Amplicon-based liquid biopsy prospectively detects more tissue-confirmed guideline-recommended biomarkers in lung cancer

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BACKGROUND

- Tissue genotyping is the gold standard in biomarker testing for treatment selection in non-squamous non-small cell lung cancer (NSCLC).
- Tissue genotyping fails in 15-40%[1] of patients due to insufficient or unavailable tissue for biopsy.
- In NSCLC, these actionable (G9) bio-markers include specific somatic alterations in EGFR, ALK, ROS1, RET, BRAF V600E, MET, KRAS G12C, ERBB2/HER2 and NTRK1/2/3.
- LiquidHALLMARK® is an amplicon-based next-generation sequencing (NGS) liquid biopsy assay, intended to detect alterations in 80 genes, including 10 fusions in plasma.

METHODS

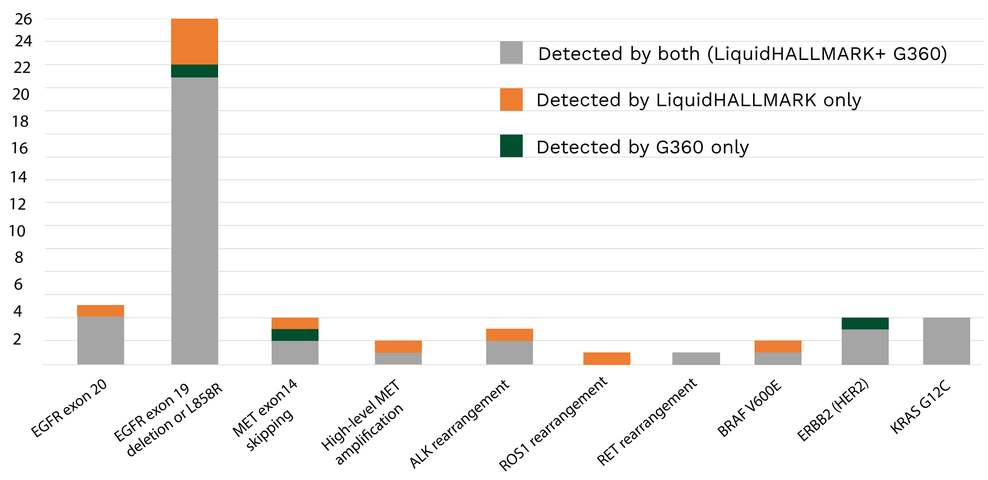
- LIQUIK (LIQUId Biopsy for Detection of Actionable Genomic BiomarKers in Patients with Advanced Non-small Cell Lung Cancer; NCT04703153) is a prospective multi-center international study comparing different liquid biopsies with conventional tissue genotyping. 200 treatment-naïve metastatic non-squamous NSCLC subjects were planned for enrollment from 11 USA and Singapore sites.
  - Primary endpoints include non-inferiority of LiquidHALLMARK(Lucence, Palo Alto; Singapore) compared with tissue genotyping in G9 biomarker detection; and a comparison of LiquidHALLMARK with Guardant360 (Guardant Health, Palo Alto), a hybrid-capture-based NGS test, for patients with tissue-confirmed G9 biomarkers.
- This is an interim analysis of the first 120 patients enrolled.

RESULTS

Table 1: Baseline characteristics of the n=120 patient population

Characteristics	All Persons (n = 120)
Median Age (Average) - Years	67 (64.84%)
Gender	
Male - No. (%)	70 (58.33%)
Female - No. (%)	50 (41.67%)
NSCLC Subtype	
Adenocarcinoma - No. (%)	114 (95.00%)
Mixed Tumor - No. (%)	1 (0.83%)
Large Cell - No. (%)	1 (0.83%)
Unclassified - No. (%)	4 (3.33%)
Tissue Availability	
Tissue Available - No. (%)	102 (85.00%)
Tissue Unavailable - No. (%)	18 (15.00%)

Graph 1. Comparison between LiquidHALLMARK and Guardant360 (G360) for G9 detection in patients with at least one tissue-positive G9 biomarker



- **Of the 65 tissue-positive patients, LiquidHALLMARK detected at least one guideline-recommended biomarker in 72.3% (47/65) patients while Guardant360 detected at least one guideline-recommended biomarker in 66.2% (43/65) patients.**
- Of the 55 patients presenting as tissue-negative or with insufficient tissue, LiquidHALLMARK and Guardant both detected 23.6% (13/55) G9 biomarkers.
- Overall concordance between LiquidHALLMARK and Guardant360 is **92.1-100%.**

Table 2. Concordance of LiquidHALLMARK with tissue biopsy for G9 detection where both tissue and LiquidHALLMARK reports are available, n=101 (19 patients had Tissue QNS/incomplete)

		Tissue Positive	Tissue Negative	Total	Concordance
EGFR exon 19 deletion or L858R mutation	ctDNA Positive	26	2	28	93.1 %
	ctDNA Negative	5	68	73	
	Total	31	70	101	
EGFR exon 20 mutation	ctDNA Positive	5	0	5	99.0%
	ctDNA Negative	1	95	96	
	Total	6	95	101*	
MET exon 14 skipping mutation	ctDNA Positive	2	1	3	96.0%
	ctDNA Negative	3	95	98	
	Total	5	96	101	
High-level *MET* amplification	ctDNA Positive	2	0	2	99.0%
	ctDNA Negative	1	98	99	
	Total	3	98	101	
ALK rearrangement	ctDNA Positive	3	2	5	96.0%
	ctDNA Negative	2	94	96	
	Total	5	96	101	
ROS1 rearrangement	ctDNA Positive	1	0	1	97.0 %
	ctDNA Negative	3	97	100	
	Total	4	97	101	
RET rearrangement	ctDNA Positive	1	0	1	100.0 %
	ctDNA Negative	0	100	100	
	Total	1	100	101	
BRAF V600E mutations	ctDNA Positive	1	1	2	98.0 %
	ctDNA Negative	1	98	99	
	Total	2	99	101	
ERBB2/HER2 mutations	ctDNA Positive	3	0	3	98.0 %
	ctDNA Negative	2	96	98	
	Total	5	96	101	
KRAS G12C mutations	ctDNA Positive	4	1	5	99.0 %
	ctDNA Negative	0	96	96	
	Total	4	97	101	

- A G9 biomarker was identified in **65 patients (54.2%) by tissue genotyping vs 60 patients (50.0%)** identified by ctDNA analysis using LiquidHALLMARK.
- Individual concordance between LiquidHALLMARK and Tissue Genotyping is **93.1-100%**.

CONCLUSION

- LIQUIK-01 prospectively demonstrates that liquid biopsy is useful for identifying guideline-recommended biomarkers in metastatic non-squamous NSCLC.
- For this 120 patient interim analysis, guideline-recommended G9 biomarkers were detected by LiquidHALLMARK in 72.3% (47/65) tissue-confirmed patients, and by Guardant360 in 66.2% (43/65) tissue-confirmed patients.

ACKNOWLEDGMENT

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