Treatment of EGFR mutant advanced NSCLC

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Disclosure

Honoraria and consultancy fees: AstraZeneca, Boeringher Ingelheim, Lilly Oncology, Roche, Pfizer, MSD, Bristol Myers Squibb, Takeda, Janssen, Bayer and Novartis

Grants paid to Institution for conduct of clinical trials or contracted research: Roche, AstraZeneca, Pfizer, Clovis, Lilly Oncology, MSD, BMS, Abbvie, Takeda, Janssen and Novartis

Stock Ownership: LOC at TCPC

Non-remunerated activities: Principal investigator for trials with Roche, AstraZeneca, Pfizer, Clovis, Lilly Oncology,Janssen, MSD, BMS, Abbvie, Takeda and Novartis

Other non remunerated membership: ESMO, EORTC

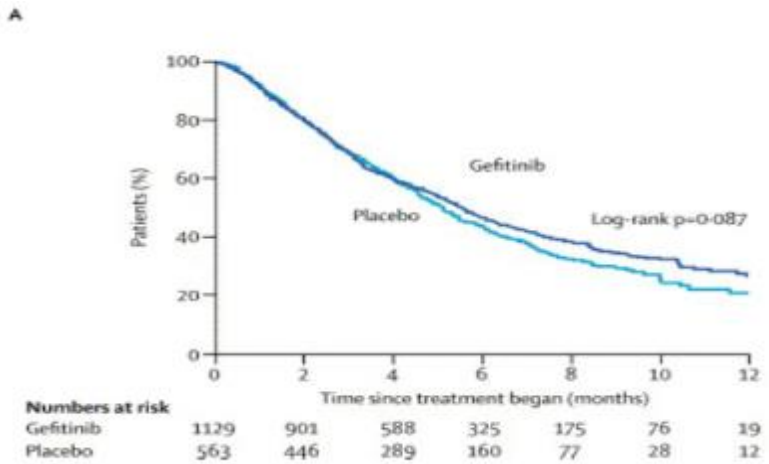
Outline

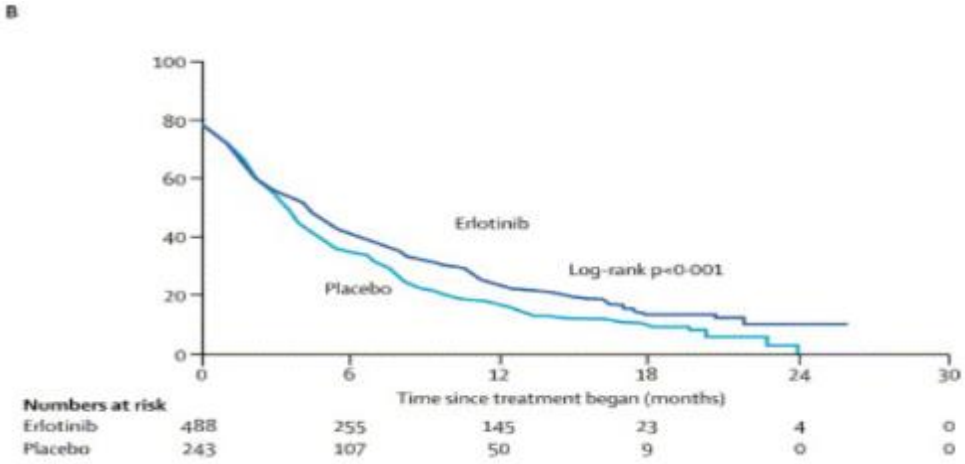
Data on first-line EGFR-TKIs

Managing resistance

Combination strategies

EGFR-TKI in pretreated patients





Thatcher et al, Lancet 2005; Shepherd et al, NEJM 2005

EGFR activating mutations

The NEW ENGLAND JOURNAL of MEDICINE

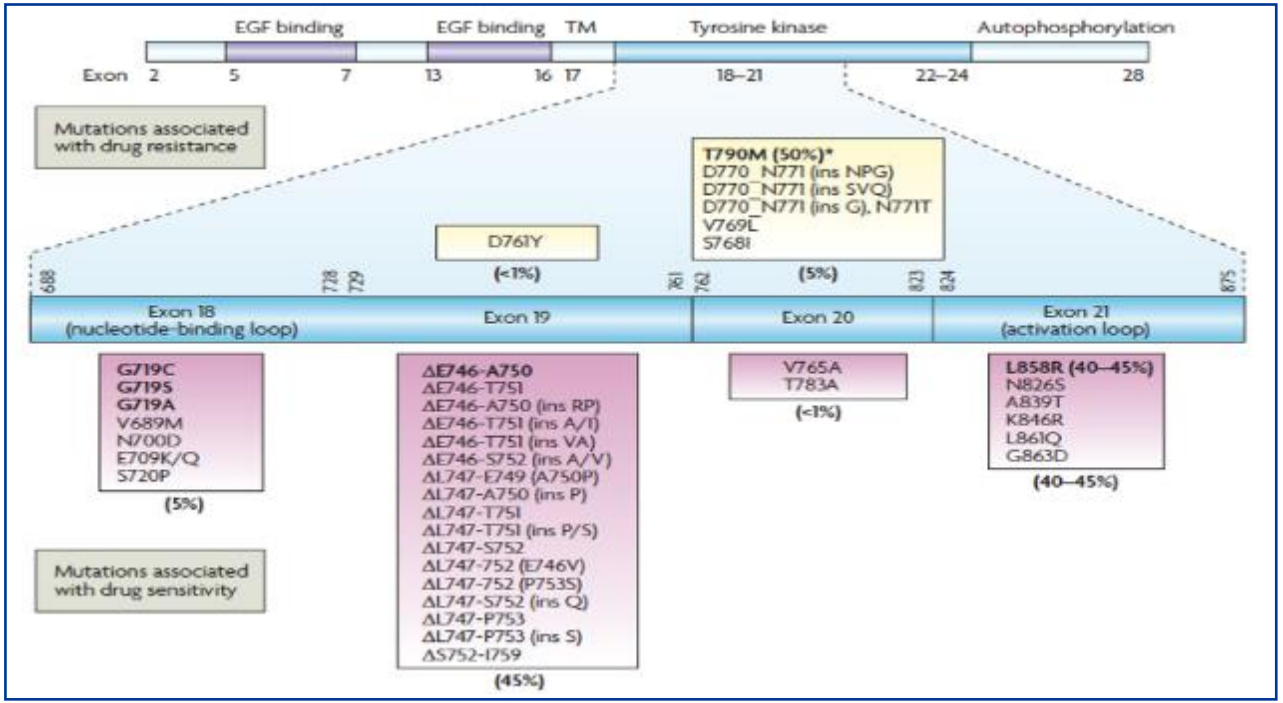
ESTABLISHED IN 1812 MAY 20, 2004 VOL. 350 NO. 21

Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib

Thomas J. Lynch, M.D., Daphne W. Bell, Ph.D., Raffaella Sordella, Ph.D., Sarada Gurubhagavatula, M.D., Ross A. Okimoto, B.S., Brian W. Brannigan, B.A., Patricia L. Harris, M.S., Sara M. Haserlat, B.A., Jeffrey G. Supko, Ph.D., Frank G. Haluska, M.D., Ph.D., David N. Louis, M.D., David C. Christiani, M.D., Jeff Settleman, Ph.D., and Daniel A. Haber, M.D., Ph.D.

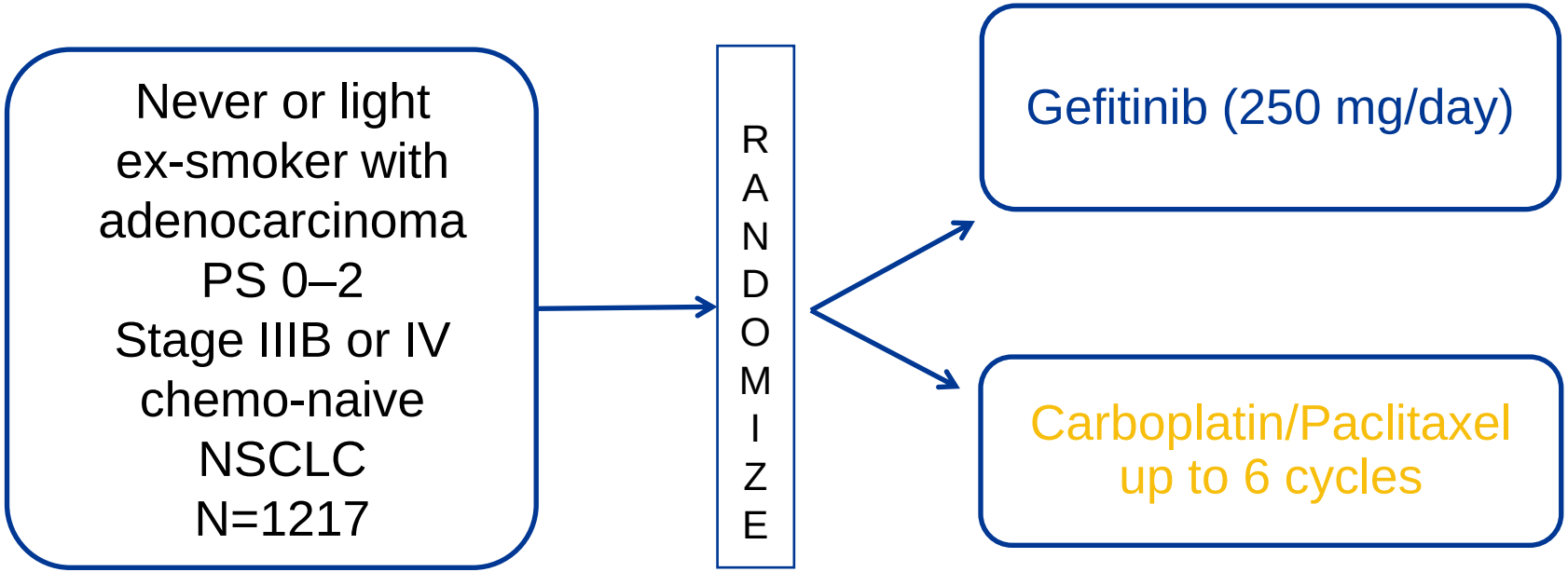
Lynch et al, NEJM 2004

EGFR activating mutations



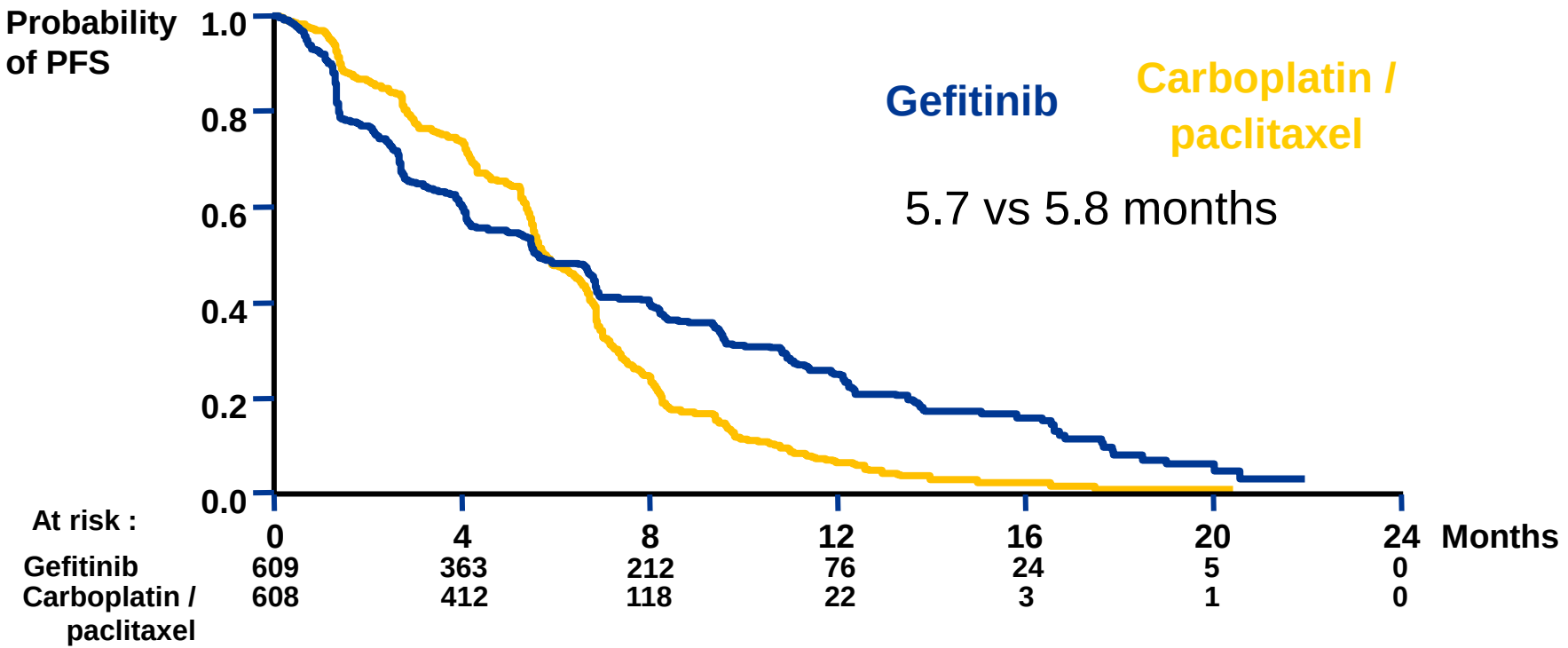
Sharma et al, Nat Rev Cancer 2007

IPASS

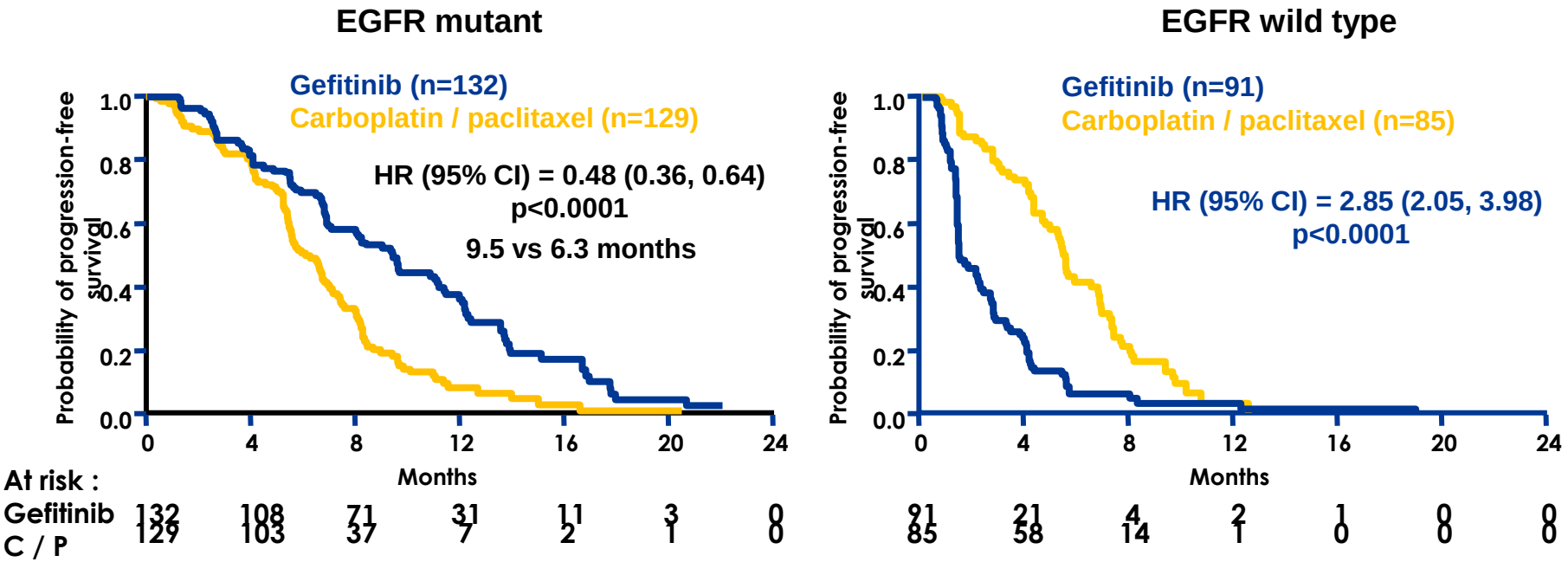


Mok et al, NEJM 2009

PFS in ITT population



PFS in EGFRmut and EGFRwt



Treatment by subgroup interaction test, p<0.0001

ITT population
Cox analysis with covariates

Gefitinib in Asian EGFR+ studies

Study	N	Regimen	RR (%)	PFS	HR
NEJ002	230	G	73.7	10.8	0.30
		C/P	30.7	5.4	
WJTOG 3405	177	G	62.1	9.2	0.48
		C/D	32.2	6.3	

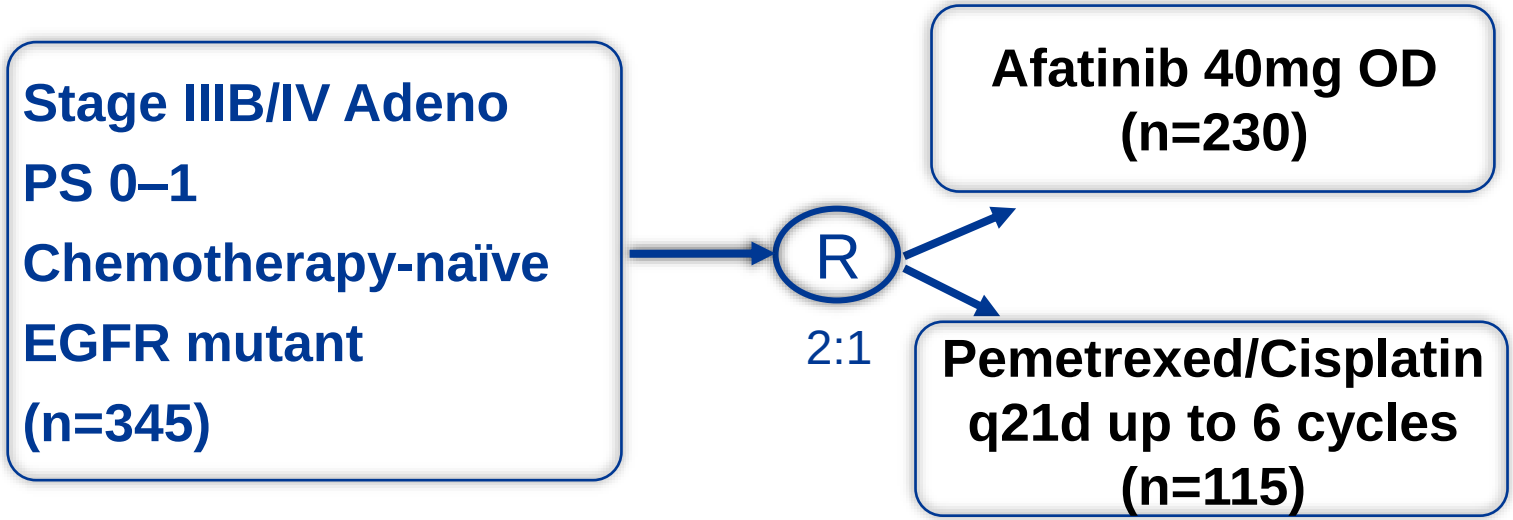
Maemondo et al, NEJM 2010; Mitsudomi et al, Lancet Oncol 2010

Erlotinib in EGFR+ studies

Study	N	Regimen	RR (%)	PFS	HR
OPTIMAL	165	E	83	13.1	0.16
		C/G	36	4.6	
EURTAC	174	E	56	9.7	0.37
		Platinum doublet	15	5.2	

Zhou et al, Lancet Oncol 2011; Rosell et al, Lancet Oncol 2012;

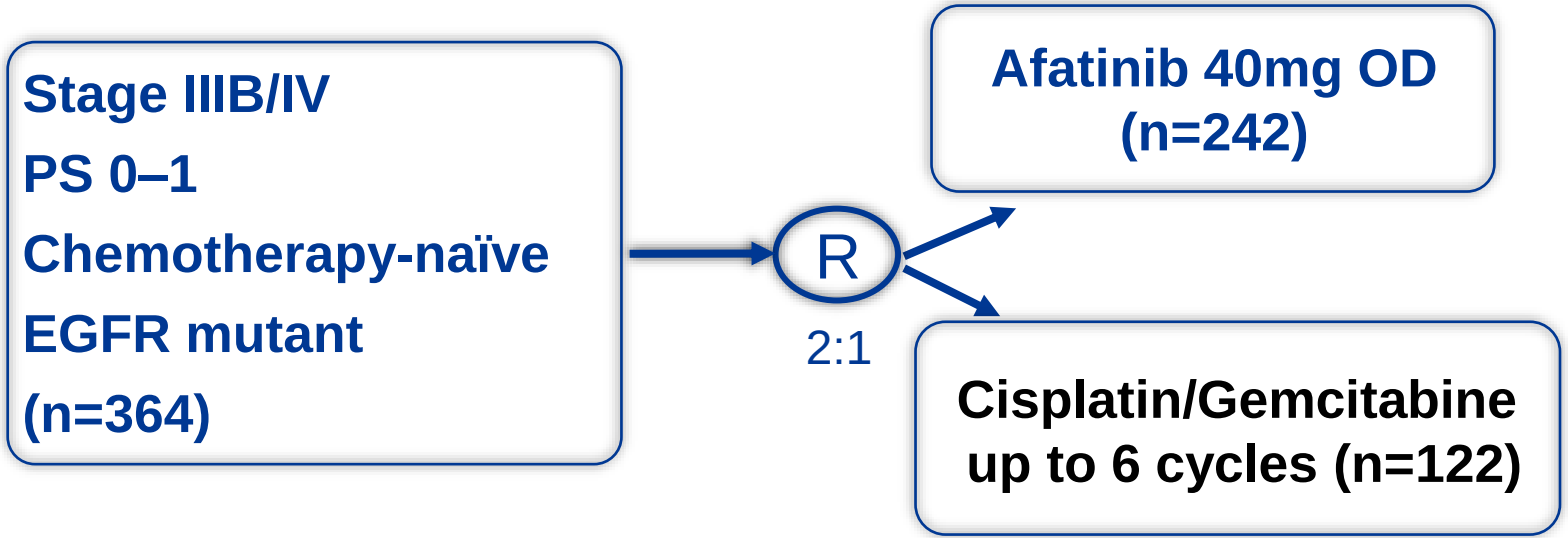
LUX-LUNG 3



Primary endpoint: PFS (IRR)

Sequist LV, et al, JCO 2013

LUX-LUNG 6



Primary endpoint: PFS (IRR)

Only East Asia

Wu Y-L, et al, Lancet Oncol 2014

LUX-Lung 3 and 6: Efficacy

	LUX-LUNG 3		LUX-LUNG 6	
	Afatinib n=230	Cis/pem n=115	Afatinib n=242	Cis/gem n=122
ORR (%)	56.1	22.5	66.9	23
Median PFS (mos)	11.1	6.9	11.0	5.6
HR (95% CIl)	0.58 (0.43–0.78) p=0.0004		0.28 (0.20-0.39) P<0.0001	
OS	28.2 vs 28.2 months HR=0.88, p=0.3850		23.1 vs 23.5 months HR=0.93, p=0.6137	

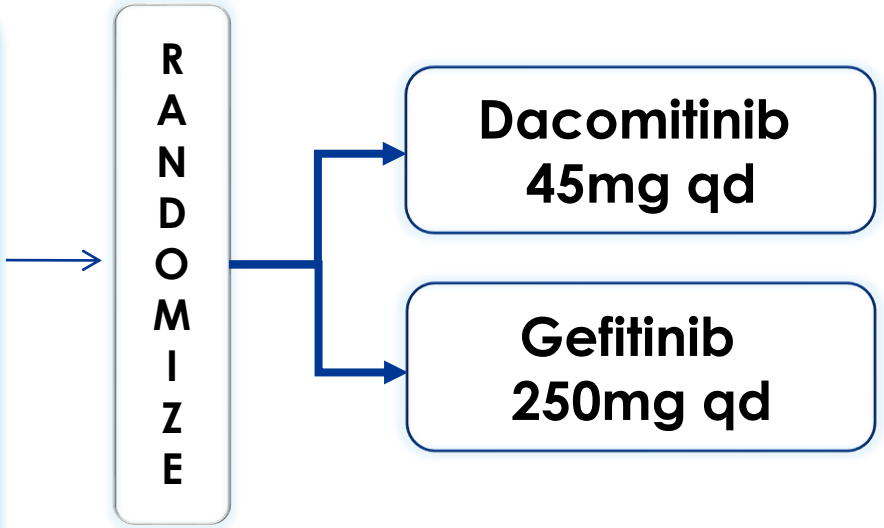
Trials of EGFR-TKIs vs CT

Study	N	Median PFS (mos)			Median OS (mos)	
		TKI	Chemo	HR (95 % CI)	TKI	Chemo
IPASS	**261**	**9.5**	**6.3**	**0.48 (0.36-0.64)**	**21.6**	**21.9**
First Signal	42	8.0	6.3	0.54 (0.26-1.10)	27.2	25.6
NEJ002	194	10.4	5.5	0.35 (0.25-0.50)	27.7	26.6
WJTOG	172	9.2	6.3	0.48 (0.33-0.71)	36	39
OPTIMAL	154	13.7	4.6	0.16 (0.10-0.26)	22.6	28.8
EURTAC	**174**	**10.4**	**5.1**	**0.34 (0.25–0.54)**	**19.3**	**19.5**
LUX-LUNG 3	**345**	**11.1**	**6.9**	**0.58 (0.43-0.78)**	**28.2**	**28.2**
LUX-LUNG 6	364	11.1	5.6	0.28 (0.20-0.39	23.1	23.5

ARCHER 1050

Advanced NSCLC
- Adenocarcinoma
- EGFR ex 19/21 mut+
- First-line treatment
- PS 0-1
- No brain mets

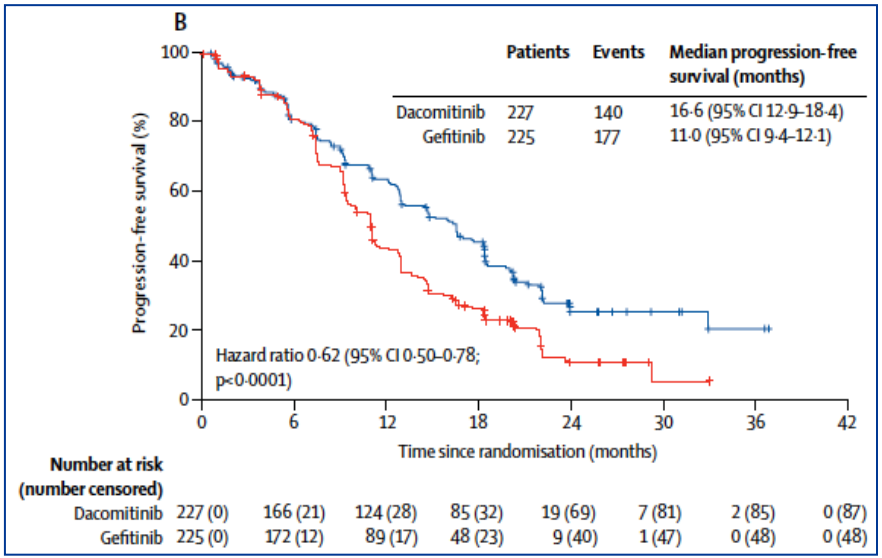
N=440

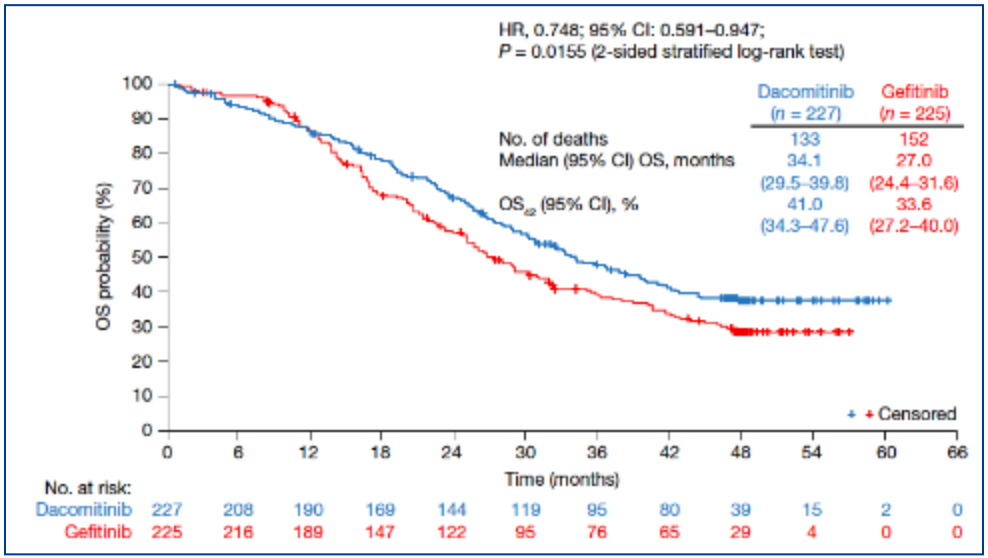


Primary endpoint: PFS

Wu et al, lancet oncology 2017; Mok et al, Drugs 2021

ARCHER 1050: PFS and OS



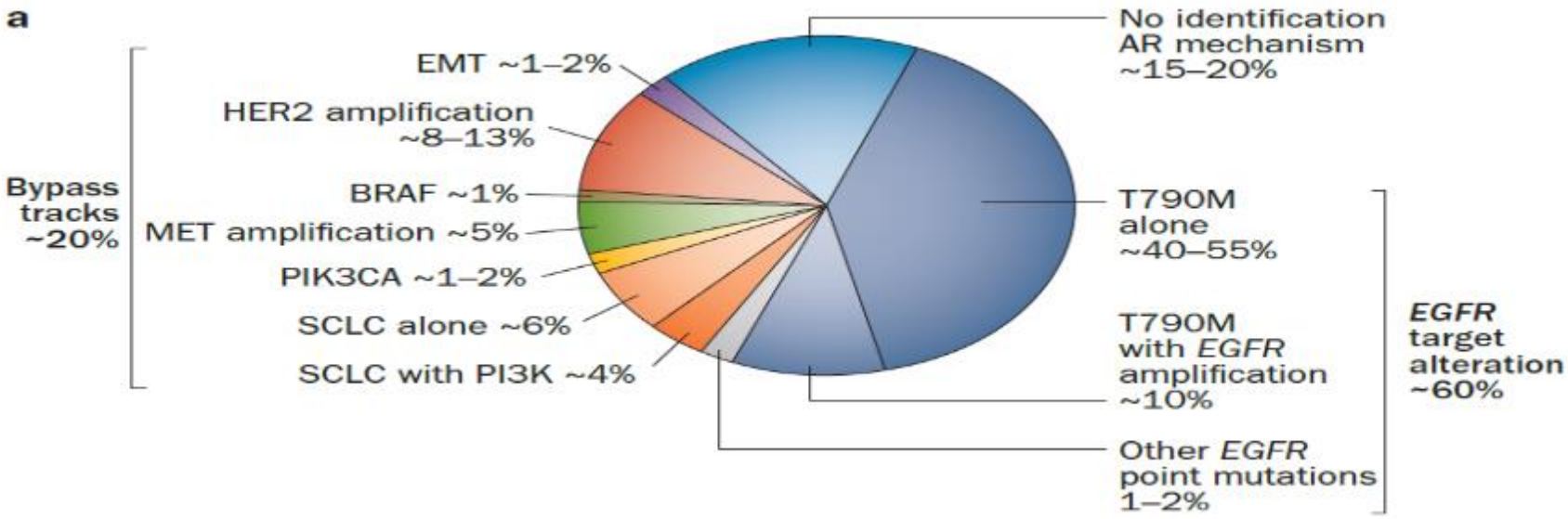


Wu et al, lancet oncology 2017; Mok et al, Drugs 2021

SAEs and dose modification

Outcome	Dacomitinib (n = 227)	Gefitinib (n = 224)
Serious AE, n (%)		
Any	62 (27.3)	50 (22.3)
Treatment related	21 (9.3)	10 (4.5)
Causing discontinuation	22 (9.7)	15 (6.7)
Causing death	2 (0.9)	1 (0.4)
Median duration of dose reduction, mos (range)	11.3 (0.1-33.6)	5.2 (0.3-17.8)
Reduced dose given, n (%)		
30 mg/day	87 (38.3)	NA
15 mg/day	63 (27.8)	
Pts requiring dose reduction, n (%)	150 (66.1)	18 (8.0)

Mechanism of resistance to 1st/2nd generation EGFR-TKIs



Camidge DR et al. Nat Rev Clin Oncol. 2014

Tackling T790M resistance mutation

AURA3

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Evidence of disease progression following first-line EGFR-TKI therapy
- Documented EGFRm and central confirmation of tumour EGFR T790M mutation after first-line EGFR-TKI treatment
- PS 0 or 1
- No more than one prior line of treatment for advanced NSCLC
- Stable asymptomatic CNS metastases allowed

R
2:1

Osimertinib
80 mg OD
(n=279)

Platinum-pemetrexed
+/- maintenance pemetrexed
(n=140)

Endpoints Primary:

•PFS by investigator assessment (RECISTv1.1)

Secondary and exploratory:

•OS

•ORR

•DoR

•DCR

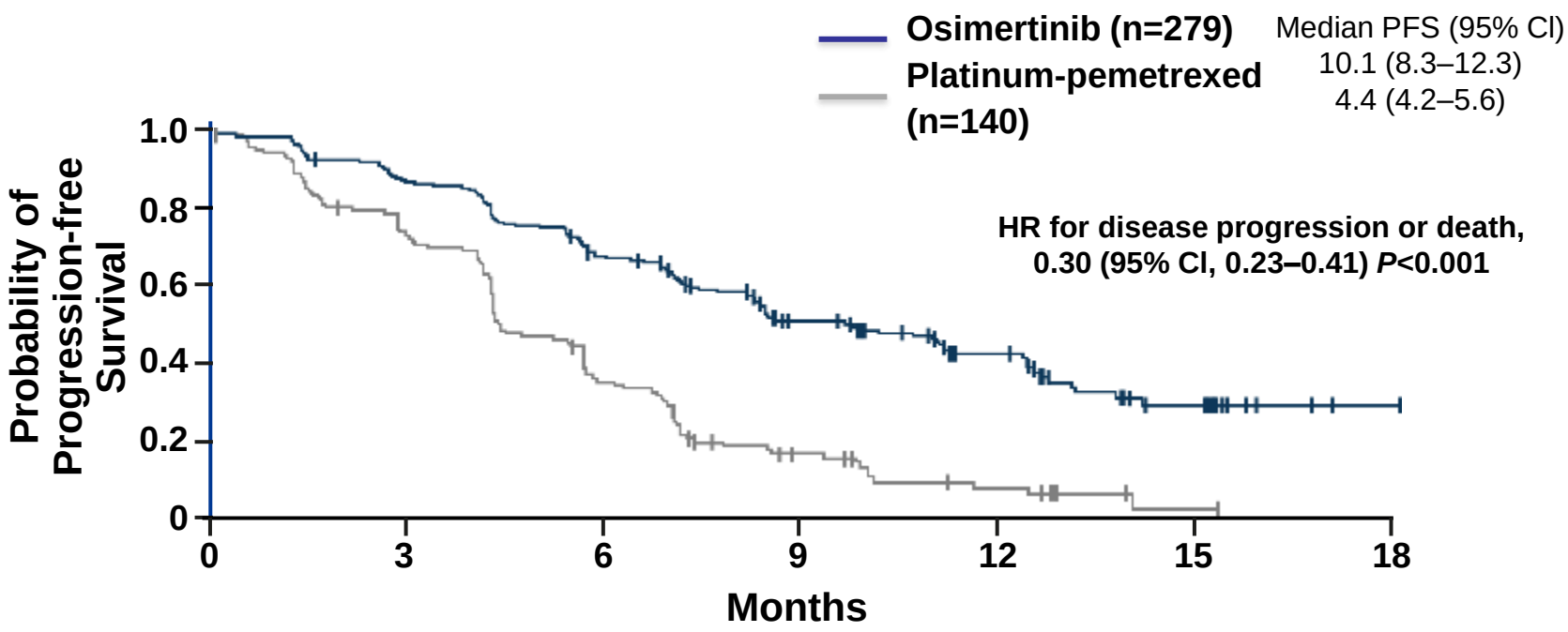
•Tumour shrinkage

•BICR-assessed PFS

Optional crossover: Protocol amendment allowed patients on chemotherapy to begin post-BICR confirmed progression open-label osimertinib treatment

Mok et al, NEJM 2016

PFS by Investigator



Mok et al, NEJM 2016

FLAURA

Patients with locally advanced or metastatic NSCLC

Key inclusion criteria

- ≥18 years*
- Performance status 0 / 1
- Exon 19 deletion / L858R (enrolment by local# or central‡ EGFR testing)
- No prior systemic anti-cancer / EGFR-TKI therapy
- Stable CNS metastases allowed

Stratification by **mutation status** (Exon 19 deletion / L858R) and **race** (Asian / non-Asian)

Osimertinib (80 mg OD) (n=279)

Randomised 1:1

EGFR-TKI SoC: **Gefitinib** or **Erlotinib** (n=277)

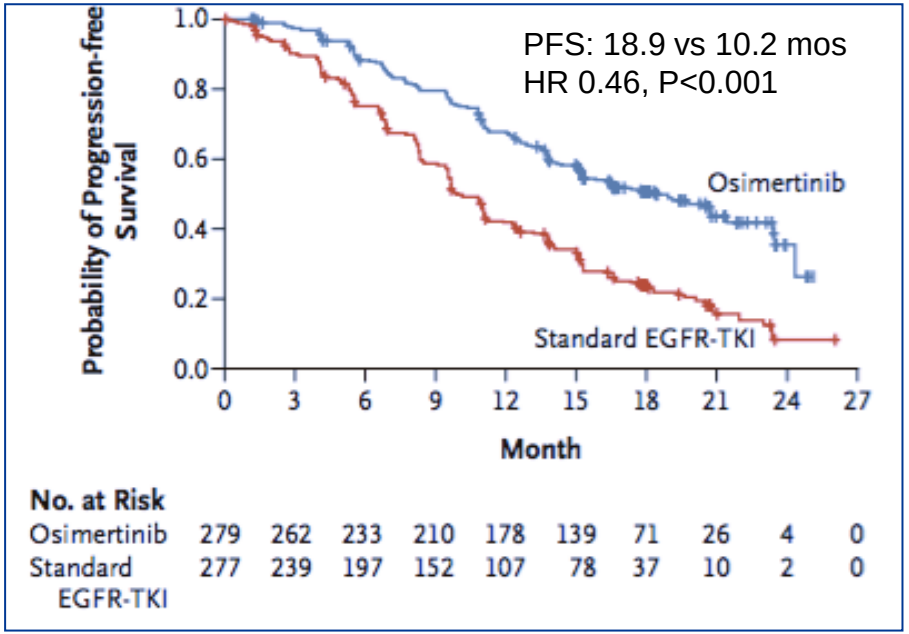
RECIST 1.1 assessment every 6 weeks until objective progressive disease

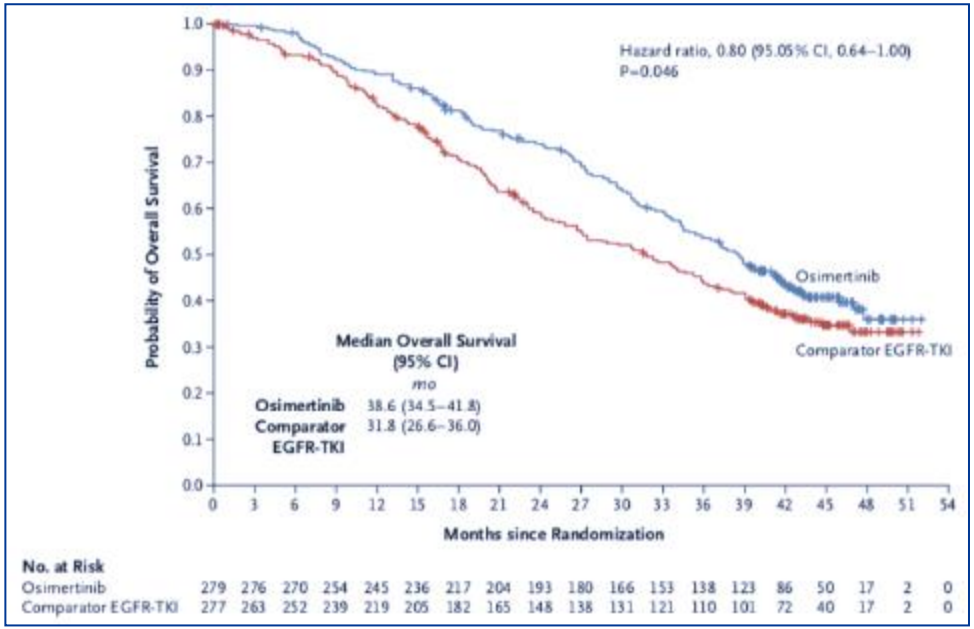
Crossover was allowed for patients in the **SoC** arm, who could receive open-label osimertinib upon central confirmation of progression and T790M positivity

Primary endpoint: PFS (investigator)
Secondary endpoints: ORR, duration of response, DCR , depth of response, OS, PRO, safety

Soria JC et al, NEJM 2017

FLAURA



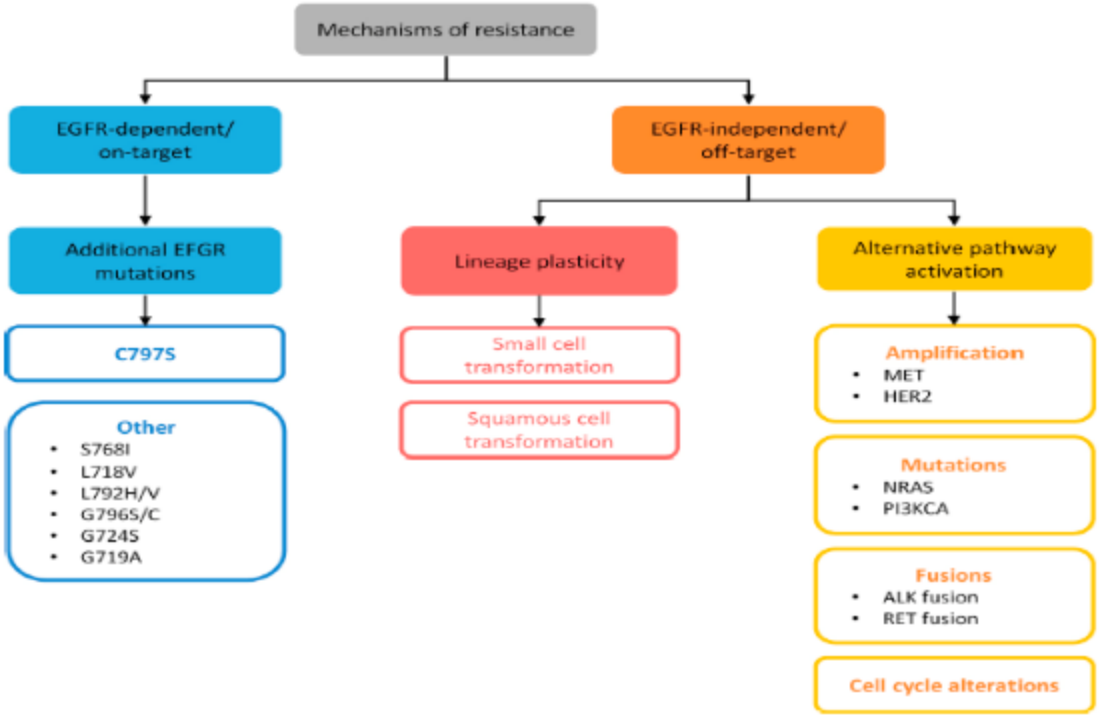


Soria JC et al, NEJM 2017; Ramalingham et al, NEJM 2020

Adverse Events

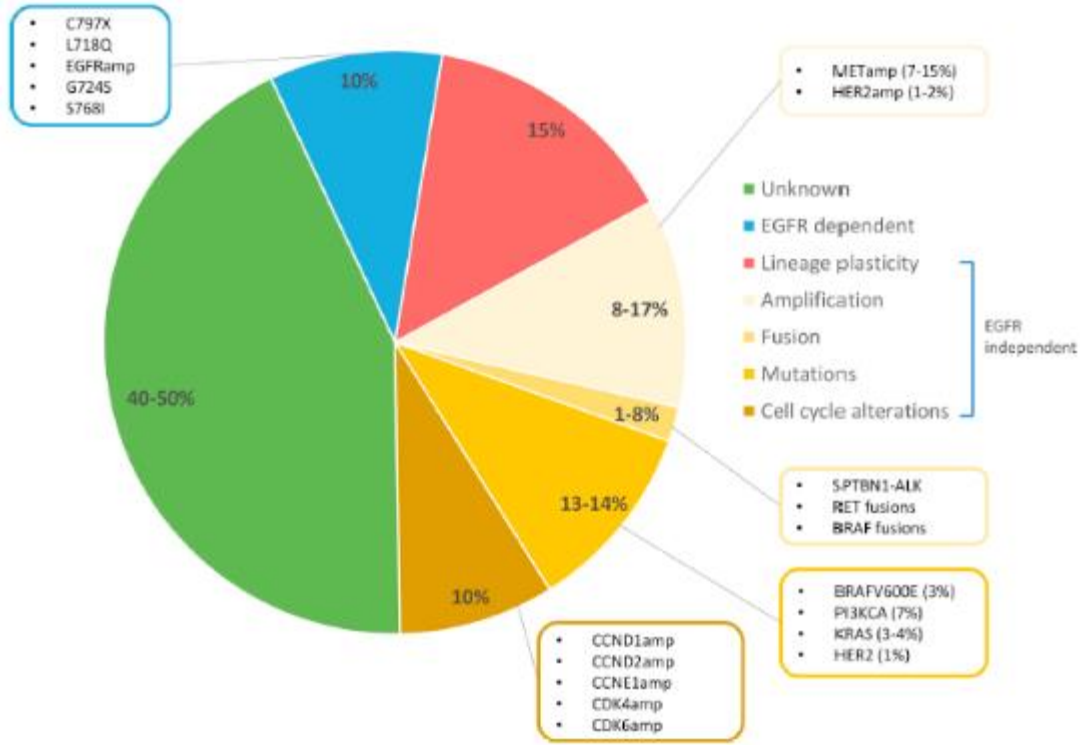
AEs n (%)	Osimertinib (n=279)					SoC (n=277)				
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
Diarrhoea	161 (58)	120 (43)	35 (13)	6 (2)	0	159 (57)	116 (42)	35 (13)	6 (2)	0
Dry skin	88 (32)	76 (27)	11 (4)	1 (<1)	0	90 (32)	70 (25)	17 (6)	3 (1)	0
Paronychia	81 (29)	37 (13)	43 (15)	1 (<1)	0	80 (29)	46 (17)	32 (12)	2 (1)	0
Stomatitis	80 (29)	65 (23)	13 (5)	1 (<1)	1 (<1)	56 (20)	47 (17)	8 (3)	1 (<1)	0
Dermatitis acneiform	71 (25)	61 (22)	10 (4)	0	0	134 (48)	71 (26)	50 (18)	13 (5)	0
Decreased appetite	56 (20)	27 (10)	22 (8)	7 (3)	0	51 (18)	24 (9)	22 (8)	5 (2)	0
Pruritis	48 (17)	40 (14)	7 (3)	1 (<1)	0	43 (16)	30 (11)	13 (5)	0	0
Cough	46 (16)	34 (12)	12 (4)	0	0	42 (15)	25 (9)	16 (6)	1 (<1)	0
Constipation	42 (15)	33 (12)	9 (3)	0	0	35 (13)	28 (10)	7 (3)	0	0
AST increased	26 (9)	18 (6)	6 (2)	2 (1)	0	68 (25)	38 (14)	18 (6)	12 (4)	0
ALT increased	18 (6)	11 (4)	6 (2)	1 (<1)	0	75 (27)	31 (11)	19 (7)	21 (8)	4 (1)

Resistance mechanisms to Osimertinib

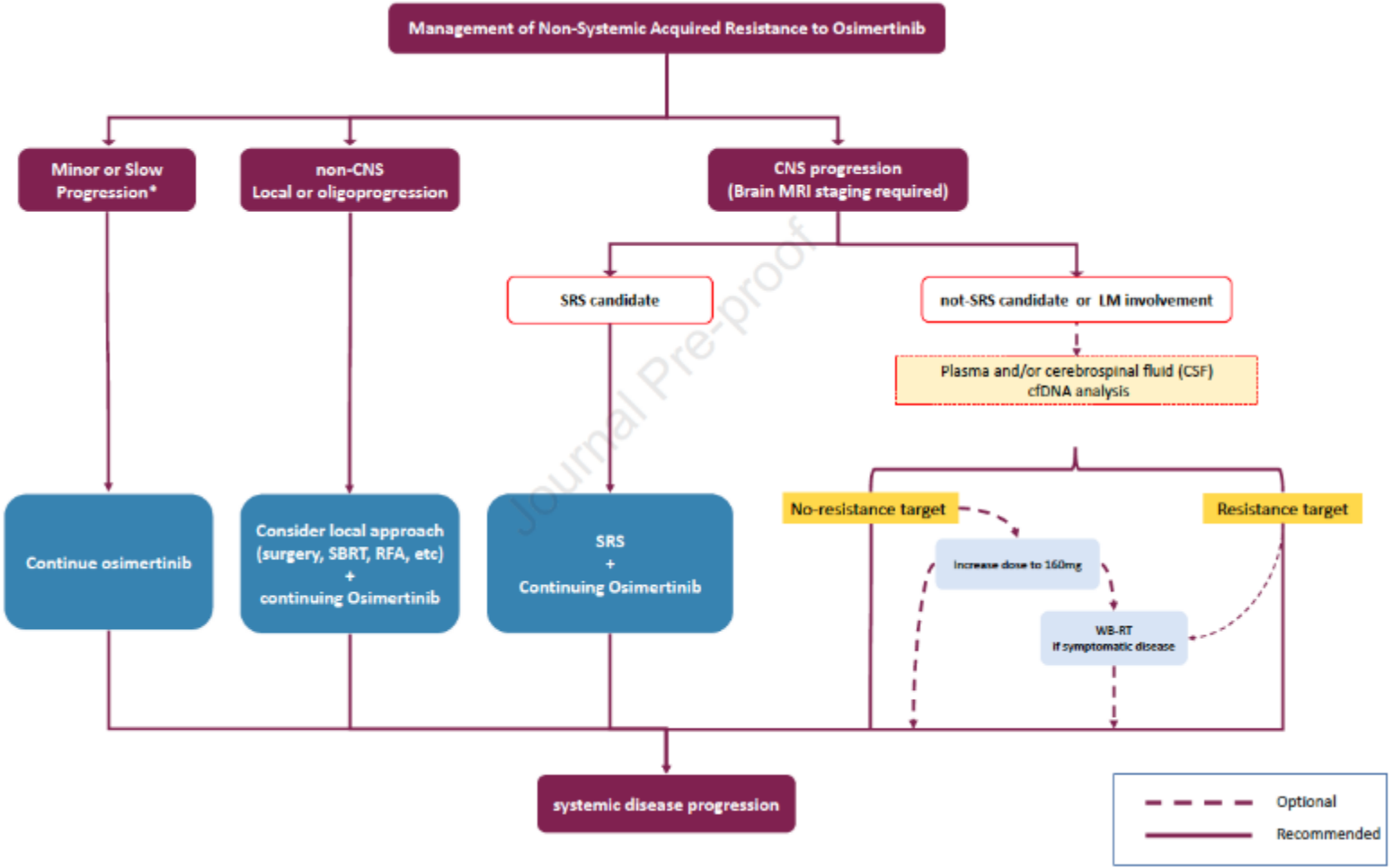


Schmid et al, Lung Cancer 2020

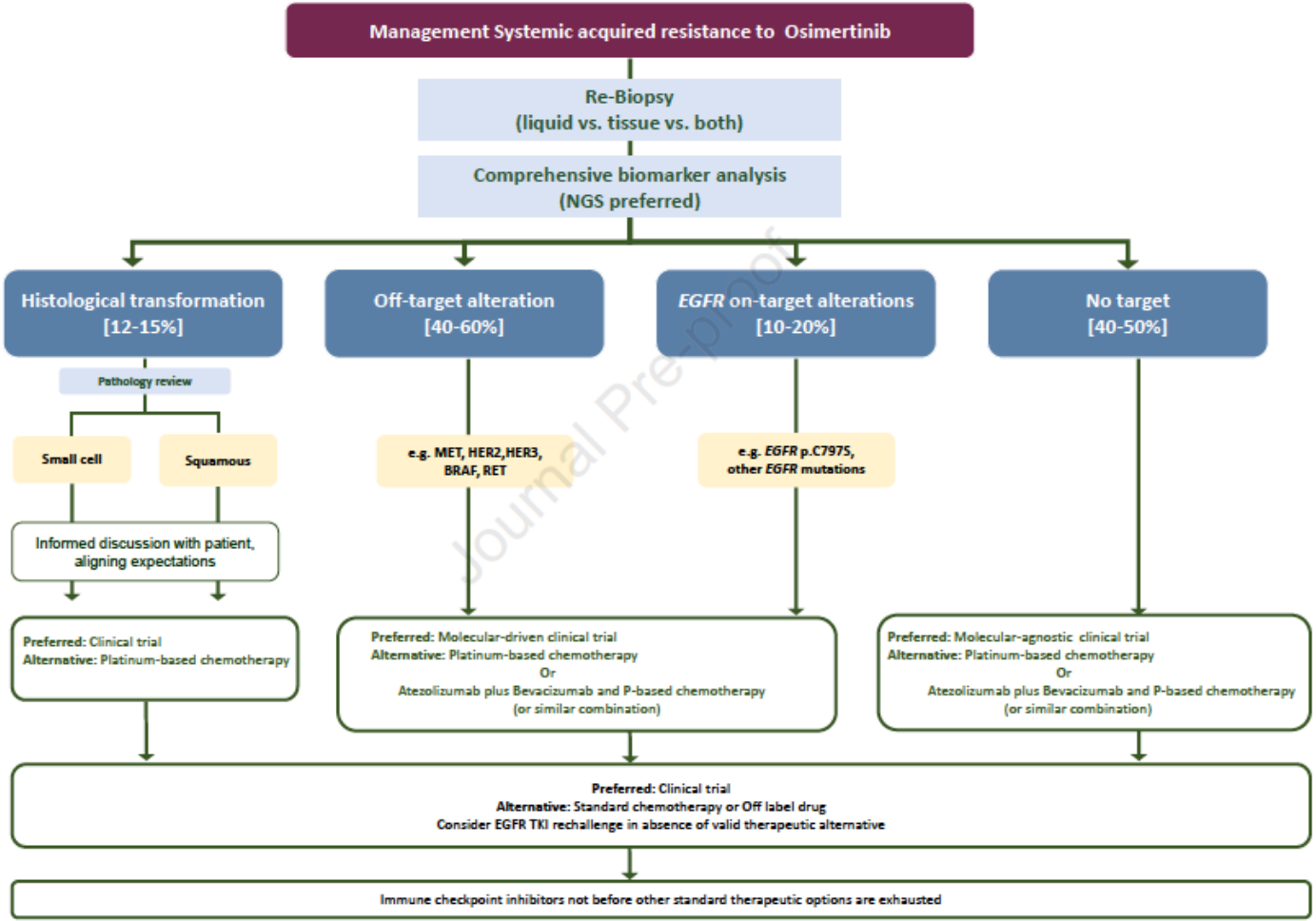
Resistance mechanisms to 1L Osi



Schmid et al, Lung Cancer 2020



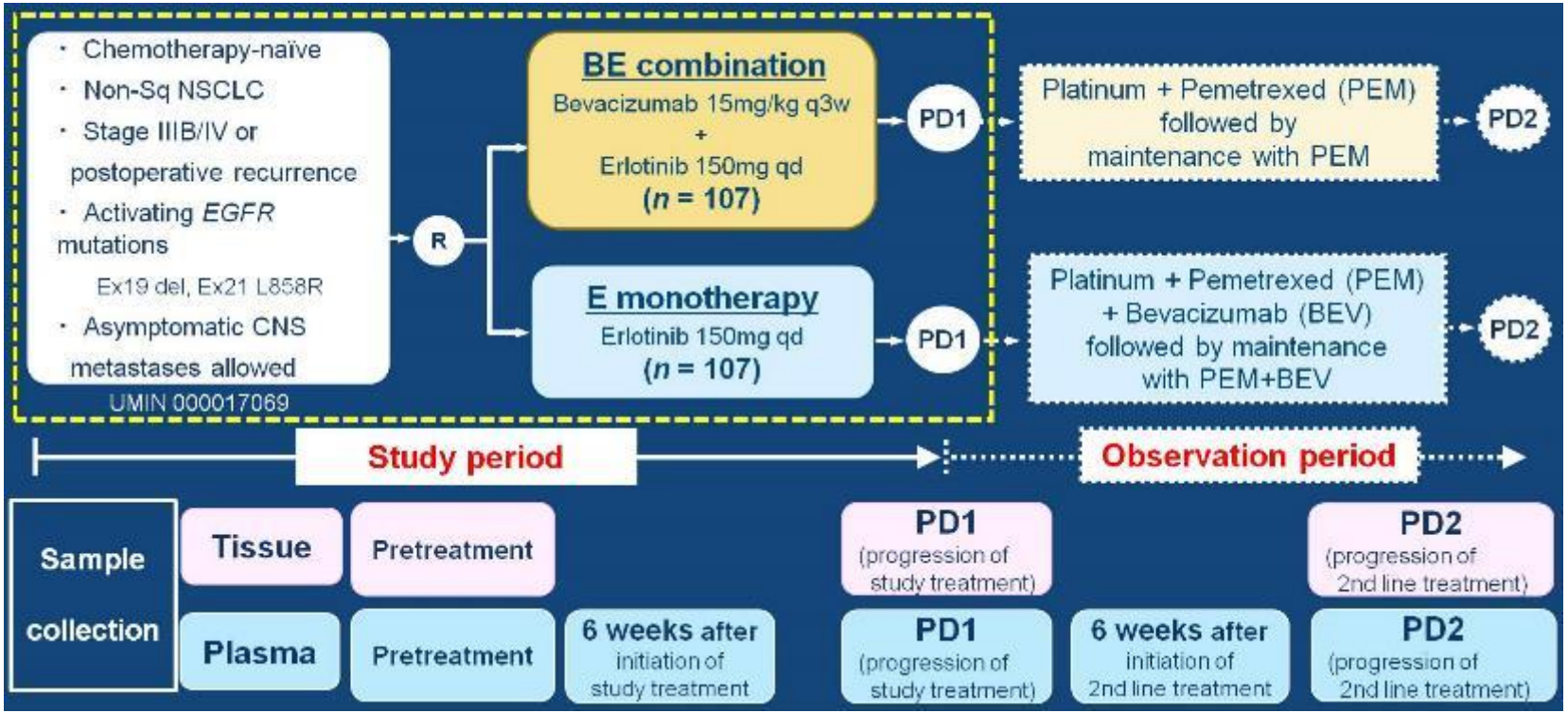
Passaro et al, Ann Onc 2022



Passaro et al, Ann Onc 2022

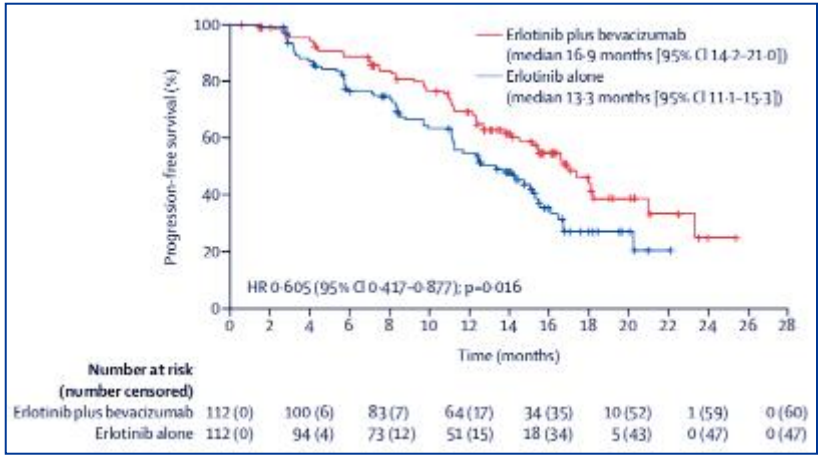
EGFR-TKI plus antiangiogenic agents

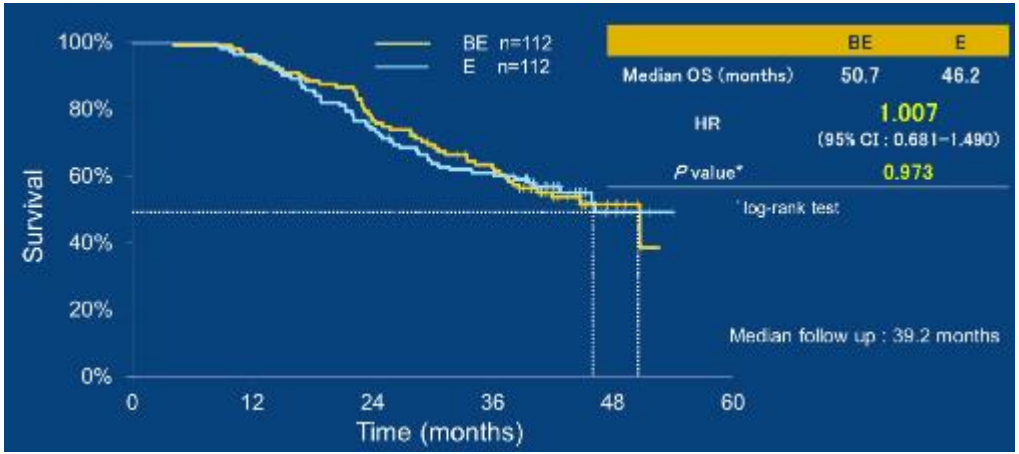
NEJ026



Saito et al, Lancet Oncology 2019; Maemondo et al, ASCO 2020

NEJ026





Saito et al, Lancet Oncology 2019; Maemondo et al, ASCO 2020

RELAY

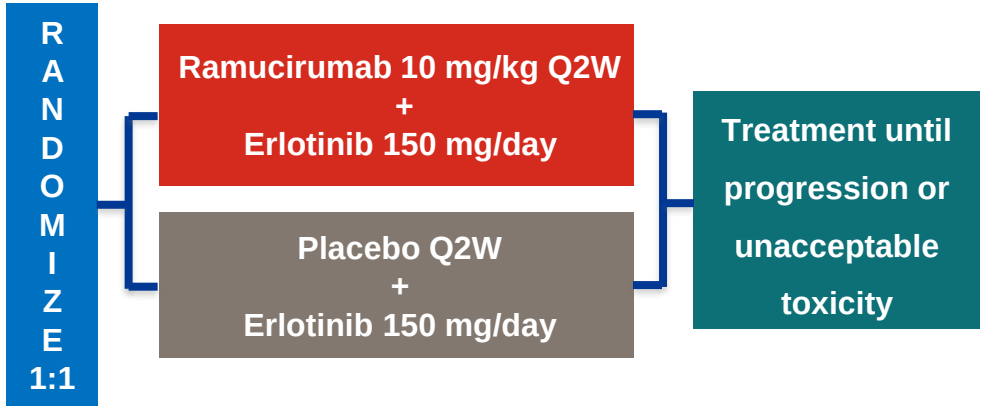
Key inclusion criteria

- Stage IV NSCLC
- *EGFR* mutation-positive (Ex19del or Ex 21 L858R)
- ECOG PS 0-1

Key exclusion criteria

- Known *EGFR* T790M mutation
- Prior treatment with EGFR TKI or chemotherapy
- **Brain metastases**

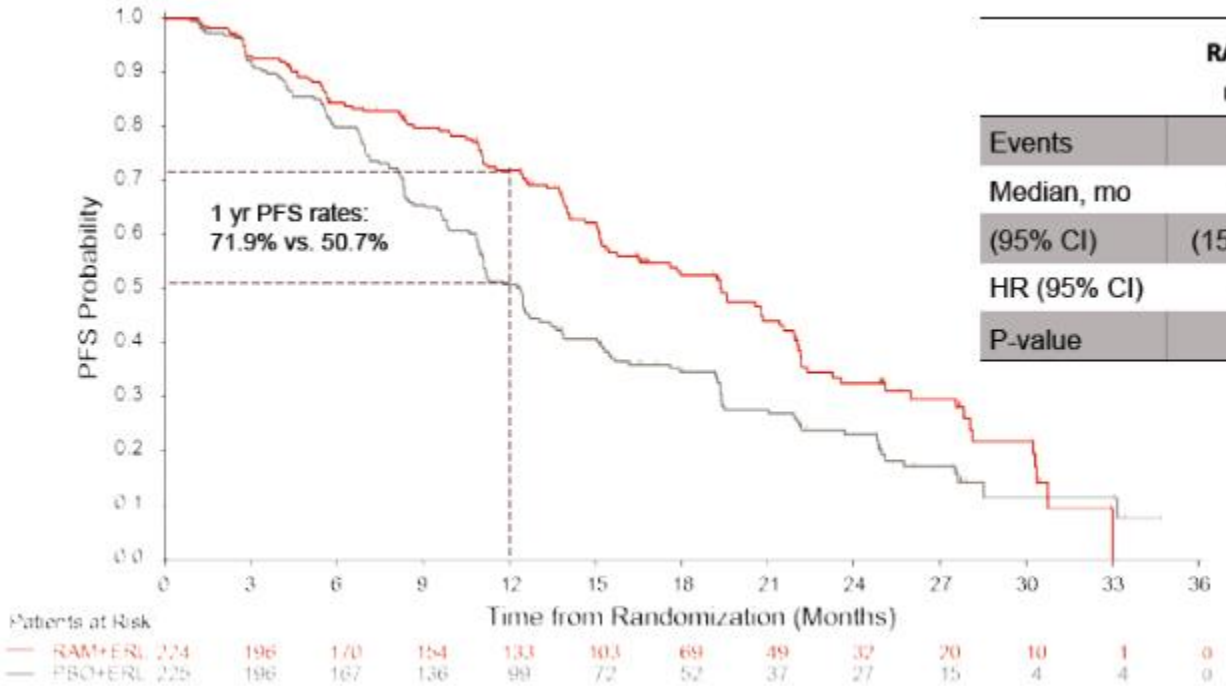
Phase 3
N=449



Primary endpoints: PFS

Nakagawa et al, Lancet Oncol 2019

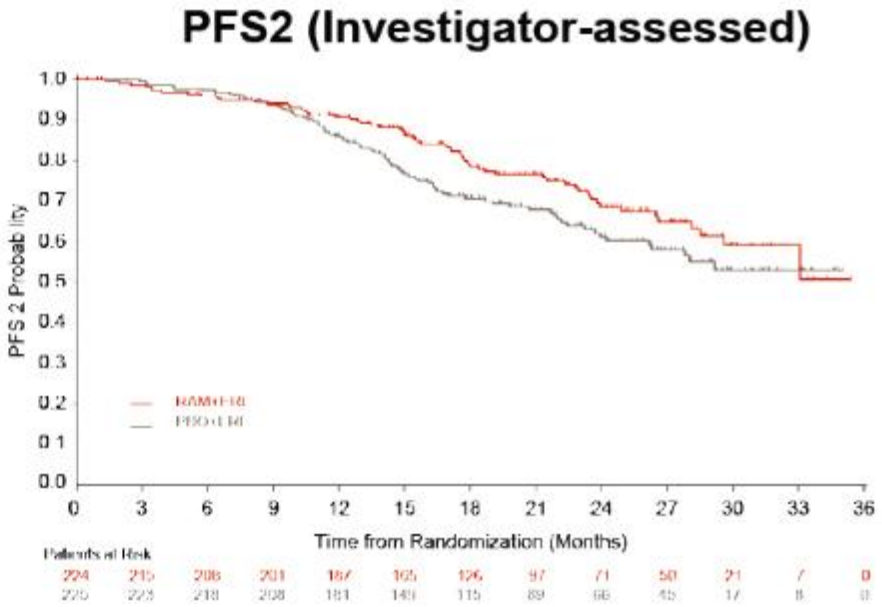
RELAY- PFS



	RAM+ERL n=224	PBO+ERL n=225
Events	122	158
Median, mo	**19.4**	**12.4**
(95% CI)	(15.4–21.6)	(11.0–13.5)
HR (95% CI)	**0.591** (0.461, 0.760)	
P-value	<0.0001	

RELAY – PFS2 and interim OS

		RAM+ERL N=224	PBO+ERL N=225
PFS2	Events,	61	79
	Censoring rate	73%	65%
	Median, mo	NR	NR
	HR (95% CI)	0.690 (0.490, 0.972)	
Interim OS	Events	37	42
	Censoring rate	83%	81%
	Median, mo	NR	NR
	HR (95% CI)	0.832 (0.532, 1.303)	



Adverse Events

	RAM+ERL N=221		PBO+ERL N=225	
n (%)	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Bleeding/Hemorrhage Events	121 (55)	4 (2)	59 (26)	4 (2)
Epistaxis	74 (34)	0	27 (12)	0
GI Hemorrhage Events[a]	23 (10)	3 (1)	6 (3)	1 (<1)
Pulmonary Hemorrhage Events	15 (7)	1 (<1)	4 (2)	1 (<1)
Hypertension	100 (45)	52 (24)*	27 (12)	12 (5)
Proteinuria[b]	76 (34)	6 (3)	19 (8)	0
Liver Failure/Liver Injury	140 (63)	31 (14)	120 (53)	28 (12)
Increased ALT	94 (43)	19 (9)	70 (31)	17 (8)
Increased blood bilirubin	68 (31)	3 (1)	70 (31)	2 (1)
Infusion-related reactions	6 (3)	0	4 (2)	0
Other TEAE of interest:				
ILD events[c]	4 (2)	1 (<1)	7 (3)	3 (1)

[a]The 2 most common GI hemorrhage events were anal hemorrhage (3% vs. <1%) and hemorrhoidal hemorrhage (2% vs. 2%)
[b]No events of nephrotic syndrome; [c]ILD events included pneumonitis

*Grade 3 only

ILD, Interstitial Lung Disease

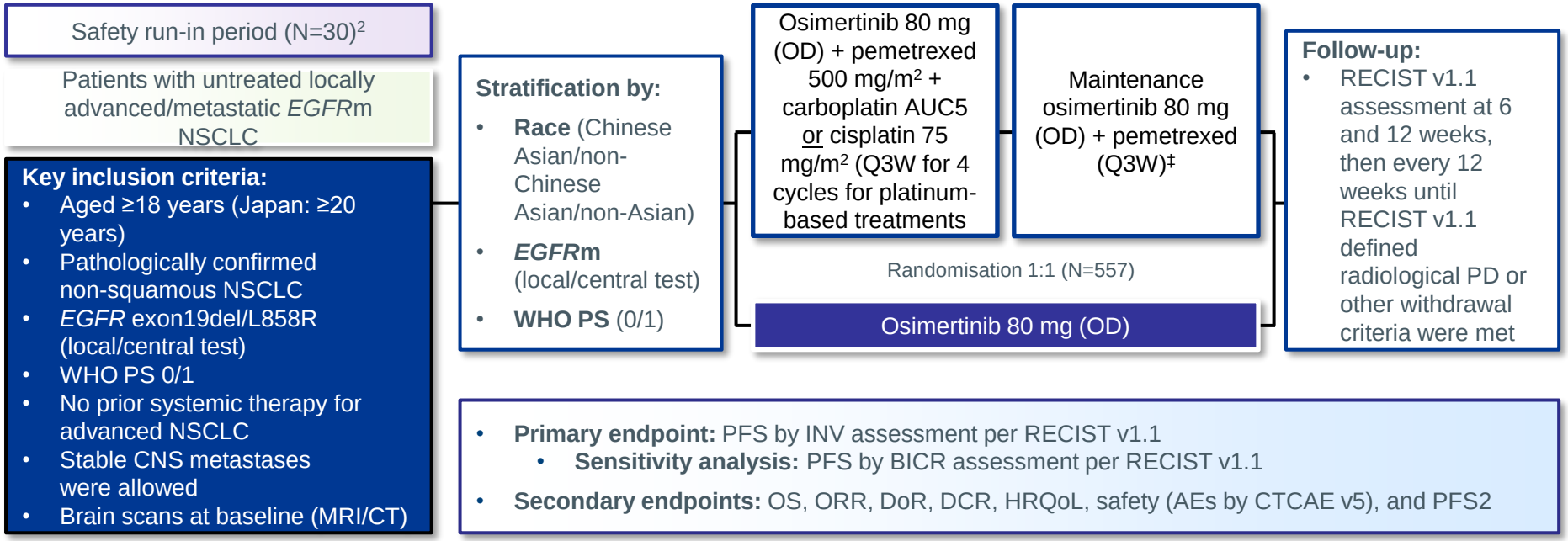
Chemo plus EGFR-TKI

Gefitinib +/- Carbo/pemetrexed

Study	Arm	PFS (mos)	HR, p	OS (mos)	HR, p
NEJ009	Gefitinib	11.9	0.49 P<0.001	38.4	0.82 P = 0.1270
	Carbo/Pem + G	**20.9**		**49**	
Noronha, et al	Gefitinib	8	0.51 P<0.001	17	0.45 P<0.001
	Carbo/Pem + G	**16**		**NR**	

Hosomi et al, JCO 2020 ; Noronha et al, JCO 2020

FLAURA2

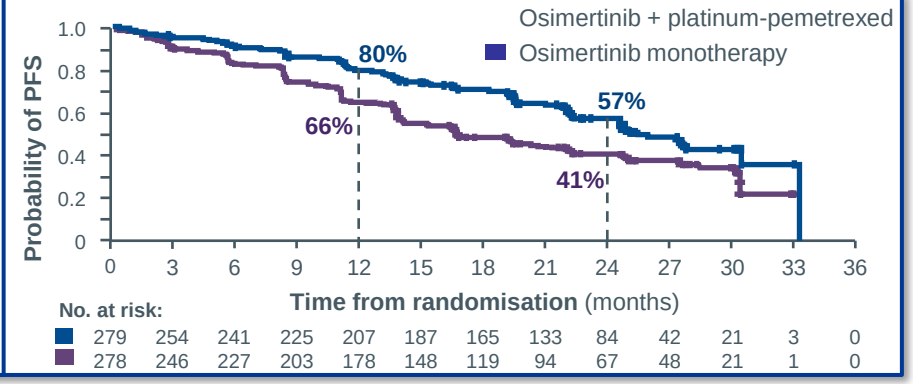


Median follow up: 19.5 months

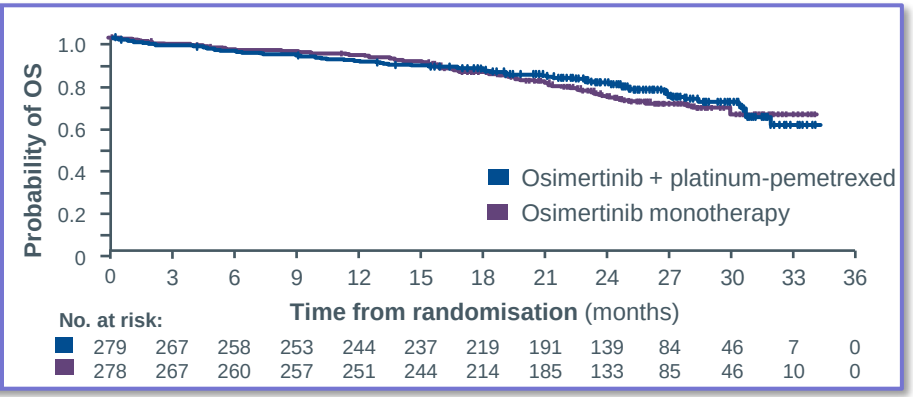
Planchard et al, NEJM 2023

FLAURA2

PFS



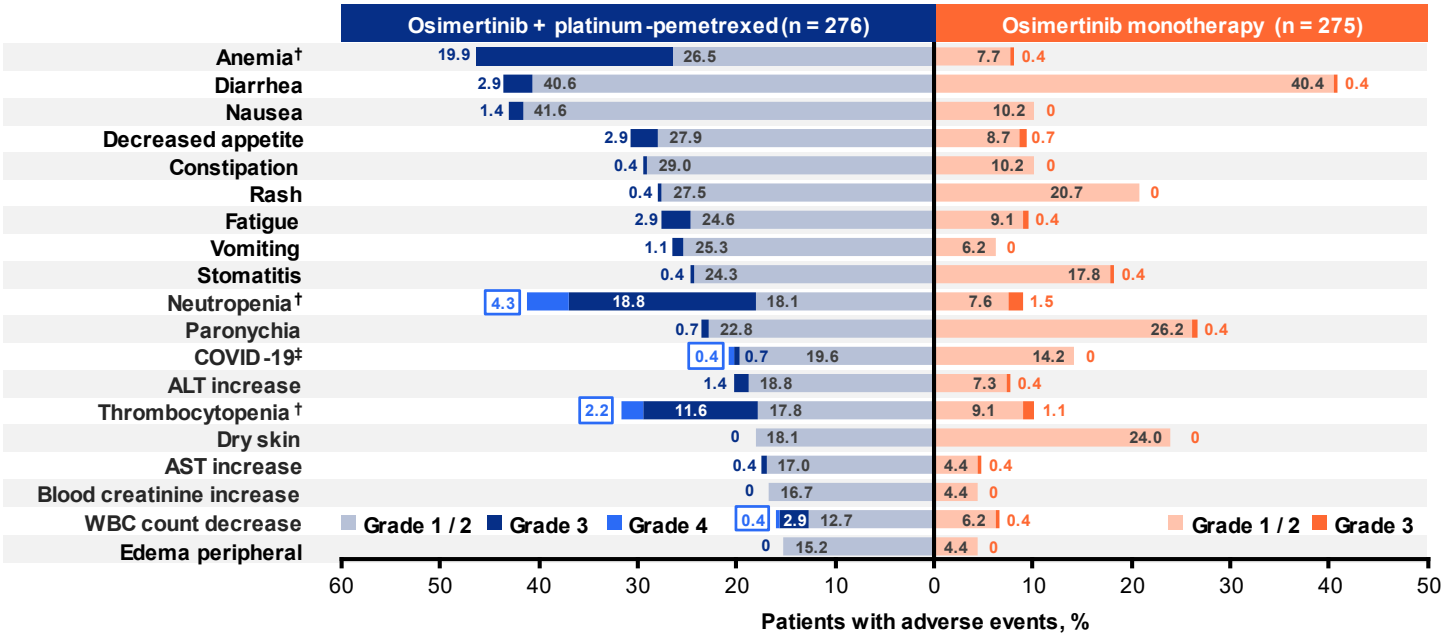
OS interim analysis



Endpoint	Osimertinib + platinum-pemetrexed (n=279)	Osimertinib monotherapy (n=278)
mPFS per INV, months (95% CI)		
Overall population	**25.5** (24.7–NC)	**16.7** (14.1–21.3)
	HR 0.62 (95% CI, 0.49–0.79); p<0.0001	
With CNS metastases	**24.9** (22.0–NC)	**13.8** (11.0–16.7)
	HR 0.47 (95% CI, 0.33–0.66)	
Without CNS metastases	**27.6** (24.7–NC)	**21.0** (16.7–30.5)
	HR 0.75 (95% CI, 0.55–1.03)	
mOS, months (95% CI)		
Overall population	**NR** (31.9–NC)	**NR** (NC–NC)
	HR 0.90 (95% CI, 0.65–1.24); p=0.5238	

CNS mets not a stratification factor

FLAURA2



- Of most common AEs (occurring in ≥15% of patients in either arm), all Grade 4 AEs in the osimertinib plus platinum-pemetrexed arm were hematological toxicities, known to be associated with chemotherapy; there were no common Grade 4 AEs in the monotherapy arm

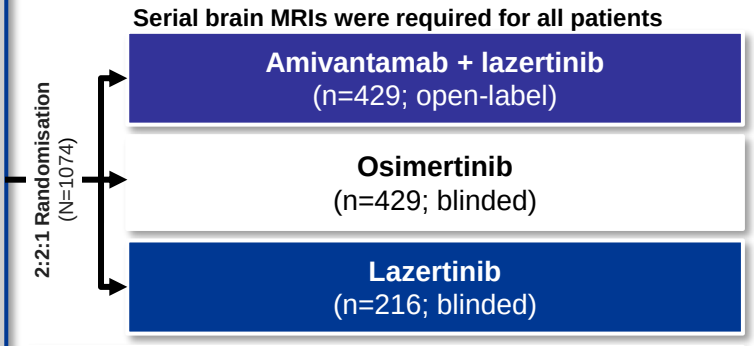
MARIPOSA

Key eligibility criteria:

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* exon19del or L858R
- ECOG PS 0 or 1

Stratification factors:

- *EGFR* mutation type (exon19del or L858R)
- Asian race (yes or no)
- History of brain metastases† (yes or no)



Dosing (in 28-day cycles):
Amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks
Lazertinib: 240 mg OD
Osimertinib: 80 mg OD

Median follow-up of 22.0 months

Primary endpoint of amivantamab + lazertinib vs osimertinib:

- PFS‡ by BICR per RECIST v1.1

Secondary endpoints of amivantamab + lazertinib vs osimertinib:

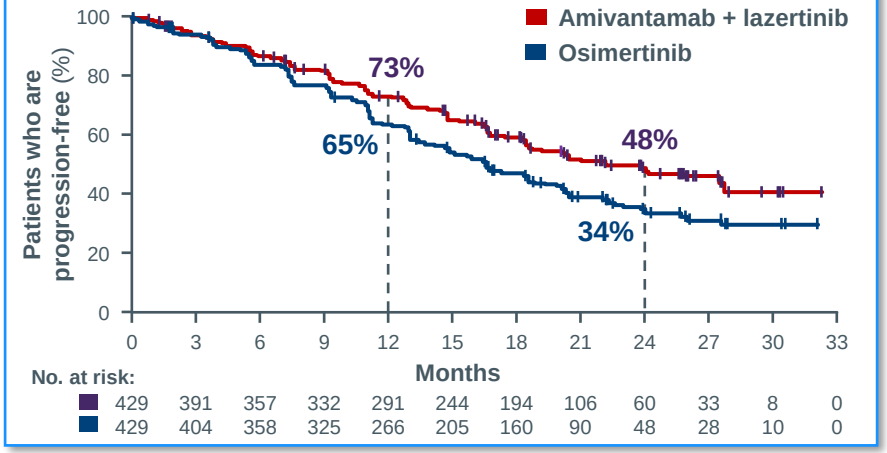
- OS‡
- ORR
- DoR
- PFS after first subsequent therapy (PFS2)
- Symptomatic PFS§
- Intracranial PFS§
- Safety

Lazertinib monotherapy arm was included to assess the contribution of components

Cho et al, ESMO 2023 LBA14

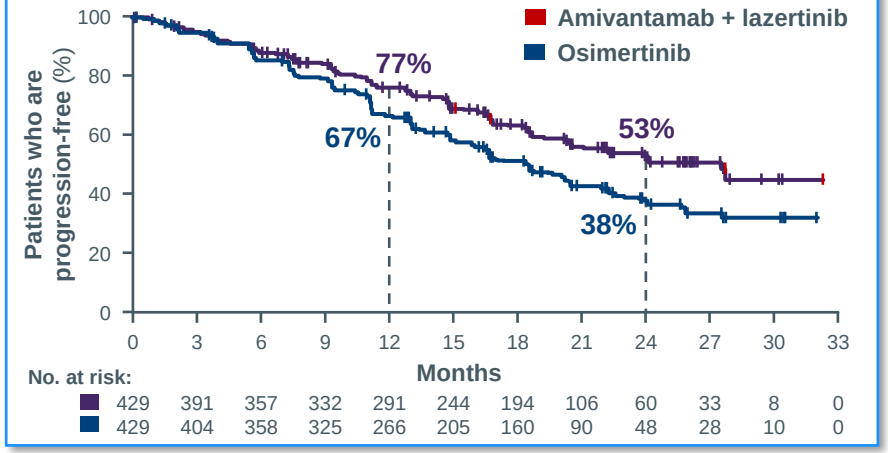
MARIPOSA

PFS



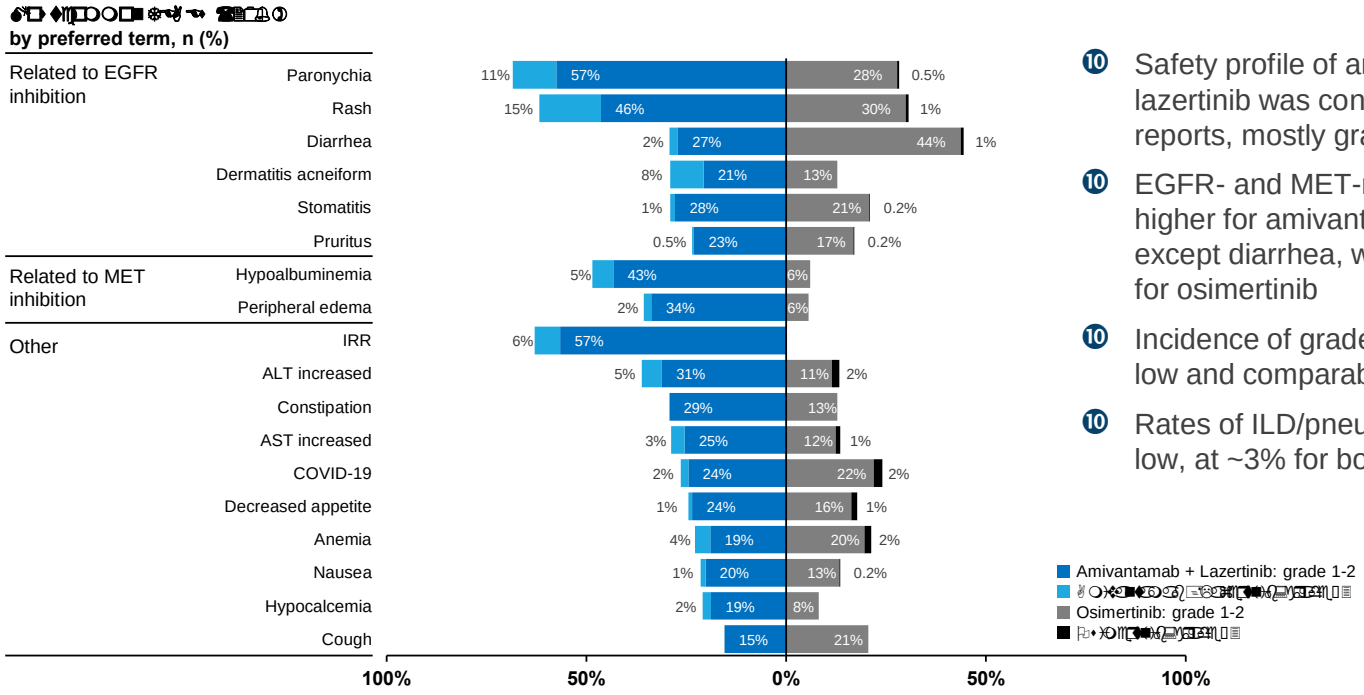
Endpoint	Amivantamab + lazertinib	Osimertinib
mPFS, months (95% CI)	**23.7** (19.1–27.7)	**16.6** (14.8–18.5)
HR (95% CI)	**0.70** (0.58–0.85); p<0.001	

Extracranial PFS



Endpoint	Amivantamab + lazertinib	Osimertinib
mPFS, months (95% CI)	**27.5** (22.1–NE)	**18.5** (16.5–20.3)
HR (95% CI)	**0.68** (0.56–0.83); p<0.001[§]	

MARIPOSA - Safety



- Safety profile of amivantamab + lazertinib was consistent with prior reports, mostly grades 1-2
- EGFR- and MET-related AEs were higher for amivantamab + lazertinib except diarrhea, which was higher for osimertinib
- Incidence of grade 4-5 AEs was low and comparable between arms
- Rates of ILD/pneumonitis remained low, at ~3% for both arms

MARIPOSA - VTE

	Amivantamab + Lazertinib (n=421)	Osimertinib (n=428)
Any VTE, n (%)	157 (37)	39 (9)
Grade 1	5 (1)	0
Grade 2	105 (25)	24 (6)
Grade 3	43 (10)	12 (3)
Grade 4	2 (0.5)	1 (0.2)
Grade 5	2 (0.5)	2 (0.5)
Any VTE leading to death, n (%)	2 (0.5)	2 (0.5)
Any VTE leading to any discontinuation, n (%)	12 (3)	2 (0.5)
Anticoagulant use at time of first VTE, n (%)		
On anticoagulants	5 (1)	0
Not on anticoagulants	152 (36)	39 (9)
Median onset to first VTE	84 days	194 days
Within first 4 months, n (%)	97 of 157 (62)	13 of 39 (33)

- VTE rates were higher for amivantamab + lazertinib
  - Most common preferred terms were pulmonary embolism and deep vein thrombosis
  - Most VTEs were grade 1-2
  - Incidence of grade 4-5 VTEs was low (<1%) and comparable between arms
- Rates of discontinuations due to VTE were low and comparable between arms
- At time of first VTE:
  - Most patients were not on anticoagulants
  - Majority in the amivantamab + lazertinib arm occurred within the first 4 months
- Prophylactic dose anticoagulation is now recommended for the first 4 months of treatment in ongoing trials of amivantamab + lazertinib

MARIPOSA-2

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1
- Stable brain metastases were allowed; radiation/definitive therapy was not required (untreated)

Stratification Factors

- Osimertinib line of therapy (1st vs 2nd)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=657)

Serial brain MRIs were required for all patients

Amivantamab-Lazertinib-Chemotherapy (n=263)

Chemotherapy (n=263)

Amivantamab-Chemotherapy (n=131)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at Cycle 3 (week 7)

Lazertinib: 240 mg daily starting after completion of carboplatin[b]

Chemotherapy administered at the beginning of every cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

Dual primary endpoint of PFS[c] by BICR per RECIST v1.1:

- **Amivantamab-Lazertinib-Chemotherapy** vs **Chemotherapy**
- **Amivantamab-Chemotherapy** vs **Chemotherapy**

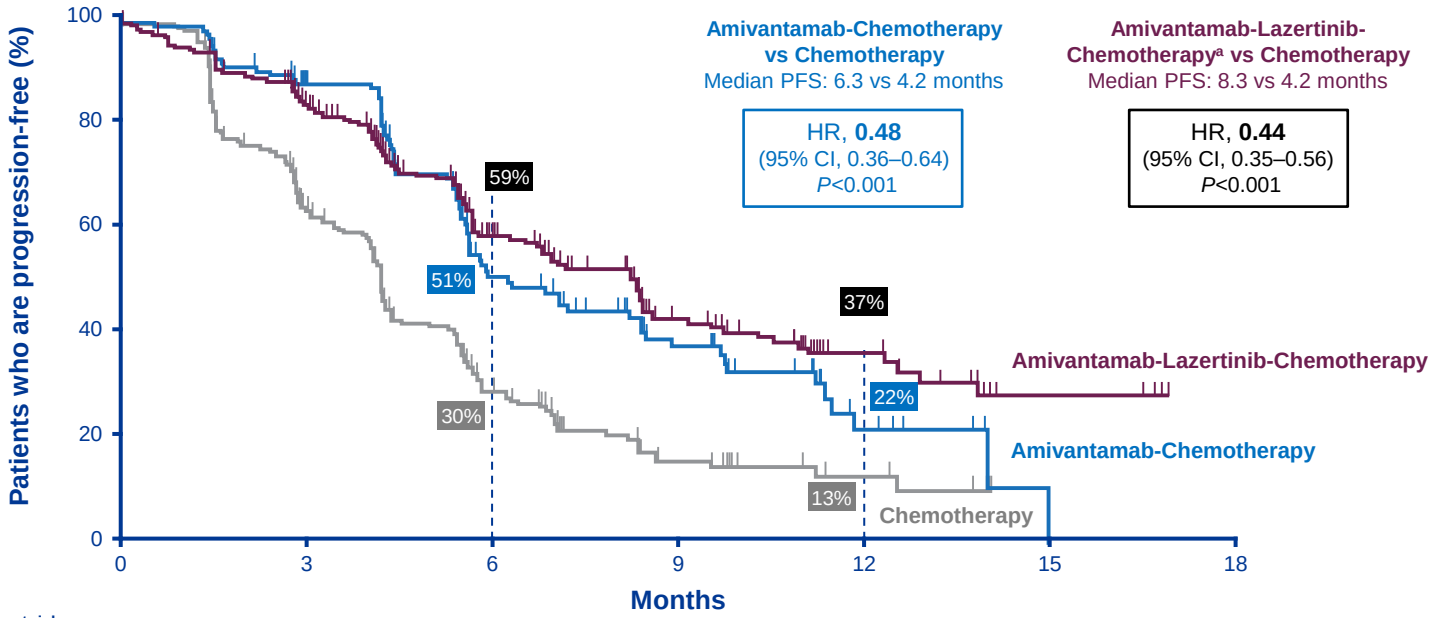
Secondary endpoints:

- Objective response rate (ORR)[c]
- Duration of response (DoR)
- Overall survival (OS)[c]
- Intracranial PFS
- Time to subsequent therapy[d]
- PFS after first subsequent therapy (PFS2)[d]
- Symptomatic PFS[d]
- Safety

Median follow-up: 8.7 months

Passaro et al, Ann Onc 2023

MARIPOSA-2 PFS



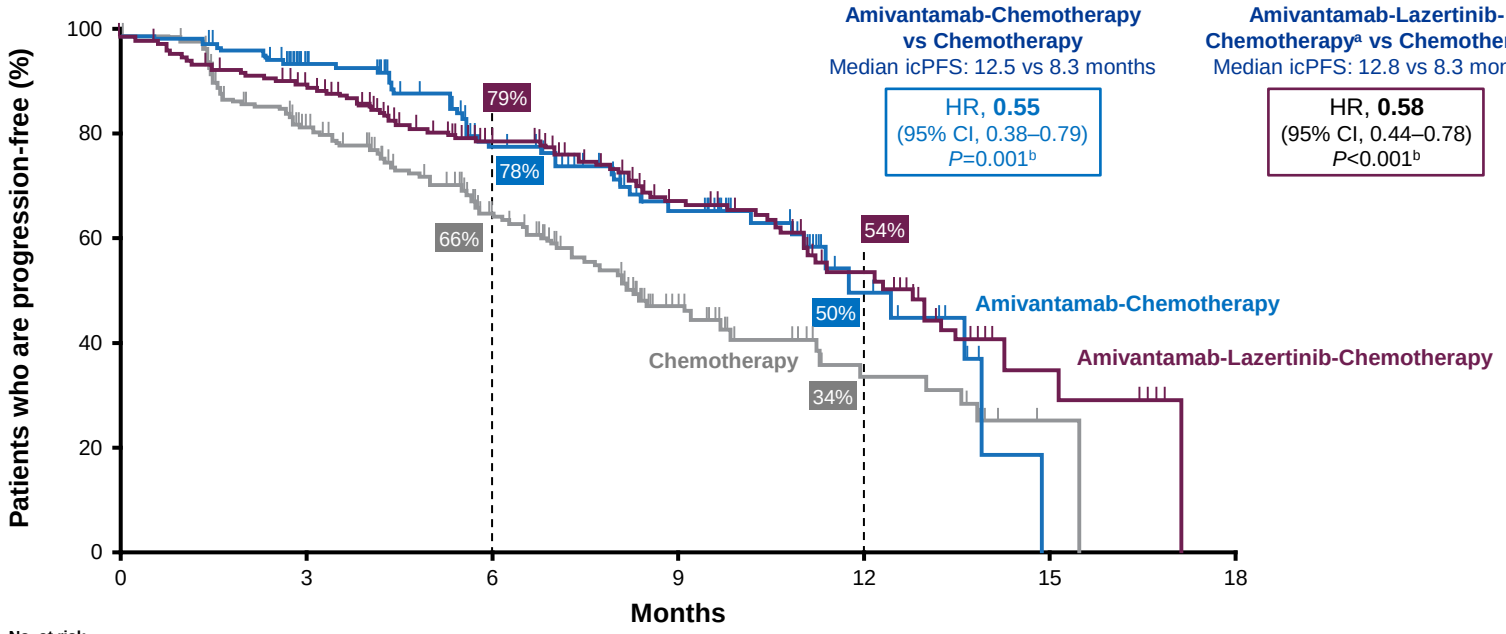
No. at risk							
Amivantamab-Chemotherapy	131	99	49	27	7	0	0
Amivantamab-Lazertinib-Chemotherapy	263	194	104	52	21	4	0
Chemotherapy	263	135	49	17	6	0	0

Consistent PFS benefit by investigator: HR, 0.41 (8.2 vs 4.2 mo; *P*<0.001[b]) & HR, 0.38 (8.3 vs 4.2 mo; *P*<0.001[b])

[a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received. [b]Nominal *P*-value; endpoint not part of hierarchical hypothesis testing.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

MARIPOSA-2 Intracranial PFS



No. at risk							
Amivantamab-Chemotherapy	131	103	72	40	11	0	0
Amivantamab-Lazertinib-Chemotherapy	263	211	135	74	32	6	0
Chemotherapy	263	167	89	37	13	1	0

MARIPOSA - Safety

Most common TEAEs (≥25%) by preferred term, n (%)	Chemotherapy (n=243)		Amivantamab-Chemotherapy (n=130)		Amivantamab-Lazertinib-Chemotherapy[a] (n=263)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition						
Paronychia	1 (0.4)	0	48 (37)	3 (2)	133 (51)	11 (4)
Rash	12 (5)	0	56 (43)	8 (6)	126 (48)	17 (6)
Stomatitis	21 (9)	0	41 (32)	1 (1)	120 (46)	24 (9)
Diarrhea	16 (7)	1 (0.4)	18 (14)	1 (1)	68 (26)	10 (4)
Associated with MET inhibition						
Hypoalbuminemia	21 (9)	1 (0.4)	29 (22)	3 (2)	104 (40)	12 (5)
Peripheral edema	15 (6)	0	42 (32)	2 (2)	85 (32)	1 (0.4)
Associated with Chemotherapy						
Neutropenia	101 (42)	52 (21)	74 (57)	59 (45)	181 (69)	144 (55)
Thrombocytopenia	72 (30)	22 (9)	57 (44)	19 (15)	158 (60)	96 (37)
Anemia	97 (40)	23 (9)	51 (39)	15 (12)	141 (54)	48 (18)
Leukopenia	68 (28)	23 (9)	37 (28)	26 (20)	106 (40)	71 (27)
Other						
Infusion-related reaction	1 (0.4)	0	76 (58)	7 (5)	148 (56)	9 (3)
Nausea	90 (37)	2 (1)	58 (45)	1 (1)	131 (50)	16 (6)
Constipation	72 (30)	0	50 (38)	1 (1)	96 (37)	3 (1)
Decreased appetite	51 (21)	3 (1)	40 (31)	0	85 (32)	7 (3)
Vomiting	42 (17)	1 (0.4)	32 (25)	1 (1)	76 (29)	10 (4)
Fatigue	47 (19)	4 (2)	36 (28)	4 (3)	69 (26)	15 (6)
Asthenia	40 (16)	5 (2)	34 (26)	1 (1)	67 (25)	14 (5)
Alanine aminotransferase increased	67 (28)	10 (4)	26 (20)	7 (5)	55 (21)	14 (5)
AESIs by grouped term, n (%)						
Rash[b]	30 (12)	0	92 (71)	13 (10)	197 (75)	40 (15)
VTE[c]	11 (5)	7 (3)	13 (10)	3 (2)	58 (22)	17 (6)
ILD	0	0	2 (2)	1 (1)	7 (3)	5 (2)

- Amivantamab-containing arms had higher rates of EGFR- and MET-related AEs
- Neutropenia and thrombocytopenia:
  - Mostly occurred during cycle 1
  - Low rates of febrile neutropenia (2%, 2%, and 8%)
  - Low rates of grade 3-4 bleeding[d] (0%, 1%, and 3%)
- VTE highest in amivantamab-lazertinib-chemotherapy arm
  - No grade 5 events
  - Rates of discontinuation due to VTE were low (0%, 1%, and 0.4%)
- Incidence of ILD was low in all arms (<3%)

Conclusions

Screen for EGFR mutations!

Novel options coming to clinical practice

Choose your strategy taking in to account patient's preference, efficacy and tolerability

The Christie
Research Division

Backup

Mariposa 2 - Summary of Adverse Events (AEs)

	Chemotherapy (n=243)	Amivantamab-Chemotherapy (n=130)	Amivantamab-Lazertinib-Chemotherapy[a] (n=263)
Treatment duration, median (range)	3.7 months (0–15.9)	6.3 months (0–14.7)	5.7 months (0.1–18.6)
No. of chemotherapy cycles, median (range)			
Carboplatin	4 (1–5)	4 (1–4)	4 (1–4)
Pemetrexed	6 (1–23)	9 (1–22)	7 (1–25)

TEAE, n (%)	Chemotherapy (n=243)	Amivantamab-Chemotherapy (n=130)	Amivantamab-Lazertinib-Chemotherapy[a] (n=263)
Any AEs	227 (93)	130 (100)	263 (100)
Grade ≥3 AEs	117 (48)	94 (72)	242 (92)
Serious AEs	49 (20)	42 (32)	137 (52)
AEs leading to death	3 (1)	3 (2)	14 (5)
Any AE leading to treatment:			
Interruptions of any agent	81 (33)	84 (65)	202 (77)
Reductions of any agent	37 (15)	53 (41)	171 (65)
Discontinuations of any agent	9 (4)	24 (18)	90 (34)
Discontinuations of all agents due to AE	10 (4)	14 (11)	38 (14)

- Median treatment duration was longer for the amivantamab-containing arms vs chemotherapy
- Amivantamab-containing arms had higher rates of grade ≥3 AEs and dose modifications vs chemotherapy
  - Highest in the amivantamab-lazertinib-chemotherapy arm
- AEs leading to death were low
- Discontinuations of all agents due to treatment-related AEs was 2%, 8%, and 10%

- [a]Amivantamab-lazertinib-chemotherapy arm includes all patients regardless of the dosing regimen received.
- TEAE, treatment-emergent adverse event.