rete oncologica
si prende cura di te

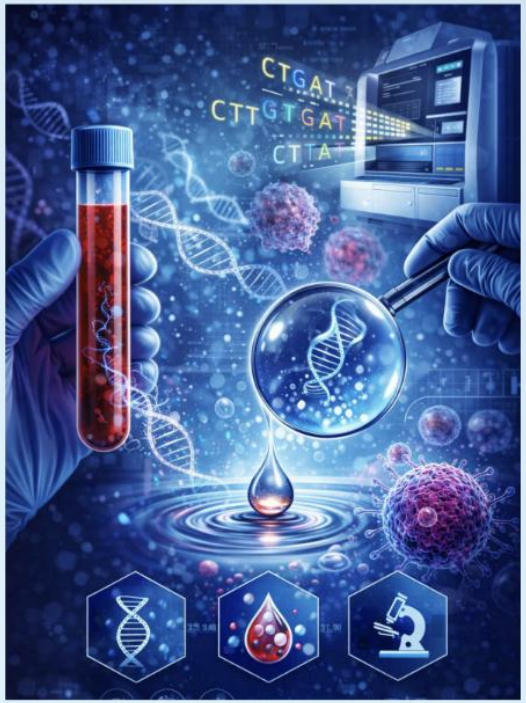
Con i Patrocini di:

AZIENDA ZERO

Aiom ASSOCIAZIONE ITALIANA ONCOLOGIA MEDICA

Scuola di Medicina
UNIVERSITÀ DI TORINO

L'INTRODUZIONE della BIOPSIA LIQUIDA nella DIAGNOSTICA ONCOLOGICA



TORINO, 8 GIUGNO 2026

AULA LENTI - Presidio Molinette
Ingresso da Corso Bramante 88 - TORINO

NSCLC

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Research grants (institutional): Pfizer, Roche
Travel expenses: Pharmamar, BeOne, Pfizer
Advisory Boards: AstraZeneca, Accord, Diaceutics, Genmab, MSD, Pharmacosmos, Pharmarmar

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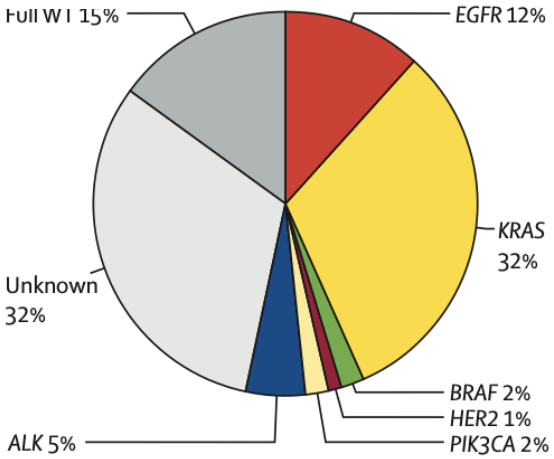
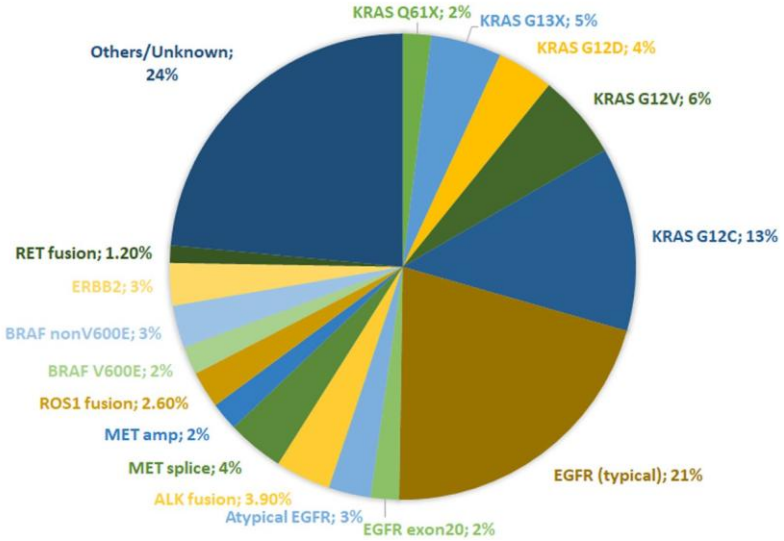
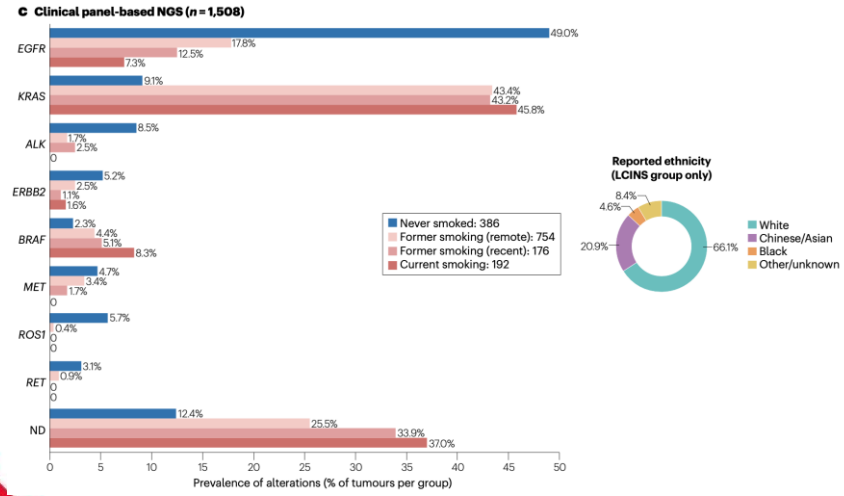
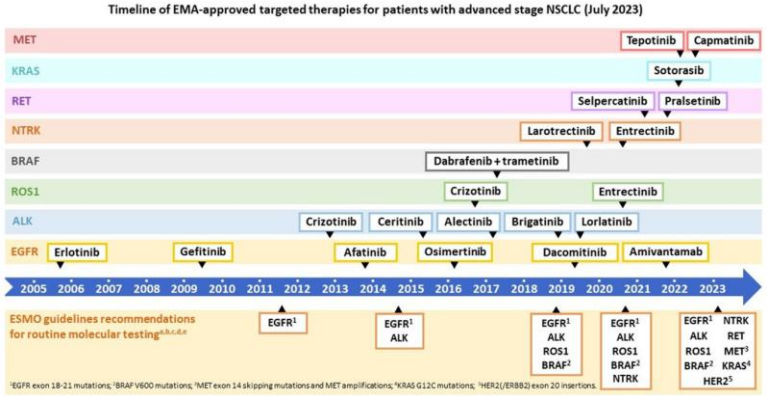
NSCLC: a pie story









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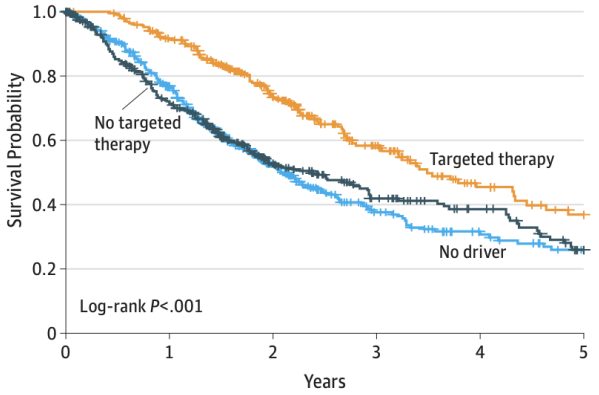
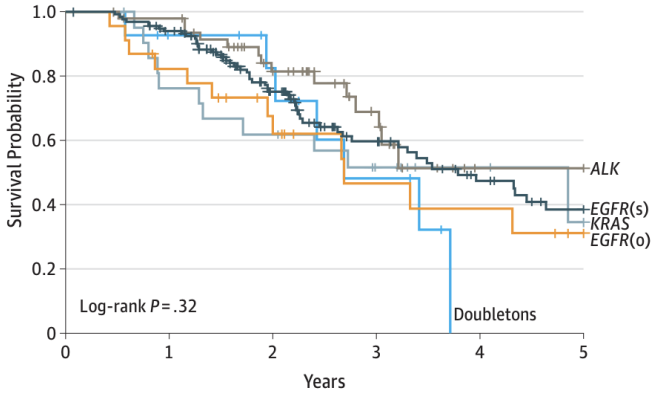
Barlesi F, Lancet Oncol 2016; Friedlander A, Biomarker Res 2024; Lo Piccolo K, Nat Rev Clin Oncol 2024; de Jager VD, Lancet RHE 2024

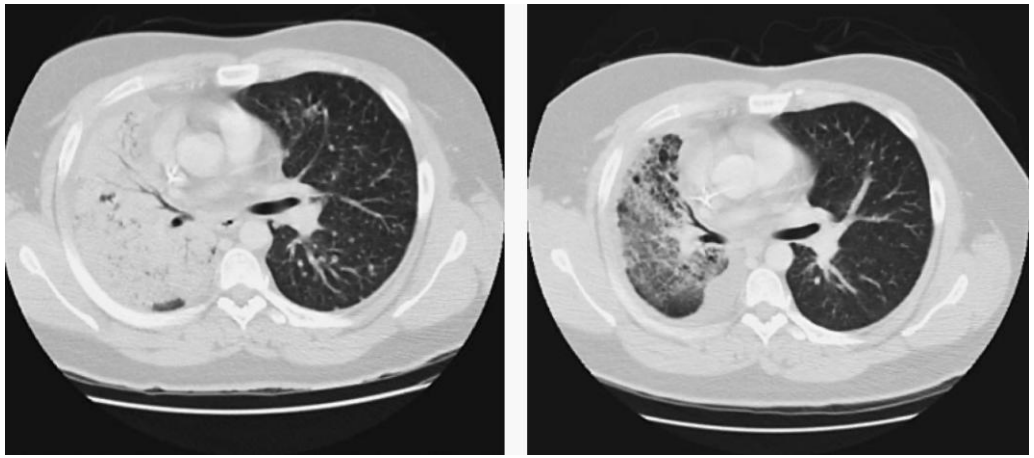
Why do we need to get a (rapid!) state-of-the art molecular profile at diagnosis?

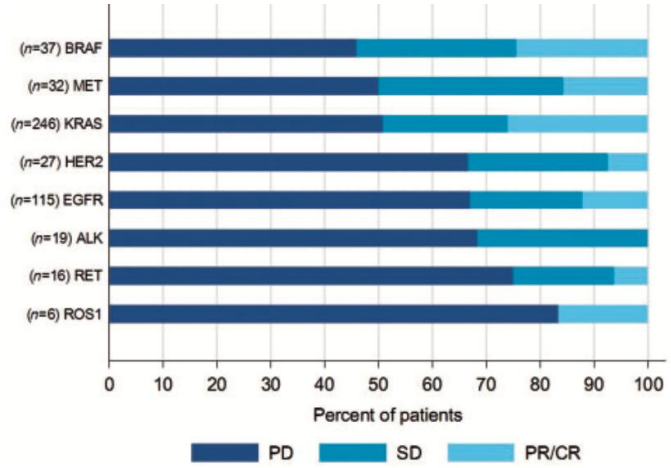


No. at risk						
Patients with oncogenic driver						
No targeted therapy	318	205	110	64	43	20
Targeted therapy	260	225	143	72	36	23
Patients with no driver	360	250	122	59	36	23



No. at risk by oncogenic driver					
EGFR(s)	136	122	72	38	24	16
EGFR(o)	23	18	12	6	5	2
ALK	49	46	31	14	2	2
KRAS	22	16	13	8	4	2
Doubletons	14	11	8	4		





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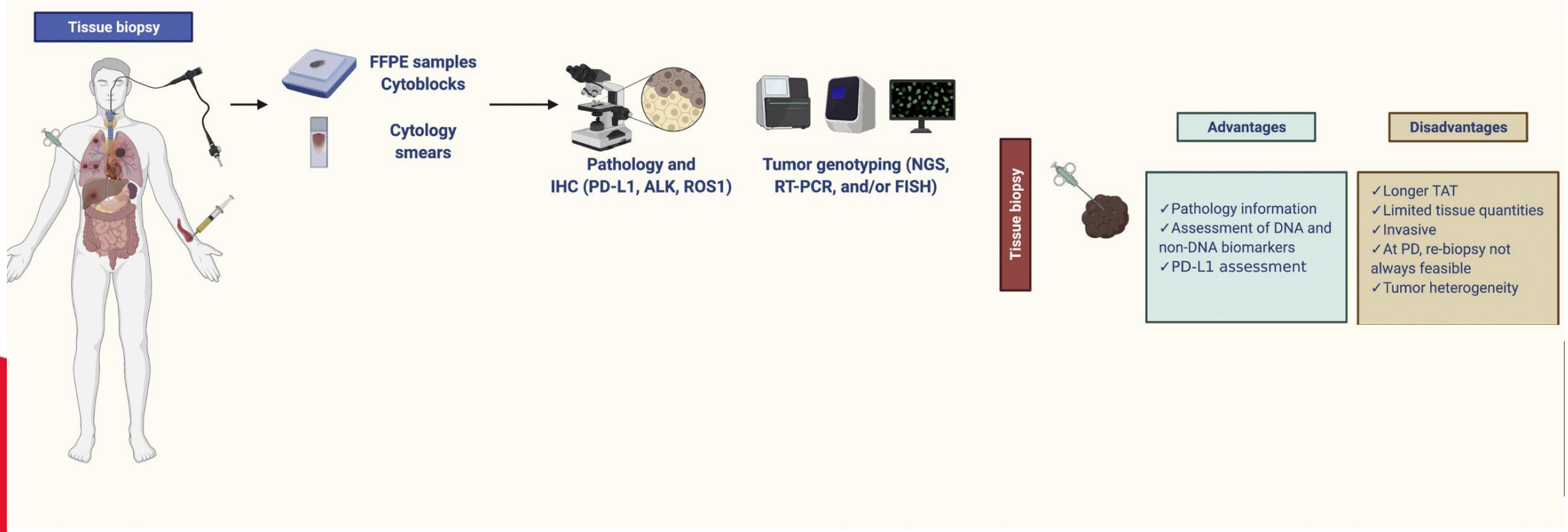
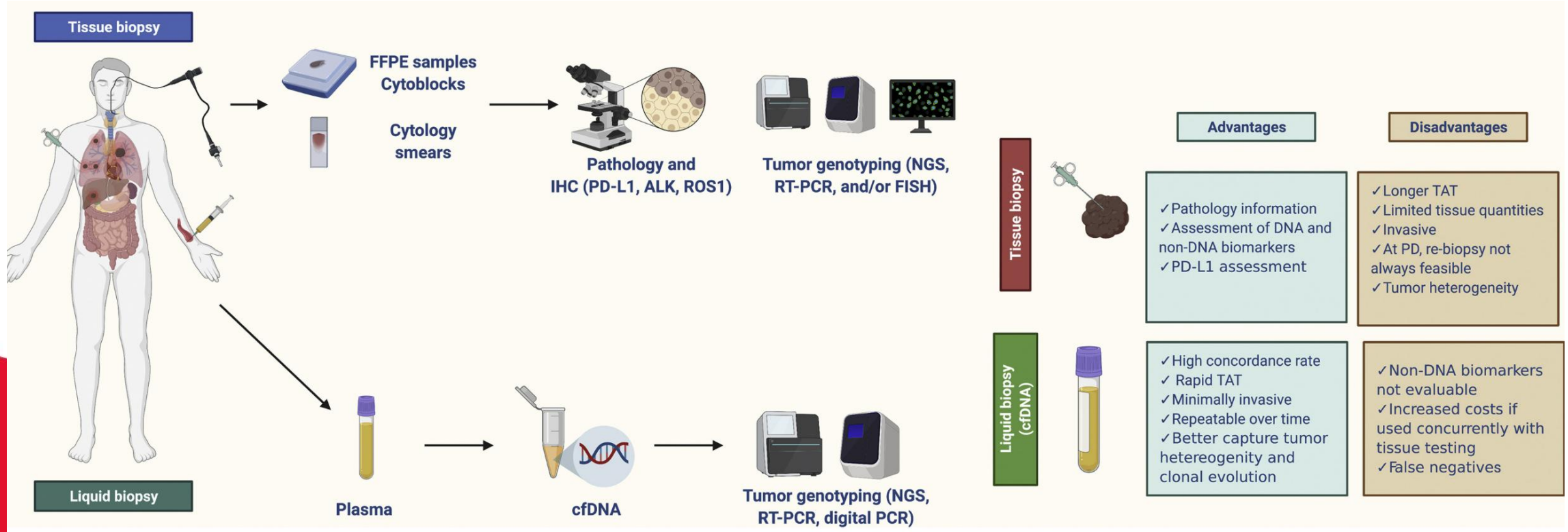
Kris MG, JAMA 2014; Paez JG, Science 2004; Mazieres J, Immunotarget 2019

Finding each slice of the cake: the classic paradigm…



Rolfo C, JTO 2021

Finding each slice of the cake: the classic paradigm…and the novel one



Rolfo C, JTO 2021

Which is the best approach for molecular profiling?

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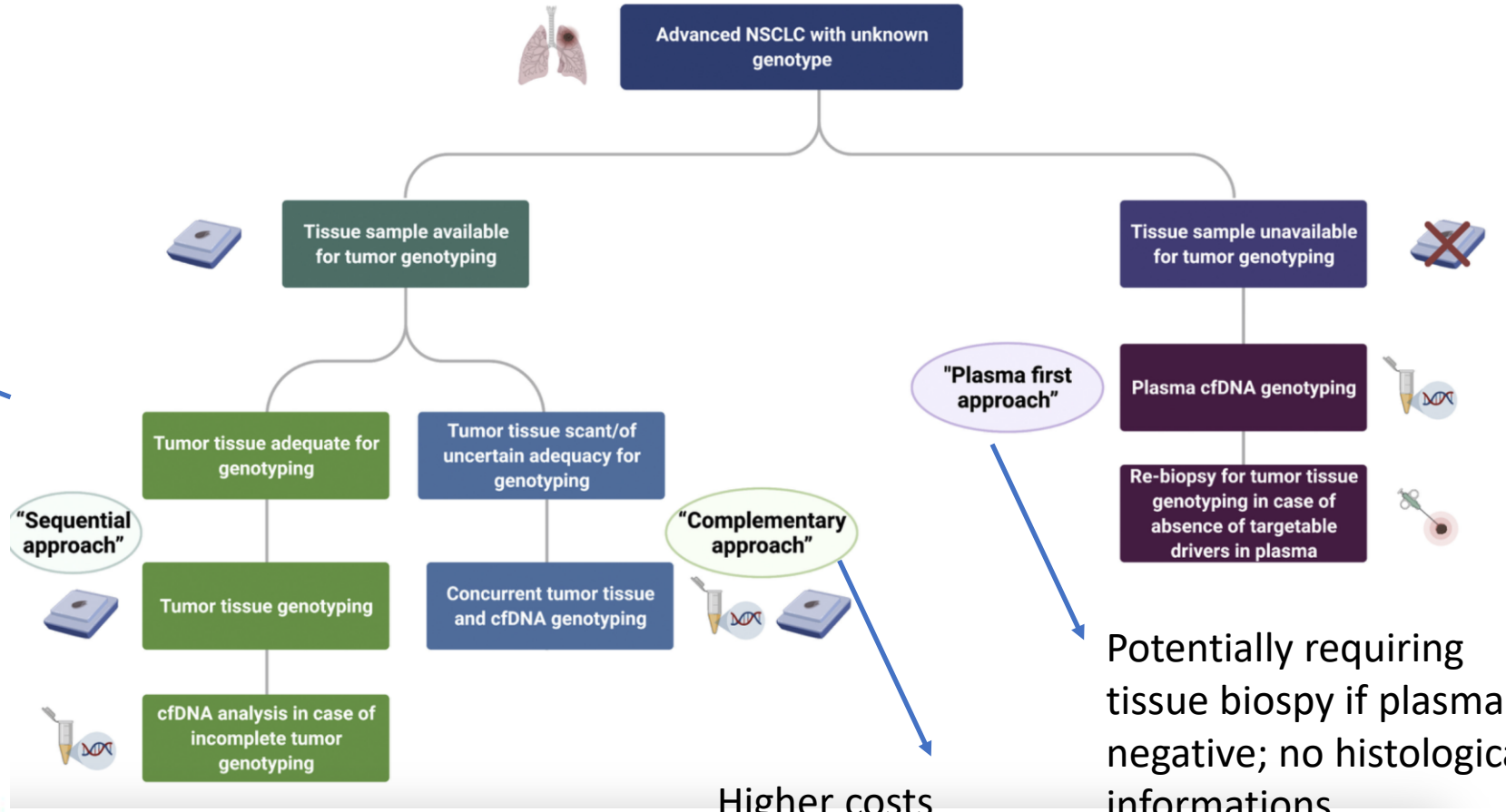
Longer turnaround time



Higher costs
Some unuseful tests

Potentially requiring tissue biospy if plasma negative; no histological informations…

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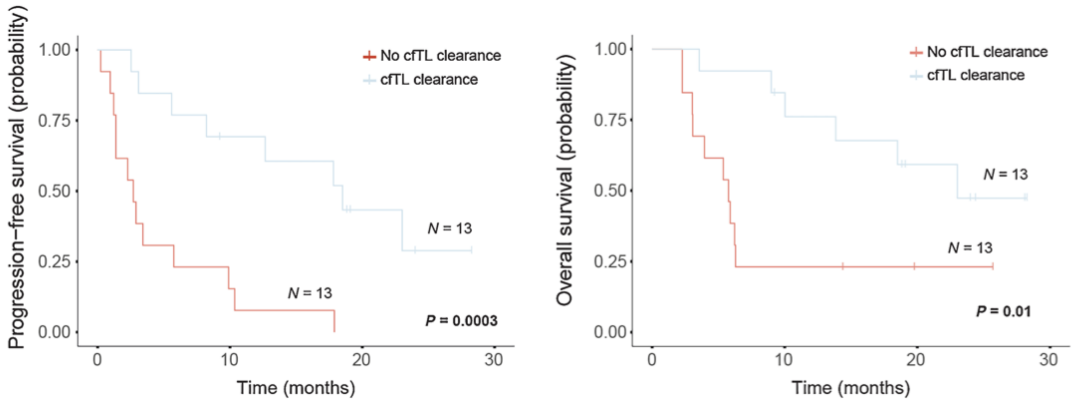
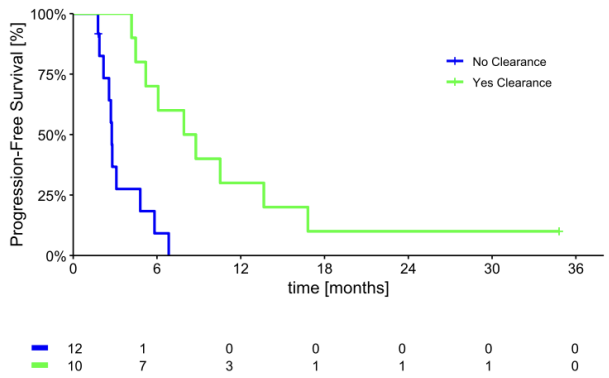
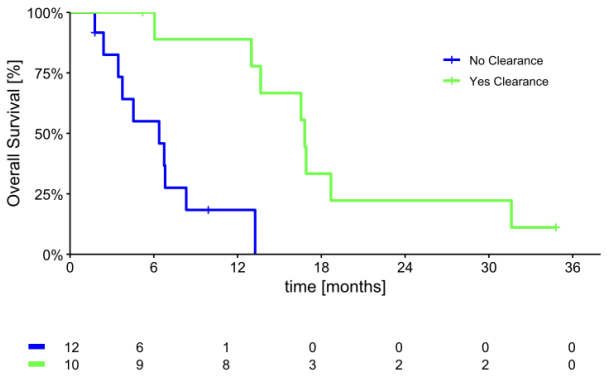
Rolfo C, JTO 2021

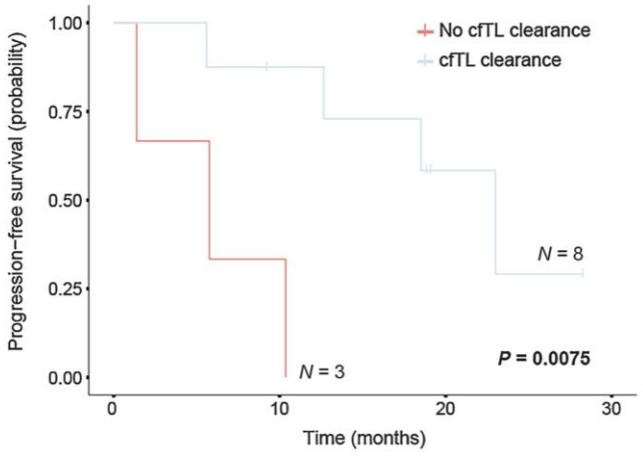
And what about exploiting liquid biopsies during treatment?

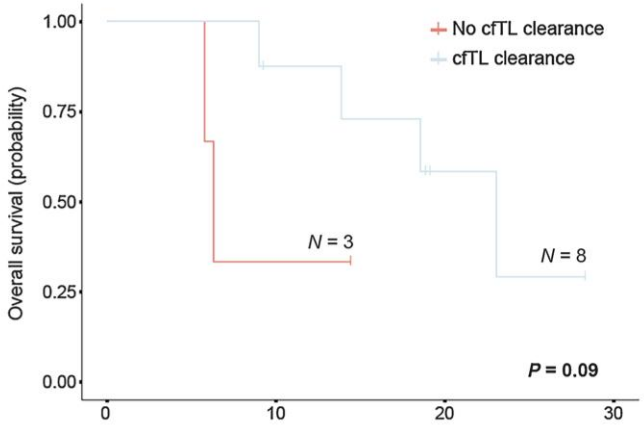






And this can better define radiologic SD!





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Murray JC,CCR 2024; Passiglia F, Cancer 2025

Liquid biopsy to tackle resistances: where did we start?

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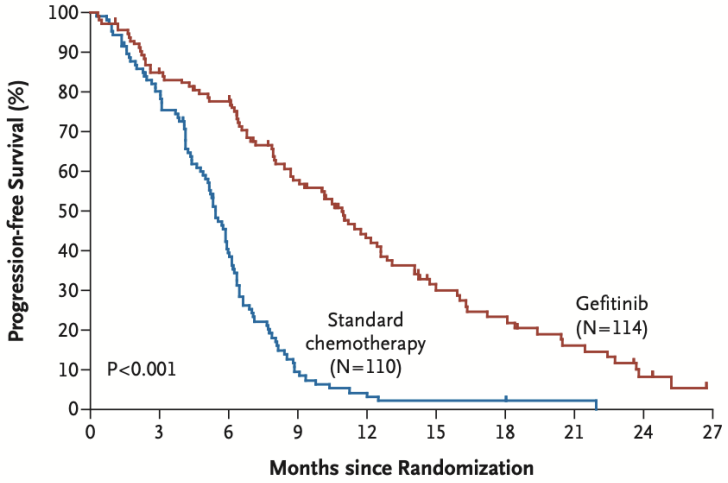

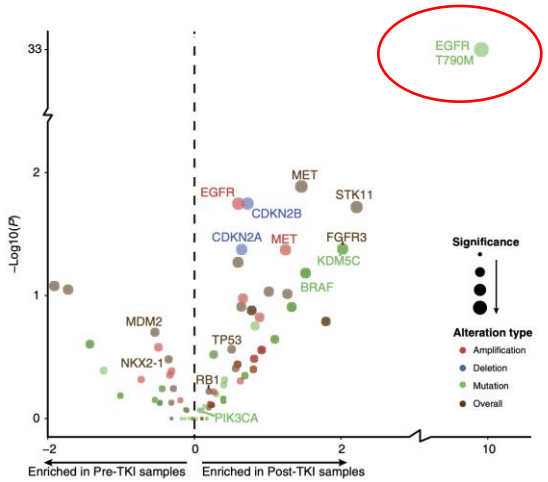

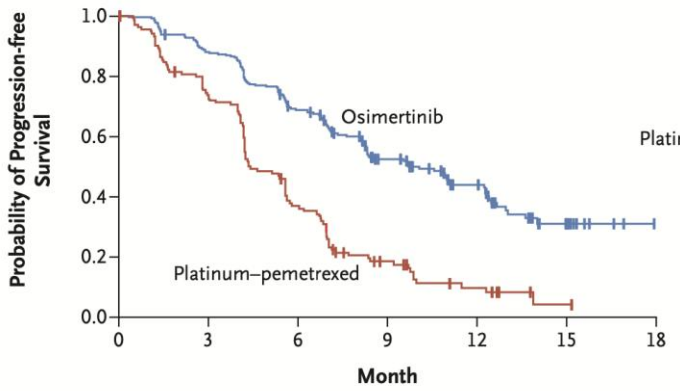

No. at Risk							
Osimertinib	279	240	162	88	50	13	0
Platinum–pemetrexed	140	93	44	17	7	1	0

	No. of Patients	Median Progression-free Survival *mo (95% CI)*
Osimertinib	279	10.1 (8.3–12.3)
Platinum–pemetrexed	140	4.4 (4.2–5.6)

Hazard ratio for disease progression or death, 0.30 (95% CI, 0.23–0.41)
P<0.001

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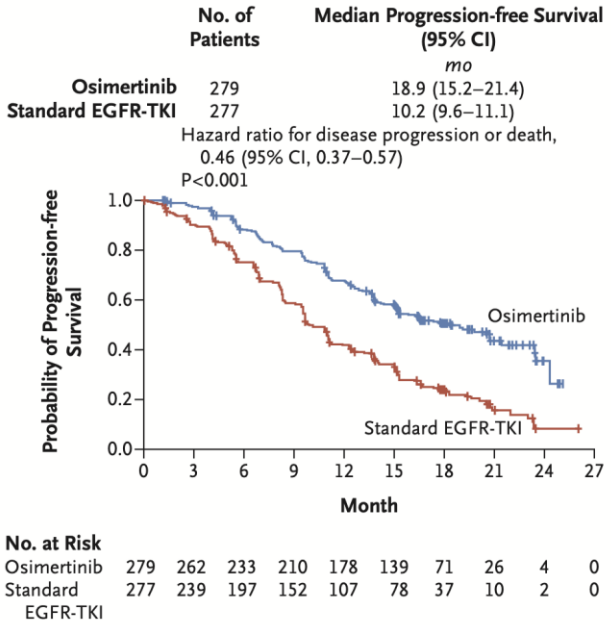
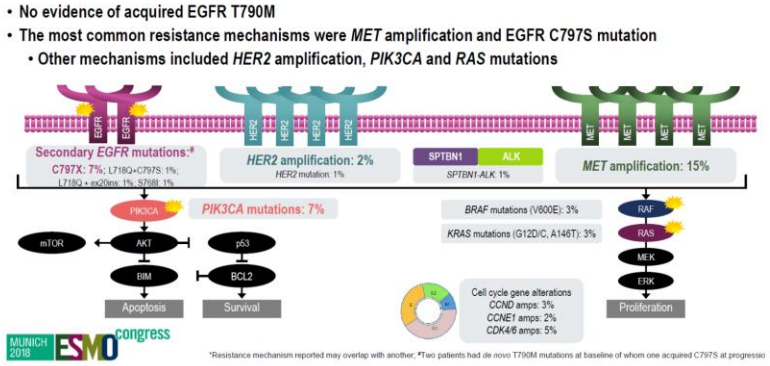
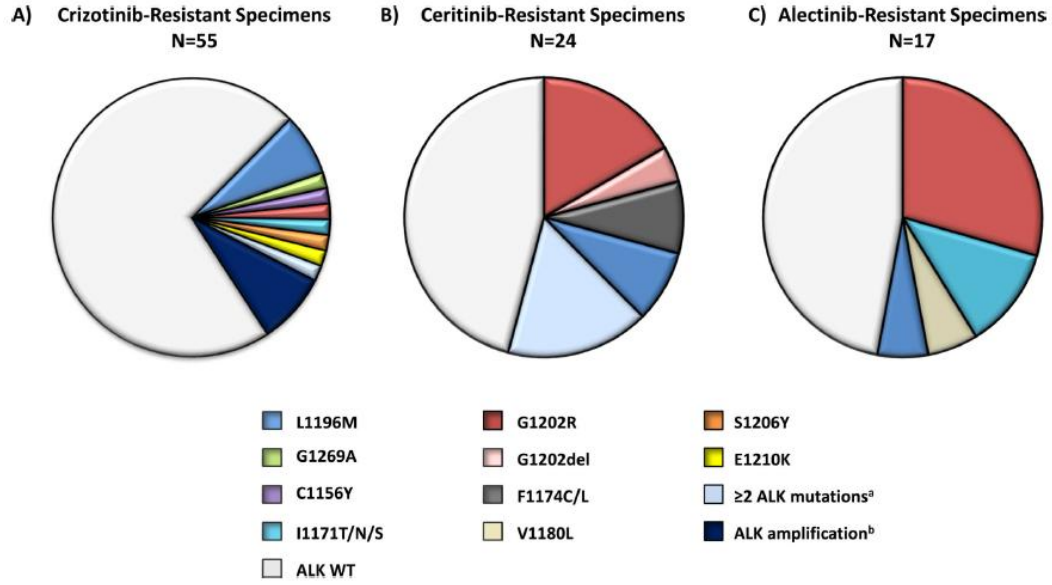
Maemondo M, NEJM 2010; Yu H, CCR 2018; Mok TS, NEJM 2017

But resistance mechanisms change as we modify upfront therapies







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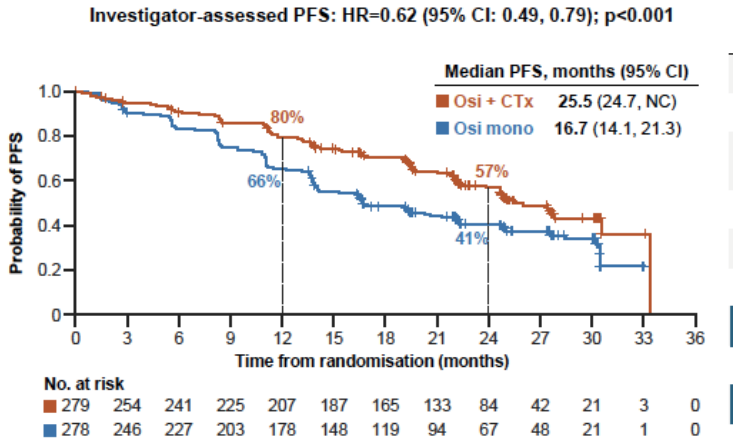
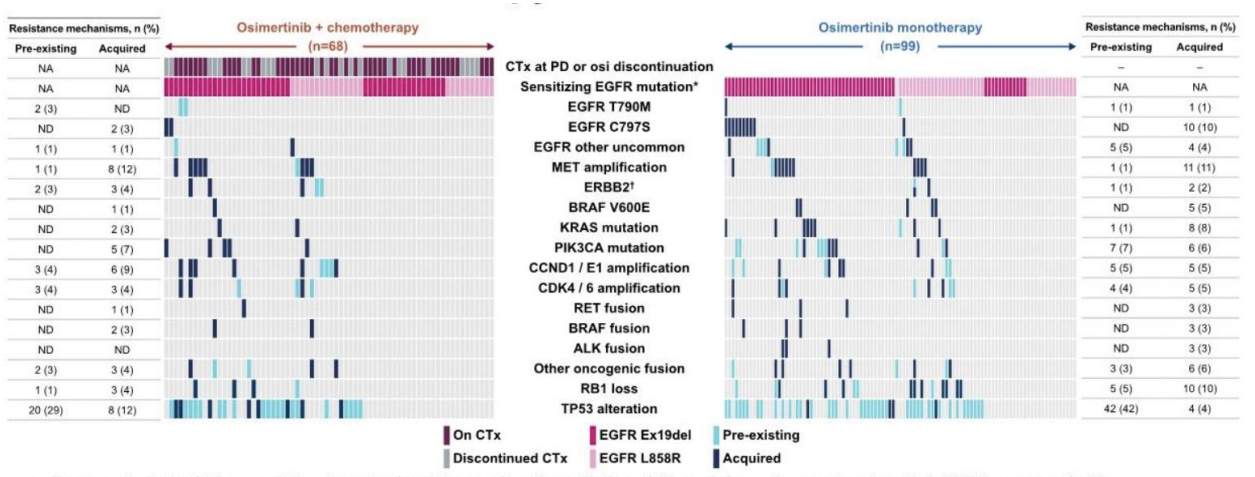
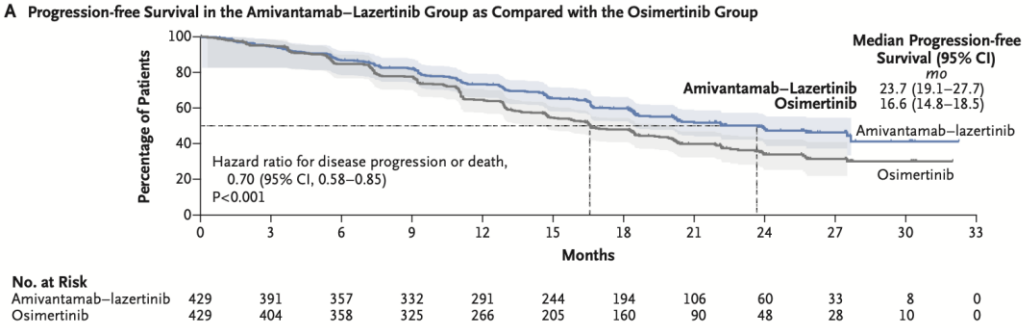
Soria JC, NEJM 2018; Ramalingam S, ESMO 2018; Gainor J, Cancer Discov 2016

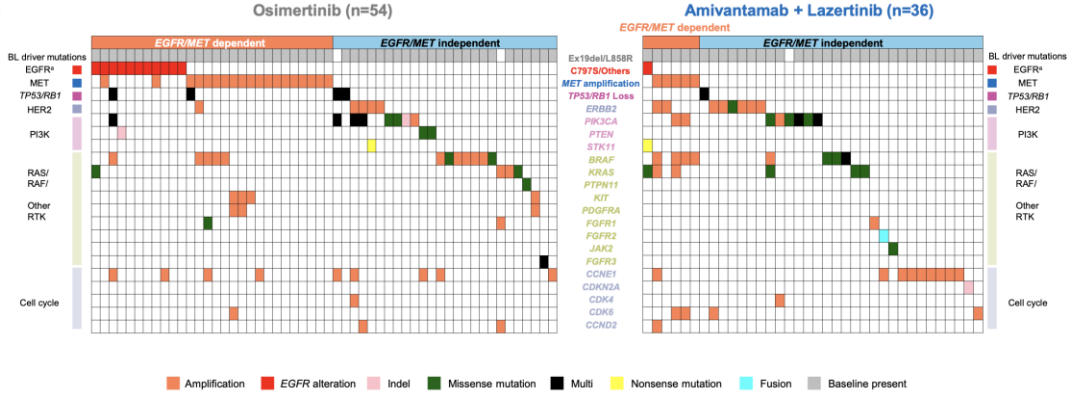
Can we use liquid biopsies to identify (novel) resistance pathways?





ctDNA, , GuardantOMNI, 29.9% of patients





ctDNA, , Guardant360°, 29.5% of patients

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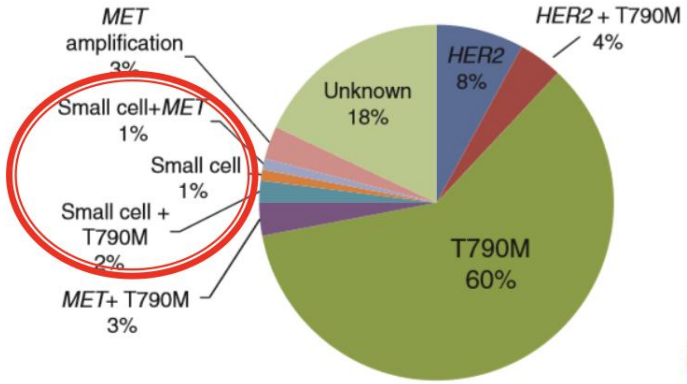
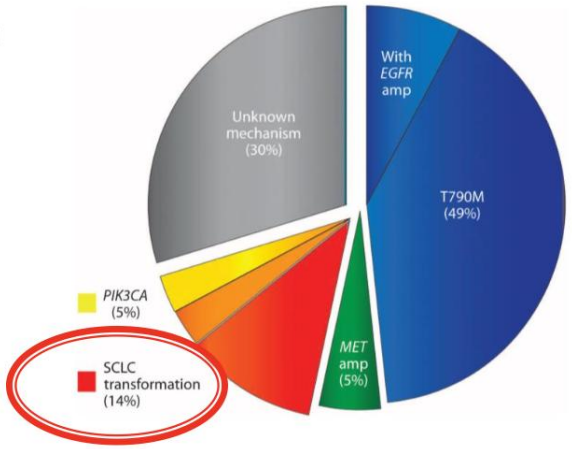
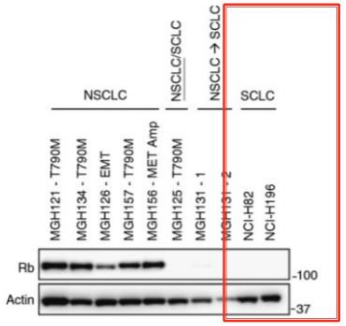
Planchard D, WCLC 2025; Yang JCH, WCLC 2024; Cho BC, NEJM 2024; Besse B, ESMO 2024

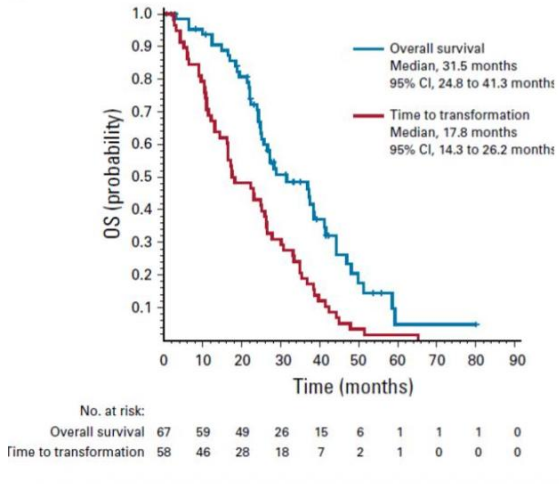
What we currently miss with ctTNA approaches…

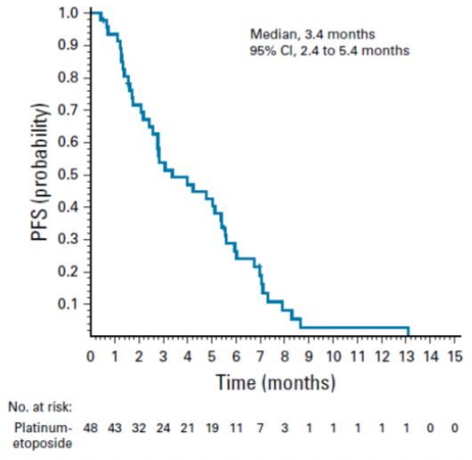


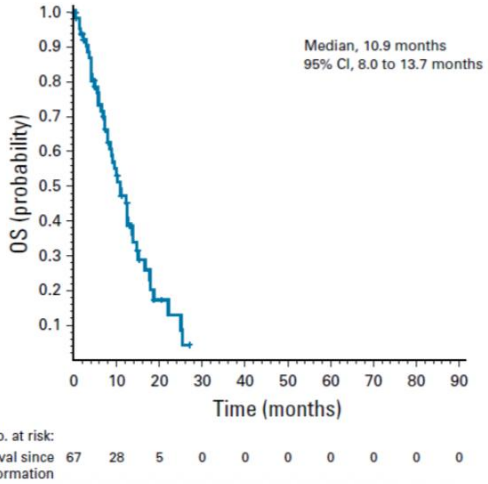




Any future role for CTCs?







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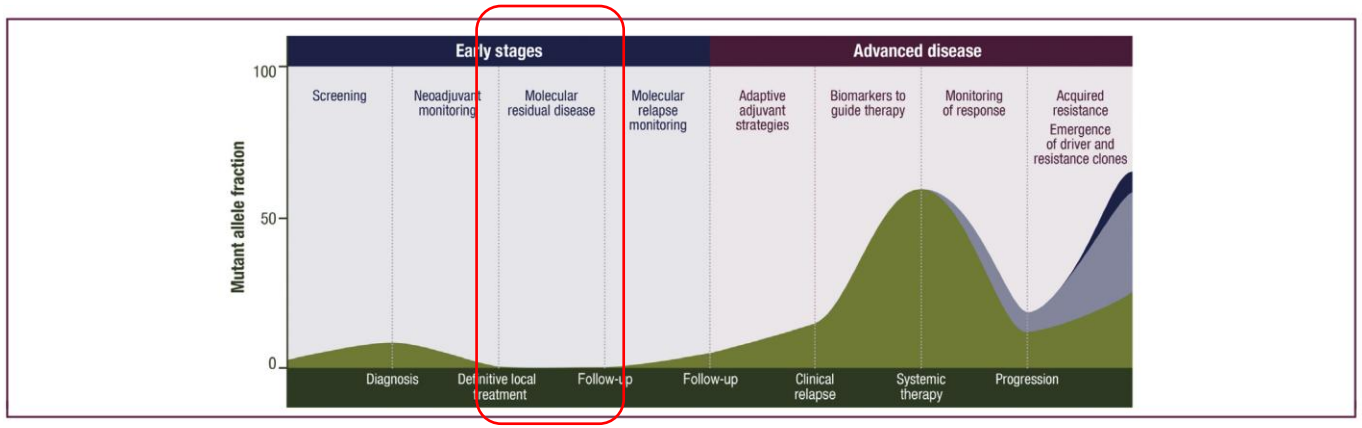
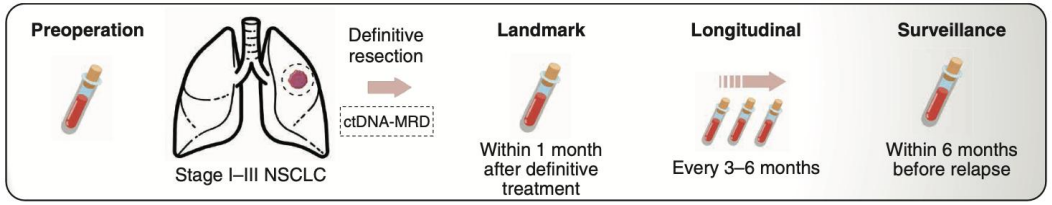
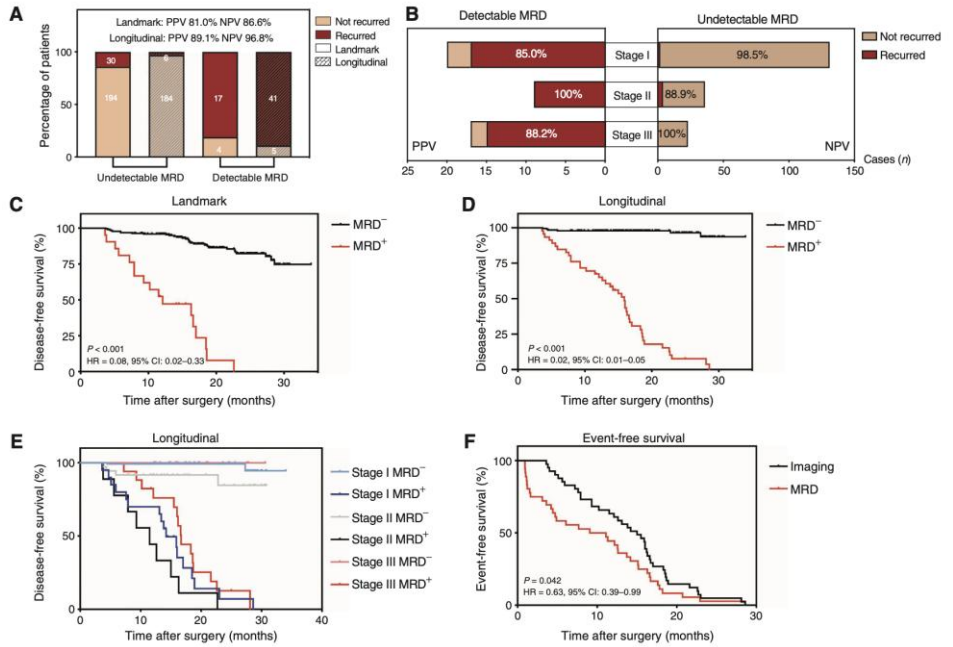
Sequist, Sci Transl Med 2011;Yu, CCR 2013; Niederst, Nat Comm 2016; Marcoux, J Clin Oncol 2019

The next frontier: MRD in early stages







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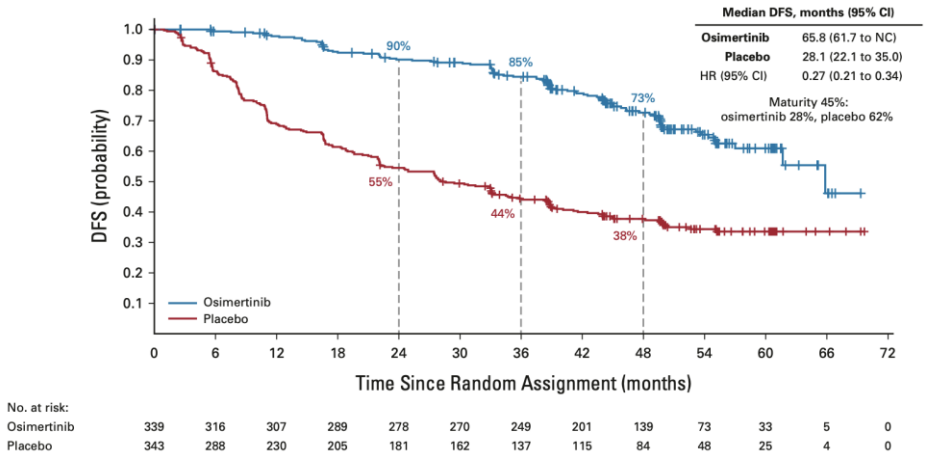
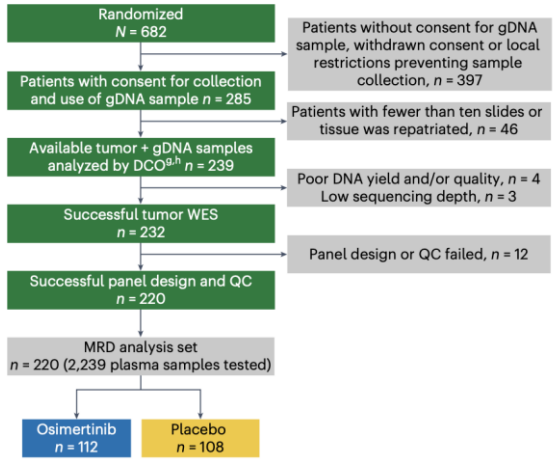
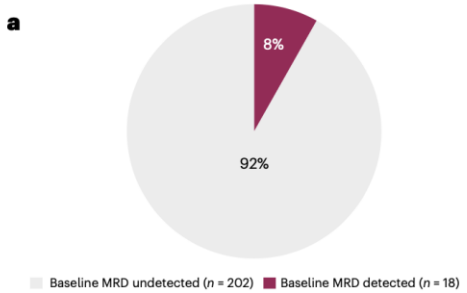
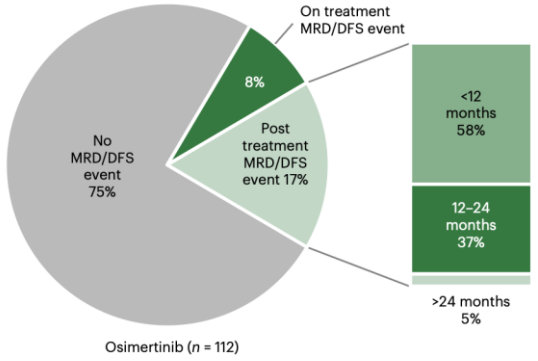
Pascual J, Ann Oncol 2021; Zhang JT, Cancer Discov 2022

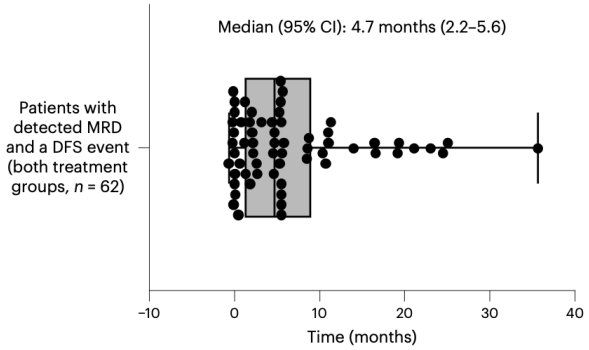
MRD as a dynamic tool to early intercept relapse











Most molecular relapses occur post treatment
Molecular relapses preceded DFS event by a median of 4.7 months (95% CI, 2.2-5.6)

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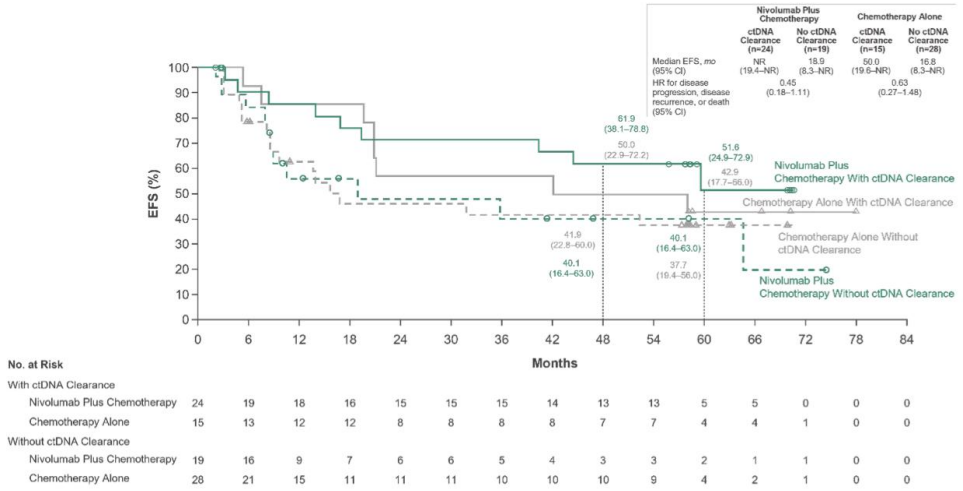
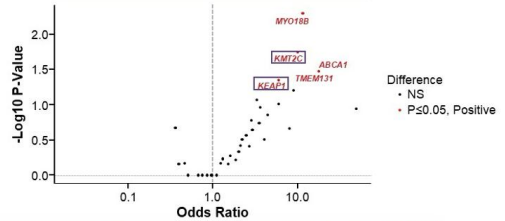
Herbst RS, JCO 2023; Herbst RS, Nat Med 2025

ctDNA clearance during neoadjuvant chemo-immunotherapy



- Within the D arm, mutated genes associated with MRD+ status included *KMT2C* and *KEAP1*

Association of Gene Mutation Status with MRD Status within the D arm*

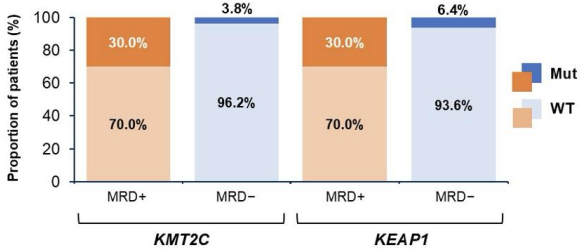


	D arm		PBO arm		Regardless of Tx	
	OR	P	OR	P	OR	P
ABCA1	17.917	0.033	0	1	4.822	0.114
TMEM131	17.917	0.033	0	1	3.189	0.188
MYO18B	11.656	0.005	0	1	4.280	0.038
KMT2C	10.165	0.018	0	0.587	2.260	0.209
KEAP1	6.042	0.044	0	1	3.345	0.107

- Within the PBO arm, mutated genes associated with MRD+ status included *SLC4A4*, *F5*, and *GRM7*

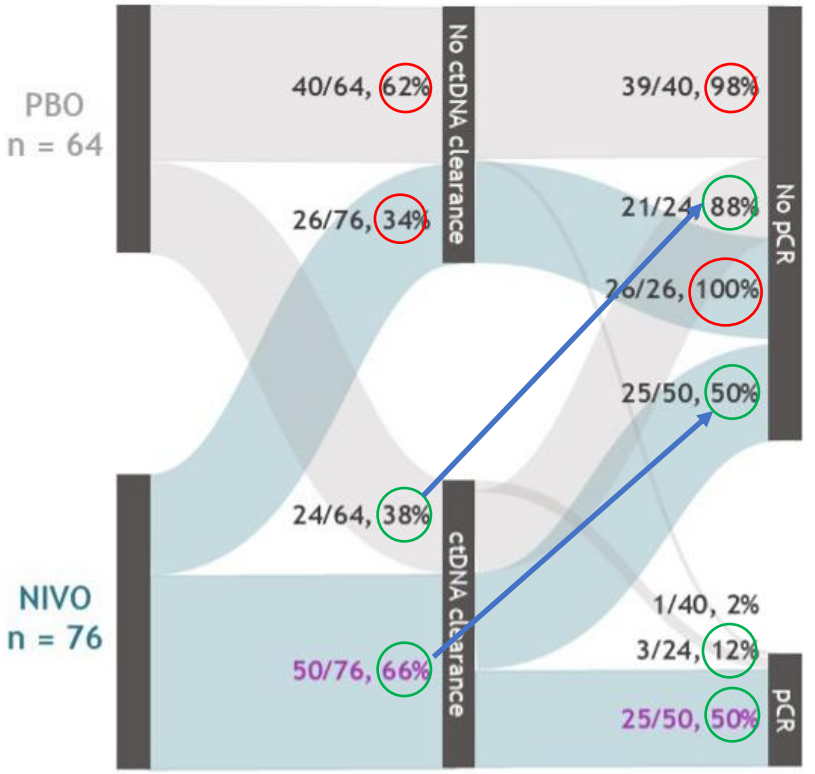
- Within the D arm, a higher proportion of MRD+ vs MRD− patients had *KMT2C* (30.0% vs 3.8%) and *KEAP1* (30.0% vs 6.4%) mutations

Prevalence of *KMT2C* and *KEAP1* Mutations in MRD-evaluable Patients within the D arm



- 62.5% (15/24) and 47.6% (10/21) of patients with *KMT2C* and *KEAP1* mutations, respectively, had persistent ctDNA at all evaluable neoadjuvant timepoints

Association between ctDNA clearance and pCR



MRD+ after neoadjuvant → very low probability of pCR
MRD- after neoadjuvant → this is like flipping a coin!!! (with chemo-IO)

Forde PM, NEJM 2025; Reck M, ASCO 2025

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Thank you