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Rotavirus Trivalent P2-VP8 Subunit Vaccine Phase 3 Study

Interim Results

Tushar Tewari, MD
Senior Medical Officer
PATH, India

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A Phase 3 Study to Evaluate the Efficacy of the Trivalent P2-VP8 Vaccine Candidate

Study title: A Phase 3 double-blind, randomized, active comparator-controlled, group-sequential, multinational trial to assess the safety, immunogenicity and efficacy of a trivalent rotavirus P2-VP8 subunit vaccine in prevention of severe rotavirus gastroenteritis in healthy infants

Sponsor: PATH

Vaccine manufacturer: SK bioscience, Co., South Korea

Clinical trial sites:

- Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, Ghana
- Malawi-Liverpool-Wellcome Trust (MLW) Clinical Research Programme, Blantyre, Malawi
- Centre for Infectious Disease Research in Zambia (CIDRZ), Lusaka, Zambia

Success, the first infant enrolled at Zingwanga, Malawi. Photo: MLW

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Study Hypothesis, Objectives, and Endpoints

Study hypotheses	• The efficacy of trivalent P2-VP8 subunit rotavirus (TV P2-VP8) vaccine in prevention of **severe rotavirus gastroenteritis** (SRVGE) will be **superior** to that of a licensed live oral vaccine, ROTARIX® • The TV P2-VP8 vaccine will be **safe and well-tolerated** in healthy infants.
Primary objectives	• To assess the **relative efficacy*** in prevention of SRVGE of the TV P2-VP8 vaccine compared to ROTARIX. • To evaluate the **safety** of the TV P2-VP8 vaccine in healthy infants compared with the safety of ROTARIX.
Primary endpoints	• Laboratory-confirmed cases of **SRVGE** (any strain). • **Serious adverse events** (SAEs), including intussusception, through 28 days after the last dose of study vaccine. • **Adverse events >grade 2** through 28 days following the last dose of study vaccine.

**Primary analysis to be performed once ≥99 cases are identified with onset at least 2 weeks after receipt of third study vaccination.*

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Secondary Objectives

Efficacy

- To assess the **relative efficacy** in prevention of SRVGE in the **first two years** of life, as well as in the **first** and **second year** of life, separately.
- To assess the relative efficacy in prevention of **very SRVGE** (VSRVGE).
- To assess the P-type specific relative efficacy in prevention of SRVGE and VSRVGE, for P[4], P[6] and P[8] strains.
- To assess the relative efficacy in prevention of rotavirus gastroenteritis (RVGE) of **any severity**.
- To assess the relative efficacy in prevention of **hospitalization** due to RVGE of any severity.

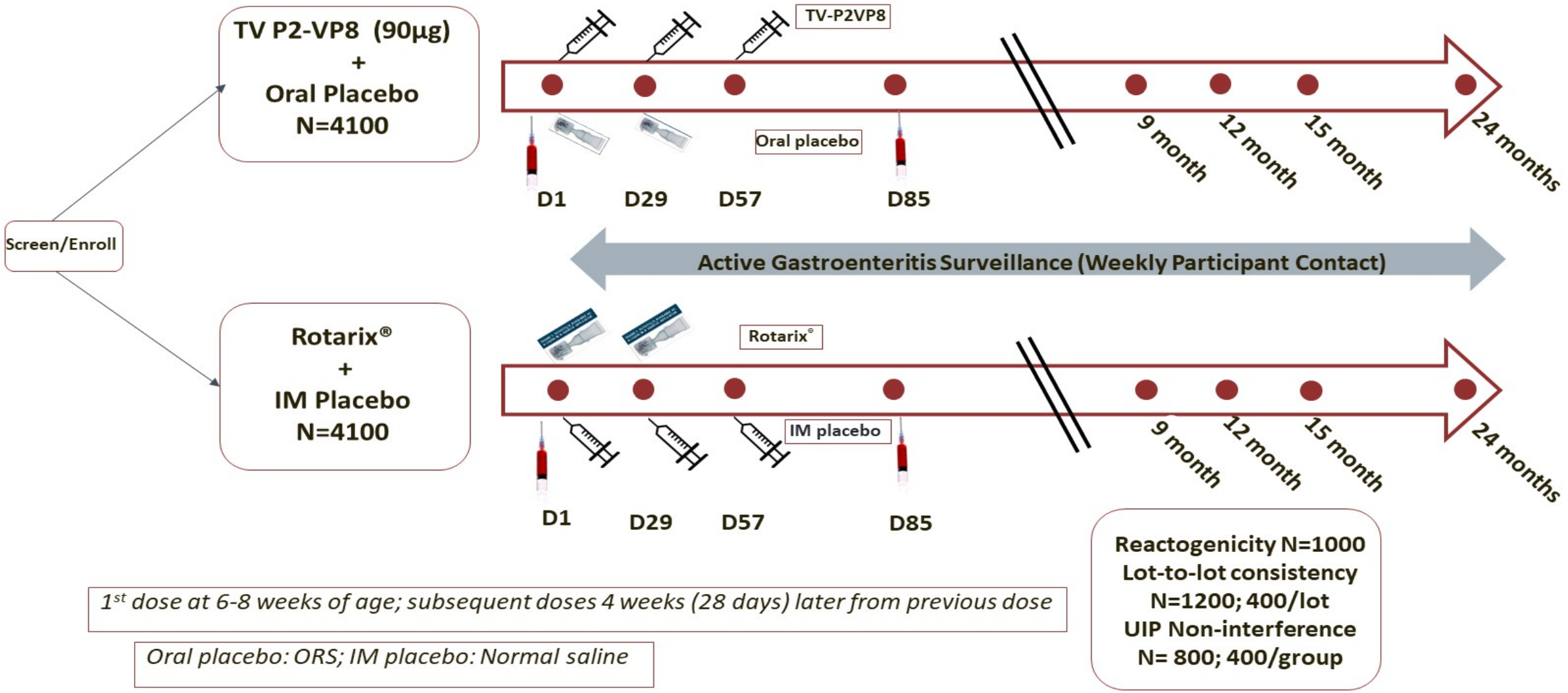
Safety

- To evaluate the **tolerability** (reactogenicity) of the TV P2-VP8 subunit vaccine (in the week following each vaccination) and compare with that of ROTARIX.
- To evaluate **longer-term safety** of the TV P2-VP8 vaccine in healthy infants and compare with that of ROTARIX.

Immunogenicity

- To evaluate the **immunogenicity** of the TV P2-VP8.
- To assess **lot-to-lot consistency** of immune responses across three lots of TV P2-VP8 vaccine, based on a subset of participants receiving TV P2-VP8.
- To compare the impact of **concomitant administration** of TV P2-VP8 on immune responses to other Universal Immunization Program vaccines to that of ROTARIX.
- To evaluate immune response to ROTARIX.

Double-Dummy Study Design



1st dose at 6-8 weeks of age; subsequent doses 4 weeks (28 days) later from previous dose

Oral placebo: ORS; IM placebo: Normal saline

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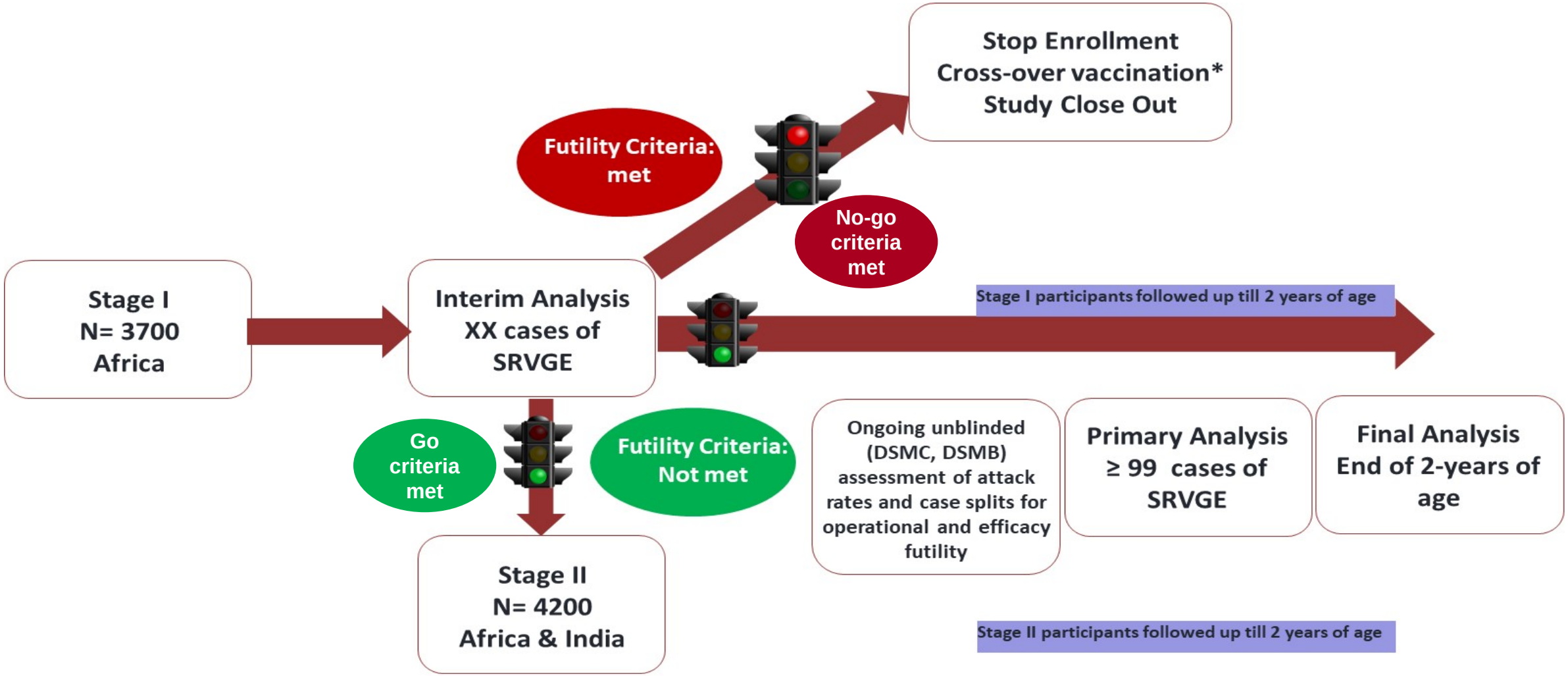
Group Sequential Design with an Interim Analysis



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Interim safety results

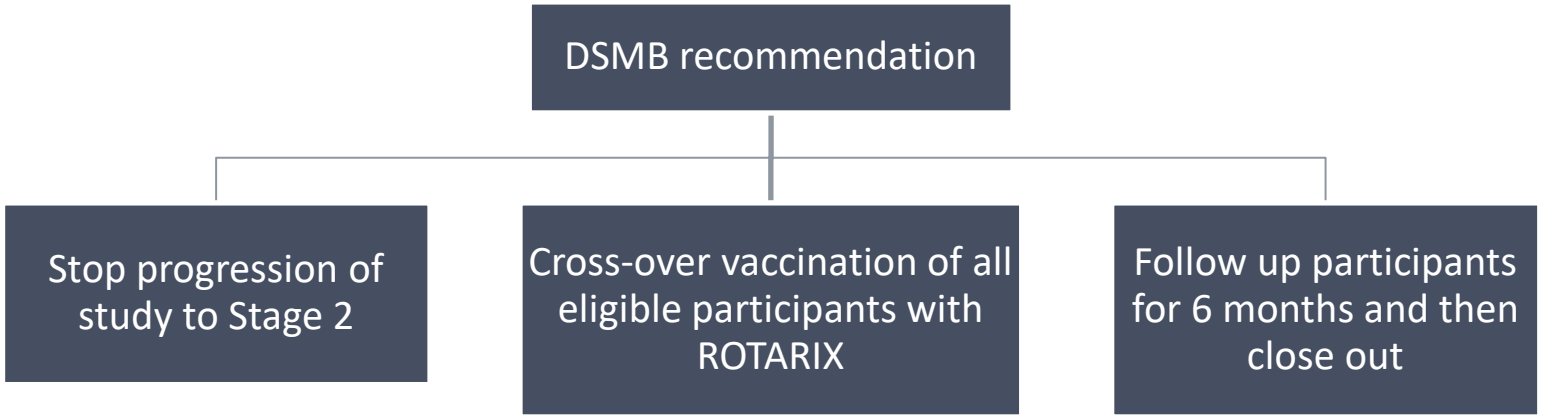
- Interim analysis occurred in August 2022 following the accrual of a predefined number of endpoints.
- No safety signals identified.

Table 1: Blinded overview of reactogenicity during the 7 days after each dose – Reactogenicity population

Solicited AEs, Reporting Period: Within 7 Days				
	Statistic: n (%), E			
Solicited AE Details	**Dose 1 (N=869)**	**Dose 2 (N=805)**	**Dose 3 (N=795)**	**Any Dose (N=869)**
At least one Solicited AE	416 (49.0), 693	315 (39.1), 548	331 (41.6), 489	609 (71.7), 1730
At least one Local Solicited AE	80 (9.4), 119	71 (8.8), 99	70 (8.8), 93	139 (16.4), 311
At least one Systemic Solicited AE	398 (46.9), 574	293 (36.4), 449	302 (38.0), 396	590 (69.5), 1419
At least one Local Solicited AE	80 (9.4), 119	71 (8.8), 99	70 (8.8), 93	139 (16.4), 311
Injection site pain or tenderness	58 (6.8), 58	51 (6.3), 51	39 (4.9), 39	106 (12.5), 148
Injection site erythema/redness	38 (4.5), 38	35 (4.3), 35	39 (4.9), 39	77 (9.1), 112
Injection site induration/swelling	14 (1.6), 14	4 (0.5), 4	5 (0.6), 5	19 (2.2), 23
Injection site pruritis	9 (1.1), 9	9 (1.1), 9	10 (1.3), 10	21 (2.5), 28
At least one Systemic Solicited AE	398 (46.9), 574	293 (36.4), 449	302 (38.0), 396	590 (69.5), 1419
Diarrhea	11 (1.3), 11	5 (0.6), 5	4 (0.5), 4	20 (2.4), 20
Fever	324 (38.2), 324	209 (26.0), 209	246 (30.9), 246	507 (59.7), 779
Vomiting	38 (4.5), 38	22 (2.7), 22	10 (1.3), 10	59 (6.9), 70
Irritability	97 (11.4), 97	110 (13.7), 110	71 (8.9), 71	186 (21.9), 278
Decreased activity	61 (7.2), 61	69 (8.6), 69	45 (5.7), 45	120 (14.1), 175
Decreased appetite	43 (5.1), 43	34 (4.2), 34	20 (2.5), 20	69 (8.1), 97

Interim Analysis Outcome and Current Status

Interim analysis: The DSMB reviewed the unblinded data and determined that the study should not continue as planned as there was insufficient evidence that the vaccine candidate would be superior to ROTARIX at primary analysis.



Current status:

- All eligible participants have received ROTARIX.
- Participants have started exiting the study.
- Study team remains blinded.
- Final analysis will be performed in Q3 2023, with results expected in mid-2024.

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Thank you!

Study Investigators

George Armah[a], Nigel Cunliffe[b], Roma Chilengi[c], Desiree Witte[b,d], Caroline.C.Chisenga[c], Vida Kukula[e], Khuzwayo Jere[b,d], Michelo Simuyandi[c], Susan Damanka[a], Edson Mwinjiwa[d], Katayi Kazimbaya[c], Frank Atuguba[e], John Williams[e], Joanne Csedrik[f], Chris Gast[f], Tushar Tewari[g] & Stan Cryz[f]

Affiliations

[a]Noguchi Memorial Institute for Medical Research, Ghana;
[b] University of Liverpool, United Kingdom;
[c] Centre for Infectious Disease Research in Zambia, Zambia;
[D] Malawi-Liverpool-Wellcome (MLW) Clinical Research Programme, Malawi;
[e] Dodowa Health Research Centre, Ghana;
[f] PATH, USA;
[g] PATH, India.

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