dosing schedule is the most effective, although the authors indicate a preference for the CET 4 × 10 mg regimen.

Serum testosterone initially drops but then recovers and stabilises at normal values for the rest of the treatment period. The effect on prostate volume reduction was also more transitory, suggesting a complex mode of action. Identifying the mechanisms for cetrorelix mediated responses may add further information to the pathophysiology of male lower urinary tract symptoms (LUTS). The mechanisms include inhibition of cellular progression with a likely apoptotic effect, as well as more complex explanations possibly involving an antiproliferative effect through inhibition of the plasminogen activator system [3].

The questions remain: (1) Will this be a competitor to drug therapy or minimally invasive surgery; (2) what is the preferred treatment schedule; and (3) will this good side effect profile be maintained in longer term therapy?

References


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Editorial Comment on: Placebo-Controlled Dose-Ranging Phase 2 Study of Subcutaneously Administered LHRH Antagonist Cetrorelix in Patients with Symptomatic Benign Prostatic Hyperplasia

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The paper by Debruyne et al reports on a phase 2 trial of a subcutaneously administered luteinising hormone-releasing hormone (LHRH) antagonist in patients with symptomatic benign prostatic hyperplasia (BPH) [1].

The aim of the study was to evaluate the efficacy and safety of different dosing schemes of the novel LHRH antagonist cetrorelix (CET). Of 140 randomised patients, 131 patients could be evaluated for the primary end point at week 12. Five centres in two countries (Belarus and Uzbekistan) were included in the study. In all CET groups, a rapid response and reduction in the International Prostate Symptom Score (IPSS) was observed. Furthermore, all secondary end points (Tables 4 and 5 and Figures 3–6 in Debruyne et al [1]) showed a statistically significant difference and all dosage schemes were well tolerated. The authors concluded that an additional study should look at the use of a long-term application that may be effective in treating symptomatic BPH patients.

The study investigates a rather new and interesting approach to treating symptomatic BPH. One drawback of the study is that no standard treatments for symptomatic BPH were included; however, this control is not mandatory in a phase 2 trial and must be considered in a phase 2 investigation. Additionally, it will be interesting to see what side effects occur in the cohort during a longer follow-up period, as suggested in the study; the study lasted 20 weeks. All four subgroups of the study presented with a median age of 66.4 to 70.5 yr and a median PSA value between 3.21 and 4.10, which is a typical group at risk for prostate cancer (pCA). Nevertheless, pCA was not excluded in this trial. There is no doubt that a patient at age 70 with a PSA of 8.9 and symptomatic BPH is less likely to harbour pCA, but it must be ruled out. It still remains unclear how the urologist should monitor PSA after the injections. How can the urologist differentiate and be sure not to miss a pCA after the initiation of treatment.

Previous studies have shown treatment to be effective using CET acetate and pamoate [2,3]. In this study, a gluconate form was chosen; unfortunately, the reader does not learn whether or not there is an advantage to this choice. One interesting finding is that the effect of CET is independent
of the extent of testosterone suppression, which indicates a beneficial role in treating clinical BPH. One point warrants further discussion: Why was the placebo response so poor compared to other alpha blocker studies?

There is no doubt that because of demographic changes, we must find ways to improve medical treatment of BPH. Even though it consists of only short-term data, this study may provide a first step to establishing a new compound. We are anxiously awaiting more data with long-term results.

References


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