

## Lung Cancer: State of the Art in 2011

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### Financial Disclosure

- I have no significant relationships to disclose.

### Topics to be Covered

- Screening for lung cancer
- NSCLC
  - First line therapy: Histologic and molecular variables
  - New drugs
  - Elderly
  - Maintenance
- SCLC
  - Amrubicin

## STAGING

### Staging Changes: T,N

- T1 – subdivided into T1a (<2cm), T1b (2-3cm)
- T2- subdivided: T2a (3-5cm), T2b (5-7cm)
- T3-
  - Tumors >7cm
  - includes multiple nodules in the same lobe (down from T4).
- T4- second nodule, non-primary lobe, ipsilateral (down from M1)
  - Pleural dissemination, pericardial or pleural effusion – now M1
- N-descriptors: No change

### M Descriptor

- Ipsilateral nodules in different lobes: down to T4
- Nodules in contralateral lung: M1a
- Pleural, pericardial effusions: M1a
- Distant disease: M1b

## Staging System

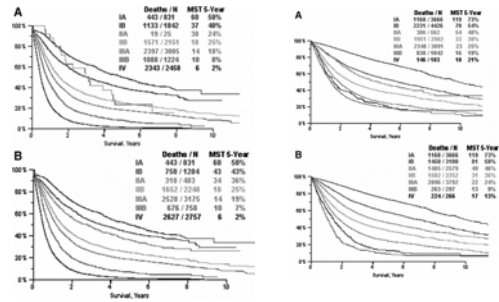
**TABLE 4.** Descriptors, Proposed T and M Categories, and Proposed Stage Groupings

Sixth Edition T/M Descriptor	Proposed T/M	N0	N1	N2	N3
T1 (≤2 cm)	T1a	IA	IIA	IIIA	IIIB
T1 (>2-3 cm)	T1b	IA	IIA	IIIA	IIIB
T2 (≤5 cm)	T2a	IB	IIA	IIIA	IIIB
T2 (>5-7 cm)	T2b	IIA	IIIB	IIIA	IIIB
T2 (>7 cm)	T3	IIIB	IIIA	IIIA	IIIB
T3 invasion	IIIB	IIIA	IIIA	IIIB	IIIB
T4 (same lobe nodules)	IIIB	IIIA	IIIA	IIIB	IIIB
T4 (extension)	T4	IIIA	IIIA	IIIB	IIIB
M1 (ipsilateral lung)	IIIA	IIIA	IIIB	IIIB	IIIB
T4 (pleural effusion)	M1a	IV	IV	IV	IV
M1 (contralateral lung)	IV	IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

Cells in bold indicate a change from the sixth edition for a particular TNM category.

JTO, August 2007

## Survival by the New System



JTO Aug 2007

Clinical

Pathological

## SCREENING

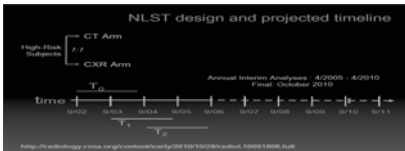
## SCREENING

Prospective, randomized trial comparing low-dose helical CT screening to chest x-ray screening with the endpoint of lung cancer specific mortality in high risk participants

### Eligibility

- Age 55-74
- Asymptomatic current or former smoker, 30 pack year smoking history
- Former smokers - quit within preceding 15 years
- No prior lung cancer diagnosis
- No evidence of other cancer within preceding 5 years

<http://ir.adiology.rma.org/content/early/2010/10/28/radiol.10091808.full>



## Compliance

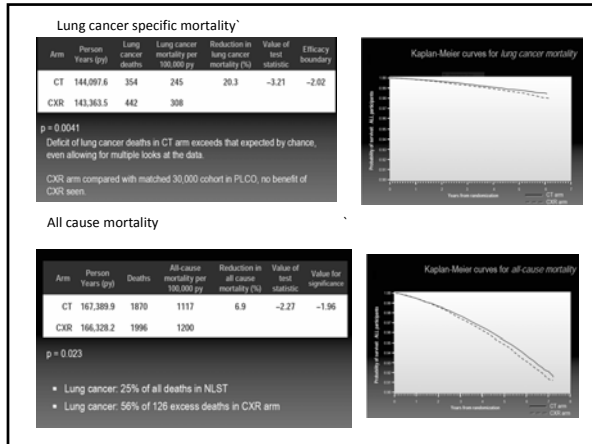
Study Year	Helical CT		Chest X-ray		Total	
	Expected	Screened	Expected	Screened	Expected	Screened
T0	26,713	98.5%	26,722	97.5%	53,435	98.0%
T1	26,282	94.0%	26,398	91.3%	52,680	92.6%
T2	25,935	92.9%	26,097	89.5%	52,032	91.2%

## Positive Screens

	Low dose helical CT			CXR		
	Number screened	Number positive	% Positive	Number screened	Number positive	% Positive
Screen 1	26,314	7,193	27.3	26,049	2,387	9.2
Screen 2	24,718	6,902	27.9	24,097	1,482	6.2
Screen 3	24,104	4,054	16.8**	23,353	1,175	5.0**
All screens	75,136	18,149	24.2	73,499	5,044	6.9

## Lung cancer detected

Screening Result	Low Dose Helical CT			CXR		
	Screen 1 N (%)	Round 2 N (%)	Round 3 N (%)	Round 1 N (%)	Round 2 N (%)	Round 3 N (%)
Total Positives	7,193 (100)	6,902 (100)	4,054 (100)	2,387 (100)	1,482 (100)	1,175 (100)
Lung cancer	270 (4)	168 (2)	211 (5)	136 (6)	65 (4)	78 (7)
No lung cancer	6,923 (96)	6,734 (98)	3,843 (95)	2,251 (94)	1,417 (96)	1,097 (93)



### NLST Conclusions and Comments

- NLST demonstrated 20% reduction in risk of lung cancer mortality.
- NNT = 300 (superior to mammography)
- Cautions:
  - Experienced institutions
  - Results appropriate for population screened
  - Very high false positive rate

## Adjuvant Chemotherapy

### ADJUVANT CHEMOTHERAPY FOR N-SCLC: A META-ANALYSIS

- Analysis of 52 randomized trials with 9387 patients and 7151 deaths.
- Surgery vs Surgery and Chemo: Hazard ratio of 0.87 (p=0.08) 13% reduction in risk of death 5% benefit at 5 years
- Surgery-XRT +/- chemotherapy. Hazard ratio of 0.94 (p=0.76), 6% reduction in risk of death. 2% benefit at 2 and 5 years

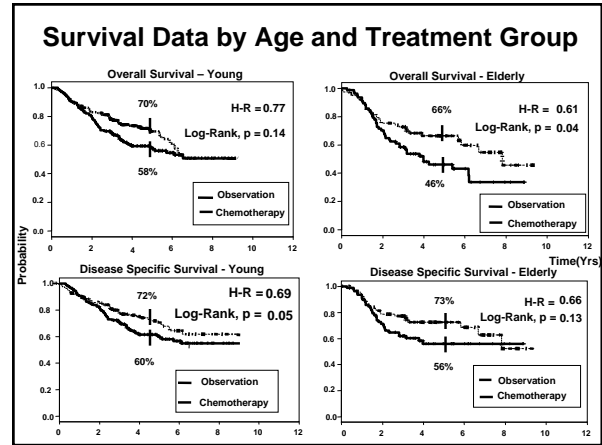
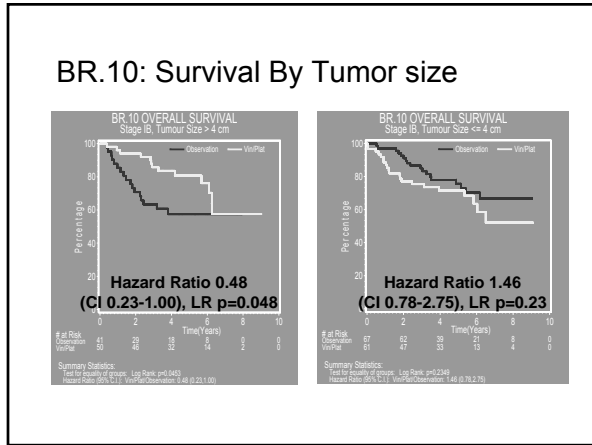
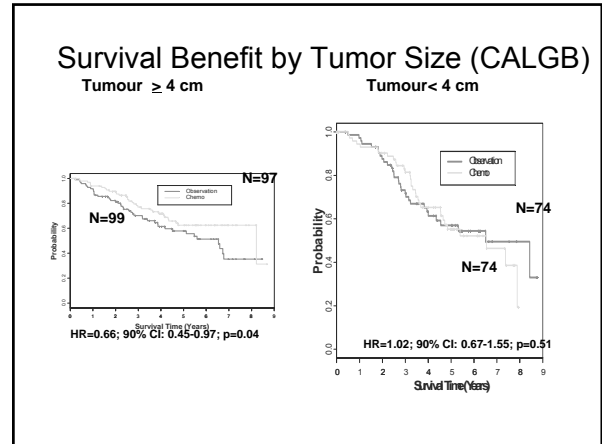
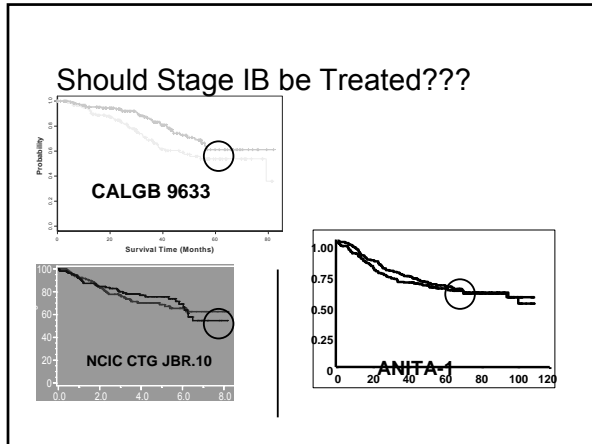
BMJ 311: 899-909, 1995

### Summary of Recent Adjuvant Trials

	N	HR (95% CI)
■ BMJ meta	1394	0.87 (0.74-1.02)
■ IALT	1867	0.86 (0.76-0.98)
■ ALPI	1209	0.94 (0.79-1.12)
■ E3590	488	0.93 (0.74-1.18)
■ BLT	381	1.02 (0.77-1.35)
■ NCIC JBR.10	482	0.70 (0.52-0.92)
■ CALGB 9633	330	0.62 (0.29-0.89)
■ ANITA 1	840	0.79 (0.66-0.95)
■ UFT meta	2003	0.74 (0.61-0.88)

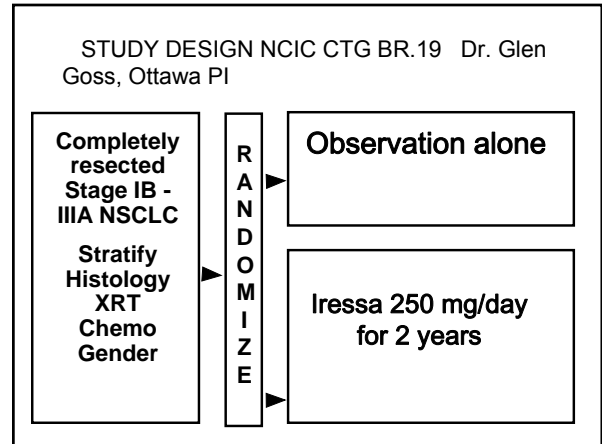
### Benefit of Adjuvant Chemotherapy

Tumor	Therapy	5-Yr S	HR	P
Breast n=11,000	Polychemo	70.8% 67.5%	NR	<0.00001
Stomach n=556	5FU/FA/RT	50% (3 yr) 41% (3 yr)	.74	<0.001
Colon n=1526	5FU/FA	83% (3 yr) 78% (3 yr)	.78	0.029
BR.10 n=480	Platinum/ Vinorelbine	69%	.70	0.012
ANITA-1	Platinum/ Vinorelbine	54% 51% 43%	.79	0.013



### ADJUVANT THERAPIES OF THE FUTURE

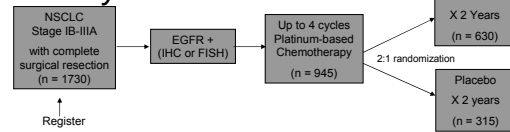
- **EGFR inhibitors**  
Tyrosine kinase inhibitors (erlotinib or gefitinib)  
Monoclonal antibodies (cetuximab)
- **Anti-angiogenesis agents**  
Bevacizumab



## NCIC BR.19

- Closed to accrual when ISEL trial did not meet its study endpoints and SWOG Stage III trial negative
- 502 patients accrued
- Negative trial. Importantly, no benefit observed for patients with gefitinib even if EGFR mutated.

## RADIANT Study Schema

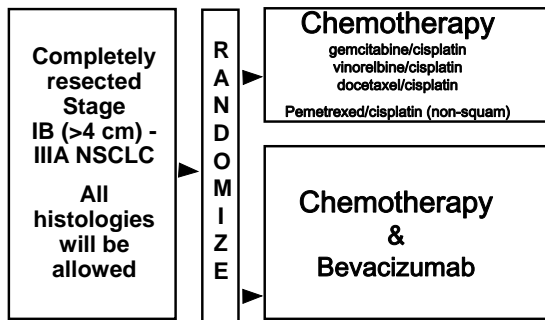


### Stratification:

- Country
- Histology (adeno vs. non-adeno)
- Stage (IB vs. II vs. IIIA)
- Adjuvant chemo (yes vs. no)
- EGFR status by FISH (+ or -)
- Smoking status (current/former vs. never)

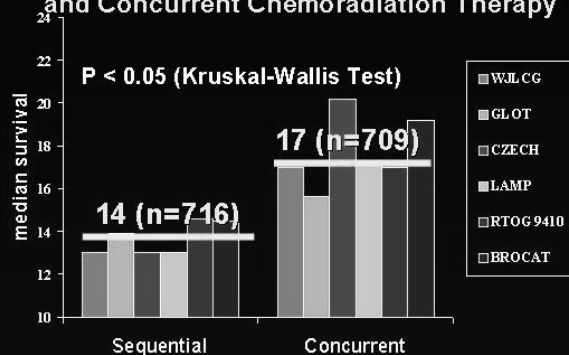
Accrual Period = 3 yr  
Follow-up Period = 4 yr  
Total Study Duration = 7 yr

## North American Intergroup Trial

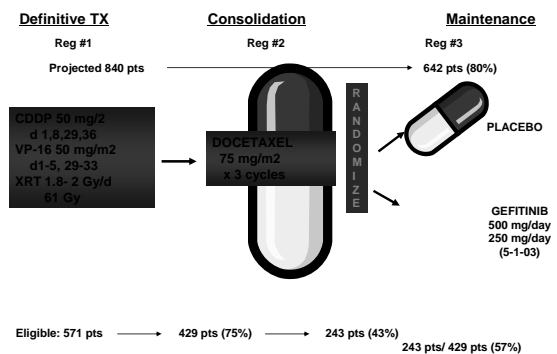


## Locally Advanced Disease (Stage IIIa, b)

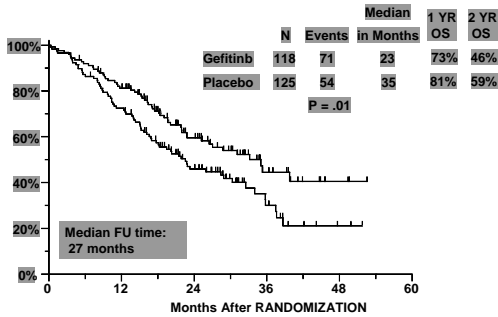
## Survival Comparison between Sequential and Concurrent Chemoradiation Therapy



## SWOG 0023



S0023: Overall Survival



Conclusions (Staging, Screening, Adjuvant and Combined Modality Approaches)

- Revised staging system rationalizes the treatment approach to NSCLC.
- Adjuvant cytotoxic chemotherapy is unequivocally established for resected stages IIa, IIb, IIIa NSCLC.
- Appropriate stage IB patients should also be considered.
- Multimodality therapy for Stage III disease is clearly established. Continuing debate as to best chemotherapy regimen, role of surgery.
- "Targeted agents" are under active investigation, but **none** have been demonstrated to be of value.

Advanced Disease (Stage IV):  
First Line Therapy

Considerations for First Line Therapy

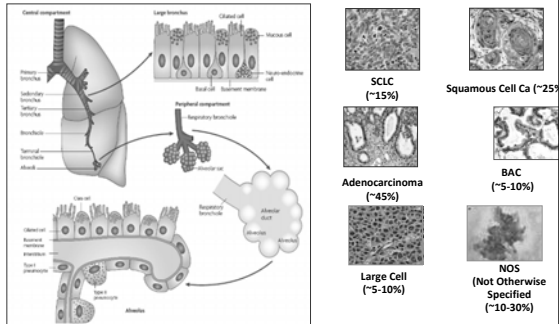
- Performance status
- Age
- Organ function, nutritional status
- Histology
- Molecular variables
- Other
  - CNS metastases: who goes first?

First Line Therapy: 2005

Platinum Agent (select one)	"1990's Agent" (select one)
Cisplatin	Vinorelbine
Carboplatin	Paclitaxel
	Docetaxel
	Gemcitabine

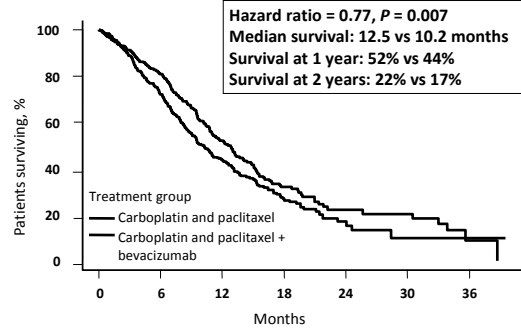
HISTOLOGY

### Complexities of lung cancer pathogenesis result in diverse histologic subtypes



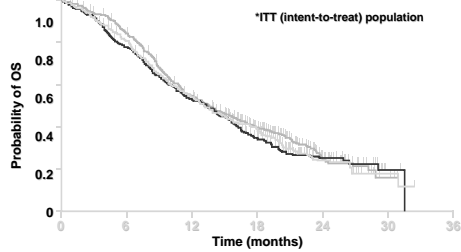
Sun S, et al. *Nat Rev Cancer*. 2007; 7:778-790

### Bevacizumab + Carboplatin and Paclitaxel: Survival



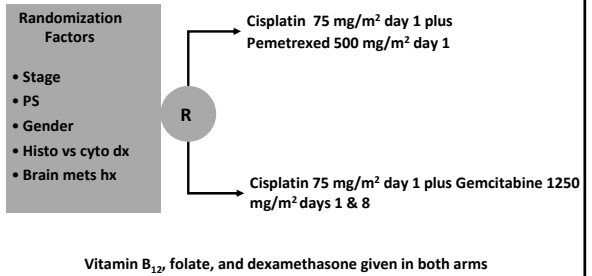
Sandler et al. ASCO 2005; Abstract LBA4.

### AVAiL: NO Difference in Overall Survival



Reck et al. *Ann Oncol* 21: 1804, 2010  
 Published 3 years after the initial presentation of PFS results

### JMDB trial: Cisplatin/pemetrexed (CP) vs cisplatin/gemcitabine (CG) in Adv NSCLC



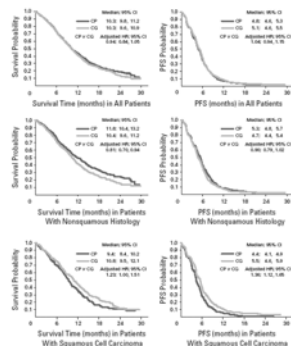
Scagliotti GV, et al. *J Clin Oncol*. 2008; 26:3543-3551

### Cisplatin/Pemetrexed (CP) vs Cisplatin/Gemcitabine (CG): Phase III

No difference in PFS or OS

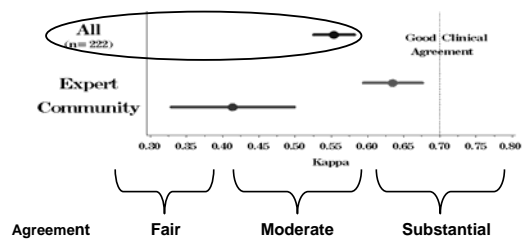
CP improves survival over CG in non-squamous histology (HR 0.81, P = .005)

CG improves survival over CP in squamous histology (HR 1.23, P = .05)



Scagliotti GV, et al. *J Clin Oncol*. 2008; 26:3543-3551

### Pathologist agreement for squamous vs. nonsquamous

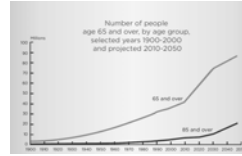


Kappa (All pathologists) = 0.55, (95% CI, 0.53 to 0.58; P<0.0001)

Grilley-Olson, ASCO 2009

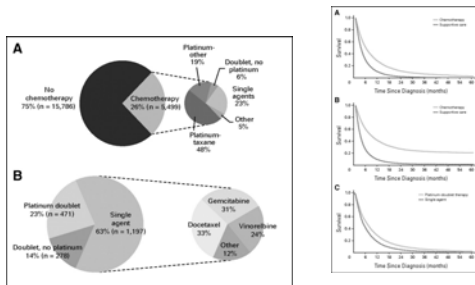
# THE ELDERLY

## The Problem of the Elderly in Lung Cancer

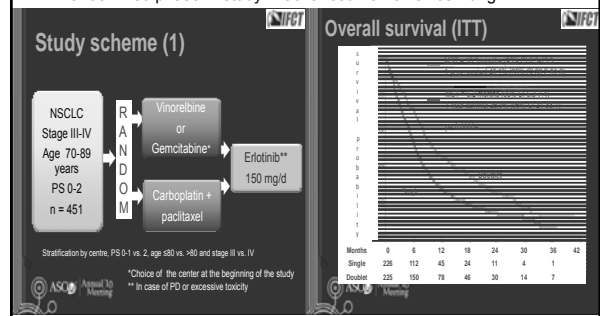


CA- A Cancer J for Clin 61, 2011

## Treatment and Outcomes of Advanced NSCLC in the Elderly: SEER/Medicare Data base

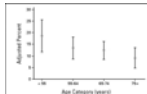


## Weekly paclitaxel combined with monthly carboplatin versus single agent therapy in patients aged 70 to 89 : IFCT-0501 randomized phase III study in advanced non-small cell lung



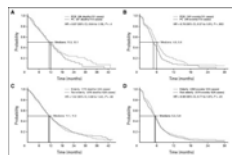
## Toxicity in the Elderly

### CANCORS



Neurotoxicity/febrile neutropenia/sepsis	N	% with event	95% CI
<55	133	8.5	3.2-13.7
55-64	208	10.8	6.5-15.0
65-74	262	15.0	10.7-19.3
≥75	169	13.2	8.2-18.2

### ECOG 4599

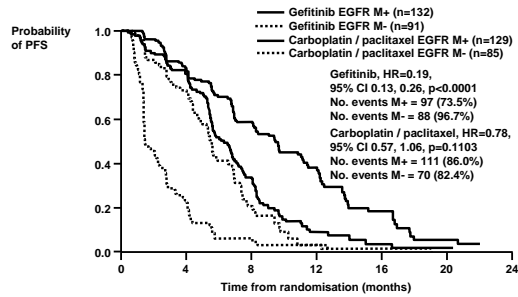


Toxicity (grade 4-5)	PC	PCB	P
Neutropenia	22	34	.06
Fever with neutropenia	.9	6.2	.03
Thrombocytopenia	0	3.5	.06
Hemorrhage (grade 3-5)	1.7	7.9	.03
Anorexia (grade 3-5)	.9	7.9	.01

## MOLECULAR VARIABLES



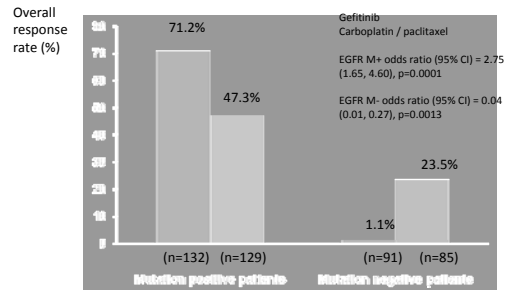
### Comparison of PFS by mutation status within treatment arms



Hazard ratio <1 implies a lower risk of progression in the M+ group than in the M- group  
 M+, mutation positive; M-, mutation negative

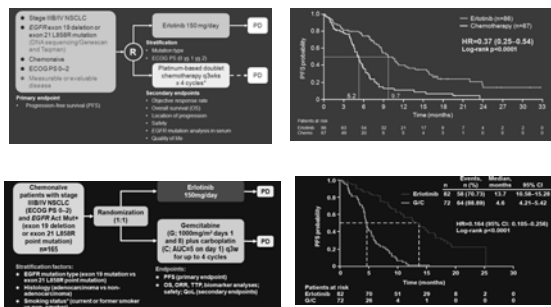
McK. ESMO 2008

### Objective response rate in EGFR mutation positive and negative patients



Odds ratio >1 implies greater chance of response on gefitinib

### EURTAC and OPTIMAL

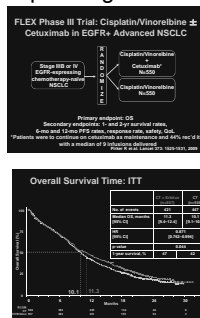


### First line treatment EGFR TKI vs. Chemotherapy in EGFR mutant (del 19, missense 21)

Study	Treatment	n	PFS	OS
Maemondo	Gefitinib	228	10.8	30.5
	CBDCA/Pac		5.4(.001)	23.6 (.31)
Mitsudomi	Gefitinib	177	9.2	30.9
	CDDP/Doc		6.3(<.001)	Not reached
OPTIMAL	Erlotinib	154	13.7	ns
	CBDCA/Gem		4.6 (<.0001)	
EURTAC	Erlotinib	174	9.7	HR=.80 (p=.42)
	Plat chemoRx		5.2 (<0001)	

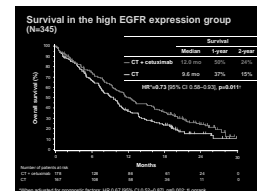
### Cetuximab: How not to develop a drug for lung cancer

- Phase II trials demonstrated tolerability and "promising activity"
- Phase III randomized trial done with "selection" based upon any indication of EGFR positivity.
- Results: Small, statistically significant, but clinically suspect.



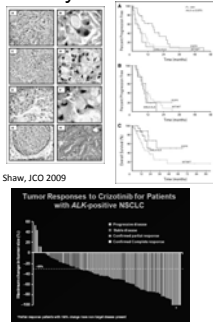
### Cetuximab development

- Three years later, analysis presented for patients with high EGFR expression (about 30% of patients).
- Failure to include a prospective analysis for degree of IHC positivity (an obvious question, given the trastuzamb precedent) has substantially reduced the potential utility of this agent.
- In the absence of a validated diagnostic, difficult to recommend the use of cetuximab.

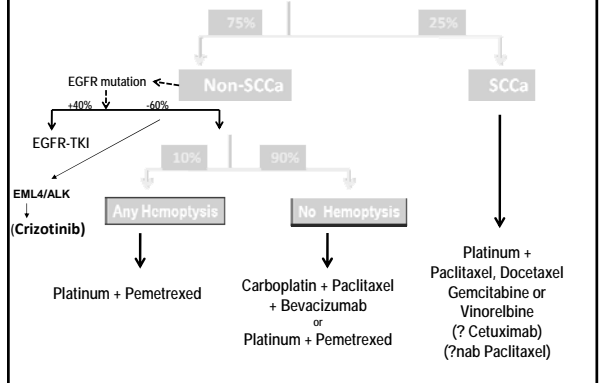


### EML4/ALK: A New Disease Entity

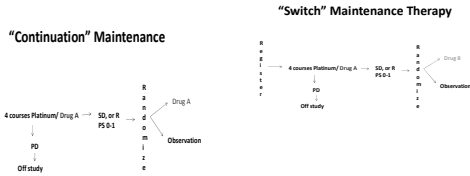
- Phenotype
  - Never/scant smokers
  - Young, male
  - Adenocarcinoma with signet ring morphology
  - Poor response to standard chemotherapy
  - Overlap with EGFR mutation phenotype
- Highly responsive to crizotinib (approved Sept 2011 w. companion diagnostic).



### 2011: 1<sup>st</sup> Line Treatment of Advanced/Metastatic NSCLC



### Maintenance Therapy



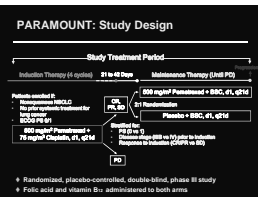
### Maintenance Therapy: Rationale

- “Continuation maintenance”: continual suppression of malignancy will be more effective than intermittent use.
- “Switch maintenance” (planned sequential)
  - transition to a proven second line therapy before the emergence of resistance will be advantageous. (Goldie-Coldman)
  - Early use assures exposure to second line therapy i.e. “no one falls off the cliff”

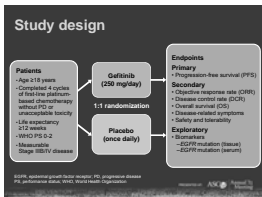


### ASCO 2011: Maintenance

#### PARAMOUNT



#### INFORM



### Top Line Results: Maintenance Trials

Study	Agent	PFS (mo)	OS (mo)
Fidias	Docetaxel Control	5.7* 2.7	12.3 9.7
JMEN	Pemetrexed Control	4.3* 2.6	13.4 10.6
SATURN	Erlotinib Control	12.3 wk** 11.1wk	12.0* 11.0
Belani 2010	Gemcitabine Control	7.4 7.7	8.0 9.3
IFCT	Gemcitabine Erlotinib Control	3.8* 2.9* 1.9	12.1 11.4 10.8
PARAMOUNT	Pemetrexed Control	3.9* 2.6	nr nr
INFORM	Gefitinib Control	4.8* 2.6	18.7 16.9

\* Significant, p<0.05

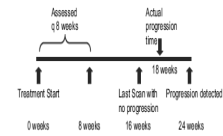
Fidias JCO 27: 591-8, 2009  
Ciuleanu Lancet 374:1432-40, 2009  
Capuzzo Lancet Oncol 11:521-529, 2010  
Belani, ASCO 2010  
Perol, ESMO, 2010

### Issues with Maintenance

- PFS endpoint
  - Accuracy
  - benefit
- Cross-over to active therapy
  - Availability
  - Reasons for non-crossover
- Definition of progression and the institution of therapy on the control arm
  - Resist RECIST?
- Heterogeneous population
  - EGFR mutations

### PFS Endpoint

- Arbitrary
  - Subject to considerable bias
  - Subject to testing interval
- Are small differences in PFS really beneficial?
  - QOL analysis
- Does not necessarily predict for OS
  - AVAIL and others



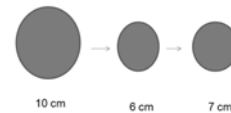
### What happens to the control arm?

- Substantial fraction of patients NEVER receive second line therapy
- Only one study (Fidias) has reported the outcome for patients who actually receive second line treatment.
- Why do patients not receive additional therapy?

Study	Agent	Cross-over %	Any agent %
Fidias	Docetaxel	62	62
JMEN (Belani)	Pemetrexed	18	67
SATURN (Cappuzzo)	Erlotinib	21	72
Belani 2010	Gemcitabine	3	17
IFCT	Gemcitabine Erlotinib	0 3	91
PARAMOUNT	Pemetrexed	?	?
INFORM	Gefitinib	30 (includes erlotinib)	67

### Control Arm: When should second line therapy be introduced?

- Protocol specified RECIST.
- Very arbitrary and not consistent with clinical practice.
- May result in delay in therapy.
- Remember, these are responding patients, with good PS. Are they falling off the cliff or are they being pushed?



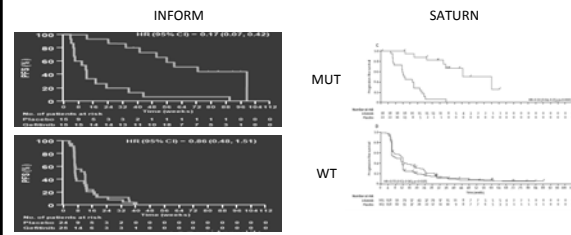
### Who should get “maintenance”

- Everybody?
- Patients who responded and are doing well?
- Patients who had stable disease/not doing so well?
- Performance status?

Study	Agent	Responder (CR/PR)	Stable Disease
Fidias	Docetaxel	n.r.	n.r.
JMEN	Pemetrexed	.81 (p=n.s.)	.61 (p < .05)
SATURN	Erlotinib	.94 (p=.618)	.72(p=.0019)
Belani	Gemcitabine	NR	NR
IFCT	Gemcitabine	NR	NR
PARAMOUNT	Pemetrexed	.48 (significant)	.74 (n.s.)
INFORM	Gefitinib	NR	NR

### EGFR mutations and maintenance

- EGFR mutations predicts substantial and sustained benefit from EGFR TKI
- All studies that involve patients with EGFR mutations and EGFR TKIs demonstrate substantial PFS advantage.
- Conversely, almost no benefit in EGFR mutation negative patients

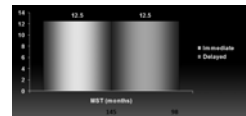


### The cost of maintenance

- While overall “well tolerated”, there is increased toxicity seen with treatment on all studies.
  - Grade 3-5 SAEs on INFORM 15% vs. 2.7%
  - Grade 3-4 fatigue on PARAMOUNT 4.2% vs. 0.6%
- Not to mention the cost (\$) of additional treatment.
- Need a cost effectiveness analysis of f/u strategies with frequent scanning/visits with “watchful waiting” vs. maintenance

### What have we learned from these and other maintenance studies?

- The drugs really do work
  - Pemetrexed approval in second line based upon response, not survival
- Drugs work in those who derive some degree of benefit from initial therapy.
- To date, there is no evidence that early introduction of therapy is inherently superior to assuring treatment, i.e. Goldie-Coldman **not** proven
  - No OS advantage for patients who receive appropriate therapy.
- EGFR TKI benefit is primarily seen in patients with mutations. Mutations predict for prolonged PFS, but not OS.



### Where should we go from here?

- How should we approach the 50% + patients who progress while receiving four cycles of initial therapy?
- Is there a benefit from this strategy in patients who have unequivocal response to initial treatment?
  - Data are conflicting or not reported. May depend upon strategy.
  - We need more information regarding “response” at the time of randomization. Is it “best response” or response after four cycles?
- What is the proper design and reporting for these trials?
  - Mandated second line therapy
  - Mandated availability of study agent (if a standard drug)
  - Mandated documentation of rationale for non-treatment
  - Mandated reporting of outcomes for the patients who actually receive treatment on the control arm.
- Is RECIST appropriate as the indication for initiation of further therapy?

### Conclusions

- Individualized care for NSCLC, based upon clinical, histologic and molecular variables is a fact.
  - FNA is no longer adequate for diagnosis
  - Crizotinib now approved for EML4/ALK NSCLC
  - Erlotinib is a first line agent for EGFR mutated NSCLC
  - The fit elderly should be treated like everyone else
  - Maintenance is an option, however, there are significant questions regarding the validity of studies that purport to show a survival advantage. Close observation (PE q mo, CT q 2mo) is a valid approach.

### Conclusions (cont'd)

- “Maintenance” chemotherapy is an option, but should be viewed with skepticism.
  - Serious methodologic flaws in trials and analysis
- Little new in SCLC
  - Amrubicin may achieve approval based upon favorable toxicity profile vs. topotecan, but not as interesting as first advertised.

## SECOND LINE THERAPY FOR ADVANCED DISEASE

### Considerations for Second Line Therapy

- Prior therapy
  - Agents
  - Indication
    - Metastatic disease
    - Adjuvant
    - Multimodality
- Performance status, ? age
- Organ function
- Histology
- Molecular variables

### Second Line Therapy

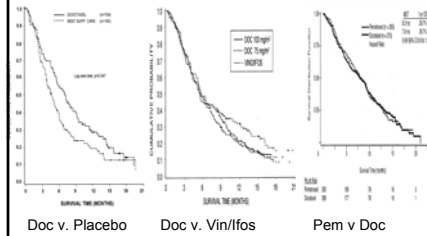
#### Second Line Drugs (select 1)

Docetaxel (approved)

Pemetrexed (approved, non-squamous)

Erlotinib (approved, also for 3<sup>rd</sup> line)

### Second Line Therapy



### Symptom Benefit with Pemetrexed

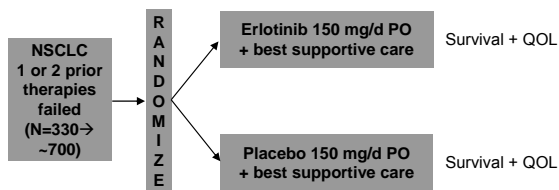
#### Change in Average Symptom Burden Index

	ALIMTA N=227	Docetaxel N=247	P value
Improved	21.2%	21.5%	
Worsened	33.0%	27.9%	0.1447
Stable	29.5%	24.7%	
Unknown	16.3%	25.9%	

Assessed by LCSS

### CAN-NCIC-BR.21 Phase III Trial in Refractory NSCLC

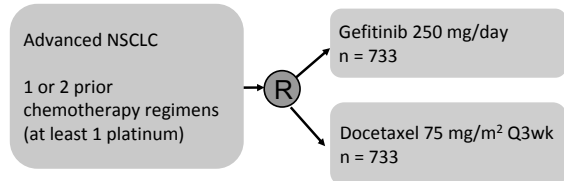
2:1 randomization to the experimental arm



90% power to detect a 33% survival benefit,  $\alpha=0.05$

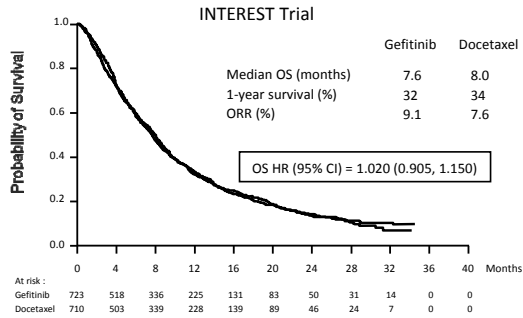
### Gefitinib vs Docetaxel in Patients Pre-treated With Platinum-Based Regimen

INTEREST Trial



Primary endpoint = OS  
Secondary endpoint: PFS, ORR, QOL, safety

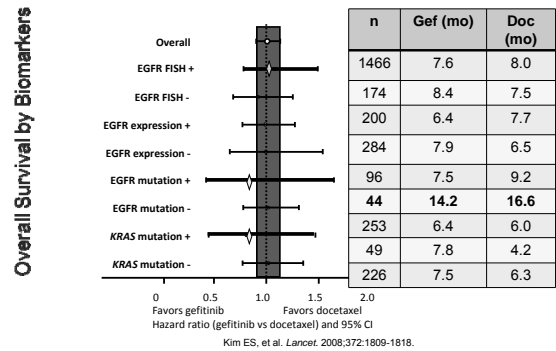
### Gefitinib vs Docetaxel in Patients Pre-treated With Platinum-Based Regimen



Kim ES, et al. *Lancet*. 2008;372:1809-1818.

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### Gefitinib vs Docetaxel in Patients Pre-treated With Platinum-Based Regimen



Kim ES, et al. *Lancet*. 2008;372:1809-1818.

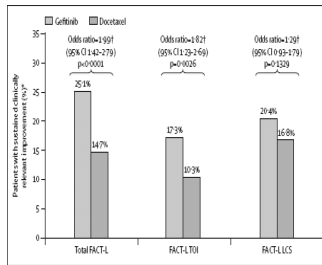
### Gefitinib vs Docetaxel in Patients Pre-treated With Platinum-Based Regimen

#### Grade 3/4 Adverse Events\* (%)

	Gef	Doc
Neutropenia	2.2	58.2
Febrile neutrop	1.2	10.1
Rash	2.1	0.6
Diarrhea	2.5	3.1
Asthenia	4.4	9.0
Neurotoxicity	0.1	2.4
Anemia	1.5	2.1

\*Includes those with a significant difference between arms and incidence > 2%.

#### Improvement Rates for QOL Scales

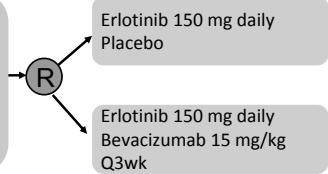


Kim ES, et al. *Lancet*. 2008;372:1809-1818.

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### Bevacizumab + Erlotinib vs Erlotinib BeTa Trial

Progression during or after chemotherapy or chemoradiotherapy  
No squamous cell carcinoma  
No prior anti-angiogenesis or EGFR therapy



Primary endpoint = OS  
Secondary endpoint: PFS, safety, correlation of markers to outcome

Hainsworth J, et al. Presented at 2008 Chicago Multidisciplinary Symposium on Thoracic Oncology, September 13-15, 2008. Abstract 189; Available at: <http://investor.osp.com/phoenix.zhtml?c=705884&p=rol-newsArticle&ID=1205579&highlight=> Accessed February 22, 2009.

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### Bevacizumab + Erlotinib vs Erlotinib BeTa Trial

- Press release 10/6/2008: primary endpoint not met
- N = 636

	E	B + E	HR [95% CI]	P
OS (mo)	9.2	9.3	0.98 [0.80-1.18]	
PFS (mo)	1.7	3.4	0.62 [0.52-0.75]	
ORR (%)	6.2	12.6		0.006

Hainsworth J, et al. Presented at 2008 Chicago Multidisciplinary Symposium on Thoracic Oncology, September 13-15, 2008. Abstract 189; Available at: <http://investor.osp.com/phoenix.zhtml?c=705884&p=rol-newsArticle&ID=1205579&highlight=> Accessed February 22, 2009.

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### Toxicity Comparison of Approved Second-Line Agents

TABLE 2. Grade 3/4 toxicities of weekly and every 3 weeks docetaxel, pemetrexed, and erlotinib

	Shepherd et al. <sup>7</sup> Docetaxel 75 mg/m <sup>2</sup> (3W)	Fossella et al. <sup>8</sup> Docetaxel 75 mg/m <sup>2</sup> (3W)	Camps et al. <sup>13</sup> Docetaxel 56 mg/m <sup>2</sup> (1W)	Hanna et al. <sup>18</sup> Pemetrexed 500 mg/m <sup>2</sup>	Shepherd et al. <sup>14</sup> Erlotinib 150 mg/day
Neutropenia	67.3%	54%	3.2%	5.3%	NR
Felicitatropenia	1.8%	8%	0.8%	1.9%	NR
Infection	5.5%	0	NR	0	2%
Asemia	5.5%	0	4.8%	4.2%	NR
Thrombocytopenia	0	2%	0.8%	2%	NR
Nausea	3.6%	3%	3.2%	2.6%	3%
Rash	NR	NR	1.6%	0.8%	9%
Diarrhea	1.8%	2%	3.2%	0.4%	6%
Pneumonitis	1.8%	NR	NR	0	<1%
Neurotoxicity	1.8%	1%	3.2%	0	NR

NR, not reported; 3W, every 3 weeks; 1W, every week.

Bedano et al. *J Thorac Oncol*. 2006;1:582-587.

## Summary of Second-Line Treatment

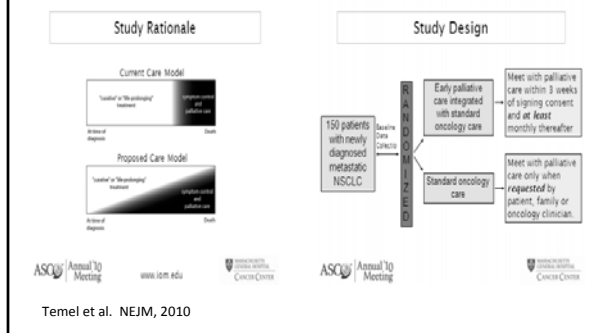
- Post-hoc analysis suggests there may be differences in efficacy based on histology
  - Pemetrexed better for large cell
  - Docetaxel better for squamous
  - Either agent similar for adenocarcinoma
- Gefitinib is an option comparable to chemotherapy
  - Less toxic and better quality of life
  - Survival similar across all subgroups
  - Erlotinib has not been directly compared to chemotherapy
- Adding bevacizumab to erlotinib does not improve overall survival

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## HOSPICE AND PALLIATIVE CARE

Early palliative care improves quality of life, reduces aggressiveness of care at the end-of-life and prolongs survival in stage IV NSCLC patients:

Results of a phase III randomized trial



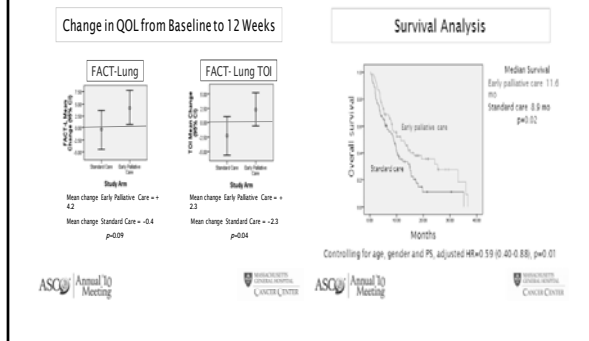
Temel et al. NEJM, 2010

## Intervention

Palliative Care Guidelines
<b>Illness understanding and education</b> Inquire about illness and prognostic understanding Offer clarification regarding treatment goals
<b>Symptom management</b> Pain Pulmonary symptoms Fatigue and sleep disturbance Mood Gastrointestinal
<b>Decision-making</b> Assess mode of decision-making Assist with treatment decision-making
<b>Coping with life-threatening illness</b> Patient Family/family caregivers

- Patients to meet with palliative care team monthly.
- Palliative care available ad hoc to control patients.

## Results



## Comments on Temel et al.

- Authors acknowledged limitations of single institution trial, lack of racial and ethnic diversity.
- Survival was not a primary endpoint.
- The definition of "palliative care" is rather hazy.
- The composition of the palliative care teams can be highly variable. Experience and knowledge of thoracic oncology likely not to be as great at other institutions. Potential for undertreatment.
- However, results should be utilized to advocate for more assistance (\$) to support aggressive interventions for symptoms (including psychiatric distress) and to limit overtreatment (i.e. find the happy medium).

## Conclusions

- Significant advances have occurred in the treatment of NSCLC in the past 20 years.
- Screening now demonstrated in high risk population
- Adjuvant therapy improves opportunity for cure after surgery for localized disease.
- Multimodality therapy (best established for *non-operative* approach) has the potential to cure patients with locally advanced (stage III disease).
- "Personalized" therapy, based on clinical, histological and molecular characteristics is the current standard in metastatic disease.
  - Reality check: advanced disease patients with poor or declining PS, progressive disease, etc are best served with non-tumor directed i.e. palliative and hospice care