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: HHI110159
Title: A randomised, double-blind, placebo-controlled, 3-period crossover study to assess the efficacy and safety of single dose intranasal GSK1004723 compared with placebo in an allergen challenge chamber in male subjects with seasonal allergic rhinitis (SAR).
Rationale: The Environmental Challenge Chamber (ECC) offers a controlled paradigm in which to reproducibly evaluate the effect of medication on allergic rhinitis. Subjects are pre-screened in order to ensure they demonstrate threshold symptoms in response to a fixed allergen load. The chamber is loaded with a qualitatively and quantitatively determined allergen load. Allergen concentration, temperature and humidity are continuously monitored, allowing for a constant humidity (40% ±10), temperature (21°C ±2) and allergen load (approximately 4000 grains per cubic metre) to be maintained throughout the exposure period. These conditions have been selected to simulate those found outdoors on a typical warm summer's day in Germany near a meadow. The doses chosen for this study had been shown to be well tolerated in the first time in human (FTIH) study conducted where volunteers received a maximum dose of 1100 µg for up to 14 days. GSK1004723 is a novel topical intranasal dual histamine H1/H3 receptor antagonist being developed for allergic rhinitis.
Phase: IIa
Study Period: 30 Jun 2008 to 28 Aug 2008
Study Design: A randomised, double-blind, placebo-controlled, 3-period crossover study.
Centres: The study was conducted at 1 centre in Germany.
Indication: Seasonal allergic rhinitis.
Treatment: Subjects who satisfied the eligibility criteria at Screening were randomised to receive single intranasal doses of GSK1004723 (1100 µg and 220 µg) and placebo in random order, in accordance with the randomisation schedule.
Objectives: To investigate the effect of single doses of intranasal GSK1004723 on nasal symptoms of allergic rhinitis following 4 hours (h) in the allergen challenge chamber post-dose on Day 1.
Statistical Methods: Fifty-four subjects were randomised into this study, to achieve 48 completed subjects. Subjects who withdrew from the study were not replaced. This sample size provided more than 90% power to detect a reduction of at least 1 in total nasal symptom score (TNSS) (0 to 4 h post-dose) between GSK1004723 and placebo using a two sided 95% confidence interval (CI), assuming a standard deviation of 1.8. The primary analysis was the comparison of GSK1004723 with placebo on Day 1 at each time-point over the 4 h post-dose in the allergen chamber. The onset of action of GSK1004723 was defined as the first time-point at which a statistically significant difference in TNSS was observed from placebo, and was maintained from this time-point onwards (for up to 3 consecutive time-points) during the allergen chamber exposure. A repeated measures analysis was carried out on the serial time-points relative to start of study medication administration. Adjusted means for each treatment and differences in adjusted means for comparisons of each dose versus placebo were presented for each time-point. The individual symptom scores of TNSS (nasal blockage, rhinorrhoea, nasal itching and sneezing) were analysed and presented in a similar manner to TNSS. Weighted mean (0 to 4 h) and weighted mean (20 to 24 h) were derived for TNSS and for the individual components. The derived parameters were statistically analysed using a mixed effects model. Adjusted means for each treatment and differences in adjusted means for comparisons of each dose versus placebo were presented. The weighted means of the individual symptom scores of TNSS (nasal blockage, rhinorrhoea, nasal itching and sneezing) were analysed and presented as for TNSS. Weighted means for the endpoints: Nasal airflow, visual analogue scale (VAS) score (congestion)

and nasal secretion were derived and analysed in the same way as weighted mean TNSS.
No formal statistical analysis was performed on safety data.

Study Population: Male subjects aged between 18 and 65 years with a known history of SAR, body weight ≥50 kg with body mass index (BMI) within the range 19 to 32 kg/m^2 were included in this study.

Number of Subjects:	**Total**
Planned N	54
Dosed N	54
Completed n (%)	51 (94)
Total Number Subjects Withdrawn N (%)	3 (6)
Withdrawn due to Adverse Events n (%)	3 (6)
Demographics	
N (ITT)	54
Females: Males	0: 54
Mean Age in Years (Range)	34.4 (19 - 61)
Mean Weight in Kg (Range)	84.0 (59 – 112)
White n (%)	53 (98)

Efficacy results:
Results from statistical analysis of TNSS are summarised in the following table.

Treatment group	**N**	**Planned time**	**n**	**Adjusted mean (95% CI)**
Placebo	52	20 min	52	5.02 (4.55, 5.49)
	52	40 min	52	5.26 (4.79, 5.74)
	52	1 h	52	5.06 (4.60, 5.53)
	52	1 h 20 min	52	5.11 (4.63, 5.59)
	52	1 h 40 min	52	5.01 (4.50, 5.52)
	52	2 h	52	5.22 (4.73, 5.71)
	52	2 h 20 min	52	5.07 (4.63, 5.51)
	52	2 h 40 min	52	5.39 (4.87, 5.90)
	52	3 h	52	5.37 (4.93, 5.81)
	52	3 h 20 min	52	5.38 (4.92, 5.83)
	52	3 h 40 min	52	5.69 (5.23, 6.16)
	52	4 h	52	5.49 (5.03, 5.96)
GSK1004723 220 µg	51	20 min	51	4.66 (4.19, 5.13)
	51	40 min	51	4.69 (4.21, 5.17)
	51	1 h	51	4.58 (4.11, 5.05)
	51	1 h 20 min	51	4.38 (3.89, 4.86)
	51	1 h 40 min	51	4.60 (4.09, 5.12)
	51	2 h	51	4.90 (4.40, 5.39)
	51	2 h 20 min	51	4.67 (4.23, 5.12)
	51	2 h 40 min	51	5.14 (4.63, 5.66)
	51	3 h	51	5.08 (4.63, 5.52)
	51	3 h 20 min	51	5.00 (4.55, 5.46)
	51	3 h 40 min	51	5.41 (4.94, 5.88)
	51	4 h	51	5.26 (4.79, 5.73)

GSK1004723 1100 µg	53	20 min	53	4.85 (4.39, 5.32)
	53	40 min	52	4.66 (4.19, 5.14)
	53	1 h	53	4.49 (4.03, 4.96)
	53	1 h 20 min	53	4.51 (4.04, 4.99)
	53	1 h 40 min	53	4.58 (4.07, 5.09)
	53	2 h	53	4.60 (4.12, 5.09)
	53	2 h 20 min	53	4.59 (4.15, 5.03)
	53	2 h 40 min	53	4.99 (4.49, 5.50)
	53	3 h	53	4.98 (4.54, 5.41)
	53	3 h 20 min	53	4.86 (4.41, 5.31)
	53	3 h 40 min	53	5.29 (4.82, 5.75)
	53	4 h	53	5.06 (4.60, 5.53)

The results were consistent across all endpoints including individual components of TNSS, VAS and nasal airflow.

Total nasal symptom score

Summary of statistical analysis of weighted mean TNSS is given in the following table.

Treatment group	N	Challenge	Adjusted mean (95% CI)	Treatment difference (95% CI) (Relative to placebo)
Placebo	52	Day 1 (0-4 h)	5.26 (4.88, 5.64)	-
		Day 1 (20-24 h)	5.62 (5.25, 5.99)	-
GSK1004723 220 µg	51	Day 1 (0-4 h)	4.89 (4.52, 5.27)	-0.37 (-0.79, 0.05)
		Day 1 (20-24 h)	5.19 (4.81, 5.56)	-0.43 (-0.85, -0.02)
GSK1004723 1100 µg	53	Day 1 (0-4 h)	4.85 (4.47, 5.22)	-0.41 (-0.84, 0.01)
		Day 1 (20-24 h)	5.19 (4.82, 5.56)	-0.43 (-0.84, -0.02)

Nasal airflow

Summary of statistical analysis of weighted mean nasal airflow (mL/s) is given in the following table.

Treatment group	N	Challenge	Adjusted mean (95% CI)	Treatment difference (95% CI) (Relative to placebo)
Placebo	52	Day 1 (0-4 h)	230.52 (201.79, 259.24)	-
		Day 1 (20-24 h)	199.19 (165.88, 232.51)	-
GSK1004723 220 µg	51	Day 1 (0-4 h)	209.35 (180.38, 238.32)	-21.17 (-50.65, 8.31)
		Day 1 (20-24 h)	188.24 (154.63, 221.84)	-10.96 (-49.25, 27.33)
GSK1004723 1100 µg	53	Day 1 (0-4 h)	247.29 (218.76, 275.81)	16.77 (-12.48, 46.02)
		Day 1 (20-24 h)	186.28 (153.24, 219.33)	-12.91 (-50.86, 25.04)

Nasal congestion VAS

Summary of statistical analysis of weighted mean VAS (cm) is given in the following table.

Treatment group	N	Challenge	Adjusted mean (95% CI)	Treatment difference (95% CI) (Relative to placebo)
Placebo	52	Day 1 (0-4 h)	4.96 (4.59, 5.34)	-
		Day 1 (20-24 h)	4.98 (4.59, 5.36)	-

GSK1004723 220 µg	51	Day 1 (0-4 h)	4.74 (4.37, 5.12)	-0.22 (-0.61, 0.17)
		Day 1 (20-24 h)	4.97 (4.58, 5.36)	-0.01 (-0.43, 0.41)
GSK1004723 1100 µg	53	Day 1 (0-4 h)	4.76 (4.39, 5.13)	-0.20 (-0.59, 0.19)
		Day 1 (20-24 h)	5.06 (4.67, 5.44)	0.08 (-0.34, 0.50)

Nasal secretion score

Summary of statistical analysis of weighted mean nasal secretion (g) is given in the following table

Treatment group	**N**	**Challenge**	**Adjusted mean (95% CI)**	**Treatment difference (95% CI) (Relative to placebo)**
Placebo	52	Day 1 (0-4 h)	6.3952 (5.8533, 6.9370)	-
		Day 1 (20-24 h)	6.6402 (5.8841, 7.3963)	-
GSK1004723 220 µg	51	Day 1 (0-4 h)	5.8439 (5.2975, 6.3904)	-0.5512 (-1.1540, 0.0515)
		Day 1 (20-24 h)	6.1563 (5.3933, 6.9194)	-0.4838 (-1.4513, 0.4836)
GSK1004723 1100 µg	53	Day 1 (0-4 h)	5.5631 (5.0255, 6.1007)	-0.8320 (-1.4310, -0.2331)
		Day 1 (20-24 h)	6.1590 (5.4094, 6.9086)	-0.4812 (-1.4407, 0.4782)

Safety results: From the time a subject received their first dose until he or she completed the study (including any Follow-up period), all adverse events (AEs) were recorded. Any serious adverse event (SAE) reported after a subject consented to participate in the study but before receiving their first dose and also after the final Follow-up visit and considered related to the investigational product by the Investigator would also be reported. The AEs are summarised in the table below. The majority of AEs were considered mild to moderate in intensity. Two severe AEs (skin laceration and bronchitis) were not considered drug-related by the Investigator.

Adverse Events:	**Placebo**	**GSK1004723 220 µg**	**GSK1004723 1100 µg**
N (ITT)	52	51	53
No. subjects with AEs n (%)	6 (12)	8 (16)	9 (17)
Headache	4 (8)	6 (12)	4 (8)
Bronchitis	0	0	1 (2)
Nasopharyngitis	1 (2)	0	0
Otitis media	0	0	1 (2)
Epistaxis	0	0	1 (2)
Nasal discomfort	0	1 (2)[a]	0
Productive cough	0	0	1 (2)
Urticaria	0	1 (2)	0
Diarrhoea	1 (2)	1 (2)	1 (2)
Skin laceration	0	0	1 (2)
Hepatic enzyme increased	0	0	1 (2)

a. Drug-related Adverse event

Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]: There were no deaths or SAEs reported in this study.

Publications: None