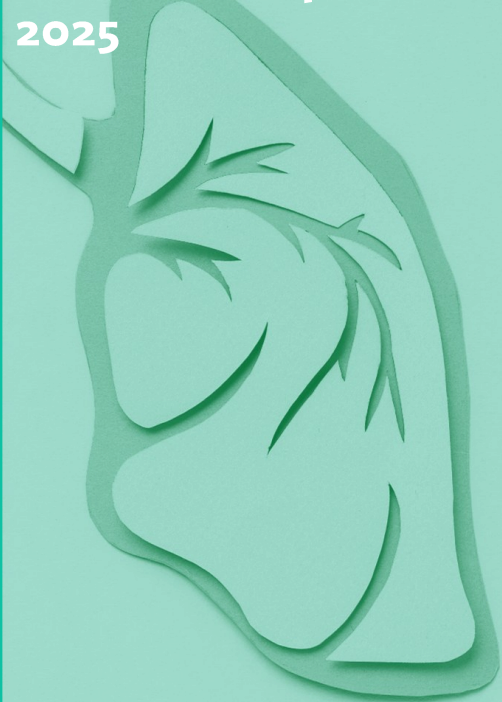


MasterClass

Radioterapia
en cáncer de pulmón
2025



ORGANIZADO POR:

GRUPO ONCOLÓGICO ESPAÑOL
DE CÁNCER DE PULMÓN (GOECP)



13
FEB
2025

1ª Sesión:

**Radioterapia en cáncer de pulmón
de célula no pequeña estadio III
irreseccable**

Ensayos clínicos en pacientes con mutación del EGFR

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SEOR
SOCIEDAD ESPAÑOLA DE
ONCOLOGÍA RADIOTERÁPICA

Consolidation with osimertinib following chemoradiotherapy in EGFRm NSCLC is the standard of care

LAURA trial

Key inclusion criteria:
≥18 years (≥20 years in Japan)
EGFR-mutated NSCLC
Ex19del or L858R
WHO performance status 0 / 1
Confirmed locally-advanced, unresectable stage IIIA/IIIB/IIIC†
No progression during or after curative-intent CRT (sequential or concurrent)‡

Randomization 2:1 (N = 216)

Stratification by:
cCRT vs. sCRT
Stage IIIA vs. stage IIIB/IIIC
China vs. non-China

Osimertinib
80 mg QD

Until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

Placebo
QD

Open-label osimertinib was offered to both treatment groups after BICR-assessed disease progression

- Patients in the placebo group were allowed to crossover to osimertinib treatment
- Patients in the osimertinib group were allowed to continue osimertinib treatment if deemed clinically beneficial by the investigator

Post-progression followed for PFS2, §TFST, TSST, TTDM and OS

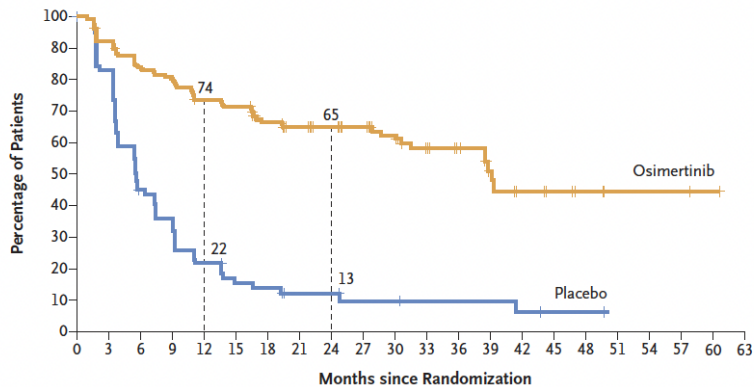
Follow-up:

- Chest CT/MRI and brain MRI: at baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

Lu et al. NEJM 2024

Consolidation with osimertinib following chemoradiotherapy in EGFRm NSCLC is the standard of care

Non-Asian 83%; non smokers 70%
EGFR del19 55%; concurrent CRT 90%



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Osimertinib	143	127	114	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

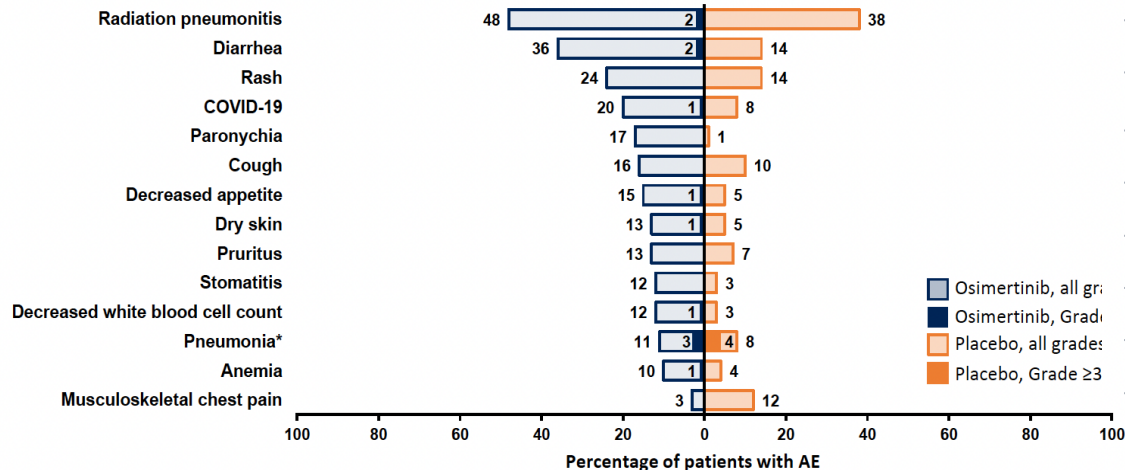
Subgroup	Osimertinib no. of events/no. of patients	Placebo no. of events/no. of patients	Hazard Ratio for Disease Progression or Death (95% CI)
Overall			
Stratified log-rank analysis	57/143	63/73	0.16 (0.10–0.24)
Unadjusted Cox proportional-hazards analysis	57/143	63/73	0.23 (0.16–0.33)
Sex			
Male	23/53	27/31	0.26 (0.15–0.46)
Female	34/90	36/42	0.21 (0.13–0.34)
Age			
<65 yr	31/81	36/39	0.16 (0.10–0.26)
≥65 yr	26/62	27/34	0.33 (0.19–0.57)
Smoking history			
Current or former	20/41	22/24	0.26 (0.14–0.48)
Never	37/102	41/49	0.22 (0.14–0.34)
Race or national group			
Chinese	7/27	11/13	NC (NC–NC)
Non-Chinese	50/116	52/60	0.26 (0.17–0.39)
Asian	43/116	55/62	0.20 (0.13–0.29)
Non-Asian	14/27	8/11	0.48 (0.20–1.19)
Stage			
IIIA	22/52	20/24	0.28 (0.15–0.52)
IIIB or IIIC	35/91	43/49	0.21 (0.13–0.33)
EGFR mutation			
Exon 19 deletion	26/74	39/43	0.17 (0.10–0.29)
L858R mutation	31/68	24/30	0.32 (0.19–0.56)
Chemoradiotherapy			
Concurrent	53/131	54/62	0.25 (0.17–0.36)
Sequential	4/12	9/11	NC (NC–NC)
Response to previous CRT			
Complete response	1/4	2/3	NC (NC–NC)
Partial response	28/67	25/27	0.20 (0.11–0.34)
Stable disease	24/61	34/37	0.18 (0.10–0.30)
Not evaluable	4/11	2/6	NC (NC–NC)

Lu et al. NEJM 2024

Consolidation with osimertinib following chemoradiotherapy in EGFRm NSCLC is the standard of care

All-causality AEs (≥10%)

- Most common AEs were as expected for patients who had received prior CRT (radiation pneumonitis) or osimertinib treatment (diarrhea and rash)

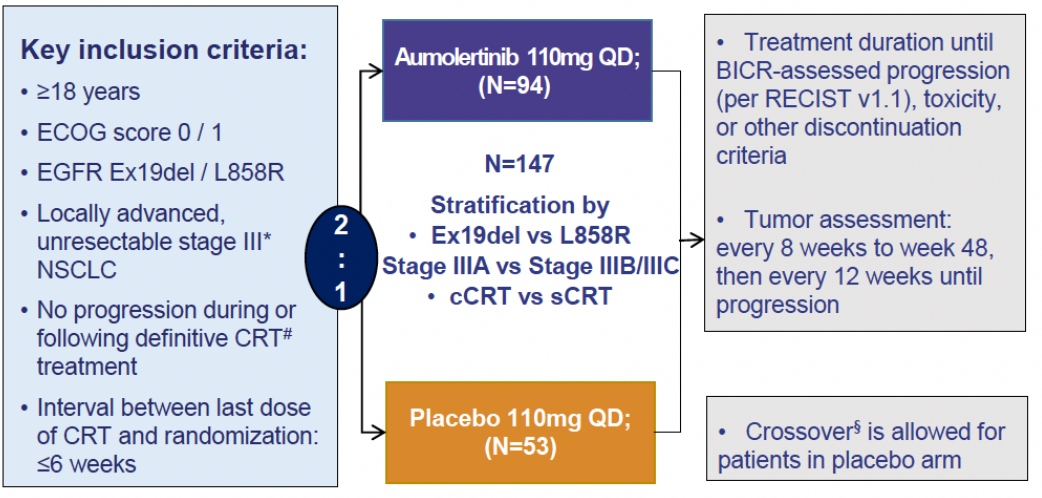


Radiation pneumonitis, n (%)	Osimertinib (n=143)	Placebo (n=73)
Total	69 (48)	28 (38)
Grade 1	22 (15)	14 (19)
Grade 2	44 (31)	14 (19)
Grade 3	3 (2)	0
CTCAE Grade ≥3	3 (2)	0
SAE	15 (10)	2 (3)
Discontinuations	7 (5)	2 (3)

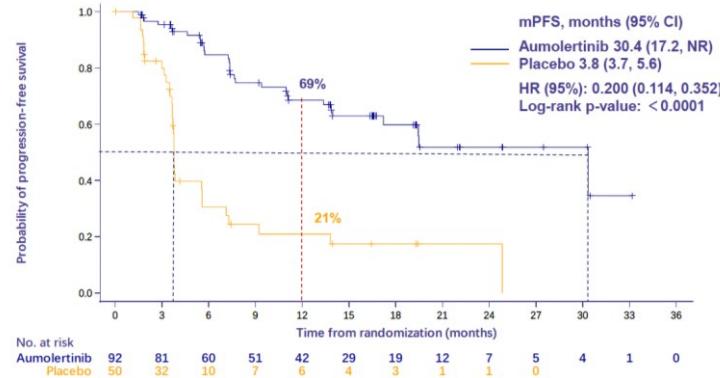
Kato et al. WCLC 2024

Another phase III clinical trial validated this strategy

POLESTAR trial

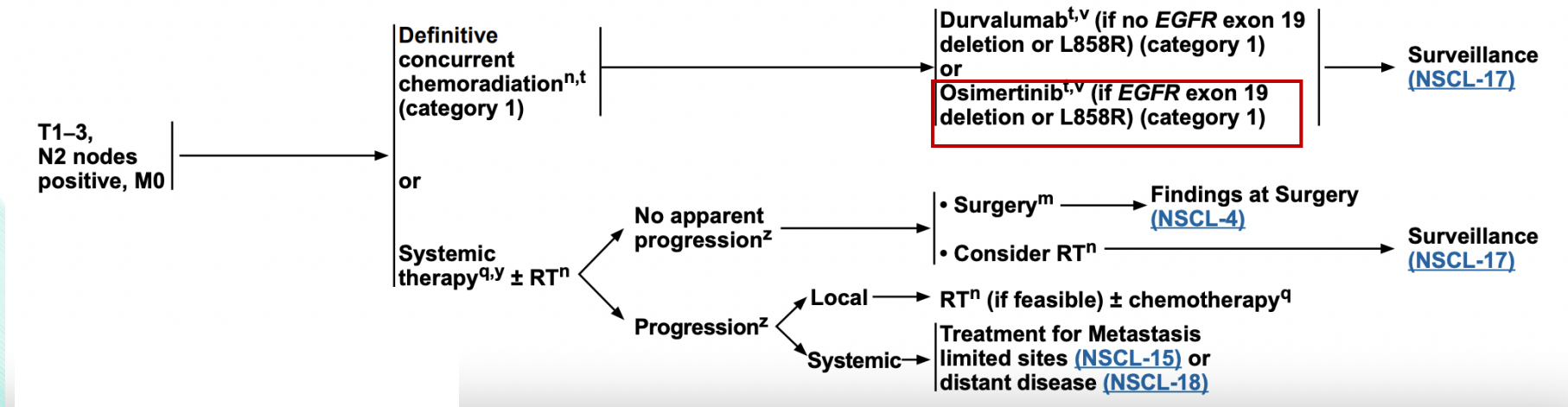


All Asian 83%; non smokers 70%
EGFR del19 41%; concurrent CRT 75%



Meng et al. WCLC 2024

Consolidation with osimertinib following chemoradiotherapy in EGFRm NSCLC is the standard of care



EMA approved osimertinib in this clinical setting in Dec 2024

NCCN guidelines Version 3.2025

Ongoing clinical trials in unresectable stage III NSCLC EGFRm

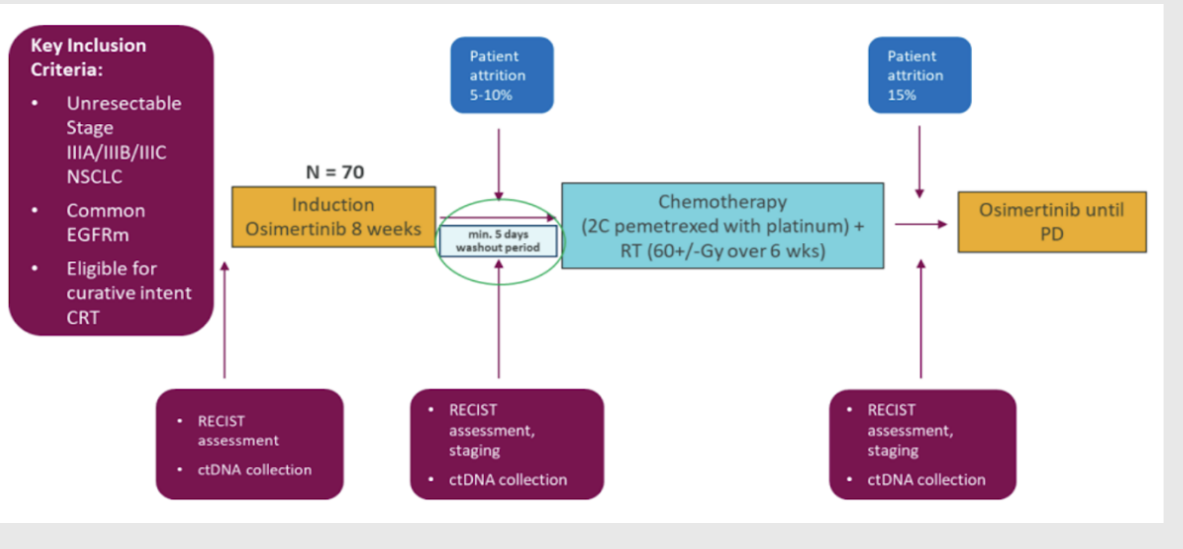
Ongoing EGFR-TKI studies in unresectable stage III EGFRm NSCLC.

Targeted therapy/Study identifier	Study design/country	Treatment	Duration of treatment	Patient population (estimated N)	Primary endpoint
cCRT → EGFR-TKI maintenance					
Osimertinib NCT03521154 LAURA [82,83]	Randomized, double-blind, placebo-controlled, multicenter, phase III; global	c/sCRT → osimertinib versus placebo (with no disease progression during or following CRT)	Until disease progression, unacceptable toxicity, or other discontinuation criteria	Unresectable stage III (8th edition staging manual) EGFRm (Ex19del/L858R +/- other mutations) NSCLC N ~216	PFS
Aumolertinib NCT04951635 [87]	Randomized, double-blind, placebo-controlled, multicenter, phase III; China	c/sCRT → aumolertinib versus placebo (with no disease progression following CRT)	Until disease progression, unacceptable toxicity, or other discontinuation criteria	Unresectable stage III (8th edition staging manual) EGFRm (Ex19del/L858R +/- other mutations) NSCLC N ~150	PFS
Lazertinib NCT05338619 PLATINUM [88,101]	Single-arm, open-label, multicenter, phase II; Republic of Korea	cCRT → lazertinib (with no disease progression during or following CRT)	Until disease progression, unacceptable toxicity, or other discontinuation criteria (at least 3 years)	Unresectable stage III EGFRm NSCLC N ~77	PFS
EGFR-TKI + cCRT/RT → EGFR-TKI consolidation					
Aumolertinib NCT04636593 [89,117]	Open-label, multicenter, phase II; China	Lung V20 <28%: Aumolertinib + RT → aumolertinib Lung V20 ≥28%: Induction aumolertinib → aumolertinib + RT → aumolertinib	Consolidation aumolertinib for 2 years or until disease progression or intolerable toxicity	Treatment-naïve unresectable stage III (8th edition staging manual) EGFRm (Ex19del/L858R) NSCLC N ~43	RP (grade ≥3) ^a
Aumolertinib NCT04952168 [90]	Open-label, single-arm, phase II; China	Aumolertinib ^b + cCRT → aumolertinib	Until disease progression or intolerable toxicity	Unresectable stage III (8th edition staging manual) EGFRm (sensitizing e.g. Ex19del/L858R) NSCLC N ~26	2-year OS rate
Induction EGFR-TKI → (RT) → EGFR-TKI (+RT) consolidation					
Aumolertinib ChiCTR2000040590 ADVANCE [91,92]	Randomized, open-label, multicenter, phase III; China	Induction aumolertinib → aumolertinib + RT versus cCRT	2 years	Treatment-naïve unresectable stage III (8th edition staging manual) EGFRm (Ex19del/L858R +/- other mutations) NSCLC N ~254	PFS
Aumolertinib NCT04841811 APPROACH [93]	Randomized, open-label, multicenter, phase II; China	Induction aumolertinib → RT → aumolertinib for 2 years versus ctDNA dynamic monitoring-guided treatment ^{c,d}	2 years	Treatment-naïve stage III (8th edition staging manual) EGFRm (Ex19del/L858R +/- other mutations) NSCLC N ~156	ORR, EFS

Kato et al.
Lung cancer 2024

Clinical trials in this setting: Induction with osimertinib followed by CRT and consolidation with osimertinib

NEOLA trial



Primary endpoint: PFS
Secondary endpoints: ORR, OS, EFS, Safety
Exploratory endpoints: CNS PFS, PFS2, MRD, ctDNA, **GTV-PTV**, **dosimetric changes**

Challenges in this clinical setting:

- Access to EGFR testing in locally advanced disease
- To incorporate NGS in the clinical pathway (reflex testing)
- Atypical EGFR mutations benefit from this strategy?
- Concurrent TKI + RT or better to avoid it?
- Induction with EGFR TKI to attack early the micrometastatic disease, CNS protection and reduce the field of RT
- Optimize treatment duration of consolidation (MRD?)
- How to follow these patients (Brain MRI?)

Thanks for your kind attention



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