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ACTIVE SURVEILLANCE: AN INDIVIDUALIZED APPROACH TO EARLY PROSTATE CANCER

Sir,

Patients with aggressive localized prostate cancer should receive radical therapy, but treating all patients will result in substantial over-intervention. The recent results of the PCPT trial, in which 25% of men in the placebo arm with normal PSA levels were biopsy-positive, confirms the risk of overtreatment [1]; the results of the Swedish randomized trial confirms the benefits of therapy [2]. How do we resolve this conundrum? Parker [3] wrote an excellent review of a selective approach to treatment based on the behaviour of the cancer over time. He appropriately raises the prospect of active surveillance becoming the basis for a change in the management of prostate. This is consistent with A. von Eschenbach's (Director, NCI) prediction that cancer management will shift from 'seek and destroy' to 'target and control', incorporating molecular and biochemical markers to stratify for risk (Von Eschenbach, Society of Urologic Oncology Annual Meeting, Anaheim, CA, May 2001). Active surveillance with selective intervention embodies that philosophy.

While the arithmetic approach to treatment decision making described by Parker makes sense, a pitfall is the phenomenon of PSA acceleration. It is not known to what degree PSA doubling time remains stable with time. We noted that some patients whose PSA doubling time has remained stable for many years have a sudden acceleration in the rate of PSA increase. Whether this precedes or is a result of the development of occult metastatic disease is unknown. More information is required on this question.

Our data suggest that a PSA doubling time of ≤ 3 years identifies patients who are at high risk of progression and are still curable in most cases [4]; $\approx 20\%$ of patients in our cohort fell into this group. Parker is correct that there is no specific threshold for intervention. The decision to treat reflects the patient's age, comorbidity and risk tolerance. This last indication is particularly important. The PSA increase slowly over time in most patients and it is critical that they understand this.

A prospective randomized trial of the active surveillance approach is clearly warranted. We have opened an initial feasibility trial randomizing good-risk patients between active surveillance and radical intervention (patient's choice of surgery, external beam irradiation or brachytherapy). The endpoint of this trial will be the proportion of patients agreeing to randomization. Assuming that

this is acceptable to patients, we anticipate rolling the feasibility trial into a large-scale trial with an objective endpoint (i.e. time to metastatic progression or survival). Active surveillance with selective delayed intervention based on PSA doubling time is an appealing option for good-risk patients who wish to avoid overtreatment but not miss the opportunity for definitive therapy if required.

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- 1 Thompson IM, Goodman PJ, Tangen CM *et al.* The influence of finasteride on the development of prostate cancer. *N Engl J Med* 2003; **349**: 215–24
- 2 Holmberg L, Bill-Axelsson A, Helgesen F *et al.* and the Scandinavian Prostatic Cancer Group Study Number 4. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. *N Engl J Med* 2002; **347**: 781–9
- 3 Parker C. Active surveillance: an individualized approach to early prostate cancer. *BJU Int* 2003; **92**: 2–3
- 4 Klotz L. Expectant management with selective delayed intervention for favorable risk prostate cancer. *Urol Oncol* 2002; **7**: 175–80