KINETICS OF HUMORAL AND CELLULAR IMMUNITY UP TO 3 YEARS AFTER MVA-BN VACCINATION

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BACKGROUND

The ongoing mpox epidemic and the limited vaccine supply have raised concerns about the long-term effectiveness of the primary MVA-BN vaccination schedule. We evaluated humoral and T-cell immune responses up to three years after MVA-BN vaccination, according to prior smallpox immunisation.

METHODS

Blood samples from individuals receiving a primary MVA-BN cycle (two doses for smallpox-naïve, one dose for previously vaccinated) were prospectively collected at each administration (T1 and/or T2) and at 1 (T2/T3), 6 (T4), 12 (T5), 24 (T6), and 36 (T7) months thereafter. Mpox virus-specific neutralising antibodies (nAbs) were measured by a 50% plaque reduction neutralisation test, and interferon-γ–producing MVA-BN–specific T cells by ELISpot. Statistical analyses included Kruskal–Wallis, Wilcoxon, and Mann–Whitney tests.

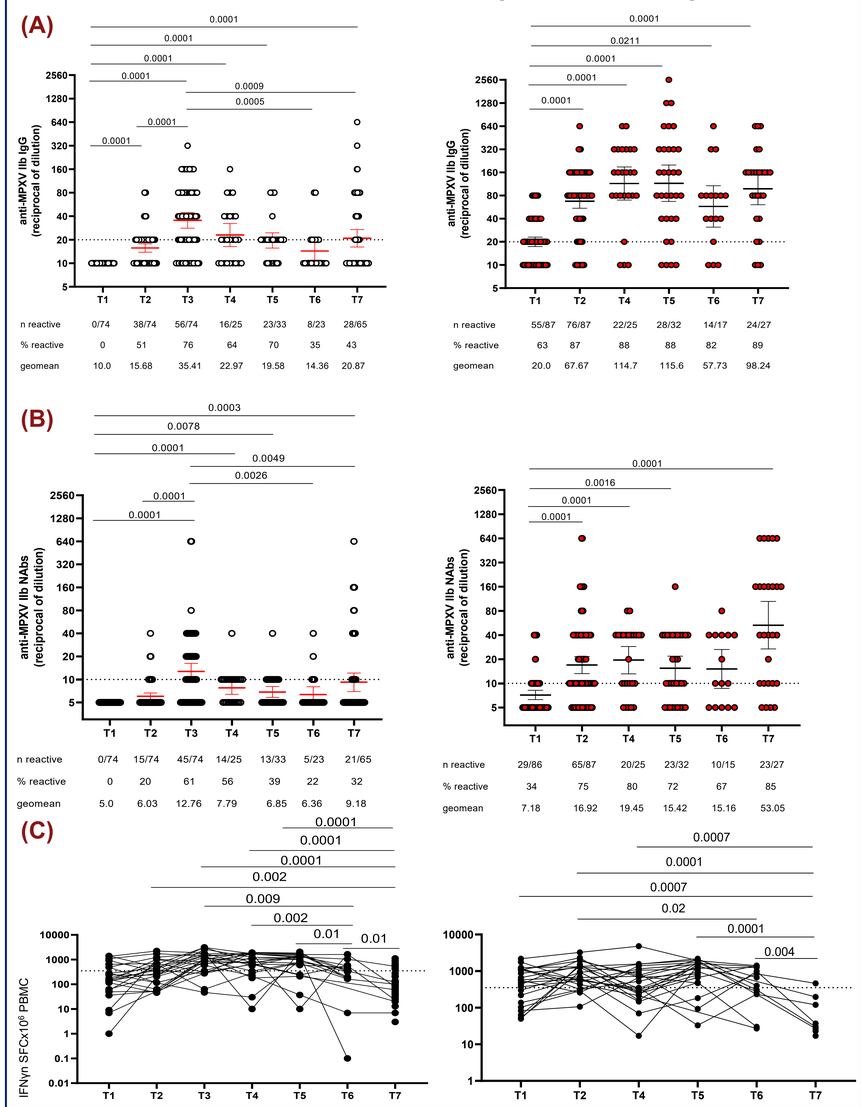
Table 1. Main characteristics of the study population

Characteristics	Overall (N=102)	Vaccine naive (N=95)	Vaccine experienced (N=7)	p-value[1]
Male at birth	102 (100%)	95 (100%)	7 (100%)	0,731
Age[2]	56,6 [53,6-61,1]	43,8 [34,6;47,3]	58,7 [57,5;60,3]	<0,001
Risk factor				0,093
Living with HIV	53 (52,0%)	50 (52,6%)	3 (43,9%)	
On PrEP	49 (48,0%)	45 (47,4%)	4 (56,1%)	
CD4 T-cells at vaccination[3]				0,278
<500	9 (17,0%)	9 (18,0%)	0 (0%)	
>500	44 (83,0%)	41 (82,0%)	3 (100%)	
Undetectable viral load at vaccination[3]	53 (100%)	53 (100%)	3 (100%)	Nd
Route of administration of the primary vaccination cycle				0,267
Subcutaneous	84 (82,5%)	77 (81,0%)	7 (100%)	
Intradermal	18 (17,5%)	18 (19,0%)	0 (0%)	

Nd = not determinable; [1]Wilcoxon-Mann-Witheny U test, Fisher's Exact test; [2]median [Q1;Q2]; [3]among people living with HIV

Three years after MVA-BN vaccination, the immune response wanes overall, especially in smallpox vaccine-naïve individuals, in whom antibody titers are largely undetectable, suggesting the need for a booster to enhance immunity in this group.

FIGURE 1. Longitudinal evaluation of MPXV-specific IgG (A), neutralising antibodies (nAbs) (B) and MVA-BN T-cells specific response (C) in vaccine-naïve and experienced individuals three years after the primary cycle.



Dot lines represent the detection limit for IgG (1:20), nAbs (1:10) and median values of T-cell response evaluated in 10 healthy controls matched for age and sex. Geometric mean IgG and nAbs titers (GMT-95% CI) are shown for each time range or study group.

RESULTS

We enrolled 102 men who have sex with men (MSM), median age 56.6 years (IQR 53.6–61.1); 6.7% had a history of childhood smallpox vaccination. Fifty-three (52%) were people living with HIV, mostly (83%) with CD4 > 500/mm³. IgG and nAb titres peaked one month after primary MVA-BN vaccination in both vaccine-naïve and previously smallpox-vaccinated participants. Thereafter, titers declined markedly in naïve individuals, with geometric mean titres falling below the detection threshold in most cases. In contrast, previously vaccinated participants maintained a robust humoral response (Figure 1A-B).

MVA-BN–specific T-cell responses followed a similar pattern in both groups: after the early rise, responses decreased substantially over time, starting to wane one year after the primary cycle up to the last timepoint, both in naïve and experienced groups (Fig. 1C). At three years, most participants were below the limit of detection (the median value detected in healthy donors).

CONCLUSIONS

Three years after primary MVA-BN vaccination, both humoral and cellular immunity waned substantially in smallpox-naïve individuals. In contrast, people with prior smallpox immunisation showed sustained antibody levels. T-cell response wanes in both groups. These findings suggest that smallpox-naïve populations may benefit from booster dosing to maintain long-term protection, whereas previously vaccinated individuals appear to preserve durable immunity.

PLAIN LANGUAGE SUMMARY

Three years after the mpox vaccine, antibodies dropped to very low or undetectable levels in most people who had not previously received the smallpox vaccine. People vaccinated against smallpox years ago kept higher antibody levels. Immune cell responses also decreased over time in both groups, suggesting that a booster may help maintain longer-term protection in smallpox-naïve individuals.

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