Cell-free Tumor DNA Test in Early Lung Cancer Detection

HTA55

Maiyani M[1,2], White L[1], Powers D[1], Quintana L[1], Nichols L[1], Dollar B[1], Bedoy R[1], Elias Martinez A[1], Raymond V[3], Lefterova M[3], & Feigelson H[1]

[1]Institute for Health Research, Kaiser Permanente Colorado, Aurora, CO.
[2]University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, [3]Guardant Health, Palo Alto, California

Background and Objective

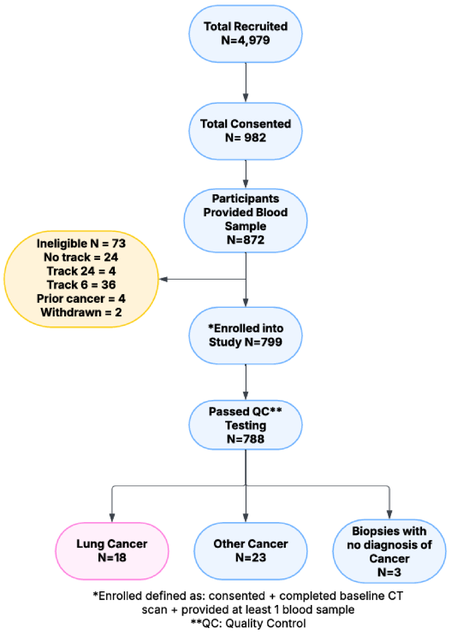
- USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults 50-80 years with 20 pack-year smoking history or current/former smoking in the past 15 years
- Unfortunately, LDCT screening rates across the US are low
  - 6.5% of those eligible have been screened
  - Screening is especially low among medically under-resourced groups
- Circulating tumor DNA (ctDNA) has been recognized as a potentially valuable analyte in identifying high-risk lung nodules using noninvasive blood collection ("liquid biopsy")
- This prospective study evaluated whether we could detect lung cancer at the time of LDCT screening from ctDNA using Guardant Health's LUNAR-2 assay

Methods

- Kaiser Permanente Colorado (KPCO) members aged ≥ 35 years with upcoming LDCT screenings were invited via email/phone
- Enrollment was limited to patients with Lung-RADS (Reporting and Data System, version 1.0)
  - categories 1-3 (Follow-up 12-month intervals)
  - category 4 (suspicious, follow-up 3-month intervals)
- Members with lung nodules >30mm, hematologic malignancies, invasive cancers within 5 years, pregnancy, or cognitive impairment were excluded
- After consent, Guardant Health LUNAR-2 research test kits were mailed with instructions
- Blood samples were collected on the LDCT visit day or within 14 days, but samples collected within 30 days were acceptable
- We collected survey and EHR data on smoking history, LDCT screening history, and other factors at (1) baseline and (2) at follow-up
- Participants were followed up to two years

Results

Figure 2. Flow diagram



*Enrolled defined as: consented + completed baseline CT scan + provided at least 1 blood sample
**QC: Quality Control

Table 1. Participant characteristics

	Cancer Free (n=747)	Lung Cancer (n=18)	Other Cancer (n=23)	Overall (n=788)	p-value*
	N (Column%)	N (Column%)	N (Column%)	N (Column%)	
Age					0.02
Mean (SD)	67.9 (7.5)	71.8 (6.3)	72 (5.6)	68.1 (7.5)	
Sex					0.95
Female	421 (56.4)	10 (55.6)	10 (43.5)	441 (56)	
Male	326 (43.6)	8 (44.4)	13 (56.5)	347 (44)	
Race/ethnicity					0.74
Black	20 (2.7)	0	1 (4.3)	21 (2.7)	
Hispanic	41 (5.5)	1 (5.6)	0	42 (5.3)	
Non-Hispanic White	658 (88.1)	17 (94.4)	21 (91.3)	696 (88.3)	
Other	28 (3.7)	0	1 (4.3)	29 (3.7)	
Personal history of cancer					<.0001
Yes	76 (10.2)	8 (44.4)	5 (21.7)	89 (11.3)	
No	656 (87.8)	9 (50)	18 (78.3)	683 (86.7)	
Unknown	15 (2)	1 (5.6)	0	16 (2)	
Smoking status					0.87
Current Smoker	289 (38.7)	8 (44.4)	5 (21.7)	302 (38.3)	
Former Smoker	402 (53.8)	9 (50)	15 (65.2)	426 (54.1)	
Never Smoker	56 (7.5)	1 (5.6)	3 (13)	60 (7.6)	
Smoking pack years					0.07
Mean (SD)	43.2 (25.4)	57.4 (35.6)	48.1 (22.8)	43.7 (25.7)	
Charlson comorbidity score					0.08
Mean (SD)	1.5 (1.6)	2.1 (1.7)	2.9 (2.2)	1.5 (1.7)	
Lung cancer screening prior to consent date					0.02
Yes	587 (78.6)	10 (55.6)	12 (52.2)	609 (77.3)	
No	160 (21.4)	8 (44.4)	11 (47.8)	179 (22.7)	

*P-values from Chi-square tests for categorical variables, Wilcoxon tests for age and pack years

Figure 1. Guardant Health's LUNAR Assay

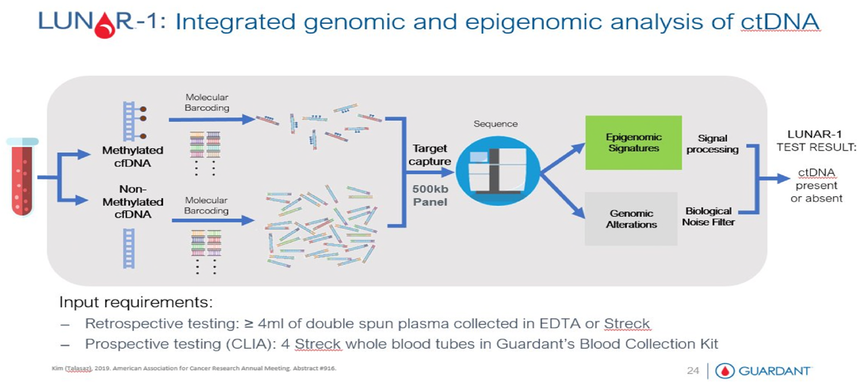
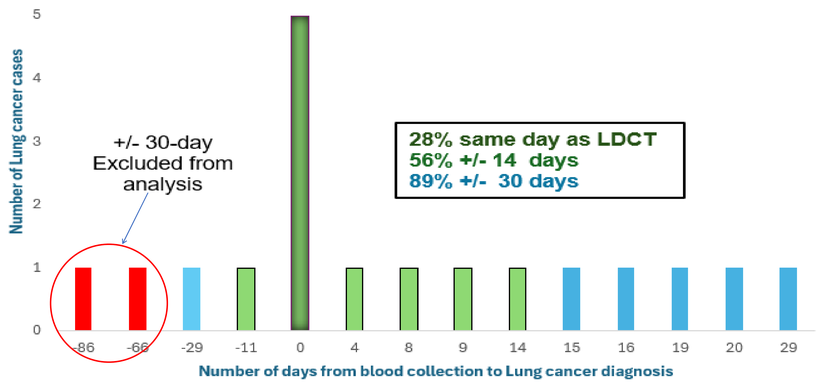


Figure 3. Timing of blood collection to diagnosis of lung cancer



Results

- The study initiated in September 2020 with 982 individuals consented and 872 blood samples collected
- Participants were on average 68 years old, 56% female, 54% former smokers, and 88% had no personal history of cancer
- About 65% of cancer cases were diagnosed within 20 days of blood sample collection
- A total of 18 lung cancer cases and 23 other cancer cases were diagnosed
- Data analysis is ongoing and expected to be completed mid-2025

Conclusion

- This study will demonstrate sensitivity and specificity of the LUNAR-2 assay to detect lung cancer relative to standard of care diagnostic work-up in high-risk populations
- We will also evaluate whether factors such as comorbidities, or pack year history affect assay accuracy
- The impact of this research can inform blood-based early detection of lung cancer

Limitations

- Remote Outreach: Due to the COVID-19 pandemic, test kits had to be mailed to participants compared to in-clinic recruitment, which impacted the blood collection window and whether the participant could complete the blood draw on the same day as their LDCT scan

Contact:

For additional information please contact:
Mahesh Maiyani, Data Specialist / PhD Student:
Mahesh.Maiyani@kp.org
Mahesh.Maiyani@cuanschutz.edu

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