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Commentary

Circulating Tumor DNA for Detection and Evaluation of Metastatic Prostate Cancer

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DESCRIPTION

The cancer system is incredibly complex and dynamic. The biology of tumors, including prostate cancer, is now widely recognized to change over time and exhibit a significant degree of geographic and temporal heterogeneity in the metastatic situation. Although the prognosis of patients with metastatic prostate cancer has improved considerably with the introduction of next-generation androgen receptor-targeted therapy, chemotherapy, and there is still a need for reliable biomarkers that can help to identify patients at high risk of treatment failure and to allow early detection of progression during on-going therapy. However, a number of difficulties with obtaining fresh tissue biopsy samples have mostly been described in metastatic prostate cancer. A multidimensional overview of the dynamics of the cancer clones can be obtained, in contrast, using liquid biopsy, which may allow the collection of sequential data reflecting several tumor sites at various time points. Circulating Tumor DNA (ctDNA), this is easily retrieved from the patient's blood and has become a key method for analyzing the biology of prostate cancer. The ctDNA testing performed on a sizable group of patients with metastatic Castration-Resistant Prostate Cancer (CRPC) received abiraterone therapy in an international, multi-institutional clinical trial. Exons of numerous known prostate cancer driver genes were covered by custom-targeted next-generation sequencing performed on plasma DNA. Importantly, by capturing 1500 pan-genome regions enriched for single nucleotide polymorphisms using the novel bioinformatics method, the assay was also capable of detecting tumor DNA. Analyses of total plasma ctDNA concentrations are unlikely to be as sensitive in detecting responders as this method. Importantly, there is a lack of validated cut-off values for ctDNA changes in prostate cancer, and the stratified patients into detectable versus non-detectable ctDNA and observed that early ctDNA change can distinguish between favorable and unfavorable disease courses. Following abiraterone medication, the baseline measurable ctDNA level serves as an independent, predictive biomarker of outcome. Baseline plasma tumor DNA was linked to both shorter Progression-Free Survival (PFS) and Overall Survival (OS) [Hazard Ratio (HR): 2.89; 95%Confidence Interval (CI): 1.77-4.73, P 0.0001]. This remained true even after taking into account established clinical prognostic variables. The patients whose ctDNA status changed from detectable to undetectable after 3 weeks of abiraterone and those who did not differed significantly in an important way.

Moreover, ctDNA clearance following two and four treatment rounds was associated with positive clinical outcomes. Together, these findings imply that ctDNA monitoring might be helpful in routine medical practice. While more effective systemic medications are now readily available for males with metastatic CRPC. These findings are consistent with studies that found changes in circulating tumor cells or prostate-specific antigen during androgen receptor targeted therapy to be similar to those reported here. The choice of the best follow-up therapies may ultimately be made using ctDNA analysis.

This may signal lineage plasticity and neuroendocrine differentiation and necessitate chemotherapy or clinical trials examining novel medicines. The acquisition of androgen receptor mutations, however, would support the use of fresh androgen receptor targeted medications that are currently being tested in healthcare situations. To show the clinical relevance of this biomarker in daily practice, that compare shifting from androgen receptor targeted therapy to subsequent therapies when ctDNA has not sufficiently decreased below a predetermined cut-off to a switch at clinical or radiographic progression are necessary. In the future, efforts should be made to compare the utility of ctDNA to that of other circulating indicators and to prospectively integrate ctDNA monitoring into treatment trials and ultimately into regular medical care.

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