Vaxchora in Children and Adolescents

James McCarty, MD
Clinical Professor of Pediatrics, Stanford University
Consultant, Emergent BioSolutions

25 February 2021

Agenda

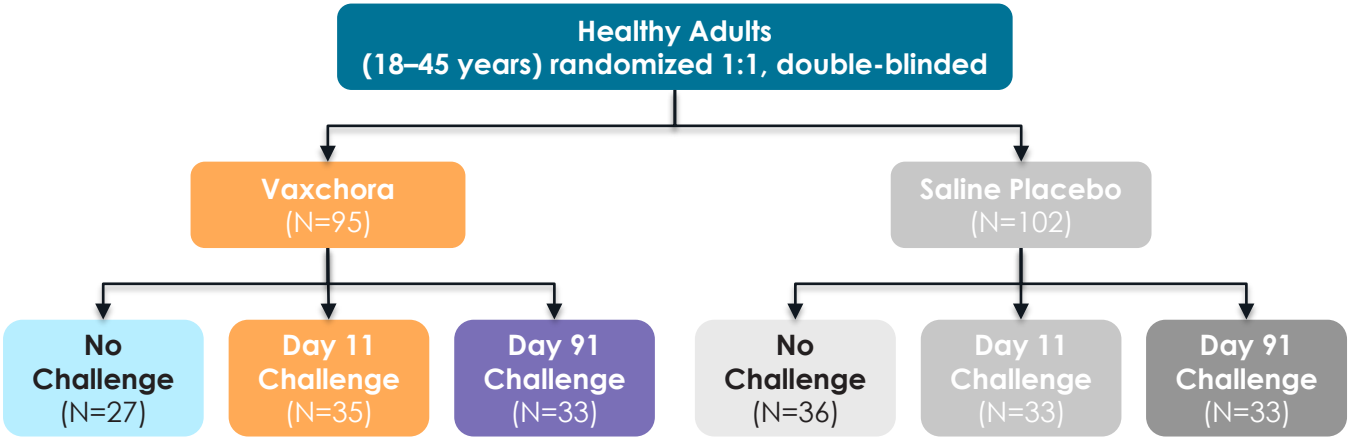
- Overview of Vaxchora clinical program
- PXVX-VC-200-006 study
  - Acceptability / Palatability
  - Safety
  - Immunogenicity
- Summary

Vaxchora Clinical Development Program

Study	Age Range	Dose	# Subjects† (Active)	Objectives	Results
Phase 1 002[1]	18 to 50	4.34 x 10^8 CFU	66 (55)	Safety Immunogenicity Kinetics (shedding)	Well-tolerated SVA 88.9% (D14) Stool+ 11% (through D7)
Challenge Phase 3 003[2]	18 to 45	5 x 10^8 CFU	197 (95)	Efficacy (challenge) Immunogenicity	SVA 79.8% (D8) SVA 89.4% (D11) Efficacy 90.3% (D11) Efficacy 79.5% (D91)
Lot Consistency Phase 3 004[3]	18 to 45	1 x 10^9 CFU	3146 (2795)	Lot consistency Safety Immunogenicity	Met consistency criteria Well-tolerated SVA: 93.5% (D11)
Older Adult Phase 3 005[4]	46 to 64	1 x 10^9 CFU	398 (299)	Safety Immunogenicity Bridging	Well-tolerated SVA 90.4% (D11) Non-inferior to 004
Pediatric Phase 4 006[5,6]	2 to 17	1 x 10^9 CFU	550 (468)	Safety Immunogenicity Bridging	Well-tolerated SVA 98.5% (D11) Non-inferior to 004

†Placebo in the phase 1 trial was lactose powder in water. Placebo was physiological saline in all other trials.
CFU=colony-forming unit; SVA=serum vibriocidal antibody.
1. Chen WH, et al. Clin Vaccine Immunol. 2014;21(1):66-73. 2. Chen WH, et al. Clin Infect Dis. 2016;62(11):1329-1335. 3. McCarty JM, et al. Vaccine. 2018;36:833-840. 4. McCarty JM, et al. Vaccine. 2019;37:1389-1397. 5. McCarty JM, et al. Am J Trop Med Hyg. 2020;102(1):48-57. 6. McCarty JM, et al. Am J Trop Med Hyg. 2020, online ahead of print.

The Efficacy of Vaxchora Was Assessed in a Placebo-Controlled Challenge Study (003)[1]



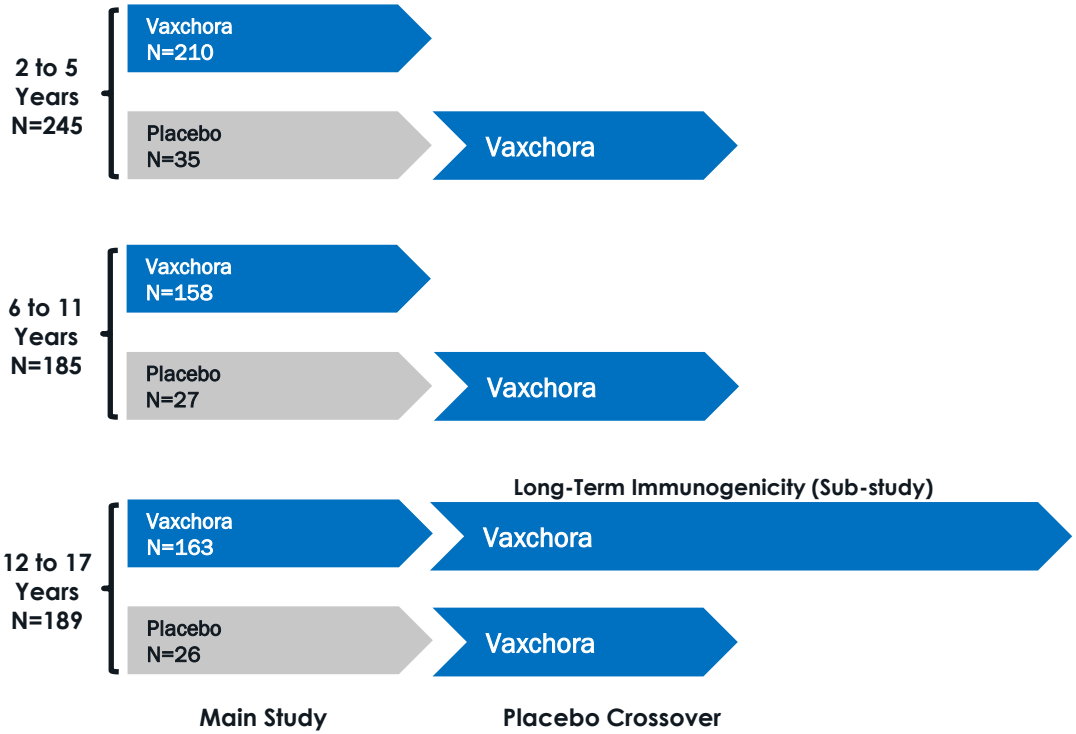
- **Protective efficacy against moderate (≥3.0 - 5 L) to severe (≥5.0 L) cholera diarrhea was 90.3% at Day 11 and 79.5% at Day 91[1]**
- **Vibriocidal antibody seroconversion was determined to be an immune correlate of protection[2]**

1. Chen WH, et al. Clin Infect Dis. 2016;62(11):1329-1335. 2. Haney DJ, et al. Clin Vaccine Immunol. 2017;24:e00098-e117.

Vaxchora 006 Pediatric Study Design[1,2]

Analysis Endpoints:

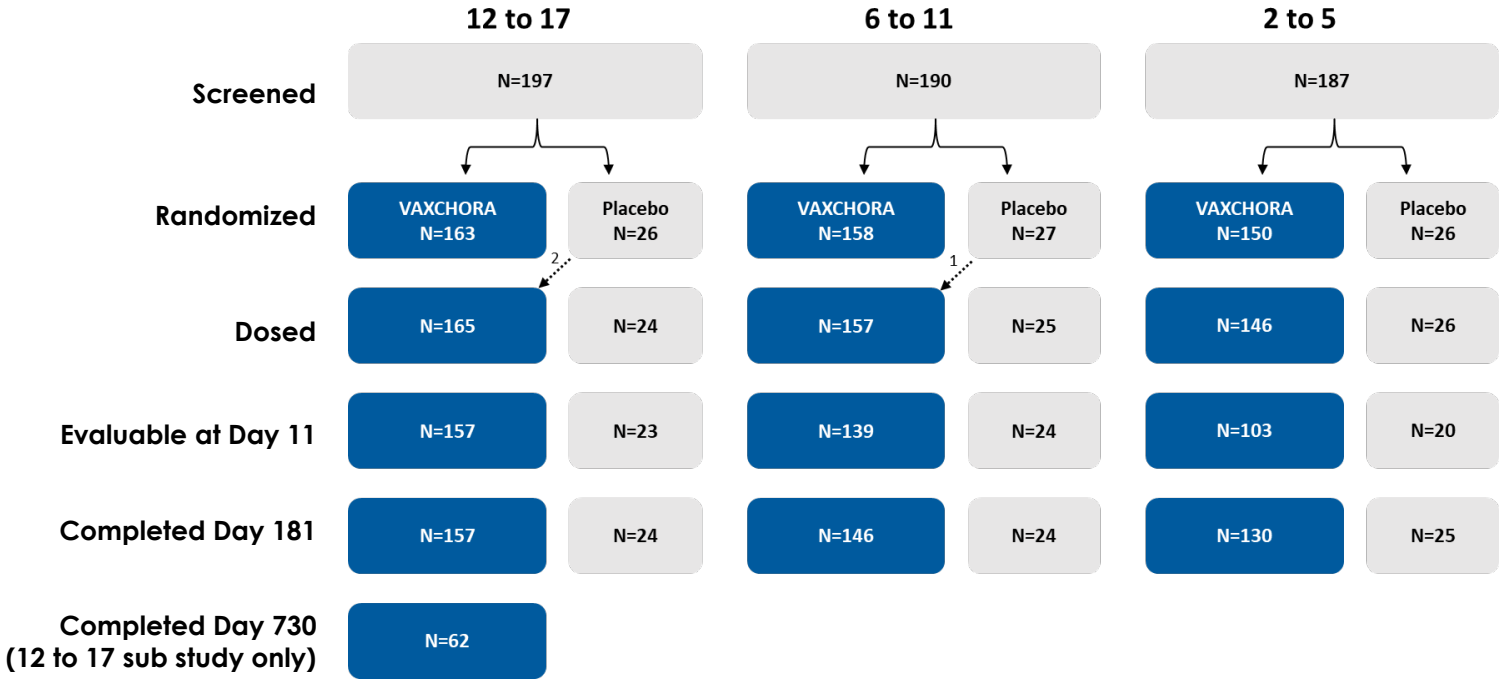
- Immunogenicity (SVA)
  - Seroconversion rate at Day 11
  - Cumulative seroconversion at Day 29
  - Geometric mean titer (GMT)
    - 12 to 17 years: through Day 730
    - 2 to 11 years: through Day 29
- Safety
  - Solicited adverse events through Day 8
  - Unsolicited adverse events (including serious adverse events)
- Dosing and Palatability
  - Percent of dose consumed
  - Reported palatability (subjective)



SVA=serum vibriocidal antibody

1. McCarty JM, et al. *Am J Trop Med Hyg.* 2020;102(1):48-57. **2.** McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

Vaxchora 006 Pediatric Study
Enrollment and Disposition[1,2]



1. McCarty JM, et al. *Am J Trop Med Hyg.* 2020;102(1):48-57. **2.** McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

Vaxchora 006 Pediatric Study
Demographics

- Mean age: 9.0 years
- 51.6% male
- Racial demographics
  - 59.5% - White
  - 31.3% - Black
  - 7.7% - Multiracial
  - 0.9% - Asian
  - 0.6% - American Indian / Alaskan Native
- Ethnic demographics
  - 8.7% Hispanic or Latinx

1. Data on file, Emergent BioSolutions Inc, Bedell L, 2020.

Vaxchora 006 Pediatric Study
Dosing and Palatability[1,2]

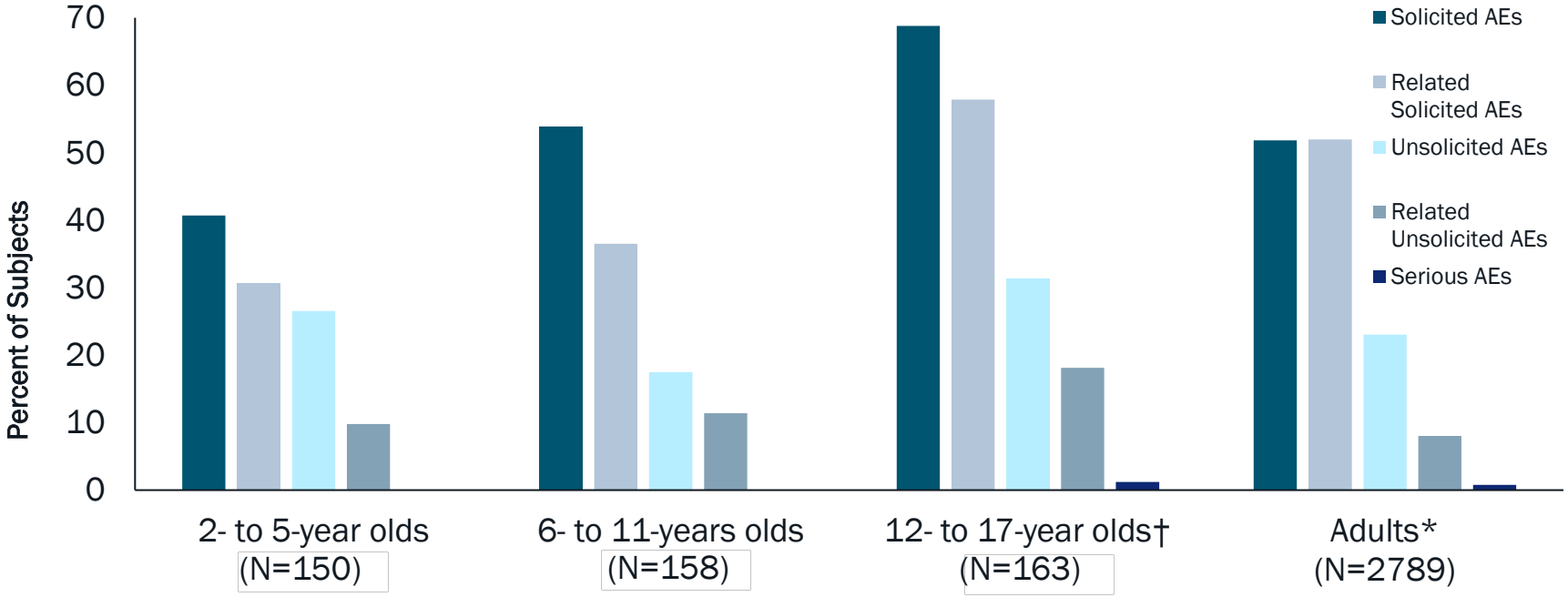
Age Group	2 to 5		6 to 11		12 to 17	
	Vaxchora N=150	Placebo N=26	Vaxchora N=158	Placebo N=27	Vaxchora N=163	Placebo N=26
Dose volume, mL	50	50	100	100	100	100
Dose given	146 (97.3%)	26 (100%)	156 (98.7%)	26 (96.3%)	163 (100%)	26 (100%)
Sweetener added*†	144 (98.6%)	26 (100%)	149 (95.5%)	25 (96.2%)	144 (88.3%)	22 (84.6%)
Complete dose consumed†	116 (79.5%)	19 (73.1%)	142 (91.0%)	25 (96.2%)	162 (99.4%)	26 (100%)
≥80% of dose consumed†	121 (82.9%)	22 (84.6%)	152 (97.4%)	25 (96.2%)	162 (99.4%)	26 (100%)
Palatability†:						
Very good	44 (30.1%)	6 (23%)	28 (17.9%)	3 (11.5%)	8 (4.9%)	2 (7.7%)
Good	28 (19.2%)	9 (35%)	27 (17.3%)	1 (3.8%)	29 (17.8%)	6 (23.1%)
Neutral	19 (13.0%)	3 (12%)	37 (23.7%)	10 (38.5%)	64 (39.3%)	10 (38.5%)
Bad	24 (16.4%)	4 (15%)	30 (19.2%)	6 (23.1%)	50 (30.7%)	7 (26.9%)
Very bad	31 (21.2%)	4 (15%)	34 (21.8%)	6 (23.1%)	12 (7.4%)	1 (3.8%)

*The unblinded dose administrator had the option to add PureVia Stevia sweetener to the oral solution at the request of the parent and/or participant.

†Percentage of subjects who received any amount of dose (Dose Given).

1. Bennett SR, CISTM, 2019. **2.** McCarty JM, et al. *Am J Trop Med Hyg.* 2020;102(1):48-57.

Safety Overview of Vaxchora (004 & 006)[1]



*In the adult population all solicited AEs were presumed to be related.

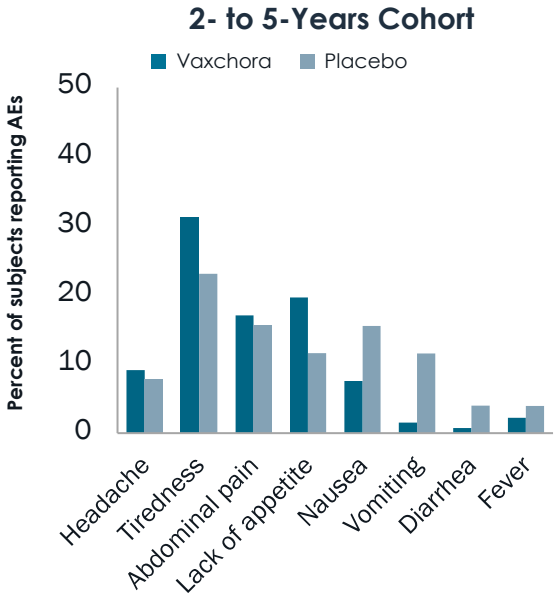
†There were no related serious AEs; 1 unrelated serious AEs of right leg fracture was noted.

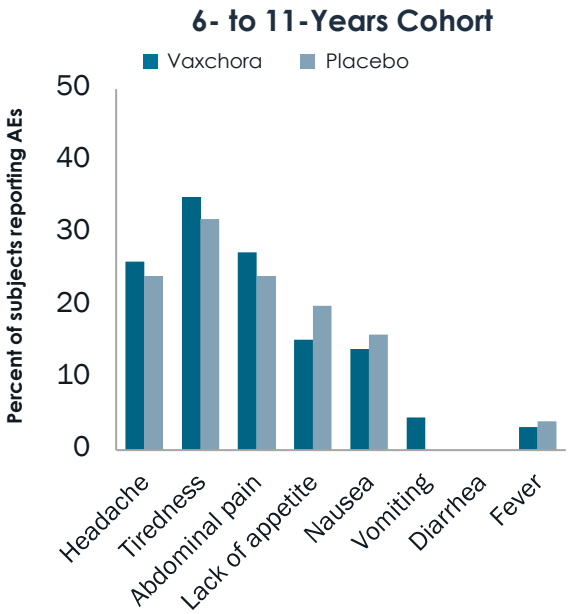
AE=adverse events.

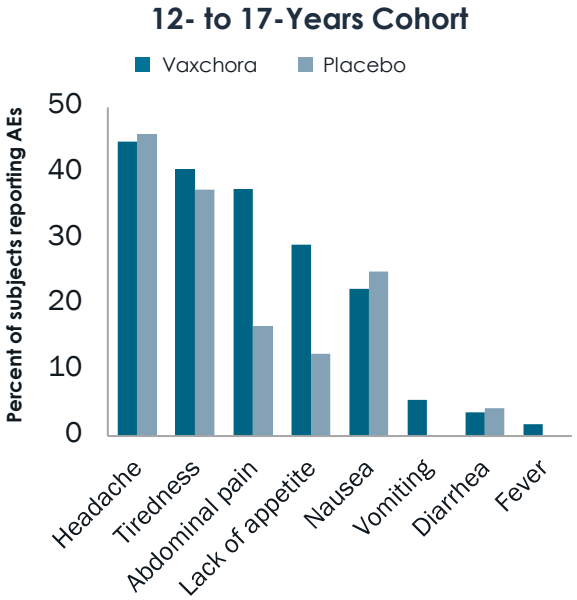
1. Bennett SR, CISTM, 2019.

Solicited AEs by Specific Event and Frequency (006)[1,2]

Abdominal pain and lack of appetite were frequent in the vaccine group in the 12- to 17-year cohort but were not significantly higher compared to placebo. Vomiting, diarrhea, and fever were relatively infrequent in all age groups.







*AE=adverse event.

1. McCarty JM, et al. *Am J Trop Med Hyg.* 2020;102(1):48-57. **2.** McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

Serious Adverse Events (SAEs) (006)[1,2]

- **SAEs were reported in 0.2% (1/468) of Vaxchora recipients and 1.3% (1/75) of placebo recipients within 6 months post-vaccination**

- **None of these events were considered related to vaccination**

1. McCarty JM, et al. *Am J Trop Med Hyg.* 2020;102(1):48-57. **2.** McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print

Primary Endpoint: SVA Seroconversion at Day 11 (006) (Adult vs Pediatric; Vaxchora Only)[1,2,3]

Age Group	2 to 5	6 to 11	12 to 17	Adults 18 to 45
N, evaluable	103	139	157	2687
N, seroconverted	101	136	156	2513
Percent seroconversion (98.3% CI)	98.1 (91.5–99.6)	97.8 (92.5–99.4)	99.4 (95.4–99.9)	93.5 (92.3–94.6)
Difference: (pediatrics minus adults) (96.7% CI)	**+4.6 (-1.0 to +6.4)**	**+4.3 (-0.3 to +6.2)**	**+5.8 (+2.4 to +7.1)**	**N/A**
P-value (Fisher's Exact test)	0.0628	0.0455	0.0009	N/A

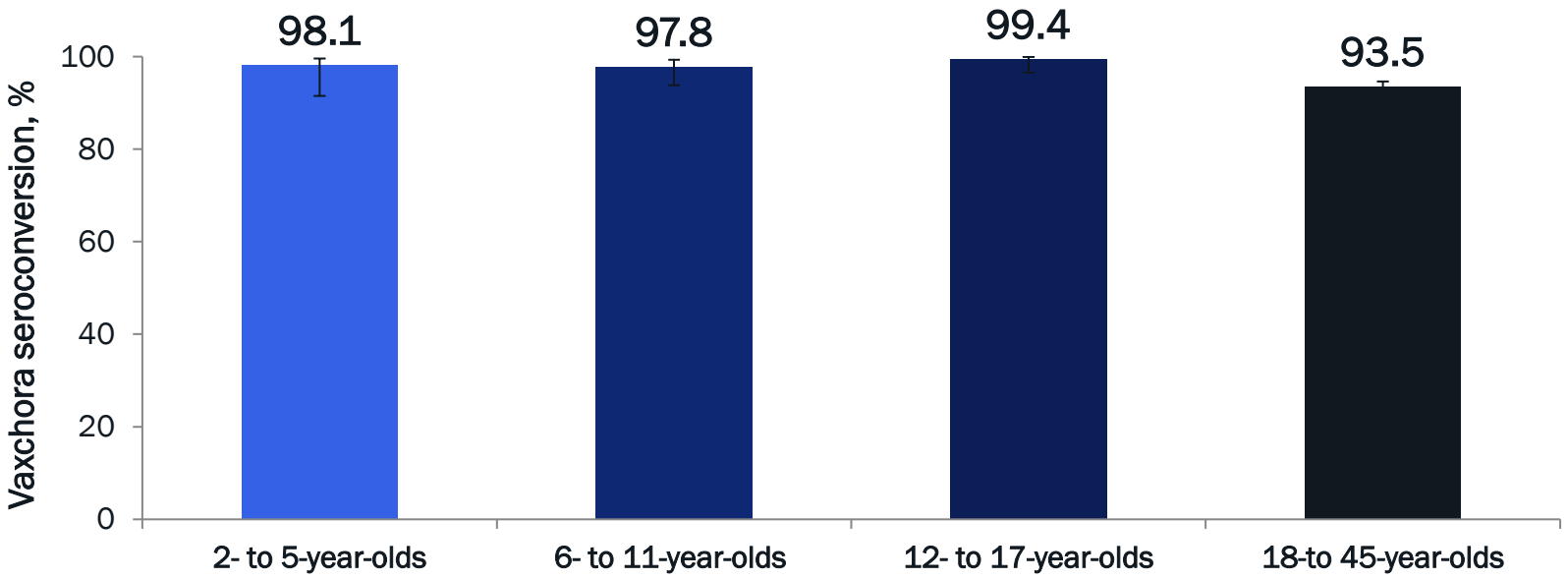
Primary objectives met for each age cohort.
Noninferiority with adults (lower bound of 96.7% CI for difference >-10%).
Minimum seroconversion (lower bound of 98.3% CI >70%).
Adult reference population from study 200-004[3]

SVA=serum vibriocidal antibody.

1. McCarty JM, et al. Am J Trop Med Hyg. 2020;102(1):48-57. 2. McCarty JM, et al. *Am J Trop Med Hyg*. 2020; online ahead of print. 3. McCarty JM, et al. Vaccine. 2018;36:833-840.

SVA Seroconversion at Day 11 (006)[1,2]

Noninferiority criteria for seroconversion were met for each age cohort and seroconversion rates were similar to adults*

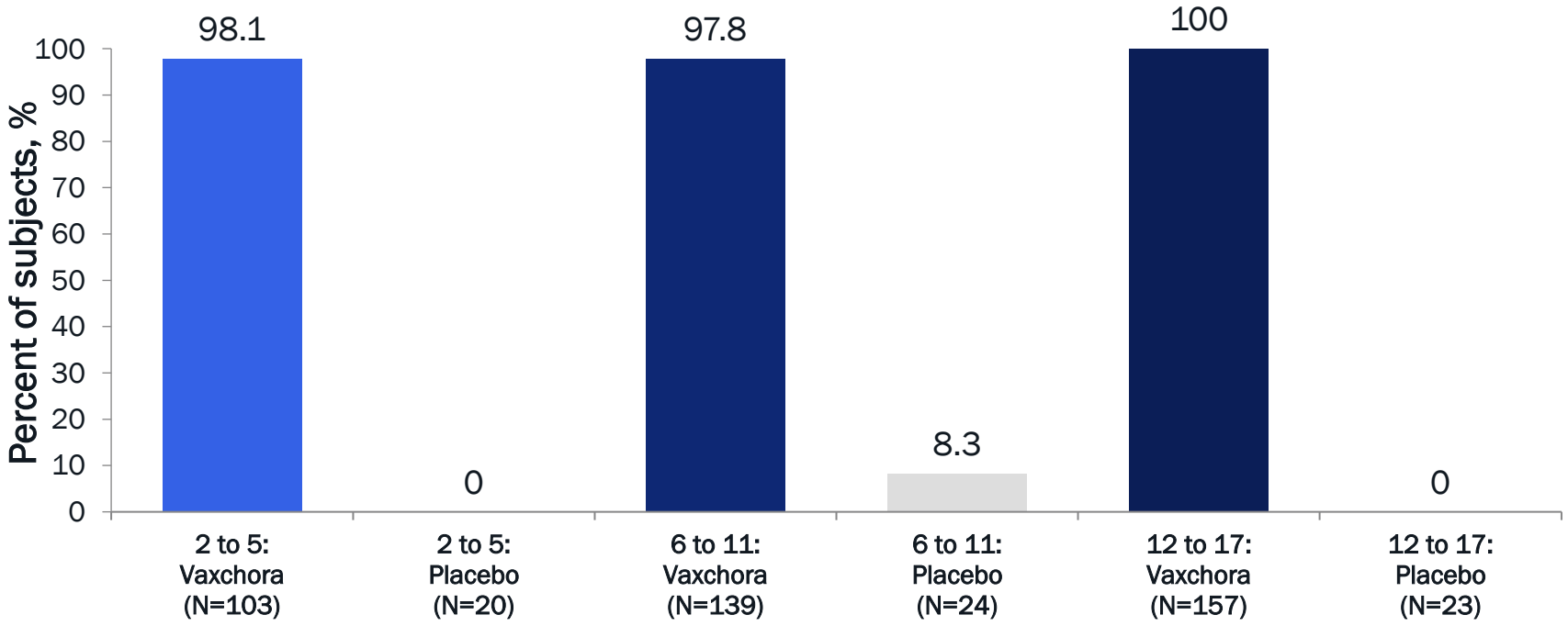


*95% CI for ages 2–5 years=91.5%–99.6%, 6–11 years=93.8%–99.3%, 12–17 years=96.5%–99.9%, 18–45 years=92.3%–94.6%.

SVA=serum vibriocidal antibody.

1. McCarty JM, et al. Am J Trop Med Hyg. 2020;102(1):48-57. 2. McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

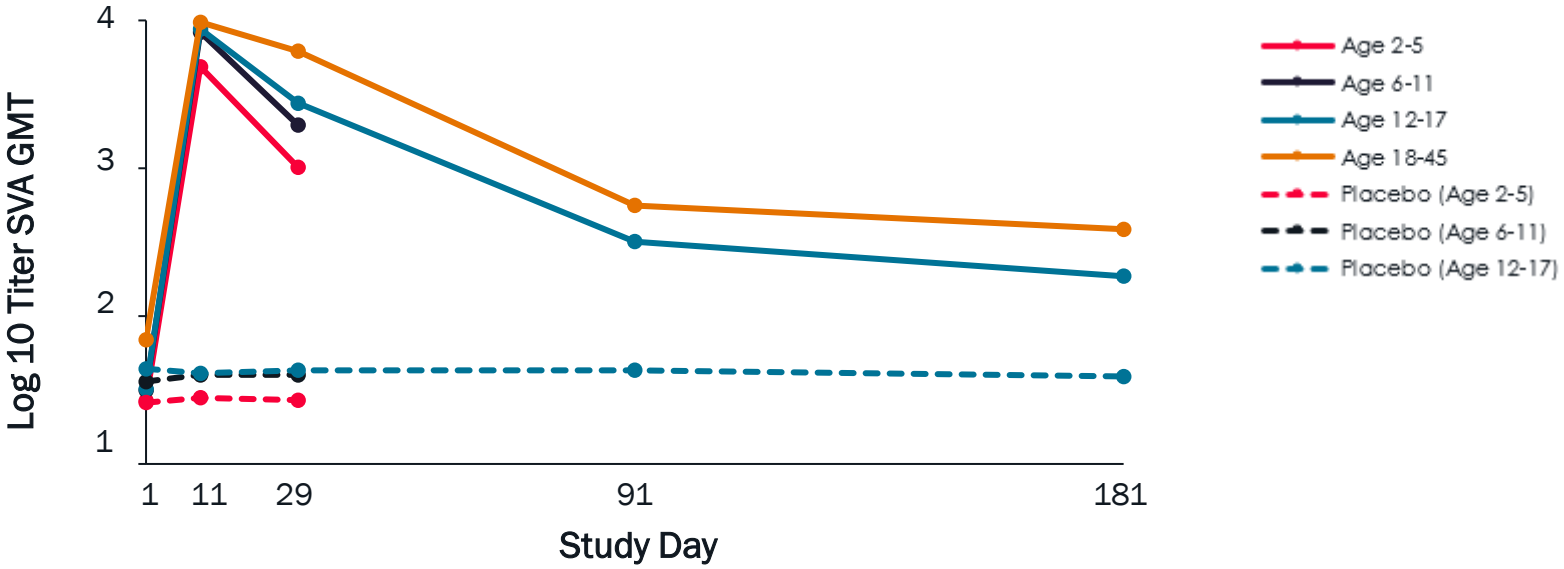
Cumulative SVA Seroconversion at Day 29 (006) (Pediatric Only; Vaxchora vs Placebo)[1,2]



*Vaxchora 95% CI for ages 2–5 years=91%–98.8%, 6–11 years=93.8%–99.3%, 12–17 years=97.6%–100%. Placebo 95% CI for ages 2–5 years=94.4%–99.7%1
SVA=serum vibriocidal antibody.

1. McCarty JM, et al. Am J Trop Med Hyg. 2020;102(1):48-57. 2. McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

GMTs of Serum Vibriocidal Antibody Through Day 181 (006)[1,2]
Children and Adults



In the 2-5 years and 6-11 years age groups, titers were followed to day 29 only.
In the 12- to 17-years age group, SVA GMTs in Vaxchora recipients remained significantly higher than placebo at day 181.

SVA=serum vibriocidal antibody; GMT=geometric mean titer.

1. McCarty JM, et al. Am J Trop Med Hyg. 2020;102(1):48-57. 2. McCarty JM, et al. *Am J Trop Med Hyg.* 2020; online ahead of print.

Vaxchora Long Term Immunogenicity Subset (006)[1]
Adolescents 12-17 years of age

Time Point	SVA Seroconversion Rate		GMT		GMFI	
	Vaxchora (n=72)	Placebo (n=23)	Vaxchora (n=72)	Placebo (n=23)	Vaxchora (n=72)	Placebo (n=23)
Day 11	100%	0	9035.4	41.2	279.2	0.9
Day 29	100%	0	2791.7	42.5	86.3	1.0
Day 91	88.9%	0	391.7	42.5	12.1	1.0
Day 181	83.1%	0	223.0	38.7	6.9	0.9
Day 365	68.6%	N/A	158.4	N/A	4.8	N/A
Day 547	73.1%	N/A	175.6	N/A	5.2	N/A
Day 730	64.5%	N/A	133.8	N/A	4.1	N/A

SVA=serum vibriocidal antibody; GMT=geometric mean titer; GMFI=geometric mean fold increase.
N/A: Seroconversion was measured in placebo subjects through Day 181.
1. McCarty JM, et al. ASTMH Annual Meeting, 2020.

Partial Dosing: SVA Seroconversion at Day 11 (006)
Stratified by Portion of Dose Consumed[1*]

Age Group	< 50% of Dose	50 to < 80% of Dose	Total (< 80% of Dose)
2 to 5 years	11/16 (68.8%)	6/6 (100%)	17/22 (77.3%)
6 to 11 years	6/9 (66.7%)	1/1 (100%)	7/10 (70.0%)
12 to 17 years	1/1 (100%)	0/0	1/1 (100%)
All age groups	18/26 (69.2%)	7/7 (100%)	25/33 (75.8%)

*Among Vaxchora subjects (modified intent-to-treat population) who consumed less than 80% of expected dose.
SVA=serum vibriocidal antibody.
1. Data on file, Emergent BioSolutions.

Summary

- Vibriocidal antibody seroconversion rates in children and adolescents 2 to 17 years of age immunized with Vaxchora were non-inferior to seroconversion rates in adults
- Vaxchora was well-tolerated in the pediatric population, with no vaccine-related serious adverse events
- In an immunogenicity subset of Vaxchora recipients 12-17 years of age, serum vibriocidal antibody GMTs remained elevated 2 years post-vaccination
- Vibriocidal antibody seroconversion occurred in most children who received only partial doses of the vaccine

Conclusion

- Vaxchora is a single-dose vaccine with demonstrated safety and efficacy
- Vaxchora may be used for the prevention of cholera in travelers 2-17 years of age visiting high risk areas

emergent biosolutions®

Discussion

emergent biosolutions®

Backup

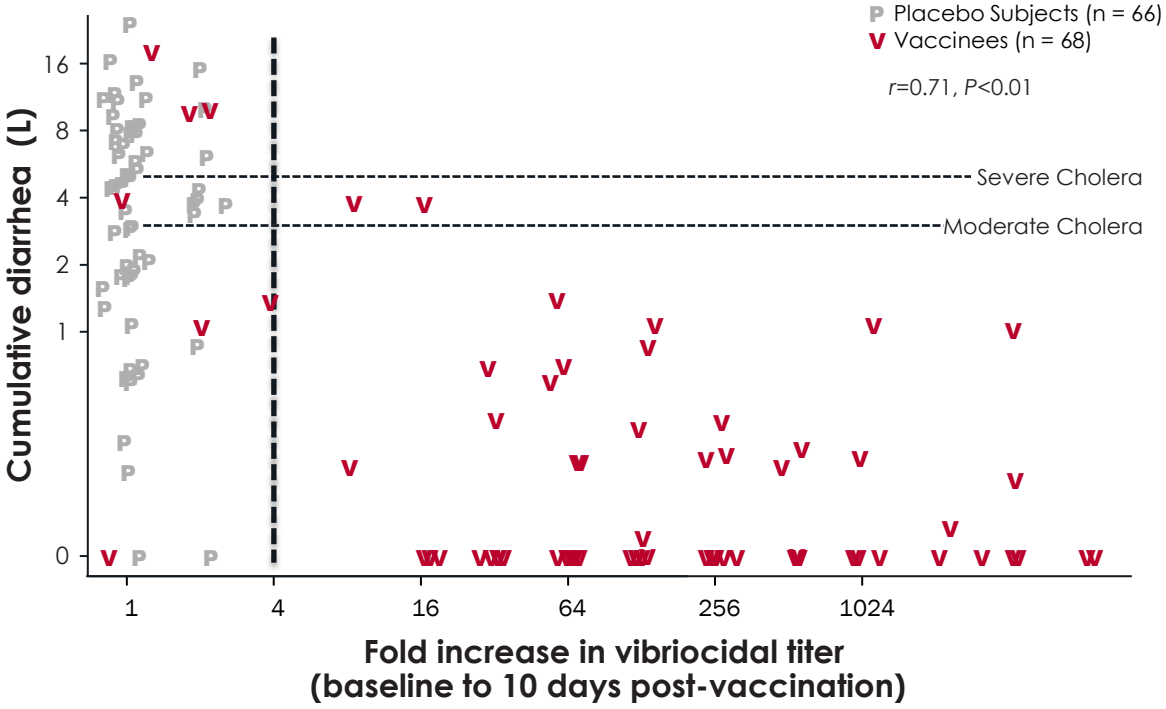
The Efficacy of Vaxchora Was Assessed in a Placebo-Controlled Challenge Study (003)[1]

Results

	Placebo All Challenge	Vaxchora D11 Challenge	Vaxchora D91 Challenge
N	66	35	33
Mild diarrhea (< 3L), n (%)	22 (33.3)	3 (8.6)	11 (33.3)
Moderate (3-5 L), n (%)	11 (16.7)	1 (2.9)	2 (6.1)
Severe (>5L), n (%)	28 (42.4)	1 (2.9)	2 (6.1)
Moderate or severe, n (%)	39 (59.1)	2 (5.7)	4 (12.1)
Protective efficacy (%)	n/a	90.3	79.5

1. Chen WH, et al. Clin Infect Dis. 2016;62(11):1329-1335.

In the Human Challenge Study (003), Vibriocidal Antibody Seroconversion Was Determined to Be an Immune Correlate of Protection[1,2]



1. Chen WH, et al. Clin Infect Dis. 2016;62(11):1329-1335. 2. PaxVax, Inc. Data on file.

Vaxchora with Sweetener or Flavoring Added: Potency Testing

- Internal testing evaluated the potency of Vaxchora over a 30-minute period after sweetener was stirred in to 50 mL reconstituted vaccine
  - The amount of CFU remained within the pre-specified range (4×10^8 to 2×10^9) of live attenuated *Vibrio cholerae* CVD 103-HgR with the addition of:
    - 1 gram of PureVia®, Truvia®, Splenda® Naturals, SweetLeaf®, or Sweet Additions® brand stevia

    OR

    - Up to 4 grams of sucrose (table sugar)
- FLAVORx® children's medicine flavoring was not compatible with the vaccine, likely because it contains propylene glycol, which is bactericidal to some organisms

CFU = colony forming units

1. Data on file, Emergent BioSolutions Inc, Duffin P, 2020.