



First Safety & Immunogenicity Data from a FIH, Placebo-controlled, Dose-escalation Trial of a Recombinant Vesicular Stomatitis Virus-based Lassa Fever Vaccine in Healthy Adults

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ABSTRACT

IAVI is developing a Lassa Fever vaccine using the attenuated chimeric VSV design (rVSVΔG-LASV-GPC) also used in the licensed Ebola Zaire vaccine, ERVEBO® (Merck). The Lassa virus (LASV) vaccine was generated by replacing the VSV surface G protein with the LASV glycoprotein complex (GPC). Vaccination with 2x10⁵ or 2x10⁷ pfus protected non-human primates from infection with LASV. A Phase 1 clinical trial enrolled 113 participants, 52 in a dose escalation (US) and 61 in a dose expansion (60 in Liberia, 1 in US). The dose escalation is unblinded and the dose expansion remains blinded.

BACKGROUND

Lassa fever (LF) is a severe viral disease endemic to West African countries and estimated to cause 500,000 cases and 10,000 deaths annually.(1) Recent unprecedented large outbreaks in Nigeria highlight the urgency to develop Lassa virus (LASV) vaccines.(1) LASV is a primary cause of hemorrhagic fever. (1) And given the potential for LASV to cause a public health emergency of international concern it was included in the 2018 WHO R&D Blueprint of priority pathogens for which there is urgent need for accelerated research and development of preventative vaccines.(2) Currently, avoidance of the rodents that carry the virus and protective measures when in contact with a LF patient are the mainstays of protection.(3)

METHODS

A total of 52 healthy participants (18-70) at US sites received rVSVΔG-LASV-GPC at IM doses: 2x10⁴ pfu, 2x10⁵ pfu, 2x10⁶ pfu, 2x10⁷ pfu, or placebo. A second dose was given to 11 participants in the 2x10⁷ pfu group between 6-20 weeks. Solicited events were collected for 14 days and unsolicited events for 28 days after vaccination. A total of 60 healthy participants (18-70) at a single site in Liberia (+ 1 in the US) received rVSVΔG-LASV-GPC at IM doses 2x10⁵ pfu, 2x10⁶ pfu or 2x10⁷ pfu or placebo. Solicited events were collected for 14 days and unsolicited events for 28 days after vaccination for all participants.

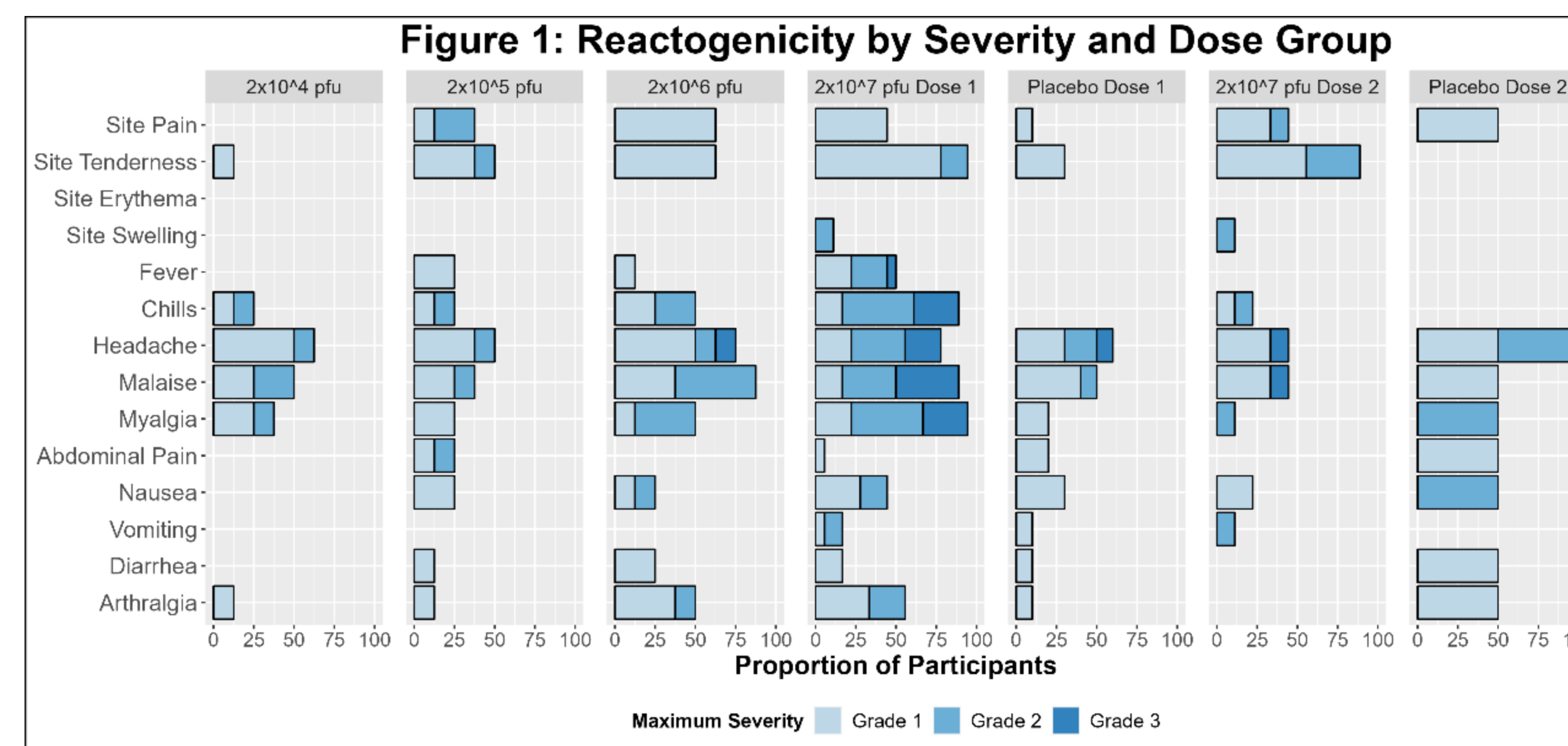
RESULTS

At the time of this presentation, all participants in the Dose Escalation portion of the trial have completed the 12-month follow-up period and the data has been locked and unblinded. The Liberian dose expansion remains ongoing and blinded. An interim review of the Liberian data (not shown) has lower reactogenicity (frequency and severity) and a similar immunology profile.

RESULTS

Solicited adverse events showed increasing frequency and severity as dose increased (Figure 1). Participants in the highest dose group who received a second dose reported decreased frequency and severity of events when compared to the first dose. Grade 3 systemic events were reported in 50% (9/18) of participants in the highest dose group following the first dose. These events started an average of 2.1 days following vaccination and lasted an average of 1.2 days.

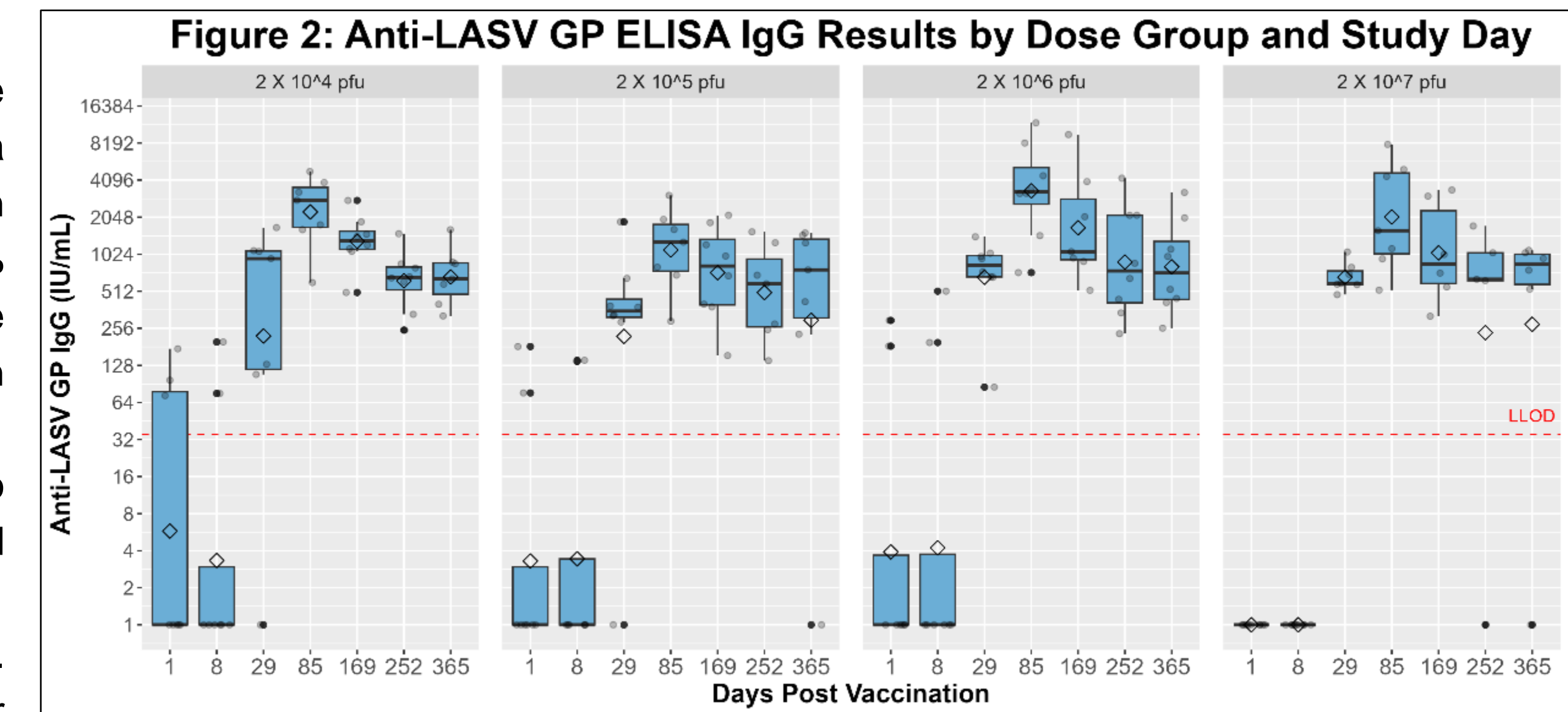
Unsolicited adverse events were reported in 52% (22/42) of participants who received active IP. Unsolicited AEs related to active vaccine were reported among 26% (11/42) of participants who received active vaccine. Only 1 participant who received active vaccine reported a related Grade 3 event. There were no related Serious Adverse Events, AEs of special interest, or hearing loss reported.



The ELISA Anti-LASV-GP binding antibodies were present for all doses by Day 29 and continued to rise through Day 84 before declining and stabilizing by Day 252. The binding antibody response was similar across dose levels (Figure 2).

Neutralizing data (not shown) shows antibodies are present by Day 29 and continue to rise through Day 169 before leveling off and remaining present through Day 252. One year assays continue to be analyzed.

Binding and neutralizing antibodies show cross reactivity across Lineages I, II and III of Lassa Viruses, indicating that the vaccine (which is based on Lineage IV) should be widely effective in West Africa. T cell responses are under study.



DISCUSSION AND CONCLUSION

The rVSVΔG-LASV-GPC vaccine was well tolerated and immunogenic over a wide dose range, from 2x10⁴ pfu to 2x10⁷ pfu. rVSVΔG-LASV-GPC vaccine in both the US and Liberian cohorts.

Binding and neutralizing antibodies were induced by all doses tested, were present at one month, increased at 3 months, and persisted for at least a year. rVSVΔG-LASV-GPC vaccine induced broadly cross-reactive antibodies against LASV Lineages common in Liberia, Sierra Leone and Nigeria.

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