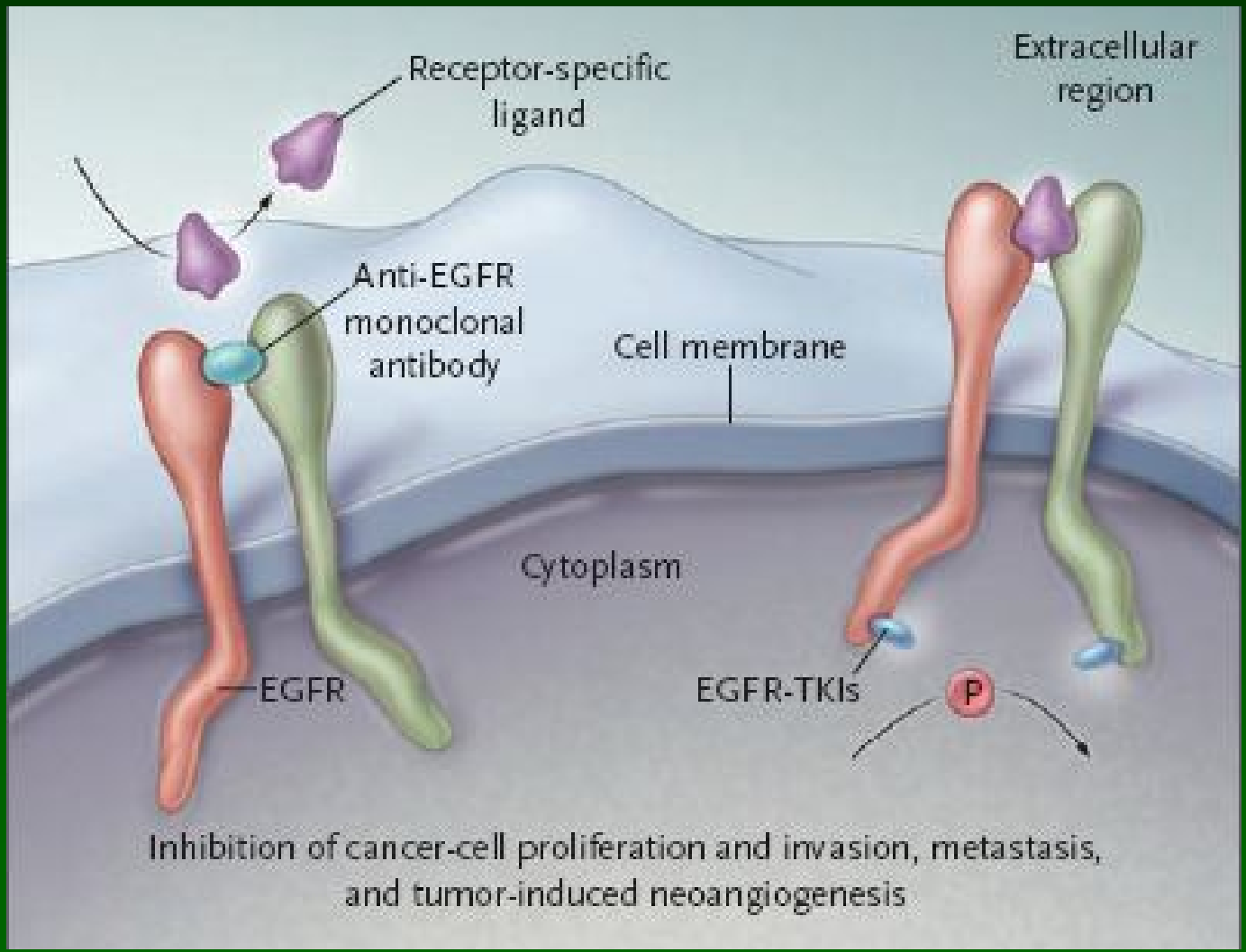
The NEW ENGLAND JOURNAL of MEDICINE

TO THE EDITOR: In their discussion of the clinical use of erlotinib or gefitinib in patients with lung cancer, Cataldo et al. recommended the permanent discontinuation of treatment with these tyrosine kinase inhibitors in cases of drug-associated interstitial lung disease. We point out three recent reports describing successful rechallenge with erlotinib after the resolution of pulmonary symptoms from interstitial lung disease that arose in association with treatment with gefitinib[1,2] or erlotinib.[3] We recognize that

1. Chang SC, Chang CY, Chen CY, Yu CJ. Successful erlotinib rechallenge after gefitinib-induced acute interstitial pneumonia. J Thorac Oncol 2010;5:1105-6.

N Engl J Med 2011; 364:2367-2368

Cetuximab - Anti-EGFR monoclonal antibody



International Journal of Clinical Pharmacology and Therapeutics, Vol. ■■ – No. ■/2010 (■■■-■■■)

Acute interstitial pneumonitis in a patient receiving FOLFOX-4 regimen plus Cetuximab treated with pulse therapy

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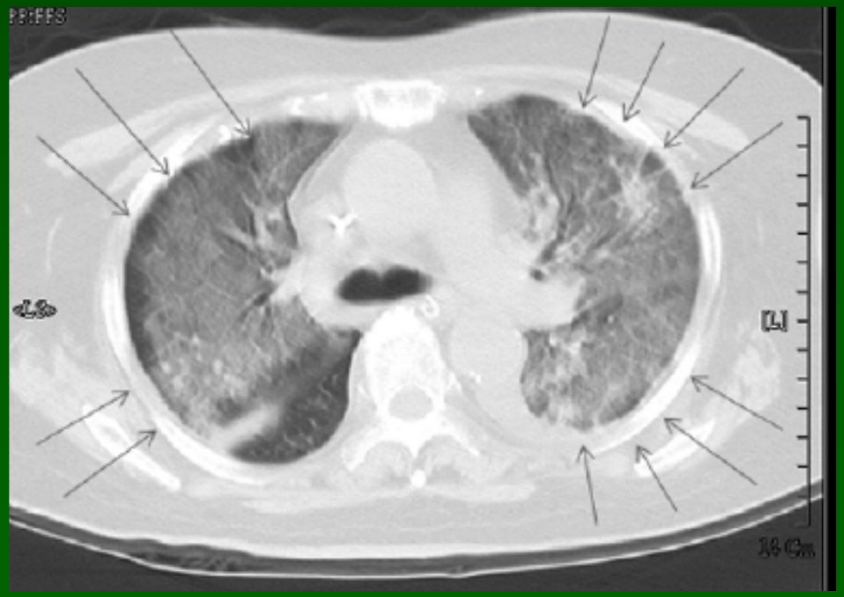
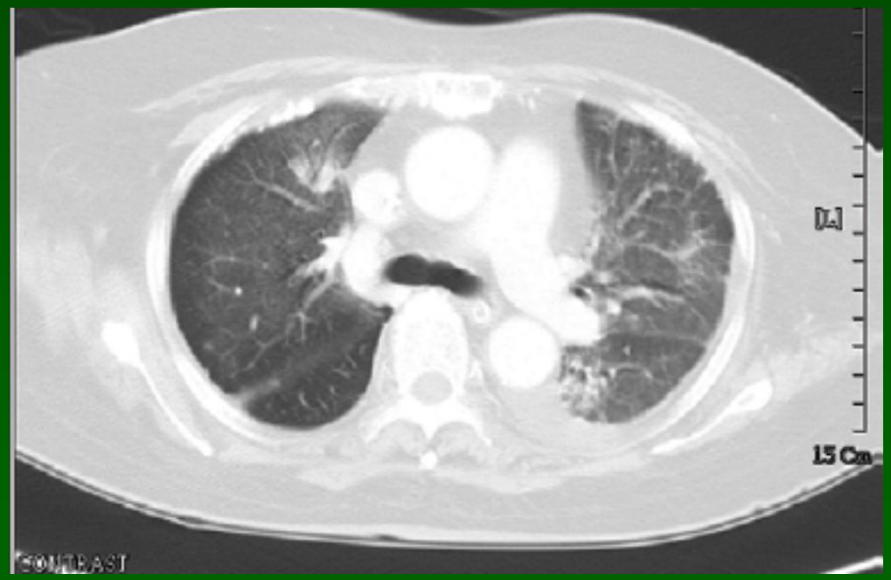
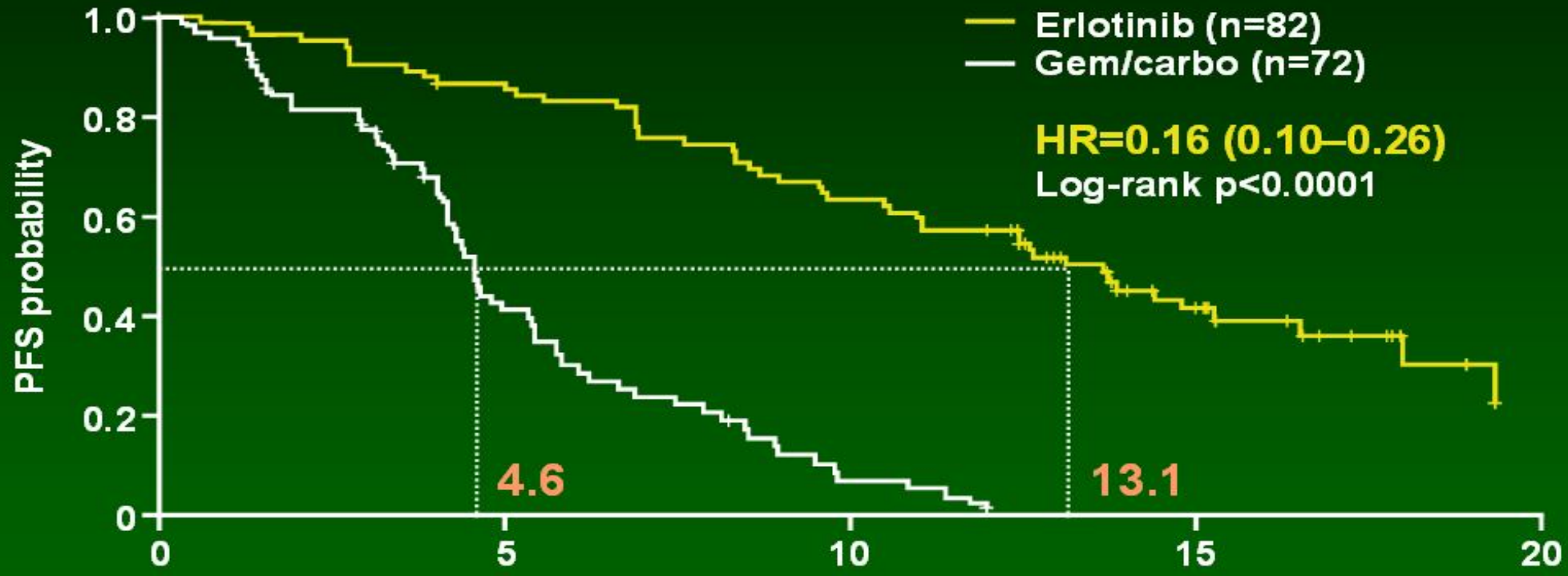
[1]National Yang-Ming University School of Medicine and [2]Department of Medicine, National Yang-Ming University Hospital, Taiwan, Republic of China





Chang et al Int. J. of Clinical Pharmacology and Therapeutics. 2010

Erlotinib First Line in Mut(+)
PFS in ITT

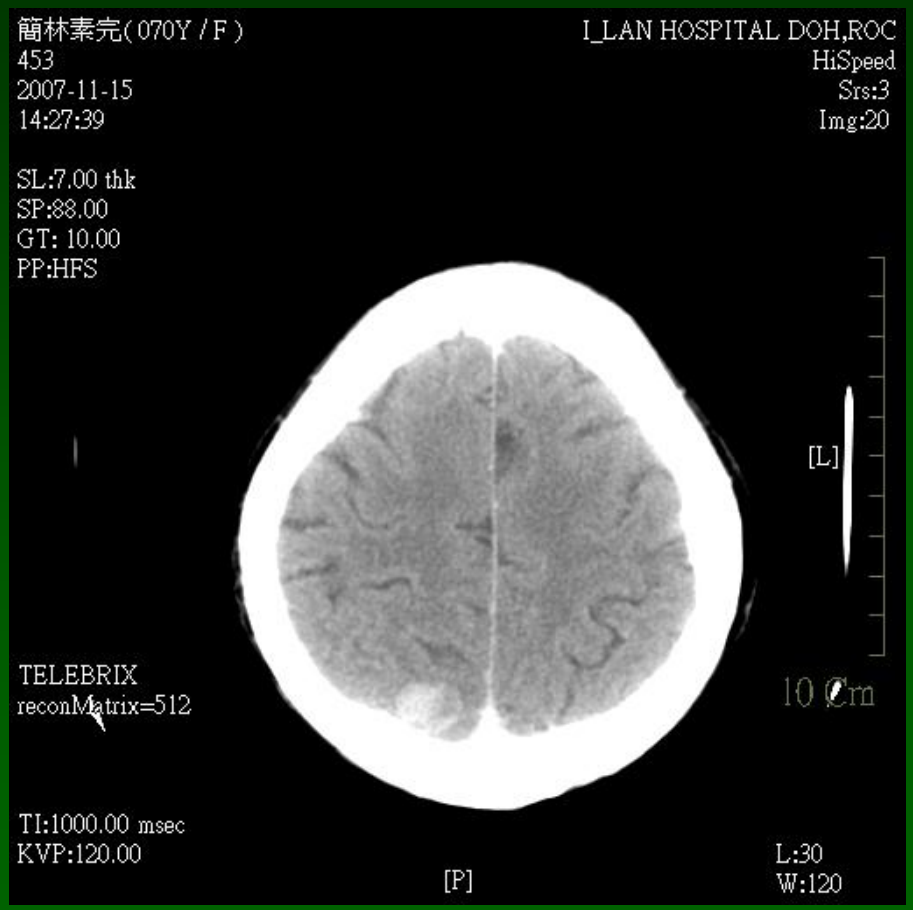


Patients at risk					
Erlotinib	82	70	51	20	2
Gem/carbo	72	26	4	0	0

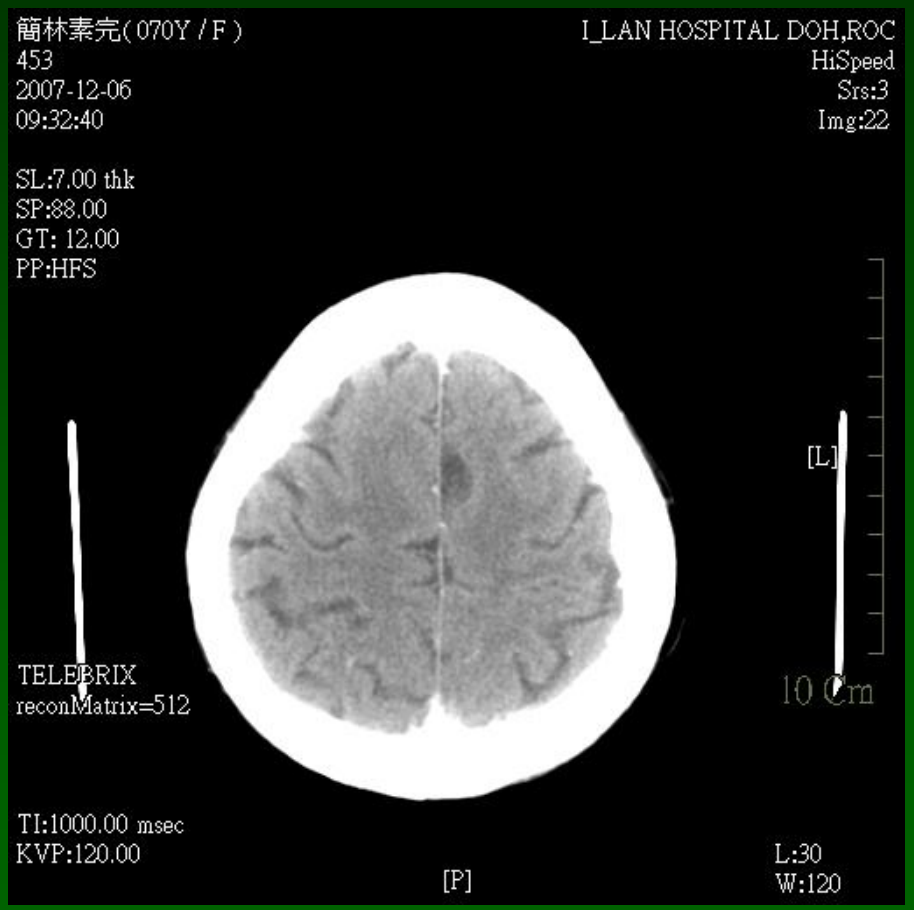
腦轉移

- 手術切除：單一腦轉移，如肺部腫瘤可以手術切除，可考慮接受腦轉移切除，再追加放射線治療，並配合化學治療
- 立體定位放射手術追加全腦照射
- 全腦照射
- 無症狀的腦轉移：少數病人在接受全身治療(如化學治療或艾瑞莎)後，可以觀察到腦腫瘤縮小

71歲女性,肺線癌併惡性胸水及腦轉移, Stage IV
艾瑞莎治療3個月



2007/11/15



2007/12/06

EGFR Mutation in Patients With Clinical Characteristics

Female + Never smoking + Adenocarcinoma

↓

55-68%

EGFR Mutation (+)

↓

32-45 %

EGFR Mutation (-)

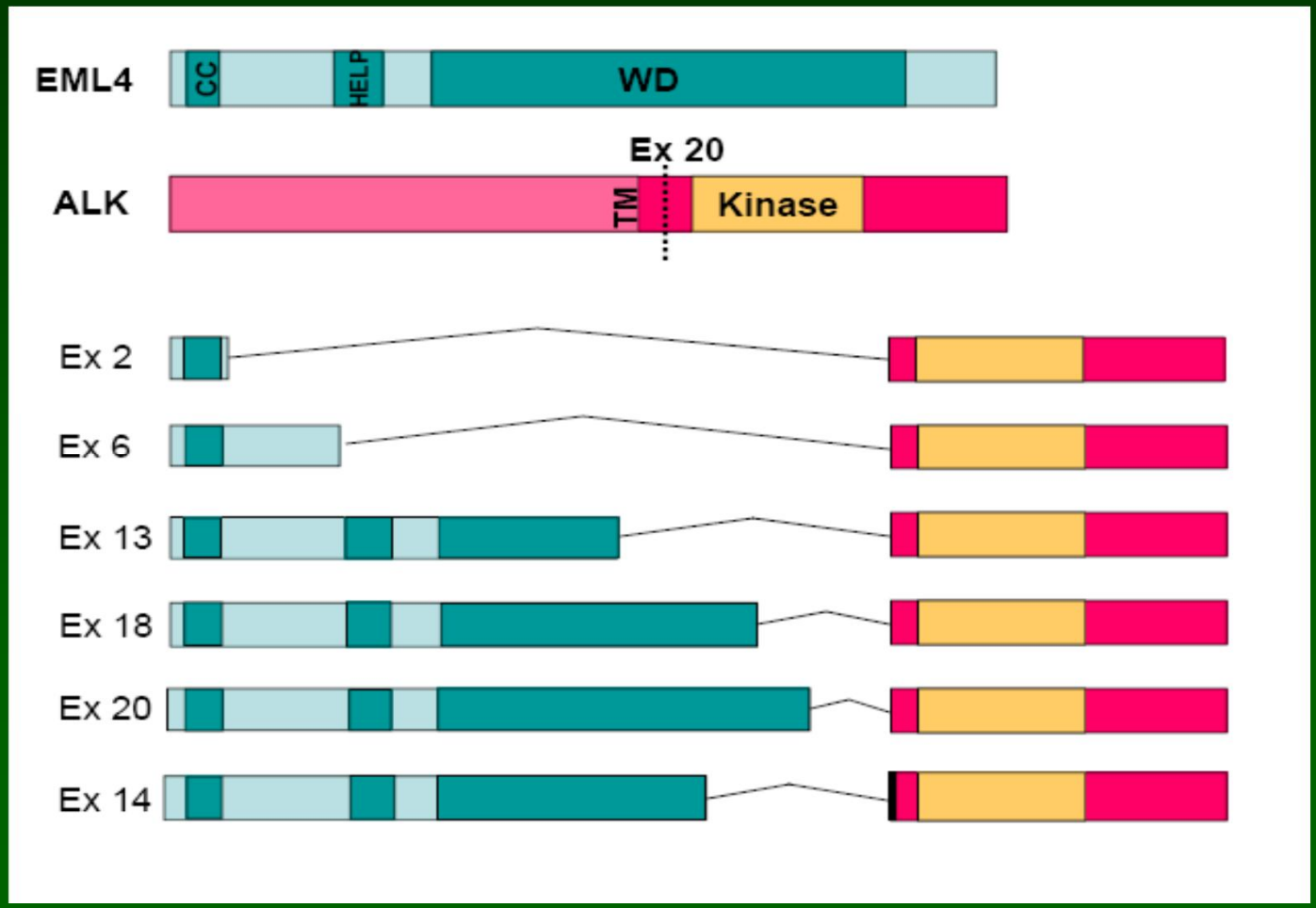
J Clin. Oncol 2011; 29

Anaplastic lymphoma kinase inhibition in NSCLC

- Oncogenic fusion genes-*EML4 and anaplastic lymphoma kinase (EML4-ALK)are* present in a subgroup of non–small-cell lung cancers (2-7%)

- Most patients with *ALK rearrangements* had little or no exposure to tobacco and had adenocarcinoma. (~20% adenocarcinoma)

Activating translocation of ALK gene → cytoplasmic chimeric protein



ALK Tyrosine Kinase Inhibitors in Development

Drug	Manufacturer	Clinical stage
Crizotinib	Pfizer	Phase III and II for NSCLC
CEP-37440	Cephalon	Preclinical
AP-26113	Ariad Pharmaceuticals	Preclinical; IND expected 2011
NMS-E628	Nerviano Medical	Preclinical
X-276/396	Xcovery	Preclinical
TAE684	Novartis	Not a clinical candidate
CH5424802	Chugai Pharmaceuticals	Preclinical; phase I trial ongoing in Japan
LDK378	Novartis	Phase I trial ongoing
ASP3026	Astellas	Phase I trial ongoing

Clin Cancer Research. 2011; Nov. 18

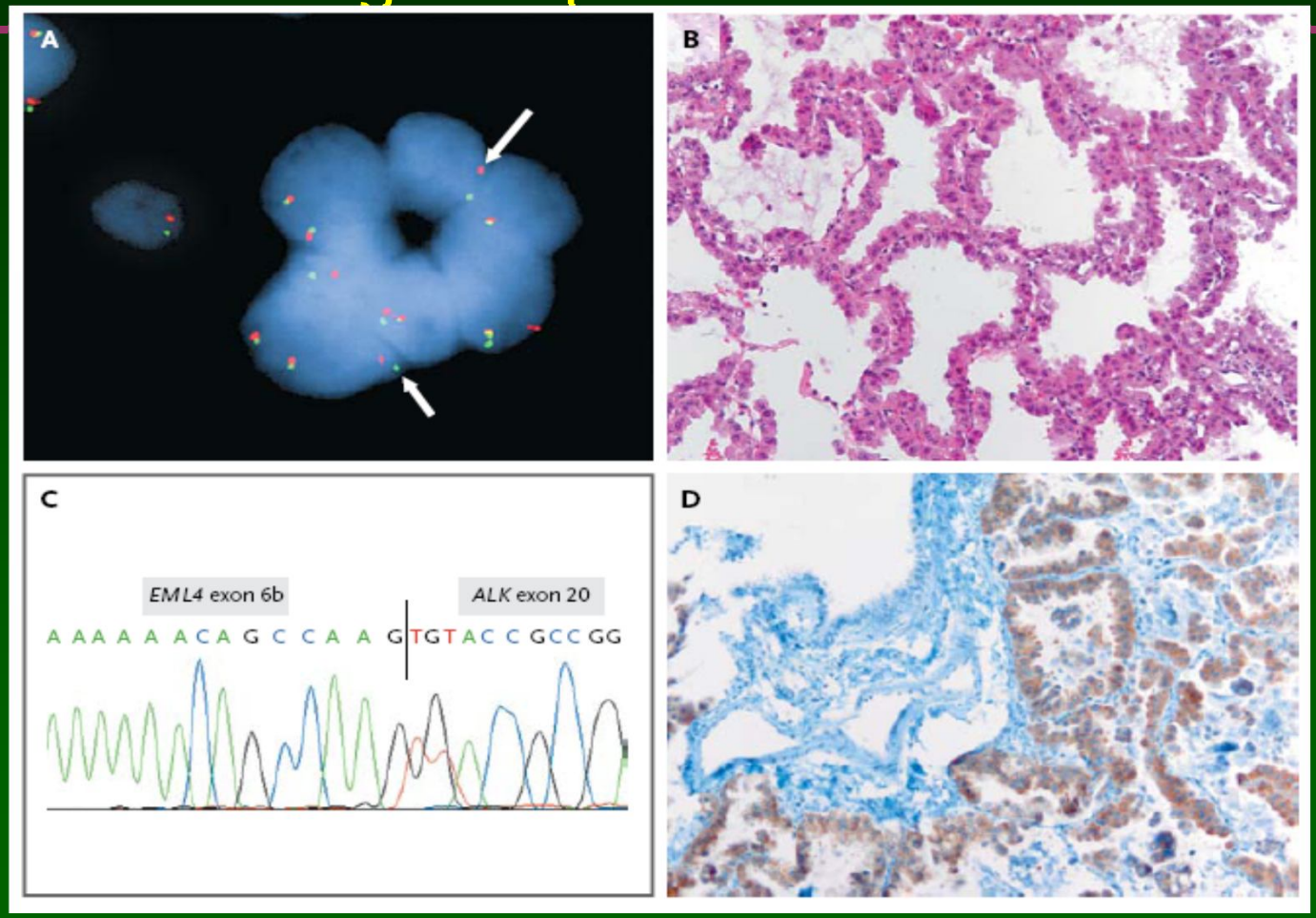
Diagnosis of an *EML4-ALK* NSCLC in a Single Representative Patient

FISH

H & E

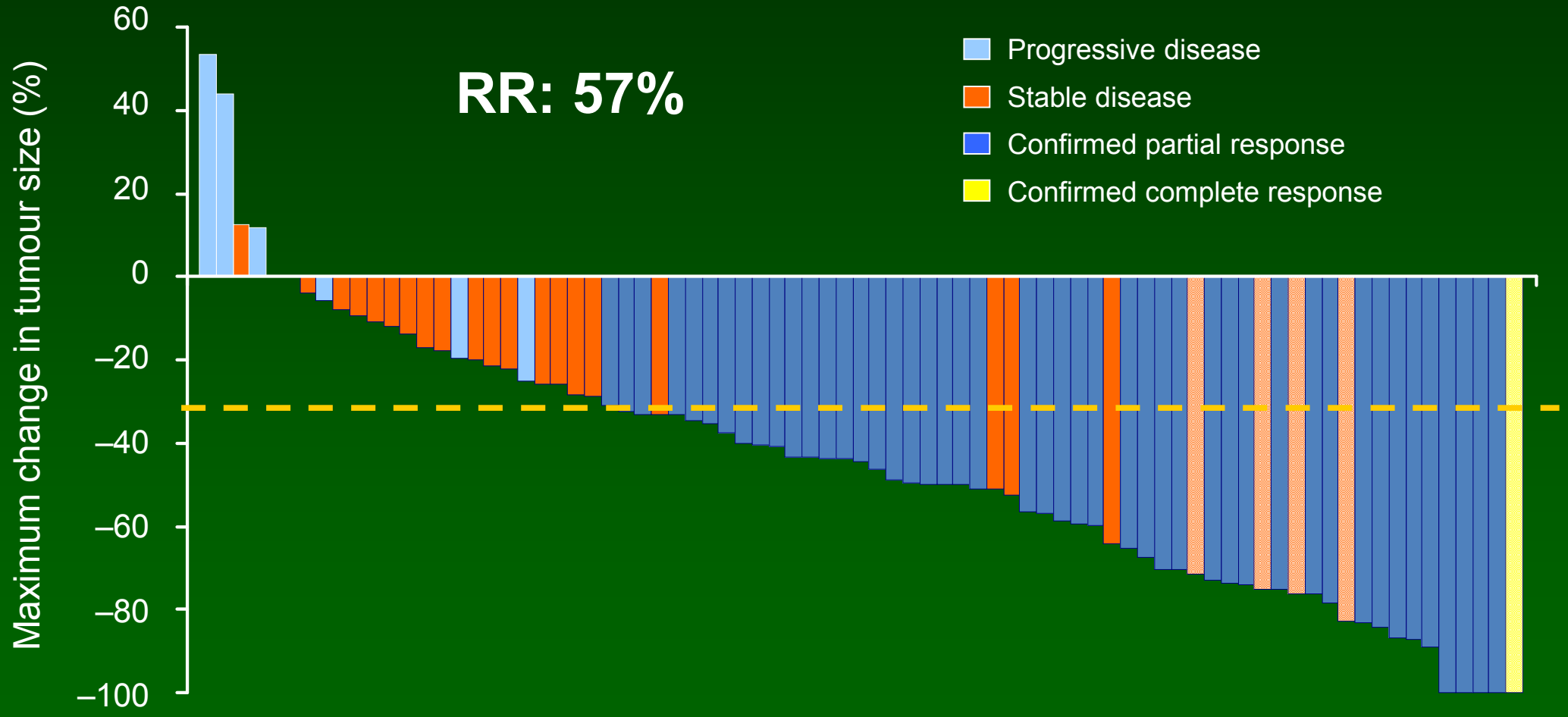
PCR

IHC



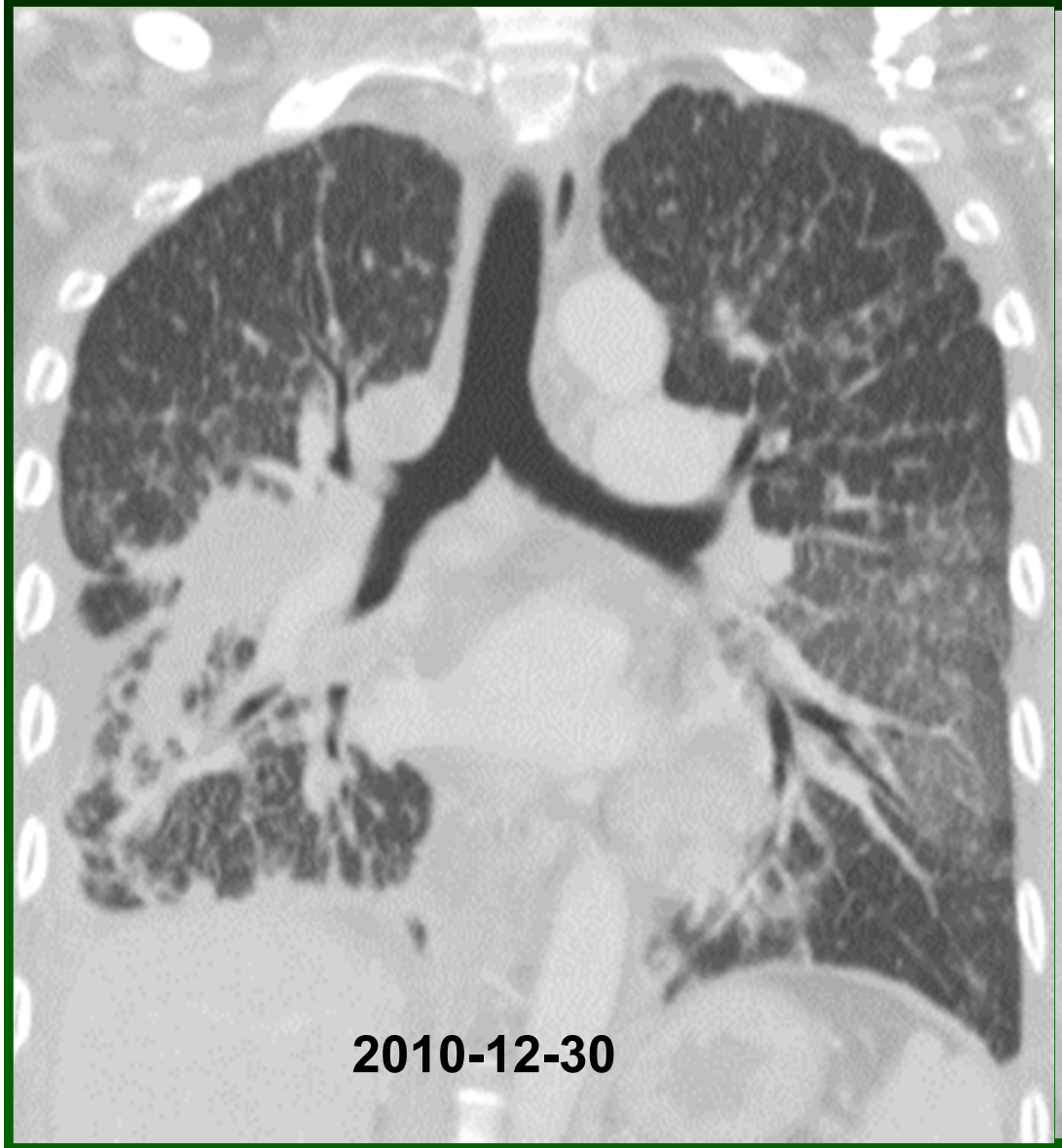
N Engl. J Med. 2010;363:1693-1793

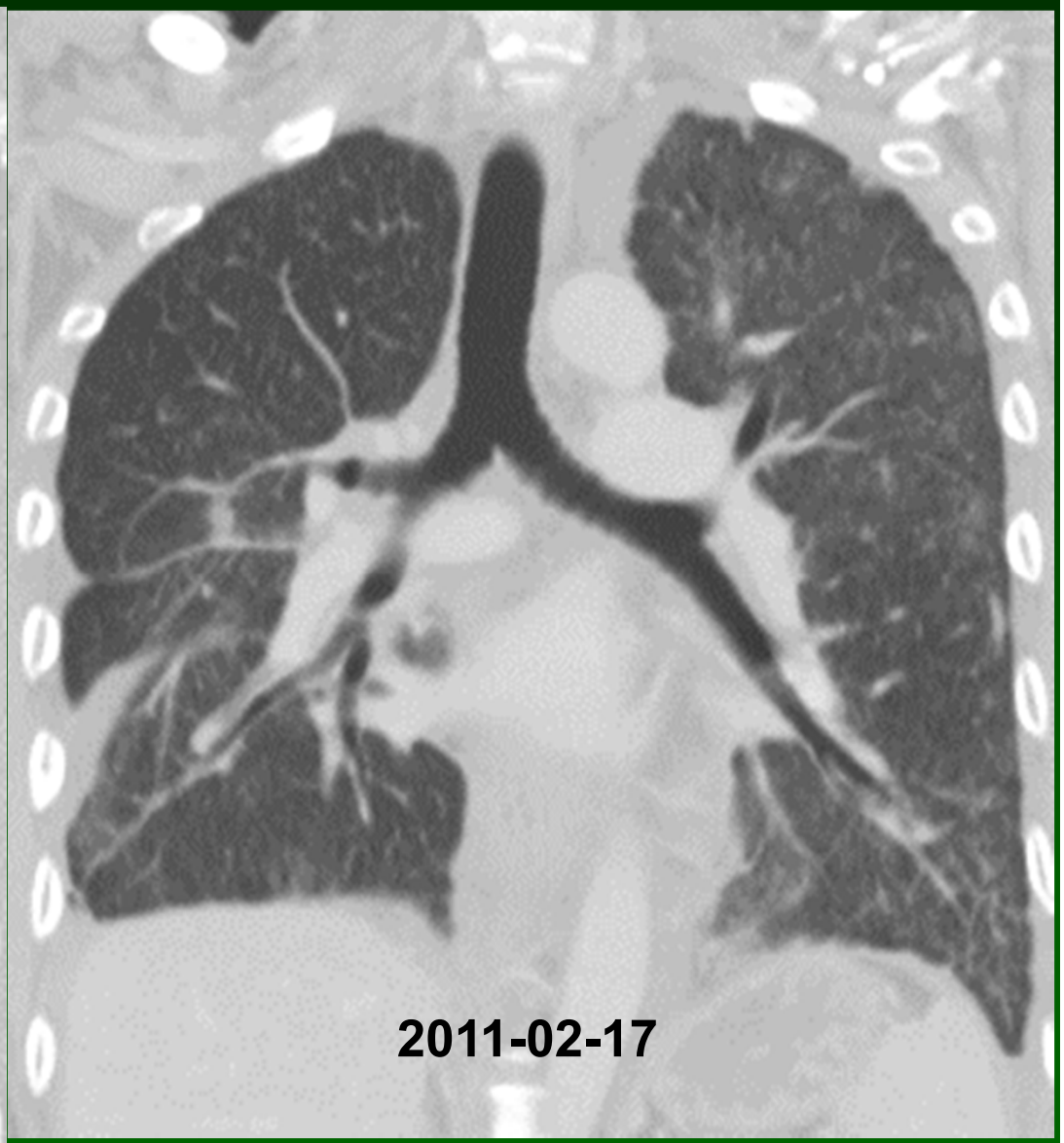
Best responses with crizotinib for 82 patients with EML4-ALK-positive lung adenoca



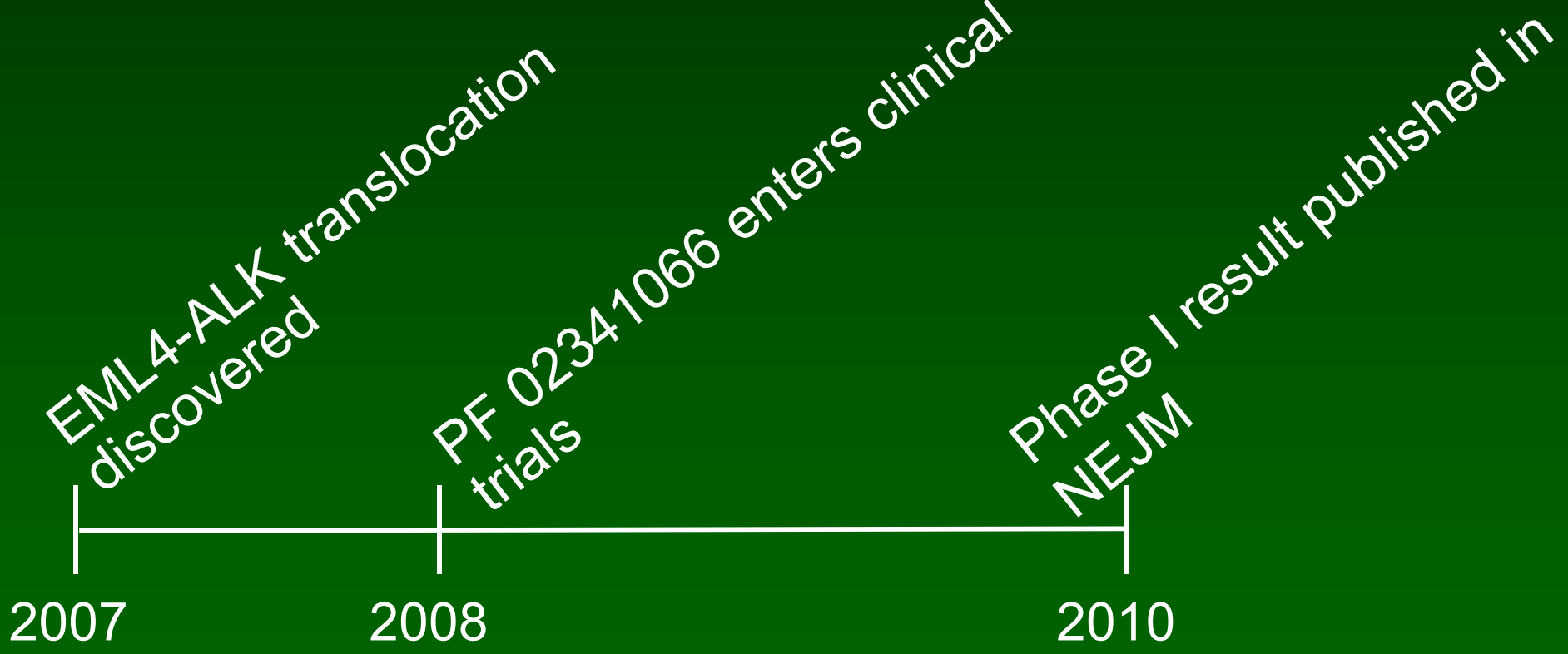
Kwak et al N Engl J Med 2010; 363:1693

Crizotinib in NSCLC

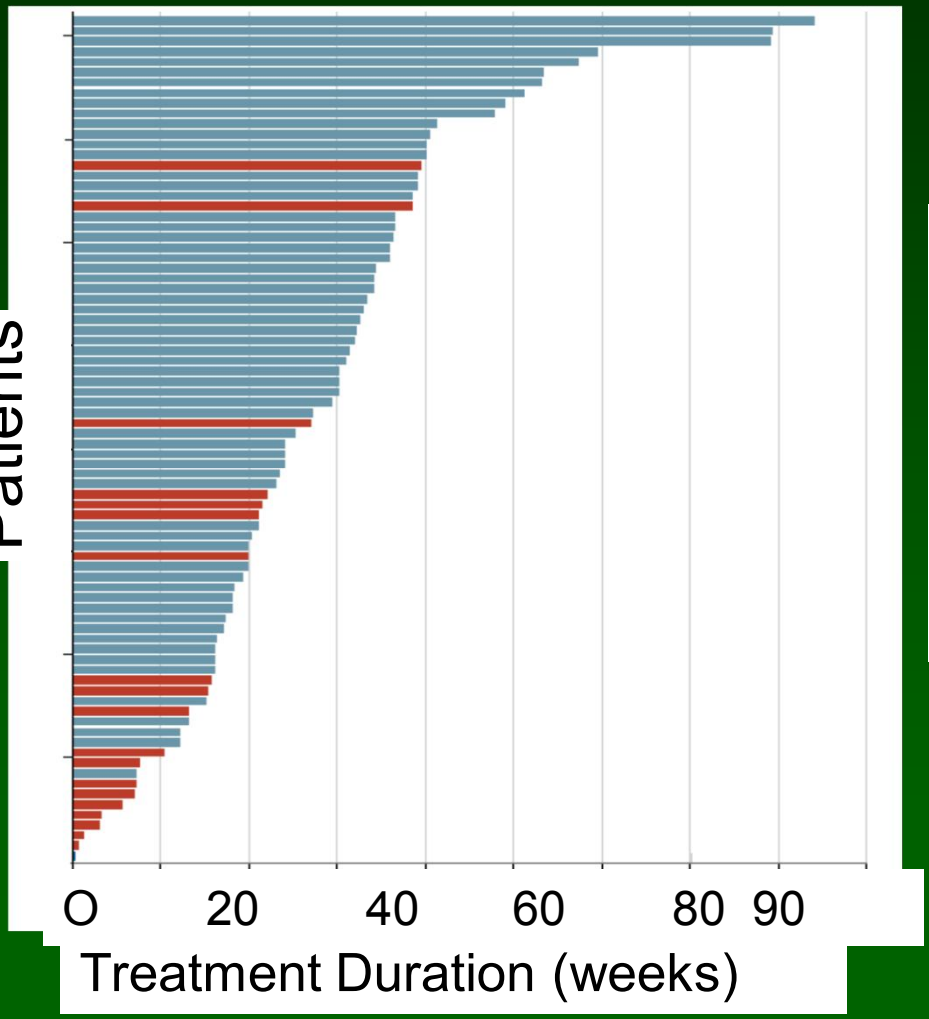


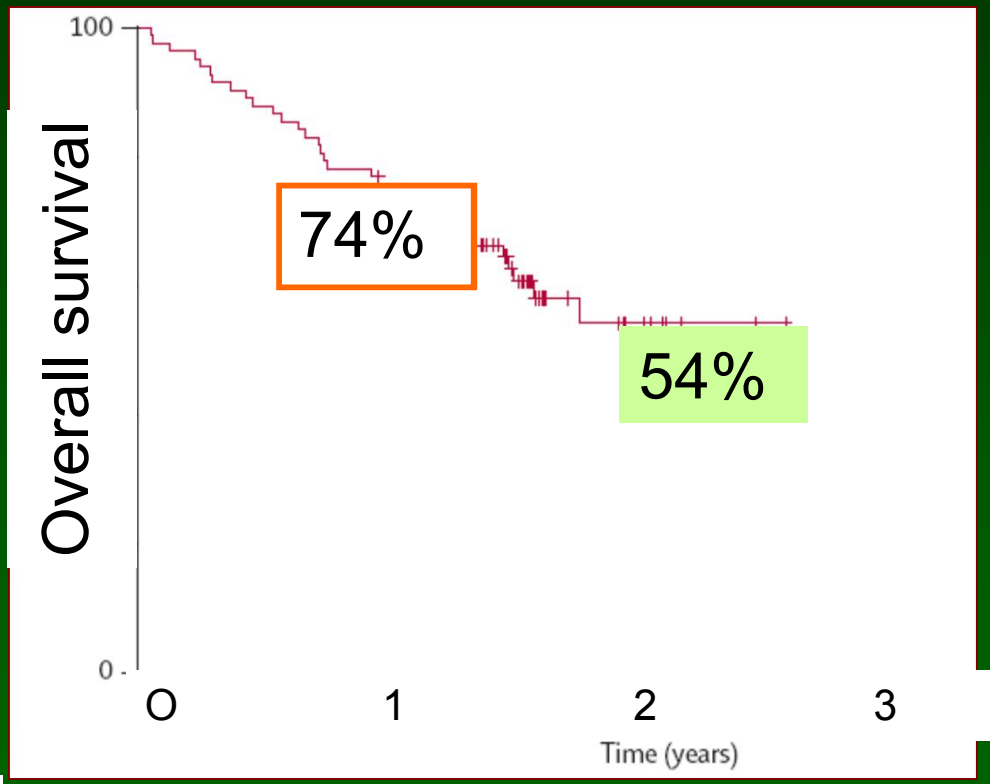


EML4-ALK Timeline



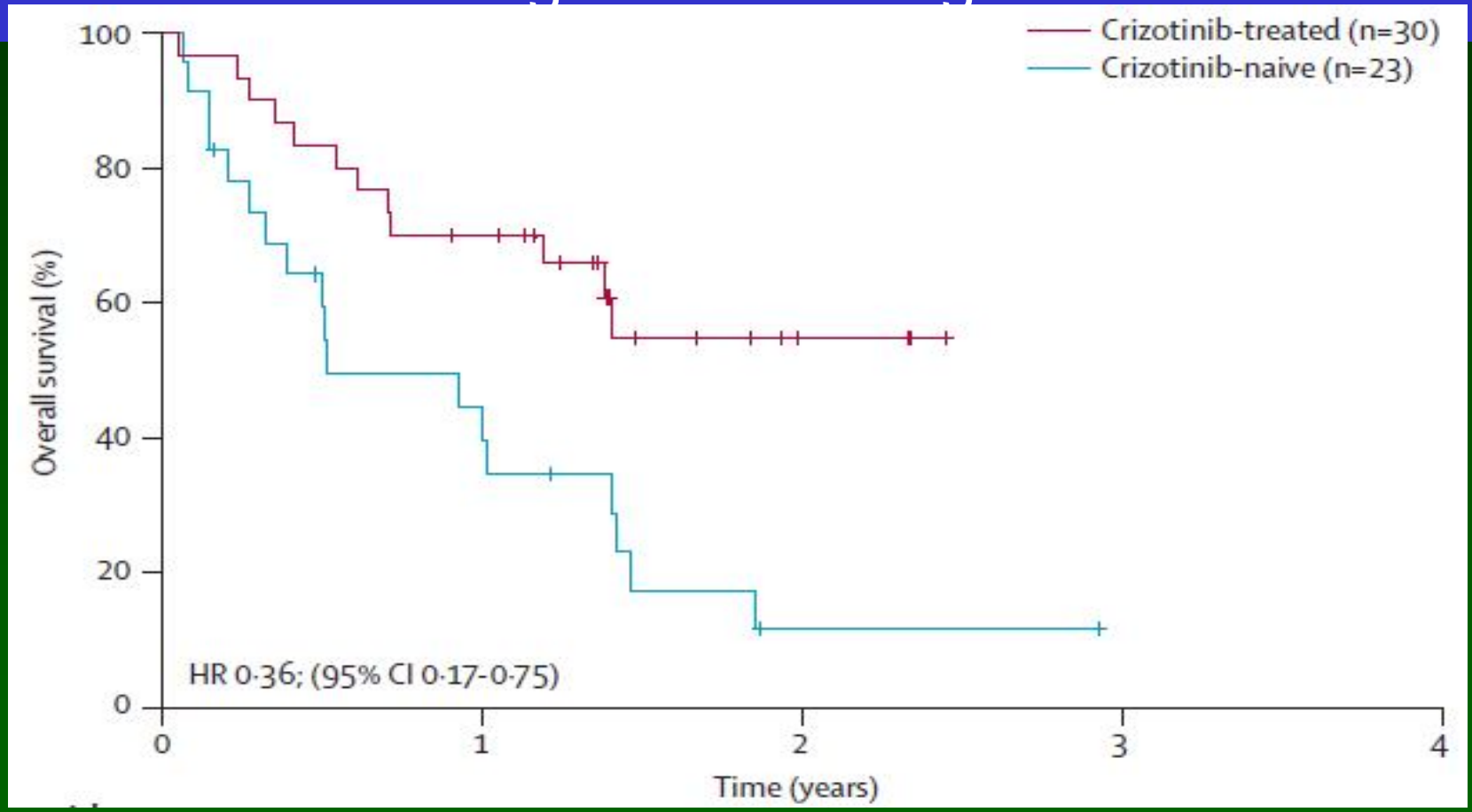
Duration of Treatment and Survival in NSCLC Patients Treated with *Crizotinib*





N Engl. J Med. 2010;363:1693-1793
Lancet Oncol 2011; 12: 1004–12

Crizotinib Prolongs Survival of Patients With NSCLC Harboring *ALK* rearrangement

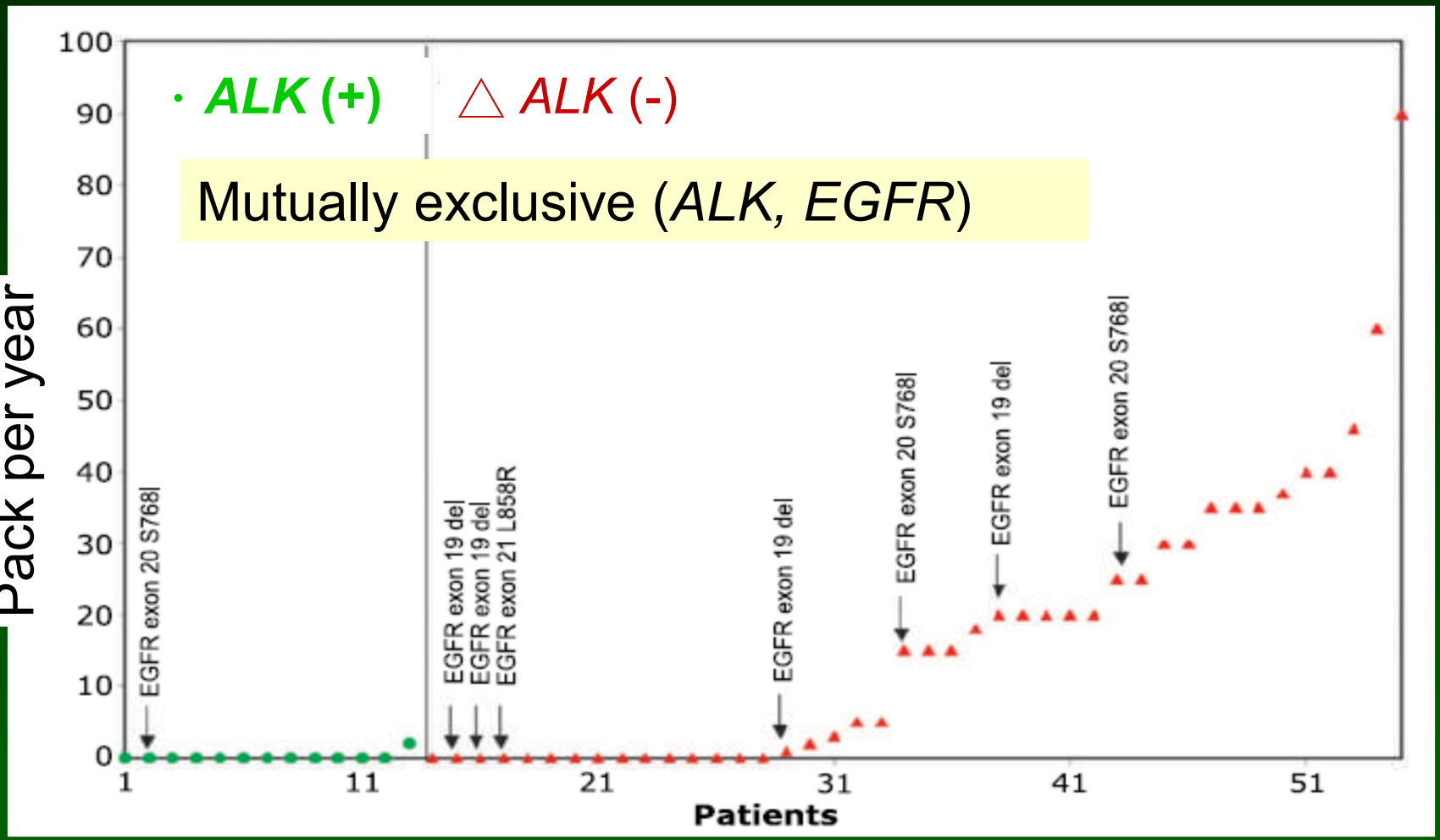


Lancet Oncol 2011; 12: 1004–12

Adverse Events in the 82 Patients (Phase I)

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Total
	no. of patients (%)				
Any adverse event†					
Nausea	43 (52)	1 (1)	0	0	44 (54)
Diarrhea	38 (46)	1 (1)	0	0	39 (48)
Vomiting	35 (43)	1 (1)	0	0	36 (44)
Visual disturbance	34 (41)	0	0	0	34 (41)
Constipation	18 (22)	2 (2)	0	0	20 (24)
Peripheral edema	13 (16)	0	0	0	13 (16)
Dizziness	12 (15)	0	0	0	12 (15)
Decreased appetite	11 (13)	0	0	0	11 (13)
Fatigue	8 (10)	0	0	0	8 (10)

N Engl. J Med. 2010;363:1693-1793

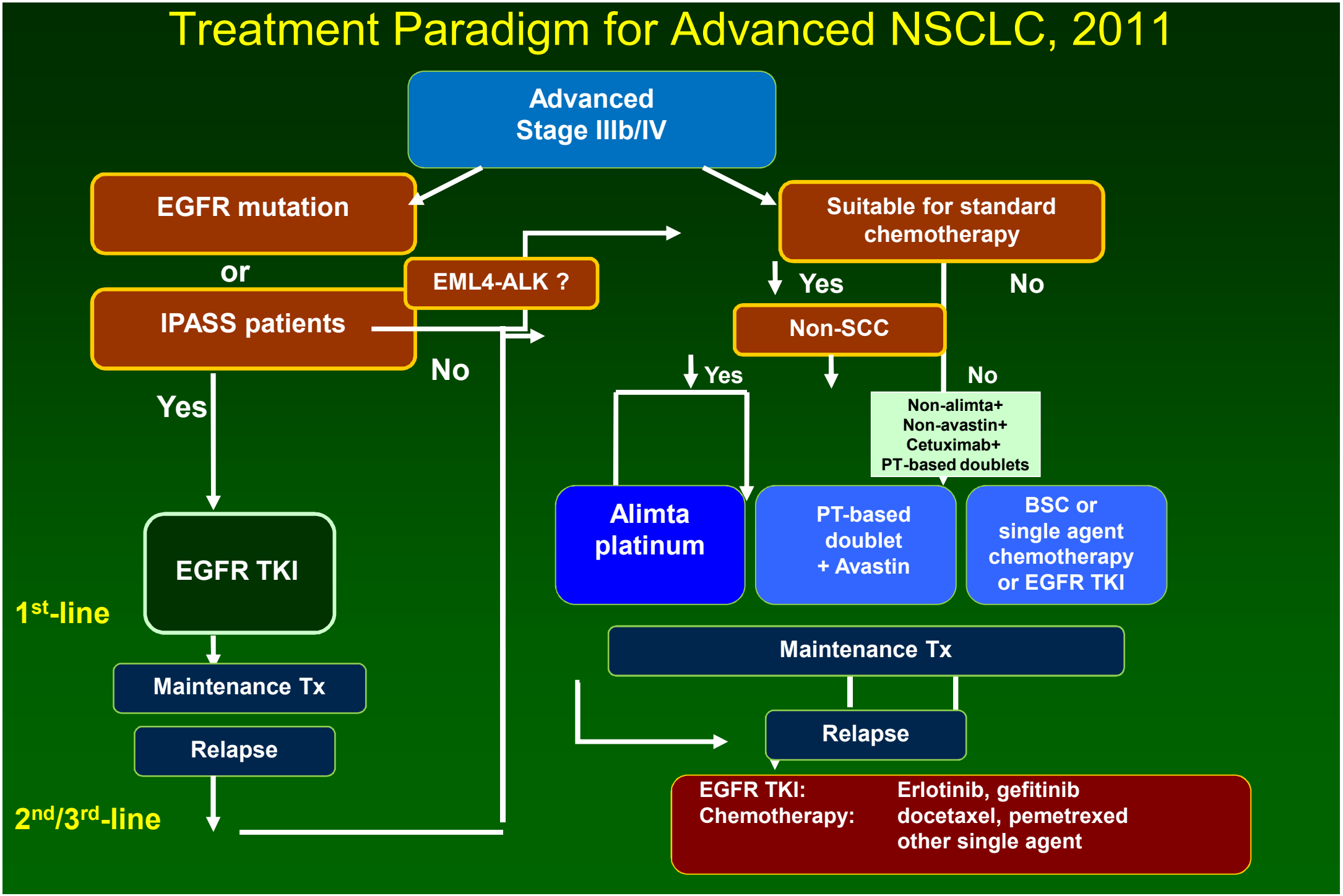


Clin Cancer Research 2011;July 14

如何選擇治療藥物？

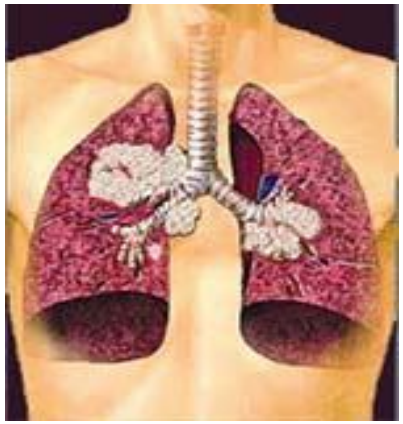
- 身體狀況佳，可優先考慮化學治療(含鉑)。四種新藥之效果大致相當，但劑量、用藥間隔、合併用藥、副作用有所不同。
- 老年人或體能狀況差，可考慮單一化學藥物治療(不含鉑)。
- 肺腺癌(尤其是女性、不吸菸者)可考慮及早使用艾瑞莎或得舒緩。

Treatment Paradigm for Advanced NSCLC, 2011



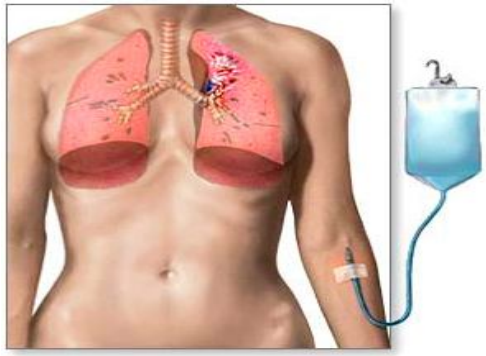
肺癌療法 -『整合治療』

手術



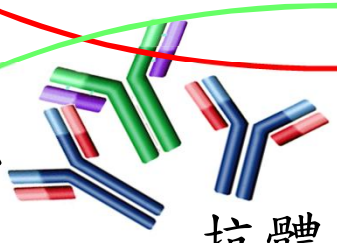
放射治療

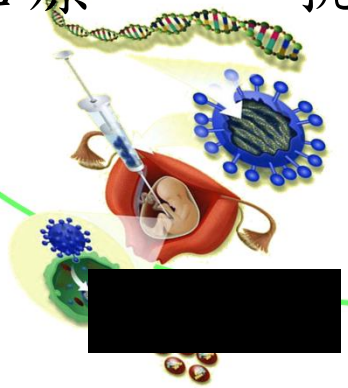
化學治療
藥物

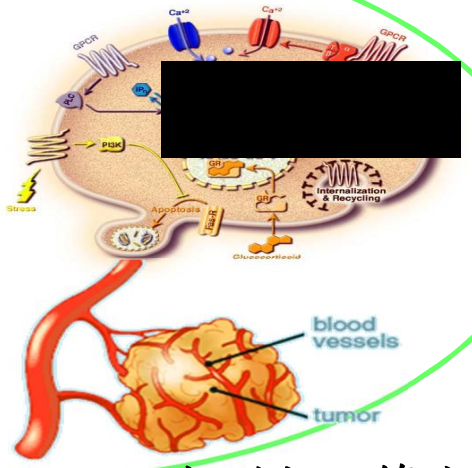


標靶
治療

抗體







抑制血管新生

Thanks for your attention