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Phase I Trials of rVSV Ebola Vaccine in Africa and Europe – Preliminary Report
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ABSTRACT: BACKGROUND: The replication-competent recombinant vesicular stomatitis virus (rVSV)-based vaccine expressing a Zaire Ebola virus (ZEBOV) glycoprotein (GP) was selected for rapid safety and immunogenicity testing prior to its use in West Africa.
METHODS: Three open-label dose-escalation phase I trials and one phase I randomized, double-blind controlled trial were performed to assess safety, tolerability and immunogenicity of rVSV-ZEBOV at various doses in healthy adults in Europe and Africa. One hundred thirty-eight subjects (Geneva: 59, Hamburg: 20, Lambaréné: 39, Kilifi: 20) were injected with doses between 3x105 and 5x107 plaque-forming units (pfu) or placebo.
RESULTS: No vaccine-related serious adverse event occurred. Mild-to-moderate early-onset reactogenicity was frequent but transient (median 1 day). Fever was observed in up to 35% of vaccinees. Vaccine (rVSV) viremia was detected within 3 days in 103/110 (94%) participants receiving ≥ 3x106 pfu; vaccine was not detected in saliva or urine. In the second week after injection, 11/51 (22%) Geneva vaccinees developed arthritis affecting 1-4 joints with pain lasting a median of 8 days (IQR 6-13). Two self-limited cases (2/40; 5%) occurred in Hamburg and Kilifi, respectively. rVSV-ZEBOV was identified in one synovial fluid aspirate and in skin vesicles of 2 other vaccinees, demonstrating peripheral viral replication in the second week after immunization. ZEBOV-GP-specific antibody responses were detected in all participants, with similar GP-binding antibody titers but significantly higher neutralizing antibody titers at higher doses.
CONCLUSIONS: rVSV-ZEBOV is reactogenic but immunogenic after a single dose and warrants further evaluation of its safety and efficacy.

STATEMENT: *We consider our work, Phase I Trials of rVSV Ebola Vaccine in Africa and Europe – Preliminary Report' published on April 1st 2015 in The New England Journal of Medicine to become the paper of the month (POM) because it describes the first-in-human safety and immunogenicity data of the replica-tion competent vaccine platform rVSV (recombinant Vesicular Stomatitis Virus).*
Until now, this vaccine platform had only been evaluated in non-human primates where it showed transient reactogenicity and robust immunogenicity. These findings represent a cornerstone for the vaccine platform, which can be further investigated for other serious infectious diseases currently without effective preventive countermeasures. We here report the first safety and immunogenicity data with an Ebola vaccine candidate expressing Ebola-Glycoprotein (GP) on its surface.

The aim of the work was to rapidly assess the safety of this potential countermeasure against the cur-rent unprecedented and still ongoing Ebola outbreak in West Africa. Up to now, the outbreak has affected over 25.000 individuals with more than 10.000 fatalities.
We demonstrate the well tolerability of the vaccine in African and European volunteers across a wide dose-range. Strikingly, all vaccinees generated Ebola-GP-specific antibodies, including neutralizing antibodies against Ebola. Viremia with the vaccine construct was detectable in the majority of participants, but was self-limited and of short duration.

BACKGROUND: The study was part of a WHO led cooperation: VEBCON (VSV Ebola Consor-tium) partners included the WHO; Institute for Tropical Medicine, University Hospital, Tübingen; Centre de Recherches Medicales de Lambaréné, Gabon; Kenya Medical Research Institute, Kilifi, Kenya; University Medical Center, Hamburg; Geneva University Hospitals; Institute of Virology, Marburg; St George's University of London, GB.
This study was conducted in close collaboration with the Clinical Trial Center North GmbH & Co. KG, the Heinrich-Pette-Institute (Leibniz-Institute for Experimental Virology) and the Bernhard-Nocht-Institute for Tropical Medicine.