

First data in African subjects for the Janssen Monovalent Ebola Zaire heterologous prime-boost vaccine regimen Ad26.ZEBOV/MVA-BN-Filo

Professor Omu Anzala¹

Gaudensia Mutua¹, Borna A. Nyaoke¹, Cynthia Robinson², Kerstin Luhn²,
Benoit Callendret², Rodolphe Thiebaut³, Deborah Watson-Jones⁴, Macaya Douoguih²

¹University of Nairobi, KAVI – Institute of Clinical Research, Nairobi, Kenya; ²Janssen Vaccines & Prevention B.V., Pennsylvania, USA;

³University of Bordeaux, INSERM U1219, Bordeaux, France; ⁴London School of Hygiene & Tropical Medicine, London, UK

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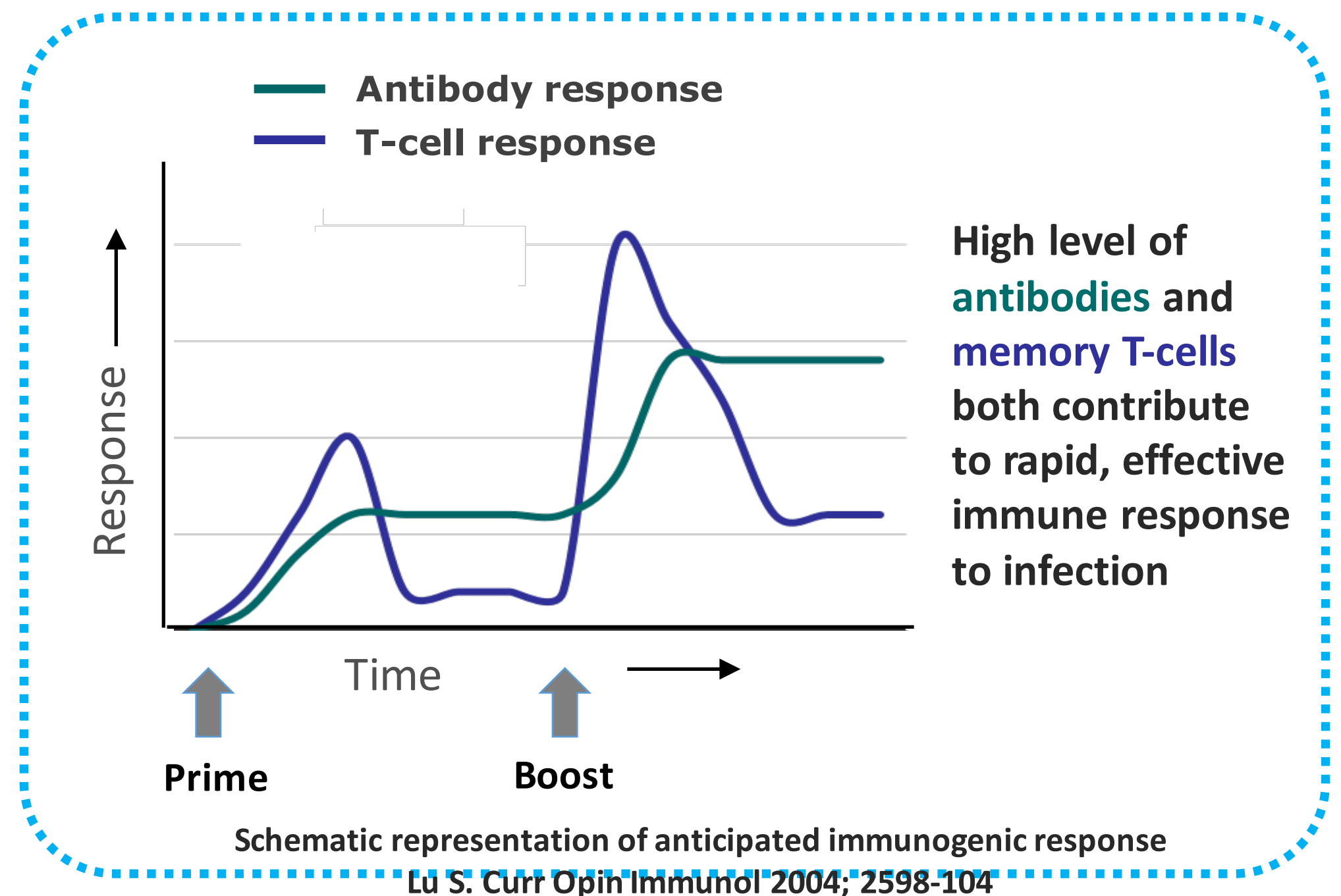
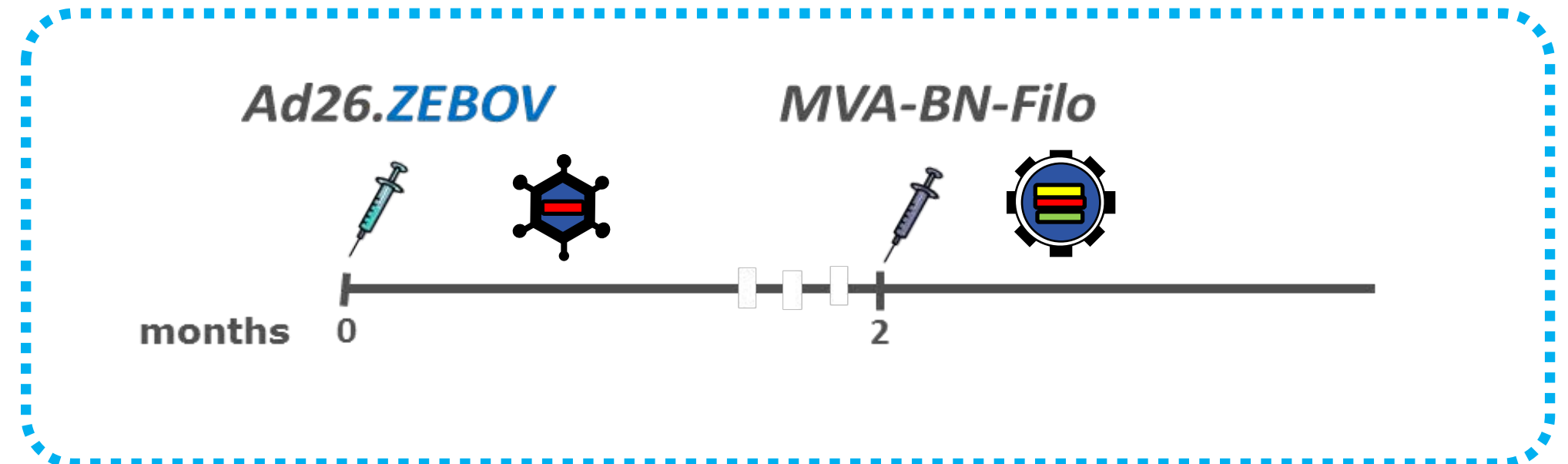
- **Professor Omu Anzala is employed by** University of Nairobi, KAVI – Institute of Clinical Research, Nairobi, Kenya and has no conflict of interest to declare
- This trial known as EBL1003 received funding from the Innovative Medicines (Initiative 2 Joint Undertaking under grant agreement numbers 115854 and 115861. 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.
- EBL1003 is sponsored by Janssen Vaccines & Prevention B.V. (formerly known as Crucell Holland B.V.), hereafter referred to as “Janssen”.
- **I AM NOT PROF OMU ANZALA**



EBL1003 Phase I study

The EBL1003 study was designed to evaluate the **safety, tolerability** and **immunogenicity** of **Ad26.ZEBOV/MVA-BN-Filo** in Kenyan healthy adult volunteers

- In response to the Ebola outbreak in West Africa in 2014, the Ebola Zaire vaccine development was accelerated
- Heterologous prime-boost monovalent Ebola Zaire vaccine regimen
 - ➔ **Ad26.ZEBOV**
 - ➔ **MVA-BN-Filo**
- **All phases of development occurring simultaneously**



Initially included sites in Ghana....

HEALTH

Ghana says locals used as 'guinea pigs' in Ebola trial

Government suspends trial by Western pharmaceutical firms, which paid volunteers a mobile phone and about \$5 each.

11 Jun 2015 18:44 GMT | Health

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PRIME SERIES

Speaker orders cessation of Ebola trials in Ghana

Source: GhanaMyjoyonline.com/Nathan Gadugah
Date: 10-06-2015 Time: 06:06:37 pm

© Photo: David Andoh-myjoyonline

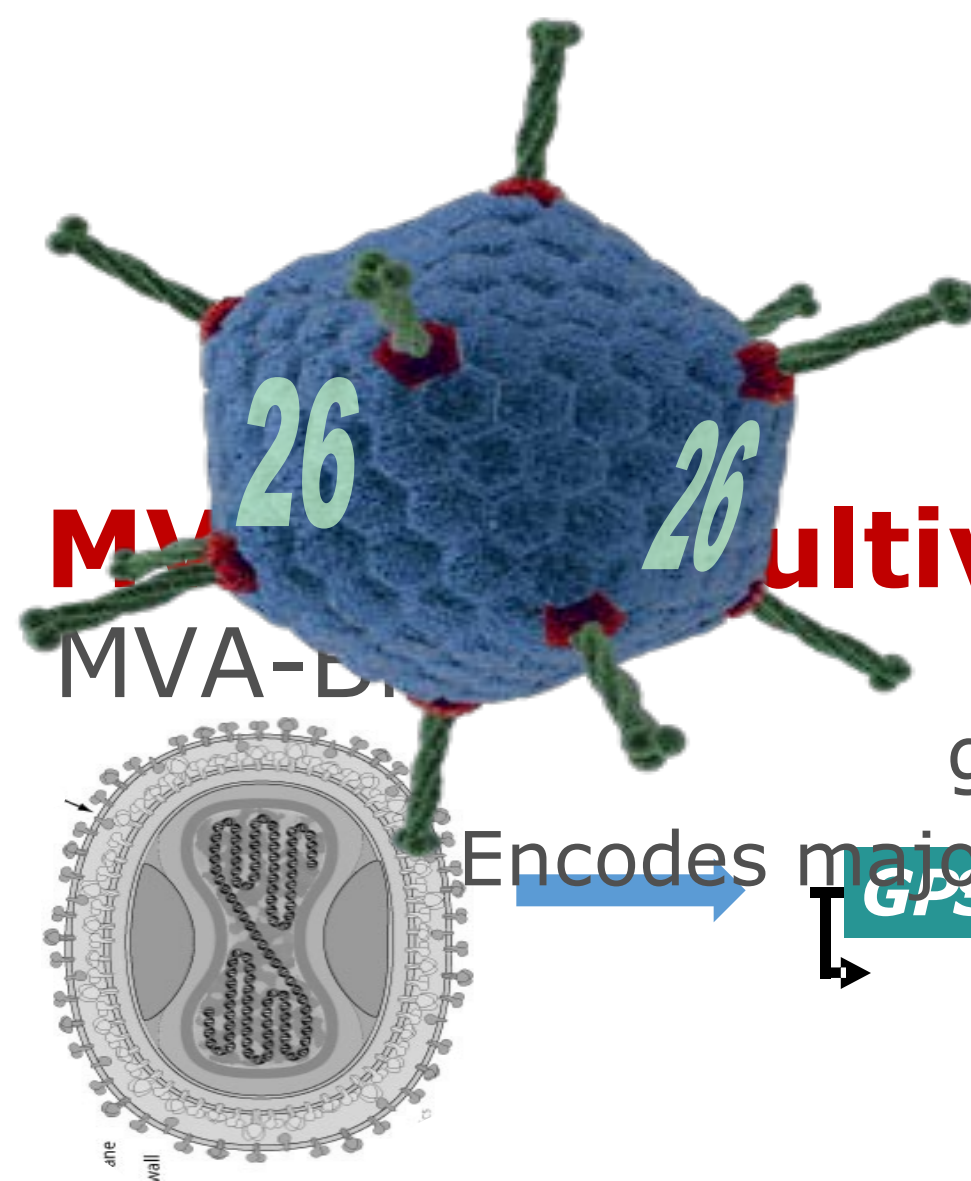


- Study Approved by Ghana FDA after significant delays
 - Followed by community protests
 - Government stops study
 - Ghana college of science in support of government action

Ad26.ZEBOV and MVA-BN-Filo Ebola vaccines

Ad26.ZEBOV

Ad26 vector



gene encoding GP antigen

GP ZEBOV

genes encoding GP and NP antigens

Encodes major antigen Glycoprotein of Ebola Zaire

GP SUDV

NP1A/FV

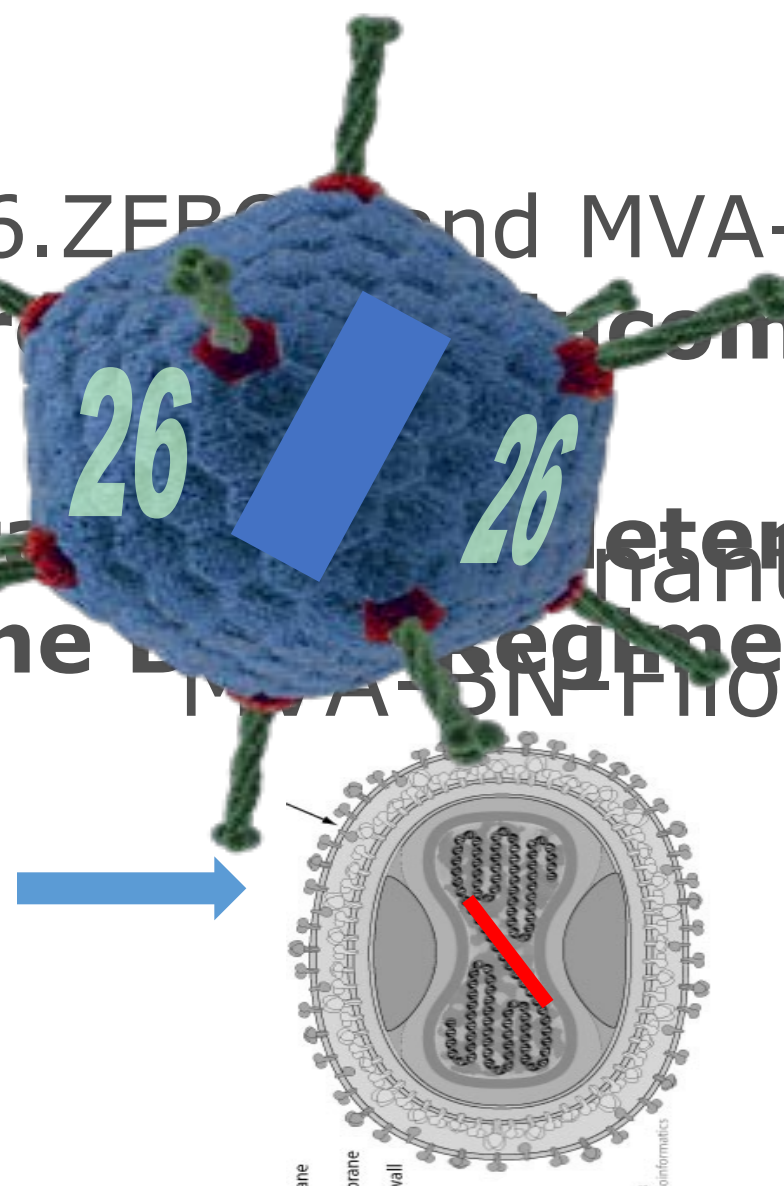
GP ZEBOV

GP MARV

Ad26-ZEBOV

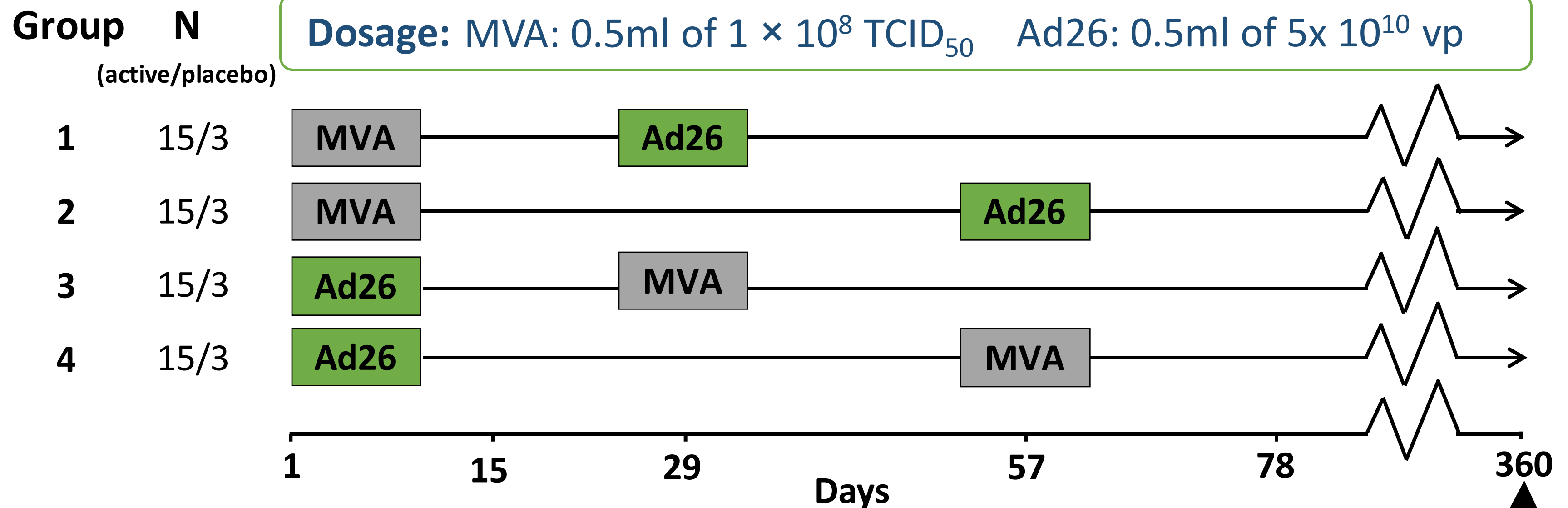
- Ad26.ZEBOV and MVA-BN-Filo are recombinant competent

- Intracellular heterologous Prime MVA-BN-Filo segment



Encodes GP antigen of all Filoviruses and the conserved nucleoprotein (NP)

EBL1003 trial design



Immunogenicity Follow-up:

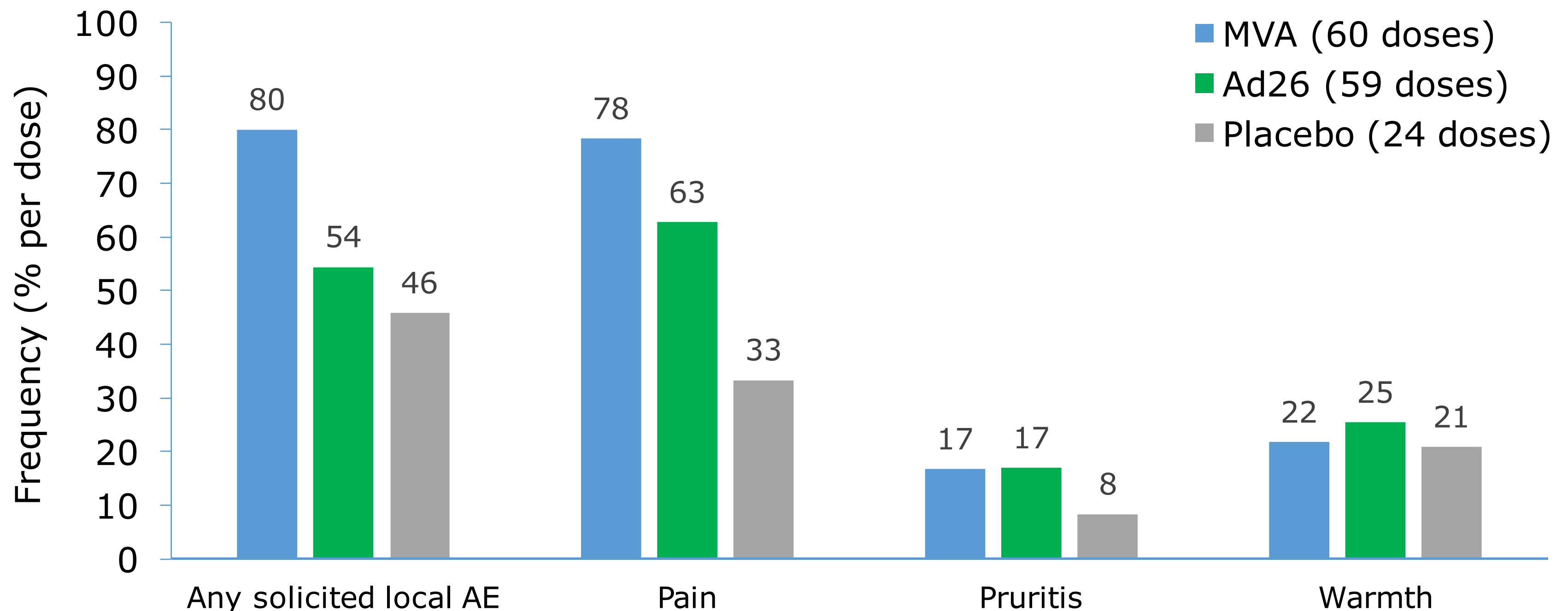
- Total IgG antibodies (ELISA)
 - IFN- γ ⁺ T cell responses (ELISpot)
 - Virus Neutralizing Antibodies (VNA)
 - CD4⁺ and CD8⁺ T cell cytokine responses (ICS)
- collected up to 1 year

EBL1003 participant characteristics

- 72 healthy adults participated in this Phase I randomised trial
- 71 completed both prime and boost
- All subjects were healthy adult Kenyans
- Subject were randomized 5:1 active to placebo

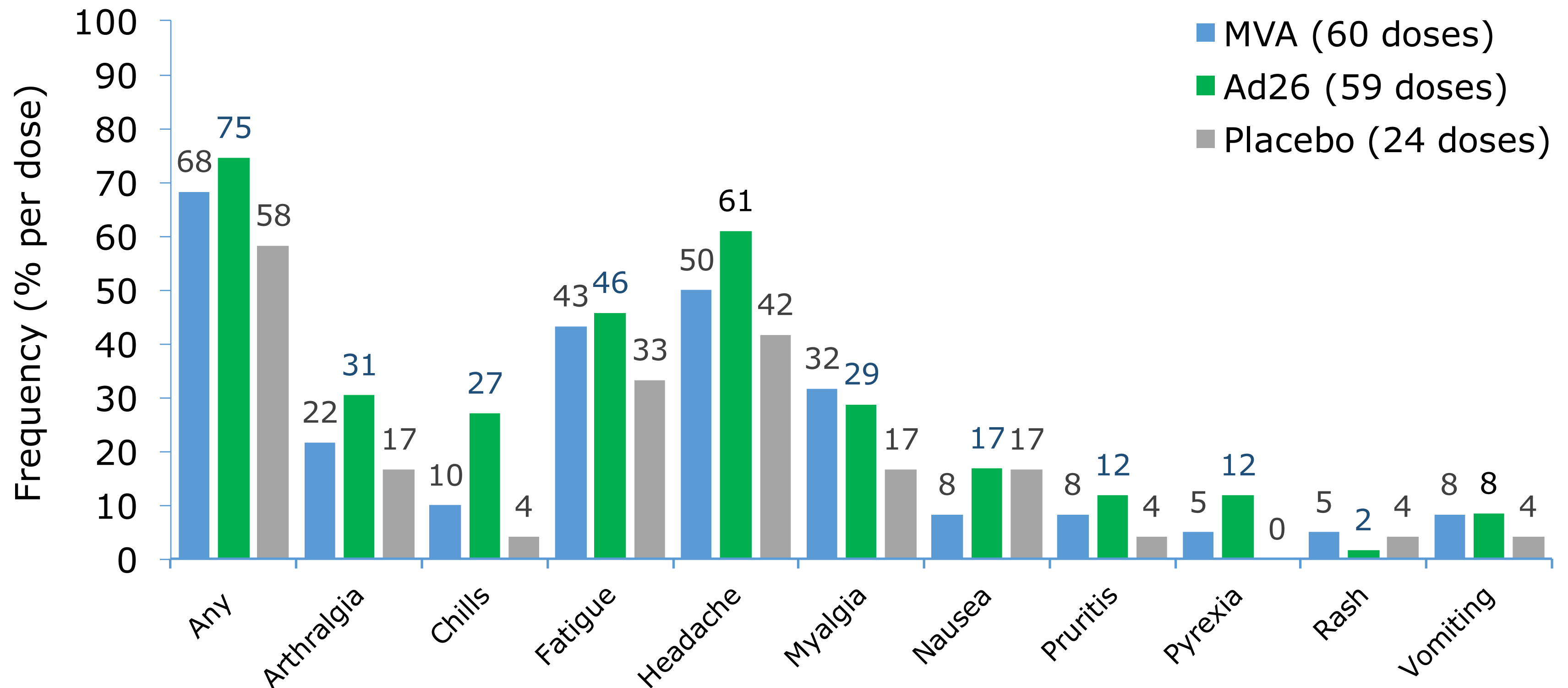
Characteristic	N=72
Male, n (%)	49 (68.1%)
Median age, years (range)	25 (18-45)
Median body mass index, kg/m ² (range)	22.6 (16.5-34.0)

Frequency of solicited local AEs (% per dose)



- The most common local solicited AE was injection site pain
- Only one participant, who had concurrent active malaria, reported grade 3 injection site pain

Frequency of solicited systemic AEs (% per dose)



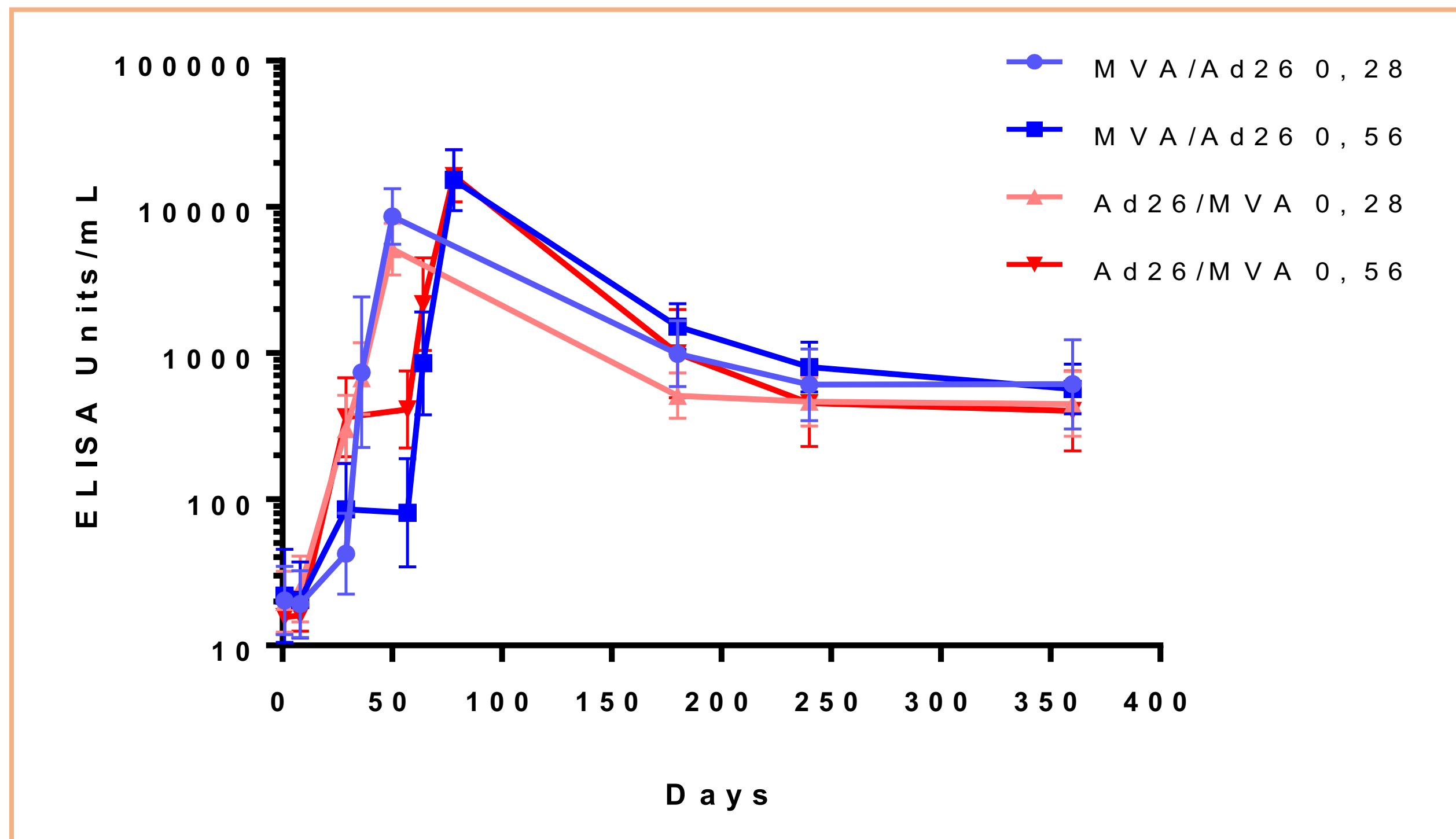
- The most common systemic solicited AEs were headache and fatigue
- Only one participant, who had concurrent active malaria, reported grade 3 headache and chills

Safety Summary

All vaccine regimens had an acceptable safety profile and were well-tolerated

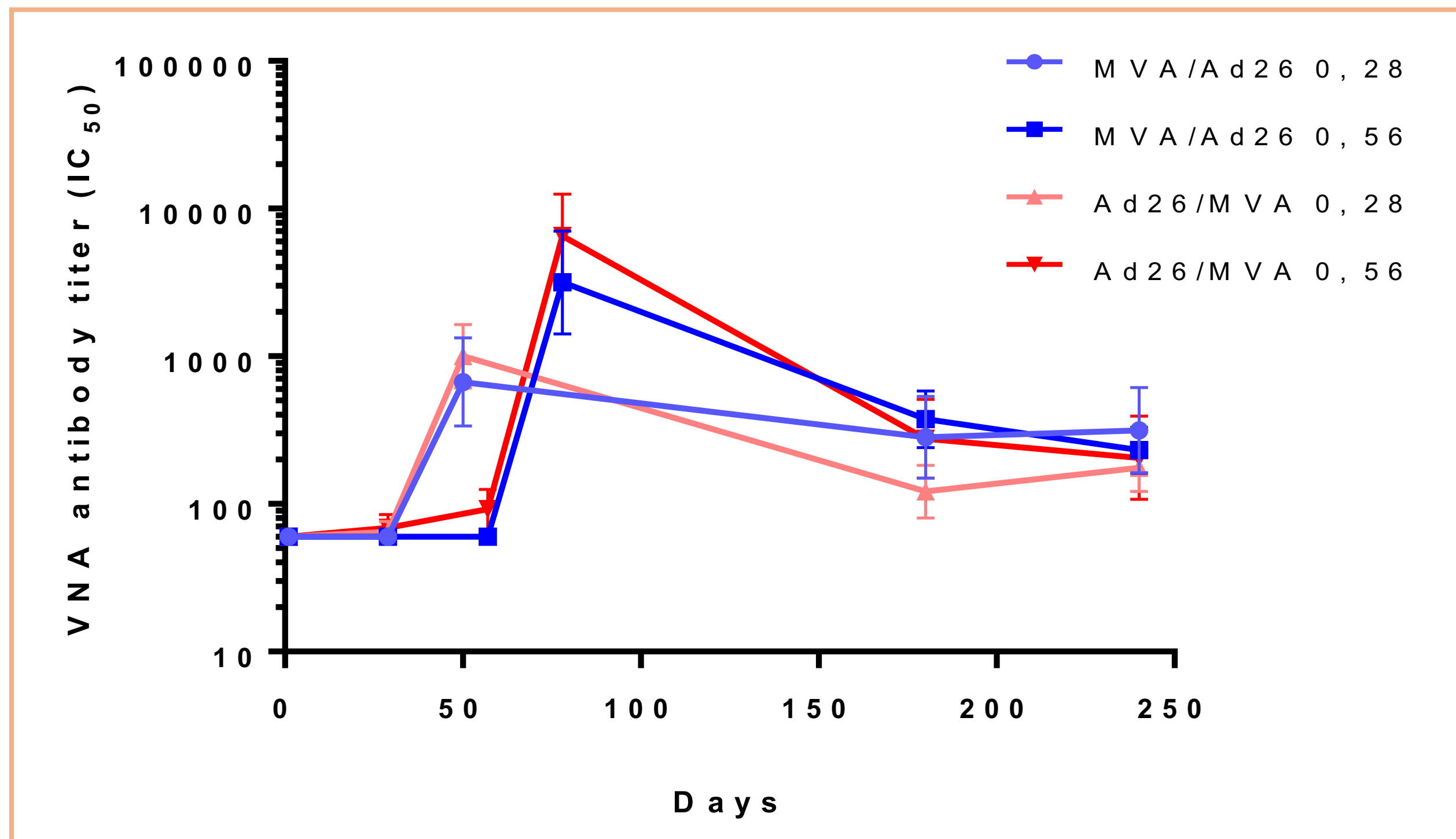
- No SAEs were reported and no discontinuations due to AE
- Solicited adverse events were typical for vaccines
- Solicited adverse events were generally mild-moderate in intensity and short-lived

Antibody responses following heterologous prime-boost up to 360 days post-prime



- Binding antibody levels are robust and stable from 6 to 12 months post-prime
- No difference between the regimens apparent at later timepoints.
- Ad26-primed regimens show an earlier antibody response than MVA-primed regimens

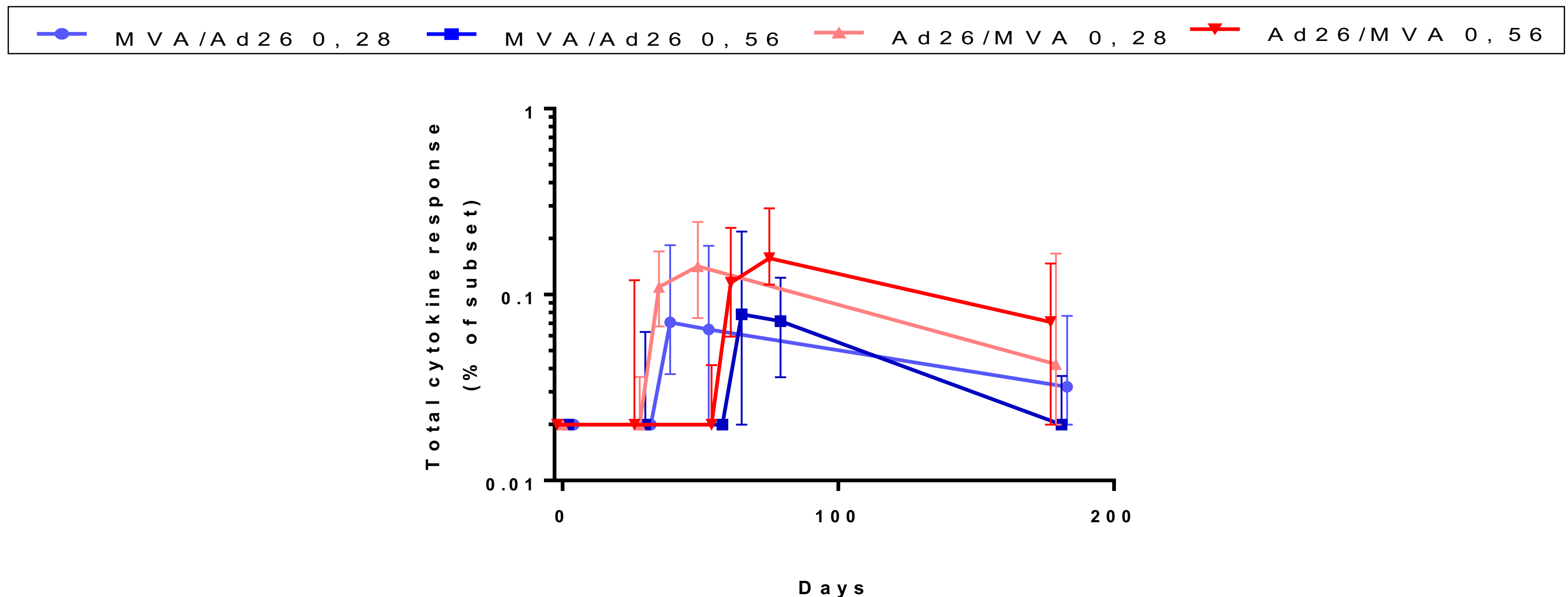
VNA responses following heterologous prime-boost up to 240 days post-prime



- Substantial, rapid boosting of neutralizing antibodies seen with all regimens
- Neutralizing antibodies detectable for ≥ 8 months post-prime with all regimens
- No difference between regimens apparent at Day 240 time point

T cell responses following heterologous prime-boost

CD4⁺ T cell cytokine response up to day 180



- CD4⁺ T cell cytokine responses of Kenyan responders are similar to those of Western participants
- Few participants displayed CD8⁺ T cell cytokine responses; However, response levels of responders are comparable to those of Western participants

Immunology Summary

- The Ad26.ZEBOV/MVA-BN-Filo heterologous prime-boost vaccine regimen was well tolerated and conferred **durable immune response to Ebola glycoprotein** in African healthy volunteers
- **Antibody responses** are sustained for at least **12 months** and **T-cell** responses for **at least 6 months** after vaccination with Ad26.ZEBOV/MVA-BN-Filo
- This regimen may therefore be suitable for use in preventive vaccination strategies in the event of a new outbreak in Africa
- Development of Janssen Ebola vaccine ongoing:
 - Further studies of Ad26.ZEBOV/MVA-BN-Filo, including Phase I studies in other African countries and **Phase 2** and 3 studies, are ongoing

Acknowledgments

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Janssen, London School of Hygiene & Tropical Medicine, Institut National de la Santé et de la Recherche Medicale (Inserm), University of Oxford, Inserm Transfert, Le Centre Muraz
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