

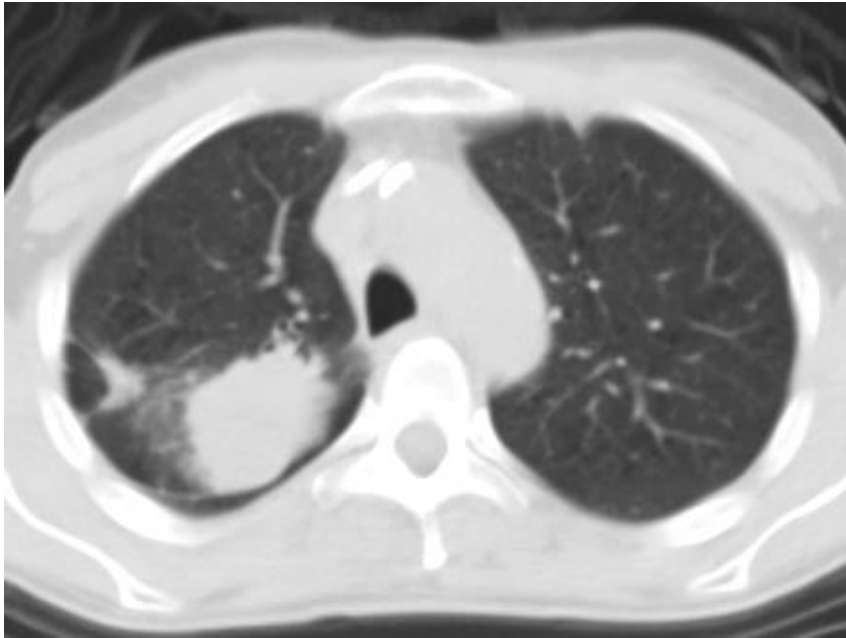
Treatment strategies for oligometastatic lung cancers

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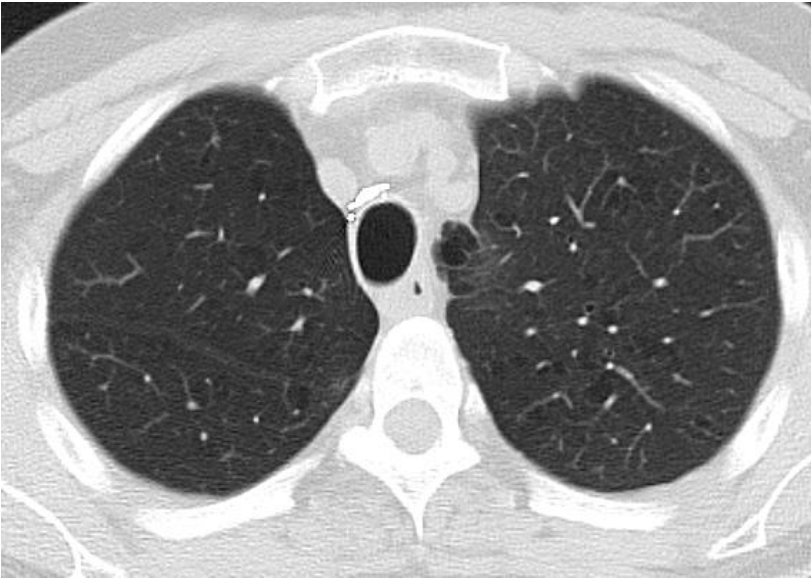
No disclosures

53 yo w/ stage IV lung adenocarcinoma



- 6/07: Presented with a 4cm RUL tumor, a 1cm satellite RUL nodule, mediastinal/hilar LN and a lesion in L1
- No known driver mutations
- 7/07-10/07: Carboplatin/paclitaxel/bevacizumab x 6
- 7/08-3/09: pemetrexed/bevacizumab

53 yo w/ stage IV lung adenocarcinoma



- 4/09 RUL lobectomy and MLND
- 6/09 IGRT to L1
- 4/11 RFA to recurrence at L1
- 12/13 CT CAP: NED

How do we select patients for local therapy, how do they do and how can we do better?

Outline

Define oligometastatic disease

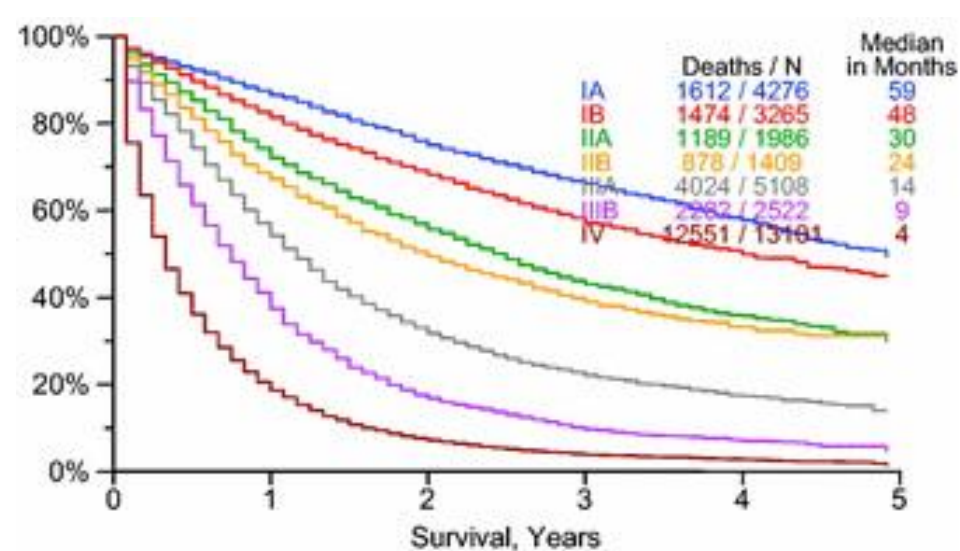
Review of the available data

Local therapy in oncogene driven cancers

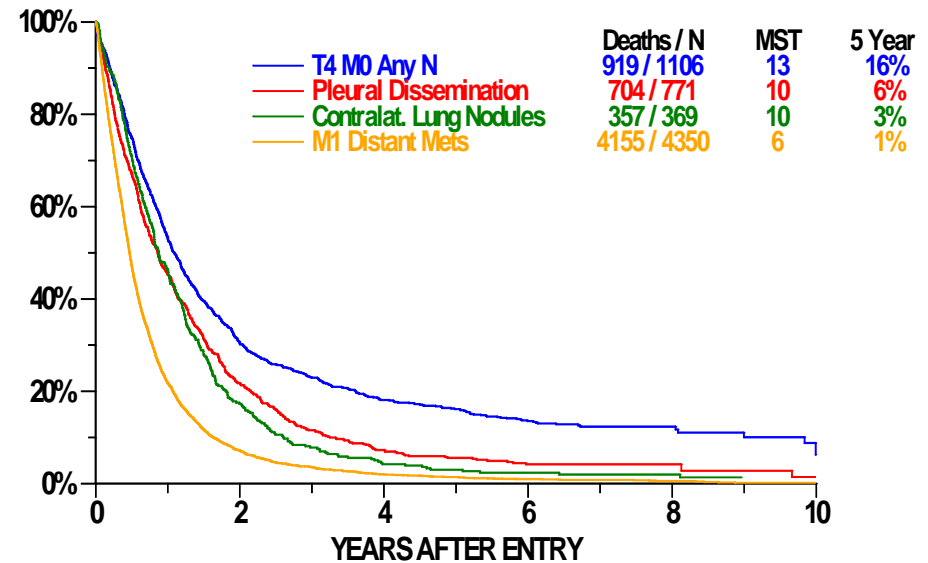
Ongoing studies/Future directions

Definitions

Overall Survival by TNM Stage



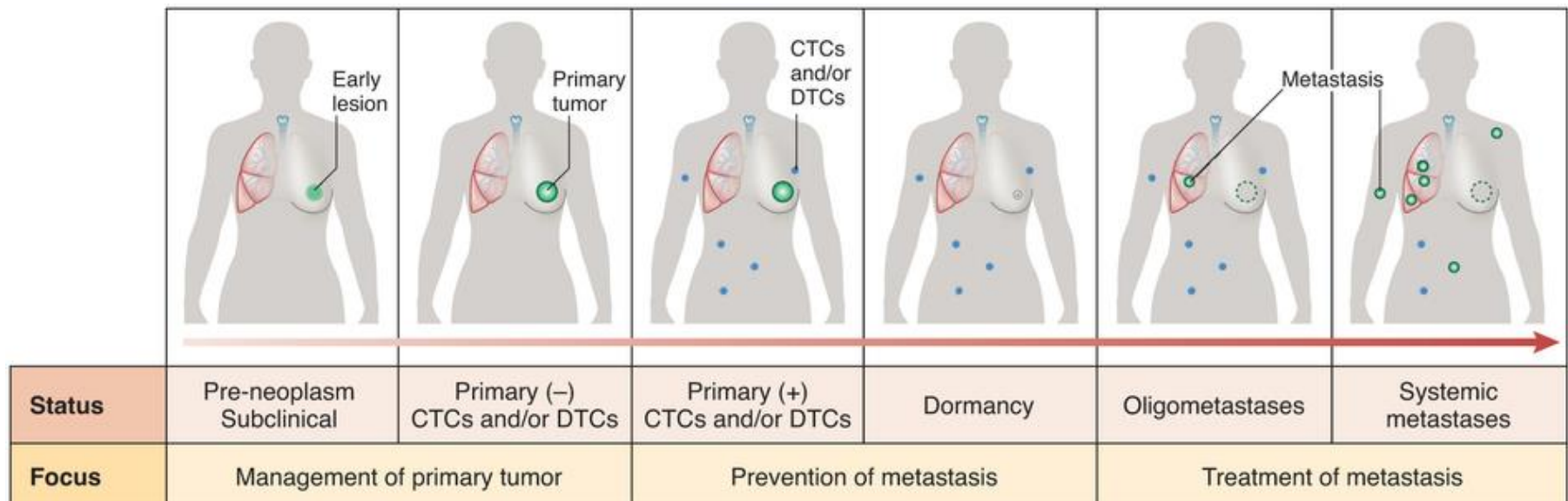
Overall Survival by M site



Definitions

Old paradigm: Early stage- Curative therapy
Metastatic disease- Palliative therapy

New Paradigm: Spectrum of tumor progression



Oligometastatic
Disease:

Possible intermediate state reflecting tumor biology

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Intra-pulmonary metastases

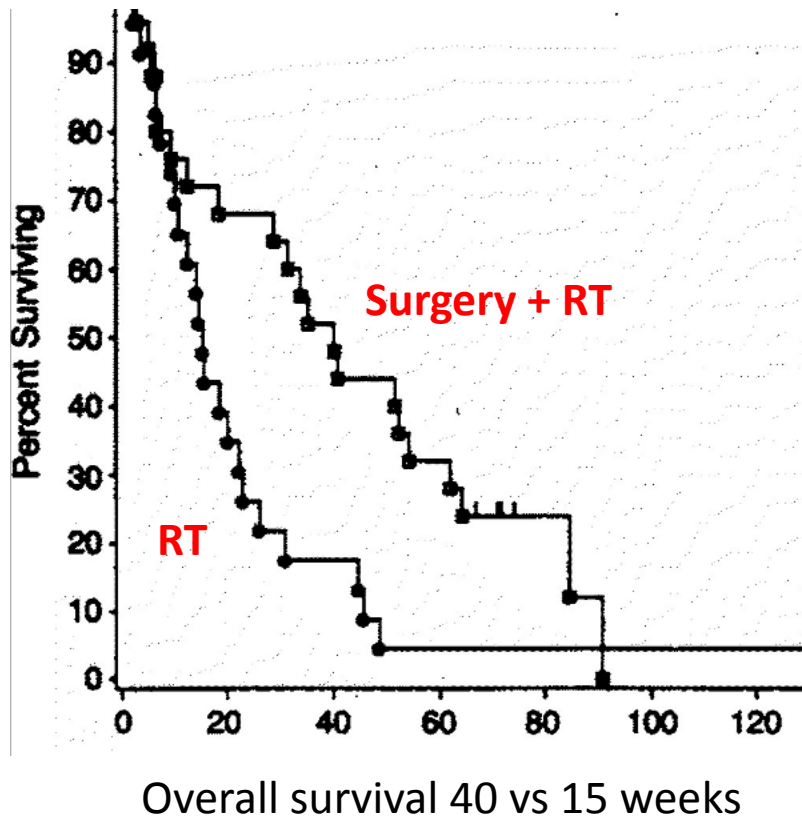
Table 5
Multivariate analysis for survival (Cox regression).

	Factor	R.R.	95% CI	<i>p</i>
Age	<67 ^a versus ≥67 years	0.667	0.207–2.144	0.496
Sex	Male versus female	3.050	0.327–28.477	0.328
Smoke	Yes versus no	1.959	0.188–20.412	0.574
Location	Unilateral versus bilateral	0.597	0.225–1.584	0.300
Type of resection	Sublobar versus lobar	1.048	0.389–2.823	0.926
Histology	Same versus different	0.519	0.185–1.454	0.212
Adjuvant treatment	No versus yes	0.603	0.195–1.862	0.379
Co-morbidity	None versus 1 or more	0.496	0.186–1.327	0.163
N stage	pN0 versus pN1–2	0.202	0.075–0.546	0.002
Period	1990–1999 versus 2000–2007	4.221	1.742–10.410	0.001

- Diagnostic challenge to differentiate between synchronous multiple primary lung cancers vs. intra-pulmonary metastases
- Overall 5 yr survival of 34%, median OS 32 months
- Lymph node positivity a persistently poor prognostic marker

Solitary brain metastases

Randomized trial of RT with and without surgery



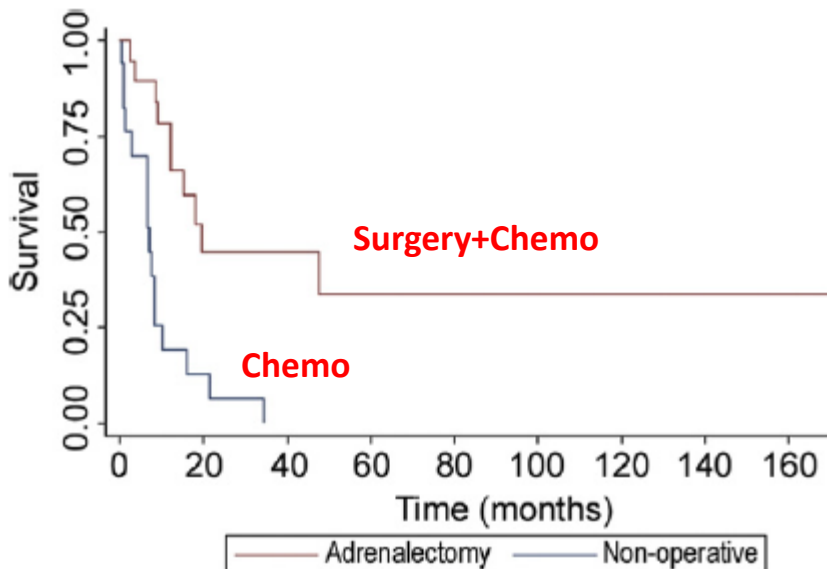
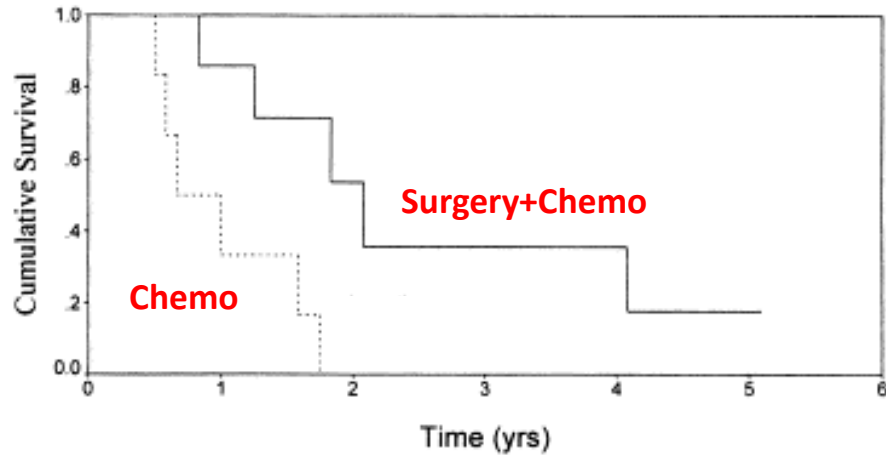
Factors associated with survival

Factor	Assigned Values	Univariate Analysis p Value	Multivariate Analysis p Value
gender	M/F	0.01	0.0088
synchronicity	synchronous/ metachronous	0.03	0.9873†
stage	1,2,3A,3B,4	0.0006	0.0872†
histology	ADCA,EPID,LARG	0.34†	0.4906†
systemic metastasis	yes/no	0.005	0.0083
extent of resection			
primary lung tumor	NT,CR,NR,PR	0.0001	0.0002
brain metastasis	total/partial	0.01	0.1025†
age	<65 yrs, ≥65 yrs	0.93†	0.2856†
	<60 yrs, ≥60 yrs	0.37†	0.0398
single metastasis	yes/no	0.02	0.3617†
supratentorial lesion	yes/no	0.04	0.0497
presurgery KPS score	≤60, ≥70	0.03	0.7624†
resection <i>en bloc</i>	yes/no	0.24†	0.1025†
diameter of brain tumor	<3 cm, ≥3 cm	0.07†	0.0530†
WBRT			
presurgery	yes/no	0.03	0.0572†
postsurgery	yes/no	0.07†	0.1187†

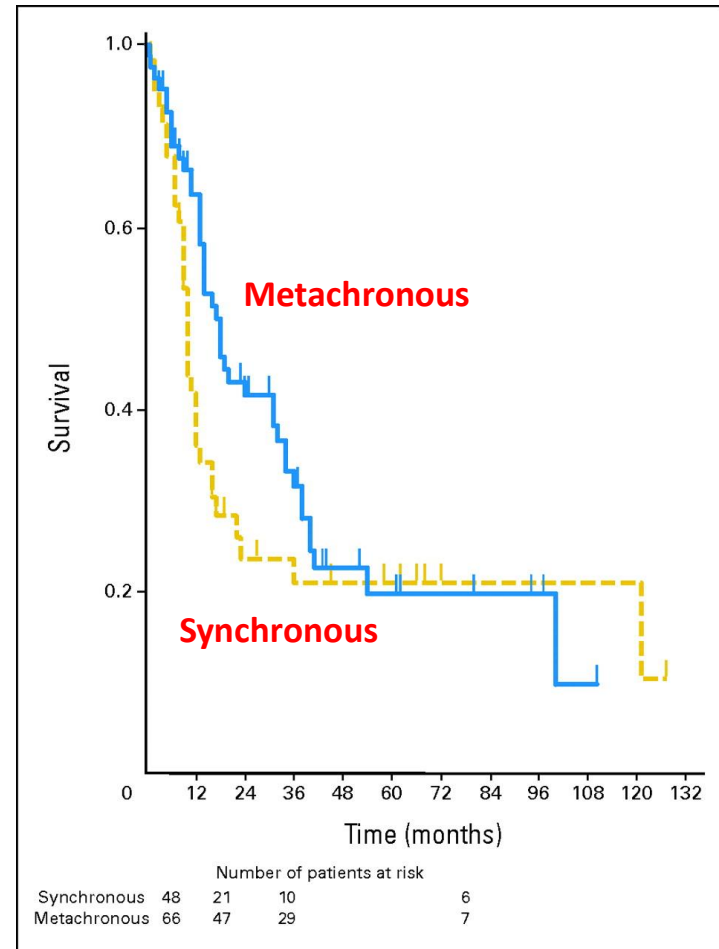
Median overall survival = 11 months

Adrenalectomy

Overall survival



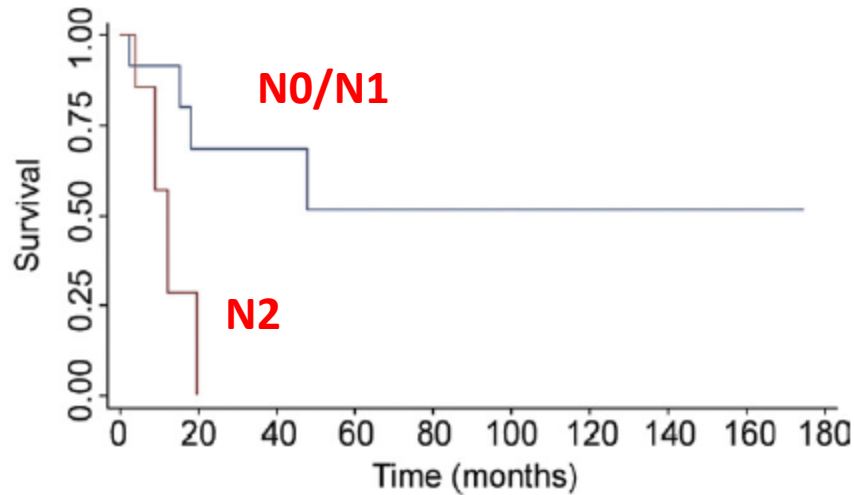
Metachronous vs synchronous tumors



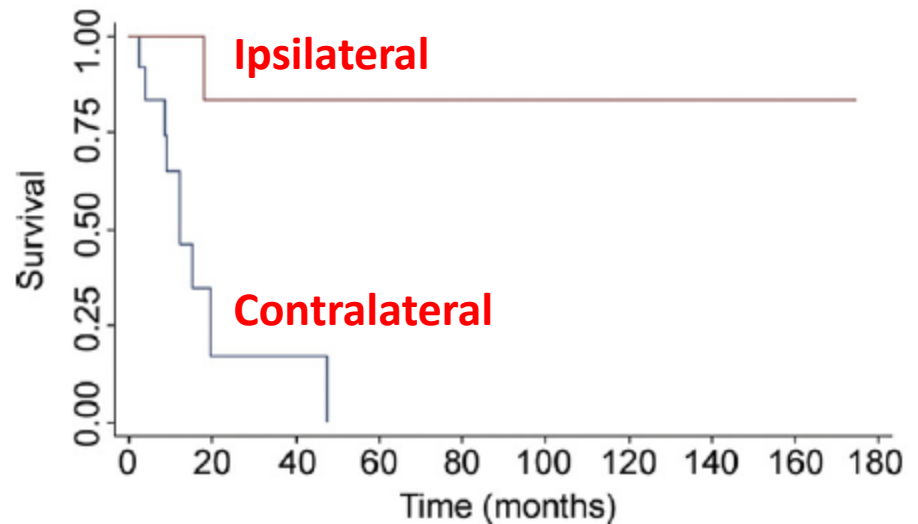
Tanvetyanon et al, JCO 2008; 26(7) 1142-1147
 Luketich et al Ann Thorac Surg 1996; 62:1614-6
 Raz et al, Ann Thorac Surg 2011; 92:1788-93

Adrenalectomy

Overall survival by nodal status



Ipsilateral vs contralateral adrenal met



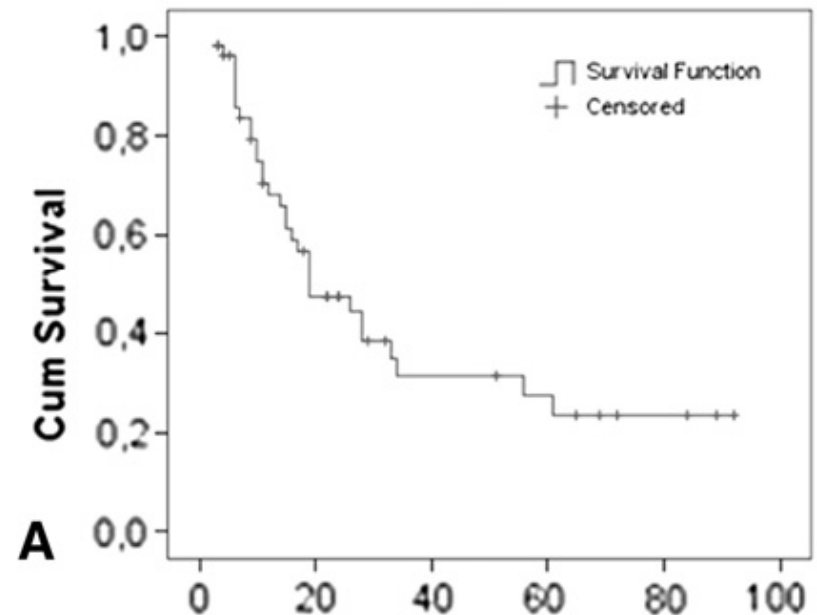
Multiple sites

Factors associated with survival

TABLE 3. Cox regression analyses

Variables analyzed	LTS	
	Univ. <i>P</i>	Multiv. [HR (95% CI)] <i>P</i>
Weight loss*	<i>P</i> < .001	[8.01 (2.73-23.51)] <i>P</i> < .00
cT stage†	<i>P</i> = .036	NS
PET-CT scan	<i>P</i> = .004	[0.46 (0.12-0.98)] <i>P</i> = .05
cN stage‡	NS	NS
Single metastases	<i>P</i> = .045	NS
Site of metastases§	<i>P</i> = .007	NS
Surgery for the metastatic lesion	<i>P</i> = .041	NS
Whole brain irradiation	NS	NS
Neoadjuvant Therapy	NS	NS
pT stage	<i>P</i> = .006	NS
pN stage¶	<i>P</i> = .030	NS
Surgical radicality (no vs yes)	<i>P</i> < .001	[4.75 (1.87-12.10)] <i>P</i> = .001
Adjuvant therapy	NS	NS
Histology#	<i>P</i> < .001	NS

Overall survival



Median Survival = 19 mo
5 yr OS = 24%

Outline

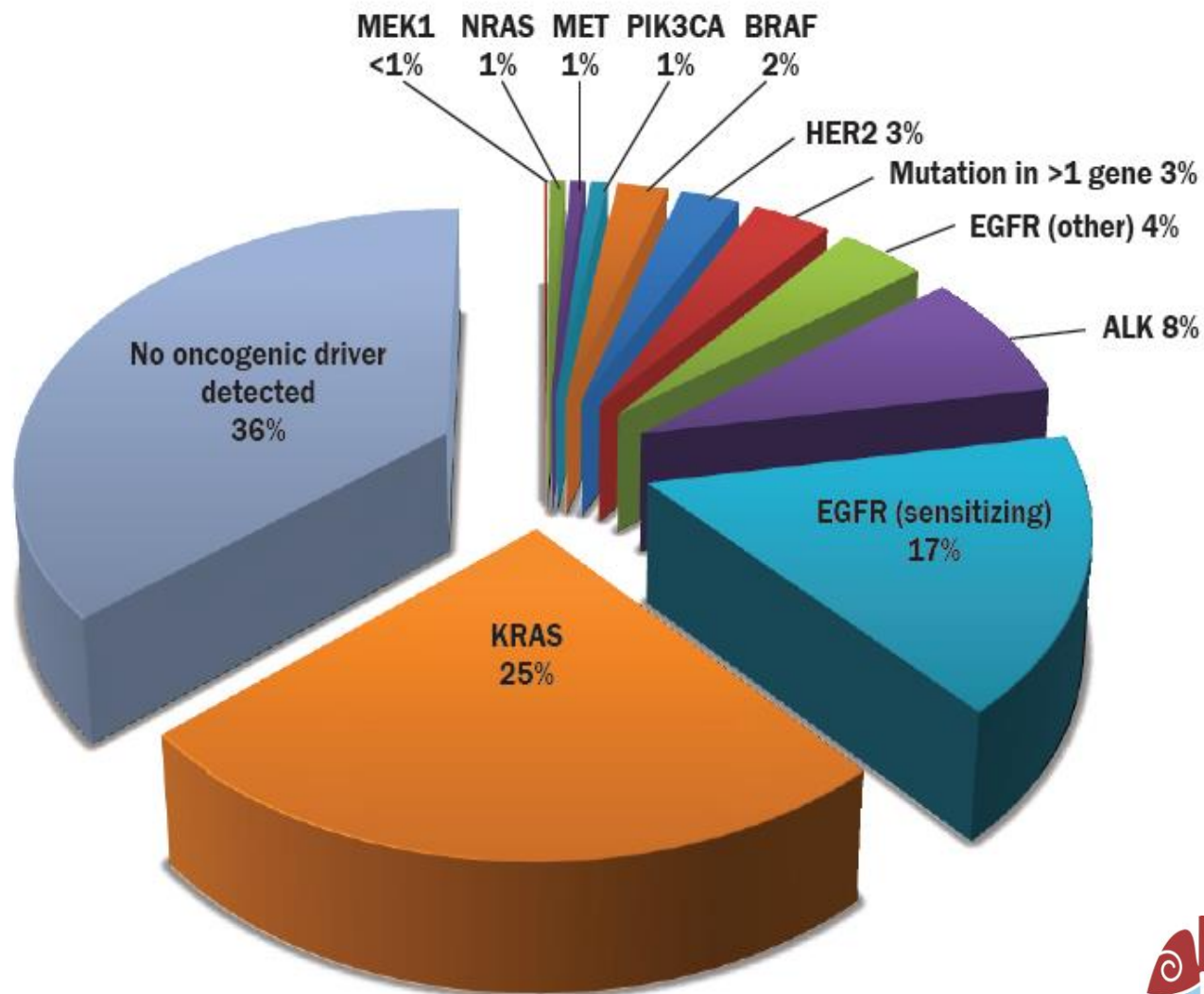
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Ongoing studies/Future directions

Driver mutations in lung adenocarcinoma



Lung Cancer
Mutation
Consortium



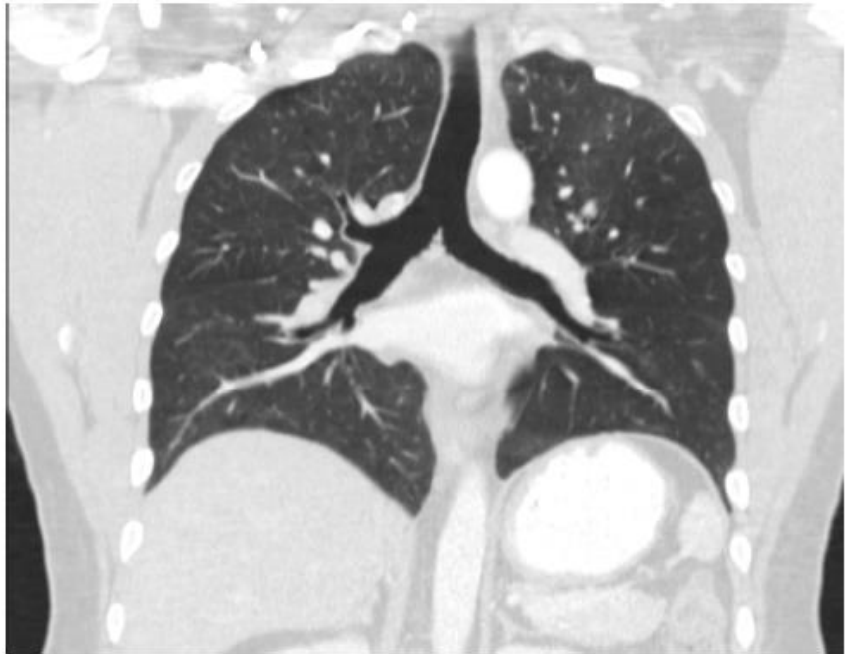
National Lung
Cancer Partnership
RESEARCH. AWARENESS. CHANGE.

Predictive implications

Patient with ROS1 positive lung cancer



Baseline

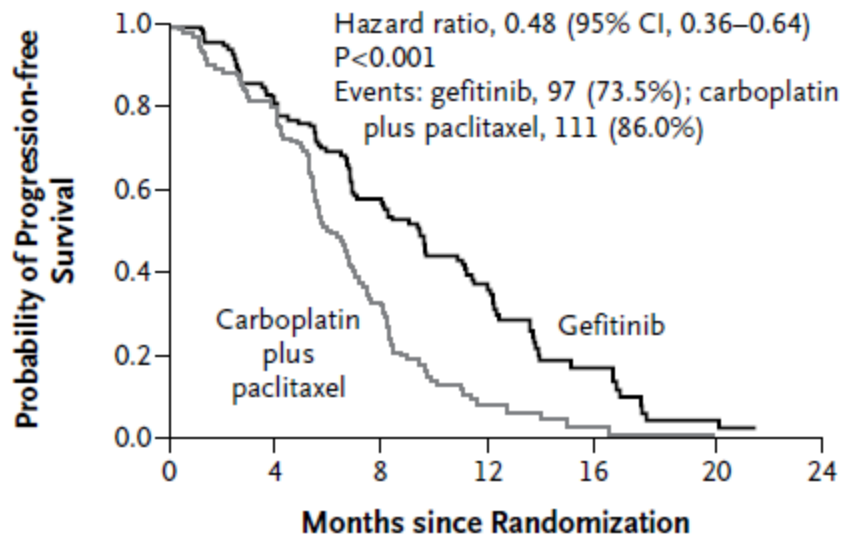


After 3 months of crizotinib

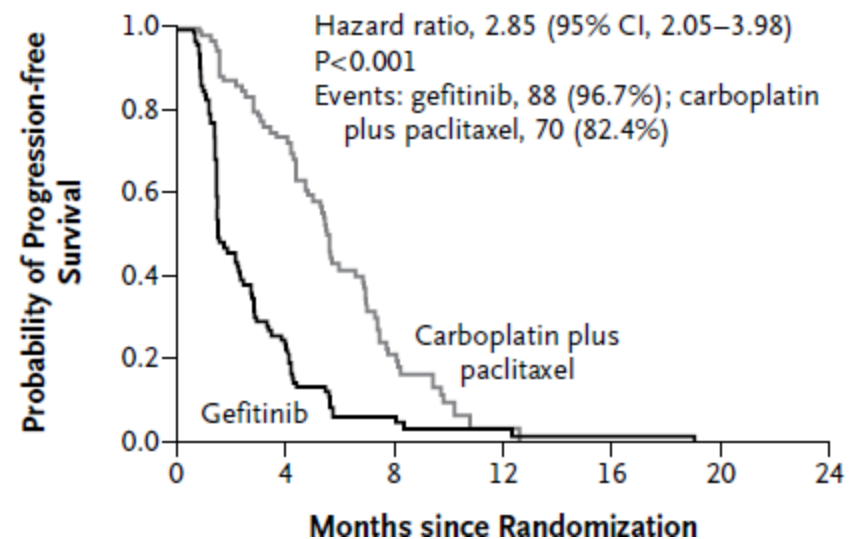
Predictive implications

Progression-Free Survival with Gefitinib and Chemotherapy

EGFR-Mutation-Positive



EGFR-Mutation-Negative

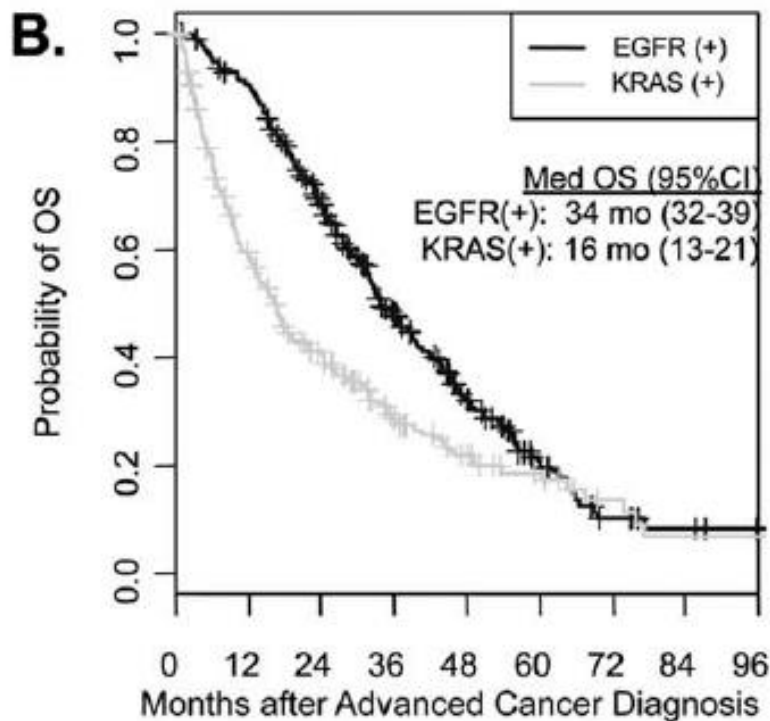


Overall Response Rate with Gefitinib and Chemotherapy

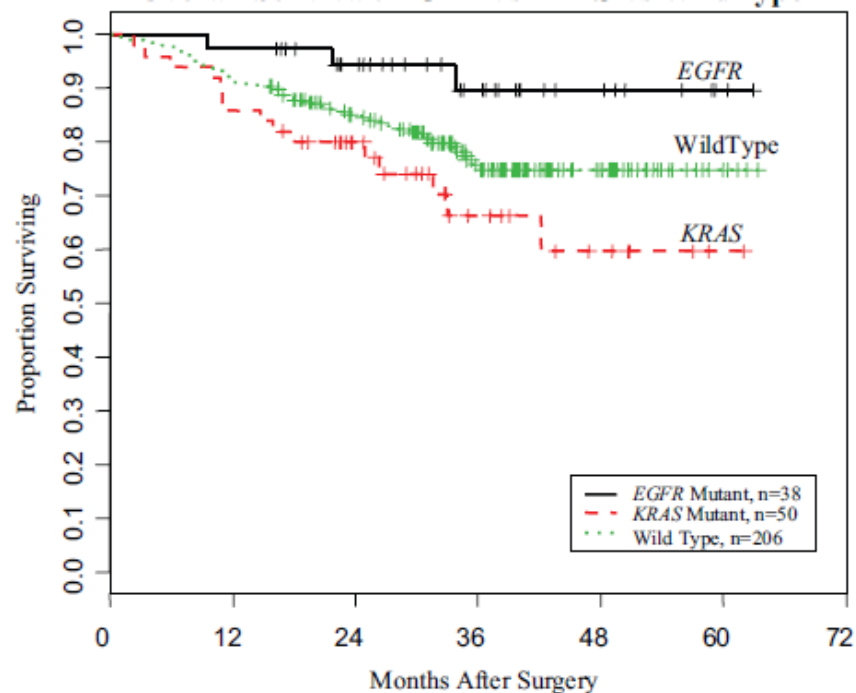
	EGFR+		EGFR-	
	Gefitinib	Chemo	Gefitinib	Chemo
ORR	71%	47%	1%	24%

Prognostic implications

Overall Survival
In Stage IV Disease



Overall Survival in
Early Stage Disease



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Ongoing studies

Induction therapy followed by local consolidative therapy

CT.gov #	Lead site	Study type	Intervention	Endpoint	Inclusion
NCT01725165	MD Anderson	Randomized	Local therapies	PFS	≤ 3 sites
NCT02045446	UTSW	Randomized	SBRT	PFS	≤ 6 sites
NCT01185639	Wake Forest	Single Arm	SBRT	PFS	≤ 5 sites

Ongoing studies

Identifying optimal time of local therapy

CT.gov #	Lead site	Study type	Intervention	Endpoint	Inclusion
NCT02076477	Sichuan	Randomized	Chemo, ChemoRT	ORR	≤ 5 sites

Oncogene specific studies

CT.gov #	Lead site	Study type	Intervention	Endpoint	Inclusion
NCT01573702	UNC	Single Arm	SRS	PFS	EGFR+ with POD on TKI

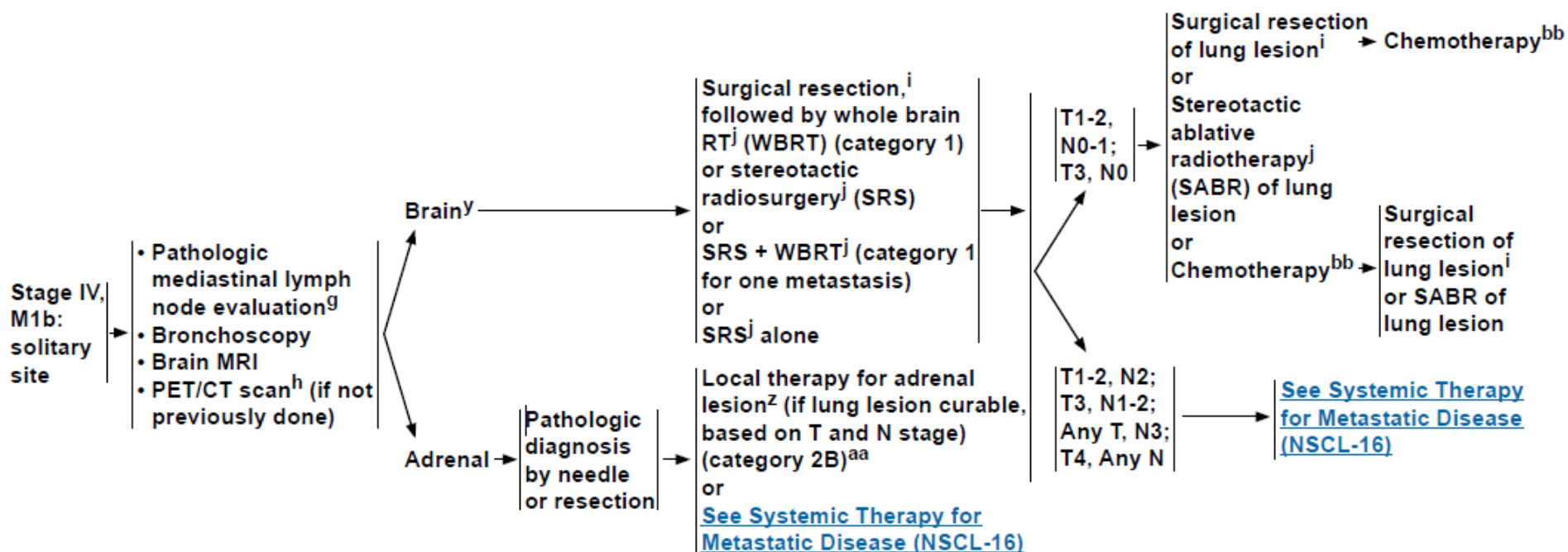


NCCN Guidelines Version 3.2014 Non-Small Cell Lung Cancer

CLINICAL ASSESSMENT

PRETREATMENT EVALUATION

INITIAL TREATMENT



Conclusions

How do we select patients:

- Allow time to understand natural history
- Local control of primary site
- Limited sites of disease (no nodal disease)
- Aim to render disease-free with local therapy

How do we do:

- Meaningful progression-free survival
- Extended survival – “Cure”

Conclusions

How can we do better:

- Appropriate patient selection
- Understand underlying tumor biology