Lassa Fever Vaccine Efficacy and Prevention For West Africa (LEAP4WA)

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Primary objectives

- **To conduct a proof-of-concept clinical trial, evaluating the efficacy of VSVΔG-LASV-GPC for the prevention of laboratory confirmed, symptomatic Lassa fever in a West African LASV-NP seronegative population.**
- **To develop state-of-the-art clinical research capacity in West Africa that can be utilized for other Emerging Infectious Diseases in the future.**

Background

Lassa fever (LF) is a severe viral disease endemic in West African countries with approximately 300,000-500,000 cases and 5,000-10,000 deaths annually. However, these numbers are likely acutely underestimated. Unprecedented recent large outbreaks in Nigeria highlight the urgency to develop Lassa virus (LASV) vaccines[1,2].

An IAVI-led consortium is advancing a Lassa vaccine candidate based on the recombinant vesicular stomatitis virus (rVSV) platform technology. The vaccine candidate demonstrated 100% efficacy against LASV in a nonhuman primate challenge study. Furthermore, it uses the same technology as Merck's ERVEBO® vaccine, which has been shown to be safe and efficacious in preventing Ebola virus disease and is licensed in multiple countries.

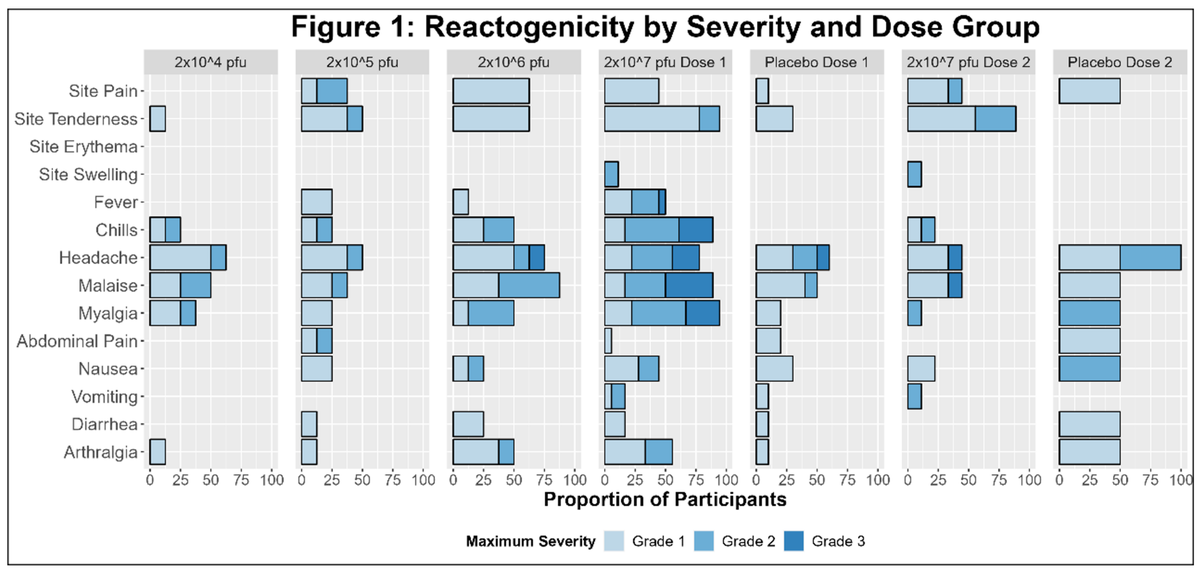
Phase 1 design (C102)

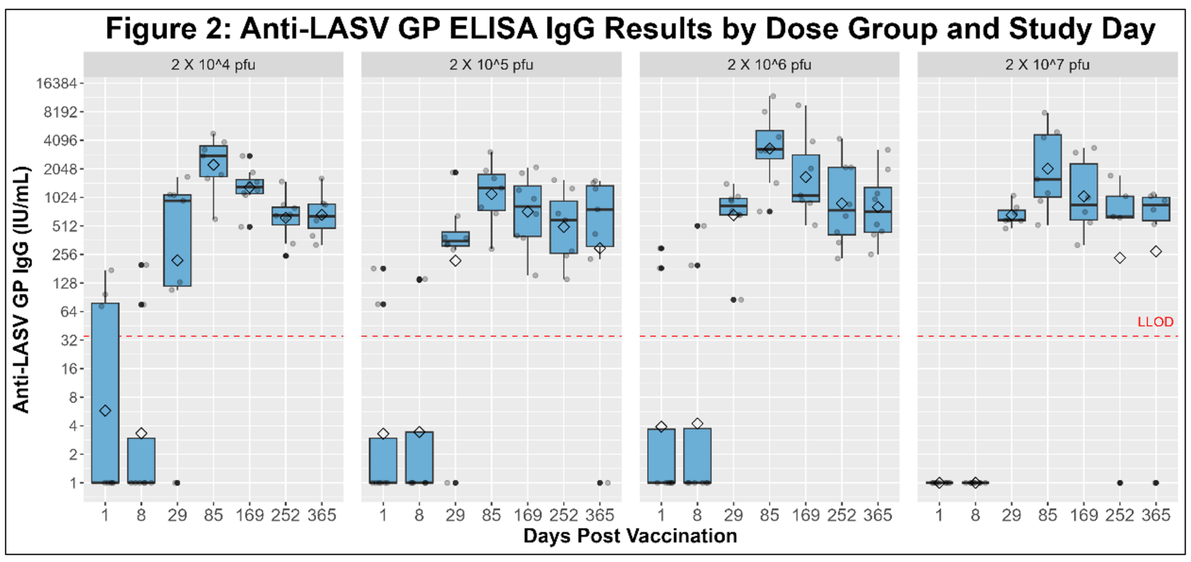
		Study Design	Vaccine Dosage (pfu)	N (Active / Placebo)	Month 0	Week 6
Dose Escalation	US Sites	1	2 10^4	8/2	X	
		2	2 X 10^5	8/2	X	
		3	2 X 10^6	8/2	X	
		4A	2 X 10^7	8/2	X	
		4B	2 X 10^7	8/2	X	X
SMC Review						
Dose Group Expansion	Liberia & US	5	2 X 10^5	16/4	X	
		6	2 X 10^6	16/4	X	
		7	2 X 10^7	16/4	X	
Total = 110 (88/22)						

Table 1 shows the design of the Phase 1 trial which will be complete in Dec 2023.

Safety & Immunogenicity data

A Phase 1 clinical trial enrolled 113 participants, 52 in a dose escalation (US, figure 1&2) and 61 in a dose expansion (60 in Liberia, 1 in US). The dose escalation is unblinded and the dose expansion remains blinded, and safety and immunogenicity data is shown (Figures 1&2, first 52 participants).





Phase 2a study design (C105)

The Phase 2a trial will enroll approximately 612 participants in Nigeria, Liberia and Ghana. This trial will confirm the dose selection and extend the populations covered to older adults, people living with HIV, adolescents and children in good general health, in preparation for a community-based efficacy trial.

Group	Population	Cohort	Day 1 Lower Dose (2x10^6 pfu)	Day 1 Higher Dose (1x10^7 pfu)	N (Active / Placebo)	Laboratory Intensive Subset
1	Healthy Adults, 18-70y	1A	X		96 (80/16)	~24
		1B		X	96 (80/16)	~24
2	HIV-infected Adults, 18-50y	2A	X		30 (25/5)	~12
		2B		X	30 (25/5)	~12
3	Adolescents 12-17y	3A	x		60 (50/10)	~12
		3B		X	60 (50/10)	~12
Data Safety Monitoring Board (DSMN) Review						
4	Children 6-11y	4A	X		60 (50/10)	~12
		4B		X	60 (50/10)	~12
DSMB Review						
5	Children 18mo-5y	5A	X		60 (50/10)	~12
		5B		x	60 (50/10)	~12
Total N = 612 (510/102) / Total Laboratory Intensive Subset = ~144 (~120/~24)						

Phase 2b Efficacy Trial Design C111 (LEAP4WA)

Study cohort	Investigational Vaccine or Licensed Comparator (IM injection)	N	N (Intensive Subset)
Baseline LASV-NP Seronegative	rVSV ΔG-LASV-GPC Vaccine	5,500	~250
	Pneumococcal conjugate vaccine (PCV) Comparator	5,500	~250
Baseline LASV-NP Seropositive	rVSV ΔG-LASV-GPC Vaccine	250	~250
	Pneumococcal conjugate vaccine (PCV) Comparator	250	~250
	Total Approximate Sample Size	11,500	1,000

This study is a proof-of-concept population-based, randomized, blinded efficacy trial in regions with high risk of LASV infection. The study will attempt to gather preliminary estimates of vaccine efficacy against symptomatic LF, hearing loss coincident with LASV infection and hospitalization or death due to LF disease. The study is designed as an endpoint-driven study with a target enrolment of approximately 11,500 participants (5,750 receiving active product and 5,750 comparator vaccine recipients). The study will be stratified by baseline LASV-NP serostatus (11,000 LASV-NP seronegative, and 500 LASV-NP seropositive). This number was calculated as the number of participants needed to observe **25 cases of LF as defined in the primary case definition**.

Conclusions and Key C111 Activities

- **Vaccine elicits strong IgG binding Neutralizing Antibodies**
- **Robust safety and immunogenicity from Phase 1 informed dose selection for Phase 2a**
- **Cross reactivity of vaccine-induced responses to lineages I, II, III and VII confirmed**
- **Site qualification visits completed**
- **SOPs provided; first batch of reagents shipped**
- **Site capacity building and preparation underway, Laboratory Information System (LIMS) being implemented**

LEAP4WA Consortium

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References

1. Asogun DA, et al. Lassa Fever: Epidemiology, Clinical Features, Diagnosis, Management and Prevention. Infect Dis Clin North Am. 2019 Dec;33(4):933-951. doi: 10.1016/j.idc.2019.08.002. PMID: 31668199.
2. https://www.who.int/teams/blueprint