PREVAC RCT: Effects of 3 Ebola vaccine strategies in West African adults and children

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BACKGROUND & OBJECTIVES

- The present study augments our understanding of the safety and rapidity and durability of antibody response of vaccines that have been used to prevent Ebola virus disease (EVD).
- To obtain additional information on the safety and immunogenicity of rVSVΔG-ZEBOV-GP and Ad26.ZEBOV/MVA-BN-Filo vaccine strategies in adults and children we conducted a randomized, placebo-controlled trial through the Partnership for Research on Ebola Vaccinations (PREVAC) consortium in Western Africa (NCT 02876328).

METHODS

- Eligible for enrolment: Adults (>18+years) and children (>1 year)
- Enrolment was staggered by age group: adults and children aged 12-17 -> children aged 5-11 years -> children aged 1-4 years.
- Randomization assignment to one of the five arms in a 2:1:2:1:1 allocation (Figure 1 and 2).
- Follow-up visits: at days 7, 14, 28, 56, 63, then months 3, 6, and 12 after the first dose of vaccine or placebo. Second or booster dose at D56.
- Anti-EBOV GP IgG antibody concentrations were measured at baseline, days 7, 14, 28, 56, and 63, and at months 3, 6, and 12.
- Primary immunogenicity endpoint: percent of responders at month 12 (participants with both ≥ 4-fold increase from baseline and an EBOV GP antibody concentration ≥ 200 EU/mL).

RESULTS

- The median (25th, 75th percentiles) age of adult participants was 27 (20, 38) years; 45% were female. One-third of children were enrolled in each of the age groups 1-4, 5-11, and 12-17 years, and 46% were female.
- The primary endpoint was assessed in more than 90% of adults and children in active vaccine or pooled placebo groups.
- The great majority of AEs occurred in the week following vaccination and were more frequent in vaccine arms than in the placebo arm (Table 1 and 2).

Figure 1: CONSORT Diagram: Adults

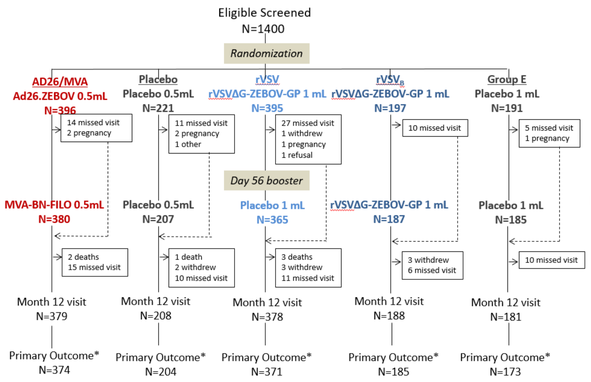
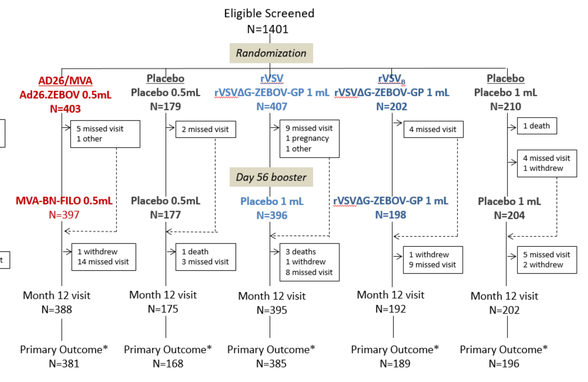


Figure 2: CONSORT Diagram: Children



Endpoint	AD26 & MVA Adults	AD26 & MVA Children	rVSV & placebo Adults	rVSV & placebo Children	rVSV & rVSV Adults	rVSV & rVSV Children	Placebo Adults	Placebo Children
% Responders at month 12 = primary endpoint	41%	78%	76%	87%	81%	93%	2.7%	3.6%
% Responders at month 3	94%	98%	81%	90%	96%	99%	1.9%	1.4%
% Responders at day 28	36%	66%	80%	90%	80%	90%	1.0%	1.1%

Figure 3. Geometric Mean Concentrations by Visit: Adults

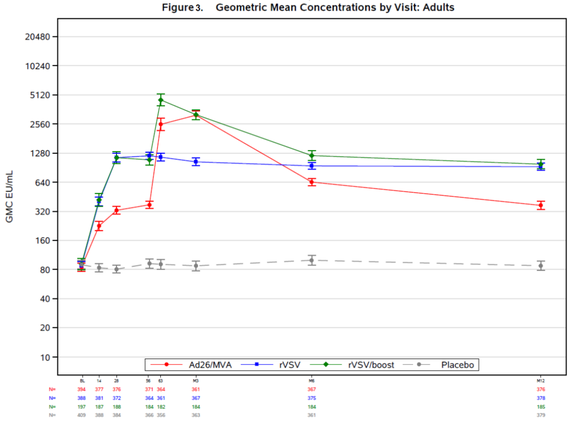
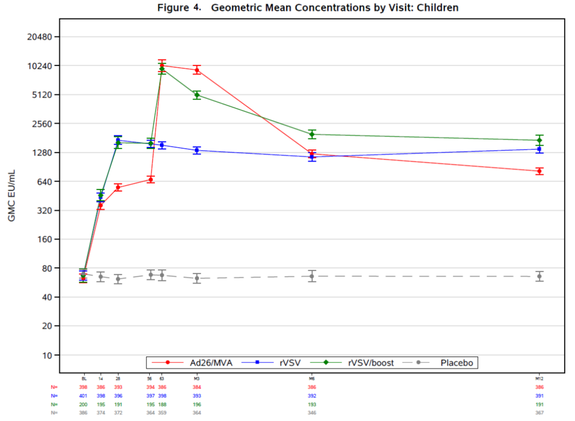


Figure 4. Geometric Mean Concentrations by Visit: Children



CONCLUSIONS

Data from this randomized, double-blind, placebo-controlled trial of Ad26.ZEBOV/MVA-BN-Filo and rVSVΔG-ZEBOV-GP Ebola vaccines add to evidence on immunogenicity and safety of these vaccines in adults and children. Immune responses were elicited by 14 days after injection for both vaccines and maintained for 12 months. The vaccines were found to be safe in children down to 1 year of age, with children exhibiting higher immune responses than adults. These data support and should facilitate wider use of these vaccines when indicated.

- By day 14, the percentages of AEs were similar for the Ad26/MVA, pooled rVSV, and placebo groups. Similar trends were observed following the second or booster vaccinations.
- Serious AEs were uncommon and did not differ significantly between the vaccine groups and the placebo group.

Table 1. Injection Site Reactions, Targeted Symptoms, and Serious Adverse Event (SAE): Adults

	Ad26/MVA		rVSV		rVSVB		Placebo	
Injection Site Reactions (post-prime)								
Day 0-7	9%*	(36/396)	22%**	(133/592)	5%	(21/412)		
Day 14	1%	(2/387)	0%	(1/579)	0%	(0/404)		
Symptoms (post-prime)								
Day 0-7	50%	(198/396)	66%**	(390/592)	44%	(182/412)		
Day 14	24%	(92/387)	23%	(133/579)	25%	(100/404)		
Injection Site Reactions (post-boost)								
Day 56-63	13%**	(49/380)	3%	(12/365)	11%*	(20/187)	5%	(20/392)
Month 3	0%	(0/369)	0%	(1/356)	1%	(1/187)	0%	(0/385)
Symptoms (post-boost)								
Day 56-63	32%	(124/382)	34%	(127/373)	40%	(76/188)	32%	(127/398)
Month 3	33%	(122/373)	26%	(95/371)	28%	(53/188)	26%	(102/393)
SAE/death	4%	(14/396)	2%	(6/395)	1%	(1/197)	1%	(5/412)
Death	1%	(2/396)	1%	(3/395)	0%	(0/197)	0%	(1/412)

Note - SAEs and deaths are measured through Month 12
Of the 26 adults with an SAE, 12 were attributed to appendicitis, all among women. There was no evidence for a difference in appendicitis among the active vaccine and placebo groups.

P-values for comparison of vaccine with placebo:
* p < .0167
** p < .001

Table 2. Injection Site Reactions, Targeted Symptoms, and Serious Adverse Events (SAE): Children

	Ad26/MVA		rVSV		rVSVB		Placebo	
Injection Site Reactions (post-prime)								
Day 0-7	15%*	(59/403)	21%*	(126/609)	5%	(19/389)		
Day 14	0%	(1/397)	0%	(1/603)	0%	(0/380)		
Symptoms (post-prime)								
Day 0-7	48%	(195/403)	60%*	(363/609)	43%	(166/389)		
Day 14	16%	(64/397)	15%	(93/603)	18%	(70/380)		
Injection Site Reactions (post-boost)								
Day 56-63	14%*	(55/398)	7%	(26/396)	12%*	(23/198)	4%	(16/381)
Month 3	0%	(0/392)	0%	(0/392)	0%	(0/197)	0%	(0/378)
Symptoms (post-boost)								
Day 56-63	32%	(127/399)	28%	(112/400)	32%	(64/198)	28%	(106/383)
Month 3	22%	(85/393)	23%	(93/396)	21%	(41/198)	24%	(90/380)
SAE/death	1%	(5/403)	2%	(9/407)	1%	(3/202)	2%	(8/389)
Death	0%	(0/403)	1%	(3/407)	0%	(0/202)	1%	(2/389)

Note - SAEs and deaths are measured through Month 12
Four of the SAEs were attributed to appendicitis.

P-values for comparison of vaccine with placebo:
* p < .001

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