BPH

The hole-punch approach to treating LUTS

Clinical trial phase IIb data published in *The Journal of Urology* have demonstrated the safety and efficacy of treating BPH-associated lower urinary tract symptoms (LUTS) with intraprostatic injection of PSA-activated pore-forming toxin PRX302.

In a double-blind placebo-controlled multicentre study of 94 Canadian men with BPH, a single ultrasonography-guided injection of PRX302 resulted in a 9-point reduction in International Prostate Symptom Score (IPSS) and a 3 ml/s increase in peak urine flow. These improvements were clinically meaningful (3–4 point decrease in IPSS compared with vehicle only), apparent after just 3 months, and sustained over 1 year.

Only mild and temporary (<2 days median duration) adverse effects were reported in PRX302-treated men, relating either to prostate inflammation (for example, dysuria and pollakiuria) or pain at the injection site. Sexual function was unaffected in treated men and there was no evidence of hypersensitivity to the drug.

Such a favourable adverse-effect profile could be explained by the fact that PRX302—a modified form of proaerolysin—contains a sequence with

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a high specificity for enzymatically-active PSA, which is only present within prostate tissue. Outside the prostate, the activation of PRX302 (by circulating PSA) is inhibited by serum protease inhibitors.

Upon activation, PRX302 spontaneously oligomerizes and forms a stable transmembrane heptameric pore. “When PRX302 is activated by PSA, it punches holes in PSA-producing cells located in the prostate,” says Mostafa Elhilali, lead researcher for the study. “All cells in the injected area die and the prostate shrinks, alleviating the LUTS.”

In accordance with this theory, serum PSA increased 10-fold within 3–5 days of injection in men treated with PRX302, compared with fourfold in controls; this transient surge represents an early inflammatory response triggered by the rapid death of PSA-producing cells.

Elhilali *et al.* are currently analysing phase II data relating to transrectal administration of PRX302, which they plan to publish soon. “Protocols for phase III studies—which will include North America and Europe—are also being finalized,” reports Elhilali. “In future studies, we will use MRI rather than ultrasound to assess prostate size change.”

According to Elhilali and his team, the clinical implications of their study extend beyond the identification of a single outpatient-based BPH treatment. Another potential use of this toxin could be to produce a focal effect against localized prostate cancer.

Melanie Clyne

Original article Elhilali, M. *et al.* Prospective, randomized, double-blind, vehicle-controlled, multicenter phase IIb clinical trial of the pore-forming protein PRX302 for targeted treatment of symptomatic benign prostatic hyperplasia. *J. Urol.* doi:10.1016/j.juro.2012.11.003