ROTARIX™
the human rotavirus vaccine:
is applied in a 2-dose schedule-
completes the course at the earliest possible age,
prevents morbidity and mortality from RV GE
regardless of the circulating strains

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Global efficacy of HRV

1-2 year follow-up

Severe RVGE: Vesikari score = ≥11; *follow-up over 2 years
Severe RVGE: requiring hospitalization and / or rehydration therapy at medical facilities
VE, vaccine efficacy

**Rotarix™ – product profile**

- **Live-attenuated human** virus, G1P[8] strain (RIX4414)\(^1,2\)
- Launched in more than 130 countries, more than 130 mill of doses have been administrated since 2004
- **Oral** vaccine: either lyophilized (1 mL), or liquid (1.5 mL)\(^1\)
- Vaccine concentration: 10\(^6\) median Cell Culture Infective Dose (CCID\(_{50}\))\(^1\)
- Two doses:\(^1\)
  - First dose as early as 6 weeks of age
  - Second dose completed by 24 weeks (preferably before 16 weeks)
  - Minimum interval between doses: 4 weeks
- Co-administration with other vaccines\(^1-3\)
  - Diphtheria-tetanus-whole cell pertussis (DTPw), diphtheria-tetanus-acellular cell pertussis (DTPa), hepatitis B vaccine (HBV), Haemophilus influenzae type B (Hib), inactivated polio vaccine (IPV), oral polio vaccine (OPV), meningitis C, Streptococcus pneumoniae
- **3 year shelf life**
  - the vaccine is stable at high temperatures of 37\(^\circ\) C for up to 7 days\(^1\)

\(^1\) Rotarix™. Summary of Product Characteristics, 2012; \(^2\) Dennehy PH et al. Pediatrics 2008; **122**: e1062–6; \(^3\) Steele AD et al. Vaccine 2008; Sep 8 [Epub].
Key clinical features

- Rotarix has demonstrated efficacy against several fully heterotypic strains, providing evidence of broad protection against rotavirus currently circulating. 1
- Rotarix has demonstrated sustained high levels of protection for 3 years, with evidence of minimal waning immunity. 2
- There is increasing evidence that widespread vaccination with Rotarix can result in herd protection, thereby enhancing the benefits of vaccination beyond the expected population based on trial data alone. 3
- Rotarix vaccination has a substantial impact on all cause gastroenteritis, reducing hospitalisation for gastroenteritis by 72% over a 2-year period in a European study. This highlights the significance of rotavirus as a causative agent. 4
- Rates of nosocomial rotavirus infection have substantially decreased by ~67% and ~87% in Austria and urban Australia respectively after rotavirus universal mass vaccination. 5, 6

Countries with rotavirus vaccination in childhood immunization calendar*

Both vaccines
Belgium
Germany (5 Federal States)

Rotarix™:
Luxemburg
Austria
Italy (Sicily)
Croatia (Risk patient)

RotaTeq™:
Finland
Israel

Both vaccines
USA,
Mexico.

Rotarix™:
Canada (Ontario + Quebec 11/2011)
Brazil,
El Salvador,
Panama,
Venezuela,
Ecuador,
Peru,
Colombia
Bolivia (GAVI)
Paraguay (2010)
Guatemala
Dominican Rep.

RotaTeq™:
Nicaragua (GAVI)
Guyana (GAVI)
Cayman Islands

Countries without national RV immunization

Countries with national/regional Rotarix™ immunization

Countries with national/regional RotaTeq™ immunization

Coming soon:
• Several GAVI-eligible countries

Rotarix™
Palau
Micronesia
Fiji
Philippines

RotaTeq™
Iraq

Rotarix™:
Bahrain
Qatar
Yemen (GAVI)
Saoudi

RotaTeq™:
Morocco
NorthSudan (GAVI)
South Africa
Ghana (GAVI)
Botswana

More specific information in notes below.

*as of 18/07/2011

1. Saxony, Mecklenburg-vorpommen, Thuringia, Branbenbrug, Schleswig-Holstein
2. Pre-terms before 33wk of age, Children with congenital heart disorder, with congenital metabolic diseases, with liver and kidney diseases, with severe CNS impairment.
Six HRV post-licensure controlled effectiveness studies

- Significant protection against rotavirus-associated hospitalization was observed in four of these studies ranging from 76 to 85% \(^{11}\).
- The effectiveness study in Belgium has shown that two doses of Rotarix offer vaccine effectiveness (overall), 91% (75% to 97%) \(^{12}\)

Twelve HRV post-licensure observational studies

- Active surveillance in sentinel centres
  - Belgium\(^{1}\), Australia\(^{2}\), Brazil\(^{3,4}\) South Africa\(^{10}\)
    - 35–93% reduction in RV GE-associated hospitalizations
    - substantial decline in gastroenteritis associated with rotavirus infection (i.e. 67%) among South African children aged 5 years\(^{10}\)
  - Passive surveillance in Australia\(^{5}\), Panama\(^{6}\), Mexico\(^{7}\), Brazil\(^{8}\)
    - 11–40% reduction in GE-associated hospitalizations
  - Reduction in GE-associated deaths
    - 22–33% reduction in diarrhea-related mortality\(^{3,8}\)


\(^{11}\)O’Ryan M et al. Expert Rev Vaccines 2011;\(^{12}\)T.Braeckman BMJ 2012;345:
RV positive test after universal RV vaccination in Belgium by birth cohorts (inpatient only)

- RV vaccination reimbursed in Belgium since November 2006
- Using **1 September 2006** as the birth date to categorise children with or without opportunity to receive RV vaccination, data show a **decline in the number of RV-positive samples across successive birth cohorts**

![Graph showing decline in RV-positive tests across birth cohorts](image)

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RV=rotavirus
Adapted from Raes M *et al.* PIDJ 2011; 30: e120–5.
The value of Rotarix™

**UNIQUE ATTRIBUTES OF ROTARIX™**

HumanRV¹
Two-dose schedule¹

**ADVANTAGES OF TWO-DOSE ROTARIX™**

Full course completed by 10 weeks of age¹
convenient in two doses

Full protection from a younger age
Potential for greater compliance³
Time, storage space and cost savings

Fewer potential cases of RV

High value potential of Rotarix™

• Potential reduction of disease burden
• Potential cost of illness reduction

Reduced cost of implementing a vaccination programme²

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Seropositivity rates at pre-dose-1 from 46,398 infants analyzed from 16 GSK sponsored studies, of which 20,099 infants had received at least one dose of placebo.

- The estimates for Vaccine Efficacy seem to be different in various regions of the world; probably due to the high level of exposure early during the first months in developing countries.
- Early protection in UMV is important to help reduce the number of infections.

Numbers on top of the bars indicate mean age with standard deviation at pre-dose-1 time point.

Htay Htay Han, PV Suryakiran, Serge Debrus, Bernd Benninghoff  WSPID - November 18-22, 2009, Buenos Aires, Argentina.
Rotarix 2 dose schedule can complete the course as early as possible

- To be optimally effective and cost-effective, a vaccination schedule should aim to induce immunity with the fewest number of doses before a sizeable proportion of the target population acquires natural infection. In countries, where natural infection occurs early, completion of the immunization schedule early in infancy is desirable.
Conclusions

• Pre-licensure trials with HRV showed high efficacy rates against clinically significant RVGE

• Post-licensure: HRV has had significant impact in reducing severe RVGE, reduced the number of deaths due to RVGE and demonstrate cost savings linked to the routine implementation of rotavirus vaccination

• Rotarix is cost effective and reduces hospitalisations/mortality and resource utilisation; in some countries Rotarix is cost-saving from a societal perspective

• Real life data continues to confirm that Rotarix results in good compliance and earlier completion with a two does schedule

• The main challenge is to increase RV vaccine use in National Vaccine Programs, especially in less developed countries – where early protection should be most impactful