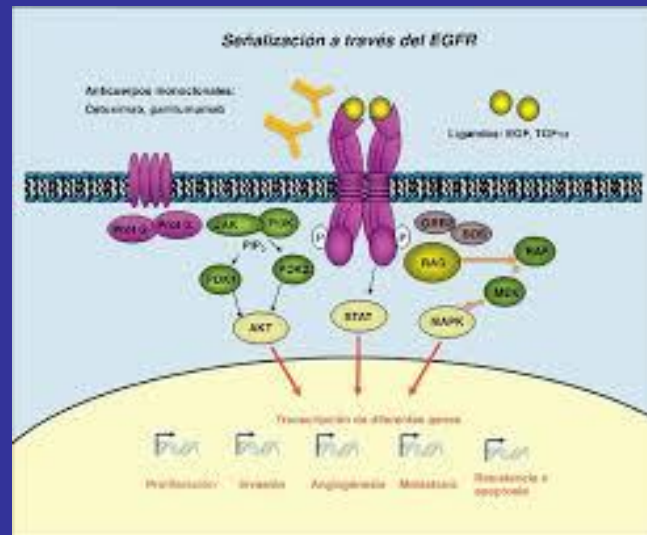


2ª línea de CPNPCP con alteraciones moleculares:

Integrar los nuevos ttos moleculares



1º LÍNEA EGFR MUTADO

Study	EGFR TKI	Sample size	Response rate (%)	Median PFS (months)	HR
IPASS	Gefitinib	261	71 vs 47	9.8 vs 6.4	0.48
First-SIGNAL	Gefitinib	NR	85 vs 37	8.4 vs 6.7	NR
WJTOC3405	Gefitinib	177	62 vs 31	9.2 vs 6.3	0.49
NEJ002	Gefitinib	198	74 vs 31	10.8 vs 5.4	0.30
OPTIMAL	Erlotinib	154	83 vs 36	13.7 vs 4.6	0.16
EURTAC	Erlotinib	174	58 vs 15	9.7 vs 5.2	0.37

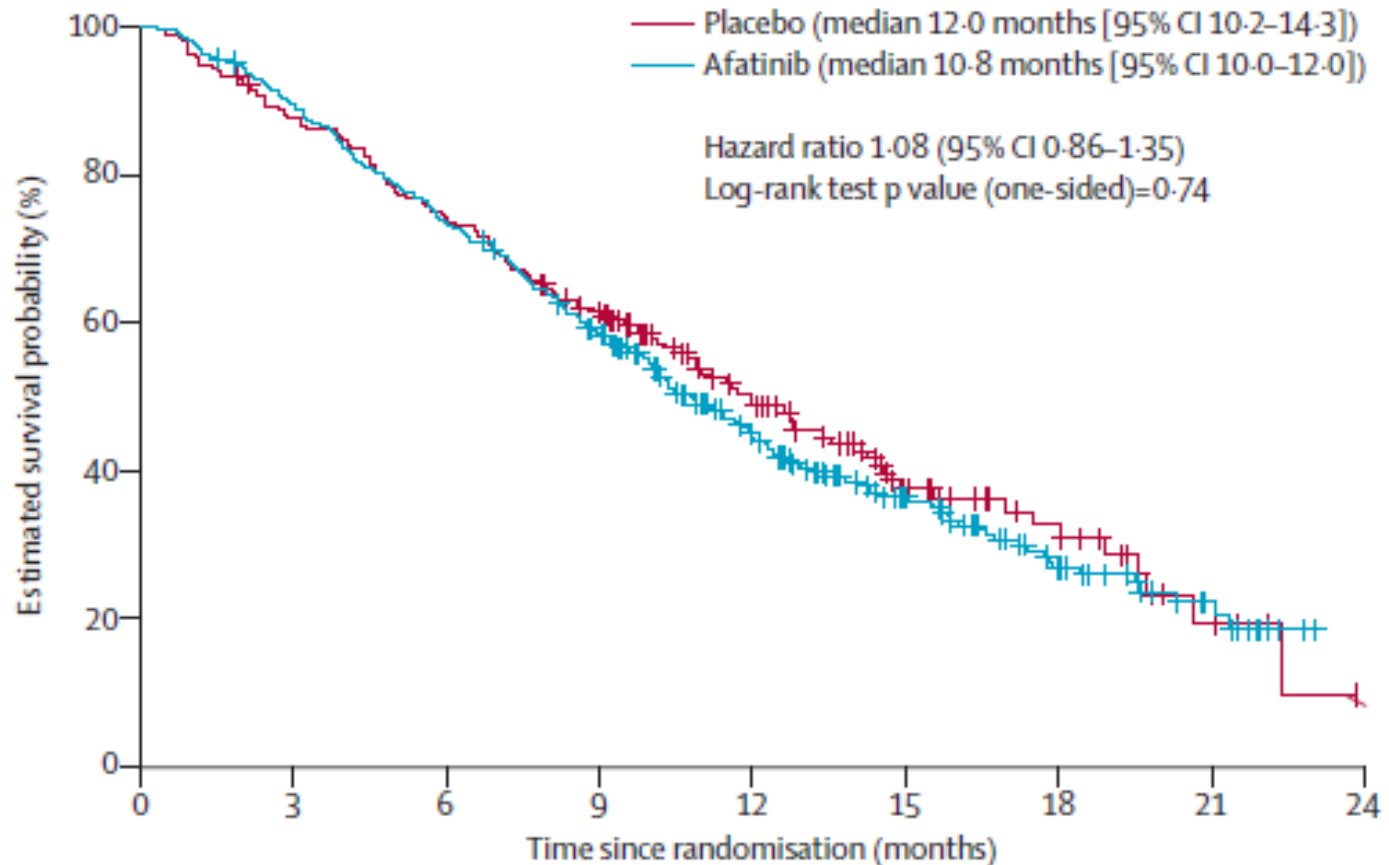
AFATINIB

Afatinib versus placebo for patients with advanced, metastatic non-small-cell lung cancer after failure of erlotinib, gefitinib, or both, and one or two lines of chemotherapy (LUX-Lung 1): a phase 2b/3 randomised trial

Vincent A Miller, Vera Hirsh, Jacques Cadranel, Yuh-Min Chen, Keunchil Park, Sang-We Kim, Caicun Zhou, Wu-Chou Su, Mengzhao Wang, Yan Sun, Dae Seog Heo, Lucio Crino, Eng-Huat Tan, Tsu-Yi Chao, Mehdi Shahidi, Xiuyu Julie Cong, Robert M Lorence, James Chih-Hsin Yang

- 585 pacientes:
 - Progresión ≥ 1 línea de QMT
 - 12 semanas con ITK
 - No imprescindible estudio EGFR

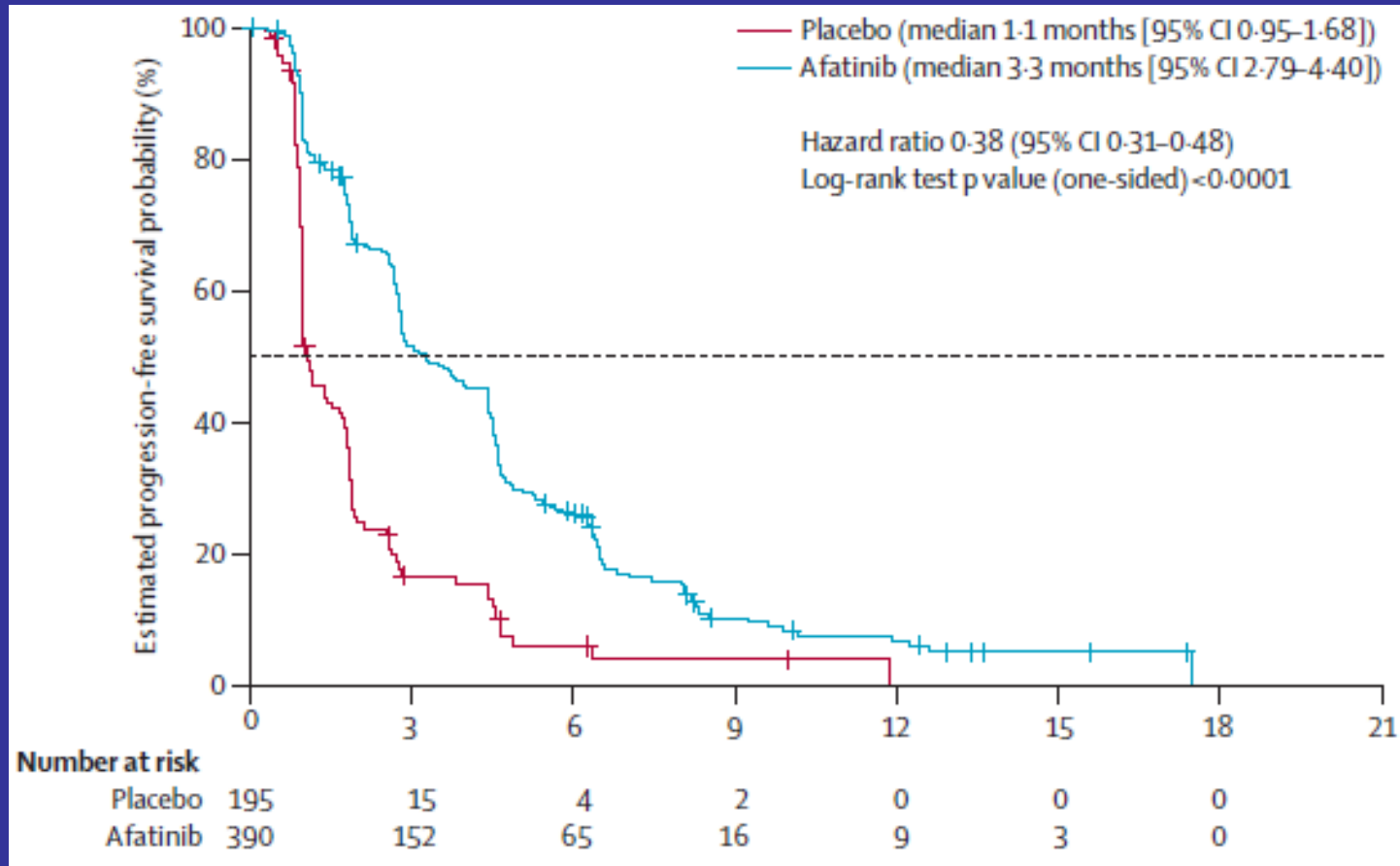
AFATINIB



Number at risk

Placebo	195	169	142	112	65	33	18	5	0
Afatinib	390	344	283	217	122	69	32	12	0

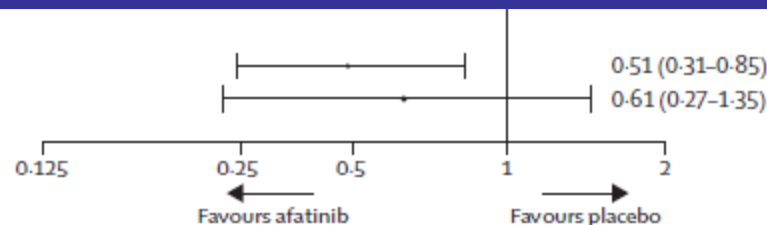
AFATINIB



EGFR mutation status

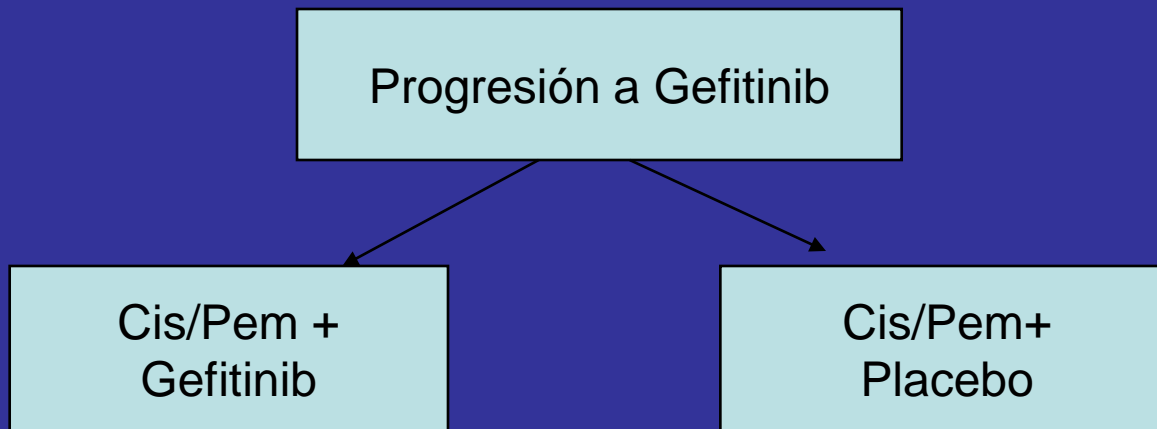
Positive (62/34)

Negative (31/14)



MANTENIMIENTO ITK

- IMPRESS fase III:

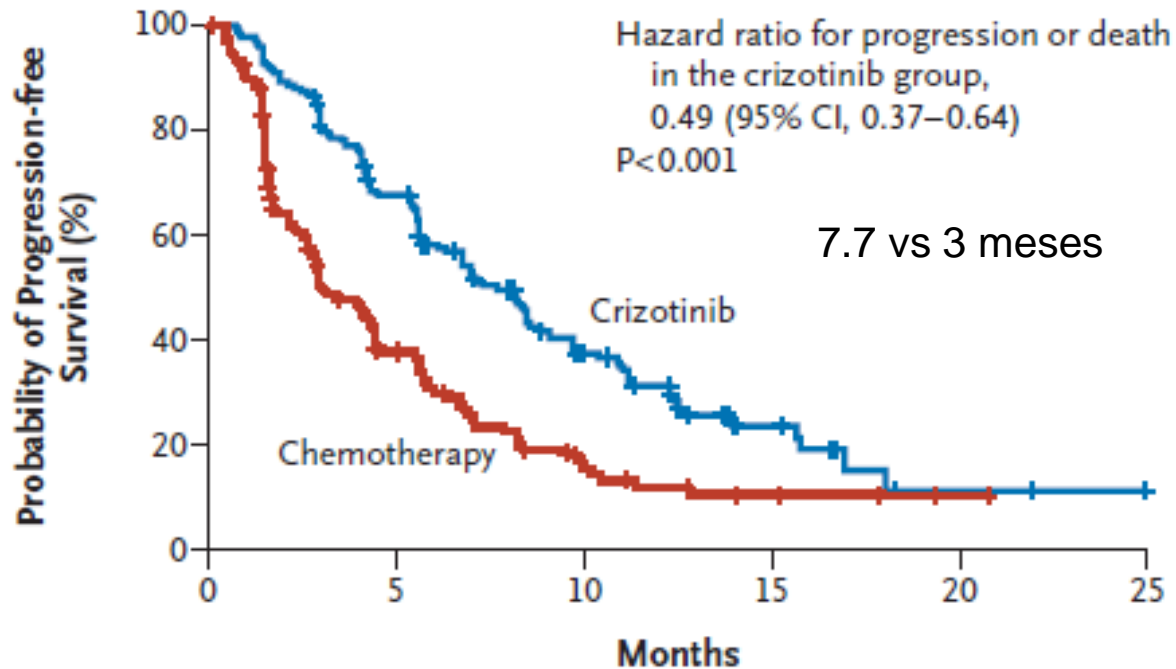


- 265 pacientes
- Objetivo primario: SLP
 - HR 0.86; $p = 0.273$. Mediana SLP 5.4 meses
- SG: datos inmaduros (33% fallecidos),
 - Mejor para placebo vs gefitinib (HR 1.62; $p = 0.029$)

CRIZOTINIB

Crizotinib versus Chemotherapy in Advanced *ALK*-Positive Lung Cancer

Progression-free Survival

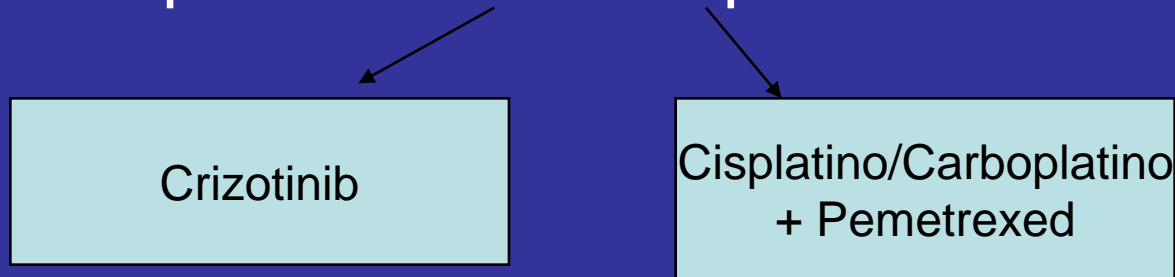


No. at Risk

Crizotinib	173	93	38	11	2	0
Chemotherapy	174	49	15	4	1	0

CRIZOTINIB

- PROFILE 1014:
 - 343 pacientes sin tto previo



- Objetivo primario: SLP
 - 11 meses Crizotinib vs 7, HR 0.45
- SG: sin diferencias

CERITINIB

Ceritinib in advanced anaplastic lymphoma kinase (ALK)-rearranged (ALK+) non-small cell lung cancer (NSCLC): Results of the ASCEND-1 trial.

Endpoint	ALKi PT N=121	ALK naive N=59	All N=180
ORR, n (%) [95% CI]	67 (55.4%) [46.1, 64.4]	41 (69.5%) [56.1, 80.8]	108 (60.0%) [52.4, 67.2]
DOR (Median [95% CI])	7.4 mos [5.4, 10.1]	NE ^a [5.6, NE]	9.7 mos [6.9, 11.4]
Time to first response (Median [min, max])	6.1 wks [4.6, 24.1]	6.1 wks [3.0, 24.1]	6.1 wks [3.0, 24.1]
PFS (Median [95% CI])	6.9 mos [5.4, 8.7]	NE ^b [6.7, NE]	7.0 mos [6.2, 10.1]

Abbreviation: NE, not estimable. ^a DOR rate at 12 mos: 71.1% (95% CI: 49.8, 84.6). ^b PFS rate at 12 mos: 58.1% (95% CI: 41.6, 71.5).

ALECTINIB

- Fase I/II 46 pacientes no tratados
 - 43 respuestas (93.5%)
- Fase I/II 47 pacientes Crizotinib previo
 - 55% respuestas, 36% EE

	All grades	Grade 3
Dysgeusia	14 (30%)	0
Increased AST	13 (28%)	0
Increased blood bilirubin	13 (28%)	1 (2%)
Increased blood creatinine	12 (26%)	0
Rash	12 (26%)	1 (2%)
Constipation	11 (24%)	0
Increased ALT	10 (22%)	1 (2%)
Decreased neutrophil count	8 (17%)	2 (4%)
Increased blood CPK	7 (15%)	2 (4%)
Stomatitis	7 (15%)	0
Increased blood ALP	6 (13%)	0
Myalgia	6 (13%)	0
Nausea	6 (13%)	0

AST=aspartate aminotransferase. ALT=alanine aminotransferase. CPK=creatine phosphokinase. ALP=alkaline phosphatase.

Table 4: Treatment-related adverse events reported in 10% or more of patients enrolled in phase 2 (n=46)

CONCLUSIONES

- EGFR mutados
 - No evidencia mantener ITK tras progresión
 - Afatinib ↑ SLP tras progresión a otros ITK
- Reordenamiento ALK
 - Crizotinib ↑ SLP vs QMT tras progresión 1^a línea
 - Podría convertirse en 1^a línea (EC Profile 1014)
 - Nuevas moléculas prometedoras

**Muchas
gracias!**

