Ixabepilone shows activity in hormone-refractory prostate cancer

Taxanes stabilize the microtubules involved in cell division, thereby inhibiting tumor growth. As some tumors are taxane-resistant, alternatives such as the epothilones (which also stabilize microtubules) are being investigated. A group of US researchers has examined the activity of one epothilone, ixabepilone, in 42 patients with chemotherapy-naive, metastatic, hormone-refractory prostate cancer.

Patients were given ixabepilone 40 mg/m^2 intravenously once every 21 days, for a minimum of two treatments. Therapy continued until the tumor progressed, unacceptable toxicity occurred, or the patient decided to withdraw. Median follow-up was 25 months. In all, 14/42 patients had a confirmed partial PSA response, defined as a ≥50% reduction in serum PSA level from baseline. The PSA levels of 10 of these patients declined by >80%, and two patients achieved undetectable PSA levels. No patient achieved a confirmed complete objective response (disappearance of all tumor tissue). Median progression-free survival was estimated at 6 months, and median survival was 18 months. Eleven patients required dose reduction to the prespecified level of 32 mg/m^2 and one to the prespecified level of 25 mg/m^2, because of low granulocyte or platelet counts.

The authors claim that, compared to their group's previous studies of single agents in hormone-refractory prostate cancer, ixabepilone shows clinically documented antitumor activity. It also compares favorably with results reported for docetaxel plus prednisone. The effects of dose level and dose schedule on ixabepilone activity are, as yet, unknown, so further study is recommended.

Katherine Sole

Original article Hussain *et al.* (2005) Ixabepilone (epothilone B analogue BMS-247550) is active in chemotherapy-naive patients with hormone-refractory prostate cancer: a Southwest Oncology Group trial S0111. *J Clin Oncol* **23:** 8724–8792

Endoscopic treatment of vesicoureteral reflux is safe but not highly effective

The standard treatment for vesicoureteral reflux (VUR) is open surgical ureteric reimplantation, but a less-invasive alternative is endoscopic subureteral injection of a bulking agent. Mevorach *et al.* have conducted a prospective, multicenter, 2-year, US trial, examining the safety and efficacy of first-line endoscopic treatment with one of the available bulking agents (synthetic calcium hydroxyapatite) in children with VUR and traditional indications for surgery.

Synthetic calcium hydroxyapatite was injected under cystoscopic guidance in 98 patients (155 ureters) with grades II–IV VUR. Of these, 44 received one injection, 51 received two injections, and 3 received three injections. Data were analyzed for the 86 patients who completed the initial follow-up period. Across the 10 centers, 32% of patients were cured at 1 and 2 years. Ureteral cure rates were 46% at 1 year and 40% at 2 years. The primary treatment center, however, produced higher success rates, with a 2 year cure rate of 66% of patients and 72% of ureters. These better results were probably the result of the primary center's greater experience. Three patients experienced serious adverse events, none of which were related to the procedure or material used.

Endoscopic subureteral injection with synthetic calcium hydroxyapatite was safe, but not highly effective, when compared to the rates of cure achieved by open surgery (typically 95–98% in grades I–IV VUR). Before a new technique can replace open surgical repair of VUR, it must demonstrate long-term surgical success and include a comparison to medically treated patients, say the authors.

Katherine Sole

Original article Mevorach RA *et al.* (2006) Results of a 2-year multicenter trial of endoscopic treatment of vesicoureteral reflux with synthetic calcium hydroxyapatite. *J Urol* **175:** 288–291

BCG plus mitomycin is more effective than BCG alone in bladder cancer

Most systemic anticancer regimens combine drugs for increased efficacy, but this approach has rarely been applied to intravesicular treatment of bladder cancer. The current standard treatment for early-stage or superficial bladder cancer is resection followed by immunotherapeutic Bacillus Calmette–Guérin (BCG) therapy. Combination therapy with ELECTROMOTIVE ADMINISTRATION of the

GLOSSARY

ELECTROMOTIVE ADMINISTRATION
Therapy that uses a local electric current to introduce the ions of a medicine into the tissues

GLOSSARY

URETHRAL RETRO-RESISTANCE PRESSURE (URP)
The pressure required to achieve and maintain an open urethral sphincter at rest; assessed by infusion of sterile fluid along the urethra into the bladder

chemotherapeutic agent mitomycin plus BCG has shown potential: electromotive administration is thought to make the bladder mucosa more permeable, thereby helping mitomycin reach its target. Italian researchers have conducted a randomized study comparing the efficacy of BCG plus electromotive mitomycin with that of BCG alone in patients with stage pT1 transitional-cell carcinoma of the bladder.

Patients received one course of treatment per week, of either BCG alone for 6 weeks ($n = 105$), or three cycles of BCG (2 weeks) and mitomycin (1 week) ($n = 107$). Patients in the sequential group had a longer disease-free interval than those in the BCG group (69 months versus 21 months, $P = 0.0012$), lower overall ($P = 0.045$) and disease-specific ($P = 0.01$) mortality rates, and a longer time to progression ($P = 0.0047$). Adverse event profiles were similar in both groups.

The authors conclude that BCG plus electromotive mitomycin was more effective than BCG alone. They recommend that further studies be undertaken to establish an optimum regimen of BCG and the precise mechanism by which BCG and mitomycin operate together. They also suggest that all patients with stage T1 bladder cancer undergo restaging transurethral resection, and that perioperative mitomycin should be used to reduce intraoperative seeding of malignant cells.

Katherine Sole

Original article Di Stasi SM *et al.* (2006) Sequential BCG and electromotive mitomycin versus BCG alone for high-risk superficial bladder cancer: a randomised controlled trial. *Lancet Oncol* **7:** 43–51

Urethral function assessment without catheterization

Several methods exist for assessing urethral function in patients with lower-urinary-tract symptoms, but most require catheterization, or, in the case of ultrasound, specialized equipment and trained personnel. There is a simple-to-perform alternative that avoids catheterization: measurement of URETHRAL RETRO-RESISTANCE PRESSURE (URP). This promising technique has now been prospectively assessed in an unselected group of 185 consecutive women with lower-urinary-tract symptoms, who were referred to three European teaching hospitals.

The authors found that URP performed poorly as a diagnostic tool, but they suggest it might be useful to assess urethral function and, therefore, direct treatment, or to predict the outcome of continence surgery. The highest mean URP values were seen in women with detrusor overactivity, and the lowest in those with urodynamic stress incontinence. Intermediate mean URP values were seen in women with mixed urodynamic incontinence and those with normal urodynamics. When the mean URP value for women with urodynamic stress incontinence was compared with the mean URP values for those with detrusor overactivity, normal urodynamics and mixed incontinence, the differences were all statistically significant ($P < 0.05$).

URP measurement cannot replace the 'gold standard' of urodynamic studies, especially before undertaking continence surgery; however, the authors conclude that URP could provide a useful 'scientific' evaluation of the urethral sphincter at rest, as it measures different aspects of urethral function from those assessed by urethral pressure profiling. They suggest that assessing urethral function with URP might be useful before undertaking conservative management strategies such as physiotherapy, and call for more studies further evaluating URP.

Caroline Barranco

Original article Digesu DA *et al.* (2006) Urethral retro-resistance pressure and urodynamic diagnoses in women with lower urinary tract symptoms. *BJOG* **113:** 34–38

Beneficial effect of statins in patients with prostate cancer

Statins have been associated with a reduced risk of cancer, possibly acting by inhibiting the activation of oncoproteins. In a retrospective study, Moyad *et al.* investigated the impact of statin therapy on the clinical presentation and long-term biochemical progression-free survival (bPFS) of 512 consecutive patients who underwent brachytherapy for prostate cancer, 65 of whom were taking statins. The authors defined bPFS as a serum PSA level of 0.4 ng/ml or less after nadir.

Pretreatment PSA levels and percentage of positive biopsies were statistically significant predictors of patient outcome. Statin users presented with lower PSA levels, lower