



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 read with interest the paper by Boevé and colleagues [1], who conducted a multicenter randomized controlled trial to investigate the effect of adding prostate external beam radiation therapy (EBRT) to androgen deprivation therapy (ADT) in patients with primary bone metastatic prostate cancer (mPCa) on overall survival (OS). For median follow-up of 47 mo, the authors did not observe a benefit with EBRT: median OS was 45 mo in EBRT plus ADT group and 43 mo in the ADT alone group ($p = 0.4$). In our opinion, several considerations in terms of undervalued criticisms should be highlighted.

Patients with metastatic disease were eligible (cT1–4, cN0–N1, M1), but considering that the primary endpoint was treatment efficacy in bone mPCa, the presence of visceral metastases or nonregional lymph node involvement should be evaluated as an exclusion criterion or at least should be evaluated in terms of results. This issue is not addressed. Moreover, in addition to the number of bone metastases, it could be important to evaluate their distribution (inside or outside the vertebral bodies or pelvis). An important bias of this study could be the lack of data regarding these clinical characteristics which did not allow a risk stratification of the population according to the definitions of a low or high burden of disease [2].

A crucial weakness seems to be the calculation of the sample size and the follow-up duration. In their statistical analysis, the authors declare that the sample size was calculated based on the assumption that the median OS for patients with primary bone metastases treated with ADT was 28 mo and a combination of ADT and EBRT will prolong median OS by 10 mo. The OS observed in the ADT group was

43 mo, with a significant gap of 15 mo. This gap could be explained by the improvement in systemic therapy [3], careful patient selection, or a combination of both. However, the 1990 study by Crawford et al. [4] showed that median OS for mPCa treated with leuprolide and flutamide was 35 mo. This factor could have an impact on the results. Moreover, the median follow-up of 47 mo is too short to draw definitive conclusions.

Despite the limitation of a subgroup analysis, for patients with a low burden of disease (<5 bone metastases and $\leq T2$ disease) the forest plot based on different covariates showed an advantage for EBRT + ADT. The recent results from STAMPEDE Trial showed that RT should be a standard option for treatment in men with newly diagnosed PCa and a low metastatic burden [5].

Finally, the emphatic conclusion from the analysis should be mitigated. These data could be strongly affected by several substantial biases and we cannot exclude the possibility of a substantial survival benefit from the addition of EBRT, especially in some subgroups.

Conflicts of interest: The authors have nothing to disclose.

References

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