IMMUNE RESPONSES AND VIRAL DYNAMICS AFTER MONKEYPOX INFECTION IN THE 2022 OUTBREAK

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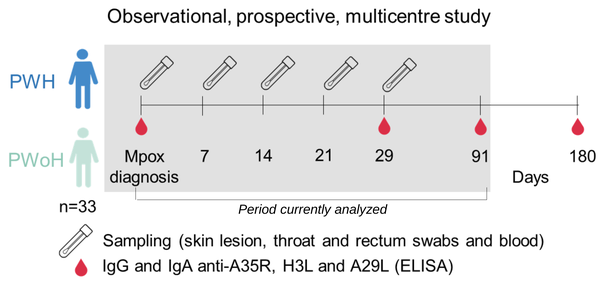
BACKGROUND

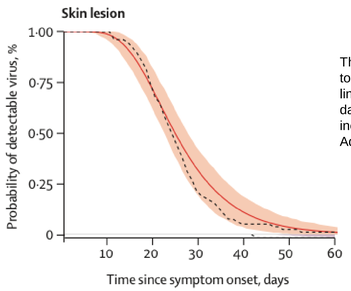
- Human immunity to Monkeypox infection (Mpox) has not been extensively characterized in people with HIV (PWH).

Here, we analyzed antibody responses in PWH and people without HIV (PWoH) diagnosed with Mpox during the 2022 outbreak in Barcelona, Spain, who had been enrolled in the MoViE study (NCT05476744).

METHODS



- DNA viral decay and time from symptom onset to viral clearance were modelled using Monolix 2019 R2 software.



The simulated means and 95% CIs of time to viral clearance are shown as a solid lines and shaded area, respectively. The dashed line represents the cumulative incidence calculated on the observed data. Adapted from *Suñer et al, Lancet ID 2022*

- A severity score was developed based on signs and symptoms.

Parameter description	Severity Score (SS)
Local skin lesions	
1	1
2-5	2
>5	3
Distal lesions	
1-4	1
5-20	2
>20	3
Proctitis	3
Fever (>38ºC)	2
Systemic symptoms*	1 for each

Examples of Severity Score for distinct individuals:



SS=4
2-5 Local skin lesions
1-4 Distal skin lesions
Lymphadenopathy

SS=9
Proctitis
1-4 Distal skin lesions
Lymphadenopathy
Asthenia
Myalgia/Arthralgia
Malaise
Fever

SS=14
>5 Local skin lesions
>20 Distal skin lesions
Lymphadenopathy
Asthenia
Headache
Malaise
Pharyngitis
Tonsillitis
Fever

*Malaise, arthralgia/myalgia, asthenia, headache, vomiting, abdominal pain, lymphadenopathy, pharyngitis, tonsillitis, etc

RESULTS

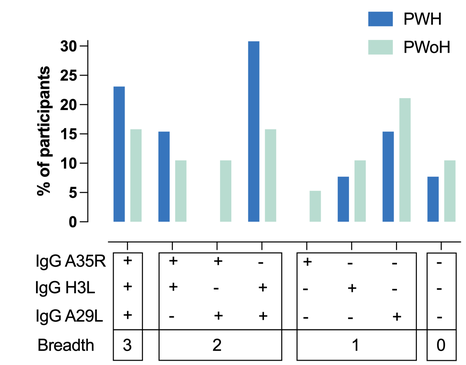
1. Demographic and clinical characteristics

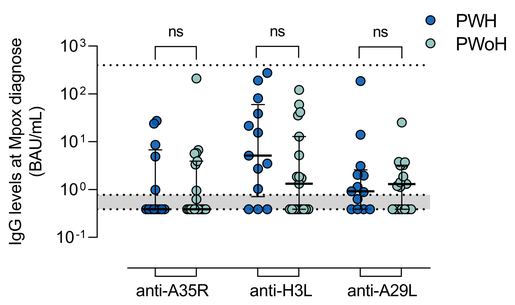
N=33, all male	PWH (n=14, 42%)	PWoH (n=19, 57%)	*P*-value
Age	40 (25-58)	33 (26-56)	0.1768
≥49 years; n (%)	5 (34%)	5 (26%)	
Country of birth; n (%)			0.8833
Spain	6 (43%)	9 (47%)	
Other European countries	4 (28%)	4 (21%)	
Latin America	4 (28%)	6 (32%)	
Previous STI; n (%)	7 (50%)	8 (42%)	0.6526
Concomitant STI; n (%)	6 (43%)	3 (16%)	**0.0484**
Current CD4	777 (**484**-1533)	NA	
ART-suppressed; n (%)	11 (**78%**)	NA	
Days since symptoms onset (SO)	6 (1-10)	5 (3-9)	0.8629
Severity Score (SS)	**9** (5-13)	**9** (4-14)	0.5233
Viral load at skin lesion (log10 DNA copies/mL)	7 (2.9-8.8)	7.2 (5.4-8.5)	0.6727
Time to viral clearance at skin lesion (days)	24 (12-40)	29 (18-55)	0.0784

Data are expressed as median (minimun-maximun) except where specified. PWH = people with HIV; PWoH = people without HIV; STI = sexually transmitted infection; ART = anitretroviral treatment

2. IgG titers at Mpox diagnosis

- Close to 90% of participants had detectable levels of at least one type of IgG at Mpox diagnosis
- Same breadth and IgG titers between PWH and PWoH

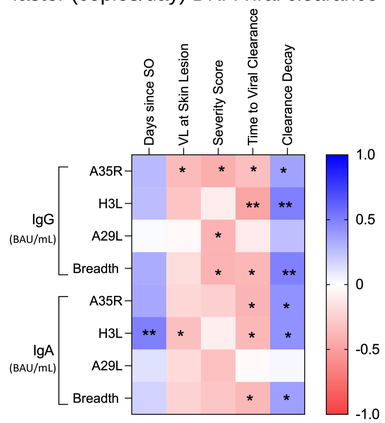




n= 14 PWH and n= 19 PWoH. Mann-Whitney tests were used to compare between 2 different groups. ns= not significant

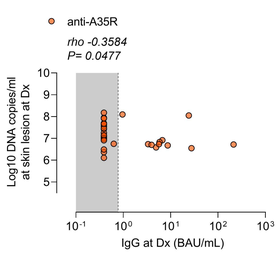
3. Preliminary Correlate Analysis

- Higher titers of anti-A35R IgG at Mpox diagnose were observed in participants with high viremic skin lesions.
- A rapid strong and polyclonal response was associated with better clinical outcomes:
  - milder presentation (lower SS),
  - shorter time to viral clearance (days) and
  - faster (copies/day) DNA viral clearance

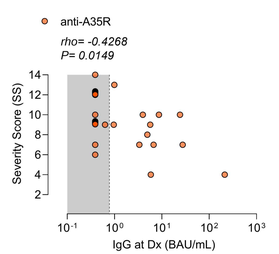


n= 32. Spearman's ρ is used for correlations. All tests are 2-sided, unadjusted for multiple comparisons, with 5% error rate. Significant correlations are shown by *$P \leq 0.05$ and ** $P \leq 0.01$.

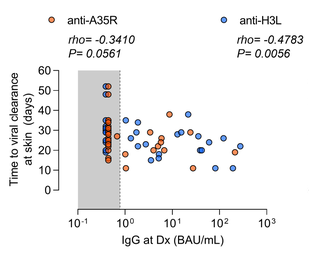
Viral Load at skin lesion



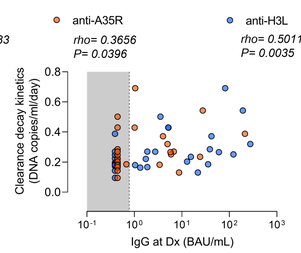
Severity Score



Time to viral clearance



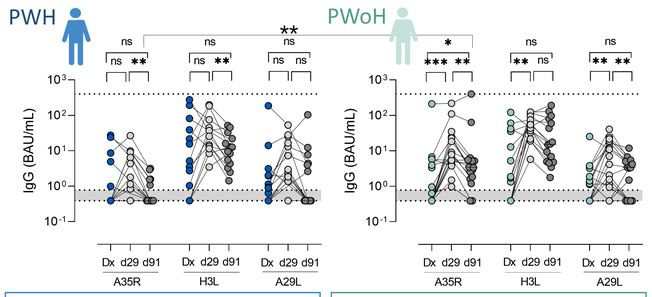
Clearance decay kinetics



n= 32. Spearman's ρ is used for correlations. All tests are 2-sided, unadjusted for multiple comparisons, with 5% error rate. Participants with determination below the limit of quantification for the anti-A35 and anti-H3 IgG (0,78 AU/mL) are represented in the gray area.

4. Longitudinal Analysis

- PWH showed lower increase and less durable levels of IgG at 29 and 91 days after Mpox diagnose, respectively, than PWoH.

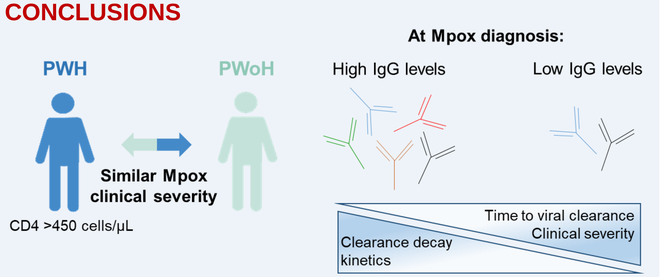


Fold Change		A35R	H3L	A29L
d29	Median	x3	x9	x4
	Range	(1-11)	(2-34)	(2-14)
d91	Median	x1	x2	x1
	Range	(0-1)	(0-21)	(0-4)

Fold Change		A35R	H3L	A29L
d29	Median	x12	x36	x5
	Range	(2-30)	(3-107)	(1-13)
d91	Median	x6	x10	x1
	Range	(1-11)	(1-62)	(1-4)

n= 14 PWH and n= 19 PWoH. Wilcoxon tests were used to compare between 2 different time points within same participant. ns= not significant. *$P \leq 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$.

CONCLUSIONS



- **PWH with good CD4 T cell counts showed similar severity than PWoH.**
- **Milder clinical presentation and shorter viral clearance at skin lesions were associated with a fast and polyclonal IgG and IgA response.**
- **However, a rapid loss of IgG after Mpox might pose PWH at a higher risk of re-infection and warrants further investigation to inform vaccination policies.**

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