

Galleri
GRAIL, Inc.

Premarket Approval (PMA) Application

**Molecular and Clinical Genetics Panel of the Medical Devices
Advisory Committee (MDAC) Meeting**

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FDA Presentation

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Topic of Panel Meeting

Premarket Approval (PMA) Application from GRAIL, Inc. for a first-of-a-kind device – **Galleri** – intended for screening for the early detection of multiple types of cancer

FDA seeks input from the Panel on whether the probable benefits to health from use of the Galleri test outweigh the probable risks for the proposed indications for use

Outline



- Part I: Background
- Part II: Clinical Studies
- Part III: Summary

Part I: Background

- Disease Background
- Device Description
- Proposed Indications for Use
- Regulatory History
- Non-Clinical Studies

Cancer Burden in the U.S.

- **Cancer is the second-leading cause of death in the U.S.** and the leading cause of death among women aged 40-79 and men aged 60-79
- In 2026, more than **2.1 million new cancer cases** and nearly **630,000 cancer deaths** are expected to occur¹
- Cancer predominantly occurs in adults aged 50 years and older

For some cancer types, earlier cancer detection may lead to significant benefits to public health

¹Siegel RL, Kratzer TB, Wagle NS, Sung H, Jemal A. Cancer statistics, 2026. CA Cancer J Clin. 2026 Jan-Feb;76(1):e70043.

Some Cancer Types Have Guideline-Recommended Screening



- The U.S. Preventive Services Task Force (USPSTF) makes evidence-based recommendations about preventive services including cancer screening
 - Grade A and B recommendations indicate the USPSTF recommends the service
 - Grade C recommendation indicates the USPSTF recommends selectively offering or providing this service to individual patients based on professional judgement and patient preferences

USPSTF has issued Grade A, B, or C screening recommendations for breast, cervical, colorectal, lung, and prostate cancer

Adherence to Guideline-Recommended Screening is Variable



Cancer Type	Eligible Population ¹	Prevalence Up-to-Date with Screening ²
Breast	Women aged 50 to 74 years	~80%
Cervical	Women aged 25 to 65 years	~76%
Colorectal	Adults aged 45 years and older	~65%
Lung	Adults aged 50 to 80 years who currently smoke or formerly smoked, with a 20+ pack-year smoking history, regardless of years since quitting	~14%
Prostate	Men aged 50 years and older	~37%

¹Eligible population as described in the ACS' Cancer Prevention & Early Detection Facts & Figures 2025-2026 report

²Prevalence estimates from 2023 for breast, colorectal, and prostate, 2022 for lung, and 2021 for cervical cancer screening

Many Cancers Do Not Have Screening Options



In 2026, about half of the cancers diagnosed and most cancer deaths are expected to occur in cancer types that lack guideline-recommended screening options

Benefit and Risk Considerations of Blood-Based Multi-Cancer Detection Tests



Benefit Considerations

- Screening for multiple cancer types at the same time
- Screening for cancer types without current screening options
- Potential to detect cancer at an earlier stage
- Potential for better adherence

Risk Considerations

- Delayed cancer detection if patients forgo guideline-recommended screening and/or ignore symptoms after receiving a false negative result
- Exposure to unnecessary diagnostic procedures and emotional distress after receiving a false positive result

Galleri Device Description

The Galleri test is a qualitative, next-generation sequencing (NGS)-based multi-cancer screening test that detects DNA methylation patterns on cell-free DNA (cfDNA) in plasma from individuals aged 50 years or older. The device workflow includes:

- Whole blood collection and shipment to GRAIL, Inc.
- Plasma isolation from whole blood
- cfDNA extraction from plasma
- Bisulfite conversion of extracted cfDNA
- Library preparation
- DNA sequencing
- cfDNA data analysis to detect methylation patterns

Device Output

The Galleri test has three possible classes of reportable results based on the cancer signal detected within the cfDNA sample, which are assessed by three distinct GRAIL-developed classifiers:

Classifier	Function	Output
Cancer Signal	Determines whether the sample is positive or negative for a cancer signal.	Cancer Signal Detected or No Cancer Signal Detected
Cancer Signal Origin (CSO)	If Cancer Signal Detected, predicts the likely anatomic location of the detected signal.	1 of 18 possible CSO predictions ¹
Cancer Signal Origin – Supplemental (CSO-S)	For a subset of Cancer Signal Detected results, predicts cancer biology	1 of 7 possible CSO-S outputs, if reported

¹anus, bladder/urothelial tract, breast, cervix, colon/rectum, head and neck, kidney [excluding renal pelvis], liver/bile duct, lung, melanocyte-containing tissues/skin, ovary, pancreas/gallbladder, prostate, stomach/esophagus, thyroid, uterus, bone and soft tissue, and hematopoietic and lymphoid organs

Proposed Indications for Use

The Galleri® test is a qualitative, next-generation sequencing (NGS)-based in vitro diagnostic test intended to detect cancer-specific methylation patterns in cell-free DNA isolated from peripheral whole blood. Galleri is intended for screening for the early detection of multiple types of cancer, in adults aged 50 years or older. The test is also intended for the prediction of Cancer Signal Origin in individuals with a Cancer Signal Detected test result.

A test result of Cancer Signal Detected, including a predicted Cancer Signal Origin, may indicate the presence of an invasive solid tumor or hematologic malignancy and should be followed by a diagnostic workup recommended by qualified healthcare professionals. A test result of No Cancer Signal Detected does not rule out the presence of cancer, and individuals should continue with guideline-recommended single-cancer screening tests.

This test is performed at GRAIL, Inc. Prescription only.

Key Sponsor Proposed Precautions and Limitations



- The Galleri test is not a replacement for existing recommended single-cancer screening tests or diagnostic modalities for cancer.
- A result of No Cancer Signal Detected does not rule out the presence of cancer. Individuals should continue with guideline-recommended single-cancer screenings.
- A result of Cancer Signal Detected requires diagnostic testing with a medically established procedure to confirm the presence of cancer. Galleri is a screening test and does not diagnose cancer. Galleri does not detect a signal for all cancers.

Regulatory History



- There are currently no FDA-authorized devices indicated for screening for the early detection of multiple types of cancer
- The Galleri test was granted Breakthrough Device Designation in 2018
- GRAIL has two approved Investigational Device Exemptions (IDEs) relevant to this panel discussion:
 - PATHFINDER 2 – IDE approved in September 2021
 - NHS-Galleri – IDE approved in November 2022



Non-Clinical Studies

- GRAIL has conducted non-clinical studies to evaluate the analytical performance of Galleri
- FDA has reviewed these studies, and we will not be seeking panel input on these studies during the panel meeting.



Part II: Clinical Studies

- Devices Used in Clinical Studies
- PATHFINDER 2
- NHS-Galleri

Devices Used in Clinical Studies



- Two different devices were used in the pivotal studies
- MCED-V2
 - Investigational device
 - Used to prospectively test subjects enrolled in the clinical studies
- Galleri
 - PMA device
 - Used to retrospectively test frozen plasma samples from a subset of subjects enrolled in the clinical studies

FDA seeks Panel input on specific questions related to the benefit/risk profile, performance, and labeling of Galleri.
Study objectives (e.g., safety) which can only be assessed by MCED-V2 are noted in the presentation

Subject Selection for Retrospective Testing with Galleri



Galleri performance in PATHFINDER 2 and NHS-Galleri was determined using frozen plasma samples from a subset of study participants, which included all available and valid plasma samples from the following groups:

- ALL eligible participants with MCED-V2 Cancer Signal Detected results
- ALL eligible participants who were diagnosed with cancer
- A subset of participants with MCED-V2 No Cancer Signal Detected results and no cancer diagnosis during 12 months of follow-up time
 - Sampling strata defined by age, race, ethnicity, prior cancer history, smoking status, and selected conditions that may affect cfDNA shedding or methylation
 - Analysis weights were applied to ensure Galleri performance results reflect the full eligible study populations

PATHFINDER 2



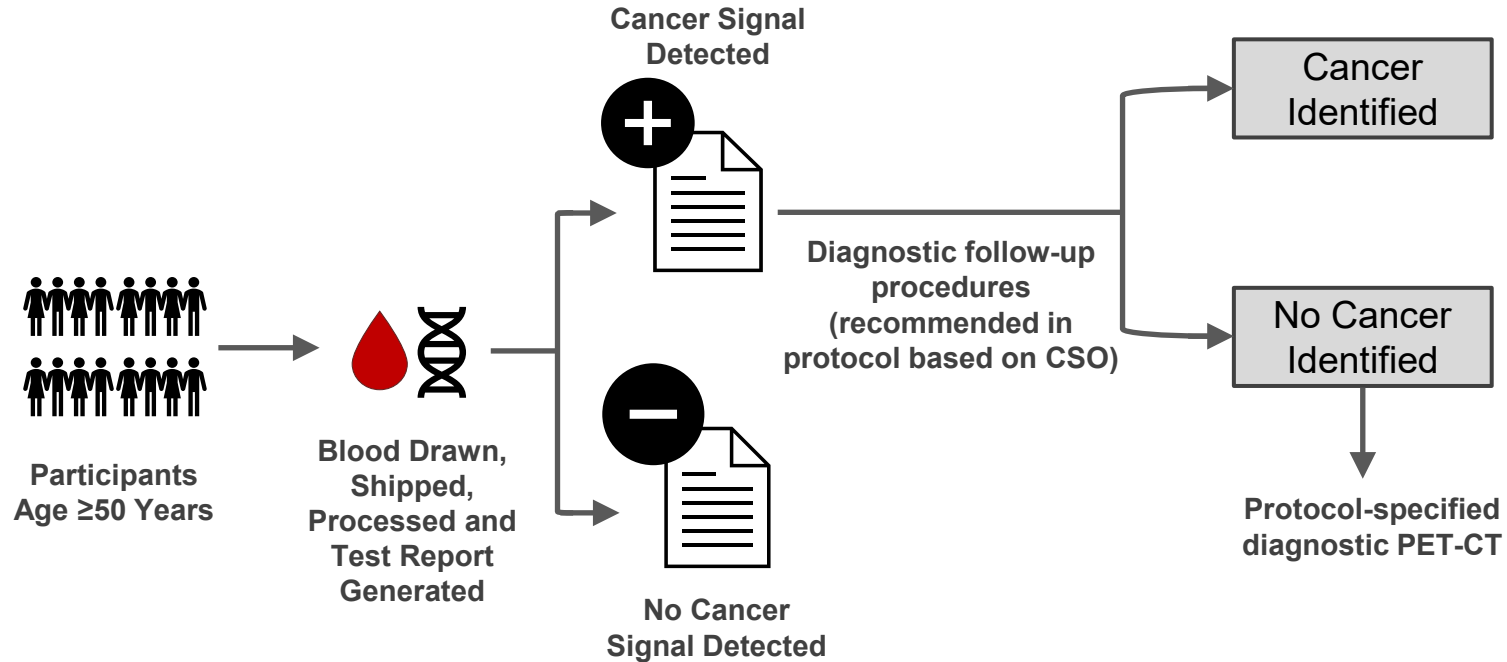
PATHFINDER 2 is a prospective, interventional multi-center study of the GRAIL MCED test in healthcare systems in North America in which participants aged 50 years or older who were not clinically suspected of having cancer were enrolled.

Primary objectives:

1. Evaluate the safety of the MCED test in terms of diagnostic testing triggered by the MCED test result
2. Evaluate performance of the MCED test in individuals eligible for cancer screening

Secondary objectives included, but were not limited to, time to diagnostic resolution, participant-reported outcomes, and evaluation of MCED test performance in selected subgroups

PATHFINDER 2 – Study Design



All participants actively followed by enrolling institutions

PATHFINDER 2 – Target Clinical Outcome



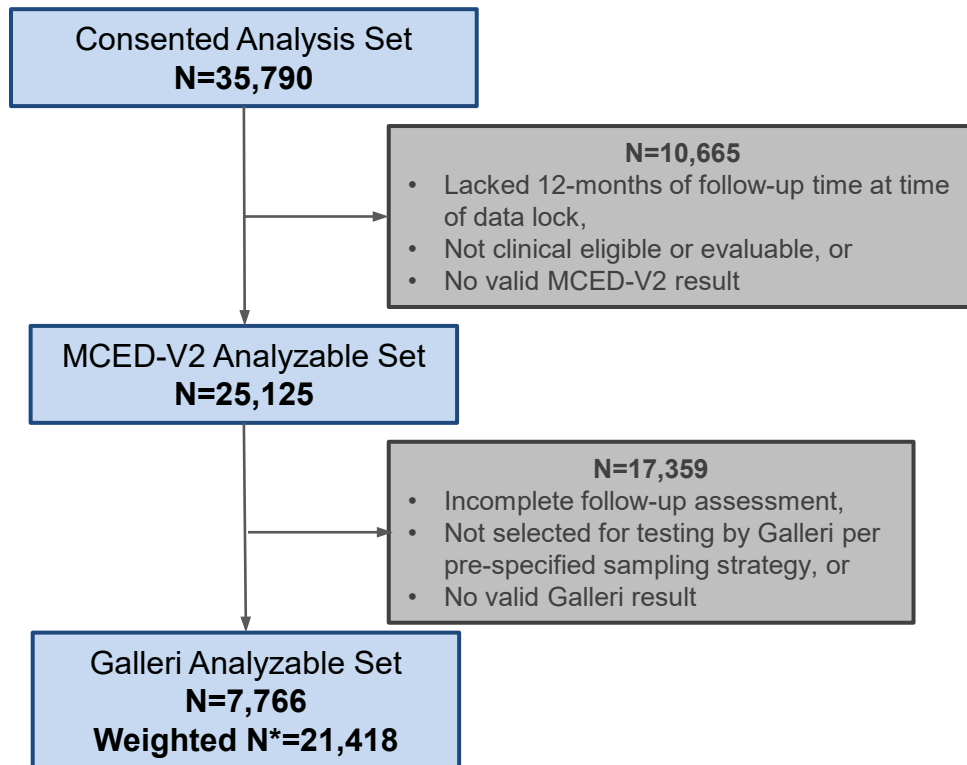
Cancer

- Pathologic confirmation of an invasive solid tumor* or hematologic malignancy, or
- Imaging confirmation in the absence of pathology, or
- Assigned clinical stage of I-IV by the treating physician, or
- Other clinical confirmation of disease per treating clinician (e.g. biochemical evidence of recurrence of prior cancer).

Non-Cancer

- Absence of the diagnosis of cancer at the time of the diagnostic resolution and at 12-months follow-up time (MCED-positive), or
- Absence of the diagnosis of cancer at the 12-month follow-up time only (MCED-negative) by review of the medical records or participant self-report through a phone call.

PATHFINDER 2 – Study Population



Characteristic	MCED-V2 Analyzable Set
Mean Age (years)	65
Female	57%
Male	43%
White only	81%
Black or African American only	8%
Asian only	6%
Hispanic or Latino	7%
Current/Former smoker	31%
Prior cancer history	10%

The demographic and clinical characteristics of the MCED-V2 Analyzable Set are highly similar to the Galleri Analyzable Set

PATHFINDER 2 – Primary Safety Analysis



FDA does not have outstanding questions for the Panel on the primary safety analysis.

The primary safety data were generated by MCED-V2 (investigational device). The primary safety objective cannot be assessed with the Galleri test (PMA device) because Galleri results were not returned to study subjects or their providers. FDA has reviewed the concordance assessment between MCED-V2 and Galleri. In the absence of direct Galleri safety data, FDA considers the primary safety analysis for PATHFINDER 2 using MCED-V2 to be an approximate estimate of the safety profile for Galleri.

PATHFINDER 2 – Primary Safety Results

Number of **MCED-V2** Analyzable Cancer Signal Detected Participants with At Least One Invasive Procedure During Diagnostic Evaluation by Cancer Status

Number of participants with at least one	MCED-V2 Cancer Signal Detected, cancer diagnosis within 12 months (N = 128)	MCED-V2 Cancer Signal Detected, no cancer diagnosis within 12 months (N = 90)	Total (N = 218)
Invasive procedure	116 (90.6%)	43 (47.8%)	159 (72.9%)
Surgical procedure	20 (15.6%)	4 (4.4%)	24 (11.0%)
Non-surgical procedure	103 (80.5%)	42 (46.7%)	145 (66.5%)
Endoscopy	47 (36.7%)	33 (36.7%)	80 (36.7%)
Biopsy	68 (53.1%)	10 (11.1%)	78 (35.8%)
Other ¹	2 (1.6%)	2 (2.2%)	4 (1.8%)
No invasive procedures	12 (9.4%)	47 (52.2%)	59 (27.1%)

¹All four (4) "other" non-surgical invasive procedures were Pap smears

PATHFINDER 2 – Primary Effectiveness Results

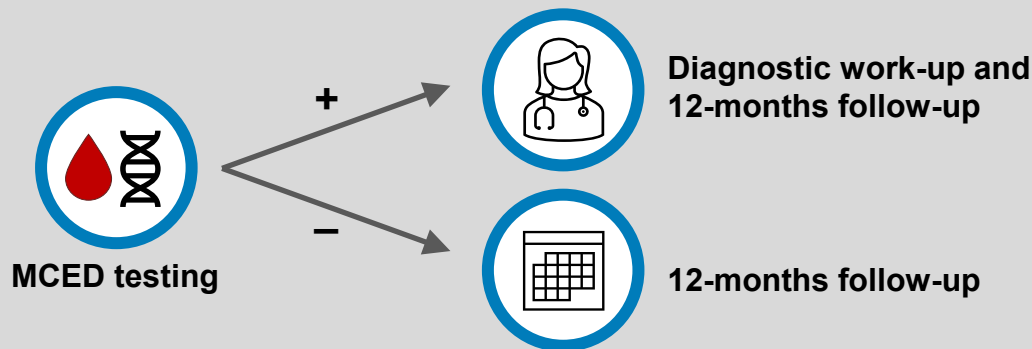


The primary effectiveness data were generated by Galleri based on retrospective testing of frozen plasma samples.

FDA seeks input from the Panel on the benefits and risks of Galleri performance for the proposed indications for use

Episode Sensitivity

The Galleri test's sensitivity is reported as "12-month episode sensitivity" – which measures the ability of Galleri to detect cancers diagnosed within 12 months of testing, not cancers present at the time of the blood draw.



True sensitivity, including stage-specific sensitivity, is unknown because cancer status at the time of testing cannot be ascertained without diagnostic work-up. The Panel should take this uncertainty into consideration during discussions of test performance.

PATHFINDER 2 – Galleri Primary Effectiveness Results



	Galleri Analyzable Set			
	Cancer diagnosis within 12M (N = 303)	No cancer diagnosis within 12 months (Weighted N* = 21115)	Total (Weighted N* = 21418)	
Galleri Cancer Signal Detected	106	32	138	PPV = 77.0% (65.8%, 85.4%)
Galleri No Cancer Signal Detected	197	21084	21281	NPV = 99.07% (98.93%, 99.20%)
	12-month Episode Sensitivity = 35.0% (29.8%, 40.5%)	Specificity = 99.85% (99.75%, 99.91%)		

*Weights were calculated for participants with no cancer diagnosis and MCED-V2 No Cancer Signal Detected group based on pre-defined sampling strata. In each stratum, analysis weights were calculated as the ratio of the number of participants eligible for Galleri sample selection to the number of participants selected and may not sum up to the marginal totals due to rounding.

PATHFINDER 2 – Galleri 12-month Episode Sensitivity for Cancers With Guideline-Recommended Screening



Cancer Type	Eligible for Screening ¹ (n/N) (95% CI)	Not Eligible for Screening (n/N) (95% CI)	Overall (n/N) (95% CI)
Colon/Rectum	50.0% (3/6) (18.8%, 81.2%)	2/2	62.5% (5/8) (30.6%, 86.3%)
Lung	0/4	61.5% (8/13) (35.5%, 82.3%)	47.1% (8/17) (26.2%, 69.0%)
Breast	23.4% (11/47) (13.6%, 37.2%)	50.0% (3/6) (18.8%, 81.2%)	26.4% (14/53) (16.4%, 39.6%)
Prostate	7.7% (3/39) (2.7%, 20.3%)	13.9% (5/36) (6.1%, 28.7%)	10.7% (8/75) (5.5%, 19.7%)
Combined	17.7% (17/96) (11.4%, 26.5%)	31.6% (18/57) (21.0%, 44.5%)	22.9% (35/153) (16.9%, 30.1%)

¹Eligibility defined per USPSTF grade A/B (breast, colon/rectum, lung) and grade C (prostate) recommendations.

No Cervical cancers were observed in PATHFINDER 2

PATHFINDER 2 – Galleri 12-month Episode Sensitivity for Cancers Without Guideline-Recommended Screening



Cancer Type	Galleri 12-Month Episode Sensitivity* (n/N) (95% CI)
Head and Neck	81.2% (13/16) (57.0%, 93.4%)
Liver, Intrahepatic Bile Duct	81.2% (13/16) (57.0%, 93.4%)
Pancreas, Extrahepatic Bile-Duct, Gallbladder	66.7% (6/9) (35.4%, 87.9%)
Lymphoid Lineage	63.0% (17/27) (44.2%, 78.5%)
Ovary or Fallopian Tubes	60.0% (3/5) (23.1%, 88.2%)
Plasma Cell Lineage	60.0% (3/5) (23.1%, 88.2%)
Bladder, Urothelial Tract	28.6% (2/7) (8.2%, 64.1%)
Kidney	18.8% (3/16) (6.6%, 43.0%)
Skin (excluding BCC/SCC)	0.0% (0/14) (0.0%, 21.5%)

Cancer Type	Galleri 12-Month Episode Sensitivity* (n/N) (95% CI)
Myeloid Lineage	0.0% (0/6) (0.0%, 39.0%)
Anus	2/4
Esophagus	1/2
Bone or Soft Tissue Sarcoma	1/4
Stomach	1/4
Uterus	1/4
Thyroid	0/4
Other ¹	71.4% (5/7) (35.9%, 91.8%)
All Combined	47.3% (71/150) (39.5%, 55.3%)

¹Other cancer types include Thymus (2), Ampulla of Vater (1), Brain and Spinal Cord (1), Unknown Primary Site (1), Small Intestine (1), Testis (1)

PATHFINDER 2 – 12-month Episode Sensitivity by Cancer Stage at Diagnosis

Galleri 12-month Episode Sensitivity By Stage for New Cancers

Participants with given cancer stage at diagnosis	12-Month Episode Sensitivity (95% CI)
Stage I	21.4% (27/126) (15.2%, 29.4%)
Stage II	33.3% (17/51) (22.0%, 47.0%)
Stage III	58.1% (18/31) (40.8%, 73.6%)
Stage IV	63.2% (24/38) (47.3%, 76.6%)
Stage I-II	24.9% (44/177) (19.1%, 31.7%)
Stage I-III	29.8% (62/208) (24.0%, 36.3%)
Stage III-IV	60.9% (42/69) (49.1%, 71.5%)
No TNM stage expected	26.7% (4/15) (10.9%, 51.9%)
Missing	0% (0/7) (0%, 35.4%)

PATHFINDER 2 – Accuracy of CSO and CSO-S Prediction



- Overall accuracy of Galleri CSO prediction for participants with true positive results based on a cancer diagnosis within 12 months of follow-up time was **94.3%** (100/106)
- The accuracy of CSO-S prediction in participants with true positive results, with assigned clinical CSO-S was **97.6%** (41/42)

NHS-Galleri



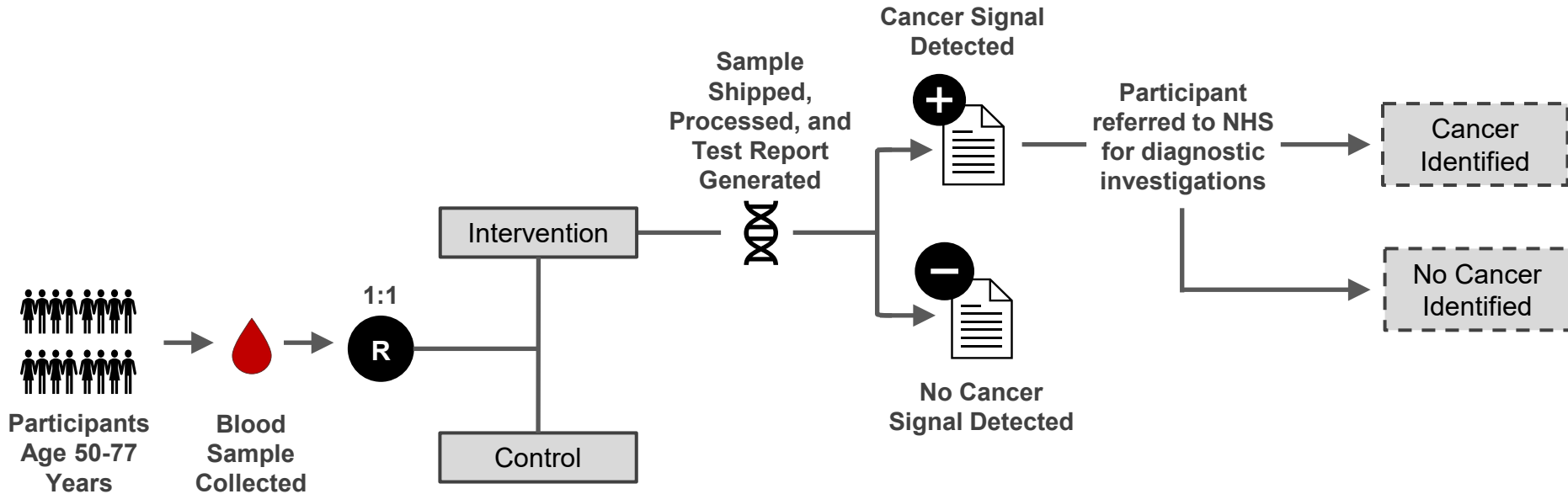
The NHS-Galleri study is a prospective, randomized controlled trial of the GRAIL MCED test in the United Kingdom (UK) in which participants aged 50-77 years who were not clinically suspected of having cancer were randomized to the intervention (MCED testing) or control (usual care) arms

Primary objective:

Evaluate the performance of the MCED test in the intervention arm in the first screening round (12 months follow-up time analysis period)

Secondary objectives included, but were not limited to, assessment of the reduction of stage IV cancers in the first screening round, participant-reported outcomes, and evaluation of MCED test performance in selected subgroups

NHS-Galleri – Study Design



Participants in both arms followed via passive linkages with NHS datasets

NHS-Galleri – Target Clinical Outcome



Cancer

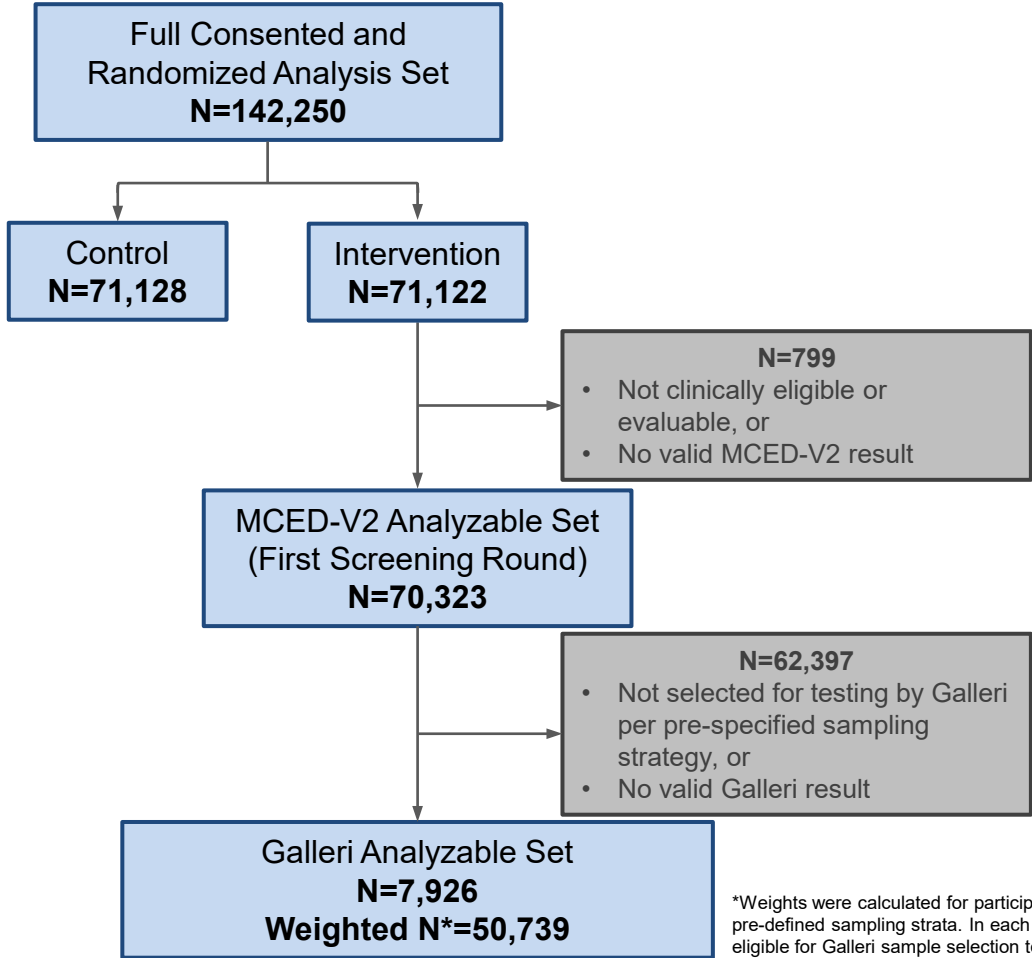
Cancer status was determined through passive follow-up via linkage to NHS datasets, including the National Cancer Registration and Analysis Service (NCRAS) database, which records all cancer diagnoses* made through the NHS in England. A participant was considered to have cancer if a qualifying cancer diagnosis was recorded in the NCRAS dataset within 12 months of their blood draw.

Non-Cancer

The clinical outcome of non-cancer was defined as absence of the diagnosis of cancer in the NCRAS dataset. A participant without cancer is defined as a participant for whom the diagnosis of cancer is absent within 12 months of follow-up.

*Recurrent cancers are not registered in NCRAS if there is sufficient evidence that the tumor represents a recurrence of a previously diagnosed cancer rather than a new primary cancer

NHS-Galleri – Study Population



Characteristic	MCED-V2 Analyzable Set
Mean Age (years)	65
Female	50%
Male	50%
White	94%
Black, African, Caribbean or Black British	1.4%
Asian or Asian British	3.3%
Current/Former smoker	45%
Prior cancer history	7%

The demographic and clinical characteristics of the MCED-V2 Analyzable Set are highly similar to the Galleri Analyzable Set

*Weights were calculated for participants with no cancer diagnosis and MCED-V2 No Cancer Signal Detected group based on pre-defined sampling strata. In each stratum, analysis weights were calculated as the ratio of the number of participants eligible for Galleri sample selection to the number of participants selected.

NHS-Galleri – Primary Effectiveness Results



The following primary effectiveness data were generated by Galleri based on retrospective testing of frozen plasma samples.

FDA seeks input from the Panel on the benefits and risks of Galleri performance for the proposed indications for use

NHS-Galleri – Primary Effectiveness Results



	Galleri Analyzable Set			
	Cancer diagnosis by 12M (N = 820)	No cancer diagnosis within 12 months (Weighted N* = 49919)	Total (Weighted N* = 50739)	
Galleri Cancer Signal Detected	259	132	391	PPV = 66.2% (56.7%, 74.6%)
Galleri No Cancer Signal Detected	561	49786	50347	NPV = 98.89% (98.78%, 98.98%)
	12-Month Episode Sensitivity = 31.6% (28.5%, 34.8%)	Specificity = 99.74% (99.61%, 99.82%)		

*Weights were calculated for participants with no cancer diagnosis and MCED-V2 No Cancer Signal Detected group based on pre-defined sampling strata. In each stratum, analysis weights were calculated as the ratio of the number of participants eligible for Galleri sample selection to the number of participants selected and may not sum up to the marginal totals due to rounding.

NHS-Galleri – Galleri 12-month Episode Sensitivity for Cancers With Guideline-Recommended Screening



Cancer Type	Eligible for Screening ¹ (n/N) (95% CI)	Not Eligible for Screening (n/N) (95% CI)	Overall (n/N) (95% CI)
Lung	63.9% (23/36) (47.6%, 77.5%)	63.6% (14/22) (43.0%, 80.3%)	63.8% (37/58) (50.9%, 74.9%)
Colon/Rectum	51.9% (40/77) (41.0%, 62.7%)	60.0% (9/15) (35.7%, 80.2%)	53.3% (49/92) (43.1%, 63.1%)
Breast	16.1% (15/93) (10.0%, 24.9%)	35.3% (6/17) (17.3%, 58.7%)	19.1% (21/110) (12.8%, 27.4%)
Prostate	11.0% (12/109) (6.4%, 18.3%)	10.4% (11/106) (5.9%, 17.6%)	10.7% (23/215) (7.2%, 15.5%)
Cervix	1/1	0/1	1/2
Combined	28.8% (91/316) (24.1%, 34.0%)	24.8% (40/161) (18.8%, 32.0%)	27.5% (131/477) (23.6%, 31.6%)

¹Eligibility defined per USPSTF grade A/B (breast, cervix, colon/rectum, lung) and grade C (prostate) recommendations.

NHS-Galleri – Galleri 12-month Episode Sensitivity for Cancers Without Guideline-Recommended Screening



Cancer Type	Galleri 12-Month Episode Sensitivity* (n/N) (95% CI)
Liver, Intrahepatic Bile Duct	80.0% (12/15) (54.8%, 93.0%)
Ovary or Fallopian Tubes	75.0% (12/16) (50.5%, 89.8%)
Esophagus	65.4% (17/26) (46.2%, 80.6%)
Stomach	57.1% (4/7) (25.0%, 84.2%)
Lymphoid Lineage	46.6% (27/58) (34.3%, 59.2%)
Head and Neck	42.9% (9/21) (24.5%, 63.5%)
Kidney	41.7% (10/24) (24.5%, 61.2%)
Pancreas, Extrahepatic Bile-Duct, Gallbladder	38.7% (12/31) (23.7%, 56.2%)
Bladder, Urothelial Tract	38.5% (5/13) (17.7%, 64.5%)
Plasma Cell Lineage	24.0% (6/25) (11.5%, 43.4%)

Cancer Type	Galleri 12-Month Episode Sensitivity* (n/N) (95% CI)
Bone or Soft Tissue Sarcoma	20.0% (1/5) (3.6%, 62.4%)
Uterus	18.5% (5/27) (8.2%, 36.7%)
Myeloid Lineage	8.3% (1/12) (1.5%, 35.4%)
Skin (excluding BCC/SCC)	3.4% (1/29) (0.6%, 17.2%)
Anus	1/3
Thyroid	0/3
Other ¹	17.9% (5/28) (7.9%, 35.6%)
All Combined	37.3% (128/343) (32.4%, 42.5%)

¹Other cancer types include Brain and Spinal Cord (N = 8), Unknown Primary Site (N = 4), Jejunum and Ileum - Neuroendocrine Tumors (N = 4), Malignant Pleural Mesothelioma (N = 4), Vulva (N = 2), Ampulla of Vater (N = 1), Eyelid Carcinoma (N = 1), Other Unspecified (N = 1), Testis (N = 1), Thymus (N = 1), Uveal Melanoma (N = 1)

NHS-Galleri – 12-month Episode Sensitivity by Cancer Stage at Diagnosis



Galleri 12-month Episode Sensitivity By Stage for New Cancers

Participants with given cancer stage at diagnosis	12-Month Episode Sensitivity (95% CI)
Stage I	13.6% (43/317) (10.2%, 17.8%)
Stage II	34.4% (54/157) (27.4%, 42.1%)
Stage III	44.3% (81/183) (37.3%, 51.5%)
Stage IV	60.0% (66/110) (50.7%, 68.7%)
Stage I-II	20.5% (97/474) (17.1%, 24.3%)
Stage I-III	27.1% (178/657) (23.8%, 30.6%)
Stage III-IV	50.2% (147/293) (44.5%, 55.9%)
No stage expected	16.0% (4/25) (6.4%, 34.6%)
Missing	39.3% (11/28) (23.6%, 57.6%)

NHS-Galleri – Accuracy of CSO and CSO-S Prediction



- Overall accuracy of Galleri CSO prediction for participants with true positive results based on a cancer diagnosis within 12 months of follow-up time was **91.9%** (238/259)
- The accuracy of CSO-S prediction in participants with true positive results, with assigned clinical CSO-S was **97.2%** (69/71)

Part III: Summary of Key Points

Overall Galleri Performance

PATHFINDER 2 & NHS-Galleri | All Cancer Types

Specificity: **99.74-99.85%**

False Positive Rate: **0.15-0.26%**

Positive Predictive Value (PPV): **~66-77%**

Positive Likelihood Ratio: **~122-233**

CSO Accuracy: **~92-94%**

12-Month Episode Sensitivity **31.6-35.0%**

False Negative Rate: **65.0-68.4%**

Negative Predictive Value: **~99%**

Negative Likelihood Ratio: **~0.65-0.69**

Key Observations:

- ~66-77% of positive Galleri results correspond to a true cancer finding
- Galleri will detect approximately 1 out of 3 cancers

Galleri Performance for Cancer Types



	12-Month Episode Sensitivity	
	PATHFINDER 2	NHS-Galleri
Per Cancer Type* (range)	<10% to >80%	
Pre-Specified Subgroup of 12 High-Mortality Cancer Types**	61.3% (95% CI: 52.4%, 69.6%)	52.1% (95% CI: 46.9%, 57.2%)
Pre-Specified Subgroup of 6 Aggressive Cancers***	60.4% (95% CI: 46.9%, 72.4%)	60.9% (95% CI: 53.0%, 68.3%)

Key Observations:

- Galleri 12-month episode sensitivity varies by cancer type
- Galleri 12-month episode sensitivity for pre-specified high-mortality cancer types and aggressive cancers is higher than overall sensitivity across all cancer types

*PATHFINDER 2 and NHS-Galleri were not powered to assess the performance of individual cancer types

**Anus, Bladder/Urothelial Tract, Colon/Rectum, Esophagus, Head and Neck, Liver/Intrahepatic Bile Duct, Lung, Lymphoid Lineage, Ovary/Fallopian Tubes, Pancreas/Extrahepatic Bile Duct/Gallbladder, Plasma Cell Lineage, and Stomach

***Esophagus, Liver/Intrahepatic Bile Duct, Lung, Ovary/Fallopian Tubes, Pancreas/Extrahepatic Bile Duct/Gallbladder, Stomach

Galleri Performance for Cancer Subgroups

For Cancer Types Without Guideline-Recommended Screening

PATHFINDER 2 12-month Episode Sensitivity 47.3% (95% CI: 39.5-55.3%)	NHS-Galleri 12-month Episode Sensitivity 37.3% (95% CI: 32.4-42.5%)
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For Cancer Types With Guideline-Recommended Screening

PATHFINDER 2 12-month Episode Sensitivity 22.9% (95% CI: 16.9-30.1%)	NHS-Galleri 12-month Episode Sensitivity 27.5% (95% CI: 23.6%-31.6%)
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Key Observations:

- Galleri detects ~37-47% of cancers for cancer types that do not have guideline-recommended screening
- Galleri detects approximately a quarter of cancers for cancer types that have guideline-recommended screening

Galleri 12-month Episode Sensitivity by Stage at Diagnosis



Participants with given cancer stage at diagnosis	12-Month Episode Sensitivity (95% CI)	
	PATHFINDER 2	NHS-Galleri
Stage I	21.4% (27/126) (15.2%, 29.4%)	13.6% (43/317) (10.2%, 17.8%)
Stage II	33.3% (17/51) (22.0%, 47.0%)	34.4% (54/157) (27.4%, 42.1%)
Stage III	58.1% (18/31) (40.8%, 73.6%)	44.3% (81/183) (37.3%, 51.5%)
Stage IV	63.2% (24/38) (47.3%, 76.6%)	60.0% (66/110) (50.7%, 68.7%)

Key Observations:

- Galleri performance increases with cancer stage
- Approximately two-thirds of Galleri-detected new cancers were diagnosed at Stages I-III
- Consider whether Galleri performance supports “early” cancer detection

Considerations for Overall Benefit-Risk Profile of Galleri



- Galleri performance:
 - Overall
 - Per cancer type
 - Per stage (overall and per cancer type)
 - For cancer types with and without guideline-recommended screening
 - For high-mortality cancer types
- Risks associated with false negative or false positive results

