Words of Wisdom

Re: Radiotherapy to the Primary Tumour for Newly Diagnosed, Metastatic Prostate Cancer (STAMPEDE): A Randomised Controlled Phase 3 Trial
Parker CC, James ND, Brawley CD, et al

Experts’ summary:
In this randomised trial, Parker et al. [1] studied the effect of radiotherapy to the prostate on overall survival (OS) in 2061 men with metastatic prostate cancer (PCa), of whom 1029 were randomised to standard of care (SOC; androgen deprivation therapy [ADT] ± docetaxel) and 1032 were randomised to SOC plus prostate radiotherapy between 2013 and 2016. In unselected newly diagnosed metastatic patients, radiotherapy to the prostate did not improve OS (0.92, 0.80–1.06; p = 0.266). In the prespecified subgroup analysis by baseline metastatic burden (a high metastatic burden was defined as four or more bone metastases with one or more outside the vertebral bodies or pelvis, or visceral metastases, or both), OS was improved in patients with a low metastatic burden who were randomised to radiotherapy (hazard ratio 0.68, 95% confidence interval 0.52–0.90; p = 0.007). The authors conclude that prostate radiotherapy should be a standard treatment option for men with a low metastatic burden.

Experts’ comments:
Several retrospective analyses have noted a survival benefit in men with metastatic PCa who underwent local treatment [2], while a few were not able to confirm these findings [3,4].

Recently, Boeve et al. [5] published data from the HORRAD trial, which randomised 432 patients with metastatic PCa to ADT with or without prostate radiotherapy between 2004 and 2014. The majority of patients (67%) had more than five bone metastases, and the median prostate-specific antigen level was 142 ng/ml. After a median follow-up of 47 mo, no significant difference was found in OS.

The present study by the STAMPEDE investigators represents the first randomised trial showing a benefit of radiotherapy to the prostate in metastatic PCa patients with a low metastatic burden [1]. The optimal definition of a low metastatic burden is still unclear and needs to be refined further, especially given the evolving landscape of more sensitive imaging tools such as prostate specific membrane antigen positron emission tomography. The current definition of a metastatic burden is based on conventional imaging.

As acknowledged by the authors, several other questions remain unanswered, which include the optimum radiotherapy dose schedule, the role of additional metastasis-directed therapy in this setting, and the value of abiraterone in men receiving radiotherapy. Furthermore, it is unknown whether the results of this trial can be extrapolated to radical prostatectomy in metastatic PCa. While it seems plausible given the hypothesis that an intact primary tumour may continue to shed metastasis, there may be radiation-specific mechanisms such as immunomodulation or an interplay between radiation and androgen deprivation, which contribute to the observed survival benefit by radiotherapy. Results from randomised studies currently underway are needed to answer this question.

Conflicts of interest: The authors have nothing to disclose.

References
