EGFR blockade: is there anything new?

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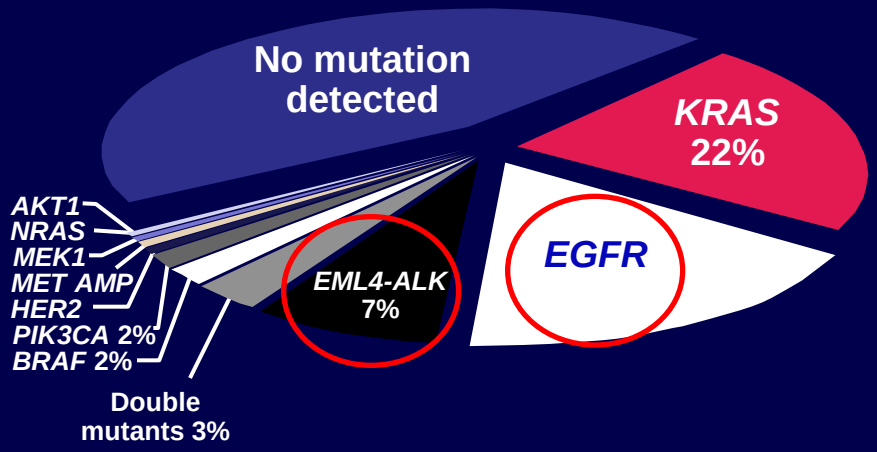
Potential "Drugable" Driver Gene in NSCLC

Lung Cancer Molecular Consortium Lung Adenocarcinoma[1,2]



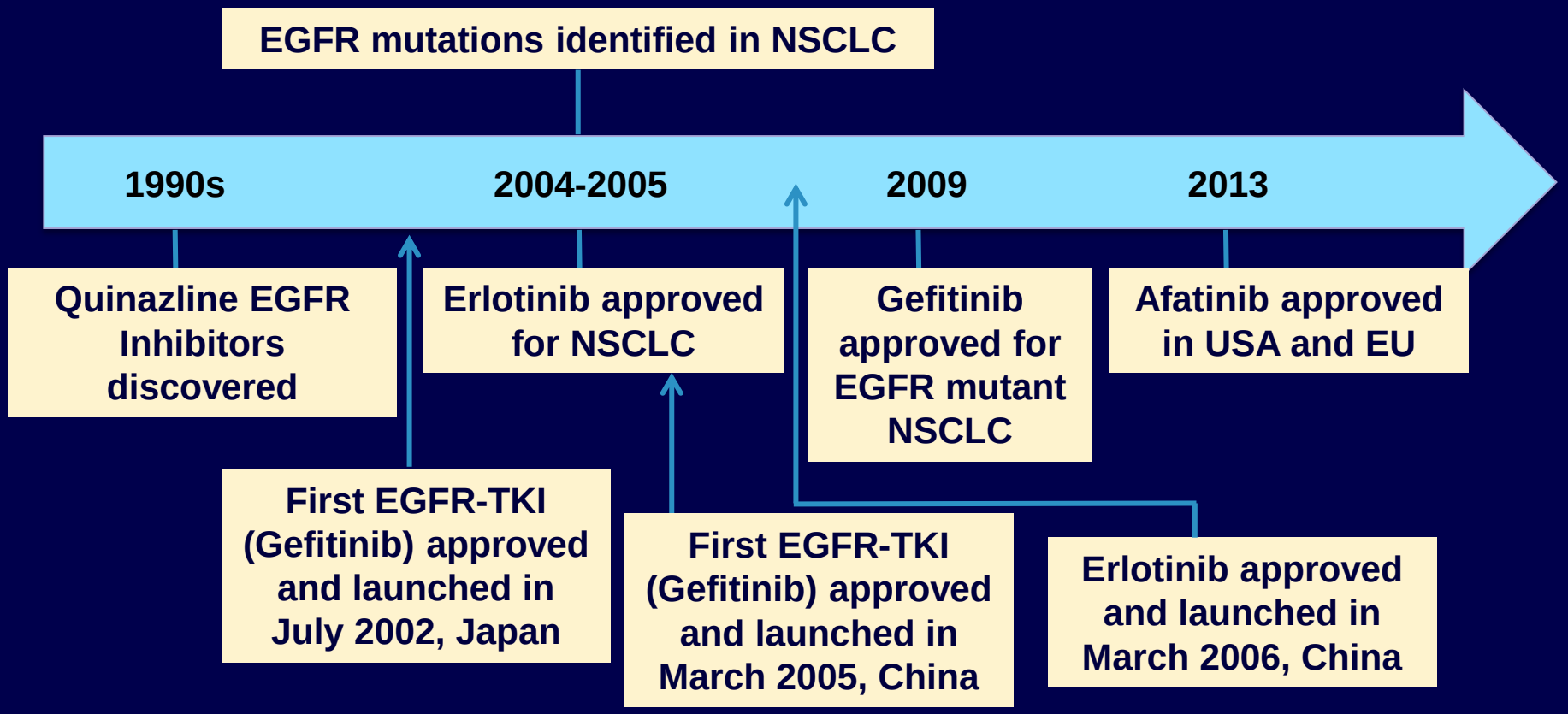
Mutations found in 54% (280/516)

Emerging "Druggable" Targets in NSCLC-Squamous Subtype[3]

Gene	Event Type	Frequency, %
FGFR1	Amplification	20-25
FGFR2	Mutation	5
PIK3CA	Mutation	9
PTEN	Mutation deletion	18
CCND1	Amplification	8
CDKN2A	Deletion/mutation	45
PDGFRA	Amplification mutation	9
EGFR	Amplification	10
MCL1	Amplification	10
BRAF	Mutation	3
DDR2	Mutation	4
ERBB2	Amplification	2

1. Kris MG, et al. ASCO 2011. CRA7506.
2. Johnson BE, et al. IASLC WCLC 2011. Abstract O16.01
3. Hammerman P, et al. IASLC WCLC 2011. Abstract PRS.1

EGFR pathway and its milestones



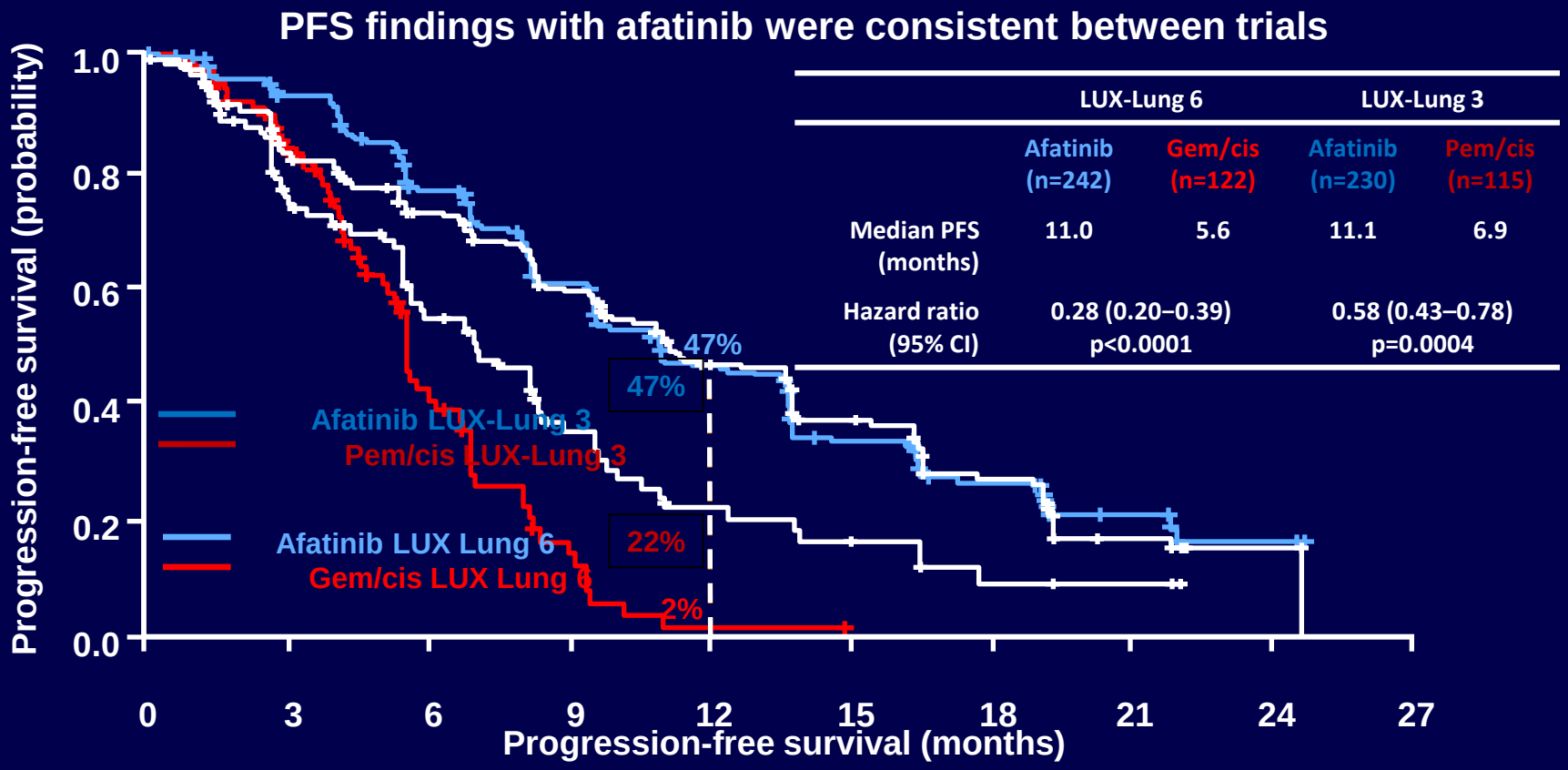
Gandhi L, et al. Clin Cancer Res 2012; 18(14):3737-3742.

EGFR-TKIs vs. Chemotheray in EGFR Mutation+ Lung Adenocarcinoma

Trial	Patient Population	TKI	Pts No.	PFS (months)			OS (months)		
				TKI	Chemo	HR(95%CI)	TKI	Chemo	HR(95%CI)
EGFR mutation+ subgroup analysis in phase III trials									
IPASS	Asia, non-smoker	Gefitinib	261	9.5	6.3	0.48 (0.36-0.64)	21.6	21.9	0.78 (0.50-1.20)
First Signal	Korea, non-smoker	Gefitinib	42	8.4	6.7	0.61 (0.31-1.22)	30.6	26.5	0.82 (0.352-1.922)
Phase III trials in EGFR mutation+ patients									
NEJ002	Japan	Gefitinib	228	10.8	5.4	0.322 (0.236-0.438)	27.7	26.6	0.88 (0.634-1.241)
WJTOG3405	Japan	Gefitinib	172	9.6	6.6	0.520 (0.378-0.715)	35.5	38.8	1.185 (0.767-1.829)
OPTIMAL	China	Erlotinib	154	13.1	4.6	0.16 (0.10-0.26)	32.1	37.5	1.065
EURTAC	Caucasian	Erlotinib	174	9.7	5.2	0.37 (0.25-0.54)	22.9	18.8	0.80 (0.47-1.37)
LUX-Lung3	Asia, non-Asia	Afatinib	345	11.1	6.9	0.58 (0.43-0.78)	NA	NA	NA
LUX-Lung6	Asia	Afatinib	364	11.0	5.6	0.28 (0.20-0.39)	NA	NA	NA
ENSURE	Asia	Erlotinib	217	11.0	5.5	0.34 (0.22-0.51)	NA	NA	NA

1. Mok, et al. NEJM 2009; 2. Han et al. JCO 2012. 3. Maemondo, et al. NEJM 2010; 4. Mitsudomi, et al. Lancet Oncol 2010; 5. Zhou, et al. Lancet Oncol 2011; 6. Rosell et al. Lancet Oncol 2012. 7. Sequist, et al. JCO 2013. 8. Wu, et al. 2013 ASCO Abstract 8016.

independent review (all randomized patients) in LUX-Lung 6 and LUX-Lung 3



	LUX-Lung 6		LUX-Lung 3	
	Afatinib (n=242)	Gem/cis (n=122)	Afatinib (n=230)	Pem/cis (n=115)
Median PFS (months)	11.0	5.6	11.1	6.9
Hazard ratio (95% CI)	0.28 (0.20–0.39) p<0.0001		0.58 (0.43–0.78) p=0.0004	

Number at risk										
Afatinib (LL6)	242	208	166	126	89	60	35	12	4	0
Gem/cis (LL6)	122	70	25	8	1	0	0	0	0	0
Afatinib (LL3)	230	180	151	120	77	50	31	10	3	0
Pem/cis (LL3)	115	72	41	21	11	7	3	2	0	0

Sequist, et al. JCO 2013. Wu, et al. 2013 ASCO Abstract 8016.

ARCHER 1009 Phase 3 Study of Dacomitinib vs. Erlotinib in 2/3rd Line NSCLC

Trial design	Endpoints	Co-primary patient populations
Double-blind, randomized, Phase 3, global	Primary: PFS‡ Secondary: OS*, safety, PROs	• All patients with *advanced NSCLC* • Patients with *NSCLC that is confirmed KRAS WT* •Global (Asia, EU, NA, SA) •First subject June 2012

‡Based on IRC review

*The study is adequately powered to show difference in OS

Advanced NSCLC*
1/2 prior CTs
ECOG PS 0–2
Tissue available
(determination of molecular markers *not* required prior to dosing)

Stratification

- Non-smokers vs. smokers
- Adenocarcinoma vs. nonadenocarcinoma
- East Asian vs. non-East Asian/Indian
- ECOG PS 0/1 vs. 2

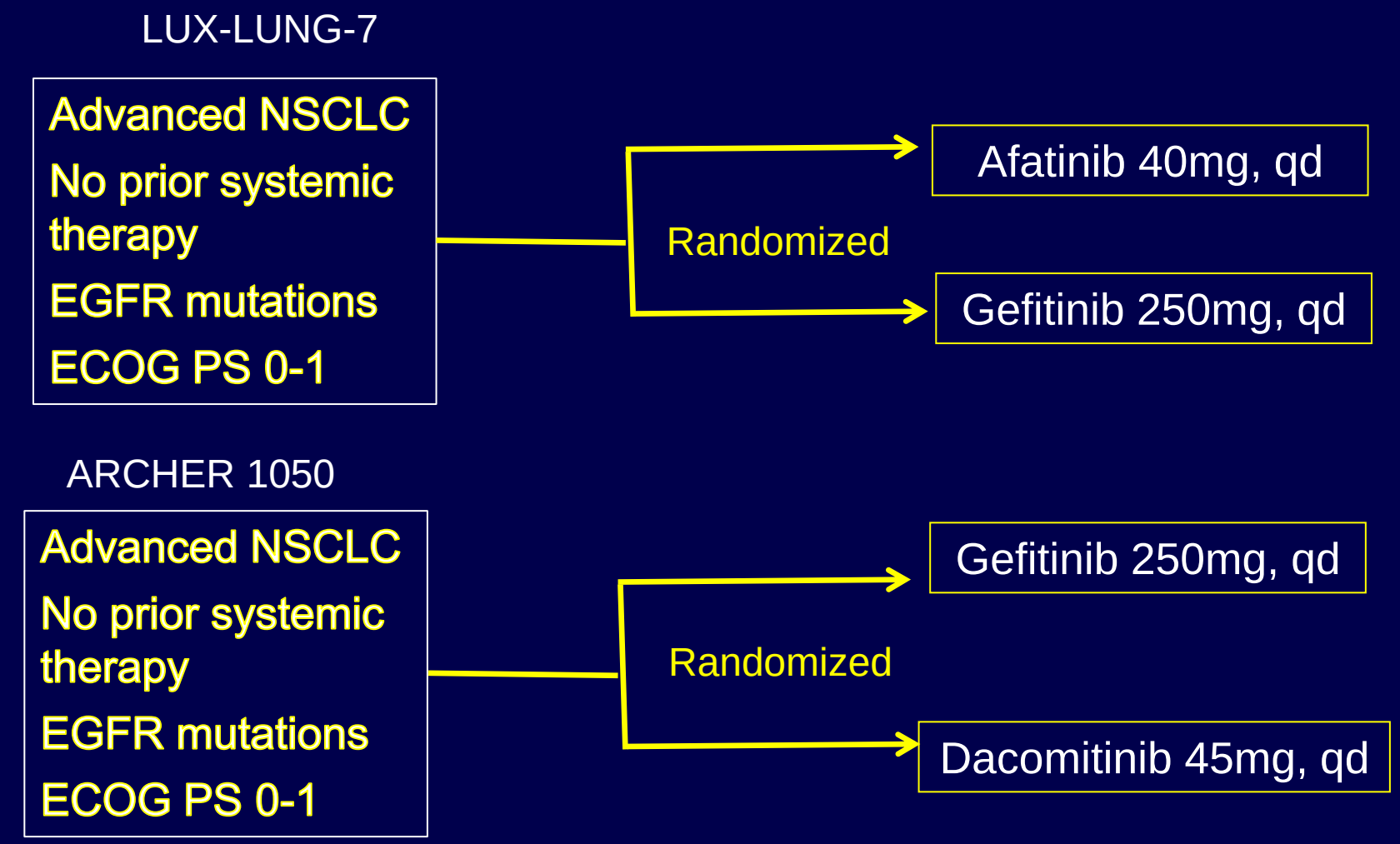
1:1

N=800

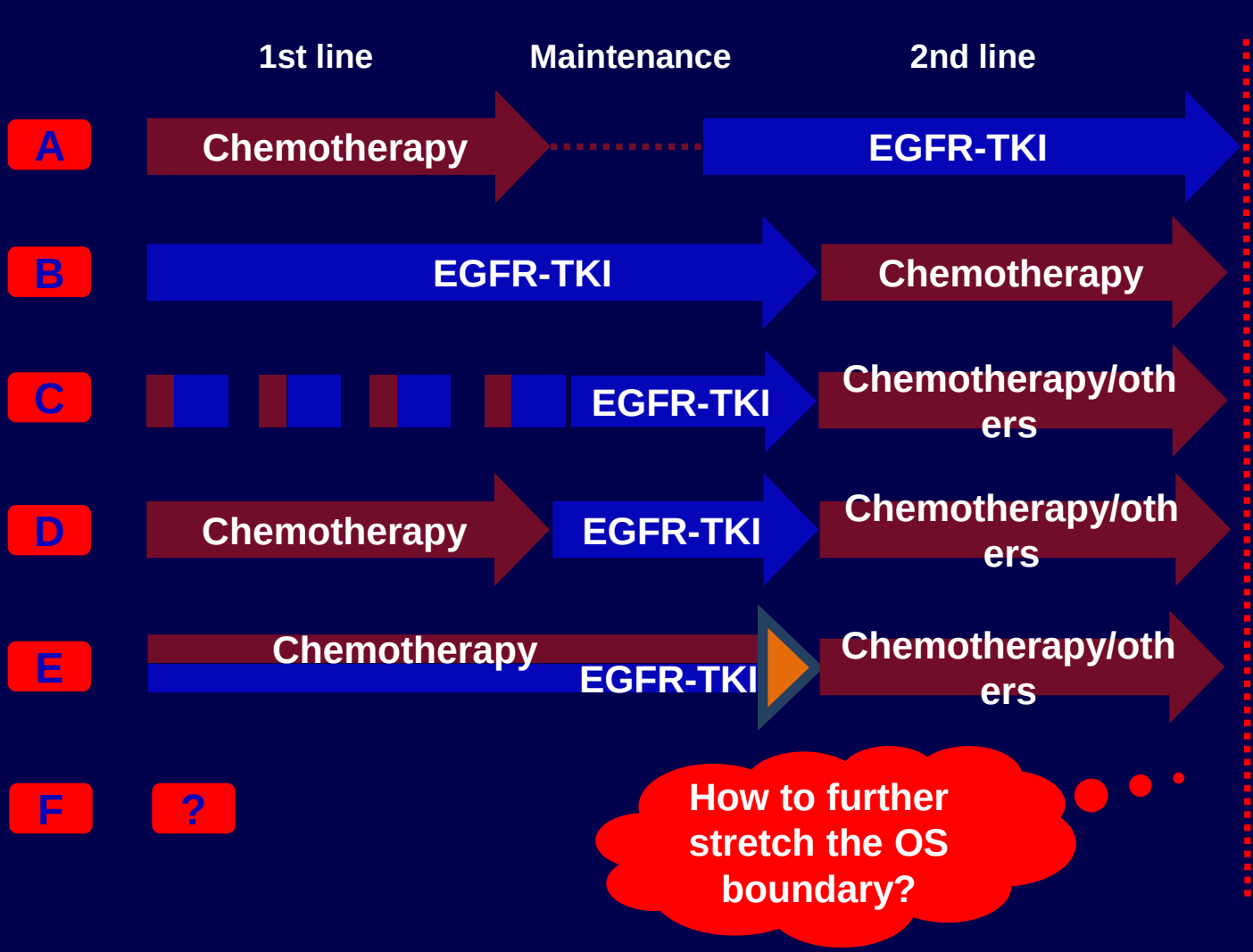
Dacomitinib
45 mg QD

Erlotinib
150 mg QD

Is there any better EGFR TKI?



Which is Better Modality for EGFR Mu+ Patients?



Questions:

① A=B ?

② C>B ?

③ D>B ?
D vs. C ?

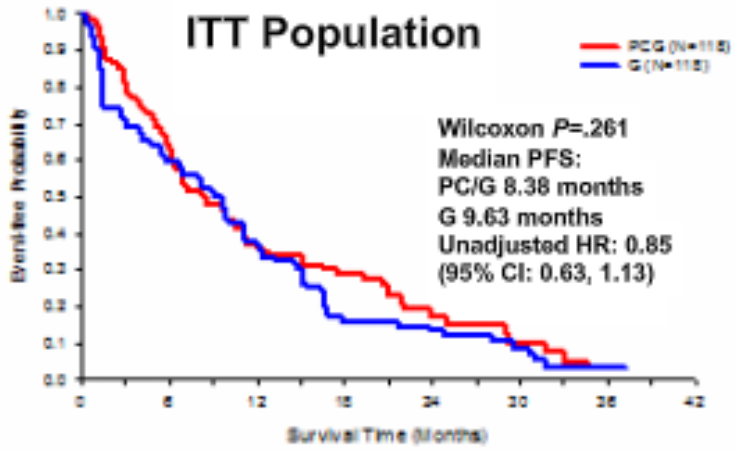
④ E in selected population?

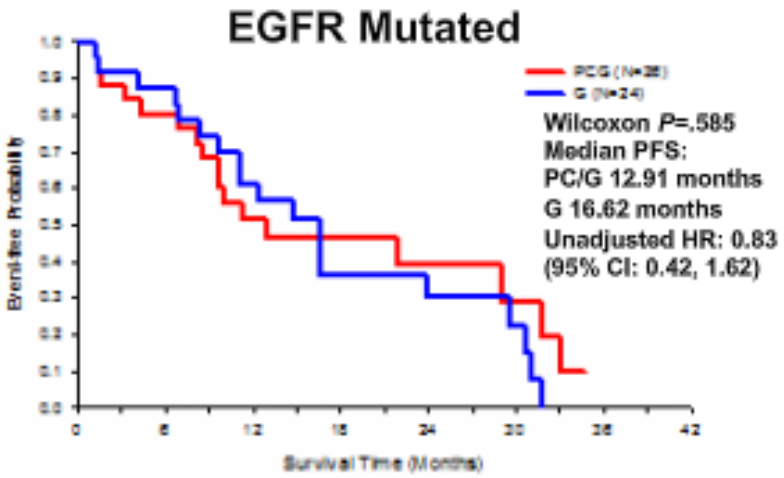
A Randomized Phase III Study Comparing First-line Pemetrexed plus Cisplatin Followed by Gefitinib as Maintenance with Gefitinib Monotherapy in East Asian Patients with Locally Advanced or Metastatic Nonsquamous Non-Small Cell Lung Cancer

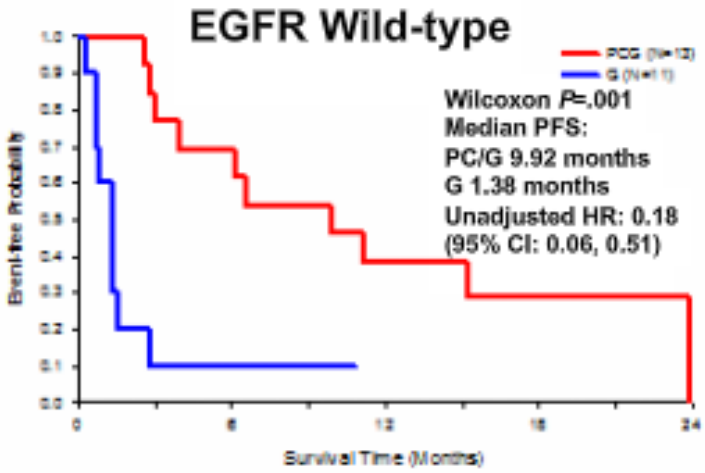
James Chih-Hsin Yang,[1] Keunchil Park,[2] Tony Mok,[3] Jin Hyoung Kang,[4] Vichien Srimunnumit,[5] Chia-Chi Lin ,[1] Dong-Wan Kim,[6] Chun-Ming Tsai,[7] HelenBarraclough,[8] Sedat Altug,[9] Mauro Orlando[10]

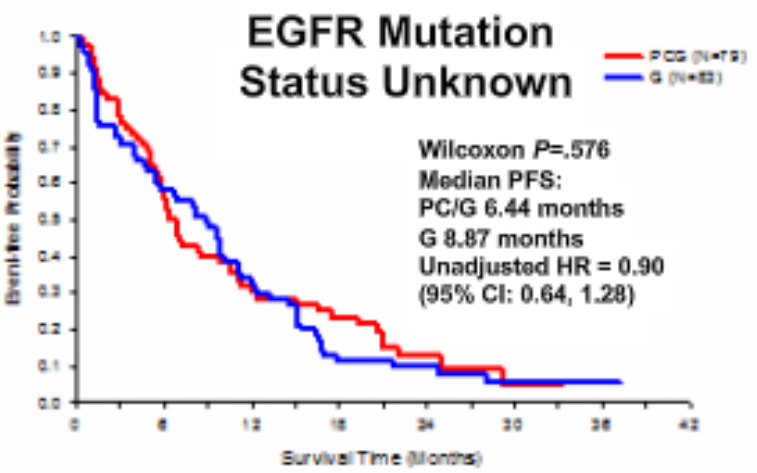
[1] National Taiwan University Hospital, Taipei, Taiwan; [2]Samsung Medical Center, Seoul, Republic of Korea; [3]Prince of Wales Hospital, Sha Tin, Hong Kong; [4]The Catholic University of Korea, ST . Mary's Hopsital, Seoul. Republic of Korea; [5]Division of Medical Oncology, Department of Faculty of Medicine, Mahidol University, Siriraj Hospital, Bangkok, Thailand; [6]Seoul National University Hospital, Seoul, Republic of Korea; [7]Taipei Veterans General Hospital, Taipei, Taiwan; [8]Eil Lilly Australia; [9]Eil Lilly Istanbul Turkey; [10]Eil Lilly Interamerica

Progression-free Survival in ITT and Biomarker-Assessable Population by EGFR Status



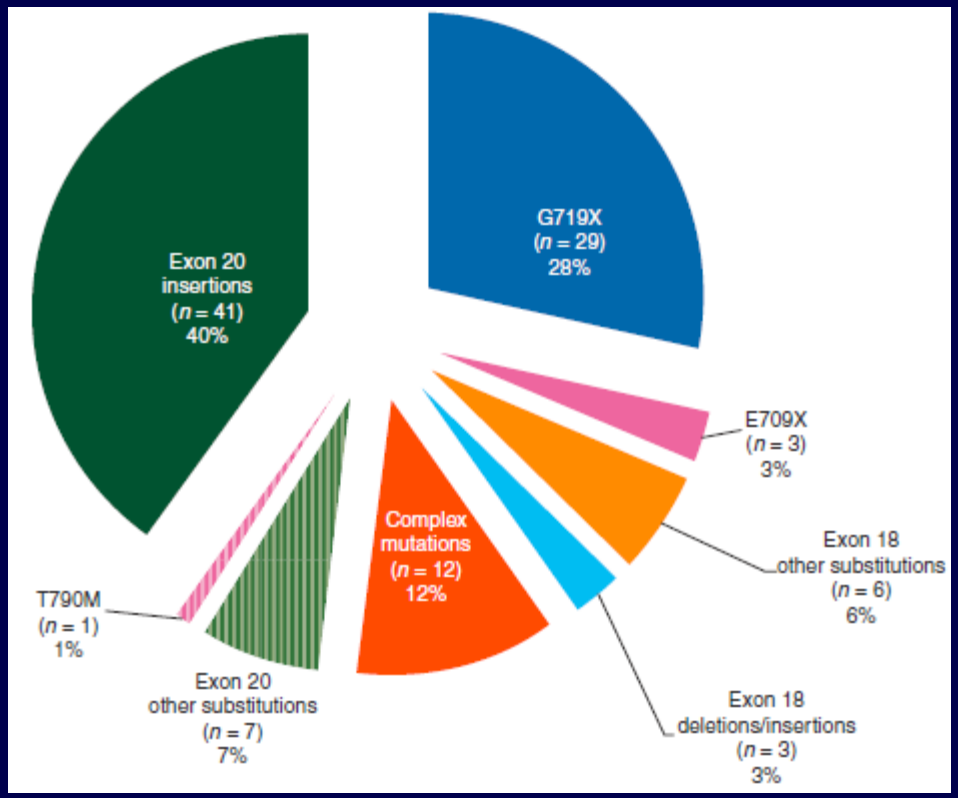






- **HRs for ITT and EGFR-mutated patients should be interpreted with caution as they were not constant.**

Frequency of rare EGFR exon 18 and 20 mutations in 10117 patients by French ERMETIC-IFCT network



- No relationship with
  - Gender
  - Age
  - Smoking Status
- Mostly seen in
  - Adenocarcinoma

Beau-Faller M, et al. Ann Oncol 2014; 25:126-131.

EGFR TKI in patients with advanced NSCLC harboring rare EGFR mutations

Keam B, Kim DW, Park JH, et al. Int J Clin Oncol 2013

	All	Classical alone	Classical+ rare	Rare± Rare	Classical +T790M
	306	269	16	16	5
ORR	71.9%	74.8%	68.8%	25%	80%
PD	7.8%	5.6%	6.3%	43.8%	20%
Median PFS	11.2	11.9	8.1	1.4	8.0

Beau-Faller M, Prim N, Ruppert Aam, et al. Ann Ann 2013

	Patients	Patients wih Exon 18 EGFR mutations	Patients with exon 20 EGFR mutations	Patients with complex exon 18 and 20 EGFR mutations
	74	28	38	8
PR	15%	7%	8%	57%
PD	53%	66%	56%	14%
PFS<3months	48%	43%	64%	0%
PFS 3-6 months	28%	36%	16%	57%

EGFR uncommon muatation in LUX-Lung trials

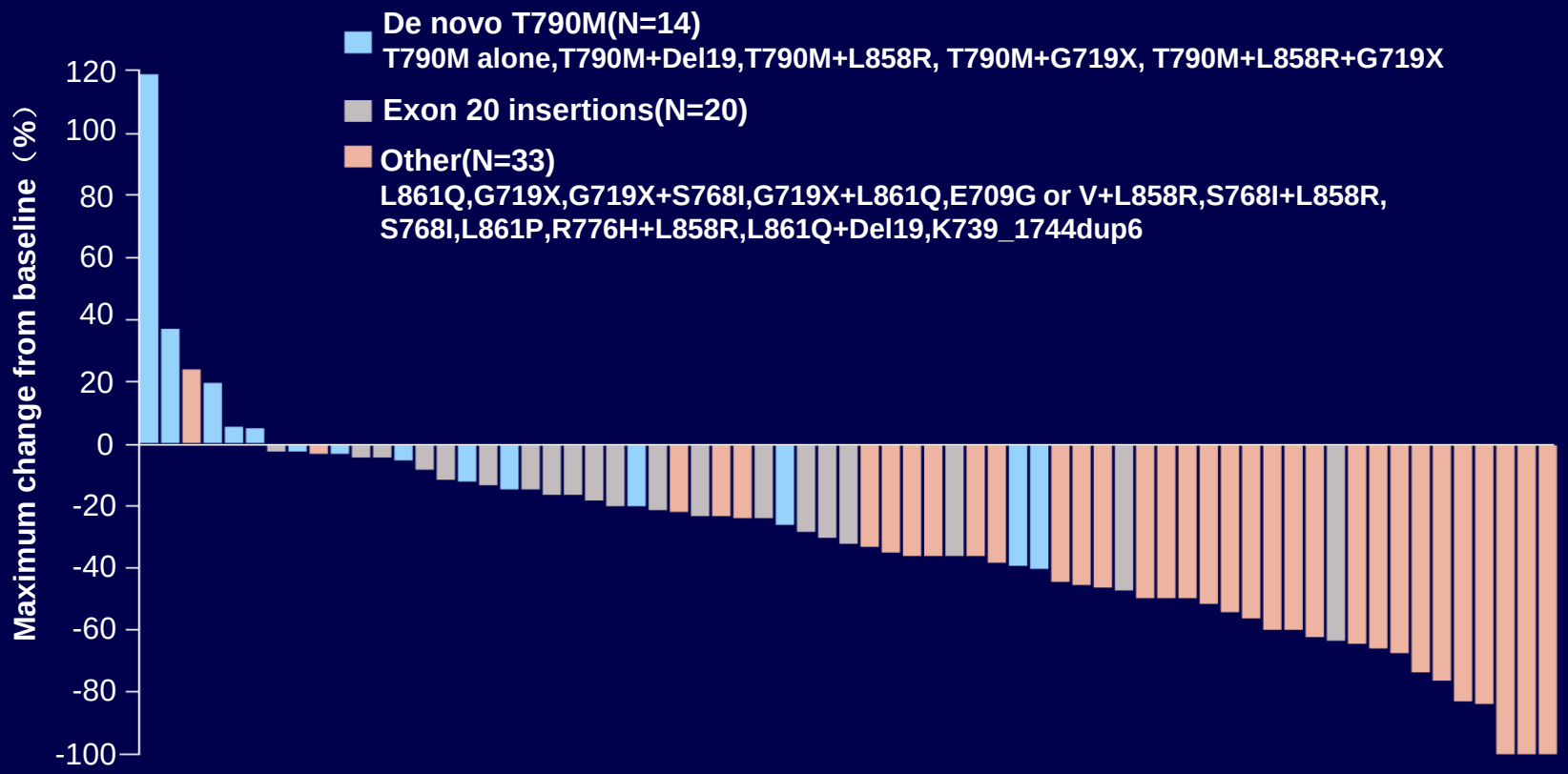
	LUX-Lung 2 Phase II N=129	LUX-Lung 3 Phase III N=345	LUX-Lung 6 Phase III N=364
Treatment	Afatinib	Afatinib vs. Pem/cis	Afatinib vs. Gem/cis
Line of treatment	First-and second-line (after chemo)	First-line	First-line
Mutation test	Direct sequencing(central)	EGFR29* (central)	EGFR29* (central)
Uncommon	n=23	n=37	n=40
	Patients with common mutations treated with afatinib		
Uncommon	n=23	n=26	n=40

Subgroups of patients with uncommon mutations

Categories	*De novo* T790M	Exon 20 insertions	Other (exon 18,19,20,21)
n=	14	23	38
Mutations （n）	T790M alone(3) T790M+Del19(3) T790M+L858R(3) T790M+G719X(1) T790M+L858R+G719X(1)	n/a	L861Q alone(12) G719X alone(8) G719X+S768I(5) G719X+L861Q(3) E709G or V+L858R(2) S786I+L858R(2) S786I alone(1) L861P alone(1) P848L alone(1) R766H+L858R(1) L861Q+Del19(1) K739_1744dup6(1）
PFS,months	2.9	2.7	10.7
OS ,month	14.9	9.4	18.6

Tumour shrinkage in patients with uncommon mutations

Independent review (n=67)



2013 WCLC, James Yang, Abstr O03.05

Uncommon EGFR mutations: PFS & OS

	De novo T790M n=14	Exon 20 Insertions n=23	Other N=38
ORR	**14.3%**	**8.7%**	**71.1%**
Median PFS, months (range)	**2.9 (0.3-13.8)**	**2.7 (0.4-11.9)**	**10.7 (0.0+-35.8+)**
Median OS, month (range)	**14.9 (1.5-30.5)**	**9.4 (0.4-32.2+)**	**18.6 (0.0+-51.3+)**

T790M+L858R, n=6

Patient	PFS	OS
1	0.8	8.7
2	2.6	24.9
3	6.7	13.2
4	8.3	30.5
5	9.6*	24.4*
6	11.0	20.8
Median	**7.5**	**22.9**

T790M+Del19, n=3

Patient	PFS	OS
1	0.3	8.1
2	1.2	7.5
3	3.0	24.6
Median	**1.2**	**8.1**

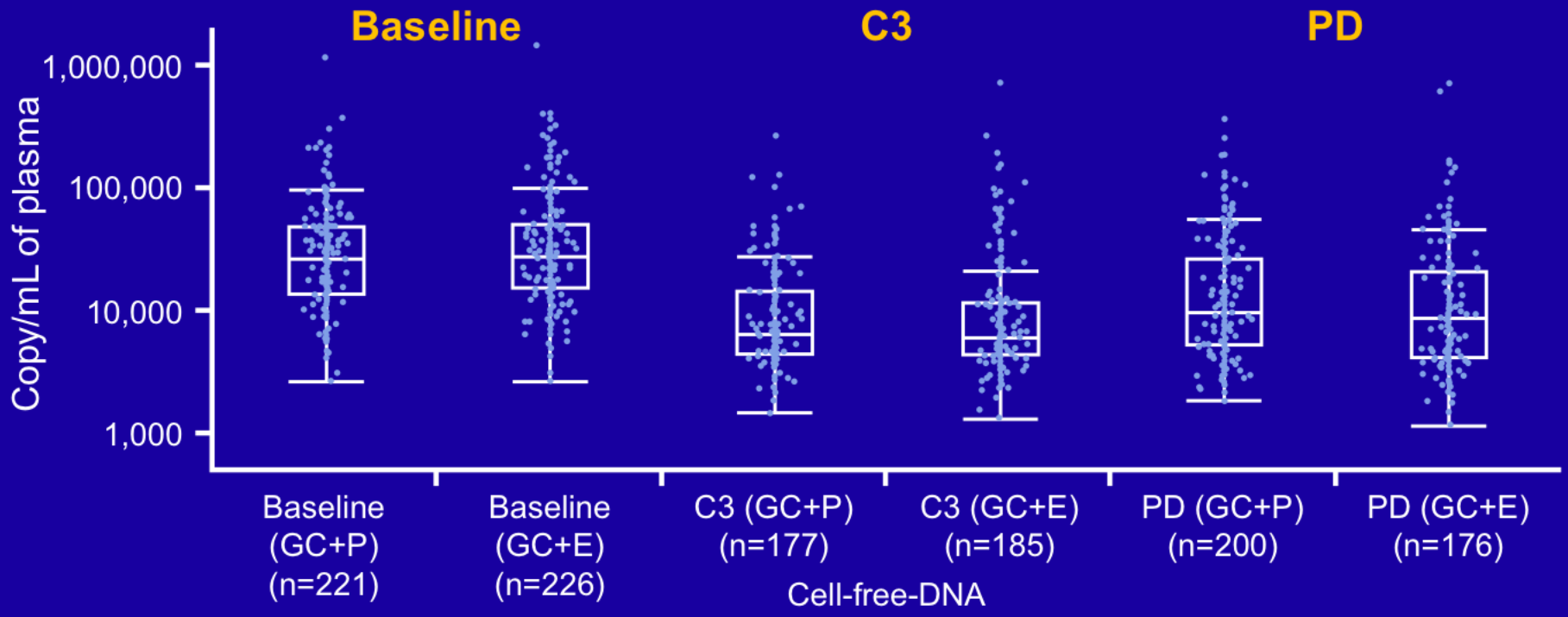
2013 WCLC, James Yang, Abstr O03.05

Cell-free DNA

- Cell-free DNA (cfDNA) is extracted directly from plasma or serum, not from CTCs.
- Majority of cfDNA is germline DNA from benign cells, but a small portion is tumor derived.
- Analysis of cfDNA is well established as a non-invasive diagnostic in pregnancy.
- An advantage over CTC analysis is the ease of blood collection and handling.

Dynamic quantitative change in total plasma free DNA at baseline, C3 and PD

One-way analysis of copy/mL of plasma by cell-free-DNA



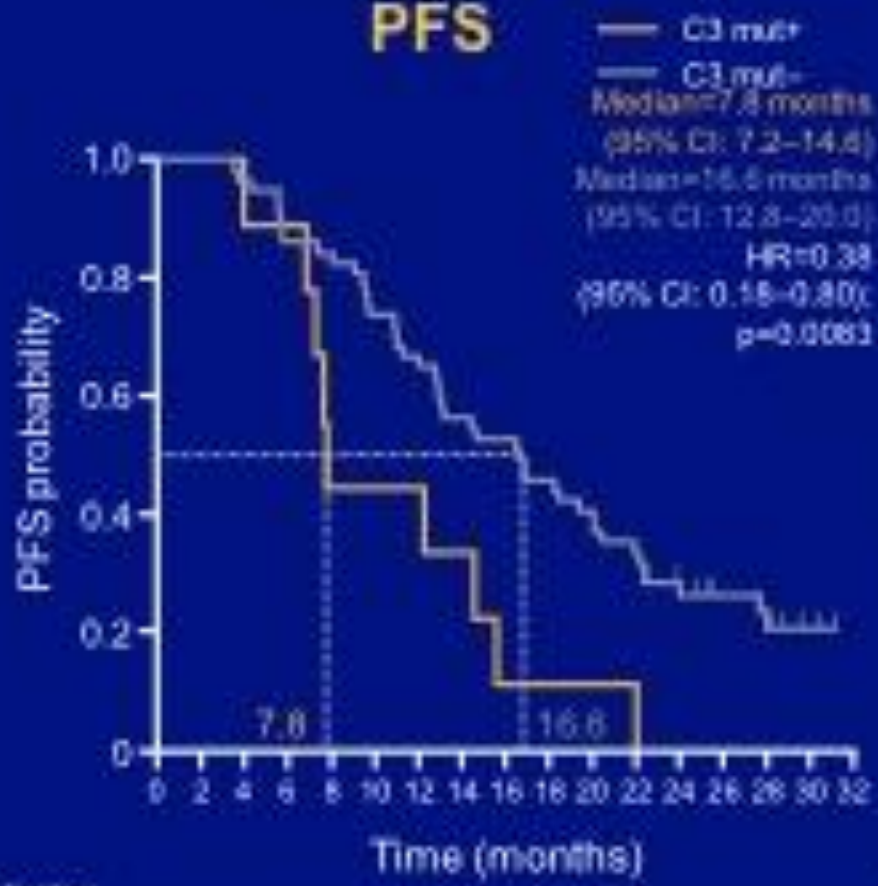
Median cell-free DNA (copy/mL of plasma)	GC+P	GC+E
Baseline	26,225	27,550
C3	6,389	5,975
PD	9,528	8,554

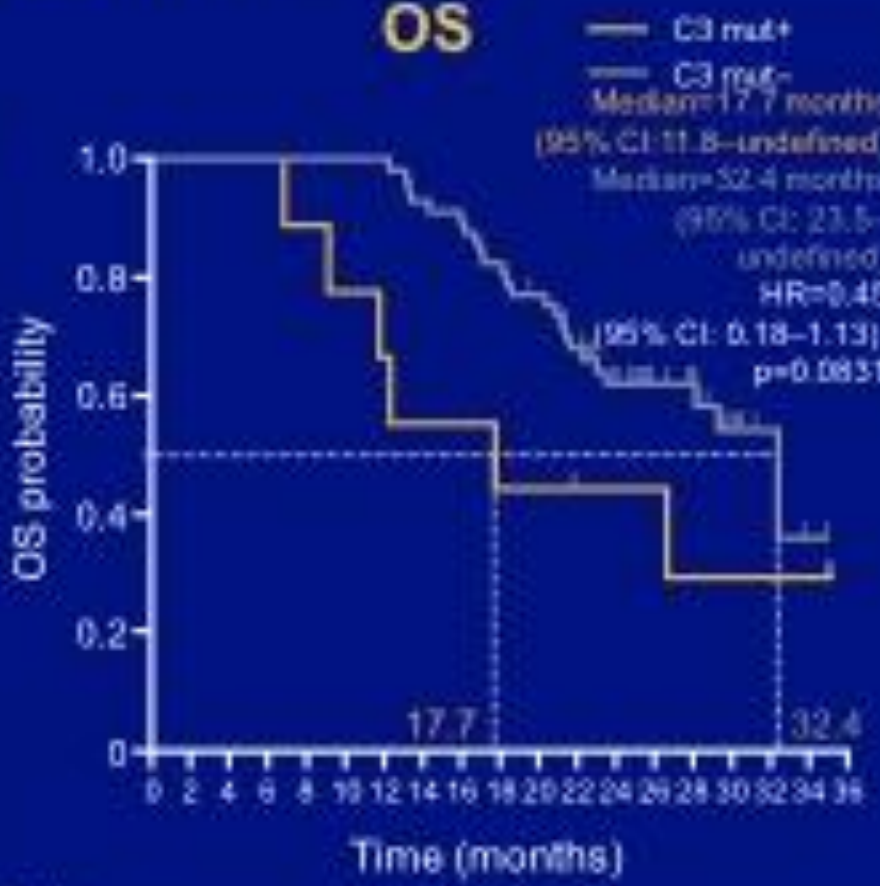
Summary of treatment outcomes according to C3 p*EGFR* mut status and treatment arms

	ORR	PFS	OS
C3 p*EGFR* mut+		Median, months	Median, months
GC+P(n=33)	24.2%	6.8	18.8
GC+E(n=9)	66.7%	7.8	17.7
	OR=6.25 (95%CI:1.26-30.90)	HR=0.38 (95%CI:0.17-0.90)	HR=0.98 (95%CI:0.40-2.42)
C3 p*EGFR* mut-		Median, months	Median, months
GC+P(n=23)	26.1%	7.8	26.3
GC+E(n=57)	82.5%	16.6	32.4
	OR=13.32 (95%CI:4.20-42.23)	HR=0.23 (95%CI:0.13-0.41)	HR=0.61 (95%CI:0.31-1.21)

All patients (n=122) p*EGFR* positive at baseline

p*EGFR* mut+ at C3 predicts PFS and OS (GC+E arm only)





Positive p*EGFR* at baseline followed by negative p*EGFR* at C3 is associated with improved outcomes; patients positive at baseline and still positive at C3 experienced worse outcomes

JO22903Trial: Phase II study on erlotinib in advanced NSCLC with positive EGFR mutations
Serum mutations and efficacy

- This analysis measured serum *EGFR* mutations before and after administration of erlotinib in the phase II JO22903 study

JO22903 criteria
−EGFR mut+ (exon 19/21)
−Stage: recurrence/IIIB/IV
−ECOG PS 0-1
N=102

→

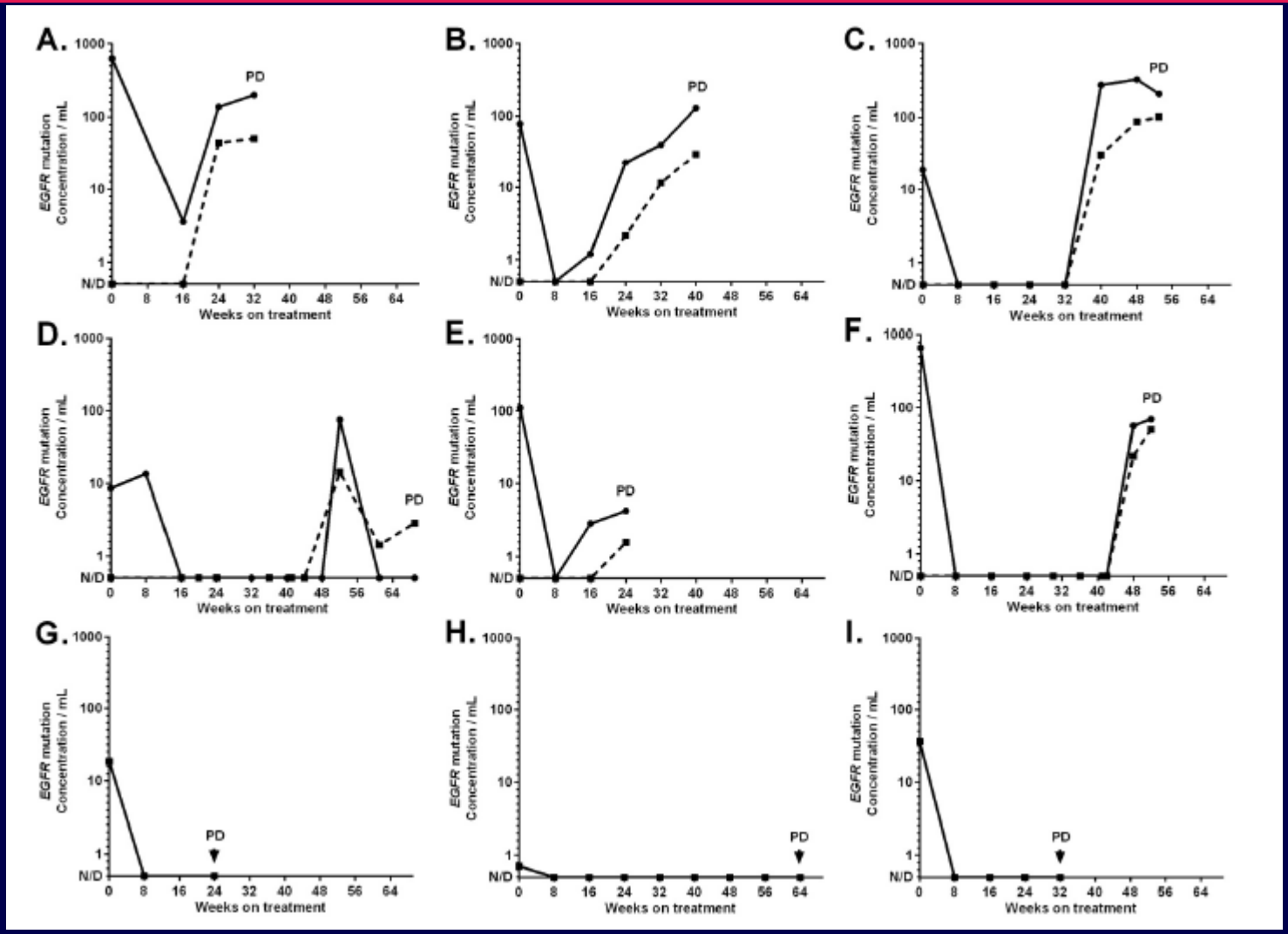
Erlotinib 150 mg/d p.o.
− until PD or unacceptable toxicity

  - Jo22903 results: PFS 11.8 months (95%CI 9.1-NR), ORR 78% (4 CR and 76 PR)[1]
- Serum samples were analysed by Scorpion-ARMs to confirm *EGFR* mutations before and after erlotinib (190 days post treatment and at disease progression)

Serum mutation status and PFS

	Mutation	n (event)	Median PFS, months	95% CI
Baseline	Yes	25 (22)	9.7	5.5-12.3
	NO	70 (54)	15.2	9.7-17.9
Day 190	Yes	5 (5)	8.5	8.0-11.1
	NO	60 (60)	17.9	13.2-20.6
At PD	Yes	16 (16)	8.4	5.4-12.3
	NO	55 (55)	10.3	8.3-12.5

Noninvasive detection of response and resistance in EGFR-mutant lung cancer using quantitative next-generation genotyping of cell-free plasma DNA



Oxnard GR, et al. CCR 2014; 20(6): 1698

EGFR-TKIs vs. Chemotheray in EGFR Mutation+ Lung Adenocarcinoma

Trial	Patient Population	TKI	Pts No.	PFS (months)			OS (months)		
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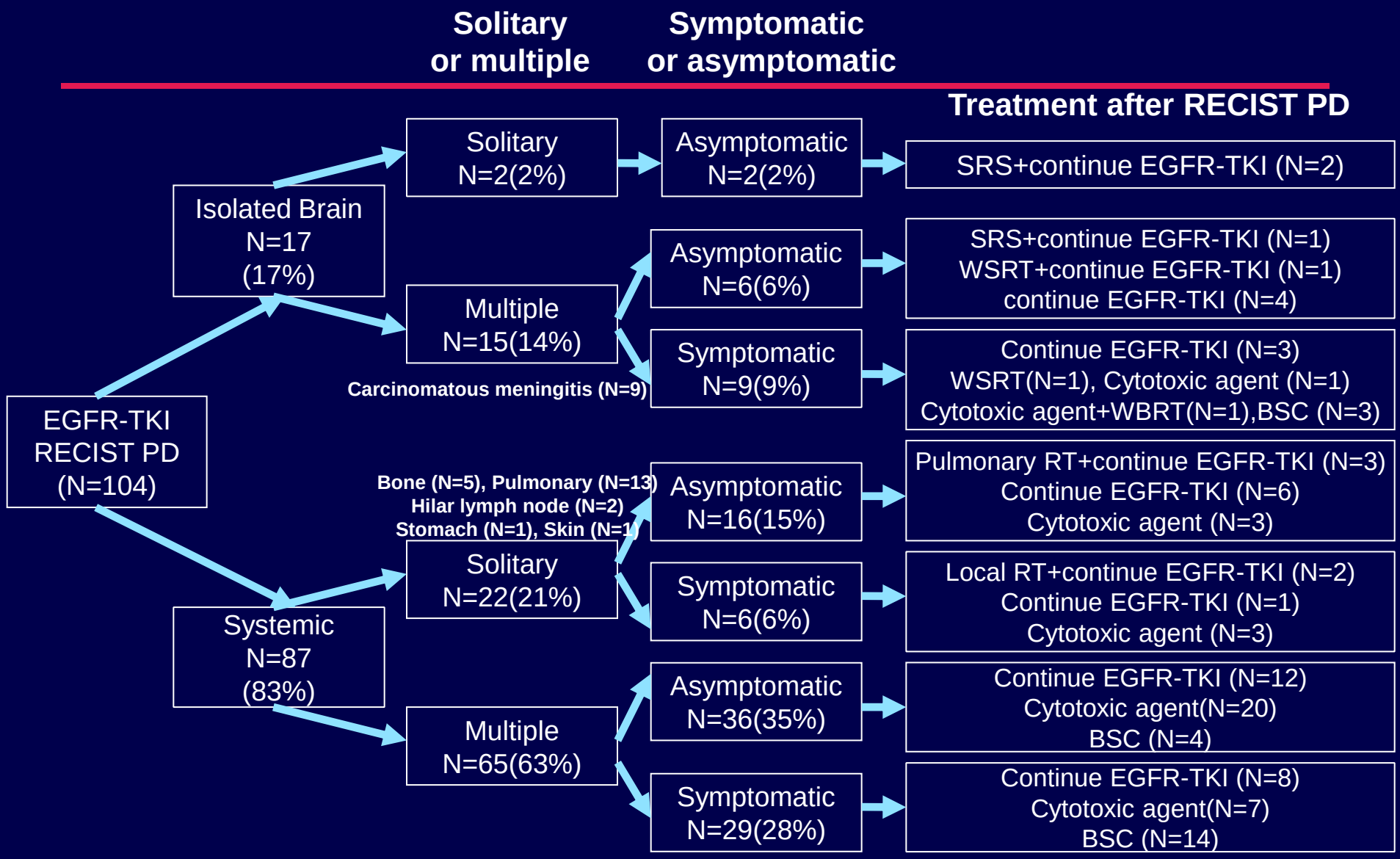
LUX-Lung6	Asia	Afatinib	364	11.0	5.6	0.28 (0.20-0.39)	NA	NA	NA

- 30% non-responders
- PFS 6 – 11 months
- Relapse unavoidable

1. Mok, et al. NEJM 2009; 2. Han et al. JCO 2012. 3. Maemondo, et al. NEJM 2010; 4. Mitsudomi, et al. Lancet Oncol 2010; 5. Zhou, et al. Lancet Oncol 2011; 6. Rosell et al. Lancet Oncol 2012. 7. Sequist, et al. JCO 2013. 8. Wu, et al. 2013 ASCO Abstract 8016.

Progression Patterns at RECIST PD



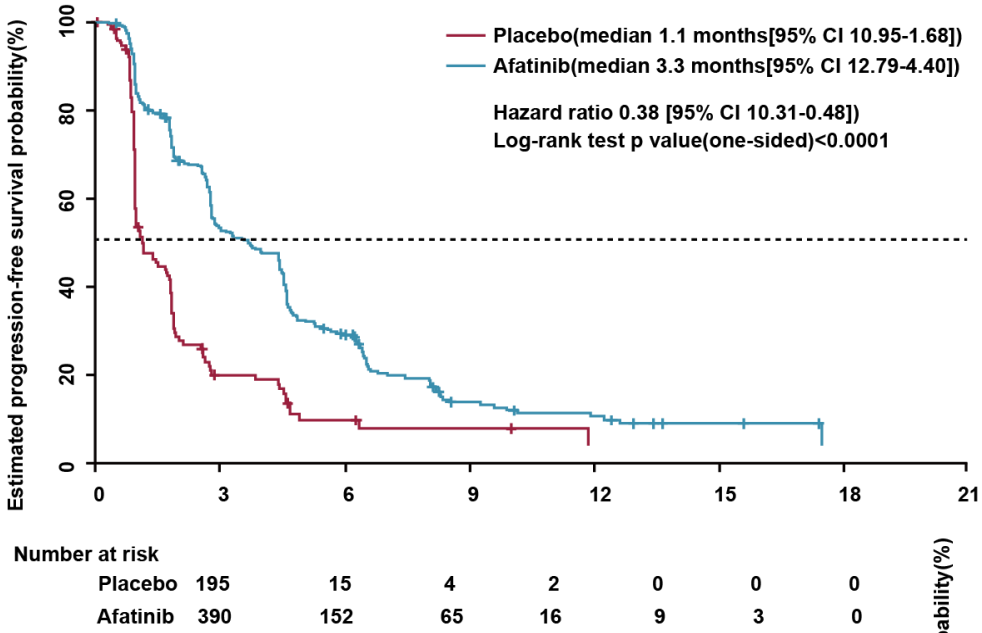
Progression patterns at RECIST PD during EGFR-TKIs in advanced NSCLC patients haboring EGFR mutation. ASCO 2013

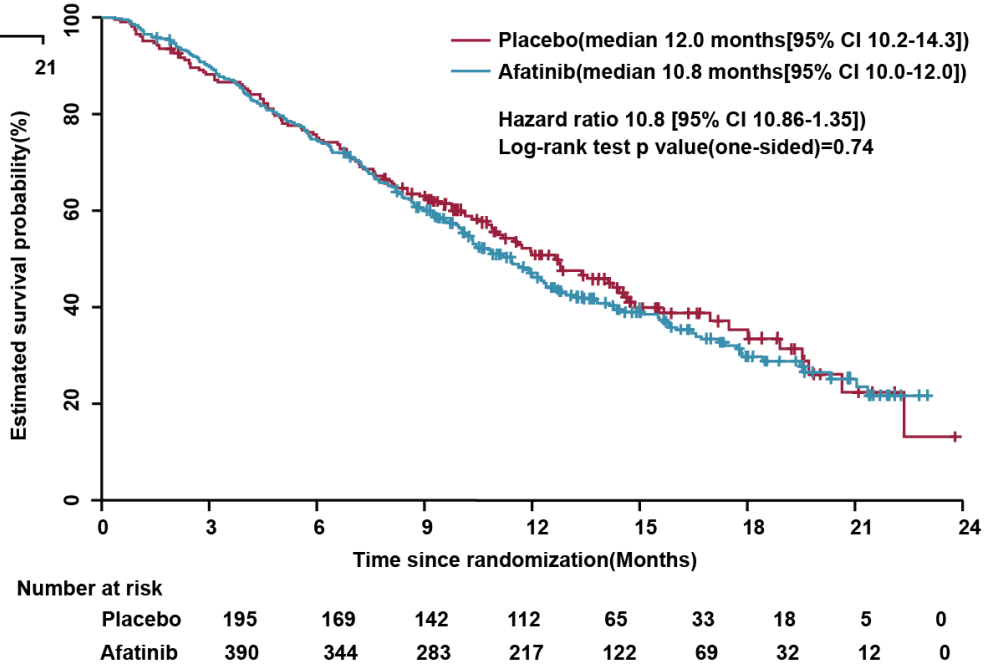
Clinical Studies for Acquired Resistance

Agent(s)	Pts(%EGFR mut)	Phase	Response	TTP/PFS
Gef/Erl& Everolimus[1]	13 (62%)	II	0%	3 mos
Everolimus[2]	43 (0%)	II	2%	2.7 mos
Neratinib[3]	91 (100%)	II	3%	3.6 mos
IPI-504[4]	28 (100%)	II	4%	NR
Erl/Cetux[5]	19 (84%)	II	0%	3 mos
Dasatinib[6]	12 (100%)	II	0%	0.5 mos
Dasatinib/Erl[6]		II	0%	0.9 mos
XL674[7]	23 (NR%)	II	4%	NR
PF299804[8]	66 (50%)	II	5%	4.5 mos
PF299804[9]	42 (21%)	II	15%	3.6 mos
XL184&Erl[10]	54 (37%)	I/II	8%	NR
Afatinib[11]	390(NR%)	III	7%	3.3 mos

[1]Riely CCR 2007; [2]Soria Ann Oncol 2009; [3]Sequist JCO 2010; [5]Janjigian CCR 2011; [6]Johnson JTO in press; [7]Miller ASCO 2008; [8]Campbell ASCO 2010; [9]Park ASCO 2010; [10]Wakelee ASCO 2010; [11]Miller ESMO 2010

LUX-Lung 1:PFS and OS





Miller et al, Lancet Oncol, Mar 26, 2012 online publication

BR.26: Advanced NSCLC After Failure of Prior EGFR Targeted Therapy (Phase 3)

Trial design	Endpoints	Study sites
Randomized, double blind placebo-controlled Interim (OS)	Primary: OS HR: 1.33 Secondary: PFS, OR and PRO	Global (Canada, Latin America, Australia and Asia)

Key entry criteria

- Prior chemo (1/2) and *EGFR TKi*
- PS 0–3
- All histologies
- Available tissue (*KRAS*)

RANDOMISE

2:1

- Dacomitinib (45 mg QD) + BSC
- Placebo + BSC

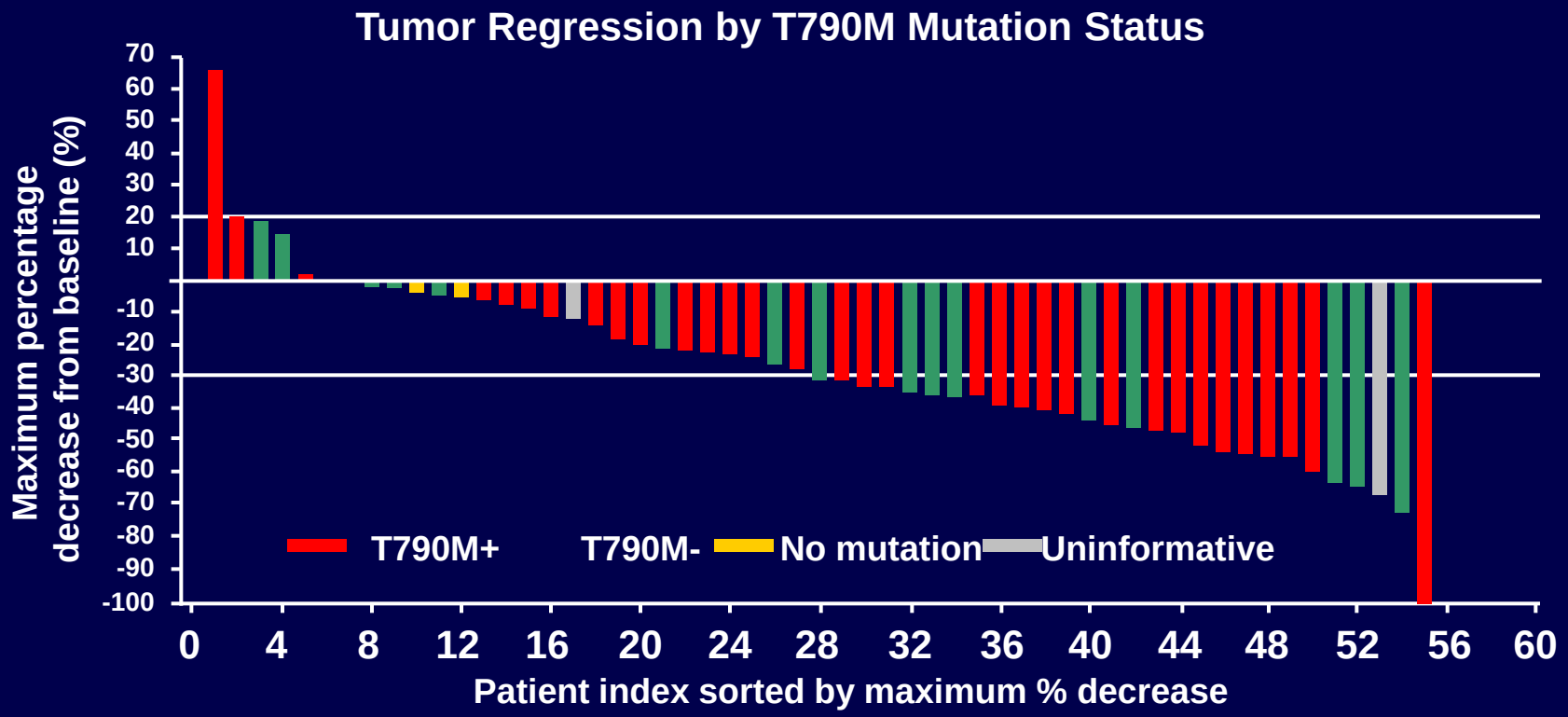
N=720

Interim analysis (N~360 patients, 200 events)

BSC= best supportive care

Clinicaltrials.gov. NCT 01000025

Trial of Afatinib-Cetuximab in EGFR MT+ NSCLC with acquired resistance to Erlotinib



- What is the mechanism of action of this combination by comparison to Afatinib alone? (Afatinib alone~10%)
- How does cetuximab modify the activity of Afatinib?
- What are the mechanisms of resistance to this combination?

Pao et al: Chicago IASLC-ASCO-ASTRO, 2012

MARQUEE Study Design

Key Eligibility Criteria

- Inoperable, locally advanced or metastatic NSCLC
- Non-squamous histology
- 1-2 prior systemic regimens, including mandatory prior platinum-based doublet therapy
- No prior EGFR TKI
- Thissue for biomarker analysis
- Stable brain metastases were permitted
- ECOG 0 or 1

Double-blind

RANDOMIZE

1:1

Tivantinib @ 360 mg PO BID
+
Erlotinib @ 150 mg QD

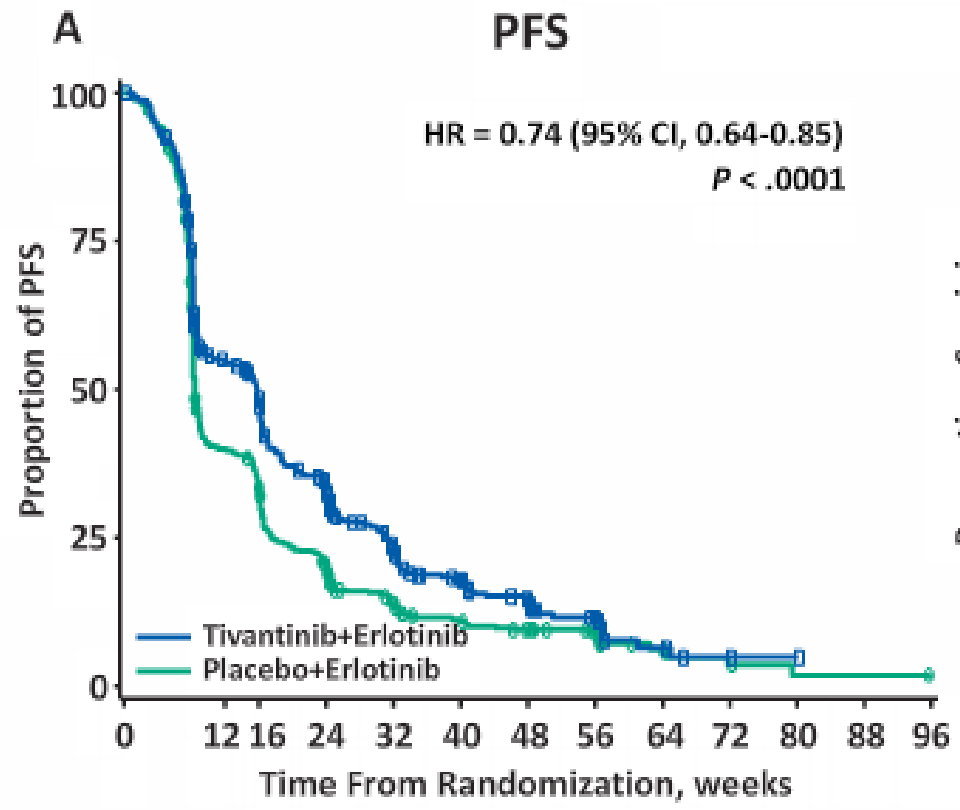
Placebo PO BID
+
Erlotinib @ 150 mg QD

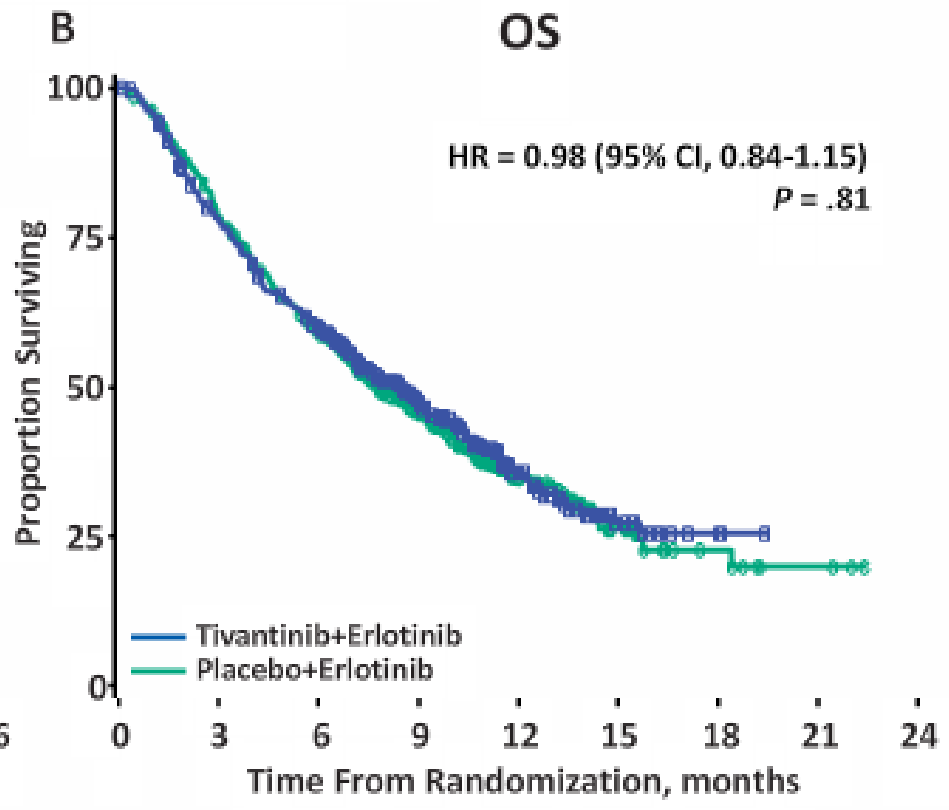
Stratification Factors

- Gender
- Smoking history
- # prior lines of systemic therapies
- *EGFR* genotype
- *KRAS* genotype

Abbreviation: BID, twice daily; EGFR, epidermal growth factor receptor; ITT, inter-to-treat; ORR, overall response rate; OS, overall survival; NSCLC, non-small cell lung cancer, PFS, progression-free survival; PO, orally, GO, once daily; wt, wild type; TKI, tyrosine kinase inhibitor.
http://clinicaltrials.gov/ct2/show/NCT01244191.

Results in ITT Population (n = 1048 randomized)





Safety (n = 1039 treated): Neutropenia (Grade 3/4 :10.0% vs 1.0%), febrile neutropenia (3.3% vs 0.4%), and anemia (Grade 3/4 : 6.5% vs 2.9%) were more common with tivantinib.

Next generation EGFR targeting in NSCLC: Mutant selectivity

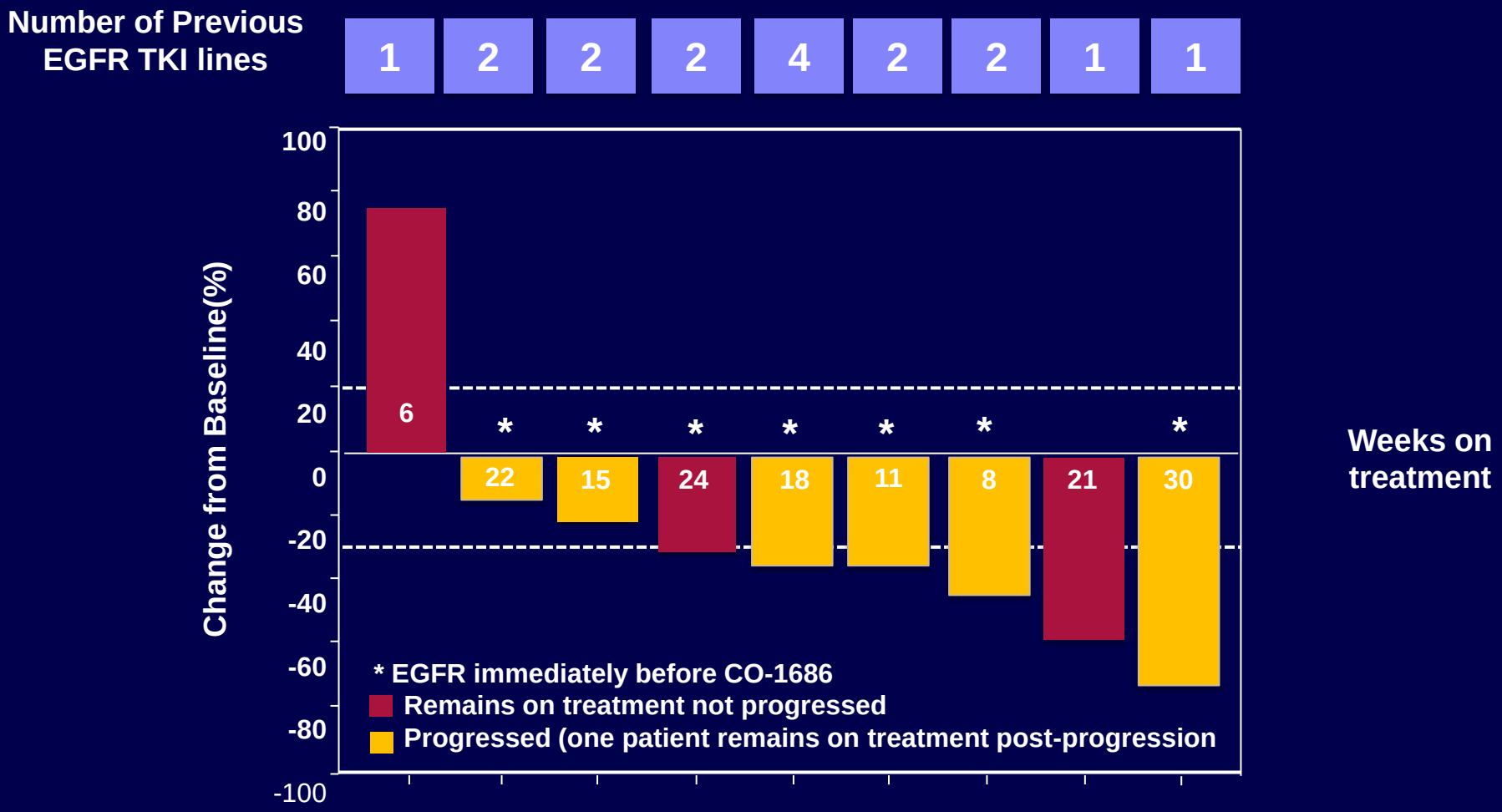
	Gefitinib & erlotinib	afatinib & dacomitinib	CO-1686 & AZD 9291
WT EGFR	++	+++	+
EGFR activating mutation	+++	+++	+++
EGFR "gatekeeper" resistance mutation (T790M)	-	++	+++

Effective for activating mutations but resistance arises

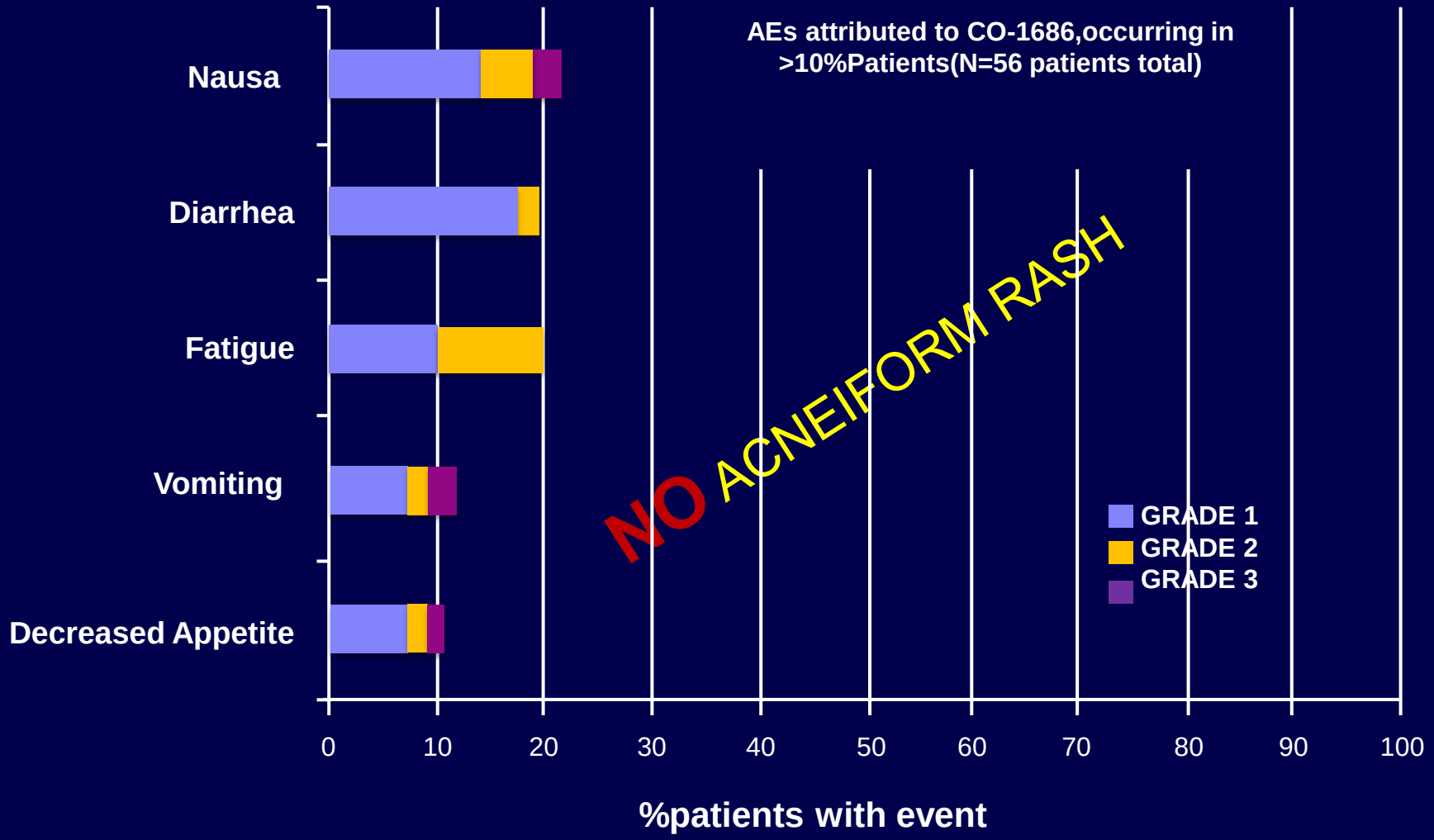
DLTs prevent dose escalation to inhibit T790M

67% RECIST response rate in evaluable T790M+ patients treated at 900mg BID

8 of 9 patients progressed on TKI immediately prior to CO-1686

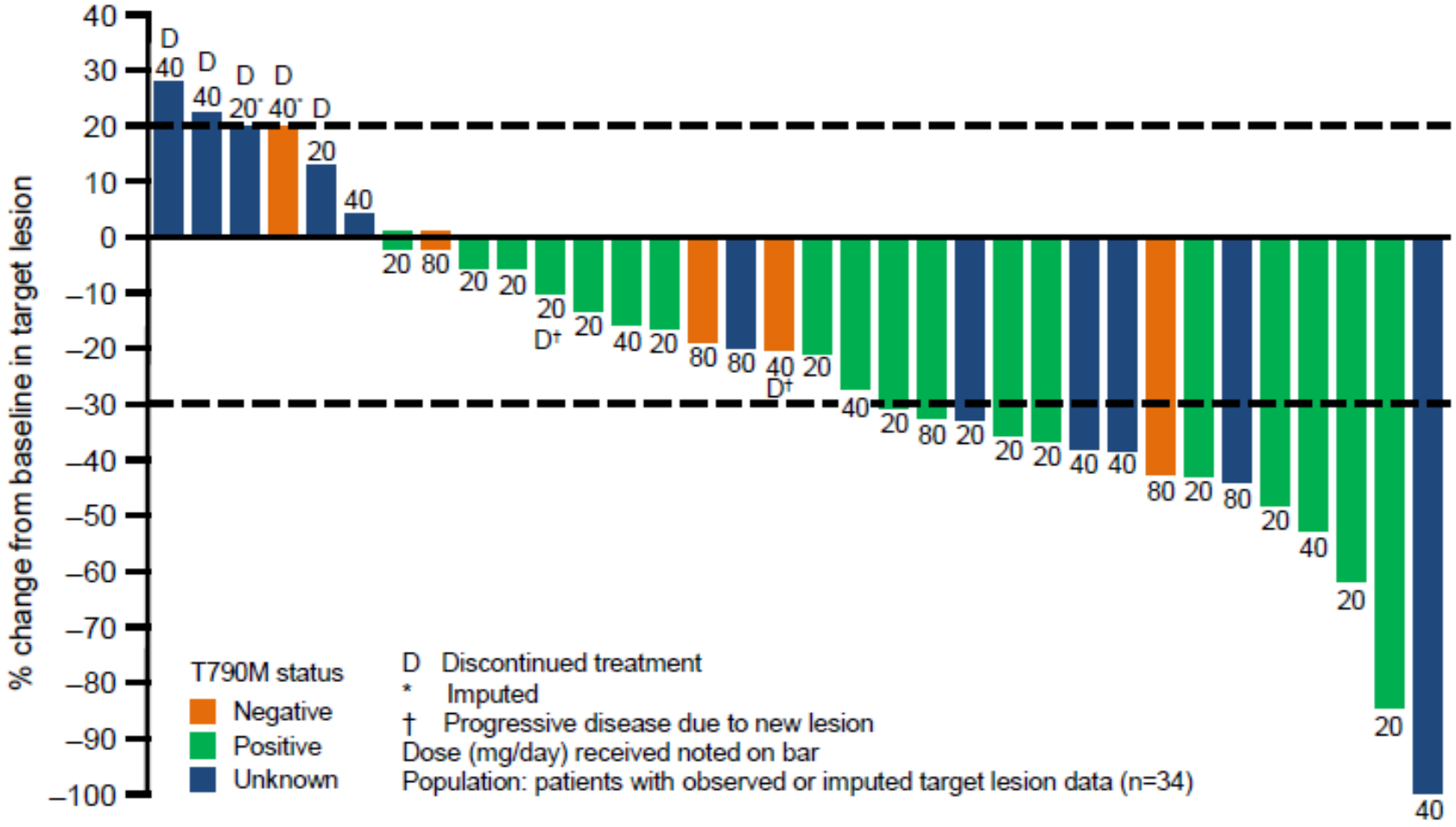


CO-1686 has demonstrated limited and low-grade adverse events in patients to date



Soria JC, et al. 2013 WCLC Abstract 1354.

AZD 9291: Best change from baseline in target lesions



15/35 patients evaluated had a partial response (confirmed + unconfirmed)

9/18 patients with T790M+ tumours achieved a partial response (confirmed + unconfirmed)

Ranson M, et al. 2013 WCLC MO21.12.

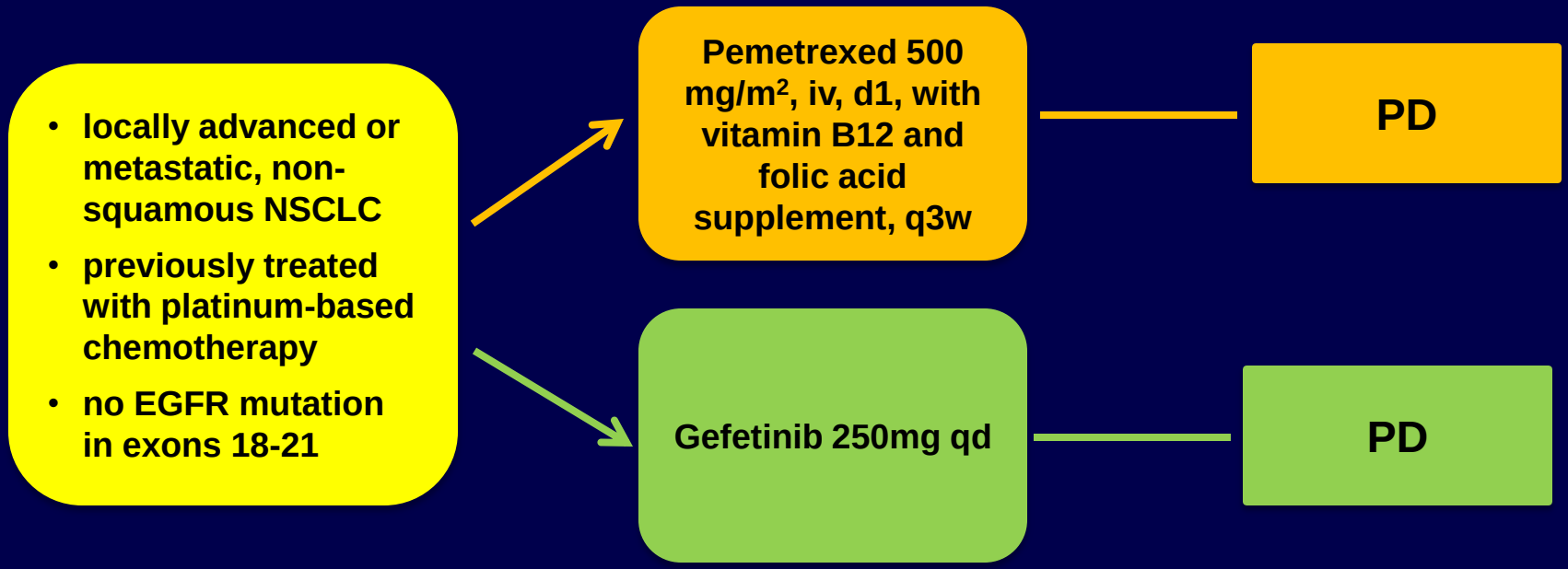
Randomized trials comparing EGFR TKI vs chemotherapy in advanced NSCLC (EGFR wild-type)

Studies	Treatment	PFS (months)	PFS HR	OS (months)	OS HR
CTONG 0806	Gefitinib Pemetrexed	1.7 5.6	1.88 (1.33-2.63)	9.6 12.4	1.38 (0.96-2.04)
DELTA	Erlotinib Docetaxel	1.3 2.9	1.45 (1.09-1.94)	9.0 10.1	0.98 (0.69-1.39)
TAILOR	Erlotinib Docetaxel	2.4 2.9	1.41 ((1.05-1.89)	5.4 8.2	1.41 (1.04-1.89
INTEREST	Gefitinib Docetaxel	1.7 2.6	1.24 (0.94-1.78)	6.4 6.0	1.02 (0.78-1.33)
TITAN	Erlotinib Pemetrexed/ docetaxel	1.4 2.0	1.25 (0.88-1.78)	6.4 4.5	0.85 (0.59-1.22)

Zhou Q, et al. 2013 WCLC O15.07.
Okano Y, et al. 2013 ASCO Abstract 8006.
Moscetti L, et al. Lancet Oncol. 2013; 14(10): 981-8.
Kim ES. et al. Lancet 2008; 372(9652): 1809-18.
Ciuleanu T, et al. 2011 WCLC Abstract O10.03.

Study Design

- A multi-center, randomized, controlled, open-label phase II trial



Primary endpoint

Progression-free survival (PFS)

Secondary endpoint

4-month and 6-month PFS rate

Overall survival(OS)

Objective response rate (ORR)

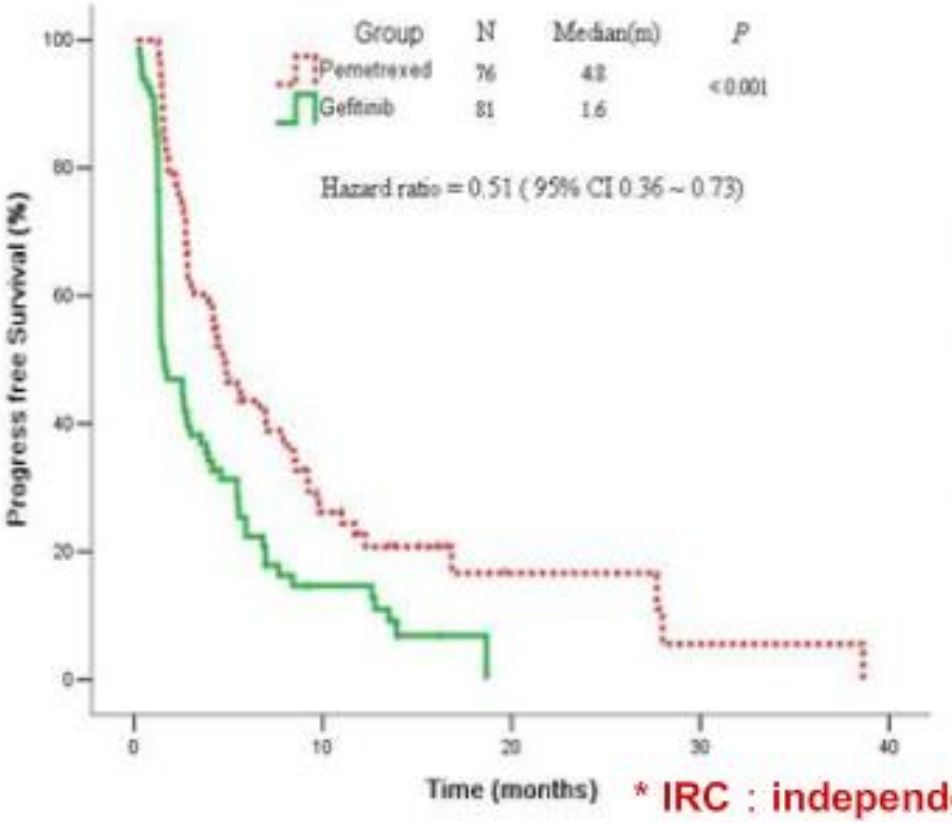
Quality of life

Safety

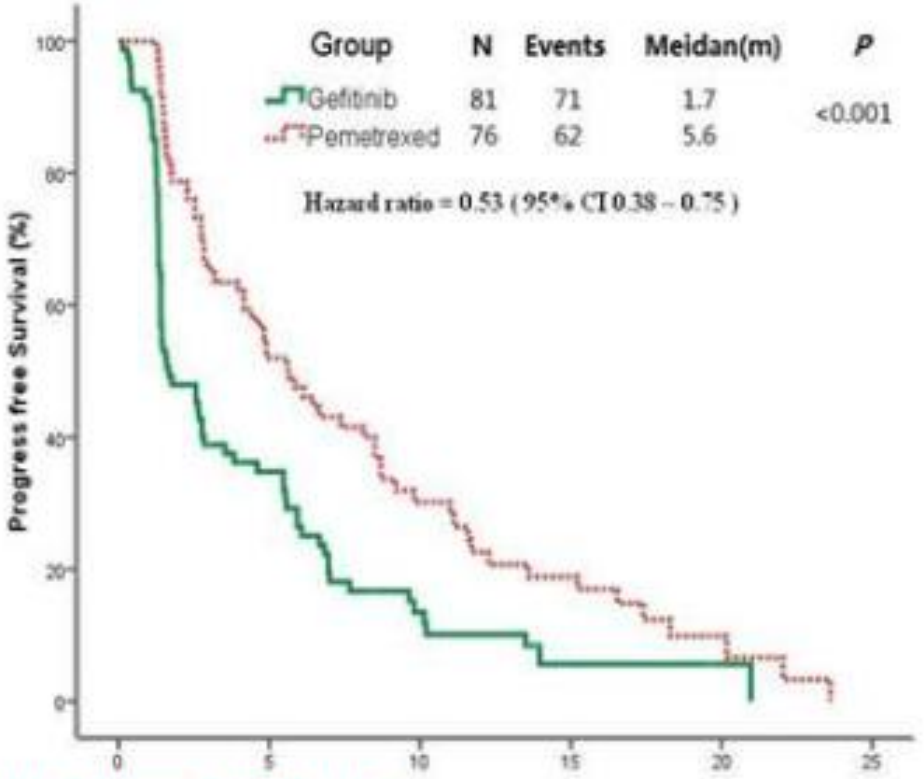
Result: Primary endpoint

- **The primary endpoint of PFS was met.**

Evaluted by investigators



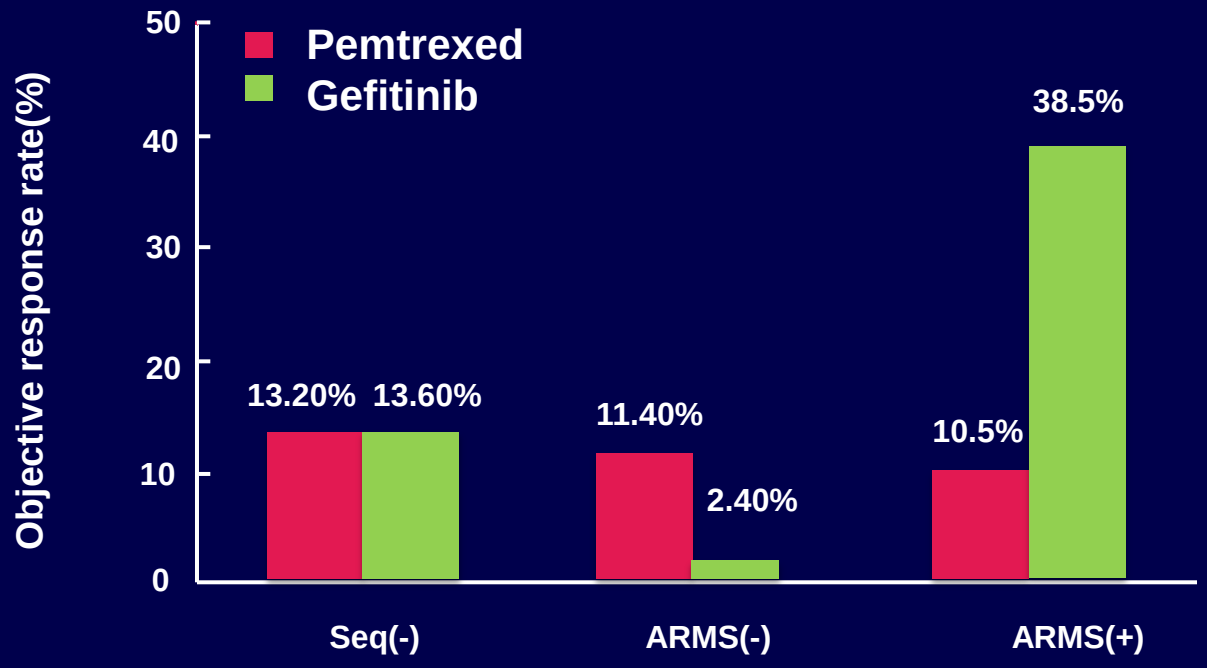
Evaluted by IRC



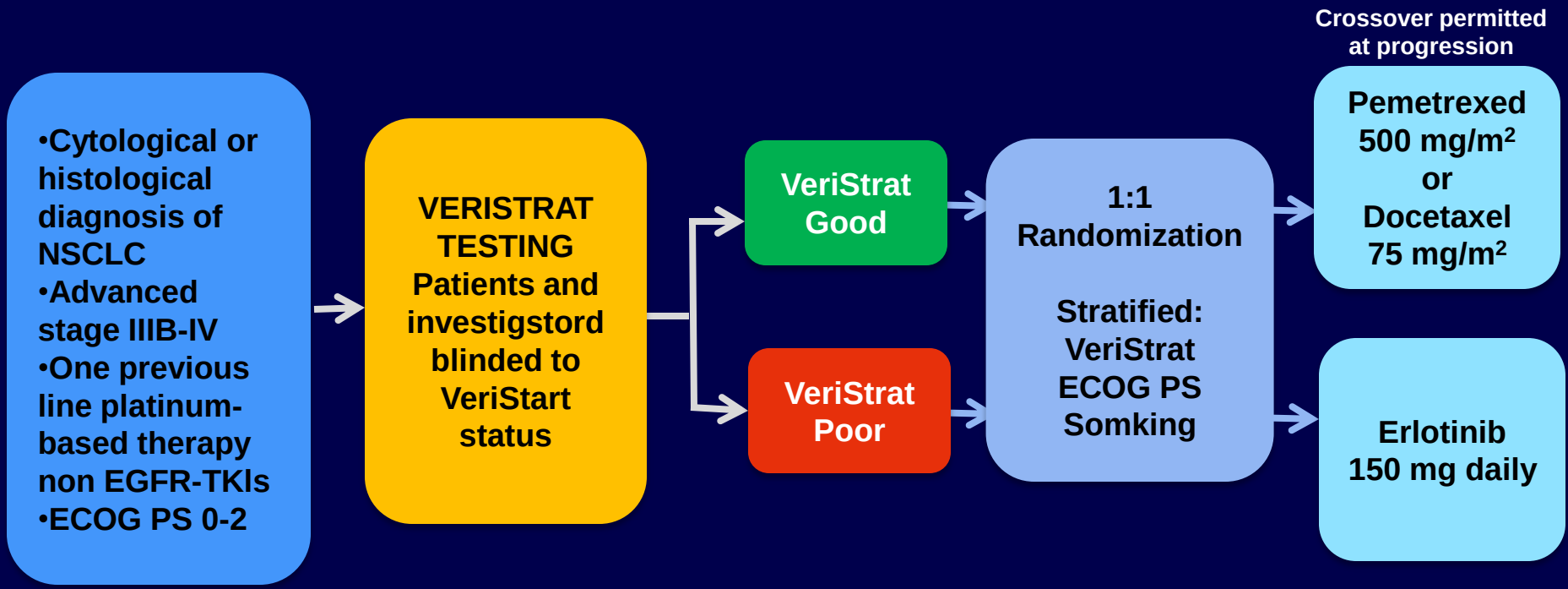
* IRC : independent review committee

Results of Abundance of EGFR mutations

- False negative rate of DNA sequencing was 29%
- 76 patients were found to harbor wild-type EGFR by DNA sequencing and ARMs
- PFS was 4.0 months in pemetrexed arm vs 1.3 months in gefitinib arm (HR+0.69, p+0.129)

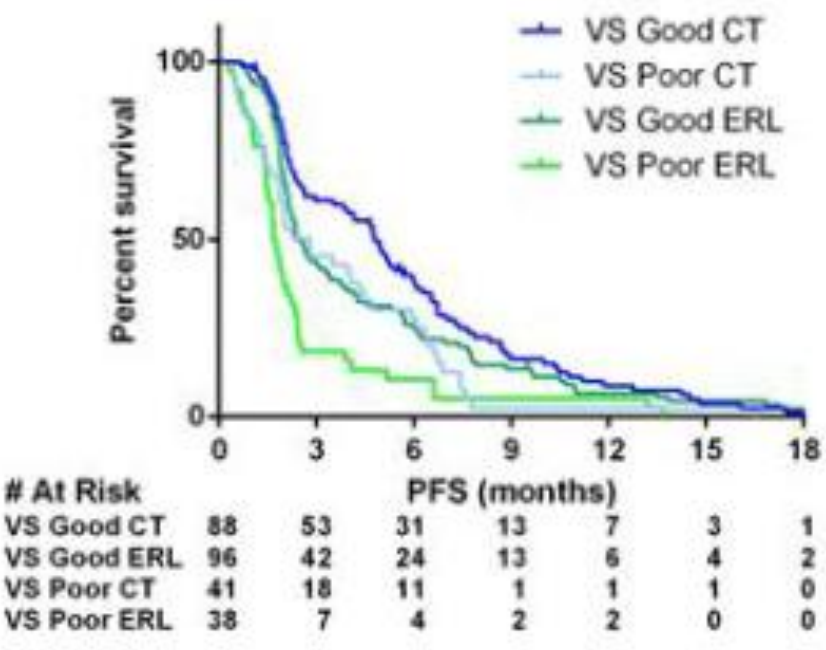


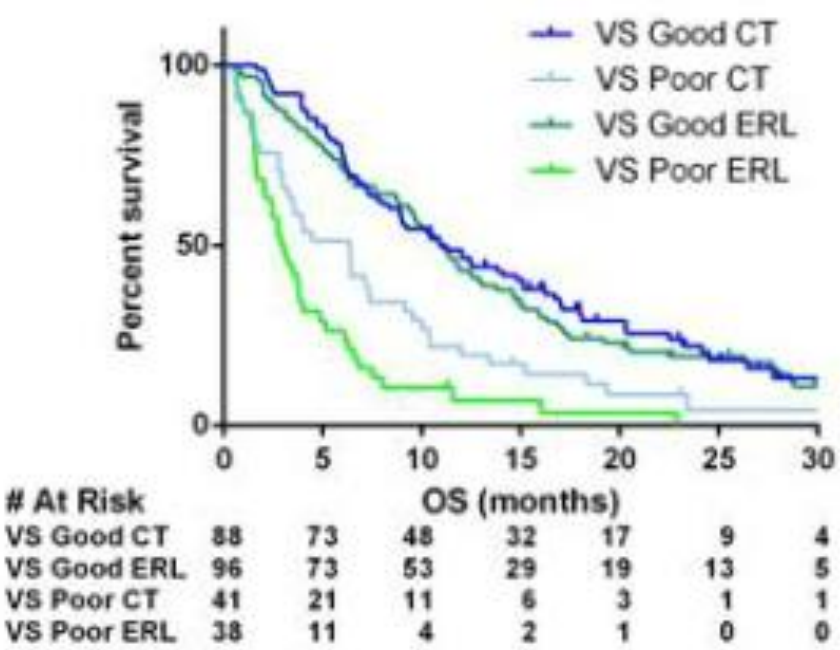
PROSE: Study Design



- **Objective: To prospectively evaluate the predictive utility of VerStrat classification on the survival outcome of erlotinib vs chemorherapy in the 2nd line NSCLC setting. Primary Endpoint: Overall Survivial reported at ASCO 2013; Secondary Endpoint: PFS, DCR and ORR.**
- **EGFR and K-Ras analysis performed in 190/263 (72%) and 166/263(63%) patients, repectively.**

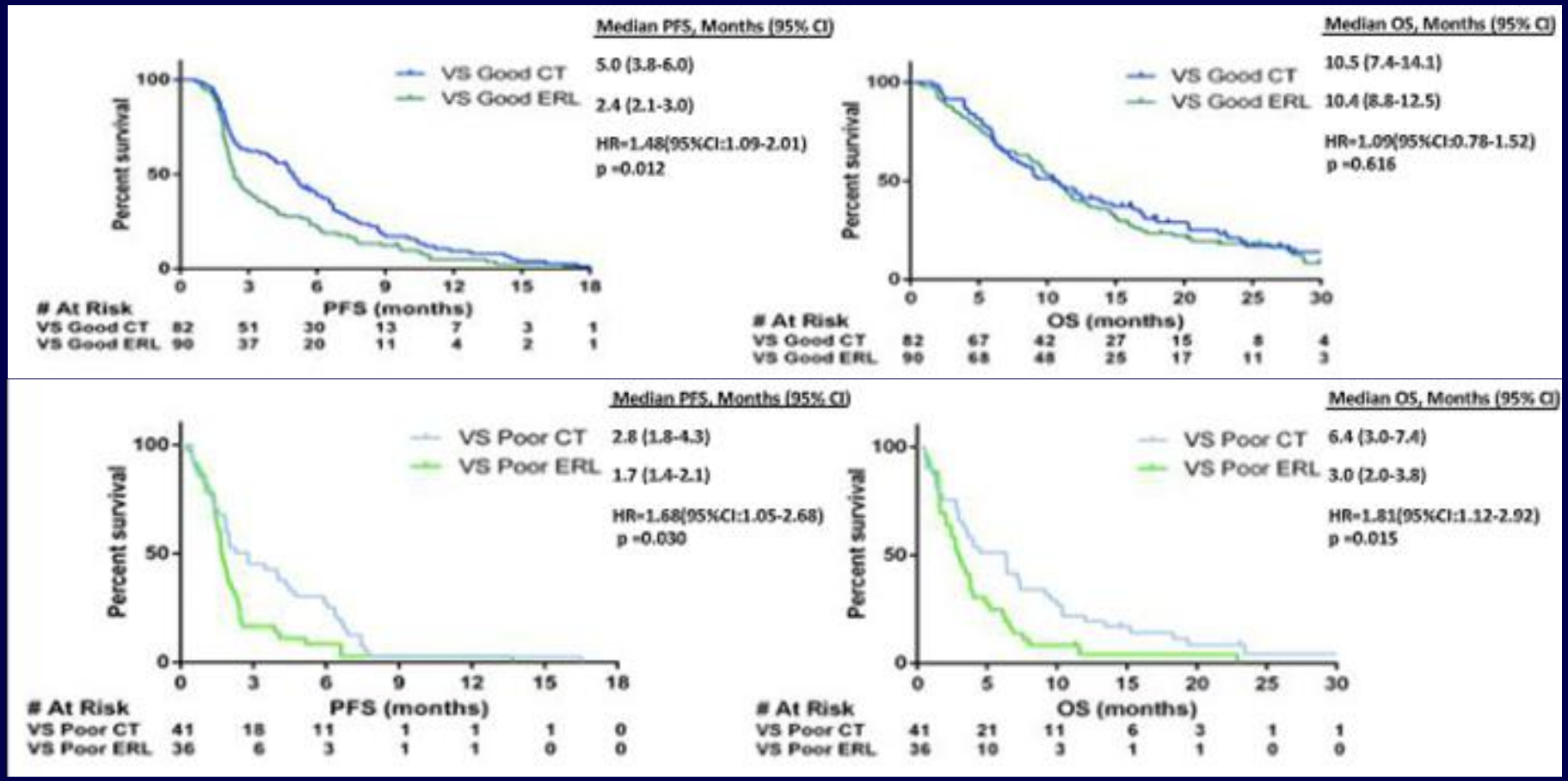
PROSE: PFS and OS Interaction Analysis





While VeriStrat is predictive for overall survival outcome between ERL and CT (VS*Tx interaction p=0.031) it is not predictive of PFS outcomes between these agents(VS*Tx interaction p=0.445).

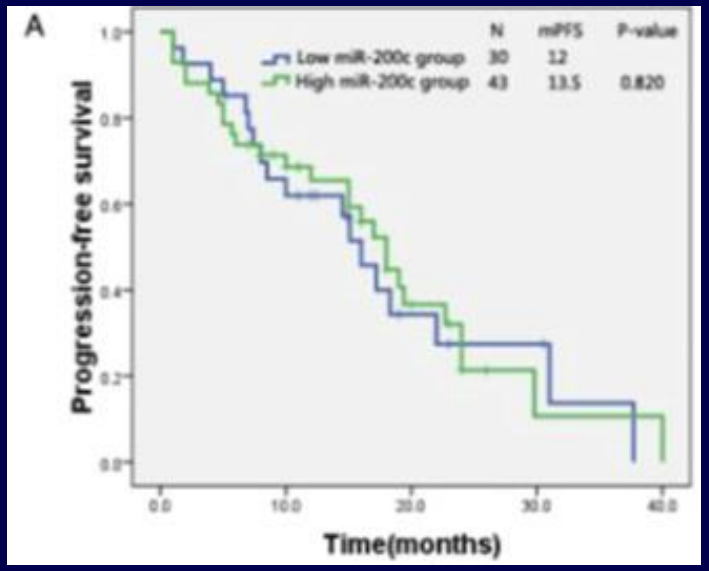
PROSE:PFS and OS by VeriStrat States in patients with EGFR w.t. or status unknown



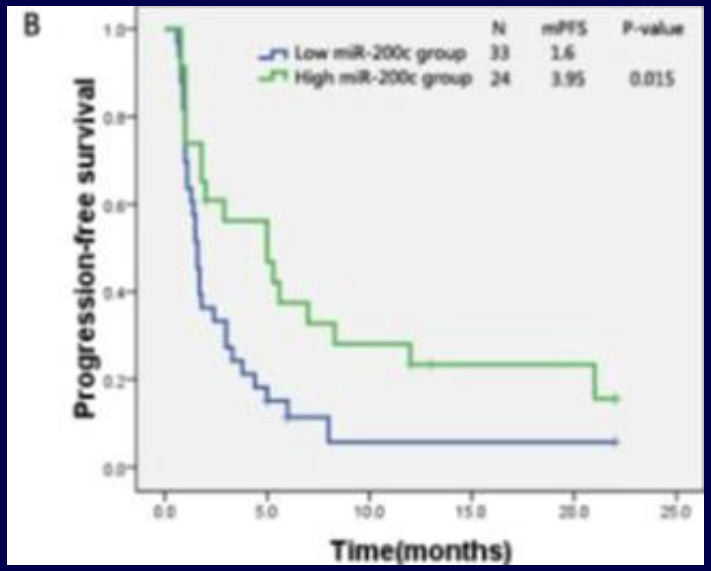
Slimilar trends are observed in this subgroup as in the overall patients population.

microRNA 200c predictive for efficacy of EGFR TKI

Patients with EGFR mutation



Patients with wild type EGFR

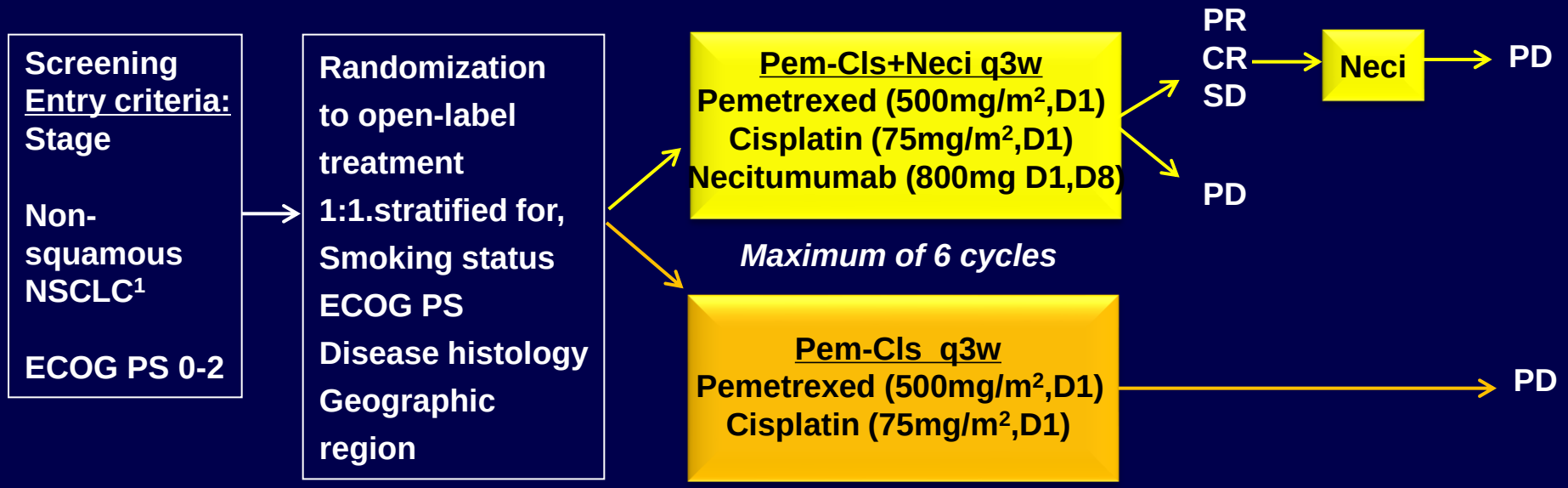


In EGFR WT patients

	HR	95%CL	P
miR-200c expression	0.375	0.198-0.712	0.003

001.05:EGFR wild-type NSCLC patients with high miR-200c expression can benefit from EGFR-TKIs-Jiayu Li

INSPIRE:Randomized Phase 3 trial of Necitumumab plus Cisplatin/pemetrexed vs. Cisplatin/pemetrexed alone as 1st line therapy in advanced non-squamous NSCLC

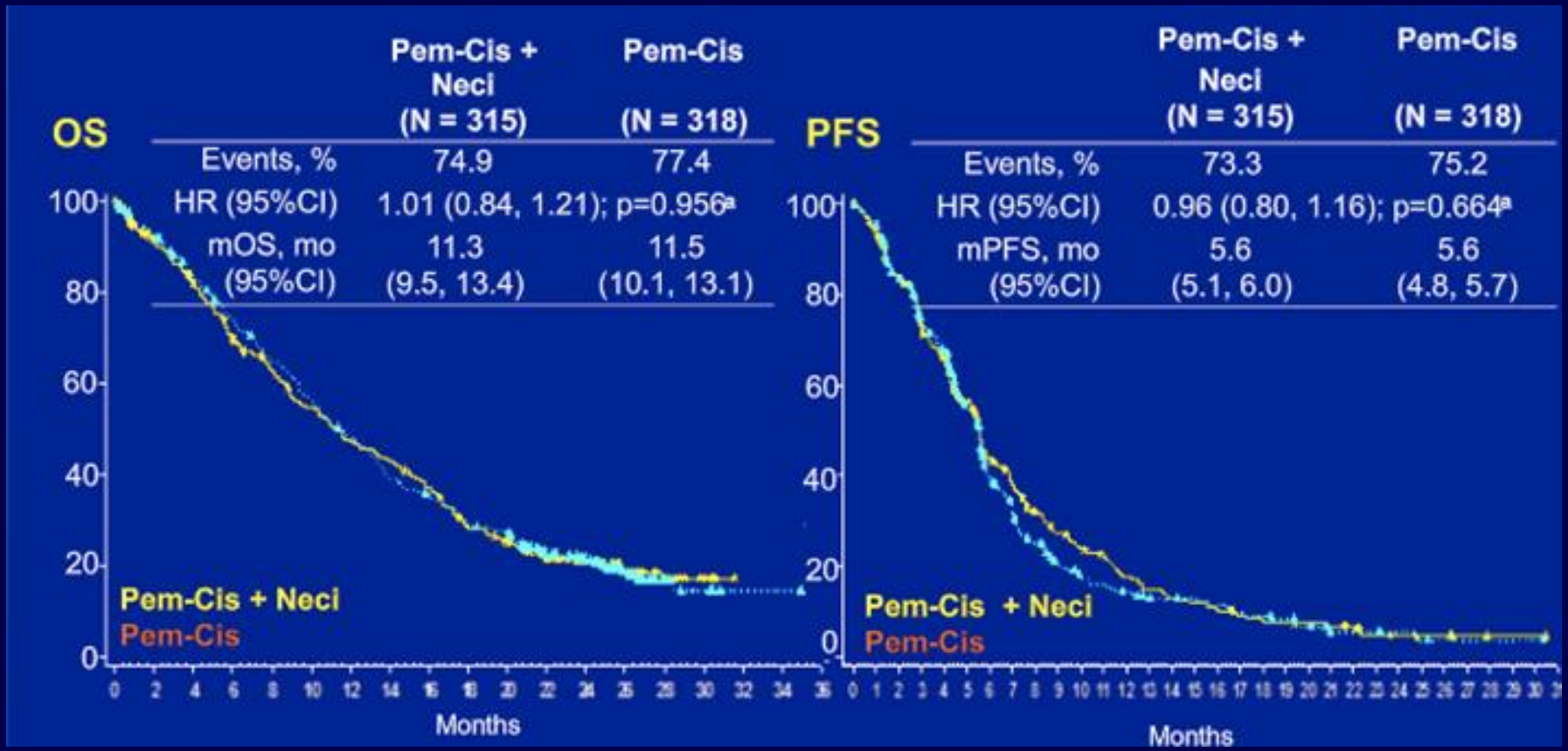


Radiographic tumor assessments: at baseline and q6w (±3 days) until radiographic Documentation of PD

Mandatory tissue collection: minimum 4 slides of paraffin embedded tissue per patient

L.Paz-Ares,J.Mezger,T.Ciuleanu,et al [1]*American Joint Commitiee on Cancer TNM Staging System for Lung Cancer.7th edition.2009.*

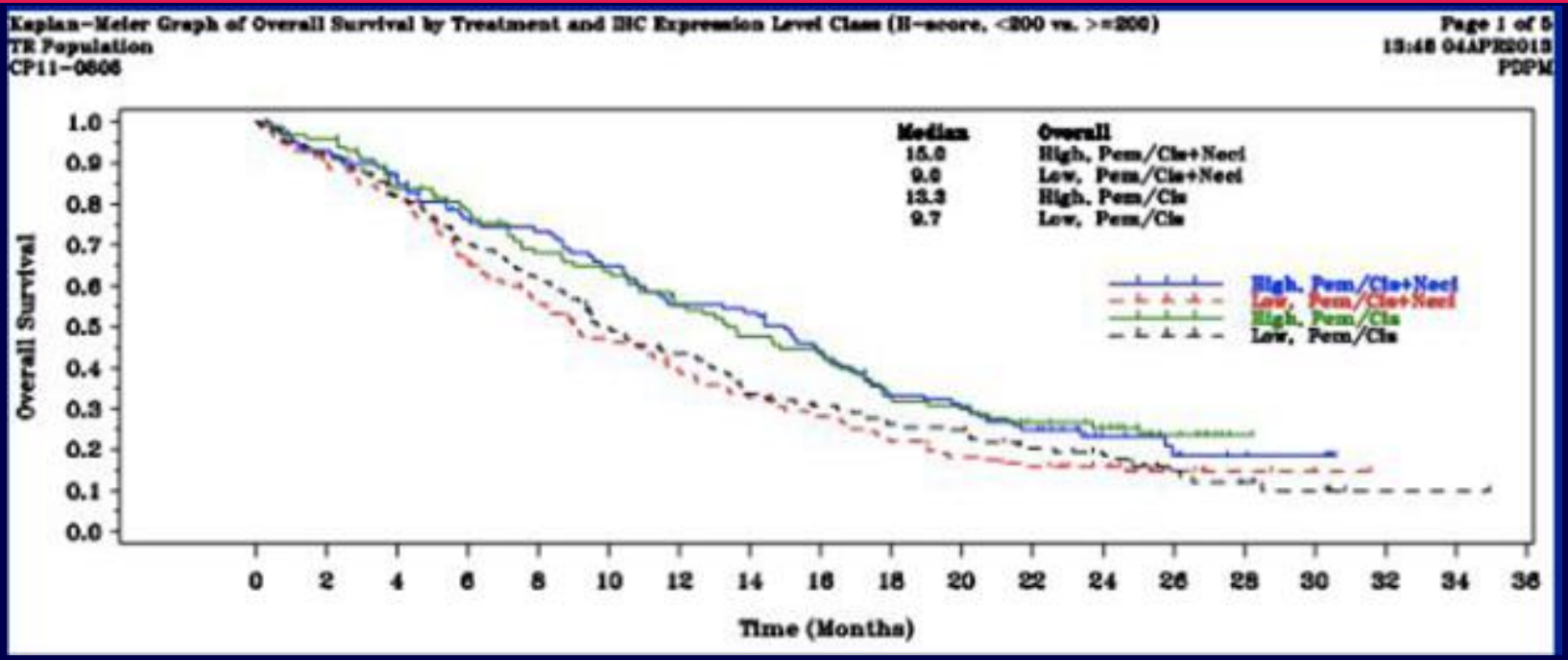
OS and PFS



- No relevant differences in ORR(CR+PR) and DCR(CR+PR+SD)
- No relevant differences in systemic post study anti-cancer treatment
- Subgroup analyses consistent across subgroups

[*] **LOG rank test (stratified)**

OS by EGFR Expression (H-Score)[a]



	H-score<200		H-score≥200	
	Pem-Cis +Neci (N=144)	Pem-Cis (N=146)	Pem-Cis +Neci (N=101)	Pem-Cis (N=99)
Events	115	122	75	72
Median OS (95%CI),months	9.0(7.6,11.3)	9.7(8.7,12.5)	15.0(10.8,16.6)	13.3(10.8,16.8)
Hazard ratio (95%CI)	1.07(0.83,1.38);p=0.592[b]		1.03(0.75,1.43;p=0.847[b]	

[a] score:0-300

[b] likelihood ratio chi square test of significance

Conclusions

- EGFR TKI is standard 1st line therapy for EGFR mutant NSCLC
- EGFR antibody does not appear effective for nonsquamous NSCLC
- Newer EGFR TKIs have encouraging activity in EGFR TKI resistant, T790M positive NSCLC
- Afatinib is effective in patients with less common mutations
- 2nd EGFR TKIs are inferior to 2nd chemotherapy in terms of PFS and ORR in EGFR wild-type NSCLC
- Dynamic change of cfDNA and mut EGFR could predict PFS of TKI and be used to monitor TKI therapy

Thank you for your kind attention!