ANRS 0515s EBO-PEP - Information for researchers

Title: **Evaluation of the efficacy of a post-exposure prophylaxis (PEP) strategy in contacts at high risk of developing Ebola virus disease (EVD)**

In brief	Coordinating Investigators: Pr Placide Mbala & Dr Marie Jaspard
	Structure/teams: ALIMA, MEREVA, INRB, CERFIG, ANSS, ISGlobal, UCAD, PANTHER, NPHIL, NPHA, INSP, Inserm
	Start dates: Not yet started End date of research: NA
	Number of participants expected: 162
	Research status: To be start
	Pathology: Ebola virus disease (EVD)
	Promotion: Inserm - ANRS MIE
	Funded under: EDCTP3
The project	EBO-PEP is a multi-country and multi-epidemic trial in which high risk contact (children, adolescents, adults) of contracting Ebola virus disease are recruited during an epidemic in several countries (Democratic Republic of Congo, Guinea, Liberia, Sierra Leone). Participants will be randomized (1:1) into one of two arms of the trial: • Ervebo® arm (control arm) ; • Ervebo® + Inmazeb® arm. The hypothesis is that administering Inmazeb® in combination with Ervebo® as PEP in the days following high-risk exposure to EVD will reduce the incidence of EVD within 21 days of administration compared to a PEP strategy using Ervebo® alone.
Latest news	Not applicable yet
Publication references	Not applicable yet
Type of study	Multicenter, multi-epidemic, phase III, comparative, controlled, randomized, one-sided, superiority trial with two parallel, unblinded arms.
Main objectives	Compare the rate of EVD at 21 days in contacts at high-risk of EVD receiving a PEP strategy of ERV+IMZ *vs*. ERV alone.
Secondary objectives	• Compare the rate of EVD at 60 days in contact at high-risk of EVD receiving a PEP strategy with ERV+IMZ versus ERV alone • Compare safety and tolerance between the different trial arms • Compare EVD severity between the different trial arms

	• Compare the rate of asymptomatic EVD between the different trial arms • Compare the proportion of deaths between the different trial arms • Describe the evolution of viral load in the different trial arms • Estimate the cost-effectiveness ratio in the different trial arms
Optional: Link to research website	www.ebo-pep.com
Inclusion criteria	• Last high-risk contact within the last 5 days • No sign or symptoms of EVD • Signed and dated informed consent from participants over the age of majority in order to participate in the trial or from a representative of parental authority for minor participants.
Non-inclusion criteria	• History of vaccination with Ervebo or any other EVD vaccine within the last 5 years (self-reported by the participant) • History of confirmed EVD within the last 5 years (self-reported by the participant) • Hypersensitivity to any of the experimental medical products (IMP) or their excipients (self-reported by the participant) • Participation in another therapeutic or vaccine trial for EVD • Any other reason which, at the investigator's discretion, that could compromise the participant's safety and cooperation in the trial.
Primary endpoints	Proportion of participants with EBOV PCR-confirmed symptomatic EVD between D1 and D21.

Secondary endpoints	• Proportion of participants with EBOV PCR-confirmed symptomatic EVD between D1 and D60*.
	• Proportion of participants with grade 3 or higher adverse event (AE) between D1 and D60*
	• Proportion of participants admitted to the Ebola Treatment Center (ETC) with confirmed EVD between D1 and D60 who met at least one of the following criteria:
	  ○ Nucleoprotein cycle threshold (NP Ct) < 22
	  ○ KDIGO stage 3[a]
	  ○ AST or ALT > 5N
	  ○ External bleeding
	  ○ NEWS2 score ≥ 7[b]
	• Proportion of asymptomatic participants with a positive EBOV PCR between Day 1 and Day 21
	• Proportion of participants who died between D1 and D60*
	• NP Ct curve between D1 and D21*

	• Incremental cost-effectiveness ratio (ICER) for ERV+IMZ arm *vs* ERV * If the participant is still hospitalized for EVD at the end of the endpoint follow-up, the follow-up will be extended until the end of hospitalization. [a] Staging criterion for acute kidney injury (KDIGO 2012) [b] National Early Warning Score 2 (https://www.rcp.ac.uk/improving-care/resources/national-early-warning-score-news-2/). Depending on the characteristics of the participant, the National Pediatric Early Warning System (PEWS - https://www.rcpch.ac.uk/resources/UK-paediatric-early-warning-systems#_-how-is-spot-being-evaluated) or the Maternity Early Warning Score (MEWS - https://www.nihr. ac.uk/news/new-maternity-early-warning-score-be-implemented-nhs) are used.

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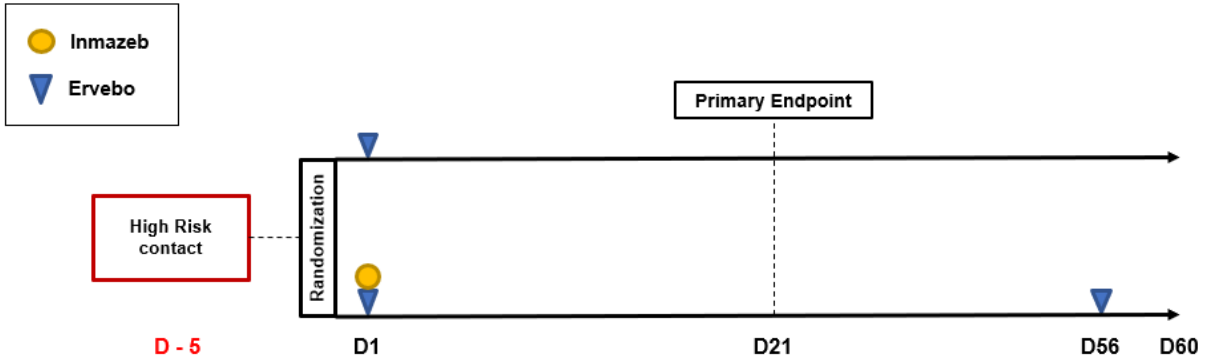
A - Study methodology and type of data and/or samples collected

Data and samples collected	**Biotech libraries**	Blood samples (EDTA) will be taken on days 1, 5, 10, and 21. There will be no samples taken specifically for the biobank; only samples remaining after analysis will be stored in a national biobank if conditions allow.
	Data	Clinical, biological, pharmacovigilance, data trial conduct data, and socioeconomic health data.

Study Design:



Trial schedule:

	Inclusion D1	**D2 - D4** Phone call	**D5** PEP Center	**D6 - D9** Phone call	**D10** PEP Center	**D11 - D20** Phone call	**D21** PEP Center	**D56[f]** PEP center/Phone call	**D60** Phone call
Time window			*+/- 1 day*		*+/- 1 day*		*+/- 2 days*	*+/- 5 days*	*+/- 5 days*
Information about the trial	X								
Checking eligibility criteria	X								
Written informed consent*	X								
Medical history	X								
Description of high-risk contact	X								
Socio-demographic data[a]	X								
Detection of clinical signs of EVD[b]	X	X	X	X	X	X	X	X	X
Randomization	X								
Blood sample (EDTA tube)[c]	X		X		X		X		
Inmazeb (150 mg/kg DU IV)	X[d]								
Ervebo (72 million PFU IM)	X							X[d]	
Information to participants about the clinical signs of EVD	X	X	X	X	X	X	X	X	X
Socio-economic data[e]	X						X	X	
Collection of adverse events	X	X	X	X	X	X	X	X	X

* In the case of minors who become adult during the trial, consent for continued participation is obtained during a visit to the PEP center.

[a] Socio-demographic data: age, gender

[b] Possibility for the participant to call the study doctor at the slightest clinical sign suggestive of EVD

[c] Samples of 1 ml for participants ≤ 3 kg, 2 ml for participants > 3 kg to ≤ 15 kg, and 4 ml for participants > 15 kg

[d] ERV+IMZ arm only

[e] Socio-economic data: Type of employment, income and loss of income - For adult participants only

[f] In-person visit for participants in the ERV+IMZ arm and by phone call for participants in the ERV arm

B - How to access the collection

1- project submission: **via the sample request form on the website**

2- project evaluation: **scientific committee or independent experts**

3- Making the collection available**: Scientific Advisory Board and final decision by ANRS MIE management**

Contact e-mail address for submitting your project: **biobanque@anrs.fr**