routine EPI vaccinations including Oral Polio Vaccine(OPV) to healthy infants in a phase III, double-blind, randomized, placebo-controlled and multi-center study (444563/024/NCT00139347) conducted in six countries in Latin-America is presented.*Methods:* Healthy infants aged 6-12 weeks were enrolled to receive two doses of RIX4414($N = 4376$) or placebo($N = 2192$) according to a 0,1—2 month schedule, administered concomitantly with Dose 1 and Dose 2 of routine pediatric vaccines including OPV, given respecting the national immunisation guidelines.Vaccine efficacy(VE) was calculated from two weeks post-Dose2 until one year of age. Severe GE was defined as an episode of diarrhea requiring hospitalization and/or re-hydration therapy in a medical facility. Diarrhoeal samples were analyzed for RV by ELISA and typed by RT-PCR based method. Safety data were collected throughout the study.

Results: During the efficacy follow-up period (mean duration of 7.4 months) RIX4414 has offered 81.6% (95%CI:54.4;93.5) protection against severe RVGE and 88.3% (95%CI:64.0;97.1) against hospitalization due to RVGE. For severe RVGE, VE against wild-type G1 was 100% (95%CI:<0;100) and 80.6% (95%CI:51.4;93.2) against pooled non-G1 RV types (G2,G9). No clinically meaningful difference between RIX4414 group and the placebo group for serious adverse events were reported.

Conclusion: Two doses of RIX4414(*Rotarix*™)offer high protection against severe RVGE and related hospitalizations when co-administered with specific childhood vaccines including OPV. These results show that co-administration with OPV does not impact the efficacy of *Rotarix*™ and are in line with the high efficacy against severe RVGE of 85% demonstrated in a large Phase III Latin America study with staggered co-administration of OPV. This finding is of significance for the implementation of RV vaccination programmes in many countries where OPV is still routinely administered.

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19.021

Immunogenicity of The Oral Live Attenuated Human Rotavirus Vaccine RIX4414 (*Rotarix*™) Oral Suspension (Liquid Formulation) Co-administered with Childhood Vaccinations in Panama

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Background: The lyophilized formulation of GlaxoSmithKline's oral, live attenuated human rotavirus vaccine RIX4414(*Rotarix*™) has shown to be immunogenic in various phase III trials in Europe and Latin America. A phase III, open-label, randomized, study(107077/NCT00363545) was conducted in Panama to assess the immunogenicity of two doses of RIX4414 oral suspension (liquid formulation) to that of the lyophilised formulation with routine vaccinations given concomitantly.

Methods: Healthy infants, 6—12 weeks old ($N = 1274$) were enrolled to receive two doses of RIX4414 oral suspension(RIX4414-liq) or RIX4414 lyophilized(RIX4414-lyo) according to a 0,2 month schedule. Routine vaccinations (oral poliovirus vaccines(OPV), DTPw-HBV/Hib) were administered concurrently following local EPI schedule. Anti-rotavirus IgA antibody concentrations were assessed at pre-vaccination and 1 to 2 months post-Dose 2 (ELISA, cut-off $\geq$20 U/mL). The anti-rotavirus IgA seroconversion rates and corresponding Geometric Mean Concentrations(GMCs) were calculated. Solicited symptoms (fever, diarrhoea, irritability, cough/runny nose, loss of appetite, vomiting) were collected for 15-days after each dose, unsolicited symptoms 31-days after each dose. Safety data were collected throughout the study.

Results: The two RIX4414-liq and RIX4414-lyo groups had a similar demographic profile. Anti-rotavirus IgA seroconversion rates at 1 to 2 months post-Dose2 was 80.8% (95%CI: 76.9%;84.4%) in the RIX4414-liq group($n = 449$) and was 73.5%(95%CI:69.1%;77.6%) in the RIX4414-lyo group($n = 434$). GMCs calculated in seropositive infants was 287.8 U/mL (95%CI:250.2;331.2) in the RIX4414-liq group and 266.6 U/mL (95%CI:228.6;310.8) in the RIX4414-lyo group. The reactogenicity profile of the RIX4414-liq group was similar to the RIX4414-lyo group. No vaccination related serious adverse events.

Conclusion: This study indicates that both formulations of RIX4414(*Rotarix*™) elicited a good immune response 1 to 2 months post-Dose2 when co-administered with routine childhood vaccines. This is of importance in considering the implementation of rotavirus UMV programmes. The two formulations were well tolerated with no clinical concerns raised based on the available safety data.

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19.023

Progress Towards Elimination of Indigenous Measles in Taiwan, 2007

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Background: Measels cases began to decline in 1990 in Taiwan just after a 5 year period in which 3 large outbreaks occurred with one to two thousand cases in the 1980's (1985:2219 cases, 97 fatal; 1988: 1386 cases; 1989: 1060 cases, 12 fatal). Since 2003 less than 10 measles cases have been confirmed annually.

Methods: Specimens including throat swabs, urine, or sera were collected from 67 patients with serological confirmed infection during the period of 1992—2007. B95a cell lines were used for virus isolation. After measles virus (MV) identification by immunofluorescence, virus gene targets (N, nucleoprotein and H, hemagglutinin) were amplified (RT-PCR), sequenced and compared to reference sequences.

Results: After diagnostic tests the 67 isolates were assigned to the following 7 genotypes: A (4), D3 (5), D5 (8), D9 (2), G2 (3), H1 (42), and H2 (3). The genotype H1 strains were responsible for cases in 1992 and outbreaks in 1994 and 2002. Most of the genotype H1 cases after 2001 were derived from China. Epidemiological information showed 16

(of 18) imported MV strains between 2003-2007. Additional information is needed to track strains prior to 2000.

Conclusions: Seven genotypes (A, D3, D5, D9, G2, H1 and H2) were recognized from MV cases during 1992-2007. Viruses of genotype H1 and D3 are implicated as indigenous strains in Taiwan. In Taiwan, one-dose measles immunization program began in 1978, and two-dose policy started in 1984. Two catch-up campaigns were implemented in 1992—1994 and 2002—2004 separately. The vaccine coverage rate with 1st dose MV (for 12—15 months) and 2nd dose MMR (for 6 years old) was over 90% and 95% since 1996. The multiple genotypes and sporadic cases discovered after 2003 (except 2 cases in 2005) were all imported. The measles mass vaccination program has successfully interrupted the transmission of indigenous MV in Taiwan.

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19.024

Human Rotavirus Vaccine RIX4414 (*Rotarix*™) Is Highly Efficacious in Infants from Asia During the First Two Years of Life

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Background and Aim: The GlaxoSmithKline oral human attenuated rotavirus (RV) vaccine RIX4414 (*Rotarix*™) has been shown to be highly effective for the prevention of RV gastroenteritis (GE) globally. Infants participating in a double-blind, randomized, placebo-controlled and multicentre trial conducted in Singapore, Hong Kong and Taiwan (e-track107070,107072,107076/NCT444563/028/029/030) were followed up to approximately two years of age to assess protection against severe RVGE.

Methods: 10708 healthy infants, 6—17 weeks of age at Dose 1 were enrolled and randomised into two groups (1:1) to receive 2 doses of RIX4414 vaccine or placebo at a 0,1-2 month schedule. Routine vaccinations were given concomitantly. Vaccine efficacy (VE) was calculated from 2-weeks post-Dose2 until approximately 24 months of age. Severity of RVGE was assessed using the 20-point Vesikari scale (severe RVGE $\geq$11). Diarrhoeal stool samples were analyzed for RV by ELISA and typed by RT-PCR based method. Safety data was collected throughout the study.

Results: During the efficacy follow-up period (mean duration of 20 months), 2 severe RVGE episodes were reported in RIX4414 and 51 in the placebo group. VE against severe RVGE was 96.1% (95%CI:85.1;99.5), 100.0% (95%CI:80.8;100.0) against wild-type G1 and 93.6% (95%CI:74.7;99.3) against pooled non-G1 RV types(G2,G3,G9) proving broad protection by RIX4414. Efficacy against hospitalized RVGE was 93.8% (95%CI:80.6;98.8). An overall reduction of 29.2%(95%CI:12.9;42.5) of hospitalization due to all cause GE episode was observed compared to placebo. There was no clinically meaningful difference between RIX4414 group and the placebo group for SAEs reported during the study.

Conclusions: Presented results demonstrate that in an Asian urban setting, two oral doses of RIX4414 (*Rotarix*™) offer high and sustained protection against severe RVGE during the first two years of life when the disease burden is highest. These data are in line with efficacy results obtained for *Rotarix*™ in Europe.

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19.025

Efficacy of Pentavalent Rotavirus Vaccine, RotaTeq™, against Hospitalizations and Emergency Department Visits through the Third Year: The Finnish Extension Study

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Background: 6—12 week-old healthy infants were randomized to receive 3 oral doses of the pentavalent rotavirus vaccine (PRV), RotaTeq™, or placebo in the Rotavirus Efficacy and Safety Trial (REST). To determine if PRV remains efficacious beyond 2 years after vaccination, approximately 21,000 REST infants in the safety cohort in Finland were followed for healthcare resource utilization (HCRU), defined as rotavirus gastroenteritis (RGE)-associated hospitalizations and/or emergency department (ED) visits, in a Finnish Extension Study (FES) for up to 3.1 years after completing vaccination.

Methods: FES infants were contacted every 12 weeks to determine whether they had any RGE-related HCRU. RGE was defined as forceful vomiting and/or $\geq$3 watery or looser-than-normal stool within a 24-hour period and detection of rotavirus antigen by enzyme immunoassay, plaque assay, and PCR assays to determine the P and G types. Infants with RGE, who received 3 vaccine doses, were included in the analysis, and follow-up started 14 days after dose 3.

Results: The maximum follow-up time in REST was 2 years (730.5 days) and in REST and FES was 3.1 years (1126 days). Overall, PRV reduced the rate of RGE-associated HCRU, regardless of rotavirus serotype, by 94% (95% confidence interval [CI]: 91.3, 95.9) for up to 3.1 years after the third dose, demonstrating an overall reduction of HCRU similar to that of REST (95% [95% CI: 91.5, 96.5]).

Conclusion: RGE-associated HCRU continues to be common in the second year of life but decreases in the third year of life. PRV significantly reduced RGE-associated hospitalizations and ED visits among FES infants, regardless of serotype, for up to 3.1 years of follow-up after completing vaccination. The results of FES are consistent with the results of REST and confirm that the efficacy of PRV remains consistent beyond two years, and up to 3.1 years, after completing vaccination.

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