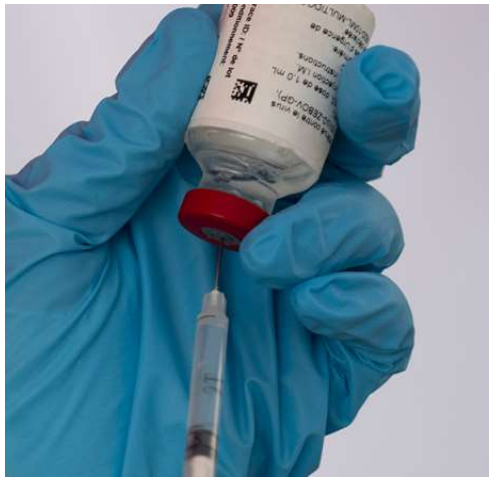
World Health Organization

FILOVIRUS CLINICAL TRIAL PROTOCOL

OBJECTIVES AND DESIGN

Bruce J Kirenga



Building research readiness for a future filovirus outbreak.

20-22 February 2024, UGANDA

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Primary Objectives: Inter-epidemic period

	Phase 1 & 2	
	Objectives	Outcomes
1	To determine the reactogenicity & safety of candidate filovirus vaccine(s) among healthy volunteers	Safety assessed by describing the proportion of vaccine recipients who experience AEs (clinical & lab) by a severity & causality assessment
2	To determine the immunogenicity of the candidate filovirus vaccine(s)	Immunogenicity assessed by measuring vaccine specific antibody titres, neutralization activity & cell mediated immune responses at pre-defined follow-up visits

Secondary Objectives: Inter-epidemic period

	During the inter-epidemic period: Phase 1 & 2	
	Objectives	Outcomes
1	To determine the durability of filovirus-specific induced immune responses following vaccination & identify factors influencing vaccine-induced immune responses among trial participants	Immunogenicity assessed by measuring vaccine specific antibody titres, neutralization activity & cell mediated immune responses at pre-defined follow up visits
2	To determine the immune cross reactivity induced by filovirus vaccine candidates	Immunogenicity assessed by measuring antibody titers & cross-neutralization activity against other filoviruses

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Exploratory objectives: Inter-epidemic period

	During the inter-epidemic period: Phase 1 & 2
1	To determine the effect of filovirus vaccines on host gene expression
2	To determine the T & B cell specific responses & immune profiling in response to vaccination
3	To determine the effect of filovirus vaccines on the host metabolome
4	To determine the effect of filovirus vaccines on host innate immune responses

Primary Objectives: During the outbreak

	Phase 1 & 2	
	Objectives	Outcomes
1	To determine the reactogenicity & safety of candidate filovirus vaccine(s) among healthy volunteers	Safety assessed by describing the proportion of vaccine recipients who experience AEs (clinical & lab) by severity & causality
2	To determine the immunogenicity of the candidate filovirus vaccine(s)	Immunogenicity assessed by measuring vaccine specific antibody titres, neutralization activity & cell mediated immune responses at pre-defined follow-up visits

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Secondary Objectives: During out break period

	During the inter-epidemic period: Phase 1 & 2	
	Objectives	Outcomes
1	To determine the durability of filovirus-specific induced immune responses following vaccination & determine the factors associated with optimal vaccine-induced immune responses among trial participants	Immunogenicity assessed by measuring vaccine specific antibody titres, neutralization activity & cell mediated immune responses at pre-defined follow up visits
2	To determine the putative cross reactivity & protection exerted by the filovirus vaccine candidates	Immunogenicity assessed by measuring antibody titers & neutralization activity

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Exploratory objectives: Inter-epidemic period

	During the outbreak period: Phase 1 & 2
1	To determine the effect of filovirus vaccines on host gene expression
2	To determine the T and B cell specific responses and immune profiling in response to vaccination
3	To determine the effect of filovirus vaccines on the host metabolome
4	To determine the effect of filovirus vaccines on host innate immune responses

Primary Objectives: During the outbreak

	Phase 3:	
	Objectives	Outcomes
1	To assess the effect of a candidate vaccine in protecting against laboratory-confirmed (Filoviruses) disease	New cases of filovirus disease in the ring to be ascertained through independent active surveillance visits by the surveillance contact tracing teams & case detection reports through the national filovirus disease surveillance system

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Secondary Objectives: During the outbreak

	Phase 3:	
	Objectives	Outcomes
1	To assess the safety of the vaccine by monitoring weekly for 21 days any adverse reactions to vaccination & any other SAEs	• Safety will be assessed by describing the proportion of vaccine recipients who experience AEs (clinical & lab) by a severity & causality assessment. • Each candidate vaccine will be compared to delayed comparator • Probable filovirus disease & death from confirmed filovirus disease are included as secondary outcomes

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Exploratory Objectives: During the outbreak

	Phase 3
1	To estimate overall vaccine effectiveness on the ring level, stratified analysis of different types of individuals in rings

Overall design

- This is a phase 1/2/3 study to evaluate the safety, tolerability, immunogenicity, and efficacy of candidate vaccines against (Filoviruses) disease in healthy individuals at risk of (Filoviruses) disease (contacts of a recently confirmed case, including health-care workers and front-line workers in affected areas)
- This study has two main components:

1. During the inter-epidemic period: Safety & Immunogenicity (Phase 1 & 2)
2. During outbreaks: Safety & efficacy (Phase 3) & for certain candidate vaccines (Phase 1 & 2)

The study is designed to move seamlessly through the phases and collect needed data on each vaccine simultaneously