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Multi-Cancer Early Detection (MCED) Test Performance in Cancer Survivors

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INTRODUCTION

- As of January 2022, there are ~18.1 million cancer survivors in the United States[1]
  - This number is projected to increase to 22.5 million by 2032
- 69% of cancer survivors have lived ≥5 years since their diagnosis[1]
  - ~16.3 million people are expected to live ≥5 years after their cancer diagnosis over the next decade, an ~30% increase
- Clear guidance is lacking, and there are few options for long-term cancer surveillance
  - Vague and inconsistent guidelines can lead to over and under use of healthcare resources, negatively impacting survivorship care[2]
- As a second cancer can develop in the same organ or a different organ system, a multi-cancer early detection (MCED) test with high specificity can greatly impact cancer survivors
- MCED tests may have higher detection rates for more aggressive cancers, which are generally associated with higher levels of circulating tumor DNA (ctDNA)[3]
- PATHFINDER (NCT04241796) was a prospective cohort study investigating the feasibility of MCED testing for cancer screening[4]
- The MCED test used in PATHFINDER (**Figure S1**) detects a cancer signal from circulating cell-free DNA in blood[3,4]

OBJECTIVE

- Analyze the performance of a refined MCED test in samples from the PATHFINDER cancer survivors group

KEY RESULTS: MCED TESTING CAN BE USED IN CANCER SURVIVORS

- Demographics for the total population tested with the refined MCED test (N=6578) are shown in **Figure 1**
- Of these, 1609 (24%) had a cancer diagnosis ≥3 years prior to study enrollment (**Figure 1** and **S2**)
- The mean number of years since previous diagnosis was 11.2 (SD=8.3) for those with prior cancer
  - Median was 9.0 years (Q1, Q3: 5, 14)
- The most common prior cancers are shown in **Figure 2**

Figure 1. Participant Demographics (N=6578)

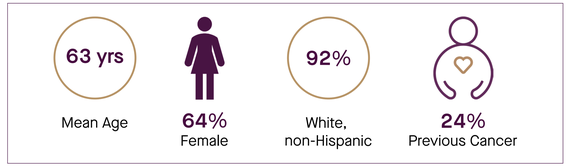
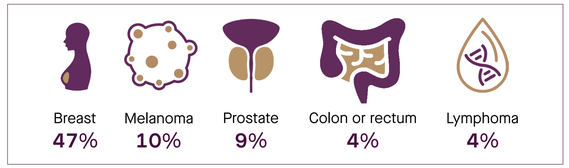


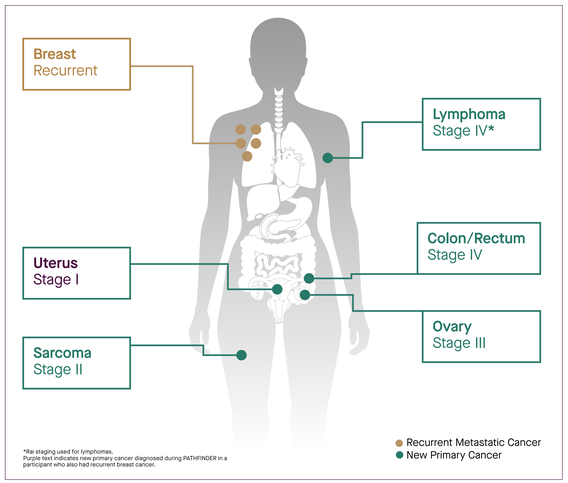
Figure 2. Most Common Prior Cancers (≥4%; n=1609)



Cancers Diagnosed After MCED Signal Detected

- 9 cancer survivors had a cancer signal detected by the refined MCED test and a cancer diagnosis (**Figure S2**)
  - 10 cancers were diagnosed in this group (**Figure 3**)
    - 5/10 were new primary cancers
      - 1 was uterine cancer found as incidental lesion on imaging during MCED-triggered workup for recurrent breast cancer
    - 5/10 were cancer recurrences (all metastatic breast)
- 8 of these individuals had a first-degree relative with cancer

Figure 3. Cancers Diagnosed After MCED Cancer Signal Detected (n=9)



MCED Test Performance

- Test performance was similar in those with and without prior cancer, with high specificity, PPV, and NPV (**Table 1**)

Table 1. MCED Test Performance in Participants With or Without Prior Cancer

	Prior Cancer n = 1609	No Prior Cancer n = 4969	Total N = 6578
PATHFINDER participants diagnosed with cancer, n (%)	**37** (2.3)	**83** (1.7)	**120** (1.8)
MCED cancer signal detected, n (%)	**20** (1.2)	**38** (0.8)	**58** (0.9)
PPV, % (n/N) (95% CI)	**45.0%** (9/20) (25.8%, 65.8%)	**42.1%** (16/38) (27.9%, 57.8%)	**43.1%** (25/58) (31.2%, 55.9%)
NPV, % (n/N) (95% CI)	**98.2%** (1517/1545) (97.4%, 98.7%)	**98.6%** (4699/4766) (98.2%, 98.9%)	**98.5%** (6216/6311) (98.2%, 98.8%)
Specificity, % (n/N) (95% CI)	**99.3%** (1517/1528) (98.7%, 99.6%)	**99.5%** (4699/4721) (99.3%, 99.7%)	**99.5%** (6216/6249) (99.3%, 99.6%)
Yield Rate, % (n/N) (95% CI)	**0.56%** (9/1609) (0.25%, 0.99%)	**0.32%** (16/4969) (0.18%, 0.48%)	**0.38%** (25/6578) (0.24%, 0.53%)
NNTS, n (N/n) (range)	**178.78** (1609/9) (101, 406)	**310.56** (4969/16) (207, 552)	**263.12** (6578/25) (188, 411)
CSO accuracy, % (n/N) (95% CI)	**88.9%** (8/9) (56.5%, 99.4%)	**81.2%** (13/16) (57.0%, 93.4%)	**84.0%** (21/25) (65.3%, 93.6%)

CI, confidence interval; CSO, first cancer signal origin; MCED, multi-cancer early detection; NNTS, number needed to screen to detect one cancer; NPV, negative predictive value; PPV, positive predictive value; Yield Rate, number of true positives among all participants tested.

Cancer Signals Not Detected

- 28 cancers were diagnosed during the PATHFINDER study in participants with no cancer signal detected (**Figure S2**)
  - 15/28 were new primary cancers
  - 13/28 were cancer recurrences (all local)
- Of the 15 new primary cancers diagnosed, 13 had staging information and 10 were early stage
  - 46% stage 1 (2 breast, 1 melanoma, 1 thyroid, 1 lymphoma, 1 lung)
  - 31% stage 2 (2 lymphomas, 1 melanoma, 1 breast)
  - 15% stage 3 (1 pancreas, 1 pleural mesothelioma)
  - 7% stage 4 (1 prostate)
- 3 diagnosed cancers were in the CNS (1 new primary, 2 recurrent)
  - MCED is unlikely to detect CNS cancer signals due to blood-brain barrier effects on ctDNA[5]
- 12 diagnosed cancers (both new and recurrent) were types that generally have lower ctDNA levels (eg, prostate, breast, thyroid and melanoma)[3]
- 6 diagnosed breast cancers had no cancer signal detected, 3 new primary and 3 recurrent
  - 5 of the 6 breast cancers were HER2-
    - 4 of 5 were ER+/HER2- (generally have lower ctDNA[3])
    - 1 of 5 was ER-/HER2-
  - 1 ER+ breast cancer did not have HER2 status reported

CONCLUSIONS

- MCED testing detected a cancer signal from both new primary and recurrent cancers in cancer survivors for whom multiple years had elapsed since their original diagnosis, when surveillance guidance can be unclear[2]
- MCED testing preferentially detects generally more aggressive cancers with higher tumor shedding, most of which also do not have available screening[3]
- The majority of diagnosed cancers with no signal detected by MCED were early stage and/or in tumor types that are known to be associated with lower tumor DNA shedding[3]
- The MCED test had high specificity, resulting in a low false positive rate, and high CSO accuracy, regardless of prior cancer history
- Taken together, these data indicate that MCED testing in cancer survivors can detect a cancer signal in individuals without symptoms or signs of cancer and earlier in the disease course, when patients may be more likely to respond to treatment[6,7]
- While MCED tests should not replace standard screening and long-term surveillance, their use can be considered in cancer survivors, especially in the years after completing treatment

METHODS

- PATHFINDER enrolled 6662 participants ≥50 years of age[4]
- 6578 samples were analyzed with a refined MCED test[4] (Galleri®; **Figure S1**)
- Exclusion criteria included
  - Anyone undergoing or referred for diagnostic evaluation due to clinical suspicion for cancer
  - Personal history of invasive or hematologic malignancy, diagnosed within the 3 years prior to expected enrollment date, or diagnosed >3 years prior to expected enrollment date and never treated
- Participants were stratified by cancer survivor status (**Figure S2**)
  - Prior cancer treated >3 years before enrollment in study
  - No prior cancer
- In cancer survivors, prior cancer type and time from diagnosis were recorded
- Cancers diagnosed during PATHFINDER were classified as new primaries or recurrent

Figure S1. MCED With Galleri Test

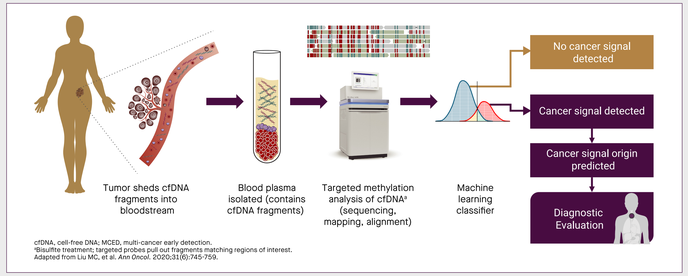
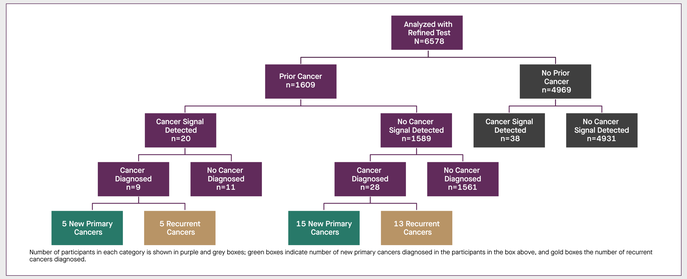


Figure S2. Flow Diagram Of Participants With Prior Cancer



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Disclosures

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