



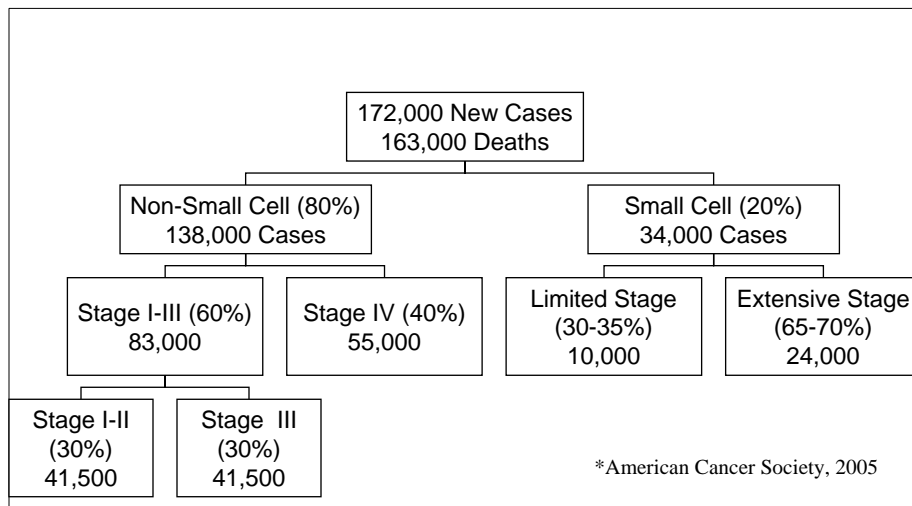
Lung Cancer Overview

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CALGB CRA Orientation, November 2006



Lung Cancer 2006*



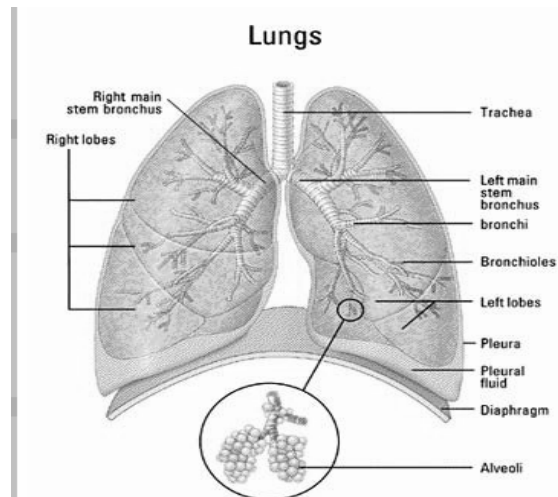


Lung Cancer Presentation

- Symptoms
 - General
 - Local
 - Regional
 - Metastatic
 - Paraneoplastic
 - Signs
-



Lung Anatomy



Diagnostic studies

- Physical exam/performance status
- Chest xrays, CTs, and MRIs
- Radionuclide scans (bone)
- PET (Positron Emission Tomography) scans
- Laboratory studies
- Biopsies
 - Bronchoscopic
 - Transthoracic biopsies
 - Needle biopsies of other organs
- Mediastinoscopy report
- Operative notes/pathology reports

Staging

- Non-small cell lung cancer (NSCLC)
- 4 stages, using the T, N, M system:
 - IA
 - IB
 - IIA
 - IIB
 - IIIA
 - IIIB
 - IV

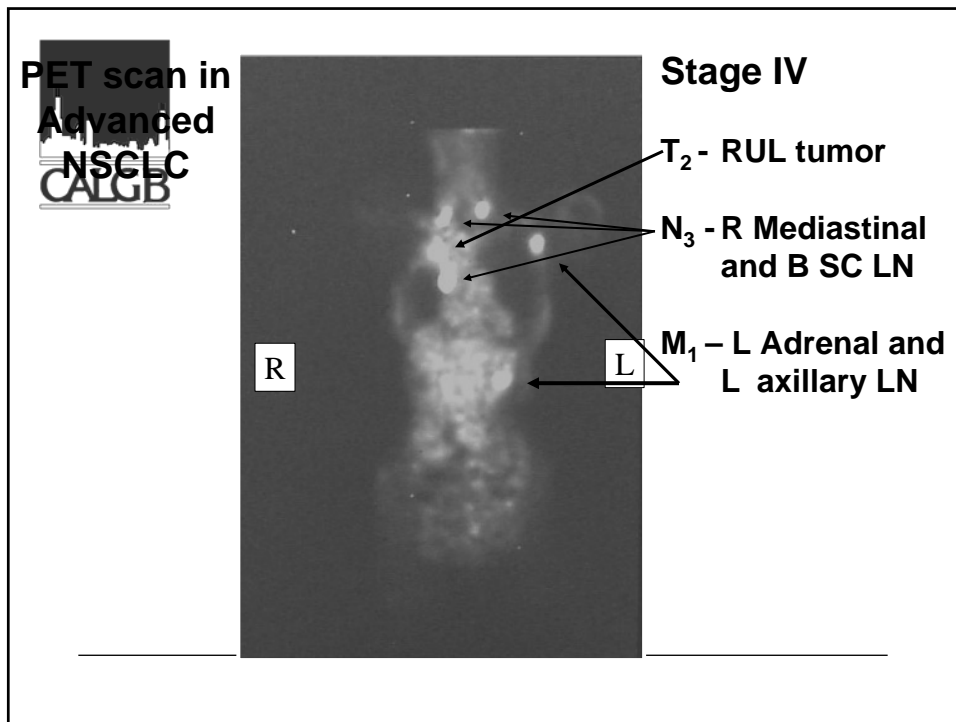


NSCLC Survival

Mountain CF. Chest. 1997;111:1710-1717.
Lababede et al. Chest. 1999;115:233-235.

Prognostic factors

- Staging
 - T (tumor) size, extension
 - N (nodes) location
 - M (metastases)
- Histologic sub-type-adenocarcinoma, squamous cell, large cell, small cell, mixed
- Sites of metastases
- Prior therapy – surgery, radiation, chemotherapy



Treatment Options

- Surgery-biopsy-lobectomy, wedge resection, pneumonectomy, VATS
- Radiation therapy
- Chemotherapy
 - Now includes “Targeted agents”
- Multimodality therapy (any combination of S, RT, or CT)
- Ancillary therapies

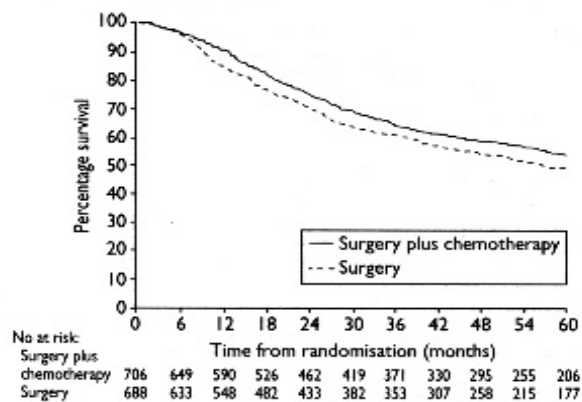


Goals of Adjuvant Therapy

- Eliminate microscopic metastases
 - Eradicate residual disease
 - Improve overall survival
 - Increase disease-free interval
 - Maximize local-regional control
 - Provide well-tolerated regimen
 - Maintain quality of life
 - Avoid long-term toxicities
-



Survival from Meta-analysis: Cisplatin-Based Adjuvant Chem



p=0.08

Non-small Cell Lung Cancer Collaborative Group. *BMJ*. 1995;311:899-909.



Adjuvant Chemotherapy

	Chemo	Control
IALT: N=1867	Cisplatin-based	-
MS	51 mo	44 mo
5-yr	44.5%	40.4%
NCIC: N=482	Cis-vinorelbine	-
MS	94 mo	73 mo
5-yr	69%	54%
CALGB: N=344	Carbo-paclitaxel	-
4-yr	71%	59%

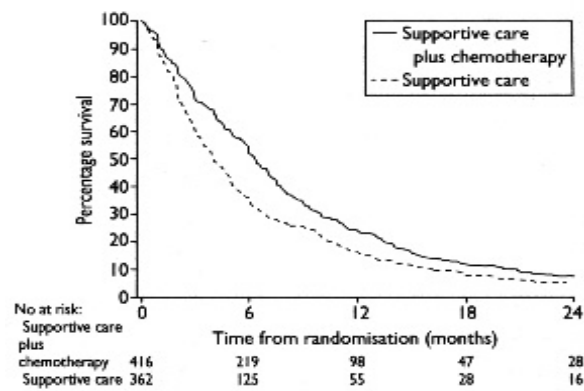


Chemotherapy in Unresectable Stage III NSCLC

Trial	Treatment	Median Surv. (mo)	5-year survival
Dillman	Chemo + RT	14	19 %
	RT alone	10	7 %
Sause	Chemo + RT	14	8 %
	RT alone	11	5 %
LeChevalier	Chemo + RT	12	12 % (3-yr)
	RT alone	10	4 % (3-yr)



ROLE OF CHEMOTHERAPY IN ADVANCED NSCLC



Chemotherapy Decision Process

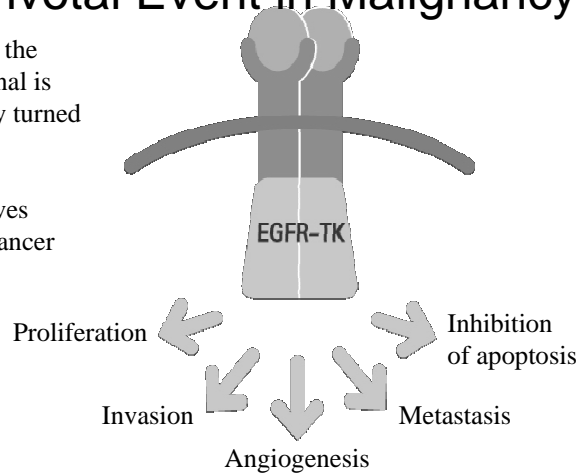
- Determine diagnosis and stage
- Evaluate prognostic factors
 - performance status
 - age
 - Co-morbidities
- Assess patient goals and preferences
 - level of aggression
 - tolerance of toxicities
- Individualize treatment strategy



Turning On the EGFR-TK Signal

A Pivotal Event in Malignancy^{1,2}

- In tumor cells, the EGFR-TK signal is inappropriately turned on
- EGFR-TK drives uncontrolled cancer cell growth



1. Woodburn JR. *Pharmacol Ther.* 1999;82:241-250. 2. Ciardiello F et al. *Clin Cancer Res.* 2001;7:1459-1465.



QOL: BR.21 Erlotinib in Refractory NSCLC

- A7018
- Both arms had similar baseline QOL scores
- MS 6.7 mo Erlotinib vs. 4.7 mo placebo

	Time to decline in QOL score (months)	
	Erlotinib	Placebo
Cough	4.9*	3.7
SOB	4.7*	2.9
Pain	2.8*	1.9

•*p=0.04

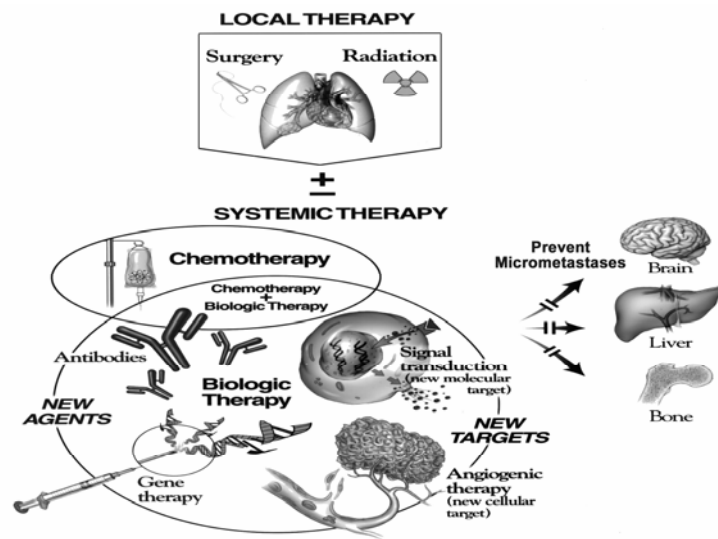


Conclusions

- Chemotherapy improves survival and QOL in pts with advanced NSCLC
 - Newer drugs offer better, less toxic options
- Chemotherapy improves survival over surgery or RT alone in stage III NSCLC
 - Concurrent chemotherapy-RT may be superior to sequential therapy
- Chemotherapy improves survival when given post-operatively to pts with stage IB-III A NSCLC
- New targeted therapy may further improve our ability to treat patients more effectively
 - Applies to both advanced and localized disease



Chemotherapy + Biologic Therapy A New Paradigm





Small Cell Lung Cancer Extensive Stage Disease

- Platinum/VP-16 x 4-6 cycles remains standard
- Cis/VP → topotecan = cis/VP alone
- Oral topotecan being studied
 - 34 chemo-naïve pts: 35% RR, MS=37 wk
- Intergroup Cis/VP/Pac vs. Cis/VP underway
- Cis/CPT improved RR/survival over cis/VP*
 - RR 89% v 67%, MS 13.5 v. 9.3 mo, 1-yr 56 v 34%

*Kudoh, et al. for JCOG. NEJM 2002.

Mesothelioma

- A rare tumor of the pleura (tissue surrounding the lung and inside the chest wall)
- Associated with asbestos exposure
- Surgery and radiation therapy are not often options, so chemotherapy is usually the therapy
- CALGB has lead the world in testing chemotherapy for mesotheliomas

Response Assessment

- Complete response
- Partial response
- Stable disease
- Progression/relapse
- Use RECIST Criteria

Follow-up

- Relapse (time to progression, sites of relapse)
- Survival
- Toxicity
- Quality of life



Teenage Smoking

