RV 460 Study: Comparative Adjuvant Study for HIV Env-C DNA and Protein Vaccines in Kenya

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ClinicalTrials.gov ID: NCT04826094

RV460 Project Information

Clinical Site:

- KEMRI/US Army Medical Research Directorate-Africa (USAMRD-A), Clinical Research Centre; Kericho, Kenya. PI: Dr. Josphat Kosgei

IND Sponsor:

- National Institute of Allergy and Infectious Diseases (NIAID) , Division of AIDS (DAIDS)

Funding Source:

- Congressionally Directed Medical Research Program (CDMRP), United States Army Medical Research Acquisition Activity (USAMRAA) - CA# W81XWH-18-2-0040. Dr. Gary Matyas, Award PI

Clinical Phase & Target Population:

- Phase 1; 126 healthy, HIV-negative male and female participants aged 18 to 40 years

Study Initiated in March 2021

Scientific Question

To determine whether these adjuvants improve the immunogenicity of the DNA priming.

ALF43

The dose was 200 µg 3D-PHAD® (synthetic monophosporyl lipid A).

dmLT

A heat-labile enterotoxin B administered at 50 µg/dose on a patch at the site of the DNA injection.

Env-C Plasmid DNA

Clade C gp120 was cloned into pSW3981 vector. The dose administered was 2 mg.

RV460: Adjuvants for DNA Priming *and* Protein Boosting

Dr. Gary Matyas, CA PI

Group	V/P	Prime at Weeks 0, 4, 12	Boost at Weeks 20, 32, 56
1	15/3	DNA alone	gp145 + Rehydragel®
2	15/3	DNA alone	gp145 + ALF43 + Rehydragel®
3	15/3	DNA + dmLT (TCI)	gp145 + Rehydragel®
4	15/3	DNA + dmLT (TCI)	gp145 + ALF43 + Rehydragel®
5	15/3	DNA + ALF43	gp145 + Rehydragel®
6	15/3	DNA + ALF43	gp145 + ALF43 + Rehydragel®
7	15/3	DNA + gp145 + ALF43	DNA + gp145 + ALF43 + Rehydragel®

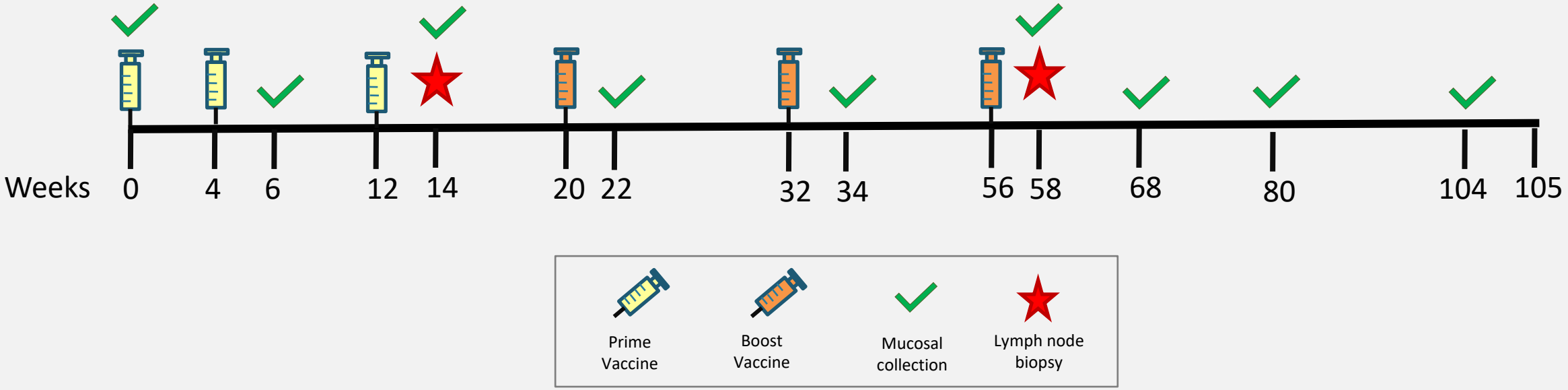
- The vaccines were given by intramuscular injection into the deltoid muscle, excluding the dmLT adjuvant which was given by transcutaneous immunization (TCI).
- RV 460 is the first human trial to evaluate dmLT delivered by TCI.

Trial Objectives

- The **primary objective** of the study is to assess the safety, reactogenicity and tolerability of the various adjuvant formulations with both HIV Env-C Plasmid DNA and gp145.

- The **secondary objectives** are to:
  - Determine whether the adjuvants improve the immunogenicity of the DNA priming.
  - Determine whether the addition of ALF43 to the Rehydragel®/HIV Env gp145 C.6980 protein boost further improves the immune response to gp145 protein.
  - Determine whether adjuvants improve humoral responses.
  - Evaluate cellular immune responses.
  - Evaluate mucosal humoral responses in cervicovaginal and rectal secretions and semen.

Study Procedures



- Each participant is followed for 108 wks (105 wks of clinic visits and then contact by phone weekly for 3 more weeks)
- Optional procedures:
  - Inguinal lymph node excision
  - Mucosal collections

Study Progress

- **Screening and Enrollment:**
  - Screening/consenting started February 2021
  - Enrollment/ vaccination began March 2021
  - Enrollment concluded January 2022

	Male	Female	Total
Screened/Consented	106	172	278
Enrolled	55	82	**137**

- **Demographics:**
  - Median age of 30 years (range 21-40yo), majority female (59.8%), single never married (36.5%)
  - Occupation ranged but largest category farmer (37.2%)

- **Vaccination Summary by Group:**

	Prime Vaccinations			Boost Vaccinations		
Study Group	**Vaccine 1**	**Vaccine 2**	**Vaccine 3**	**Vaccine 4**	**Vaccine 5**	**Vaccine 6**
ITT Total (N= 126 + 11 replacements)	137	121	118	124	118	117

- All vaccinations are complete. Clinical follow-up visits will conclude in January 2024

Local Reactogenicity

Symptom	Prime vaccinations (Vaccines 1,2,3)	Boost Vaccinations (Vaccines 4, 5, 6)
	N=126	**N=126**
Pain/Tenderness	27(21.3%)	26(20.5%)
Swelling/Induration	5(3.9%)	5(3.9%)
Itching	15(11.8%)	6(4.7%)
Redness/Erythema	4(3.1%)	2(1.5%)
Hardness	3(2.2%)	2(1.5%)
Warmth	9(7.1%)	4(3.1%)
Any Local Reaction	35(27.7%)	27(21.3%)

Systemic Reactogenicity

Symptom	Prime vaccinations (Vaccines 1,2,3)	Boost Vaccinations (Vaccines 4, 5, 6)
	N=126	N=126
Systemic		
Headache	48(38%)	22(17.3%)
Temperature	14(11%)	19(15%)
Chills	15(11.8%)	9(7.1%)
Dizziness	21(16.5%)	10(7.9%)
Tiredness/Fatigue	35(27.6%)	9(7.1%)
Nausea	12(9.5%)	5(3.9%)
Muscle pain/myalgia	20(15.7%)	10(7.9%)
Joint pain/arthralgia	15(11.8%)	2(1.5%)
Rash	2(1.5%)	1(0.7%)
Other	1(0.7%)	0
Any Systemic Reaction	66(52.3%)	40(31.6%)

Safety Review

- Reactogenicity and tolerability of the vaccine has been excellent
- No severe or life-threatening local injection or systemic reactions
- 1 Serious adverse event (SAE)
  - Hospitalization for new onset Type 1 diabetes mellitus in 23 yo female in Group 1 (unrelated to study)
- 2 Potentially immune-mediated medical conditions (PIMMCs)
  - Type 1 diabetes mellitus (as noted above)
  - Graves' disease in 27 yo female in Group 3 (unrelated to study)
- No deaths

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All RV460 participants!