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

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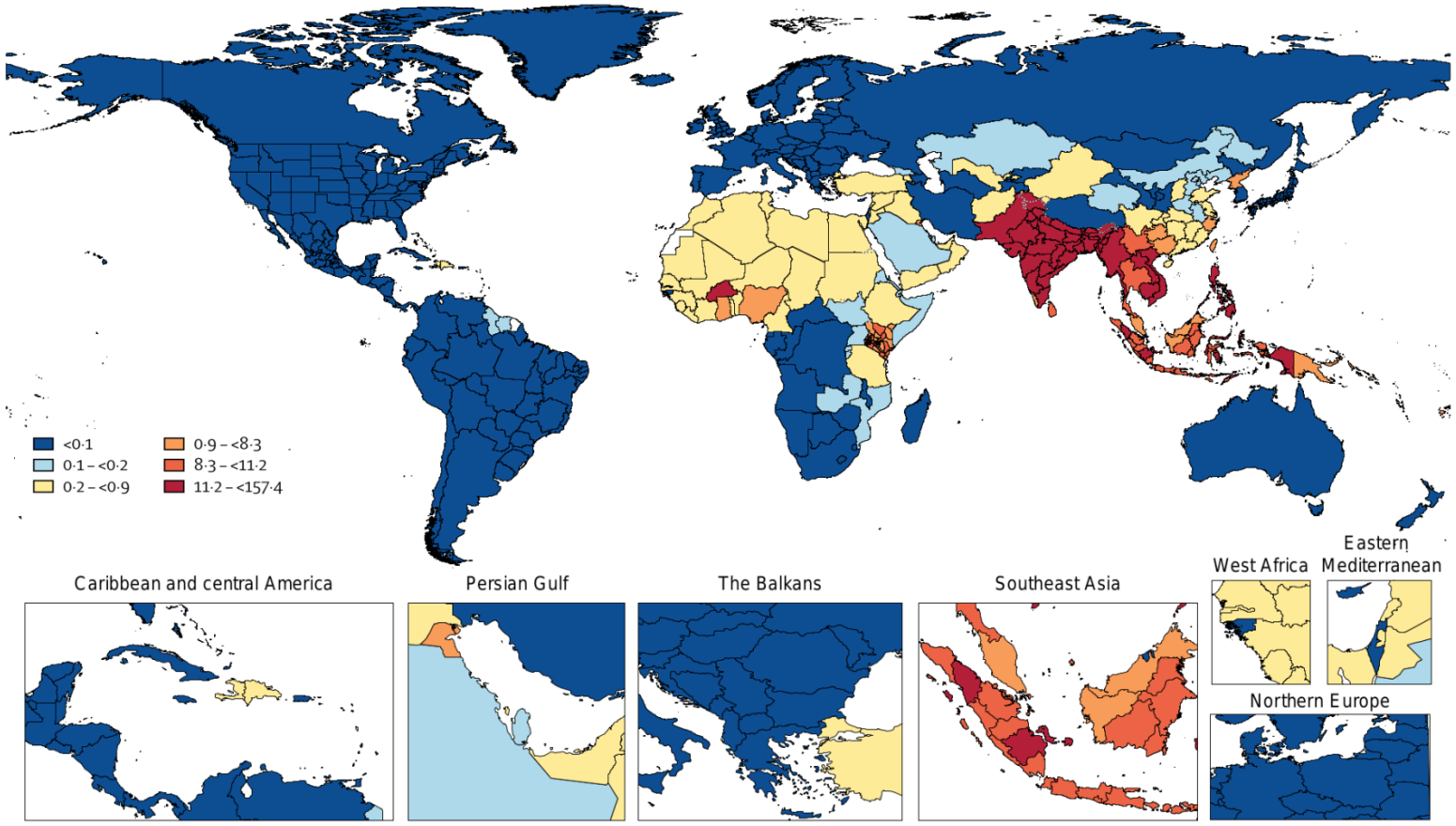
7th December 2023

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



3.8 million cases & 23 300 deaths in 2019

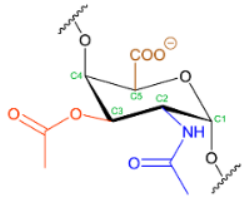
Increasing incidence *S.* Paratyphi A infections

Emergence of multidrug resistant strains

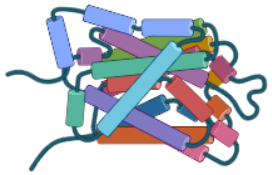
Figure from: https://www.healthdata.org/results/gbd_summaries/2019/paratyphoid-fever-level-4-cause

Paratyphoid A-Typhoid Bivalent Conjugate Vaccine

S. Typhi

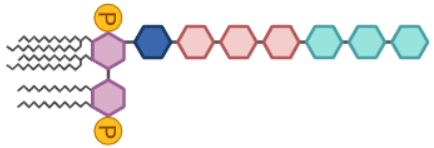


25 µg purified Vi

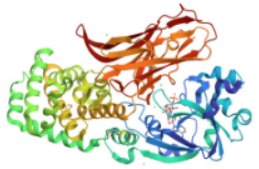


Conjugated to tetanus toxoid

S. Paratyphi A



25 µg purified LPS



Conjugated to diptheria toxoid

Sii - PTCV

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Study Site And Facilities

Site	Human Pharmacology Unit , Syngene International Limited Bangalore, India.
Immunogenicity Laboratory Facility	Oxford Vaccine Laboratory, University of Oxford, United Kingdom

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.

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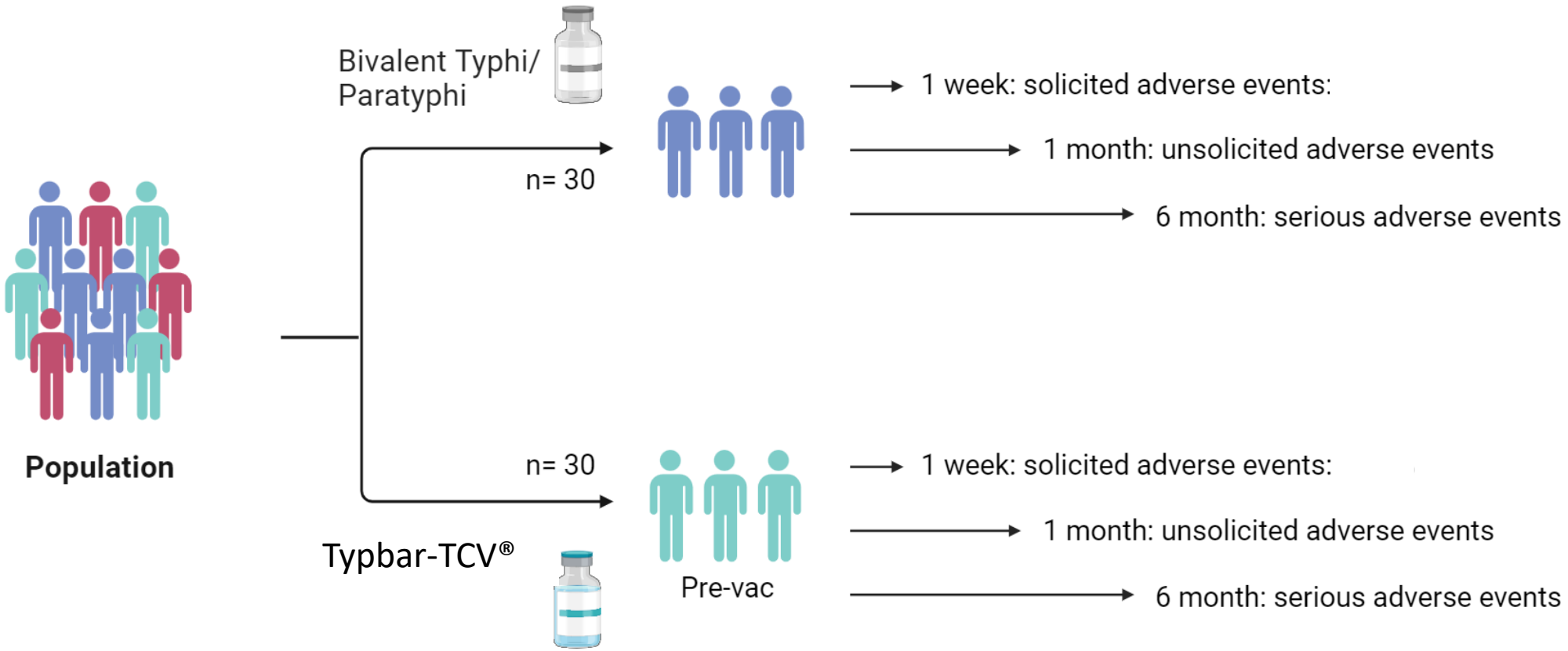
Study Design – Safety



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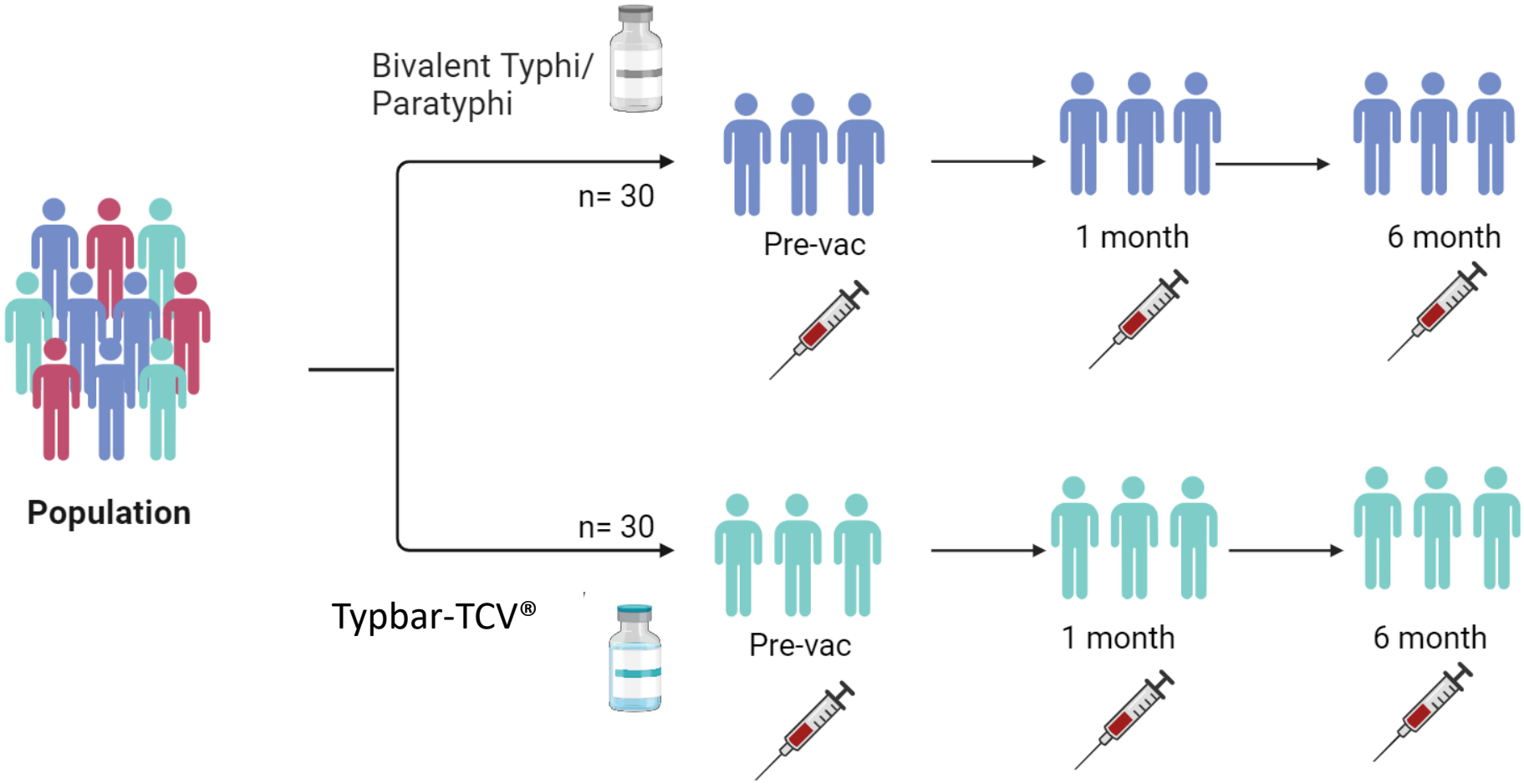
Study design - Immunogenicity



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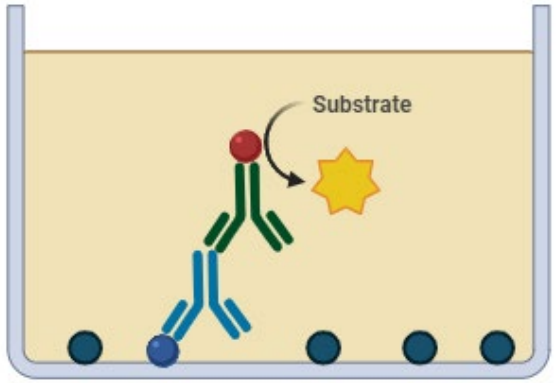
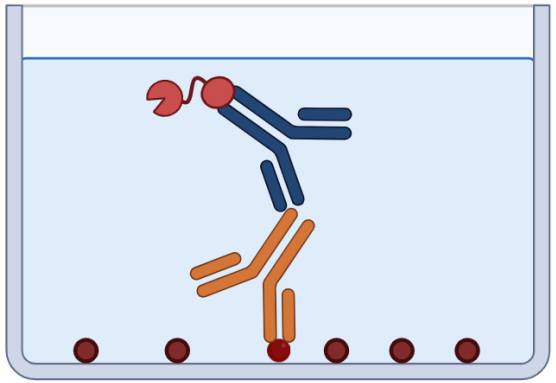
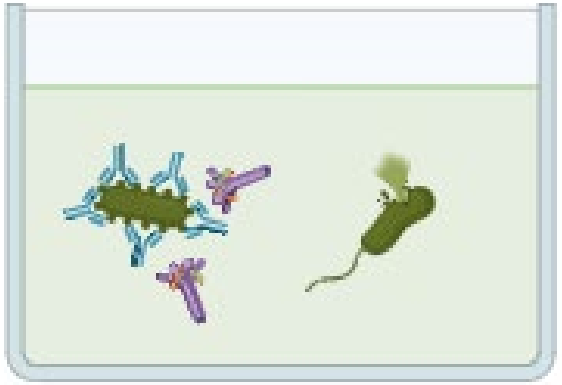
Immunogenicity sample analysis



Anti-Vi IgG & IgA



Anti-LPS IgG



Serum bactericidal activity

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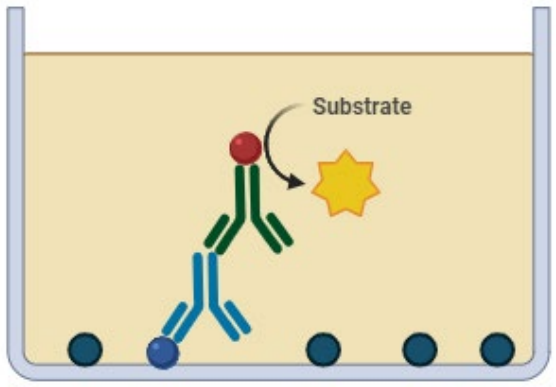
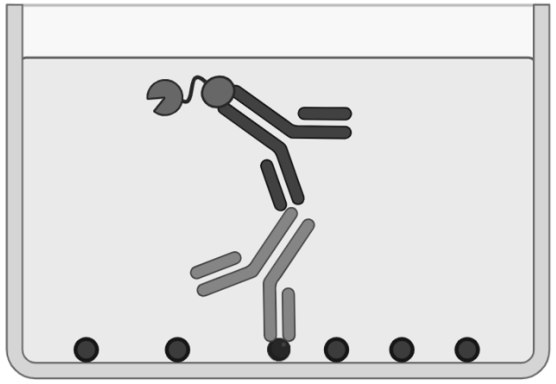
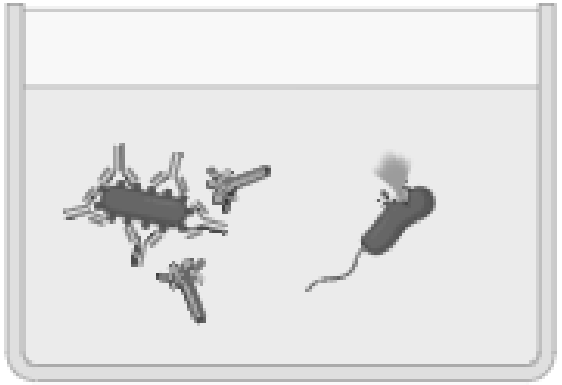
Immunogenicity sample analysis



Anti-Vi IgG & IgA



Anti-LPS IgG



Serum bactericidal activity

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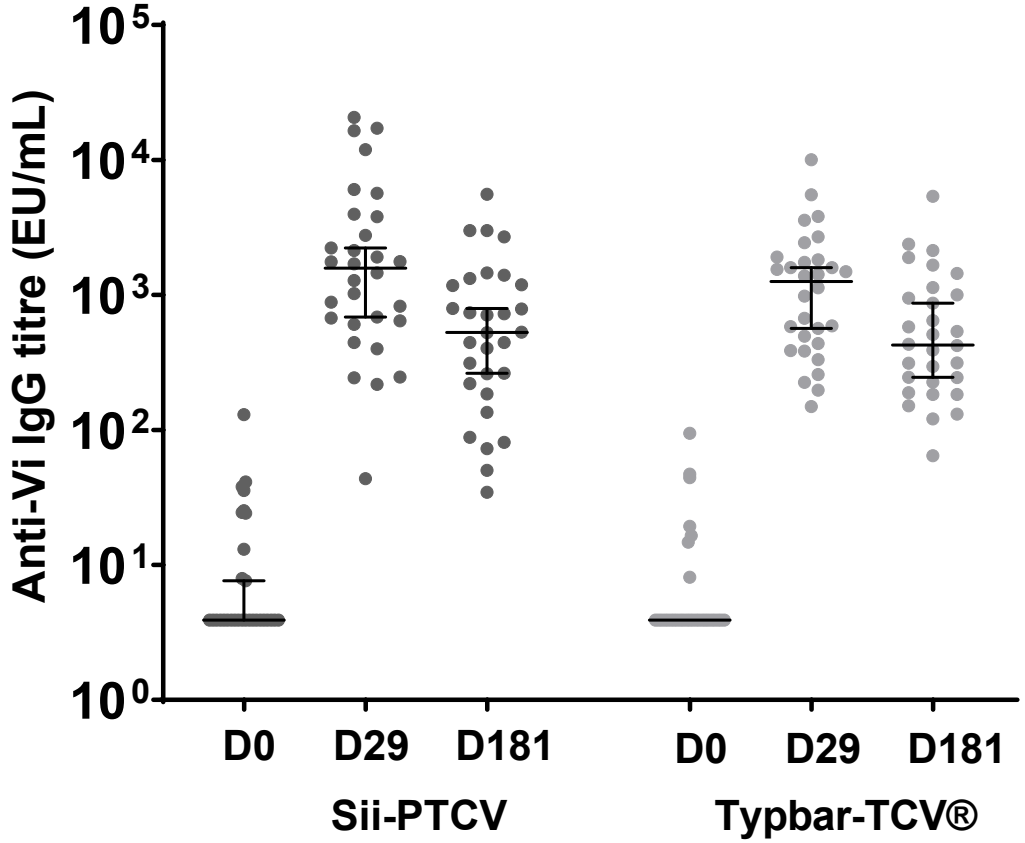
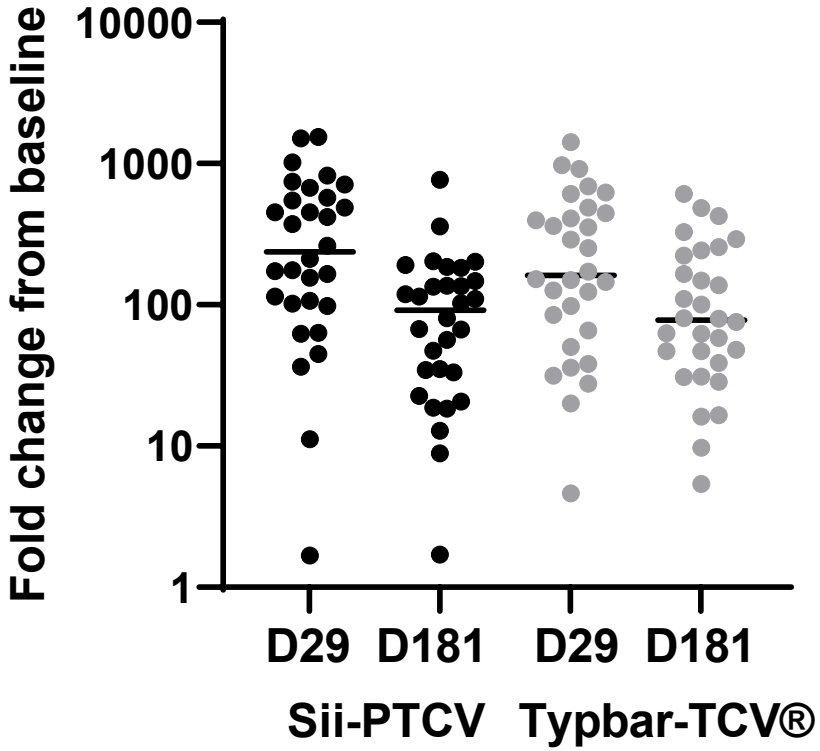
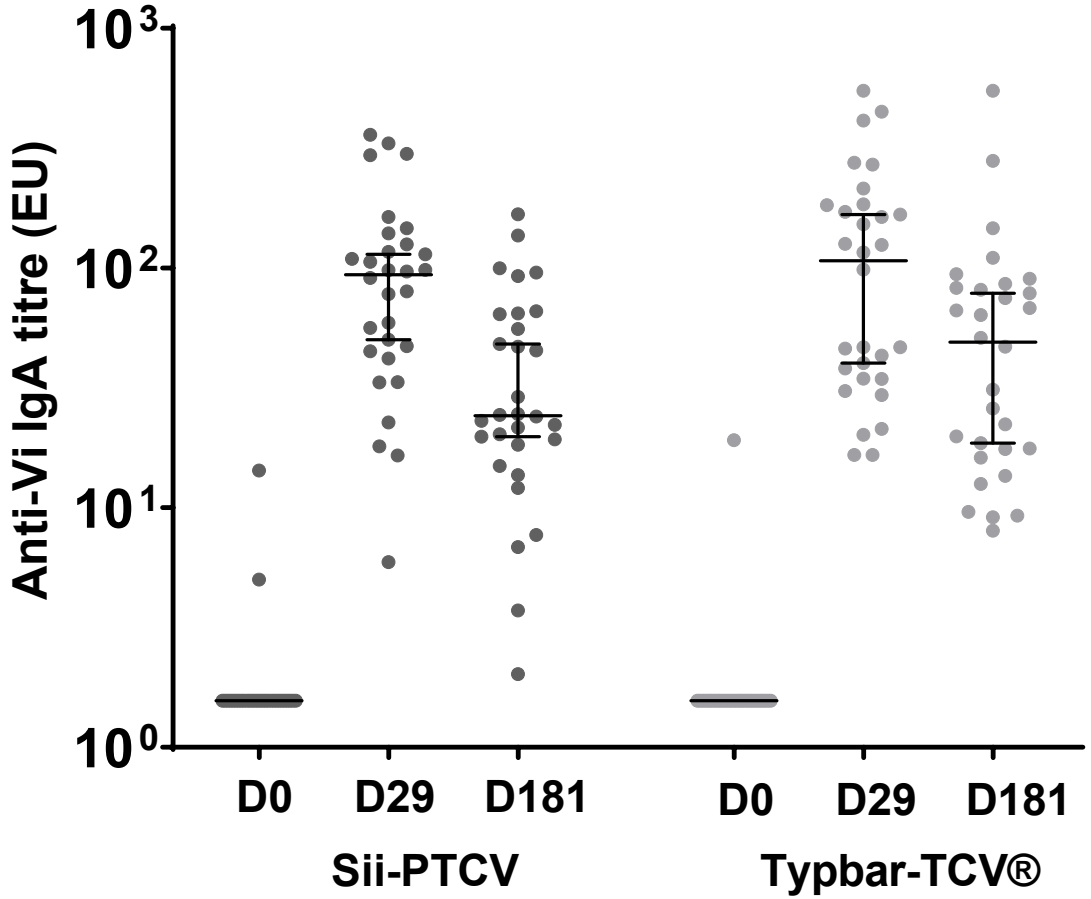
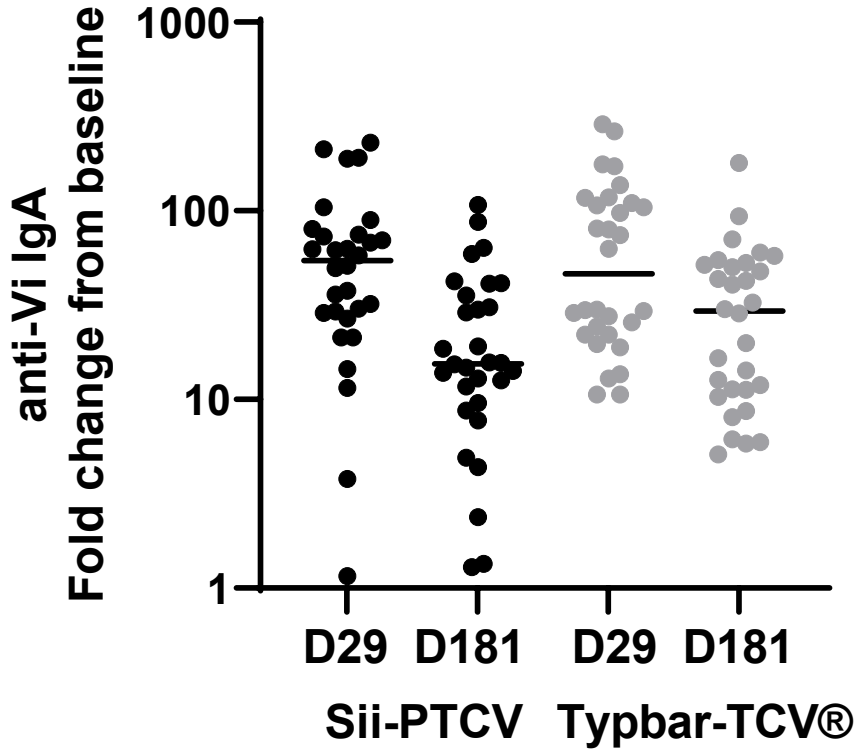
Vi IgG responses are equivalent in both vaccine arms



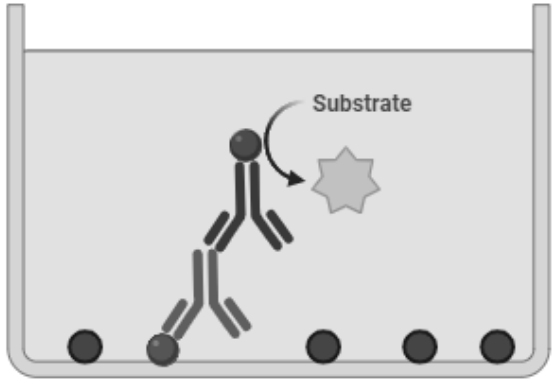


Vi IgA responses are equivalent in both vaccine arms

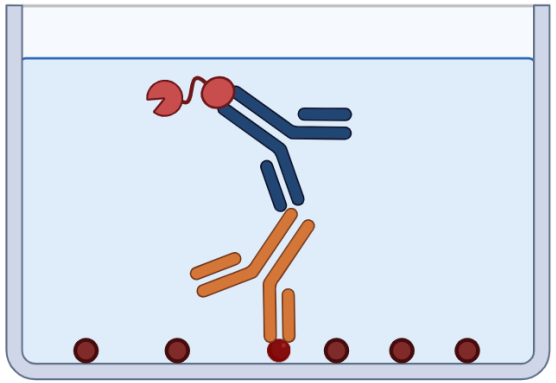




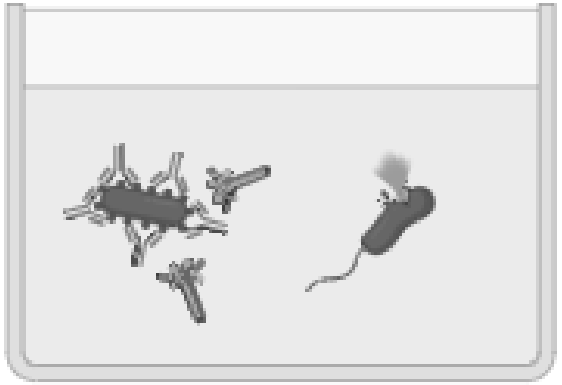
Immunogenicity sample analysis



Anti-Vi IgG & IgA



Anti-LPS IgG



Serum bactericidal activity

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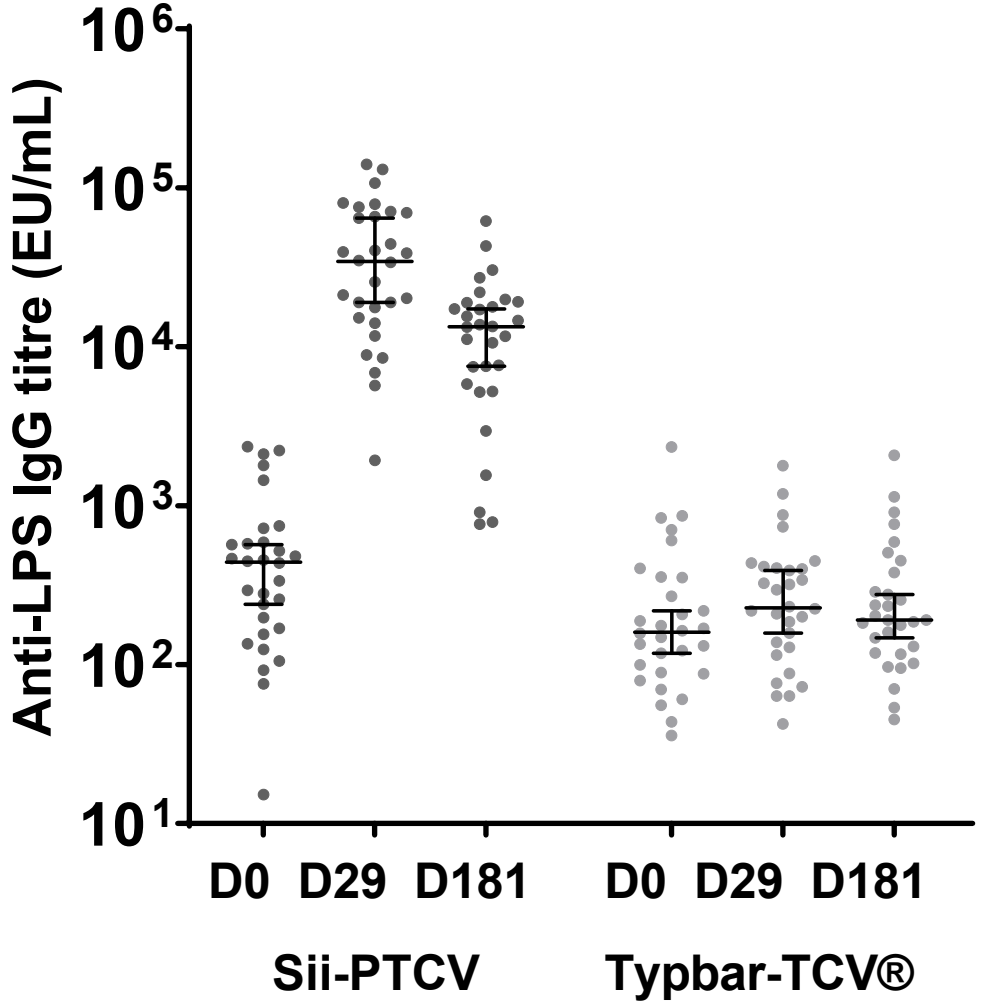
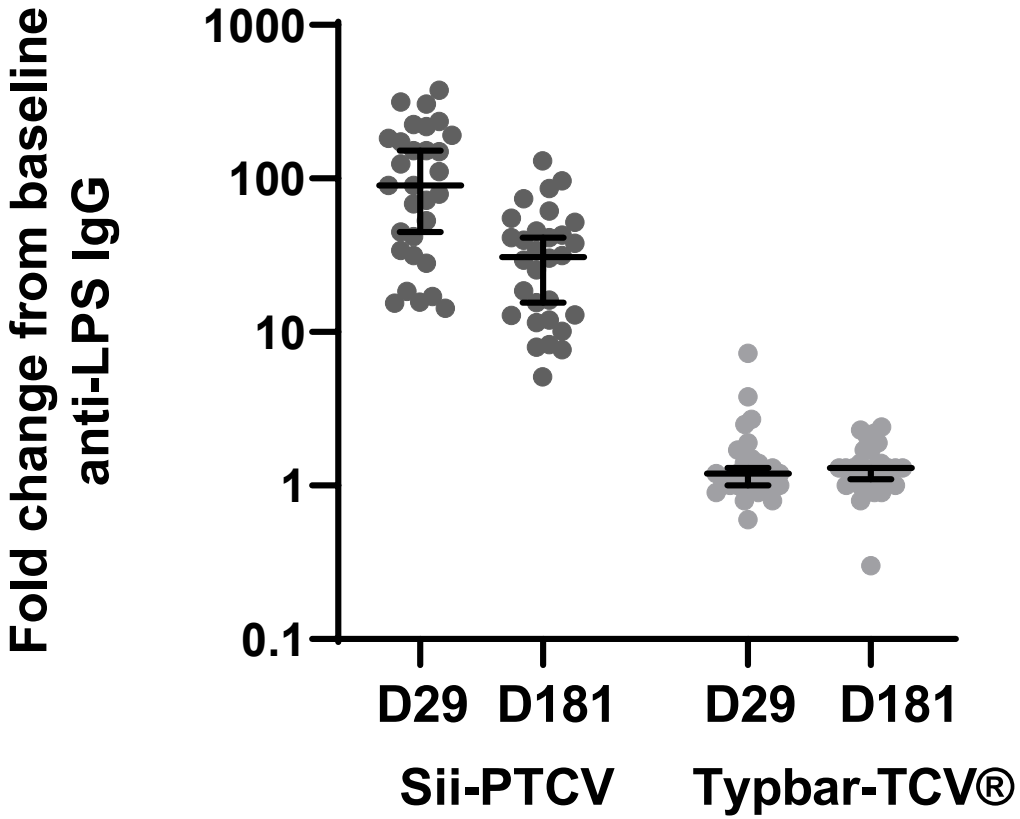
Sii-PTCV induces strong anti-LPS IgG responses





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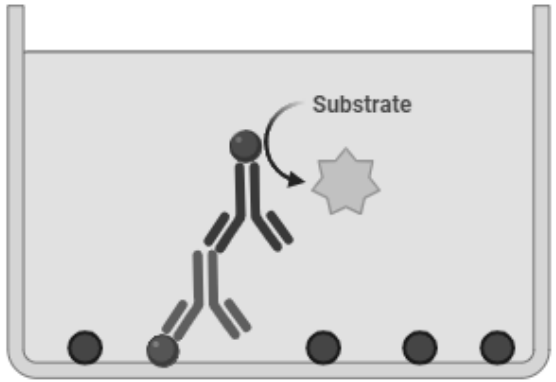
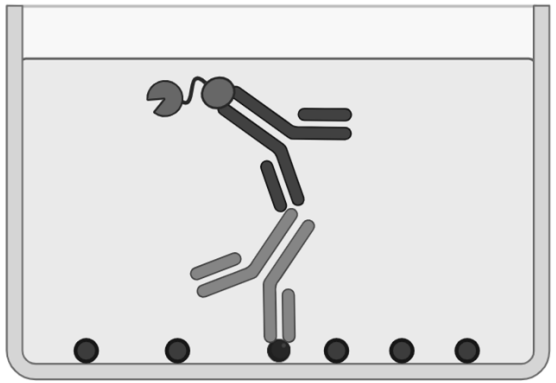
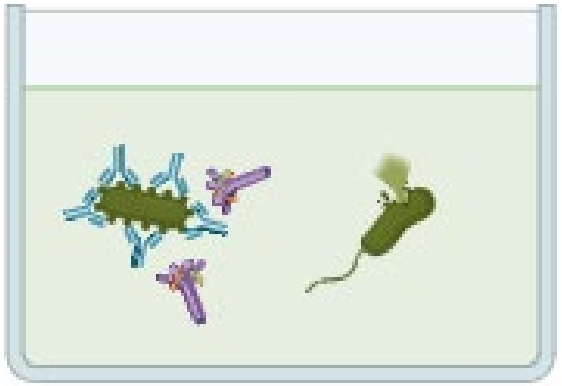
Immunogenicity sample analysis



Anti-Vi IgG & IgA

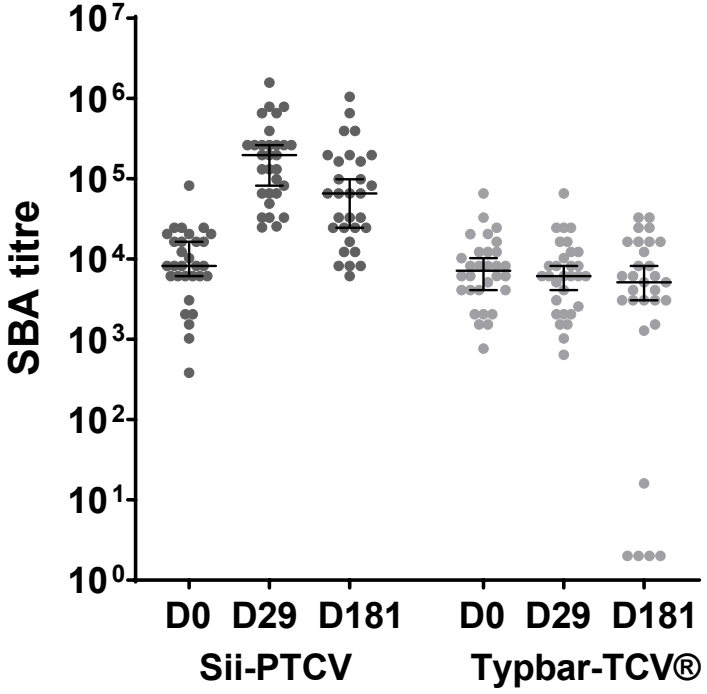


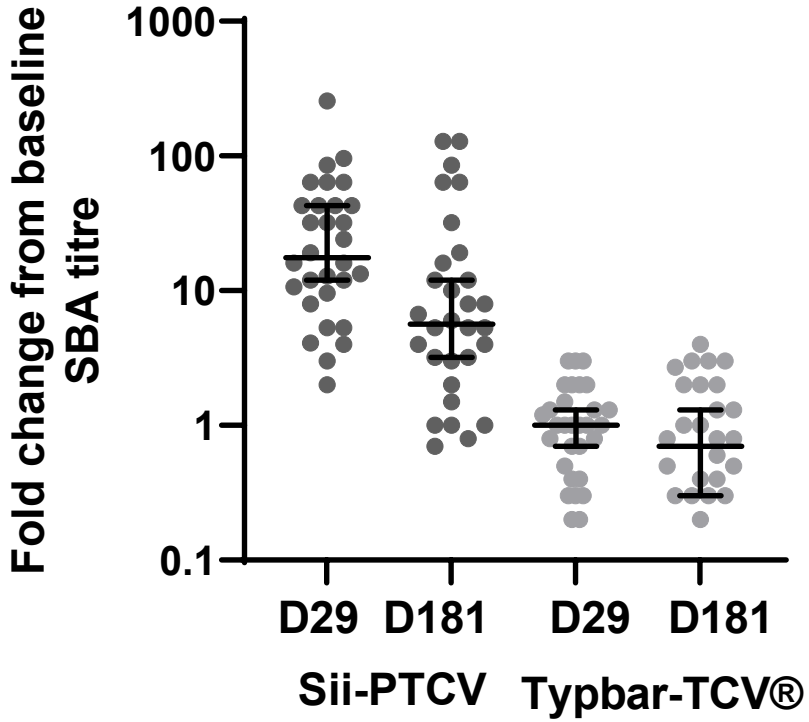
Anti-LPS IgG

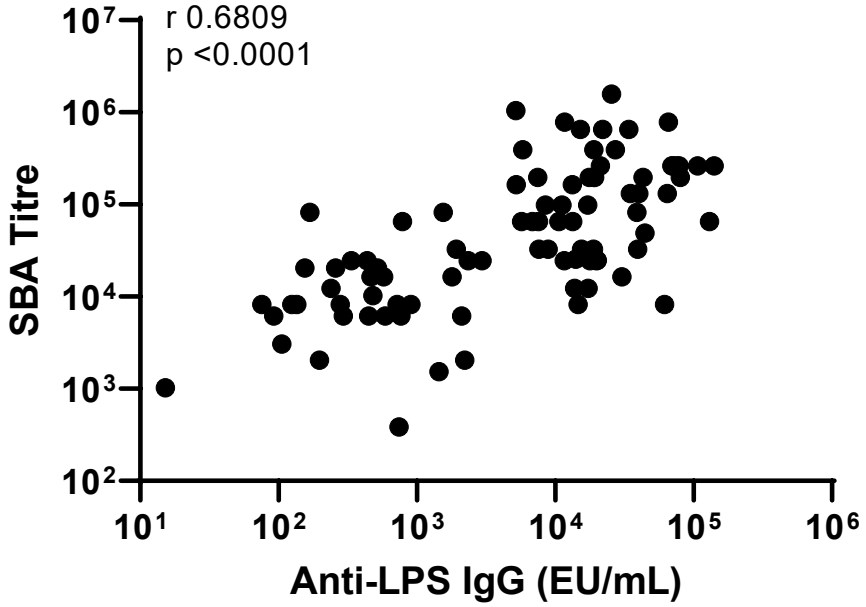


Serum bactericidal activity

Sii-TCV induces significant increase in bactericidal antibodies







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Safety data results

	SII-TCV(B) %	Typbar-TCV® %
Solicited Local Events	90	76.7
→ Pain	90	76.7
Redness	-	6.7
Swelling	-	3.3
Solicited Systemic Events	23.3	26.7
→ Headache	10	13.3
Malaise	10	6.7
Anorexia	6.7	6.7
→ Myalgia	16.7	13.3
Arthralgia	6.7	3.3

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

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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
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Sandesh Bharati
Vinay Gavade
Chandrashekhar Kamat
Anil Kunhihitlu
Bharath Narasimha
Sindhu Yallapa
Abhijeet Dharmadhikari
Asha Mallya
Annamraju D Sarma
Sunil Goel
Sambhaji S Pisal
Cyrus S Poonawalla
Rajaram Venkatesan

	Sii-PTCV N=30			Typbar-TCV® N=30		
	GMT (95%CI)	GMFR (95%CI)	Seroconversion n[%] (95%CI)	GMT (95%CI)	GMFR (95%CI)	Seroconversion n[%] (95%CI)
Anti-Vi IgG						
Day 1	6.97 (4.75, 10.22)	-	-	5.82 (4.13, 8.20)	-	-
Day 29	1477 (867.80, 2513.89)	211.96 (121.69, 369.20)	29 [96.7] (82.78, 99.92)	996.38 (676.58, 1467.35)	171.25 (103.13, 284.38)	30 [100.0] (88.43, 100.00)
Day 181	480.46 (297.94, 774.79)	68.95 (43.18, 110.10)	29 [96.7] (82.78, 99.92)	482.54 (327.32, 711.36)	82.93 (53.25, 129.16)	30 [100.0] (88.43, 100.00)
Anti-Vi IgA						
Day 1	1.75 (1.48, 2.07)	-	-	1.7 (1.43, 2.01)	-	-
Day 29	75.66 (53.25, 107.51)	43.27 (28.42, 65.87)	28 [93.3] (77.93, 99.18)	85.19 (57.93, 125.28)	50.15 (34.82, 72.23)	30 [100.0] (88.43, 100.00)
Day 181	27.75 (18.9, 40.74)	15.89 (10.51, 23.95)	27 [90] (73.47, 97.89)	40.6 (27.2, 60.59)	23.9 (16.74, 34.12)	30 [100.0] (88.43, 100.00)
Anti-LPS						
Day 1	360.46 (237.07, 548.07)	-	-	181.04 (126.08, 259.96)	-	-
Day 29	28845.24 (19679.44, 42280.06)	80.02 (54.93, 116.58)	30 [100.0] (88.43, 100.00)	236.81 (169.24, 331.37)	1.31 (1.09, 1.58)	1 [3.3] (0.08, 17.22)
Day 181	9535.52 (6281.40, 14475.46)	26.45 (19.31, 36.25)	30 [100.0] (88.43, 100.00)	222.86 (159.58, 311.22)	1.23 (1.05, 1.44)	0 [0] (NC)
SBA						
Day 1	8044.6 (5326.37, 12150.05)	-	-	6765.7 (4672.43, 9796.85)	-	-
Day 29	155737.8 (102803.95, 235927.33)	19.4 (12.61, 29.73)	28 [93.3] (77.93, 99.18)	5993.7 (4047.46, 8875.91)	0.9 (0.66, 1.19)	0 [0.0] (0.00, 11.57)
Day 181	56367.4 (33580.12, 94617.93)	3.98 (3.98, 12.32)	20 [66.7] (47.19, 82.71)	1782.3 (520.64, 6101.18)	0.3 (0.09, 0.81)	1 [3.3] (0.08, 17.22)