



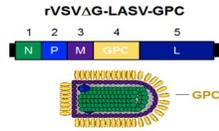
Lassa Fever Vaccine Efficacy and Prevention For West Africa (LEAP4WA)

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Background

Lassa fever (LF) is a severe viral disease endemic in West African countries with approximately 300,000 cases and 5,000-10,000 deaths annually. However, these numbers are likely severely underestimated because of limited disease surveillance. Unprecedented recent large outbreaks in Nigeria further highlight the urgency to develop vaccines against Lassa virus (LASV).

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.



Primary objectives

- To conduct a pivotal clinical trial that will generate proof-of-concept efficacy data to support VSVΔG-LASV-GPC licensure.
- To develop state-of-the-art clinical research capacity in West Africa that can be utilized for other EIDs in the future.

LEAP4WA Partner Consortium

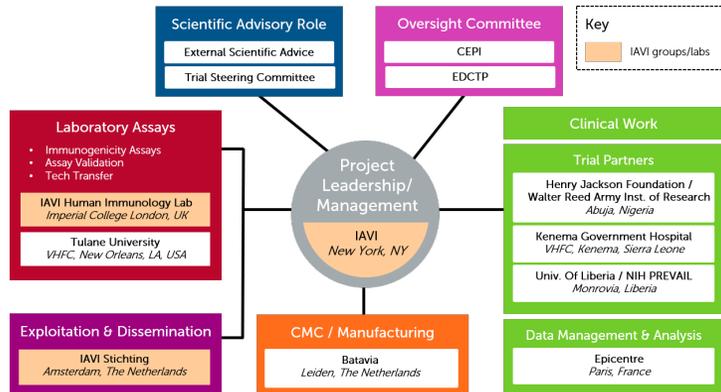


Table 1: Phase 1 design

	Study Design	rVSVΔG-LASV-GPC Vaccine ¹ Dosage (pfu)	N (Active Product/ Placebo)
Dose Escalation	US Sites	1	2 X 10 ⁴
		2	2 X 10 ⁵
		3	2 X 10 ⁶
		4	2 X 10 ⁷
Safety Monitoring Committee Planned Review			
Dose Group Expansion	Liberia (and US sites if needed)	5	2 X 10 ⁵
		6	2 X 10 ⁶
		7	2 X 10 ⁷
Total = 105 (84/21)			

Design and status of Phase 1, 2a, 2b clinical trials

Table 1 shows the design of the phase 1 trial. Dose escalation is currently underway; when complete, enrollment in Liberia will begin. The initial Phase 2a trial will enroll approximately 375 participants in countries where the efficacy trial is planned (Nigeria, Liberia and Sierra Leone). This trial will confirm the dose selection and extend the populations covered to adults, including elders, adolescents and children in good general health, in preparation for a community-based efficacy trial. The phase 2b trial (Table 2) will be conducted in West Africa, with proof-of-concept efficacy as the main outcome.

Table 2: Phase 2b Efficacy Trial design (LEAP4WA)

Population	Study Group	N Main Study	N Substudy ²	N Total	
Seronegative for Lassa Virus	1	rVSVΔG-LASV-GPC Vaccine	2,740	60	2,800
	2	Comparator ¹	1,370	30	1,400
Seropositive for Lassa Virus	3	rVSVΔG-LASV-GPC Vaccine	460	40	500
	4	Comparator	230	20	250

- Comparator is a licensed single-dose vaccine that will benefit this population
- Substudy is an immunogenicity subset of 150 participants, most or all selected from a Health Care Worker population

Lassa Fever Epidemiology

Lassa fever is a viral hemorrhagic virus endemic to West Africa thought to cause thousands of deaths annually in the region. Researchers are hampered by limited knowledge of the virus epidemiology. To address this gap, CEPI and the Wellcome Trust have launched large, population-based epidemiology studies in the region (See Grant et al. at this conference 1, and 2 for more information). These studies propose to enroll up to 31,000 volunteers at seven sites in five West African countries (Figure) with the aim to better understand the incidence of Lassa fever infection, and to characterize the frequency and presentation of Lassa fever. Study enrollment is underway, and initial data are expected in Q4 2021.



Figure: West African countries (blue) participating in current Lassa fever epidemiology studies (left-to-right: Guinea, Sierra Leone, Liberia, Benin, Nigeria)

REFERENCES

- Donald Grant, Henshaw Mandi, J. Gabrielle Bruegelmans "The Enable Lassa Research Programme in West Africa: a major opportunity to strengthen site and investigator capacity to conduct vaccine trials and address Lassa fever knowledge gaps" 10th EDCTP Forum, Maputo, Mozambique, 17 – 21 October 2021
- <https://epi.ighn.org/epidemiology/epi-studies/>

