Updates on Rotasiil® development

13th International Rotavirus Symposium
Minsk, Belarus
30 August 2018

Dr Sajjad Desai MD
Serum Institute of India Pvt Limited, Pune
Rotasiil

• Bovine-human reassortant strains received from NIH
• Sterile, pentavalent, lyophilized powder
• 2.5 ml antacid as diluent
• Rotavirus serotypes G1, G2, G3, G4 and G9 at $\geq 10^{5.6}$ FFU/Serotype/dose.
• Three doses at 6, 10 and 14 weeks of age
Serotypes & Severity

• G1, G2, G3, G4 and G9 serotypes cause over 90% of rotavirus disease worldwide

• **G9** – The emerging serotype associated with
  — a significantly longer duration and higher frequency of diarrhea
  — longer duration of vomiting
  — increased hospitalization rate
  — more-severe dehydration

C. Linhares. CID 2006:43; 312–4
Tarun Saluja *Hum Vaccin Immunother*. 2017 Mar; 13(3): 711–716
Linhares et al. 2011
Three dose Schedule

- Natural rotavirus infection confers protection against subsequent infection and
- protection increases with each new infection

[Velázquez et al, NEJM, 1996]
Thermostable vaccine

- Lyophilized vaccine
  - 36 months at 25°C
  - 18 months at 40°C
- Reconstituted Vaccine
  - 5 ±3°C for six hours
- Assures potency during power failures and transport

Recommended storage ≤ 25°C for 30 months

First heat-stable vaccine in the world
Stability of heat stable, live attenuated Rotavirus vaccine (ROTASiLL®)

Sameer P. Naik, Jagdish K. Zade *, Rajendra N. Sabale, Sambhaji S. Pisal, Ravi Menon, Subhash G. Bankar, Sunil Gairola, Rajeev M. Dhere

Serum Institute of India PVT LTD, 212/2, Hadapsar, Pune 411028, India

ABSTRACT

Vaccines currently available across the globe are stored and transported in a continuous cold-chain at 2–8 °C or below −20 °C. A temperature excursion outside this range affects the potency of the vaccines. Such vaccines need to be discarded leading wastage. The Rotavirus disease burden is predominantly reported in developing and low-income countries and therefore, has entered or poised to enter their national immunization programs. These countries already have several limitations for effective storage, maintenance and distribution of vaccines in a cold-chain and this introduction is expected to further stress this fragile ecosystem. To help mitigate the cold chain related issues, SIIPL has developed a thermostable rotavirus vaccine ROTASiLL®, which can be stored at a temperature below 25 °C for 36 months, completely by-passing the standard 2–8 °C cold storages. In addition it has the capability to withstand temperatures of 37 °C and 40 °C for 18 months and short term exposure to 55 °C. It can also tolerate a temperature shock of being thawed from an extreme cold temperature of −20 °C to a high temperature of 42 °C. The vaccine contains serotypes G1, G2, G3, G4 and G9 (UK-Bovine reassortant strains procured from National Institute of Health-USA). The vaccine is recently licensed in India.

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Economic impact of thermostable vaccines

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\textsuperscript{d} Médecins Sans Frontières, Geneva, Switzerland
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\textbf{Abstract}

\textbf{Background:} While our previous work has shown that replacing existing vaccines with thermostable vaccines can relieve bottlenecks in vaccine supply chains and thus increase vaccine availability, the question remains whether this benefit would outweigh the additional cost of thermostable formulations.

\textbf{Methods:} Using HERMES simulation models of the vaccine supply chain for the Republic of Benin, the state of Bihar (India), and Niger, we simulated replacing different existing vaccines with thermostable formulations and determined the resulting clinical and economic impact. Costs measured included the costs of vaccines, logistics, and disease outcomes averted.

\textbf{Results:} Replacing a particular vaccine with a thermostable version yielded cost savings in many cases even when charging a price premium (two or three times the current vaccine price). For example, replacing the current pentavalent vaccine with a thermostable version without increasing the vaccine price saved from $366 to $10,945 per 100 members of the vaccine's target population. Doubling the vaccine price still resulted in cost savings that ranged from $300 to $10,706, and tripling the vaccine price resulted in cost savings from $234 to $10,468. As another example, a thermostable rotavirus vaccine (RV) at its current (year) price saved between $131 and $1065. Doubling and tripling the thermostable rotavirus price resulted in cost savings ranging from $102 to $936 and $73 to $808, respectively. Switching to thermostable formulations was highly cost-effective or cost-effective in most scenarios explored.

\textbf{Conclusion:} Medical cost and productivity savings could outweigh even significant price premiums charged for thermostable formulations of vaccines, providing support for their use.

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United States Patent

Dhere et al.

STABLE, DRIED ROTAVIRUS VACCINE, COMPOSITIONS AND PROCESS FOR PREPARATION THEREOF

Inventors: Rajeev M. Dhere, Pune (IN); Sambhaji S. Pital, Pune (IN); Jagdish K. Zade, Pune (IN)

Assignee: Serum Institute of India, Pune (IN)

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 493 days.

Appl. No.: 13/056,557

PCT Filed: Nov. 6, 2009

Patent No.: US 8,795,686 B2

Date of Patent: Aug. 5, 2014

Field of Classification Search
None

See application file for complete search history.

References Cited
U.S. PATENT DOCUMENTS

2008/0274197 A1 11/2008 Mizuno

FOREIGN PATENT DOCUMENTS

WO WO 02/09749 * 2/2002

OTHER PUBLICATIONS
USPTO announced humanity award to NIH patent for rotavirus vaccine developed in partnership with SIIPL

USPTO Announces 2018 Patents for Humanity Winners

August 9, 2018  Press Release 10-15

WASHINGTON—The United States Patent and Trademark Office (USPTO) today announced the latest winners of the Patents for Humanity program. The Patents for Humanity program was launched by the USPTO in February 2012 as part of an initiative promoting game-changing innovations to address long-standing development challenges.

“Each of these recipients showcases the power of innovation to help the less fortunate around the globe,” said Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark

U.S. National Institutes of Health

Rotavirus is a disease that affects nearly every child worldwide. While most cases have mild symptoms, it is responsible for one third of infant hospitalizations for severe diarrhea and kills an estimated 200,000 children a year, mostly in developing countries. Researchers at the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) developed vaccine formulations to address the six most common forms of rotavirus. In 2005, they partnered with the Serum Institute of India Limited (SIIIL), one of the largest vaccine manufacturers in the world, to produce the affordable RotaSIIL vaccines in India for use in developing countries. The vaccine is suitable for use in developing countries, lasting up to two years without refrigeration. The government of India has ordered 3.8 million doses for their Universal Immunization Programme.
Need for antacid

- Rotaviruses are acid labile viruses.
- To protect the attenuated vaccine in the gastric acid, the acid needs to be neutralized.
- Rotasiil has 2.5 ml antacid as diluent.
- Ensures survival of vaccine virus during gastric pH.
## Preclinical & Clinical Development

<table>
<thead>
<tr>
<th>Phase</th>
<th>Objective</th>
<th>Number of doses</th>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity</td>
<td>Safety</td>
<td>Single and repeated</td>
<td>Rabbits and Rats</td>
</tr>
<tr>
<td>I</td>
<td>Safety</td>
<td>1</td>
<td>Adults</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Toddler</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infant</td>
</tr>
<tr>
<td>II</td>
<td>Safety, Immunogenicity</td>
<td>3</td>
<td>Infant</td>
</tr>
<tr>
<td></td>
<td>Safety, Immunogenicity</td>
<td>3</td>
<td>Infant</td>
</tr>
<tr>
<td>III</td>
<td>Efficacy, Safety</td>
<td>3</td>
<td>Infant (India)</td>
</tr>
<tr>
<td>III</td>
<td>Efficacy, Safety</td>
<td>3</td>
<td>Infant (Niger)</td>
</tr>
<tr>
<td>III</td>
<td>Lot-to-Lot consistency</td>
<td>3</td>
<td>Infant (India)</td>
</tr>
<tr>
<td>III</td>
<td>Non-interference with EPI vaccines</td>
<td>3</td>
<td>Infant (India)</td>
</tr>
</tbody>
</table>
Bovine rotavirus pentavalent vaccine development in India

Jagdish K. Zade, Prasad S. Kulkarni *, Sajjad A. Desai, Rajendra N. Sabale, Sameer P. Naik, Rajeev M. Dhere

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Serum Institute of India Ltd.
Development
Clinical trials

A B S T R A C T

A bovine rotavirus pentavalent vaccine (BRV-PV) containing rotavirus human-bovine (UK) reassortant strains of serotype G1, G2, G3, G4 and G9 has been developed by the Serum Institute of India Ltd, in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), USA. The vaccine underwent animal toxicity studies and Phase I and II studies in adults, toddlers and infants. It has been found safe and immunogenic and will undergo a large Phase III study to assess efficacy against severe rotavirus gastroenteritis.

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Phase III efficacy clinical trials

• Two studies: One in India and another in Niger (MSF)
• Similar study designs
• Sample size
  ▪ India – 7500
  ▪ Niger – 7770
• Storage in Niger
  ▪ ≤ 25°C in Maradi
  ▪ Ambient temperature at dispatch to vaccination sites

https://www.youtube.com/watch?v=cK8Wpixu2WA
# Niger Clinical Trial Results

## Vaccine Efficacy

<table>
<thead>
<tr>
<th>Type of Gastroenteritis</th>
<th>RotaSIIL</th>
<th>Placebo</th>
<th>Vaccine Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe RVGE</td>
<td>6</td>
<td>27</td>
<td><strong>78.8%</strong></td>
</tr>
<tr>
<td>SRVGE</td>
<td>31</td>
<td>87</td>
<td><strong>66.7%</strong></td>
</tr>
</tbody>
</table>


## Vaccine Safety

<table>
<thead>
<tr>
<th>Events</th>
<th>RotaSIIL</th>
<th>Placebo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAE</td>
<td>395</td>
<td>419</td>
<td>0.36</td>
</tr>
</tbody>
</table>

One participant had confirmed intussusception, 542 days after receiving the third dose of RotaSIIL.

Vaccine 36 (2018) 3674–3680
Efficacy of a Low-Cost, Heat-Stable Oral Rotavirus Vaccine in Niger

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Brian D. Pikayis, M.Sc., Nathan Sayinzoga-Makombe, M.P.H.,
Monica M. McNeil, M.Sc., Nicole Meyer, M.Sc., Eric Adevori, M.D.,
Ali Djibo, M.D., Bruno Jochem, M.S., and Rebecca F. Grais, Ph.D.

ABSTRACT

BACKGROUND
Each year, rotavirus gastroenteritis is responsible for about 37% of deaths from diarrhea among children younger than 5 years of age worldwide, with a disproportionately high rate in sub-Saharan Africa.

METHODS
We conducted a randomized, placebo-controlled trial in Niger to evaluate the efficacy of a live, oral bovine rotavirus pentavaccine (BRV-PV, Serum Institute of India) to prevent severe rotavirus gastroenteritis. Healthy infants received three doses of the vaccine or placebo at 6, 10, and 14 weeks of age. Episodes of gastroenteritis were assessed through active and passive surveillance and were graded on the basis of the score on the Vesikari scale (which ranges from 0 to 20, with higher scores indicating more severe disease). The primary end point was the efficacy of three doses of vaccine as compared with placebo after a first episode of laboratory-confirmed severe rotavirus gastroenteritis (Vesikari score ≥11) beginning 28 days after dose 3.

RESULTS
Among the 3588 infants who were included in the per-protocol efficacy analysis, there were 31 cases of severe rotavirus gastroenteritis in the vaccine group and 87 cases in the placebo group (2.4 vs. 6.4 cases per 100 person-years, respectively), for a vaccine efficacy of 65.7% (95% confidence interval [CI], 49.9 to 77.9). Similar efficacy was seen in the intention-to-treat analyses, which showed a vaccine efficacy of 69.1% (95% CI, 55.0 to 78.7). There was no significant between-group difference in the risk of adverse events, which were reported in 68.7% of the infants in the vaccine group and in 67.2% of those in the placebo group, or in the risk of serious adverse events (in 8.3° in the vaccine group and in 9.1% in the placebo group); there were 27 deaths in the vaccine group and 22 in the placebo group. None of the infants had confirmed intussusception.

CONCLUSIONS
Three doses of BRV-PV, an oral rotavirus vaccine, had an efficacy of 66.7% against severe rotavirus gastroenteritis among infants in Niger. (Funded by Médecins sans Frontières Operational Center and the Kavli Foundation; ClinicalTrials.gov number, NCT02145000.)

Safety of a heat-stable rotavirus vaccine among children in Niger: Data from a phase 3, randomized, double-blind, placebo-controlled trial

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b Siprotein, Maradi, Niger
c Centre Suisse Projetaires, 78 rue de Lausanne, Geneva, Switzerland

ABSTRACT

Background: Rotavirus remains a major cause of diarrhea among children under 5 years of age. The efficacy of RotaSILIL, a pentavalent rotavirus vaccine, was shown in an event-driven trial in Niger. We describe the two-year safety follow-up of this trial.

Methods: Follow-up of safety outcomes began upon administration of the first dose of RotaSILIL or placebo. Adverse events were followed until 28 days after the third dose, and serious adverse events were followed until 2 years of age. Skeptical cases of intussusception were evaluated at first point of contact and then referred to hospital for surgical evaluation. Causes of death were obtained by chart review and verbal autopsy. Passive surveillance was carried out in health centers. Community health workers carried out active surveillance in villages. Between-person differences were evaluated using the chi-squared test and Fisher’s exact test.

Results: A total of 4092 children were randomized, and 4086 received at least one dose of RotaSILIL or placebo, constituting the intention-to-treat population. A total of 3835 child-years of follow-up time. At two years of follow-up, 58 (2.8%) participants who received RotaSILIL and 49 (2.4%) participants who received placebo had died (p 0.36). Most deaths were due to infectious causes common to the study area. One participant had confirmed intussusception, 542 days after receiving the third dose of RotaSILIL. A total of 395 (19.3%) participants receiving RotaSILIL and 419 (20.5%) participants receiving placebo experienced any serious adverse event (p 0.36). Most serious adverse events were hospitalizations due to infection (malaria, lower respiratory tract infection and gastroenteritis) or marasmus. Overall, 1474 (72.3%) participants receiving RotaSILIL and 1456 (71.1%) participants receiving placebo had at least one adverse event (p 0.49) in the follow-up period.

Conclusions: At two years of follow-up, RotaSILIL was found to be safe.

Trial registration: ClinicalTrials.gov: NCT02145000.
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## Indian Clinical Trial Results

### Vaccine efficacy (Primary Analysis)

<table>
<thead>
<tr>
<th>Type of Gastroenteritis</th>
<th>Rotasiil (n=3749)</th>
<th>Placebo (n=3751)</th>
<th>Vaccine Efficacy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe RVGE</td>
<td>10</td>
<td>25</td>
<td>60.5 %</td>
<td>0.0131</td>
</tr>
<tr>
<td>SRVGE</td>
<td>61</td>
<td>94</td>
<td>36.0 %</td>
<td>0.0067</td>
</tr>
</tbody>
</table>

### Vaccine efficacy (Final Analysis)

<table>
<thead>
<tr>
<th>Type of Gastroenteritis</th>
<th>Rotasiil</th>
<th>Placebo</th>
<th>Vaccine Efficacy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very severe RVGE</td>
<td>29</td>
<td>63</td>
<td>54.7 %</td>
<td>0.0004</td>
</tr>
<tr>
<td>SRVGE</td>
<td>171</td>
<td>275</td>
<td>39.5 %</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Better efficacy even in very severe RVGE - the highest risk of dehydration, hospitalization and deaths
A randomized Phase III clinical trial to assess the efficacy of a bovine-human reassortant pentavalent rotavirus vaccine in Indian infants


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b PATH, Delhi, India
c Hinda Sadaba Rural Hospital, Vadu, India
d Center for Health Research & Development, Society for Applied Studies, New Delhi, India
e Mahatma Gandhi Institute of Medical Sciences, Sevagram, India
f Government Medical College, Jammu, India
g National Institute of Cholera & Enteric Diseases, Kolkata, India
h Kasturba Medical College, Manipal, India
i Christian Medical College, Vellore, India
j PATH, Washington D.C., United States
k DignoSearch Pvt Ltd, Mumbai, India

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Vaccine
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ABSTRACT

Rotavirus is the most common cause of moderate-to-severe infant diarrhoea in developing countries, resulting in enormous morbidity, mortality, and economic burden. A bovine-human reassortant pentavalent rotavirus vaccine (BRV-PV) targeting the globally most common strains was developed in India and tested in a randomized, double-blind, placebo-controlled end-point driven Phase III efficacy clinical trial implemented at six sites across India. Infants 6 to 8 weeks of age were randomized (1:1) to receive three oral doses of BRV-PV or placebo at 6, 10, and 14 weeks of age along with routine vaccines. Home visit surveillance was conducted to detect severe rotavirus gastroenteritis (SVRG) and safety outcomes until the children reached two years of age. A total of 3749 infants received BRV-PV while 3751 received placebo. At the time of the primary end-point (when the minimum number of cases needed for analysis were accrued) the vaccine efficacy against SVRGE was 36% (95% CI 11.7, 53.6, p = 0.0067) in the per protocol (PP) analysis, and 41.9% (95% CI 21.1, 57.3, p = 0.0005) in the intent to treat (ITT) analysis. Vaccine efficacy over the entire follow-up period (until children reached two years of age) was 35.5% (95% CI 26.7, 40, p < 0.0001) in the PP analysis and 38.8% (95% CI 26.4, 49, p < 0.0001) in the ITT analysis. Vaccine efficacy against the very severe rotavirus cases (SVRGE, Vesilari score ≥ 16) was 60.5% (95% CI 17.7, 81, p = 0.0131) at the time of the primary analysis and 54.7% (95% CI 29.7, 70.8, p = 0.0004) for the complete follow-period in the PP population. The incidence of solicited, unsolicited, and serious adverse events were similar in both the vaccine and placebo groups. Likewise, the number of intussusceptions and deaths were similar between both groups. Thus, BRV-PV is an effective, well tolerated and safe vaccine in Indian infants. (Trial registration: Clinical Trials.gov [NCT 02133090] and Clinical Trial Registry of India [CTRI/2013/05/003867]).
## Comparative Efficacy

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Country</th>
<th>SRVGE</th>
<th>Very severe RVGE</th>
<th>RVGE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ITT%</td>
<td>95% CI</td>
<td>PP %</td>
</tr>
<tr>
<td>RotaTeq</td>
<td>Africa</td>
<td>40.3</td>
<td>(20.6, 55.3)</td>
<td>40.7</td>
</tr>
<tr>
<td></td>
<td>Asia</td>
<td>47.8</td>
<td>(21.9, 65.6)</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>Mali</td>
<td>1</td>
<td>(-431.7 , 81.6)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Bangladesh</td>
<td>42.7</td>
<td>(10.4, 63.9)</td>
<td>-</td>
</tr>
<tr>
<td>Rotarix</td>
<td>Malawi</td>
<td>44.7</td>
<td>(19.2, 68.5)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Bangladesh</td>
<td>48</td>
<td>(27, 63)</td>
<td>-</td>
</tr>
<tr>
<td>ROTAVAC</td>
<td>India</td>
<td>54.7</td>
<td>(37.2–67.3)</td>
<td>54.4</td>
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<tr>
<td>BRV-PV</td>
<td>India</td>
<td>41.7</td>
<td>(21.1, 57.3)</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Niger</td>
<td>69.1</td>
<td>(55.0, 78.7)</td>
<td>78.8</td>
</tr>
</tbody>
</table>

Armah GE et al 2010; Zaman K et al 2010

Results comparable to other rotavirus vaccines
Phase III EPI Study

- 1500 infants in India
- Lot-to-lot consistency was demonstrated
- No interference with EPI vaccines was seen
- IgA GMCs were 19.16 (95% CI 17.37 – 21.14) in the combined Rotasiil group and 10.92 (95% CI 9.36 – 12.74) in the Rotarix® group
Non-interference of Bovine-Human reassortant pentavalent rotavirus vaccine ROTASIL® with the immunogenicity of infant vaccines in comparison with a licensed rotavirus vaccine

Sajjad Desai a, Niraj Rathi b, Anand Kawade c, Padmasani Venkatraman d, Ritabrata Kundu e, Sanjay K. Lalwani f, A.P. Dubey g, J. Venkateswara Rao h, D. Narayanappa i, Radha Ghildiyal j, Nithya J Gogtay k, P. Venugopal l, Sonali Palkar m, Renuka Munshi n, Ashish Bavdekar o, Sanjay Juvekar c, Nupur Ganguly c, Prabal Niyogi c, Kheya Ghosh Uttam c, Alpana Kondekar p, Dipti Kumbar r, Smilu Mohanlal s, Mukesh C. Agarwal t, Parvan Shetty u, Kalpana Antony v, Bhagwat Ganale w, Abhijeet Dharmadhikari x, Jagdish Deshpande y, Uma Navalade z, Deepa Sharma m, Anurag Bansal n, Yuxiao Tang o, Jorge Flores p, Prasad S. Kulkarni a, b

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bPATH, India
cVadu Rural Health Program KEM Hospital Research Centre Vadu, Pune, India
dSri Ramachandra Medical Centre, Chennai, India
eInstitute of Child Health, Kolkata, India
fBharati Vidyapeeth Medical College & Hospital, Pune, India
gManipal Arad Medical College, New Delhi, India
hGandhi Medical College & Gandhi Hospital, Secunderabad, India
iJSS Medical College & Hospital, Mysore, India
jT.N. Medical College & B.V.L. Nar Charitable Hospital, Mumbai, India
kSeth GS Medical College & KEM Hospital, Mumbai, India
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Bovine-human reassortant pentavalent rotavirus vaccine (BRV-PV) DTwP-HepB-Hib vaccine Oral polio vaccine (OPV) Interference Immune response

A B S T R A C T

Background: A newly developed bovine-human reassortant pentavalent vaccine (BRV-PV, ROTASIL®) was tested for its potential effect on the immunogenicity of concomitantly administered EPI vaccines in infants in a randomized controlled study in India.

Methods: In this Phase III, multicenter, open label, randomized, controlled study, three doses of BRV-PV or two doses of Rotarix® and one dose of placebo were given to healthy infants at 6, 10, and 14 weeks of age. Subjects also received three doses of DTwP-HepB-Hib (diphtheria, tetanus, whole-cell pertussis, hepatitis B, and haemophilus influenzae type b conjugate – pentavalent vaccine) and oral polio vaccine concomitantly at 6, 10, and 14 weeks of age and a single dose of inactivated polio vaccine at 14 weeks of age. Blood samples were collected four weeks after the final vaccination to assess immune responses to all the vaccines administered. For diphtheria, tetanus, hepatitis B, Hib, polio type 1, and polio type 3 antibodies, non-interference was to be supported if the lower limit of the two-sided 90% confidence interval (CI) for the seroprotection rate difference for the BRV-PV group minus the Rotarix® group was >10.0%. For pertussis antibodies, non-interference was to be supported if the lower limit of the two-sided 90% CI for the ratio of geometric mean concentrations (GMCs) was >0.5.

Results: A total of 1500 infants were randomized to either BRV-PV (7125 infants) or Rotarix® (7875 infants), of which 1341 completed the study as per the protocol. More than 97% of subjects achieved seroprotective antibody titres against diphtheria, tetanus, hepatitis B, Hib, polio type 1, and polio type 3 in
Current Status

- Licensed in India in December 2016.
- Introduced in EPI in Jharkhand in April 2018.
- > 1 million doses distributed
- Three PSURs prepared so far; no safety concern reported
- Phase IV studies planned
Live, Liquid Pentavalent Rotavirus vaccine
Product Profile

- Ready-to-use liquid vaccine with same strains and manufacturing process as Rotasiil
- Volume 2 ml, Stored at 2-8° C
<table>
<thead>
<tr>
<th>Phase</th>
<th>No. of doses</th>
<th>Vaccine recipients</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity</td>
<td>Single and repeated</td>
<td>Rabbits and Rats</td>
<td>Completed</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>Adults</td>
<td>Completed</td>
</tr>
<tr>
<td>II/III</td>
<td>3</td>
<td>Infants</td>
<td>Completed; analysis ongoing</td>
</tr>
</tbody>
</table>
Short communication

Safety and tolerability of a liquid bovine rotavirus pentavalent vaccine (LBRV-PV) in adults

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A R T I C L E   I N F O

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Adults
Safe
Phase I

A B S T R A C T

Background: Rotavirus Gastroenteritis (RVGE) is an important global public health problem. Recently a Lyophilized Pentavalent Human Bovine Reassortant Rotavirus vaccine (BRV-PV, RotaSII) was licensed in India. A Liquid formulation of the same vaccine (LBRV-PV) was tested in a Phase I clinical trial.

Methods: Total 20 healthy adults were given a single oral dose of LBRV-PV and were followed for one month for safety outcomes: immediate reactions, solicited reactions, unsolicited adverse events and serious adverse events.

Results: All 20 adults completed the study without any major protocol deviations. No immediate reaction, solicited reactions and unsolicited adverse events were reported during the study. No clinically significant changes were seen in the vital parameters and safety laboratory test results.

Conclusions: LBRV-PV developed in India was safe and well tolerated in adults. Further clinical development of this vaccine in infants should be undertaken.

Conclusions: Trial Registration – CTRI/2015/11/006384.
Summary

- Rotasiil is found highly safe and efficacious
- No safety concern reported since licensure
- Liquid formulation – Phase II/III trial results are awaited
Acknowledgement

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Quest Diagnostics

DSMB Members

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Thank You