

A multi-centre, double-blind, randomised, placebo-controlled, parallel-group study to determine the efficacy and safety of PSD502 in patients with premature ejaculation

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Introduction

Premature ejaculation (PE) is a common condition affecting over 30% of the general male population¹. Incidence is thought to be higher than that of erectile dysfunction (ED). In contrast to ED, however, no effective pharmacological therapy has been approved for the treatment of PE.

Men with PE generally exhibit abnormal autonomic reflex pathways for the ejaculatory process, which includes lower vibratory threshold to ejaculation². Reducing this heightened sensitivity of the glans penis with topical anaesthetics could therefore be a way of improving intravaginal ejaculatory latency time (IELT) without adversely affecting the sensation of ejaculation.

PSD502 is a metered dose spray of lidocaine and prilocaine under development as a topical treatment for PE. The spray has a rapid onset of action, being applied to the glans penis approximately 15 minutes prior to intercourse. Early pilot studies show that PSD502 at a treatment regimen of 3 sprays (delivering a total of 22.5mg lidocaine and 7.5mg prilocaine) is effective in prolonging the time to ejaculation and is well tolerated.

Objectives

The aim of this study was to evaluate the efficacy, safety and tolerability of PSD502 compared with placebo in treating PE patients. The primary endpoints were the mean change in IELT from baseline and the proportion of men with PE responding to treatment (defined as a subject who had at least two sexual encounters where the IELT was ≥ 4 minutes). Secondary endpoints were the proportion of men with PE who had an IELT of ≥ 2 or 3 minutes on at least 2 occasions and changes in the Index of Ejaculatory Control (IEC) and sexual quality of life (in both patients and partners).

Materials and Methods

The study recruited patients with a history of primary PE (defined using DSM-IV criteria) from across the UK and the Netherlands. The men were aged 18 to 75, all of whom were in stable sexual monogamous relationships. Exclusion criteria included the use of antidepressants (including selective serotonin re-uptake inhibitors), non-registered drugs within 30 days of screening, a history of ED, any previous treatment for PE within 4 weeks of screening, patients with physical or psychological conditions, those with clinically significant abnormal urinalysis and sensitivity of either the subject or his partner to amide-type local anaesthetics.

Participants recorded their baseline, treatment-free IELT using a stopwatch on three consecutive sexual encounters (Study Month 1). Patients were randomised to PSD502 or placebo spray to be used prior to sexual intercourse on a total of four, preferably consecutive occasions (Study Month 2). Each sexual encounter was separated by an interval of more than 24 hours. Sexual Quality of Life (SQoL) Questionnaires and the IEC were completed at the end of Study Months 1 and 2. (Figure 1).

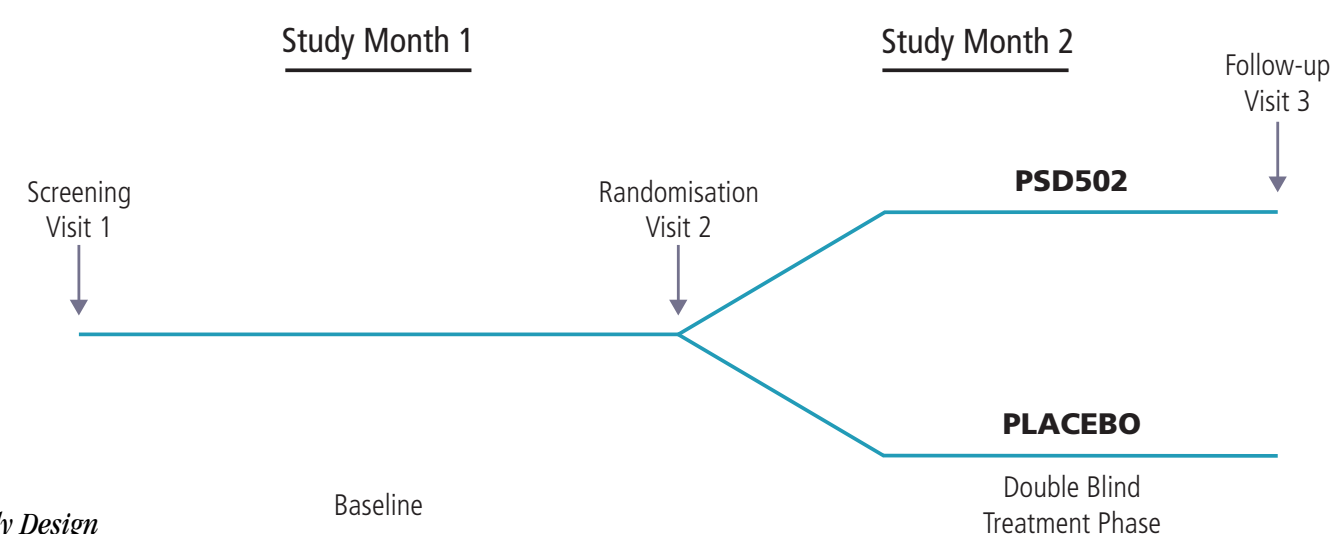


Figure 1: Study Design

The mean IELT during Study Month 1 was used as the baseline, and the mean IELT during Study Month 2 was used to calculate the change from baseline.

Results

A total of 26 patients were randomised to PSD502 with 20 completing treatment and 28 to placebo with 23 patients completing treatment. The mean age of patients in PSD502 group was 39 years with a mean duration of PE of 11 years. The mean age of patients in the placebo group was also 39 years with a mean duration of PE of 9 years.

The primary endpoint, change in IELT from baseline showed a statistically significant increase over baseline for PSD502 patients, which was 2.4 times greater than that for placebo-treated patients (Table 1).

	IELT (minutes)		Treatment comparison
	PSD502 (n=20)	Placebo (n=23)	
Baseline Mean	1.0	0.9	
Follow-up	4.9	1.6	
Observed change from Baseline to Follow-up	3.8	0.7	
Geometric Mean change* [95% CI]	2.50 [1.60 - 3.89]	1.04 [0.69 - 1.55]	2.4 times greater for PSD502 vs placebo (p<0.01)

* adjusted for baseline and centre

Table 1: The mean IELT change from baseline for PSD502 and placebo-treated patients

The number of responders (men with an IELT of ≥ 4 minutes on at least two occasions) was greater with PSD502, 25% (5/20) than placebo 13% (3/23); however the difference between treatments was not statistically significant.

The number of patients who achieved IELT responses of ≥ 2 or ≥ 3 minutes during at least two sexual encounters also showed evidence of a trend towards greater efficacy in PSD502-treated patients compared with the placebo-treated group (Figure 2). An IELT of ≥ 2 minutes was achieved by 55% of PSD502 patients compared to 35% of placebo-treated patients.

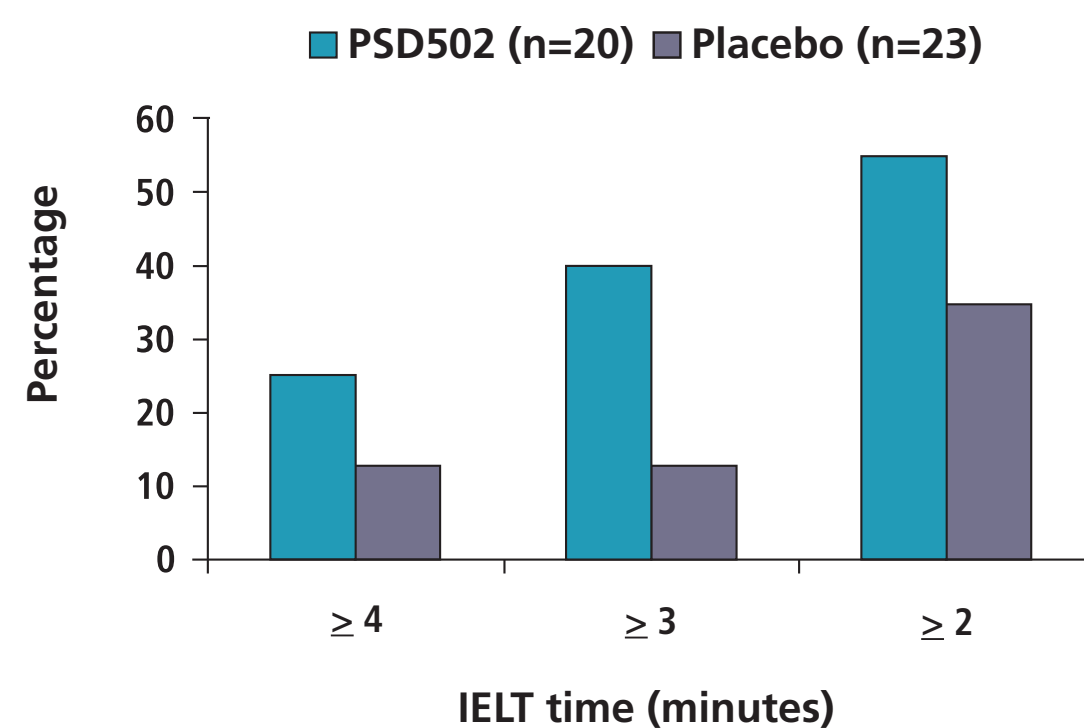


Figure 2: Percentage of patients who achieved IELTs ≥ 2 on two occasions

The observed mean change from baseline in total IEC scores was clinically meaningful for PSD502 patients and was 1.3 times greater than that of placebo patients (6.7 vs 3.0 points, p=0.12).

SQoL questionnaires also showed a trend towards improvement over baseline, for both patients and their partners in the PSD502 treated group. The observed mean change from baseline for PSD502 treated men was 7.0 points compared to 5.5 points in the placebo group and for partners 3.3 versus 1.8 points respectively. Nearly all the patients (83%) found the spray formulation (either active or placebo) easy to use.

No serious adverse events (AEs) were reported. Treatment emergent AEs occurring in PSD502-treated patients were; mild local numbness (n=2), moderate local numbness (n=1) and erectile dysfunction (n=1). PSD502 was also well tolerated by the female partners. A total of four AEs were considered to be related to study medication, all of which occurred in the partner of one PSD502-treated patient. She recorded a mild burning sensation during intercourse each time the spray was used. There were no discontinuations due to any of these AEs.

Discussion

PE is a distressing condition that occurs across all age groups and affects a similar number of men as ED. The lack of approved therapies for PE means that most men remain untreated.

The aim of this phase II study was to explore the utility and acceptability of PSD502 as a topical treatment for PE. The primary objective of showing a statistically significant improvement in IELT from baseline for PSD502 compared to placebo was achieved. This finding was supported by positive, although not significant trends in the other primary endpoint (IELT ≥ 4 minutes on 2 or more occasions) and the secondary endpoints.

PSD502 was well tolerated and effective when applied to the glans penis with a relatively short time to onset of action.

The components of PSD502 have an established long-term safety profile and the formulation offers the potential advantage of being a topical, on-demand treatment which reduces the risk of systemic exposure and side effects compared to long-term oral treatments.

Conclusion

PSD502, a topical spray (delivering a total of 22.5mg lidocaine and 7.5mg prilocaine) significantly increases IELT for PSD502 treated patients compared to placebo (2.4 fold increase), is well tolerated and improves sexual satisfaction in both patients and their partners. These findings indicate that PSD502 might be a suitable first-line, on-demand therapy for PE and warrant further investigation in larger scale, randomised studies.

References

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