Durability of Anti-Vi IgG and IgA Responses in 15-month-old Children Vaccinated with a Typhoid Conjugate Vaccine in Burkina Faso

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Introduction

• Typhoid is a public health threat that disproportionately impacts children in sub-Saharan Africa.

• Typhoid conjugate vaccine (TCV) has demonstrated efficacy against S. Typhi.

• TCV-induced IgA and IgG responses correlate to protection in a controlled human infection model (Jin et al., 2021).
Study Overview and Aims

• **Aim**
  • Assess long-term immunogenicity of Vi-TT, co-administered with EPI vaccines, among healthy children from the 15 - 23 months of age cohort in Burkina Faso

• **Objective**
  • Compare anti-Vi IgA and IgG responses at 28 days and 30-35 months after Vi-TT versus control vaccination

• **Study Vaccines**
  • Typbar TCV® (Vi-TT, Bharat Biotech, Hyderabad, India)
  • Inactivated Poliovirus Vaccine (IPV)
Site-Specific Information

• Groupe de Recherche Action en Santé (GRAS), Burkina Faso

• Schiphra Hospital in Ouagadougou, Burkina Faso

• Center for Vaccine Development and Global Health, University of Maryland School of Medicine
Trial Design

Infants 15-23 months of age who present for second MR and MCV-A EPI visit

**Abbreviations**
MR: Measles-rubella vaccine  
YFV: Yellow fever vaccine  
EPI: Expanded Program on Immunization  
Vi-TCV: Vi-typhoid conjugate vaccine  
IPV: Inactivated polio vaccine  
MCV-A: Meningooccal A conjugate vaccine
Methods

• Symptoms solicited at days 3 & 7
  • Local: pain/tenderness, swelling and redness at injection site
  • Systemic: fever or feverishness, and irritability

• TCV immunogenicity
  • Enzyme-linked immunosorbent assay (ELISA) at days 0, 28 and 30-35 months
  • VaccZyme *Salmonella* Typhi anti-Vi IgG & IgA ELISA

• Seroconversion at day 28 and 30-35 months
  • Seroconversion: >4-fold rise in anti-Vi IgG antibody titer from baseline day 0
  • Participants re-contacted & re-enrolled for immunogenicity at 30-35 months
Results

Study Time Period: 03 December 2018 - 24 September 2021
### Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>Group 1: TCV + IPV (delayed MCV-A)</th>
<th>Group 2: TCV + MCV-A</th>
<th>Group 3: MCV-A + IPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>49</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td>Attended final visit (%)</td>
<td>38 (78%)</td>
<td>33 (66%)</td>
<td>44 (86%)</td>
</tr>
<tr>
<td>Female Sex (%)</td>
<td>16 (42%)</td>
<td>15 (45%)</td>
<td>26 (59%)</td>
</tr>
<tr>
<td>Age at enrollment ± SD (months)</td>
<td>16.4 ±1.7</td>
<td>16.1 ±1.7</td>
<td>15.7 ±1.2</td>
</tr>
<tr>
<td>Age final visit ± SD (months)</td>
<td>47.4 ±1.6</td>
<td>47.3 ±1.8</td>
<td>46.6 ±0.9</td>
</tr>
</tbody>
</table>
# Anti-Vi IgG Seroconversion at 28 days and 30-35 months after vaccination

<table>
<thead>
<tr>
<th>Group 1: TCV + IPV (delayed MCV-A)</th>
<th>Day 0 to 28</th>
<th>Day 0 to 30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>Percent (95%CI)</td>
<td>n/N</td>
</tr>
<tr>
<td>44/47*</td>
<td>93.6% (82.5-98.7)</td>
<td>34/38</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2: TCV + MCV-A</th>
<th>Day 0 to 28</th>
<th>Day 0 to 30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>Percent (95%CI)</td>
<td>n/N</td>
</tr>
<tr>
<td>48/50</td>
<td>96.0% (86.3-99.5)</td>
<td>29/33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 3: MCV-A + IPV</th>
<th>Day 0 to 28</th>
<th>Day 0 to 30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>Percent (95%CI)</td>
<td>n/N</td>
</tr>
<tr>
<td>2/51</td>
<td>3.9% (0.5-13.5)</td>
<td>3/44</td>
</tr>
</tbody>
</table>

Data are % (95% CI). n=number of participants. N= total number. CI=confidence interval.

*One participant excluded in analysis for late Day 28 visit.
### Anti-Vi IgG Antibody Titers
Baseline (day 0), and 28 days & 30-35 months after vaccination

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 28</th>
<th>30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>GMT (95% CI)</td>
<td>n</td>
</tr>
<tr>
<td><strong>Group 1: TCV +IPV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(delayed MCV-A)</td>
<td>49</td>
<td>5.0 (3.9-6.2)</td>
<td>47*</td>
</tr>
<tr>
<td><strong>Group 2: TCV +MCV-A</strong></td>
<td>50</td>
<td>4.7 (3.7-5.8)</td>
<td>50</td>
</tr>
<tr>
<td><strong>Group 3: MCV-A +IPV</strong></td>
<td>51</td>
<td>4.8 (3.8-6.2)</td>
<td>51</td>
</tr>
</tbody>
</table>

Data are mean (95% CI). n=number of participants. GMT=geometric mean titer. CI=confidence interval.

*One participant excluded in analysis for late Day 28 visit.*
Anti-Vi IgG Antibody Titers
Baseline (day 0), and 28 days & 30-35 months after vaccination

* Using two sample t-test with unequal variances on log_{10} transformed data
** Using paired t-test on log_{10} transformed data
Anti-Vi IgG Antibody Titers
Baseline (day 0), and 28 days & 30-35 months after vaccination

Groups 1+2: TCV

Group 3: Control

Using two sample t-test with unequal variances on log10 transformed data

Using paired t-test on log10 transformed data † MCV-A and IPV

* Using two sample t-test with unequal variances on log10 transformed data
** Using paired t-test on log10 transformed data † MCV-A and IPV
## Anti-Vi IgA Antibody Titers
### 28 days & 30-35 months after vaccination

<table>
<thead>
<tr>
<th></th>
<th>Day 28</th>
<th>30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>GMT (95% CI)</td>
</tr>
<tr>
<td><strong>Group 1: TCV +IPV (delayed MCV-A)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>47*</td>
<td>45.5 (33.1-62.4)</td>
</tr>
<tr>
<td><strong>Group 2: TCV +MCV-A</strong></td>
<td>50</td>
<td>37.3 (29.3-47.6)</td>
</tr>
<tr>
<td><strong>Group 3: MCV-A +IPV</strong></td>
<td>51</td>
<td>1.7 (1.5-1.8)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI). n=number of participants. CI=confidence interval. GMT=geometric mean titre.

*One participant excluded in analysis for late Day 28 visit.*
Anti-Vi IgA Antibody Titers
28 days & 30-35 months after vaccination

Group 1:
Vi-TCV + IPV
(delayed MCV-A dose)

Group 2:
Vi-TCV + MCV-A

Group 3:
MCV-A + IPV

* Using two sample t-test with unequal variances on log_{10} transformed data
** Using paired t-test on log_{10} transformed data
Using two sample t-test with unequal variances on log_{10} transformed data

** Using paired t-test on log_{10} transformed data † MCV-A and IPV.
Comparison: Nepal & Burkina Faso Anti-Vi IgG Antibody Titers
Baseline (day 0), and 28 days & 30-35/18 months after vaccination

<table>
<thead>
<tr>
<th>Study Area</th>
<th>Day 0</th>
<th>Day 28</th>
<th>30-35 months</th>
<th>% Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Burkina Faso</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups 1+2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCV</td>
<td>99</td>
<td>4.8</td>
<td>(4.1-5.6)</td>
<td>97*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3210.1</td>
<td>(2311.7-4457.6)</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>79.3</td>
<td>(63.1-99.6)</td>
<td>92/97</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>94.9 (88.4-98.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>63/71</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>88.7 (79.0-95.1)</td>
</tr>
<tr>
<td>Group 3:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control*</td>
<td>51</td>
<td>4.8</td>
<td>(3.8-6.2)</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.3</td>
<td>(4.1-6.9)</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.7</td>
<td>(4.4-7.3)</td>
<td>2/51</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.9 (0.5-13.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3/44</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.8 (1.4-18.7)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI) or % (95% CI). n=number of participants. N=total number. CI=confidence interval. GMT=geometric mean titre.

*One participant excluded in analysis for late Day 28 visit. * MCV-A and IPV.

<table>
<thead>
<tr>
<th>Nepal*</th>
<th>Day 0</th>
<th>Day 28</th>
<th>18 months</th>
<th>% Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCV</td>
<td>99</td>
<td>4.5</td>
<td>(3.9-5.1)</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1488.3</td>
<td>(1160.8-1908.2)</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>81.0</td>
<td>(67.3-97.6)</td>
<td>54/5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>55/58</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>94</td>
</tr>
<tr>
<td>MCV-A</td>
<td>66</td>
<td>4.6</td>
<td>(3.9-5.6)</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.5</td>
<td>(3.8-5.2)</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.5</td>
<td>(3.8-5.4)</td>
<td>0/46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1/47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

Data are mean (95% CI) or % (95% CI). n=number of participants. N=total number. GMC=geometric mean concentration. CI=confidence interval.

### Comparison: Nepal & Burkina Faso Anti-Vi IgA Antibody Titers before (day 0), 28 days and 18/30-35 months after vaccination

#### Burkina Faso

<table>
<thead>
<tr>
<th></th>
<th>Day 28</th>
<th>30-35 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>GMT</td>
</tr>
<tr>
<td>15-month cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groups 1 +2: TCV</td>
<td>97*</td>
<td>41.1 (33.8-49.9)</td>
</tr>
<tr>
<td>Group 3: Control†</td>
<td>51</td>
<td>1.7 (1.5-1.8)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI). n=number of participants. CI=confidence interval. GMT=geometric mean titre. *One participant excluded in analysis for late Day 28 visit. † MCV-A and IPV.

#### Nepal*

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 28</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>GMC</td>
<td>n</td>
</tr>
<tr>
<td>&lt; 5 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCV</td>
<td>55</td>
<td>1.6 (1.5-1.9)</td>
<td>55</td>
</tr>
<tr>
<td>MCV-A</td>
<td>46</td>
<td>1.6 (1.5-1.7)</td>
<td>46</td>
</tr>
</tbody>
</table>

Conclusions

- TCV is highly immunogenic in young children
- Demonstrated durability of the immune response for ~3 years
- TCV efficacy + durability = longer-term protection
- 4-year efficacy data together with this evidence of durable immunogenicity in Burkina Faso when co-administered with routine immunizations makes a strong case for TCV introduction in endemic countries
- Burkina Faso has submitted an application to Gavi for TCV and intends to implement it during the 9-month vaccination visit in January 2025.
Durable Anti-Vi IgG and IgA Antibody Responses in 15-Month-Old Children Vaccinated With Typhoid Conjugate Vaccine in Burkina Faso

Alphonse Ouedraogo,1 Amidou Diarra,1 Issa Nébié,1 Nouchou Barry,1 Jean Moise Kabore,1 Alfred B. Tiono,1 Shrimati Datta,2* Yuanyuan Liang,2 Ifayet Mayo,2 Jennifer J. Oshinsky,2 J. Kathleen Tracy,2 Tsion Girmay,2 Marcela F. Pasetti,2 Leslie P. Jamka,2* Kathleen M. Neuzil,2 Leslie P. Jamka,2* Kathleen M. Neuzil,2

Durable Anti-Vi IgG and IgA Antibody Responses in 15-Month-Old Children Vaccinated With Typhoid Conjugate Vaccine in Burkina Faso

[4]. In Burkina Faso, TCV was safe and immunogenic when coadministered with measles-rubella (MR) and yellow fever vaccines at 9–11 months [5], and with MR and meningococcal serogroup A conjugate vaccine (MCV-A) at 15–23 months in a double-blind, randomized, controlled Phase 2 clinical trial [6].

We evaluated anti-Vi IgA antibodies 28 days after vaccination, and anti-Vi IgG and IgA antibodies 30–35 months post-vaccination in participants from a clinical trial where TCV was coadministered with routine MR vaccine, with and without MCV-A, at the 15-month vaccination visit [6]. The study was approved by ethics committees in Burkina Faso and Maryland, USA. Parents/guardians of study participants provided informed consent (Clinicaltrials.gov NCT03614533).

METHODS

Detailed methods of this randomized, double-blinded, controlled, Phase 2 trial were published previously [6]. Briefly,
Learn more at:
http://takeontyphoid.org
Extra Slides
## TCV Immunogenicity in Malawian Children


### Table 2: Anti-Vi immunoglobulin G antibody immunogenicity 28 days and 730-1035 days after vaccination by ELISA, in the intention-to-treat population

<table>
<thead>
<tr>
<th>Age stratum: 1–5 years</th>
<th>Group 1 TCV</th>
<th>Group 2 MCV-A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n or n/N</td>
<td>Mean or percentage (95% CI)</td>
</tr>
<tr>
<td><strong>GMT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 28</td>
<td>91</td>
<td>2085.9 (1635.6-2660.2)</td>
</tr>
<tr>
<td>Day 730*</td>
<td>74</td>
<td>36.9 (27.1-50.3)</td>
</tr>
<tr>
<td><strong>GMFR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 0 to 28</td>
<td>90</td>
<td>490.6 (378.6-635.6)</td>
</tr>
<tr>
<td>Day 0 to 730*</td>
<td>74</td>
<td>8.9 (6.5-12.1)</td>
</tr>
<tr>
<td>Seroconversion four times or higher increase from:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 0 to 28</td>
<td>88/90</td>
<td>97.8 (92.3-99.4)</td>
</tr>
<tr>
<td>Day 0 to 730*</td>
<td>58/74</td>
<td>78.4 (67.7-86.2)</td>
</tr>
</tbody>
</table>

Data are mean (95% CI) or percentage (95% CI). TCV=typhoid conjugate vaccine. MCV-A=meningococcal serogroup A conjugate vaccine. n=number of participants. N=total number. GMT=geometric mean titre. GMFR=geometric mean-fold rise. *Day 730 visits were extended by a year because of COVID-19 restrictions (730–1035 days).