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 irresecable

Ensayos clínicos en pacientes con mutación del EFGR

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Generalitat de Catalunya Departament de Salut

ICO Institut Català d'Oncologia

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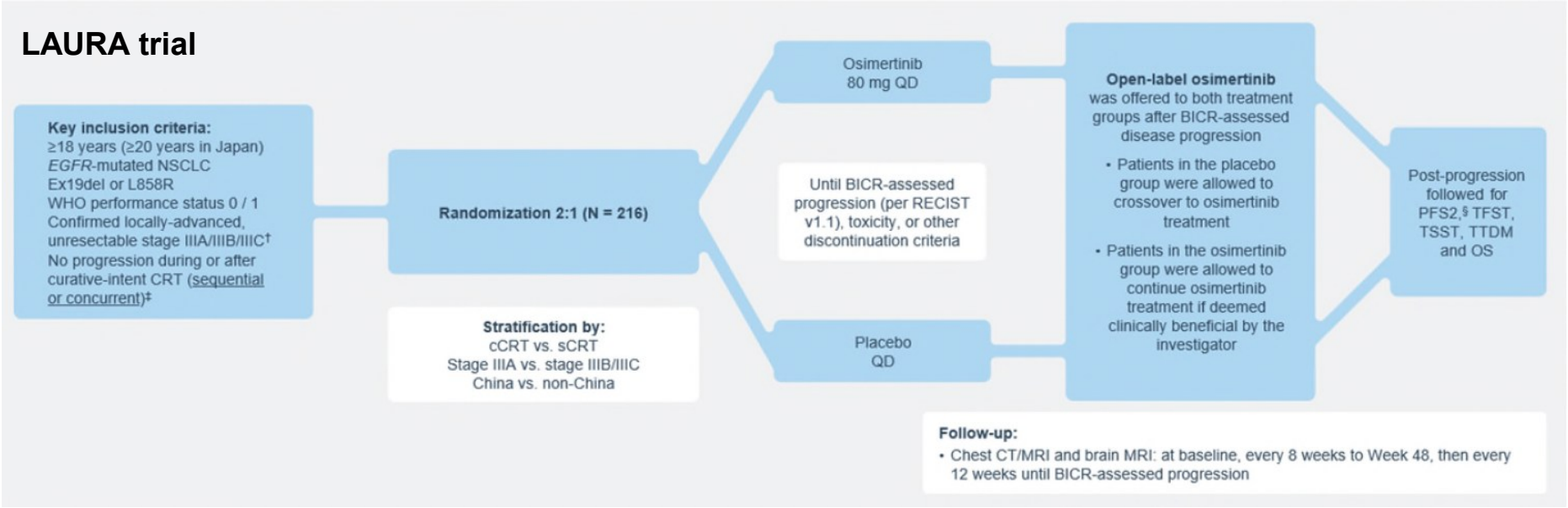
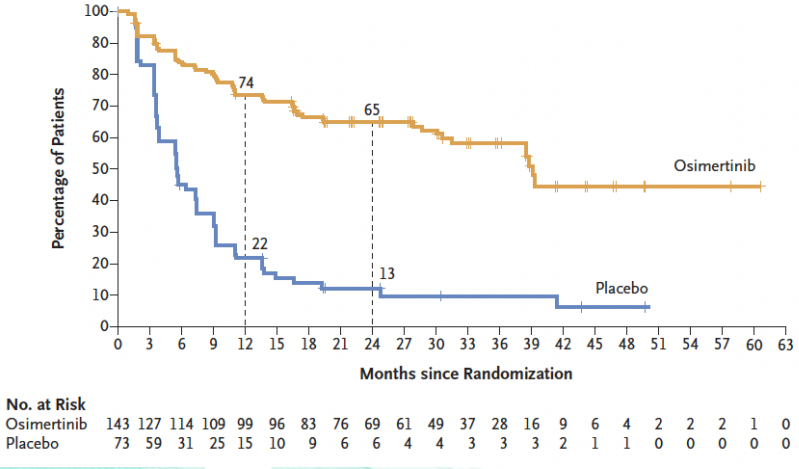
Consolidation with osimertinib following chemoradiotherapy in EGFRm NSCLC is the standard of care



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%



Median Progression-free Survival (95% CI)

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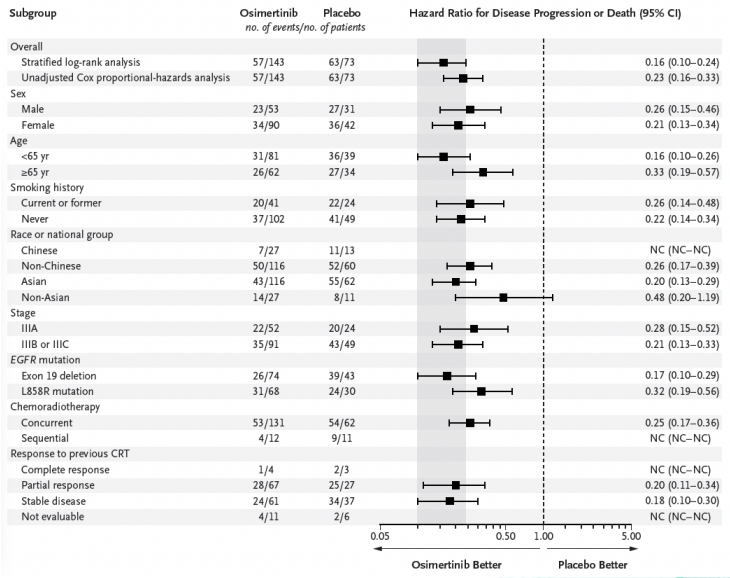
Osimertinib	39.1 (31.5–NC)
Placebo	5.6 (3.7–7.4)

Hazard ratio for disease progression or death, 0.16 (95% CI, 0.10–0.24)
P<0.001



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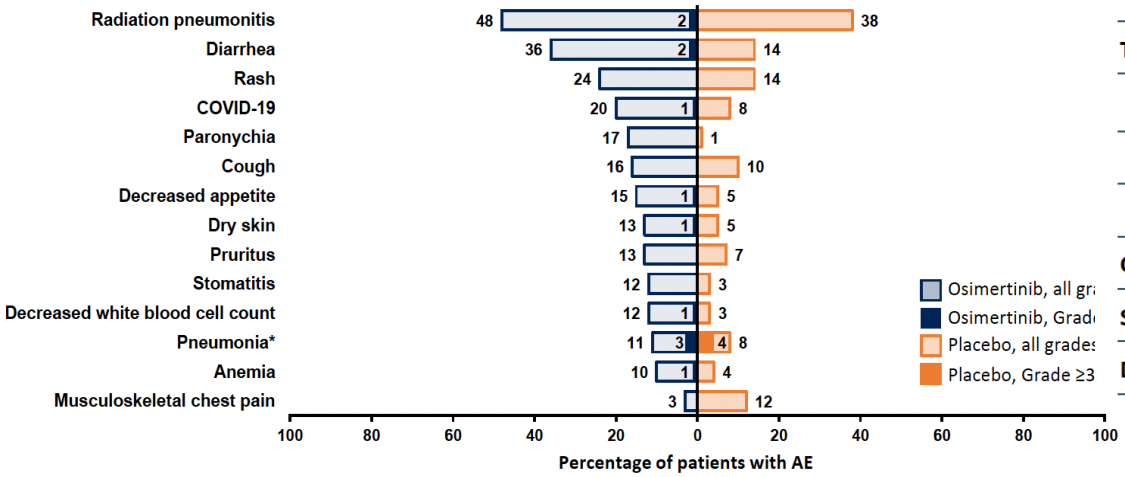
All-causality AEs (≥10%)

- 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

Key inclusion criteria:
- ≥18 years
- ECOG score 0 / 1
- EGFR Ex19del / L858R
- Locally advanced, unresectable stage III* NSCLC
- No progression during or following definitive CRT# treatment
- Interval between last dose of CRT and randomization: ≤6 weeks

2 : 1

Aumolertinib 110mg QD; (N=94)

N=147

Stratification by
- **Ex19del vs L858R**

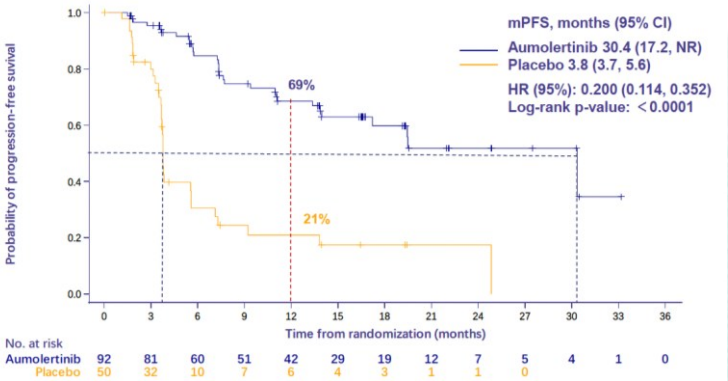
Stage IIIA vs Stage IIIB/IIIC
- **cCRT vs sCRT**

Placebo 110mg QD; (N=53)

- Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria
- Tumor assessment: every 8 weeks to week 48, then every 12 weeks until progression

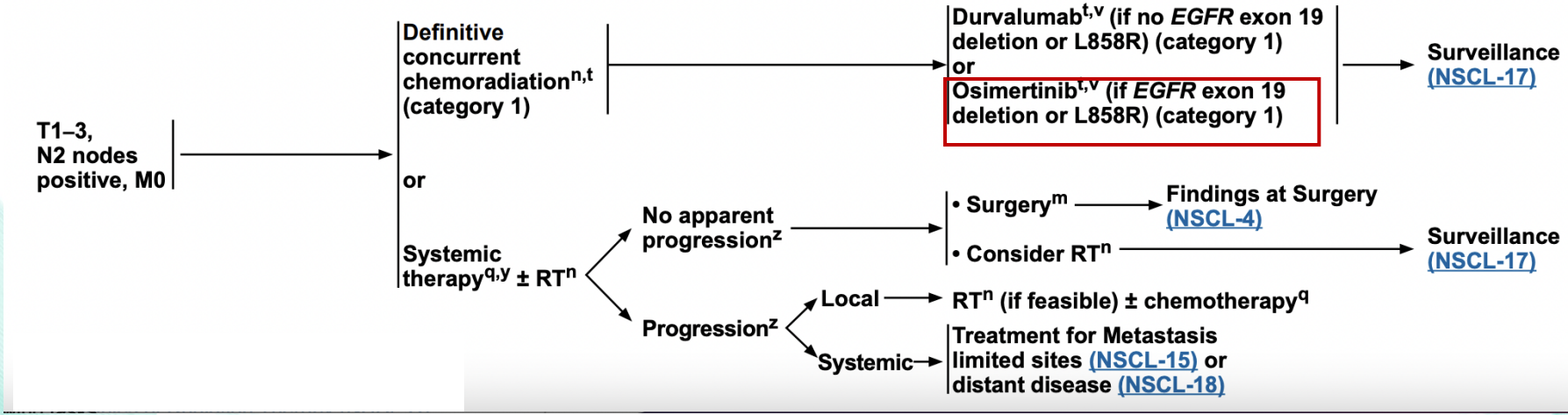
- Crossover§ is allowed for patients in placebo arm

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

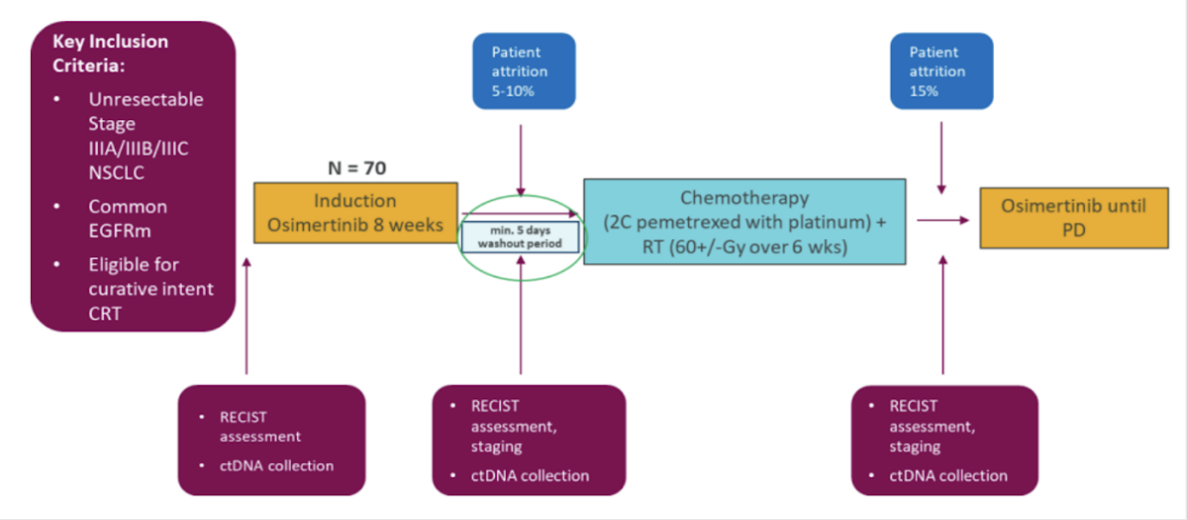
Ongoing EGFR-TKI studies in unresectable stage III EGFRm NSCLC.

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[c]) 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 micrometastic disase, 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

/Salut
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