International Journal of Clinical Practice

Current Perspectives in Bladder Cancer Management

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Disclosures

Int J Clin Pract. 2013;67(5):435-448.

Abstract

More than 350,000 new cases of bladder cancer are diagnosed worldwide each year; the vast majority (> 90%) of these are transitional cell carcinomas (TCC). The most important risk factors for the development of bladder cancer are smoking and occupational exposure to toxic chemicals. Painless visible haematuria is the most common presenting symptom of bladder cancer; significant haematuria requires referral to a specialist urology service. Cystoscopy and urine cytology are currently the recommended tools for diagnosis of bladder cancer. Excluding muscle invasion is an important diagnostic step, as outcomes for patients with muscle invasive TCC are less favourable. For non-muscle invasive bladder cancer, transurethral resection followed by intravesical chemotherapy (typically Mitomycin C or epirubicin) or immunotherapy [bacillus Calmette-Guérin (BCG)] is the current standard of care. For patients failing BCG therapy, cystectomy is recommended; for patients unsuitable for surgery, the choice of treatment options is currently limited. However, novel interventions, such as chemohyperthermia and electromotive drug administration, enhance the effects of conventional chemotherapeutic agents and are being evaluated in Phase III trials. Radical cystectomy (with pelvic lymphadenectomy and urinary diversion) or radical radiotherapy are the current established treatments for muscle invasive TCC. Neoadjuvant chemotherapy is recommended before definitive treatment of muscle invasive TCC; cisplatin-containing combination chemotherapy is the recommended regimen. Palliative chemotherapy is the first-choice treatment in metastatic TCC.

Bladder-Sparing Treatments After BCG Failure

Radical cystectomy remains the mainstay of treatment for patients who have failed BCG treatment. For patients who are unwilling or unfit to undergo this procedure, the treatment options are limited.

Intravesical chemotherapeutic agents, such as gemcitabine and docetaxel, novel immunotherapies, such as interferon-alpha, and device-assisted treatments have all shown promise. However, to date, much of the evidence to support their potential benefit is based on non-randomised or small Phase II studies. At best, currently available bladder-sparing treatments for those with BCG-refractory TCC are associated with 2-year DFS of approximately 50%.[90]

Electromotive drug administration (EMDA) is an alternative way of enhancing MMC absorption and urothelial exposure, by creating an electrical gradient across the bladder wall using electrodes placed within the catheter and on the lower abdominal wall. In patients with BCG-naïve high-risk NMIBC, EMDA-MMC has shown promise.[95,96] To date, no studies have specifically evaluated EMDA-MMC in the BCG-refractory setting, although one RCT allowed crossover of patients to EMDA-MMC alone if they did not respond to primary BCG treatment