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European Association of Urology

## Letter to the Editor

**Re: Jutta Engel, Patrick J. Bastian, Helmut Baur, et al. Survival Benefit of Radical Prostatectomy in Lymph Node–Positive Patients with Prostate Cancer. Eur Urol 2010;57:754–61**

Retrospective studies of patients with lymph node–positive prostate cancer suggest that radical prostatectomy (RP) with early adjuvant orchiectomy may provide a significant advantage in overall and cause-specific survival compared to orchiectomy alone [1]. Also, in a long-term retrospective study, patients with treatment failure after RP had a better response to androgen ablation than those in whom radiation failed. Because patients with radiation had a high rate of uncontrolled local disease, it would appear that the bulk of local disease affects the response to systemic therapy [2].

As shown in the latest study, patients with positive lymph nodes and completed RP may have a survival benefit compared to patients with abandoned surgery, and we noticed that a majority of lymph node–positive patients received adjuvant hormone therapy [3]. We think this study added to the evidence that cytoreduction of the primary tumor allows a better response of advanced prostate cancer to androgen ablation, as was suggested by our own experience in metastatic hormone-sensitive prostate cancer (mHSPC). In our cohort of mHSPC patients, transurethral resection of the prostate resulted in better and more prolonged response to hormone therapy, with a trend toward positive influence in disease-specific survival and overall survival [4].

One possible mechanism that underlies the increased response to systemic therapy in advanced prostate cancer after cytoreductive surgery to the primary tumor is the different androgen microenvironment in and out of the prostate [4]. Previous investigation has found that medical castration reduces tissue androgens by 75% and also reduces the expression of several androgen-regulated genes. However, many androgen-response genes, including the androgen receptor and prostate-specific antigen, are not suppressed after short-term castration or after 9 mo of neoadjuvant androgen deprivation therapy. The degree of medical castration based on serum testosterone levels cannot be equated with the thoroughness of androgen ablation in the prostate microenvironment.

Standard androgen deprivation does not consistently suppress androgen-dependent gene expression because of higher levels of intraprostatic androgens. Suboptimal suppression of tumoral androgen activity may lead to adaptive cellular changes, allowing prostate cancer cell survival in a low-androgen environment [5]. Because the primary tumor might be the primordial source of metastatic disease and because newly disseminated cancer cells from the castrated prostate are probably more hormone refractory, reducing the volume of intraprostatic cancer cells by cytoreductive surgery before they are castration adaptive may reduce the proportion of hormone refractory cells disseminated later. We hope you agree that the role of cytoreductive surgery to the primary tumor in advanced prostate cancer in the setting of hormone therapy merits further investigation.

***Conflicts of interest:*** The authors have nothing to disclose.

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