

Phase 1 Safety and Immunogenicity of an Attenuated VesiculoVax™ Vectored EBOV Vaccine

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Viral hemorrhagic fevers (VHFs) are a group of infectious diseases with common symptoms in humans. The causative viruses affect the vascular system and can cause a hemorrhagic fever characterized by edema, hypotension, shock, and multi-organ failure. The hemorrhagic fever viruses include members of the *Filoviridae*, *Bunyaviridae*, *Flaviviridae*, and *Arenaviridae* families. Profectus BioSciences is developing vaccines to protect against the major VHF viruses using the VesiculoVax™ vector platform. The platform uses live, replication-competent, attenuated, vesiculoviruses to safely deliver the surface glycoproteins (GP) from VHF viruses. The prototype vector is an Indiana serotype vesicular stomatitis virus attenuated by “shuffling” of the N gene to position 4 in the genome, and truncation of the cytoplasmic tail of the G protein (rVSVN4CT1). The rVSVN4CT1 vector has been used to create a trivalent vaccine that has been shown to provide single dose protection of NHPs challenged intramuscularly (IM) with low-passage isolates of EBOV(Kikwit), SUDV(Gulu), and MARV(Angola). Here we present interim safety and immunogenicity data from a phase 1 trial of the mono-valent rVSVN4CT1-EBOV vaccine. This was a randomized, double-blind, placebo-controlled, truncated dose escalation trial evaluating vaccine doses of 2.5×10^4 , 2.5×10^5 , and 2.0×10^6 PFU administered by IM injection in 3 groups of 13 healthy adult subjects (10 active/3 placebo). Subjects were administered two doses of vaccine separated by 28 days. The primary endpoints were measures of safety, and the secondary endpoints were measures of cellular and humoral immune responses to the EBOV GP. Although the data from this trial remain blinded with respect to the subjects receiving vaccine vs. placebo, adverse events (AE) across all dose groups were generally mild. The most common AEs were injection site pain followed by fatigue. Notably, there were no reports of the arthritis and skin vesicles attributed to peripheral viral replication seen with an EBOV vaccine vectored with non-attenuated VSV. Anti-EBOV GP-specific antibody responses as measured by ELISA were detected in 10/13, 9/12, and 10/13 subjects at the 2.5×10^4 , 2.5×10^5 , and 2.0×10^6 PFU dose levels, respectively. Similarly, EBOV GP-specific T cell responses as measured by INF γ -secreting cells detected in an ELISpot assay were detected in 8/13, 8/12, and 9/13 subjects. Thus, the data are consistent with a well-tolerated vaccine that induces antibody responses in 100% of vaccine recipients across all tested dose levels of vaccine. Assays to determine if vaccine virus enters the blood circulation, saliva, or urine are in progress and will be discussed.

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