

# TEMPE, a novel aerosol delivery form of lidocaine-prilocaine for the treatment of premature ejaculation

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## Introduction

Premature ejaculation (PE) is a common condition affecting over 30% of the general male population<sup>1</sup>. 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 ejaculation<sup>2</sup>. Reducing this heightened sensitivity of the glans penis with topical desensitising agents might therefore be a way of improving intravaginal ejaculatory latency time (IELT) without adversely affecting the sensation of ejaculation.

TEMPE is a topical eutectic mixture of lidocaine and prilocaine in an easy to use spray, under development as a first line therapy for PE<sup>3</sup>. 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 TEMPE at a treatment regimen of three sprays (delivering a total of 22.5mg lidocaine and 7.5mg prilocaine) is effective and well tolerated<sup>3</sup>.

## Objectives

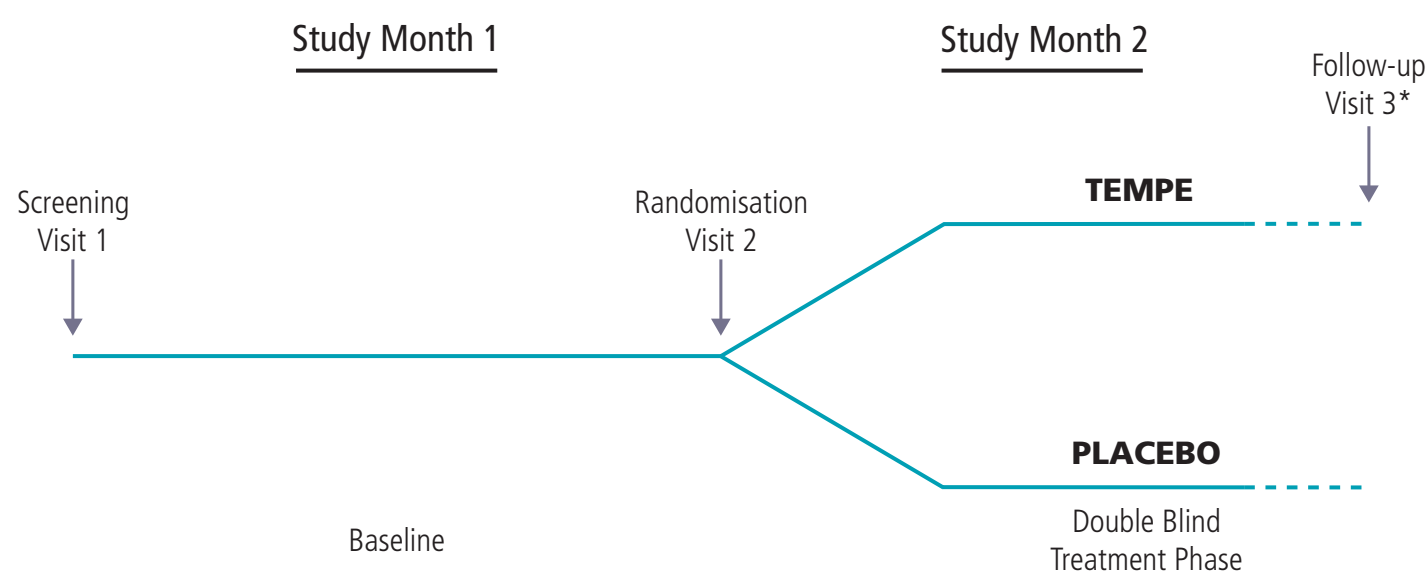
The primary objective of this study was to evaluate the efficacy of TEMPE compared to placebo in treating men with PE. Secondary objectives included the evaluation of the effect of TEMPE on ejaculatory control and sexual quality of life and the assessment of the safety and tolerability of treatment.

## Methods

The efficacy and safety of TEMPE was determined in patients with PE in this phase II, multi-centre, double-blind, randomised, placebo controlled, parallel-group study (Figure 1).

The study recruited men aged 18 to 75 with a history of primary PE (defined using DSM-IV criteria), and in stable heterosexual, monogamous relationships, from across the UK and the Netherlands. Exclusion criteria were standard for studies in PE populations but in addition, men with known drug sensitivity to amide-type local anaesthetics were also excluded.

Participants recorded their baseline IELT using a stopwatch on three consecutive sexual encounters (Study Month 1). Patients were randomised to TEMPE 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) and the Index of Ejaculatory Control (IEC) questionnaires were completed at the end of Study Months 1 and 2.



\* Follow-up Visit 3 - carried out 2 weeks after end of Study Month 2 or last IELT recording, whichever was sooner.

Figure 1: Study Design

## Results

A total of 26 patients were randomised to TEMPE, with 20 completing treatment, and 28 to placebo, with 23 patients completing treatment. The mean age of patients in both groups was 39 years. The mean duration of PE was 11 years in the TEMPE group and 9 years in the placebo group. At baseline both groups had a mean IELT of approximately 1 minute.

TEMPE-treated patients showed a statistically significant increase in stopwatch-recorded IELT over baseline, which was 2.4 times greater than that observed with placebo ( $p < 0.01$ , Table 1).

	IELT (minutes)		Treatment comparison
	TEMPE (n=20)	Placebo (n=23)	
Baseline Mean (SD)	1.0 (1.2)	0.9 (0.7)	
Follow-up (SD)	4.9 (4.9)	1.6 (1.6)	
Observed change from Baseline to Follow-up (SD)	3.8 (4.5)	0.7 (1.4)	
Geometric Mean change* [95% CI]	2.50 [1.6 - 3.9]	1.04 [0.7 - 1.6]	Increase 2.4 times greater on TEMPE than on placebo ( $p < 0.01$ , CI: 1.3, 4.4)

\* adjusted for baseline and centre

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

The number of patients who achieved IELTs of  $\geq 2$ ,  $\geq 3$  or  $\geq 4$  minutes during at least two sexual encounters also showed evidence of a trend towards greater efficacy with TEMPE than placebo (Figure 2). Fifty five percent (11/20) of TEMPE-treated patients achieved an IELT time of  $\geq 2$  minutes compared to 35% (8/23) of placebo-treated patients.

Ejaculatory control, measured by the IEC questionnaire, was 1.3 times greater after treatment with TEMPE than placebo. Although when adjusted for baseline and centre, the difference was not statistically significant.

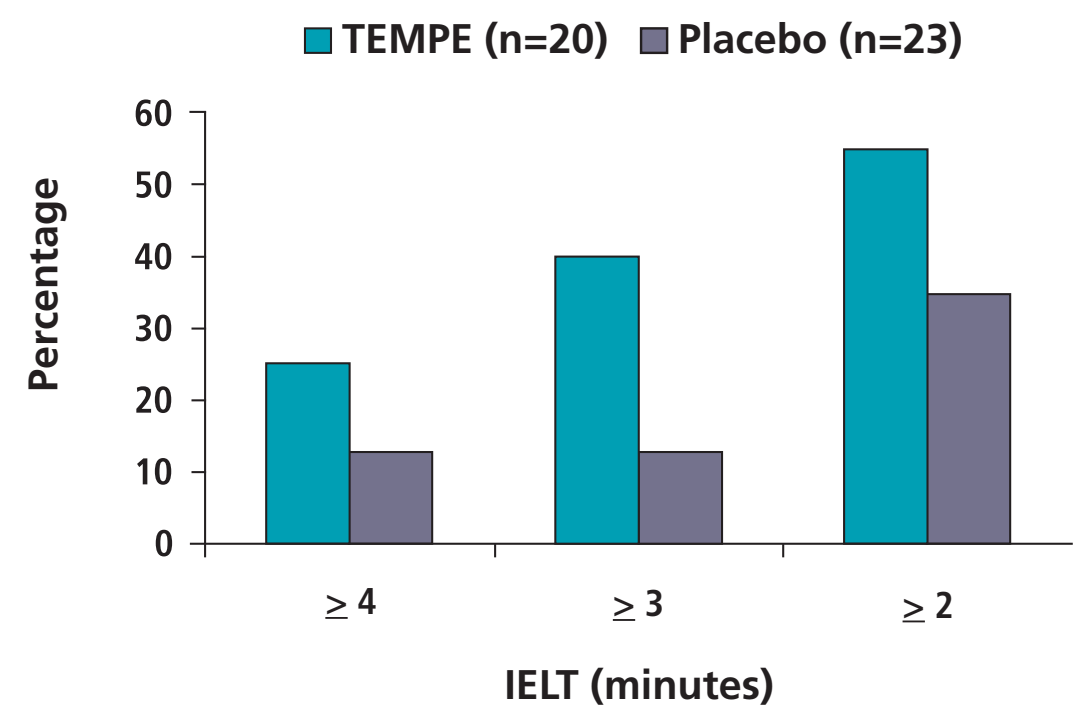


Figure 2: The mean IELT change from baseline for TEMPE and placebo-treated patients.

Despite the short duration of the study, an encouraging trend was also seen in the SQoL scores for patients and their partners, with a trend towards greater improvements over baseline in the TEMPE group than in the placebo group.

Both patient and partners perception of TEMPE was positive; the majority of patients (70%) and partners (60%) believed that the spray prolonged the time to ejaculation or improved their partner's ability to control ejaculation, respectively (Figure 3). Nearly all the patients (81%) found the spray easy to use.

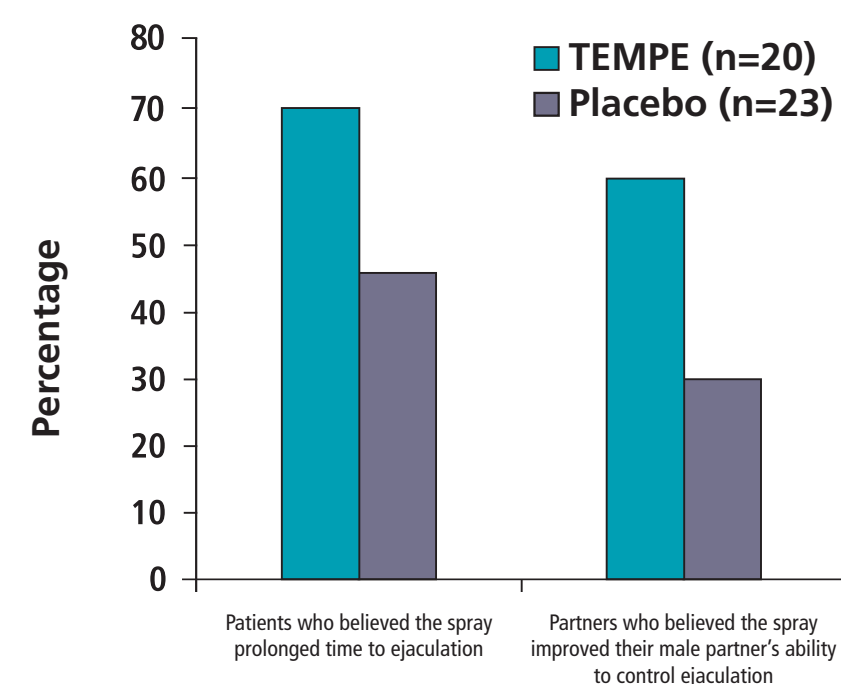


Figure 3: Perception of treatment effect on prolonging time to ejaculation or improving male partner's ability to control ejaculation.

No serious adverse events were reported and TEMPE was well tolerated by patients and their partners. Three TEMPE-treated men (11.5%) experienced mild or moderate hypoaesthesia (numbness) of penis and a fourth reported erectile dysfunction. One female partner of a TEMPE-treated patient reported a mild burning sensation during intercourse. None of the adverse events led to discontinuation.

## Discussion

PE is a distressing condition that occurs across all age groups, but the lack of approved therapies for PE means that most men remain untreated. The aim of this study was to evaluate the efficacy and tolerability of TEMPE compared to placebo. Treatment with TEMPE resulted in a mean IELT of 4.9 minutes, i.e. within the 'normal' range of 2-7 minutes<sup>4</sup>, compared to 1.6 minutes in the placebo group. However, it is now generally accepted that prolongation of a previously unacceptable IELT is more relevant to patient satisfaction than achieving pre-defined goals. This study showed, with clinical and statistical significance, that TEMPE was 2.4 times more effective at prolonging IELT than placebo.

Subjective measures of improvement in PE, such as ejaculatory control and sexual quality of life may be as important (if not more so) to patients and their partners than IELTs. This study showed an encouraging trend towards improvements in these measures in patients using TEMPE, despite the limited duration of the study. Longer-term studies are required in order to assess this further. TEMPE was well tolerated by patients and their partners and both patient and partner perception of TEMPE was positive. Nearly all the patients found the spray easy to use.

## Conclusion

TEMPE, a topical eutectic mixture (delivering 22.5mg lidocaine and 7.5mg prilocaine) in a spray formulation, significantly increases IELT compared to placebo in men with PE and is well tolerated. TEMPE appears to offer comparable efficacy to cream formulations but without the compliance limiting issues associated with their application. It has the potential to offer a convenient, novel, first-line treatment option for patients with PE.

## References

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