



## 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 Randomised Clinical Trial: Data from the HORRAD Trial. *Eur Urol* 2019;75:410–8**

### ***Future Steps for Definitive Therapy in Metastatic Prostate Cancer: Lessons from the HORRAD Trial***

We read with great interest the results of the HORRAD trial reported by Boevé et al. [1] on the role of local therapy in prostate cancer patients with distant metastatic disease. The authors are to be congratulated for undertaking this poignant and relevant work. This trial refutes previous nonrandomized studies and national registry database studies suggesting a potential role for definitive local therapy in metastatic prostate cancer. On the basis of the initial results from the randomized phase 2 STOMP trial, the current primary interest in the use of radiation in this patient population is in oligometastatic prostate cancer ( $\leq 3$  extracranial metastatic sites) [2]. As the authors of the HORRAD trial suggest, the protocol was developed more than a decade ago and treatment approaches for prostate cancer have evolved. Specifically, current trials in oligometastatic prostate cancer incorporating radiation for tumor-directed therapy use stereotactic body radiation therapy (SBRT) to metastatic sites and surgery/radiation to the primary (NCT03298087, NCT03304418, NCT03361735). In the HORRAD trial, 67% of patients had more than five sites of disease, which current guidelines would not define as oligometastatic. Sites of metastatic disease were not treated with definitive local therapy such as SBRT. Figure 3 [1] shows a potential trend to benefit with the addition of prostatic radiation in patients with fewer than five bone metastases, but without metastasis-directed therapy to control gross metastatic disease and prevent systemic

reseeding it is not surprising that there was not a time to prostate-specific antigen (PSA) progression or survival benefit. In addition, the median PSA in this patient population (126–149 ng/ml) is approximately ten times the median PSA in the STOMP trial (10.5–14.4 ng/ml) [2]. The authors attempted to specifically exclude patients with PSA levels above 20 ng/ml when the trial was developed. This stark difference in median PSA probably affects outcomes as well as being a surrogate marker for the burden of disease throughout the entire body. According to the scatter plot in Figure 3 [1], additional factors to consider in aggressive management include ideal performance status and lack of symptoms from the metastatic disease as having potential for benefit from definitive therapy to both the primary and metastatic sites.

The authors are to be commended for performing a randomized trial determining that addition of local therapy to only the prostate in metastatic cancer does not confer a PSA progression or overall survival benefit compared to androgen deprivation therapy alone. We agree with the authors that future trials should ideally focus on the management of oligometastatic disease given the trend in results seen in Figure 3 [1]. However, what is of paramount importance for future trials is that definitive therapy should not be limited to the primary site, but should also include metastasis-directed therapy using either SBRT or surgery, as has been done in other oligometastatic studies in both prostate and non-prostate cancer [2,3].

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

### References

- [1] Boevé LMS, Hulshof MCCM, Vis AN, 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 randomised clinical trial: data from the HORRAD trial. *Eur Urol* 2019;75:410–8. <http://dx.doi.org/10.1016/j.eururo.2018.09.008>.



- [2] Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. *J Clin Oncol* 2018;36:446–53. <http://dx.doi.org/10.1200/jco.2017.75.4853>.
- [3] Gomez DR, Blumenschein GR, Lee JJ, et al. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. *Lancet Oncol* 2016;17:1672–82. [http://dx.doi.org/10.1016/S1470-2045\(16\)30532-0](http://dx.doi.org/10.1016/S1470-2045(16)30532-0).

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