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: OTB109059

Title : A Phase II Study to Evaluate: Delay in Intravaginal Ejaculatory Latency Time (IELT), Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Two Oral Doses of GSK557296 in a Randomized, Double Blind, Placebo-Controlled, Parallel Group Study in Men with Premature Ejaculation

Rationale: The purpose of this study was to to evaluate the efficacy and safety of two fixed-doses (50 mg or 150 mg) of GSK557296 taken in an at home setting on demand compared to placebo in male subjects with premature ejaculation

Phase: II

Study Period: Initiation Date: 23 Dec 2011
Completion Date: 05 May 2011

Study Design: This was a multicenter randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of two fixed-doses (50 mg or 150 mg) of GSK557296 taken in an at home setting on demand compared to placebo in male subjects with premature ejaculation. Subjects who met the inclusion/exclusion criteria were eligible for the one-to-one-to-one randomization into three treatment groups (GSK557296 50 mg, GSK557296 150 mg or placebo) for 8 weeks. A follow-up visit occurred at the end of the 8 week treatment period to assess AEs and SAEs.

Centres: 6 sites in the US and 2 centers in the Netherlands

Indication: Premature Ejaculation

Treatment: Subjects were assigned to placebo, GSK557296 50mg or GSK557296 150mg in a 1:1:1 randomization

Objectives:

Primary

- To determine if an on demand dosing of 50 or 150 mg of GSK557296 demonstrated superior efficacy with respect to duration of IELT during an 8 week study period compared to placebo in men with premature ejaculation (PE)

Secondary

- To assess safety and tolerability of 50 mg and 150 mg of GSK557296.
- To assess change in the Index of Premature Ejaculation (IPE) from baseline and at the end of the 8 weeks of treatment
- To characterize the pharmacokinetics of GSK557296 in men with PE.

Statistical Methods: A sample size of 20 evaluable subjects per arm was chosen to provide approximately 83% power to detect a 2.5 fold difference between a single dose of GSK557296 and placebo in geometric mean IELT. A step-down procedure was used to determine if the efficacy of on-demand GSK557296 therapy was superior to placebo. First, the average of the geometric mean IELTs of the 150mg and 50mg doses of GSK557296 was tested against placebo, and if significance was achieved with this global plateau trend test (p must be < 0.05), then the simultaneous pairwise comparisons of the 150mg and 50mg doses to placebo would occur (each at an alpha level of 0.05).

An un-blinded interim analysis of the IELT endpoint was performed in November 2010. An objective of the interim analysis was to explore the possibility of stopping the study early for futility. No recommendation to terminate the trial was made.

For primary efficacy analysis, geometric mean IELT for each treatment (overall 8 weeks) was compared using analysis of covariance (ANCOVA), adjusting for baseline and center. The least squares (LS) geometric means post-randomization were presented together with the standard error of the LS geometric means for each treatment. A point estimate and corresponding 95% confidence interval (CI) for the LS geometric mean IELT treatment difference was constructed.

The secondary and exploratory endpoints were compared using the same methods as the primary analysis. In these secondary and exploratory analyses no adjustments for multiple comparisons were made.

Individual subject diary questions, individual IIEF questions and domains, and individual questions and domains of the IPE were summarized with descriptive statistics by treatment and visit, but no formal statistical analysis was performed.

Study Population: Male subjects with Premature Ejaculation

Number of Subjects:	**Placebo**	**GSK557296 50mg**	**GSK557296 150mg**
Planned n	20	20	20
Randomized n	27	22	28
Completed n (%)	23 (85%)	17 (77%)	25 (89%)
Total Number Subjects Withdrawn n (%)	4 (15%)	5 (23%)	3 (11%)
Withdrawn due to Adverse Events n (%)	1 (4%)	0	0
Withdrawn due to Lack of Efficacy n (%)	2 (7%)	2 (9%)	0
Withdrawn for Other Reasons n (%)	1 (4%)	3 (14%)	3 (11%)
Demographics	**Placebo**	**GSK557269 50mg**	**GSK557296 150mg**
n (ITT)	27	22	28
Mean Age in Years (sd)	38.4 (8.9)	37.9 (9.9)	34.0 (9.0)
Mean Weight in Kg (sd)	89.3 (18.2)	89.2 (21.4)	88.5 (19.8)
White n (%)	24 (89%)	20 (91%)	21 (75%)

Pharmacodynamics (PD), Endpoints: Median Intervaginal Ejaculatory Time(ITT) Population

	Placebo (n=27)	GSK557269 50mg (n=22)	GSK557269 150 mg (n=28)	Pooled GSK557296 (n=50)
Number of Subjects	25	20	26	46
Geometric LS Mean of the Median IELT (minutes)	0.62	0.72	0.69	0.71
Standard Error	0.090	0.117	0.099	0.075
Geometric LS Mean Fold Difference From Placebo	---	1.16	1.11	1.13
95% Confidence Interval	---	0.75, 1.79	0.74, 1.65	0.79, 1.61
p-value	---	0.50	0.62	0.50

Pharmacokinetics (PK),pharmacodynamics (PD), PK/PD Endpoints:
AUC, T_{max}, C_{max}

Treatment	n	AUC(0-∞) (ng*hr/mL)	AUC(0-t) (ng*hr/mL	CL/F (L/hr)	Cmax (ng/mL)	Vz/F (L)	t1/2[2] (hr)	tlast[2] (hr)	tmax[2] (hr)
50 mg GSK557296	21	854 (45)	773 (43)	58.5 (45)	387 (49)	196 (40)	2.4 (1.8-2.9)	8.0 (7.8-8.2)	0.5 (0.3-2.0)
150 mg GSK557296	28	2490 (33)	2300 (31)	60.3 (33)	1410 (41)	183 (27)	2.1 (1.4-.2.8)	8.0 (7.8-8.0)	0.5 (0.3-2.0)

Safety results:
The investigator or site staff was responsible for detecting, documenting and reporting events that met the definition of an AE or SAE.
AEs were collected from the start of Investigation Product until the follow-up contact and entered into the eCRF. If they had occurred, SAEs would have been collected over the same time period as stated for AEs. An AE is any untoward medical occurrence in a subject or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An on therapy serious adverse event (SAE) was defined as a SAE with onset on or after the start date of study medication and up to 30 days after the last dose of medication.

Adverse Events:	**Placebo**	**GSK557296 50mg**	**GSK557296 150mg**
n (Safety)	25	22	28
No. subjects with AEs n (%)	8 (32%)	6 (27%)	10 (36%)
Most Frequent AEs n (%) Headache	3 (12%)	3 (14%)	5 (18%)

Serious Adverse Events, n (%) 0 (%)

Conclusion: This study did not reach a statistically significant or clinically relevant result for the primary IELT endpoint or for other secondary endpoints. The safety population of this study does not exhibit cause for concern.