Evaluation of candidate VACCINES integrated into outbreak response

Trial designs to evaluate candidate vaccines – immunological studies.

Pontiano Kaleebu (UVRI)

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Tokomeza Immuno

Add-on Study to the Solidarity against Ebola/ Tokomeza Ebola trial protocol.

Study to assess the Laboratory Safety and Immunogenicity profiles of a Sudan ebolavirus vaccine among primary contacts of active cases.

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2025 outbreak

- Ready protocol: Solidarity against Ebola/ Tokomeza Ebola trial protocol Version 4.0 November 10, 2022 had been approved. It remained active.
- Makerere University REC; UNCST and WHO Ethics Review Committee.
- The IAVI rVSVΔG-SEBOV-GP vaccine was already in the country.

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Added immunogenicity

- The Tokomeza-Plus which added the blood safety and immunogenicity had not been approved in 2022.
- We developed this protocol and added it as “Add-on Study to the Solidarity against Ebola/ Tokomeza Ebola trial protocol”. Version 5.0.
- This was therefore behind the main protocol.

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Tokomeza-immune Primary objectives

1. To evaluate the laboratory safety of SUDV vaccine by assessing hematology, clinical chemistry and other soluble biomarkers as needed (e. g. inflammatory parameters).
2. To determine the immunogenicity of the Ebola Sudan Vaccine candidate.

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Secondary objectives

1. To determine the durability of SUDV-specific induced immune responses in the ring trial.
2. To determine the putative cross reactivity exerted by the SUDV vaccine candidate against other ebolaviruses (e.g. *Bundibugyo ebolavirus* (BUDV) and EBOV).
3. To determine whether host factors, viral factors or immune responses are related to clinical outcomes, potentially supporting a correlate of risk or a correlate of protection for SUDV.

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Exploratory objectives

1. To determine the T and B cell specific responses and immune profiling in response to vaccination.

2. To determine the effect of SUDV vaccine on the host metabolome.

3. To determine the effect of SUDV vaccine on host innate immune responses.

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Methodology

Sample size

- All participants in the ring trial willing to consent/assent were to be included in the Tokomeza immuno study.

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Sample collection time points

Blood sampling schedule for participants who provided consent in the immediate and delayed vaccination arms.

	Visits already included in Tokomeza Ebola							New visits for Add-on study					Number of samples
AIM	Assess primary immune response							Assess duration of immunity					
DAY	**0**	**7**	**14**	**21**	**28**	**35**	**42**	**63**	**180**	**201**	**360**	**381**	
Immediate	X	X	X	X	X		X		X		X		Eight
Delayed	X			X	X	X	X	X		X		X	Eight

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Sampling

- All samples from SUDV case primary contacts are potentially infectious and hence a detailed biosafety protocol was developed for the study.
- Sample inactivation protocols were developed and used to inactivate the samples. (If PCR +ve only store).

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Blood sample volumes

- Briefly, for adults, 3x 9ml tubes of EDTA blood as well as 2x 7.5ml serum vacutainer tubes were collected at the baseline at the time points described above.
- For children between 6 and 12 years, the total blood volume collected per visit followed guidelines. For children between 13 and 17 years, similar blood volumes as adult were to be collected.

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Circulating SUDV-specific immunoglobulins

- Serum IgG and IgM antibody titres specific for SUDV GP antigen as detected by ELISA and or MSD Serology.
- Geometric mean titer (GMT); Geometric mean ratio (GMR); antibody concentration.
- A response defined as a significant increase in the ELISA titer post vaccination compared to baseline.

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Antibody neutralization assays

- Serum SUDV neutralizing antibody reciprocal titers as detected by a VSV pseudotype method.
- Geometric mean 50% and 90% titer (GMT); Geometric mean titre fold increase.
- Neutralization breadth (SUDV, Zaire, Bundibugyo).

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Cell-mediated immune responses (CMI)

- Interferon-gamma ELISPOT assays using overlapping peptide libraries as well as whole GP antigen.

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Challenges

- Some cases had moved over wide geographical areas – identifying all contacts took longer than anticipated.
- Samples had to be transported over long distances to processing laboratory.
- High volumes of blood collected caused fear among some participants.

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Other opportunities of conducting these studies during out breaks

- Capacity building to have ready teams, i.e community, clinical and laboratory teams working together
- Safety and immunogenicity data in real-world setting
- Opportunity to identify correlates of protection
- Data and samples for immuno-bridging to accelerate vaccine licensure

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Moving forward

Mobile research laboratories with capacity to do safety tests and PBMC isolation could help overcome the challenge of distance.

This year a phase 2 trial (UKRI/MRC funded).

Use of the IAVI construct as opposed to the Merck construct.

At UVRI we are developing more assay capacity as a CEPI centralised lab.

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(PI) Bruce J Kirenga; **(Co-PI)** Pontiano Kaleebu

(Co-investigators) Winters Muttamba, Henry Kyobe Bosa, Misaki Wayengera, Andrew Obuku, Maria Sekimpi, Geofrey Kimbugwe, Wilber Sabiiti, Pauline Byakika, Noah Kiwanuka, Rebecca Nantanda, Stephen Balinandi, Jennifer Serwanga, Diana Atwine, Charles Olaro, Diallo Abdourahamane, Simon Funnell, Riveros Balta Ximena , Cesar Muñoz Fontela, Ana Maria Henao-Restrepo.

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THANK YOU

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