EBOPEP

EBOla Zaïre Post-Exposure Prophylaxis, preparedness and efficacy evaluation during outbreak in Central and West-Africa

This project Grant Agreement No 101145675 is supported by the Global Health EDCTP3 Joint Undertaking and its members Médecins Sans Frontières does not receive any funds from the European Commission.

Global Health EDCTP

Funded by the European Union

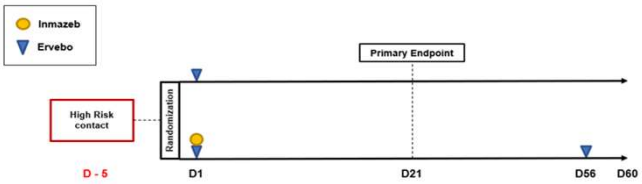
1

EBO-PEP Clinical Trial for Ebola Zaïre outbreak

EBOPEP

Phase III Randomized Controlled Trial

Primary objective : To compare the rate of **confirmed EVD at D21** in high-risk contacts of EVD receiving a PEP strategy of Ervebo + Inmazeb *vs.* Ervebo alone.



Target population: High-risk contacts

Protocol pre-positioned and approved by ethics & regulatory in:

- Guinea
- Democratic Republic of Congo
- Sierra Leone
- Liberia

Database and CRF ready

Global Health EDCTP3

2

EBO-PEP Clinical Trial

Population

- Last high-risk contact ***within the past 5 days***
- No signs or symptoms of EVD

Definition of high-risk contacts

- **Direct contact with a person with EBOV PCR-confirmed EVD** with diarrhoea, vomiting or external bleeding **("wet symptoms"),** or with their **body fluids ;**
- **Direct contact with the dead body** of a person with **confirmed or probable EVD ;**
- **Needlestick injury with a syringe contaminated by a person with confirmed or probable EVD**
- **Or a child born to or breastfed** by an individual with EVD.

3

EBO-PEP Clinical Trial

Community Engagement and community communication (lead by UCAD)

- Design of a **community engagement strategy** to be implemented for involving the population and promoting their civic engagement to increase their acceptability and ownership of the trial
- In close collaboration national outbreak response and contact traçing

Cost-effectiveness analysis (lead by ISGlobal)

- Objective : Estimate the cost-effectiveness ratio in the different trial arms by the Incremental cost-effectiveness ratio (ICER) for ERV+IMZ arm vs ERV
- EC models feed by datas from
  - Intervention Costs : cost of vaccines, IMPs, medical supplies, patients monitoring, staff time, etc
  - Efficiency: infection prevented, DALYs, etc

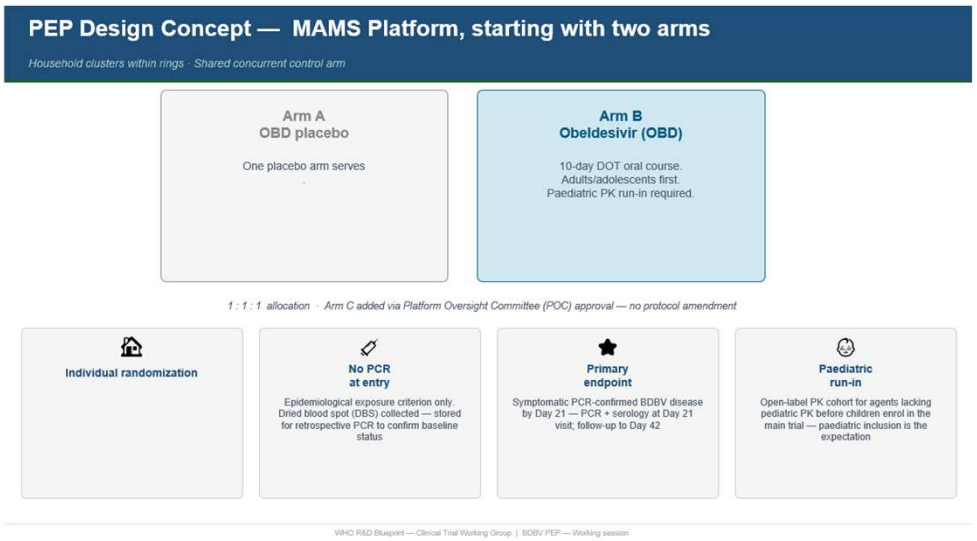
4

Therapeutics options for Bundibugyo PEP

VACCIN	OBELDESIVIR	MOLNUPIRAVIR
To date, no r-VSV-BDBV vaccine is readily available. Limited cross-protection data with the ERBEVO vaccine against subsequent exposure to BDBV on NHP *Mire and al., PLoS Negl Trop. Dis., 2013* *Woolsey and al., J. Infect Dis., 2023*	**Pro-drug of Remdesivir** *In vitro* and pre-clinical datas Efficacy on MARV, EBOV and SUDV - **No data on BDBV** *Cross et al., Science, 2024* *Cross et al., Nat Med, 2025* *Woolsey et al., Sci. Adv, 2025* Good Safety datas Phase 3 for COVID-19 : 350 mg BID for 5 days *Ogbuagu et al., Lancet, 2025* Phase I N=19, 350 mg BID for 10 days *Abstract for the 34th ECCMID 2024* Phase II, loading doses RSV trial, 700mg BID *Unpublished* Gilead selected dose : **700 mg BID on D1 followed by 700 mg morning - 350 mg evening from D2 to D10** ⇒ Approved by Rwanda ethics committee on a PEP protocol (MARV) NCT06682234.	**Prodrug of N-hydroxycytidine (NHC), a ribonucleoside analog that targets viral RNA polymerase** Pre-clinical data In vitro reduction of virus titer of Marburg and EBOV *Reynard et al., Viruses, 2015* Study in murine models on EBOV *Bluemling et al., Antiviral Res, 2023* Clinical datas Phase 1 data on 5 and 10 days of treatment at 800 mg BID *Iwamoto et al., Clin. Transl., 2023* *Painter et al., AAC, 2021* Phase 3 data : clinical efficacy against moderate COVID-19 in non-hospitalized patients - dose of 800 mg BID, 5 days *Bernal, et al, NJEM, 2022* The proposed dosing regimen : **To be defined**

5

WHO R&D blue print proposition of design for PEP - BUNDI



6

Adaptation of EBO-PEP to the Bundibugyo strain

EBO-PEP BUNDI

Working group of methodologist to transform EBO-PEP into a MAMS Platform is ongoing

Arms under evaluation by the consortium partners

- Control arm: waiting TAG vaccine recommendations, DRC/Uganda view on placebo use
- Interventional arms: Agree with Obeldesivir; DRC propose to also evaluate Molnupiravir

⇒ **Objective: DRC protocol amendment + Uganda submission next week**

7

BUNDI-CO

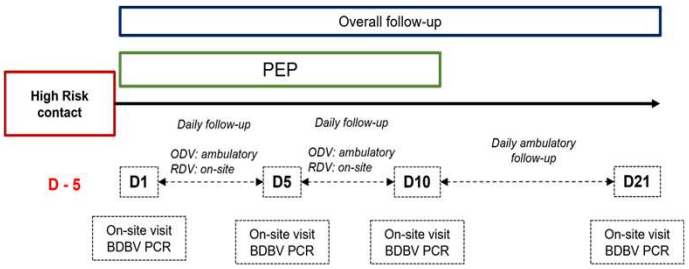
Prospective cohort of contacts at high risk of developing BVD that received a PEP strategy

Sponsor : ANRS

PI: Pr. Placide Mbala, Dr. Marie Jaspard & Dr. Pauline Byakika

Population:

- Last high-risk contact within the last 5 days
- No signs or symptoms of BVD
- Depending of the treatment administered on-site (ODV or Remdesivir)



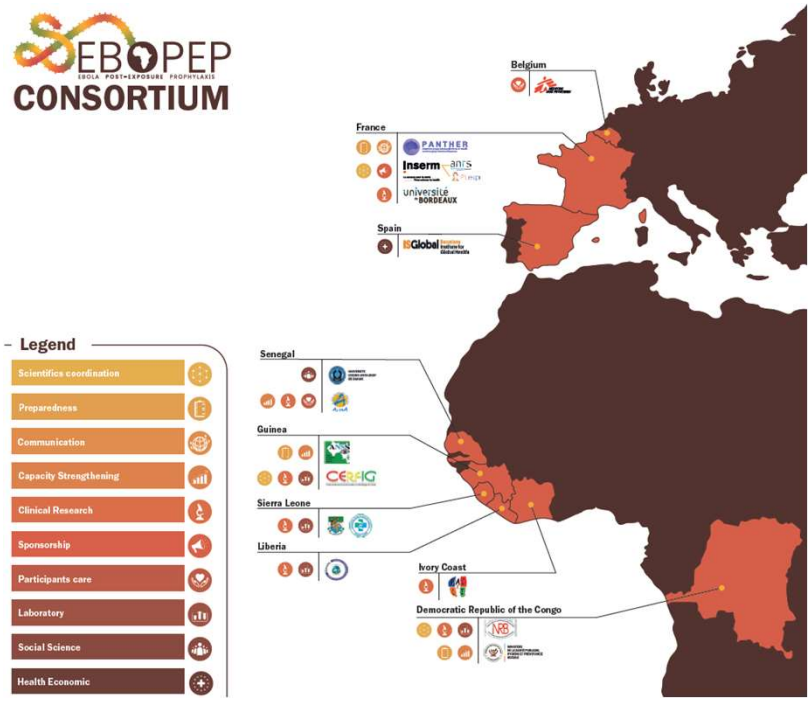
8

Thank you

This project Grant Agreement No 101145675 is supported by the Global Health EDCTP3 Joint Undertaking and its members

9

EBOPEP CONSORTIUM



CONSORTIUM OBJECTIVES

Expand the portfolio of **therapeutic tools** against EVD, by evaluating **PEP strategies for high-risk contacts**.

Maintain a **network of knowledge-sharing and collaboration** around PEP.

EDCTP Funding

10

Therapeutics options for EBO-PEP-Bundi

VACCINE

To date, no r-VSV-BDBV vaccine is readily available.

Limited cross-protection data with the ERBEVO vaccine against subsequent exposure to BDBV on NHP

Mire and al., PLoS Negl Trop. Dis., 2013
Woolsey and al., J. Infect Dis., 2023

11

Therapeutics options for EBO-PEP-Bundi

OBELDESIVIR **Pro-drug of Remdesivir**

In vitro and pre-clinical datas

Efficacy on MARV, EBOV and SUDV - **No data on BDBV**

Cross et al., Science, 2024
Cross et al., Nat Med, 2025
Woolsey et al., Sci. Adv, 2025

Clinical datas

Good safety profile in phase 3 for COVID-19 : (350 mg BID for 5 days

Ogbuagu et al., Lancet, 2025

No safety warning on a drug-drug interaction study : Phase I, N=19, Dosage of 350 mg BID for 10 days

Abstract for the 34th ECCMID 2024

Loading dose (700 mg BID) evaluated on Phase 2 RSV trial without safety warning

Unpublished

Gilead selected dose :

700 mg BID on D1 followed by 700 mg morning - 350 mg evening from D2 to D10.

⇒ Approved by Rwanda ethics committee on a PEP protocol proposed by Gilead for the last Marburg outbreak (NCT06682234).

12

New therapeutics options for EBO-PEP-Bundi

MOLNUPIRAVIR

Prodrug of N-hydroxycytidine (NHC), a ribonucleoside analog that targets viral RNA polymerase.

Pre-clinical data on filoviruses – No datas on BDBV

In vitro reduction of virus titer of Marburg and EBOV

Reynard et al., Viruses, 2015

Study in murine models on EBOV

Bluemling et al., Antiviral Res, 2023

Clinical datas

Phase 1 data on 5 and 10 days of treatment at 800 mg BID

Iwamoto et al., Clin. Transl., 2023
Painter et al., AAC, 2021

Phase 3 data : clinical efficacy against moderate COVID-19 in non-hospitalized patients, with a satisfactory safety profile - dose of 800 mg BID, 5 days

Bernal, et al, NJEM, 2022

The proposed dosing regimen : **To be defined**

13

EBO-PEP Clinical Trial for Ebola Zaïre outbreak

Definition of high-risk contacts

- **Direct contact with a person with EBOV PCR-confirmed EVD** with diarrhoea, vomiting or external bleeding **("wet symptoms"),** or with their **body fluids ;**
- **Direct contact with the dead body** of a person with **confirmed or probable EVD ;**
- **Needlestick injury with a syringe contaminated by a person with confirmed or probable EVD**
- **Or a child born to or breastfed** by an individual with EVD.

14

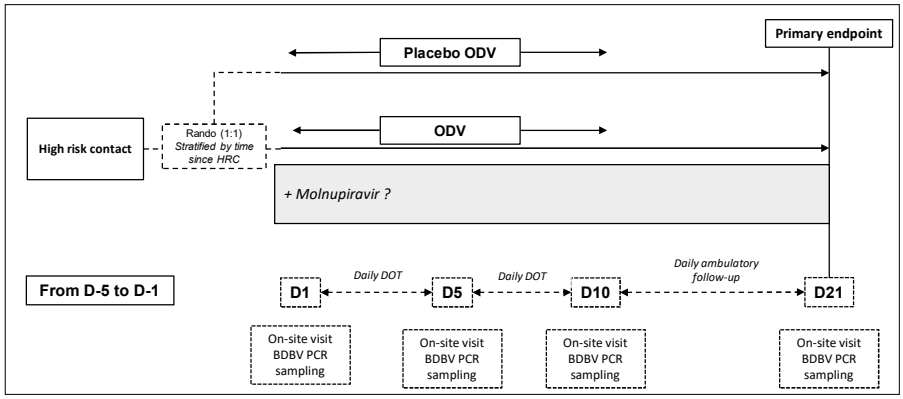
EBO-PEP-Bundi design proposition

⇒ Agree with proposed WHO arms if DRC/Uganda for a placebo arm

⇒ The team propose to add Molnupiravir as a potential arm

⇒ The protocol could be redesigned to a MAMS platform trial if it does not alter a rapid deployment of the trial and would be beneficial on the long term (e.g. pipeline of potential treatments to be evaluated)

⇒ The team propose to revise trial hypotheses to fit the current situation (evaluation of antivirals on a large outbreak)



Sample size considerations
- BVD rate in placebo arm: 20%
- BVD rate in ODV arm: 8% (RR 60%)
- SS = 140/arm (Power 80%, 1P <2.5%, 3IA)

Multi-arm considerations
- Placebo availability
- Impact on placebo design (double, triple placebo,…)
- Different eligibility criteria?
- Impact on sample size
- Design considered
  - Shared concurrent control arm
  - Pairwise comparison IMP vs. Placebo
  - No adj. for multiplicity

15

EBO-PEP Project

Community Engagement and community communication (lead by UCAD)

- Design of a **community engagement strategy** to be implemented for involving the population and promoting their civic engagement to increase their acceptability and ownership of the trial
- In close collaboration national outbreak response and contact traçing

Cost-effectiveness analysis (lead by ISGlobal)

- Objective : Estimate the cost-effectiveness ratio in the different trial arms by the Incremental cost-effectiveness ratio (ICER) for ERV+IMZ arm vs ERV
- EC models feed by datas from
  - Intervention Costs : cost of vaccines, IMPs, medical supplies, patients monitoring, staff time, etc
  - Efficiency: infection prevented, DALYs, etc

16

EBO-PEP Project

EDCTP Funding

- Expand the portfolio of **therapeutic tools** against EVD, by evaluating **PEP strategies for high-risk contacts**.
- Maintain a **network of knowledge-sharing and collaboration** around PEP.

Objective 1: Set up a multi-epidemic, multi-site, multi-country Phase III clinical trial in Africa to test the efficacy of mAbs used as PEP for high-risk contacts (**EBO-PEP study**).

Objective 2: **Strengthen the capacity of clinical researchers** and **increase the community's knowledge** of Ebola virus research.

Objective 3: **Define the best PEP strategy for high-risk contacts** and **advocate** the implementation of PEP in Ebola-affected countries.

17