interdisipliner onkoloji derneği

GENÇLERLE ONKOLOJİYE BAKIŞ KONGRESİ

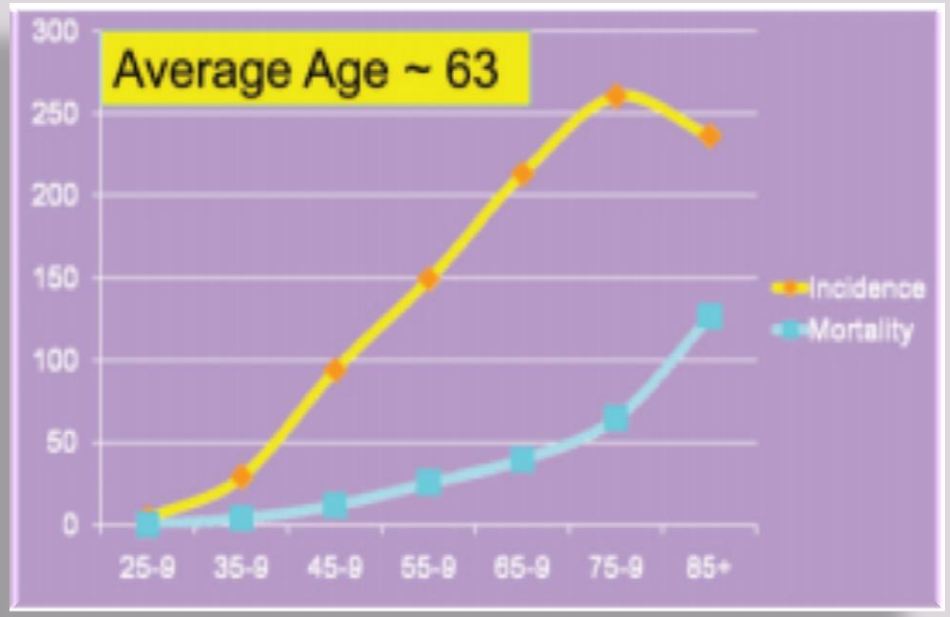
T2N1M0 TRİPLE NEGATİF OPERE MEME KANSERİ POSTMENAPOZAL,KAH ve KBY/DİYALİZ hastasında ADJUVAN TEDAVİ

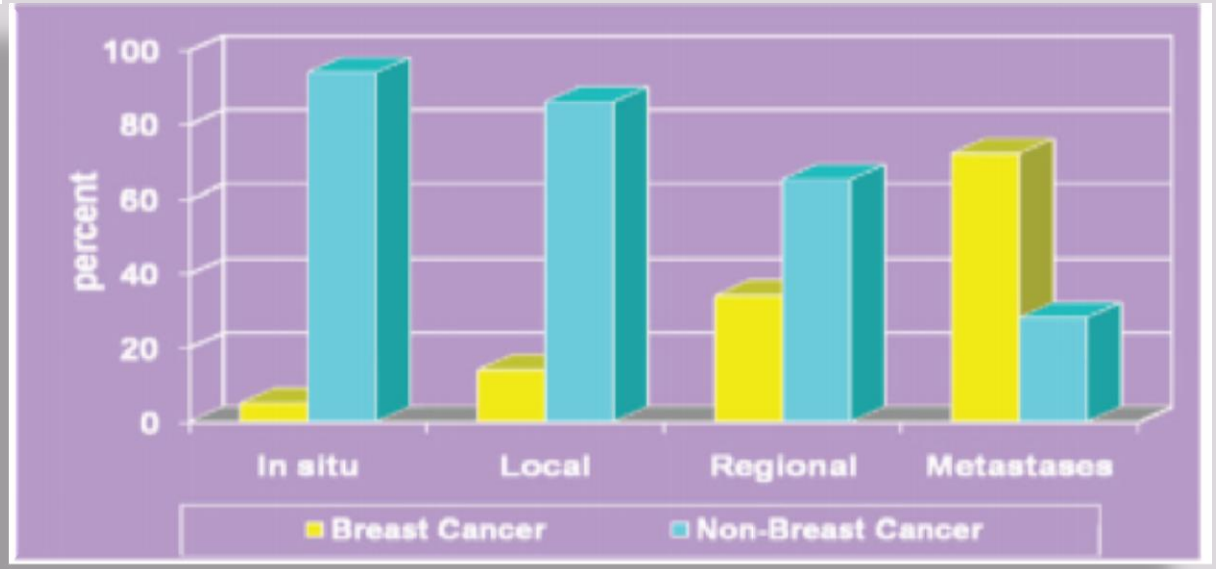
DR NİLÜFER AVCI
VM MEDİKAL PARK BURSA
MEDİKAL ONKOLOJİ

15-18 ŞUBAT 2018

The Oncologist®

Coming of Age: Breast Cancer in Seniors





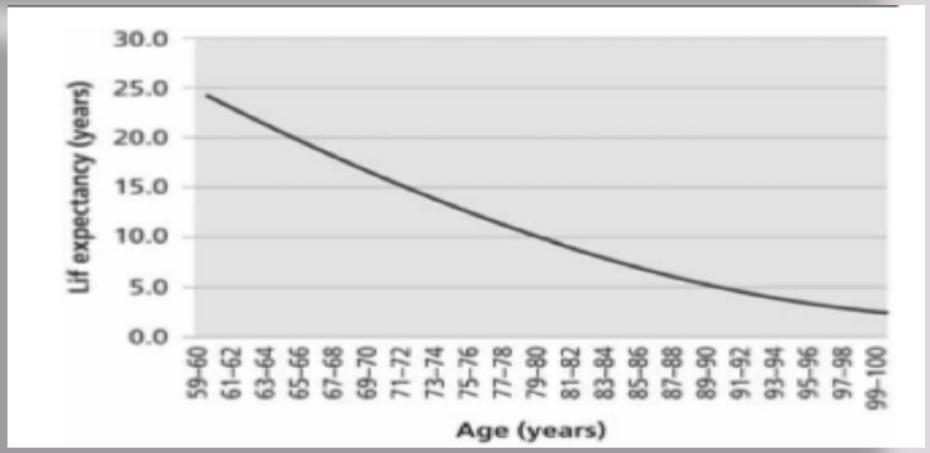
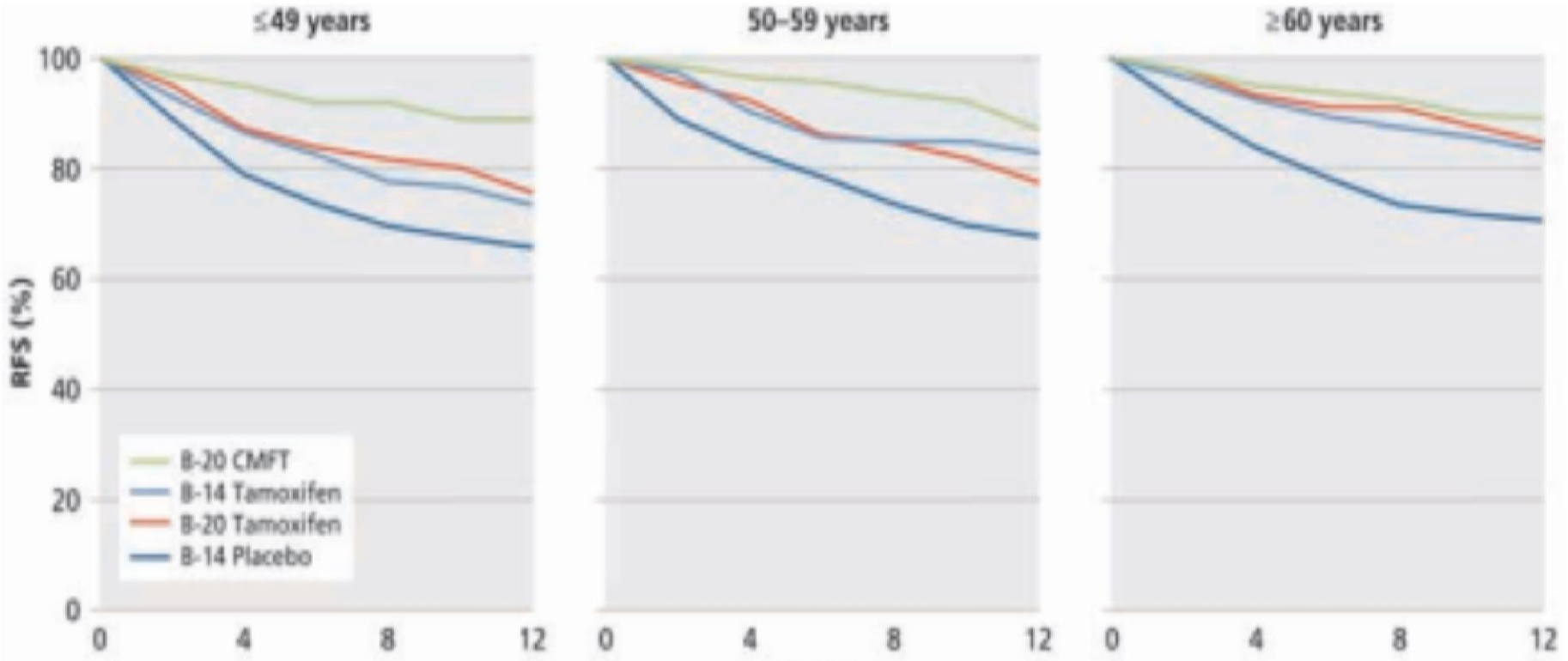


Figure 1. Surveillance, Epidemiology and End Results 2002–2006: Breast cancer incidence and mortality rates.

Figure 4. Cause of death after approximately 28 years of follow-up: white women aged ≥70 years with breast cancer (395,000 patients 1973–2000).

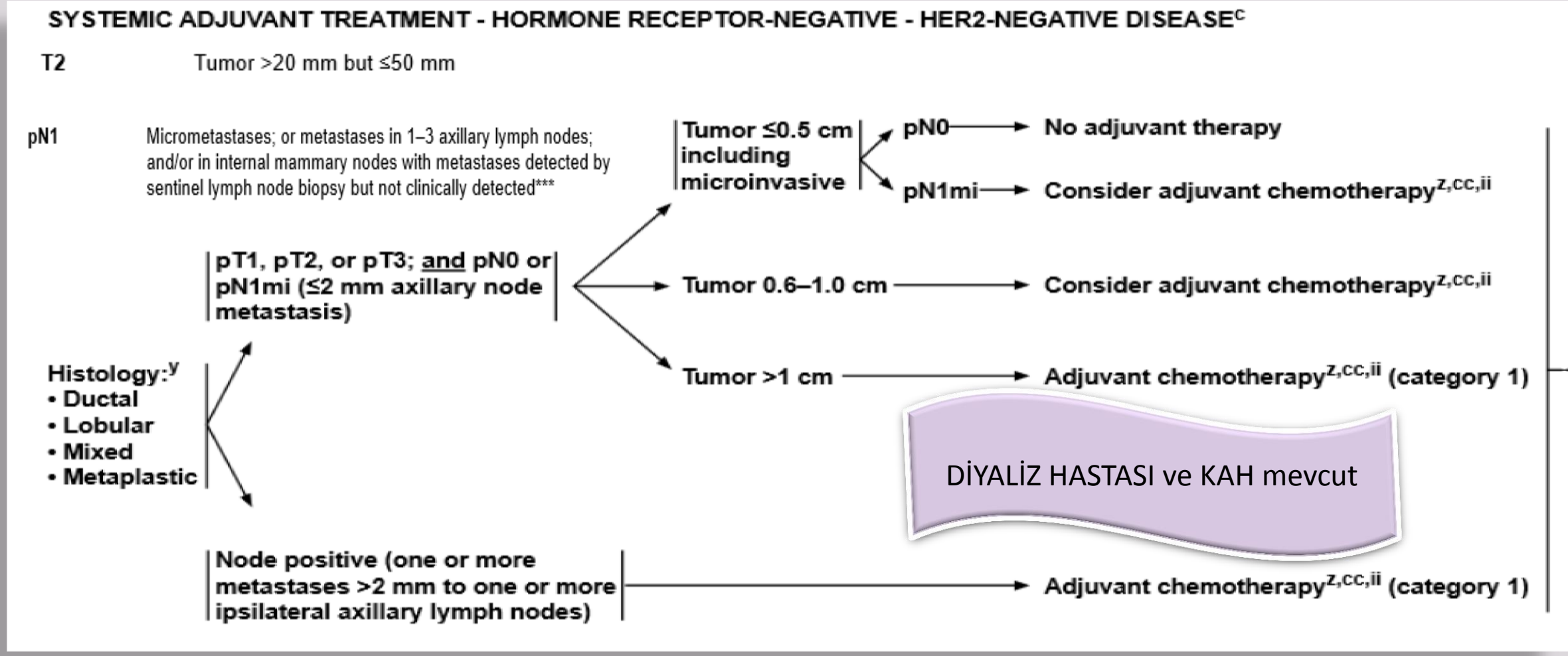


Number at risk									
B-14 Placebo	317	261	215	354	290	238	405	313	252
B-14 Tamoxifen	362	306	263	358	307	258	462	388	303
B-20 Tamoxifen	288	252	88	188	159	56	187	160	59
B-20 CMFT	324	292	93	195	167	58	178	145	52

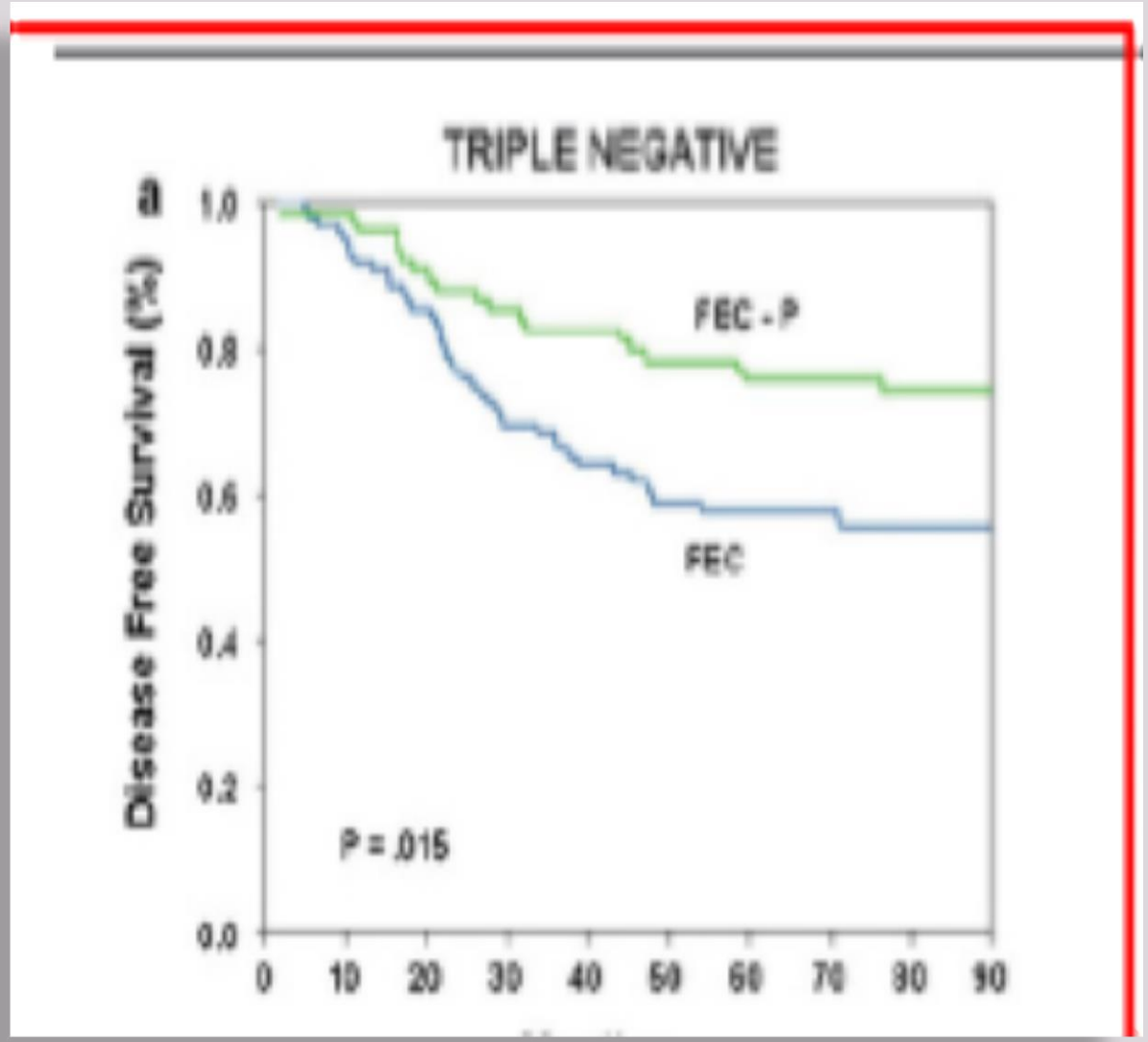
OLGU

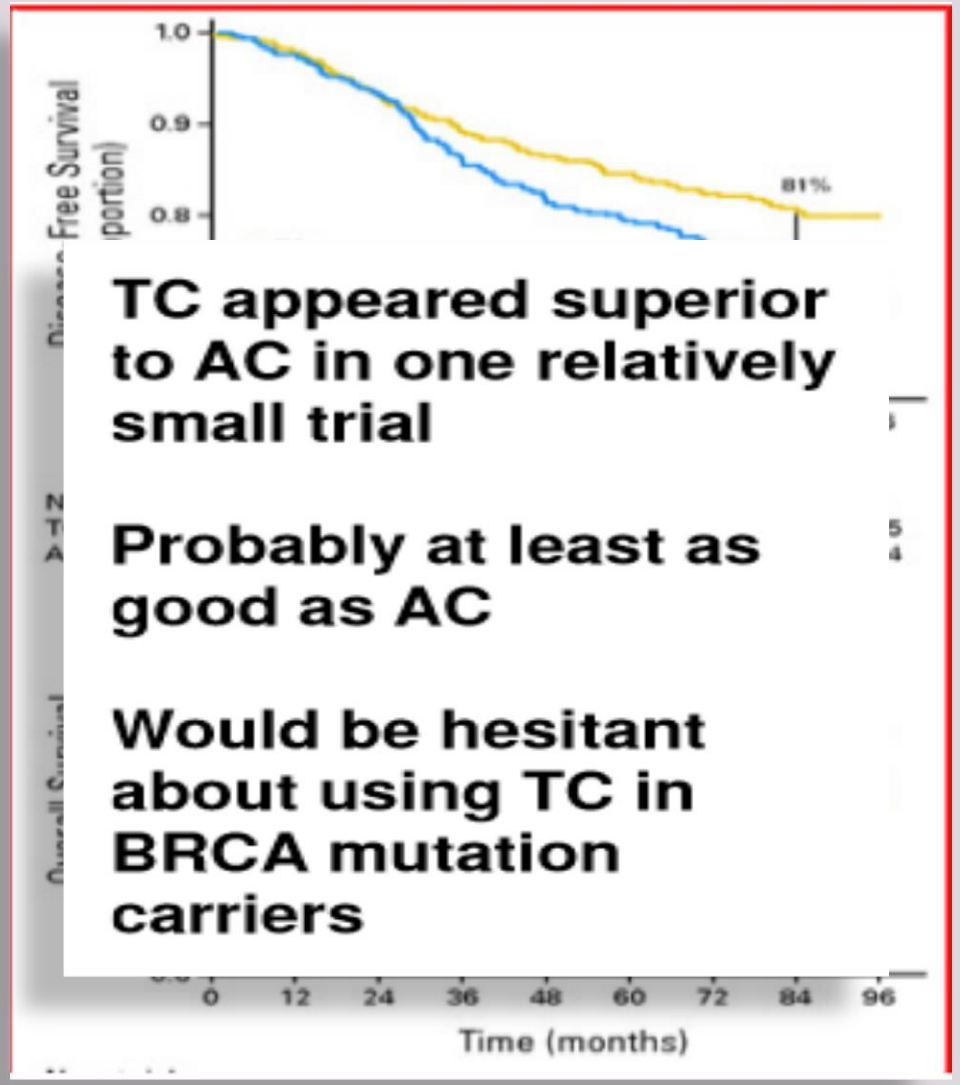
- ✓ 75 yaş, Boy:160cm, Kilo:50kg
- ✓ Hipertansiyon, 2 yıldır Hemodiyaliz programında, KAH
- ✓ Kitle 3.5cm, 2LN+, grade 3, ER-, PR-, HER2-
- ✓ EF:??

T2N1M0,opere triple negatif



NCCN Guidelines Version 4.2017





TC appeared superior to AC in one relatively small trial

Probably at least as good as AC

Would be hesitant about using TC in BRCA mutation carriers

Breast Cancer Res Treat (2010) 123:149–157

Jones, S. et al. J Clin Oncol; 27:1177-1183 2009

- **Standard of Care**
  - based on direct comparisons, subset analyses and considerations of toxicity/tolerability
  - **sequential anthracycline, cyclophosphamide and taxane-based therapy**
  - **arguably ddAC → paclitaxel**
- Alternative regimens
  - Preferred regimen without anthracyclines: TC
  - Preferred regimen without taxanes: AC or CMF
- Neoadjuvant regimens = adjuvant regimens

SİZİN ÖNERİNİZ

- Patients with ESRD undergoing chemotherapy need coordinated care between oncologists, nephrologists and [illegible] to optimise drug delivery and timing of dialysis.
- The decision to initiate an anticancer treatment should be based on a discussion of prognosis and therapy options for both conditions. Frailty scores, like in oncogeriatrics, should be built to optimally adapt cancer treatments in these dialysis patients.
- Drug clearance by dialysis must be taken into account for appropriate chemotherapy timing in order to avoid drug removal, which may result in a loss of efficacy.
- Chemotherapeutic agents without or with limited renal excretion (ie, taxanes and anthracycline) can be given at full doses in patients with ESRD.
- Drugs predominantly eliminated through the kidney, such as cisplatin, should be substitute when equally effective and more manageable agents are available (ie, carboplatin).
- Multiagent chemotherapy is feasible in ESRD; it must be cautiously checked before administration with appropriate dosage adjustment whenever necessary also based on the limited literature in this setting.

kardiyoloji

Breast J. 2017 Nov;23(6):630-637. doi: 10.1111/tbj.12813. Epub 2017 May 9.

Triple-negative breast cancer in the elderly: Prognosis and treatment.

Kaplan HG[1], Malmgren JA[2,3], Atwood MK[1].

Author information

Abstract

Our objective is to chara[illegible] measure mortality risk relative to younger women. We co[illegible]ry TNBC, age 25-93, stage I-III from 1990 to 2014, identified[illegible]ted at diagnosis and follow-up. The Kaplan-Meier method w[illegible]n modeling for relative contribution of patient and clinical characteristics. Of patients, 80% were <65 years (n=612), 13% were 65-74 years (n=100), and 7% were 75 and older (n=5[illegible]ee age group[illegible]-95%, 65-7[illegible]ree age g[illegible] diagnosis year, radiation and chemotherapy treatment, age was not significantly associated with disease-specific mortality. TNBC survival appears equivalent by age despite less aggressive treatment in patients 75 years and older. This may be a result of lower stage at diagnosis and decreased disease virulence resulting in comparative survival despite less treatment.

older patients were less often treated with adjuvant chemotherapy

In Cox regression analysis controlling for stage, histologic and nuclear grade,

diagnosis year, radiation and chemotherapy treatment, age was not significantly associated with disease-specific mortality.

Factor	Tools for assessment
Functional status	Activities of daily living Instrumental activities of daily living Performance status
Comorbidity	Charlson Comorbidity Index Cumulative Illness Rating Scale—G
Socioeconomic issues	
Nutritional status	
Polypharmacy	
Geriatric syndromes	Geriatric Depression Scale Folstein Mini Mental Status

- ✓ **YAŞAM BEKLENTİSİ**
- ✓ **YAŞAM KALİTESİ**
- ✓ **AİLENİN TERCİH**
- ✓ **YAŞLILARDA FARMAKOKİNETİK ve FARMAKODİNAMİK DEĞİŞİKLİKLERE DİKKAT**

Physiologic change
NA damage
mass and hematopoiesis
l reserve of organ systems
estinal absorptive surfaces, gastric
tric secretion
Reduced fat-free mass
Greater anemia
Decreased liver mass
Decreased nephrons mass

REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 18 (2013) 26–33

Table 4 Independent Risk Factors for 4-Year Mortality

Risk Factor	Adjusted OR (95% CI)*	Points
Demographics		
Age (y)		
60–64	1.9 (1.4–2.5)	1
65–69	2.8 (2.1–3.7)	2
70–74	3.7 (2.8–4.9)	3
75–79	5.4 (4.1–7.1)	4
80–84	8.3 (6.3–11.0)	5
≥ 85	16.2 (12.2–21.6)	7
Male gender	2.0 (1.8–2.3)	2
Comorbidities and behaviors		
Diabetes mellitus	1.8 (1.5–2.1)	1
Cancer	2.1 (1.7–2.4)	2
Lung disease	2.3 (1.8–2.9)	2
Heart failure	2.3 (1.8–3.1)	2
BMI < 25 kg/m²	1.7 (1.4–1.9)	1
Current smoker	2.1 (1.7–2.5)	2
Functional measures		
Bathing	2.0 (1.6–2.4)	2
Managing finances	1.9 (1.6–2.3)	2
Walking several blocks	2.1 (1.8–2.4)	2
Pushing/pulling	1.5 (1.3–1.8)	1

- ✓ **0-5 puan :%4**
- ✓ **6-9 puan:%15**
- ✓ **10-13 puan:%42**
- ✓ **14 ve üzeri:%64**

OLGU

- ✓ 65 yaşında, Boy:160cm, Kilo:50kg
- ✓ Hipertansiyon, 2 yıldır Hemodiyaliz programında,KAH
- ✓ Kitle 3.5cm, 2LN+, grade 3, ER-, PR-, HER2-
- ✓ EF:??

- ✓ Dünyada yıllık hemodiyaliz hastası 1 milyondan fazla
- ✓ Kronik replasman tedavisi ile birlikte sağ kalım artıyor
- ✓ **Diyaliz tedavisi sırasında**
- ✓ Hücresel-humaral immunitede bozulma
- ✓ Viral enf
- ✓ DNA tamir mekanizmalarınıda içeren genomik değişiklikler
- ✓ Antioksidan aktivitede azalma
- ✓ Üremik toksinler ve inflamatuvar sitokinlerin artışı

Drug	Dose adjustment	Timing of administration
5-Fluorouracil	Standard dose	After HD
Capecitabine	Limited data to recommend its use*	No data
Carboplatin	AUCx25	Non-dialysis day
Cisplatin	Reduction of	After HD
Cyclophos		After HD
Docetaxel		Before or after HD
Doxorubic		After HD
Epirubicin		After HD
Etoposide		Before or after HD
Gemcitabi		6–12 hours before HD
Ifosfamide		
Irinotecan		After HD
Methotrexate	Reduction of 75%†	After HD
Oxaliplatin	Reduction of 30%	After HD
Paclitaxel	Standard dose	Before or after HD
Vinorelbine	Reduction of 25%–33%	After HD

Male (1)

Female (0.85)

$$GFR = Sex * ((140 - Age) / (SerumCreat)) * (Weight / 72)$$

$$CarboplatinDose = TargetAUC * (GFR + 25)$$

Breast cancer	Epirubicin+CTX	Epirubicin standard dose+CTX reduced of 25%	24 hours after CT
	Epirubicin+TXL	Standard dose	24 hours after CT
	FEC75	Epirubicin and 5-FU standard dose+CTX reduced of 25%	24 hours after CT

NOT!!

<u>Eritropoetin sitimüle eden ajanlar</u>:

kanserin evresi,

kür oranı,

hastanın yaşı ve performansı, diğer komorbiditeler

değerlendirilmelidir.

Sık kan transfüzyonları allosensitizasyona neden olacağı için HGB 10gr/dl az olan olgularda düşük doz ESAs yapılabilir

- ✓ **KORONER ARTER HASTALIĞI**
- ✓ **KRONİK BÖBREK YETERSİZLİĞİ**
- ✓ *ANTRASİKLİNLER!*
- ✓ *TAKSANLAR!*
- ✓ *FLUOROPİRİMİDİNLER*
- ✓ *ALKİLLEYİCİ AJANLAR!*
- ✓ *PLATİNLER!*

KARDİYOTOKSİSİTE

ANTRASİKLİNLER

- ✓ Akut sol ventrikül yetersizliği ve miyokard hasarı
- ✓ Kümülatif doz:300-500mg/m2
- ✓ %1-20
- ✓ LVEF önemlidir
- ✓ EKO veya radyonüklid ventrikülografi
- ✓ Eş zamanlı kardiyotoksik ilaçlar***

Risk fakt

- ✓ 65 yaş
- Kadın
- LVEF<5
- ✓ Sigara,
- ✓ Obezite
- ✓ Göğüse

İZLEM

Her siklusda
öykü ve kardiyak muayene
Kalp yetm bulguları varsa EKG-EKO

Clinical manifestations, monitoring, and diagnosis of anthracycline-induced cardiotoxicit

This topic last updated: Apr 03, 2017.

İLK MUAYENEDE

TEDAVİ SIRASINDA

- Patients with (sympt
- Asymptomatic patier
- Asymptomatic patients with LVEF ≥50 percent

rilmemelidir

vor ise!

- ✓ DOZ REDÜKSİYONU???
- ✓ ACEİ ve BETA BLOK preventifmidir ?
- ✓ SİTATİNLER??
- ✓ Dexrazoxane??
- ✓ DXR kümülatif doz:450mg/m2
- ✓ EPİ:900mg/m2

TAKSANLAR

- ✓ Dosetaksel ile kardiyovasküler kollaps ve anjina
- ✓ Paklitaksel ile bradikardi fazladır, asemptomatik
- ✓ DXR+PAK ile KKY riski%20
- ✓ Nabpaklitaksel ile asemptomatik EKG!!

SİKLOFOSFAMİD

- ✓ Kardiyotoksisite için kümülatif doz yoktur
- ✓ Endokardiyal kapiller hasara bağlı perikardiyal effüzyon olabilir
- ✓ Yüksek doz protokollerde kardiyotoksisite ye neden olur

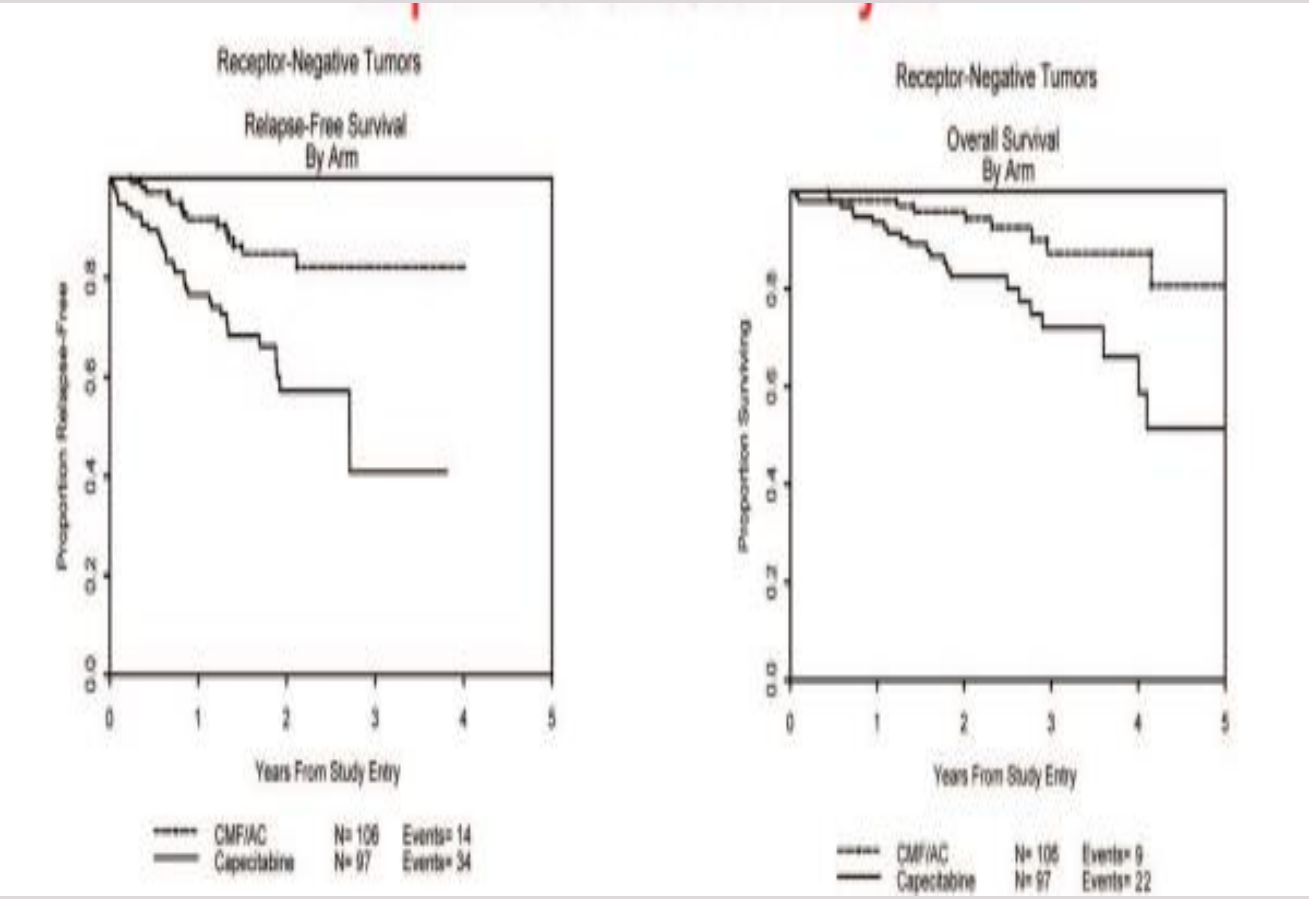
5-FLUOROURACİL

- Angina – 45 percent
- Myocardial infarction – 22 percent
- Arrhythmias – 23 percent
- Acute pulmonary edema – 5 percent
- Cardiac arrest – 1.4 percent
- Pericarditis – 1.4 percent

- ✓ T1/2:15-20dk
- ✓ Bolus dozlarda:%1.6-3
- ✓ Metaboliti:alfa fluoro beta alanin fluoroasetat oldukça kardiyotoksik
- ✓ Vazospazm
- ✓ Miyokardiyal toksisite ve disfonksiyon
- ✓ Semptomlar ilk siklusda, ilk 12saatte
- ✓ EKO:EF takibi
- ✓ Tekrarlanan dozlar kardiyotoksisiteyi artırır ve ölüme

Fluoropyrimidine-associated cardiotoxicity: Incidence, clinical manifestations, mechanisms, and management

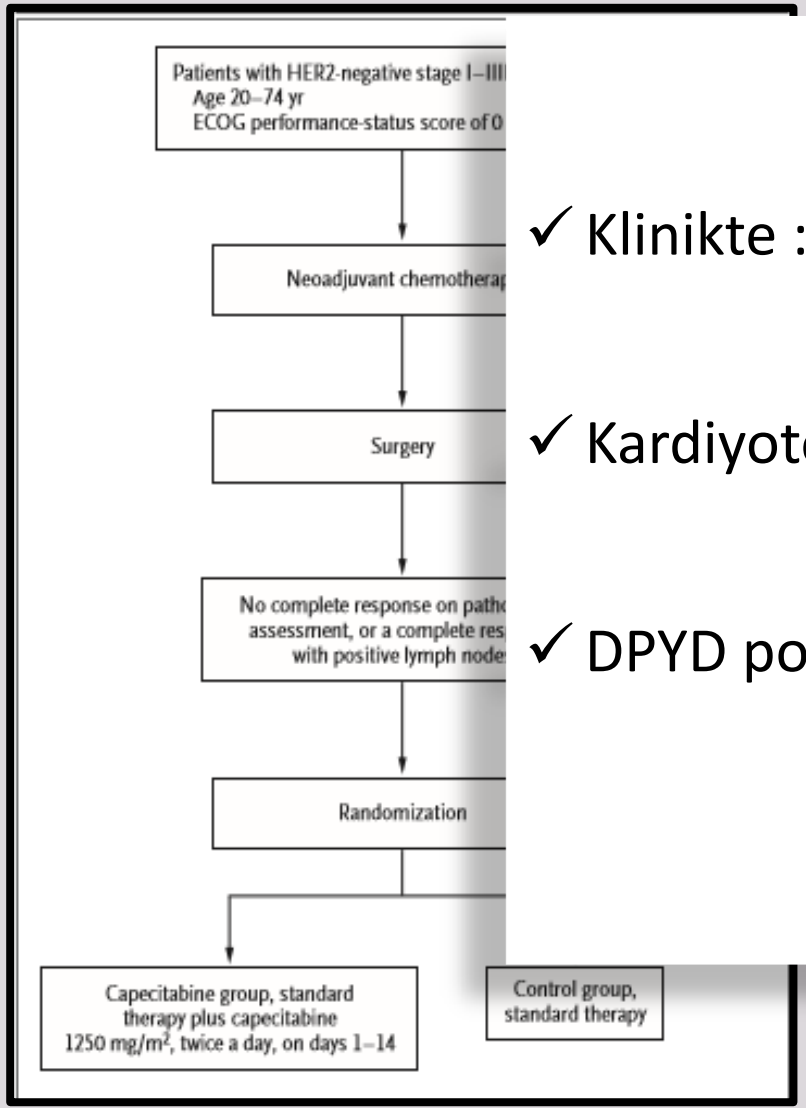
>65 yaş, CMF X AC X Kapesitabin



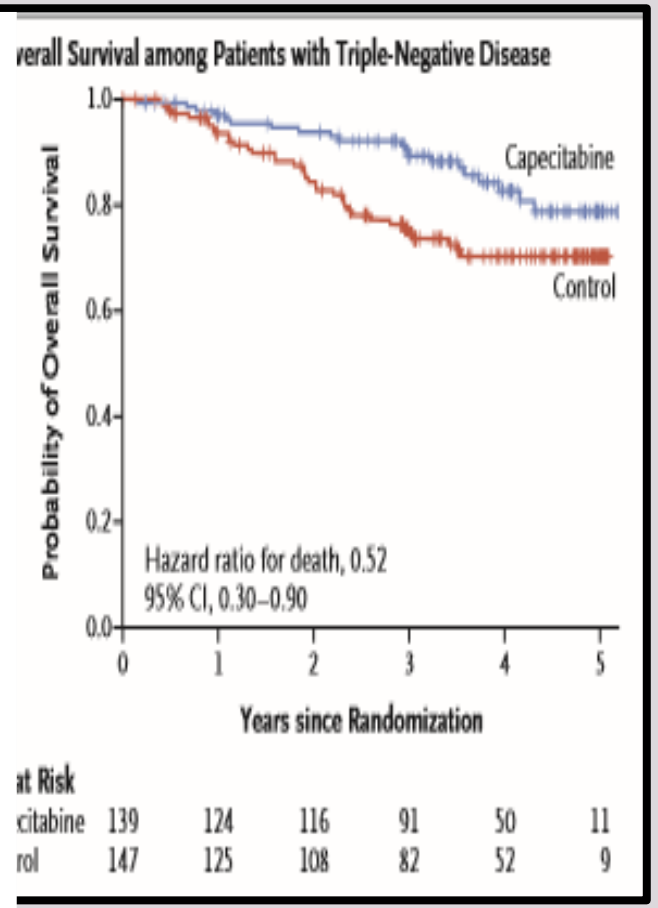
	Standard therapy	Capecitabine	*p*-value
n of patients (%)	326 (100)	307 (100)	–
Relapse-free survival	89%	80%	<.001[a]
Overall survival	93%	88%	0.02[a]
Maximum grade 3–5 toxicity	60%, AC 70%, CMF	34%	–
Completed all courses	92%, AC 62%, CMF	80%	–

Breast Cancer in Seniors

HASTA NEOADJUVAN KT SONRASI T2N1M0 ise adjuvan kemoterapi??



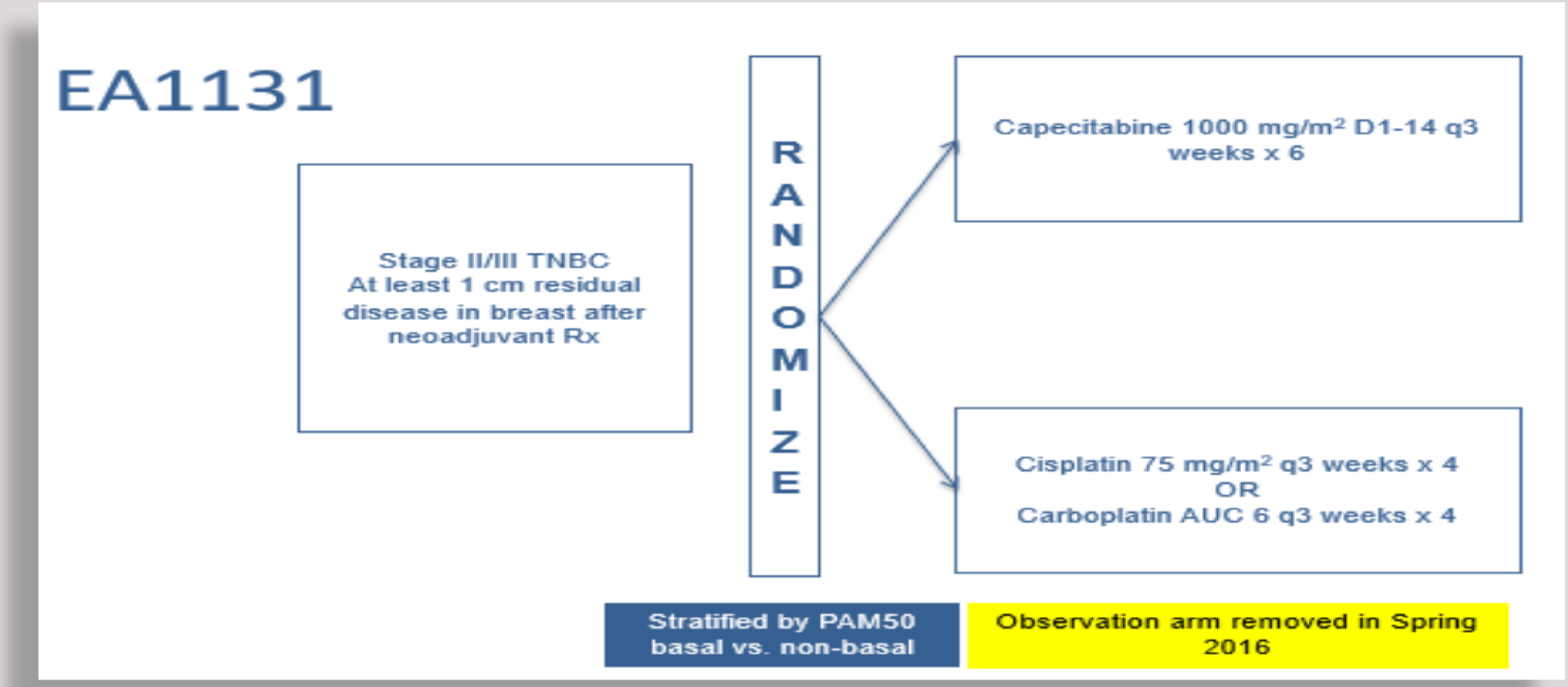
- ✓ Klinikte :anjina
- ✓ Kardiyotoksisite:%3-9
- ✓ DPYD polimorfizm de kardiyotoksisite ??



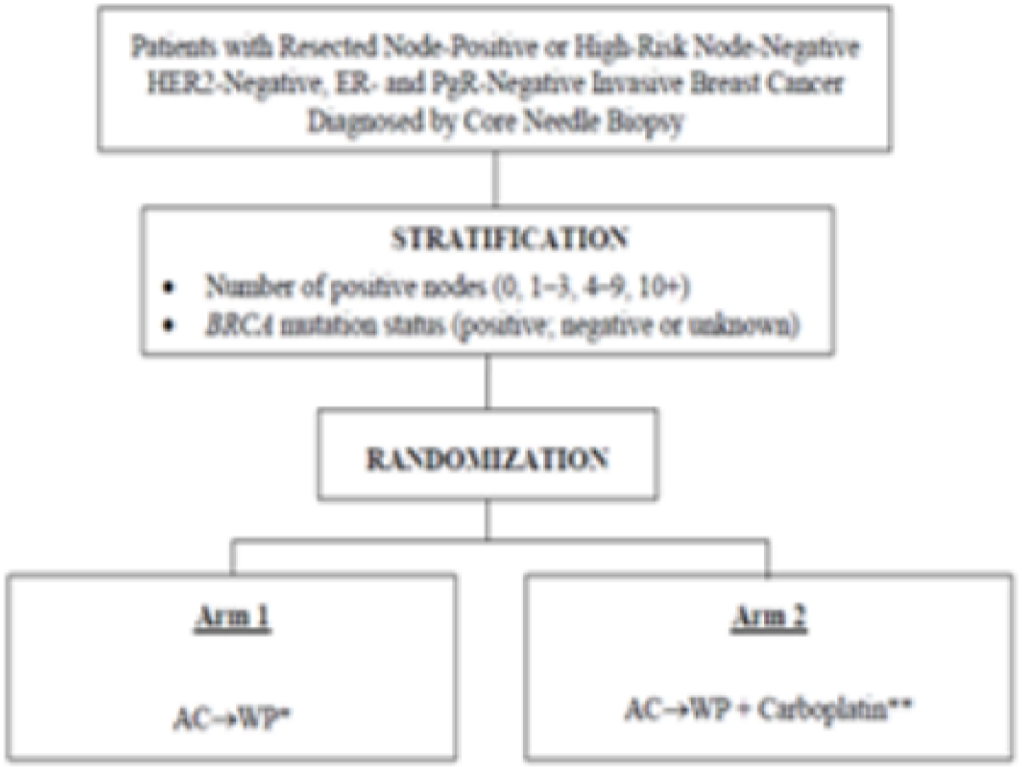
N Engl J Med 2017;376:2147-59.

Fluoropyrimidine-associated cardiotoxicity: Incidence, clinical manifestations, mechanisms, and management

HASTA NEOADJUVAN KT SONRASI T2N1M0 ise adjuvan kemoterapi??



Adjuvant Platinum?: NRG-BR003



Primary hypothesis: The addition of carboplatin to AC->T will improve IDFS

Secondary endpoints: OS, BCFS, toxicity

* **Chemotherapy regimen for Arm 1**

AC→ Weekly Paclitaxel (WP): Doxorubicin (A) 60 mg/m^2 IV + cyclophosphamide (C) 600 mg/m^2 IV every 2 weeks for 4 cycles (dose-dense schedule) followed by paclitaxel 80 mg/m^2 IV weekly for 12 doses.

** **Chemotherapy regimen for Arm 2**

AC→ Weekly Paclitaxel (WP) + Carboplatin: Doxorubicin (A) 60 mg/m^2 IV + cyclophosphamide (C) 600 mg/m^2 IV every 2 weeks for 4 cycles (dose-dense schedule) followed by paclitaxel 80 mg/m^2 IV weekly for 12 doses plus carboplatin AUC of 5 IV every 3 weeks for 4 cycles.

Is Carboplatin Ready for Primetime in Unselected TNBC in the Adjuvant or Neoadjuvant Setting?

NO

- Need definitive study showing improvement in DFS and/or OS
- If platinum is ultimately used, should it be added to standard therapy or substituted for one or more drugs?
- Are there triple negative subtypes that are particularly sensitive to platinum, ie biomarker driven?

Breast cancer	Epirubicin+CTX	Epirubicin standard dose+CTX reduced of 25%	24 hours after CT
	Epirubicin+TXL	Standard dose	24 hours after CT
	FEC75	Epirubicin and 5-FU standard dose+CTX reduced of 25%	24 hours after CT

TEŞEKKÜR EDERİM