

American Academy of Family Physicians (AAFP) Family Medicine Experience (FMX) September 20-23, 2022

Charles H. McDonnell III,¹ Andrew G. Hudnut,¹ Deepti Behl,¹ Roger Ang,¹ Barbara Spinelli,¹ Debbie Jacobs,¹ Ina Kim,¹ Patrick D. Ogilvie¹ and Kristie Bobolis¹
¹Sutter Health, Sacramento, CA

INTRODUCTION

- Encouraging cancer screening is a core responsibility in family medicine, yet the US Preventive Services Task Force guidelines recommend single cancer screening for only a few select cancers^{1,2}
- A multi-cancer early detection (MCED) test (Galleri®) that allows for earlier detection of shared cancer signal across multiple cancers and provides a prediction of the cancer signal origin (CSO) with a simple blood draw is available in the US³⁻⁵
- PATHFINDER (NCT04241796) is a prospective cohort study in asymptomatic adults ≥50y evaluating clinical implementation of MCED testing

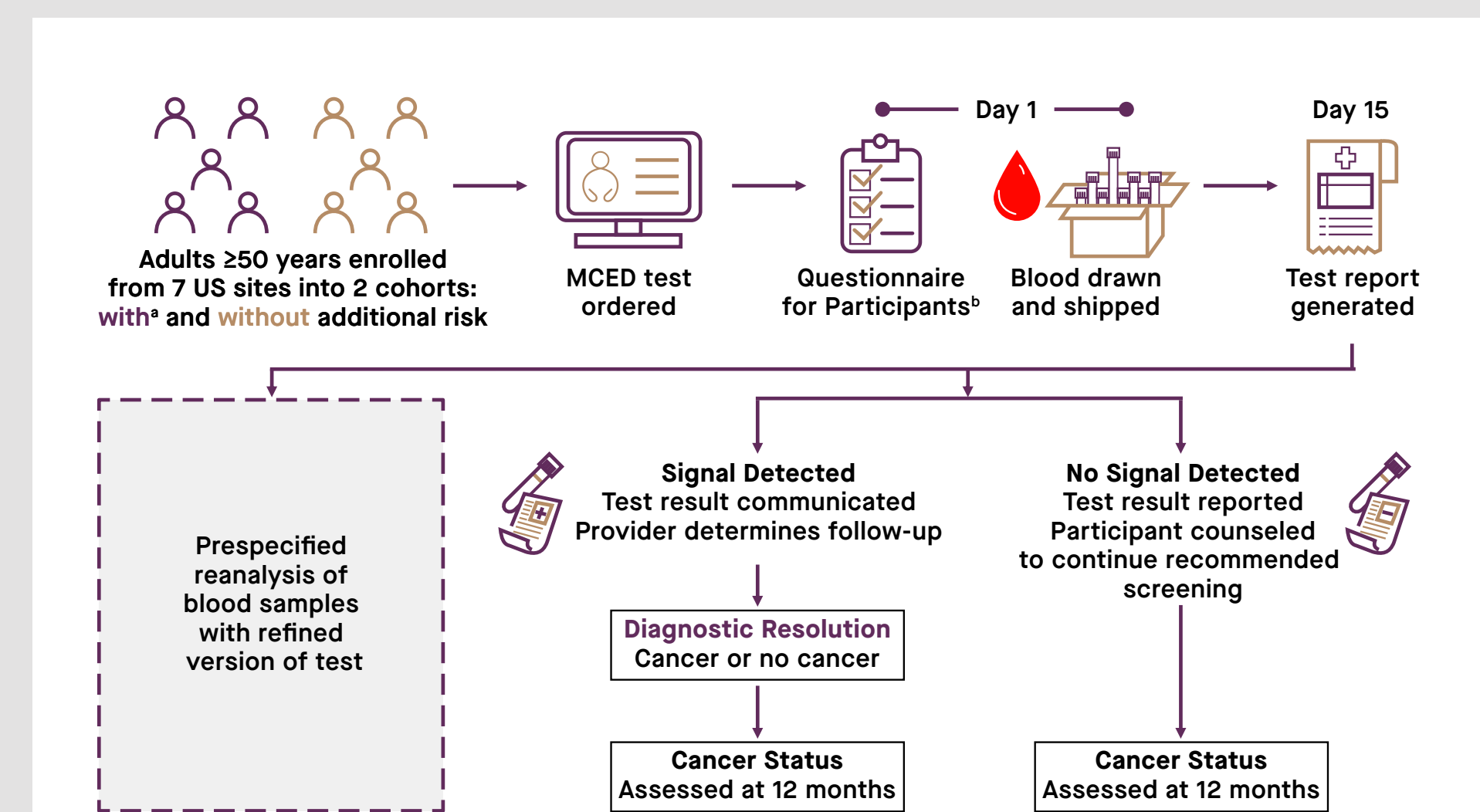
OBJECTIVE

- To provide clinical insight on the challenges and opportunities following a cancer signal detected result, the diagnostic workups of participants from an interim analysis (cutoff Mar-19-2021) of the PATHFINDER study are summarized

METHODS

- A blood-based MCED test was evaluated in the PATHFINDER study by assessing extent of clinical evaluation required to achieve diagnostic resolution following a signal detected result (Figure S1)^{6,7}
- Selection criteria as follows were applied to identify participants for whom a more detailed view of diagnostic progression may provide early clinical insights on use of MCED testing as follows: available staging information and CSO prediction (not "Indeterminate"), complete clinical notes, a predicted or diagnosed solid cancer (not hematologic), and a confirmed new cancer
- Data for the 5 participants meeting these criteria were reviewed, and key diagnostic steps from signal detected (Day 1) to resolution are summarized

Figure S1. Pathfinder Study Design



*Previous history of cancer, smoking, and genetic risk; ^aAlso collected at other timepoints during the study; ^cDefined as date when study team determines to end diagnostic evaluation triggered by a "signal detected" test result.

MCED TESTING DETECTED CANCER SIGNAL AND DIRECTED DOWNSTREAM DIAGNOSTIC EVALUATION OF MULTIPLE CANCER TYPES, INCLUDING THOSE WITHOUT CURRENT SCREENING METHODS

Individual 1

- Individual 1 was a female >60 y without additional cancer risk factors (CSO=Colon/Rectum, Upper GI Tract)

Individual 1 CSO 1 = Colon, Rectum
CSO 2 = Upper GI Tract

Day 1: Signal Detected

Day 4: Results Communicated and Multidisciplinary Panel Convened

Day 7: CT (Abdomen, Pelvis) With Contrast

Day 35: GI referral

Day 43: Upper Endoscopy, Colonoscopy, and Pathology

Day 48: Clinic Visit and Referral

Day 60: Clinic Visit and EUS

Day 60: DIAGNOSIS: Small Intestine Adenocarcinoma, Clinical Stage I (T2N0M0)

Through July 2022 (Day 840)

Treatment and Status: Surgery (Pathologic Stage III) and adjuvant chemotherapy. Patient tolerated the treatment and remains disease free as of July 2022, though follow up imaging identified new lung nodules that are concerning for metastases. Evidence for probable enlargement of sub-centimeter lung nodules (not FDG avid on PET) has been documented, and patient is being followed off treatment

Individual 2

- Individual 2 was a male former smoker >65 y with a history of hepatitis C (CSO=Liver/Bile-duct)

Individual 2 CSO 1 = Liver, Bile Duct

Day 1: Signal Detected

Day 2: Results Communicated and Multidisciplinary Panel Convened

Day 36: Chemistry Panel

Day 40: Quad Phase wwo CT Abdomen and Chest CT With Contrast

Day 45: Referral to Liver Surgeon and Multidisciplinary Panel Convened

Day 57: Clinic Visit

Day 57: DIAGNOSIS: Liver tumor, Clinical Stage I (T1N0M0)

Through July 2022 (Day 225)

Treatment and Status: Treatment was declined following surgical referral and participant died <9 months post-test result (Day 225) from progression of cancer

Individual 3

- Individual 3 was a male former smoker >70 y (CSO=Pancreas/Gallbladder, Lung)

Individual 3 CSO 1 = Pancreas/Gallbladder
CSO 2 = Lung

Day 1: Signal Detected

Day 3, Day 4: Multidisciplinary Panel Convened and Results Communicated

Day 9: Lab Work (Comprehensive Metabolic Panel and Tumor Markers)

Day 14: CT Chest and Abdomen wwo Contrast

Day 19: PET-CT

Day 38: CT-guided Core Biopsy

Day 38: DIAGNOSIS: Pancreatic Adenocarcinoma, Clinical Stage IIb (T3N1M0)

Through July 2022 (Day 650)

Treatment and Status: Surgery revealed pathologic stage IIa disease. Adjuvant chemotherapy followed. Follow up imaging July 2022 shows an enlarging lung mass suspicious for a primary lung cancer. Stable post-operative changes in the abdomen

Individual 4

- Individual 4 was a male former smoker >60 y (CSO=Head and Neck)

Individual 4 CSO 1 = Head and Neck

Day 1: Signal Detected

Day 2: Results Communicated and Review Board Convened

Day 3: Lab Work (Chemistry Panel)

Day 11: Endoscopy (Laryngoscopy)

Day 41: CT (Soft Tissue Neck) With Contrast

Day 46-59: Thyroid Ultrasound and Multiple Biopsies

Day 63, 64: Clinic Visit and Referral

Day 73: PET-CT

Day 81: Surgical Biopsy

Day 81: DIAGNOSIS: Head/Neck Squamous Cell Carcinoma, Stage II (T2N2M0)

Through July 2022 (Day 580)

Treatment and Status: Radiation therapy, chemotherapy, and nephrectomy. Patient alive with no evidence of cancer as of June 2022

Individual 5

- Individual 5 was a female former smoker >60 y (CSO=Lung)

Individual 5 CSO 1=Lung
CSO 2=Pancreas, Gall Bladder

Day 1: Signal Detected

Day 4: Results Communicated and Review Board Convened

Day 8: CT (Chest) Without Contrast

Day 11, 13: Referral and Review Board Convened

Day 18: PET-CT

Day 19, 20: Clinic Visit and Review Board

Day 22: Lab Tests and Biopsy

Day 22: DIAGNOSIS: Lung Adenocarcinoma, Stage IIIB (T1N3M0)

Through July 2022 (Day 800)

Treatment and Status: Radiation therapy, chemotherapy, and immunotherapy. Treatment for metastatic disease initiated. As of June 2022, imaging shows worsening metastatic disease in lymph nodes

CONCLUSIONS

- This MCED test detected cancer signals in these participants, all of whom received a confirmatory diagnosis of cancer in <3 months
- Guidance provided by the CSO prediction was used to direct the workup required to achieve a definitive diagnosis, including for cancers for which there is currently no recommended screening method
- Given the role that family practitioners can play in advocating for early cancer screening, an increased awareness and understanding of MCED testing can support their ability to interpret and take appropriate action based on MCED test results
- Importantly, insights here show that diagnostic testing prompted by MCED test results was consistent with existing clinical guidance and reflective of the steps and procedures that would be taken in any instance of suspicion of cancer with the corresponding patient attributes

References

- Gates TJ. Am Fam Physician. 2014 Nov 1;90(9):625-631.
- <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation-topics/uspstf-and-b-recommendations>
- www.galleri.com
- Liu MC, Oxnard GR, Klein EA, et al. Ann Oncol. 2020;31(6):745-759. doi:10.1016/j.annonc.2020.02.011
- Klein EA, Richards D, Cohn A, et al. Ann Oncol. 2021;32(9):1167-1177.
- Nadauld LD, McDonnell CH, 3rd, Beer TM, et al. Cancers. 2021;13(14).
- Beer TM MC, Nadauld L, Liu MC, et al. J Clin Oncol. 2021;May 20;39(15_suppl):3010.1.

Disclosures

Study funded by GRAIL, LLC, a subsidiary of Illumina, Inc. All other financial relationships disclosed at abstract submission.

Acknowledgements

Funded by GRAIL, LLC, a subsidiary of Illumina Inc.* Writing, editorial, and graphic assistance provided by Prescott Medical Communications Group (Chicago, IL).

*GRAIL, LLC, is currently held separate from Illumina Inc. under the terms of the Interim Measures Order of the European Commission dated 29 October 2021.