AIRO Associazione Italiana Radioterapia e Oncologia clinica

LA CURA DI PRECISIONE

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA



Sessione: L'Oncologo Radioterapista al centro del cambiamento

HIGHLIGHTS 2025

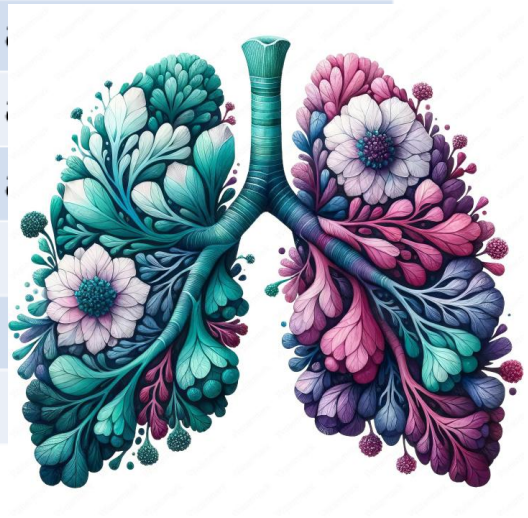
(ELCC, ESTRO, WCLC, ASTRO)

Sara Ramella
Università Campus Bio-Medico di Roma
Fondazione Policlinico Universitario Campus Bio-Medico

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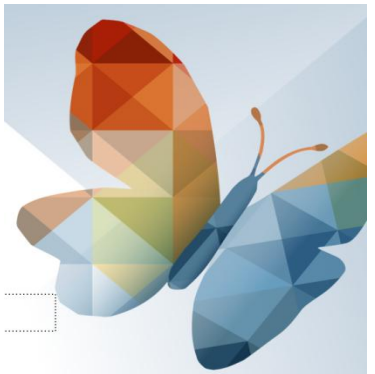
DECLARATION OF INTERESTS

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

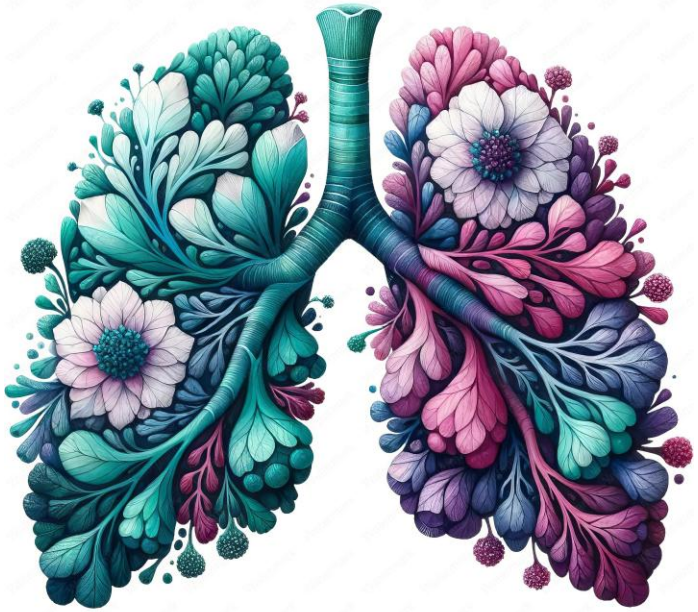
ASTRO'S 67TH ANNUAL MEETING

SEPTEMBER 27 – OCTOBER 1, 2025

MOSCONE CENTER | SAN FRANCISCO

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1. CHEMORADIATION IN EGFR (post-PD and PNEUMONITIS of LAURA TRIAL)
2. CHEMORADIATION and IO (EA5181-KN799)
3. MODALITY of RT (STANDARD RTCT vs SBRT+NFRT-PROTONS vs PHOTONS)
4. FRACTIONATION in LS-SCLC (CHINESE TRIAL and LU005 QoL)

LAURA PHASE III STUDY DESIGN[1]

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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

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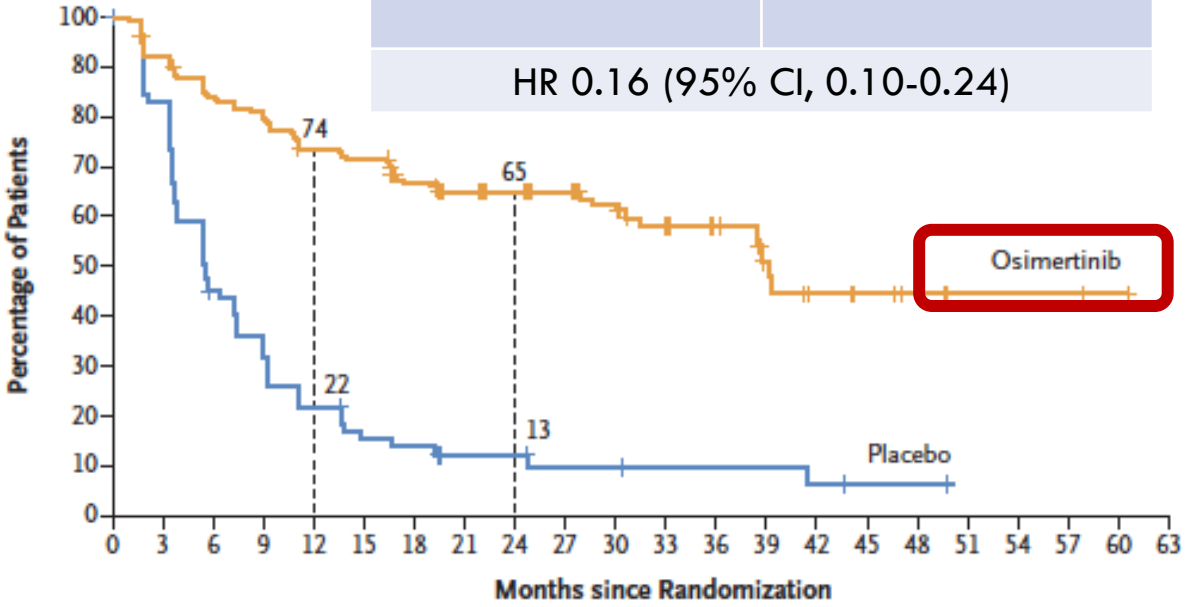
OSIMERTINIB AFTER CHEMORADIOTHERAPY IN STAGE III EGFR-MUTATED NSCLC

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)	



PATIENTS CHARACTERISTICS %

Characteristics, %	Osimertinib (n=143)	Placebo (n=73)
Sex: male / female	37 / 63	42 / 58
Age: median (range), years	62 (36–84)	64 (37–83)
AJCC / UICC staging (8th edition) at diagnosis:‡ IIIA / IIIB / IIIC	**36 / 47 / 17**	**33 / 52 / 15**
EGFR mutation at screening:‖ Ex19del / L858R	**52 / 48**†	**59 / 41**
Type of CRT: concurrent / sequential¶	**92 / 8**	**85 / 15**



Subgroup categories with fewer than 20 events across the two groups were excluded from the analysis, and hazard ratios were not calculable (NC).

Sara Ramella: discussant of abstract LBA4 and 1860

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LAURA - CUMULATIVE INCIDENCE OF DISTANT OR LOCAL PROGRESSION

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PLACEBO

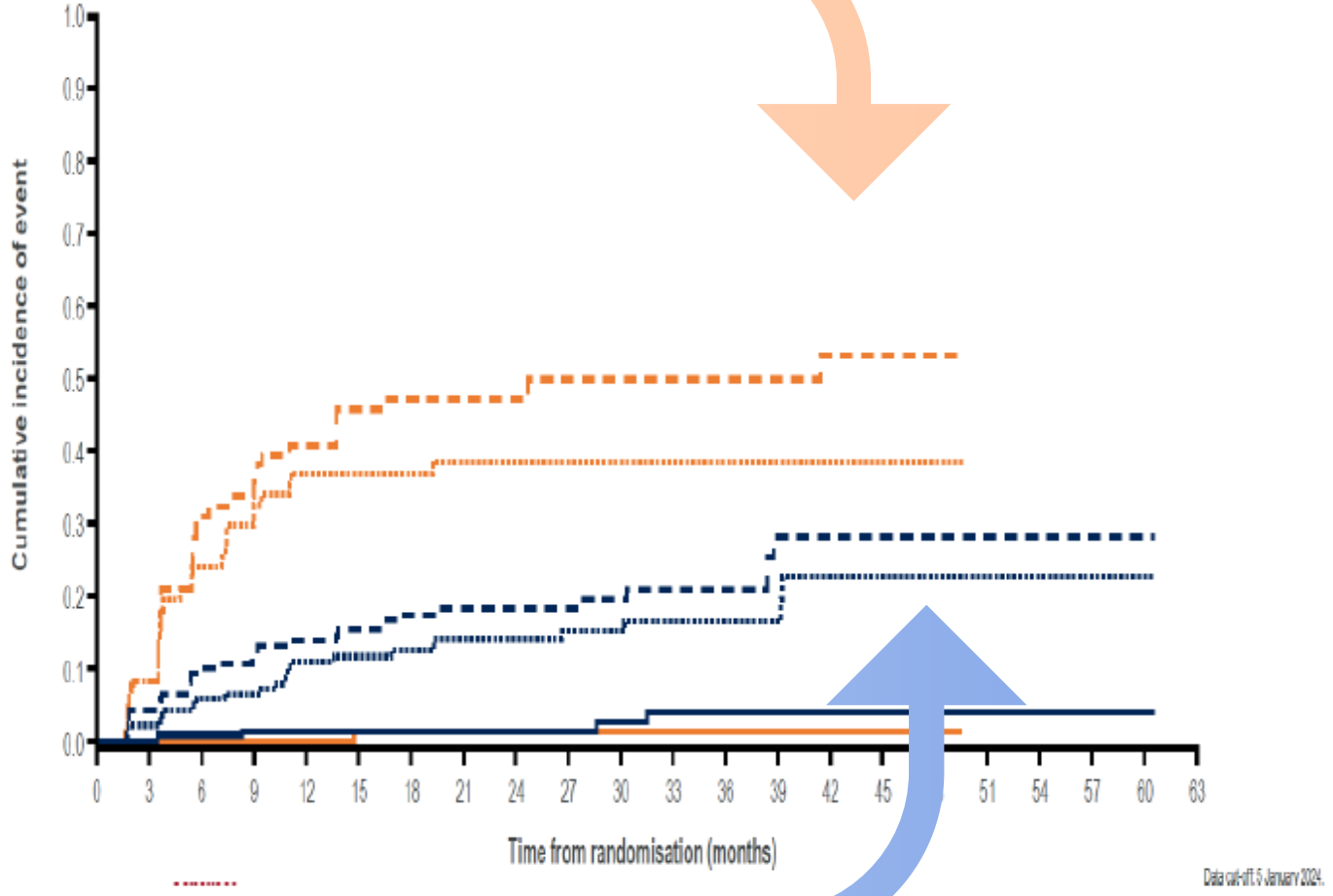
LOCAL PD: 48%

DISTANT M+ 37%

OSIMERTINIB

LOCAL PD: 21%

DISTANT M+ 16%

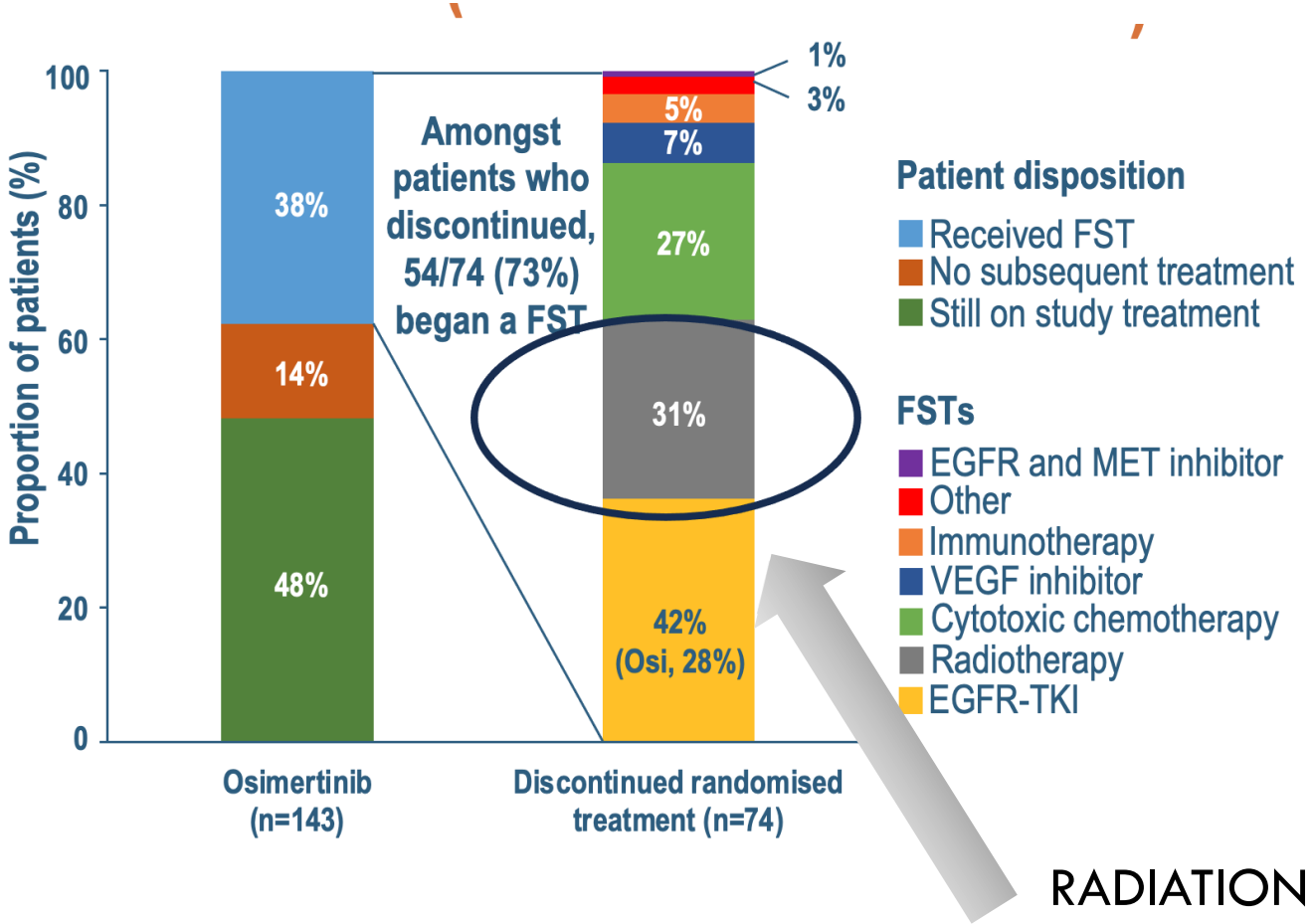


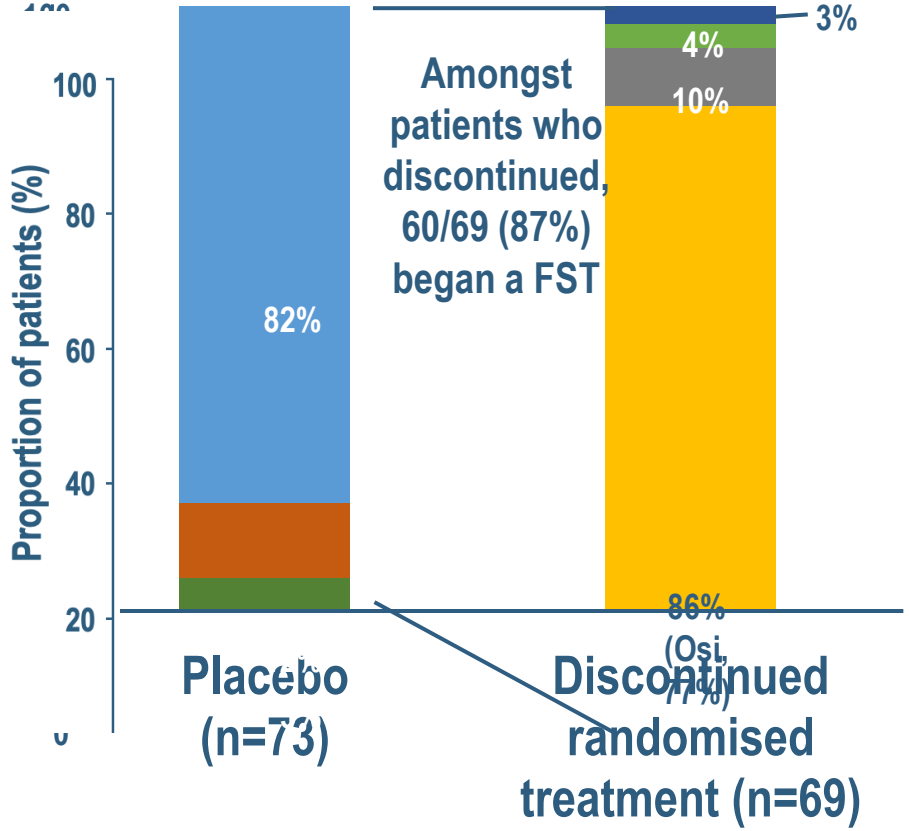
S Lu et al, ESMO 2024

POST-PROGRESSION OUTCOME

elcc European Lung Cancer Congress 2025





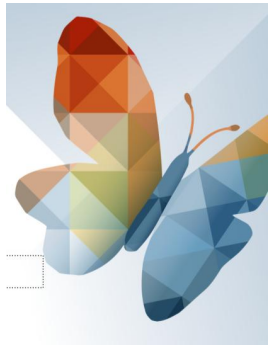


RADIATION THERAPY FOR OLIGOPROGRESSION?

Suresh S. Ramalingam

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Data cut-off: 29 November 2024
Subsequent anticancer treatments were given after discontinuation of study treatment.
A patient may be counted in multiple groups if they received more than one first subsequent anticancer treatment or a combination therapy
EGFR, epidermal growth factor receptor; FST first subsequent treatment; MET, mesenchymal epithelial transition; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor

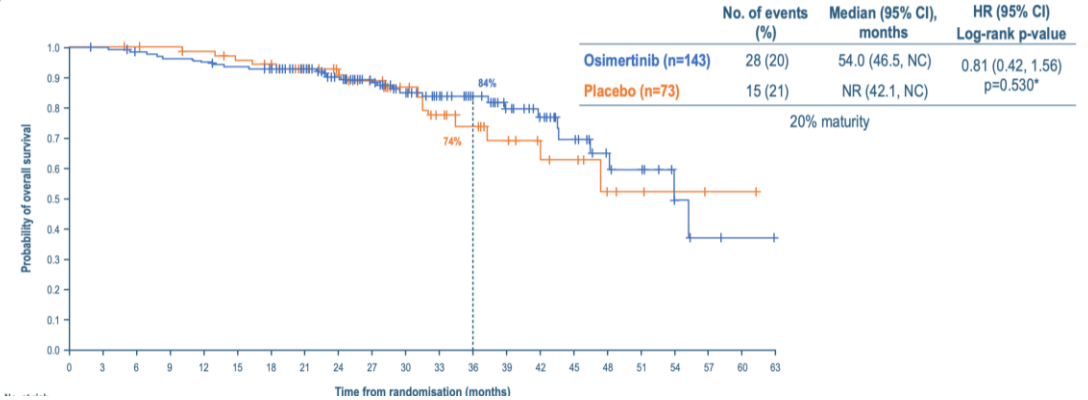


WHAT QUESTIONS DO OUR PATIENTS ASK?

✓ "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]

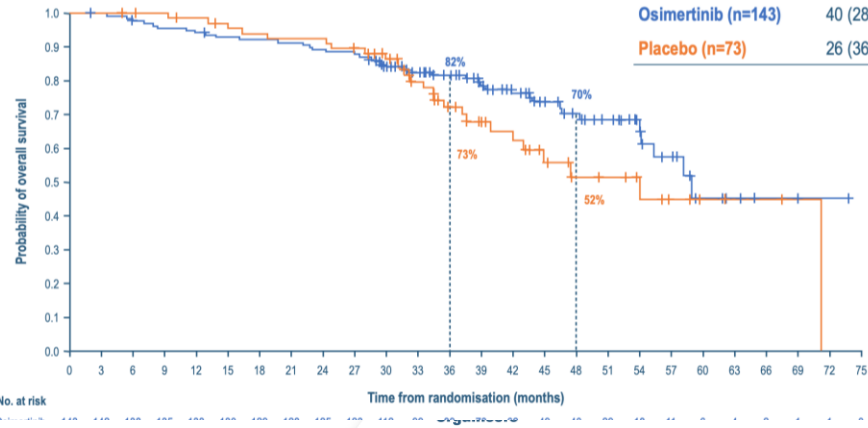


	No. of events (%)	Median (95% CI), months	HR (95% CI) Log-rank p-value
Osimertinib (n=143)	28 (20)	54.0 (46.5, NC)	0.81 (0.42, 1.56) p=0.530*
Placebo (n=73)	15 (21)	NR (42.1, NC)	

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

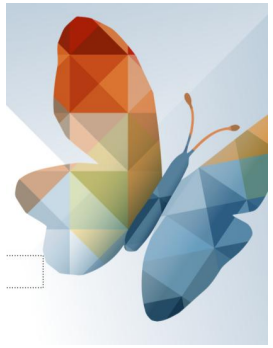


	No. of events (%)	Median (95% CI), months	HR (95% CI) Log-rank p-value
Osimertinib (n=143)	40 (28)	58.8 (54.1, NC)	0.67 (0.40, 1.14) p=0.140
Placebo (n=73)	26 (36)	54.0 (42.1, NC)	

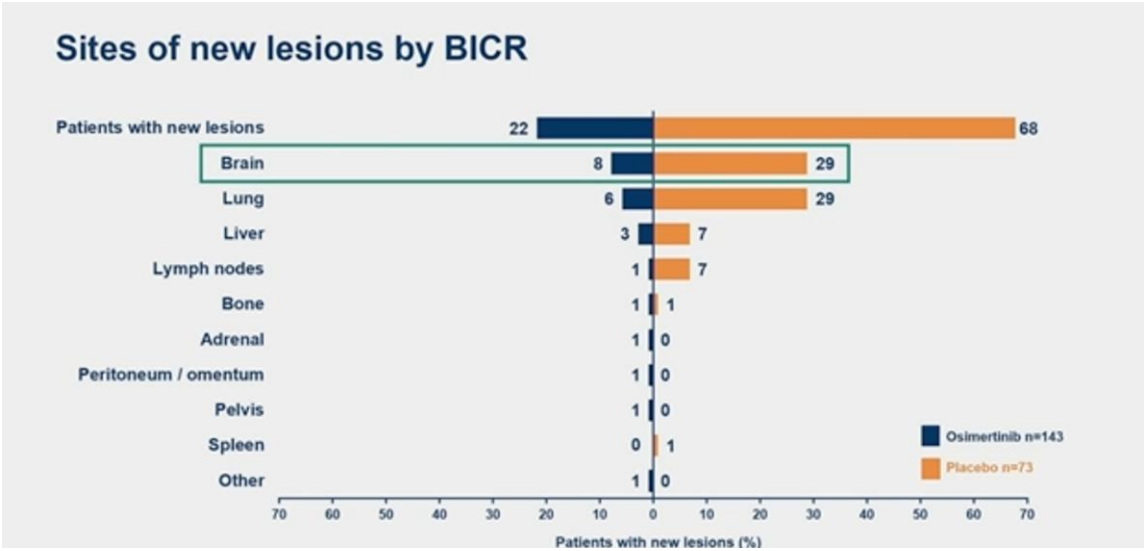
31% maturity

Sara Ramella: discussant of abstract LBA4 and 1860

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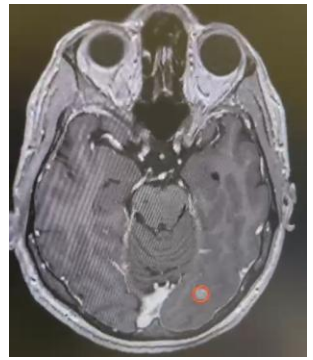


WHAT QUESTIONS DO OUR PATIENTS ASK?



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

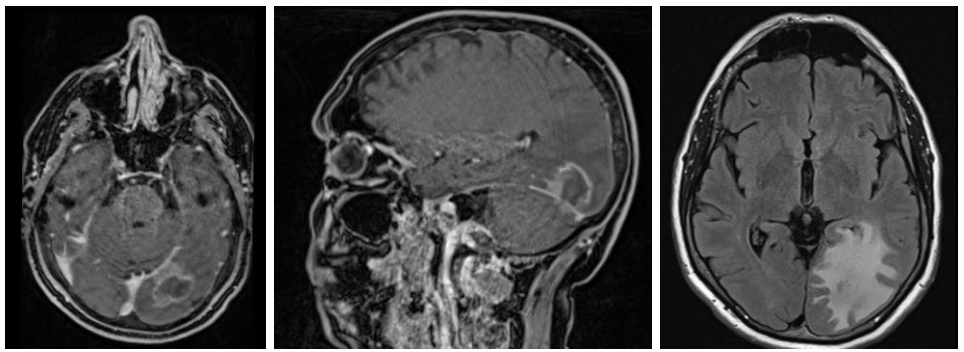
STEREOTACTIC RADIATION THERAPY





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)

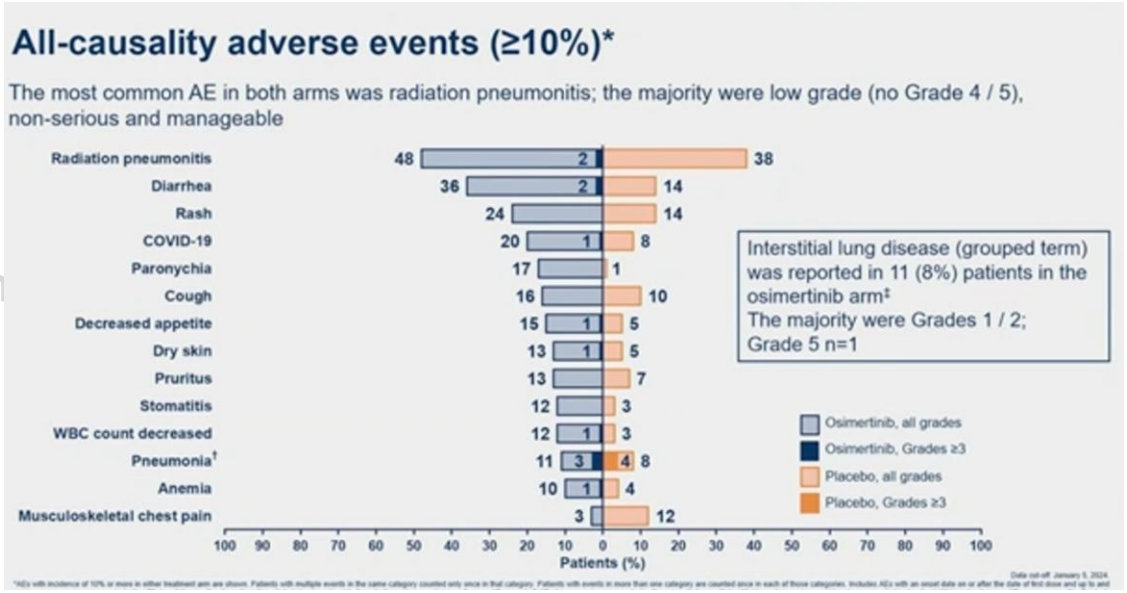


Sara Ramella: discussant of abstract LBA4 and 1860

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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

Sara Ramella: discussant of abstract LBA4 and 1860

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ESTRO 2025

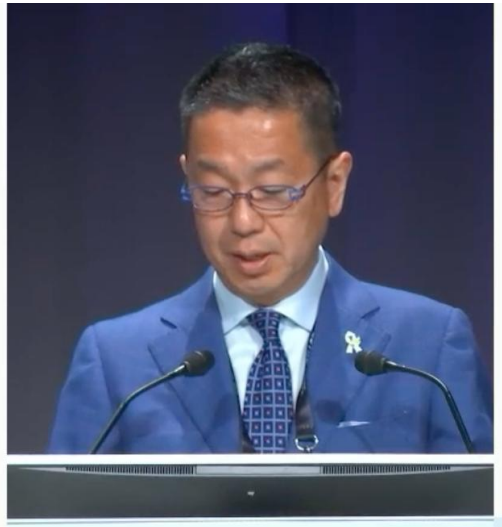
2-6 May 2025

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

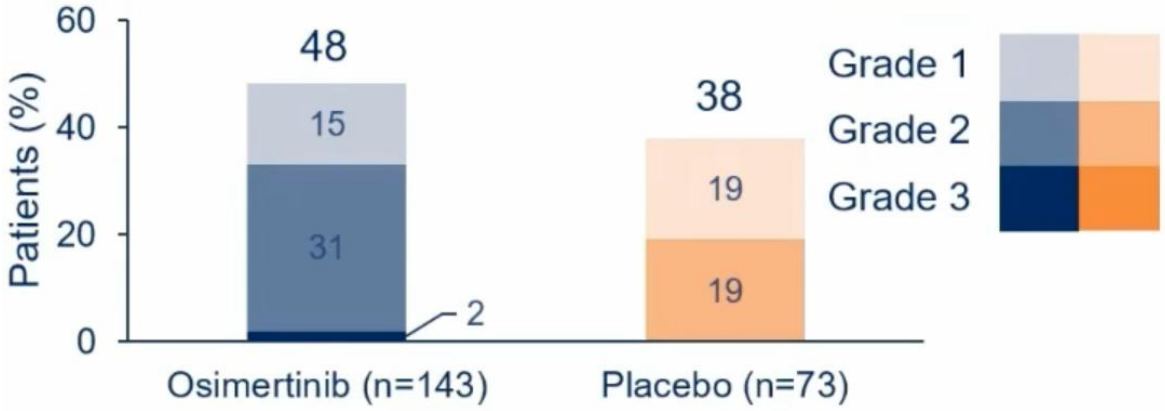


Terufumi Kato
Japan

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

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%



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



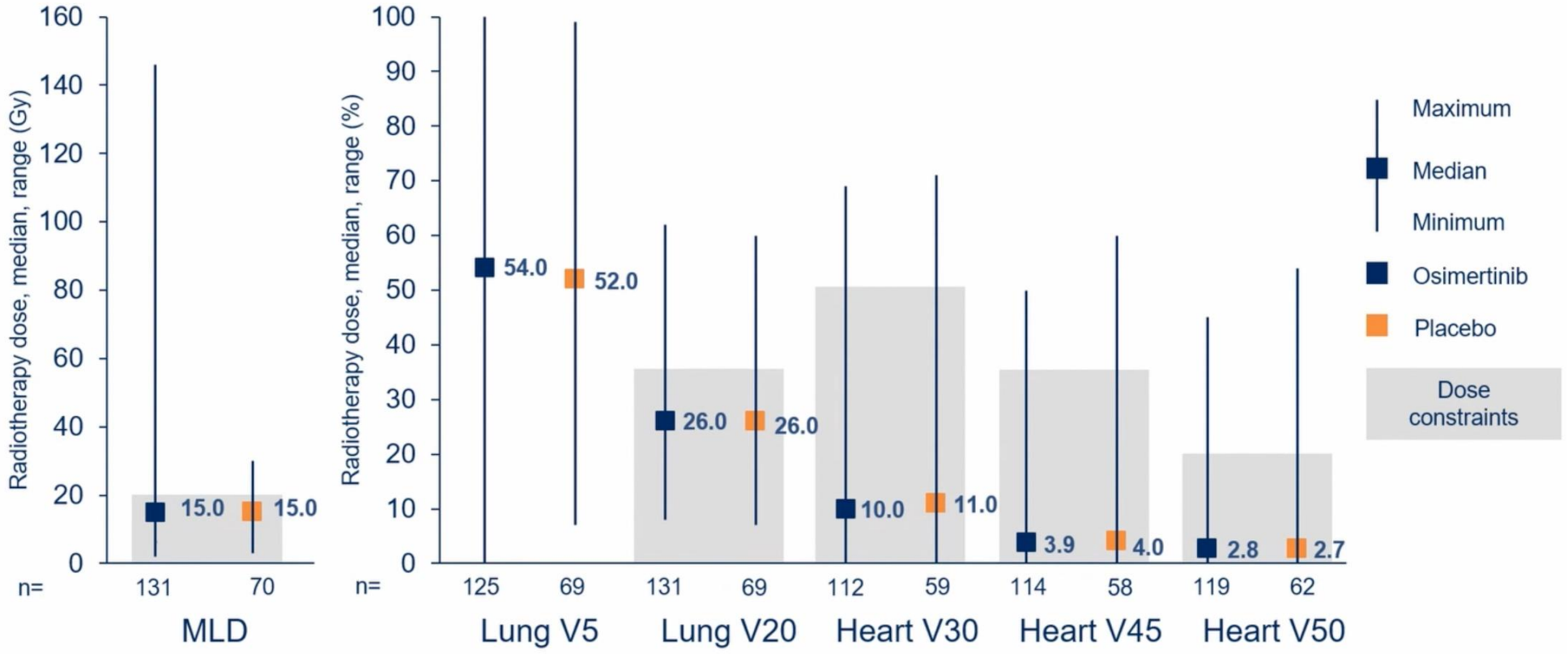


LAURA TRIAL: OSIMERTINIB AFTER CHEMORADIO IN STAGE III EGFR-MUTATED NSCLC

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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….

LAURA SAFETY OUTCOMES

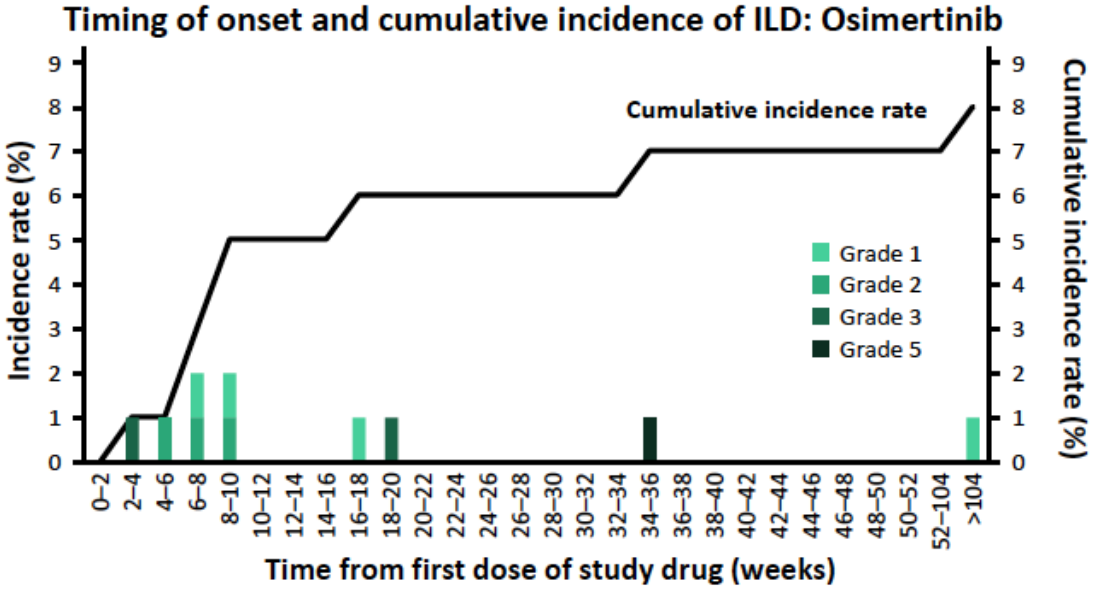
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Safety analysis: ILD

- 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

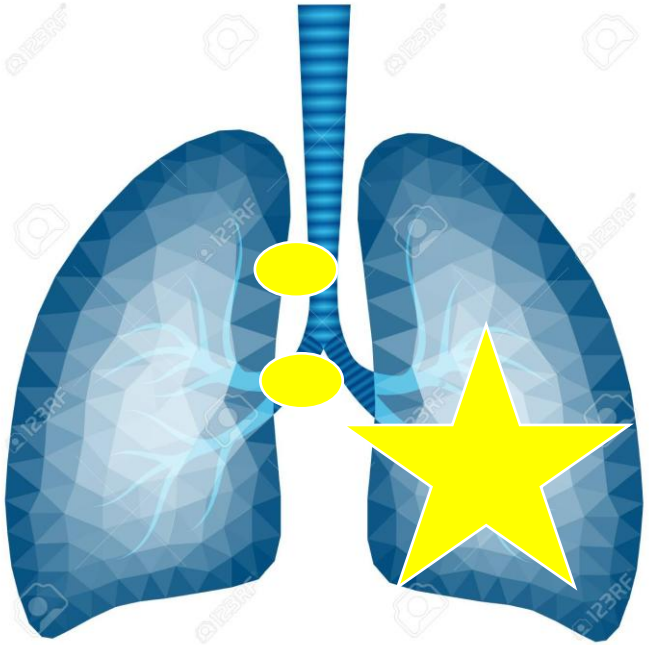


Time to onset of ILD, median (range), days	Osimertinib (n=11)
From first dose of osimertinib	57 (26–755)
From last dose of prior CRT	91 (38–793)

T Kato et al, WCLC 2024

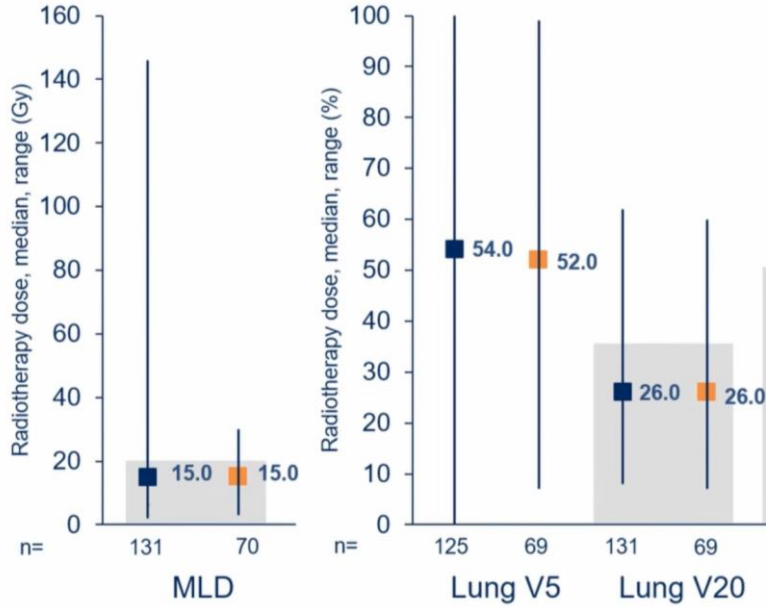
ILD-RT/DOSIMETRIC PARAMETERS:

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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?

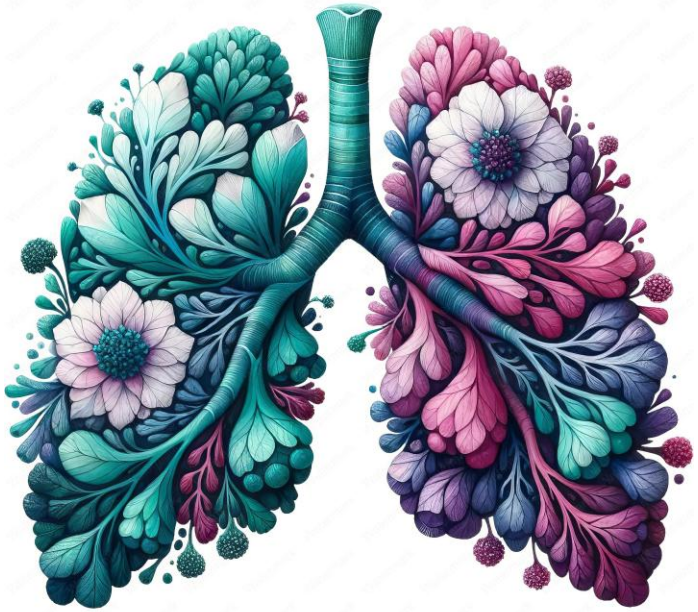
Radiotherapy for Lung Cancers in Patients with Interstitial Lung Disease: AIRO (Italian Association of Radiotherapy and Clinical Oncology) Delphi Consensus

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

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1. CHEMORADIATION IN EGFR (post-PD and PNEUMONITIS of LAURA TRIAL)
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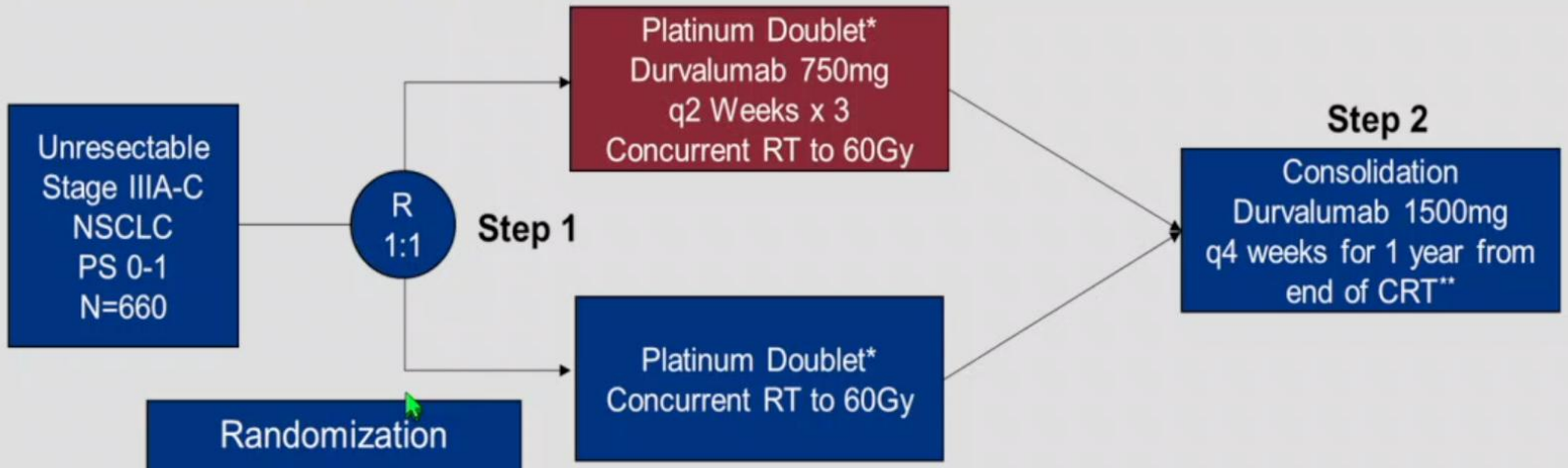


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EA5181 Schema



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

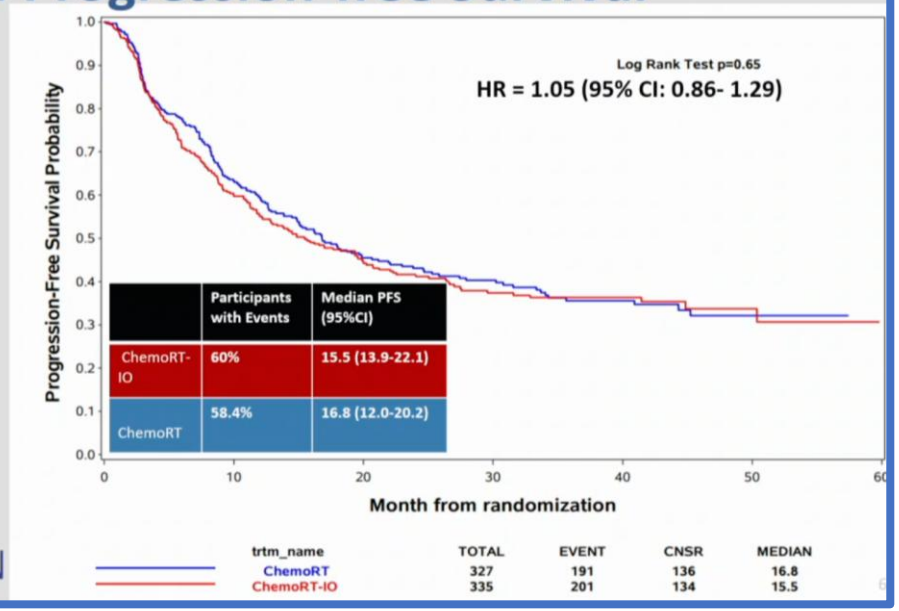
**Starting within 14 days of CRT unless toxicity has not resolved to ≤ grade 2, but not later than 45 days post-CRT

Primary endpoint – OS intention to treat population; 25% reduction in OS HR

Secondary endpoint –PFS, toxicity, ORRs, and Recurrence patterns

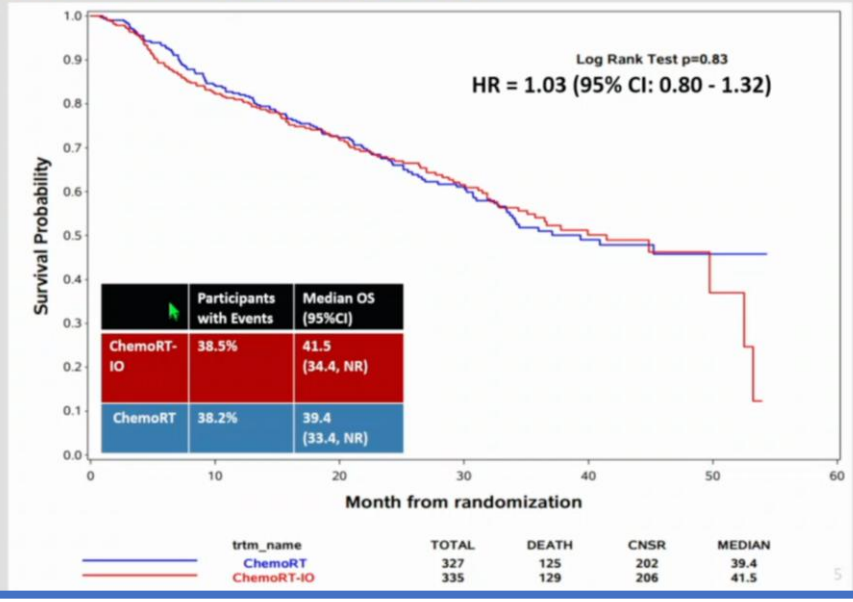
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EA5181: Progression-free Survival



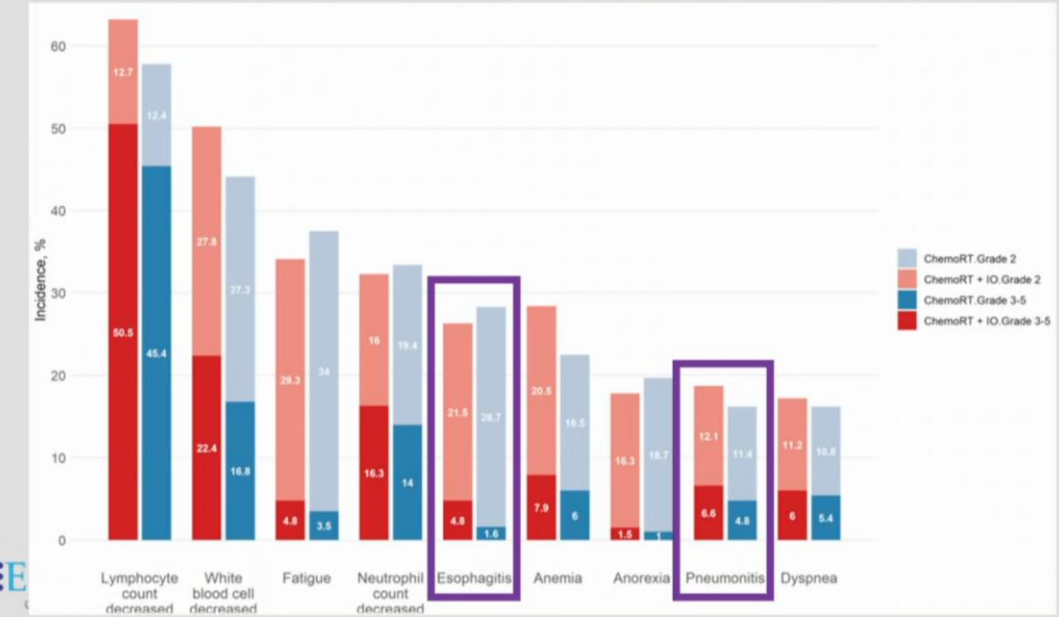
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EA5181: Overall Survival



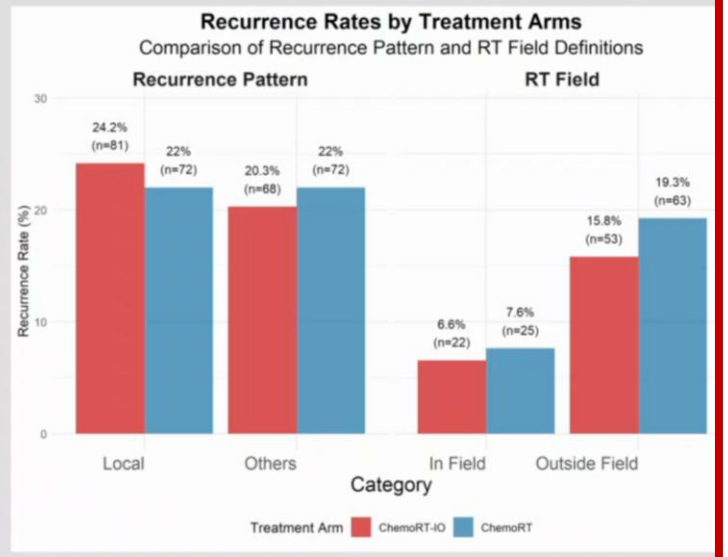
ECOG-ACRIN cancer research group

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

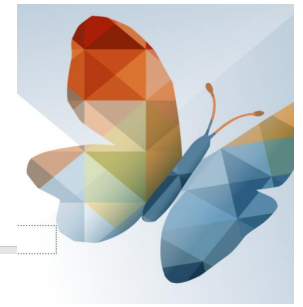
Recurrence Rates



ECOG-ACRIN cancer research group

KEYNOTE-799 Study Design

Nonrandomized, Open-Label, Phase 2 Study (NCT03631784)



Key Eligibility Criteria

- Age ≥18 y
- Previously untreated, unresectable stage IIIA–C NSCLC
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- Adequate pulmonary function test[a]
- No prior systemic immunosuppressive therapy ≤7 d
- Provided tumor sample for PD-L1 evaluation

N = 216

Cohort A (squamous or nonsquamous NSCLC)

Cycle 1	Cycles 2–3	Cycles 4–17
Pembrolizumab 200 mg Q3W + Paclitaxel 200 mg/m² Q3W / Carboplatin AUC 6 mg/mL/min Q3W	Pembrolizumab 200 mg Q3W + Paclitaxel 45 mg/m² QW / Carboplatin AUC 2 mg/mL/min QW / Standard thoracic radiotherapy[b]	Pembrolizumab 200 mg Q3W[c]

Cohort B (nonsquamous NSCLC)

Cycle 1	Cycles 2–3	Cycles 4–17
Pembrolizumab 200 mg Q3W + Pemetrexed 500 mg/m² Q3W / Cisplatin 75 mg/m² Q3W	Pembrolizumab 200 mg Q3W + Pemetrexed 500 mg/m² Q3W / Cisplatin 75 mg/m² Q3W / Standard thoracic radiotherapy[b]	Pembrolizumab 200 mg Q3W[c]

Primary endpoints: ORR per RECIST v1.1 by BICR and incidence of grade ≥3 pneumonitis

Secondary endpoints: PFS per RECIST v1.1 by BICR, OS, and safety

Median time to response (range):

2.1 (1.1–20.7) months

2.1 (0.5–10.5) months

At the END of CHEMORADIO

ORR is obteined at the end of CHEMORADIATION

KEYNOTE-799



PRIMARY ENDPOINTS	Cohort A (squamous and non-squamous)	Cohort B (nonsquamous)
ORR (95% CI), %	71.4 (62.1–79.6)	74.5 (64.9–82.6)
Grade ≥3 pneumonitis	8.0%	6.9%

WITHOUT IMMUNO	
RTOG 0617	7%
PROCLAIM Arm A	1.8%
PACIFIC Placebo arm	2.6% + 3.8% pneumonia
PACIFIC 2 Placebo arm	5.6%

WITH IMMUNO CONSOLIDATION	
PACIFIC Durva arm	3.4% +4.4% pneumonia
GEMSTONE 301 sugemalimab arm	3%
CM 73L Durva arm	1%

WITH CONCURRENT IMMUNO	
DETERRED Atezo-concurrent	3% + 17% lung infection
NICOLAS Nivo-concurrent	11.7%
PACIFIC 2 Durva concurrent	4.6%
CM 73L Nivo-concurrent	9%

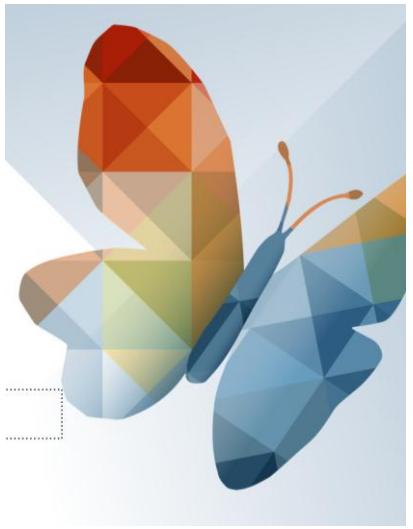
Sara Ramella: discussant of abstract LBA4 and 1860

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RADIATION TREATMENT





This study required a pretreatment **REVIEW OF THE TREATMENT PLAN** for each patient that was evaluated centrally

Technique: 3DCRT or IMRT **(NO INFORMATION)**

KN 799: PROTOCOL CONSTRAINTS

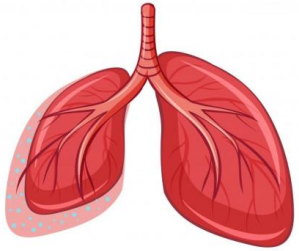
Table. Summary of protocol constraints and compliance criteria for thoracic radiotherapy

Structure	Metric	Per protocol	Variation acceptable	Deviation acceptable
Lungs (minus GTV)	V20Gy	≤31%	None	>31
	V5Gy	≤60%	≤65%	>65%
	Mean dose	≤20 Gy	≤22 Gy	>22 Gy

Chun, JCO 2017: a secondary analysis of RTOG 0617

Results – Severe Long-term Toxicity Profile

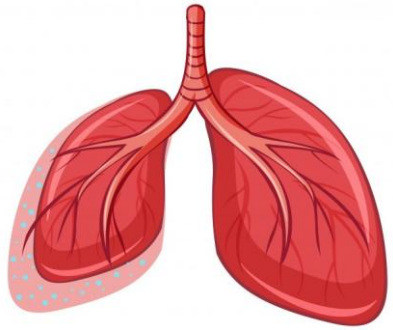
Grade ≥ 3 Adverse Event	Radiation Technique Comparison		Univariate logistic regression
	IMRT	3D-CRT	Lung V5Gy
Pneumonitis	3.5%	8.2%	OR = 1.02 (95% CI: 0.99-1.05) p = 0.13
	p = 0.03		
Esophagitis	13.2%	15.3%	OR = 1.01 (95% CI: 0.996-1.03) p = 0.15
	p = 0.50		
	3.9%	3.1%	OR = 1.01 (95% CI: 0.98-1.04) p = 0.52
	p = 0.63		
	5.3%	8.2%	OR = 1.00 (95% CI: 0.98-1.02) p = 0.99
	p = 0.20		
	5.7%	5.9%	OR = 1.00 (95% CI: 0.98-1.03) p = 1.00
	p = 0.93		
	58.8%	50.2%	OR = 1.00 (95% CI: 0.99-1.01) p = 0.66
	p = 0.06		



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RADIATION TREATMENT LUNG CONSTRAINTS



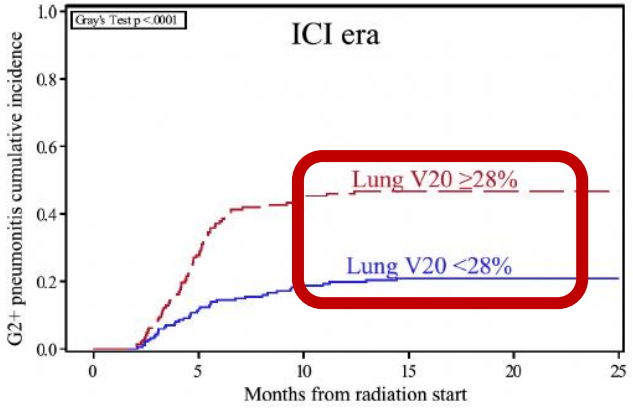
eTable 2. Summary of radiotherapy dose specification in patients who experienced grade 3–5 pneumonitis (all of whom received radiotherapy).

V20	Cohort A (n=9)	Cohort B (n=7)
Actual total lung V20 (%)	n=8	n=6
Mean (SD)	27.3 (4.13)	24.8 (5.74)
Median (range)	27.0 (22.0–34.0)	25.0 (17.0–32.0)
≤31%, n (%)	6 (75.0)	5 (83.3)
>31%, n (%)	2 (25.0)	1 (16.7)
Actual Total Lung V5 (%)	n=8	n=6
Mean (SD)	57.8 (4.40)	5[illegible]
Median (range)	59.0 (51.0–63.0)	
≤60%, n (%)	6 (75.0)	
>60%, n (%)	2 (25.0)	
Mean Lung Dose (cGy)	n=8	[illegible]=6
Mean (SD)	1525.[illegible]	[illegible]455.0 (276.21)
Median (range)	1573.0 (1288.0–	1466.5 (1076.0–1814.0)

REDUCED LUNG CONSTRAINTS FOR RT-CT-IO TREATMENTS

Pne[illegible]ore and After Adoption [illegible]Consolidation in Patients [illegible]vanced Non-Small Cell Lung [illegible]ed With Concurrent RTCT

[illegible]aman IJROBP, Volume 118 • Number 5 • 2024



Evaluation of Radiation Pneumonitis in a Phase 2 Study of Consolidation Immunotherapy With Nivolumab and Ipilimumab or Nivolumab Alone Following Concurrent Chemoradiation Therapy for Unresectable Stage IIIA/IIIB Non-Small Cell Lung Cancer

Int J Radiation Oncol Biol Phys, Vol. 121, No. 3, pp. 720–727, 2025

Table 4 Grade 2 and 3 pneumonitis rates by V20 of 23%

Pneumonitis grade	Total	V20 group ≤23% N = 37	V20 group >23% N = 62
At least grade 2 pneumonitis			
No	70 (70.7)	31 (83.8)	39 (62.9)
Yes	29 (29.3)	6 (16.2)	23 (37.1)
Grade 3 pneumonitis			
No	85 (85.9)	34 (91.9)	51 (82.3)
Yes	14 (14.1)	3 (8.1)	11 (17.7)

Values are expressed as n (%).
Abbreviation: V20 = percentage of normal lung tissue receiving 20 gy or more.

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RT-CT

RT-CT followed by IO

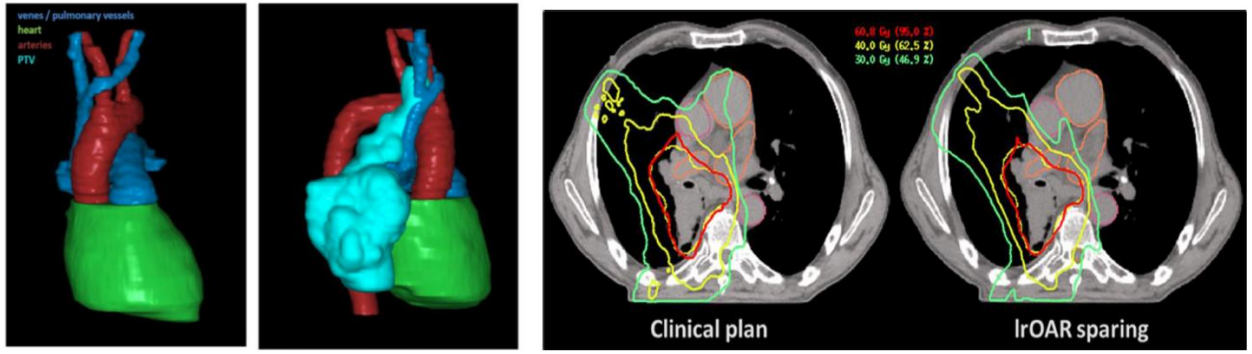
RT-CT concomitant and followed by IO

	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

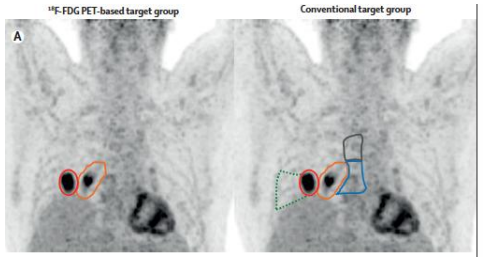


132 pts RT+IO; Grade 3+ Hemathological Tox: Dmean EQD2 ≧ 30.2 Gy,V5 EQD2 ≧ 69.1%, V10 EQD2 ≧ 64.6%, and V20 EQD2 ≧ 53.5%.).

- 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; $p = 0.01$).

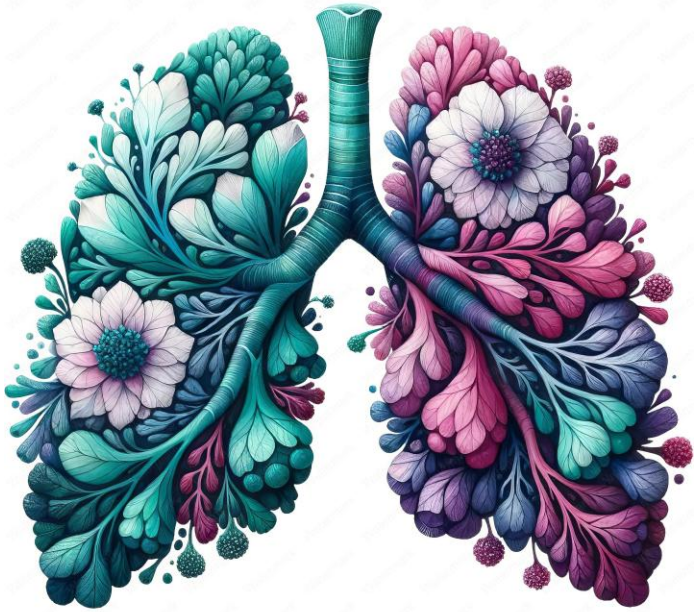


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Locally Advanced LUNG CANCER

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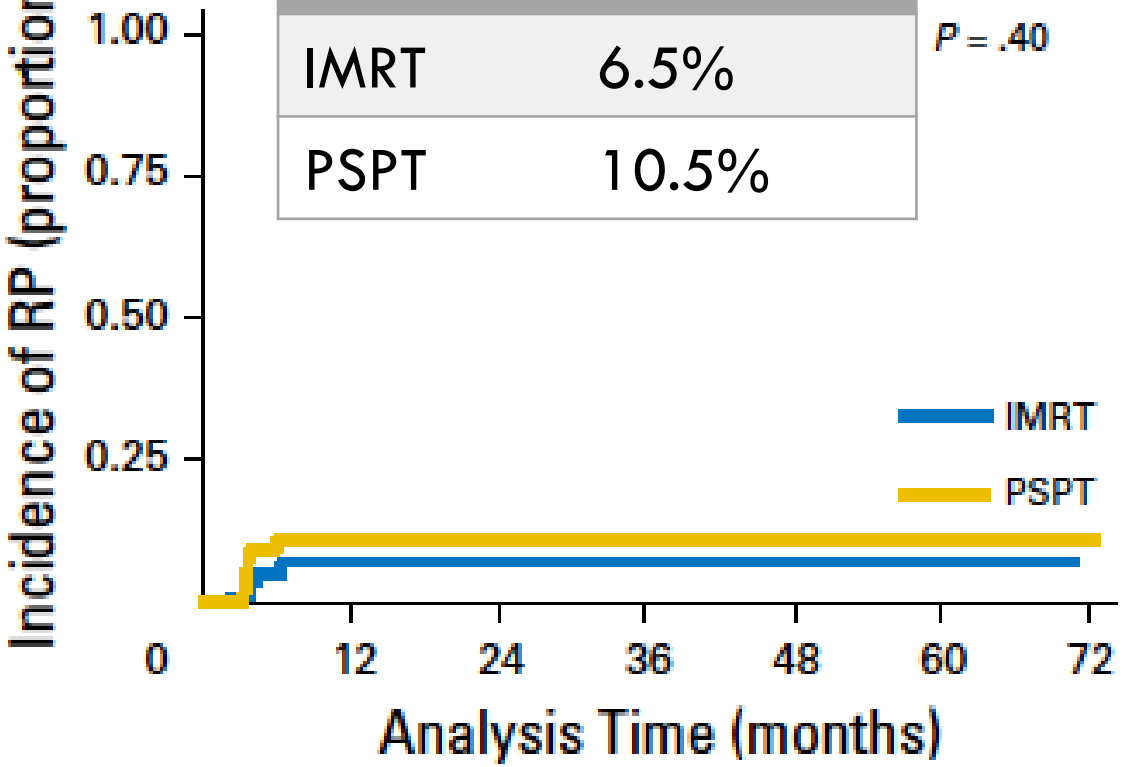
1. CHEMORADIATION IN EGFR (post-PD and PNEUMONITIS of LAURA TRIAL)
2. CHEMORADIATION and IO (EA5181-KN799)
3. MODALITY of RT (STANDARD RTCT vs SBRT+NFRT-PROTONS vs PHOTONS)
4. FRACTIONATION in LS-SCLC (CHINESE TRIAL and LU005 QoL)

Bayesian Adaptive Randomization Trial of Passive Scattering Proton Therapy and Intensity-Modulated Photon Radiotherapy for Locally Advanced Non–Small-Cell Lung Cancer

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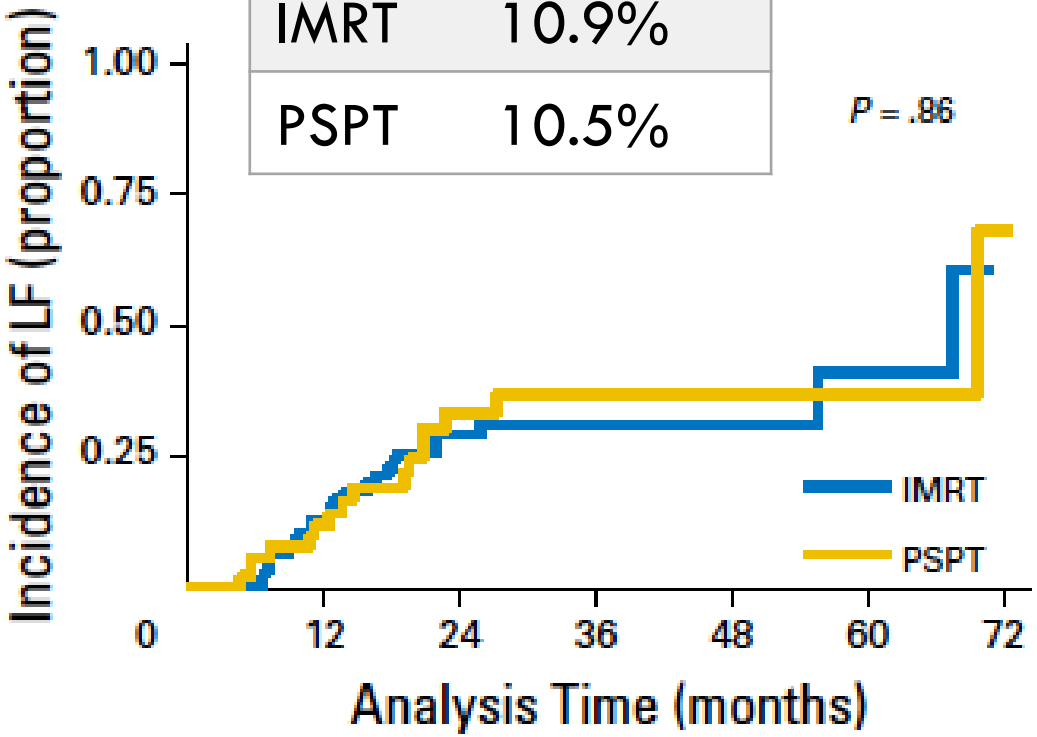
Rad Pneumo ≥G3	
IMRT	6.5%
PSPT	10.5%

$P = .40$



Local Failure	
IMRT	10.9%
PSPT	10.5%

$P = .86$



Liao Z et al, J Clin Oncol 2018 36:1813-1822.

SS 25 - Lung 1: Randomized Trials for Lung Cancer

243 - Long-Term Outcomes of a Prospective Randomized Trial of Passive Scattering Proton Therapy vs. Intensity-Modulated Photon Radiotherapy for Locally Advanced Non-Small-Cell Lung Cancer

Presenter(s)



Tingshi Su, MD, PhD

MD Anderson Cancer Center
Houston, TX

ASTRO 2024
Targeting Provider Wellness
FOR EXCEPTIONAL PATIENT CARE

	IMRT	PSPT	P-value
RP >=G3	9.8%	22.8%	0.052
Esophagitis >=G2	47.8%	64.9%	0.062
Cardiac events	30.4%	31.6%	0.99
Local failure	22.8%	24.6%	0.965
5yOS	33%	22.7%	>0.05
mOS	29.5m	24.5m	0.074
mPFS	9.85m	9.43m	0.35
LRFS	21.7m	17.2	0.12
DMFS	16.8m	10.4	0.23



ESTRO 2025 2-6 May 2025 Vienna, Austria

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Bradley M. Sugden
Maastro Clinic / Maastricht University Medical Centre

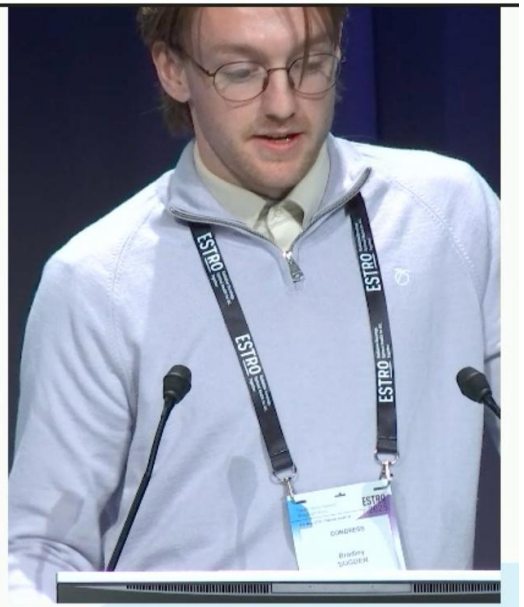
The impact of proton versus photon therapy on health-related quality of life for patients with lung cancer

Sugden BM[1 2], Witlox WJA[1], Cortiula F[2], Hattu D[2], Joore M[1], Ramaekers B[1], De Ruysscher, DKM[2].

1. Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre (MUMC+), The Netherlands.

2. Department of Radiation Oncology (Maastro Clinic), Maastricht University Medical Centre (MUMC+), GROW School on Oncology and Developmental Biology, Maastricht, The Netherlands.

Maastro



Bradley Sugden
Netherlands

THE IMPACT OF PROTONS VERSUS PHOTONS

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Background

- External Beam Radiotherapy (EBRT) important treatment modality for lung cancer
  - → Potential treatment-induced toxicity impacting Health-Related Quality of Life (HRQoL)
- Intensity-Modulated Proton Therapy (IMPT) for reducing normal tissue exposure vs Intensity-Modulated Radiotherapy (IMRT)
- Eligibility (NL) determined through *model-based approach*
  - Current NTCP models: Mortality, oesophagitis, pneumonitis
- Impact of IMPT vs IMRT on HRQoL not studied in lung cancer
- Research aim:
  - **To assess the impact of protons versus photons on HRQoL for patients with lung cancer in The Netherlands**

Methods (2)

- Many indicated for IMPT received proton/photon combination
  - n=137 (57%)
  - In-line with previously reported implementation challenges*

=> Need to define treatment group

- Base-case analyses:
  - IMPT = patients that received ≥ 30% of total fractions as protons**
- Scenario analyses:

Proton fractions cut-off (%)	IMPT group	IMRT group
30%	171 (71%)	71 (29%)
50%	164 (68%)	78 (32%)
80%	123 (51%)	119 (49%)
100%	41 (17%)	201 (83%)

Jacobs et al. (2022); ** Cortiula et al. (2024)

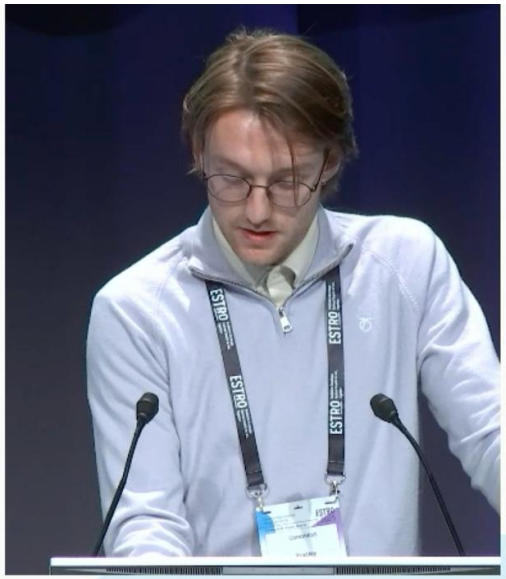
THE IMPACT OF PROTONS VERSUS PHOTONS

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Results: Impact of protons on HRQoL *(base-case)*

HRQoL	Proton coefficient (*vs photons*)	95% CI	Minimal Important Difference
EQ-5D-5L	-0.026	-0.058, 0.007	0.03
EQ-VAS	-0.015	-0.043, 0.014	0.03
Global Health Status	-0.017	-0.047, 0.013	0.05

Coefficient interpretation:
0: no difference in HRQoL; **Positive**: Protons favoured; **Negative**: Photons favoured



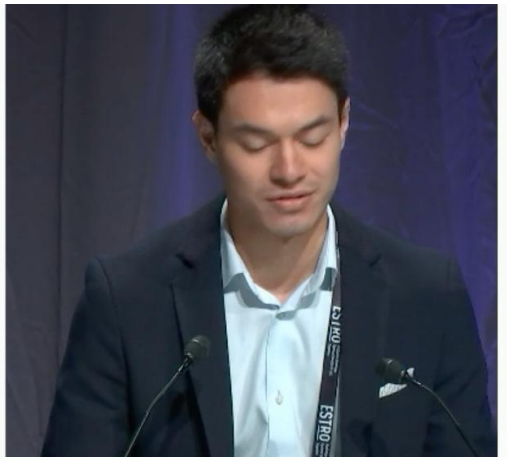
Bradley Sugden
Netherlands

Conclusion: NO SIGNIFICANT IMPACT OF PROTONS ON HRQoL (vs photons)

Applicability of results: INFORM UTILITY PARAMETERS IN A FUTURE COST_EFFECTIVENESS ANALYSES

STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

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Highly Hypofractionated versus Standard Tumor Irradiation in Locally Advanced NSCLC with Durvalumab Maintenance: A Multicenter Retrospective Study

Etienne CEDOZ[1], Antonin LEVY[2], Isabelle MARTEL-LAFAY[1], Pierre-Yves BONDIAU[3], Cécile LE PECHOUX[2], Christos CHOUAID[4], Myriam AYADI-ZAHRA[1], Jérôme DOYEN[3], Benoit ALLIGNET[1]

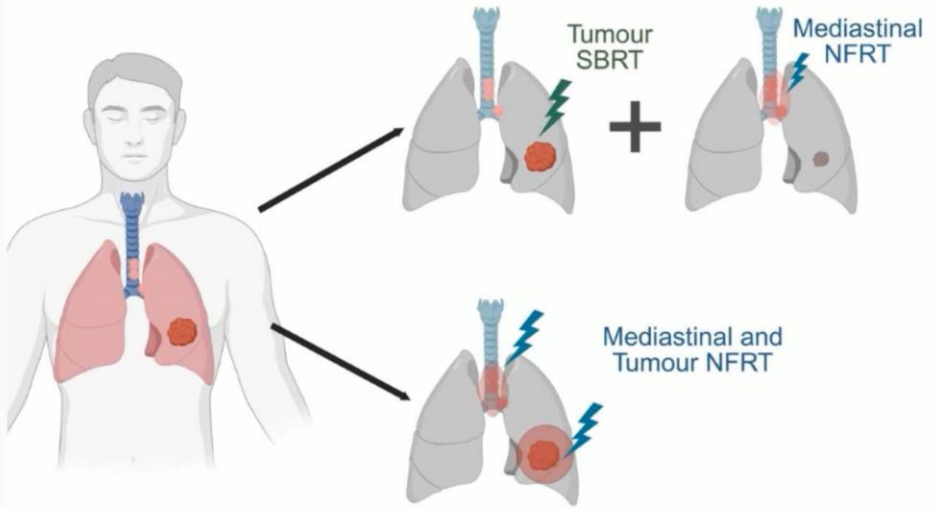
1 - Department of Radiation Oncology, Centre Léon Bérard, Lyon, France.
2 - Department of Radiation Oncology, Gustave Roussy, Villejuif, France
3 - Department of Radiation Oncology, Centre Antoine Lacassagne, Nice, France
4 - Department of Pneumology, Centre Hospitalier Intercommunal de Créteil, Créteil, France

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

GUSTAVE ROUSSY CANCER CAMPUS RAND PARIS



MATERIAL AND METHODS - RADIOTHERAPY TREATMENT



TUMOUR-SBRT GROUP

- *Primary tumour*: **SBRT**
  - in 3 to 8 fractions
- *Mediastinum*: **NFRT**
  - 60-66 Gy

STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

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MATERIAL AND METHOD - STUDY DESIGN and PATIENTS SELECTION



- **Retrospective multicentric cohort**
- 3 French Cancer centers performing SBRT to primary tumours
- Included patients treated from **July 2017** to **January 2023**
- *Inclusion criteria:*
  - Age ≥ 18 years
  - **Stage II–III NSCLC** deemed **unresectable** or **unfit** for surgery
  - ≥ 1 cycle of **platinum-based chemotherapy**
  - ≥ 1 cycle of **durvalumab**

PROPENSITY SCORE MATCHING (PSM)

Overall cohort

PSM cohort

	NRFT only (N=188)	NFRT and SBRT (N=21)	NRFT only (N=63)	NFRT and SBRT (N=21)
Sex				
Woman	**58 (30.9%)**	8 (38.1%)	**26 (41.3%)**	8 (38.1%)
Men	**130 (69.1%)**	13 (61.9%)	**37 (58.7%)**	13 (61.9%)
Age				
Median (Q1-Q3)	**63.6 (58.1-69.0)**	65.0 (62.0-72.0)	**64.6 (59.0-70.6)**	65.0 (62.0-72.0)
Performance status				
0	**91 (48.4%)**	13 (61.9%)	**37 (58.7%)**	13 (61.9%)
1	**87 (46.3%)**	8 (38.1%)	**23 (36.5%)**	8 (38.1%)
2	**10 (5.3%)**	0 (0%)	**3 (4.8%)**	0 (0%)

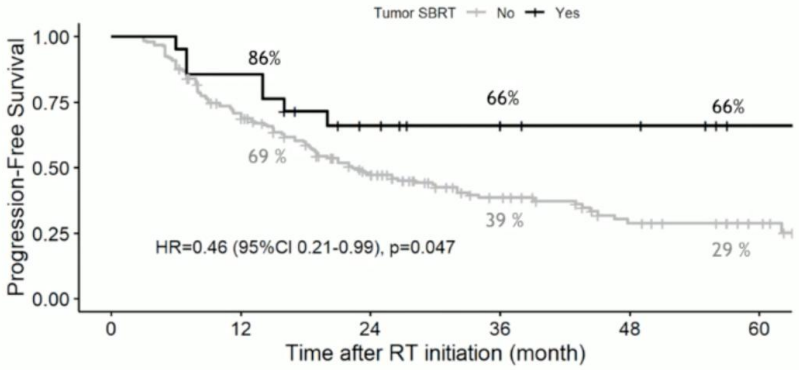
STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

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RESULTS- PFS

Overall cohort

Tumor SBRT	Events (n ; %)	Median (%95 CI)	HR (95% CI)	P-Value
Yes	7/21 (33%)	NA (20- NA)	0.46 (0.21-0.99)	0.047
No	111/188 (59%)	22.3 (18.6-32)	--	--

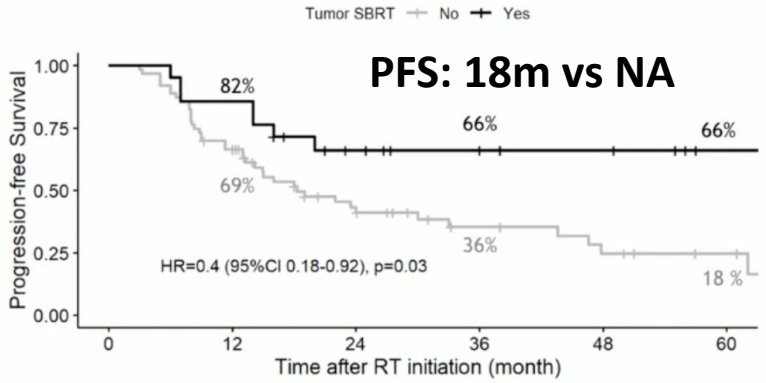


Number at risk

Yes	21	18	10	7	5	1
No	188	128	72	36	19	10

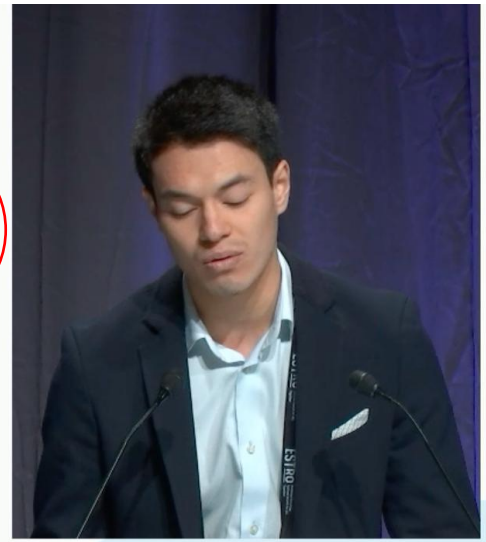
PSM cohort

Tumor-SBRT	Events (n ; %)	Median (95% CI)	HR (95% CI)	P-Value
Yes	7/21 (33)	NA (20.0-NA)	0.40 (0.18-0.92)	0.03
No	40/63 (63)	18.3 (14.2-43.6)	--	--



Number at risk

Yes	21	18	10	7	5	1
No	63	41	20	11	7	4



Etienne Cedoz
France

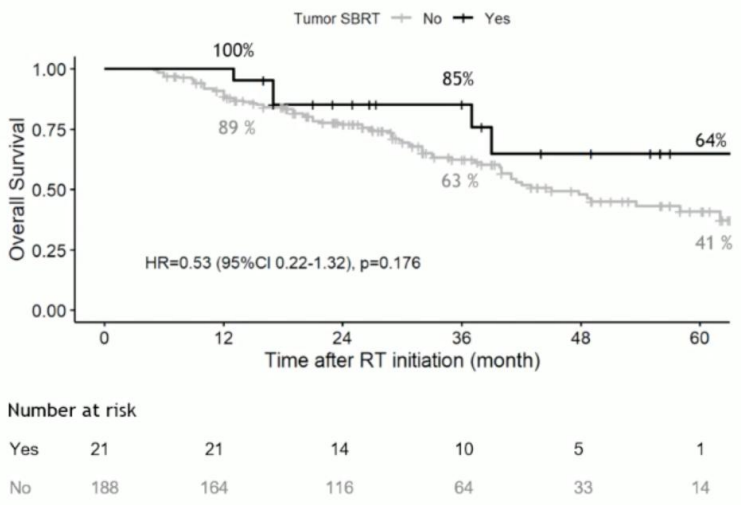
STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

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RESULTS- OS

Overall cohort

Tumor SBRT	Events (n ; %)	Median(%95 IC)	HR (95% CI)	P-Value
Yes	5/21 (24)	NA (39-NA)	0.53 (0.22-1.32)	0.2
No	75/188 (39)	45 (40-NA)	--	--

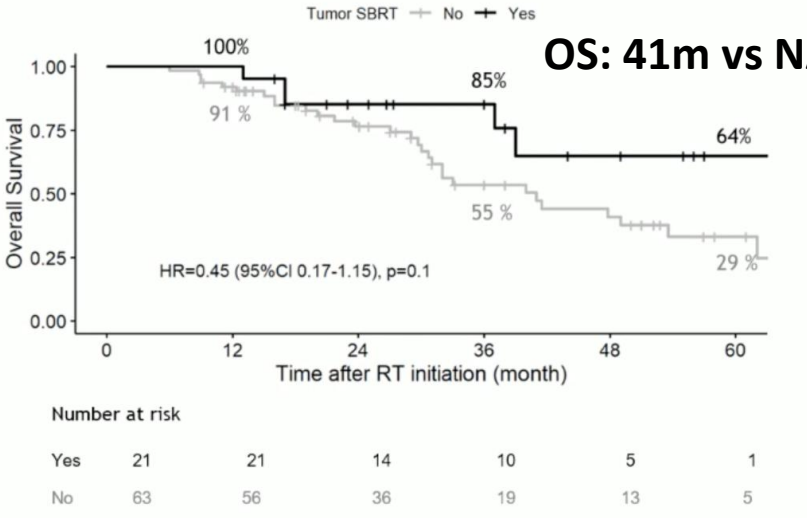


Number at risk

Yes	21	21	14	10	5	1
No	188	164	116	64	33	14

PSM cohort

Tumor SBRT	Events (n ; %)	Median (95% CI)	HR (95% CI)	P-Value
Yes	5/21 (24)	NA (39-NA)	0.45 (0.17-1.15)	0.1
No	29/63 (46)	41 (31-NA)	--	--



Number at risk

Yes	21	21	14	10	5	1
No	63	56	36	19	13	5

OS: 41m vs NA

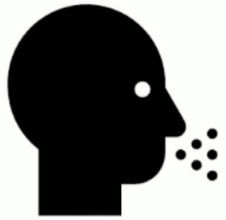


Etienne Cedoz
France

STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

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RESULTS- SAFETY OVERVIEW - GRADE 3 EVENTS



Mainly Esophagitis and Pneumonitis

No grade 4 or 5 events

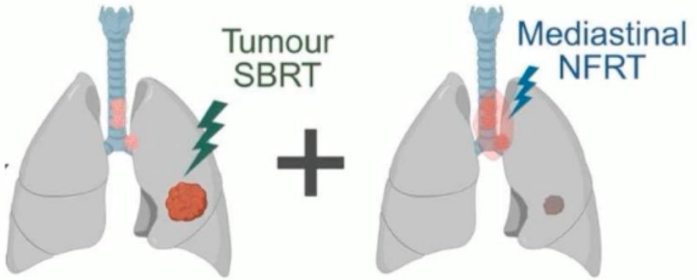
	Overall cohort		PSM cohort	
	NRFT only (N=188)	NFRT and SBRT (N=21)	NRFT only (N=63)	NFRT and SBRT (N=21)
Grade 3 toxicity related to RT				
No	166 (88.3%)	19 (91.5%)	57 (90.5%)	19 (91.5%)
Yes	22 (11.7%)	2 (9.5%)	6 (9.5%)	2 (9.5%)
Grade 3 RT related - details				
None	166 (88.2%)	19 (91.5%)	55 (90.5%)	19 (91.5%)
Esophagitis	10 (5.3%)	2 (9.5%)	3 (4.8%)	2 (9.5%)
Pneumonitis	8 (4.2%)	0 (0%)	2 (3.2%)	0 (0%)
				0 (0%)



Etienne Cedoz
France

CONCLUSION - PERSPECTIVE

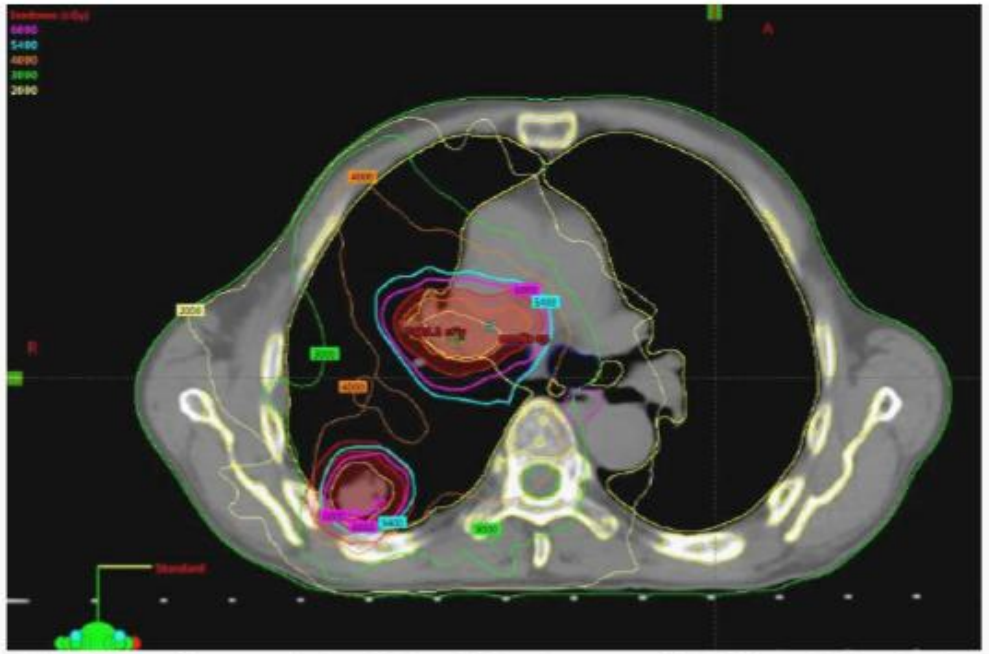
- In this cohort, Tumor-SBRT was associated with **an improvement in PFS,** and a **trend toward better OS**
- However, **small sample size** may explain the **lack of statistical significance** of some results



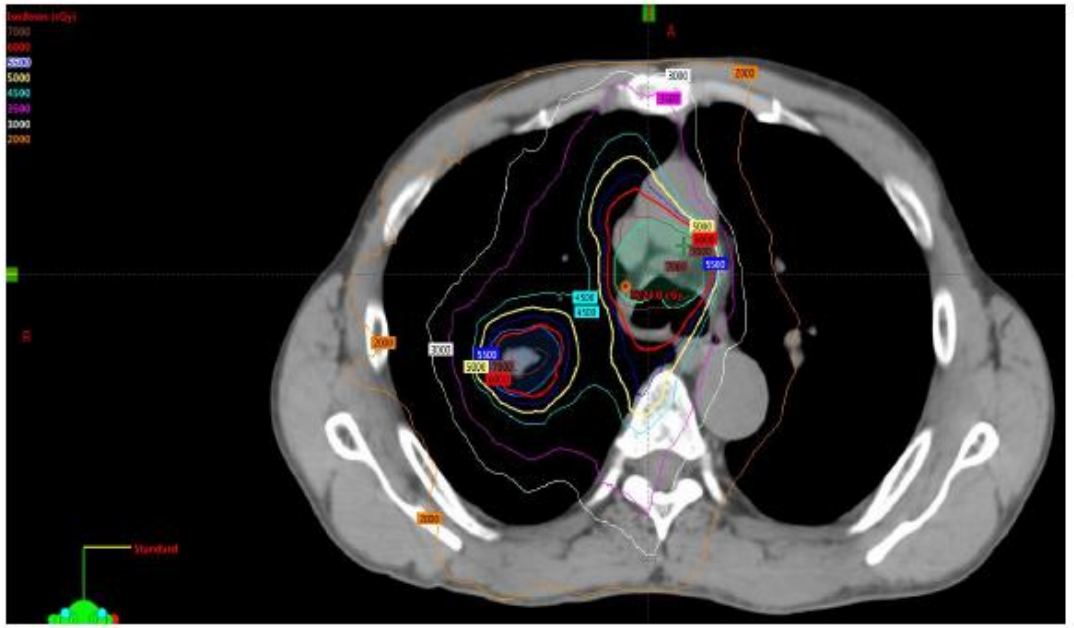
STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB



Representative Cases



Total volume of lung receiving 40 Gy= 332 cc (compared to 590 cc, 44% reduction)
Total volume of lung receiving 20 Gy=922 cc (compared to1300 cc, 29% reduction)
Total volume of lung receiving 10 Gy=2168 cc (compared to 2360, 8% reduction)



STANDARD RT-CT versus SBRT PRIMARY + MEDIASTINAL NFRT ->> DURVALUMAB

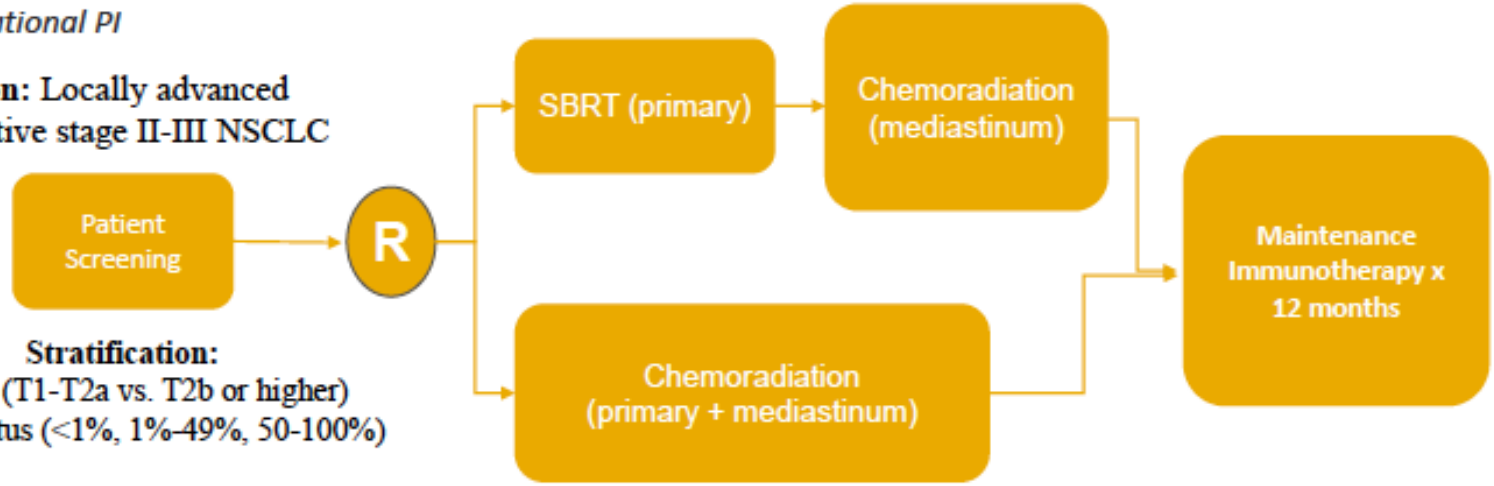
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LU008: Phase IIIR Trial of Primary Lung Tumor SBRT Followed by Concurrent Mediastinal Chemoradiation for LA-NSCLC

Charles Simone - National PI

Population: Locally advanced node-positive stage II-III NSCLC

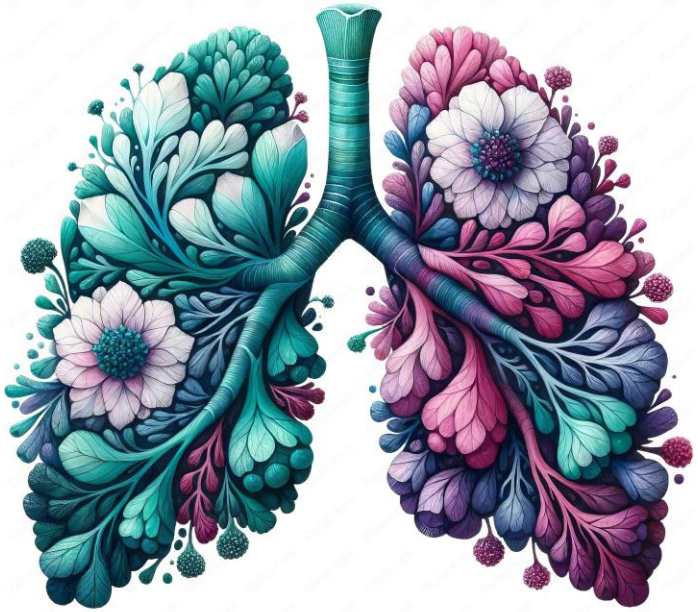
Stratification:
T Stage (T1-T2a vs. T2b or higher)
PD-L1 Status (<1%, 1%-49%, 50-100%)



- Control arm: chemoradiation to the primary and mediastinal disease (60 Gy/2 Gy) → immunotherapy maintenance x 12 months
- Experimental arm: SBRT to the primary (standard BED ≥100 Gy dose regimen) → chemoradiation to mediastinal disease (60 Gy/2 Gy) → immunotherapy maintenance x 12 months
  - SBRT to primary tumor:
    - 3 fractions to 54 Gy (BED10 of 151.2 Gy) [peripheral]
    - 4 fractions to 50 Gy (BED10 of 112.5 Gy) [peripheral or central]
    - 5 fractions to 50 Gy (BED10 of 100 Gy) [peripheral or central]
  - Radiation to involved hilar/mediastinal lymph nodes: 2 Gy x 30 fx to 60 Gy, IMRT or proton therapy
  - Concurrent chemotherapy: carboplatin + paclitaxel or cisplatin + etoposide or cisplatin + pemetrexed or carboplatin + pemetrexed
  - Maintenance immunotherapy: durvalumab x 12 months [if durvalumab is NOT given, carbo/paclitaxel pts receive 2 cycles of consolidation]

Locally Advanced LUNG CANCER

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1. CHEMORADIATION IN EGFR (post-PD and PNEUMONITIS of LAURA TRIAL)
2. CHEMORADIATION and IO (EA5181-KN799)
3. MODALITY of RT (STANDARD RTCT vs SBRT+NFRT-PROTONS vs PHOTONS)
4. FRACTIONATION in LS-SCLC (CHINESE TRIAL and LU005 QoL)

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DI ROMA



IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

wclc.iaslc.org #WCLC25

Hypofractionated vs Conventional Fractionated Radiotherapy With Concurrent Chemotherapy for LS-SCLC: A Multi-Center Phase III Trial

Presenter: Nan Bi[1], MD, PhD

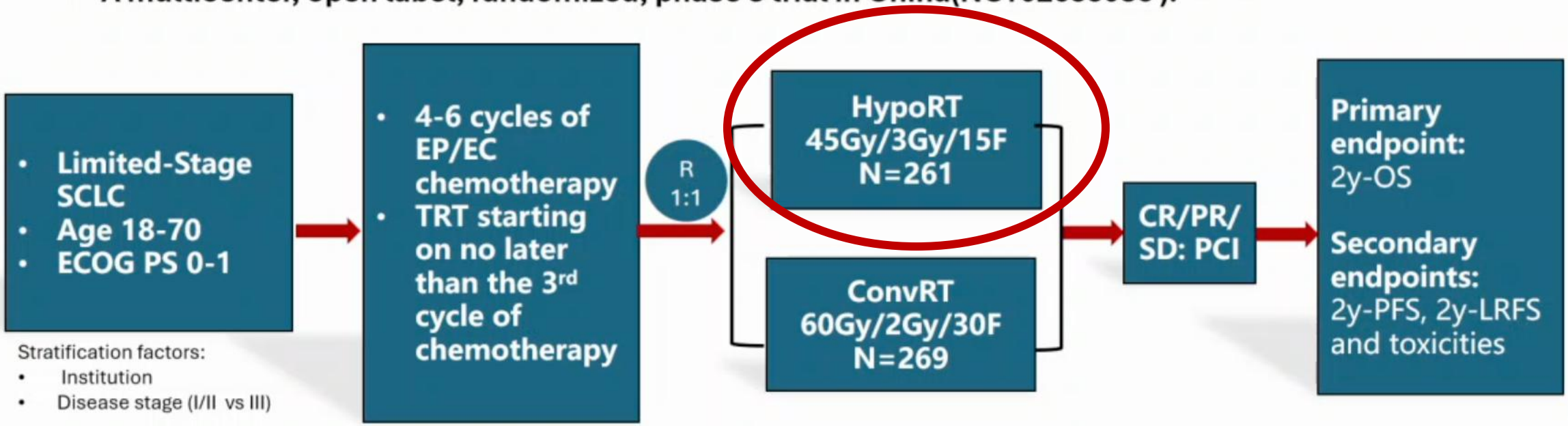
Principal Investigator: Luhua Wang[2]

National Cancer Center/National Clinical Research Center for Cancer/[1]Cancer Hospital and [2]Shenzhen Cancer Hospital , Chinese Academy of Medical Science and Peking Union Medical College

CONQUERING LUNG AND OTHER THORACIC CANCERS WORLDWIDE IN THE 21ST CENTURY

Methods

- A multicenter, open label, randomized, phase 3 trial in China(NCT02688036).

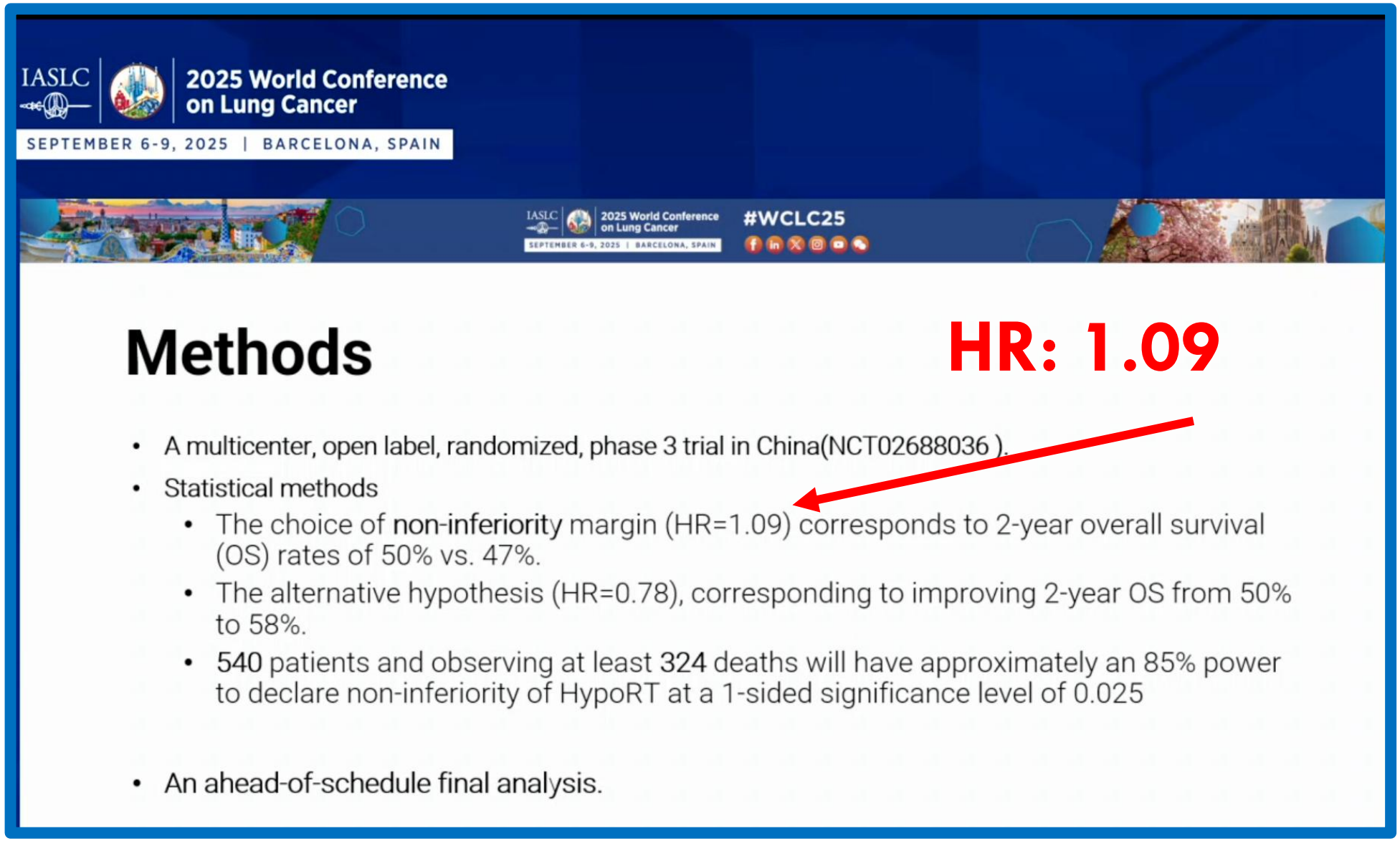


- EP/EC: Etoposide 100mg/m2 IV d1-3, Cisplatin 75mg/m2 IV d1 or Carboplatin AUC 5 IV d1; every 3 weeks

T: thoracic radiation therapy; CR: complete response; PR: partial response; SD: stable disease; PCI: prophylactic cranial irradiation;
: overall survival; PFS: progression-free survival; LRFS: local regional recurrence-free survival.

HYPO vs STANDARD FX in LS-SCLC

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HYPO vs STANDARD FX in LS-SCLC

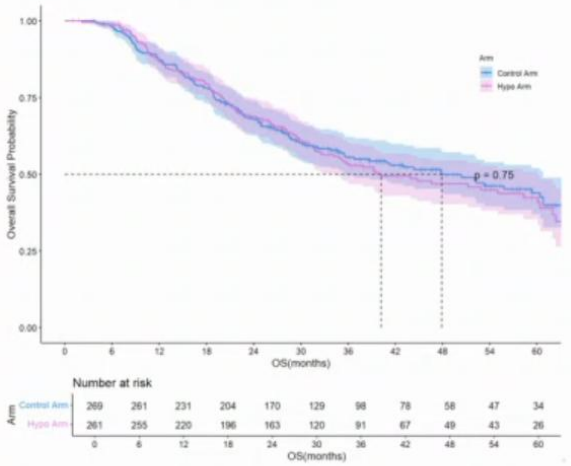
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IASLC 2025 World Conference on Lung Cancer #WCLC25
SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

Primary Endpoint

- A median follow-up of 43.4 months
- HypoRT did not meet the non-iferiority threshold compared to ConvRT in OS.
- Numerically similarity between ConvRT and HypoRT.

	ConvRT	HypoRT	
Number	269	261	
OS events	129	127	
Median OS	47.9 months	40.2 months	P=0.752 HR=1.04 (0.81-1.33)
1y-OS	87.2%	86.6%	
2y-OS	68.0%	68.9%	
3y-OS	55.5%	53.5%	
5y-OS	43.9%	42.4%	



wclc.iaslc.org



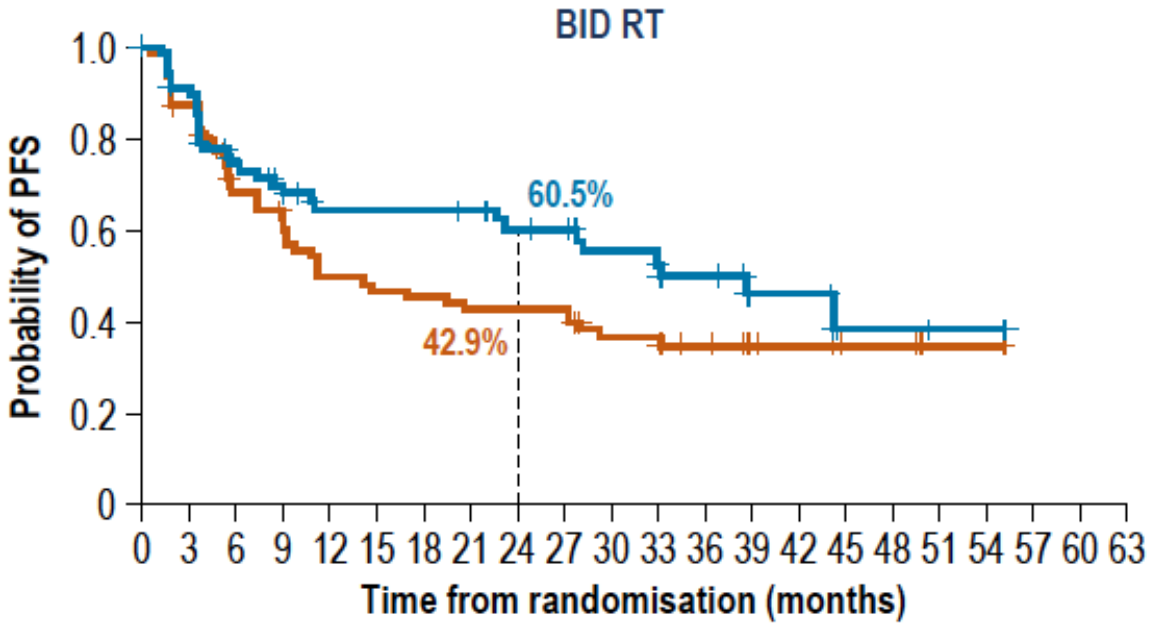
LO STUDIO E' INCONCLUSIVO PERCHE' IL RISULTATO PUO' PORTARE A CONCLUSIONI OPPOSTE (beneficio 20%-aumento dei morti del 33%)

REPORTING BIAS

FRACTIONATION is an HOT TOPIC….

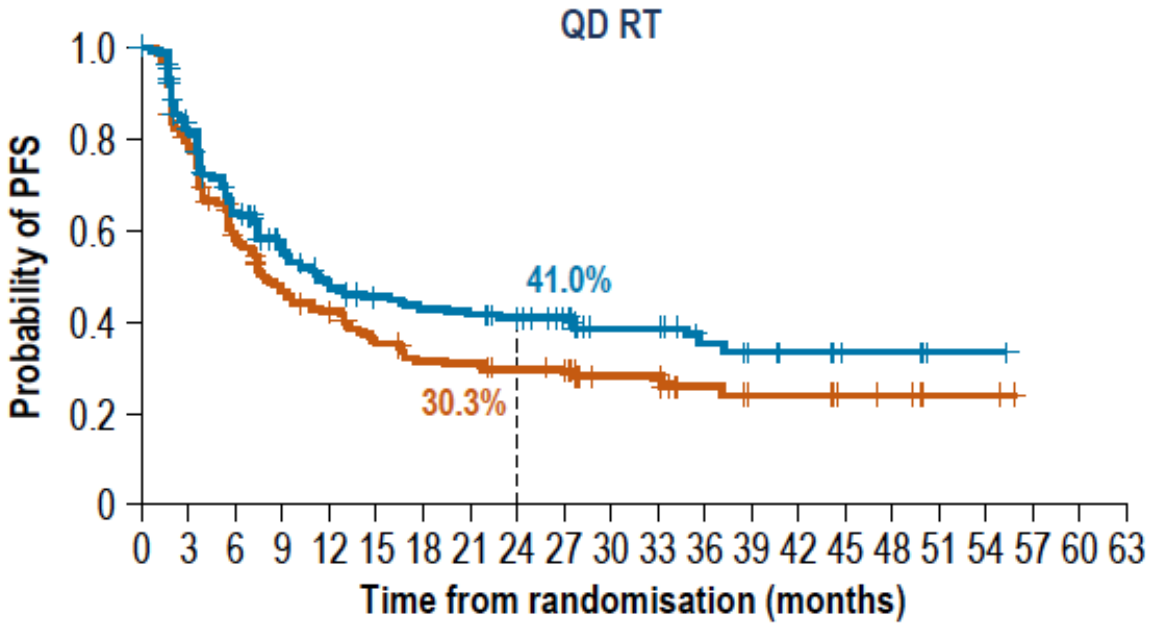
ADRIATIC: BID and QD subgroup - PFS

	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



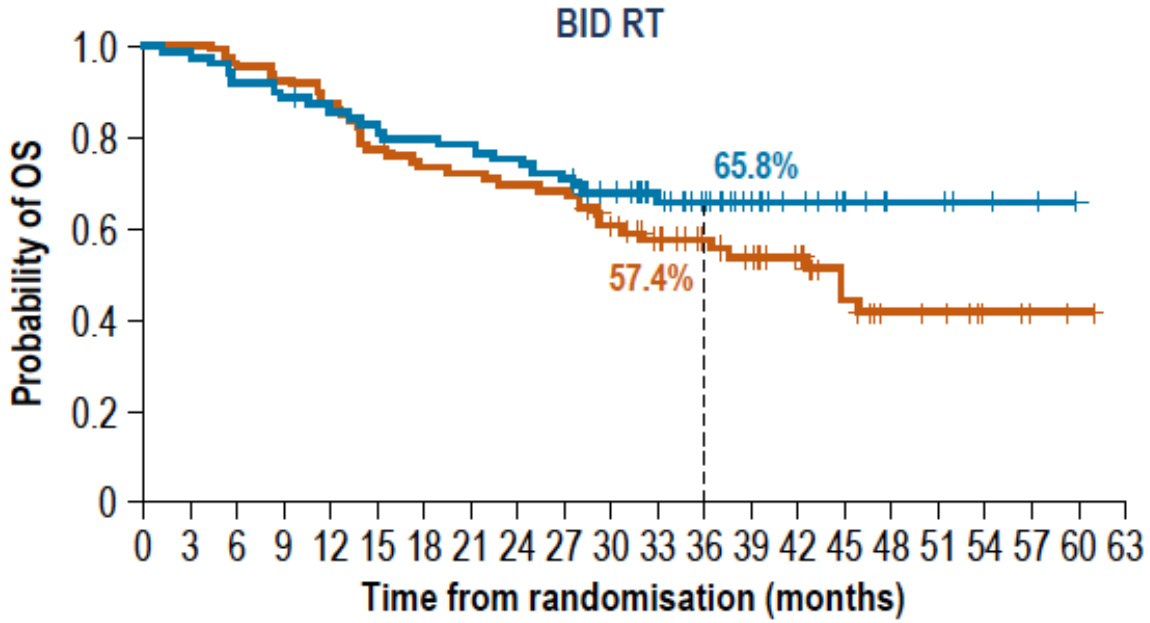
No. at risk:

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.

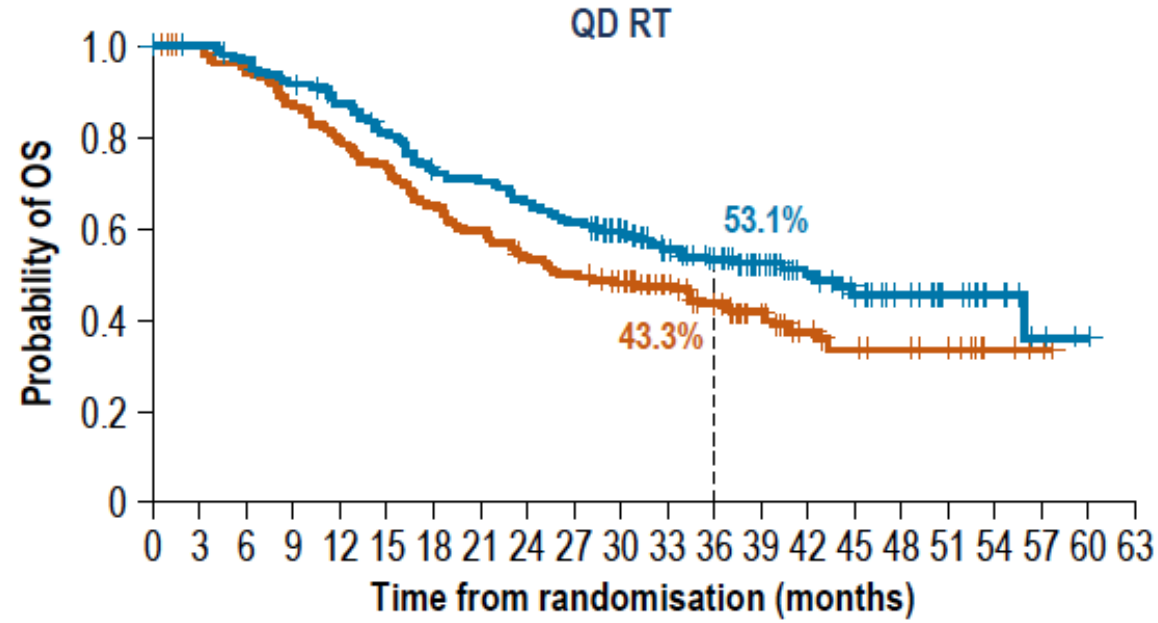
ADRIATIC: BID and QD subgroup - OS

	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:

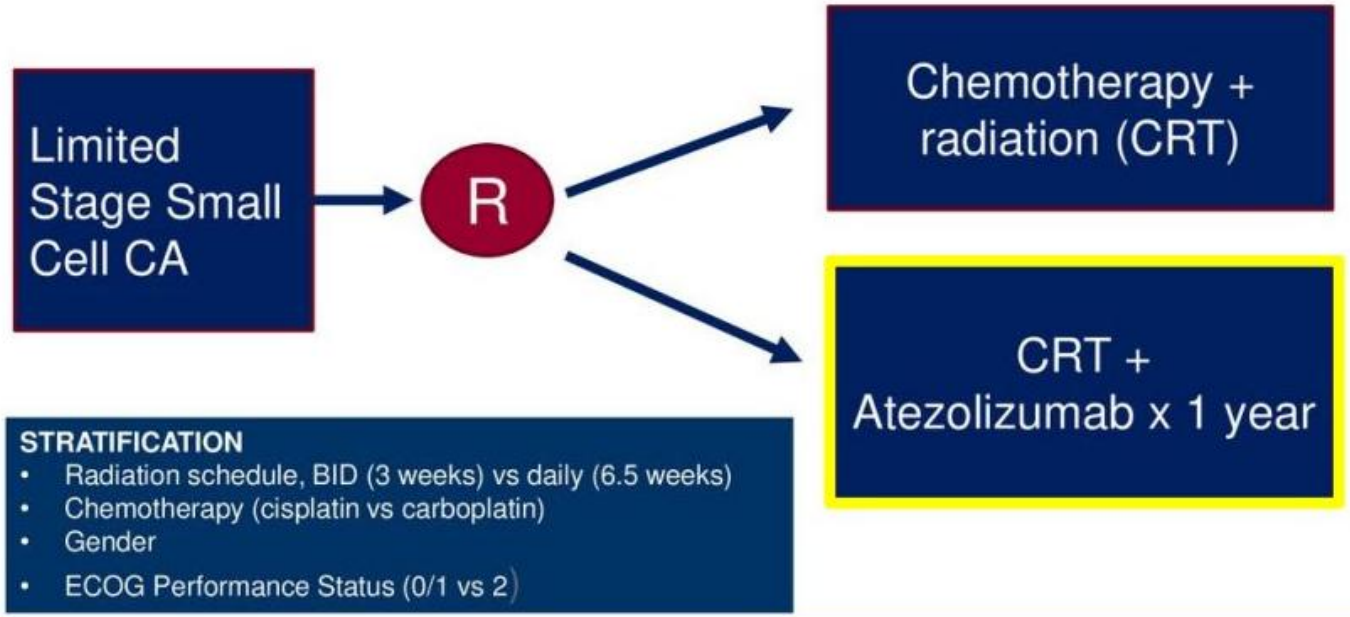
D, QD	195	193	185	175	164	151	135	130	121	114	99	75	63	50	38	29	22	14	8	3	1	0
P, QD	187	181	171	158	145	134	118	108	97	90	78	60	48	35	22	17	14	11	4	2	0	0

*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

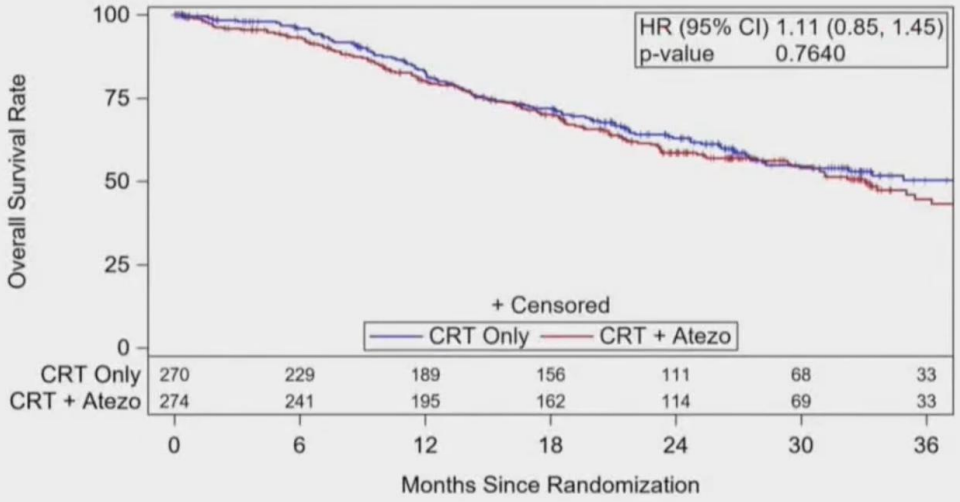
No concerning safety signals for atezo +cCRT.

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

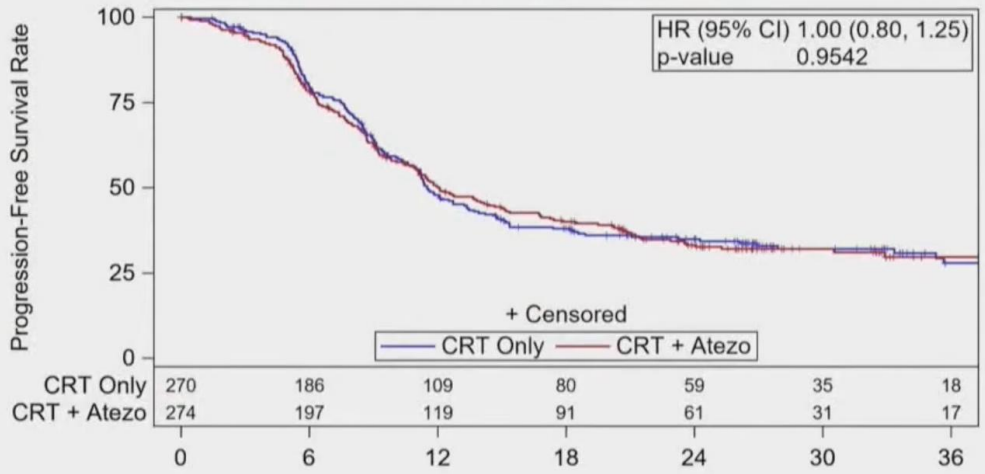
Chemoradiation with concurrent and consolidation atezo did not improve survival in LS-SCLC

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

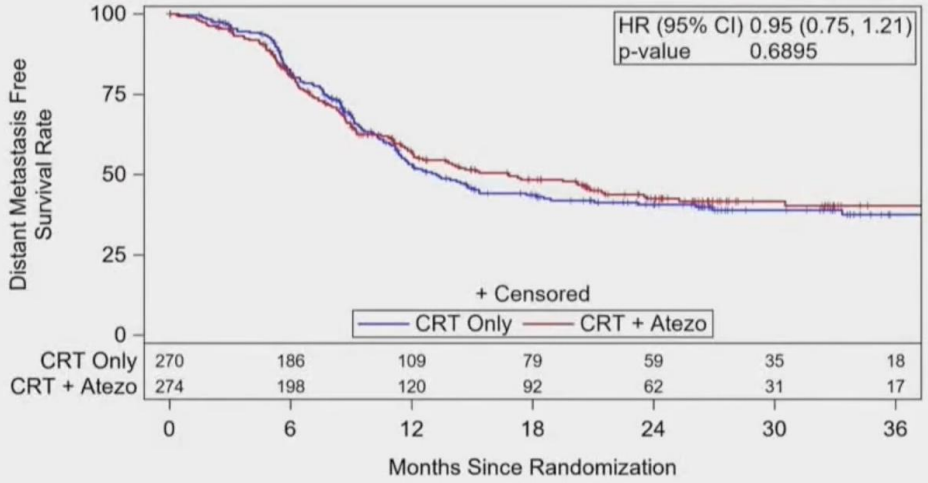
Overall Survival



Progression Free Survival



Distant Metastasis Free Survival

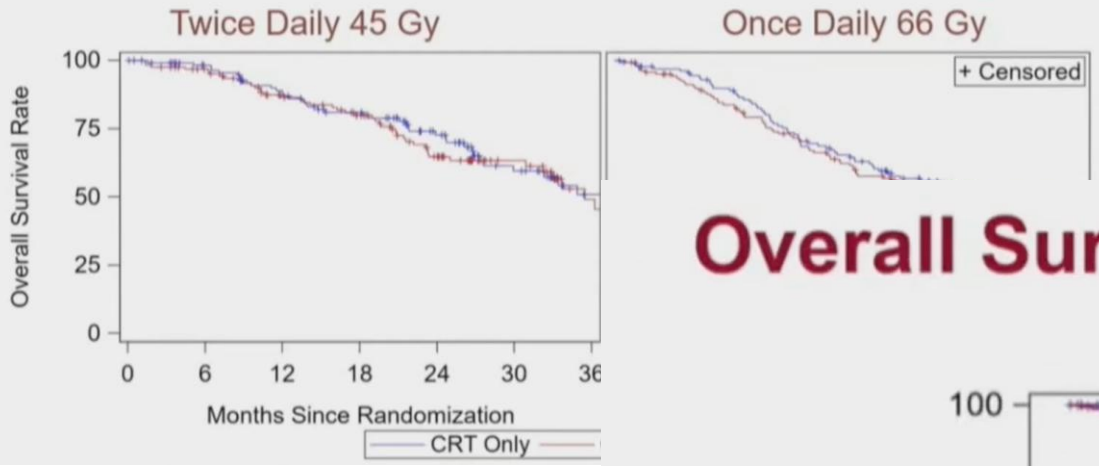


Time to Local Failure

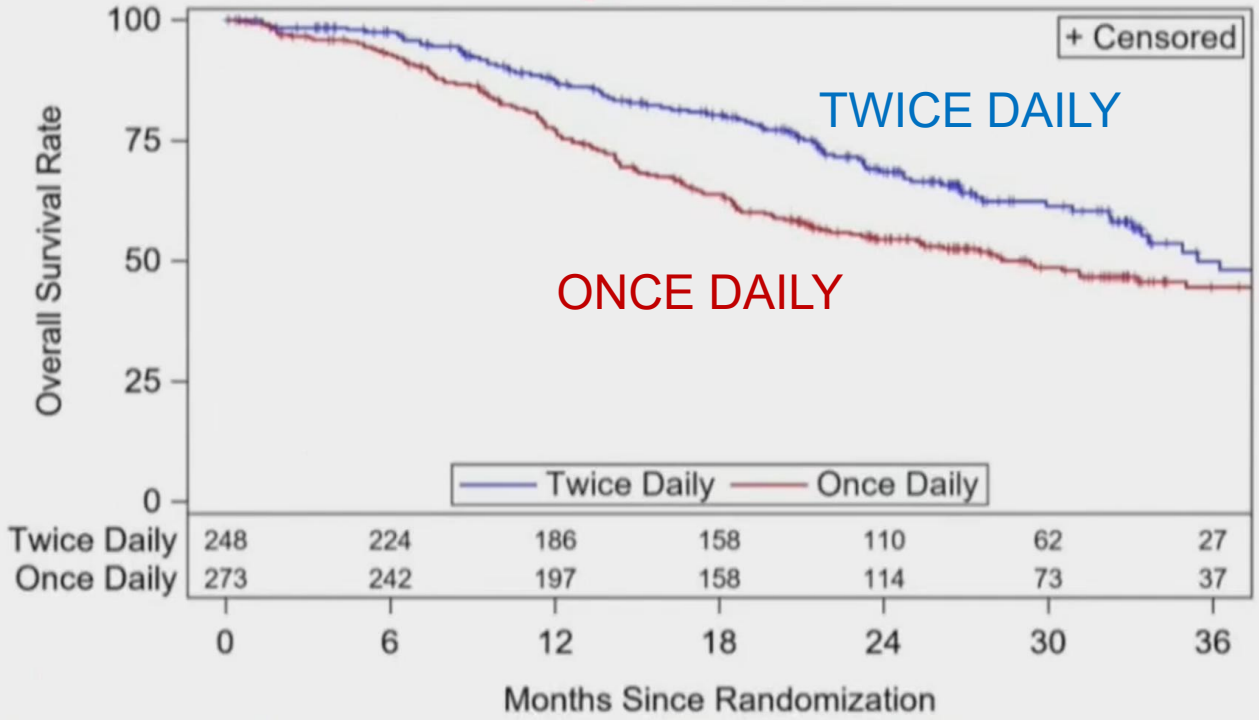


ASTRO 2024

Overall Survival: RT Schedule Subgroups



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

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

DLCA
DUTCH LUNG CANCER AUDIT

Real-world treatment outcomes comparing once- versus twice-daily RT in Limited Stage SCLC

Floris Bosch, **Zeno Gouw**, Ronald Damhuis, Liselotte van Bockel, Ida Coremans, Corine van Es, Annelies van der Geest, Katrien De Jaeger, Barbara Wachters, Hans Knol, Friederike Koppe, Bart Reymen, Dominic Schinagl, Femke Spoelstra, Caroline Tissing-Tan, Max Peters, Noëlle van der Voort van Zyp, Antoinet van der Wel, Erwin Wiegman, Robin Wijsman, Judith Dasselaar, José Belderbos

REAL WORLD DATA: ONCE vs BID in LS-SCLC

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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	

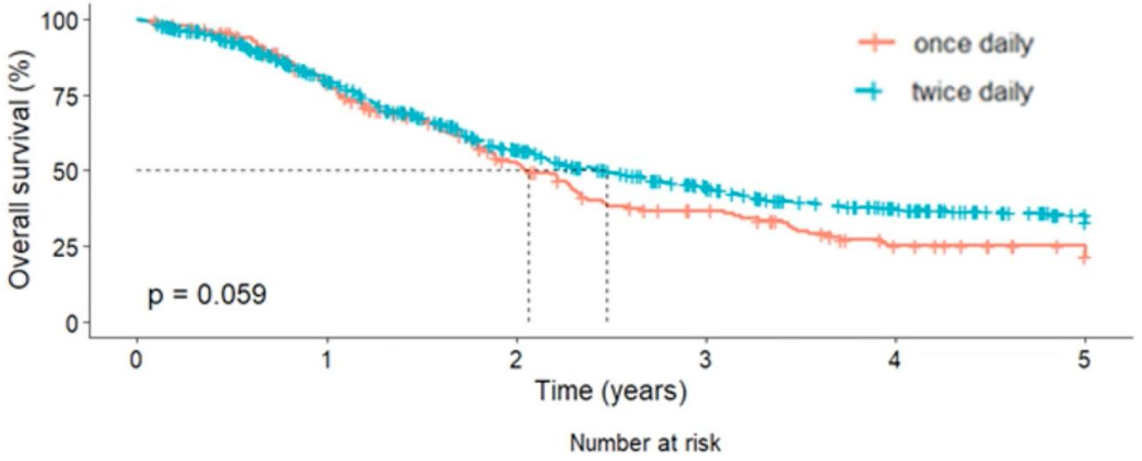
Baseline characteristics

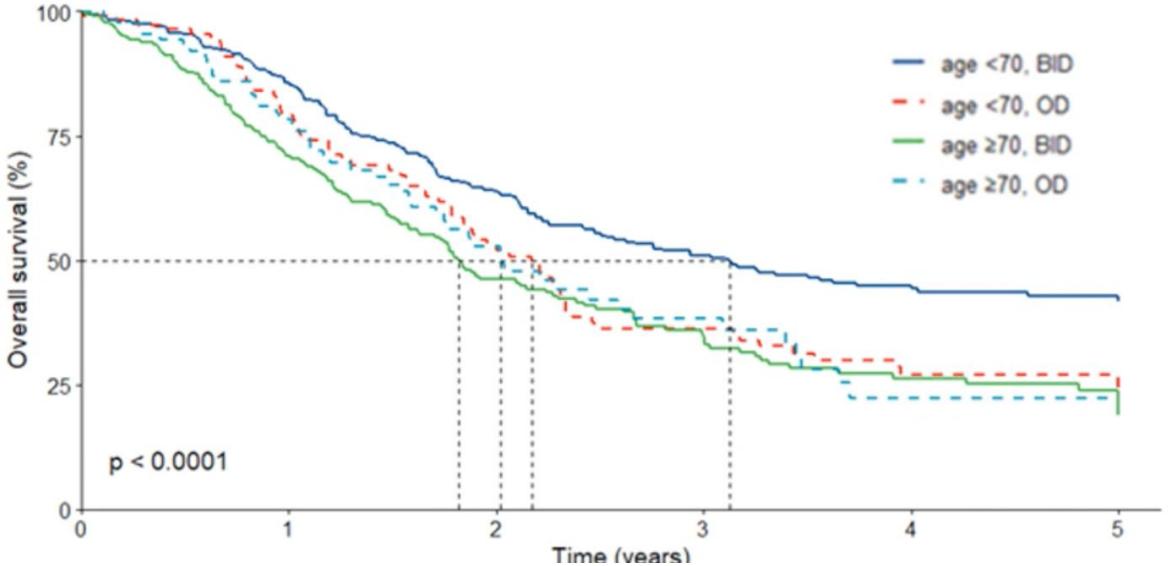
REAL WORLD DATA: ONCE vs BID in LS-SCLC

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

- **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)





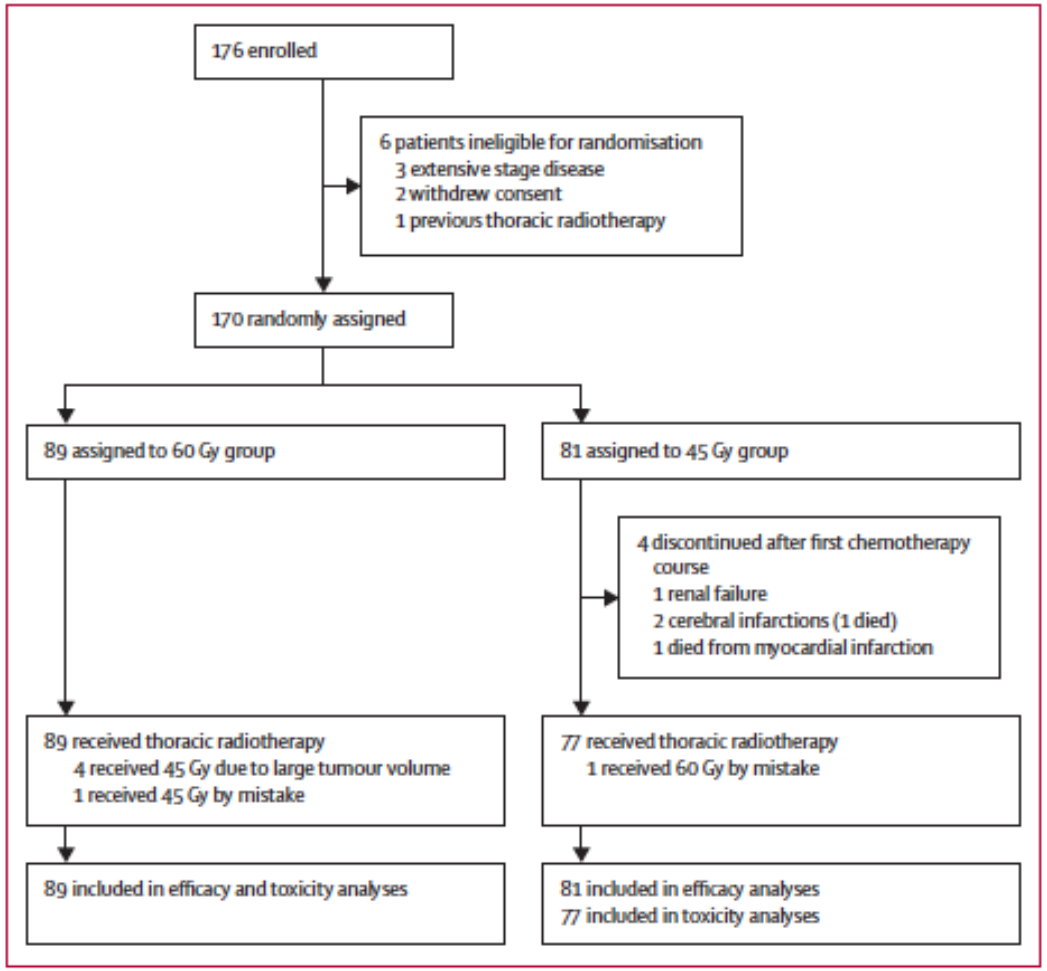
High-dose versus standard-dose twice-daily thoracic radiotherapy for patients with limited stage small-cell lung cancer: an open-label, randomised, phase 2 trial

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)

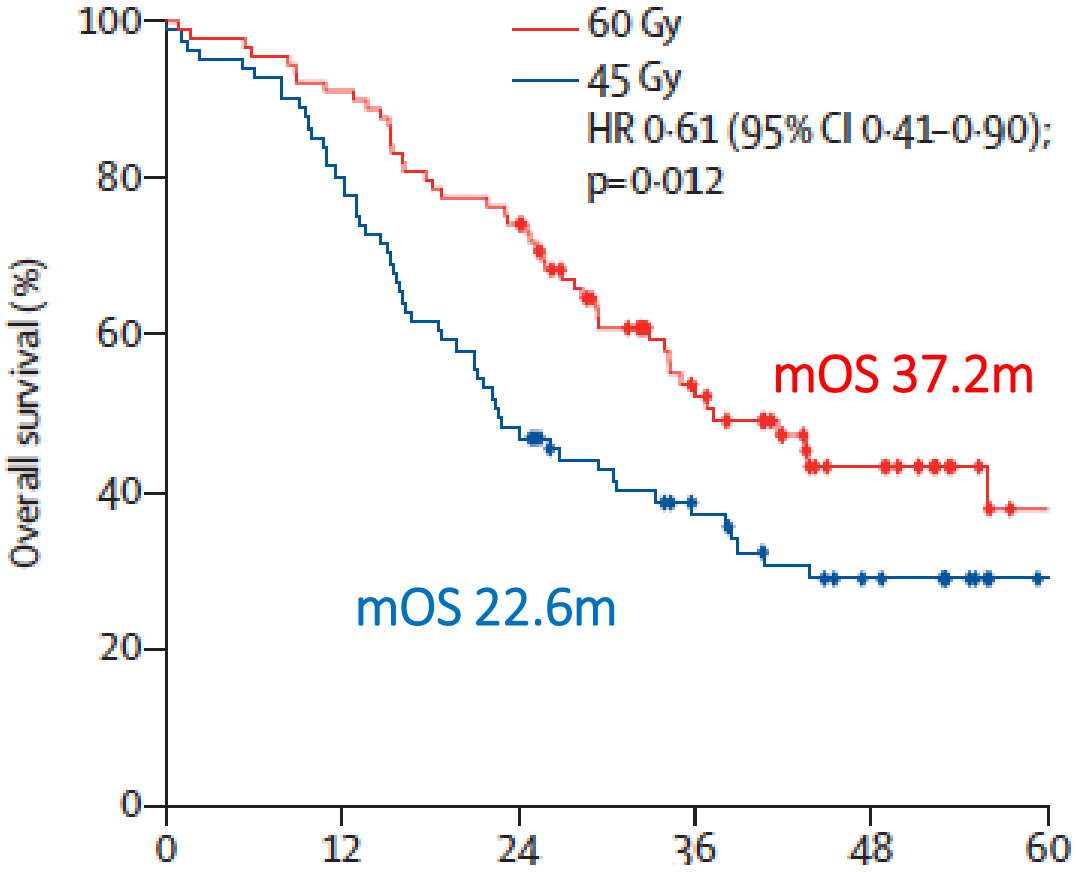


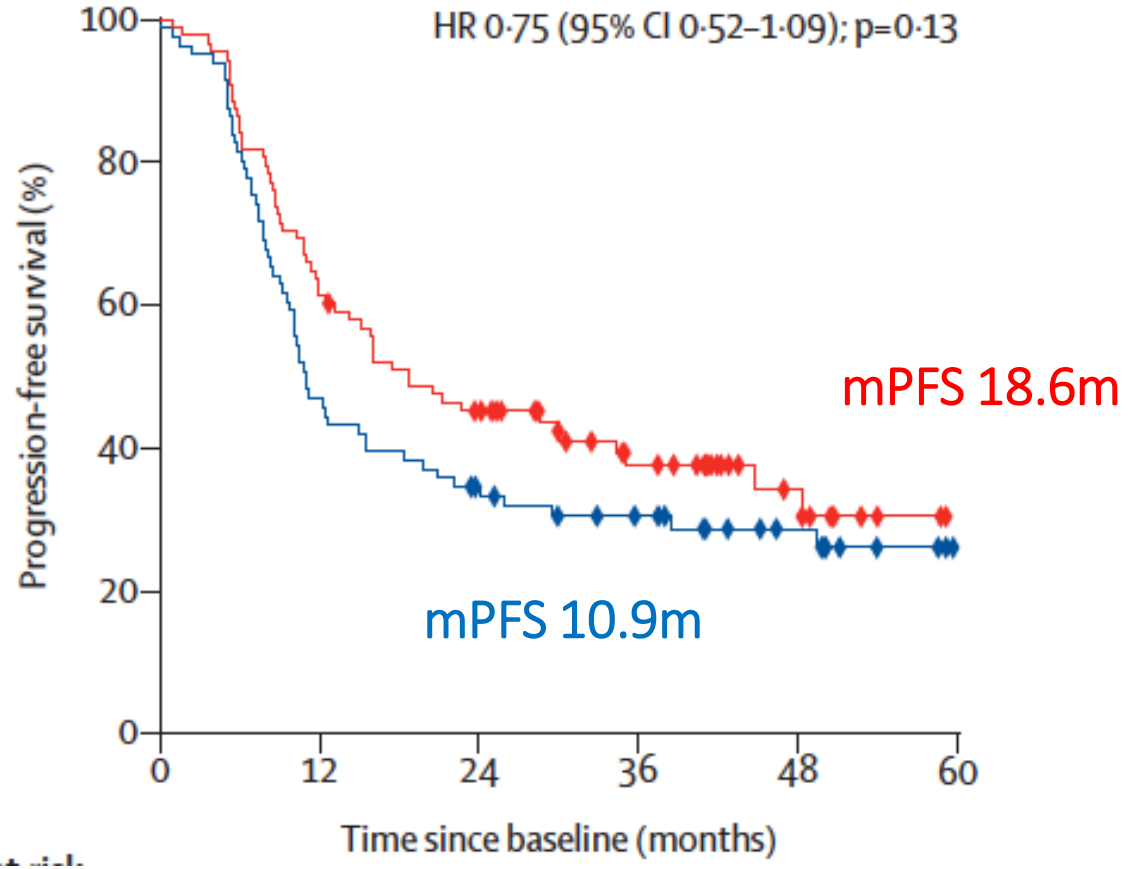
Lancet Oncol 2021; 22: 321–31

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

Median follow-up 49 months





Low increase of G3 toxicity (3%)

Lancet Oncol 2021; 22: 321–31

OVERALL SURVIVAL-NORVEGEAN TRIAL, Lancet Oncology 2021

Certainty assessment							Summary of findings				
							№ of patients		Effect		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Overal survival (follow-up: median 49 months)											
1	randomised trials	not serious [a,b,c]	not serious [d]	not serious	serious [e]	none	89 participants -	81 participants 72.0%	**HR 0.61** (0.41 to 0.90) [Overal survival]	- **18 fewer per 100** (from 31 fewer to 4 fewer)	⨁⨁⨁◯ Moderate

GRADEpro

TWICE DAILY HIGH DOSE RT: HIGH CLINICAL BENEFIT WITH MODERATE CERTAINTY

Explanations | References

- ☐ no detection for OS
- ☐ no performance for OS
- ☐ no attrition, 100% evaluable
- ☐ not applicable
- ☑ NNT 5 (from 3 to 25)

Durvalumab in Small-Cell Lung

The NEW ENGLAND JOURNAL of MEDICINE

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:

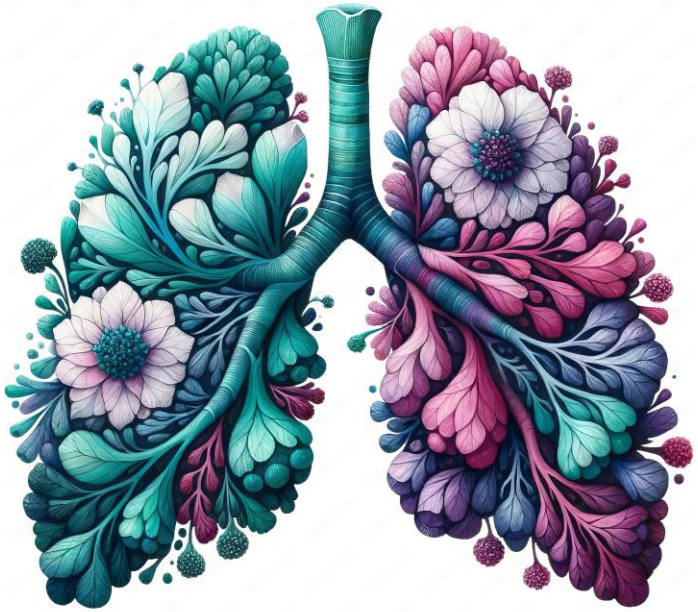
Ramella et al. suggest that a twice-daily thoracic radiotherapy dose of 60 Gy, as investigated in a randomized phase 2 trial in Scandinavia, could be a preferred radiation schedule.[2] The radiation doses and schedules used in our trial were guideline-recommended worldwide standards in 2018, when we 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-look into the black box!!)
3. MODALITY of RT (Higher doses to the primary)
4. FRACTIONATION in LS-SCLC (BID is better!!!)


Thank You...
UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA
«Le cose vere nella vita non si studiano né si imparano, ma si incontrano»

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

UNIVERSITÀ CAMPUS BIO-MEDICO DI ROMA

FATAL PULMONARY HEMORRHAGE IN PATIENTS TREATED WITH HYPOFRACTIONATED RT FOR STAGE II-III NSCLC

To boost statistical power, data from 2 studies were combined.
The randomized ARTFORCE PET-Boost trial (NCT01024829) ("PB cohort") l

Miedian fraction dose was 3.3 Gy (IQR 3.2-3.4 Gy) and 3.5 Gy (IQR 3.4 -3.8 Gy), for 24 fractions, respectively. Involved lymph nodes received 24 x 2.75 Gy.

In the retrospective "LN cohort" patients with node-positive

NSCLC received 2.75 Gy to the primary tumor, while involved lymph nodes received either 2.75 Gy or 2.42 Gy over 24 fractions.

S. Cooke[1], J. Belderbos[1], J. van Diessen[1], C. Faivre-Finn[2], B. Reymen[3], M. Lambrecht[4,5], E. M. Dieleman[6], G. Fredberg Persson[7,8], B. Stam[9], D. de Ruysscher[10], and J. J. Sonke[11];

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FATAL PULMONARY HEMORRHAGE IN PATIENTS TREATED WITH HYPOFRACTIONATED RT FOR STAGE II-III NSCLC

The current analysis included 398 patients (PB n=103; LN n=295).

The randomized ARTFORCE PET-Boost trial (NCT01024829) ("PB cohort") I → FPH occurred in 6 (5.8%)

In the retrospective "LN cohort" patients with node-positive → FPH occurred in 4 (1.4%)

CONCLUSION: Tumor pathology, PBT compression and vessel encasement may be more critical determinants of FPH than high maximum doses to broncho-vascular structures in patients with stage II-III NSCLC receiving moderately hypofractionated (chemo)radiotherapy. These findings may help refine **patient selection for hypofractionated treatment**.