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Letter to the Editor

Mpox Immune response elicited by MVA-BN vaccine over 12 months of follow-up

Dear Editor,

In this Journal, Raccagni et al. reported 23 breakthrough mpox infections following previous smallpox or recent MVA-BN vaccination, raising the question of how long immune protection conferred by vaccination lasts.[1] To date, more than 100,000 mpox cases have been reported.[2] Currently, the rise of new cases in Africa, with the spread of the new MPXV Clade Ib together with the Clade IIb, led the World Health Organization to declare mpox as a public health emergency of international concern again.[3]

Modified-Vaccinia-Ankara Bavarian Nordic (MVA-BN) vaccine has been recommended to tackle the epidemic. According to epidemiological models, its effectiveness ranged between 36–86%.[4–7] MVA-BN was reported to be safe and immunogenic early after vaccination[8] and to elicit a strong cellular response, while a moderate humoral one.[9,10] Raising concerns about the possible spread of a new epidemic have posed the question of protection persistence after vaccination, but limited data are available on the duration of immunity.[11] Here, we describe the kinetics of humoral and cellular immune responses up to one year after vaccination.

Fifty high-risk people vaccinated at the Lazzaro Spallanzani Institute in Rome, Italy, during the 2022–2023 outbreak were included. All were men, with 94% self-reporting having sex with men. The median age was 50 years (IQR 45–57), and 21 (42%) were people living with HIV (PLWH), all on antiretroviral therapy, and 71% with a CD4 cell count higher than 500 μL. 25 (50%) have been primed with previous smallpox vaccination and received a single-dose course of immunization (Appendix 1). Blood samples were prospectively collected at the time of each dose administration (T1-T2) and then one (T3), six (T4), and twelve (T5) months from vaccination. Protocol and laboratory assays were previously described [8] (Appendix 2).

In non-primed people, anti-MPXV IgG titers significantly increased from T1 to T3 and, despite a slight reduction, were still higher than T1 up to T4 and then gradually decreased until T5, when 64% of sera were still reactive (Appendix 3). MPXV-nAb titers peaked at T3 and then dropped, with 56% and 32% of sera reactive at T4 and T5, respectively. IFN-γ production by MVA-BN-specific T-cells progressively rose across time, peaked at T3, and remained significantly higher than the baseline after 6 and 12 months from vaccination. (Fig. 1).

Furthermore, a single-dose course of MVA-BN vaccination in smallpox-primed participants elicited an early increase in IgG and nAb titers, which remained significantly higher than baseline after 6 and 12 months (Fig. 1 and Appendix 3). Notably, MPXV-nAbs were detected in 80% and 72% of vaccinees at T4 and T5, respectively. We observed a similar improvement and maintenance in the MVA-BN-specific T-cell response (Fig. 1). No evidence for a difference in both humoral and cellular responses was found between PLWH and PLWoH in our cohort (Appendix 4). Limitations are stated in Appendix 5.

One year after vaccination, our data showed the persistent detectability of low levels of nAb against MPXV in one-third of non-primed individuals. At the same time, humoral response was still detectable in most previously vaccinated participants. Concurrently, the MVA-BN-specific T-cell response was robust and persistent. Whether this T-cell response can contribute to ensuring long-term protection against mpox, even in individuals with a significant reduction in the humoral response, remains to be demonstrated. This will be better clarified through epidemiological studies and longer follow-ups of vaccinated individuals. These data may be informative for public health recommendations on the need and time for booster doses after a primary course of MVA-BN.

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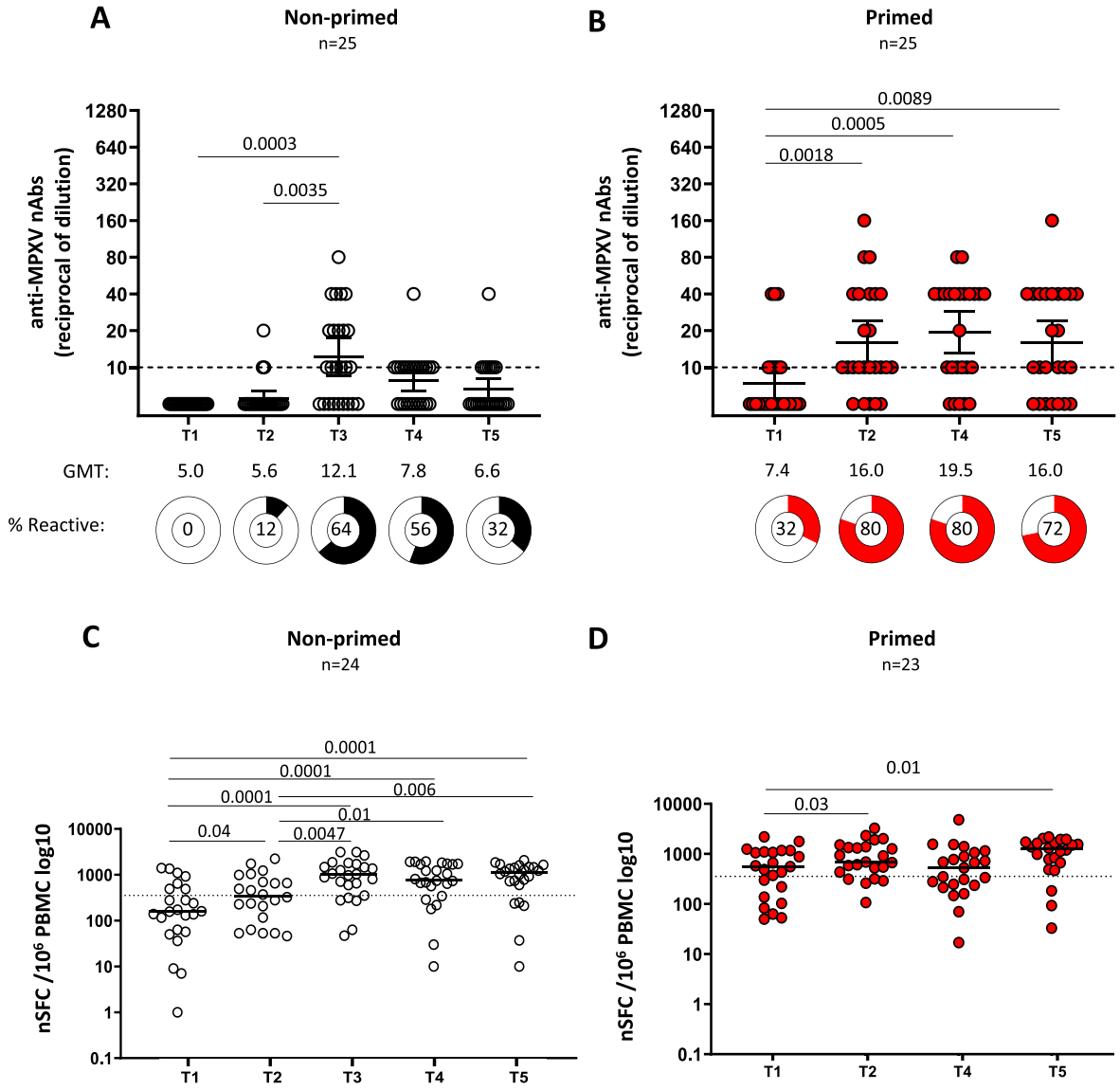

Fig. 1. Kinetics of the neutralizing and cellular immune response in non-primed and primed MVA-BN vaccinated individuals. Panels A and B show the kinetics of anti-MPXV neutralizing antibody levels. The Dot line represents the limit of the assay detection, GMT= geometric mean titre. Panels C and D show the kinetics of T-cell-specific response after stimulation with MVA-BN. Black dots represent non-primed individuals; red dots represent primed individuals. Friedman and Wilcoxon's tests were used for statistical comparisons.

Declaration of Competing Interest

The authors GM, VM, EC, FV and FM declare no conflict of interest.

AA received honoraria for presentation at IAS conference from Bavaria Nordic.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106309.

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