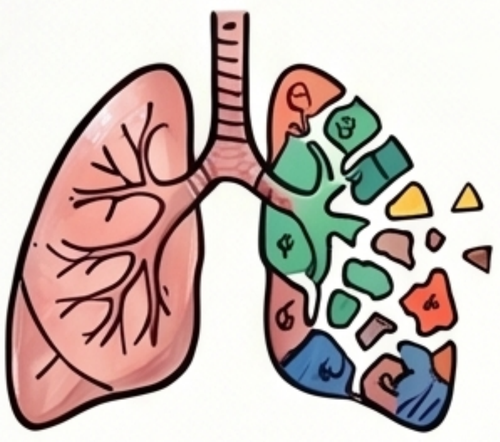
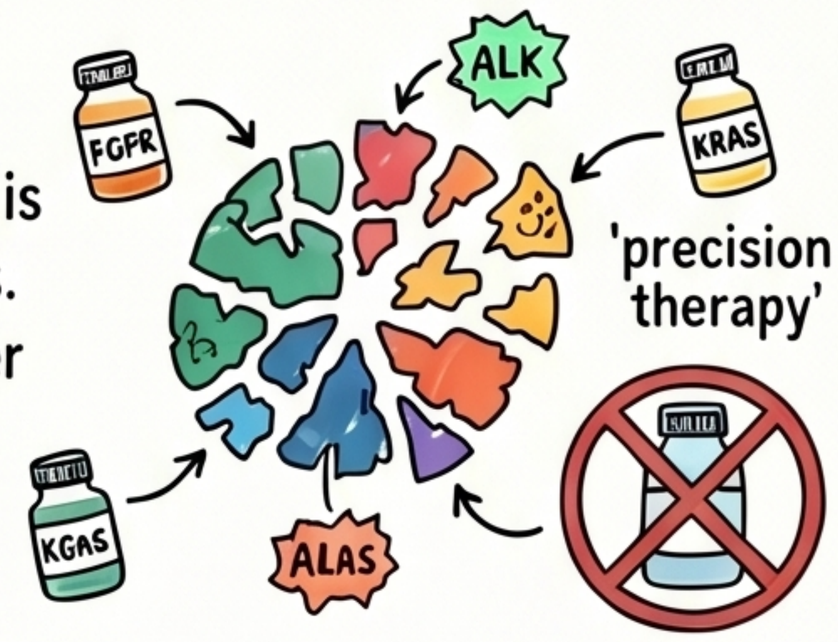
Precision Oncology in NSCLC: Mapping the Targetable Genome



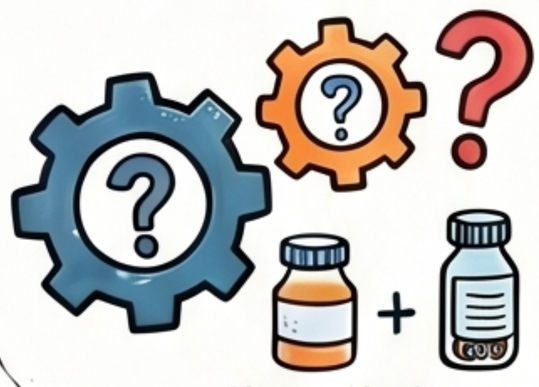
CONTEXT SUMMARY:

NSCLC, once seen as a single disease, is now a collection of molecular subtypes. Treatment is dictated by specific 'driver mutations' for significant survival extension, not organ of origin.



EGFR & ALK: The Established Giants

KEY FINDING: Osimertinib is the EGFR Front-line Standard.
Median Overall Survival: 38.6 months.



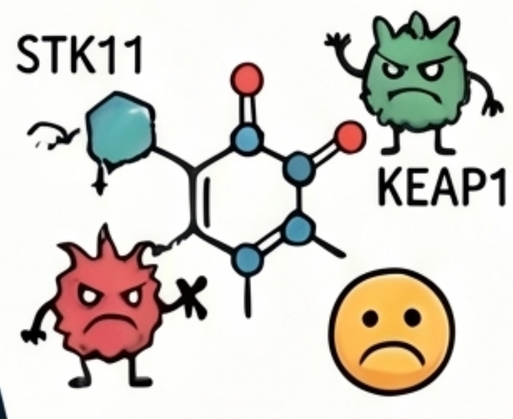
TIMELINE EVENT:
FLAURA2 & MARIPOSA: The Next Frontier.
Testing combinations to extend progression-free survival, toxicity remains a key debate.

ALK SUCCESS

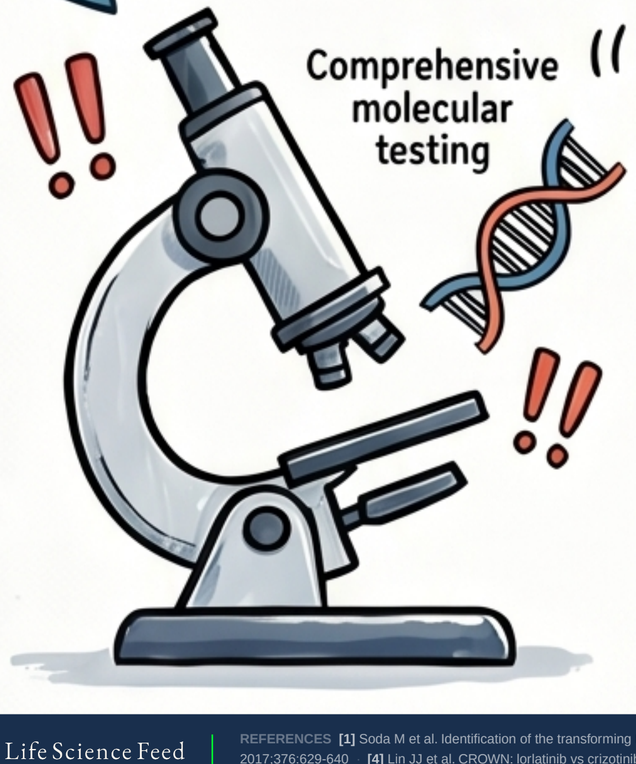
STATISTIC:
60% Progression-Free at 5 Years (CROWN trial for Lorlatinib).
'Extraordinary' long-term efficacy, 82% intracranial response rates for brain metastases.

KRAS & The Diagnostic Mandate

DEFINITION:
Cracking the 'Undruggable' Pocket. Sotorasib and Adagrasib target a 'switch II' binding pocket previously inaccessible.



EXAMPLE:
KRAS Resistance & Co-mutations. Benefit blunted by co-mutations (e.g., STK11, KEAP1), driving research into new combination strategies.



NGS

PROCESS STEP:
NGS: The Non-Negotiable Standard. Comprehe molecular testing (Next-Generation Sequencing) at diagnosis is mandatory to catch fusions and rare alterations.

LANDMARK EFFICACY SNAPSHOT

Biomarker	Landmark Trial	Key Efficacy Result
EGFR	FLAURA	38.6 months Median Overall Survival
ALK	CROWN	60% of patients remain progression-free at 5 years
KRAS G12C	CodeBreaK 200	5.6 months PFS vs 4.5 months (Docetaxel)

Life Science Feed

REFERENCES [1] Soda M et al. Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature. 2007;448:561-566 · [2] Shaw AT et al. ALEX: alectinib vs crizotinib in ALK-positive NSCLC. N Engl J Med. 2017;377:829-838 · [3] Mok TS et al. FLAURA: osimertinib vs gefitinib/erlotinib in EGFR-mutant NSCLC. N Engl J Med. 2017;376:629-640 · [4] Lin JJ et al. CROWN: lorlatinib vs crizotinib in ALK-positive NSCLC. N Engl J Med. 2020;383:2018-2029 · [5] Drilon A et al. Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. N Engl J Med. 2018;378:731-739

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