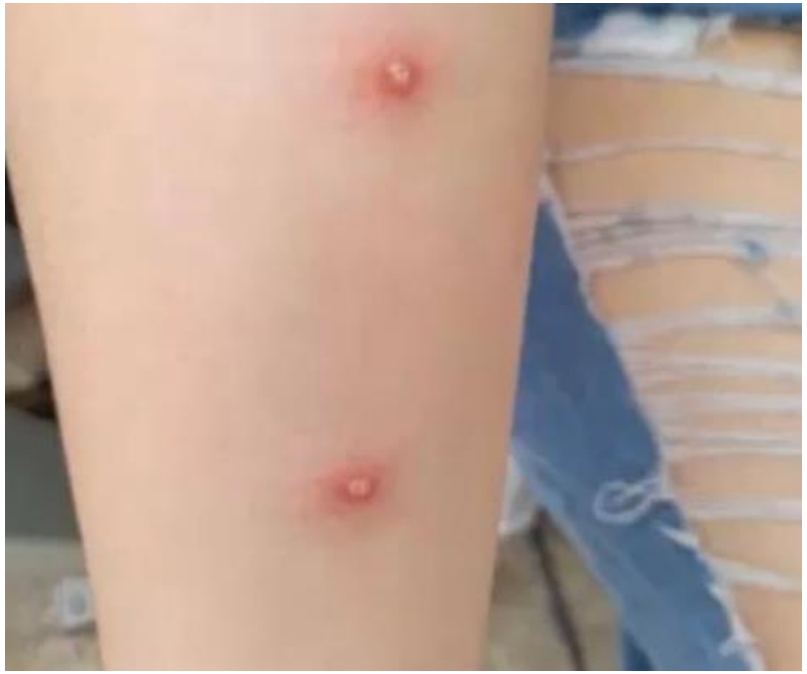
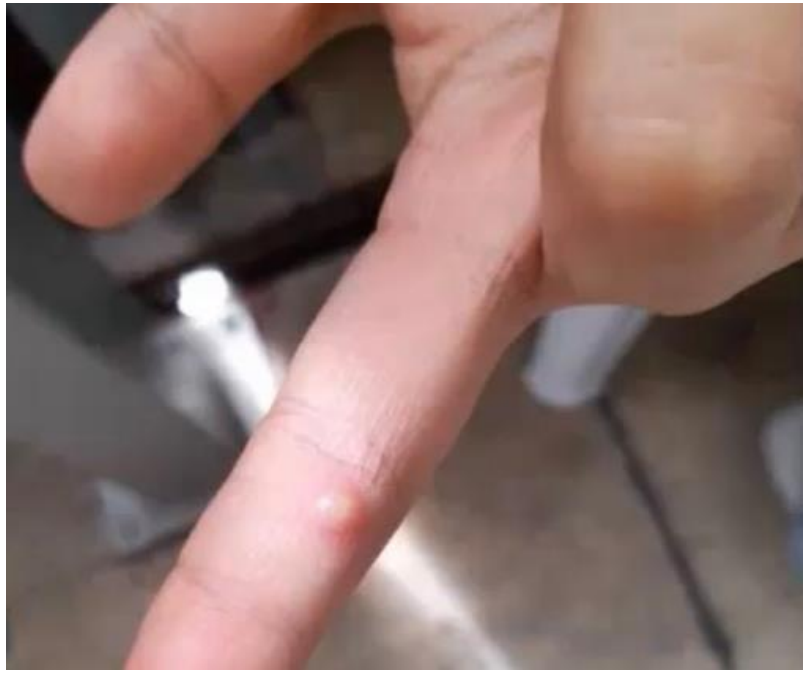
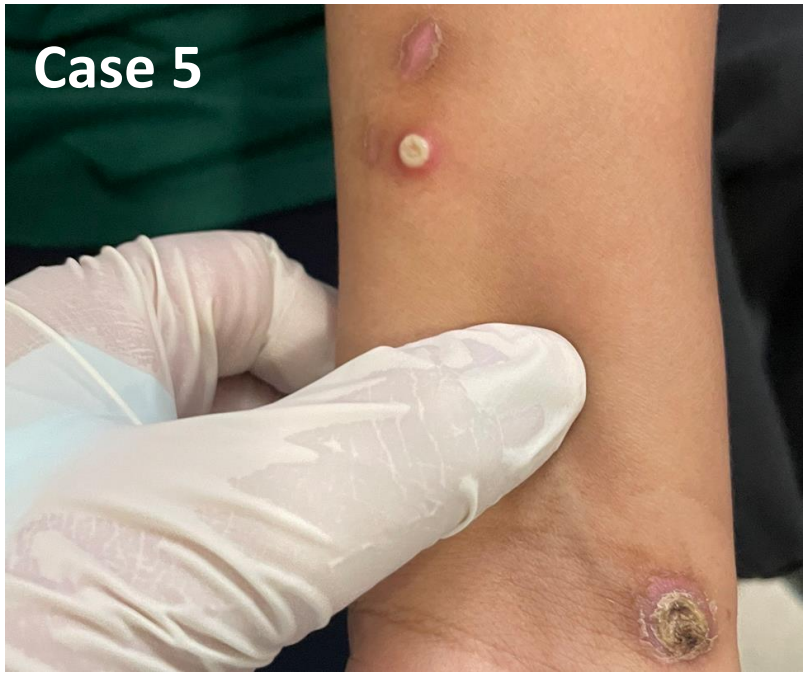


Photo credits: Benjawan Skulsujirapa and Rome Buathong


Case 4



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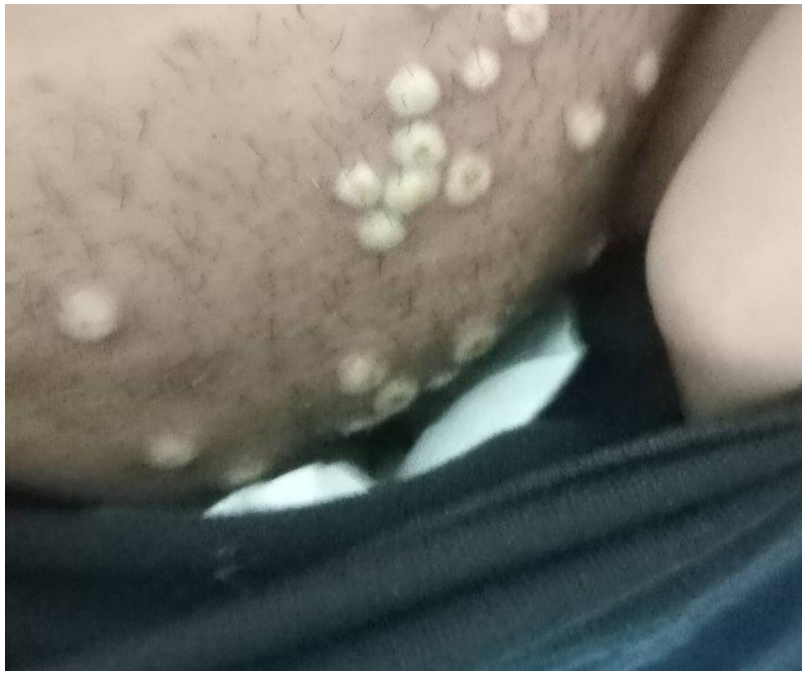
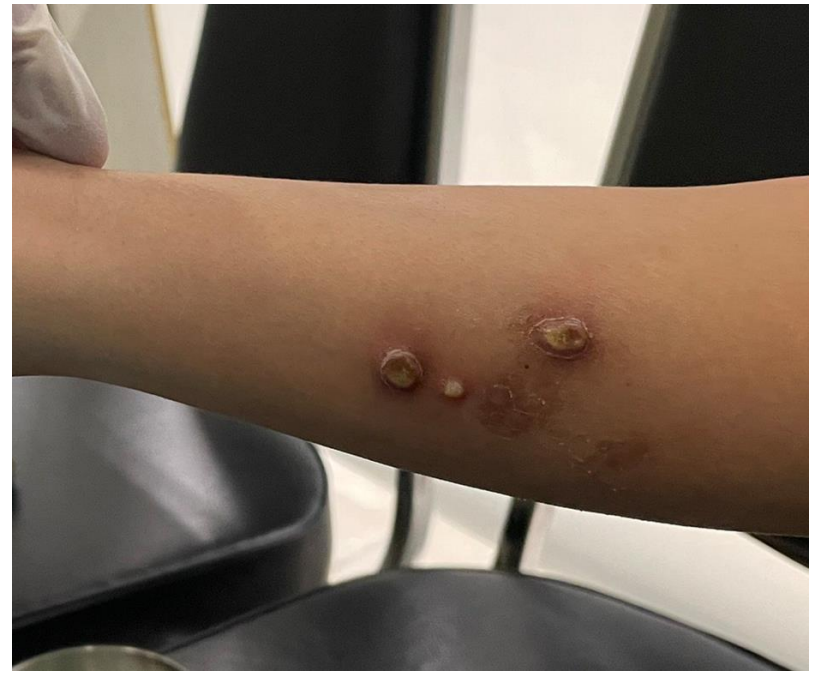
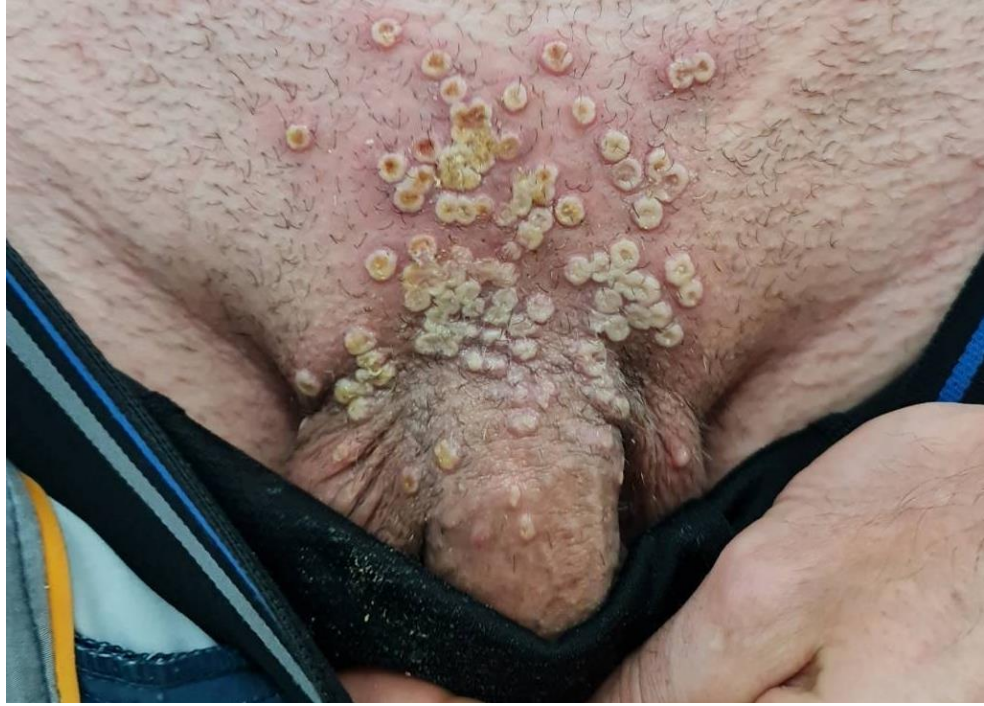
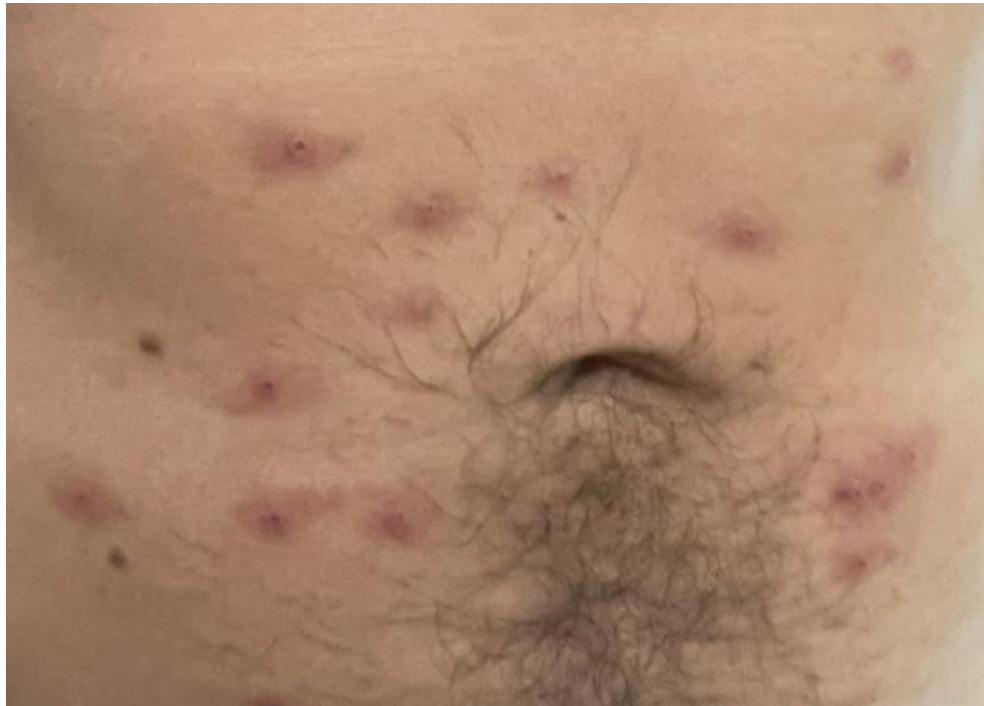
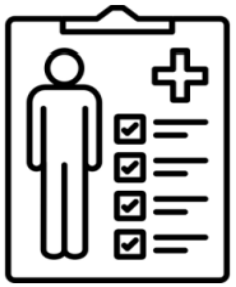










Treatment

Symptomatic and supportive

ผู้ป่วยส่วนใหญ่ที่ติดเชื้อมักมีอาการน้อย และสามารถหายได้เองโดยไม่ต้องได้รับการรักษาเฉพาะ

ความรุนแรงของอาการในผู้ติดเชื้อฝีดาษวานรขึ้นกับหลายปัจจัย ได้แก่ ประวัติการได้รับวัคซีนมาก่อนหน้า โรคประจำตัวที่พบร่วม
ผู้ป่วยต่อไปนี้ควรปรึกษาผู้เชี่ยวชาญเพื่อพิจารณาการรักษาเฉพาะ ได้แก่

- ผู้ที่มีอาการของโรคแบบรุนแรง (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization)
- ผู้ที่อาจจะมีความเสี่ยงสูงที่จะมีอาการของโรครุนแรง
  - ผู้ที่มีภาวะภูมิคุ้มกันบกพร่อง (immunocompromise)
  - ผู้ป่วยเด็กโดยเฉพาะอายุต่ำกว่า 8 ปี
  - หญิงตั้งครรภ์ หรือให้นมบุตร
  - ผู้ที่มีภาวะแทรกซ้อน เช่น secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities
- ผู้ที่ติดเชื้อฝีดาษวานรที่มีลักษณะอาการผิดปกติจากผู้ป่วยทั่วไป เช่น ติดเชื้อบริเวณตา ปาก หรือบริเวณอื่นที่อาจก่อให้เกิดอันตรายโดยเฉพาะ เช่นบริเวณอวัยวะเพศ หรือทวาร

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Medical Countermeasures Available for the Treatment of Monkeypox

ปัจจุบันยังไม่มียาที่ได้รับอนุมัติให้ใช้ในการรักษาฝีดาษวานรโดยเฉพาะ จึงมีการนำยาต้านไวรัสที่ถูกพัฒนามาเพื่อรักษาคนไข้ฝีดาษ (smallpox) เดิมมาใช้เป็นทางเลือกหนึ่งในการรักษาฝีดาษวานร

Tecovirimat

Orthopoxvirus VP37 Envelope Wrapping Protein Inhibitor

เป็นยาต้านไวรัสที่ USFDA อนุมัติให้ใช้ในการรักษา smallpox ในผู้ใหญ่ และเด็กที่น้ำหนักมากกว่า 3 กิโลกรัมขึ้นไป ปัจจุบัน CDC และ EMA อนุมัติให้ใช้ในการรักษาฝีดาษวานรในช่วงที่มีการระบาด แม้ยังมีข้อมูลทดสอบในมนุษย์ไม่เพียงพอ ยามีทั้งรูปแบบเม็ดเป็นแคปซูล และยาฉีด

- ไม่มีข้อมูลประสิทธิภาพของยานี้ในการรักษาฝีดาษวานรในมนุษย์ มีการศึกษาในสัตว์หลายชนิด พบว่ายานี้มีประสิทธิภาพในการรักษาโรคที่เกิดจากเชื้อกลุ่ม orthopoxvirus
- มีการศึกษาในคนที่มีสุขภาพดี พบว่ายานี้มีความปลอดภัย และสามารถทนยาได้โดยพบอาการไม่พึงประสงค์เล็กน้อยเท่านั้น

inhibiting viral DNA polymerases

Cidofovir และ Brincidofovir

ไม่มีข้อมูลประสิทธิภาพของยาในการนำมาใช้รักษาฝีดาษวานร มีเพียงข้อมูลในหลอดทดลอง และการทดลองในสัตว์ ว่ามีประสิทธิภาพต่อต้าน poxvirus ปัจจุบันยังไม่ทราบแน่ชัดว่าผู้ป่วยฝีดาษวานรที่มีอาการรุนแรงจะได้ประโยชน์จากการใช้ยาดังกล่าวหรือไม่ แม้ว่าปัจจุบันมีการนำมาพิจารณาใช้ในบางภาวะ

- ยา Brincidofovir มีข้อมูลความปลอดภัยมากกว่า cidofovir

Vaccinia Immune Globulin Intravenous (VIGIV)

FDA รับรองให้ใช้รักษาภาวะแทรกซ้อนจากการได้วัคซีนที่ผลิตมาจากเชื้อ Vaccinia ได้แก่ eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, การติดเชื้อ vaccinia ในคนที่เป็นโรคผิวหนังผื่นแพ้อยู่เดิม และการติดเชื้อ vaccinia ในบริเวณที่ไม่ปกติ ยกเว้นการติดเชื้อที่กระจกตา

- ไม่มีข้อมูลประสิทธิภาพของยานี้ในการนำมารักษาภาวะแทรกซ้อนจากฝีดาษวานร ยังไม่แน่ใจว่าผู้ป่วยที่มีอาการรุนแรงจะมีประโยชน์การการได้รับยานี้หรือไม่
- สามารถพิจารณานำมาใช้เพื่อป้องกันในคนไข้ที่สัมผัสฝีดาษวานร และมี severe immunodeficiency in T-cell function ทำให้ไม่สามารถได้รับวัคซีนหลังสัมผัสได้

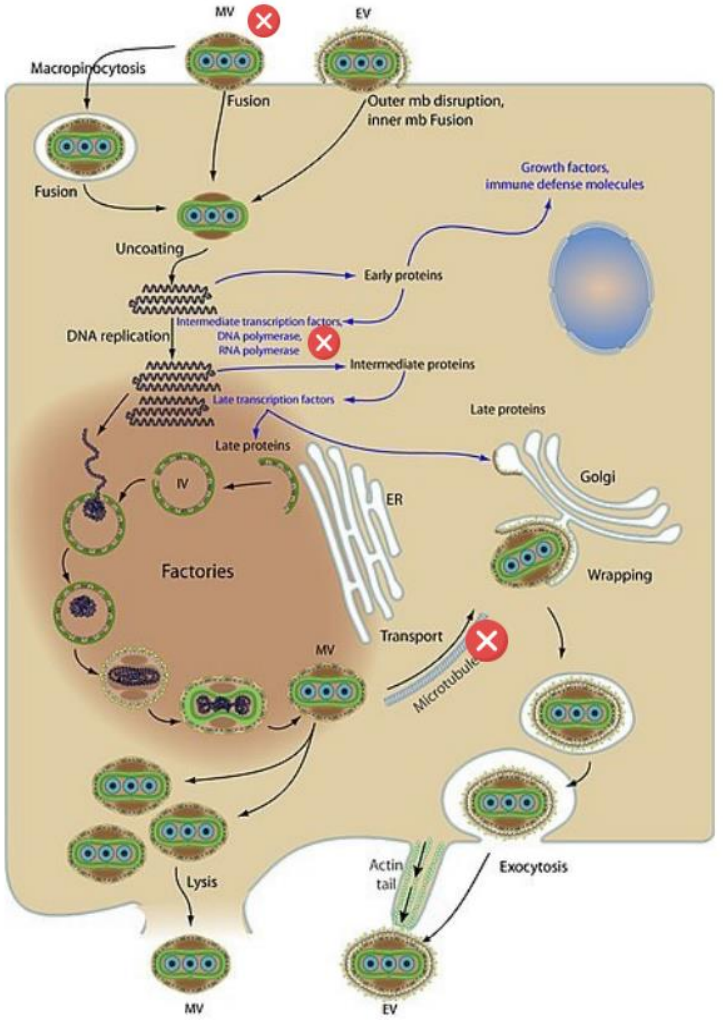
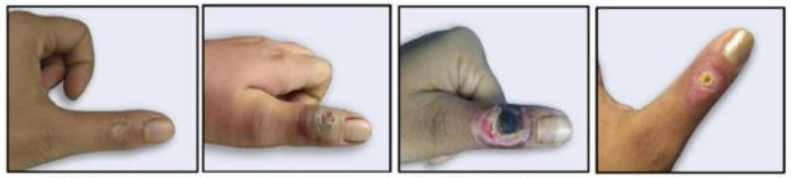


Figure 1 **Progression of infection after accidental inoculation with vaccinia virus, Pune, India, September 2020**
Figure 1 **Évolution de l'infection après inoculation accidentelle par le virus de la vaccine, Pune, Inde, septembre 2020**

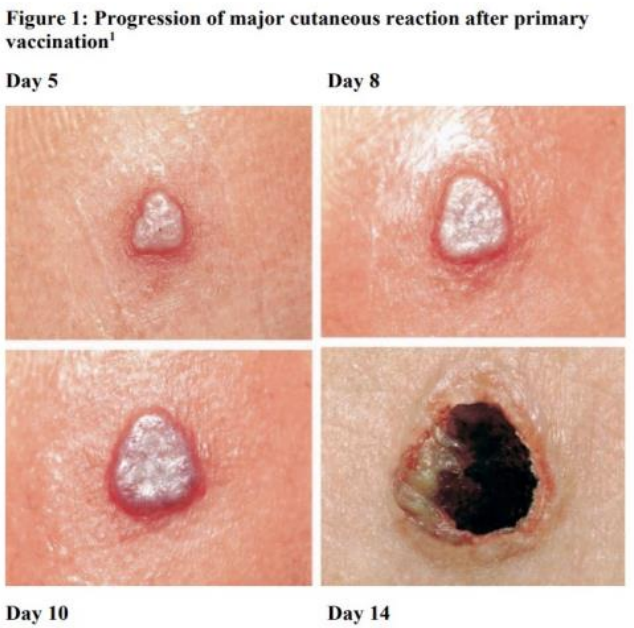


Riyesh T, et al. Emerg Infect Dis. 2014 Feb;20(2):324-6.
Hoy SM et al, Drugs. 2018 Sep;78(13):1377-1382.
https://viralzone.expasy.org/resources/Poxviridae_cycle.jpg

Vaccine prevent smallpox and monkeypox

- *Vaccinia virus* vaccine (against smallpox 95-100% , monkeypox 85%)
- **1st generation: Dryvax** – a freeze-dried live-virus smallpox vaccine, cultured in the skin of calves, used during 1940-1980, serious side effects 1-2%
- **2nd generation: ACAM 200** – live vaccine, cultured in Vero cells, 2007 – percutaneous route (scarification), considered vaccinated within 28 days
  - SE: Myocarditis, cardiomyopathy, encephalitis, blindness
- **3rd generation: MVA-BN, Jynneos, Imvanex, Imvamune**–non-replicating live modified vaccinia Ankara virus
  - 0.5 ml subcutaneous
    - Naïve: 2 doses 4 weeks apart
    - Previous vaccinated: 1 dose
  - consider vaccinated 14 days after the 2nd dose

15 jabs of a bifurcation needle in diameter of 5 mm



https://www.cdc.gov/poxvirus/monkeypox/clinicians/smallpox-vaccine.html

ACAM2000 Product Insert (fda.gov)

Indication of vaccination

UK Health Security Agency

CDC

Pre-exposure prophylaxis (PrEP)

- For occupational exposure – Clinical or research laboratory personnel, health care workers
- ACAM200: revaccination q 3 years

Post-exposure prophylaxis (PEP)

- Within 4 days from the date of exposure in order to prevent the onset of the diseases
- Within 4-14 days: may reduce the symptoms of the disease
- If exposure has been intermittent or continuous, post-exposure vaccination should ideally be given within 4 days of the last exposure.

https://www.cdc.gov/poxvirus/monkeypox/clinicians/smallpox-vaccine.html

Recommendations for the use of pre and post exposure vaccination during a monkeypox incident: UKHSA Updated 1 June 2022 v7

TRC EIDCC
Thai Red Cross Emerging Infectious Diseases Clinical Center

Monkeypox

- **อาการและอาการแสดงที่เปลี่ยนไปจากเดิม อาจจะแยกยากจากโรคติดต่อทางเพศสัมพันธ์อื่น ๆ**
- คาดว่ามีผู้ป่วยเพิ่มขึ้นเรื่อย ๆ แต่การระบาดอยู่ในวงจำกัดเฉพาะบุคคลที่มีความเสี่ยงเช่นเดียวกับการระบาดโรคเอชไอวีในอดีต
- การเตรียมความพร้อม
  - ค้นหาผู้ป่วยที่มีความเสี่ยงทั้งในระดับบุคคลและในชุมชน
  - พัฒนาการตรวจให้เข้าถึงได้ง่ายขึ้น
  - การให้ความรู้แก่บุคคลากรทางการแพทย์และประชาชนทั่วไป