Performance of a Multi-Cancer Detection Test as a Tool for Diagnostic Resolution of Symptomatic Gynecological Cancers

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Disclosure

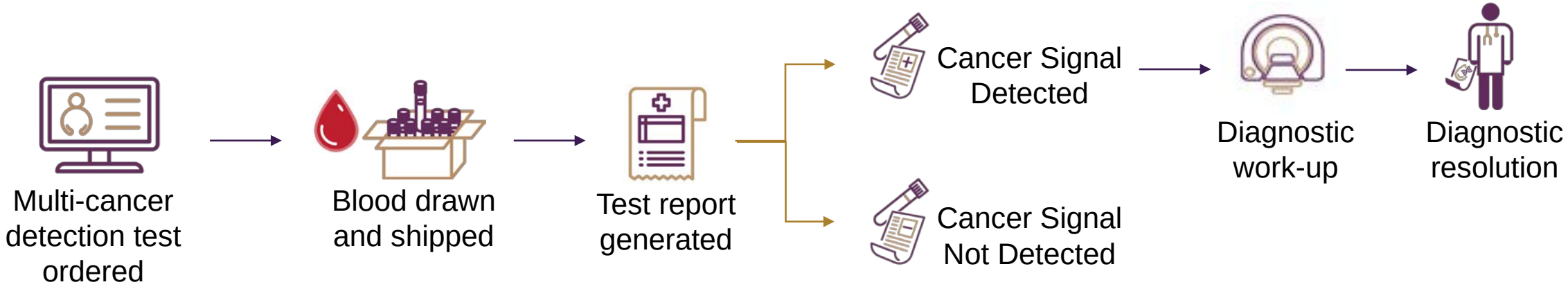
- Uncompensated Consultant: GRAIL, LLC, a subsidiary of Illumina, Inc.
- The Mayo Clinic was compensated for Dr. Liu’s institutional responsibilities for the Circulating Cell-free Genome Atlas (CCGA) study protocol oversight and advisory board activities for GRAIL, LLC, a subsidiary of Illumina, Inc.

Objective

- To assess the performance of a multi-cancer detection test for detection of symptomatic gynecological cancers

Multi-Cancer Detection Test

Blood-based test using cell-free DNA



Multi-Cancer Detection Tests can:

- Detect the presence of cancer signals in blood
- Predict the anatomic cancer signal origin
- Potentially be used for diagnostic resolution of symptomatic cancers

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The Circulating Cell-Free Genome Atlas Study (CCGA Study; NCT02889978)

Prospective, multicenter, case-control, observational study

Study Goals

Develop and validate a blood-based multi-cancer detection test analyzing plasma cell-free DNA (cfDNA) to detect cancer signals across multiple cancer types & simultaneously predict the signal origin

Study Design

15,254 participants with/without cancer
(142 sites)

Blood samples
all participants

Tissue samples
cancer only

Follow-up for 5 years
(vital status, cancer status)

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CCGA: Divided Into 3 Pre-Specified Substudies

Discovery[1,2]	Assay Refinement and Classifier Development[3]	Further Assay Refinement and Clinical Validation[4]
Whole Genome Methylation (identified as method for further development)	**Targeted Methylation** (identified key informative methylation regions; training and validation of a machine-learning classifier)	**Further refined for use** as screening tool **Clinical validation** supporting product launch

[1]Klein E, et al. *J Clin Oncol*. 2018;36(15) suppl. DOI: 10.1200/JCO.2018.36.15_suppl.12021. [2]Razavi P, et al. Poster presented at: American Society for Clinical Oncology 2017 Annual Meeting; June 2-7, 2017; Chicago, IL. Abstract 11526. [3]Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. DOI: 10.1016/j.annonc.2020.02.011. [4]Klein E, et al. *Ann Oncol*. 2021;32(9):1167-1177. DOI: https://doi.org/10.1016/j.annonc.2021.05.806.

Study Participants

CCGA Substudy 2
Validation Analyzable Set
N=1308 (Cancer n=703; Non-cancer n=605)

↓

Applicable Population for Current Analysis
Clinically Presenting Cancer n=518
Non-cancer[a] n=398

↓

Population with Gynecological Cancers
n=60
(cervix, ovary, uterus, vagina, vulva)

[a]Non-cancer status confirmed at Year 1 follow-up

The Multi-Cancer Detection Test Performed with High Specificity

Participant Group	Cancer Signal Not Detected/ Total (n/N)	Specificity (95% CI)
Non-cancer participants[a]	396/398	99.5% (98.2-99.9%)
Non-cancer participants with non-malignant confounding conditions at enrollment[b]	15/16	93.8% (71.7-99.7%)

False Positive Rate: **0.5%**

[a] Cancer status confirmed at 1 year follow-up
[b] Includes endometriosis
CI, confidence interval.

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Sensitivity of the Multi-Cancer Detection Test Varied by Cancer and Clinical Stage

Cancer	Sensitivity in Participants with Clinically Presenting Cancer (95%-CI; Cancer Signal Detected/Total [n/N])				
	Stage I	Stage II	Stage III	Stage IV	All Stages
All Clinically Presenting Cancer[a]	27.0% (20.0%, 35.5%; 33/122)	58.8% (49.1%, 67.9%; 60/102)	85.1% (77.7%, 90.4%; 103/121)	92.5% (87.1%, 95.8%; 136/147)	66.4% (62.2%, 70.3%; 344/518)
Cervix	33.3% (1.7-79.2%; 1/3)	-	100.0% (5.1-100.0%; 1/1)	-	50.0% (15.0-85.0%; 2/4)
Ovary	0.0% (0.0-94.9%; 0/1)	0.0% (0.0-94.9%; 0/1)	83.3% (55.2-95.3%; 10/12)	66.7% (20.8-98.3%; 2/3)	70.6% (46.9-86.7%; 12/17)
Uterus	15.6% (6.9-31.8%; 5/32)	-	100.0% (43.9-100.0%; 3/3)	100.0% (5.1-100.0%; 1/1)	25.0% (13.8-41.1%; 9/36)
Vagina	-	-	100.0% (5.1-100.0%; 1/1)	-	100.0% (5.1-100.0%; 1/1)
Vulva	-	-	50.0% (2.6-97.4%; 1/2)	-	50.0% (2.6-97.4%; 1/2)

[a]Excludes those with multiple or unknown primaries, or “other” cancers
CI, confidence interval.

Accuracy of Cancer Signal Origin Prediction was High

Cancer	Cancer Signal Origin Prediction Accuracy[a] (95% CI; Correct Signal Origin Detected/Total [n/N])
All Clinically Presenting Cancer[b]	91.7% (88.3-94.3%; 300/327)
Cervix	100.0% (34.2-100.0%; 2/2)
Ovary	100% (75.8-100.0%; 12/12)
Uterus	88.9% (56.5-99.4%; 8/9)
Vagina	100% (5.1-100%; 1/1)
Vulva	0% (0.0-94.9%; 0/1)

[a]Data are reported for true positive cases.
[b]Excludes those with multiple or unknown primaries, or “other” cancers
CI, confidence interval.

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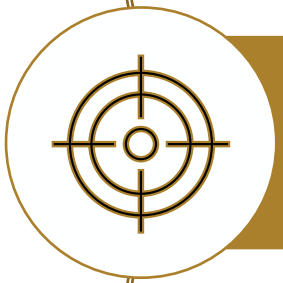
Conclusions

In this subgroup analysis from the pre-specified, second CCGA sub-study:

The multi-cancer detection test performed with:

-High specificity

-High accuracy for cancer signal origin prediction



Sensitivity of the test varied depending on the cancer and clinical stage

-Subgroups had limited sample size

Findings support the potential use of this multi-cancer detection test for diagnostic resolution of symptomatic gynecological cancers

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Study participants and their families

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