INRB-ANRS 0515s EBO-PEP - Information for researchers

Title: **Evaluation of the efficacy of a post-exposure prophylaxis (PEP) strategy in contacts at risk of developing a Filovirus Disease: an adaptive platform trial**

In brief	Coordinating Investigators: Pr Placide Mbala & Dr Marie Jaspard & Pr Pauline Byakika-Kibwika
	Structure/teams: ALIMA, MEREVA, INRB, CERFIG, ANSS, ISGlobal, UCAD, PANTHER, NPHIL, NPHA, INSP, MUST, Inserm
	Start date: 16 July 2026 End date of research: NA
	Number of participants expected: • Subprotocol No. 1 (ODV-BDBV): 998 • Subprotocol No. 2 (RDV-BDBV): 350
	Research status: • Subprotocol No. 1 (ODV-BDBV): Ongoing • Subprotocol No. 2 (RDV-BDBV): Ongoing
	Pathology: Filovirus disease (FVD)
	Sponsorship: National Institute for Biomedical Research (INRB) & Inserm - ANRS MIE
	Funded under: EDCTP3
The project	EBO-PEP is a randomized controlled platform trial designed to evaluate different post-exposure prophylaxis (PEP) strategies among contacts (children, adolescents, adults) at risk of contracting a filovirus disease (FVD) such as Zaire Ebola virus (EBOV), Sudan Ebola virus (SUDV), Bundibugyo Ebola virus (BDBV), or Marburg virus (MARV). Participants are recruited from countries reporting an FVD outbreak and are individually randomized to different intervention arms based on the virus and the available PEP options. Two subprotocols on Bundibugyo Ebola virus disease (BDV) are currently underway:

	<u>Subprotocol No. 1 (ODV-BDV):</u> a double-blind, placebo-controlled, superiority trial with two parallel arms to evaluate the safety and efficacy of Obeldesivir (ODV) compared to placebo in preventing symptomatic Bundibugyo Ebola virus disease (BVD) in participants who have had high-risk exposure. **<u>Subprotocol No. 2 (RDV–BDBV):</u>** a prospective interventional cohort study aimed at providing insights into the efficacy and safety of Remdesivir in preventing symptomatic Bundibugyo Ebola virus disease (BVD) in children under 12 years of age and in pregnant and breastfeeding women who have had high-risk exposure. This cohort allows for the proposal and evaluation of a potentially effective PEP treatment for vulnerable populations who cannot be included in the ODV-BDBV trial.
Latest news	Not applicable yet
Publication references	Not applicable yet
Type of study	Multicenter, multi-epidemic, phase III, comparative, adaptative trial.
Main objectives	To determine whether the investigational PEP strategy, administered as PEP to contacts of confirmed FVD cases, reduce the risk of developing symptomatic PCR-confirmed FVD compared with the control arm over the 21-day incubation window.
Secondary objectives	<u>For all interventional subprotocols:</u> • To determine whether the investigational PEP strategy, administered as PEP to contacts of confirmed FVD cases, reduce the risk of developing symptomatic PCR-confirmed FVD compared with the control arm over 42-days (two incubation period); • To evaluate the safety and tolerability of investigational PEP strategy relative to the control arm.Compare EVD severity between the different trial arms; • To determine whether the investigational PEP strategy reduces the severity of PCR-confirmed FVD, compared with the control arm; • To determine whether the investigational PEP strategy reduces the rate of asymptomatic FVD, compared with the control arm; • To determine whether the investigational PEP strategy reduces mortality, compared with the control arm; • To describe the evolution of viral load across trial arms; • To estimate the cost-effectiveness ratio in the different trial arms;

	Additional Secondary Objective for Subprotocol No. 1 (ODV-BDBV): To determine whether Obeldesivir, administered as PEP to contacts, reduce the risk of developing symptomatic PCR-confirmed BVD compared with the placebo on the optimal window combining a PEP and a PrEP effect (i.e. 10 to 21 days following randomization). Secondary objectives for Subprotocol No. 2 (RDV-BDBV): Adaptation of the objectives applicable to all subprotocols for the intervention cohort.
Optional: Link to research website	www.ebo-pep.com

Inclusion criteria	For all subprotocols:
	• Registered contact of an FVD confirmed case (level of risk defined in each sub-protocol);
	• No sign or symptoms of FVD;
	• Signed and dated informed consent to participate in the trial from the adult participant or their legal guardian in the case of a minor participant or adult with cognitive disorder.
	
	Additional inclusion criteria for Subprotocol No. 1 (ODV-BDBV):
	• Last high-risk contact within the last 5 days with a BDBV PCR confirmed case, defined as one of the following:
	  ○ Direct contact with an individual with PCR-confirmed BVD with diarrhea, vomiting or external bleeding ("wet symptoms"), or with their bodily fluids;
	  ○ Direct contact with the dead body of an individual with confirmed or probable BVD;
	  ○ Needlestick with a syringe contaminated by the blood of a person with confirmed or probable BVD.
	
	Additional inclusion criteria for Subprotocol No. 2 (RDV-BDBV):
	• Age <12 years or,
	• Pregnant or positive pregnancy test or,
	• Women with plans to breastfeed during the study period and 21 days following the last dose of study intervention. World Health Organization guidance on breastfeeding should be followed.
	• Last high-risk contact within the last 5 days with a BDBV PCR confirmed case, defined as one of the following:
	  ○ Direct contact with an individual with PCR-confirmed BVD with diarrhea, vomiting or external bleeding ("wet symptoms"), or with their bodily fluids;

	○ Direct contact with the dead body of an individual with confirmed or probable BVD; ○ Needlestick with a syringe contaminated by the blood of a person with confirmed or probable BVD.
Non-inclusion criteria	<u>For all subprotocols:</u> • History of confirmed FVD within the last 5 years (self-reported by the participant); • Hypersensitivity to any of the IMP or their excipients (self-reported by the participant); • Ongoing participation in another therapeutic or vaccine trial for FVD; • Any other reason which, at the investigator's discretion, that compromise the participant's safety and cooperation in the trial. <u>Additional non-inclusion criteria for Subprotocol No. 1 (ODV-BDBV):</u> • Children <12 years; • Pregnant or positive pregnancy test; • Individuals with plans to breastfeed during the study period and 21 days following the last dose of study intervention. World Health Organization guidance on breastfeeding should be followed; • Known moderate or severe renal impairment or known estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m2 (based on participant declaration); • Decompensated cirrhosis (Child-Pugh Class C), acute liver injury/failure (eg, new onset [< 2 weeks] of easy bruising, jaundice, ascites, hepatic encephalopathy, asterixis), and/or known alanine aminotransferase ≥5 × upper limit of normal (based on participant declaration); • Any inability to take study drug or comply with study procedures that, in the opinion of the investigator, would make the participant unsuitable for the study.
Primary endpoints	Incidence of PCR-confirmed symptomatic FVD between D1 and D21.
Secondary endpoints	<u>For all interventional subprotocols:</u> • Incidence of PCR-confirmed symptomatic FVD between D1 and D42. • Incidence of AEs, SAE, and SUSARs over the entire follow-up

	• Proportion of participants admitted to the Ebola Treatment Center (ETC) with confirmed FVD between D1 and D42 who met at least one of the following criteria:
	  ○ Nucleoprotein cycle threshold (NP Ct) < 22
	  ○ KDIGO stage 3a
	  ○ AST or ALT > 5N
	  ○ External bleeding
	  ○ NEWS2 score ≥ 7b
	• Proportion of asymptomatic participants with a positive PCR between D1 and D21.
	• Incidence of all-cause death over the entire follow-up and Incidence of FVD-related death over the entire follow-up.
	• NP Ct curve between D1 and D21, or between D1 and ETC discharge for PCR-confirmed FVD.
	• Incremental cost-effectiveness ratio (ICER).
	
	[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.
	
	Additional Secondary Endpoints for Subprotocol No. 1 (ODV-BDBV): Incidence of PCR-confirmed symptomatic FVD between D10 and D21.

Contents

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

Data and samples collected	**Biotech libraries**	Blood samples (EDTA or DBS) 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.

Trial schedule common to all subprotocols:

	Inclusion D1	D2 to D4	D5	D6 to D9	D10	D11 to D20	D21	D42
Visit type (on-site, ambulatory, phone)	See sub-protocols							
Visit window (days)								+/- 7
Blood sampling window (days)			+/-1		+/-1		+/-1	
Information about the trial	X							
Checking eligibility criteria	X							
Written informed consent	X							
Urine pregnancy test	X							
Medical history	X							
Description of contact	X							
Socio-demographic data	X							
Clinical signs of FVD	X	X	X	X	X	X	X	X
Randomization	X							
PEP administration	See sub-protocols							
Blood sample for filovirus RT-PCR	(X)		(X)		(X)		X	
Socio-economic data	X						X	X
Collection of AE	X	X	X	X	X	X	X	X

Specific Features of Subprotocol No. 1 (ODV-BDBV):

	D1	**D2 to D4**	**D5**	**D6 to D9**	**D10**	**D11 to D20**	**D21**	**D42**
PEP center visit	X		X		X		X	
Ambulatory visit		X		X		X		X
Urine pregnancy test	X						X	
Placebo (Oral, DOT administration)	X	X	X	X	X			
Obeldesivir (Oral, DOT administration)	X	X	X	X	X			

Creatinine, liver enzyme and hematology analysis	X		X		X		X	

Specific Features of Subprotocol No. 2 (RDV-BDBV):

	D1	D2 to D4	D5	D6 to D9	D10	D11 to D20	D21	D42
PEP center visit	X	X	X	X	X		X	
Ambulatory visit						X		X
Remdesivir IV	X	X	X	X	X			
Creatinine, liver enzyme and hematology analysis*	X		X		X		X	

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**: Steering Committee and final decision by the Sponsors**

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