# Final Results From PATHFINDER Study of GRAIL's Multi-Cancer Early Detection Blood Test Published in The Lancet

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*PATHFINDER Results Support Feasibility of Multi-Cancer Early Detection (MCED) Testing in Clinical Practice of Eligible Patients*

*Accuracy of Cancer Signal Origin Prediction of MCED Testing Enabled Targeted Diagnostic Evaluations; Majority of Participants Achieved Diagnostic Resolution in Less Than Three Months*

*Adding MCED Testing to Standard of Care Screening More Than Doubled the Number of New Cancers Detected With Nearly Half in Early Stages*

**MENLO PARK, Calif., Oct. 5, 2023** — GRAIL, LLC, a healthcare company whose mission is to detect cancer early when it can be cured, today announced that detailed findings from the PATHFINDER study of its multi-cancer early detection (MCED) blood test have been published in *The Lancet*. The study, conducted in 6,662 adults over the age of 50 without symptoms suggestive of cancer, demonstrated that an earlier version of GRAIL's MCED test identified many cancer types that do not currently have recommended screening tests, enabled targeted cancer diagnostic evaluations, and supported diagnostic resolution for the majority of participants in less than three months.

"The possibility of screening for multiple types of cancer simultaneously using a blood specimen is promising both because there are no effective screening strategies for many types of cancer and because strategies with established effectiveness require considerable time and effort," noted Deb Schrag, MD, MPH, Chair, Department of Medicine at Memorial Sloan Kettering in New York and a PATHFINDER investigator. "The PATHFINDER study was a pilot non-randomized study to evaluate how patients and clinicians would respond to a blood test to screen for multiple cancer types. The screening test identified a cancer signal in 1.4% of participants, 0.5% of whom were confirmed to have cancer. In the vast majority of cases, the test accurately predicted the type of cancer. This study demonstrates the feasibility of screening for multiple cancers using a blood test and lays the foundation for large, controlled trials necessary to establish clinical utility and cost-effectiveness."

The prospective cohort assessed use of GRAIL's targeted methylation-based MCED test with 6,662 enrolled participants in U.S. outpatient settings to determine the time required and diagnostic testing necessary to reach a diagnostic resolution following a cancer signal detected test result (primary endpoint). Study results showed that the GRAIL test cancer signal origin (CSO) prediction was 97% accurate and directed the clinical workup, leading to resolution of the cancer diagnosis in less than three months (median 79 days) among participants who received a cancer signal detected result.

In the study, when added to U.S. Preventive Services Task Force (USPSTF) standard of care screening, GRAIL's MCED test more than doubled the number of cancers detected compared to standard screening alone. Of those who received a cancer signal detected result, 36 cancers were diagnosed in 35 participants (one participant was diagnosed with two cancers). Standard screenings identified 29 cancers.

"The PATHFINDER study provides crucial insights into how MCED testing can be used in clinical settings and demonstrates its additive benefit for cancer screening in clinical practice for eligible patients," said Jeffrey Venstrom, MD, chief medical officer at GRAIL. "MCED tests have the potential to expand the number of cancers detected with a low false-positive rate when added to recommended single-cancer screenings. In addition, our MCED test can predict the cancer signal of origin, resulting in a more efficient and targeted diagnostic evaluation to help decrease unnecessary tests, radiation and costs. We believe this study helps pave the way for its clinical adoption, with the aim of reducing the burden of late-stage cancer."

Among participants who received an MCED cancer signal detected result and had a confirmed new cancer diagnosis (true positives), nearly half (48%) were detected at an early stage (I-II) when the potential for curative treatment is increased. Importantly, 74% of the MCED-detected cancers were cancer types that do not currently have recommended screening tests. These included cancers of the bile duct, small intestine, pancreas and spindle cell neoplasm, all highly lethal cancers that may be amenable to surgical resection at early stages.

"The PATHFINDER trial gave us a glimpse into the future of cancer, early detection and cancer screening and showed us how a multi-cancer early detection blood test can have tremendous potential to impact patient outcomes," said Charles McDonnell, MD, radiologist at Sutter Medical Group and PATHFINDER investigator. "The more broadly that we can get the message out about multi-cancer early detection technology, the more people can continue to study and incorporate this into clinical practice, the better for our patients."

After the PATHFINDER study was launched, a refined version of the MCED test, now available by prescription as Galleri, was developed for clinical use. The refined test only changed the threshold for detecting a cancer signal for hematologic malignancies, removed indeterminate as a returned cancer signal origin result and limited the number of CSOs. The study assessed performance of both the early version and the refined version as a key secondary endpoint. Results showed the positive predictive value (PPV, the percent of cancer signal detected results that were confirmed to be cancer) of the refined test was 43.1% compared to 38% with the earlier version. The refined test version also improved specificity, or the percentage of true negatives, to 99.5%, increasing from 99.1% with the earlier version. The CSO prediction accuracy of the refined test was 88%.

No study-related serious adverse events were reported as a result of MCED testing in the study, and there were no adverse events reported from diagnostic workups.

**About GRAIL**
GRAIL is a healthcare company whose mission is to detect cancer early, when it can be cured. GRAIL is focused on alleviating the global burden of cancer by using the power of next-generation sequencing, population-scale clinical studies, and state-of-the-art machine learning, software, and automation to detect and identify multiple deadly cancer types in earlier stages. GRAIL's targeted methylation-based platform can support the continuum of care for screening and precision oncology, including multi-cancer early detection in symptomatic patients, risk stratification, minimal residual disease detection, biomarker subtyping, treatment and recurrence monitoring. GRAIL is headquartered in Menlo Park, CA with locations in Washington, D.C., North Carolina, and the United Kingdom. GRAIL, LLC, is a subsidiary of Illumina, Inc. (NASDAQ:ILMN) currently held separate from Illumina Inc. under the terms of the Interim Measures Order of the European Commission.

For more information, visit **grail.com**.

**About Galleri®**
Galleri is the first-of-its-kind multi-cancer early detection (MCED) test that has demonstrated the ability to detect a shared cancer signal across more than 50 types of cancer through a routine blood draw. The Galleri test can improve the opportunity for asymptomatic early detection by screening for multiple cancers, most of which lack recommended screening tests. Galleri has demonstrated a low false positive rate and high positive predictive value (the proportion of people with a positive screening result who are diagnosed with cancer) in asymptomatic people at an elevated risk for cancer.

The Galleri test uses next-generation sequencing and machine-learning algorithms to isolate cell-free DNA and analyze methylation patterns to detect if a cancer signal is present. If a cancer signal is detected, the Galleri test predicts the cancer signal origin, or the tissue or organ where the cancer signal originated, to help guide diagnostic evaluation.

The Galleri test requires a prescription from a licensed health care provider and should be used in addition to recommended cancer screenings such as mammography, colonoscopy, prostate-specific antigen (PSA) test, or cervical cancer screening. It is intended for use in people with an elevated risk of cancer, such as those aged 50 or older.

For more information, visit **galleri.com**.

**Important Galleri Safety Information**
The Galleri test is recommended for use in adults with an elevated risk for cancer, such as those aged 50 or older. The Galleri test does not detect all cancers and should be used in addition to routine cancer screening tests recommended by a healthcare provider. Galleri is intended to detect cancer signals and predict where in the body the cancer signal is located. Use of Galleri is not recommended in individuals who are pregnant, 21 years old or younger, or undergoing active cancer treatment.

Results should be interpreted by a healthcare provider in the context of medical history, clinical signs and symptoms. A test result of “Cancer Signal Not Detected” does not rule out cancer. A test result of “Cancer Signal Detected” requires confirmatory diagnostic evaluation by medically established procedures (e.g., imaging) to confirm cancer.

If cancer is not confirmed with further testing, it could mean that cancer is not present or testing was insufficient to detect cancer, including due to the cancer being located in a different part of the body. False-positive (a cancer signal detected when cancer is not present) and false-negative (a cancer signal not detected when cancer is present) test results do occur. Rx only.

**Laboratory/Test Information**
GRAIL’s clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and accredited by the College of American Pathologists. The Galleri test was developed, and its performance characteristics were determined by GRAIL. The Galleri test has not been cleared or approved by the U.S. Food and Drug Administration. GRAIL’s clinical laboratory is regulated under CLIA to perform high-complexity testing. The Galleri test is intended for clinical purposes.

Corporate Communications
Trish Rowland
Cammy Duong
pr@grail.com