BLADDER CANCER

GEMCITABINE REDUCES RECURRENCE

A phase III, randomized, double-blind clinical trial has shown that immediate intravesical instillation with gemcitabine reduced recurrence of non-muscle-invasive bladder cancer after transurethral resection of the bladder tumour (TURBT).

Overall, 406 eligible patients with suspected low-grade papillary urothelial cancer were included in the study. Participants were randomly assigned to receive 2 g gemcitabine in 100 ml saline (201 patients) or 100 ml saline alone (205 patients) within 3 h of TURBT. Patients were monitored for 4 years, undergoing cystoscopy and cytology quarterly for the first 2 years and semiannually for the second 2 years.

In total, 383 patients received TURBT, 190 in the gemcitabine group and 193 in the saline group. Recurrences occurred in 67 patients in the gemcitabine group and 91 patients in the saline group ($P < 0.001$). Immediate postresection instillation of gemcitabine reduced the risk of recurrence in the intention-to-treat population with an absolute reduction in risk of 12% at 4 years.

In the predefined target population with low-grade non–muscle-invasive urothelial cancer, 34 of 102 patients in the gemcitabine group and 59 of 113 patients in the saline group experienced disease recurrence ($P < 0.001$). The absolute reduction in risk of recurrence in this target population was 20% at 4 years.

Intravesical gemcitabine was well tolerated; no grade 4 or 5 toxic effects were reported. Grade 1–3 adverse events were similar between groups.

These results show that immediate intravesical instillation of gemcitabine after TURBT can reduce disease recurrence in patients with low-grade bladder cancer.

Louise Stone

ORIGINAL ARTICLE Messing, E. M. et al. Effect of intravesical instillation of gemcitabine vs saline immediately following resection of suspected low-grade non–muscle-invasive bladder cancer on tumor recurrence SWOG S0337 randomized clinical trial. *JAMA* **319**, 1880–1888 (2018)

BPH

Signal of GV1001 efficacy

Findings of a phase II trial in men with BPH show that treatment with the peptide vaccine GV1001 results in significant reductions in prostate symptom scores and prostate gland volume in comparison with placebo.

GV1001 is a 16-amino-acid peptide fragment representing a part of the catalytic site of telomerase. The agent was initially developed as a cancer vaccine, for example, against pancreatic and prostate cancer. In rat models of BPH, GV1001 seemed to limit disease progression, prompting investigation for the treatment of BPH. Now, the results of a multicentre, placebo-controlled, single-blind phase II trial in men with BPH have been published in *BJU International*. A total of 161 patients were equally randomized to 4 groups, receiving intradermal injections of 0.4 mg GV1001 every 2 weeks, 0.56 mg GV1001 every 2 weeks or every 4 weeks, or placebo. The primary efficacy measure was change from baseline (CFB) in International Prostate Symptom Score (IPSS) at weeks 4, 8, 12, 13, and 16.

In all three treatment groups, IPSS CFB was lower than in the control group at all five time points. Statistical analysis in the per-protocol set showed significant differences in IPSS CFB at time points >4 weeks for the 2 groups that received the vaccine every 2 weeks compared with the placebo group ($P < 0.05$). In addition, CFB in prostate volume at week 16, which was a secondary efficacy measure, was significantly different from that in the control group for all treatment groups ($P < 0.05$). Other secondary end points, such as CFB in PSA levels, erectile function, and testosterone levels were not significantly different between groups, but CFB of Qmax and post void residual seemed to improve in the treatment groups compared with the control group.

> “…treatment with the peptide vaccine GV1001 results in significant reductions in prostate symptom scores…”

BLADDER DYSFUNCTION

TRPV4 targeting improves function in DUA rat model

Detrusor underactivity (DUA) is a common sequela of pelvic surgery owing to iatrogenic damage to efferent and sensory nerves. “Underactive bladder is a very prevalent problem without effective treatments,” explains Wouter Everaerts, senior author of a new study in *European Urology*. “As targeting efferent pathways in the bladder has proven to be ineffective, we hypothesize that the bladder’s sensory systems are malfunctioning in some patients with DUA. An alternative strategy could be to increase the sensory output of the bladder by afferent nerve stimulation.”

Several transient receptor potential (TRP) channels have been identified in the lower urinary tract (LUT), in particular TRP vanilloid 4 (TRPV4), which is highly expressed in the urothelium. *Trpv4*$^{-/-}$ mice display abnormal voiding and treatment with TRPV4 agonists results in bladder hyperactivity. Thus, it represents a potential treatment target.

> “*Trpv4*$^{-/-}$ mice display abnormal voiding”

In order to test this hypothesis, Everaerts and his team developed a rat model of DUA. Wild-type and *Trpv4*$^{-/-}$ rats underwent bilateral pelvic nerve injury (bPNI) and subsequent cystometry. Compared with sham-operated rats, bPNI rats demonstrated an almost threefold increase in mean intercontractile interval (ICI) and voided volume (VV), as well as decreases in voiding contractions and a significant increase in post-void residual (PVR).

The effect of TRPV4 targeting on bladder function in DUA rats was investigated by instillation of TRPV4 agonist GSK1016790A, which significantly reduced ICI and VV in both bPNI and sham wild-type