

Controversies on individualized prostate cancer care: gaps in current practice

Steven Joniau, David Pfister, Alexandre de la Taille, Franco Gaboardi, Alan Thompson and Maria J. Ribal

Ther Adv Urol
 (2013) 5(5) 233–244
 DOI: 10.1177/
 1756287213490053
 © The Author(s), 2013.
 Reprints and permissions:
[http://www.sagepub.co.uk/
 journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)

Abstract: Prostate cancer (PCa) is a heterogeneous disease with a wide spectrum of aggressiveness. Evidence-based guidelines are invaluable but cannot be expected to be extensive enough to provide detailed guidance on the management of all patients. As such, the use of individualized, risk-adapted approaches to the management of PCa is indispensable. However, wide variation in treatment approaches observed for patients in practice suggests that there is an unmet need to improve the individualized approach towards patient care. A holistic approach that encompasses guidelines and evidence-based medicine could be used to guide individualized care for patients with PCa, from first contact through to final outcomes. As a result of an international expert meeting, this paper proposes this approach and highlights some of the factors that can be considered when aiming to identify patients' profiles; individualize treatment; and improve communication between patients and the healthcare teams.

Keywords: cancer, guidelines, multidisciplinary communication, prostate, prostatic neoplasm, therapy

Introduction

Prostate cancer (PCa) is the most common cancer in men [National Institute for Health and Clinical Excellence, 2008], but it is difficult to treat due to its heterogeneity and wide spectrum of aggressiveness, from indolent to rapidly progressing. In the last 20 years, with the widespread use of prostate-specific antigen (PSA) as a screening tool, a greater proportion of patients present with localized PCa and many patients have low-risk disease [Cooperberg *et al.* 2007]. As not all diagnosed patients will require treatment, and only patients at high risk of having a deadly cancer will require aggressive therapy, overtreatment must be avoided to prevent the unnecessary exposure to the risk of treatment-related adverse events [Adami, 2010]. Conversely, even localized cancer has a significant impact upon mortality after 15 years [Johansson *et al.* 2004], highlighting the need for risk-adapted approaches to treatment.

Challenges in optimizing prostate cancer management

It is thought that 30–40% of patients with PCa do not receive optimum care (either overtreatment

or undertreatment), possibly indicating a lack of adherence to diagnosis and staging guidelines, such as those produced by the European Association of Urology (EAU) [Heidenreich *et al.* 2011]. However, adherence to guidelines may be limited by local variations in the availability of specialists and equipment, and inability of guidelines to encompass every clinical presentation of PCa seen in practice. As such, there are often wide variations in treatment approaches offered to individual patients in practice; this variation occurs worldwide and at all stages of the disease [Cooperberg *et al.* 2010; Fairley *et al.* 2009; Jonsson *et al.* 1995; Payne and Gillatt, 2007].

The factors that result in the variation in PCa management are numerous. Detection and staging of PCa is a difficult process with many uncertainties. PSA level is widely used for diagnosis of PCa, but the association between PSA-based screening and reduced mortality from PCa is uncertain and the use of screening may be associated with overdiagnosis [Andriole *et al.* 2009; Schroder *et al.* 2009, 2012]. Prostate biopsies are usually taken following the second consecutive measurement of elevated PSA level [Heidenreich

Correspondence to:
Maria J. Ribal, MD, PhD
 Head of Uro-oncology Unit,
 Hospital Clinic, University
 of Barcelona, Villarroel
 170, Escalera 12, planta
 1ª, 08036 Barcelona, Spain
mjribal@clinic.ub.es
Steven Joniau, MD, PhD
 University Hospitals
 Leuven, Leuven, Belgium
David Pfister, MD
 Universitätsklinikum
 Aachen-Klinik für
 Urologie, Aachen,
 Germany
**Alexandre de la Taille,
 MD, PhD**
 Department of Urology,
 CHU Henri Mondor,
 INSERM U955Eq07,
 Creteil, France
Franco Gaboardi, MD
 University of Milan, Milan,
 Italy
**Alan Thompson, FRCS
 (Urol)**
 Royal Marsden Hospital,
 London, UK

et al. 2012]. However, urologists use different biopsy techniques that are associated with varied detection rates and risk of complications. For example, while cancer detection rate is similar between transrectal and transperineal standard biopsies (12–14 cores) [Hara *et al.* 2008; Takenaka *et al.* 2008], transperineal saturation biopsies (>20 cores) can detect an additional 38% of PCa compared with transrectal saturation biopsies. Transperineal approaches are, however, limited due the proportion of patients (10%) reporting urinary retention [Moran *et al.* 2006].

Because PSA-based screening is not sufficiently robust to standardize clinical decision making in the management of PCa [Church, 2006], other prognostic biomarkers have been sought. Measurement of prostate cancer gene 3 (PCA3) mRNA and the TMPRSS2-ERG gene fusion mRNA in urine are potentially useful biomarkers for the diagnosis and prognosis of localized PCa respectively [Hessels *et al.* 2003, 2007; Rice *et al.* 2010; Salagierski and Schalken, 2012; Tomlins *et al.* 2011], but as these tests are not yet reimbursed, their application in routine clinical practice is limited.

To help identify patients at most need of treatment, risk stratification of PCa has been proposed. Risk stratification tools include the D'Amico classification system, CAPRA score, Partin tables and Kattan nomograms. Although these may correlate with risk, these tools are not widely accepted and may need to be validated in individual centers. Therefore, identifying the presence and stage of disease, as a first step to making management decisions, is fraught with difficulty and contributes to the variations in treatment received.

At each stage of PCa, a number of treatment options are available and are recommended by guidelines [Heidenreich *et al.* 2011]. In general, there is no clear evidence base to recommend one mode of management over another [Wilt *et al.* 2008]. Despite guidance, therefore, it is physician and patient preference and values that can be the most significant factors in the approach to management [Kramer *et al.* 2005]. Other factors relating to the healthcare team can also have a major impact on management. For example, in the use of radical prostatectomy, the choice of surgeon may be more important than the choice of surgical technique. Furthermore, new hormonal agents will become available, such as the inhibitors of

cytochrome P17 (Cyp17) abiraterone [recently licensed for the treatment of castrate-resistant PCa (CRPC)] and orteronel, the androgen receptor antagonist enzalutamide, and other agents, such as the immunomodulatory/antimetastatic/antiangiogenic agent tasquinimod, and the radioisotope alpharedin (radium-223 chloride). These agents may help treatment of CRPC [Adamo *et al.* 2012; Pili *et al.* 2011; Scher *et al.* 2010; Yap *et al.* 2011], which is currently the biggest challenge to overcome in the management of PCa.

The choice of treatment will also be affected by their associated side effects that may have an impact upon quality of life (QoL) to a different extent in different patients. A wide variety of other factors also influence management decisions, and these include financial, legal and other incentives, as well as sociodemographic factors, such as ethnicity, socioeconomic status, income and place of residence [Bauvin *et al.* 2003; Cooperberg *et al.* 2004; Fairley *et al.* 2009; Harlan *et al.* 2001; Krupski *et al.* 2005]. Even within relatively small geographical areas, these factors can result in important variations and inequalities in the management of PCa [Fairley *et al.* 2009].

Beyond guidelines

There is an unmet need to improve the individualized approach towards patient care, particularly increasing the understanding of who to treat, when to intervene, and what treatment to use. The factors outlined above highlight the inadequacy of guidelines and evidence-based medicine alone for providing consistent and optimum individualized management of PCa. While ongoing clinical research into more reliable early detection and classification of PCa, new therapeutic agents, and improved surgical methodology will help improve care in the future; sharing experiences and knowledge can also enhance current practices. The internet offers an opportunity for collaboration between healthcare professionals and patients, enhancing communication, and improving advice on the individualization of treatment of informed patients. One everyday way of enhancing communication is by following the DREAM interview technique (accurate history taking, relationship building, education, providing advice, and encouraging realistic goals) during consultations. Likewise, sharing experiences with experts from other therapy areas (such as breast cancer) may help PCa specialists optimize treatment decisions.

A holistic strategy to the management of PCa is proposed to improve individualized patient care. This should encompass the application of evidence-based medicine and clinical guidelines, alongside the use of nomograms, novel disease biomarkers, novel treatments and techniques, consideration of the patient's general health and comorbidities, and improved communication between the patient and the multidisciplinary team (MDT).

On 7–9 October 2011, a multidisciplinary meeting entitled 'Individualized prostate cancer care in an advancing world' was held. The aim of the meeting was to discuss how a holistic approach could be used to guide individualized care for patients with PCa, from first contact through to final outcomes. A total of 182 participants, who came from Western Europe (approximately 60%), Eastern Europe (approximately 20%), Asia (approximately 10%) and North Africa/Middle-East (approximately 10%), attended the meeting; attendees were principally urologists, radio-oncologists and medical oncologists. In order to test whether a worldwide group of experts could implement a holistic approach to care, participants were presented with several hypothetical patient scenarios (patients with localized, locally advanced, or metastatic disease) during workshop sessions. The group was asked to integrate guidelines, and other evidence-based medicine, to determine the following: how each patient's profile could be identified; which treatment options would be appropriate in order to provide individualized care; and ways in which communication could be improved. Key discussion points for the workshop are outlined in Table 1.

Identifying, individualizing, and improving patient care

Scenario 1: localized prostate cancer

A 65-year-old man with no medical history presented with normal digital rectal examination (DRE), PSA of 4.5 ng/ml, prostate volume of 50 cc³, International Prostate Symptom Score (IPSS) of 10, and QoL score of 2. A prostate biopsy found 1 out of 12 positive biopsies, 1 mm cancer, Gleason score 6 (3+3). A computed tomography (CT) scan showed no metastasis and magnetic resonance imaging (MRI) found no suspicious nodules.

The patient underwent radical prostatectomy, pT2a, Gleason score 6 (3 + 3), no residual tumor

after resection, unknown regional lymph node status, and no distant metastasis (R0N_xM0). At 6 weeks, PSA was 0.001 ng/ml, continence was one pad per day and the patient had weak erection.

Discussion centered on the need for treatment or active surveillance (AS) in low-risk PCa.

Identifying patient profiles. Low-risk PCa is a controversial topic because the exact definition is not yet standardized. As AS was an option in the case presented, the discussion was focused first on how to identify those patients that are the best candidates for AS. The most widely used diagnostic tools were DRE and PSA (both velocity and doubling time). Given the importance of a good initial selection of patients for AS, the use of MRI and an early confirmatory biopsy may also be important. Rebiopsy during AS is mandatory, but while the use of MRI is not widely validated and its use depends on the experience of urologists, data suggest that MRI may also be a useful tool for PCa detection in this setting [Lawrence *et al.* 2012; Nagarajan *et al.* 2012; Quentin *et al.* 2012; Shukla-Dave *et al.* 2012]. PCA3 is a useful biomarker to determine whether prostate biopsies should be performed following an initially negative biopsy outcome, but its use in AS is controversial and there is no specific reimbursement in most countries.

There are insufficient data for the use of genetic markers in urine for diagnosis or prognosis, and because nomograms can be misleading in approximately 30% of cases, these should not be used at diagnosis, but may have benefits later in the course of disease. One point that was stressed during the discussion was that one of the most important factors for accurate diagnosis is the availability of an experienced uropathologist. The lack of a dedicated uropathologist may lead to incorrect classification of the disease and, in turn, suboptimal treatment.

Individualizing treatment. Most participants at the meeting did not use nomograms routinely (<20% stated that nomograms were used in assessing localized PCa). A number of factors contributed to the concerns about nomograms: they can be time consuming and difficult to translate to individual patients; they are not always conclusive; most are developed with a single patient population, at a single center at a single time point and, as such, they lose validity at different centers and with improvements in

Table 1. Questions and key discussion points for the workshop sessions.

	Localized	Locally advanced	Metastatic
Controversy	<ul style="list-style-type: none"> How to identify significant <i>versus</i> insignificant cancers 	How to choose between different therapeutic options	When to start treatment
Identify patient profiles	<ul style="list-style-type: none"> How to carry out biopsies and MRIs How to use markers such as PCA3 	<ul style="list-style-type: none"> Understanding and optimizing staging tools (MRI/CT scans) The use of lymphadenectomy Who can benefit from a multimodality approach? 	<ul style="list-style-type: none"> Identifying the potential for new tools (e.g. choline PET scan) Defining CRPC
Individualize treatment	<ul style="list-style-type: none"> When and how to use nomograms effectively Understanding the impact on patient QoL and comorbidities 	<ul style="list-style-type: none"> Discussing treatment options within guideline recommendations Establishing a MDT 	<ul style="list-style-type: none"> How to manage comorbidities How to undertake pain assessments Balancing improved life expectancy without diminishing QoL Taking the MDT approach
Improve communication	<ul style="list-style-type: none"> Explaining to a patient that his cancer does not need to be treated aggressively 	<ul style="list-style-type: none"> Understanding the importance of open discussion within a MDT Discussing the opportunities offered by collaborative group trials 	<ul style="list-style-type: none"> Explaining the opportunities and parameters presented by investigational therapies Discussing QoL and outpatient management

CT, computed tomography; CRPC, castrate-resistance prostate cancer; MDT, multidisciplinary team; MRI, magnetic resonance imaging; PCA3, prostate cancer gene 3; PET, positron emission tomography; QoL, quality of life.

diagnostic procedures over time; and the possibility that they can be affected by regional and racial differences.

Individual factors are important when selecting the best management strategies for patients with low-risk PCa. Patient QoL, and the impact treatment may have upon this, is the first factor to be considered before choosing the course of management. Factors that may have a detrimental effect on QoL are age, comorbidities, anxiety about AS, and cultural and social circumstances [Huang *et al.* 2010; Johansson *et al.* 2009; Thong *et al.* 2011; van de Poll-Franse *et al.* 2008]. Continence and erectile function are often the most important factors to affect QoL, and therefore, the importance of these to the patient and the possible impact of the different therapy

options should be discussed [Johansson *et al.* 2011; Kyrдалen *et al.* 2013].

Improving communication. Before proposing AS, it is important that a psychological evaluation of the patient is carried out, and that the MDT considers the patient's sociodemographic status. While AS is a well documented treatment modality in low-risk PCa, it is not well accepted in some countries. Physicians at the meeting believed that greater understanding of AS among patients and their families is required (i.e. it is important that patients understand that it is not the same as doing nothing), because the decision on AS can only be made with the patient's full cooperation and agreement. Clear and homogenous recommendations are needed to help patients understand the concept of AS [Van Poppel and Joniau, 2013].

In clinical practice, the greatest fears expressed by patients about their disease are generally: a fear of death; a fear of losing their QoL; sexuality issues; incontinence; repeated biopsies; and waiting and the uncertainties of treatment success. This is consistent with published studies [Bellizzi *et al.* 2008; Denis *et al.* 2012; Ihrig *et al.* 2011; Xu *et al.* 2011]. Many people expect treatment once they are diagnosed, making AS unacceptable to them. The potential impact of surgery or treatment on QoL must, therefore, be discussed in detail with patients. It is particularly important to provide clear information on incontinence or erectile dysfunction, as these are often the biggest concerns of patients [Bellizzi *et al.* 2008; Johansson *et al.* 2011].

The participants at the meeting suggested a number of measures that could aid communication between patients and the healthcare teams, and thus empower patients to make more informed choices. These included providing written information to all newly diagnosed patients; allocating more time for well trained nurses to discuss issues with patients; ensuring that a MDT is formed and the various members are involved in communication with patients; and giving patients time to decide on treatment options.

Scenario 2: locally advanced prostate cancer

Hypothetical clinical case. A 52-year-old sexually active married man with PSA of 13.5 ng/ml (rising from 9 ng/ml 2 years earlier), DRE T2a, and hypoechoic nodule at the posterior zone of the right lobe. A prostate biopsy found five of six positive biopsies on the right side [Gleason score 3 + 4 (70%)], and two of six positive biopsies on the left side [Gleason score 4 + 4 (<30%)].

A number of options were offered, including radical prostatectomy plus lymphadenectomy; external beam radiation with androgen deprivation therapy or without adjuvant treatment; androgen deprivation; or high-dose-rate brachytherapy. In this case, the patient was submitted for radical prostatectomy with lymphadenectomy. The lymphadenectomy options discussed were none, limited or extended lymphadenectomy. The pathological report was pT3 PCa; Gleason score 4 + 4 in two areas of 1 cm³; one positive margin (3 mm posterior); 15 lymph node negative; and immediate postoperative PSA at 6 weeks less than 0.1 ng/ml.

Discussion centered on the therapy options for locally advanced disease, use of adjuvant therapies and the need for a multimodal approach.

Identifying patient profiles. Defining locally advanced disease or high-risk localized disease was a matter of debate. DRE, bone scans, positron emission tomography computed tomography (PET CT; where available), PSA (both velocity and kinetics), biopsy, and MRI (if available) or transrectal ultrasonography were regularly used as staging tools among participants at the meeting.

In the management of locally advanced disease, lymphadenectomy should always be used when radical prostatectomy is considered, and extended pelvic lymph node dissection (PLND) should be performed according to EAU guidelines [using nomograms, which include PSA level, stage and Gleason score, to predict lymph node invasion (LNI) risk] [Heidenreich *et al.* 2011]. Limited PLND is of less value due to the high rates of false-negative findings. Some participants suggested that LNI could be predicted by a positive CT scan, but published data show that a positive scan is not a reliable measure [Briganti *et al.* 2011]. The inclusion of biopsy-derived information is very important when predicting LNI due to the predictive value of percentage positive cores for nodal metastases [Briganti *et al.* 2012]. While acknowledging that the use of lymphadenectomy in PCa is a controversial point [Briganti *et al.* 2009a, 2009b; Miki and Egawa, 2011; Spahn *et al.* 2010], some believe that lymphadenectomy can be curative. However, more data are needed to confirm this belief. In some European countries, lymphadenectomy is underused in everyday clinical practice.

When considering which patients may benefit from which treatment approach, the group agreed that, in addition to disease characteristics, patient characteristics should be closely considered (e.g. younger patients may be more suitable for multimodal treatment to preserve QoL).

Individualizing treatment. In most patients with locally advanced disease, adhering to evidence-based guidelines provides optimal treatment, and in most cases this would be radical prostatectomy with lymphadenectomy or irradiation and androgen deprivation therapy [Heidenreich *et al.* 2011; Mottet *et al.* 2011].

When patients with high-risk localized PCa or locally advanced disease undergo radical prostatectomy, approximately 50% will require subsequent therapy [Lu-Yao *et al.* 1996; Swanson *et al.* 2002],

but there was no consensus on whether this should be immediate or salvage, which reflects the uncertainty of the evidence [Cozzarini and Di Muzio, 2011; Nielsen *et al.* 2010]. In lower-risk locally advanced disease, there were different preferences for radiation therapy and surgery among participants. With radiation therapy, androgen blockade is recommended as adjuvant therapy for a period of 2 years, but with surgery, androgen blockade therapy is only recommended for node-positive patients [Mottet *et al.* 2011]. Participants agreed that the number of lymph nodes affected could be used as a prognostic factor in order to determine the need for immediate adjuvant therapy; however, when less than two nodes are involved, then there was no consensus on whether androgen blockade should be immediate or delayed [Briganti *et al.* 2009b; Steuber *et al.* 2011]. Guidelines state that it is unclear whether early androgen blockade should still be used in the era of increased detection of microscopic involvement as a result of more extensive LND [Heidenreich *et al.* 2012].

A concept that was generally accepted among participants was that the MDT approach is important when treating this kind of patient, with involvement of urologists, radiotherapists, oncologists, radiologists and pathologists. Involvement of the MDT should represent the future approach to PCa management. However, due to time constraints in practice, discussion of cases in MDT sessions is often restricted to highly selected patients only (usually patients with a number of possible treatment options, for which a discussion and shared decision may be needed).

Improving communication. It was agreed that the advantage of the MDT approach is that it encourages the team to consider evidence-based guidelines, and therefore, optimize patient management. In discussions with the patient and their spouses, it is important to discuss the side effects of treatment and issues of sexual function and incontinence. Psychological support may be needed for some patients to deal with these issues [Heidenreich *et al.* 2012; White *et al.* 2012], and so a psychologist may be an important addition to the MDT. Generally, participants felt that the MDT should meet weekly [Gomella, 2012; Lamb *et al.* 2011a, 2011b].

Scenario 3: metastatic prostate cancer

A 65-year-old man who was asymptomatic had a performance status of 0, DRE cT3, PSA of 430

ng/ml with a PSA doubling time of 6 months. He had no hypercalcemia or renal insufficiency. Prostate biopsy found 8 of 12 positive biopsies. He had adenocarcinoma with Gleason score 9 (4 + 5). A bone scintigraphy showed bone metastases.

A high PSA, low PSA doubling time and high Gleason score may indicate poor prognosis. A number of options were suggested, including immediate androgen blockade; deferred androgen blockade; continuous androgen blockade; intermittent androgen blockade; or chemotherapy plus hormonal treatment. In this case, hormonal therapy with complete androgen blockade was initiated. A PSA nadir of 0.1 ng/ml was reached and remained stable for approximately 9 months. However, 6 months after this, three consecutive PSA measurements confirmed a rise to 0.8 ng/ml.

Discussion centered on treatment options, such as stopping antiandrogen therapy, starting chemotherapy with docetaxel, stopping all hormonal treatment, or enrolling the patient in a clinical trial with new-generation hormone therapy.

Identifying patient profiles. Several tools are used to diagnose tumor spreading in metastatic PCa. In many countries, bone scintigraphy and CT or MRI of the pelvis and abdomen are used; however, this two-step approach has limited sensitivity and specificity. Whole-body MRI (WBMRI) as a one-step screening test has been shown to outperform bone scintigraphy with targeted x-rays for detection of PCa bone metastases, and performs as well as CT for evaluating enlarged lymph nodes [Lecouvet *et al.* 2012]. It is therefore thought that WBMRI may replace the current multimodality metastatic workup for the concurrent evaluation of bones and lymph nodes in high-risk patients with PCa.

PET scans are useful for identifying metastases in patients with PSA relapse following radical prostatectomy [Cirillo *et al.* 2009; Heinisch *et al.* 2006; Kotzerke *et al.* 2002]. The role of choline PET scan was discussed but the results achieved are not as good as initially anticipated [Bauman *et al.* 2012]. Choline PET scans were proposed as a helpful tool in very specific situations, such as when there is visceral involvement, when there is a slow PSA rise after irradiation or radical prostatectomy, and in other demanding scenarios (for example, in patients with rapidly progressive PSA but no evidence of metastasis using conventional tools such as MRI, CT scan or bone scans).

However, cost and availability limit the use of choline PET scans in some countries. The ‘trigger’ PSA (the cutoff for obtaining good results with a PET scan) may need to be more clearly defined before this technique is widely accepted [Castellucci *et al.* 2011; Graute *et al.* 2012].

A wide variety of tools and markers are used to predict survival in patients with metastatic disease: PSA doubling time and levels; Gleason score; bone scans; and presence of visceral metastases [Crnalic *et al.* 2012; Kambara *et al.* 2010; Robinson *et al.* 2008]. Nomograms may be useful in some circumstances and there is some evidence that testosterone levels may have some predictive qualities [Xylinas *et al.* 2011]. Ultimately, the use of various tools to predict prognosis depends upon local facilities and resources, which are limited in some regions (such as many parts of Eastern Europe).

Individualizing treatment. In the individualization of treatment, a clear definition of CRPC is needed. The current definition of CRPC is generally regarded as sufficient: serum testosterone levels of less than 50 ng/dl; three consecutive rises of PSA level, 1 week apart (the final PSA level reaching >2 ng/ml); PSA progression despite hormonal manipulations; antiandrogen withdrawal for at least 4 weeks for flutamide or 6 weeks for bicalutamide; and progression of clinical or bone lesions [Mottet *et al.* 2011]. However, it needs to be determined whether two consecutive rises in PSA would be enough to identify CRPC.

In most clinical practices of meeting participants, hormone therapy with luteinizing hormone-releasing hormone (LHRH) agonists is usually incorporated. In some countries, LHRH agonists are combined with bicalutamide. Generally, LHRH agonists are either prescribed for 2–4 weeks after flareup, or for 6 months continuously and then intermittently if PSA levels are low (or the patient has underlying cardiovascular risk factors). If patients do not respond to LHRH agonist therapy (or if the patient has cardiovascular risk factors) they are generally referred to oncologists for chemotherapy [Heidenreich *et al.* 2012].

The participants at the meeting estimated that in their countries, less than 10% of patients with metastatic disease undergo orchiectomy (usually indicated due to age or nonadherence with medical therapies); it was generally accepted that discussion of potential side effects is important. In some

countries, bisphosphonates are used to prevent bone events, or are indicated in the case of symptomatic bone metastasis in patients with CRPC.

Although new agents are currently being developed and some of them are already accepted by regulatory authorities in Europe and North America, they are not yet considered as common therapies in clinical practice. However in the near future, it may be possible to use newer agents even before using chemotherapy. At the time of the meeting, preclinical and clinical data suggested that agents such as abiraterone (recently approved for use in CRPC), enzalutamide (also recently approved), tasquinimod and cabazitaxel represented a strong opportunity for future treatment [Heidenreich *et al.* 2012], and they may maintain QoL for longer. Skeletal-related events may also be managed better in future with, for example, monoclonal antibodies to receptor activator of nuclear factor κ B ligand (RANKL), such as denosumab [Bekker *et al.* 2004; Boyle *et al.* 2003; Fizazi *et al.* 2011].

Improving communication. Again the MDT is crucial for metastatic PCa management. Investigational therapies are discussed within the MDT and with the patient in most centers, but patient reluctance and lack of facilities may prevent newer therapies being tried in some centers.

Supportive care was discussed and it was suggested that patients need a local contact within the health-care team to ensure that QoL issues are handled on an outpatient basis. However, some issues (such as pain) still need to be discussed with, and managed by, the MDT. Pain is the main QoL concern in these patients [Cleeland, 2006; Serlin *et al.* 1995]; other key concerns are skeletal events, hot flashes, and fatigue [Jonler *et al.* 2005; Weinfurt *et al.* 2005]. All of these need an integrated approach to management and usually the patient and their family require psychological help.

Key points

Identifying patients with prostate cancer

- (1) Since clinical factors are important in identifying patients suitable for AS or intervention, particular attention must be paid to the tools for classification. The availability of an experienced uropathologist is crucial to ensure correct pathological classification.

- (2) MRI is generally considered underused in localized PCa. EAU guidelines suggest the use of MRI when a clinical suspicion of PCa persists despite negative biopsy [Heidenreich *et al.* 2011], but its wider use may be beneficial.
- (3) In locally advanced disease, the selection of patients for a multimodal approach may depend more on patient characteristics (e.g. age and presence of comorbidities) than is currently acknowledged in guidelines.
- (4) In assessing metastatic disease, some specific situations were proposed in which choline PET scans and WBMRI may be helpful; however, use of these techniques may be limited by local availability.

Individualizing management of patients with prostate cancer and improving communication

- (1) To help with management decisions in low-risk localized disease, patients need to be provided with clear and consistent information on AS, the impact that treatment and management decisions will have on QoL (particularly on continence and erectile function), and the risks and benefits of newer therapies. As these factors are not always understood by patients, good communication is essential.
- (2) Equally importantly, the MDT needs to understand the main concerns and preferences of the patient, and provide individualized information to allow patients to make informed choices.
- (3) EAU guidelines mention the need for MDT involvement [Heidenreich *et al.* 2011], but this should be emphasized more strongly, because the establishment of a MDT is important not just to aid optimum treatment of patients, but also to ensure that communication between the various members of the team and the patient and their families is efficient and meets the needs of the patient.
 - (a) The team should involve urologists, radiotherapists, oncologists, radiologists and pathologists.
 - (b) A specialist nurse can be a crucial inclusion in the MDT to maintain regular contact with the patient and their relatives/carers.
 - (c) Psychological support may be needed for some patients to deal with issues of sexual function and incontinence, and so a psychologist may be an important addition to the MDT.
 - (d) Generally, the MDT should meet weekly.

Conclusion

Published guidelines on PCa provide excellent information on the evidence available, but by their nature cannot give specific guidance on individual cases. A more individualized approach to patient care that is based on guidelines and evidence, but which draws upon many other factors, is essential for the management of PCa.

Appropriate imaging tools and predictive models, such as nomograms and staging tools, and genetic markers, should be used if available and in an evidence-based manner for assessment of the disease. Patient-specific factors, such as comorbidities, QoL issues and treatment preferences, also need to be assessed along with the availability of the relevant medical specialists and equipment. Only then should evidence-based guidelines be used to guide individualized treatment. The introduction of a MDT is crucial for designing local care programs and for enhancing efficient communication so the patient fully understands the options available to them.

It is hoped that meetings such as the 'Individualized prostate cancer care in an advancing world' meeting, and reports of their key discussion points will encourage more MDTs worldwide to consider the individual factors that influence the management of PCa and to adopt a holistic and individualized approach to patient care.

Acknowledgements

The authors thank all participants in the 'Individualized prostate cancer care in an advancing world' meeting and in particular they thank Thomas Wiegel and Andrea Gallina. We acknowledge the editorial assistance provided by Martin Gilmour of ESP Bioscience (Crowthorne, UK), supported by Ipsen, during the preparation of this manuscript.

Funding

This paper originates from a report from a meeting on 'Individualized prostate cancer care in an advancing world' held in Nice, France, 7–9 October 2011. The meeting was supported by an unrestricted educational grant from Ipsen, and was EACCME accredited.

Conflict of interest statement

S.Joniau, M.J. Ribal, A. de la Taille and F. Gaboardi have received lecture fees from Ipsen. D. Pfister has received fees from Ipsen, Astellas and Janssen for advisory boards and lectures. A. Thompson

received fees from Ipsen to participate in the advisory board for the meeting described herein.

References

- Adami, H. (2010) The prostate cancer pseudo-epidemic. *Acta Oncol* 49: 298–304.
- Adamo, V., Noto, L., Franchina, T., Chiofalo, G., Picciotto, M., Toscano, G. *et al.* (2012) Emerging targeted therapies for castration-resistant prostate cancer. *Front Endocrinol (Lausanne)* 3: 73.
- Andriole, G., Crawford, E., Grubb, R. 3rd, Buys, S., Chia, D., Church, T. *et al.* (2009) Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med* 360: 1310–1319.
- Bauman, G., Belhocine, T., Kovacs, M., Ward, A., Beheshti, M. and Rachinsky, I. (2012) 18F-fluorocholine for prostate cancer imaging: a systematic review of the literature. *Prostate Cancer Prostatic Dis* 15: 45–55.
- Bauvin, E., Soulie, M., Menegoz, F., Mace-Lesec'h, J., Buemi, A., Velten, M. *et al.* (2003) Medical and non-medical determinants of prostate cancer management: a population-based study. *Eur J Cancer* 39: 2364–2371.
- Bekker, P., Holloway, D., Rasmussen, A., Murphy, R., Martin, S., Leese, P. *et al.* (2004) A single-dose placebo-controlled study of AMG 162, a fully human monoclonal antibody to RANKL, in postmenopausal women. *J Bone Miner Res* 19: 1059–1066.
- Bellizzi, K., Latini, D., Cowan, J., DuChane, J. and Carroll, P. (2008) Fear of recurrence, symptom burden, and health-related quality of life in men with prostate cancer. *Urology* 72: 1269–1273.
- Boyle, W., Simonet, W. and Lacey, D. (2003) Osteoclast differentiation and activation. *Nature* 423: 337–342.
- Briganti, A., Abdollah, F., Nini, A., Suardi, N., Gallina, A., Capitanio, U. *et al.* (2011) Performance characteristics of computed tomography in detecting lymph node metastases in contemporary patients with prostate cancer treated with extended pelvic lymph node dissection. *Eur Urol* 61: 1132–1138.
- Briganti, A., Blute, M., Eastham, J., Graefen, M., Heidenreich, A., Karnes, J. *et al.* (2009a) Pelvic lymph node dissection in prostate cancer. *Eur Urol* 55: 1251–1265.
- Briganti, A., Karnes, J., Da Pozzo, L., Cozzarini, C., Gallina, A., Suardi, N. *et al.* (2009b) Two positive nodes represent a significant cut-off value for cancer specific survival in patients with node positive prostate cancer. A new proposal based on a two-institution experience on 703 consecutive N+ patients treated with radical prostatectomy, extended pelvic lymph node dissection and adjuvant therapy. *Eur Urol* 55: 261–270.
- Briganti, A., Larcher, A., Abdollah, F., Capitanio, U., Gallina, A., Suardi, N. *et al.* (2012) Updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection: the essential importance of percentage of positive cores. *Eur Urol* 61: 480–487.
- Castellucci, P., Fuccio, C., Rubello, D., Schiavina, R., Santi, I., Nanni, C. *et al.* (2011) Is there a role for (1)(1)C-choline PET/CT in the early detection of metastatic disease in surgically treated prostate cancer patients with a mild PSA increase <1.5 ng/ml? *Eur J Nucl Med Mol Imaging* 38: 55–63.
- Church, T. (2006) Prostate-specific antigen and prostate cancer prognosis. *J Natl Cancer Inst* 98: 1509–1510.
- Cirillo, S., Petracchini, M., Scotti, L., Gallo, T., Macera, A., Bona, M. *et al.* (2009) Endorectal magnetic resonance imaging at 1.5 Tesla to assess local recurrence following radical prostatectomy using T2-weighted and contrast-enhanced imaging. *Eur Radiol* 19: 761–769.
- Cleeland, C. (2006) The measurement of pain from metastatic bone disease: capturing the patient's experience. *Clin Cancer Res* 12: 6236s–6242s.
- Cooperberg, M., Broering, J. and Carroll, P. (2010) Time trends and local variation in primary treatment of localized prostate cancer. *J Clin Oncol* 28: 1117–1123.
- Cooperberg, M., Broering, J., Kantoff, P. and Carroll, P. (2007) Contemporary trends in low risk prostate cancer: risk assessment and treatment. *J Urol* 178: S14–S19.
- Cooperberg, M., Lubeck, D., Meng, M., Mehta, S. and Carroll, P. (2004) The changing face of low-risk prostate cancer: trends in clinical presentation and primary management. *J Clin Oncol* 22: 2141–2149.
- Cozzarini, C. and Di Muzio, N. (2011) Contemporary role of radiation therapy in the adjuvant or salvage setting following radical prostatectomy. *Curr Opin Urol* 21: 206–210.
- Crnalic, S., Lofvenberg, R., Bergh, A., Widmark, A. and Hildingsson, C. (2012) Predicting survival for surgery of metastatic spinal cord compression in prostate cancer: a new score. *Spine (Phila Pa 1976)* 37: 2168–2176.
- Denis, L., Joniau, S., Bossi, A., Baskin-Bey, E. and Fitzpatrick, J. (2012) PCA: prostate cancer, patient-centred approach or both? *BJU Int* 110: 16–22.
- Fairley, L., Baker, M., Whiteway, J., Cross, W. and Forman, D. (2009) Trends in non-metastatic prostate

- cancer management in the Northern and Yorkshire region of England, 2000-2006. *Br J Cancer* 101: 1839-1845.
- Fizazi, K., Carducci, M., Smith, M., Damiao, R., Brown, J., Karsh, L. *et al.* (2011) Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *Lancet* 377: 813-822.
- Gomella, L. (2012) Prostate cancer: the benefits of multidisciplinary prostate cancer care. *Nat Rev Urol* 9: 360-362.
- Graute, V., Jansen, N., Ubleis, C., Seitz, M., Hartenbach, M., Scherr, M. *et al.* (2012) Relationship between PSA kinetics and [18F]fluorocholine PET/CT detection rates of recurrence in patients with prostate cancer after total prostatectomy. *Eur J Nucl Med Mol Imaging* 39: 271-282.
- Hara, R., Jo, Y., Fujii, T., Kondo, N., Yokoyama, T., Miyaji, Y. *et al.* (2008) Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. *Urology* 71: 191-195.
- Harlan, L., Potosky, A., Gilliland, F., Hoffman, R., Albertsen, P., Hamilton, A. *et al.* (2001) Factors associated with initial therapy for clinically localized prostate cancer: prostate cancer outcomes study. *J Natl Cancer Inst* 93: 1864-1871.
- Heidenreich, A., Bastian, P., Bellmunt, J., Bolla, M., Joniau, S., van der Kwast, V. *et al.* (2012) Guidelines on prostate cancer. Available at: http://www.uroweb.org/gls/pockets/english/07_Prostate_Cancer.pdf (accessed 1 May 2013).
- Heidenreich, A., Bellmunt, J., Bolla, M., Joniau, S., Mason, M., Matveev, V. *et al.* (2011) EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and treatment of clinically localised disease. *Eur Urol* 59: 61-71.
- Heinisch, M., Dirisamer, A., Loidl, W., Stoiber, F., Gruy, B., Haim, S. *et al.* (2006) Positron emission tomography/computed tomography with F-18-fluorocholine for restaging of prostate cancer patients: meaningful at PSA < 5 ng/ml? *Mol Imaging Biol* 8: 43-48.
- Hessels, D., Klein Gunnewiek, J., van Oort, I., Karthaus, H., van Leenders, G., van Balken, B. *et al.* (2003) DD3(PCA3)-based molecular urine analysis for the diagnosis of prostate cancer. *Eur Urol* 44: 8-15; discussion 15-16.
- Hessels, D., Smit, F., Verhaegh, G., Witjes, J., Cornel, E. and Schalken, J. (2007) Detection of TMPRSS2-ERG fusion transcripts and prostate cancer antigen 3 in urinary sediments may improve diagnosis of prostate cancer. *Clin Cancer Res* 13: 5103-5108.
- Huang, G., Sadetsky, N. and Penson, D. (2010) Health related quality of life for men treated for localized prostate cancer with long-term followup. *J Urol* 183: 2206-2212.
- Ihrig, A., Keller, M., Hartmann, M., Debus, J., Pfitzenmaier, J., Hadaschik, B. *et al.* (2011) Treatment decision-making in localized prostate cancer: why patients chose either radical prostatectomy or external beam radiation therapy. *BjU Int* 108: 1274-1278.
- Johansson, E., Bill-Axelsson, A., Holmberg, L., Onelov, E., Johansson, J. and Steineck, G. (2009) Time, symptom burden, androgen deprivation, and self-assessed quality of life after radical prostatectomy or watchful waiting: the Randomized Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4) clinical trial. *Eur Urol* 55: 422-430.
- Johansson, E., Steineck, G., Holmberg, L., Johansson, J., Nyberg, T., Ruutu, M. *et al.* (2011) Long-term quality-of-life outcomes after radical prostatectomy or watchful waiting: the Scandinavian Prostate Cancer Group-4 randomised trial. *Lancet Oncol* 12: 891-899.
- Johansson, J., Andren, O., Andersson, S., Dickman, P., Holmberg, L., Magnuson, A. *et al.* (2004) Natural history of early, localized prostate cancer. *JAMA* 291: 2713-2719.
- Jonler, M., Nielsen, O., Groenvold, M., Hedlund, P., Damber, L., Hedelin, H. *et al.* (2005) Quality of life in patients with skeletal metastases of prostate cancer and status prior to start of endocrine therapy: results from the Scandinavian Prostate Cancer Group Study 5. *Scand J Urol Nephrol* 39: 42-48.
- Jonsson, P., Danneskiold-Samsøe, B., Heggstad, T., Iversen, P. and Leisti, S. (1995) Management of early prostatic cancer in the Nordic countries: variations in clinical policies and physicians' attitudes toward radical treatment options. *Int J Technol Assess Health Care* 11: 66-78.
- Kambara, T., Oyama, T., Segawa, A., Fukabori, Y. and Yoshida, K. (2010) Prognostic significance of global grading system of Gleason score in patients with prostate cancer with bone metastasis. *BjU Int* 105(11): 1519-1525.
- Kotzerke, J., Volkmer, B., Neumaier, B., Gschwend, J., Hautmann, R. and Reske, S. (2002) Carbon-11 acetate positron emission tomography can detect local recurrence of prostate cancer. *Eur J Nucl Med Mol Imaging* 29: 1380-1384.
- Kramer, K., Bennett, C., Pickard, A., Lyons, E., Wolf, M., McKoy, J. *et al.* (2005) Patient preferences in prostate cancer: a clinician's guide to understanding health utilities. *Clin Prostate Cancer* 4: 15-23.

- Krupski, T., Kwan, L., Afifi, A. and Litwin, M. (2005) Geographic and socioeconomic variation in the treatment of prostate cancer. *J Clin Oncol* 23: 7881–7888.
- Kyrdalen, A., Dahl, A., Hernes, E., Smastuen, M. and Fossa, S. (2013) A national study of adverse effects and global quality of life among candidates for curative treatment for prostate cancer. *BJU Int* 111: 221–232.
- Lamb, B., Brown, K., Nagpal, K., Vincent, C., Green, J. and Sevdalis, N. (2011a) Quality of care management decisions by multidisciplinary cancer teams: a systematic review. *Ann Surg Oncol* 18: 2116–2125.
- Lamb, B., Sevdalis, N., Mostafid, H., Vincent, C. and Green, J. (2011b) Quality improvement in multidisciplinary cancer teams: an investigation of teamwork and clinical decision-making and cross-validation of assessments. *Ann Surg Oncol* 18: 3535–3543.
- Lawrence, E., Gnanapragasam, V., Priest, A. and Sala, E. (2012) The emerging role of diffusion-weighted MRI in prostate cancer management. *Nat Rev Urol* 9: 94–101.
- Lecouvet, F., El Mouedden, J., Collette, L., Coche, E., Danse, E., Jamar, F. *et al.* (2012) Can whole-body magnetic resonance imaging with diffusion-weighted imaging replace Tc 99m bone scanning and computed tomography for single-step detection of metastases in patients with high-risk prostate cancer? *Eur Urol* 62: 68–75.
- Lu-Yao, G., Potosky, A., Albertsen, P., Wasson, J., Barry, M. and Wennberg, J. (1996) Follow-up prostate cancer treatments after radical prostatectomy: a population-based study. *J Natl Cancer Inst* 88: 166–173.
- Miki, J. and Egawa, S. (2011) The role of lymph node dissection in the management of prostate cancer. *Int J Clin Oncol* 16: 195–202.
- Moran, B., Braccioforte, M. and Conterato, D. (2006) Re-biopsy of the prostate using a stereotactic transperineal technique. *J Urol* 176: 1376–1381; discussion 1381.
- Mottet, N., Bellmunt, J., Bolla, M., Joniau, S., Mason, M., Matveev, V. *et al.* (2011) EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration-resistant prostate cancer. *Eur Urol* 59: 572–583.
- Nagarajan, R., Margolis, D., Raman, S., Sarma, M., Sheng, K., King, C. *et al.* (2012) MR spectroscopic imaging and diffusion-weighted imaging of prostate cancer with Gleason scores. *J Magn Reson Imaging* 36: 697–703.
- National Institute for Health and Clinical Excellence (2008) *Prostate Cancer: Diagnosis and Treatment*. Clinical guideline 58. London: NICE.
- Nielsen, M., Trock, B. and Walsh, P. (2010) Salvage or adjuvant radiation therapy: counseling patients on the benefits. *J Natl Compr Canc Netw* 8: 228–237.
- Payne, H. and Gillatt, D. (2007) Differences and commonalities in the management of locally advanced prostate cancer: results from a survey of oncologists and urologists in the UK. *BJU Int* 99: 545–553.
- Pili, R., Haggman, M., Stadler, W., Gingrich, J., Assikis, V., Bjork, A. *et al.* (2011) Phase II randomized, double-blind, placebo-controlled study of tasquinimod in men with minimally symptomatic metastatic castrate-resistant prostate cancer. *J Clin Oncol* 29: 4022–4028.
- Quentin, M., Blondin, D., Klasen, J., Schek, J., Buchbender, C., Miese, F. *et al.* (2012) Evaluation of a structured report of functional prostate magnetic resonance imaging in patients with suspicion for prostate cancer or under active surveillance. *Urol Int* 89: 25–29.
- Rice, K., Chen, Y., Ali, A., Whitman, E., Blase, A., Ibrahim, M. *et al.* (2010) Evaluation of the ETS-related gene mRNA in urine for the detection of prostate cancer. *Clin Cancer Res* 16: 1572–1576.
- Robinson, D., Sandblom, G., Johansson, R., Garmo, H., Aus, G., Hedlund, P. *et al.* (2008) PSA kinetics provide improved prediction of survival in metastatic hormone-refractory prostate cancer. *Urology* 72: 903–907.
- Salagierski, M. and Schalken, J. (2012) Molecular diagnosis of prostate cancer: PCA3 and TMPRSS2:ERG gene fusion. *J Urol* 187: 795–801.
- Scher, H., Beer, T., Higano, C., Anand, A., Taplin, M., Efstathiou, E. *et al.* (2010) Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1–2 study. *Lancet* 375: 1437–1446.
- Schroder, F., Hugosson, J., Roobol, M., Tammela, T., Ciatto, S., Nelen, V. *et al.* (2009) Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med* 360: 1320–1328.
- Schroder, F., Hugosson, J., Roobol, M., Tammela, T., Ciatto, S., Nelen, V. *et al.* (2012) Prostate-cancer mortality at 11 years of follow-up. *N Engl J Med* 366: 981–990.
- Serlin, R., Mendoza, T., Nakamura, Y., Edwards, K. and Cleeland, C. (1995) When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. *Pain* 61: 277–284.
- Shukla-Dave, A., Hricak, H., Akin, O., Yu, C., Zakian, K., Udo, K. *et al.* (2012) Preoperative nomograms incorporating magnetic resonance imaging and spectroscopy for prediction of insignificant prostate cancer. *BJU Int* 109: 1315–1322.

- Spahn, M., Joniau, S., Gontero, P., Fieuws, S., Marchioro, G., Tombal, B. *et al.* (2010) Outcome predictors of radical prostatectomy in patients with prostate-specific antigen greater than 20 ng/ml: a European multi-institutional study of 712 patients. *Eur Urol* 58: 1–7; discussion 10–11.
- Steuber, T., Budaus, L., Walz, J., Zorn, K., Schlomm, T., Chun, F. *et al.* (2011) Radical prostatectomy improves progression-free and cancer-specific survival in men with lymph node positive prostate cancer in the prostate-specific antigen era: a confirmatory study. *BjU Int* 107: 1755–1761.
- Swanson, G., Riggs, M., Earle, J. and Haddock, M. (2002) Long-term follow-up of radical retropubic prostatectomy for prostate cancer. *Eur Urol* 42: 212–216.
- Takenaka, A., Hara, R., Ishimura, T., Fujii, T., Jo, Y., Nagai, A. *et al.* (2008) A prospective randomized comparison of diagnostic efficacy between transperineal and transrectal 12-core prostate biopsy. *Prostate Cancer Prostatic Dis* 11: 134–138.
- Thong, M., van de Poll-Franse, L., Hoffman, R., Albertsen, P., Hamilton, A., Stanford, J. *et al.* (2011) Diabetes mellitus and health-related quality of life in prostate cancer: 5-year results from the Prostate Cancer Outcomes Study. *BjU Int* 107: 1223–1231.
- Tomlins, S., Aubin, S., Siddiqui, J., Lonigro, R., Sefton-Miller, L., Miick, S. *et al.* (2011) Urine TMPRSS2:ERG fusion transcript stratifies prostate cancer risk in men with elevated serum PSA. *Sci Transl Med* 3: 94ra72.
- van de Poll-Franse, L., Sadetsky, N., Kwan, L. and Litwin, M. (2008) Severity of cardiovascular disease and health-related quality of life in men with prostate cancer: a longitudinal analysis from CaPSURE. *Qual Life Res* 17: 845–855.
- Van Poppel, H. and Joniau, S. (2013) Active surveillance and focal therapy: a European perspective. In: Polascik, T. (ed.), *Imaging and Focal Therapy of Early Prostate Cancer*, 2nd ed. New York: Humana Press, pp. 37–52.
- Weinfurt, K., Li, Y., Castel, L., Saad, F., Timbie, J., Glendenning, G. *et al.* (2005) The significance of skeletal-related events for the health-related quality of life of patients with metastatic prostate cancer. *Ann Oncol* 16: 579–584.
- White, K., D'Abrew, N., Katris, P., O'Connor, M. and Emery, L. (2012) Mapping the psychosocial and practical support needs of cancer patients in Western Australia. *Eur J Cancer Care (Engl)* 21: 107–116.
- Wilt, T., MacDonald, R., Rutks, I., Shamliyan, T., Taylor, B. and Kane, R. (2008) Systematic review: comparative effectiveness and harms of treatments for clinically localized prostate cancer. *Ann Intern Med* 148: 435–448.
- Xu, J., Dailey, R., Eggly, S., Neale, A. and Schwartz, K. (2011) Men's perspectives on selecting their prostate cancer treatment. *J Natl Med Assoc* 103: 468–478.
- Xylinas, E., Ploussard, G., Durand, X., Fabre, A., Salomon, L., Allory, Y. *et al.* (2011) Low pretreatment total testosterone (< 3 ng/mL) predicts extraprostatic disease in prostatectomy specimens from patients with preoperative localized prostate cancer. *BjU Int* 107: 1400–1403.
- Yap, T., Zivi, A., Omlin, A. and de Bono, J. (2011) The changing therapeutic landscape of castration-resistant prostate cancer. *Nat Rev Clin Oncol* 8: 597–610.