The EBOVAC projects have received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grants agreements EBOVAC1 n°115854, EBOVAC2 n°115861 and EBOVAC3 n°800176. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Association.

**EBOVAC projects Stakeholder meeting**

June 22nd, 2021
14:00 – 17:00 CET
Housekeeping rules

Keep your microphone muted

This meeting is being recorded. With turning on your video/audio, you consent that your images/video/audios will be recorded.

For technical support, please contact “Elodie Acloque” via chat or via email.

Thank you for joining the EBOVAC stakeholder meeting!
EBOVAC projects Stakeholder meeting

June 22nd, 2021
14:00 – 17:00 CET

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Opening address

Pr. Yves LEVY
Opening address

Welcome!

- More than 120 registered participants to this virtual event
- All partners from the EBOVAC projects are represented
- Number of the most prominent actors of the vaccine R&D from Africa, the USA and Europe are represented:

...Thank you for attending the EBOVAC project stakeholder meeting!
Today’s objectives

- Acknowledge the support of IMI2 and the involvement of our partners
- Present some of the major achievements of the EBOVAC projects
- To have an opportunity to reflect on the future of the Ebola vaccine deployment strategy
Opening address

Speakers

Invited Speakers
- Pr. Steve AHUKA-MUNDEKE (INRB)
- Dr. Pierre MEULIEN (IMI2)

EBOVAC Project coordination
- Dr. Cynthia ROBINSON (Janssen) Project leader
- Pr. Deborah WATSON-JONES (LSHTM) Coordinator EBOVAC1 & EBOVAC3
- Pr. Rodolphe THIEBAUT (Inserm) Coordinator EBOVAC 2

EBOVAC presenters
- Dr. Gaudensia MUTUA (IAVI)
- Dr. Frank BAIDEN (LSHTM/COHMAS),
- Dr. Houreratou BARRY (Centre Muraz)
- Elizabeth CLUTTERBUCK (University of Oxford),
- Christine LACABARATZ (Inserm),
- Martin GOODIER (LSHTM)
- Mélanie PRAGUE (Inserm)
- Pr. Hypolite MUHINDO (UNIKIN)
- Dr. Melanie SAVILLE (CEPI)
- Dr. Valerie ORIOLE-MATHIEU (Janssen)
Opening address

Discussion panel

- Pr. Deborah WATSON-JONES (LSHTM)
- Dr. Johan VAN HOOF (Janssen)
- Pr. Nicolas MEDA (Centre Muraz)
- Pr. Hypolite MUHINDO (University of Kinshasa)
- Pr. Pierre VAN DAMME (University of Antwerp)
- Pr. Andrew POLLARD (University of Oxford)
- Dr. Pierre MEULIEN (IMI2)
- Pr. Rodolphe THIEBAUT (Insem)
- Pr. Yves LEVY (VRI Insem)

Chairman:
- Pr. Daniel G. BAUSCH (LSHTM)

Thank you for participating in the EBOVAC projects stakeholder meeting!
Some elements of context

A response to March 2014 Ebola outbreak in Western-Africa

- Multivalent filovirus vaccine development ongoing at Janssen since 2008
  - A heterologous 2-dose vaccine regimen for optimal and durable immunity
  - Proof-of-concept obtained in highly stringent NHP model using multivalent vaccines against Marburg, Sudan and Ebola (100% protection)

- In response to the Ebola outbreak, decision was made in August 2014 to establish an accelerated Ebola Monovalent Vaccine Program
  - Heterologous 2-dose monovalent Ebola Zaire vaccine
  - Two vaccine regimen based on replication incompetent vectors:
    1. Janssen’s Ad26.ZEBOV
    2. MVA-BN-Filo manufactured by Bavarian Nordic

- Joining forces to combat Ebola, Innovative Medicines Initiative 2 (IMI2) awarded funding to EBOVAC1 and EBOVAC2 consortia in December 2014 in the frame of the EBOLA+ program.
EBOVAC projects overview

- The overall aim of the EBOVAC programme was to assess the safety, immunogenicity and efficacy of a novel Ad26.ZEBOV + MVA-BN-Filo 2-dose heterologous preventive vaccine regimen against EVD.

1. **EBOVAC1**
   - Phase 1 and 3 development of 2-dose heterologous vaccine based on Ad26.ZEBOV and MVA-BN-Filo
   - 5 partners
   - 12/2014-11/2021

2. **EBOVAC2**
   - Phase 2 Phase II development of 2-dose heterologous vaccine based on Ad26.ZEBOV and MVA-BN-Filo
   - 6 partners
   - 12/2014-05/2021

3. **EBOVAC3**
   - Bringing a prophylactic Ebola vaccine to licensure
   - Additional clinical trials in infants and front line workers
   - 7 partners
   - 06/2019-05/2023

**EBO MAN**
- Manufacturing of 2-dose Ebola vaccine regimen

**EBO Reed**
- Promote the acceptance and uptake of new Ebola vaccines
An epic journey...

An incredibly fast implementation: end of 2015, after 12 months we had:

- Initiated 6 clinical studies ongoing in 6 countries
  - Completed enrollment in 3 Phase 1 clinical studies in 3 different countries
  - 11 sites were initiated (with 11 more sites to follow within the next 6 months for Phase 2 in EU/Africa)
- Contributed to 35% of expected subjects vaccinated in the Ebola Monovalent Vaccine Program
- Underwent 3 AVAREF joint reviews for 4 protocols
  - Phase 1: 3-4 Feb 2015 in Arusha, Tanzania, >400 questions
  - Phase 3: 9-10 Apr 2015 in Accra, Ghana, ~160 questions
  - Phase 2: 9-11 Jun 2015 in Accra, Ghana, ~169 questions
- JnJ had frequent interactions with regulatory agencies including MHRA, FAMHP, ANSM, EMEA Scientific advice, US FDA meetings, WHO...
An epic journey...

We had to face many difficulties...

- Rumors in Ghana forbidding the start of the trial there...
- A coup in Burkina Faso in 2016...
- Terrorist attacks in Paris in 2015, Ouagadougou 2016 and Nairobi 2020 every time we were planning to have a meeting there...
- Rebellion in RDC
- Recent outbreaks of Ebola in Guinea and RDC
- The SARS-COV2 pandemic...
- ...

Now: the vaccine got MAA from EMA (01/07/20) and SAGE recommendation (04/06/21)

The commitment of all PIs and staff involved made it possible

The volunteers who accepted to enter the studies made it possible

THANK YOU!
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Opening presentations

June 22nd, 2021
14:15 – 14:25 CET
EBOLA+ IMI2 program and the European support following the 2014 Ebola outbreak

Dr. Pierre MEULIEN
IMI2 Ebola+ programme

Pierre Meulien
IMI Executive Director
22 June 2021
Starting point of the IMI2 EBOLA + programme

Epidemic in West Africa, from December 2013 to January 2016
The largest Ebola disease outbreak ever

>28 000 confirmed cases and >11 000 deaths
Main Challenges at the time

- No licensed treatment specific for Ebola virus disease
- No good and rapid diagnostic test available
- Rapid scaling up of candidate vaccine doses difficult
- Vaccine candidates require very cold temperatures for stability during transport
- Deployment (reaching those most in need) challenging
- Adherence to vaccination regimens challenging
- Range of products needed for current and future outbreaks
- Lack of local capacity with Ebola or clinical research
Why the Innovative Medicines Initiative?

IMI is a neutral trusted platform where all involved can engage in open collaboration on shared challenges and aligned interests.

- IMI’s flexibility to fast-track the launch process in an outbreak situation
- IMI’s flexibility to allow projects to adapt as Ebola epidemic evolved
- Collaboration b/w stakeholders and disciplines is a MUST to address the threat
- Low expected return on investment into Ebola and other filoviral haemorrhagic fevers drug and vaccine development
A fast-track single-stage process

Decision IMI2 Ebola+ Call
21-28 Oct 2014

Call launch
6 Nov 2014

Submission deadline
1 Dec 2014
First 4 projects start!

Evaluation by independent experts
Dec 2014

Signature grant agreements
Jan–Feb 2015

First fast-track call!
First single-stage call!
First projects to start under IMI2!
EU fast-track response

European Commission & EFPIA

- Other funders
- Situation of current epidemic
- Short term goals
- Long term strategy
- Need for collaboration

A programmatic approach in IM:
6 Nov 2014 IMI2 Call 2 launching the Ebola+ programme with first five topics

- Filoviral haemorrhagic fevers
- Fast impact and longer term
- Broad scope from early discovery to compliance, diagnostics

18 Dec 2015 Call 8: open call, two years with 5 cut-off dates
IMI2 Ebola+ programme overview

IMI2 Ebola and other filoviral haemorrhagic fevers programme
Joint Information repository, Scientific Advisory Board, Ethics Board

Pipelines
- PEVIA
  - APHP, Vaxeal

Development
- VSV-EBOVAC
  - Sclavo Vacc. Assoc.
- EBOVAC 1
  - LSHTM, Janssen
- EBOVAC 2
  - Inserm, Janssen
- VSV-EBOPLUS
  - Sclavo Vacc, MSD
- EBOVAC 3
  - LSHTM, Janssen

Manufacturing
- EBOMAN
  - Vibalogics, Janssen

Deployment
- EBODAC
  - LSHTM, Janssen

Diagnostics
- EbolaMoDRAD
  - Public Health Institute Sweden
- FILODIAG
  - GNA Biosolutions
- Mofina
  - Public Health England, Altona
- VHFMoDRAD
  - FHM, Cepheid

Total budget: > € 300 million
EBOMAN
Janssen, Vibalogics, Bavarian Nordic
Budget: EFPIA in-kind: 36.0 m EUR
IMI JU: 1.0 m EUR
Other: 3.2 m EUR

EBOVAC1
Coordinator: LSHTM
Other partners: Janssen, INSERM, Oxford University, University of Sierra Leone
Budget: EFPIA IKC: 39.9 m EUR
IMI JU: 58.3 m EUR

EBOVAC2
Coordinator: INSERM
Other partners: Janssen, LSHTM, Oxford U., Le Centre Muraz (Burkina Faso), Inserm Transfert, Chu Hopitaux Bordeaux, U. Bordeaux, U. Paris XII Val de Marne
Budget: EFPIA IKC: 27.9 m EUR
IMI JU: 22.8 m EUR

EBOVAC3
Coordinator: LSHTM
Budget: EFPIA IKC: 21.4 m EUR
IMI JU: 29.4 m EUR

EBODAC
Coordinator: LSHTM
Other partners: Janssen, World Vision of Ireland, World Vision Sierra Leone, Grameen Foundation
Budget: EFPIA in-kind: 5.4 m EUR - IMI JU: 20.3 m EUR
Thank you

EBOLA + Programme

www.imi.europa.eu

@IMI_JU
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EBOVAC Achievements

June 22nd, 2021
14:35 - 16:10 CET
General Janssen Ebola vaccine development overview

Dr. Cynthia ROBINSON
Primary vaccination: 2-Dose Vaccine Regimen, given approximately 8 weeks apart, IM

Non-replicating viral vectored vaccines

- **Dose 1**
  - **Ad26.ZEBOV**
    - encoding EBOV GP
    - $5 \times 10^{10}$ vp

- **Dose 2**
  - **MVA-BN-Filo**
    - encoding EBOV, SUDV, MARV GP, TAFV NP
    - $1 \times 10^8$ Inf.U.

Booster: 1 Dose of Ad26.ZEBOV can be given to individuals who are at imminent risk of exposure to EBOV

The Ebola vaccine regimen contains vaccines based on platform technologies:

- **Ad26.ZEBOV**
  - (Janssen’s AdVac® technology)
  - Encoding EBOV GP (Mayinga)

- **MVA-BN-Filo**
  - (Bavarian Nordic’s MVA-BN® technology)
  - Encoding GP of EBOV, SUDV, MARV & NP of TAFV

Both vaccines are non-replicating in humans
Overview: Janssen’s Filovirus Vaccine Programs

Monovalent Ebola Vaccine

- **2002 – 2008 NIH/VRC collaboration**
- **2008 NIH contract Filovirus Vaccine Development**

- **2014** BN Agreement signed
- **2015** Manufacturing campaigns
- **2016** FIH Monovalent
- **2017** EUAL Filing
- **2018** Manufacturing campaigns
- **2019** WHO Pre-Qualification
- **2020** Conditional Approval Rwanda
- **2021** Temporary Use Approval DRC
- **2022...**

- **2018** EU license
- **2019** WHO SAGE recommendation

---

WHO list of prequalified vaccines: https://extranet.who.int/pqweb/vaccines/prequalified-vaccines
West African Epidemic & Accelerated Clinical Development of Janssen Prophylactic Ebola Vaccine

2014

- 2002 – 2008 NIH/VRC collaboration
- 2008 NIH contract Filovirus Vaccine Development

2014

- J&J’s Decision to accelerate

2015

- FIH: 30 Dec 2014
- Commercial scale Manufacturing
- P1 Africa: 22 Apr 2015
- P2: 7 Jul 2015
- P3: Sierra Leone Oct 2015
# Vaccine Regimen is well-tolerated in Adults

<table>
<thead>
<tr>
<th>Adverse Reactions Following Vaccination with Zabdeno</th>
<th>Adverse Reactions Following Vaccination with Mvabea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>System Organ Class</strong></td>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>very common</td>
</tr>
<tr>
<td></td>
<td>uncommon</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>common</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>very common</td>
</tr>
<tr>
<td></td>
<td>uncommon</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>common</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Vaccine Regimen is well-tolerated in Children

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Adverse reactions</th>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>very common</td>
<td>decreased appetite</td>
<td>System Organ Class</td>
<td>Frequency</td>
<td>Adverse reactions</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>very common</td>
<td>irritability</td>
<td>Musculoskeletal and connective tissue disorders</td>
<td>common</td>
<td>myalgia, arthralgia</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>common</td>
<td>vomiting, nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>common</td>
<td>arthralgia, myalgia</td>
<td>General disorders and administration site</td>
<td></td>
<td>fatigue, injection site</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>rare</td>
<td>febrile seizures</td>
<td>conditions</td>
<td></td>
<td>pyrexia, chills, injection site</td>
</tr>
<tr>
<td>General disorders and administration site</td>
<td>very common</td>
<td>fatigue, decreased activity, injection site pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>conditions</td>
<td>common</td>
<td>pyrexia, injection site pruritus, injection site swelling, injection site erythema</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Zabdeno® (Ad26.ZEBOV), Mvabea® (MVA-BN-Filo) vaccine regimen indicated for active immunization to prevent disease caused by Ebola virus (Zaire) in individuals ≥1 year of age in the EU

**EU Marketing Authorization obtained 01 July 2020 (EC Decision)**

- Approval pathway: exceptional circumstances*
- European Public Assessment Report (EPAR)
  - The overall benefit/risk of the Zabdeno®, Mvabea® vaccine regimen is positive
  - High unmet need for a prophylactic vaccine
  - Janssen committed to conduct effectiveness study as post-approval commitment if opportunity arises (status to be reported annually/study to be done in context of an outbreak)

**WHO prequalification in April 2021**

- Based on EMA dossier
- Parallel review with two National Regulatory Authorities in Africa
- Facilitated process with approximately 20 countries in Africa is under planning with WHO
- It will complement conditional approval in Rwanda in Sept 2019, and the temporary use in DRC in May 2021

* Annex I to Directive 2001/83/EC – Marketing Authorisation under exceptional circumstances
  
  
  
  
  WHO list of prequalified vaccines: https://extranet.who.int/pqweb/vaccines/prequalified-vaccines
Strategic Group of Experts (SAGE) has clarified Ebola vaccination strategies

Complementary tools for comprehensive public health strategy to contain/prevent Ebola outbreaks

<table>
<thead>
<tr>
<th>Merck vaccine (rVSV-ZEBOV-GP, Ervebo®)</th>
<th>Janssen Vaccine Regimen (Ad26.ZEBOV, MVA-BN-Filo, Zabdeno®, Mvabea®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outbreak response</strong> (Reactive use)</td>
<td>Ring vaccination and HCWs/FLWs in affected areas</td>
</tr>
<tr>
<td>People living in affected areas, and those living in neighboring areas but who are not eligible for Merck’s vaccine</td>
<td></td>
</tr>
<tr>
<td><strong>In the absence of outbreak</strong> (Preventive or prophylactic use)</td>
<td><strong>National response teams</strong></td>
</tr>
<tr>
<td>National response teams</td>
<td>International responders</td>
</tr>
<tr>
<td>Laboratory workers with possible exposure to Ebola virus and those working in specialized research units and Ebola Treatment Units</td>
<td></td>
</tr>
<tr>
<td>(large scale preventive vaccinations in the absence of an outbreak not recommended)</td>
<td></td>
</tr>
</tbody>
</table>

https://www.fda.gov/vaccines-blood-biologics/ervebo
https://www.who.int/immunization/policy/position_papers/interim_emoji_recommendations_may_2019.pdf
SAGE 24 March 2021
Steps Toward Widespread Vaccine Deployment

- Approval by Stringent Regulatory Authority (EMA, FDA, MHRA, etc.)
- Formal SAGE Group Meeting & Recommendation
- WHO Prequalification (PQ)

Facilitated Process

National Licenses by African Regulatory Authorities

Prophylactic Vaccine Deployment by African National Authorities
Private-public partnerships **critical** for successful registration of the vaccine
- Financial support
- Partners’ contributions
- Unique set up of partnership

Ongoing partnerships’ support **critical** for setting up the vaccine for its intended use
- Answering additional questions about vaccine

Lasting legacy of these commitments
- Publications
- Capacity maintenance (training of personnel, attraction for new projects)
- Lessons learned for accelerated development
Presentations of some major projects achievements:

Clinical trials

Chaired by Pr. Deborah WATSON-JONES
Presentations of some major projects achievements:

Clinical trials

Phase 1 clinical trials

Dr. Gaudensia MUTUA
Presentations of some major projects achievements:

**Phase 1 Clinical trials sites**

**FIH UK & US**

**EBL1001 & EBL1002**
- Establish preliminary safety and immunogenicity
- Identify optimal heterogenous prime-boost regimen
- Investigate durability of immune responses
- Number of volunteers: 72 (UK) and 127 (US)

**AFRICA**

**EBL1003 (KE/GH**) EBL1004 (UG/TZ)**
- Replicate data from FIH studies in countries unaffected by the EBL outbreak
- Confirm preliminary safety and immunogenicity
- Number of volunteer 148
Presentations of some major projects achievements:

Phase 1 Clinical trials sites

In Ghana....

Study Approved by Ghana FDA after significant delays

- Followed by community protests
- Government stops study
- Ghana college of science in support of government action
Presentations of some major projects achievements:

**EBL1001 and EBL1002 FIH clinical trials**

**EBL1001 (UK)**

<table>
<thead>
<tr>
<th>Group</th>
<th>N (active/placebo)</th>
<th>Dosage</th>
<th>MVA: $1 \times 10^8$ TCID$_{50}$</th>
<th>Ad26: $5 \times 10^{10}$ vp</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15/3</td>
<td>MVA</td>
<td>Ad26</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15/3</td>
<td>MVA</td>
<td>Ad26</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15/3</td>
<td>Ad26</td>
<td>MVA</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15/3</td>
<td>Ad26</td>
<td>MVA</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Ad26</td>
<td>MVA</td>
<td></td>
</tr>
</tbody>
</table>

In **EBL1001**: Randomized (5:1) to receive MVA and Ad26 or placebo. 15 participants were included in a non-randomized group and received open-label Ad26/MVA with 14-day prime-boost interval.

**EBL1002 (US)**

<table>
<thead>
<tr>
<th>Group</th>
<th>N (active/placebo)</th>
<th>Dosage</th>
<th>MVA: $1 \times 10^8$ TCID$_{50}$</th>
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<tbody>
<tr>
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<td>2</td>
<td>15/3</td>
<td>MVA</td>
<td>Ad26</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15/3</td>
<td>MVA</td>
<td>Ad26</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15/3</td>
<td>Ad26</td>
<td>MVA</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>9/1</td>
<td>MVA</td>
<td>MVA</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>9/1</td>
<td>Ad26</td>
<td>Ad26</td>
<td></td>
</tr>
</tbody>
</table>

In **EBL1002**: Four heterologous prime-boost schedules randomized (5:1) to receive MVA and Ad26 or placebo in each schedule. Separately, MVA and Ad26 homologous prime-boost schedules with 14-day interval were randomized (9:1) to receive MVA or Ad26 or placebo in each schedule.
Presentations of some major projects achievements:

Antibody Responses

Humoral responses
- Significant boosting of antibody responses with all heterologous prime-boost regimens

Cellular Responses (Not shown)
- Similar trajectories observed for CD4+ and CD8+ T cell responses

Prime-boost interval (28 vs 56 days) had no impact on responses

Marginal insignificant differences between MVA/AD26 vs AD26/MVA regimens
Presentations of some major projects achievements:
Durability of Immune Responses

- Durability of humoral and cellular immune responses induced by AD26/MVA
- No significant difference with different time intervals (Not shown)
- No significant difference between AD26/MVA and MVA/Ad26 (Not Shown)
Presentations of some major projects achievements:

**EBL1003 (N=72) and EBL1004 (N=72) trial design**

<table>
<thead>
<tr>
<th>Group (active/placebo)</th>
<th>N</th>
<th>MVA</th>
<th>Ad26</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15/3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15/3</td>
<td></td>
<td>MVA</td>
<td>Ad26</td>
</tr>
<tr>
<td>15/3</td>
<td></td>
<td>Ad26</td>
<td>MVA</td>
</tr>
<tr>
<td>15/3</td>
<td></td>
<td>Ad26</td>
<td>MVA</td>
</tr>
</tbody>
</table>

**Dosage:**
- MVA: 0.5ml of $1 \times 10^8$ TCID$_{50}$
- Ad26: 0.5ml of $5\times10^{10}$ vp

**Immunogenicity Follow-up:**
- Total IgG antibodies (ELISA)
- IFN-γ+ T cell responses (ELISpot)
- Virus Neutralizing Antibodies (VNA)
- CD4+ and CD8+ T cell cytokine responses (ICS) collected up to 1 year

**Safety Follow-up:**
- Local and systemic reactogenicity events (7 days post each vaccination)
- SAEs throughout the study
- Unsolicited AEs

Clinicaltrials.gov: NCT02376426/ NCT02376400.

TCID$_{50}$, 50% tissue culture infectious dose; vp, viral particles
Presentations of some major projects achievements: EBL1003 & EBL1004 Results Confirmed....

**SAFETY**

- Safety profile comparable to EBL1001
  - Most frequent Reactogenicity events Local site pain and headache and no IP related SAE

**IMMUNOGENICITY**

- Robust binding antibody responses sustained up to 12 months post-prime
- Substantial, rapid and sustained boosting of neutralizing antibodies seen with all regimens
- Ad26-primed regimens show an earlier antibody response than MVA-primed regimens (but no difference at later time points)
- CD4+ T cell cytokine responses similar to those of Western participants
- Fewer participants displayed CD8+ T cell cytokine responses compared to US/UK studies
Presentations of some major projects achievements:

**Phase 1: Summary of Results**

The Ad26.ZEBOV and MVA-BN-Filo heterologous prime-boost vaccine regimen was safe and well tolerated in healthy ADULT American/European and African Populations.

The Ad26.ZEBOV and MVA-BN-Filo heterologous prime-boost vaccine regimen was conferred robust and durable immune responses to Ebola glycoprotein in healthy ADULT US, UK and African volunteers.

---

**EBL Phase 2 Trials**
Presentations of some major projects achievements:
Clinical trials

Phase 1 and 3 clinical trials in Sierra Leone

Dr. Frank BAIDEN
Presentations of some major projects achievements:

Kambia district in rural northern Sierra Leone

Kambia District Population
~325,000

Kambia & Mambolo
Presentations of some major projects achievements:

**EBOVAC studies in Sierra Leone – May 2015 to date**

**EBOVAC1:**
- EBL3001 Phase 3 Ad26.ZEBOV, MVA-BN-Filo D0/56 regimen trial (**Completed**)
- EBL2011 Children Booster Study (**About to start in Kambia**)
- Ancillary studies (e.g. malaria infection and vaccine immune responses; Ebola serology in screened population)

**PREVAC trial**: Multi-site evaluation of two Ebola vaccines (with Guinea, Liberia, Mali) (**Data analysis is ongoing**)

**Social science**: Community dynamics, attitudes and perceptions on clinical trials

**EBOVAC3**:  
- EBL3005 - Long term follow-up of EBL3001 participants (to 5 years)  
- EBL2005 infant study (**Analysis to commence soon**
Presentations of some major projects achievements:

**EBL3001 study design**

**Stage 1**
- 43 adults received Ad26, MVA and were followed up for 2 years
- Ad26 booster at 2yrs and followed up for an additional year

**Stage 2**
- 400 adults and 576 children (age de-escalation)
- Randomised 3:1 to Ad26, MVA or active control (MenACWY, Placebo)
- Follow-up for 2 years (adults) and 1 year (children)

Ebola vaccine (Ad26.ZEBOV, MVA-BN-Filo) regimen
Active control (MenACWY, Placebo)
Presentations of some major projects achievements:

**Anti-GP Binding Antibody Response in Adults**

![Graph showing antibody concentrations over time](image)

- **Ad26 MVA**
- **Time (days)**
- **LLOQ**

**Antibody Arbitrary Concentration (ELISA Units/mL)**

- **4784 EU/mL**
- **3810 EU/mL**

Stage 1: Ad26, MVA (Ad26)

Stage 2: MenACWY, Placebo

Stage 2: Ad26, MVA
Presentations of some major projects achievements:

**Anti-GP Binding Antibody Response in children**

Immune responses paediatric participants were higher compared to adults in the same study
Presentations of some major projects achievements:

Challenges and lessons learnt

Epidemic declined making efficacy trial impossible
- Change from efficacy to immunogenicity and safety study

Limited onsite experience in clinical trials
- Training and refresher training
- Community engagement

Eligibility
- Working with EPI programme to identify eligible children

Personnel, equipment & maintenance
- External expertise to fill critical gaps
- Importations e.g. equipment for ER in district hospital
Presentations of some major projects achievements:

**Cold chain & Laboratory capacity**

- **Vaccine depot**
  - 24/7 generator power. Storage capacity: 2-8°C, -20°C & -80°C
- **Haematology, biochemistry, malaria & ELISA**
- **GeneXpert Ebola PCR assay**
Presentations of some major projects achievements:

Upcoming and future work

• **EBOVAC 1**
  
  o Phase 2, **open label** - Safety and immunogenicity of Ad26.ZEBOV booster.

  o EBL2011 booster study on healthy children previously (>2 years) vaccinated with Ad26.ZEBOV (dose 1) followed by MVA-BN-Filo (dose 2) 56 days later. (**Starting in July 2021**)

• **Malaria**: Impact of repeated malaria infections on vaccine immune response using bead-based assay
Presentations of some major projects achievements:

Clinical trials

**Phase 2 clinical trials in Europe and Africa**

Dr. Houreratou BARRY

![Centre Muraz logo](image)
A total of 20 clinical studies contribute to the safety and immunogenicity profile of Ad26.ZEBOV, MVA-BN-Filo. 4 studies include children from 4 months to 17 years of age (EBL2002, PREVAC (2004), 2005 and 3001). Study EBL2002 is first study to include children in east Africa vaccinated with Ad26.ZEBOV and MVA-BN-Filo.
Presentations of some major projects achievements:

**Phase 2 clinical trials**

### STUDY DESIGN

- **EBL2001**

#### Ratio

Active/placebo for each cohort

- **Cohort II:** 14:1
- **Cohort III:** 10:3

#### Group and Dosage

<table>
<thead>
<tr>
<th>Group</th>
<th>Dosage: $Ad26: 5 \times 10^{10}$ vp $MVA: 1 \times 10^{8}$ Inf.U</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$Ad26$ $MVA$</td>
</tr>
<tr>
<td>2</td>
<td>$Ad26$ $MVA$</td>
</tr>
<tr>
<td>3</td>
<td>$Ad26$ $MVA$</td>
</tr>
</tbody>
</table>

Calendar days:

- **Day 29**
- **Day 57**
- **Day 85**
- **Day 365**
Presentations of some major projects achievements:

**Phase 2 clinical trials**

**STUDY DESIGN:** EBL2002

A randomized, blinded, placebo-controlled, Phase 2 Study

**Objectives**

**Primary**
- Assess the safety and tolerability of different vaccination schedules in healthy adults, elderly, and HIV-infected subjects and healthy children

**Secondary**
- Assess immune responses to the EBOV GP of different vaccination schedules

**2-Dose Vaccine Regimen, IM**

Non-replicating viral vectored vaccines

- **Dose 1**
  - Ad26.ZEBOV
  - $5 \times 10^{10}$ vp

- **Dose 2**
  - MVA-BN®-Filo
  - $1 \times 10^8$ Inf.U.

**Days**

- **Days 0**
- **28 or 56 or 84**

**Group 1:**
- Day 1, Day 29
  - Healthy adult and elderly subjects ($288/44$ in Group 1, $268/43$ in Group 2 and $132/22$ in Group 3)

**Group 2:**
- Day 1, Day 57

**Group 3:**
- Day 1, Day 85
  - (in Cohort 1 only)

**Cohort 2a**
- HIV-infected subjects ($71/12$ in Groups 1 and 2)

**Cohort 2b**
- Adolescents (12-17 years incl.)
  - ($66/11$ in Group 1 and $65/10$ in Group 2)

**Cohort 3**
- Children (4-11 years incl.)
  - ($66/12$ in Groups 1 and 2)

EBOVAC projects Stakeholder meeting, 22 June 2021
Presentations of some major projects achievements:

**Phase 2 clinical trials**

**SAFETY RESULTS**

EBL2001: most frequent unsolicited adverse events (AEs) and serious adverse events (SAEs) throughout the study in Cohorts II and III.

<table>
<thead>
<tr>
<th>Incidence, reports following n doses (%)</th>
<th>Ad26.ZEBOV</th>
<th>MVA-BN-Filo</th>
<th>All Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 332</td>
<td>N = 236</td>
<td>N = 72</td>
<td></td>
</tr>
<tr>
<td><strong>Any Unsolicited AE</strong></td>
<td>115 (34·6)</td>
<td>81 (34·3)</td>
<td>24 (33·3)</td>
</tr>
<tr>
<td><strong>MEDRA classes of main reported AEs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>30 (9·0)</td>
<td>28 (11·9)</td>
<td>7 (9·7)</td>
</tr>
<tr>
<td>Upper respiratory tract Infection</td>
<td>4 (1·2)</td>
<td>12 (5·1)</td>
<td>3 (4·2)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>10 (3·0)</td>
<td>7 (3·0)</td>
<td>0</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>17 (5·1)</td>
<td>12 (5·1)</td>
<td>3 (4·2)</td>
</tr>
<tr>
<td>Headache</td>
<td>5 (1·5)</td>
<td>7 (3·0)</td>
<td>2 (2·8)</td>
</tr>
<tr>
<td>Investigations</td>
<td>16 (4·8)</td>
<td>13 (5·5)</td>
<td>2 (2·8)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>17 (5·1)</td>
<td>7 (3·0)</td>
<td>2 (2·8)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>9 (2·7)</td>
<td>8 (3·4)</td>
<td>5 (6·9)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>12 (3·6)</td>
<td>6 (2·5)</td>
<td>3 (4·2)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>10 (3·0)</td>
<td>5 (2·1)</td>
<td>3 (4·2)</td>
</tr>
</tbody>
</table>

**SAEs throughout study**

<table>
<thead>
<tr>
<th>Ad26.ZEBOV &amp; MVA-BN-Filo</th>
<th>All placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 332</td>
<td>N = 44</td>
</tr>
<tr>
<td>Any reported SAE</td>
<td>11 (3·3)</td>
</tr>
<tr>
<td>SAE related to vaccination</td>
<td>0</td>
</tr>
</tbody>
</table>
### SAFETY RESULTS

**EBL2002: Frequency of solicited and unsolicited adverse events in adults**

<table>
<thead>
<tr>
<th></th>
<th>Healthy Adults</th>
<th>Adults with HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall solicited AEs</strong></td>
<td>70.7%</td>
<td>72.1%</td>
</tr>
<tr>
<td><strong>Any solicited Grade 3</strong></td>
<td>2.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td><strong>Overall solicited local AEs</strong></td>
<td>54.0%</td>
<td>57.3%</td>
</tr>
<tr>
<td><strong>Any solicited local Grade 3</strong></td>
<td>0.3%</td>
<td>0.8%</td>
</tr>
<tr>
<td><strong>Overall solicited systemic AEs</strong></td>
<td>62.7%</td>
<td>59.2%</td>
</tr>
<tr>
<td><strong>Any solicited systemic Grade 3</strong></td>
<td>2.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td><strong>Most frequent local solicited AE</strong></td>
<td>Injection site pain</td>
<td>Injection site pain</td>
</tr>
<tr>
<td><strong>Most frequent systemic solicited AE</strong></td>
<td>Fatigue</td>
<td>Fatigue</td>
</tr>
<tr>
<td><strong>Any pyrexia (defined as ≥38°C)</strong></td>
<td>4.6%</td>
<td>6.4%</td>
</tr>
<tr>
<td><strong>Grade 3 pyrexia (defined as ≥39°C)</strong></td>
<td>0.8%</td>
<td>1.7%</td>
</tr>
<tr>
<td><strong>Overall unsolicited AEs</strong></td>
<td>35.4%</td>
<td>32.1%</td>
</tr>
</tbody>
</table>
Presentations of some major projects achievements:

**Phase 2 clinical trials**

### SAFETY RESULTS

**EBL2002**: Frequency of solicited and unsolicited adverse events in Children and adolescents

<table>
<thead>
<tr>
<th></th>
<th>Adolescents</th>
<th></th>
<th></th>
<th>Children</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ad26.ZEBOV</td>
<td>MVA-BN-Filo</td>
<td>Pbo</td>
<td>Ad26.ZEBOV</td>
<td>MVA-BN-Filo</td>
<td>Pbo</td>
</tr>
<tr>
<td></td>
<td>N=110</td>
<td>N=109</td>
<td>N=41</td>
<td>N=108</td>
<td>N=108</td>
<td>N=47</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Overall solicited local AEs</td>
<td>50.9</td>
<td>45.0</td>
<td>34.1</td>
<td>50.9</td>
<td>40.7</td>
<td>31.9</td>
</tr>
<tr>
<td>Any solicited local grade 3</td>
<td>0</td>
<td>0.9</td>
<td>2.4</td>
<td>2.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Overall solicited systemic AEs</td>
<td>53.6</td>
<td>47.7</td>
<td>43.9</td>
<td>43.5</td>
<td>18.5</td>
<td>23.4</td>
</tr>
<tr>
<td>Any solicited systemic grade 3</td>
<td>1.8</td>
<td>0</td>
<td>0</td>
<td>0.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Most frequent local solicited AE (injection site pain)</td>
<td>45.5</td>
<td>44.0</td>
<td>14.6</td>
<td>41.7</td>
<td>33.3</td>
<td>21.3</td>
</tr>
<tr>
<td>Most frequent systemic solicited AE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>42.7</td>
<td>35.8</td>
<td>36.6</td>
<td>18.5</td>
<td>9.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Decreased activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any pyrexia (defined as ≥38°C)</td>
<td>5.5</td>
<td>4.6</td>
<td>4.9</td>
<td>22.2</td>
<td>3.7</td>
<td>4.3</td>
</tr>
<tr>
<td>Grade 3 pyrexia (defined as ≥40°C)</td>
<td>0.9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Overall unsolicited AEs</td>
<td>53.6</td>
<td>40.4</td>
<td>41.5</td>
<td>38.9</td>
<td>38.9</td>
<td>48.9</td>
</tr>
</tbody>
</table>
Presentations of some major projects achievements:

**Phase 2 clinical trials**

**EBL2001: Binding Antibody Responses (Cohort I and II) EBOV GP FANG ELISA; ELISA units/mL**

![Graph showing antibody responses over time](image_url)
Presentations of some major projects achievements:

Phase 2 clinical trials

EBL2002: Adults Binding Antibody Responses EBOV GP FANG ELISA (EU/mL)

**Healthy Adults**

- Ad26.ZEBOV, MVA-BN-Filo induces humoral memory that can rapidly be re-activated
- Strong anamnestic responses within 7 days post booster (55-fold increase)
- 21 days post booster, binding antibody levels 5 to 9-fold greater than 21 days post dose 2 levels
- Post booster antibodies persist at ± 10-fold higher level than post 2-dose regimen
- Binding antibody response levels similar between the binding antibody responses in HIV-infected versus healthy adults

**HIV+ Adults**

- Ad26.ZEBOV, MVA-BN-Filo induces humoral memory that can rapidly be re-activated
- Strong anamnestic responses within 7 days post booster (55-fold increase)
- 21 days post booster, binding antibody levels 5 to 9-fold greater than 21 days post dose 2 levels
- Post booster antibodies persist at ± 10-fold higher level than post 2-dose regimen
- Binding antibody response levels similar between the binding antibody responses in HIV-infected versus healthy adults
Presentations of some major projects achievements:

**Phase 2 clinical trials**

**EBL2002:** Geometric mean concentrations of EBOV-specific binding antibodies (FANG ELISA, 95% CI) in adolescents and children
Presentations of some major projects achievements:

Phase 2 clinical trials

MAIN POINTS

The Ad26.ZEBOV, MVA-BN-Filo vaccine regimens (0.28 – 0.56 – 0.84 intervals) were well-tolerated and no safety concerns were identified in healthy adults or in adults with HIV and children.

Heterologous 2-dose Ad26.ZEBOV, MVA-BN-Filo vaccine regimen induces **humoral memory** that can rapidly be re-activated.

**Strong anamnestic antibody responses** within **7 days** post booster (40-55-fold increase).

21 days post-booster dose, binding antibody levels 3-5-fold greater than peak post-dose 2 levels.

Post-booster antibodies **persist at ± 10-fold higher level** than post 2-dose regimen.

The Ad26.ZEBOV, MVA-BN-Filo vaccine regimen was well tolerated in pediatric cohorts and produced robust vaccine-induced immune responses, which persisted up to one year post AD26.ZEBOV in both EBL2002 and EBL3001.
Immunology and Modelling

Chaired by Pr. Rodolphe THIEBAUT
Presentations of some major projects achievements:

**Immunology and Modelling**

Little was known in the mechanisms of the vaccine triggered immune response before the EBOVAC projects.

The objective of the EBOVAC 2 exploratory work was to **perform detailed analysis of the immune response to the heterologous 2-dose Ad26.ZEBOV, MVA-BN-Filo vaccine regimen in phase 2 trials** conducted in European and African populations, with 3 major purposes:

- To measure the humoral and cellular response to the vaccine
- To further explore the immune pathways triggered by vaccination
- To use these data to build and refine an in silico model of the immune response to the vaccine
Presentations of some major projects achievements:

**Immunological pathways**

- **Ad26.ZEBOV**
  - Stimulate innate response
  - Antigen uptake and presentation

- **MVA-BN-Filo**
  - Induce cellular responses
  - Effector of memory CD8+ T cell

**Innate responses**
- Blood vessels
- PRR
- NK

**Adaptive responses**
- Plasma cells
- Memory B cells
- Naïve B cells
- Naïve T cell
- T<sub>FH</sub>
- T<sub>TH</sub>
- T<sub>HI</sub>
- Other T<sub>TH</sub> cells
- CD8+ T cell

**Multiple actors involved in the vaccine response**
Presentations of some major projects achievements:

Immunology and Modelling

Immunology of the vaccine response

T cell response

Dr. Christine LACABARATZ

Inserm
Explored Immunological Pathways

Ad26.ZEBOV

MVA-BN-Filo

Innate responses
- Blood vessels
- PRR
- Stimulate innate response

Ebola vaccine
- Antigen uptake and presentation

B Cell activation

Humoral responses
- Naïve B Cell
- Plasma cells
- Memory B cells

Cellular responses
- Naïve T cell
- TCR
- MHC-II
- Co-stimulatory molecules
- Effector CD8+ (CTL)
- Memory CD8+
Immunology of the vaccine response

B cell response

Dr. Elizabeth C LUTTERBUC K
Explored Immunological Pathways

Innate responses

Ad26.ZEBOV

MVA-BN-Filo

Adaptive responses

Humoral responses

Cellular responses

Blood vessels

PRR

B Cell activation

Antigen uptake and presentation

Induce cellular responses

Humoral responses

Plasma cells

Memory B cells

Naïve B Cell

Naïve T cell

Other T H Cells

Naïve T cell

MHC-I

TCR

CD4+

TH1

CD8+

TH1

CD8+

Effector CD8+ (CTL)

Naïve T cell

MHC-I

TCR

Co-stimulatory molecules

NK

DC

DC

B-Cells

CD4+

CD8+
Presentations of some major projects achievements:
Immunology and Modelling

Immunology of the vaccine response

NK cell response

Dr. Martin GOODIER
Explored Immunological Pathways

Innate responses
- Blood vessels
- PRR

Adaptive responses
- Naïve B cells
- Plasma cells
- Memory B cells
- CD4+
- CD8+

Humoral responses
- Antigen uptake and presentation
- MHC-II
- TCR

Cellular responses
- DC
- NK Cells
- Naïve T cell
- Memory CD8+
- Effector CD8+ (CTL)

Ad26.ZEBOV
MVA-BN-Filo

Stimulate innate response
B Cell activation
Antigen uptake and presentation
Induce cellular responses
Presentations of some major projects achievements: NK cell response data EBL2002

**ex vivo analysis**
CD56dimFceR1γ⁺ NK cells (Canonical)

**Subset redistribution**

**Proliferation**

* Anti-GP Antibody dependent activation *in vitro*

**Standard readout**
**Autologous NK cells**

**Degranulation**

Study Visit

- Redistribution and proliferation towards less differentiated NK cells
- Robust antibody dependent activation with a standard readout and autologous NK cells
## Presentations of some major projects achievements:

### NK cell response data EBL1001, 2001, 2002

<table>
<thead>
<tr>
<th>Study</th>
<th>Dosing intervals</th>
<th>Ex-vivo</th>
<th>Assay</th>
<th>Innate Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBL1001 Oxford UK</td>
<td>28 days 56 days</td>
<td>Activation (A) Proliferation (P)</td>
<td>Antibody- dependent degranulation in-vitro Standard NK cell readout</td>
<td>ND</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subset redistribution (SR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>21 days post dose 2 A *</td>
<td>21 days post dose 2 ****</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P ***</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SR **</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBL2001 Inserm France</td>
<td>28 days 56 days</td>
<td>Up to 180 days post dose 2 A *</td>
<td>14 days post dose 2 ****</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td>84 days</td>
<td>P ns</td>
<td>180 days post dose 2 ***</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SR **</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBL2002 Kenya Uganda</td>
<td>28 days 56 days</td>
<td>21 days post dose 2 A ns</td>
<td>21 days post dose 2 ****</td>
<td>ND</td>
</tr>
<tr>
<td>Burkina-Faso</td>
<td></td>
<td>P **</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SR *</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reference 1. Wagstaffe et al. JID. 2019: [https://doi.org/10.1093/infdis/jiz657](https://doi.org/10.1093/infdis/jiz657) 2. Wagstaffe et al. JCI. 2020: [https://doi.org/10.1172/jci132438](https://doi.org/10.1172/jci132438)

Reference 3. Wagstaffe et al. NPJ vaccines. 2021: [https://doi.org/10.1038/s41541-021-00280-0](https://doi.org/10.1038/s41541-021-00280-0)


1. P value compared to baseline: * < 0.05; ** < 0.01; *** < 0.001; **** < 0.0001;   ns: not significant     ND: not determined

2. P value compared to unstimulated: ++++ <0.0001
Presentations of some major projects achievements:

Immunology: CONCLUSION

**Vaccine regimen elicits:**

- Durable EBOV GP-specific CD4+ and CD8+ T cell proliferation and polyfunctional cytotoxic CD8+ T cells until at least 6 months.

- Strong induction of EBOV GP-specific BMEM by Ad26.ZEBOV observed, along with TFH induction, differential gene expression, and BCR sequence changes, indicative of Germinal Centre activation. Maintained for at least 6 months post dose 2.

- Increased frequency of less differentiated NK cells associated with proliferative activity, robust antibody-dependent activation of NK cells up to 6 months post dose 2.
Presentations of some major projects achievements: Immunology and Modelling

Modelisation of the immune response

Dr. Mélanie PRAGUE

Inserm

Inria
Presentations of some major projects achievements:  
Modelisation of the immune response

**Within host model of response to Ebola vaccination**

- Pasin et al. (2019) *Journal of Virology* Dynamics of the humoral immune response to a prime-boost Ebola vaccine: quantification and sources of variation

![Diagram showing the model of the immune response](image)

- Lower bound for long-life antibodies secreting cells: 6 ans
Within host model of persistence to Ebola vaccination (model calibration)

Presentations of some major projects achievements:

Modelisation of the immune response

Extend the results for available data

- Estimation (vs. calibration) on EBL2001 Data

Antibodies secreting cells  B memory cells  Antibodies
Presentations of some major projects achievements:

Modelisation of the immune response

**Extend the results for available data**

- Estimation (vs. calibration) on EBL2001 Data
- Prediction of two years response to vaccination on EBL3001 Data

Lower bound for long-life antibodies secreting cells: 14 ans
Future and ongoing work

Chaired by Dr. Cynthia ROBINSON
EBL2007 Study population and anthropological angle

Pr. Hypolite MUHINDO
EBL2007 Study population and anthropological angle

**EBL2007 SHORT OVERVIEW**

Open-label, monocentric, phase 2 clinical trial

- 699 enrolled participants
  - Day 1: Ad26.ZEBOV
  - Day 57: MVA-BN-Filo

- Two randomization groups
  - Y1 booster: Ad26.ZEBOV
  - Y2 booster: Ad26.ZEBOV

Safety and immunogenicity

**Accomplishment:** 91% retention rate after 1 year

**Currently ongoing:** Group 1 phone contacts 6 months post booster
EBL2007 SHORT OVERVIEW

Location trial: Boende General Reference Hospital, Tshuapa province, DR Congo

Start date: 19/DEC/2019  Foreseen ending: OCT/2022
EBL2007 Study population and anthropological angle

**STUDY POPULATION DEMOGRAPHICS**

- Active health care providers (HCPs) and frontliners
- Mean age: 45 years old
- Many more male (76.39%) HCP and frontliners than females (23.61%)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>N</th>
<th>%</th>
<th>Mean</th>
<th>SD</th>
<th>Min-Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>699</td>
<td>45.01</td>
<td>11.99</td>
<td>19.00-71.00</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>534</td>
<td>76.39</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>165</td>
<td>23.61</td>
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</table>
Top three professions: community health workers, nurses and first aid workers

Main workplace: Boende health center

<table>
<thead>
<tr>
<th>Professions</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Health workers</td>
<td>236</td>
<td>33.76</td>
</tr>
<tr>
<td>Nurse</td>
<td>182</td>
<td>26.04</td>
</tr>
<tr>
<td>First aid worker</td>
<td>177</td>
<td>25.32</td>
</tr>
<tr>
<td>Hygienist</td>
<td>37</td>
<td>5.29</td>
</tr>
<tr>
<td>Midwife</td>
<td>30</td>
<td>4.29</td>
</tr>
<tr>
<td>Medical doctors</td>
<td>13</td>
<td>1.86</td>
</tr>
<tr>
<td>Health facility cleaners</td>
<td>10</td>
<td>1.43</td>
</tr>
<tr>
<td>Care giver</td>
<td>7</td>
<td>1.00</td>
</tr>
<tr>
<td>Laboratory technician</td>
<td>2</td>
<td>0.29</td>
</tr>
<tr>
<td>Nutritionist</td>
<td>2</td>
<td>0.29</td>
</tr>
<tr>
<td>Pharmacist assistant</td>
<td>2</td>
<td>0.29</td>
</tr>
<tr>
<td>Vaccination campaigner</td>
<td>1</td>
<td>0.14</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Establishment of work</th>
<th>N</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Health center</td>
<td>371</td>
<td>53.08</td>
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<tr>
<td>Other (e.g. red-cross)</td>
<td>198</td>
<td>28.33</td>
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<tr>
<td>Hospital</td>
<td>85</td>
<td>12.16</td>
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<td>Health post</td>
<td>37</td>
<td>5.29</td>
</tr>
<tr>
<td>Health zone</td>
<td>8</td>
<td>1.14</td>
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</table>
ANTHROPOLOGICAL ANGLE

Improving preparedness by vaccination of a well-known population at risk (e.g. HCPs) is necessary, but without community engagement (CE), it will be useless.

With the support of social sciences:
- Address complex social relations between participants and community members with the four Rs (reciprocity, relatability, relationships, and respect) (see Dada et al., 2019)
- Understand social dynamics and power structures by being careful about the concept of ‘the community’. (see Wilkinson et al., 2017)
- Conduct more in-depth research on effective models of CE for both global health emergency and disease preparedness settings

Building trust with those people (in)directly involved
EBL2007 Study population and anthropological angle

FOR EBL2007 SPECIFICALLY:

- Explore community experiences of previous outbreak (Boende, 2014) and perceptions of Ebola vaccine options
  Among the medical staff, the trial participants and the “community” while taking complex social and political relationships into account

- Compare Trials EBL3008 (Goma) and EBL2007 (Boende)
  E.g. perception of inclusion/exclusion of pregnant-lactating women for Ebola vaccination

- Describe Local Ebola - ecosystem - livelihood dynamics with a participative modelling approach

- Summarize the regulatory authorities’ experience of studying and deploying an unlicensed vaccine under compassionate use during an epidemic

- Map the landscape of preparedness activities in DRC - Boende site from a One Health perspective + identify gaps
CONCLUSION

Crucial for (Ebola) epidemic preparedness
  o Relatively weak surveillance system
  o HCP & frontliners at higher risk of Ebola
  o Duration of the protection of vaccination to be determined
  o Integrate the socio-anthropological components

Within the EBOVAC projects: first time focus on HCP

Original approach
Future challenges of an improved and sustainable emergency response system for future epidemics

Dr. Melanie SAVILLE
Director of Research and Development
The global need for an organisation like CEPI was recognised after the devastating West African Ebola epidemic, which killed more than 11,000 people and had an economic and social burden of over $53 billion.

CEPI was launched at Davos in 2017 by Norway, India, the Bill & Melinda Gates Foundation, the Wellcome Trust, and the World Economic Forum, as the result of a consensus that a coordinated, international, and intergovernmental plan was needed to develop and deploy new vaccines to prevent future epidemics.
Future challenges of an improved and sustainable emergency response system for future epidemics

**CEPI’s vaccine portfolio**

- **MERS**
  - 5 vaccine candidates

- **Lassa**
  - 6 vaccine candidates

- **Nipah**
  - 4 vaccine candidates

- **Chikungunya**
  - 3 vaccine candidates

- **Rift Valley fever**
  - 2 vaccine candidates

- **COVID-19**
  - 10 vaccine candidates

- **Disease X**
  - 3 platform technologies

**Ebola clinical trial support**
Future challenges of an improved and sustainable emergency response system for future epidemics

Lessons learned from COVID-19 vaccine R&D
Future challenges of an improved and sustainable emergency response system for future epidemics

Rapid progress in vaccine innovation

- Year in which pathogen was linked to disease
- Year in which US vaccine was licensed

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year Pathogen Linked</th>
<th>Year US Vaccine Licensed</th>
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</thead>
<tbody>
<tr>
<td>Typhoid Fever</td>
<td>1880</td>
<td>1927</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1984</td>
<td>1985</td>
</tr>
<tr>
<td>Whooping Cough</td>
<td>1983</td>
<td>1983</td>
</tr>
<tr>
<td>Polio</td>
<td>1936</td>
<td>1955</td>
</tr>
<tr>
<td>Measles</td>
<td>1991</td>
<td>1993</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1957</td>
<td>1959</td>
</tr>
<tr>
<td>Ebola</td>
<td>1976</td>
<td>2019</td>
</tr>
<tr>
<td>COVID-19</td>
<td>2019</td>
<td>2020</td>
</tr>
</tbody>
</table>

CEPI
Future challenges of an improved and sustainable emergency response system for future epidemics

**Speed is of the essence in outbreak response**

**Ebola**

Significant research prior to the outbreak
Rapid deployment of vaccine but outbreak largely managed through non-pharmaceutical interventions

**COVID**

With COVID-19 it took about 300 days from virus characterisation to submission of phase 3 data.

A moonshot to reduce this time to 100 days for future outbreaks.

First test with new variants for COVID-19
Future challenges of an improved and sustainable emergency response system for future epidemics

How can we do better?

Vaccine Development
- Role of rapid response platforms
- Preclinical/clinical development

Regulatory
- Platform master file labelling
- Based on benefit risk assessment

Manufacturing
- Better global geographical footprint
- Regional capacity

Vaccine introduction
- Post approval safety and effectiveness
- Recommendations
Future challenges of an improved and sustainable emergency response system for future epidemics

COVAX: paradigm shift
Future challenges of an improved and sustainable emergency response system for future epidemics

**COVAX: has brought a paradigm shift to global health**

**COVAX firsts**

**Beyond numbers…**

... many "firsts" created by COVAX

- **190** Confirmed and eligible COVAX participants
- **>6B** USD raised within a year for AMC countries
- **>2B** Vaccine doses secured in 2021

- First vaccine EULs granted for global use
- First labelling harmonization of its kind
- First global health safety monitoring system updated weekly
- First model I&L for AMCs with uniform language
- First no-fault compensation programme of its kind
- First global vaccine allocation mechanism
- First pandemic vaccine rollout to L(M)ICs within <3 months of first vaccinations
- First time global rollout of a vaccine requiring UCC

87.9Mn doses shipped to 131 countries and territories (as of June 16)
Future challenges of an improved and sustainable emergency response system for future epidemics

COVAX

CEPI, Gavi and the WHO are co-leading COVAX, with key delivery partner UNICEF, to ensure equitable access to COVID-19 vaccines and end the acute phase of the pandemic by the end of 2021.

COVAX aims to deliver 2 billion doses by the end of 2021.

COVAX has so far shipped over 87.9 million COVID-19 vaccines to 131 participating economies.
Future challenges of an improved and sustainable emergency response system for future epidemics

Another pandemic need never happen

- Universal coronavirus vaccines
- 100-day vaccine development
- Vaccine libraries for whole virus families
- Global networks for lab capacity, assays, and preclinical models
When handling epidemics is not enough: the importance of prevention

Dr. Valérie O Riol-Mathieu
Overall health consequences of Ebola outbreaks go far beyond EVD morbidity and mortality

Ebola virus disease indirect effects on population health because resources are diverted from other health programs:

- HIV infections, malaria, tuberculosis, and human African trypanosomiasis, Maternal and infant health and primary care, Vaccination programs

**EVD risk** in HCW

- 21-32-fold higher in HCWs than in non-HCW adults

**Social impact** of West Africa outbreak with food insecurity, closure of schools, orphans, and heavy psychological impact on affected people, communities and HCWs

**Economy**

- Global economic and social burden of the West Africa epidemic estimated up to US$53.19 billion

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1. Malvy, Ebola Virus Disease, The Lancet 2019
4. Ngatu Occupational EVD in Africa 2017
Multiple Ebola Virus Disease risk groups can be identified

3 drivers of risk of EVD exposure

Occupation

- HCWs (Physicians, Nurses and Midwives, Labworkers, Dentists, Pharmacists, Other hospital personnel, such as admin, cleaning and washing staff, Community health workers, Traditional healers)
- People working with animals and/or meat, such as forest rangers
- Burial workers
- Front line workers:
  - Security personnel (Military, Airport staff, police, border staff)
  - Transportation personnel, e.g. Ambulance / Taxi drivers
  - Other people having multiple interpersonal contacts (Religious/ Community leader, workers on markets / shops, sex workers)

Geography

- Regions prone to Ebola outbreaks (endemic in animals, chronic human carriers)

Temporary mission

- National/ International response teams: people who are being deployed to areas with an outbreak

References:
1. Rugarabamu et al. BMJ Global Health 2020
2. WHO. Disease outbreak news DRC, 10 Feb 2021
3. Adapted from: CDC. ACIP categories of essential workers. Available at: https://www.cdc.gov/vaccines/covid-19/categories-essential-workers.html
Despite progress, EVD prevention, treatment and control strategies are sub-optimal

Guidelines on EVD prevention and control strategies: 5-8
- Travel restrictions / Traveler screening measures
- EVD case detection
- Contact-tracing
- Community-based education
- Management of ill and deceased patients
- Infection prevention for HCWs

Limited treatment options1-4
- EVD management based on supportive care
- 2 US approved treatments / limited availability in Africa (a combination of three monoclonal antibodies and a human monoclonal antibody- mAb114)

Sub-optimal implementation of measures in challenging environments:
- Limited resources in outbreak countries such as running water, stable power, PPE, and technical skills10
- Incoherent contact tracing methods resulting in incomplete identification of contacts11,12,13
- Political unrest and violence against civils14
Compared to reactive vaccination, prophylactic vaccination has a greater impact on the mitigation and prevention of future Ebola epidemics.\(^1\-^3\)

Prophylactic vaccination of populations at high risk of acquiring and transmitting Ebola virus infection—such as HCWs—can significantly reduce the number of cases in the whole community, even at modest levels of coverage.\(^2\)

57% reduction of community cases achieved when prophylactically vaccinating 5% of the general population in addition to 30% of HCWs.\(^1\)

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WHO SAGE recommendations on Ebola have clarified Janssen Ebola vaccine use

**Outbreak response (Reactive use)**

- **Merck vaccine**
  - Contacts of an EVD patient and contacts of contacts

- **Janssen vaccine regimen**
  - Those at some, but lower, risk of EVD. At-risk individuals, such as health workers and frontline workers, in neighboring areas and countries where the outbreak may spread

**In the absence of outbreak (Preventive or prophylactic use)**

- **Janssen vaccine regimen**
  - National Response Teams
    - + International responders, Lab workers, Specialized research Units, Ebola Treatment Units

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SAGE : Strategic Advisory Group of Experts on Immunization
Potential broadening of SAGE recommendation

Broader preventive vaccination

SAGE did not recommend yet widespread preventive use:
- vaccine supply constraints
- unknown duration of protection
- more clarity on vaccine demand

“If Ebola vaccine supply were to increase, SAGE would be able to consider recommendations for preventive vaccination of people at risk in areas and countries that have a history of Zaire-strain EVD outbreaks.”
Stakeholder mobilization needs to continue to ensure progress towards broader preventive Ebola vaccination strategies

- WHO prequalification
- Conditional Approval in Rwanda
- Temporary Use Approval in DRC
- SAGE recommendation
- Expected WHO facilitated meeting with ~20 NRAs

- Expected involvement of GAVI and UNICEF
- Virtuous circle of increased demand and supply

- Continuing evidence generation (special populations, durability, effectiveness...)
- Modelling of various Ebola vaccination impact

- Building Ebola vaccination implementation experience (large studies, campaigns)
- Community engagement and use of technologies to support implementation
- Countries delineating national strategies and expressing demand
PANEL DISCUSSION

June 22nd, 2021
16:10 – 17:00 CET
Panel members:

Pr. Yves LEVY
Pr. Nicolas MEDA
Dr. Pierre MEULIEN
Pr. Hypolite MUHINDO
Pr. Rodolphe THIEBAUT
Pr. Andrew POLLARD
Pr. Pierre Van DAMME
Dr. Johan Van HOOF
Pr. Deborah WATSON-JONES

Moderator:

Pr. Daniel G. BAUSCH
The EBOVAC projects have received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grants agreements EBOVAC1 n°115854, EBOVAC2 n°115861 and EBOVAC3 n°800176. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Association.

THANK YOU FOR YOUR PARTICIPATION!
Thank you to all volunteers, investigators and their staff and all our partners