ASO Author Reflections: Clinical Utility of Circulating Tumor DNA Analysis in Colorectal Cancer: Current Status

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PAST

Current clinical practice in advanced colorectal cancer (CRC), similar to the management of other cancers, heavily relies on genetic profiling of tumor tissue to match patients with targeted therapy. However, the success of this precision oncology approach often is limited by the lack of archived tissue, the prolonged time required to deliver the needed information, and the small number of effective targeted agents.¹ Liquid biopsy using circulating tumor DNA (ctDNA) has, in recent years, become a minimally invasive tool to provide valuable molecular information in a dynamic fashion for clinical decision-making in CRC.²

PRESENT

This article starts by comparing different methods for ctDNA analysis, then describes the clinical evidence for the application of genetic and epigenetic biomarkers from ctDNA in the screening, surveillance, and treatment-monitoring of CRC.³ The use of genetic biomarkers from ctDNA as a tool for CRC surveillance has been most extensively evaluated in the adjuvant setting. Prospective studies have clearly demonstrated the association between ctDNA clearance and improved recurrence-free survival.⁴ In contrast, to address the unique challenge of early cancer detection, the use of epigenetic biomarkers from ctDNA has been evaluated more for CRC screening.⁵ However, several critical limitations remain including but not limited

to the heterogeneity and lack of standardized methods used for ctDNA analysis, the modest performance in detecting early disease and minimal residual disease after curative-intent treatment, and the coexistence of molecular aberrations from clonal hematopoiesis.³

FUTURE

Given these limitations, further evidence is needed to establish the clinical utility and validity of ctDNA analysis in the screening, surveillance, and treatment-monitoring of CRC. But the field is rapidly evolving and getting close to its prime time. The results from currently ongoing observational and interventional trials will provide important perspective on the utility of biomarkers from ctDNA as a predictive tool to guide therapy.

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REFERENCES

1. Moorcraft SY, Gonzalez de Castro D, Cunningham D, et al. Investigating the feasibility of tumour molecular profiling in gastrointestinal malignancies in routine clinical practice. *Ann Oncol.* 2018;29:230–6. <https://doi.org/10.1093/annonc/mdx631>.
2. Wan JCM, Massie C, Garcia-Corbacho J, et al. Liquid biopsies come of age: towards implementation of circulating tumour DNA. *Nat Rev Cancer.* 2017;17:223–38. <https://doi.org/10.1038/nrc.2017.7>.
3. Xie H, Kim RD. The application of circulating tumor DNA in the screening, surveillance, and treatment monitoring of colorectal cancer. *Ann Surg Oncol.* 2020. <https://doi.org/10.1245/s10434-020-09002-7>.
4. Dasari A, Grothey A, Kopetz S. Circulating tumor DNA-defined minimal residual disease in solid tumors: opportunities to accelerate the development of adjuvant therapies. *J Clin Oncol.* 2018;36:3437–40. <https://doi.org/10.1200/jco.2018.78.9032>.
5. Aravanis AM, Lee M, Klausner RD. Next-generation sequencing of circulating tumor DNA for early cancer detection. *Cell.* 2017;168:571–4. <https://doi.org/10.1016/j.cell.2017.01.030>.