TRATAMIENTO INDIVIDUALIZADO CON TKIs EN CÁNCER DE PULMÓN

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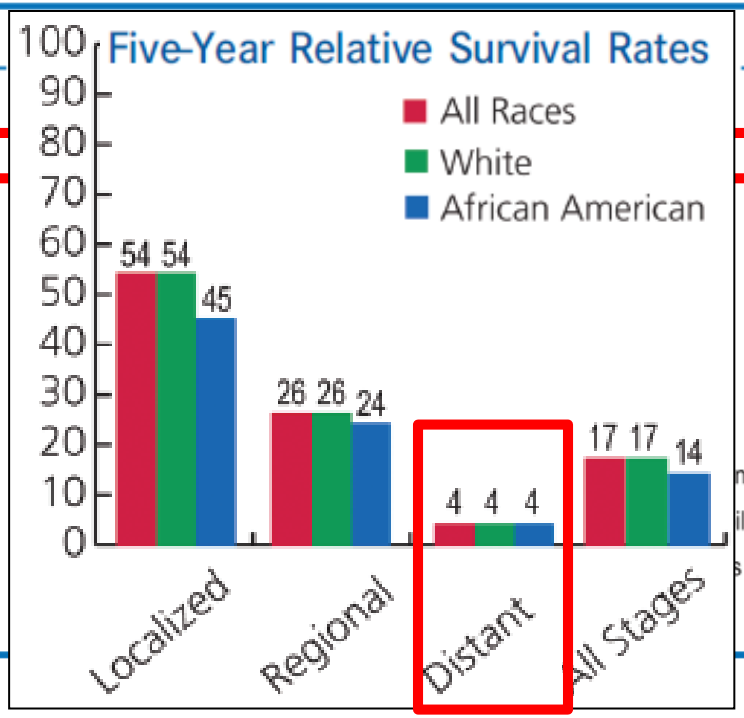
Estimated New Cases*

Males			Females		
Prostate	233,000	27%	Breast	232,670	29%
Lung & bronchus	116,000	14%	Lung & bronchus	108,210	13%
Colorectum	71,830	8%	Colorectum	65,000	8%
Urinary bladder	56,390	7%	Uterine corpus	52,630	6%
Melanoma of the skin	43,890	5%	Thyroid	47,790	6%
Kidney & renal pelvis	39,140	5%	Non-Hodgkin lymphoma	32,530	4%
Non-Hodgkin lymphoma	38,270	4%	Melanoma of the skin	32,210	4%
Oral cavity & pharynx	30,220	4%	Kidney & renal pelvis	24,780	3%
Leukemia	30,100	4%	Pancreas	22,890	3%
Liver & intrahepatic bile duct	24,600	3%	Leukemia	22,280	3%
All Sites	**855,220**	**100%**	**All Sites**	**810,320**	**100%**

Estimated Deaths

Lung & bronchus	72,330	26%
Prostate	40,000	15%
Colorectum	24,040	9%
Pancreas	19,420	7%
Liver & intrahepatic bile duct	14,270	5%
Leukemia	10,050	4%
Esophagus	8,590	3%
Urinary bladder	8,520	3%
Non-Hodgkin lymphoma	7,130	3%
Kidney & renal pelvis	6,230	2%
All Sites	**275,710**	**100%**



Siegel. Cancer CA Cancer J Clin 2014

TRATAMIENTOS DIRIGIDOS

- Fármacos contra **vías de señalización críticas para el crecimiento tumoral** sin comprometer órganos y tejidos normales:
  - Solo funciona contra tumores que contengan la diana.
  - En pacientes seleccionados más eficaces que la QT y menos efectos secundarios.

- **La diana debe poder ser medida y esta medida debe correlacionarse con la eficacia del tratamiento.**

NCI Diccionary of Cancer Terms. Retrieved 2009-01-25.
Sledge. JCO 2005

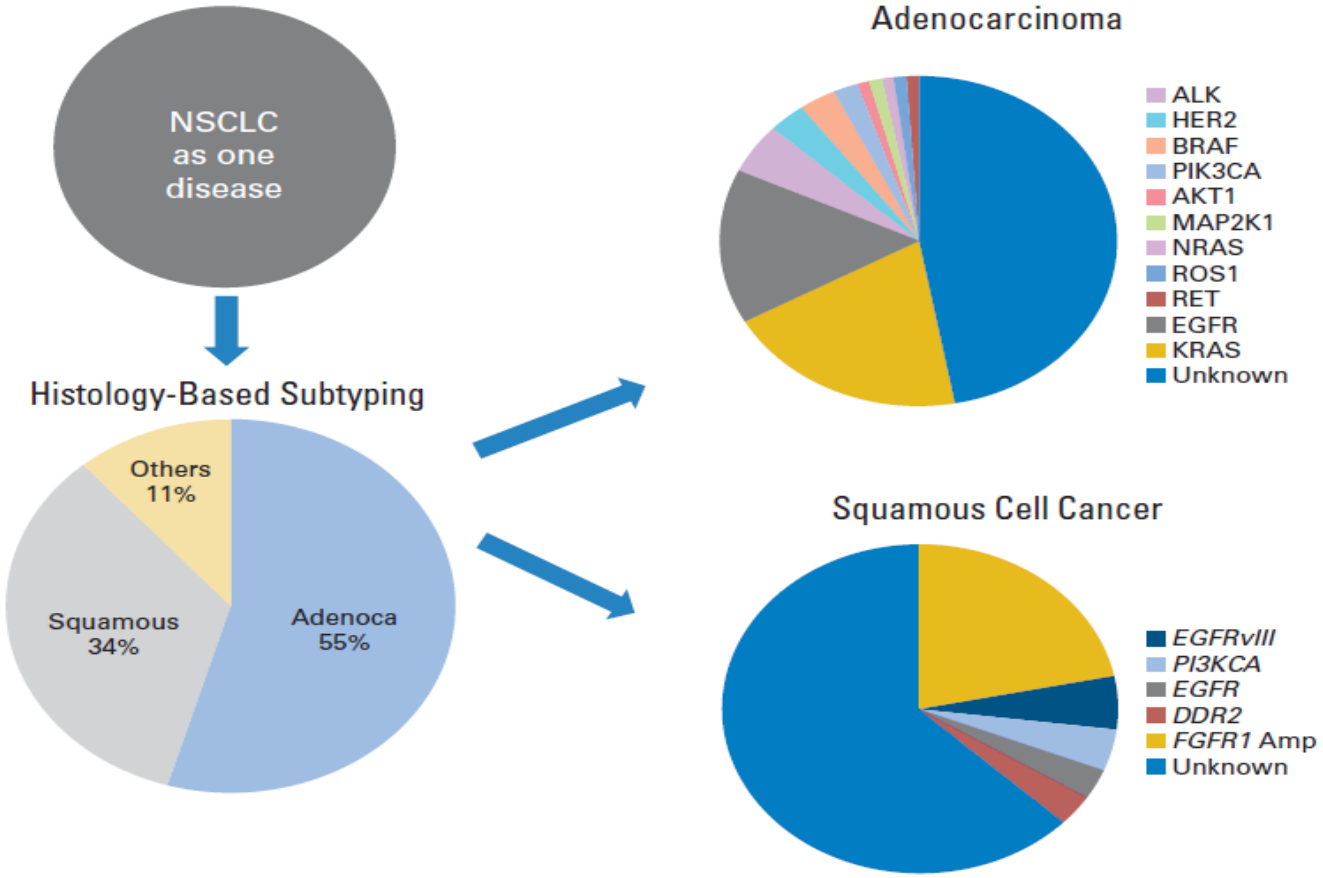
CAMBIO PARADIGMA EN CPCNP

CCR Translations
Commentary on Sakairi et al., p. 4938

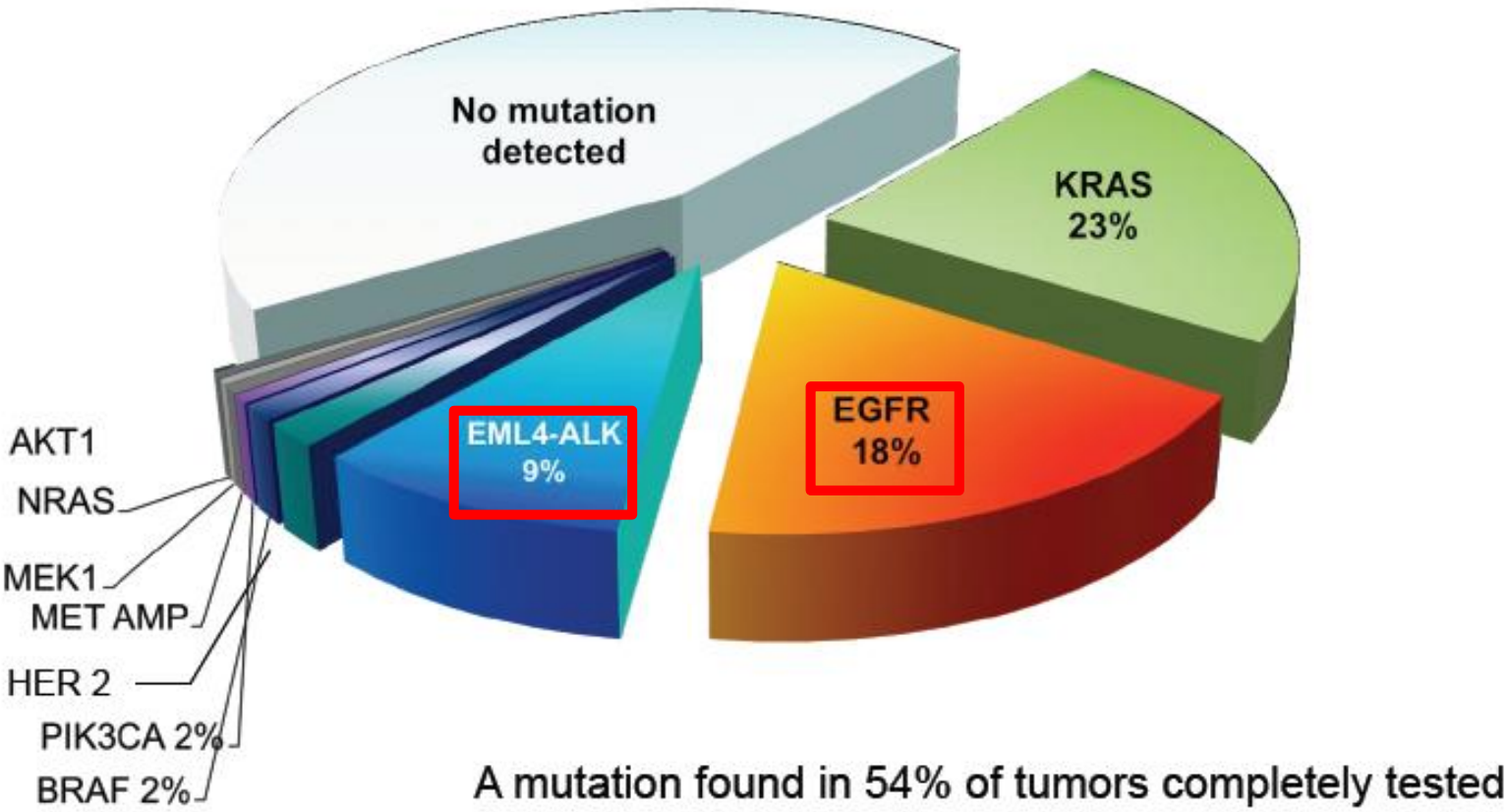
Clinical Cancer Research

The Tissue Is the Issue: Personalized Medicine for Non-Small Cell Lung Cancer

Fred R. Hirsch[1], Murry W. Wynes[1], David R. Gandara[2], and Paul A. Bunn, Jr.[1]



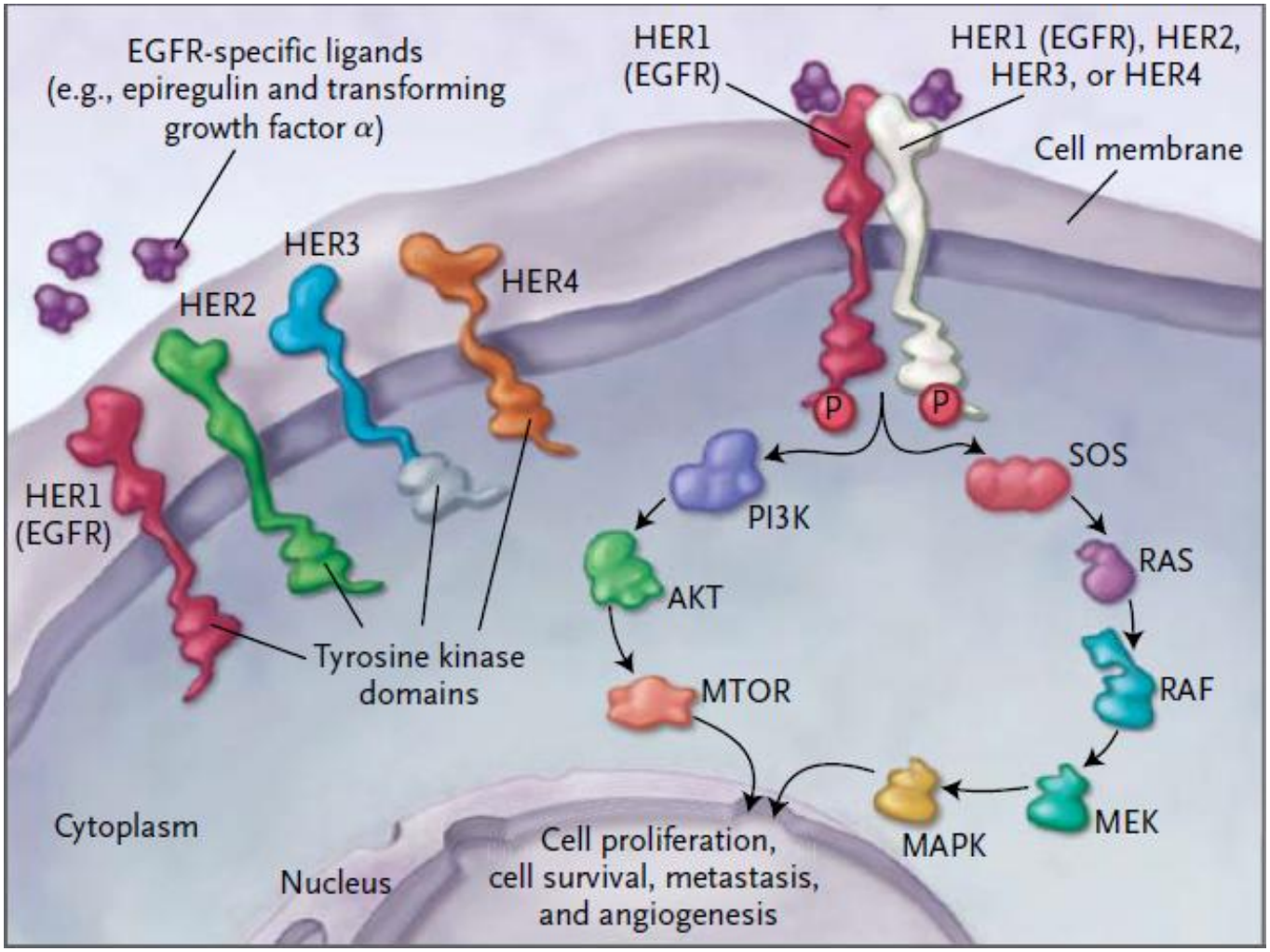
MUTACIONES EN CPCNP (ADC)



Lung Cancer Mutation Consortium

EGFR

EGFR

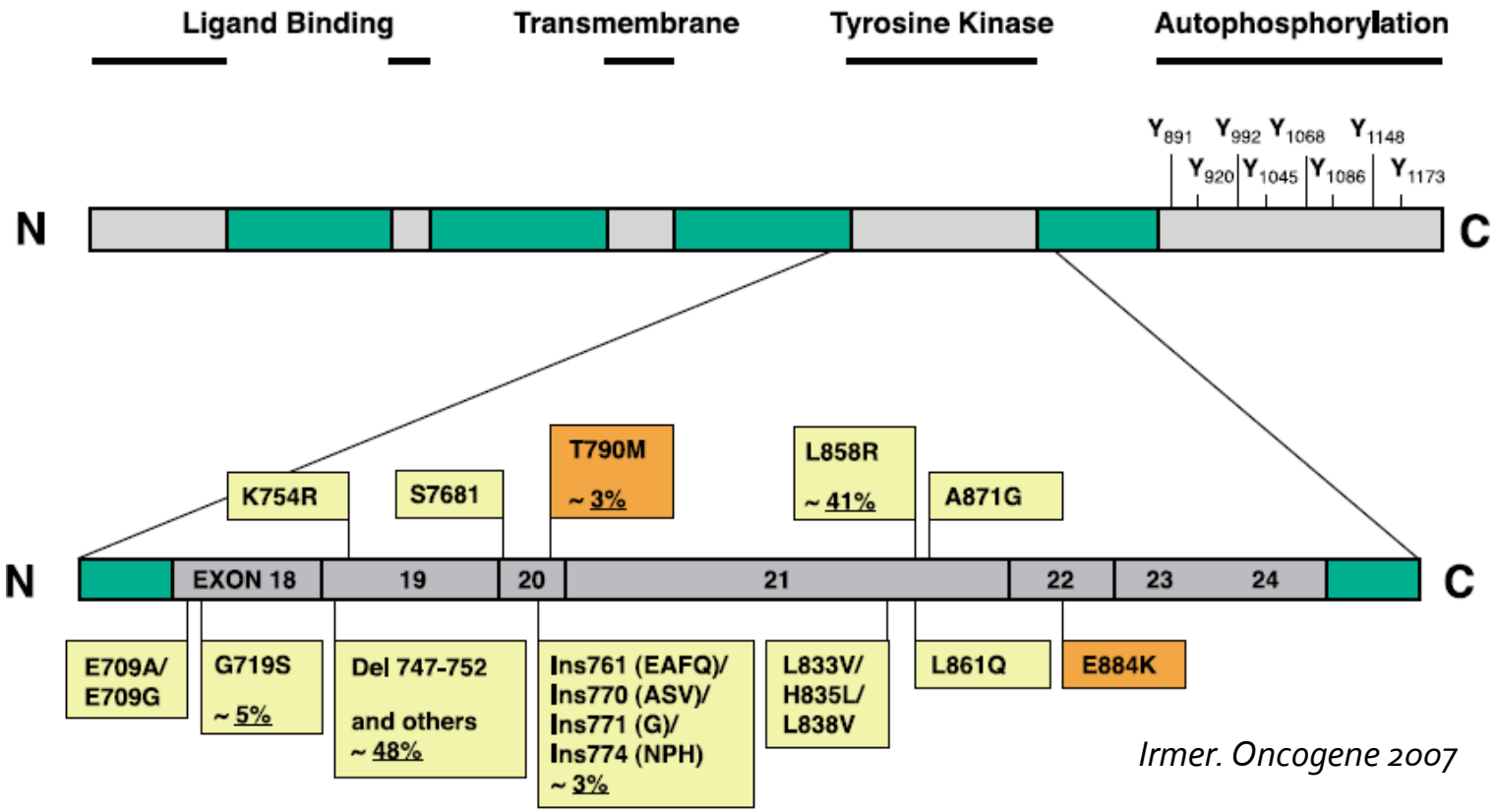


Cataldo NEJM 2011

Frequency of *EGFR* mutations in different NSCLC patient subgroups

	Total, %	Non-east Asian, %	East Asian %
All subgroups	19	10	30
Smokers	11	4	17
Nonsmokers	54	35	60
Adenocarcinoma	42	16	49
Non-adenocarcinoma	3	1	4
Male	16	1	22
Female	46	20	58

Adapted from Jänne and Johnson, 2006.

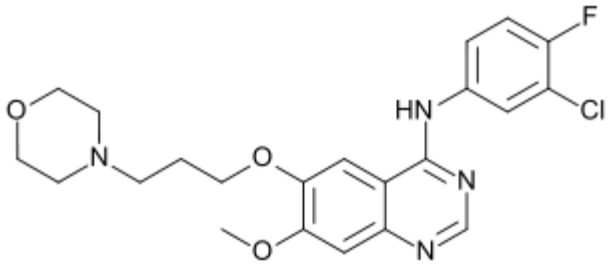


Irmer. Oncogene 2007

EGFR

GEFITINIB

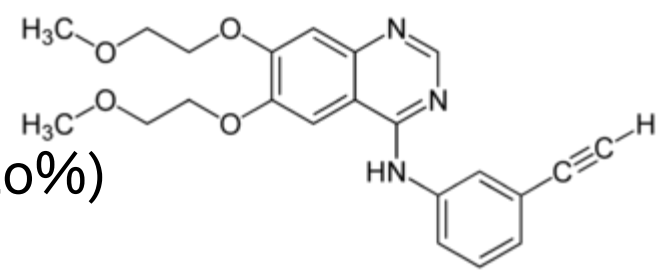
Inhibidor reversible EGFR



ERLOTINIB

Inhibidor reversible EGFR

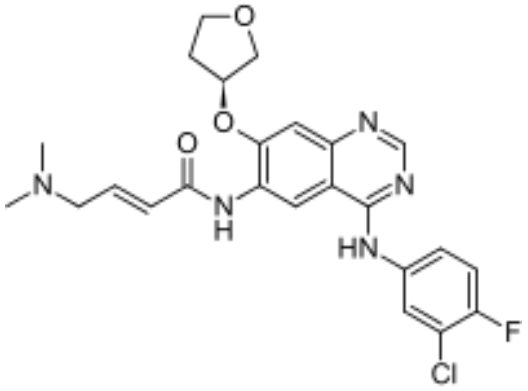
Actividad en EGFR no mutados (Resp.<10%)



AFATINIB

Inhibidor **irreversible** EGFR, HER2, ErbB4

Actividad tras fallo de Gefitinib / Erlotinib



EGFR. Gefitinib

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2010;362:2380-8.

Gefitinib or Chemotherapy for Non–Small-Cell Lung Cancer with Mutated EGFR

Makoto Maemondo, M.D., Ph.D., Akira Inoue, M.D., Ph.D.,

CPNCP IIIb-IV, 1ª línea

Mut. Sensibilidad EGFR**

Ausencia T790M exon20

n: 230

RANDOMIZACIÓN*

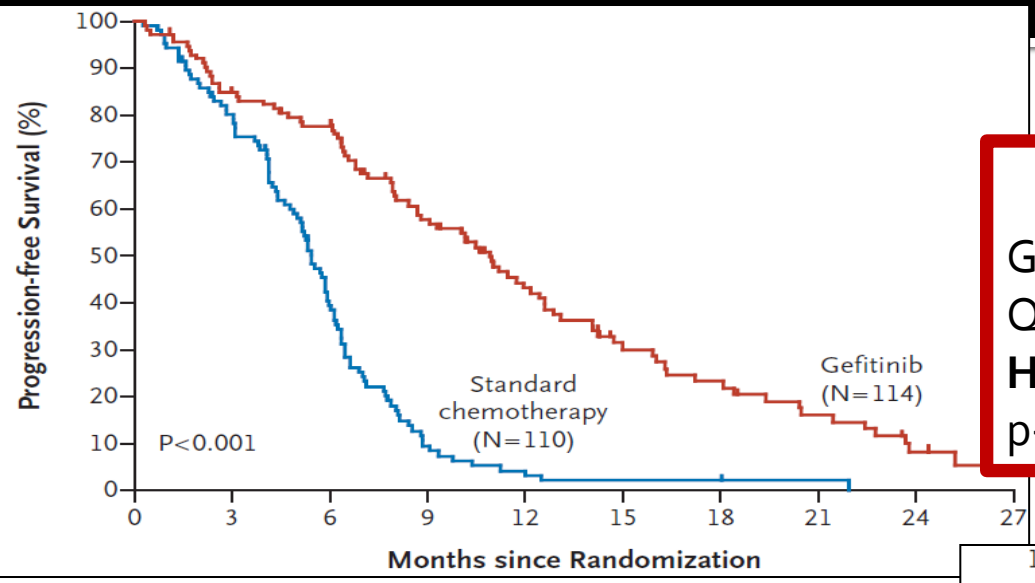
Gefitinib
250mg día

Carboplatino/Paclitaxel
AUC 5-6/200mg/m²
cada 21d

***randomización 1:1**

****delección exon19, L858R exon21**

Eficacia



PFS

Gefitinib 10.8 m

QT 5.4 m

HR 0.30,

p<0.001

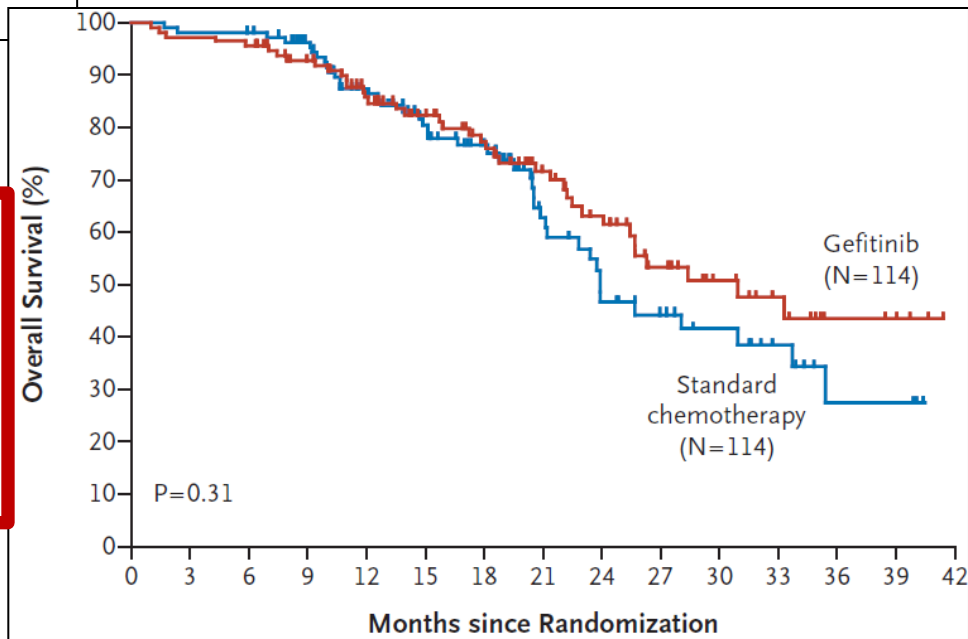
OS

Gefitinib 30.5 m

QT 23.6 m

P=0.31

Cross-over: 95%



Toxicidad

Table 3. Common Toxic Effects in the Safety Population, According to Treatment Group.*

Toxic Effect	Gefitinib (N=114)					Carboplatin–Paclitaxel (N=113)					P Value for Grade ≥3
	Grade 1	Grade 2	Grade 3	Grade 4	Grade ≥3	Grade 1	Grade 2	Grade 3	Grade 4	Grade ≥3	
	no. of patients				*no. (%)*	*no. of patients*				*no. (%)*	
Diarrhea	32	6	1	0	1 (0.9)	7	0	0	0	0	<0.001
Appetite loss	7	4	6	0	6 (5.3)	39	18	7	0	7 (6.2)	<0.001
Fatigue	8	1	3	0	3 (2.6)	19	11	1	0	1 (0.9)	0.002
Rash	38	37	6	0	6 (5.3)	8	14	3	0	3 (2.7)	<0.001
Neuropathy (sensory)	0	1	0	0	0	28	27	7	0	7 (6.2)	<0.001
Arthralgia	1	2	1	0	1 (0.9)	25	21	8	0	8 (7.1)	<0.001
Pneumonitis	3	0	2	1†	3 (2.6)	0	0	0	0	0	0.02
Aminotransferase elevation	20	13	29	1	30 (26.3)	31	5	0	1	1 (0.9)	<0.001
Neutropenia	5	1	0	1	1 (0.9)	4	9	37	37	74 (65.5)	<0.001
Anemia	19	2	0	0	0	35	32	6	0	6 (5.3)	<0.001
Thrombocytopenia	8	0	0	0	0	25	3	3	1	4 (3.5)	<0.001
Any	17	44	43	4†	47 (41.2)	4	25	41	40	81 (71.7)	<0.001

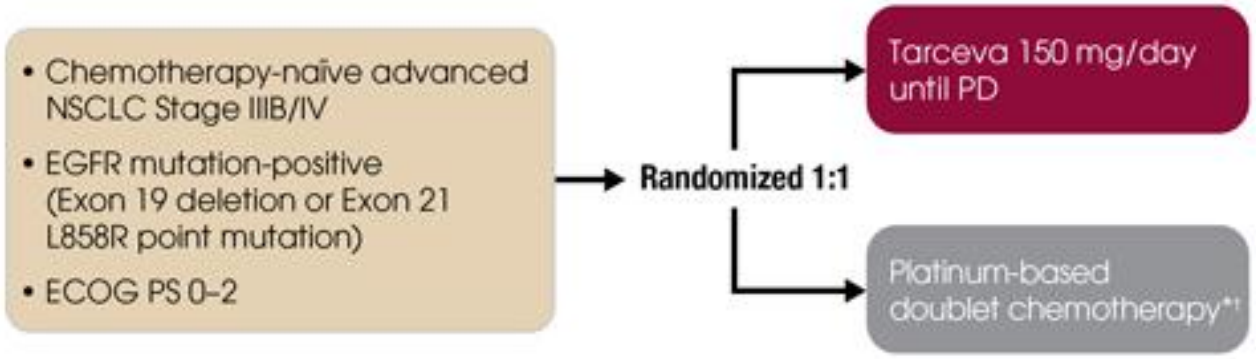
* Toxic-effect grades are based on the National Cancer Institute Common Terminology Criteria (version 3.0).
† One patient counted here had a grade 5 toxic effect.

EGFR. Erlotinib

Lancet Oncol 2012

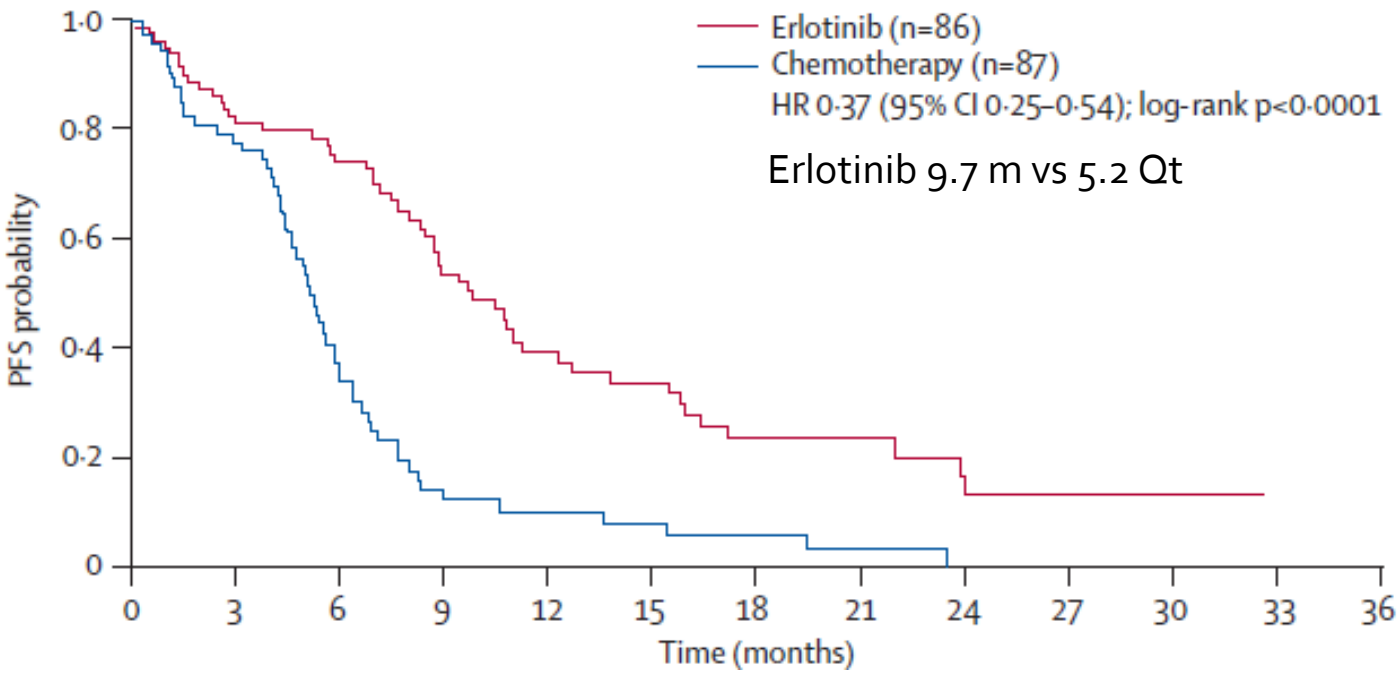
Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial

Rafael Rosell, Enric Carcereny, Radj Gervais, Alain Vergnenegre, Bartomeu Massuti, Enriqueta Felip, Ramon Palmero, Ramon Garcia-Gomez, Cinta Pallares, Jose Miguel Sanchez, Rut Porta, Manuel Cobo, Pilar Garrido, Flavia Longo, Teresa Moran, Amelia Insa, Filippo De Marinis, Romain Corre, Isabel Bover, Alfonso Illiano, Eric Dansin, Javier de Castro, Michele Milella, Noemi Reguart, Giuseppe Altavilla, Ulpiano Jimenez, Mariano Provencio, Miguel Angel Moreno, Josefa Terrasa, Jose Muñoz-Langa, Javier Valdivia, Dolores Isla, Manuel Domine, Olivier Molinier, Julien Mazieres, Nathalie Baize, Rosario Garcia-Campelo, Gilles Robinet, Delvys Rodriguez-Abreu, Guillermo Lopez-Vivanco, Vittorio Gebbia, Lioba Ferrera-Delgado, Pierre Bombaron, Reyes Bernabe, Alessandra Bearz, Angel Artal, Enrico Cortesi, Christian Rolfo, Maria Sanchez-Ronco, Ana Drozdowskyj, Cristina Queralt, Itziar de Aguirre, Jose Luis Ramirez, Jose Javier Sanchez, Miguel Angel Molina, Miquel Taron, Luis Paz-Ares, on behalf of the Spanish Lung Cancer Group in collaboration with the Groupe Français de Pneumo-Cancérologie and the Associazione Italiana Oncologia Toracica



*EURTAC regimens included: cisplatin/gemcitabine, cisplatin/docetaxel, carboplatin/gemcitabine and carboplatin/docetaxel.

Eficacia



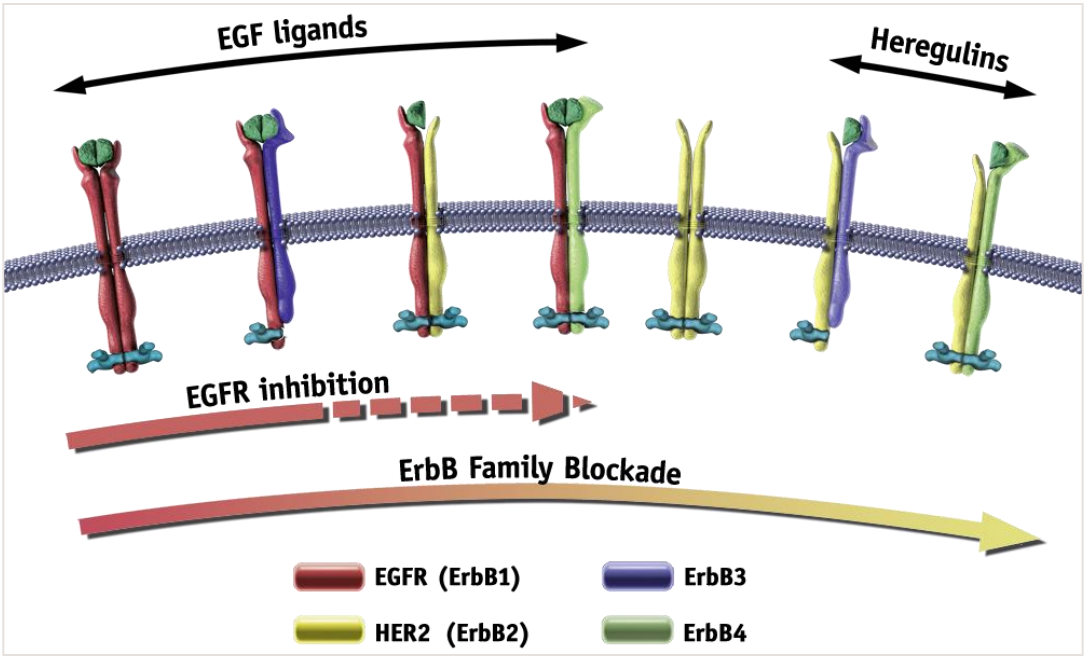
Erlotinib 9.7 m vs 5.2 Qt

Toxicidad

	Erlotinib (n=84)			Standard chemotherapy (n=82)			p value for grade 3–4
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	
Fatigue	43 (51%)	5 (6%)	0	43 (52%)	16 (20%)	0	0·0086
Rash	56 (67%)	11 (13%)	0	4 (5%)	0	0	0·0007

	Erlotinib group (n=84)	Standard chemotherapy group (n=82)
Any adverse event (all grades)	82 (98%)	81 (99%)
Treatment-related adverse event (all grades)	78 (93%)	78 (95%)
Grade 3 or 4 adverse event	38 (45%)	55 (67%)
Dose reduction due to adverse event	18 (21%)	23 (28%)
Dose reduction due to drug-related adverse event	18 (21%)	21 (26%)
Discontinuation due to an adverse event	11 (13%)	19 (23%)
Discontinuation due to drug-related adverse event	5 (6%)	16 (20%)
Any severe adverse event	27 (32%)	25 (30%)
Treatment-related severe adverse event	5 (6%)	16 (20%)
Treatment-related death*	1 (1%)	2 (2%)
Interstitial lung disease-like events	1 (1%)	1 (1%)

EGFR. Afatinib



- Afatinib es un inhibidor **irreversible** oral de la familia ErbB.
  - Inhibicion de la heterodimerización de la familia de receptores ErbB

Li D, et al. *Oncogene* 2008;**27**:4702–11.

EGFR. Afatinib

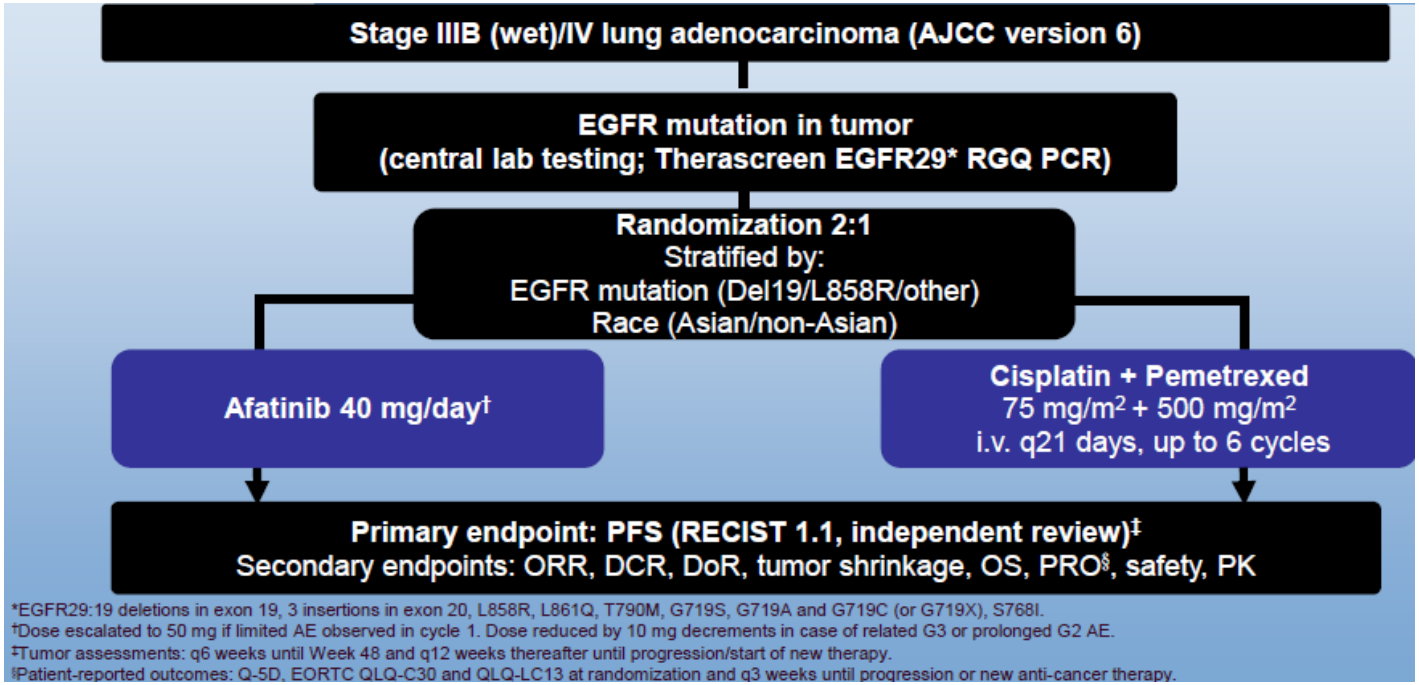
VOLUME 31 · NUMBER 27 · SEPTEMBER 20 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

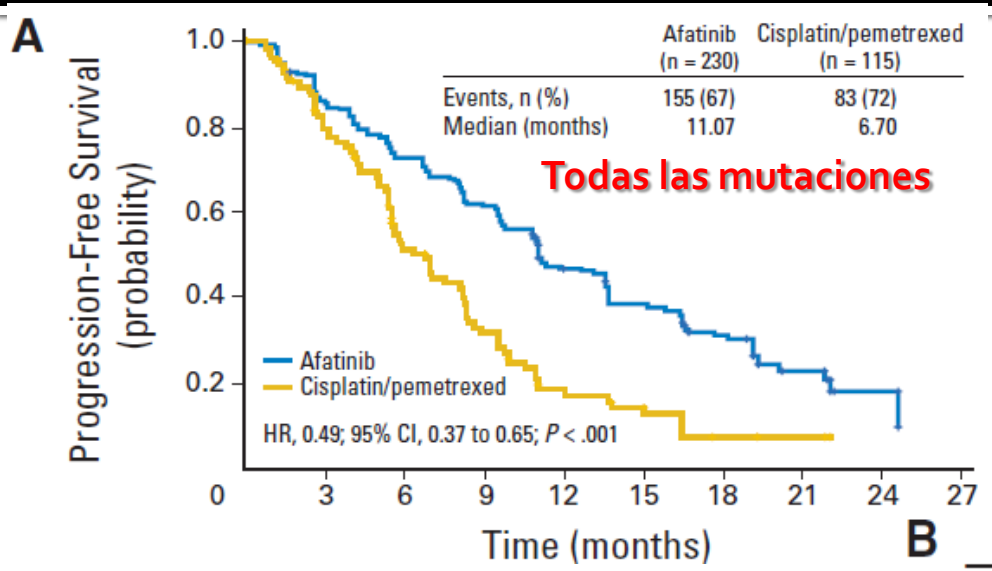
Phase III Study of Afatinib or Cisplatin Plus Pemetrexed in Patients With Metastatic Lung Adenocarcinoma With *EGFR* Mutations

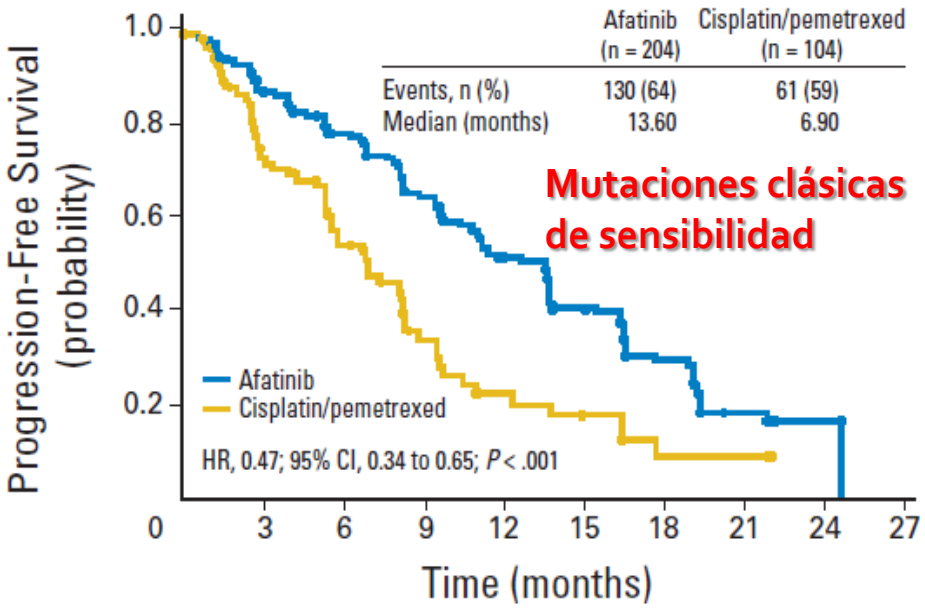
Lecia V. Sequist, James Chih-Hsin Yang, Nobuyuki Yamamoto, Kenneth O'Byrne, Vera Hirsh, Tony Mok, Sarayut Lucien Geater, Sergey Orlov, Chun-Ming Tsai, Michael Boyer, Wu-Chou Su, Jaafar Bennouna, Terufumi Kato, Vera Gorbunova, Ki Hyeong Lee, Riyaz Shah, Dan Massey, Victoria Zazulina, Mehdi Shahidi, and Martin Schuler



*EGFR29:19 deletions in exon 19, 3 insertions in exon 20, L858R, L861Q, T790M, G719S, G719A and G719C (or G719X), S768I.
†Dose escalated to 50 mg if limited AE observed in cycle 1. Dose reduced by 10 mg decrements in case of related G3 or prolonged G2 AE.
‡Tumor assessments: q6 weeks until Week 48 and q12 weeks thereafter until progression/start of new therapy.
§Patient-reported outcomes: Q-5D, EORTC QLQ-C30 and QLQ-LC13 at randomization and q3 weeks until progression or new anti-cancer therapy.

Eficacia


A
Progression-Free Survival (probability)
1.0
0.8
0.6
0.4
0.2
0
3
6
9
12
15
18
21
24
27
Time (months)
Afatinib (n = 230)
Cisplatin/pemetrexed (n = 115)
Events, n (%) 155 (67) 83 (72)
Median (months) 11.07 6.70
Todas las mutaciones
Afatinib
Cisplatin/pemetrexed
HR, 0.49; 95% CI, 0.37 to 0.65; P < .001


B
Progression-Free Survival (probability)
1.0
0.8
0.6
0.4
0.2
0
3
6
9
12
15
18
21
24
27
Time (months)
Afatinib (n = 204)
Cisplatin/pemetrexed (n = 104)
Events, n (%) 130 (64) 61 (59)
Median (months) 13.60 6.90
Mutaciones clásicas de sensibilidad
Afatinib
Cisplatin/pemetrexed
HR, 0.47; 95% CI, 0.34 to 0.65; P < .001

Toxicidad

Table 2. Treatment-Related AEs*

	Afatinib (n = 229)				Cisplatin Plus Pemetrexed (n = 111)			
	All Grades		≥ Grade 3		All Grades		≥ Grade 3	
AE	No.	%	No.	%	No.	%	No.	%
Diarrhea	218	95.2	33	14.4	17	15.3	0	0.0
Rash/acne†	204	89.1	37	16.2	7	6.3	0	0.0
Stomatitis/mucositis†	165	72.1	20	8.7	17	15.3	1	0.9
Paronychia	130	56.8	26	11.4	0	0.0	0	0.0
Dry skin	67	29.3	1	0.4	2	1.8	0	0.0
Decreased appetite	47	20.5	7	3.1	59	53.2	3	2.7
Pruritus	43	18.8	1	0.4	1	0.9	0	0.0
Nausea	41	17.9	2	0.9	73	65.8	4	3.6
Fatigue†	40	17.5	3	1.3	52	46.8	14	12.6
Vomiting	39	17.0	7	3.1	47	42.3	3	2.7
Epistaxis	30	13.1	0	0.0	1	0.9	1	0.9
Cheilitis	28	12.2	0	0.0	1	0.9	0	0.0
Anemia‡	7	3.1	1	0.4	31	27.9	7	6.3
Constipation	6	2.6	0	0.0	21	18.9	0	0.0
Leukopenia‡	4	1.7	1	0.4	21	18.9	9	8.1
Neutropenia‡	2	0.9	1	0.4	35	31.5	20	18.0

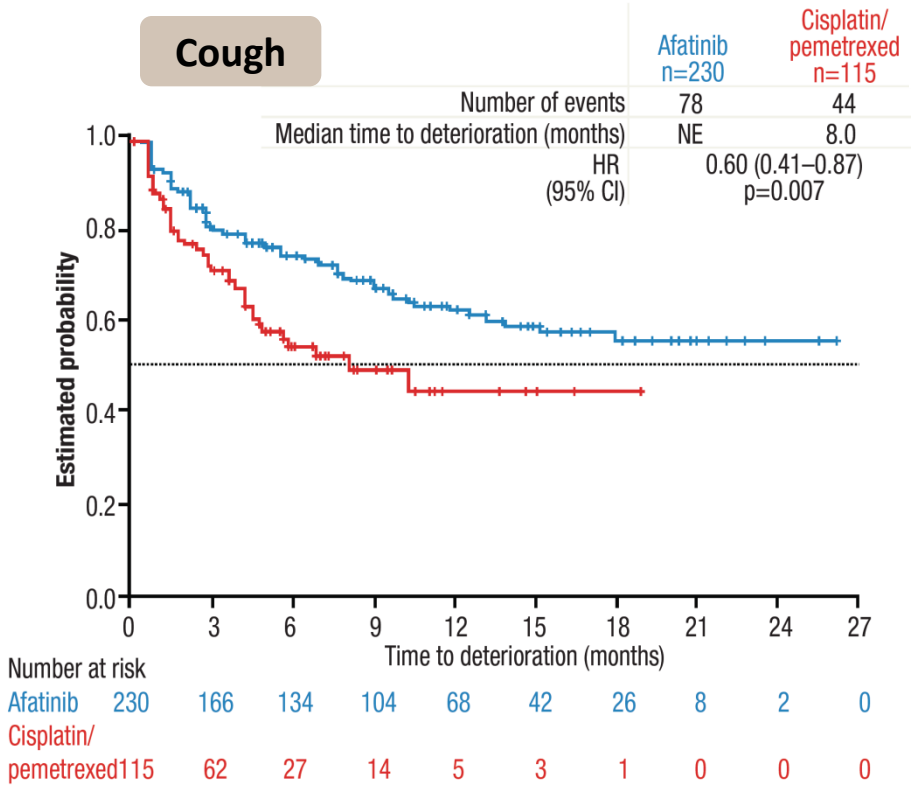
	Afatinib (n=229) n (%)	Cis/pem (n=111) n (%)
Any AEs	229 (100.0)	109 (98.2)
Drug-related AEs	228 (99.6)	106 (95.5)
Any AEs grade ≥3	139 (60.7)	63 (56.8)
Drug-related AEs ≥3	112 (48.9)	53 (47.7)
AE leading to discontinuation	23 (10.0)	16 (14.4)
Drug-related AEs leading to discontinuation	18 (7.9)*†	13 (11.7)
SAE	66 (28.8)	25 (22.5)
Drug-related SAE	33 (14.4)	16 (14.4)
Drug-related AEs leading to death	4 (1.7)‡	0 (0.0)

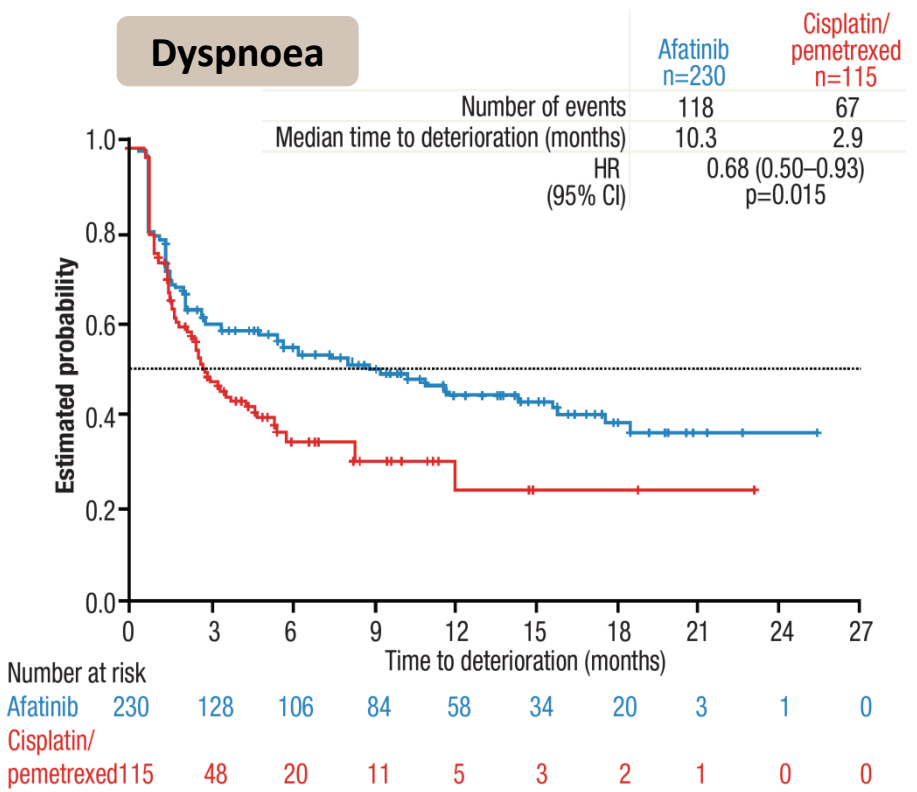
*Includes 3 patients (1%) who discontinued due to diarrhea, no discontinuations for rash.
†Includes 3 patients (1%) with ILD-like events (1 G1, 1 G3; 1 G5).
‡Preferred terms: dyspnea, sepsis, ARDS, death (unknown cause).

Treatment duration (median)
- Afatinib: 16 cycles (336 days; range 7–827 days), 38% one dose reduction, 19% two dose reductions
- Cis/pem: 6 cycles (range 1–6); 75% patients ≥4 cycles, 55% 6 cycles

Sequist et al., J Clin Oncol 31:3327–3334. Yang et al., ASCO 2012

Control de síntomas





Time to deterioration for pain favoured afatinib (HR=0.83; p=0.1913)

- **First-line afatinib significantly delayed time to deterioration for cough and dyspnoea**

Sequist et al., J Clin Oncol 31:3327–3334. Yang et al., ASCO 2012. James Chih-Hsin Yang et al., J Clin Oncol 2013 Sep 20;31(27):3342-3350

EGFR. Afatinib

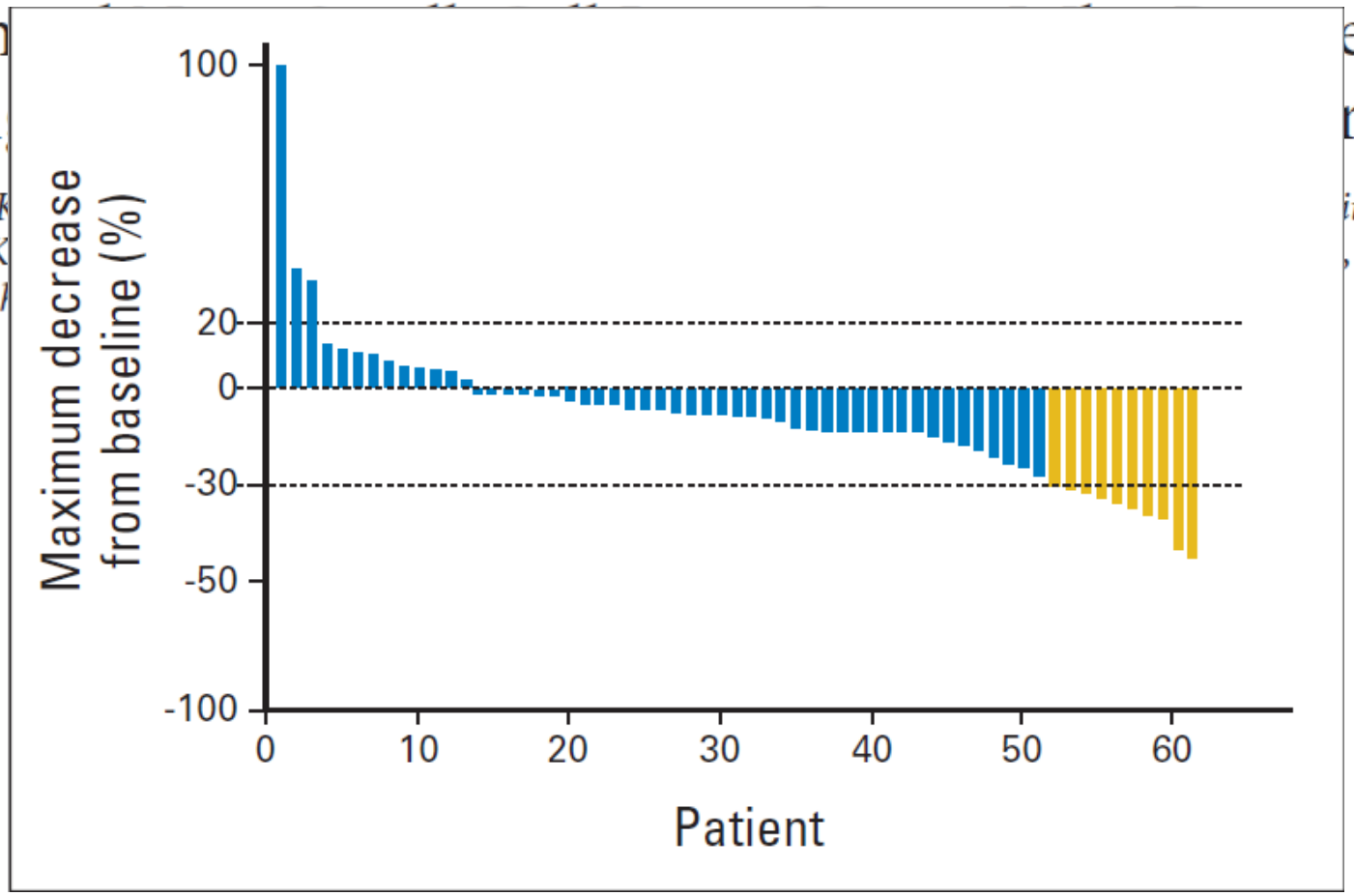
VOLUME 31 · NUMBER 27 · SEPTEMBER 20 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

LUX-Lung 4: A Phase II Trial of Afatinib in Patients With Advan essed Durin r Both

Nobuyuki K ito Ichinose, Kunihiko K Mehdi Shah



Caso Clínico EGFR

- Paciente mujer de 70 años, no fumadora.

- Antecedentes patológicos:
  - HTA en tratamiento con valsartan
  - DM en tratamiento con metformina
  - Dislipemia en tratamiento con simvastatina

Primer síntoma:

- Abril 2013:
  - Disnea de medianos esfuerzos progresiva
- Rx tórax(3/6/13):
  - Condensación lóbulo inferior derecho: antibiótico
- Ante la no mejoría se deriva a nuestro centro al circuito de diagnóstico rápido de cáncer de pulmón

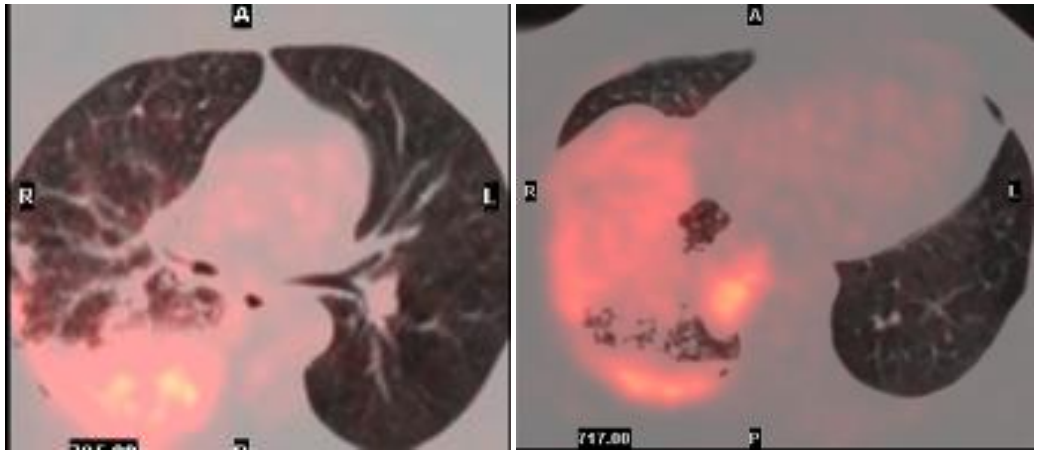
Analítica y TC:

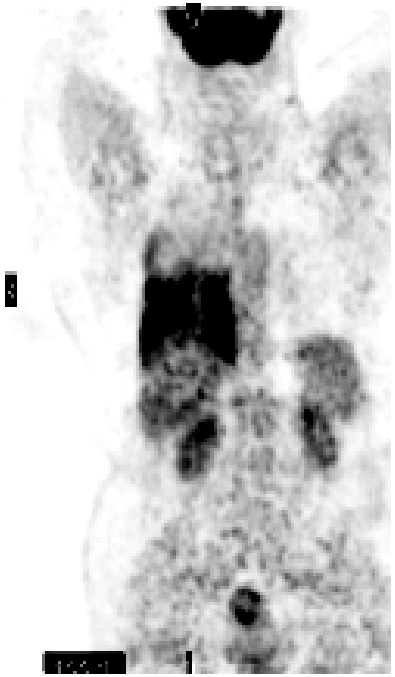
- Analítica (25/07/2013): normal.

- TC toráx-abdomen superior (04/07/2013): Ocupación del espacio aéreo en pulmon derecho por parte de componente solido todo indicativo de proceso neoformativo tipo adenocarcinoma como primera opción. No se aprecian adenopatias ni claras lesiones secundarias. El estadiaje TC seria T4 N0 M0 asociado a presencia de probable linfangitis

PET/TC:

- PET (29/07/2013): lesión hipermetabólica (SUV 8) pulmonar derecha con afectación del LM, LID y probablemente del LSD sugestiva de un proceso neoproliferativo primario.





FBS y AP:

- BRONCOFIBROSCÒPIA (31/07/2013): estenosis concéntrica sin infiltración del bronquio lobar inferior derecho. BAS, cepillado bronquial i biopsias transbronquiales.

- AP: Adenocarcinoma con patrón de crecimiento predominantemente acinar

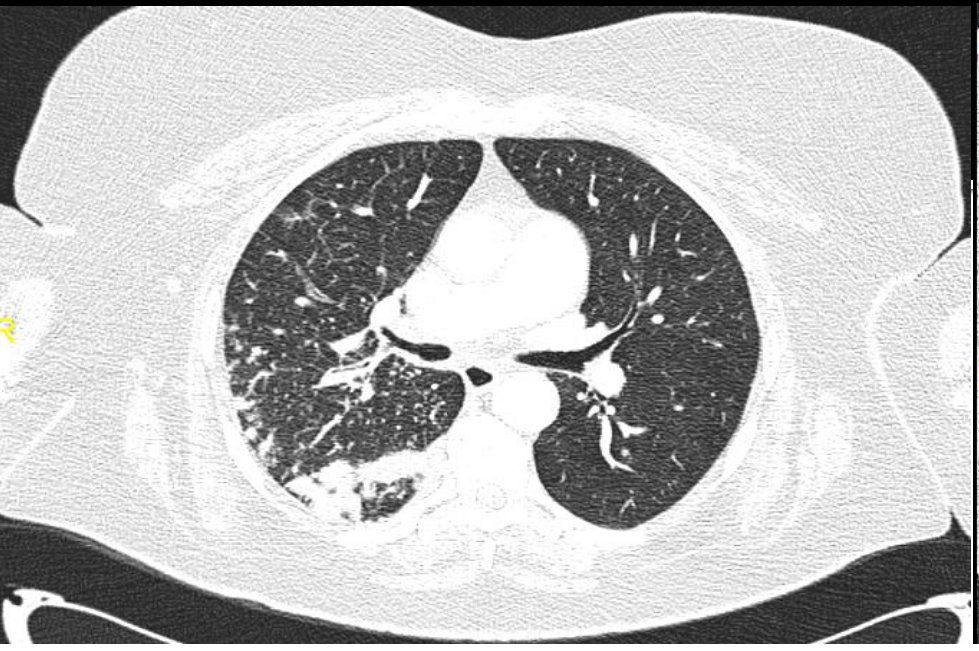
- ***EGFR* mutación exón 19** (E746_S752delinsV).

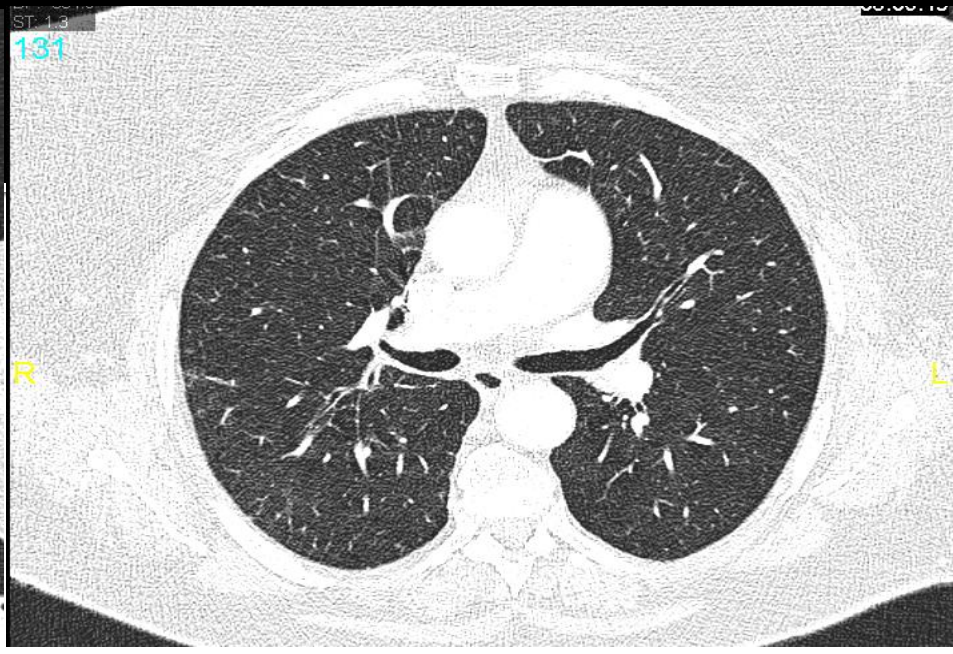
Tratamiento:

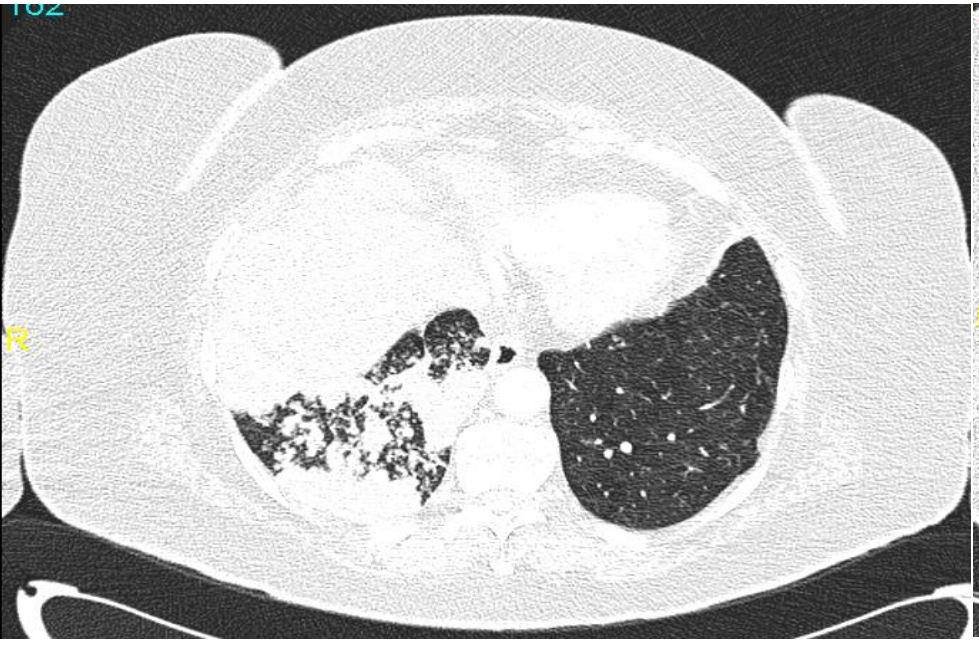
- Agosto 2013: Inicia afatinib 40mg/día
- Síntomas:
  - Resolución de la disnea, ECOG PS:0
- Toxicidades:
  - Rash cutáneo G1
  - Mucositis G2
  - Diarreas G2
- Disminución dosis afatinib a 30mg/día
- Desde entonces, resolución toxicidades

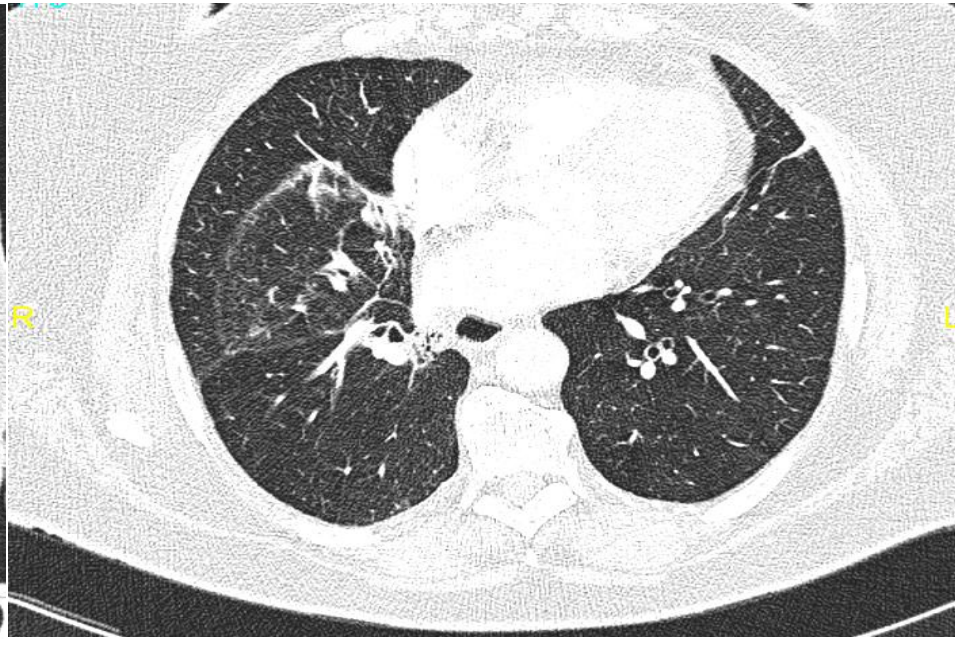
Pre afatinib

Post afatinib







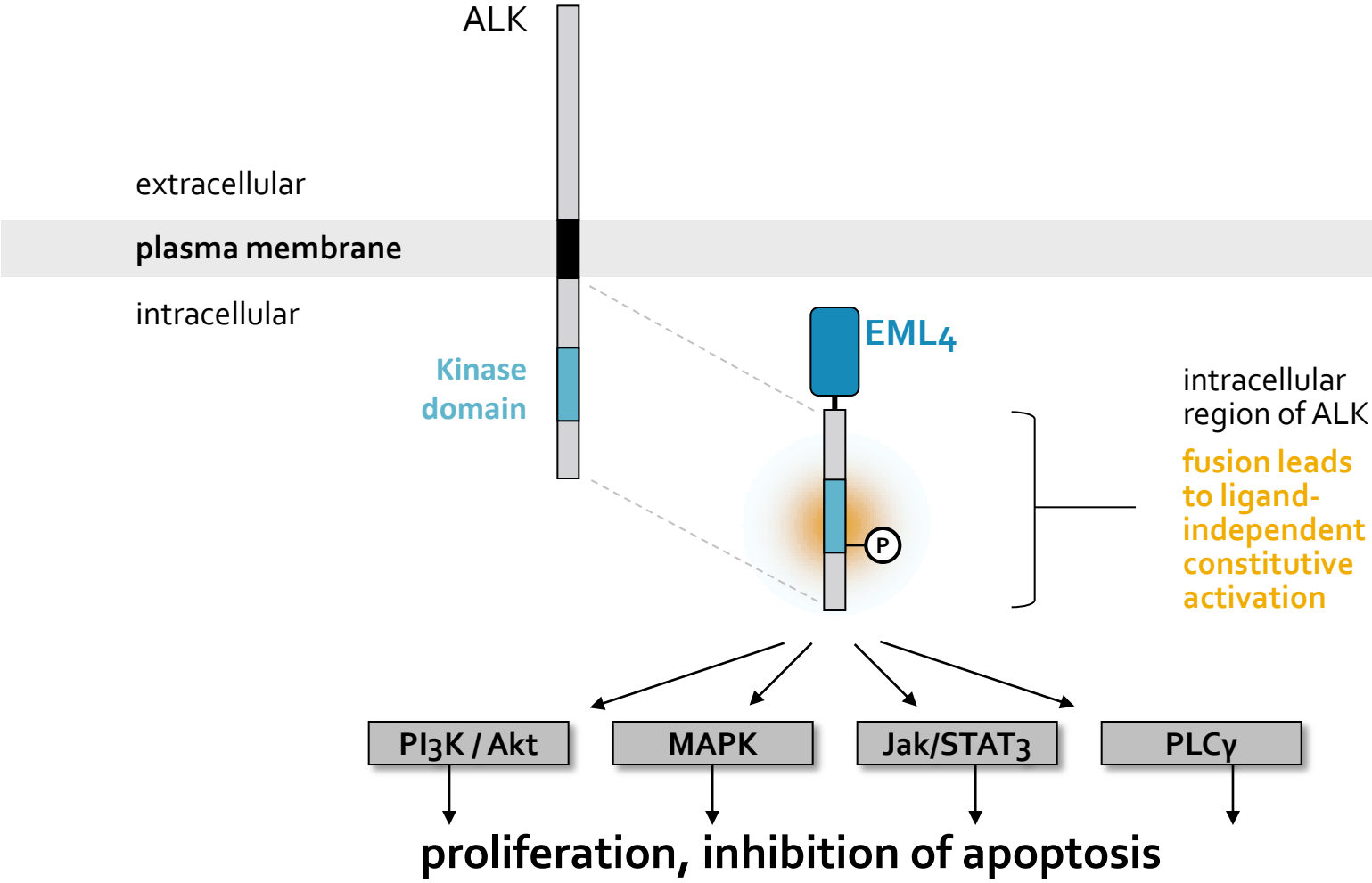


Seguimiento:

- Abril 2014: Último control clínico y por TC
  - Asintomática
  - No toxicidades
  - No evidencia de progresión

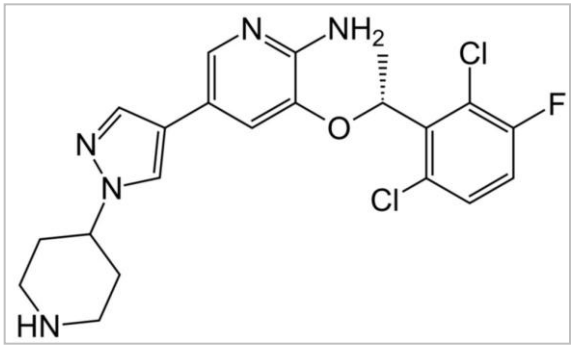
ALK

Signaling via the ALK Mutant Fusion Proteins

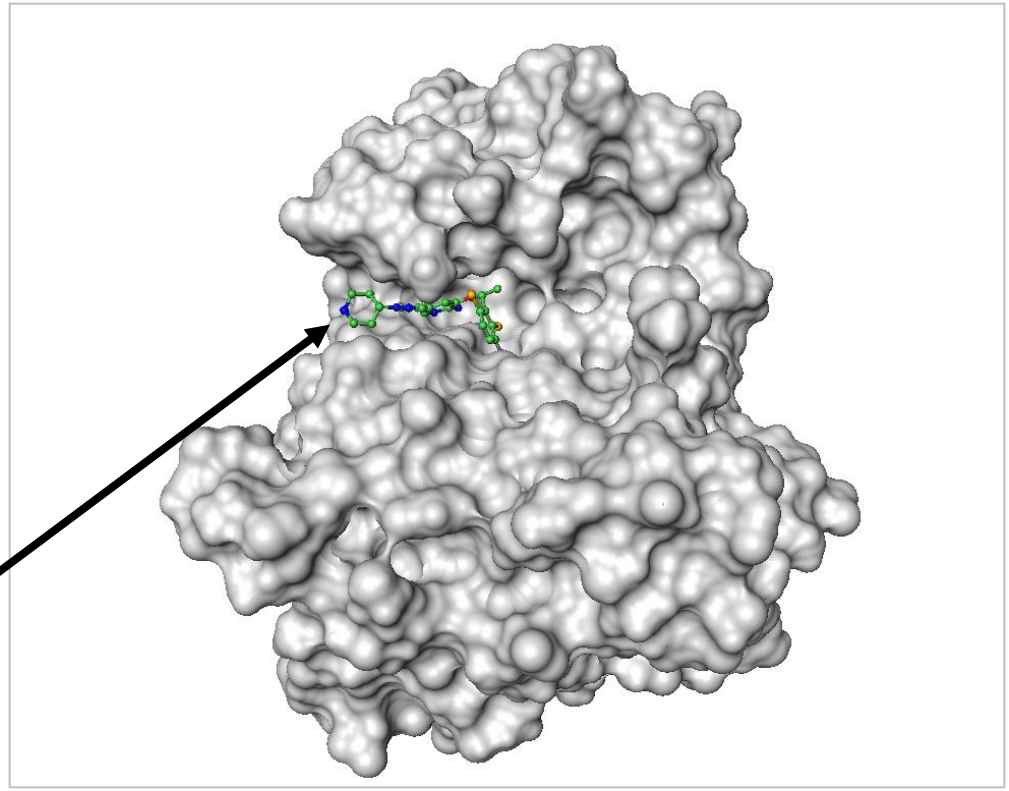


CRIZOTINIB

- Crizotinib es un Inhibidor tirosin-kinasa dual de ALK y c-Met oral

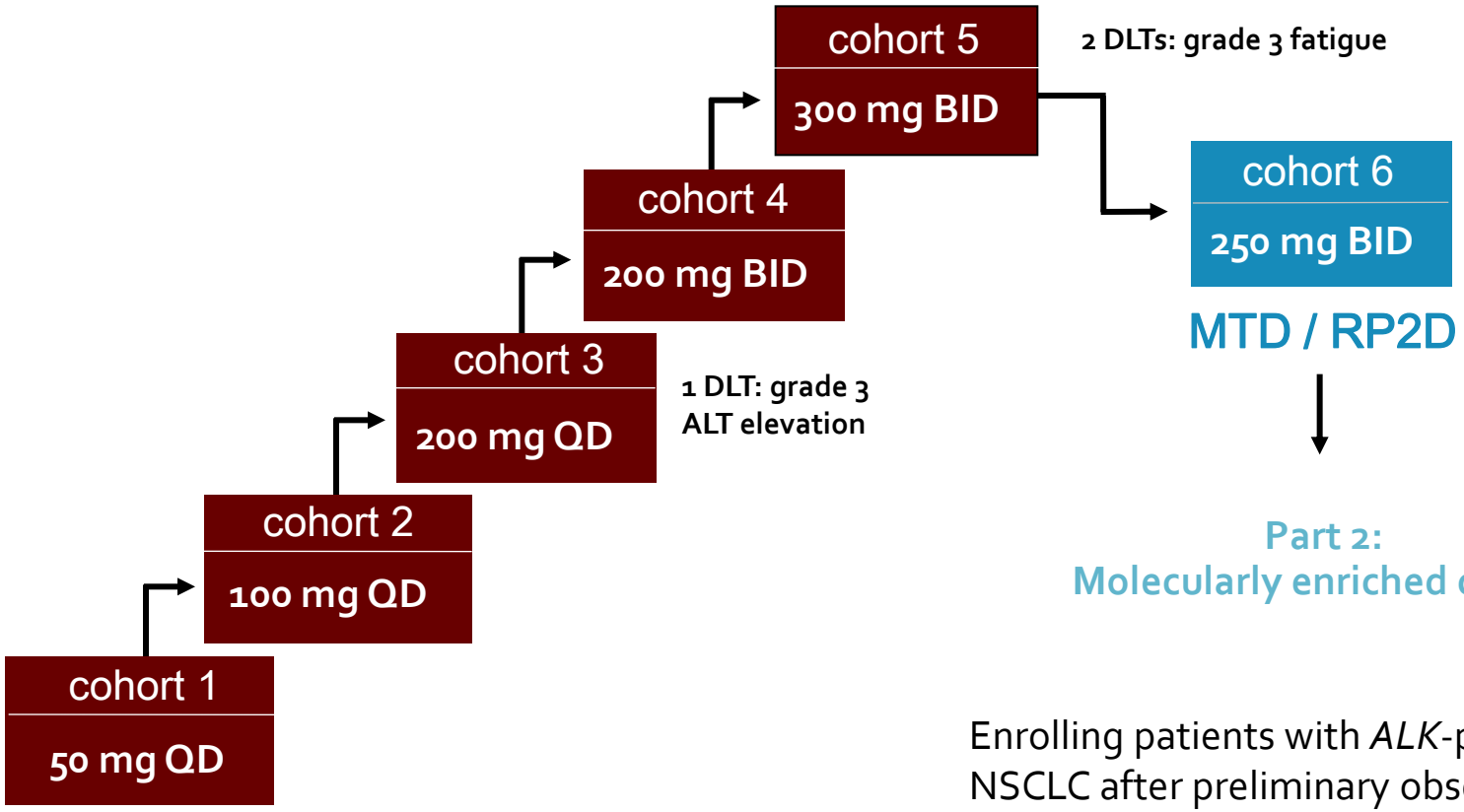


Molecular structure of crizotinib



Crizotinib in the ATP binding pocket of the ALK protein

Phase I Study A8081001 & Expanded Cohort



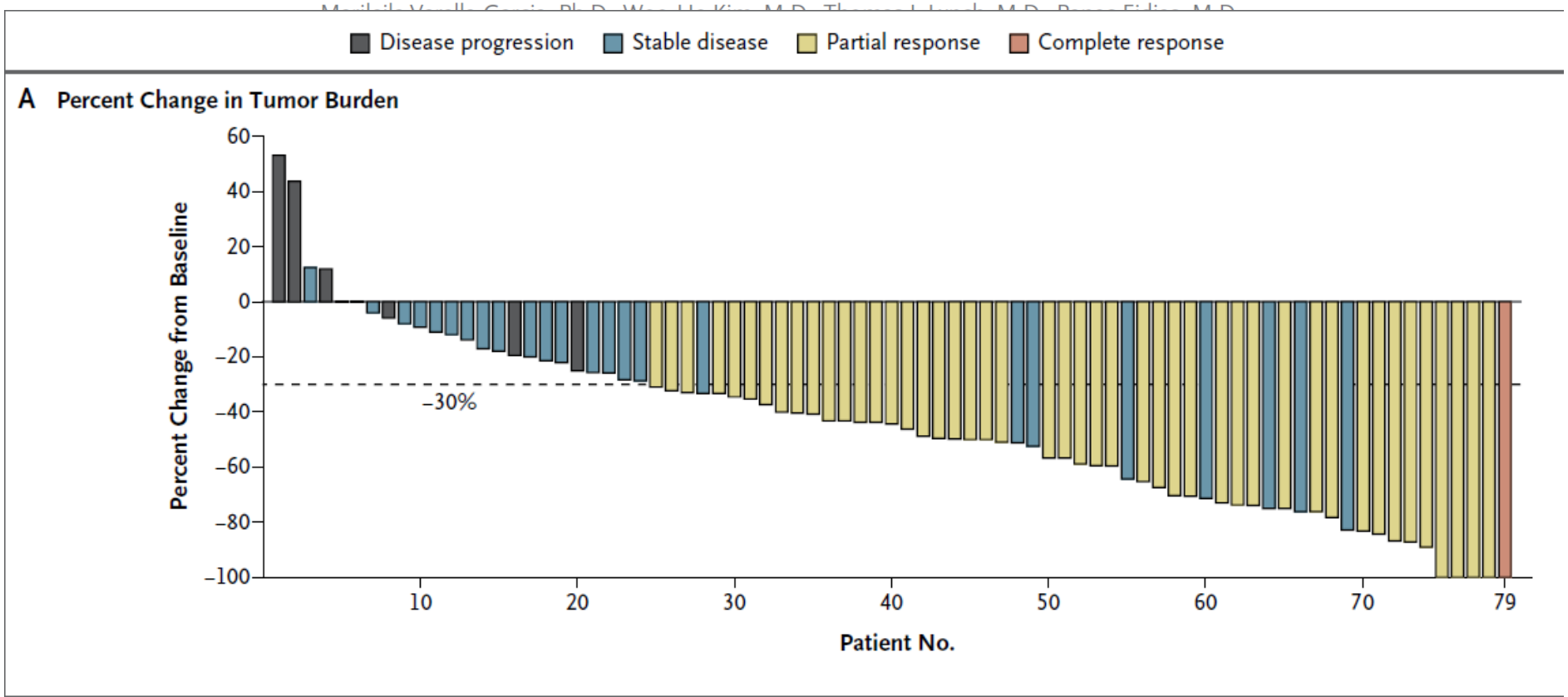
Enrolling patients with *ALK*-positive NSCLC after preliminary observation of impressive activity in a few patients

The NEW ENGLAND JOURNAL of MEDICINE

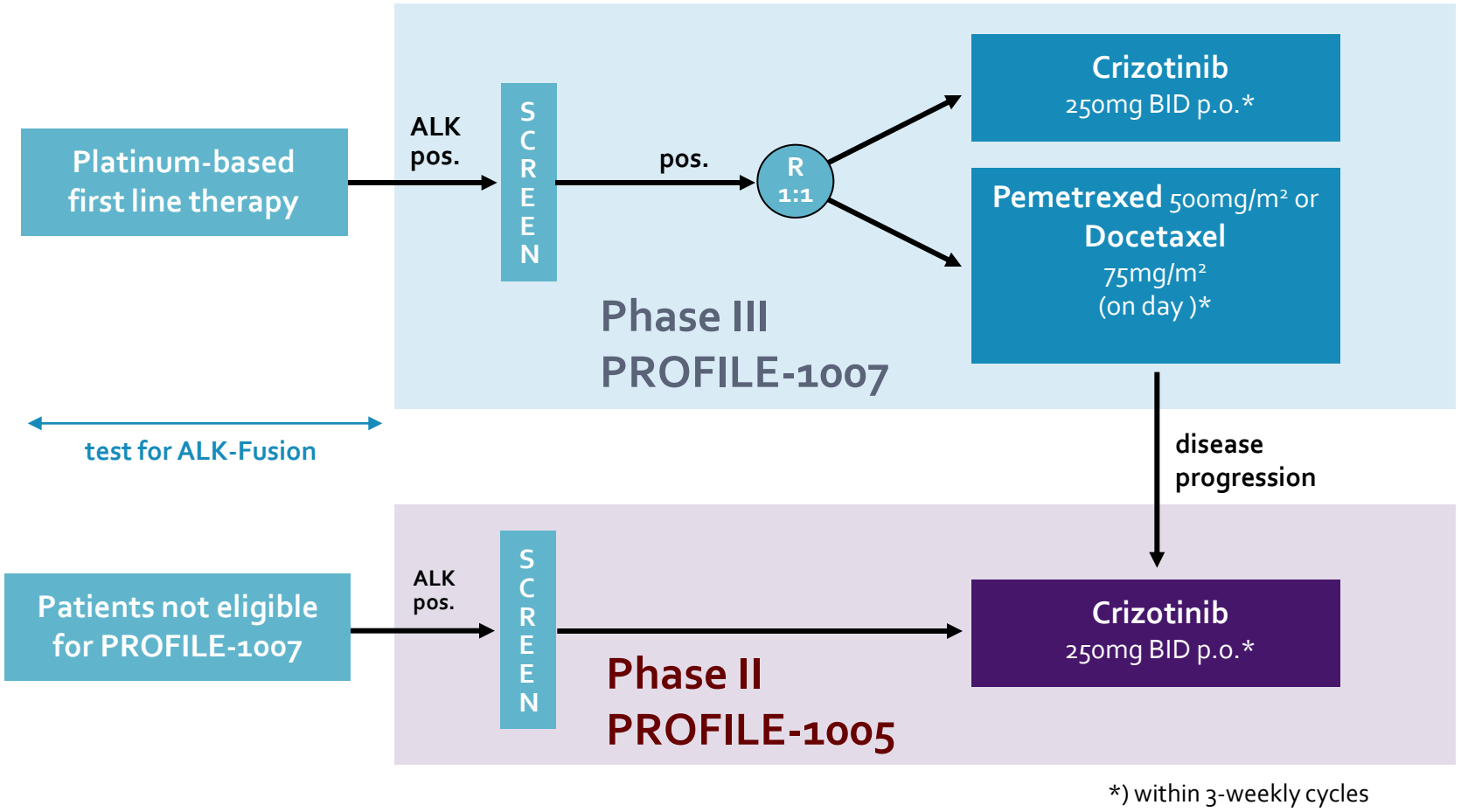
ESTABLISHED IN 1812 OCTOBER 28, 2010 VOL. 363 NO. 18

Anaplastic Lymphoma Kinase Inhibition in Non–Small-Cell Lung Cancer

Eunice L. Kwak, M.D., Ph.D., Yung-Jue Bang, M.D., Ph.D., D. Ross Camidge, M.D., Ph.D., Alice T. Shaw, M.D., Ph.D., Benjamin Solomon, M.B., B.S., Ph.D., Robert G. Maki, M.D., Ph.D., Sai-Hong I. Ou, M.D., Ph.D., Bruce J. Dezube, M.D., Pasi A. Jänne, M.D., Ph.D., Daniel B. Costa, M.D., Ph.D.,



Overview - PROFILE-1005 & 1007



*) within 3-weekly cycles

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

N Engl J Med 2013.

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

Alice T. Shaw, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Ph.D., Takashi Seto, M.D., Lucio Crinó, M.D., Myung-Ju Ahn, M.D., Tommaso De Pas, M.D., Benjamin Besse, M.D., Ph.D., Benjamin J. Solomon, M.B., B.S., Ph.D., Fiona Blackhall, M.D., Ph.D., Yi-Long Wu, M.D., Michael Thomas, M.D., Kenneth J. O'Byrne, M.D., Denis Moro-Sibilot, M.D., D. Ross Camidge, M.D., Ph.D., Tony Mok, M.D., Vera Hirsh, M.D., Gregory J. Riely, M.D., Ph.D., Shrividya Iyer, Ph.D., Vanessa Tassell, B.S., Anna Polli, B.S., Keith D. Wilner, Ph.D., and Pasi A. Jänne, M.D., Ph.D.

Key entry criteria

- *ALK*-positive advanced or metastatic stage IIB/IV NSCLC
- ECOG 0-2
- 1 prior platinum-based chemotherapy

RANDOMISE

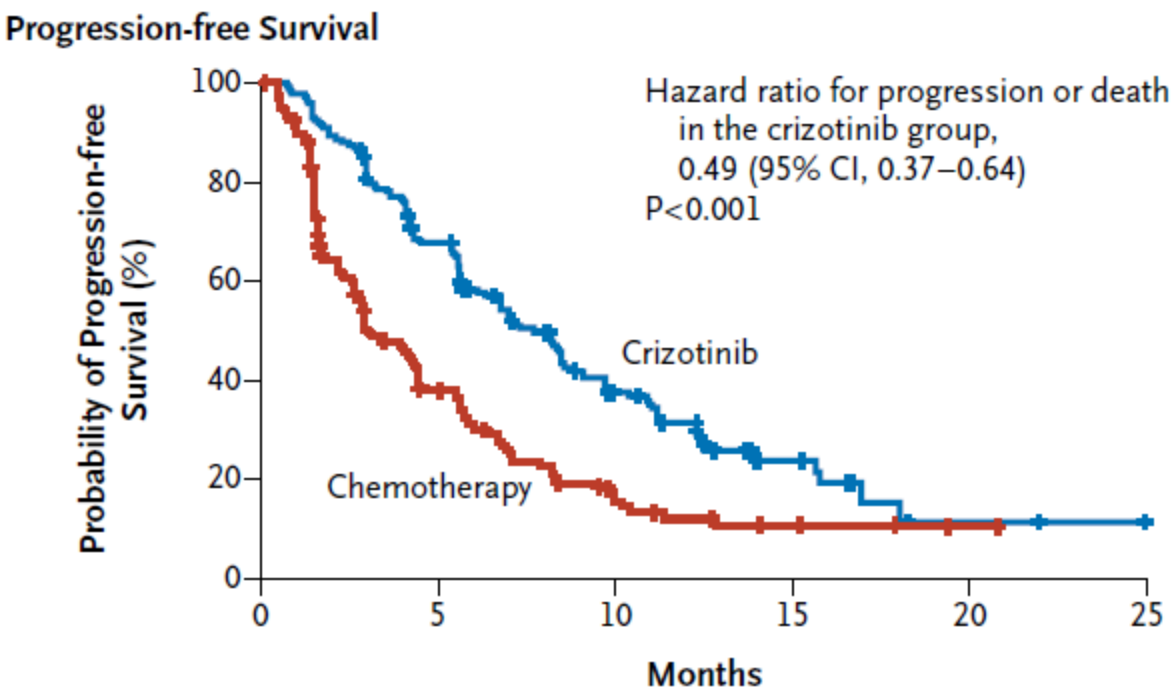
N=318

N=159

Crizotinib 250 mg BID continuous dosing schedule

N=159

Pemetrexed 500 mg/m² OR Docetaxel 75 mg/m² (Day 1/21)


Progression-free Survival
Probability of Progression-free Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
Months
Hazard ratio for progression or death in the crizotinib group, 0.49 (95% CI, 0.37–0.64)
P<0.001
Crizotinib
Chemotherapy

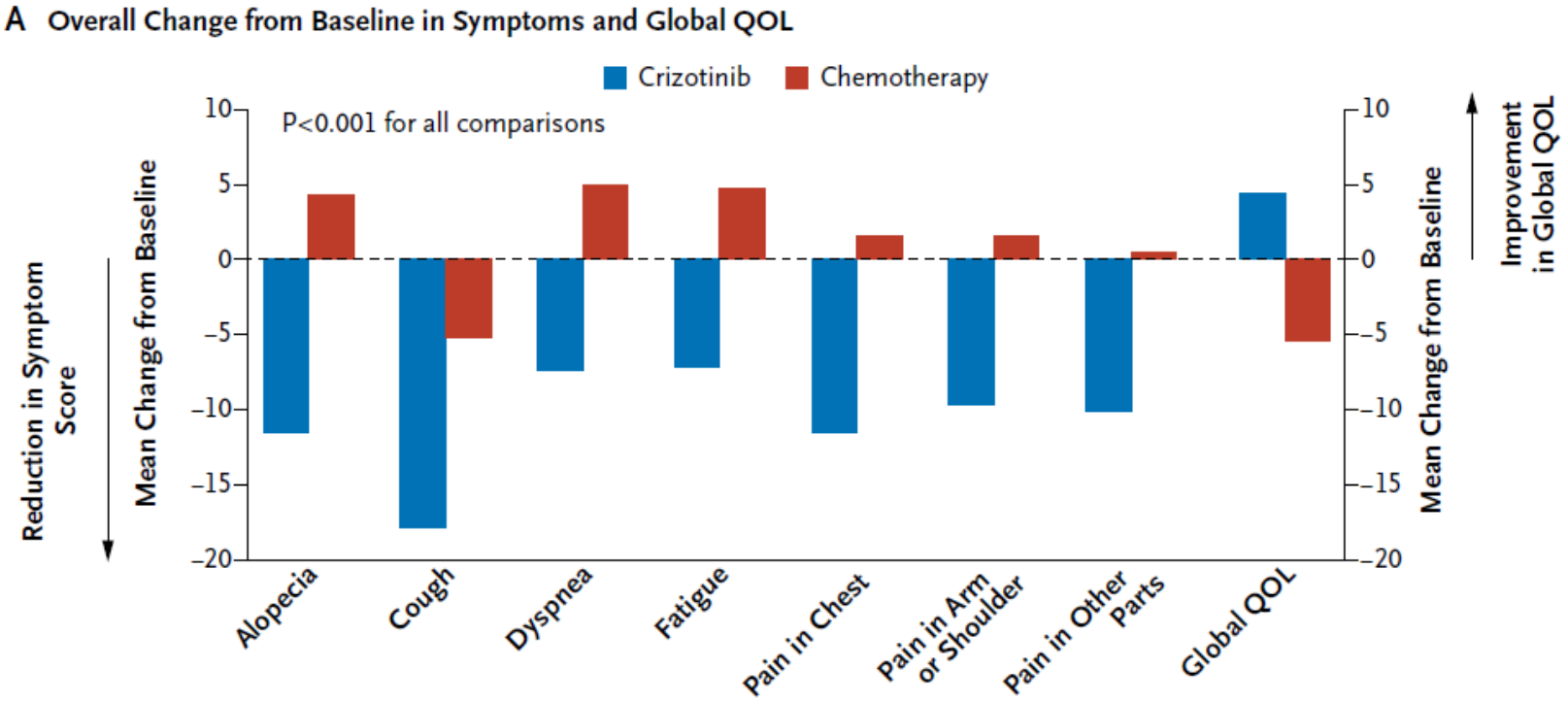
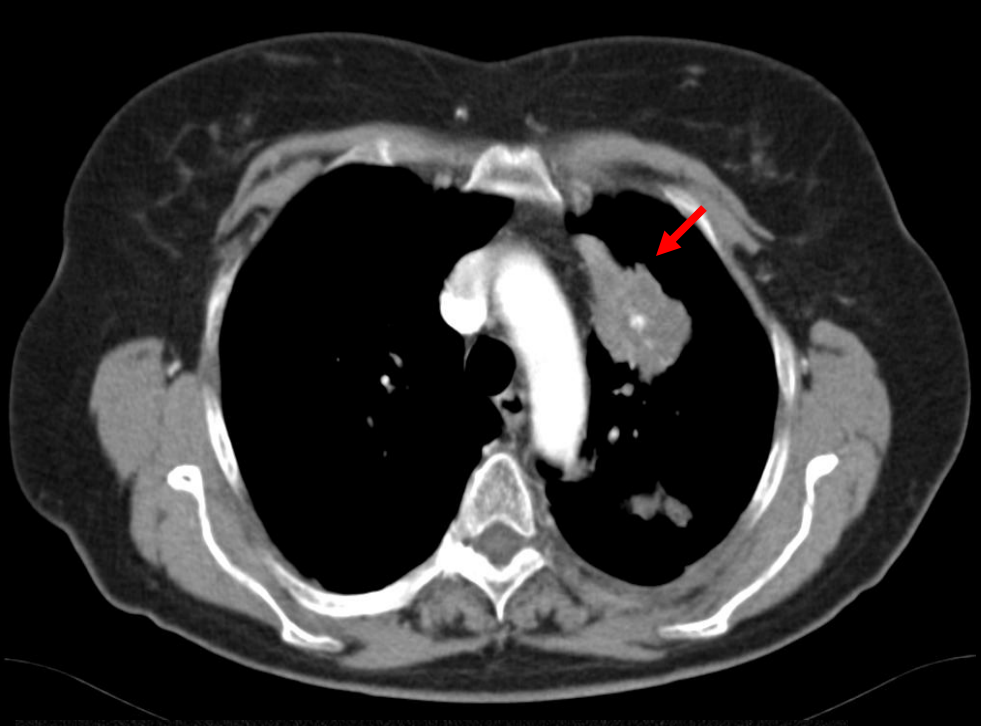

A Overall Change from Baseline in Symptoms and Global QOL
Crizotinib
Chemotherapy
P<0.001 for all comparisons
Reduction in Symptom Score
Mean Change from Baseline
Improvement in Global QOL
10
5
0
−5
−10
−15
−20
Alopecia
Cough
Dyspnea
Fatigue
Pain in Chest
Pain in Arm or Shoulder
Pain in Other Parts
Global QOL

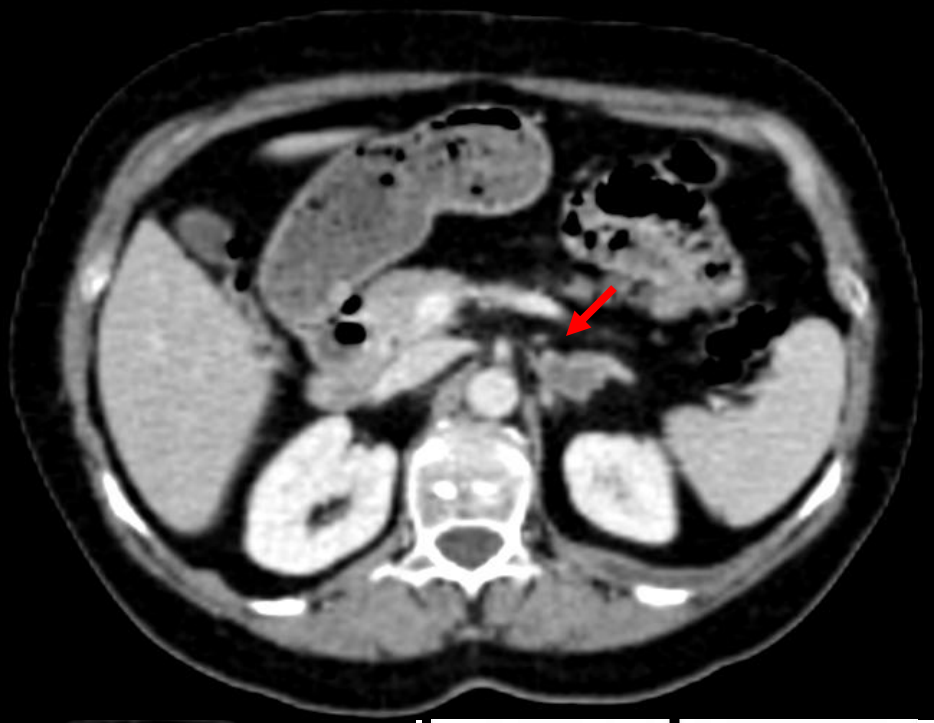
Table 3. Adverse Events of Any Cause.*

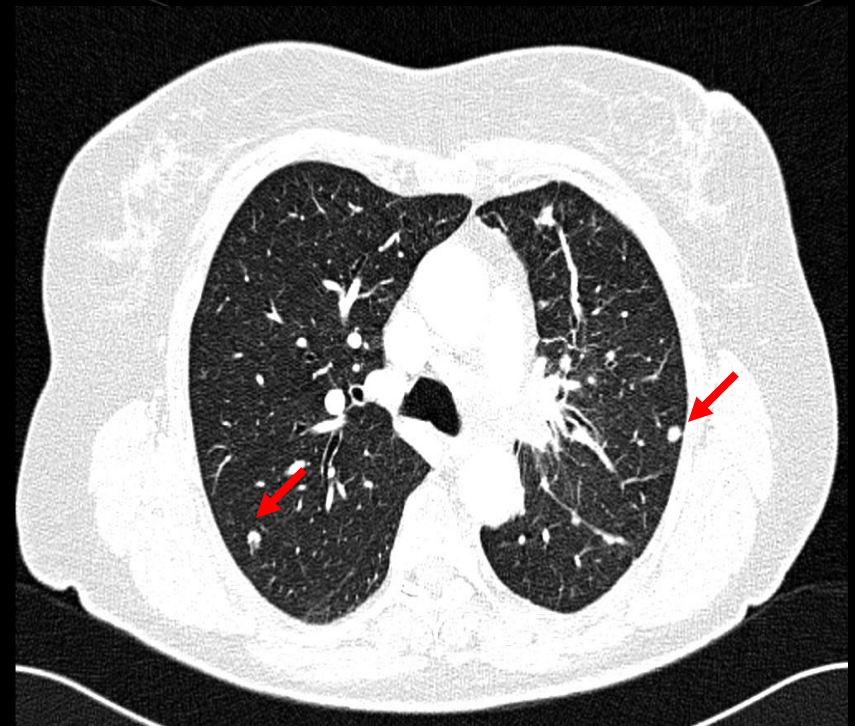
Adverse Event	Crizotinib (N=172)		Chemotherapy (N=171)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	no. of patients (%)			
Vision disorder†‡	103 (60)	0	16 (9)	0
Diarrhea	103 (60)	0	33 (19)	1 (1)
Nausea§	94 (55)	2 (1)	64 (37)	1 (1)
Vomiting§	80 (47)	2 (1)	30 (18)	0
Constipation	73 (42)	4 (2)	39 (23)	0
Elevated aminotransferase levels†	66 (38)	27 (16)¶	25 (15)	4 (2)
Edema†	54 (31)	0	27 (16)	0
Fatigue	46 (27)	4 (2)	57 (33)	7 (4)
Upper respiratory infection†	44 (26)	0	22 (13)	1 (<1)
Dysgeusia	44 (26)	0	16 (9)	0
Dizziness†	37 (22)	1 (1)	14 (8)	0
Dyspnea†‖	23 (13)	7 (4)	32 (19)	5 (3)
Rash	15 (9)	0	29 (17)	0
Alopecia	14 (8)	0	35 (20)	0

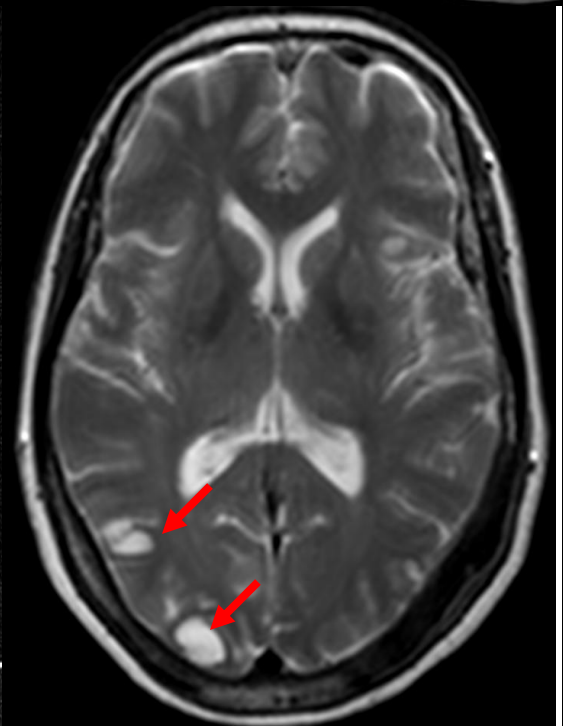
Caso Clínico ALK

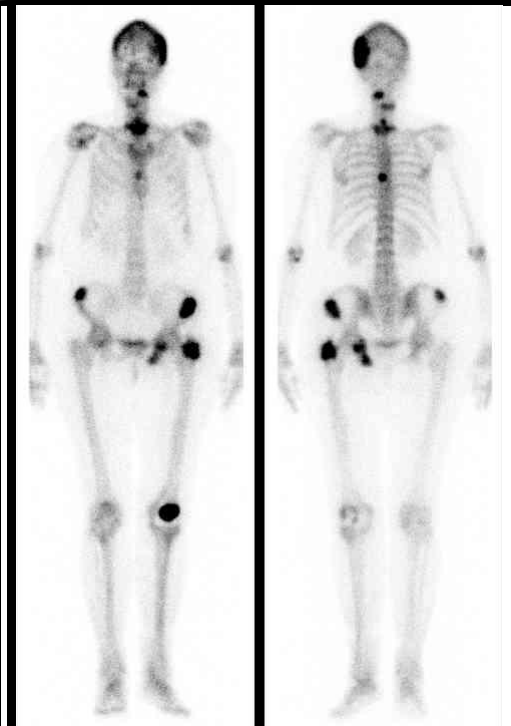
- Mujer de 60 años, no fumadora.
- Abril 2011:
  - TC:
    - Masa irregular de 6 x 3 cm LSI
    - M1 pulmonares bilaterales
    - Derrame e implantes pleurales Izq
    - M1 suprarrenal Izq
    - M1 óseas
    - M1 cerebrales





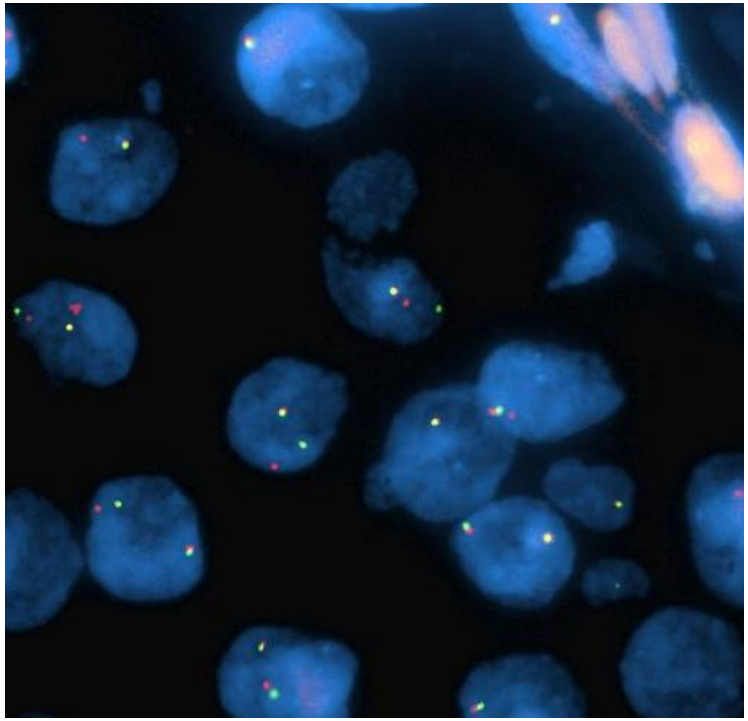






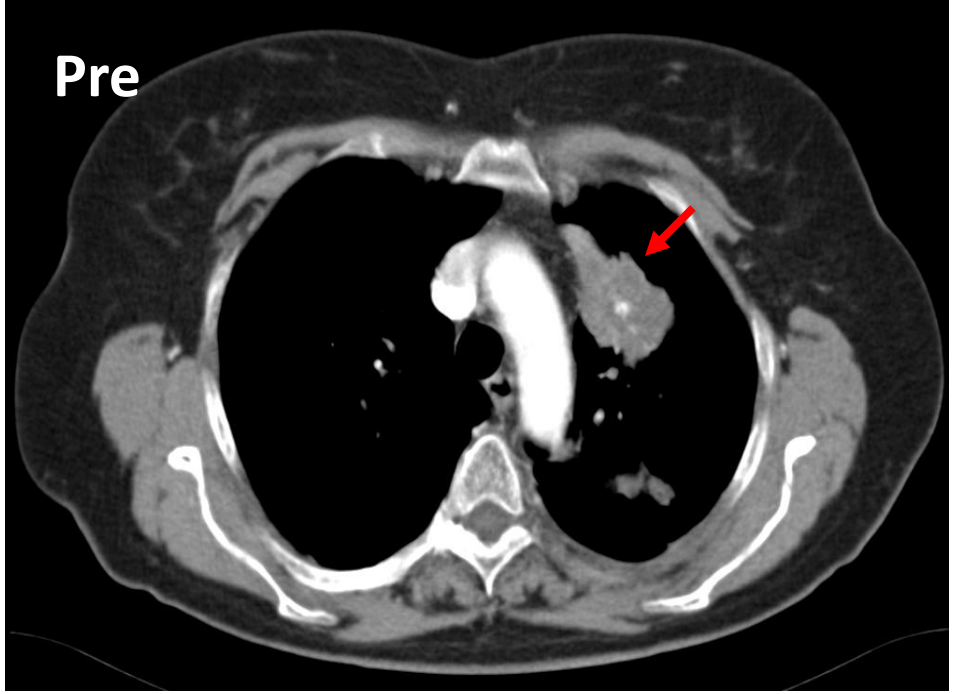
Caso Clínico ALK

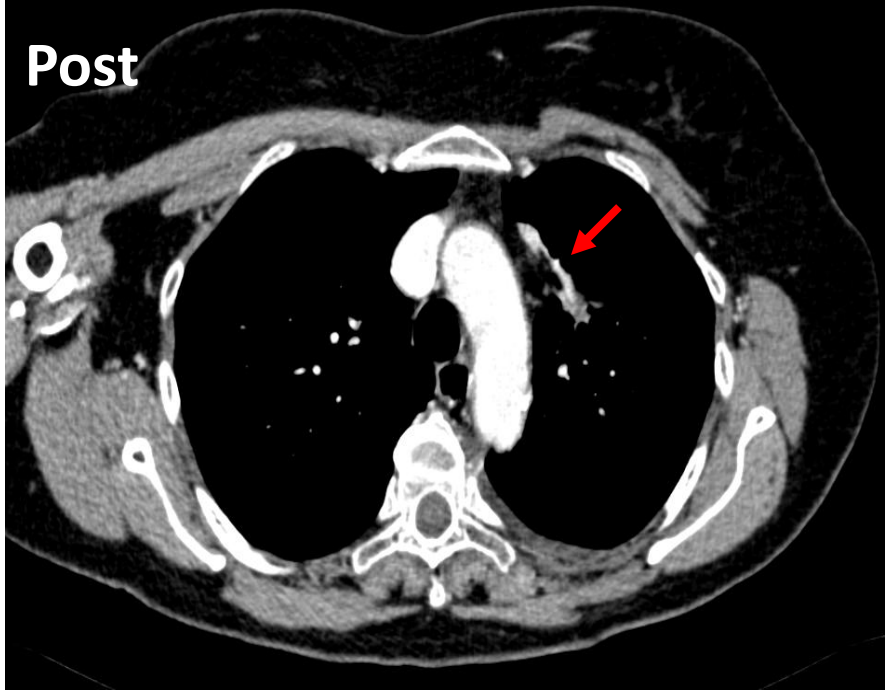
- Estudio molecular:
  - Determinación **ALK: POSITIVO**



Caso Clínico ALK

- Radioterapia holocraneal 20 Gy
- Mayo 2011: Ensayo Clínico PROFILE-1007 (Fase III)
  - **Docetaxel** 6 ciclos (EE como mejor respuesta)
    - Stop por mala tolerancia
    - Mantiene ac. Zoledrónico
- Enero 2012: Progresión local y suprarrenal
  - Ensayo Clínico PROFILE-1005→ **Crizotinib**


Pre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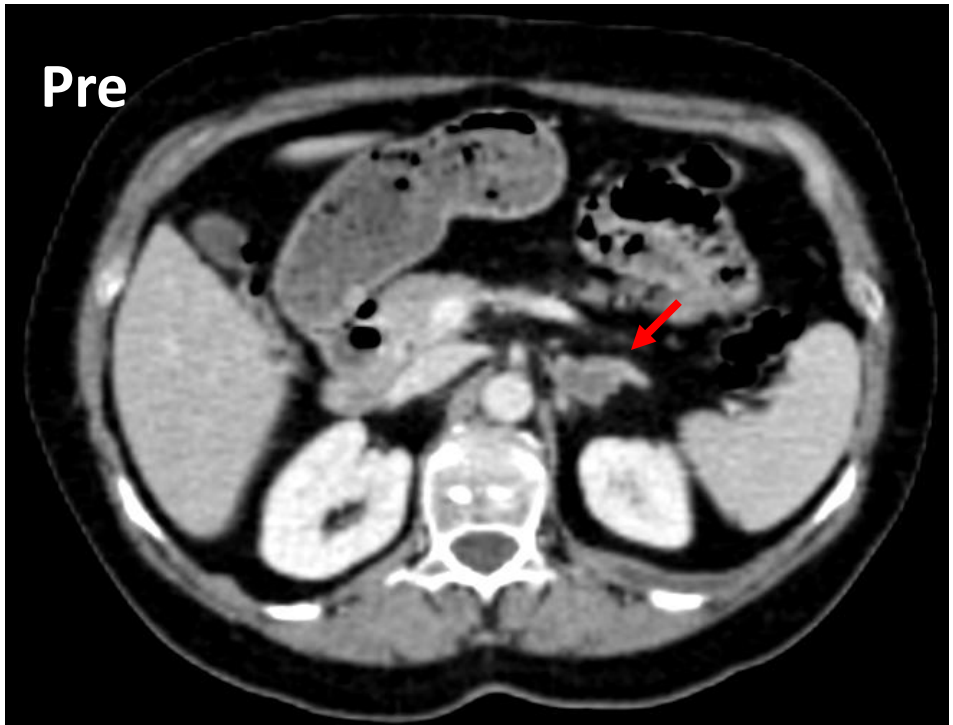
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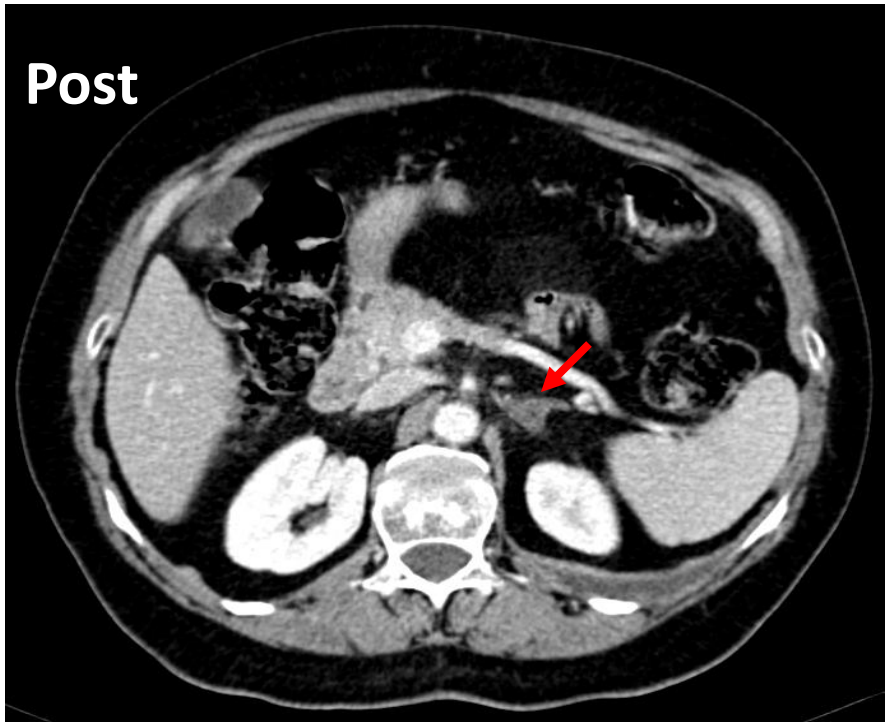
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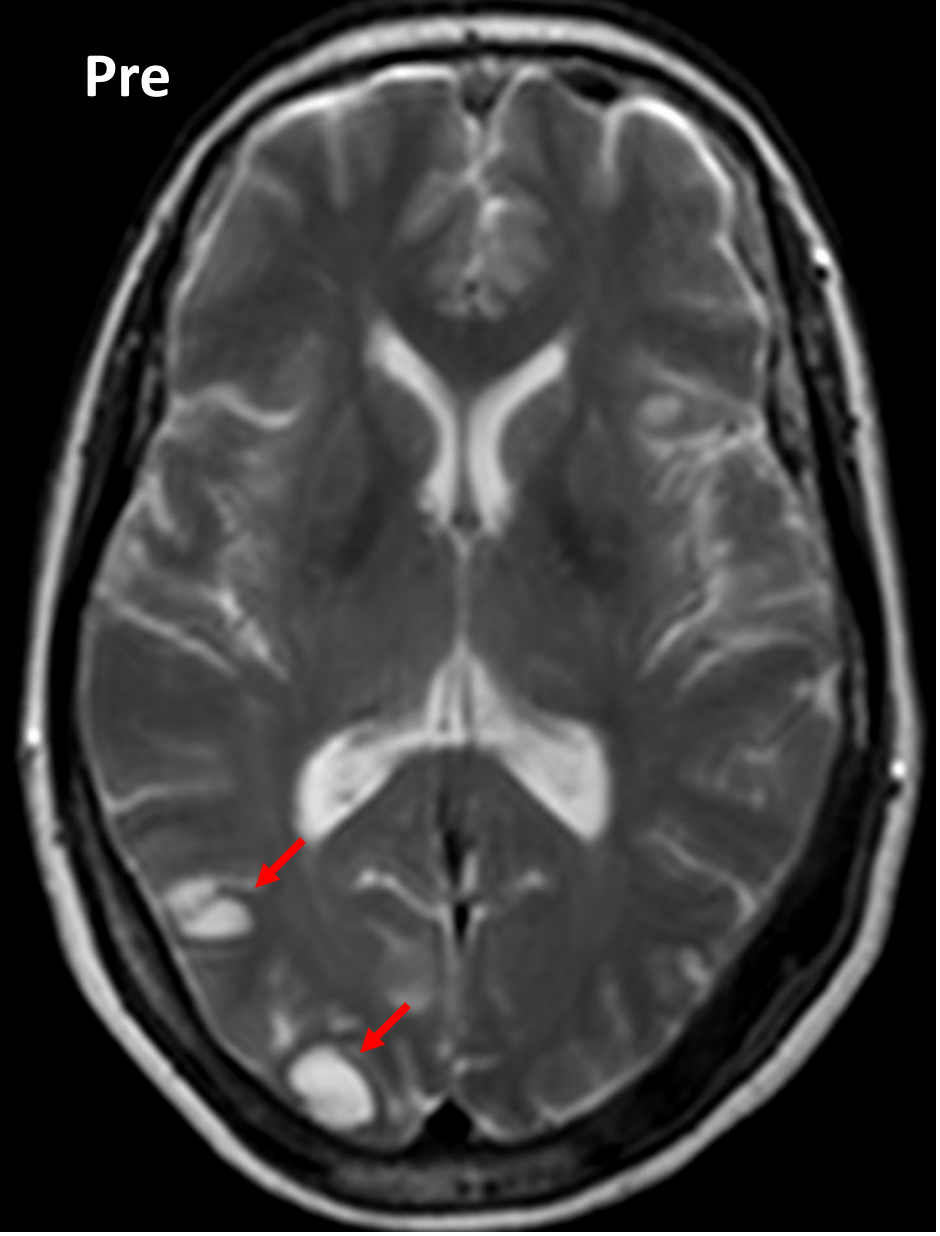
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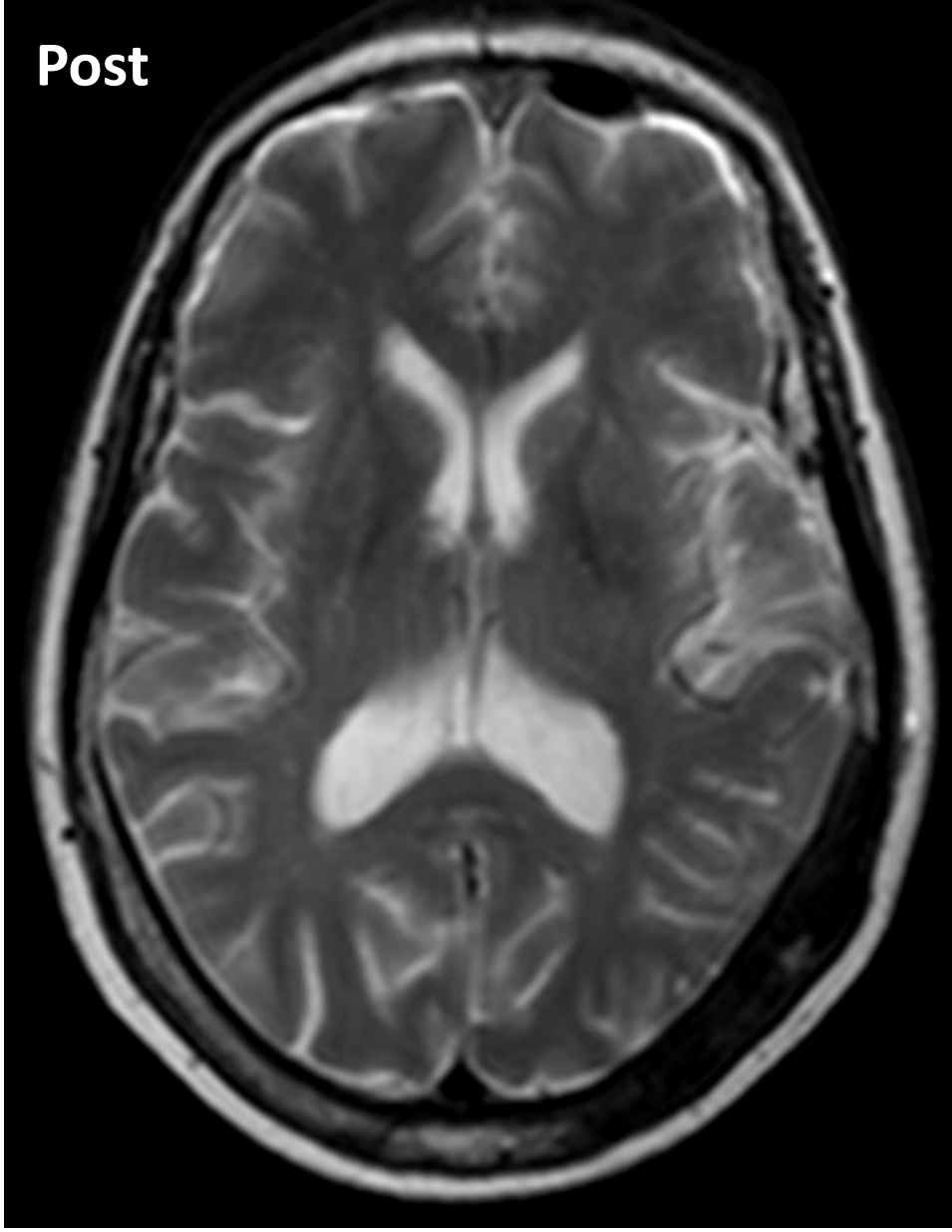
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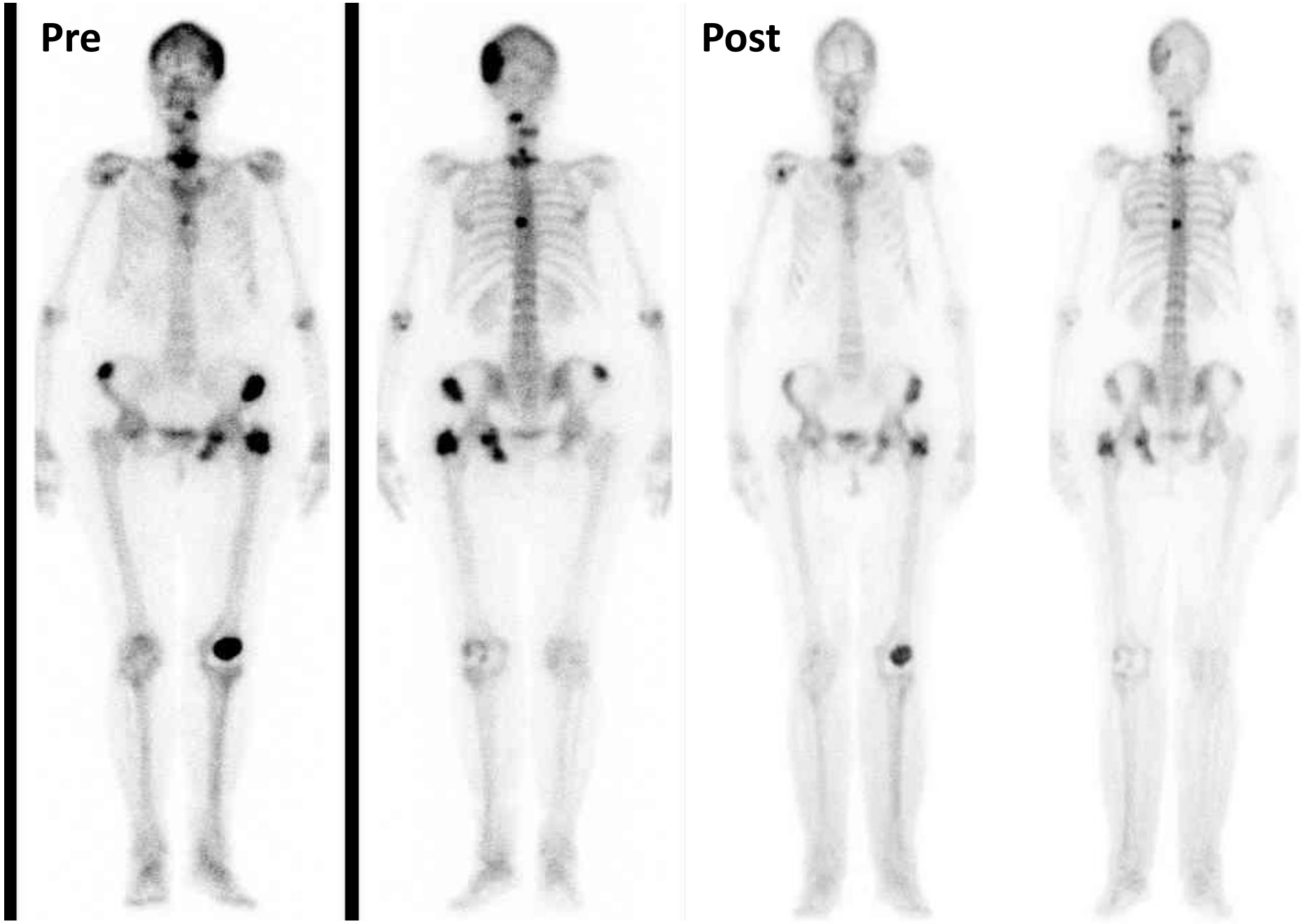
Pre
Post

Seguimiento

- Tiempo de tratamiento con Crizotinib: 24 meses
  - Vida activa
  - ECOG 1
  - Buena tolerancia de toxicidades
- Progresión en enero 2014
  - Ensayo clínico con nuevo inhibidor ALK (alectinib)
  - Enfermedad estable en 1ª valoración

CONCLUSIONES

- La oncología avanza hacia la identificación de nichos de pacientes con alteraciones moleculares tratables con tratamiento dirigidos

- **EGFR**
  - Gefitinib/Erlotinib/Afatinib aprobados en 1ª línea
  - No estudios comparativos publicados (en marcha LUX-LUNG 7 y 8)

- **ALK**
  - Crizotinib aprobado en 2ª línea

- Multitud de estudios en marcha frente a otras dianas (KRAS, MET, BRAF, HER3 …)

Most frequent related AEs with afatinib

	LL3: Afatinib n=229 (%)			LL6: Afatinib n =239 (%)		
	All	g3	g4	All	g3	g4
Diarrhoea	95	14		88	5	
Rash/acne*	89	16		81	14	0.4
Stomatitis/mucositis*	72	8	0.4	52	5	
Paronychia	57	11		34		
ALT increase	7	0.4		20	2	
AST increase	5	0.4		15	0.4	
Epistaxis	13			13	0.4	
Pruritus	19	0.4		11	0.4	
Decreased appetite	21	3		10	1	
Fatigue*	18	1		10	0.4	
Ocular*	18	0.4		6		
Dry skin	29	0.4		5		
Cheilitis	12	0		3		

* Grouped term

1. Sequist LV, et al. *J Clin Oncol*. 2013;31:3327-3334.
2. Wu Y-L, et al. Abstract 8016. Poster presented at ASCO 2013.

EFICACIA

	GEFITINIB[1]	ERLOTINIB[2]	AFATINIB[3]
PFS	10.8 m (HR 0.30)	9.7 m (HR 0.37)	13.6 m (0.49)
RR	73.7%	58%	69%
OS	30.5 m	-	-

1. *Maemondo, NEJM 2010*
2. *Rosell, Lancet Oncol 2012*
3. *Sequist, JCO 2013*

TOXICIDAD G3 O SUPERIOR

	GEFITINIB[1]	ERLOTINIB[2]	AFATINIB[3]
Diarrea	1%	5%	14.4%
Rash	5.3%	13%	16.2%
Elevación transaminasas	26.3%	0%	-

1. *Maemondo, NEJM 2010*
2. *Rosell, Lancet Oncol 2012*
3. *Sequist, JCO 2013*