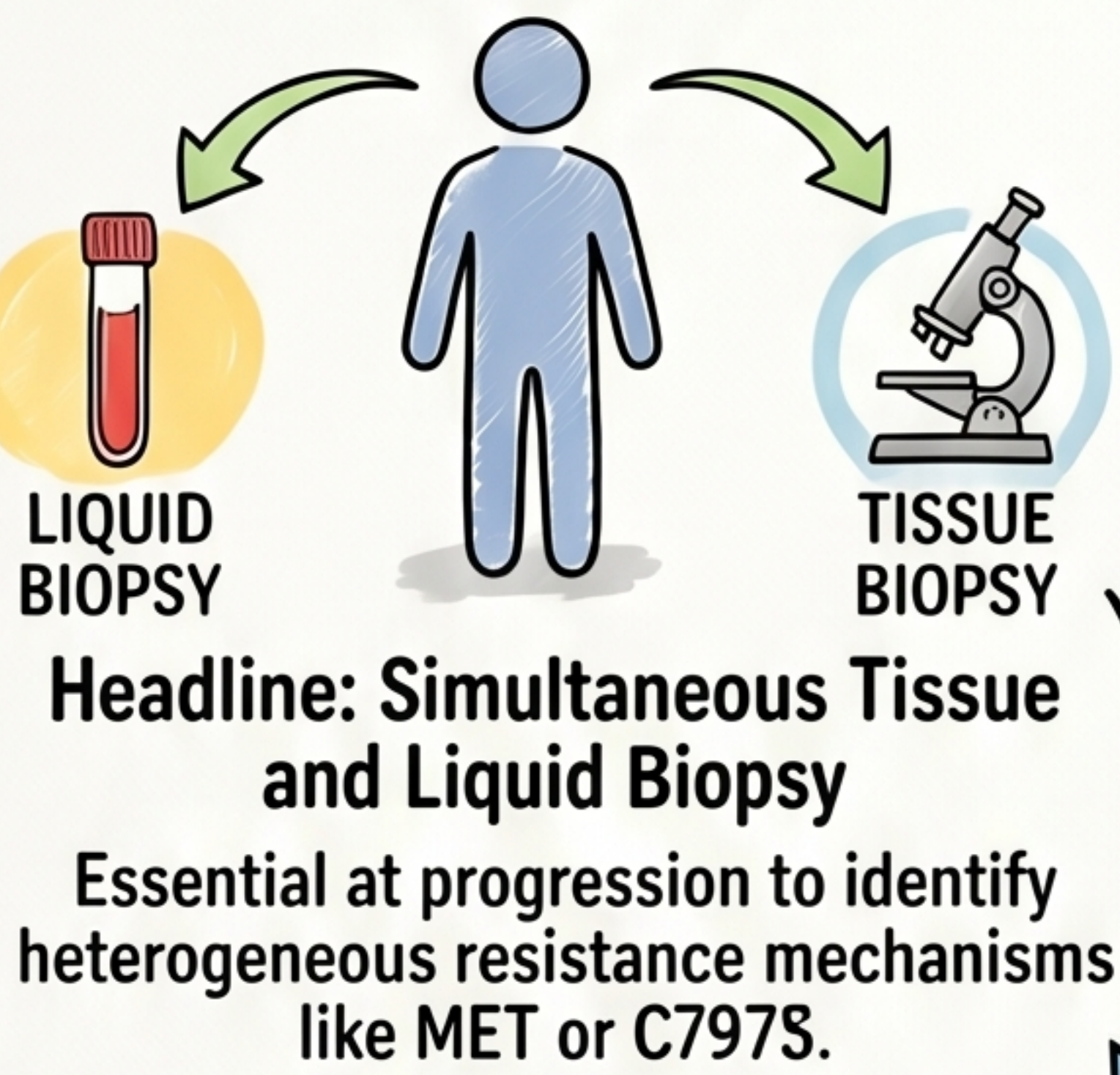


Navigating NSCLC Resistance: Precision Sequencing Beyond Progression

CONTEXT SUMMARY: 2026 & Beyond

Managing resistance post-1st line. Shift to **MANDATORY RE-BIOPSY & NEW THERAPIES** (ADCs, Bispecifics) redefining standard of care.

POST-OSIMERTINIB: THE MANDATORY RE-BIOPSY



RESISTANCE MECHANISMS (Approx. Frequency)

Resistance Mechanism	Frequency	Potential Action/Therapy
MET Amplification	15–20%	MET inhibitors (Savolitinib)
EGFR C797S Mutation	15–20%	Novel EGFR inhibitors (BLU-701)
SCLC Transformation	5–14%	Platinum-Etoposide

KEY FINDING

Headline: 5–14% Small Cell Transformation

Requires a shift to platinum-etoposide; missing this is a consequential error.

STATISTIC

33%

Headline: 33% ORR for Amivantamab + Chemo

MARIPOSA-2 established this combination as a superior active regimen post-osimertinib progression.

POST-IO/CHEMO: THE DRIVER-NEGATIVE PATIENT

PREFERRED



STANDARD



Headline: Dato-DXd vs. Docetaxel

TROPION-Lung01 shows Dato-DXd as a preferred, more tolerable backbone than traditional docetaxel.

KEY FINDING

Headline: Ivonescimab: The New PD-L1 Standard?

This PD-1/VEGF bispecific showed a striking 11.1-month PFS in PD-L1-high patients.

SUPPORTING FACT

Headline: Molecular Profiling Beyond Diagnosis

Status of STK11 and KEAP1 should guide treatment choice even in second-line settings.