# Amplicon-Based Liquid Biopsy Platform Complements Tissue Genotyping in Detection of Guideline-Recommended Biomarkers in Metastatic NSCLC

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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

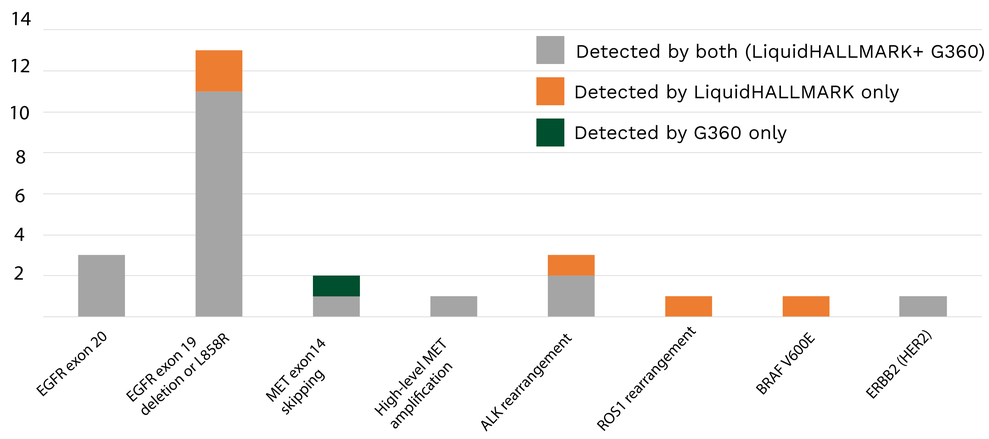
- LIQUIK-01 (LIQUId Biopsy for Detection of Actionable Genomic BiomarKers in Patients with Advanced Non-small Cell Lung Cancer; NCT04703153) is a prospective multicenter study in 200 treatment-naïve, newly diagnosed, histologically or cytologically confirmed metastatic non-squamous NSCLC subjects enrolled from 11 US and Singapore-based centers from April 2021. The following are the primary endpoints:
  - Non-inferiority of LiquidHALLMARK ctDNA testing (Lucence, Palo Alto, CA; Singapore) in comparison with tissue biopsy in the detection of G9 biomarkers.
  - Comparison of LiquidHALLMARK ctDNA testing with Guardant360 (Guardant, Redwood City, CA), a hybrid-capture-based NGS test, for patients who had at least one G9 biomarker detected by tissue-genotyping performed at a CAP-accredited clinical laboratory.
- This is an interim analysis of the first 60 patients enrolled, with complete data entry.

## RESULTS

***Table 1. Characteristics of the patients (n=60) at baseline***

| Characteristics | All Persons (n = 60) |
|---|---|
| *Median Age (Average) - Years* | 65 (64.1) |
| *Gender* | |
| Male - No. (%) | 33 (55.0) |
| Female - No. (%) | 27 (45.0) |
| *Lung Cancer Subtype* | |
| Adenocarcinoma - No. (%) | 55 (91.7) |
| Mixed Tumor - No. (%) | 1 (1.67) |
| Unclassified - No. (%) | 4 (6.67) |
| *Tissue Availability* | |
| Tissue Available - No. (%) | 56 (93.3) |
| Tissue Unavailable - No. (%) | 4 (6.67) |

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




- **Of the 33/60 patients with tissue-positive G9 biomarkers, LiquidHALLMARK detected at least one G9 biomarker in 24 patients (72.7%), and Guardant360 detected at least one G9 biomarker in 21 patients (63.6%).**
- Of the 27/60 patients presenting as tissue-negative or with insufficient tissue, LiquidHALLMARK detected 5 G9 biomarkers (5/27 = 18.5%), and Guardant360 detected 6 G9 biomarkers (6/27 = 22.2%).
- Overall concordance between LiquidHALLMARK and Guardant360 is **93.5-100%.**

***Table 2. Concordance of LiquidHALLMARK with tissue biopsy for G9 detection***

| | | Tissue Positive | Tissue Negative | Total | Concordance |
|---|---|---|---|---|---|
| *EGFR* exon 19 deletion or L858R mutation | ctDNA Positive | 14 | 1 | 15 | 94.5 % |
| | ctDNA Negative | 2 | 38 | 40 | |
| | **Total** | 16 | 39 | 55 | |
| *EGFR* exon 20 mutation | ctDNA Positive | 3 | 0 | 3 | 100 % |
| | ctDNA Negative | 0 | 52 | 52 | |
| | **Total** | 3 | 52 | 55 | |
| *MET* exon 14 skipping | ctDNA Positive | 1 | 0 | 1 | 96.4 % |
| | ctDNA Negative | 2 | 52 | 54 | |
| | **Total** | 3 | 52 | 55 | |
| High-level MET amplification | ctDNA Positive | 1 | 0 | 1 | 100 % |
| | ctDNA Negative | 0 | 54 | 54 | |
| | **Total** | 1 | 54 | 55 | |
| *ALK rearrangement* | ctDNA Positive | 3 | 2 | 5 | 94.5% |
| | ctDNA Negative | 1 | 49 | 50 | |
| | **Total** | 4 | 51 | 55 | |
| *ROS1 rearrangement* | ctDNA Positive | 1 | 0 | 1 | 95.2 % |
| | ctDNA Negative | 3 | 51 | 54 | |
| | **Total** | 4 | 51 | 55 | |
| BRAF V600E mutation | ctDNA Positive | 0 | 1 | 1 | 96.4 % |
| | ctDNA Negative | 1 | 53 | 54 | |
| | **Total** | 1 | 54 | 55 | |
| *ERBB2/HER2 mutations* | ctDNA Positive | 1 | 0 | 1 | 100 % |
| | ctDNA Negative | 0 | 54 | 54 | |
| | **Total** | 1 | 54 | 55 | |

- A G9 biomarker was identified in 33 patients (55%) by tissue genotyping vs **29 patients** (48.3%) **identified by ctDNA analysis using LiquidHALLMARK.**
- Individual concordance between LiquidHALLMARK and Tissue Genotyping is **94.5-100%.**

## CONCLUSION

- LIQUIK-01 prospectively demonstrates that liquid biopsy is useful for identifying guideline-recommended biomarkers in metastatic non-squamous NSCLC.
- For this 60 patient interim analysis, guideline-recommended biomarkers were detected by LiquidHALLMARK in 24 / 33 (72.7%) tissue-confirmed patients, and by Guardant360 in 21 / 33 (63.6%) tissue-confirmed patients.

## ACKNOWLEDGEMENT

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## REFERENCES

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