Incidence

Table 2 Incidence of ILD in gefitinib-treated patients (Forsythe and Faulkner, 2003b)

Gefitinib-treated patients	Incidence of ILD (death), %
Globally ($n = \sim 92\,750$)	0.99 (0.36)
Japan marketed use ($n = \sim 39\,600$)	1.86 (0.69)
Outside Japan ($n = \sim 53\,150$)	0.34 (0.11)
US EAP ($n = \sim 24\,200$)	0.39 (0.08)
Rest of world EAP ($n = \sim 15\,000$)	0.38 (0.21)

EAP = expanded access programme; ILD = interstitial lung disease.

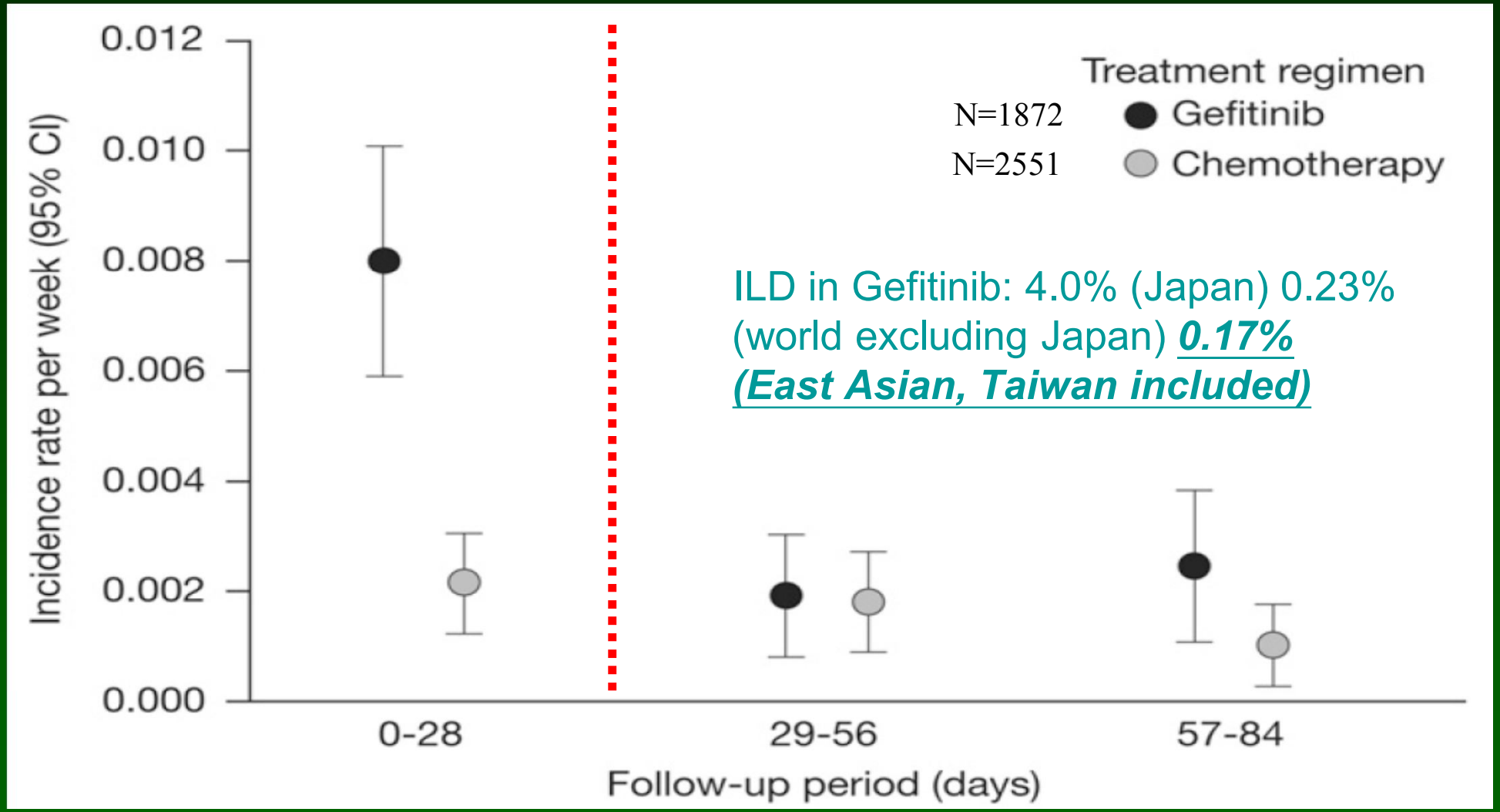
British Journal of cancer 2004; 91:S18-S23

Risk factor of ILD

Table 2. Risk Factors for Interstitial Lung Disease Identified by Multivariate Logistic Regression Analysis (n = 1,586*)

Variable	Odds Ratio	95% CI	*P*
Male	3.10	1.15 to 8.36	.025
Positive smoking history	4.79	1.69 to 13.54	.003
Coincidence of IP	2.89	1.06 to 7.84	.038
BSA of < 1.5 m^2	1.67	0.98 to 2.83	.059

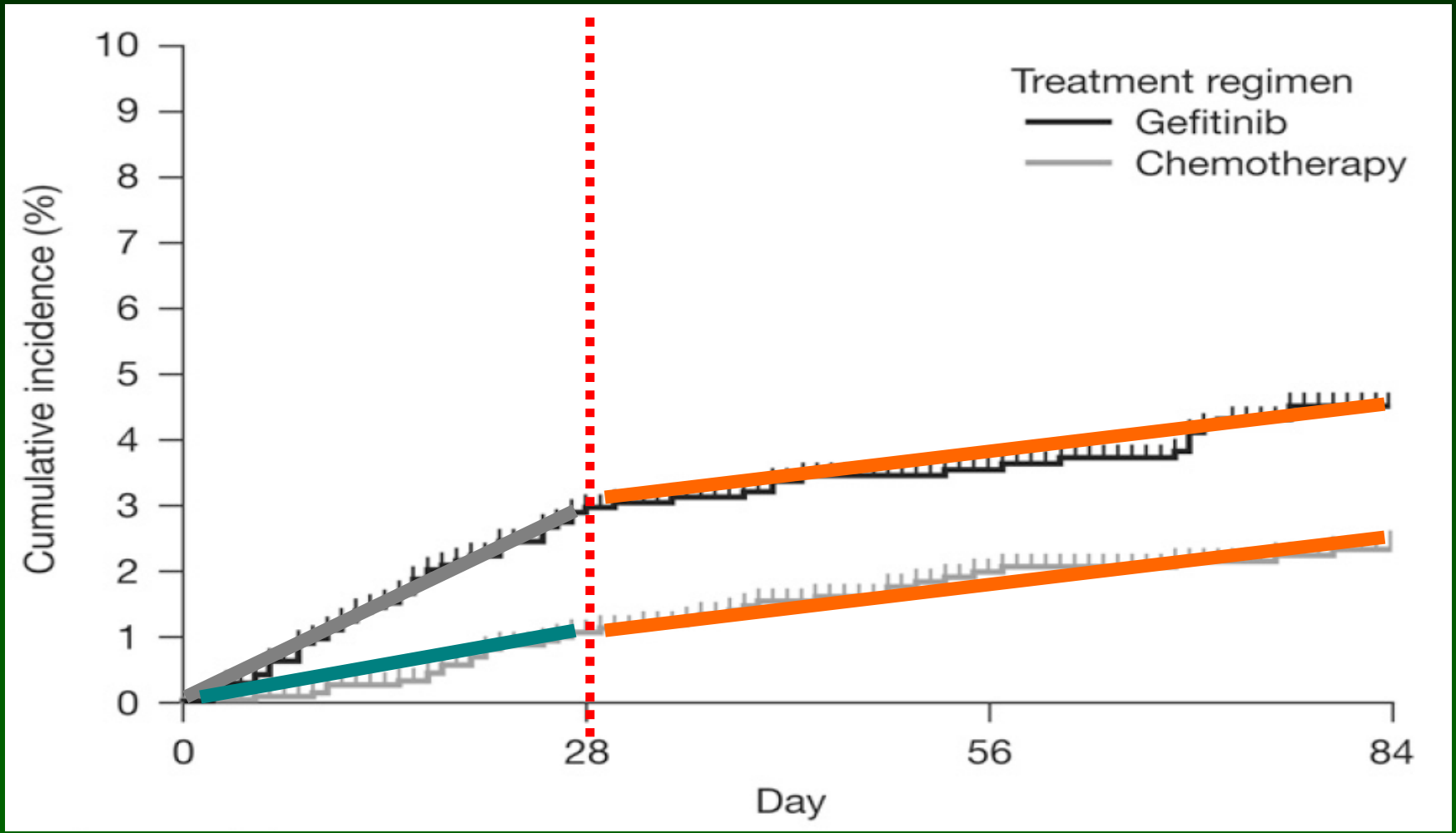
Abbreviations: IP, interstitial pneumonia; BSA, body-surface area.
*Including 66 patients with gefitinib-induced interstitial lung disease.



ILD in Gefitinib: 4.0% (Japan) 0.23% (world excluding Japan) ***0.17%***
(East Asian, Taiwan included)

AJRCCM 2008; 177:1348-57

Asia Pac J Clin Oncol 2007;3:66–78.

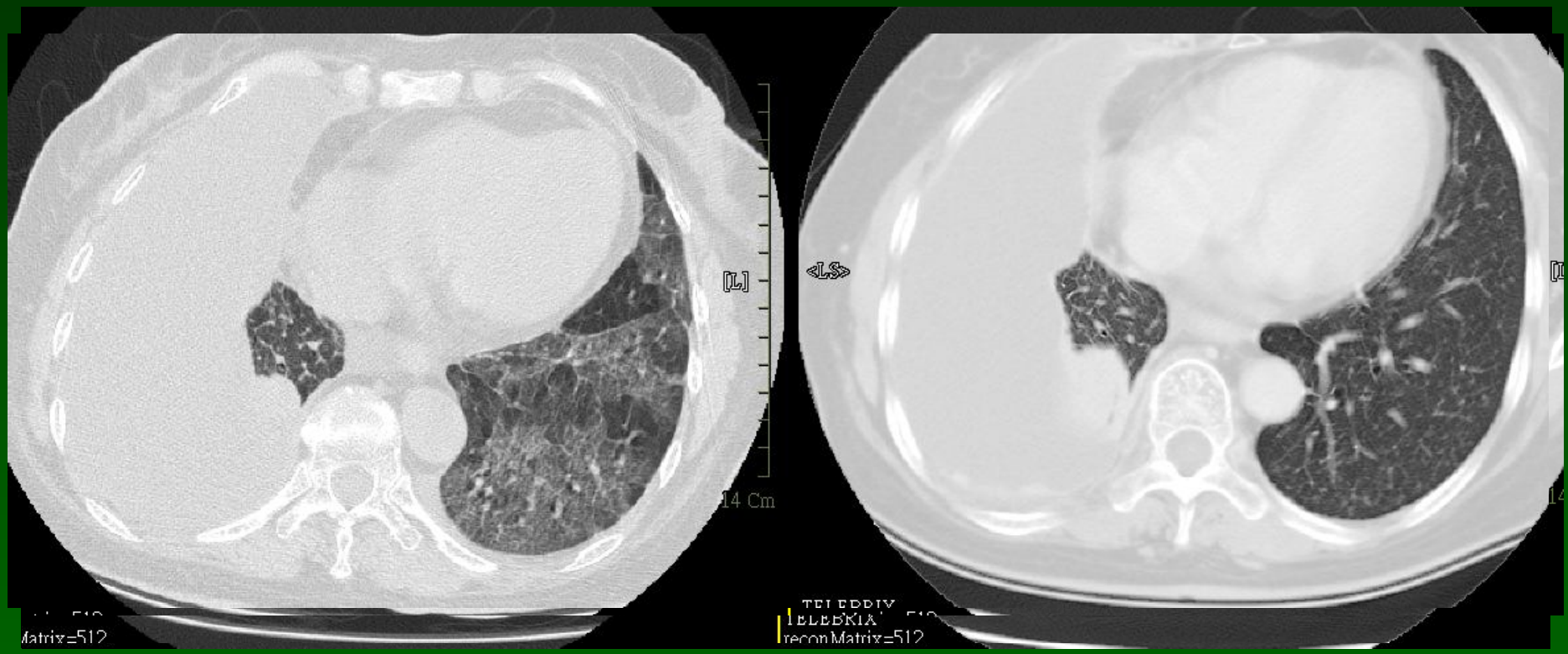

Cumulative incidence (%)
10
9
8
7
6
5
4
3
2
1
0
0
28
56
84
Day
Treatment regimen
Gefitinib
Chemotherapy

Our experience in NYMUH

- Name: 徐XX; 72 y/o female
- Adenocarcinoma of lung, RLL, with malignant pleural effusion, diagnosed 97/11
- s/p Navelbine x 7, shifted to Iressa (98/5/22)

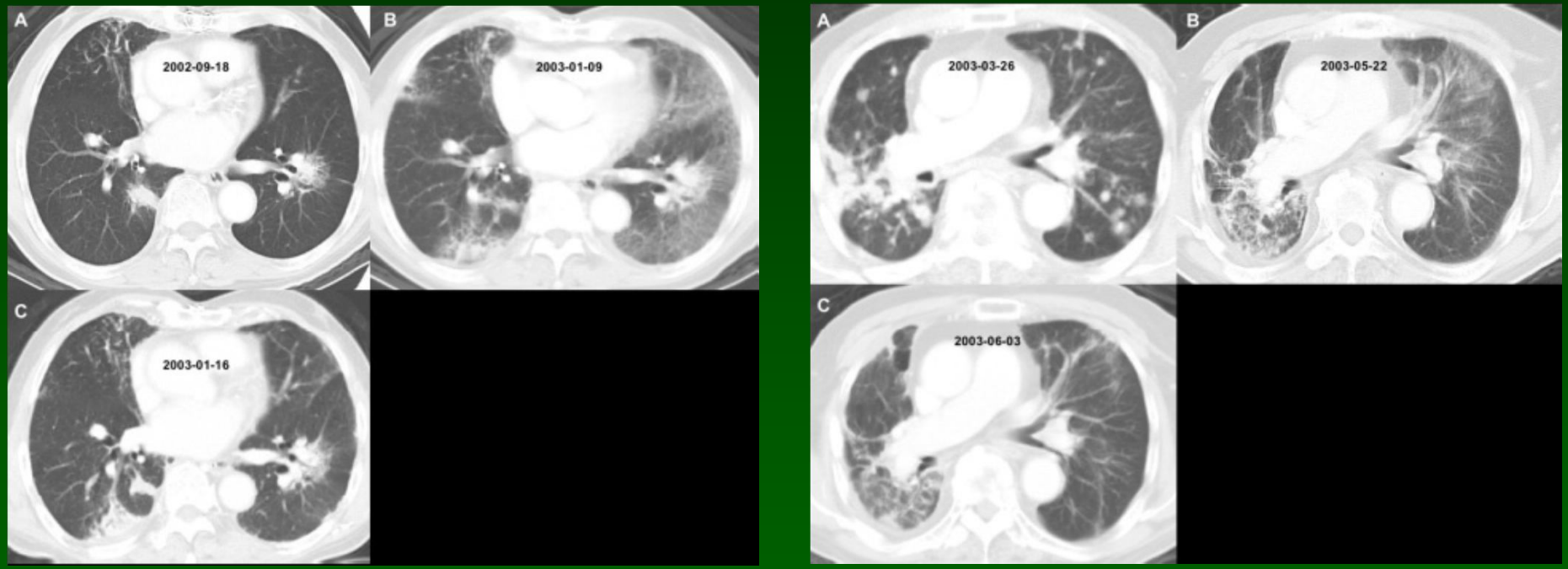
→ Fever, SOB, non productive cough (5/25)

Chest CT scan



2009/5/29 Iressa since 98/5/22 2009/4/29

Incidence of ILD during Gefitinib treatment in Taiwan: 0.17 % ????



4 *(5.8%)* of 69 patients developed ILD during gefitinib treatment

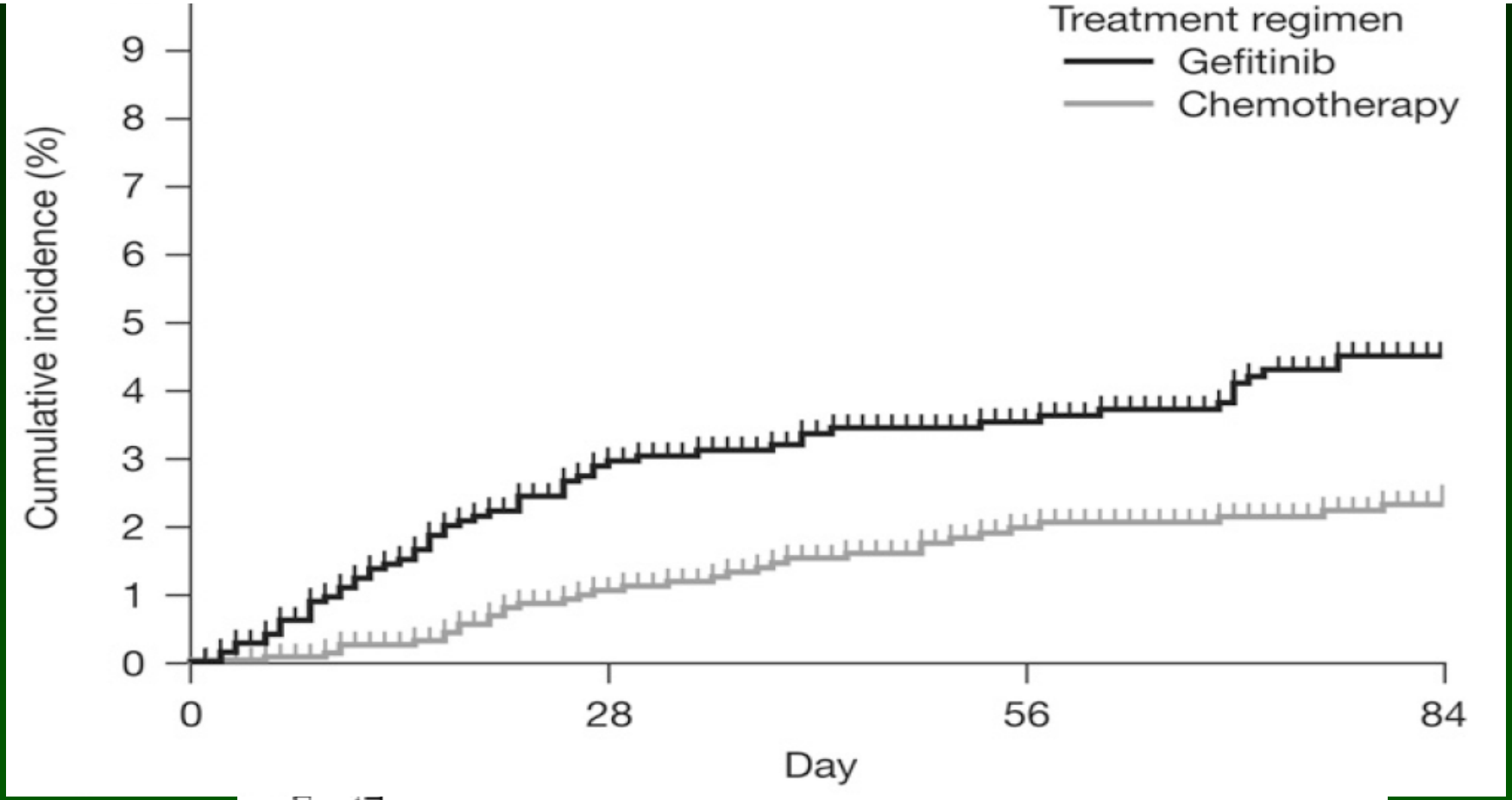
VGH Chun-Ming Tsai **JCMA** 2005; 68:183-186

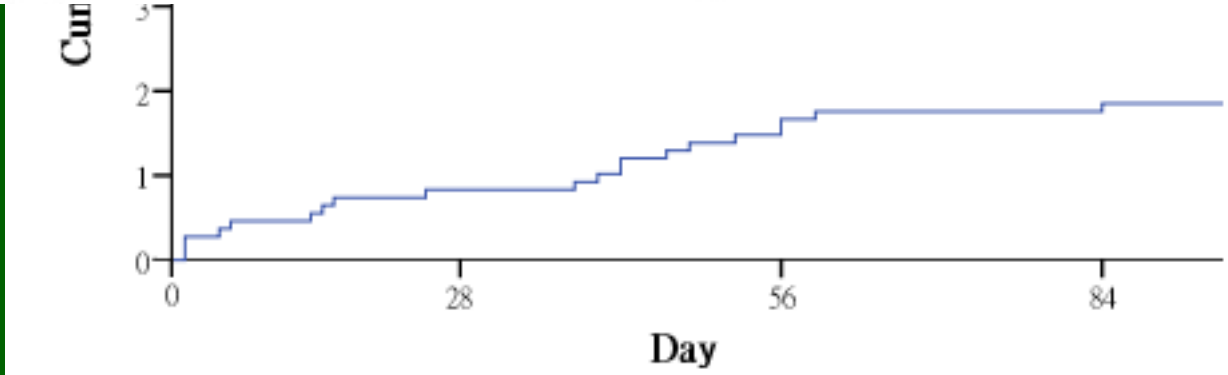
We consecutively recruited 1080 patients treated with gefitinib

	Patients (%)		
	NTUH	FEMH	NYMUH
Gefitinib use	969	85	26
ILD	21	2	2
Incidence (%)	2.1	2.3	7.7

From April 2004 to May 2009, 25 (2.3%) of 1080 patients developed ILD during gefitinib treatment

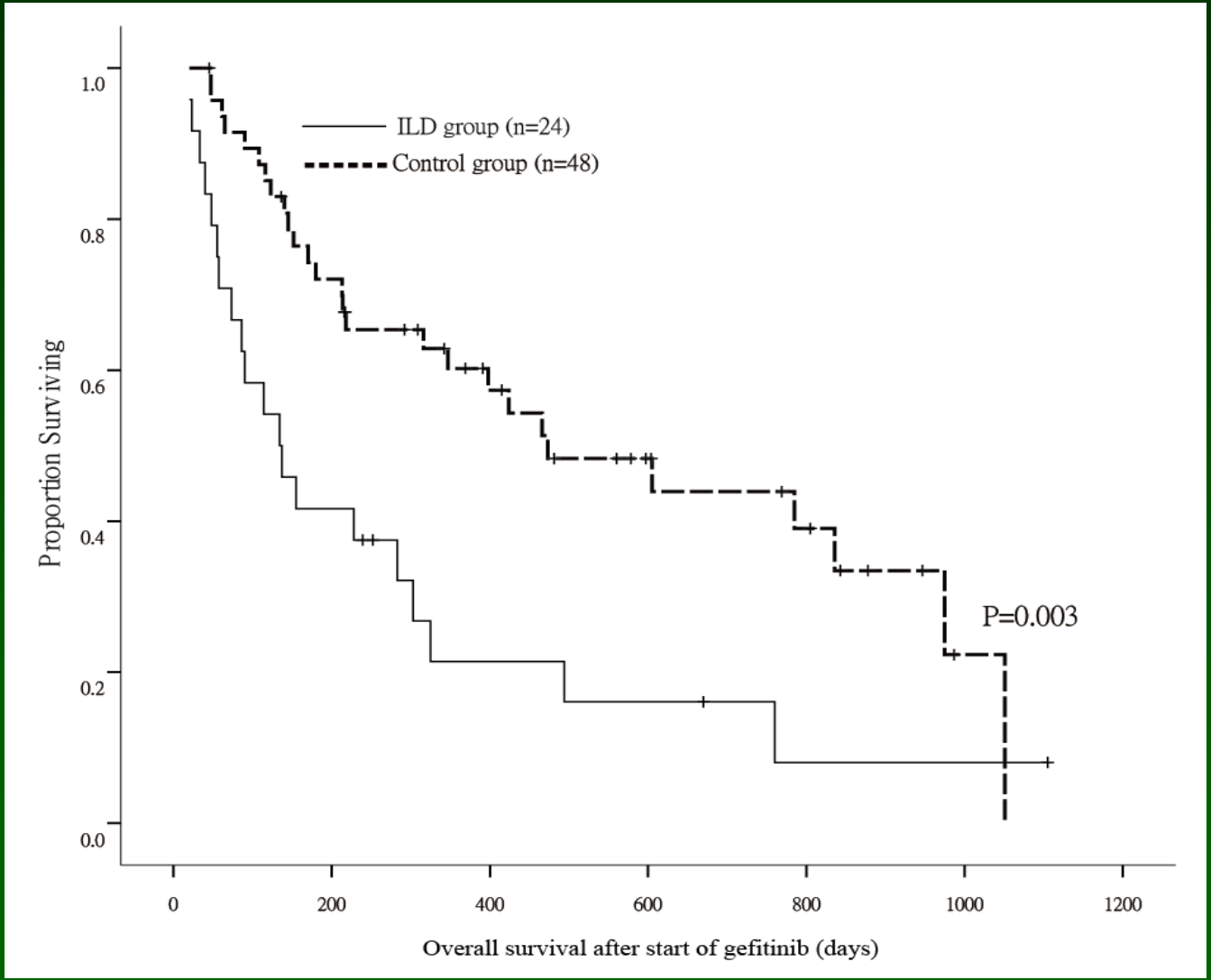
Chang SC et al. Clinical lung cancer, 2012 accepted





Chang SC et al 2010, lung cancer, revised

ILD is a serious adverse effect



In-hospital mortality=54.2 %

1 year survival after ILD onset=21.8%

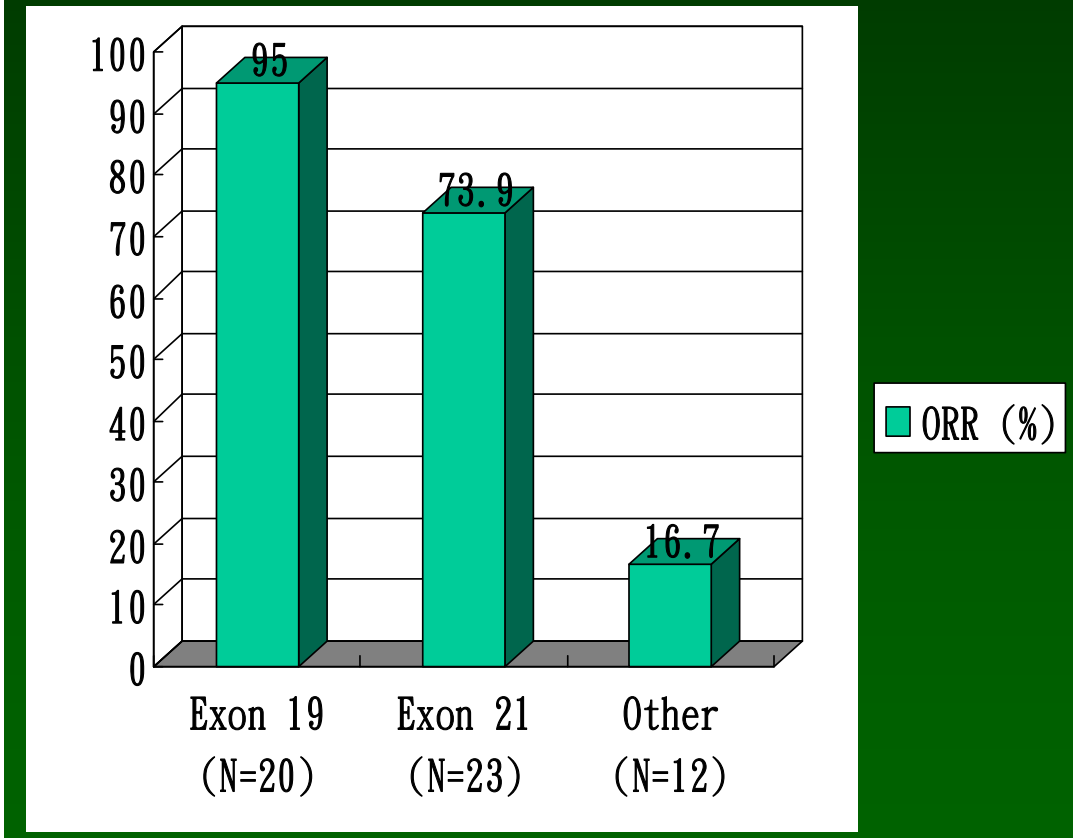
Chang SC et al. Clinical lung cancer, 2012 accepted

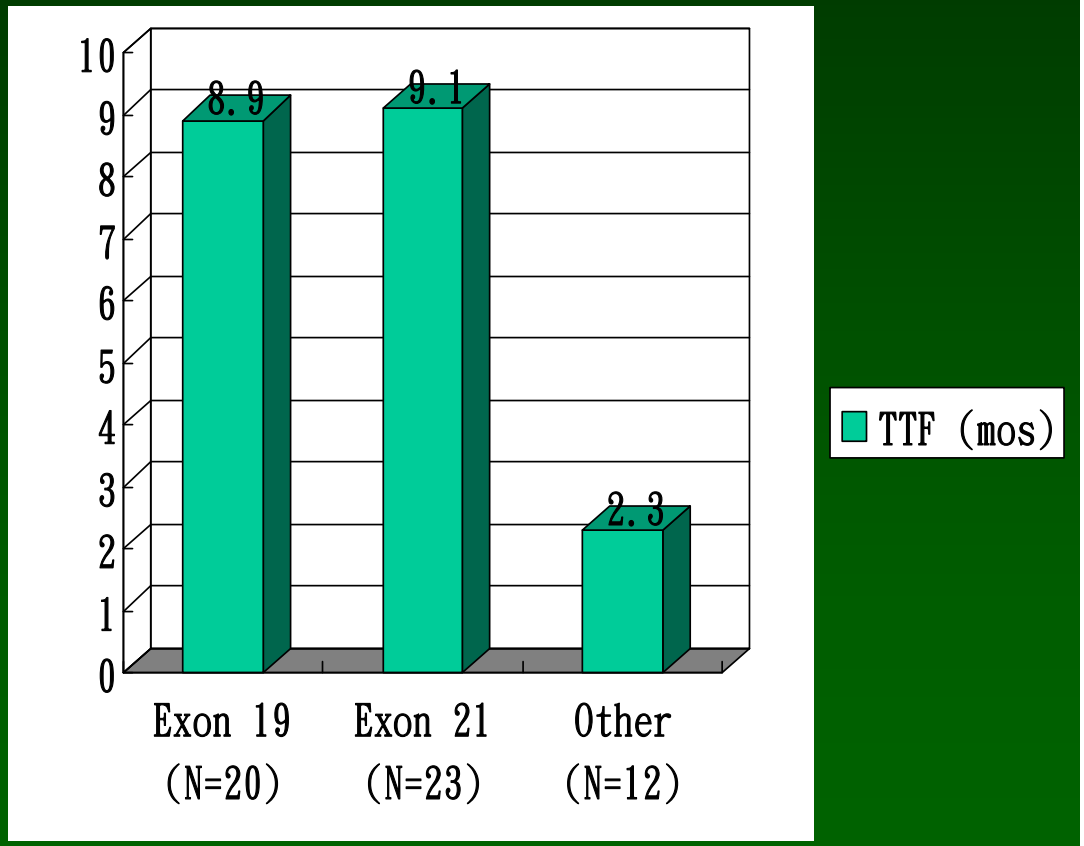
Cox regression analysis in-hospital mortality

Variables	Hazard ratio	95% C.I.	P value
Gefitinib non-responder	10.55	1.20 – 92.40	0.03
Non 1st-line use	4.30	0.79 – 23.58	0.09
SpO2<80 %	0.33	0.07 – 1.60	0.17
Mechanical ventilation	3.02	0.65 – 9.41	0.13

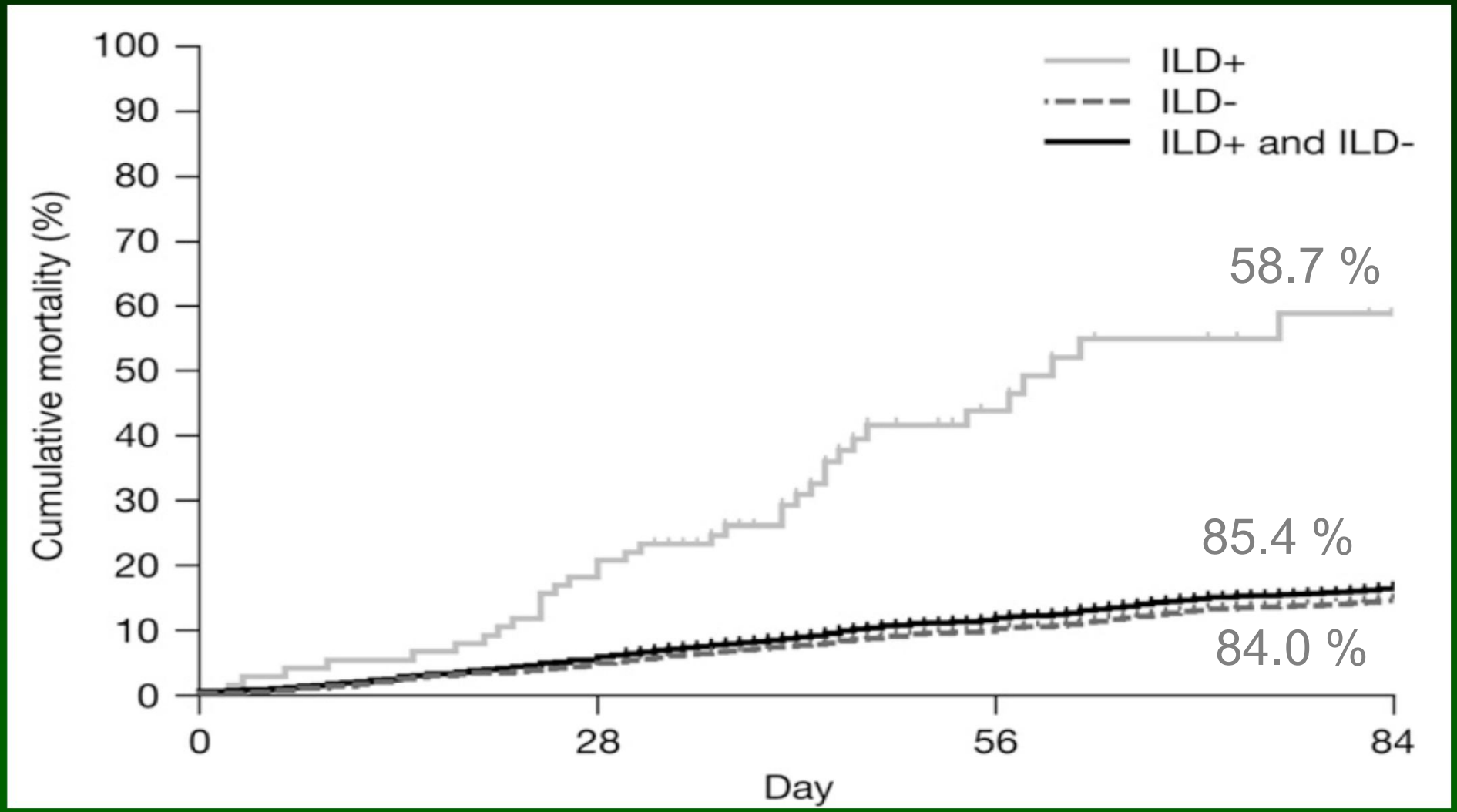
Chang SC et al. Clinical lung cancer, 2012 accepted

Prediction by specific EGFR mutations





Chih-Hsin Yang et al. JCO 2008;26:2745-53



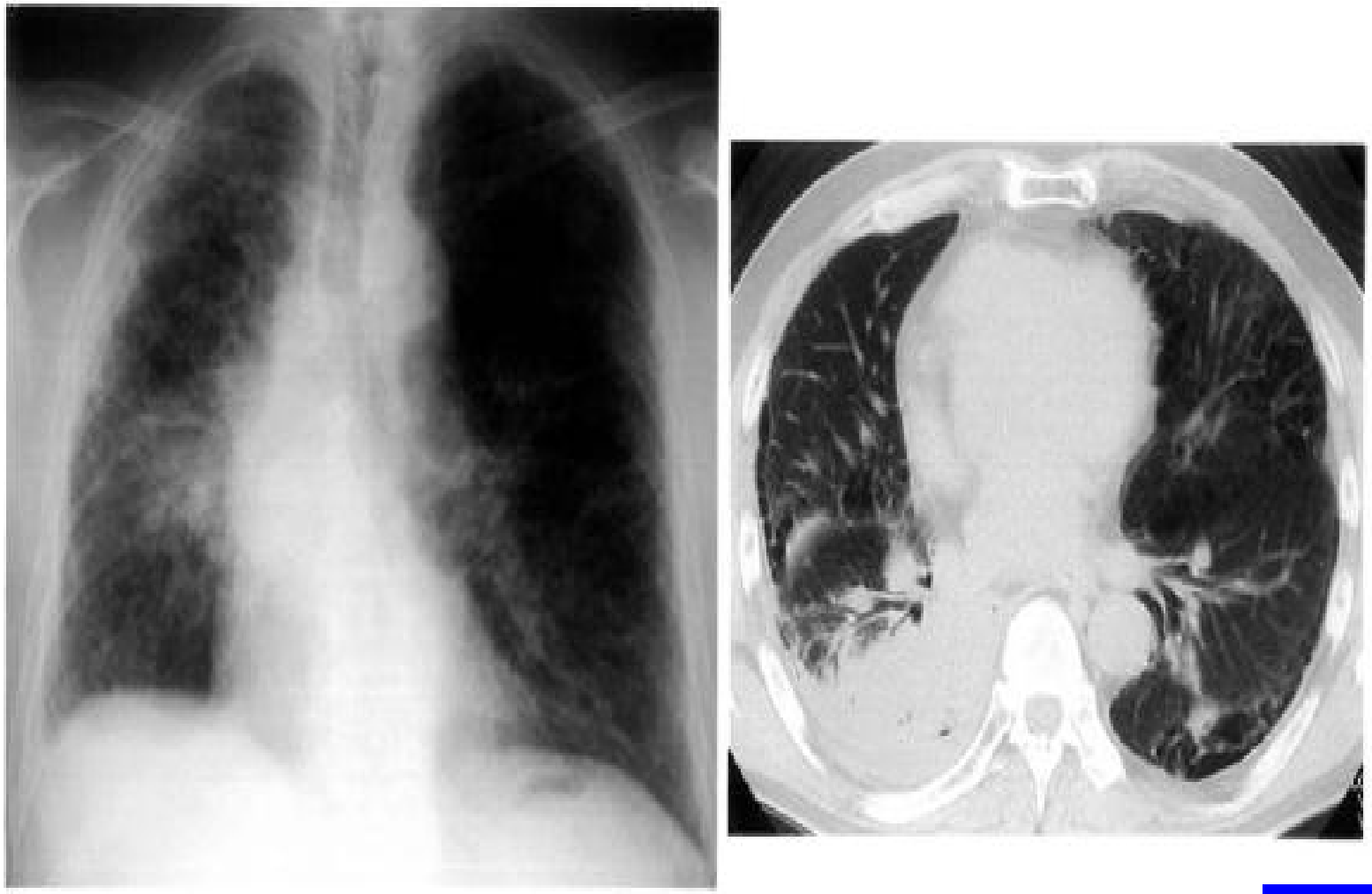
AJRCCM 2008; 177:1348-57

Table 2 Frequency of radiological patterns of ILD induced by gefitinib and mortality

Radiological pattern	Frequency		Mortality
	Chest radiography	CT	
A	29 (43.8%)	24 (47.1%)	9 (31.0%)
B	7 (10.0%)	7 (13.7%)	2 (28.6%)
C	3 (4.3%)	1 (2.0%)	0 (0.0%)
D	20 (28.6%)	12 (23.5%)	15 (75.0%)
Others	11 (15.7%)	7 (13.7%)	5 (45.5%)
Total	70	51	31 (44.3%)

- A: Non specific area with ground glass attenuation
- B: A multifocal area of airspace consolidations
- C: Patchy distribution of ground glass attenuation accompanied by interlobar septal thickening
- D: Extensive bilateral ground glass attenuation or airspace consolidation with traction bronchiectasis

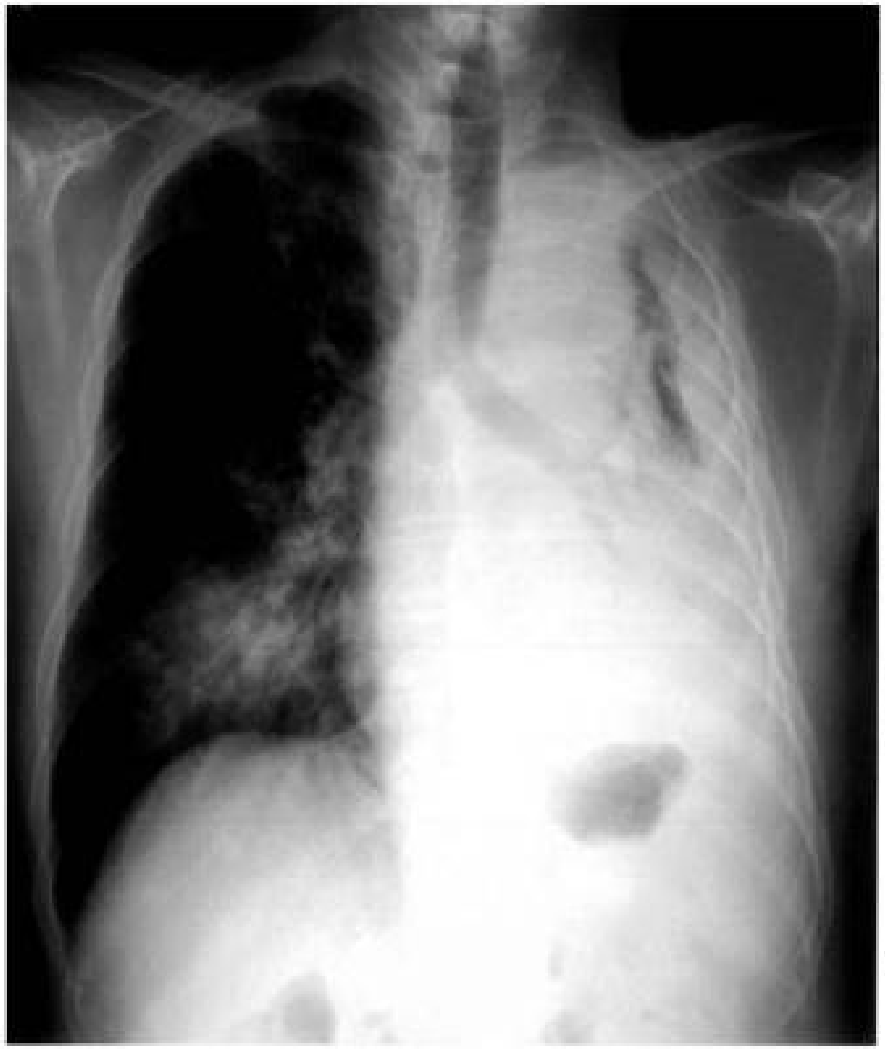
Endo et al Lung cancer 2006;52:135-140



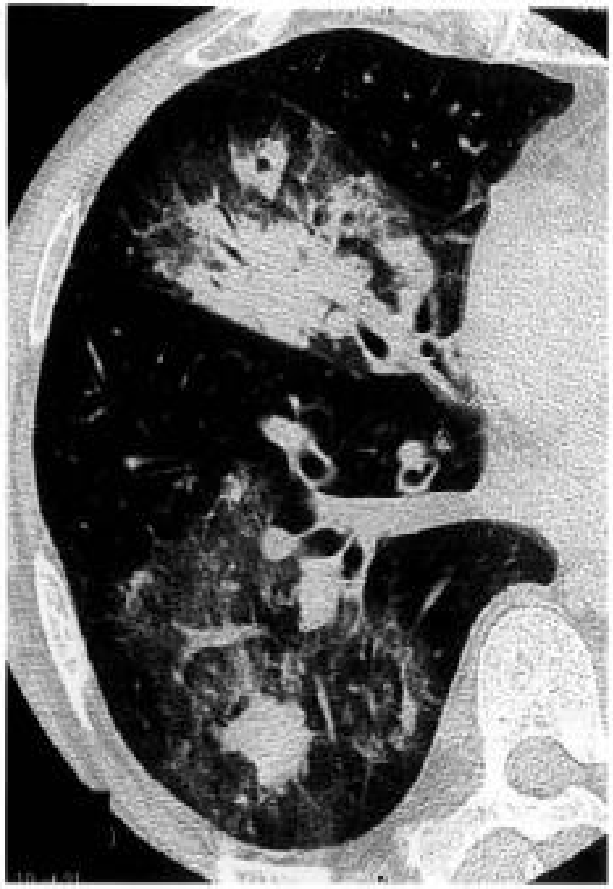
(a) (b)

pattern A

Fig. 1 A 60-year-old male with stage IV non-small cell lung cancer who had been treated with platinum-based chemotherapy developed mild dyspnea on day 10 after administration of gefitinib. The chest radiography reveals a mass opacity in the right hilum and diffuse ground-glass density over the entire lung field against a background of emphysema and fibrosis (a). The CT scan shows nonspecific areas with ground-glass attenuation throughout the lung parenchyma (b).



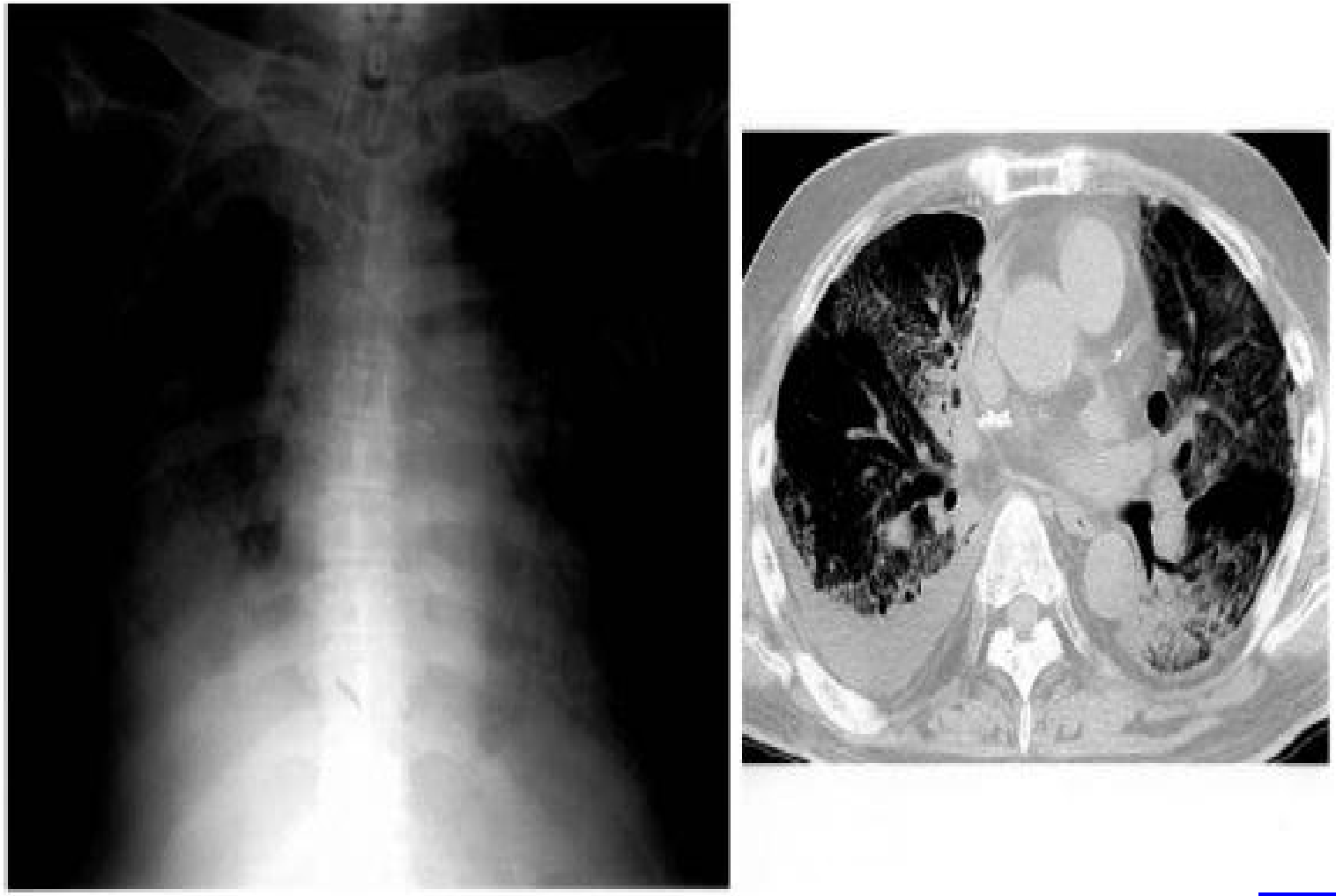
(a)



(b)

pattern B

Fig. 2 A 70-year-old male with stage IIIB adenocarcinoma who had been treated with platinum-based chemotherapy was started on gefitinib, and developed a severe cough and mild dyspnea on day 30 of gefitinib therapy. The chest radiography shows areas of consolidation on the upper and lower field of the right lung (a), and multifocal areas of airspace consolidation are seen on the thin-section CT scan (b).



(a) (b)

pattern D

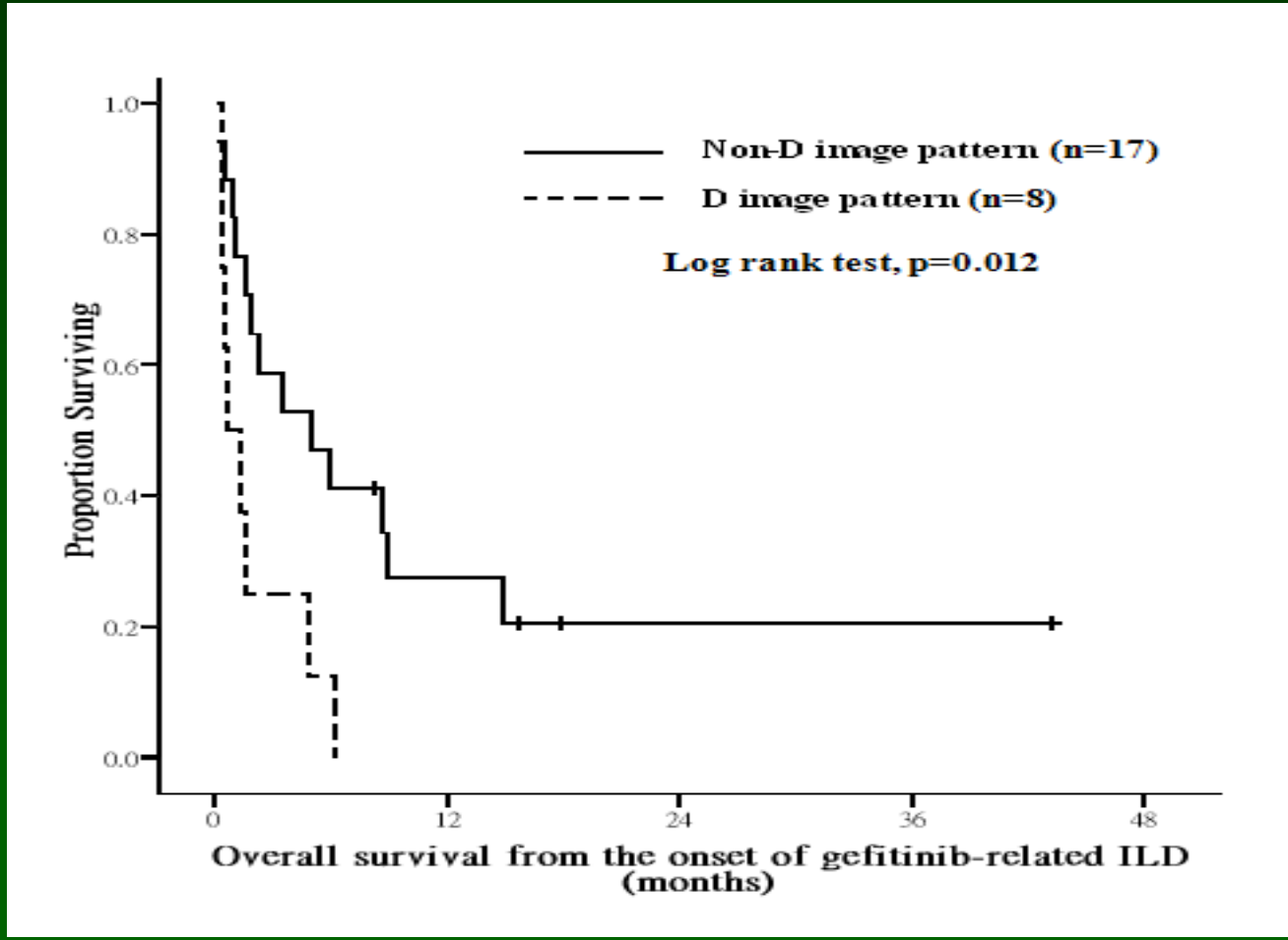
Fig. 3 A 62-year-old male who had undergone right upper lobectomy complained of the acute onset of dyspnea on day 5 after the start of gefitinib therapy. The anterio-posterior chest radiography shows diffuse ground-glass densities in the lung parenchyma (a). The CT scan shows extensive bilateral ground-glass attenuation and airspace consolidations with traction bronchiectasis (b). The patient died 10 days after the onset of ILD despite treatment by steroid pulse therapy.

Our Experience in Radiological Patterns of ILD Induced by Gefitinib and Mortality

Radiological Pattern	Chest X-ray	CT	Mortality
A	8 (32.0%)	8 (34.8%)	3 (34.8 %)
B	3 (12.0%)	3 (13.0%)	0 (0.0%)
C	6 (24.0%)	5 (21.7%)	2 (33.3%)
D	8 (32.0%)	7 (30.4%)	8 (100%)
Total	25	23	13 (56.5%)

Yuan MK, Chang SC, Int J Clin Pharmacol Ther. 2011 Oct

Imaging patterns and prognosis of patients with gefitinib-related ILD



Yuan MK, Chang SC, Int J Clin Pharmacol Ther. 2011 Oct

Treatments

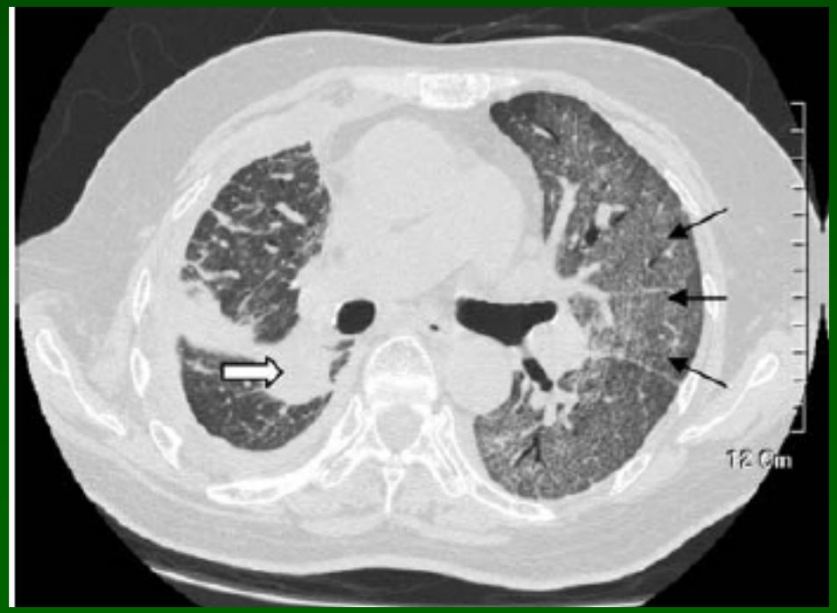
- There is no specific treatment, but supportive therapy including
  - DC iressa
  - Oxygen
  - Corticosteroids
    - (Rigimen)
      - MTP IV (1 g/day) x 3 days
        - (Respirology, 2006 11, 113–116) case report
      - MTP IV (2mg/kg/day~1 g/day) -> Prednisolone PO (20-30 mg/day)
        - Respiratory Medicine (2006) 100, 698–704
    - steroid less effective in AIP
  - Assisted ventilation is indicated

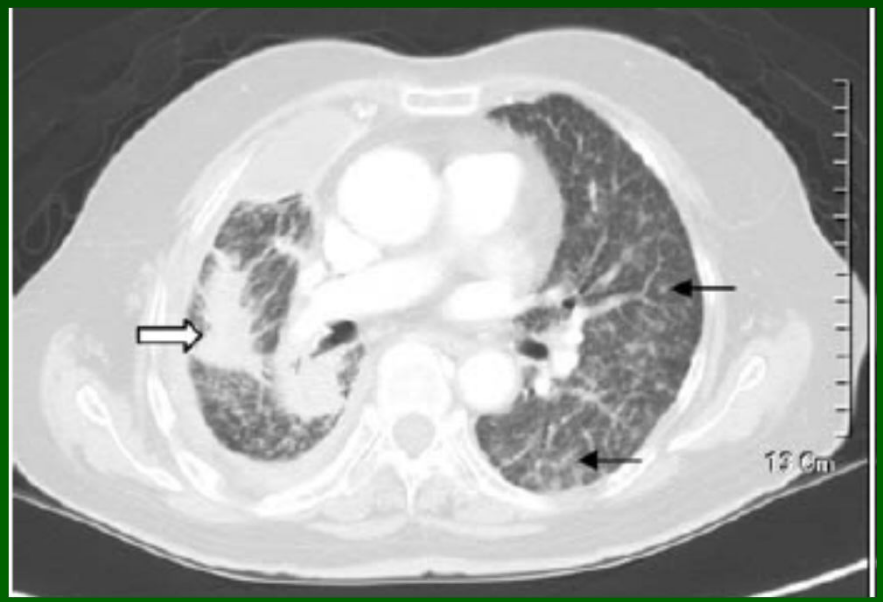
Med Oncol
DOI 10.1007/s12032-010-9424-4

ORIGINAL PAPER

Successful treatment of gefitinib-induced acute interstitial pneumonitis with high-dose corticosteroid: a case report and literature review

Li-Chiao Kuo · Po-Chou Lin · Ko-Fan Wang · Mei-Kang Yuan · Shih-Chieh Chang

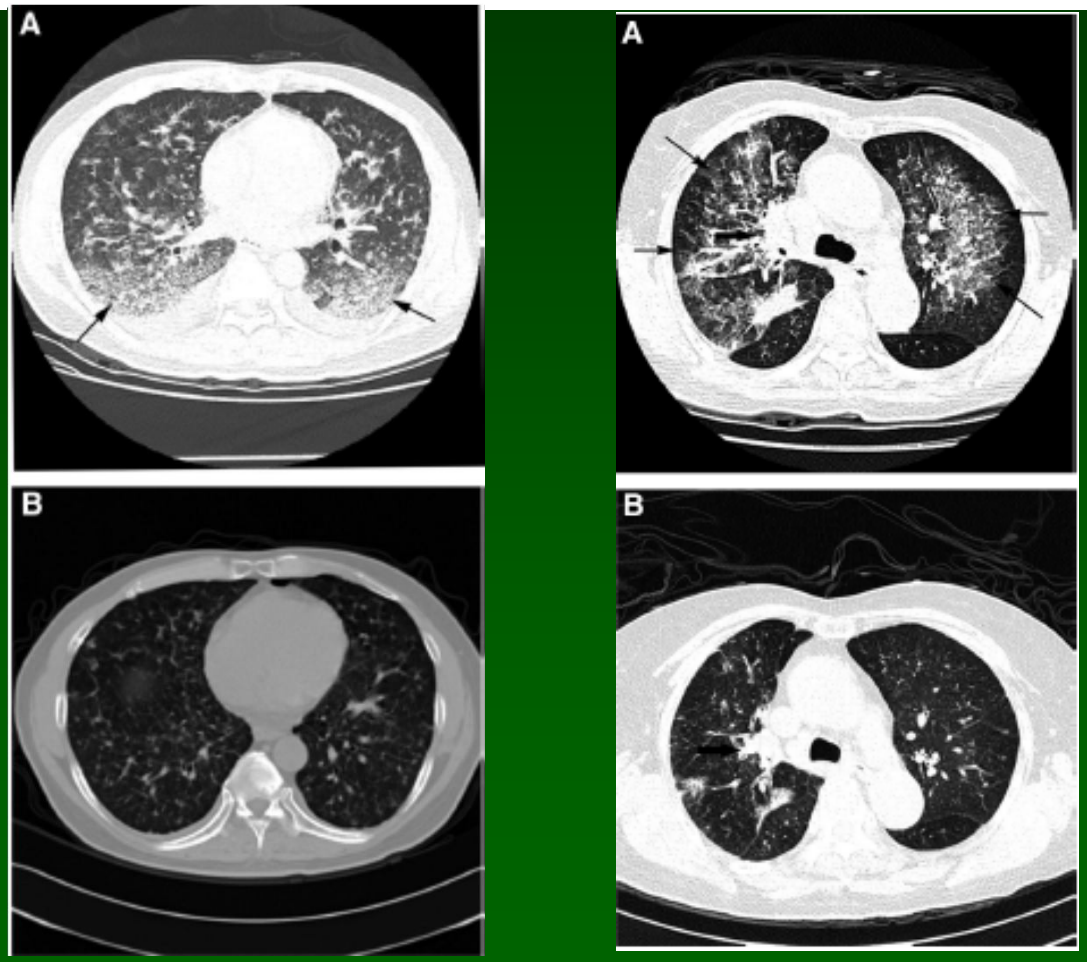




Kuo LC, Chang SC Med Oncol. 2011/1

Successful Erlotinib Rechallenge after Gefitinib-Induced Acute Interstitial Pneumonia

Shih-Chieh Chang, Cheng-Yu Chang,† Chiung-Yu Chen,‡ and Chong-Jen Yu‡*



Chang SC et al Journal of Thoracic Oncology 2010 June