



Worldwide Post Marketing Experience with Rotarix™

European Expert Meeting on Rotavirus Vaccination

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Overview: Rotarix™

- Clinical Trials Safety Summary
- Pharmacovigilance
- Post Authorization Safety Studies
- Post Marketing Vaccine Impact and Effectiveness Studies
 - Objectives and expected outcomes
 - Impact in Belgium
- Conclusion: Overall Benefit/Risk ratio



Rotarix™ Clinical Trials: Safety Summary

Robust safety and tolerability profile

- SAEs occurred in 1.7% of vaccinees (N = 36,755) compared to 1.9% of placebo recipients (N = 34,454)
- No increased risk of intussusception within a 31-day period following any dose
 - In a subset of 20,169 infants followed up to 1yr after dose 1 (10,159 vaccinees and 10,010 placebo) : 4 cases in vaccinees compared with 14 cases with placebo
[Relative Risk: 0.28 (95% CI: 0.10, 0.81)]
- Acceptable safety data on specific populations (preterm and HIV infants) (ESPID 2009)

Rotarix™ Broad Post Marketing Exposure and Experience

- Registered in more than 110 countries, distributed in 87 countries
- 43 millions (lyo + liquid) doses distributed worldwide up to Jan.2009,

Region	N of countries	Doses distributed
Europe	30	1,705,000
Latin America	17	38,756,000
ROW	40	2,531,000



Rotarix™ Pharmacovigilance: Adverse Events update

1,892 spontaneous reports from 69 countries
4.4 reports/100,000 doses

Diarrhoea
Vomiting
Abdominal pain
Crying
Anorexia
Pyrexia
Intussusception
Gastroenteritis rotavirus
Haematochezia



Rotarix™ Pharmacovigilance: Selected Events with Special Monitoring

Event	Reason for interest	Current status: <i>Rotarix™</i>
Maladministration	Post-marketing reports	Action taken; education and change to Liquid formulation
Kawasaki disease 1 case	<i>RotaTeq™</i> / FDA	No concern
Fatal pneumonia 4 cases	Imbalance in 1 clinical study	No concern
Intussusception 204 cases (Brigton level 1)	<i>Rotashield™</i>	No concern



Rotarix™ Pharmacovigilance: Intussusception

Intussusception confirmed cases¹:

204	level 1 Brighton criteria ²
120	within 30 days
7	unknown time to onset

Reporting rate¹ (IS within 30 days):

World:	0.3/100,000 doses
Europe:	2.1/100,000 doses

¹DLP: 11 Jan 2009 (PSUR); ²Vaccine 2004 Jan 26;22(5-6):569-74

Incidence rates of Intussusception, 1st year of life - Selected studies

Country	Population & methods	Rate / 100,000 per year	Reference or data source
Australia	Hospitals, nationwide, 1994-2000	101	Justice <i>et al.</i> 2005
Australia	Single hospital, 2002-2004	71	Bines <i>et al.</i> 2006
Austria	2005-2006	56.2	Karl Zwiauer, personal communication
Austria	2006	43.6	Karl Zwiauer, personal communication
Belgium	Health Insurance, whole country 2000-2006	82	Hospital discharges per year (Pers Comm.)
Denmark	Complete birth cohort + hospital discharge 1980-2001	78.2	Fischer <i>et al.</i> 2004; table 2
Germany	BavariPro; OPS code only	37.4	Study report
Germany	BavariPro; ICD-10 or OPS code	72	Study report
Germany	ESPED	72.2	Study report; Adjusted for underreporting
Germany	Federal Health statistics, whole country, 2000-2005	96.7	Eva-Chritina Schnabel, pers comm
Japan	Hospital records, 1978-2002	185	Nakagomi <i>et al.</i> 2006
Latin America	2003-2005 (12 countries)	40.4	GSK study 204; Saez-Llorens, Velazquez et al, MS.
Switzerland	Surveillance network + capture-recapture adj., 2003-2006	49.3	Buettcher <i>et al.</i> 2007
USA	Hospitalisations, Claims db, 1993-2004	35	Tate <i>et al.</i> 2008
Vietnam	Single hospital, 2003	302	Bines <i>et al.</i> 2006



*Rotarix*TM Post-Authorization Safety Studies (PASS): Ongoing

○ Mexico

- Active surveillance for IS
- Self-controlled case series analysis
- Birth cohort: 575,000 with UMV
- Primary outcome: Intussusception
- Initiated Jan 2008; Results by 2012

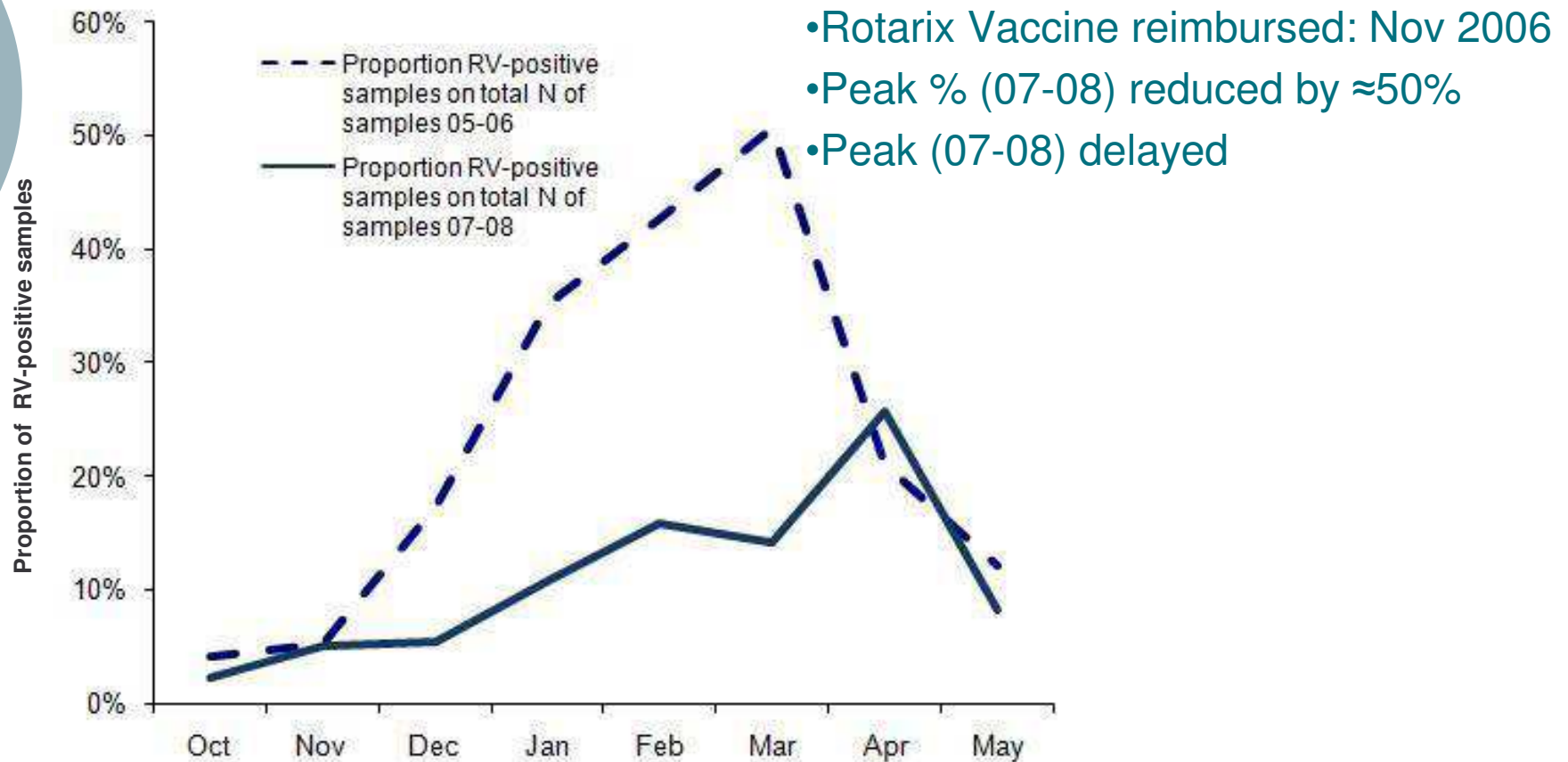
○ USA

- Healthcare database study
- Matched cohorts:
 - Rotarix*TM+ 2 control: concurrent and historical, IPV
 - 55,700 infants in *Rotarix*TM cohort; 167,100 / control cohorts
- Outcomes: IS, Kawasaki's disease, convulsions, hospitalisations for LRTI, fatalities
- Initiated March 2009; Results by 2012

Rotarix™ GSK Vaccine Effectiveness Studies

Country/ Hospitals	Rotarix Vaccination	Design	Primary objective	Study Start (duration)
Belgium	UMV instituted Current vaccine coverage (VC) ~ 90%	Age Matched Case Control	Effectiveness in preventing community- acquired rotavirus severe gastroenteritis among hospitalised children	Feb 2008 (2 years)
Singapore	Current VC ~ 30%			Apr 2008 (2 years)
Panama	UMV instituted Current VC >80%			Mar 2008 (1 year)
Brazil	UMV instituted Current VC >50%			May 2008 (1 year)
Australia, (Northern Territory)	UMV instituted Current VC >65%			Mar 2008 (3 years)
Bangladesh	Vaccine registered, not commercialized/ Vaccine administered in Study by EPI	Cluster randomized Intervention Trial		Sept 2008 (3 years)

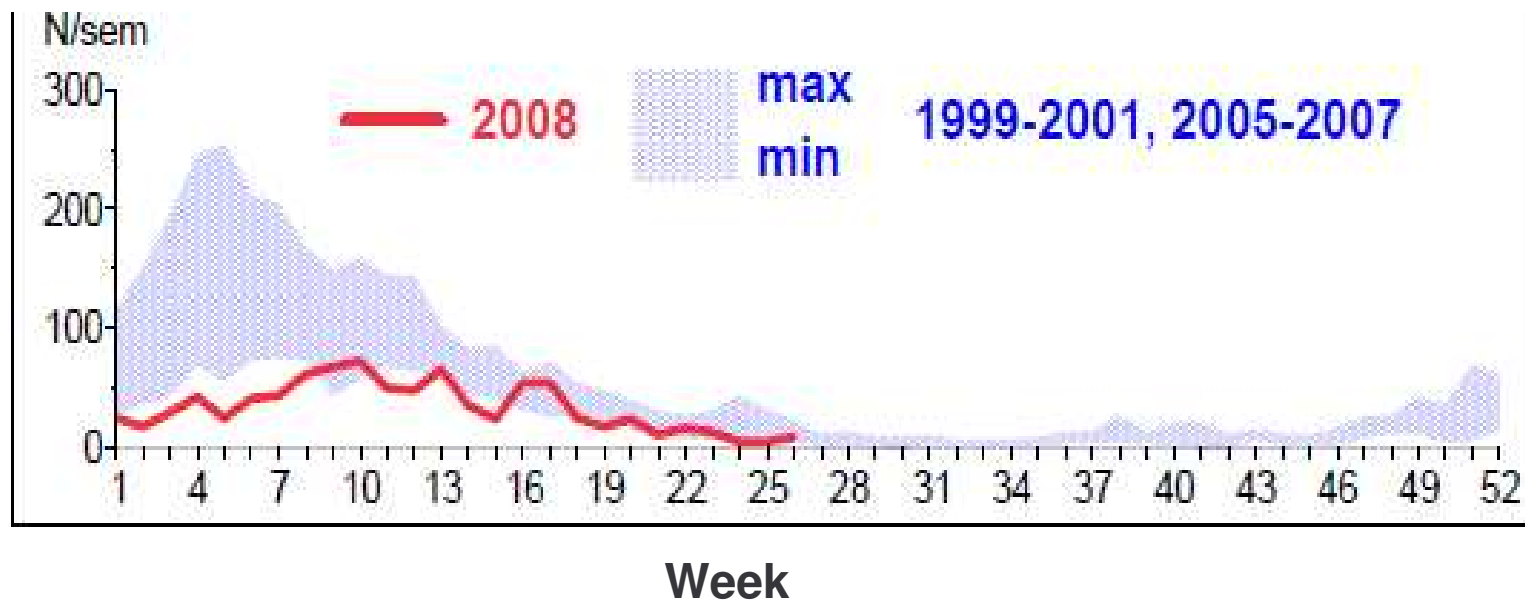
Impact of RV Vaccination on RV Disease Burden: Belgium, 11 hospitals; children ≤ 5 y old



D Strens et al, TO INVESTIGATE THE EFFECT OF PAEDIATRIC VACCINATION ON ROTAVIRUS DISEASE BURDEN IN BELGIUM, Abstract A-132-0018-00778 submitted to ESPID 2009 and accepted as poster, In press.

Impact of RV Vaccination: Belgium Public Health Institute, Surveillance (« Laboratoires Vigies »)

Number of rotavirus diagnoses, from 92 laboratories, 1991- June 2008



Source: surveillance network run by the National Public Health Institute



Conclusion

- *Rotarix*[™] has a broad global distribution
- GSK continues to monitor relevant and important safety event
- Impact data are being documented in Effectiveness and Surveillance studies
- To date, the benefit-risk ratio is clearly in favour of rotavirus vaccination with *Rotarix*[™]