

Low serum tumor marker profile and tissue genomic rescue after plasma NMD in stage IV lung adenocarcinoma

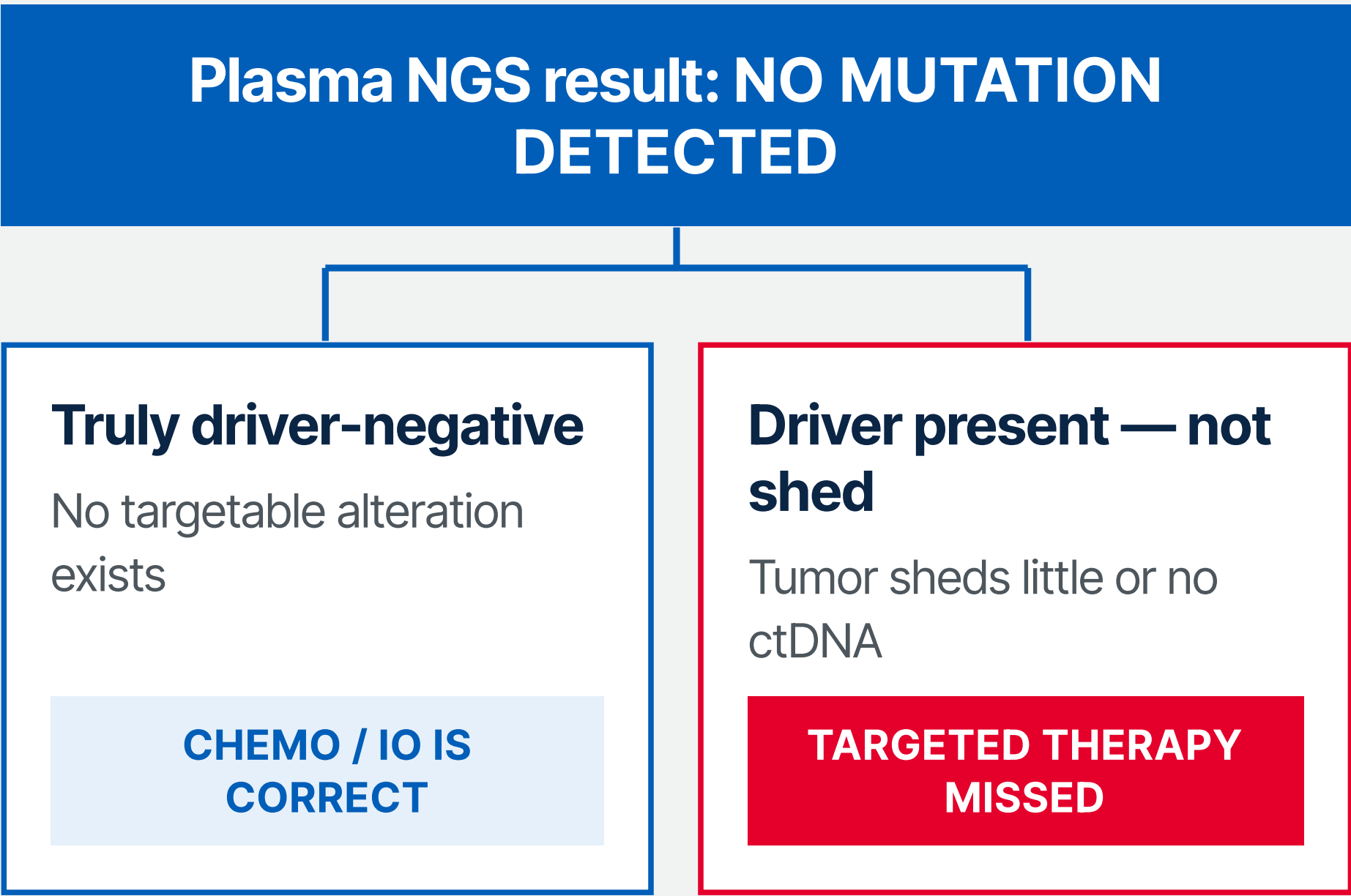
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INTRODUCTION

- Plasma NGS is standard of care for identifying targetable drivers in stage IV lung adenocarcinoma.
- No mutation is detected (NMD) in 13–14%** of plasma NGS reports in advanced NSCLC.^{1,2}
- NMD is **ambiguous**: it may mean no driver exists — or that a driver is present in a tumor not shedding ctDNA. Only the second is a missed targeted therapy.

ONE RESULT, TWO VERY DIFFERENT MEANINGS



The plasma report alone cannot tell these apart — both return the same result.

HYPOTHESIS

Can routine serum tumor markers — **CEA, CA-125 and CA19-9**, already measured in most patients — identify plasma-NMD patients in whom tissue genotyping still recovers an actionable driver?

METHODS

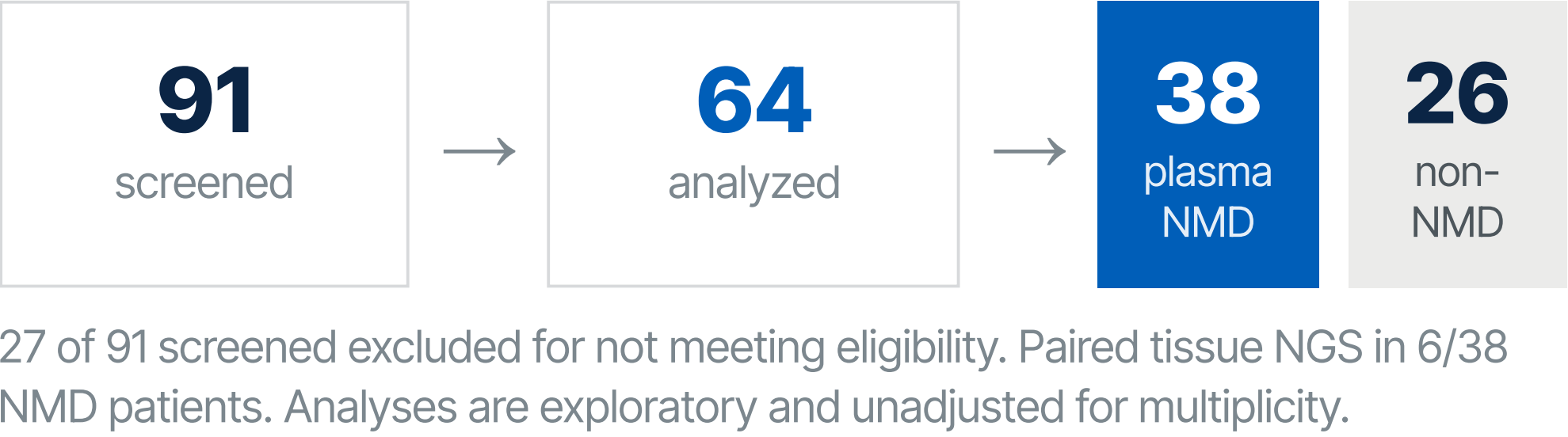
Design	Retrospective · 3 medical centers, Taiwan · Oct 2019 – Apr 2026
Eligibility	Pathologically confirmed stage IV lung adenocarcinoma; plasma NGS; CEA, CA-125 and CA19-9 all within ±35 d of plasma draw
Cohort	64 of 91 screened → plasma NMD n=38 · non-NMD n=26
Plasma NGS	Guardant360 v2.11 · 74 genes · SNV / indel / CNV / fusion reportable
Tissue NGS	Guardant360 TissueNext v1.0 · 84 genes · at physician discretion in 6/38 NMD (15.8%); median 21.5 d after plasma
Tumor markers	Abbott Alinity i · ULN CEA 5 ng/mL · CA-125 35 U/mL · CA19-9 37 U/mL
Statistics	Mann–Whitney U · Fisher exact · Cochran–Armitage trend · multivariable logistic regression (adjusted for extrathoracic metastases) · Clopper–Pearson exact CI

KEY DEFINITIONS

NMD — no somatic alteration reported on plasma NGS, excluding synonymous variants, VUS and CHIP-filtered calls.

Targetable — OncoKB level I; counted as recovered only if absent from the plasma report and not known from prior testing.

COHORT FLOW

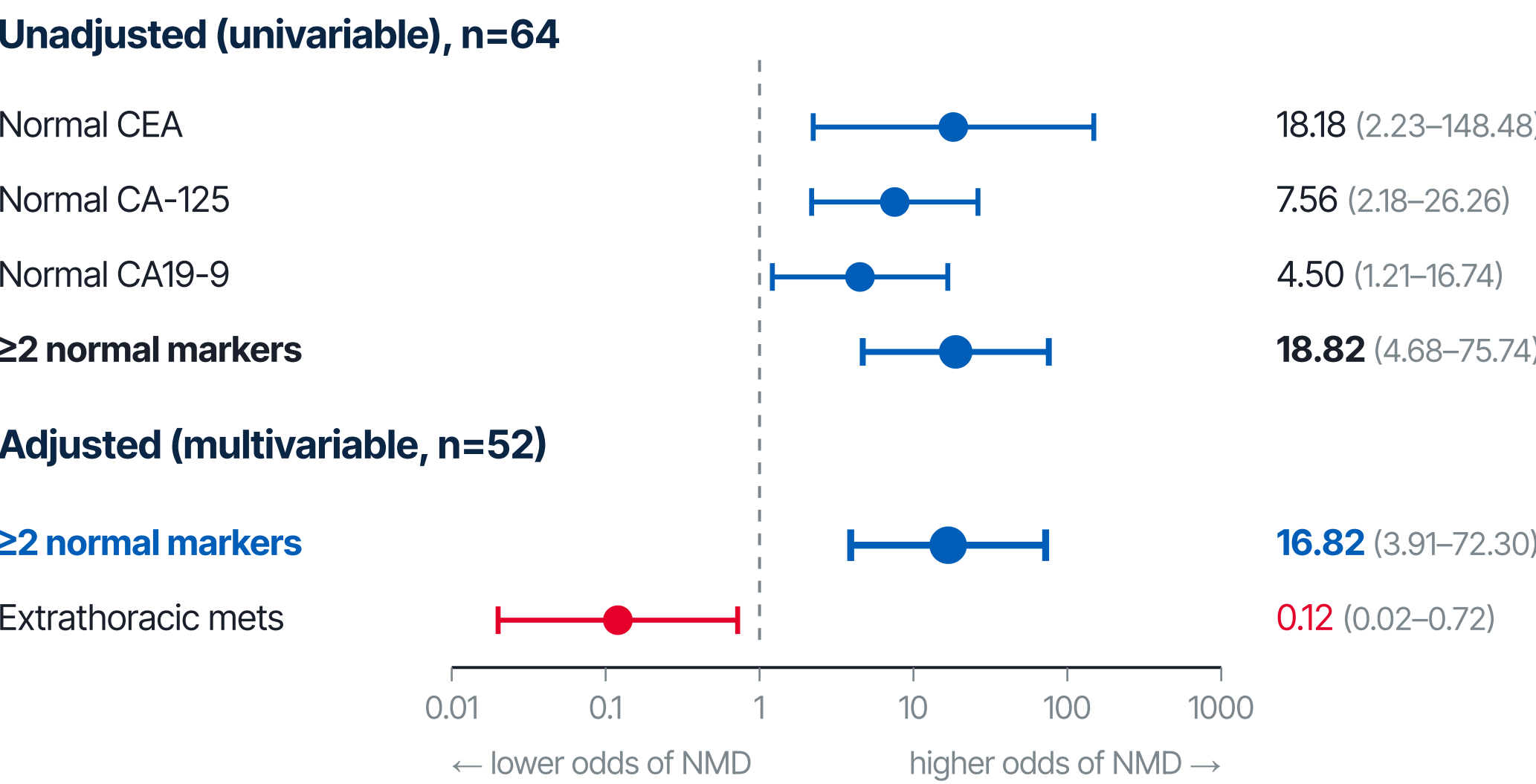


RESULTS — COHORT & ASSOCIATIONS

	Plasma NMD n=38	Non-NMD n=26	P
Age, median (range)	59 (41–89)	64 (50–92)	—
Female, n (%)	24 (63.2)	17 (65.4)	1.00
Never-smoker, n (%)	34 (89.5)	23 (88.5)	—
Extrathoracic mets (M1b/c)	58%	92%	0.009
On treatment at draw, n (%)	7 (18.4)	0 (0)	0.017
On EGFR TKI at draw, n (%)	21 (55.3)	13 (50.0)	—

Groups differed markedly in metastatic extent; the multivariable model adjusts for this.

ODDS OF PLASMA NMD — ODDS RATIO (95% CI)



Having **≥2 normal tumor markers** stayed strongly associated with plasma NMD after adjustment — adjusted **OR 16.82** (95% CI 3.91–72.30; P<0.001).

Unadjusted ORs from 2×2 tables (Woolf 95% CIs, Fisher exact P); adjusted OR from multivariable logistic regression, complete-case n=52. The inverse association for extrathoracic metastases is expected — more extensive disease sheds more ctDNA. OR was not estimable for “all 3 normal” (0 events in non-NMD; Fisher exact P=0.017).

TISSUE RESCUE & CONCLUSIONS

4/6

plasma-NMD patients biopsied had a **targetable driver recovered** in tissue — **66.7%** (95% CI 22.3–95.7). All four were EGFR alterations; none seen in plasma.

PT	TISSUE FINDING	ONCOKB	THERAPY AT DRAW
1	EGFR exon 19 del	I	Naïve
2	EGFR exon 19 del	I	Progression
3	EGFR L747P	I	Progression
4	EGFR L858R + ERBB2 amp	I	Progression
5	STK11, KEAP1	—	Naïve
6	TP53 G244D	—	Naïve

All biopsies were thoracic lesions. Lower bound: 4/38 (10.5%) of all plasma-NMD patients. Tissue NGS was discretionary in 6/38 (15.8%).

9 of 10 patients with ≥2 normal markers had a plasma-NMD result — versus ~1 in 3 with fewer — a stepwise rise from 0 to 3 markers (P for trend <0.001).

CONCLUSIONS

- Markers track shedding, not driver status.**
- Plasma NMD is not a driver-negative result.**
- It changes how a report is read, not who is biopsied** — the profile flags the group worth biopsying, not the individual.

TAKE-AWAY

Normal tumor markers after a plasma-NMD result flag a tumor that isn't shedding — not one without a driver. Read NMD in that light and consider tissue genotyping.

NEXT STEP

Prospective cohort measuring quantitative ctDNA shedding alongside tumor markers, with tissue genotyping in all plasma-NMD patients.

LIMITATIONS, REFERENCES & ACKNOWLEDGEMENTS

Selected tissue subgroup (6/38); groups imbalanced in disease extent (adjusted analysis complete-case, n=52); residual treatment effect (7/38 NMD on therapy at draw).

¹Clin Cancer Res 2018;24:3528. ²Curr Oncol 2022;29:174.

Disclosures: The presenting author declares no conflict of interest. Co-authors H-Y.J. and N.S. are employees of Guardant Health AMEA.

AI USE DISCLOSURE

Claude 4.8 Opus (Anthropic) was used to refine the poster text and generate the conceptual diagrams. No primary data or experimental results were altered or simulated using artificial intelligence.