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European Association of Urology

Letter to the Editor

Reply to Dr. A.E. Friedman letter to the editor re: Re: Russell Szmulewitz, Supriya Mohile, Edwin Posadas, et al. A Randomized Phase 1 Study of Testosterone Replacement for Patients with Low-Risk Castration-Resistant Prosate Cancer EurUrol 2009; 56: 97–104

We thank Professor Friedman for his interesting comments [1] on our study [2]. We agree that the hormonal milieu of castration-resistant prostate cancer (CRPC) and the interaction of various steroid hormone receptors is complex and underappreciated.

Although the role of estrogen receptor (ER)–α and ER-β should be considered, we note that the limited studies with metastatic castrate-resistant tissue and the limited therapeutic studies with ER agonists, antagonists, and aromatase inhibitors do not fully clarify the role that these pathways play in castration-resistant disease. Others have also suggested that intratumoral steroidogenesis and the relative growth-promoting effects versus differentiating effects of these androgenic steroids in prostate cancer also may be critical [3]. Finally, and as suggested by Professor Friedman, steroid hormone receptor pathways may have different roles in tumor cells, as opposed to the supporting tumor stroma.

Perhaps most important, CRPC in patients is highly heterogeneous, and studies to date suggest that multiple mechanisms contribute to the castration-resistant state [4]. Consequently, a single hormonal manipulation can have multiple theoretical effects on CRPC in an individual patient. Given this complex interaction and the difficulty of predicting clinical outcome, we suggest that only one experimental variable be manipulated at a time in carefully controlled clinical research studies.

The current study was simply a phase 1 study to confirm safety and feasibility for our current randomized phase 2 study of testosterone versus placebo in early CRPC patients. We look forward to reviewing the results of this study and will certainly consider them in context of Professor Friedman's comments.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Friedman AE. Re: Russell Szmulewitz, Supriya Mohile, Edwin Posadas, et al. A randomized phase 1 study of testosterone replacement for patients with low-risk castration-resistant prostate cancer. Eur Urol. In press.
[2] Szmulewitz R, Mohile S, Posadas E, et al. A randomized phase 1 study of testosterone replacement for patients with low-risk castration-resistant prostate cancer. Eur Urol 2009;56:97–104.
[3] Montgomery RB, Mostaghel EA, Vessella R, et al. Maintenance of intratumoral androgens in metastatic prostate cancer: a mechanism for castration-resistant tumor growth. Cancer Res 2008;68:4447–54.
[4] Scher HI, Sawyers CL. Biology of progressive, castration-resistant prostate cancer: directed therapies targeting the androgen-receptor signaling axis. J Clin Oncol 2005;23:8253–61.

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