

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 208108-083 (Hib-083)				
Title: A phase IV, open, multicentric, post-marketing surveillance study to monitor the safety and reactogenicity of GlaxoSmithKline Biologicals' <i>Haemophilus influenzae</i> type b vaccine (Hiberix™) in Korean subjects administered according to the Prescribing Information.				
Rationale: The aim of this study was to monitor the safety of Hib vaccine in Korean children administered according to the Prescribing Information.				
Phase: IV				
Study Period: 25 March 1999 to 03 May 2005				
Study Design: Open, single group, multi-centric study.				
Centres: 86 sites in Korea				
Indication: Active immunization against <i>Haemophilus influenzae</i> type b disease.				
Treatment: Subjects received 3 doses of Hib as an intramuscular injection within 1-2 months interval, starting after 2 months of age.				
Objectives: To assess the occurrence of rare adverse events (AEs) reported after vaccination with Hib vaccine in Korean subjects.				
Primary Outcome/Efficacy Variable: Occurrence of severe (Grade 3) unsolicited AEs during the entire study period.				
Secondary Outcome/Efficacy Variable(s): <ul style="list-style-type: none"> • Occurrence of solicited local and general symptoms during the 4-day follow-up (Day 0-3) after vaccination. • Occurrence of serious adverse events (SAEs) during the entire study period. • Occurrence of related unsolicited AEs. 				
Statistical Methods: The analysis was performed on the Total Vaccinated Cohort. The Total Vaccinated Cohort included all subjects with at least one vaccine administered. <i>Safety analysis</i> The percentage of subjects with any solicited local and general symptoms reported during the 4-day (Day 0-3) follow-up after vaccination was tabulated with their exact 95% Confidence Interval (CI). The same tabulations were performed for Grade 3 solicited local and general symptoms and solicited general symptoms with relationship to vaccination. The percentage of subjects with any, Grade 3 and related unsolicited AEs during the 31-day (Day 0-30) follow-up after vaccination was tabulated by the Medical Dictionary for Regularity Activities (MedDRA) preferred terms. The occurrence of SAEs during the entire study period was tabulated according to MedDRA preferred terms.				
Study Population: Male or female subjects ≥ 2 months of age at the time of the first vaccination, free of obvious health problems as established by medical history or clinical examination prior to study entry. Written informed consent was obtained from the parent(s)/guardian(s) of the subjects before study entry.				
Number of Subjects:		Hib group		
Planned, N		> 600		
Randomised, N (Total Vaccinated Cohort)		726		
Completed, n (%)		Not Available		
Total Number Subjects Withdrawn, n (%)		Not Available		
Withdrawn due to Adverse Events, n (%)		Not Available		
Withdrawn due to Lack of Efficacy, n (%)		Not Applicable		
Withdrawn for other reasons, n (%)		Not Available		
Demographics		Hib group		
N (Total Vaccinated Cohort)		726		
Females: Males		340:386		
Mean Age, months (SD)		3.0 (3.19)*		
Race, n (%)		Not Available		
*Age at first dose was not computed for 94 subjects due to missing or unknown information.				
Secondary Outcome Variable(s): Number (%) of subjects with solicited local symptoms during the 4-day follow-up (Day 0-3) post-vaccination period (Total Vaccinated Cohort)				
Symptom	Intensity	Dose 1	Dose 2	Dose 3

		n	%	95%CI		n	%	95%CI		n	%	95%CI	
				LL	UL			LL	UL			LL	UL
		N = 671				N = 611				N = 501			
Pain	Any	71	10.6	8.4	13.2	45	7.4	5.4	9.7	34	6.8	4.7	9.4
	Grade 3	2	0.3	0.0	1.1	0	0.0	0.0	0.6	0	0.0	0.0	0.7
Redness	Any	80	11.9	9.6	14.6	53	8.7	6.6	11.2	36	7.2	5.1	9.8
	> 30 mm	2	0.3	0.0	1.1	0	0.0	0.0	0.6	0	0.0	0.0	0.7
Swelling	Any	46	6.9	5.1	9.0	26	4.3	2.8	6.2	18	3.6	2.1	5.6
	> 30 mm	1	0.1	0.0	0.8	0	0.0	0.0	0.6	0	0.0	0.0	0.7

N = number of subjects having received the considered dose
n (%) = number (percentage) of subjects for whom the symptom was reported at least once
95% CI = exact 95% confidence interval; LL = lower limit; UL = upper limit
Any = incidence of a specified solicited local symptom irrespective of intensity grade
Grade 3 pain = cried when limb was moved/spontaneously painful

Secondary Outcome Variable(s): Number (%) of subjects with solicited general symptoms during the 4-day follow-up (Day 0-3) post-vaccination period (Total Vaccinated Cohort)

Symptom	Intensity/ Relationship	Dose 1				Dose 2				Dose 3			
		n	%	95% CI		n	%	95% CI		n	%	95%CI	
				LL	UL			LL	UL			LL	UL
		N = 671				N = 611				N = 501			
Fever (Axillary)	≥ 37.5°C	31	4.6	3.2	6.5	10	1.6	0.8	3.0	15	3.0	1.7	4.9
	> 39°C	0	0.0	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	19	2.8	1.7	4.4	5	0.8	0.3	1.9	4	0.8	0.2	2.0
Unusual Crying	Any	18	2.7	1.6	4.2	1	0.2	0.0	0.9	3	0.6	0.1	1.7
	Grade 3	2	0.3	0.0	1.1	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	12	1.8	0.9	3.1	0	0.0	0.0	0.6	1	0.2	0.0	1.1
Vomiting	Any	7	1.0	0.4	2.1	6	1.0	0.4	2.1	6	1.2	0.4	2.6
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	2	0.3	0.0	1.1	2	0.3	0.0	1.2	1	0.2	0.0	1.1
Diarrhoea	Any	7	1.0	0.4	2.1	4	0.7	0.2	1.7	5	1.0	0.3	2.3
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	1	0.1	0.0	0.8	1	0.2	0.0	0.9	0	0.0	0.0	0.7
Loss Of Appetite	Any	10	1.5	0.7	2.7	4	0.7	0.2	1.7	5	1.0	0.3	2.3
	Grade 3	0	0.0	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	6	0.9	0.3	1.9	3	0.5	0.1	1.4	1	0.2	0.0	1.1
Restlessness	Any	53	7.9	6.0	10.2	27	4.4	2.9	6.4	13	2.6	1.4	4.4
	Grade 3	2	0.3	0.0	1.1	0	0.0	0.0	0.6	0	0.0	0.0	0.7
	Related	33	4.9	3.4	6.8	13	2.1	1.1	3.6	2	0.4	0.0	1.4

N = number of subjects having received the considered dose
n (%) = number (percentage) of subjects for whom the symptom was reported at least once
95% CI = exact 95% confidence interval; LL = lower limit; UL = upper limit
Any = incidence of a specified solicited general symptom irrespective of intensity grade and relationship to study vaccination
Grade 3 symptom = symptom which prevented normal everyday activities
Grade 3 loss of appetite = not eating at all
Grade 3 restlessness = crying that could not be comforted
Related = incidence of a specified symptom considered by the investigator as related to the vaccination.

Safety Results: Number (%) of subjects with unsolicited adverse events (Total Vaccinated Cohort)

Most Frequent Adverse Events - On-Therapy- (occurring within Day 0-30 following vaccination)	Hib Group N = 726
Subjects with any AE(s), n (%)	18 (2.5)
Subjects with severe AE(s), n (%)	0 (0.0)
Subjects with related AE(s), n (%)	2 (0.3)
Upper respiratory tract infection	8 (1.1)
Restlessness	4 (0.6)

Gastroenteritis	3 (0.4)
Bronchiolitis	2 (0.3)
Pyrexia	2 (0.3)
Abdominal distension	1 (0.1)
Angioneurotic oedema	1 (0.1)
Anorexia	1 (0.1)
Diarrhoea	1 (0.1)
Injection site pain	1 (0.1)
Pharyngitis	1 (0.1)
Pharyngotonsillitis	1 (0.1)
Urticaria	1 (0.1)
*Primary efficacy result	
Safety Results: Number (%) of subjects with Serious Adverse Events (SAEs) (Total Vaccinated Cohort)	
Serious adverse event, n (%) [n considered by the investigator to be related to study medication]	
All SAEs	Hib Group N = 726
Subjects with any SAE(s), n (%) [related]	1 (0.1) [0]
Bronchiolitis	1 (0.1) [0]
Fatal SAEs	Hib Group N = 726
Subjects with fatal SAEs, n (%) [related]	0 (0.0) [0]

Conclusion: No severe AEs were reported during the course of the study. Redness at the injection site was the most frequently reported solicited local symptom after each dose; restlessness was the most frequently reported solicited general symptom after Doses 1 & 2, while it was fever after Dose 3. At least one unsolicited AE was reported for 18 subjects (2.5%). One SAE was reported; it was considered by the investigator to be not related to the study vaccination. No fatal SAEs were reported during the course of the study.

Publications: No publications

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