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P0398 Anamnestic response after antigen re-exposure following Ebola vaccine regimen with Ad26.ZEBOV and MVA-BN-Filo in a phase I study

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Background: The West African 2014–16 Ebola epidemic highlights the need for vaccines providing long-term protection. Heterologous Ebola vaccine regimens based on Ad26.ZEBOV (Ad26) and MVA-BN®-Filo (MVA) are in development.

We report a phase 1 study (EBL1002) evaluating safety and immunogenicity of heterologous and homologous 2-dose Ad26, MVA primary series and a 3rd dose using Ad26 or MVA one year after initial vaccination in healthy adults in USA.

Materials/methods: In this randomized, placebo-controlled study, volunteers (aged ≥18 to ≤50) were randomized and vaccinated with Ad26 or MVA on day 1, followed by the alternate vaccine on day 8,15,29 or 57 (day 57 only for MVA, Ad26). A booster dose using Ad26 or MVA was administered at day 360 (n=82). Serious adverse events (AEs) were assessed until end of study, AEs until 21 days post-dose 2 and booster dose and solicited AEs until 7 days post-dose. Humoral and cellular immune responses were assessed by EBOV GP FANG ELISA for binding antibodies and IFNγ Elispot and Intracellular Cytokine Staining for GP specific T cells.

Results: In total, 163 volunteers were vaccinated (n=137 active vaccine; n=26 placebo).

All vaccination schedules were well tolerated.

Responses (defined as 3x over positive baseline or >Limit of Detection if baseline negative) were observed 21 days post-dose 2 in all heterologous regimens; all participants developed anti-EBOV GP IgG (GMC:1271–14048 EU/ml) and 44–93% developed IFNγ T cell responses. Although responses declined after peak response, both humoral and cellular responses were maintained and detectable at Day 360.

A booster vaccination with Ad26 on Day 360 induced a marked increase of binding antibody levels 7 days later, higher than peak responses observed post-dose 2, that increased until 21 days post-booster dose (GMC:26823–82561 EU/ml). After day 381, response levels gradually decreased but remained 1.6- to 5.8-fold higher at Day 720 compared to 1 year post-prime with binding antibody responses observed in 91%–100% of subjects (GMC:2449–9668 EU/ml).

Conclusions: Ad26, MVA vaccine regimens were well tolerated, consistent with previous phase 1 findings. They induced strong humoral memory response that could be rapidly boosted with a third dose of vaccine.

Figure 1: **Anamnestic Response after 3rd Dose Vaccination on Day 360 Following 2-Dose Regimen with Ad26, MVA in 28-Day Interval (EBL1002; US; $ELISA_{Battelle}$, N=15)**