

Safety and tolerability of a novel typhoid conjugate vaccine in African infants and children

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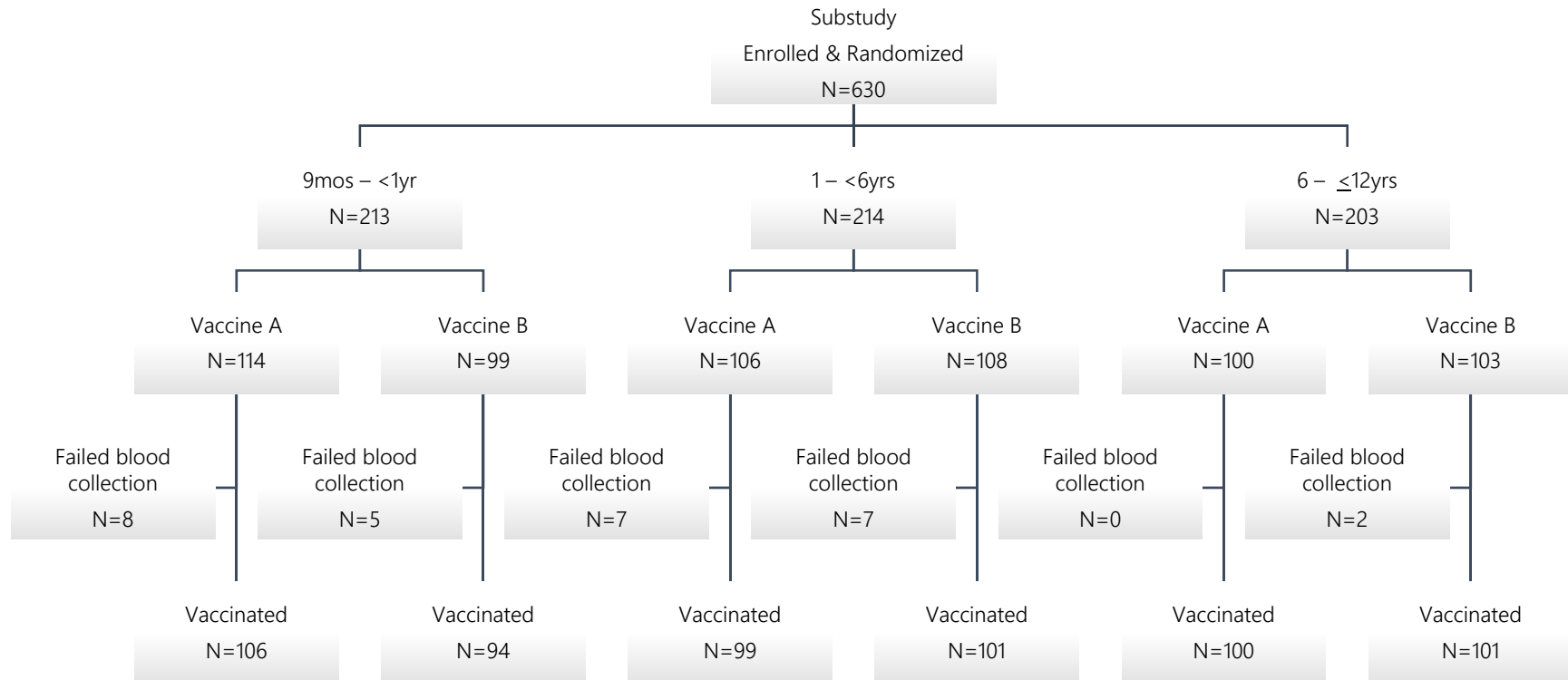


TyVAC Malawi

- **Design**
 - Individually randomized (1:1 ratio), controlled efficacy trial with two vaccine groups: typhoid conjugate vaccine (TCV) and meningococcal group A vaccine (MCV-A); N= 28,142
 - Immunogenicity and reactogenicity substudy; n= 601
- **Safety Objectives**
 - To determine the safety profile of vaccination with TCV or MCV-A
 - **ALL PARTICIPANTS:**
 - Reactions within 30 minutes of vaccination
 - Serious adverse events within 6 months of vaccination
 - **SUBSTUDY PARTICIPANTS:**
 - Local and systemic solicited and unsolicited events within 7 days of vaccination



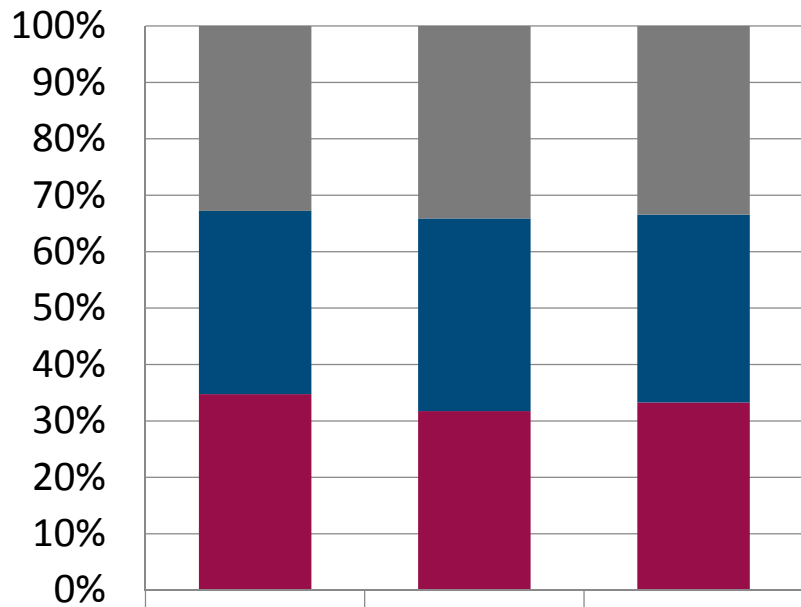
Immunogenicity & Reactogenicity Substudy recruitment



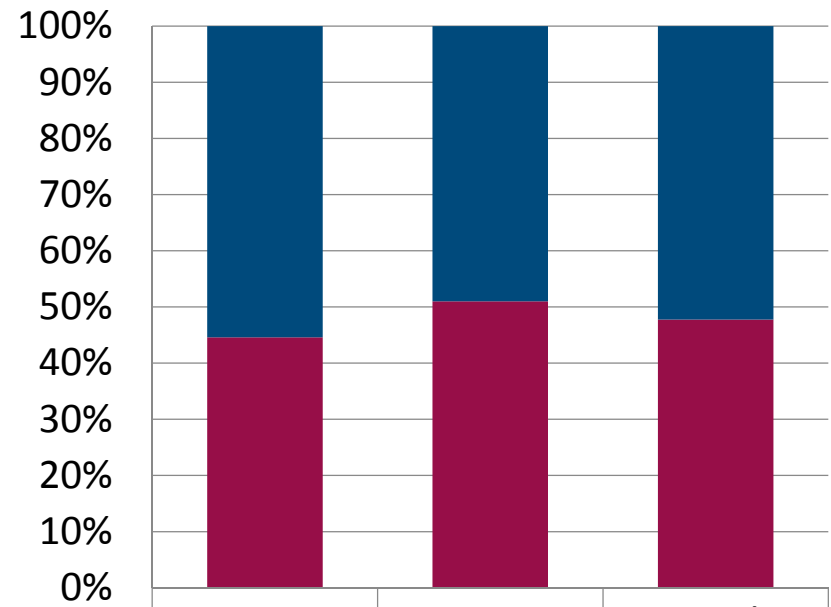
Screening period: 22 Feb 2018 to 06 Sep 2018
Total subjects enrolled: 630
Total subjects vaccinated: 601
Total vaccinated with vaccine A: 305
Total vaccinated with vaccine B: 296

Baseline Characteristics – Immunogenicity and Reactogenicity Substudy

Age at enrollment



Gender



	Vaccine A	Vaccine B	Total
6 - ≤12yrs	100	101	201
1 - <6yrs	99	101	200
9mos - <1yr	106	94	200

	Vaccine A	Vaccine B	Total
Male	169	145	314
Female	136	151	287

² Chi-squared test.

Safety and Reactogenicity Data



Summary of Adverse Events Following Immunization

Adverse Effects	Age 9mos – <1yr	Age 1—<6yrs	Age 6— ≤12yrs	Total
Systemic				
Mild	25	7	7	39
Moderate	4	2	2	8
Severe	1	0	0	1
Local				
Mild	5	1	6	12
Moderate	1	0	0	1
Severe	0	0	0	0

Adverse Events Following Immunization Day 0 (asked during day 3 visit)

Variable	Age 9mos – <1yr (N = 198)	Age 1—<6yrs (N = 200)	Age 6— ≤12yrs (N = 201)	Total (N = 599)
Did the participant have a fever or symptoms of feverishness? N				
No	172	187	194	553
Yes	16	7	2	25
Missing	10	6	5	21
Did the participant have Irritability -Intensity N				
None	181	190	196	567
Mild	5	3	0	8
Moderate	1	1	1	3
Severe	1	0	0	1
Missing	10	6	4	20
Did the participant have Malaise -Intensity N				
None	182	192	196	570
Mild	5	1	0	6
Moderate	1	1	1	3
Missing	10	6	4	20

Adverse Events Following Immunization Day 0 cont.

Variable	Age 9mos – <1yr (N = 198)	Age 1—<6yrs (N = 200)	Age 6— ≤12yrs (N = 201)	Total (N = 599)
Did the participant have Pain – Intensity N				
None	183	195	193	571
Mild	4	0	4	8
Moderate	1	0	0	1
Missing	10	5	4	19
Did the participant have Swelling – Intensity N				
None	188	194	196	578
Mild	0	0	1	1
Missing	10	6	4	20
Did the participant have Erythema – Intensity N				
None	188	194	197	579
Missing	10	6	4	20
Did the participant have Myalgia – Intensity N				
None	187	193	195	575
Mild	1	1	2	4
Missing	10	6	4	20
Did the participant have Arthralgia – Intensity N				
None	185	192	195	572
Mild	1	0	1	2
Missing	12	8	5	25

Adverse Events Following Immunization Day 3

Variable	Age 9mos – <1yr (N = 197)	Age 1—<6yrs (N = 200)	Age 6— ≤12yrs (N = 201)	Total (N = 598)
Today, does participant have a fever or symptoms of feverishness? N				
No	178	191	195	564
Yes	9	2	1	12
Missing	10	7	5	22
Irritability – Intensity N				
None	186	195	198	579
Mild	4	2	1	7
Missing	7	3	2	12
Malaise – Intensity N				
None	188	196	198	582
Mild	2	0	1	3
Missing	7	4	2	13

Adverse Events Following Immunization Day 3 cont.

Variable	Age 9mos – <1yr (N = 197)	Age 1—<6yrs (N = 200)	Age 6— ≤12yrs (N = 201)	Total (N = 598)
Pain – Intensity N				
None	189	197	198	584
Mild	1	0	1	2
Missing	7	3	2	12
Swelling – Intensity N				
None	190	196	199	585
Missing	7	4	2	13
Erythema – Intensity N				
None	190	196	199	585
Missing	7	4	2	13
Myalgia – Intensity N				
None	189	196	198	583
Mild	0	0	1	1
Missing	8	4	2	14
Arthralgia – Intensity N				
None	189	196	195	580
Mild	0	0	1	1
Missing	8	4	5	17

Adverse Events Following Immunization Day 7

Variable	Age 9mos – <1yr (N = 196)	Age 1—<6yrs (N = 198)	Age 6— ≤12yrs (N = 201)	Total (N = 595)
Today, does participant have a fever or symptoms of feverishness? N				
None	186	195	199	580
No	177	190	197	564
Yes	14	5	1	20
Missing	5	3	3	11
Irritability – Intensity N				
None	186	195	199	580
Mild	4	0	0	4
Moderate	1	0	0	1
Missing	5	3	2	10
Malaise – Intensity N				
None	189	195	199	583
Mild	1	0	0	1
Moderate	1	0	0	1
Missing	5	3	2	10

Adverse Events Following Immunization Day 7 cont.

Variable	Age 9mos – <1yr (N = 196)	Age 1—<6yrs (N = 198)	Age 6— ≤12yrs (N = 201)	Total (N = 595)
Pain – Intensity N				
None	191	195	199	585
Missing	5	3	2	10
Swelling – Intensity N				
None	190	194	199	583
Mild	0	1	0	1
Missing	6	3	2	11
Erythema – Intensity N				
None	191	195	199	585
Missing	5	3	2	10
Myalgia – Intensity N				
None	189	195	199	583
Mild	1	0	0	1
Missing	6	3	2	11
Arthralgia – Intensity N				
None	188	193	199	580
Mild	1	0	0	1
Missing	7	5	2	14

Adverse Events within 30 minutes of vaccination among 28,142 participants

Adverse event	N	Relatedness to vaccination
Number of AEs within 30mins of vaccination	3	
Rash	1	Yes
Diarrhea	1	No
Vasovagal Syncope	1	Yes

Serious Adverse Effects and Deaths Among 28,142 participants

- 141 SAEs were observed in 127 participants
 - No SAE was determined related to the study product
- 5 deaths were observed
 - No death was determined related to the study product



Conclusions

- The typhoid conjugate vaccine and meningococcal serogroup A conjugate vaccine were associated with few solicited reactogenicity events after vaccination
- No serious adverse event was considered related to vaccination
- The vaccinations were well-tolerated and no safety signal was detected



The Typhoid Vaccine Acceleration Consortium (TyVAC)

Reduce the global burden of typhoid fever by accelerating the introduction of typhoid conjugate vaccines (TCVs) in countries eligible for support from Gavi, the Vaccine Alliance



COLLABORATING ORGANIZATIONS



Learn more at: <http://takeontyphoid.org>

Thank you

