13th International Conference: Typhoid & Other Invasive Salmonelloses

Dr. Raches Ella,
Chief Development Officer

BHARAT BIOTECH – OVERVIEW

Vision

To offer affordable, safe and effective healthcare solutions to combat mankind's most dreaded illnesses, and to thus eradicate or at least control their occurrence in the years to come.

Mission

Developing next-generation remedies through Genetic Engineering Technologies so as to create a healthier world.

Established	Promoters	Business Line	First Project	Investment	Facility	Personnel	Accreditations
1996	Dr. Krishna & Ms. Suchitra Ella	5th largest Vaccine Manufacturers (volumes)	Hepatitis B Vaccine – US $ 3.5 Mn	Over US $ ~250 Mn	One of the largest facilities in Asia	Over 4000 resources including scientists	WHO PQ. ANVISA, KFDA, PIC(S), other Countries

PLETHORA OF INNOVATIVE PRODUCTS

A wide product portfolio of more than 15 vaccines & 4 bio- therapeutics

Our portfolio includes vaccines for Hepatitis-B, influenza H1N1, Polio, Rotavirus, Japanese Encephalitis, Rabies, Chikungunya, Zika and the world's first tetanus-toxoid conjugated vaccine for Typhoid.

Vaccines

- BioHib
- BIOPOLIO® M1
- BIOPOLIO® M3
- BIOPOLIO B1/3
- ComVac 3
- ComVac 4 Hb
- ComVac 5
- COVAXIN
- HNVAC
- INDIRAB
- JENVAC
- REVAC- B+®
- Revac-B mcf
- ROTAVAC
- ROTAVAC 5D®
- TYPBAR
- Typbar TCV

Biotherapeutics

- BIOGIT®
- REGEN-D® 60
- REGEN-D® 150
- SLVRGEN
- ZELECT®

OUR PRODUCT PIPELINE

Trivalent *Salmonella* (*S.* Enteritidis, *S.* Typhimurium, *S.* Typhi) Conjugate Vaccine Partnership

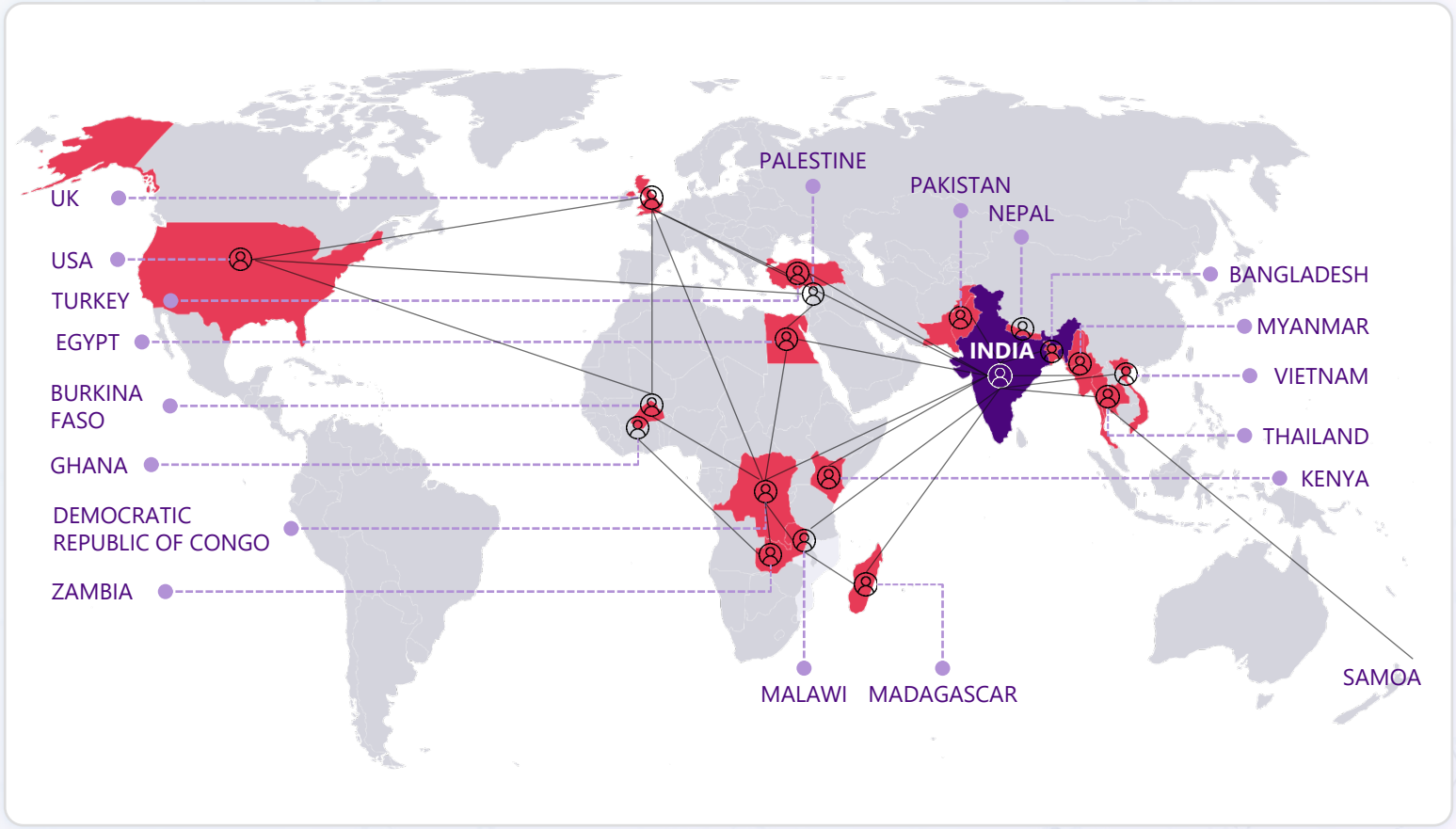
The Partners:

CVD, University of Maryland, Baltimore, USA

Bharat Biotech International Limited, Hyderabad, India

Wellcome Trust, UK

CLINICAL TRIALS CONDUCTED ACROSS THE WORLD



102
CLINICAL TRIALS

ACROSS 20 COUNTRIES

150,000
ADULTS

700,000
VOLUNTEERS

550,000
INFANTS

PARTNERS WORLDWIDE

TYPBAR TCV® EVIDENCE BASED CLINICAL STUDIES

TYPHOID CONJUGATE VACCINE

A conjugate vaccine is a substance that is composed of a polysaccharide antigen fused (conjugated) to a carrier molecule. This enhances the efficacy of the vaccine.

Purity of components

Polysaccharide: **Vi-polysaccharide**- Culturing & processing

Carrier Protein: **High purity Tetanus Toxoid** enhances the conjugation.

De-O-Acetylation

Immunogenicity of Vi is closely related to its **degree of O-acetylation**. Partial de-O-acetylation on Vi enhance immunogenicity due to **hidden epitopes that are revealed**.

Alkaline hydrolysis by sodium carbonate and bicarbonate buffer can do partial de-O-acetylation on ViPS.

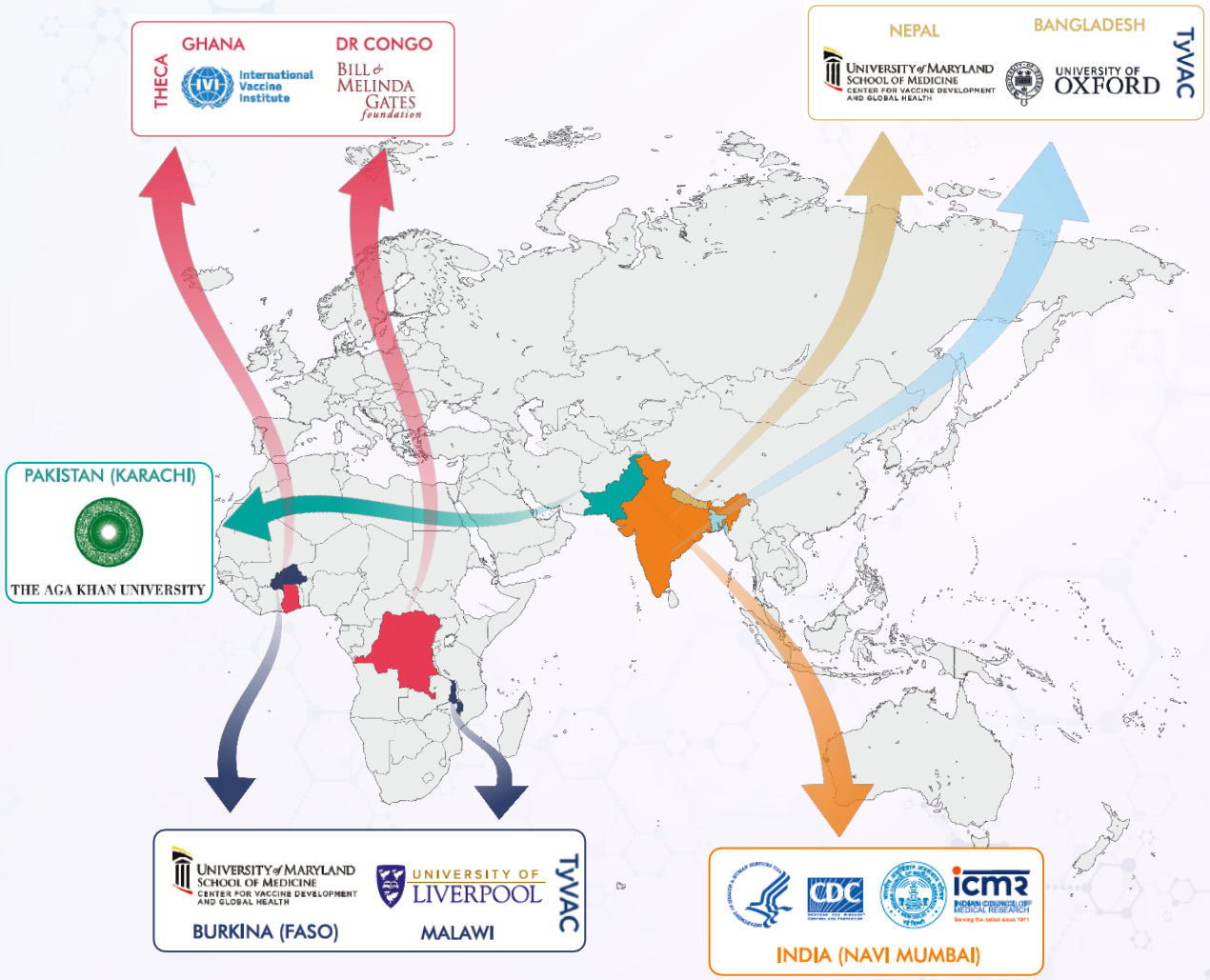
Length of the Polysaccharide

Intermediate Oligo saccharides (11-16 repeated units) gives optimum immunogenicity, compared to shorter and longer polysaccharides.

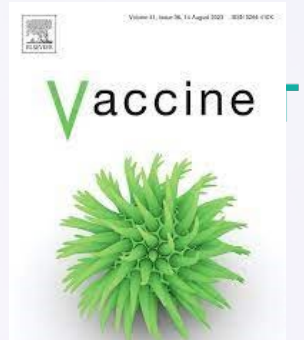
PRE-CLINICAL & CLINICAL DEVELOPMENT

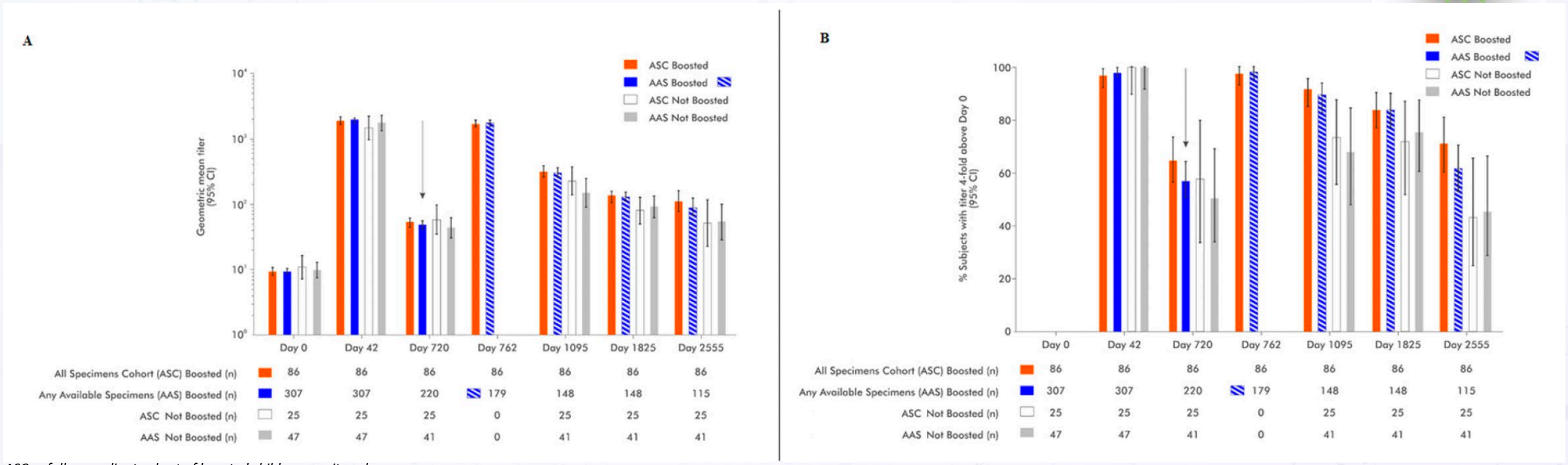
TYPBAR TCV®

EFFECTIVENESS STUDIES ACROSS THE WORLD



LONG TERM IMMUNOGENICITY





ASC: a fully compliant cohort of boosted children monitored over seven years.

Estimating the decline in antibody titers is required to decide the time point of a booster vaccination.

Does Typbar-TCV and other TCVs share the same antibody decay rates?

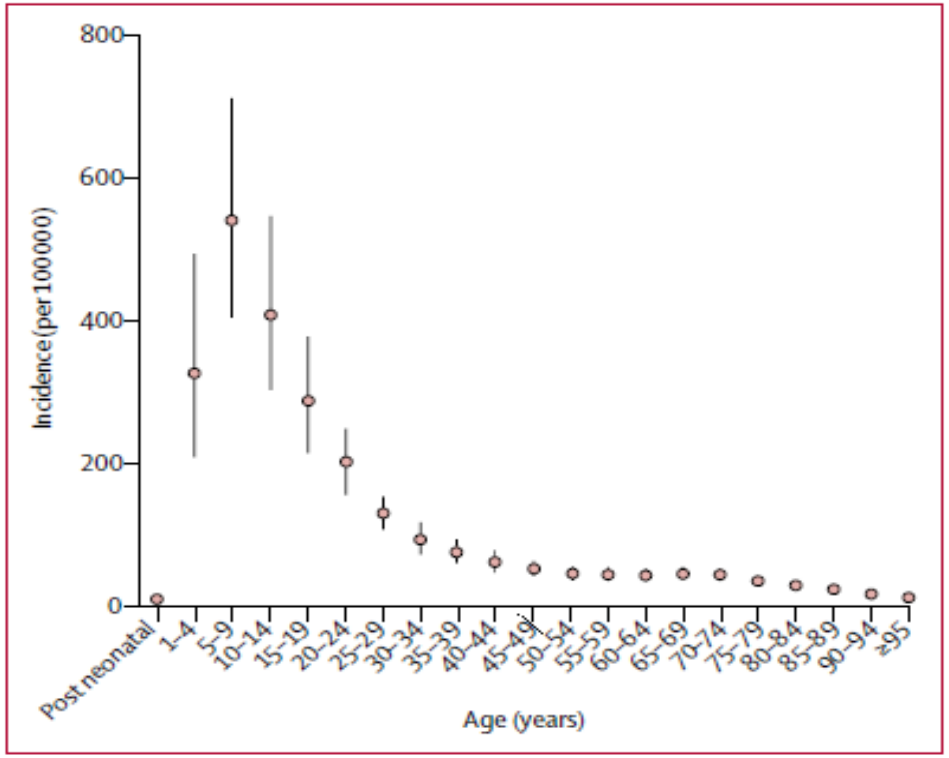
Data Inequity with other TCVs?

10.1016/j.vaccine.2021.07.073

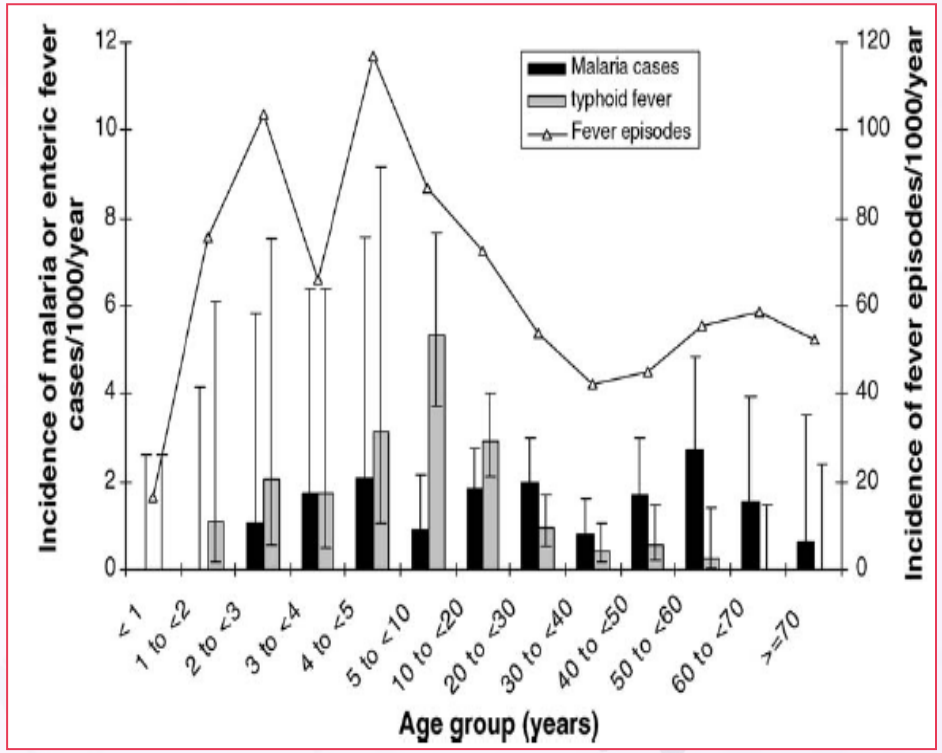
The need for TCVs in Adults

Typhoid Disease Burden

World wide



India



- **Moderate incidence in Older adults**
- **1 to 6 % of patients with typhoid fever become chronic biliary carriers of *Salmonella* Typhi. These carriers are potential factors in the continued transmission of the disease.**

1. Sur D., et al. Trans R Soc Trop Med Hyg. 2006 Aug;100(8):725-33. Epub 2006 Jan 18.
2. Stanaway JD,. et al. Lancet Infect Dis. 2019 Apr;19(4):369-381. doi: 10.1016/S1473-3099(18)30685-6. Epub 2019 Feb 18.
3. Warren D. Johnson. et al., Antimicrobial Agents And Chemotherapy, Mar. 1973, p. 439-440.
4. Zavala Trujillo et al., Eur. J. Clin. Microbiol: Infect. Dis., April 1991, p. 334-341

PHASE IV: ADULTS

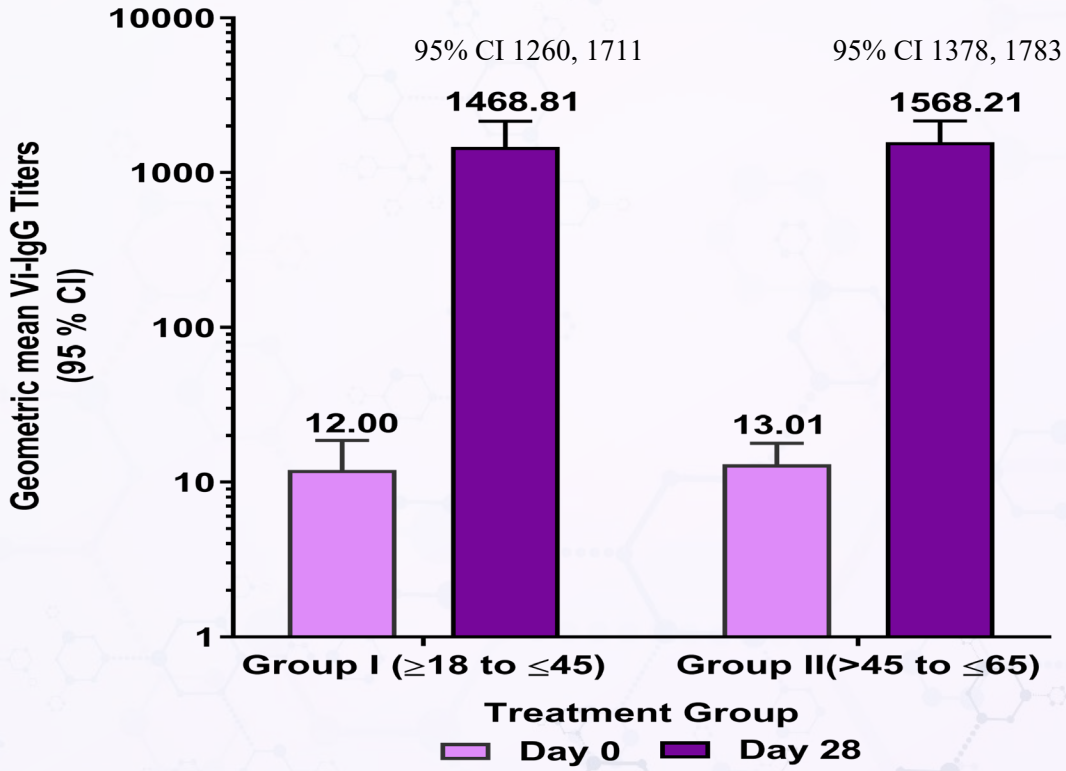
Typbar TCV® is a vaccine **licensed for individuals aged ≥6 months to ≤45 years** to protect against typhoid fever.

As typhoid fever is known to affect people of all ages, a Phase IV Adults study was conducted to test the safety and immunogenicity of Typbar TCV® in adults aged **≥18 to ≤65 years.**

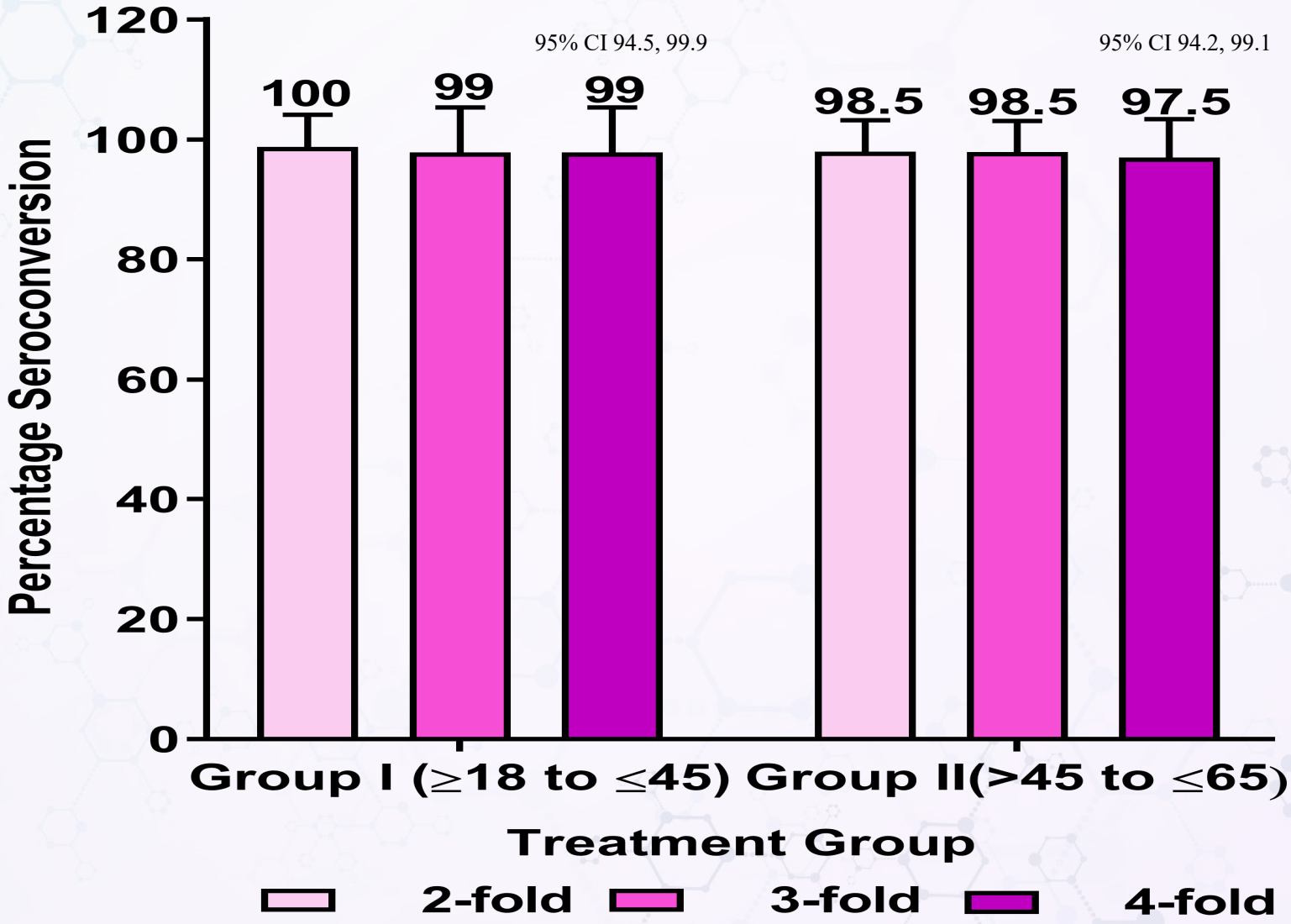
An **open-labeled study** to evaluate the immunogenicity and safety of the Typhoid Conjugate vaccine (Typbar-TCV®) in adults within the age group of ≥18 to ≤65 years

- **300 subjects were enrolled** and randomized to one of the two groups based on the age criteria.
  - ✓ **Group I: ≥18 to ≤45 – 100 subjects**
  - ✓ **Group II: >45 to ≤65 – 200 subjects**
- All subjects received a single dose of Typbar TCV®

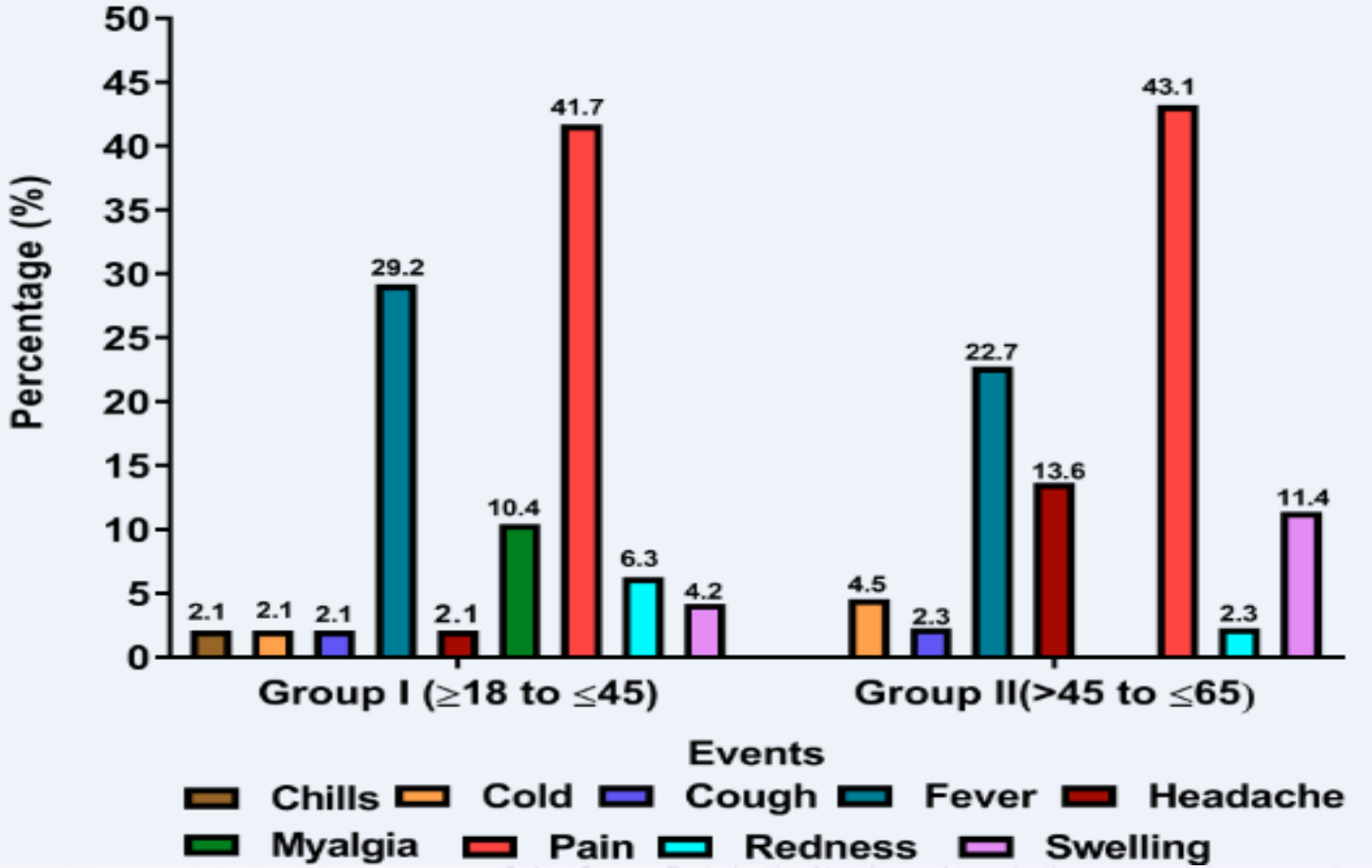
Geometric Mean Titres



Seroconversion



Safety



Conclusion

1. Both treatment groups had comparable immune responses with **no statistically significant difference** detected. Seroconversions and GMTs achieved by Group I were similar to those of Group II.

2. The r**eactogenicity and safety of Typbar-TCV® were comparable** across both groups, with no statistically significant difference regarding solicited and unsolicited adverse events. These findings indicate that Typbar TCV® is well-tolerated, with no significant safety concerns.

3. Typbar TCV® can be safely administered to individuals up to 65 years of age.

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THANK YOU