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Bladder Cancer: Highlights from 2006

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Abstract

Objectives: This paper provides an overview of the most relevant findings on bladder cancer (BCa) presented at the 2006 annual meetings of the European Association of Urology, American Urological Association, and the American Society of Clinical Oncology.
Methods: Experts in the field of BCa selected and discussed relevant new findings in BCa during a closed meeting in Marbella, Spain. Furthermore, the participants' opinions on representative clinical cases were assessed via interactive voting. Voting results were commented on by an expert panel.
Results: Many studies examined the diagnostic and prognostic value of the biomarkers survivin and nuclear matrix protein-22, but results were not consistent. With respect to superficial BCa, a major revelation was the introduction of the European Organisation for Research and Treatment of Cancer tables to calculate the risk for recurrence and progression of superficial BCa patients. In addition, one study showed that Bacillus Calmette-Guérin + interferon-alpha might be a good alternative treatment for patients with recurrent superficial BCa. For patients with minimally invasive BCa who had undergone radical transurethral resection, a bladder-sparing treatment was cautiously suggested. For those with recurrent urothelial cancer, one study presented a new salvage chemotherapy consisting of paclitaxel, ifosfamide, and nedaplatin. Finally, two studies demonstrated that there was no difference in oncologic outcome between patients who underwent open or laparoscopic radical cystectomy or nephroureterectomy.
Conclusions: Many interesting new findings in the field of BCa have been presented at 2006 urologic/oncologic meetings, which aim to improve the diagnosis and treatment of patients with BCa.
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1. Introduction

Bladder cancer (BCa) is a common malignancy, being the fourth most frequent cancer in men and the ninth most frequent cancer in women in the United States [1]. In Europe, approximately 36,500 males and 13,000 females die from BCa each year [2]. The incidence of BCa varies considerably across

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Europe. The highest mortality rates are observed in Southern and Western European men. The majority of newly diagnosed BCas, 70–80%, are classified as superficial disease. The remaining tumours initially present as either invasive or metastatic disease. About 70% of individuals with superficial BCa have a low-grade papillary tumour that involves only the urothelium. Although these patients will have numerous interventions after diagnosis, their overall prognosis is good and most of them will die from other causes. The other 30% of superficial BCas have a higher histologic grade, involve the lamina propria, and are often accompanied by a flat carcinoma in situ (CIS). Therefore, this population is at high risk for both progression and death from BCa. Since BCa has the highest recurrence rate of all cancers, not only patients with a high-grade tumour but also those with a low-grade tumour need very thorough surveillance [3].

This paper provides a selection of data on BCa presented in 2006 at annual meetings from the European Association of Urology (EAU), the American Urological Association (AUA), and the American Society of Clinical Oncology (ASCO). A selection of abstracts on BCa presented at these congresses was discussed during the ''New Horizons in Urology'' meeting in Marbella, Spain. In addition, participants in this meeting were engaged in an interactive voting procedure to assess their opinions on representative clinical case studies illustrative of the chosen abstracts. Voting results were commented on by experts in the field of BCa.

2. Biomarkers for the detection and surveillance of BCa

Because of the high recurrence rate of BCa, a rigorous patient follow-up is necessary to monitor the disease by allowing appropriate detection and treatment in both low- and high-grade tumour patients to maximise their cure rate. The most important evaluation methods used so far include cystoscopy, voided urine cytology (VUC), and urinary tract imaging. However, because of the rather low sensitivity of VUC in detecting transitional cell carcinoma (TCC) of the urinary tract, particularly in low-grade disease, the invasive character of cystoscopy, and the significant costs associated with the elaborate surveillance protocol, additional follow-up strategies were investigated. Therefore, various biomarkers were introduced to detect disease in the urinary tract by analysing voided urine samples. Current biomarkers investigate biologic characteristics associated with different levels of the cancer cell evolution and can be grouped into several categories such as tumour-associated antigens, blood group antigens, growth factors, apoptosis/cell-cycle and extracellular matrix proteins, and DNA alterations [4].

Although these biomarkers have promising diagnostic and prognostic value, they are scarcely used in practise because of their rather insufficient sensitivity and/or specificity. A stumbling block in the generalised use of these biomarkers may be the lack of straightforward studies supporting their use for decision making, treatment, and prognosis of BCa. However, it has also been put forward that cost, difficult interpretation of results, or the unsuitability for use in the office contribute to their minimal use.

At the EAU 2006 congress, several new data on the biomarkers survivin and nuclear matrix protein-22 (NMP-22) was presented.

2.1. *Survivin*

Survivin, a 16.5-kDa protein, belongs to the type of proteins that serve to inhibit apoptosis. In contrast to normal cells, survivin is highly expressed in a large number of malignant neoplasms and is generally associated with adverse prognosis. In the case of BCa, survivin is differentially expressed in the neoplastic epithelium, but not in the normal epithelium or in the uninvolved mucosa. Therefore, several research groups have already explored the possibility of using urinary survivin as a molecular biomarker for the early detection of BCa, and the prognostic and diagnostic potentials of survivin remain under investigation by several groups [5–10].

Several teams found a correlation between high survivin levels and urothelial invasion, size, pathologic stage and grade, progression and/or mortality in primary or recurrent TCC [5,6,8]. However, in one study [7], the level of survivin messenger RNA (mRNA) measured by real-time polymerase chain reaction was not correlated to stage and grade. This discrepancy may be due to different methods that were used to analyse the survivin levels in the urine samples. Nevertheless, this latter study showed that urinary survivin mRNA is a highly specific (100%) and sensitive (75%) marker for the detection of TCC [7].

Although these data support the use of survivin as a diagnostic and prognostic tool for superficial BCa, one study did not support these findings. Using an enzyme-linked immunosorbent assay to detect survivin in serum or voided urine samples, the authors were unable to identify those patients with BCa [9].

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