Emerging Multi-Cancer Early Detection Strategies

Presented by Tomasz M. Beer, MD
Disclosures

- Consultant for AbbVie, Arvinas, Astellas Pharma, AstraZeneca, Bayer, Bristol-Myers Squib, Constellation, Grail Inc., Janssen, Myovant Sciences, Pfizer, Sanofi, Sapience Therapeutics
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Learning Objectives

• To review currently available recommended cancer screening strategies
• To compare and contrast single cancer and multiple cancer early detection strategies
• To introduce blood-based multi-cancer early detection technologies
• To review current results from multi-cancer early detection clinical trials
Overall Burden of Cancer in the US

10 leading causes of death in the US in 2020

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>No. of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>700,000</td>
</tr>
<tr>
<td>Cancer</td>
<td>600,000</td>
</tr>
<tr>
<td>COVID-19</td>
<td>500,000</td>
</tr>
<tr>
<td>Unintentional injury</td>
<td>200,000</td>
</tr>
<tr>
<td>Stroke</td>
<td>150,000</td>
</tr>
<tr>
<td>Chronic lower respiratory disease</td>
<td>100,000</td>
</tr>
<tr>
<td>Alzheimer disease</td>
<td>75,000</td>
</tr>
<tr>
<td>Diabetes</td>
<td>50,000</td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>25,000</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>15,000</td>
</tr>
</tbody>
</table>

Ahmad FB et al., MMWR Morb Mortal Wkly Rep 2021
## Current Cancer Screening Guidelines

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Screening Modality</th>
<th>Age at First Screening</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Low-dose CT</td>
<td>50 if meets high-risk criteria</td>
<td>Annually</td>
</tr>
<tr>
<td>Breast</td>
<td>Mammogram, Ultrasound, MRI</td>
<td>40-50</td>
<td>Every 1-2 years</td>
</tr>
<tr>
<td>Colorectal</td>
<td><strong>Stool-based methods</strong></td>
<td></td>
<td>1-10 years, depending on test</td>
</tr>
<tr>
<td></td>
<td>-FIT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Stool DNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-High-sensitivity guaiac-based</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>fecal occult blood test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Direct Visualization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-CT colonography</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Colonoscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Flexible sigmoidoscopy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>Pap test</td>
<td>21-25</td>
<td>3-5 years</td>
</tr>
<tr>
<td></td>
<td>HPV test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>PSA</td>
<td>50-55</td>
<td>1-4 years</td>
</tr>
</tbody>
</table>
Colorectal Cancer Mortality
Minnesota Colon Cancer Control Study: FOBT vs usual care

Relative risk screening vs. controls:
Biennial: 0.78 (95% CI: 0.96, 0.93)
Annual: 0.68 (95% CI: 0.56, 0.82)

Years since Randomization

Cumulative Colorectal-Cancer Mortality

Lung Cancer Diagnosis and Mortality

Randomized trial of low-dose CT vs chest radiography in 53,454 high-risk individuals

Prostate Cancer Mortality
ERSPC

1 PCa death averted
Per 781 men screened
Per 27 PCa detected

Rate ratio – 0.79

Schroder F, Lancet, 2014
<table>
<thead>
<tr>
<th>Cancer</th>
<th>Prevalence (%)</th>
<th>USPSTF Recommended Screening</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Compliance With Recommended Screening (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast¹</td>
<td>0.6</td>
<td>Biennial mammography, women ages 55–79</td>
<td>87</td>
<td>89</td>
<td>4.4</td>
<td>78.3</td>
</tr>
<tr>
<td>Cervical²</td>
<td>&lt;0.1</td>
<td>Triennial cytology or quinquennial cytology/HPV test, women ages 21–65</td>
<td>95</td>
<td>85.5</td>
<td>&lt;1%</td>
<td>80</td>
</tr>
<tr>
<td>Colorectal³</td>
<td>0.65</td>
<td>Decennial Colonoscopy</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>69.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Triennial Stool-based screening (Cologuard)</td>
<td>92.3</td>
<td>86.6</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Annual Stool-based screening (FIT)</td>
<td>73.8</td>
<td>94.9</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>Lung⁴</td>
<td>1.1 (high risk)</td>
<td>Annual low-dose CT for high-risk persons ages 55–80⁵</td>
<td>85</td>
<td>87</td>
<td>6.9</td>
<td>14</td>
</tr>
</tbody>
</table>

CT, computed tomography; FIT, fecal immunochemical test; HPV, human papillomavirus; USPSTF, United States Preventive Services Task Force.
Cumulative False Positive Rate From Single-Cancer Screening

Existing paradigms are associated with a high cumulative false positive rate

- Each false positive from a screening test would require follow-up tests or interventions with attendant risks
- These risks are not well understood at the population level because current paradigms only evaluate one cancer at a time
- An opportunity for a multi-cancer approach to early cancer detection

A 60-year-old female with a history of smoking screened for 4 cancers would have a 43% false positive rate (FPR)*

*Assumes eligibility for all 4 tests.

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Cancers Without Recommended Screening Tests Account for 71% of Cancer Deaths in the United States in 2020\(^1,2\)

Deaths due to cancers with recommended screening tests (prostate, breast, cervical, colorectal and lung) account for 29% of cancer deaths, while cancers without recommended screening tests account for 71% of cancer deaths in the United States in 2020.

Lethal Cancers Without Effective Screenings Are Often Diagnosed Late

Stage distribution of SEER Incidence Cases

5-year Relative Survival By Stage at Diagnosis

Survival

Stage

Pre Localized Regional Distant

Pancreas
Lung and Bronchus
Thyroid
Breast
Colon and Rectum
Ovarian

Low Prevalence of Individual Cancers Presents a Challenge to Early Detection

Ahlquist DA. *NPJ Precis Oncol*. 2018;2:23.
Integrated Multi-omic Analysis of Circulating Cancer Biomarkers Provides a Potential Avenue for Revolutionizing Early Detection of Cancer

- A range of biomarkers can be comprehensively analyzed
  - DNA (mutations, methylation)
  - Proteins
  - Extracellular Vesicles / Exosomes
  - CTCs and CTC clusters
  - RNA, tumor educated platelets, etc.
- Tissue of origin identification is possible
  - DNA methylation patterns
Promise and Applications of Circulating Tumor-derived Material

Development Of Blood-Based Cancer Early Detection Tests

- Assay development
- Test development and initial validation
  - Case control design
- Prospective studies measured against current SOC tests
  - Testing simultaneously with a standard screening procedure
  - Focus on single cancer
  - No return of results
- Prospective studies with return of results
  - Multi-cancer application
Key Clinical Studies

CancerSEEK Test:
• Evaluates the levels of 8 cancer proteins and the presence of cancer gene mutations

Galleri Test:
• Targeted methylation assay
CANCER-SEEK
Multicenter prospective trial in 10,006 women ages 65-75 women not known to have cancer to examine the feasibility and safety of CancerSEEK coupled with PET-C imaging

Feasibility of blood testing combined with PET-CT to screen for cancer and guide intervention

Anne Marie Lennon1,4,10*, Adam H. Buchanan11*, Isaac Klindel2*, Andrew Warren12,13*, Ashley Honushofsky11*, Ariella T. Cohain12, David H. Ledbetter11, Fred Sanfilippo14, Kathleen Sheridan11, Dillenia Rosica11, Christian S. Adonizio11,14, Hee Jung Hwang12, Kamel Lahouel16, Joshua D. Cohen1,2,3,6,7, Christopher Douville1,4, Aalpen A. Patel11, Leonardo N. Hagmann12, David D. Rolston11, Nilav Malani12, Shlomn Zhou1,3,4, Chetan Bettegowda1,3,6, David L. Diehl11, Bobbi Urban12, Christopher D. Still11, Lisa Kann12, Julie I. Woods11, Zachary M. Salvati11, Joseph Vadakara11, Rosemary Leeming11, Prianka Bhattacharya11, Carroll Walter13, Alex Parker12, Christoph Lengauer12,13, Allison Klein1,4,15, Cristian Tomasetti1,6,7, Elliot K. Fishman1,4,10, Ralph H. Hruban1,4,9, Kenneth W. Kinzler1,3,4, Bert Vogelstein1,2,3,4, Nickolas Papadopoulos1,3,4,9,11

Cite as: A. M. Lennon et al., Science 10.1126/science.abb9601 (2020).
Scored positive if any DNA or protein analytes were above present threshold

Scored positive if CHIP excluded and identical analyte elevated in baseline test remained abnormal

PET-CT used to provide orthogonal evidence of cancer and localize it if present

If PET-CT signals cancer, participant rereferred to specialist

12 month follow up assessments

Baseline test

Confirmation test

Imaging

Return of results & continued follow-up

Baseline test

Confirmation test

Imaging

Return of results & continued follow-up

Safety Features

➢ Participants counseled about implications of test results
➢ Continued SOC screening advised

➢ Retesting performed on equal number of individuals with negative baseline results to minimize anxiety

➢ PET-CT reviewed by radiologists

➢ Follow-up recommended by Multidisciplinary Review Committee
➢ Continued SOC Screening advised

TESTING PROCESS

DETECT-A Testing Process
DETECT-A Results

- 9911 women screened
- 490 positive on baseline test
- 127 positive on both tests
- 26 cancers detected

Stage at Diagnosis

- 30% Stage 1
- 40% Stage 2
- 20% Stage 3
- 10% Stage 4

Cancers:
- Breast
- Lung
- Kidney
- Ovary
- Colorectal
- Appendix
- Uterine
- Carcinoma of Unknown Primary
- Lymphoma
- Thyroid
DETTECT-A Results (cont.)

- 9911 women screened
- 490 positive on baseline test
- 127 positive on both tests
- 26 cancers detected
- 101 participants had imaging based on false-positive test
- 22 invasive diagnostic procedures after false-positive test
- 24 cancers detected with routine screening
- 46 cancers detected with neither approach
## Test Performance

Performance with and without confirmation test and 95% confidence intervals

<table>
<thead>
<tr>
<th></th>
<th>Blood Test Without Confirmation</th>
<th>Blood Test With Confirmation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive Predictive Value</strong></td>
<td>5.9% (4.0-8.4)</td>
<td>19.4% (13.1-27.1)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>95.3% (94.9-95.7)</td>
<td>98.9% (98.7-99.1)</td>
</tr>
<tr>
<td><strong>Negative Predictive Value</strong></td>
<td>99.3% (99.1-99.4)</td>
<td>99.3% (99.1-99.4)</td>
</tr>
<tr>
<td><strong># Needed to Screen to Detect 1 Cancer</strong></td>
<td>342 (238-510)</td>
<td>381 (260-583)</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cancers</td>
<td>30.2 (21.3-40.3)</td>
<td>27.1% (18.5-37.1)</td>
</tr>
<tr>
<td>Cancers with SOC Screening</td>
<td>27.5% (15.9-41.7)</td>
<td>23.5% (12.8-37.5)</td>
</tr>
<tr>
<td>Cancers with no SOC Screening</td>
<td>33.3% (20.0-49.0)</td>
<td>31.1% (18.2-46.6)</td>
</tr>
</tbody>
</table>
GALLERI
Methylation Biology Differentiates Cancer From Non-Cancer

Characteristics of GRAIL’s Targeted Methylation Panel

Approximately 100,000 genomic regions

<table>
<thead>
<tr>
<th>Panel Version 1.0</th>
<th>Size/Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targeted regions (Mb)</td>
<td>17.1</td>
</tr>
<tr>
<td>Probe regions covering target regions (Mb)</td>
<td>31.3</td>
</tr>
<tr>
<td>Probes (n)</td>
<td>1,121,325</td>
</tr>
<tr>
<td>Probe size (bp)</td>
<td>120 (60 bp overlap)</td>
</tr>
<tr>
<td>CpGs (n)</td>
<td>1,116,720</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of CpGs</th>
<th>Probe</th>
<th>CpGs (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypo</td>
<td>363,033</td>
<td></td>
</tr>
<tr>
<td>Hyper</td>
<td>585,181</td>
<td></td>
</tr>
<tr>
<td>Binary</td>
<td>218,506</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1,116,720</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Genomic Region</th>
<th>CpGs (n)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5 kb upstream of start codon</td>
<td>193,818</td>
<td>17</td>
</tr>
<tr>
<td>Promoter</td>
<td>278,872</td>
<td>24</td>
</tr>
<tr>
<td>Introns</td>
<td>500,996</td>
<td>43</td>
</tr>
<tr>
<td>Exons</td>
<td>292,798</td>
<td>25</td>
</tr>
<tr>
<td>Intron/Exon Boundaries</td>
<td>247,752</td>
<td>21</td>
</tr>
<tr>
<td>5’ UTR</td>
<td>134,144</td>
<td>11</td>
</tr>
<tr>
<td>Between genes</td>
<td>182,174</td>
<td>16</td>
</tr>
<tr>
<td>Not annotated</td>
<td>1,817</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

UTR, untranslated region.
Grail MCED Clinical Trials

**CCGA**¹
NCT02889978
15,254 participants
♂♀
Demonstrate feasibility of detecting cancer and predicting tissue of origin with minimal false positives

**STRIVE**
NCT03085888
99,308 participants
♀
Confirm performance in a population with no known active cancer diagnosis

**PATHFINDER**
NCT04241796
~6,200 participants
♂♀
Evaluate implementation of test in clinical practice

**SUMMIT**
NCT03934866
~25,000 participants
♂♀
Additional performance in a population with no known active cancer diagnosis and clinical utility in a high-risk population

¹Circulating Cell-Free Genome Atlas study.
Multi-Cancer Early Detection Test

Sensitivity and Specificity

### Overall sensitivity and specificity

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Non-cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test positive</td>
<td>1453</td>
<td>1254</td>
</tr>
<tr>
<td>Test negative</td>
<td>1370</td>
<td>1248</td>
</tr>
</tbody>
</table>

Sensitivity = 1453/2823
51.5% (49.6% - 53.3%)

Specificity = 1248/1254
99.5% (99.0% - 99.8%)

Two-sided 95% Wilson confidence intervals were calculated.

### Sensitivity by cancer class

![Graph showing sensitivity by cancer class]

Circulating Cell-free Genome Atlas (CCGA) Sub-Study 2

- 76.4% (71.6-80.7%) sensitivity in pre-specified† cancers (validation set)
- 54.9% (51.0-58.8%) overall sensitivity in >50 cancers (validation set)
- Single fixed false positive rate (0.7%) across all cancers

†Anus, bladder, colon/rectum, esophagus, head and neck, liver/bile-duct, lung, lymphoma, ovary, pancreas, plasma cell neoplasm, stomach.
Plot excludes unstaged cancers.
Circulating Cell-free Genome Atlas (CCGA) Sub-Study 2

Sensitivity

Clinical Stage (n)

Breast

Colon/Rectum

Esophagus

Head and Neck

Prostate

Kidney

Lung

Lymphoma

Pancreas

Uterus

0%
25%
50%
75%
100%

0%
25%
50%
75%
100%

I
143 (62)
1 (14 | 7)
1 (6 | 1)
(37 | 19)
(15 | 7)
(28 | 12)
(12 | 8)
(73 | 32)

II
110 (40)
11 (10 | 6)
5 (8 | 5)
(40 | 11)
(23 | 11)
(27 | 12)
(14 | 6)
(3 | 2)

III
27 (12)
41 (15)
17 (17)
(31 | 15)
(23 | 11)
(27 | 12)
(16 | 8)
(5 | 3)

IV
8 (4)
(15 | 7)
(19 | 8)
(21 | 8)
(12 | 8)
(14 | 6)
(16 | 8)
(3 | 1)

I
14 (7)
6 (1)
(14 | 7)
(59 | 27)

II
11 (10)
(11 | 10)
(10 | 5)
(72 | 31)

III
4 (1)
(41 | 15)
(17 | 7)
(106 | 42)

IV
4 (2)
(40 | 21)
(19 | 8)
(42 | 17)

Includes cancers with >50 samples.
Overall survival by stage

Galleri-Detected Cancers Have a Worse Prognosis than not Detected Cancers

Xiaoji Chen et al. Clin Cancer Res 2021;27:4221-4229
Key Performance Features of
Galleri Test

Demonstrated in CCGA Case Control Study

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancers detected</td>
<td>&gt; 50</td>
<td>&gt; 50 cancers, including unscreened cancers</td>
</tr>
<tr>
<td>Positive predictive value (modeled)</td>
<td>43%</td>
<td>Anorectal, Bladder/urothelial, Esophageal, Gastric, Head and neck, Liver/bile-duct, Lymphoid neoplasm², Melanoma, Myeloid neoplasm, Ovarian, Pancreas/gallbladder, Plasma cell neoplasm, Renal, Sarcoma, Seminoma, Skin, Testicular, Thyroid, Uterine, Vaginal, Vulva</td>
</tr>
<tr>
<td>False-positive rate</td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity stages I-III for all cancer</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity stages I-III for prespecified cancers representing ⅔ of cancer mortality in US</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Rate tissue of origin predicted correctly¹</td>
<td>93%</td>
<td></td>
</tr>
</tbody>
</table>

¹Based on tissue of origin class assigned in 96% of cases where cancer was detected.
²Lymphoid neoplasm includes lymphoma and leukemia. Leukemia includes chronic lymphocytic leukemia and hairy cell leukemia.
*USPSTF A, B, or C rating.

CCGA, Circulating Cell-free Genome Atlas.
The Pathfinder Study: Assessment of A Multi-Cancer Early Detection Test In Clinical Practice

Prospective, multicenter, interventional, return-of-results study (NCT04241796)

**Study Objectives**

**Primary**
- Assess extent of diagnostic testing required to achieve diagnostic resolution following a “signal detected” test result

**Secondary**
- Evaluate test performance
- Assess participant-reported outcomes and perceptions of the MCED test

**Study Design**

- Adults ≥50 years enrolled from 7 US sites into 2 cohorts: with and without additional risk
- MCED test ordered
- Participant Questionnaire
- Blood drawn and shipped
- Test report generated

- **Signal Detected**
  - Test result communicated
  - Provider determines follow-up
  - Diagnostic Resolution:
    - Cancer or no cancer
  - Cancer Status: Assessed at 12 months

- **Signal Not Detected**
  - Test result reported
  - Participant continues recommended screening
  - Cancer Status: Assessed at 12 months

---

*a*Also collected at other timepoints during the study.

*b*Defined as date when study team determines to end diagnostic evaluation triggered by a “signal detected” test result.

MCED, multi-cancer early detection.
Grail Pathfinder Study: Overall Study Accrual

![Bar chart showing PATHFINDER Total Study Enrollment]

- OHSU: 1743
- SUTTER: 1563
- MAYO: 1027
- CLEVELAND_CLINIC: 902
- DFCI: 500
- INTERMOUNTAIN: 446
- USOR: 400
Interim Primary Outcome: Extent of Diagnostic Testing

Most participants with diagnostic resolution had at least 1 imaging test (57/63; 90%)
More true positives (21/27; 78%) than false positives (9/36; 25%) had at least 1 invasive procedure
Most invasive procedures were minimally invasive (88%)

*2 participants with 'signal detected' MCED test result (true positives) were excluded from the diagnostic workup analysis because diagnostic testing was initiated before MCED test results were returned.
As of March 2021, 30 participants had ≥1 invasive procedure (26 minimally invasive, 2 surgical, 2 both).
Interim Secondary Outcome: Test Performance

<table>
<thead>
<tr>
<th></th>
<th>With Additional Risk</th>
<th>Without Additional Risk</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cancer Signal Detection, No.</strong></td>
<td>n=3695</td>
<td>n=2934</td>
<td>N=6629</td>
</tr>
<tr>
<td>Detected, No. (%)</td>
<td>56 (1.5)</td>
<td>36 (1.2)</td>
<td>92 (1.4)</td>
</tr>
<tr>
<td>True Positive</td>
<td>20 (0.5)</td>
<td>9 (0.3)</td>
<td>29 (0.4)</td>
</tr>
<tr>
<td>False Positive</td>
<td>15 (0.4)</td>
<td>21 (0.7)</td>
<td>36 (0.5)</td>
</tr>
<tr>
<td>No Current Diagnostic Resolution</td>
<td>21 (0.6)</td>
<td>6 (0.2)</td>
<td>27 (0.4)</td>
</tr>
<tr>
<td>Not Detected</td>
<td>3639 (98.5)</td>
<td>2898 (98.8)</td>
<td>6537 (98.6)</td>
</tr>
<tr>
<td><strong>PPV for Cancer Signal Detection, No.</strong></td>
<td>n=35</td>
<td>n=30</td>
<td>n=65</td>
</tr>
<tr>
<td>% (95% CI)</td>
<td>57.1 (40.9–72.0)</td>
<td>30.0 (16.7–47.9)</td>
<td>44.6 (33.2–56.7)</td>
</tr>
<tr>
<td><strong>CSO Prediction Accuracy</strong></td>
<td>n=19(^a)</td>
<td>n=8(^a)</td>
<td>n=27(^a)</td>
</tr>
<tr>
<td>First CSO, % (95% CI)</td>
<td>84.2 (62.4–94.5)</td>
<td>87.5 (52.9–99.4)</td>
<td>85.2 (67.5–94.1)</td>
</tr>
<tr>
<td>First/Second CSO</td>
<td>100 (83.2–100.0)</td>
<td>87.5 (52.9–99.4)</td>
<td>96.3 (81.7–99.8)</td>
</tr>
</tbody>
</table>

Cancer signal was detected in 1.4% of all analyzable participants
Nearly half with diagnostic resolution had confirmed cancer, for an estimated 45% PPV
Cancer signal origin was predicted with high accuracy

Data as of March 2021. CSO, cancer signal origin; PPV, positive predictive value. \(^a\)Excludes 1 participant with unknown cancer type and 1 with indeterminate CSO from the true positive set.
# Cancer Characteristics of True Positive Set (n=28)

<table>
<thead>
<tr>
<th>Cancer Type Diagnosed</th>
<th>Clinical AJCC Stage of New Cancers</th>
<th>Recurrent Cancers</th>
<th>First Predicted Cancer Signal Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>III</td>
</tr>
<tr>
<td>Colon or rectum</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Head and Neck</td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Liver, bile duct</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoid leukemia</td>
<td></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Ovary, peritoneum/FT</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma cell neoplasm</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waldenstrom macroglobulinemia</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Breast cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

AJCC, the American Joint Committee on Cancer version 8; CSO, cancer signal origin; FT, fallopian tube; GI, gastrointestinal; NA, not applicable; pt, participant; SIV, stage IV; unk, unknown.
## CEDAR Clinical Trials

<table>
<thead>
<tr>
<th>Status at CEDAR</th>
<th>Disease Location</th>
<th>Study</th>
<th>Population</th>
<th>Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled 1743</td>
<td>Multi</td>
<td>GRAIL Pathfinder</td>
<td>Age&gt;50, Cohort A: elevated risk (smoking, hx of CA, genetic markers); Cohort B: non-elevated risk</td>
<td>Prospective Interventional with return of results</td>
</tr>
<tr>
<td>Enrolling 500+</td>
<td>Multi</td>
<td>GRAIL Pathfinder II</td>
<td>Age&gt;50, new diversity goals</td>
<td>Prospective Interventional with return of results</td>
</tr>
<tr>
<td>Enrolled 5</td>
<td>UNK</td>
<td>GRAIL Galleri-EAP</td>
<td>CA with unknown tissue of origin For compassionate use in late stage treatment</td>
<td>Pilot Interventional with return of results</td>
</tr>
<tr>
<td>Enrolling 229</td>
<td>Colorectal</td>
<td>Freenome PREEMPT</td>
<td>Age 45-85, colonoscopy as SOC</td>
<td>Prospective observational</td>
</tr>
<tr>
<td>Enrolling 117</td>
<td>Multi</td>
<td>Freenome Danube</td>
<td>Age 45-85, dx of IBD, or untreated CA, or no CA</td>
<td>Case Control</td>
</tr>
<tr>
<td>Pending</td>
<td>Lung</td>
<td>Delfi Lung</td>
<td>Age &gt;50, 20 pk/day history</td>
<td>Prospective observational</td>
</tr>
<tr>
<td>Pending</td>
<td>Multi</td>
<td>Exact</td>
<td>Age&gt;50, untreated cancer or control group</td>
<td>Prospective observational</td>
</tr>
</tbody>
</table>
The Pathfinder 2 Study

- Multicenter Early Detection Blood Test
- Compared to Pathfinder 1:
  - Refined test
  - Recruitment goal of 20,000 over 18 months
    - 3,600 at OHSU
  - Diverse study population
- Population:
  - Age 50 or older
  - Did not participate in Pathfinder 1
  - No suspicion of cancer, or any cancer since 2018
Community Preparation
Community stakeholders identified and data collected

Workgroup Formed
Review the data with a community perspective

Process Development
Create a cultural landscape summary of the region
Customize the submission process & forms

Local Advisory Council
Takes over full implementation of the process
Reviews proposals
Approves, suggests changes, or declines projects

Community owns it!

OHSU Community Engagement team walks alongside the community
Rural Oregonians in Coos County take part in the Region Research Assessment System and implement the PATHFINDER2 interventional trial as a subsite with OHSU.

Knight Cancer Advisory Council representatives from the Portland Black community, trusted leaders, help spread the word about the trial which will benefit members of their community.
Partnerships: a result of years of relationship building (PATHFINDER2 subsites)
What Partnership May Look Like

• Subsite Contributes
  • Regional relationships and expertise for recruitment
  • Local blood draws and diagnostic work-up for signal positives (1%)
  • Medical Co-Investigator

Communities need to retain their patients, but might not have research capacity

OHSU has institutional recognition for Early Detection but lacks a diverse patient population

• OHSU Contributes
  • Pharma relationships
  • Contracting, IRB oversite, regulatory compliance
  • Participant enrollment and follow-up for signal negatives (99%)
  • Marketing
Pathfinder 2 Participation

• More OHSU Employee Early Detection Days to come

• Contact us to participate and for more information!
  – Email: PATHFINDER@ohsu.edu
  – Phone: (503) 418-8150
Thank you.

The CEDAR Clinical Trials Team