

MSI detection via liquid biopsy shows high concordance with results from tissue samples

5 August 2019

Bottom Line: Incorporation of pan-cancer microsatellite instability (MSI) detection into the 74-gene panel Guardant360 liquid biopsy assay showed high concordance with matched tissue samples in nearly 1,000 patients.

Journal in Which the Study was Published: *Clinical Cancer Research*, a journal of the American Association for Cancer Research

Authors: Martina Lefterova, MD, Ph.D., laboratory director and medical director at Guardant Health in Redwood City, California; and Scott Kopetz, MD, Ph.D., associate professor of Gastrointestinal Medical Oncology at The University of Texas MD Anderson Cancer Center

Background: "Following the tissue-agnostic approval of pembrolizumab for patients with MSI-high tumors, a barrier to improved outcomes for many patients is the awareness and testing of MSI status," said Kopetz.

Evaluation of MSI status, which is typically performed via tumor biopsy, is underutilized for several reasons, noted Kopetz. Reasons include the inherent invasive nature of traditional biopsies, which may not be feasible in some patients; a lack of viable tissue, which may be required for other analyses; and a lack of routine testing, as MSI-high tumors are relatively rare, he noted. "The addition of MSI detection into a routine, noninvasive sequencing panel following the diagnosis of metastatic cancer could direct clinicians to prescribe immunotherapy and provide patients with better outcomes," Kopetz said.

How the Study Was Conducted and Results: To develop a pan-cancer MSI detection panel, the researchers identified 90 relevant microsatellite loci to include in the Guardant360 panel. The assay

was validated by comparing the MSI status as determined via the liquid biopsy test with the MSI status previously determined via standard-of-care tissue testing on 1,145 patients spanning 40 distinct cancer types.

In 949 evaluable patients, the liquid biopsy test identified 87 percent of patients previously reported as MSI-high and 99.5 percent of patients previously reported as MSI-low or microsatellite-stable, representing an overall accuracy of 98.4 percent.

The researchers also evaluated MSI status using the liquid biopsy test in 28,459 consecutive samples from patients with advanced cancer. Among this cohort, 278 samples representing 16 unique tumor types were identified as MSI-high; MSI prevalence was high in endometrial, colorectal, and gastric cancers, while MSI prevalence was low in lung, bladder, and head and neck cancers, which is consistent with previous reports using tissue samples, noted Lefterova.

Additionally, the researchers evaluated the clinical outcomes of 16 patients with metastatic gastric cancer that had previously progressed following standard-of-care chemotherapy; these patients had MSI-high tumors detected using the liquid biopsy test and were treated with either pembrolizumab (15 patients) or nivolumab (one patient). Among these patients, the objective response rate and disease control rate were 63 percent and 81 percent, respectively, which are comparable to the responses for patients identified as MSI-high through tissue testing, explained Kopetz.

Authors' Comments: "The results from our study show that Guardant360, a liquid biopsy test, can deliver valid MSI-high results that can be used to guide treatment planning for patients with advanced [cancer](#)," said Lefterova. "The addition of MSI

detection increases the utility of the assay to direct clinicians beyond targeted therapies to include immunotherapies," she said.

"By adding MSI testing into a non-invasive screening panel, clinicians can routinely scan for this prognostic factor without ordering a separate test," added Kopetz.

"Our results show that MSI detection in blood samples is not only possible, but valid and informative for immunotherapy selection in patients with a wide range of advanced solid tumors," said Lefterova.

Study Limitations: As a limitation to the study, of the more than 28,000 plasma samples evaluated for MSI status, only a subset of them were matched to [tissue samples](#), noted Kopetz. Another limitation of the study is that only one liquid [biopsy](#) test was studied, and the results cannot be applied more broadly to other tests, noted Lefterova.

Funding & Disclosures: This study was sponsored by Guardant Health. Lefterova is a current employee of Guardant Health. Kopetz declares no conflict of interest.

Provided by American Association for Cancer Research

APA citation: MSI detection via liquid biopsy shows high concordance with results from tissue samples (2019, August 5) retrieved 12 June 2021 from <https://medicalxpress.com/news/2019-08-msi-liquid-biopsy-high-concordance.html>

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