Improving Outcomes for Patients with Lung Cancer: Multidisciplinary Approaches, New Agents and Supportive Therapy

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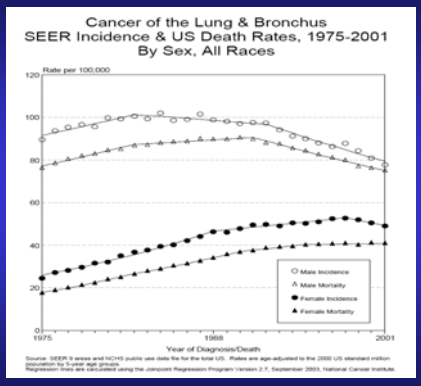
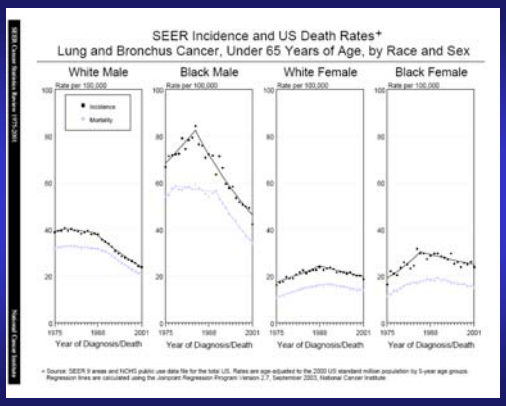
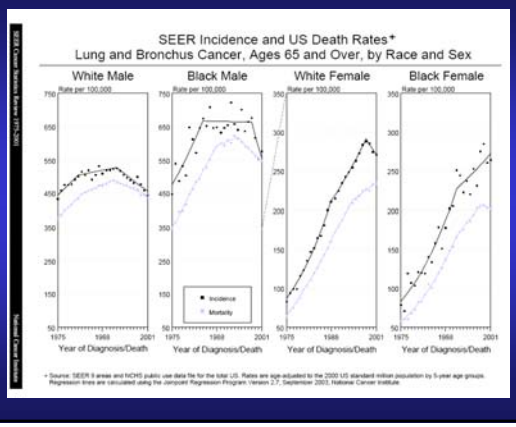
Non Small Cell Lung Cancer
Circa 1980

- **Screening - None**
- **Staging**
  - **CT (in development)**
  - **Thoracotomy**
- **RX Options**
  - **Surgery**
  - **Radiation (unimodality)**
  - **Chemotherapy**
    Nitrogen Mustard
  - **Palliative Care**







The Rolling Stones World Tour

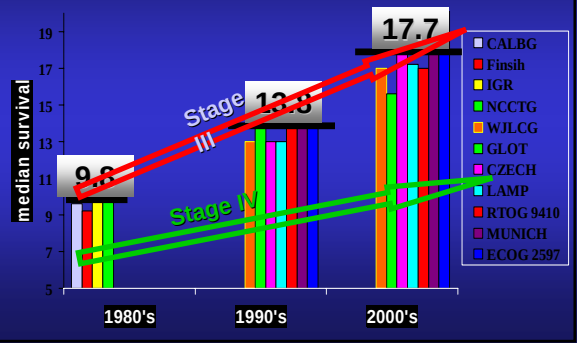
The Rolling Stones World Tour

It's all about survivorship!

Adjuvant Chemotherapy: Standard of Care for Early Stage NSCLC

Trial	Stage	N	Chemo	Survival
IALT	I-III	1867	Cis+Etop/Vinca	+4%
NCIC	IB-II	482	Cis+Vinorelbine	+15%
CALGB	IB	344	Carbo+Tax	+14%
ANITA	I-III	840	Cis+Vinorelbine	+9%

Survival Improvement in Stage III vs IV NSCLC



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Clinical Practice Guidelines in Oncology – v.2.2006

Non-Small Cell Lung Cancer
Version 2.2006

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NON-SMALL CELL LUNG CANCER

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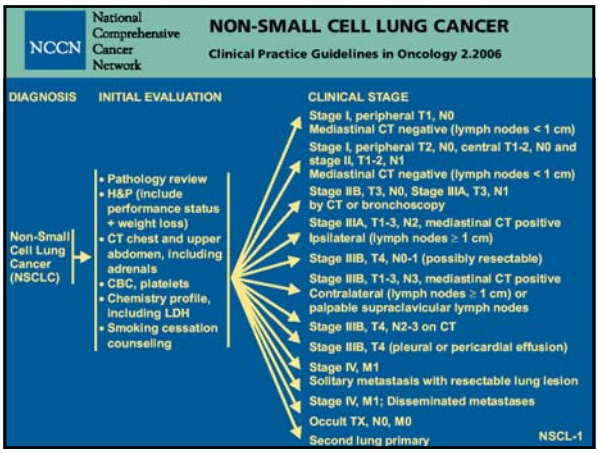
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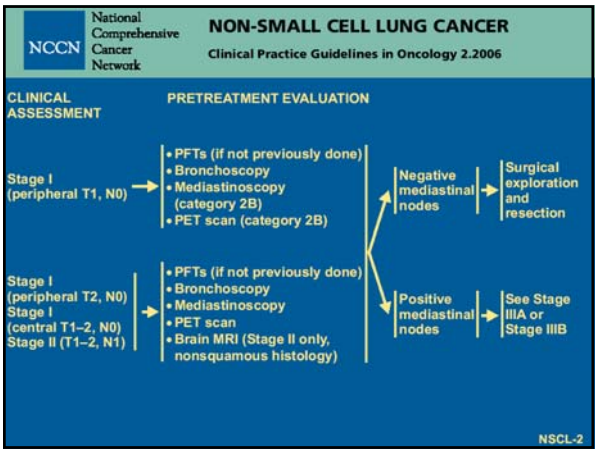
DIAGNOSIS
INITIAL EVALUATION
CLINICAL STAGE
Non-Small Cell Lung Cancer (NSCLC)
• Pathology review
• H&P (include performance status + weight loss)
• CT chest and upper abdomen, including adrenals
• CBC, platelets
• Chemistry profile, including LDH
• Smoking cessation counseling
Stage I, peripheral T1, N0
Mediastinal CT negative (lymph nodes < 1 cm)
Stage I, peripheral T2, N0, central T1-2, N0 and stage II, T1-2, N1
Mediastinal CT negative (lymph nodes < 1 cm)
Stage IIB, T3, N0, Stage IIIA, T3, N1
by CT or bronchoscopy
Stage IIIA, T1-3, N2, mediastinal CT positive
Ipsilateral (lymph nodes ≥ 1 cm)
Stage IIIB, T4, N0-1 (possibly resectable)
Stage IIIB, T1-3, N3, mediastinal CT positive
Contralateral (lymph nodes ≥ 1 cm) or palpable supraclavicular lymph nodes
Stage IIIB, T4, N2-3 on CT
Stage IIIB, T4 (pleural or pericardial effusion)
Stage IV, M1
Solitary metastasis with resectable lung lesion
Stage IV, M1; Disseminated metastases
Occult TX, N0, M0
Second lung primary
NSCL-1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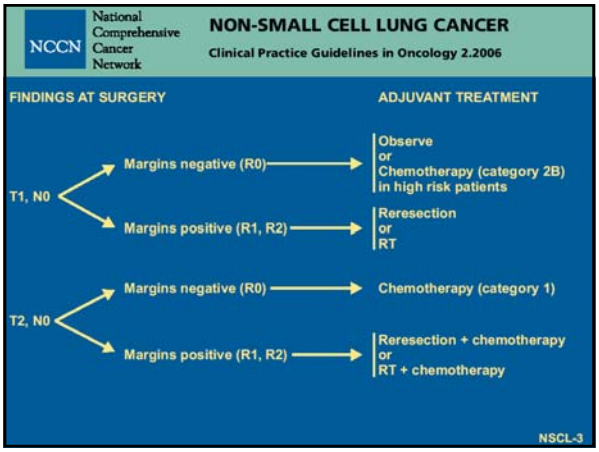
CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
Stage I (peripheral T1, N0)
• PFTs (if not previously done)
• Bronchoscopy
• Mediastinoscopy (category 2B)
• PET scan (category 2B)
Negative mediastinal nodes
Surgical exploration and resection
Stage I (peripheral T2, N0)
Stage I (central T1–2, N0)
Stage II (T1–2, N1)
• PFTs (if not previously done)
• Bronchoscopy
• Mediastinoscopy
• PET scan
• Brain MRI (Stage II only, nonsquamous histology)
Positive mediastinal nodes
See Stage IIIA or Stage IIIB
NSCL-2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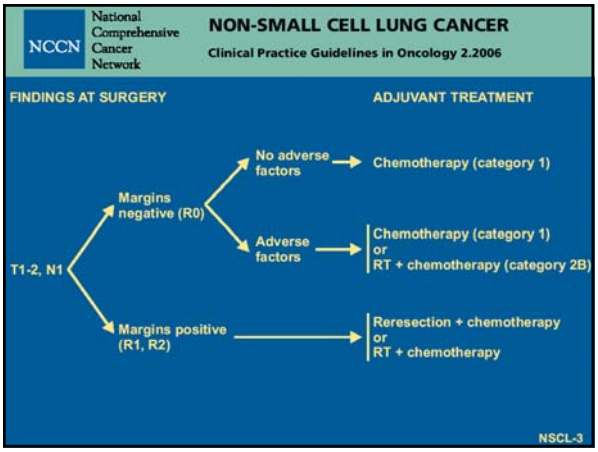
FINDINGS AT SURGERY
ADJUVANT TREATMENT
T1, N0
Margins negative (R0)
Observe or Chemotherapy (category 2B) in high risk patients
Margins positive (R1, R2)
Reresection or RT
T2, N0
Margins negative (R0)
Chemotherapy (category 1)
Margins positive (R1, R2)
Reresection + chemotherapy or RT + chemotherapy
NSCL-3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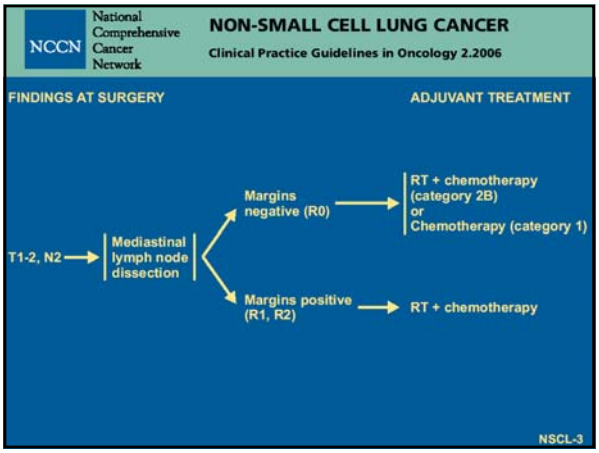
FINDINGS AT SURGERY
ADJUVANT TREATMENT
T1-2, N1
Margins negative (R0)
No adverse factors
Chemotherapy (category 1)
Adverse factors
Chemotherapy (category 1) or RT + chemotherapy (category 2B)
Margins positive (R1, R2)
Reresection + chemotherapy or RT + chemotherapy
NSCL-3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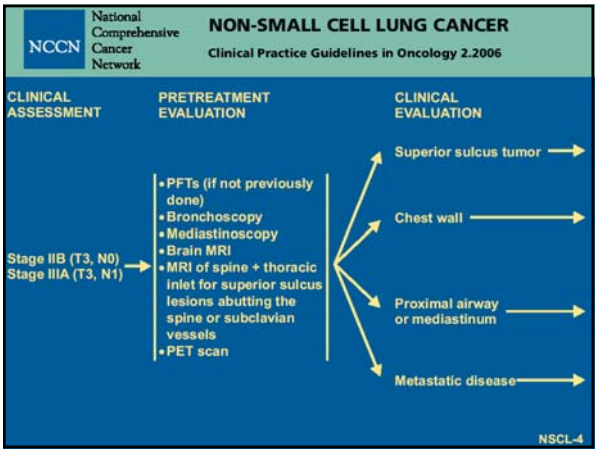
FINDINGS AT SURGERY
ADJUVANT TREATMENT
T1-2, N2
Mediastinal lymph node dissection
Margins negative (R0)
RT + chemotherapy (category 2B) or Chemotherapy (category 1)
Margins positive (R1, R2)
RT + chemotherapy
NSCL-3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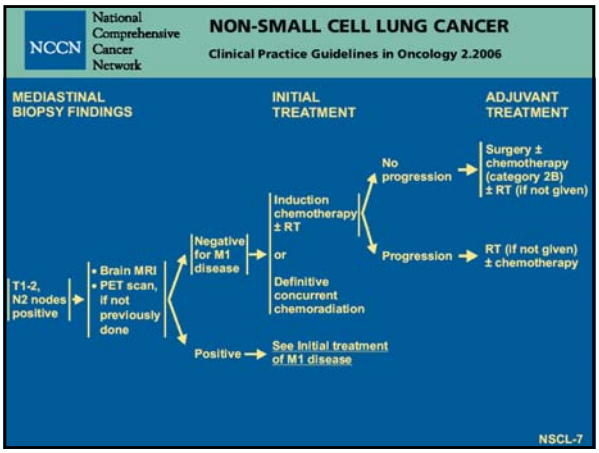
CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
CLINICAL EVALUATION
Stage IIB (T3, N0)
Stage IIIA (T3, N1)
• PFTs (if not previously done)
• Bronchoscopy
• Mediastinoscopy
• Brain MRI
• MRI of spine + thoracic inlet for superior sulcus lesions abutting the spine or subclavian vessels
• PET scan
Superior sulcus tumor
Chest wall
Proximal airway or mediastinum
Metastatic disease
NSCL-4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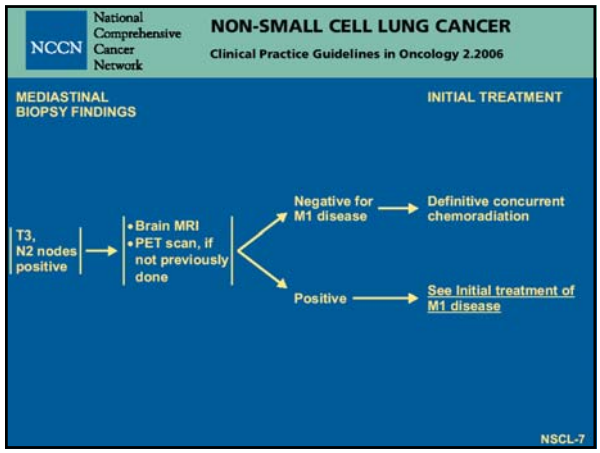
MEDIASTINAL BIOPSY FINDINGS
INITIAL TREATMENT
ADJUVANT TREATMENT
T1-2, N2 nodes positive
• Brain MRI
• PET scan, if not previously done
Negative for M1 disease
Induction chemotherapy ± RT
or
Definitive concurrent chemoradiation
No progression
Surgery ± chemotherapy (category 2B) ± RT (if not given)
Progression
RT (if not given) ± chemotherapy
Positive
See Initial treatment of M1 disease
NSCL-7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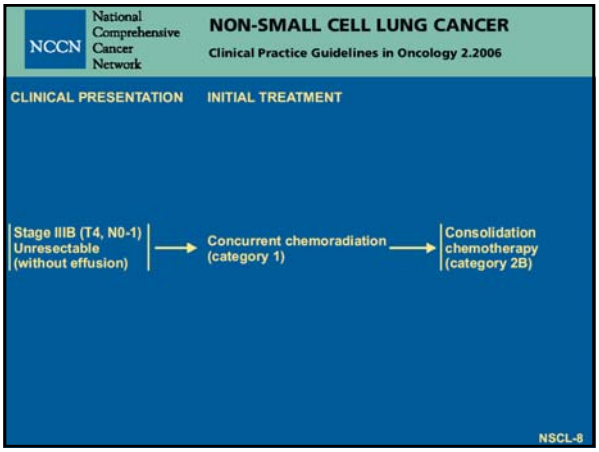
MEDIASTINAL BIOPSY FINDINGS
INITIAL TREATMENT
T3, N2 nodes positive
• Brain MRI
• PET scan, if not previously done
Negative for M1 disease
Definitive concurrent chemoradiation
Positive
See Initial treatment of M1 disease
NSCL-7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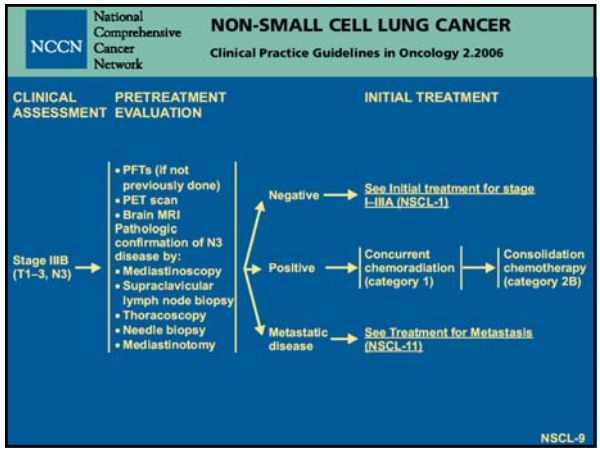
CLINICAL PRESENTATION
INITIAL TREATMENT
Stage IIIB (T4, N0-1) Unresectable (without effusion)
Concurrent chemoradiation (category 1)
Consolidation chemotherapy (category 2B)
NSCL-8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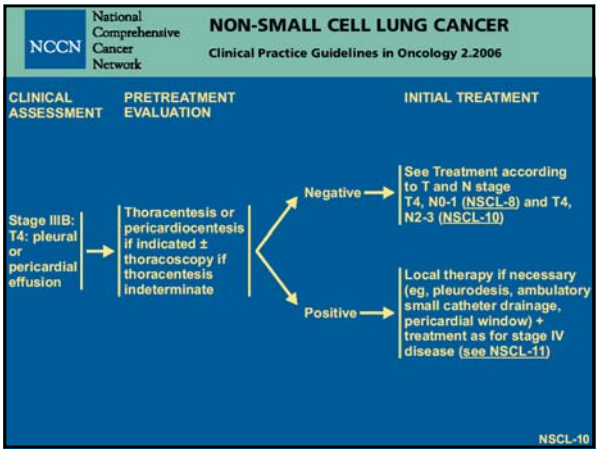
CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
INITIAL TREATMENT
Stage IIIB (T1–3, N3)
• PFTs (if not previously done)
• PET scan
• Brain MRI
Pathologic confirmation of N3 disease by:
• Mediastinoscopy
• Supraclavicular lymph node biopsy
• Thoracoscopy
• Needle biopsy
• Mediastinotomy
Negative
See Initial treatment for stage I–IIIA (NSCL-1)
Positive
Concurrent chemoradiation (category 1)
Consolidation chemotherapy (category 2B)
Metastatic disease
See Treatment for Metastasis (NSCL-11)
NSCL-9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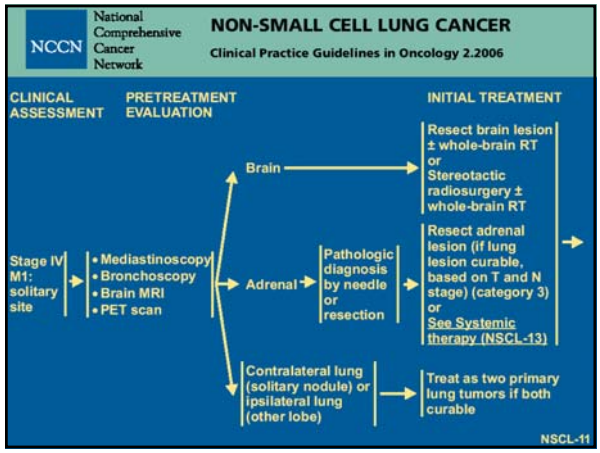
CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
INITIAL TREATMENT
Stage IIIB: T4: pleural or pericardial effusion
Thoracentesis or pericardiocentesis if indicated ± thoracoscopy if thoracentesis indeterminate
Negative
See Treatment according to T and N stage T4, N0-1 (NSCL-8) and T4, N2-3 (NSCL-10)
Positive
Local therapy if necessary (eg, pleurodesis, ambulatory small catheter drainage, pericardial window) + treatment as for stage IV disease (see NSCL-11)
NSCL-10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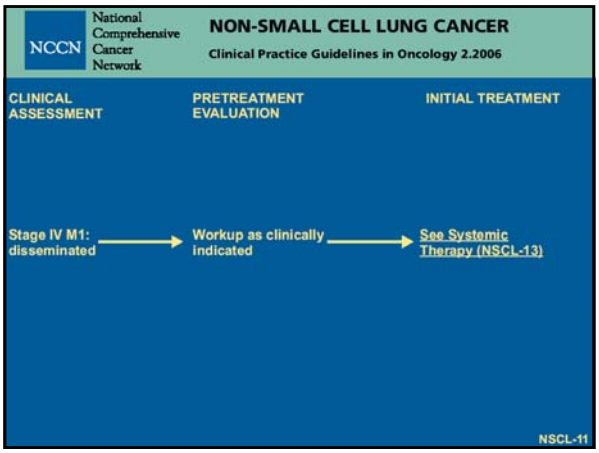
CLINICAL ASSESSMENT
PRETREATMENT EVALUATION
INITIAL TREATMENT
Stage IV M1: solitary site
• Mediastinoscopy
• Bronchoscopy
• Brain MRI
• PET scan
Brain
Resect brain lesion ± whole-brain RT or Stereotactic radiosurgery ± whole-brain RT
Adrenal
Pathologic diagnosis by needle or resection
Resect adrenal lesion (if lung lesion curable, based on T and N stage) (category 3) or See Systemic therapy (NSCL-13)
Contralateral lung (solitary nodule) or ipsilateral lung (other lobe)
Treat as two primary lung tumors if both curable
NSCL-11



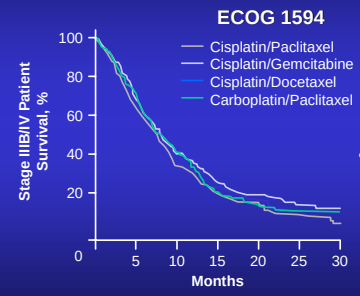
Paradigms in Advanced NSCLC

- Platinum-based combination chemotherapy improves survival over BSC
  - NSCLC Collaborative Group meta-analysis (BMJ 311:899, 1995)
  - Big Lung Trial (Proc ASCO 21:291a, 2002, abstr 1161)
- Selected single agents improve survival over BSC
  - Paclitaxel, docetaxel, vinorelbine

Paradigms in Advanced NSCLC

- "New" agents modestly improve outcomes over 2nd generation regimens
  - -Yana T et al. Proc ASCO 21:328a, 2002 (abstr 1309)
  - -Baggstrom MQ et al. Proc ASCO 21:306a, 2002 (abstr 1222)
- Platinum-based doublets remain the standard (2 drugs superior to 1; 3 drugs offer no survival advantage)
  - -Delbaldo C et al. Proc ASCO 22:623, 2003 (abstr 2507)
  - -Baggstrom MQ et al. Proc ASCO 22:624, 2003 (abstr 2510)

Cytotoxic Chemotherapy Survival Plateau



- New paradigm is needed

ECOG = Eastern Cooperative Oncology Group.

Adapted with permission from Schiller JH et al. *N Engl J Med*. 2002;346:92-98.

Polyglutamated Paclitaxel (PPX)

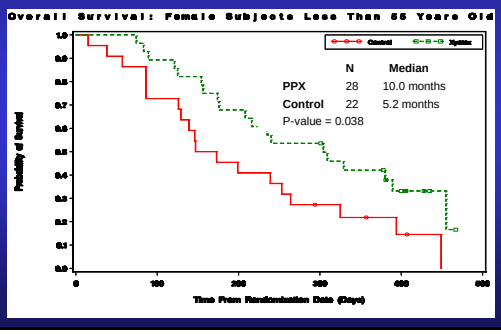
- PPX is designed to have improved tolerability without sacrificing efficacy
- PPX had significant activity in NSCLC patients in phase II studies
- Consequently, PPX is of interest in PS2 patients, both as a single agent and in combination with platinum therapy
- PPX has also been investigated in a phase III study for use in PS0-2 patients who are undergoing second-line treatment

NSCLC Phase III Program Trial Summary

Trial	Comparator	Xyotax (PPX)	Sample Size
STELLAR 4 First-line PS2 superiority	Gemcitabine 1000 mg/m^2 on days 1, 8,15 q4w or Vinorelbine 30 mg/m^2 on days 1, 8, 15, q3w	PPX 175 mg/m^2 q3w	477*
STELLAR 3 First-line PS2 superiority	Paclitaxel 225 mg/m^2 and carboplatin (AUC 6) q3w	PPX 210 mg/m^2 and carboplatin (AUC 6) q3w	400*
STELLAR 2 Second-line superiority	Docetaxel 75 mg/m^2 q3w	PPX 210 mg/m^2 - PS0-1 175 mg/m^2 - PS2 q3w	840

*370 planned

Efficacy of PPX in STELLAR 3 and 4: Survival in Females <55 Years (Pre-menopausal)



Future Directions PGT-305: Trial Design

Chemotherapy-naïve PS2 female patients with advanced NSCLC

RANDOMIZED

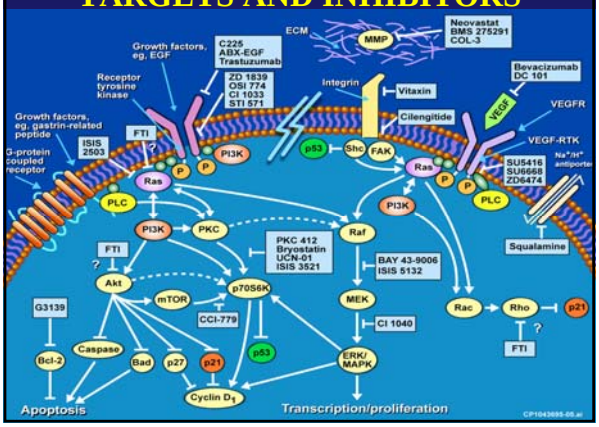
- PPX 175 mg/m² every 3 weeks (N= ~300)
- Paclitaxel 175 mg/m² every 3 weeks (N= ~300)

Stratified by:
- Stage
- Age >/< 55
- Geographic region

1° Objective: Overall survival

unstratified log-rank test
80% power to detect a HR=1.30

TARGETS AND INHIBITORS



Molecularly Targeted Therapy

- Is the target important in driving the disease process? Is it predictive and/or prognostic?
- Can expression of the target be reliably and simply measured?
- Can a biologic effect of the targeted agent be demonstrated in humans?
- Does the targeted agent produce single-agent responses in the disease under study?
- Can the target be used to enrich the population?
- What is the optimal way to evaluate the therapeutic potential of the targeted agent?
- How does the targeted agent interact with standard drugs/regimens used in the disease?

Targeted Therapies in Advanced NSCLC - Phase III

• MMPI	Negative X4
• EGFR	Negative X4
• PKC Antisense	Negative X2
• FTIs	Negative X1
• Retinoids	Negative X2

Targeted Therapies in Advanced NSCLC - Phase III

• MMPI	Negative X4
• EGFR	Negative X4
• PKC Antisense	Negative X2
• FTIs	Negative X1
• Retinoids	Negative X2
• Anti-VEGF	Positive

Bevacizumab

Recombinant Humanized Monoclonal Antibody to VEGF-A

Bevacizumab plus chemotherapy has provided a survival advantage to patients with metastatic colorectal carcinoma

Hurwitz, H. NEJM 350:2335-42, 2004.

Phase III Trial of Bevacizumab in Non-Squamous NSCLC: ECOG 4599

Sandler AB et al. ASCO 2005, abstr #4

Eligibility:
- Non-squamous NSCLC
- No Hx of hemoptysis
- No CNS metastases

Stratification Variables:
- RT *vs* no RT
- Stage IIIB vs IV *or* recurrent
- Wt loss <5% *vs* ≥5%
- Measurable *vs* non-measurable

(PC)
Paclitaxel 200 mg/m^2
Carboplatin AUC = 6
(q 3 weeks) x 6 cycles

(PCB)
PC x 6 cycles
+
Bevacizumab
(15mg/kg q 3 wks) to PD

No crossover to Bevacizumab permitted

Patient Characteristics

(eligible patients)

	PC *N* = 431	PCB *N* = 424
Stage IIIB	14%	13%
Measurable disease	91%	91%
Prior wt. loss ≥ 5%	28%	28%
Age ≥ 65	44%	43%
ECOG PS 0	38%	40%
Male	58%	50%
Caucasian	91%	90%

Hematologic Toxicity

	PC (N = 427) Grade 4	PCB (N = 420) Grade 4	P value
Neutropenia	16.4%	24%	0.006
Thrombocytopenia	0%	1.4%	0.01
Anemia	0.7%	0%	NS
FN	1.9%*	3.3%*	NS

*includes one death on each arm due to neutropenic fever

Non-Hematologic Toxicity

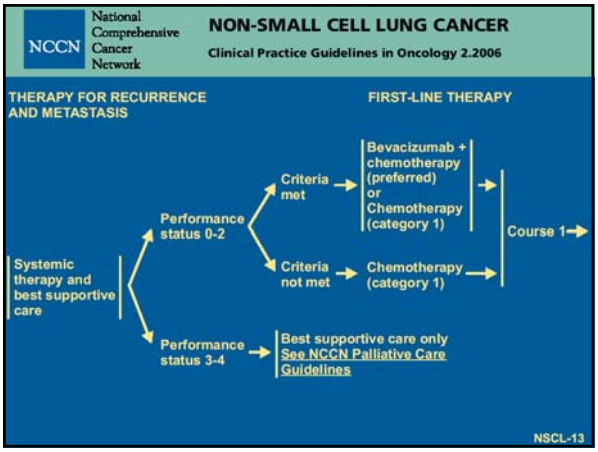
	PC (% n) ≥Grade 3	PCB (% n) ≥Grade 3	p-value
Hemorrhage	3 (0.7)	19 (4.5)	<.001
Hemoptysis	1 (0.2)	8 (1.9)	0.04
CNS	0	4 (1.0)	0.03
GI	2 (0.5)	5 (1.2)	NS
Other	1 (0.2)	4 (1.0)	NS
Hypertension	3 (0.7)	25 (6.0)	<.001
Venous Thrombosis	13 (3.0)	16 (3.8)	NS
Arterial Thrombosis	4 (1.0)	8 (1.9)	NS

Treatment Related Deaths

	PC 427	PCB 420
Hemorrhage		
Hemoptysis	0	5
GI bleed	1	2
Neutropenic fever	1	1
Total	2	8

Response Rate:
Measurable Disease

	PC	PCB	P value
No. of Pts.	350	357	
CR	0 (0%)	5 (1.4%)	
PR	35 (10.0%)	92 (25.8%)	
Overall RR	35 (10.0%)	97 (27.2%)	**<0.0001**



Current Issues with Bevacizumab in NSCLC

- Is it safe to use it with any chemotherapy regimen?
- How long do we continue it?
- Will it work as maintenance therapy?
- Does it work in the second-line and beyond setting?
- How safe is it in patient populations excluded from ECOG 4599 (brain mets, squamous histology, anti-coagulation, etc)?
- Can we identify patients at high risk for severe hemorrhage?
- What is the best way to manage the HTN?
- Reimbursement issues

The 2005 National Champions
University of North Carolina
Tar Heels

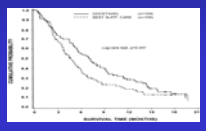
Is there a role for treatment after first-line platinum-based therapy in advanced NSCLC?

- Docetaxel vs BSC improved survival at 1-yr from 12% to 37% (p<0.01)- Approved by FDA 1999
- Gefitinib (Iressa) shown to be active and palliative in 2nd/3rd line setting- Approved by FDA May 2003
- Pemetrexed (Alimta) shown to be equally efficacious but less toxic than docetaxel- Approved by FDA August 2004
- Erlotinib (Tarveca) shown to improve survival over BSC- Approved by FDA November 2004

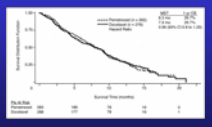
Second Line Therapy in NSCLC

- Docetaxel superior to BSC.
- Pemetrexed comparable to docetaxel with less toxicity.

Docetaxel vs BSC

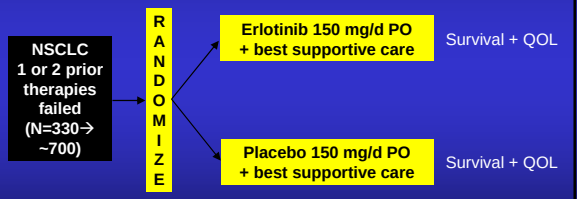


Docetaxel vs Pemetrexed



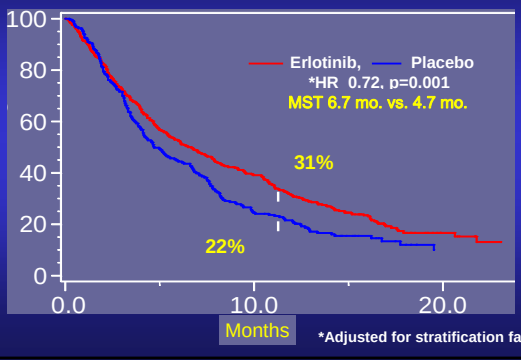
CAN-NCIC-BR.21 Phase III Trial in Refractory NSCLC

2:1 randomization to the experimental arm



90% power to detect a 33% survival benefit, α=0.05

BR.21 Overall Survival



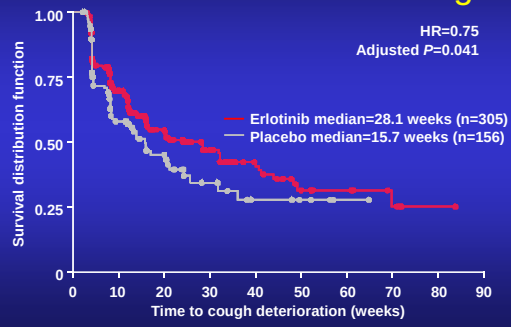
*Adjusted for stratification factors

Symptom Response in NSCLC Pts treated with Erlotinib: QoL Analysis of BR.21

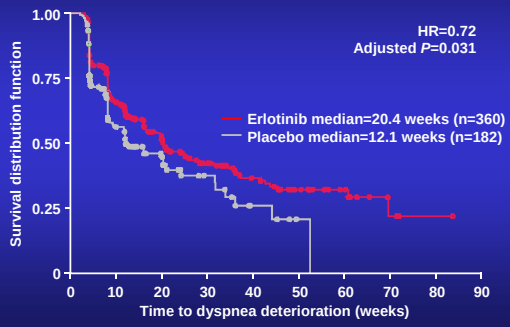
Bezjak A et al. ASCO 2005, abstr #7018

- QoL- secondary endpoint of the trial; 1^0 endpoint of QoL was time to symptom deterioration
- Assessed by EORTC QLQ-C30 and lung cancer module baseline and q4wks
- Compliance was good (87% baseline, >70% @ 12 wks)
- Erlotinib pts had significantly longer times to symptom deterioration
- Global QoL and physical function improved in erlotinib vs placebo (35% vs 26%, p<0.01 and 31% vs 19%, p=0.01)

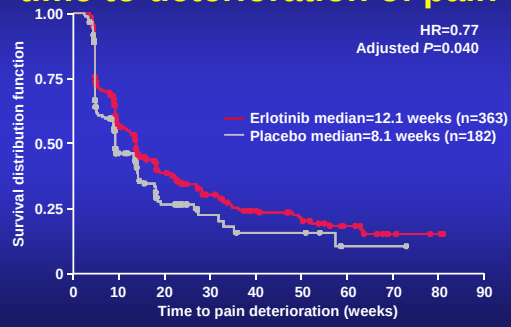
BR.21 symptom benefit: time to deterioration of cough



BR.21 symptom benefit: time to deterioration of dyspnea



BR.21 symptom benefit: time to deterioration of pain

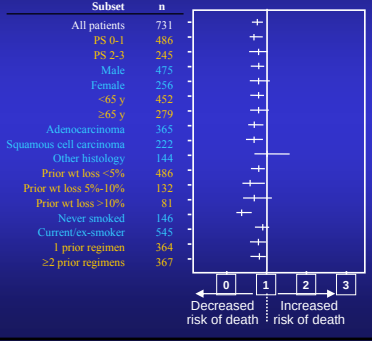


BR.21: Adverse Events

	% of Patients					
	Erlotinib (n=485)			Placebo (n=242)		
AE*	Any	Grade 3	Grade 4	Any	Grade 3	Grade 4
Rash	75	8	<1	17	0	0
Diarrhea	54	6	<1	18	<1	0
Anorexia	52	8	1	38	5	<1
Fatigue	52	14	4	45	16	4
Dyspnea	41	17	11	35	15	11
Cough	33	4	0	29	2	0
Nausea	33	3	0	24	2	0
Infection	24	4	0	15	2	0
Vomiting	23	2	<1	19	2	0

*AE = adverse event; occurring in ≥10% of Erlotonib-treated patients.

BR.21 Exploratory Study: Survival Across Subgroups



Tarceva (erlotinib) PI.

NCIC CTG BR.21: Best Response (N=638)

	Erlotinib (N=427)	Placebo (N=211)
Complete response	1%	<1%
Partial response	8%	<1%
Stable disease	35%	27%
Progression	38%	57%
Inevaluable / Not assessed	18%	15%
Response duration	7.9 mo (95% CI 5.7-10.6)	3.7 mo (95% CI 2.9-4.4)

NCCN National Comprehensive Cancer Network

NON-SMALL CELL LUNG CANCER

Clinical Practice Guidelines in Oncology 2.2006

PRINCIPLES OF SYSTEMIC THERAPY FOR NON-SMALL CELL LUNG CANCER

Second-line therapy

- In patients who have experienced disease progression either during or after first-line therapy, single agent docetaxel and pemetrexed, and recently tyrosine kinase inhibitor, erlotinib are established second-line agents.
  - Docetaxel has been proven superior to BSC, vinorelbine, or ifosfamide with improved survival/QOL.
  - Pemetrexed has been shown to be equivalent to docetaxel with less toxicity.
  - Erlotinib has proven superior to BSC with significantly improved survival and delayed time to symptom deterioration.

Third-line therapy

- Erlotinib has proven statistically superior to BSC with respect to survival.

NSCL-D 2 of 3

NCCN National Comprehensive Cancer Network

NON-SMALL CELL LUNG CANCER

Clinical Practice Guidelines in Oncology 2.2006

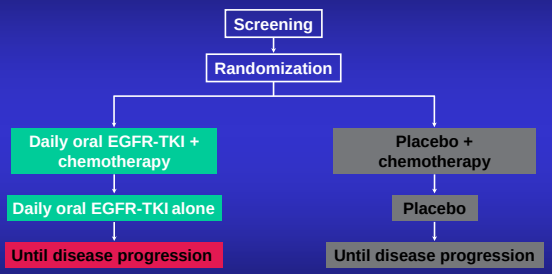
PRINCIPLES OF SYSTEMIC THERAPY FOR NON-SMALL CELL LUNG CANCER

ESTABLISHED AGENTS TO TREAT NON-SMALL CELL LUNG CANCER:

• Cisplatin	• Gemcitabine	• Ifosfamide
• Carboplatin	• Etoposide	• Pemetrexed
• Paclitaxel	• Irinotecan	• Erlotinib
• Docetaxel	• Vinblastine	• Bevacizumab (not as a single agent)
• Vinorelbine	• Mitomycin	

NSCL-D 3 of 3

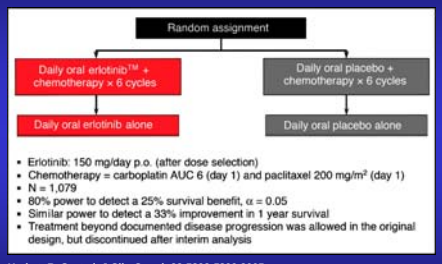
INTACT, TALENT & TRIBUTE: Study design



Chemotherapy - Gemcitabine/Cisplatin or Paclitaxel/Carboplatin

EGFR-TKI - Gefitinib 250 mg or 500 mg daily
Erlotinib 150 mg po daily

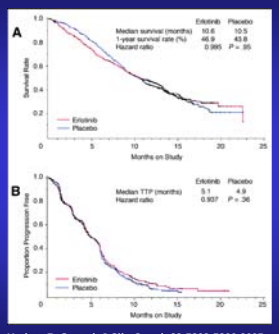
Tribute Trial
Fig 1. Study schema



- Erlotinib: 150 mg/day p.o. (after dose selection)
- Chemotherapy = carboplatin AUC 6 (day 1) and paclitaxel 200 mg/m² (day 1)
- N = 1,079
- 80% power to detect a 25% survival benefit, $\alpha = 0.05$
- Similar power to detect a 33% improvement in 1 year survival
- Treatment beyond documented disease progression was allowed in the original design, but discontinued after interim analysis

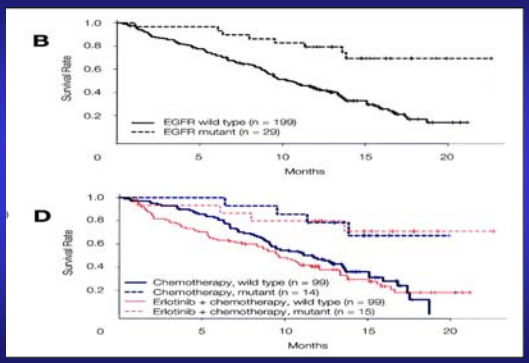
Herbst, R. S. et al. J Clin Oncol; 23:5892-5899 2005

Fig 2. Survival (A) and time to progression (B) intent-to-treat population



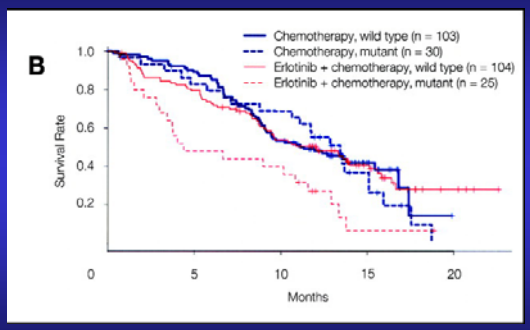
Herbst, R. S. et al. J Clin Oncol; 23:5892-5899 2005

Survival Based on EGFR Mutation in Tribute Trial



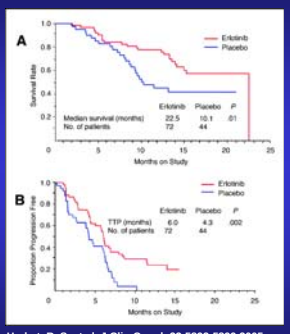
Eberhard PA, et al. JCO 23:5900-7, 2005

Survival Based on K-ras Mutation in Tribute Trial



Eberhard PA, et al. JCO 23:5900-7, 2005

Fig 3. Survival (A) and time to progression (B) for never smokers



Herbst, R. S. et al. J Clin Oncol; 23:5892-5899 2005

JOURNAL OF CLINICAL ONCOLOGY

CALGB 30406: Erlotinib vs. Chemo/Erlotinib in a clinically enriched population

- Stage IIIB/IV
- Non-smokers
- Light smokers
- Chemotherapy naïve
- Adenocarcinoma
- Mandatory tissue acquisition

Randomize

Erlotinib

Erlotinib + Carboplatin/Paclitaxel

Light smoker: quit ≥ 1 year ago and ≤ 10 pack years

Patients with known EGFR mutations eligible if they fit other criteria

CALGB 30406: Sample size and Stats

- Primary endpoint: TTP
- Secondary: response rate, median and overall survival, correlative science
- TTP for chemo alone in TRIBUTE never smokers: 4.3 months
- Erlotinib: median TTP ≥ 4.3 months –74 pts.
- Erlotinib/Chemo:median TTP ≥ 6.0 months – 72 pts.
- Total patients:158 (78 erlotinib/76 erlotinib/chemo; 5% dropout rate)

CALGB 30406: Correlative Science

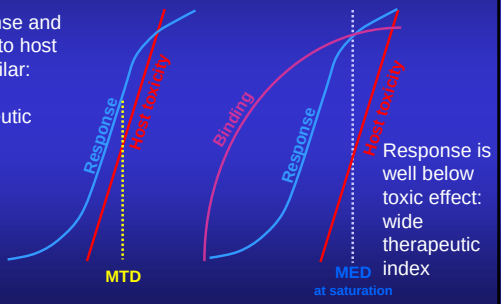
- EGFR and K-ras sequencing on all pts
- Pts with FNAs not eligible
- Sequencing performed at Harvard – CLIA certified
- Support: translational research funds or R21 (in conjunction with specimens from 2nd line study)
- Additional screening tests being developed

Conclusions

- We have had a paradigm shift in the management of advanced NSCLC!
  - Antiangiogenic and anti EGFR therapies improve patient survival
  - The integration of targeted agents has transformed chemotherapy into systemic therapy
  - Treatment plans will be individualized based on patient characteristics and tumor biology

Dosing of Cytotoxic Chemotherapy vs Cytostatic Targeted Agents

Response and cell kill to host are similar: narrow therapeutic index



Response is well below toxic effect: wide therapeutic index

MTD = maximum tolerated dose; MED = maximum effective dose.

Chemotherapy-induced Neutropenia and Outcome in Advanced NSCLC Patients

Hypothesis:
Neutropenia is a biological measure of drug activity and marker of efficacy.

Methods:
Landmark Analysis of survival from 3 randomized trials – ELVIS, MILES, GEMVIN

Of 1265 pts, 436 received all 6 planned cycles and were alive at 180 days.

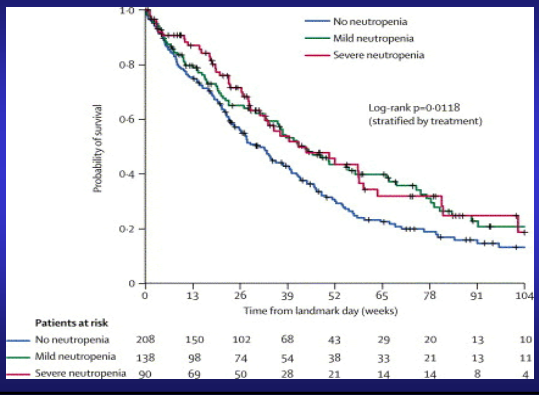
Results:

	HR	Median Survival (wks)	
No Neutropenia	1.0	31.4	
G1-2 ANC	.74	42.0	
G3-4 ANC	.65	43.7	p=.01

Age, gender, PS, Stage and histological subtype non-significant.

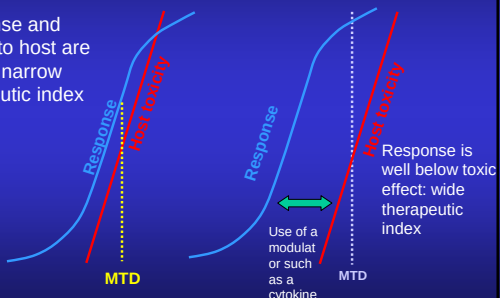
DiMaio M. Lancet Oncology 6:669-77.

Overall survival by grade of neutropenia for patients in landmark analysis.



Changing Therapeutic Index

Response and cell kill to host are similar: narrow therapeutic index



Response is well below toxic effect: wide therapeutic index

MTD = maximum tolerated dose; MED = maximum effective dose.

Platinum-Etoposide Chemotherapy in Elderly Patients with Small-Cell Lung Cancer: Results of a Randomized Multicenter Phase II Study Assessing Attenuated-Dose or Full-Dose With Lenograstim Prophylaxis

FONICAP-GSTPV Study – A. Ardizzoni, A. Favaretto, L. Boni, E. Baldini, F. Castiglioni, P. Antonelli, F. Pari, C. Tibaldi, A. M. Altieri, S. Barbera, G. Cacciani, M. Raimondi, L. Tixi, M. Stefani, S. Monfardini. A. Antilli, R. Rosso, and A. Paccagnella
Journal of Clinical Oncology 23: 569-575, 2005

Attenuated or Full Dose Cisplatin/Etoposide

Study Design

SCLC patients >70 years of age

AD
Cisplatin 25 mg/m^2 d 1,2
Etoposide 60 mg/m^2 d 1,2,3

FD
Cisplatin 40mg/m^2 d 1,2
Etoposide 100mg/m^2 d 1, 2, 3
Lenograstim 5 mg/kg d 5-12

Treatment Plan – 4 cycles

[1^0 Endpoint – "Therapeutic Success"]

(≥ 3 cycles at planned dose/schedule with objective response, without G ¾ toxicity)

Ardizzoni, JCO 23: 569-575, 2005

Attenuated or Full Dose Cisplatin/Etoposide

Results

Objective Tumor Response/Survival

	AD (n-28)	FD (n=67)
CR	-	9%
PR	39.3%	55.2%
Survival		
1 yr	18%	39%
2 yr	0%	12%
Median (weeks)	31	41

Ardizzoni, JCO 23: 569-575, 2005

Attenuated versus Full Dose Cisplatin/Etoposide

1) Delivery of full dose platinum/etoposide with neutrophil growth factor support is feasible and active in elder patients with SCLC

2) Delivery of attenuated doses of platinum/etoposide without GF support was well tolerated, but with substantially less clinical activity (lower response, shorter survival)

Ardizzoni, JCO 23: 569-575, 2005

Conclusions

- Neutropenia in the cancer chemotherapy patient has serious consequences in terms of morbidity and mortality.
- Neutropenia may also compromise dose delivery and clinical outcome for cancer patients.
- Clinical trials have documented the benefit of myeloid growth factors in reducing neutropenic complications across a wide range of patient risks.

Conclusions

- Patient risk models are needed to help further define the population at risk to maximize the benefit of myeloid growth factors.
- Delivery of standard full dose chemotherapy is a quality measure in oncology that warrants prospective study to validate the impact on cancer survivors.