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INTRODUCTION

Identifying actionable driver mutations is crucial for managing advanced non-small cell lung cancer (NSCLC), but tissue availability for next-generation sequencing (NGS) is often limited. We investigated whether routinely available serum tumor markers (STM) could help to identify patients who are more likely to harbor actionable genomic alterations (AGA) prior to biopsy.

METHODS

Design:

A total of 155 patients with stage IIIB/IV NSCLC were included (102 adenocarcinoma, 30 squamous cell carcinoma, 23 non-specified). Pre-treatment CEA, CA15-3, CYFRA 21-1, and CA125 levels were quantitatively analyzed on a COBAS e801 multiparametric analyzer using an electrochemiluminescent assay (ECLIA), and correlated with genomic alteration status (EGFR=27, ALK=6, KRASG12C=6, BRAFv600=4, MET=3, ERBB2=3 and ROS1=2).

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The clear association between elevated CEA/CA15-3 levels and the presence of actionable mutations presents a substantial operational advantage.
- By predicting the likelihood of actionable mutations prior to biopsy, clinicians are guided to proactively secure adequate and high-quality tissue samples specifically earmarked for NGS from the very outset.
- This data-driven workflow avoids frustrating delays, reduces the need for re-biopsy, and accelerates the initiation of the most appropriate precision therapy.

Future Direction for Research

- While these initial predictive thresholds (CEA >10 / CA15-3 >60) exhibit high sensitivity and negative predictive value, subsequent research is essential. Future efforts must focus on validating this model across larger, independent multi-center cohorts to standardize pre-biopsy testing protocols on a global scale.

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Google Gemini (Imagen 3, 2026) was used to generate the illustrative conceptual images. Claude (Anthropic, Sonnet 4.6, August 2026) was used to format the reference list, generate QR codes, and assist with poster layout and English-language editing. No AI tools were used in the data analysis, clinical interpretation, or drafting of the scientific conclusions.

RESULTS

AGA were found in 51 patients (32.9%). Patients with mutations tended to have higher levels of CEA and CA15-3 compared to non-mutated cases, while differences in other markers were less consistent. Table 1 shows the medians concentrations of tumor markers according to AGA. A model using CEA >10 ng/mL and/or CA15-3 >60 U/mL shows 94.1% sensitivity, 36.2% specificity, 92.7% negative predictive value and 41.7% positive predictive value for detecting AGA (OR 9.07; 95% CI 2.65–31.1). Among the 41 patients with results below these thresholds, only three had mutations. Figure 1 illustrates the proposed diagnostic workflow.

94.1%

Sensitivity

92.7%

Negative predictive value

9.07

Odds ratio (95% CI 2.65–31.1)

3 / 51

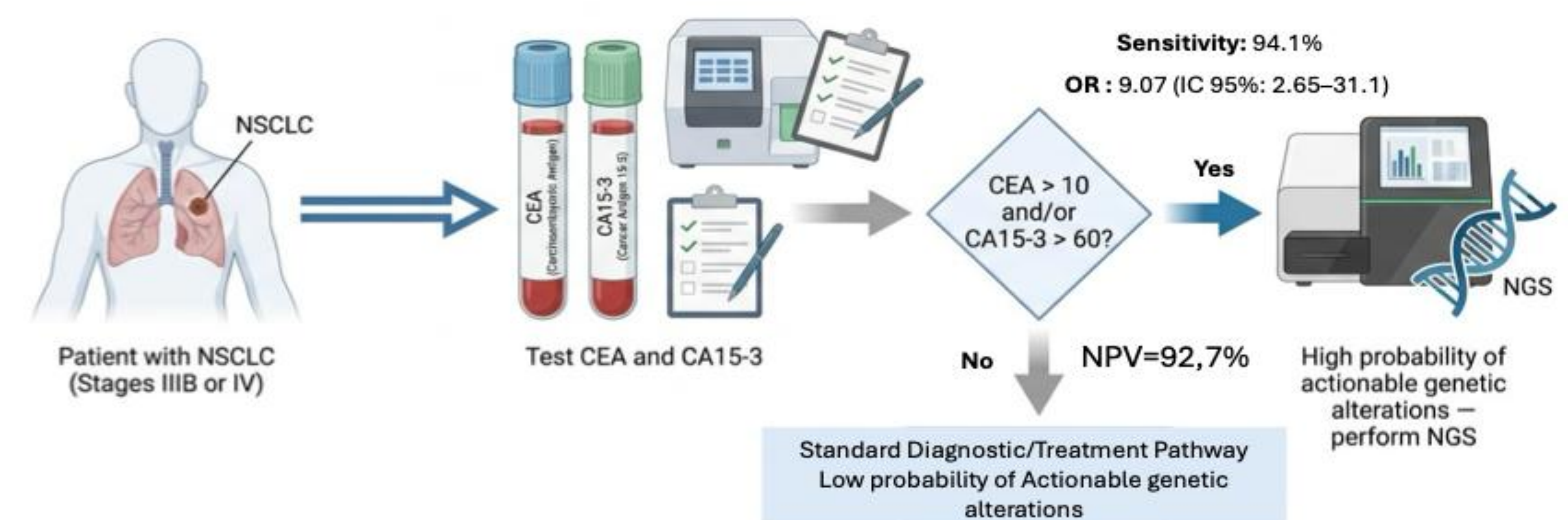
AGA missed below thresholds

Table 1 Medians of tumor markers according to AGA

	CEA (ng/mL)	CA15-3 (U/mL)	CA125 (U/mL)	CYFRA21-1 (ng/mL)
EGFR	226.0	32.7	149.0	12.0
ALK	75.0	81.0	82.0	2.6
KRASG12C	72.5	90.1	73.0	5.1
BRAFV600	21.5	25.4	40.0	9.0
MET	82.3	90.1	237.0	8.9
ERBB2	11.1	81.0	124.0	13.2
ROS1	22.4	55.1	148.6	16.1
Non-mutated	16.4	24.8	54.4	9.1

Figure 1

NSCLC Rapid Diagnostic Workflow for Identifying Actionable Genetic Alterations



CEA: Carcinoembryonic Antigen | CA15-3: Cancer Antigen 15-3