非小細胞肺癌用藥
Crizotinib (Xalkori®)
健保價申覆口頭報告

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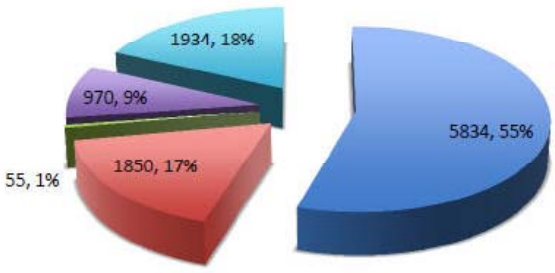
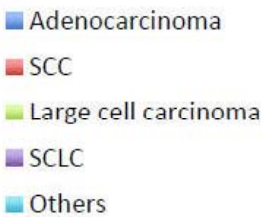
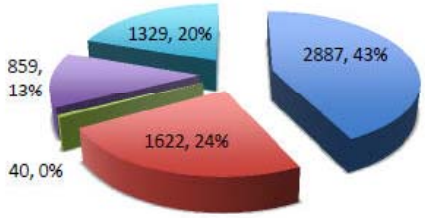
Jun 18, 2015

NSCLC Histology – Taiwan

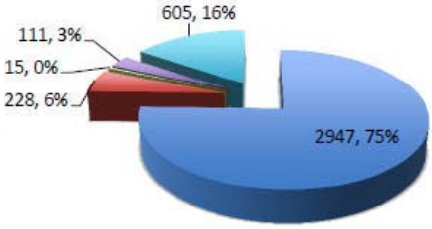


Overall (n = 10643)





Male (n = 6737)



Female (n = 3906)

癌症登記資料 民國98年

標靶治療

- **標靶：driver mutations-影響細胞生長及存活的信息傳導路徑中某一個基因發生突變。這個突變的基因可以讓正常細胞變成腫瘤並且存活下來**(癌細胞過度依賴此腫瘤蛋白，又稱 oncogene addiction)
- **標靶治療的藥物，大多是以小分子化合物，作用在 driver mutations 。**
- **作用機轉特定，效果增加，副作用減少**

肺癌標靶治療主要的藥物

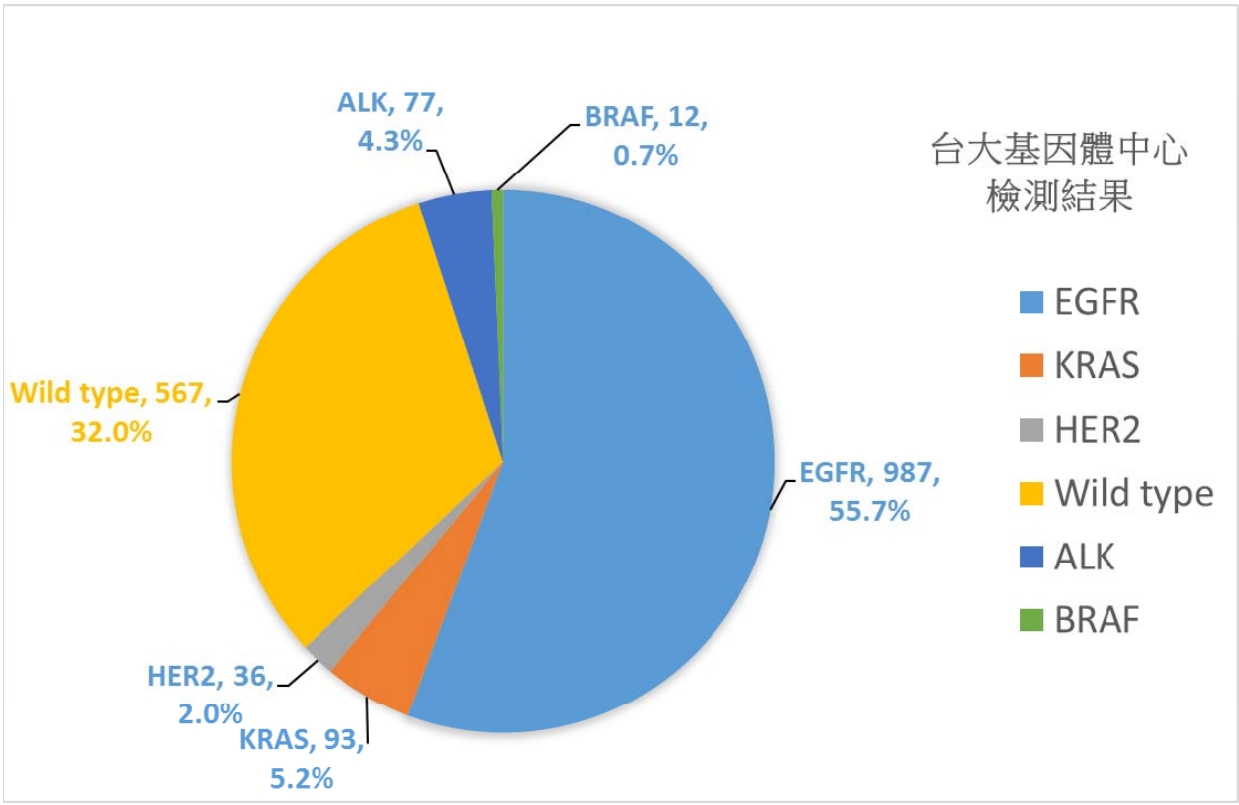
- 上皮生長因子接受器抑制劑(EGFR TKI):

  gefitinib (Iressa)、erlotinib (Tarceva) 、afatinib (Giotrif)

- 間變性淋巴瘤激酶抑制劑 (ALK TKI):

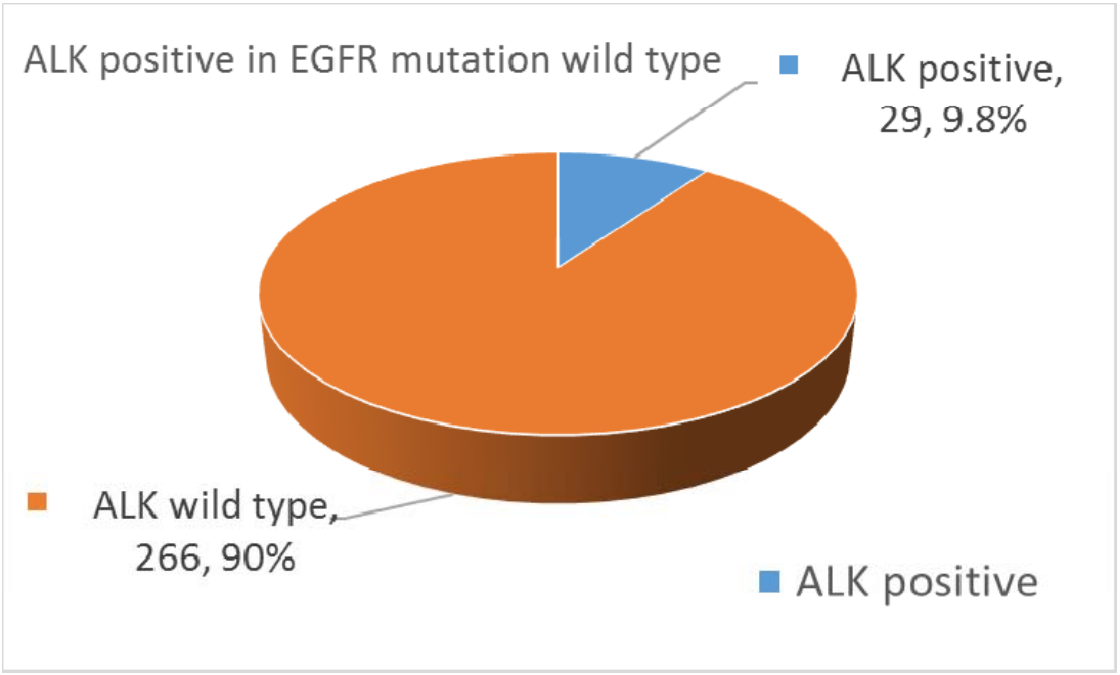
  crizotinib (Xalkori)

台大基因體中心檢測 Lung adenocarcinoma 病人中 ALK positive 比率為 4.3%



ALK 陽性的病人不多，與Iressa 使用族群不同。

台大基因體中心檢測 EGFR mutation wild type 病人中 ALK positive 比率為 9.8%



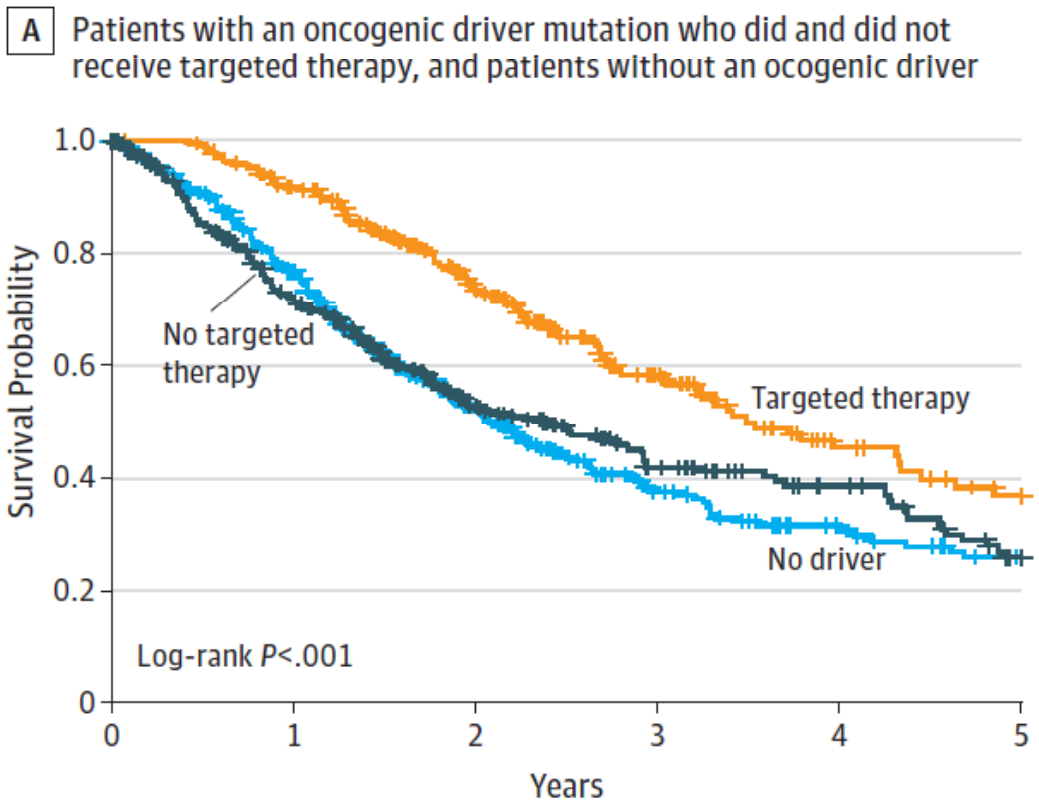
ALK positive 病人特性

Total 29 patients

Characteristics	ALK No (%)	p-value
Age, median	53 y/o (30-78)	
Age (years)		
≤ 65	25 (86%)	0.002
> 65	4 (14%)	
Gender		
Male	12 (41%)	0.331
Female	17 (59%)	
Smoking status		
Non-smokers	21 (72%)	0.167
Current/former smoker	8 (28%)	

ALK 陽性的病人多為不吸菸、年輕的族群。

Lung Adenocarcinoma pts with drivers receiving a matched targeted agent lived longer



Kris et al JAMA 2014

Crizotinib vs. 化學治療　用於第二線治療

Key entry criteria
- *ALK*+ by central FISH testing[a]
- Stage IIIB/IV NSCLC
- 1 prior chemotherapy (platinum-based)
- ECOG PS 0–2
- Measurable disease
- Treated brain metastases allowed

RANDOMIZE[b]

- Crizotinib 250 mg BID PO, 21-day cycle (n=159)
- Pemetrexed 500 mg/m² or Docetaxel 75 mg/m² IV, day 1, 21-day cycle (n=159)
  - CROSSOVER TO CRIZOTINIB ON PROFILE 1005

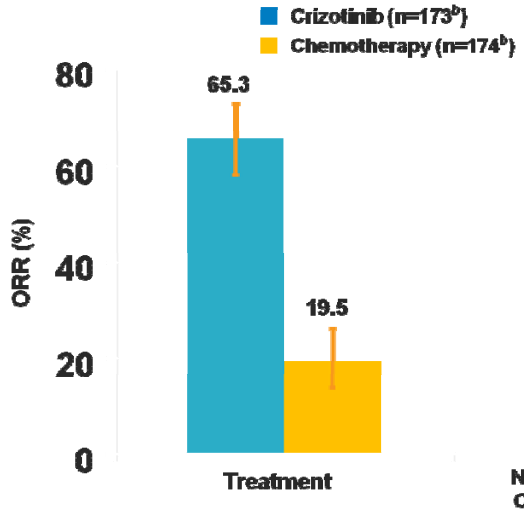
Endpoints
- Primary
  - PFS (RECIST 1.1, independent radiology review)
- Secondary
  - ORR, DCR, DR
  - OS
  - Safety
  - Patient reported outcomes (EORTC QLQ-C30, LC13)

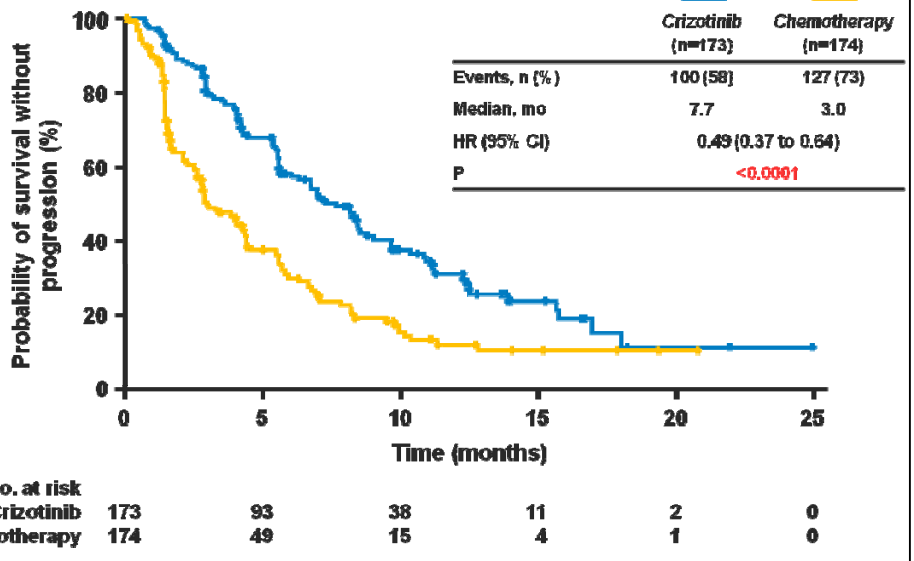
Shaw et al NEJM 2013

[a]*ALK* status determined using standard *ALK* break-apart FISH assay
[b]Stratification factors: ECOG PS (0/1 vs 2), brain metastases (present/absent), and prior EGFR TKI (yes/no)

ORR 及 PFS by Independent Radiologic Review

ORR ratio: 3.4 (95% CI: 2.5 to 4.7); P<0.0001





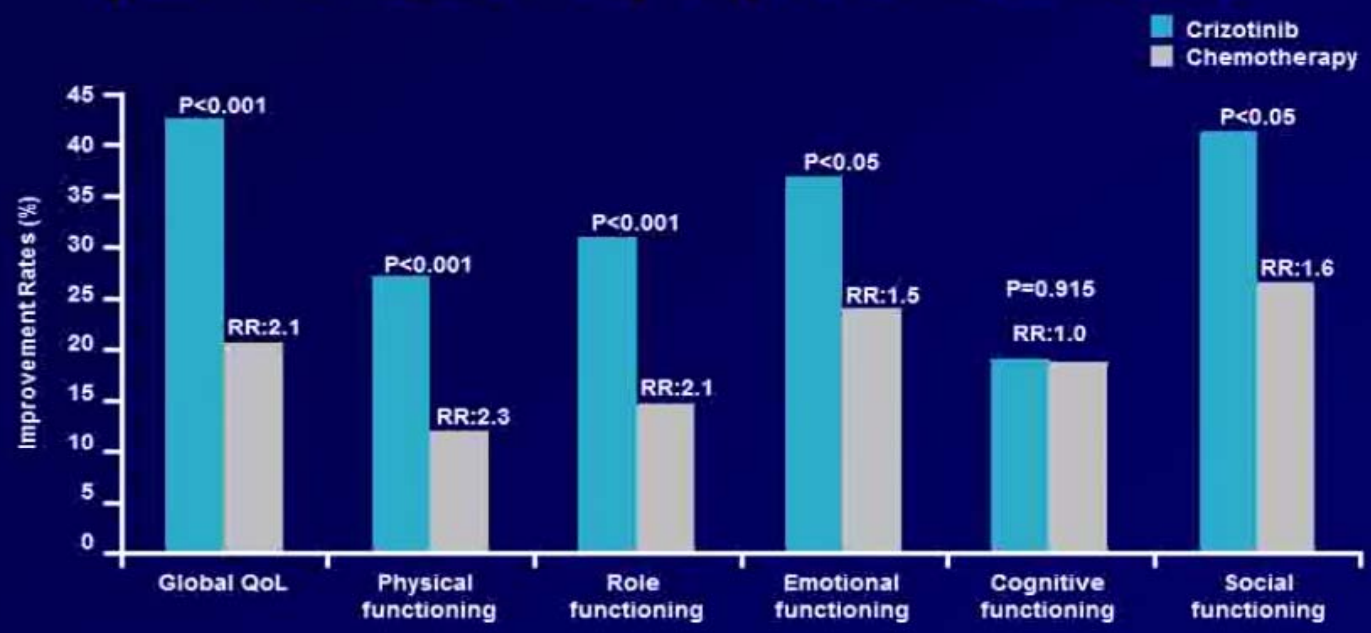
	Crizotinib (n=173)	Chemotherapy (n=174)
Events, n (%)	100 (58)	127 (73)
Median, mo	7.7	3.0
HR (95% CI)	0.49 (0.37 to 0.64)	
P	<0.0001	

No. at risk						
Crizotinib	173	93	38	11	2	0
Chemotherapy	174	49	15	4	1	0

[a]RECIST v1.1; [b]ITT population; [c]as-treated population

第二線Crizotinib vs. 化學治療 Global QOL

Functioning Domains and Global QOL (EORTC–QLQ-C30) Improvement Rates

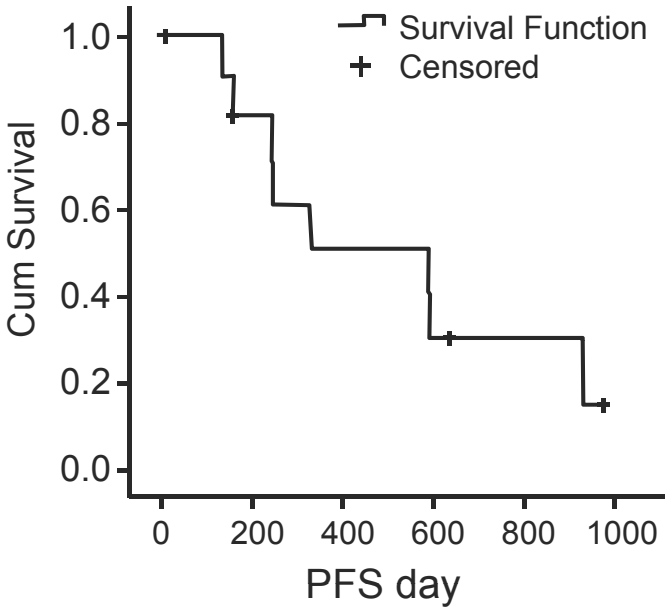


- A significantly greater percentage of patients in the crizotinib versus the chemotherapy arm showed improvements for global QOL, physical, role functioning and emotional functioning

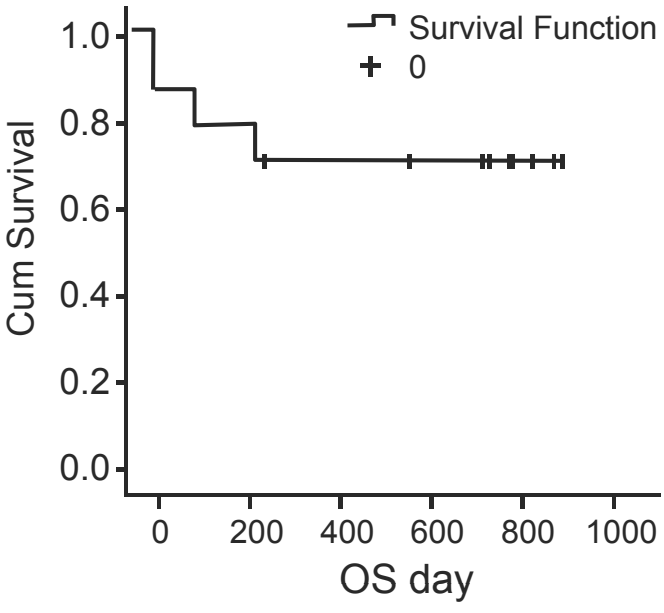
臺大醫院研究者發起之Crizotinib 臨床試驗

N＝12

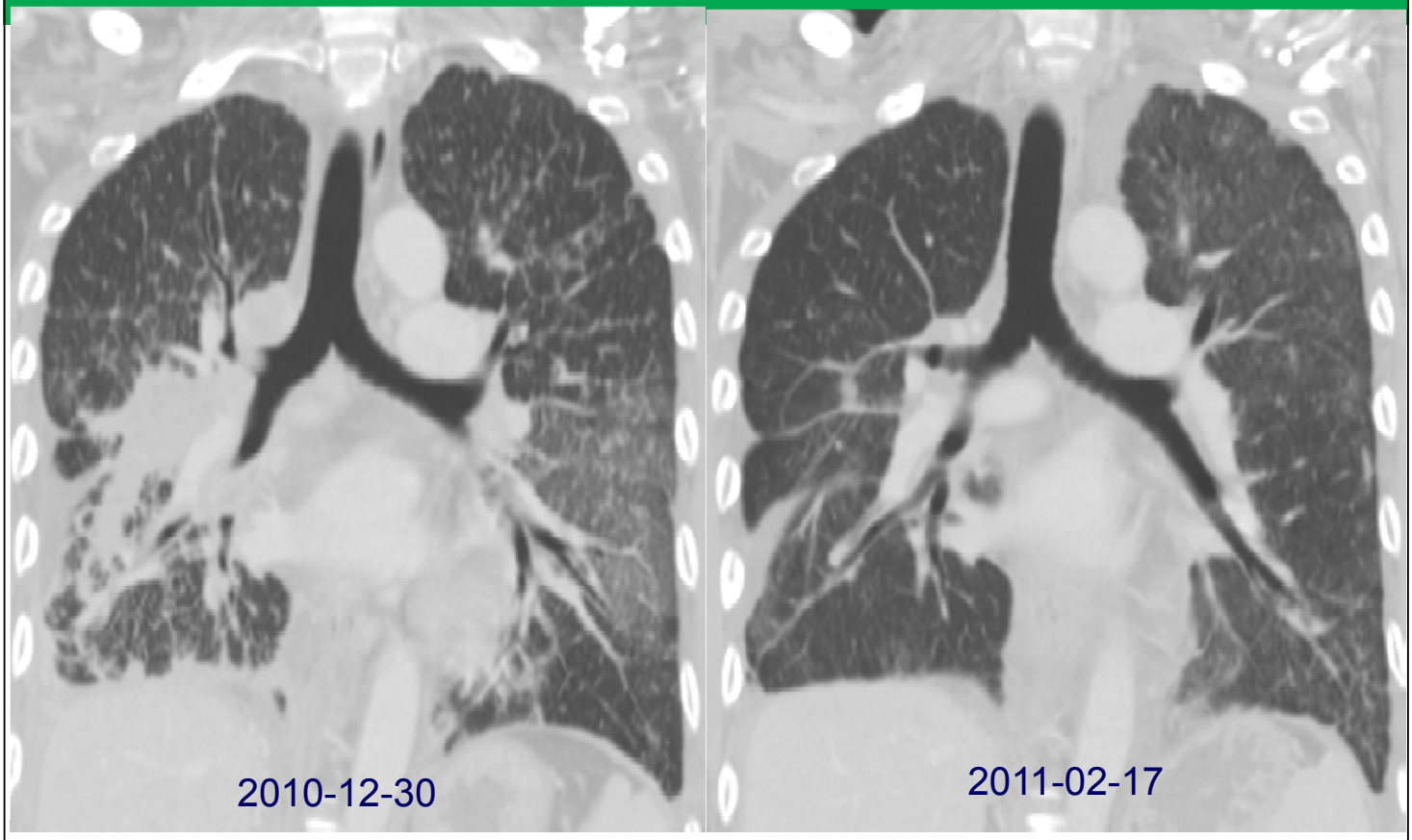
Survival Function



Survival Function

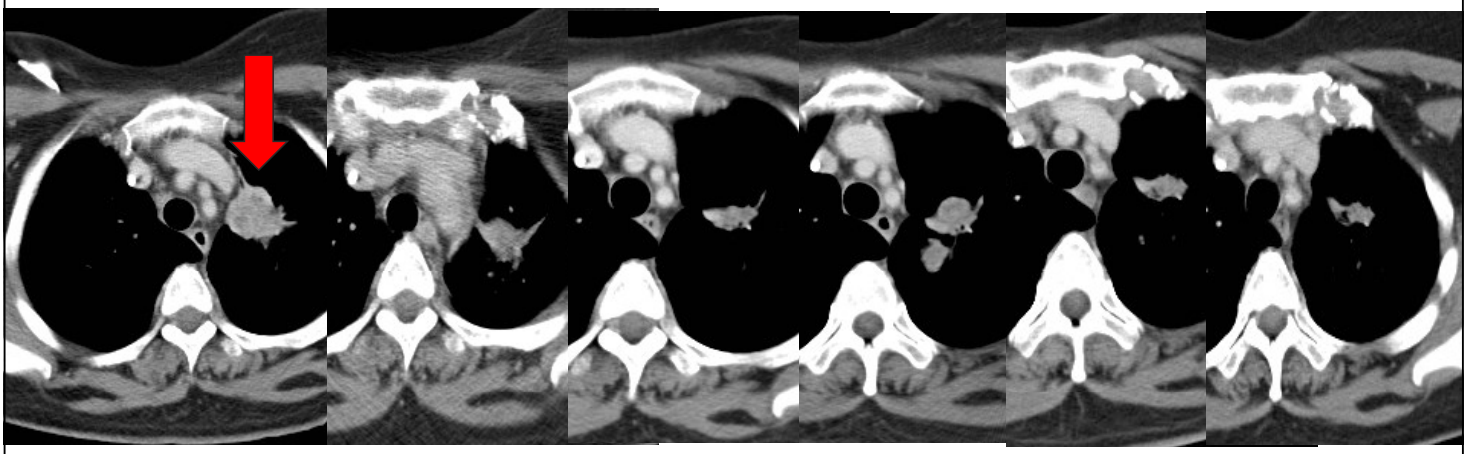


Crizotinib in Critical Patient



49 y/o man, never smoker, diagnosed in 2009/10, 6th line crizotinib

34 y/o female, brain, pelvic metastases, diagnosed in 2012



2013/3 2013/6 2013/9 2014/2 2014/5 2015/5


Thank you!