Inside the Issue: Integrating ALK-Targeted Therapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, July 18, 2024
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Professor Ben Solomon, MBBS, PhD

Moderator

Neil Love, MD

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Faculty

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Chair, Thoracic Malignancies
Oncology Department
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Lausanne, Switzerland

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Research To Practice
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Medical Oncologist
Head of Lung Medical Oncology Service
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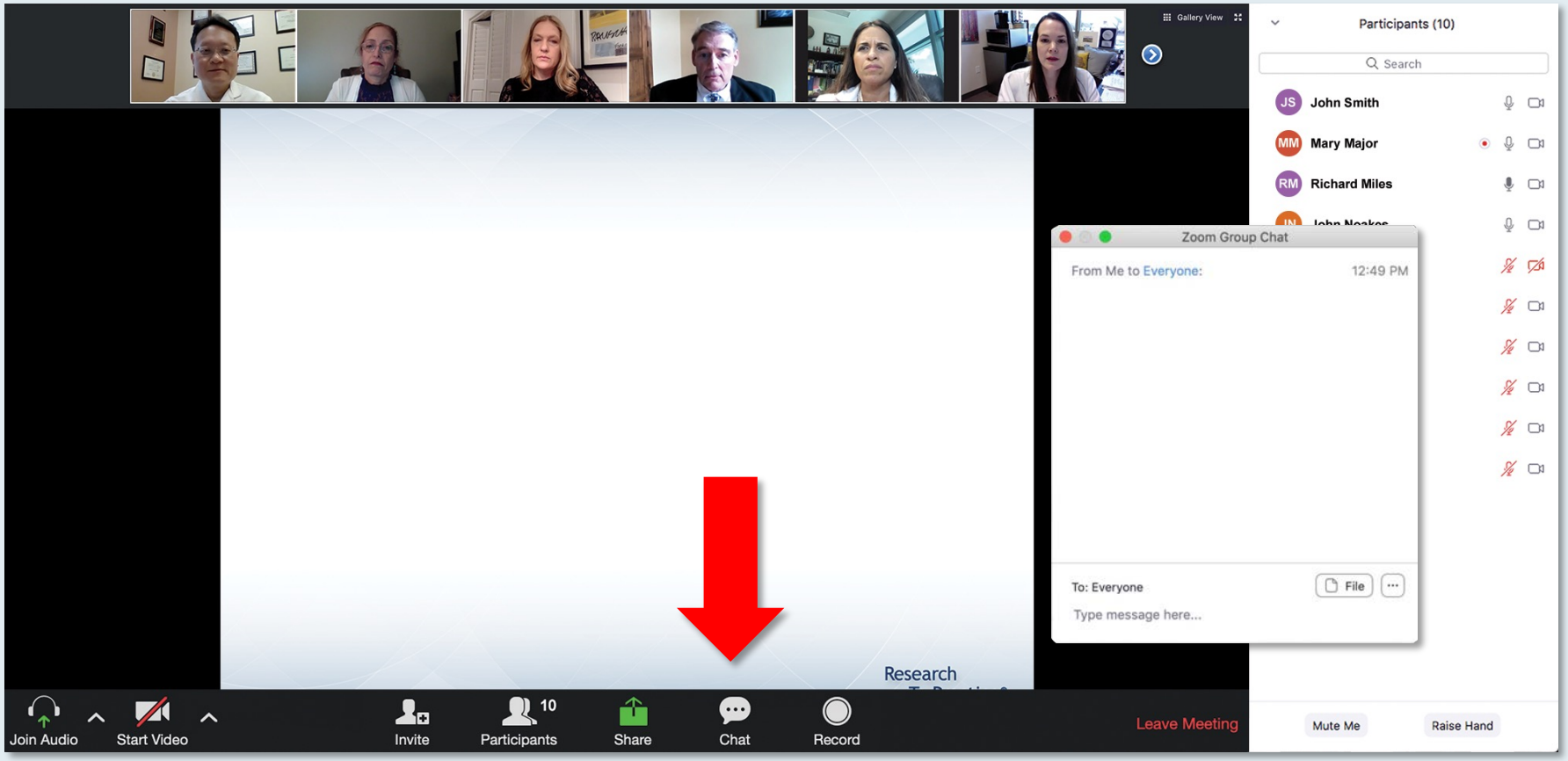

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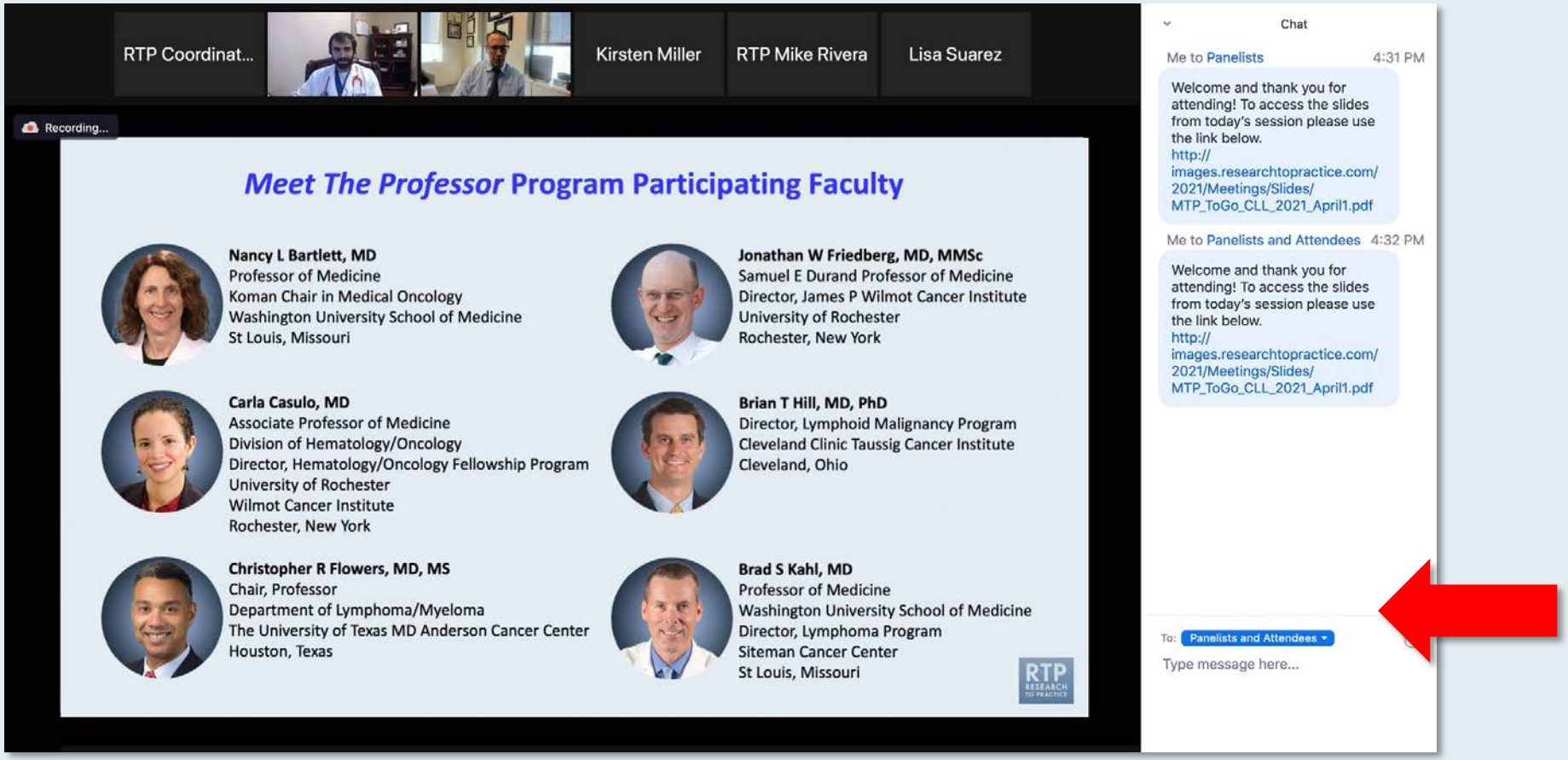

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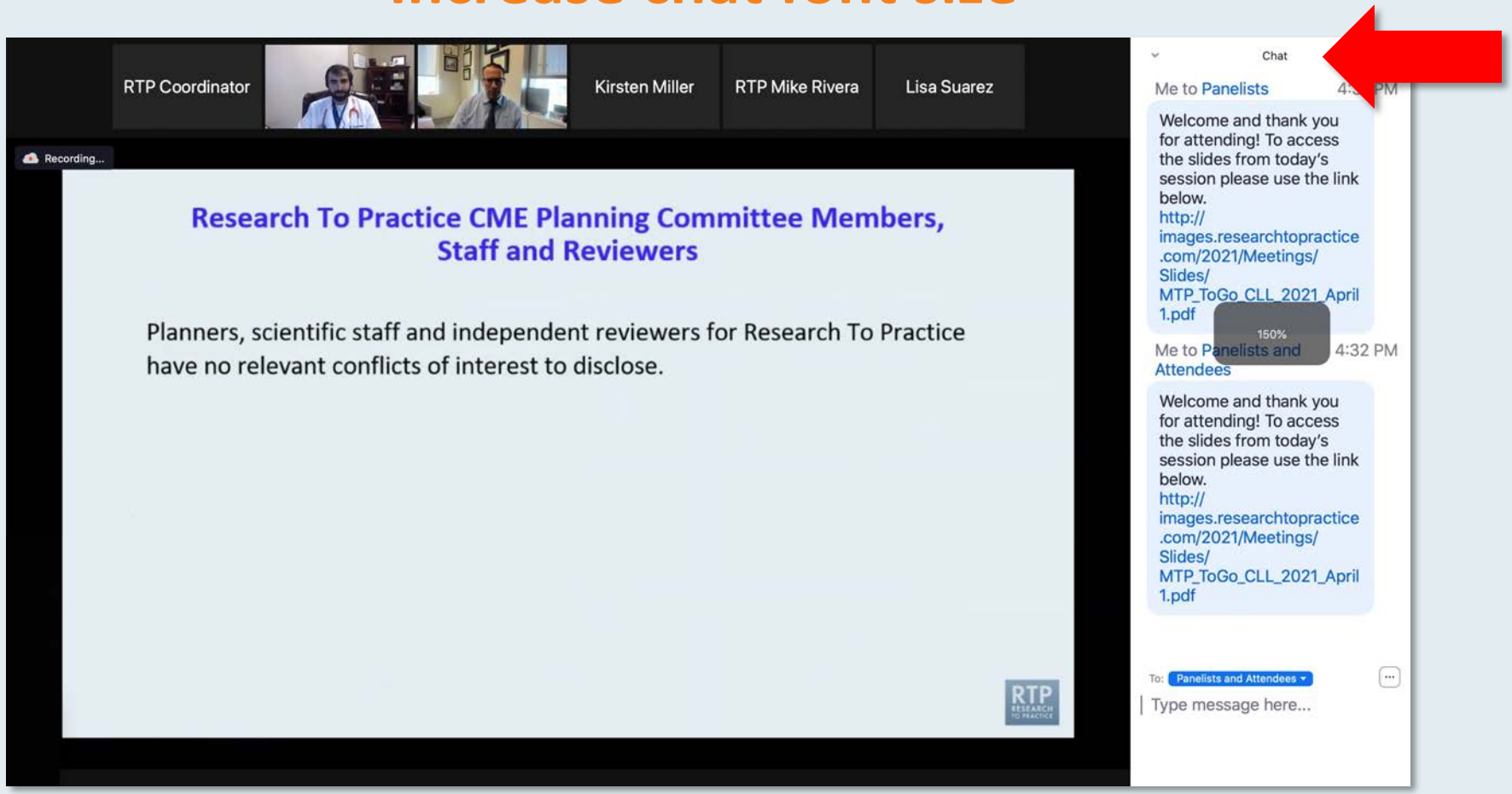

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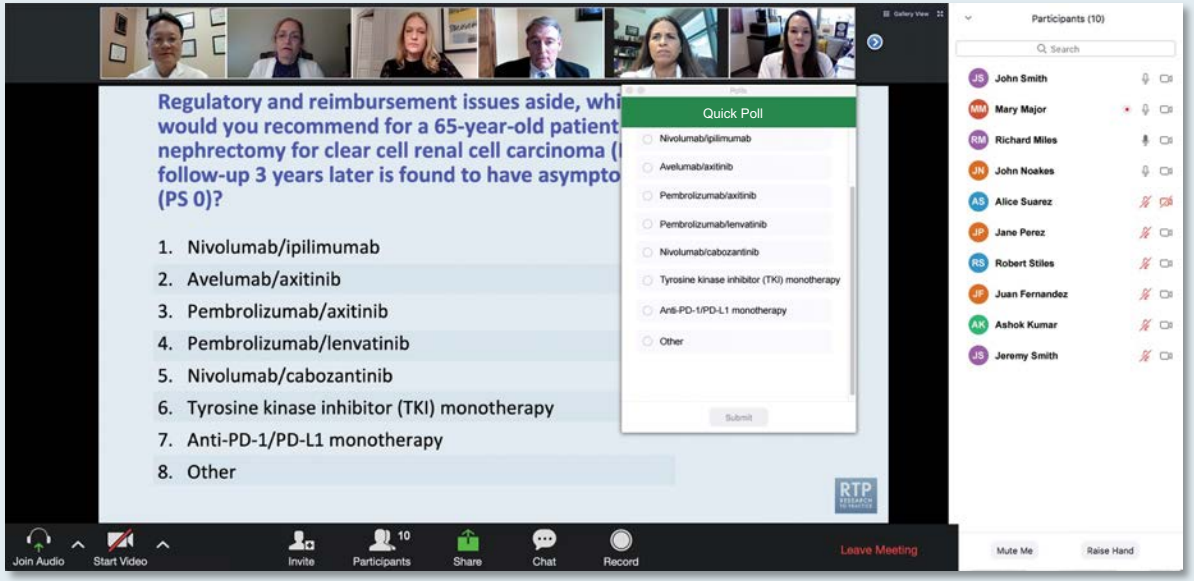

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WITH DR NEIL LOVE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Targeted Therapy for Non-Small Cell Lung Cancer

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MASSACHUSETTS GENERAL HOSPITAL

DR KAREN RECKAMP
CEDARS-SINAI CANCER

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Inside the Issue: Integrating HER2-Targeted Strategies into the Management of Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 21, 2024
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD
John Strickler, MD

Moderator

Neil Love, MD

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Inside the Issue: Optimizing the Diagnosis and Treatment of Neuroendocrine Tumors

A CME/MOC-Accredited Live Webinar

Thursday, August 29, 2024
5:00 PM – 6:00 PM ET

Faculty

Pamela Kunz, MD
Simron Singh, MD, MPH

Moderator

Neil Love, MD

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Data + Perspectives: Clinical Investigators Discuss the Role of CAR T-Cell Therapy for Patients with Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia

Part 1 of a 2-Part CME Satellite Symposium Series During the Society of Hematologic Oncology 2024 Annual Meeting

Wednesday, September 4, 2024

11:46 AM – 12:46 PM CT

Faculty

Jason Westin, MD, MS

Additional faculty to be announced.

Moderator

Matthew Lunning, DO

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Data + Perspectives: Clinical Investigators Discuss the Current and Future Management of Diffuse Large B-Cell Lymphoma

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Laurie H Sehn, MD, MPH

Moderator

Christopher R Flowers, MD, MS

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Thank you for joining us!

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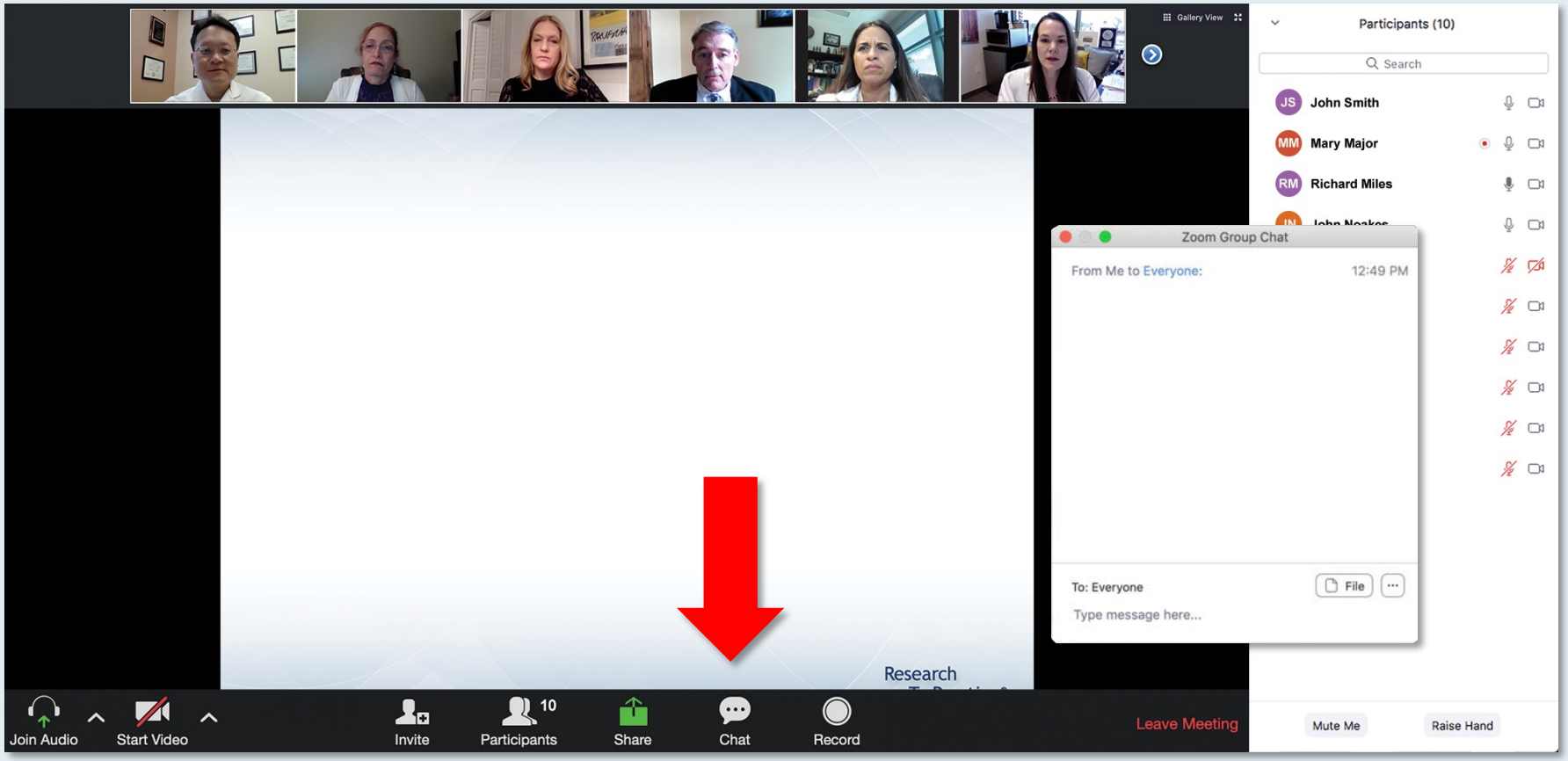

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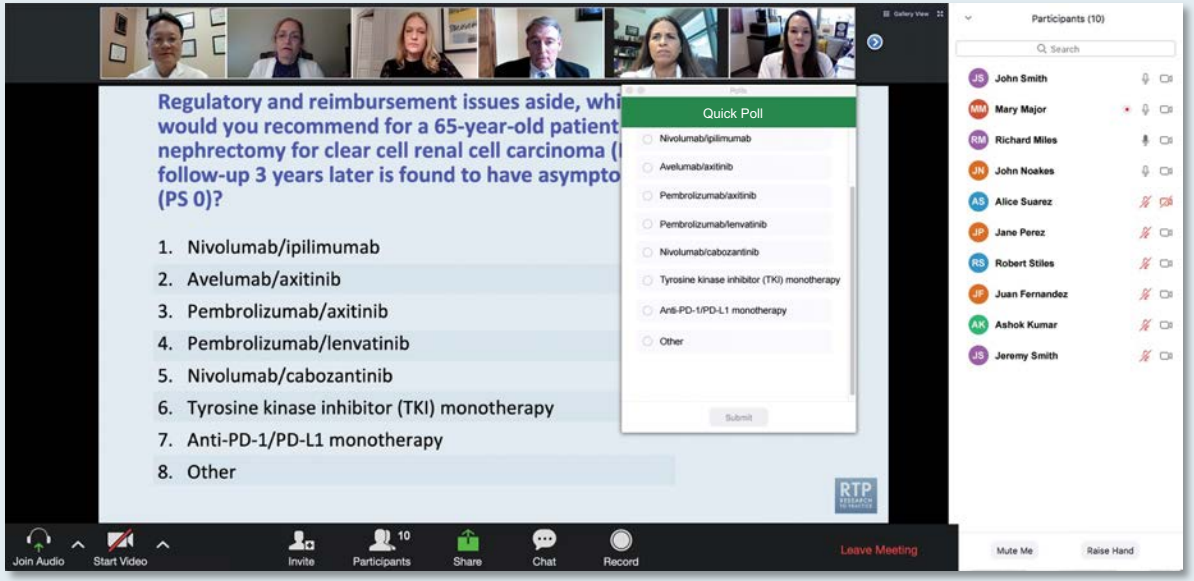

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Chair Medical Oncology

Oncology Department – CHUV

Lausanne University

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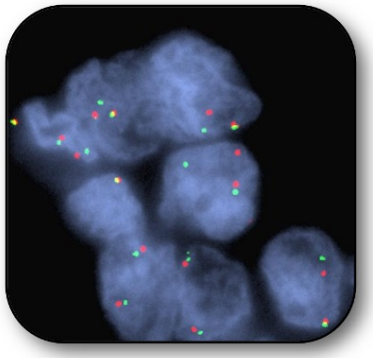

Significance of Biomarker Testing in Early-Stage Non-Small Cell Lung Cancer and Historical Management Paradigm for ALK-Positive Disease

Emerging Role and Practical Application of ALK-Targeted Therapy in Localized NSCLC

Ben Solomon

Peter MacCallum Cancer Centre

Melbourne, Australia

Agenda

Module 1: Significance of Biomarker Testing in Localized Non-Small Cell Lung Cancer (NSCLC) and Historical Management Paradigm for ALK-Positive Disease — Prof Peters

Module 2: Emerging Role and Practical Application of ALK-Targeted Therapy in Localized NSCLC — Prof Solomon

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Module 2: Emerging Role and Practical Application of ALK-Targeted Therapy in Localized NSCLC — Prof Solomon

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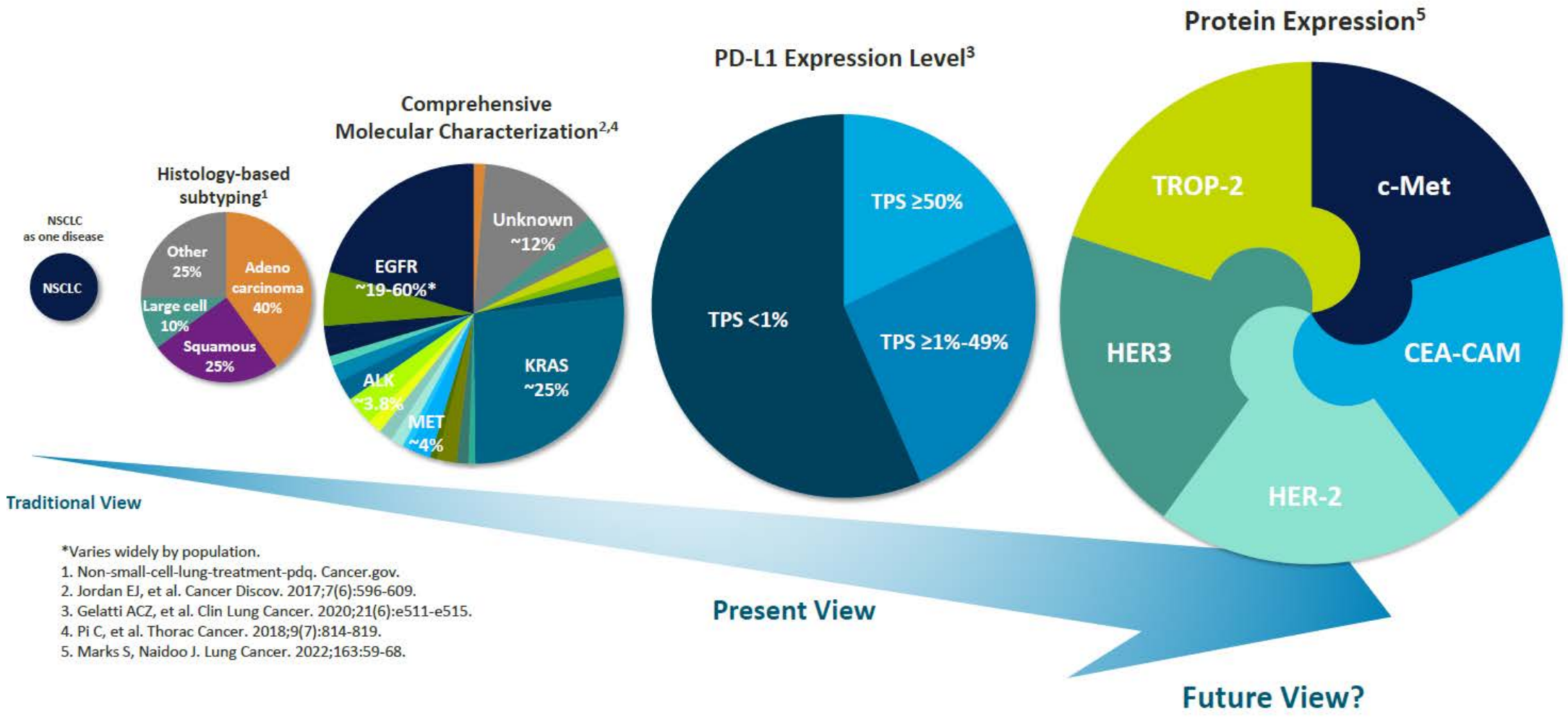
In general, do you routinely perform testing for actionable genomic alterations (AGAs) in patients with localized nonsquamous NSCLC? What testing platform(s) do you generally employ to assess for AGAs in patients with localized NSCLC?

	Perform testing?	Testing platforms
 Prof Peters	Yes, for all patients	DNA- and RNA-based NGS, RT-PCR, FISH, IHC
 Prof Solomon	Yes, for all patients	DNA- and RNA-based NGS, RT-PCR, IHC
 Dr Camidge	Yes, for all patients	DNA- and RNA-based NGS, FISH, ctDNA
 Dr Chaft	Yes, for all patients	DNA- and RNA-based NGS, RT-PCR, IHC
 Dr Dagogo-Jack	Yes, for all patients except those with tumors <3 cm and negative lymph nodes	DNA- and RNA-based NGS; for Stage IB, selective EGFR PCR
 Dr Liu	Yes, for all patients	DNA- and RNA-based NGS, IHC

NGS = next-generation sequencing; RT-PCR = reverse transcription polymerase chain reaction; FISH = fluorescence in situ hybridization; IHC = immunohistochemistry
ctDNA = circulating tumor DNA

Paradigms in Lung Cancer Molecular Pathology – 2024



*Varies widely by population.

1. Non-small-cell-lung-treatment-pdq. Cancer.gov.
2. Jordan EJ, et al. Cancer Discov. 2017;7(6):596-609.
3. Gelatti ACZ, et al. Clin Lung Cancer. 2020;21(6):e511-e515.
4. Pi C, et al. Thorac Cancer. 2018;9(7):814-819.
5. Marks S, Naidoo J. Lung Cancer. 2022;163:59-68.

Slide (modified) courtesy of Dr. David Planchard, Institute Gustav Roussy

1. Non-small-cell-lung-treatment-pdq. Cancer.gov; 2. Jordan EJ et al. *Cancer Discov.* 2017;7(6):596-609; 3. Gelatti ACZ et al. *Clin Lung Cancer.* 2020;21(6):e511-e515; 4. Pi C et al. *Thorac Cancer.* 2018;9(7):814-819; 5. Marks S and Naidoo J. *Lung Cancer.* 2022;163:59-68.

Courtesy of Prof Solange Peters, MD, PhD

Biomarkers in NSCLC

Mandatory and highly recommended molecular biomarkers		
MANDATORY **ESCAT I**	***ALK***	Fusion Mutation as a mechanism of resistance
	BRAF	V600E mutation
	EGFR	Common mutation: Del19, L858R Uncommon mutation: G719X, L861Q, S7681 T790M mutation
	MET	Mutation exon 14 skipping
	NTRK	Fusion
	RET	Fusion
	ROS1	Fusion Mutation as a mechanism of resistance
Highly RECOMMENDED **ESCAT II**	***EGFR***	Exon 20 Insertion
	HER2	Mutations
	KRAS	G12C mutation
	MET	Amplification

Emerging molecular biomarkers		
Predictive biomarkers for TARGETED THERAPY ESCAT III	***BRAC1*** ***BRAC2***	Mutation
	FGFR	Fusion Mutation
	HER2, HER3 ***B7-H3*** ***CEACAM5*** ***MET, TROP2***	Protein expression
	PI3KA	Mutation
	NRG1	Fusion
Predictive biomarkers for IMMUNO THERAPY	***KEAP1***	Mutation
	MTAP	Protein expression
	NOTCH	Mutation
	STK11	Mutation
	SMARCA4	Mutation
	TMB	Mutations

Exploratory and potential molecular biomarkers		
Predictive biomarkers for TARGETED THERAPY	***TP53*** ***RB1***	Mutation
	RBM10	Mutation
	AKT ***CTNNB1*** ***JAK2/3***	Mutation
	NRAS	Mutation
	HRAS	Mutation
Predictive biomarkers for IMMUNO THERAPY	High **TCR** clonality	
	High **CD8** density	
	High **dNLR/LIPI**	
	Adequate **microbiota** Gut and tumor DNA, metabolites, products	

Hofman P et al. Virchows Arch 2023 Oct 6. doi: 10.1007/s00428-023-03651-1.

Courtesy of Prof Solange Peters, MD, PhD

Different biomarkers: different technology

Mutations[1,2]	Fusion genes[1,2]	Gene copy number[1–5]	Protein expression[1,2,6,7]
EGFR (many)	*ALK*	*MET*	PD-L1
KRAS G12C	*ROS1*		CD_3, CD8, CD68
BRAF V600E	*NTRK1/2/3*		*ALK, ROS1, NTRK*
MET ex14 skipping	*RET*		MET, $CEACAM_5$
HER2	*NRG1*		Trop2?, HER_2, HER_3?
Appropriate technology			
DNA sequencing	RNA sequencing FISH? IHC screening	FISH CISH CGH NGS	IHC

- We need more than (just) NGS[8]
- But we do need NGS, for comprehensive coverage[8]
- IHC still has a place[8]
- And so does ISH[8]

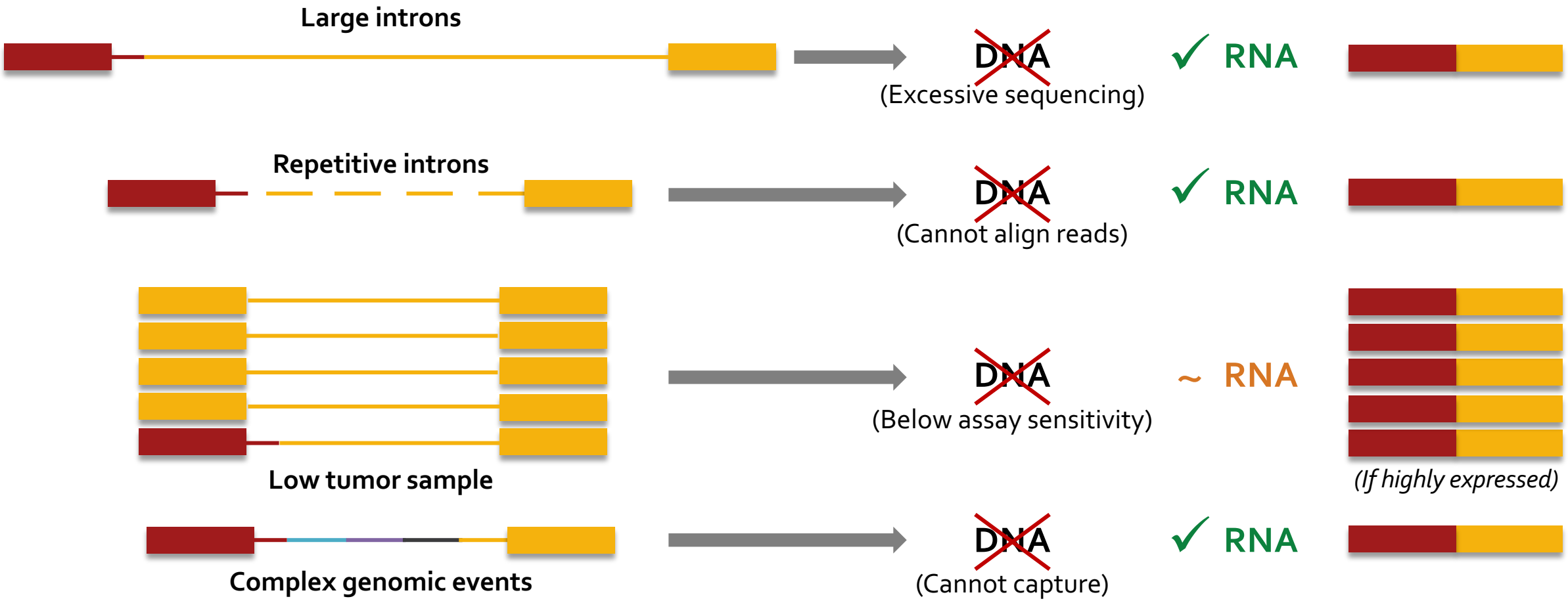
- CGH, comparative genomic hybridisation; CISH, chromogenic *in situ* hybridisation; ex14, exon 14; FISH, fluorescence *in situ* hybridisation; IHC, immunohistochemistry; ISH, in *situ* hybridisation; NGS, next-generation sequencing.

- 1. Kerr KM et al. Lung Cancer 2021;154:161–75; 2. Penault-Llorca F et al. Virchows Arch 2022;481:351–66; 3. Dimou A et al. PLoS One 2014;9:e107677; 4. Tchinda J et al. BioTechniques 2006;41:385–92; 5. Yoo SB et al. Lung Cancer 2010;67:301–5; 6. Wang J et al. J Exp Clin Cancer Res 2014;33:109; 7. Yaegashi LB et al. Front Immunol 2021;12:714230; 8. Speaker's personal communication.

Courtesy of Prof Solange Peters, MD, PhD

Proper Biomarker Testing Matters: DNA vs RNA

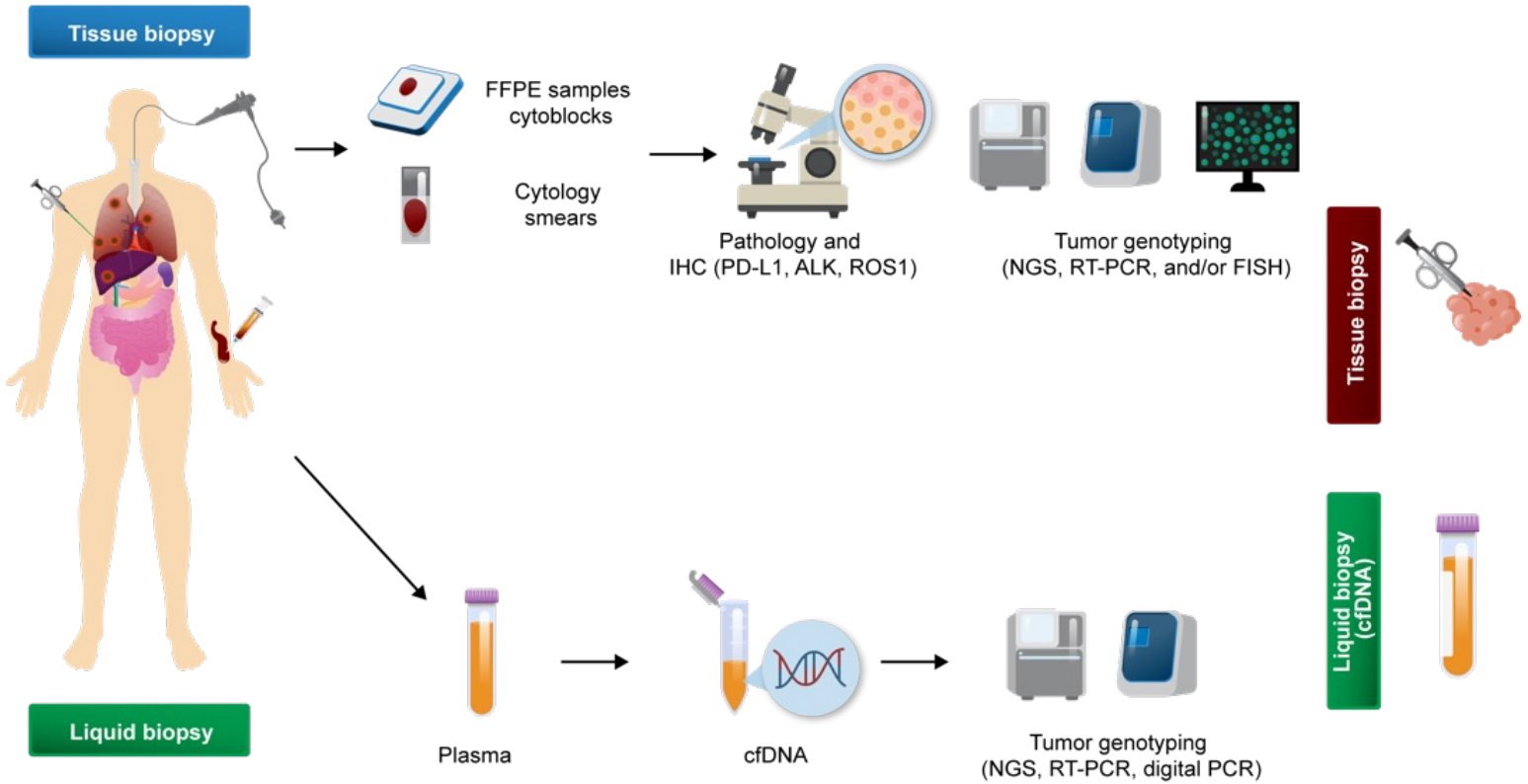
False Negatives With DNA-Based NGS: RNA-Based Approaches May Overcome Limitations[1]



Courtesy of Prof Solange Peters, MD, PhD

Proper Biomarker Testing Matters: Tissue vs Liquid Biopsy

Liquid Biopsy in Advanced NSCLC (2021 IASLC Consensus)[1]



Advantages	Disadvantages
• Pathology information • Assessment of DNA and non-DNA biomarkers • PD-L1 assessment	• Longer TAT • Limited tissue quantities • Invasive • At PD, rebiopsy not always feasible • Tumor heterogeneity
• High concordance rate • Rapid TAT • Minimally invasive • Repeatable over time • Better capture heterogeneity and clonal evolution	• Non-DNA biomarkers not evaluable • Increased costs if used concurrently with tissue testing • False negatives

Sequential
(when tissue fails)

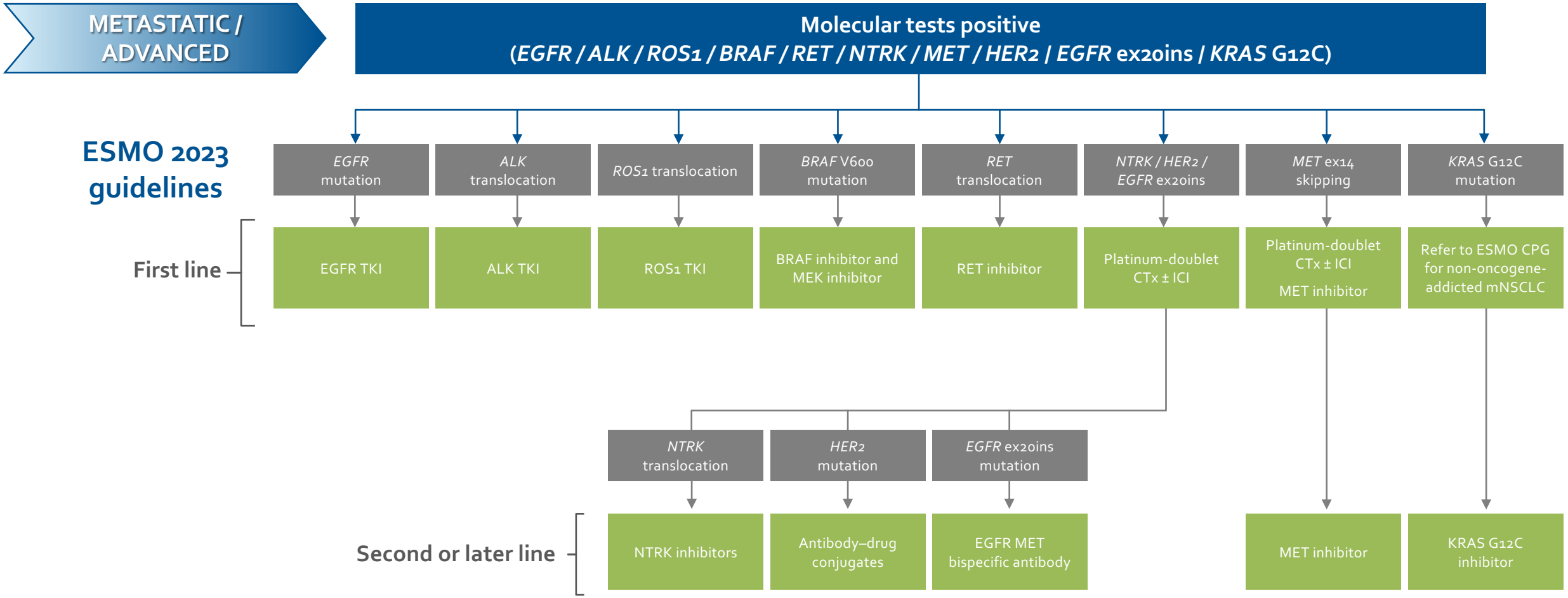
Complementary
(initiate tissue and liquid)

Plasma First
(when biopsy not possible, delayed)

Treatment Resistance

Courtesy of Prof Solange Peters, MD, PhD

Oncogene-addicted metastatic NSCLC treatment

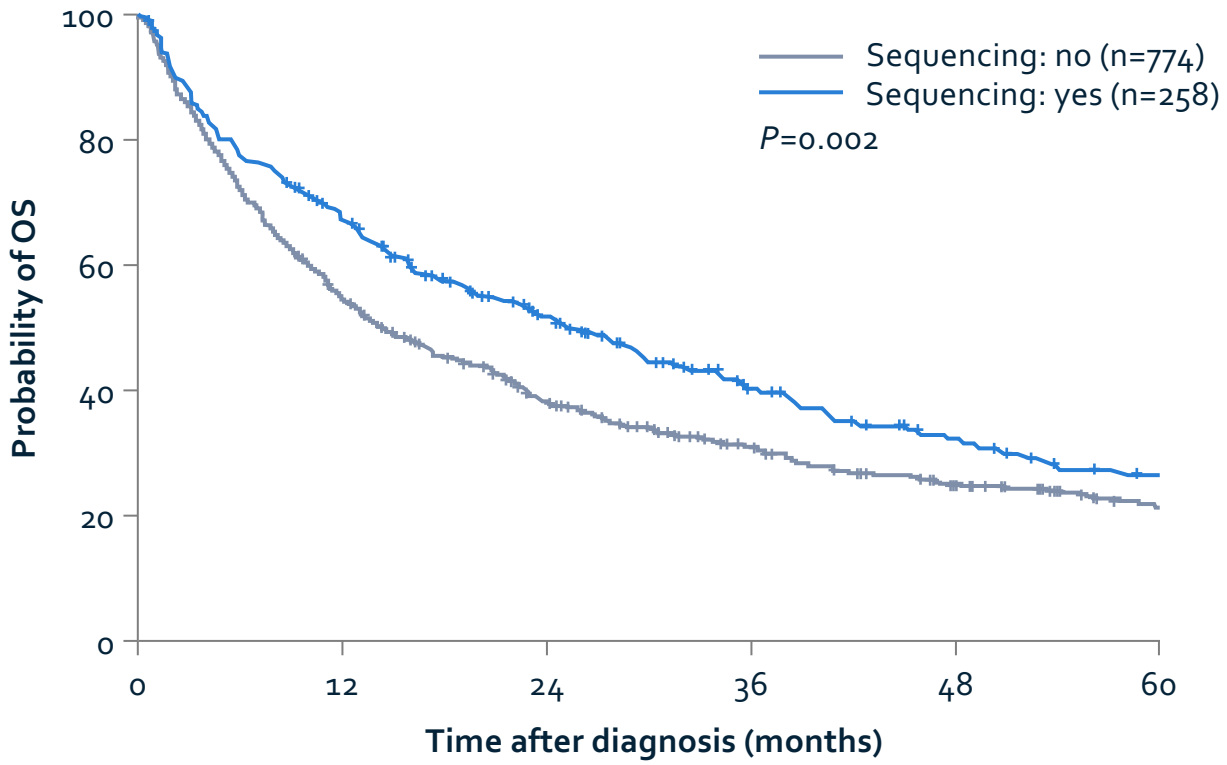


Adapted from: Hendriks LE et al. Ann Oncol 2023;34:339–57.

Courtesy of Prof Solange Peters, MD, PhD

Patients with advanced NSCLC undergoing NGS testing have longer OS

- Retrospective analysis using a large institutional database of US patients with stage IV NSCLC
- Of 928 patients with stage IV NSCLC, 295 patients underwent NGS



	NGS	No sequencing
Median OS, months (95% CI)	25.3 (19.6, 32.2)	14.6 (12.8, 17.2)

CI, confidence interval; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; OS, overall survival.

Al-Ahmadi A et al. Clin Lung Cancer 2021;22:16–22.

Courtesy of Prof Solange Peters, MD, PhD

Typical characteristics of patients with ALK+ NSCLC

Younger age compared with the general NSCLC population
Median age ~50 years[1]

CNS metastases are present in:

- **>30% patients at diagnosis [2,3]**
- **70% patients who are still living at 3 years without 2nd/3rd gen TKI[3]**

Light smokers or never smoked [1]

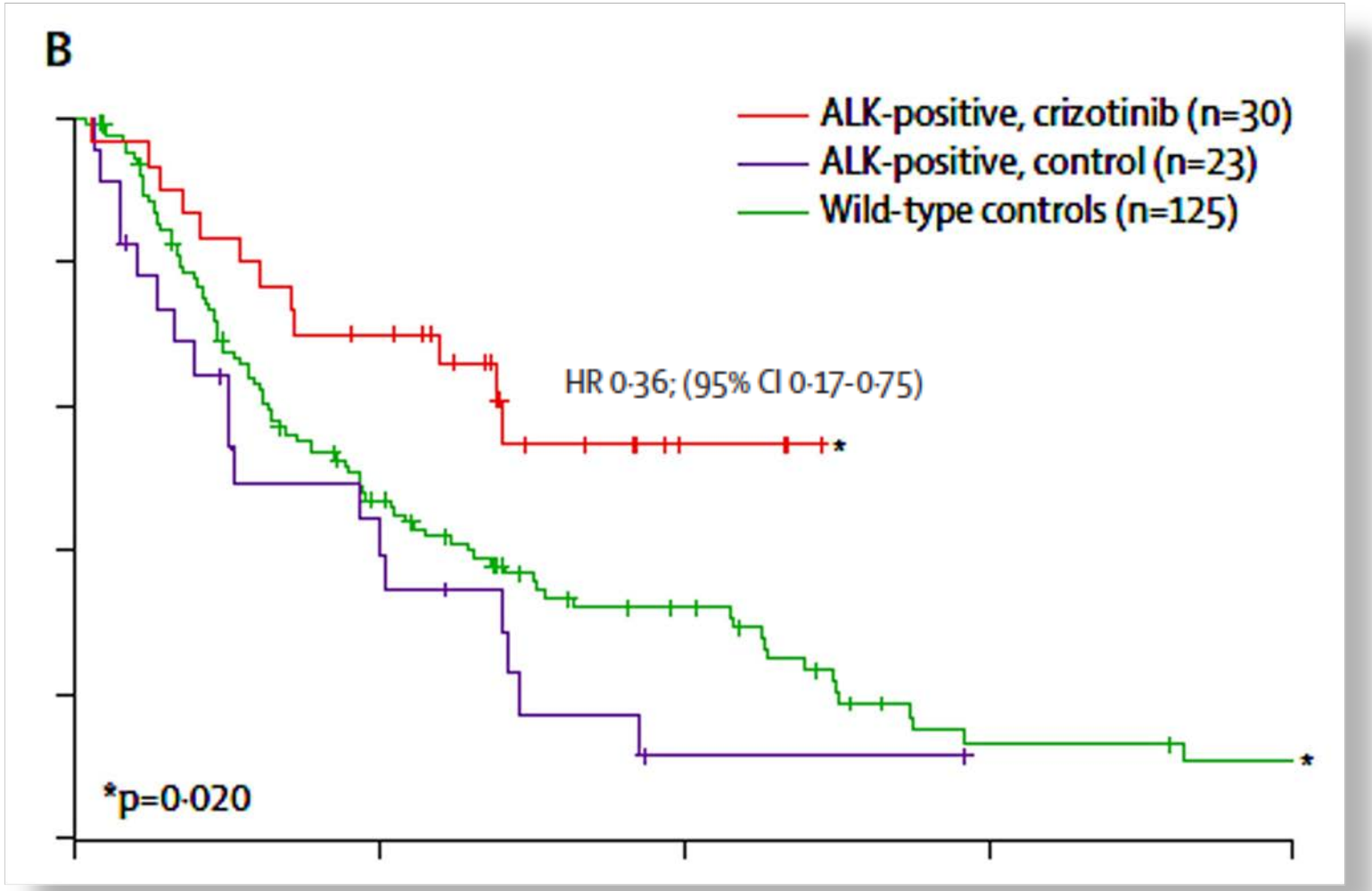
Adenocarcinoma histology [1]

ALK+, anaplastic lymphoma kinase positive; NSCLC, non-small cell lung cancer.

1. Le T, Gerber DE. *Semin Cancer Biol* 2017;42:81–8; 2. Shaw AT *et al. Lancet Oncol* 2011;12:1004–12. 2. Guerin A *et al. J Med Econ* 2015;18:312–22;
3. Rangachari D *et al. Lung Cancer* 2015;88:108–11.

Courtesy of Prof Solange Peters, MD, PhD

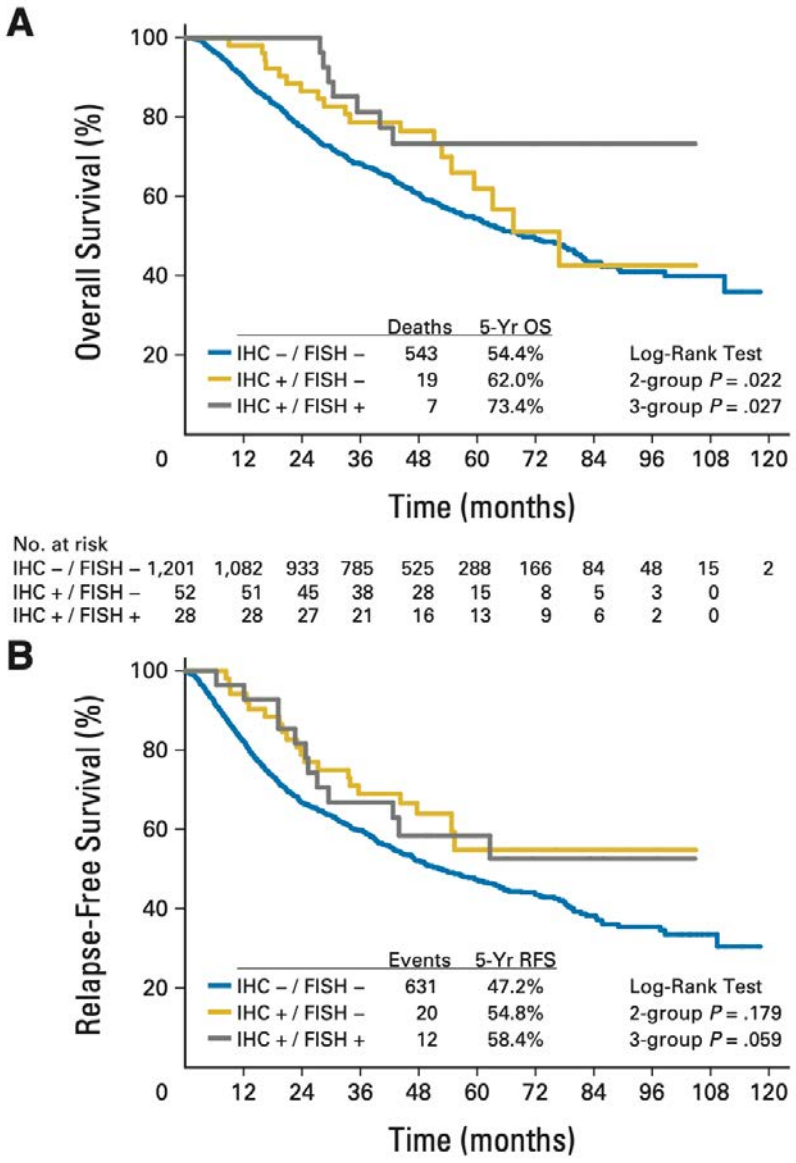
Prognostic impact of ALK rearrangement in advanced NSCLC



Shaw, Lancet Oncol 2011

Courtesy of Prof Solange Peters, MD, PhD

Prognostic impact of ALK rearrangement in localized NSCLC



Prevalence and Clinical Outcomes for Patients With ALK-Positive Resected Stage I to III Adenocarcinoma: Results From the European Thoracic Oncology Platform Lungscape Project

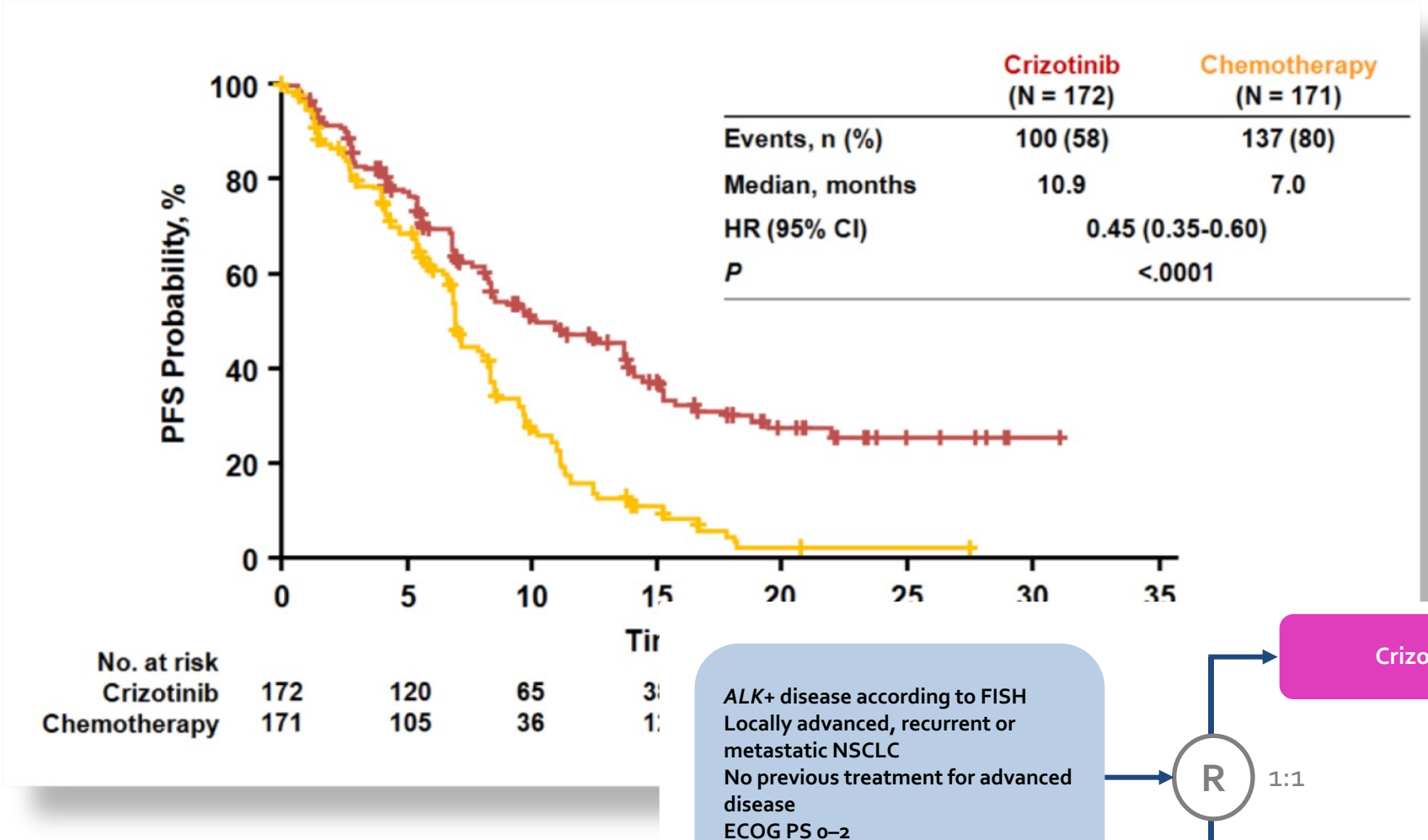
Fiona H. Blackhall, Solange Peters, Lukas Bubendorf, Urania Dafni, Keith M. Kerr, Henrik Hager, Alex Soltermann, Kenneth J. O'Byrne, Christoph Dooms, Aleksandra Sejda, Javier Hernández-Losa, Antonio Marchetti, Spasenija Savic, Qiang Tan, Erik Thunnissen, Ernst-Jan M. Speel, Richard Cheney, Daisuke Nonaka, Jeroen de Jong, Miguel Martorell, Igor Letovanec, Rafael Rosell, and Rolf A. Stahel

Other small series in early disease suggest a neutral or negative prognostic impact of ALK rearrangement.

Chaft, Lung Cancer, 2018; Wang Lung Cancer 2017; Shi Cancer Man and Res, 2020

Courtesy of Prof Solange Peters, MD, PhD

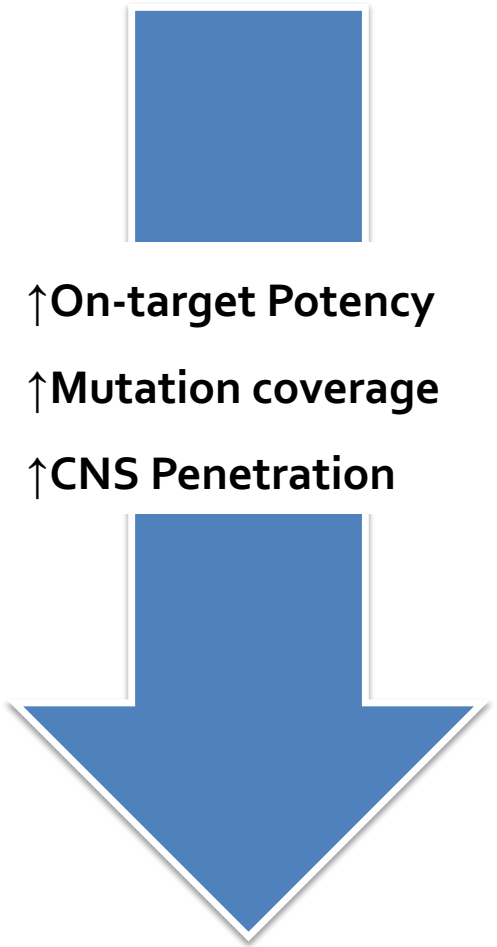
Crizotinib instead of chemotherapy in naïve patients



Solomon BJ, et al. *N Engl J Med* 2014;371:2167-77.

Courtesy of Prof Solange Peters, MD, PhD

Landscape of ALK inhibitors in clinical use

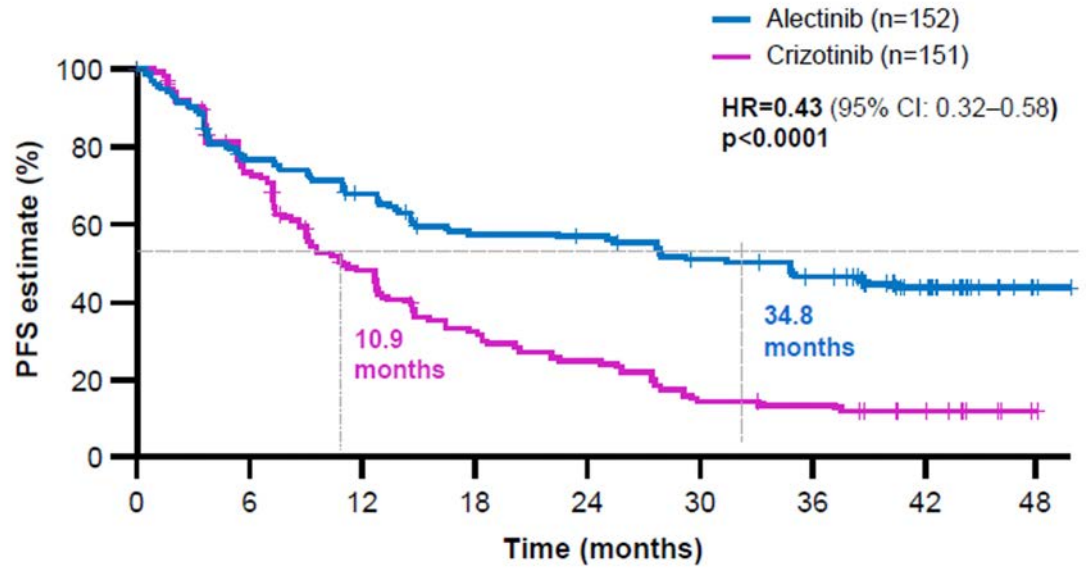


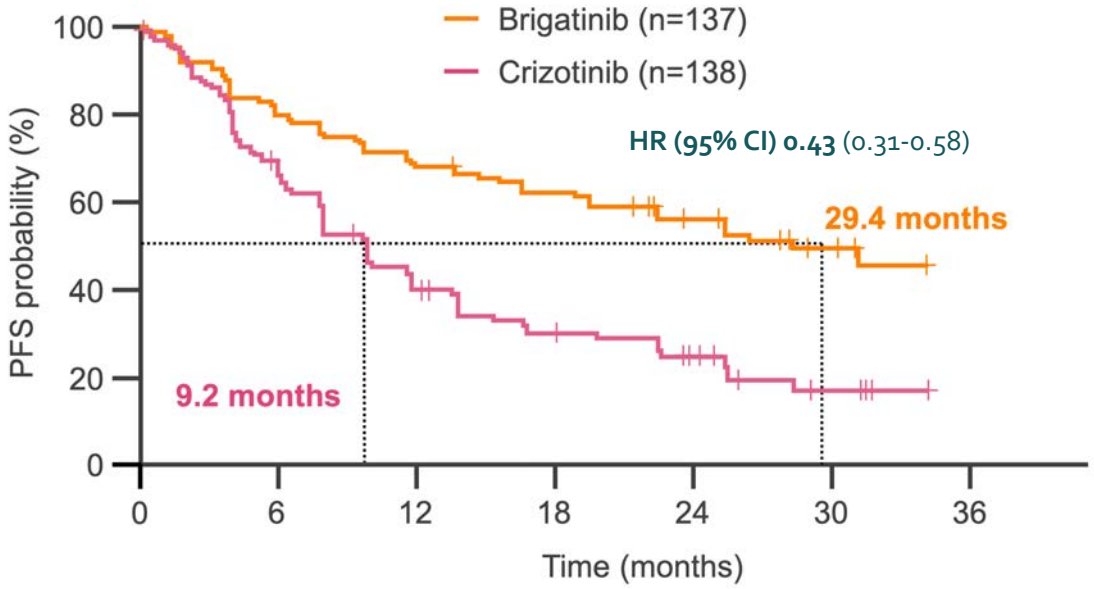
ALK TKI		STATUS
1st generation	**Crizotinib**	▪ FDA-approved, EMA-approved
2nd generation	**Ceritinib**	▪ FDA / EMA approved, post crizotinib ▪ FDA / EMA approved, first line
	Alectinib	▪ FDA / EMA approved, post crizotinib ▪ FDA / EMA approved, first line
	Brigatinib	▪ FDA / EMA approved, post crizotinib ▪ FDA/EMA approved, first line
	Ensartinib	▪ *Investigational*, approved in China
3rd generation	**Lorlatinib**	▪ FDA / EMA approved, in patients who have received 1 or more ALK inhibitors ▪ FDA/ EMA approved, first line

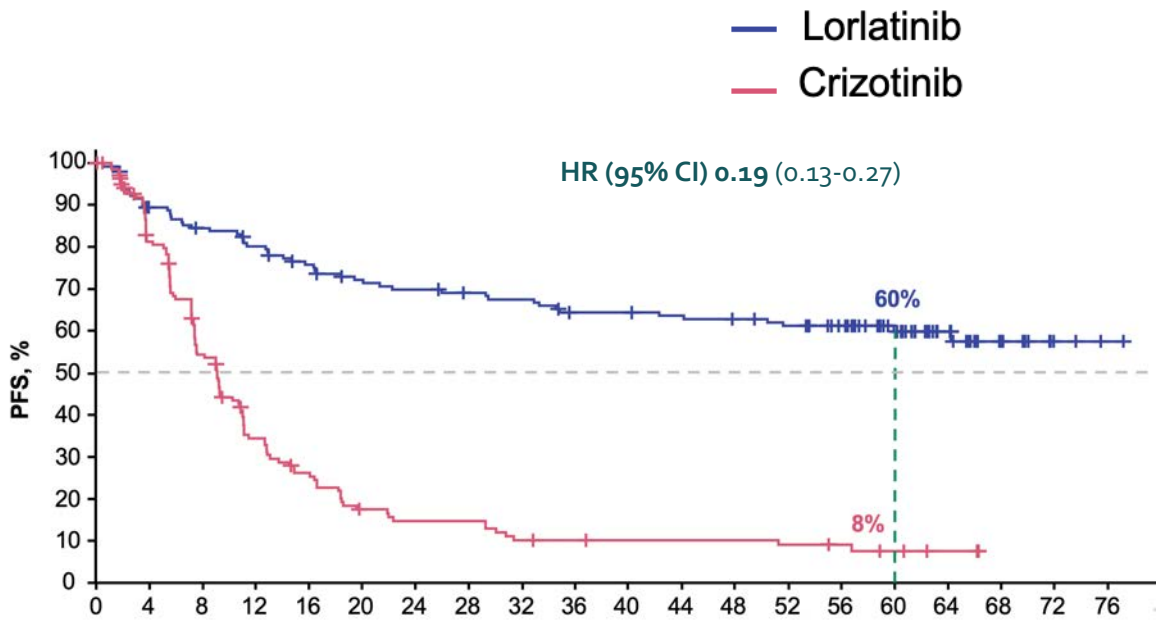
ALK, anaplastic lymphoma kinase; CNS, central nervous system; EMA, European Medicines Agency; FDA, United States Food and Drug Administration

Courtesy of Prof Solange Peters, MD, PhD

PFS for new generation ALK TKIs



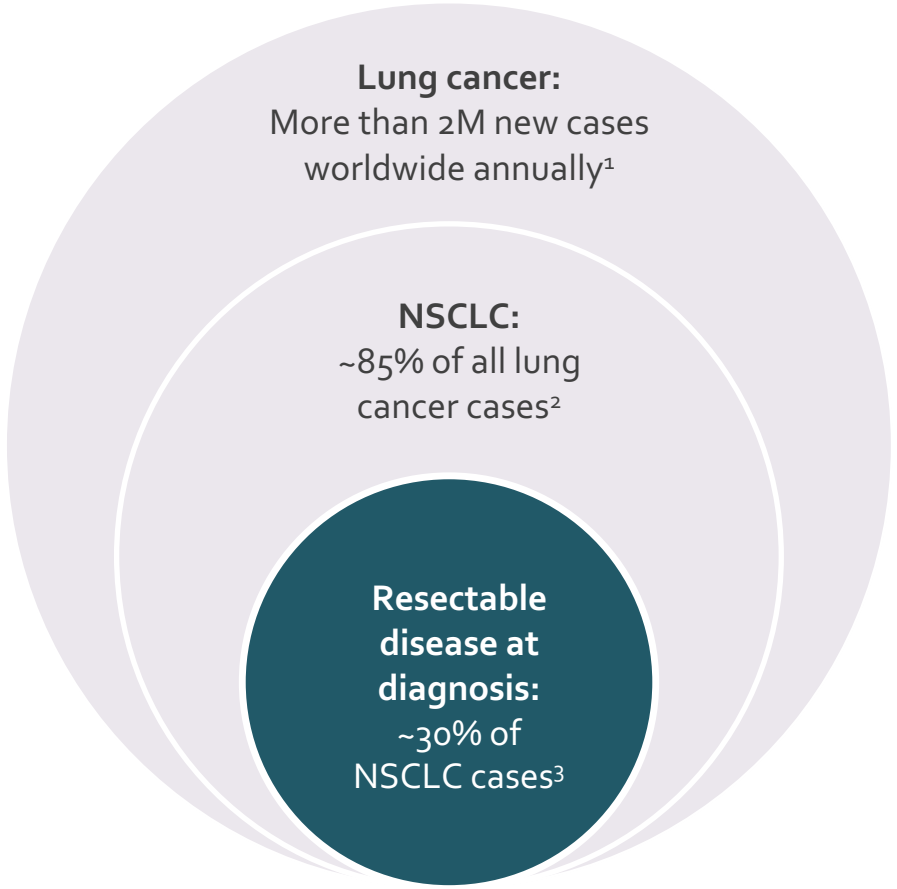




Courtesy of Prof Solange Peters, MD, PhD

WHY TESTING IN EARLY-DISEASE?

Outcomes in Resectable NSCLC Need to be Improved



Disease recurrence/death rates increase with advancing disease stage[4]

Early stage	Regional / locally advanced disease	
Stage IB	Stage II	Stage III
		
45% chance of recurrence or death	**62%** chance of recurrence or death	**76%** chance of recurrence or death

Adjuvant cytotoxic chemotherapy delivers a moderate survival benefit[4]

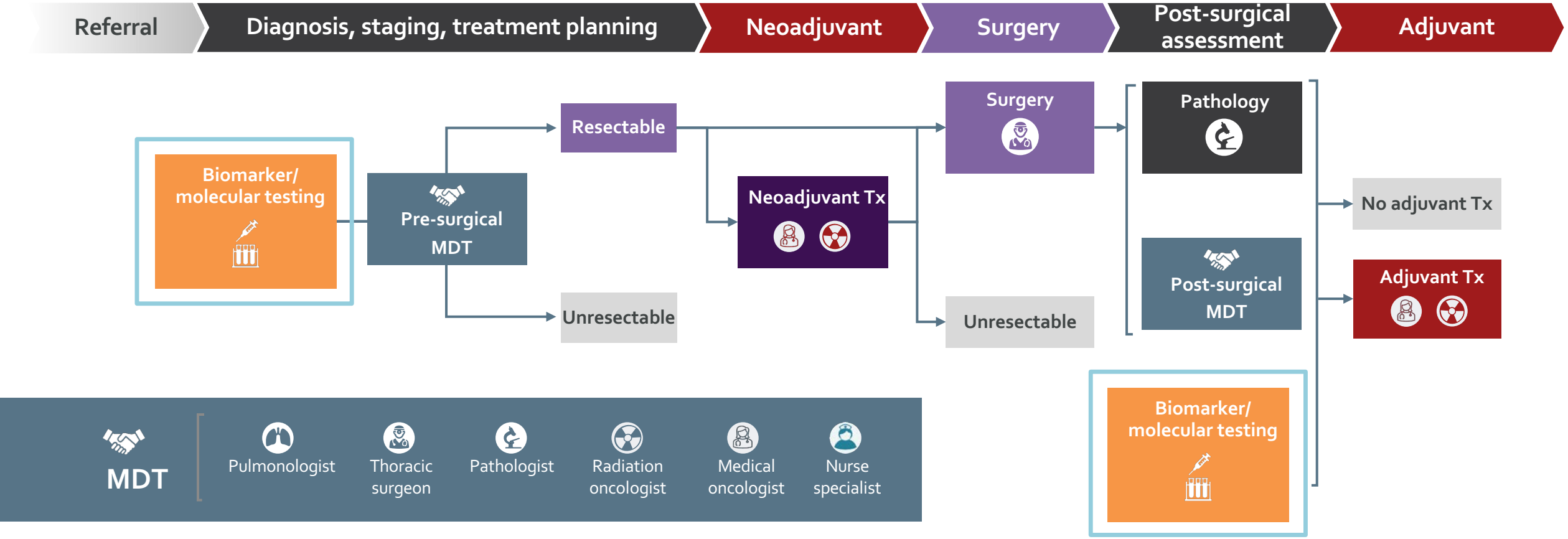
5.4%

5-year absolute benefit[4]

1. World Health Organization. Cancer Fact Sheet. Available at: https://www.who.int/news-room/fact-sheets/detail/cancer. Accessed August 2021;
2. Cancer.org. Lung Cancer Statistics. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8703.00.pdf. Accessed August 2021;
3. Cagle PT, et al. Arch Pathol Lab Med 2013;137:1191–8; 4. Pignon JP, et al. J Clin Oncol 2008;26:3552–9

Courtesy of Prof Solange Peters, MD, PhD

Patient journey and MDT practices are changing due to the evolving (neo)adjuvant treatment landscape



There are several opportunities in the early-stage NSCLC patient journey to assess the molecular and biomarker profile

Targeted treatments – instead of immunotherapy - must be given in the adjuvant setting in EGFR mutated and ALK rearranged NSCLC

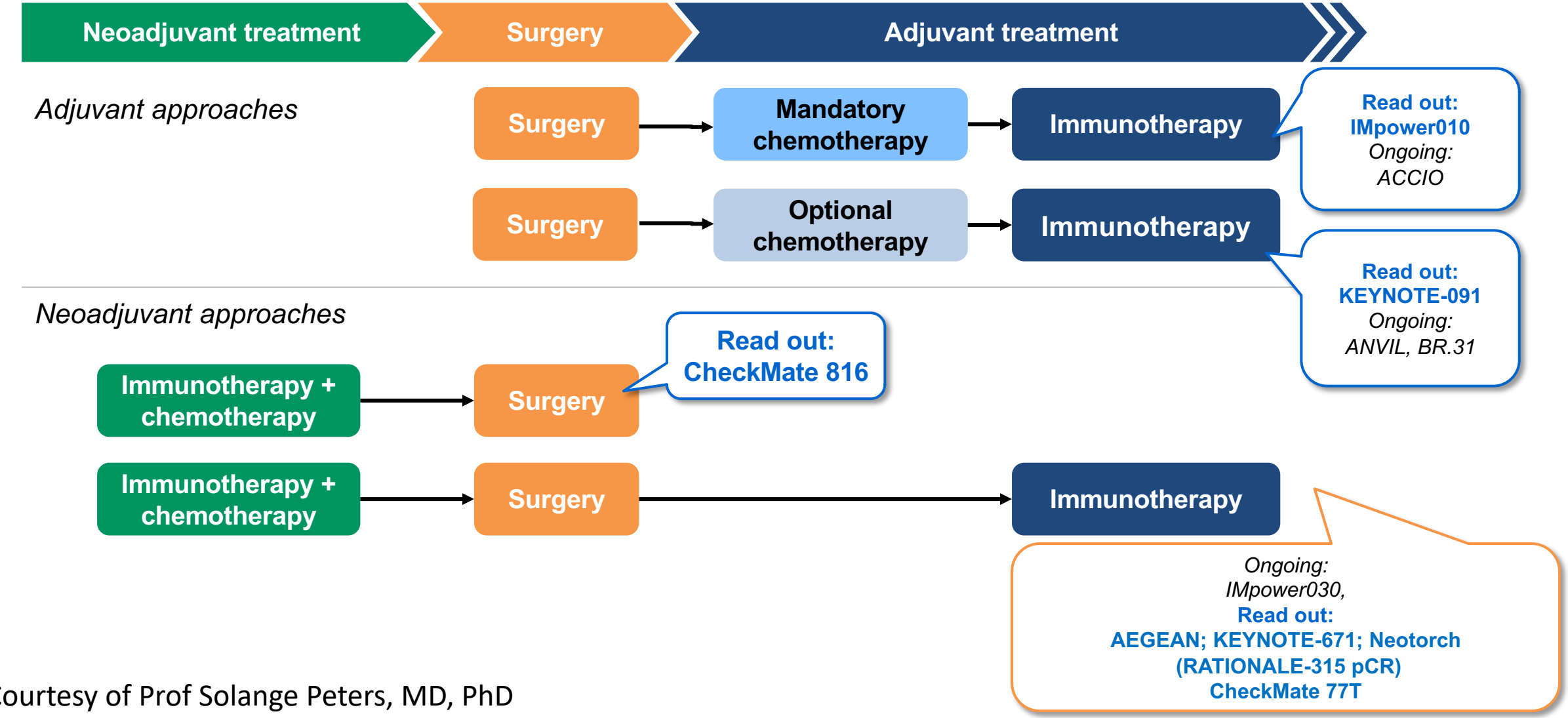
Courtesy of Prof Solange Peters, MD, PhD

Biomarker testing has become an essential prerequisite in patients with resectable early-stage NSCLC

Guideline	CAP/IASLC/AMP (2018)[2]	NCCN Guidelines® (2024)[3]	ASCO (2017)[4]	ASCO (2022)[5]	Canadian consensus recommendations (2020)[6]	ESMO (2021)[7]	Asian Thoracic Oncology Research Group (2020)[8]	Chinese guidelines for diagnosis and treatment of primary lung cancer (2019)[9]	Indian consensus guidelines (2019)[10]	Society for Translational Medicine consensus (2019)[11]
Disease stage	I–IIIA	IB–IIIA, IIIB	I–IIIA	III	All/any	IB–III*	III	II–IIIA†	Early/any	IB–IIIA
***EGFR* mutations**		✓		✓	✓	✓	✓	✓	✓	✓
PD-L1 expression		✓				✓			✓	
***ALK* rearrangements**		✓				✓			✓	
***ROS1* rearrangements**									✓	
Comments	Insufficient data for evidence-based recommendation. Each institution to set own policy, evaluating cost–benefit of testing all patients		No specific recommendations regarding molecular testing However, the recommendation is for treatment to be guided by test results							

Courtesy of Prof Solange Peters, MD, PhD

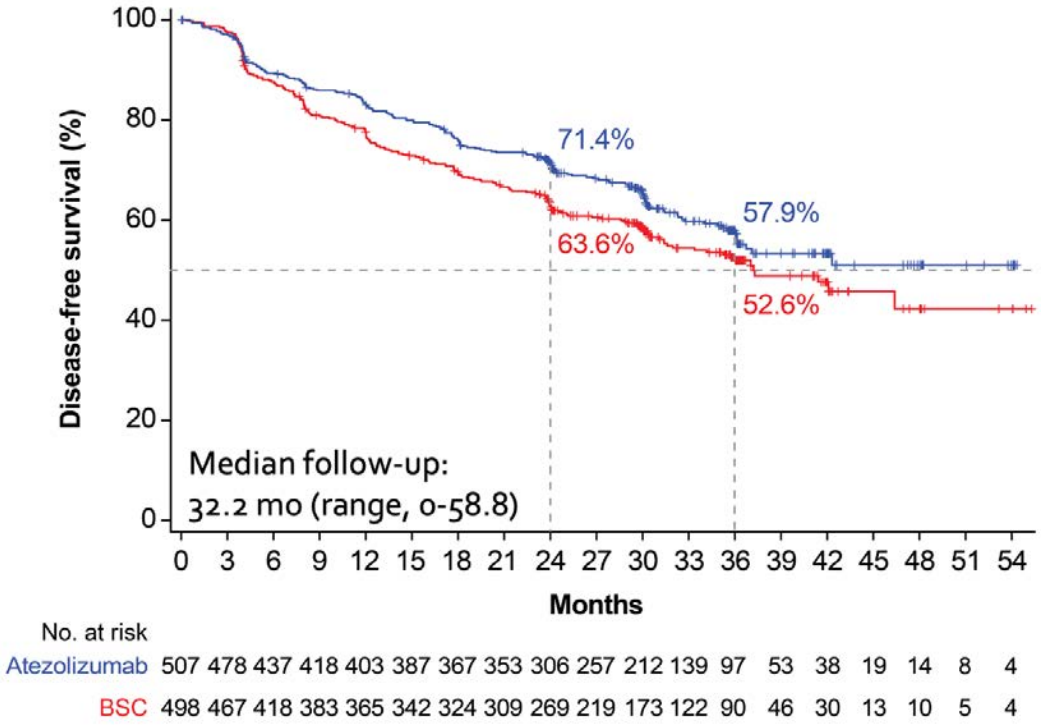
Several positive phase III studies with immunotherapy in resectable NSCLC taking different approaches



Courtesy of Prof Solange Peters, MD, PhD

Adjuvant IO Phase III randomised trials: DFS benefit

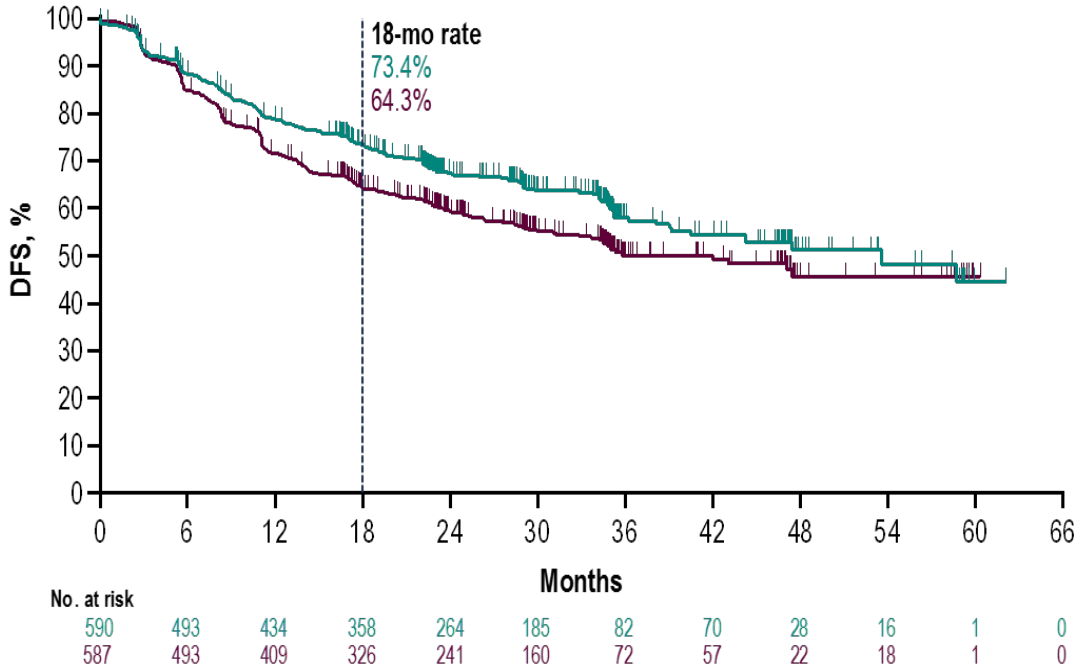
IMpower010



Stage IB to IIIA

HR: 0.81
mDFS: NE vs 37.2 months

PEARLS/KEYNOTE-091



Stage IB to IIIA

HR: 0.76
mDFS: 53.9 vs 42 months

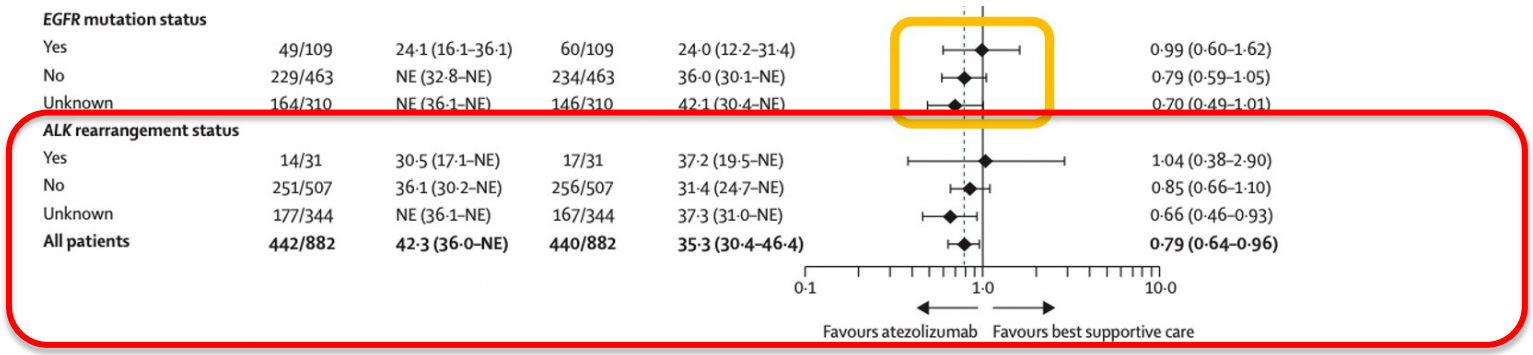
Felip E et al. *Lancet Oncol.* 2021; 398: 1344-57
O'Brien M et al. *Lancet Oncol*. 2022;23(10):1274-1286.

Courtesy of Prof Solange Peters, MD, PhD

Adjuvant ICB in ALK+ NSCLC

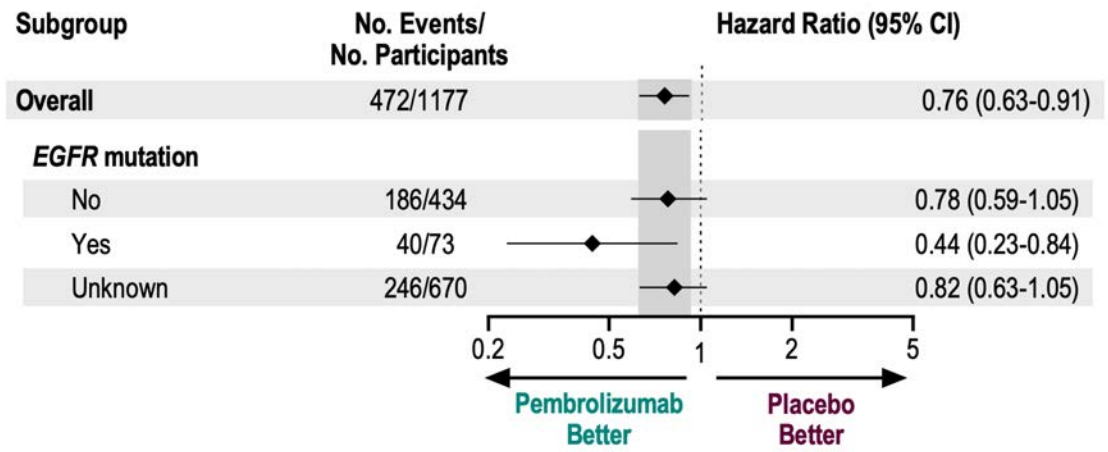
EGFRm allowed only in:

- IMpower010 (Stage II/IIIA)



- KEYNOTE-091

	Overall intention-to-treat population		PD-L1 TPS of ≥50% population	
	Pembrolizumab group (n=590)	Placebo group (n=587)	Pembrolizumab group (n=168)	Placebo group (n=165)
(Continued from previous page)				
EGFR mutation‡				
No	218 (37%)	216 (37%)	57 (34%)	67 (41%)
Yes	39 (7%)	34 (6%)	6 (4%)	5 (3%)
Unknown	333 (56%)	337 (57%)	105 (63%)	93 (56%)
ALK translocation‡				
No	226 (38%)	190 (32%)	55 (33%)	58 (35%)
Yes	7 (1%)	7 (1%)	3 (2%)	0
Unknown	357 (61%)	390 (66%)	110 (65%)	107 (65%)



?

Felip E et al. *Lancet Oncol.* 2021; 398: 1344-57
O'Brien M et al. *Lancet Oncol*. 2022;23(10):1274-1286.

Courtesy of Prof Solange Peters, MD, PhD

Do we have perioperative ICI data in early stage ALK+ NSCLC?

	CM816 N=358	KEYNOTE-671 N=797	AEGEAN N=802	CHECKMATE-77T N=461	RATIONALE-315 N=453	NEOTORCH N=500*
Neoadjuvant chemo-ICI	3 cycles nivo-ChT Platinum: cis or carbo	4 cycles pembro-ChT Platinum: cis	4 cycles durva-ChT Platinum: cis or carbo	4 cycles nivo-ChT Platinum: cis or carbo	3-4 cycles tisl-ChT Platinum: cis or carbo	3 cycles torip – ChT Platinum: cis or carbo
Adjuvant ICI	No, but chemo optional	Yes, 13 cycles Q3W	Yes, 12 cycles Q4W	Yes, 13 cycles Q4W	Yes, 8 cycles Q6W	Yes 13 cycles Q3W (+ 1 cycle ChT-ICI)
Stages	IB (≥4cm)-IIIA, TNM7	II-IIIB (N2), TNM8	II-IIIB(N2), TNM8	II-IIIB(N2), TNM8	II-III, TNM8	II-III, TNM8
Stratification factors	Stage, PD-L1 (+ vs -), sex	Stage, PD-L1 (50% cutoff), histology, region	Stage, PD-L1 (+ vs –)	Stage, PD-L1 (+ vs -), histology	Stage, histology, PD-L1 (+ vs -)	Stage, type surgery, histology, PD-L1
EGFR/ALK allowed?	No, testing acc to inv. EGFR mandatory Asia NSQCC	**Yes** **NA** **?**	**After amendment: no**	No	No, testing not mandatory	No
Prim endpoints	pCR by BIPR, EFS by BICR	EFS per inv, OS	pCR by BIPR, EFS by BICR	EFS by BICR	MPR, EFS by BICR	EFS by inv, MPR by BIPR

Forde NEJM 2022; Wakelee NEJM 2023; Heymach NEJM 2023; Cascone ESMO 2023; Lu ASCO 2023; Wang JTO 2021 supp *so far only stage III data presented; modified and cortesy of Hendricks 2023

Courtesy of Prof Solange Peters, MD, PhD

For a patient with NSCLC and an ALK rearrangement, have you offered or would you offer targeted treatment in the adjuvant setting, and which specific targeted agent have you employed or would you employ?

 Prof Peters	I have, alectinib
 Prof Solomon	I have, alectinib
 Dr Camidge	I have, alectinib
 Dr Chaft	I have, alectinib
 Dr Dagogo-Jack	I have, alectinib
 Dr Liu	I have, alectinib

For the following AGAs, have you offered or would you offer targeted treatment in the adjuvant setting?

	EGFR activating mutation	EGFR exon 20 insertion
 Prof Peters	I have, osimertinib	I have not and would not
 Prof Solomon	I have, osimertinib	I have not and would not
 Dr Camidge	I have, osimertinib	I have not and would not
 Dr Chaft	I have, osimertinib	I have not and would not
 Dr Dagogo-Jack	I have, osimertinib	I have not and would not
 Dr Liu	I have, osimertinib	I have not and would not

For the following AGAs, have you offered or would you offer targeted treatment in the adjuvant setting?

	ROS1 rearrangement	NTRK fusion
 Prof Peters	I have not and would not	I have not and would not
 Prof Solomon	I have not but would for the right patient	I have not but would for the right patient
 Dr Camidge	I have, entrectinib	I have not but would offer larotrectinib for the right patient
 Dr Chaft	I have not but would for the right patient	I have not and would not
 Dr Dagogo-Jack	I have not but would offer repotrectinib or crizotinib for the right patient	I have not and would not
 Dr Liu	I have not and would not	I have not and would not

For the following AGAs, have you offered or would you offer targeted treatment in the adjuvant setting?

	BRAF V600E mutation	KRAS G12C mutation
 Prof Peters	I have not and would not	I have not and would not
 Prof Solomon	I have not and would not	I have not and would not
 Dr Camidge	I have not and would not	I have not and would not
 Dr Chaft	I have not and would not	I have not and would not
 Dr Dagogo-Jack	I have not and would not	I have not and would not
 Dr Liu	I have not and would not	I have not and would not

For the following AGAs, have you offered or would you offer targeted treatment in the adjuvant setting?

	MET exon 14 skipping mutation	RET rearrangement
 Prof Peters	I have not and would not	I have not and would not
 Prof Solomon	I have not and would not	I have not but would for the right patient
 Dr Camidge	I have not and would not	I have not but would offer selpercatinib for the right patient
 Dr Chaft	I have not and would not	I have not and would not
 Dr Dagogo-Jack	I have not and would not	I have not and would not
 Dr Liu	I have not and would not	I have not but would offer selpercatinib for the right patient

For the following AGAs, have you offered or would you offer targeted treatment in the adjuvant setting, and which specific targeted agent have you employed or would you employ?

	HER2 mutation	HER2 overexpression
 Prof Peters	I have not and would not	I have not and would not
 Prof Solomon	I have not and would not	I have not and would not
 Dr Camidge	I have not but would offer T-DXd for the right patient	I have not and would not
 Dr Chaft	I have not and would not	I have not and would not
 Dr Dagogo-Jack	I have not and would not	I have not and would not
 Dr Liu	I have not and would not	I have not and would not

T-DXd = trastuzumab deruxtecan

To approximately how many patients with localized NSCLC have you administered the following treatments?

	Adjuvant alectinib (or another ALK inhibitor)	Chemoradiation followed by adjuvant alectinib (or another ALK inhibitor)
 Prof Peters	2	0
 Prof Solomon	5	1
 Dr Camidge	3	1
 Dr Chaft	4	2
 Dr Dagogo-Jack	2	1
 Dr Liu	4	4

Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you recommend for a patient with completely resected Stage IB nonsquamous NSCLC with an ALK rearrangement?

 Prof Peters	None
 Prof Solomon	Alectinib
 Dr Camidge	Chemotherapy → alectinib
 Dr Chaft	Alectinib if tumor at least 4 cm, otherwise none
 Dr Dagogo-Jack	Alectinib
 Dr Liu	Alectinib

What would you estimate to be the approximate risk of recurrence for a patient with completely resected Stage IB nonsquamous NSCLC with an ALK rearrangement without and with your preferred adjuvant therapy?

	Recurrence risk without adjuvant therapy	Recurrence risk with adjuvant therapy
 Prof Peters	20%-25%*	Maybe 20%*
 Prof Solomon	40%	10%
 Dr Camidge	15%	10%
 Dr Chaft	20%	5%
 Dr Dagogo-Jack	40%	20%-30%
 Dr Liu	40%	10%

*According to 8/9th TNM (3-4 cm N0)

Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you recommend for a patient with completely resected Stage IIA nonsquamous NSCLC with an ALK rearrangement?

 Prof Peters	Chemotherapy or alectinib
 Prof Solomon	Alectinib
 Dr Camidge	Chemotherapy → alectinib
 Dr Chaft	Chemotherapy → alectinib
 Dr Dagogo-Jack	Chemotherapy → alectinib
 Dr Liu	Alectinib

What would you estimate to be the approximate risk of recurrence for a patient with completely resected Stage IIA nonsquamous NSCLC with an ALK rearrangement without and with your preferred adjuvant therapy?

	Recurrence risk without adjuvant therapy	Recurrence risk with adjuvant therapy
 Prof Peters	30%*	20%*
 Prof Solomon	50%	15%
 Dr Camidge	35%	30%
 Dr Chaft	25%	5%
 Dr Dagogo-Jack	60%	20%
 Dr Liu	50%	10%

*According to 8/9th TNM (3-4 cm N0)

Regulatory and reimbursement issues aside, in general, which adjuvant treatment would you recommend for a patient with completely resected Stage IIIA nonsquamous NSCLC with an ALK rearrangement?

 Prof Peters	Alectinib or chemotherapy → alectinib
 Prof Solomon	Alectinib
 Dr Camidge	Chemotherapy → alectinib
 Dr Chaft	Chemotherapy → alectinib
 Dr Dagogo-Jack	Chemotherapy → alectinib
 Dr Liu	Alectinib

RTP RESEARCH TO PRACTICE

What would you estimate to be the approximate risk of recurrence for a patient with completely resected Stage IIIA nonsquamous NSCLC with an ALK rearrangement without and with your preferred adjuvant therapy?

	Recurrence risk without adjuvant therapy	Recurrence risk with adjuvant therapy
 Prof Peters	50%*	35%-40%*
 Prof Solomon	60%	20%
 Dr Camidge	75%	70%
 Dr Chaft	80%	30%
 Dr Dagogo-Jack	>75%	<30%
 Dr Liu	60%	10%

*According to 8/9th TNM (3-4 cm N0)

For patients able to receive adjuvant chemotherapy, do you offer it in addition to adjuvant alectinib for patients with localized NSCLC and ALK rearrangements?

 Prof Peters	Yes
 Prof Solomon	No
 Dr Camidge	Yes
 Dr Chaft	Yes
 Dr Dagogo-Jack	Yes if Stage III; no for Stage II
 Dr Liu	No

RTP RESEARCH TO PRACTICE

For patients able to receive adjuvant chemotherapy, do you offer it in addition to adjuvant osimertinib for patients with localized NSCLC and EGFR mutations?

 Prof Peters	Yes
 Prof Solomon	Yes
 Dr Camidge	Yes
 Dr Chaft	Yes
 Dr Dagogo-Jack	Yes, unless tumor is 3 to 4 cm and node-negative
 Dr Liu	Yes

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Significance of Biomarker Testing in Localized Non-Small Cell Lung Cancer (NSCLC) and Historical Management Paradigm for ALK-Positive Disease — Prof Peters

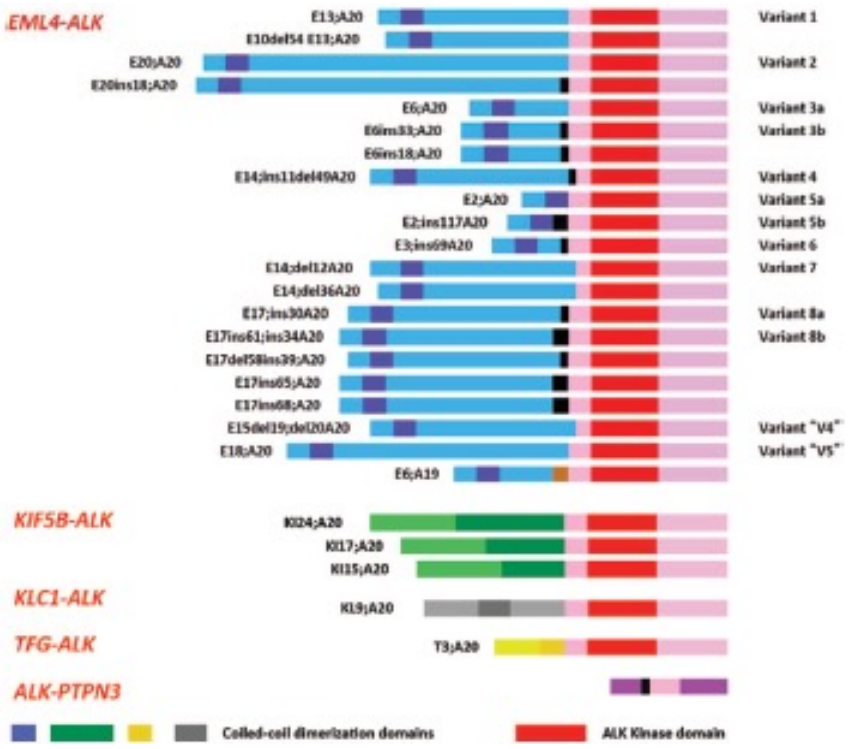
Module 2: Emerging Role and Practical Application of ALK-Targeted Therapy in Localized NSCLC — Prof Solomon

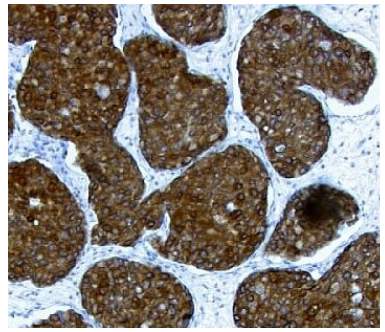
RTP RESEARCH TO PRACTICE

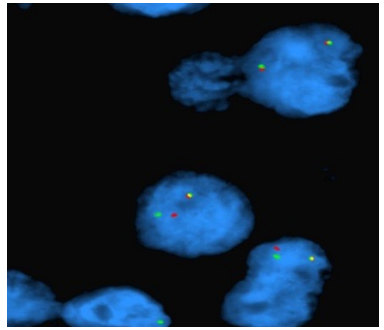
ALK gene rearrangements in NSCLC

- ***EML4-ALK* and other fusion variants present in ~5% of NSCLC.**
  - Detected in tumors by IHC, FISH, PCR or ideally NGS

- Guidelines recommend testing all newly diagnosed non-squamous NSCLC (and selected SCC)







Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA phase 3 trial of adjuvant alectinib vs chemotherapy

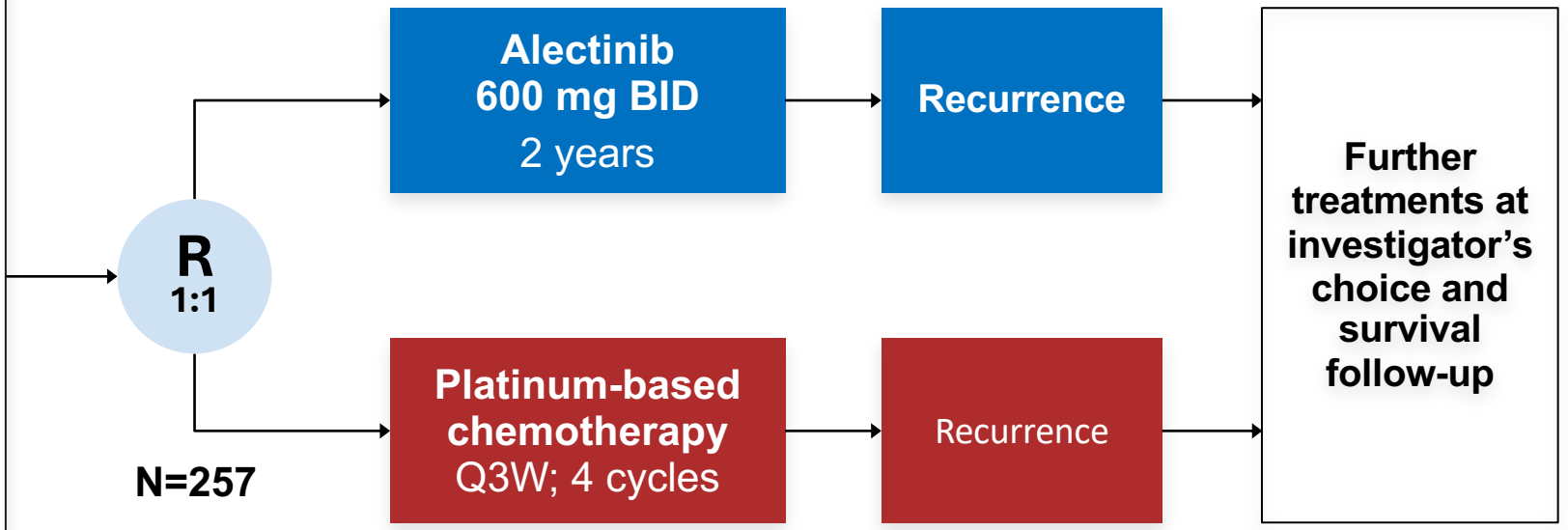
Resected Stage IB (≥4cm)–IIIA *ALK*+ NSCLC
per UICC/AJCC 7th edition

Other key eligibility criteria:

- ECOG PS 0–1
- Eligible to receive platinum-based chemotherapy
- Adequate end-organ function
- No prior systemic cancer therapy

Stratification factors:

- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian



Primary endpoint

- DFS per investigator, tested hierarchically:
  - Stage II–IIIA → ITT (Stage IB–IIIA)

Other endpoints

- CNS disease-free survival
- OS
- Safety

Disease assessments (including brain MRI) were conducted: at baseline, every 12 weeks for year 1–2, every
24 weeks for year 3–5, then annually

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Patient demographics and baseline characteristics

Characteristic	Alectinib (n=130)	Chemotherapy (n=127)
Median age <65 / ≥65 years, %	54 years 79 / 21	57 years 73 / 27
Sex: female / male, %	58 / 42	46 / 54
Smoking status: never / former / current, %	65 / 32 / 4	55 / 43 / 2
Race: Asian / non-Asian, %	55 / 45	56 / 44
ECOG PS: 0 / 1, %	55 / 45	51 / 49
Stage at diagnosis: IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
Nodal status: N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
Histology: squamous / non-squamous, %	5 / 95	2 / 98

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Surgical characteristics

Characteristic	Alectinib (n=130)	Chemotherapy (n=127)
Surgical procedure: lobectomy / pneumonectomy / other*, %	97 / 2 / 2	92 / 3 / 5
Median time from last surgery to randomization†	1.7 months	1.7 months
<8 weeks / ≥8 weeks, %	55 / 45	55 / 45
Nodal assessment, %		
MLND	83	83
Lymph node sampling	15	12
MLND and lymph node sampling not performed‡	2	6
Nodal status: N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
Stage at diagnosis per AJCC 7th edition: IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
Stage at diagnosis per AJCC 8th edition: IB§ / IIA / IIB / IIIA / IIIB, %	5 / 8 / 31 / 51 / 5	4 / 3 / 35 / 54 / 5

Surgical characteristics were generally well balanced across treatment arms

Data cut-off: 26 June 2023

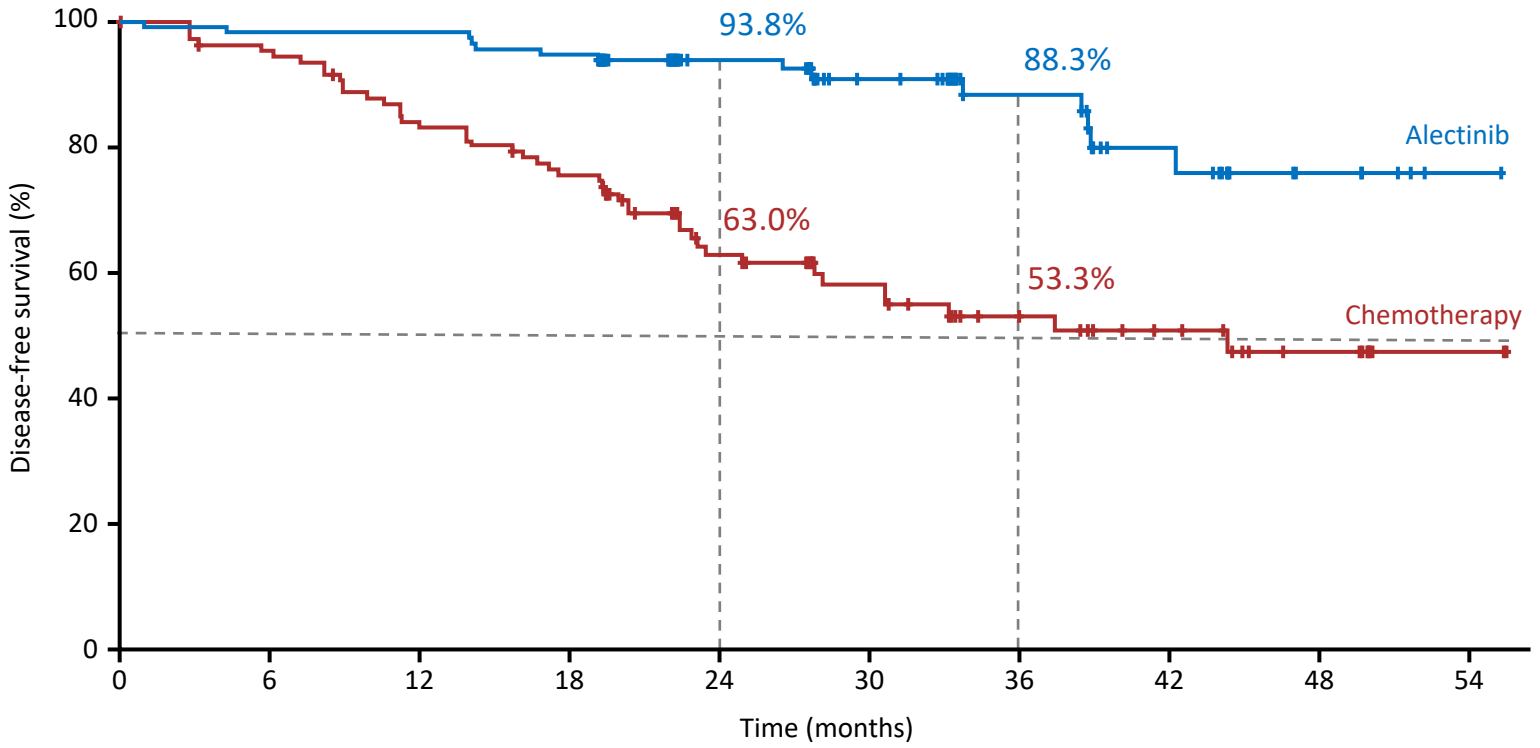
*Bilobectomy (alectinib arm, 2%; chemotherapy arm, 4%); sleeve lobectomy (0%; 1%). †First dose of the study drug was to be administered immediately after randomization and no later than seven days post randomization

‡An exception was granted for patients who had documented N2 disease in one nodal station or who had negative preoperative staging imaging (CT and PET scan) in the mediastinum

§ Nine patients had tumor size=4 cm, the remaining two patients had tumors <4cm (major protocol deviations reported)

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Disease-free survival: stage II–IIIA*



No. at risk

Alectinib	116	111	111	107	67	49	35	21	10	3
Chemo	115	102	88	79	48	35	23	17	10	2

	Alectinib (N=116)	Chemotherapy (N=115)
Patients with event Death Recurrence	14 (12%) 0 14	45 (39%) 1 44
Median DFS, months (95% CI)	Not reached	44.4 (27.8, NE)
DFS HR (95% CI)	0.24 (0.13, 0.45) p†<0.0001	

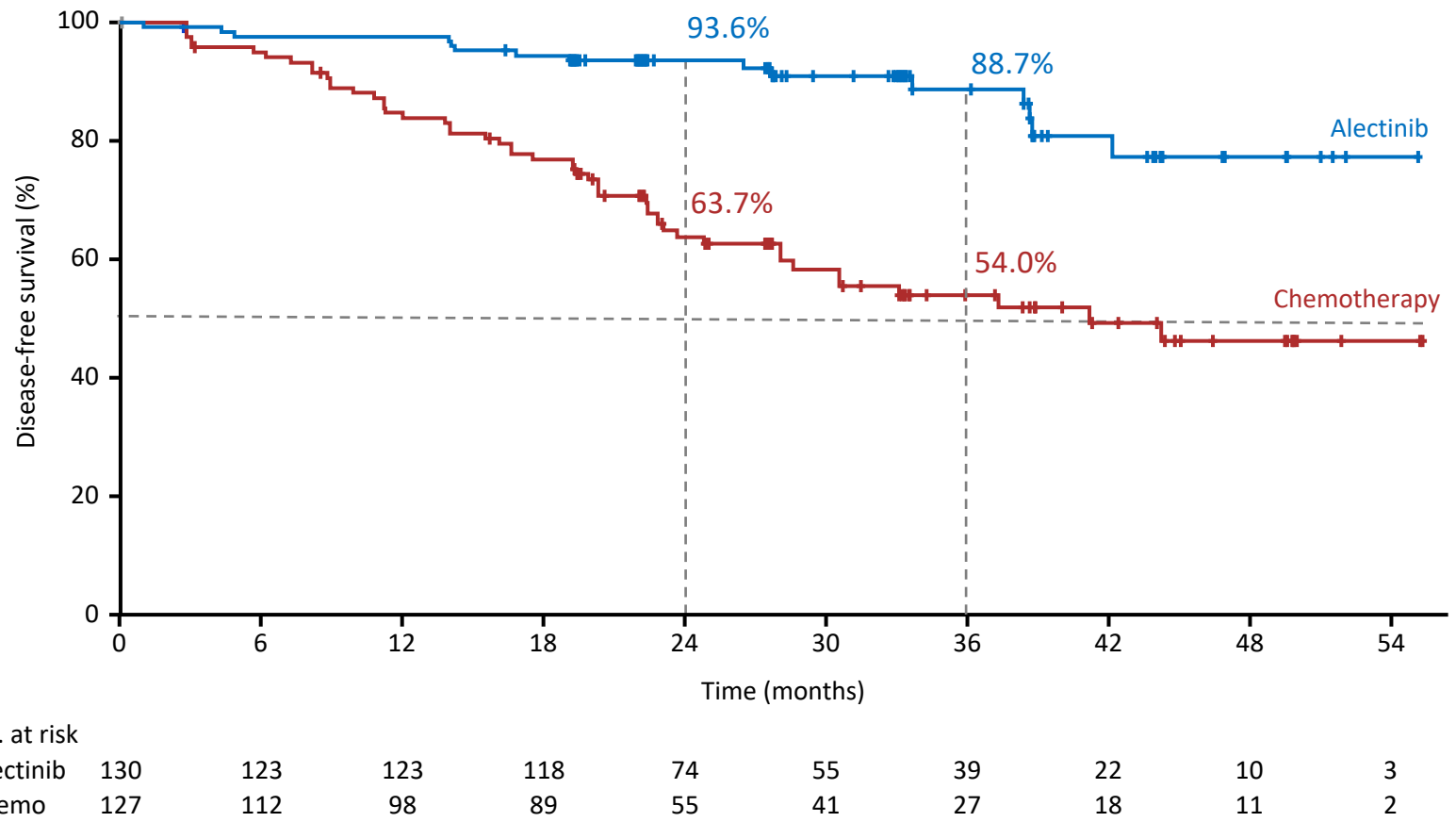
Median survival follow up: alectinib, 27.9 months; chemotherapy, 27.8 months

Data cut-off: 26 June 2023; Time from last patient in to data cut off was ~18 months

*Per UICC/AJCC 7th edition; †Stratified log rank; DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Disease-free survival: stage IB–IIIA(ITT)



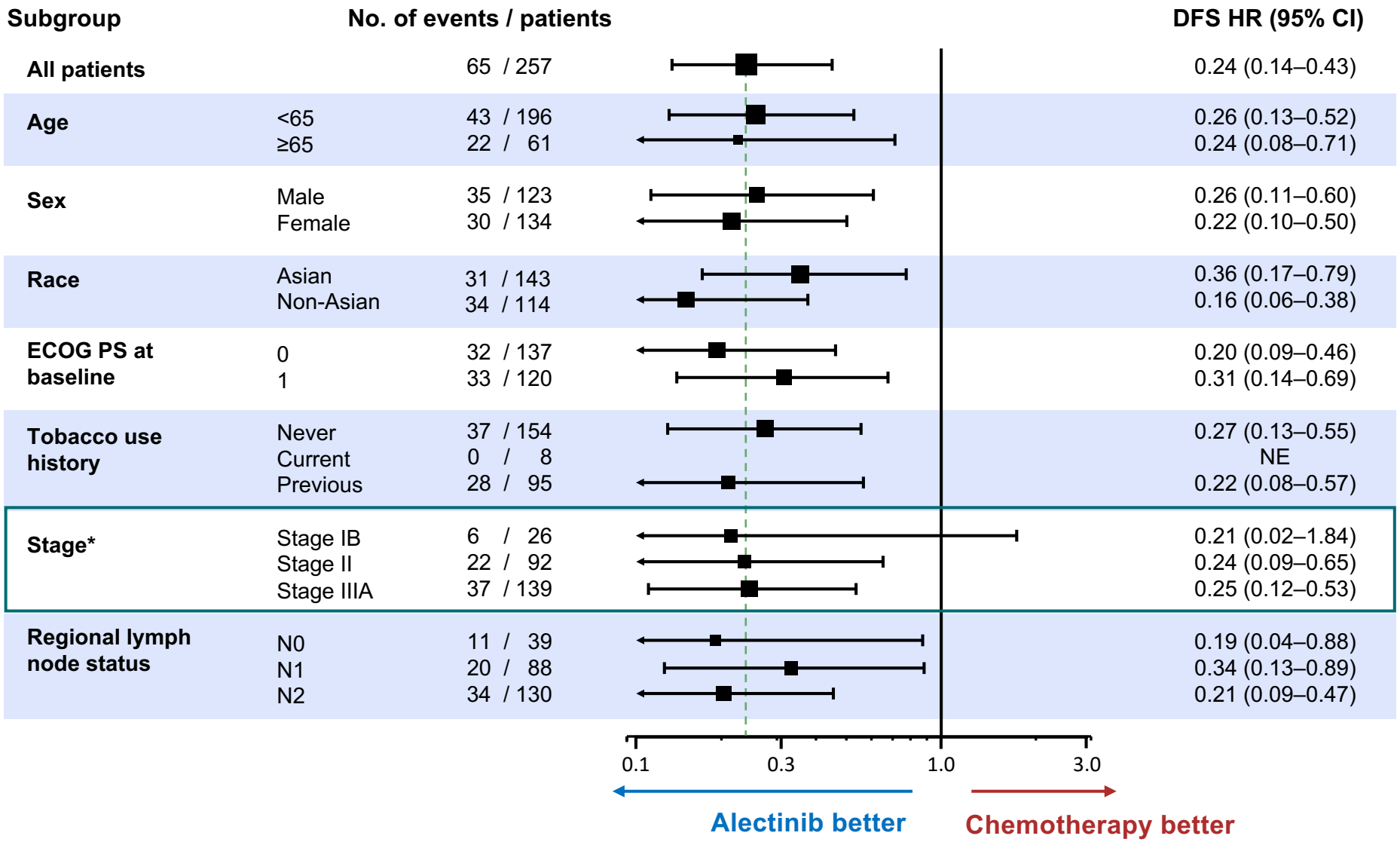
	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	15 (12%)	50 (39%)
Death	0	1
Recurrence	15	49
Median DFS, months (95% CI)	Not reached	41.3 (28.5, NE)
DFS HR (95% CI)	0.24 (0.13, 0.43) $p^{\dagger}<0.0001$	

At the data cutoff date, OS data were immature with only 6 (2.3%) OS events reported‡

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Disease-free survival subgroup analysis (ITT)



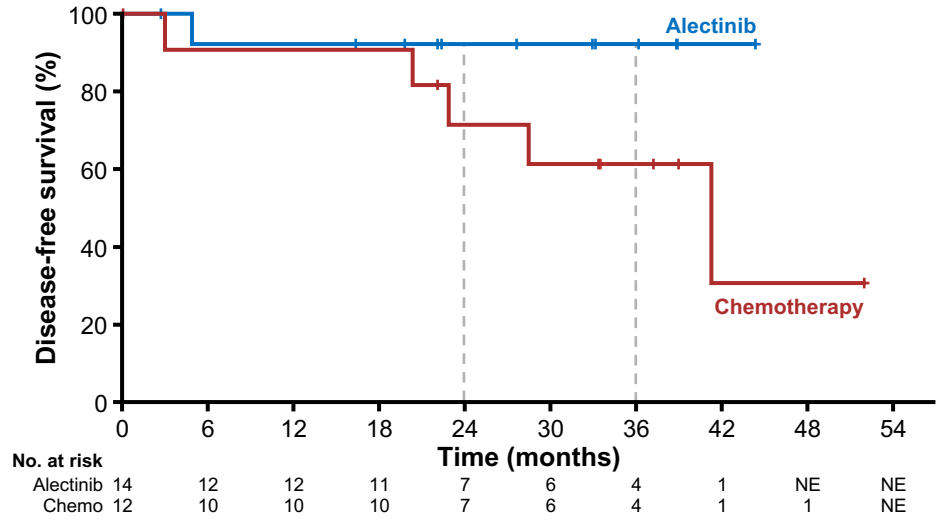
Data cut-off: 26 June 2023

Arrows indicate lower bound of the CI<0.1; *Per UICC/AJCC 7th edition

Courtesy of Prof Ben Solomon, MBBS, PhD

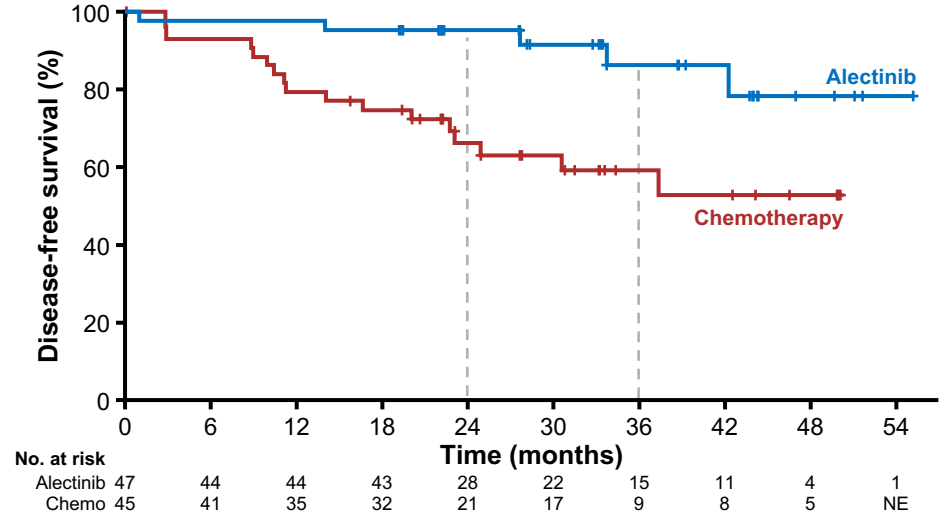
ALINA: Disease-free survival by stage*

Stage IB

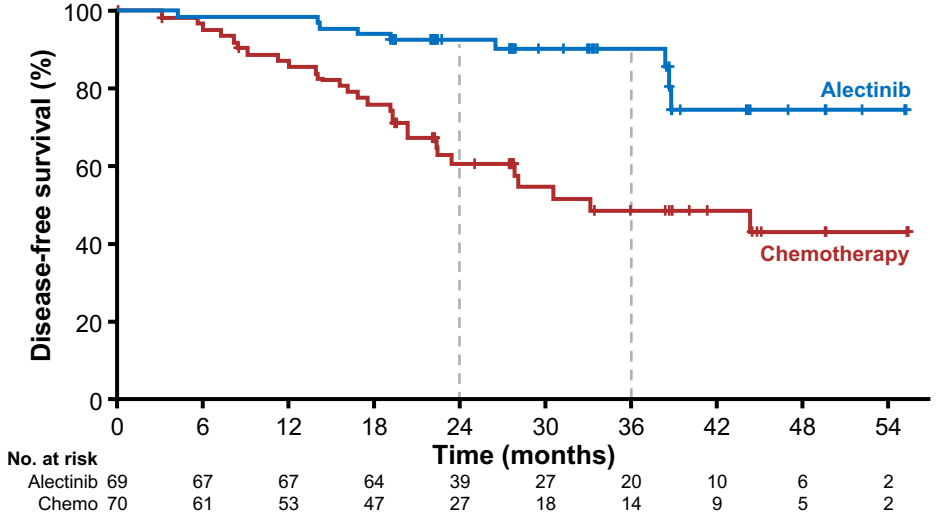


2-year DFS rate, % (95% CI)	Stage IB (n=26)	Stage II (n=92)	Stage IIIA (n=139)
Alectinib	**92.3** (77.8, 100.0)	95.6 (89.5, 100.0)	**92.7** (86.4, 98.9)
Chemotherapy	**71.6** (44.2, 99.0)	66.3 (51.7, 81.0)	**60.7** (47.9, 73.5)
HR† (95% CI)	**0.21** (0.02, 1.84)	**0.24** (0.09, 0.65)	**0.25** (0.12, 0.53)

Stage II



Stage IIIA

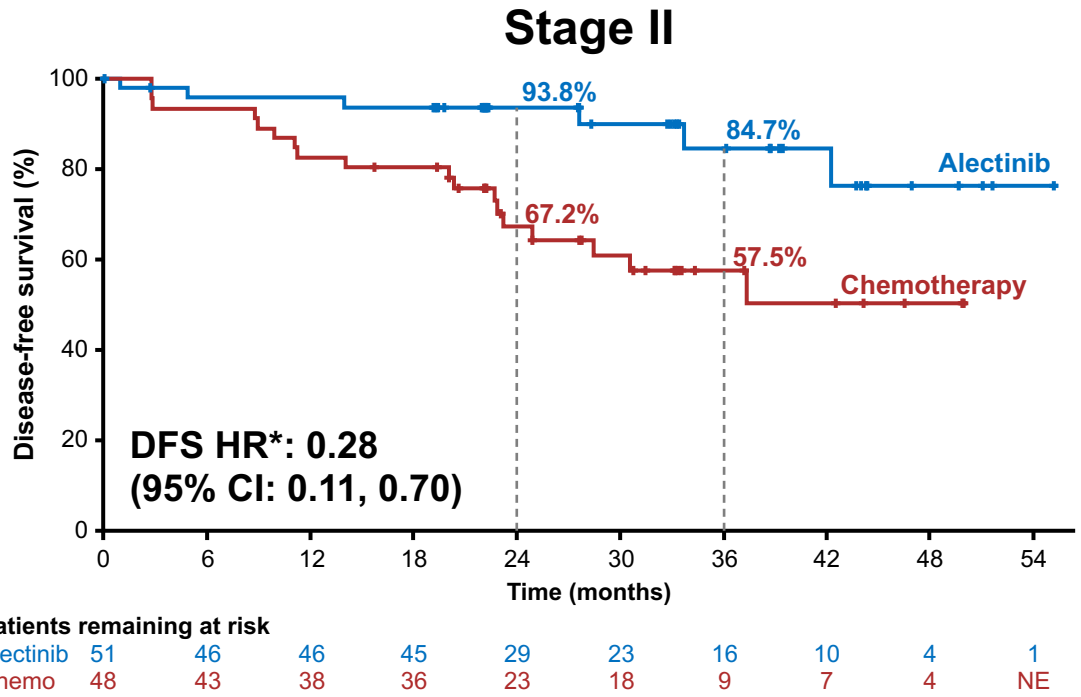


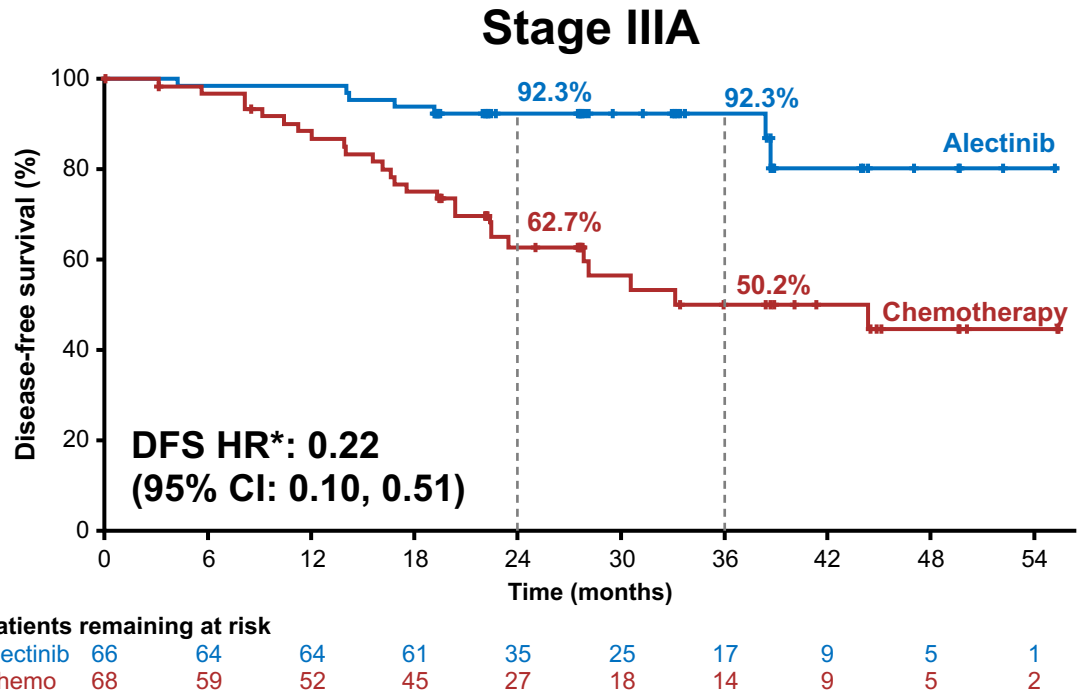
Data cut-off: 26 June 2023

*Per UICC/AJCC 7th edition; †Unstratified analysis

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Disease-free survival by stage (AJCC 8th edition)



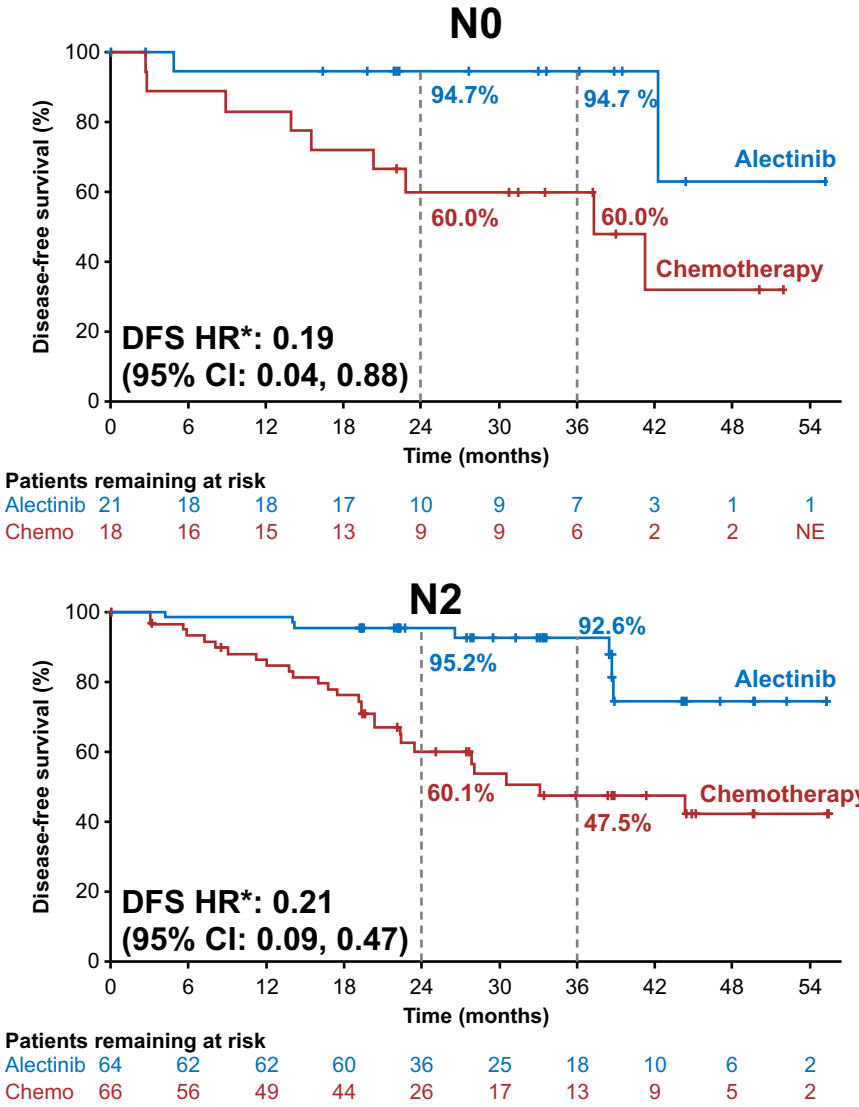


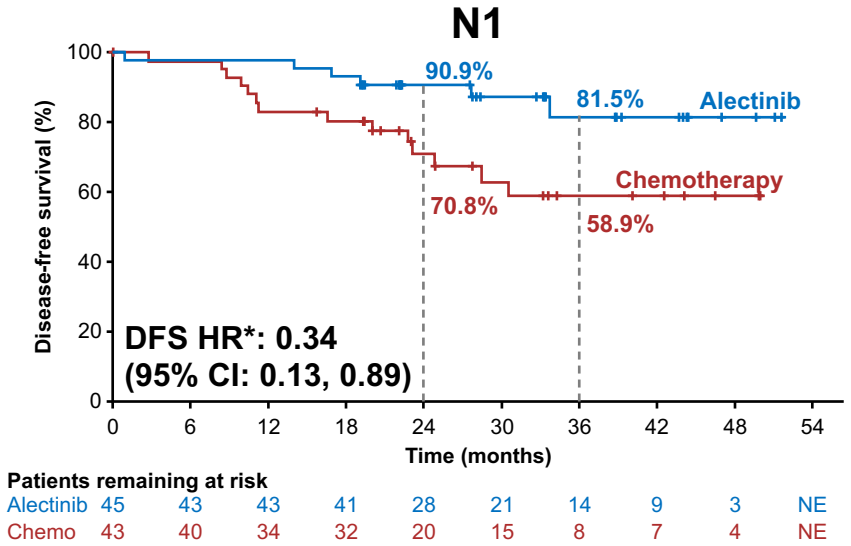
A consistent DFS benefit with alectinib was observed across all disease stages per AJCC 8th staging edition

Data cut-off: 26 June 2023
*Unstratified analysis
Six patients in the alectinib arm and five patients in the chemotherapy arm had stage IB (AJCC 8th edition); DFS HR* was <0.01 (95% CI: 0.00, NE)
2-year / 3-year DFS rates for patients with stage IB disease (AJCC 8th edition) and who received alectinib and chemotherapy were: 100% / 100% and 100% / 100%, respectively
Seven patients in the alectinib arm and six patients in the chemotherapy arm had stage IIIB (AJCC 8th edition); DFS HR*: 0.16 (95% CI: 0.03, 0.85)
2-year / 3-year DFS rates for patients with stage IIIB disease (AJCC 8th edition) and who received alectinib and chemotherapy were: 100% / 85.7% and 16.7% / 16.7%, respectively

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Disease-free survival by nodal status



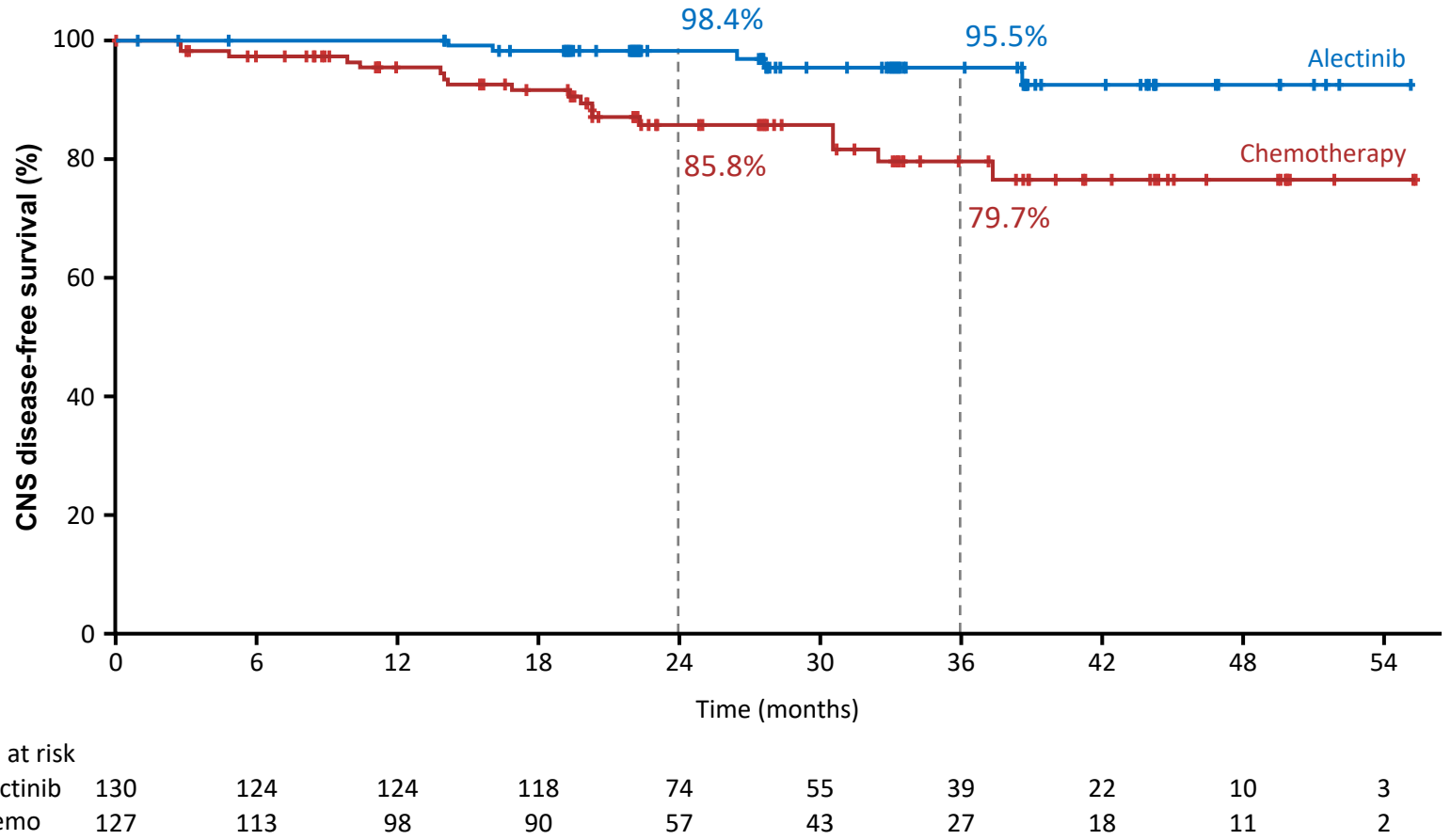


A consistent DFS benefit with alectinib was observed across subgroups by nodal stage

Data cut-off: 26 June 2023
*Unstratified analyses

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: CNS disease-free survival in the ITT population



	Alectinib (N=130)	Chemotherapy (N=127)
Patients with event	5	18
Death	1	4
Brain recurrence	4	14
CNS-DFS HR* (95% CI)	0.22 (0.08, 0.58)	

Median survival follow up: alectinib, 27.8 months; chemotherapy, 28.4 months

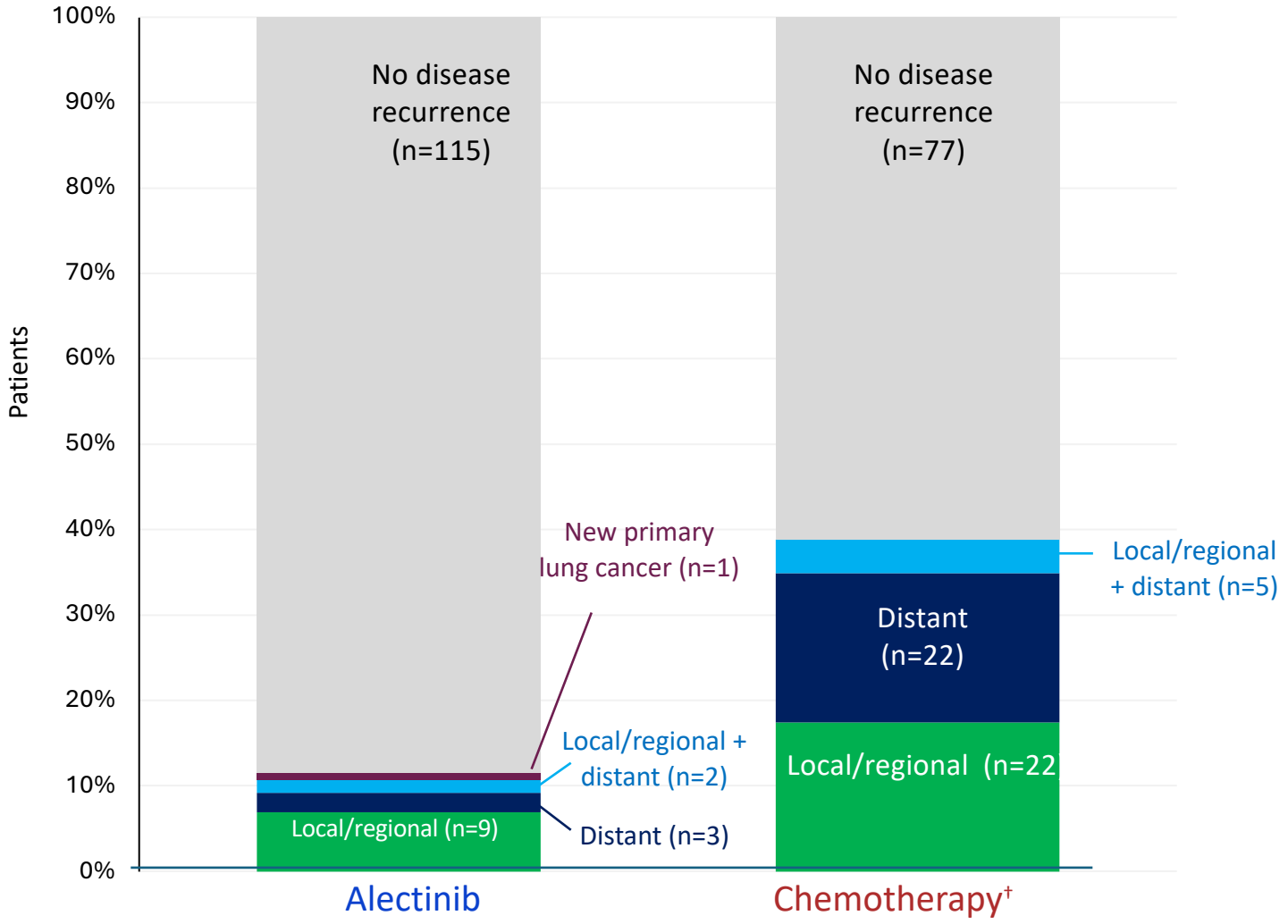
Data cut-off: 26 June 2023

*Stratified analysis with race and stage as stratification factors

CNS-DFS defined as time from randomisation to the first documented recurrence of disease in the CNS or death from any cause

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Sites of disease recurrence (ITT)



Site(s) of distant recurrence*	Alectinib (n=130)	Chemotherapy (n=127)
Brain	4	14
Bone	1	8
Adrenal gland	0	3
Lymph node	0	2
Kidney	0	1
Peritoneum	0	1
Other	1	0

Data cut-off: 26 June 2023; *At disease assessment where first recurrence detected; patients may have multiple sites of disease recurrence counted; †One patient died without a recurrence event reported

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: Post-recurrence subsequent therapy

Number of patients with disease recurrence, n (%)	Alectinib (n=15)	Chemotherapy (n=49)
Patients with any subsequent therapy	13 (87)	43 (88)
Systemic therapy	13 (87)	38 (78)
ALK TKI	7 (47)	37 (76)
Alectinib	4 (27)	29 (59)
Brigatinib	4 (27)	4 (8)
Crizotinib	0	4 (8)
Lorlatinib	0	2 (4)
Ceritinib	0	1 (2)
Chemotherapy	6 (40)	2 (4)
Immunotherapy	1 (7)	1 (2)
Other anti-cancer therapy	1 (7)	1 (2)
Radiotherapy	5 (33)	9 (18)
Surgery	1 (7)	3 (6)

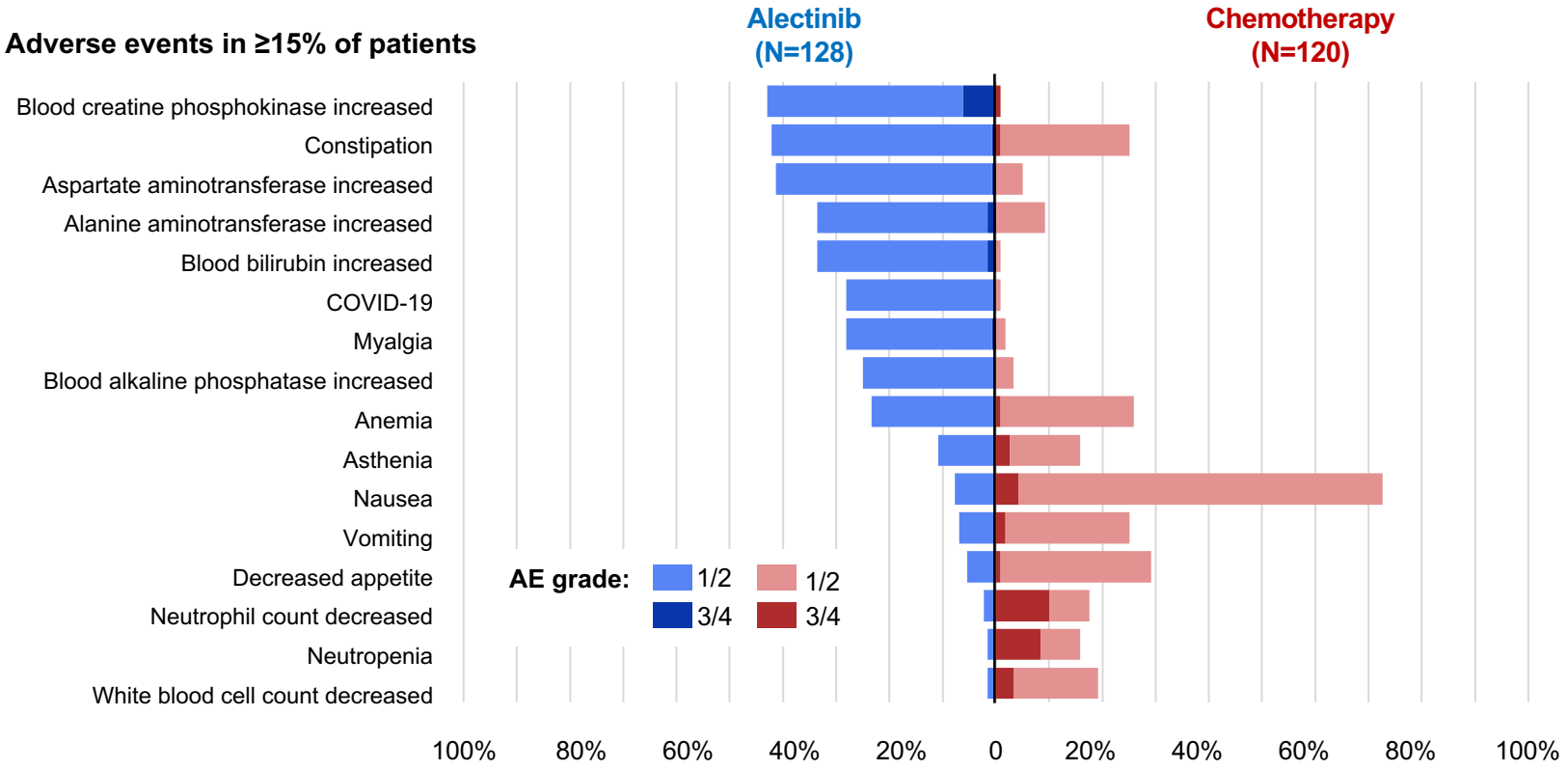
Data cut-off: 26 June 2023

Includes any subsequent therapy reported on or after date of earliest contributing event to disease recurrence;
Patients may have received more than one subsequent anticancer therapy

Courtesy of Prof Ben Solomon, MBBS, PhD

ALINA: AEs occurring in ≥15% of patients

Adjuvant alectinib was tolerable, with a manageable safety profile which was in line with the known profile of alectinib[1,2]



AEs leading to:

- Dose reduction
  Alectinib: **26%** / Chemo: **10%**
- Dose interruption
  Alectinib: **27%** / Chemo: **18%**
- Treatment withdrawal
  Alectinib: **5%** / Chemo: **13%**

Median treatment duration

Alectinib: **23.9 months**
Chemo: **2.1 months**

AE, adverse event;
1. Solomon et al. ESMO 2023 (LBA2); 2. Wu et al. N Engl J Med 2024

Prof. Makoto Nishio

Courtesy of Prof Ben Solomon, MBBS, PhD

Questions following ALINA

How can therapy be optimized?

What is the optimal duration of alectinib therapy?
Does chemotherapy add any benefit to alectinib?
What about neoadjuvant alectinib?

Who may benefit?

Will pts with Stage IA disease or locally advanced disease benefit?
Role of ctDNA?

What happens after relapse?

Do tumors retain sensitivity to ALK TKIs?

What are mechanisms of resistance?

Courtesy of Prof Ben Solomon, MBBS, PhD

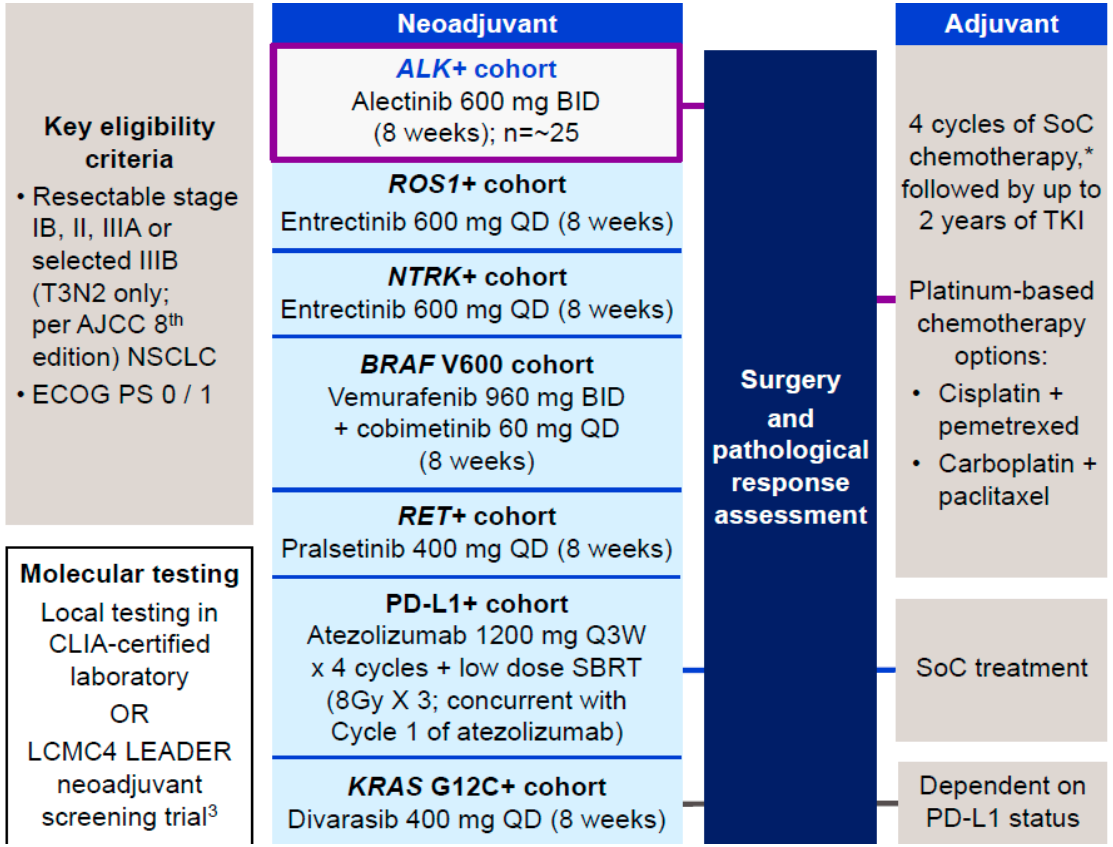
Other key trials of alectinib in stage I–III NSCLC are ongoing

NAUTIKA1 **USA** **NCT04302025**	Phase II study in resectable stage IB–IIIA NSCLC, which includes a cohort of patients receiving perioperative alectinib (neoadjuvant and adjuvant) + adjuvant chemotherapy[1]
ALNEO Italy **NCT05015010**	Phase II study of perioperative alectinib in patients with resectable stage III, ALK+ NSCLC[2]
HORIZON-01 International NCT05170204	Phase III, open-label, randomised cohort of patients with unresectable stage III, ALK+ NSCLC receiving alectinib vs durvalumab following chemoradiotherapy[3]

1. Lee et al. WCLC 2023 (Abs EP02.04); 2. Leonetti et al. Clin Lung Cancer 2021; 3. Paz-Ares et al. ELCC 2023 (Abs 131TiP)

Courtesy of Prof Ben Solomon, MBBS, PhD

NAUTIKA1



Primary endpoint: MPR
Secondary endpoints: ORR, pCR, surgical outcomes/safety

Table 2. Response outcomes of patients from the *ALK*+ cohort

Pathological response, n (%)*	*ALK*+ cohort (n=9)
Major pathological response†	6 (66.7)
Pathological complete response‡	3 (33.3)
Radiographic response, n (%)	***ALK*+ cohort (n=9)**
Complete response	0
Partial response	4 (44.4)
Stable disease	5 (55.6)
Progressive disease	0

Of the 9 patients, 8 with R0 resection. 1 patient did not proceed with surgery due to need for pneumonectomy

Lee J et al. WCLC 2023.

Courtesy of Prof Ben Solomon, MBBS, PhD

Based on your clinical experience and knowledge of available data, what are the top 3 tolerability issues patients experience when receiving adjuvant alectinib for NSCLC with ALK rearrangements?

 Prof Peters	Elevated liver tests, muscular pain, constipation
 Prof Solomon	LFT issues, myalgia, constipation
 Dr Camidge	Arthralgia, weight gain, constipation
 Dr Chaft	Fatigue, weight gain, edema
 Dr Dagogo-Jack	Fatigue, muscular pain, constipation
 Dr Liu	Fatigue, myalgia, abnormal LFTs

LFT = liver function test

Approximately what proportion of patients with localized NSCLC with ALK rearrangements will experience toxicity during treatment with adjuvant alectinib that requires dosing to be held? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding adjuvant alectinib dose	Primary toxicity leading to withholding dosing
 Prof Peters	25%	Abnormal LFTs
 Prof Solomon	20%	Abnormal LFTs
 Dr Camidge	20%	Transaminitis
 Dr Chaft	10%	Abnormal LFTs
 Dr Dagogo-Jack	25%-35%	Labs (CPK elevation, LFT elevation)
 Dr Liu	10%	Abnormal LFTs

CPK = creatine phosphokinase; LFT = liver function test

For how long do you (or would you) typically continue adjuvant alectinib for a patient with localized NSCLC with an ALK rearrangement who is tolerating therapy well? What variables, if any, affect your decision about duration of therapy with adjuvant alectinib?

	Duration of adjuvant alectinib	Factors influencing duration decision
 Prof Peters	2 years	Reimbursement and evidence-based medicine
 Prof Solomon	2 years	Although longer seems better, am guided by clinical trials
 Dr Camidge	Until PD or unacceptable toxicity	Cost, tolerability
 Dr Chaft	3 years (LN-negative); PD or unacceptable toxicity (Stage III or LN-positive)	LN status
 Dr Dagogo-Jack	If can get approved, PD or unacceptable toxicity	Tolerability and reimbursement; concerned cancer will return if tx stopped
 Dr Liu	Until PD or unacceptable toxicity	Cost, tolerability

PD = progressive disease; LN = lymph node

Approximately what proportion of patients do you expect to complete your intended duration of adjuvant alectinib? To what degree do you believe adherence is an issue for patients receiving adjuvant alectinib for localized NSCLC?

	Proportion of patients able to complete adjuvant alectinib	Degree adherence is an issue
 Prof Peters	80%-90%	Somewhat
 Prof Solomon	95%	Somewhat
 Dr Camidge	75%	Moderate
 Dr Chaft	90%	Somewhat
 Dr Dagogo-Jack	70%-80% (if duration is 2 y)	Somewhat
 Dr Liu	90%	Not at all

Outside of a clinical trial setting, have you employed or would you employ neoadjuvant ALK-targeted therapy for a patient with resectable NSCLC and a documented ALK rearrangement?

 Prof Peters	I have not and would not
 Prof Solomon	I have not and would not
 Dr Camidge	I have
 Dr Chaft	I have
 Dr Dagogo-Jack	I have
 Dr Liu	I have not but would for the right patient

For a patient with unresectable locally advanced disease with an ALK rearrangement, would you administer durvalumab or targeted therapy as consolidation after chemoradiation therapy? If targeted therapy, which specific targeted agent would you employ?

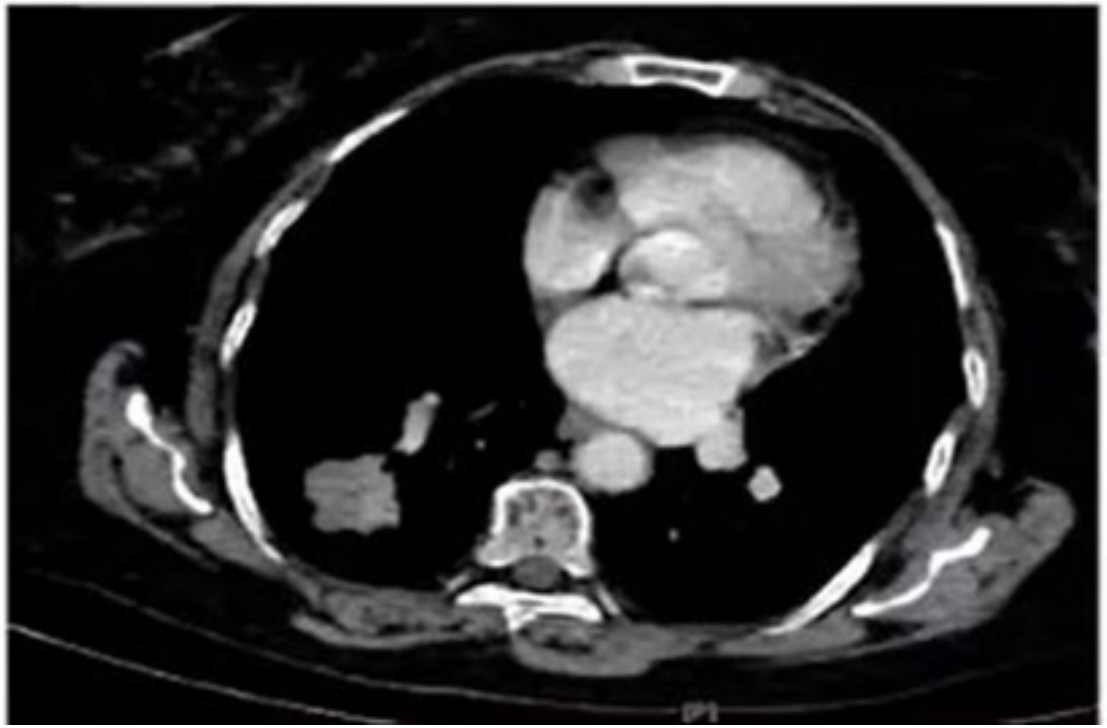
 Prof Peters	Durvalumab
 Prof Solomon	Would prefer targeted therapy but not reimbursed
 Dr Camidge	Alectinib
 Dr Chaft	Alectinib
 Dr Dagogo-Jack	Alectinib
 Dr Liu	Alectinib

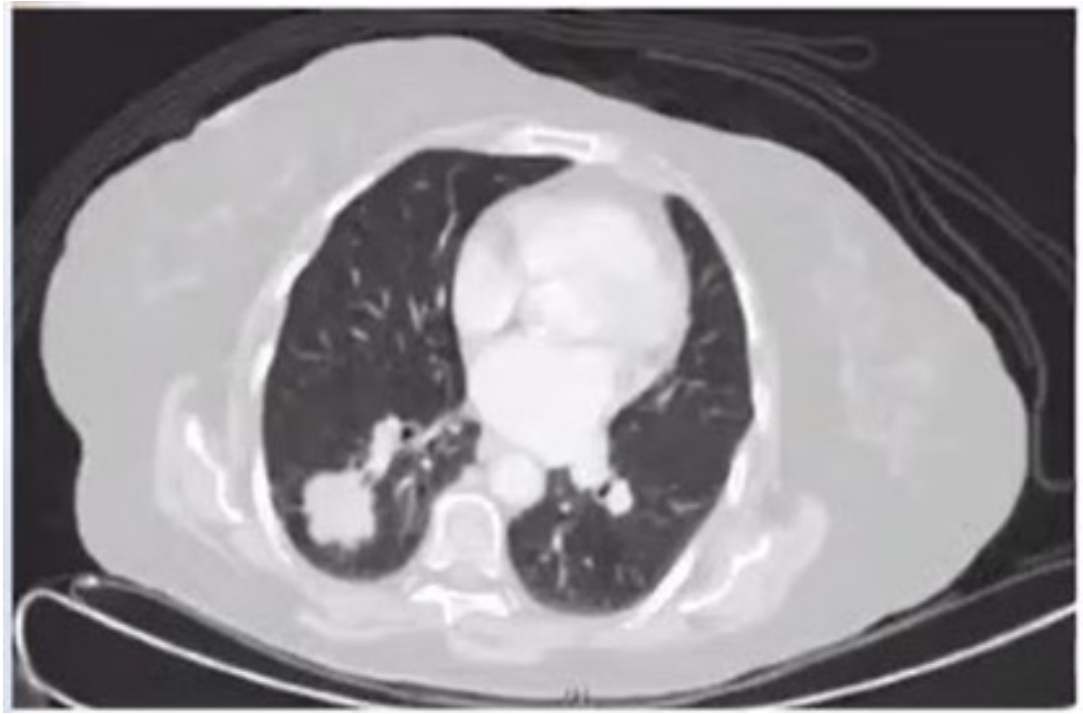
A patient completes 2 years of adjuvant alectinib but 18 months later experiences metastatic disease recurrence in the lungs and liver. Regulatory and reimbursement issues aside, what would be your most likely second-line treatment recommendation if they had acquired the gene mutations below associated with resistance to ALK inhibitor therapy?

	ALK I1171N mutation	ALK G1202R mutation	MET amplification
 Prof Peters	Lorlatinib	Lorlatinib	Lorlatinib
 Prof Solomon	Lorlatinib	Lorlatinib	ALK inhibitor + capmatinib
 Dr Camidge	Lorlatinib	Lorlatinib	Alectinib + capmatinib or lorlatinib + capmatinib
 Dr Chaft	Lorlatinib	Lorlatinib	Crizotinib + MET inhibitor
 Dr Dagogo-Jack	Lorlatinib	Lorlatinib	Lorlatinib + capmatinib
 Dr Liu	Ceritinib	Lorlatinib	Alectinib + capmatinib

Case Presentation – Prof Peters: 63-year-old woman with T2aN0M0, Stage IB lung adenocarcinoma

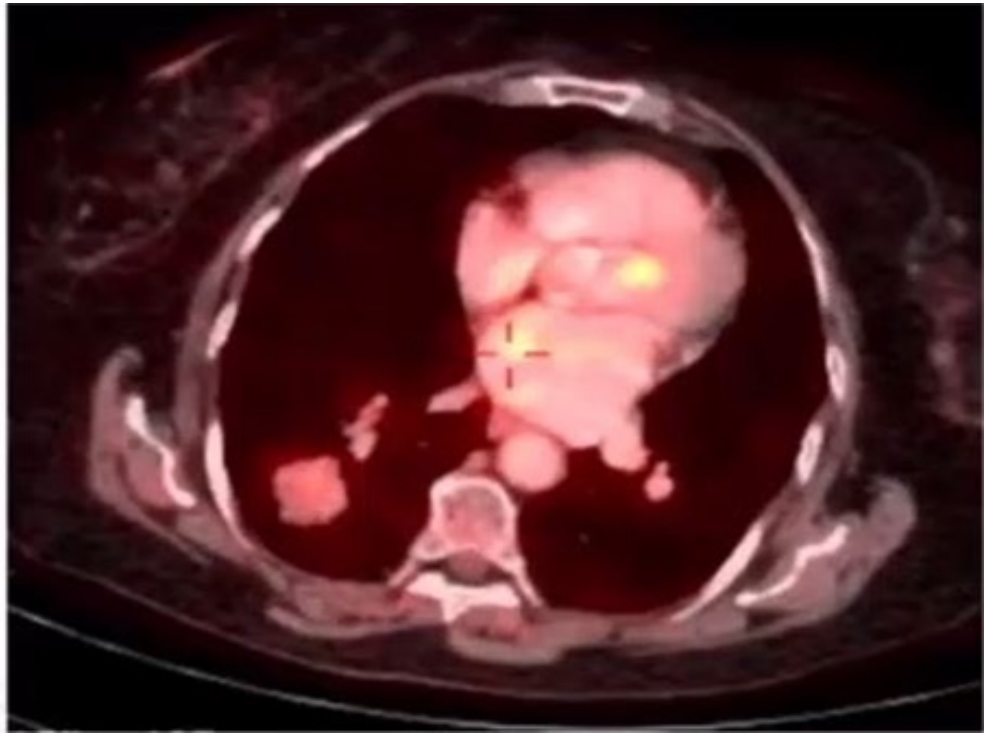
- A 63-year-lady, never smoker, ECOG 1, presented with chest pain (right-side), cough, & loss of appetite for three months
- Comorbidities: diabetes mellitus (well controlled on OHA) for last four years
- CECT thorax: 3.3×3.5×2.5 cm right lower lobe mass with no significant mediastinal & hilar lymphadenopathy





Case Presentation – Prof Peters: 63-year-old woman with T2aNoMo, Stage IB lung adenocarcinoma (continued)

- Biopsy – adenocarcinoma, TTF-1 & Napsin A – positive
- PET-CET: 3.4×3.5×2.5 cm right lower lobe lesion with an SUV max of 5.13 with no other significant uptake elsewhere in the body.



- MRI brain – no metastases
- EBUS FNA – Station 7, 4R & 4L – negative
- clinical stage was T2aNoMo, Stage IB
- PFT: FEV1 – 77%, DLCO – 77%
- 2D-Echo – EF-60%, No RWMA

WHAT ELSE DO YOU NEED?

Case Presentation – Prof Peters: 63-year-old woman with T2aN0M0, Stage IB lung adenocarcinoma (continued)

Management

- Surgery: right lower lobectomy with systematic mediastinal lymph node dissection was planned.
- Histopathology revealed a tumor of size-3.4 cm, adenocarcinoma, TTF-1 positive.
- Ipsilateral hilar node positive for malignancy. All mediastinal nodes were negative for malignancy (0/10).
- EGFR was positive; negative for ALK and ROS
- The final AJCC 8th TNM stage was pT2aN1M0, Stage IIB
- Adjuvant Osimertinib was planned.

Learning Points

- Testing should ideally be done in the initial biopsy
- If neoadjuvant chemo/IO is given, Osimertinib administration has to be delayed. This is not the best treatment
- Nodal upstaging happens in at least 15% of patients, creating a reality for adjuvant treatments, In addition to traditional surgical practices

Case Presentation – Prof Solomon: 74-year-old man with pT1N2M0 ALK+ lung adenocarcinoma

74 year-old former smoker (20 pkt year history) with resected **pT1N2M0** Adenocarcinoma ALK+ NSCLC

4/12/19 - VATs right lower lobectomy + mediastinal lymph node dissection

Pathology: 18x16x15mm Adenocarcinoma – mod differentiated, predominantly acinar; Lymph nodes: Intrapulmonary nodes 3/3 no ECE; R middle lobe nodes: 2/2; R lower paratracheal: 0/1; Subcarinal 2/3; Interlobar node: 0/1; Inferior pulmonary ligament node: 0/1. ALK IHC and FISH positive. EGFR mutation negative

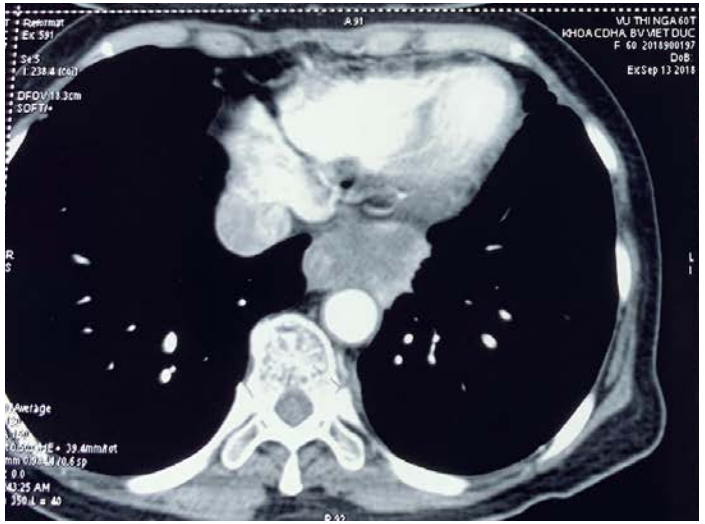
Enrolled on the ALINA adjuvant trial:

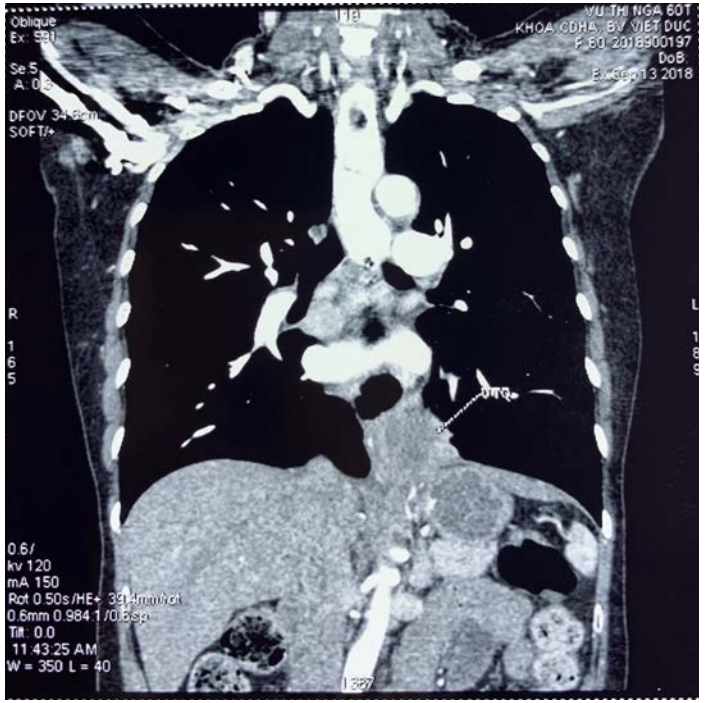
Randomised to the Alectinib arm commenced 3/2/2020 - Completed Alectinib 31st January 2022

Remains well to date with no evidence of recurrent disease on scans

Case Presentation – Prof Peters: 61-year-old woman with ALK+ Stage IIIB lung adenocarcinoma – PD-L1 <1%

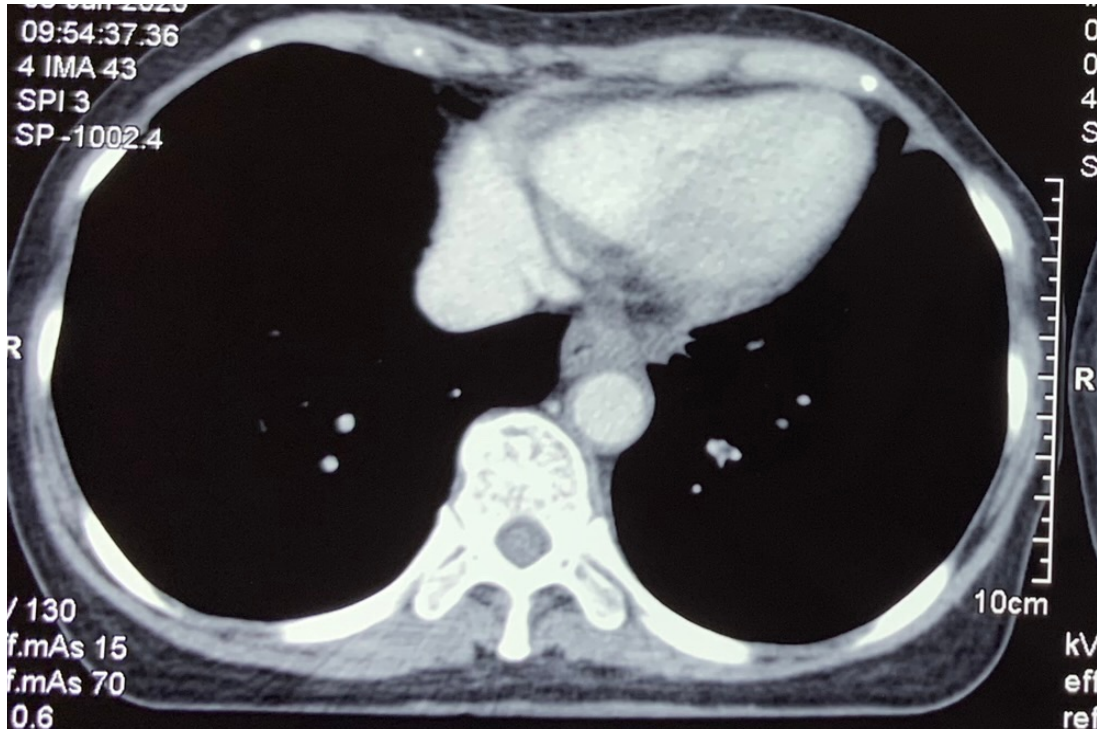
- A 61-year-old, nonsmoking housewife, without occupational chemical exposure or family history of lung cancer
- She complained she has had difficulty swallowing for last 10 months, admitted to Cancer Hospital for nutrition by percutaneous gastrostomy
- Detection of a mass near by the lung and esophagus on thoraco-abdominal tomography. Lesion invasive to pericardium, pleural and diaphragm.
- Bronchoscopy was done but can't reach to lesion





Case Presentation – Prof Peters: 61-year-old woman with ALK+ Stage IIIB lung adenocarcinoma – PD-L1 <1% (continued)

- PET-CT: no other lesions were detected.
- Esophagus endoscopy biopsy was done, no mucosal invasion
- Lung adenocarcinoma, EGFR negative, ALK-rearranged variant type 1 (v1) positive. PDL1 < 1%, cT4 cNo cMo, stage IIIB
- The patient started treatment with alectinib at a dosage of 600 mg twice per day for two months, achieving a partial response. CR of the disease with 100% shrinkage of the mass at 4 months.



WAS THE DECISION CORRECT AND WHAT ELSE COULD HAVE BEEN DONE?

Case Presentation – Prof Peters: 61-year-old woman with ALK+ Stage IIIB lung adenocarcinoma – PD-L1 <1% (continued)

- A lobectomy of the left lower lobe and systemic lymphadectomy under video-assisted thoracoscopic approach was successfully performed 10 days after the last dose of alectinib. Postoperative pathology showed pathological complete response (pCR) ypTo ypNo cMo

WHAT COMES NEXT:
- **RESUME ALECTINIB?**
- **CHEMO?**
- **RT?**
- **FU?**

Case Presentation – Prof Solomon: 76-year-old woman with recurrent metastatic ALK+ lung adenocarcinoma

76 year-old never-smoker presented with an incidentally detected mass in lung

→VATs Left lower lobectomy (November 2018) – for pT3N0M0 (stage IIB)ALK+ lung adenocarcinoma

Pathology: moderately and poorly differentiated adenocarcinoma (acinar and micropapillary growth pattern). Main component 35x25x40 mm and separate 5 mm satellite nodule in same lobe

No nodes involved: 0/4 Hilum 0/2 9L 0/1 and 11L 0/1

ALK IHC (D5F3) – strong membranous staining and FISH+ (Vysis)

Post-operative adjuvant therapy

→Cisplatin/Pemetrexed x4

Developed recurrent disease in bone

Case Presentation – Prof Solomon: 76-year-old woman with recurrent metastatic ALK+ lung adenocarcinoma (continued)

Commenced alectinib 600 mg bid October 2019

Complete metabolic response

Alectinib dose reduced to 450mg because of myalgia and increased CK

Remains well with no evidence of disease on scans

Inside the Issue: Integrating HER2-Targeted Strategies into the Management of Gastrointestinal Cancers

A CME/MOC-Accredited Live Webinar

Wednesday, August 21, 2024
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD
John Strickler, MD

Moderator

Neil Love, MD

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Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

CME and MOC credit information will be emailed to each participant within 5 business days.

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