

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: DB1112016						
Title : Phase I study of GSK233705 - A randomised, double blind, placebo-controlled, 2-parts study to investigate the safety, tolerability, and pharmacokinetics of single and repeat inhaled doses of GSK233705 from a novel dry powder device in healthy Japanese male subjects -						
Rationale: GSK233705 is a high affinity specific reversible mAChR antagonist developed for once-daily treatment of chronic obstructive pulmonary disease. This study was conducted to provide safety, tolerability and pharmacokinetics (PK) data of single and repeat dose of GSK233705 in healthy Japanese male subjects.						
Phase: I						
Study Period: 20 September 2008 – 15 December 2008						
Study Design: This was a two-part study to investigate the safety, tolerability, and pharmacokinetics of single and repeat inhaled doses of GSK233705 in healthy Japanese male subjects. Part 1 was a randomised, double-blind, placebo-controlled, 4way cross-over design of single inhaled doses of GSK233705. Part 2 was a randomised, double-blind, placebo-controlled, parallel-group design of repeat inhaled doses with GSK233705 or placebo once daily for 7 days.						
Part	Group	Single dose phase				Repeat dose phase
		Period 1	Period 2	Period 3	Period 4	Period 5
Part 1	A (n=3)	Placebo	50µg	100µg	200µg	-
	B (n=3)	50µg	Placebo	100µg	200µg	-
	C (n=3)	50µg	100µg	Placebo	200µg	-
	D (n=3)	50µg	100µg	200µg	Placebo	-
Part 2	E (n=12)	-	-	-	-	200µg (QD for 7days)
	F (n=4)	-	-	-	-	Placebo (QD for 7days)
Centres: A single center in Japan.						
Indication: None						
Treatment: Twenty-eight subjects received inhaled doses of GSK233705 (50, 100 and 200 µg) or placebo. In part 1, twelve subjects participated and received a single inhaled dose during each of the 4 treatment periods. In part 2, sixteen subjects participated and received repeat inhaled doses with GSK233705 200µg once daily for 7 days.						
Objectives: The primary objective was to evaluate the safety and tolerability of single and repeat inhaled doses of GSK233705 in healthy Japanese male subjects. The secondary objective was to investigate the pharmacokinetics of single and repeat inhaled doses of GSK233705 in healthy Japanese male subjects.						
Statistical Methods: All safety data were listed and summarized descriptively, as appropriate. No formal inferential analysis of the safety data was performed. Safety endpoints, including adverse events, blood pressure, heart rate, body temperature, 12-lead ECG, 24 hour Holter monitoring and clinical laboratory safety tests results were tabulated and listed by treatment. Pharmacokinetic parameters of GSK233705 were derived using non-compartmental pharmacokinetic analysis following single and repeat dosing. For each of the derived parameters, except t_{max} , the following summary statistics were calculated: n, arithmetic mean, standard deviation, 95% confidence interval for the arithmetic means, coefficient of variation, minimum, median, maximum, geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data for each session. For t_{max} , n, arithmetic mean, standard deviation, 95% confidence interval for the arithmetic means, median, maximum, minimum were summarised for each session. Dose proportionality was assessed for PK data using the power model from Part 1. To evaluate the observed GSK233075 accumulation ratio, statistical analysis of C_{max} and AUC(0–t) was performed after a log transformation of the data from days 1 and 7 of Part 2.						
Study Population: Healthy Japanese male subjects aged between 20 and 64 years inclusive with a body weight ≥ 50 kg and body mass index within the range 18.5–25.0 kg/m ² .						
Number of Subjects:		Part 1		Part 2		
Planned N		12		16		
Dosed N		12		16		
Completed n (%)		12		16		
Total Number Subjects Withdrawn N (%)		0		0		

Demographics	Part 1				Part 2	
	Group A	Group B	Group C	Group D	Group E	Group F
N	3	3	3	3	12	4
Females: Males	0:3	0:3	0:3	0:3	0:12	0:4
Mean Age in Years (sd)	24.7 (1.15)	23.3 (0.58)	22.7 (1.53)	28.0 (6.00)	22.5 (1.57)	22.3 (0.96)
Mean Height in cm (sd)	173.0 (1.00)	168.3 (4.16)	172.7 (4.51)	176.3 (5.51)	169.3 (5.28)	168.3 (5.44)
Mean Weight in Kg (sd)	68.23 (8.70)	58.77 (3.16)	57.90 (0.46)	64.13 (6.65)	59.37 (5.44)	63.38 (3.95)
Mean BMI in kg/m ² (sd)	22.80 (2.97)	20.77 (1.79)	19.43 (0.90)	20.67 (1.94)	20.68 (0.97)	22.35 (0.13)
Asian-Japan Heritage n (%)	3 (100)	3 (100)	3 (100)	3 (100)	12 (100)	4 (100)
Safety results: Adverse events (AEs) were collected from screening until follow-up. All AEs are presented below.						
Adverse Events (Part 1):		Placebo		GSK233705		
				50µg	100µg	200µg
N		12		12	12	12
No. subjects with AEs n (%)		0		0	1 (8)	0
Investigations						
Alanine aminotransferase increased		0		0	1 (8)	0
Adverse Events (Part 2):		Placebo		GSK233705 200µg		
N		4		12		
No. subjects with AEs n (%)		0		1 (8)		
Investigations						
Alanine aminotransferase increased		0		1 (8)		
Serious Adverse Events, n (%): There were no serious adverse events in this study.						
Pharmacokinetics (PK): PK parameters for GSK233705 are summarized in the table below.						
Parameter (Part 1)	Dose	N	Maen (sd)	Geometric Mean	95% CI	
C _{max} (pg/mL)	50µg	12	234.99 (53.166)	229.65	199.214-264.741	
	100µg	12	539.53 (96.233)	530.79	469.094-600.607	
	200µg	12	1088.58 (283.434)	1056.30	897.664-1242.969	
AUC(0-t) (pg.hr/mL)	50µg	12	53.44 (16.875)	50.84	40.891-63.208	
	100µg	12	202.45 (53.513)	195.63	163.879-233.521	
	200µg	12	627.58 (146.279)	607.15	504.860-730.167	
t _{max} (hr)	Dose	N	Median	Minimum	Maximum	
	50µg	12	0.033	0.03	0.03	
	100µg	12	0.033	0.03	0.03	
	200µg	12	0.033	0.03	0.08	
Parameter (Part 2)	Dose	Day	N	Maen (sd)	Geometric Mean	95% CI
C _{max} (pg/mL)	200µg	1	12	1075.65 (557.453)	933.14	642.835-1354.555
	200µg	7	12	1124.97 (609.598)	952.11	633.007-1432.071
AUC(0-t) (pg.hr/mL)	200µg	1	12	513.42 (214.035)	452.92	311.484-658.580
	200µg	7	12	987.45 (256.959)	956.40	807.307-1133.031
t _{max} (hr)	Dose	Day	N	Median	Minimum	Maximum
	200µg	1	12	0.033	0.03	0.08
	200µg	7	12	0.033	0.03	0.08
Dose proportionality of GSK233705: The statistical summary of dose proportionality from Part 1 is presented below.						
Parameter	Slop		SE		90% CI	
C _{max} (pg/mL)	1.10		0.049		1.017 – 1.184	
AUC(0-t) (pg.hr/mL)	1.79		0.074		1.662 – 1.916	
Accumulation ratios of GSK233705: The statistical summary of accumulation assessment is from Part 2 presented below.						
Parameter	Ratio of Geometric Means			95% CI		
C _{max} (Day 7/Day 1)	1.020			0.6710 – 1.5516		
AUC(0-t) (Day 7/Day 1)	2.112			1.6261 – 2.7422		
Publications: There are no publications as of May 2009.						