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Letter to the Editor

Reply to Piet R. Dirix, Carole Mercier, and Luc Y. Dirix's Letter to the Editor re: Fabian Lohaus, Klaus Zöphel, Steffen Löck, et al. Can Local Ablative Radiotherapy Revert Castration-resistant Prostate Cancer to an Earlier Stage of Disease? *Eur Urol* 2019;75:548–51

We thank Dirix and colleagues for their interest in and for comments on our article on whether local ablative radiotherapy can revert castration-resistant prostate cancer (CRPC) to an earlier disease stage [1]. We agree that the title is provocative for our small, retrospective, and hypothesis-generating study.

Nonetheless, the majority of patients in this cohort had a lasting prostate-specific antigen (PSA) response, similar to the three cases mentioned in the letter from Dirix et al. The generally accepted definition of CRPC (testosterone at a castrate level, PSA > 2 ng/ml and rising, or radiological progression) was no longer fulfilled [2]. We hypothesize that prostate-specific membrane antigen (PSMA) ligand-based positron emission tomography (PET) hybrid imaging may identify patients with oligoprogressive prostate cancer and that ablative therapy may eliminate the tumor cell clones that have overcome androgen dependence. We want to emphasize that our patients had PSMA-based PET rather than the choline PET used in other studies, such as the one by Triggiani et al. [3].

In this brief correspondence, we did not focus on the technique or on the schedules for local ablative radiotherapy. For primary radiotherapy alone, the fractionation sensitivity (α/β ratio) is probably <3 Gy, but there is a broad range across studies [4]. However, for CRPC the fractionation sensitivity is not yet known. As 3×10 Gy (80% isodose line encompassing the planning target volume, assuming $\alpha/\beta = 3$ Gy) equals 53 Gy in terms of equivalent dose, the two fractionation schedules used have to be considered comparable. In general, we apply the conventionally fractionated schedule for larger target volumes and in cases of overlap with a previously irradiated volume.

In this retrospective study, no regular imaging was performed during follow-up; and it should definitely be part of prospective clinical trials. In addition, such trials must focus on clinically relevant endpoints (eg, progression-free survival and quality of life) and compare local ablative radiotherapy to systemic treatment options to establish its role in patients with CRPC, e.g. [5]. Furthermore, predictive parameters need to be developed to stratify patients who benefit from early systemic therapy, those who benefit from systemic therapy and local ablative radiotherapy, and those who are best off with local ablative radiotherapy alone.

Conflicts of interest: The authors have nothing to disclose.

References

- [1] Lohaus F, Zöphel K, Löck S, et al. Can local ablative radiotherapy revert castration-resistant prostate cancer to an earlier stage of disease? *Eur Urol* 2019;75:548–51.
- [2] Mottet N, van den Bergh RCN, Briers E, et al. EAU guidelines: prostate cancer. Arnhem, The Netherlands: European Association of Urology. <https://uroweb.org/guideline/prostate-cancer/>.
- [3] Triggiani L, Mazzola R, Magrini SM, et al. Metastasis-directed stereotactic radiotherapy for oligoprogressive castration-resistant prostate cancer: a multicenter study. *World J Urol*. In press. <https://doi.org/10.1007/s00345-019-02717-7>.
- [4] Datta NR, Stutz E, Rogers S, Bodis S. Clinical estimation of α/β values for prostate cancer from isoeffective phase III randomized trials with moderately hypofractionated radiotherapy. *Acta Oncol* 2018;57:883–94.
- [5] Fizazi K, Shore N, Tammela TL, et al. Darolutamide in nonmetastatic, castration-resistant prostate cancer. *N Engl J Med* 2019;380:1235–46.

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