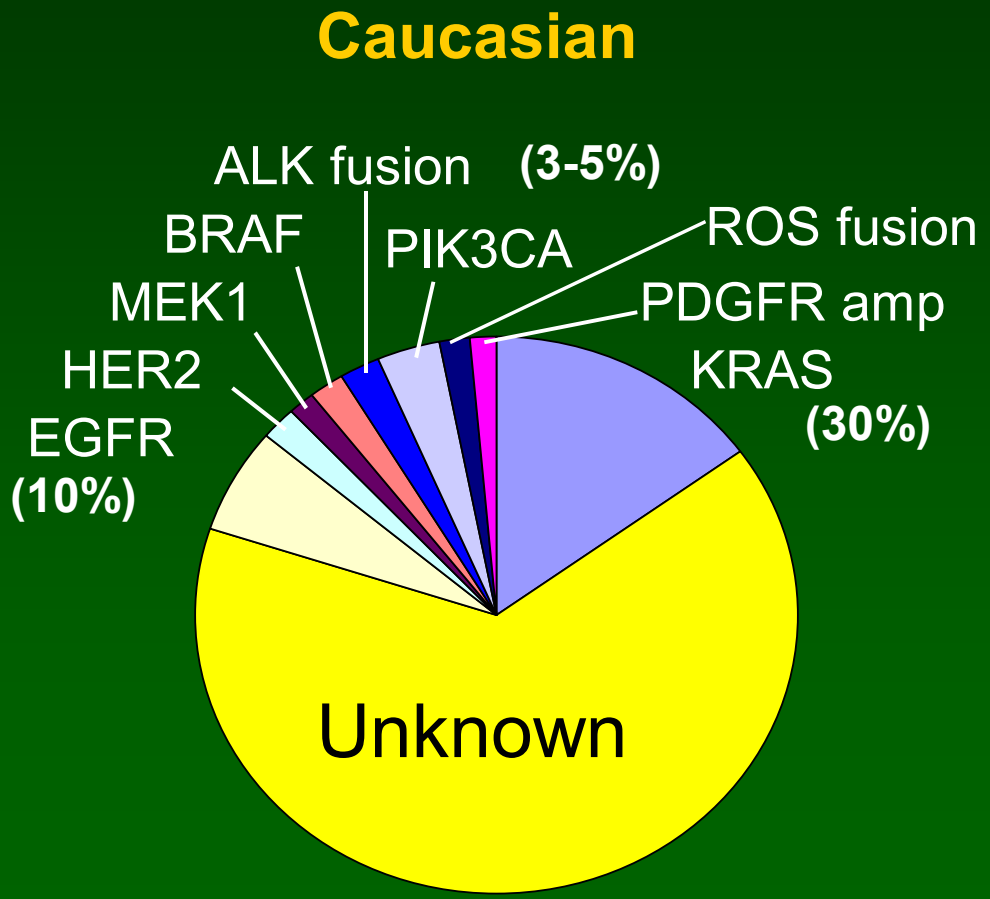
EGFR mutation rates (10-40%) in each group

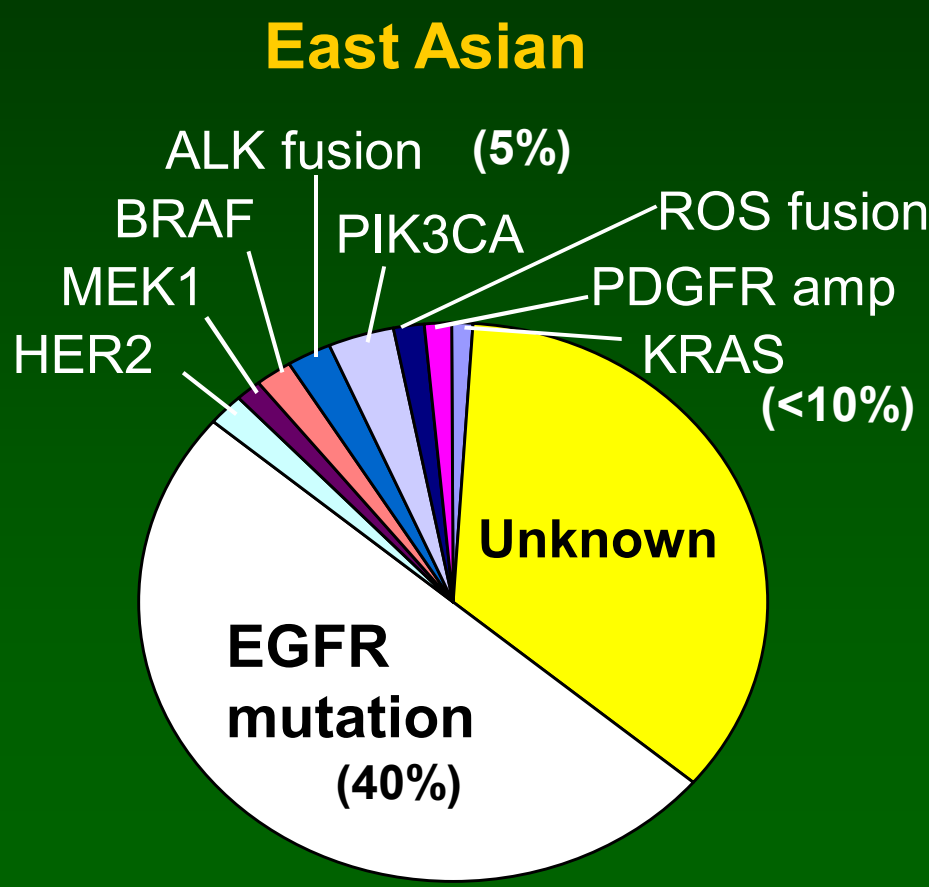
Study	Centre	No. of patients	AdenoCa (+BAC) (%)	M (%)	F (%)	Smokers (%)	n-smokers (%)
Taiwan[1]	NTUH	62	49	25	61	29	56
Taiwan[2]	VGH-T	37	67.4	52	72	44	69
Korea[3]	Seoul NU	90	21	9	33	13	26
Japan[4]	NCC Tokyo	66	61	53	69	35	68
Japan[5]	Aichi CCH	59	64	44	70	42	71
HK[6]	Chinese U	72	32	—	—	—	—
China[7]	Pek UMCH	76	48.6	32.3	34.8	—	—
Italy[8*]	U Chieti	375	10	6	30	7	25

1. Shih et al, IJC 2005
2. Chou et al, CCR 2005
3. Han et al, JCO 2005
4. Takano et al, JCO 2005
5. Mitsudomi et al, JCO 2005
6. Lung et al, PAACR 2005
7. Mu et al, CCR 2005
8. Machetti et al, JCO 2005

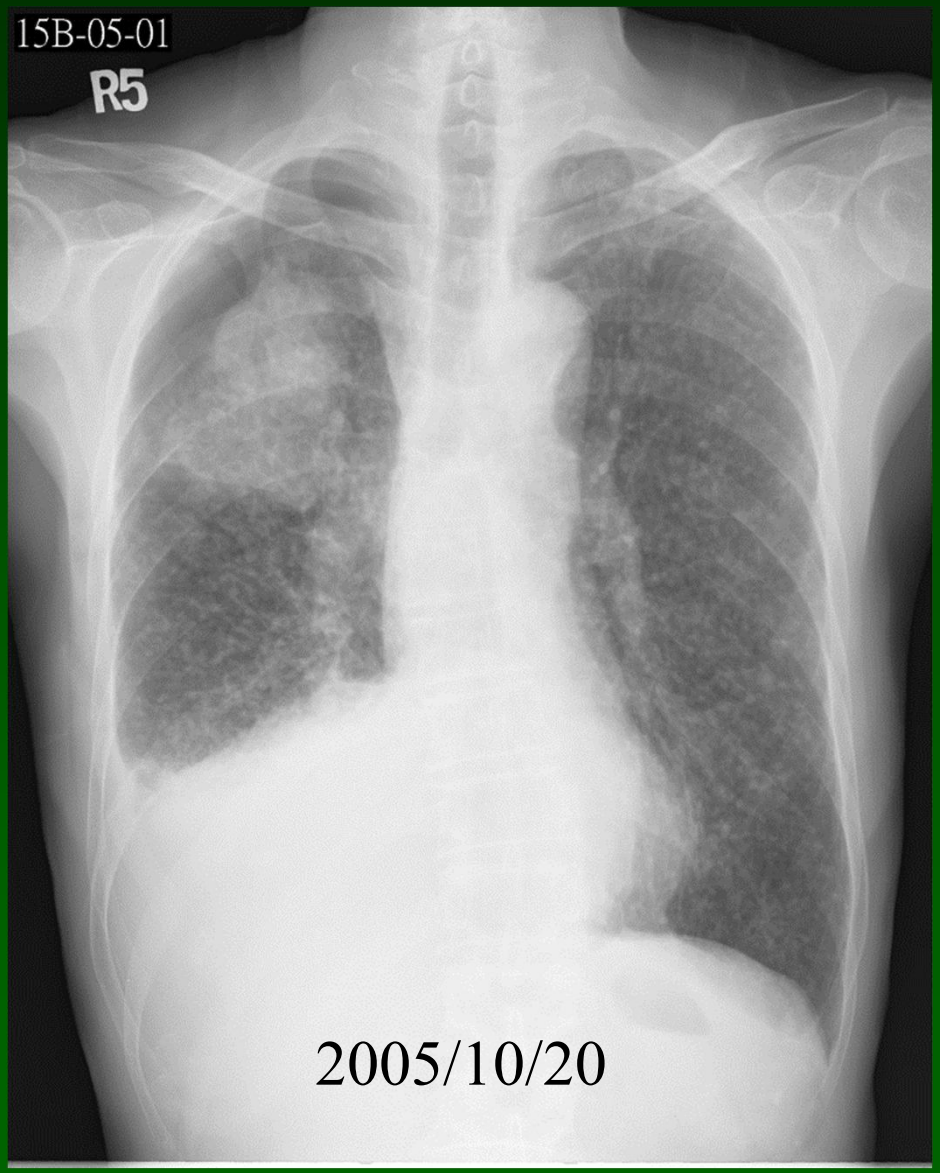
*only AdenoCa

Lung Adenocarcinoma
Different in east from west

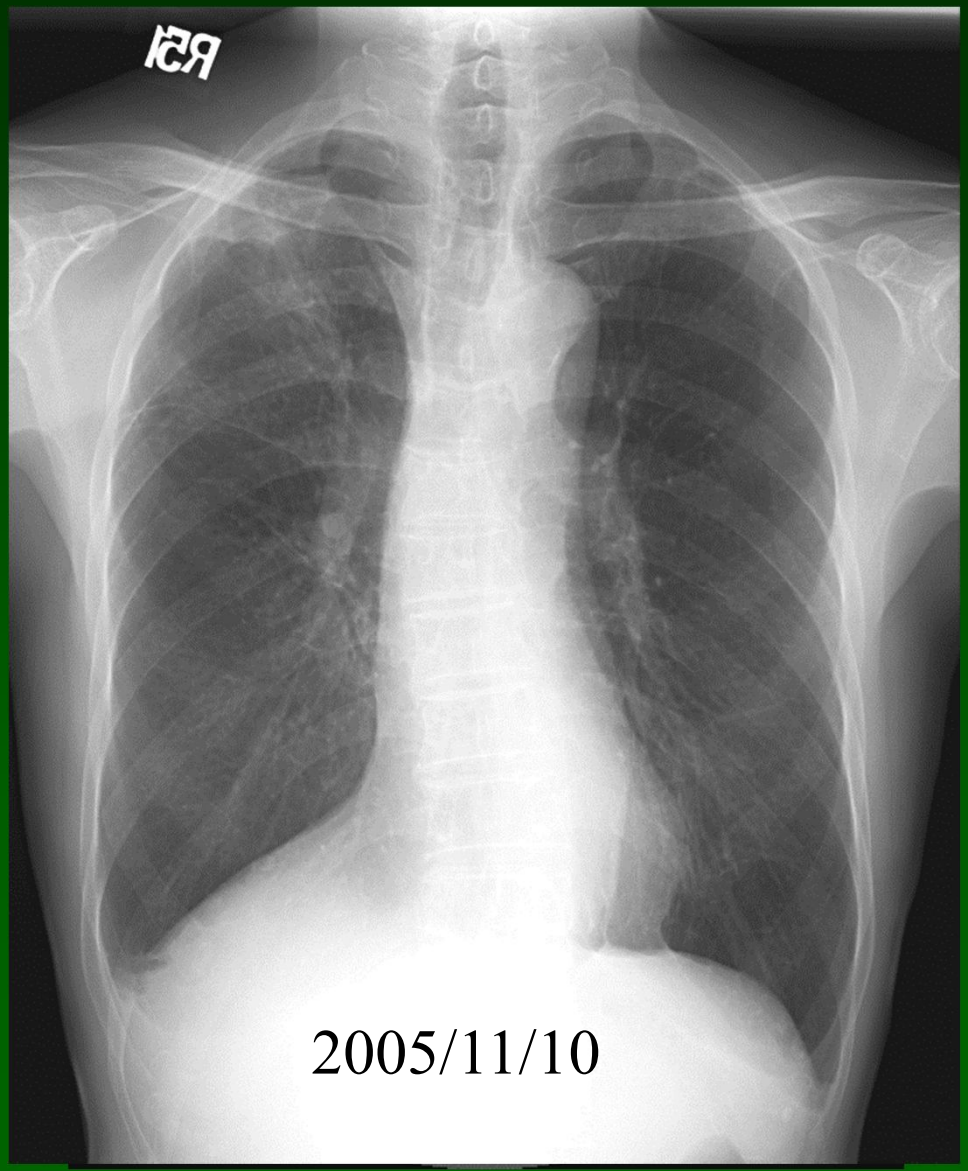




EGFR TKI 艾瑞莎 for NSCLC



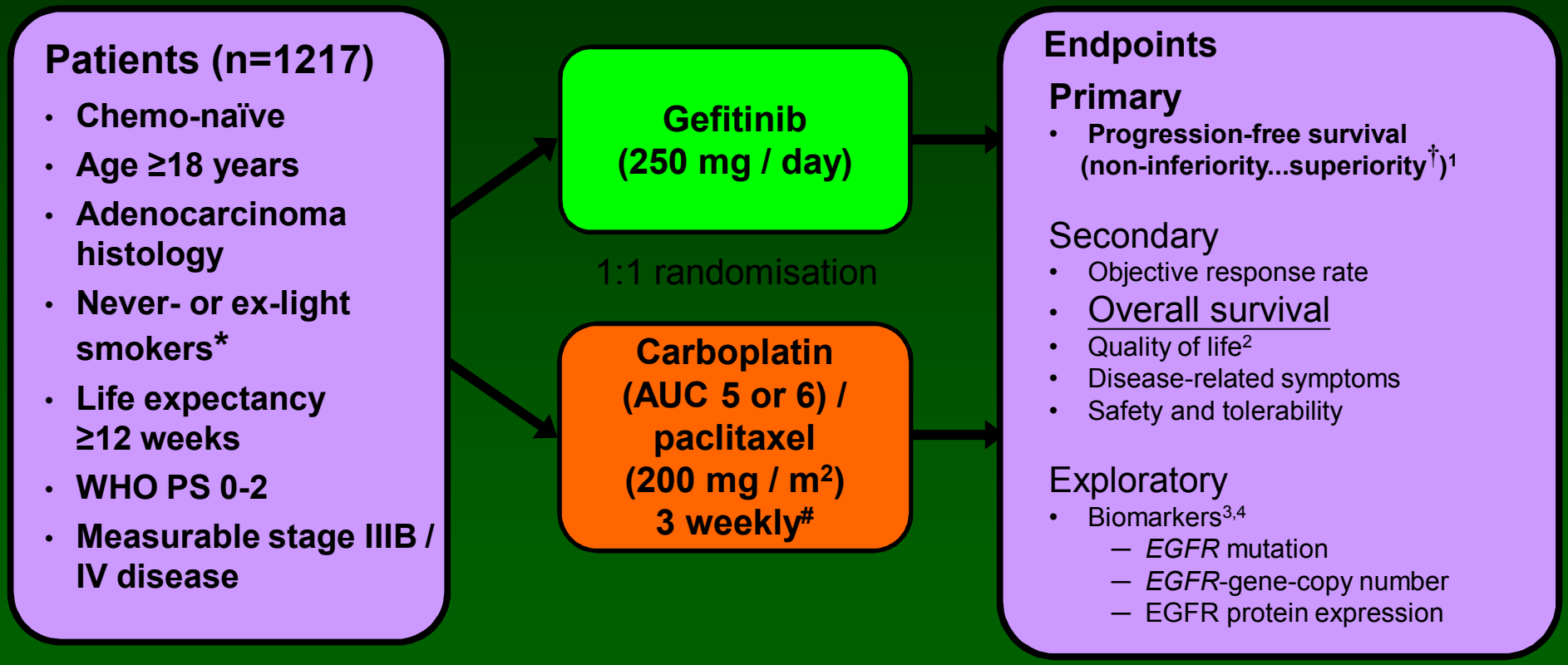
2005/10/20



2005/11/10

IPASS: study design

Conducted in China, Japan, Thailand, Taiwan, Indonesia, Malaysia, Philippines, Hong Kong and Singapore

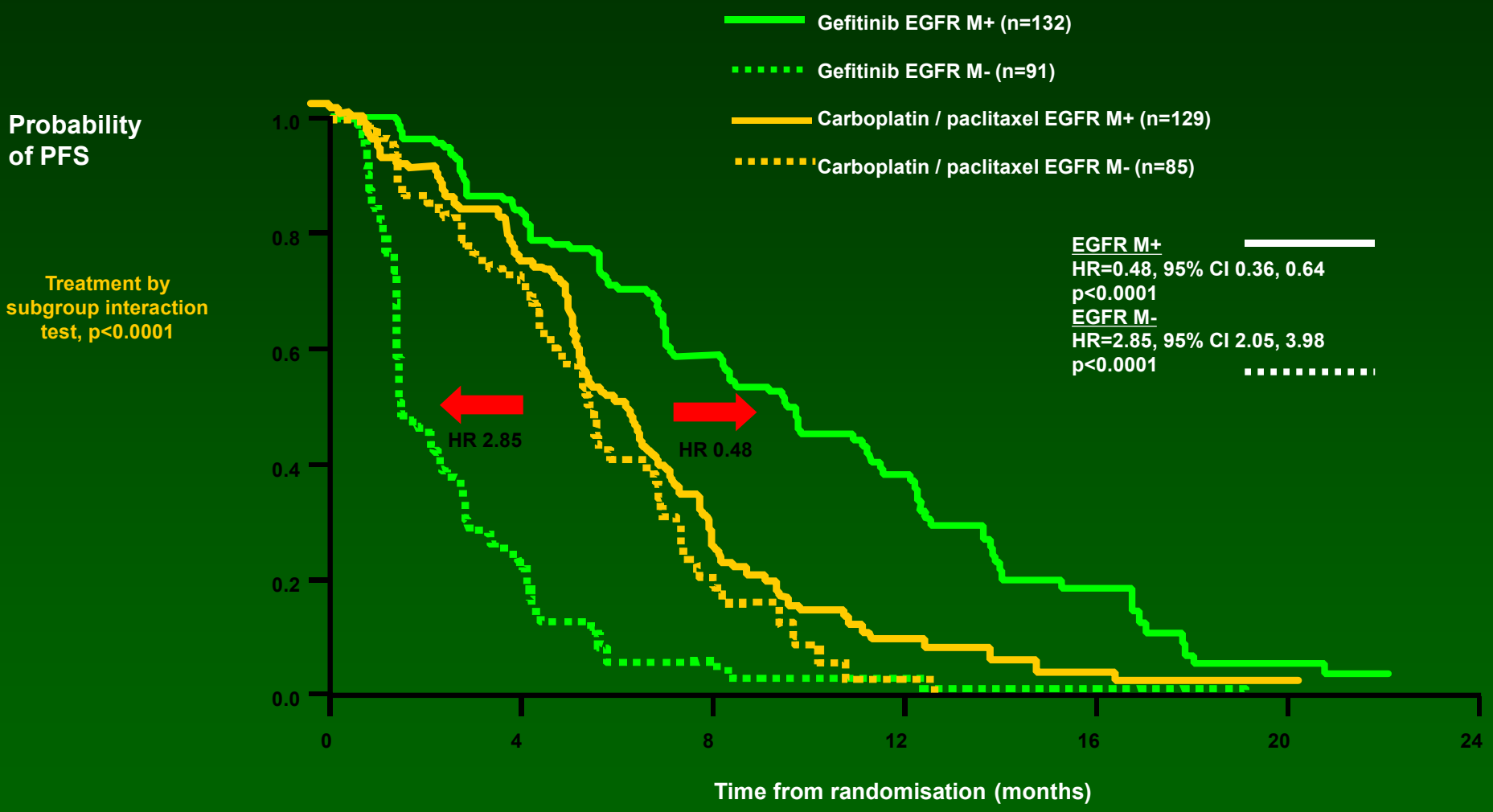


*Never-smokers, <100 cigarettes in lifetime; ex-light smokers, stopped ≥15 years ago and smoked ≤10 pack-years; #limited to a maximum of 6 cycles; †If the primary objective of non-inferiority was reached, then superiority could be assessed
Carboplatin / paclitaxel was offered to gefitinib patients upon progression

Presented at: [1]ESMO 2008, [2]ELCC 2010; [3]ASCO 2009, [4]WCLC 2009

Yang CH et al. presented at ESMO Ann Oncol 21(s8) viii1;2010

IPASS: Comparison of PFS by mutation status within treatment arms

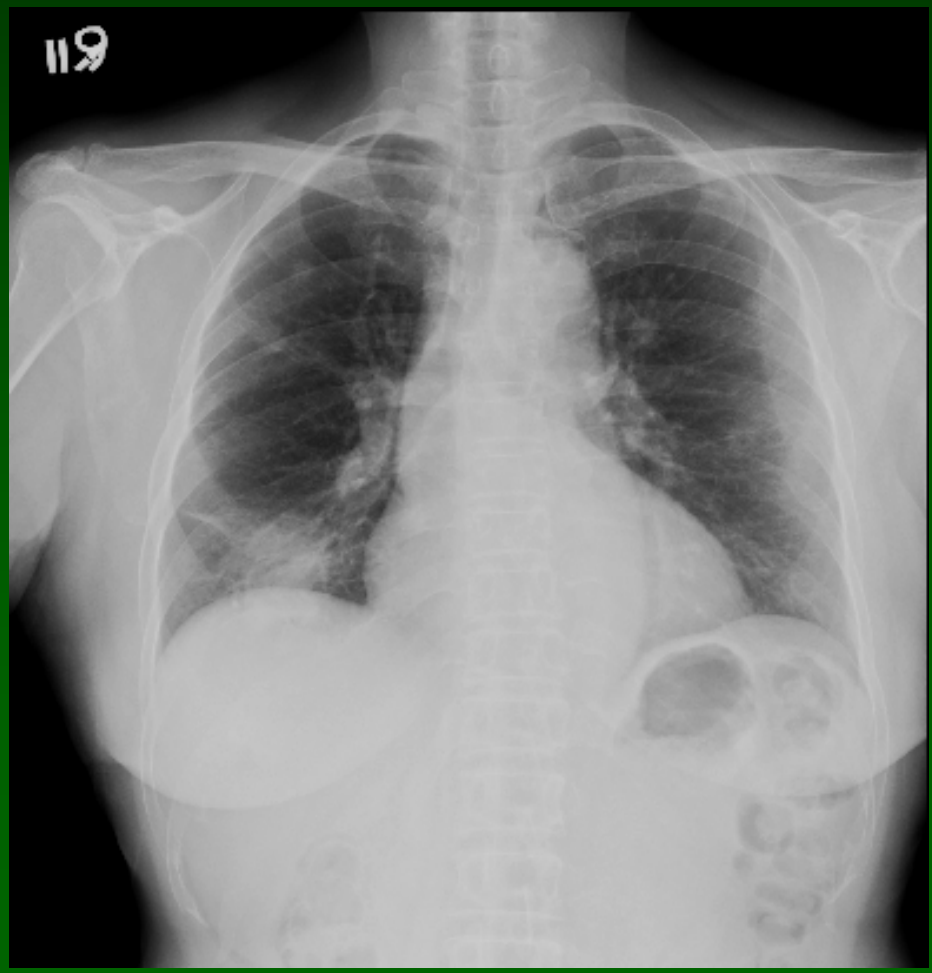


Treatment by subgroup interaction test, p<0.0001

M+, mutation positive; M-, mutation negative

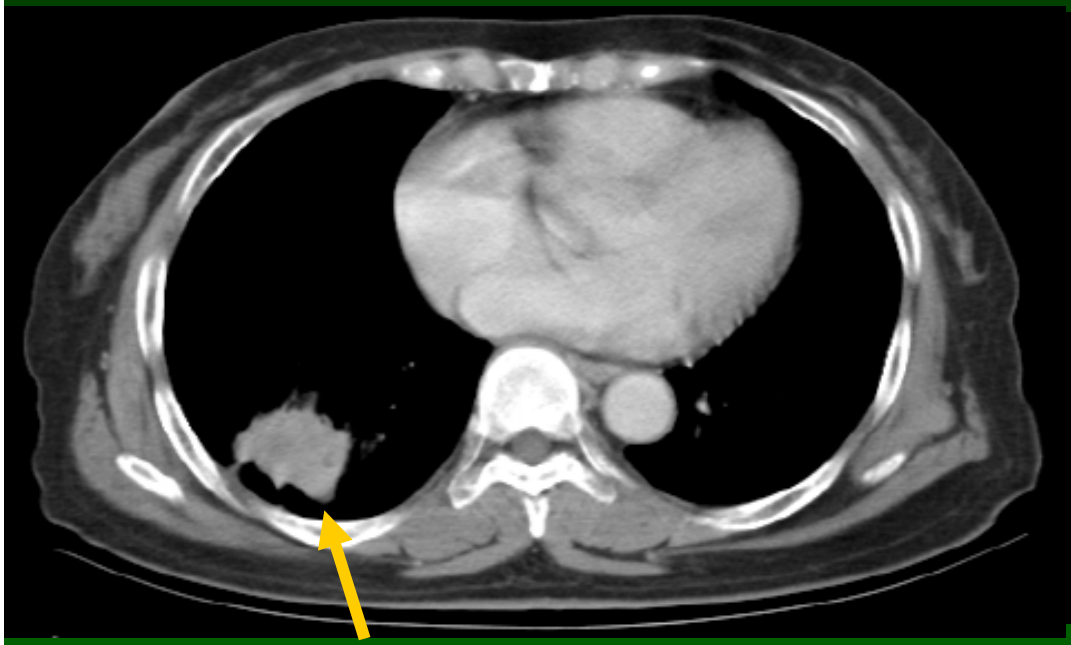
Case experience

- 68 y/o woman, non-smoker, 過去職業為家庭主婦,2008/1因為咳嗽求診
- 無過去病史
- PS: 1

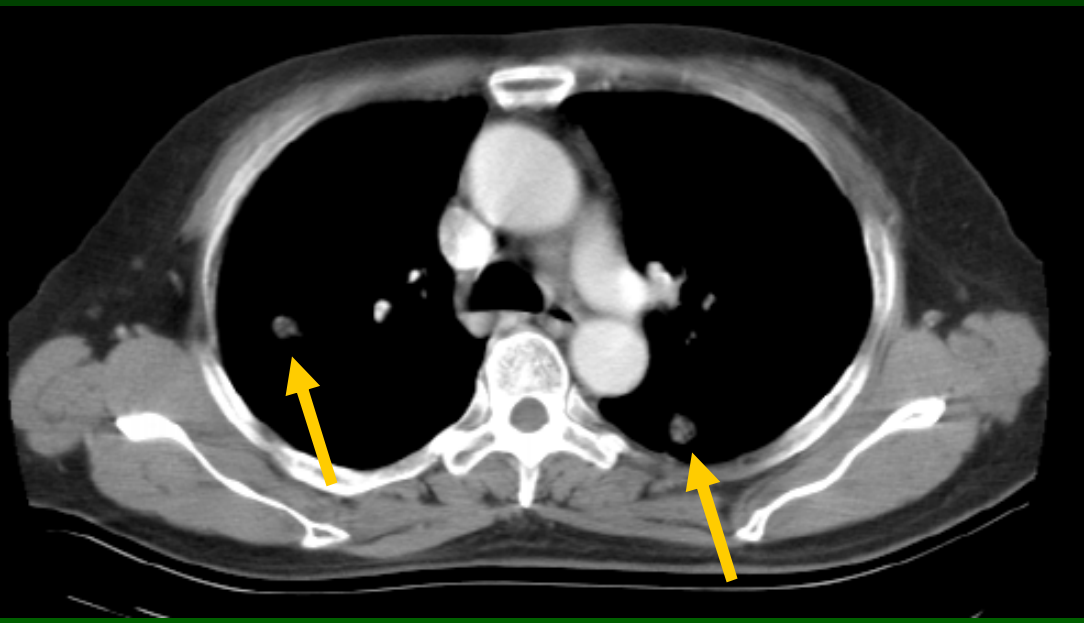


Case experience

- 切片檢查(97/01/25)為adenocarcinoma,分期為T4N2M1

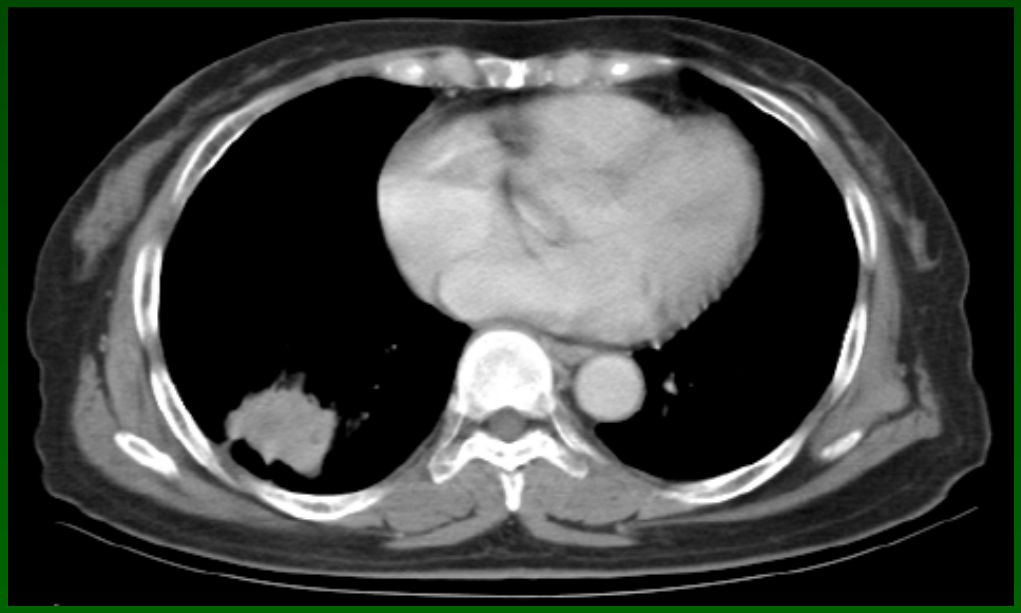


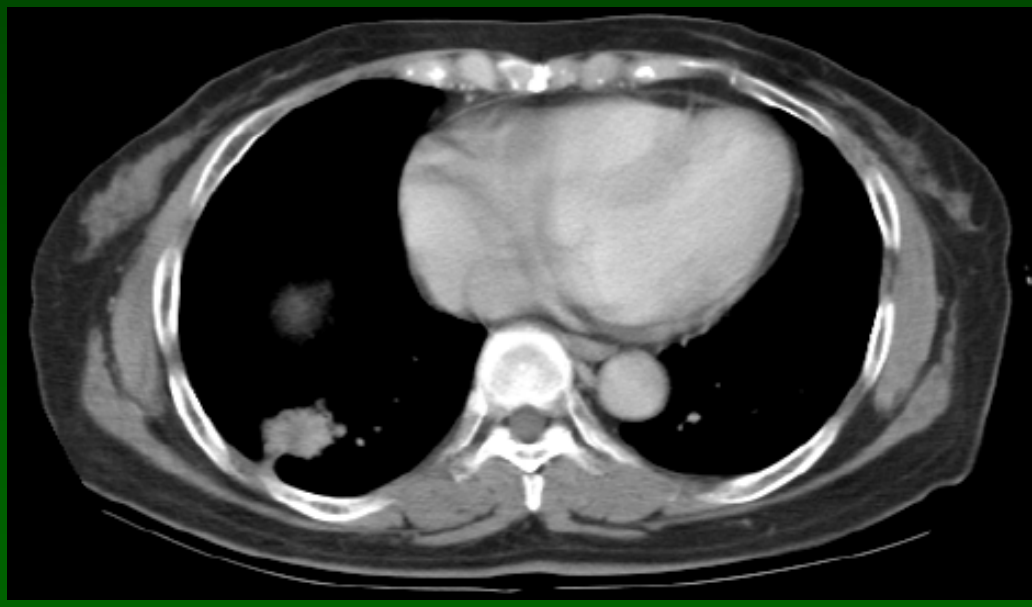
Primary tumor在右下肺葉



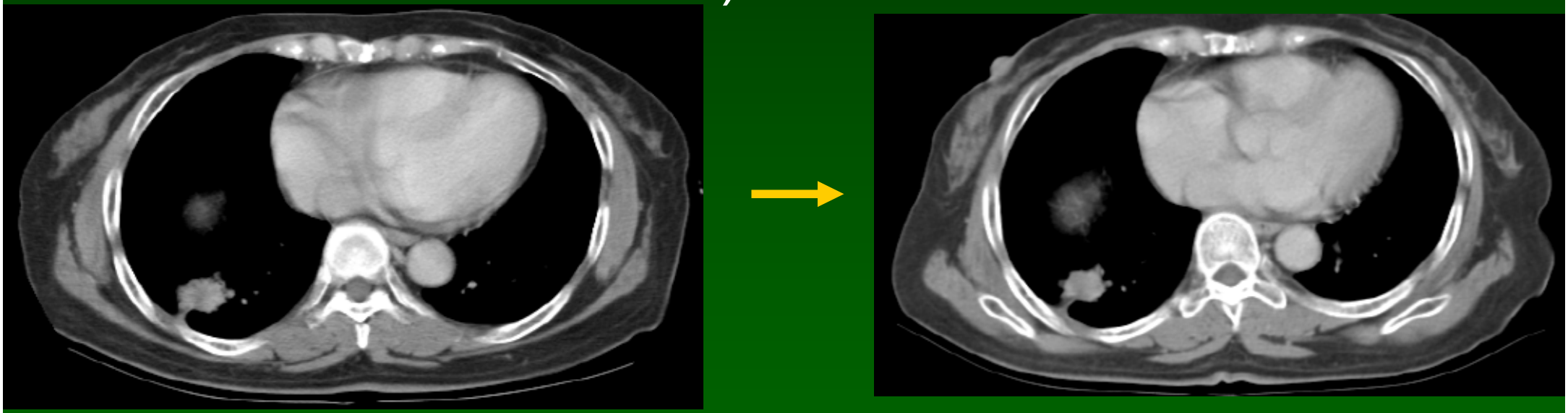
合併多處肺葉轉移

- 診斷後開始化療
- Taxotere + Cisplatin (70mg/m^2) for 6 cycles (97-01-29 to 97-05-13)
- Partial remission



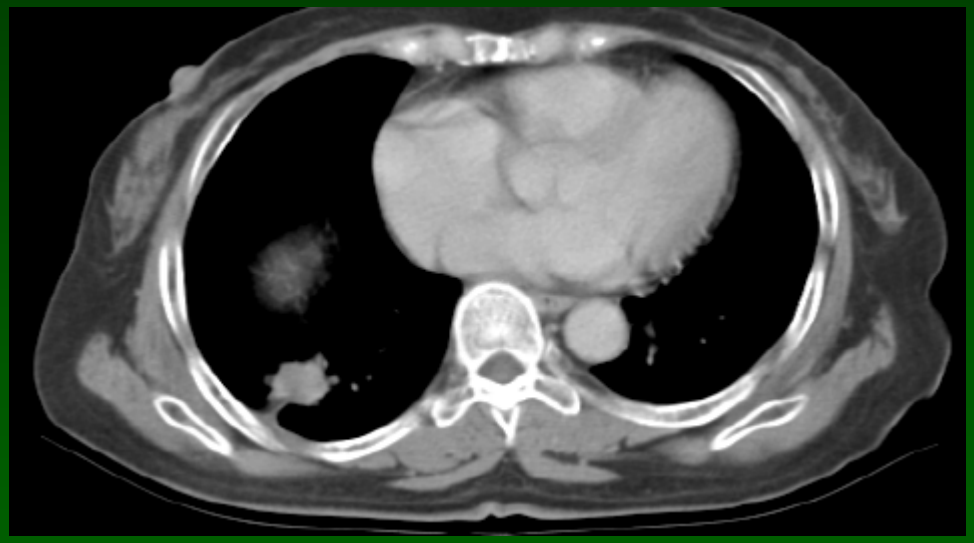


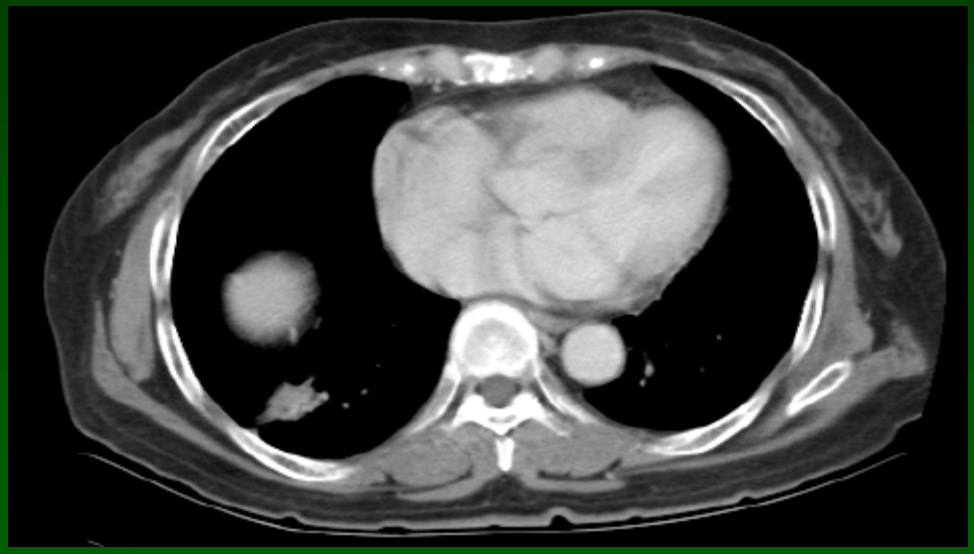
- 第一線化療完後, close observation
- 97/08/13 disease progression with bone pain, new rib metastasis), CEA逐漸上升 (PFS-1st line C/T: 6.5 months)



Start Gefitinib since 97-08-27

- 97-08-27Gefitinib: partial remission, bone pain 消失,CEA 下降

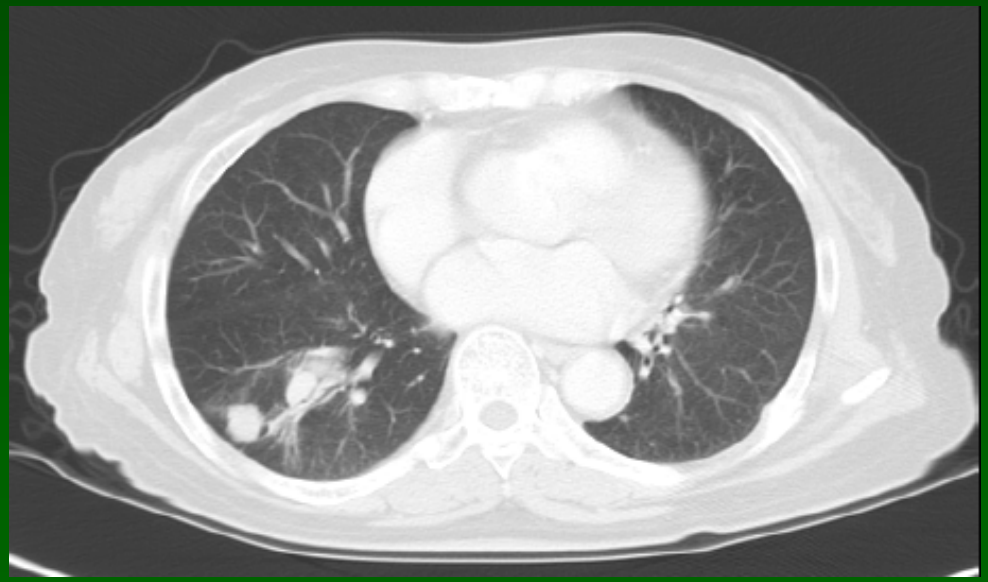




日期	1/23	5/28	9/3	12/16
CEA	40.5	6.8	13.1	4.9

The remission duration up to….?

- 15 times (q3m) NHI application
- PFS-2nd line gefitinib: 43.3 months
- PFS-1st line C/T: 6.5 months



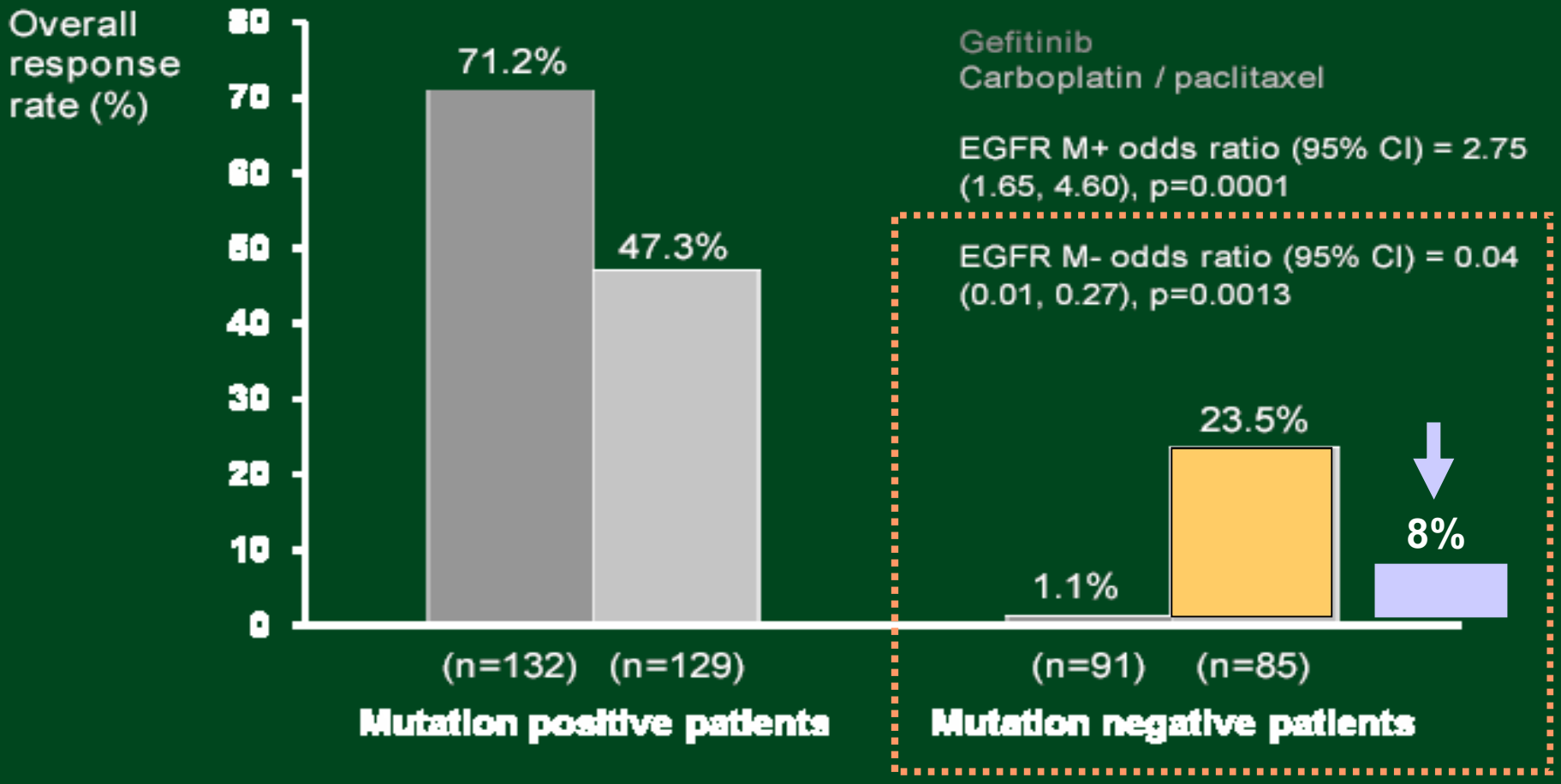
101/04/05

Prospective Studies of Patients with EGFR Mutations Treated with EGFR TKIs

Trial	No. of Pts	EGFR Mutations	Agent	RR(%)	TTP (mo)
Paz-Ares et al	1047	127	Erlotinib	82	13.3
Miller et al	81	18	Erlotinib	83	13
Inoue et al	99	16	Gefitinib	75	9.7
Sutani et al	100	38	Gefitinib	78	9.4
Asahina et al	82	16	Gefitinib	75	8.9
ONCOBELL	37	24	Gefitinib	62	3.8
Sunaga et al	33	21	Gefitinib	76	12.9
IPASS	1217	132	Gefitinib	71	9.8
WJTOG0403	118	32	Gefitinib	75	11.5

West et al JTO 2009, Sep, S1029-1039

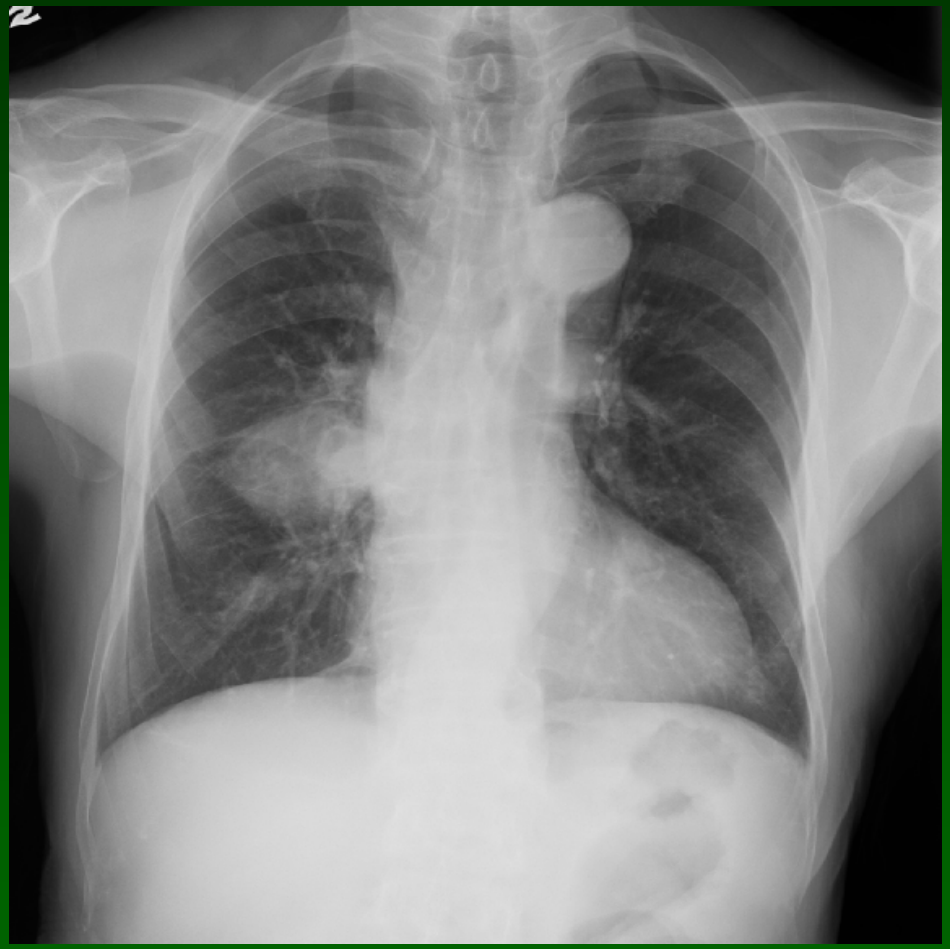
Objective response rate in EGFR mutation positive and negative patients



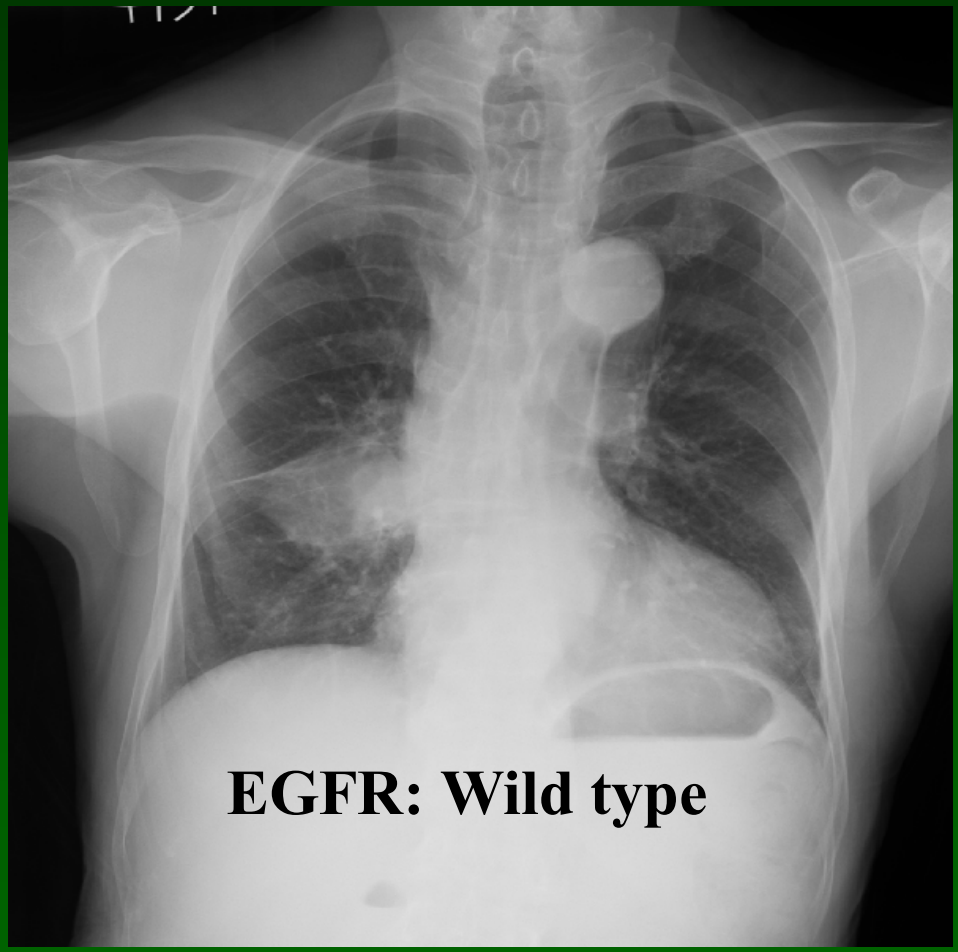
Odds ratio >1 implies greater chance of response on gefitinib

Case experience

76 y/o male smoker with RLL adenocarcinoma receive gefitinib (100/11/29-100/12/13)

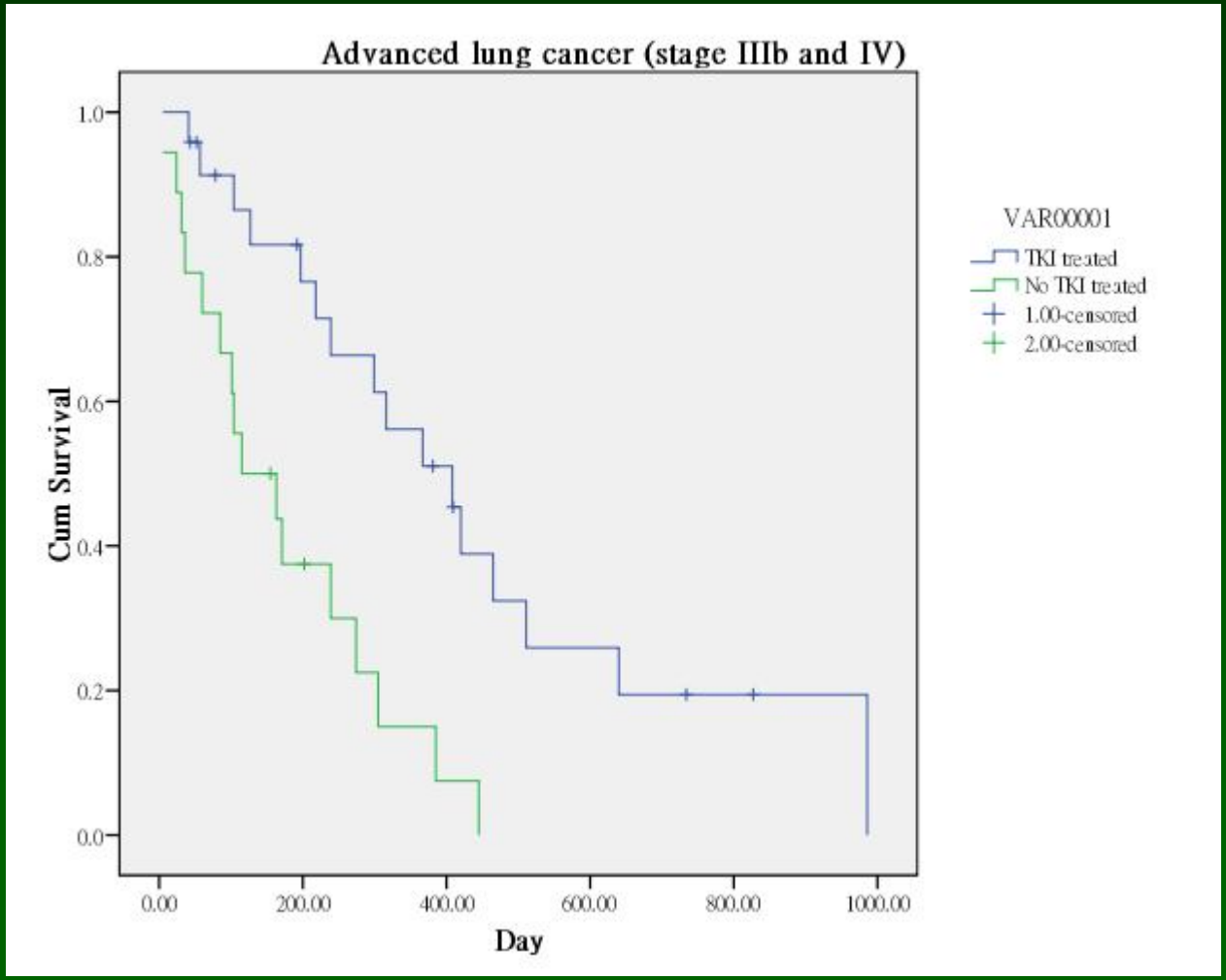


Pre-treatment



2-week treatment

Impact of EGFR-TKI on survival in NYMUH



P=0.001

Predictive markers of response

- Female, never smoker, adenocarcinoma, Asian ethnic
- Presence of cutaneous adverse toxicity
- Performance status
- Molecular markers
  - EGFR expression level (unlikely)
  - EGFR mutation (susceptible- exon 19, 21)
    (resistance- exon 20)

Potential of EGFR-targeted therapy in special patient groups with NSCLC

- In addition to those patients who have failed prior chemotherapy, certain other patient groups with NSCLC may benefit from therapy, including
  - patients with poor PS (>2)
  - elderly patients (aged >70 years)
  - patients with brain metastases

Argiris 2003; Pino et al 2003; Soto Parra 2003

Tolerability of second-line therapies: haematological toxicities

Adverse event (grade 3/4)	Patients (%)		
	EGFR-TKI (Tarceva)	Docetaxel (75mg/m^2)	Pemetrexed (500mg/m^2)
Neutropenia	<1	40.2	5.3
Febrile neutropenia	<1	12.7	1.9
Anaemia	<1	4.3	4.2
Thrombocytopenia	<1	0.4	1.9

Shepherd F, et al. N Engl J Med 2005;353:123–32
Hanna N, et al. J Clin Oncol 2004;22:1589–97

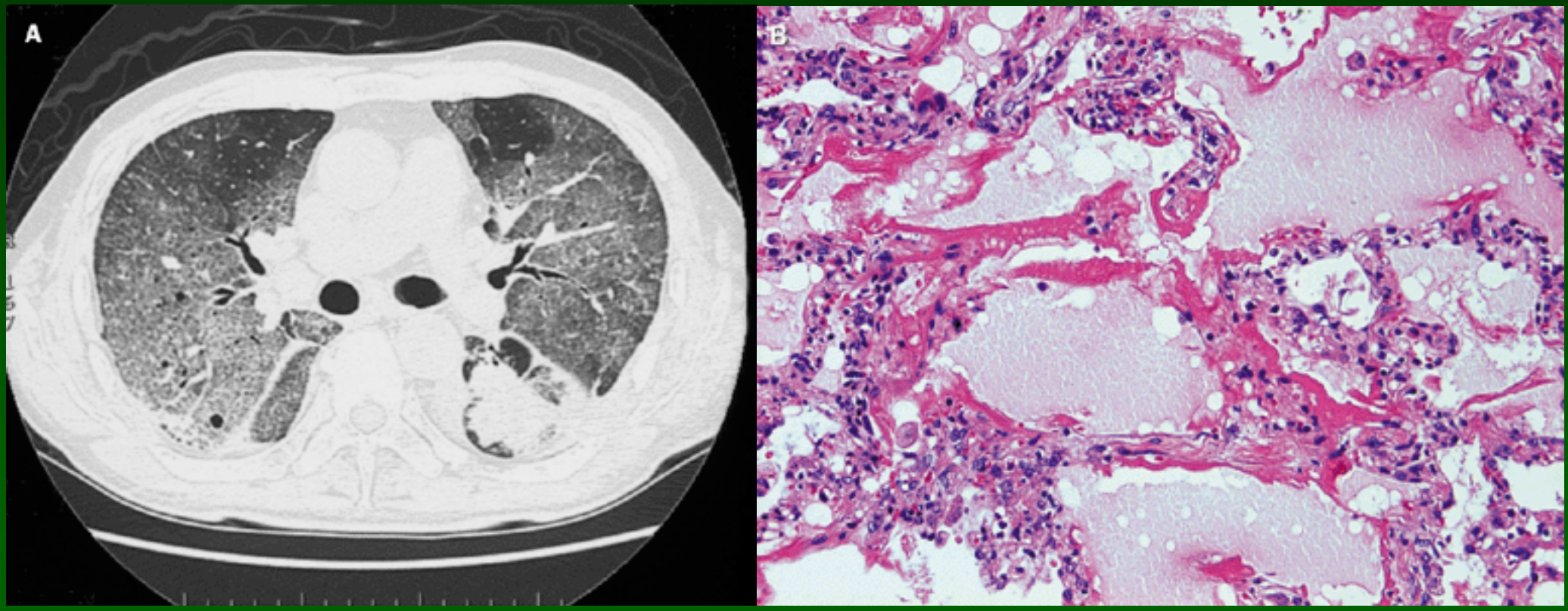
Conventional chemotherapy plus TKI

Regimen	Survival advantage
Gem+Cisplatin+Iressa	No
Taxol+Carboplatin+Iressa	No
Taxol+Carboplatin+Tarceva	No
Gem+Cisplatin+Tarceva	No

TKI: Monotherapy was preferred

J Clin Oncol. 2004; 22:785-94
J Clin Oncol. 2004; 22:777-84
J Clin Oncol. 2005; 23:5892-9
J Clin Oncol. 2007; 25:1545-52

艾瑞莎 - 急性間質性肺炎

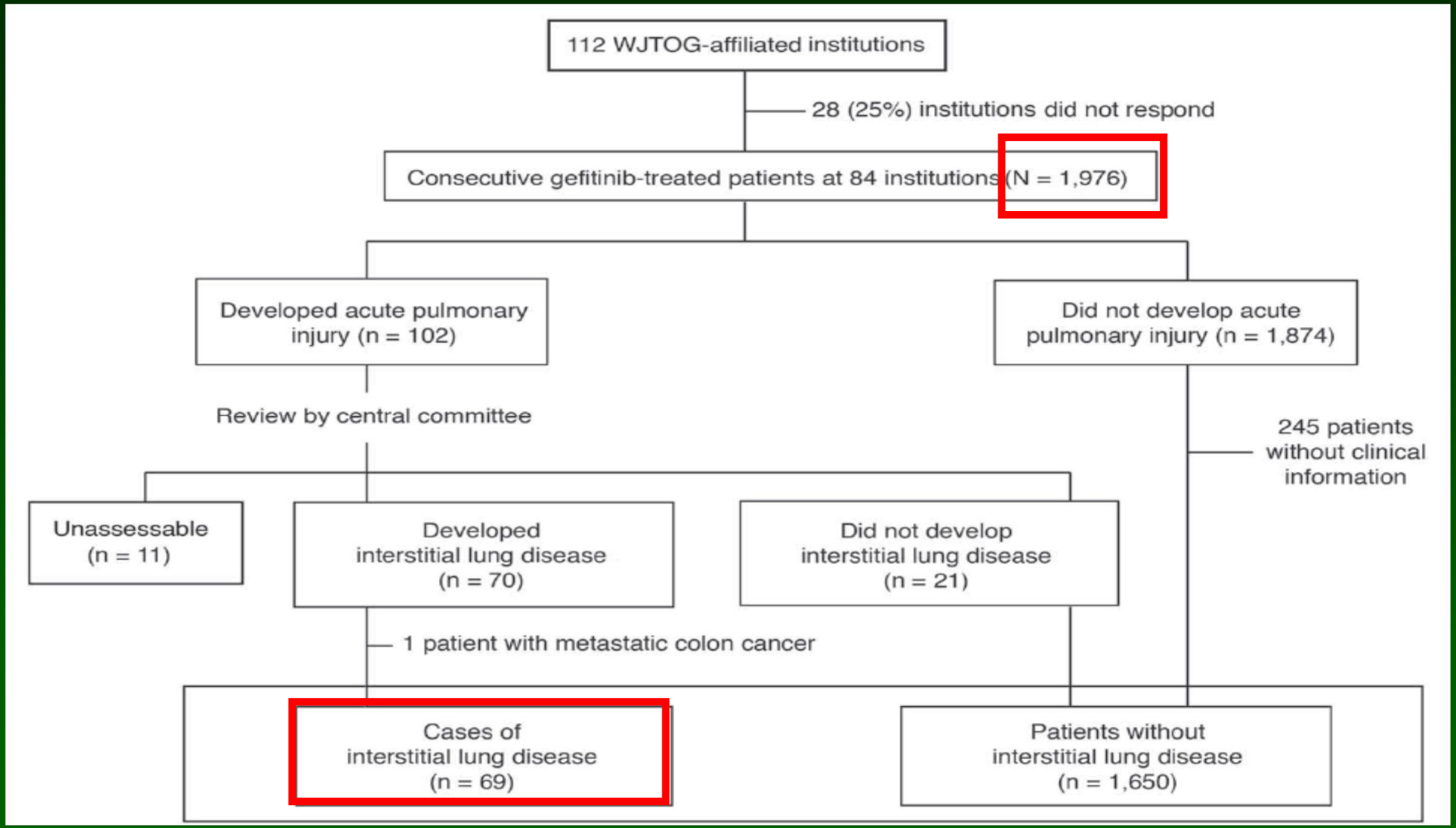


艾瑞莎或得舒緩在有肺部慢性疾病者使用可能發生急性間質性肺炎，可能導致死亡

Predictive Factors for Interstitial Lung Disease, Antitumor Response, and Survival in Non–Small-Cell Lung Cancer Patients Treated With Gefitinib

Masahiko Ando, Isamu Okamoto, Nobuyuki Yamamoto, Koji Takeda, Kenji Tamura, Takashi Seto, Yutaka Ariyoshi, and Masahiro Fukuoka

JCO 2006;24:2549-56 A cohort study in Japan (N=1976)



69/1976=3.5% incidence