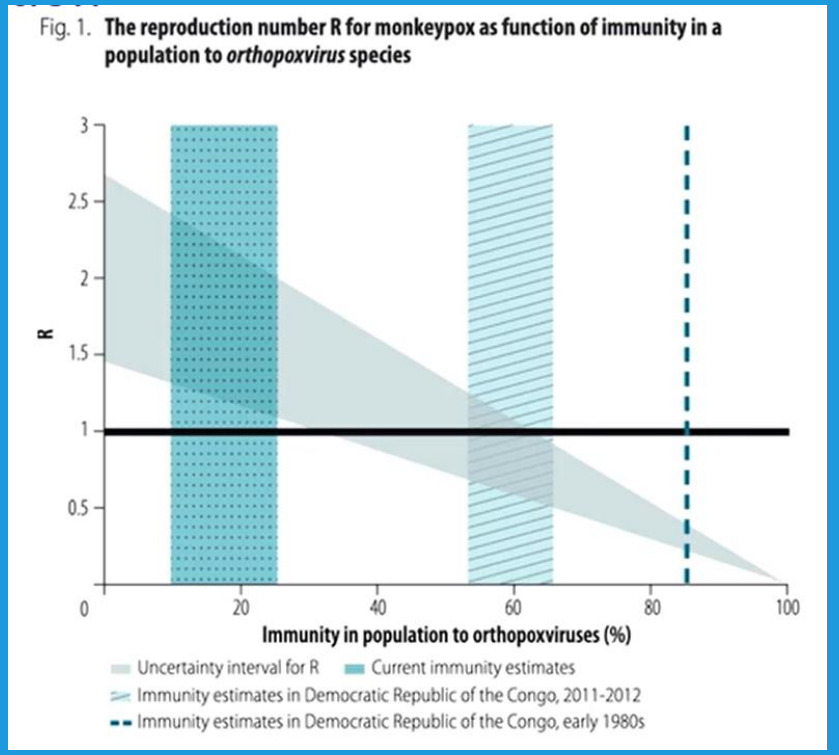
Viruela Símica Consideraciones clínicas

Omar Sued, MD, PhD
Asesor de tratamiento y Atención de VIH
Punto focal clínico MPOX IMST
03 Marzo 2023

OPS Organización Panamericana de la Salud
Organización Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas

Características epidemiológicas

- Periodo de incubación: 5,6 (IC95% 4,3-7,8) días [1]
- R0: 2,44 (0.8 en heterosexuales)[2]
- Factores modificadores del R0 [3]
  - Número de contactos (>o <14 contactos)
  - Inmmunidad (por vacuna o infección)
- 53% de la transmisión en estado presintomático [4]
- 6,5% de los casos asintomáticos [5,6]



1) Madewell Z, EID 2023.
2) Branda F, JM Virol 2023.
3) Grant BWHO 2022.
4) Ward BMJ 2022,
5) Ferre AIM 2022,
6) de Baetselier Nature Medicine 2022

Características clínicas del casos confirmados de VS

Indicator	Región de las Américas	
	n	%
Hospitalización		
Información disponible	34,562	60.1%
No hospitalizado	31,380	90.8%
Hospitalizado	3,182	9.2%
Manejo clínico	949	29.8%
Aislamiento	305	9.6%
Causa desconocida	1,928	60.6%
UCI	37	1.2%
Otras características		
Hombres	49,059	95.8%
HSH	14,673	71.5%
VIH+	13,303	52.4%

Datos actualizados hasta: 02/03/2023
Fuentes de datos: Información recibida de los Puntos Focales Nacionales (CNE) del Reglamento Sanitario Internacional (RSI) o publicada en los sitios web de los Ministerios de Salud, Agencias de Salud o similares

https://www.paho.org/es/brote-por-enfermedad-viruela-simica-2022

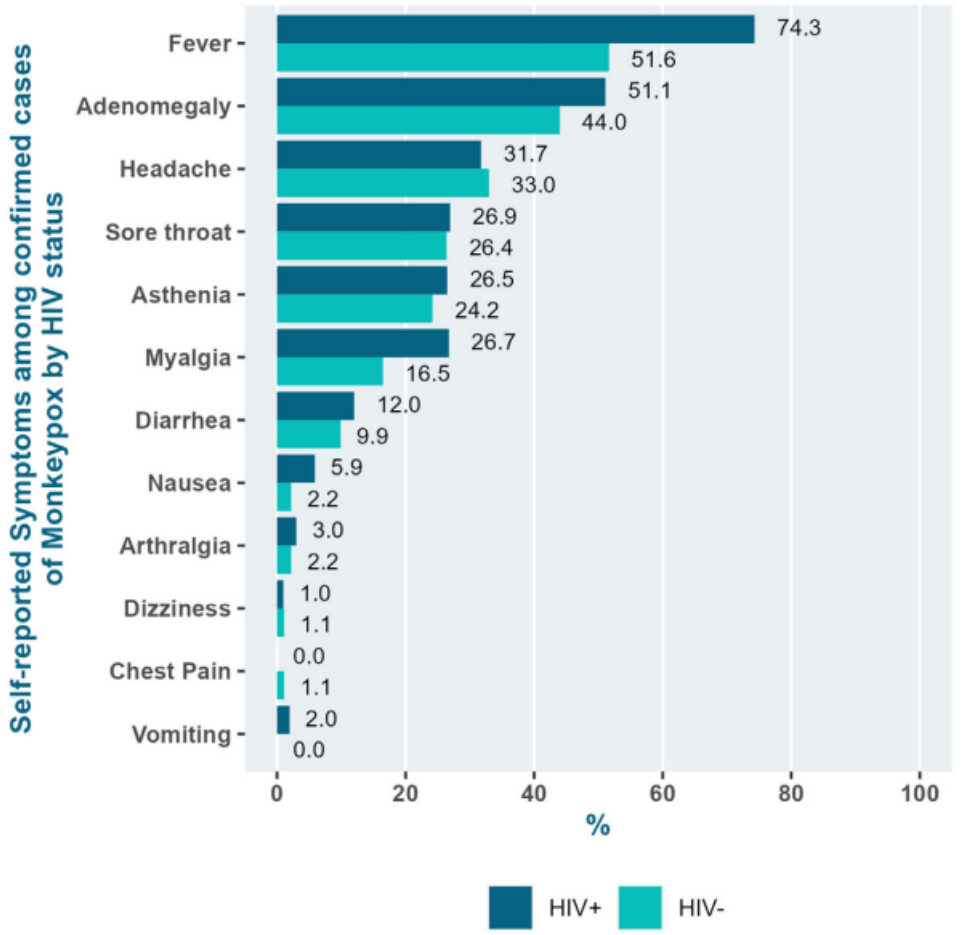


Fig. 3: Self-reported clinical symptoms among confirmed mpox cases according to HIV status (%).

Mayara Secco, LANCET the Americas, 2022 (online)

Las próximas imágenes pueden resultar sensibles, debido a la naturaleza de las fotos

OPEN ACCESS

Check for updates

FAST TRACK

Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: descriptive case series

Aatish Patel, Julia Bilinska, Jerry C H Tam, Dayana Da Silva Fontoura, Claire Y Mason, Anna Daunt, Luke B Snell, Jamie Murphy, Jack Potter, Cecilia Tuudah, Rohan Sundramoorthi, Movin Abeywickrema, Caitlin Pley, Vasanth Naidu, Gaia Nebbia, Emma Aarons, Alina Botgros, Sam T Douthwaite, Claire van Nispen tot Pannerden, Helen Winslow, Aisling Brown, Daniella Chilton, Achyuta Nori

Lancet Infect Dis 2022; 22: 883–92

197 pacientes, 38 años, 99.5% HSH

35.9% HIV+, todos >200 CD4

51.8% menos de 10 lesiones

36% dolor rectal

13% sin manifestaciones sistémicas

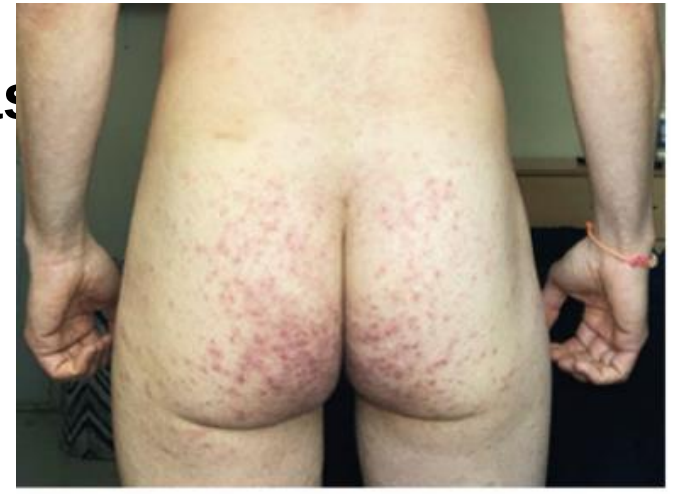
10% requirió admisión hospitalaria

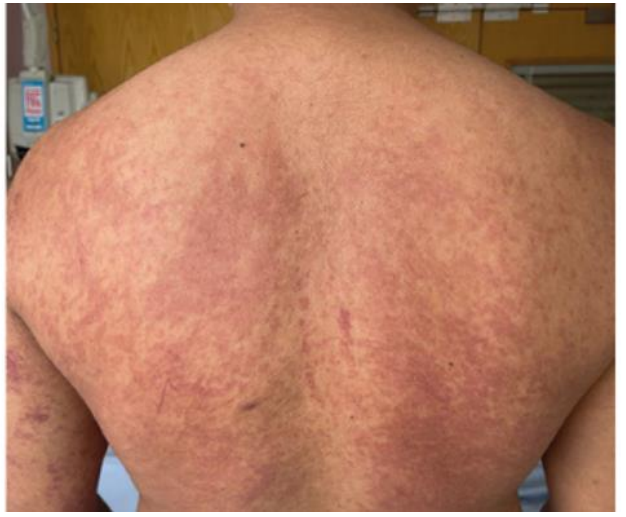
Lesiones atípicas

- Lesiones solitarias (11%)
- Lesiones polimorficas (35%)
- Rash maculopapular
- Sin pródromo

Complicaciones

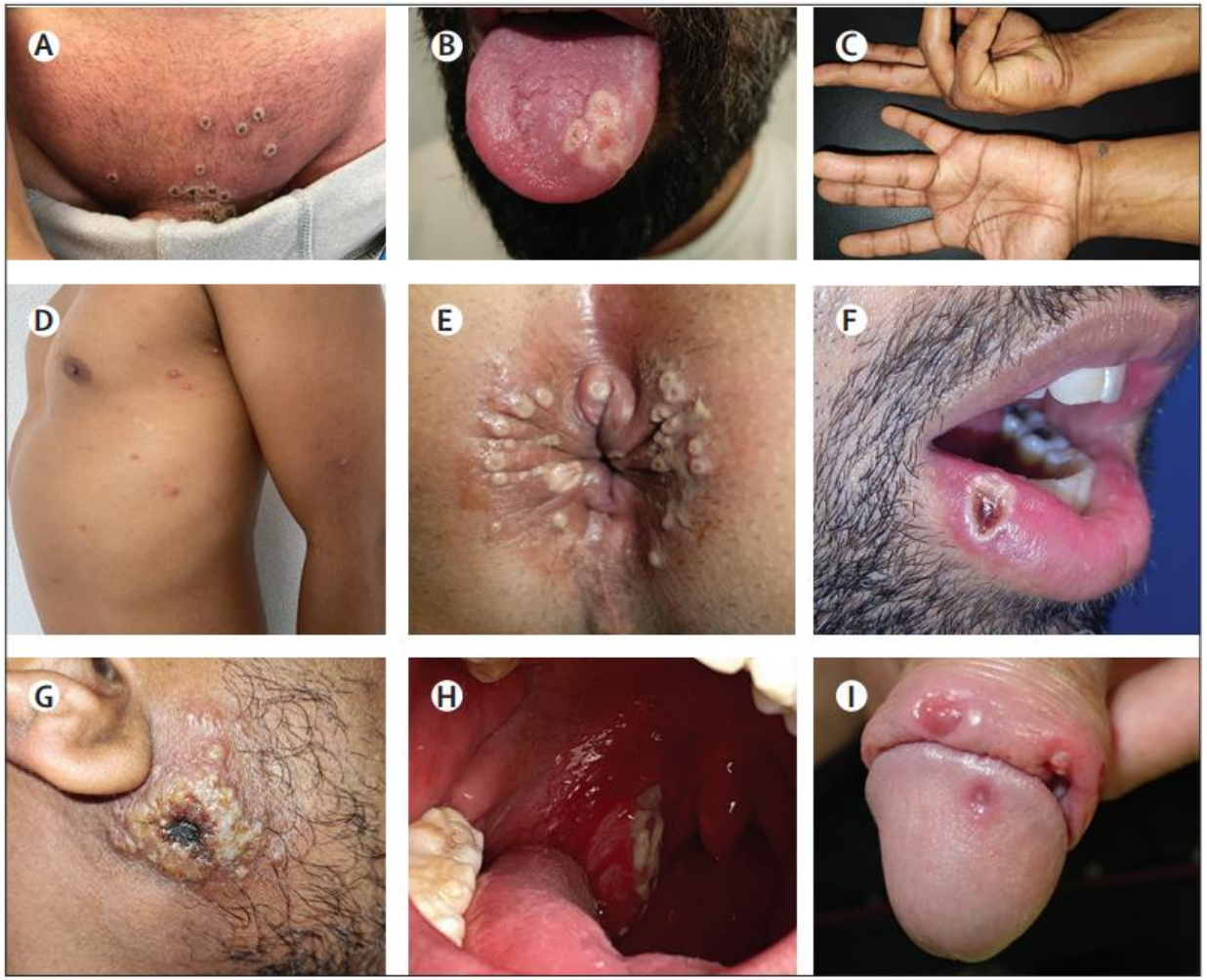
- Proctitis, abscesos rectales y tonsilares
- Edema de pene
- Perforación rectal





Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: a prospective observational cohort study

Eloy José Tarín-Vicente, Andrea Alemany, Manuel Agud-Dios, Maria Ubals, Clara Suñer, Andrés Antón, Maider Arando, Jorge Arroyo-Andrés, Lorena Calderón-Lozano, Cristina Casañ, José Miguel Cabrera, Pep Coll, Vicente Descalzo, María Dolores Folgueira, Jorge N García-Pérez, Elena Gil-Cruz, Borja González-Rodríguez, Christian Gutiérrez-Collar, Águeda Hernández-Rodríguez, Paula López-Roa, María de los Ángeles Meléndez, Julia Montero-Menárguez, Irene Muñoz-Gallego, Sara Isabel Palencia-Pérez, Roger Paredes, Alfredo Pérez-Rivilla, María Piñana, Nuria Prat, Aida Ramirez, Ángel Rivero, Carmen Alejandra Rubio-Muñiz, Martí Vall, Kevin Stephen Acosta-Velásquez, An Wang, Cristina Galván-Casas, Michael Marks*, Pablo L Ortiz-Romero*, Oriol Mitjà**



181 pacientes, 97% hombres

17% con otras ITS concomitantes

2% internación

8% edema peneano

Celulitis mas frecuente en cara o perianal

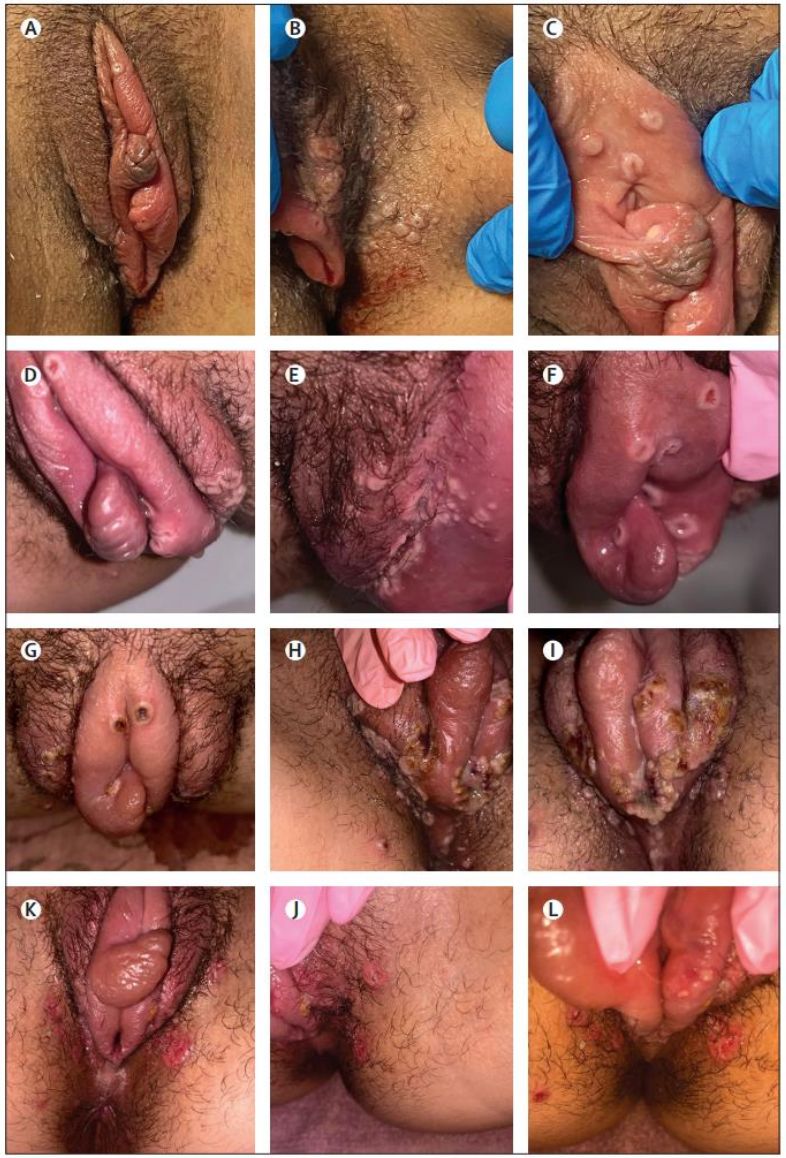
Ninguno recibió tecovirimat.

40% vivian con VIH, todos buen control. No eventos graves

La actividad sexual se relacionó con la clínica:

- **Proctitis: 91% reportaron sexo anal**
- **Tonsilitis: 95% reportaron sexo oral**

Casos en mujeres: 2153 (4,2%)



Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series

Thornhill P, Lancet 2022

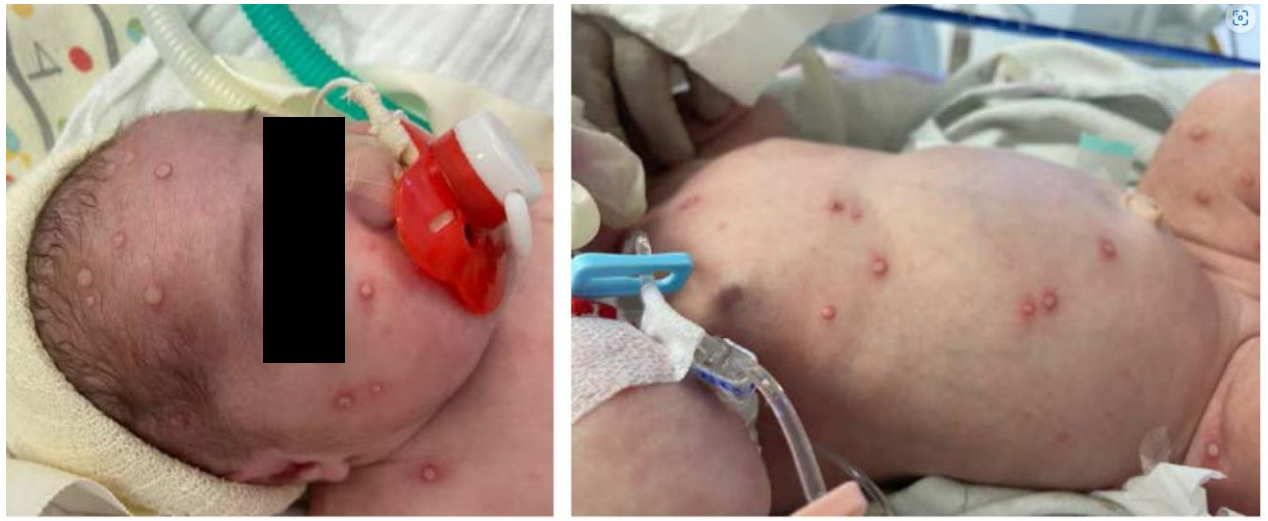
	Mujeres trans (62)	Mujeres cis (74)
Mal diagnóstico inicial	**10%**	**34%**
Más de una visita	23%	42%
Raza Blanca	13%	43%
Trabajo sexual	55%	1%
Parejas	10	1
Viven con VIH	50%	8%
Otras ITS	26%	8%

Casos en niños: 736 casos en <18 años confirmados en las Américas

- Tasa de ataque global: 4.7%
- Tasa de ataque en 0-9 años: 7.1%
- No se reportó transmisión secundaria
- Cargas virales mas bajas que en adultos

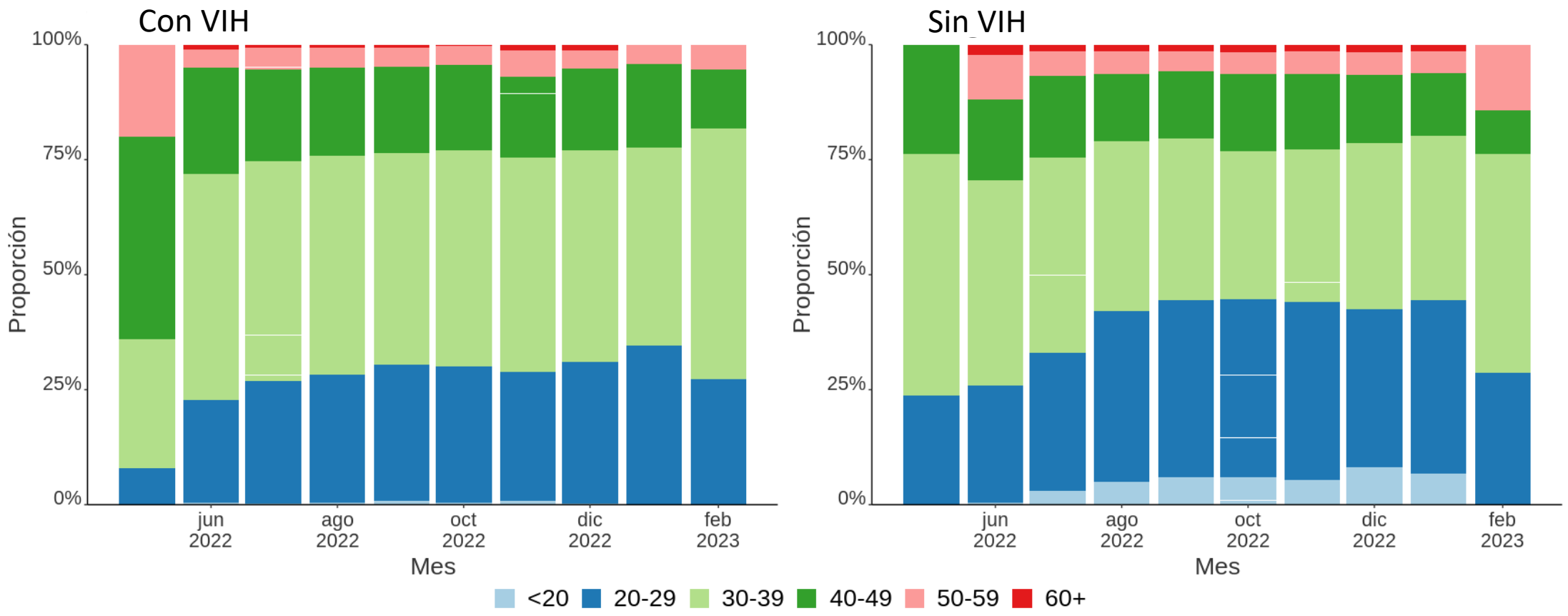
Sachdev, CROI 2023

- Manifestaciones neonatales potencialmente graves



Antonello V, Ped ID Journal,2023

Casos confirmados de mpox por edad y estatus VIH Región de las Américas



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022

J.P. Thornhill, S. Barkati, S. Walmsley, J. Rockstroh, A. Antinori, L.B. Harrison, R. Palich, A. Nori, I. Reeves, M.S. Habibi, V. Apea, C. Boesecke, L. Vandekerckhove, M. Yakubovsky, E. Sendagorta, J.L. Blanco, E. Florence, D. Moschese, F.M. Maltez, A. Goorhuis, V. Pourcher, P. Migaud, S. Noe, C. Pintado, F. Maggi, A.-B.E. Hansen, C. Hoffmann, J.I. Lezama, C. Mussini, A.M. Cattelan, K. Makofane, D. Tan, S. Nozza, J. Nemeth, M.B. Klein, and C.M. Orkin, for the SHARE-net Clinical Group*

ABSTRACT

BACKGROUND

Before April 2022, monkeypox virus infection in humans was seldom reported outside African regions where it is endemic. Currently, cases are occurring worldwide. Transmission, risk factors, clinical presentation, and outcomes of infection are poorly defined.

METHODS

We formed an international collaborative group of clinicians who contributed to an international case series to describe the presentation, clinical course, and outcomes of polymerase-chain-reaction–confirmed monkeypox virus infections.

RESULTS

We report 528 infections diagnosed between April 27 and June 24, 2022, at 43 sites in 16 countries. Overall, 98% of the persons with infection were gay or bisexual men, 75% were White, and 41% had human immunodeficiency virus infection; the median age was 38 years. Transmission was suspected to have occurred through sexual activity in 95% of the persons with infection. In this case series, 95% of the persons presented with a rash (with 64% having <10 lesions), 73% had anogenital lesions, and 41% had mucosal lesions (with 54 having a single genital lesion). Common systemic features preceding the rash included fever (62%), lethargy (41%), myalgia (31%), and headache (27%); lymphadenopathy was also common (reported in 56%). Concomitant sexually transmitted infections were reported in 109 of 377 persons (29%) who were tested. Among the 23 persons with a clear exposure history, the median incubation period was 7 days (range, 3 to 20). Monkeypox virus DNA was detected in 29 of the 32 persons in whom seminal fluid was analyzed. Antiviral treatment was given to 5% of the persons overall, and 70 (13%) were hospitalized; the reasons for hospitalization were pain management, mostly for severe anorectal pain (21 persons); soft-tissue superinfection (18); pharyngitis limiting oral intake (5); eye lesions (2); acute kidney injury (2); myocarditis (2); and infection-control purposes (13). No deaths were reported.

CONCLUSIONS

In this case series, monkeypox manifested with a variety of dermatologic and systemic clinical findings. The simultaneous identification of cases outside areas where monkeypox has traditionally been endemic highlights the need for rapid identification and diagnosis of cases to contain further community spread.

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Drs. Thornhill,
contributed eq

This article was
at NEJM.org.

DOI: 10.1056/N

Table 1. Demographic and Clinical Characteristics of the Persons with Monkeypox.*

Characteristic	All Persons (N=528)
Median age (range) — yr	38 (18–68)
Sex or gender — no. (%)	
Male	527 (>99)
Female	0
Trans or nonbinary	1 (<1)
Sexual orientation — no. (%)†	
Heterosexual	9 (2)
Homosexual	509 (96)
Bisexual	10 (2)
Race or ethnic group — no. (%)†	
White	398 (75)
Black	25 (5)
Mixed race	19 (4)
Latinx	66 (12)
Other or unknown	20 (4)
HIV positive — no. (%)	218 (41)
HIV negative or status unknown — no. (%)	310 (59)
Use of preexposure prophylaxis against HIV — no./total no. (%)	176/310 (57)
Foreign travel in month before diagnosis — no. (%)‡	147 (28)
Continent of travel — no./total no. (%)	
Europe	132/147 (90)
North America	9/147 (6)
Australasia	0/147
Africa and Middle East	2/147 (1)
Central and South America	2/147 (1)
Not stated	2/147 (1)
Known to have undergone STI screening — no. (%)	377 (71)
Microbiologically confirmed concomitant STI present — no./total no. screened (%)	109/377 (29)
Gonorrhea	32/377 (8)
Chlamydia	20/377 (5)
Syphilis	33/377 (9)
Herpes simplex virus infection	3/377 (1)
Lymphogranuloma venereum	2/377 (1)
Chlamydia and gonorrhea	5/377 (1)
Other or not stated	14/377 (4)
HIV test taken — no./total no. with previously unknown or negative HIV status (%)	122/310 (39)
New HIV infection diagnosis — no./total no. (%)	3/122 (2)
Sexual history not known — no./total no. (%)	122/528 (23)
Median no. of sex partners in previous 3 months (IQR)	5 (3–15)
"Chemsex" reported in the previous month — no. (%)	106 (20)
Reported attendance at a sex-on-site event in the previous month — no. (%)	169 (32)
Known hepatitis infection — no. (%)	
Hepatitis B virus surface antigen positive	6 (1)
Hepatitis C virus antibody positive	30 (6)
Hepatitis C virus RNA positive	8 (2)
Reported history of smallpox vaccination — no. (%)	49 (9)

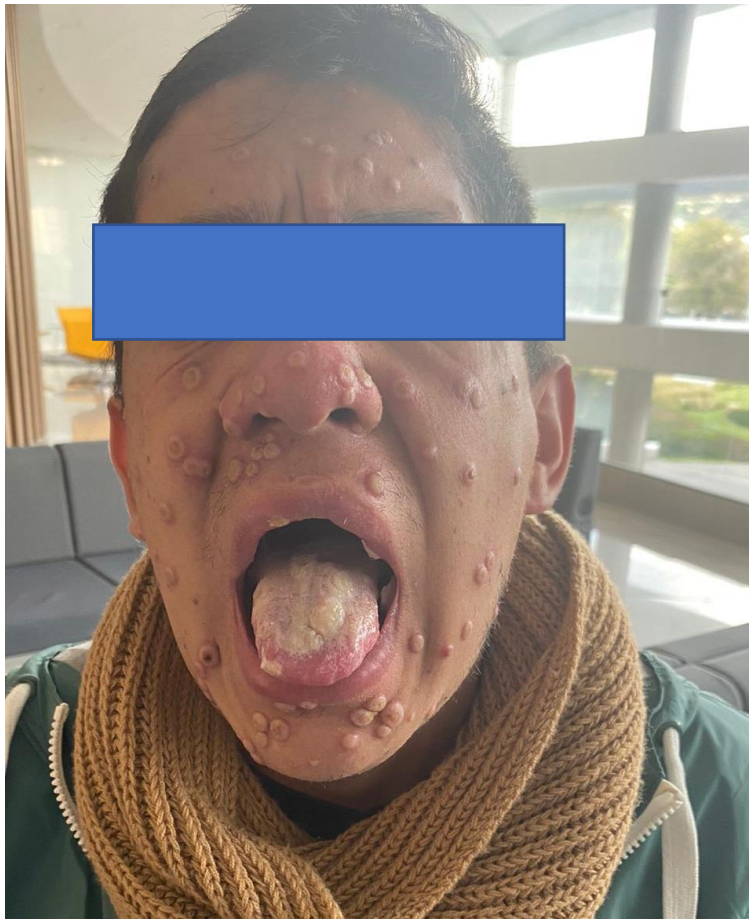
Table 2. Demographic and Clinical Characteristics of Persons with HIV Infection in the Case Series.*

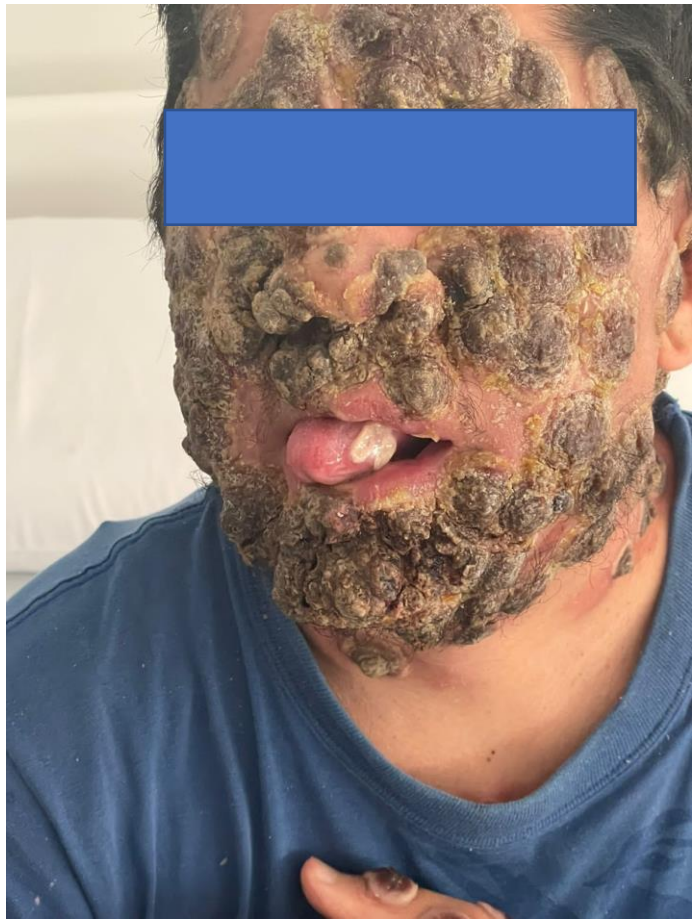
Characteristic	Persons with HIV Infection (N=218)
Median age (range) — yr	39 (21–62)
Male sex — no. (%)	218 (100)
Sexual orientation — no. (%)	
Homosexual	212 (97)
Heterosexual	2 (1)
Bisexual	4 (2)
Median CD4 cell count (IQR) — cells/mm^3	680 (513–861)
Missing CD4 cell-count data — no. (%)	33 (15)
HIV viral load — no./total no. with data (%)	
<50 copies/ml	180/190 (95)
<200 copies/ml	185/190 (97)
Missing HIV viral load data — no. (%)	28 (13)
Known to be taking ART — no. (%)	210 (96)
ART regimen among those taking ART	
Backbone — no./total no. (%)	
Tenofovir-based three-drug regimen	102/210 (49)
Abacavir-based three-drug regimen	20/210 (10)
Zidovudine-based three-drug regimen	2/210 (1)
Two-drug regimen	48/210 (23)
Missing or unknown	38/210 (18)
Third agent — no./total no. (%)†	
Integrase inhibitor	129/210 (61)
NNRTI	31/210 (15)
bPI	11/210 (5)
Missing or unknown	39/210 (19)

* ART denotes antiretroviral therapy, bPI boosted protease inhibitor, and NNRTI nonnucleoside reverse-transcriptase inhibitor.
† Percentages were calculated with the total number of persons taking three-drug regimens (or two-drug regimens with integrase inhibitors included as a third agent) used as the denominator.

2% tecovirimat
2% cidofovir
1% vaccinia Ig

Casos graves asociados con VIH





CD4 bajos
Sin TARV
Neoplasias asociadas

Credit Dr. C Alvarez, Colombia

Severe disseminated clinical presentation of monkeypox virus infection in an immunosuppressed patient: first death report in Brazil

Yargos Rodrigues Menezes[1] *and Alexandre Braga de Miranda*[2]

Journal of the Brazilian Society of Tropical Medicine Vol.:55 | (e0392-2022) | 2022

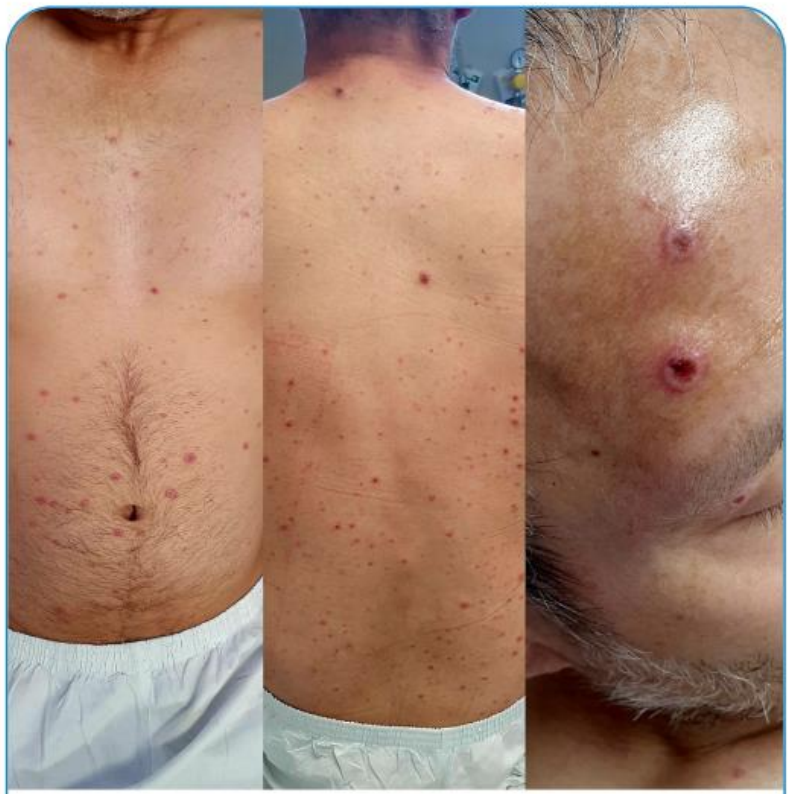


FIGURE 1: Hospital admission on July 15, 2022.

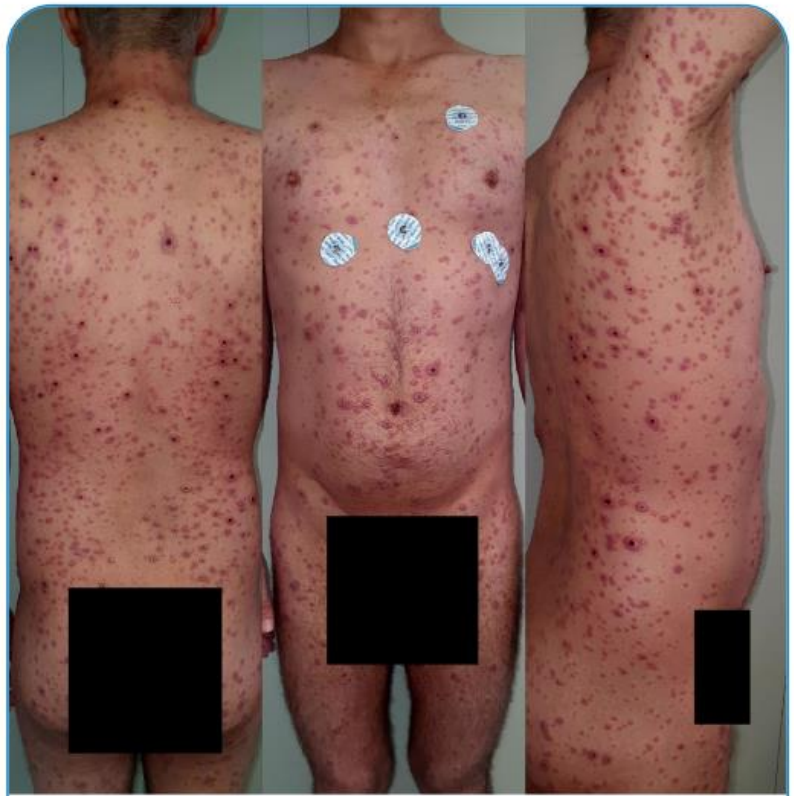


FIGURE 3: July 21, 2022.

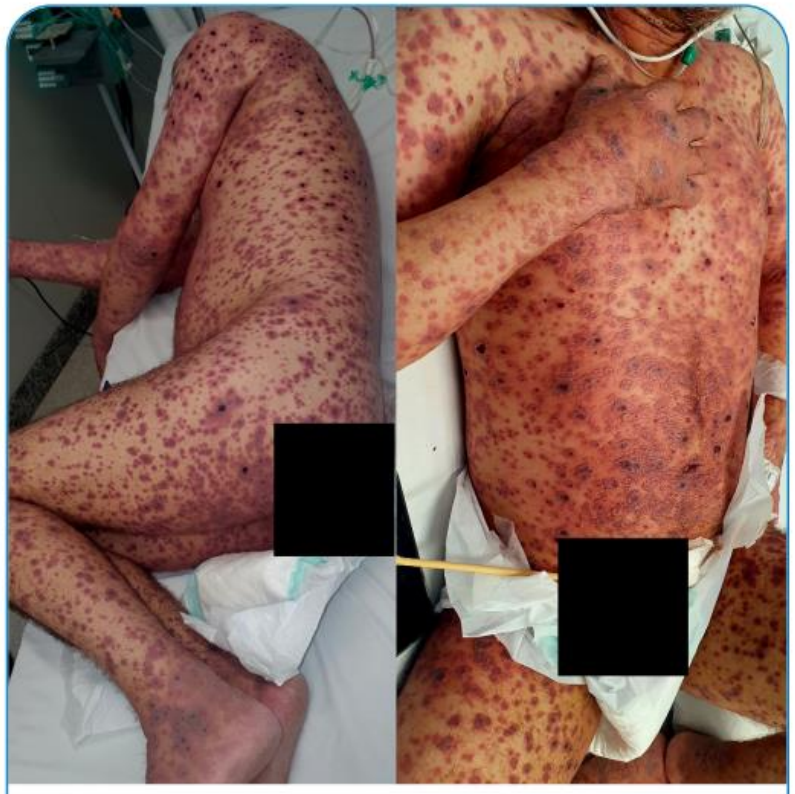


FIGURE 4: July 27, 2022.

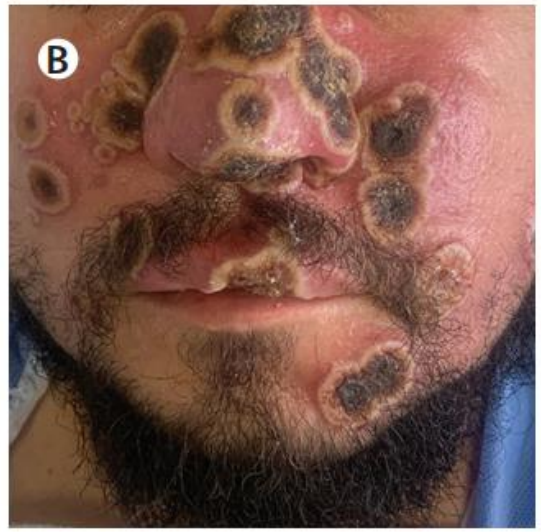
Mpox in people with advanced HIV infection: a global case series

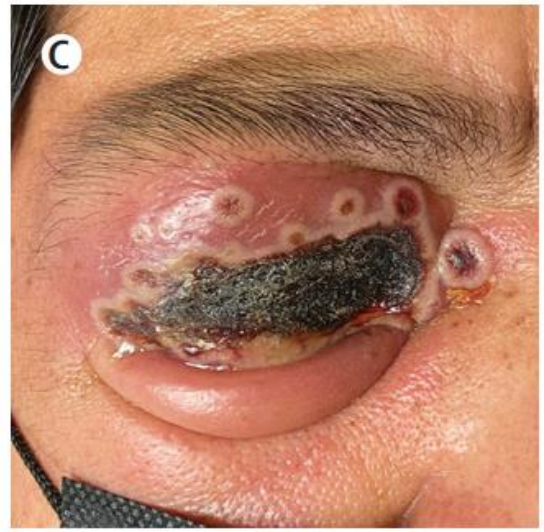
Oriol Mitjà, Andrea Alemany*, Michael Marks*, Jezer I Lezama Mora, Juan Carlos Rodríguez-Aldama, Mayara Secco Torres Silva, Ever Arturo Corral Herrera, Brenda Crabtree-Ramirez, José Luis Blanco, Nicolo Girometti, Valentina Mazzotta, Aniruddha Hazra, Macarena Silva, Juan José Montenegro-Idrogo, Kelly Gebo, Jade Ghosn, María Fernanda Peña Vázquez, Eduardo Matos Prado, Uche Unigwe, Judit Villar-García, Noah Wald-Dickler, Jason Zucker, Roger Paredes, Alexandra Calmy, Laura Waters, Cristina Galvan-Casas, Sharon Walmsley, Chloe M Orkin, on behalf of SHARE-NET writing group*

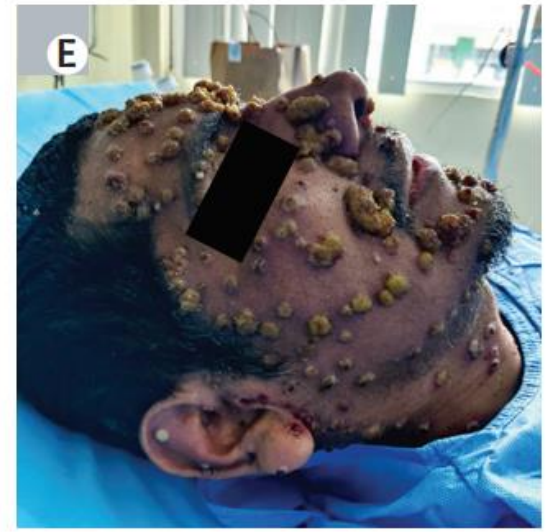
Serie de casos de pacientes con VIH y <350 cel CD4.

- 382 casos: 367 hombres, 4 mujeres y 10 mujeres trans
- 349 (91%) conocían el estatus VIH;
- Mediana de CD4 211 cels/mm^3, 85 (22%) tenían menos de 100
- 193 (51%) tenían carga viral indetectable
- 35% tenían mala adherencia
- 107 (28%) se hospitalizaron
- 27 personas fallecieron

Lancet 2023







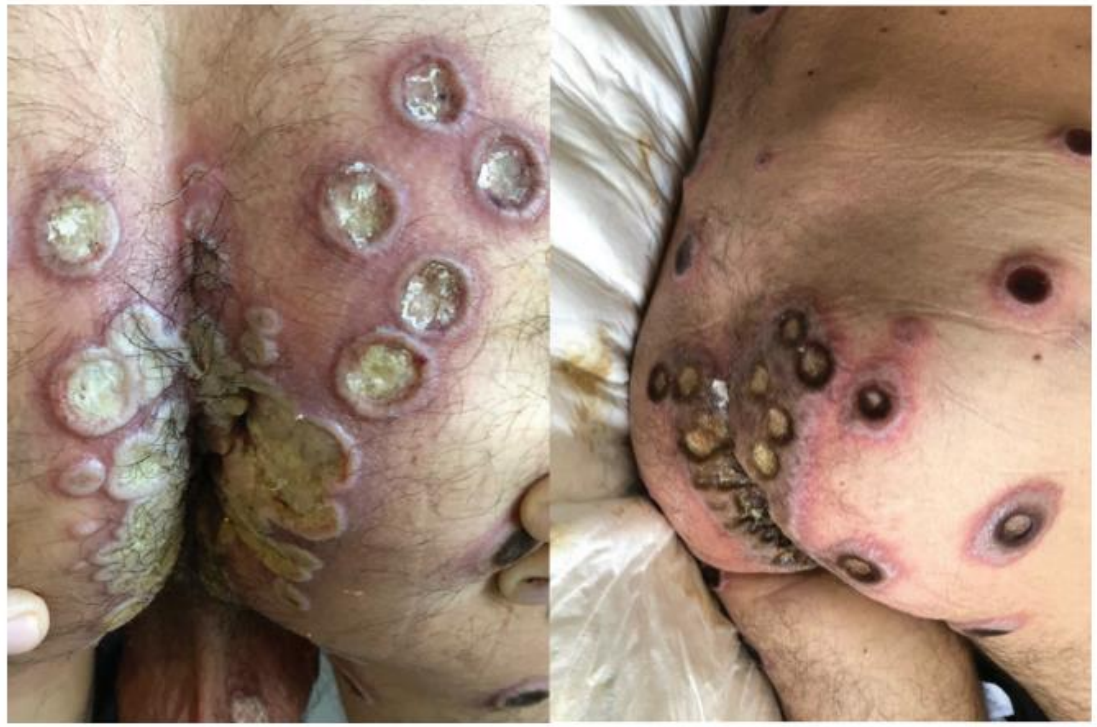
F

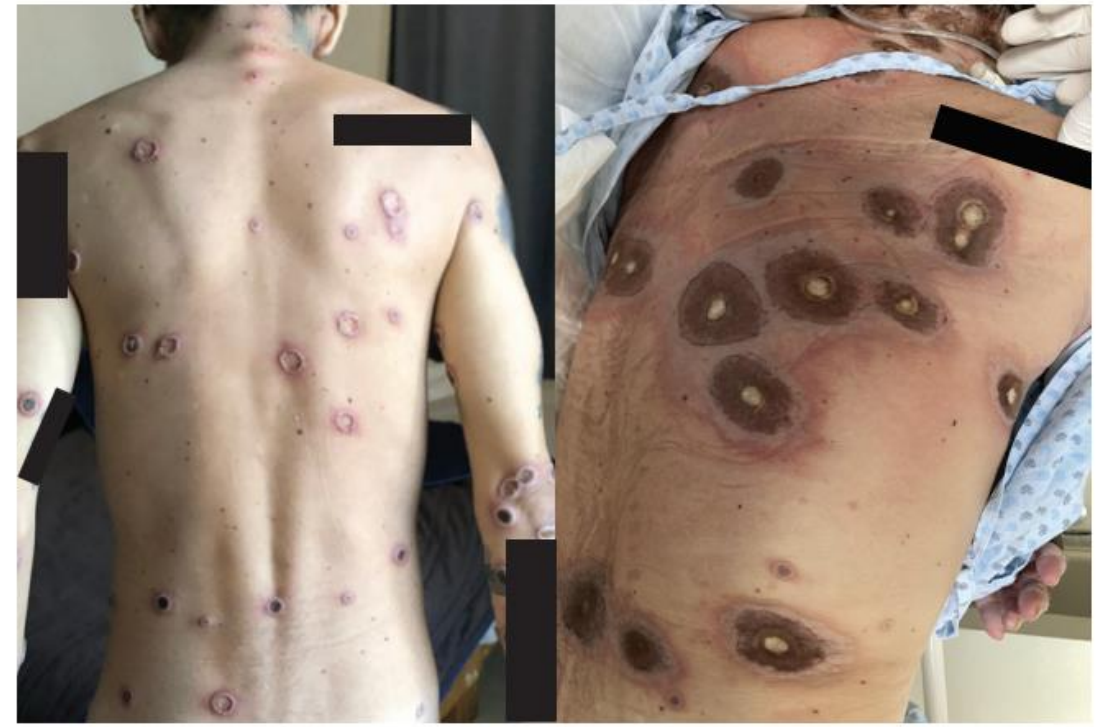
Day 33

Day 44

Day 33

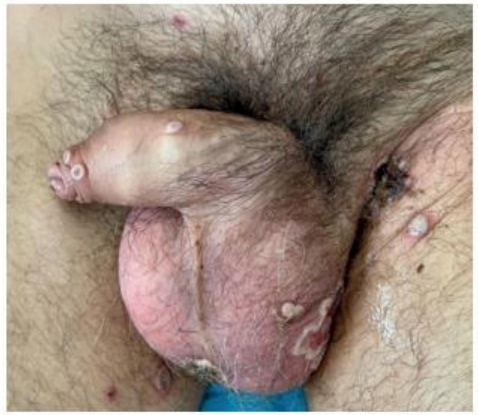
Day 44



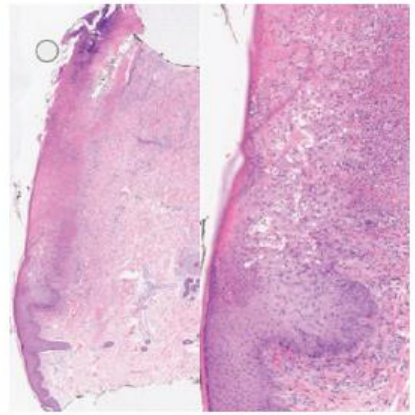


A

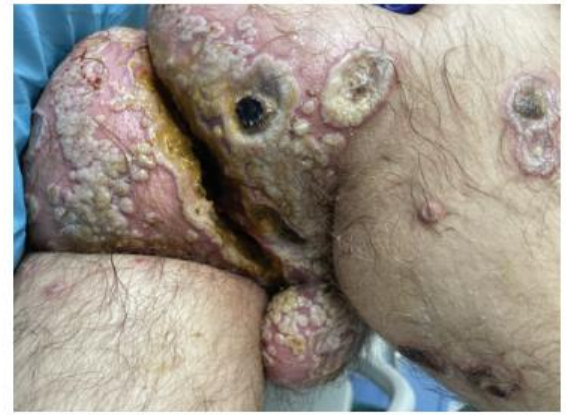
Day 0: genital lesions



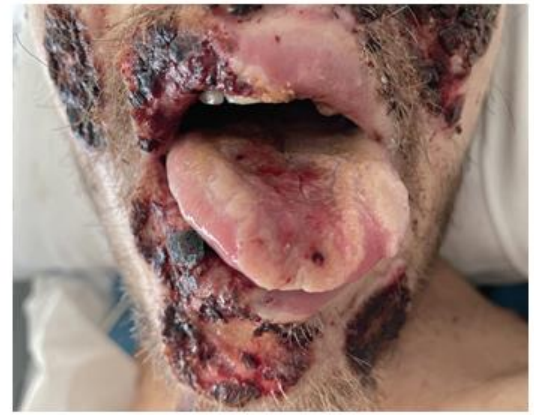
Day 19: skin biopsy



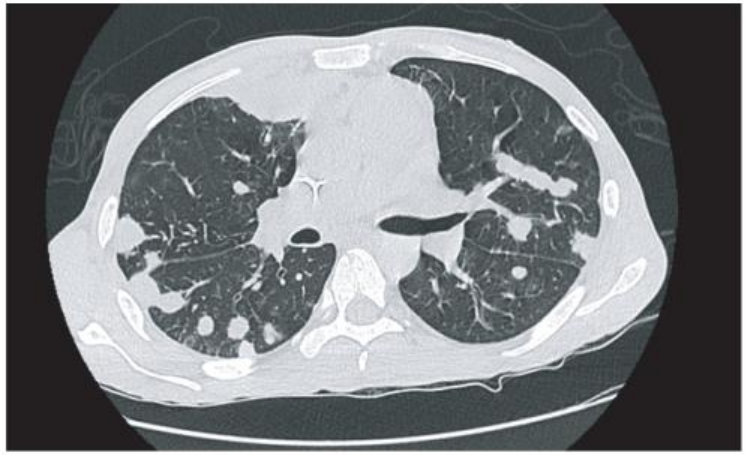
Day 81: worsening of lesions



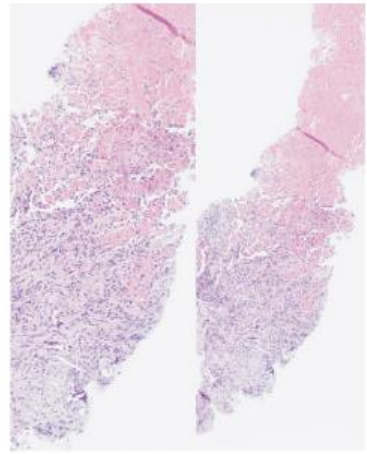
Day 81: necrotising lesions



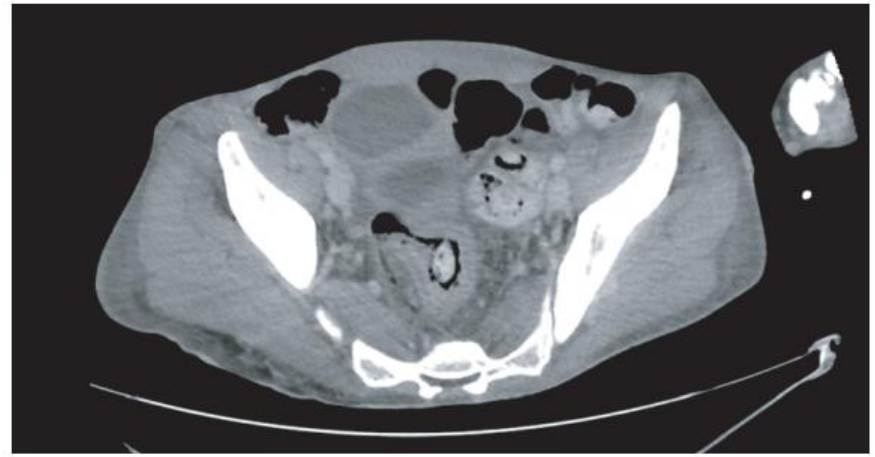
Day 89: CT larger lung nodules



Day 89: lung biopsy



Day 96: CT bowel perforation



Day 0: monkeypox virus PCR-positive, rash, and proctitis. CD4 13 cells per mm^3, viral load log5 copies per mL

Day 10: skin biospy consistent with monkeypox virus. Perianal abscess and bacteremia (*Escherichia coli* ESBL)

Day 25: ocular and lung involvement. Lung fine-needle aspiration monkeypox virus PCR positive

Day 48: start on ART. Progressive and disseminated disease

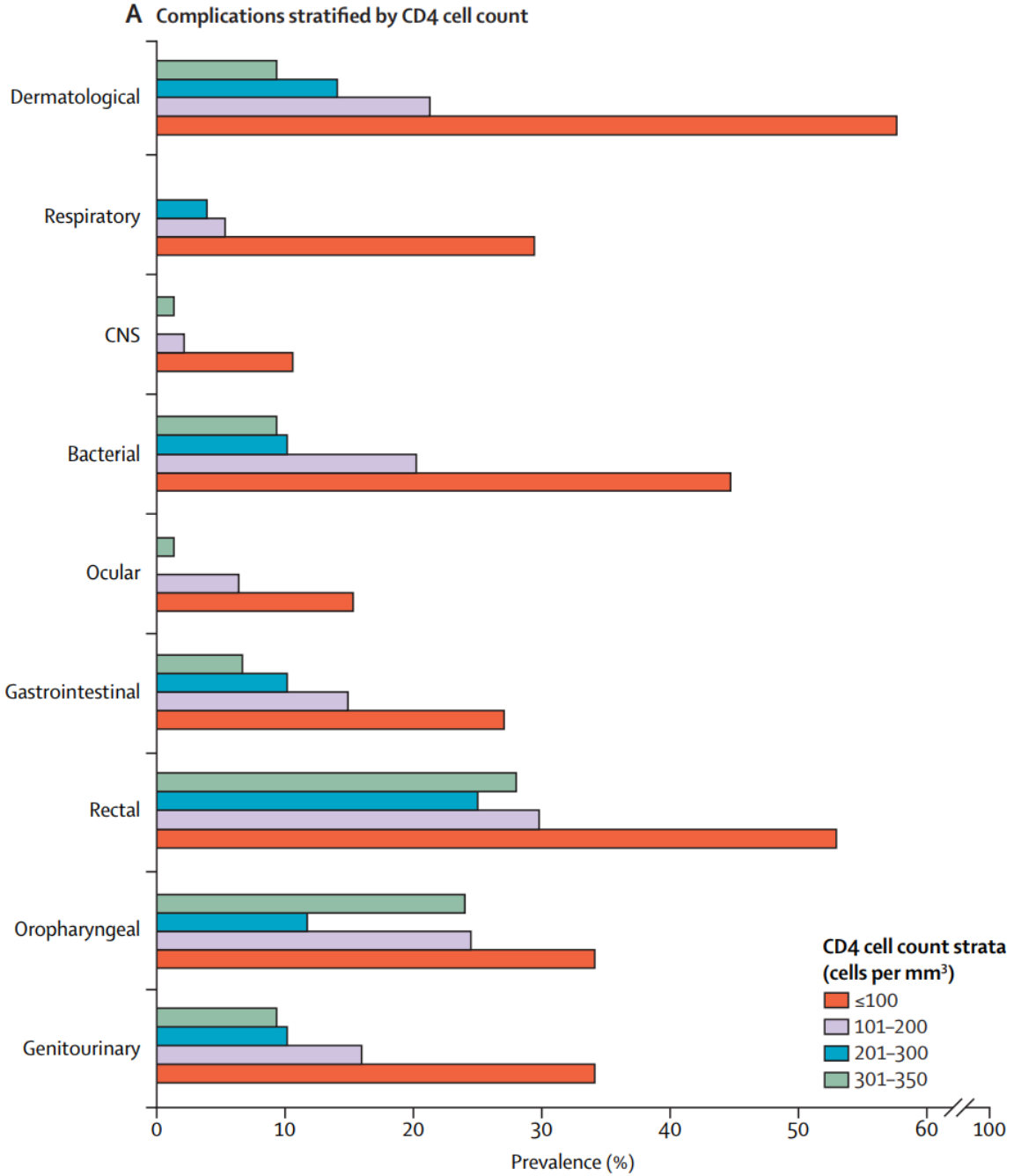
Day 81: increase CD4 to 80 cells per mm^3. Worsening of skin, anal, ocular and lung lesions

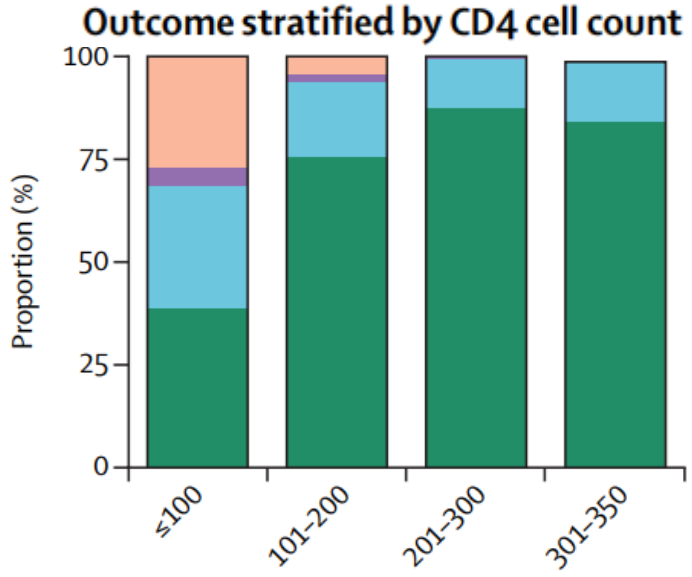
Day 89: lung CT larger nodules compared with day 25. Transthoracic biopsy monkeypox virus PCR positive, *Mycobacterium tuberculosis* PCR negative. Pathology rules out granulomatosis

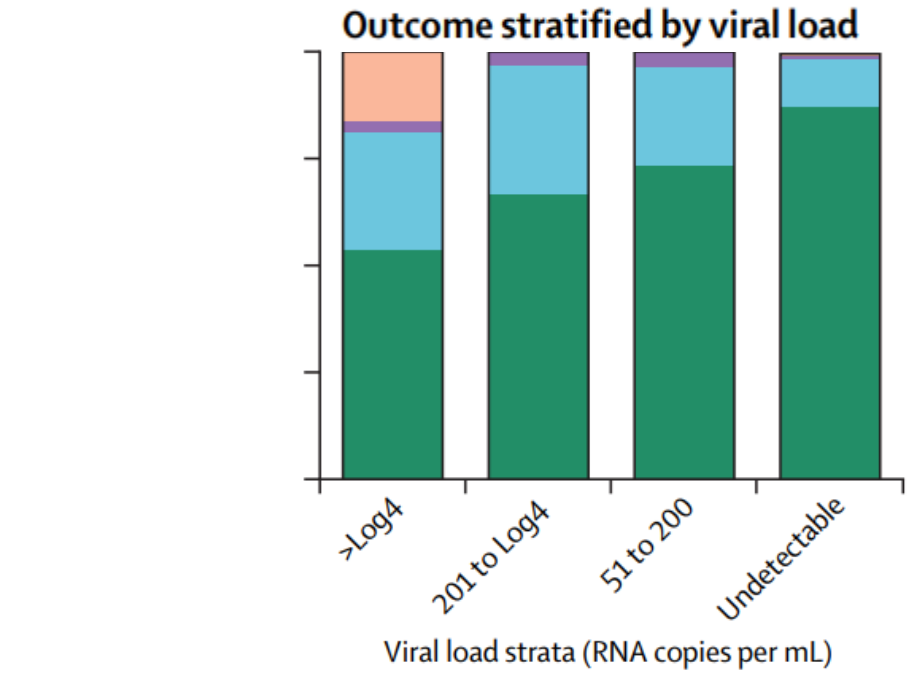
Day 96: Bowel perforation and sepsis

Day 103: patient died

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
HIV status					
Previously known PLWH currently adherent to ART	228 (60%)	17 (20%)	53 (56%)	100 (78%)	58 (77%)
Previously known PLWH not on ART or non-adherent	121 (32%)	53 (62%)	33 (35%)	25 (20%)	10 (13%)
Newly diagnosed with HIV infection	33 (9%)	15 (18%)	8 (9%)	3 (2%)	7 (9%)
CD4 cell count (cells per mm³)	211 (117–291)	47 (27–77)	156 (125–184)	259 (221–280)	326 (316–338)
HIV viral load strata RNA copies per mL					
≥log4	105 (27%)	47 (55%)	28 (30%)	20 (16%)	10 (13%)


A Complications stratified by CD4 cell count
Dermatological
Respiratory
CNS
Bacterial
Ocular
Gastrointestinal
Rectal
Oropharyngeal
Genitourinary
0
10
20
30
40
50
60
100
Prevalence (%)
CD4 cell count strata (cells per mm³)
≤100
101–200
201–300
301–350


Outcome stratified by CD4 cell count
Proportion (%)
100
75
50
25
0
≤100
101–200
201–300
301–350
CD4 cell count strata (cells per mm³)


Outcome stratified by viral load
>Log4
201 to Log4
51 to 200
Undetectable
Viral load strata (RNA copies per mL)


Death
Intensive care unit
Hospitalisation
Outpatient care

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
Mpox rash presentation					
Peak number of skin lesions	15 (8–35)	30 (15–100)	20 (12–35)	12 (6–20)	10 (4–15)
Rash duration in days	23 (18–33)	31 (21–45)	26 (19–40)	21 (16–28)	21 (15–30)
Highest care level					
Outpatient	275 (72%)	32 (38%)	69 (73%)	111 (87%)	63 (84%)
Hospitalisation in general ward	73 (19%)	26 (31%)	19 (20%)	16 (13%)	12 (16%)
Intensive care unit§	34 (9%)	27 (32%)	6 (6%)	1 (1%)	0
Ultimate Outcome					
Death§	27 (7%)	23 (27%)	4 (4%)	0	0

15%

	Total (n=382)	CD4 <100 cells per mm³* (n=85)	CD4 100–200 cells per mm³ (n=94)	CD4 201–300 cells per mm³ (n=128)	CD4 >300 cells per mm³ (n=75)
(Continued from previous page)					
Antimicrobial and antiviral treatment					
Antibiotics	144 (38%)	52 (61%)	34 (36%)	38 (30%)	20 (27%)
Tecovirimat (oral)	52 (14%)	21 (25%)	11 (12%)	15 (12%)	5 (7%)
Tecovirimat (intravenous)	15 (4%)	13 (15%)	1 (1%)	1 (1%)	0
Intravenous immune globulin	6 (2%)	6 (7%)	0	0	0
Cidofovir or brincidofovir	7 (2%)	5 (6%)	2 (2%)	0	0
Genotypic resistance to tecovirimat, n					
Samples sequenced	5	4	1	0	0
Presence of F13L mutations conferring resistance	3	3	0	0	0
Immune restitution inflammatory syndrome					
Antiretroviral started or restarted	85 (22%)	40 (47%)	23 (24%)	15 (12%)	7 (9%)
Deterioration consistent with immune restitution inflammatory syndrome	21 (5%)	15 (18%)	6 (6%)	0	0
Immune restitution inflammatory syndrome treatment provided	19 (5%)	14 (16%)	5 (5%)	..	..

Ninguna persona que falleció había recibido vacuna

10 personas con menos de 200 CD4 fallecieron a pesar de haber cumplido uno o dos cursos completos de tecovirimat

3 casos de resistencia documentada

Se sospechó síndrome de reconstitución inmune en 21 de 85 personas que iniciaron tratamiento

12/21 personas con sospecha de SRI fallecieron

- **Mejorar diagnóstico de VIH**
- **Mejorar vacunación**
- **Estudiar SIR**

Antivirales

Estudios en marcha (STOMP, PLATINIUM, PALM007 y UNITY) en marcha para evaluar la eficacia de Tecovirimat vs placebo en humanos. El studio PROTECT-HUGTiP específico para personas con enfermedad avanzada por VIH

Tecovirimat

- Aprovado para el tratamiento de viruela en USA y Canada.
- Aprovado para MPOX por la EMA bajo 'circunstancias excepcionales'.
- La OMS recomienda que si se utiliza debe aplicarse el marco **Meuri (del inglés Monitored Emergency Use of Unregistered and Experimental Interventions)**

Uso excepcional en algunos casos en Brasil, Chile, Costa Rica y Argentina mediante pequeñas donaciones de OMS, SIGA o el CDC

La OPS está trabajando con países para efectivizar la donación de 2160 cursos completes de tecovirimat, para ser usados bajo el marco MEURI y un protocol específico

OPS Organización Panamericana de la Salud | Organización Mundial de la Salud Américas

OPS 120 ANIVERSARIO

En resumen

- La vasta mayoría de los casos son hombres, mayormente HSH, 52% PVVIH
- Se observa una disminución global de casos, y al menos en nuestra región esto no se asocia a campañas de vacunación
- La carga de enfermedad, gravedad clínica, mortalidad es mucho mayor en personas viviendo con VIH con menos de 200 CD4, y en particular con menos de 100
- Todavía no hay datos de eficacia de tecovirimat ni de las otras medidas potencialmente terapeuticas (cidofovir, brincidofovir, inmunoglobulinas)
- Se han documentado casos de fracaso y emergencia de resistencia con tecovirimat

Desafios

- Búsqueda de contactos
- Transmisión comunitaria considerando los casos asintomáticos
- Riesgo de zoonosis
- Prevención en grupos vulnerables

Nuevas preguntas

- Duración de la inmunidad y riesgo de reinfección
- Tratamientos combinados para evitar la resistencia
- Estudios de vigilancia centinela
- Sindrome de reconstitución immune en VIH Avanzado
- VS como enfermedad oportunista

Muchas gracias!

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