

Detecting Cancer Signal Across Multiple Cancers With One Blood Draw: Validating a Multi-Cancer Early Detection (MCED) Test

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INTRODUCTION

- Cancer is a leading cause of death worldwide.¹
- USPSTF-recommended screening tests currently are available for only five cancers (breast, cervical, colorectal, lung [in high-risk patients], and prostate).²⁻⁶
- Most cancers still are identified only when a patient is symptomatic and, therefore, more likely to have a higher treatment burden and lower chance for cure.
 - Detecting cancer before a person has symptoms can lead to better outcomes, including fewer deaths.⁷⁻⁹
 - It has been estimated that cancer detection before stage IV could reduce cancer-related deaths by 15% within 5 years.¹⁰
- A multi-cancer early detection (MCED) test that can detect cancer signals in cell-free DNA (cfDNA) from a single blood-draw has been developed and validated in the Circulating Cell-free Genome Atlas study (CCGA; NCT02889978).^{11,12}
 - Galleri™, an MCED test that analyzes plasma cfDNA to detect signals across >50 cancers and predict the cancer signal origin (CSO), was developed for use as a screening tool in adults with an elevated risk for cancer, such as those aged 50 and older.¹³

OBJECTIVE

- The results of the third and final pre-specified CCGA validation substudy for the MCED test in a large cohort in preparation for clinical use are reported.

KEY RESULTS: THE MCED TEST HAS HIGH SPECIFICITY, DETECTS CANCER SIGNALS FROM DIVERSE CANCERS, AND PROVIDES ACCURATE CSO PREDICTION THAT MAY INFORM PATIENT MANAGEMENT

Overall Test Performance

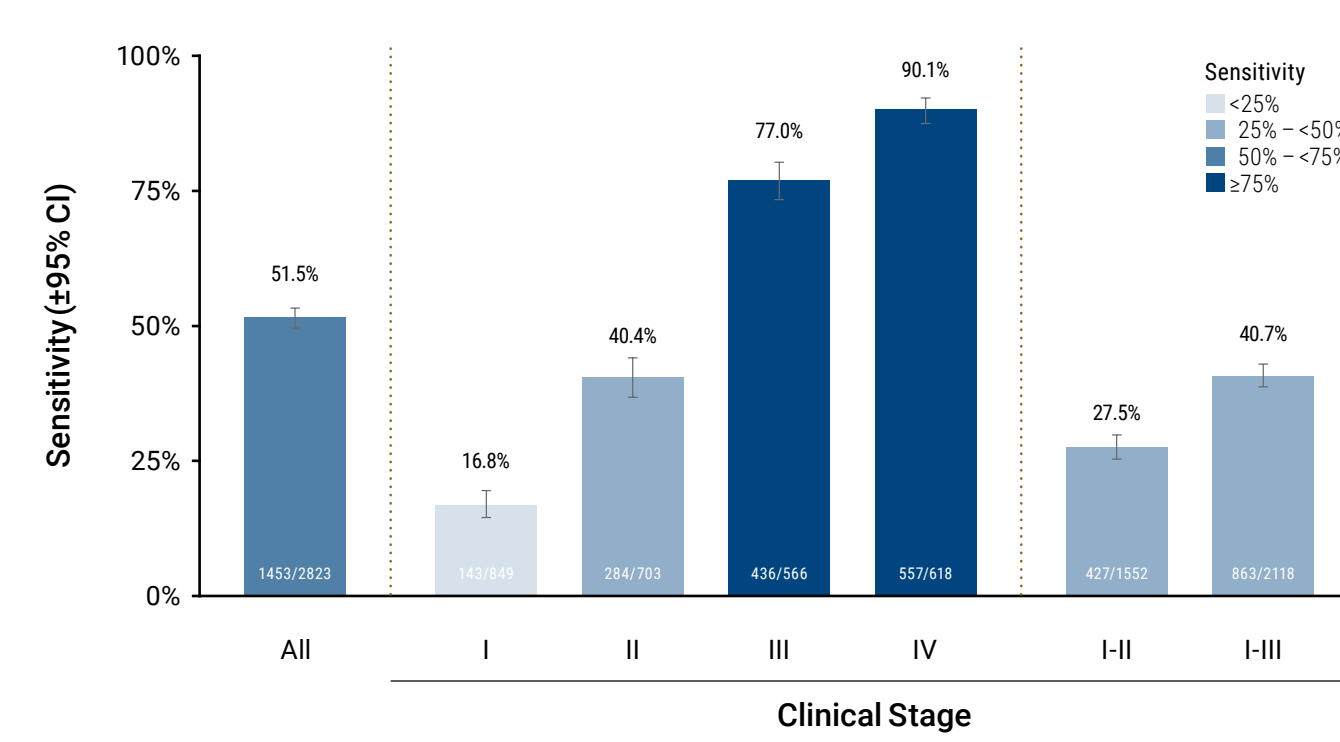
- The MCED test demonstrated 99.5% specificity and 88.7% accuracy of CSO prediction; overall sensitivity was 51.5%, and sensitivity increased with cancer stage (Figures 1 and 2).
- The extrapolated positive predictive value of the MCED test in the screening-eligible 50-79 year age group is higher than that of currently recommended screening tests.¹⁴⁻¹⁶
- Cancer signals from a diversity of cancers were detected by the MCED test as shown by sensitivity across individual cancer classes (Figure 3)

Figure 1. Key Metrics of Overall Test Performance

Sensitivity	51.5% (49.6%-53.3%)
Specificity	99.5% (99.0%-99.8%) False-positive rate of 0.5%
Accuracy of CSO Prediction	88.7% (87.0-90.2%) ^a
PPV	44.4% (28.6-79.9%) ^b

^aAccuracy was defined as the number of correctly predicted top 1 signal origin (n=1273) divided by all cancer participants with a positive cancer signal, excluding participants with unknown primary (n=1435).
^bExtrapolated; SEER-adjusted for the 50-79 years age group.
CI, two-sided 95% Wilson confidence intervals (shown within parentheses); CSO, cancer signal origin; PPV, positive predictive value.

Figure 2. Sensitivity Increased with Clinical Stage



"All" comprises all cancer stages, including missing stage and cancer classes that do not have staging per American Joint Committee on Cancer (AJCC) staging manual.
CI, confidence interval.

Figure 3. Cancer Signals from a Diversity of Cancers were Detected

