P0356

Detection of Gastrointestinal Cancer in Individuals Without Clinical Suspicion of Cancer Using a Multi-Cancer Early Detection Test in the PATHFINDER Study

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INTRODUCTION

- Colorectal cancer (CRC) is the only gastrointestinal (GI) cancer with United States Preventive Services Task Force (USPSTF)-recommended screening guidelines[1]
- Other GI cancer (eg, esophageal, liver) screening guidelines are based on predisposing risk factors; however, not all patients who develop cancer would have met the clinical criteria for screening described in the guidelines[1,2]
- A blood-based multi-cancer early detection (MCED) test was evaluated in the prospective PATHFINDER study (NCT04241796; n=6662)[3]
  - PATHFINDER was designed to provide insight into how physicians and patients would respond to MCED testing, including what diagnostic steps would follow a positive MCED test result and if the test information helped facilitate a diagnosis[4]
  - In the study, a final diagnosis in those with a cancer signal detected was often achieved within 3 months
  - A refined version of the test (Galleri®, GRAIL, LLC, Menlo Park, CA), which is intended to complement USPSTF-recommended screening, is available with accreditations from the College of American Pathologists (CAP) and certification under Clinical Laboratory Improvement Amendments (CLIA)[5]

OBJECTIVE

- An overall objective of the PATHFINDER study was to assess clinical feasibility of the use of MCED testing. Although the MCED test has been shown to detect a signal shared by over 50 cancer types (both GI and non-GI), this presentation provides a focused subanalysis of test performance with GI cancers specifically from the PATHFINDER study

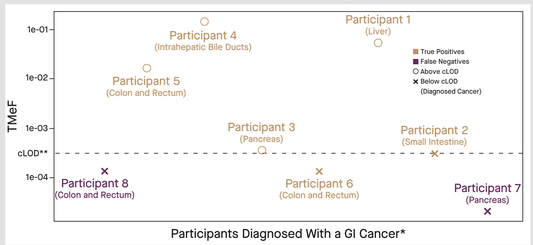
METHODS

- The MCED test uses machine learning to detect cancer-specific methylation patterns in tumor cell-free DNA and predict a cancer signal origin (CSO)
- Participants in PATHFINDER were ≥50 years of age with/without additional cancer risk factors beyond age (eg, smoking), were not under clinical investigation for cancer, and consented to 1 year of follow-up surveillance[4]
- Participants with a confirmed GI cancer diagnosis were reviewed for cancer signal detected or signal not detected result, CSO prediction accuracy, cancer type and stage, and time to diagnostic resolution

SUPPORTING DATA

- The 2 participants diagnosed with GI cancer after receiving a signal not detected MCED test result had a circulating tumor fraction below the clinical limit of detection
- These included a stage I CRC (n=1) and a stage III pancreatic cancer (n=1) diagnosed 6 months after MCED testing due to new symptom development (**Figure S1**)

Figure S1. Circulating Tumor Fraction in 8 Participants Diagnosed With a GI Cancer in the PATHFINDER Study.

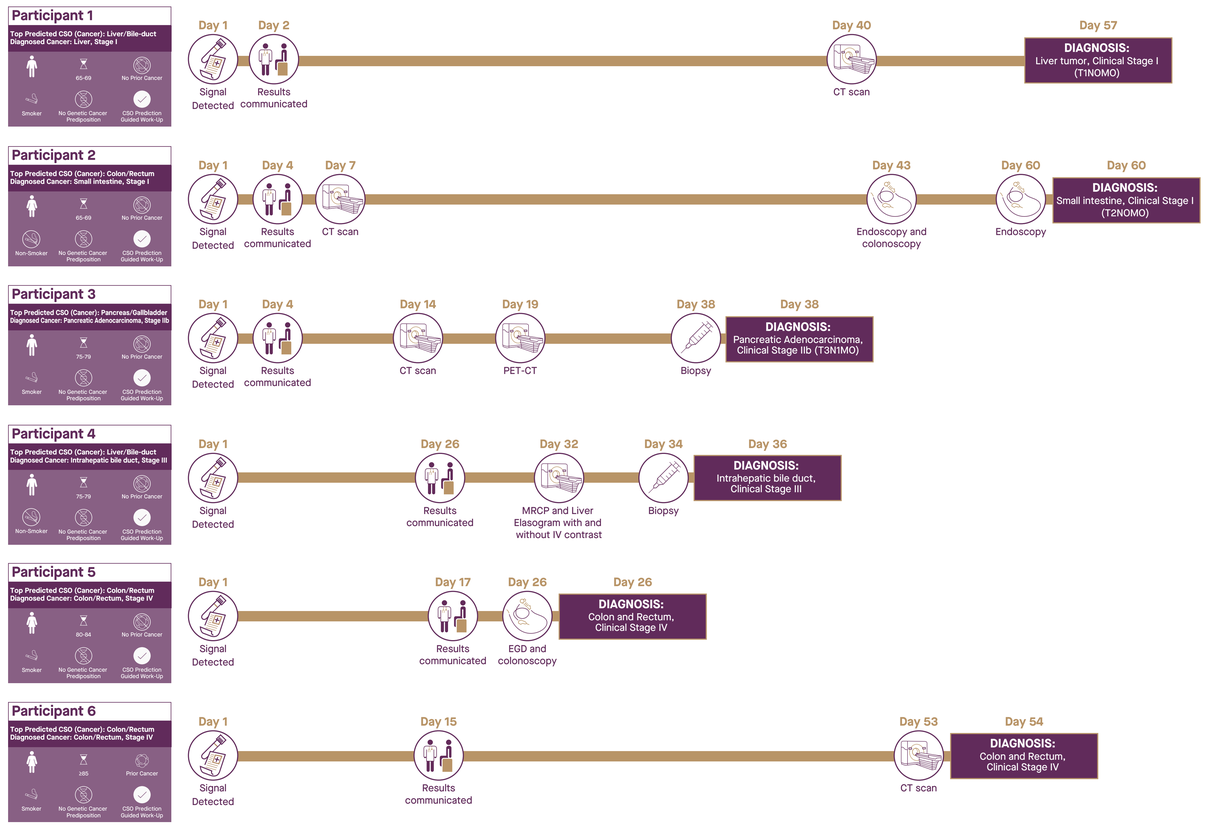


*Participants are shown from left to right by increasing time to achieve diagnosis following the MCED test.
**cLOD indicates a TMeF at which 50% of cases are detected.
cLOD, clinical limit of detection; GI, gastrointestinal; TMeF, tumor methylated fraction (a methylation-based quantification of the circulating tumor allele fraction that can be used to estimate circulating tumor DNA abundance)

KEY RESULTS: A BLOOD-BASED MULTI-CANCER EARLY DETECTION TEST DETECTED 75% OF GI CANCERS, HALF OF WHICH WERE EARLY STAGE, AND MOST DID NOT HAVE OTHER RECOMMENDED SCREENING OPTIONS

- Among 8 participants diagnosed with a GI cancer, 6 were detected by the MCED test (**Figure 1**)
  - CSO prediction was accurate for 5/6 diagnoses, and the 6th case was a diagnosis of small intestine cancer that was obtained after a CSO-directed workup utilizing upper and lower endoscopy
  - All cases with a cancer signal detected result achieved diagnostic resolution in <2 months from test result
  - Notably, 3/6 had early-stage, non-metastatic cancer, and 4/6 had cancer without USPSTF-recommended screening (small intestine, liver, bile duct, pancreatic)
  - All 6 were detected prior to clinical presentation, including the stage IV CRC (n=2)

Figure 1. Diagnostic Journey of the 6 True Positive Participants Diagnosed with GI Cancers Following a Signal Detected Result With an MCED Test.



CSO, cancer signal origin; CT, computed tomography; EGD, esophagogastroduodenoscopy; MRCP, magnetic resonance cholangiopancreatography; PET, positron emission tomography.

CONCLUSIONS

- PATHFINDER was a prospective cohort study evaluating the feasibility of MCED testing for cancer screening and was designed to provide insight into how physicians and patients would respond to MCED testing
- This blood-based MCED test detected 75% of GI cancers in PATHFINDER. The majority were in GI cancer types that have no current USPSTF screening recommendations, and half were detected at early stages (I/II). As the PATHFINDER study was a one-time screen, the 2 individuals diagnosed with a stage IV cancer might have been detected at an earlier stage with earlier administration of the MCED test
- These data support the utility of an MCED test that predicts a CSO. Time to diagnosis was rapid (<2 months), prediction accuracy was high (83%), and the cancers were diagnosed in participants not under clinical investigation for cancer, even those diagnosed with stage IV CRC

References

1. https://www.uspreventiveservicestaskforce.org/uspstf/topic_search_results?topic_status=P&searchterm=cancer. Accessed August 2023.
2. Cabebe E and Espat, *J. Esophageal Cancer Guidelines*. https://emedicine.medscape.com/article/2500007-overview?form=fpf.
3. Schrag, DS et al. *Lancet*. 2023; TBD (In Press).
4. Nadauld LD, et al. *Cancers* 2021; 13: 3501.
5. Galleri® | Multi-Cancer Early Detection | Homepage. Galleri®. Accessed August, 2023. https://www.galleri.com/

Disclosures

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