The Lancet Oncology Publishes Results from SYMPLIFY, The First Prospective Study of a Multi-Cancer Early Detection Test in a Symptomatic Patient Population

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Study Demonstrated Overall Positive Predictive Value of 75.5%

Negative Predictive Value was 99.1% and 97.8% for Patients Referred for Upper and Lower Gastrointestinal Cancer Suspicion, Respectively

Overall Cancer Signal Origin Prediction Accuracy was 85.2%

MENLO PARK, Calif., June 20, 2023 — GRAIL, LLC, a healthcare company whose mission is to detect cancer early when it can be cured, and the University of Oxford today announced that results from the SYMPLIFY study have been published in The Lancet Oncology. SYMPLIFY is the first large-scale evaluation of a multi-cancer early detection (MCED) test in individuals who presented with symptoms to primary care and were referred for diagnostic follow-up for suspicion of cancer. The analysis showed strong performance of GRAIL's MCED methylation-based platform in the population of more than 6,000 patients and demonstrated the feasibility of using an MCED test to assist clinicians with decisions regarding referral from primary care.

"For the majority of cancers, there are no organized screening programs and most patients diagnosed with cancer first attend primary care with symptoms. These can be non-specific, such as weight loss or abdominal pain and can result in a lengthy diagnostic path of invasive and expensive work-ups, with associated anxiety for the patient. The use of MCED testing, with an accurate prediction of the site of origin in symptomatic patients can speed up diagnosis where we are not sure which diagnostic pathway is the right one," said Mark Middleton, MD, PhD, FRCP, Head of Oncology at the University of Oxford and co-lead investigator of the study. "In the SYMPLIFY study, a significant minority of cancers were diagnosed in organs that were different from those originally suspected, given the symptoms experienced. This was particularly true in patients referred for upper gastrointestinal and gynecological investigation. In these cases, the high accuracy of cancer signal origin prediction of the MCED blood test can add valuable information to inform test sequencing and reduce both the time to diagnosis and costs in patients referred for urgent cancer investigation. It is also encouraging to see the performance of the test in esophagus, stomach, liver, pancreas and bile duct cancers. We really need to be able to diagnose these hard-to-treat cancers earlier so that we can improve outcomes."

The SYMPLIFY study enrolled 6,238 patients, aged 18 and older, in England and Wales who were referred for urgent imaging, endoscopy or other diagnostic modalities to investigate symptoms suspicious for possible gynecological, lung, lower gastrointestinal (GI) or upper GI cancer, or who had presented with non-specific symptoms. Of the total enrolled, there were 5,461 evaluable patients who achieved diagnostic resolution. Participants provided a blood sample, from which cell-free DNA was isolated and stored until GRAIL's MCED test was performed in batches, blinded to clinical outcome. GRAIL's MCED test's predictions (cancer signal detected, and if so, cancer signal origin [CSO]) were compared with the diagnosis obtained by standard of care to assess the test's performance. Among evaluable patients, the most commonly reported symptoms leading to referral were unexpected weight loss (24.1%), change in bowel habit (22.0%), post-menopausal bleeding (16.0%), rectal bleeding (15.7%), abdominal pain (14.5%), pain (10.6%), difficulty swallowing (8.8%) and anemia (7.1%). Within the study, 368 (6.7%) of the evaluable patients were diagnosed with cancer through standard of care. The most common cancer diagnoses were colorectal (37.2%), lung (22.0%), uterine (8.2%), oesophago-gastric (6.0%) and ovarian (3.8%). The mean age of patients in the study was 62.1 years old.

GRAIL's MCED test detected a cancer signal in 323 people (6.7%), 244 in whom cancer was diagnosed, resulting in a positive predictive value (PPV) of 75.5%, negative predictive value (NPV) of 97.6%, and specificity of 98.4%. The overall sensitivity of the MCED test was 66.3%, ranging from 24.2% in stage I cancers to 57.1% in stage II and 95.3% in stage IV, increasing with age and later cancer stage. The overall accuracy of the top CSO prediction after a positive MCED test was 85.2%. Additionally, many cancers were diagnosed at sites other than those inferred by the symptoms that led to referral. This was most pronounced in the upper GI and gynecological pathways, for which 47% and 25% of cancers, respectively, were incongruent with the referral pathway.

Results were particularly strong within the GI pathways. The sensitivity for lower and upper GI cancer were 68.5% and 80.5%, respectively. Considering the groups of patients included in this study, MCED test performance was the strongest in patients referred for investigation of a possible upper GI cancer, with a negative predictive value of 99.1%, offering the potential to make more efficient use of endoscopy resources.

"The high overall positive predictive value and signal origin accuracy results seen in the SYMPLIFY study provide further evidence that GRAIL's MCED methylation-based platform can help clinicians in difficult non-specific symptomatic situations determine the likelihood that an individual might have cancer, and if so, where to direct them next," said Harpal Kumar, President of GRAIL Europe. "These are very exciting results that have the potential to transform the way clinicians manage patients with nonspecific symptoms to achieve a faster diagnosis, hopefully leading to a better outcome if we can find those cancers faster. We look forward to using these results to further improve test performance in this patient population."

The University of Oxford sponsored the SYMPLIFY study and was responsible for data collection, analysis and interpretation. The study was funded by GRAIL with support from National Health Service (NHS) England, NHS Wales, the National Institute for Health and Care Research (NIHR) and NIHR Oxford Biomedical Research Centre.

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.

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. GRAIL's clinical laboratory is regulated under CLIA to perform high-complexity testing.

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