Oligometastatik Küçük Hücreli Dışı Akciğer Kanserlerine Yaklaşım

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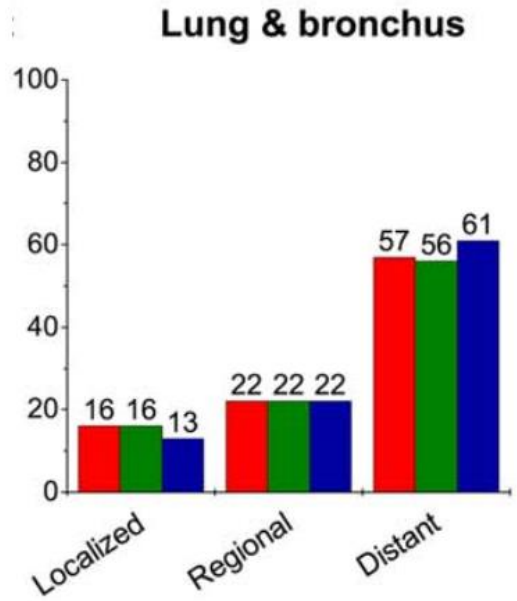
Antalya Memorial Hastanesi
16/02/2018

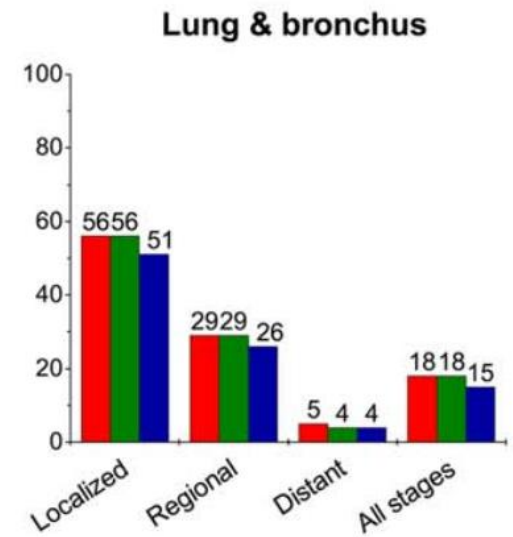
Estimated New Cases

	Males			Females		
Prostate	164,690	19%		Breast	266,120	30%
Lung & bronchus	121,680	14%		Lung & bronchus	112,350	13%
Colon & rectum	75,610	9%		Colon & rectum	64,640	7%
Urinary bladder	62,380	7%		Uterine corpus	63,230	7%
Melanoma of the skin	55,150	6%		Thyroid	40,900	5%
Kidney & renal pelvis	42,680	5%		Melanoma of the skin	36,120	4%
Non-Hodgkin lymphoma	41,730	5%		Non-Hodgkin lymphoma	32,950	4%
Oral cavity & pharynx	37,160	4%		Pancreas	26,240	3%
Leukemia	35,030	4%		Leukemia	25,270	3%
Liver & intrahepatic bile duct	30,610	4%		Kidney & renal pelvis	22,660	3%
All Sites	**856,370**	**100%**		**All Sites**	**878,980**	**100%**

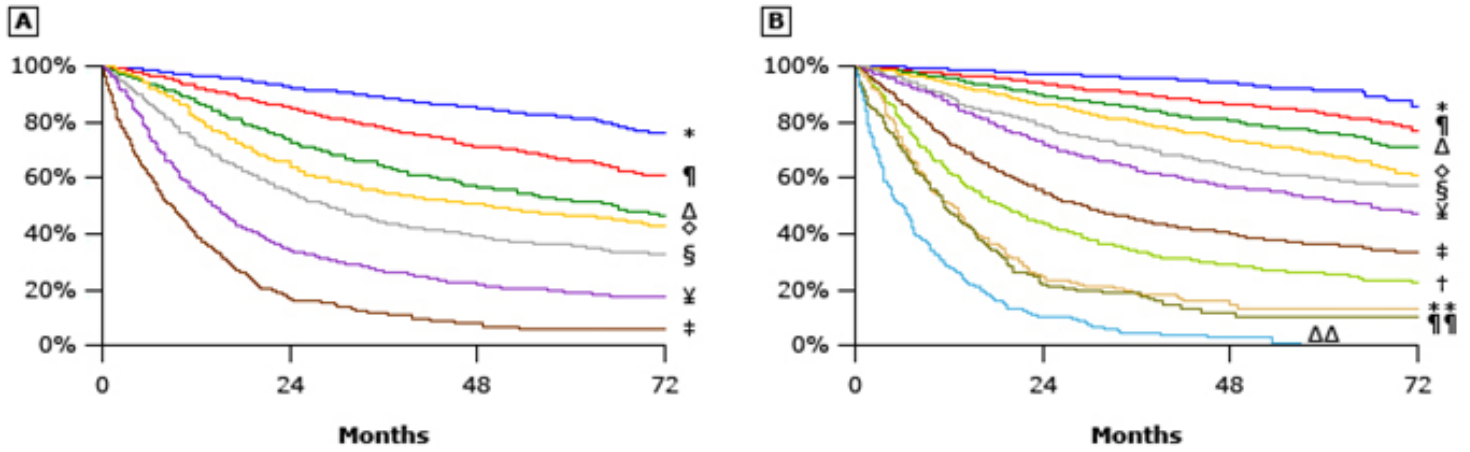


Estimated Deaths

	Males			Females		
Lung & bronchus	83,550	26%		Lung & bronchus	70,500	25%
Prostate	29,430	9%		Breast	40,920	14%
Colon & rectum	27,390	8%		Colon & rectum	23,240	8%
Pancreas	23,020	7%		Pancreas	21,310	7%
Liver & intrahepatic bile duct	20,540	6%		Ovary	14,070	5%
Leukemia	14,270	4%		Uterine corpus	11,350	4%
Esophagus	12,850	4%		Leukemia	10,100	4%
Urinary bladder	12,520	4%		Liver & intrahepatic bile duct	9,660	3%
Non-Hodgkin lymphoma	11,510	4%		Non-Hodgkin lymphoma	8,400	3%
Kidney & renal pelvis	10,010	3%		Brain & other nervous system	7,340	3%
All Sites	**323,630**	**100%**		**All Sites**	**286,010**	**100%**



Overall survival by clinical stage according to the seventh edition (A) and the eighth edition (B) groupings using the entire database available for the eighth edition



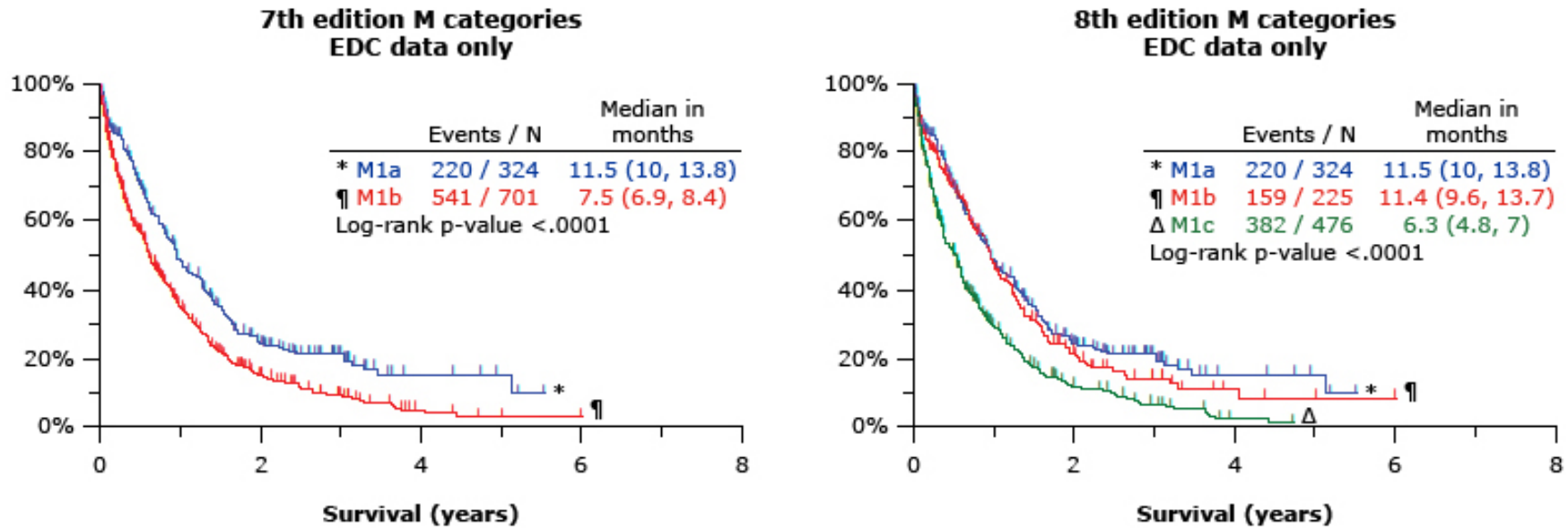
7th edition	Events / N	MST	24 month	60 month
* IA	1119 / 6303	NR	93%	82%
¶ IB	768 / 2492	NR	85%	66%
Δ IIA	424 / 1008	66.0	74%	52%
◇ IIB	382 / 824	49.0	64%	47%
§ IIIA	2139 / 3344	29.0	55%	36%
¥ IIIB	2101 / 2624	14.1	34%	19%
‡ IV	664 / 882	8.8	17%	6%

8th edition	Events / N	MST	24 month	60 month
* IA1	68 / 781	NR	97%	92%
¶ IA2	505 / 3105	NR	94%	83%
Δ IA3	546 / 2417	NR	90%	77%
◇ IB	560 / 1928	NR	87%	68%
§ IIA	215 / 585	NR	79%	60%
¥ IIB	605 / 1453	66.0	72%	53%
‡ IIIA	2052 / 3200	29.3	55%	36%
† IIIB	1551 / 2140	19.0	44%	26%
** IIIC	831 / 986	12.6	24%	13%
¶¶ IVA	336 / 484	11.5	23%	10%
ΔΔ IVB	328 / 398	6.0	10%	0%

Overall survival by clinical stage according to the seventh edition (A) and the eighth edition (B) groupings using the entire database available for the eighth edition. Survival is weighted by type of database submission: registry versus other.

%25 hasta oligometastatik

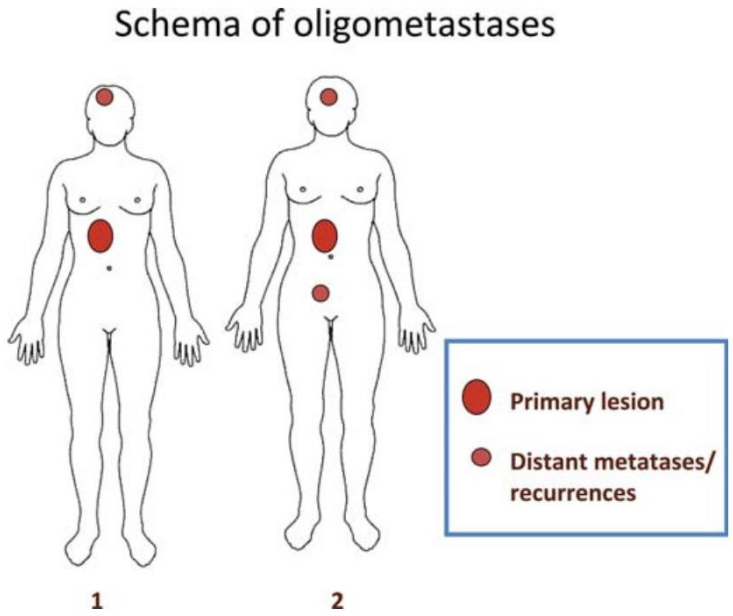
The 7th edition and 8th edition M categories

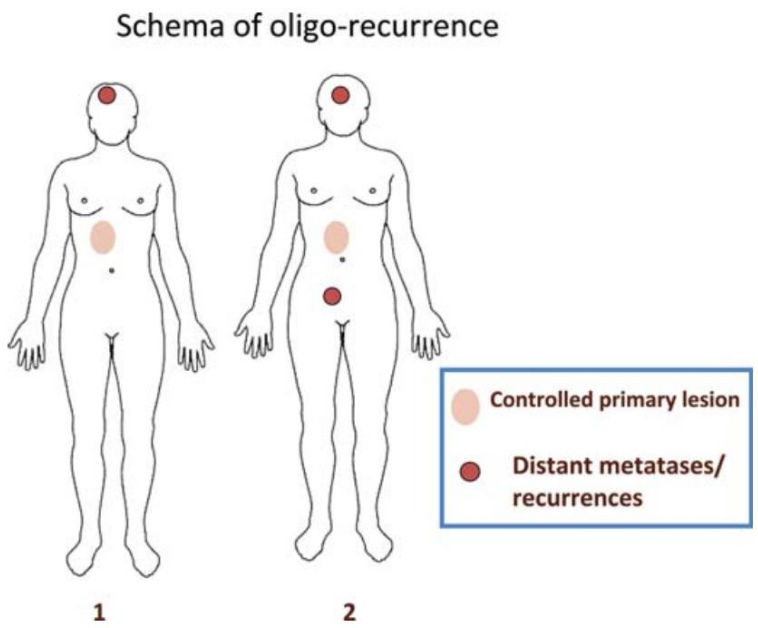


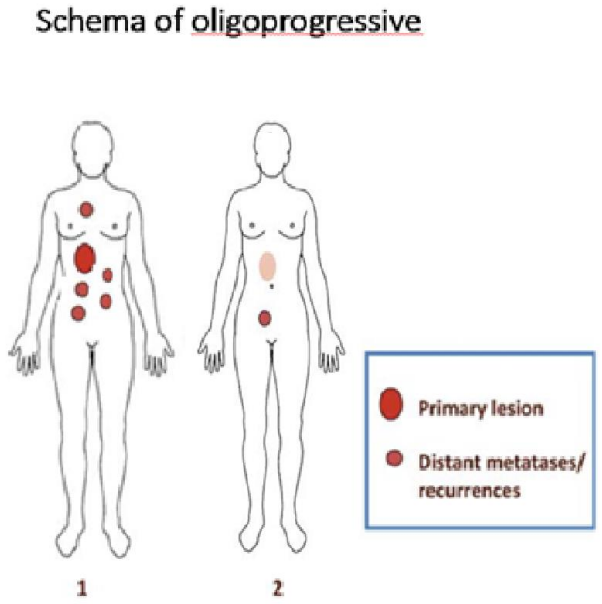
EDC: electronic data capture; N: number of patients.

Reproduced from: Eberhardt WE, Mitchell A, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for the Revision of the M Descriptors in the Forthcoming Eighth Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2015; 10:1515. Illustration used with the permission of Elsevier Inc. All rights reserved.

Tanımlama ve Klasifikasyonu:







Hellman S, Weichselbaum RR. Oligometastases. JCO 1995 Jan;13(1):8-10, Niibe Y, Hayakawa K. Oligometastases and oligo-recurrence: the new era of cancer therapy. Jpn J Clin Oncol. 2010 Feb;40(2):107-11.

Hasta Seçimi

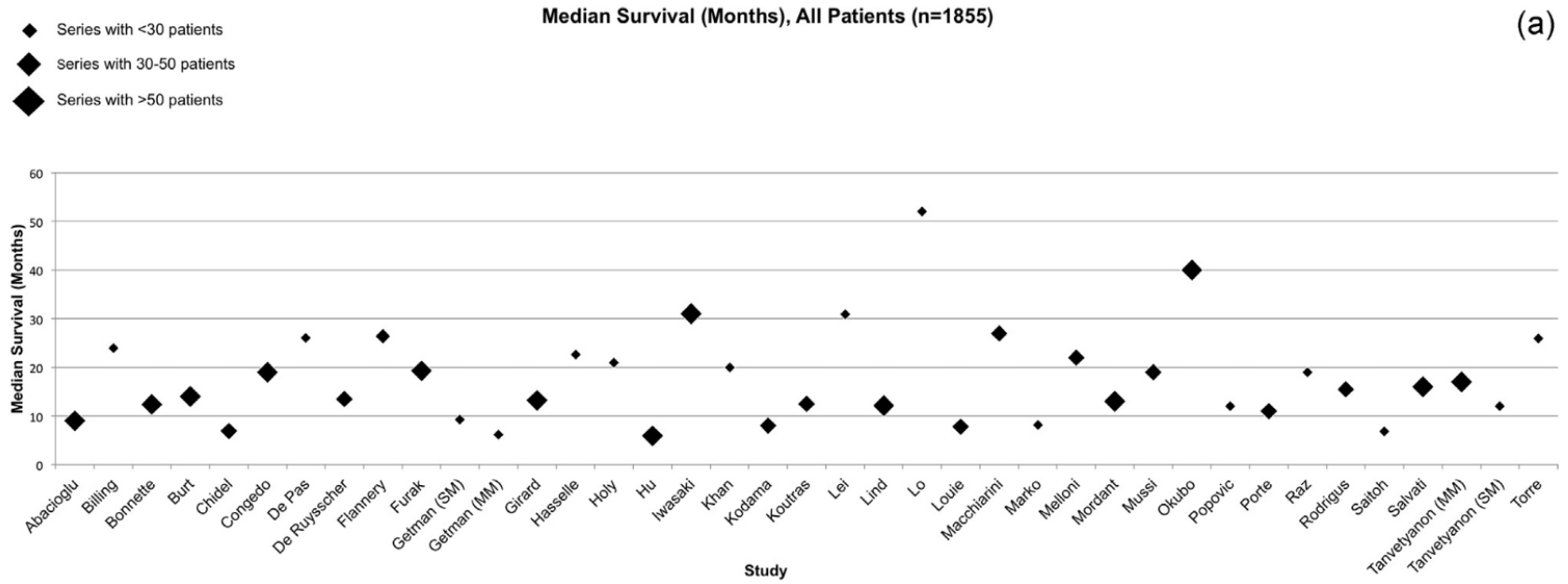
Is there an oligometastatic state in non-small cell lung cancer? A systematic review of the literature

Allison Ashworth, George Rodrigues, Gabriel Boldt, David Palma*

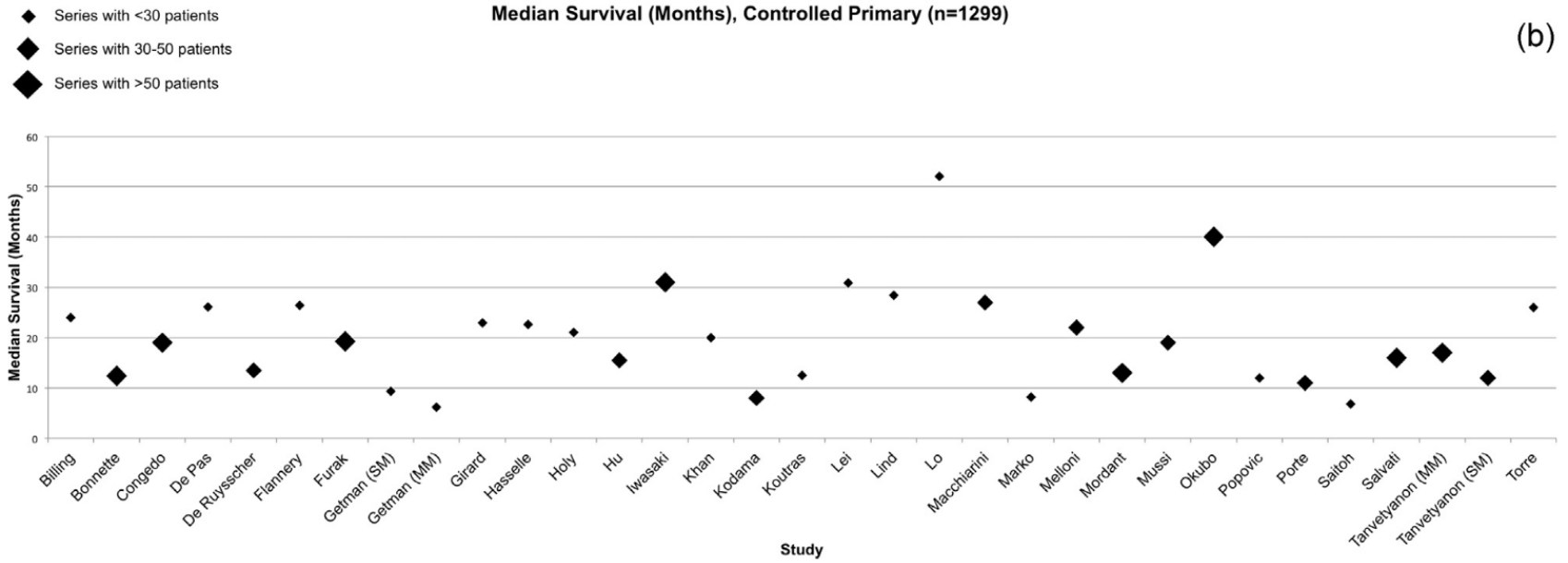
Department of Radiation Oncology, London Regional Cancer Program, London, Canada

Lung Cancer 82 (2013) 197–203

- 49 çalışma
- 1-5 metastazı olan 2176 hasta
- Hastaların %80'i primer kontrol altında
- %60 sadece beyin metastatik



Median 14.9 ay



Median 19 ay

Prognostic factors for survival assessed by multivariate analyses (MVA) in at least two studies.

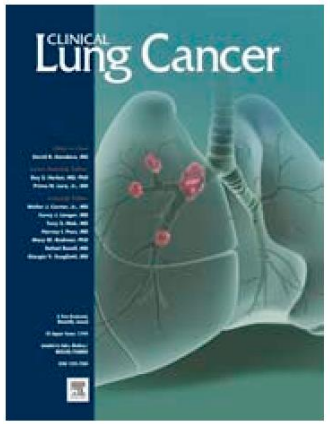
	Prognostic factor	# Studies reporting	# Studies significant/#studies reporting	Comments
Group 1	Controlled primary tumor	13	7/13	Better OS with radical/definitive treatment/controlled primary/complete resection vs. supportive/palliative treatment/uncontrolled primary/incomplete resection
	Primary tumor N-stage	12	6/12	*N*0 better OS than *N*+ (5 studies) *N*0/1 better OS than N2/3 (1 study)
	Disease free interval	4	3/4	Better OS with DFI > 360 days vs. < 360 days (brain metastases) with DFI > 1 year vs. < 1 year (multiple metastatic sites), better OS if DFI > 6 months vs. less (adrenal metastases)
Group 2	Presence of extra-cranial metastases	2	2/2	Decreased OS with presence of extra-cranial metastases
	Use of PET-CT	2	2/2	PET CT associated with better OS than CT alone
	RPA classification	2	1/2	RPA 1 better OS than RPA 2
	Primary tumor size	2	1/2	1–3 cm vs. 3–5 cm vs. > 5 cm, better OS with smaller primary tumor
	Type of thoracic resection	2	1/2	Lobectomy vs. pneumonectomy (better OS with lobectomy)
Group 3	Primary tumor histology	16	5/16	Adenocarcinoma better OS than other histologies
	Age	11	2/11	Age ≤50≥ or age ≤70≥ better OS
	Use of chemotherapy	8	1/8	Use of peri-operative chemotherapy associated with better OS
	# of oligometastases	7	2/7	1 vs. > 1 (1 study: lung mets), 1 vs. 2–3 vs. 4–6 (1 study: brain mets)
	Thoracic AJCC stage group	5	1/5	Stage I better than stage III or IV (no stage II pts in study)
	Sex	9	0/9	
	Primary tumor T-stage	7	0/7	
	Synchronous vs. metachronous oligometastases	4	0/4	
	Location of oligometastases	5	0/5	(visceral vs. non-visceral, ipsilateral vs. contralateral lung, ipsilateral vs. contralateral adrenal)
	Use of whole brain radiotherapy	3	0/3	

An Individual Patient Data Meta-Analysis of Outcomes and Prognostic Factors after Treatment of Oligometastatic Non-Small Cell Lung Cancer

Allison B. Ashworth , Suresh Senan , David A. Palma , Marc Riquet , Yong Chan Ahn , Umberto Ricardi , Maria T. Congedo , Daniel R. Gomez , Gavin M. Wright , Giulio Melloni , Michael T. Milano , Claudio V. Sole , Tommaso M. De Pas , Dennis L. Carter , Andrew J. Warner , George B. Rodrigues

PII: S1525-7304(14)00077-1

DOI: 10.1016/j.cllc.2014.04.003



20 merkez

757 hasta

1-5 metastazlı

Senkron/ metakron metastazı olan hastalar

53 aylık takip

Table II. Baseline clinical characteristics (*N*=757).

Variable	No. with data available	Median (range) or *N* (%)	Variable	No. with data available	Median (range) or *N* (%)
Male	671	483 (72.0%)	Good Performance Status*	358	352 (98.3%)
Age			No. of Oligometastases		
< 50	712	96 (13.5%)	1	757	668 (88.2%)
≥ 50, < 60		211 (29.6%)	2		63 (8.3%)
≥ 60, < 70		246 (34.6%)	3		12 (1.6%)
≥ 70		159 (22.3%)	4		9 (1.2%)
			5		5 (0.7%)
Synchronous vs. Metachronous	605		Location of Oligometastases	757	
Synchronous		457 (75.5%)	Adrenal		98 (13.0%)
Metachronous		148 (24.5%)	Bone		64 (8.5%)
			Brain		269 (35.5%)
			Lung		254 (33.6%)
			Liver		18 (2.4%)
			Lymph Node		18 (2.4%)
			Other		59 (7.8%)
T Stage	655		N Stage	658	
T1		163 (24.9%)	N0		342 (52.0%)
T2		348 (53.1%)	N1		129 (19.6%)
T3		110 (16.8%)	N2		171 (26.0%)
T4		34 (5.2%)	N3		16 (2.4%)
Thoracic Stage	652		Histology	743	
IA		115 (17.6%)	Adenocarcinoma		499 (67.2%)
IB		159 (24.4%)	Large Cell		57 (7.7%)
IIA		20 (3.1%)	Squamous		166 (22.3%)
IIB		134 (20.6%)	Other		21 (2.8%)
IIIA		178 (27.3%)			
IIIB		46 (7.1%)			
Oligometastases Treatment	544		Primary Lung Cancer Treatment	757	
Radiotherapy:		205 (37.7%)	Radiotherapy:		122 (16.1%)
EBRT		28 (5.2%)	EBRT		94 (12.4%)
SBRT/SABR		88 (16.2%)	SBRT/SABR		28 (3.7%)
SRS		62 (11.4%)			
RT (Other)		27 (5.0%)			
Surgical Metastasectomy:		339 (62.3%)	Surgery:		635 (83.9%)
Surgery		285 (52.4%)	Surgery		609 (80.4%)
Surgery + EBRT		3 (0.6%)	Surgery + EBRT		26 (3.4%)
Surgery + SBRT/SABR		3 (0.6%)			
Surgery + SRS		1 (0.2%)			
Surgery + RT (Other)		47 (8.6%)			

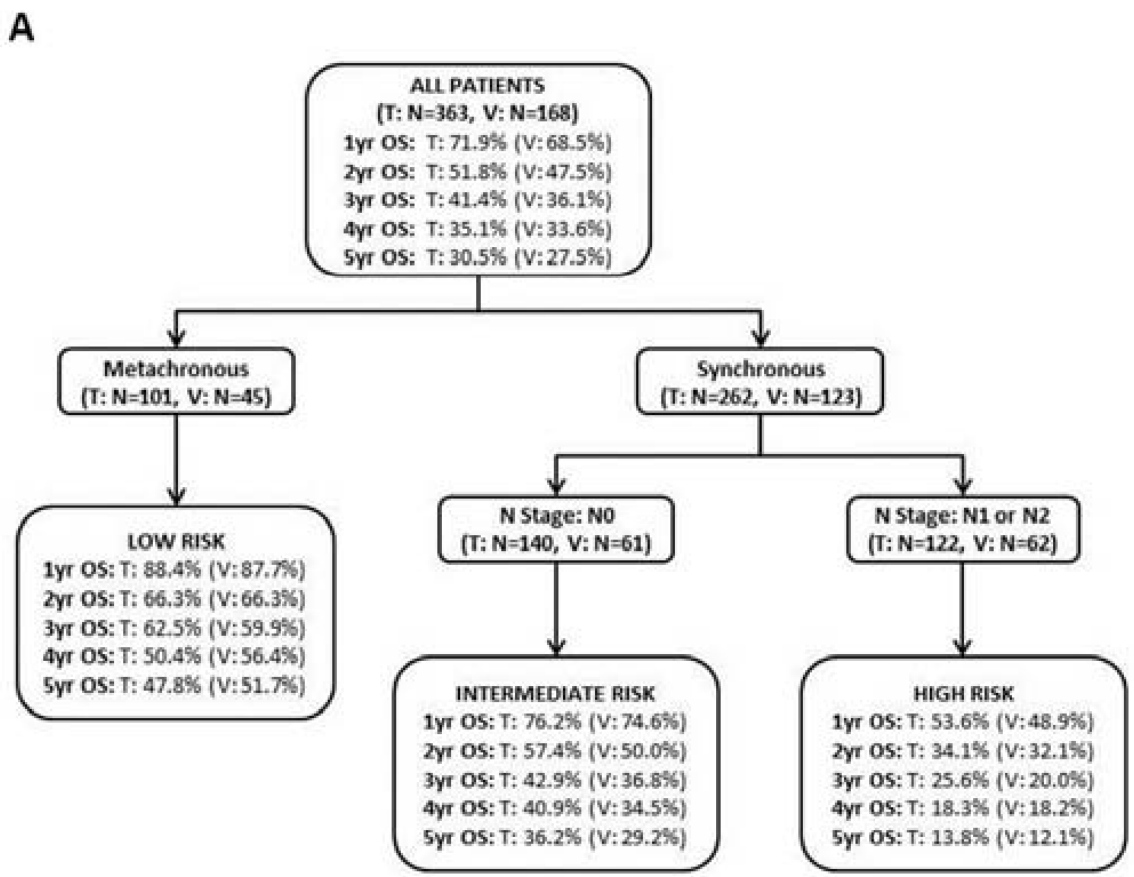
Abbreviations: RT – Radiotherapy; CT – Chemotherapy; SBRT – Stereotactic Body Radiotherapy; SABR – Stereotactic Ablative Radiotherapy; SRS – Stereotactic Radiosurgery; WBRT – Whole Brain Radiotherapy; EBRT – External Beam Radiotherapy.
*Defined as Eastern Cooperative Oncology Group Performance Status of 0-1 or Karnofsky Performance Status of ≥70.

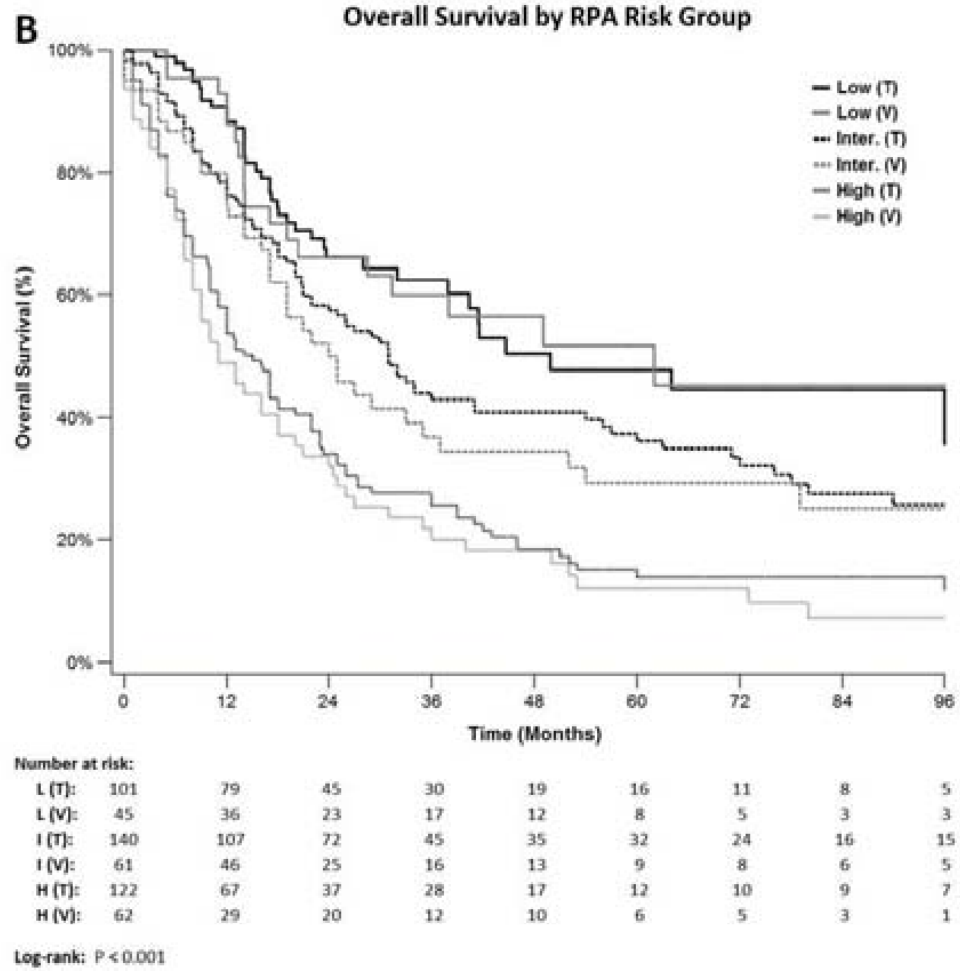
Table III: Univariable and multivariable cox regression of factors predicting overall survival in the training set (*N*=505) and validating set (*N*=252).

	Training set				Validating set	
Factor	**Univariable Hazard Ratio (95% CI)**	**p-value**	**Multivariable Hazard Ratio (95% CI)**	**p-value**	**Multivariable Hazard Ratio (95% CI)**	**p-value**
Synchronous vs. Metachronous		< 0.001		< 0.001		< 0.001
Synchronous	2.12 (1.51, 2.98)		1.96 (1.37, 2.79)		3.02 (1.74, 5.26)	
Metachronous	1 Reference		1 Reference		1 Reference	
N Stage		***< 0.001*		***0.002*		***0.002*
N0	1 Reference		1 Reference		1 Reference	
N1	1.58 (1.16, 2.15)	0.004	1.59 (1.12, 2.25)	0.01	1.69 (1.00, 2.85)	0.051
N2	1.72 (1.31, 2.27)	< 0.001	1.72 (1.27, 2.33)	< 0.001	1.93 (1.25, 2.97)	0.003
N3	2.12 (1.08, 4.17)	0.03	-- --	--	8.28 (1.82, 37.68)	0.006
Thoracic Stage		***0.002*				
IA	1 Reference					
IB	1.16 (0.78, 1.72)	0.456	-- --	--	-- --	--
IIA	1.55 (0.70, 3.45)	0.285	-- --	--	-- --	--
IIB	1.53 (1.03, 2.26)	0.035	-- --	--	-- --	--
IIIA	1.99 (1.37, 2.88)	< 0.001	-- --	--	-- --	--
IIIB	1.91 (1.14, 3.20)	0.015	-- --	--	-- --	--
Brain Metastases		0.003				
Present	1.41 (1.12, 1.76)		-- --	--	-- --	--
Absent	1 Reference		-- --	--	-- --	--
Lung Metastases		0.022				
Present	1 Reference		-- --	--	-- --	--
Absent	1.32 (1.04, 1.67)		-- --	--	-- --	--
Histology		***0.040*		***0.036*		***0.001*
Adenocarcinoma	1 Reference		1 Reference		1 Reference	
Large Cell	1.42 (0.95, 2.13)	0.088	1.54 (0.98, 2.42)	0.063	2.39 (1.26, 4.51)	0.007
Squamous	1.00 (0.77, 1.30)	0.991	1.07 (0.78, 1.46)	0.687	1.86 (1.16, 2.98)	0.01
Other	2.03 (1.13, 3.64)	0.017	2.98 (1.21, 7.34)	0.018	6.26 (1.38, 28.38)	0.017
Primary Lung Cancer Treatment		0.048				
Non-surgical	1 Reference		-- --	--	-- --	--
Surgical	0.74 (0.55, 1.00)		-- --	--	-- --	--

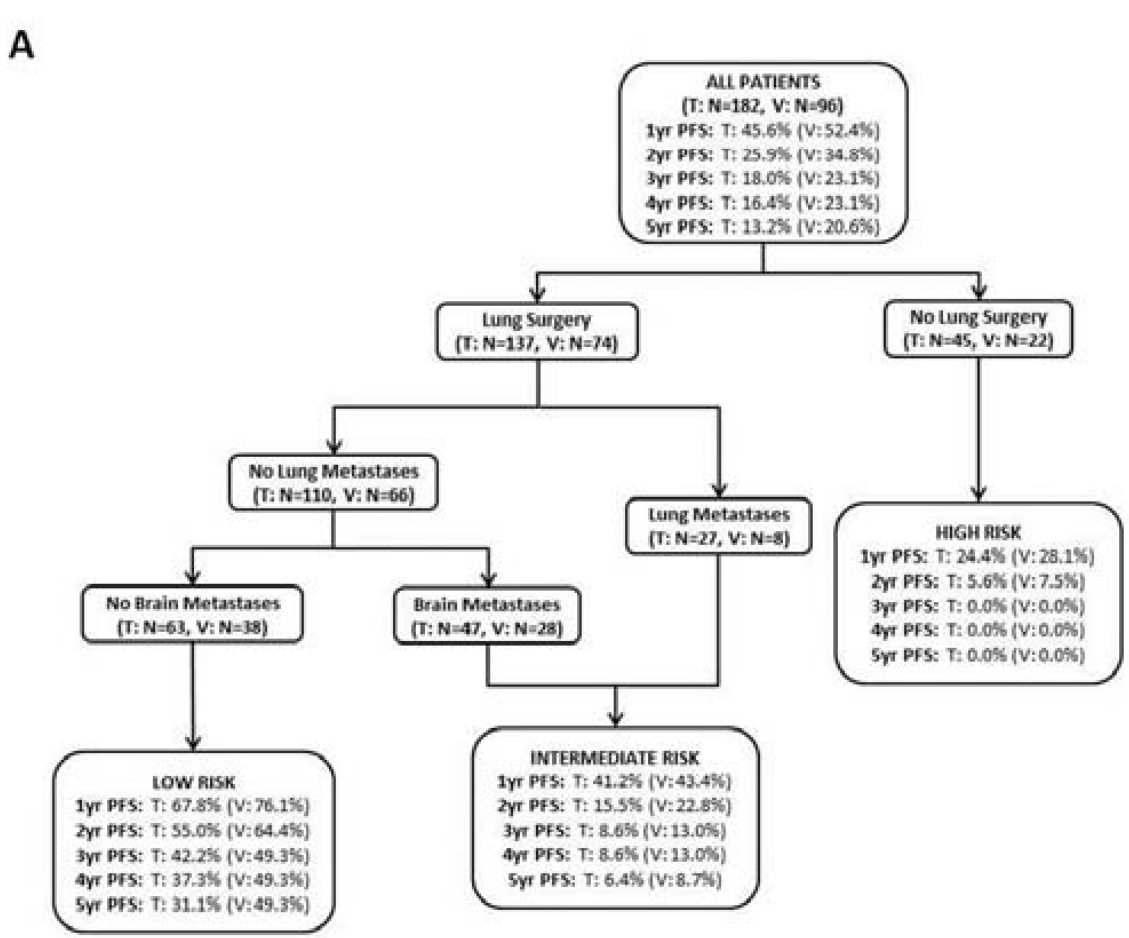
**overall analysis of effects.

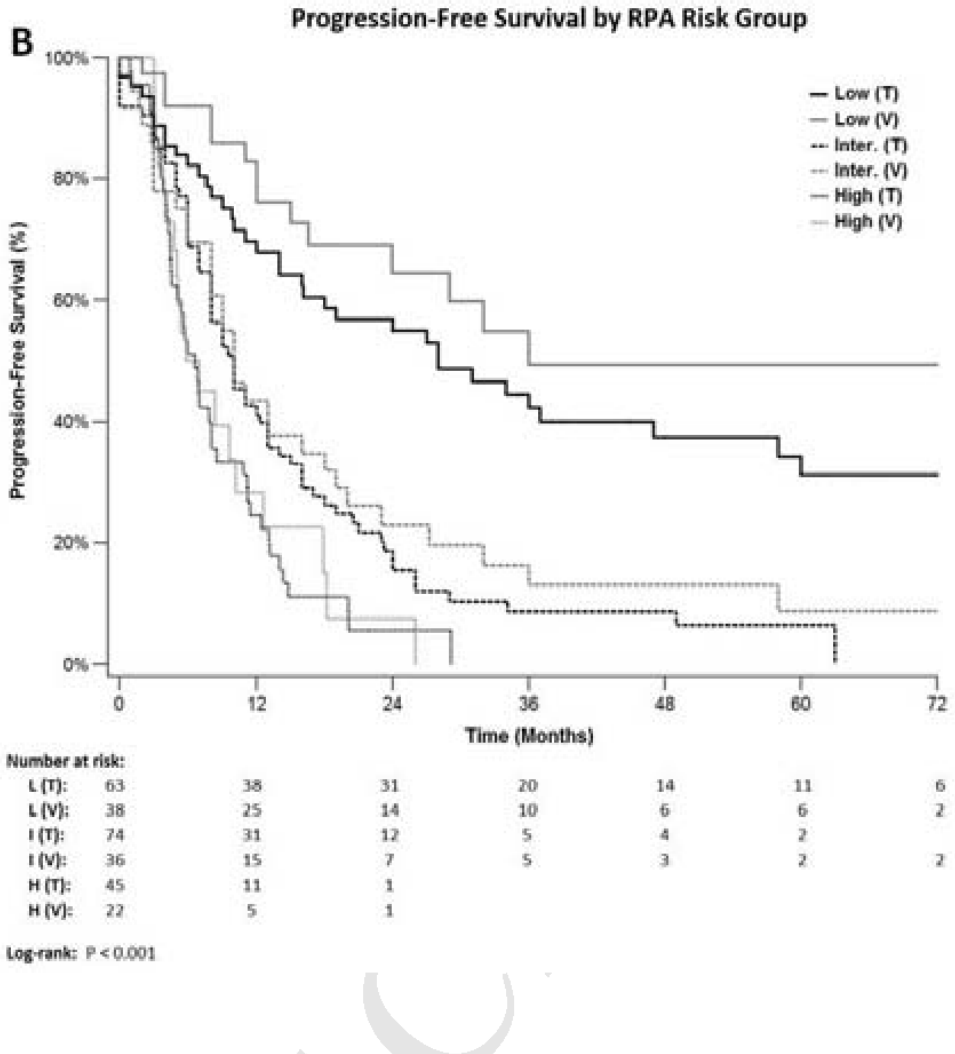
median OS: 26 ay





Median PFS: 11 ay





Sonuç itibariyle

- ECOG PS 0-1
- Primeri kontrol altındaki hastalar
- Mediasten LN tutulumu olmayanlar
- Adenokarsinom alt tip
- Perioperatif kemoterapi almış olanlar
- DFS 6 Aydan uzun olanlar daha iyi

Hangi Tedavi Modalitesi

Sistemik tedavi

- Metastatik veya nüks hastalıkta standart tedavidir.
- Oligometastatik hastalıkta lokal ablatif tedavilerle kombine edilmelidir.
  - Hedefe yönelik tedavi
  - Kemoterapi
  - immünoterapi

Hedefe Yönelik Ajanlar

Local Ablative Therapy of Oligoprogressive Disease Prolongs Disease Control by Tyrosine Kinase Inhibitors in Oncogene-Addicted Non–Small-Cell Lung Cancer

Andrew J. Weickhardt, MBBS, DmedSc, Benjamin Scheier, MD,* Joseph Malachy Burke, MD,* Gregory Gan, MD,‡ Xian Lu, MSc,‡ Paul A. Bunn, Jr., MD,* Dara L. Aisner, MD, PhD,§ Laurie E. Gaspar, MD, MBA,‡ Brian D. Kavanagh, MD, MPH,‡ Robert C. Doebele, MD, PhD,* and D. Ross Camidge, MD, PhD**

Journal of Thoracic Oncology • Volume 7, Number 12, December 2012

Stereotactic Radiotherapy Can Safely and Durably Control Sites of Extra-CNS Oligoprogressive Disease in ALK-Positive Lung Cancer Patients on Crizotinib

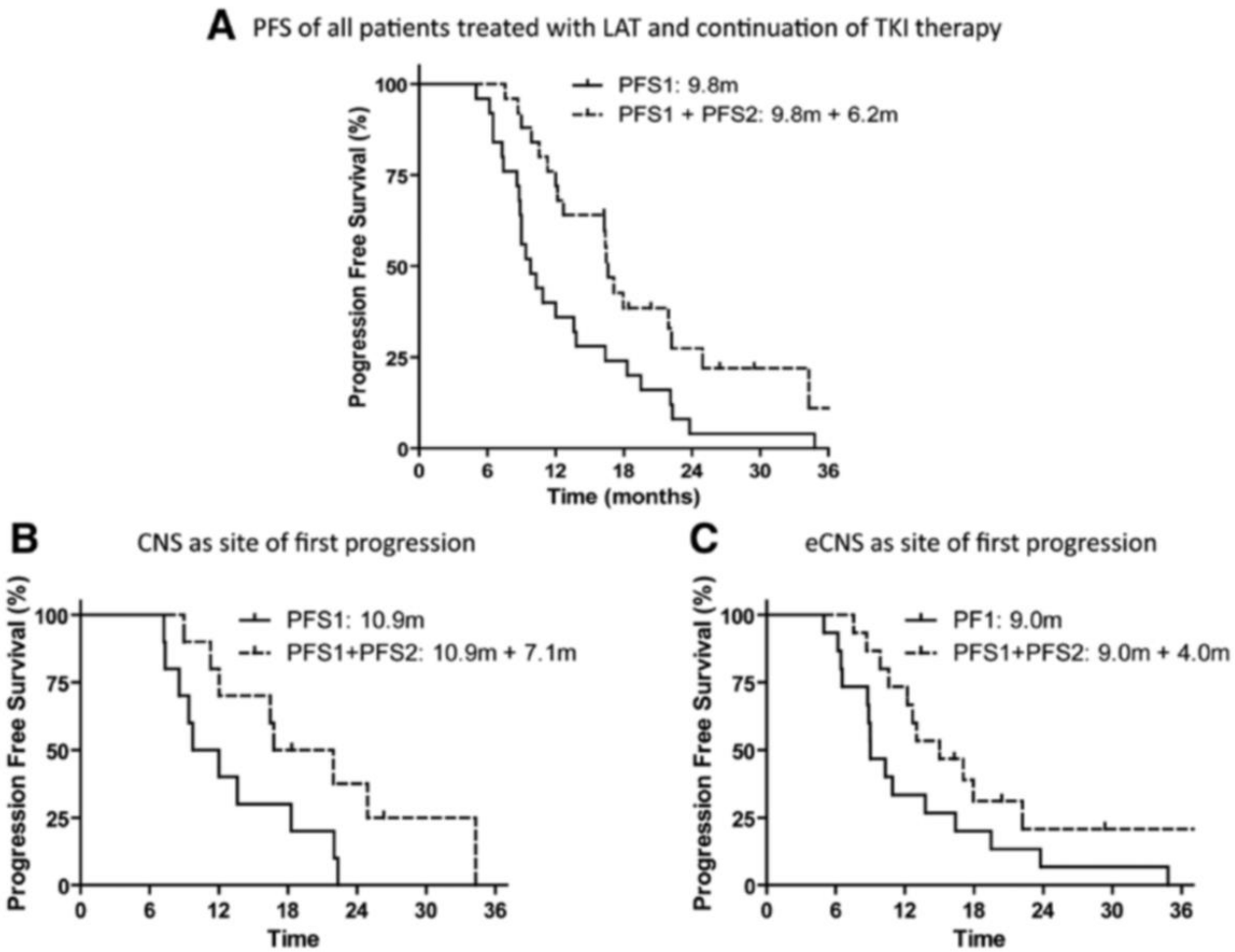
Gregory N. Gan, M.D., Ph.D.[*], Andrew J. Weickhardt, MBBS, D.Med.Sc.[‡], Benjamin Scheier, M.D.[‡], Robert C. Doebele, M.D., Ph.D.[‡], Laurie E Gaspar, M.D., MBA[*], Brian D. Kavanagh, M.D., MPH[*], and D. Ross Camidge, M.D., Ph.D.[‡]

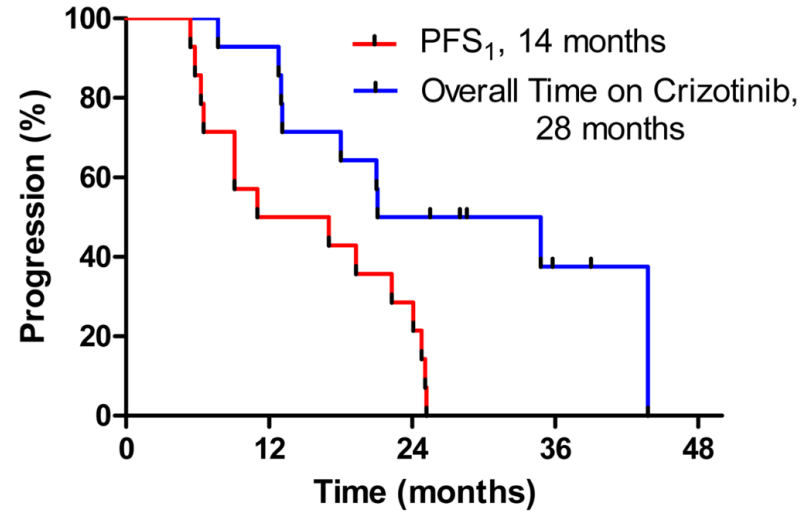
[*]Department of Radiation Oncology, University of Colorado, Colorado

[‡]Department of Medical Oncology, University of Colorado, Colorado

Int J Radiat Oncol Biol Phys. 2014 March 15; 88(4): 892–898.

- EGFR (+) erlotinib altında , ALK (+) Crizotinib altında progrese hastalar
- Progresyon alanı 4 ve <4
- Lokal ablatif tedavi sonrası
  - PFS katkısı ek 6 ay
  - Lokal kontrol oranı 1 yıl %86


A PFS of all patients treated with LAT and continuation of TKI therapy
PFS1: 9.8m
PFS1 + PFS2: 9.8m + 6.2m
Progression Free Survival (%)
Time (months)
B CNS as site of first progression
PFS1: 10.9m
PFS1+PFS2: 10.9m + 7.1m
Progression Free Survival (%)
Time
C eCNS as site of first progression
PF1: 9.0m
PFS1+PFS2: 9.0m + 4.0m
Progression Free Survival (%)
Time


PFS1, 14 months
Overall Time on Crizotinib, 28 months
Progression (%)
Time (months)

Cerrahi:

Original Article

Cancer March 1, 2015

The Rise in Metastasectomy Across Cancer Types Over the Past Decade

Edmund K. Bartlett, MD; Kristina D. Simmons, PhD; Heather Wachtel, MD; Robert E. Roses, MD; Douglas L. Fraker, MD; Rachel R. Kelz, MD; and Giorgos C. Karakousis, MD

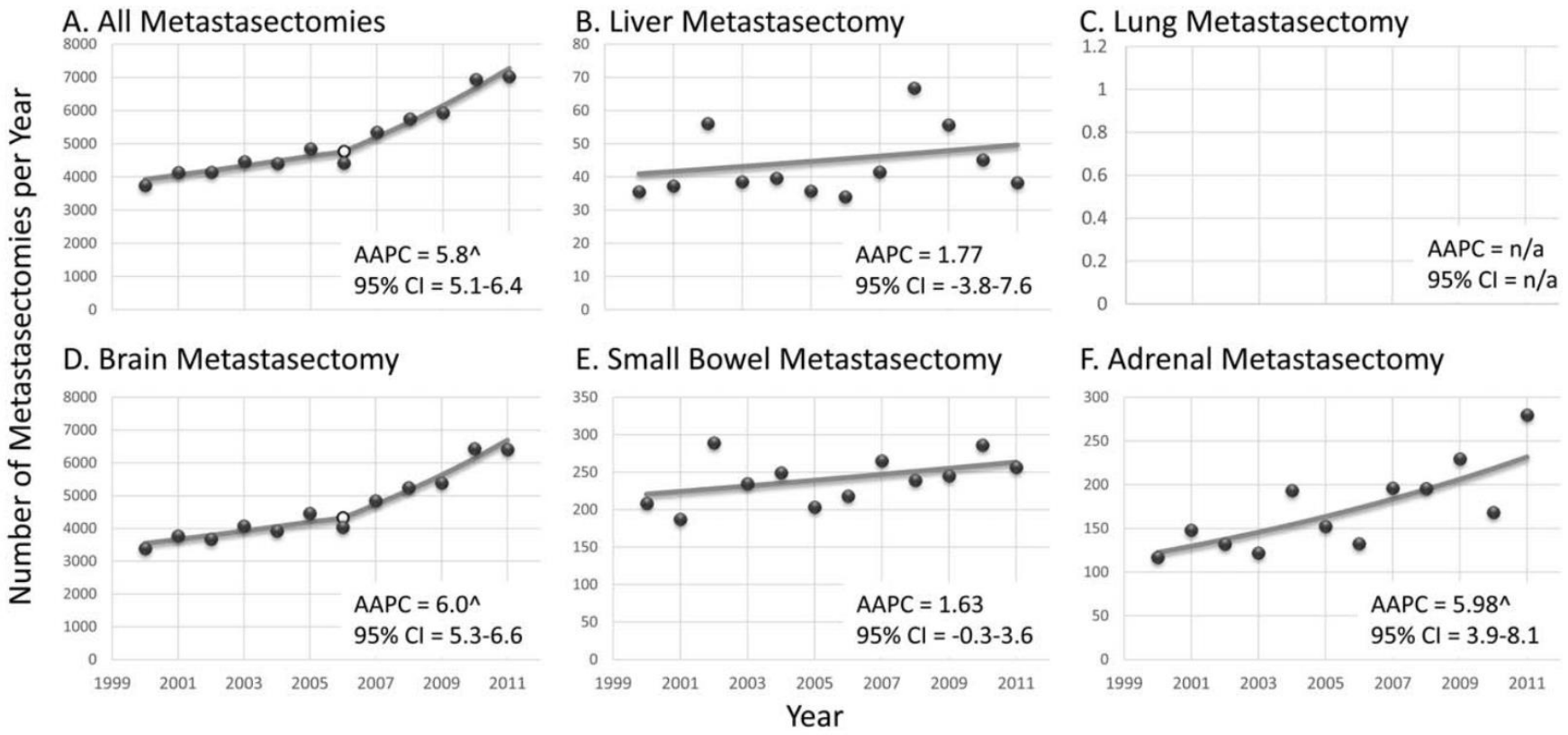


Figure 2. Metastasectomy rates for lung cancer are shown for (A) all metastasectomies and (B) liver metastasectomy. (C) Lung metastasectomy was omitted. Rates are also shown for (D) brain metastasectomy, (E) small bowel metastasectomy, and (F) adrenal metastasectomy. AAPC indicates average annual percent change; ^, an AAPC that is significantly different from 0 ($P<.05$); 95% CI, 95% confidence interval; n/a, not applicable. An open circle indicates a joinpoint (trend change). Note that the y-axis values vary for each panel.

- Doğru evreleme
- Kemoterapi rejimleri
- Hedefe yönelik tedaviler
- Cerrahi tekniklerdeki gelişmeler

Radyoterapi

- Cerrahinin morbidite ve mortalite riski nedeniyle sıklıkla tercih edilir
- Cerrahi ile radyoterapiyi karşılaştıran klinik çalışma yok
- Retrospektif çalışmalarda kemoterapiye eklenmesi oligometastaik hastalar için cerrahiye benzer sonuçlar.

- FazI/II çalışmalarda metastazlara yönelik SBRT ile %70-90 lokal kontrol oranı
- Grade3 ve üstü yan etki < %10

Stereotactic Body Radiotherapy for Multisite Extracranial Oligometastases

Final Report of a Dose Escalation Trial in Patients With 1 to 5 Sites of Metastatic Disease

Joseph K. Salama, MD[1]; Michael D. Hasselle, MD[2]; Steven J. Chmura, MD, PhD[2,3]; Renuka Malik, MD[2]; Neil Mehta, MD[2];

113 ekstrakranal metastaz 15 aylık takipte

Çalımada RT dozu düşük olmasına ragmen local kontrol oranı

%64

Garde 3 toksisite %3

SARON: Stereotactic Ablative Radiotherapy for Oligometastatic Non-Small Cell Lung Cancer (NSCLC). A UK Randomized Phase III Trial

Topic: Clinical Studies

Yenting Ngai,[1] Gerard Hanna,[2] John Conibear,[3]

Control Arm:

Screening	Registration	Modality	No. of Chemotherapy cycles		Randomisation			End of primary chemotherapy	Maintenance
			1	2		3	4		
		Platinum based doublet	X	X		X	X		X

Investigational Arm:

ALL RT IS SEQUENTIAL TO CHEMOTHERAPY									
Screening	Registration	Modality	No. of cycles		Randomisation			End of chemotherapy	2-6 weeks after day 1 of cycle 4 chemotherapy
			1	2		3	4		
		Platinum based doublet	X	X		X	X		
		Radical RT primary							X
		SABR/SRS							X**

** concurrent with CR sequential to primary RT

340 Hasta

1-3 metastatik

Primer sonlanım noktası OS

9.9 vs 14.3 ay

Diğer Lokal Ablatif yöntemler

- RFA
- Kriyoablasyon

RFA

Pulmonary Radiofrequency Ablation: Long-term Safety and Efficacy in 153 Patients[1]

Radiology

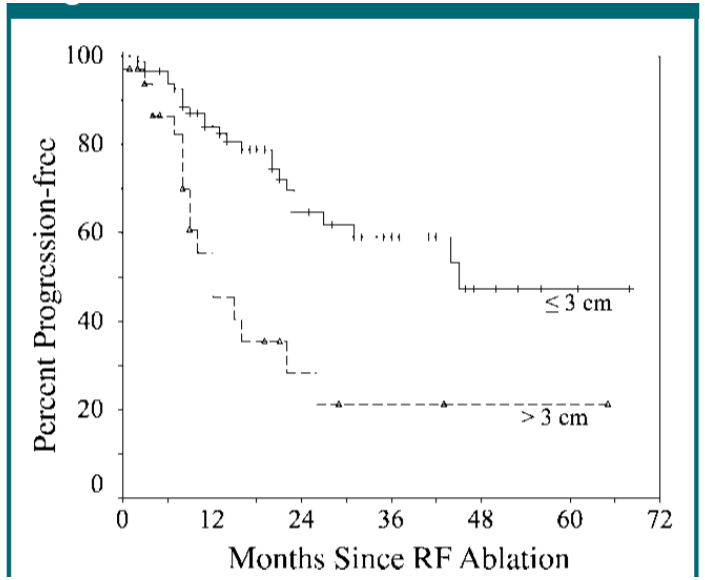
Simon et al

Characteristics of 153 Patients and 189 Lung Lesions Treated with Pulmonary RF Ablation according to Disease Stage

Characteristic	Local Control Group ($n = 132$)		Symptom Palliation Group ($n = 21$)
	Stage I NSCLC*	Stage IV Metastatic Lung Cancer†	Stage IV Metastatic Lung Cancer‡
No. of patients	75 (56.8)	57 (43.2)	21
No. of lesions treated	80 (49.4)§	82 (50.6)§	27
Mean lesion diameter (cm)‖	3.0 (1.0–7.5)	2.5 (0.6–8.5)	6.1 (1.5–19.0)

Complications of 183 Ablation Sessions

Complication	Rate (%)
Pneumothorax	28.4 (52/183)
Mild—grade 1, asymptomatic	18.6 (34/183)
Moderate or severe—grade 2, symptomatic, requiring chest tube	9.8 (18/183)
Hemoptysis—grade 1, mild, less than 100 mL, intervention not required	2.7 (5/183)
Infection—grade 3, intravenous antibiotic therapy required	2.2 (4/183)
Complication requiring admission*	10.4 (19/183)



Kryoablasyon

J Vasc Interv Radiol. 2012 June ; 23(6): 761–769. doi:10.1016/j.jvir.2012.02.013.

Percutaneous cryoablation of metastatic lesions from non-small cell lung carcinoma: Initial survival, local control, and cost observations

Hyun J. Bang, M.D.[1], Peter J. Littrup, M.D.[2], Brandt P. Currier, B.S.[2], Dylan J. Goodrich[3],

Location	Lung	Liver	Soft Tissue					Total*
			Superficial	*Adrenal*	*Para-aortic or isolated*	*Bone*	*Subtotal**	
# of Patients	13	6	4	7	2	6	15	31
# of Procedures	18	7	11	7	2	7	25	49
# of Tumors	20	9	12	7	2	10	31	60
Average Tumor Diameter (cm^3)	2.6	2.7	2.8	4.3	2.2	4.3	3.6	3.1
Average Ablation Diameter (cm^3)	4.4	5.2	5.1	5.9	4.5	6.5	5.7	5.2

*

- 31 hasta
- Median OS 15.9 ay
- 1yıl OS %53

İzole beyin metastazı

- Evre 4 KHDAK li hastaların %25'inde beyin metastazı mevcuttur
- Metastatik adenokanserli hastaların %10'u izole beyin metastazı
- PS uygun primer tümörü de küratif tedavi potasına alınabilecek hastalarda tam rezeksiyon veya ablasyon yöntemleri düşünülmelidir

Survival Outcomes for Patients With Isolated Brain Metastasis Following Local Therapy of Primary Tumor and Metastasis

	Synchronous			Metachronous		
		Survival (%)			Survival (%)	
Author	No.	2 years	5 years	No.	2 years	5 years
Bonnette et al[7]	103	28	11	-	-	-
Girard et al[8]	51	42	N/R	-	-	-
Granone et al[6]	30	47	14	-	-	-
Wroński et al[4]	86	14	8	145	29	17
Nakagawa et al[5]	60	10	N/R	28	11	N/R
Flannery et al[17]	42	34	21	33	59	13
Furak et al[10]	-	-	-	45	N/R	16

Abbreviation: N/R, not recorded.

CHEST Supplement
DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

Special Treatment Issues in Non-small Cell Lung Cancer

Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Benjamin D. Kozower, MD, MPH, FCCP; James M. Larner, MD; Frank C. Detterbeck, MD, FCCP; and David R. Jones, MD, FCCP

- Küratif cerrahi rezeksiyon yapılacaksa invaziv mediastinal evreleme ve ekstratorasik görüntüleme yapılamalı
- Senkron rezektabl N0, N1; diğer bölgelerde metastaz yoksa primer rezeksiyonu ve beyin met rezeksiynu /SBRT önerilir.
- Metakron tümörde ek metastaz yoksa beyin metastazının rezeksiyonu /SBRT önerilir.
- İzole beyin metastazı rezeke olduysa beyine adjuvant RT önerilir
- Küratif rezeksiyon yapılan hastalaa adjuvant kemoterapi önerilir.

FIGURE 10. [Section 6.2] Isolated brain metastases.

First Author	No. of patients	% Survival	
		2-year	5-year
Synchronous Presentation			
Bonnette[214]	103	28	11
Wronski[220]	86	14	8
Hu[223]	84	16	7
Xu[224]	64	20	13
Nakagawa[225]	60	10	-
Mordant[226]	57	-	13
Girard[217]	51	42	-
Flannery[228]	42	34	21
Flannery[229]	39	11	8
Louie[220]	35	22	-
Arrieta[230]	30	60	-
Granone[213]	30	47	14
Billing[215]	28	54	21
Average		**30**	**13**
Metachronous Presentation			
Wronski[220]	145	29	17
Moazami[222]	91	10	6
Furak[210]	45	-	16
Flannery[228]	33	59	13
Mussi[229]	30	47	19
Nakagawa[225]	28	11	-
Average		**31**	**13**

Inclusion criteria were studies of ≥20 patients reporting specific data for synchronous or metachronous brain metastases and curative-intent treatment from December 1989-April 2012.

İzole Adrenal Metastazı

- Küratif cerrahi rezeksiyon yapılacaksa invaziv mediastinal evreleme ve ekstratorasik görüntüleme yapılamalı
- Senkron rezektabl N0, N1; diğer bölgelerde metastaz yoksa primer ve adrenal rezeksiyonu
- Metakron tümörde ek metastaz yoksa izole adrenal rezeksiyon önerilir.
- Küratif rezeksiyon yapılan hastalara adjuvant kemoterapi önerilir.

CHEST Supplement
DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

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FIGURE 11. [Section 7.1] Adrenal metastasectomy.

First Author	No. of patients	% Lung Cancer	% 5-y Survival of Lung Cancer Patients	Positive Prognostic Factors
Tanvetyanon[245]	110	100	25	None
Pham[246]	78	100	40	Negative intrathoracic nodes
Porte[247]	43	100	12	None
Mercier[240]	23	100	23	DFI > 6 months
Raz[241]	20	100	34	Ipsilateral metastasis, N2 negative
Lucchi[242]	14	100	36	None
Strong[243]	94	39	29	None
Wade[244]	47	30	26	None
Average			**27**	

Inclusion criteria were patients with adrenal metastasis undergoing curative-intent surgical therapy reported in publications with ≥10 patients with lung cancer from December 1989-April 2012. DFI = disease-free interval from lung resection.

Akciğer metastazları

Resection of Pulmonary Metastasis of Non-small Cell Lung Cancer

Kenichi Okubo, MD,† Toru Bando, MD,* Ryo Miyahara, MD,* Hiroaki Sakai, MD,* Tsuyoshi Shoji, MD,* Makoto Sonobe, MD,* Takuji Fujinaga, MD,* Kiyoshi Sato, MD,* Hiromi Wada, MD,* and Toru Tanaka, MD†*

Journal of Thoracic Oncology • Volume 4, Number 2, February 2009

66 NSCLC

- 18 senkron aynı lob 5 yıl OS %80;
- 16 Senkron farklı lob 5 yıl OS %30,
- 42 metakron 5 yıl OS %34

Kötü prognostik

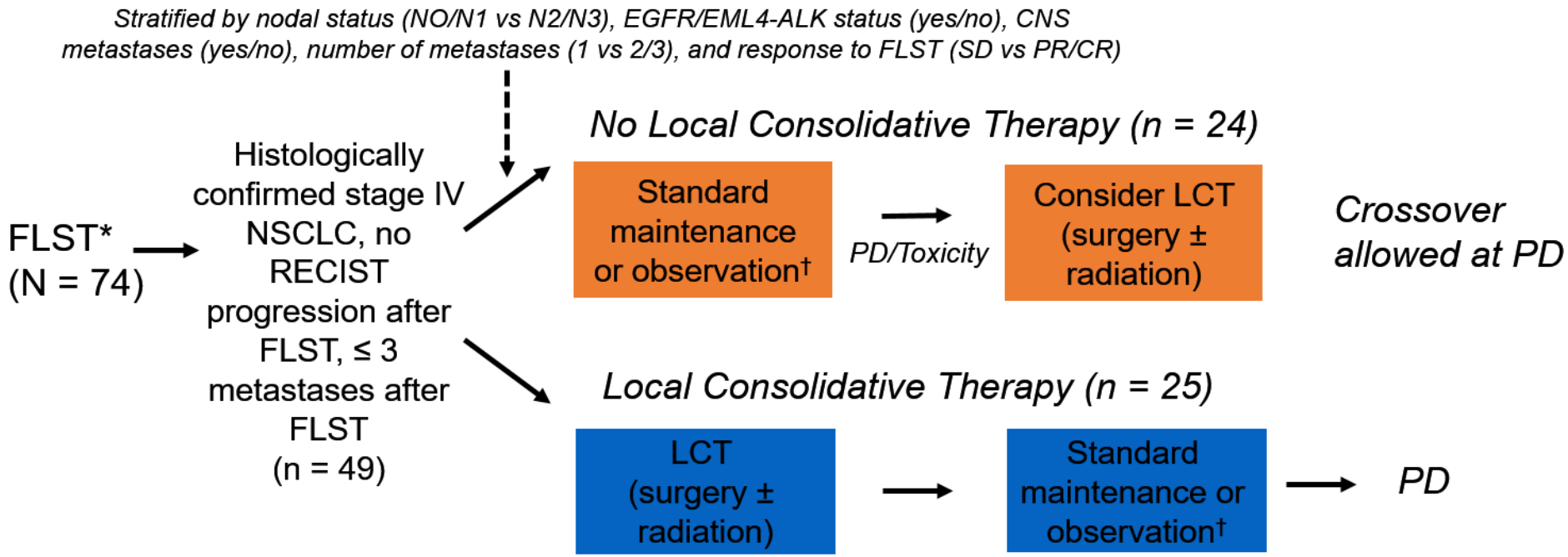
- Mediasten LN (+)
- Multpl pulmoner nodül

Önce primer mi yoksa metastaz mı?

- Optimal zamanlama net değil
- Devamında gelecek olan diffüz metastatik hastalığın görünümü olabilir
- Sistemik tedavi ile başlamak daha uygun gibi

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

Daniel R Gomez, George R Blumenschein Jr, J Jack Lee, Mike Hernandez, Rong Ye, D Ross Camidge, Robert C Doebele, Ferdinandos Skoulidis, Laurie E Gaspar, Don L Gibbons, Jose A Karam, Brian D Kavanagh, Chad Tang, Ritsuko Komaki, Alexander V Louie, David A Palma, Anne S Tsao, Boris Sepesi, William N William, Jianjun Zhang, Qiuling Shi, Xin Shelley Wang, Stephen G Swisher*, John V Heymach*



*≥ 4 cycles of platinum-doublet chemotherapy, or ≥ 3 mos of afatinib, erlotinib, or gefitinib in setting of *EGFR* mutation, or ≥ 3 mos of crizotinib if *EML4-ALK* fusion; pts could enroll before or during FLST, but randomization occurred after completion of FLST without progression. †Physician choice.

- Primary outcome: PFS

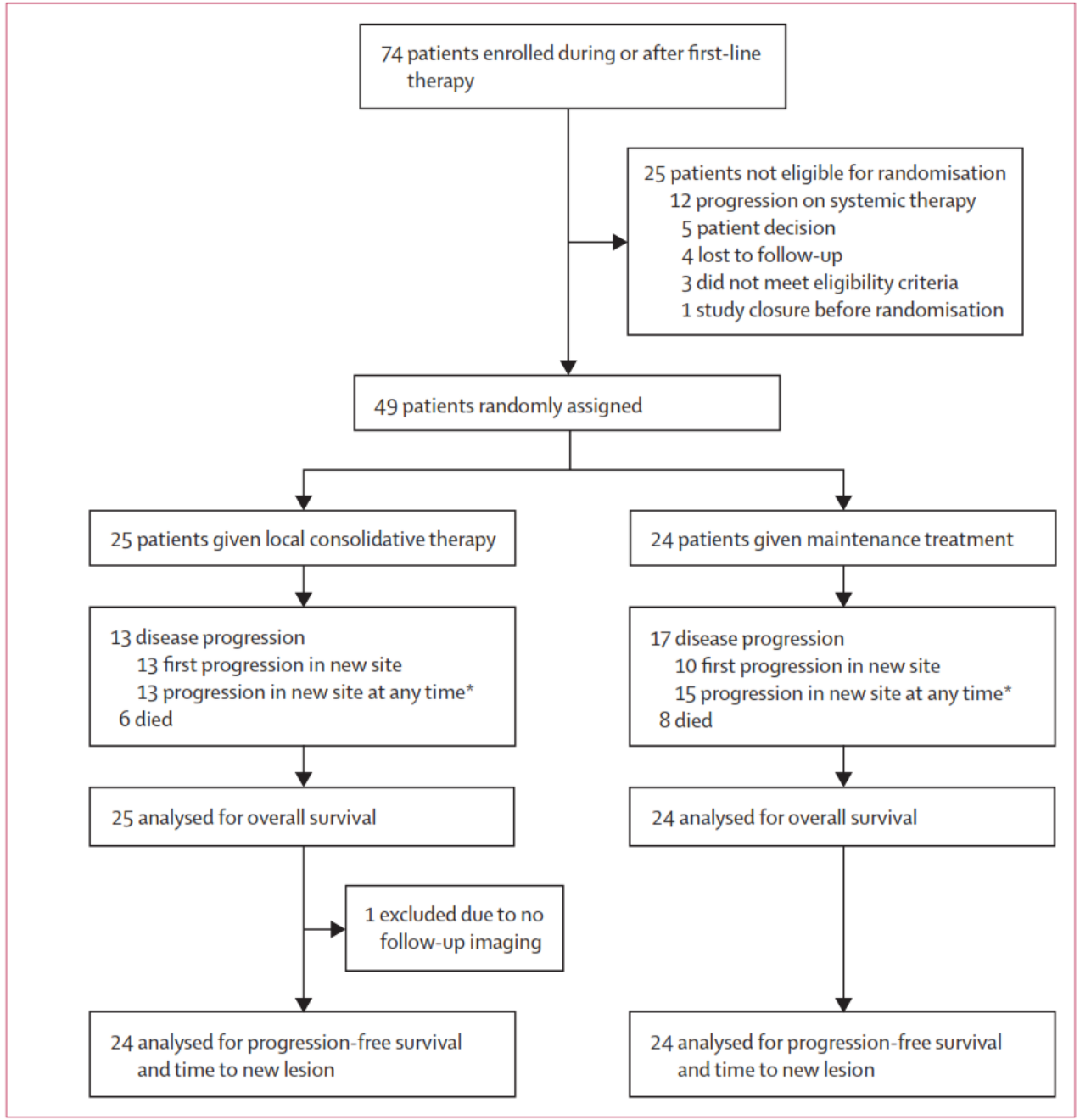


Figure 1: **Trial profile**

*Includes patients who developed a new lesion after their first progression event.

Hasta Özellikleri:

	Local consolidative therapy (n=25)	Maintenance treatment (n=24)
Age		
Mean (SD)	64 (10)	63 (10)
Median (IQR)	63 (43–83)	61 (43–80)
Sex		
Male	12 (48%)	10 (42%)
Female	13 (52%)	14 (58%)
Ethnicity		
White	20 (80%)	18 (75%)
Black	2 (8%)	3 (12%)
Hispanic	2 (8%)	0
Asian	1 (4%)	3 (12%)
Tumour histology		
Adenocarcinoma	21 (84%)	18 (75%)
Adenosquamous	0	1 (4%)
NSCLC, NOS	1 (4%)	0
Poorly differentiated NSCLC, NOS	2 (8%)	0
SCC	1 (4%)	4 (17%)
Sarcomatoid carcinoma	0	1 (4%)

	Local consolidative therapy (n=25)	Maintenance treatment (n=24)
Time of metastases		
Metachronous	1 (4%)	2 (8%)
Synchronous	24 (96%)	22 (92%)
Non-regional metastases after first-line systemic therapy		
0–1	17 (68)	15 (62)
2–3	8 (32)	9 (38)
Response to first-line chemotherapy		
Partial response or complete response	9 (36%)	9 (38%)
Stable disease	16 (64%)	15 (62%)
CNS metastases		
No	18 (72%)	18 (75%)
Yes	7 (28%)	6 (25%)
Nodal status		
N0/N1	12 (48%)	11 (46%)
N2/N3	13 (52%)	13 (54%)
Mutation type		
None	20 (80%)	21 (88%)
EGFR	3 (12%)	3 (12%)
EML4ALK	2 (8%)	0

Hasta Özellikleri:

Treatment Regimens in LCT Arm, n (%)	**Pts (N = 25)**
Hypofractionated RT/SBRT	13 (52)
Combination CRT and hypofractionated RT	4 (16)
Combination surgery and RT	3 (12)
CRT alone	3 (12)
Surgery alone	1 (4)
Progressed prior to local treatment	1 (4)

Treatment Regimens in No-LCT Arm	Pts (N=24)
Pemetrexet	16 (67%)
Erlotinib	2 (8%)
Afatinib	1 (4%)
Bevasizumab	1(4%)
Gözlem	4(17%)

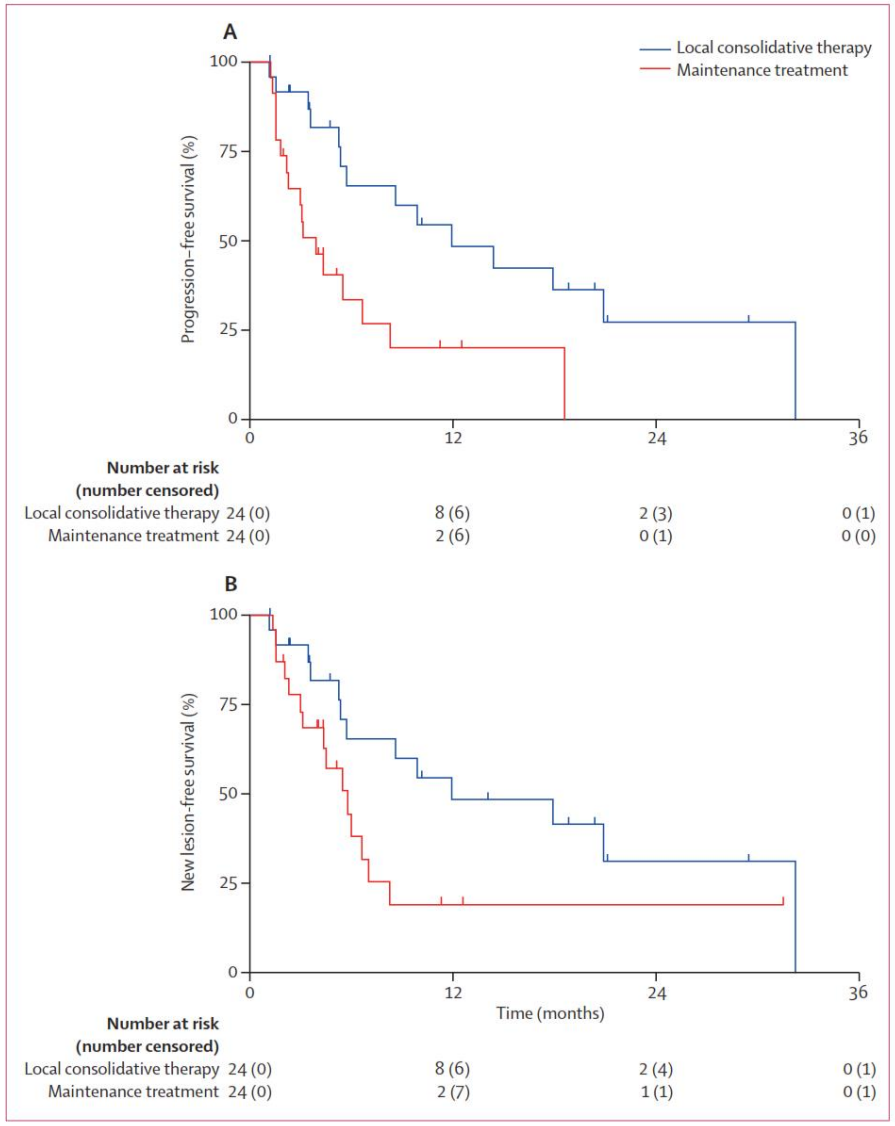


Figure 2: **Progression-free survival (A) and time to appearance of disease at a new site (B)**

- Median takip 18.9 ay
- Median PFS
  - 11.9 ay vs 3.9 ay
- PFS ilişkili faktörler
  - Metastaz sayısı
  - EGFR/ALK pozitifliği
- Genel sağkalım verilerine henüz ulaşılamadı

- 30 hastada (%61) progresyon (LCT:13, No-LCT: 17 hasta)
  - Yeni lezyon (14 hasta)
  - Uzak metastaz (16 Hasta)

	No-LCT	LCT
Bölgesel progresyon	%17	%4
Metastatik progresyon	%25	%40
Bölgesel+Metastatik	%29	%8

Toksisite

- Toksisite farklılığı yok
  - No-LCT:
    - 1 anemi, 1 halsizlik, 1 renal yetersizlik
    - 1 kişi çalışmadan çıkmış bilateral alt ekstremite ödemi nedeniyle
  - LCT :
    - Grade 3 özefajit: 2
    - 1 anemi, 1 pnömotoraks, 1 ağrı

Bu çalışmayla oligometastatik NSCLC’de lokal ablatif tedavi ile

- PFS de katkı
  - Az sayıda hasta, heterojen grup, heterojen tedavi
- Analizlerde yeni lezyon gelişene kadarki süreyi uzattığı gösterildi
  - Bu strateji metastatik yayılımı azaltıyor diyebiliriz
- Toksisite profile yönetilebilir ve her iki kol arasında fark yok

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Non-Small Cell Lung Cancer

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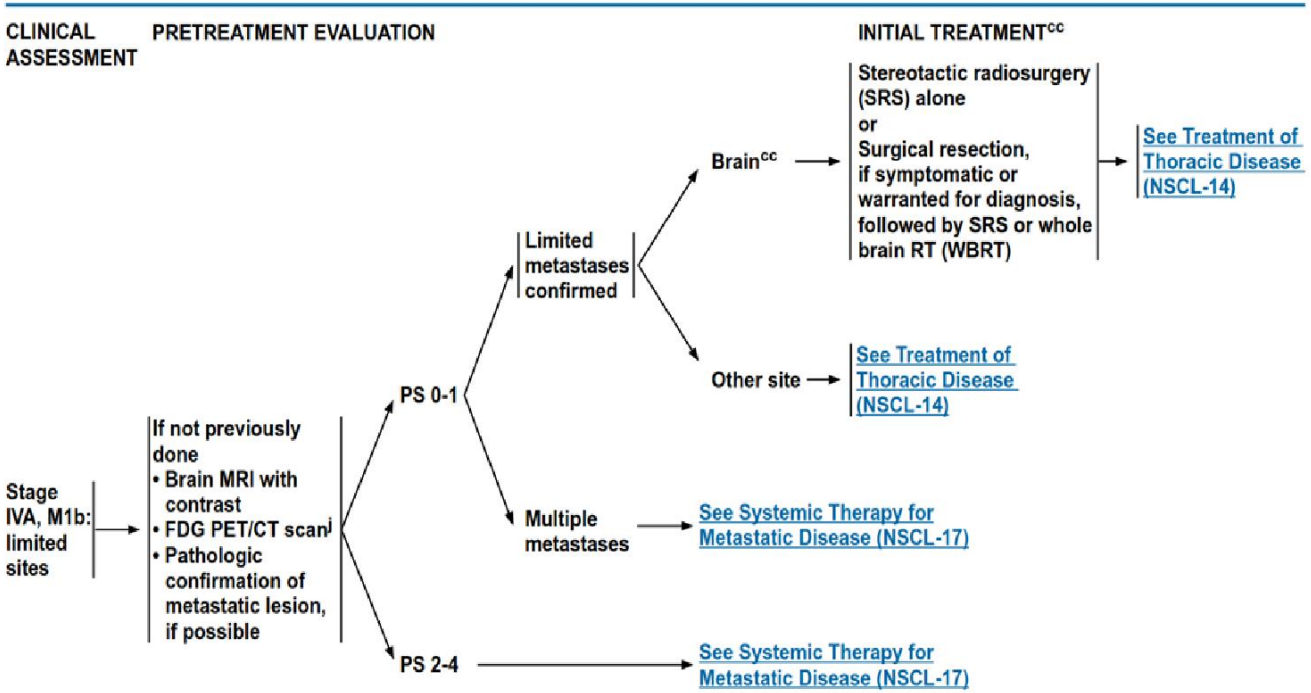

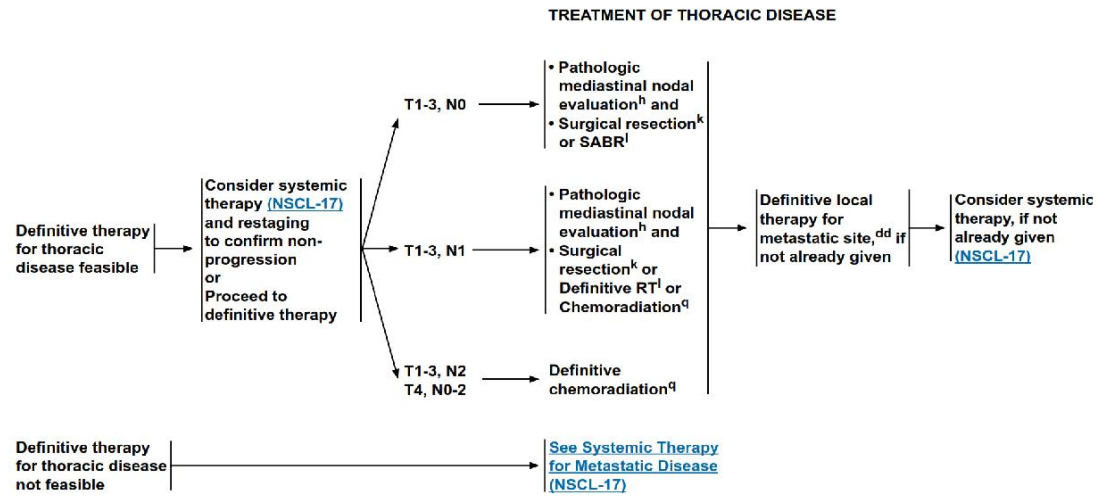

Sonuç olarak

- Oligometastaz kavramı sınırlı sayıdaki organda sınırlı sayıda olan metastatik hastalıktır.
- Çalışmalarda 1-5 arası metastazla sınırlıdır
- Primer tedavisi primer tümörle birlikte cerrahi veya radyoterapi ile küratif yaklaşım ve bunu sistemik tedavi ile kombine etmektir.
- Primeri kontrol altındaki oligometastatik hastalarda da küratif tedavi yaklaşımları düşünülebilir.

TEŞEKKÜRLER…..