Androgen dependence of prostate cancer (PCA) cells was set in a new light with the recent findings on androgen receptor alterations and expression as well as local testosterone production in PCA [1]. The role of estrogen receptors α and β in PCA progression further increased complexity of the mechanisms [2].

It is clearly novel and counterintuitive to use testosterone in the management of men with seemingly hormone-independent PCA, although randomization in a phase 1 trial is somewhat unusual [1]. Intermittent androgen ablation studies showed an improved quality of life (QoL) during off-treatment intervals, supporting the notion that androgen resupplementation may improve QoL in these men. It seems evident that within physiologic levels, testosterone suppletion is not associated with an increased risk of PCA [3], yet in men with androgen-independent PCa, based on above-mentioned results, one may assume a higher sensitivity of cells to even lower levels of androgens. Careful titration of androgens in these men is essential, and I would personally prefer histologic analysis of data such as androgen receptor levels or mutations to possibly available in any future study plan.

The fact that one man experienced a myocardial infarction urges us to be extremely careful with the suggested use of testosterone in these patients. It cannot be ignored that (local) aromatase activity converting testosterone into estrogens plays a role in the prostate-specific antigen effects observed in these men, and it is far from clear whether these increased estrogen levels are, by definition, beneficial [4,5]. More than ever, these data [1] should be interpreted with great care.

Thorough evaluation of tumor characteristics and response criteria are required before we become tempted to treat hormone-refractory PCA patients with androgens. Then again, new insight into the mechanisms of hormone-refractory PCA is desperately needed, and studies like this one will help us to further it.
References


DOI: 10.1016/j.eururo.2009.02.023
DOI of original article: 10.1016/j.eururo.2009.02.022