Impact of delays in molecular diagnostics – how can we speed things up?

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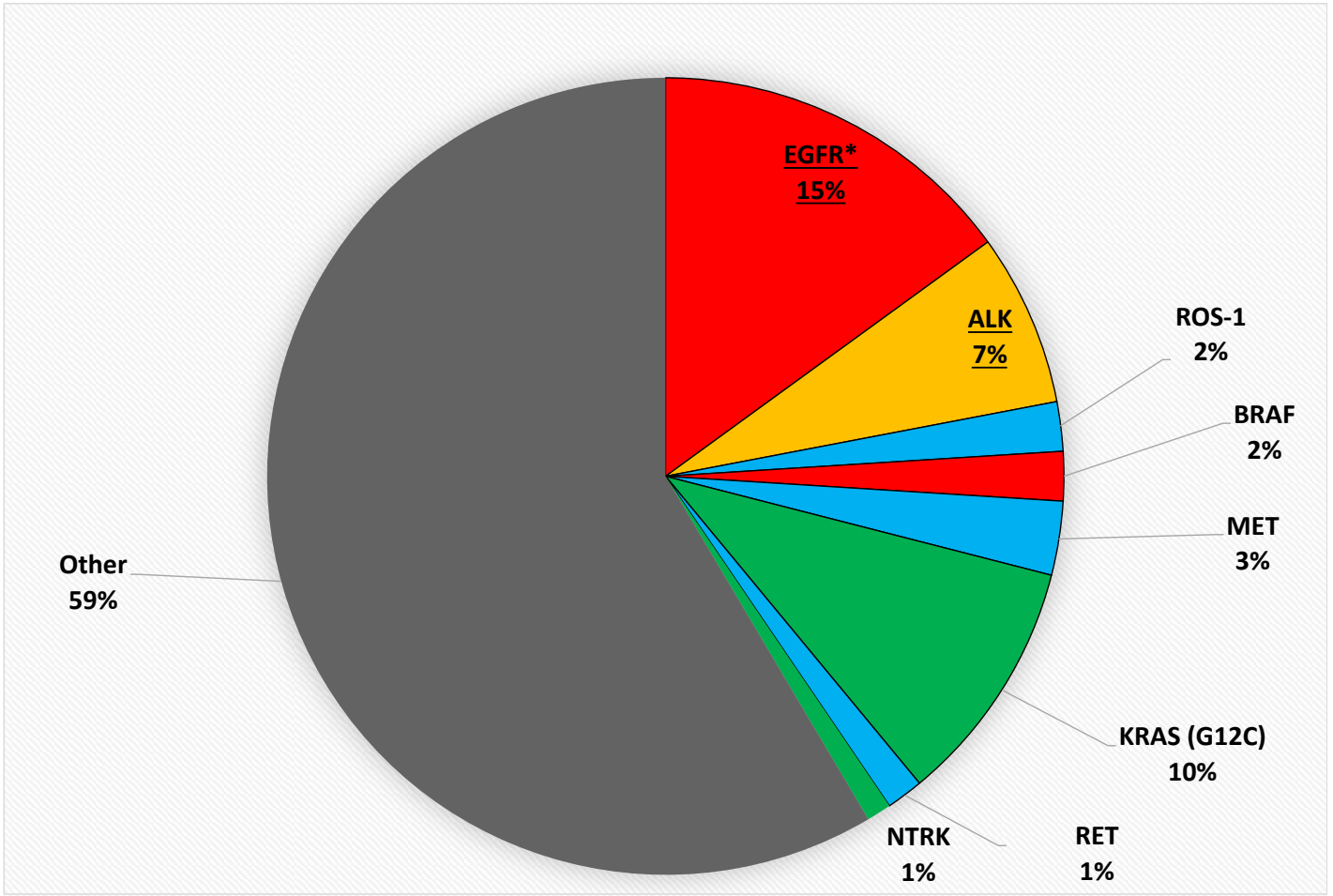
The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

Newcastle University / Centre for Cancer

Increasing numbers of Targeted Therapies available in Non-Squamous NSCLC



- Optimal TT only available 1st line
- One option TT only available 1st line
- TT available any line
- TT only available 2nd line (+)

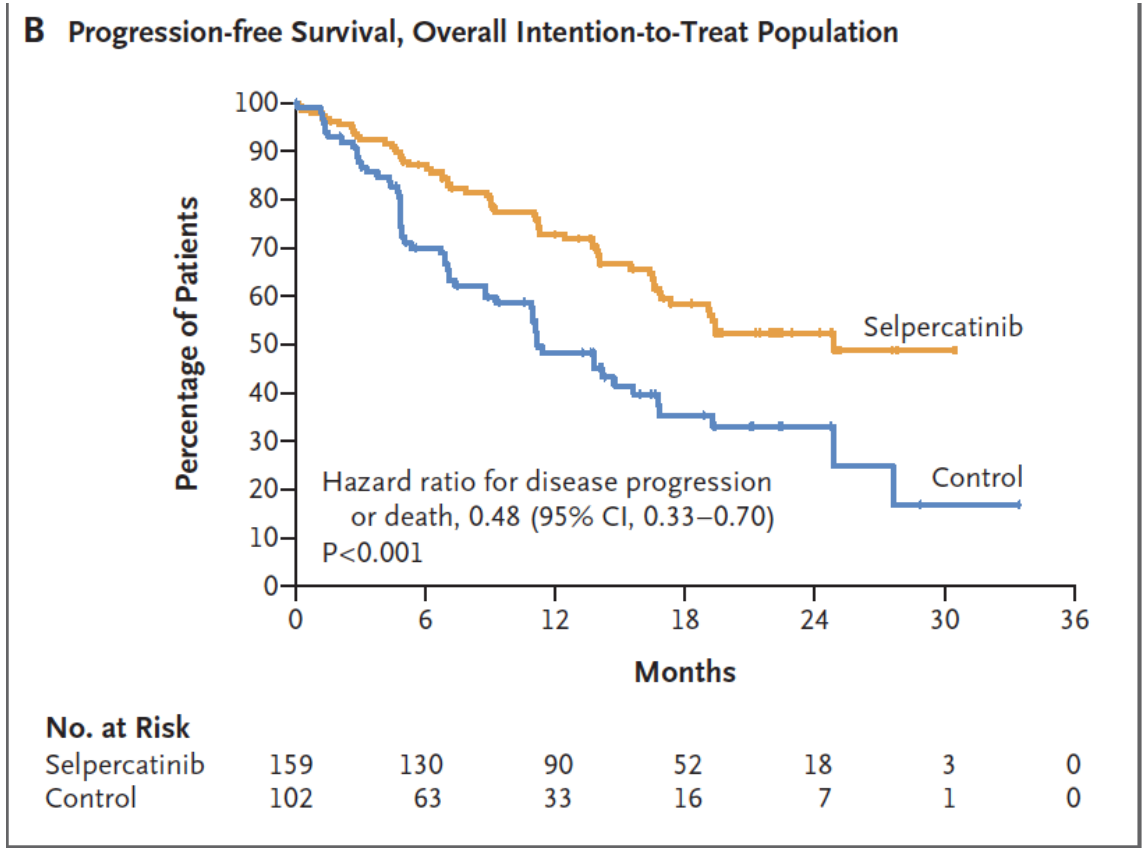
Current England access situation, November 2023

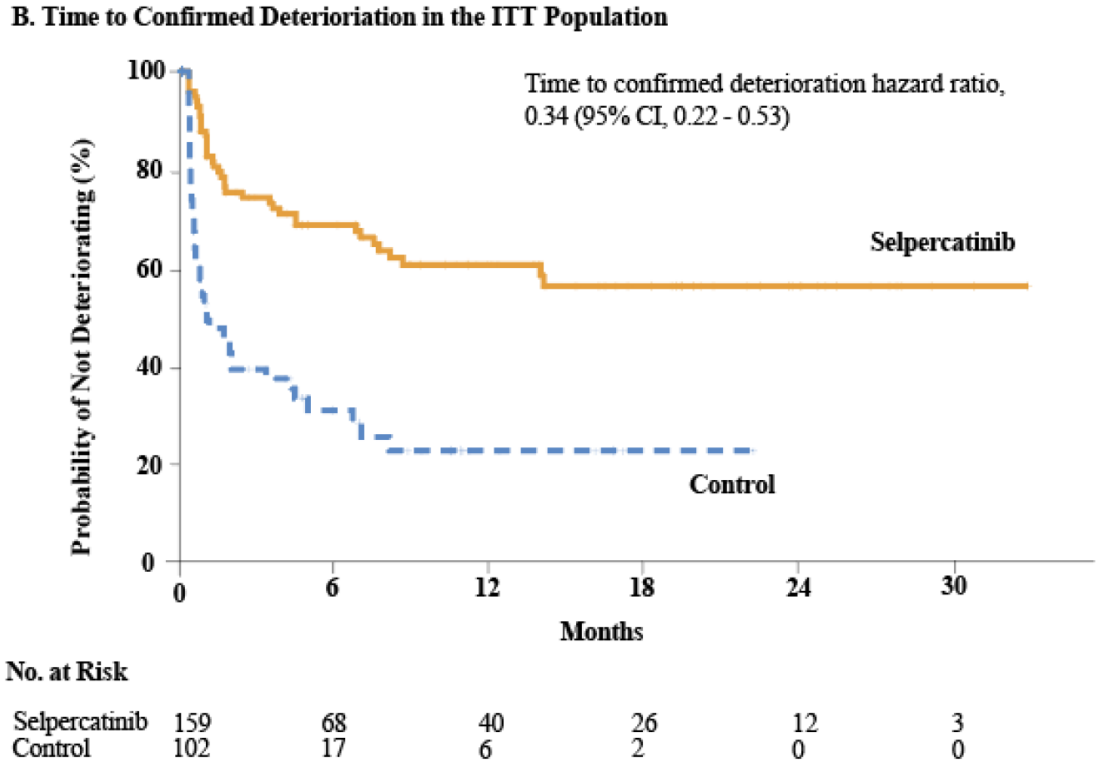
Biomarker	Therapy approved in the UK	NHS funded therapy
EGFR common/rare	erlotinib, gefitinib, afatinib, dacomitinib, osimertinib,	erlotinib, gefitinib, afatinib, dacomitinib, osimertinib,
EGFR adjuvant	osimertinib	osimertinib
EGFR exon 20 insertions	~~mobocertinib~~, amivantamab	~~mobocertinib~~
ALK 1st line	crizotinib, alectinib, ceritinib, brigatinib, lorlatinib	crizotinib, alectinib, ceritinib, brigatinib
ROS1	crizotinib, entrectinib	crizotinib, entrectinib
BRAF V600	dabrafenib-trametinib	dabrafenib-trametinib
NTRK	larotrectinib, entrectinib	larotrectinib, entrectinib
MET exon 14 skipping mutations	tepotinib	tepotinib
RET	selpercatinib, pralsetinib	selpercatinib
KRAS	Sotorasib, adagrasib	sotorasib
HER2		

National Cancer Drugs Fund List. September 202. Available at: https://www.england.nhs.uk/wp-content/uploads/2017/04/NationalCDF_List_ver1.277_-22092023_MASTER-.pdf

Please refer to individual SmPCs for full details of indications and posology

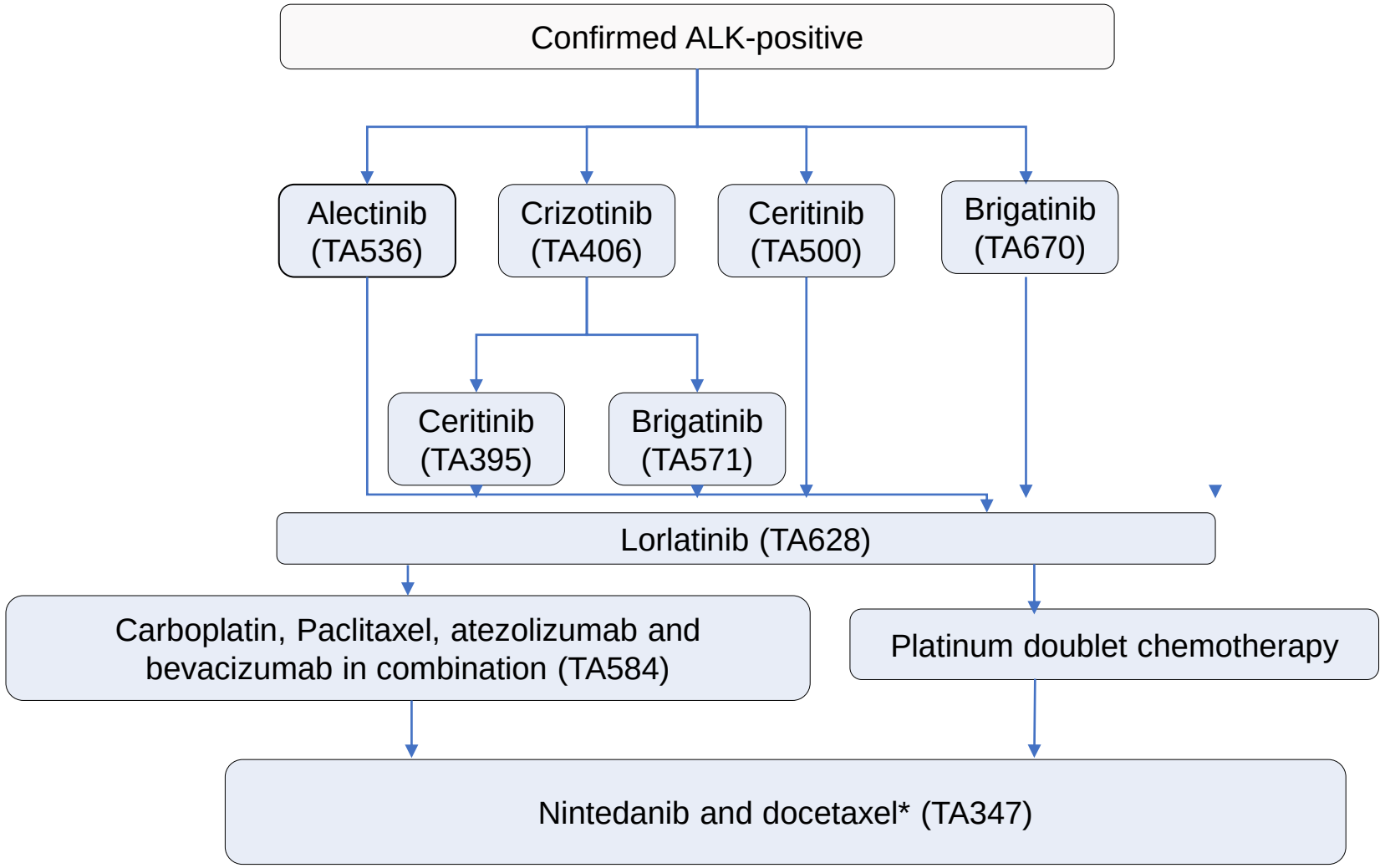
Its not just about radiological response





Zhou C, et al .N Engl J Med. 2023 Oct 21. doi: 10.1056/NEJMoa2309457. Epub ahead of print.

Additional lines of therapy



Please refer to individual SmPCs for full details of indications and posology

Please consult the individual NICE technology appraisal guidances for further information.

* Licensed in NSCLC (not specifically ALK+ patients)

Apples and Pears

Administration time and place

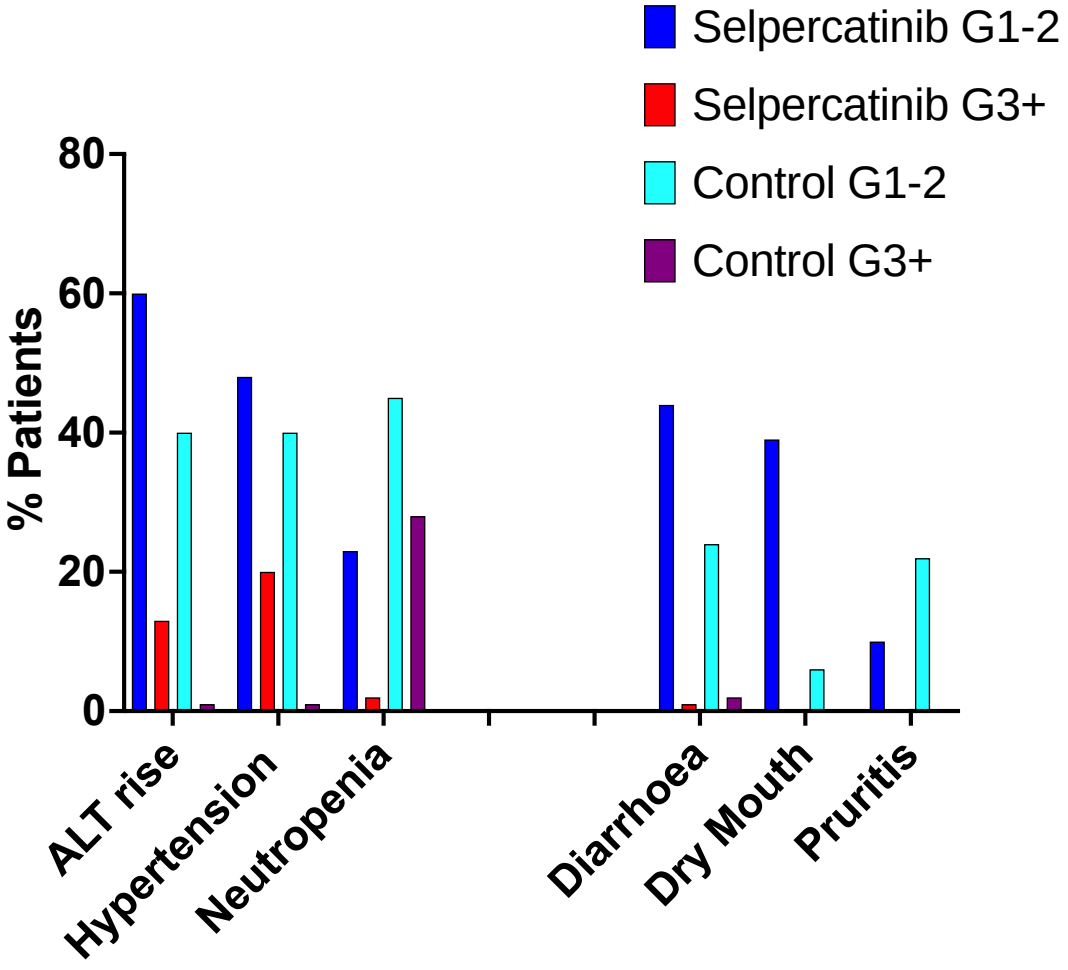
- Patient and health care system
- Waiting times

Side –effects

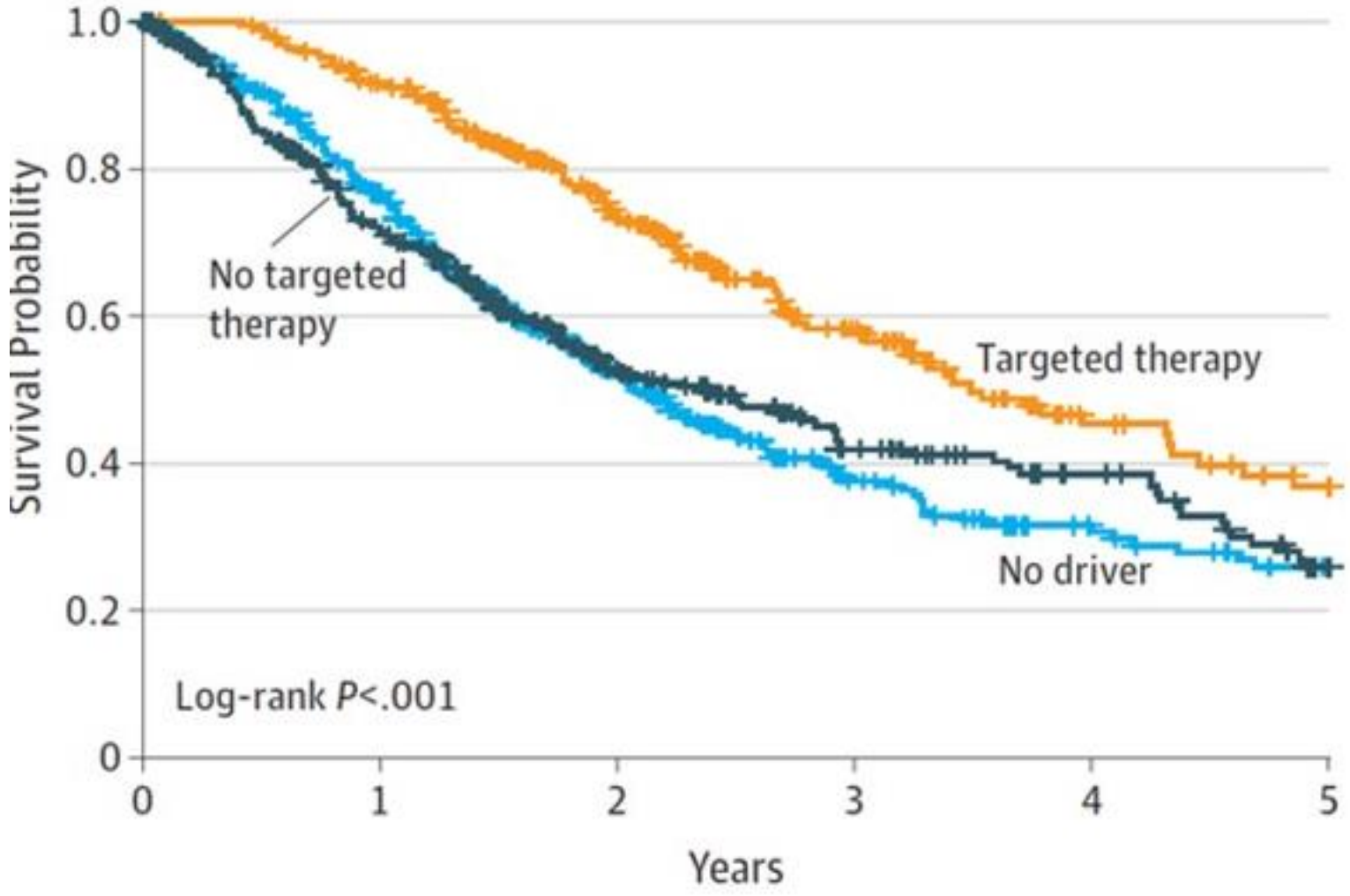
- Patient and health care system

Intermittent vs continuous administration

Cannulation

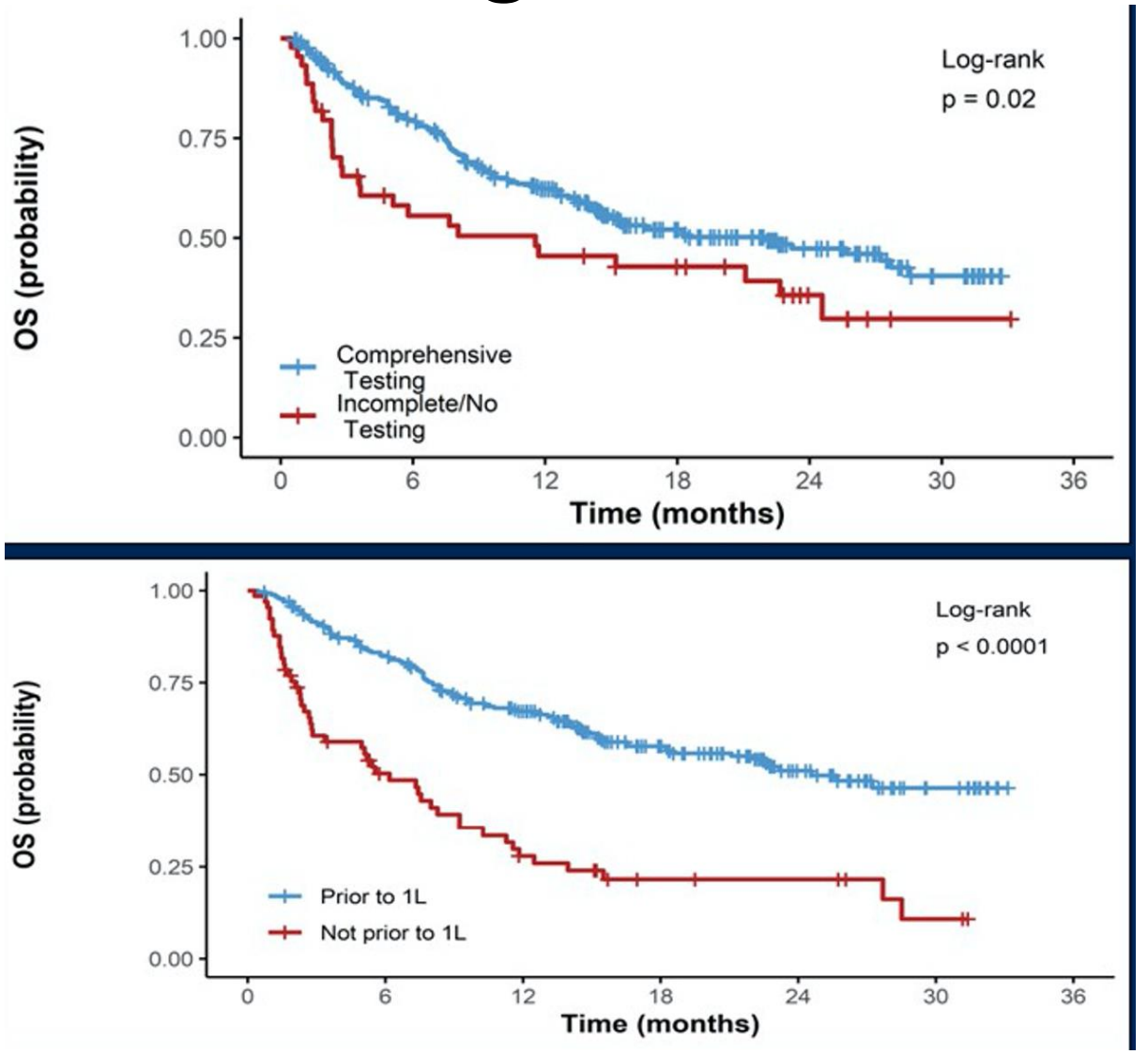


Appropriate Treatment Needed to Improve Outcomes



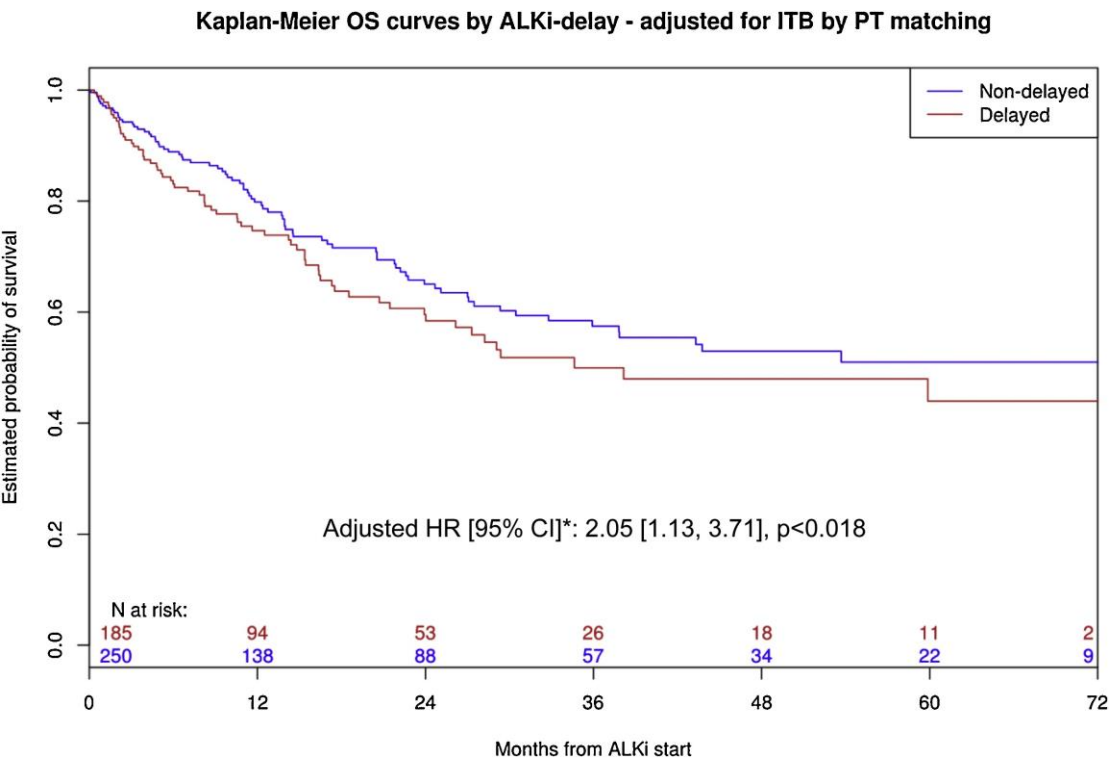
Singal et al. JAMA. 2019 Apr 9;321(14):1391-1399. doi: 10.1001/jama.2019.3241.

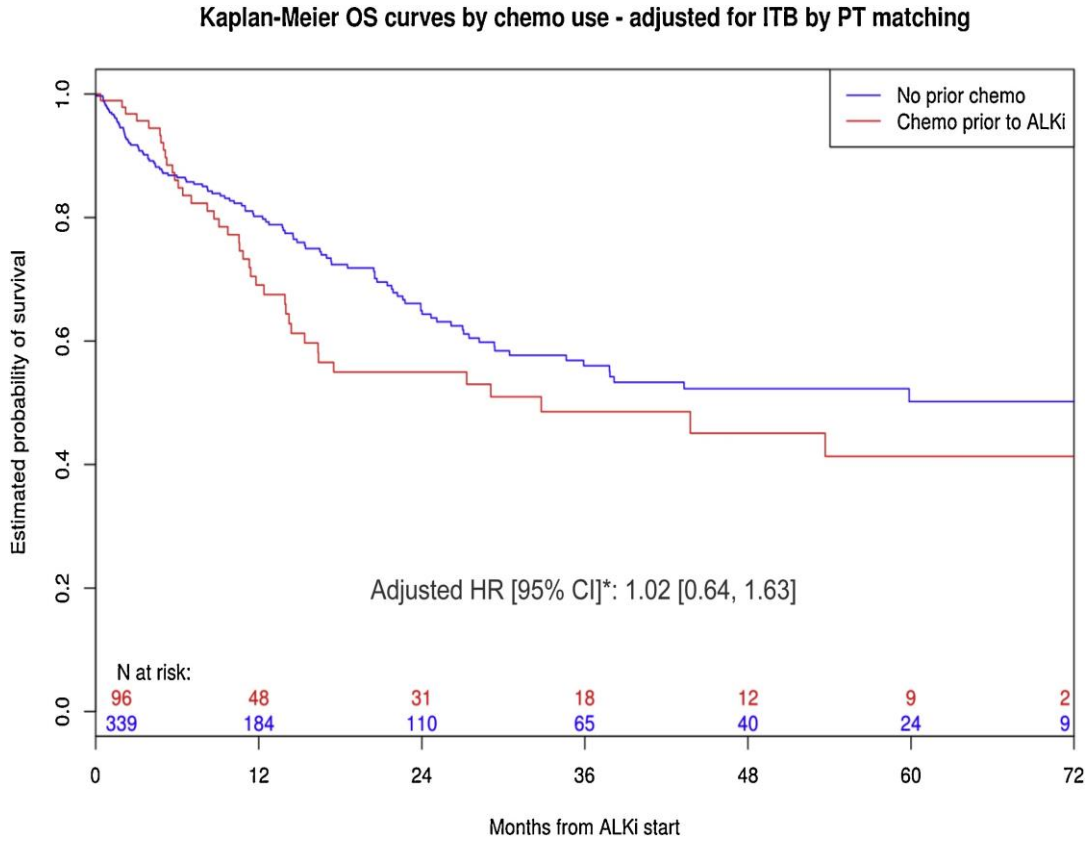
Comprehensive testing needed



•Aggarwal C, et al. J Clin Oncol. 2022;doi:10.1200/JCO/2022.40.16_suppl9022.

Timely





Impact of delaying initiation of anaplastic lymphoma kinase inhibitor treatment on survival in patients with advanced non-small-cell lung cancer Sheinson et al.Lung Cancer (2020) **143** Pages 86-92 (DOI: 10.1016/j.lungcan.2020.03.005

Need for Biomarker status for MDT discussion

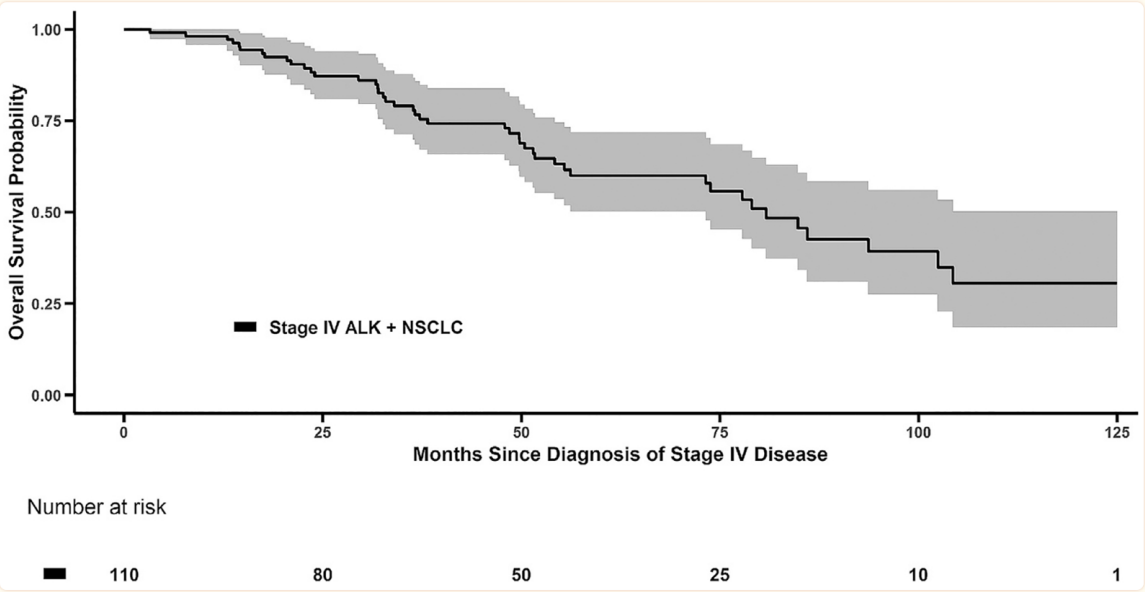
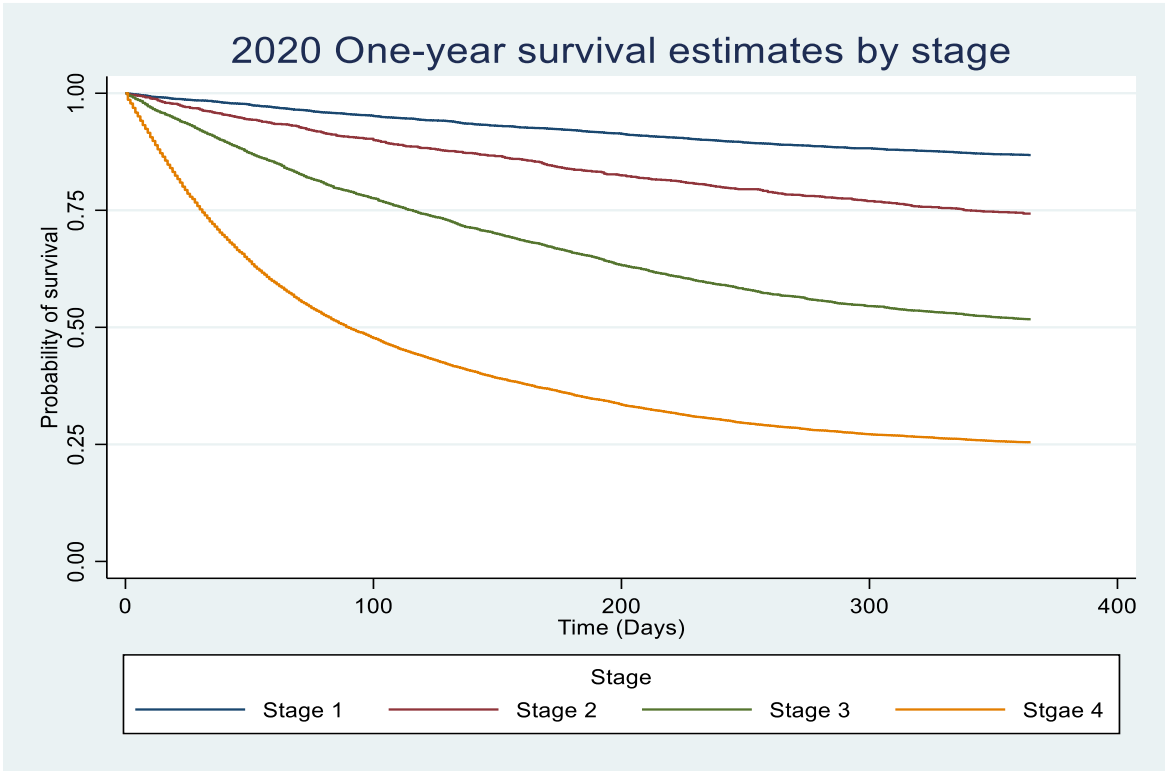


Figure 1.

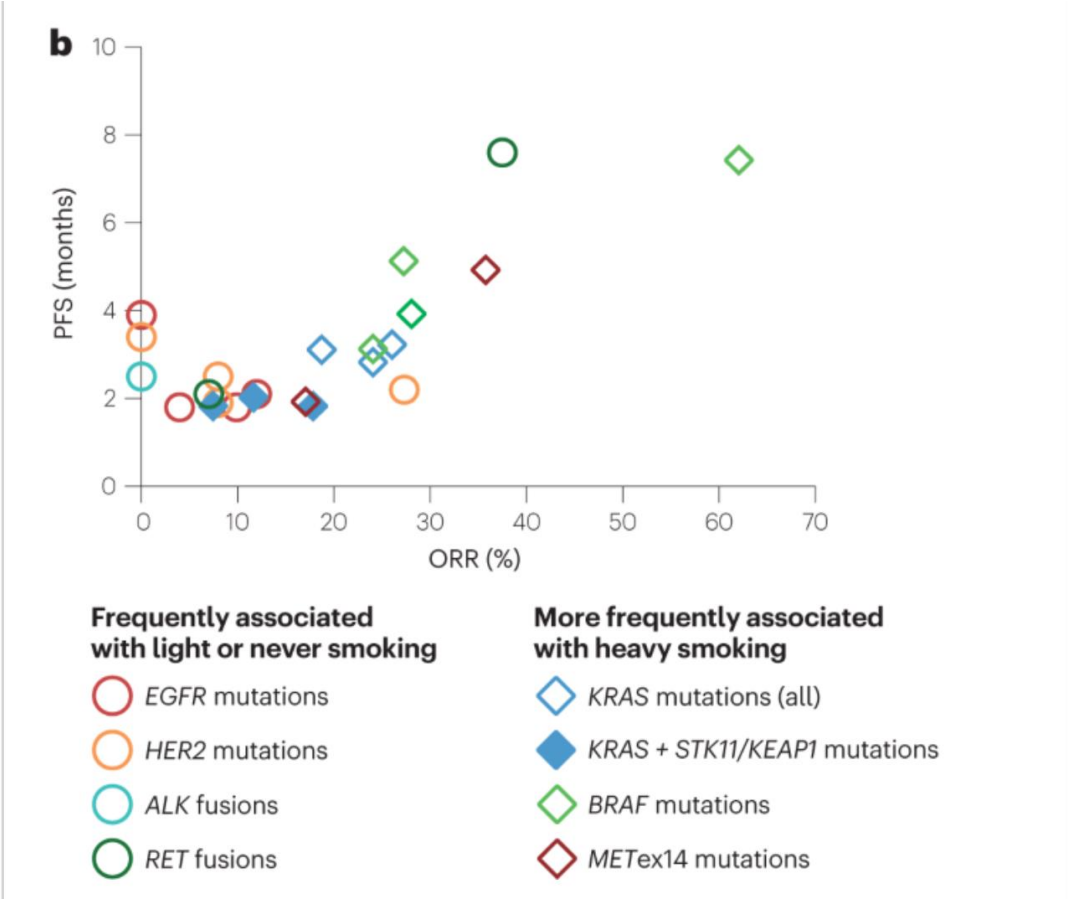
Overall survival from diagnosis of stage IV anaplastic lymphoma kinase gene rearrangement positive (*ALK*-positive) NSCLC. The 95% confidence interval is indicated by the shaded area.



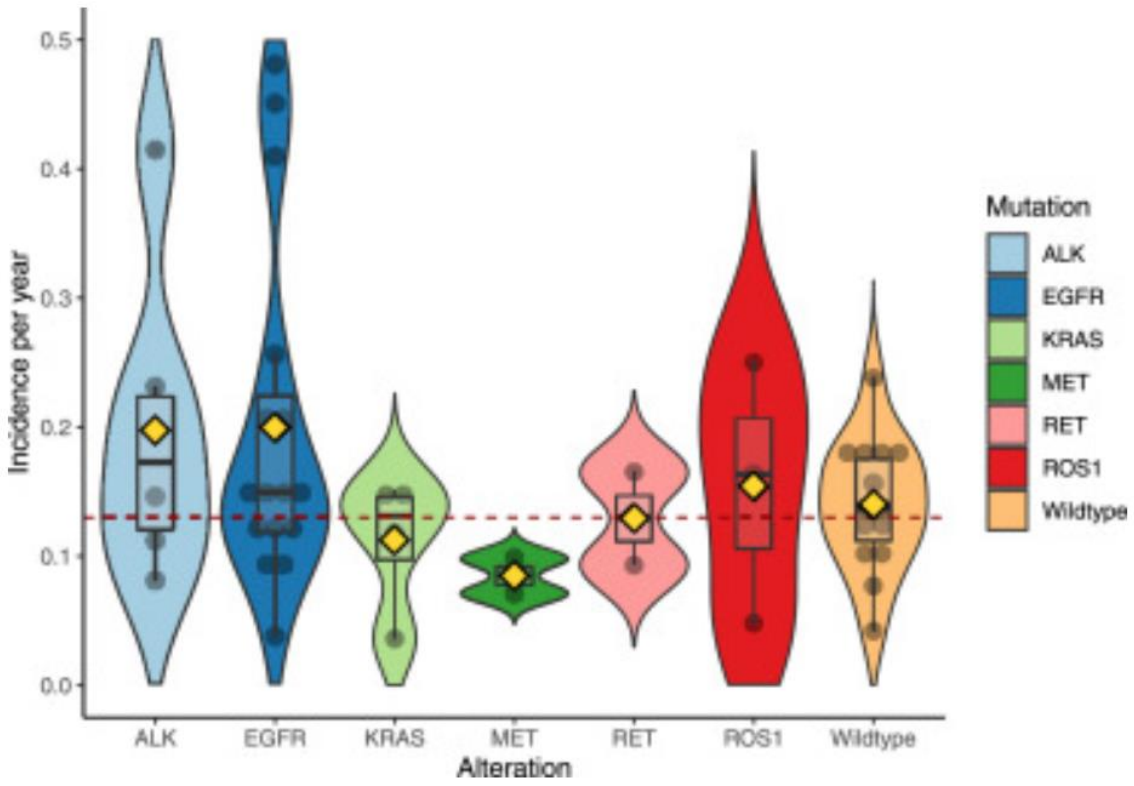
Pacheco et al J Thorac Oncol. 2019 Apr;14(4):691-700. doi: 10.1016/j.jtho.2018.12.014. Epub 2018 Dec 30. PMID: 30599201; PMCID: PMC7310567.

National Lung Cancer Audit Report 2020
https://www.rcplondon.ac.uk/projects/outputs/nlca-annual-report-2022

Genomics give important insights into behaviour and response to other treatments

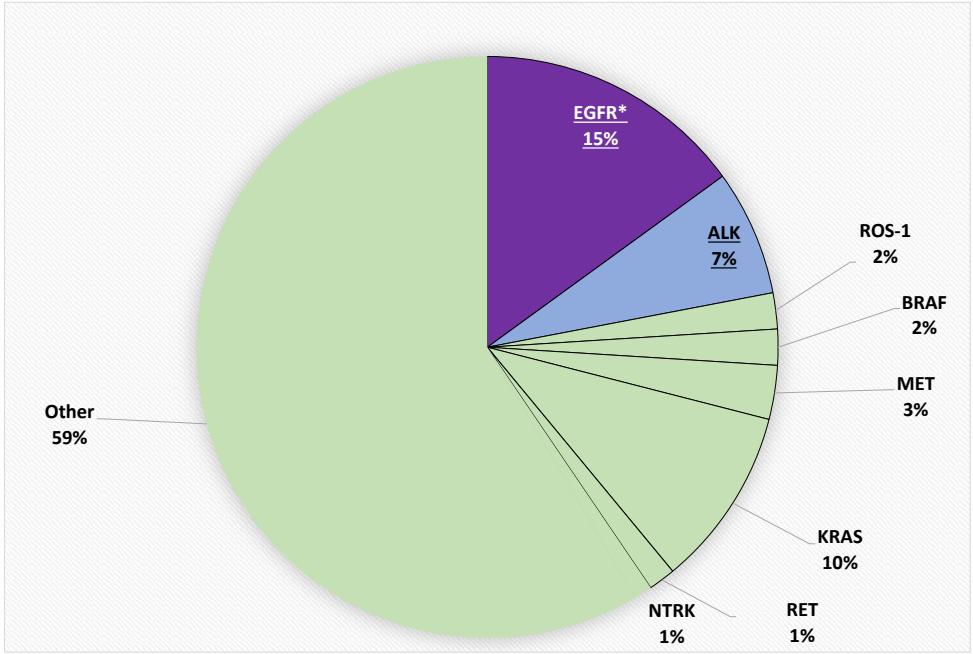


Otano, I., Ucero, A.C., Zugazagoitia, J. *et al.* *Nat Rev Clin Oncol* **20**, 143–159 (2023).



Gillespie et al JTO 2023
DOI:https://doi.org/10.1016/j.jtho.2023.06.017

Biomarker Status Impact on Surgically Treated Lung Cancer



Common EGFR Mutations

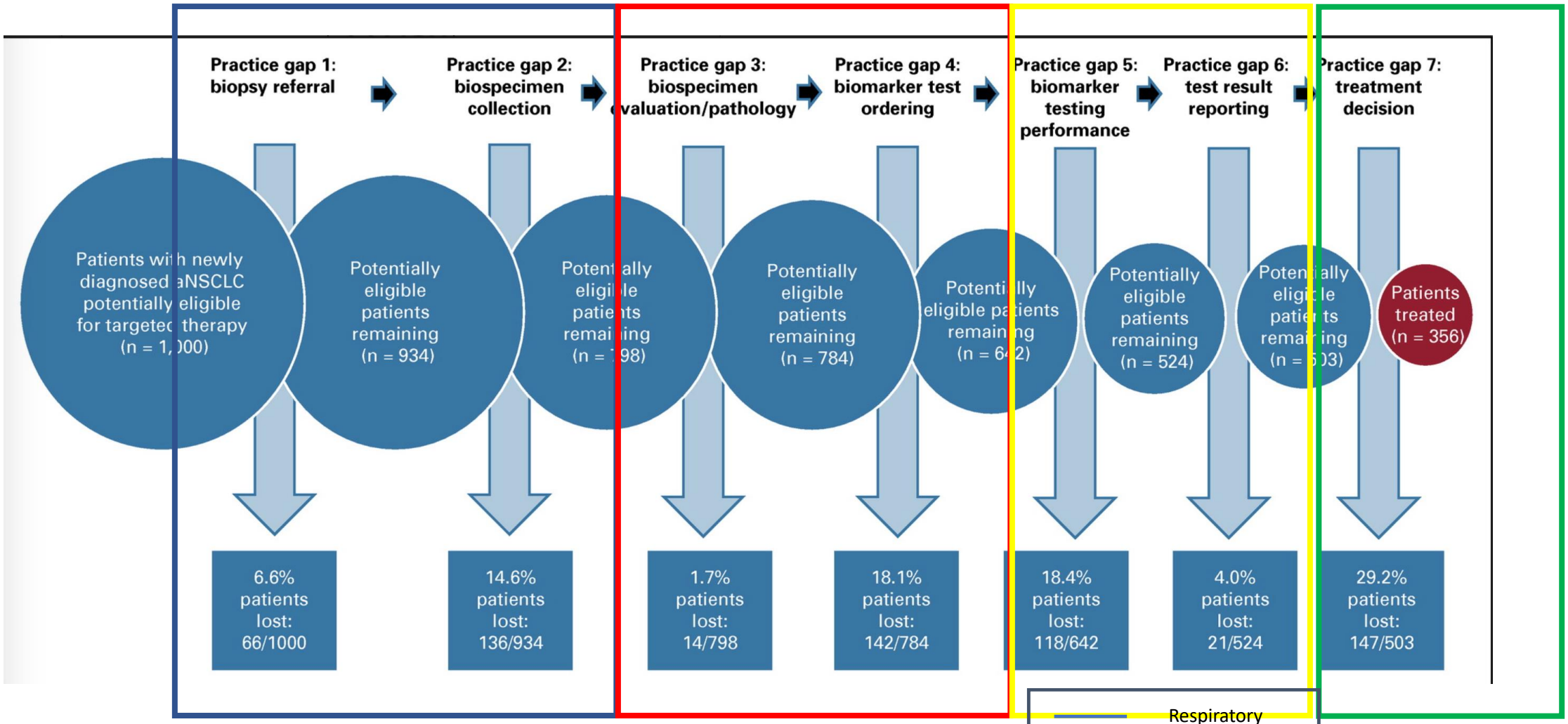
Surgery → Adjuvant chemotherapy (if appropriate) → Osimertinib

EGFR/ ALK Wildtype

Neo-Adjuvant chemotherapy-immunotherapy → Surgery

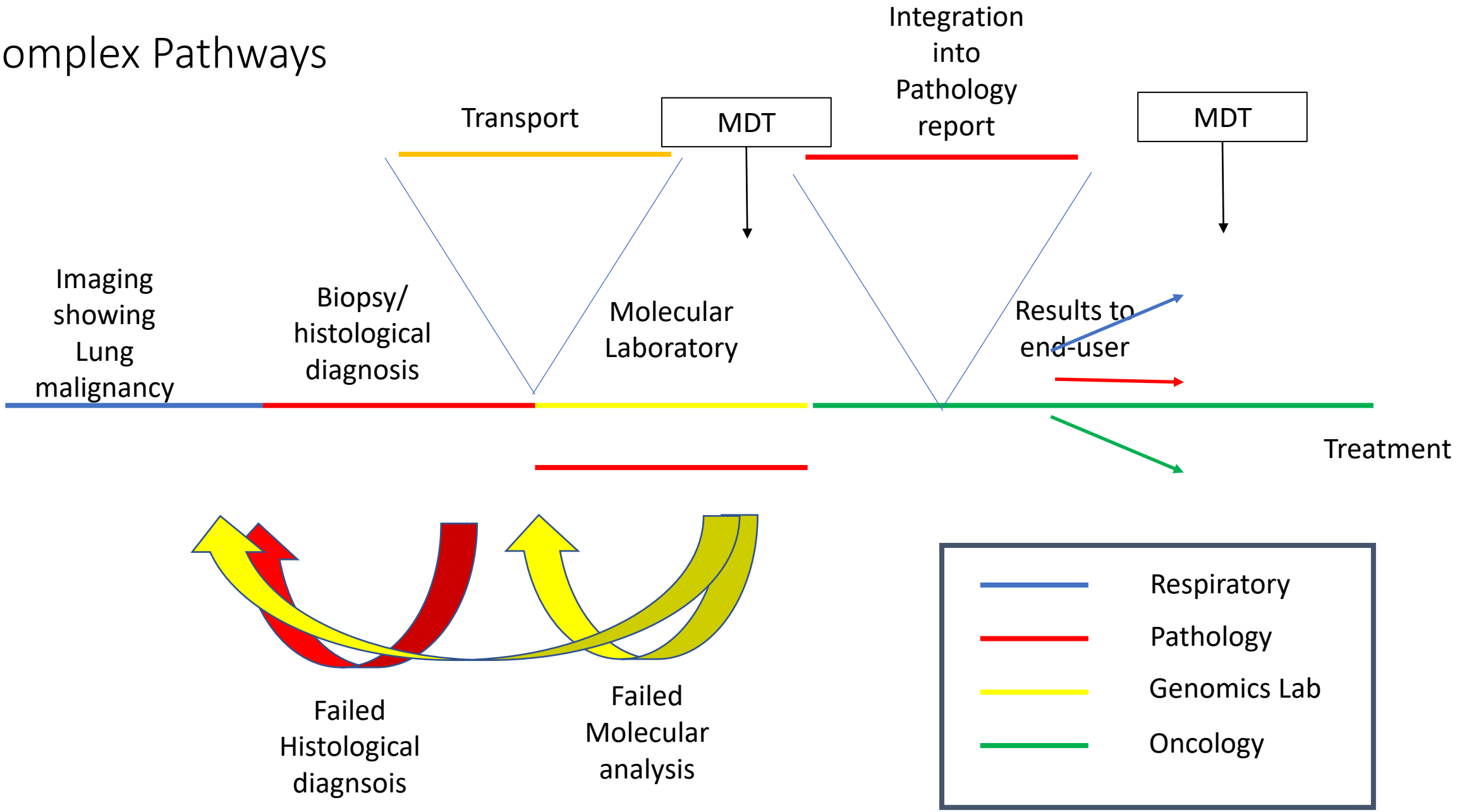
Surgery → Adjuvant chemotherapy (if appropriate) → Adjuvant Immunotherapy (if received chemotherapy and PDL1 >50%)

Barriers to Precision Therapy : a Team Problem



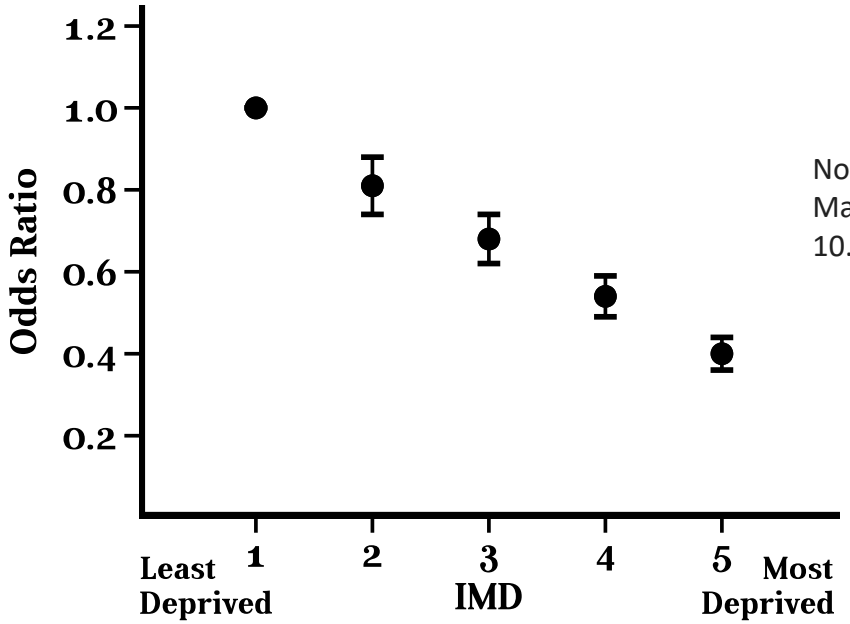
Impact of Clinical Practice Gaps on the Implementation of Personalized Medicine in Advanced Non–Small-Cell Lung Cancer
Sadik et al.
JCO Precision Oncology 2022 :6

Complex Pathways



Biology	Technical	Organisational	Society
Small Biopises	Evolving testing/technologies	Complexity of pathways: limited ownership	Pressure from patient/ family
Necrosis/ Low tumour content	Evolving treatment landscape	Artificial split between genomic tests and pathology tests	Pressure from Government/ Management
Rare but significant abnormalities	Fusions/ Complex abnormalities	Limited involvement of end users in set-up of centralisation model	Pressure from colleagues
Detioriating patient	Incompatible requesting and reporting systems	Separation of Test Directory from funding decisions	Data protection legislation Risk adverse/ poor knowledge in IG department
	Separate funding for hardware	Funding decisions match to trial entry criteria	
		Time limited funding	

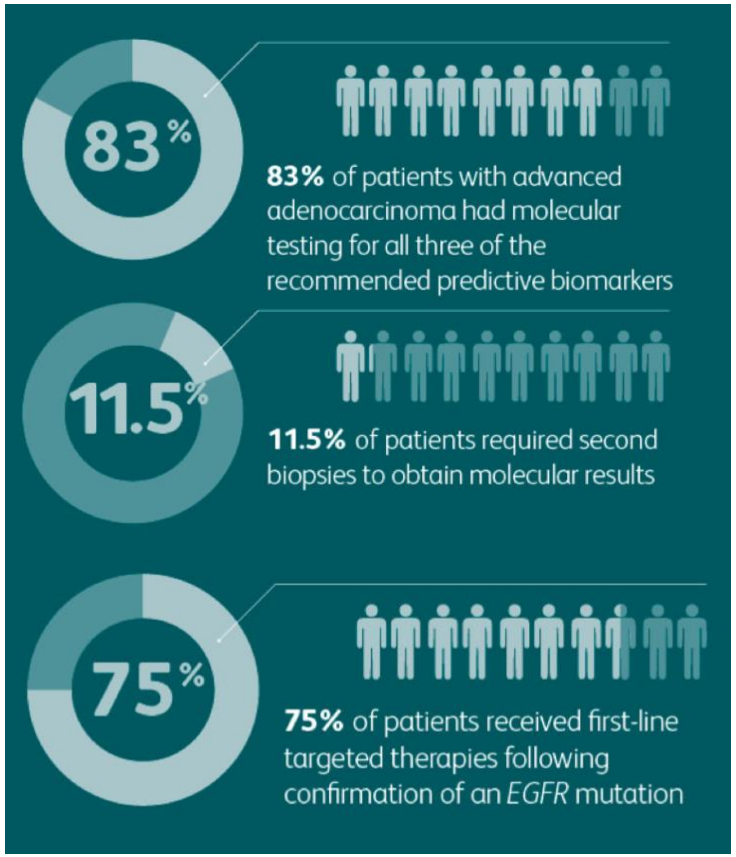
Need equitable access



Norris et al J Thorac Oncol. 2023 May 4:S1556-0864(23)00522-1. doi: 10.1016/j.jtho.2023.04.018

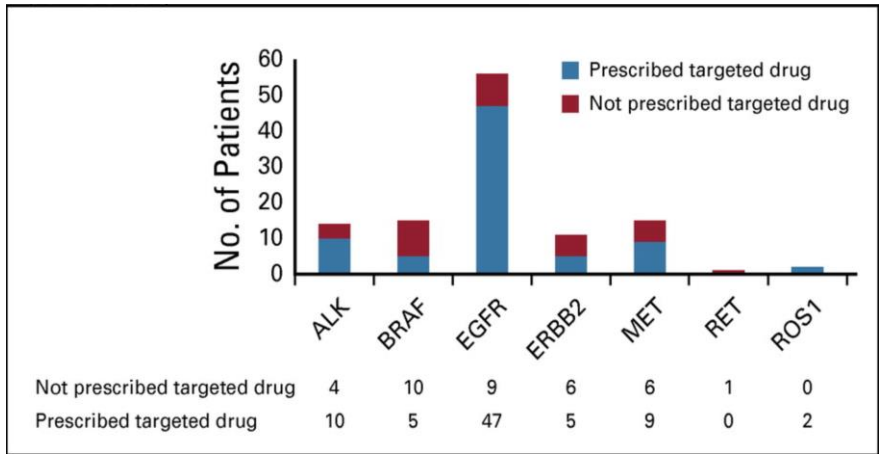
Molecular testing in advanced lung cancer*

- * UK NHS 2017



- Median turnaround time from tissue acquisition to result was 18 days for EGFR mutation testing

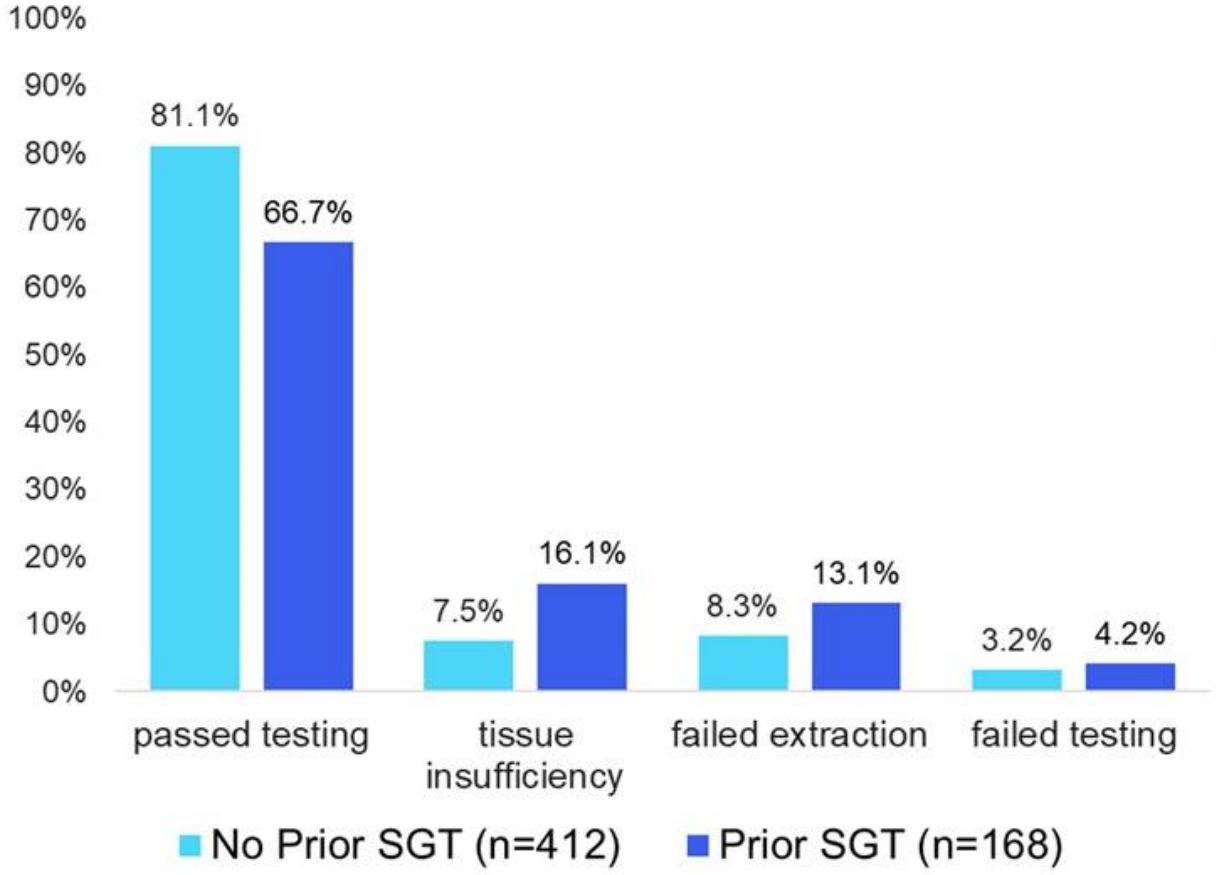
Barriers to prescribing targeted therapies

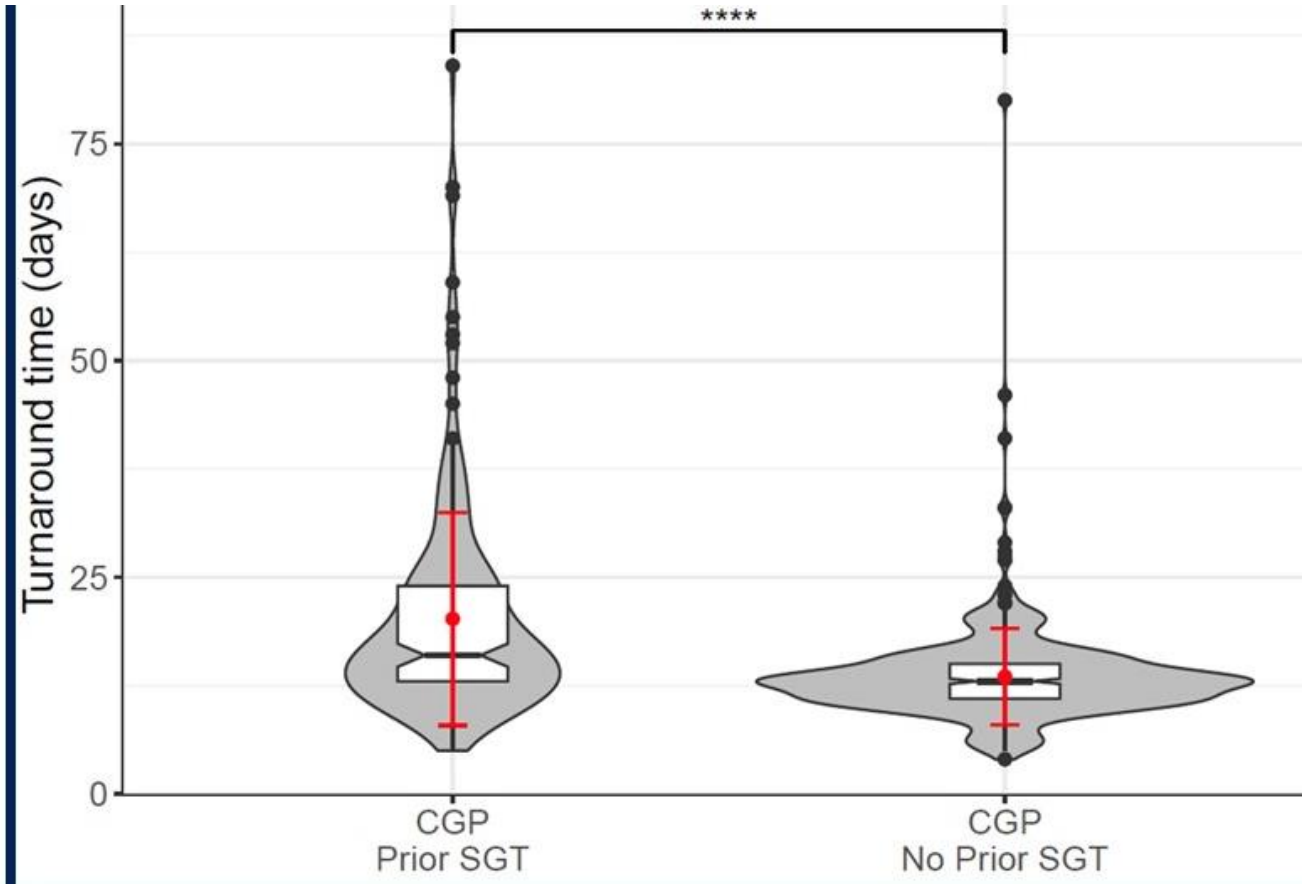


Reasons for not prescribing included:

- Preference
- Toxicity concerns or poor PS
- Urgent treatment required while awaiting NGS results
- Absence of metastatic disease
- NGS result not documented

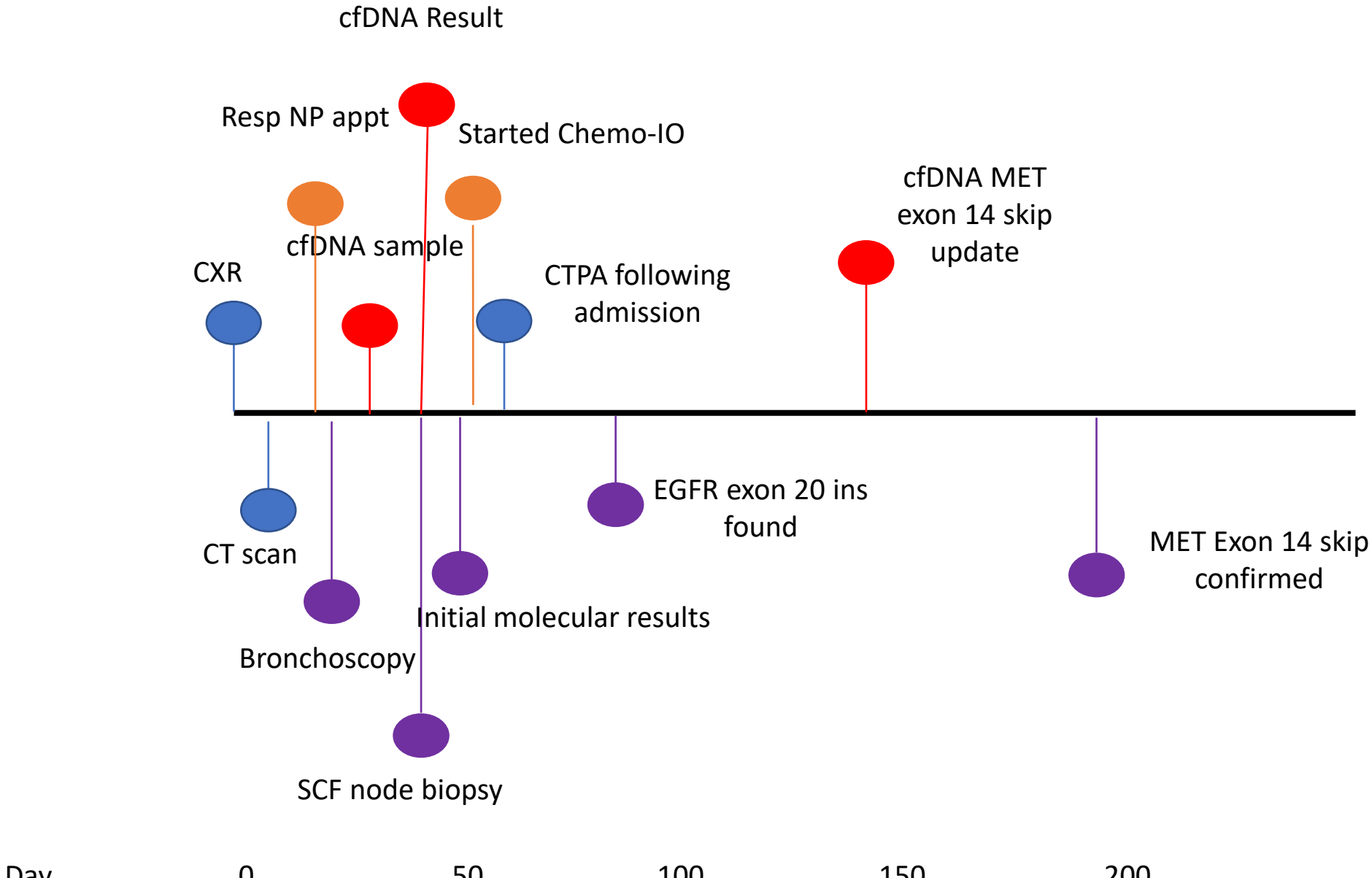
Single Gene Testing is detrimental to comprehensive molecular testing





Nesline et al
DOI: 10.1200/JCO.2023.41.16_suppl.6506 *Journal of Clinical Oncology* 41, no. 16_suppl (June 01, 2023) 6506-6506.

Clive's Timeline



	Priority	Cost	Pathway Redesign	Benefits	Dependencies
Single comprehensive report	High	Minimal	Variable	Minimises error Maximises opportunities for treatment	Easier with integrated LIMS (Laboratory Information Management System)
TAT Audit (Biopsy to end-user: + all steps in pathway)	High	Minimal	Minimal	Allows identification of problems	-
Rationale use of cfDNA	High	Moderate to High	Moderate	Speed time to molecular results and treatment Reduced rebiopsy rate Somatic vs germline	Stage dependent Commercial vs non-commercial testing
Daily Transport	High	Minimal to moderate	Minimal	Prevent delays	
Genomic Friendly Tissue handling	High	Minimal to moderate	Minimal to moderate	Reduce failure rate	6 day working
Tissue Coordinator	High	Minimal	Nil	Ownership/ smooth pathway Reduce “Chasing”	

	Priority	Cost	Pathway Redesign	Benefits	Dependencies
Funding for molecular test regardless of technology used	Medium	Minimal	Moderate	”Fairer” Allows appropriate integration of and move between technologies	NHS Management
Fully Integrated requesting/ reporting	Medium	Moderate to high	Moderate	Speed information flow Ensure all parties have full information	IT investment (hardware and people)
Report full analysis of panel beyond NTD	Medium	Moderate	Minimal	Reduces retrospective reporting Enable research Maximises benefit of panel anlysis	Workforce Training Clinician acceptance
Sharing of Genomic analysis and outcomes	Future	Minimal	Moderate	Reduces Analysis time Assessment of impact of genomics on SoC therapies Enable research	IG hurdles IT hurdles
Marry up costs/ savings of molecular testing with those of drugs	Future	?	Large	Most effective use of resources in **National** HS Promote best practice	Completion of data gaps Clinician buy-in

Summary

- Lung Cancer is not just one disease
- Timely and comprehensive genomic analysis key component
- Not just in stage IV!
- Multiple barriers to overcome