Safety and Immunogenicity of an Accelerated Two-Dose Ebola Vaccine Regimens

MAJ Gina L. Griffith[1], Betty Mwesigwa[2], COL Julie A. Ake[1]

[1] U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, Maryland, USA
[2] Makerere University Walter Reed Project, Kampala, Uganda

Summary: Given the rapid onset of Ebola Viral Disease (EVD) outbreaks, first responders and deploying military personnel may benefit from accelerated Ebola vaccine regimens. EVD occurs in areas of HIV endemicity, prompting vaccine evaluation in people living with HIV (PLH). In RV456/EBL2003, we conducted a two-part Phase 2 randomized placebo-controlled trial to assess the safety and immunogenicity of accelerated two-dose Ebola vaccine regimens in PLH and HIV uninfected populations.

Methods-Results: RV456/EBL2003 was conducted in two sequential parts. Part 1 enrolled 75 US participants (50 people living without HIV (PWOH) and 25 PLH) randomized 4:1 to receive intramuscular injection of MVA-BN-Filo (1×10^8 Inf.U) then Ad26.ZEBOV (5×10^{10} viral particles) 14 days apart or 2 doses of placebo 14 days apart. Part 2 enrolled a total of 499 participants in two groups at sites in Uganda, Mozambique, Nigeria, Tanzania, and Kenya. Group 1 included 200 HIV PWOH and 200 PLH randomized 4:1 to receive AD26.ZEBOV then MVA-BN-Filo 28 days apart or 2 doses of placebo 28 days apart. Group 2 included 49 PWOH and 50 PLH randomized to receive MVA-BN-Filo then Ad26.ZEBOV 14 days apart or placebo 14 days apart. Safety was determined by collection of solicited/unsolicited adverse events (AEs) and safety laboratory testing. Immunogenicity was assessed by evaluation of the EBOV glycoprotein (GP) specific binding antibodies (bAb) measured by FANG ELISA. CD4+ and CD8+ T cell responses were measured against EBOV GP by intracellular cytokine staining.

Part 1 participants were 37% female (mean age 44 years); part 2 participants were 52% female (mean age 33 years). Both regimens were safe with mild/moderate solicited AEs with no deaths or vaccine related serious AEs. Part 1 EBOV GP-specific bAb responder rates were very high (95%) in PLH as well as PWOH (100%), with slightly lower geometric mean concentrations (2005 EU/mL and 6286 EU/mL, respectively). This pattern was observed in Part 2, in which GMCs were also slightly higher in the 28 vs. 14-day regimen. Both accelerated schedules induced a durable polyfunctional T-cell response with balanced Ebola specific CD4+ and CD8+ components.

Conclusions: The compressed vaccine schedules studied in this trial were found to be well-tolerated and immunogenic in adults living with and without HIV.