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EDITORIAL

Developments in oligometastatic hormone-sensitive prostate cancer

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"Suddenly a solitary horseman appeared on the horizon, then another, and another, and then six. In a few moments a whole crowd of solitary horsemen swooped down upon him."

This quote by Stephen Leacock was in included in the *Introduction* for the first definitive work on low-volume metastatic cancer by Philip Rubin and Jerold Green, entitled *Solitary Metastases*, and encompasses the fears of all those who endeavor to understand and treat patients with what is now termed oligometastatic disease [1]. Formally hypothesized by Hellman and Weichselbaum, the *oligometastatic state* is an intermediate state along a spectrum of cancer metastasis whereby local therapies may alter the natural history of patients with metastatic disease [2]. With the recent coalescence of developments in biology, imaging and metastasis-directed therapies (MDT) such as stereotactic ablative radiotherapy (SABR), this *state* has become an area of growing biologic and clinical interest [3, 4].

It is in this context we are pleased to present a special issue in the *Journal* on *Developments in oligometastatic hormone-sensitive prostate cancer*. Briefly, we preview and highlight the work covered in this issue and place them in a cohesive picture of we believe are key future big picture outstanding biological and clinical questions that will be important in the field of primarily hormone-sensitive oligometastatic prostate cancer. First, what is oligometastatic prostate cancer? Then, how do we best treat this condition?

Taking the lead is Christopher Hovens and his group who produce a cogent review of the multiple molecular and clinical studies in support of this meta-stable metastatic state [5]. They argue as we develop greater understanding of oligometastases in prostate cancer we will be able to molecularly define the oligometastatic state and depart from our current simple clinical numerical definition with hopefully significant clinical benefits [6]. We do include an original investigative report by Dhondt et al. who chronicle the failed validation of a miRNA serum signature as a biomarker for oligometastatic prostate cancer [7]. Preliminary data suggest that tissue microRNAs (miRNAs), small 18–24 nucleotide RNAs that regulate gene expression, may drive metastatic competency by adaptive communication between cancer cells and their local and distant environment [8, 9], but unfortunately this did not hold true in this case for the serum miRNAs profiled in prostate cancer. Consequently, until we have such a molecular definition, work that includes clinical models will be needed. Along this vein, Buelens et al. then describe their development of a pragmatic and prognostic clinical model comprised of tumor burden using the CHAARTED metastatic volume definition (high-volume = visceral metastasis or ≥ 4 bone metastases with ≥ 1 appendicular lesion) and alkaline phosphatase to stratify metastatic hormone-naive prostate cancer (mHNPC) [10]. These data support the prognostic significance of the low-volume or oligometastatic state in prostate cancer.

Newer and highly sensitive imaging modalities for prostate cancer cannot be ignored and will be a critical bridge towards a molecular definition of oligometastatic prostate cancer [11]. We have two specific contributions to this imaging work in this special issue, the first by Jurgen J. Futterer and company describe a level setting review of imaging modalities that sheds light on the role of conventional and functional imaging in the setting of synchronous oligometastatic prostate cancer [12]. Pasoglou et al. then present some original work using whole-body magnetic resonance imaging (WB-MRI) to assess the anatomical distribution of oligometastatic and polymetastatic prostate cancer and the impact of the initial treatment on metastatic distribution [13]. They found that oligometastatic men showed different distribution of bone metastases

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compared to polymetastatic men and that the distribution of disease was not influenced by the primary treatment. An important aspect of the emerging data from these more sensitive imaging modalities is that our current clinical definitions of oligometastatic prostate cancer are based almost entirely on conventional imaging and thus we must proceed carefully in parallel with prospective clinical trials validating these new advanced imaging techniques to eventual incorporate them into better definitions of oligometastatic disease.

Next, what are the best approaches for treatment of oligometastatic prostate cancer? In the modern era with conventional imaging, metastatic prostate cancer as a whole is only a minority of newly diagnosed cases making *synchronous* or de novo oligometastatic prostate cancer an even smaller subset of these men. Nonetheless, this is an exciting and important clinical space where Nicholas Nickols and his group review the existing data evaluating primary tumor therapy for patients with metastatic prostate cancer and describe ongoing clinical trials testing the hypothesis that primary tumor therapy may benefit patients with metastatic prostate cancer [14]. Oligorecurrent or metachronous prostate cancer on the other hand comprises a large number of men [15–18]. These patients are presumably in a potentially curable state before castration-resistance develops so we need additional studies to examine this potentially large group of patients. We have a trio of reports either reviewing the current landscape of imaging and treatment for prostate cancer nodal oligorecurrence, by Fodor et al. [19], or two original retrospective single-institutional investigations by Patel et al. [20] and Moyer et al. [21] from the Royal Marsden and Johns Hopkins, respectively, that suggest potential benefits of MDT in this population. Lastly, oligoprogressive prostate cancer, in particular, castration-resistant is an area with little clinical evidence for the utility of MDT. Herein, we present a multi-institutional report by Triggiani et al. [22] comprising 86 men with metastatic castration-resistant prostate cancer (mCRPC) treated with SABR MDT that appears to show a promising clinical outcomes signal.

In closing, we are pleased to present a wonderful collection of reviews and original investigative work to enlighten the *Journal* reader on the rapidly progressing field of oligometastatic prostate cancer. We are optimistic that with the knowledge gleaned from this special issue future prospective initiatives will be performed to accelerate the knowledge to benefit men with oligometastatic prostate cancer in the near future.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest related to this work.

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