Safety and Immunogenicity of a bivalent Paratyphoid A-Typhoid Conjugate Vaccine: Phase I study

Anirudha Potey & Lizzy Jones

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Why do we need an *S.* Paratyphi vaccine?

3.8 million cases & 23,300 deaths in 2019

Increasing incidence *S.* Paratyphi A infections

Emergence of multidrug resistant strains

Figure from:
https://www.healthdata.org/results/gbd_summaries/2019/paratyphoid-fever-level-4-cause
Paratyphoid A-Typhoid Bivalent Conjugate Vaccine

- S. Typhi
- 25 µg purified Vi
- Conjugated to tetanus toxoid

- S. Paratyphi A
- 25 µg purified LPS
- Conjugated to dipheria toxoid

Sii - PTCV
## Study Site And Facilities

<table>
<thead>
<tr>
<th>Site</th>
<th>Human Pharmacology Unit, Syngene International Limited, Bangalore, India.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunogenicity Laboratory Facility</strong></td>
<td>Oxford Vaccine Laboratory, University of Oxford, United Kingdom</td>
</tr>
</tbody>
</table>
Key Inclusion criteria

- Healthy adult male or female participants between 18-45 years age.

Key Exclusion criteria

- Fever or any acute infection.
- Known hypersensitivity.
- Previous documented exposure to S. Typhi or S. Paratyphi A.
- Impaired immunity.
- History or presence of clinically significant diseases.
Study Design – Safety

- Population
- Bivalent Typhi/Paratyphi
  - n=30
  - 1 week: solicited adverse events
  - 1 month: unsolicited adverse events
  - 6 month: serious adverse events

- Typbar-TCV®
  - n=30
  - 1 week: solicited adverse events
    - 1 month: unsolicited adverse events
    - 6 month: serious adverse events
Study design - Immunogenicity

Population

Bivalent Typhi/Paratyphi

n=30

Pre-vac  1 month  6 month

Typbar-TCV®

n=30

Pre-vac  1 month  6 month
Immunogenicity sample analysis

- Anti-Vi IgG & IgA
- Anti-LPS IgG
- Serum bactericidal activity
Immunogenicity sample analysis

- Anti-Vi IgG & IgA
- Anti-LPS IgG
- Serum bactericidal activity
Vi IgG responses are equivalent in both vaccine arms
Vi IgA responses are equivalent in both vaccine arms
Immunogenicity sample analysis

- Anti-Vi IgG & IgA
- Anti-LPS IgG
- Serum bactericidal activity
Sii-PTCV induces strong anti-LPS IgG responses
Immunogenicity sample analysis

- Anti-Vi IgG & IgA
- Anti-LPS IgG
- Serum bactericidal activity
Sii-TCV induces significant increase in bactericidal antibodies

<table>
<thead>
<tr>
<th></th>
<th>Sii-PTCV</th>
<th>Typbar-TCV®</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0</td>
<td>0.1</td>
<td>1</td>
</tr>
<tr>
<td>D29</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>D181</td>
<td>1000</td>
<td>10000</td>
</tr>
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</table>

Fold change from baseline

SBA titre

SBA titre

SBA Titre

r 0.6809
p < 0.0001

Anti-LPS IgG (EU/mL)
## Safety data results

<table>
<thead>
<tr>
<th>Event</th>
<th>SII-TCV(B)</th>
<th>Typbar-TCV®</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solicited Local Events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>90%</td>
<td>76.7%</td>
</tr>
<tr>
<td>Redness</td>
<td>-</td>
<td>6.7%</td>
</tr>
<tr>
<td>Swelling</td>
<td>-</td>
<td>3.3%</td>
</tr>
<tr>
<td><strong>Solicited Systemic Events</strong></td>
<td>23.3%</td>
<td>26.7%</td>
</tr>
<tr>
<td>Headache</td>
<td>10%</td>
<td>13.3%</td>
</tr>
<tr>
<td>Malaise</td>
<td>10%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>6.7%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>16.7%</td>
<td>13.3%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6.7%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

- No causally related unsolicited events reported
- No serious AEs reported
Conclusion

Sii-PTCV is safe and well tolerated

Similar Vi specific antibody responses after Sii-PTCV compared with licensed Typbar-TCV®

Vaccine responses were sustained for at least 6 months

Induces strong immune responses against typhoid and paratyphoid
Thank you...

The study participants

**Oxford Vaccine Group**
Andrew Pollard
Florence McLean
Amy Flaxman
Young Kim
Rachel Atherton
Tanya Dinesh
Sarthak Sahoo
Nicole Day
JuYeon Park
Eirini Pantazi

**Serum Institute India PL**
Prasad S Kulkarni
Anirudha Vyankatesh Potey
Sandesh Bharati
Vinay Gavade
Chandrashekhar Kamat
Anil Kunhihitlu
Bharath Narasimha
Sindhu Yallapa
Abhijeet Dharmadhikari
Asha Mallya
Annamraju D Sarma
Sunil Goel
Sambhaji S Pital
Cyrus S Poonawalla
Rajaram Venkatesan
<table>
<thead>
<tr>
<th></th>
<th>Anti-Vi IgG</th>
<th>Anti-Vi IgA</th>
<th>Anti-LPS</th>
<th>SBA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[GMT (95%CI)]</td>
<td>[GMFR (95%CI)]</td>
<td>[Seroconversion n[%]] (95%CI)</td>
<td>[GMT (95%CI)]</td>
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<tr>
<td><strong>GMT (95%CI)</strong></td>
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<tr>
<td><strong>Anti-Vi IgG</strong></td>
<td></td>
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<tr>
<td><strong>SII-PTCV</strong> N=30</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>6.97 (4.75, 10.22)</td>
<td>-</td>
<td>-</td>
<td>5.82 (4.13, 8.20)</td>
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<tr>
<td>Day 29</td>
<td>(867.80, 2513.89)</td>
<td>211.96</td>
<td>(121.69, 369.20)</td>
<td>996.38</td>
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<tr>
<td>Day 181</td>
<td>480.46</td>
<td>68.95</td>
<td>(43.18, 110.10)</td>
<td>482.54</td>
</tr>
<tr>
<td><strong>Anti-Vi IgA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Typbar-TCV®</strong> N=30</td>
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<tr>
<td><strong>Anti-LPS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>360.46</td>
<td>-</td>
<td>-</td>
<td>181.04</td>
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<tr>
<td>Day 29</td>
<td>(237.07, 548.07)</td>
<td>80.02</td>
<td>(54.93, 116.58)</td>
<td>236.81</td>
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<tr>
<td>Day 181</td>
<td>9535.52</td>
<td>26.45</td>
<td>(19.31, 36.25)</td>
<td>222.86</td>
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<tr>
<td><strong>SBA</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>8044.6</td>
<td>-</td>
<td>-</td>
<td>6765.7</td>
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<tr>
<td>Day 29</td>
<td>(5326.37, 12150.05)</td>
<td>19.4</td>
<td>(12.61, 29.73)</td>
<td>5993.7</td>
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<tr>
<td>Day 181</td>
<td>56367.4</td>
<td>3.98</td>
<td>(4.719, 82.71)</td>
<td>1782.3</td>
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</tbody>
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