Next-Gen Cholera Vaccines

GTFCC OCV Working Group Meeting

Sourabh Sobti

December 5-6th 2018, Annecy, France
HILLCHOL IS AN INNOVATIVE VACCINE WITH STREAMLINED MANUFACTURING PROCESS

PROBLEM STATEMENT

Current prequalified vaccines effective but complex to manufacture:
- 3 or 4 different strains
- Two different inactivation methods

APPROACH

Single vaccine strain (Hikojima) incorporating desirable characteristics of the current Cholera vaccine:
- Ogawa and Inaba dual expression
- Single fermentation run
- One inactivation method
- Efficient process results in lower COGs

SCIENCE

Inaba
- wbeT gene mutated and inactive in Inaba phenotype

Ogawa
- Fully functional wbeT gene

Hikojima
- Partially functional wbeT gene

Co-expression of Inaba and Ogawa serotype antigens

However, no stable Hikojima strains exist in nature

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### Study Objective

- Evaluate and compare the safety following immunization with 2 dose of OCV using WHO-PQ Shanchol as comparator
- To establish Non inferiority of Hillchol vs Shanchol in terms of Vibriocidal response with ~ 840 patients
  - Adult (18-45 years): 360 subjects
  - Young Children and Adolescents (5-17 years): 240 subjects
  - Kids (1-4 years): 240 subjects
- Study cohorts for both test vaccine were powered to demonstrate Non-Inferiority to Shanchol

### Study Centre

- Mirpur field site of icddr,b, Bangladesh

### Study Endpoints

- Proportion of subjects receiving test vaccine or Shanchol with any AE/ SAEs
- Proportion of subjects demonstrating four fold rise vibriocidal response at 14 days after each dose
HILLCHOL HAS BEEN PROVEN SAFE AND NON-INFERIOR IN PHASE I/II CLINICAL TRIALS CONDUCTED BY ICDDR,B IN BANGLADESH

Study Design

- Active controlled randomized study
- Monitored for immunogenicity up to 2 weeks after each dose; for safety up to 1 month after second dose

Study Results

Analysis of safety and immunogenicity results from adult cohort indicate that:

- HL 246 Formulation was safe, and the frequency and severity of adverse events as similar to that of Shanchol.
- The vibriocidal antibody response was elicited by HL 246 formulation, against both Ogawa and Inaba serotypes.
- Immune response elicited by HL246 was non-inferior to that of Shanchol in terms of GMT as evident from GMR & Reverse cumulative curves and also for sero-conversion rates.
- We observed a dose dependent response with high dose (HD) HL246 eliciting superior immune response to that of low dose HL246 (LD).
**HILLEMAN IS IN DISCUSSION WITH PARTNERS TO ACHIEVE WHO PQ BY 2021**

<table>
<thead>
<tr>
<th>MILESTONE</th>
<th>STATUS</th>
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<tbody>
<tr>
<td>Technology Development at scale done in Hilleman Labs</td>
<td>✔️</td>
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<tr>
<td>Pre-clinical and Toxicity studies conducted in Korea</td>
<td>✔️</td>
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<td>Technology Transfer to CMO</td>
<td>✔️</td>
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<tr>
<td>Phase I/II clinical trial in ~ 840 subjects completed at ICDDR, Bangladesh</td>
<td>✔️</td>
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<tr>
<td>In-discussion with DCVM to make GMP Phase III clinical trial material</td>
<td>In-Progress</td>
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<td>Phase III clinical trials to commence by Q3 2019 with licensure by Q4 2020</td>
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<td>WHO-PQ by 2021</td>
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<tr>
<td>Attribute</td>
<td>HL 246</td>
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<tr>
<td><strong>Indication</strong></td>
<td>• Diarrhea caused by Vibrio Cholera</td>
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<td><strong>Active Ingredients</strong></td>
<td>• Whole cell inactivated Stable Hikojima expressing both Inaba and Ogawa LPS</td>
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<td><strong>Dosing</strong></td>
<td>• 2 Oral doses given 14 days apart</td>
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<tr>
<td><strong>Minimum Age</strong></td>
<td>• 1 year</td>
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<td><strong>Duration of Protection</strong></td>
<td>• &gt;3 years</td>
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<td><strong>Presentation</strong></td>
<td>• 2mL liquid in vial or BFS</td>
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<tr>
<td><strong>Current Status</strong></td>
<td>• Completed Phase II</td>
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<td><strong>Notes</strong></td>
<td>• In-discussion with partner to commence Phase III clinical trials</td>
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#Thanks#
HILLEMAN LABS IS A GLOBAL VACCINE R&D ORGANIZATION COMMITTED TO DEVELOPING AFFORDABLE VACCINES FOR PEOPLE IN LOW & MIDDLE INCOME COUNTRIES

- We function as a biotech company translating our innovation into important vaccine products and technology platforms.

- Our focus is on transforming ideas into products and technologies through translational R&D and by building partnerships with vaccine manufacturers.

- Sustainability for funding Hilleman Lab’s R&D
  - Founding contribution from MSD and Wellcome Trust
  - Licensing and Royalty payments
  - Raising project specific funding
  - Grants & Innovative financing

- To date, our focus has been largely on Vaccines and Infectious Disease, technologies and opportunities that meet the unmet needs of the developing world.