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Editorial

The Renaissance clinician: Essential for the modern management of prostate cancer

This special issue of the *European Journal of Cancer*, focusing on the biology and management of prostate cancer, illustrates clearly the changing demands on the clinician treating this complex disease. This series of update reviews spans the biomedical research on prostate cancer, ranging from molecular and clinical epidemiology to the subtleties of population screening and public health issues, in addition to covering the interplay between prognostic and predictive factors in characterising outcomes of treatment. The assessment of outcome has become more complex, requiring consideration of the impact of stage migration, compounded by the increasing use of quality of life measures, the importance of framing reference in questionnaires, and the application of surrogate markers to the assessment of standard and novel therapies. The genitourinary oncologist of the modern era needs to master molecular biology, behavioural science, philosophy and fiscal management, in addition to the more conventional medical skills, and is thus a veritable Renaissance clinician! This is clearly illustrated by the range and complexity of the topics covered in this volume.

It is clear that there has been a substantial increase in the available information on the biology and management of prostate cancer, accompanying a quite dramatic change in the biology of the disease itself. Gee and Cheng illustrate clearly that a new pattern of disease is emerging in Asia – a virtual epidemic of this 'Western' disease, with a rapidly increasing incidence rate – perhaps consequent upon diet, occupational exposure or other aspects of lifestyle. Whether the significance of the interplay between transforming growth factor-β (TGF-β) and the Smad proteins with androgen receptor function and insulin-like growth factor-1 (IGF-1) expression, characterised by Danielpour, will explain this changing demography remains to be seen. However, we are acquiring a much clearer understanding of the fundamental steps in the genesis of prostate cancer, with disruptions in the balance between cellular regulation, apoptosis and mutation. Quinn and colleagues have reviewed in considerable detail the collision between molecular characterisation and its application to predictive and prognostic determination for early prostate cancer, presenting a series of novel indices to be evaluated in current and future clinical trials.

Klein and an international team of contributors show that even the traditionally 'simple' area of surgical management of early stage prostate cancer now involves consideration of screening technology, application of molecular prognostication to decisions about incorporation of adjuvant systemic therapies, and extraordinarily sophisticated surgical techniques. Similarly, Horwich and colleagues demonstrate equivalent complexity in the use of different particle therapies, field construction and enhancers of radiation response to improve tumour kill, while ameliorating treatment toxicity. The whole situation has shifted with the evolution of more sophisticated indicators of quality of life and the changing algorithm of weighting of length versus quality of survival. Talcott and Clark demonstrate that the traditionally simple indices of outcome for localised therapies may not reflect the results with complete accuracy, and patients are now seeking more complex information from the domains of lifestyle, sexuality and the psychological aspects that constitute the costs of cure.

The actual process of patient selection through population screening tools and the investigation of the optimal timing of treatment, simultaneously increasing and reducing the potential pool of patients, is an area of intense controversy, as summarised elegantly by Postma and Schroder. National medical advisory bodies have been unable to reach a consensus opinion on the role of screening, and it will require the final presentation of the results of the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) studies to rationalise the international approach to

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screening for prostate cancer. Sadly, this debate is currently characterised more by passion and rhetoric than by rational thought, but Postma and Schroder give us hope for the future.

Advanced and metastatic prostate cancer, with a subtle interaction between hormone-responsive and refractory/resistant tumour cell populations, presents an even more challenging set of problems. The discussions of Bhandari, Petrylak and Hussain about 'conventional' systemic therapies, overlapping with those of Strother, Beer and Dreicer about new approaches, illustrate clearly an extension of the molecular principles presented by Quinn, Henshall and Sutherland to the application of targeted therapies focused on molecular or biochemical targets. It should not be forgotten that the appreciation of true progress can be confounded by stage and outcome migration – that is, the application of surrogate markers, such as prostate-specific antigen (PSA) response and quality of life measures, may well create an illusion of progress when outcome data from current trials are compared with those obtained in the studies from 20 years ago when response was defined in terms of objective and measurable tumour shrinkage.

The key question relates to outcomes – are we really making important progress? While stage migration and case selection may have an impact on mortality rates, it is clear that we are improving outcomes, both with respect to quality and duration of life in important subsets of our patients. Real progress has been achieved for patients with locally advanced prostate cancer, hormone-resistant disease, and perhaps even in identifying the more dangerous variants of early stage tumours. The trajectory of this change can clearly be appreciated if one contrasts the symposium edition of the *European Journal of Cancer* [1] that I edited on this topic in 1997 with the data reported here. The work described in the current edition, contributed by many of the leading investigators in the field of prostate cancer treatment and research, allows us to set this progress into context. These reviews are intense, demanding and packed with data… truly requiring the skills of a Renaissance clinician to be appreciated fully!

Reference

1. *Eur J Cancer* 1997, **33**, 329–330, 340–356, 544–574.

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