

# Metastatic prostate cancer gets into the biomarker era

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Outcomes of patients with metastatic castrate-resistant prostate cancer have improved substantially since the addition of docetaxel, abiraterone, and enzalutamide for patients progressing on androgen deprivation therapy (ADT).<sup>1-3</sup> The benefit has extended to patients with metastatic hormone-sensitive prostate cancer,<sup>4</sup> where combining ADT and docetaxel or androgen receptor antagonist therapy has shown that more complex interventions in metastatic prostate cancer (mPCa) offer better overall survival (OS) and quality of life (QoL).

It is not until recently, however, that treatment selection is based on the use of biomarkers that play a significant role in informing prognosis and predicting response to novel therapies (such as poly-adenosine-receptor inhibitors [PARP-i]). The TOPARP-A trial<sup>5</sup> reported an 88% response rate in patients carrying one of the mutations of interest, and in PROFOUND,<sup>6,7</sup> olaparib was able to demonstrate a five-month survival advantage when compared to standard of care. Initial clinical trials have demonstrated the utility in identifying a biomarker that will potentially translate into a better response, as well as the complexity of identifying this patient population; the best example is PROFOUND, where 2792 patients had to be screened to identify 387 patients that were included in the final analysis.

Although it is expected that approximately 20–30% of patients with mPC will carry pathogenic variants of interest in genes associated with homologous recombination pathway and potentially receive the OS and QoL benefit of a PARP-I, we still have to learn how prevalent these alterations are in our population and which strategies should be put in place to identify those patients.<sup>8</sup>

In this issue of *CUAJ*, Selvarajah et al present their recommendations for the implementation of genetic testing for mPCa patients in Canada.<sup>9</sup> Their approach provides a good example of the multidisciplinary modality required in the management of patients with mPCa, which includes medical and radiation oncology and urology, as well as pathology and familial oncology, the latter two playing a more active role in the context of newer therapies requiring biomarker assessment.

Testing for genetic alterations of interest has challenges — the difference in resources between academic and community settings, among others — that can complicate implementation of this type of diagnostic program, potentially limiting the quality of care for patients. The work presented is relevant to understand and address those challenges. Sharing experiences between cancer centers across the country can help expand ideas and move the implementation process forward quicker.

A potential first step is to work in parallel, constructing a clinical registry of patients enrolled in diagnostic programs and reviewing the screening information of all Canadian patients enrolled in the different PARP-i trials. This can help refine the developing testing programs and create a clinical picture of biomarker-positive patients.

Selvarajah et al have made an important step, highlighting recommendations and actions that will impact equitable access for testing and, consequently, treatment in a timely manner.

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