

20. ULUSAL KANSER KONGRESİ

19 - 23 Nisan 2013
Susesi Otel - ANTALYA



**Yaygın metastatik akciğer kanserinde
konsolidasyon radyoterapisi verilmelidir?**



BAŞKENT ÜNİVERSİTESİ
ADANA UYGULAMA VE ARAŞTIRMA MERKEZİ
KIŞLA YERLEŞKESİ

Dr. Erkan Topkan
Radyasyon Onkolojisi A.D.

Yaygın nedir? Ne kadar yaygın?

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English
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Clinical Trials

Cancer Statistics

NCI Dictionary of Cancer Terms

In English

En español

Dictionary » D » Disseminated

Disseminated

Disseminated

scattered, distributed over a consid

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SEARCH

A B C D E F G H I J K L

In English En español

disseminate  (dih-SEH-mih-NAYT)

Scatter or distribute over a large area or range.

Bir metastaz=3metastaz=20 metastaz.....

(?)

Kanser Yayılım Teorileri

- **Ortodoks Yaklaşım: Sıralı hastalık yayılımı (Halstead WS; 1907)**
 - Lokal
 - Rejyonel
 - Sistemik
- **Non-ortodoks Yaklaşım: Başlangıçtan itibaren sistemik hastalık (Hellman S; 1994)**
 - Metastaz başlangıçta da vardı
- **Dialektik Yaklaşım: Değişken hastalık süreci (Hellman-Weichselbaum-2005)**
 - Lokal hastalık
 - Rejyonel yayılım
 - Sistemik Yayılım
 - Lokorejyonel hastalık
 - Sistemik başlangıç

TEZ

ANTİTEZ

SENTEZ

EDITORIAL

Oligometastases

Samuel Hellman
Ralph R. Weichselbaum
*The University of Chicago
Chicago, IL*

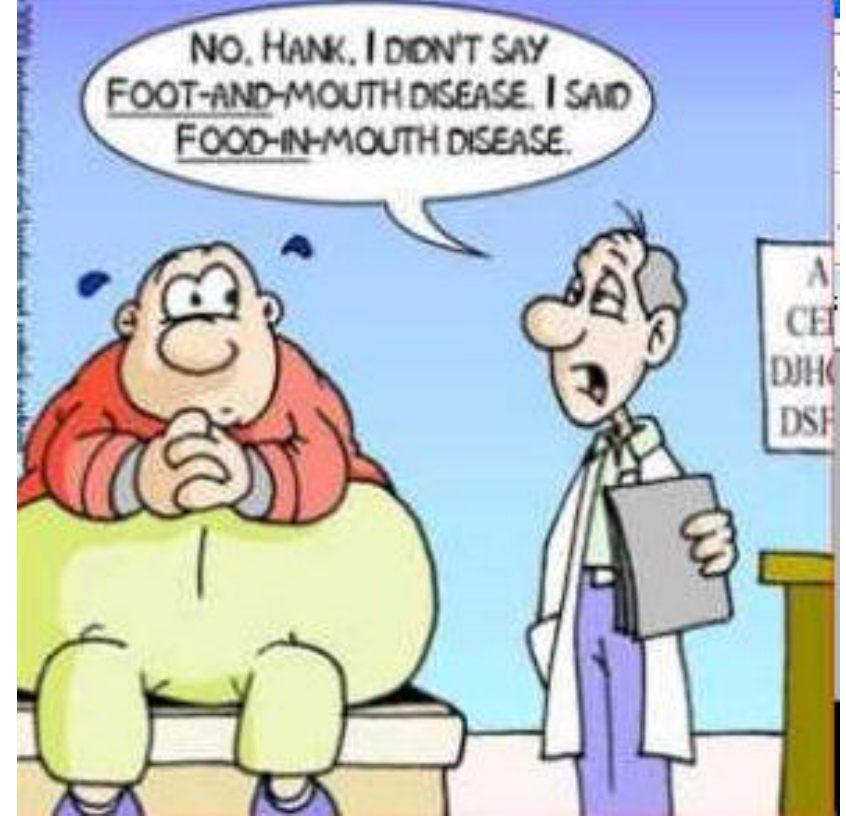


Both the contiguous and systemic theories of cancer pathogenesis are too restricting and do not consider what is now known about tumor progression during clinical evolution. A third paradigm, one that synthesizes the contiguous-systemic dialectic, has been suggested by one of us⁶ to explain the natural history of breast cancer. This thesis argues that cancer comprises a biologic spectrum extending from a disease that remains localized to one that is systemic when first detectable but with many intermediate states. Metastases are a function of both tumor size and tumor progression.

From considerations of these theories of cancer dissemination, in the light of the emerging information on the multistep nature of cancer progression, we propose the existence of a clinically significant state of **oligometastases**. For certain tumors, the anatomy and physiology may limit or concentrate these metastases to a single or a limited number of organs. The likelihood of the oligometastatic state should correlate with the biology of tumor progression, rough clinical surrogates of which, for many tumors, might be primary tumor size and grade. Metastasizing cells may seed specific organs as a function of the seeding tumor cell number and characteristics as well as the receptivity of the host organ. The importance of “seed and soil” have been considered elsewhere^{14,15} and will not be discussed further. Tumors early in the chain of progression may have metastases limited in number and location because the facility for metastatic growth has not been fully developed and the site for such growth is restricted (this is in contrast to micrometastases, which, although small in size, are extensive in number). With further pro-

Oligometastaz

- Tm yaygın met hale gelmeden önce sınırlı met olabilir (1-5)
- Oligometastaz lokalize hastalıkla sınırlı met hastalık arasında bir durumu temsil eder
- Oligometastaz türleri
 - Başlangıçta oligometastatik
 - İndüklenmiş oligometastatik
 - Relaps oligometastatik (Oligorekürrens)



Oligomet ablate olursa potansiyel kür mümkün olabilir

Oligometastaz İnsidansı Nedir?

- Net insidans ? Görüntülemeledeki iyileşmeyle paralel artış +
- MSKCC datası: Sarkomlarda ilk nüks yeri %19 izole AC

Gadd MA, Casper ES, Woodruff JM, et al: Development and treatment of pulmonary metastases in adult patients with extremity soft tissue sarcoma. Ann Surg 218:705-712, 1993

- Metastatik kolorektal ca: %46 izole KC, %38 1-3 met

Ksienski D, Woods R, Speers C, et al: Patterns of referral and resection among patients with liver-only metastatic colorectal cancer (MCRC). Ann Surg Oncol 17:3085-3093, 2010

- Evre I-III meme ca= %16 oligomet, ortalama 1.7 lezyon/hasta.
Ayrıntılı görüntülemelede oran daha yüksek

Dorn P, Meriwether A, LeMieux M, et al: Patterns of distant failure and progression in breast cancer: Implications for the treatment of oligometastatic disease. Int J Radiat Oncol 81:S643, 2011

- **PET/CT ile evre I-III AC ca= %19 occult met +**

MacManus MP, Hicks RJ, Matthews JP, et al: High rate of detection of unsuspected distant metastases by PET in apparent stage III non-small-cell lung cancer: Implications for radical radiation therapy. Int J Radiat Oncol Biol Phys 50:287-293, 2001

- **Çoğu hastada adrenal met +**

Tanvetyanon T, Robinson LA, Schell MJ, et al: Outcomes of adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non-small-cell lung cancer: A systematic review and pooled analysis. J Clin Oncol 26:1142-1147, 2008



Barney JD, Churchill EJ

Adenocarcinoma of the kidney with metastasis
to the lung cured by nephrectomy and lobectomy

J Urol 42:269-276, 1939

In 1939, Barney et al reported a case of renal adenocarcinoma metastatic to the lung, treated with pulmonary metastasectomy and nephrectomy. The patient died 23 years later and demonstrated no evidence of tumor recurrence.

A dark, possibly black, door with a glowing yellow border. The door has a classic six-panel design. In the center of the door, there is a white rectangular box with a thin yellow border containing red text. The text reads "GİRİLMEZ!" on the top line and "Metastatik Kanserler" on the bottom line. The background is dark, and the lighting is focused on the door and the text box.

GİRİLMEZ!
Metastatik Kanserler

Rektum Kanseri Kanıtları

Rees M, Tekkis PP, Welsh FK, et al: Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: A multifactorial model of 929 patients. Ann Surg 247:125-135, 2008

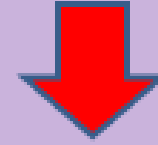
Nordlinger B, Guiguet M, Vaillant JC, et al: Surgical resection of colorectal carcinoma metastases to the liver: A prognostic scoring system to improve case selection, based on 1568 patients—Association Française de Chirurgie. Cancer 77:1254-1262, 1996

Pawlik TM, Scoggins CR, Zorzi D, et al: Effect of surgical margin status on survival and site of recurrence after hepatic resection for colorectal metastases. Ann Surg 241:715-722, 2005; discussion 722-724

Fong Y, Fortner J, Sun RL, et al: Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: Analysis of 1001 consecutive cases. Ann Surg 230:309-318, 1999; discussion 318-321



KC rezeksiyonu



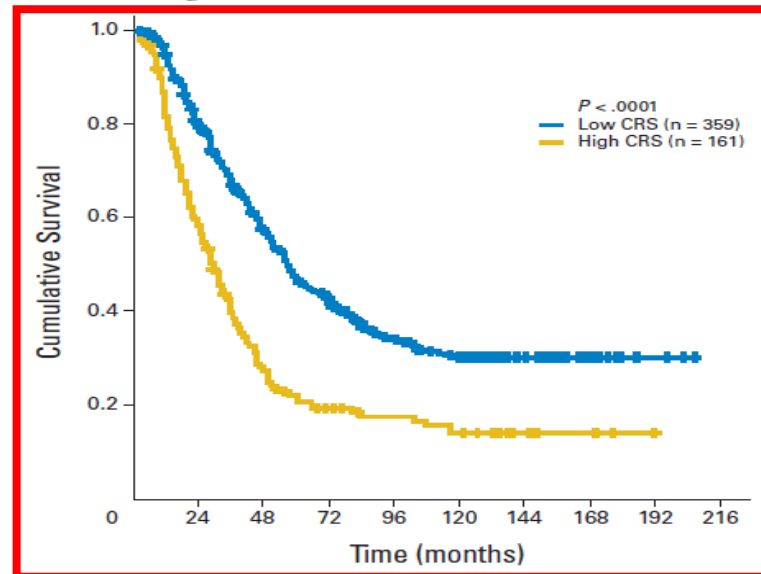
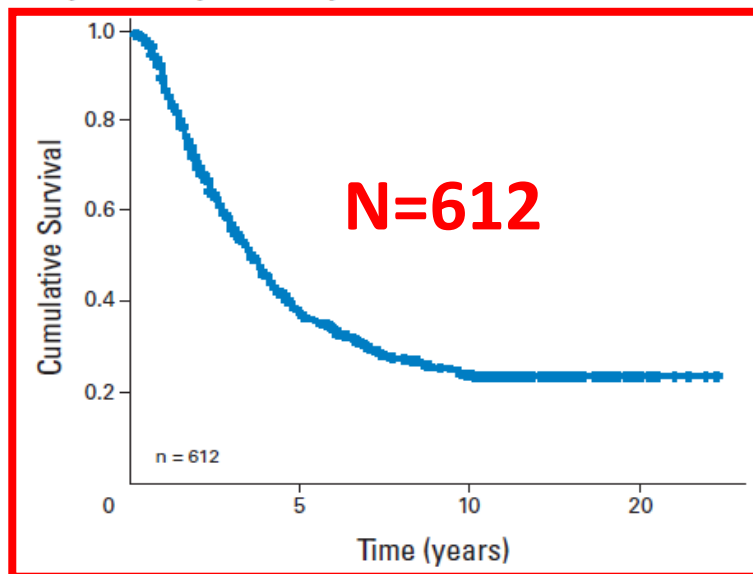
5 yıllık OS %25-50



10-yıl OS: %22

Actual 10-Year Survival After Resection of Colorectal Liver Metastases Defines Cure

James S. Tomlinson, William R. Jarnagin, Ronald P. DeMatteo, Yuman Fong, Peter Kornprat, Mithat Gonen, Nancy Kemeny, Murray F. Brennan, Leslie H. Blumgart, and Michael D'Angelica



Results

There were 612 consecutive patients identified with 10-year follow-up. Median DSS was 44 months. There were 102 actual 10-year survivors. Ninety-nine (97%) of the 102 were disease free at last follow-up. Only one patient experienced a disease-specific death after 10 years of survival. In contrast, 34% of the 5-year survivors suffered a cancer-related death. Previously identified poor prognostic factors found among the 102 actual 10-year survivors included 7% synchronous disease, 36% disease-free interval less than 12 months, 25% bilobar metastases, 50% node-positive primary, 39% more than one metastasis, and 35% tumor size more than 5 cm.

AC Metastazları

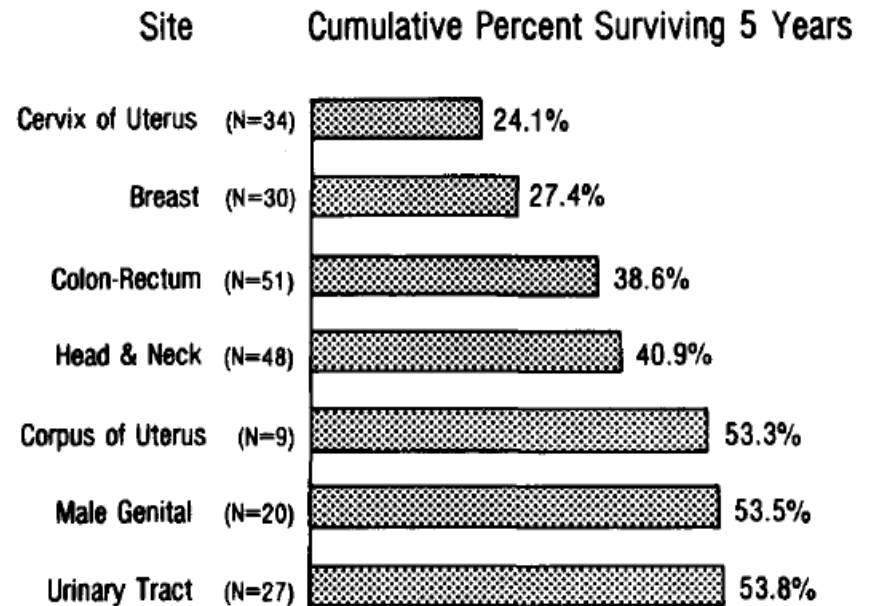
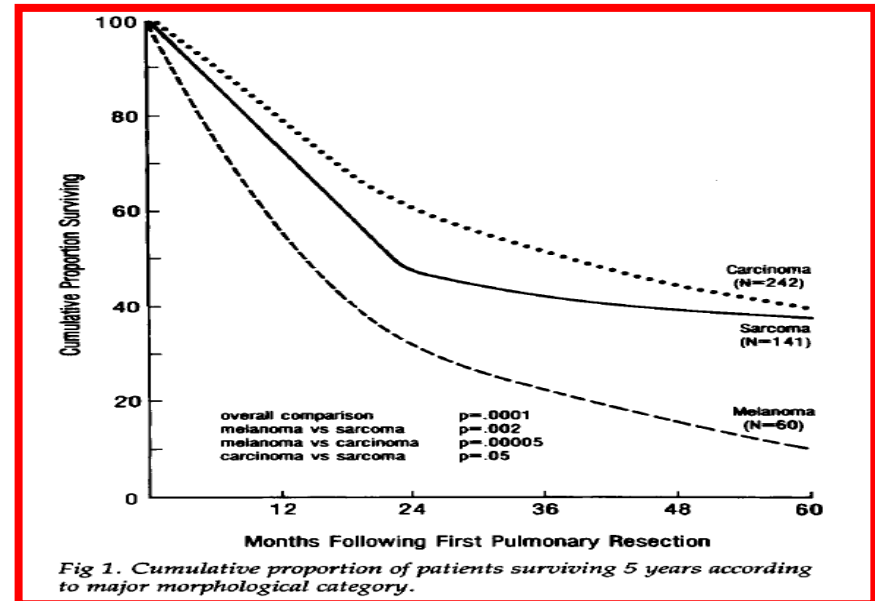
THE ANNALS OF THORACIC SURGERY

Surgery for Pulmonary Metastasis: A 20-Year Experience

Clifton F. Mountain, M.D., Marion J. McMurtrey, M.D., and Kay E. Hermes, B.S.

Ann Thorac Surg 1984;38:323-330

ABSTRACT During a recent 20-year period, 556 patients underwent operation for pulmonary metastasis at the University of Texas M. D. Anderson Hospital and Tumor Institute at Houston. The surgical mortality was 1.5% for 772 resections. A selection of 443 patients was made to evaluate the contribution of operative intervention as a primary treatment, with selective adjunctive therapy when applicable. The success of a surgical approach is dependent



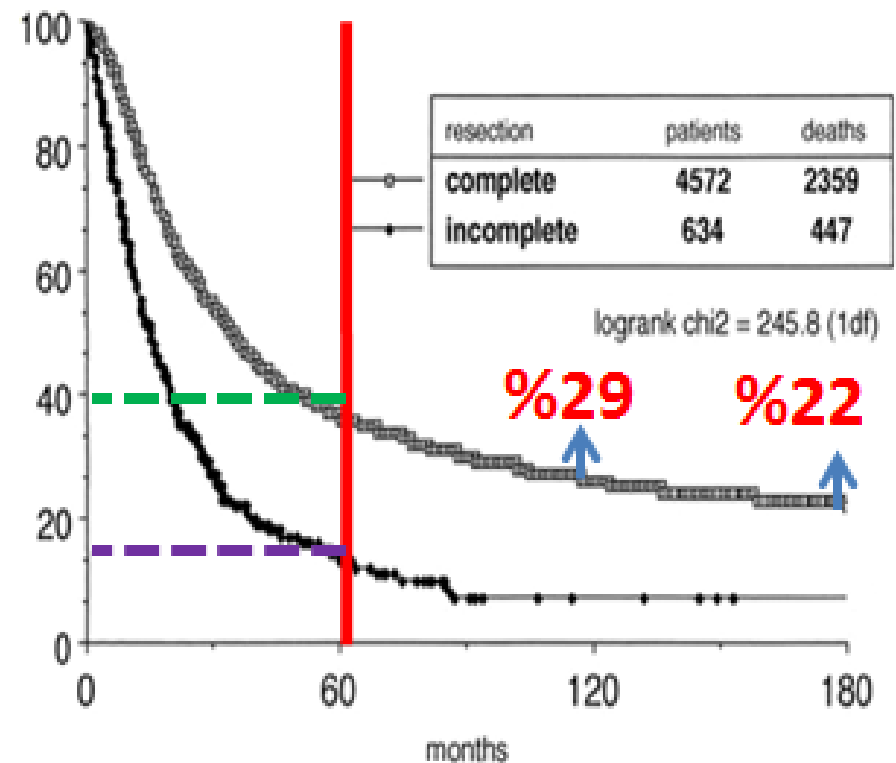
The Journal of THORACIC AND CARDIOVASCULAR SURGERY

LONG-TERM RESULTS OF LUNG METASTASECTOMY: PROGNOSTIC ANALYSES BASED ON 5206 CASES

The International Registry of Lung Metastases, Writing Committee: Ugo Pastorino, MD, Marc Buyse, ScD, Godehard Friedel, MD, Robert J. Ginsberg, MD, Philippe Girard, MD, Peter Goldstraw, MD, Michael Johnston, MD, Patricia McCormack, MD, Harvey Pass, MD, Joe B. Putnam, Jr., MD

Patients' features

| | <i>Complete</i> | <i>Incomplete</i> | <i>Total</i> |
|---------------|-----------------|-------------------|--------------|
| Type | | | |
| Epithelial | 1984 | 276 | 2260 |
| Sarcoma | 1917 | 256 | 2173 |
| Germ cell | 318 | 45 | 363 |
| Melanoma | 282 | 46 | 328 |
| Other | 70 | 11 | 81 |
| Free interval | | | |
| 0 | 469 | 87 | 556 |
| 1-11 mo | 915 | 132 | 1047 |
| 12-35 mo | 1662 | 195 | 1857 |
| 36+ mo | 1416 | 204 | 1620 |



Extracranial Oligometastases: A Subset of Metastases Curable With Stereotactic Radiotherapy

Kimberly S. Corbin, Samuel Hellman, and Ralph R. Weichselbaum, *University of Chicago Medical Center, Chicago, IL*

Table 1. Summary of Surgical Metastasectomy and SBRT for Metastasis Therapy to Multiple Sites

| Surgical Series | Year | No. of Patients | 5-Year Survival (%) | 10-Year Survival (%) | Site |
|----------------------------------------------------|------|-----------------|---------------------|----------------------|----------------------------|
| Rees et al (colorectal cancer) | 2008 | 929 | 36 ^a | 23 ^a | Liver |
| Fong et al (colorectal cancer) | 1999 | 1,001 | 37 | 22 | Liver |
| Pawlik et al (colorectal cancer) | 2005 | 557 | 58 | No 10-year follow-up | Liver |
| Carpizo et al (colorectal cancer) | 2009 | 1,369 | | No 10-year follow-up | |
| Liver only | | 1,242 | 49 | | Liver |
| Limited EHD | | 127 | 26 | | Liver and EHD ^b |
| De Haas et al (colorectal cancer) | 2008 | | | | Liver |
| R0 resection | | 234 | 61 | 43 | |
| R1 resection | | 202 | 57 | 37 | |
| Elias et al (colorectal cancer) | 1998 | 269 | 24.7 | No 10-year follow-up | Liver |
| Elias et al (noncolorectal only) | 1998 | 147 | 36 | No 10-year follow-up | Liver |
| Scheele et al (colorectal cancer) | 1995 | 350 | 39.3 | 23.6 | Liver |
| de Jong et al (colorectal cancer) | 2009 | 1,669 | 47.3 | No 10-year follow-up | Liver |
| Pastorino et al (many primary tumors) ^c | 1997 | 4,572 | 36 | 26 | Lung |
| Choong et al (soft tissue sarcoma) | 1995 | 274 | 40 | No 10-year follow-up | Lung |
| Casiraghi et al (many primary tumors) ^d | 2011 | 575 | 46 | No 10-year follow-up | Lung |
| Pfannschmidt et al (renal cell carcinoma) | 2002 | 191 | 39.6 | No 10-year follow-up | Lung |
| Pfannschmidt et al (colorectal cancer) | 2003 | 167 | 32.4 | 10-year follow-up | Lung |
| Kanemitsu et al (colorectal cancer) | 2003 | 313 | 38.3 | No 10-year follow-up | Lung |
| Petersen et al (melanoma) | 2007 | | | No 10-year follow-up | Lung |
| Complete resection | | 249 | 21 | | |
| Incomplete resection | | 69 | 13 | | |
| Saito et al (colorectal cancer) | 2002 | 165 | 39.6 | 37.2 | Lung |
| Kim et al (multiple primary tumors) ^e | 1998 | 37 | 24 | No 10-year follow-up | Adrenal |
| Porte et al (NSCLC) | 2001 | 43 | 11 ^f | No 10-year follow-up | Adrenal |
| Mercier et al (NSCLC) | 2005 | 23 | 23 | No 10-year follow-up | Adrenal |
| Burt et al (NSCLC) | 1992 | 185 | 13 | 7 | Brain |
| Bonnette et al (NSCLC) | 2001 | 103 | 11 | No 10-year follow-up | Brain |

Extracranial Oligometastases: A Subset of Metastases Curable With Stereotactic Radiotherapy

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| Radiation Series | Year | No. | | Local Control (%) | Survival (%) | Site |
|---------------------------------|------|----------|---------|-----------------------------------|-----------------------------------|----------------------------------|
| | | Patients | Lesions | | | |
| Blomgren et al | 1995 | 31 | 42 | 80 | Not reported | Liver, lung, and retroperitoneum |
| Wulf et al | 2004 | 41 | 51 | 80 | 33 ^a | Lung |
| Hoyer et al (colorectal cancer) | 2006 | 64 | 141 | 86 ^a | 38 ^a , 13 ^h | Lung, liver, and adrenal |
| Hof et al | 2007 | 61 | 71 | 63 ⁱ | 47.8 ⁱ | Lung |
| Rusthoven et al | 2009 | 47 | 63 | 92 ^a | 30 ^a | Liver |
| Rusthoven et al | 2009 | 38 | 63 | 96 ^a | 39 ^a | Lung |
| Kang et al (colorectal cancer) | 2010 | 59 | 78 | 66 ⁱ | 49 ⁱ | Multiple |
| Okunieff et al | 2006 | 49 | 125 | 83 ⁱ | 25 ^j | Lung |
| Katz et al | 2007 | 69 | 174 | 57 ^k | 24 ^{l,m} | Liver |
| Lee et al | 2009 | 70 | 143 | 71 ^m | 47 ⁿ | Liver |
| Milano et al | 2011 | 121 | | | | Multiple ^p |
| Breast cancer | | 39 | | 87 ^o | 74 ^a , 47 ^o | |
| All others | | 82 | | 65 ^o | 39 ^a , 9 ^o | |
| Salama et al | 2011 | 61 | 111 | 66.7 ^{a,q} | 56.7 ^a | Multiple |
| Bae et al (colorectal cancer) | 2012 | 41 | 50 | 64 ⁱ , 57 ^h | 64 ⁱ , 38 ^h | Lung, liver, and lymph node |
| Norihisa et al | 2008 | 34 | | 90 ^a | 84.3 ^a | Lung |

- 5-y lokal kontrol %63-96 (%80)
- 5-y OS (30-94)

YAYGIN EVRE KÜÇÜK HÜCRELİ AKCİĞER KANSERİNDE (KHAK) KÜRATİF RADYOTERAPİ

- **PCI**
- **TRT**
- **Met. RT**

ORIGINAL ARTICLE

Prophylactic Cranial Irradiation in Extensive Small-Cell Lung Cancer

Ben Slotman, M.D., Ph.D., Corinne Faivre-Finn, M.D., Ph.D., Gijs Kramer, M.D.,*
Elaine Rankin, M.D., Michael Snee, D.M., Matthew Hatton, F.R.C.R.,
Pieter Postmus, M.D., Ph.D., Laurence Collette, Ph.D., Elena Musat, M.D.,
and Suresh Senan, Ph.D., F.R.C.R., for the EORTC Radiation Oncology Group
and Lung Cancer Group†

ABSTRACT

BACKGROUND

We conducted a randomized trial of prophylactic cranial irradiation in patients with extensive small-cell lung cancer who had had a response to chemotherapy.

METHODS

Patients between the ages of 18 and 75 years with extensive small-cell lung cancer were randomly assigned to undergo prophylactic cranial irradiation (irradiation group) or receive no further therapy (control group). The primary end point was the time to symptomatic brain metastases. Computed tomography or magnetic resonance imaging of the brain was performed when any predefined key symptom suggestive of brain metastases was present.

RESULTS

The two groups (each with 143 patients) were well balanced regarding baseline characteristics. Patients in the irradiation group had a lower risk of symptomatic brain metastases (hazard ratio, 0.27; 95% confidence interval [CI], 0.16 to 0.44; $P < 0.001$). The cumulative risk of brain metastases within 1 year was 14.6% in the irradiation group (95% CI, 8.3 to 20.9) and 40.4% in the control group (95% CI, 32.1 to 48.6). Irradiation was associated with an increase in median disease-free survival from 12.0 weeks to 14.7 weeks and in median overall survival from 5.4 months to 6.7 months after randomization. The 1-year survival rate was 27.1% (95% CI, 19.4 to 35.5) in the irradiation group and 13.3% (95% CI, 8.1 to 19.9) in the control group. Irradiation had side effects but did not have a clinically significant effect on global health status.

CONCLUSIONS

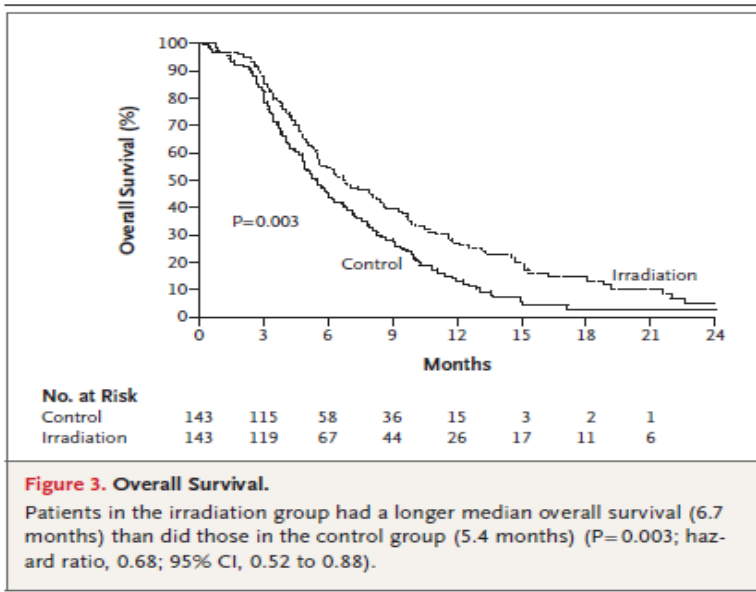
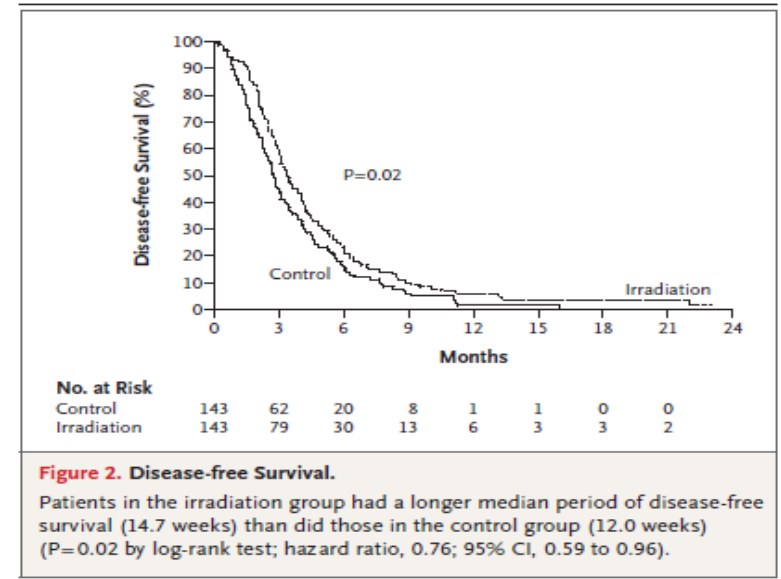
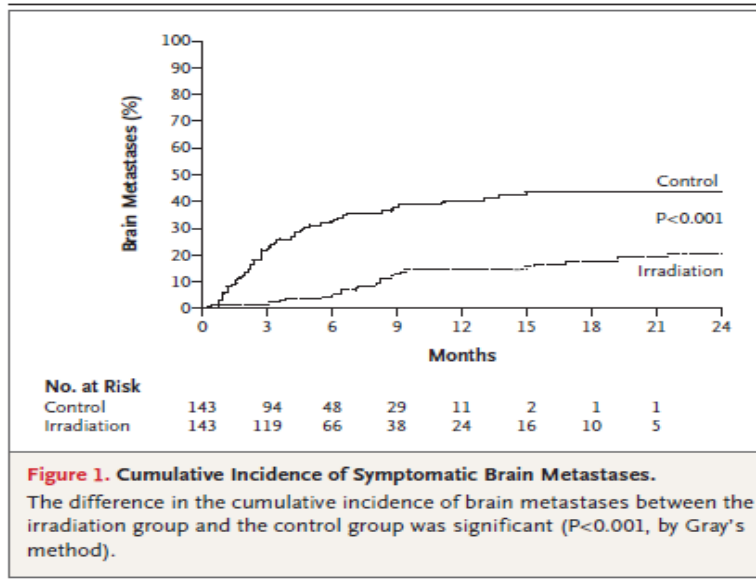
Prophylactic cranial irradiation reduces the incidence of symptomatic brain metastases and prolongs disease-free and overall survival. (ClinicalTrials.gov number, NCT00016211.)

Table 1. Characteristics of the Patients.*

| Variable | Prophylactic Cranial Irradiation (N=143) | Control (N=143) |
|----------------------------------|------------------------------------------------|--------------------|
| Median age — yr (range) | 62 (37–75) | 63 (39–75) |
| Median time after diagnosis — mo | 4.2 | 4.2 |
| Sex — no. (%) | | |
| Male | 97 (67.8) | 82 (57.3) |
| Female | 46 (32.2) | 61 (42.7) |
| WHO performance score — no. (%)† | | |
| 0 | 52 (36.4) | 52 (36.4) |
| 1 | 80 (55.9) | 76 (53.1) |
| 2 | 11 (7.7) | 15 (10.5) |
| Persistent disease — no. (%) | | |
| Primary | 108 (75.5) | 110 (76.9) |
| Distant | 99 (69.2) | 104 (72.7) |

* There were no significant differences between patients in the irradiation group and those in the control group in any category.

† Higher scores on the World Health Organization (WHO) scale indicate poorer performance status.



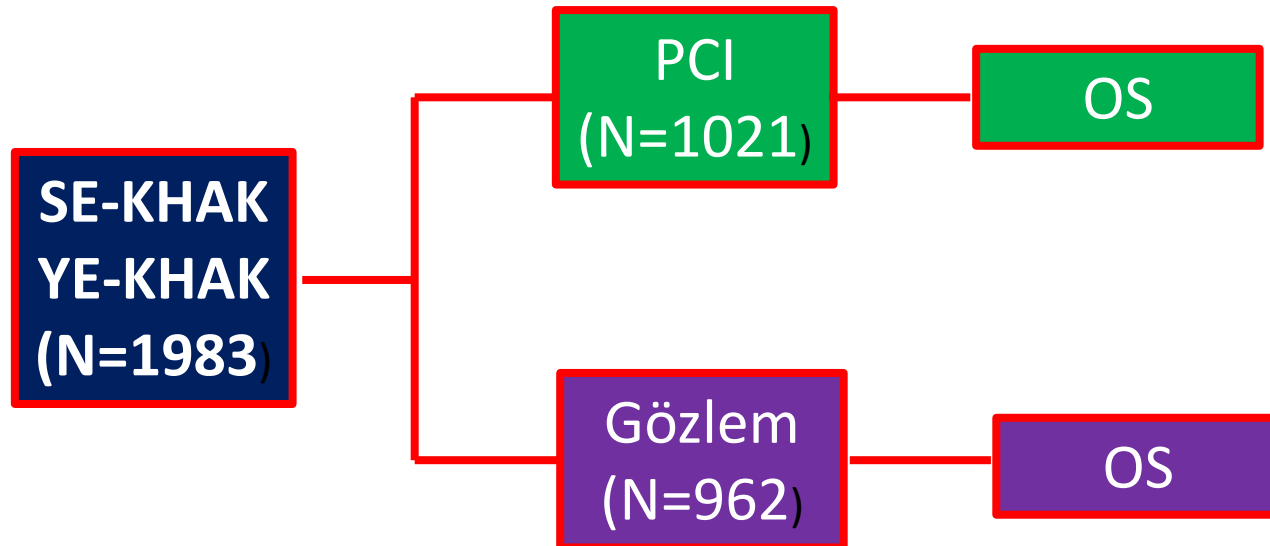
- PCI ile mikrometastaz tedavisi mümkün
- RT ile metastaz gelişimi engellenebilir

Thirty years of prophylactic cranial irradiation in patients with small cell lung cancer: a meta-analysis of randomized clinical trials*

Gustavo Arruda Viani, André Campiolo Boin, Veridiana Yuri Ikeda,
Bruno Silveira Vianna, Rondinelli Salvador Silva, Fernando Santanella

J Bras Pneumol. 2012;38(3):372-381

- Son 30 yılda yapılmış 16 RCT



Viani meta analizi

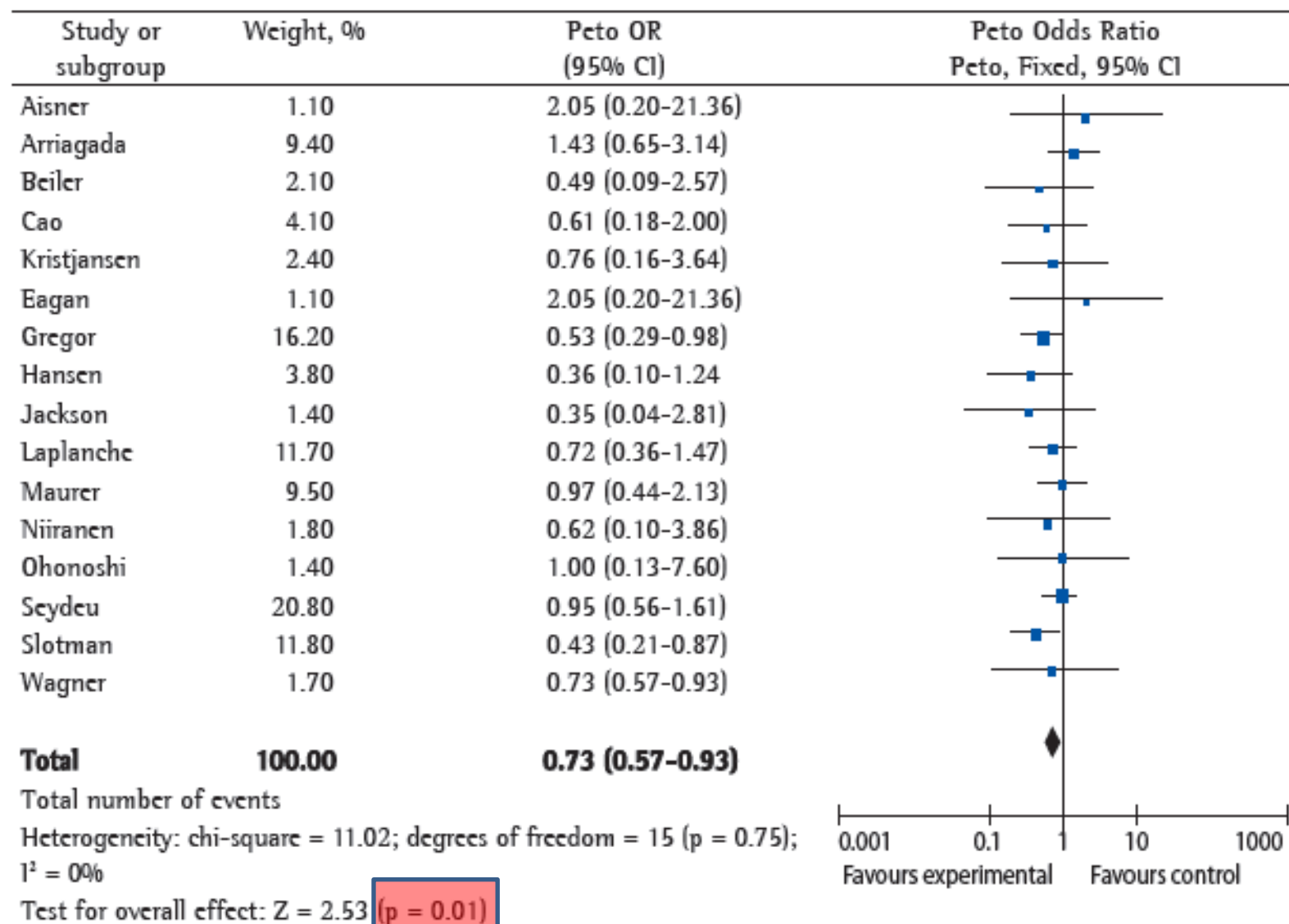
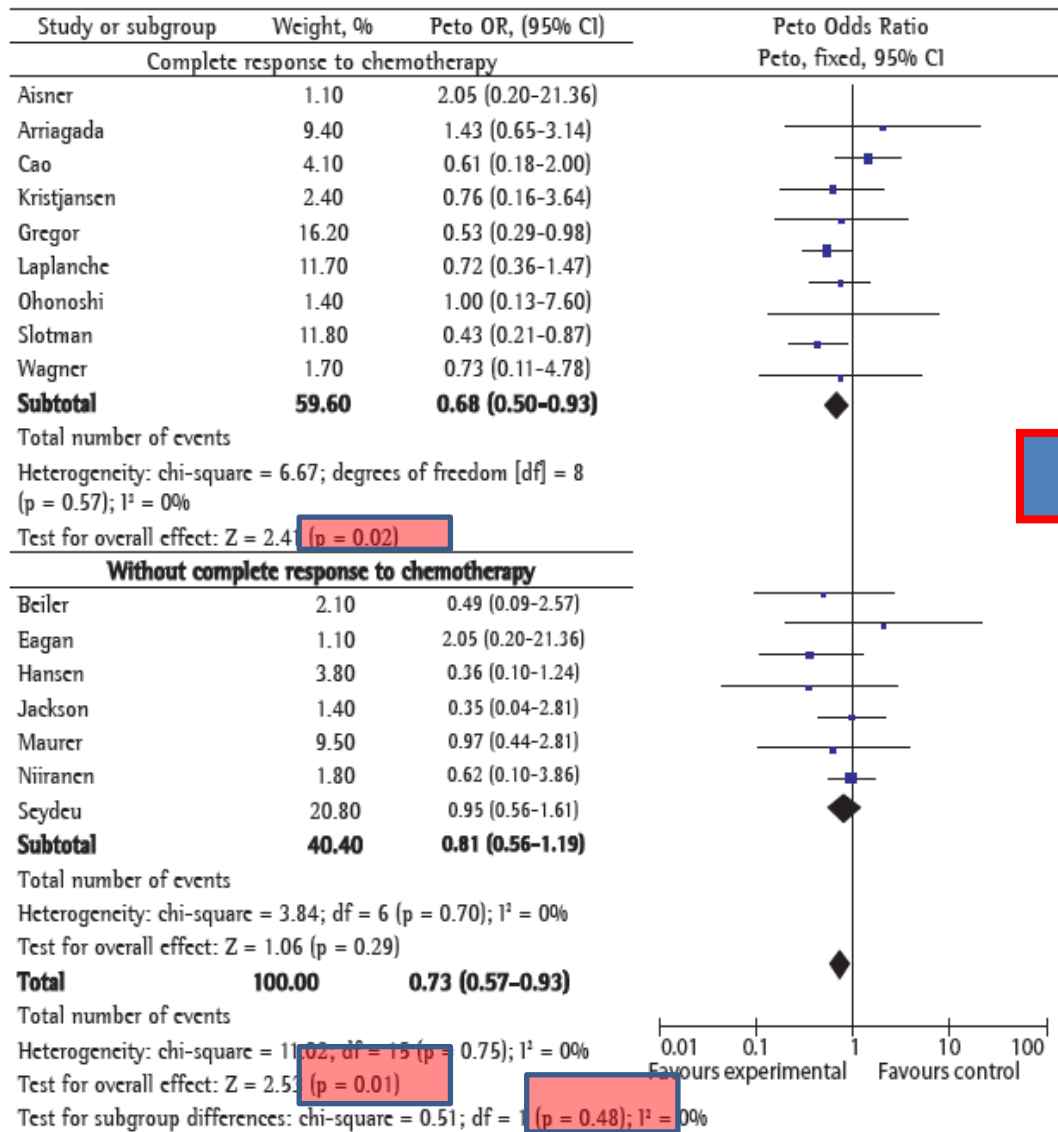


Figure 1 - Overall mortality.



PCI ile mortalite
%4.4 azalir

Etki evreden
bagimsizdir

Figure 2 - Mortality and chemotherapy response.

Konsolidasyon TRT

- Medyan OS:10 ay
- 5-y OS: %0-2
- Multiajan KT ile sonuç deęişmiyor
- KT'ye cevap genellikle iyi ama kalıcı deęil
- En sık nüks yeri: Primer hastalık bölgesi
- Toraks nüksü, uzak metastaz ve ölüm kaçınılmaz
- Konsolidasyon TRT: KT ile elde edilen cevap kalıcı hale getirilebilir mi?
- Tedaviye cevap tm yükü ile sıklıkla doęru orantılı
- Tercihen CR, PR belki de SD hastalarda denenebilir mi?

Role of Radiation Therapy in the Combined-Modality Treatment of Patients With Extensive Disease Small-Cell Lung Cancer: A Randomized Study

By Branislav Jeremic, Yuta Shibamoto, Nebojsa Nikolic, Biljana Milicic, Slobodan Milisavljevic, Aleksandar Dagovic, Jasna Aleksandrovic, and Gordana Radosavljevic-Asic

Purpose: To investigate the efficacy and toxicity of cisplatin/etoposide (PE) chemotherapy (CHT) with or without accelerated hyperfractionated radiation therapy (ACC HFX RT) and concurrent daily carboplatin/etoposide (CE) in patients with extensive-disease small-cell lung cancer.

Patients and Methods: A total of 210 patients were treated with three cycles of standard PE. Patients with a complete response (CR) at both the local and distant levels (CR/CR) or a partial response (PR) at the local level and CR at the distant level (PR/CR) received either thoracic ACC HFX RT with 54 Gy in 36 fractions over 18 treatment days in combination with CE followed by two cycles of PE (group 1, $n = 55$) or an additional four cycles of PE (group 2, $n = 54$). Patients who experienced less response were treated nonrandomly (groups 3, 4, and 5). All patients with a CR at the distant level received prophylactic cranial irradiation.

Results: For 206 assessable patients, the median survival time (MST) was 9 months and the 5-year survival rate was 3.4%. Patients in group 1 had significantly better survival rates than those in group 2 (MST, 17 v 11 months; 5-year survival rate, 9.1% v 3.7%, respectively; $P = .041$). Local control was also better in group 1, but the difference was only marginally not significant ($P = .062$). There was no difference in distant metastasis-free survival between groups 1 and 2. Acute high-grade toxicity was higher in group 2 than in group 1.

Conclusion: The addition of ACC HFX RT to the treatment of the most favorable subset of patients led to improved survival over that obtained with CHT alone.

J Clin Oncol 17:2092-2099. © 1999 by American Society of Clinical Oncology.

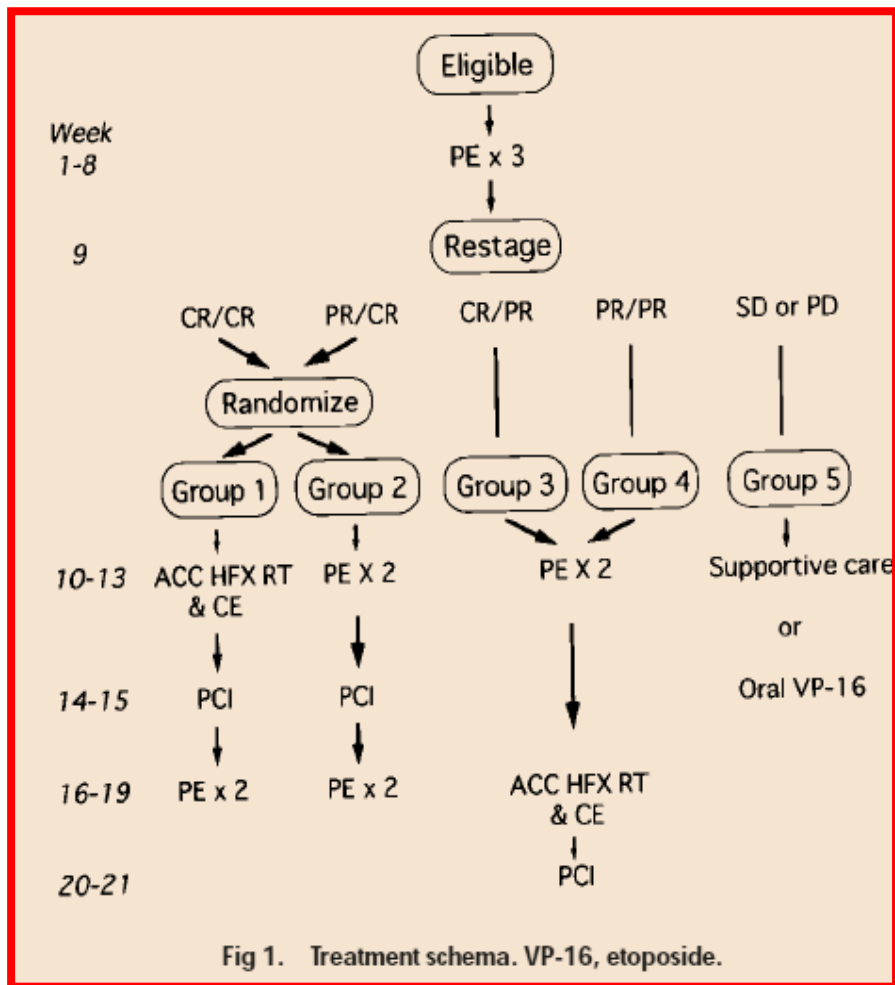
Role of Radiation Therapy in the Combined-Modality Treatment of Patients With Extensive Disease Small-Cell Lung Cancer: A Randomized Study

By Branislav Jeremic, Yuta Shibamoto, Nebojsa Nikolic, Biljana Milicic, Slobodan Milisavljevic, Aleksandar Dagovic, Jasna Aleksandrovic, and Gordana Radosavljevic-Asic

Table 1. Patient Characteristics

| Characteristic | Total of All Patients | Group | | | | | P |
|--------------------------------|-----------------------|-------|-------|-------|-------|-------|-----|
| | | 1 | 2 | 3 | 4 | 5 | |
| Sex | | | | | | | |
| Male | 124 | 33 | 32 | 21 | 17 | 21 | .99 |
| Female | 82 | 22 | 22 | 13 | 11 | 14 | |
| Age, years | | | | | | | |
| Median | 59 | 59 | 59 | 58 | 60 | 59 | .99 |
| Range | 38-71 | 38-70 | 39-71 | 41-70 | 44-69 | 41-69 | |
| KPS score | | | | | | | |
| 70 | 31 | 8 | 8 | 7 | 4 | 4 | .99 |
| 80 | 37 | 10 | 10 | 5 | 5 | 7 | |
| 90 | 80 | 20 | 23 | 12 | 13 | 12 | |
| 100 | 58 | 17 | 13 | 10 | 6 | 12 | |
| Weight loss | | | | | | | |
| ≥ 5% | 95 | 25 | 23 | 16 | 12 | 19 | .85 |
| < 5% | 111 | 30 | 31 | 18 | 16 | 16 | |
| No. of metastatic sites | | | | | | | |
| 1 | 97 | 23 | 25 | 18 | 14 | 17 | .91 |
| 2 | 87 | 27 | 23 | 12 | 11 | 14 | |
| 3 | 17 | 4 | 5 | 3 | 2 | 3 | |
| 4 | 4 | 1 | 1 | 1 | 0 | 1 | |
| 5 | 1 | 0 | 0 | 0 | 1 | 0 | |

Abbreviation: KPS, Karnofsky performance status.



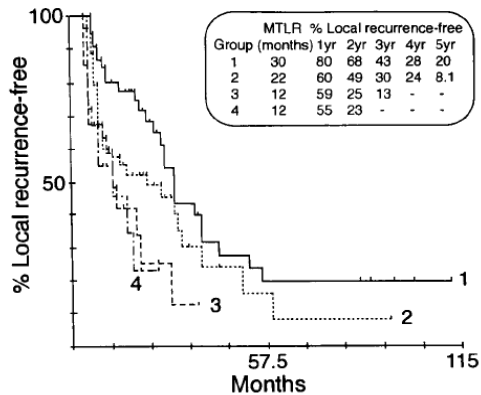


Fig 3. LRFS in group 1 (—), group 2 (- · - · -), group 3 (- - - -), and group 4 (· · · · ·).

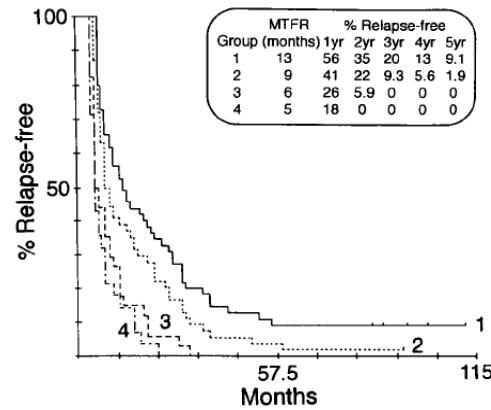


Fig 5. First relapse-free survival in group 1 (—), group 2 (- · - · -), group 3 (- - - -), and group 4 (· · · · ·).

Table 2. Response at Local Level in Groups 1 and 2 After Week 9

| Group | Week 9 | | Week 15 | | Week 21 | |
|-------|-------------------------------------------|-----|-------------------------------------------|---------|-------------------------------------------|--------|
| | No. of Patients/ Total No. of Patients | % | No. of Patients/ Total No. of Patients | % | No. of Patients/ Total No. of Patients | % |
| 1 | 26/55 | 47 | 53/55 | 96 | 53/55 | 96 |
| 2 | 24/54 | 44 | 33/54 | 61 | 35/53* | 66 |
| P | | .77 | | .000007 | | .00005 |

NOTE. All patients in groups 1 and 2 had CR at the distant level.

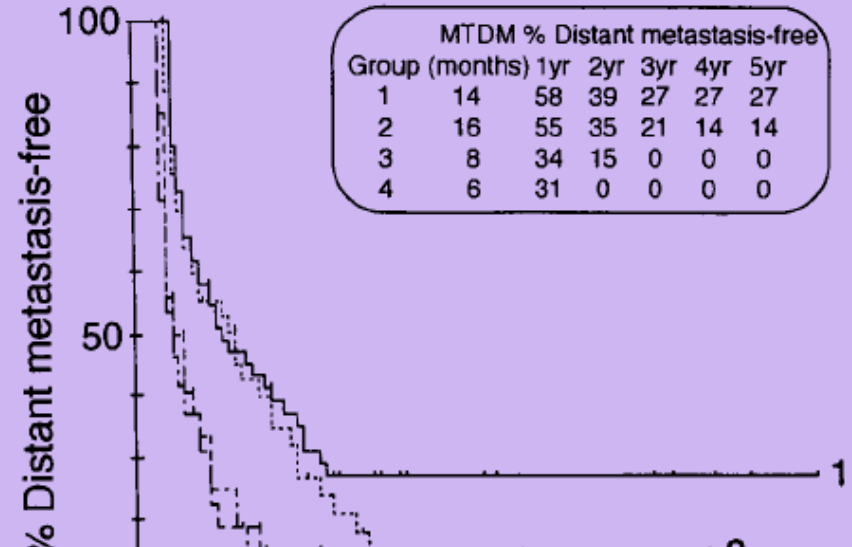
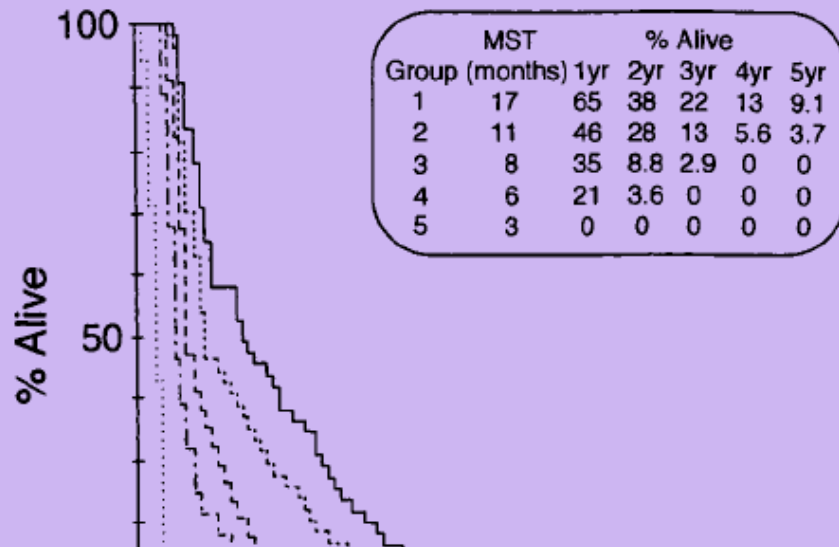
*One patient in group 2 had died of toxicity by week 21.

Table 3. Acute High-Grade Toxicity

| Toxicity/Group | Grade 3 | | Grade 4 | | Grade 5 | | p |
|----------------------------|-----------------|----|-----------------|----|-----------------|----|---------------|
| | No. of Patients | % | No. of Patients | % | No. of Patients | % | |
| Leukopenia | | | | | | | |
| 1 | 17 | 31 | 7 | 13 | — | — | 1 v 2 .18 |
| 2 | 22 | 40 | 11 | 20 | — | — | All .33 |
| 3 | 12 | 36 | 4 | 12 | — | — | |
| 4 | 10 | 36 | 4 | 14 | — | — | |
| 5 | 11 | 31 | 11 | 31 | — | — | |
| Thrombocytopenia | | | | | | | |
| 1 | 9 | 16 | 6 | 11 | — | — | 1 v 2 .23 |
| 2 | 15 | 27 | 8 | 14 | — | — | All .81 |
| 3 | 6 | 18 | 3 | 9 | — | — | |
| 4 | 5 | 18 | 3 | 11 | — | — | |
| 5 | 9 | 26 | 4 | 11 | — | — | |
| Anemia | | | | | | | |
| 1 | 3 | 5 | 3 | 5 | — | — | 1 v 2 .39 |
| 2 | 5 | 9 | 6 | 11 | — | — | All .21 |
| 3 | 2 | 6 | 2 | 6 | — | — | |
| 4 | 1 | 4 | 1 | 4 | — | — | |
| 5 | 7 | 20 | 1 | 6 | — | — | |
| Infection | | | | | | | |
| 1 | 7 | 13 | 5 | 9 | 1 | 2 | 1 v 2 .64 |
| 2 | 11 | 20 | 5 | 9 | 2 | 4 | All .048 |
| 3 | 4 | 12 | 2 | 6 | 1 | 3 | |
| 4 | 5 | 18 | 1 | 4 | 1 | 4 | |
| 5 | 1 | 3 | — | — | 6 | 17 | |
| Nausea and vomiting | | | | | | | |
| 1 | 2 | 4 | 3 | 5 | — | — | 1 v 2 .0038 |
| 2 | 11 | 20 | 8 | 14 | — | — | All .0076 |
| 3 | 3 | 9 | 1 | 3 | — | — | |
| 4 | 1 | 94 | 1 | 4 | — | — | |
| 5 | 7 | 20 | 1 | 3 | — | — | |
| Alopecia | | | | | | | |
| 1 | 5 | 99 | 2 | 4 | — | — | 1 v 2 .000003 |
| 2 | 20 | 36 | 12 | 22 | — | — | All .000003 |
| 3 | 4 | 12 | 1 | 3 | — | — | |
| 4 | 2 | 7 | 1 | 4 | — | — | |
| 5 | 7 | 20 | 5 | 14 | — | — | |
| Kidney | | | | | | | |
| 1 | — | — | — | — | — | — | 1 v 2 .0010 |
| 2 | 11 | 20 | 1 | 2 | — | — | All .000019 |
| 3 | — | — | — | — | — | — | |
| 4 | — | — | — | — | — | — | |
| 5 | — | — | — | — | — | — | |
| Esophageal | | | | | | | |
| 1 | 11 | 20 | 4 | 7 | — | — | 1 v 2 .00020 |
| 2 | — | — | — | — | — | — | All .00023 |
| 3 | 8 | 24 | 2 | 6 | — | — | |
| 4 | 6 | 21 | 1 | 4 | — | — | |
| 5 | — | — | — | — | — | — | |
| Bronchopulmonary | | | | | | | |
| 1 | 3 | 5 | — | — | — | — | 1 v 2 .082 |
| 2 | — | — | — | — | — | — | All .28 |
| 3 | 2 | 6 | — | — | — | — | |
| 4 | 1 | 4 | — | — | — | — | |
| 5 | — | — | — | — | — | — | |

Role of Radiation Therapy in the Combined-Modality Treatment of Patients With Extensive Disease Small-Cell Lung Cancer: A Randomized Study

By Branislav Jeremic, Yuta Shibamoto, Nebojsa Nikolic, Biljana Milicic, Slobodan Milisavljevic, Aleksandar Dagovic, Jasna Aleksandrovic, and Gordana Radosavljevic-Asic



Konsolidasyon TRT ilave 4 kür PE'den daha etkin ve sağ kalımı uzatıyor
Medyan OS: 17 vs. 11 ay
5-y OS : %9.1 vs. %3.7

Fig 2. Overall survival in group 1 (—), group 2 (---), group 3 (·····), group 4 (- · - · -), and group 5 (· · · · ·).

Fig 4. DMFS in group 1 (—), group 2 (---), group 3 (·····), and group 4 (- · - · -).

Sonuçları Beklenen Grup Çalışmaları

RTOG 0937

Randomized Phase II Study Comparing Prophylactic Cranial Irradiation Alone to Prophylactic Cranial Irradiation and Consolidative Extra-Cranial Irradiation for Extensive Disease Small Cell Lung Cancer (ED-SCLC)

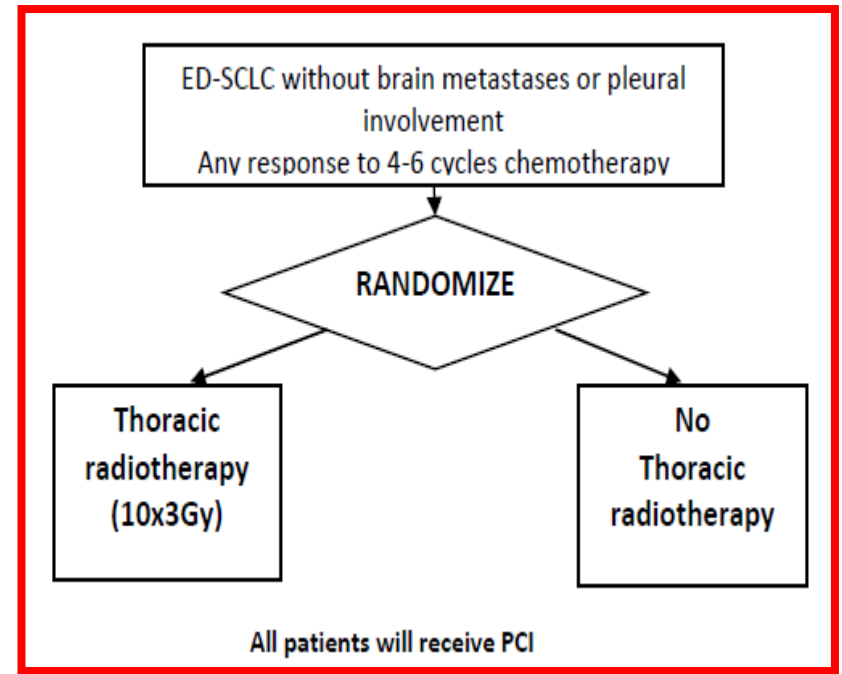
SCHEMA (10/21/11)

| | | | |
|----------|-------------------------------------|----------|------------------------------------------------------------|
| | | | |
| S | Response to Treatment | R | Arm 1: Prophylactic Cranial Irradiation |
| T | 1. Complete Response (CR) | A | 2.5 Gy per fraction for a total of 25 Gy |
| R | 2. Partial Response (PR) | N | |
| A | | D | Arm 2: Prophylactic Cranial Irradiation |
| T | | O | 2.5 Gy per fraction for a total of 25 Gy |
| I | Number of Metastatic Lesions | M | and |
| F | 1. 1 | I | Consolidative Radiation to |
| Y | 2. 2-4 | Z | Locoregional and Residual Metastatic Disease |
| | | E | 45 Gy at 3 Gy per fraction* |
| | | | |
| | | | *Acceptable alternative regimens: 30-40 Gy in 10 fractions |

Chest
Radiotherapy
Extensive stage
Small cell lung cancer
Trial

CREST Trial

Randomized trial on chest irradiation in extensive disease small cell lung cancer



KHDAK Oligometastaz ve Oligonükslerinde

Küratif RT

KHDAK Oligometastaz ve Oligonükslerinde RT

- İyi performans: Palyatif kemoterapi ve/veya RT
- Kötü performans: Destekleyici tedavi
- OS: 8-12 ay
- İnsidans: %20 ve görüntüleme iyileşmeyle artıyor
- Sıklıkla oligomet/nüks hastalar yaygın met hastalarla benzer tedaviler alıyor
- Potansiyel ablatif tedavilerle LRPFS, DFS, CSS ve/veya OS uzayabilir mi?
- Ablatif tedavilerin amaçları
 - Oligomet başka met yok Ablate edilirse kür mümkün olabilir
 - Oligomet met odağı. Ablate edilirse başka met gelişmeyebilir
 - Küçük tm yüksek kemoterapi etkisi: Ablate olmasa bile küçülürse etki artar
(Norton-Smith Hipotezi-1986)
- Potansiyel ablatif tedaviler %25-30 hastada 5-y OS ile sonuçlanıyor

Destekleyici Kanıtlar Var mı?

JAMA The Journal of the American Medical Association

November 4, 1998, Vol 280, No. 17

Original Contributions

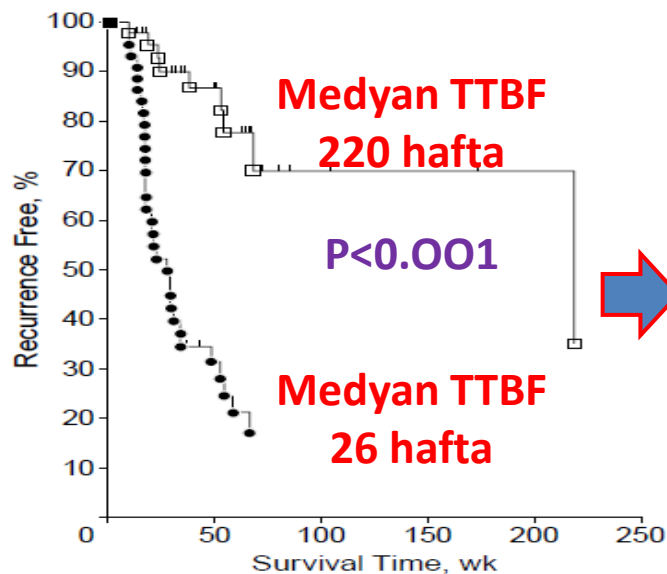
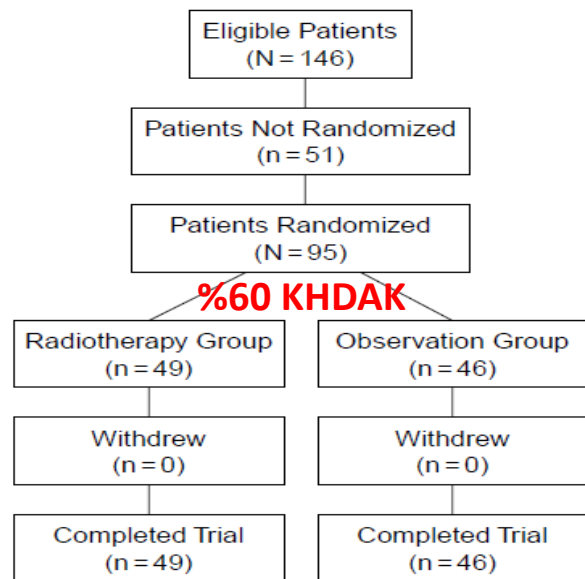
Postoperative Radiotherapy in the Treatment of Single Metastases to the Brain

A Randomized Trial

Roy A. Patchell, MD; Phillip A. Tibbs, MD; William F. Regine, MD; Robert J. Dempsey, MD; Mohammed Mohiuddin, MD; Richard J. Kryscio, PhD; William R. Markesbery, MD; Kenneth A. Foon, MD; Byron Young, MD

Location of Recurrence of Metastatic Cancer in the Brain

| Recurrence | No. (%) | |
|-----------------------|----------------------------|--------------------------|
| | Observation Group (n = 46) | Radiation Group (n = 49) |
| None | 14 (30) | 40 (82) |
| Original only* | 15 (33) | 2 (4) |
| Original and distant† | 6 (13) | 3 (6) |
| Distant only | 11 (24) | 4 (8) |



Beyin met. hastalarda 15 hf OS burada 40 haftaya çıkmış

Adrenal met. rezeksiyonu veya SBRT

- KHDAK: Otopsi serilerinde %40+
- Genellikle diğer uzak met+
- Retroperitoneal lenfatik akımla gelebilir (Rejyonel hastalık)
- Twomey ve ark-1982-JAMA
 - Large cell KHDAK, 2 hastada adrenalectomi sonrası 6 ve 14 yıl DFS

VOLUME 26 · NUMBER 7 · MARCH 1 2008

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Outcomes of Adrenalectomy for Isolated Synchronous Versus Metachronous Adrenal Metastases in Non–Small-Cell Lung Cancer: A Systematic Review and Pooled Analysis

Tawee Tanvetyanon, Lary A. Robinson, Michael J. Schell, Vivian E. Strong, Rachna Kapoor, Daniel G. Coit, and Gerold Bepler

Outcomes of Adrenalectomy for Isolated Synchronous Versus Metachronous Adrenal Metastases in Non–Small-Cell Lung Cancer: A Systematic Review and Pooled Analysis

Tawee Tanvetyanon, Lary A. Robinson, Michael J. Schell, Vivian E. Strong, Rachna Kapoor, Daniel G. Coit, and Gerold Bepler

A B S T R A C T

Purpose

Several small studies have reported that an adrenalectomy for isolated adrenal metastasis in non–small-cell lung cancer (NSCLC), along with a surgical resection for the primary lung cancer, can be curative. However, some suggest that the survival outcome among patients with a synchronous metastasis is poor. It remains unclear whether this treatment approach is warranted among those with synchronous metastasis.

Methods

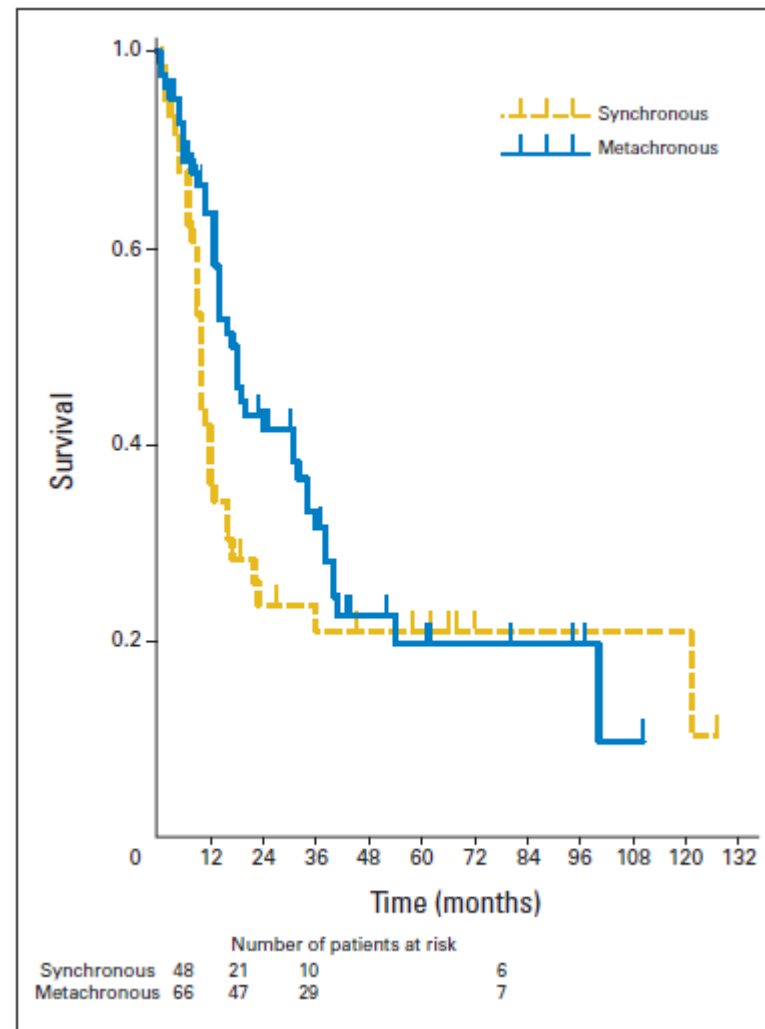
A search for publications on adrenalectomy for NSCLC was performed via the MEDLINE database. Studies reporting on survival outcomes and containing at least four analyzable patients who had surgery for primary lung cancer were included. Those not allowing separation of outcomes between synchronous and metachronous metastases were excluded. Synchronous metastasis was defined as a disease-free interval (DFI) of 6 months or less.

Results

There were 10 publications contributing 114 patients; 42% of patients had synchronous metastases and 58% had metachronous metastases. The median DFIs were 0 and 12 months, respectively. Patients in the synchronous group were younger than those in the metachronous group (median age 54 v 68 years). Complications from adrenalectomy were infrequent. Median overall survival was shorter for patients with synchronous metastasis than those with metachronous metastasis (12 months v 31 months, generalized Wilcoxon P value = .02). However, the 5-year survival estimates were equivalent at 26% and 25%, respectively.

Conclusion

For an isolated adrenal metastasis from NSCLC, patients with a synchronous metastasis who underwent adrenalectomy had a shorter median overall survival than those with a metachronous metastasis. However, a durable long-term survival is achieved in approximately 25% in both groups.



izole adrenal met eksizyonu
sonrası 5-y OS

%25

SBRT kanıtları



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 0360-3016/\$ - see front matter

doi:10.1016/j.ijrobp.2010.11.060

CLINICAL INVESTIGATION

Genitourinary Cancer

STEREOTACTIC RADIOTHERAPY FOR ADRENAL GLAND METASTASES: UNIVERSITY OF FLORENCE EXPERIENCE

FRANCO CASAMASSIMA, M.D., PH.D.,* LORENZO LIVI, M.D.,[†] STEFANO MASCIULLO, M.D.,*
 CLAUDIA MENICHELLI, M.D.,* LAURA MASI, PH.D.,* ICRO MEATTINI, M.D.,[†] IVANO BONUCCI, M.D.,*
 BENEDETTA AGRESTI, M.D.,[†] GABRIELE SIMONTACCHI, M.D.,[†] AND RAFFAELA DORO, PH.D.*

*Clinical Radiobiological Institute and [†]Department of Radiation-Oncology, University of Florence, Florence, Italy

Purpose: To evaluate a retrospective single-institution outcome after hypofractionated stereotactic body radiotherapy (SBRT) for adrenal metastases.

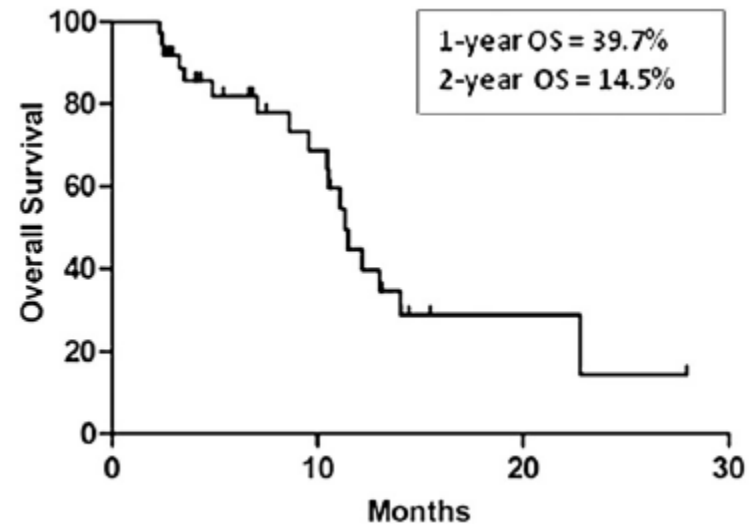
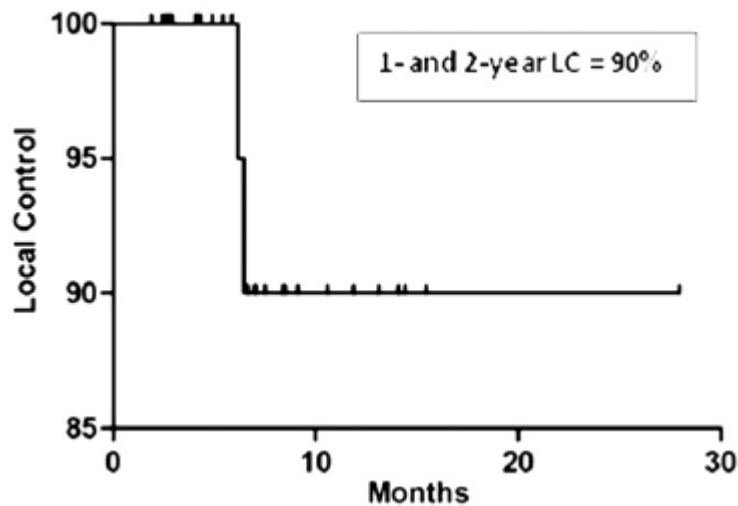
Methods and Materials: Between February 2002 and December 2009, we treated 48 patients with SBRT for adrenal metastases. The median age of the patient population was 62.7 years (range, 43-77 years). In the majority of patients, the prescription dose was 36 Gy in 3 fractions (70% isodose, 17.14 Gy per fraction at the isocenter). Eight patients were treated with single-fraction stereotactic radiosurgery and forty patients with multi-fraction stereotactic radiotherapy.

Results: Overall, the series of patients was followed up for a median of 16.2 months (range, 3-63 months). At the time of analysis, 20 patients were alive and 28 patients were dead. The 1- and 2-year actuarial overall survival rates were 39.7% and 14.5%, respectively. We recorded 48 distant failures and 2 local failures, with a median interval to local failure of 4.9 months. The actuarial 1-year disease control rate was 9%; the actuarial 1- and 2-year local control rate was 90%.

Conclusion: Our retrospective study indicated that SBRT for the treatment of adrenal metastases represents a safe

Table 2. Main characteristics of 48 patients treated at University of Florence

| Feature | No. of patients (%) |
|------------------------------------------------------------|---------------------|
| Gender | |
| Male | 30 (62.5) |
| Female | 18 (37.5) |
| Age (y) | |
| Mean | 62.7 |
| Range | 43-77 |
| Primary site | |
| Lung | 24 (50.0) |
| Colon | 12 (25.0) |
| Melanoma | 4 (8.4) |
| Breast | 3 (6.3) |
| Kidney | 3 (6.3) |
| Uterus | 1 (2.0) |
| Unknown | 1 (2.0) |
| Interval from primary diagnosis to adrenal metastases (mo) | |
| Median | 37.2 |
| Range | 0-132 |
| Unilateral adrenal metastasis | |
| Right | 23 (48.0) |
| Left | 15 (31.2) |
| Bilateral metastasis | 10 (20.8) |



Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

FILIPPO ALONGI,^a STEFANO ARCANGELI,^a ANDREA RICCARDO FILIPPI,^b UMBERTO RICARDI,^b MARTA SCORSETTI^a

Table 4. Summary of published trials of stereotactic body radiation therapy for adrenal metastases

| Study | <i>n</i> of patients | Median dose/ <i>n</i> of fractions | Median (range) follow-up, mos | Local control rate | Overall survival | Toxicity |
|-------------------------|----------------------|------------------------------------|-------------------------------|------------------------------|---------------------------------|-------------------------------------------|
| Casamassima et al. [26] | 48 | 36 Gy/3 | 16.2 (3–63) | 1–2 yrs, 90% | 1-yr, 39.7%; 2-yr, 14.5% | 1 case of grade II adrenal insufficiency |
| Chawla et al. [24] | 30 | 40 Gy/10 | 9.8 (3.2–28.3) | 1-yr, 55% | 1-yr, 44%; 2-yr, 25% | Mild grade 1 fatigue and nausea, “common” |
| Oshiro et al. [25] | 19 | 45 Gy/10 | 11.5 (5.4–87.8) | Objective response rate, 68% | 1-yr, 56%; 2-yr, 33%; 3-yr, 22% | 1 grade 2 duodenal ulcer |
| Holy et al. [54] | 18 | 20 Gy/5 or 40 Gy/8 | 21 | Objective response rate, 77% | Median, 23 mos | – |
| Torok et al. [55] | 7 | 16 Gy/1 or 27/3 | 14 (1–60) | 1-yr, 63% | Median, 8 mos | – |

- Cerrahi SBRT'den daha iyi görünüyor. İlk tercih cerrahi olmalı
 - SBRT: 2-y LC: %55-90
 - SBRT: 2-Y OS: %25-40
- ➔
- Cerrahi: 5-y sonuçlar benzer**

AC oligomet/oligonükslerinde SBRT



The
Oncologist[®]

Radiation Oncology

Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

FILIPPO ALONGI,^a STEFANO ARCANGELI,^a ANDREA RICCARDO FILIPPI,^b UMBERTO RICARDI,^b
MARTA SCORSETTI^a

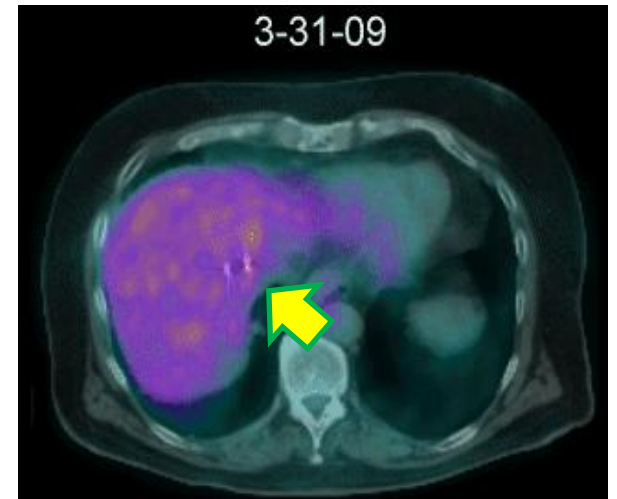
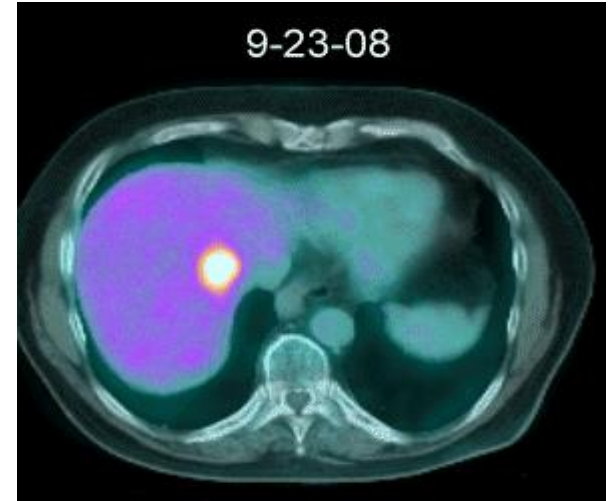
Table 1. Outcomes of stereotactic body radiation therapy for lung metastases from selected trials

| Study | <i>n</i> of patients | Median dose/ <i>n</i> of fractions | Median (range) follow-up, mos | Local control rate | Overall survival | Toxicity |
|---------------------|----------------------|------------------------------------|-------------------------------|---------------------------------------|------------------|-------------------|
| Onimaru et al. [5] | 45 | 48 Gy/8; 60 Gy/8 | 18 (2–44) | 3-yr, 69.6% for 48 Gy, 100% for 60 Gy | 2-yr, 47.1% | Grade 5, 1 (2.2%) |
| Wulf et al. [32] | 27 | 30 Gy/3; 36 Gy/3 | 13–17 | 2-yr, 71% | 1-yr, 48% | Grade 3, 1 (3.7%) |
| Ricardi et al. [17] | 61 | 45 Gy/3; 26 Gy/1 | 20.4 (3–77) | 2-yr, 89% | 2-yr, 66.5% | Grade 3, 1 (1.6%) |

- Cerrahi hastalar seçilmiş vakalardan oluşsa da SBRT ile sonuçlar benzer
- Yeterli SBRT dozlarında (>52 Gy) 2-3 y LC: %70-100
- SBRT: 2-y OS: %21-84

KHDAK ve KC met

- Sıklıkla AC, meme, GIS kökenli
- Yaygın met bir parçası
- Tek met organı olabilir
- Kolorektal ca hariç genellikle palyatif KT
- Rezeksiyon, SBRT, RFA vs ile bazı hastalarda uzun süreli tm kontrolü, yaşam ve kür mümkün
- Cerrahi vs. gözlem RCT yok



KHDAK ve KC met

- EORTC 40004-COCC Faz II çalışması
 - Kemo+RFA vs. kemo
 - DFS: 17 VS. 10 ay
- ASCO Derlemesi
 - RFA: 5-y OS 14-55%
- Çok merkezli Fransız çalışması: N=1452 non-CRC, non-NE hasta
 - 5-y OS: %36
 - 10-y OS: %23
- SBRT
 - 1-y LC: %70-100, 2-y LC: %60-90
 - Doz ve etkinlik paralellik gösteriyor
 - 48-52 Gy/3 ile >%90 LC mümkün
 - Medyan OS: 10-34 ay
 - 2-y OS: %30-83

KHDAK ve KC met

- Unrezektabl (%80-90) KC met SBRT %60-90 LC ile ümit verici
- KT+SBRT± Hedefle yönelik ajanlarla daha iyi sonuçlar alınabilme potansiyeli yüksek
- PMH Çalışması: SBRT +Sorafenib
- MDACC Yttrium-90 radyoembolizasyon + kemoterapi
- RAS-Trial (SBRT vs. RFA): İlk kafa-kafaya çalışma

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

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Example: "Heart attack" AND "Los Angeles"

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Search for studies:

Example: "Heart attack"

Advanced Search

Sorafenib-RT Treatment for

Yttrium Microspheres

Find Studies

About Clinical Studies

Submit Studies

Resources

About This Site

Home > Find Studies > Study Record Detail

This study is ongoing, but not

Sponsor:
University Health Network, Toronto

Information provided by (Responsible Party):
University Health Network, Toronto

This study has been withdrawn

(Slow Accrual and withdrawn/terminated)

Sponsor:
M.D. Anderson Cancer Center

Collaborator:
Sirtex Medical

Information provided by (Responsible Party):
M.D. Anderson Cancer Center

Radiofrequency Ablation Versus Stereotactic Radiotherapy in Colorectal Liver Metastases (RAS01)

This study is currently recruiting participants.

Verified June 2012 by University of Aarhus

Sponsor:
University of Aarhus

Collaborator:
Danish Center for Interventional Research in Radiation Oncology (CIRRO)

Information provided by (Responsible Party):
University of Aarhus

ClinicalTrials.gov Identifier:
NCT01233544

First received: November 2, 2010
Last updated: June 18, 2012
Last verified: June 2012
[History of Changes](#)

KHDAK ve spinal met

THE LANCET Oncology



Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Merina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Cl Peter J Ostler, Nicholas J van As

Review

Lancet Oncol 2013; 14: e28-37

| Study | Study year | Number of patients (number of lesions) | Dose | Primary site | Treated site(s) | Treated metastasis control | Toxicity |
|-------------------------------|------------|----------------------------------------|--------------------------------------------------------------------|-------------------------------------------------|--------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| Muacevic et al ⁶⁷ | 2011 | 40 (64) | 20 Gy in 1 fraction (median) | Prostate | Bone (34/64 spine) | 2-year control 95.5% | No grade 3 or higher |
| Wang et al ^{68*} | 2012 | 149 (166) | 27-30 Gy in 3 fractions | Mixed (32% renal) | Spine | 72% (median follow-up 15.9 months) | 7% grade 3 (non-cardiac chest pain, other pain, nausea, fatigue) |
| Yamada et al ^{69*} | 2008 | 93 (103) | 18-24 Gy in 1 fraction | Mixed (high proportion of renal-cell carcinoma) | Vertebrae | 90% at 15 months | 1 acute grade 3 (1%), 1 late grade 3 (1%) |
| Gerstzen et al ^{70*} | 2007 | 393 (500) | Mean maximum dose 20 Gy in 1 fraction | Mixed | Vertebrae | 88% at median follow-up 21 months (100% for breast and lung primaries, 75% for melanoma) | No significant neurological effects recorded |
| Zelevsky et al ⁷¹ | 2011 | 105 (105) | Varied, but mostly 24 Gy in 1 fraction or 30 Gy in 5 fractions | Renal-cell carcinoma | 99% bone metastases | 3-year local control 44%, but 88% for 24 Gy in 1 fraction | 1 grade 4 skin (1%), 4 fractures (not graded) |
| Nguyen et al ^{72*} | 2010 | 48 (55) | 24 Gy in 1 fraction, 27 Gy in 3 fractions, or 30 Gy in 5 fractions | Renal-cell carcinoma | Spine (one or two sites) | 82% 1-year spine progression-free survival | 2% pain, 2% anaemia |

* Percentage of patients with oligometastatic disease is not known for these studies.

Table 3: Stereotactic body radiotherapy for treatment of spinal metastases



Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

FILIPPO ALONGI,^a STEFANO ARCANGELI,^a ANDREA RICCARDO FILIPPI,^b UMBERTO RICARDI,^b MARTA SCORSETTI^a

Table 5. Summary of published trials of stereotactic body radiation therapy for spinal metastases

| Study | <i>n</i> of patients | Median dose/ <i>n</i> of fractions | Median follow-up, mos | Local control rate | Pain response |
|----------------------|----------------------|---------------------------------------|-----------------------|--------------------|----------------------------------|
| Yamada et al. [73] | 93 | | | | NS |
| Ryu et al. [74] | 49 | | | | 85% |
| Sahgal et al. [56] | 14 | | | | NS |
| | 25 | | | | NS |
| Nguyen et al. [75] | 48 | | | | 52% |
| Tsai et al. [76] | 69 | | | | Improved pain control, 88% |
| Chang et al. [58] | 63 | | | | Narcotic use declined 60% to 36% |
| Gibbs et al. [77] | 74 | 14–25 Gy/1–5 | 9 | NS | Clinical benefit, 84% |
| Gerstzen et al. [78] | 393 | 20 Gy/1 | 21 | 88% (imaging) | Clinical benefit, 86% |

SBRT

- Uzun süreli LC: %72-100
- Ağrı kontrolü: %85

Abbreviation: NS, not significant.

**KHDAK'de primer tm ve oligometastazların
RT ile konsolidasyonu (Küratif Yaklaşım)**

Uzun süreli sağkalım mümkün mü?

Radiotherapy and Oncology 81 (2006) 163–167
www.thegreenjournal.com

Lung cancer



Long term disease-free survival resulting from combined modality management of patients presenting with oligometastatic, non-small cell lung carcinoma (NSCLC)

Atif J. Khan^a, Par S. Mehta^a, Thomas W. Zusag^a, Philip D. Bonomi^b,
L. Penfield Faber^c, Susan Shott^b, Ross A. Abrams^{a,b,*}

^aDepartment of Radiation Oncology, ^bDepartment of Internal Medicine, Section of Medical Oncology, and ^cDepartment of Surgery, Rush University Medical Center, Chicago, IL, USA

Abstract

We report outcomes on 23 patients with oligometastatic (1 or 2 sites) NSCLC treated with aggressive local, regional, and systemic treatment. The results suggest that this is a favorable subset of patients who may benefit from such an approach, with a 22% rate of long-term survival. This treatment strategy is a departure from the usual practice of palliative-only therapy for all NSCLC patients presenting with metastatic disease.

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Keywords: Lung cancer; NSCLC; Oligometastasis; Oligometastases

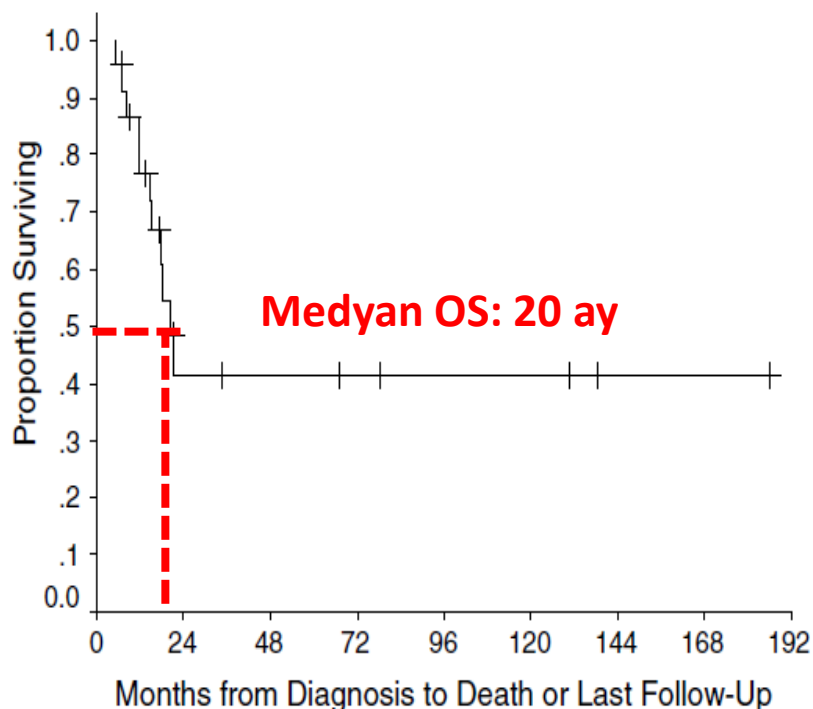
Table 1
Patient characteristics

| | | |
|------------------|----------------|------|
| Age | ≤65 | 13 |
| | >65 | 10 |
| Gender | Male | 10 |
| | Female | 13 |
| ECOG | 0 | 11 |
| PS ^a | 1 | 12 |
| Weight loss ≥10% | Y/N | 1/22 |
| Metastatic sites | Brain | 14 |
| | Intrapulmonary | 3 |
| | Adrenals | 2 |
| | Bone | 2 |
| | Celiac node | 1 |
| | Soft tissue | 1 |
| T stage | TX | 1 |
| | T1 | 5 |
| | T2 | 10 |
| | T3 | 5 |
| | T4 | 2 |
| N stage | 0 | 3 |
| | 1 | 3 |
| | 2 | 13 |
| | 3 | 4 |
| Chest only stage | IA/IB | 1/1 |
| | IIA/IIIB | 0/3 |
| | IIIA/IIIB | 12/6 |

^a Abbreviations: ECOG PS, = Eastern Cooperative Oncology Group performance status.

Long term disease-free survival resulting from combined modality management of patients presenting with oligometastatic, non-small cell lung carcinoma (NSCLC)

Atif J. Khan^a, Par S. Mehta^a, Thomas W. Zusag^a, Philip D. Bonomi^b,
L. Penfield Faber^c, Susan Shott^b, Ross A. Abrams^{a,b,*}



- **Medyan TTR: 12 ay**
- **Medyan TTLR: 30 ay**
- **5 (%22) : Relaps+, sağ**
- **7 (%30): NED yaşıyor**

We report outcomes on 23 patients with oligometastatic (1 or 2 sites) NSCLC treated with aggressive local, regional, and systemic treatment. The results suggest that this is a favorable subset of patients who may benefit from such an approach, with a 22% rate of long-term survival. This treatment strategy is a departure from the usual practice of palliative-only therapy for all NSCLC patients presenting with metastatic disease.

Clinical Investigation: Metastases

Oligometastases Treated With Stereotactic Body Radiotherapy: Long-Term Follow-Up of Prospective Study

Michael T. Milano, M.D., Ph.D.,* Alan W. Katz, M.D., M.P.H.,*
Hong Zhang, Ph.D., M.D.,* and Paul Okunieff, M.D.*†

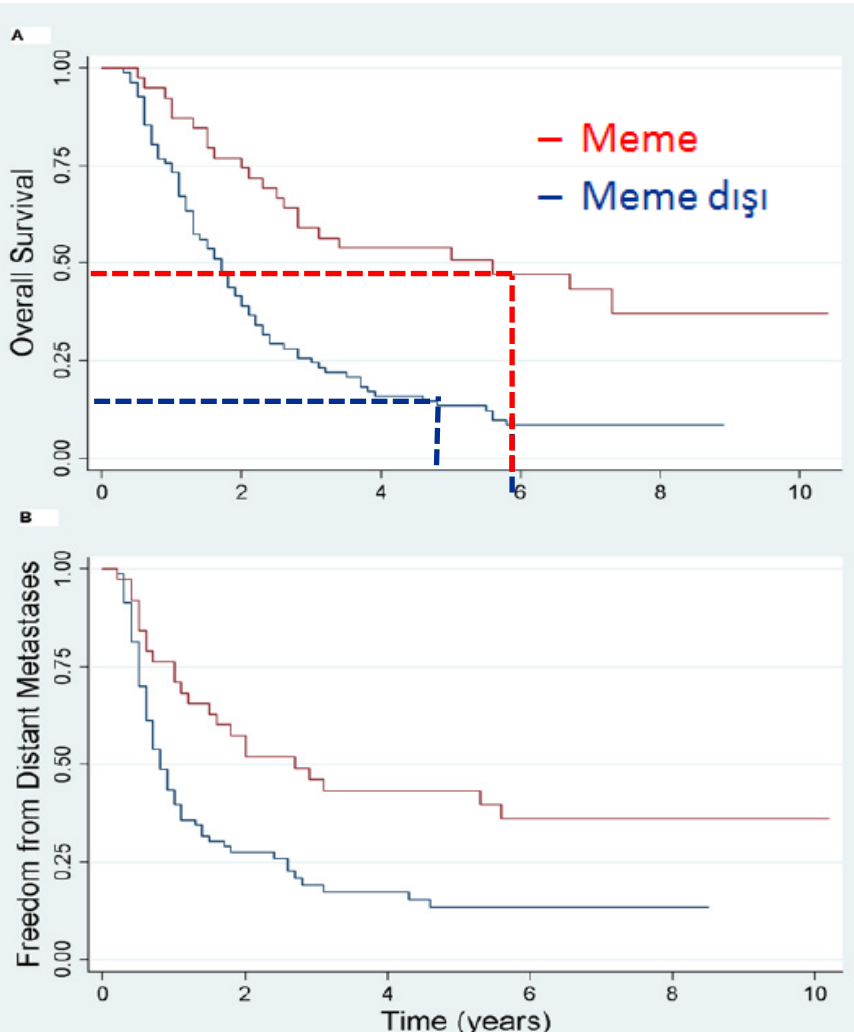
*Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY; and †Department of Radiation Oncology, University of Florida, Gainesville, FL

Purpose: To analyze the long-term survival and tumor control outcomes after stereotactic body radiotherapy (SBRT) for metastases limited in number and extent.

Methods and Materials: We prospectively analyzed the long-term overall survival (OS) and cancer control outcomes of 121 patients with five or fewer clinically detectable metastases, from any primary site, metastatic to one to three organ sites, and treated with SBRT. Freedom from widespread distant metastasis (FFDM) was defined as metastatic disease not amenable to local therapy (*i.e.*, resection or SBRT). Prognostic variables were assessed using log-rank and Cox regression analyses.

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- Meme kanseri sonuçları daha iyi
- Meme dışı tm: Medyan OS 1.7 yıl
- En iyi tedavilerle Evre IIIB
- KHDAK'de güncel medyan sağkalım 20-26 ay
- 1.7 yıl = 21 ay
- Tm hacmi küçük olanlarda LC ve OS daha iyi

Clinical Investigation: Thoracic Cancer

Prognostic Impact of Radiation Therapy to the Primary Tumor in Patients With Non-small Cell Lung Cancer and Oligometastasis at Diagnosis

Jose Luis Lopez Guerra, MD,^{*,§} Daniel Gomez, MD,^{*} Yan Zhuang, MD,^{*} David S. Hong, BA,^{*} John V. Heymach, MD, PhD,[†] Stephen G. Swisher, MD,[‡] Steven H. Lin, MD, PhD,^{*} Ritsuko Komaki, MD,^{*} James D. Cox, MD,^{*} and Zhongxing Liao, MD^{*}

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Summary

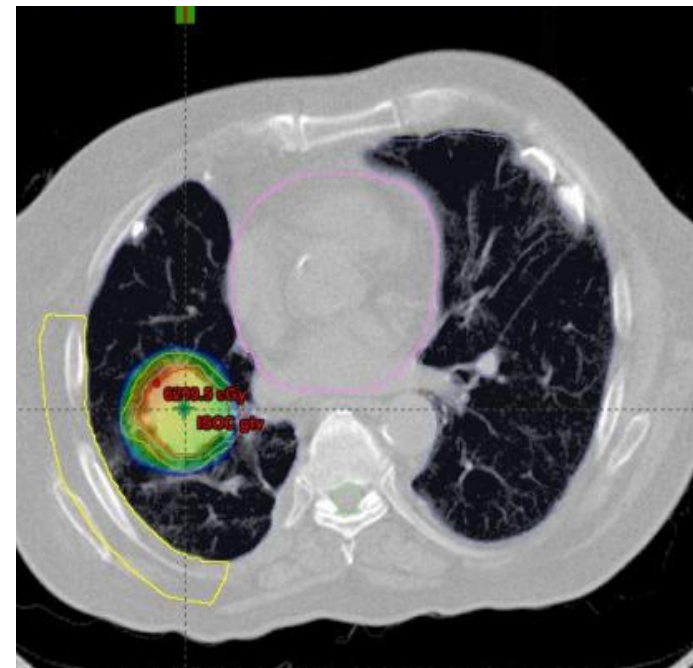
We investigated prognostic factors associated with overall survival in patients with oligometastatic non-small cell lung cancer, including local treatment to the primary tumor site. We found that patients receiving a higher radiation dose to the primary tumor (≥ 63 Gy), having a lower gross tumor volume ($GTV \leq 124$ cm³), or having better Karnofsky performance scores (KPS > 80) had better outcomes.

Purpose: We investigated prognostic factors associated with survival in patients with non-small cell lung cancer (NSCLC) and oligometastatic disease at diagnosis, particularly the influence of local treatment to the primary site on prognosis.

Methods and Materials: From January 2000 through June 2011, 78 consecutive patients with oligometastatic NSCLC (< 5 metastases) at diagnosis underwent definitive chemoradiation therapy (≥ 45 Gy) to the primary site. Forty-four of these patients also received definitive local treatment for the oligometastases. Survival outcomes were estimated using the Kaplan-Meier method, and risk factors were identified by univariate and multivariate analyses.

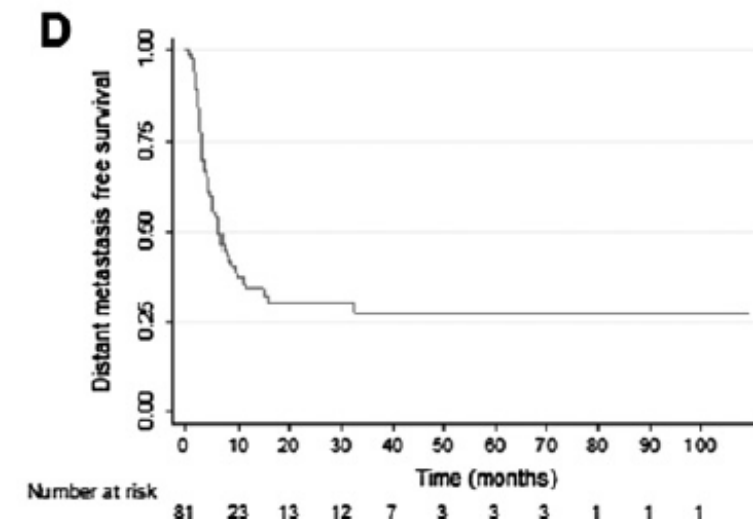
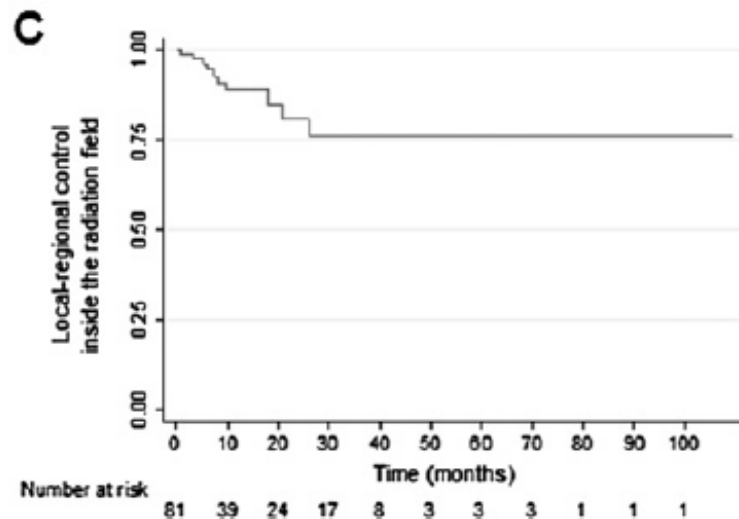
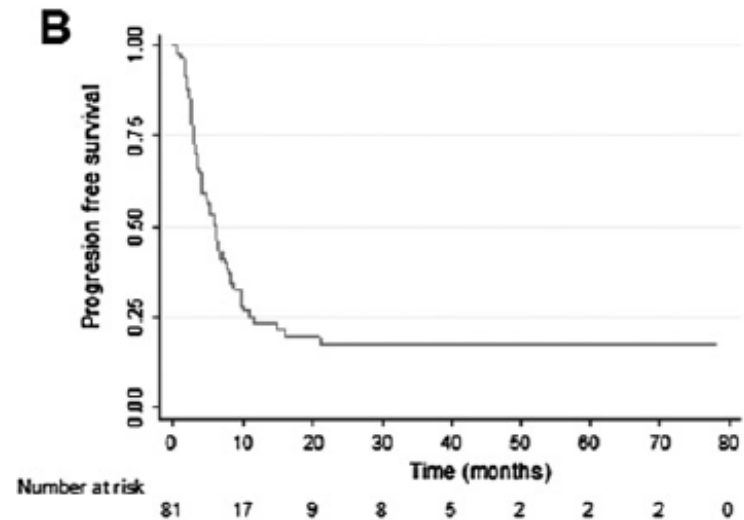
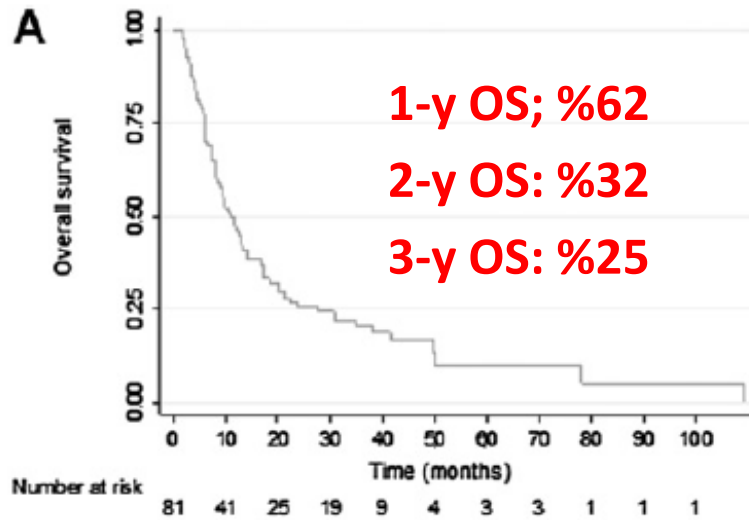
Results: Univariate Cox proportional hazard analysis revealed better overall survival (OS) for those patients who received at least 63 Gy of radiation to the primary site ($P = .002$), received definitive local treatment for oligometastasis ($P = .041$), had a Karnofsky performance status (KPS) score > 80 ($P = .007$), had a gross tumor volume ≤ 124 cm³ ($P = .002$), had adenocarcinoma histology ($P = .002$), or had no history of respiratory disease ($P = .016$). On multivariate analysis, radiation dose, performance status, and tumor volume retained significance ($P = .004$, $P = .006$, and $P < .001$, respectively). The radiation dose also maintained significance when patients with and without brain metastases were analyzed separately.

Conclusions: Tumor volume, KPS, and receipt of at least 63 Gy to the primary tumor are associated with improved OS in patients with oligometastatic NSCLC at diagnosis. Our results suggest that a subset of such patients may benefit from definitive local therapy.
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Prognostic Impact of Radiation Therapy to the Primary Tumor in Patients With Non-small Cell Lung Cancer and Oligometastasis at Diagnosis

Jose Luis Lopez Guerra, MD,^{*,§} Daniel Gomez, MD,^{*} Yan Zhuang, MD,^{*}



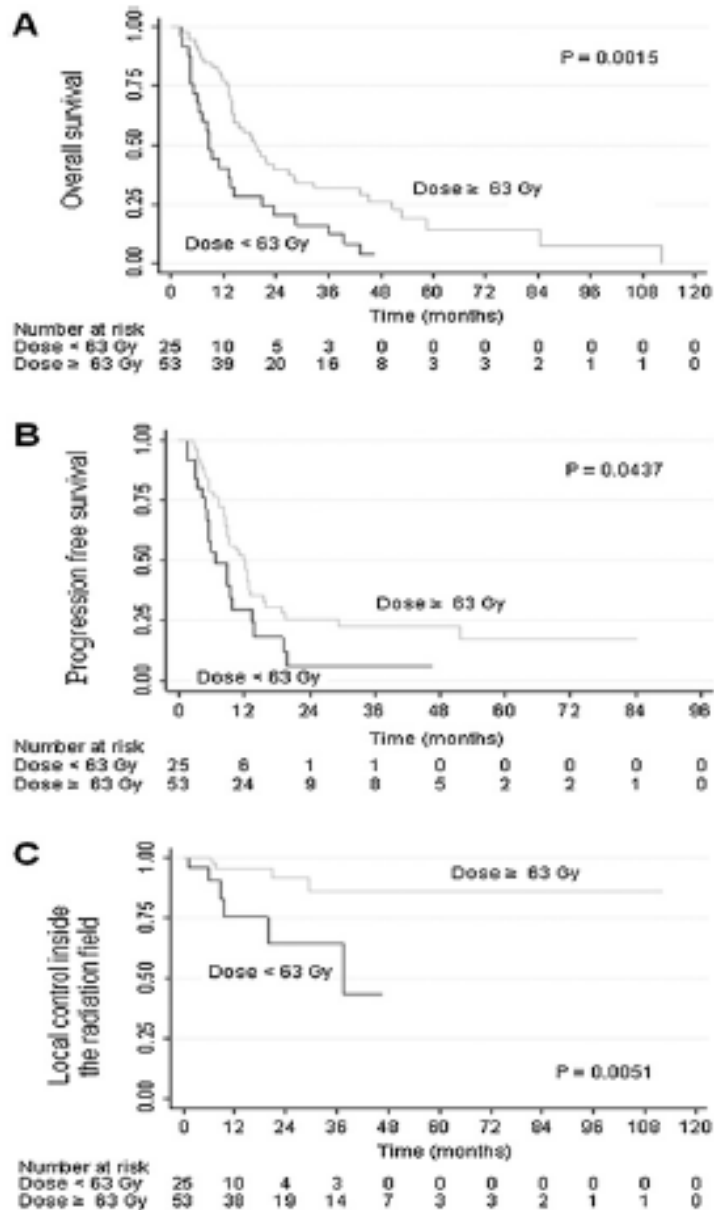


Fig. 2. Overall survival (A), progression-free survival (B), and local-regional control (C) according to the radiation dose to the primary tumor.

Prognostic Impact of Radiation Therapy to the Primary Tumor in Patients With Non-small Cell Lung Cancer and Oligometastasis at Diagnosis

Jose Luis Lopez Guerra, MD,^{*,§} Daniel Gomez, MD,^{*} Yan Zhuang, MD,^{*}

Table 3 Factors associated with overall survival and local tumor control in multivariate analyses

| Variables | Overall survival | | LRC inside the field | | LRC inside + outside the field | |
|--------------------------------------------|------------------|----------|----------------------|---------|--------------------------------|---------|
| | HR | P value | HR | P value | HR | P value |
| T category | | | | | | |
| T1 or T2 | - | - | - | - | 1.00 | - |
| T3 or T4 | - | - | - | - | 4.61 | .008 |
| Karnofsky performance status | | | | | | |
| ≤ 80 | 1.00 | - | - | - | - | - |
| > 80 | 0.38 | .006 | - | - | - | - |
| Gross tumor volume (cm³) | | | | | | |
| ≤ 124 | 1.00 | - | - | - | - | - |
| > 124 | 2.74 | $< .001$ | - | - | - | - |
| Radiation total dose | | | | | | |
| < 63 Gy or GyE | 1.00 | - | 1.00 | - | - | - |
| ≥ 63 Gy or GyE | 0.44 | .004 | 0.24 | .033 | - | - |

Abbreviations: GyE = cobalt-Gray equivalent; HR = hazard ratio; LRC = local-regional control.

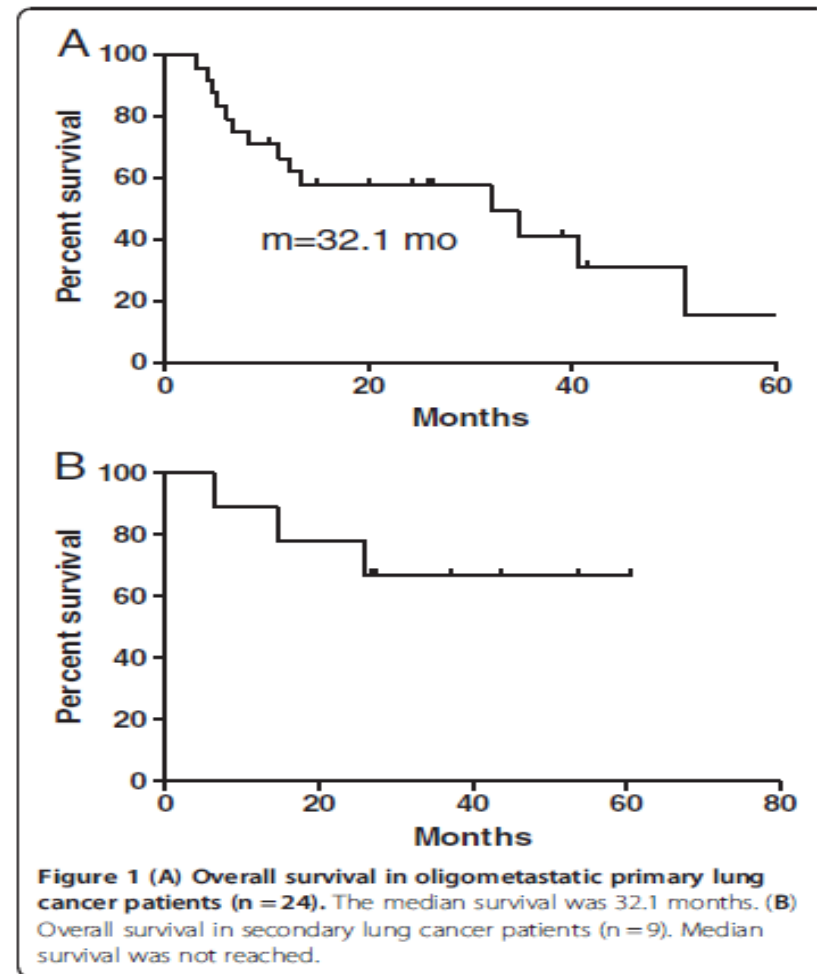
RESEARCH

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Hypofractionated radiotherapy for primary or secondary oligometastatic lung cancer using Tomotherapy

Heng-Jui Chang¹, Hui-Ling Ko¹, Cheng-Yen Lee¹, Ren-Hong Wu¹, Yu-Wung Yeh², Jiunn-Song Jiang², Shang-Jyh Kao² and Kwan-Hwa Chi^{1,3*}

| Variable | Distribution | Numbers | |
|-----------------------------|------------------------|----------|----|
| Sex | Male | 24 | |
| | Female | 9 | |
| Age (years) | Range | 31-82 | |
| | Median | 68 | |
| Performance Status | 0 | 20 | |
| | 1 | 10 | |
| | 2 | 3 | |
| Primary tumor site | Lung | 24 | |
| | Mesothelioma | 1 | |
| | Head and neck | 1 | |
| | Colorectum | 3 | |
| | Esophagus | 1 | |
| | Stomach | 1 | |
| | Liver | 1 | |
| | Sarcoma | 1 | |
| | Primary lung cancer | Stage IV | 24 |
| | Extrapulmonary disease | No | 18 |
| Yes | | 15 | |
| No of total RT targets | 1 | 20 | |
| | 2 | 6 | |
| | 3 | 3 | |
| | 4 | 1 | |
| | 5 | 3 | |
| Concurrent systemic therapy | No | 10 | |
| | Yes | 23 | |



RESEARCH

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(EPD: Extrapulmonary disease)

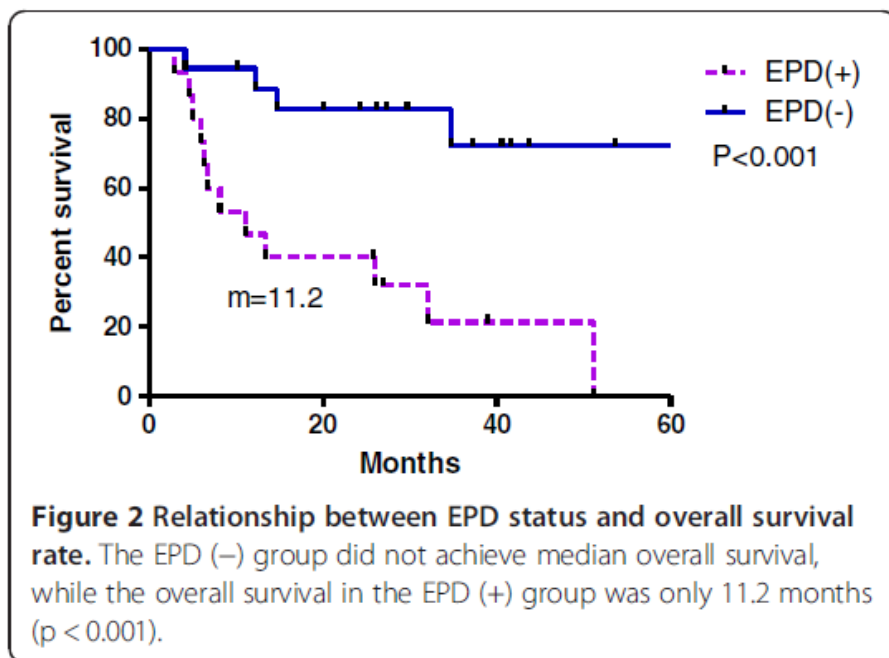


Figure 2 Relationship between EPD status and overall survival rate. The EPD (-) group did not achieve median overall survival, while the overall survival in the EPD (+) group was only 11.2 months ($p < 0.001$).

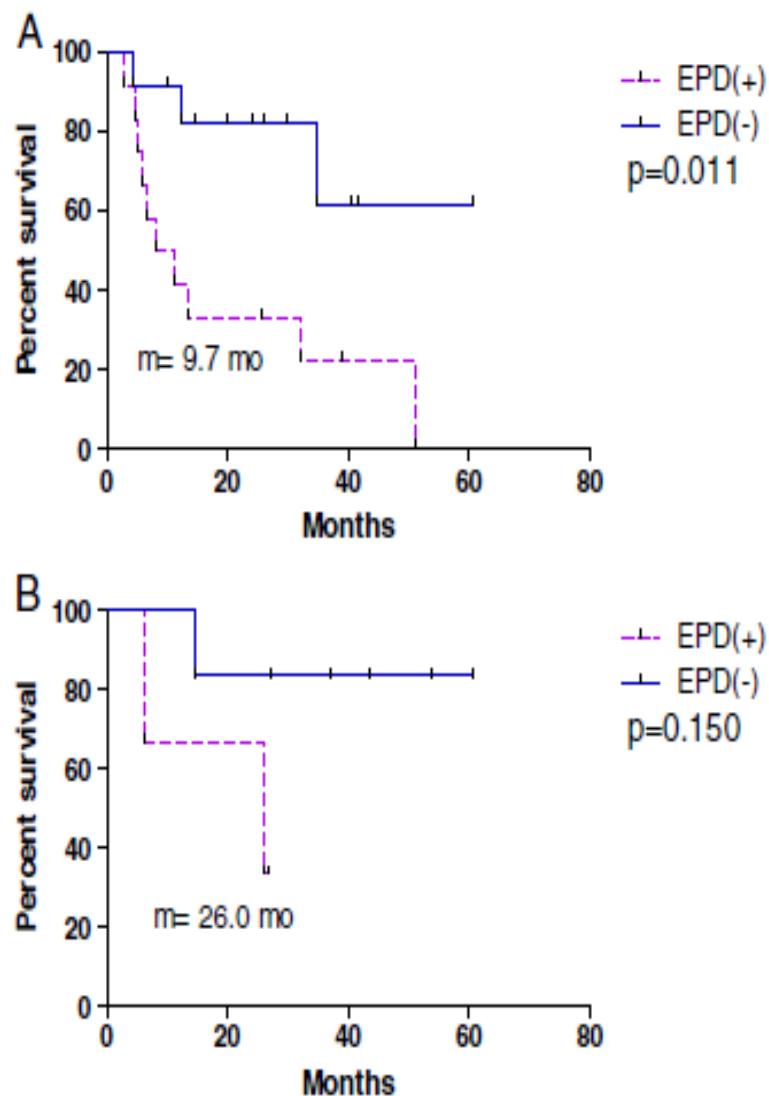


Figure 4 (A) EPD status in primary lung cancer also leads survival difference. EPD(+) vs EPD(-): 9.7 months vs not reached ($p = 0.011$). (B) EPD status in secondary lung cancer. EPD(+) vs EPD (-): 26 months vs not reached ($p = 0.150$).

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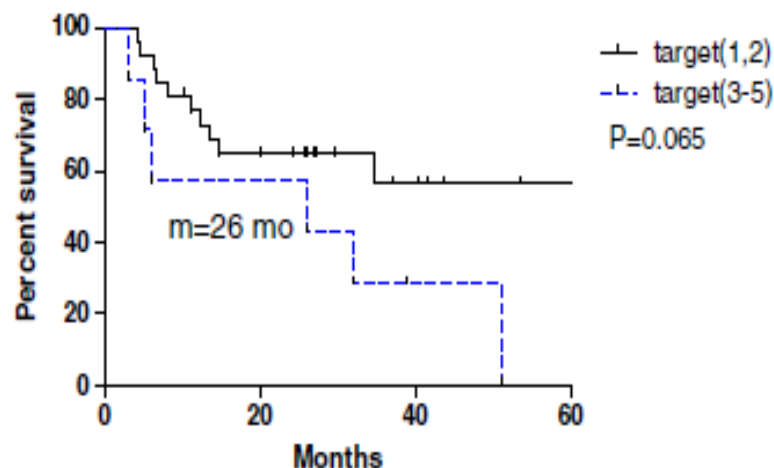


Figure 3 Overall survival difference of 2 and 3 total oligometastatic lesions in all 33 patients. Median survival were undefined and 26 months separately ($p = 0.065$).

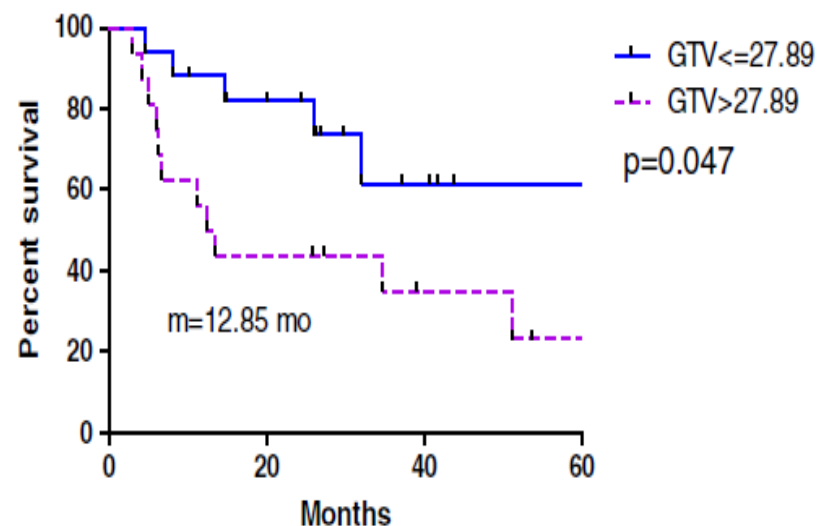


Figure 6 Use GTV volume to predict survival.

RESEARCH

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Comparison of outcomes in patients with stage III versus limited stage IV non-small cell lung cancer

Praveena Cheruvu¹, Su K Metcalfe¹, Justin Metcalfe¹, Yuhchyan Chen¹, Paul Okunieff² and Michael T Milano^{1*}

Abstract

Background: Standard therapy for metastatic non small cell lung cancer (NSCLC) includes palliative systemic chemotherapy and/or radiotherapy. Recent studies of patients with limited metastases treated with curative-intent stereotactic body radiation therapy (SBRT) have shown encouraging survival. We hypothesized that patients treated with SBRT for limited metastases have comparable outcomes with those treated with curative-intent radiation for Stage III NSCLC.

Methods: We retrospectively reviewed the records of NSCLC patients treated with curative-intent radiotherapy at the University of Rochester from 2000-2008. We identified 3 groups of patients with NSCLC: stage III, stage IV, and recurrent stage IV (initial stage I-II). All stage IV NSCLC patients treated with SBRT had ≤ 8 lesions.

Results: Of 146 patients, 88% had KPS $\geq 80\%$, 30% had $> 5\%$ weight loss, and 95% were smokers. The 5-year OS from date of NSCLC diagnosis for stage III, initial stage IV and recurrent stage IV was 7%, 14%, and 27% respectively. The 5-year OS from date of metastatic diagnosis was significantly ($p < 0.00001$) superior among those with limited metastases (≤ 8 lesions) versus stage III patients who developed extensive metastases not amenable to SBRT (14% vs. 0%).

Conclusion: Stage IV NSCLC is a heterogeneous patient population, with a selected cohort apparently faring better than Stage III patients. Though patients with limited metastases are favorably selected by virtue of more indolent disease and/or less bulky disease burden, perhaps staging these patients differently is appropriate for prognostic and treatment characterization. Aggressive local therapy may be indicated in these patients, though prospective clinical studies are needed.

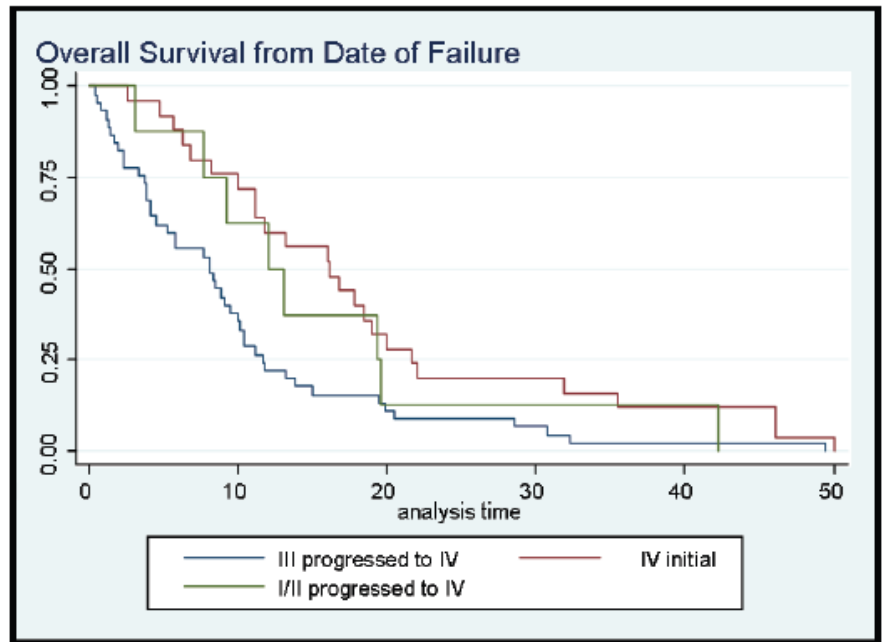
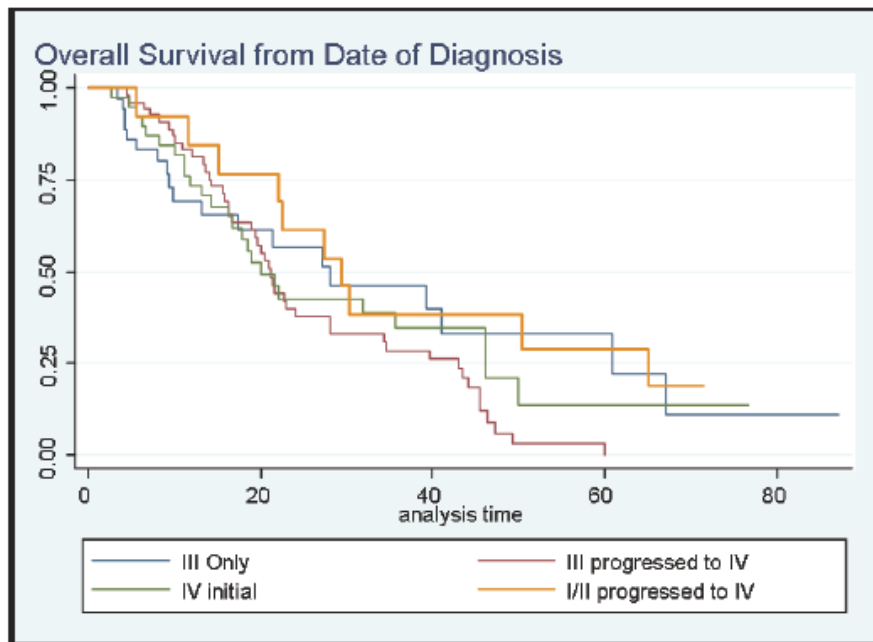
Keywords: Stereotactic Body Radiotherapy, Oligometastases, Non-Small Cell Lung Cancer

RESEARCH

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Comparison of outcomes in patients with stage III versus limited stage IV non-small cell lung cancer

Praveena Cheruvu¹, Su K Metcalfe¹, Justin Metcalfe¹, Yuhchayou Chen¹, Paul Okunieff² and Michael T Milano^{1*}



- **Oligometastatik evre IV hastalık prognozu evre III ve evre IV'e progrese hastalıktan daha iyi**



PROSPECTIVE STUDY OF EPIDERMAL GROWTH FACTOR RECEPTOR TYROSINE KINASE INHIBITORS CONCURRENT WITH INDIVIDUALIZED RADIOTHERAPY FOR PATIENTS WITH LOCALLY ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER

JING WANG, M.D., PH.D., TING-YI XIA, M.D., PH.D., YING-JIE WANG, M.D., HONG-QI LI, M.D.,
PING LI, M.D., JI-DONG WANG, M.D., DONG-SHU CHANG, M.D., LIY-YUAN LIU, M.D.,
YU-PENG DI, M.D., XUAN WANG, M.D., AND WEI-ZHANG WU, PH.D.

Table 1. Patient characteristics and previous treatment

| Variable | n | % |
|--------------------------|-------|----|
| Age (y) | | |
| Median | 56 | – |
| Range | 30–84 | – |
| Gender | | |
| Male | 11 | 42 |
| Female | 15 | 58 |
| Smoking | | |
| Yes | 7 | 27 |
| No | 19 | 73 |
| ECOG PS scores | | |
| 0 | 1 | 4 |
| 1 | 22 | 85 |
| 2 | 3 | 11 |
| AJCC stage | | |
| IIIA | 2 | 8 |
| IIIB | 3 | 11 |
| IV | 21 | 81 |
| Histology | | |
| Adenocarcinoma | 19 | 73 |
| Squamous cell cancer | 4 | 15 |
| Others | 3 | 12 |
| No. of metastatic organs | | |
| 0 | 9 | 35 |
| 1 | 11 | 42 |
| 2 | 2 | 8 |
| 3 | 4 | 15 |

| Variable | n | % |
|-------------------------------|----|----|
| Distant metastatic site | | |
| Lung | 10 | 48 |
| Pleural | 6 | 29 |
| Brain | 6 | 29 |
| Bone | 3 | 14 |
| Adrenal gland | 2 | 10 |
| Liver | 1 | 5 |
| Skin | 1 | 5 |
| Previous treatment | | |
| Untreated | 9 | 35 |
| Radiation alone | 3 | 12 |
| Chemotherapy alone | 9 | 35 |
| Combined modality | 5 | 18 |
| Previous chemotherapy regimen | | |
| 0 | 12 | 46 |
| 1 | 8 | 30 |
| 2 | 3 | 12 |
| ≥3 | 3 | 12 |
| No. of chemotherapy cycles | | |
| 0 | 12 | 46 |
| 1–4 | 7 | 27 |
| >4 | 7 | 27 |

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Table 2. Selective adverse events for EGFR-TKIs concurrent with individualized radiation in patients with Stage III/IV NSCLC

| Toxicities | Grade 1/2 | | Grade 3 | | Grade 4 | | Total | |
|-----------------------|-----------|----|----------|---|----------|---|----------|----|
| | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % |
| Acne-like rashes | 20 | 77 | 2 | 8 | 0 | – | 22 | 85 |
| Pruritus | 10 | 38 | 1 | 4 | 0 | – | 9 | 42 |
| Esophagitis | 6 | 23 | 1 | 4 | 0 | – | 7 | 27 |
| Dysphagia | 5 | 19 | 0 | – | 0 | – | 5 | 19 |
| Pneumonitis | 9 | 35 | 1 | 4 | 0 | – | 10 | 39 |
| Lung fibrosis | 3 | 12 | 0 | – | 0 | – | 3 | 12 |
| Diarrhea | 14 | 54 | 1 | 4 | 0 | – | 15 | 58 |
| Anorexia | 11 | 42 | 2 | 8 | 0 | – | 13 | 50 |
| Nausea | 14 | 54 | 0 | – | 0 | – | 14 | 54 |
| Vomiting | 7 | 27 | 0 | – | 0 | – | 7 | 27 |
| Fatigue | 17 | 65 | 1 | 4 | 0 | – | 18 | 69 |
| Neutropenia | 6 | 23 | 0 | – | 1 | 4 | 7 | 27 |
| Anemia | 8 | 31 | 2 | 8 | 0 | – | 10 | 38 |
| Thrombocytopenia | 1 | 4 | 1 | 4 | 2 | 8 | 4 | 15 |
| Elevated transaminase | 2 | 8 | 0 | – | 0 | – | 2 | 8 |

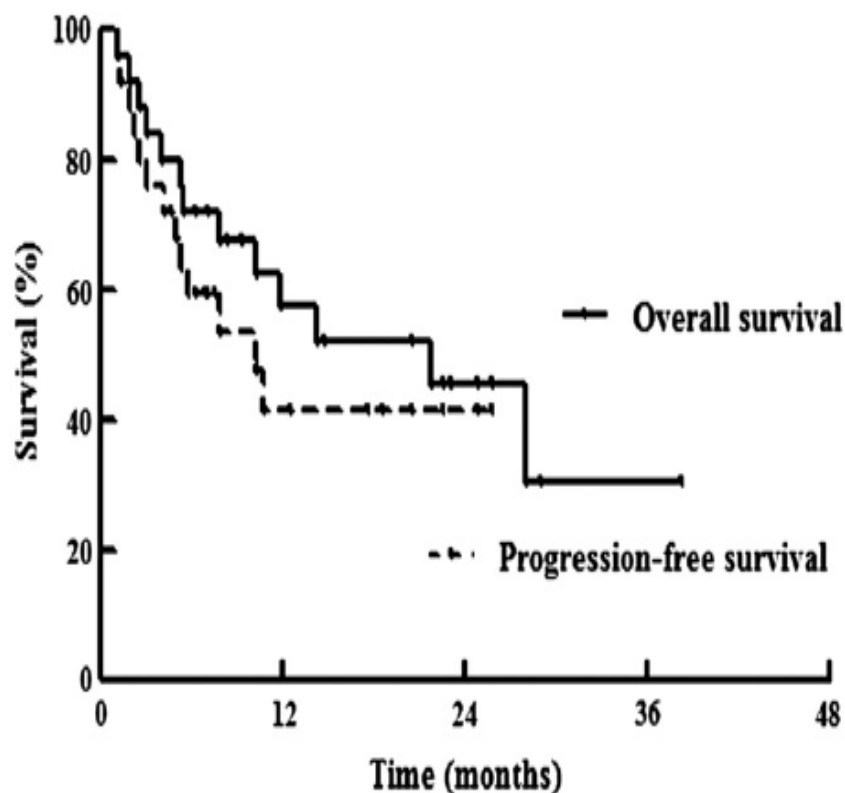
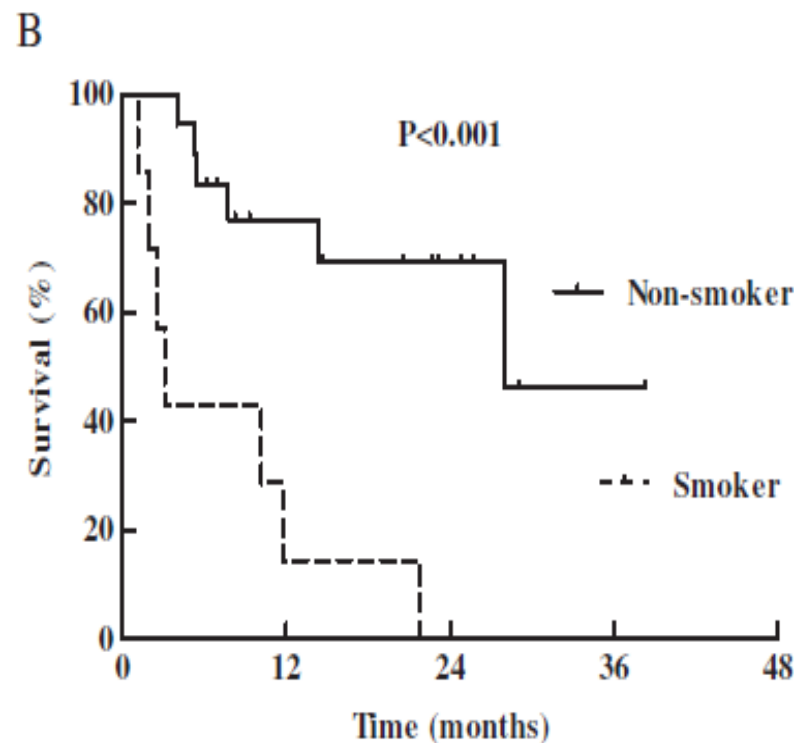
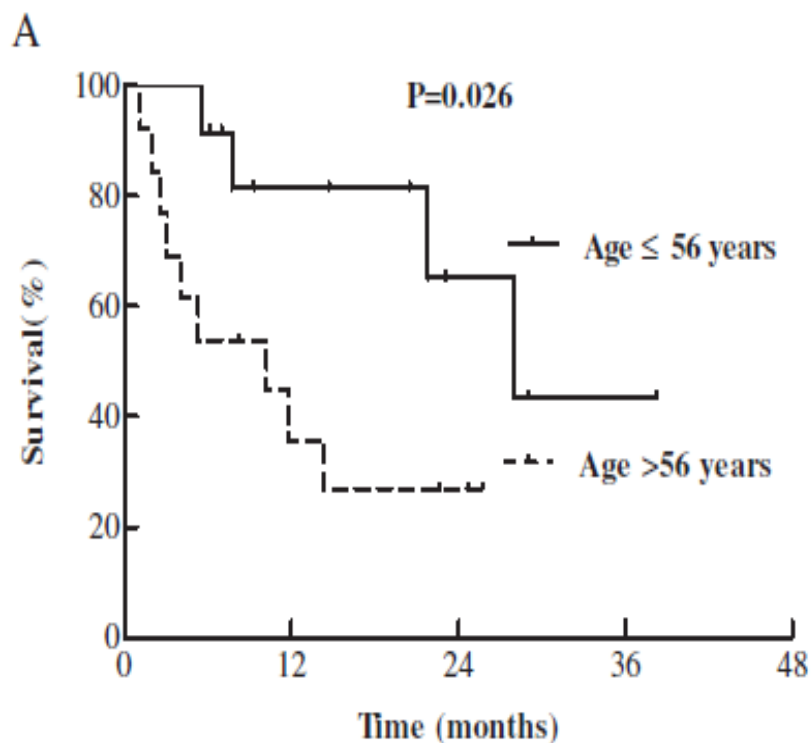


Fig. 1. Overall survival and progression-free survival for all patients.

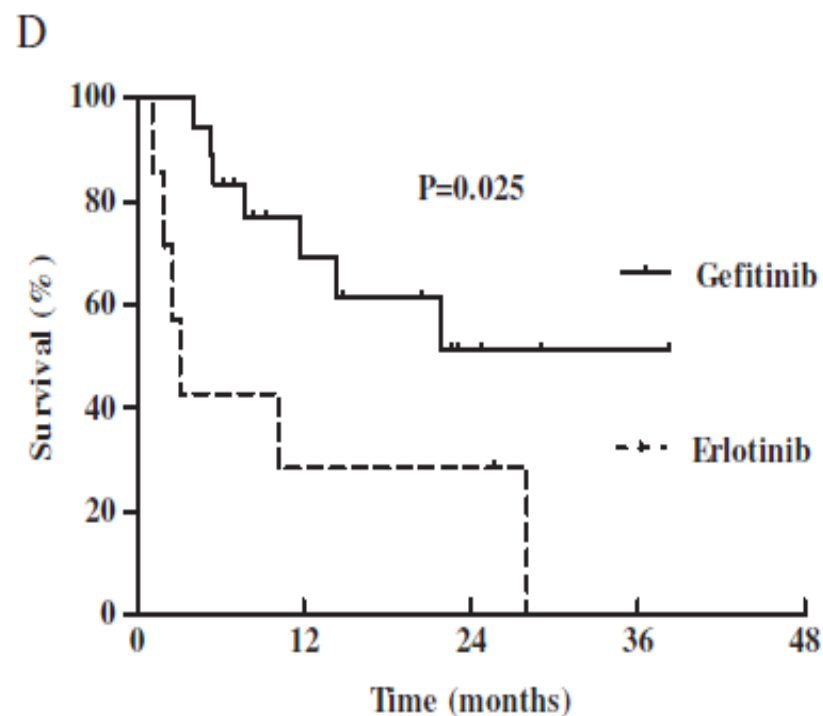
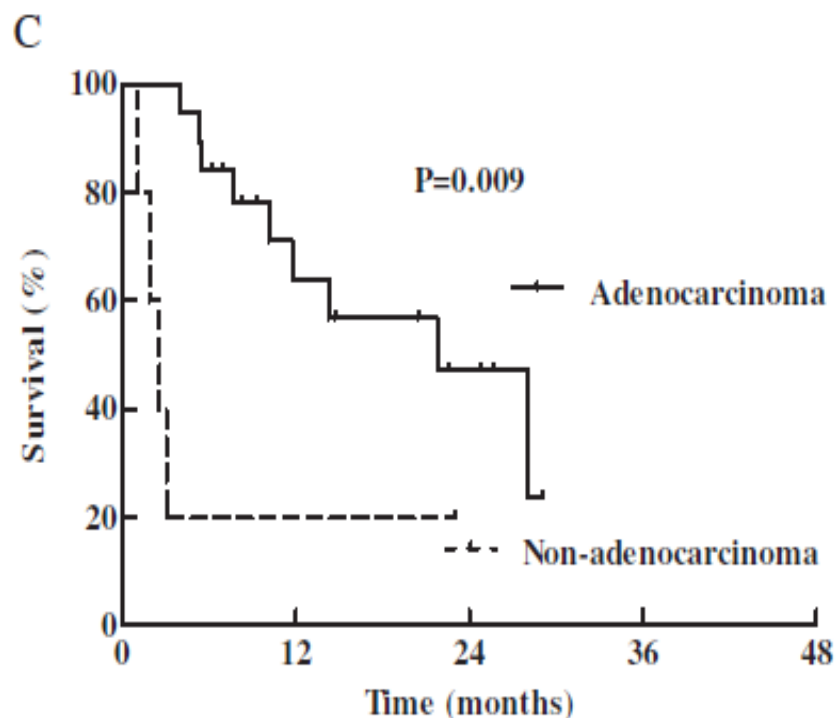
PROSPECTIVE STUDY OF EPIDERMAL GROWTH FACTOR RECEPTOR TYROSINE KINASE INHIBITORS CONCURRENT WITH INDIVIDUALIZED RADIOTHERAPY FOR PATIENTS WITH LOCALLY ADVANCED OR METASTATIC NON-SMALL-CELL LUNG CANCER

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73, 89–194, 2011

Upfront gefitinib/erlotinib treatment followed by concomitant radiotherapy for advanced lung cancer: A mono-institutional experience

Chih-Chia Chang^a, Kwan-Hwa Chi^{a,b,*}, Shang-Jyh Kao^c, Pei-Sung Hsu^c, Yuk-Wah Tsang^a, Heng-Jui Chang^a, Yu-Wung Yeh^c, Yei-San Hsieh^d, Jiunn-Song Jiang^c

| Characteristics | No. of patients (n=25) | % |
|-----------------------------|------------------------|------|
| Sex | | |
| Male | 8 | 32.0 |
| Female | 17 | 68.0 |
| Age (years) | | |
| Median | 66 | |
| Range | 37–84 | |
| Performance status | | |
| 1 | 25 | 100 |
| Histology | | |
| Adenocarcinoma | 21 | 84.0 |
| Non-squamous cell carcinoma | 4 | 16.0 |
| Metastatic sites | | |
| Lung to lung | 9 | 36.0 |
| Mediastinal LNs | 17 | 68.0 |
| Brain | 3 | 12.0 |
| Pleural cavity | 5 | 20.0 |
| Bone | 10 | 40.0 |
| Others | 8 | 32.0 |
| Stage | | |
| IIIb | 2 | 8.0 |
| IV | 23 | 92.0 |
| Initial TKI | | |
| E | 10 | 40.0 |
| G | 15 | 60.0 |

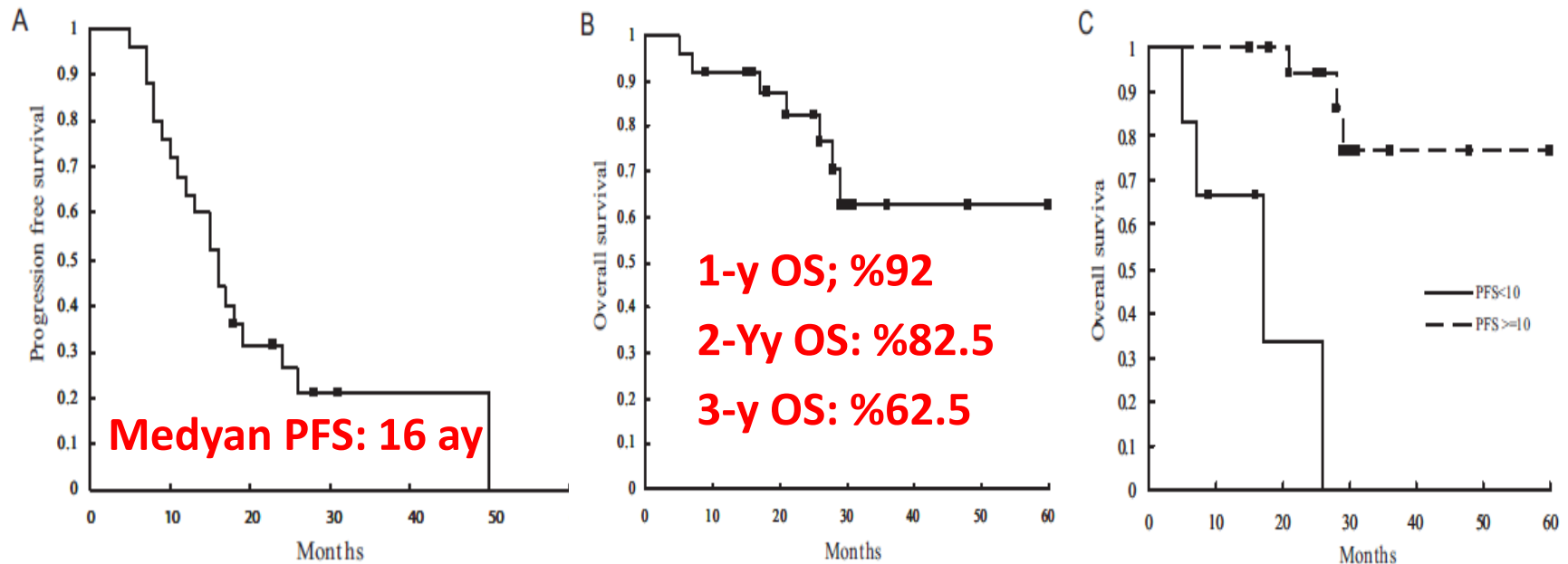
| Toxicity | No. of patients (n=25) | | | |
|--------------------------------------|------------------------|---------|---------|---------|
| | Grade 1–2 | Grade 3 | Grade 4 | Grade 5 |
| Dermatology (rash, acne, paronychia) | 14 | 1 | 0 | 0 |
| GI tract | | | | |
| Anorexia | 9 | 0 | 0 | 0 |
| Nausea/vomiting | 4 | 0 | 0 | 0 |
| Diarrhea | 9 | 1 | 0 | 0 |
| Mucositis | 4 | 0 | 0 | 0 |
| Esophagitis | 5 | 1 | 0 | 0 |
| Hematology | | | | |
| Anemia | 7 | 1 | 0 | 0 |
| Neutropenia | 2 | 2 | 0 | 0 |
| Thrombocytopenia | 10 | 2 | 0 | 0 |
| Constitutional symptoms | | | | |
| Myalgia (arthralgia) | 3 | 0 | 0 | 0 |
| Fatigue | 23 | 0 | 0 | 0 |
| Pulmonary | | | | |
| Pneumonitis | 18 | 1 | 0 | 2 |

TKI, tyrosine kinase inhibitor; E, erlotinib; G, gefitinib; SCF, supraclavicular; LN, lymph node.

73, 89–194, 2011

Upfront gefitinib/erlotinib treatment followed by concomitant radiotherapy for advanced lung cancer: A mono-institutional experience

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- A) Progression-free survival for all patients. The median PFS was 16 months.
- B) Overall survival for all patients. The 1-year, 2-year, and 3-year survival rates were 92.0%, 82.5%, and 62.5%, respectively.
- C) Overall survival for patients with PFS more than and less than 10 months.

73, 89–194, 2011

Upfront gefitinib/erlotinib treatment followed by concomitant radiotherapy for advanced lung cancer: A mono-institutional experience

Chih-Chia Chang^a, Kwan-Hwa Chi^{a,b,*}, Shang-Jyh Kao^c, Pei-Sung Hsu^c, Yuk-Wah Tsang^a, Heng-Jui Chang^a, Yu-Wung Yeh^c, Yei-San Hsieh^d, Jiunn-Song Jiang^c

Univariate analysis for overall survival.

| | HR | 95% CI | P |
|--------------------------------------------------------|-------|--------------|-------|
| RT response to primary GTV (\geq PR vs. <PR) | 0.238 | 0.042–1.342 | 0.104 |
| Stage (IIIb vs. IV) | 2.170 | 0.258–18.258 | 0.476 |
| TKI (E vs. G) | 3.791 | 0.734–19.587 | 0.112 |
| Time interval from TKI to RT (<3 months vs. >3 months) | 0.135 | 0.016–1.126 | 0.064 |
| Sex (female vs. male) | 0.549 | 0.122–2.464 | 0.434 |
| Bone (yes vs. no) | 0.158 | 0.019–1.320 | 0.088 |
| Pleural (yes vs. no) | 2.281 | 0.507–10.272 | 0.283 |
| Lung (yes vs. no) | 1.638 | 0.359–7.466 | 0.524 |

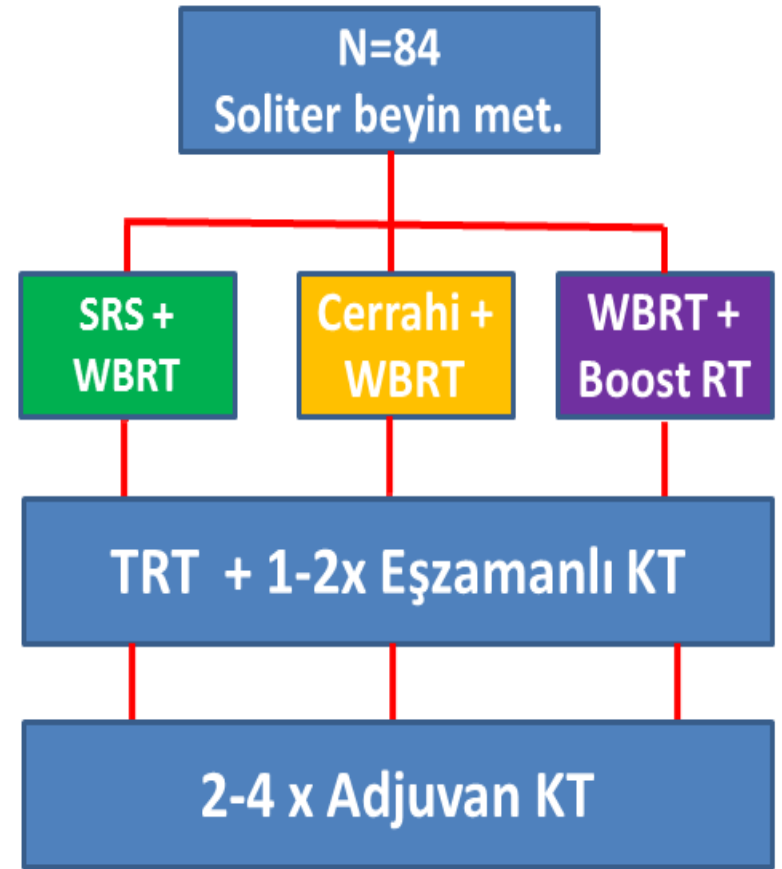
PR, partial response; TKI, tyrosine kinase inhibitor; E, erlotinib; G, gefitinib; RT, radiotherapy.



Başkent Ün. Rad Onkol A.D. Deneyimi

BAŞKENT ÜNİVERSİTESİ

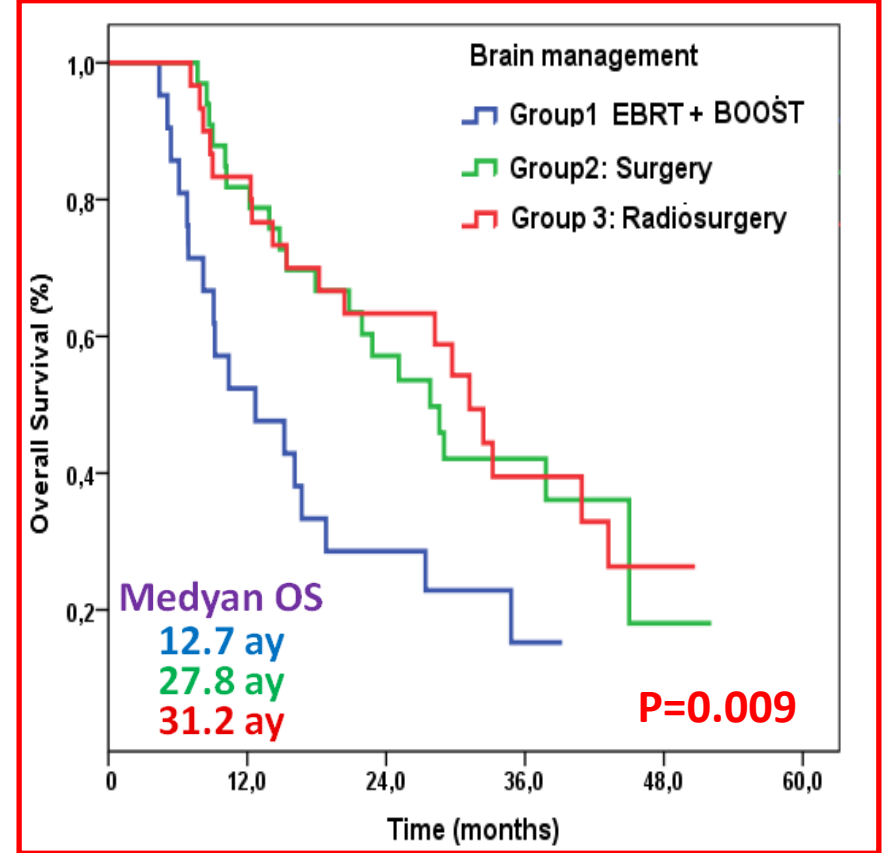
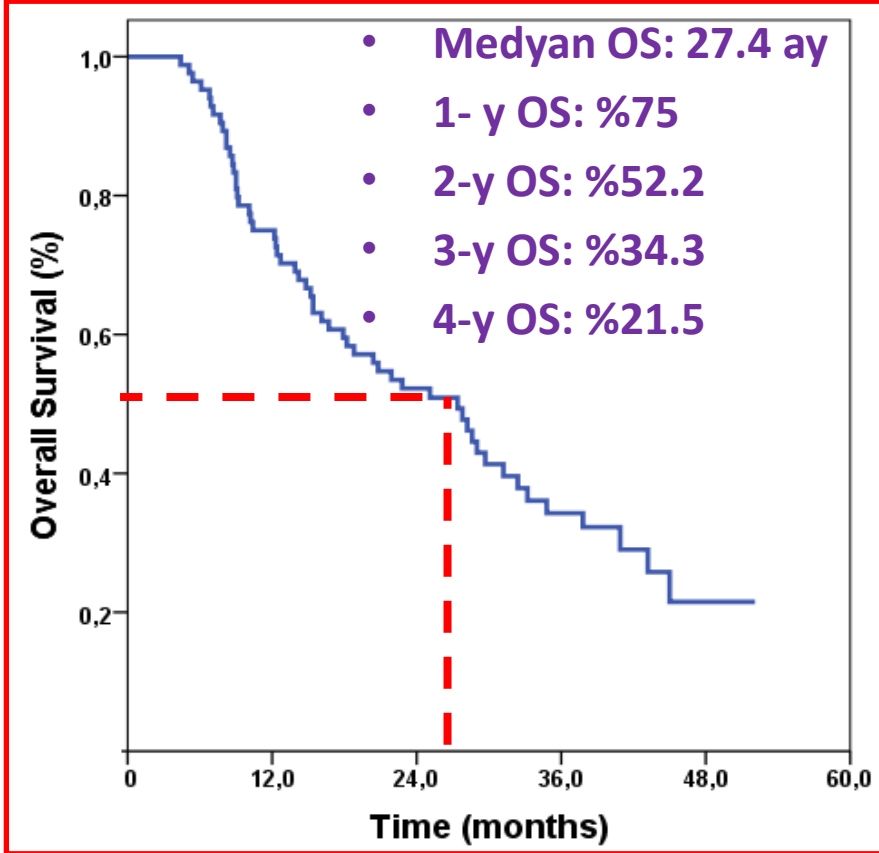
- Ocak 2007- Aralık 2011 (retrospektif analiz)
- 1197 potansiyel kür olabilir KHDAK
- 103 beyin soliter oligomet olgu (18-70 yaş)
- Toraks CT, Beyin MRG, PET/CT +
- 84 potansiyel küratif TRT (60-66 Gy/ 2Gy fr) + Eşzamanlı KT
- Beyin RT
- Primer sonlanım: OS
- Sekonder sonlanım: Prognostik faktörler





Başkent Ün. Rad Onkol A.D. Deneyimi

BAŞKENT ÜNİVERSİTESİ



Ablatif tedaviler WBRT+ EBRT boost tedaviden anlamlı üstün



BAŞKENT ÜNİVERSİTESİ

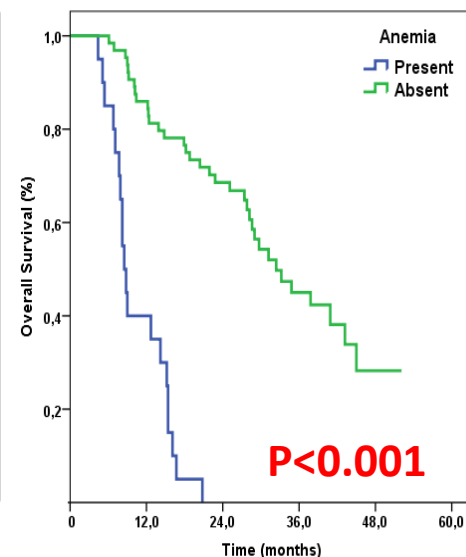
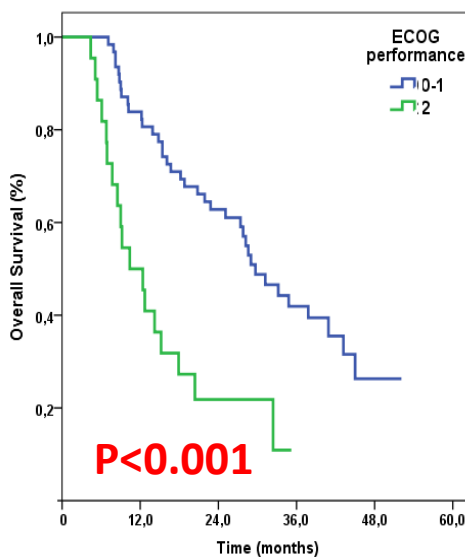
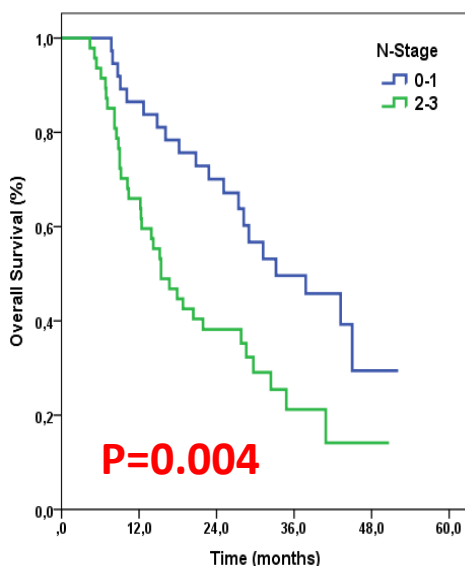
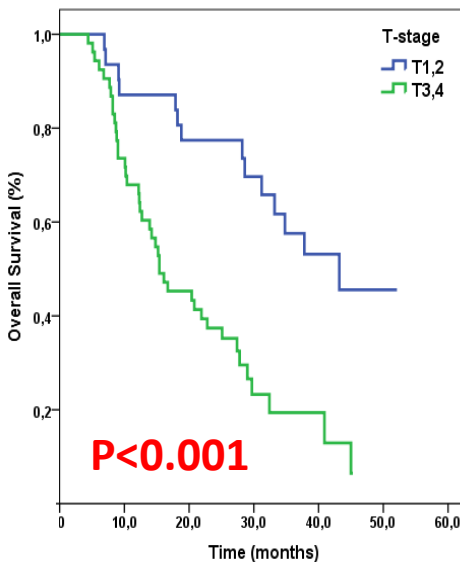
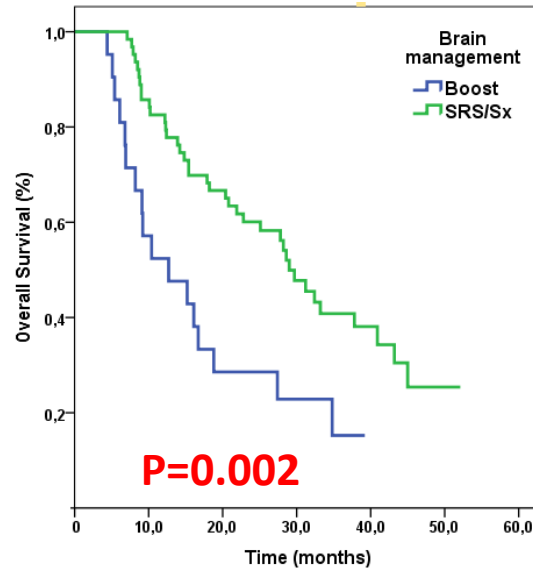
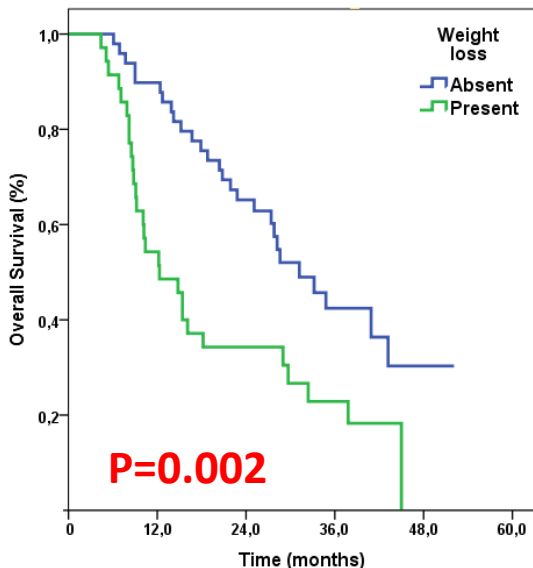
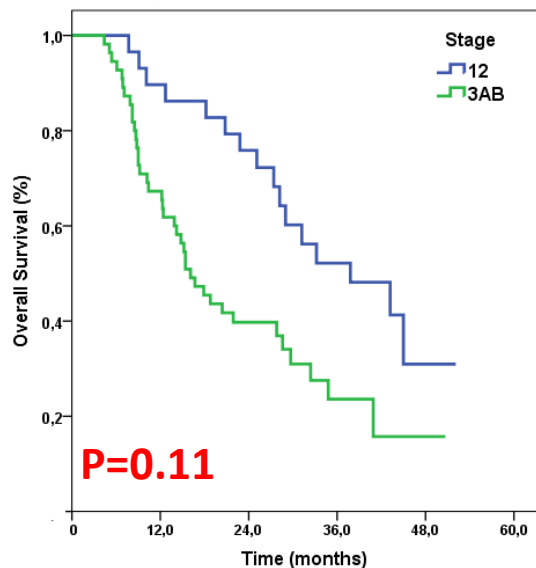
Başkent Ün. Rad Onkol A.D. Deneyimi

| Variables | B | SE | Wald | df | Exp(B) | Sig (p) |
|-----------------------------|--------|------|--------|----|--------|---------|
| Stage (12vs. 3A/B) | -,568 | ,599 | ,899 | 1 | ,566 | ,110 |
| Weight loss (- vs. +) | ,814 | ,292 | 7,757 | 1 | 2,257 | ,005 |
| Brain tx (SRS/Sx vs. Boost) | -1,191 | ,326 | 13,331 | 1 | ,304 | < ,001 |
| T-stage (1,2 vs. 3,4) | 1,126 | ,353 | 10,173 | 1 | 3,083 | ,001 |
| N-stage (0,1 vs. 2,3) | 1,175 | ,544 | 4,672 | 1 | 2,181 | ,012 |
| ECOG (0,1 vs. 2) | ,780 | ,310 | 6,334 | 1 | 1,580 | ,034 |
| Anemia(- vs. +) | -1,628 | ,400 | 16,520 | 1 | ,196 | < ,001 |



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RESEARCH

Open Access

Long-term survival in patients with non-small cell lung cancer and synchronous brain metastasis treated with whole-brain radiotherapy and thoracic chemoradiation

Oscar Arrieta^{1,2,3*}, Cynthia Villarreal-Garza², Jesús Zamora^{1,4}, Mónica Blake-Cerda⁴, María D de la Mata^{1,4}, Diego G Zavala², Saé Muñoz-Hernández² and Jaime de la Garza¹

Abstract

Background: Brain metastases occur in 30-50% of Non-small cell lung cancer (NSCLC) patients and confer a worse prognosis and quality of life. These patients are usually treated with Whole-brain radiotherapy (WBRT) followed by systemic therapy. Few studies have evaluated the role of chemoradiotherapy to the primary tumor after WBRT as definitive treatment in the management of these patients.

Methods: We reviewed the outcome of 30 patients with primary NSCLC and brain metastasis at diagnosis without evidence of other metastatic sites. Patients were treated with WBRT and after induction chemotherapy with paclitaxel and cisplatin for two cycles. In the absence of progression, concurrent chemoradiotherapy for the primary tumor with weekly paclitaxel and carboplatin was indicated, with a total effective dose of 60 Gy. If disease progression was ruled out, four chemotherapy cycles followed.

Results: Median Progression-free survival (PFS) and Overall survival (OS) were 8.43 ± 1.5 and 31.8 ± 15.8 months, respectively. PFS was 39.5% at 1 year and 24.7% at 2 years. The 1- and 2-year OS rates were 71.1 and 60.2%, respectively. Three-year OS was significantly superior for patients with N0-N1 stage disease vs. N2-N3 (60 vs. 24%, respectively; Response rate [RR], 0.03; $p=0.038$).

Conclusions: Patients with NSCLC and brain metastasis might benefit from treatment with WBRT and concurrent thoracic chemoradiotherapy. The subgroup of N0-N1 patients appears to achieve the greatest benefit. The result of this study warrants a prospective trial to confirm the benefit of this treatment.

Keywords: NSCLC, brain metastases, chemoradiotherapy, survival

Table 1 Baseline characteristics of patients and disease

| | |
|---------------------------------|------------|
| Median age (years) | 57 ± 11.1 |
| Gender (Female) | 17 (56.7%) |
| ECOG | |
| 0 | 8 (26.7%) |
| 1 | 19 (63.3%) |
| 2 | 3 (10%) |
| Comorbidities | |
| EPOC | 4 (13.3%) |
| Diabetes | 3 (10%) |
| Hypertension | 3 (10%) |
| Histology | |
| Adenocarcinoma | 24 (80%) |
| Squamous | 4 (13.3%) |
| Other | 2 (6.7%) |
| Smoking history | |
| Yes | 23 (76.7%) |
| No | 7 (23.3%) |
| Nodal status | |
| N 0-1 (n) | 16 (53.3%) |
| N 2-3 (n) | 14 (46.7%) |
| RPA class 2 | 30 (100%) |
| Median brain metastatic lesions | 3 ± 2 |

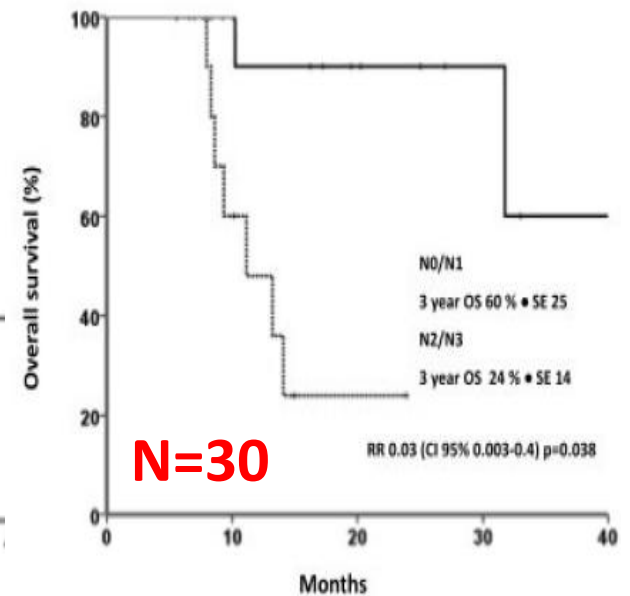
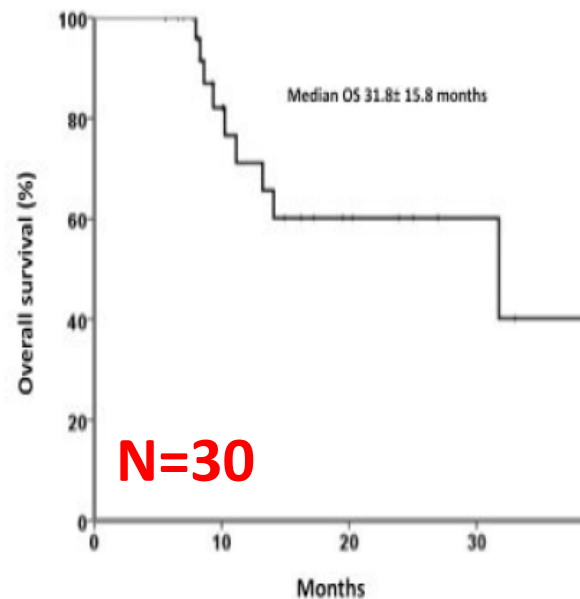
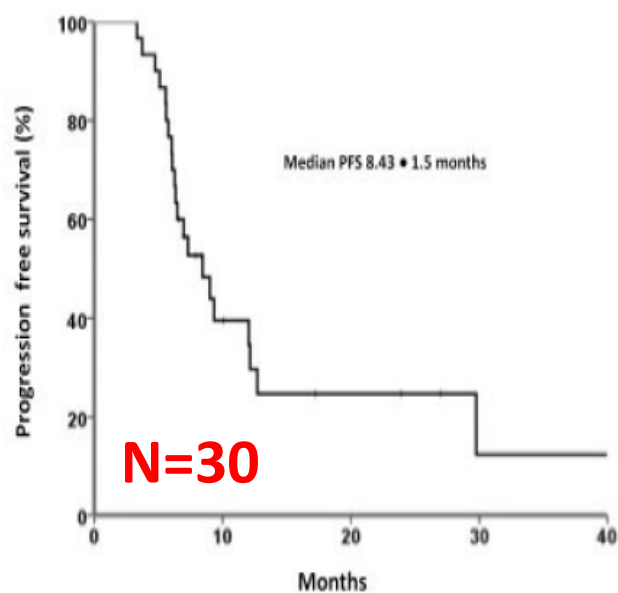
ECOG: Eastern Cooperative of Gynecologists; RPA: Radiation Therapy Oncology Group Recursive partitioning analysis (RPA).

RESEARCH

Open Access

Long-term survival in patients with non-small cell lung cancer and synchronous brain metastasis treated with whole-brain radiotherapy and thoracic chemoradiation

Oscar Arrieta^{1,2,3*}, Cynthia Villarreal-Garza², Jesús Zamora^{1,4}, Mónica Blake-Cerda⁴, María D de la Mata^{1,4}, Diego G Zavala², Saé Muñoz-Hernández² and Jaime de la Garza¹





Bünyamin Hocamızın
muhtemel söylemleri
neler olacak?

Bu hastalar seçilmiş hastalar mı?

Bünyamin Hocamız der ki?

- Hastalar çok iyi seçilmiş
- Prognozu standart tedaviyle de iyi olurdu



Guideline önerisi yok?

Bünyamin Hocamız der ki?

- Guideline önerisi yok, bu tür yaklaşımlar deneysel olmaktan öteye geçemez



Guideline önerisi yok

Martin John Rees, Baron Rees of Ludlow



“ Absence of evidence is not evidence of absence”

The difference between evidence that something is absent (e.g. an observation that suggests there were no dragons here today) and a simple absence of evidence (e.g. no careful research has been done) can be nuanced. Indeed, scientists will often debate whether an experiment's result should be considered evidence of absence, or if it remains absence of evidence. The debate is whether the experiment would have detected the phenomenon of interest if it was there.

Kanıt yokluğu yokluğun kanıtı olamaz

Kanıtları kim bulacak?

- Metastaz sayısı, ortaya çıkış zamanı ile tutulu organ(lar)ın önemi ve tedavi edilebilirliği göz önüne alınmadan bütün metastatik AC ca tanılı hastaların aynı şekilde palyatif tedavilerle idame edilmeleri akıl dışıdır

- Genel durumu iyi, görece sınırlı sayıda metastazı olan hastaların bilimin ve teknolojinin getirdiği yeniliklerden yararlanma şansı tanınmalı ve metastazları ablate edilmiş bir grup hastanın erken evre hastalara benzer sağkalım gösterebileceği unutulmamalıdır
- En yüksek faydayı görece hastaları ile en iyi “hasta ve hastalığa” özgü tedaviler için gerekli kanıtları bulacak olan bizleriz

Kanıtları kim bulacak?

- Kanıt yok diyerek vazgeçmek de akıl dışıdır





**Multidisipliner ve önyargısız yaklaşımlarla
başarısız olma şansımız yok!**



...hürriyetin de,
eşitliğin de,
adaletin de
dayanak noktası,
**ULUSAL
EGEMENLİKTİR.**

K. Atatürk

23



Ulusal Egemenlik ve
Çocuk Bayramı

KUTLU OLSUN

TEŞEKKÜRLER