MRO . ART
MODERN RADIATION ONCOLOGY
35° RESIDENTIAL COURSE

Gemelli
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

GART
Advanced Radiation Therapy

LUNG CANCER: WHICH STRATEGIES DELIVERS THE BEST VALUE: INNOVATION, EQUITY and COST-EFFECTIVENESS

BEST OF THE YEAR

(from ELCC,ESTRO,WCLC, ASTRO, ESMO)

Sara Ramella

s.ramella@unicampus.it

Rome, 27 October 2025

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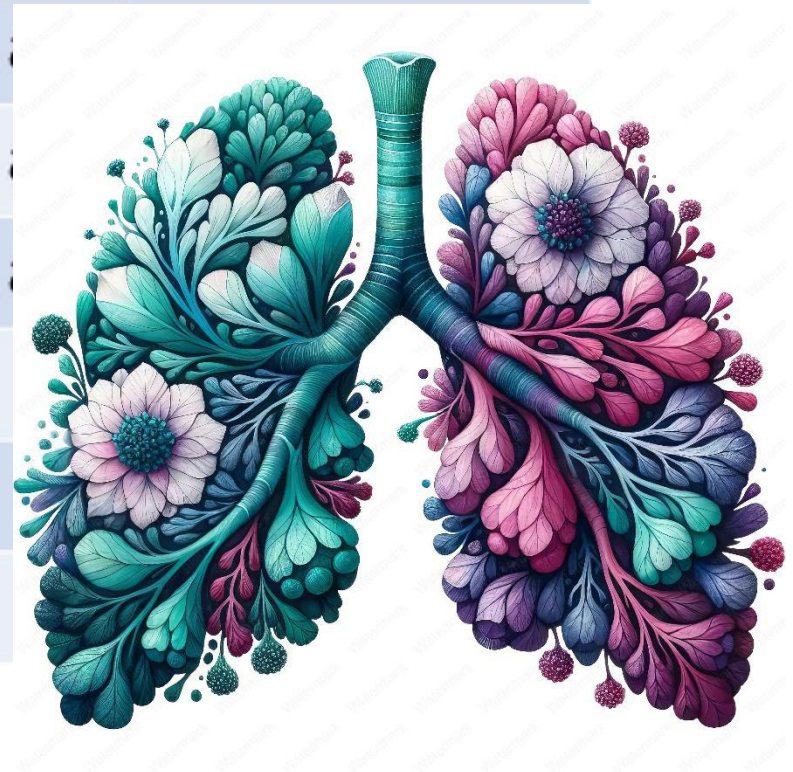
DECLARATION OF INTERESTS

AstraZeneca	Advisory Board, Research Funding, Honoraria for lectures
Roche	Advisory Board, Research Funding, Honoraria for lectures
Merck (MSD)	Advisory Board, Research Funding, Honoraria for lectures
Amgen	Honoraria for lectures and presentations
Tema Sinergie	Honoraria for lectures and presentations
Elekta	Support for attending meetings and/or travel



LUNG CANCER NEWS

elcc European Lung Cancer Congress 2025

ESTRO 2025 2-6 May 2025 Vienna, Austria

IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

2025 ASTRO'S 67TH ANNUAL MEETING

SEPTEMBER 27 – OCTOBER 1, 2025

MOSCONE CENTER | SAN FRANCISCO

BERLIN 2025 ESMO congress

BERLIN GERMANY

17-21 OCTOBER 2025

Locally Advanced LUNG CANCER

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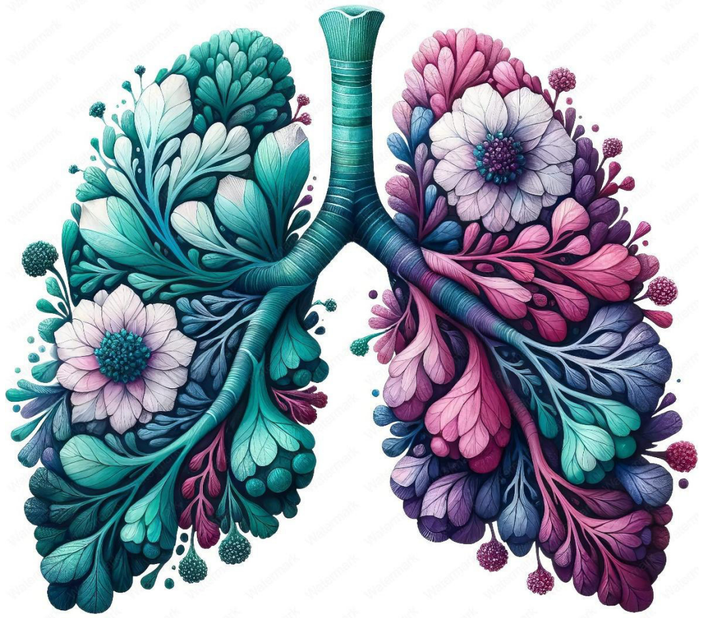


1. CHEMORADIATION IN EGFR (post-PD and PNEUMONITIS of LAURA TRIAL)
2. CHEMORADIATION and IO (EA5181- SKYSCRAPER 03)
3. OLIGOMETASTATIC EGFR+ DISEASE (ABLATE and NORTHSTAR)
4. FRACTIONATION in LS-SCLC (LU005 QoL and DUTCH trial)

LAURA PHASE III STUDY DESIGN[1]

elcc European Lung Cancer Congress 2025

Patients with locally advanced, unresectable stage III* EGFRm NSCLC, with no progression during / following definitive CRT†

Key inclusion criteria:

- ≥18 years (Japan: ≥20 years)
- WHO performance status 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomisation: 6 weeks

R
2:1††

N=216

- **Osimertinib 80 mg, once daily**
- **Placebo, once daily**

Endpoints

- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Key secondary endpoints:** OS, CNS PFS
- **Secondary post-progression endpoints:** TFST,‖ PFS2,¶ TSST**

Treatment continued until BICR-assessed progression (per RECIST 1.1), toxicity, or other discontinuation criteria met

Open-label osimertinib after progression offered to both treatment arms§

Tumour assessments:

- Chest CT / MRI and brain MRI
  - At baseline, every 8 weeks to Week 48, then every 12 weeks until progression
  - After progression, PFS2 was assessed by the investigator every 12 weeks and defined by local practice

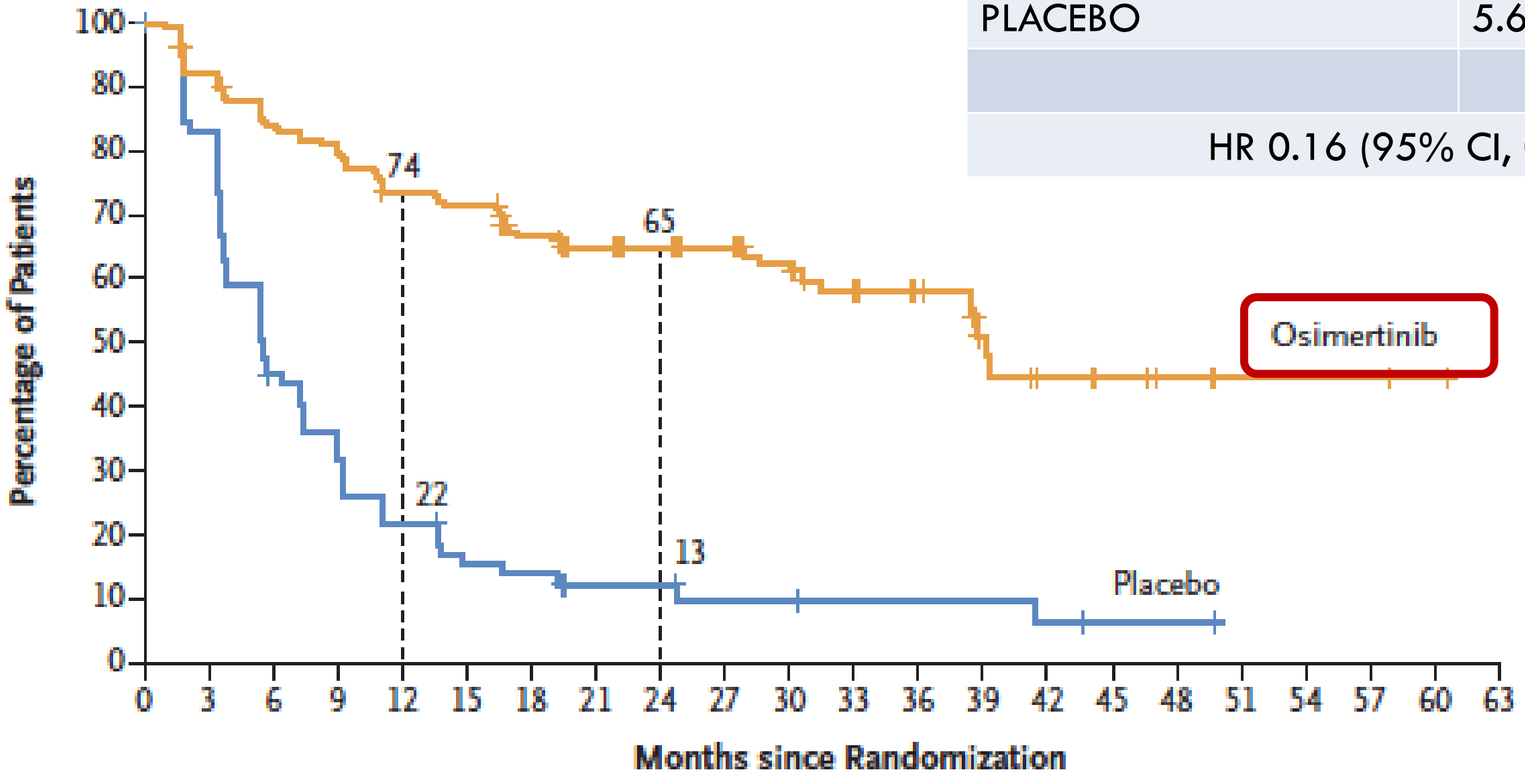
Sara Ramella: discussant of abstract LBA4 and 1860

OSIMERTINIB AFTER CHEMORADIOTHERAPY IN STAGE III EGFR-MUTATED NSCLC

Lu et al. N Engl J Med 2024;391:585–597

MEDIAN PROGRESSION FREE SURVIVAL

	mPFS (95%CI)
OSIMERTINIB	39.1 (31.5-NC)
PLACEBO	5.6 (3.7-7.4)
HR 0.16 (95% CI, 0.10-0.24)	



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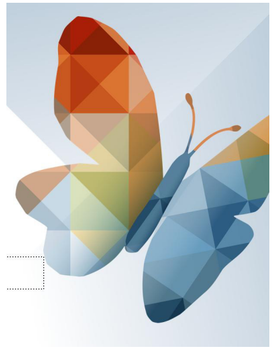


WHAT QUESTIONS DO OUR PATIENTS ASK?

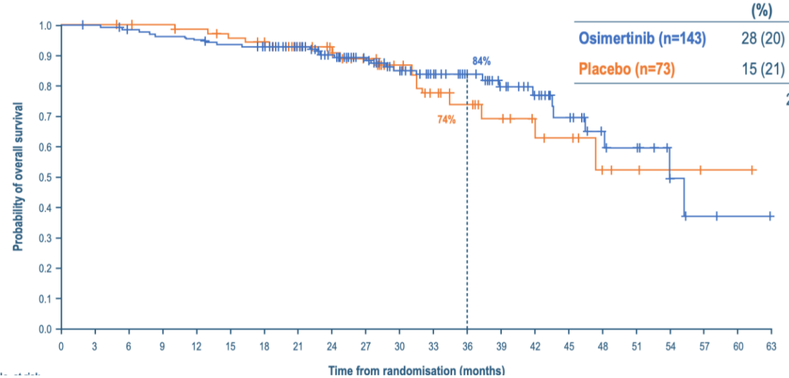
✓ "I would like to live as long as possible.»

INTERIM ANALYSIS OF OS DEMONSTRATED A POSITIVE TREND IN SURVIVAL FAVOURING OSIMERTINIB[1]

- 52/66 (79%) patients who discontinued study treatment in the placebo group received subsequent treatment with a 3rd-generation EGFR-TKI[1]

	No. of events (%)	Median (95% CI), months	HR (95% CI) Log-rank p-value
Osimertinib (n=143)	28 (20)	54.0 (46.5, NC)	0.81 (0.42, 1.56) p=0.530*
Placebo (n=73)	15 (21)	NR (42.1, NC)	

20% maturity

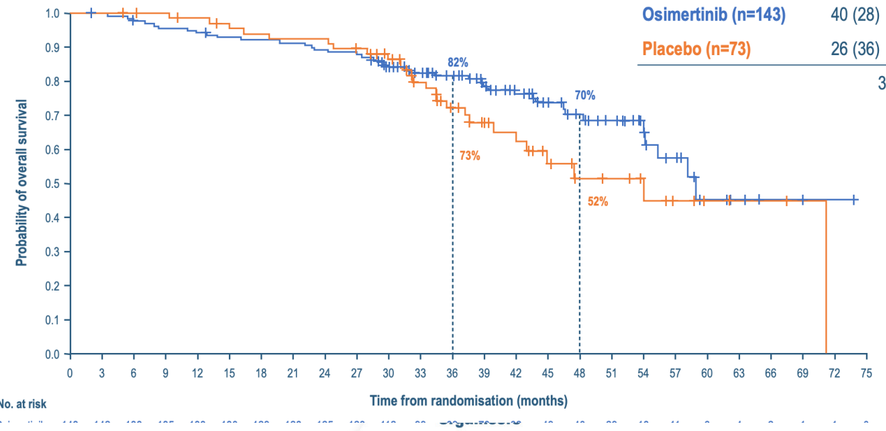


IMPROVED TREND TOWARDS OS BENEFIT SEEN WITH OSIMERTINIB AT UPDATED ANALYSIS

- 55/69 (80%) patients who discontinued study treatment in the placebo group received subsequent treatment with a 3rd-generation EGFR-TKI

	No. of events (%)	Median (95% CI), months	HR (95% CI) Log-rank p-value
Osimertinib (n=143)	40 (28)	58.8 (54.1, NC)	0.67 (0.40, 1.14) p=0.140
Placebo (n=73)	26 (36)	54.0 (42.1, NC)	

31% maturity



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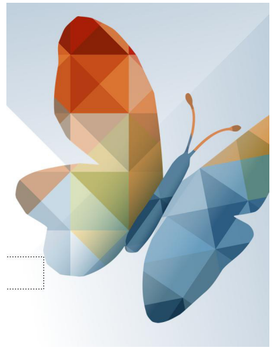
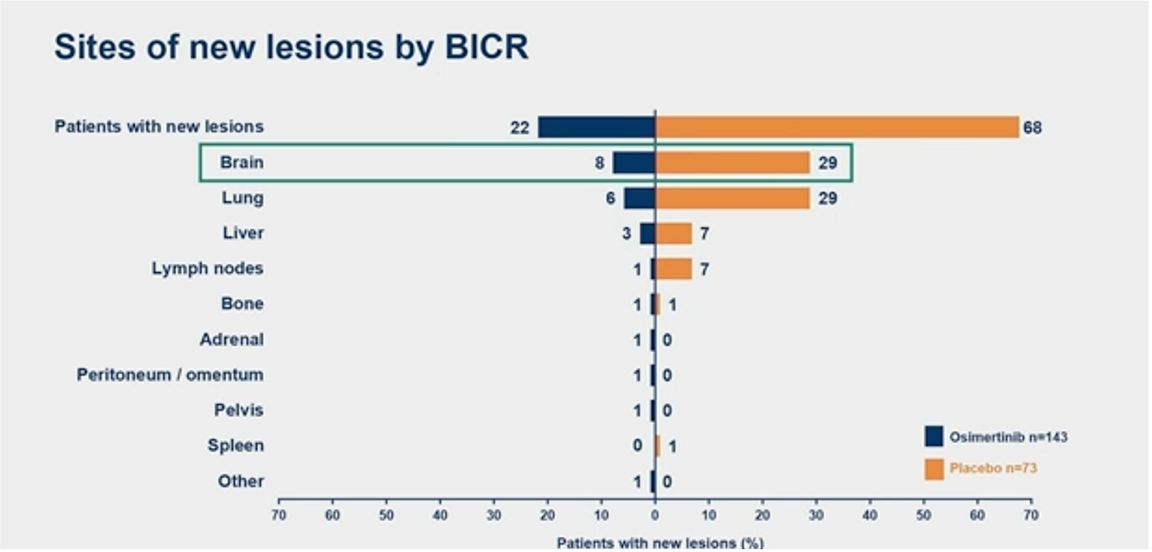
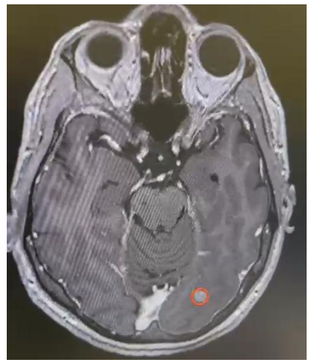


WHAT QUESTIONS DO OUR PATIENTS ASK?



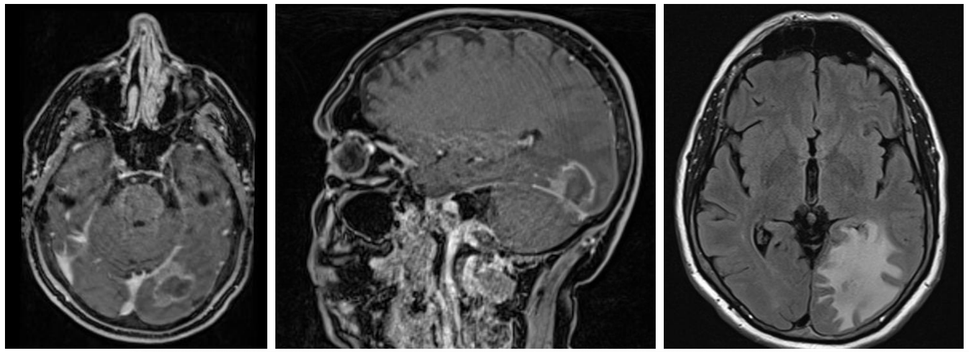
- ✓ "I would like to live as long as possible.»
- ✓ "I would like to live as long as possible free from disease relapses."

STEREOTACTIC RADIATION THERAPY



RADIONECROSIS

"Although patients receiving EGFR-TKI concurrently or after SRS (200 pts) had significantly longer OS, the local treatment efficacy and toxicity of SRS did not differ between patients with/without EGFR-TKI use. " (J Neurooncol. 2019;145:151-157)



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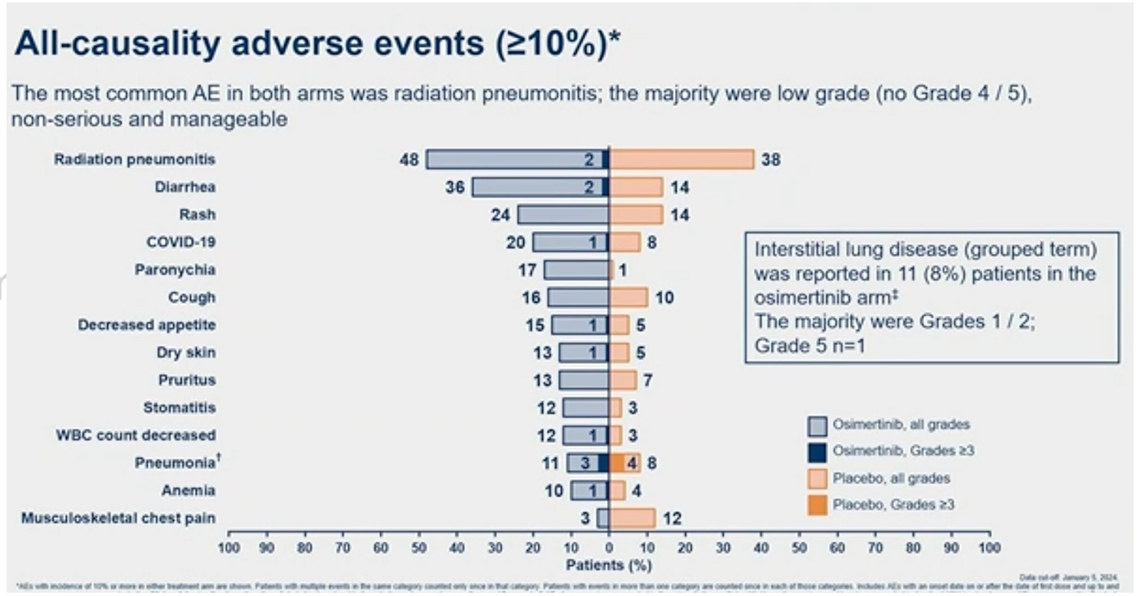
WHAT QUESTIONS DO OUR PATIENTS ASK?

- ✓ "I would like to live as long as possible.»
- ✓ "I would like to live as long as possible free from disease relapses."
- ✓ "I would like to live without side effects.»



PNEUMONITIS

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ESTRO 2025

2-6 May 2025

Vienna, Austria

Osimertinib after chemoradiotherapy in unresectable stage III EGFRm NSCLC: chemoradiotherapy regimens and radiation pneumonitis in LAURA (NCT03521154)

Terufumi Kato,[1] Hong Jian, Thanyanan Reungwetwattana, Edurne Arriola, Hidetoshi Hayashi, Ki Hyeong Lee, Shuanghu Yuan, James Chih-Hsin Yang, Manuel Cobo, Ahmet Alacacioğlu, Lucy Thompson, Feruza Nasirova, Ellie Grainger, Azura Evans, Ana Bolanos, Suresh S. Ramalingam

[1]Kanagawa Cancer Center, Yokohama, Japan

Terufumi Kato
Japan

ESTRO 2025

LAURA TRIAL: OSIMERTINIB AFTER CTRT in STAGE III EGFR-MUTATED NSCLC

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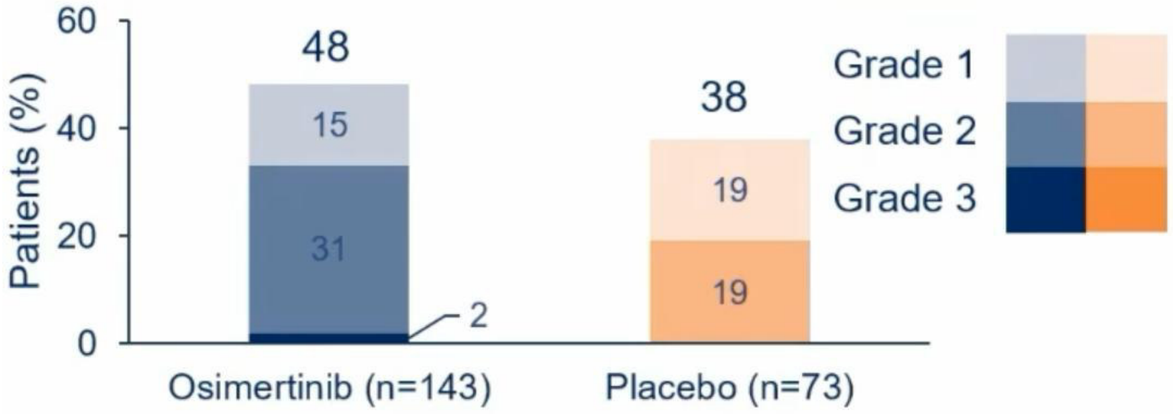
Radiation pneumonitis summary

Patients with RP (grouped term)*



Of patients with RP (n=69 osimertinib vs n=28 placebo):

- 87% versus 93% continued treatment, or restarted treatment following interruption due to RP, without subsequent recurrence of RP
- 10% versus 7% discontinued due to RP (5% vs 3% for all randomised patients)
- 36% versus 36% had RP that resolved while on treatment

G3 NO DIFFERENCE

G2: 31% vs 19%

OSI PLACEBO

LAURA TRIAL: OSIMERTINIB AFTER CTRT in STAGE III EGFR-MUTATED NSCLC

LAURA TRIAL: OSIMERTINIB AFTER CHEMORADIO IN STAGE III EGFR-MUTATED NSCLC

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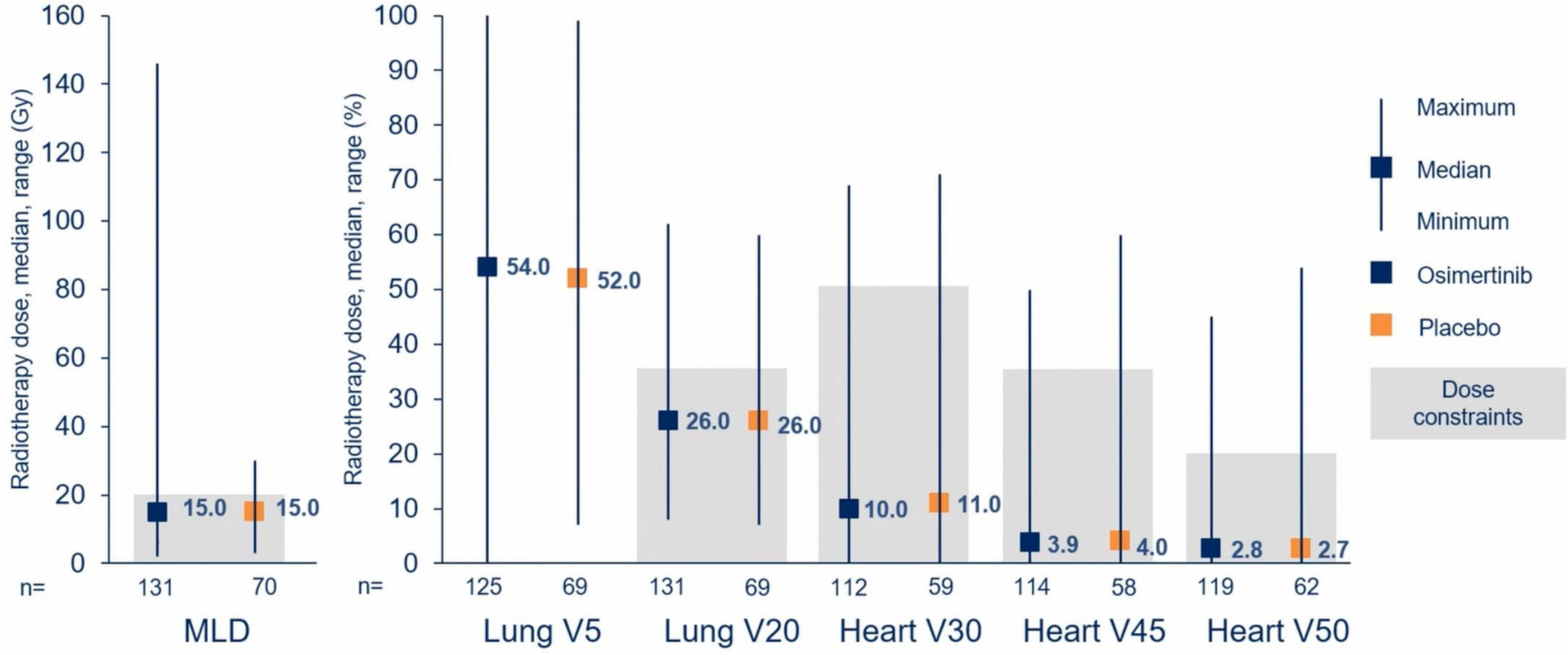
Lung and heart radiotherapy doses

- Protocol-advised dose constraints for MLD (<20 Gy) and V20 (<35%) were met in a majority of patients



LAURA TRIAL: OSIMERTINIB AFTER CHEMORADIO IN STAGE III EGFR-MUTATED NSCLC

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G2: 31% vs 19%

EGFR-MUTATED PATIENTS ARE NEVER-SMOKERS….

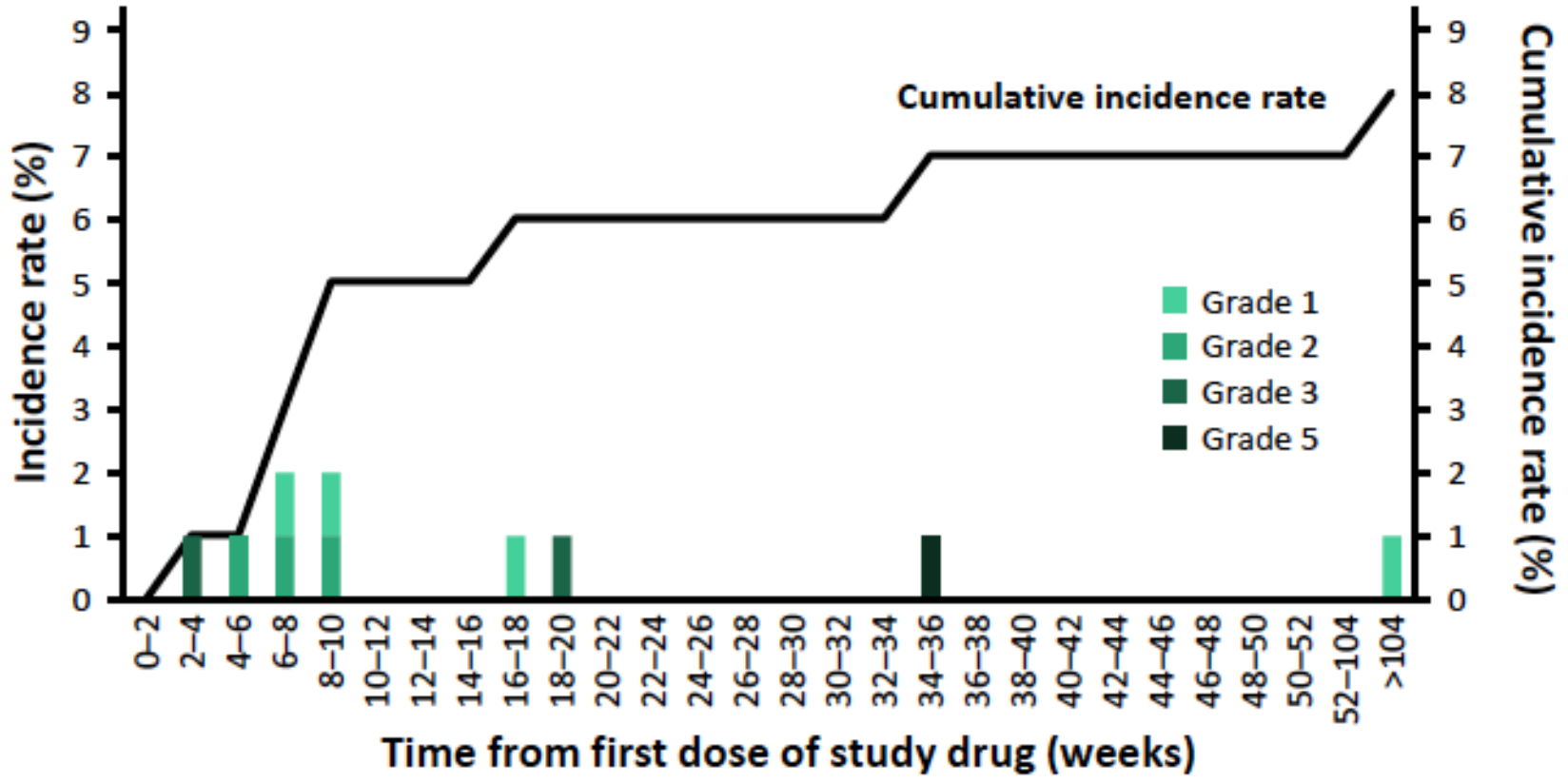
Safety analysis: ILD

- ILD (grouped term) included PTs of ILD, pneumonitis and pulmonary fibrosis

ILD, n (%)	Osimertinib (n=143)	Placebo (n=73)
Total	**11 (8)**	**1 (1)**
Grade 1	4 (3)	1 (1)
Grade 2	4 (3)	0
Grade 3	2 (1)	0
Grade 5	1 (1)	0
CTCAE Grade ≥3	3 (2)	0
SAE	3 (2)	0
Discontinuations	3 (2)	0

- Majority of ILD events were Grade 1–2 and manageable
- 11 patients in the osimertinib arm reported 12 events:
  - ILD n=1, pneumonitis n=8, pulmonary fibrosis n=3
  - No Grade 4 events; one Grade 5 event (pneumonitis with confounding factors)* reported

Timing of onset and cumulative incidence of ILD: Osimertinib



Time to onset of ILD, median (range), days	Osimertinib (n=11)
From first dose of osimertinib	57 (26–755)
From last dose of prior CRT	91 (38–793)

T Kato et al, WCLC 2024

ILD-RT/DOSIMETRIC PARAMETERS:

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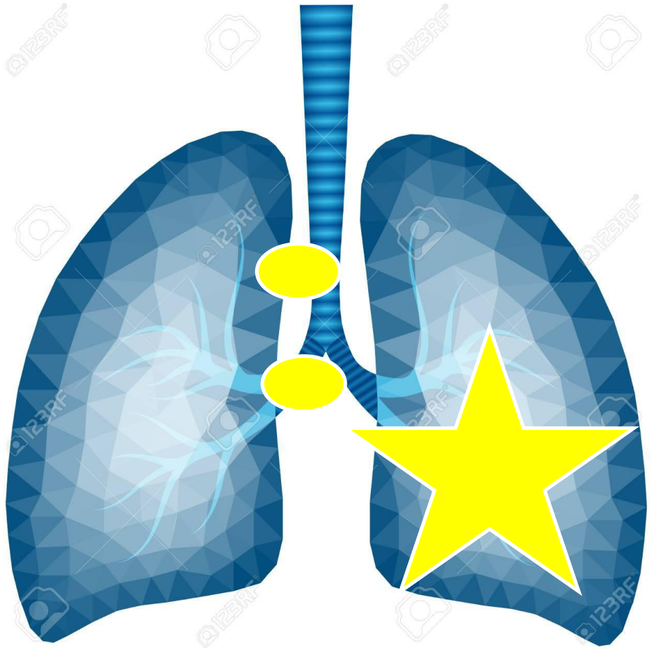
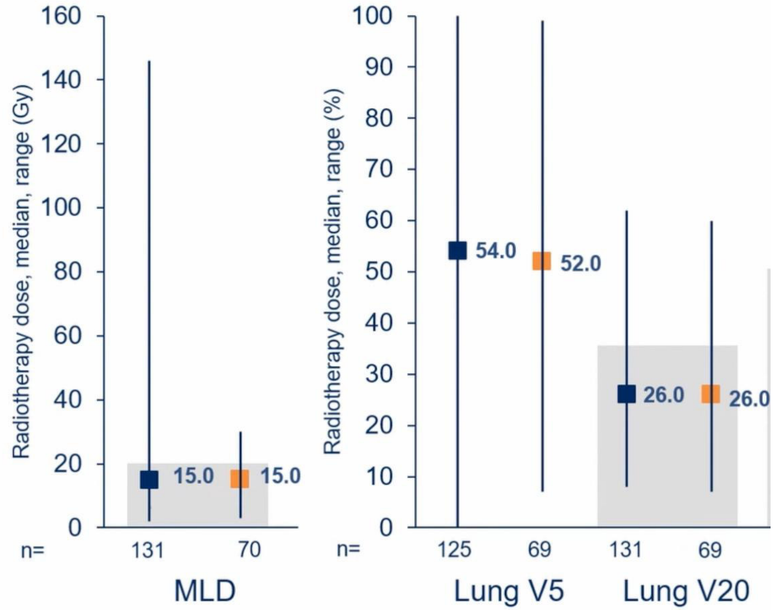


LA-NSCLC:

LAURA ILD	
MLD=15	MLD<12Gy
V20= 26	V20<25%
V5=54	V5<50%



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NEW CONSTRAINTS FOR ONCOGENE ADDICTED PATIENTS?

Radiotherapy for Lung Cancers in Patients with Interstitial Lung Disease: AIRO (Italian Association of Radiotherapy and Clinical Oncology) Delphi Consensus

21 Pages • Posted: 13 May 2025

Li F, Radiat Oncol 2021,16(1):70
Higo, Jpn JCO 2019, 49(5): 458-464
Saha et al. Clin Oncol 34 (2022) e493-e504
Kashihara, Radiotherapy and Oncology 2023

Locally Advanced LUNG CANCER

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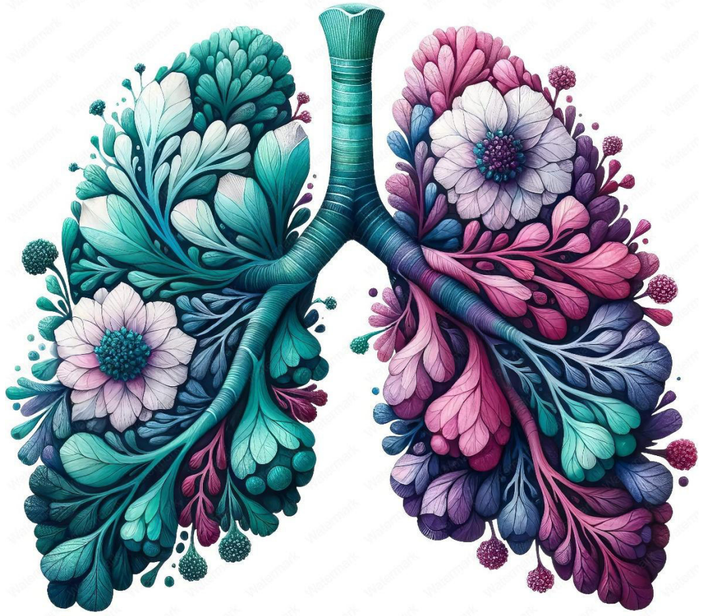

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2. CHEMORADIATION and IO (EA5181-SKYSCRAPER 03)
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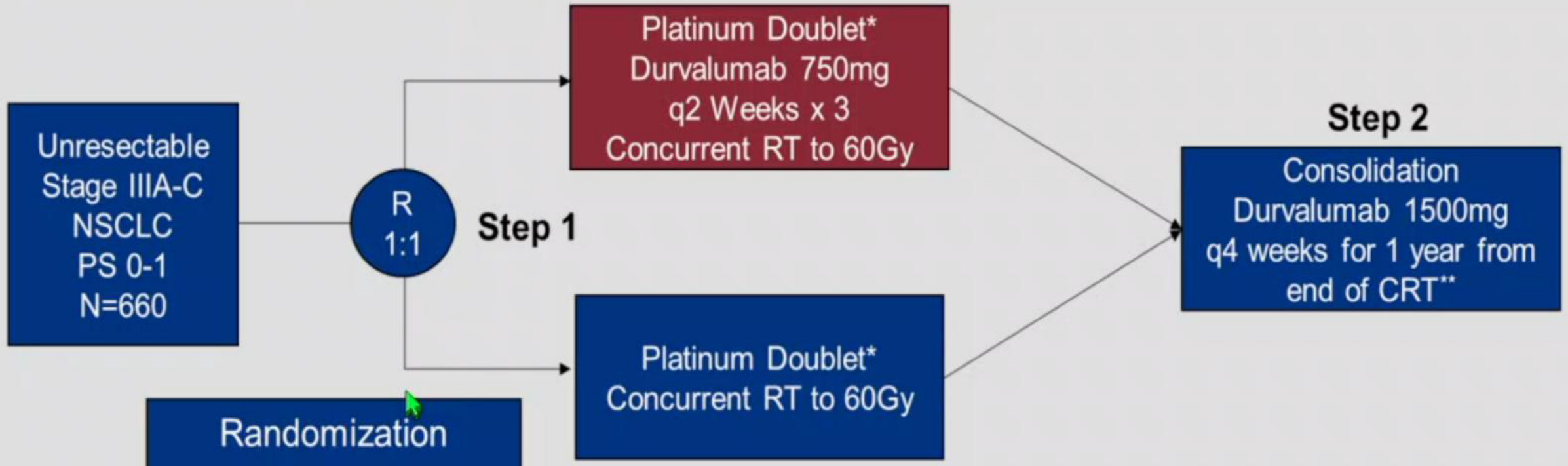
4. FRACTIONATION in LS-SCLC (LU005 QoL and DUTCH trial)

IASLC 2025 World Conference on Lung Cancer
SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

EA5181 Schema



Randomization

Stratified by:
1) Planned chemotherapy
2) Age
3) Sex
4) Stage (IIIA vs IIIB vs IIIC)

Investigator choice

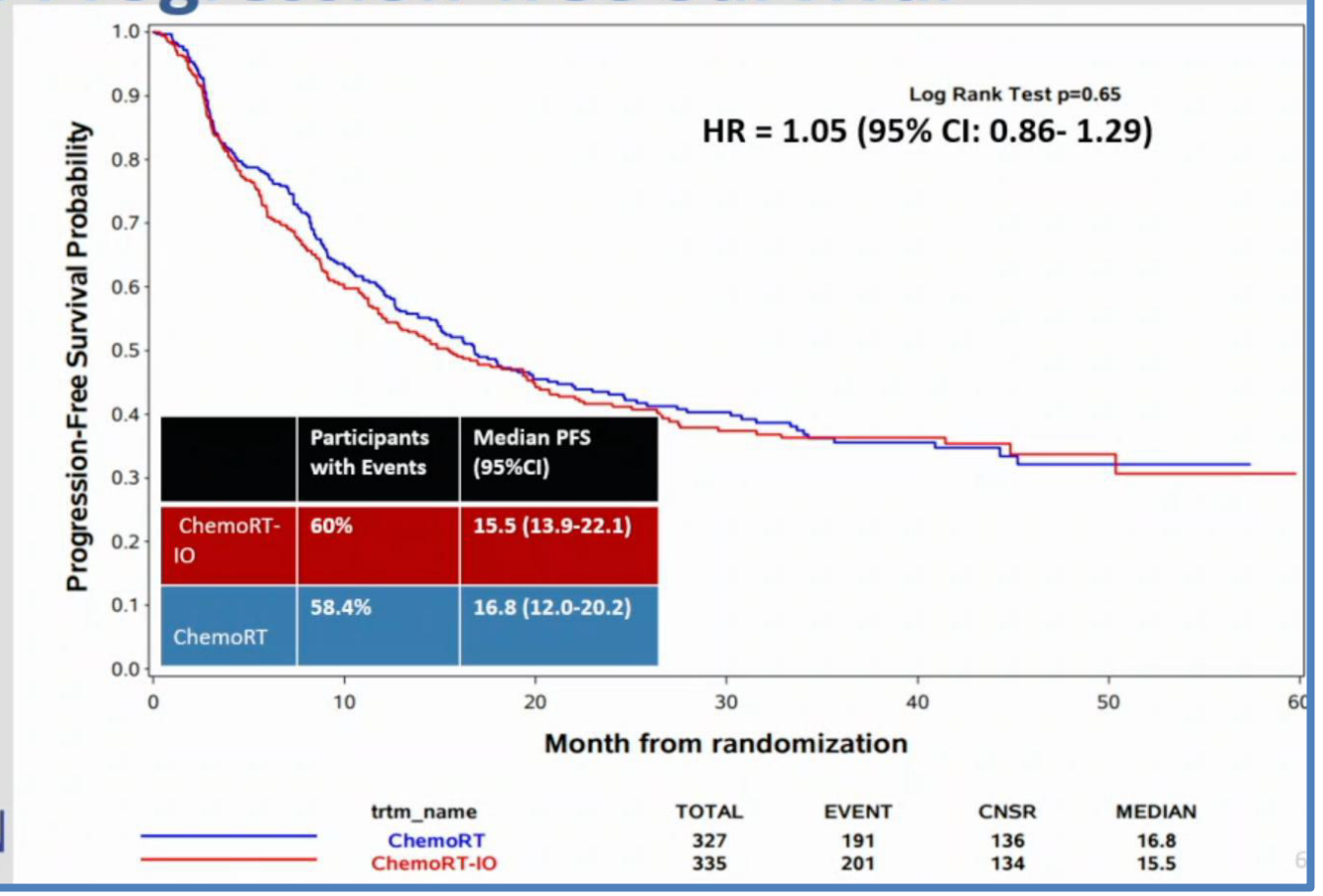
Cisplatin 50 mg/m2 D1, 8, 29, 36; etoposide 50 mg/m2 D1-5, 29-33
Cisplatin 75 mg/m2 D1, 22; pemetrexed 500 mg/m2 D1, 22 (nonsquamous only)
Carboplatin AUC 2 D1, 8, 15, 22, 29, 36; paclitaxel 45 mg/m2 D1, 8, 15, 22, 29, 36

**Starting within 14 days of CRT unless toxicity has not resolved to ≤ grade 2, but not later than 45 days post-CRT

Primary endpoint – OS intention to treat population; 25% reduction in OS HR
Secondary endpoint –PFS, toxicity, ORRs, and Recurrence patterns

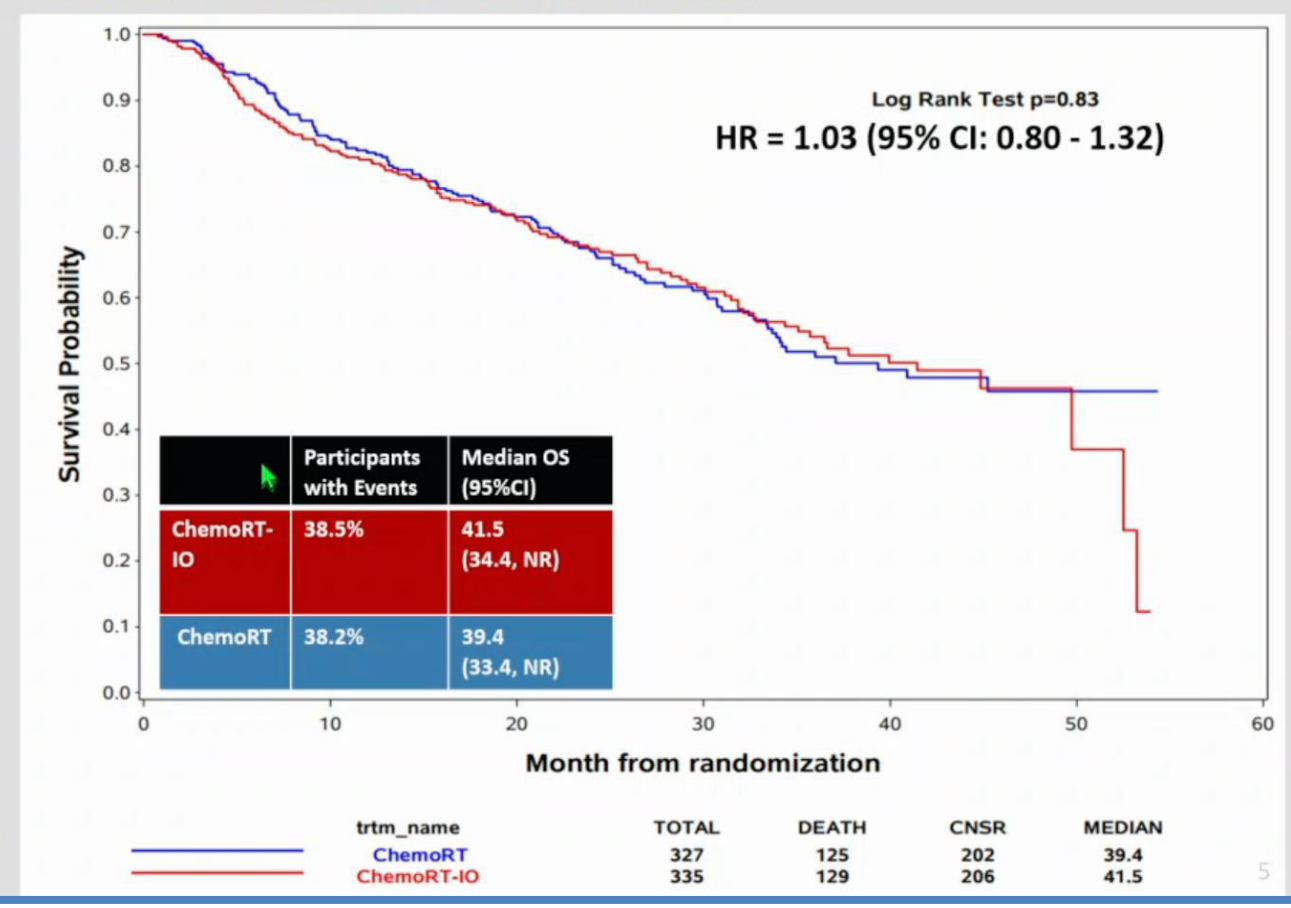
ECOG-ACRIN cancer research group

EA5181: Progression-free Survival



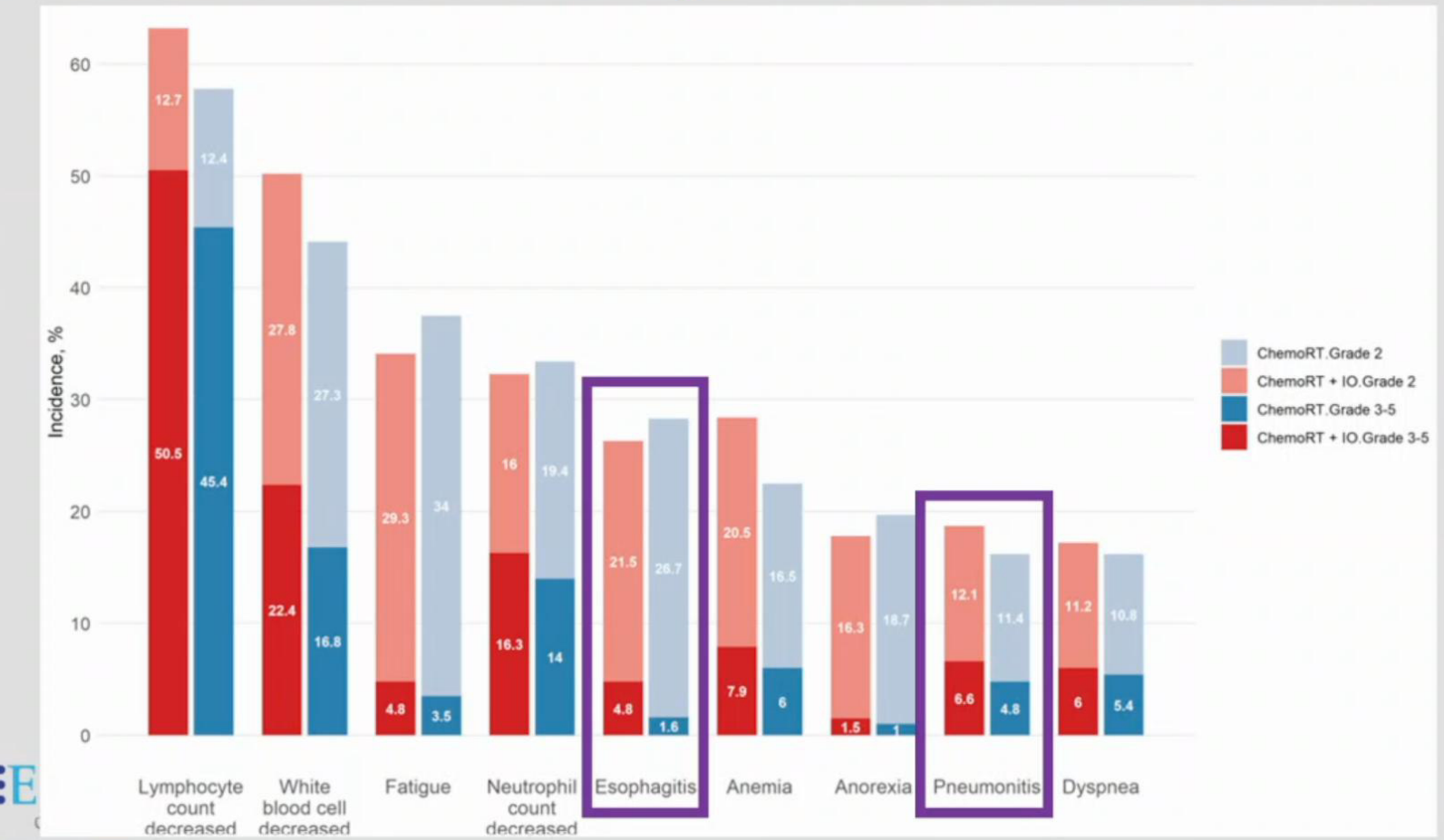
ECOG-ACRIN cancer research group

EA5181: Overall Survival



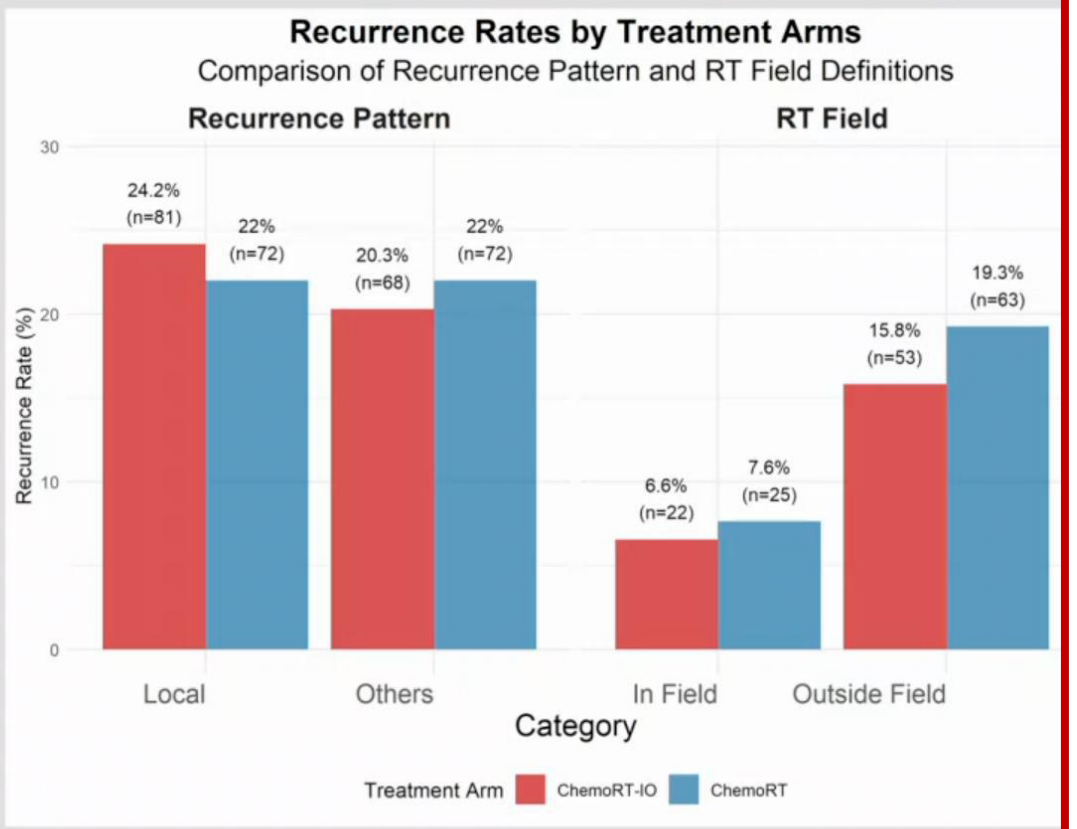
ECOG-ACRIN cancer research group

Treatment-related Toxicity Incidence >10%, Top 9 AEs



- **Local recurrences** were 24.2%(Arm ChemoRT-IO) and 22%(Arm ChemoRT), p = 0.52.
- **Radiation in-field recurrences** were noted in 6.6% (Arm ChemoRT-IO) and 7.6% (Arm ChemoRT), p=0.65.
- **Step 1**, the overall best **response rates (CR and PR)** were 51.3% (Arm A) and 47.1% (Arm B), p = 0.28.
- **Step 2**, the overall best **response rates (CR and PR)** were 71.5% (Arm A) and 67.1% (Arm B), p = 0.31.
- **Median and mean number of cycles of consolidative** durvalumab was 10 and 8 in both Arms

Recurrence Rates



ECOG-ACRIN cancer research group

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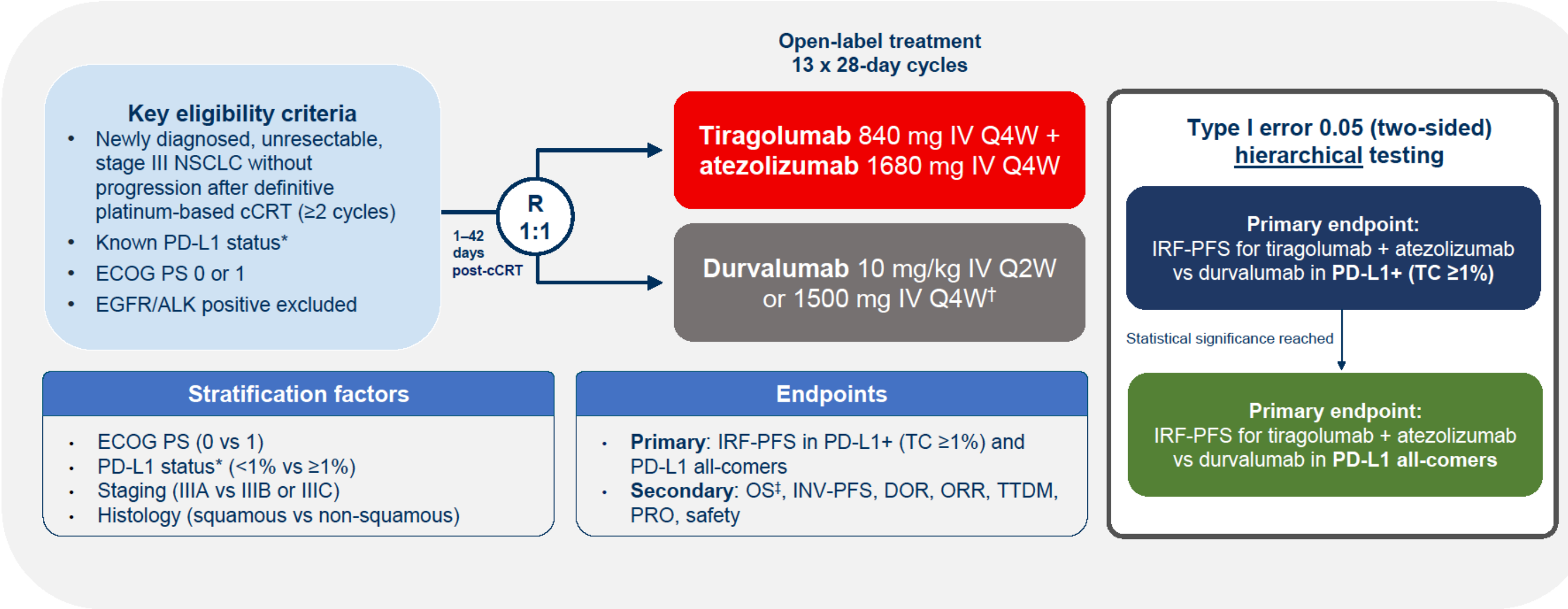
Anti- TIGIT monoclonal antibody

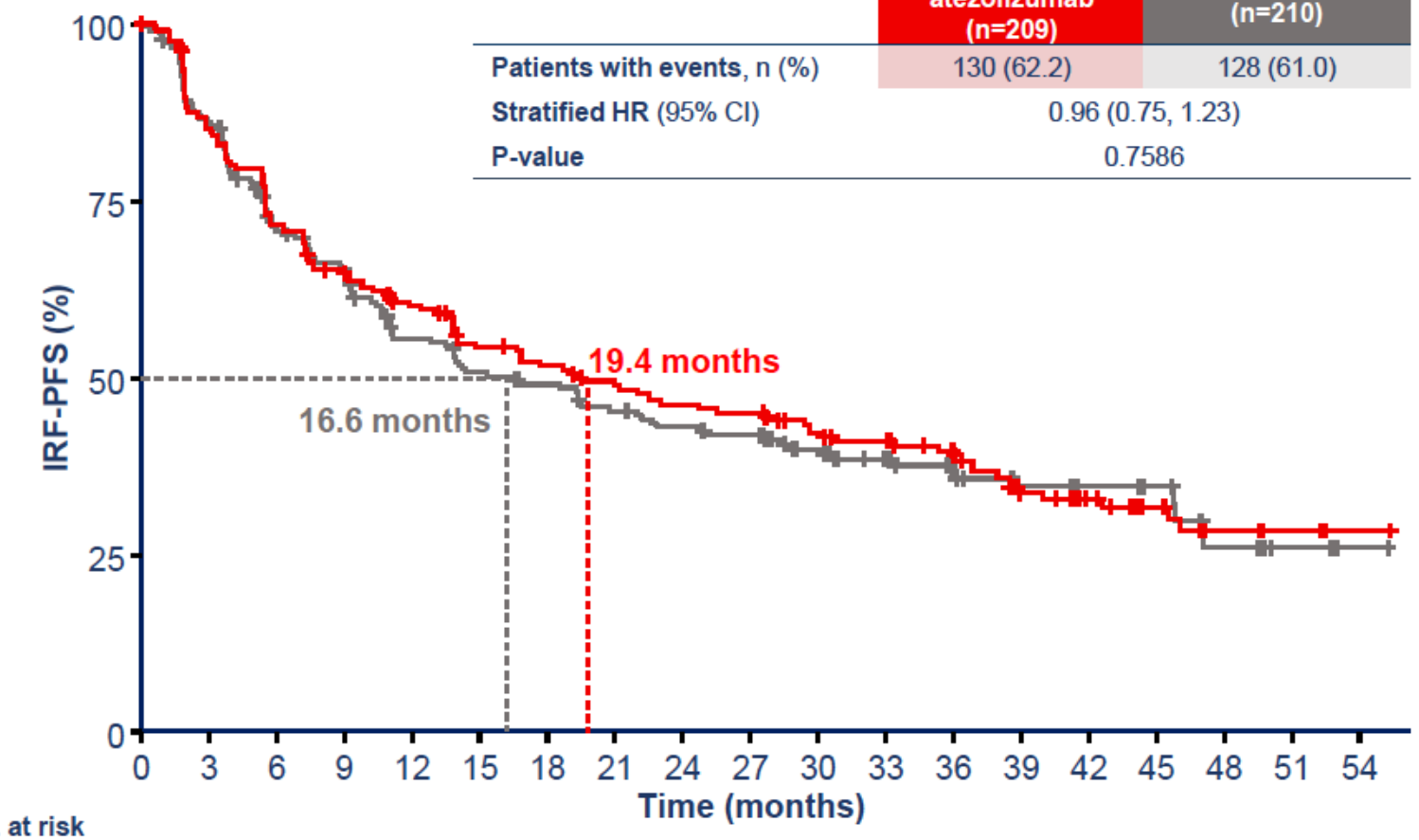
SKYSCRAPER-03: a phase 3, open-label, randomised study



IRF-PFS and OS in PD-L1+ (TC ≥1%)

Primary endpoint: PFS

	Tiragolumab + atezolizumab (n=209)	Durvalumab (n=210)
Patients with events, n (%)	130 (62.2)	128 (61.0)
Stratified HR (95% CI)	0.96 (0.75, 1.23)	
P-value	0.7586	

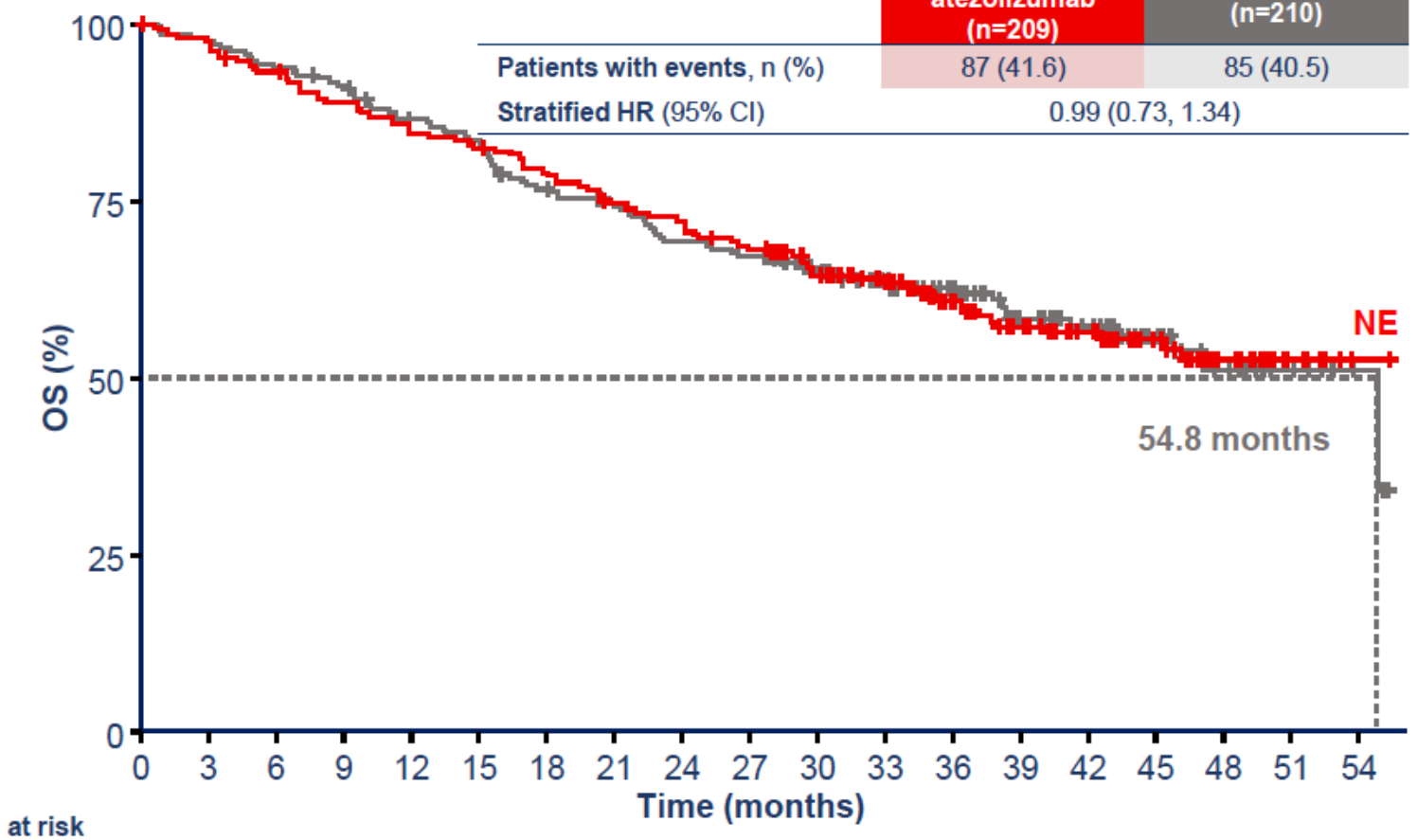


No. at risk																			
Tira + atezo	209	173	145	130	116	102	96	89	84	82	72	68	58	40	30	20	11	4	1
Durva	210	180	143	130	105	95	90	82	77	73	57	48	38	23	20	15	7	3	1

	Tiragolumab + atezolizumab (n=209)	Durvalumab (n=210)
Median PFS, months (95% CI)	19.4 (13.8, 29.5)	16.6 (11.1, 22.8)
12-month event free rate (%)	60.0	55.4
24-month event free rate (%)	46.1	42.9

Secondary endpoint: OS

	Tiragolumab + atezolizumab (n=209)	Durvalumab (n=210)
Patients with events, n (%)	87 (41.6)	85 (40.5)
Stratified HR (95% CI)	0.99 (0.73, 1.34)	



No. at risk																			
Tira + atezo	209	203	192	182	174	169	161	151	146	137	123	110	89	72	59	41	24	7	1
Durva	210	204	196	190	177	171	156	148	138	134	117	100	83	60	51	29	19	9	3

	Tiragolumab + atezolizumab (n=209)	Durvalumab (n=210)
Median OS, months (95% CI)	NE (40.0, NE)	54.8 (41.2, NE)
12-month event free rate (%)	84.9	86.5
24-month event free rate (%)	72.2	69.2

Data cutoff: 27 May 2025

Minimum follow-up: 27.3 months; median follow-up: 33.0 months

Atezo, atezolizumab; CI, confidence interval; Durva, durvalumab; HR, hazard ratio; NE, not evaluable; Tira, tiragolumab

RT-CT

RT-CT followed by IO

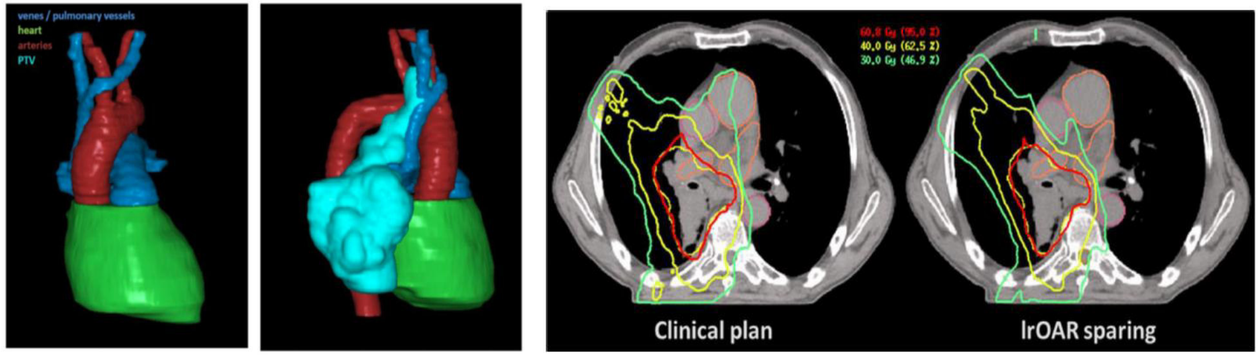
RT-CT concomitant and followed by IO

	IIIB-C	mFUP	mPFS	1y PFS	2y PFS	3y PFS	4y PFS	5y PFS	mOS	1y OS	2y OS	3y OS	4y OS	5y OS
RTOG 0617	(7°ed)	60	**12.0**	49	29	25	19	18	**28.7**	80	58	45	36	32.1
PROCLAIM arm A	(7°ed)	22.2	**11.4**	48	28	20	18	18	**26.8**	76	52	40	34	32
PACIFIC placebo	(7°ed)	61.6	**5.6**	35	25	21	20	19	**29.1**	75	55	44	36	33
PACIFIC 2 placebo	65	-	**9.4**	40	26	22	17	-	**29.5**	80	57	41	36	-
PACIFIC durva	(7°ed)	61.6	**19.6**	56	45	40	35	33	**47.5**	83	66	57	50	43
GEMSTONE 301 sugemal	70	22.4	**15.7**	55	43	34	-	-	**NR**	84	66	54	-	-
CM 73L durva	65	30.5	**15.6**	51	24	-	-	-	**40.2**	79	45	18	-	-
EA5181 durva	*47.7*	-	**16.8**	-	-	-	-	-	**39.4**	-	-	-	-	-
DETERRED Atezo-conc	44	41.7	**15.1**	52	-	-	-	-	**NR**	80	-	54	47	-
NICOLAS Nivo-conc	(7°ed)	32.6	**12.7**	54	-	-	-	-	**38.8**	76	64	-	-	-
PACIFIC 2 Durva conc	65		**13.8**	46	31	26	19	-	**36.4**	73	57	49	41	-
CM 73L Nivo-conc	67	30.5	**16.7**	52	27	-	-	-	**34.6**	75	42	21	-	-
KN 799-A Pembro.conc	**63**	**59.2**	**29.0**	**67**	**55**	**43**	**39**	**-**	**35.6**	**81**	**64**	48	40	-
KN 799-B Pembro.conc	**62**	**54.4**	**45.3**	**69**	**58**	**54**	**46**	**-**	**56.7**	**88**	**73**	64	55	-
EA5181 Durva conc.	**49.9**	**-**	**15.5**	**-**	**-**	**-**	**-**	**-**	**41.5**	**-**	**-**	-	-	-

THE BLACK BOX: RADIATION THERAPY

- Lymphocyte-Sparing Radiotherapy: The Rationale Protecting Lymphocyte-rich Organs When Combining Radiotherapy With IO

  Lambin P, Semin Radiat Oncol. 2020 April ; 30(2): 187-193.



- The Role of Thoracic Vertebral Body Dosimetry in Minimizing Acute Hematologic Toxicities of Patients With Non Small Cell Lung Cancer Receiving Lung Radiation Therapy and IO

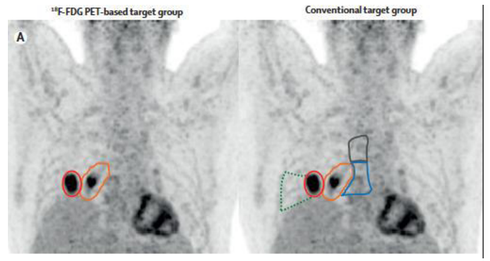
  Ma J et al. Int J Radiation Oncol Biol Phys, 119(1), 78–89, 2024

132 pts RT+IO; Grade 3+ Hematological Tox: Dmean EQD2 ≧ 30.2 Gy,V5 EQD2 ≧ 69.1%, V10 EQD2 ≧ 64.6%, and V20 EQD2 ≧ 53.5%.).

- Impact of mediastinal tumor burden and lymphatic spread in locally advanced non-small-cell lung cancer: A secondary analysis of the multicenter randomized PET-Plan trial

  Gkika E et al, Radiotherapy and Oncology 200 (2024) 110521

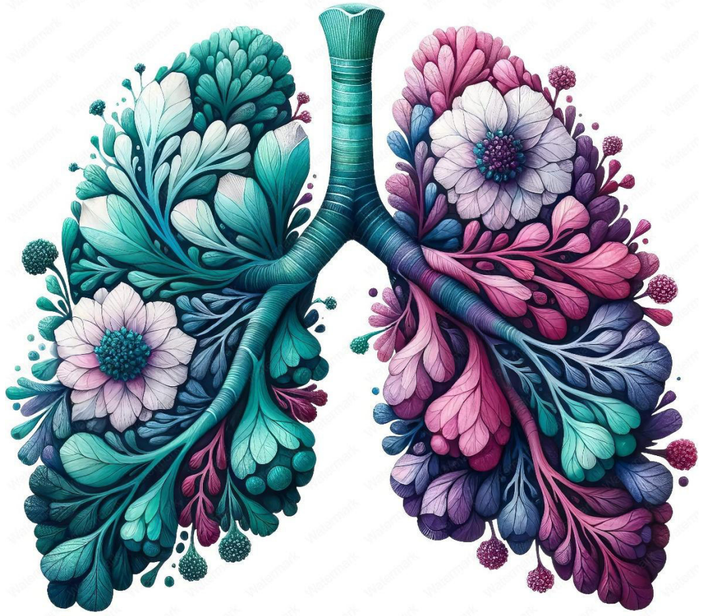
In patients PET-based selective nodal irradiation, prescribed RT dose to each LN station correlated significantly with freedom from local progression (HR=0.45; p = 0.01).



Sara Ramella: discussant of abstract LBA4 and 1860

Locally Advanced LUNG CANCER

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA



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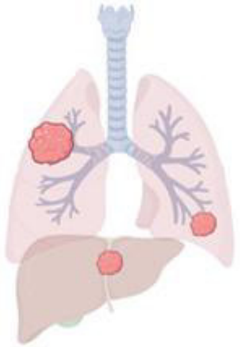
3. OLIGOMETASTATIC EGFR+ DISEASE (ABLATE and NORTHSTAR)
4. FRACTIONATION in LS-SCLC (LU005 QoL and DUTCH trial)

TRIALS INVESTIGATING OLIMETS DE NOVO EGFR+:

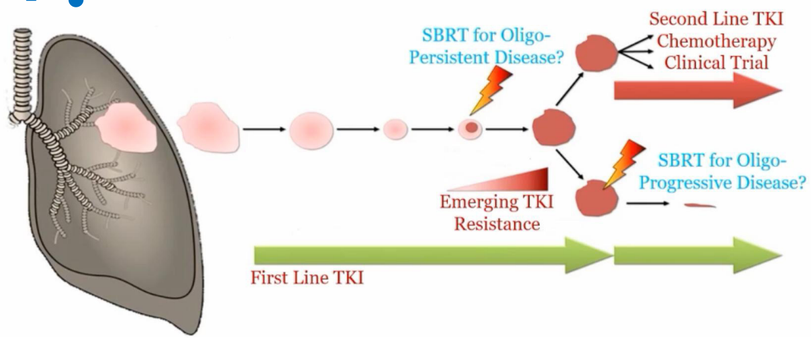
SINDAS Trial

ABLATE Trial



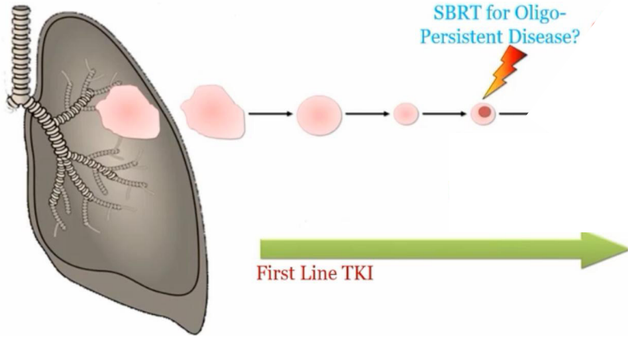
TRIALS INVESTIGATING OLIGOPD EGFR+:

CURB Trial



TRIALS INVESTIGATING OLIGOPERSISTENCE EFGR+:

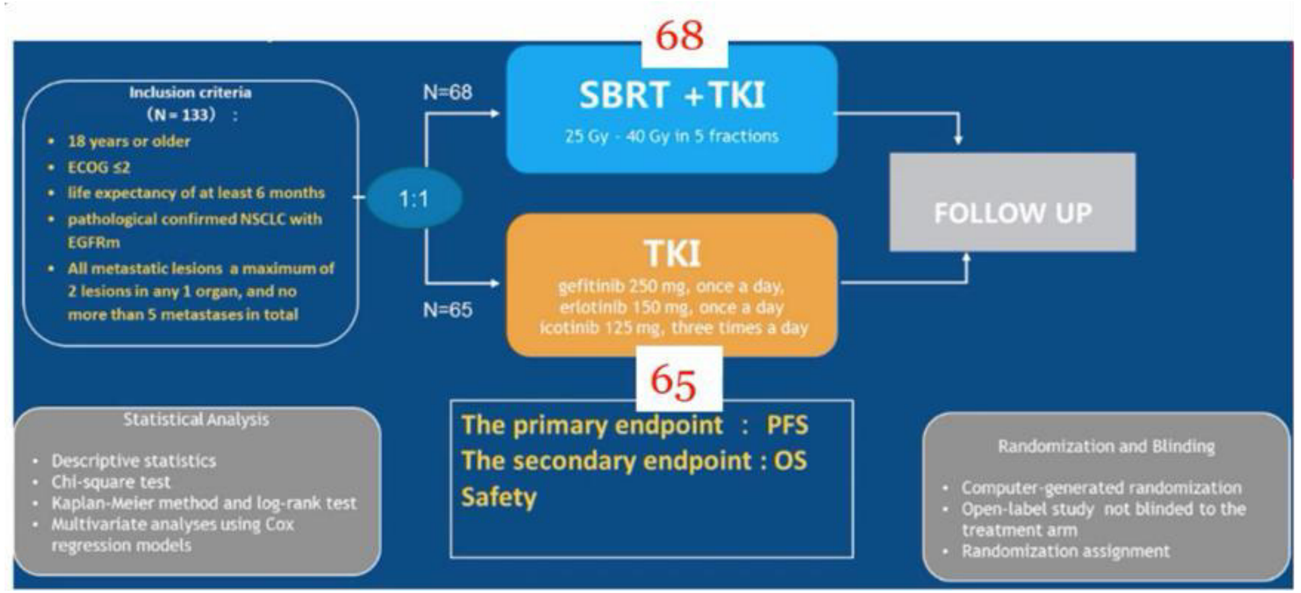
NORTHSTAR Trial

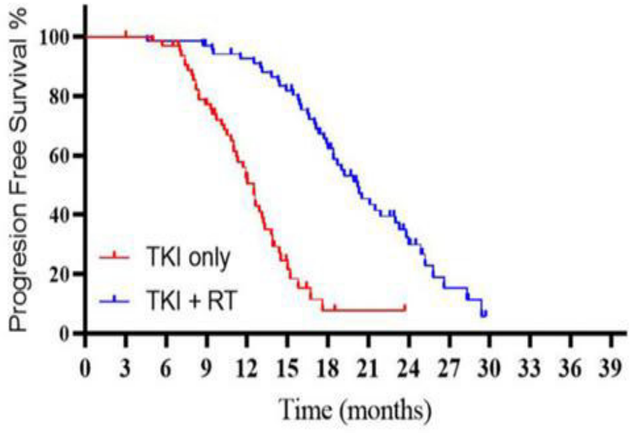


TRIALS INVESTIGATING OLIGOMETS DE NOVO IN EGFR-MUTATED PATIENTS:

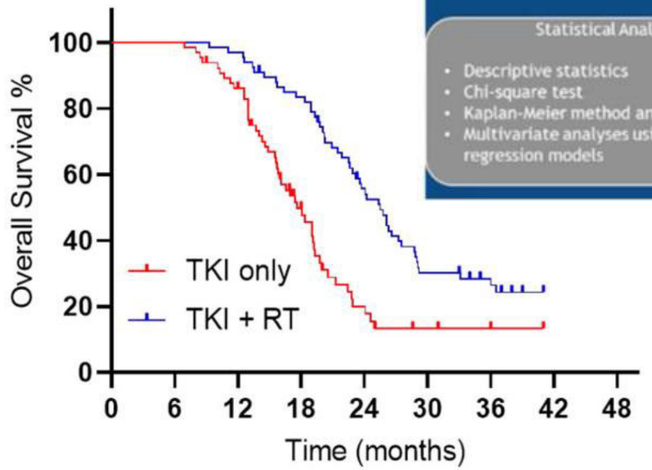
SINDAS Trial (EGFR+)

Wang et al JNCI: Journal of the National Cancer Institute 2023





mPFS: 12.5months vs 20.2months (P<.001)



mOS was 17.4months vs 25.5months (P<.001)

6% G3-G4 pneumonitis in the Tki arm+RT

IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

ABLATE (EGFR+)

First-line lazertinib with or without local ablative radiotherapy in oligo-metastatic, *EGFR*-mutant non-small cell lung cancer (ABLATE, KCSG-LU21-11)

Jii Bum Lee,[1*] Kyung Hwan Kim,[2*] Shinkyo Yoon,[3] Si Yeol Song,[4] Sung Sook Lee,[5] Sunmi Jo,[6] Hee Kyung Ahn,[7] Hyun Ju Kim,[8] Min Hee Hong,[1] Byoung Chul Cho, Hong In Yoon,[1**] Sun Min Lim[1**]

IASLC 2025 World Conference on Lung Cancer
SEPTEMBER 6-9, 2025
BARCELONA, SPAIN

Purpose: To evaluate the efficacy and safety of **LAZERTINIB**, a third-generation EGFR tyrosine kinase inhibitor, with or without stereotactic body radiotherapy (SBRT) in patients with oligo-metastatic, EGFR-mutant non-small cell lung cancer (NSCLC)

Key Inclusion Criteria

- Synchronous oligo-metastatic disease was defined as metastatic lesion ≤ 5 and involved organs ≤ 3.
- All lesions were deemed amenable for SBRT at the discretion of radiologist. Patients were stratified by *EGFR* mutation status (Ex19del vs. L858R), and randomized to receive 240 mg of oral lazertinib monotherapy with or without the addition of SBRT.

Endpoints

- The primary endpoint was investigator-assessed PFS.
- Secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response (DoR), and safety.

First-line lazertinib with or without local ablative radiotherapy in oligo-metastatic, *EGFR*-mutant non-small cell lung cancer (ABLATE, KCSG-LU21-11)

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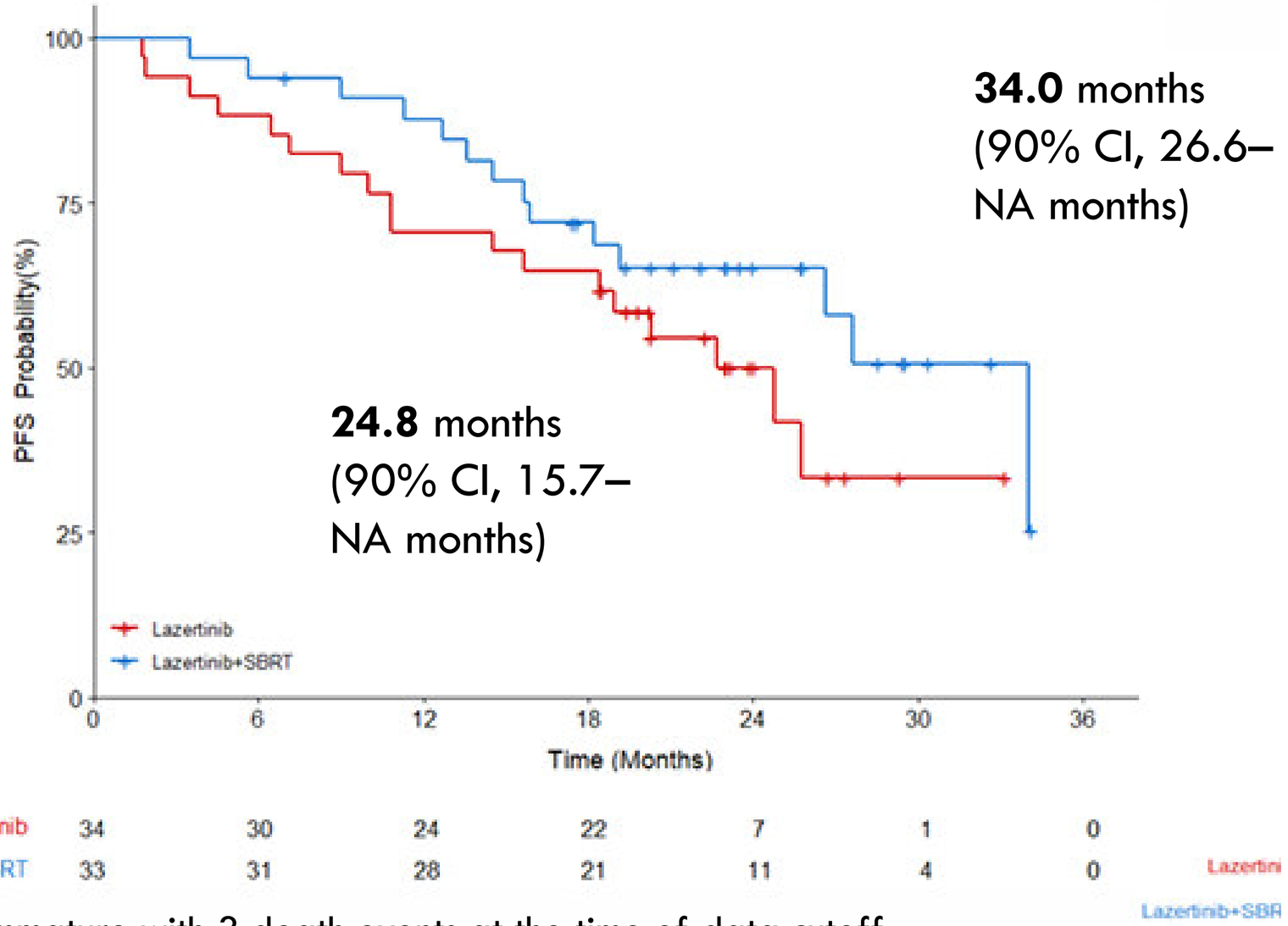


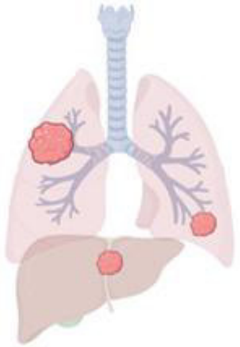
- OS data remain immature with 3 death events at the time of data cutoff.

No Grade 3 or higher radiation pneumonitis and there were no grade 4 or 5 adverse events in both arms

TRIALS INVESTIGATING OLIMETS DE NOVO EGFR+:

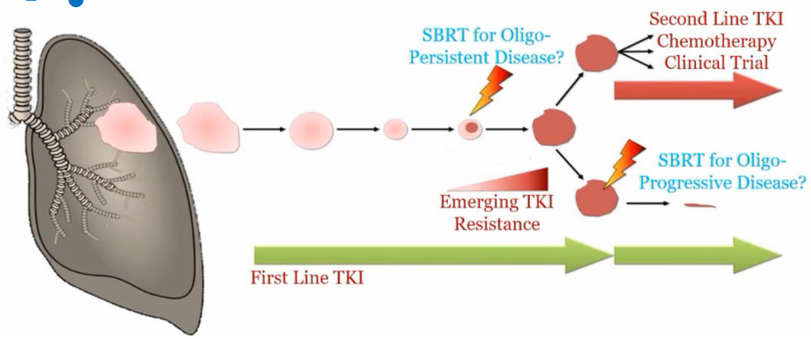
SINDAS Trial

ABLATE Trial



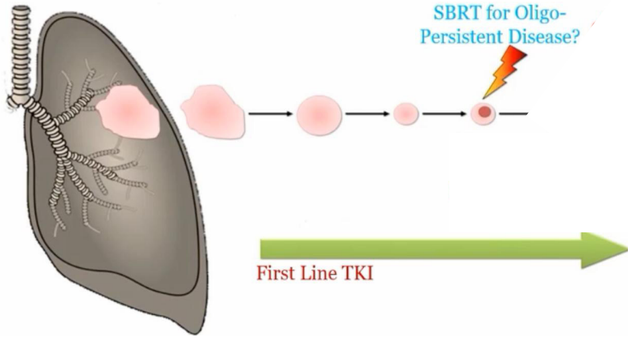
TRIALS INVESTIGATING OLIGOPD EGFR+:

CURB Trial



TRIALS INVESTIGATING OLIGOPERSISTENCE EFGR+:

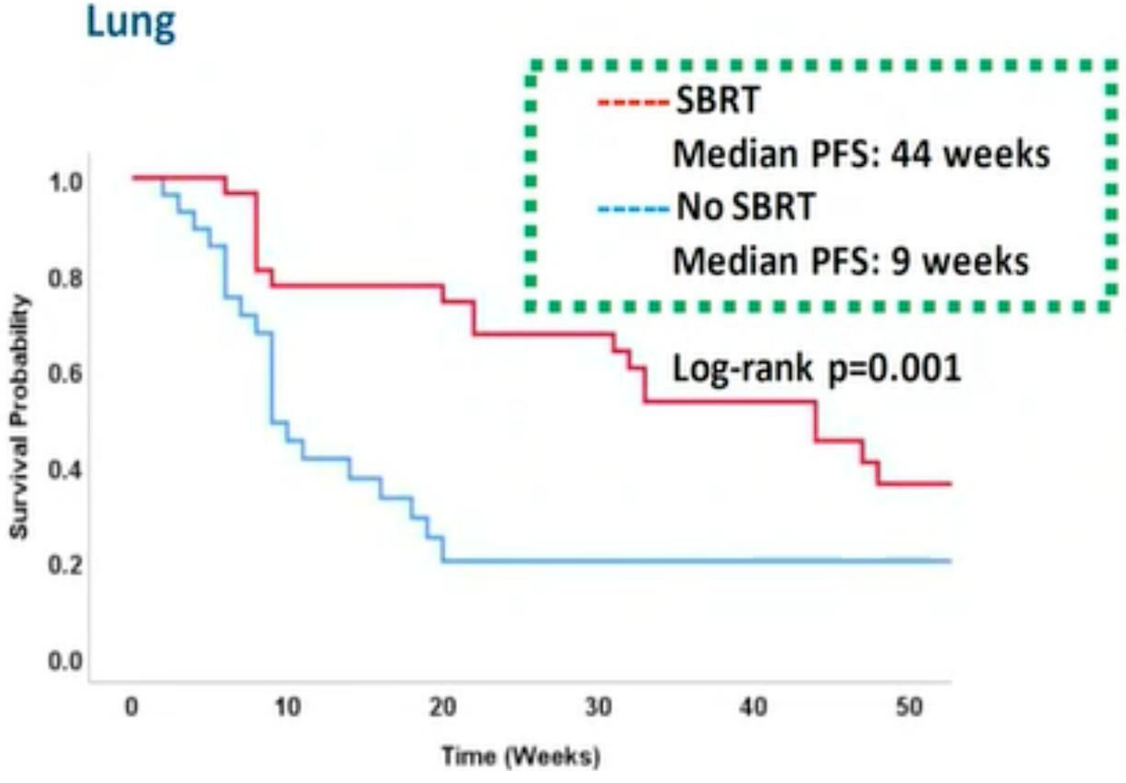
NORTHSTAR Trial



Consolidative Use of Radiotherapy to Block (CURB) Oligoprogression: Interim Analysis of the First Randomized Study of Stereotactic Body Radiotherapy in Patients with Oligoprogressive Metastatic Cancers of the Lung and Breast

C. Jillian Tsai, MD, PhD

Memorial Sloan Kettering Cancer Center



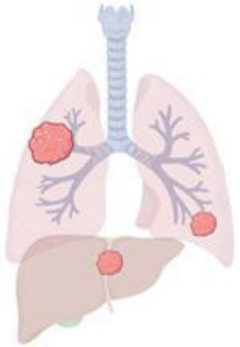
NSCLC	No SBRT (51)	SBRT (55)	p value
No driver mutations	24	22	
Driver mutations	4	9	
Median no. of oligoprogressive lesions	2 (1 to 5)	2 (1 to 5)	0.45
Median no. of total metastatic lesions	5 (1 to >10)	4 (1 to >10)	0.69
Median lines of systemic tx	2 (1 to 9)	2 (1 to 9)	0.10

New lesions	Lung (40)	Breast (38)
Yes	18 (45%)	34 (89.5%)
No	18 (45%)	3 (7.9%)
Unk	4 (10%)	1 (2.6%)

TRIALS INVESTIGATING OLIMETS DE NOVO EGFR+:

SINDAS Trial

ABLATE Trial



TRIALS INVESTIGATING OLIGOPD EGFR+:

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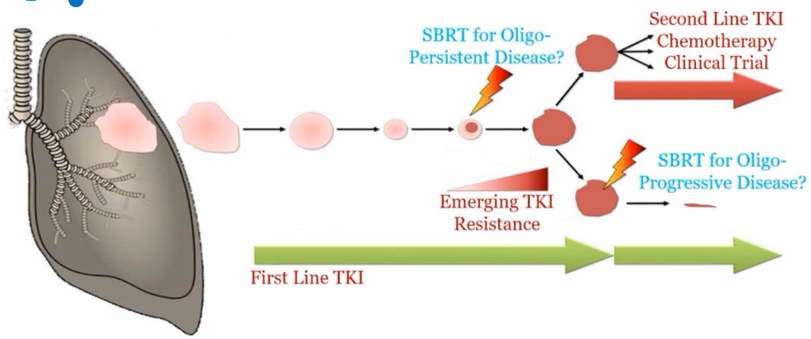

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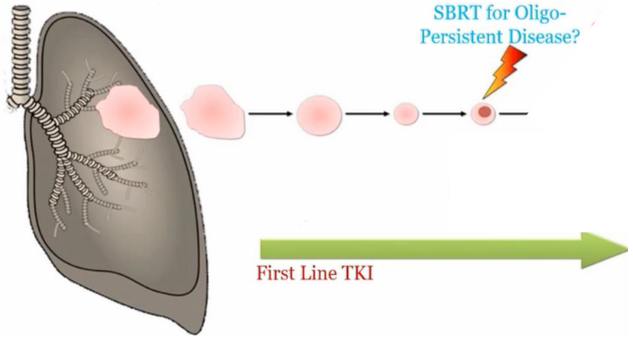

BERLIN 2025 ESMO congress

BERLIN GERMANY
17-21 OCTOBER 2025

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NorthStar Study Design

Randomized, multicenter, phase II trial, NCT03410043

Key Eligibility
- Locally advanced or metastatic NSCLC
- ECOG PS 0 or 1
- Measurable disease
- TKI naïve EGFR Ex19del or L858R

or
- Acquired T790 no prior 3rd gen TKI

Stratification Factors
- TKI naïve vs prior 1/2 gen TKI
- Number of metastases (≤3 vs >3)
- PR vs SD
- Brain metastases

Induction osimertinib 6-12 weeks

Non-PD R 1:1 N=120

Osimertinib*

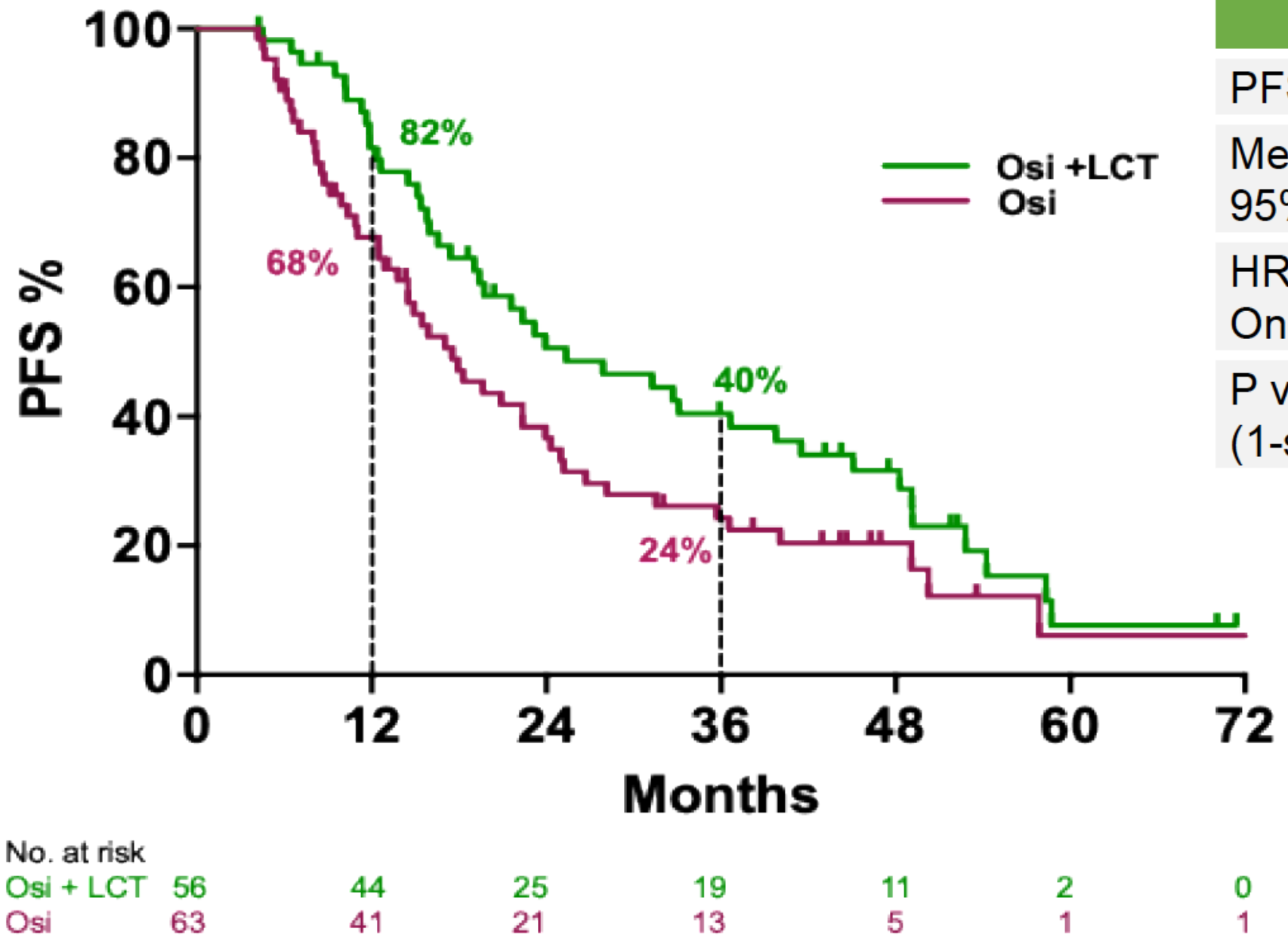
Osimertinib* plus LCT

Primary Endpoint
- PFS

Key Secondary Endpoints
- Safety of osimertinib and LCT
- OS
- PFS in ≤3 mets
- PFS in TKI naïve

*Osimertinib continued until disease progression or unacceptable toxicity

Progression-Free Survival



	Osimertinib (n=63)	Osimertinib plus LCT (n=56)
PFS events, n (%)	50 (79.3%)	42 (75%)
Median PFS month 95% CI	**17.5** (14.5, 24.3)	**25.3** (19.4, 45.0)
HR One-sided 90% CI	**0.66** 0.50 - 0.87	
P value (1-sided log rank)	0.025	

LCT-Specific Adverse Events

Adverse Event	Osimertinib plus LCT (n=56)		
	Grade 1	Grade 2	Grade 3
Pneumonitis	1 (1.8%)	5 (8.9%)	1 (1.8%)
Dyspnea	15 (26.8%)	2 (3.6%)	-
Arterial injury	-	-	1 (1.8%)
Empyema	-	-	1 (1.8%)
Esophagitis	1 (1.8%)	1 (1.8%)	-
Dysphagia	7 (12.5%)	-	-

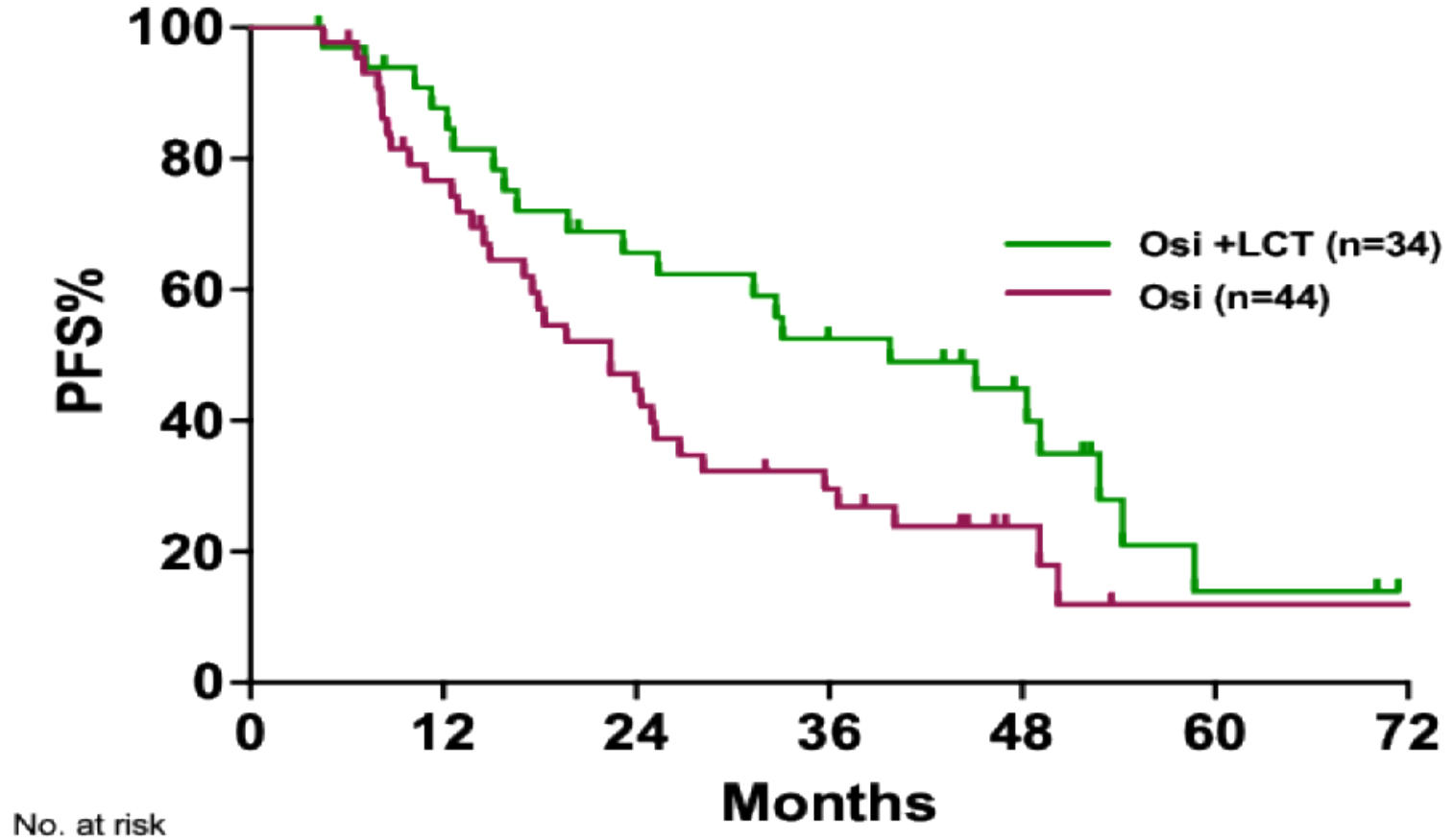
No grade 4 or 5 LCT related adverse events

Yasir Elamin, MD

Progression Free Survival per *EGFR* mutation subtype

Ex19del

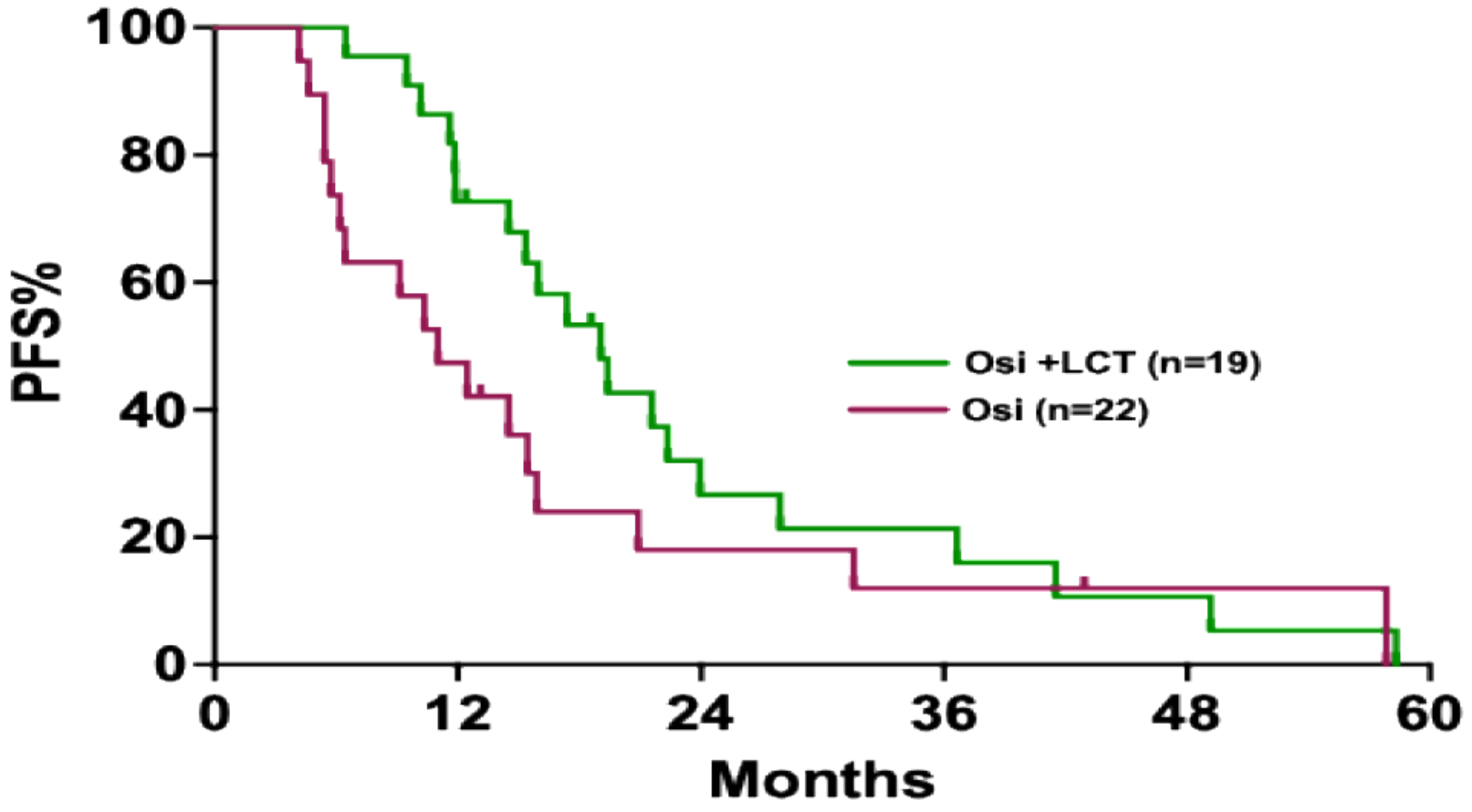
	mPFS (95% CI)	HR (1-sided 90% CI)
Osimertinib + LCT	39.8 (25.4 – 58.7)	0.57 (0.40 – 0.82)
Osimertinib	22.4 (17.0 – 35.7)	



No. at risk							
Osi + LCT	34	28	20	15	9	2	0
Osi	44	32	18	11	4	1	1

L858R

	mPFS (95% CI)	HR (1-sided 90% CI)
Osimertinib + LCT	19.0 (15.4 – 36.6)	0.60 (0.39 – 0.92)
Osimertinib	11.0 (6.4 – 20.9)	



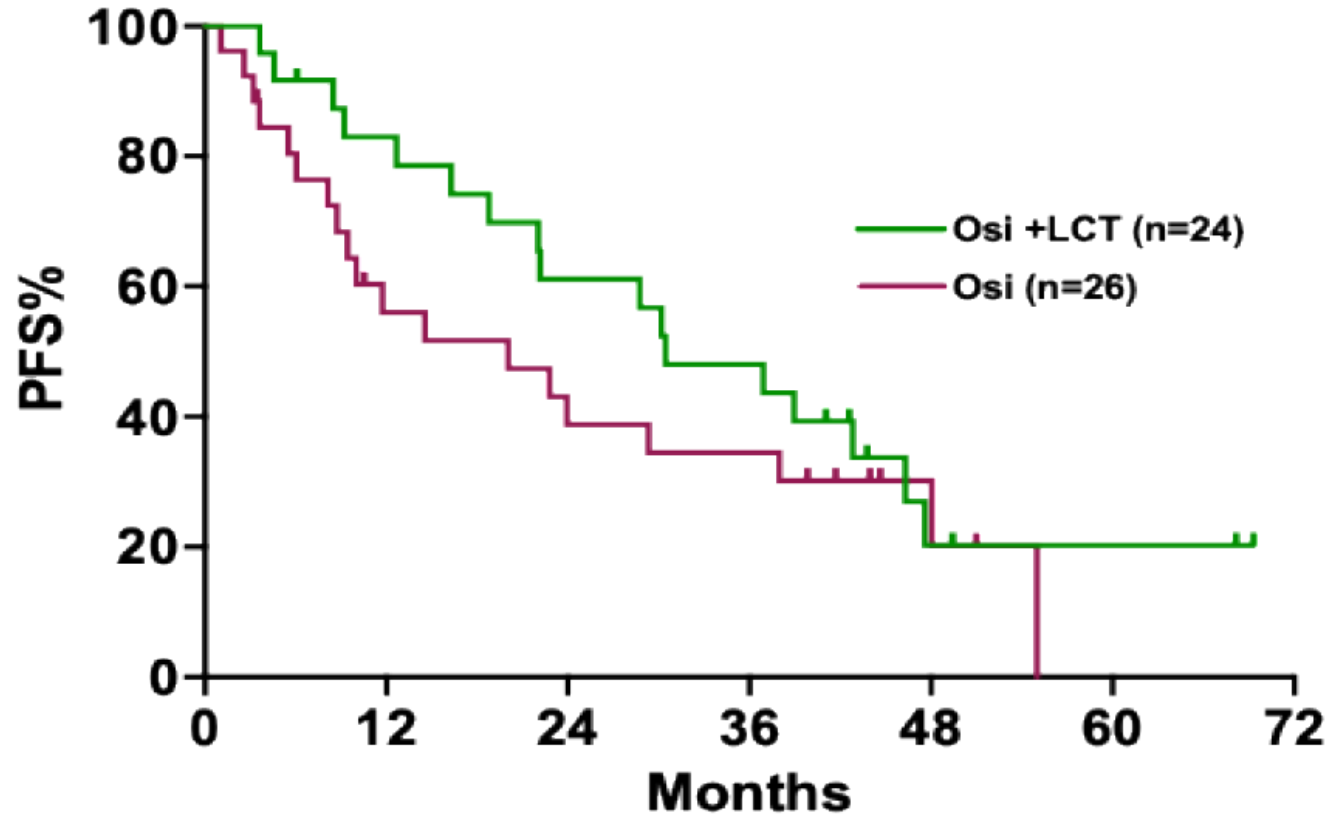
No. at risk							
Osi + LCT	19	9	3	3	2	1	0
Osi	22	16	5	4	4	2	0

Yasir Elamin, MD

Progression-Free Survival in ≤ 3 and >3 metastases at randomization

Metastases ≤3

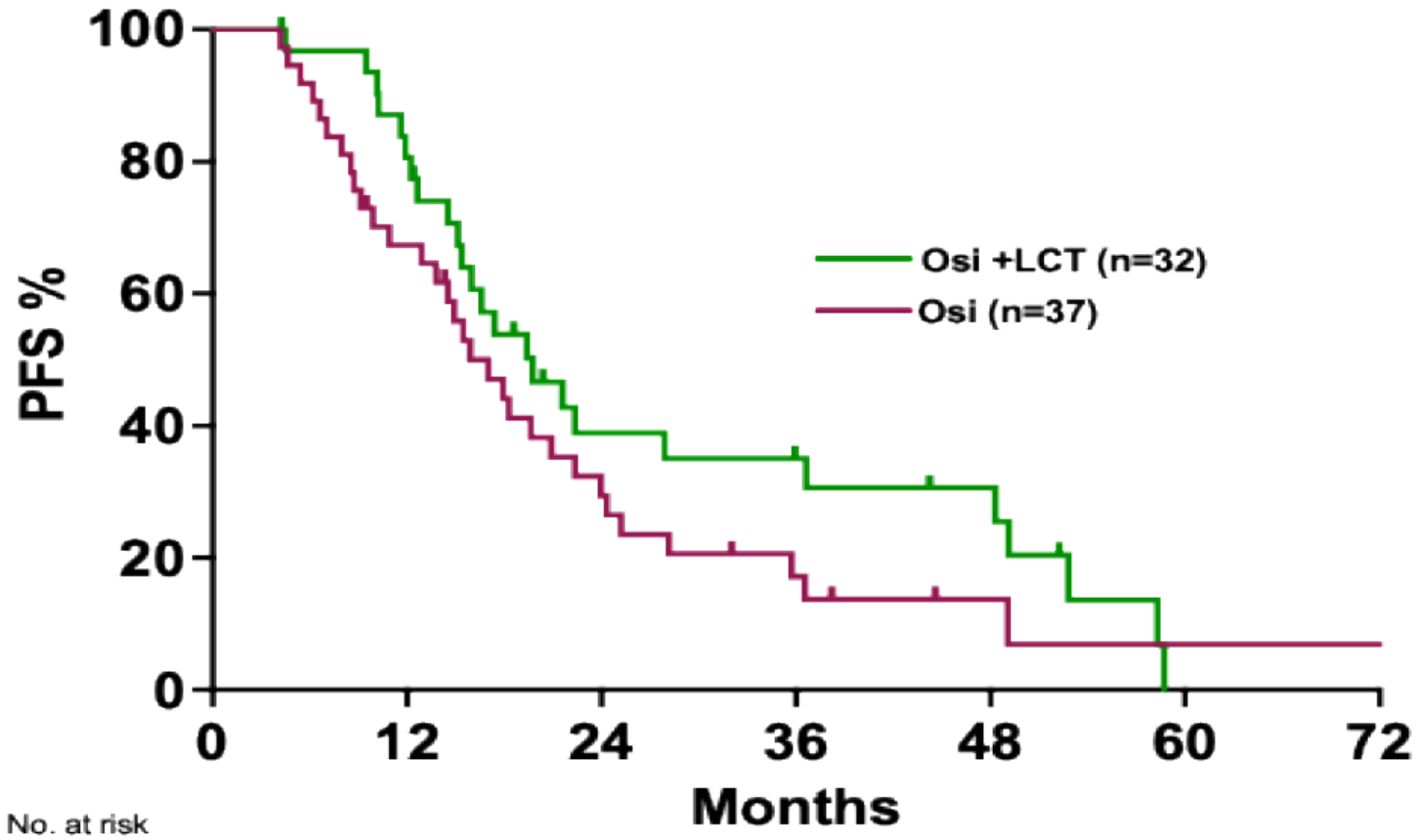
	mPFS (95% CI)	HR (1-sided 90% CI)
Osimertinib + LCT	33.1 (23.9 - NA)	0.67 (0.43 - 1.03)
Osimertinib	22.4 (12.5 - NA)	



No. at risk							
Osi + LCT	24	19	14	11	3	2	2
Osi	26	13	9	8	3	0	0

Metastases >3

	mPFS (95% CI)	HR (1-sided 90% CI)
Osimertinib + LCT	19.7 (15.4 – 48.3)	0.70 (0.50 - 1.00)
Osimertinib	15.9 (13.8 – 23.9)	

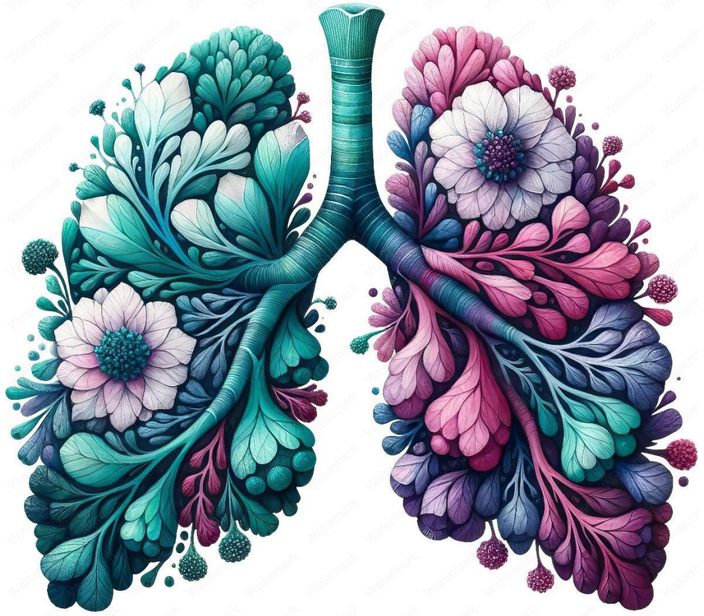


No. at risk							
Osi + LCT	32	25	10	8	6	0	0
Osi	37	24	10	5	2	1	1

Yasir Elamin, MD

Locally Advanced LUNG CANCER

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA



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3. OLIGOMETASTATIC EGFR+ DISEASE (ABLATE and NORTHSTAR)
4. FRACTIONATION in LS-SCLC (LU005 QoL and DUTCH trial)

2024 ASCO ANNUAL MEETING

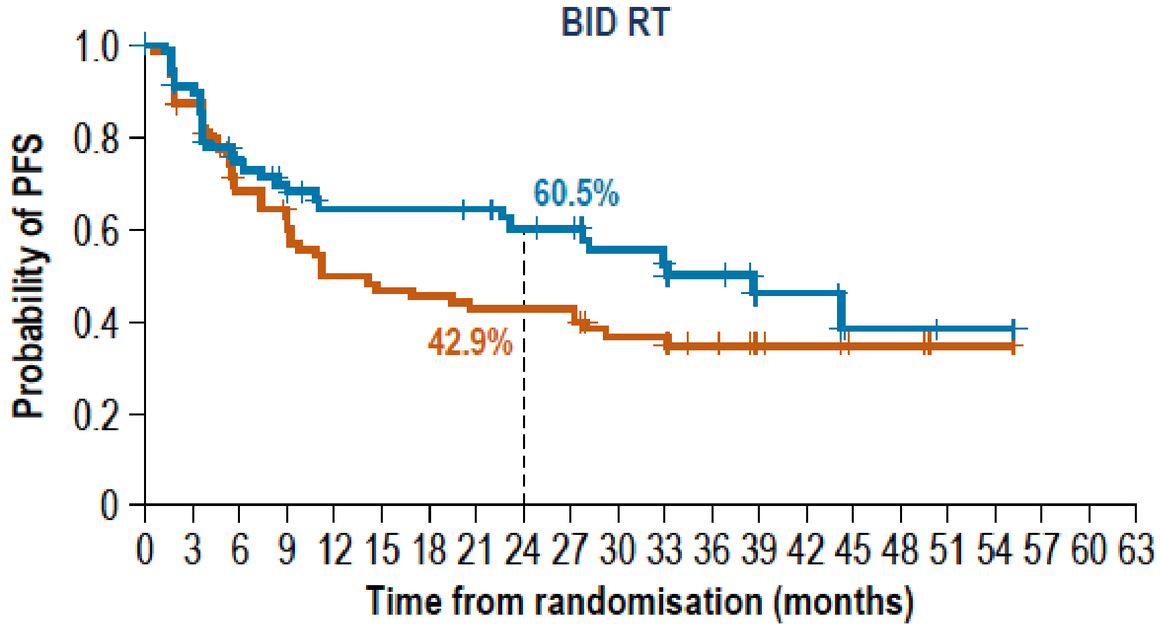
ADRIATIC: durvalumab as consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC)

David R. Spigel, Ying Cheng, Byoung Chul Cho, Konstantin Laktionov, Jian Fang, Yuanbin Chen, Yoshitaka Zenke, Ki Hyeong Lee, Qiming Wang, Alejandro Navarro, Reyes Bernabe, Eva Buchmeier, John Wen-Cheng Chang, Isamu Okamoto, Sema Sezgin Goksu, Andrzej Badzio, Bethany Gill, Hema Gowda, Haiyi Jiang, Suresh Senan

PRESENTED BY: Dr David R. Spigel, Sarah Cannon Research Institute, Nashville, TN, USA

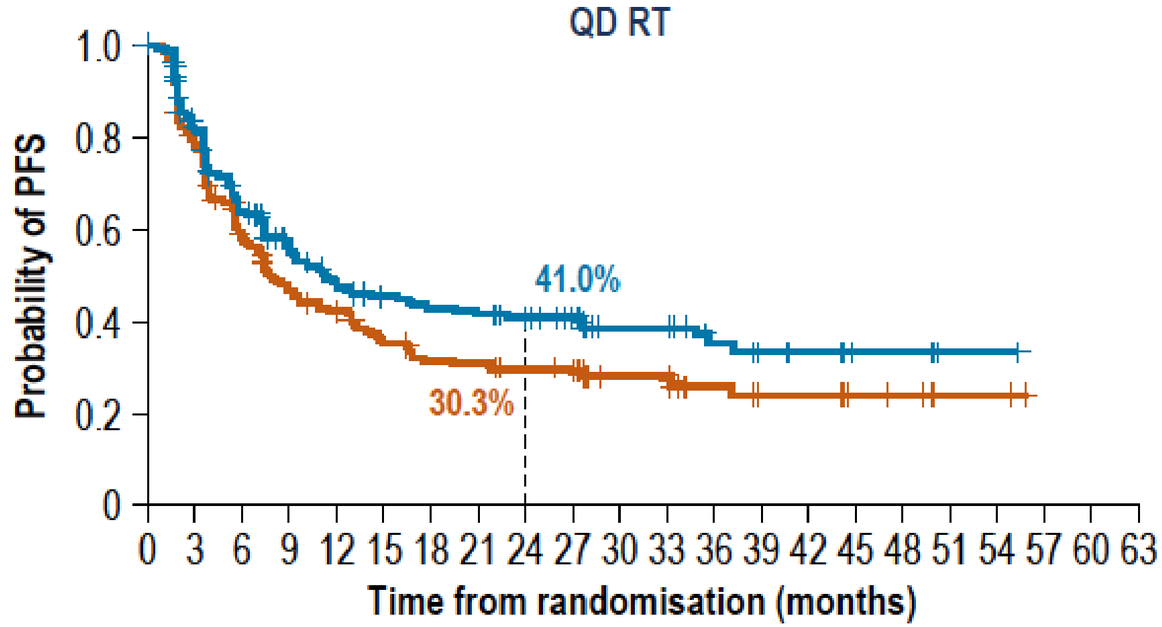
ADRIATIC: BID and QD subgroup - PFS

	BID RT		QD RT		ITT	
	D (n = 69)	P (n = 79)	D (n = 195)	P (n = 187)	D (n = 264)	P (n = 266)
Median PFS (95% CI), months	38.7 (22.7–NE)	14.3 (9.1–28.1)	11.4 (9.0–19.5)	7.8 (6.4–11.5)	16.6 (10.2–28.2)	9.2 (7.4–12.9)
2-year PFS, %	60.5	42.9	41.0	30.3	46.2	34.2
HR (95% CI)	0.72 (0.45–1.13)*		0.77 (0.60–1.00)*		0.76 (0.61–0.95)†	
Multivariable HR (95% CI)	0.73 (0.46–1.14)‡		0.79 (0.61–1.03)‡		–	



No. at risk:

D, BID	69	61	47	42	36	36	36	35	30	29	22	22	14	7	7	3	3	2	2	0	0	0
P, BID	79	67	49	46	35	33	32	30	30	30	23	23	19	12	11	8	8	3	3	0	0	0



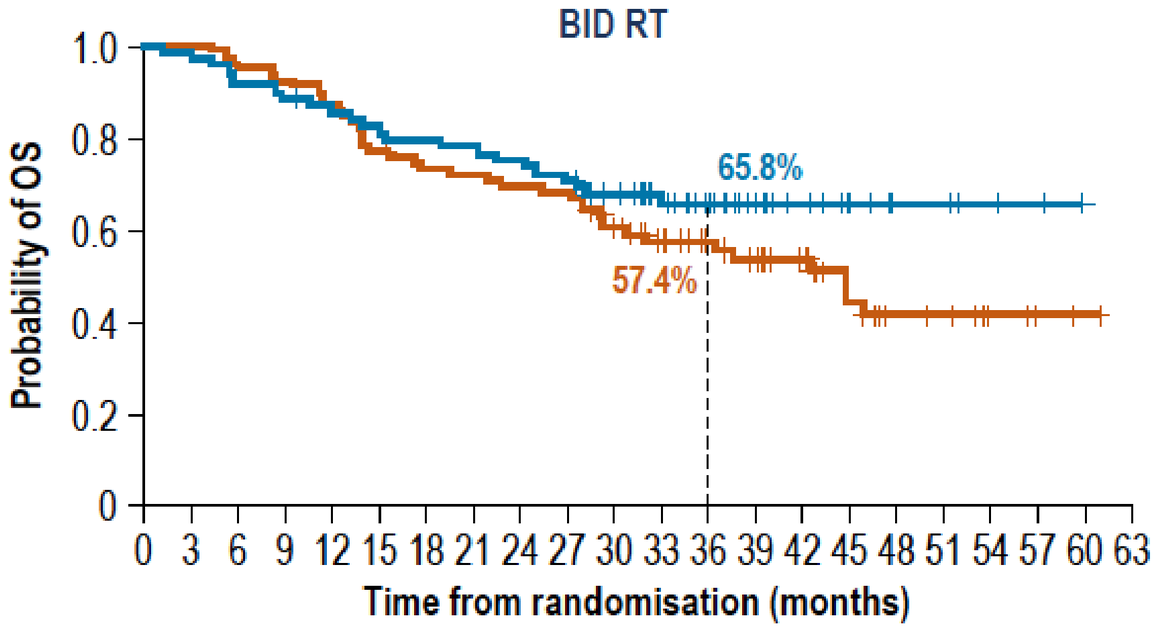
No. at risk:

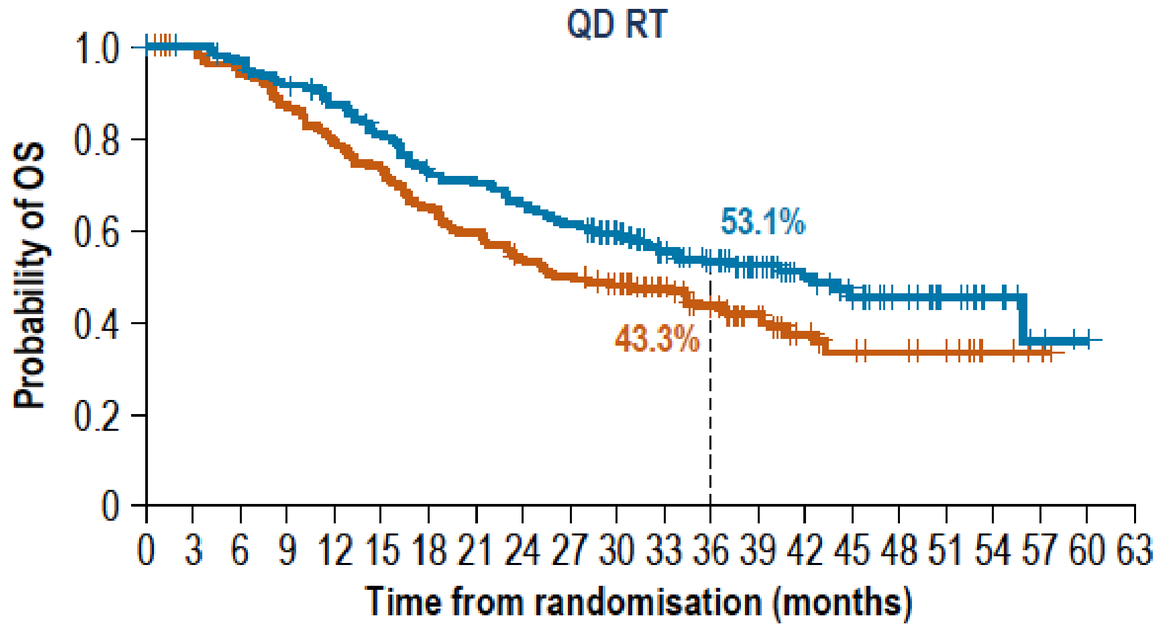
D, QD	195	151	114	93	77	69	65	63	54	49	29	29	19	14	12	7	7	2	2	0	0	0
P, QD	187	141	97	76	65	55	47	46	41	39	24	24	15	11	11	7	6	2	2	0	0	0

*Subgroup HRs and CIs calculated using an unstratified Cox proportional hazards model.
†ITT HR and CIs calculated using a Cox proportional hazards model stratified by TNM stage and receipt of PCI.
‡Multivariable analysis interaction p-value 0.75.

ADRIATIC: BID and QD subgroup - OS

	BID RT		QD RT		ITT	
	D (n = 69)	P (n = 79)	D (n = 195)	P (n = 187)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (NE–NE)	44.8 (29.4–NE)	41.9 (32.0–NE)	26.1 (21.7–36.8)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	65.8	57.4	53.1	43.3	56.5	47.6
HR (95% CI)	0.68 (0.40–1.14)*		0.72 (0.55–0.96)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.71 (0.42–1.18)‡		0.73 (0.55–0.96)‡		–	





No. at risk:																							
D, BID	69	68	63	61	59	56	54	53	51	48	42	35	27	18	13	10	5	5	3	2	0	0
P, BID	79	79	76	73	69	61	57	56	54	53	45	37	32	27	22	14	9	8	4	3	1	0

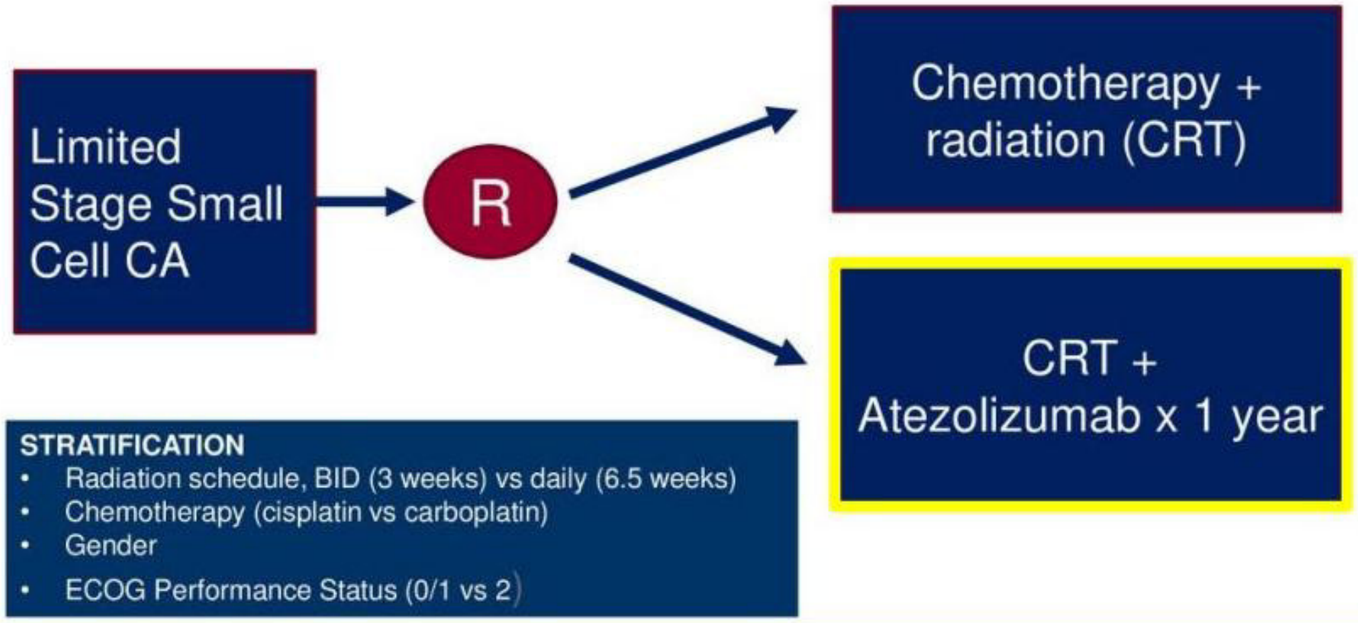
No. at risk:																									
D, QD	195	193	185	175	164	151	135	130	121	114	99	75	63	50	38	29	22	14	8	3	1	0
P, QD	187	181	171	158	145	134	118	108	97	90	78	60	48	35	22	17	14	11	4	2	0	0

*Subgroup HRs and CIs calculated using an unstratified Cox proportional hazards model.
†ITT HR and CIs calculated using a Cox proportional hazards model stratified by receipt of PCI.
‡Multivariable analysis interaction p-value 0.95.

LU005 Trial

ASTRO 2024

LU005: SCLC: A Phase II/III Randomized Study of Chemoradiation Versus Chemoradiation Plus Atezolizumab



544 pts randomized from May 2019 and December 2023

Median OS: 39.5 mos (95% CI 27.5- Not reached) vs 33.1 mos (95% CI 27.8- 43.9) for cCRT and atezo+cCRT, respectively
HR= 1.11, 95% CI: 0.85-1.45

Median PFS: 11.5 mos (95% CI: 10.713.4) vs 12.0 mos (95% CI: 10.8-15.1) for cCRT and atezo+cCRT, respectively
HR=1.00, 95% CI: 0.80-1.25

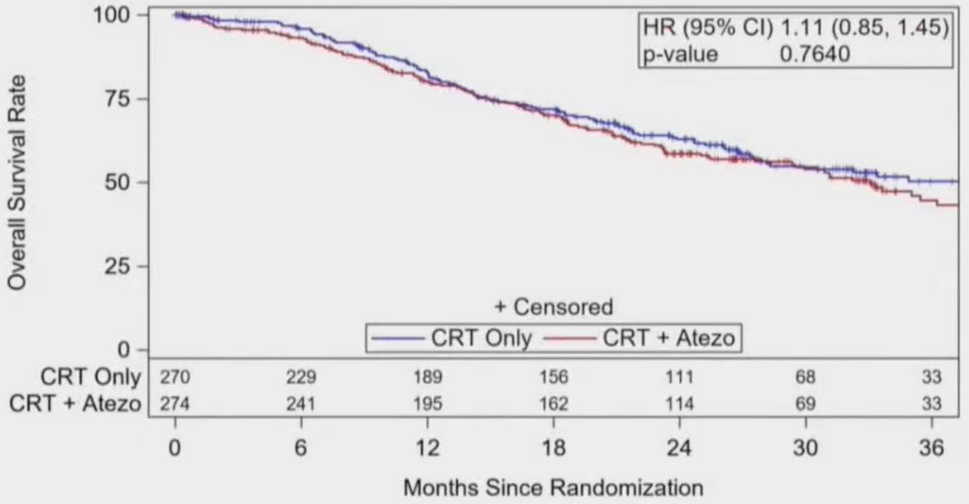
No concerning safety signals for atezo +cCRT.

Pts treated with BID had higher survival (median OS 35.4 mos, 95% CI: 32.3- not reached) than daily RT (median OS 28.3 mos 95% CI: 21.7- 40.6)
HR=1.44, 95% CI: 1.10-1.89

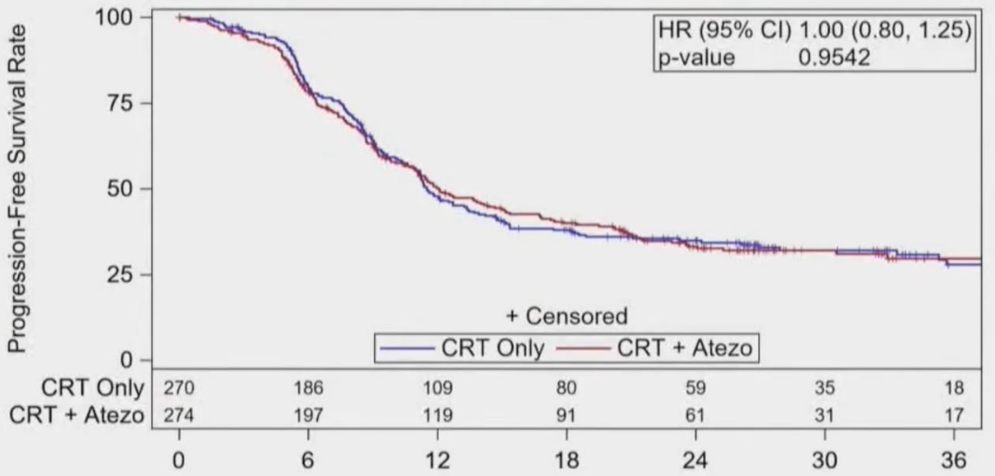
Chemoradiation with concurrent and consolidation atezo did not improve survival in LS-SCLC

LU-005: No Benefit in Survival or Local Failure with Concurrent and Adjuvant Atezolizumab

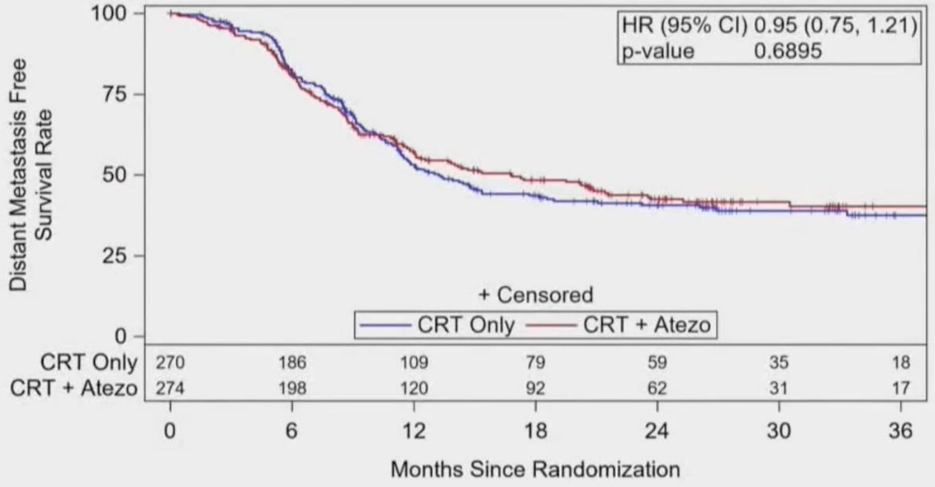
Overall Survival



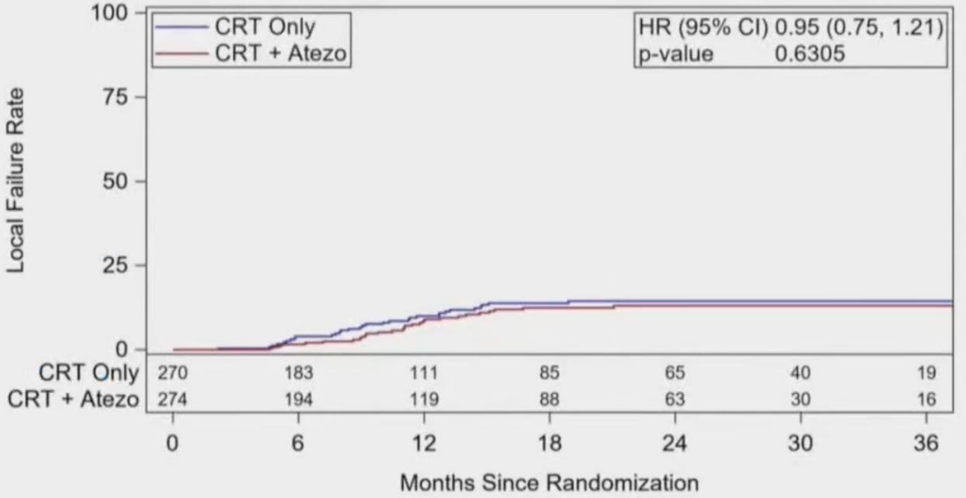
Progression Free Survival



Distant Metastasis Free Survival



Time to Local Failure



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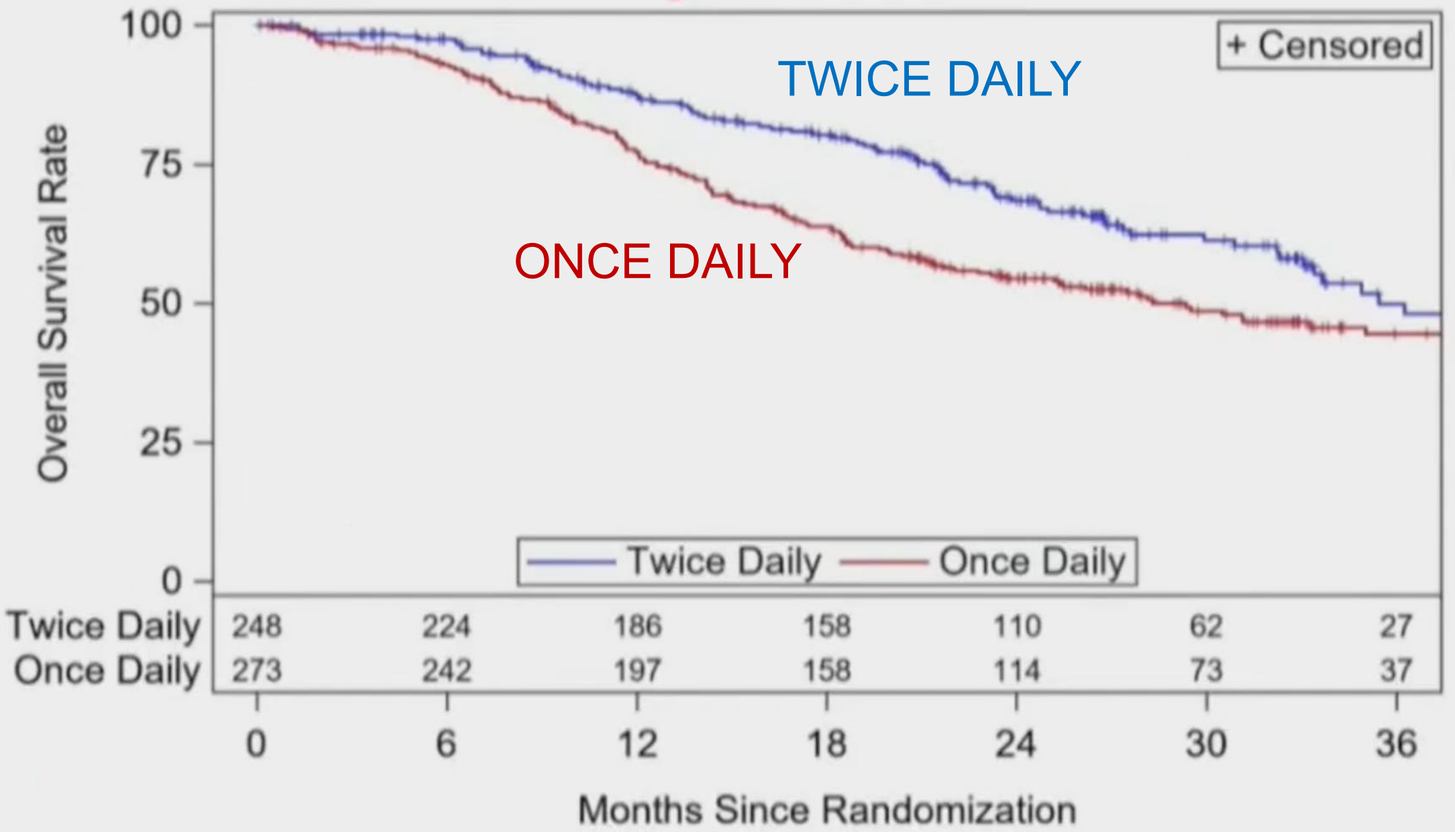
Overall Survival: Unadjusted RT Schedule Comparison



Note: Preliminary findings. Patients may have received twice daily RT over once daily for a numbe reasons, including better performance status. Excludes patients who received no RT.

ASTRO'S 67TH ANNUAL MEETING
SEPTEMBER 27 – OCTOBER 1, 2025
MOSCONE CENTER | SAN FRANCISCO

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LBA 08

Comprehensive Patient Reported Outcomes (PROs) from NRG LU005: A Randomized Trial Of Chemoradiation (CRT) ± Atezolizumab In Limited-Stage Small Cell Lung Cancer (LS-SCLC)

Validated PRO instruments were employed to assess different aspects of health-related quality of life:
•FACT-TOI (Functional Assessment of Cancer Therapy – Trial Outcome Index) for general well-being and symptom burden.
•EQ-5D-5L, used to derive Quality-Adjusted Survival (QAS).
•PROMIS-Fatigue, to measure treatment-related fatigue.

Compliance with PRO assessments was high, exceeding 85% at baseline and remaining steady at 60–68% through 21 months

At 15 months, FACT-TOI changes were comparable between treatment arms, but **by 21 months, a lower proportion of patients** receiving atezolizumab experienced CMD (25% vs. 38%).

Nearly 50% of patients received **BID radiotherapy**, which consistently correlated with better QOL than once-daily RT at every timepoint.
Rates of CMD favored BID RT both acutely and long-term:
- At end of CRT: 36% vs. 60%
- At 15 months: 28% vs. 41%
- At 21 months: 22% vs. 39%

In multivariable analysis, predictors of lower CMD included BID RT at all timepoints, cisplatin (at 15 months), and atezolizumab (at 21 months), reinforcing the independent positive effects of both treatment intensity and immunotherapy on sustained QOL.

ESTRO 2025 2-6 May 2025 Vienna, Austria

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REAL WORLD DATA: ONCE vs BID

Methods

Real-world data from the Dutch Lung Cancer Audit-Radiotherapy

Patients diagnosed with LS-SCLC between Jan 2016 and Dec 2023

Treated with concurrent OD or BID chemoradiation

Outcomes (corrected for age, sex, T stage, N stage and WHO-status):

-**Overall Survival** (cox proportional hazards)

-**Severe Acute Toxicity** gr ≥2+ pneumonitis/ gr ≥3 non-hematological tox (multivariable logistic regression)

Results

	BID group N=593	OD group N=202	P-value
Age (mean, SD)	66.4 (9.6)	67.1 (9.1)	0.41
Sex, female (%)	55.5	57.9	0.57
WHO performance (%)			**0.02**
0-1	89.7	85.1	
≥2	8.6	14.4	
N-stage (%)			0.87
0	7.1	7.4	
1-3	92.9	92.6	
TNM-stage (%)			0.53
I	1.9	2.5	
II	9.9	7.4	
III	87.2	90.1	
PCI (%)			**<0.01**
Yes	35.1	15.8	
No	19.9	10.4	
Unknown	45.1	73.8	

Baseline characteristics

NETHERLANDS CANCER INSTITUTE ANTONI VAN LEEUWENHOEK

REAL WORLD DATA: ONCE vs BID in LS-SCLC

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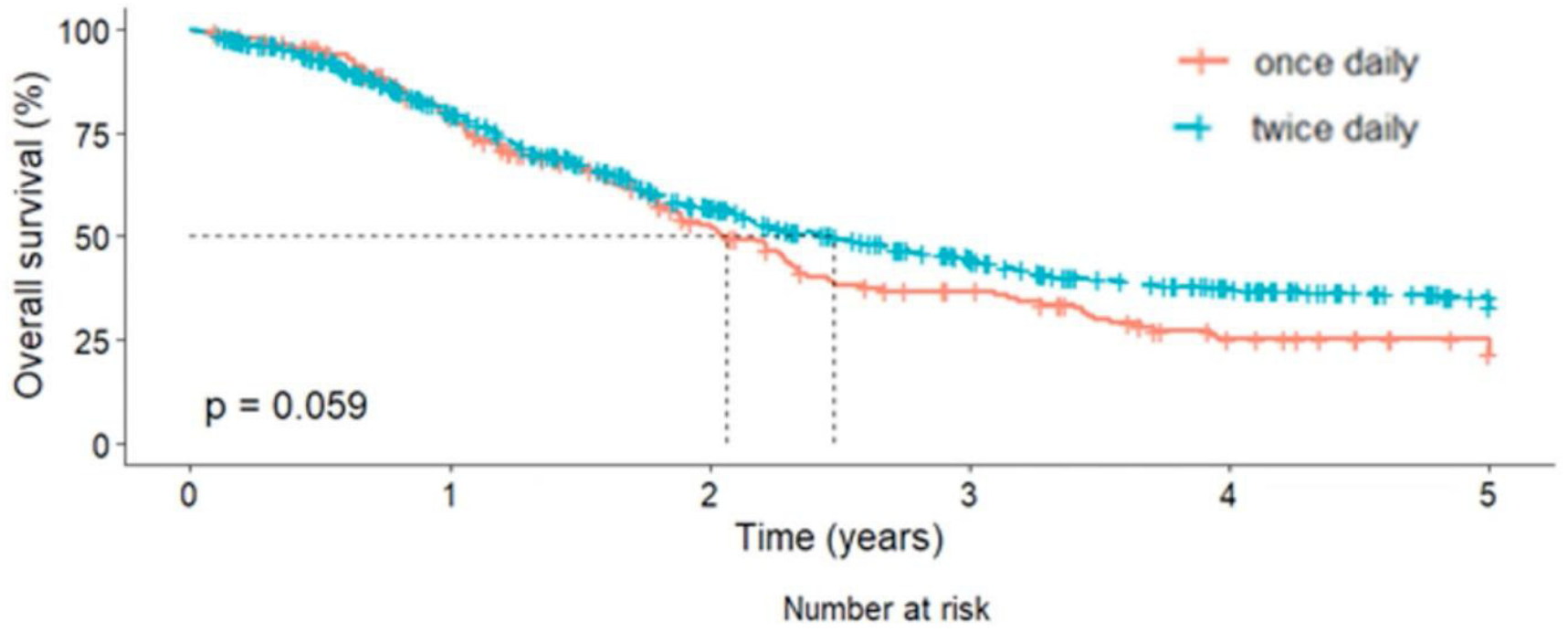
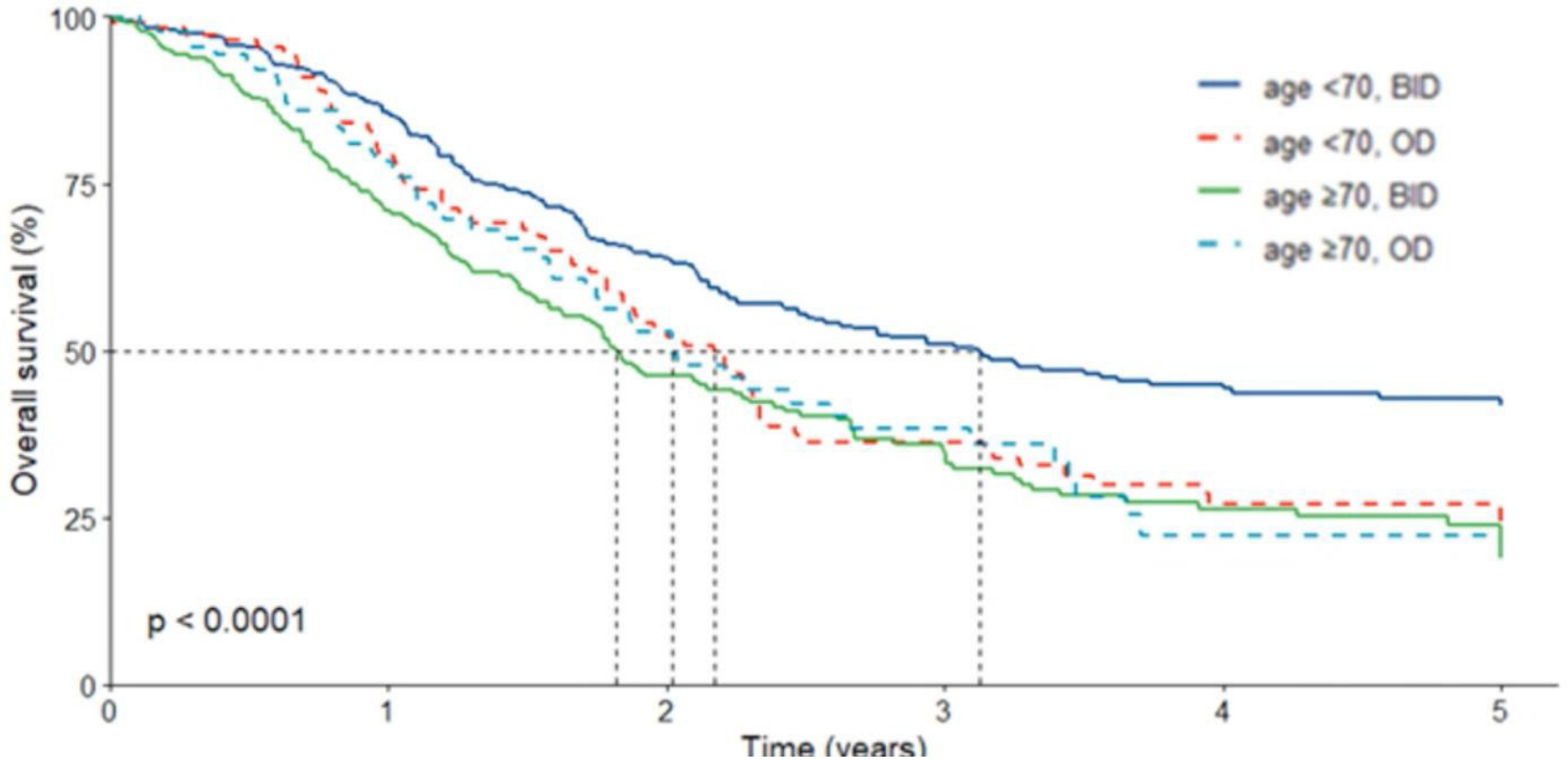
- **Median OS**
  - BID 29.7 months (95% CI 25.8 – 35.9)
  - OD 24.7 months (95% CI 22.1 – 28.1)
  - aHR 0.83 (95% CI 0.67 – 1.03)
- **Acute toxicity**
  - BID 27.3%
  - OD 21.6%
  - OR 1.38 (95% CI 0.93 – 2.08)

- **Median OS (<70)**
  - BID 37.5 months (95% CI 25.8 – 35.9)
  - OD 26.1 months (95% CI 22.1 – 28.1)
  - aHR 0.67 (95% CI 0.50 – 0.88)
- **Acute toxicity (<70)**
  - BID 26.0%
  - OD 23.9%
  - OR 1.1 (95% CI 0.78 – 1.55)





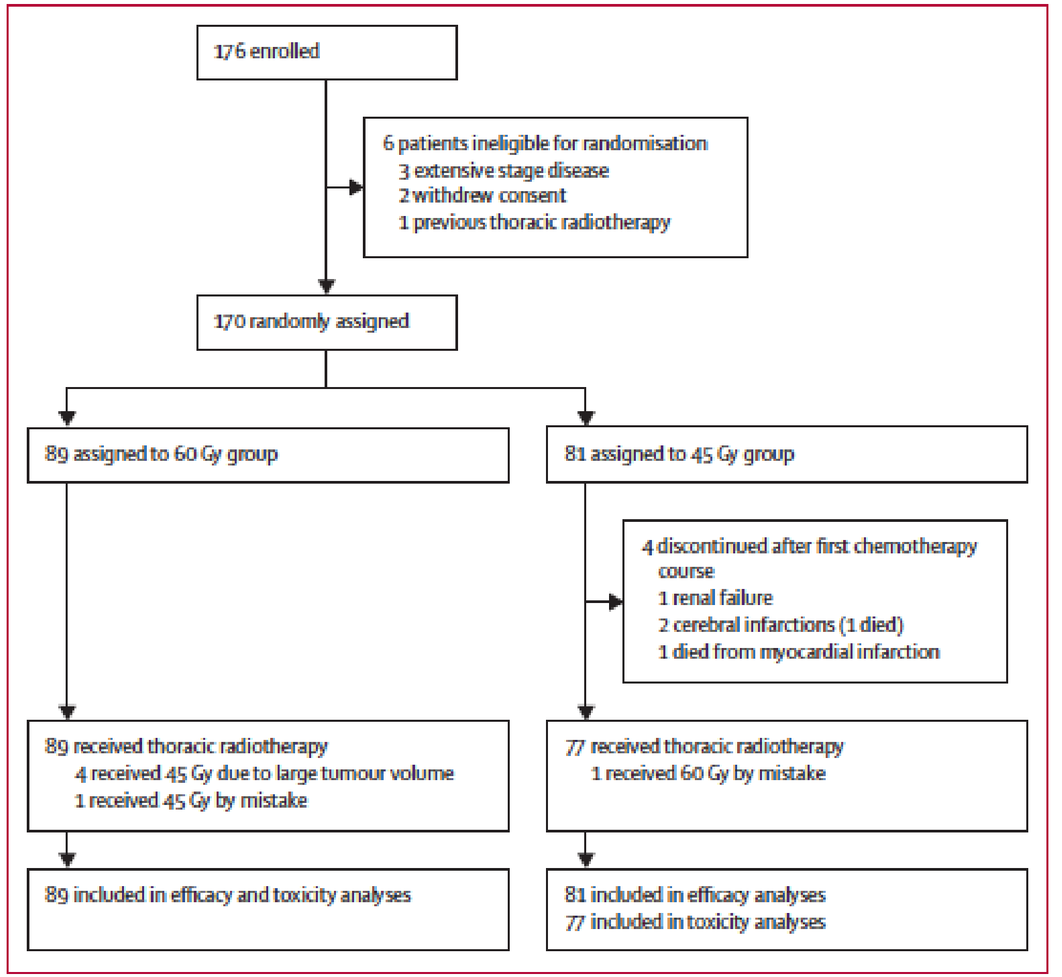
High-dose versus standard-dose twice-daily thoracic radiotherapy for patients with limited stage small-cell lung cancer: an open-label, randomised, phase 2 trial

Bjørn Henning Grønberg, Kristin Toftaker Killingberg, Øystein Fløtten, Odd Terje Brustugun, Kjersti Hornslien, Tesfaye Madebo, Seppo Wang Langer, Tine Schytte, Jan Nyman, Signe Risum, Georgios Tsakonas, Jens Engleson, Tarje Onsøien Halvorsen

Norway, Denmark, and Sweden.

TOTAL DOSE OF 45Gy in 30 FX
(twice daily in 150cGy fractions)

TOTAL DOSE OF 60Gy in 40 FX
(twice daily in 150cGy fractions)



Lancet Oncol 2021; 22: 321–31

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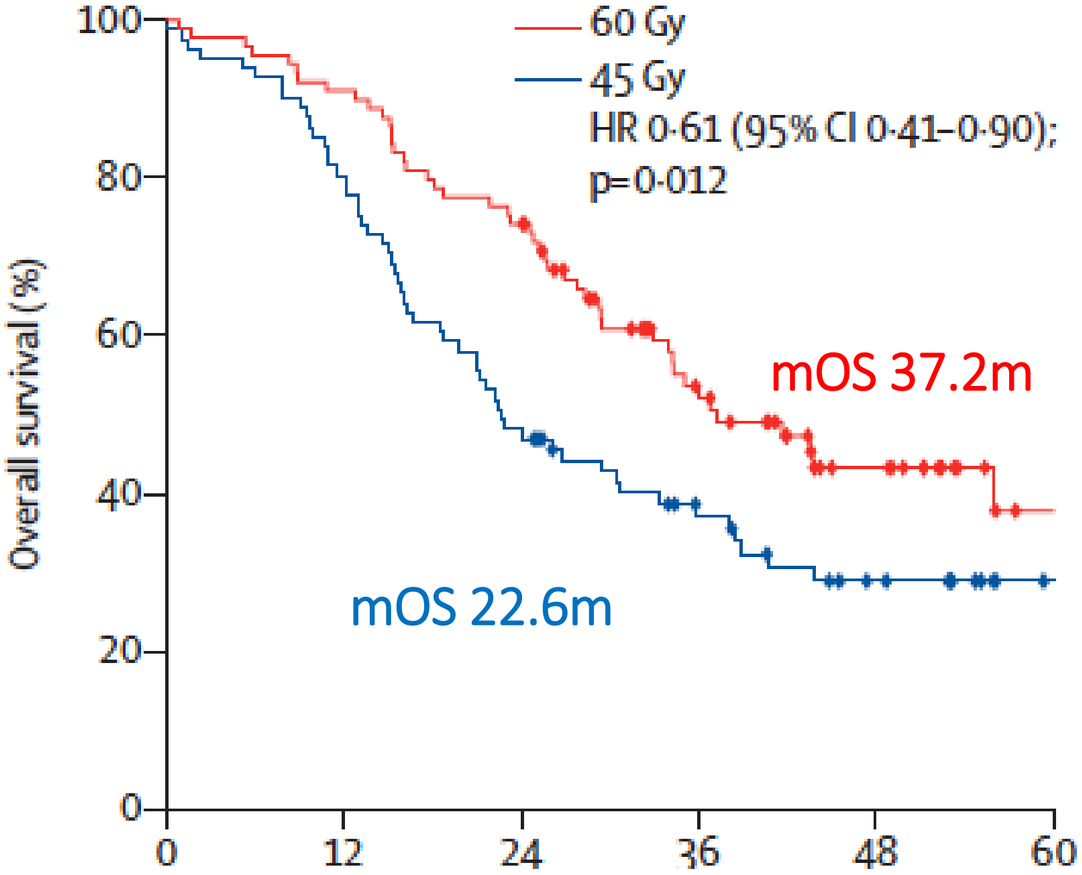
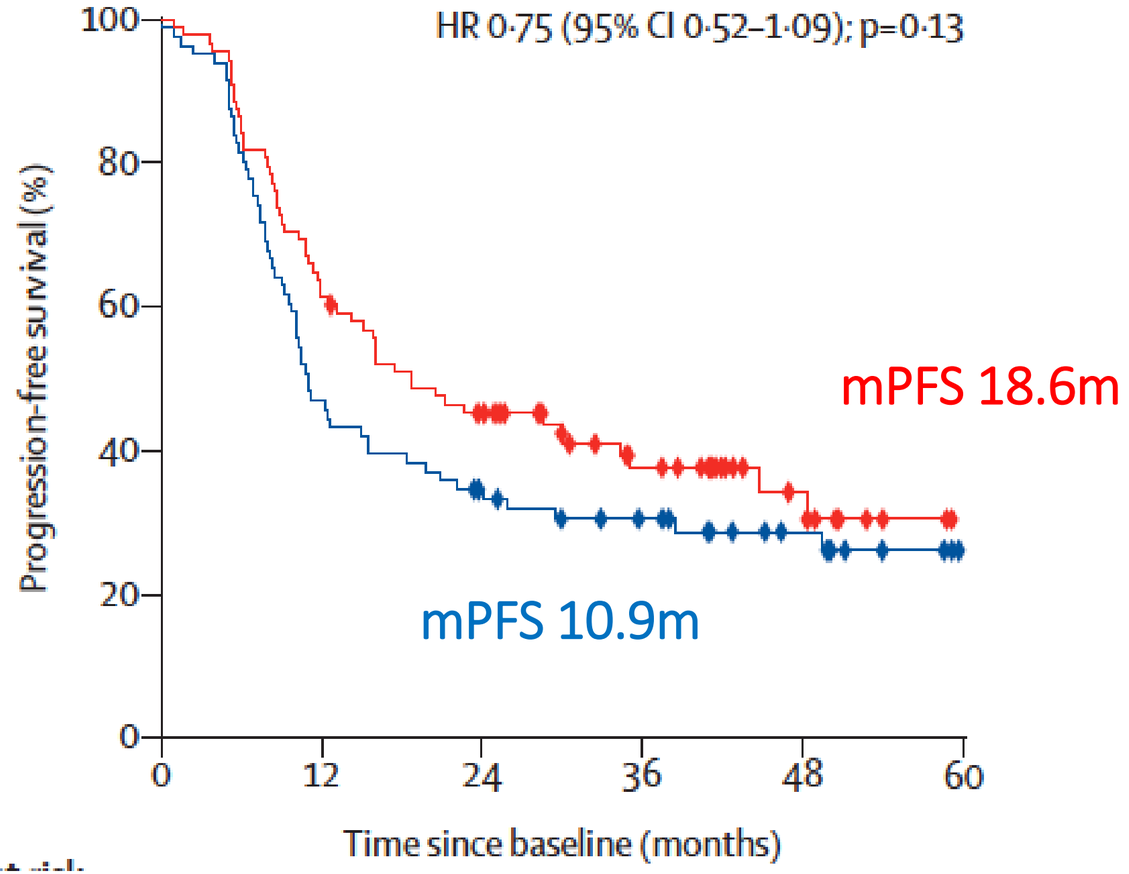
Median follow-up 49 months





Low increase of G3 toxicity (3%)

Lancet Oncol 2021; 22: 321–31

The NEW ENGLAND JOURNAL of MEDICINE

Durvalumab in Small-Cell Lung

TO THE EDITOR: Results of the phase 3 ADRIATIC trial (Oct. 10 issue)[1] marked a breakthrough in the treatment of limited-stage small-cell lung cancer, but some questions remain unanswered. According to the protocol, the radiotherapy dose was 60 to 66 Gy once daily or 45 Gy twice daily. Are these doses the best options for limited-stage small-cell lung cancer?

In a randomized phase 2 trial, Gronberg et al.[2] found that high-dose thoracic radiotherapy of 60 Gy twice daily improved survival as compared with the standard dose of 45 Gy twice daily (hazard ratio for death from any cause, 0.61; 95% confidence interval, 0.41 to 0.90). The authors also observed that the high-dose regimen led to the longest median overall survival duration (43.5 months)[3] that has been reported in trials of chemoradiotherapy for limited-stage small-cell lung cancer.[4-6] Although this trial is a phase 2 trial with a limited sample size, it has remarkable clinical relevance, with an absolute effect of 18 fewer deaths per 100 patients treated (number needed to treat to avoid one death, 5; range, 3 to 25).

Notwithstanding the impressive results of the ADRIATIC trial, will we be compelled to use a less effective radiation schedule such as that in the trial? The scientific world is called to answer this question, and efforts should be made to add evidence in this area.

WHICH DOSE????:
45Gy twice daily
60Gy twice daily

REPLY TO RAMELLA ET AL:

Ramella et al. suggest that a twice-daily thoracic radiotherapy dose of 60 Gy, as investigated in a randomized phase 2 trial in Scandinavia, could be a preferred radiation schedule.[2] The radiation doses and schedules used in our trial were guideline-recommended worldwide standards in 2018, when we initiated the trial. Some limitations of the findings from the Scandinavian trial, as well as promising results of other randomized trials of different radiotherapy schedules, have recently been highlighted.[3] A phase 3 trial investigating these different doses and schedules is warranted. Ongoing translational research in our trial may provide insights into the role of radiotherapy when combined with immunotherapy in patients with limited-stage small-cell lung cancer.

Suresh Senan, M.B., B.S., Ph.D.

Ramella, Ippolito, D'Angelillo. NEJM December 2024

Locally Advanced LUNG CANCER

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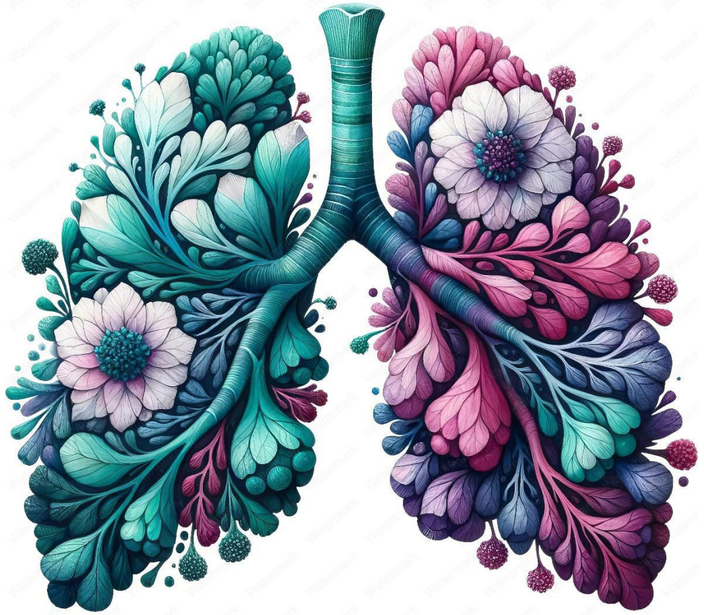

1. CHEMORADIATION IN EGFR (FOCUS ON ILD- dose constraints)
2. CHEMORADIATION and IO (no conco- no doublets-look into the black box!!)
3. OLIGOMETASTATIC EGFR+ DISEASE (Local therapy offers advantage!)
4. FRACTIONATION in LS-SCLC (BID is better!!!)


Thank You...
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IN HONOREM PRINCIPIS APOST PAVLVS V BVRGHESIVS ROMANVS PONT MAX AN MDCXII PONT VII
«The true things in life are not studied or learned, but encountered.»