HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Dr. Deniz Tural
Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi
Tıbbi Onkoloji

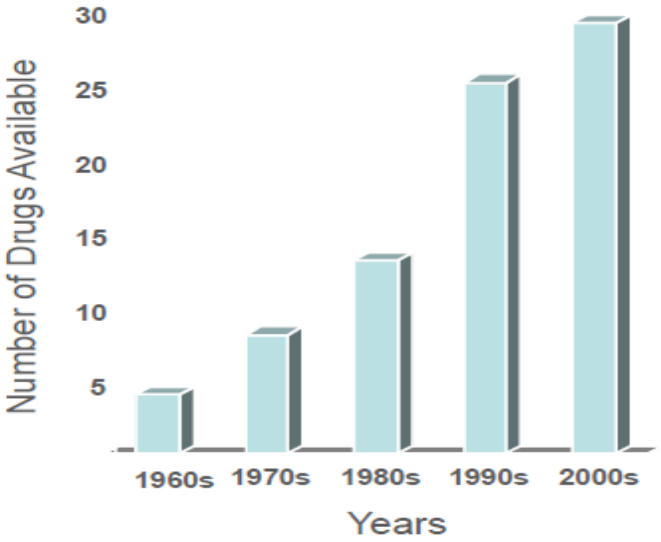
İnsidans ve Epidemiyoloji

	Common Types of Cancer	Estimated New Cases 2016	Estimated Deaths 2016
1.	**Breast Cancer (Female)**	**246,660**	**40,450**
2.	Lung and Bronchus Cancer	224,390	158,080
3.	Prostate Cancer	180,890	26,120
4.	Colon and Rectum Cancer	134,490	49,190
5.	Bladder Cancer	76,960	16,390
6.	Melanoma of the Skin	76,380	10,130
7.	Non-Hodgkin Lymphoma	72,580	20,150
8.	Thyroid Cancer	64,300	1,980
9.	Kidney and Renal Pelvis Cancer	62,700	14,240
10.	Leukemia	60,140	24,400

Female breast cancer represents 14.6% of all new cancer cases in the U.S.

14.6%

İnsidans ve Epidemiyoloji



1950s: Cyclophosphamide, methotrexate

1960s: 5-fluorouracil

1970s: Doxorubicin, tamoxifen

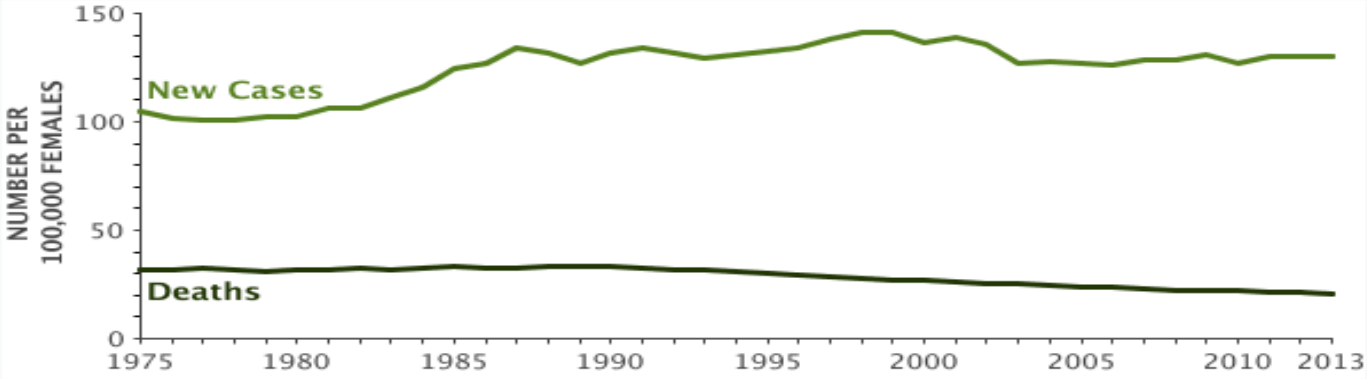
1980s: Mitoxantrone, megestrol acetate, goserelin, leuprolide

1990s: Paclitaxel, docetaxel, vinorelbine, trastuzumab, capecitabine, gemcitabine, epirubicin, toremifene, anastrozole, letrozole, exemestane

2000s: *nab*-paclitaxel, lapatinib, ixabepilone, eribulin, denosumab, everolimus, palbociclib, fulvestrant, T-DM1, pertuzumab…

İnsidans ve Epidemiyoloji

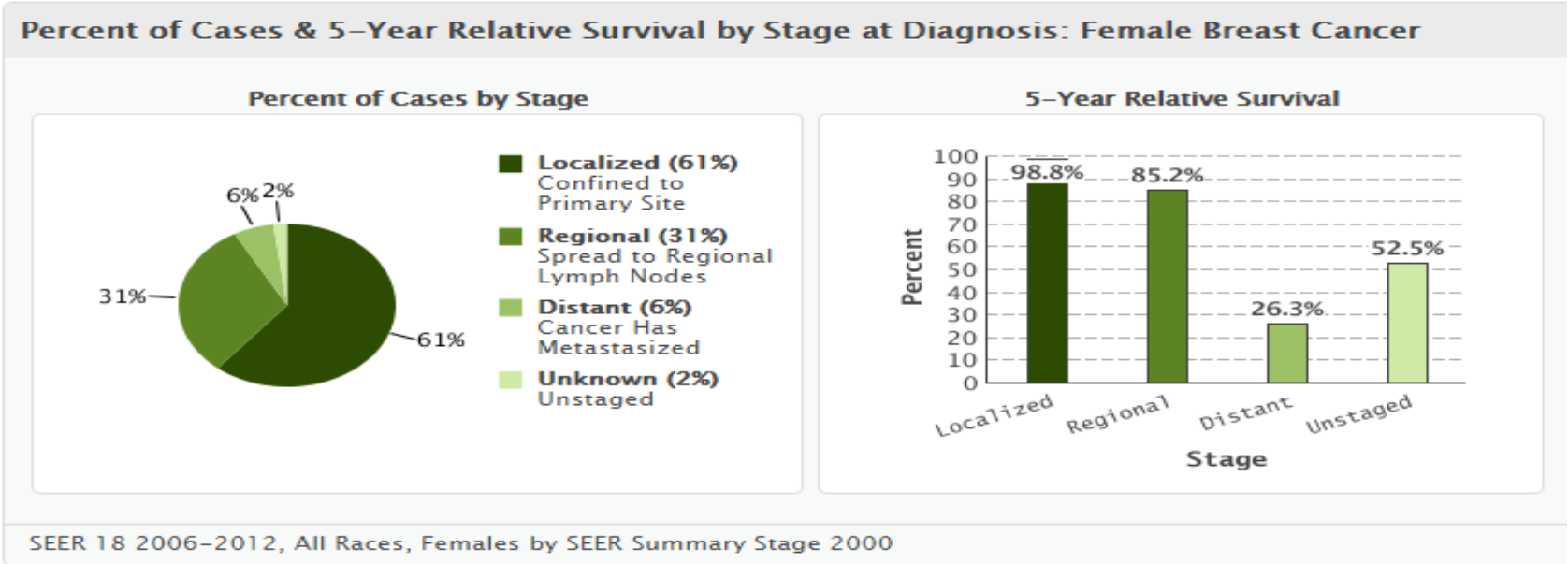
New Cases, Deaths and 5-Year Relative Survival View Data Table



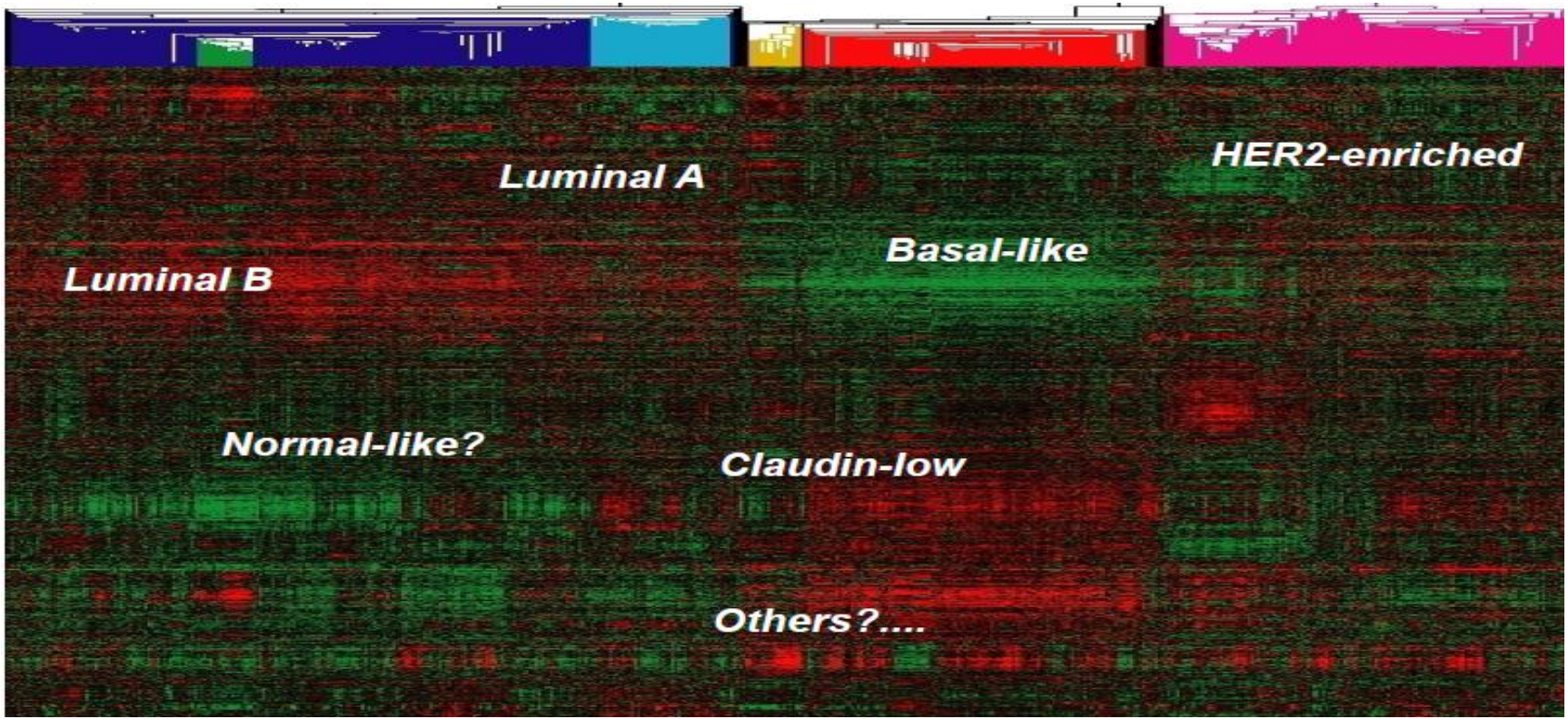
Year	1975	1980	1985	1990	1995	2000	2004	2008
5-Year Relative Survival	75.2%	74.9%	78.4%	84.6%	86.8%	90.2%	89.9%	90.6%

SEER 9 Incidence & U.S. Mortality 1975-2013, All Races, Females. Rates are Age-Adjusted.

İnsidans ve Epidemiyoloji

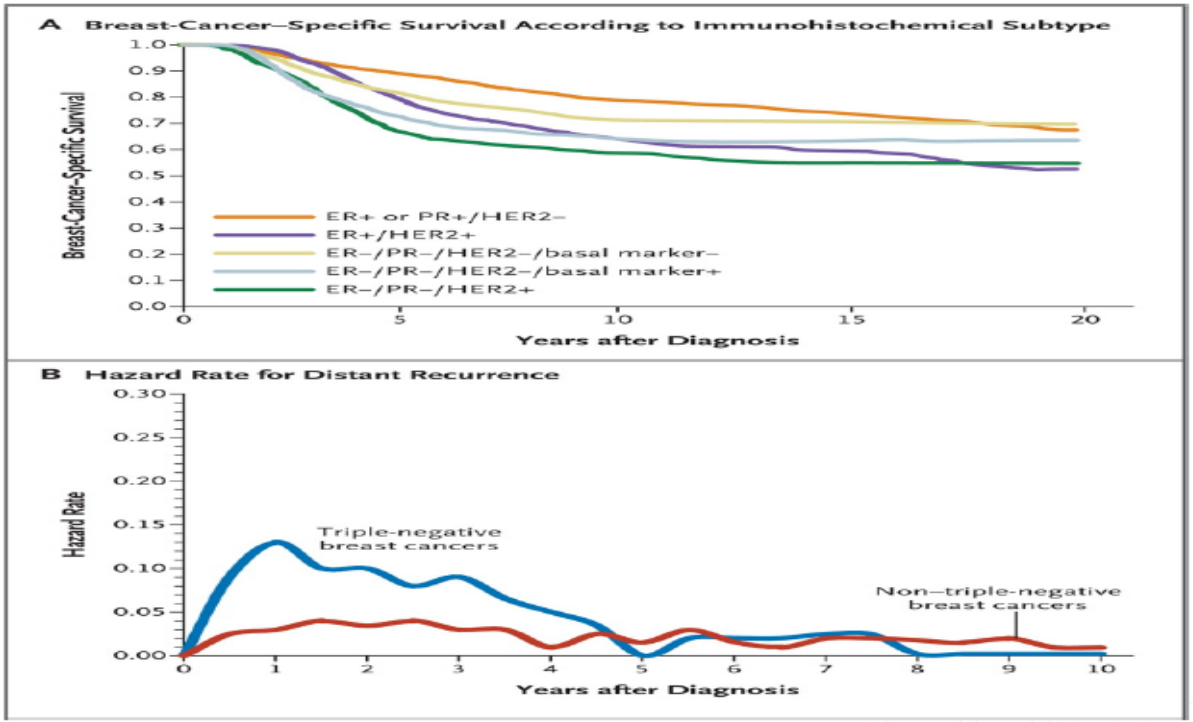


Meme Kanseri Moleküler Alt Grupları



Meme Kanseri Moleküler Alt Grupları

Breast Cancer Recurrences Occur Late

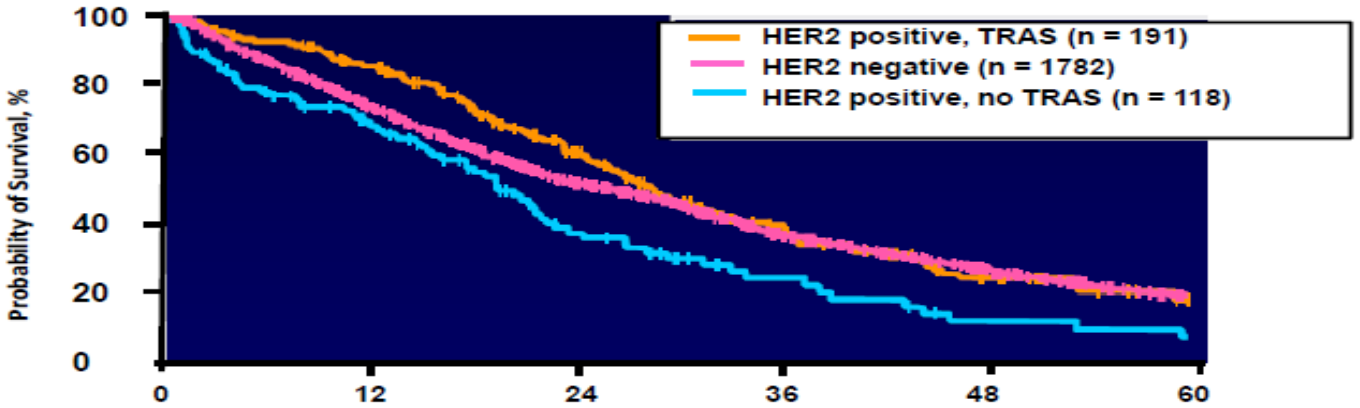


Foulkes WD et al. N Engl J Med 2010;363:1938-1948.

Meme Kanseri Moleküler Alt Grupları
HER2 Pozitif- Trastuzumab

Trastuzumab Has Changed the Natural History of HER2-Positive Breast Cancer

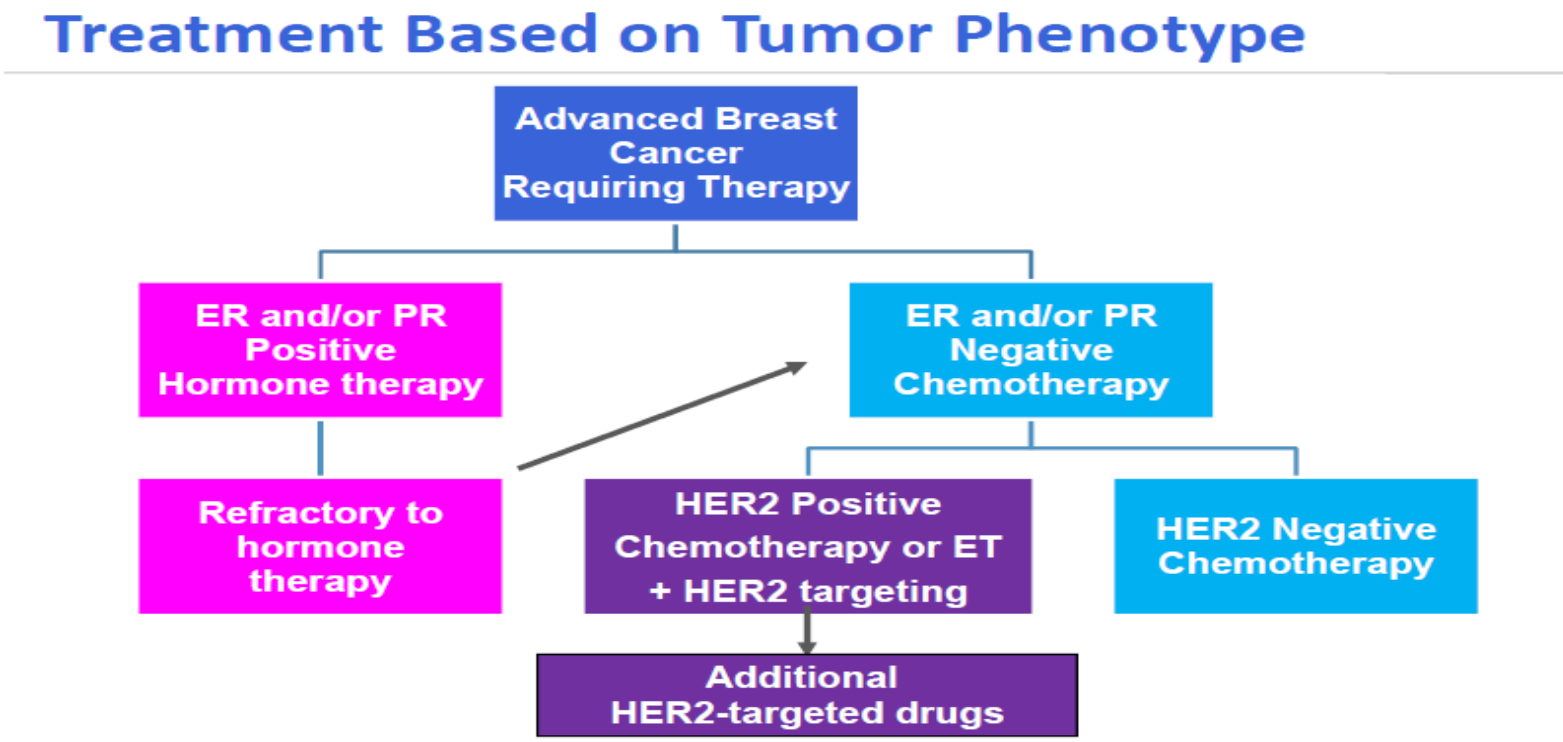
- Patients with HER2-positive metastatic breast cancer (MBC) now have comparable outcomes with HER2-negative MBC



TRAS, trastuzumab

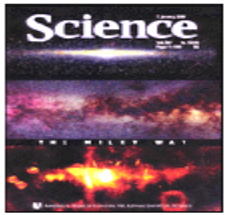
Dawood S, et al. *J Clin Oncol.* 2010;28(1):92-98.

Meme Kanseri Moleküler Alt Gruplara Göre Tedavi



HER2 Pozitif Meme Kanserindeki Tedavinin Tarihsel Seyri

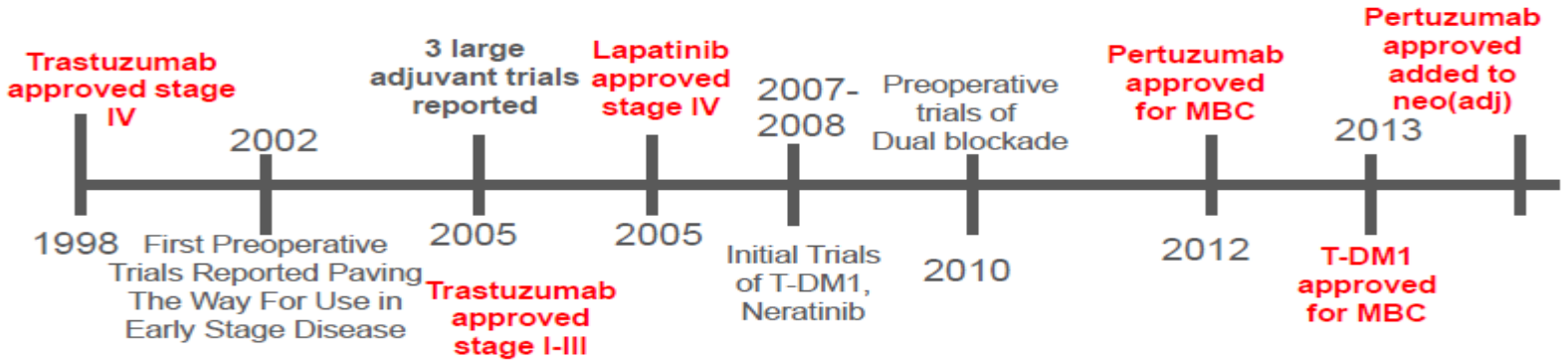
HER2+ Disease: Major Clinical Advances



Studies of the HER-2/*neu* Proto-oncogene in Human Breast and Ovarian Cancer

DENNIS J. SLAMON,* WILLIAM GODOLPHIN, LOVELL A. JONES, JOHN A. HOLT, STEVEN G. WONG, DUANE E. KEITH, WENDY J. LEVIN, SUSAN G. STUART, JUDY UDOVE, AXEL ULLRICH, MICHAEL F. PRESS

1989



Meme Kanseri Moleküler Alt Grupları

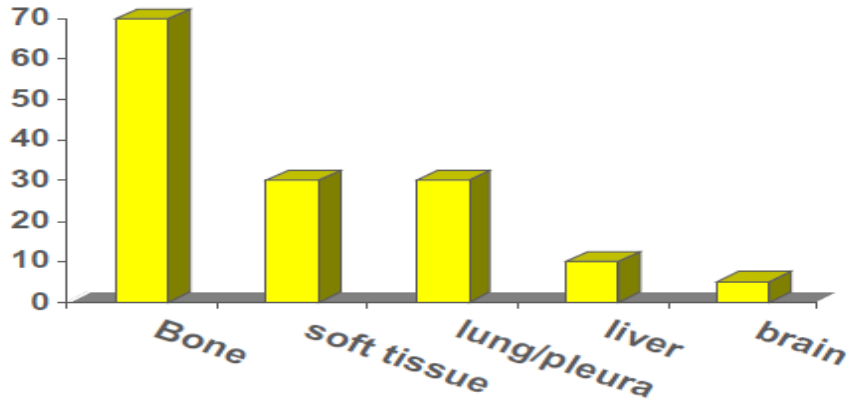
New Patients With Metastatic Breast Cancer in U.S.

Subtype	Percentage
HER2+	~15-20% (↓ing)
Triple Neg	~ 15-20%
ER+ and HER2-	~ 60-70%

About 50% of total HR+ are highly sensitive to endocrine Rx

Meme Kanseri Metastaz Bölgeleri

Metastatic Sites



Breast cancer tropisms differ by subtype
Bone more dominant in hormone receptor positive
Visceral and CNS in hormone receptor negative

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Heterogeneity of Metastatic Breast Cancer

Disease Characteristics

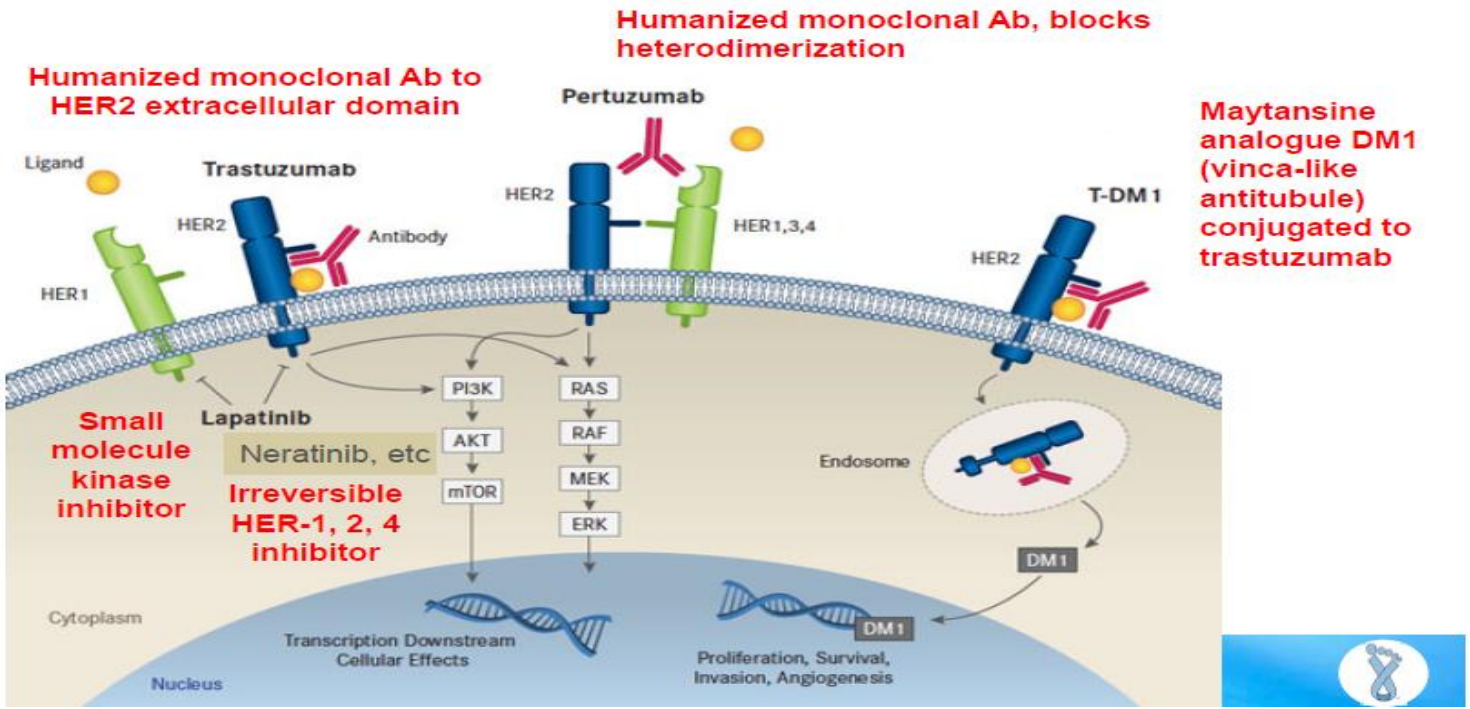
- Disease-free interval
- Sites and volume of disease
- Tempo of disease
- Prior therapy
- ER and PR status
- HER-2 status

Patient Characteristics

- Performance status
- Comorbidity
- Host factors
  - ? Immune response
  - ? Drug metabolism

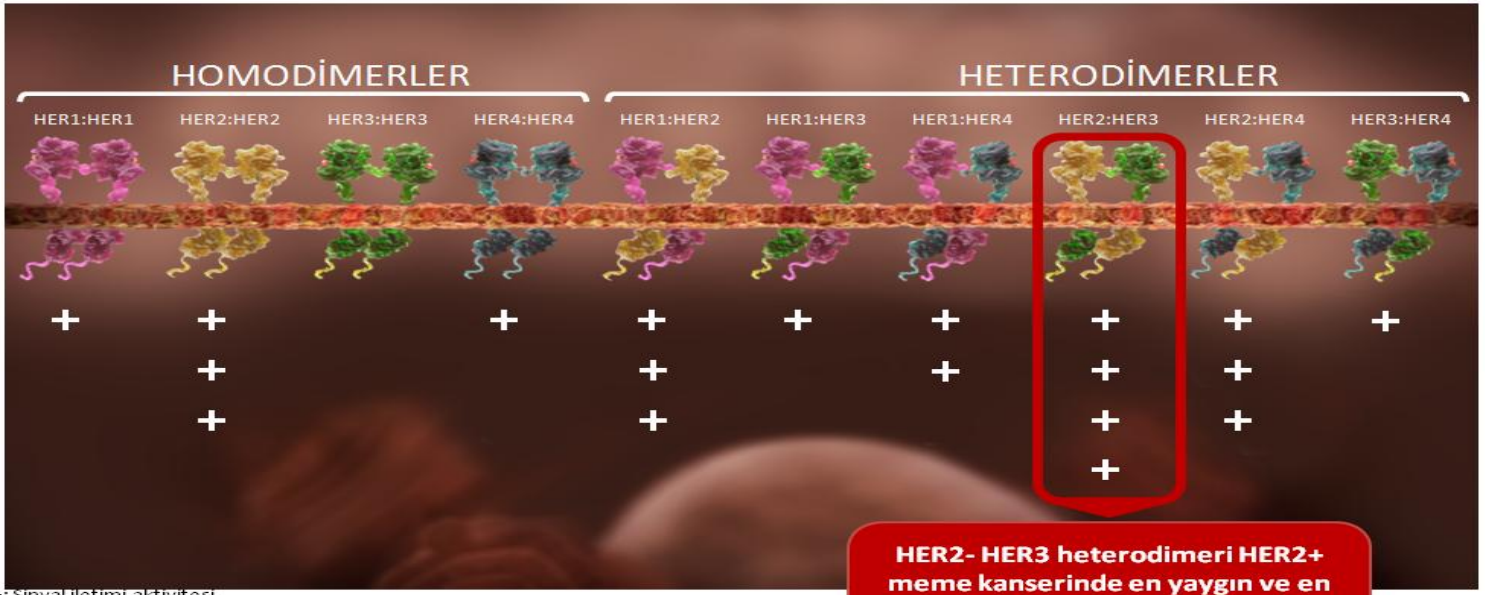
HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Targeting HER2



HER2 Pozitif Metastatik Meme Kanserinde Tedavi

HER AİLESİNDE DİMERİZASYON

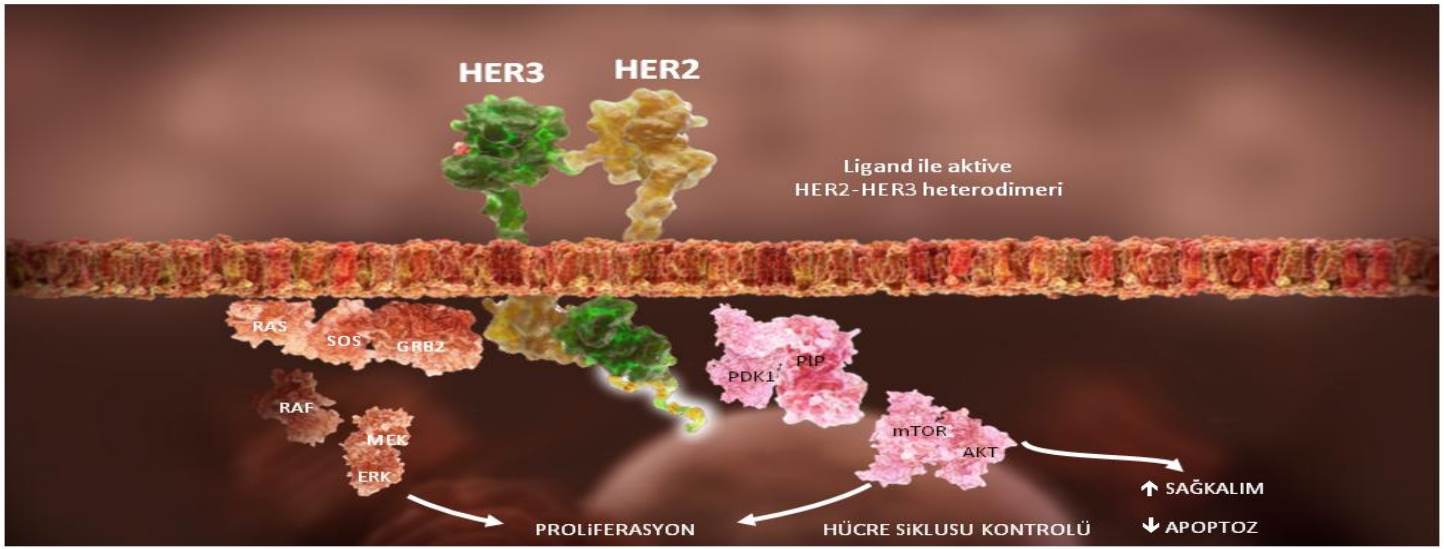


+: Sinyal iletimi aktivitesi

Tzahar E, et al. Mol Cell Biol 1996; 16:5276–5287; Citri A, et al. Exp Cell Res 2003; 284:54–65.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

HER2-HER3 DİMERİZASYONU



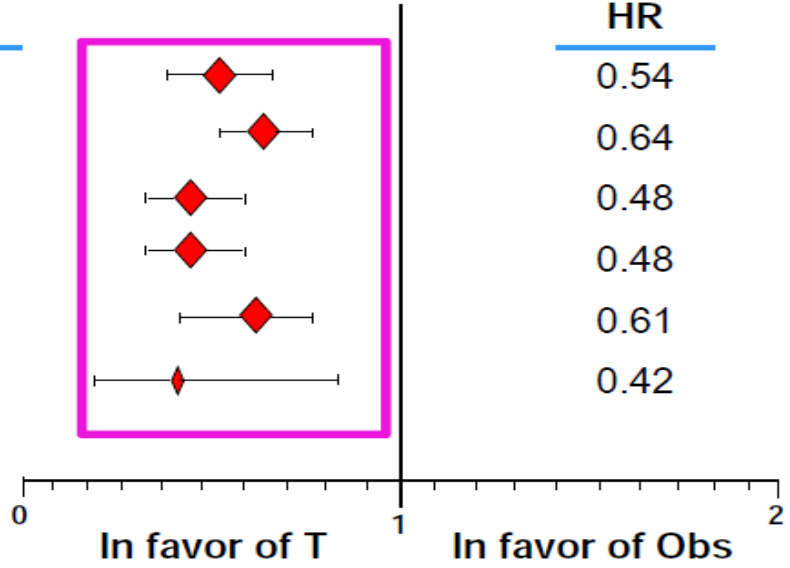
- HER2: HER3 dimerizasyonu , artmış hücre proliferasyonu dahil birden çok sinyal iletimi yolağını indükler.
- Bu reseptör dimerizasyonu , PI3K/Akt ve Ras/MEK/MAPK yolaklarının aktivasyonuna yol açar ve böylece proliferasyon, sağkalım ve migrasyon desteklenir; apoptoz ise inhibe edilir.

Yarden Y & Sliwkowski MX. Nat Rev Mol Cell Biol 2001; 2:127–137;
Baselga J & Swain SM. Nat Rev Cancer 2009; 9:463–475.

HER2 Pozitif Meme Kanserinde Adjuvan Tedavi

Adjuvant Trastuzumab Confers DFS Benefits in HER2-Positive Breast Cancer

Study	FU, yr	N	HR
HERA	1	3,387	0.54
	2	3,401	0.64
NSABP B-31/ NCCTG 9831	2	3,351	0.48
	4	3,968	0.48
BCIRG 006	3	3,222	0.61
FinHer	3	231	0.42



Meme Kanseri Neoadjuvan Tedavi

Pathological Complete Response and Accelerated Drug Approval in Early Breast Cancer

Tatiana M. Prowell, M.D., and Richard Pazdur, M.D.

New drugs for breast cancer have historically been approved first for patients with metastatic disease who have few remaining options for systemic treatment. Approval for an adjuvant indication occurs years later, after large, randomized trials with prolonged follow-up have been conducted in patients with early-stage disease. Recently, neoadjuvant trials have introduced new drugs preoperatively in patients with localized breast cancer. Such treatment aims to render locally advanced cancers operable, facilitate breast-conserving surgery, and ultimately improve survival. The rate of pathological complete response — absence of residual invasive cancer on pathological evaluation of resected breast specimens and lymph nodes after preoperative therapy — has been used as the primary end point in many neoadjuvant trials.

Promising investigational drugs should be incorporated into standard treatment for early-stage

Meme Kanseri Neoadjuvan Tedavi

CTNeoBC Selected Trials

- 12 neoadjuvant randomized controlled trials
- pCR clearly defined with all necessary data collected
- Long-term follow-up EFS and OS data collected

TRIALS	Patients (n)
GBG/AGO: 7	6377
NSABP: 2	3171
EORTC/BIG: 1	1856
ITA: 2	1589
Total # patients	12993

Cortazar et al, SABCS 2012

Meme Kanseri Neoadjuvan Tedavi

HER2 pozitif

San Antonio Breast Cancer Symposium- Cancer Therapy and Research Center at UT Health Science Center- December 10-14, 2013

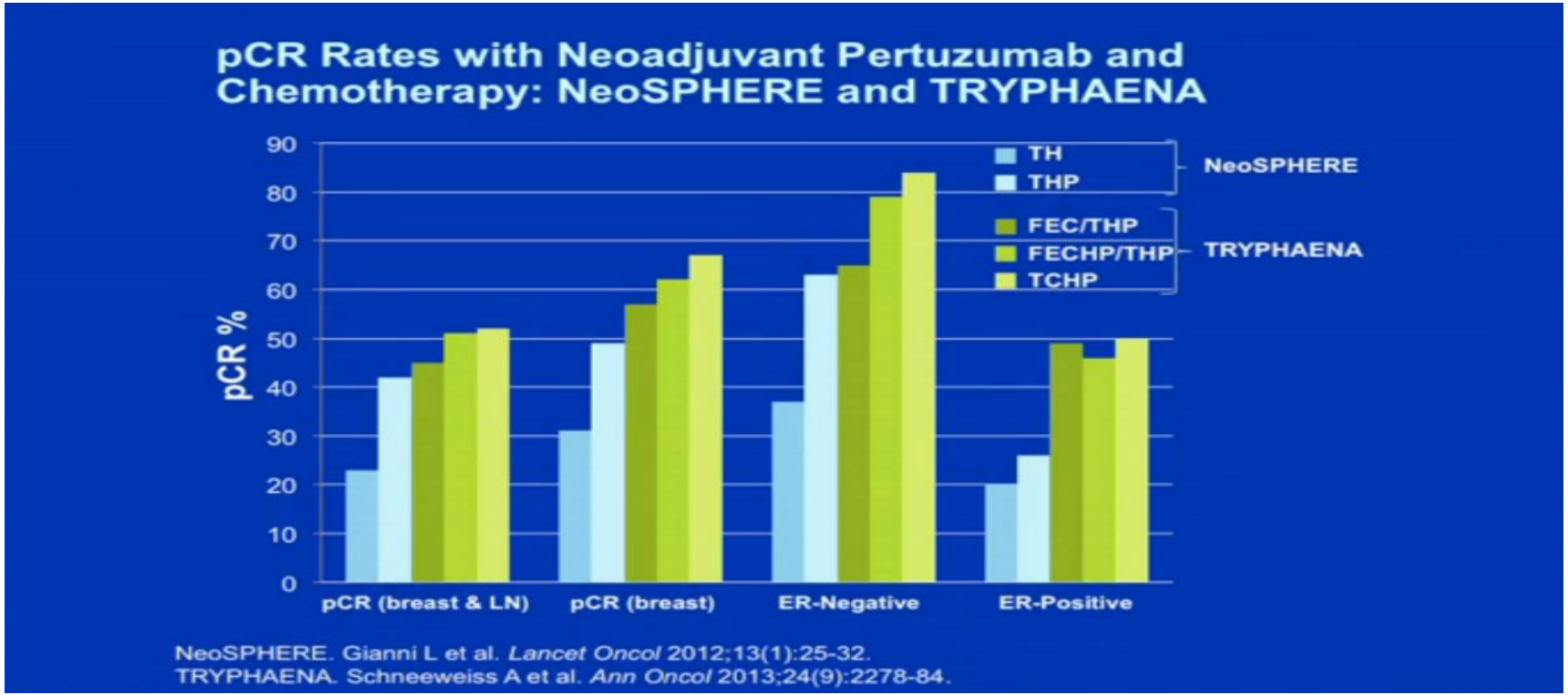
Neoadjuvant Trastuzumab + Pertuzumab

	Regimen	Duration	pCR	P value
NEOSPHERE (N=417)	DH		29%	
	DP	12 w	24%	
	DHP		45.8%	0.0141
	HP		16.8%	
TRYPHAENA (N=225)	FECHP → DHP		61.6%	
	FEC → DHP	24 w	57.3%	
	DCbHP		66.2%	

E=epirubicin; C=cyclophosphamide; F=fluorouracil;
D=docetaxel;
Cb=carboplatin; H=trastuzumab; P=pertuzumab

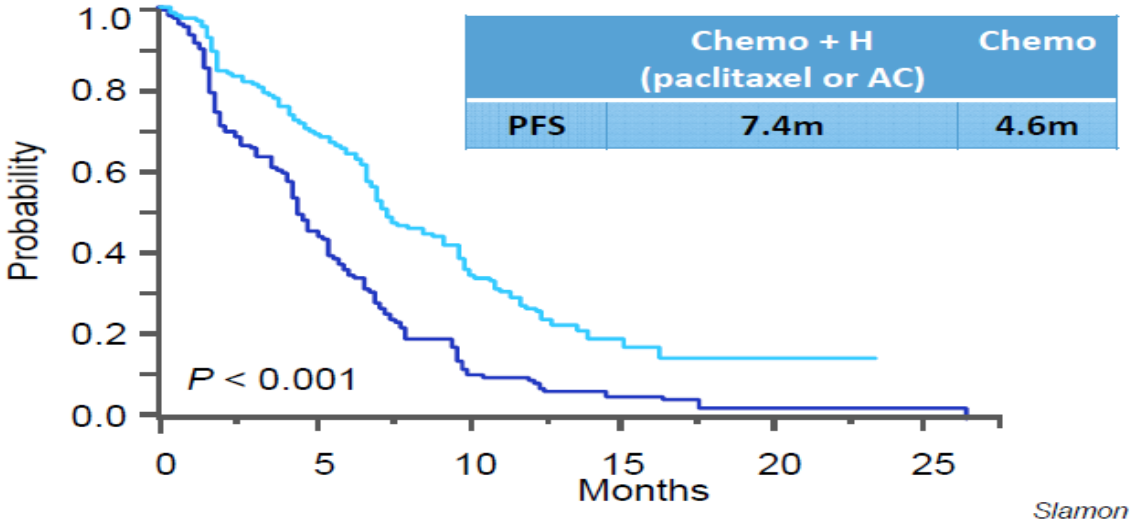
Meme Kanseri Neoadjuvan Tedavi

HER2 pozitif



HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Trastuzumab Added To Chemotherapy

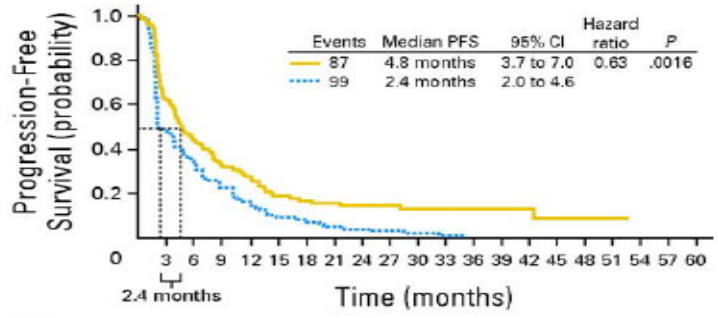


	Chemo + H (paclitaxel or AC)	Chemo
PFS	7.4m	4.6m

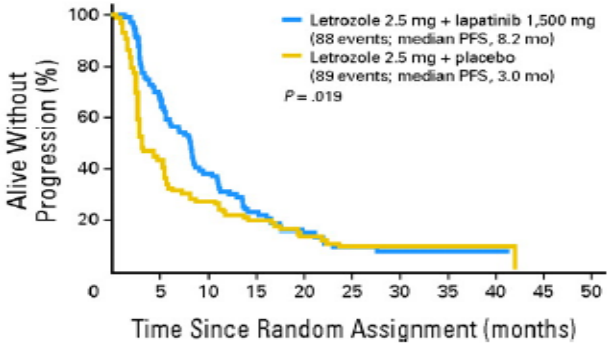
Slamon DJ, et al. NEJM 2001

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

HER2-Targeting Added To Endocrine Therapy



anastrozole vs
anastrozole + trastuzumab
Kaufman et al, JCO 2008



letrozole vs
letrozole + lapatinib
Johnston et al, JCO 2009

Adds toxicity with modest changes in outcome. Most co-target but ok in individual patients to just use ET.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Hormonal Therapy in HER2-Positive Metastatic Breast Cancer

Regimen	ORR, %	Median PFS, months
Trastuzumab (N = 114; HER2 positive, n = 79)[1]	26	3.5-3.8
Anastrozole/trastuzumab (n = 103)[2]	20	4.8
Anastrozole (n = 104)[2]	7	2.4
Lapatinib/letrozole (n = 642)[3]	28	8.2
Letrozole (n = 644)[3]	15	3.0
Lapatinib (N = 138)[4]	24	NA

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Summary: Optimal Choice First-Line Setting 2016

VOLUME 32 · NUMBER 19 · JULY 1 2014

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Systemic Therapy for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline

Sharon H. Giordano, Sarah Temin, Jeffrey J. Kirshner, Sarat Chandarlapaty, Jennie R. Crews, Nancy E. Davidson, Francisco J. Esteva, Ana M. Gonzalez-Angulo, Ian Krop, Jennifer Levinson, Nancy U. Lin, Shanu Modi, Debra A. Patt, Edith A. Perez, Jane Perlmutter, Naren Ramakrishna, and Eric P. Winer

- **Clinicians should recommend combination of trastuzumab, pertuzumab and a taxane for first-line treatment, unless contraindication to taxane use**
- **If ER+, can consider endocrine therapy + trastuzumab or lapatinib in selected cases**

Giordano SH, et al. *J Clin Oncol.* 2014;32(19):2078-2099.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

HER2-Targeting: The First Generation

Post-H progression ongoing HER2-targeting works

- Lapatinib
- TDM1
- Trastuzumab!

Multiple chemotherapy partners for HER2-targeting

- Platinums, vinorelbine, gemcitabine, capecitabine
- What is optimal?

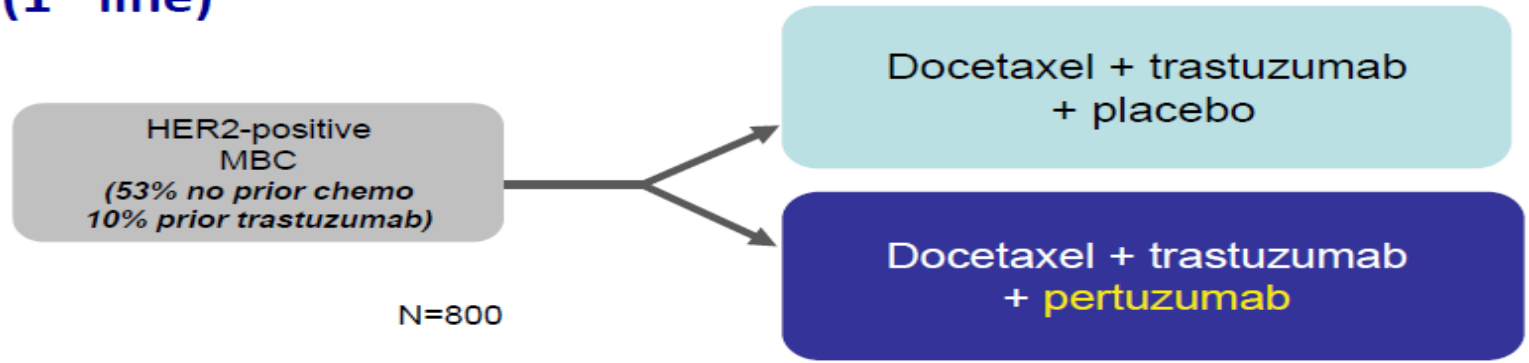
ER+ HER2+ disease benefits from dual targeting

- AI + either trastuzumab or lapatinib
- Ok to omit HER2-targeting in strongly ER+, indolent, asymptomatic.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Newer Anti-HER2 Drugs

CLEOPATRA: Phase III trial testing addition of pertuzumab (1st line)



End points

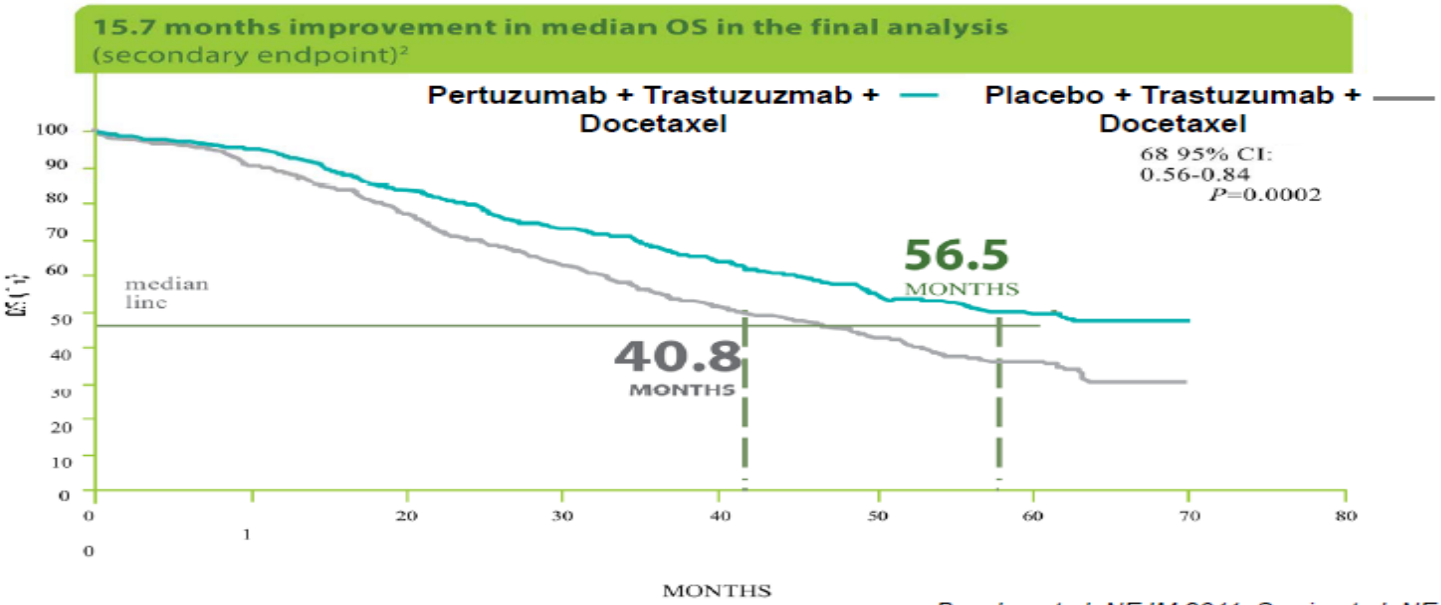
- PFS and OS
- quality of life
- biomarker analysis

Baselga J et al. NEJM 2012

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

CLEOPATRA: Overall Survival

PFS 18.5 vs 12.4m, p<0.0001

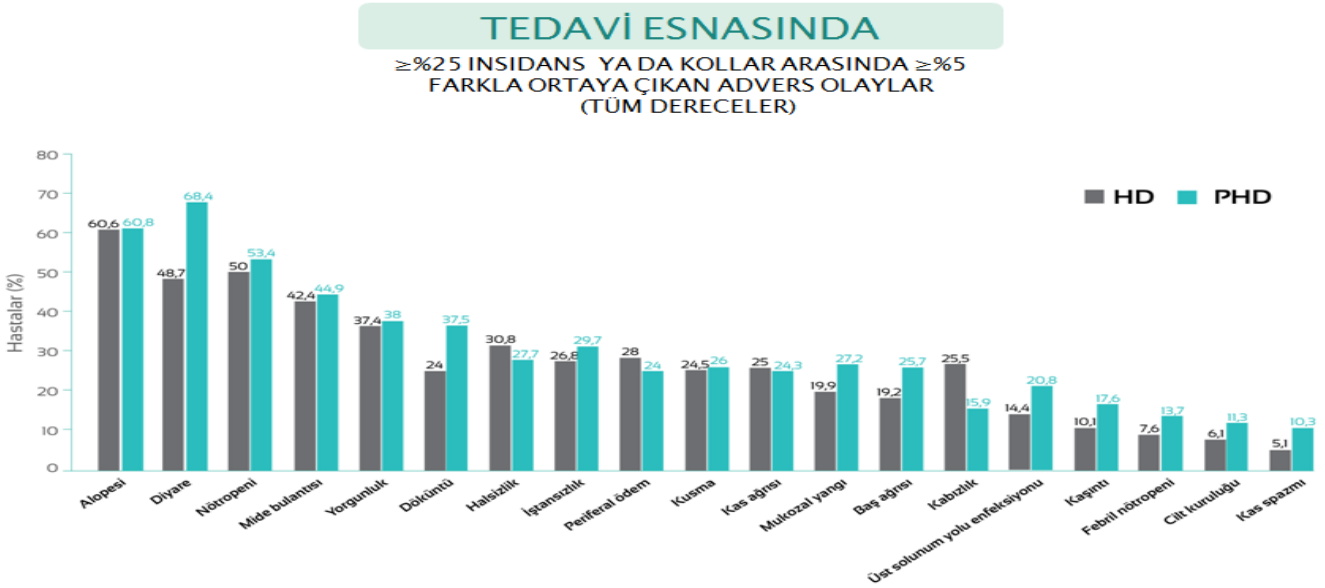


Baselga et al, NEJM 2011; Swain et al, NEJM 2015

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

CLEOPATRA

Advers Olaylar



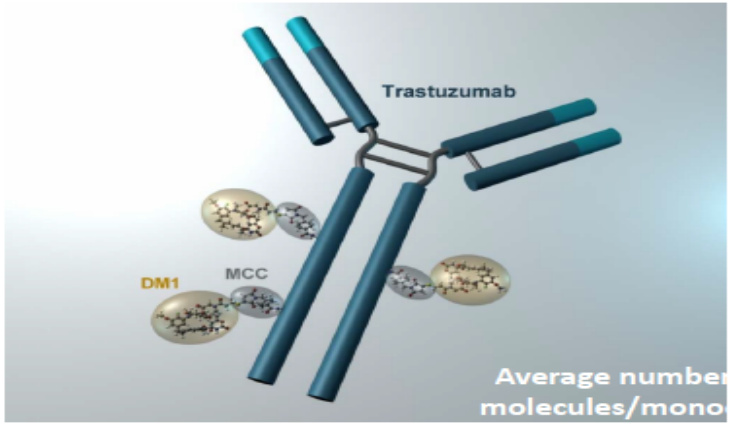
H, trastuzumab; P, pertuzumab; D, dosetaksel

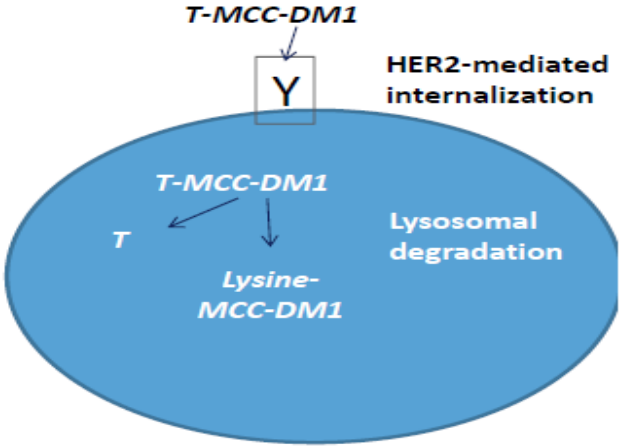
Swain SM, et al. N Engl J Med 2015; 372: 724-734.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

Trastuzumab-emtansine (T-DM1), HER2 Antibody-Drug Conjugate

- Maytansine analogue DM1 (antitubule akin to vincas) conjugated to trastuzumab – similar to gemtuzumab (Myelotarg)
- Will it allow omission of separate cytotoxic?



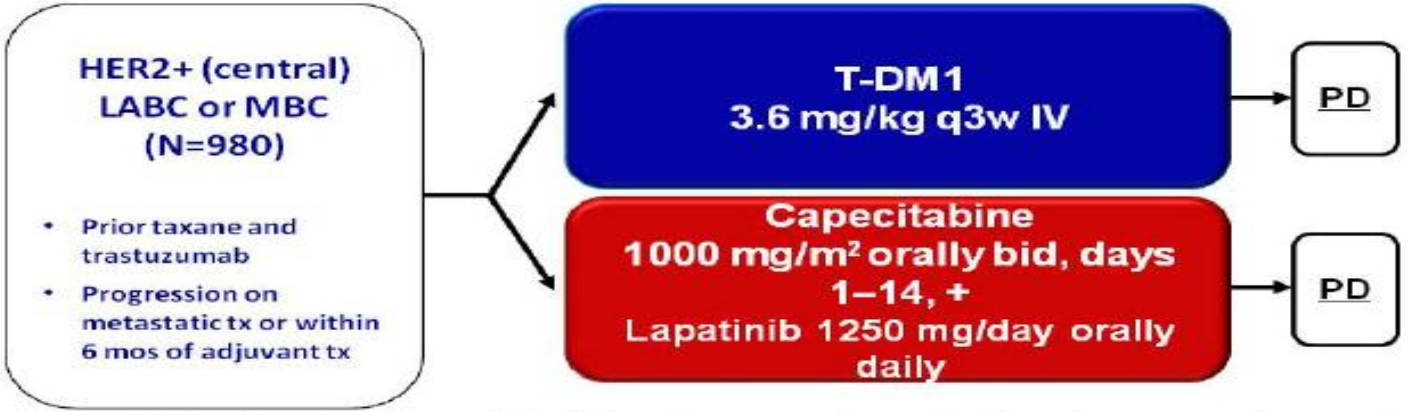


Active metabolite can't cross plasma membrane (no bystander effect)

Beeram et al. J Clin Oncol 2008.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

EMILIA Study Design



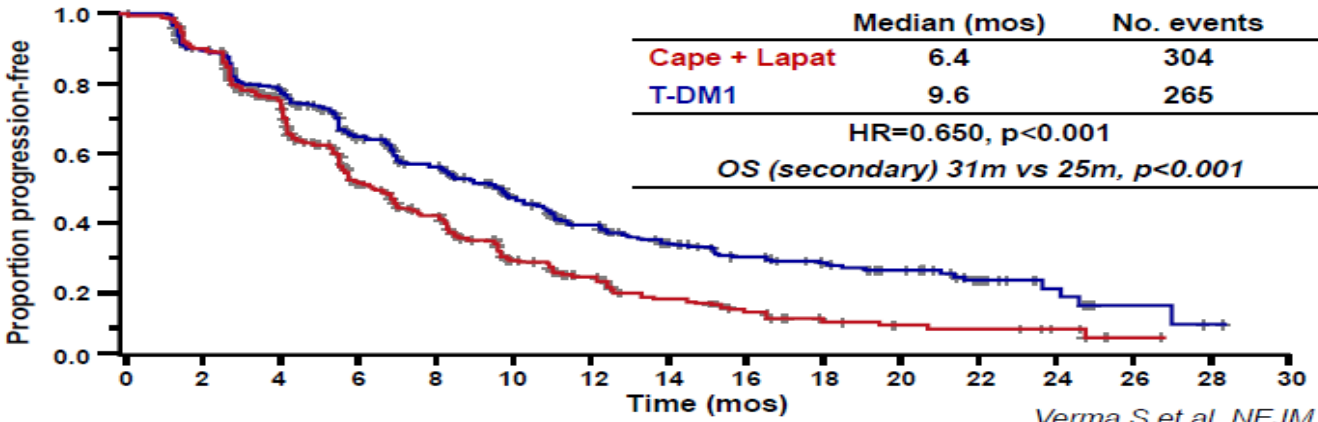
- **Stratification factors:** World region, number of prior chemo regimens for MBC or unresectable LABC, presence of visceral disease
- **Primary end points:** PFS by independent review, OS, and safety
- **Key secondary end points:** PFS by investigator, ORR, duration of response, time to symptom progression

Blackwell et al, ASCO 2012
Verma et al, NEJM 2012

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

EMILIA: Phase III Trial T-DM1 versus XL

Pre-treated setting



	Median (mos)	No. events
Cape + Lapat	6.4	304
T-DM1	9.6	265

HR=0.650, p<0.001

OS (secondary) 31m vs 25m, p<0.001

Verma S et al, NEJM 2012

Toxicity better (and different) with T-DM1: grade 3+ 57% vs 41%
T-DM1 – thrombocytopenia, LFT↑
XL – N/V, hand-foot syndrome

Win-Win

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

San Antonio Breast Cancer Symposium, December 8-12, 2015

Trastuzumab emtansine (T-DM1) improves overall survival versus treatment of physician's choice in patients with previously treated HER2-positive metastatic breast cancer: final overall survival results from the phase 3 TH3RESA study

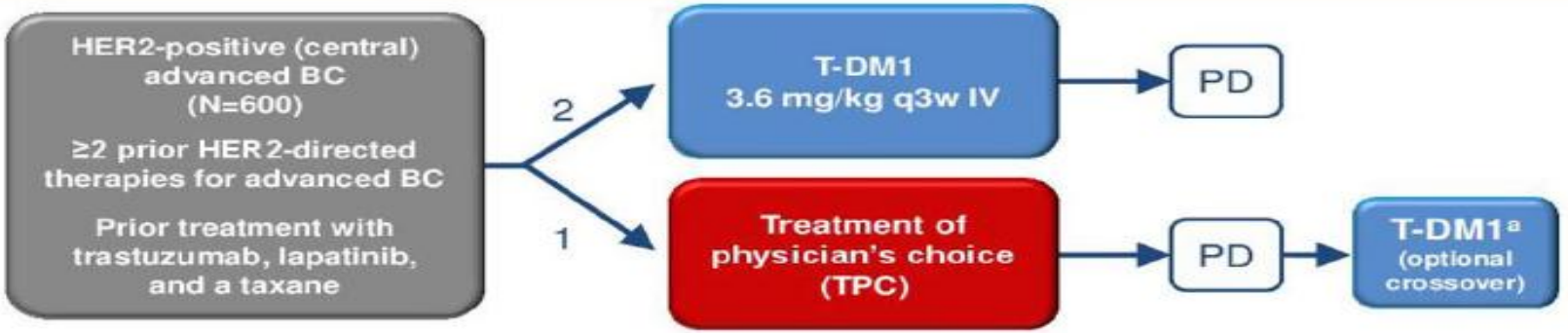
Hans Wildiers,[1] Sung-Bae Kim,[2] Antonio Gonzalez Martin,[3] Patricia M. LoRusso,[4] Jean-Marc Ferrero,[5] Tanja Badovinac-Crnjevic,[6] Ron Yu,[7] Melanie Smitt,[7] Ian E. Krop[8]

[1]University Hospitals Leuven, Leuven, Belgium; [2]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [3]MD Anderson Cancer Center, Madrid, Spain; [4]Yale Cancer Center, Yale University Medical Center, New Haven, CT, USA; [5]Department of Medical Oncology, Centre Antoine Lacassagne, Nice, France; [6]F. Hoffmann-La Roche, Ltd, Basel, Switzerland; [7]Genentech, Inc, South San Francisco, CA, USA; [8]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

San Antonio Breast Cancer Symposium, December 8-12, 2015

TH3RESA Study Schema



Stratification factors: World region, number of prior regimens for advanced BC, presence of visceral disease

Co-primary endpoints: PFS by investigator and OS

Key secondary endpoints: ORR by investigator and safety

[a]First patient in: Sept. 2011. Study amended: Sept. 2012 following EMILIA 2nd interim OS results to allow patients in the TPC arm to receive T-DM1 after documented PD.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

San Antonio Breast Cancer Symposium, December 8-12, 2015

Treatment of Physician's Choice Regimen

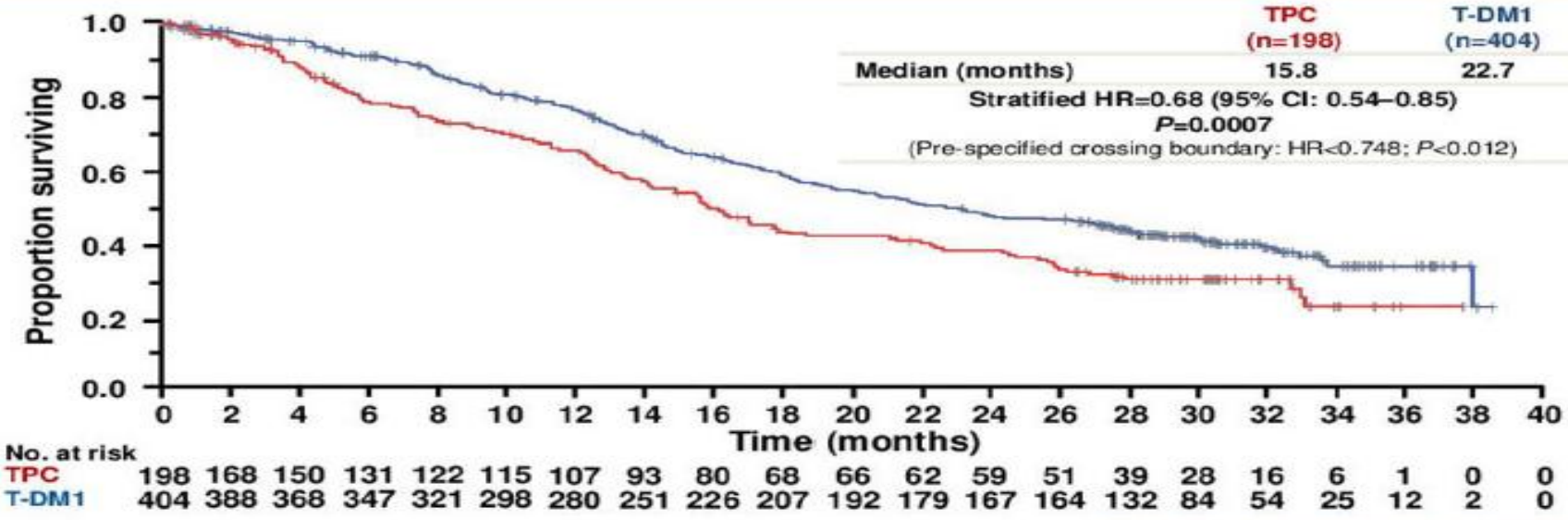
TPC treatment regimen	TPC (n=184[a])	
Combination with HER2-directed agent, %	**83.2**	
Chemotherapy[b] + trastuzumab	68.5	**Trastuzumab-containing 80.4**
Lapatinib + trastuzumab	10.3	
Hormonal therapy + trastuzumab	1.6	
Chemotherapy[b] + lapatinib	2.7	
Single-agent chemotherapy,[b] %	**16.8**	

[a]Includes patients who received study treatment. Excludes one patient who was randomized to the TPC arm but received two cycles of T-DM1 by mistake.
[b]The most common chemotherapy agents used were vinorelbine, gemcitabine, eribulin, paclitaxel, and docetaxel.

HER2 Pozitif Metastatik Meme Kanserinde Tedavi

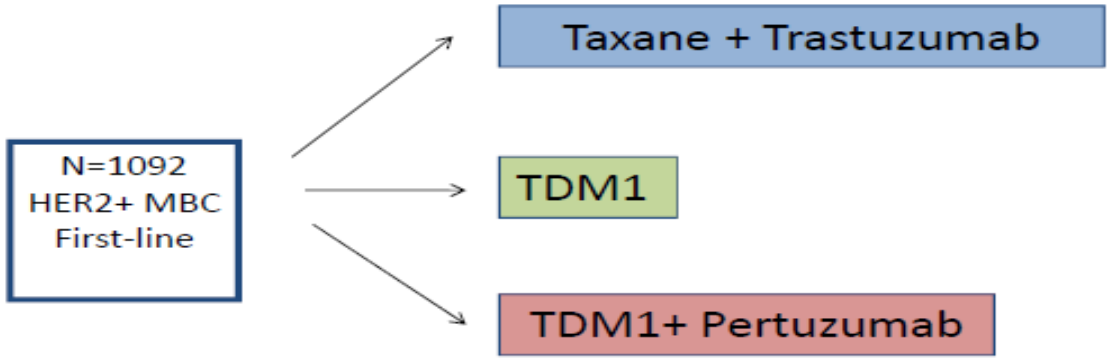
San Antonio Breast Cancer Symposium, December 8-12, 2015

Final OS Analysis



HER2 Pozitif Metastatik Meme Kanserinde Tedavi

MARIANNE Phase III



1° Endpoint: PFS
2° Endpoints: OS, TTF, DOR, ORR, CBR

T= paclitaxel 80 m/m weekly or docetaxel at 75-100 m/m q 3 w
H=trastuzumab 2 mg/kg q w or 6 mg/kg q 3 w
P=pertuzumab at 840 mg load → 420mg q 3 w
TDM= trastuzumab/DM1 at 3.6 mg/kg q 3 w

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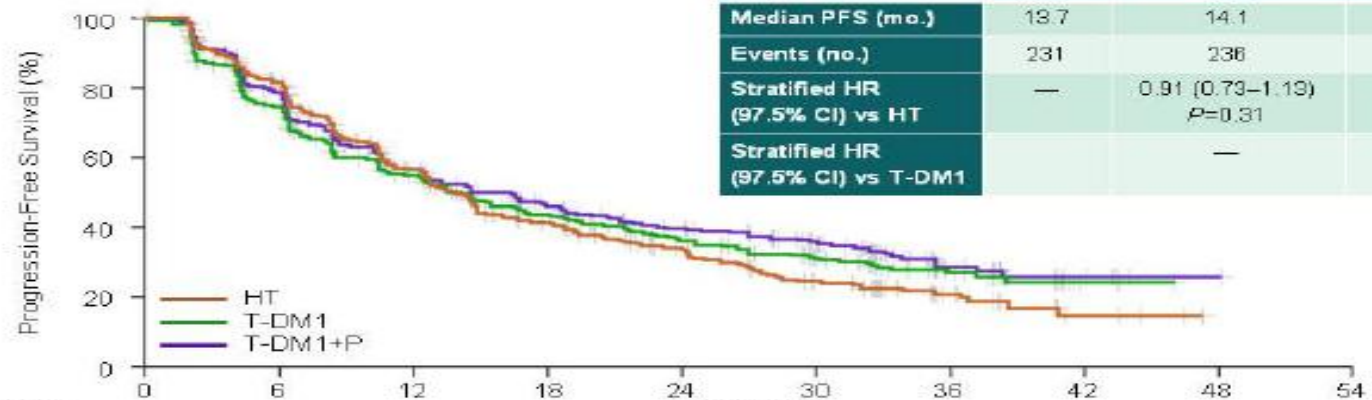
Progression-Free Survival by IRF

	HT	T-DM1	T-DM1+P
Median PFS (mo.)	13.7	14.1	15.2
Events (no.)	231	236	217
Stratified HR (97.5% CI) vs HT	—	0.91 (0.73–1.13) P=0.31	0.97 (0.69–1.09) P=0.14
Stratified HR (97.5% CI) vs T-DM1		—	0.91 (0.73–1.13)



No. at Risk

HT	365	265	163	107	75	50	21	5
T-DM1	367	257	176	133	104	67	28	3
T-DM1+P	363	261	177	135	109	75	25	5

Non-inferiority: Established if the upper limit of the 97.5% CI for the HR is below 1.1785 (non-inferiority margin).

PRESENTED AT: ASCO Annual '15 Meeting

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Key Differences Between CLEOPATRA and MARIANNE

MARIANNE

- Poorer prognosis population
  - Shorter DFI required: > 6m
  - Less *de novo* MBC
  - More patients have prior taxane exposure
  - More patients have previous trastuzumab exposure

CLEOPATRA

- Better prognosis population
  - Longer DFI required: > 12m
  - More *de novo* MBC
  - Fewer patients have prior taxane exposure
  - Fewer patients have previous trastuzumab exposure

DFI = disease free interval from neoadjuvant or adjuvant setting

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CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

Preferred first-line agents for HER2-positive disease:
- Pertuzumab + trastuzumab + docetaxel (category 1)
- Pertuzumab + trastuzumab + paclitaxel

Other agents for HER2-positive disease:
- Ado-trastuzumab emtansine (T-DM1)
- Trastuzumab + paclitaxel ± carboplatin
- Trastuzumab + docetaxel
- Trastuzumab + vinorelbine
- Trastuzumab + capecitabine

Agents for trastuzumab-exposed HER2-positive disease:
- Lapatinib + capecitabine
- Trastuzumab + capecitabine
- Trastuzumab + lapatinib (without cytotoxic therapy)
- Trastuzumab + other agents

BINV-O

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Next Generation of HER2-Targeting

Trial	Line	Regimens	PFS	OS
CLEOPATRA	**1**	**TH ± Pert**	**19 v. 12m (HR 0.69*)**	**56 v. 41m (HR 0.68*)**
MARIANNE[&]	1	TH v. TDM1 v. TDM1+P	ns	-
NEfERTT[&]	1	TH v. TN	17 v. 17m (ns)	?fewer CNS with TN?
BOLERO-1	1	TH ± Eve	15 v. 14m	-
EMILIA	**2**	**TDM1 v. XL**	**10 v. 6m (HR 0.65*)**	**31 vs 29m (HR 0.68*)**
BOLERO-3	2	VH ± Eve	7 v. 6m (HR 0.78*)	-
TH3RESA	**3+**	**TDM1 v. MD choice**	**6 v. 3m (HR 0.53)**	**HR 0.55 (interim)**

* significant

T=taxane; N=neratinib; V=vinorelbine; E=everolimus

Baselga NEJM'12; Swain ESMO'14; Hurvitz SABCS'14; Verma NEJM'12; Andre Lancet Oncol'14; Krop Lancet Oncol'14

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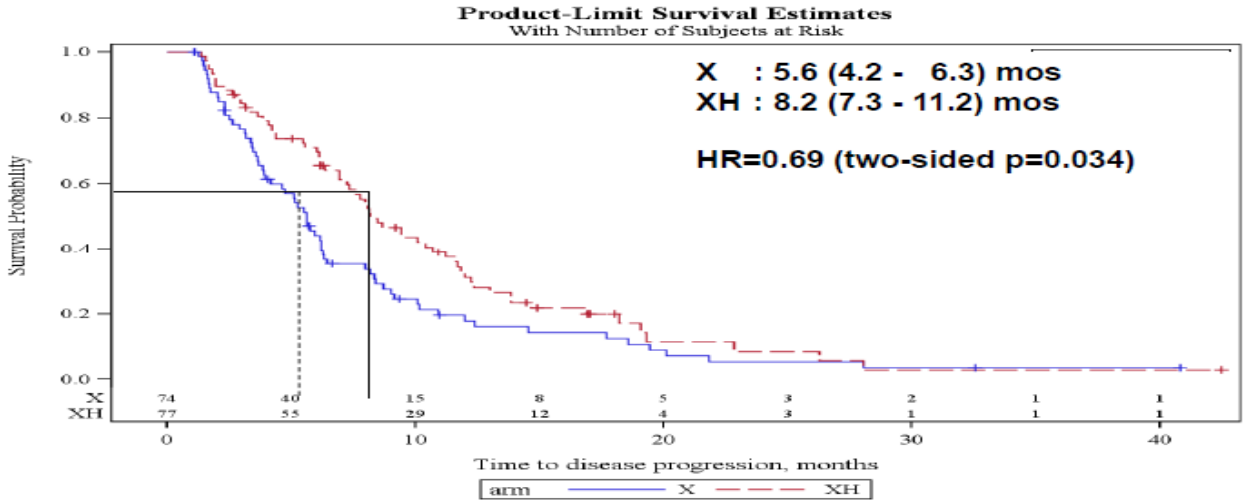
Capecitabine ± Trastuzumab: Time To Progression (after prior trastuzumab)



ORR 48% vs 27%, p=0.0011

von Minckwitz. JCO 2009

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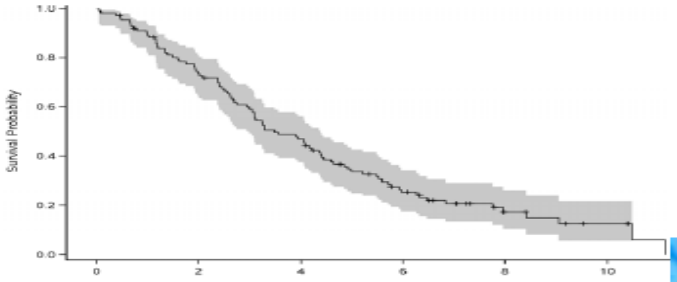
Summary: Metastatic Options for HER2+

Line of therapy	Regimen Options	
	Chemotherapy-based	*Endocrine therapy-based*
First	Taxane + trast + pert	AI + lapatinib or trastuzumab
Second	T-DM1	Fulvestrant + lapatinib or trastuzumab
Third	Capecitabine + lapatinib	
Later	Other drugs + trastuzumab	



Olsen et al, The Breast 2012

Median survival > 4 years, likely to rise
Multiple drug choices

How do we treat most thoughtfully?

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Treatment Approach HER2+ MBC in 2016

First Line: Taxane + Trastuzumab + Pertuzumab

Who Should Receive Endocrine Therapy Upfront?

↓

Second Line: TDM-1

↓

Third, Fourth, Fifth, Sixth Line:

Capecitabine + Lapatinib
Capecitabine + Trastuzumab
Vinorelbine + Trastuzumab
Lapatinib + Trastuzumab
Other chemotherapy + Trastuzmab
Endocrine Therapy + Trastuzumab

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CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER[1,2]

Preferred single agents:

Anthracyclines
- Doxorubicin
- Pegylated liposomal doxorubicin

Taxanes
- Paclitaxel

Anti-metabolites
- Capecitabine
- Gemcitabine

Other microtubule inhibitors
- Vinorelbine
- Eribulin

Other single agents:
- Cyclophosphamide
- Carboplatin
- Docetaxel
- Albumin-bound paclitaxel
- Cisplatin
- Epirubicin
- Ixabepilone

Chemotherapy combinations:
- CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)
- FEC (fluorouracil/epirubicin/cyclophosphamide)
- AC (doxorubicin/cyclophosphamide)
- EC (epirubicin/cyclophosphamide)
- CMF (cyclophosphamide/methotrexate/fluorouracil)
- Docetaxel/capecitabine
- GT (gemcitabine/paclitaxel)
- Gemcitabine/carboplatin
- Paclitaxel/bevacizumab[3]

Preferred first-line agents for HER2-positive disease:
- Pertuzumab + trastuzumab + docetaxel (category 1)[4]
- Pertuzumab + trastuzumab + paclitaxel[4]

Other agents for HER2-positive disease:
- Ado-trastuzumab emtansine (T-DM1)
- Trastuzumab + paclitaxel ± carboplatin
- Trastuzumab + docetaxel
- Trastuzumab + vinorelbine
- Trastuzumab + capecitabine

Agents for trastuzumab-exposed HER2-positive disease:
- Lapatinib + capecitabine
- Trastuzumab + capecitabine
- Trastuzumab + lapatinib (without cytotoxic therapy)
- Trastuzumab + other agents[4,5,6]

[1]There is no compelling evidence that combination regimens are superior to sequential single agents.
[2]Nab-paclitaxel may be substituted for paclitaxel or docetaxel due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of nab-paclitaxel should not exceed 125 mg/m^2.
[3]Randomized clinical trials in metastatic breast cancer document that the addition of bevacizumab to some first- or second-line chemotherapy agents modestly improves time to progression and response rates but does not improve overall survival. The time-to-progression impact may vary among cytotoxic agents and appears greatest with bevacizumab in combination with weekly paclitaxel.

[4]Patients previously treated with chemotherapy plus trastuzumab in the absence of pertuzumab in the metastatic setting may be considered for one line of therapy including both trastuzumab plus pertuzumab in combination with or without cytotoxic therapy (such as vinorelbine or taxane). Further research is needed to determine the ideal sequencing strategy for anti-HER2 therapy.
[5]Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided.
[6]Trastuzumab may be safely combined with all non-anthracycline containing preferred and other single agents listed above for recurrent or metastatic breast cancer.

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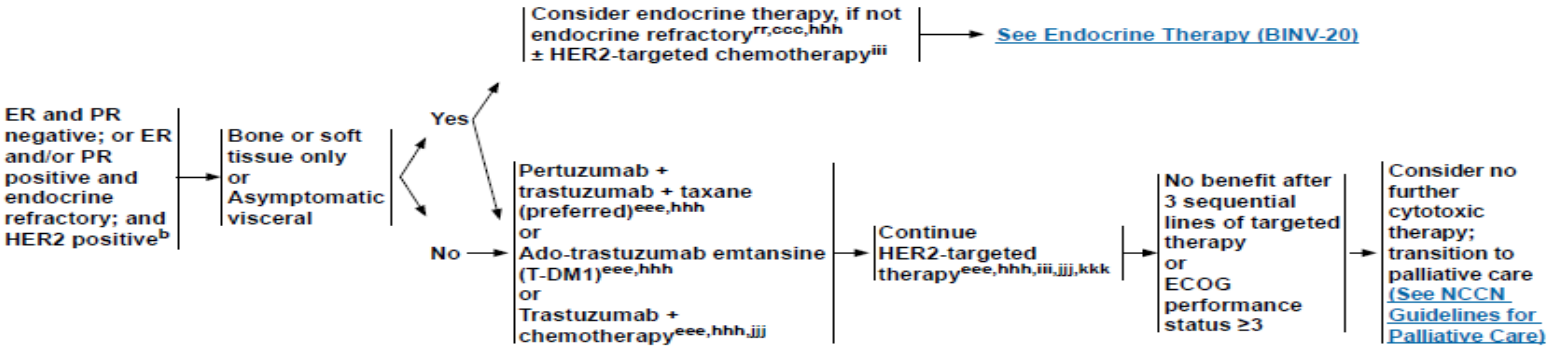
SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE
ER and PR NEGATIVE; or ER and/or PR POSITIVE and ENDOCRINE REFRACTORY; and HER2 POSITIVE



[b] See Principles of HER2 Testing (BINV-A).
[rr] False-negative ER and/or PR determinations occur, and there may be discordance between the ER and/or PR determination between the primary and metastatic tumor(s). Therefore, endocrine therapy with its low attendant toxicity may be considered in patients with non-visceral or asymptomatic visceral tumors, especially in patients with clinical characteristics predicting for a hormone receptor-positive tumor (eg, long disease-free interval, limited sites of recurrence, indolent disease, older age).
[ccc] See Endocrine Therapy for Recurrent or Stage IV Disease (BINV-N).
[eee] See Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer (BINV-O).
[hhh] See Principles of Monitoring Metastatic Disease (BINV-P).
[iii] Continue HER2-targeted therapy following progression on first-line HER2-targeted chemotherapy for metastatic breast cancer. The optimal duration of trastuzumab in patients with long-term control of disease is unknown.
[jjj] Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided.
[kkk] Patients previously treated with chemotherapy plus trastuzumab in the absence of pertuzumab may be considered for one line of therapy including both trastuzumab plus pertuzumab in combination with or without cytotoxic therapy (such as vinorelbine or taxane). Further research is needed to determine the ideal sequencing strategy for anti-HER2 therapy.

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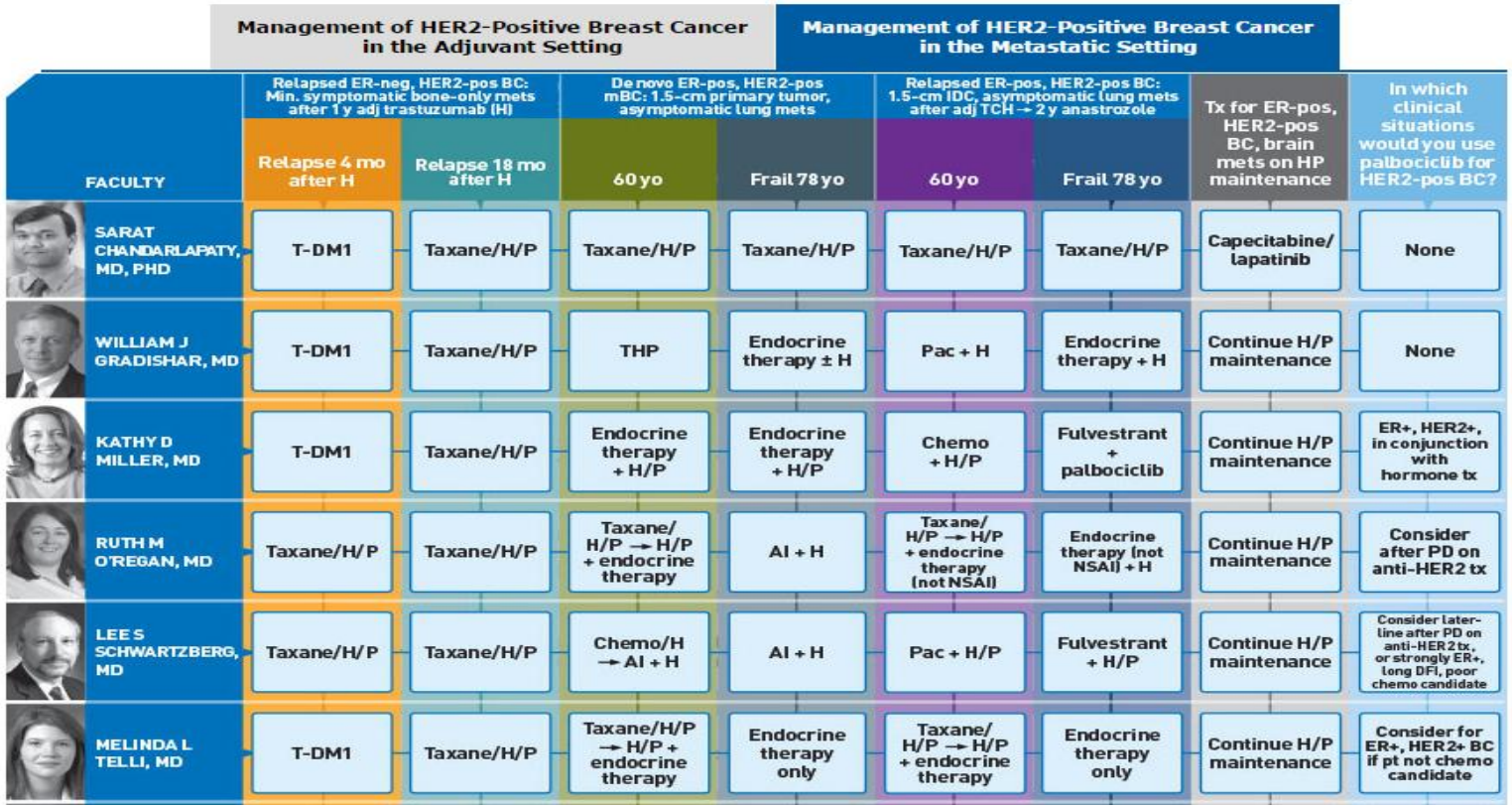
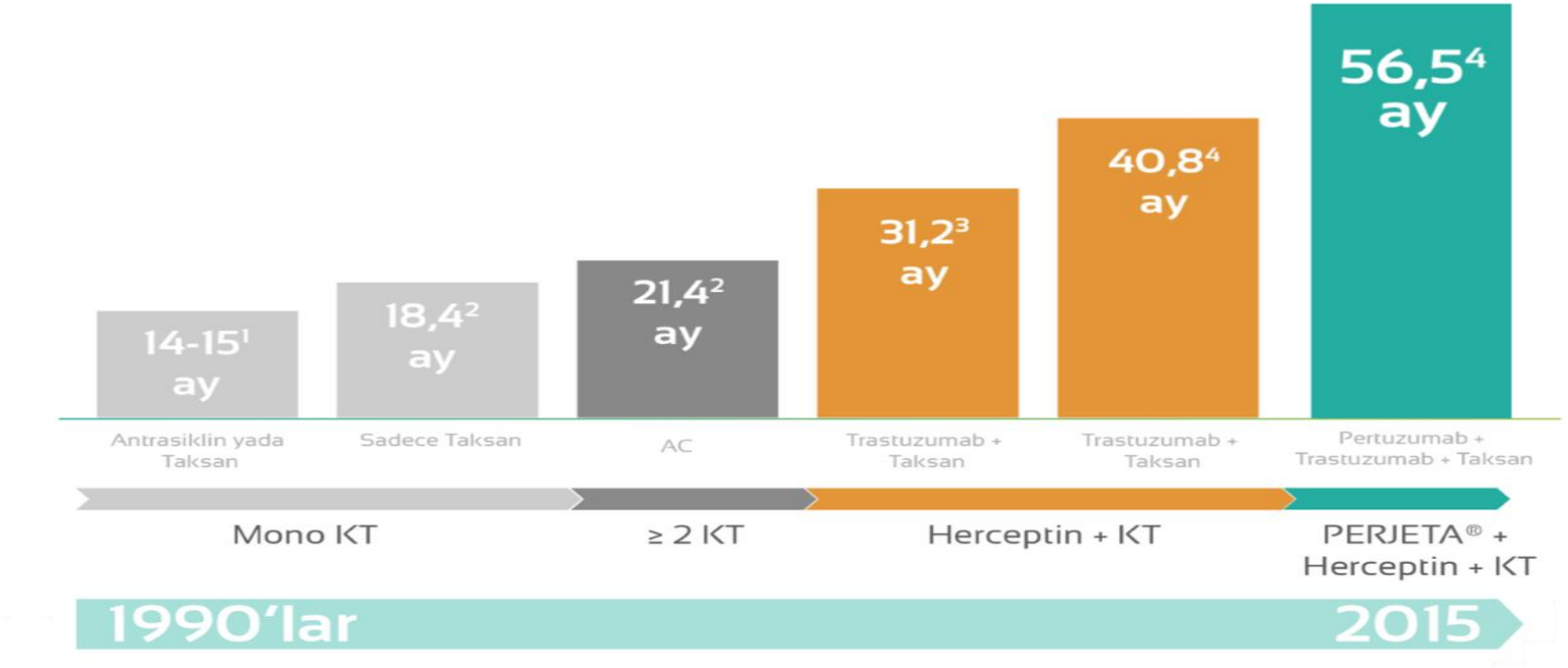


	Management of HER2-Positive Breast Cancer in the Adjuvant Setting		Management of HER2-Positive Breast Cancer in the Metastatic Setting					
	Relapsed ER-neg, HER2-pos BC: Min. symptomatic bone-only mets after 1 y adj trastuzumab (H)		De novo ER-pos, HER2-pos mBC: 1.5-cm primary tumor, asymptomatic lung mets		Relapsed ER-pos, HER2-pos BC: 1.5-cm IDC, asymptomatic lung mets after adj TCH → 2 y anastrozole		Tx for ER-pos, HER2-pos BC, brain mets on HP maintenance	In which clinical situations would you use palbociclib for HER2-pos BC?
FACULTY	Relapse 4 mo after H	Relapse 18 mo after H	60 yo	Frail 78 yo	60 yo	Frail 78 yo		
SARAT CHANDARLAPATY, MD, PHD	T-DM1	Taxane/H/P	Taxane/H/P	Taxane/H/P	Taxane/H/P	Taxane/H/P	Capecitabine/ lapatinib	None
WILLIAM J GRADISHAR, MD	T-DM1	Taxane/H/P	THP	Endocrine therapy ± H	Pac + H	Endocrine therapy + H	Continue H/P maintenance	None
KATHY D MILLER, MD	T-DM1	Taxane/H/P	Endocrine therapy + H/P	Endocrine therapy + H/P	Chemo + H/P	Fulvestrant + palbociclib	Continue H/P maintenance	ER+, HER2+, in conjunction with hormone tx
RUTH M O'REGAN, MD	Taxane/H/P	Taxane/H/P	Taxane/ H/P → H/P + endocrine therapy	AI + H	Taxane/ H/P → H/P + endocrine therapy (not NSAI)	Endocrine therapy (not NSAI) + H	Continue H/P maintenance	Consider after PD on anti-HER2 tx
LEE S SCHWARTZBERG, MD	Taxane/H/P	Taxane/H/P	Chemo/H → AI + H	AI + H	Pac + H/P	Fulvestrant + H/P	Continue H/P maintenance	Consider later-line after PD on anti-HER2 tx, or strongly ER+, long DFI, poor chemo candidate
MELINDA L TELLI, MD	T-DM1	Taxane/H/P	Taxane/H/P → H/P + endocrine therapy	Endocrine therapy only	Taxane/ H/P → H/P + endocrine therapy	Endocrine therapy only	Continue H/P maintenance	Consider for ER+, HER2+ BC if pt not chemo candidate

SAĞKALIM ÖYKÜSÜ

HER2+ METASTATİK MEME KANSERİ



Grafik referanslardan uyarlanmıştır.
1.Chan S, et al. J Clin Oncol 1999; 17:2341-2354 2.Slamon DJ, et al. N Engl J Med 2001; 344:783-792
3.Marty M, et al. J Clin Oncol 2005; 23:4265-4274 4. Swain SM, et al. N eng J Med 2015; 372:724-34

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