

Rutin Pratiđi Deđiřtirecek Literatür Güncellemesi : Radyoterapi

Dr. Gökhan Özyiđit

Hacettepe Üniversitesi, Tıp Fakültesi

Radyasyon Onkolojisi Anabilim Dalı

MA-20 Çalışması

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 23, 2015

VOL. 373 NO. 4

Regional Nodal Irradiation in Early-Stage Breast Cancer

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ABSTRACT

BACKGROUND

Most women with breast cancer who undergo breast-conserving surgery receive whole-breast irradiation. We examined whether the addition of regional nodal irradiation to whole-breast irradiation improved outcomes.

METHODS

We randomly assigned women with node-positive or high-risk node-negative breast cancer who were treated with breast-conserving surgery and adjuvant systemic therapy to undergo either whole-breast irradiation plus regional nodal irradiation (including internal mammary, supraclavicular, and axillary lymph nodes) (nodal-irradiation group) or whole-breast irradiation alone (control group). The primary outcome was overall survival. Secondary outcomes were disease-free survival, isolated locoregional disease-free survival, and distant disease-free survival.

RESULTS

Between March 2000 and February 2007, a total of 1832 women were assigned to the nodal-irradiation group or the control group (916 women in each group). The median follow-up was 9.5 years. At the 10-year follow-up, there was no significant between-group difference in survival, with a rate of 82.8% in the nodal-irradiation group and 81.8% in the control group (hazard ratio, 0.91; 95% confidence interval [CI], 0.72 to 1.13; $P=0.38$). The rates of disease-free survival were 82.0% in the nodal-irradiation group and 77.0% in the control group (hazard ratio, 0.76; 95% CI, 0.61 to 0.94; $P=0.01$). Patients in the nodal-irradiation group had higher rates of grade 2 or greater acute pneumonitis (1.2% vs. 0.2%, $P=0.01$) and lymphedema

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Whelan at the Juravinski Cancer Centre at Hamilton Health Sciences, 699 Concession St., Rm. 4-204, Hamilton, ON L8V 5C2, Canada, or at twhelan@hhsc.ca.

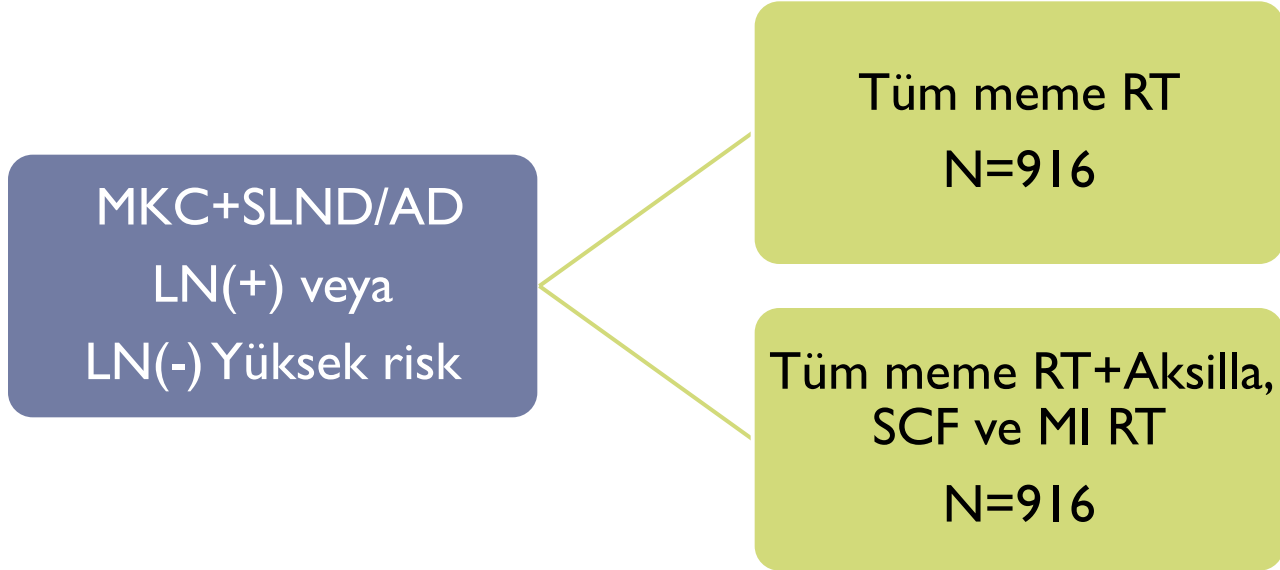
*A list of the MA.20 study investigators is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2015;373:307-16.

DOI: 10.1056/NEJMoa1415340

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MA 20 Çalışması



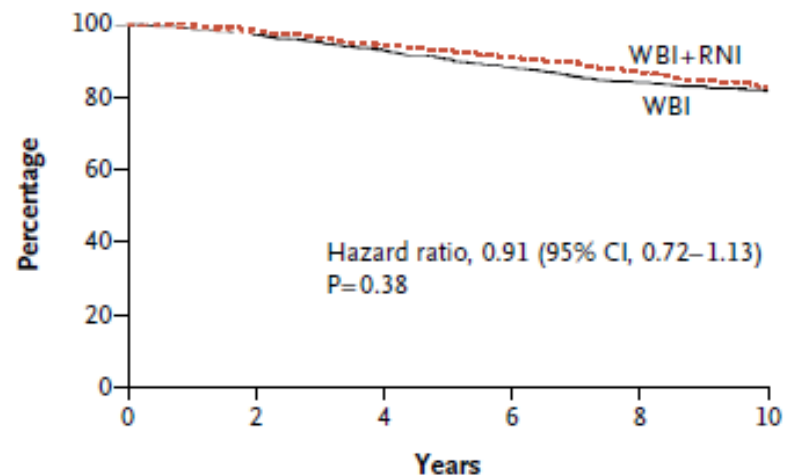
Hasta Özellikleri

► Kriterler;

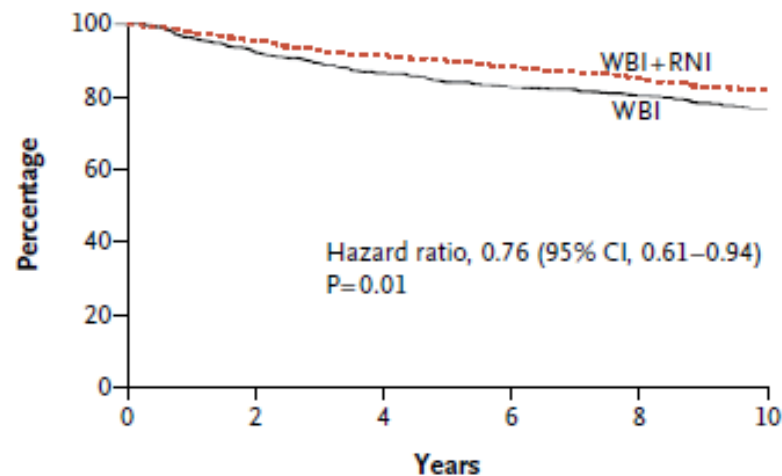
- MKC+SLND/AD
- $T \geq 5$ cm
- ≥ 2 cm ve
 - <10 LN diseksiyonda ve
 - Aşağıdakilerden en az 1 (+)
 - Grad III
 - ER(-)
 - LVI(+)
- T4, cN2-3 (fikse LN veya MI(+)) (Çalışma dışı)

Table 1. Characteristics of the Patients at Baseline.*

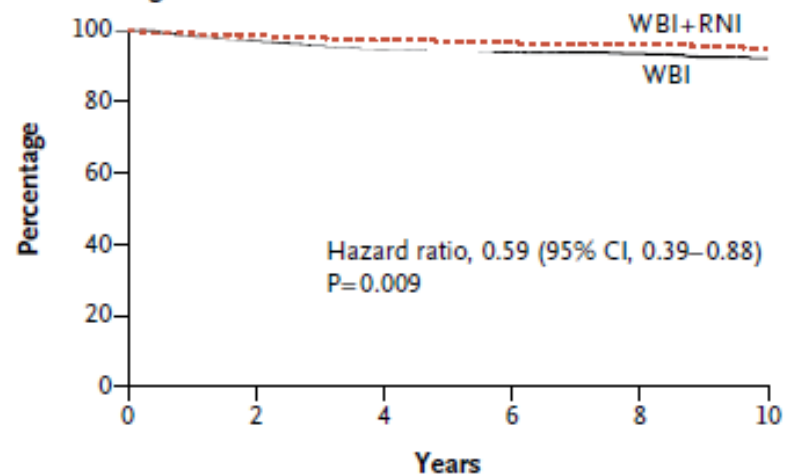
Characteristic	WBI (N=916)	WBI+RNI (N=916)
Median age (range) — yr	53 (26–84)	54 (29–84)
Patients who underwent initial sentinel-lymph-node biopsy — no. (%)†	357 (39.0)	360 (39.3)
No. of axillary nodes removed		
Median (interquartile range)	12 (8–16)	12 (9–16)
1–9 — no. (%)	303 (33.1)	294 (32.1)
≥10 — no. (%)	612 (66.8)	622 (67.9)
No. of positive axillary nodes — no. (%)		
0	89 (9.7)	88 (9.6)
1	447 (48.8)	460 (50.2)
2	233 (25.4)	209 (22.8)
3	100 (10.9)	109 (11.9)
>3	47 (5.1)	50 (5.5)
Tumor size — no. (%)		
≤2 cm	501 (54.7)	459 (50.1)
2.1–5 cm	409 (44.7)	443 (48.4)
>5 cm	6 (0.7)	13 (1.4)
Estrogen-receptor status — no. (%)		
Positive	682 (74.5)	685 (74.8)
Negative	234 (25.5)	231 (25.2)
Progesterone-receptor status — no. (%)		
Positive	549 (59.9)	553 (60.4)
Negative	365 (39.8)	360 (39.3)
Adjuvant chemotherapy — no. (%)		
Anthracycline without taxane	540 (59.0)	554 (60.5)
Anthracycline with taxane	244 (26.6)	230 (25.1)
Other‡	45 (4.9)	47 (5.1)
No chemotherapy	87 (9.5)	85 (9.3)
Adjuvant endocrine therapy — no. (%)§		
Aromatase inhibitor¶	529 (57.8)	521 (56.9)
Tamoxifen	167 (18.2)	172 (18.8)
No endocrine therapy	220 (24.0)	223 (24.3)
Boost irradiation — no. (%)	317 (34.6)	294 (32.1)

A Overall Survival**No. at Risk**

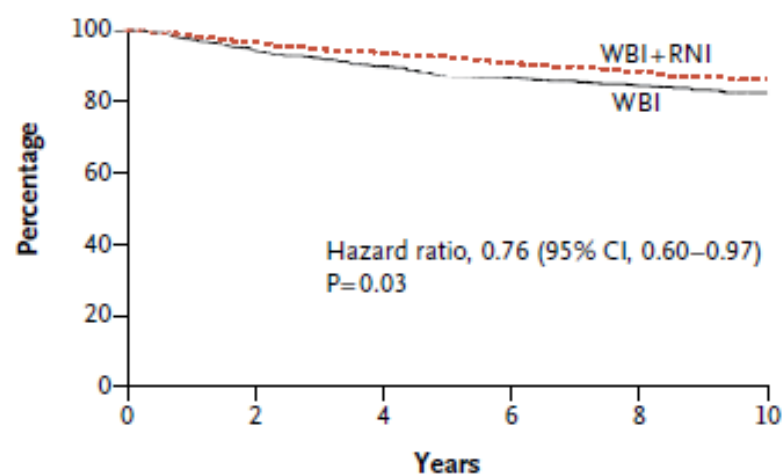
WBI	916	879	828	773	602	317
WBI+RNI	916	890	841	806	635	331

B Disease-free Survival**No. at Risk**

WBI	916	833	764	710	553	279
WBI+RNI	915	861	800	758	592	297

C Isolated Locoregional Disease-free Survival**No. at Risk**

WBI	916	836	769	720	563	288
WBI+RNI	915	863	806	764	602	307

D Distant Disease-free Survival**No. at Risk**

WBI	916	851	793	743	579	304
WBI+RNI	916	871	823	781	617	318

SONUÇLAR

Ortanca İzlem: 9.5 YIL

▶ Tüm meme RT

▶ 10-y GS

▶ ER(-) %73.9

▶ DFS

▶ ER (-) %61.6

▶ Tüm meme+Lenfatik RT

▶ %81.3 (p=0.05)

▶ %76.2 (p=0.03)



Toksisite

▶ Akut (<3 ay);

- ▶ Radyasyon dermatit ve pnömoni (Nodal RT grubunda daha fazla)

▶ RT Pnömoni

- ▶ 2 (%0.2) vs. 11 (%1.2)

▶ Geç:

- ▶ Lenfödem, telanjiektazi, subkutan fibrozis (Nodal RT grubunda daha fazla)

▶ Lenfödem:

- ▶ %4.5 vs. %8.4

- ▶ Kardiyak hastalık, brakial pleksopati, veya 2. kanser (benzer)
-



Tartışma

- ▶ 4 ve üzeri LN hasta çok az (GS farkı açısından önemli)
- ▶ Modern KT rejimleri bu etkiyi daha da gölgelemiş olabilir.
- ▶ LNI: Gerek lokal bölgesel kontrol gerekse uzak metastaz anlamlı şekilde azaldı.
- ▶ Sonuçlar nod (-)lere uygulanabilir mi? Hasta sayısı çok az.
- ▶ Mikrometastatik hastalara uygulanabilir mi?
- ▶ AD %96; SLN durum?



EORTC Çalışması (Medial SCF ve MI RT)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, S. Collette, C. Kirkove, E. Van Limbergen, V. Budach, H. Struikmans, L. Collette, A. Fourquet, P. Maingon, M. Valli, K. De Winter, S. Marnitz, I. Barillot, L. Scandolaro, E. Vonk, C. Rodenhuis, H. Marsiglia, N. Weidner, G. van Tienhoven, C. Glanzmann, A. Kuten, R. Arriagada, H. Bartelink, and W. Van den Bogaert, for the EORTC Radiation Oncology and Breast Cancer Groups*

ABSTRACT

BACKGROUND

The effect of internal mammary and medial supraclavicular lymph-node irradiation (regional nodal irradiation) added to whole-breast or thoracic-wall irradiation after surgery on survival among women with early-stage breast cancer is unknown.

METHODS

We randomly assigned women who had a centrally or medially located primary tumor, irrespective of axillary involvement, or an externally located tumor with axillary involvement to undergo either whole-breast or thoracic-wall irradiation in addition to regional nodal irradiation (nodal-irradiation group) or whole-breast or thoracic-wall irradiation alone (control group). The primary end point was overall survival. Secondary end points were the rates of disease-free survival, survival free from distant disease, and death from breast cancer.

RESULTS

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Poortmans at the Department of Radiation Oncology, Radboud University Medical Center, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands, or at philip.poortmans@radboudumc.nl.

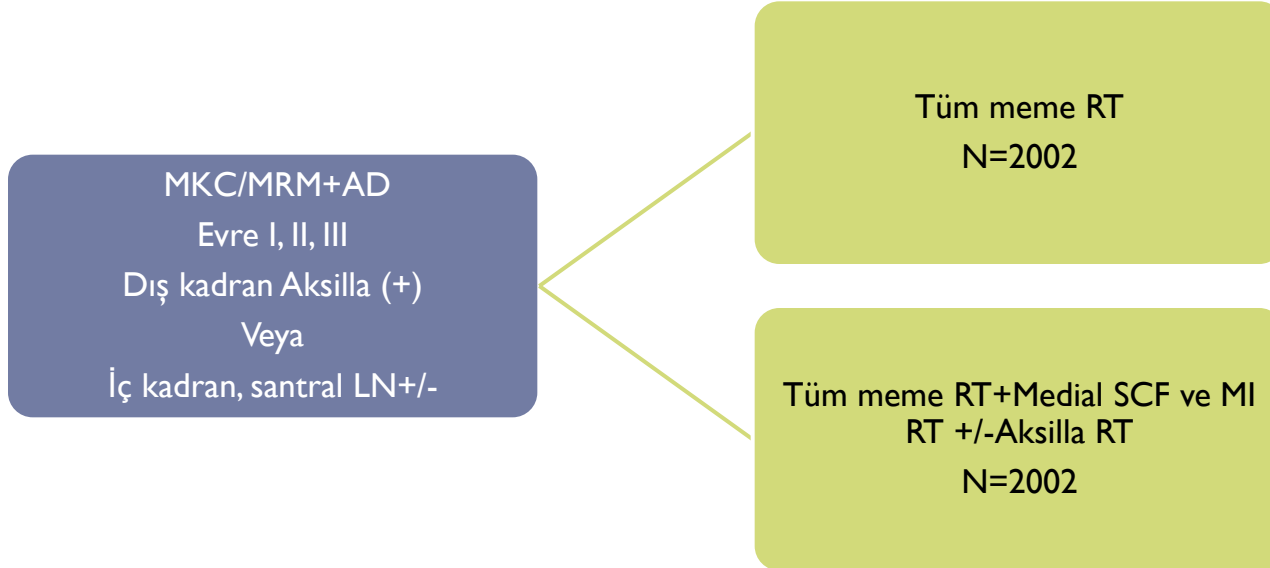
*A complete list of investigators in the European Organization for Research and Treatment of Cancer (EORTC) Radiation Oncology and Breast Cancer Groups is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2015;373:317-27.

DOI: 10.1056/NEJMoa1415369

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EORTC Çalışması



Hasta Özellikleri

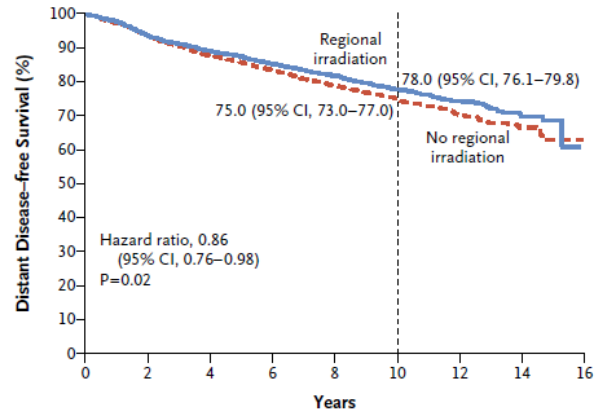
Table 1. Baseline Characteristics of the Patients, According to Study Group.*

Characteristic	Control Group (N=2002)	Nodal-Irradiation Group (N=2002)	Total (N=4004)
Age — yr			
Median	54.0	54.0	54.0
Range	22.0–75.0	19.0–75.0	19.0–75.0
Type of surgery — no. (%)			
Mastectomy	479 (23.9)	476 (23.8)	955 (23.9)
Breast-conserving surgery	1523 (76.1)	1526 (76.2)	3049 (76.1)
Pathological tumor stage — no. (%)			
pT1: ≤2 cm	1203 (60.1)	1205 (60.2)	2408 (60.1)
pT2: 2–5 cm	714 (35.7)	716 (35.8)	1430 (35.7)
pT3: >5 cm	71 (3.5)	70 (3.5)	141 (3.5)
Pathological nodal stage — no. (%)			
pN0: no axillary lymph nodes involved	890 (44.5)	888 (44.4)	1778 (44.4)
pN1a: 1–3 axillary lymph nodes involved	866 (43.3)	859 (42.9)	1725 (43.1)
pN2a: 4–9 axillary lymph nodes involved	201 (10.0)	195 (9.7)	396 (9.9)
pN3a: >9 axillary lymph nodes involved	44 (2.2)	59 (2.9)	103 (2.6)
Adjuvant treatment — no. (%)			
None	301 (15.0)	324 (16.2)	625 (15.6)
Chemotherapy	500 (25.0)	494 (24.7)	994 (24.8)
Hormonal therapy	599 (29.9)	586 (29.3)	1185 (29.6)
Both chemotherapy and hormonal therapy	602 (30.1)	598 (29.9)	1200 (30.0)

* The control group received whole-breast or thoracic-wall irradiation alone, as compared with the nodal-irradiation group, which received whole-breast or thoracic-wall irradiation in addition to regional nodal irradiation. There were no significant differences between the groups.

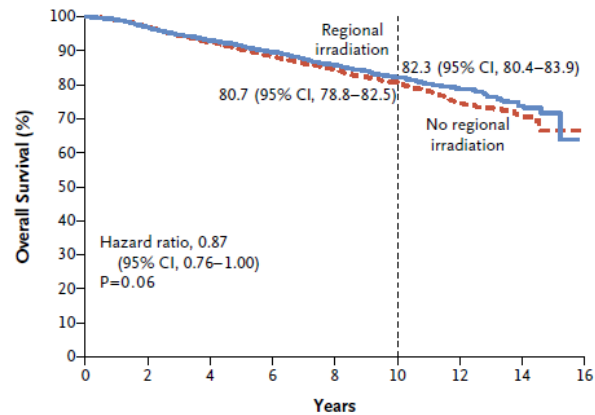
Sonuçlar

A



No. at Risk										No. of Events
No regional irradiation	2002	1862	1728	1606	1382	890	403	113		523
Regional irradiation	2002	1866	1764	1650	1464	939	437	117		462

B



No. at Risk										No. of Events
No regional irradiation	2002	1926	1819	1698	1475	969	434	119		429
Regional irradiation	2002	1931	1839	1732	1532	988	466	124		382

Toksisite

- ▶ 10-y toksisite (RNI vs Kontrol)
 - ▶ Pulmoner Fibroz:
 - ▶ %4.4 vs. %1.7 ($p < 0.001$)
 - ▶ Kardiyak Fibroz:
 - ▶ %1.2 vs. %0.6 ($p = 0.06$)
 - ▶ Kardiyak Hastalık:
 - ▶ %6.5 vs. %5.6 ($p = 0.25$)
 - ▶ İkinci Kanser
 - ▶ 191 olgu vs. 222 olgu



Tartışma

- ▶ Medial ve Santral yerleşimli tümörlerde Aksilla (-) olsa bile RNI katkısı var.
- ▶ Lenfödem sıklığı az. Çünkü Aksilla RT: Kontrol %7.4 vs. RNI %8.3
- ▶ Mevcut veriler dışı kadran, LN(-) olgulara uygulanamaz



MA-20 ve EORTC Ortak Yorum

- ▶ **Genel sağkalım farkı yok.**
 - ▶ EORTC çalışmasında trend mevcut, MA-20 ER(-) fark var.
 - ▶ Daha uzun dönem izlemde fark olması için potansiyel var.
 - ▶ **EORTC;**
 - ▶ DFS, DMFS ve Meme ca. mortalitesi
 - ▶ **MA-20;**
 - ▶ DFS, UM azalması ve lokal-bölgesel nüks azalması
 - ▶ DFS=meme ca mortalitesi azalma
 - ▶ =Yaşam kalitesi
 - ▶ =Daha az sistemik tedavi ihtiyacı
 - ▶ =Maliyet azalması
-



MA-20 ve EORTC Ortak Yorum

▶ Toksikite:

- ▶ Her ikisinde de oransal olarak çok az.
- ▶ EORTC: Sadece pulmoner fibrozisde artış anlamlı (%4.4).
- ▶ Kardiyak hastalık benzer.

▶ NSABP-B28;

- ▶ +Paklitaksel ilavesi ile
- ▶ %4 DFS artışı (5-yıl)
- ▶ Genel sağkalımda 5 yılda fark yok.
- ▶ Grad III düzeyinde;
 - ▶ Nörosensory toksisite: %15
 - ▶ Nöromotor toksisite: %7
 - ▶ AML/Myelodisplastik sendrom artışı da BONUS.



MA-20 ve EORTC Ortak Sonuç

- ▶ Nod pozitif (1-3 LN dahil): RNI yapılması için çok kuvvetli kanıtlardır.
- ▶ Sistemik tedavi ve nodal örnekleme tekniklerindeki ilerlemeler olsa dahi 1-3 LN (+) olgularda RT'nin katkısı aşikardır.



Surgical Excision Without Radiation for Ductal Carcinoma in Situ of the Breast: 12-Year Results From the ECOG-ACRIN E5194 Study

Lawrence J. Solin, Robert Gray, Lorie L. Hughes, William C. Wood, Mary Ann Lowen, Sunil S. Badve, Frederick L. Baehner, James N. Ingle, Edith A. Perez, Abram Recht, Joseph A. Sparano, and Nancy E. Davidson

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Published online ahead of print at www.jco.org on September 14, 2015.

Supported in part by Public Health Service Grants No. CA180820, CA180794, CA188859, CA180864, CA180795, CA180844, CA180802, CA25224 from the National Cancer Institute, National Institutes of Health, Department of Health and Human Services, and by the Breast Cancer Research Foundation.

Presented in part at the San Antonio Breast Cancer Symposium, San Antonio, TX, December 9-13, 2014.

A B S T R A C T

Purpose

To determine the 12-year risk of developing an ipsilateral breast event (IBE) for women with ductal carcinoma in situ (DCIS) of the breast treated with surgical excision (lumpectomy) without radiation.

Patients and Methods

A prospective clinical trial was performed for women with DCIS who were selected for low-risk clinical and pathologic characteristics. Patients were enrolled onto one of two study cohorts (not randomly assigned): cohort 1: low- or intermediate-grade DCIS, tumor size 2.5 cm or smaller ($n = 561$); or cohort 2: high-grade DCIS, tumor size 1 cm or smaller ($n = 104$). Protocol specifications included excision of the DCIS tumor with a minimum negative margin width of at least 3 mm. Tamoxifen (not randomly assigned) was given to 30% of the patients. An IBE was defined as local recurrence of DCIS or invasive carcinoma in the treated breast. Median follow-up time was 12.3 years.

Results

There were 99 IBEs, of which 51 (52%) were invasive. The IBE and invasive IBE rates increased over time in both cohorts. The 12-year rates of developing an IBE were 14.4% for cohort 1 and 24.6% for cohort 2 ($P = .003$). The 12-year rates of developing an invasive IBE were 7.5% and 13.4%, respectively ($P = .08$). On multivariable analysis, study cohort and tumor size were both significantly associated with developing an IBE ($P = .009$ and $P = .03$, respectively).

Conclusion

For patients with DCIS selected for favorable clinical and pathologic characteristics and treated with excision without radiation, the risks of developing an IBE and an invasive IBE increased through 12 years of follow-up, without plateau. These data help inform the treatment decision-making process for patients and their physicians.

J Clin Oncol 33:3938-3944. © 2015 by American Society of Clinical Oncology

Çalışma Detayı: Prospektif (randomize değil)

▶ Kohort 1:

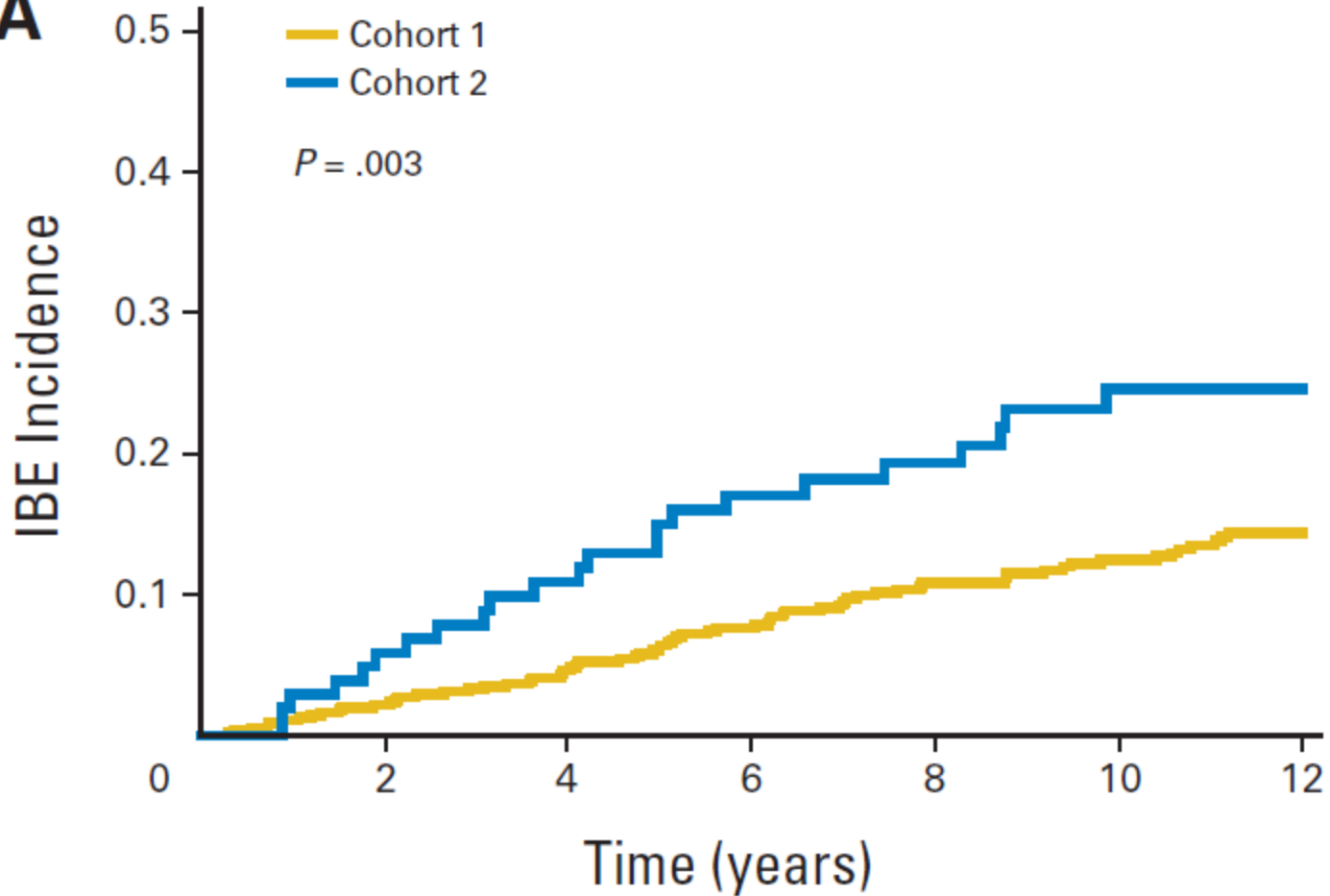
- ▶ $T_m \leq 2.5$ cm
- ▶ Düşük-Orta Grad

▶ Kohort 2:

- ▶ $T_m \leq 1$ cm
- ▶ Yüksek grad

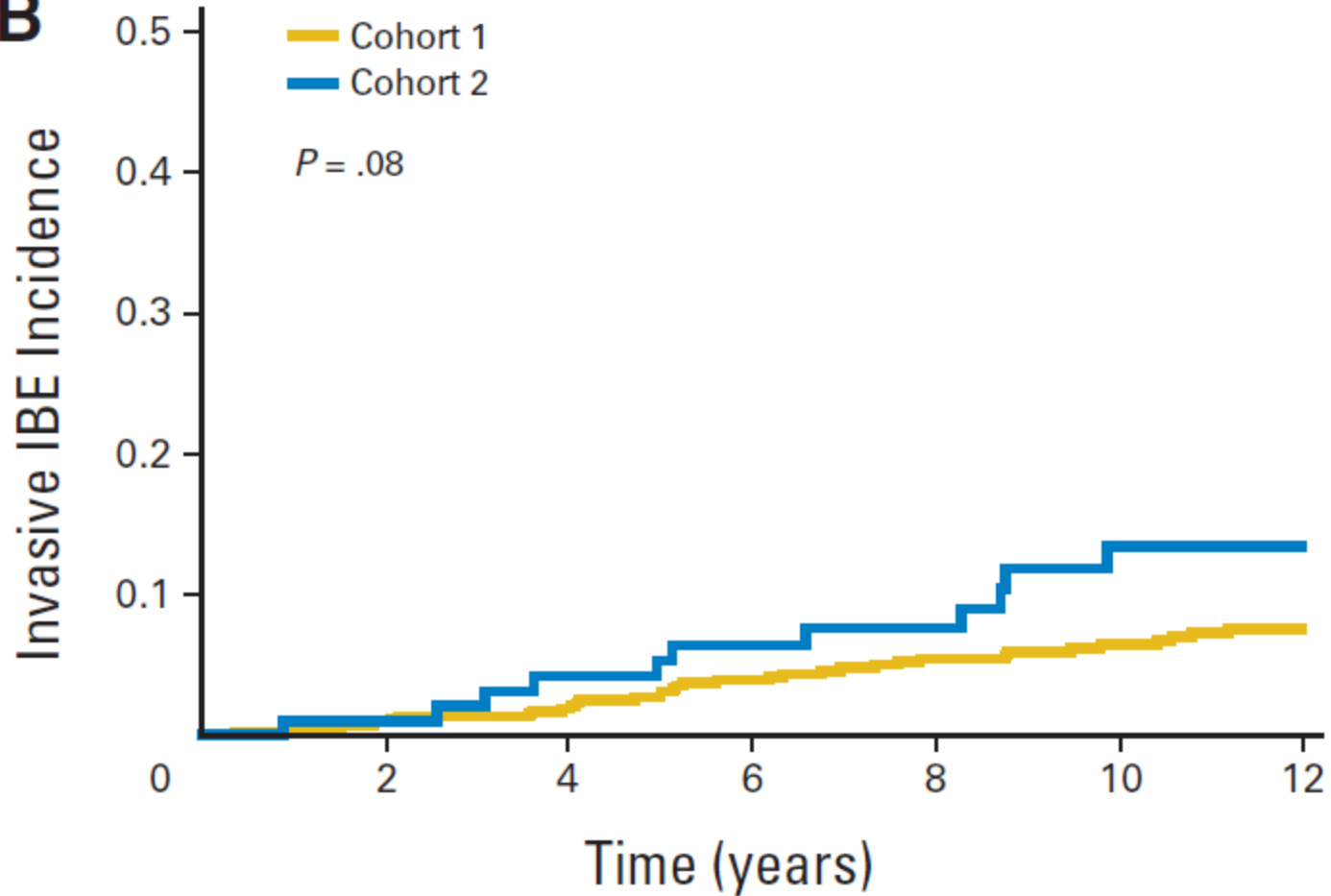
Cerrahi sınır ≥ 3 mm



A

No. at risk

Cohort 1	561	525	492	449	402	352	206
Cohort 2	104	95	88	78	67	53	34

B

No. at risk

Cohort 1 561

528

497

458

414

366

214

Cohort 2 104

97

90

80

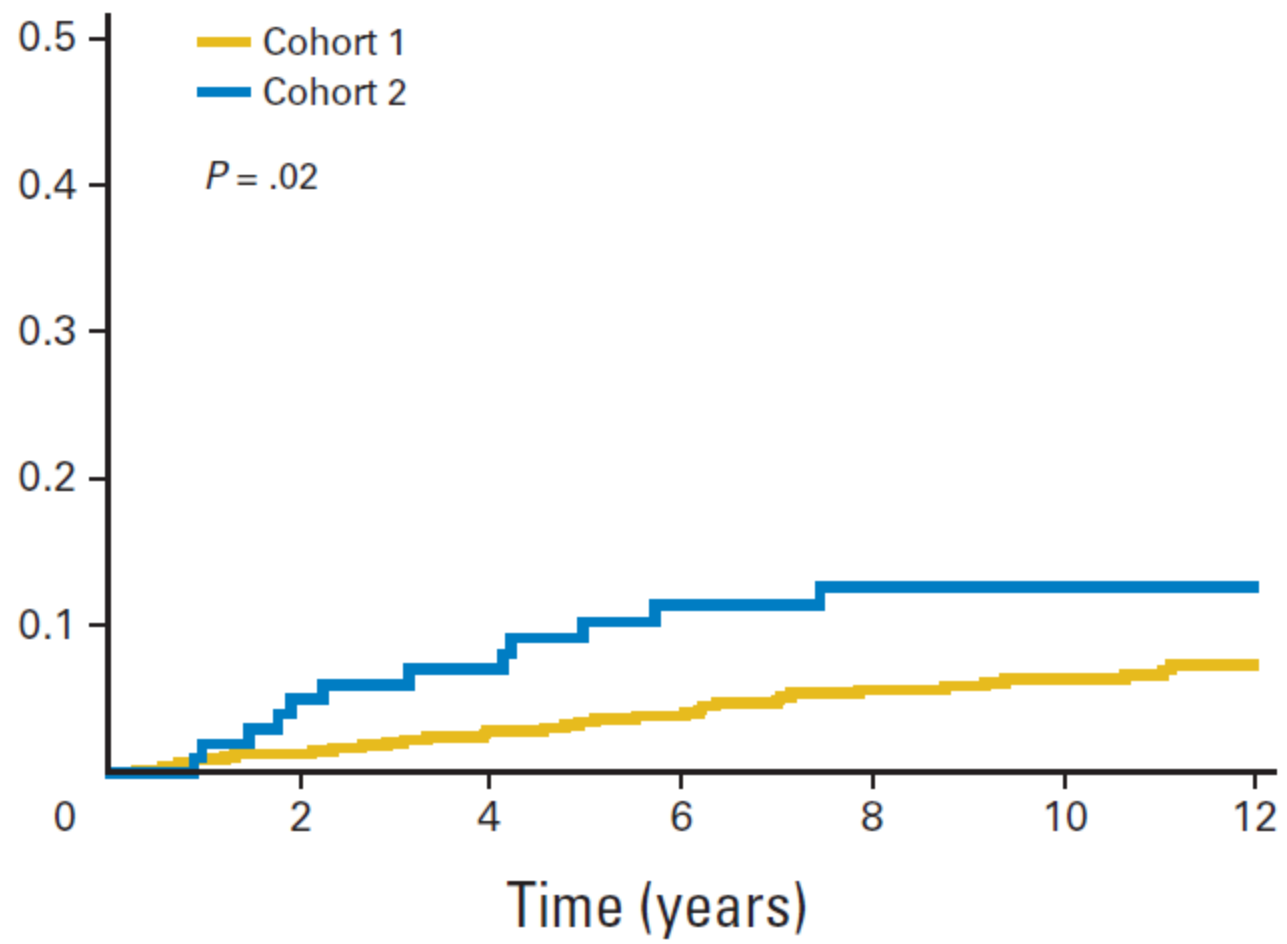
69

55

36

C

DCIS-Only IBE Incidence



No. at risk

Cohort 1	561	525	492	449	402	352	206
Cohort 2	104	95	88	78	67	53	34

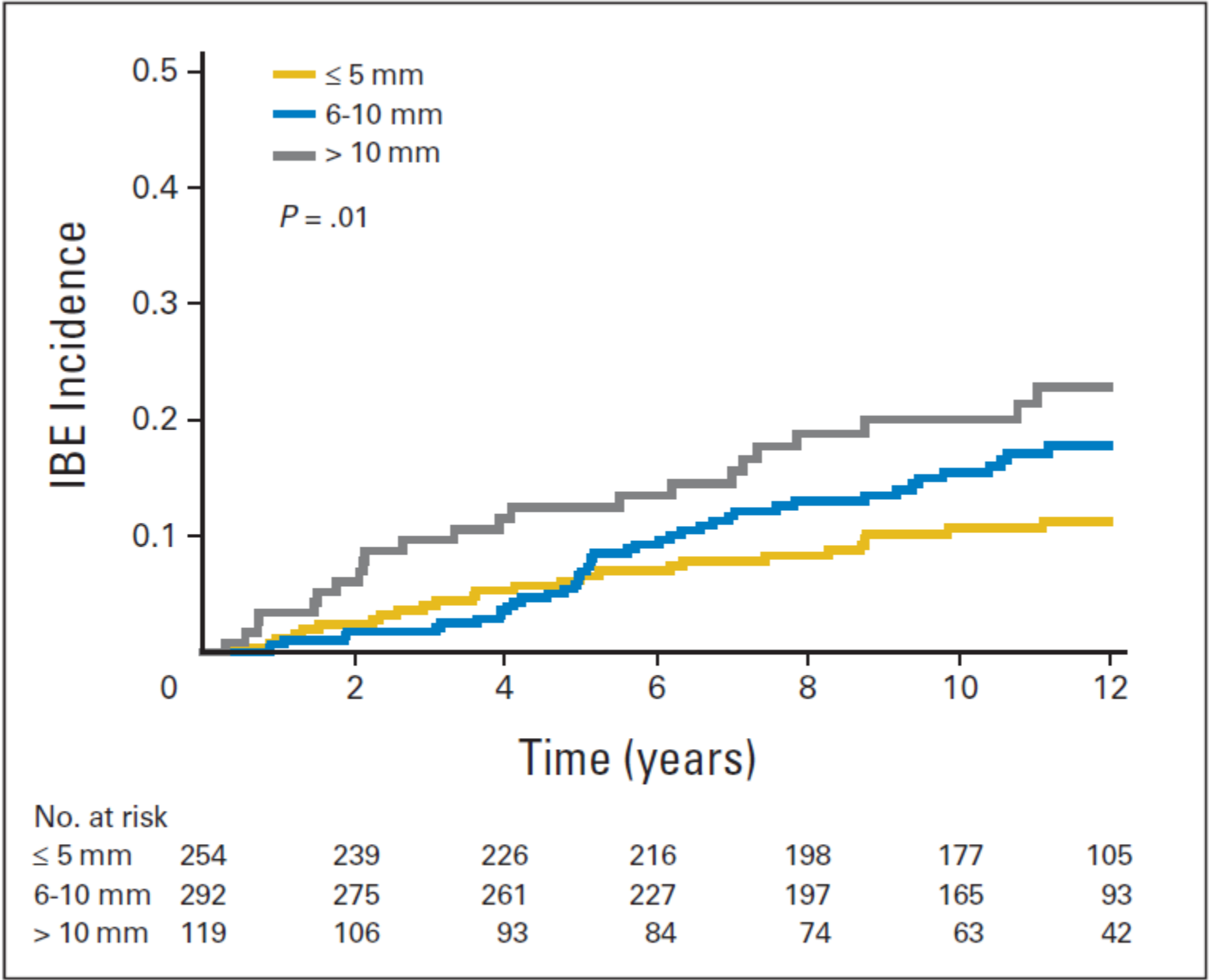


Fig 2. Ipsilateral breast events (IBEs) according to tumor size. The numbers at risk are given beneath the x-axis.

Yorum:

- ▶ Cerrahi eksizyon sonrası RT almayan DKİS olgularında iyi klinik ve patolojik karakterli olsa dahi **istikrarlı** bir şekilde tüm riskler 12. yılda plato dahi göstermeden artıyor.
- ▶ Cerrahlarımıza ve hastalarımıza duyurulur!

