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O1059 Safety and immunogenicity of a 2-dose Ebola vaccine regimen with Ad26.ZEBOV and MVA-BN-Filo in a Phase III clinical trial in Sierra Leone

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Background: The West African 2014–16 Ebola epidemic highlights the need for safe and effective Ebola vaccines for at-risk populations. A 2-dose prophylactic Ebola vaccine regimen based on Ad26.ZEBOV (Ad26) and MVA-BN®-Filo (MVA) is in Phase 3 development.

We report a Phase 3 study (EBL3001) funded by the European Commission Innovative Medicines Initiative under EBOVAC 1, evaluating the safety and immunogenicity of this regimen in healthy adults in Sierra Leone.

Materials/methods: In this two-stage study (Stage 1: Open-label; Stage 2: Randomized, double-blind, controlled) adults aged ≥18 years with no Ebola vaccination or infection history were vaccinated with Ad26 (dose 1) followed by MVA (dose 2) 56 days later in Kambia District, Sierra Leone.

Serious adverse events (AEs) were assessed until end of study, AEs until 28 days post-dose and solicited AEs until 7 days post-dose.

Humoral responses (measured by EBOV GP FANG ELISA) were evaluated at baseline, pre-dose 2, 21 days post-dose 2 and 1 year post-dose 1.

Results: A total of 443 healthy adults (Stage 1:N=43; Stage 2:N=400) were vaccinated with Ad26, MVA regimen (N=341) or MenACWY placebo (N=102).

Overall, the Ad26, MVA (0, 56) regimen was well tolerated with no significant safety signals. The majority of solicited AEs were mild-to-moderate. Serious AEs were reported in 8 subjects (2.5%) receiving Ad26, MVA (none vaccine related) and 3 subjects (2.9%) with placebo.

At baseline, 176 (59.5%) subjects were positive for Ebola Zaire antibodies, of whom 24–33% had antibody levels >100 EU/mL. A robust immune response was observed in those given Ad26, MVA with 98% responders (defined as 2.5x over positive baseline or 2.5x over LLOQ) post-dose 2 (GMC:3810-4784 EU/ml) representing a ~41–58 fold increase from baseline. No clear correlation was observed between baseline ELISA values and 21 days post-dose 2 response. Antibody responses persisted up to at least day 360.

Conclusions: The Ad26, MVA (0, 56) vaccine regimen was well tolerated in adults in a country previously affected by Ebola. Robust and persistent immune responses to the vaccine regimen were observed. Ad26, MVA vaccine regimens may be suitable for vaccination strategies in countries susceptible to Ebola outbreaks.