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Update on PREVAIL Vaccine Studies

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UPDATE ON PREVAIL VACCINE STUDIES

Presented by

Dr. Mark Kieh for the PREVAIL TEAM

February 27, 2019

HISTORICAL HIGHLIGHTS

- 2014 Ebola outbreak in West Africa was the largest in history
- It placed unprecedented burdens upon our healthcare system and workers
- There is a critical need for a safe and effective vaccine to prevent future outbreaks of this devastating disease.

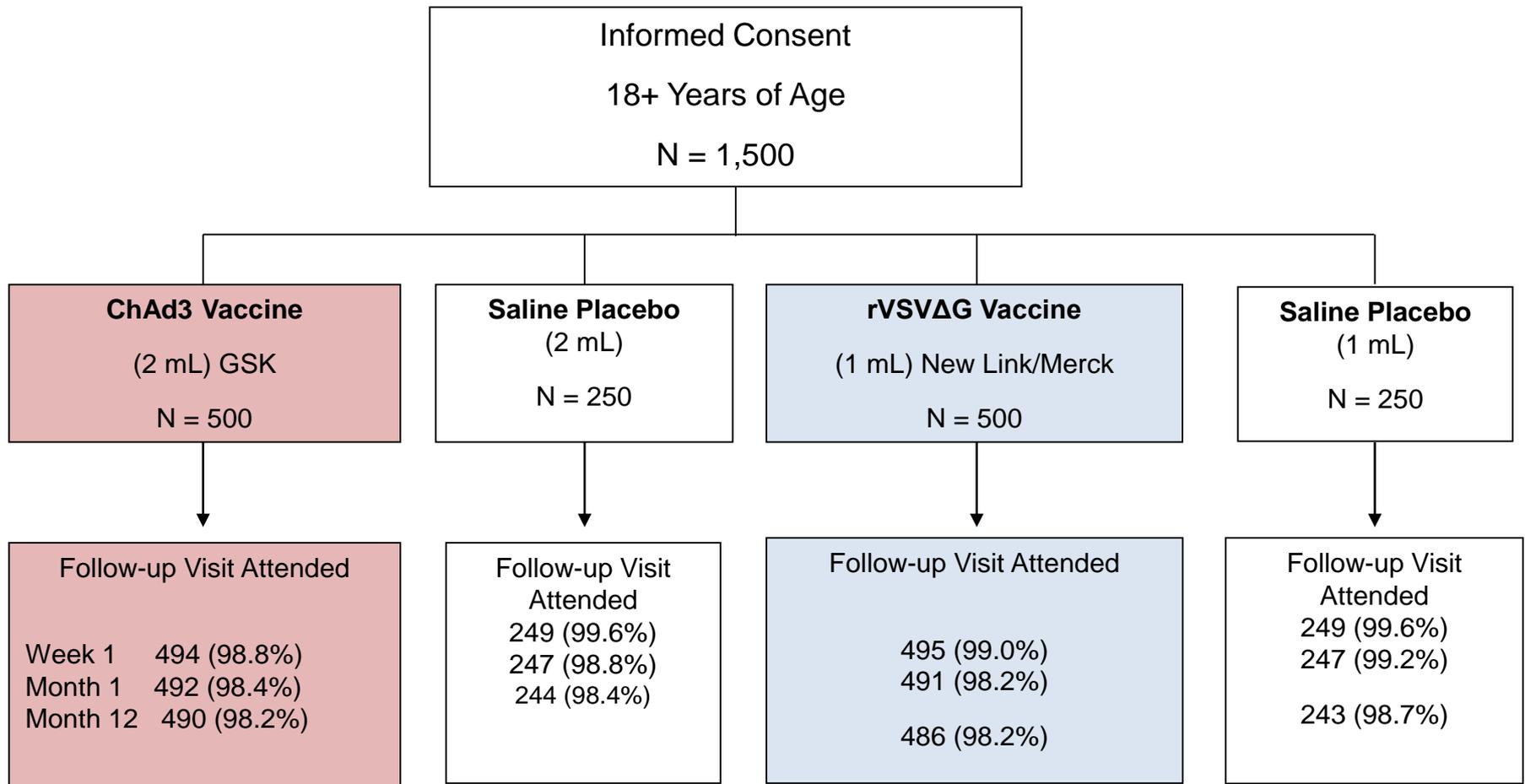
PREVAIL UPDATE-HISTORICAL HIGHLIGHTS

- The Liberian/U.S. Partnership for Research on Ebola Virus in Liberia (PREVAIL) was established in October 2014 based upon an exchange of letters between the then Liberian Minister of Health Gwenigale and U.S. Health and Human Services Secretary Burwell.
- A research plan to test candidate Ebola Vaccines and Therapeutics was initiated.

PREVAIL UPDATE-HISTORICAL HIGHLIGHTS

- * Two candidate Ebola virus vaccines had just entered phase 1 testing in September 2014.
 - Recombinant chimpanzee adenovirus Type-3 (ChAd3)
 - Recombinant vesicular stomatitis virus (rVSV)
 - On February 1, 2015, the PREVAIL I Vaccine Study was launched at a ceremony at Redemption Hospital which was graced by His Excellency, former Vice President of the Republic of Liberia, Ambassador Joseph N. Boakai

PREVAIL I Study Design and consort Flow Diagram



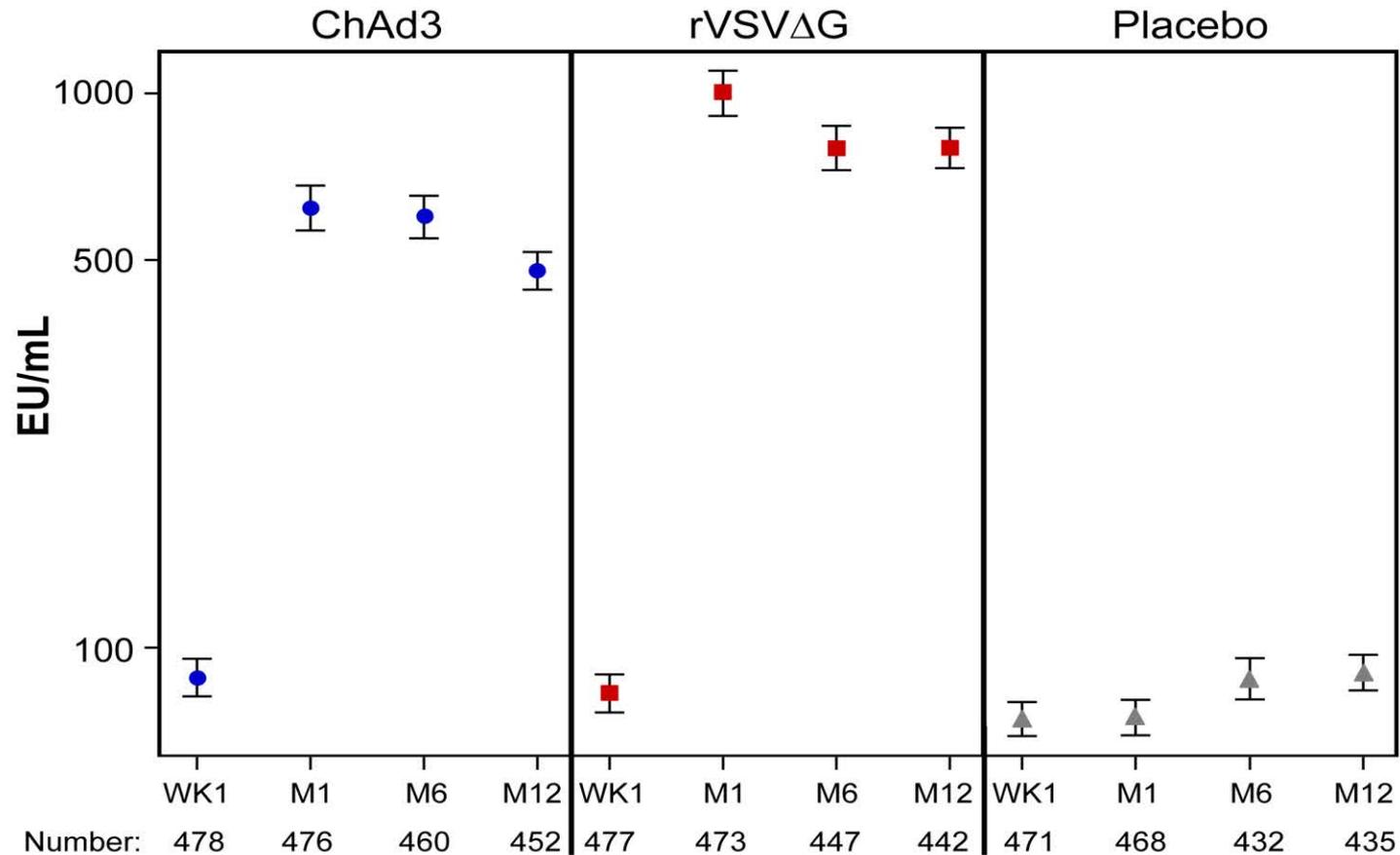
UPDATE

- Participants were followed post-vaccination at week 1, month 1, and every two months for 12 months
- Overall, the vaccines were well tolerated, and no significant differences in reported side effects were found between those who received either of the vaccines or the placebo.

UPDATE

- Compared to placebo, both vaccines are safe and elicited an immune response (antibodies to the Ebola surface glycoprotein) by one month post-vaccination that was largely maintained through 12 months.
- Common side effects were headaches, muscle pain, feverishness, and fatigue.
- No major Serious Adverse Event reported.

Geometric Mean Titers Following Randomization+



+Among participants without elevated levels at entry. P-values between each active vaccine and placebo are significant at level $p < 0.001$ at each visit, except at week 1 for ChAd3 vs. placebo ($p = 0.004$).

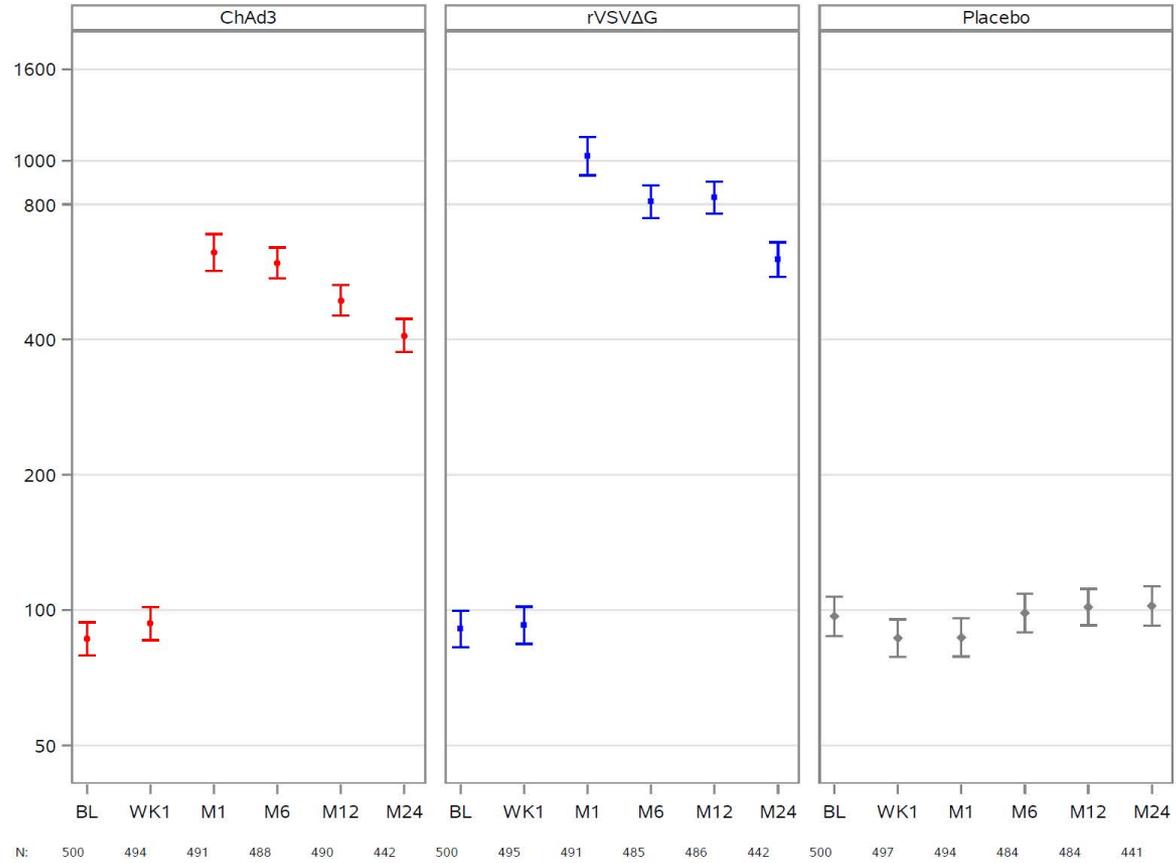
PREVAIL I Close- out and Follow up Plan

- Extended to follow-up the original cohort of PREVAIL I study participants(1500)
- To conduct long-term immunogenicity testing and collection of SAE's for an additional 4 years after the original 12-month visit.
- To determine the duration of the immune response.
- Participants have been followed up to 36months.

PREVAIL I Close-out and Follow-up Plan

- All participants were invited in February of 2016 and educated on the close-out plan
- Participants randomized assignments were revealed individually.
- All participants were asked if they wanted to volunteer for follow-up every 12 months with blood draw at each follow-up visit. SAE's events will be assessed at each follow-up visit.

Geometric Mean Titers at Vaccination Through 24 Months: All Participants



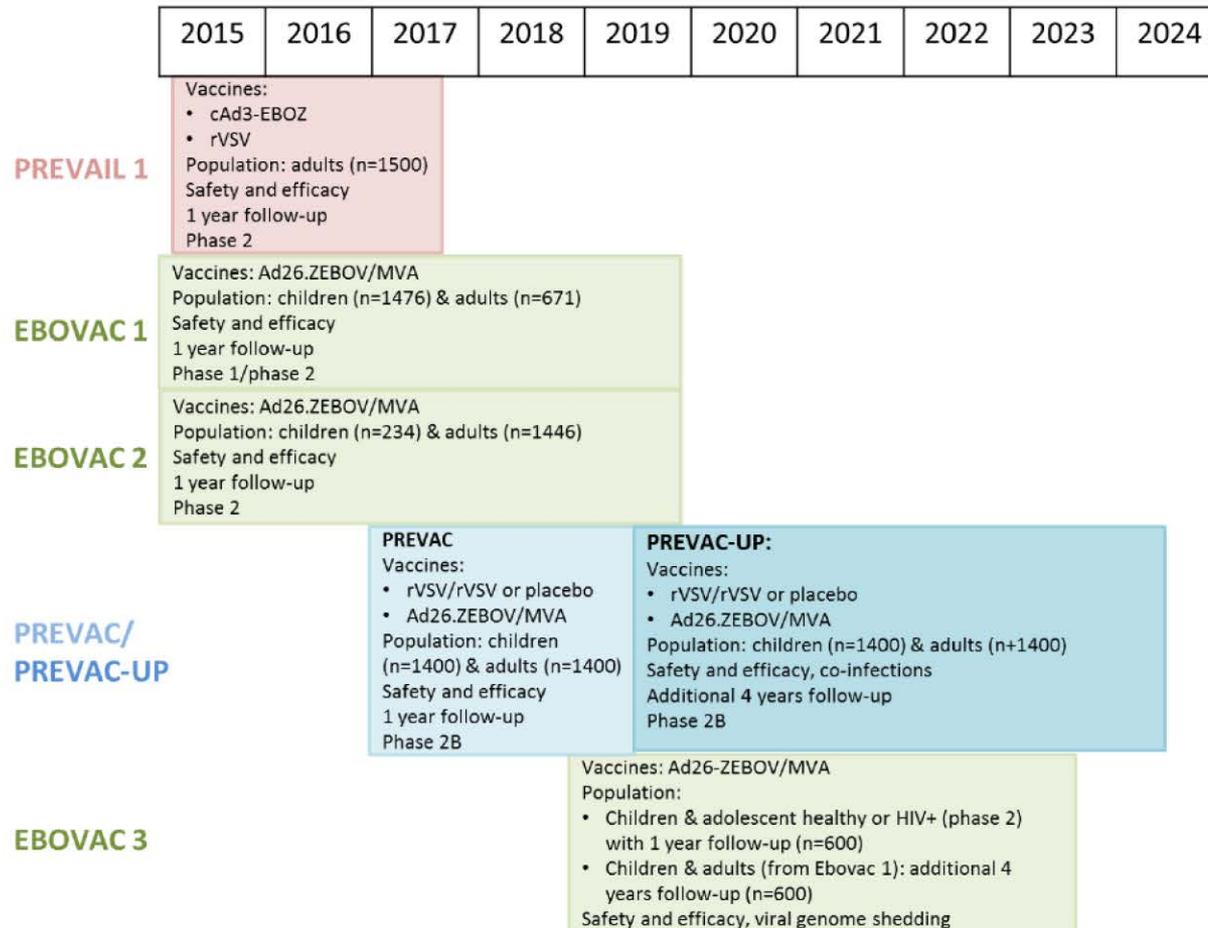
PARTNERSHIP FOR RESEARCH ON EBOLA VACcination (PREVAC)

- PREVAC means Partnership for Research on Ebola VACcination. It is a regional study ongoing in the three countries most affected by Ebola, Guinea, Liberia, and Sierra Leone plus Mali
- This is an extension of other vaccine studies that have been conducted in these three countries to investigate many unanswered questions about the safety and efficacy of the vaccines,

PARTNERSHIP FOR RESEARCH ON EBOLA VACCINATION (PREVAC)

- including the immediacy (how quickly does a participant elicit an immune response)
- duration of the immune response,
- and safety issues especially among children.

PREVAC in Ebola Research



PARTNERSHIP FOR RESEARCH ON EBOLA VACCINATION (PREVAC)

- Little is known about the effects of the vaccines on children.
- During the epidemic, children were the most vulnerable, with high mortality rates recorded among the very young to the oldest. So, it was decided on that evidence to include children since they were the most vulnerable.

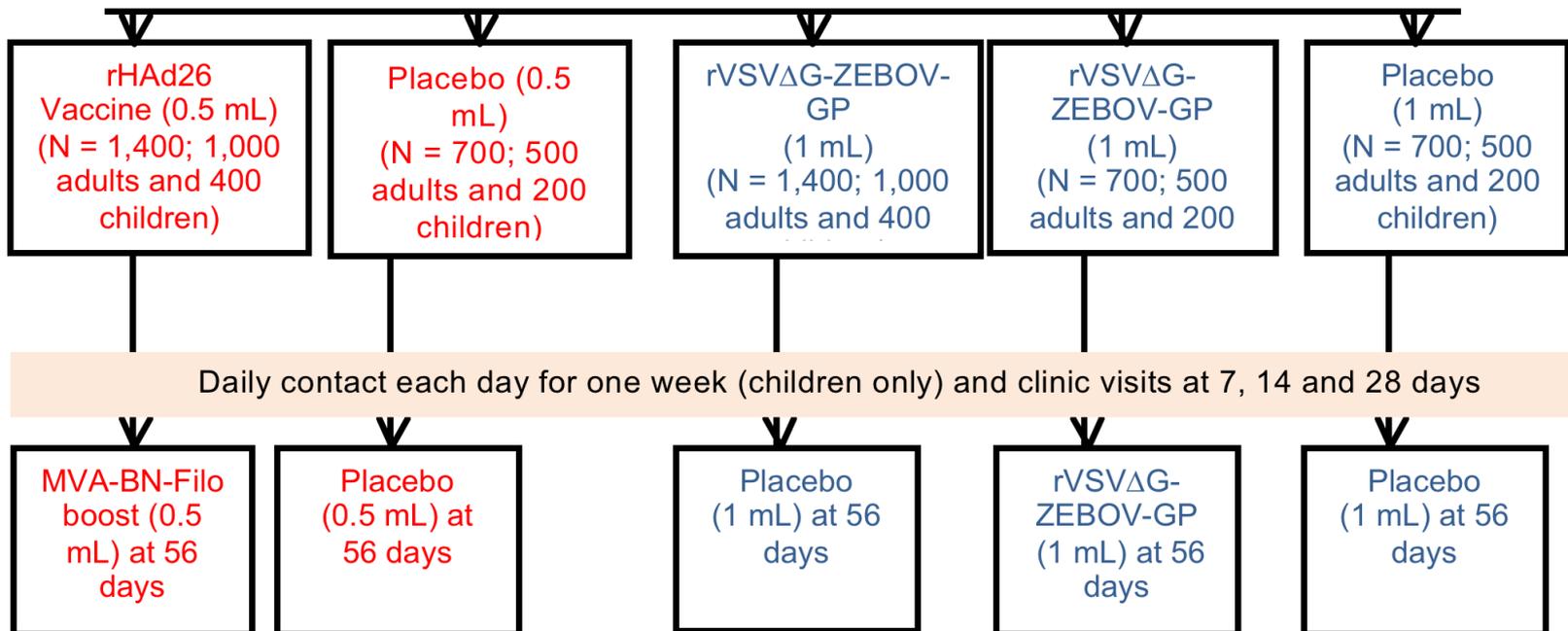
Objective

- **To compare 3 vaccine strategies each with placebo for safety and immunogenicity in adults and children in three countries in West Africa where EVD was active during 2014 and 2015 (Guinée, Liberia, Sierra Leone). Mali Joined**
- **Vaccine strategies:**
 - rVSV Δ G-ZEBOV-GP vaccine without a boost
 - rVSV Δ G-ZEBOV-GP vaccine, with a boost at 56 days
 - Ad26.ZEBOV vaccine (prime vaccination) and MVA-BN-Filo at 56 days (boost)

Study Design Overview: a phase 2 randomized controlled study

4,900 Eligible Participants: 3,500 Adults and 1,400 Children

Randomized 2:1:2:1:1



Daily contact each day for one week (children only) and clinic visits at 63 days, and 3, 6 and 12 months and then annually through 5 years (if funding permits)

Blinding

- Study participants and clinical staff assessing the study participants for safety and laboratory outcomes are fully blinded until all participants complete 12 months of follow-up.

Data and Safety Monitoring Board (DSMB)

- DSMB closely monitored accumulating safety data for adults and children in each age group (1-4, 5-11, and 12-17 years).
 - Safety data for children were reviewed at least monthly until the DSMB was satisfied that the vaccines were safe and that now less frequent reviews are being carried out

Enrollment: age 1-17 years for the trial in children

Initially, only adults and children ≥ 12 to ≤ 17 years of age.



70 children aged ≥ 12 to ≤ 17 years enrolled and followed for 28 days

DSMB: consider vaccination of children ≥ 5 to ≤ 11 years?



70 children aged ≥ 5 to ≤ 11 years of age



DSMB: consider vaccination of children 1 to ≤ 4 years?



enrol 100 children between 1 and 4 years.



Safety: definition of Serious Adverse Events (SAE)

- Death
- Events that are life-threatening
- Events requiring hospitalisation or requiring prolongation of existing hospitalisation
- Events resulting in a persistent or significant incapacity
- Congenital anomaly or birth defects

*For this protocol, EVD events and laboratory confirmed malaria events that do not require hospitalization will not be considered as SAEs. Laboratory diagnostic criteria for confirmation of malaria should be based on local criteria

Safety

- Injection site reactions: redness of skin, swelling/induration, pain/tenderness with activity, and itching a injection site
- Targeted symptoms: reduced activity, somnolence, fatigue, vomiting, chills, abnormal sweating. skin lesions, mouth ulcers, decreased appetite, feverishness, diarrhea, nausea, headache, dizziness, abdominal pain, muscle pain, joint swelling, and joint pain
- For non-verbal children, subjective symptoms may not be assessed and irritability/fussiness, crying, and screaming will be assessed.

PREVAC in Numbers

➤ Key dates

First participant in: 27 March 2017 (Guinea, Landreah)
 3 April 2017 (Liberia, Redemption)
 24 May 2017 (Guinea, Mayferinyah)
 22 May 2018 (Sierra Leone, Mambolo)
 12 July 2018 (Mali, CVD and UCRC)

➤ To date: 4789 participants randomized
(preliminary phases and current phase)

- 2560 Adults
- 2229 Children (1 to 17 years old)

PREVAC in Numbers

➤ To date: Participants randomized per country

- Guinea: 1214 Adults / 1116 Children
- Liberia: 657 Adults / 476 Children
- Sierra Leone: 397 Adults / 311 Children
- Mali: 292 Adults / 326 Children



PREVAC-UP



EDCTP

European & Developing Countries
Clinical Trials Partnership

- Funding secured through EDCTP for 4 more years of follow-up
- PREVAC-UP will start in 2019
- 1 follow-up visit per year until 2023 = total of 5-year follow-up post vaccination

Prevail Upcoming New Studies

- Honor Study
 - > Sites: JFK/Redemption
- Malaria Study
 - > Sites : Duport Rd/Rennie
- Fever Etiology Study
 - > Sites : Redemption/?

PREVAIL

THANK YOU.

QUESTIONS