Promises and Pitfalls of Primary Local Treatment in Metastatic Prostate Cancer

TO THE EDITOR: The retrospective analysis by Rusthoven et al\(^1\) on improved survival in men who have undergone prostate radiation in addition to androgen deprivation therapy brings to light one of the more recent ongoing controversies in the field of prostate cancer treatment: Do we subject men with metastatic cancer to definitive primary therapy? This area has gained a lot of interest because retrospective analyses have shown surprising benefit in men who undergo primary therapy, especially younger men.\(^2\) In addition, debates continue about treating not only the primary prostate site but also metastatic disease sites, especially for those who have oligometastatic disease, although the appropriate definition of oligometastatic disease also remains a subject for debate. The approach lends itself to both a scientific and pragmatic rationale because other disease sites, such as colon or renal cell cancer, have seen paradigm shifts of addressing the primary and metastatic sites whenever feasible. In addition, this is among many other prospective data that support primary treatment of the prostate in the setting of overt metastatic disease (eg, a treatment arm in the Systemic Therapy for Advancing or Metastatic Prostate Cancer [STAMPEDE] trial, the accrued Netherlands Hormone Versus Radiation [HORRAD] trial, the MD Anderson Cancer Center Best Systemic Therapy or Best Systemic Therapy [BST] Plus Definitive Treatment trial). Furthermore, lethal prostate cancer has been increasingly recognized as emanating not just from the primary tumor but also from metastatic sites through the spread of daughter clones or metastases between metastatic sites, as elegantly shown in the Johns Hopkins biopsy series.\(^3\)

Although these studies raise important issues and provide encouraging results for both patients and physicians who must navigate through the intrinsic management of those who present with de novo metastatic disease, the retrospective database study by Rusthoven et al\(^1\) has several limitations that warrant cautious interpretation of the results. Specifically, the burden of disease that patients presented with was not included. Certainly, patients who may have been deemed fit to undergo primary therapy may have been selected for such an approach. The burden of disease was also not disclosed, and perhaps not able to be determined in a retrospective database analysis. Patients who may have had equivocal disease on scans may have been committed to primary therapy given the uncertainty of a true metastatic diagnosis. Other questions are: What was the time interval between initiation of radiation and the start of hormonal therapy? Would this have altered the decision for primary definitive therapy such that patients who exhibited early castration-resistant disease would have precluded benefit from primary local radiation? Most importantly, what would be the impact in terms of adverse effects? Although we continue to debate the potential harms of curative-intent primary prostate therapy, we have to be similarly cognizant of the potential harms of primary definitive therapy of the prostate when complete extirpative radiation or surgery cannot be achieved in patients with overt metastatic disease. An increasing number of patients query about the benefit of local therapy in the face of a metastatic disease diagnosis. Improved response to multimodality treatment, including the use of early chemotherapy, has swung the pendulum toward more aggressive treatment in men with de novo metastatic disease. However, it is incumbent upon us to interpret the data in the best way possible so we may recognize the absolute benefits and not lose sight of potential harms, especially in the absence of prospective randomized trials.

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AUTHOR’S DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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REFERENCES

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