Update on Pentavalent Human-Bovine Rotavirus Vaccine

RotaTeq
(Rotavirus Vaccine, Live, Oral, Pentavalent)

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India, September 2014
Outline

• Characteristics of RotaTeq and its worldwide use
• Recent data evaluating correlation between immunogenicity and efficacy
• Introduction in GAVI-eligible countries and activities
• Key clinical trials and events
• Introduction to work being performed by Hilleman Laboratories
### Characteristics of RotaTeq - Worldwide Product Circular

<table>
<thead>
<tr>
<th>Composition:</th>
<th>Human–bovine reassortant</th>
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<tbody>
<tr>
<td>Indications:</td>
<td>Prevention of RGE caused by G1, G2, G3, G4, and G-serotypes that contain P1A[8] (e.g. G9)</td>
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<td>Contraindications:</td>
<td>History of hypersensitivity to vaccine or any vaccine component. Children with history of intussusception and Severe Combined Immunodeficiency Disease (SCID)</td>
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<td>Dosing Schedule:</td>
<td>First dose at 6 to 12 weeks of age, subsequent doses administered at minimum 4-week intervals and all 3 doses completed by 32 weeks of age. Same for preterm infants.</td>
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<td>Concomitant Use:</td>
<td>Can be administered with other routine pediatric vaccines</td>
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<td>Presentation:</td>
<td>Oral, Liquid, Ready to use</td>
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If an incomplete dose is administered (e.g., infant spits or regurgitates the vaccine) a replacement dose should not be administered.
Worldwide Use of RotaTeq

• US Licensure (February 2006)
• Global WHO pre-qualification (March 2010)
• Licensed in >110 countries and ~119 million doses distributed worldwide (as of June 2014)
• Demonstrated safety profile
  • Large, comprehensive pre- and post-licensure studies
    • Global post-licensure spontaneous reporting for > 8 years
• Efficacy in low & high-income countries
  • North America, Europe, Latin America, and Asia
  • GAVI-eligible countries in Africa and Asia
• Gastroenteritis reduction after introduction
  • North America, Europe, Latin America, and Asia
Correlation between Immunogenicity and Efficacy from Clinical Trials of RotaTeq

- Data from clinical trials of RotaTeq were pooled to evaluate association between immunogenicity and efficacy
  - Phase II - P005 (dose-ranging; Finland)
  - Phase III - P006 and P007 (11 industrialized countries)
  - Phase III - P015 (5 GAVI-eligible countries in Asia and Africa)
- Two analyses were conducted
  - Individual subjects from Phase II (P005) and two Phase III studies (P006 and P007)
  - Population level: Aggregated data from all four efficacy trials
Results from Phase II and III Studies

- **Individual subjects**
  - Higher Post Dose (PD) 3 G1 serum neutralization antibody (SNA) titers are associated with lower odds of contracting any rotavirus gastroenteritis (RVGE)

- **Population level**
  - Aggregated data show higher efficacy associated with higher PD3 G1 SNA and PD3 serum anti-RV IgA titers

- **Both individual and aggregated data analyses**
  - PD 3 G1 SNA shows good correlation
  - Single cut-off value that provides high degree sensitivity & specificity not identified

- Among high-income countries, efficacy may be on a plateau over the range of PD3 G1 SNA and PD3 serum anti-RV IgA titers
  - Consistent with conclusion from Patel et al. (JID 2013) that higher efficacy estimates occur when serum anti-RV IgA titer > 90
  - G1 SNA titers not evaluated in Patel et al.

- Future studies needed to support use of PD3 G1 SNA titers as correlate
National Introduction of RotaTeq in GAVI-Eligible Countries
After Introduction of RotaTeq in Nicaragua (2006), Rotavirus is No Longer a Common Cause of Diarrhea

2007-2009
- Evaluation in 5 cities
- Vaccine coverage: 70-92% (3 doses)
- Vaccine effectiveness against severe rotavirus disease resulting in hospitalization or ED visit
  - All ages*: 76% (63,84)†
  - <12 months*: 85% (66,93)†

2010-2011
- Evaluation in 1 city
- Vaccine coverage: 82% (≥1 dose)
- Incidence and frequency of rotavirus in children <2 years via household visits
  - Pre-vaccine: 11.5 episodes*; 12.4%
  - Post-vaccine: 4.2 episodes*; 2.7%

*Age at time of disease onset. Median age=14 months
†2 age-matched control groups: community controls, hospital controls; combined results

Programmatic Evaluation of RotaTeq Implementation in Burkina Faso

October 31, 2013: 16th GAVI-eligible Country to Introduce Rotavirus Vaccine

- Agence de Médecine Préventive (AMP) conducted independent evaluation
- Three activities, all site visits:
  1. Desk review of EPI programmatic and logistic official documents
  2. Interview staff from EPI, Planning & Finance, vaccination partners (WHO, UNICEF) and health care personnel
     - Central, regional and district levels
     - SWOT (strengths, weaknesses, opportunities, threats) structure
  3. Review in-country rotavirus surveillance data
- Specific objectives
  - Document activities conducted before, during and after introduction
  - Identify strengths and weaknesses related to introduction
  - Describe key lessons learned by country
- Results will be published soon
Hilleman Laboratories : Heat-Stable Oral Rotavirus Vaccine

• Hilleman Laboratories is a joint venture between Merck & Co and Wellcome Trust focused on making vaccines for low resource settings
• Based in New Delhi
• Evaluating use of rotavirus strains from RotaTeq
• To develop a new dried vaccine formulation to improve stability, ease of use, transportation and affordability
• Dr. Davinder Gill to present details later in conference