

# Testing for Molecular Markers and Sequencing of Treatments in Advanced NSCLC

## Fit Elderly Man with Metastatic Squamous Cell NSCLC



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## Conflicts of Interest

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### Dr. Thomas Hensing

Speaker's Bureau: Eli Lilly, Genentech

### Dr. David Jackman

Consultant: Foundation Medicine

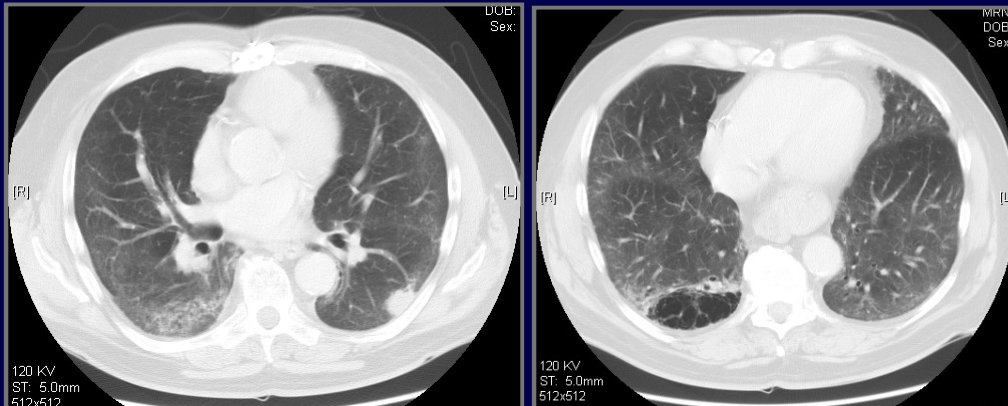
## Stage IV NSCLC, Background

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- 76 year-old male retired insurance broker with significant PMH newly diagnosed with advanced NSCLC, squamous histology
- Previously smoked 2 ppd x 40 years, quit 1991
- Cough w/green sputum x few weeks, mentioned to PCP
- CXR: peripheral LLL nodule
- CT: 3.3 cm subpleural mass superior segment LLL; nodes in precarinal window and AP window borderline enlarged
- CT-guided Bx: squamous cell NSCLC

## Imaging, 76 yo man with Squamous NSCLC

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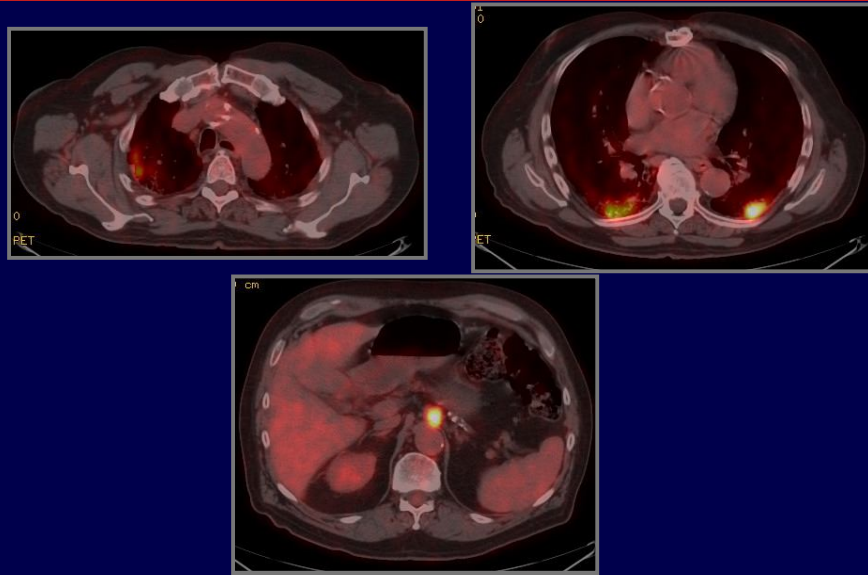


## Stage IV NSCLC, Background (cont.)

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- Referred to thoracic surgeon
- PET CT reveals hypermetabolism in LLL lesion, SUV 14, but also uptake of 5.5 in RUL and 9.6 in R lung base, possibly representing pulmonary fibrosis, but also 2.1 cm PET avid lesion in upper abdomen

## 76 yo man with Squamous NSCLC: PET/CT



### Stage IV NSCLC, Background (cont.)

- Ultrasound (U/S) guided-guided biopsy (Bx) of abdominal lesion: squamous NSCLC
- Past medical history (PMH):
  - coronary artery bypass graft (CABG) x 3 in 1993
  - carotid atherosclerosis (no surgery needed per vasc surgeon)
  - migraines
  - diverticulosis
  - misc.
- Stage IV NSCLC, good performance status

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Would you consider it important to send for molecular markers in this patient? If so, which test(s)?

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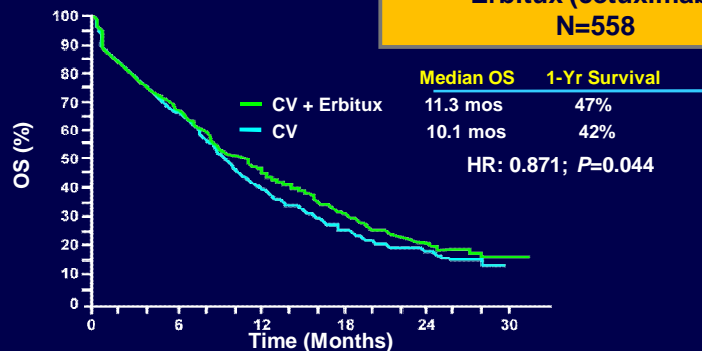
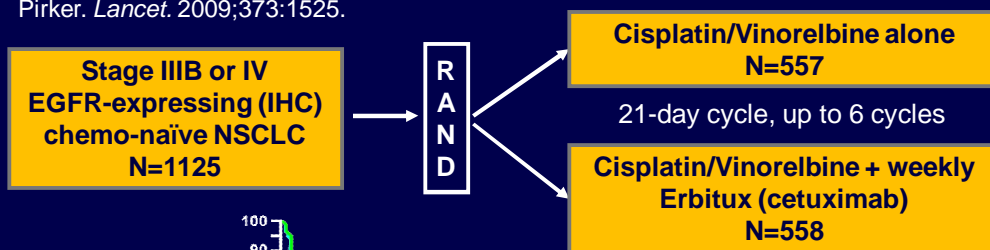
What treatment approach would you generally advocate for good PS advanced squamous NSCLC?

How much of a factor is his age and PMH?

Have you had a particular challenge with low blood counts in older patients receiving the carboplatin/gemcitabine regimen?

## FLEX: Phase III Trial of Chemo ± Erbitux (Cetuximab) in EGFR IHC-Positive Advanced NSCLC

Pirker. *Lancet*. 2009;373:1525.



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Has the FLEX trial led to much use of Erbitux (cetuximab) in combination with chemo for initial treatment of advanced NSCLC?

## FLEX Trial: Safety Profile

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<u>Grade 3/4 AEs</u>	<u>Chemotherapy + Cetuximab (N=548)</u>	<u>Chemotherapy Alone (N=562)</u>	<u>P Value</u>
Any event	91%	86%	0.01
Neutropenia	52%	52%	0.67
Febrile neutropenia	22%	15%	0.0086
Anemia	13%	17%	0.21
Acne-like rash (grade 3 only)*	10%	<1%	0.0001
Diarrhea	5%	3%	0.047
Infusion reactions	4%	1%	0.017
Treatment-related deaths	3%	2%	NR

\*No grade 4 acne-like rash.

NR=not reported.

Pirker. *Lancet*. 2009;373:1525.

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Are there any encouraging signals for biomarker-defined subsets who might benefit more or less with Erbitux (cetuximab)?

### Stage IV NSCLC, Response to Treatment

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- He receives carboplatin and gemcitabine chemotherapy
- He has significant cytopenias and requires dose reduction, also has some significant but not prohibitive fatigue, but otherwise tolerates treatment well.
- CT after two cycles shows a good minor response
- CT after four cycles shows stable disease
- Cumulative myelosuppression and fatigue, but he could continue with ongoing treatment

What is your generally approach for maintenance therapy vs. a break from treatment in this setting?  
Continuation maintenance (single agent gemcitabine?), switch maintenance, or follow off therapy?

## How Long to Treat? Four Cycles vs. More

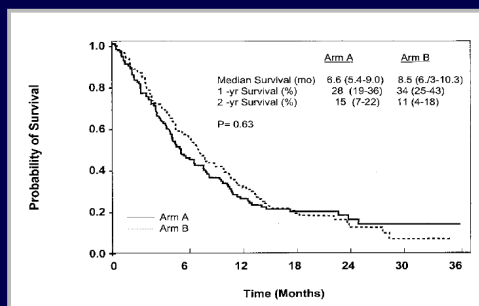
Socinski, J Clin Oncol , 2002

Advanced NSCLC  
Good Perf Status  
N=230

R  
A  
N  
D

Carbo/Taxol (Paclitaxel)  
x 4 cycles only

Carbo/Taxol (Paclitaxel)  
ongoing until progression



- All efficacy endpoints equal
- Only difference is more neurotoxicity with ongoing Rx

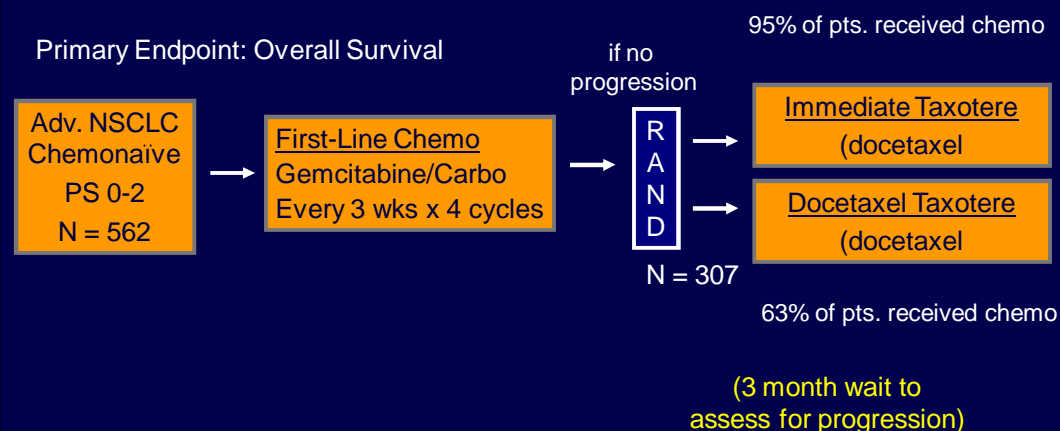
## Alimta (Pemetrexed) vs. Placebo: Efficacy by Histologic Groups

	Median Prog-Free Surv, mos			CR+PR+SD*, %			Median OS, mos		
	Pem	Plac	p-value	Pem	Plac	p-value	Pem	Plac	p-value
<b>Non-squam</b> (n=482)	4.37	1.84	<0.00001	54.3	26.6	<0.001	14.4	9.4	0.005
<b>Adeno</b> (n=329)	4.60	2.66	<0.00001	58.2	29.6	<0.001	16.4	11.7	0.091
<b>Large cell</b> (n=20)	4.53	1.45	0.104	30.0	25.0	0.999	9.1	5.5	0.154
<b>Other</b> (n=133)	4.11	1.58	0.0001	47.5	18.9	0.004	11.3	7.0	0.005
<b>Squamous</b> (n=181)	2.43	2.50	0.896	33.3	34.5	0.999	9.6	11.9	0.231

\*Clinical response (CR+PR+SD) was significantly improved with pemetrexed vs placebo in the intent-to-treat population (49% vs 29%,  $p < 0.001$ ).

Ciuleanu, Lancet 2010.

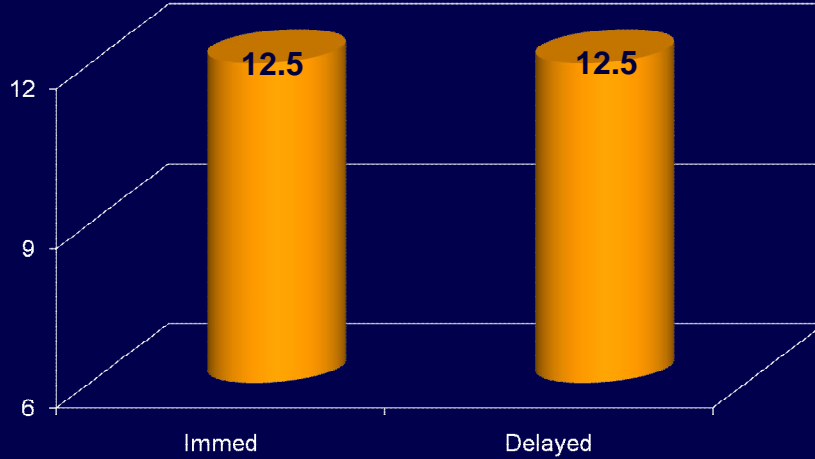
## Immediate vs. Delayed Second-Line Docetaxel (Taxotere)



Fidas, J Clin Oncol 2009

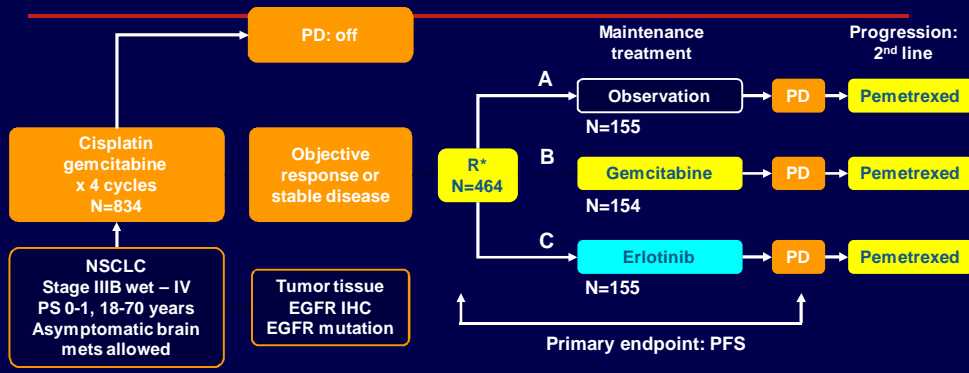
## Survival Among Patients Actually Receiving Second Line Chemotherapy

Median Overall Survival (months)



Fidias, J Clin Oncol 2009

## IFCT-GFPC 0502 study design



**Induction chemo:** cisplatin 80mg/m<sup>2</sup> d1  
+ gemcitabine 1,250mg/m<sup>2</sup> d1, d8  
**Arm B:** gemcitabine 1,250mg/m<sup>2</sup> d1, d8 /3 wks  
**Arm C:** erlotinib 150mg daily

\*Stratification factors:

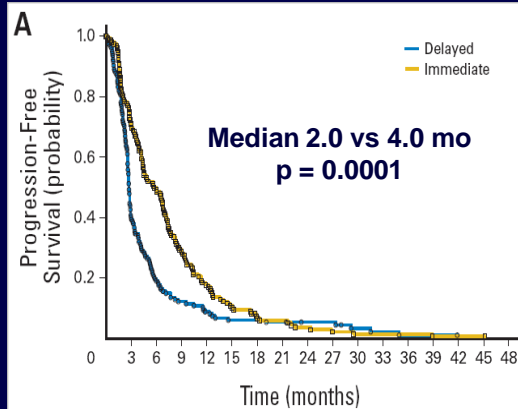
- gender
- histology: adenocarcinoma vs other histology
- smoking status: non-smokers vs current/former smokers
- center
- response vs stabilization to induction chemotherapy

Perol, ASCO 2010, A# 7507

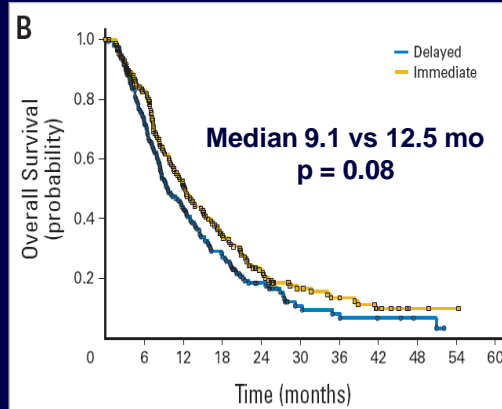
EGFR = epidermal growth factor receptor  
IHC = immunohistochemistry; PD = progressive disease

## Immediate vs. Delayed Second-Line Taxotere (Docetaxel) Efficacy

Progression-Free Survival



Overall Survival

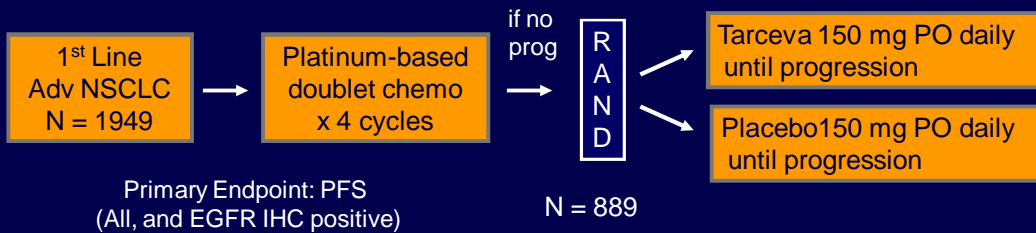


Fidias, J Clin Oncol 2009

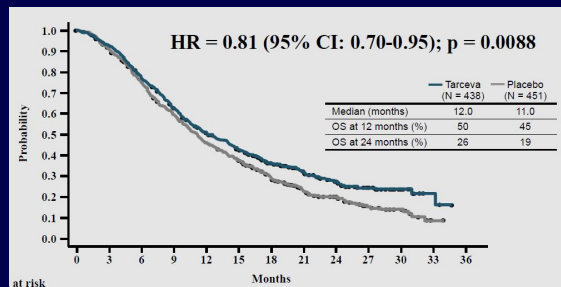
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Are the data with Taxotere (docetaxel) comparable to those seen with FDA approved options of Alimta (pemetrexed) and Tarceva (erlotinib) as maintenance therapy for advanced NSCLC?

# SATURN: Maintenance Tarceva (Erlotinib) vs. Placebo after First Line Chemo for Four Cycles



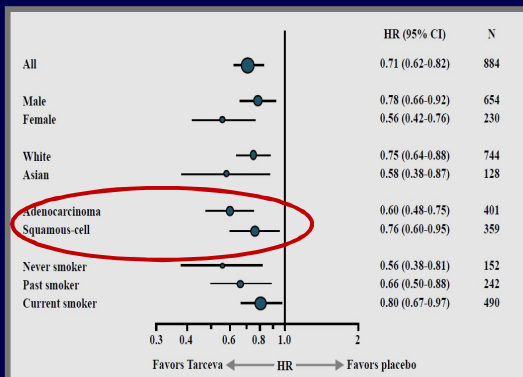
## Overall Survival



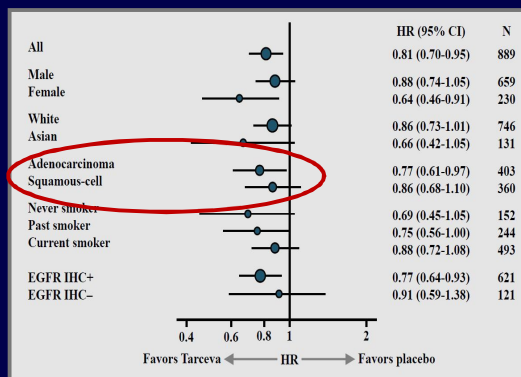
Cappuzzo, Lancet Oncology, 2010

# SATURN: Efficacy of Maintenance Tarceva by Patient Subgroup

## Progression-Free Survival by Subgroup



## Overall Survival by Subgroup



Cappuzzo, Lancet Oncology, 2010

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