EBOVAC projects Stakeholder meeting

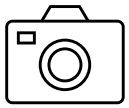
June 22nd, 2021

14:00 – 17:00 CET

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.

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

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.

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!

Opening address

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 tor reflect on the future of the Ebola vaccine deployment strategy**

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 EBOVAC2*

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 ORIOL-MATHIEU (Janssen)*

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 (Inserm)*
- *Pr. Yves LEVY (VRI Inserm)*

Chairman:

- *Pr. Daniel G. BAUSCH (LSHTM)*

Thank you for participating in the EBOVAC projects stakeholder meeting!

Opening address

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.

Opening address

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.**

12/2014-11/2021

- 5 partners
- Phase1and 3 development of 2-dose heterologous vaccine based on Ad26.ZEBOV and MVA-BN-Filo

12/2014-05/2021

- 6 partners
- Phase 2 Phase II development of 2-dose heterologous vaccine based on Ad26.ZEBOV and MVA-BN-Filo

06/2019-05/2023

- 7 partners
- Bringing a prophylactic Ebola vaccine to licensure
- Additional clinical trials in infants and front line workers

EBOMAN manufacturing of 2-dose Ebola vaccine regimen

promote the acceptance and uptake of new Ebola vaccines

Opening address

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…

Opening address

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!

Opening presentations

June 22nd, 2021

14:15 – 14:25 CET

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.

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

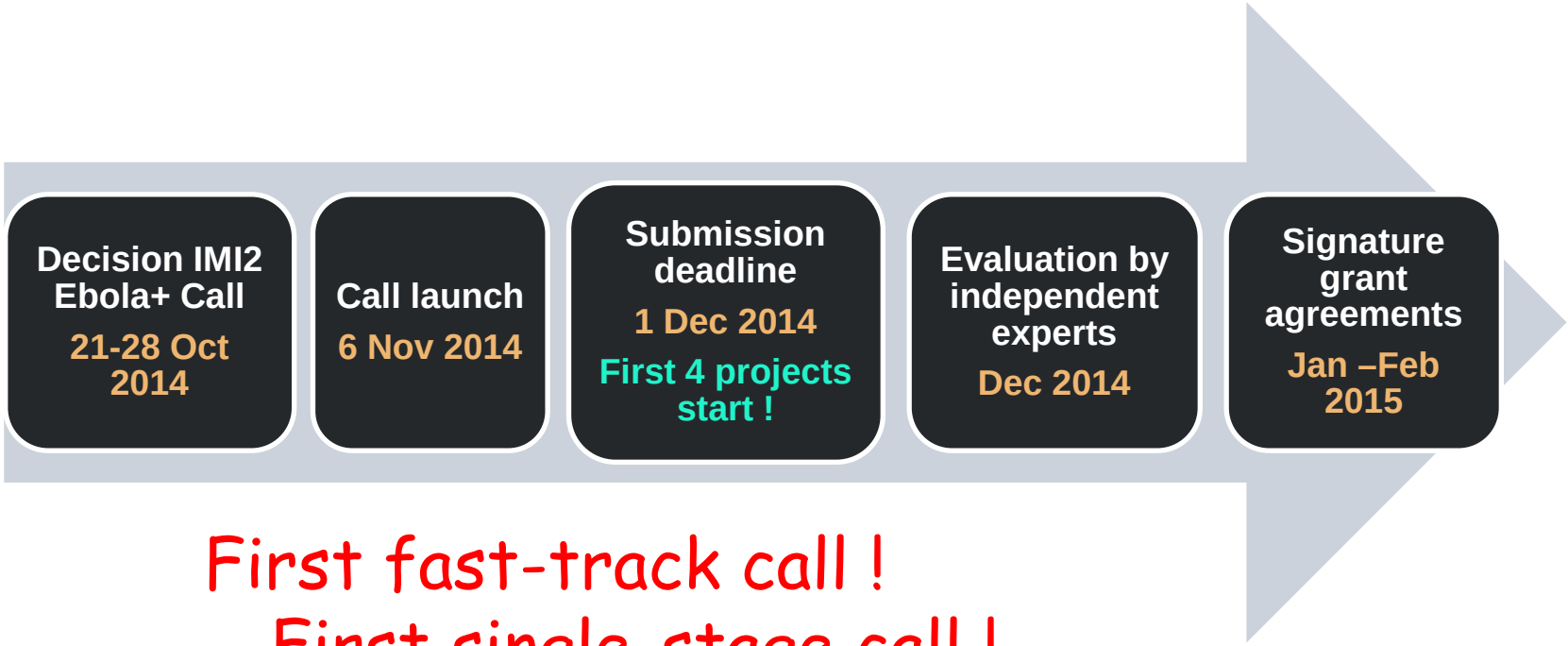
Why the Innovative Medicines Initiative ?

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

imi innovative medicines initiative

A fast-track single-stage process



First fast-track call !

First single-stage call !

First projects to start under IMI2 !

innovative medicines initiative

EU fast-track response

European Commission & EFPIA

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

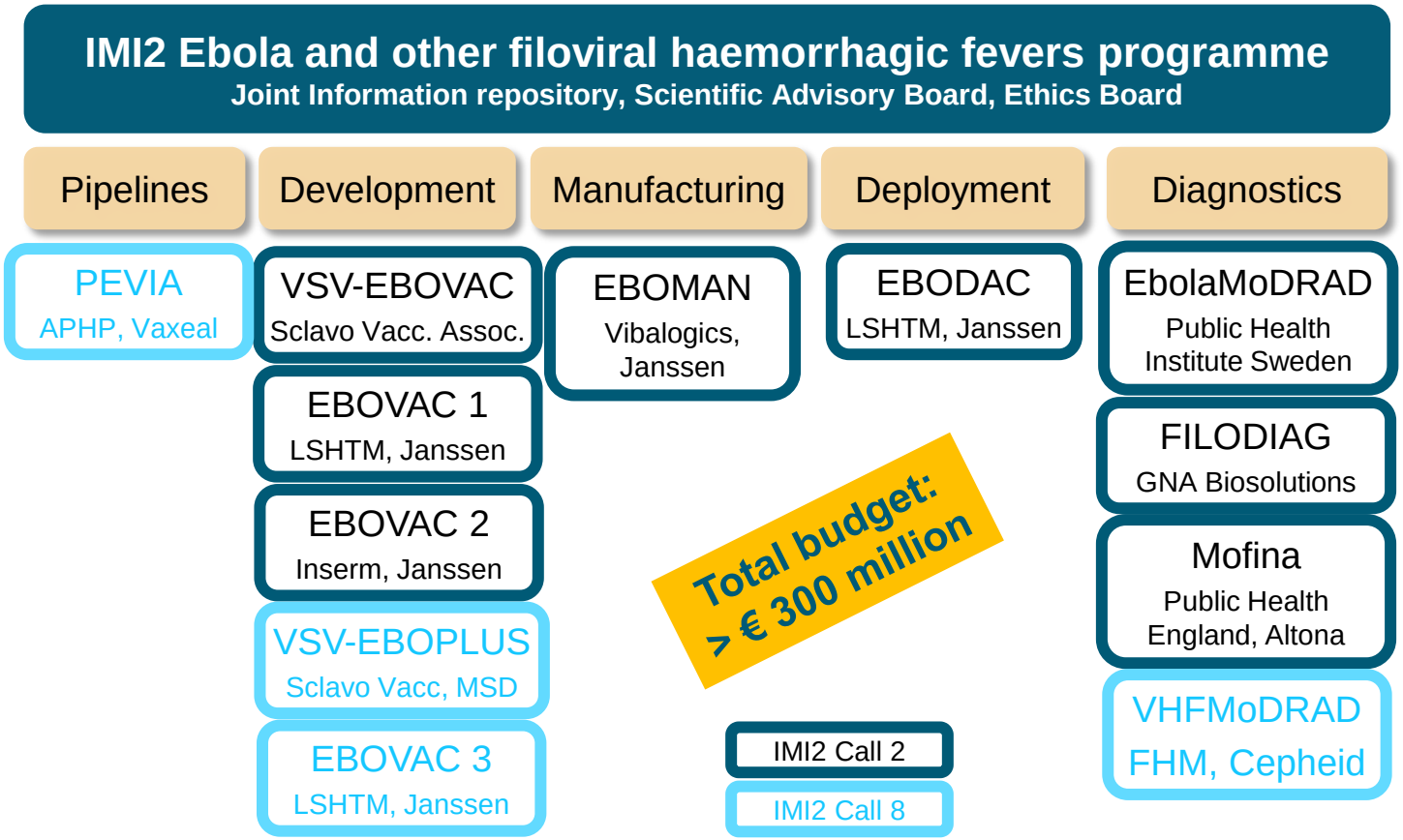
A programmatic approach in IM:

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



EBOVAC programme

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

Other partners: Janssen, INSERM, U. Antwerpen, U. Sierra Leone, Chu Hopitaux Bordeaux, U. Bordeaux, U.Paris Diderot - Paris 7, Universite De Kinshasa, Kinshasa (DRC), CEPI

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

EBOVAC Achievements

June 22nd, 2021

14:35 – 16:10 CET

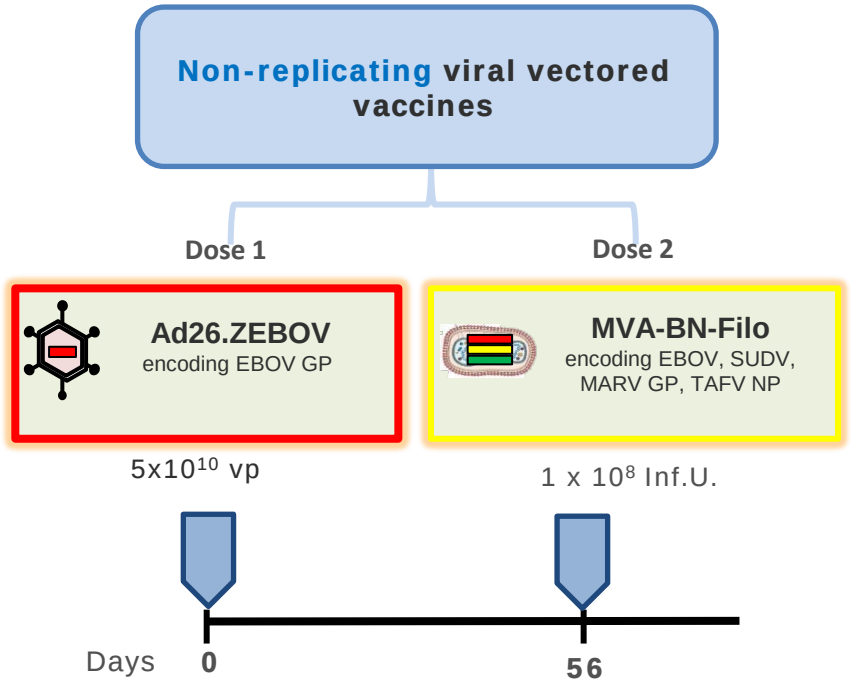
The EBOVAC projects have received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grants agreements EBOVAC1 n°115854, EBOVAC2 n°115861 and EBOVAC3 n°800176. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and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

General Janssen Ebola vaccine development overview

Dr. Cynthia ROBINSON

Janssen Monovalent Ebola Prophylactic Vaccine Regimen

Primary vaccination: 2-Dose Vaccine Regimen, given approximately 8 weeks apart, IM



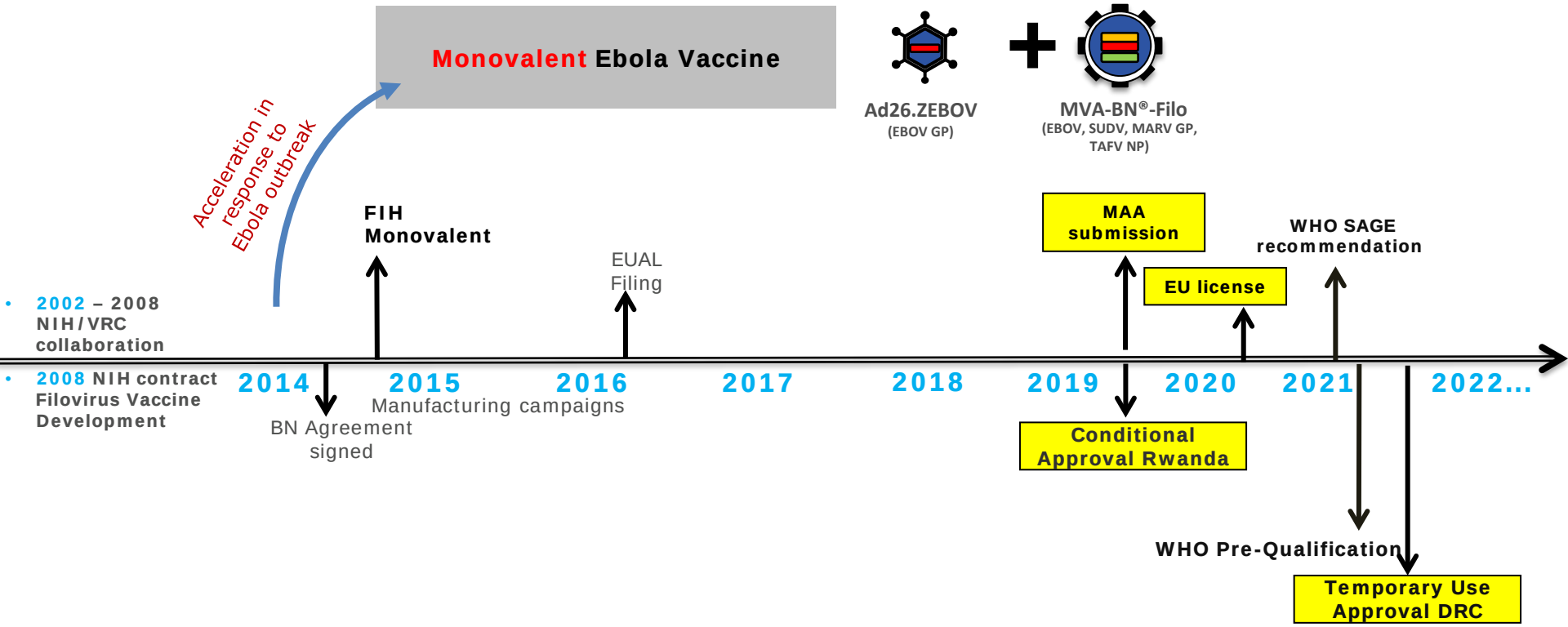
Booster: 1 Dose of Ad26.ZEBOV can be given to in individuals who are at imminent risk of exposure to EBOV

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

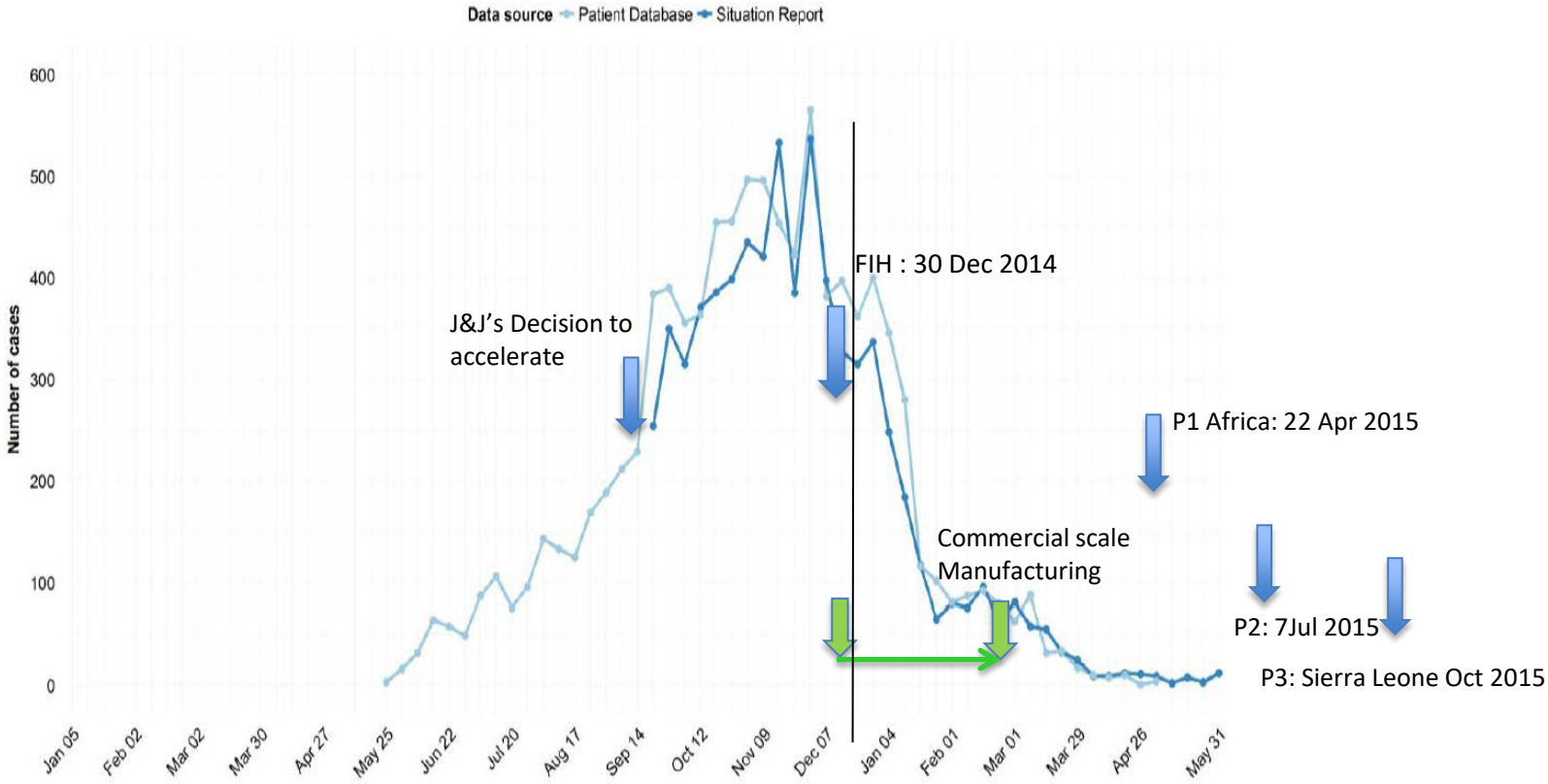


https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf
https://www.ema.europa.eu/en/documents/product-information/mvabea-epar-product-information_en.pdf
WHO list of prequalified vaccines: https://extranet.who.int/pqweb/vaccines/prequalified-vaccines

West African Epidemic & Accelerated Clinical Development of Janssen Prophylactic Ebola Vaccine

2014 2015

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



2014 2015

Vaccine Regimen is well-tolerated in Adults

Ad26.ZEBOV

Adverse Reactions Following Vaccination with Zabdeno		
System Organ Class	Frequency	Adverse reactions
Nervous system disorders	very common	headache
	uncommon	dizziness postural
Gastrointestinal disorders	common	vomiting
Musculoskeletal and connective tissue disorders	very common	arthralgia, myalgia
Skin and subcutaneous tissue disorders	common	pruritus
General disorders and administration site conditions	very common	chills, fatigue, injection site pain, injection site swelling, injection site warmth
	common	pyrexia, injection site pruritus
	uncommon	injection site induration, injection site erythema

MVA-BN-Filo

Adverse Reactions Following Vaccination with Mvabea		
System Organ Class	Frequency	Adverse reactions
Gastrointestinal disorders	common	vomiting
Musculoskeletal and connective tissue disorders	very common	myalgia, arthralgia
Skin and subcutaneous tissue disorders	uncommon	pruritus
General disorders and administration site conditions	very common	fatigue, injection site pain, injection site swelling, injection site warmth
	common	injection site pruritus
	uncommon	injection site induration, injection site erythema

https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf
https://www.ema.europa.eu/en/documents/product-information/mvabea-epar-product-information_en.pdf

Vaccine Regimen is well-tolerated in Children

Ad26.ZEBOV

Adverse Reactions Reported Following Vaccination with Zabdeno		
System Organ Class	**Frequency**	**Adverse reactions**
Metabolism and nutrition disorders	very common	decreased appetite
Psychiatric disorders	very common	irritability
Gastrointestinal disorders	common	vomiting, nausea
Musculoskeletal and connective tissue disorders	common	arthralgia, myalgia
Nervous system disorders	*rare*	*febrile seizures*
General disorders and administration site conditions	very common	fatigue, decreased activity, injection site pain
	common	pyrexia, injection site pruritus, injection site swelling, injection site erythema

MVA-BN-Filo

Adverse Reactions Reported Following Vaccination with Mvabea		
System Organ Class	**Frequency**	**Adverse reactions**
Musculoskeletal and connective tissue disorders	common	myalgia, arthralgia
General disorders and administration site conditions	very common	fatigue, injection site pain
	common	pyrexia, chills, injection site pruritus, injection site swelling, injection site erythema

https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf
https://www.ema.europa.eu/en/documents/product-information/mvabea-epar-product-information_en.pdf

Indication and Regulatory Status

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
https://www.ema.europa.eu/en/documents/assessment-report/zabdeno-epar-public-assessment-report_en.pdf
https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf
https://www.ema.europa.eu/en/documents/product-information/mvabea-epar-product-information_en.pdf
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

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

https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf
https://www.ema.europa.eu/en/documents/product-information/mvabea-epar-product-information_en.pdf
https://www.fda.gov/vaccines-blood-biologics/ervebo
https://www.fda.gov/news-events/press-announcements/first-fda-approved-vaccine-prevention-ebola-virus-disease-marking-critical-milestone-public-health
https://www.who.int/immunization/policy/position_papers/interim_ebola_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

Summary

- 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

Clinical trials

Chaired by Pr. Deborah WATSON-JONES

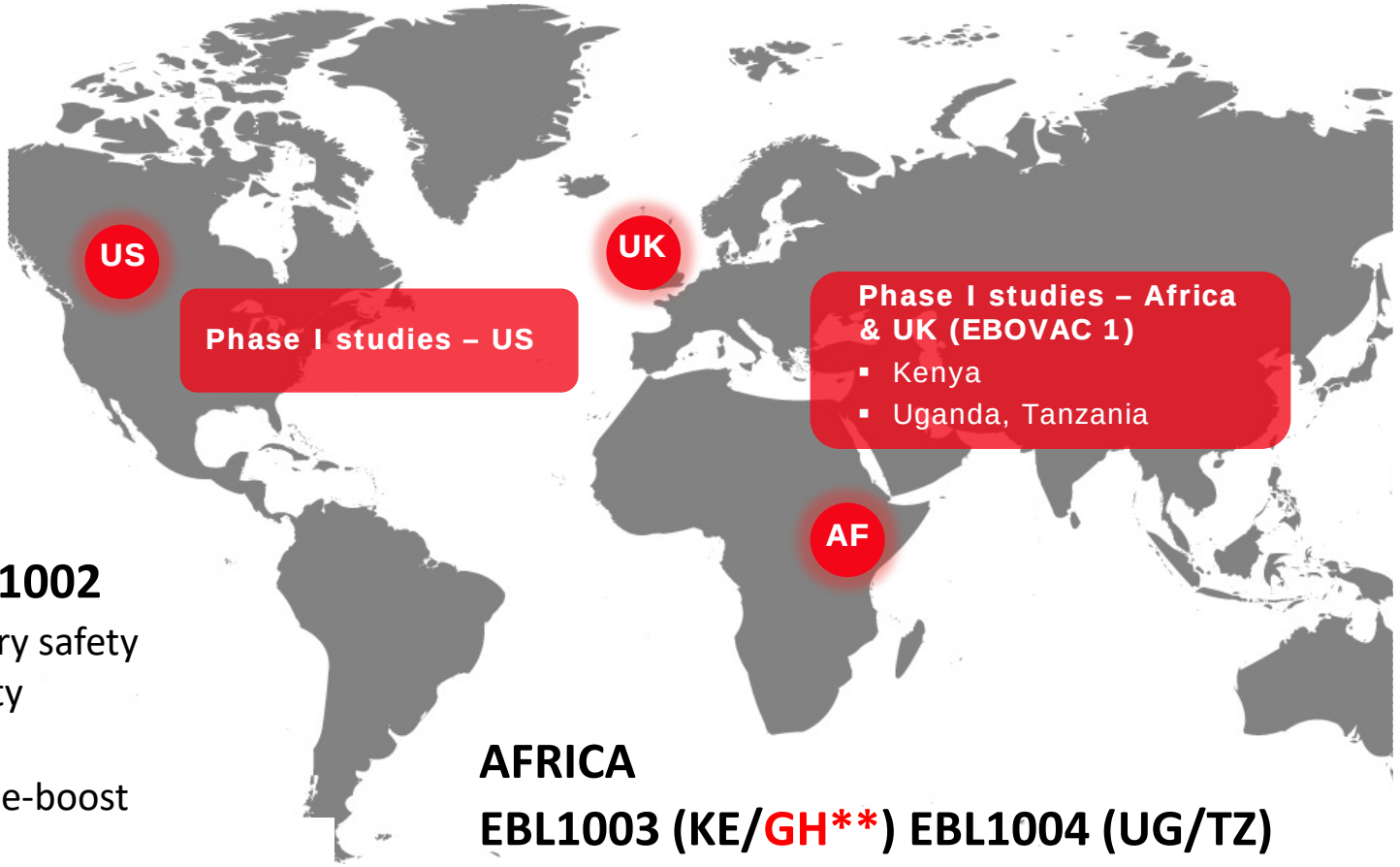
Phase 1 clinical trials

Dr. Gaudensia MUTUA

iavi Translating science into global health impact

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

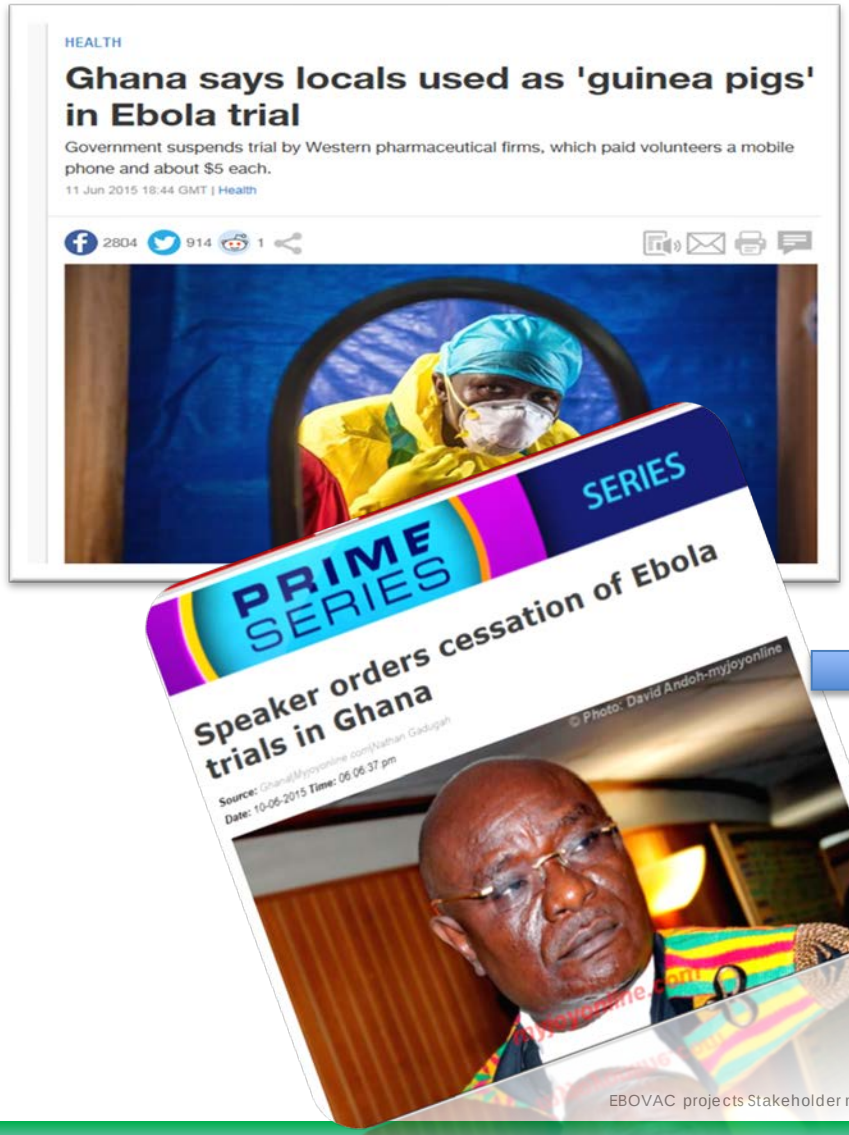
EBL1003 (KE/GH**) EBL1004 (UG/TZ)

- 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….



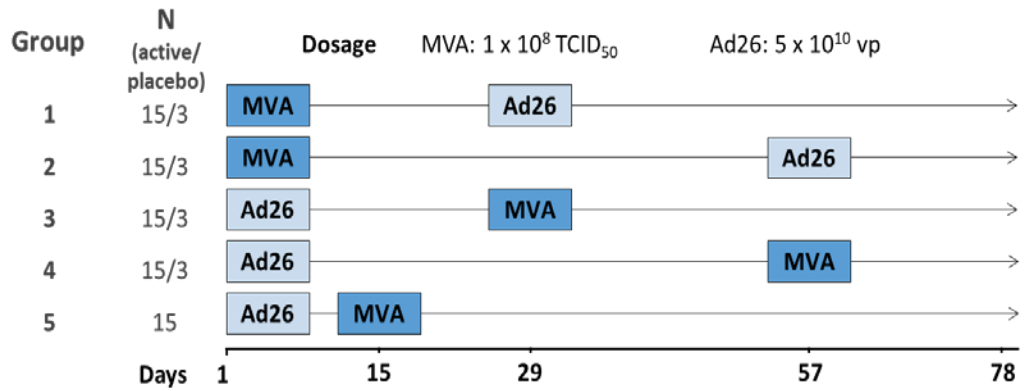
Study Approved by Ghana FDA after significant delays

- Followed by community protests
- Government stops study
- Ghana college of science in support of government action

Presentations of some major projects achievements:

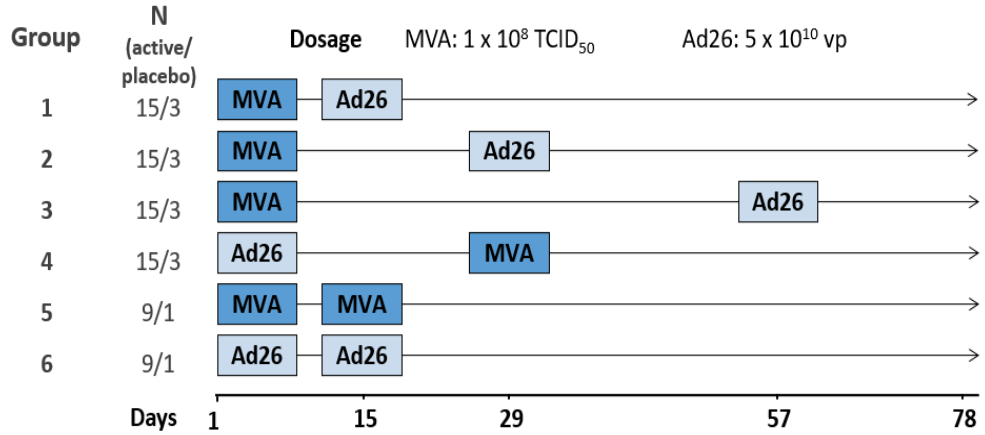
EBL1001 and EBL1002 FIH clinical trials

EBL1001 (UK)



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.

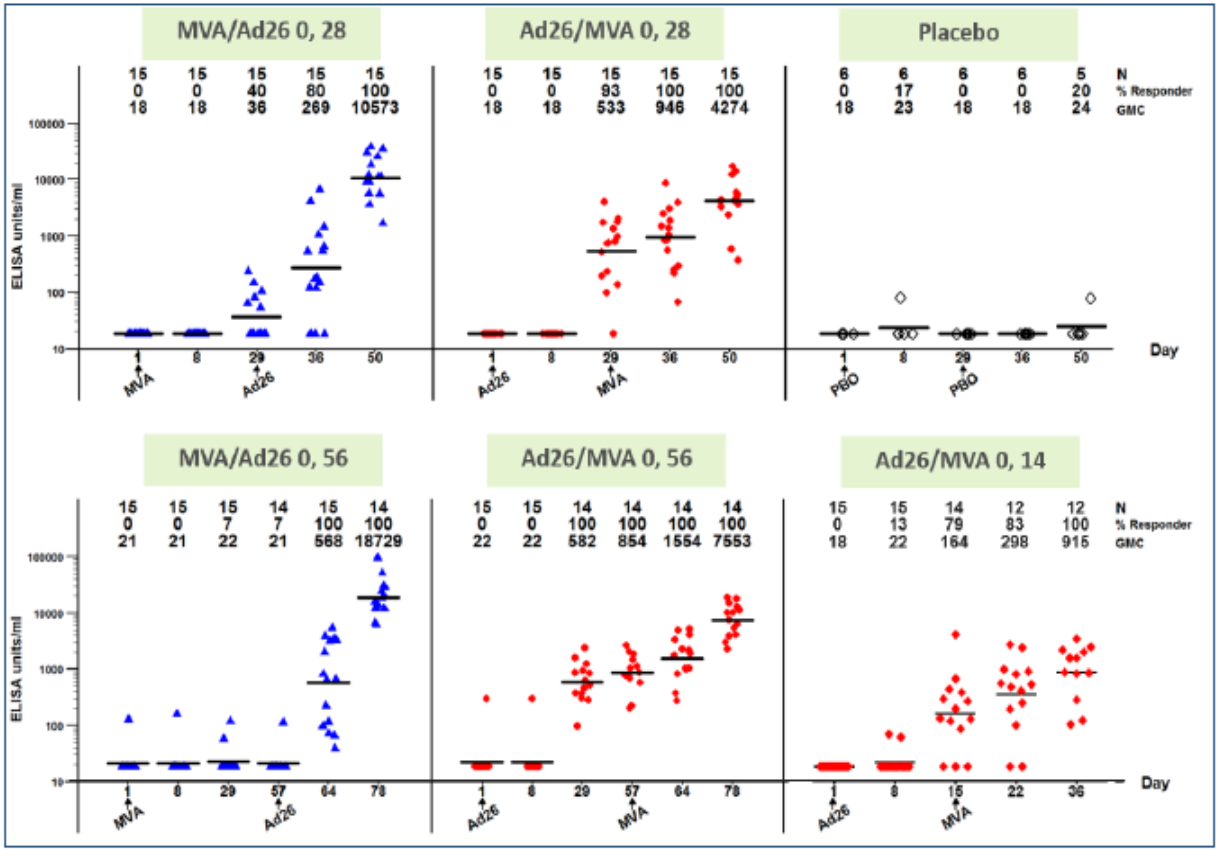
- **EBL1002 (US)**



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 <u>(Not shown)</u>

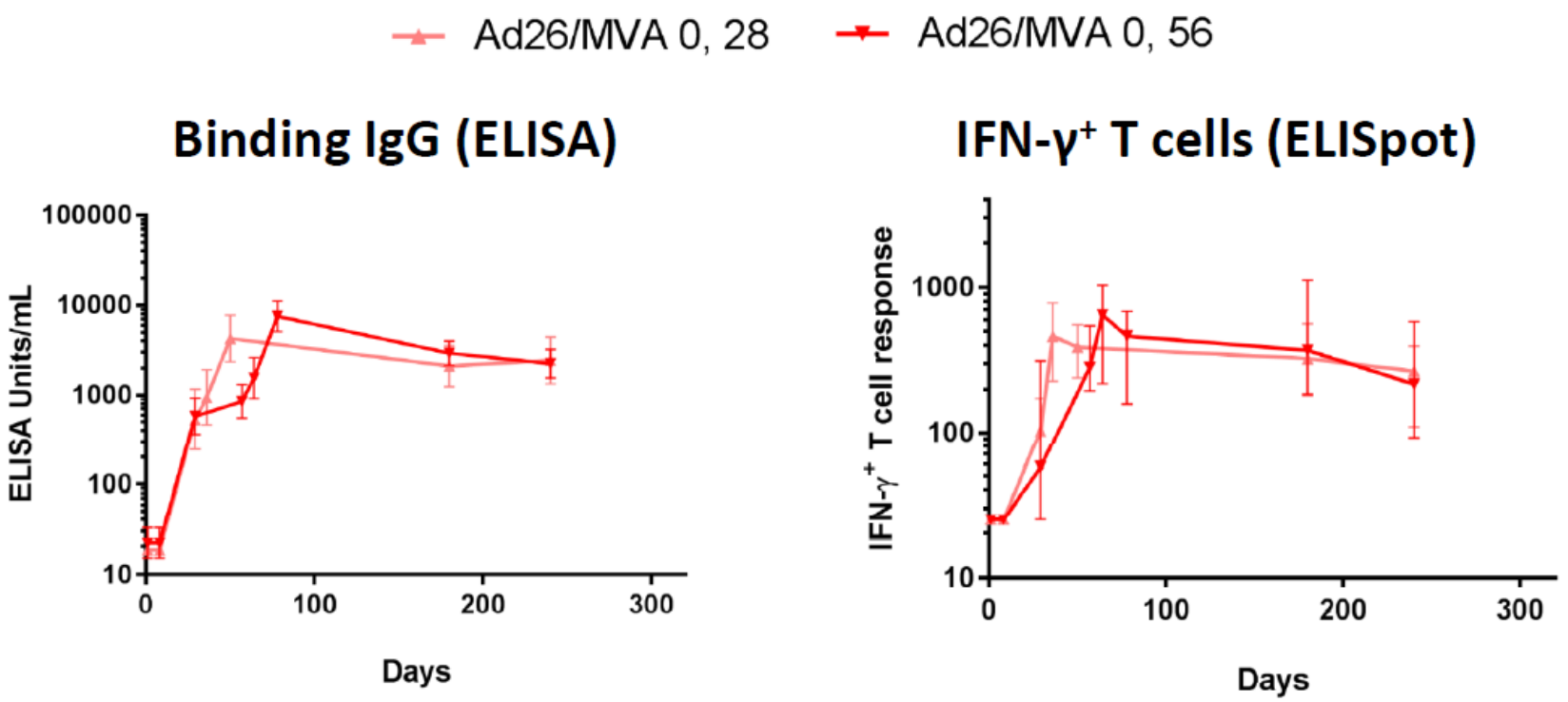
- Similar trajectories observed for CD4+ and CD8+ T cell responses

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

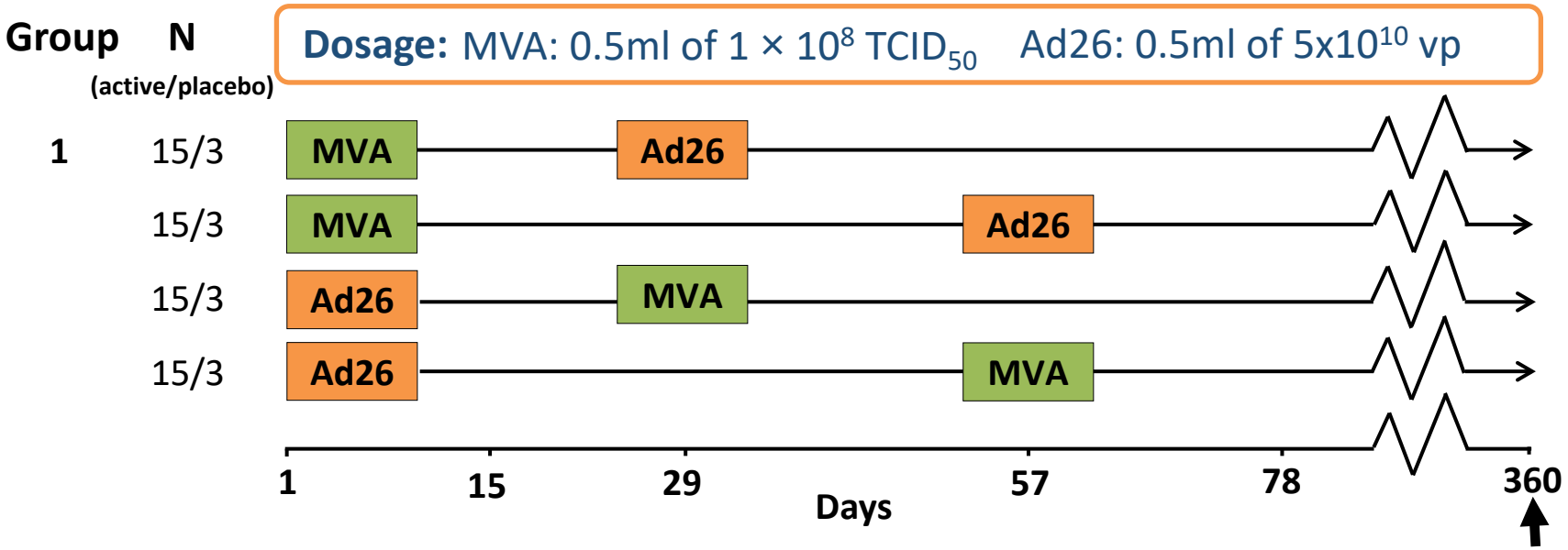


Durability of humoral and cellular immune responses induced by AD26/MVA

- 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



Safety Follow-up:

- Local and systemic reactogenicity events (7 days post each vaccination)
- SAEs throughout the study
- Unsolicited AEs

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

53

Clinicaltrials.gov: NCT02376426/ NCT02376400.

$TCID_{50}$, 50% tissue culture infectious dose; vp, viral particles

Presentations of some major projects achievements:

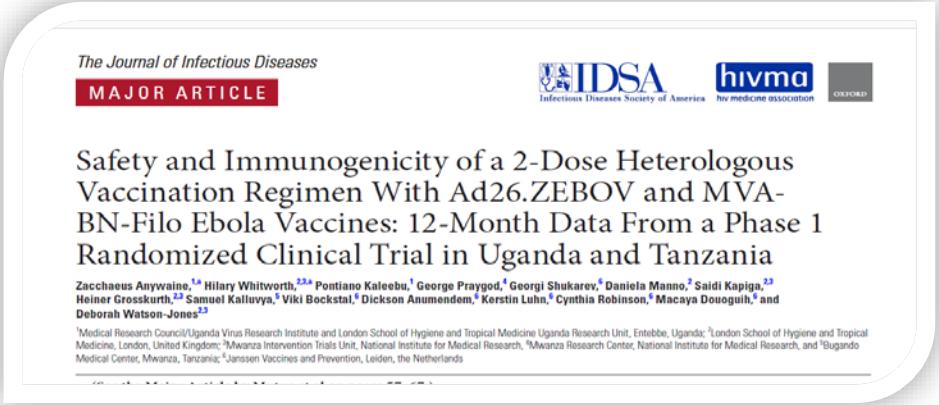
EBL1003 & EBL1004 Results Confirmed….

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 12months 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


The Journal of Infectious Diseases

MAJOR ARTICLE

Safety and Immunogenicity of a 2-Dose Heterologous Vaccination Regimen With Ad26.ZEBOV and MVA-BN-Filo Ebola Vaccines: 12-Month Data From a Phase 1 Randomized Clinical Trial in Uganda and Tanzania


The Journal of Infectious Diseases

MAJOR ARTICLE

Safety and Immunogenicity of a 2-Dose Heterologous Vaccine Regimen With Ad26.ZEBOV and MVA-BN-Filo Ebola Vaccines: 12-Month Data From a Phase 1 Randomized Clinical Trial in Nairobi, Kenya

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

Phase 1 and 3 clinical trials in Sierra Leone

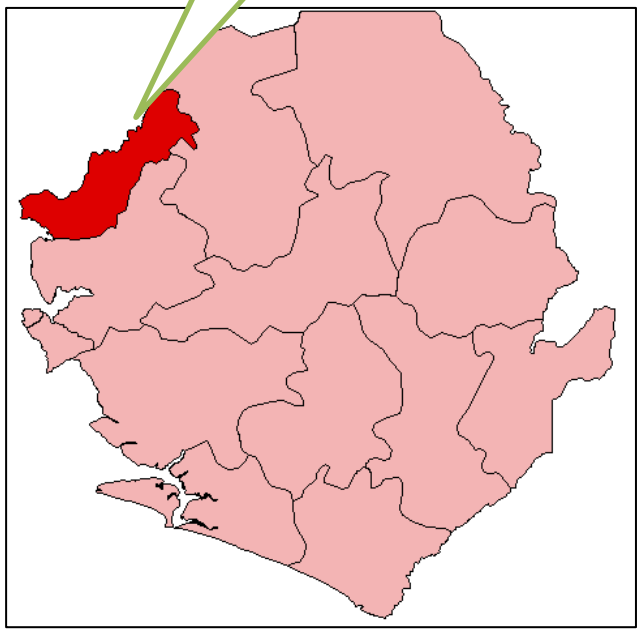
Dr. Frank BAIDEN

Presentations of some major projects achievements:

Kambia district in rural northern Sierra Leone

Kambia & Mambolo

Kambia District Population
~325,000



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***)

PREVAC
PARTNERSHIP FOR RESEARCH ON EBOLA VACCINATION

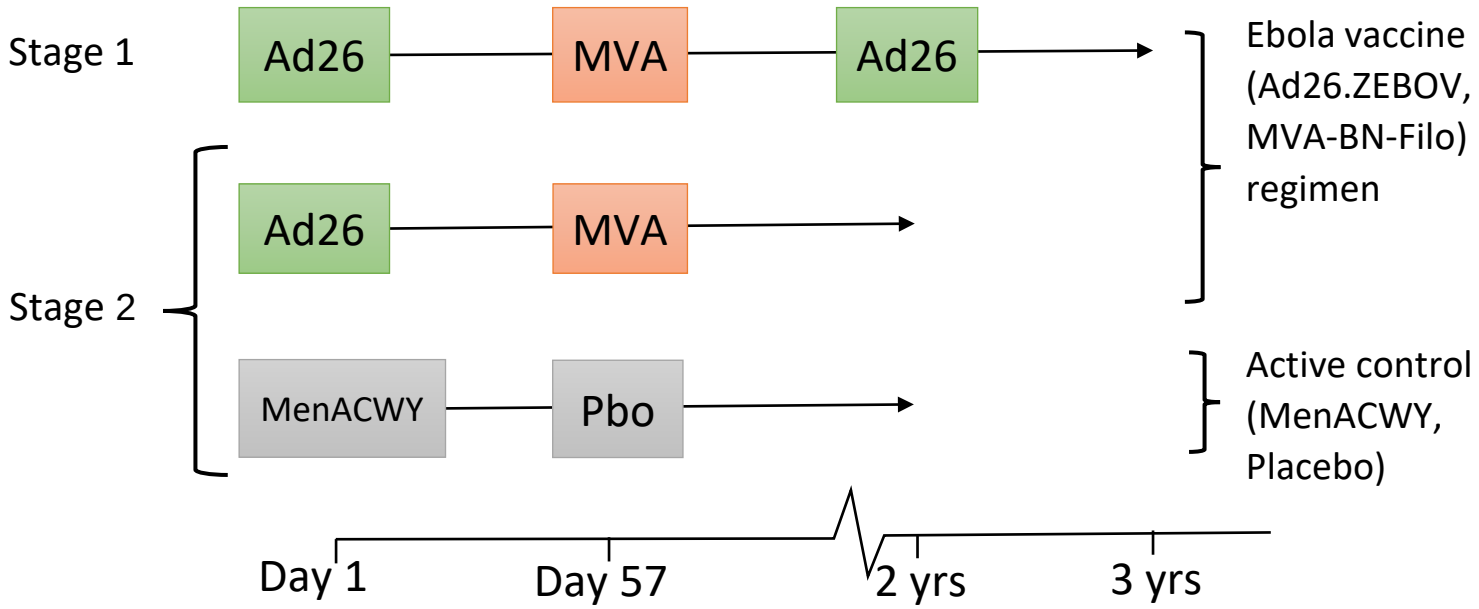
Social science: Community dynamics, attitudes and perceptions on clinical trials

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



In Stage 1

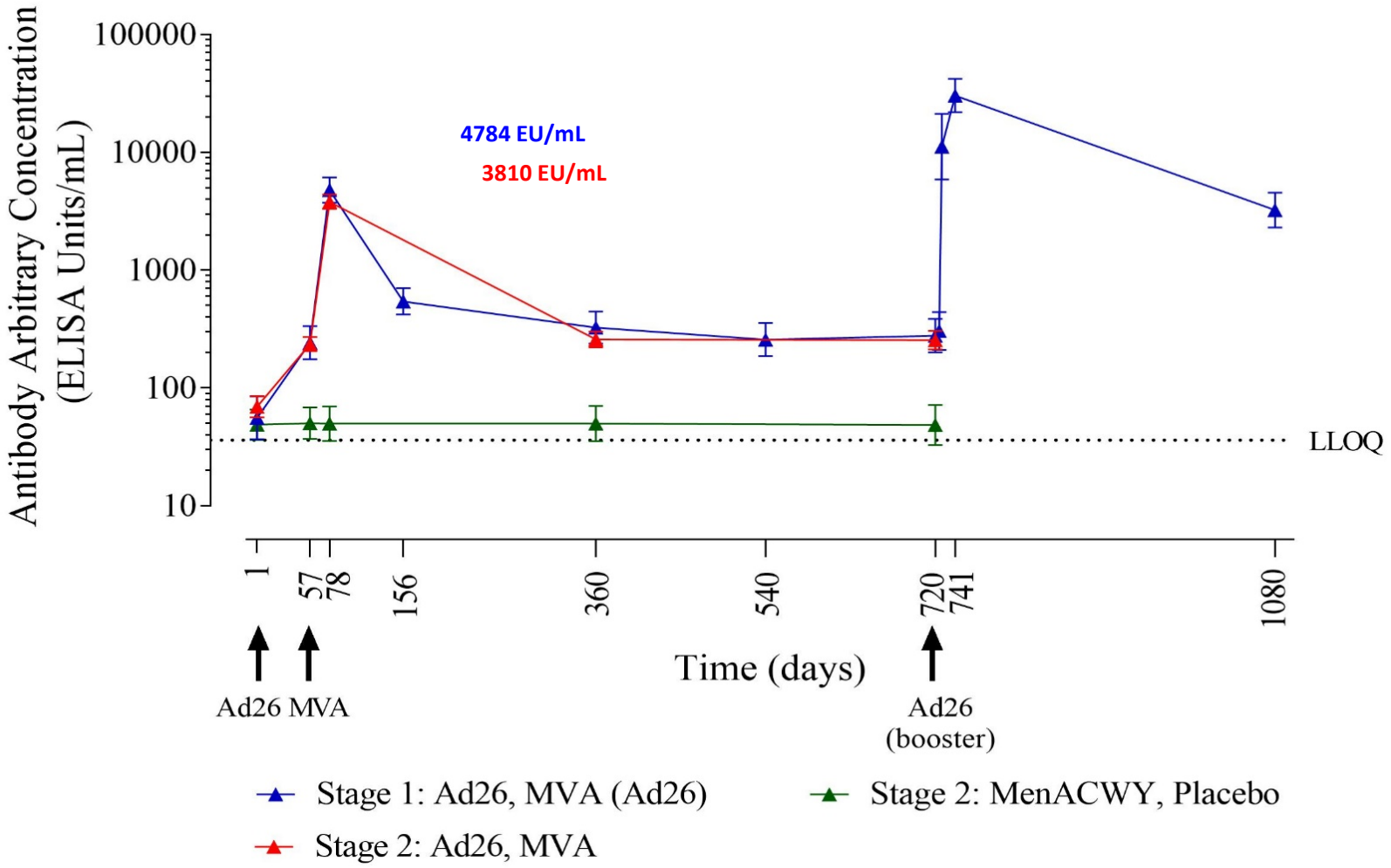
- 43 adults received Ad26, MVA and were followed up for 2 years
- Ad26 booster at 2yrs and followed up for an additional year

In 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)

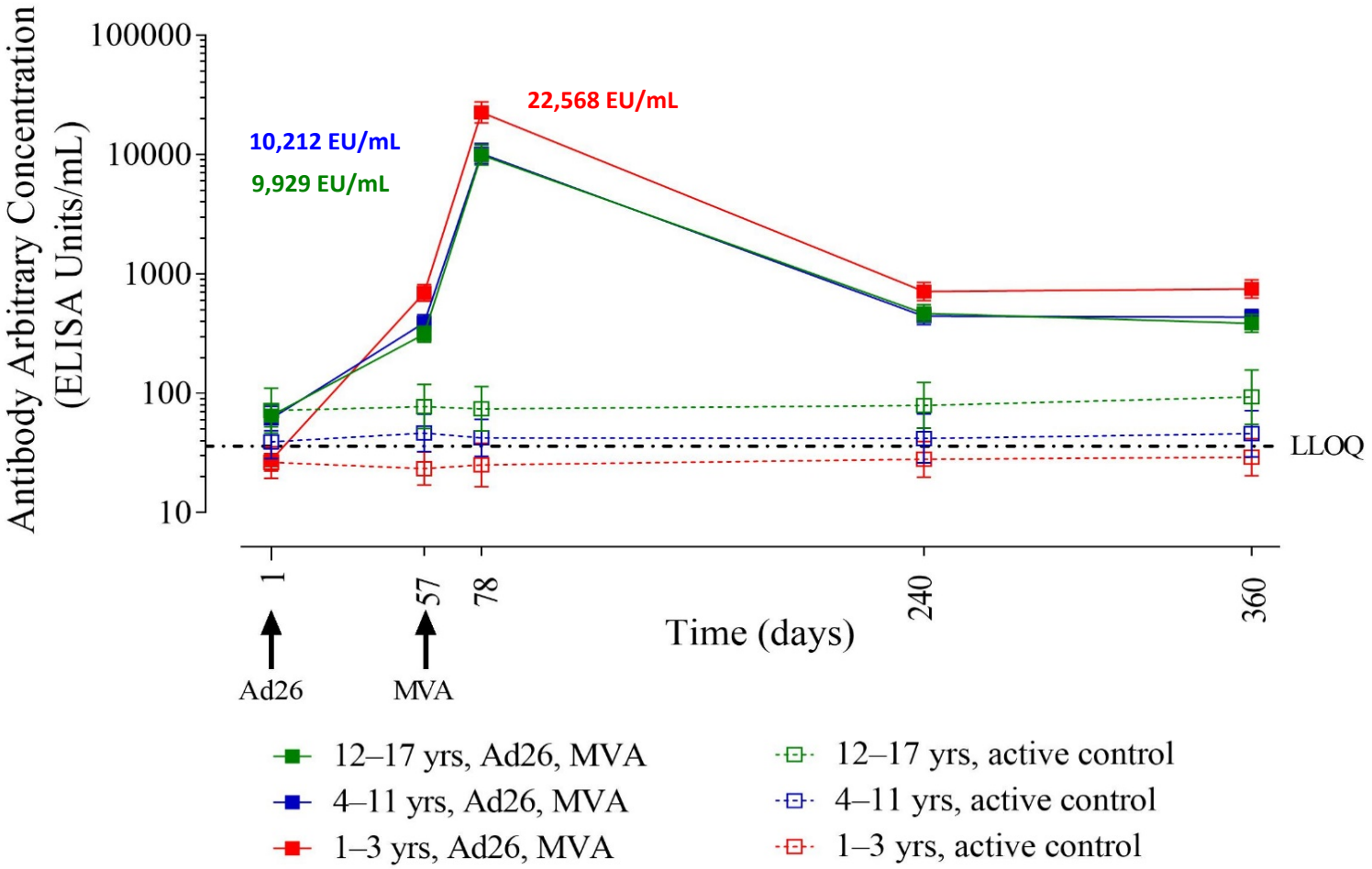
Presentations of some major projects achievements:

Anti-GP Binding Antibody Response in Adults



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

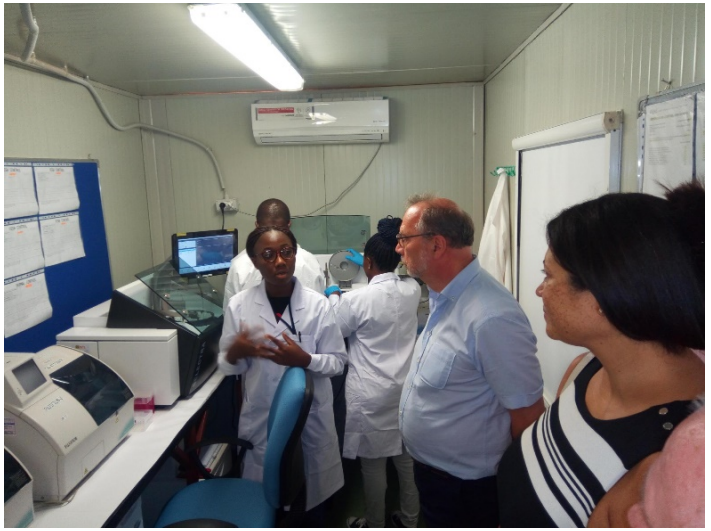
Personnel, equipment & maintenance

- 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**
  - Phase 2, **open label** - Safety and immunogenicity of Ad26.ZEBOV booster.
  - 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

Phase 2 clinical trials in Europe and Africa

Dr. Houreratou BARRY

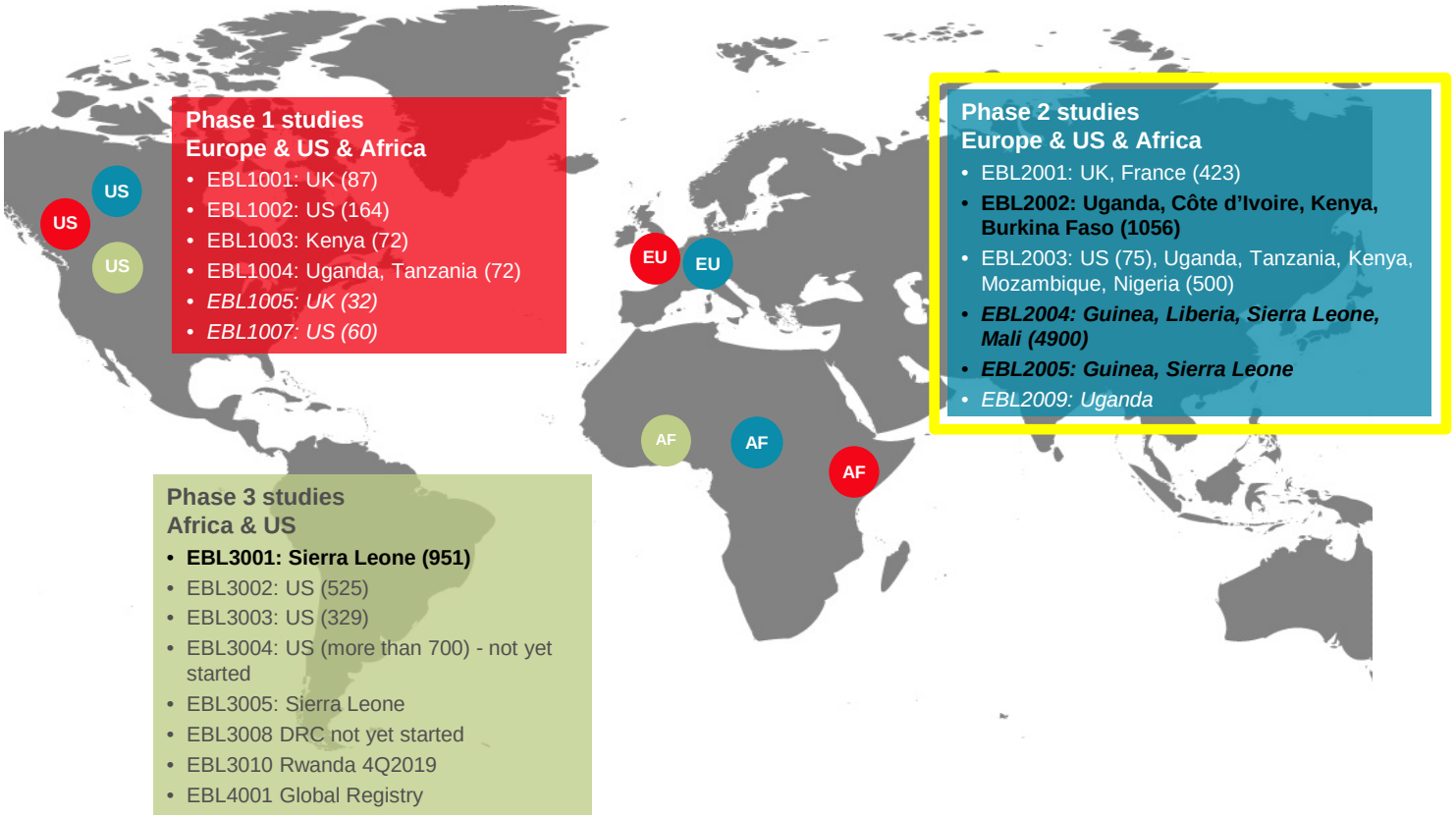
Centre MURAZ
Recherche - Formation - Expertise

Presentations of some major projects achievements:

Phase 2 clinical trials

EBOVAC2 STUDIES

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

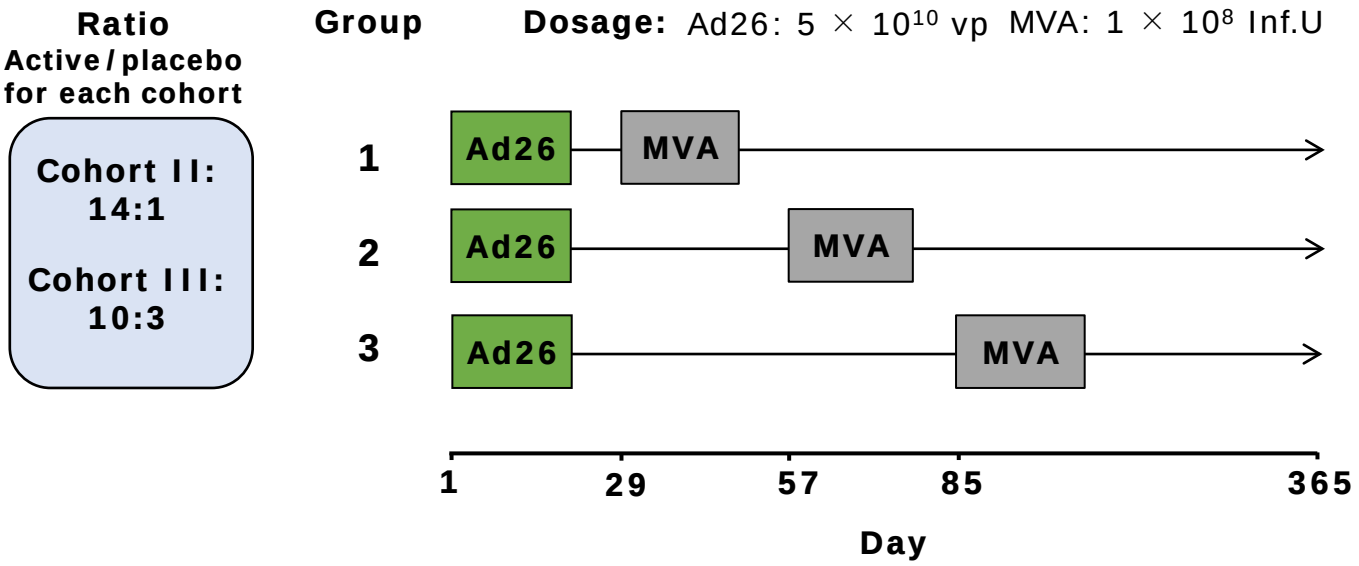


Presentations of some major projects achievements:

Phase 2 clinical trials

STUDY DESIGN

o EBL2001

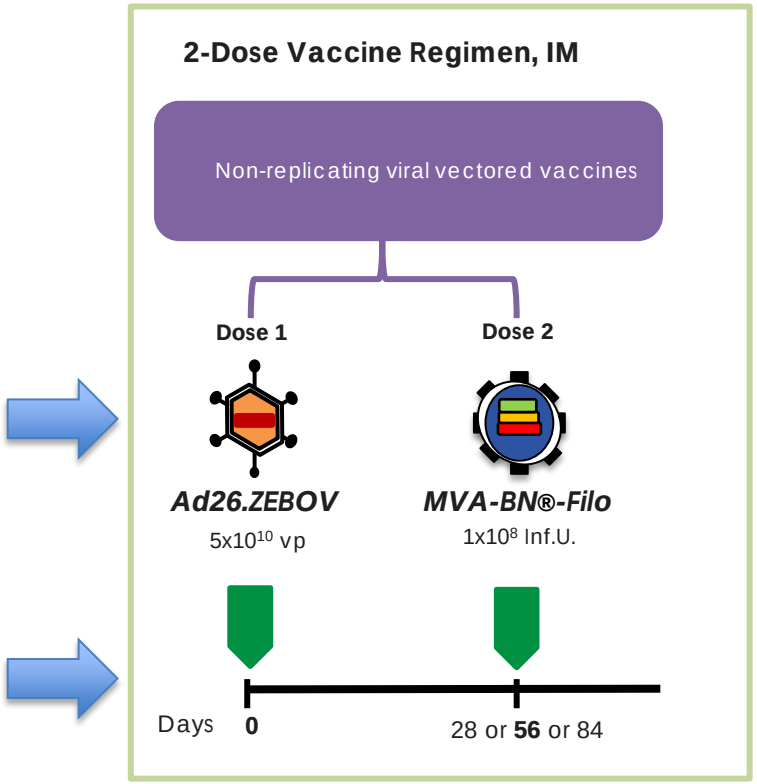


Presentations of some major projects achievements:

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

Group 1:
Day 1, Day 29

Group 2:
Day 1, Day 57

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

Cohort 1
Healthy adult and elderly subjects (268/44 in Group 1, 268/43 in Group 2 and 132/22 in Group 3)

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)

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.

	Incidence, reports following n doses (%)		
	Ad26.ZEBOV	MVA-BN-Filo	All Placebo
Doses	N = 332	N = 236	N = 72
Any Unsolicited AE	115 (34·6)	81 (34·3)	24 (33·3)
MEDRA classes of main reported AEs			
Infections and infestations	30 (9·0)	28 (11·9)	7 (9·7)
Upper respiratory tract Infection	4 (1·2)	12 (5·1)	3 (4·2)
Rhinitis	10 (3·0)	7 (3·0)	0
Nervous system disorders	17 (5·1)	12 (5·1)	3 (4·2)
Headache	5 (1·5)	7 (3·0)	2 (2·8)
Investigations	16 (4·8)	13 (5·5)	2 (2·8)
Respiratory, thoracic and mediastinal disorders	17 (5·1)	7 (3·0)	2 (2·8)
Gastrointestinal disorders	9 (2·7)	8 (3·4)	5 (6·9)
Musculoskeletal and connective tissue disorders	12 (3·6)	6 (2·5)	3 (4·2)
General disorders and administration site conditions	10 (3·0)	5 (2·1)	3 (4·2)
SAEs throughout study	Ad26.ZEBOV & MVA-BN-Filo		All placebo
	N = 332		N = 44
Any reported SAE	11 (3·3)		2 (4·5)
SAE related to vaccination	0		0

Presentations of some major projects achievements:

Phase 2 clinical trials

SAFETY RESULTS

EBL2002: Frequency of solicited and unsolicited adverse events in adults

	Healthy Adults			Adults with HIV		
	Ad26.ZEBOV N=632 %	MVA-BN-Filo N=517 %	Placebo N=225 %	Ad26.ZEBOV N=118 %	MVA-BN-Filo N=117 %	Placebo N=48 %
Overall solicited AEs	70.7	72.1	61.3	78.8	55.6	43.8
Any solicited Grade 3	2.5	2.5	2.2	2.5	0	2.1
Overall solicited local AEs	54.0	57.3	37.8	58.5	43.6	20.8
Any solicited local Grade 3	0.3	0.8	0	0	0	0
Overall solicited systemic AEs	62.7	59.2	54.2	49.6	67.8	39.6
Any solicited systemic Grade 3	2.5	2.1	2.2	0	2.5	2.1
Most frequent local solicited AE	Injection site pain **48.3**	**51.3**	**30.7**	Injection site pain 43.2	35.9	18.8
Most frequent systemic solicited AE	Fatigue **46.4**	**38.1**	**38.2**	Fatigue 51.7	36.8	31.3
Any pyrexia (defined as ≥38^{0}C)	4.6	6.4	3.1	11.0	2.6	10.4
Grade 3 pyrexia (defined as ≥39^{0}C)	0.8	1.7	0.4	2.5	0	2.1
Overall unsolicited AEs	35.4	32.1	34.7	42.4	37.6	37.5

Presentations of some major projects achievements:

Phase 2 clinical trials

SAFETY RESULTS

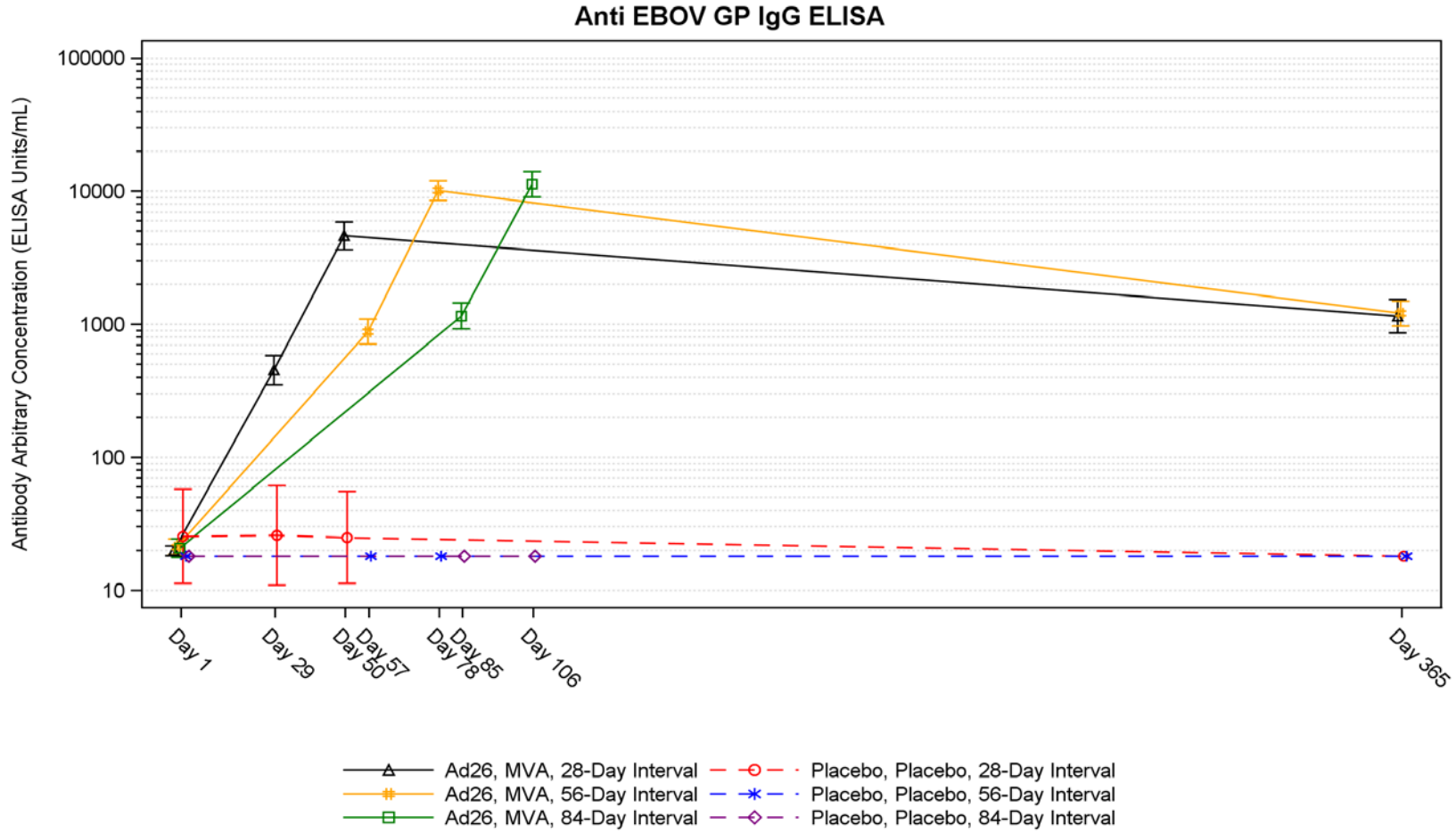
EBL2002: Frequency of solicited and unsolicited adverse events in Children and adolescents

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

Presentations of some major projects achievements:

Phase 2 clinical trials

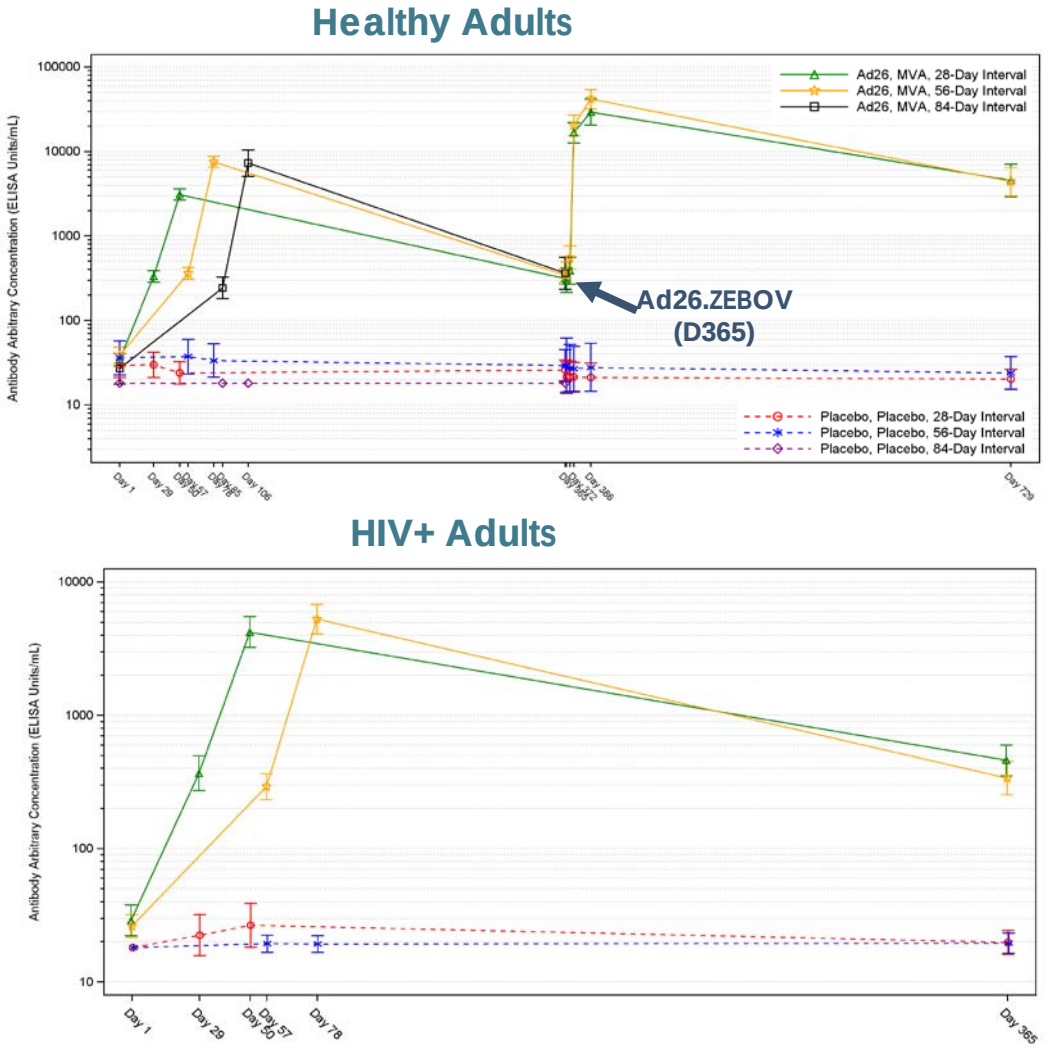
EBL2001: Binding Antibody Responses(Cohort liand III) EBOV GP FANG ELISA; ELISA units/mL



Presentations of some major projects achievements:

Phase 2 clinical trials

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

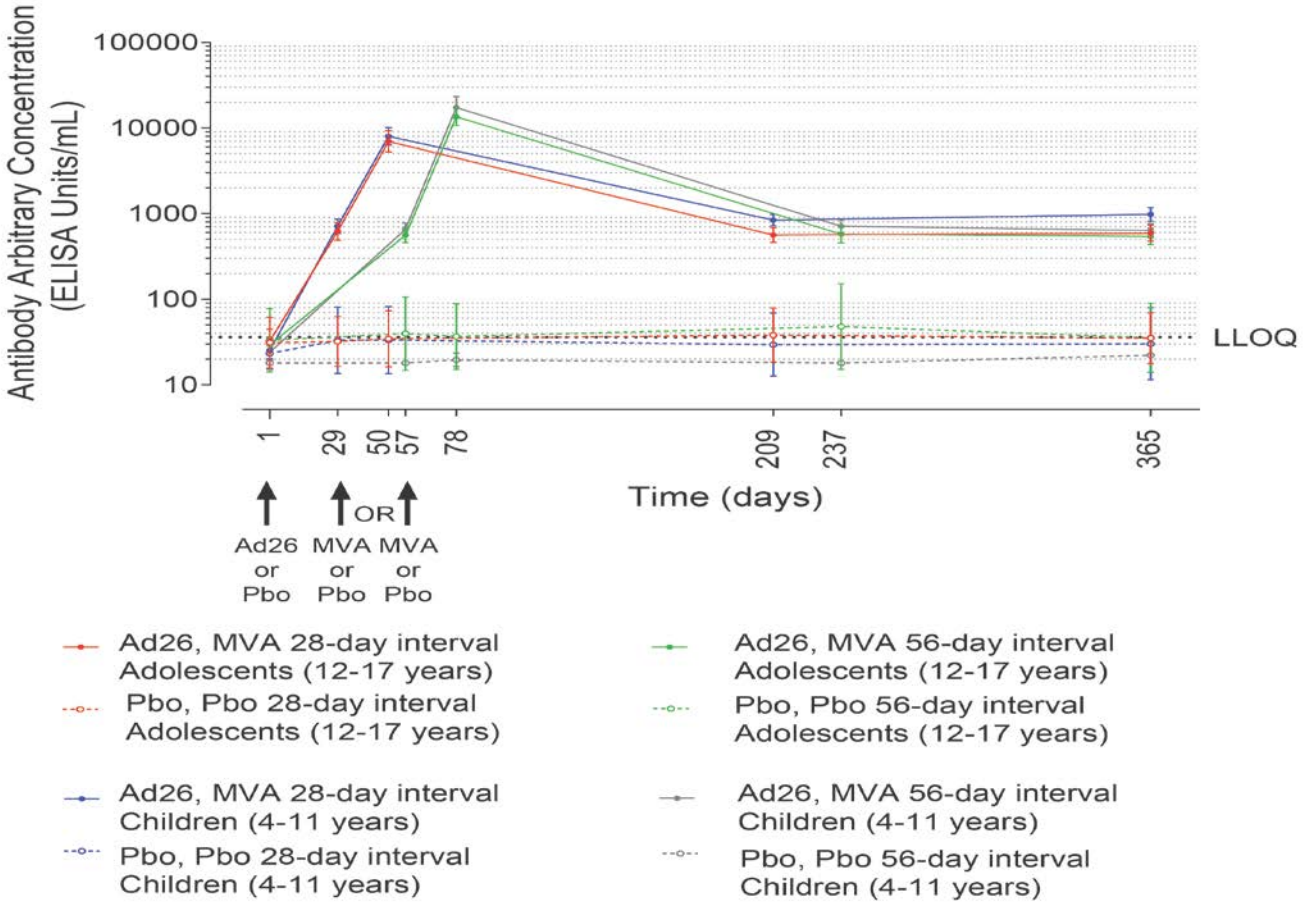


- Ad26.ZEBOV, MVA-BN-Filo induces **humoral memory** that can rapidly be re-activated
- **Strong anamnestic responses** within **7 days** post booster (55-fold increase)
- 21 days post booster, binding antibody levels **5 to 9-fold greater** than 21 days post dose 2 levels
- Post booster antibodies **persist 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

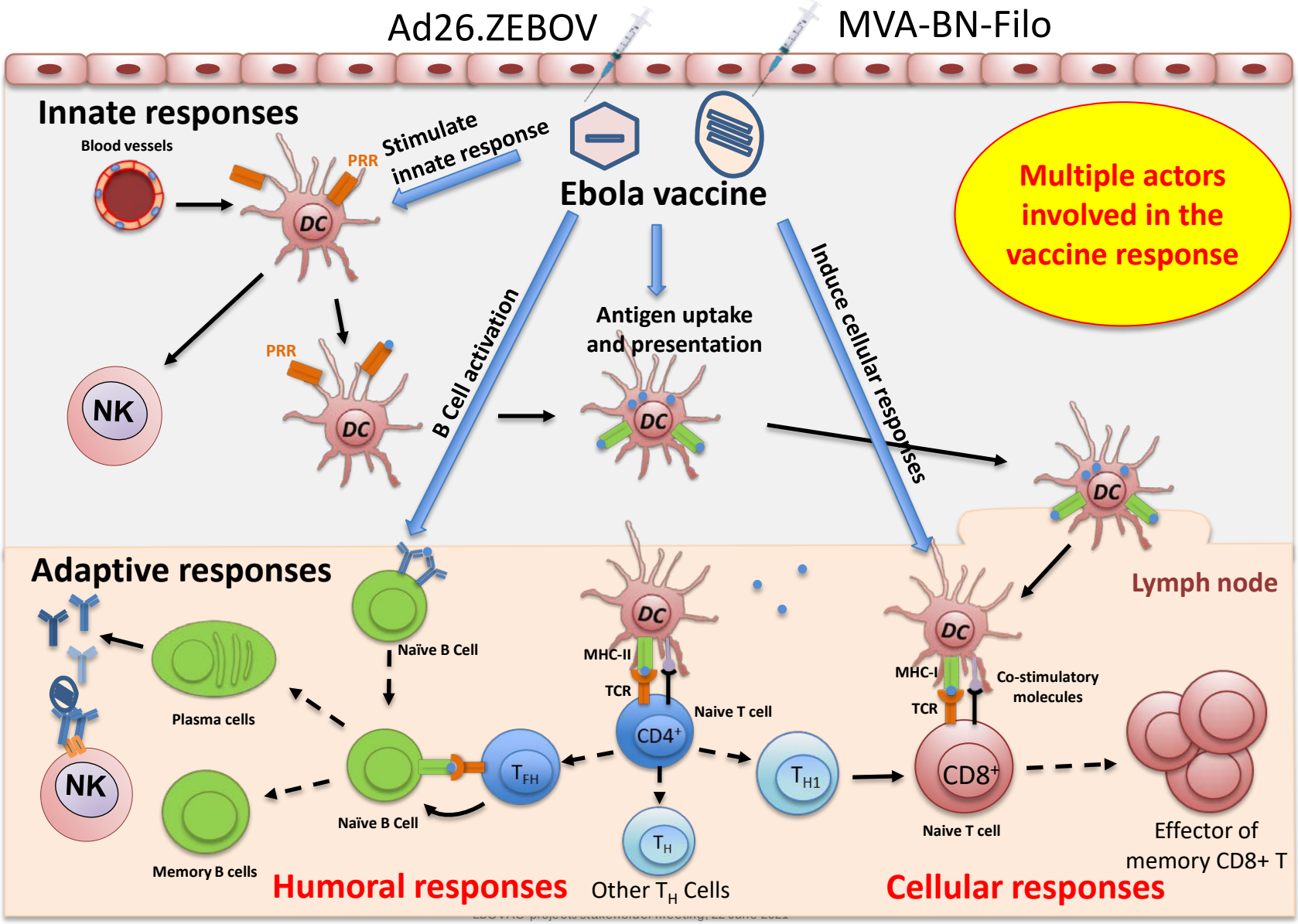
Little was known in the mechanisms of the vaccine triggered immune response before the EBOVAC projects.

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

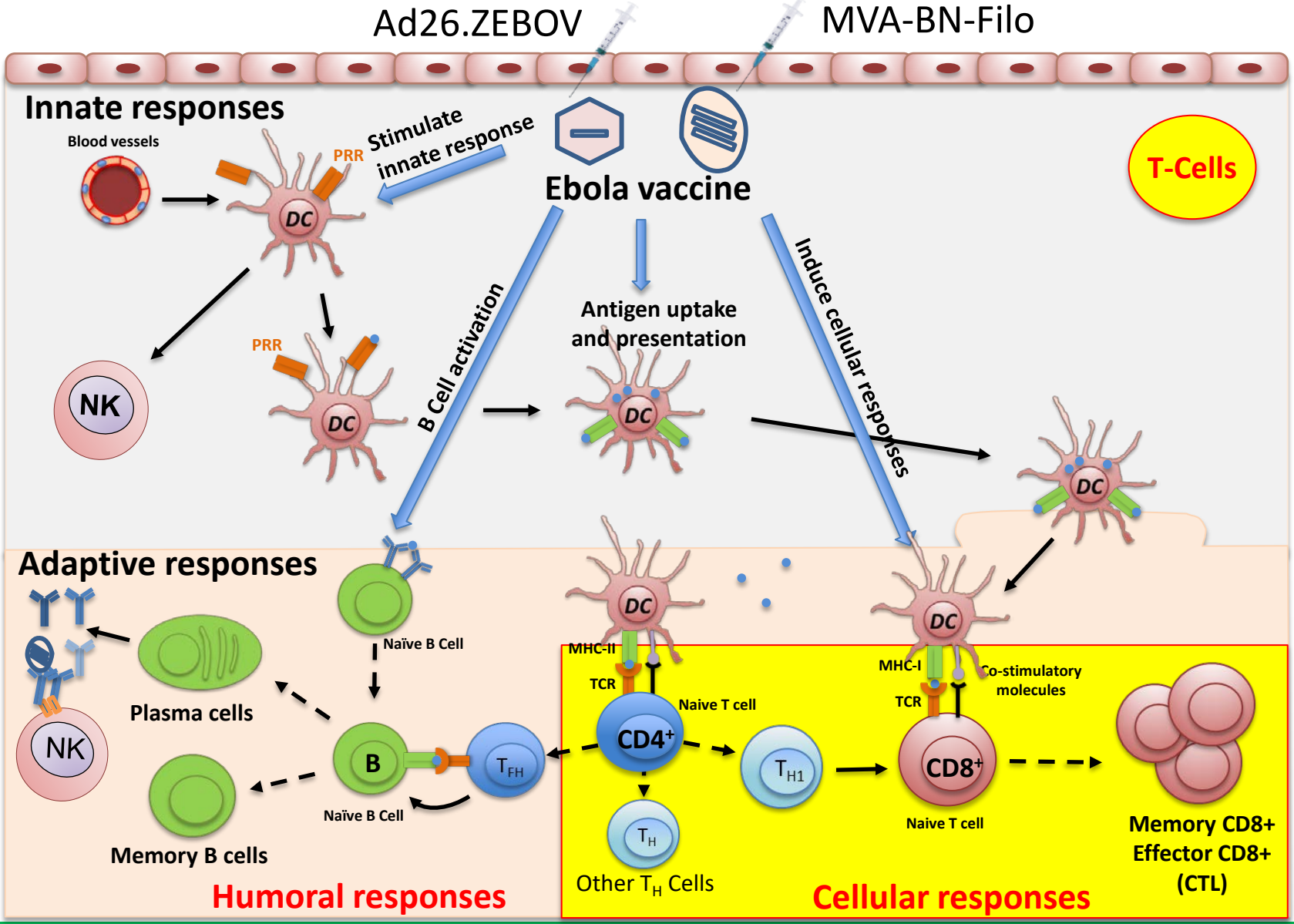


Immunology of the vaccine response

T cell response

Dr. Christine LACABARATZ

Explored Immunological Pathways



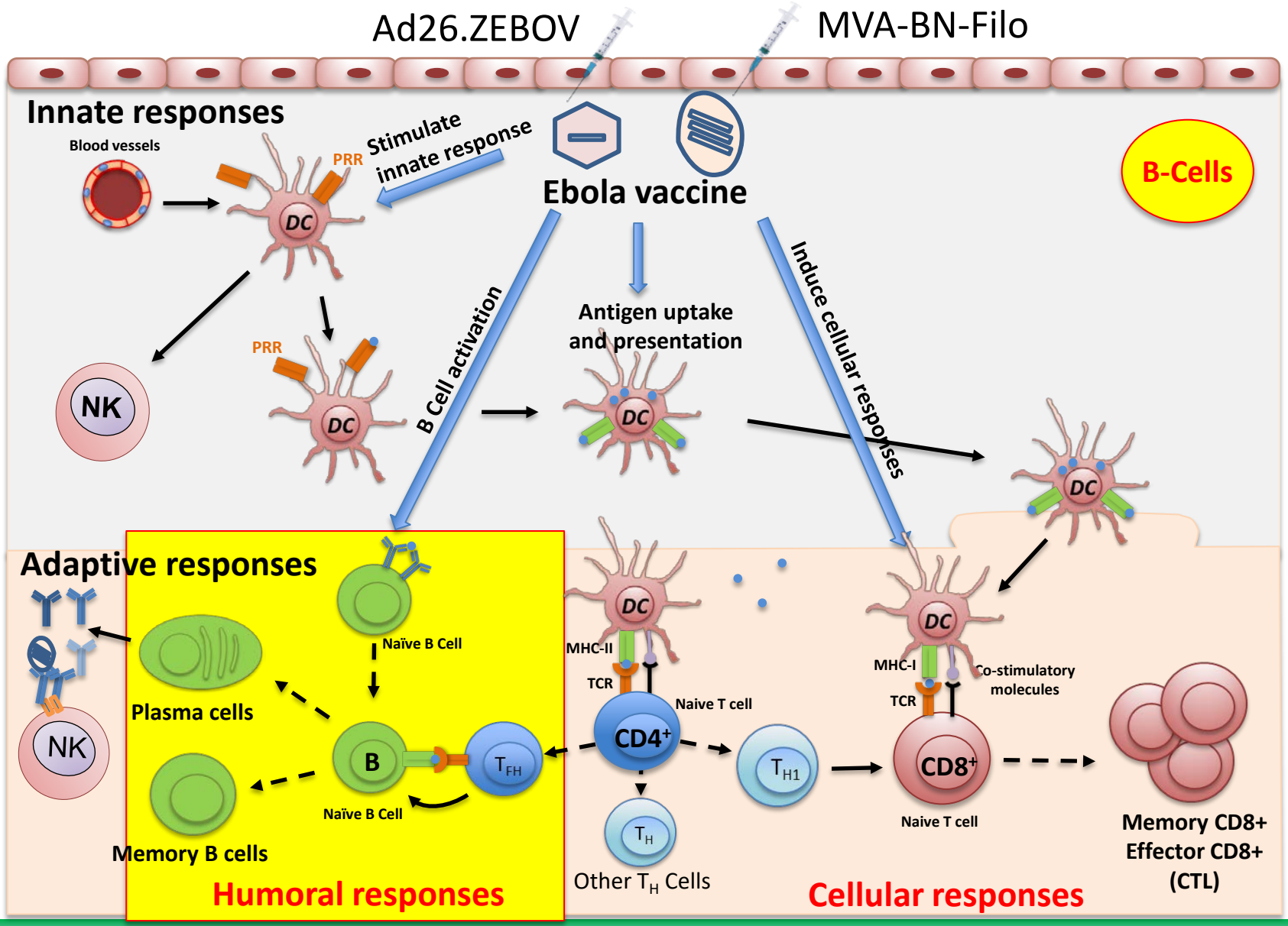
Immunology of the vaccine response

B cell response

Dr. Elizabeth CLUTTERBUCK

UNIVERSITY OF OXFORD

Explored Immunological Pathways

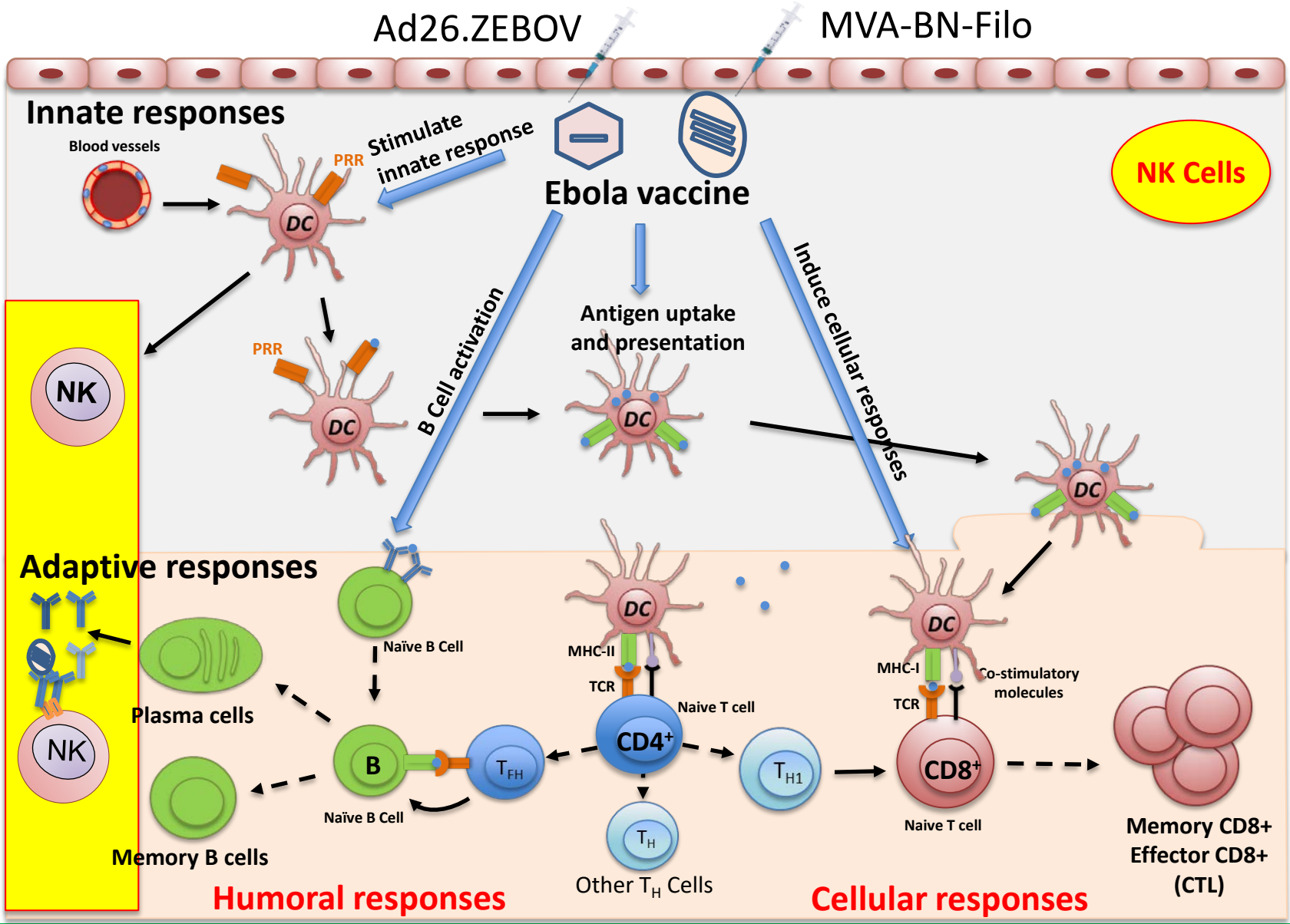


Immunology of the vaccine response

NK cell response

Dr. Martin GOODIER

Explored Immunological Pathways

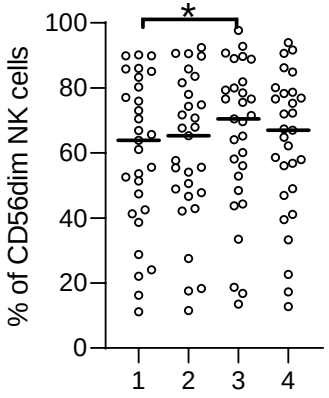


Presentations of some major projects achievements:

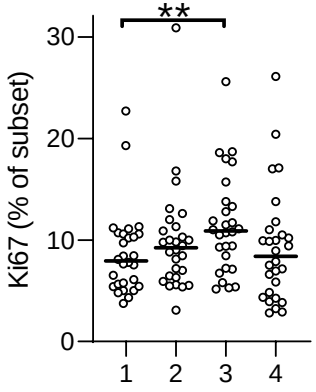
NK cell response data EBL2002

ex vivo analysis
CD56dimFcεR1γ⁺ NK cells (Canonical)

Subset redistribution



Proliferation

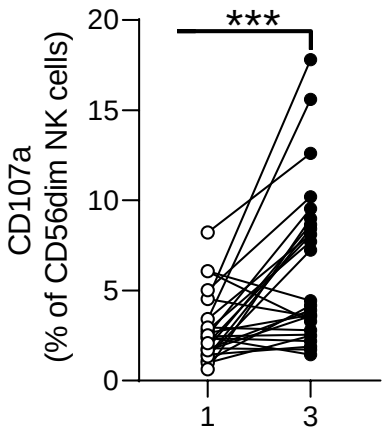


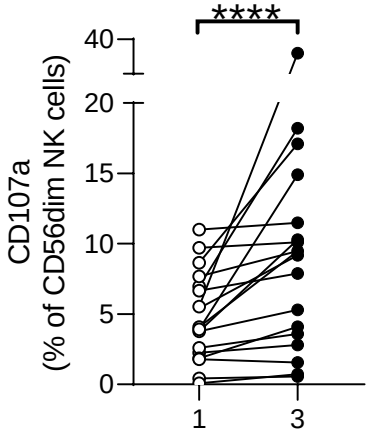
Study Visit

Anti-GP Antibody dependent activation *in vitro*

Standard readout *Autologous NK cells*

Degranulation





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

Sequence of dosing Ad26, MVA					
Study		Assay			
	Dosing intervals	***Ex-vivo*** Activation (A) Proliferation (P) Subset redistribution (SR)[1]	Antibody- dependent degranulation ***in-vitro*** Standard NK cell readout [1]	Antibody- dependent degranulation ***in-vitro*** Autologous NK cell readout [1]	Innate Activation ***In-vitro*** Ebola-GP [2]
EBL1001 Oxford UK	28 days 56 days	21 days post dose 2 A * P *** SR **	21 days post dose 2 ****	ND	+++
Reference 1. Wagstaffe et al. JID. 2019: https://doi.org/10.1093/infdis/jiz657 2. Wagstaffe et al. JCI. 2020: https://doi.org/10.1172/jci132438					
EBL2001 Inserm France	28 days 56 days 84 days	Up to 180 days post dose 2 A * P ns SR **	14 days post dose 2 **** 180 days post dose 2 ***	14 days post dose 2 * 180 days post dose 2 ***	++++
Reference 3. Wagstaffe et al. NpJ vaccines. 2021: https://doi.org/10.1038/s41541-021-00280-0					
EBL2002 Kenya Uganda Burkina-Faso	28 days 56 days	21 days post dose 2 A ns P ** SR *	21 days post dose 2 ****	21 days post dose 2 ***	ND
Reference 4. 2021. Manuscript in preparation.					

*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.

Modelisation of the immune response

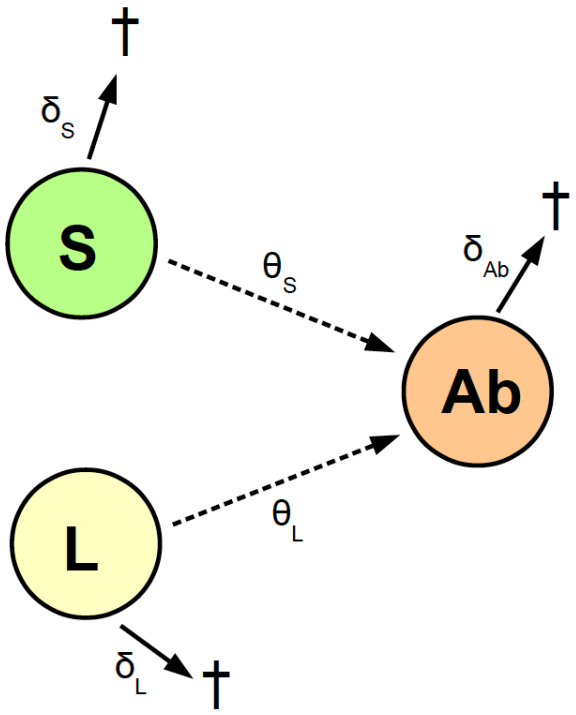
Dr. Mélanie PRAGUE

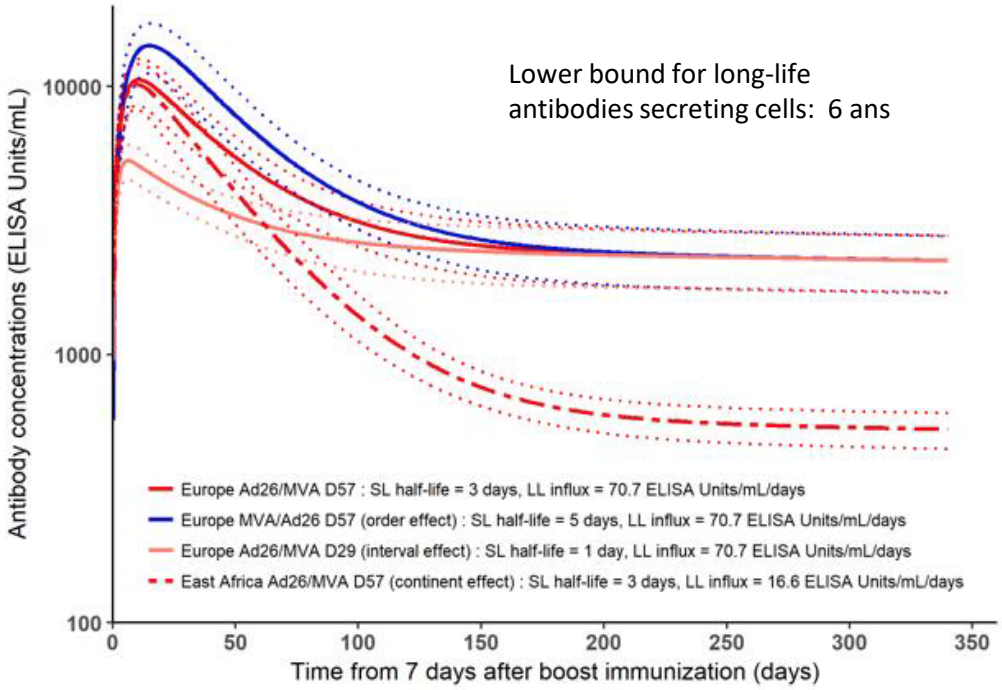
Presentations of some major projects achievements:

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



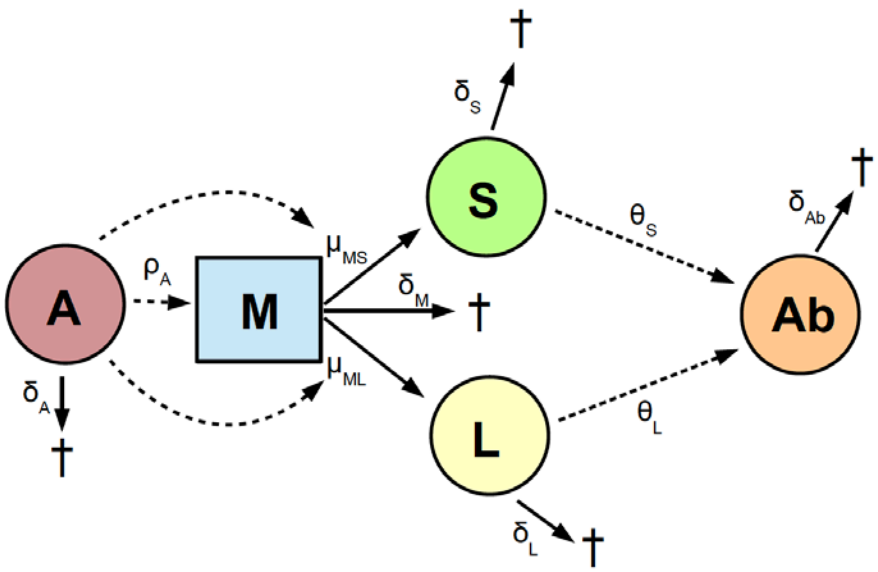


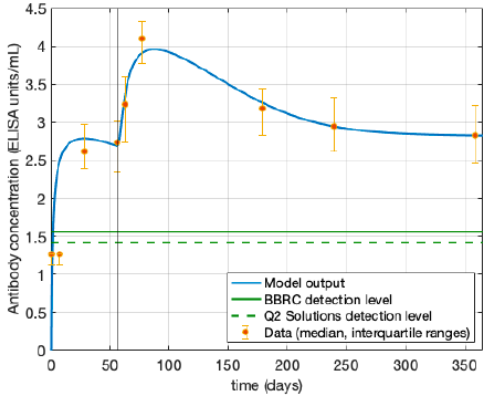
Presentations of some major projects achievements:

Modelisation of the immune response

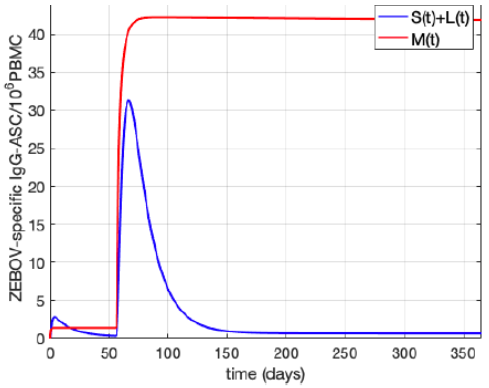
Within host model of persistence to Ebola vaccination (model calibration)

- Balelli et al. (2020) Journal of theoretical biology. A model for establishment, maintenance and reactivation of the immune response after vaccination against Ebola virus





(a) $Ab(t)$, Ad26/MVA D57



(b) B cells, Ad26/MVA D57

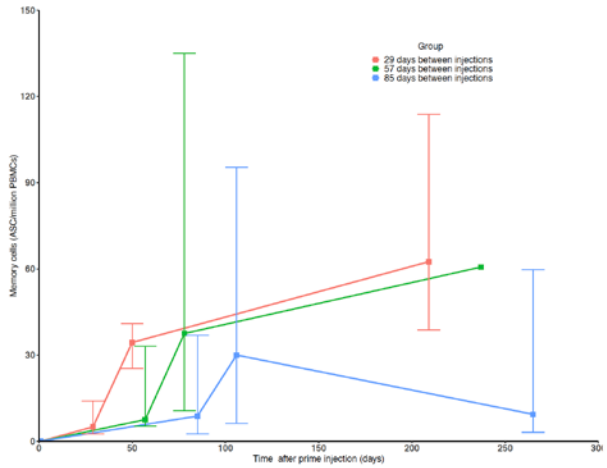
Presentations of some major projects achievements:

Modelisation of the immune response

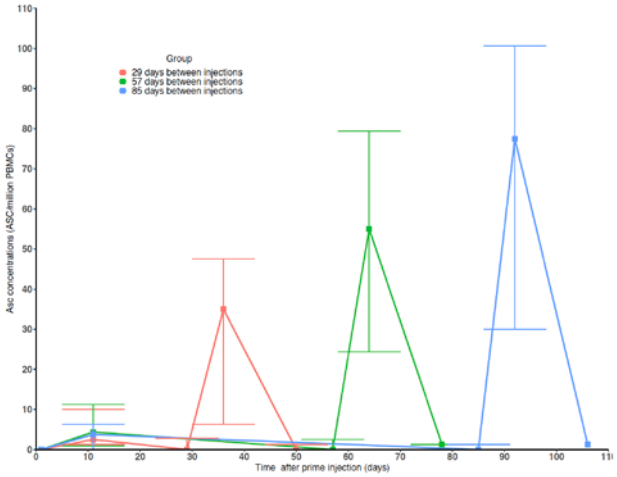
Extend the results for available data

- Estimation (vs. calibration) on EBL2001 Data

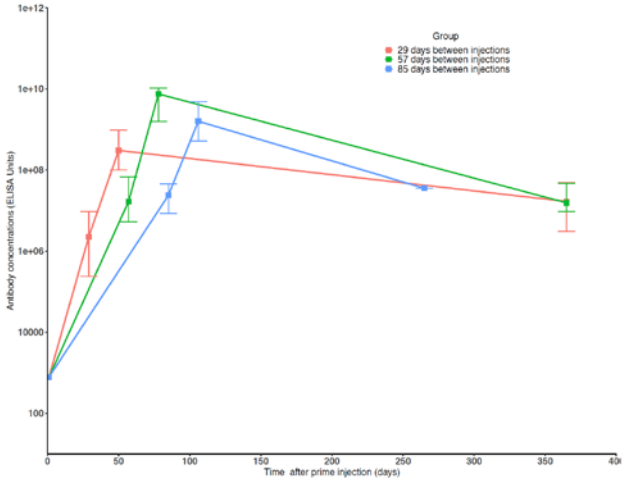
Antibodies secreting cells



B memory cells



Antibodies

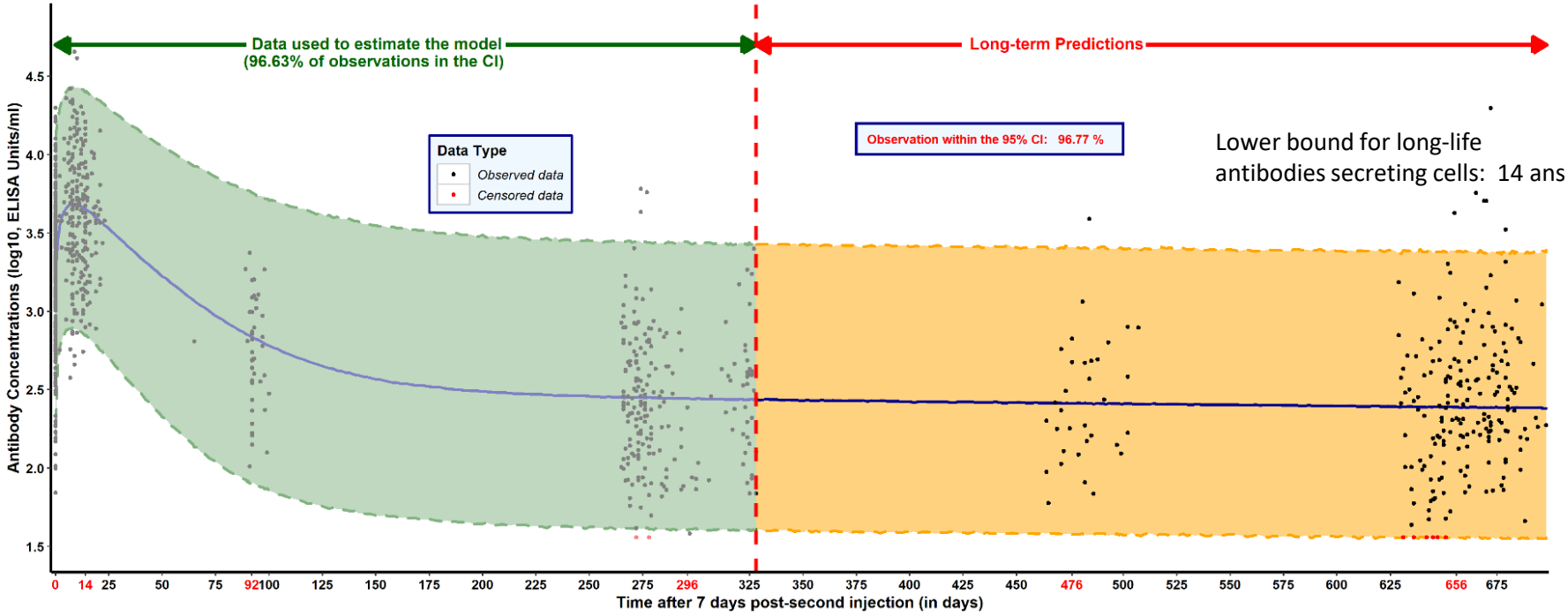


Presentations of some major projects achievements:

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



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

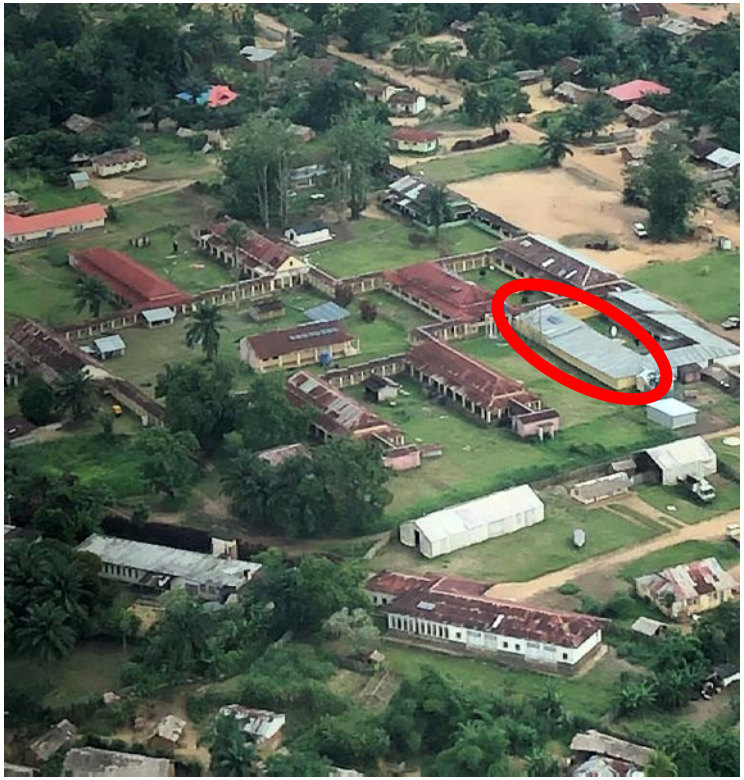
- Safety and immunogenicity

Accomplishment: 91% retention rate after 1 year
Currently ongoing: Group 1 phone contacts 6 months post booster

EBL2007 Study population and anthropological angle

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%)

Demographics	N	%	Mean	SD	Min-Max
Age	699		45.01	11.99	19.00-71.00
Gender					
Male	534	76.39			
Female	165	23.61			

EBL2007 Study population and anthropological angle

STUDY POPULATION PROFESSION & ESTABLISHMENT OF WORK

- Top three professions : community health workers, nurses and first aid workers
- Main workplace: Boende health center

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

Establishment of work	N	%
Health center	371	53.08
Other (e.g. red-cross)	198	28.33
Hospital	85	12.16
Health post	37	5.29
Health zone	8	1.14

EBL2007 Study population and anthropological angle

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

EBL2007 Study population and anthropological angle

CONCLUSION

Crucial for (Ebola) epidemic preparedness

- Relatively weak surveillance system
- HCP & frontliners at higher risk of Ebola
- Duration of the protection of vaccination to be determined
- 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

CEPI

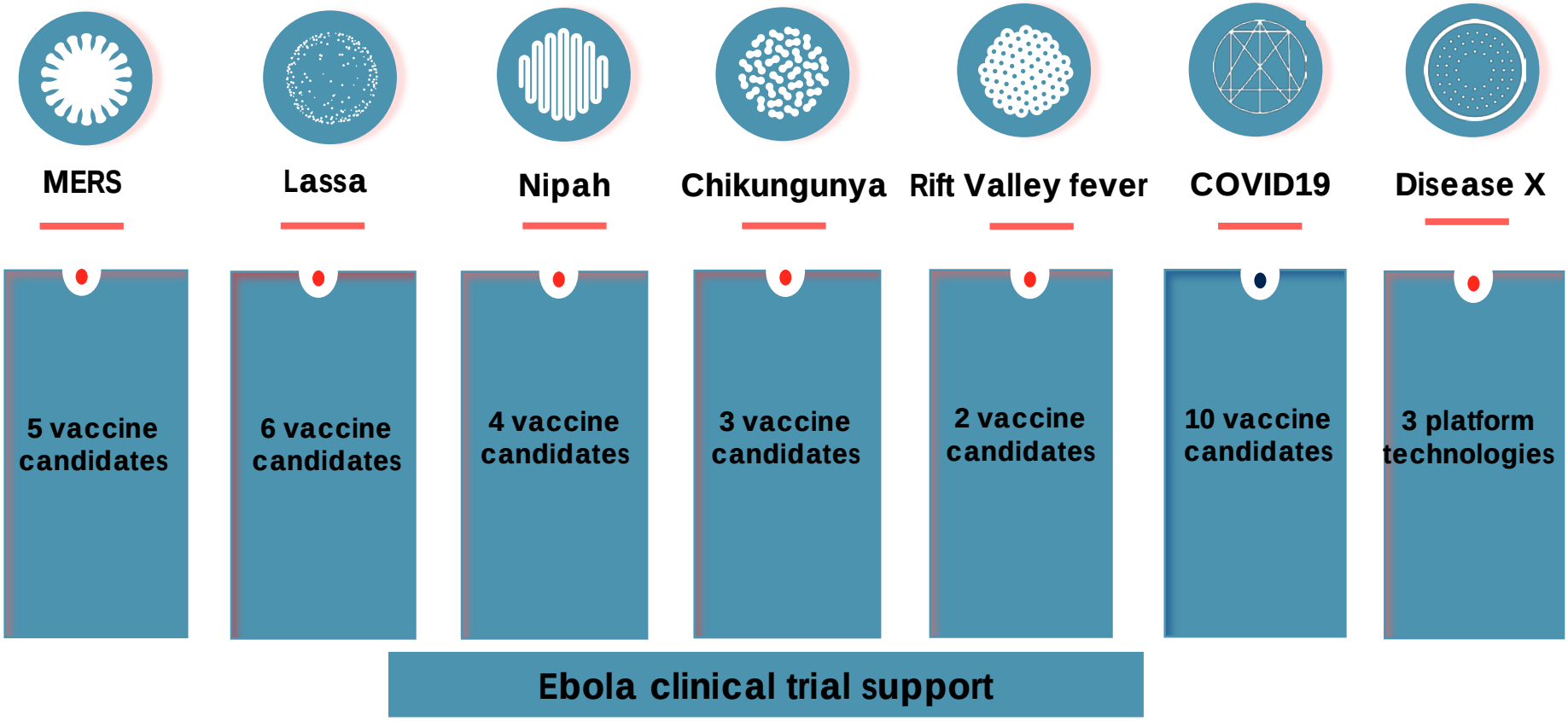
Formation of CEPI

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



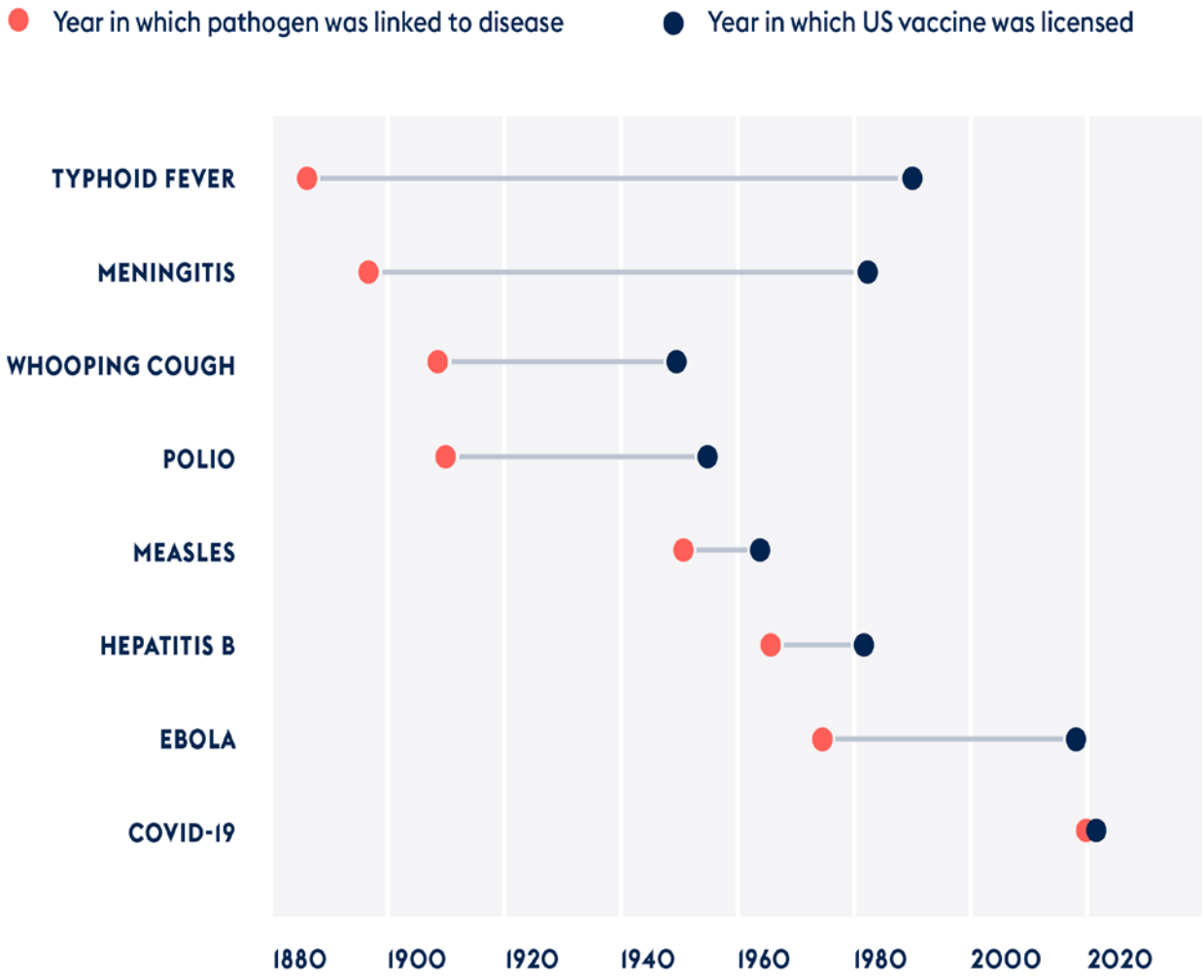
CEPI

Lessons learned from COVID-19 vaccine R&D

CEPI

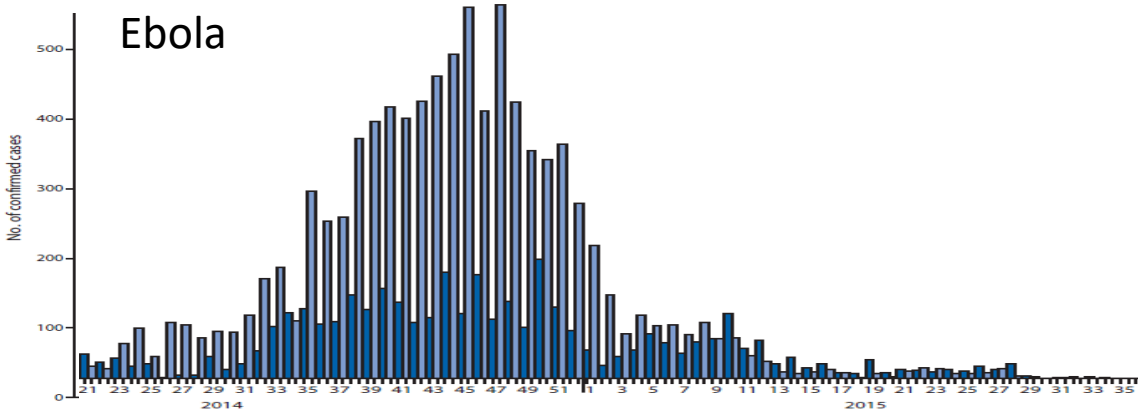
Future challenges of an improved and sustainable emergency response system for future epidemics

Rapid progress in vaccine innovation

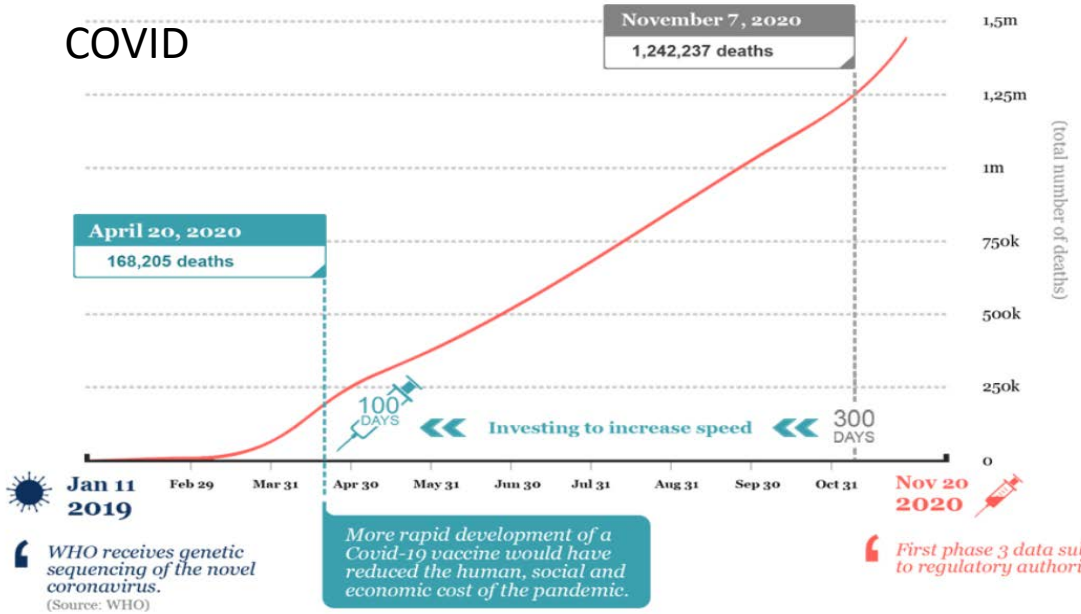


CEPI

Speed is of the essence in outbreak response



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



*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

COVAX: paradigm shift

CEPI

COVAX: has brought a paradigm shift to global health

COVAX firsts

Beyond numbers…

190 Confirmed and eligible COVAX participants

>6B USD raised within a year for AMC countries

>2B Vaccine doses secured in 2021

… many **"firsts"** created by COVAX

- 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)

CEPI

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**

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

CEPI

When handling epidemics is not enough: the importance of prevention

Dr. Valérie ORIOL-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 [1,3]

EVD risk in HCW [2,4]

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

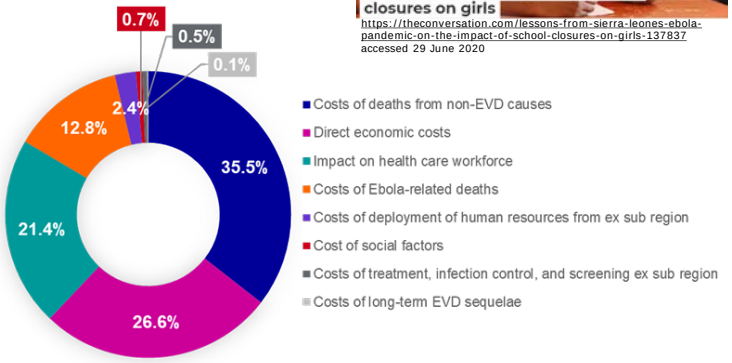
https://www.who.int/teams/health-product-and-policy-standards/access-to-assistive-technology-medical-devices/medical-devices/ppe/ppe-ebola accessed 19 June 2021

Social impact of West Africa outbreak with food insecurity, closure of schools, orphans, and heavy psychological impact on affected people, communities and HCWs[3,4]

https://theconversation.com/lessons-from-sierra-leones-ebola-pandemic-on-the-impact-of-school-closures-on-girls-137837 accessed 29 June 2020

Economy [1,3]

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



Estimates of the economic and social burden of the 2014-2016 Ebola virus disease outbreak, in billions USD[1]

1. Malvy, Ebola Virus Disease, The Lancet 2019
2. Evans et al. "Health-care worker mortality and the legacy of the Ebola epidemic." The Lancet Global Health 3, no. 8 (2015): 439-440
3. Huber and colleagues (2018) The economic and social burden of the 2014 Ebola outbreak in West Africa
4. Ngatu Occupational EVD in Africa 2017

Multiple Ebola Virus Disease risk groups can be identified

3 drivers of risk of EVD exposure [1-3]

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 forrest 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

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 options[1-4]

- 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)

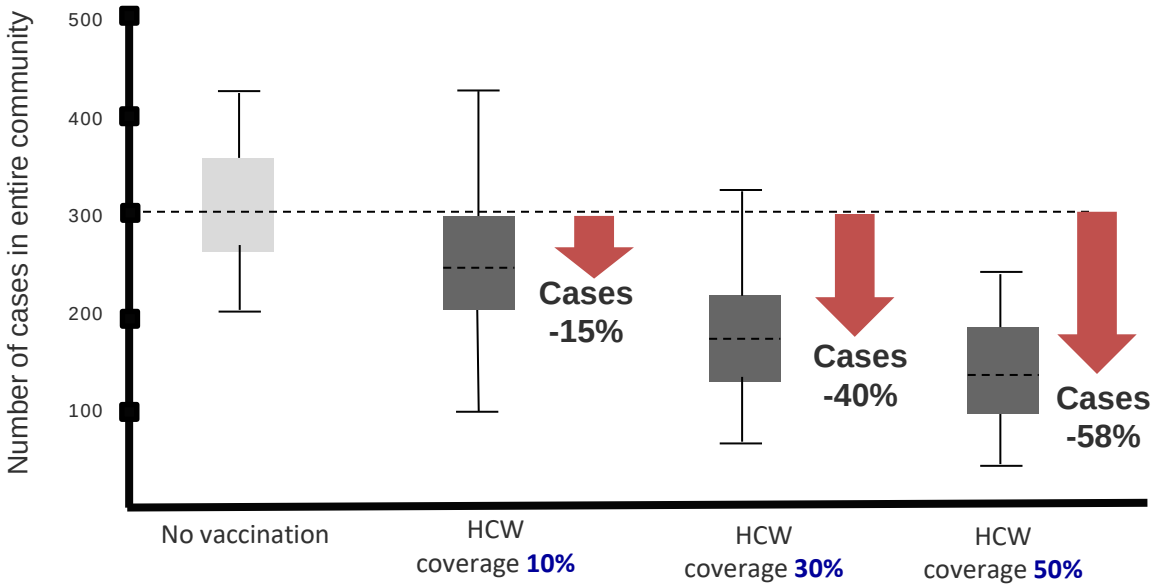
Sub-optimal implementation of measures in challenging environments:

- Limited resources in outbreak countries such as running water, stable power, PPE, and technical skills[10]
- Incoherent contact tracing methods resulting in incomplete identification of contacts[11,12,13]
- Political unrest and violence against civils[14]

1. FDA Approves First Treatment for Ebola Virus | FDA. (2020)
2. FDA Approves Treatment for Ebola Virus | FDA. (2020)
3. Mulangu, S. et al. A randomized, controlled trial of Ebola virus disease therapeutics. N. Engl. J. Med. 2019
4. WHO https://www.who.int/news/item/23-09-2019-second-ebola-vaccine-to-complement-ring-vaccination-given-green-light-in-drc.
5. WHO. WHO | Infection prevention and control (IPC) guidance summary. WHO (2014).
6. ECDC. Public health management of healthcare workers returning from Ebola affected areas
7. ECDC. Entry and exit screening options for EVD
8. WHO | Ebola and Marburg virus disease epidemics: preparedness, alert, control, and evaluation. WHO (2014).
9. IPAC. Ebola Virus Resources | IPAC Canada. https://ipac-canada.org/ebola-virus-resources.php.
10. Cooper C. et al. Infection prevention and control of the Ebola outbreak in Liberia, 2014-2015: Key challenges and successes. BMC Medicine 2016
11. WHO | Contact tracing. https://www.who.int/csr/disease/ebola/training/contact-tracing/en/
12. Greiner, A. L. et al. Addressing contact tracing challenges-critical to halting Ebola virus disease transmission. International Journal of Infectious Diseases 2015
13. Olu, O. O. et al. Contact Tracing during an Outbreak of Ebola Virus Disease in the Western Area Districts of Sierra Leone. Front. Public Heal. 2016
14. Kelly J.D. et all Impact of Different Types of Violence on Ebola Virus Transmission During the 2018–2020 Outbreak in DRC. JID 2020

Potential impact of Ebola prophylactic vaccination

Compared to reactive vaccination, **prophylactic vaccination** has a greater impact on the mitigation and prevention of future Ebola epidemics [1-3]



Impact of different vaccination coverage rates in healthcare workers (Adapted from Robert, 2019)[2]

Prophylactic vaccination of populations at high risk of acquiring and transmitting Ebolavirus infection – such as **HCWs** – can significantly reduce the number of cases in the whole community, **even at modest levels of coverage**[2]

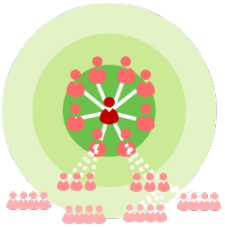
57% reduction of community cases achieved when prophylactically vaccinating **5% of the general population** in addition to 30% of HCWs[1]

1. Potluri, R. et al. Impact of prophylactic vaccination strategies on Ebola virus transmission: A modeling analysis. PLoS One, 2020
2. Robert, A. et al. Control of Ebola virus disease outbreaks: Comparison of health care worker-targeted and community vaccination strategies. Epidemics 2019
3. Coltart, C. E. M., Johnson, A. M. & Whitty, C. J. M. Role of healthcare workers in early epidemic spread of Ebola: Policy implications of prophylactic compared to reactive vaccination policy in outbreak prevention and control. BMC Medicine 2015

WHO SAGE recommendations on Ebola have clarified Janssen Ebola vaccine use

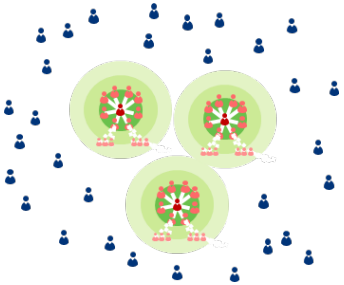

World Health Organization
Organisation mondiale de la Santé
Weekly epidemiological record
Relevé épidémiologique hebdomadaire
Contents
Meeting of the Strategic Advisory Group of Experts on Immunization, 22–24 March 2021: conclusions and recommendations
Sommaire
Réunion du Groupe stratégique consultatif d'experts sur la vaccination, 22-24 mars 2021 – conclusions et recommandations

Outbreak response (Reactive use)



Merck vaccine

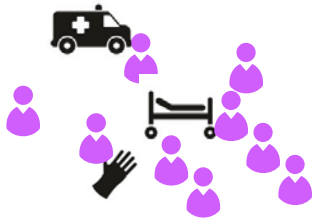
Contacts of an EVD patient and contacts of contacts



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

Index case | Contacts of the index case | Contacts of contacts | People in neighboring areas | National Response Teams

SAGE : Strategic Advisory Group of Experts on Immunization
WHO Weekly Epidemiological Record 4 JUNE 2021, 96th YEAR /No 22, 2021, 96, 197–216/http://www.who.int/wer

Potential broadening of SAGE recommendation

Broader preventive vaccination

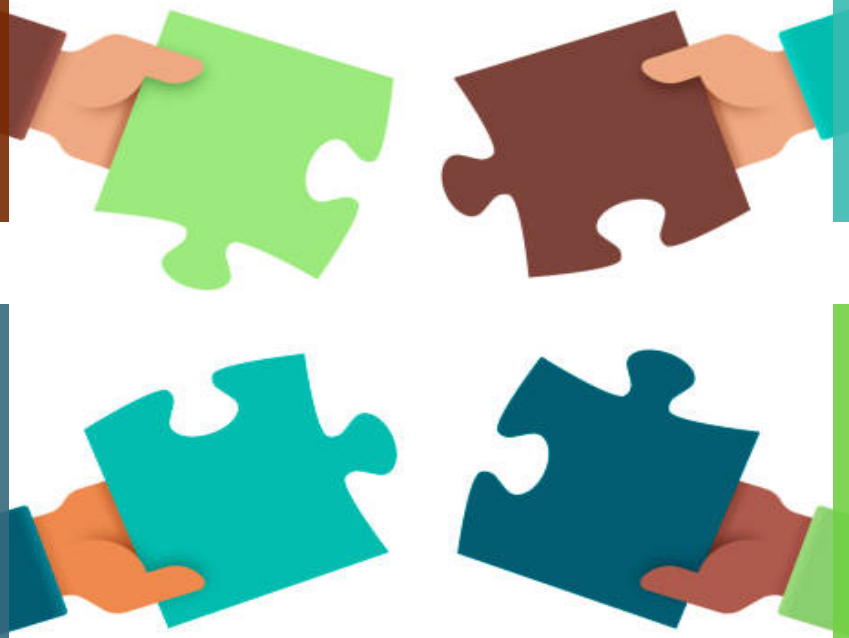
SAGE did not recommend yet widespread preventive use:
- o vaccine supply constraints
- o unknown duration of protection
- o more clarity on vaccine demand

"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**."

SAGE : Strategic Advisory Group of Experts on Immunization
WHO Weekly Epidemiological Record 4 JUNE 2021, 96th YEAR /No 22, 2021, 96, 197–216/http://www.who.int/wer

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



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

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

- 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

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.

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

THANK YOU FOR YOUR PARTICIPATION!

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.

ACKNOWLEDGEMENTS

Thank you to all volunteers, investigators and their staff and all our partners

BAVARIAN NORDIC

Inserm
Institut national
de la santé et de la recherche médicale

BARDA

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

NRB

NIH National Institute of Allergy and Infectious Diseases

CEPI

UNIVERSITY OF OXFORD

MINISTERE DE LA santé

imi innovative medicines initiative

Republic of Rwanda
Ministry of Health

CENTER FOR FAMILY HEALTH RESEARCH

COMAHS

World Vision

Centre MURAZ
Recherche - Formation - Expertise

efpia
European Federation of Pharmaceutical Industries and Associations

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

wellcome

University of Antwerp

SCIENTIA SPLENDET ET CONSCIENTIA

U.S.ARMY

MEDICAL COUNTERMEASURE SYSTEMS (MCS) – JOINT VACCINE ACQUISITION PROGRAM (JVAP) AND BIOSCAVENGER

Vibalogics

BATTELLE

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

HIV VACCINE TRIALS NETWORK

epicentre
EPIDEMIOLOGIE • EPIDEMIOLOGY

GRAMEEN FOUNDATION
Empowering people. Changing lives.
Innovating for the world's poor.

Walter Reed Army Institute of Research
Soldier Health • World Health

InsermTransfert