Meme Kanserinde Neoadjuvan Tedavi

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Tıbbi Onkoloji

Ders Planı

- İnsidans ve epidemiyoloji
- Klinik ve radyolojik evreleme
- Hangi hasta gurubuna neoadjuvan kemoterapi
- Alt guruplarda uygun kemoterapi seçenekleri
- Kemoterapi sonrası aksilanın değerlendirilmesi

İnsidans ve Epidemiyoloji

	Common Types of Cancer	Estimated New Cases 2015	Estimated Deaths 2015
1.	**Breast Cancer (Female)**	**231,840**	**40,290**
2.	Lung and Bronchus Cancer	221,200	158,040
3.	Prostate Cancer	220,800	27,540
4.	Colon and Rectum Cancer	132,700	49,700
5.	Bladder Cancer	74,000	16,000
6.	Melanoma of the Skin	73,870	9,940
7.	Non-Hodgkin Lymphoma	71,850	19,790
8.	Thyroid Cancer	62,450	1,950
9.	Kidney and Renal Pelvis Cancer	61,560	14,080
10.	Endometrial Cancer	54,870	10,170

Female breast cancer represents 14.0% of all new cancer cases in the U.S.

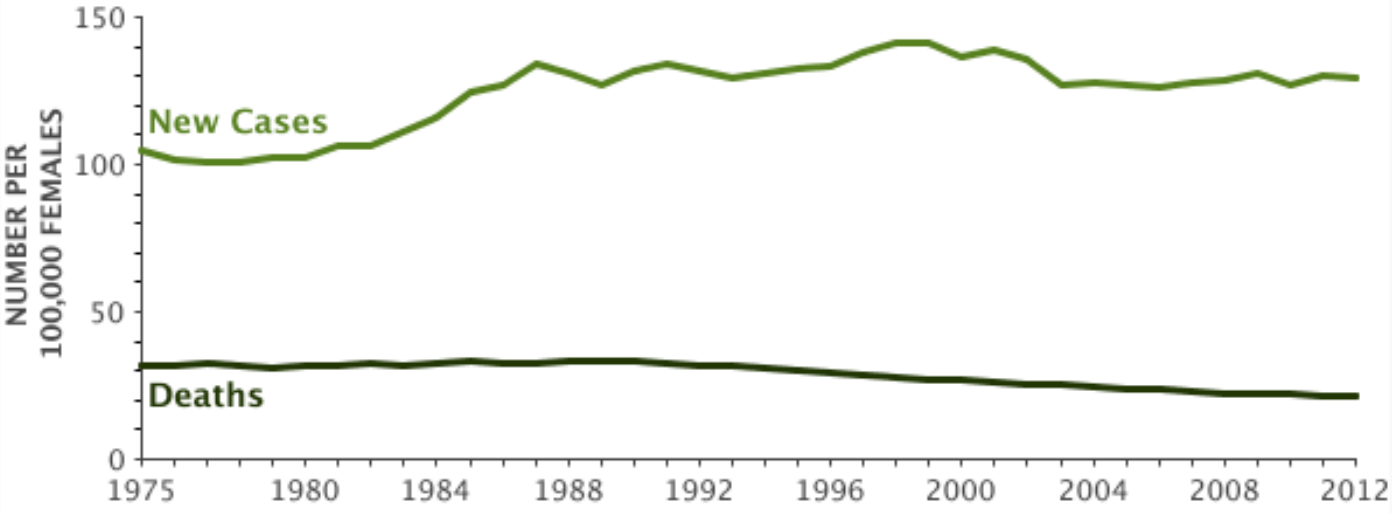
14.0%

In 2015, it is estimated that there will be 231,840 new cases of female breast cancer and an estimated 40,290 people will die of this disease.

İnsidans ve Epidemiyoloji

New Cases, Deaths and 5-Year Relative Survival

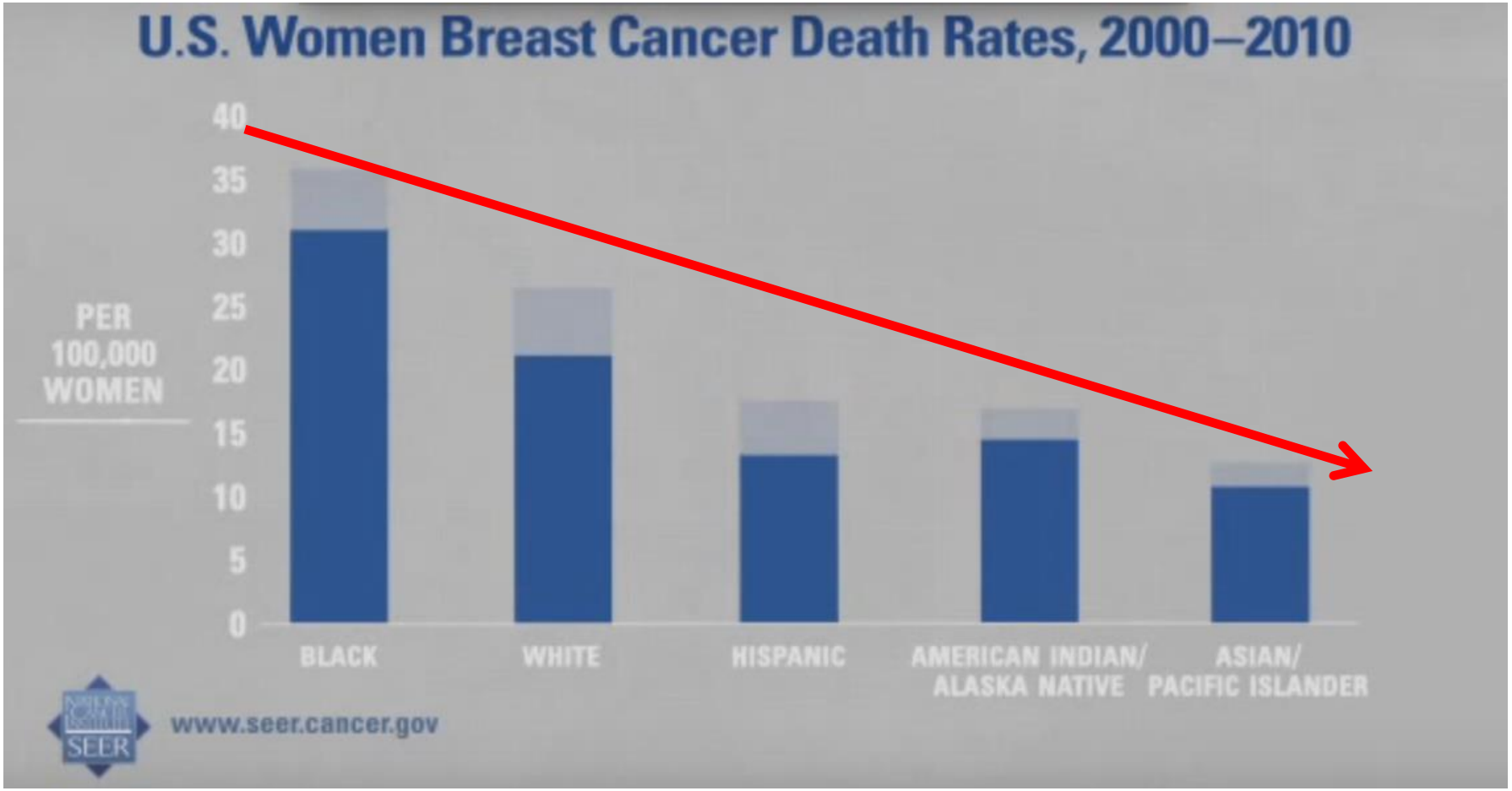
View Data Table



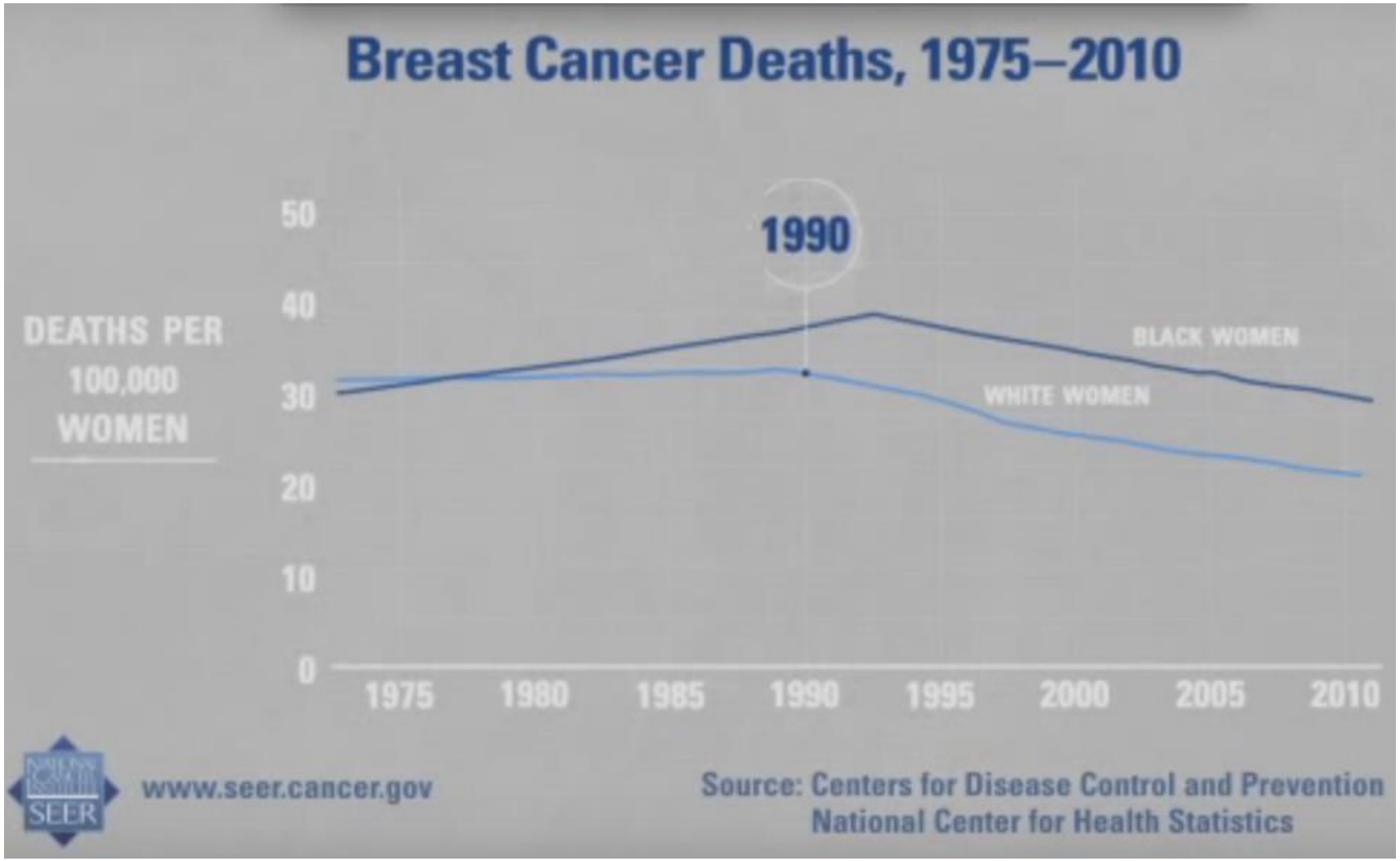
Year	1975	1980	1985	1990	1995	1999	2003	2007
5-Year Relative Survival	75.2%	74.8%	78.4%	84.6%	86.8%	89.6%	89.7%	91.0%

SEER 9 Incidence & U.S. Mortality 1975-2012, All Races, Females. Rates are Age-Adjusted.

İnsidans ve Epidemiyoloji

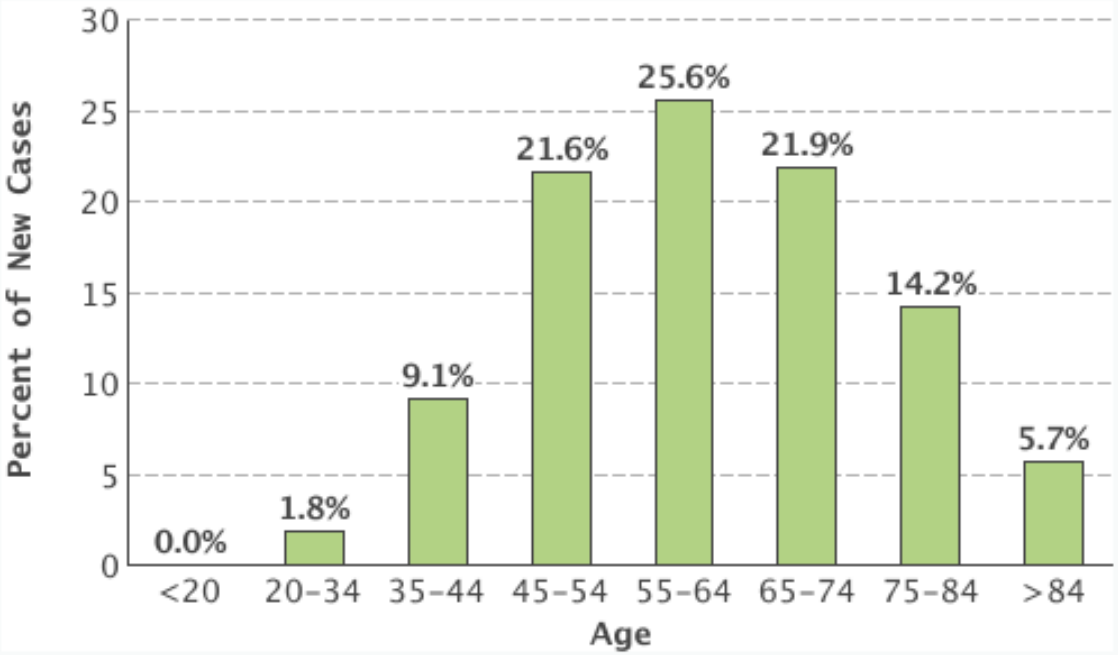


İnsidans ve Epidemiyoloji



İnsidans ve Epidemiyoloji

Percent of New Cases by Age Group: Female Breast Cancer



Female breast cancer is most frequently diagnosed among women aged 55-64.

Median Age At Diagnosis

61

SEER 18 2008-2012, All Races, Females

Meme Kanseri Risk Faktörleri

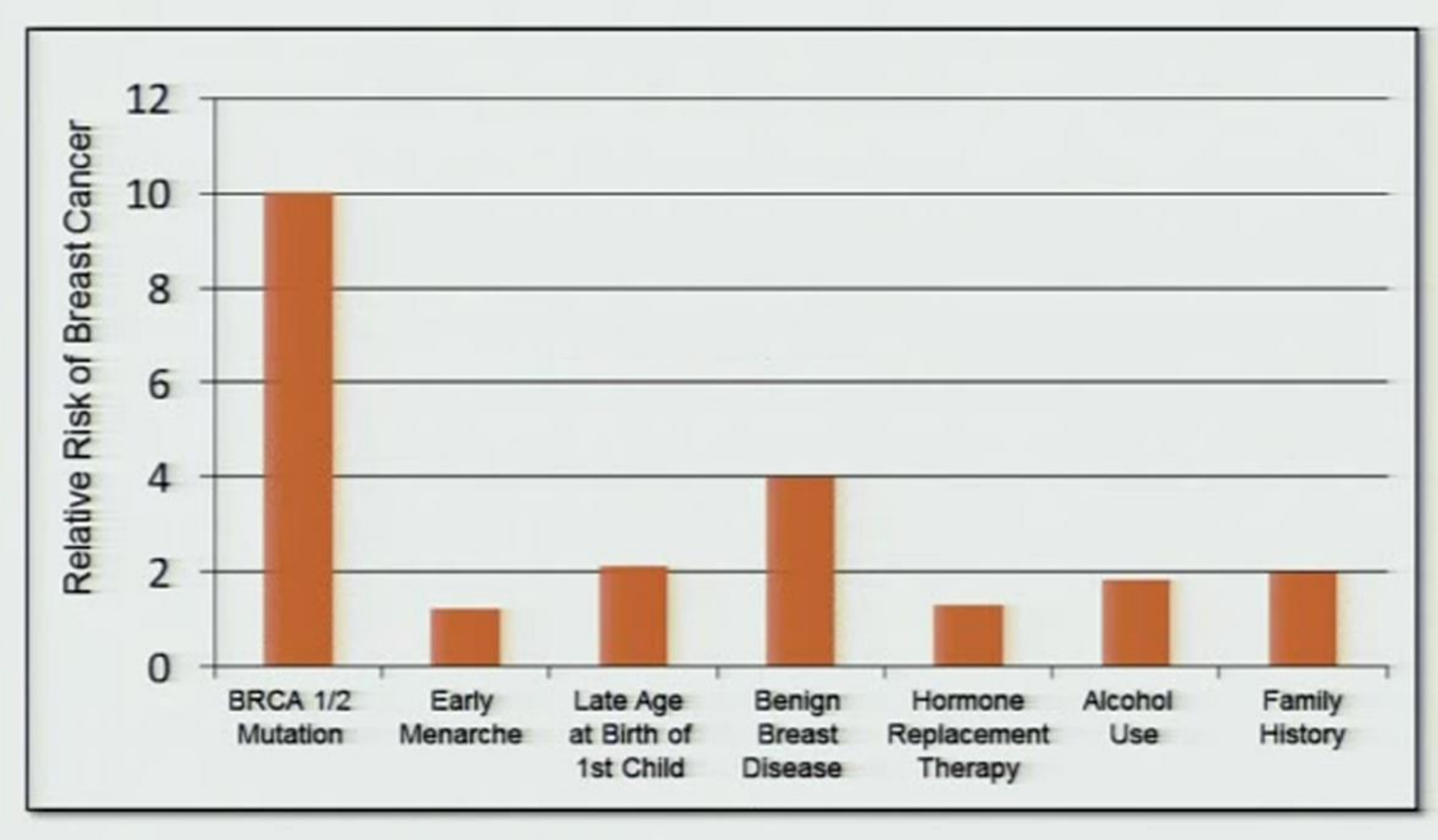
- İleri Yaş
- Meme kanseri öyküsü, bening meme hastalıkları öyküsü
- Ailesel meme kanseri öyküsü
- Genetik yatkınlık
- Endojen östrojen maruziyetin olması
- Yoğun meme dokusuna sahip olmak
- İlaç şeklinde verilen östrojen bazlı tedaviler
- Göğüs bölgesine radyoterapi almak
- Obezite
- Alkol tüketimi

Meme Kanseri Risk Faktörleri

Age-specific probabilities of developing invasive breast cancer

If current age is ...	The probability of devloping breast cancer in the next 10 years is:	or 1 in:
20	0.06%	1,681
30	0.43%	232
40	1.45%	69
50	2.38%	42
60	3.45%	29
70	3.74%	27
Lifetime risk	12.15%	8

Meme Kanseri Risk Faktörleri



Meme Kanseri Risk Faktörleri

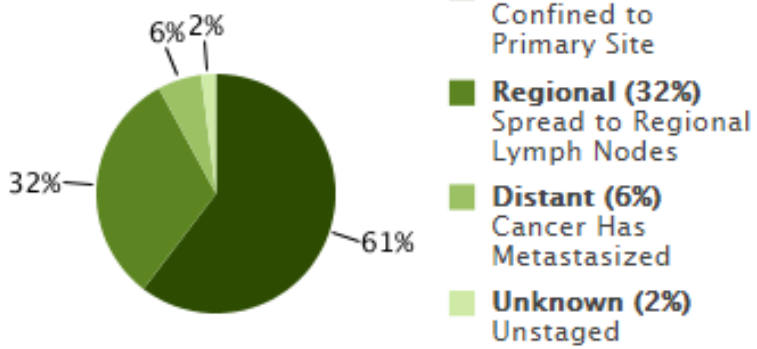
Benign Breast Disease			
No Risk	RR 1.5-2		RR 3-5
Cysts	Papilloma	Atypical Ductal Hyperplasia	
Duct ecatsia	Sclerosing adenosis	Atypical Lobular Hyperplasia	
Fibroadenoma			LCIS
Mastitis			DCIS
Fibrosis			

Arpino G, et al. *Ann Intern Med.* 2005;143:446-457.
Travis LB, et al. *J Natl Cancer Inst.* 2005;97:1428-1437.

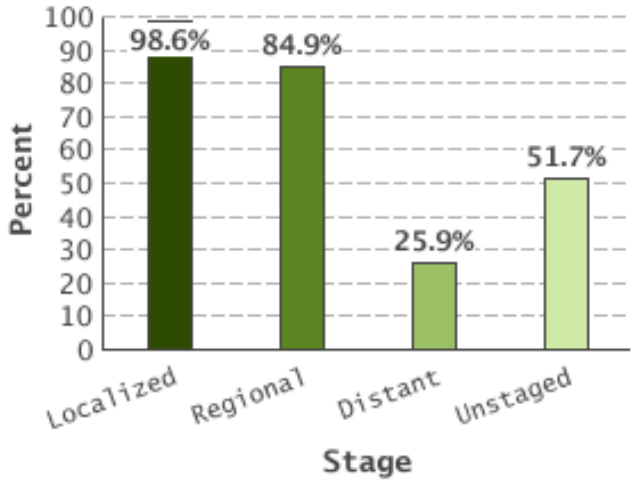
İnsidans ve Epidemiyoloji

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Female Breast Cancer

Percent of Cases by Stage

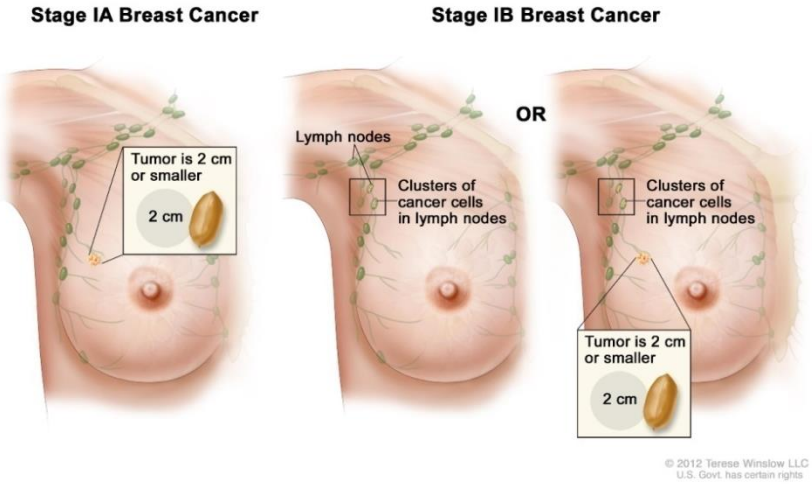


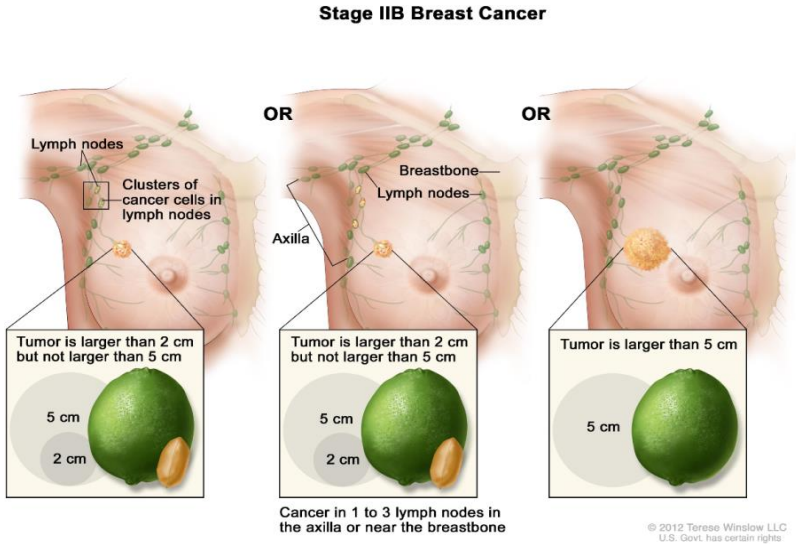
5-Year Relative Survival

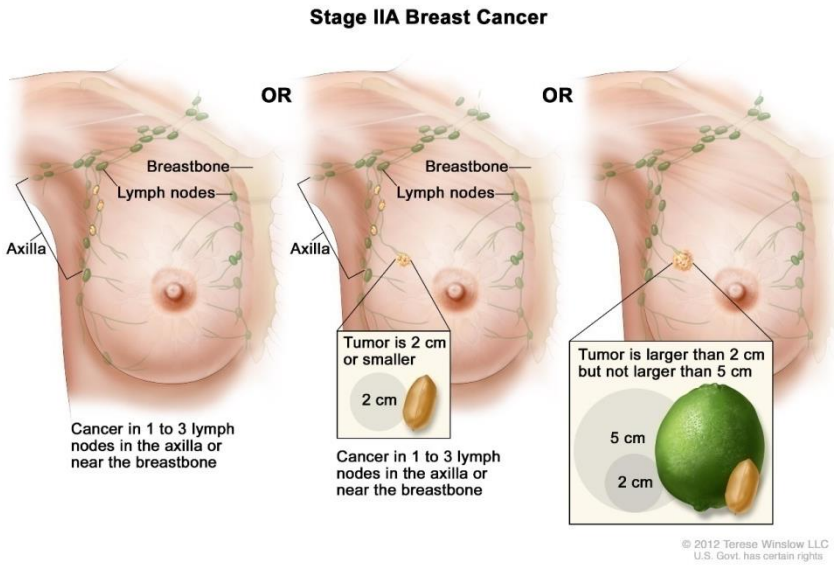


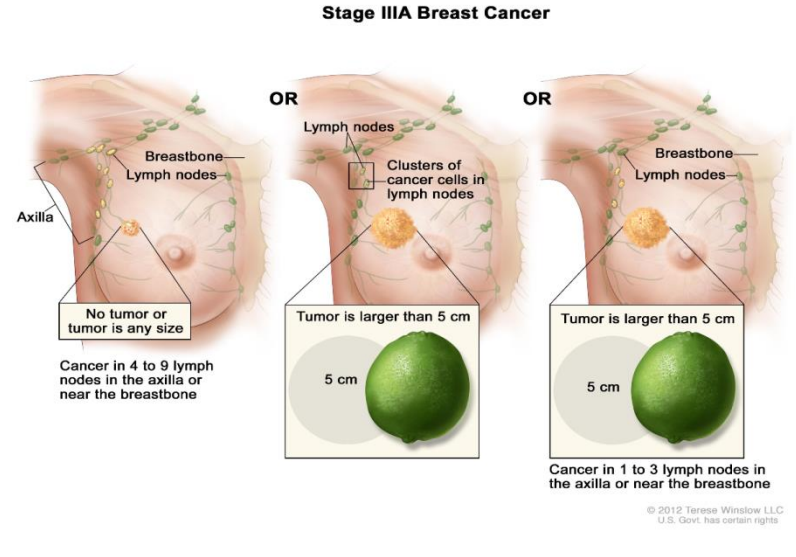
SEER 18 2005-2011, All Races, Females by SEER Summary Stage 2000

Meme Kanseri Evreleme









Meme Kanseri Evreleme

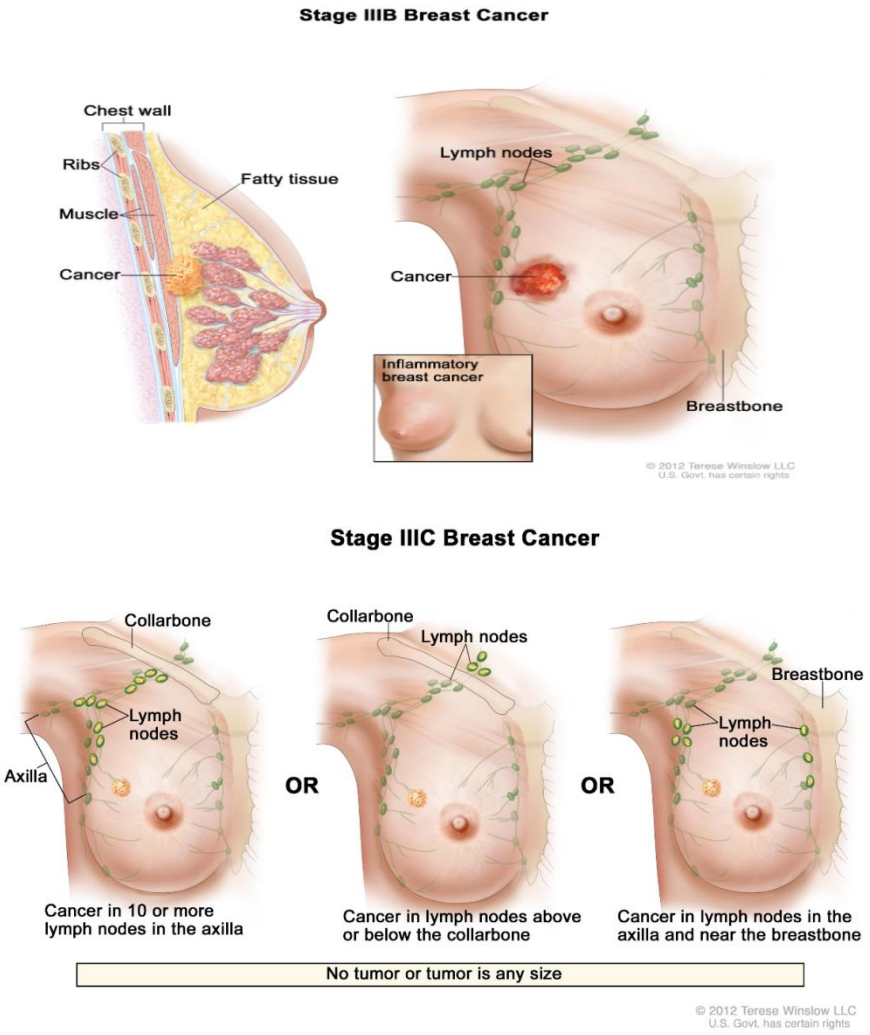


Table 1 (continued)

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage 0	Tis	N0	M0	**Stage IIIA**	T0	N2	M0
Stage IA	T1*	N0	M0		T1*	N2	M0
Stage IB	T0	N1mi	M0		T2	N2	M0
	T1*	N1mi	M0		T3	N1	M0
Stage IIA	T0	N1**	M0		T3	N2	M0
	T1*	N1**	M0	**Stage IIIB**	T4	N0	M0
	T2	N0	M0		T4	N1	M0
Stage IIB	T2	N1	M0		T4	N2	M0
	T3	N0	M0	**Stage IIIC**	Any T	N3	M0
				Stage IV	Any T	Any N	M1

* T1 includes T1mi

** T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

- M0 includes M0(i+).
- The designation pM0 is not valid; any M0 should be clinical.
- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.
- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.
- Postneoadjuvant therapy is designated with “yc” or “yp” prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

Meme Kanseri Evreleme

- Operable

  Evre I, II ve evre IIIA hastaların bir kısmı

- İnoperable

  Evre III B, IIIC ve evre IIIA hastaların bir kısmı

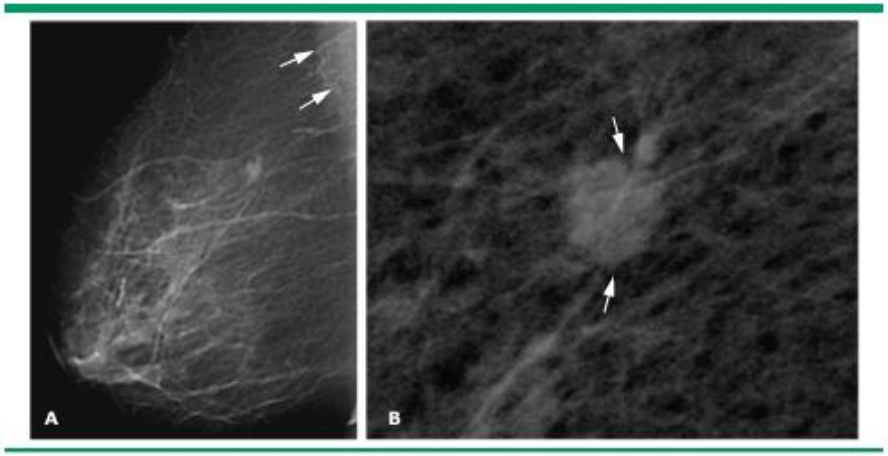
- Metastatik

  Evre IV

Meme Kanserinde Klinik Evreleme

- Mamografi
- Meme USG
- Meme MRI
- PET-CT

Meme Kanserinde Klinik Evreleme
Mamografi/USG



These images illustrate the benefits of spot compression and magnification. In the left panel (A), a medial lateral oblique (MLO) mammographic image, there is a mass at the posterior edge of the film (arrows) which is incompletely characterized. The borders of the lesion can be better characterized with regional spot compression and magnification. The spot magnification MLO view (B) shows that the lesion has irregular borders and spiculation. In addition, associated microcalcifications are seen. The lesion can now be characterized as suspicious, BIRADS 4c, requiring biopsy. Pathology revealed infiltrating duct cell carcinoma with papillary features.

- **Meme kanseri hastaların %10'da hastalarda fizik muayene**
- **%90 mamografi ile tanı konulur**
- **USG regional lenf nodlarının değerlendirilmesi ve biyopsi**

Smart CR, Cancer 1993

Meme Kanserinde Evreleme

MR

- Sensitivitesi yüksek
- Spesitivitesi düşük
- Yanlış pozitiflik oranı yüksek
- MR bulgusu tek başına tedavi yaklaşımını değiştirmez
- MR-guide ile biyopsi almak gerekir

Meme Kanserinde Evreleme

MR

J Clin Oncol. 2008 Jul 1;26(19):3248-58. doi: 10.1200/JCO.2007.15.2108. Epub 2008 May 12.

Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer.

Houssami N[1], Ciatto S, Macaskill P, Lord SJ, Warren RM, Dixon JM, Irwig L.

Author information

Abstract

PURPOSE We review the evidence on magnetic resonance imaging (MRI) in staging the affected breast to determine its accuracy and impact on treatment. METHODS Systematic review and meta-analysis of the accuracy of MRI in detection of multifocal (MF) and/or multicentric (MC) cancer not identified on conventional imaging. We estimated summary receiver operating characteristic curves, positive predictive value (PPV), true-positive (TP) to false positive (FP) ratio, and examined their variability according to quality criteria. Pooled estimates of the proportion of women whose surgery was altered were calculated. Results Data from 19 studies showed MRI detects additional disease in 16% of women with breast cancer (N = 2,610). MRI incremental accuracy differed according to the reference standard (RS; P = .016) decreasing from 99% to 86% as the quality of the RS increased. Summary PPV was 66% (95% CI, 52% to 77%) and TP:FP ratio was 1.91 (95% CI, 1.09 to 3.34). Conversion from wide local excision (WLE) to mastectomy was 8.1% (95% CI, 5.9 to 11.3), from WLE to more extensive surgery was 11.3% in MF/MC disease (95% CI, 6.8 to 18.3). Due to MRI-detected lesions (in women who did not have additional malignancy on histology) conversion from WLE to mastectomy was 1.1% (95% CI, 0.3 to 3.6) and from WLE to more extensive surgery was 5.5% (95% CI, 3.1 to 9.5). CONCLUSION MRI staging causes more extensive breast surgery in an important proportion of women by identifying additional cancer, however there is a need to reduce FP MRI detection. Randomized trials are needed to determine the clinical value of detecting additional disease which changes surgical treatment in women with apparently localized breast cancer.

Meme Kanserinde Evreleme
MR

- Mastektomi oranı artırabilir
- %7.8–33.3 tedavi yaklaşımını değiştirir
- Meme sağkalım sonuçları üzerinde etkisi yok
- Pirimeri bilinmeyen aksila metastazlarında primer odak bulmada ek fayda görür

Meme Kanserinde Evreleme
MR

NCCN önerileri

- Yoğun meme dokusuna sahip hastalarda
- Multisentrik Tümör olanlarda
- Göğüs duvarı invaziyonu şüphesi olanlarda
- Primeri bilinmeyen aksila metastazı

Meme Kanserinde Evreleme

Ann Oncol. 2005 Feb;16(2):263-6.

Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications.

Puglisi F[1], Follador A, Minisini AM, Cardellino GG, Russo S, Andreetta C, Di Terlizzi S, Piga A.

Author information

Abstract

BACKGROUND: Bone scanning (BS), liver ultrasonography (LUS) and chest radiography (CXR) are commonly used in patients with newly diagnosed breast cancer as part of baseline staging. However, in the absence of symptomatic disease, the usefulness of this routine diagnostic work-up is not evidence-based.

METHODS: We selected the study sample from 516 consecutive patients with newly diagnosed invasive breast cancer. For each diagnostic test (BS, LUS, CXR), we analyzed the prevalence defined as the number of patients with diagnosis of metastatic disease after an imaging technique divided by the total number of patients tested. In addition, sensitivity and specificity were calculated. Initial suspicion was confirmed by other independent tests (bone X-ray, computerized tomography scan, magnetic resonance imaging) in order to identify "true" positive diagnoses.

RESULTS: At baseline, BS was carried out in 412 patients, LUS in 412 patients and CXR in 428 patients. Thirty-three patients were correctly diagnosed by the initial staging investigations as having metastatic disease (true positive cases). BS detected skeletal metastases in 6.31% of patients, LUS detected liver metastases in 0.72% of patients and CXR detected lung metastases in 0.93% of patients. Before imaging tests, all patients with either LUS or CXR evidence of metastases were previously classified as having stage III disease. On the other hand, only 26.9% of bone metastases were detected in patients with stage III. Accordingly, the detection rate in stage III patients was 14%, 5.6% and 7.2%, respectively for BS, LUS and CXR.

CONCLUSIONS: These findings indicate that a complete diagnostic work-up to detect metastases is unnecessary in the majority of patients with newly diagnosed breast cancer, whereas it may be indicated for specific patient categories such as those with stage III disease.

Semptomatik olmayan evre I/II Hastalarda sistemik tarama yapılması önerilmez. Evre III≥ hastalarda yapılması önerilir

Meme Kanserinde Evreleme

- Semptomatik ve bulgu olmayan erken meme kanserinde rutin sistemik görüntüleme istenmez.
- Tüm vücut sintigrafisi semptom ve bulgu olmayan evre I, II, III hastalarında, metastaz saptama oranı sırasıyla, %5.1, %5.6 ve %14
- Semptomu olmayan, Evre I ve II hastalarında PA akciğer ve Batın USG ile metastaz saptanmamış

Meme Kanserinde Evreleme

- Pulmoner semptom ve bulgu varsa; Thoraks BT
- Alkali fosfataz yüksek ya da semptom var; tüm vücut kemik sintigrafisi
- Karaciğer enzimleri yüksek ya da bulgu ve semptom varsa; batın BT/ MRI

Meme Kanserinde Evreleme

NCCN önerileri

Evre I-II

- Semptomu olmayan hastalarında görüntüleme tetkiği istemenin faydası gösterilememiş.

Evre IIIA≥

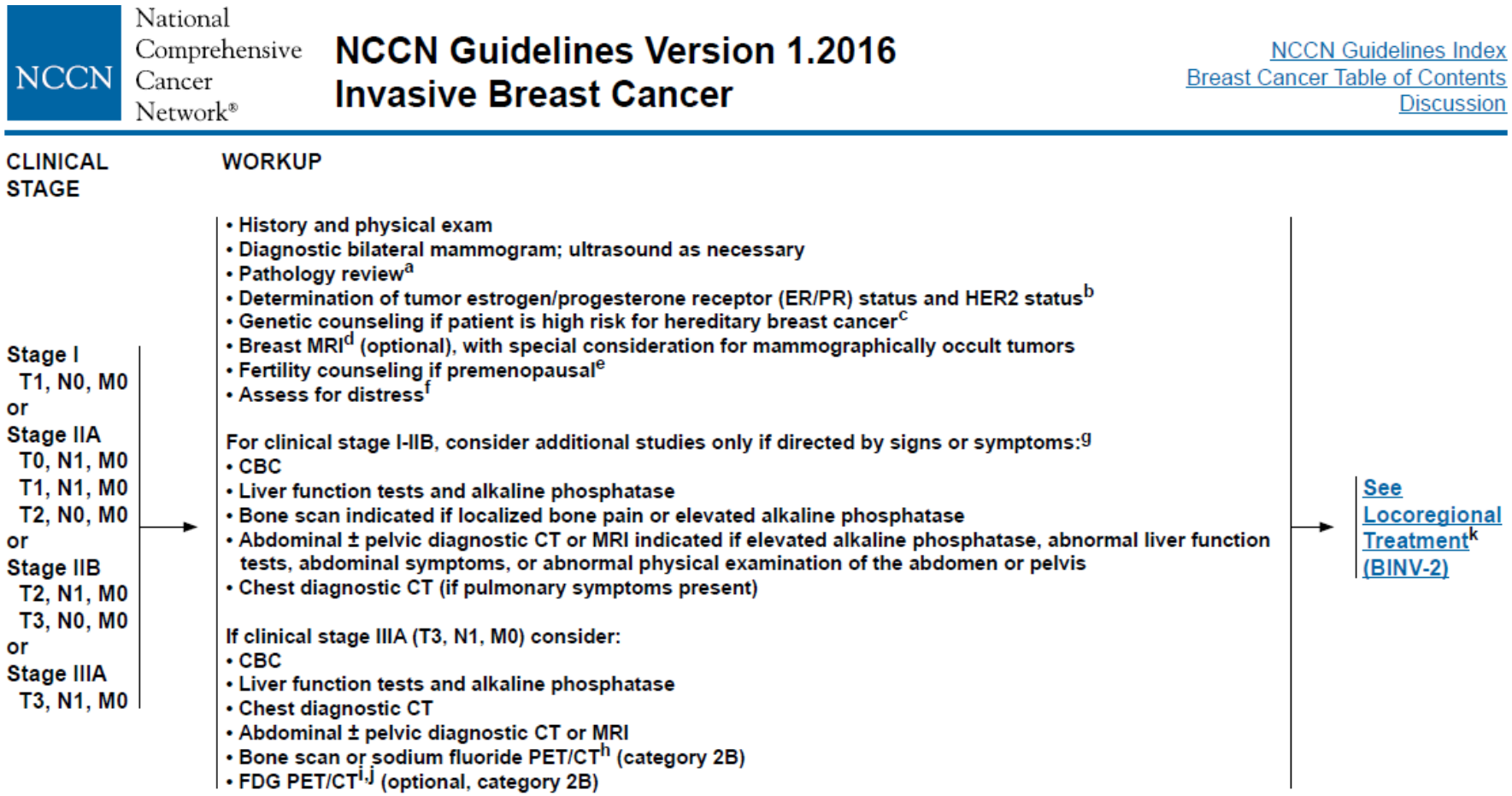
- Thoraks BT/Tüm batın BT/MR, Kemik sintigrafis
- PET-CT kategori 2B

Meme Kanserinde Evreleme

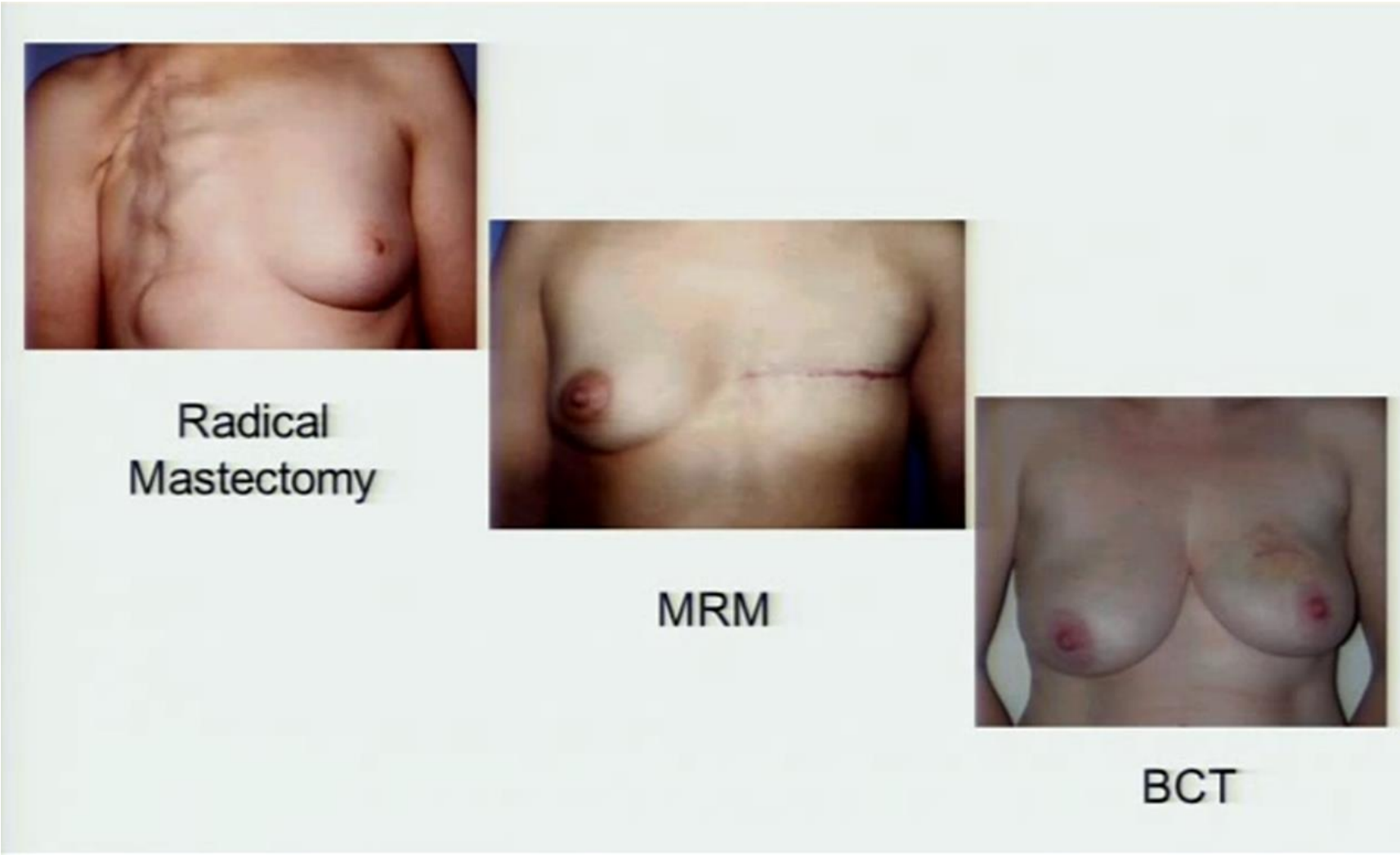
PET-CT

- Evre I, II ve operable evre III meme ca endikasyonu yok
- Erken evre, 1 cm altındaki lezyonlar ve düşük grad'lı tümörlere yanlış negatiflik yüksek
- Aksila metastazı göstermede sensitivitesi düşük
- Lokal ileri, metastatik evrede rutin tetkiklerde görülen anormal görüntülerin ayrımında yardımcı olabilir.

Meme Kanserinde Evreleme



Meme Cerrahisinin Seyri



Meme Cerrahisinin Seyri


William Stewart Halsted

Johns Hopkins Press, 1930

- **Radikal Mastektomi ile kanser cerrahisinde bir ekolün öncüsü oldu**
- **Yetiştirdikleri öğrencileri, Harvey Cushing, Joseph Bloodgood**
- **1989 yılında William Halsted Amerikan Cerrahi Birliği'nin New Orleans 'taki konferansında ameliyat ettiği 76 meme kanserli hatanın verilerini sundu, hastalarının yarısı 3 yıl üçünde kaybedilmişti**
- **1896 yılında 21 yaşında bir öğrenci olan Emil Grubbe hastalığı tekrar etmiş bir meme kanserli hastasında X ışınlı tüpüyle tedavi ediyor**
- **Bonadonanın 1970 yılların sonlarında CMF rejmininin meme kanserinde kullanılmaya başlanmasıyla uzun yıllar kemoterapi kanserle mücadelede önemli silah olarak görüldü.**
- **1990 sonrası Taksanlar ve Transtusumab, 2010 sonrası Pertusumab**

Meme Cerrahisinin Seyri

- Halsted Ameliyatlarında kendine eşlik eden hemşiresinin ellerinde gelişen kontak dermatit için literatürde ilk cerrahi eldiven kullanıyor
- Büyük ameliyatlarda ağrıyı azaltmak için lokal kokain kullanıyor. Kokaini kendi üzerinde deniyor ve kokain bağımlısı oluyor
- Bağımlılıktan kurtulmak için Butler Sanatoryumuna yatıyor, orada eroin bağımlısı olarak geri dönüyor

Meme Kanseri Neoadjuvan Tedavi

- Meme koruyucu cerrahi, daha çok meme dokusunu korumak
- İnoperable meme kanserlerini operable hale getirmek
- Tedavinin etkinliğini(Kemoterapi, yeni molekül) erken değerlendirebilmek(Patolojik tam yanıt oranı)
- Genetik testler için zaman kazanmak(BRCA vs, operasyon şeklini belirlemek)

Meme Kanseri Neoadjuvan Tedavi
Handikapları

- Klinik everenin, patolojik evreye göre ileri olarak değerlendirilmesi buna bağlı olarak overtreatment
- Klinik evere, patolojik evreye göre alt evre olarak değerlendirilmesi buna bağlı undertreatment(RT alamayabilir)
- Tedavi esnasında progresyon ve cerrahi şansını kaybetme

Meme Kanseri Neoadjuvan Tedavi

CTNeoBC Pooled Analysis: Pathologic Complete Response (pCR) versus No pCR

Endpoint	Event-free survival HR (95% CI)	Overall survival HR (95% CI)
pCR (ypT0 ypN0)[1] (n = 1,554)	0.44 (0.39-0.51)	0.36 (0.31-0.44)
pCR (ypT0/is ypN0)[2] (n = 2,131)	0.48 (0.43-0.54)	0.36 (0.31-0.42)
pCR (ypT0/is)[3] (n = 2,598)	0.60 (0.55-0.66)	0.51 (0.45-0.58)

[1] No invasive or in situ disease in breast or axillary nodes
[2] No invasive disease in breast or axillary nodes, irrespective of DCIS
[3] No invasive disease in breast irrespective of DCIS or nodal involvement

Cortazar P et al. *Lancet* 2014;384(9938):164-72.

Meme Kanseri Neoadjuvan Tedavi

CTNeoBC Pooled Analysis: Association of pCR and Outcomes

- The association between pCR and long-term outcomes was strongest among patients with
  - Triple-negative breast cancer
  - HER2-positive, hormone receptor (HR)-negative tumors who received trastuzumab

Cortazar P et al. *Lancet* 2014;384(9938):164-72.

Meme Kanseri Neoadjuvan Tedavi
Tümör Boyutu

Neoadjuvant Chemotherapy for Breast Cancer Increases the Rate of Breast Conservation: Results from the National Cancer Database

Brigid K Killelea, MD, MPH, FACS, Vicky Q Yang, MS, Sarah Mougalian, MD, Nina R Horowitz, MD, FACS, Lajos Pusztai, MD, DPhil, Anees B Chagpar, MD, MSc, MPH, MA, MBA, FACS, Donald R Lannin, MD, FACS

BACKGROUND: Neoadjuvant chemotherapy has been shown to increase the rate of breast conservation in clinical trials and small institutional series, but it has never been studied on a national level.

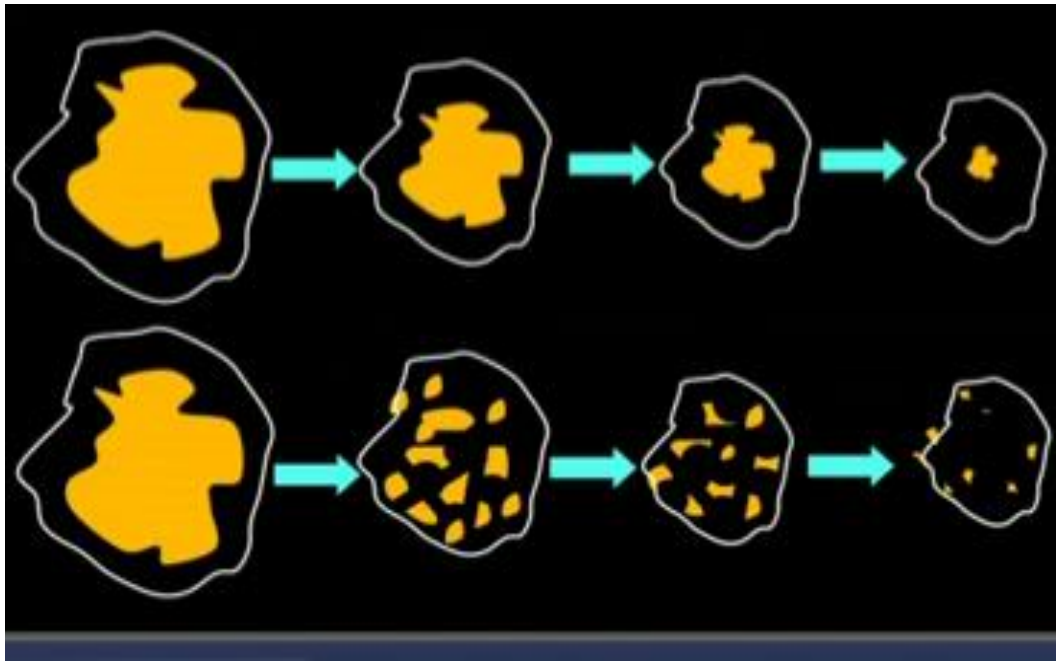
STUDY DESIGN: We performed a retrospective review of the National Cancer Database (NCDB). The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society and contains about 80% of the cancer cases in the United States. All women in the NCDB diagnosed with invasive breast cancer from 2006 through 2011, who underwent definitive breast surgery and received either neoadjuvant or adjuvant chemotherapy, excluding patients with distant metastases or T4 tumors, were included and rates of breast preservation were determined.

RESULTS: Of 354,204 patients who met the inclusion criteria, 59,063 (16.7%) underwent neoadjuvant chemotherapy. This proportion steadily increased from 13.9% in 2006 to 20.5% in 2011 ($p < 0.001$). Receipt of neoadjuvant chemotherapy was associated with larger tumor size (7% cT1, 25% cT2, and 58% cT3; $p < 0.001$), more advanced nodal disease (11% cN0, 39% cN1-3; $p < 0.001$), younger patient age (21% <50 years vs 14% >50 years; $p < 0.001$), higher tumor grade (18% grade 3, 15% grade 2, vs 12% grade 1; $p < 0.001$), and estrogen receptor (ER)-negative tumors (21% ER negative vs 15% ER postive; $p < 0.001$). Multivariate logistic regression showed that when adjusted for the above variables, patients with tumors larger than 3 cm undergoing neoadjuvant chemotherapy were more likely to receive breast preservation than those who opted for primary surgery (odds ratio 1.7, 95% CI 1.6 to 1.8).

CONCLUSIONS: Neoadjuvant chemotherapy increases breast preservation for patients with breast tumor size larger than 3 cm. (J Am Coll Surg 2015;220:1063–1069. © 2015 by the American College of Surgeons)

Tümör boyutu 3 cm büyük olan olgularda neoadjuvan KT, meme koruyucu cerrahi oranını artırıyor.

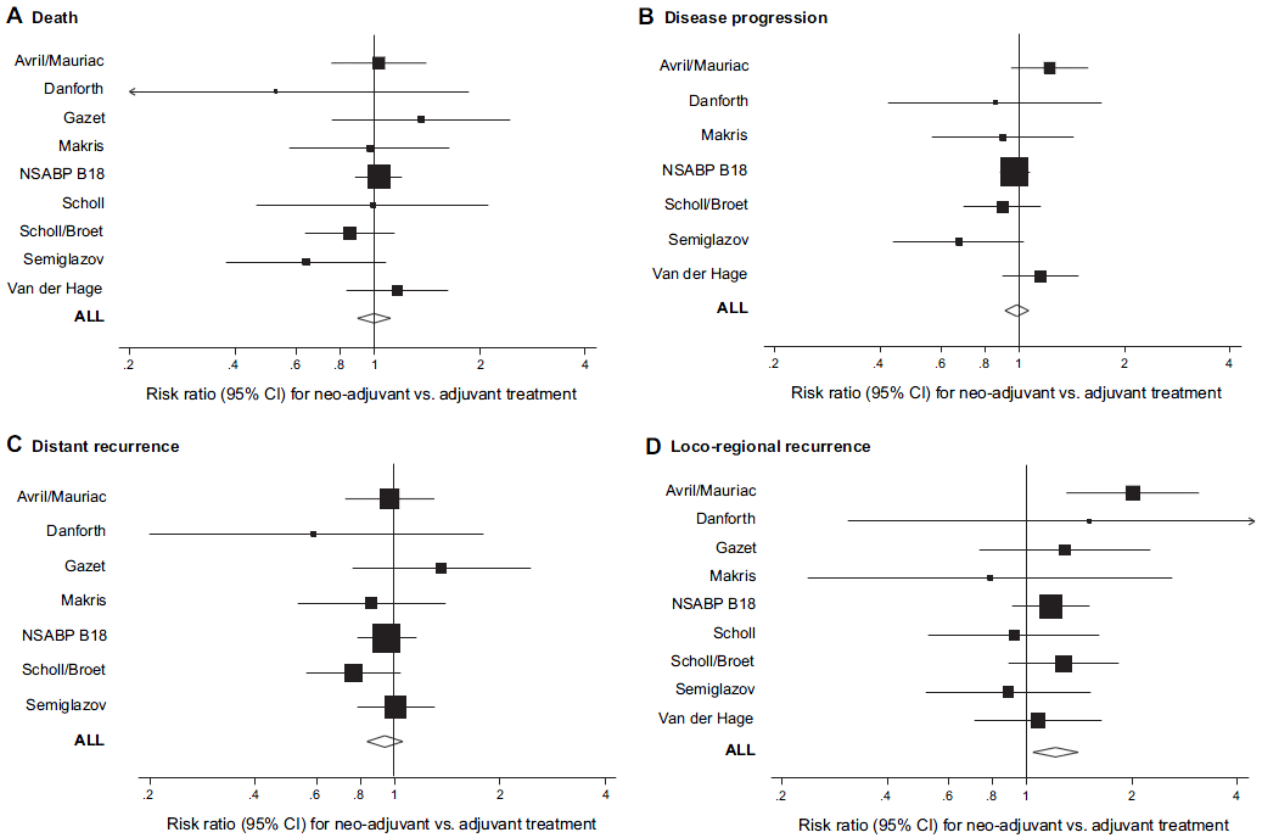
Meme Kanseri Neoadjuvan Tedavi



- ❑Triple Negatif
- ❑HER2 Pozitif
- ❑High Grade

- ❑HER2-/HR +
- ❑Düşük grade
- ❑Multisentrik tümör
- ❑Lobüler histoloji
- ❑Yaygın mikrokalsifikasyon

Meme Kanseri Neoadjuvan Tedavi



Cerrahi öncesi yada Cerrahi sonrası Kemoterapi Vermenin Sağkalım Yönünde Birbirine Üstünlüğü Yoktur

Mauri D , J Natl Cancer Inst, 2005

Meme Kanseri Neoadjuvan Tedavi
HER2 pozitif

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PREOPERATIVE/ADJUVANT THERAPY REGIMENS [1,2,3,4]

Regimens for HER2-negative disease[5]

Preferred regimens:
- Dose-dense AC (doxorubicin/cyclophosphamide) followed by paclitaxel every 2 weeks
- Dose-dense AC (doxorubicin/cyclophosphamide) followed by weekly paclitaxel
- TC (docetaxel and cyclophosphamide)

Other regimens:
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- AC (doxorubicin/cyclophosphamide) every 3 weeks (category 2B)
- CMF (cyclophosphamide/methotrexate/fluorouracil)
- AC followed by docetaxel every 3 weeks
- AC followed by weekly paclitaxel
- EC (epirubicin/cyclophosphamide)
- FEC/CEF followed by T (fluorouracil/epirubicin/cyclophosphamide followed by docetaxel) or (fluorouracil/epirubicin/cyclophosphamide followed by weekly paclitaxel)
- FAC followed by T (fluorouracil/doxorubicin/cyclophosphamide followed by weekly paclitaxel)
- TAC (docetaxel/doxorubicin/cyclophosphamide)

Regimens for HER2-positive disease[6,7,8]

Preferred regimens:
- AC followed by T + trastuzumab ± pertuzumab[9] (doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab ± pertuzumab, various schedules)
- TCH (docetaxel/carboplatin/trastuzumab) ± pertuzumab

Other regimens:
- AC followed by docetaxel + trastuzumab ± pertuzumab[9]
- Docetaxel + cyclophosphamide + trastuzumab
- FEC followed by docetaxel + trastuzumab + pertuzumab[9]
- FEC followed by paclitaxel + trastuzumab + pertuzumab[9]
- Paclitaxel + trastuzumab[10]
- Pertuzumab + trastuzumab + docetaxel followed by FEC[9]
- Pertuzumab + trastuzumab + paclitaxel followed by FEC[9]

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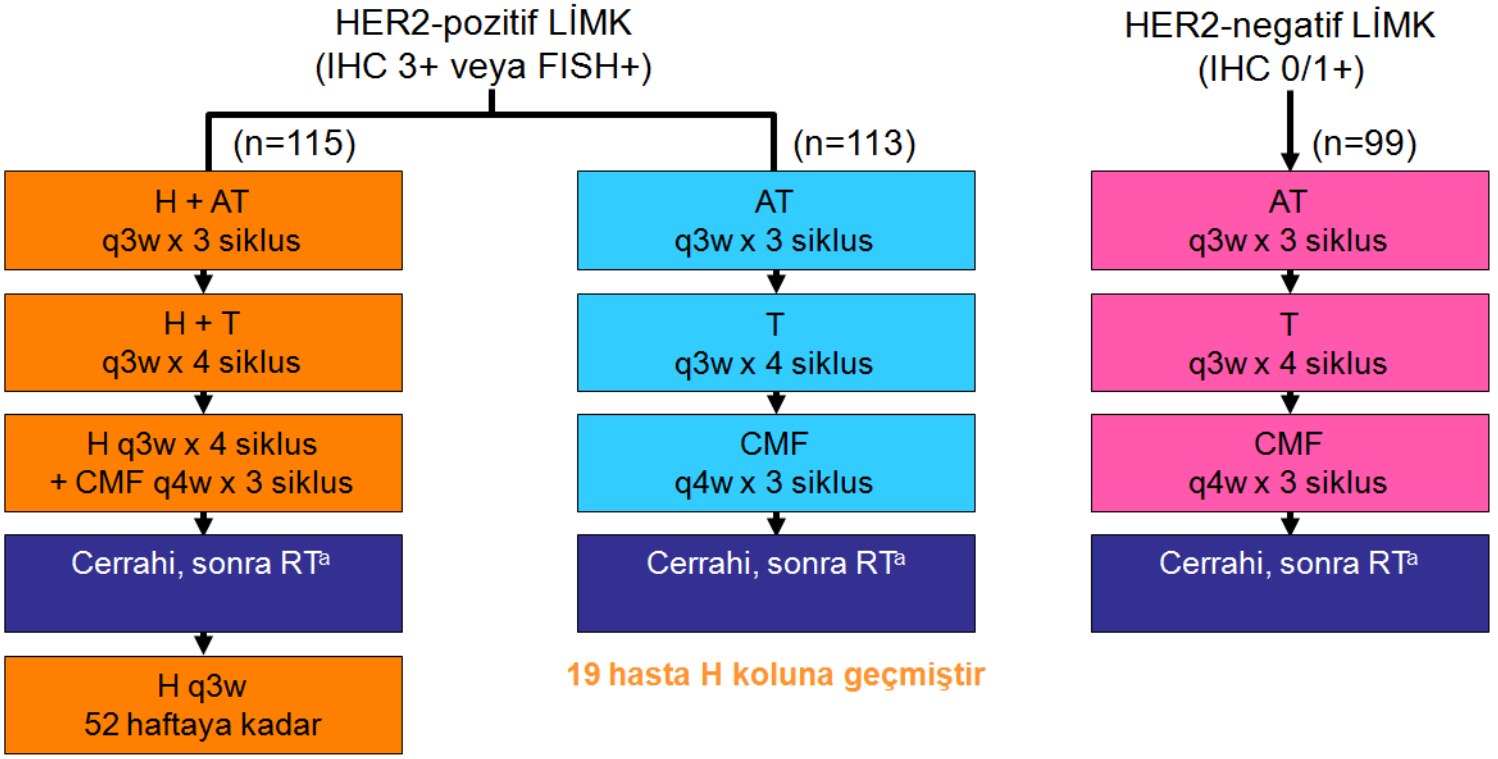
HER2 pozitif

NOAH çalışma düzeni



H, trastuzumab (8 mg/kg yükleme dozu sonrası 6 mg/kg);
AT, doksorubisin (60 mg/m²), paklitaksel (150 mg/m²); q3w;
T, paklitaksel (175 mg/m²); q4w
[a]Hormon reseptor-pozitif hastalar adjuvan tamoksifen almaktadır

Gianni L, et al. SABC Sempozyumu, Genel Oturum 3, 12 Aralık 2008

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HER2 pozitif

Sonlanım Noktaları

- Primer (final analiz)
  - EFS: tedavi sırasında progresyon veya cerrahi sonrası relaps veya herhangi bir sebebe bağlı ölüm
- Sekonder
  - pCR oranı
  - ORR
  - Güvenlilik ve tolerabilite

EFS, olaysız sağkalım (event-free survival);
pCR, patolojik tam yanıt (pathological complete response)

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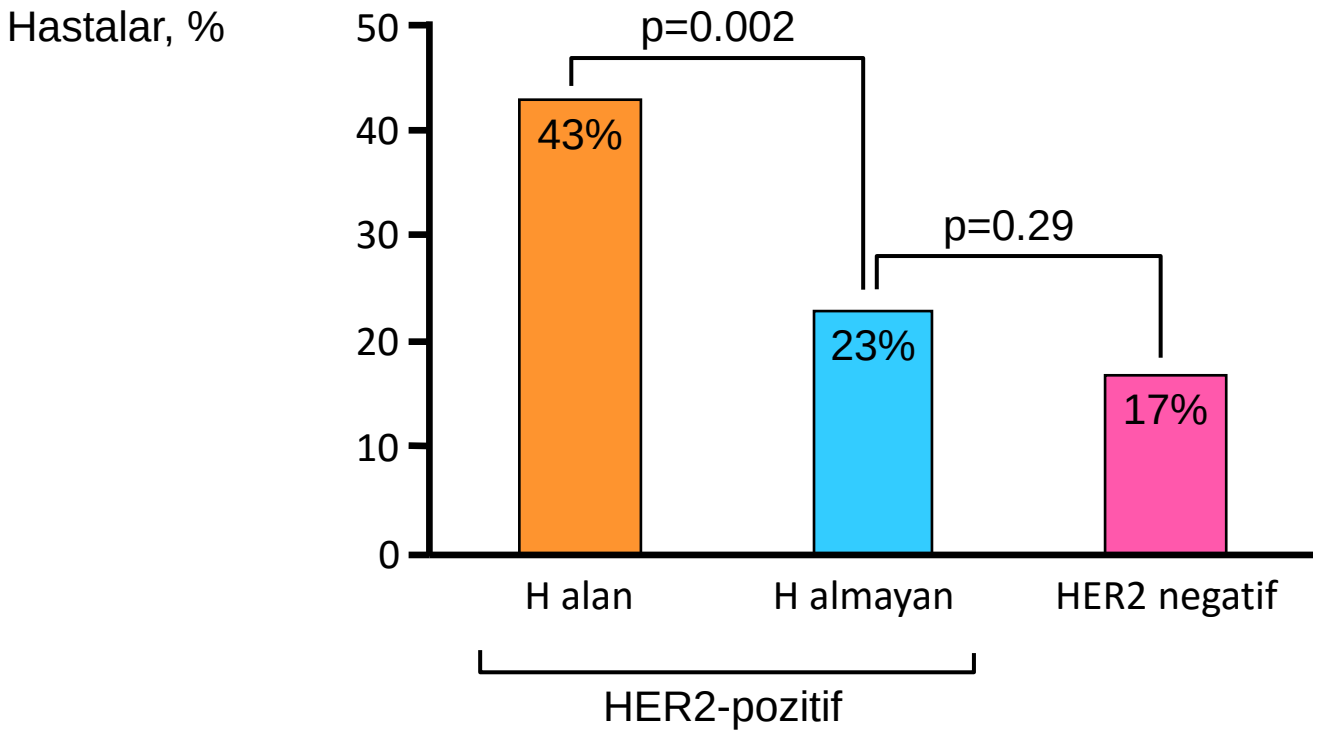
Primer tümörde pCR: ITT popülasyon*



* Tedavi edilmesi planlanan grubun analizi

Gianni L, et al. SABC Sempozyumu, Genel Oturum 3, 12 Aralık 2008

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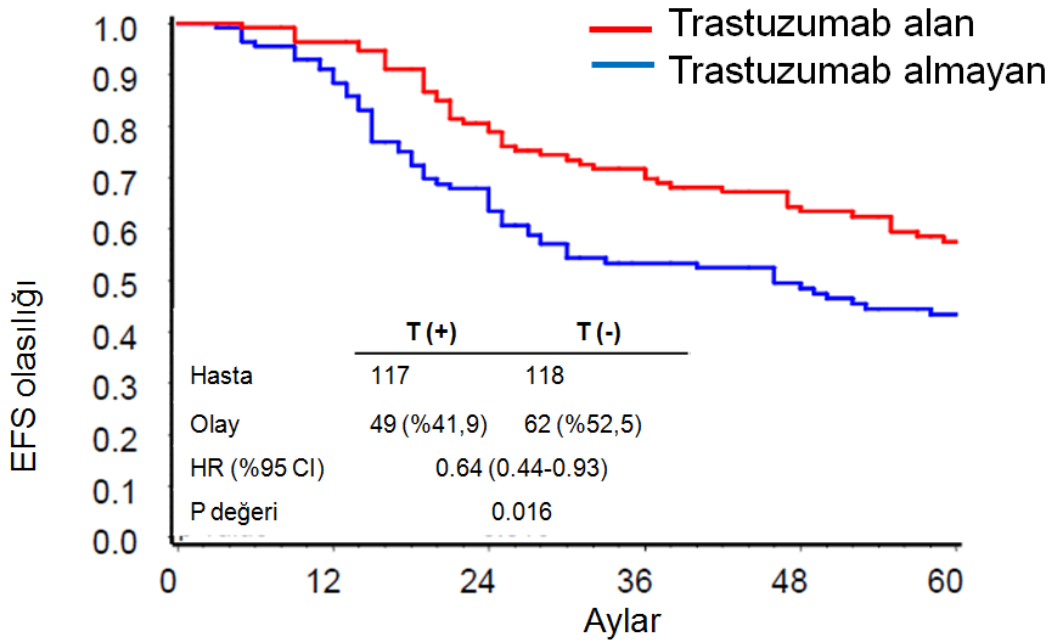
EFS: HER2 (+) grup



Gianni L, et al. **Lancet Oncol 2014; 15: 640–47**

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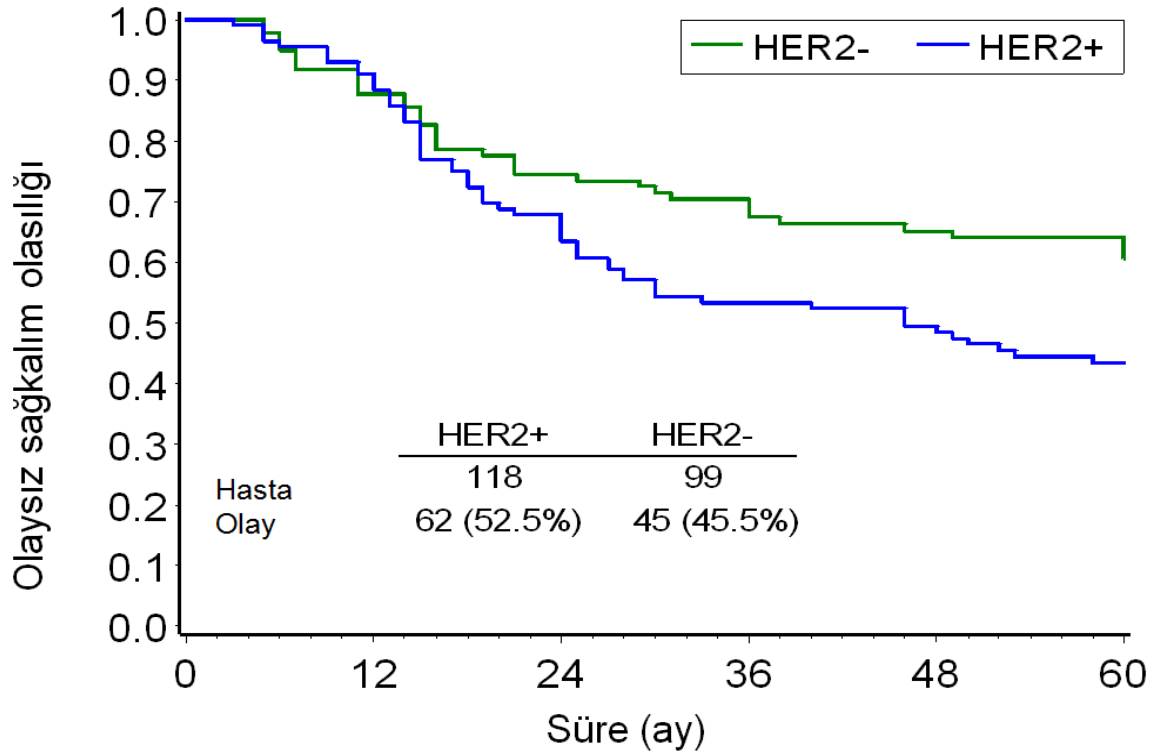
HER2 pozitif

EFS analizi
HER2 (+) (trastuzumab almayan) vs HER2 (-) Hastalar



Gianni L, et al. Lancet 2010

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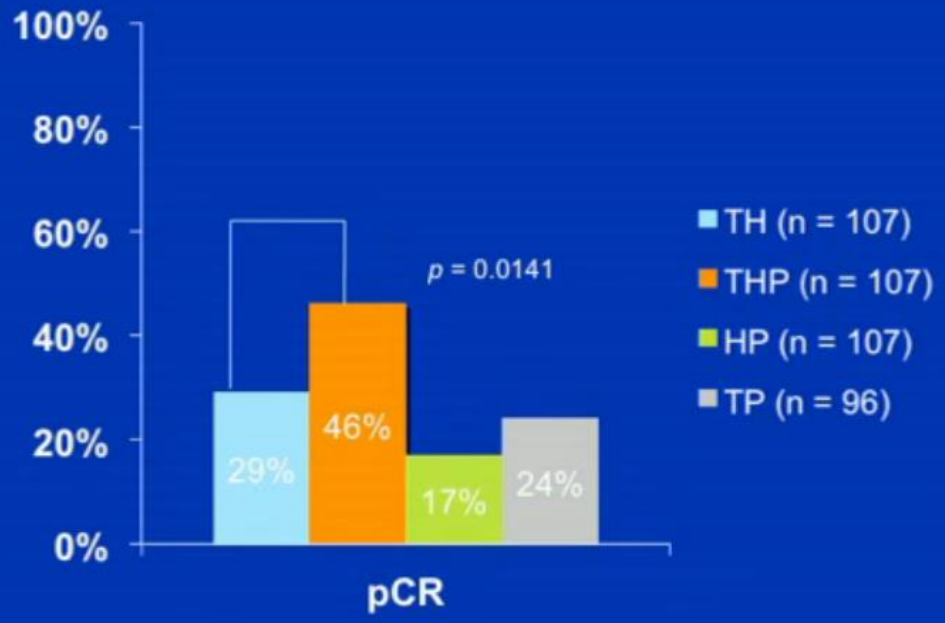
HER2 pozitif

NEOSPHERE Primary Outcome Measure: pCR



T = docetaxel; H = trastuzumab, P = pertuzumab

* Pathologic complete response (pCR) rate defined as the absence of invasive cancer in the breast at the time of surgery

Gianni L et al. *Lancet Oncol* 2012;13(1):25-32.

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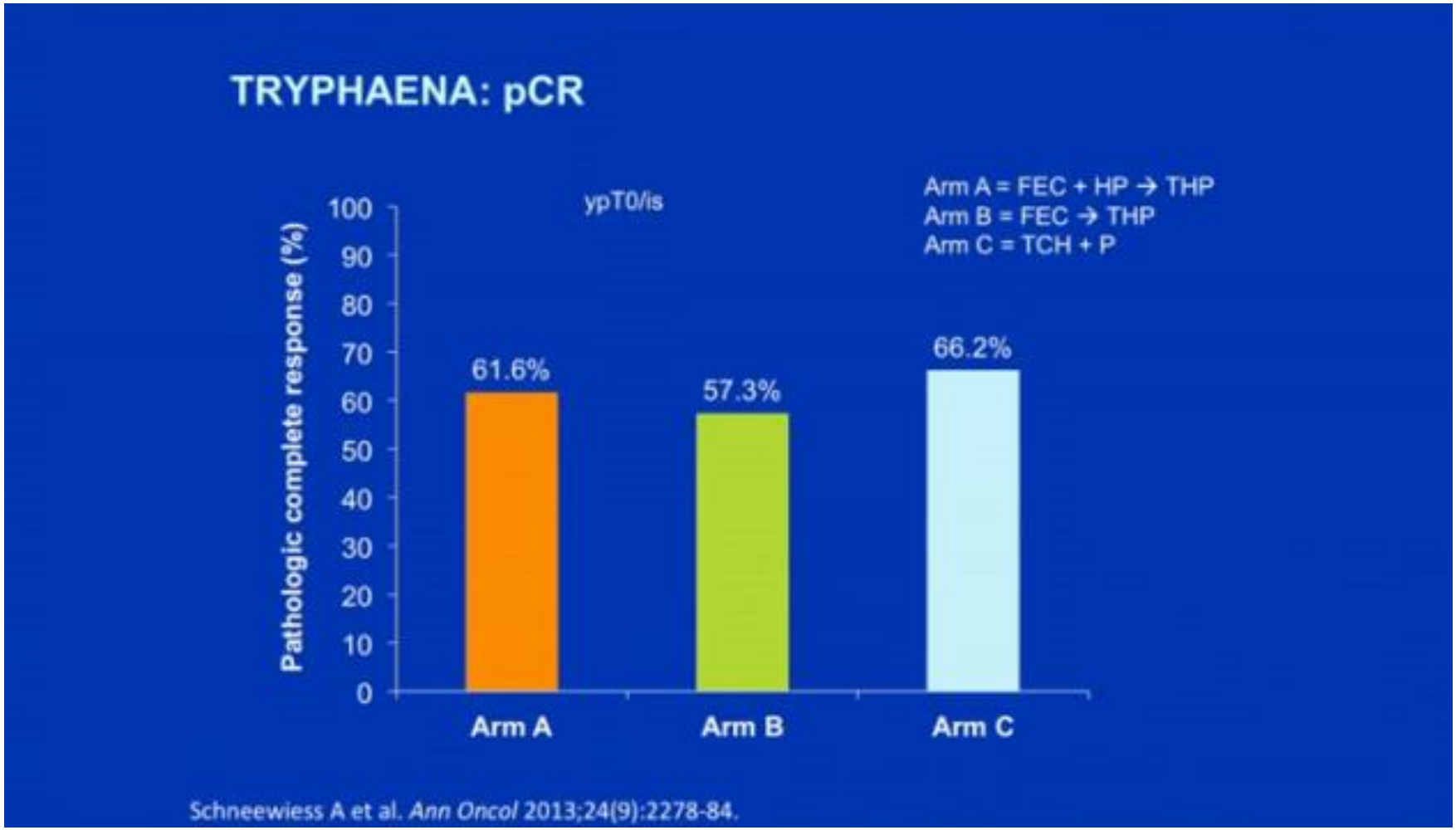
HER2 pozitif



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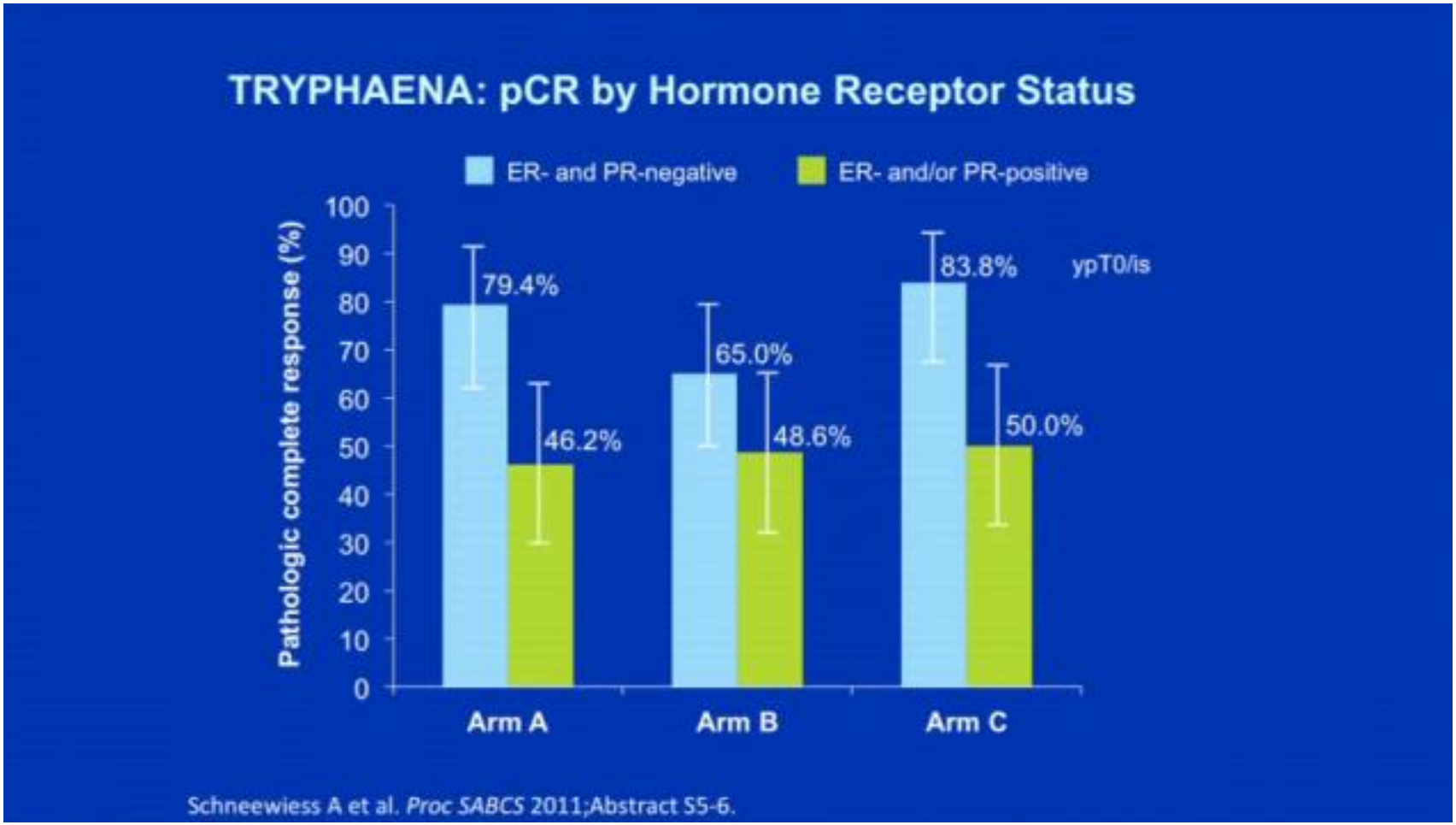
HER2 pozitif



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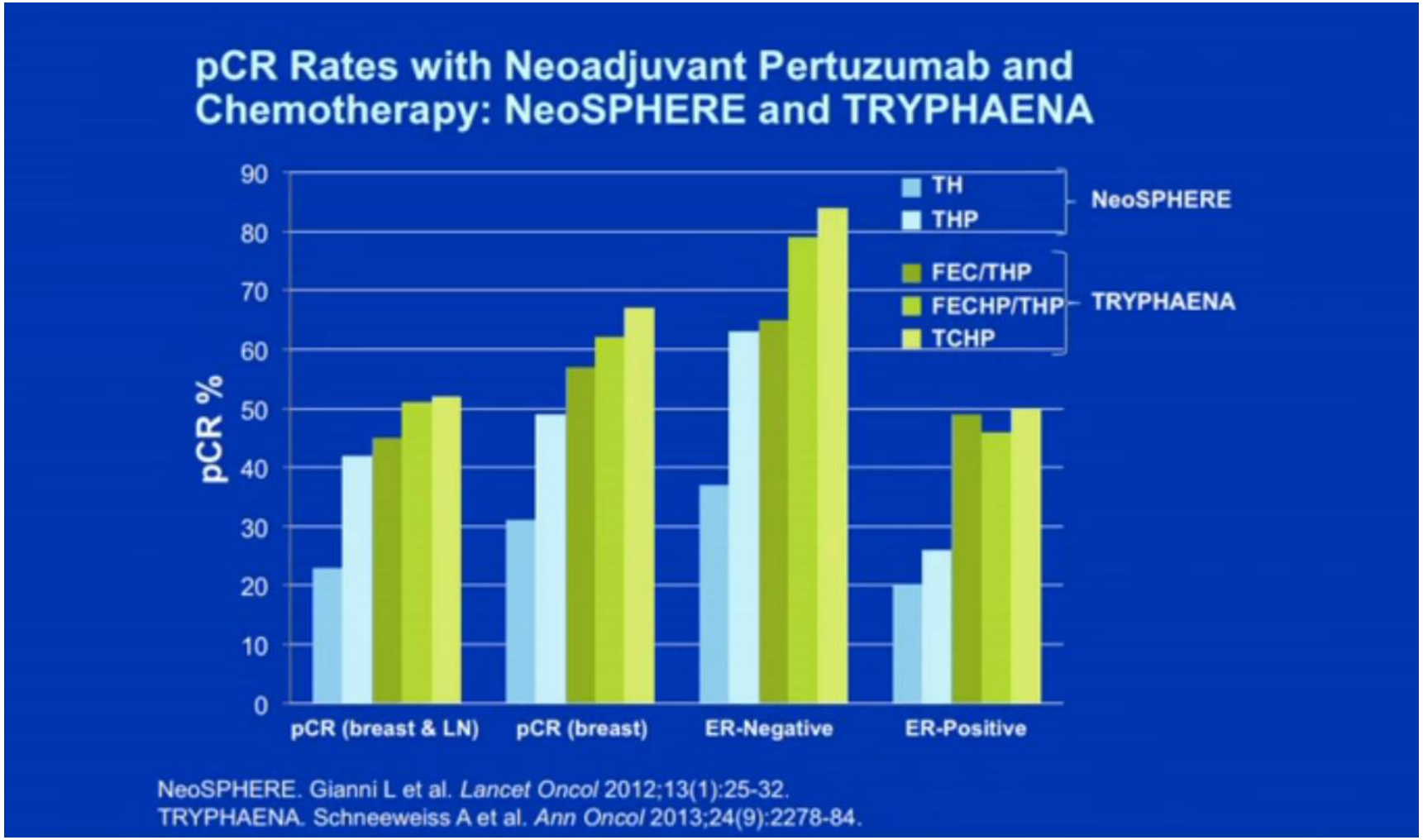
HER2 pozitif



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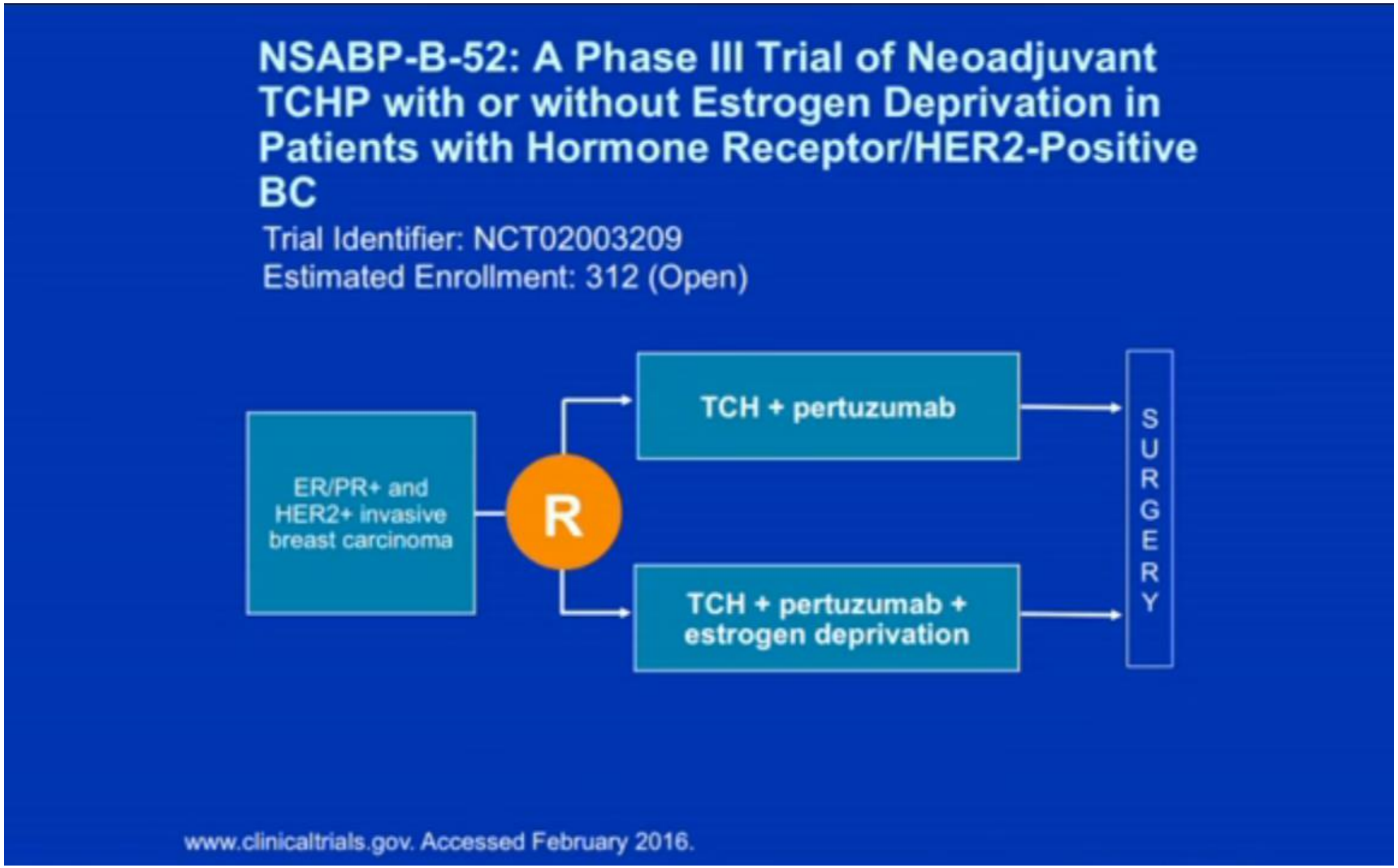
HER2 pozitif



Meme Kanseri Tedavi

HER2 pozitif

CLEOPATRA: Updated Survival Analyses

Clinical parameter	Ptz + T + D (n = 402)	Pla + T + D (n = 406)	HR (*p*-value)
Median overall survival	56.5 mo	40.8 mo	0.68 (<0.001)
Median progression-free survival	18.7 mo	12.4 mo	0.68 (<0.001)

Ptz + T + D = pertuzumab + trastuzumab + docetaxel
Pla + T + D = placebo + trastuzumab + docetaxel

Swain SM et al. *N Engl J Med* 2015;372(8):724-34.

Meme Kanseri Neoadjuvan Tedavi
Triple Negatif

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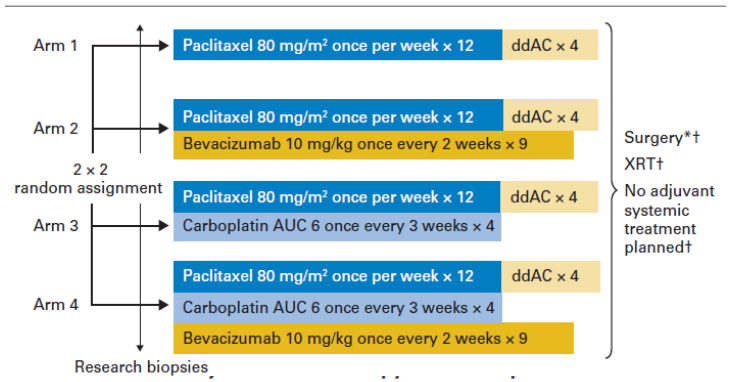
Triple Negatif



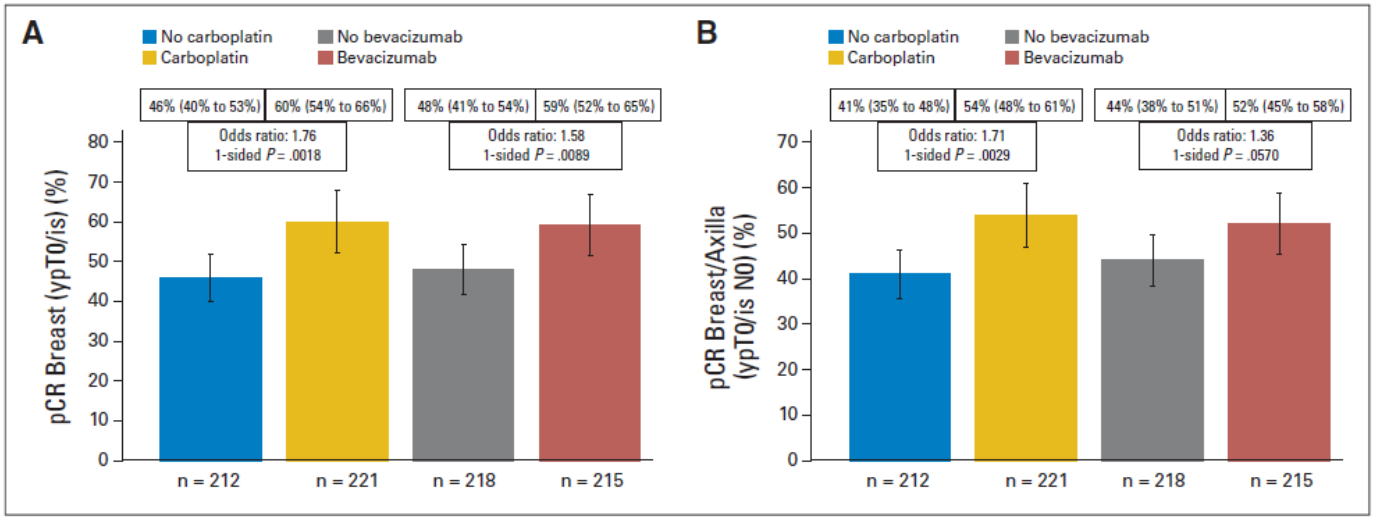


Fig 2. (A) Pathologic complete response (pCR) breast (ypT0/is); (B) pCR breast/axilla (ypT0/is N0); 95% CIs shown in parentheses.

Carboplatine, triple negatif hastalarda neoadjuvan tedaviye eklenmesi pCR artırır, DFS ve OS üzerine etkisi bilinmediğinden kılavuzlar rutin önermez

CALGB 40603, JCO 2014

Meme Kanseri Neoadjuvan Tedavi
HR+/HER2-

Table 2. Reductions in Relative Risks of Recurrence and Death and Absolute Differences in 5-Year Disease-Free and Overall Survival, According to ER Status*

Study and ER Status	Reduction in Risk, (95% Confidence Interval)†		Absolute Difference in 5-Year Survival, %‡	
	Recurrence	Death	Disease-Free	Overall
8541 (high dose vs low dose)				
ER-negative	21 (9 to 31)	17 (4 to 29)	13.9	6.6
ER-positive	9 (–6 to 22)	6 (–11 to 20)	6.6	4.0
9344 (paclitaxel vs no paclitaxel)				
ER-negative	25 (12 to 36)	24 (10 to 37)	8.2	7.4
ER-positive	12 (–3 to 25)	11 (–8 to 26)	2.1	0.0
9741 (every 2 wk vs every 3 wk)				
ER-negative	24 (1 to 42)	28 (1 to 47)	9.1	7.4
ER-positive	8 (–20 to 29)	8 (–28 to 35)	2.8	–0.2
Overall (every 2 wk in 9741 vs low dose in 8541)				
ER-negative*	55 (37 to 68)	55 (38 to 69)	22.8	16.7
ER-positive*	26 (–4 to 48)	23 (–17 to 49)	7.0	4.0

Abbreviation: ER, estrogen-receptor; CAF, cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil.

*The interaction between higher chemotherapy and ER status was assessed using proportional hazards model with added terms for study and main effects for higher chemotherapy and ER status. The interaction was statistically significant ($P = .02$ for recurrence and $P = .05$ for survival) for the overall comparison but not when comparing the studies separately.

†Relative risks were assessed from multivariate proportional hazards models (adjusted for menopausal status, number of positive axillary lymph nodes, and tumor size).

‡Absolute differences for the individual studies were estimated from Kaplan-Meier survival curves. Absolute differences overall were calculated from the relative risk reduction comparing patients in low-dose CAF of study 8541 vs those patients modeled as though receiving biweekly doxorubicin and cyclophosphamide followed by paclitaxel as in study 9741 (see Figure 5 as regards disease-free survival).

Berry Da, JAMA;2006

Meme Kanserinde Neoadjuvan Hormonal Tedavi

Table 1 Summary of the letrozole P024, IMPACT and PROACT trials

	Letrozole P024	IMPACT	PROACT
	Postmenopausal women with HR+ breast cancer		
	337 randomised	**330 randomised**	**451 randomised**
Patient characteristics at baseline	None were BCS candidates at baseline; 14% deemed inoperable	Pretreatment surgical assessment available for 220 patients – 96 eligible for BCS	386 of the patients either required a mastectomy or were deemed inoperable at baseline
Definition of HR positivity	ER/PgR staining >10%	ER staining >1%	'ER+/PgR+'
Neoadjuvant endocrine therapy	L for 4 months T for 4 months	A for 12 weeks A+T for 12 weeks T for 12 weeks	A for 3 months T for 3 months
Concomitant chemotherapy?	No	—	Yes
Primary end point	Clinical response by palpation	Overall response by caliper measurements	Overall response by ultrasound measurements
Response (per primary end point)	55% (L) *vs* 36% (T); $P<0.001$	37% (A) *vs* 39% (A+T) *vs* 36% (T)	39.5% (A) *vs* 35.4% (T)
Rate of down staging to BCS	45% (L) *vs* 35% (T); $P=0.022$	44%(A) *vs* 24% (A+T) *vs* 31% (T)	43.0% (A) *vs* 30.8% (T) in improved feasible surgery in hormone therapy-only group ($n=314$)

Abbreviations: A = anastrozole 1 mg daily; BCS = breast conserving surgery; ER = oestrogen receptor; HR = hormone receptor; IMPACT = Immediate Preoperative Anastrozole, Tamoxifen or Combined with Tamoxifen; L = letrozole 2.5 mg daily; PROACT = Preoperative 'Arimidex' Compared to Tamoxifen; PgR = progesterone receptor; T = tamoxifen 20 mg daily.

Chia Y et al, Br J Cancer 2010

Meme Kanserinde Tedavi
HR+/HER2-

Table 2. Multivariate Analysis.*

End Point	Hazard Ratio (95% CI)	P Value
Recurrence, second primary breast cancer, second primary nonbreast invasive cancer, or death without recurrence of cancer		
Tumor grade		0.13
Intermediate vs. low	1.56 (0.92–2.63)	
High vs. low	2.05 (0.92–4.55)	
Tumor size >2 cm vs. ≤2 cm	1.17 (0.71–1.92)	0.54
Age		0.07
51–60 yr vs. ≤50 yr	0.87 (0.46–1.64)	
61–75 yr vs. ≤50 yr	1.53 (0.87–2.70)	
Lumpectomy vs. mastectomy	0.63 (0.38–1.06)	0.07
Recurrence at a distant site		
Tumor grade of high or intermediate vs. low†	3.83 (0.48–30.69)	0.14
Tumor size >2 cm vs. ≤2 cm	1.55 (0.38–6.31)	0.55
Age		0.27
51–60 yr vs. ≤50 yr	1.28 (0.12–4.22)	
61–75 yr vs. ≤50 yr	3.49 (0.42–29.16)	
Lumpectomy vs. mastectomy	0.57 (0.12–2.82)	0.47
Recurrence at any site		
Tumor grade		0.02
Intermediate vs. low	8.07 (1.06–61.45)	
High vs. low	4.73 (0.29–76.42)	
Tumor size >2 vs. ≤2 cm	1.06 (0.33–3.33)	0.93
Age		0.33
51–60 yr vs. ≤50 yr	0.41 (0.10–1.73)	
61–75 yr vs. ≤50 yr	0.98 (0.32–3.02)	
Lumpectomy vs. mastectomy	0.93 (0.32–2.71)	0.89

* Data from 1578 of 1626 patients with a recurrence score of 0 to 10 were included in these analyses. Data from 48 patients for whom the histologic grade of the tumor was not reported were excluded from these analyses.

† Data from patients with a high tumor grade and those with an intermediate tumor grade were combined for the analysis of freedom from the recurrence of breast cancer at a distant site because of the small number of events.

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d affiliations are listed in the Ap-
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re Medical Center, 1695 East-
Rd., Bronx, NY 10461, or at
@montefiore.org.

e was published on September 28,
NEJM.org.

056/NEJMoa1510764

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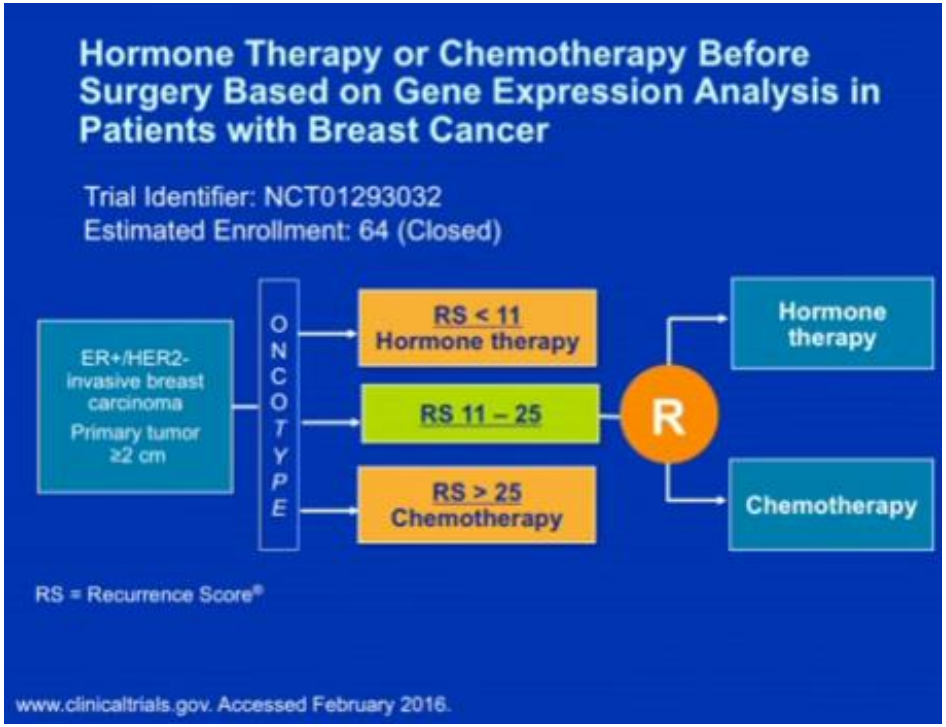

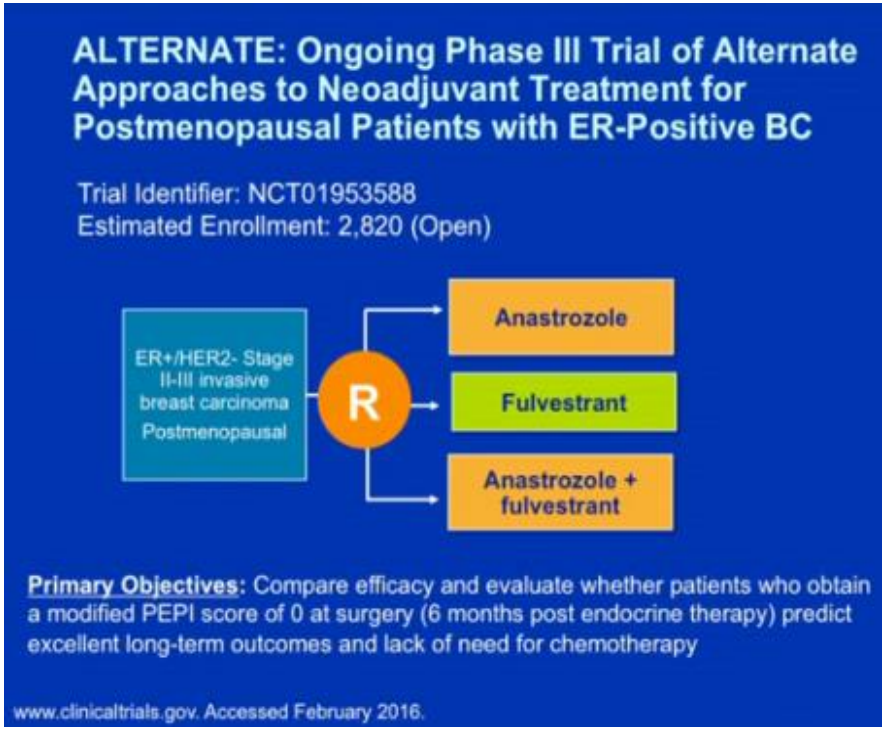

Meme Kanseri Cerrahi Öncesi
Aksila Değerlendirilmesi

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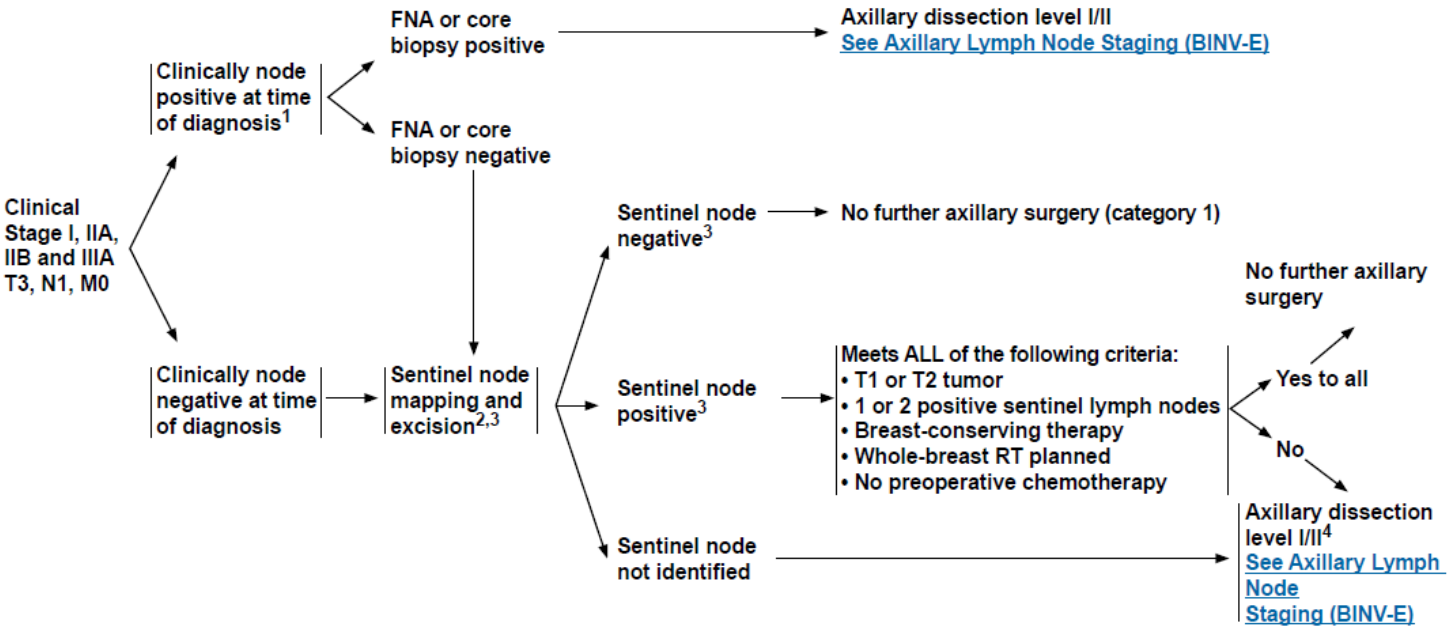
SURGICAL AXILLARY STAGING - STAGE I, IIA, IIB and IIIA T3, N1, M0



[1]Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound-guided FNA or core biopsy in determining if a patient needs axillary lymph node dissection.
[2]Sentinel lymph node mapping injections may be peritumoral, subareolar, or subdermal.
[3]Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.
[4]For patients with clinically negative axillae who are undergoing mastectomy and for whom radiation therapy is planned, axillary radiation may replace axillary dissection level I/II for regional control of disease.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Meme Kanseri Tedavi Sonrası
Aksila Değerlendirilmesi

Multi-Institutional Registry

- 99 surgeons enrolled 806 patients
- Attempted SLN dissection followed by ALND in all patients
- Single-agent (blue dye or radiocolloid alone (n=244),or dual-agent (n=562)

	Single-agent	Dual-agent	P value
SLN ID-rate	86%	90%	ns
# SLN	1.5	2.1	.001
False Negative Rate	11.8%	5.8%	<.05

McMasters K, et al. *J Clin Oncol* 2000;18(13):2560-2566

Meme Kanseri Tedavi Sonrası
Aksila Değerlendirilmesi

Cancer. 2006 Jan 1;106(1):4-16.

Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma: a metaanalysis.

Kim T[1], Giuliano AE, Lyman GH.

Author information

Abstract

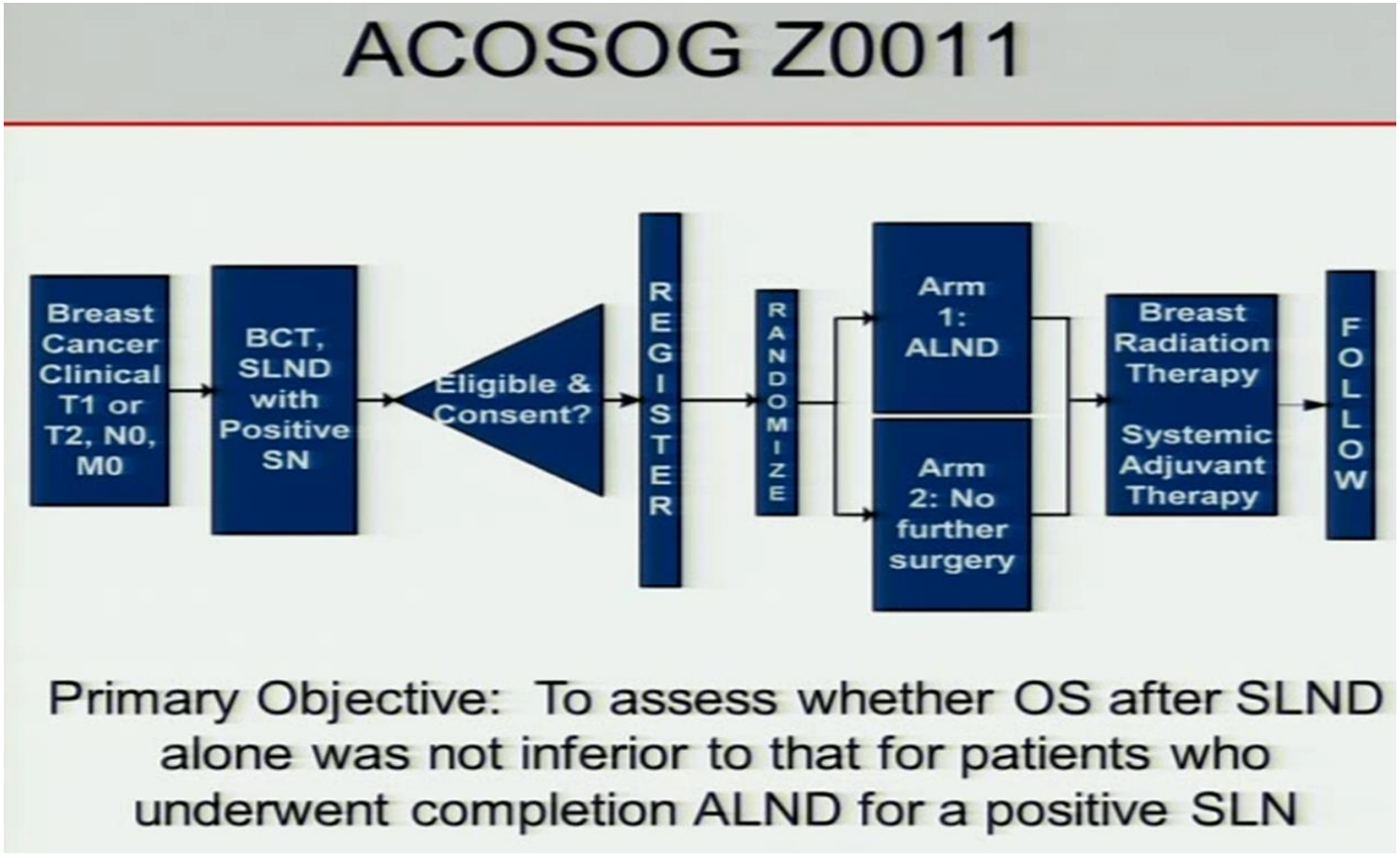
BACKGROUND: Lymphatic mapping with sentinel lymph node biopsy has the potential for reducing the morbidity associated with breast carcinoma staging. It has become a widely used technology despite limited data from controlled clinical trials.

METHODS: A systematic review of the world's literature of sentinel lymph node (SLN) biopsy in patients with early-stage breast carcinoma was undertaken by using electronic and hand searching techniques. Only studies that incorporated full axillary lymph node dissection (ALND), regardless of SLN results, were included. Individual study results along with weighted summary measures were estimated using the Mantel-Haenszel method. The correlations of outcomes with the study size, the proportion of positive lymph nodes, the technique used, and the study quality were evaluated.

RESULTS: Between 1970 and 2003, 69 trials were reported that met eligibility criteria. Of the 8059 patients who were studied, 7765 patients (96%) had successfully mapped SLNs. The proportion of patients who had successfully mapped SLNs ranged from 41% to 100%, with > 50% of studies reporting a rate < 90%. Lymph node involvement was found in 3132 patients (42%) and ranged from 17% to 74% across studies. The false-negative rate (FNR) ranged from 0% to 29%, averaging 7.3% overall. Eleven trials (15.9%) reported an FNR of 0.0, whereas 26 trials (37.7%) reported an FNR > 10%. Significant inverse correlations were observed between the FNR and both the number of patients studied ($r = -0.42$; $P < 0.01$) and the proportion of patients who had successfully mapped SLNs nodes ($r = -0.32$; $P = 0.009$).

CONCLUSIONS: Lymphatic mapping with SLN biopsy is used widely to reduce the complications associated with ALND in patients with low-risk breast carcinoma. This systematic review revealed a wide variation in test performance.

Meme Kanseri Cerrahi Öncesi
Aksila Değerlendirilmesi



6.3 yıllık takip sonucu, sağkalım, lokal ve lokoregional nüks açısından iki kol arasında fark yok

Meme Koruyucu Cerrahi Sonrası
Adjuvan RT

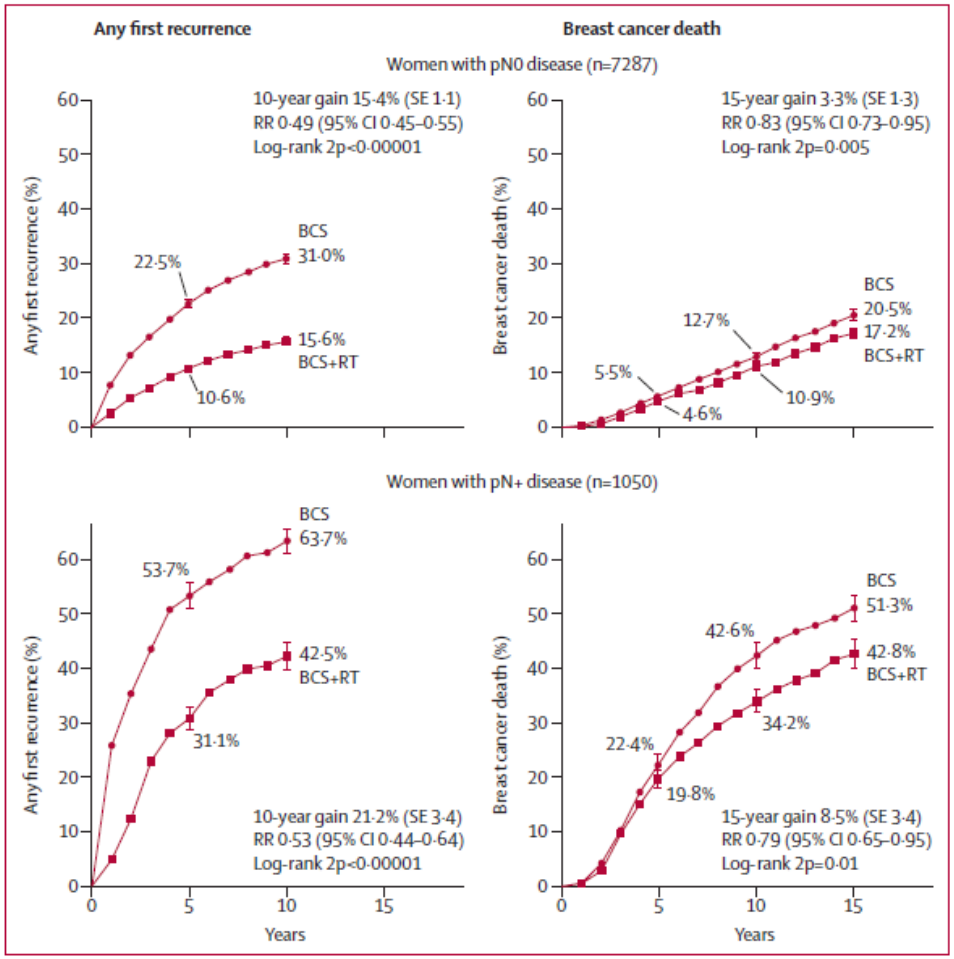
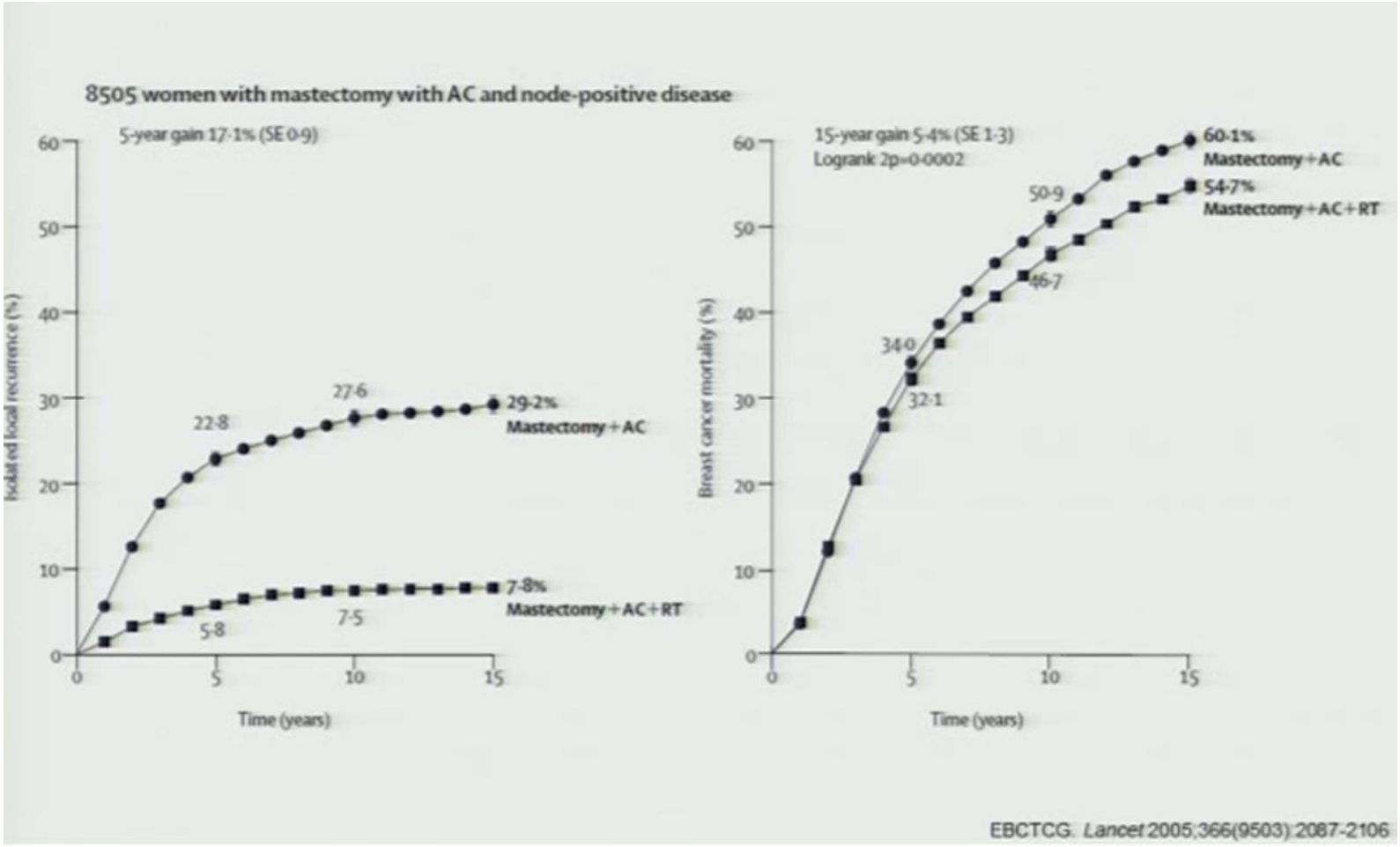


Figure 2: **Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risk of breast cancer death in women with pathologically verified nodal status**

Vertical lines indicate 1 SE above or below the 5, 10, and 15 year percentages. Further details are in webappendix pp 6–7. pN0=pathologically node-negative. pN+=pathologically node-positive. RR=rate ratio. Rate ratios in this figure include all available years of follow-up.

EBCTCG, Lancet 2011

Meme Kanseri Cerrahi Sonrası
Aksila pozitif Adjuvan RT



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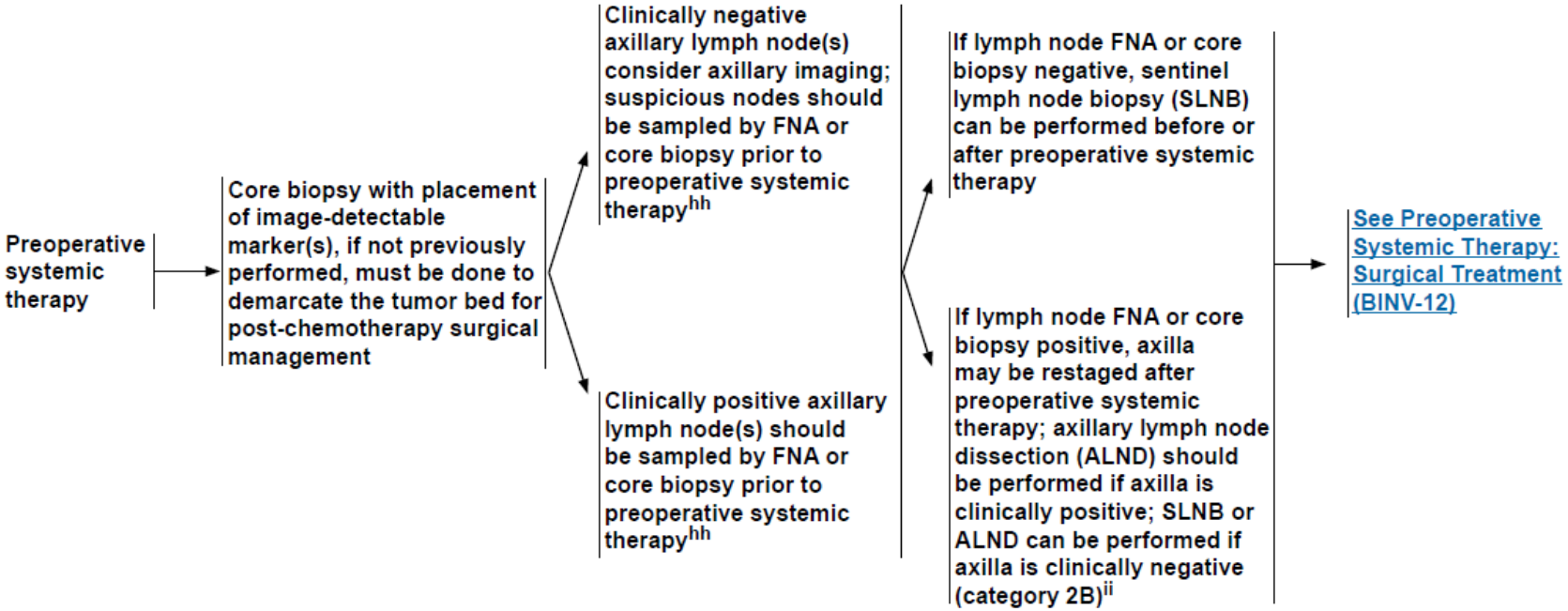
Discussion

PREOPERATIVE SYSTEMIC THERAPY: BREAST AND AXILLARY EVALUATION



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Aksila Değerlendirilmesi

FNR with Sentinel Node Biopsy After NAC in Patients with Node-Positive Breast Cancer

Clinical trial	Patient population	FNR
ACOSOG Z1071	N = 525 patients with cN1 disease and ≥2 lymph nodes examined	12.6%
SENTINA	N = 592 cN1-2 patients converted to cN0 after NAC	14.2%
SN FNAC	N = 153 patients with cN1-2 disease	8.4%

Boughey JC et al. *JAMA* 2013;310(14):1455-61.
Kuehn T et al. *Lancet Oncol* 2013;14(7):609-18.
Boileau J-F et al. *J Clin Oncol* 2015;33(3):258-64.

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Aksila Değerlendirilmesi

ASCOSOG Z1071: FNR and Number of SLNs Examined

Number of SLNs examined	FNR	*p*-value*
2	19/90 (21.1%)	0.007
3 or more	20/220 (9.1%)	

* Fisher exact test

Boughey JC et al. *JAMA* 2013;310(14):1455-61.

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Aksila Değerlendirilmesi

GANEA: Sentinel Lymph Node (SLN) Biopsy After Neoadjuvant Chemotherapy (NAC)

Patient group	Detection rate	*p*-value*	False-negative rate	*p*-value*
All patients (n = 195)	90.1%	0.008	11.5%	0.66
N0 patients (n = 130)	94.6%		9.4%	
N1 patients (n = 65)	81.5%		15.0%	

* Chi square or Fisher exact test. N0 = patients with axilla clinically free of involved nodes; N1 = patients with clinical axillary suspicious nodes not fixed

"The detection rate, false-negative rate, and accuracy do not differ from those obtained in the case of early breast cancer without NAC, thus demonstrating the feasibility of SLN biopsy after NAC."

Classe J-M et al. *J Clin Oncol* 2009;27(5):726-32.

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Aksila Değerlendirilmesi

Comparison of False-Negative Rates (FNR) Between Sentinel Node Multicenter Studies

Study	FNR	(SN-/N+)
Multicenter SB-2 trial	11%	(13/114)
Italian randomized trial	9%	(8/91)
Ann Arundel	13%	(25/193)
University of Louisville	7%	(24/333)
NSABP-B-32 randomized trial	10%	(75/766)
NSABP-B-27 (after NC)	**11%**	**(15/140)**
Meta-analysis (after NC)	**12%**	**(65/540)**

Krang DN. *Surg Oncol* 1993; Veronesi U. *N Engl J* Med 2003; Mc Masters KM. *J Clin Oncol* 2000; Mamounas EP. *J Clin Oncol* 2005; Tafra L. *Am J Surg* 2001; Xing Y. *Br J Surg* 2005; Jualian JB. SABCS 2004.

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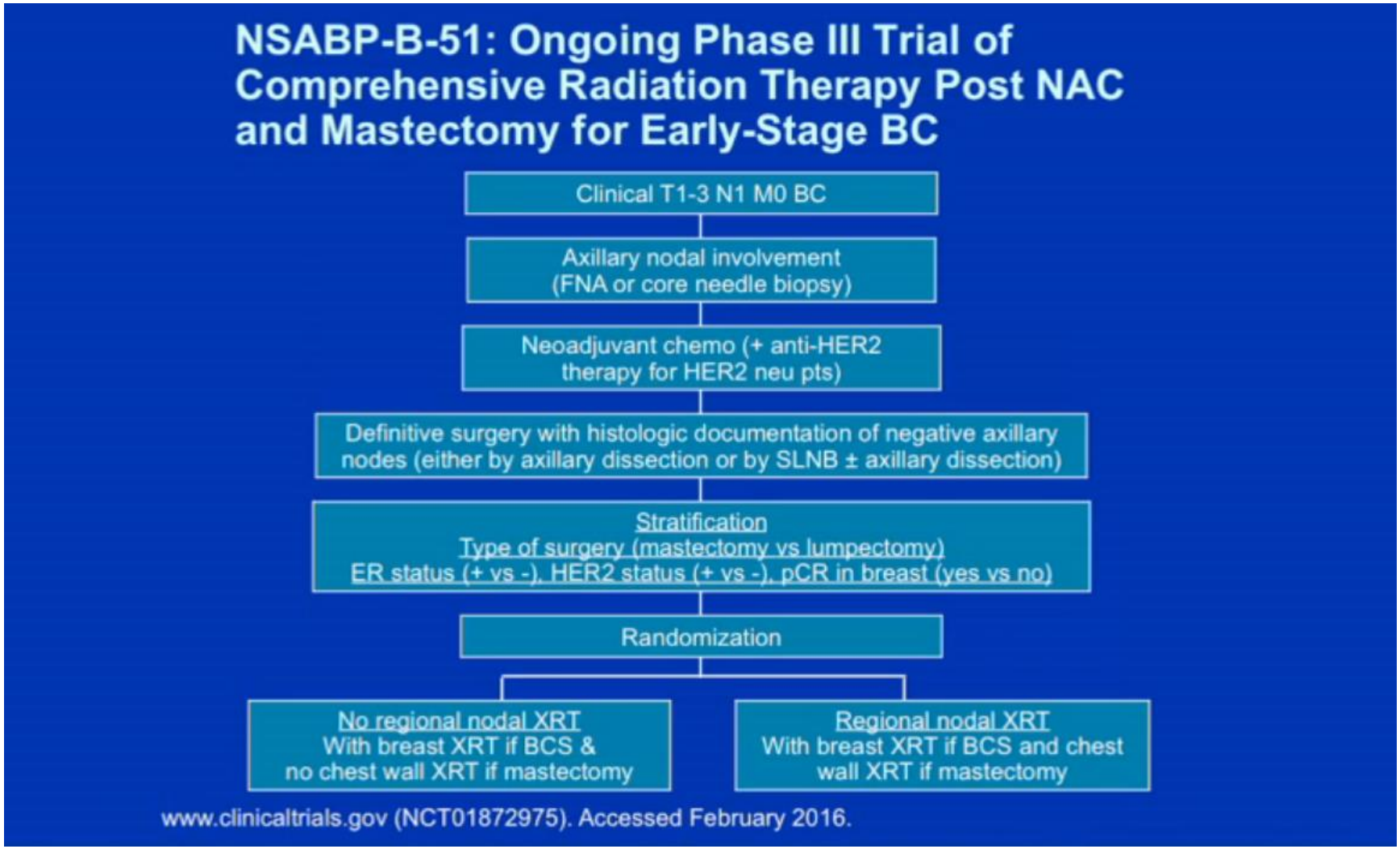
Aksila Değerlendirilmesi



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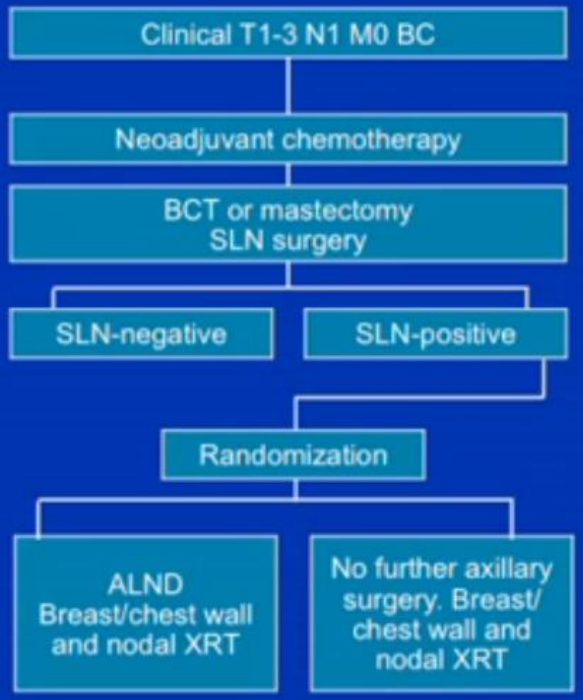
Aksila Değerlendirilmesi

Alliance A011202: Ongoing Phase III Trial of Axillary Lymph Node Dissection (ALND) in Patients Who Have SLN-Positive Disease After NAC



www.clinicaltrials.gov (NCT01901094); Accessed February 2016.