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EDITORIAL

Report from London

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The management of patients with prostate cancer continues to create controversy on both sides of the Atlantic. Now the regulators are getting in on the act. Last month guidelines for the management of localized prostate cancer were issued by the National Institute of Clinical Excellence (NICE) in the UK: http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11924. Among other recommendations, these have emphasized the role of active surveillance for men with so called 'low risk' prostate cancer. But can we really define with certainty those men with cancers, who have a minimal risk of progression? And can we truly recognize that progression is occurring at a time when the situation is still remediable?

The parameters of so-called 'low-risk' prostate cancers best managed by active surveillance include a presenting prostate-specific antigen (PSA) less than 10 ng/ml, a Gleason score of 6 or less, as well as no disease that is palpable on digital rectal examination. Others have suggested rather more rigorous protocols for active surveillance. Most include an evaluation of the number and percentage of cores involved by cancer followed by quarterly digital rectal examinations together with PSA determination, followed by a repeat ultrasound-guided biopsy of the prostate and MRI within a year. Provided that there is no evidence of progression of the cancer at that stage the surveillance protocol is relaxed to two times in a year with a further biopsy within 3–5 years.

Those readers who have firsthand experience of managing patients with localized prostate cancer will recognize the frequent occurrence of under-staging and under-grading this disease on biopsy compared with subsequent radical prostatectomy specimens. They will also be aware how difficult it can be to diagnose progression through and beyond the capsule of the gland. A further word of caution, however, comes from a paper published online in *Cancer*, Harnden *et al*. report a meta-analysis on whether patients with microfocal CaP on biopsy have adverse pathologic findings or any significant risk of PSA recurrence after undergoing radical prostatectomy (Harnden *et al*. *Cancer* 2008; **112** (5): 971–998). A total of 238 articles were evaluated and in the final review 29 articles addressed the specific question of the correlation between small-volume cancer on biopsy and pathologic findings, biochemical or clinical progression, or mortality.

Regarding the likelihood that no cancer at all would be found in the radical prostatectomy specimen, the occurrence rate was 0.8%. The overall estimate of the risk that patients with microfocal prostate cancer would have extracapsular extension (ECE) at RP was 17.6%. The combined estimate for a positive surgical margin among men with microfocal prostate cancer was 12%. The range of PSA recurrences among this population was 0–26%, with an estimated risk of 8.6%. Among watchful waiting studies, the number of patients was small and a rising PSA was reported in nine of 15 patients who had a microfocus of prostate cancer. Conversion to definitive therapy occurred in 30%. The overall conclusion was that a small volume of prostate cancer in biopsies is not necessarily indicative of a good prognosis. Clearly more data are required confirming the safety and efficacy of active surveillance before the recommendations of NICE are widely adopted by clinicians in the frontline.

Across the other side of the Atlantic the FDA's decision to delay the approval of Provenge, a recombinant therapeutic vaccine developed by Dendreon for use in patients with androgen independent prostate cancer has also resulted in controversy. Cancer patients have been exasperated by the agency's decision to ignore an advisory committee recommendation made in March last year which gave the green light for approval. Efficacy is the issue here because in both the Dendreon trials presented to the FDA, Provenge failed to meet its primary end points. In certain respects, Dendreon did set an overoptimistic efficacy/hazard ratio for the trial of 0.585, which no conventional drug or chemotherapeutic regime has ever achieved in a comparable setting of late-stage disease. At the same time, however, Provenge did extend median survival by 4.5 months, and after 3 years, 34% of the men who received the therapy were still alive, compared with only 11% who received a placebo.

Thus the trial was not designed to demonstrate survival advantages, but reanalysis showed that it did. Is it right that the FDA ignored this? When the sole evidence-based therapy for hormone-relapsed prostate cancer is taxotere (docetaxel)—which extends survival by only two and a half months and has considerable toxicity—it is easy to see why patients feel that the data were strong enough. And it seems that the advisory body thought so too. Many feel that the FDA should now explain its decision. Others developing other cancer vaccines would welcome the clarity, and prostate cancer patients, denied a potentially life-saving therapy, deserve an answer.

This, and so many other controversial issues involved in the diagnosis and management of prostate cancer and prostatic diseases, will continue to be the focus of this journal. We are grateful that more and more of you are choosing to submit your research to the journal for and also reading the journal, both in print and online.

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