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
1996

Promoters
Dr. Krishna & Ms. Suchitra Ella

Business Line
5th largest Vaccine Manufacturers (volumes)

First Project
Hepatitis B Vaccine – US $ 3.5 Mn

Investment
Over US $ ~250 Mn

Facility
One of the largest facilities in Asia

Personnel
Over 4000 resources including scientists

Accreditations
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

- BioHiib
- BIOPOLIO® M1
- BIOPOLIO® M3
- BIOPOLIO® B1/3
- ComVac3
- ComVac4 Hb
- ComVac5
- COVAXIN®
- HNVAC®

Biotherapeutics

- INDIRAB®
- JENVAC®
- REVAC-B®
- Revac-B®mcf
- ROTAVAC
- ROTAVAC 5D®
- TYPBAR
- Tybar®TCV®

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OUR PRODUCT PIPELINE

Vaccine Candidate

- Chikungunya
- Zika
- Cholera
- NTS Conjugates
- S. Paratyphi
- HPV
- Sabin IPV
- Malaria (RTS,S)
- SARS COV 2-M2SR
- SARS COV 2-Rabies Vector
- THR-100
- Lysostophin Topical
- Lysostophin IV

Therapeutics

Product Development | Preclinical Testing | Phase-1 | Phase-2 | Phase-3

- Chikungunya
- Zika
- Cholera
- NTS Conjugates
- S. Paratyphi
- HPV
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- Malaria (RTS,S)
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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

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TYPBAR TCV®
EVIDENCE BASED
CLINICAL STUDIES
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 enhances 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

ANIMAL STUDIES

- Rodents & Non-Rodent Studies

DEVELOPMENT

Safety and Immunogenicity

- Phase II (Dose Determination)
- Phase III
- Phase IV (Comparator)
- Phase IV (Non-Interference)
- Phase IV (Adults)
- PMS (Safety)
- Phase II (Burkina Faso)

Efficacy Studies

- Phase IIb (UK)
- Phase III (Malawi)
- Phase III (Nepal)
- Sero-Efficacy (India)

Effectiveness Studies

- PMS Study (Pakistan)
- PHASE IIIb (Bangladesh)
- Navi Mumbai (India)
- Phase-IV (Malawi)
- Zimbabwe

CLINICAL TRIALS ACROSS THE WORLD

- Phase II (Burkina Faso)
- Phase II (Dose Determination)
- Phase III
- Phase III (Nepal)
- Phase III (Malawi)
- Phase IV (Comparator)
- Phase IV (Non-Interference)
- Phase IV (Adults)
- PMS (Safety)
- Phase II (Burkina Faso)
TYPBAR TCV®
EFFECTIVENESS STUDIES ACROSS THE WORLD

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LONG TERM IMMUNOGENICITY

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?

ASC: a fully compliant cohort of boosted children monitored over seven years.
The need for TCVs in Adults
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.

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

95% CI 1260, 1711
95% CI 1378, 1783
Seroconversion

95% CI 94.5, 99.9
95% CI 94.2, 99.1

Percentage Seroconversion

Group I (≥18 to ≤45) Group II(>45 to ≤65)

Treatment Group
- 2-fold
- 3-fold
- 4-fold
Safety

![Safety Chart]

- **Events:**
  - Chills
  - Cold
  - Cough
  - Fever
  - Headache
  - Myalgia
  - Pain
  - Redness
  - Swelling

- **Group I (≥18 to ≤45):**
  - 2.1%
  - 2.1%
  - 2.1%
  - 2.1%
  - 2.1%
  - 6.3%
  - 4.2%
- **Group II (>45 to ≤65):**
  - 4.5%
  - 2.3%
  - 22.7%
  - 13.6%
  - 43.1%
  - 11.4%
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 reactogenicity 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.