Oral drug effectively improves premature ejaculation

Investigational agent increases ejaculatory latency time by 1.5 minutes over baseline

Cheryl Guttman
UT CONTRIBUTING EDITOR

Buenos Aires, Argentina—The serotonin transport inhibitor dapoxetine appears to be a well-tolerated and effective agent for the treatment of premature ejaculation, according to the results of a phase II study presented at the International Society for Sexual and Impotence Research world congress.

Dr. Hellstrom

Researchers say the drug, which is still investigational, may offer a safer, more tolerable alternative to the selective serotonin reuptake inhibitors (SSRIs) currently used to treat this common sexual condition.

The randomized, double-blind, placebo-controlled trial enrolled 166 adult, heterosexual men with a baseline intravaginal ejaculatory latency time (IELT, as measured by a stopwatch held by the female partner) <2 minutes (mean time, 1.01 minutes). Subjects were randomized to initial treatment with dapoxetine, 60 mg or 100 mg taken 1 to 2 hours prior to anticipated sexual activity, or placebo. Patients were crossed over to both alternate treatments. Treatment periods lasted 2 weeks and were separated by a 72-hour washout period.

In the primary efficacy analysis, there were significant differences favoring both doses of dapoxetine compared with placebo for increasing IELT ($p<.0001$). At the end of treatment, mean IELT was 2.06 minutes in the placebo group compared with 2.93 minutes for dapoxetine, 60 mg, and 3.20 minutes for dapoxetine, 100 mg.

Efficacy was immediate, as well. After the first dose, mean change from baseline IELT was 0.33 minutes for placebo; 1.52 minutes for dapoxetine, 60 mg; and 1.39 minutes for dapoxetine, 100 mg (60 mg vs. placebo, $p=.014$; 100 mg vs. placebo, $p=.025$).

Ten patients—one taking placebo and nine receiving dapoxetine, 100 mg—withdrew from the study due to adverse events. However, the 60-mg dose of dapoxetine was well tolerated and associated with a relatively low incidence of minor side effects.

Based on the phase II results, phase III studies were conducted to investigate dapoxetine, both 30 mg and 60 mg, and some preliminary results from those investigations are encouraging, said lead author Wayne J.G. Hellstrom, MD, professor of urology and chief, section of andrology, at Tulane University Health Sciences Center in New Orleans.

"Considering the favorable efficacy and safety profile demonstrated so far for dapoxetine, we look forward to this novel agent as being the first medication approved by the FDA for the treatment of premature ejaculation," he said.

A common problem

Dr. Hellstrom noted there is a genuine need for modalities to treat premature ejacula-

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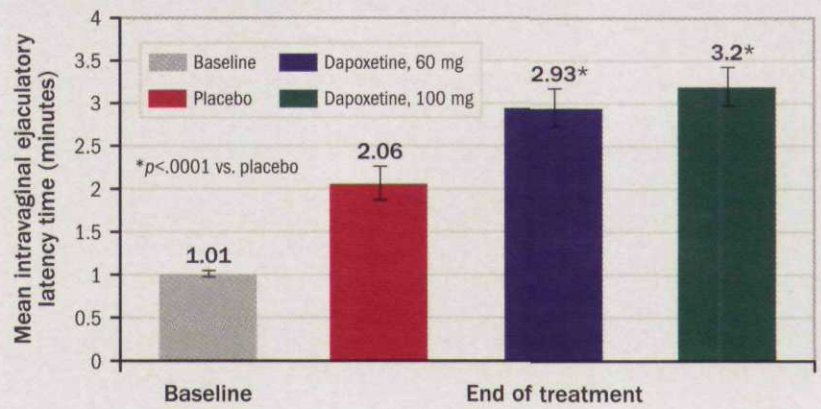
UT Figure

Intravaginal ejaculatory latency time: Placebo vs. dapoxetine



Source: Wayne J.G. Hellstrom, MD

Oral ED agent has rapid onset of action, study shows

Cheryl Guttman
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Buenos Aires, Argentina—The onset of action may be very rapid—within 10 minutes—in some men who take vardenafil (Levitra) to treat erectile dysfunction, according to the results of a multinational study.

At a Glance

Quick Response » One-fifth of participants respond to vardenafil within 10 minutes in a multicenter, multinational trial.

Designed to identify the earliest time to onset of action leading to successful sexual intercourse after vardenafil dosing, the "Onset of vardenafil in men with erectile dysfunction" (ONTIME) trial—overseen by Luc Valiquette, MD, professor of urology at the Hospital Saint-Luc du CHUM in Montreal—randomized 732 patients to treatment with vardenafil, 10 mg; vardenafil, 20 mg; or placebo. The study participants had a baseline International Index of Erectile Function score of 13.4 (moderate severity), and all had demonstrated a response to vardenafil.

Each participant was instructed to initiate sexual activity immediately after taking the medication and was issued a stopwatch to time the interval between dosing and attainment of erection perceived to be adequate for penetration with subsequent intercourse completion—recorded as a positive response to question 3 in the Sexual Encounter Profile (SEP3).

The study results, based on an intention-to-treat population of 708 men, showed the SEP3 responder rate was significantly higher among men taking vardenafil, 10 mg, than among placebo recipients beginning at 10 minutes (21% vs. 14%, $p<.025$), and this difference was maintained at all later time points tested for statistical significance (15, 20, 25, and 30 minutes).

In men taking vardenafil, 20 mg, SEP3 responder rates were statistically higher than those of placebo at 11 minutes (23% vs. 15%, $p<.025$) and at all time points beyond, according to the researchers, whose data were presented at the International Society for Sexual and Impotence Research world congress and published in the *Journal of Sexual Medicine* (2004; 1:168-78).

Sexual Dysfunction

"In the clinical trials leading to vardenafil approval, men were instructed to initiate sexual activity about 1 hour after taking their study medication. That protocol represented a best-case scenario, taking into account pharmacokinetic studies showing that the peak serum concentration of vardenafil is achieved after 50 to 60 minutes," said Randall B. Meacham, MD, associate professor of urology, University of Colorado Health Sciences Center, Denver.

"However, it is also known that some men respond more rapidly, and this study was specifically designed to identify how early the onset of action of vardenafil might be."

> **"This study was specifically designed to identify how early the onset of action of vardenafil might be."**
>
> RANDALL B. MEACHAM, MD

Dr. Meacham noted that the findings of this study provide important information for counseling patients who are being prescribed the drug.

"I tell my patients that, for the most reliable results when first starting the medication, they should wait 50 to 60 minutes before attempting intercourse," Dr. Meacham said. "However, as they find they are responding to the treatment, they can identify whether they fit into a group of earlier responders and then adjust the time of administration depending on their personal experience."

75% complete intercourse

ONTIME was conducted in 80 centers across eight countries in Europe and North America. The study began with a 4-week unmedicated run-in period, followed by a 4-week double-blind phase during which men took their assigned treatment on demand. The time to earliest response used in the analyses represented the best time achieved with the first four doses.

Other analyses showed that about half of men taking vardenafil achieved erections adequate for penetration leading to successful intercourse within 25 minutes after ingestion (50% of men taking vardenafil, 10 mg, and 53% of men taking vardenafil, 20 mg). The responder rate after 25 minutes in the placebo group was 26% and was significantly different compared with the vardenafil rates ($p<.0001$).

Between 15 and 30 minutes after dosing, 75% to 77% of all attempts with an erection sufficient for penetration led to intercourse completion among men who took vardenafil, either dosage, compared with only 45% to 47% of all attempts for the men in the control group.

The ONTIME study was sponsored by Bayer and GlaxoSmithKline. Dr. Meacham is a speakers bureau member for GlaxoSmithKline and other companies that market products for the treatment of erectile dysfunction. UT