Management of Prostate Cancer: Global Strategies

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Abstract

As in any malignancy, the management of prostate cancer (pCA) is highly dependent on stage and grade, as well as on the patient’s condition. The European Association of Urology (EAU) guidelines on the primary treatment of pCA advise watchful waiting, radical prostatectomy, radiotherapy, hormonal treatment, or a combination of various therapies, depending on the stage and grade of the tumour, as well as the patient’s remaining life expectancy and condition. Cytotoxic therapy is recommended for hormone-refractory pCA with metastatic disease. Comparing the results of a survey among urologists on how they treat pCA in clinical practice to the recently updated EAU guidelines shows that the EAU guidelines are followed by the majority of urologists, but these guidelines do not provide guidance for all patients that urologists are confronted with in clinical practice. Considerable variations in practice between urologists were recorded.

New data presented at the EAU 2006 annual congress on the use of prostate specific antigen (PSA) in diagnosis/screening, surgery, radiotherapy, hormone therapy, and chemotherapy for the management of pCA is discussed. Whereas the value of serum PSA levels for initial screening is debated, PSA levels in combination with PSA doubling time and PSA velocity may prove more reliable for assessing the presence and severity of pCA. PSA remains important for follow-up after treatment to detect disease recurrence. Several studies on novel surgical techniques including laparoscopic and robot-assisted surgery as well as high-intensity focused ultrasound (HIFU) showed promising results. Data on efficacy and safety of two novel luteinising hormone-releasing hormone antagonists were presented, as well as data comparing intermittent versus continuous hormonal therapy. Furthermore, the beneficial effects of biphosphonates in preventing bone complications in pCA patients on androgen-deprivation therapy and for metastatic disease were highlighted.

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1. Introduction

Prostate cancer (pCA) remains one of the most commonly diagnosed and lethal malignancies in men. During the past decade the incidence of pCA has increased but mortality has decreased, which offers increasing numbers of patients a curative rather than palliative treatment [1]. The debate remains whether this reduction in mortality is due to improved screening, with some groups reporting a lower pCA-related mortality in highly screened populations [2] but which has been contradicted by others [3].

However, not all pCA detected is equally aggressive, and systematic screening and treating may expose patients with clinically insignificant pCA to unnecessary treatment and its associated morbidity. Hence, the challenge remains to identify and adequately treat those patients at risk for progression, while avoiding overtreatment in those with clinically insignificant disease. Guidelines, for instance those issued by the European Association of Urology (EAU), may aid in diagnosis and treatment decisions for the management of pCA.

In this paper we outline the updated EAU guidelines on treatment of pCA and compare them with the results of a survey on how urologists actually treat their patients in clinical practice. Subsequently, we discuss new data that was presented during the EAU 2006 annual congress on diagnosis, screening, and treatment of pCA.

2. Management of pCA in Europe: EAU guidelines versus clinical practice

The EAU guidelines on the primary treatment of pCA have been updated recently [4,5]. However, it remains unclear if clinicians indeed rely on these guidelines for treating their pCA patients. Hence, to what extent the guidelines are being applied in clinical practice was assessed during a meeting in October 2005, the detailed results of which have been published elsewhere [6]. Briefly, 150 urologists from various European countries attended a symposium in Malta, during which an interactive voting session was held on four patient cases. Subsequently, Professor Alcaraz and Professor Teillac chaired a debate with the audience and 10 experts.

The EAU guidelines recommend radical prostatectomy (RP) as standard therapy for localised pCA (tumour stage: T1b–T2) in patients with a life expectancy >10 yr and otherwise fit for surgery. In case the patient does not meet one of these criteria, radiotherapy (RT) should be offered [4]. This treatment was agreed upon by the majority of the delegates. Age and physical conditions were the major criteria for differentiating between RP and RT. Disagreement was mainly related to the question of whether these patients should receive additional adjuvant and/or neoadjuvant hormone therapy (luteinising hormone-releasing hormone [LHRH] agonists) [6].

Watchful waiting may be suitable for asymptomatic patients with well-defined tumours and <10 yr life expectancy. For advanced pCA (T3–T4) the combination of RT and hormone therapy is recommended as standard therapy in symptomatic patients [5]. The delegates’ opinions were divided between LHRH agonist monotherapy in older patients, and the combination of RT and hormone therapy in younger patients, whereas the EAU guidelines do not take into account the patient’s age [6].

About one third to one half of the patients who have undergone radical therapy will relapse within 10 yr after initial therapy [4]. As pCA recurrence is almost invariably preceded by a PSA rise [7]—although disease recurrence in the absence of detectable PSA has been described in patients with undifferentiated tumours [8]—treatment failure has been defined as “a rising PSA level after radical therapy”. The EAU guidelines consider two consecutive PSA values of ≥0.2 ng/ml after RP as recurrent cancer. In case of RT, three consecutive increasing PSA values measured at 3-mo intervals above a previous nadir are considered recurrent pCA [4]. In case of local recurrence a PSA increase >3 yr after surgery and a PSA doubling time (PSADT) ≥11 mo are observed. Distant failure after RP is predicted by a PSA increase <1 yr after surgery and a PSADT between 4 and 6 mo. Local recurrence after RP or RT should be treated with salvage RT or RP, respectively, before the PSA level has reached 1.5 ng/ml. Watchful waiting with possible hormone therapy later on may also be offered to those patients. Distant failure can be managed with early hormone therapy. The experts agreed unanimously that PSA level as well as PSADT constitute the most important predictors to differentiate between local and distant recurrence. Around half (49%) of the attending urologists indicated RT to be their treatment of choice for patients with local recurrence. Around one third (31%) of the delegates stated that they used LHRH agonist monotherapy in these patients to avoid treatment-related side-effects and to improve the patients’ quality of life (QoL). Active surveillance was preferred for those patients with a long PSADT. While the experts and delegates tended to follow the EAU guidelines with respect to

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salvage RT after initial RP, they indicated that these guidelines do not take into account the patients’ QoL [6].

The outcomes of this meeting clearly showed that there are large variations in the management of patients with pCA among urologists. The EAU guidelines provide guidance in the management of pCA, but do not give direction for all patients seen in daily clinical practice. This deficiency reveals the need for continued medical education of practising urologists.

3. New data on the management of pCA presented at the EAU 2006 congress

3.1. Diagnosis and screening

The value of PSA levels for the detection of pCA has been questioned because some have argued that a PSA rise may also be due to benign prostatic hyperplasia (BPH) [9]. Others have argued that even considerable numbers of men with low PSA levels (defined as a PSA <4 ng/ml) have pCA, with some even having high-grade pCA [10,11], and hence that the PSA cutoff value should be <4 ng/ml. However, this value would expose millions more men to biopsies [9], which are costly and, even if they are negative, have a considerable psychological morbidity on the men involved, as shown in a study in which almost 20% of biopsy-negative patients fulfilled the criteria for posttraumatic stress disorders and depression [12]. Furthermore, others point out that not the PSA level alone, but rather the PSA level in combination with the rate of PSA increase (PSA velocity [PSAV] and PSADT) are important aids in discriminating not only between BPH and pCA, but also between more- and less-aggressive pCA [13]. Roobol et al. [13] used data from 588 men who were biopsied because of a PSA ≥3.0 ng/ml. These men were subdivided into three groups: (1) men diagnosed with a less-aggressive (LA) pCA, (2) men diagnosed with a more-aggressive (MA) pCA, and (3) men with a benign biopsy result. This study showed that using a PSAV cutoff value of 2.0 ng/ml/yr along with the PSA 3.0 ng/ml cutoff would have resulted in 32% fewer benign biopsies, 28% fewer LA biopsies, and no reduction in MA biopsies. A PSAV cutoff of 4.0 ng/ml/yr would have resulted in 58%, 55%, and 19% fewer biopsies, whereas a PSAV cutoff of 0.75 ng/ml/yr would have resulted in 82%, 83%, and 38% fewer biopsies (Fig. 1). In sum, Roobol et al. showed that applying a screening algorithm using a PSAV cutoff of 0.2 ng/ml/yr along with a PSA value of at least 3 ng/ml allowed for a considerable decrease in the number of biopsies, while at the same time all aggressive cancers were detected. A mean PSAV of 0.96 ng/ml/yr was significantly related to MA pCA.

Furthermore, contrary to earlier belief, fluctuating PSA levels are not associated with LA pCA or decreased risk of pCA [14,15].

A multicentre study [16] inviting asymptomatic men between 45 and 49 for screening on pCA reported a low response rate (39%), suggesting that younger men are less interested in routine screening for pCA. Only nine cancers, all of them low grade, were detected among 515 men, which questions the value of PSA screening in younger men.

New ways for enhancing the diagnostic performance of PSA in pCA are being explored. For instance, prostate cancer gene 3 (PCA3) encodes messenger RNA (mRNA) that is prostate-specific and highly expressed in pCA cells. Fradet et al. [17] reported their assay to have a specificity of 76% and a sensitivity of 50%, which was considerably higher than the specificity of serum PSA (22%).

Another study [18] assessed human glandular kallikrein (hK2), which is a serum marker with 80% structure similarity to PSA to identify pCA in patients with a PSA <4 ng/ml. It was shown that hK2 could discriminate significantly between pCA and BPH, and could increase specificity of PSA.

Boccon-Gibod et al. [19] presented the first study on the use of saturation biopsy in the reevaluation of microfocal pCA in 30 patients with potentially insignificant pCA (1 single positive core out of 10, with <5 mm of Gleason score <6 tumour on a primary biopsy). Taking repeat biopsies (32 cores)
by means of transrectal ultrasound was shown to aid in distinguishing among patients with minimal disease, those with probably minimal disease, and those who almost certainly have significant disease. In their study, 63% of the patients had positive repeat biopsies, and 20% of these were upgraded to a Gleason score ≥7; 37% were negative for pCA, suggesting these patients may be managed with observation and delayed treatment, and hence avoid having RP.

3.2. Active surveillance

Active surveillance with selective delayed intervention has been advocated for patients with good-risk pCA, meaning they have a Gleason score ≤6, PSA <10–15 ng/ml, and tumour stage T1c–T2a [20]. Around 50% of newly diagnosed pCA cases belong to this group, for whom the disease is indolent, hence posing no threat during the lifetime of most patients. The challenge remains to identify the patients who most likely will not progress, while simultaneously offering radical treatment to those who are at risk. Klotz et al. [20] proposed to stratify patients in risk groups for progression according to PSADT. In this approach, patients with a PSADT ≤3 yr based on a minimum of three assays over 6 mo are offered radical therapy, whereas the others are closely monitored with serial PSA and periodic biopsies at 2, 5, and 10 yr.

However, a study [21] presented at the annual EAU 2006 congress showed that the criteria for nonsignificant pCA (Gleason score ≤6, PSA <10 ng/ml, T1c, 1 positive biopsy of 21, tumour size <3 mm) underestimate tumour aggressiveness. More than half of the pCA patients who preoperatively responded to these criteria were shown to have a MA tumour (pT3, Gleason ≥7, and/or tumour volume >0.5 cc).

Another study assessed (1) which patients with T0–4 N0–2 M0 pCA who were treated with watchful waiting and were unfit for local definitive treatment were not in immediate need of hormone therapy [22] and (2) the prognostic value of PSADT in the same patients [23]. The authors concluded that patients older than 70 yr with a baseline PSA ≤50 ng/ml might not benefit from immediate treatment, whereas in patients ≤70 yr the serum PSA threshold to benefit from immediate treatment appeared lower [22]. Furthermore, patients with an initial PSA between 8–50 ng/ml and a PSADT <12 mo apparently constituted a subgroup of patients at high risk of progression and death attributable to pCA, and hence these patients might be in need of immediate hormone therapy [23].

3.3. Treatment

3.3.1. Treatment with curative intent: surgery and radiotherapy

Radical prostatectomy remains the golden standard for surgical treatment of localized pCA in patients with a life expectancy >10 yr [4]. The large retrospective European Study on Radical Prostatectomy (ESPRE) involving 10,553 men who underwent RP between 1993 and 2004 revealed a favourable trend over time in operation time, complication rates, and biochemical recurrence. A considerable decrease in positive surgical margins (PSMs; or the evidence that surgery may not have entirely removed the cancer) was observed, and a larger proportion of T1c and pT2 cancers were operated. Furthermore, the prevalence of nerve-sparing procedures had also increased (Fig. 2) [24]. Postoperative continence and potency rates had improved as well [25]. The authors concluded that RP had significantly evolved over the years of the study. Best outcomes were noticed for centres performing >200 cases per year and in those with the lowest surgeon/case ratio. Another study [26] assessing long-term survival after RP showed that 71% of the patients remained free of progression 10 yr after the operation. Independent risk factors for progression after RP comprised Gleason score, organ-confined disease, seminal vesicle involvement, lymph node metastasis, and surgical margin status.

Whereas RP yields good results for T1 and T2 stage tumours, the management of locally advanced disease (T3) is controversial because RP in these patients often results in incomplete tumour resection and, hence, a higher probability of disease...
At the EAU 2006 congress several presented studies assessed the outcomes of RP in cT3 pCA. Joniau et al. [27] assessed the technical feasibility of surgery in 139 cT3 patients who underwent retropubic RP with pelvic lymphadenectomy. The positive surgical margin rate amounted to 15%. There was no perioperative mortality, and no serious in-hospital complications were recorded. Furthermore, complete continence 12 mo postoperatively was 87.8%, whereas erectile function recovered in 6% of the patients who underwent a non–nerve-sparing procedure versus 10% of those who had a nerve-sparing procedure. It was concluded that RP in cT3 pCA is technically feasible with morbidity comparable to RP in clinically localised pCA. Hsu et al. [28] reported on 200 patients with unilateral clinical stage T3 pCA who underwent RP and bilateral pelvic lymphadenectomy. The authors reported very high 10-yr overall and cancer-specific survival (CSS) outcomes in this patient group (Fig. 3) in whom 23.5% were confirmed with organ-confined disease (pT2), but 72.5% were confirmed pT3, whereas 4% had pT4. Surprisingly, in their analysis, Gleason score and pelvic lymph node status were not independent risk factors in predicting CSS, biochemical progression-free survival, or clinical progression-free survival. Only pathologic stage was a significant independent factor for CSS. Over half (56%) of the patients needed adjuvant or salvage treatment. The authors concluded that RP is a valuable treatment option in unilateral cT3a pCA.

Before the publication of the revised EAU guidelines, no randomised controlled trials (RCTs) that compared RP with RT for localised pCA had been published, but the National Institutes of Health had set up a consensus in 1988 that external irradiation yields the same long-term survival results as those of RP [4]. This consensus appears to be confirmed by the results of the first RCT [29] comparing clinical progression, survival, and QoL of patients subjected to either external beam radiotherapy (EBRT) or RP, which was presented at the EAU 2006 congress. After a (however limited) follow-up of 67 mo, no significant differences were recorded in disease progression or survival (Fig. 4). RP patients tended to have worse urinary function ($p < 0.001$) but better bowel function ($p < 0.001$) than EBRT patients.

Whereas the open or retropubic RP has been standard treatment to date and remains the recommended surgical option in the EAU guidelines [4], laparoscopic and robotic procedures are becoming increasingly common in prostatectomy, although long-term oncologic and functional results for these minimally invasive procedures are lacking. A study [30] with a follow-up of 2.5 yr on 1177 patients who underwent either RP or laparoscopic prostatectomy (LP) for clinically localised pCA showed comparable PSM rates (respectively 11% and 11.3%). Furthermore, a significant decrease over time in PSM was noted for LP, whereas the PSM rate for RP remained unchanged, indicating a considerable learning curve for this recent technique. LP improved results on postoperative erectile function without increasing PSM rates at 18 mo of follow-up compared with open retrograde RP in a study on 210 patients [31], provided that a retrograde laparoscopic approach was used. Another study [32] showed that patients who underwent LP and who had PSM with margin size $<1$ mm had a biochemical disease-free survival similar to that of patients with negative margins after LP. These data are congruent with earlier results on PSM after RP. Obesity, prior pelvic surgery, or large prostate size does not appear to be a contraindication for LP [33–35]. Nevertheless, obese
patients exhibit a trend towards slower recovery of potency and continence than nonobese patients [33], and a significantly longer operation time has to be taken into account for these patients [33,35].

Whereas no reference to robot-assisted surgery has been made in the EAU guidelines to date, several contributions at the EAU 2006 congress assessed the outcomes of robotic surgery for prostatectomy. Oncologic and functional results of robotic approaches appeared to be similar to current established techniques [36–38]. However, long-term outcome data are still lacking.

Several contributions at the EAU congress reported on the efficacy of high-intensity focused ultrasound (HIFU), a minimally invasive therapy for e.g., local pCA [39–41]. The aim is to heat malignant tissues and to destroy them through coagulative necrosis. HIFU is considered an experimental treatment in the EAU guidelines [4]. Evaluation of HIFU results in 190 patients treated for localised pCA showed an actuarial 7-yr disease-free rate of 61% [40]. The authors concluded that HIFU might be a treatment option for patients with localised pCA who are unsuitable for RP or watchful waiting. Likewise, salvage treatment with HIFU in patients with localised pCA who relapsed after EBRT showed that 84% of the patients had negative control biopsies and 62% had a nadir PSA level <0.5 ng/ml within 4 mo after HIFU [41]. The main side-effects of HIFU appeared to be urinary retention, stress urinary incontinence (SUI), and impotence [4]. These adverse effects were confirmed in a prospective cohort study [39] involving 1078 patients who had undergone HIFU 10 yr earlier, which showed a low treatment-related morbidity on a short- and medium-term basis, with erectile dysfunction, urinary tract infection, and SUI being the most prevalent treatment-related side-effects.

3.3.2. Hormonal treatment

Ever since the pivotal studies of Huggins and Hodges [42,43], who demonstrated the dependence of pCA growth on testosterone, androgen-deprivation therapy (ADT) has been the mainstay of treatment of advanced and metastatic pCA.

Surgical castration (bilateral orchiectomy) remains the gold standard against which all other treatment modalities are compared [4]. Later years have seen the introduction of pharmacotherapy, in casu oestrogens (e.g., diethylstilbestrol [DES]), LHRH agonists and antagonists, and antiandrogens. DES has good therapeutic efficacy but has fallen out of favour because it is associated with a high cardiotoxicity.

Repeat administration (every 1, 2, 3, or 6 mo) of LHRH agonists (leuprolide, triptorelin, buserelin, goserelin) has become the standard of care in ADT. LHRH agonists initially stimulate LHRH receptors, resulting in a testosterone flare at onset of therapy. However, chronic exposure to LHRH agonists results in downregulation of the LHRH receptors, and suppresses LH and follicle-stimulating hormone (FSH) release, and hence ultimately testosterone production [4]. Hormonal therapy also has beneficial effects on lower urinary tract symptoms in pCA patients with a statistically significant increase in maximum flow rate and voided volume, whereas voiding frequency, Danish Prostatic Symptom Score (DAN-PSS), prostate volume, and postvoid residual urine decrease [44].

A drawback of LHRH agonist therapy is that 10% of patients fail to achieve castration levels [45]. Furthermore, potential detrimental effects of LHRH agonists may occur with the "flare" phenomenon (testosterone escape) [48]. Although only a minority (4–10%) of M1 patients appear to be at risk for a clinically significant flare reaction, the potential side-effects are serious enough (e.g., bone pain, spinal cord compression, renal failure, bladder outlet obstruction, or fatal cardiovascular events) to warrant special caution. Concomitant administration of an antiandrogen decreases, but does not completely eliminate the incidence of a clinically relevant flare reaction [4]. In this respect, the novel LHRH agonist Eligard® (leuprolide acetate delivered by means of a novel system capable of delivering 2-fold higher doses of the drug than conventional systems) has been shown to effectively suppress testosterone to below surgical castrate levels (<20 ng/dl) in 94–98% of the patients with minimal injection-related and breakthrough testosterone escapes [46,47].

In contrast, LHRH antagonists bind competitively to LHRH receptors in the pituitary, which results in a rapid decline in LH, FSH, and testosterone. While no flare is observed, these antagonists have been associated with life-threatening allergic reactions. At the EAU congress data was presented on two novel LHRH antagonists [49,50]. The efficacy and safety of degarelix were assessed in 187 patients during a 1-yr study. A rapid and sustained decrease in testosterone (<50 ng/dl) was observed in the majority of patients. Importantly, no systemic allergic reactions were reported, and side-effects were mainly related to the androgen deprivation [49]. Teverelix, another LHRH antagonist, was tested in a phase 2 trial in 14 patients and showed promising results with respect to efficacy and safety [50]. It was concluded that these compounds might
have potential for treating pCA; however, more data are needed to confirm these findings.

**Antiandrogens** are also applied in patients with advanced disease. These compounds compete with testosterone for the binding sites on the receptors of the prostate cell nucleus. Nonsteroidal antiandrogens may serve as primary monotherapy as an alternative to castration in patients with locally advanced pCA. Short-term administration concomitantly with an LHRH agonist reduces the risk of a “flare” phenomenon with the latter. The survival benefit of combining antiandrogens with LHRH agonists for maximal androgen blockade is small at best [4]. Recent results from the Scandinavian Prostatic Cancer Group (SPCG-6) study of the Early Prostate Cancer Programme with a median follow-up of 7.1 yr showed that patients with early nonmetastatic pCA also may benefit from antiandrogen treatment (bicalutamide) in terms of survival, compared with standard treatment alone, but only those with locally advanced disease. Patients with localised disease did not benefit from bicalutamide treatment [51]. This finding confirms earlier data with a follow-up of 5.4 yr from the same research programme [52].

**Intermittent hormone therapy (IHT)**, which could theoretically delay the appearance of androgen-independent pCA as well as improve the patients’ QoL during the periods they are off therapy, is considered investigational in the EAU 2005 guidelines [4]. The first phase 3 RCT [53] on intermittent versus continuous ADT with an LHRH agonist combined with a steroidal antiandrogen involved 626 patients whose PSA fell < 4 ng/ml or 80% below initial value after 3 mo of induction treatment. No difference was found between the two groups except for sexual activity; significantly more patients on IHT reported sexual activity compared with those on continuous ADT. The authors concluded that IHT could be standard in clinical practice for selected patients. Another study on IHT [54] presented at the EAU 2006 congress involved 103 patients with PSA recurrence who received three monthly injections of LHRH agonist combined with a nonsteroidal antiandrogen. Treatment was stopped when PSA fell <4 ng/ml and resumed when PSA reached >20 ng/ml, pain or urinary symptoms recurred, or the PSA progression slope over the previous 3 mo was >5 ng/ml/mo. Median duration of treatment cycle (ON/OFF) decreased from 24 mo at onset of IHT to 10 mo at the fifth cycle, and remained at 10 mo during the sixth and seventh cycles. Three (2.9%) patients died from their pCA. It was concluded that IHT ensures adequate disease control on a medium-term basis in a selected group of patients.

3.3.3. Treatment of hormone-refractory pCA

The growth of most prostate tumours will eventually become androgen-independent and thus will no longer respond to ADT. Upon cessation of the response, the hormone-refractory pCA (HRPC) patient can be treated with chemotherapy. No clearcut guidelines are available for this phase, and treatment options should be discussed with the individual patient [4].

In case cytotoxic therapy is administered, the EAU guidelines recommend docetaxel 75 mg/m³ every 3 wk as reference treatment [4]. Docetaxel may also be beneficial as second-line therapy in HRPC, following PSA relapse after first-line docetaxel therapy [55]. Other compounds that may be used for chemotherapy of HRPC include mitoxantrone, hydrocortisone, and prednisone [4]. Novel agents and combinations are being investigated. For instance, Serretta et al. [56] reported promising results for low-dose estramustine phosphate in combination with etoposide. Combining somatostatin with dexamethasone and an LHRH agonist [57] or the biphosphonate zoledronate [58] yielded better outcomes in somatostatin-treated patients relative to those who were not treated with somatostatin.

The majority of HRPC patients have painful bone metastases that may lead to bone pain, spinal cord compression, vertebral collapse or deformity, and pathologic fractures. These complications may be counteracted by administering biphosphonates (e.g., zoledronate, alendronate, pamidronate). Considering that bone metastases are amongst the most debilitating consequences of HRPC, along with the proven efficacy of biphosphonates, these compounds should be considered early in the treatment of HRPC [4].

![Fig. 5 – Long-term risk for first and second skeletal-related events (SREs) in patients with metastatic pCA treated with zoledronic acid (ZA) compared with placebo [61].](image-url)
Biphosphonates are also effective against ADT-induced osteoporosis and subsequent skeletal-related events (SREs) in nonmetastatic patients. Only 20% of the pCA patients were shown to have normal values of one mineral density at baseline, a percentage that further decreases to 0% after 10 yr of ADT, indicating that even without ADT they are already at increased risk for SREs [59]. The risk of incurring an SRE is significantly reduced when the biphosphonate zoledronic acid (ZA) is administered concomitantly with ADT [60,61]. Even if the patient has already suffered an SRE, the risk for a second SRE remains significantly lower in ZA-treated patients compared with placebo-treated patients (Fig. 5) [60]. The importance of preventing SREs is illustrated by a recent study showing that patients who had experienced an SRE had significantly worse survival and a lower health-related QoL [62].

4. Conclusions

The recently updated EAU guidelines for the management of pCA provide guidance on the diagnosis, treatment, and follow-up of men with pCA, but are not applicable to all patients in daily urologic practice. Large differences exist in treatment of pCA among urologists.

New data on pCA presented at the EAU 2006 congress confirm the importance of serum PSA, PSADT, and PSAV for assessing the presence and severity of (recurrent) pCA. The diagnostic value of other serum markers is being explored for improving the diagnosis of pCA. Novel therapeutic agents as well as minimally invasive surgical techniques show promising results, but more long-term data are awaited.

References


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