Vaxchora in Children and Adolescents

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Agenda

• Overview of Vaxchora clinical program

• PXVX-VC-200-006 study
  • Acceptability / Palatability
  • Safety
  • Immunogenicity

• Summary
## Vaxchora Clinical Development Program

<table>
<thead>
<tr>
<th>Study</th>
<th>Age Range</th>
<th>Dose</th>
<th># Subjects† (Active)</th>
<th>Objectives</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 002¹</td>
<td>18 to 50</td>
<td>4.34 x 10⁸ CFU</td>
<td>66 (55)</td>
<td>Safety Immunogenicity</td>
<td>Well-tolerated SVA 88.9% (D14)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Kinetics (shedding)</td>
<td>Stool+ 11% (through D7)</td>
</tr>
<tr>
<td>Challenge Phase 3 003²</td>
<td>18 to 45</td>
<td>5 x 10⁸ CFU</td>
<td>197 (95)</td>
<td>Efficacy (challenge) Immunogenicity</td>
<td>SVA 79.8% (D8) SVA 89.4% (D11) Efficacy 90.3% (D11) Efficacy 79.5% (D91)</td>
</tr>
<tr>
<td>Lot Consistency</td>
<td>18 to 45</td>
<td>1 x 10⁹ CFU</td>
<td>3146 (2795)</td>
<td>Lot consistency</td>
<td>Met consistency criteria Well-tolerated SVA: 93.5% (D11)</td>
</tr>
<tr>
<td>Phase 3 004³</td>
<td>46 to 64</td>
<td>1 x 10⁹ CFU</td>
<td>398 (299)</td>
<td>Safety Immunogenicity</td>
<td>Well-tolerated SVA 90.4% (D11) Non-inferior to 004</td>
</tr>
<tr>
<td>Pediatric Phase 4 006⁵ ⁶</td>
<td>2 to 17</td>
<td>1 x 10⁹ CFU</td>
<td>550 (468)</td>
<td>Safety Immunogenicity Bridging</td>
<td>Well-tolerated SVA 98.5% (D11) Non-inferior to 004</td>
</tr>
</tbody>
</table>

†Placebo in the phase 1 trial was lactose powder in water. Placebo was physiological saline in all other trials.

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

Healthy Adults (18–45 years) randomized 1:1, double-blinded

Vaxchora (N=95)

- No Challenge (N=27)
- Day 11 Challenge (N=35)
- Day 91 Challenge (N=33)

Saline Placebo (N=102)

- No Challenge (N=36)
- Day 11 Challenge (N=33)
- Day 91 Challenge (N=33)

• 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 91¹

• Vibriocidal antibody seroconversion was determined to be an immune correlate of protection²

Vaxchora 006 Pediatric Study Design

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)

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SVA=serum vibriocidal antibody
### Vaxchora 006 Pediatric Study
#### Enrollment and Disposition

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Screened</th>
<th>Randomized</th>
<th>Dosed</th>
<th>Evaluable at Day 11</th>
<th>Completed Day 181</th>
<th>Completed Day 730 (12 to 17 sub study only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 to 17</td>
<td>N=197</td>
<td>VAXCHORA N=163</td>
<td>N=165</td>
<td>N=157</td>
<td>N=157</td>
<td>N=62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo N=26</td>
<td>N=24</td>
<td>N=23</td>
<td>N=24</td>
<td></td>
</tr>
<tr>
<td>6 to 11</td>
<td>N=190</td>
<td>VAXCHORA N=158</td>
<td>N=157</td>
<td>N=139</td>
<td>N=146</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo N=27</td>
<td>N=25</td>
<td>N=24</td>
<td>N=24</td>
<td></td>
</tr>
<tr>
<td>2 to 5</td>
<td>N=187</td>
<td>VAXCHORA N=150</td>
<td>N=146</td>
<td>N=103</td>
<td>N=130</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo N=26</td>
<td>N=26</td>
<td>N=20</td>
<td>N=25</td>
<td></td>
</tr>
</tbody>
</table>

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

# Vaxchora 006 Pediatric Study
## Dosing and Palatability

**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).

### Table: Dosing and Palatability

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2 to 5</th>
<th></th>
<th></th>
<th>6 to 11</th>
<th></th>
<th></th>
<th>12 to 17</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaxchora</td>
<td>Placebo</td>
<td>Vaxchora</td>
<td>Placebo</td>
<td>Vaxchora</td>
<td>Placebo</td>
<td>Vaxchora</td>
<td>Placebo</td>
</tr>
<tr>
<td>Dose volume, mL</td>
<td>N=150</td>
<td>N=26</td>
<td>N=158</td>
<td>N=27</td>
<td>N=163</td>
<td>N=26</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose given</td>
<td>146 (97.3%)</td>
<td>26 (100%)</td>
<td>156 (98.7%)</td>
<td>26 (96.3%)</td>
<td>163 (100%)</td>
<td>26 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweetener added‡</td>
<td>144 (98.6%)</td>
<td>26 (100%)</td>
<td>149 (95.5%)</td>
<td>25 (96.2%)</td>
<td>144 (88.3%)</td>
<td>22 (84.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete dose consumed‡</td>
<td>116 (79.5%)</td>
<td>19 (73.1%)</td>
<td>142 (91.0%)</td>
<td>25 (96.2%)</td>
<td>162 (99.4%)</td>
<td>26 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥80% of dose consumed‡</td>
<td>121 (82.9%)</td>
<td>22 (84.6%)</td>
<td>152 (97.4%)</td>
<td>25 (96.2%)</td>
<td>162 (99.4%)</td>
<td>26 (100%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Palatability‡:

<table>
<thead>
<tr>
<th></th>
<th>Very good</th>
<th>Good</th>
<th>Neutral</th>
<th>Bad</th>
<th>Very bad</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=150</td>
<td>N=26</td>
<td>N=158</td>
<td>N=27</td>
<td>N=163</td>
</tr>
<tr>
<td>Very good</td>
<td>44 (30.1%)</td>
<td>6 (23%)</td>
<td>28 (17.9%)</td>
<td>3 (11.5%)</td>
<td>8 (4.9%)</td>
</tr>
<tr>
<td>Good</td>
<td>28 (19.2%)</td>
<td>9 (35%)</td>
<td>27 (17.3%)</td>
<td>1 (3.8%)</td>
<td>29 (17.8%)</td>
</tr>
<tr>
<td>Neutral</td>
<td>19 (13.0%)</td>
<td>3 (12%)</td>
<td>37 (23.7%)</td>
<td>10 (38.5%)</td>
<td>64 (39.3%)</td>
</tr>
<tr>
<td>Bad</td>
<td>24 (16.4%)</td>
<td>4 (15%)</td>
<td>30 (19.2%)</td>
<td>6 (23.1%)</td>
<td>50 (30.7%)</td>
</tr>
<tr>
<td>Very bad</td>
<td>31 (21.2%)</td>
<td>4 (15%)</td>
<td>34 (21.8%)</td>
<td>6 (23.1%)</td>
<td>12 (7.4%)</td>
</tr>
</tbody>
</table>

*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).

Safety Overview of Vaxchora (004 & 006)\(^1\)

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

\(^1\)There were no related serious AEs; 1 unrelated serious AE of right leg fracture was noted.

AE=adverse events.

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.
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

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

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

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\(^3\)

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**Primary Endpoint: SVA Seroconversion at Day 11 (006) (Adult vs Pediatric; Vaxchora Only)**


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**ACIP CHOLERA PRESENTATION**
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.

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

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Vaxchora (N)</th>
<th>Placebo (N)</th>
<th>Percent of subjects, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 5: Vaxchora</td>
<td>103</td>
<td>20</td>
<td>98.1</td>
</tr>
<tr>
<td>2 to 5: Placebo</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 to 11: Vaxchora</td>
<td>139</td>
<td>24</td>
<td>97.8</td>
</tr>
<tr>
<td>6 to 11: Placebo</td>
<td>24</td>
<td>8.3</td>
<td></td>
</tr>
<tr>
<td>12 to 17: Vaxchora</td>
<td>157</td>
<td>23</td>
<td>100</td>
</tr>
<tr>
<td>12 to 17: Placebo</td>
<td>23</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*SVA=serum vibriocidal antibody.

GM Ts of Serum Vibriocidal Antibody Through Day 181 (006)\textsuperscript{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.

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

<table>
<thead>
<tr>
<th>Time Point</th>
<th>SVA Seroconversion Rate</th>
<th>GMT</th>
<th>GMFI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaxchora (n=72)</td>
<td>Placebo (n=23)</td>
<td>Vaxchora (n=72)</td>
</tr>
<tr>
<td>Day 11</td>
<td>100%</td>
<td>0</td>
<td>9035.4</td>
</tr>
<tr>
<td>Day 29</td>
<td>100%</td>
<td>0</td>
<td>2791.7</td>
</tr>
<tr>
<td>Day 91</td>
<td>88.9%</td>
<td>0</td>
<td>391.7</td>
</tr>
<tr>
<td>Day 181</td>
<td>83.1%</td>
<td>0</td>
<td>223.0</td>
</tr>
<tr>
<td>Day 365</td>
<td>68.6%</td>
<td>N/A</td>
<td>158.4</td>
</tr>
<tr>
<td>Day 547</td>
<td>73.1%</td>
<td>N/A</td>
<td>175.6</td>
</tr>
<tr>
<td>Day 730</td>
<td>64.5%</td>
<td>N/A</td>
<td>133.8</td>
</tr>
</tbody>
</table>

SVA=serum vibriocidal antibody; GMT=geometric mean titer; GMFI=geometric mean fold increase.

N/A: Seroconversion was measured in placebo subjects through Day 181.

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

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

*Among Vaxchora subjects (modified intent-to-treat population) who consumed less than 80% of expected dose.  
SVA=serum vibriocidal antibody.  
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
Discussion
Backup
The Efficacy of Vaxchora Was Assessed in a Placebo-Controlled Challenge Study (003)\(^1\)

**Results**

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

In the Human Challenge Study (003), Vibriocidal Antibody Seroconversion Was Determined to Be an Immune Correlate of Protection\textsuperscript{1,2}

\begin{itemize}
  \item Placebo Subjects (n = 66)
  \item Vaccinees (n = 68)
\end{itemize}

\[ r=0.71, \quad P<0.01 \]

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 x 10^8 to 2 x 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