



Letter to the Editor

Reply to Fabiana Gregucci and Alba Fiorentino's Letter to the Editor re: Liselotte M.S. Boevé, Maarten C.C.M. Hulshof, André N. Vis, et al. Effect on Survival of Androgen Deprivation Therapy Alone Compared to Androgen Deprivation Therapy Combined with Concurrent Radiation Therapy to the Prostate in Patients with Primary Bone Metastatic Prostate Cancer in a Prospective Randomized Clinical Trial: Data from the HORRAD Trial. Eur Urol 2019;75:410–8

We thank Gregucci and Fiorentino for their comments on our paper [1]. We take this opportunity to address some of their remarks.

As the trial protocol was written more than a decade ago, changes in clinical management and in the availability of new effective treatment options in advanced prostate cancer (PC) could not have been foreseen. This relates to the outcome of seminal PC trials in the early 2010s such as AFFIRM [2] and PREVAIL [3] (enzalutamide), COU-AA-301 [4] (abiraterone), ASYMPCA [5] (radium-223), and TROPIC [6] (cabazitaxel), which all showed an overall survival benefit in patients with metastatic castration-resistant PC. Thus, at the time at which the protocol for HORRAD was written, overall survival among men with hormone-naïve metastatic PC was expected to be lower than that actually observed in the late 2010s. However, as HORRAD was a randomized clinical trial, these new treatment modalities were shown to be evenly distributed among treatment arms, refuting an explanation for a difference in overall survival between those who received local radiation therapy and those who did not [1].

As Gregucci and Fiorentino indicated, the number of osseous metastases and their location in the skeleton were shown to be of prognostic importance. The CHARTED trial [7] revealed that a distinction between high-volume disease (defined as visceral metastases, or four or more bone metastases, with at least one outside the spine and pelvis) and low-volume disease could mandate treatment with docetaxel in patients with primary hormone-naïve metastatic PC. In many clinics today, patients with high-volume disease receive

docetaxel accompanied by castration therapy, whereas those with low-volume disease do not. The number of osseous metastases and their location is a matter of further study in the HORRAD trial.

Again, we should stress that the HORRAD trial was negative for all its prognostic subgroups for the endpoint of overall survival. Contradictory to the data from the recently published STAMPEDE trial [8], this holds true for those with low prostate-specific antigen (<60 ng/ml), low Gleason scores (≤ 7), and those with low-volume bone metastatic (<5 metastases) PC.

Conflicts of interest: The authors have nothing to disclose.

References

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André N. Vis^a
Liselotte M.S. Boevé^{a,b,*}

*Corresponding author. Department of Urology, OLVG Amsterdam,
Oosterpark 9, Amsterdam, The Netherlands. Tel. +31 61 8463222.
E-mail address: l.boeve@olvg.nl (L.M. Boevé).

^aDepartment of Urology, VU University Medical Centre, Amsterdam,
The Netherlands

^bDepartment of Urology, OLVG, Amsterdam, The Netherlands

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