Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

WCLC HIGHLIGHTS

12 - 15 **SEPTIEMBRE** 2026

Seoul, Republic of South Korea



#WCLCUPDATES

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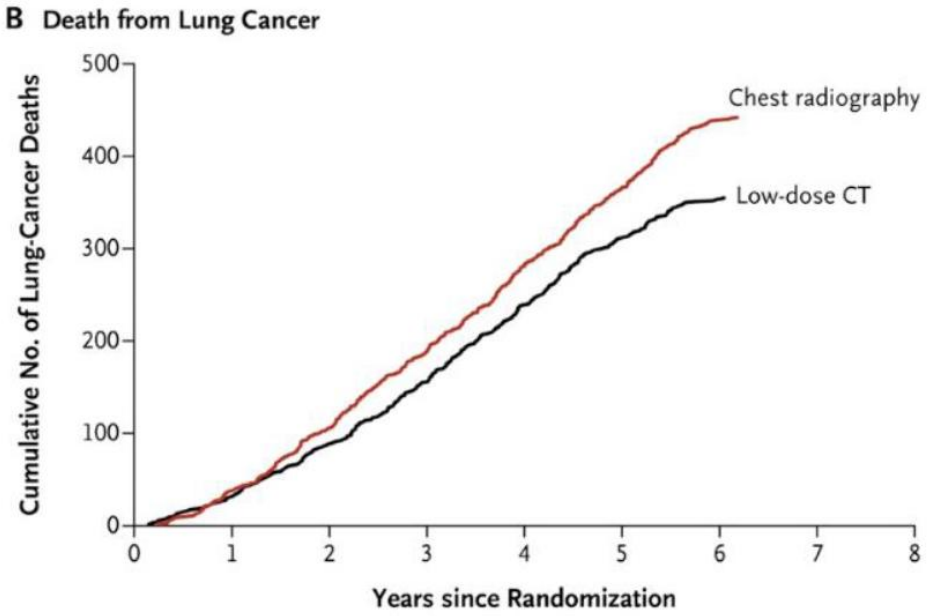
Biomarcadores, screening y cáncer de pulmón no microcítico estadio precoz - (Parte I)

Silvia Sequero Lopez

Hospital Universitario San Cecilio, Granada

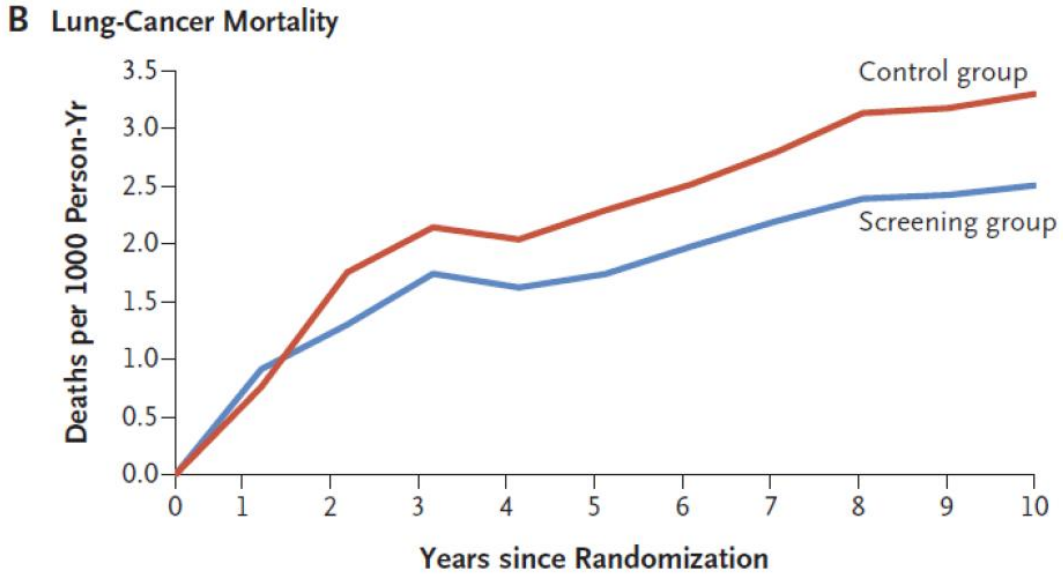
SCREENING EN CÁNCER DE PULMÓN

Evidence of lung cancer screening: mortality reduction in smokers



<NLST trial>

Age 55–75 years, ≥30 PY smoking, <10 years ex-smoker (*n* = 53,454)



<NELSON trial>

Age 55–75 years, ≥15 PY smoking, <10 years ex-smoker (*n* = 15,789)

The NLST research team. N Engl J Med. 2011.
de Koning et al. N Engl J Med. 2020.

Risk-model based calculation for the screening criteria – PLCOm2012

Table 2. Modified Logistic-Regression Prediction Model ($PLCO_{M2012}$) of Cancer Risk for 36,286 Control Participants Who Had Ever Smoked.*

Variable	Odds Ratio (95% CI)	P Value	Beta Coefficient
Age, per 1–yr increase†	1.081 (1.057–1.105)	<0.001	0.0778868
Race or ethnic group‡			
White	1.000		Reference group
Black	1.484 (1.083–2.033)	0.01	0.3944778
Hispanic	0.475 (0.195–1.160)	0.10	−0.7434744
Asian	0.627 (0.332–1.185)	0.15	−0.466585
American Indian or Alaskan Native	1		0
Native Hawaiian or Pacific Islander	2.793 (0.992–7.862)	0.05	1.027152
Education, per increase of 1 level†§	0.922 (0.874–0.972)	0.003	−0.0812744
Body-mass index, per 1-unit increase†	0.973 (0.955–0.991)	0.003	−0.0274194
Chronic obstructive pulmonary disease (yes vs. no)	1.427 (1.162–1.751)	0.001	0.3553063
Personal history of cancer (yes vs. no)	1.582 (1.172–2.128)	0.003	0.4589971
Family history of lung cancer (yes vs. no)	1.799 (1.471–2.200)	<0.001	0.587185
Smoking status (current vs. former)	1.297 (1.047–1.605)	0.02	0.2597431
Smoking intensity¶			−1.822606
Duration of smoking, per 1-yr increase†	1.032 (1.014–1.051)	0.001	0.0317321
Smoking quit time, per 1-yr increase†	0.970 (0.950–0.990)	0.003	−0.0308572
Model constant			−4.532506

Table 4. Accuracy of Lung-Cancer Classification According to Alternative Criteria in the PLCO Intervention-Group Smokers.*

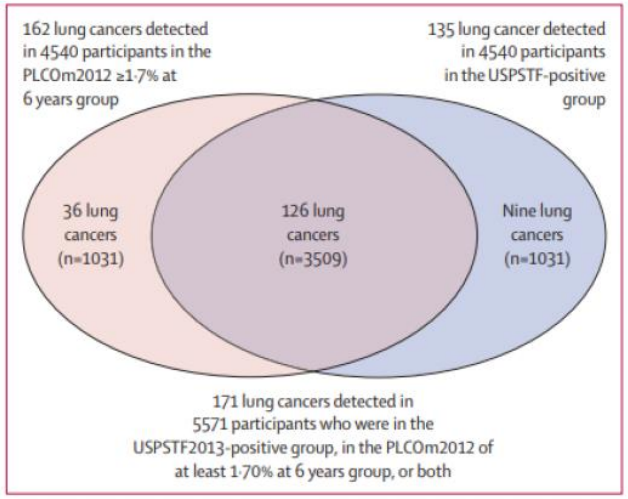
Criteria†	Participants with Lung Cancer (N=678)	Participants without Lung Cancer (N=36,654)	Total Participants (N=37,332)	Predictive Value
NLST				
Criteria positive	482 TP (3.4%)	13,662 FP (96.6%)	14,144	PPV, 3.4%
Criteria negative	196 FN (0.8%)	22,992 TN (99.2%)	23,188	NPV, 99.2%
Sensitivity	71.1%			
Specificity		62.7%		
$PLCO_{M2012}$ ‡				
Criteria positive	563 TP (4.0%)	13,581 FP (96%)	14,144	PPV, 4.0%
Criteria negative	115 FN (0.5%)	23,073 TN (99.5%)	23,188	NPV, 99.5%
Sensitivity	83.0%			
Specificity		62.9%		

- Calculation of the 6 year-lung cancer risk: suitable threshold for screening = 1.5%/6y

Yeon Wook Kim

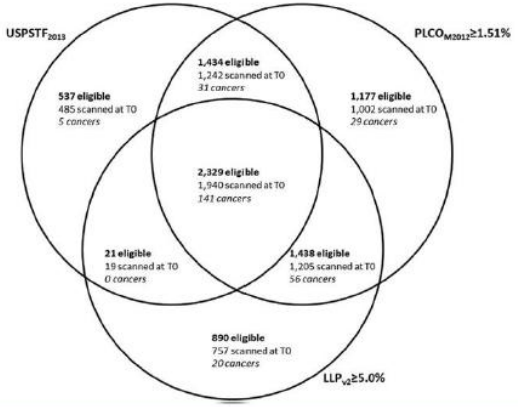
Tammemagi M. et al. NEJM. 2013.

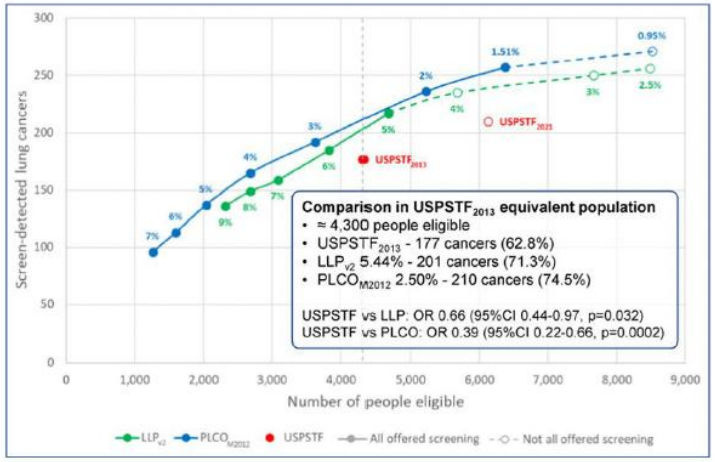
Benefits of risk-prediction models: higher sensitivity



	USPSTF eligible	PLCOm2012 ≥1·70% at 6 years	p value
ILST data			
Cancer detection rate*	135/177 (76·3% [69·3–82·3])	162/177 (91·5% [86·4–95·2])	$p_{McNemar}$=0·0001
Cancer detection rate†	135/171 (78·9% [72·1–84·8])	162/171 (94·7% [90·2–97·6])	$p_{McNemar}$=0·0001
Positive predictive value†	135/4540 (2·97% [2·90–3·51])	162/4540 (3·57% [3·05–4·15])	p=0·11
False-negative proportion†	42/1279 (3·28% [2·38–4·41])	15/1279 (1·17% [0·66–1·93])	p=0·0003
Negative predictive value	96·72%	98·83%	..

International Lung Screening Trial





Yorkshire Lung Screening Trial

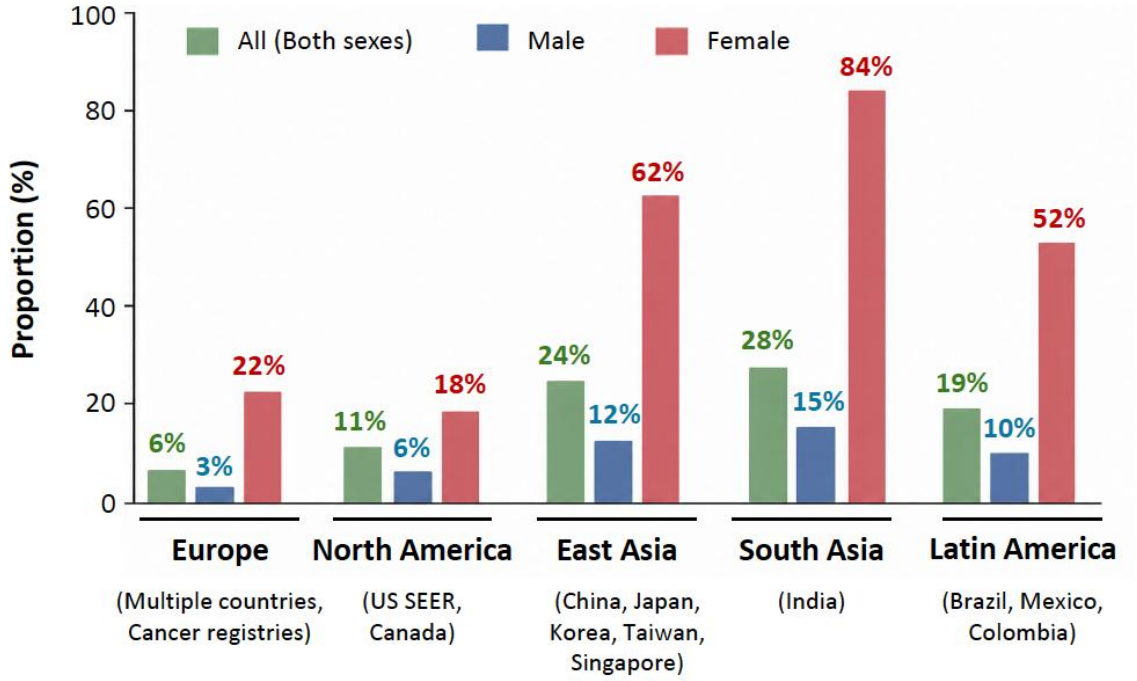
Yeon Wook Kim

Tammemagi et al. Lancet Oncol. 2022.
Gabe et al. J Thorac Oncol. 2025.

Persons Who Never Smoked and Women are Missed Burden

Proportion of Lung Cancer Among Never-Smokers (%)

Marked sex and regional differences: highest among women in Asia



Estimates are derived from population-based cancer registries and cohort studies summarized in recent reviews. Regions are aggregated from multiple countries within each region.

100% Total Lung Cancer Population

35% Under Current US guidelines

- Only **35%** lung cancer pts meet US screening criteria

>65% The Missed Burden

- In US, women lung cancer incidence has surpassed men
- **80%** of women lung cancers are excluded from guidelines

Data from Potter AL et al, JCO 2024; Jemal A et al NEJM 2018

Data synthesized from international cancer registries and cohort studies as reported in the following references: LoPiccolo J, et al. Nat Rev Clin Oncol. 2024;21:121–146; Murphy C, et al. JAMA. 2025;334(20):1836–1845.

Pan-Chyr Yang

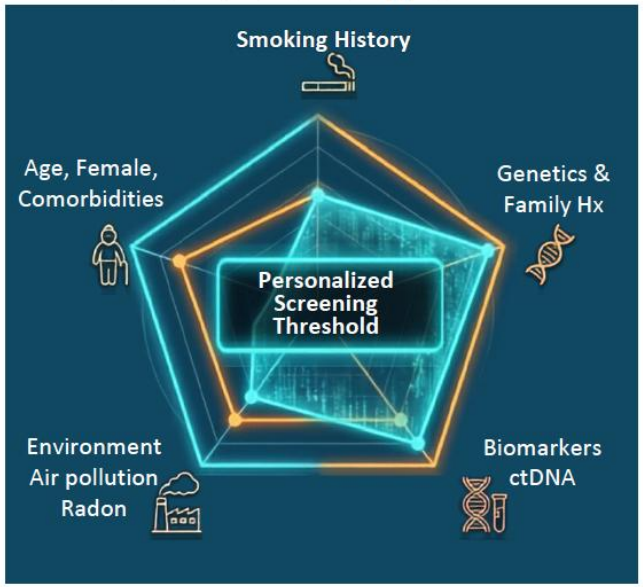
Lung Cancer Risk: A Continuum, Not a Binary

LCINS in East Asia and LATAM exhibit a different epidemiologic profile, heavily modified by gender, geography, endogenous and exogenous exposomes, demanding loco-regional screening architectures.

East Asian Profile — Latin America Profile — US/ Western Profile

Never-Smokers | **Light/Moderate Smokers** | **Heavy smokers**

Risk factors for lung cancer



Precision Screening should base on personalized cumulated risks not just smoking alone

[Moderate Factors] + [Moderate Factors] ≥ Risk of Heavy Smoking

$$P(Risk) = \alpha \times Age + \beta \times BMI + \gamma \times \text{pack-yr} + \text{SNPs, Biomarkers etc.}$$

Osarogiagbon, Yang, and Sequist 2023 ASCO EDUCATIONAL BOOK

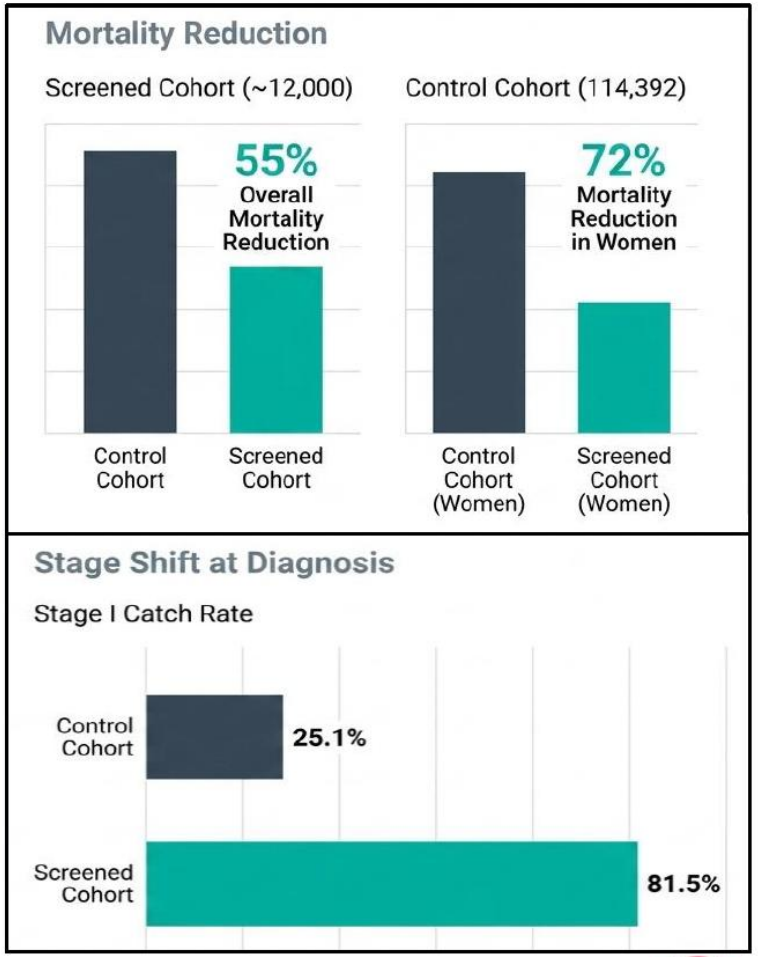
Pan-Chyr Yang

Cost Effectiveness and Evidence of Lung Cancer Screening in Never Smokers

- **Chinese Lung-Care Project**: 12,000 adults (40-74 yrs) LDCT screening vs 114,392 controls, 7 yrs follow up
- 55% reduction in overall mortality (HR 0.45; p<0.001),
- 72% reduction in female lung cancer mortality (HR 0.28; p<0.001)
- 81.5% diagnosed at Stage 1 compared to 25% unscreened cohort

Region	Strategy & Starting Age	Resulting ICER (Per QALY Gained)	Economic Status
Japan	LDCT screening for **never-smokers** at 60yrs	Negative ICER (save $117B over lifetime)	**Cost-Saving**
China	Targeted screening **non-smokers** (LCFH) at 55yrs	Males: CNY 68,932 / Females: CNY 80,056	**Cost-Effective**
USA	LDCT screening for **never smokers** at 60 yrs	Males: $3,001,304 / Females: $2,097,969	Highly Inefficient (>WTP threshold of $100k)

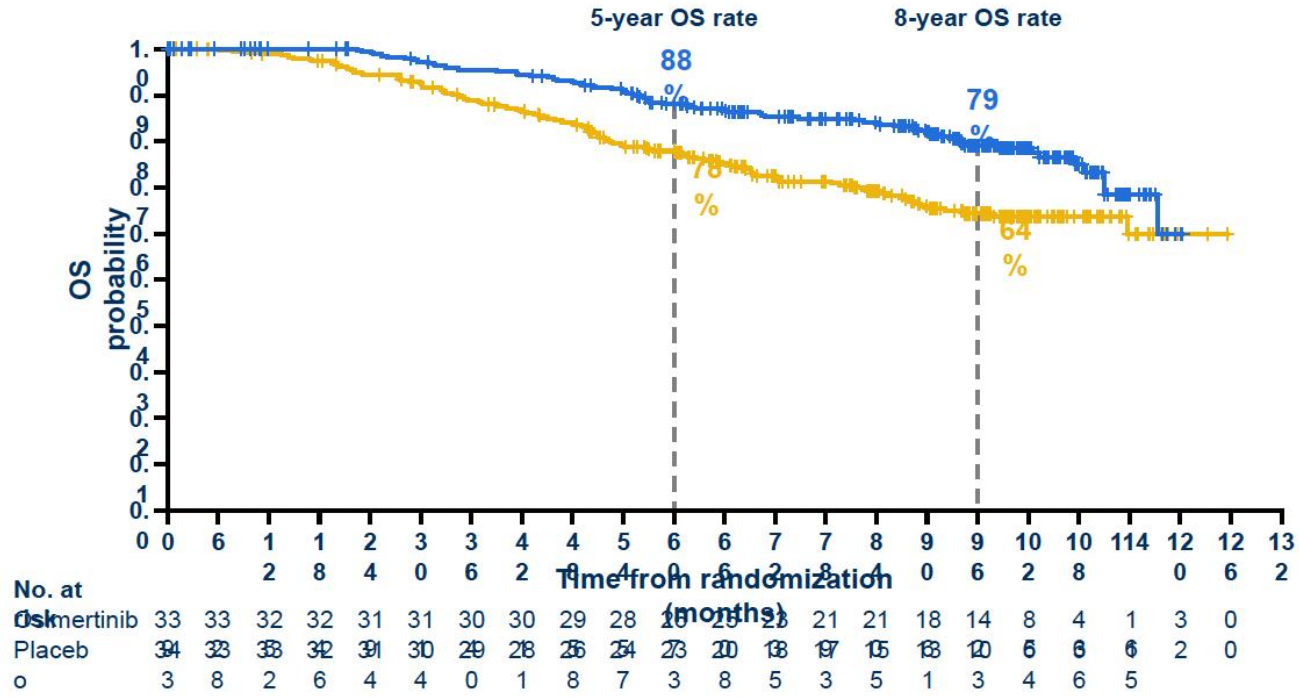
LCFH: Lung cancer family history; Li, JAMA 2026, Li, ELCC 2026 Kowada, BMC Pulmonary Medicine, 2022; Liu, BMC Public Health, 2025.



Pan-Chyr Yang

BIOMARCADORES Y CÁNCER DE PULMÓN ESTADIO PRECOZ

Osimertinib continued to show an OS benefit versus placebo in the overall population (stage IB□IIIA disease) at the current DCO*



8-year OS rate, % (95% CI)	
Osimertinib (n=339)	79 (74, 83)
Placebo (n=343)	64 (58, 70)

OS HR (95% CI)	**0.52 (0.39, 0.71)**

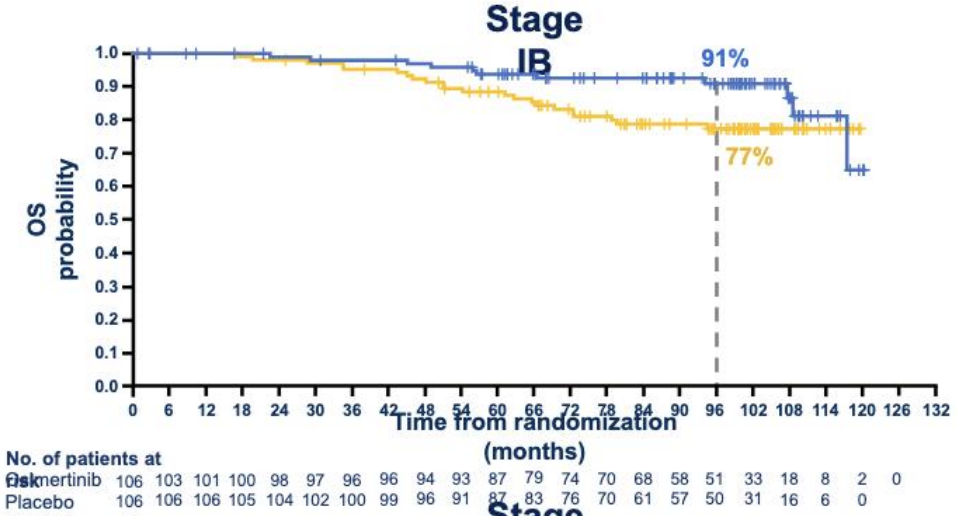
Maturity: 26%
osimertinib 20%; placebo 31%

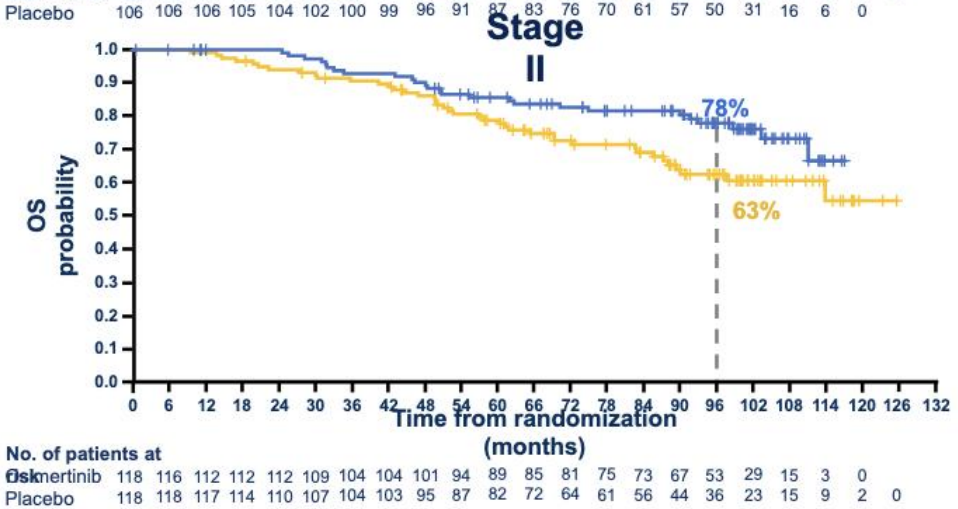
Median follow-up for OS (all patients):
osimertinib 93.3 months; placebo 79.6 months

Roy S. Herbst,

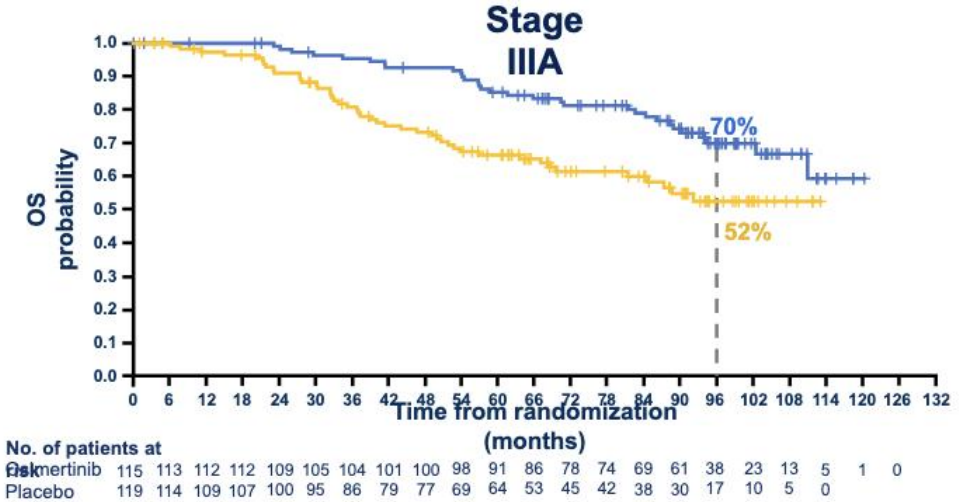
DCO: May 4, 2026. Tick marks indicate censored data. *Among patients who were alive at the planned final OS analysis (DCO: Jan 27, 2023), updated survival data were collected through yearly follow-up until the current DCO (May 4, 2026; additional consent provided) and from accessible records / information from last contact date after the final planned OS DCO. Patients for whom no additional long-term OS data were available remained censored at their last known alive date, survival time unchanged from the final planned OS analysis DCO (Jan 27, 2023). CI, confidence interval; DCO, data cut-off; HR, hazard ratio; OS, overall survival.

OS benefit was observed across disease stages (IB / II / IIIA)*





	Stage IB	Stage II	Stage IIIA
8-year OS rate, % (95% CI)			
Osimertinib	91 (82, 95)	78 (68, 85)	70 (59, 78)
Placebo	77 (68, 85)	63 (52, 71)	52 (41, 63)
OS HR (95% CI)	**0.50 (0.23, 1.01)**	**0.60 (0.36, 0.97)**	**0.49 (0.31, 0.77)**

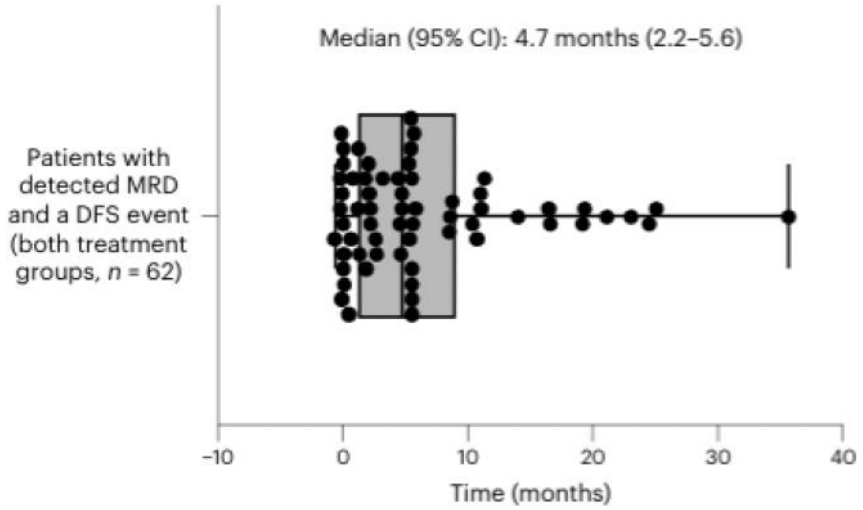


DCO: May 4, 2026. *AJCC / UICC 7th edition. AJCC, American Joint Committee on Cancer; CI, confidence interval; HR, hazard ratio; OS, overall survival; UICC, Union for International Cancer Control.

Roy S. Herbst,

Optimizing Adjuvant Targeted Therapy

Can Molecular Residual Disease Tell Us Who Needs Longer Therapy?

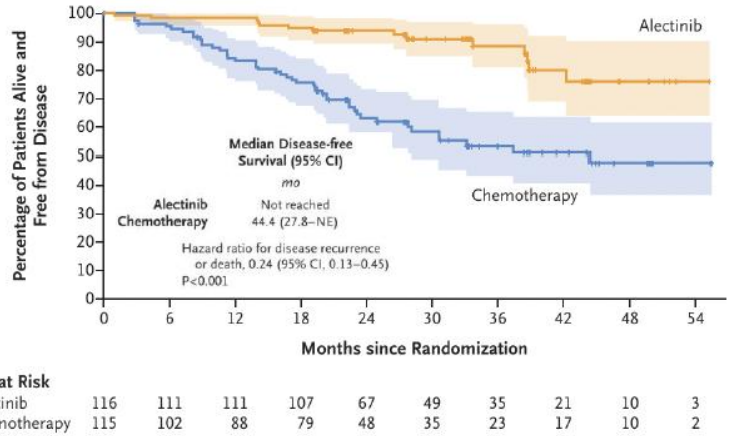


- MRD preceded imaging DFS events in this study by a median of **4.7 months** (95% confidence interval, 2.2–5.6).
- Most MRD or DFS events occurred **after osimertinib** treatment discontinuation or completion.
- MRD detection could identify patients who may benefit from longer adjuvant osimertinib, although this requires clinical confirmation.

Herbst RS, et al. Nat Med. 2025;31(6):1958-1968.

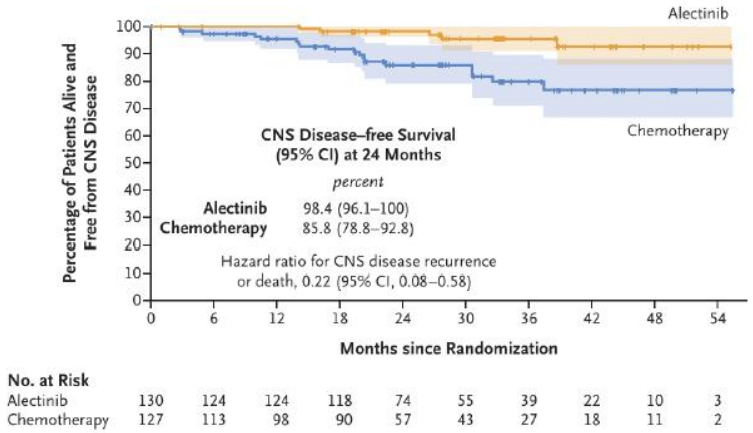
ALINA: Adjuvant Alectinib

2-year Disease-free Survival



76% Reduction in Risk of Recurrence or Death
(HR = 0.24 vs. chemotherapy in resected Stage **II-IIIA** NSCLC)

CNS Disease-free Survival



78% Reduction in Risk of CNS Recurrence or Death
(HR = 0.22 vs. chemotherapy in resected Stage **II-IIIA** NSCLC)

- Adjuvant Alectinib demonstrated substantial DFS and CNS protection over chemotherapy in resected ALK+ NSCLC (2-yr DFS: 93.8% vs. 63.0%, HR = 0.24; CNS DFS HR = 0.22)
- Updated follow-up: Durable efficacy maintained post 2-year treatment completion in stage II-IIIA NSCLC (4-yr DFS: 74.5% vs 46.3%, HR = 0.36); CNS DFS HR = 0.37 in ITT (stage IB-IIIA).

Solomon BJ, et al. N Engl J Med. 2024;390(14):1265-1276. Dziadziuszko R, et al. Ann Oncol 2025;36(Suppl 2):S971–S972 (Abstract 1787MO

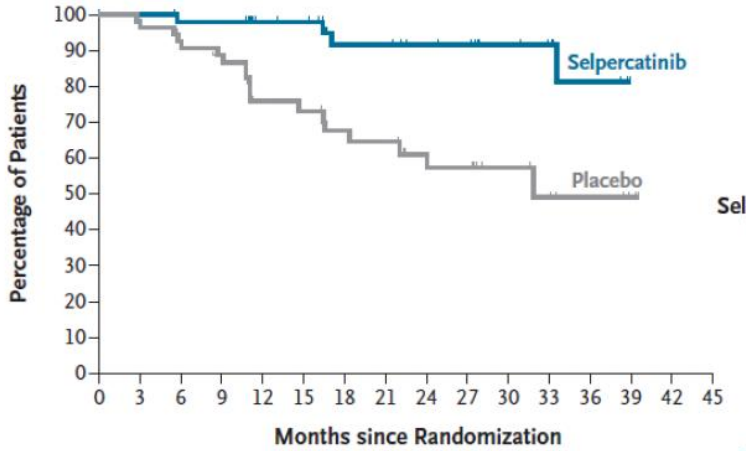
LIBRETTO-432: Adjuvant Selpercatinib

Study Design
- Phase 3, double-blind, 1:1 randomized, placebo-controlled trial
- Resected Stage IB–IIIA, RET fusion-positive NSCLC (post-definitive therapy ± adjuvant chemotherapy)
- **Adjuvant Selpercatinib (N=75) vs. Placebo (N=76) (up to 3 years)**

- Primary Endpoint: EFS (Stage II–IIIA)
- Secondary Endpoints: EFS in ITT (Stage IB–IIIA), BICR-assessed EFS, OS, Safety

2-year Event-free Survival

A Event-free Survival in the Primary Analysis Population



	No. of Patients	No. of Events	Median Event-free Survival (95% CI)
			mo
Selpercatinib	54	4	NE (33.5 to NE)
Placebo	55	19	31.8 (18.4 to NE)

Hazard ratio for disease recurrence, progression, or death, 0.17 (95% CI, 0.06–0.51)
P<0.001

No. at Risk															
Selpercatinib	54	49	45	45	37	36	27	27	22	21	15	12	7	0	0
Placebo	55	54	47	44	28	27	22	21	16	15	8	6	4	2	0

83% Reduction in Risk of Recurrence or Death
(HR = 0.17 vs. placebo in resected Stage **II-IIIA** NSCLC)

- EFS in Stage II–IIIA: 83% reduction in risk of recurrence or death (92% vs. 61%, HR = 0.17, *P*<0.001)
- EFS in stage IB-IIIA: 94% vs. 70%, HR 0.16, *P*<0.001
- CNS Protection: Brain recurrence in only 1 patient (1.9%; Selpercatinib) vs. 3 patients (5.5%; Placebo)

Wu YL, Goldman J, Drilon A, et al. N Engl J Med 2026;395(7):660–670

A Randomized Phase III Multicenter Trial of Adjuvant Gefitinib Plus Chemotherapy Versus Chemotherapy in EGFR-Mutant NSCLC: RAPHAEL Trial (KM-07, LU15-12)

Method

Multicenter, Randomized, Phase III trial

Eligibility:
Completely Resected pStage II-IIIB (excluding N3)

Non-squamous NSCLC

EGFR mutation: E19del or L858R

1:1 R

Stratified by
-pStage (II or III)
-exon 19del vs. L858R

Arm A: Intercalating arm

Pemetrexed (D1) + Cisplatin (D1)
Gefitinib (D5-18), q3wks x 4 cycles

Intercalating phase (3week * 4 cycle)

Gefitinib maintenance 1 year

Arm B: Chemotherapy arm

Vinorelbine (D1,8) + Cisplatin (D1)
q3wks x 4 cycles

Two-sided α = 0.05 and 80% power, N=102 in each arm

Treatment continues until:
Disease recurrence
Treatment completed
Discontinuation criterion met

Chemotherapy

Gefitinib

Primary endpoint : Disease-free survival
Secondary endpoints : Overall survival, safety & tolerability

Exploratory Analysis

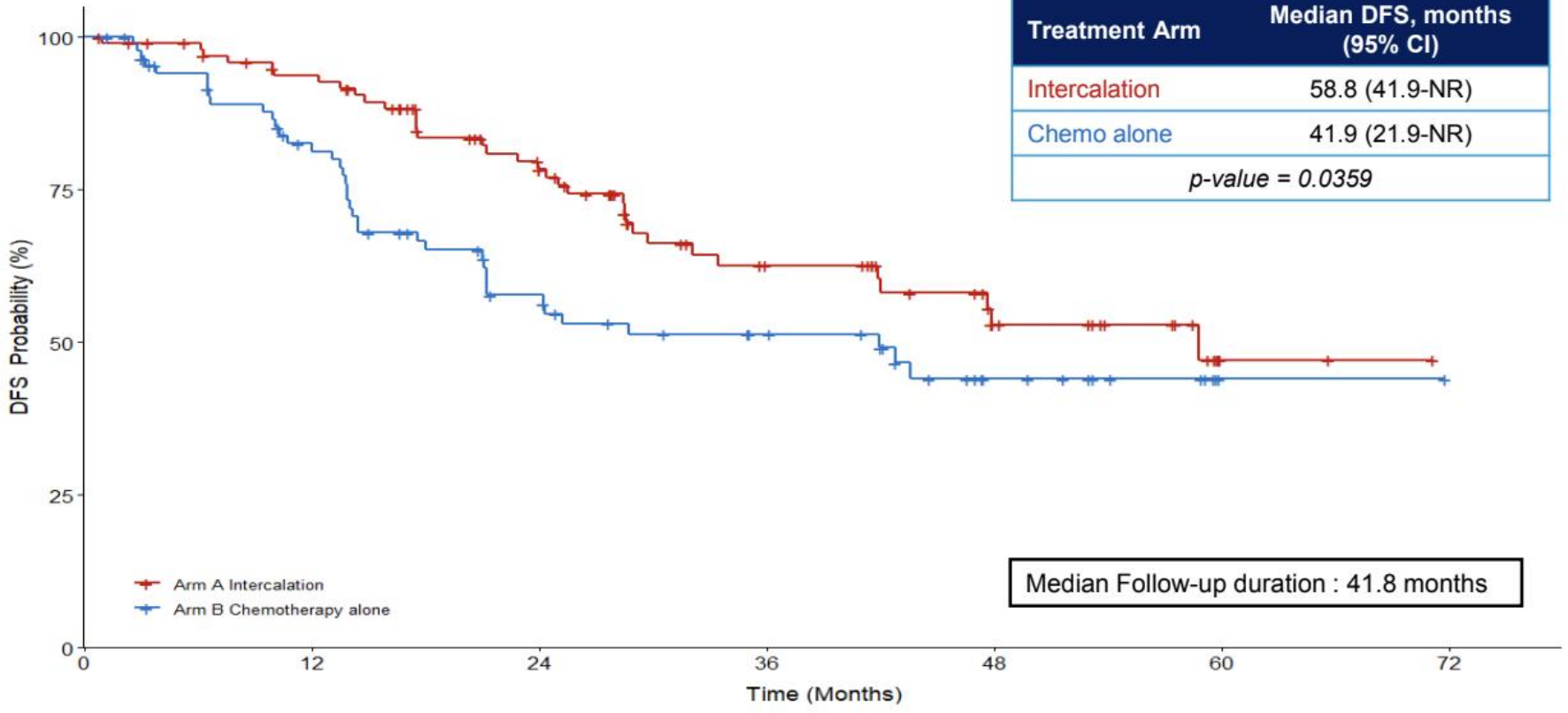
- **Exploration of biomarkers predictive of recurrence using next-generation sequencing (NGS) of surgical tumor specimens**
- **Longitudinal assessment of changes in EGFR mutation patterns in cell-free DNA**
- **Blood-based analysis of inflammatory biomarkers**
- **Optional acquisition of tumor tissue at recurrence to investigate mechanisms of resistance using NGS**

Beung Chul Ahn

A Randomized Phase III Multicenter Trial of Adjuvant Gefitinib Plus Chemotherapy Versus Chemotherapy in EGFR-Mutant NSCLC: RAPHAEL Trial (KM-07, LU15-12)

Results

Disease-Free Survival



Treatment Arm	Median DFS, months (95% CI)
Intercalation	58.8 (41.9-NR)
Chemo alone	41.9 (21.9-NR)
p-value = 0.0359	

Median Follow-up duration : 41.8 months

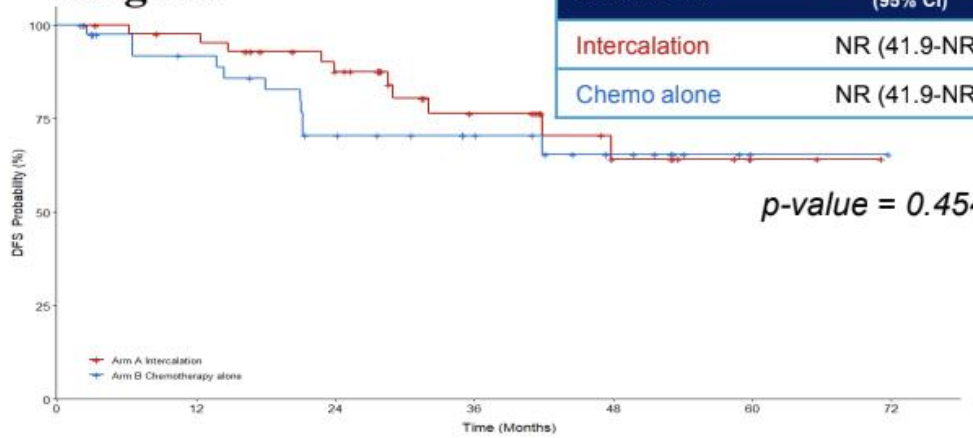
Arm A Intercalation	100	87	59	33	17	2	0
Arm B Chemotherapy alone	88	61	38	26	12	2	0

Beung Chul Ahn

Results

Stage II

Treatment Arm	Median DFS, months (95% CI)
Intercalation	NR (41.9-NR)
Chemo alone	NR (41.9-NR)

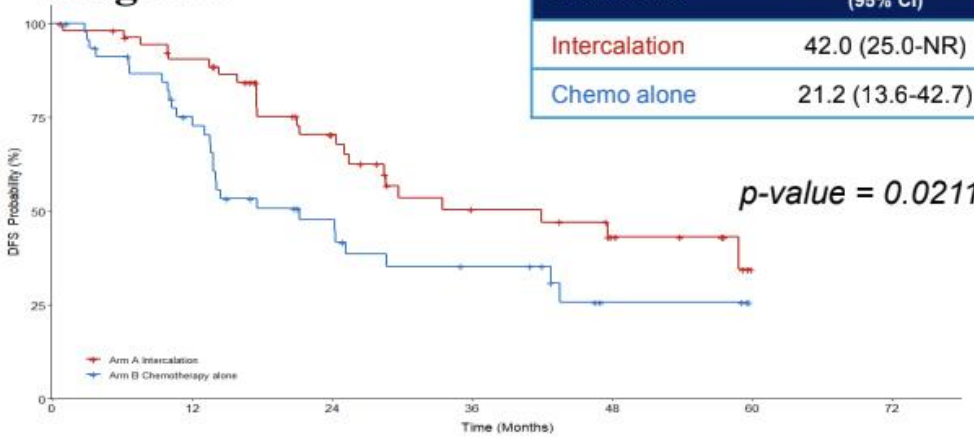


p-value = 0.4547

Arm A Intercalation	45	41	32	18	8	2	0
Arm B Chemotherapy alone	41	31	22	16	9	2	0

Stage III

Treatment Arm	Median DFS, months (95% CI)
Intercalation	42.0 (25.0-NR)
Chemo alone	21.2 (13.6-42.7)

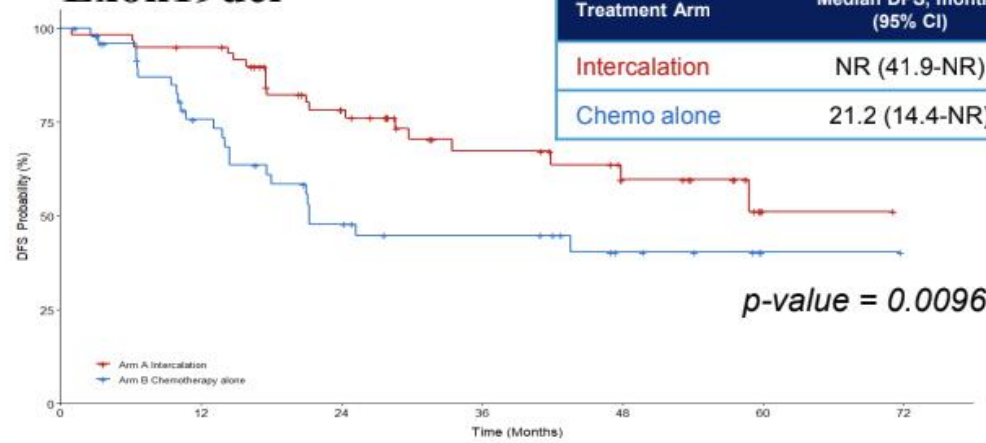


p-value = 0.0211

Arm A Intercalation	55	46	27	15	9	0	0
Arm B Chemotherapy alone	47	30	16	10	3	0	0

Exon19del

Treatment Arm	Median DFS, months (95% CI)
Intercalation	NR (41.9-NR)
Chemo alone	21.2 (14.4-NR)

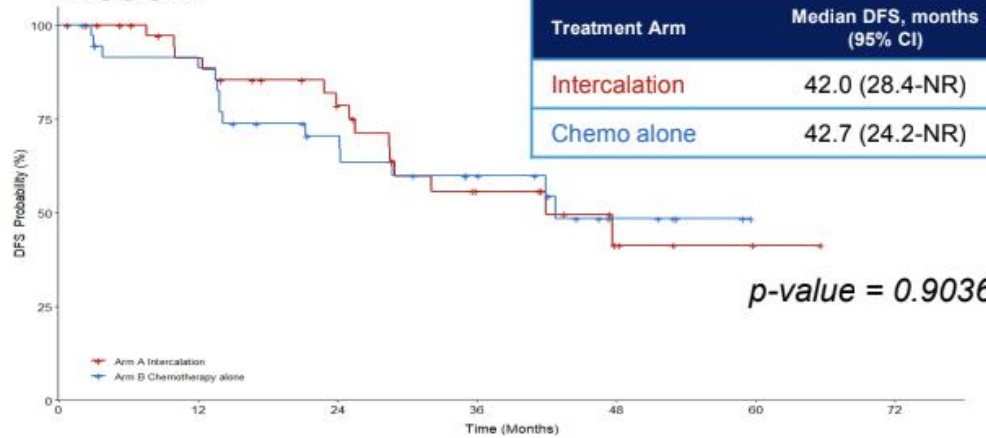


p-value = 0.0096

Arm A Intercalation	60	56	37	21	13	1	0
Arm B Chemotherapy alone	51	31	18	13	7	2	0

L858R

Treatment Arm	Median DFS, months (95% CI)
Intercalation	42.0 (28.4-NR)
Chemo alone	42.7 (24.2-NR)



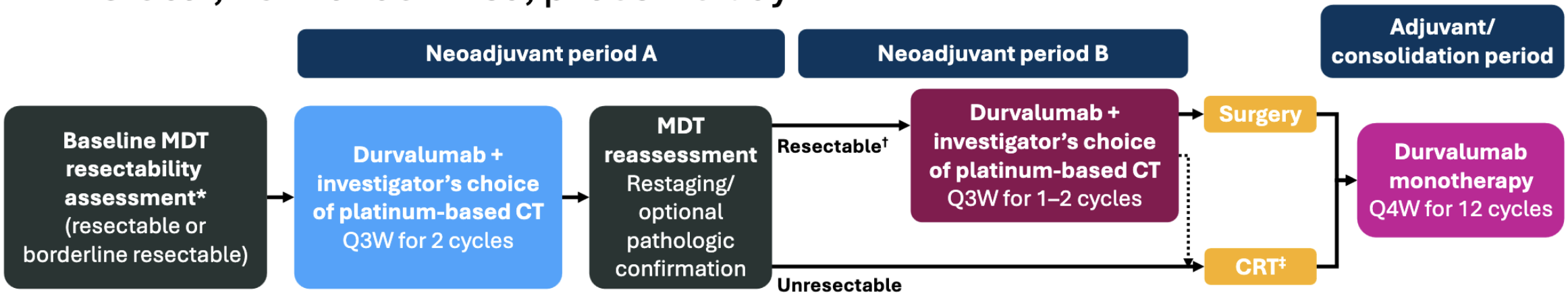
p-value = 0.9036

Arm A Intercalation	40	31	22	12	4	1	0
Arm B Chemotherapy alone	37	30	20	13	5	0	0

MDT-BRIDGE study design

Global, non-randomized, phase 2 study

Martin Reck



Key inclusion criteria and study requirements

- Aged ≥18 years
- Previously untreated
- Pathologically confirmed, resectable or borderline resectable stage IIB–IIIB NSCLC (AJCC 8th edition[1])
- *EGFR*/*ALK* wild type (per local test)
- WHO/ECOG PS 0–1
- At least 1 target lesion not previously irradiated
- Pre-operative RT not allowed

Primary endpoint

- Resection rate, defined as proportion of all patients (FAS) who underwent definitive surgery

Secondary endpoints¶

- Resection rate in patients deemed resectable/borderline resectable at baseline
- Surgical outcomes in patients who underwent surgery
- ORR in patients deemed resectable/unresectable at MDT reassessment
- pCR and EFS in all patients (FAS) and patients deemed resectable at MDT reassessment
- PFS in patients deemed unresectable at MDT reassessment
- Safety

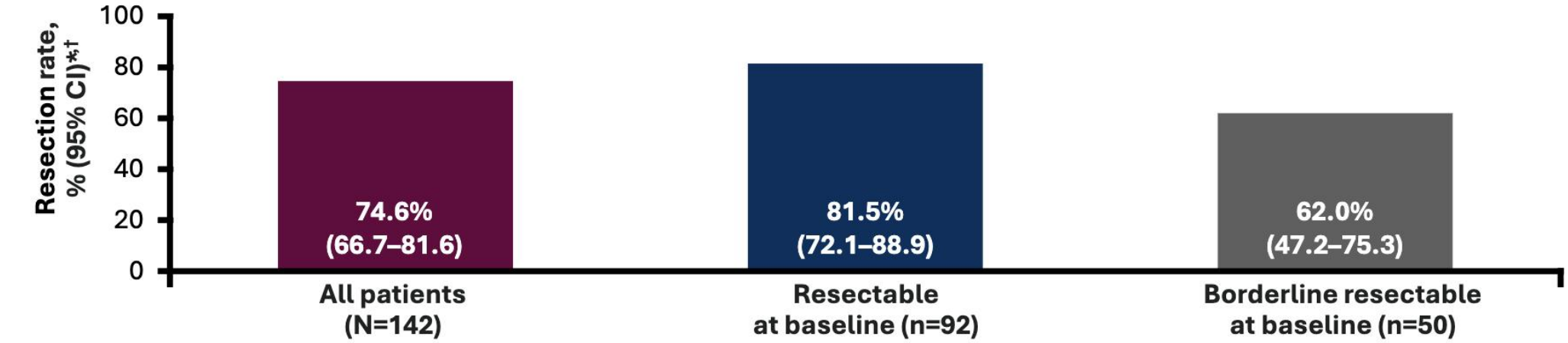
*MDT comprised a medical/pulmonary oncologist, thoracic surgeon, radiation oncologist, and pathologist at a minimum; resectable/borderline resectable status determined per MDT decision based on baseline available assessments. †Patients who were deemed eligible for surgery at MDT evaluation but then deemed unresectable/progressed locally at the pre-surgery assessments entered the unresectable cohort. ‡Five fractions/week for ~6 weeks (± 3 days) (total 60 Gy ± 10%). ¶Efficacy outcomes are reported, unless otherwise indicated, according to prespecified analysis populations except for pCR (assessed per local pathology review), which was not prespecified for analysis in all patients. AJCC, American Joint Committee on Cancer; ECOG, Eastern Cooperative Oncology Group; FAS, full analysis set (i.e., all patients who received at least one dose of study intervention); Gy, gray; ORR, objective response rate; PS, performance status; QXW, once every X weeks; RT, radiotherapy; WHO, World Health Organization.

1. Amin MB, et al. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017.

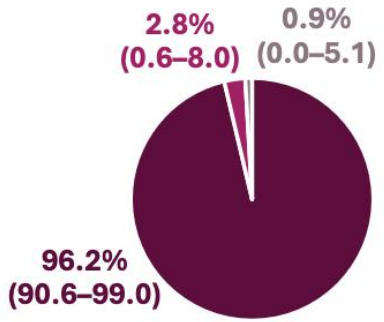
Resection rates and outcomes (FAS)

Martin Reck

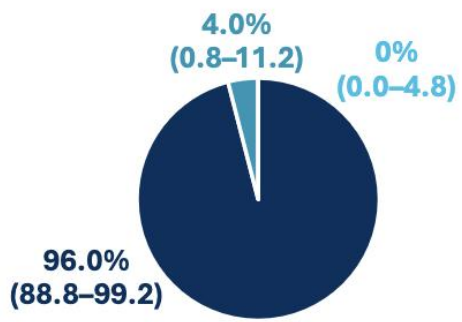
- The overall resection rate was 74.6% and most patients had R0 resection



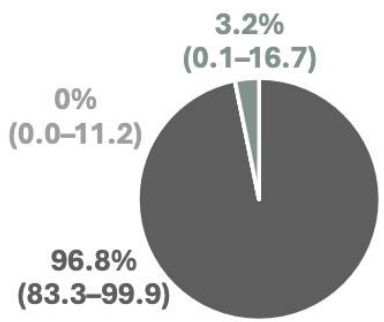
Resection outcomes, % (95% CI)‡



Resected cohort: all patients (n=106)



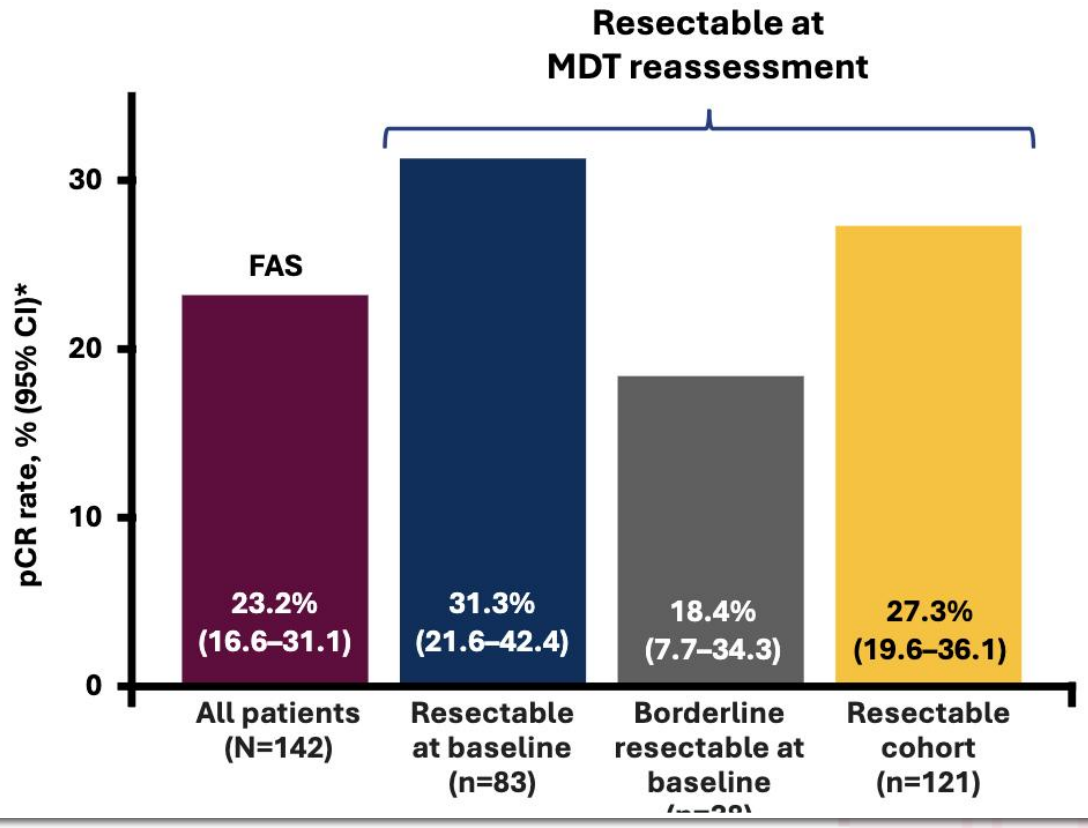
Resected cohort: resectable at baseline (n=75)



Resected cohort: borderline resectable at baseline (n=31)

pCR

- 27.3% of all patients resectable at MDT reassessment had pCR, including 31.3% who were resectable at baseline

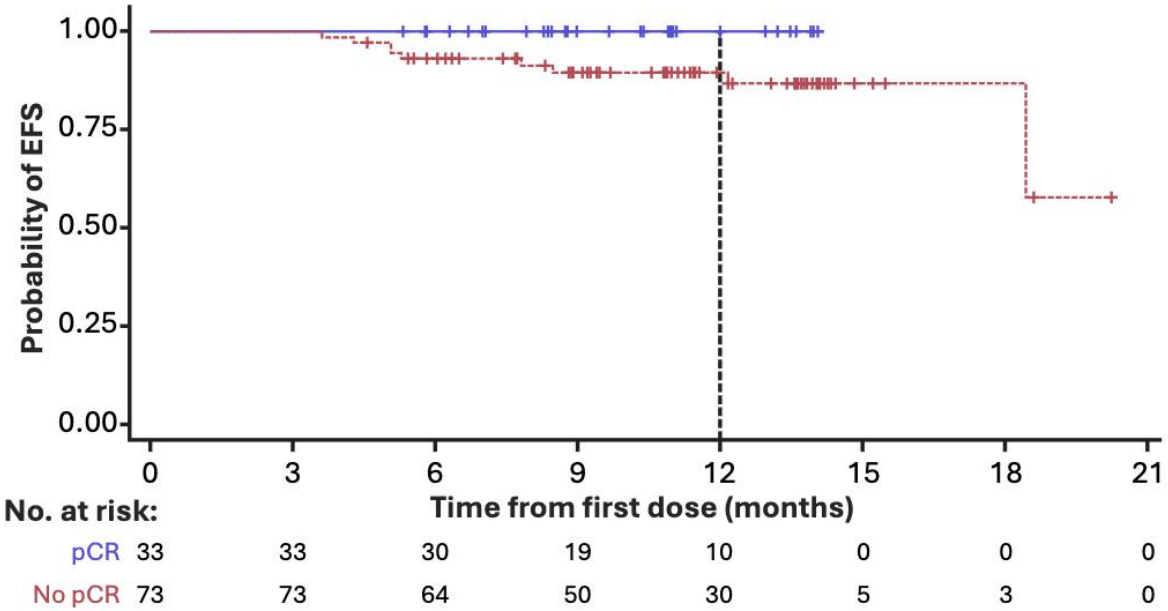


EFS by pCR

Martin Reck

- 12-month EFS was higher in patients with vs without pCR (100% vs 89.8%)

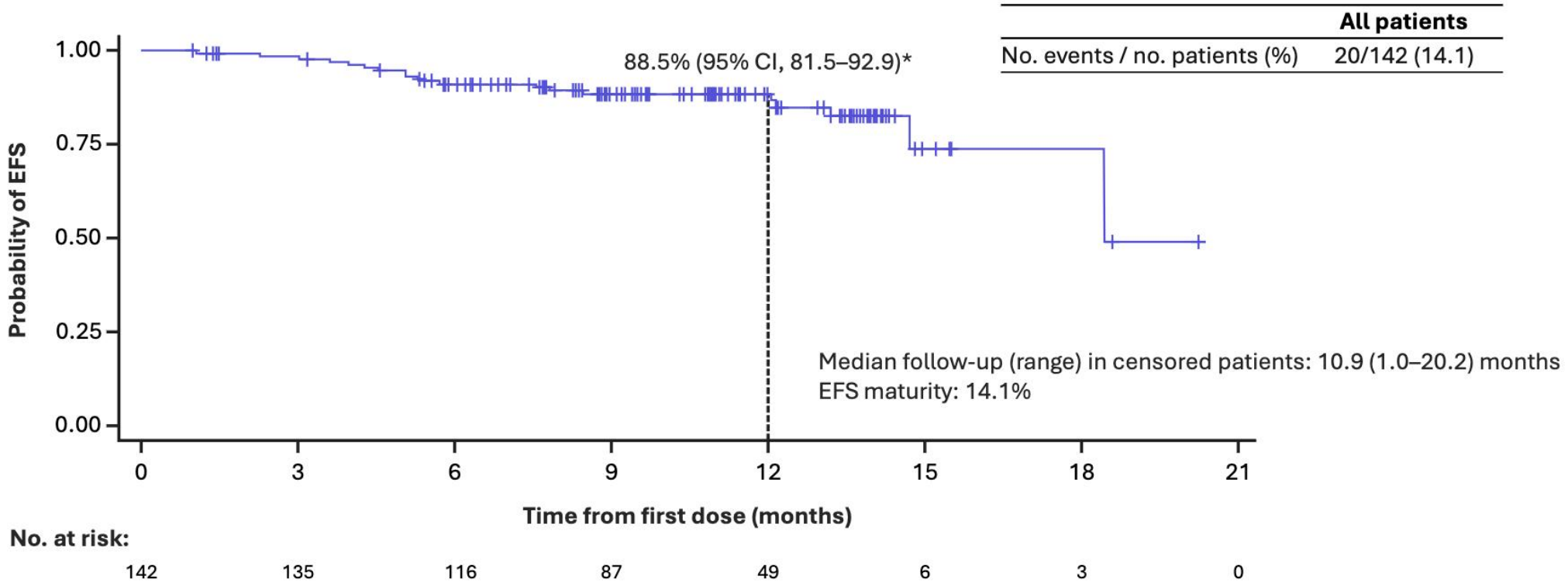
	pCR	No pCR
No. events / no. patients (%)	0/33 (0)	9/73 (12.3)
12-month EFS, % (95% CI)*	100.0 (100.0–100.0)	89.8 (79.6–95.0)



EFS in all patients (FAS)

Martin Reck

- Based on 14.1% maturity, the 12-month EFS was 88.5% in all patients

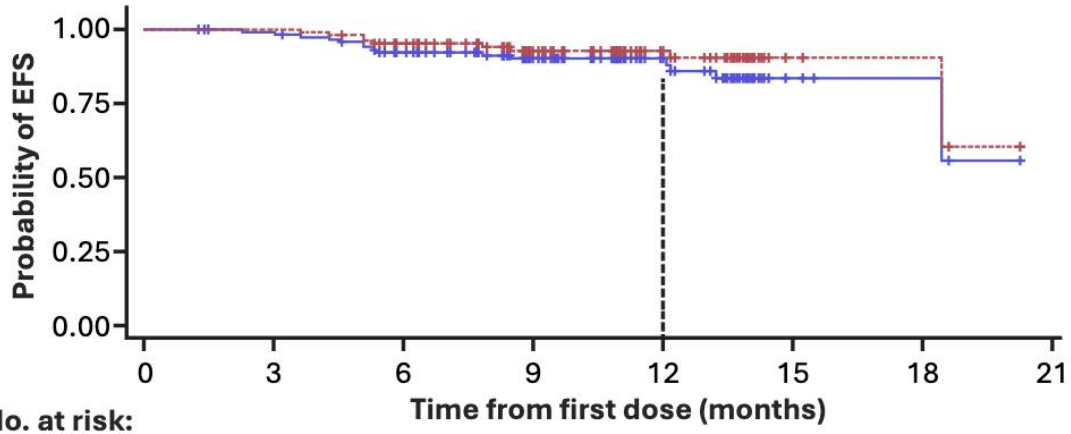


EFS and PFS in subgroups of interest

Martin Reck

EFS in patients resectable at MDT reassessment and in resected patients

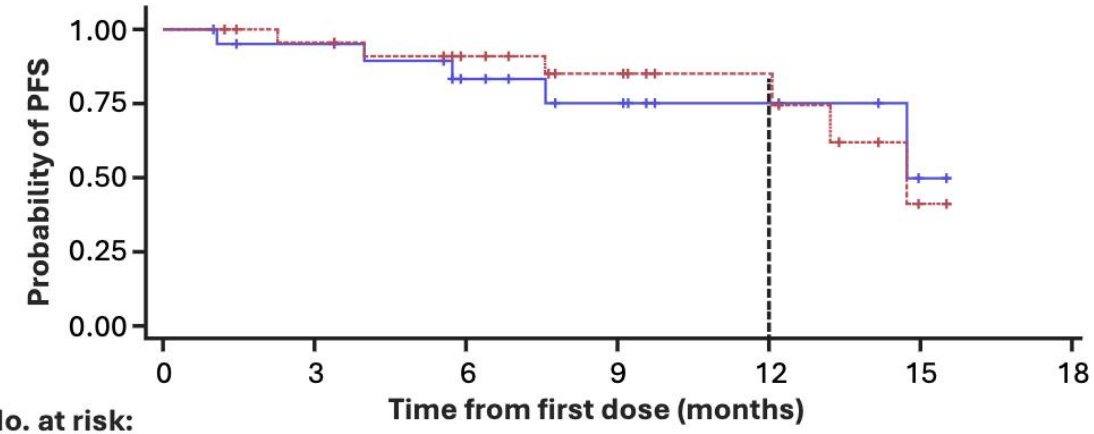
	Resectable	Resected
No. events / no. patients (%)	15/121 (12.4)	9/106 (8.5)
12-month EFS, % (95% CI)*	90.1 (82.8–94.4)	92.9 (85.5–96.6)



No. at risk:								
Resectable	121	117	101	75	43	5	3	0
Resected	106	106	94	69	40	5	3	0

PFS in patients unresectable at MDT reassessment and in CRT-treated patients

	Unresectable	CRT-treated
No. events / no. patients (%)	5/21 (23.8)	6/25 (24.0)
12-month PFS, % (95% CI)*,†	75.1 (45.2–90.2)	85.0 (59.8–95.0)



No. at risk:							
Unresectable	21	18	12	8	5	1	0
CRT-treated	25	22	17	12	8	1	0


Gracias