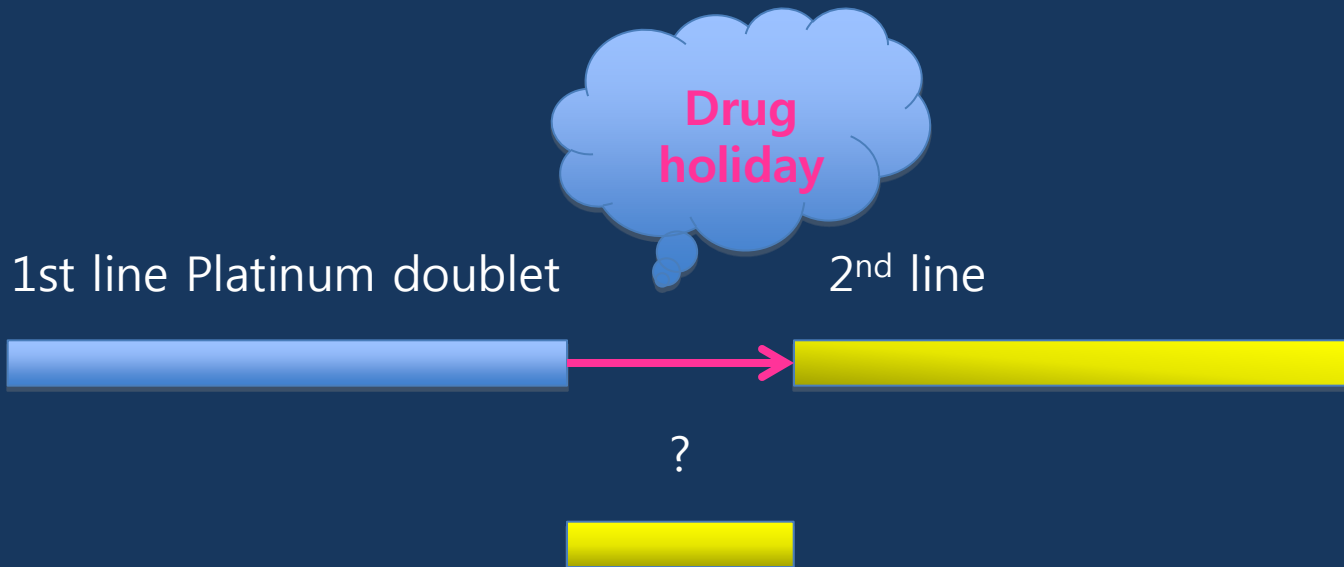


# Evidence Updates of Maintenance Therapy

Chungnam national university hospital,  
Department of internal medicine, Pulmonology division

Jeong Eun Lee

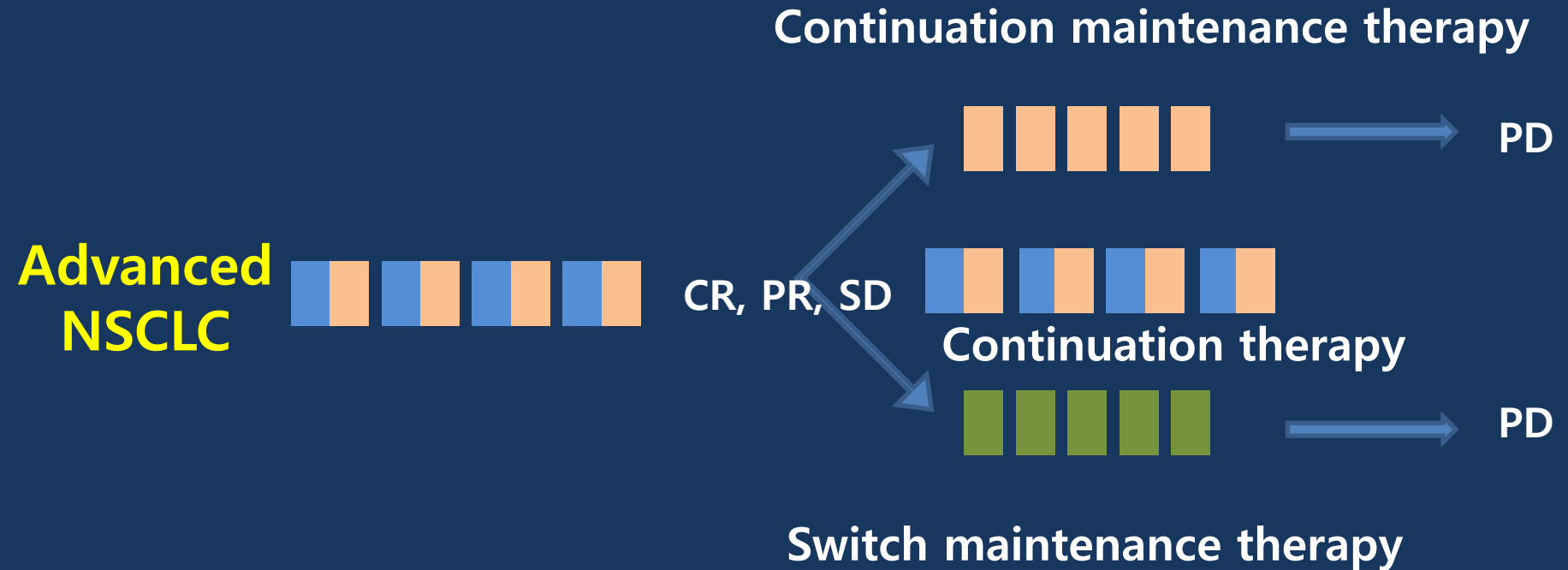
# Maintenance therapy



# Wishful-Purpose

- To sustain maximal tumor shrinkage
- To reduce cancer-related symptoms
- To prolong the time to progression and onset of related symptoms

# Maintenance therapy



# Maintenance therapy in solid tumor

- **NSCLC**
  - SCLC
  - Malignant pleural mesothelioma
- **Colorectal cancer**
- **Ovarian cancer**
- **Breast cancer**
  - Head and neck cancer
  - Melanoma
  - Brain tumor
  - Renal cell cancer
  - Urothelial tumor
  - Prostate cancer

# NCCN Guideline

# NCCN v2, 2010

NCCN®

Practice Guidelines  
in Oncology – v.2.2010

## Non-Small Cell Lung Cancer

[Guidelines Index](#)  
[NSCL Table of Contents](#)  
[Staging, Discussion, References](#)

### THERAPY FOR RECURRENCE AND METASTASIS

Systemic therapy<sup>w</sup>  
and best  
supportive care

Performance  
status 0-1<sup>x</sup>

Performance  
status 2

Performance  
status 3-4

### FIRST-LINE THERAPY

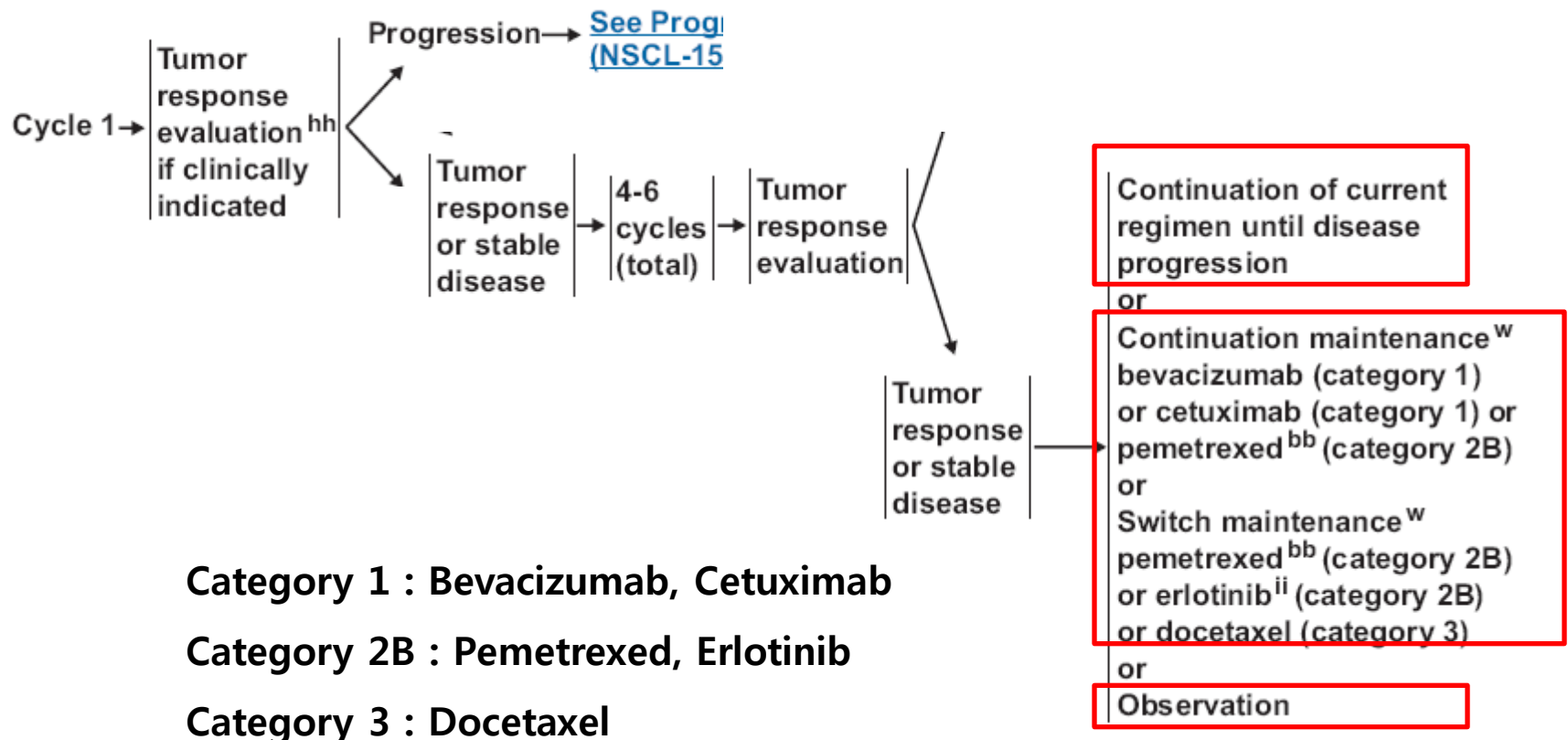
Chemotherapy<sup>w</sup> (category 1) →  
or  
Bevacizumab + chemotherapy<sup>w,y,z</sup> (if criteria met)<sup>aa</sup>  
or  
Cisplatin/pemetrexed<sup>bb</sup> (category 1) (if criteria met)<sup>cc</sup>  
or  
Cetuximab/vinorelbine/cisplatin<sup>dd</sup>  
(category 2B)  
or  
Erlotinib for EGFR mutation positive patients<sup>ee</sup> →

Cetuximab/vinorelbine/cisplatin<sup>dd,ff</sup>  
(category 2B)  
or  
Chemotherapy<sup>w</sup> →  
or  
Erlotinib for EGFR mutation positive patients<sup>ee</sup> →

Erlotinib for EGFR mutation positive patients<sup>gg</sup>  
or  
Best supportive care only ([See NCCN Palliative Care Guidelines](#))

→ [See NSCL-14](#)

# NCCN v2, 2010

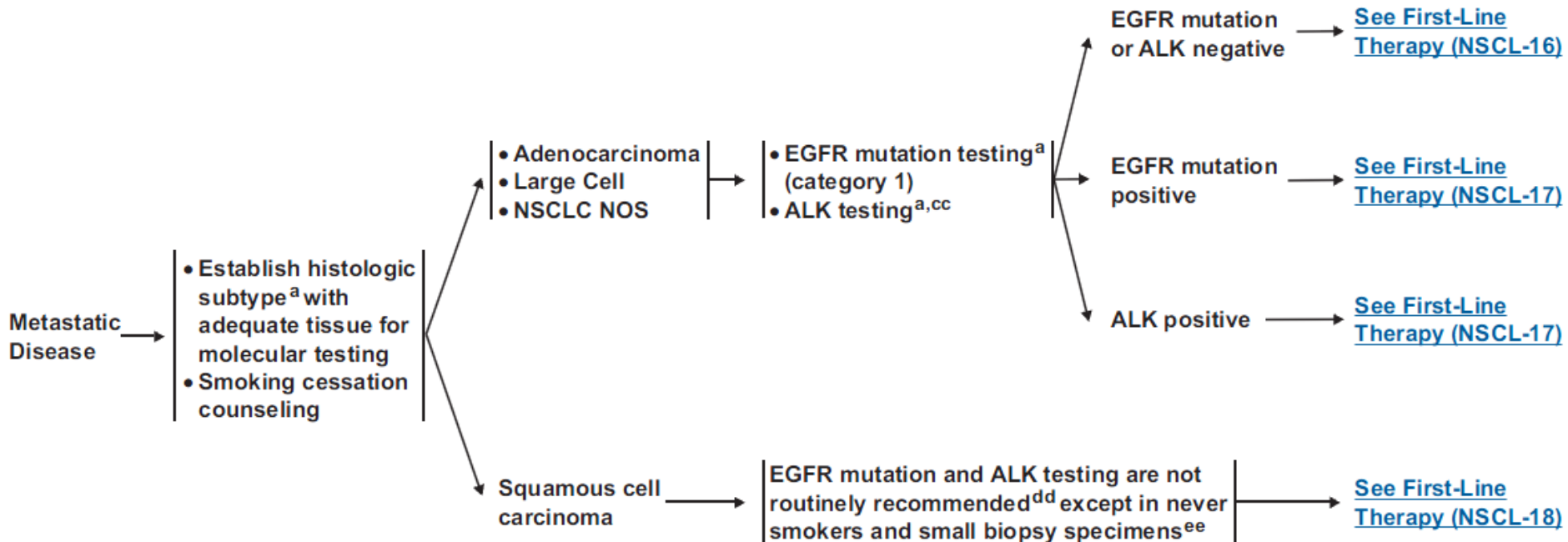


# Updated Guideline

# NCCN v2, 2013

### SYSTEMIC THERAPY FOR METASTATIC DISEASE

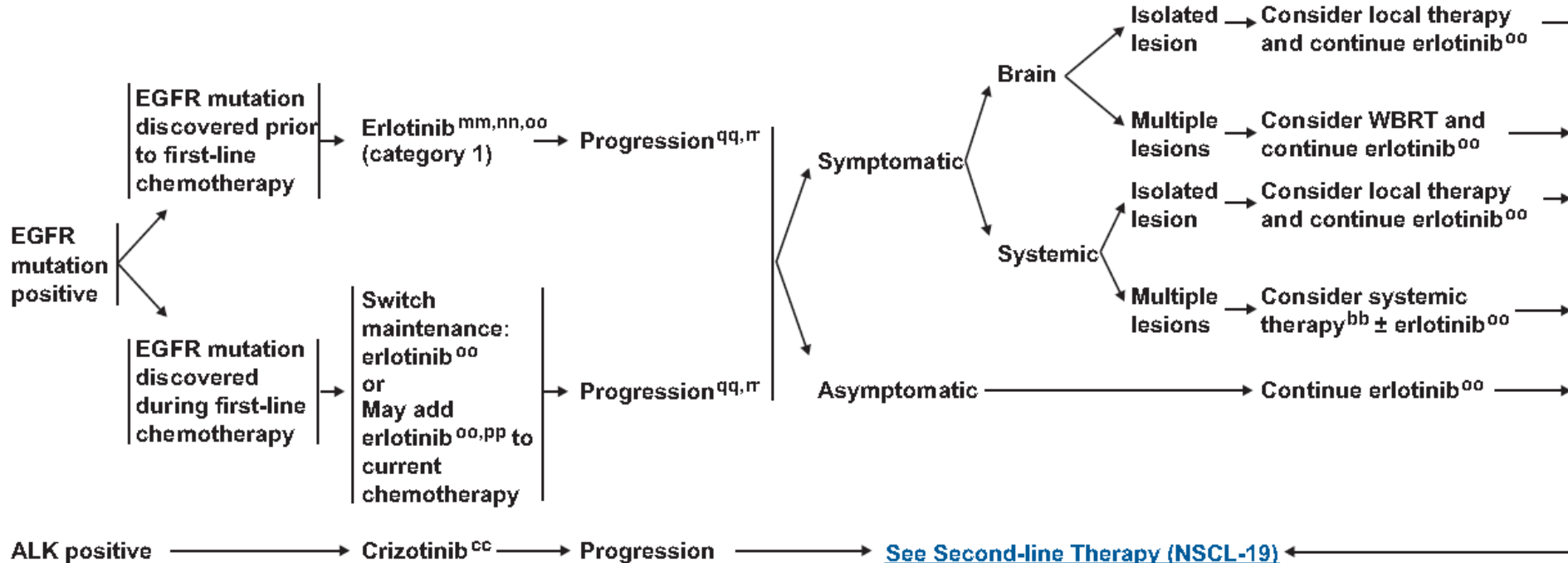
### HISTOLOGIC SUBTYPE



# NCCN v2, 2013

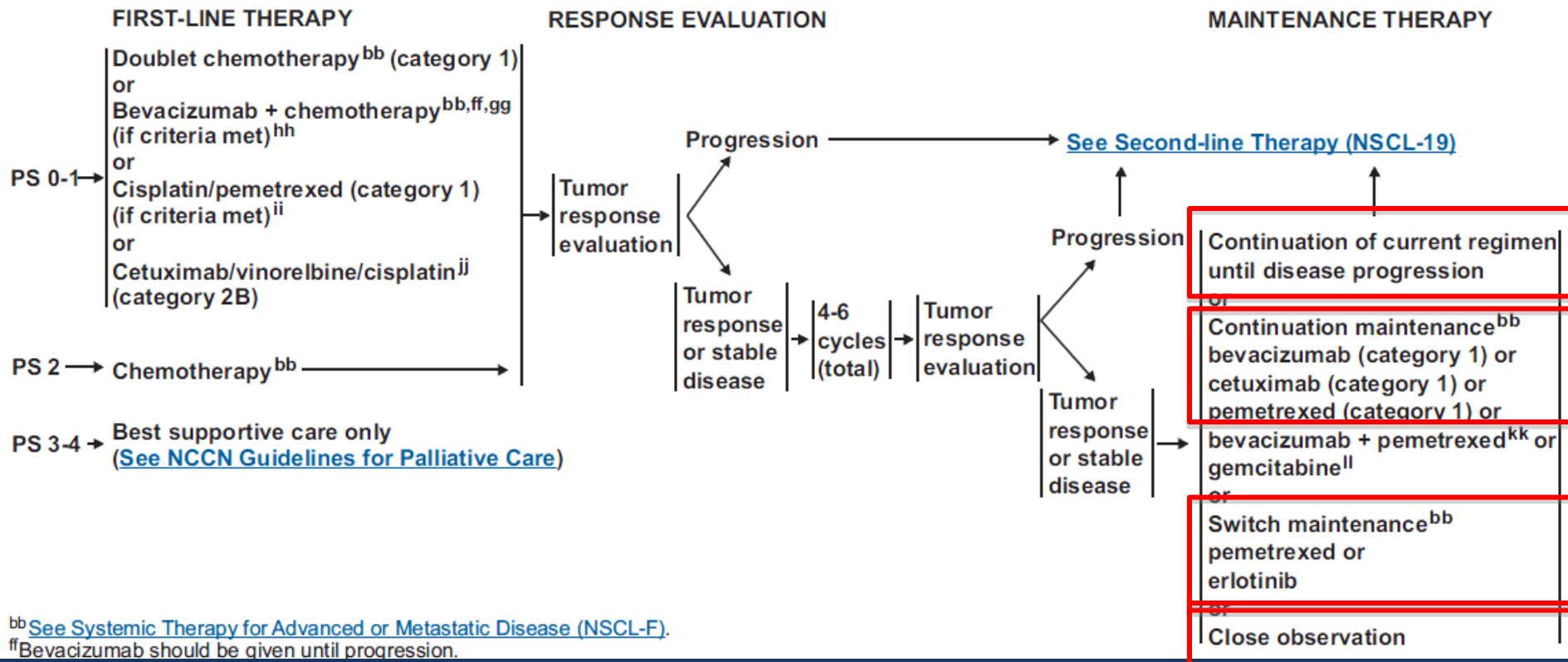
ADENOCARCINOMA, LARGE CELL, NSCLC NOS: EGFR MUTATION OR ALK POSITIVE

FIRST-LINE THERAPY<sup>bb</sup>



# NCCN v2, 2013

ADENOCARCINOMA, LARGE CELL, NSCLC NOS: EGFR MUTATION AND ALK NEGATIVE



<sup>bb</sup> See [Systemic Therapy for Advanced or Metastatic Disease \(NSCL-F\)](#).

<sup>ff</sup> Bevacizumab should be given until progression.

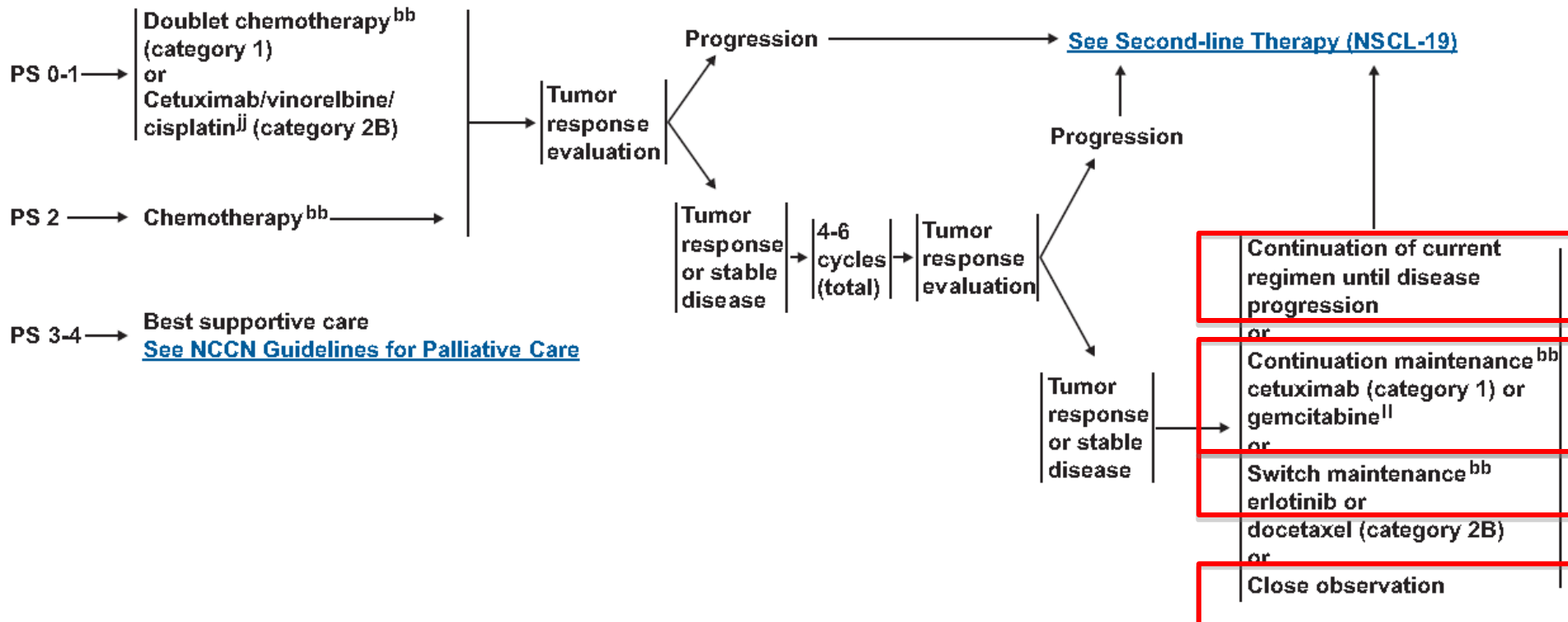
# NCCN v2, 2013

## SQUAMOUS CELL CARCINOMA

### FIRST-LINE THERAPY

### RESPONSE EVALUATION

### MAINTENANCE THERAPY



# Continuation therapy

# Phase III trials of platinum combination chemotherapy duration

VOLUME 25 · NUMBER 33 · NOVEMBER 20 2007

JOURNAL OF CLINICAL ONCOLOGY

- 2<sup>nd</sup> line Tx : 62.7% (6-cycle group)  
74.4% (4-cycle group)  
why? Toxicity, PS

## Phase III Trial of Two Versus Four Additional Cycles in Patients Who Are Nonprogressive After Two Cycles of Platinum-Based Chemotherapy in Non-Small-Cell Lung Cancer

*Joon Oh Park, Sang-We Kim, Jin Seok Ahn, Cheolwon Suh, Jung Shin Lee, Joung Soon Jang, Eun Kyung Cho, Sung Hyun Yang, Jin-Hyuk Choi, Dae Seog Heo, Suk Young Park, Sang Won Shin, Myung Ju Ahn, Jong Seok Lee, Young Ho Yun, Jae-Won Lee, and Keunchil Park*

Von Plessen et al	(Carboplatin-vinorelbin)	6	147	10	21 weeks	32 weeks
Park et al	2007 (3 <sup>rd</sup> platinum doublet)	4	156	74	4.6 months	15.9 months
		6	158	63	6.2 months	14.9 months
Barata et al	2007 (carboplatin-gemcitabine)	4	110	14 (docetaxel)	4 months	7 months
		6	110	15 (docetaxel)	5 months	12 months

# ASCO guidelines 2009

- In patients with stage IV NSCLC, first-line cytotoxic chemotherapy should be stopped at disease progression or after four cycles in patients whose disease is not responding to treatment.
- Two-drug cytotoxic combinations should be administered for no more than six cycles. For patients who have stable disease or who respond to first-line therapy, evidence does not support the continuation of cytotoxic chemotherapy until disease progression or the initiation of a different chemotherapy prior to disease progression.

# Continuation maintenance

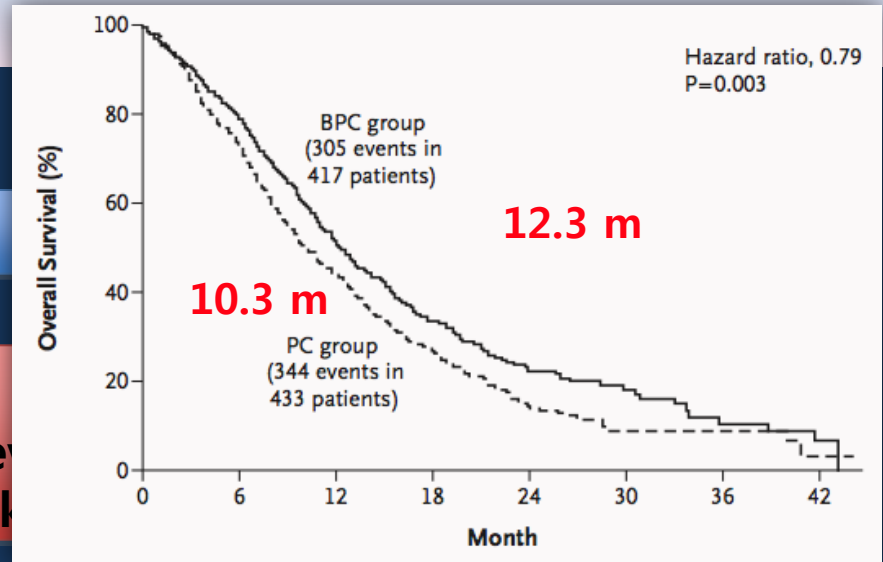
- Target agent
  - Bevacizumab
  - cetuximab
- Cytotoxic agent
  - Pac~~ax~~axel
  - Gemcitabine
  - Pemetrexed

# Bevacizumab with standard CTx

## ECOG 4599: Carbo/Taxol

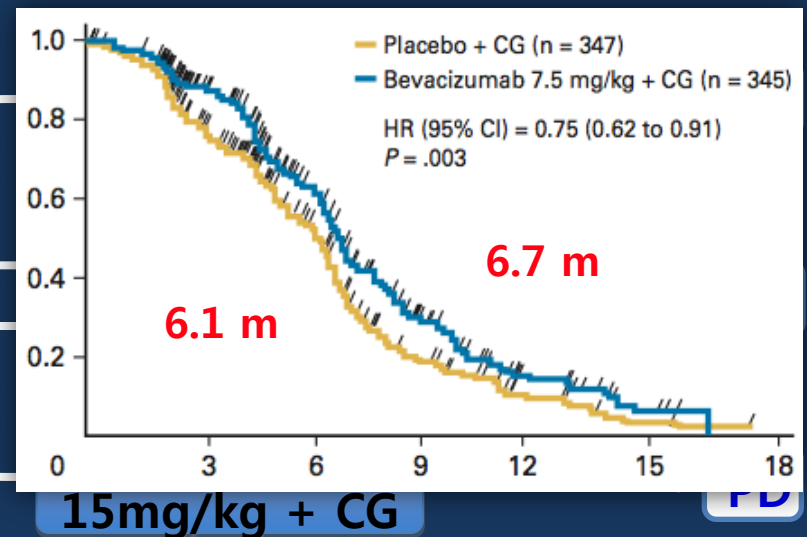
Previously untreated stage IIIB/IV non-squamous NSCLC

Bev  
g) e  
eel



## AVAiL: Cis/Gem

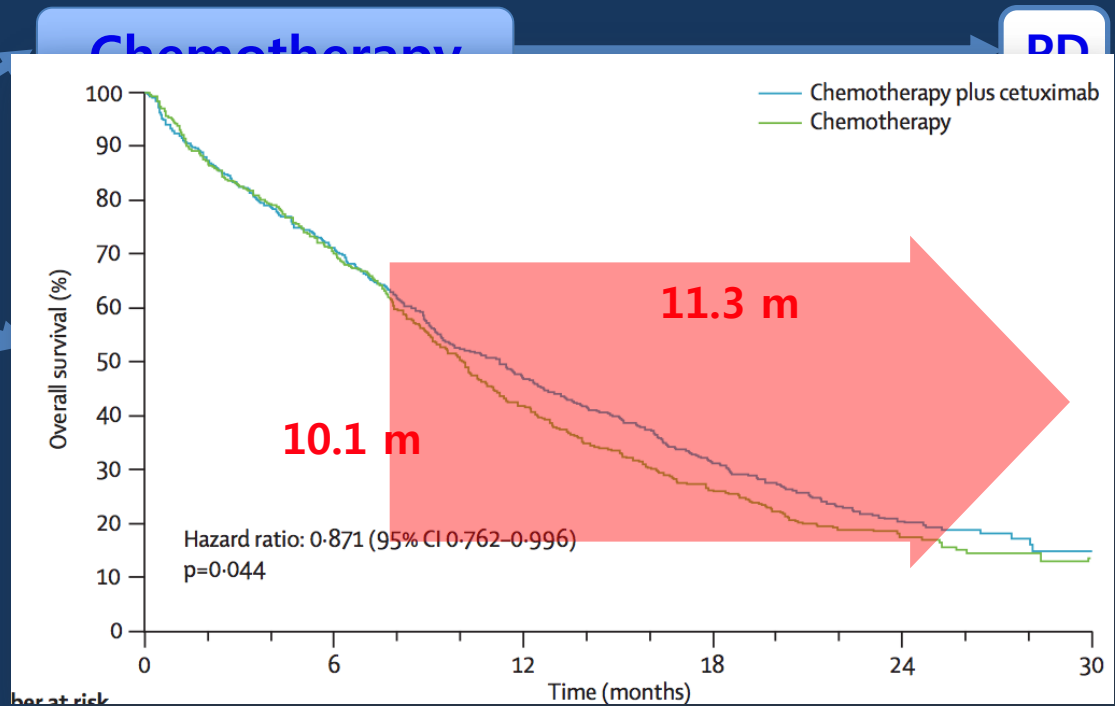
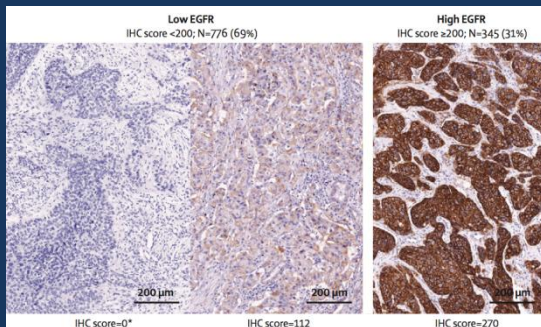
Previously untreated, stage IIIB/IV non-squamous NSCLC



# Cetuximab with standard CTx

**FLEX: Cisplatin/vinorelbine**

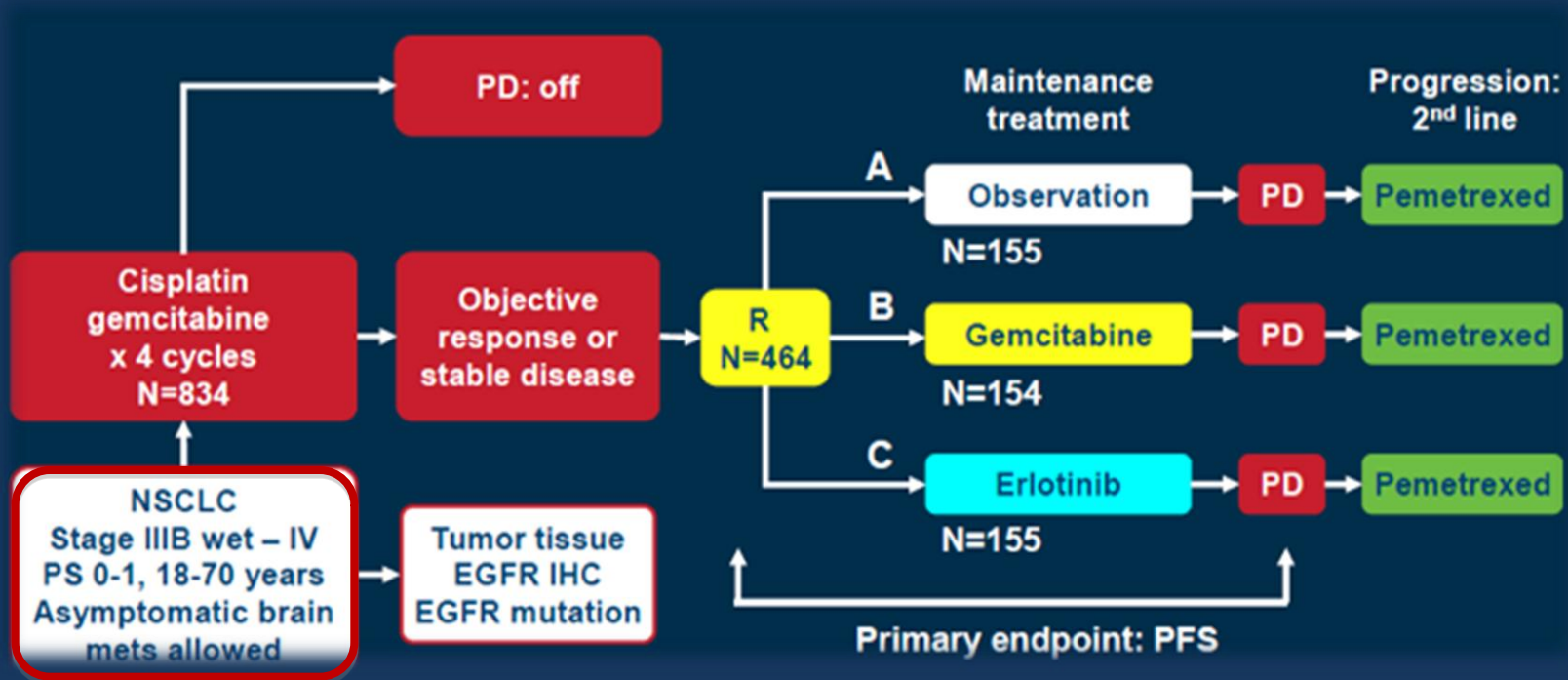
**Previously untreated stage IIIB/IV EGFR expressing NSCLC**



# Continuation maintenance

Trial (Year)	Induction CTx		Maintenance Tx.		Therapy at PD (%)	PFS (months)	OS (months)
	Regimen	No.	Regimen	No.			
IFCT-GFPC 0502 (2010)	Cis+gem	834	Gemcitabine	154	119(74.0% pemetrexed)	3.8	12.1
			observation	155	141 (83.8% pemetrexed)	1.9 (HR 0.56)	10.8
Belani et al (2010)	Carbo+Gem.	519	gemcitabine	128	16	*3.9 (7.4)	8.0
			BSC	127	17	*3.8 (7.7)	9.3 (HR 1.97)
PARAMOUNT (2012)	Cis+Pem	939	Pem.+ BSC	359	64	4.1	16.9
			Placebo +BSC	180	72	2.8 (HR 0.62)	14.0 (HR 0.78)
AVAPERL	Cis+Pem + bevacizumb	376	Pem.+ Bevacizumab	125	Not reported	10.2	Not reported
			Bevacizumab	120	Not reported	6.6 (HR 0.5)	15.7(HR 0.75)

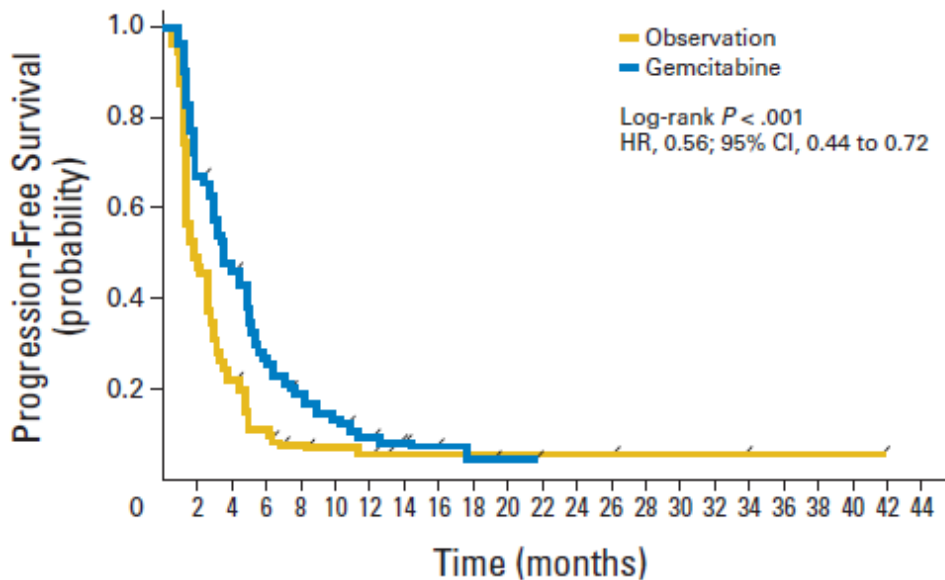
# IFCT-GFPC 0502



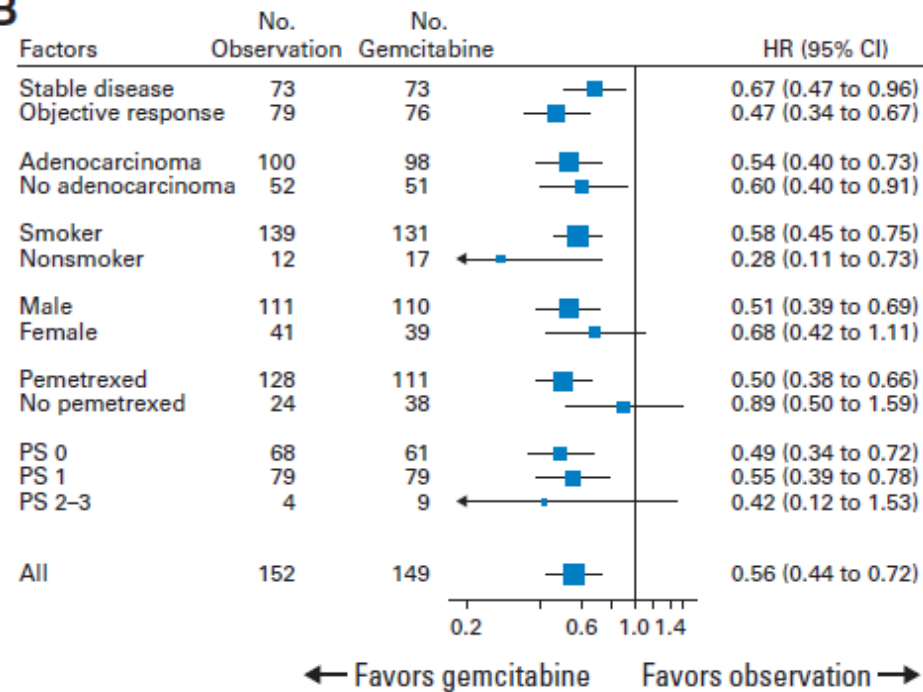
- Primary endpoint :PFS
- Secondary endpoints: OS, safety, symptom control, prognostic and predictive effect of tumor EGFR status (IHC, EGFR mut)

# Continuation maintenance with gemcitabine

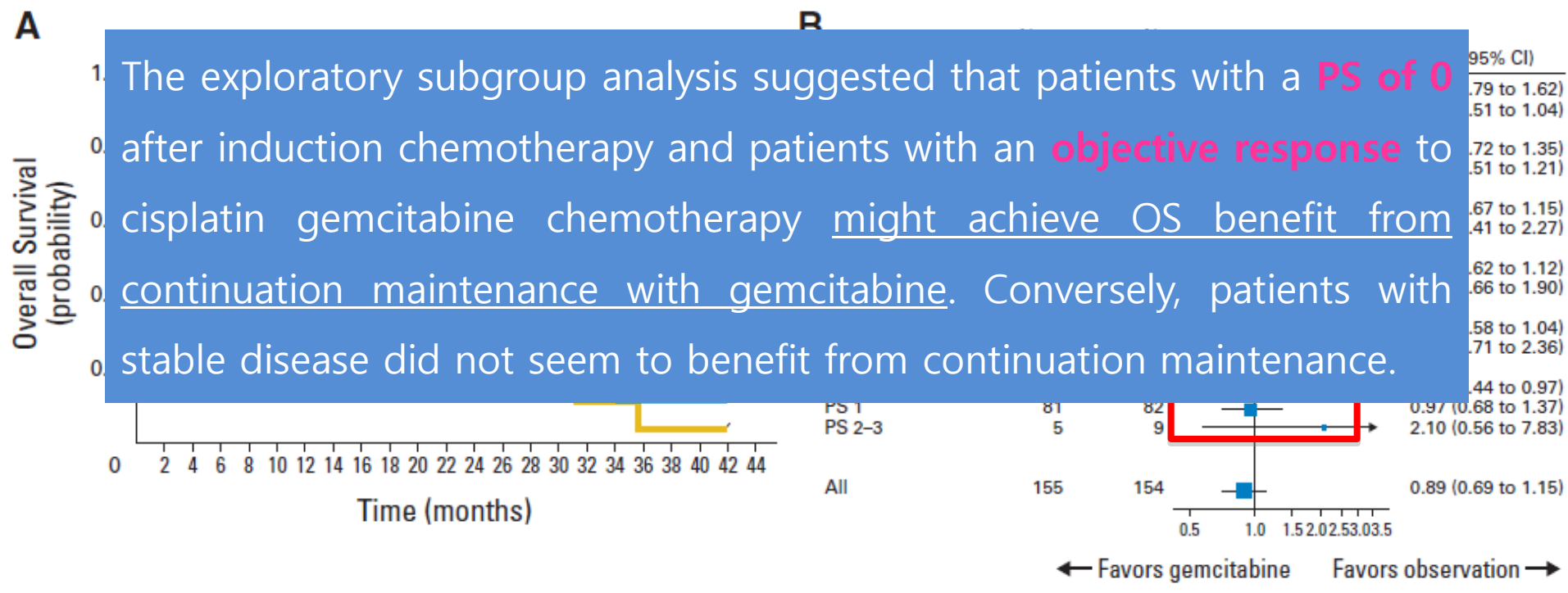
**A**



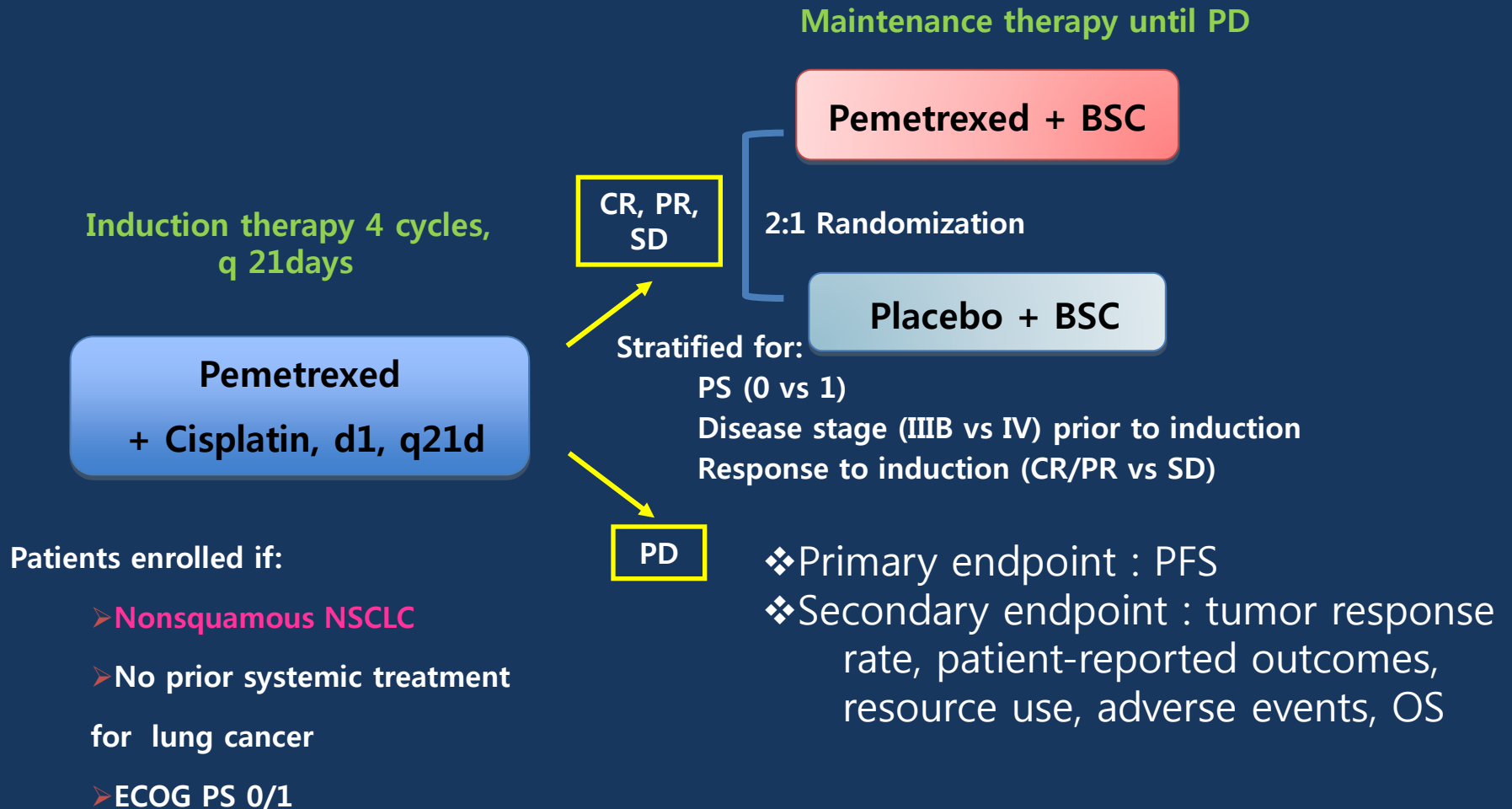
**B**



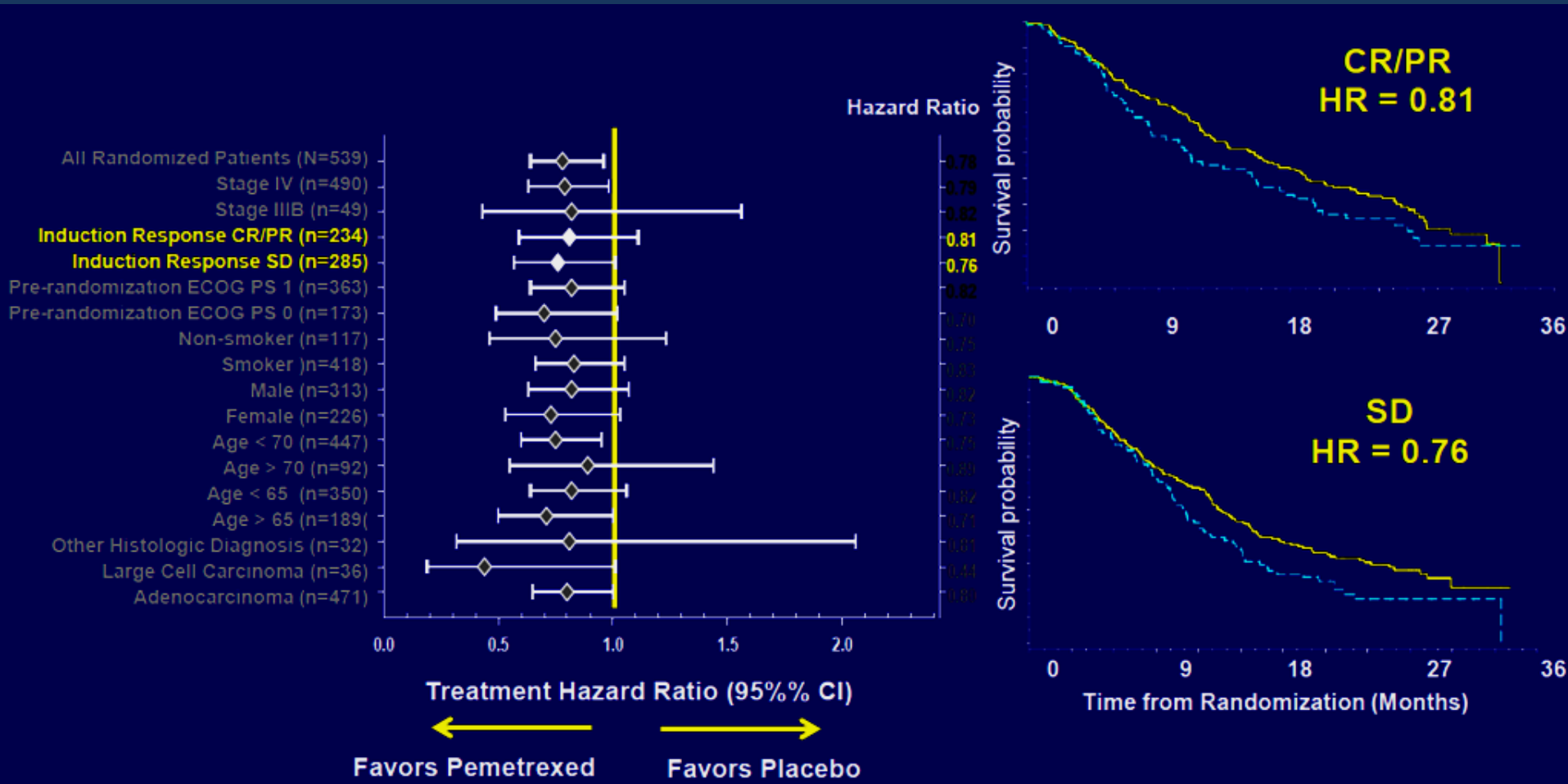
# Continuation maintenance with gemcitabine



# PARAMOUNT(2012)



# PARAMOUNT: Induction response subgroups OS Hazard ratios



# Switch maintenance

- Cytotoxic agent
  - Vinc~~ristine~~ristine
  - Pac~~litaxel~~litaxel
  - Docetaxel
  - Pemetrexed
- Target agent
  - Erlotinib
  - gefi~~nib~~nib

# Switch maintenance

Trial (Year)	Induction CTx		Maintenance Tx.		Therapy at PD (%)	PFS	OS (months)
	Regimen	No. Pt.	Regimen	No. Pt.			
JMEN, Ciuelanu et al (2009)	Platinum doublet (4 cycles)	745	Pemetrexed	441	51	4.0 m.	13.4 m.
			BSC	222	67 (19% pemetrexed)	2.0 m. (HR 0.6)	10.6 m. (HR 0.79)
Fidias et al (2009)	Carbo-gemcitab (4 cycles)	566	Docetaxel q 3 weeks (to 6 cycles)	153	Not reported	5.7 m.	12.3 m.
			Observation	156	63 (Docetaxel q 3 weeks (to 6 cycles))	2.7 m.	9.7 m.
SATURN (2010)	Platinum doublet (4 cycles)	1949	Erlotinib	438	55	12.3 w.	12.0 m.
			Placebo	451	64	11.1 w (HR 0.71)	11.0 m.

# JMEN (2009)

Pemetrexed treatment resulted in a **50% reduction** in the risk of disease progression or death. Moreover, we noted a **21% reduction** in the risk of death, and long-term exposures were well tolerated.

Stage IIIB/IV  
NSCLC

PS 0-1

Platinum doublet  
(except pem.)

Placebo (d1, q21d)  
+ BSC (n = 222)

Pemetrexed 500  
mg/m<sup>2</sup> (d1,q21d) +  
BSC (n = 441)

PD

PD

Primary endpoint : PFS

## Randomization factors:

gender

PS

stage

best tumor response to induction

non-platinum induction drug

brain mets

# Switch maintenance with pemetrexed

OS : squamous /non-squamous

OS	Pemetrexed	Placebo	HR (95% CI)	<i>p</i> -value
non-squamous (n = 481)	15.5 mo	10.3 mo	0.70 (0.56-0.88)	0.002
squamous (n = 182)	9.9 mo	10.8 mo	1.07 (0.49-1.73)	0.678

# Switch maintenance with pemetrexed

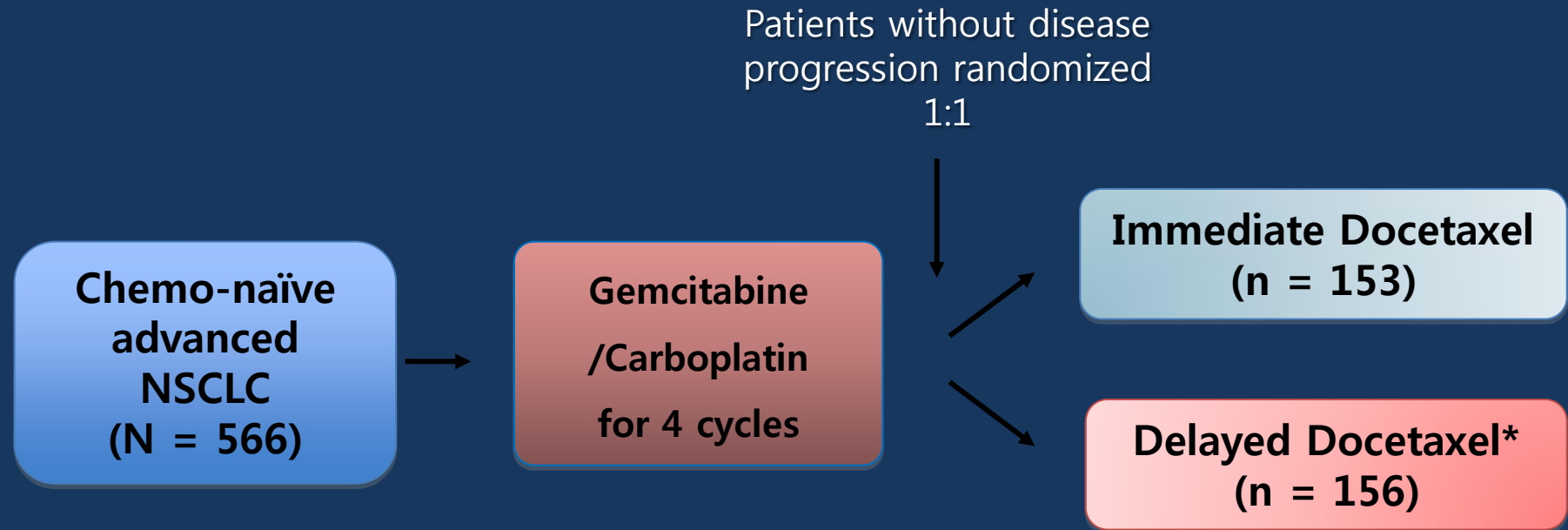
Response after induction CTx / non-squamous

OS	Pemetrexed	Placebo	HR (95% CI)	<i>p</i> -value
Non-squamous pts with CR/PR	14.4 mo	11.7 mo	0.81 (0.58, 1.12)	0.19854
Non-squamous pts with SD	16.6 mo	8.6 mo	0.61 (0.45, 0.83)	0.00171

Ciuleanu et al, Lancet 2009

Belani et al, J Clin Oncol 2010 (suppl; abstr 7506)

# Switch maintenance with docetaxel



- ▣ Primary endpoint: OS
- ▣ Other endpoints: PFS, ORR, safety, QOL

# Switch maintenance with docetaxel

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

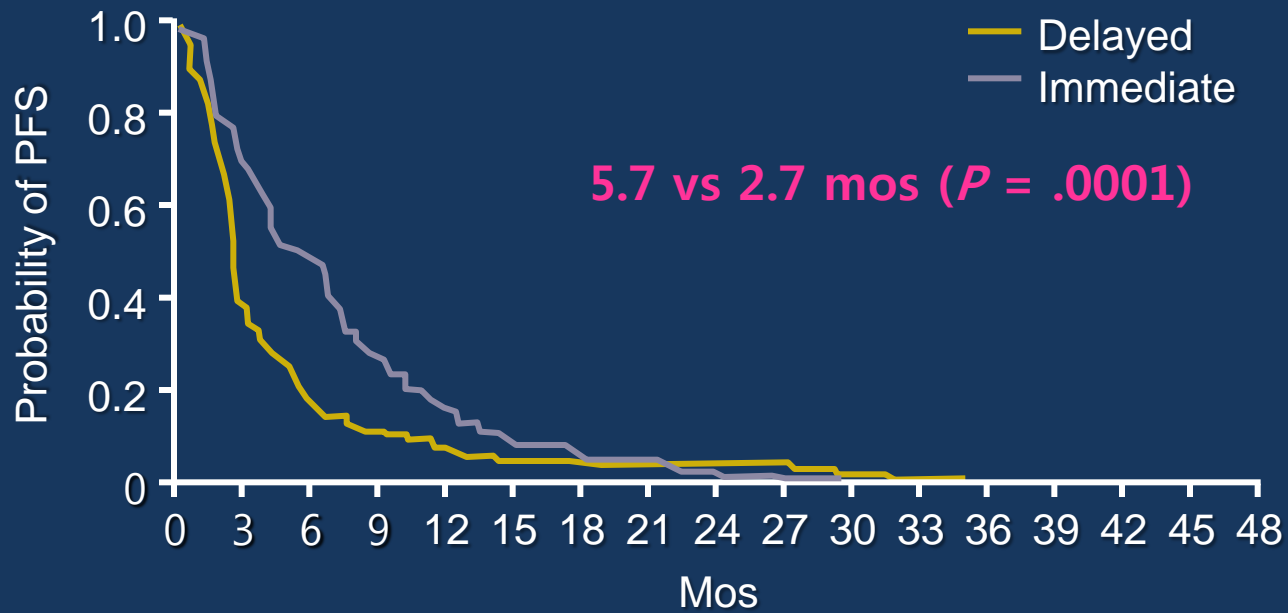
## Phase III Study of Immediate Compared With Delayed Docetaxel After Front-Line Therapy With Gemcitabine Plus Carboplatin in Advanced Non–Small-Cell Lung Cancer

*Panos M. Fidas, Shaker R. Dakhil, Alan P. Lyss, David M. Loesch, David M. Waterhouse, Jane L. Bromund, Ruqin Chen, Maria Hristova-Kazmierski, Joseph Treat, Coleman K. Obasaju, Martin Marciniak, John Gill, and Joan H. Schiller*

For patients without progression, **timing of second-line chemotherapy** for optimum clinical benefit remains uncertain.

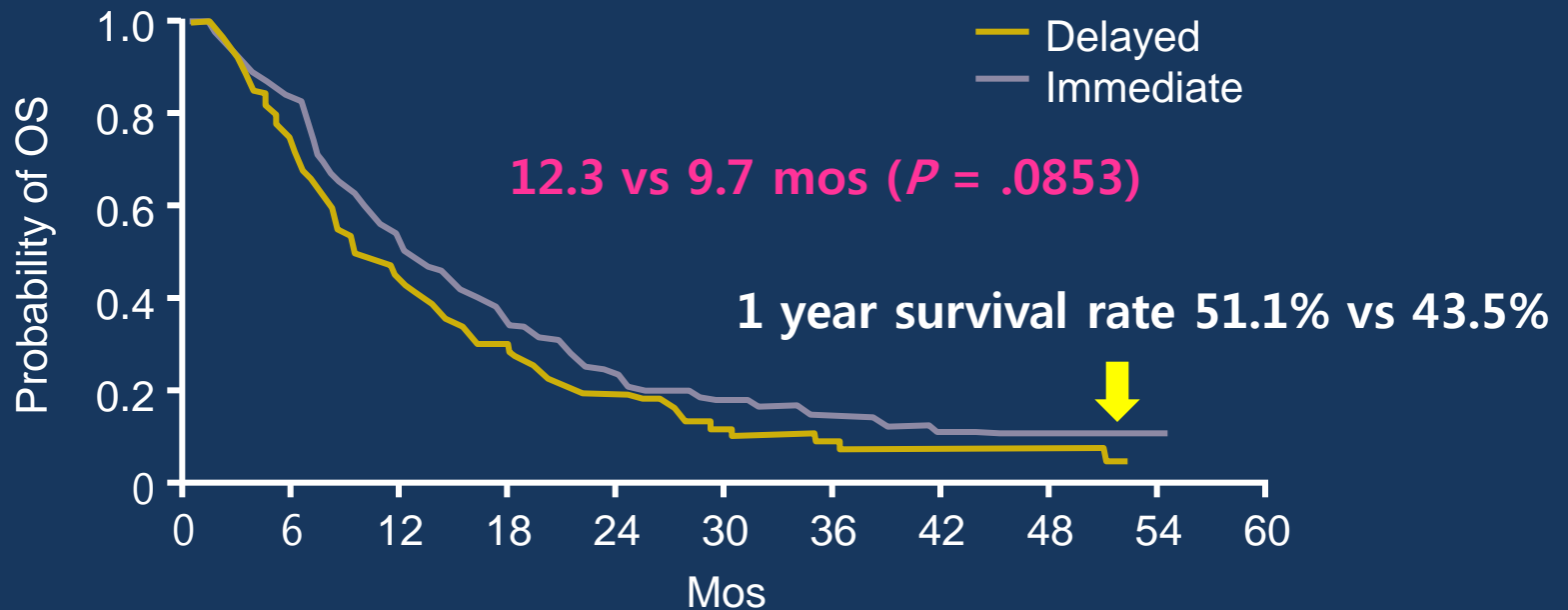
# Switch maintenance with docetaxel

## PFS



Patients at Risk, n							
Delayed	156	59	28	18	13	6	1
Immediate	153	109	72	42	26	5	2

# Switch maintenance with docetaxel OS



Patients at Risk, n	
Delayed	156 109 65 42 21 6 2
Immediate	153 119 73 49 28 13 2

These results suggest that NSCLC patients **may be healthier and more likely to proceed to additional therapy** if it is offered immediately after front-line treatment.

Chemo-naïve  
advanced  
NSCLC  
(N = 566)



Gemcitabine  
/Carboplatin  
for 4 cycles

94.8% (145/153)



Immediate Docetaxel  
(n = 153)

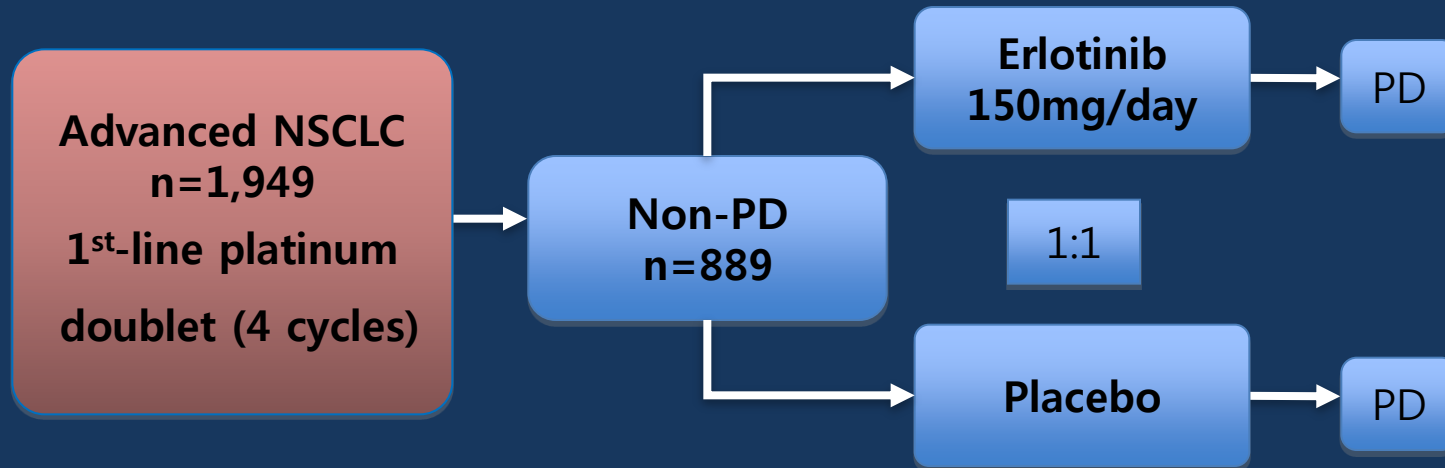


Delayed Docetaxel\*  
(n = 156)

62.8% (98/156)

37.2% ; PD (Sx. Deterioration)  
patient decision

# SATURN(2010)



	<b>PFS</b>	<b>OS</b>
Erlotinib	12.3 w.	12.0 m
placebo	11.1 w (HR 0.71)	11.0 m (HR 0.81)

## Co-primary endpoints:

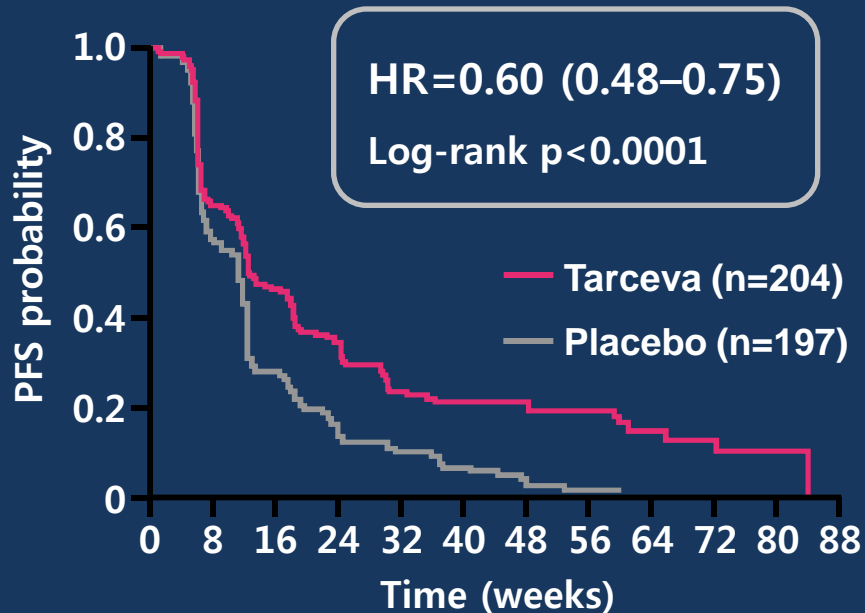
- PFS in all patients
- PFS in patients with EGFR IHC+ tumours

## Secondary endpoints:

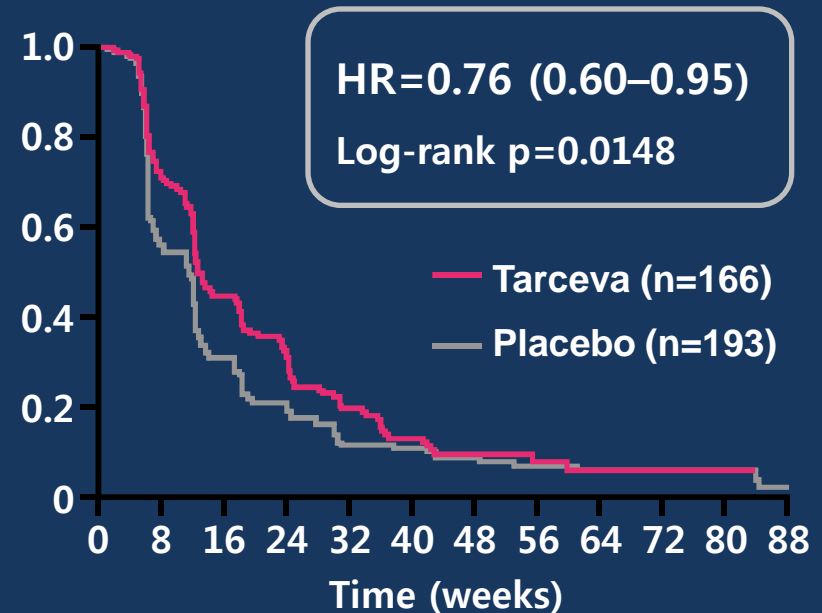
- OS in all patients and those with EGFR IHC+ tumours,
- safety;
- time to symptom progression
- QoL

# Switch maintenance with erlotinib in adenocarcinoma and squamous cell carcinoma

## Adenocarcinoma



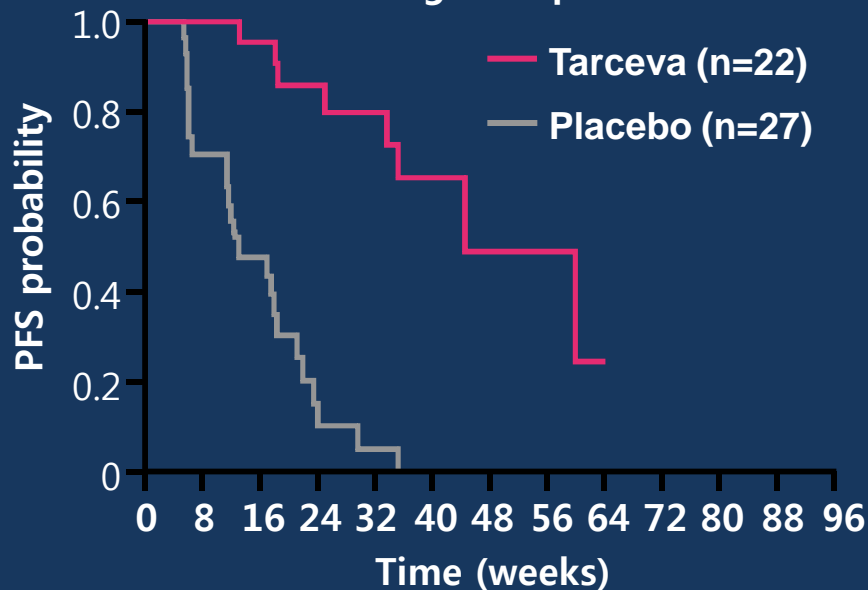
## Squamous-cell carcinoma



# Switch maintenance with erlotinib in EGFR mutation + and EGFR mutation wild

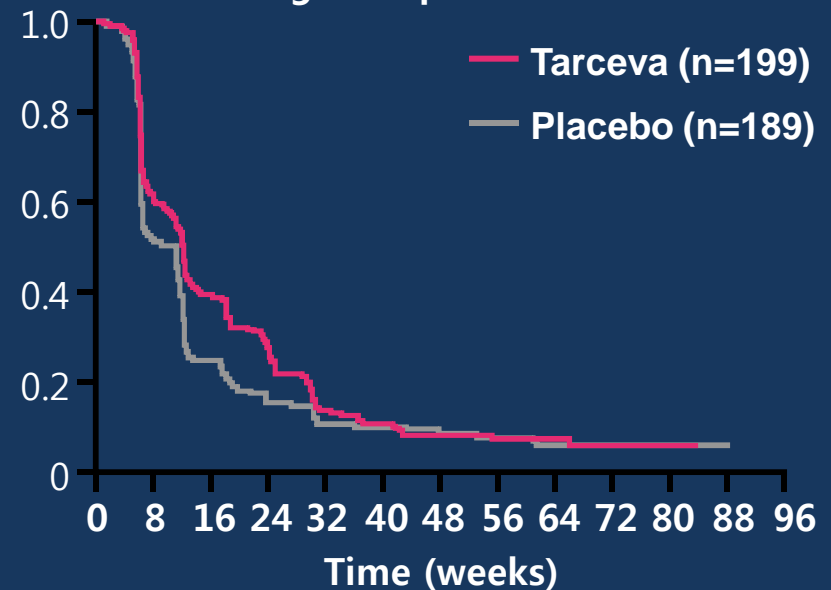
*EGFR* mutation+

HR=0.10 (0.04–0.25)  
Log-rank p<0.0001



*EGFR* wild-type

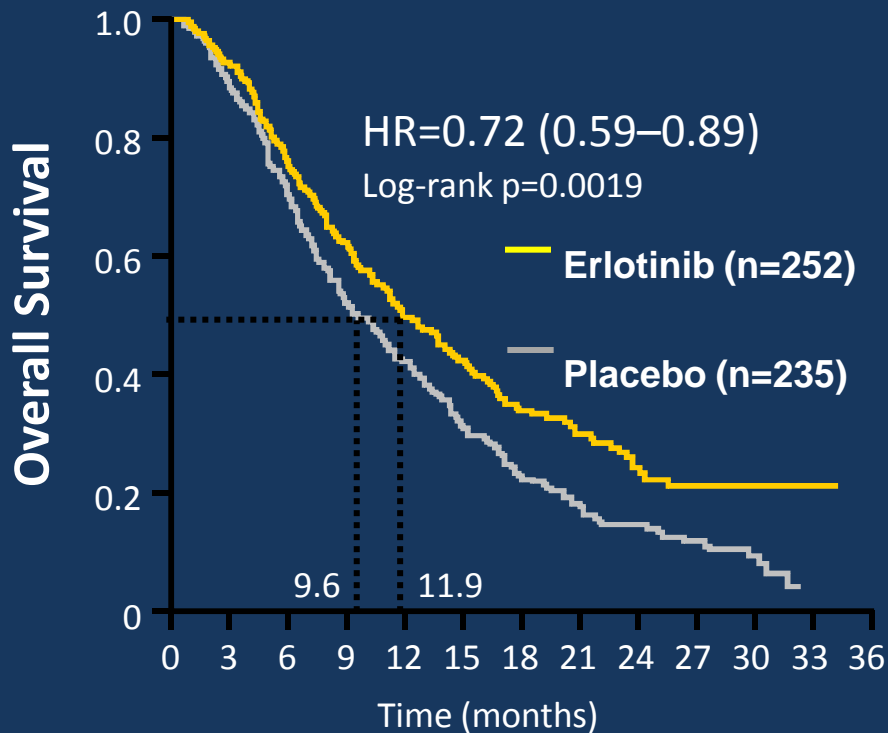
HR=0.78 (0.63–0.96)  
Log-rank p=0.0185



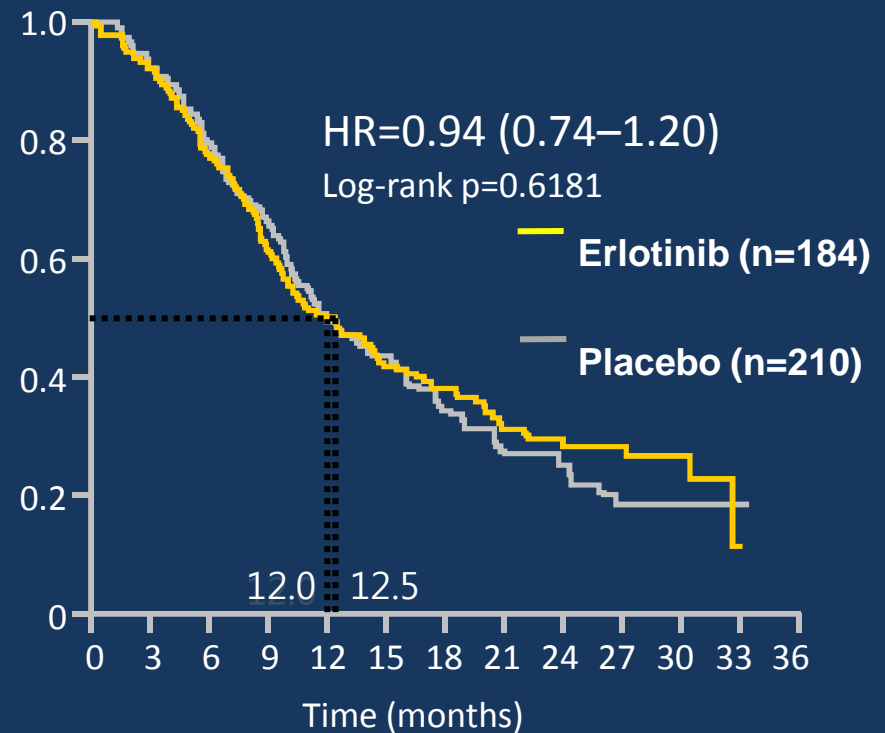
# Switch maintenance with Erlotinib

## Overall survival by response

**SD**



**CR/PR**



Measured from time of randomisation into the maintenance phase

# SATURN(2010)

Advanced NSCLC

Erlotinib  
150mg/day

PD

Experience from clinical practice suggests that less than half of patients with advanced NSCLC receive a second-line therapy. Theoretically, maintenance therapy should improve survival **not** because these agents are **more effective** when given earlier, **but** simply because this approach enables us to give patients access to **more lines of effective treatment** and treat a greater number of patients, including those who might otherwise be unsuitable for additional lines of therapy.

Erlotinib  
placebo

(HR 0.71)

(HR 0.81)

tumours,

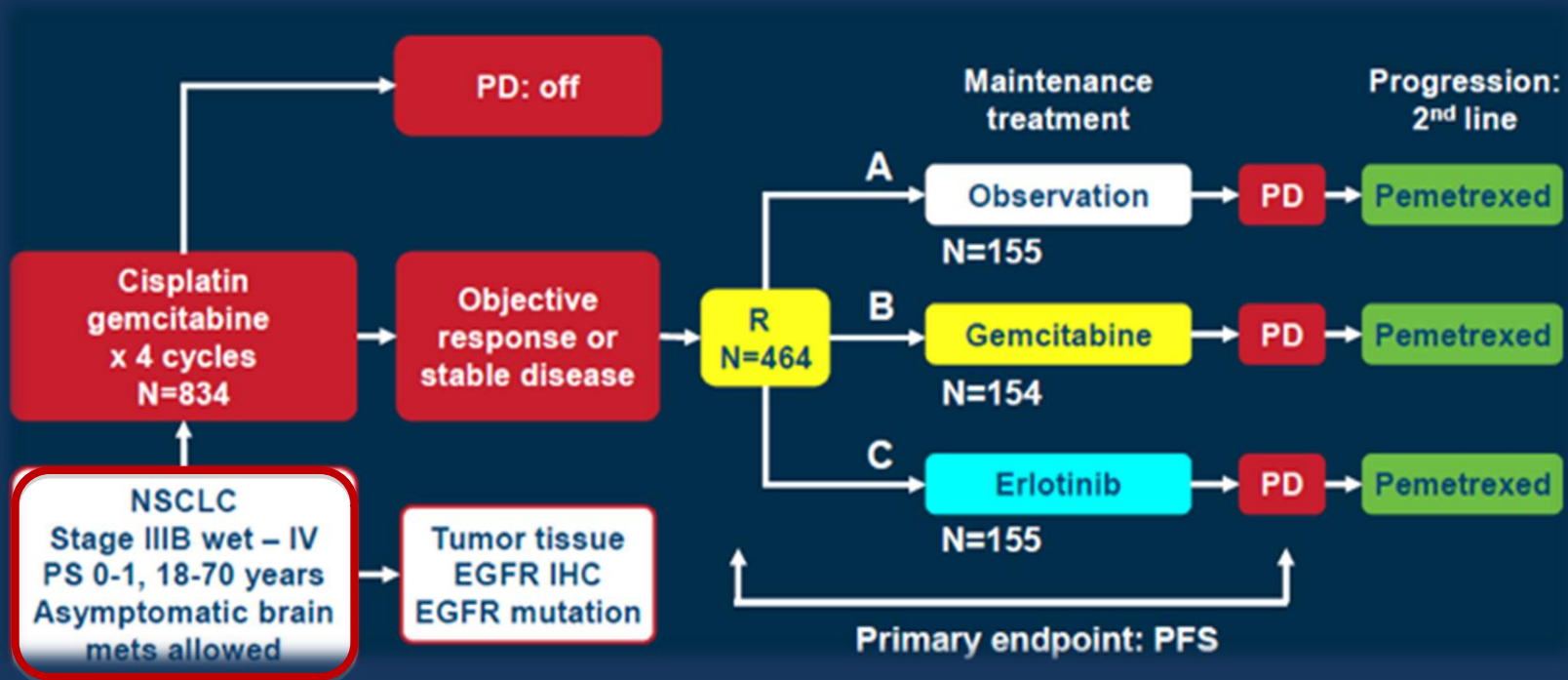
- safety;
- time to symptom progression
- QoL

C+

# Switch maintenance with EGFR-TKI

Trial (Year)	Induction CTx		Maintenance Tx.		Therapy at PD (%)	PFS (months)	OS (months)
	Regimen	No.	Regimen	No.			
IFCT-GFPC 0502 (2010)	Cis+gem	834	erlotinib	155	63	2.9	11.8
			observation	155	82 (64% EGFR-TKI)	1.9 (HR 0.82)	10.7(HR 0.91)
WJTOG 0203 (2010)	Platinum doublet 3 vs 6cycles	302/301	gefitinib	(172)	65%	4.6	13.7
			observation	297	73.0(54% EGFR-TKI)	4.3 (HR 0.68)	12.9 (HR 0.86)
INFORM (C-TONG 0804)	Platinum doublet 4 cycles	298	gefitinib	148	43	4.8	18.7
			Placebo	148	62(EGFR-TKI)	2.6 (HR 0.42)	16.9 (HR 0.84)
ATLAS(2009)*	Platinum doublet+bevacizumab(15) 4 cycles	1160	Bevacizumab +erlotinib	743	NR	4.8	15.9
			Bevacizumab +placebo		56 (40% EGFR-TKI)	3.7 (HR 0.72)	13.9 (HR 0.9)

# IFCT-GFPC 0502



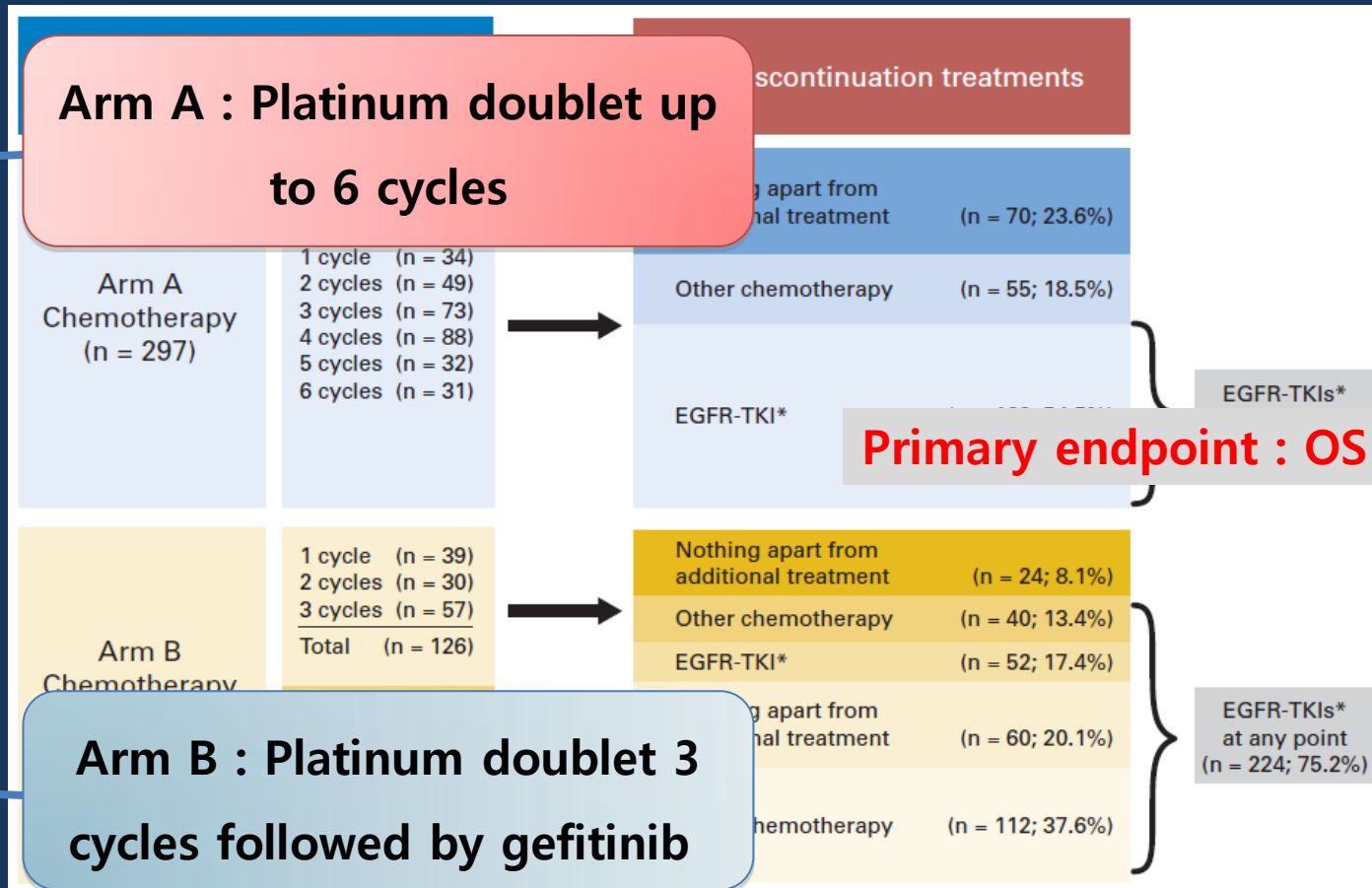
- Primary endpoint :PFS
- Secondary endpoints: OS, safety, symptom control, prognostic and predictive effect of tumor EGFR status (IHC, EGFR mut)

# IFCT-GFPC 0502 versus SATURN

	<b>IFCT-GFPC 0502</b>	<b>SATURN</b>
PFS	2.9 months	≈3.0 months
OS	11.8 months (without significance)	12.0 months
2nd line Tx	pemetrexed	Not controlled (pem. : 24% in erlotinib, 23% in placebo)
Therapy at progression	90% of control group (45% EGFR-TKI)	64% of control group (21% EGFR-TKI)
ORR after Induction CTx	non-specific	Benefit in SD

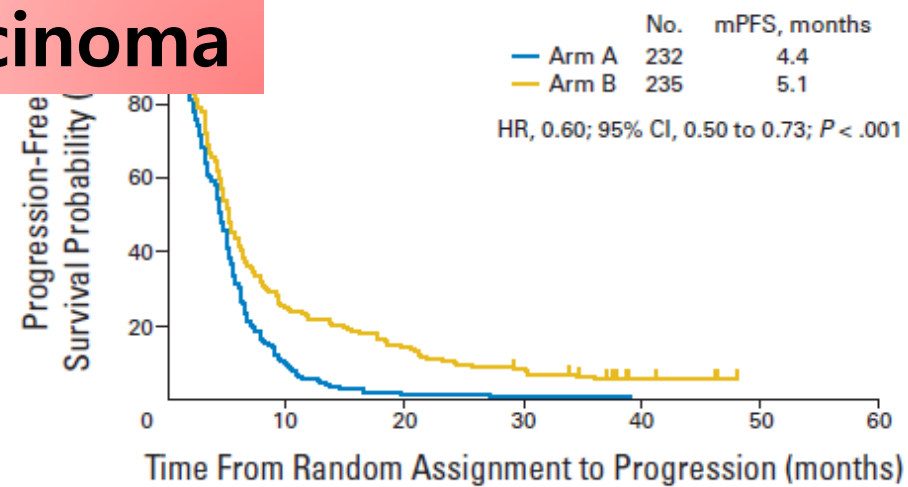
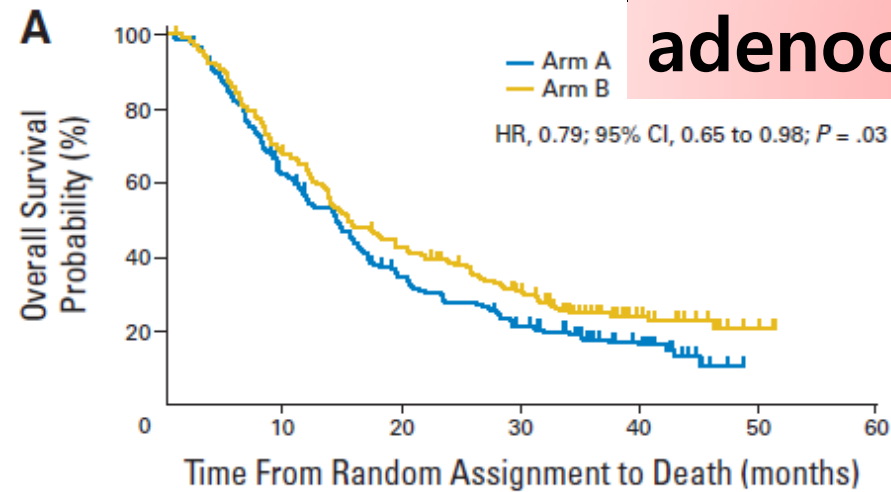
# WJTOG 0203(2010)

Non-squamous  
NSCLC  
Randomization  
N=604

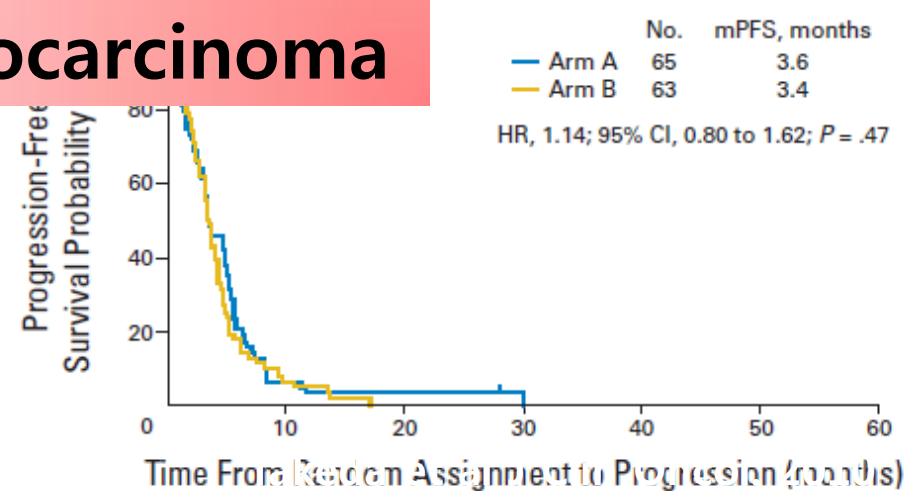
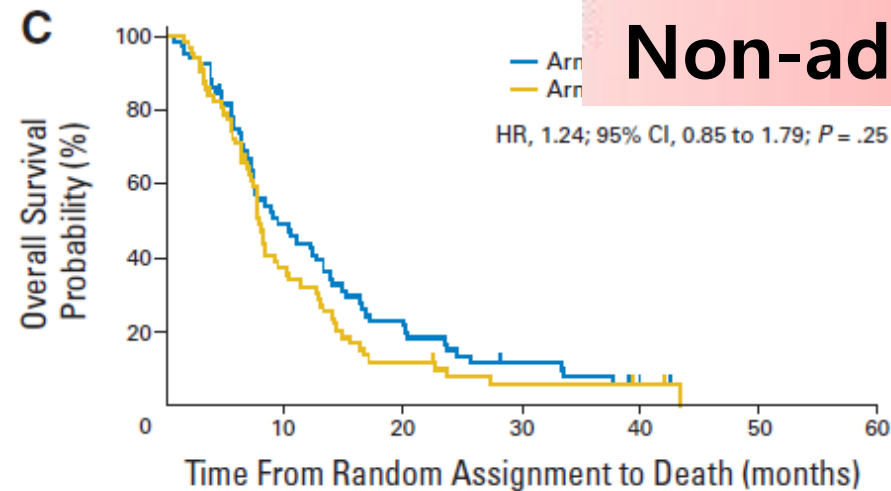


# WJTOG 0203

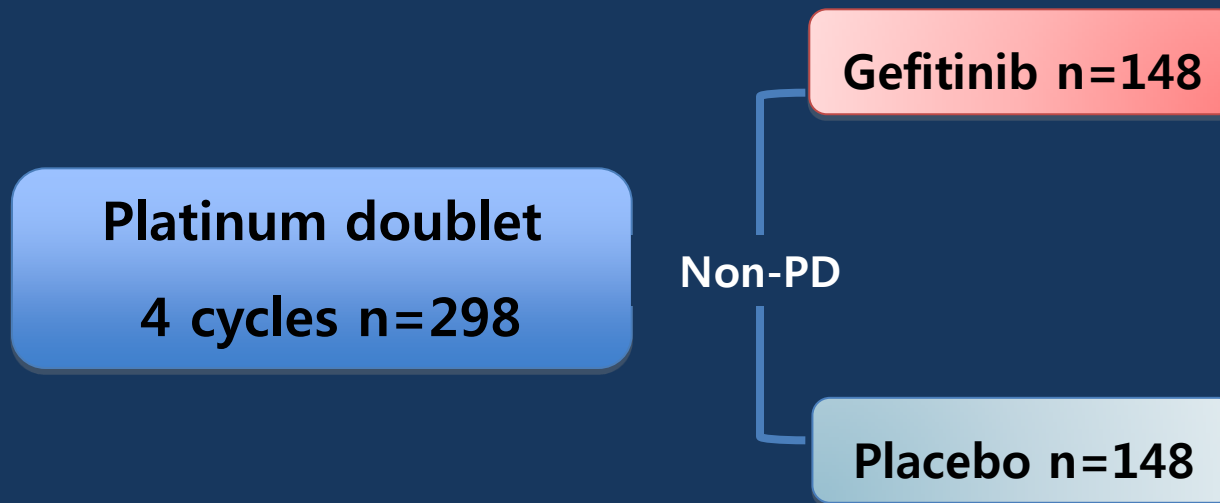
## adenocarcinoma



## Non-adenocarcinoma



# INFORM (C-TONG 0804)



- Primary endpoint = PFS
- 2ndary endpoints : OS

time to worsening symptom(QOL)  
disease control rate,

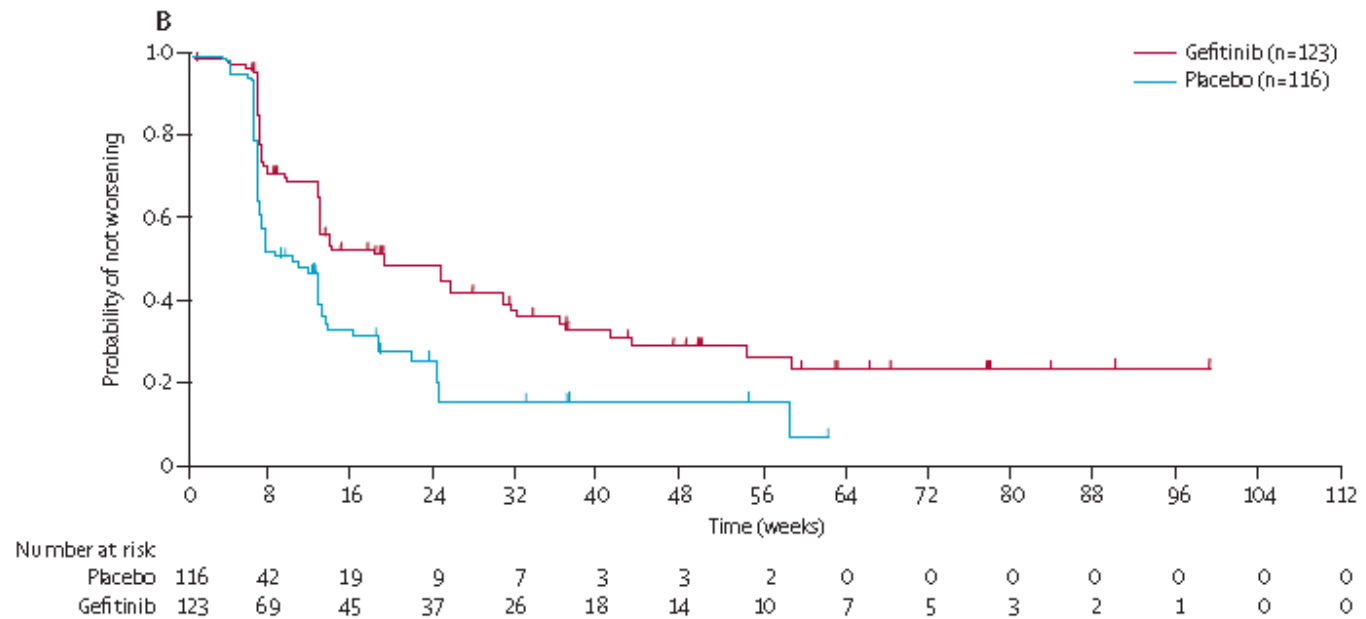
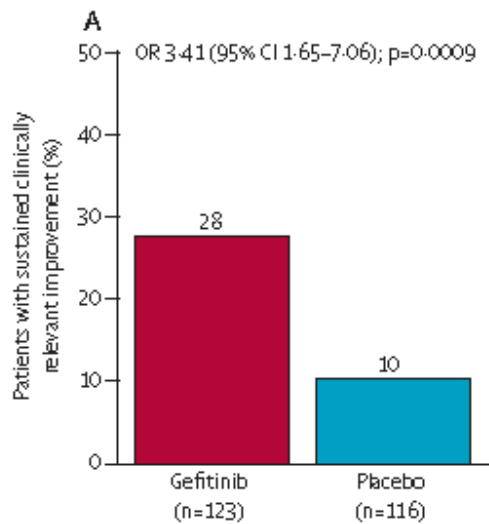
# Switch maintenance with gefitinib

## PFS, OS



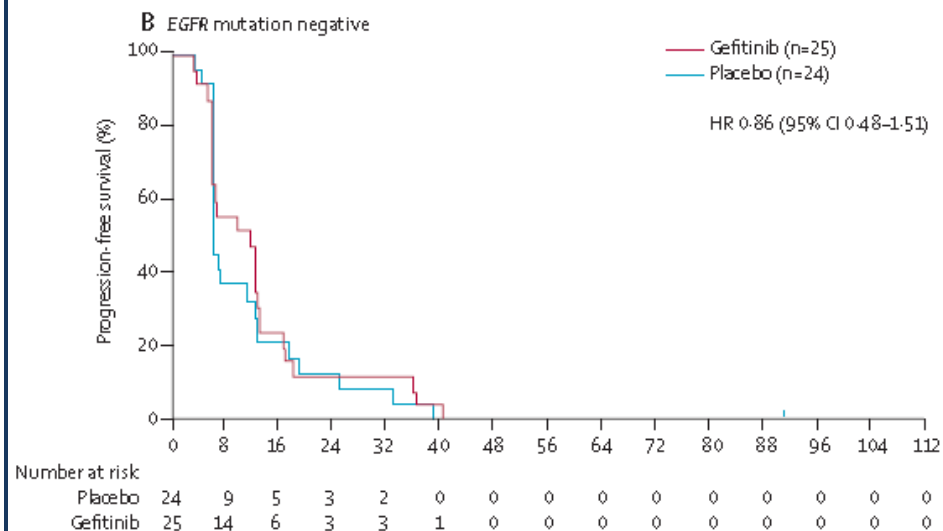
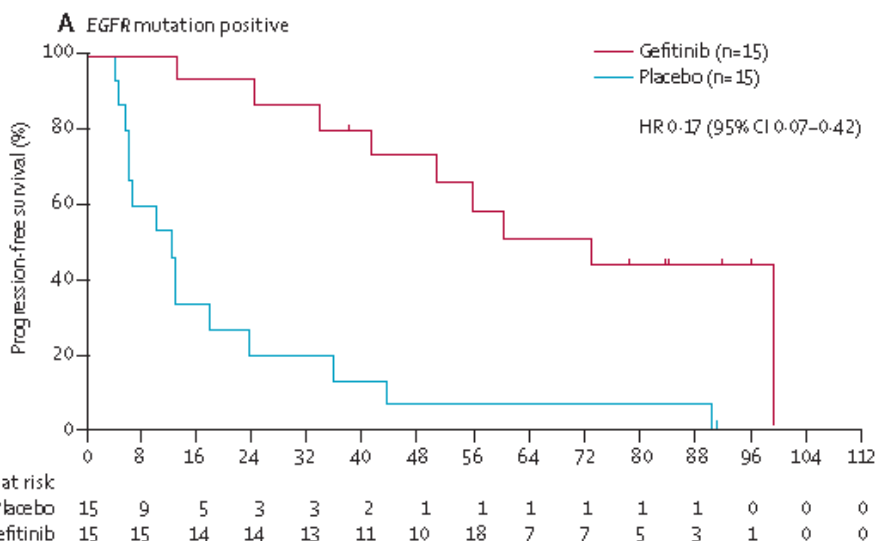
# Switch maintenance with gefitinib

## Symptom improvement



# Switch maintenance with gefitinib EGFR mutation

Maintenance treatment with gefitinib can significantly prolong the progression-free survival of patients from east Asia with advanced NSCLC who have achieved disease control after first-line chemotherapy



**Who will benefit from maintenance  
therapy?**

# Who will benefit from maintenance therapy?

- Response to 1<sup>st</sup> line therapy
  - Switch vs Continuation  
(JMEN, SATURN vs PARAMOUNT)

# Who will benefit from maintenance therapy?

- Performance status **KPS > 80**
  - **CECOG (2006)** ; Cisplatin and gemcitabine first-line chemotherapy followed by maintenance gemcitabine or best supportive care in advanced non-small cell lung cancer: a phase III trial

Table 3 Median survival (months) by KPS

	GEM arm	BSC arm	Hazard ratio (95% CI)
Throughout the study <sup>a</sup>			
Overall survival			
KPS > 80 (n = 99)	25.3	12.2	2.1 (1.2–3.8)
KPS ≤ 80 (n = 107)	10.0	10.8	0.8 (0.5–1.3)
Maintenance period <sup>b</sup>			
Overall survival			
KPS > 80 (n = 99)	22.9	8.3	2.1 (1.2–3.8)
KPS ≤ 80 (n = 107)	7.0	7.7	0.8 (0.5–1.3)

<sup>a</sup> The time interval between the date of first treatment administration and death due to any cause.

<sup>b</sup> The time interval between the date of randomization with maintenance therapy and death due to any cause.

# Who will benefit from maintenance therapy?

- Likelihood of therapy at progression

US

Markers of socioeconomic status, symptom burden, and response to and tolerance of 1<sup>st</sup> line chemotherapy were associated with receipt of 2<sup>nd</sup> line chemotherapy.

Korea

Maintenance therapy may be of greater benefit to patients with NSCLC who have clinical characteristics including poor performance status after 1<sup>st</sup> line therapy, large initial target lesions, or smaller decrease in target lesions after first-line therapy.

JTO. 2011

Sun et al. JTO. 2010

# Who will benefit from maintenance therapy?

- **Histology** (adenocarcinoma, non-squamous histology)
  - Erlotinib
  - Pemetrexed
  - Cytotoxic agent
  - Cetuximab
  - Bevacizumab

# Who will benefit from maintenance therapy?

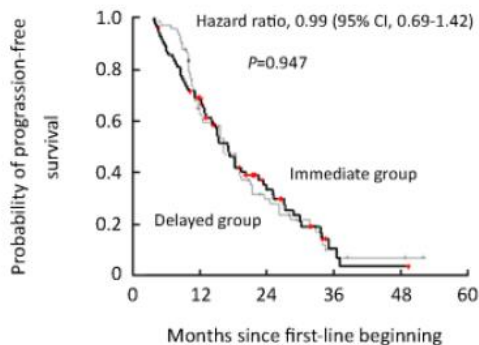
- **Molecular characteristics : EGFR mutation positive**

**PFS**

- **SATURN (erlotinib)**
- IFCT-GFPC 0502 (gefitinib)
- WJTOG0203
- **INFORM**

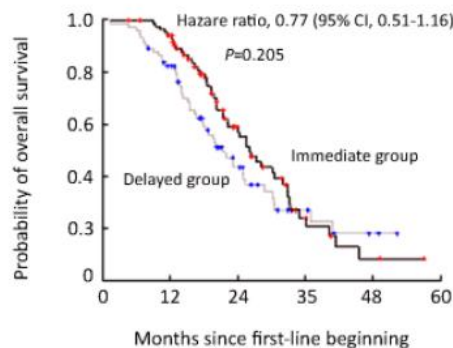
# Who will benefit from maintenance therapy?

**A Overall PFS**



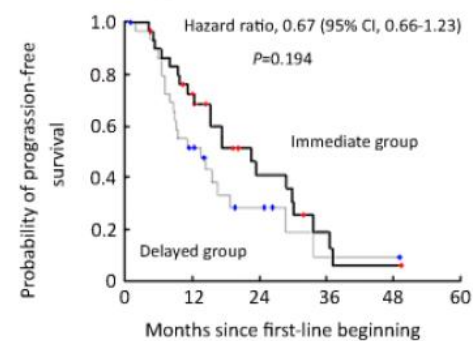
No. at risk	0	12	24	36	48	60
Immediate group	85	57	18	3	1	0
Delayed group	74	45	15	4	2	0

**B Overall OS**



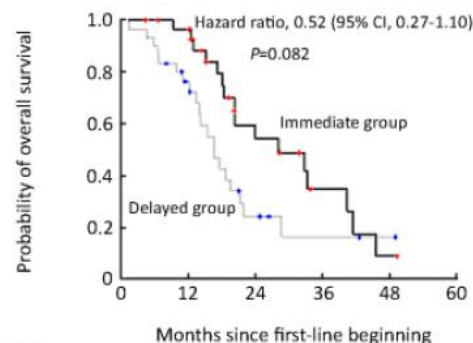
No. at risk	0	12	24	36	48	60
Immediate group	85	77	33	8	2	0
Delayed group	74	57	22	7	2	0

**C PFS for first-line 4 cycles**



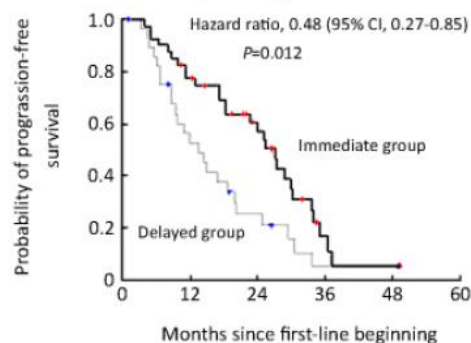
No. at risk	0	12	24	36	48	60
Immediate group	30	20	8	3	1	0
Delayed group	30	14	5	1	1	0

**D OS for first-line 4 cycles**



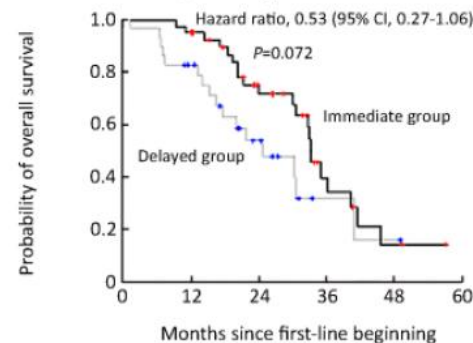
No. at risk	0	12	24	36	48	60
Immediate group	30	27	11	4	1	0
Delayed group	30	21	7	2	1	0

**E PFS for EGFR mutation-positive type**



No. at risk	0	12	24	36	48	60
Immediate group	40	30	17	3	1	0
Delayed group	29	14	6	1	1	0

**F OS for EGFR mutation-positive type**



No. at risk	0	12	24	36	48	60
Immediate group	40	38	22	7	2	0
Delayed group	29	22	10	2	1	0

**Clinical trials lacks...**

# Raised Concerns

- **Primary endpoint : PFS**
  - Subjective criteria
  - OS?

# Raised Concerns

- **Quality of life**
  - No clinical trial showing significant improvement in QOL with maintenance therapy
- **SATURN**
  - Time to pain
  - Time to analgesic use

# Raised Concerns

- JMEN **Hemoptysis, Pain**

	Pemetrexed (N=441)*		Placebo (N=222)†		HR (95% CI)	p value
	Censored	Median (months)	Censored	Median (months)		
Loss of appetite	236 (54%)	3.78 (2.86-4.44)	140 (63%)	4.40 (2.96-15.61)	1.12 (0.87-1.45)	0.374
Fatigue	237 (54%)	3.06 (2.63-5.29)	130 (59%)	3.09 (2.43-3.98)	0.98 (0.77-1.26)	0.886
Cough	274 (62%)	6.05 (4.21-7.82)	146 (66%)	4.67 (3.06-15.61)	0.90 (0.69-1.19)	0.470
Dyspnoea	271 (61%)	5.36 (4.21-10.87)	143 (64%)	4.40 (2.83-15.61)	0.93 (0.71-1.22)	0.596
Haemoptysis‡	404 (92%)	NE	198 (89%)	NE	0.58 (0.34-0.97)	0.038
Pain	271 (61%)	6.11 (4.57-9.56)	135 (61%)	4.63 (3.32-5.98)	0.76 (0.59-0.99)	0.041
Symptom distress	247 (56%)	4.21 (3.56-5.55)	141 (64%)	3.78 (2.99-18.53)	1.00 (0.77-1.29)	0.972
Interference with activity level	267 (61%)	6.51 (4.34-8.18)	141 (64%)	3.98 (2.83-15.61)	0.92 (0.70-1.19)	0.512
Overall quality of life	262 (59%)	5.75 (4.37-8.41)	137 (62%)	3.71 (2.99-5.49)	0.86 (0.66-1.12)	0.267

Data are n (%) or median (95% CI) unless otherwise specified. HR=hazard ratio. NE=not estimable. \*420-423 patients completed the Lung Cancer Symptom Scale (LCSS) questionnaire at baseline; 400-403 of these patients had post-baseline data. †209-211 patients completed the LCSS questionnaire at baseline; 195-197 of these patients had post-baseline data. ‡Median time to worsening for haemoptysis could not be calculated because of a high level of censoring.

**Table 3:** Time to worsening of symptoms

# Patient's perspective

# But, Patient attitudes

Patient Perception, Preference and Participation

Patient comprehension and attitudes toward maintenance chemotherapy for lung cancer

David E. Gerber<sup>a,d</sup>, Heidi A. Hamann<sup>b,c,d</sup>, Drew W. Rasco<sup>a,e</sup>, Sharon Woodruff<sup>d</sup>, Simon J. Craddock Lee<sup>b,d,\*</sup>

- Watchful waiting = doing nothing
- Maintenance chemotherapy = doing something

👉 Important consideration of maintenance therapy

✓ quality of life

✓ meaningful activities (e.g., socializing, cooking, cleaning)

**Awaiting results of ongoing trials**

# Ongoing trials

- **AVAPERL**
- **Point Break**
  - Carboplatin+paclitaxel+bevacizumab→ bevacizumab
  - Carboplatin+pemetrexed+bevacizumab→  
pemetrexed+bevacizumab

# Ongoing trials

Rank	Status	Study
1	Recruiting	<p><u><a href="#">Study of Nivolumab (BMS-936558) in Combination With Gemcitabine/Cisplatin, Pemetrexed/Cisplatin, Carboplatin/Paclitaxel, Bevacizumab Maintenance, Erlotinib, Ipilimumab or as Monotherapy in First-Line or in Switch Maintenance in Subjects With Stage IIIB/IV Non-small Cell Lung Cancer (NSCLC)</a></u></p> <p><b>Condition:</b> Non-small Cell Lung Cancer</p> <p><b>Interventions:</b> Biological: Nivolumab; Drug: Gemcitabine; Drug: Cisplatin; Drug: Pemetrexed; Drug: Paclitaxel; Drug: Carboplatin; Drug: Bevacizumab; Drug: Erlotinib; Biological: Ipilimumab</p>
2	Recruiting	<p><u><a href="#">A Study of First-line Maintenance Tarceva (Erlotinib) Versus Tarceva at Time of Disease Progression in Patients With Advanced Non-small Cell Lung Cancer After Chemotherapy</a></u></p> <p><b>Condition:</b> Non-Small Cell Lung Cancer</p> <p><b>Interventions:</b> Drug: erlotinib [Tarceva]; Drug: Placebo</p>
3	Recruiting	<p><u><a href="#">Maintenance Gemcitabine in the Chinese Advanced Lung Cancer</a></u></p> <p><b>Condition:</b> Non Small Cell Lung Cancer</p> <p><b>Interventions:</b> Drug: Gemcitabine; Drug: Best supportive care</p>
4	Recruiting	<p><u><a href="#">Maintenance Therapy With Autologous Cytokine-induced Killer Cells for Nonsquamous Non-small Cell Lung Cancer</a></u></p> <p><b>Condition:</b> Non-small Cell Lung Cancer</p> <p><b>Interventions:</b> Biological: Autologous cytokine-induced killer cell; Other: Pemetrexed</p>
5	Recruiting	<p><u><a href="#">Genius Study Study to Compare Efficacy and Safety of Gefitinib/ Pemetrexed With Pemetrexed Alone as Maintenance Therapy in Patients With Stage IV EGFR Mutation Negative or T790M Single Mutation Who Respond to Pemetrexed/ Platinum as First-line Therapy</a></u></p> <p><b>Condition:</b> NSCLC</p> <p><b>Interventions:</b> Drug: Pemetrexed 500mg/m2 iv; Drug: Pemetrexed 500mg/m2 iv and Gefitinib 250 mg</p>

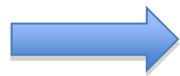
# Conclusions

# In Non-squamous NSCLC

ADENOCARCINOMA, LARGE CELL, NSCLC NOS: EGFR MUTATION OR ALK POSITIVE

FIRST-LINE THERAPY<sup>bb</sup>

● EGFR mutation +



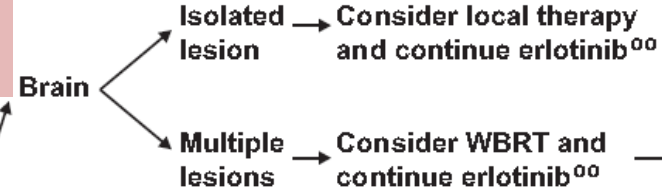
EGFR-TKI

EGFR mutation discovered prior to first-line therapy

Erlotinib<sup>mm,nn,oo</sup> (category 1)

Progression<sup>qq,rr</sup>

Symptomatic



● EGFR mutation + but, unknown



Platinum doublet followed by maintenance with erlotinib

EGFR mutation discovered during first-line chemotherapy

Switch maintenance: erlotinib<sup>oo</sup> or May add erlotinib<sup>oo,pp</sup> to current chemotherapy

Progression<sup>qq,rr</sup>

Asymptomatic

lesions therapy<sup>oo</sup> ± erlotinib<sup>oo</sup>

Continue erlotinib<sup>oo</sup>

ALK positive

Crizotinib<sup>cc</sup>

Progression

[See Second-line Therapy \(NSCL-19\)](#)

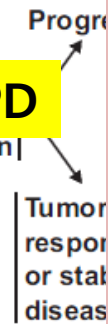
# In Non-squamous NSCLC

ADENOCARCINOMA, LARGE CELL, NSCLC NOS: EGFR MUTATION  
FIRST-LINE THERAPY      RESPONSE EVALUATION

## 1<sup>st</sup> line CTx

- Platinum doublet \*
- Cisplatin/pemetrexed\*
- Bevacizumab/platinum doublet
- Cetuximab/vinorelbine/cisplatin

**Non-PD**



- Continuation maintenance  
bevacizumab\*, cetuximab\*, pemetrexed, gemcitabine
- Switch maintenance  
Pemetrexed, erlotinib
- Close observation

Switch maintenance  
pemetrexed or erlotinib  
or  
Close observation

<sup>bb</sup> See [Systemic Therapy for Advanced or Metastatic Disease \(NSCLC-F\)](#).  
<sup>ff</sup> Bevacizumab should be given until progression.

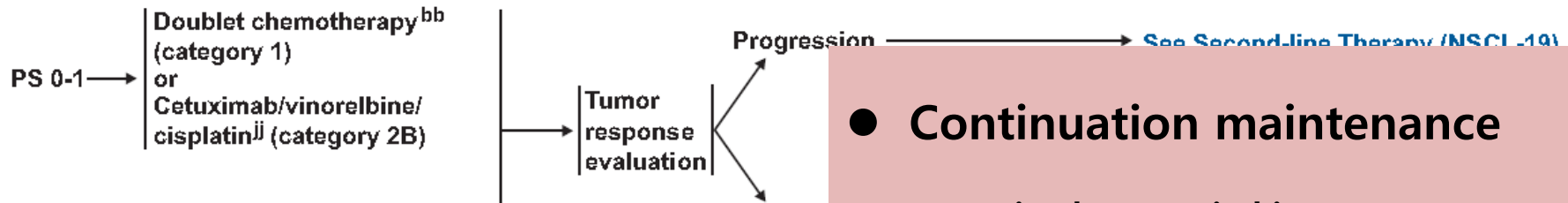
# In squamous NSCLC

## SQUAMOUS CELL CARCINOMA

### FIRST-LINE THERAPY

### RESPONSE EVALUATION

### MAINTENANCE THERAPY



### 1<sup>st</sup> line CTx

Platinum doublet \*

Cetuximab/vinorelbine/cisplatin

Non-PD

- Continuation maintenance

cetuximab\*, gemcitabine

- Switch maintenance

Erlotinib, docetaxel

- Close observation

docetaxel (category 2B) or Close observation

**Thank you**