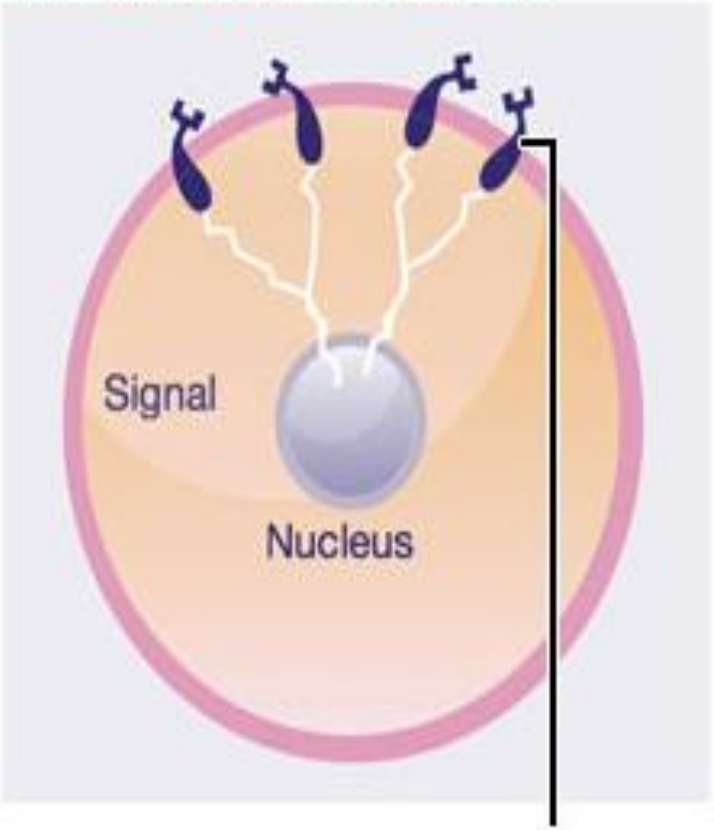
Her2 Pozitif ve Lokal İleri Meme Kanserinde Neoadjuvan Tedavi

Dr. Gökhan ERDEM

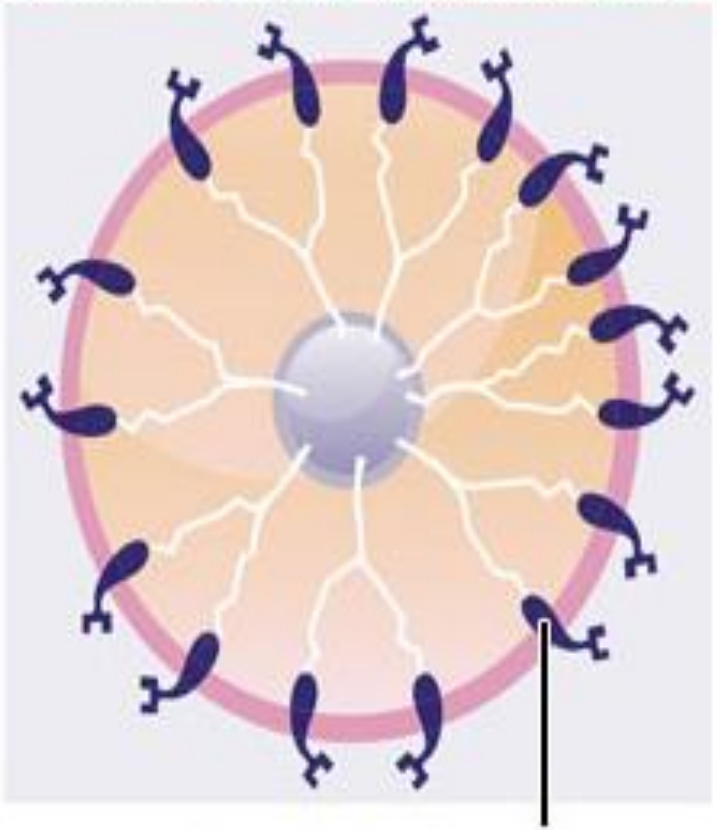
LİV Hospital Ankara Hastanesi, Tıbbi Onkoloji

Normal breast cancer cell



Normal amount of HER2 receptors send signals telling cells to grow and divide.[1]

Abnormal HER2+ breast cancer cell



Too many HER2 receptors send more signals, causing cells to grow too quickly.[1]

VOLUME 33 · NUMBER 1 · JANUARY 1 2015

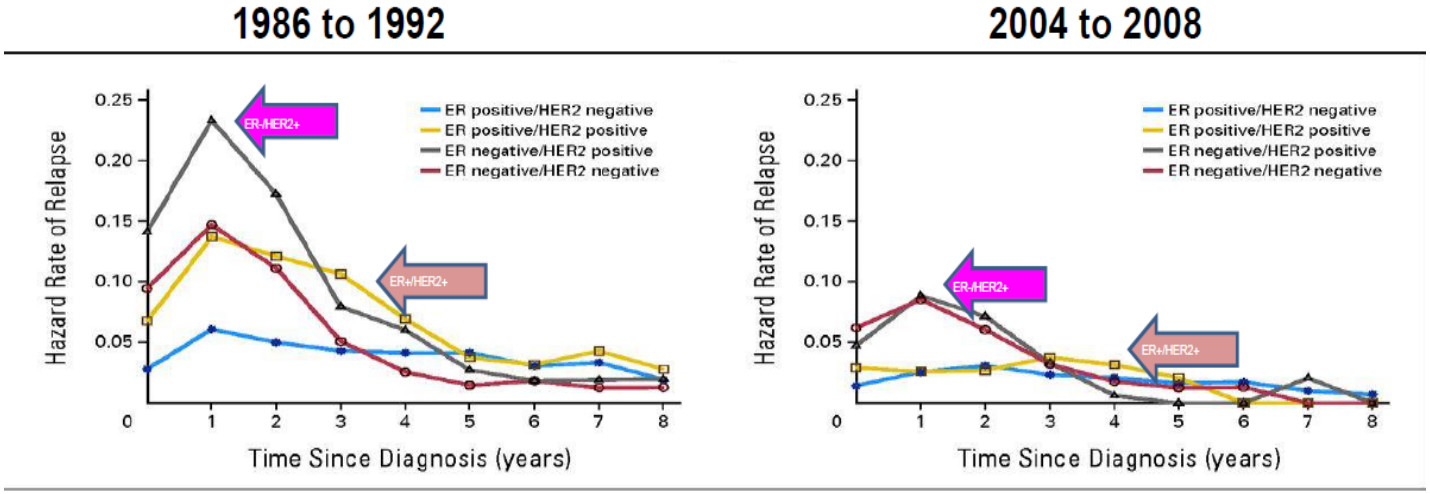
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Comparison of Breast Cancer Recurrence and Outcome Patterns Between Patients Treated From 1986 to 1992 and From 2004 to 2008

Rachel J.D. Cossetti, Scott K. Tyldesley, Caroline H. Speers, Yvonne Zheng, and Karen A. Gelmon

Hazard Rate of Relapse by Tumor Subtype and Year of Diagnosis: British Columbia Population Based Data



7178 patients from British Columbia registry
Matched by stage, grade, ER, HER2

Cossetti RJ, et al. J Clin Oncol. 2015;33(1):65-73

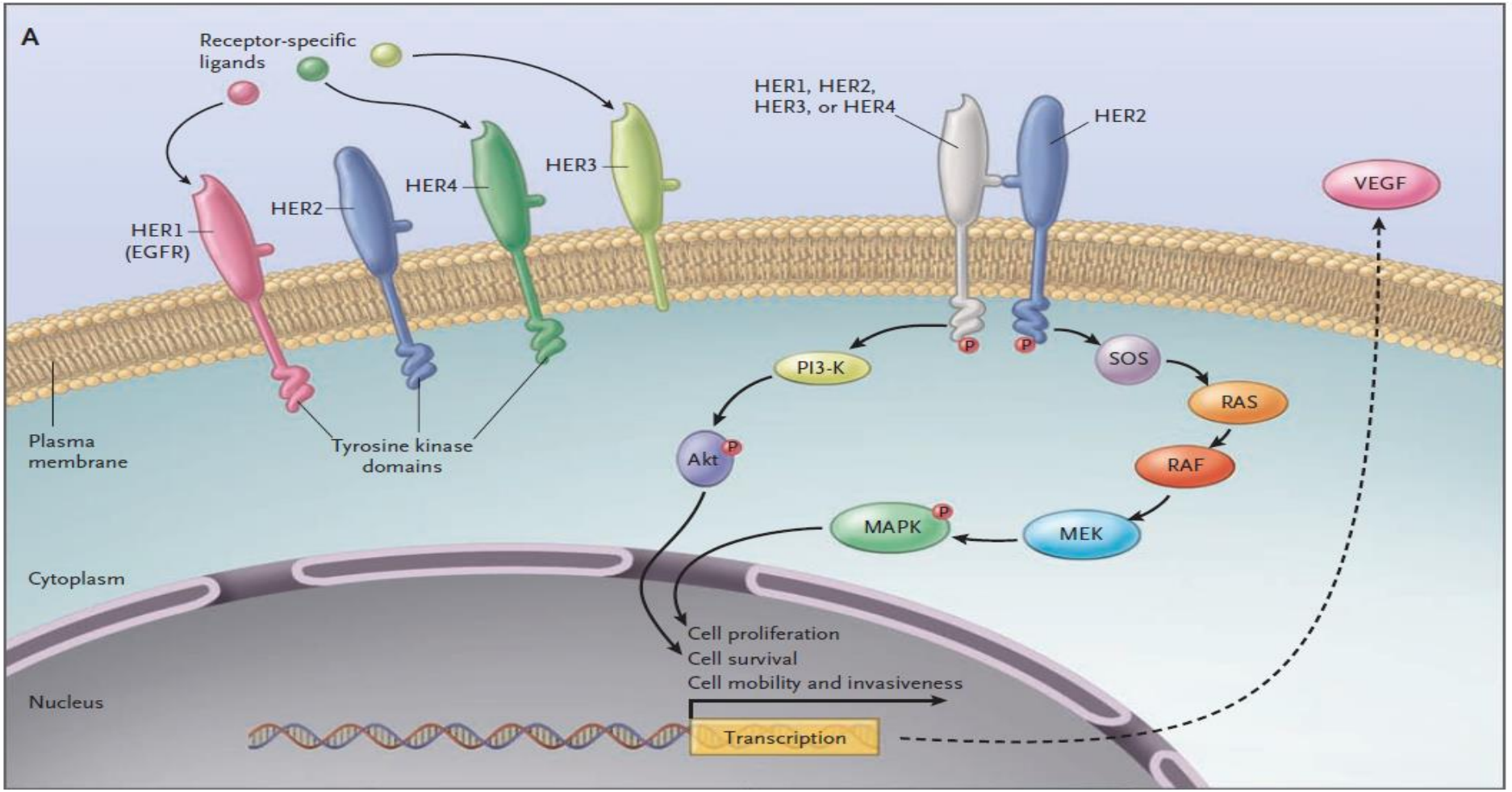
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Trastuzumab — Mechanism of Action and Use in Clinical Practice

Clifford A. Hudis, M.D.



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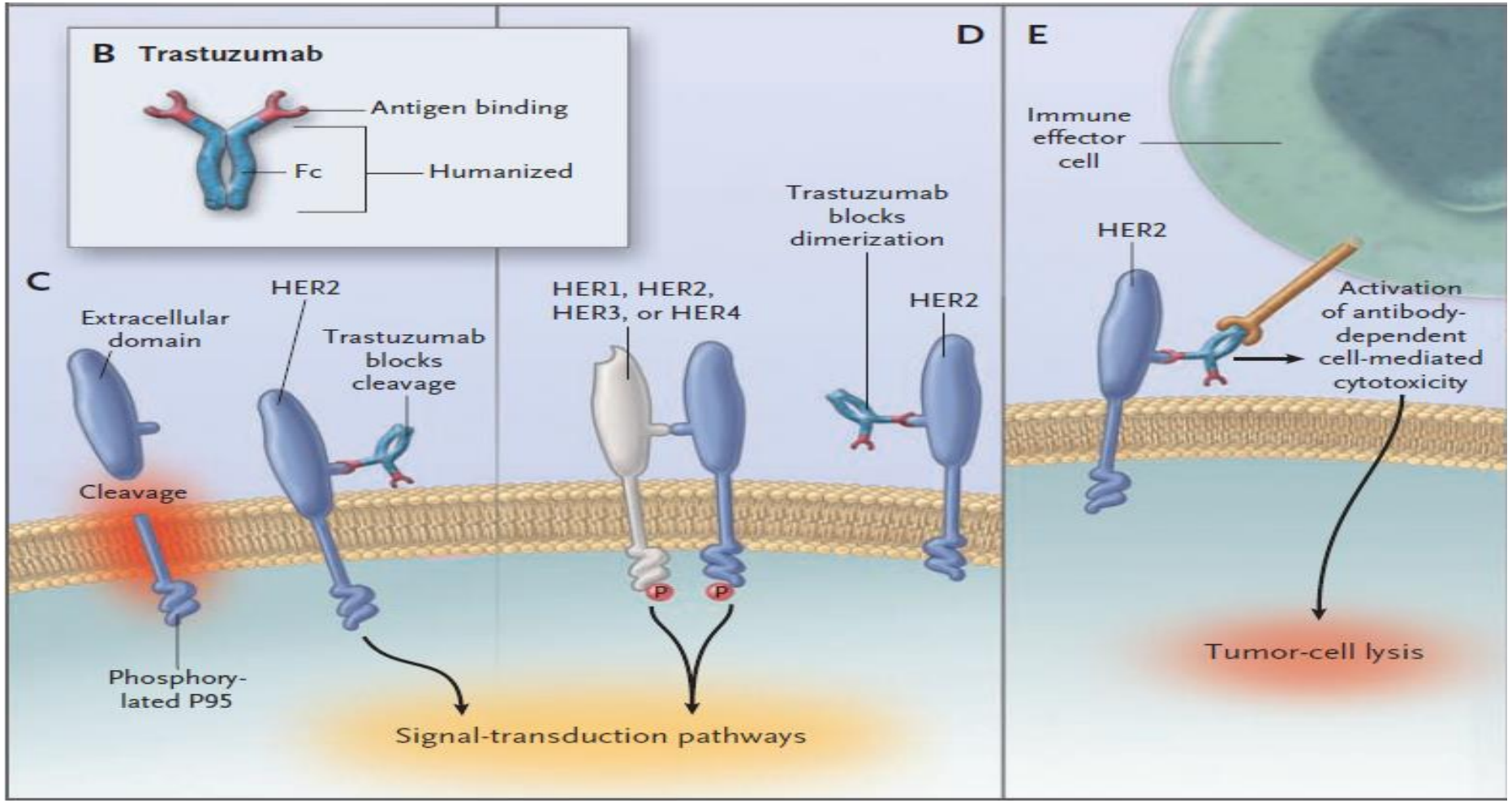
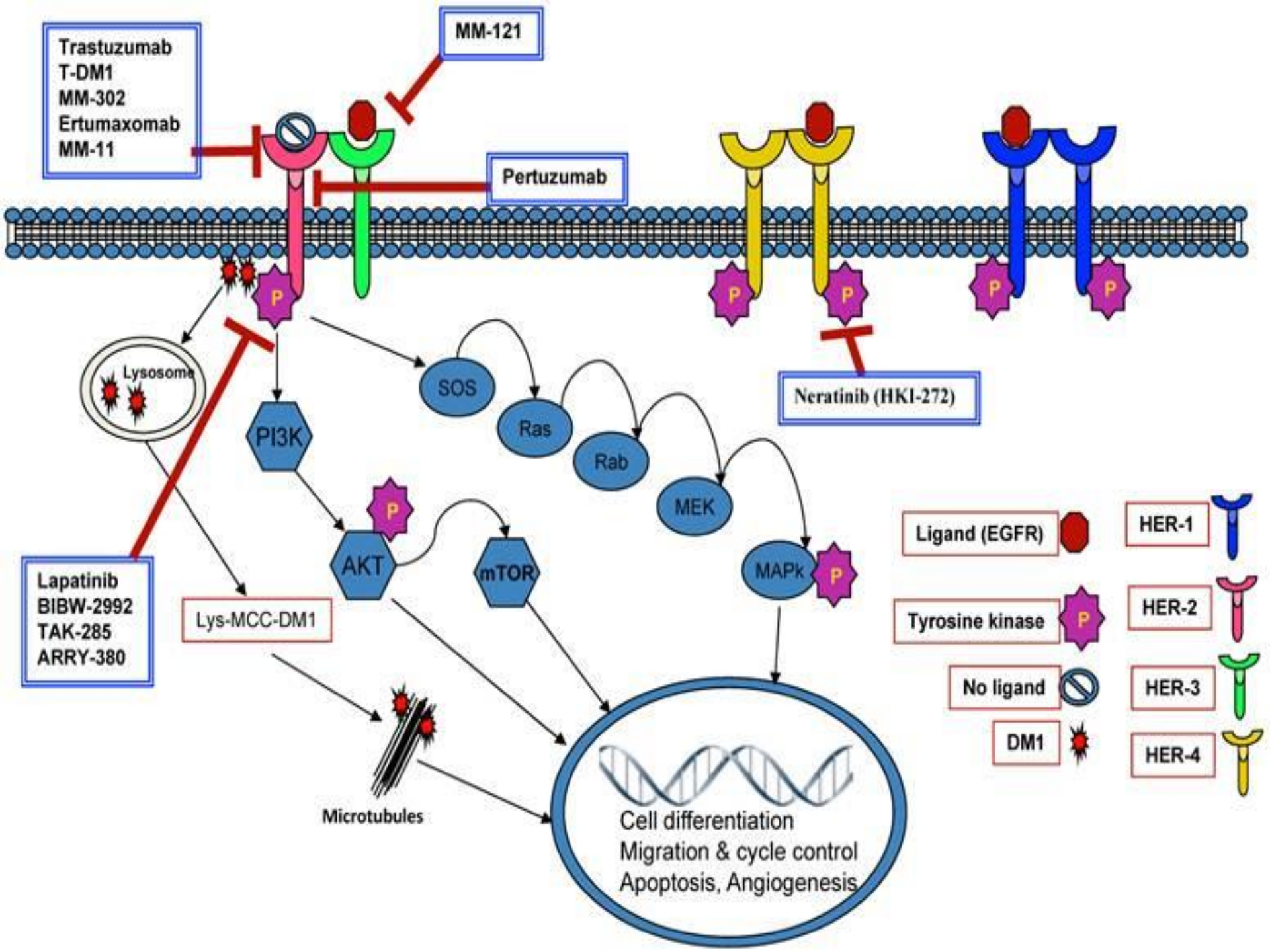



Trastuzumab
T-DM1
MM-302
Ertumaxomab
MM-11
MM-121
Pertuzumab
Neratinib (HKI-272)
Lysosome
SOS
Ras
Rab
MEK
PI3K
AKT
mTOR
MAPk
P
Lapatinib
BIBW-2992
TAK-285
ARRY-380
Lys-MCC-DM1
Microtubules
Cell differentiation
Migration & cycle control
Apoptosis, Angiogenesis
Ligand (EGFR)
Tyrosine kinase
No ligand
DM1
HER-1
HER-2
HER-3
HER-4

NEOADJUVAN TEDAVİ ENDİKASYONLARI…

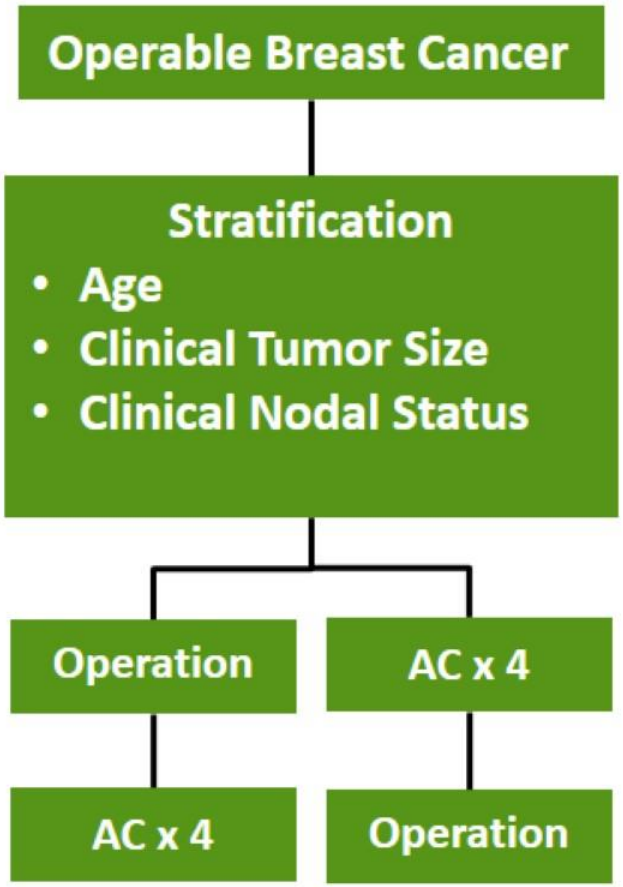
Neoadjuvan Tedavi Endikasyonları
İnflamatuvar meme kanseri
T4 tümör
N2 veya N3 hastalık
Meme koruyucu cerrahi için tümör/meme oranı uygun olmayan hastalar

NEOADJUVAN TEDAVİDE HEDEFLER

- Mikro-metastatik hastalığın erken tedavisi
- Tümörün cerrahi tedavi için uygun hale gelmesi
- Meme koruyucu cerrahi ↑
- Aksillar lenf nodları ↓
- Yeni sistemik ajanlara verilen patolojik cevabın değerlendirilmesi
- Direnç ve duyarlılık için prediktif belirteçlerin belirlenmesi

NSABP B-18

Neoadjuvant vs Adjuvant Doxorubicin + Cyclophosphamide (AC)



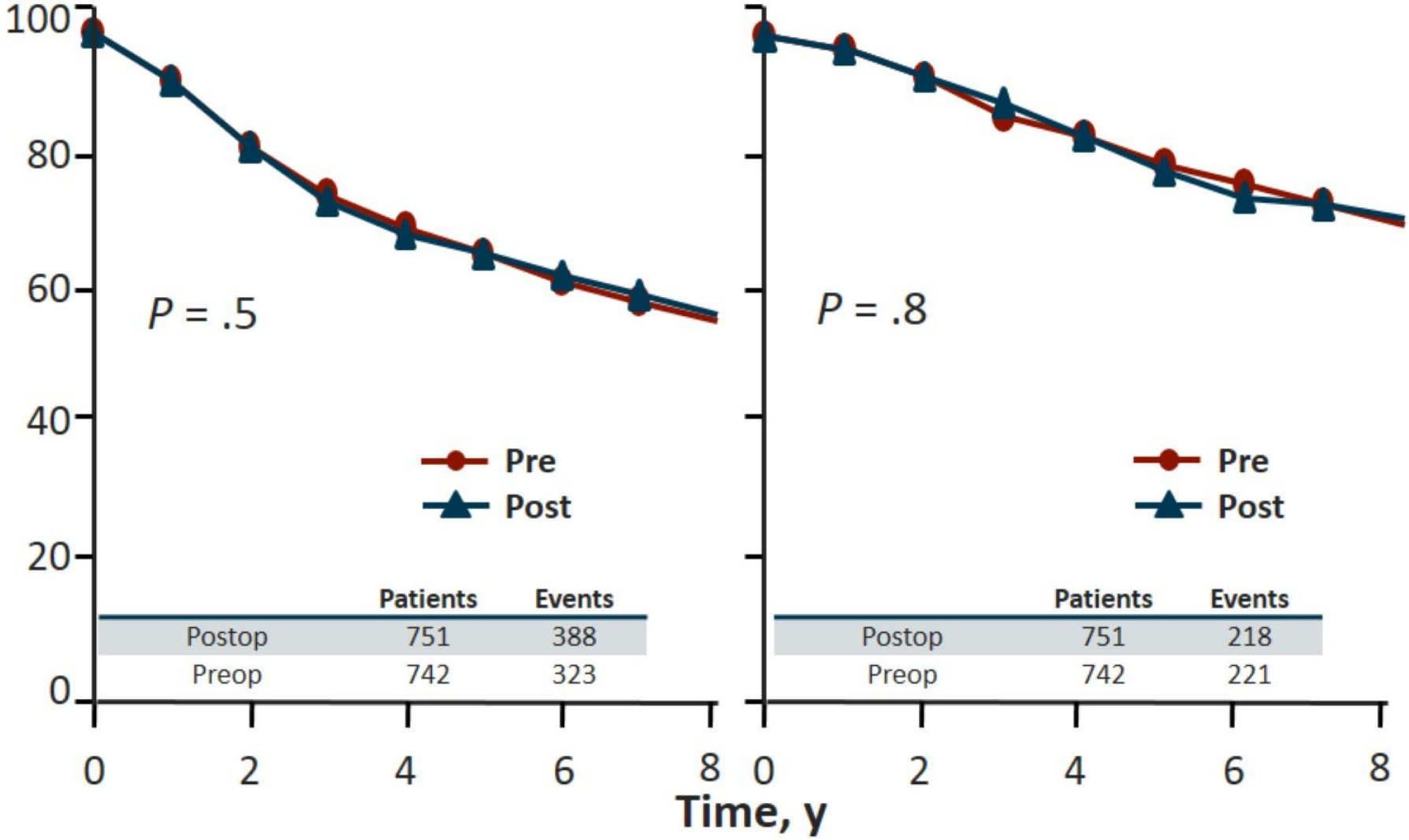
Key Principles

- High clinical response rate: 79%
  - cCR: 36% cPR: 43%
    - pCR: 13%
- Increase in lumpectomy rate: 68% vs 60%
- Downstaging of (+) axillary nodes: 58% vs 40%
- No difference in DFS and OS
- Significant correlation between pCR and outcome

Wolmark N, et al. *J Natl Cancer Inst Monogr* 2001;30:96-102.

NSABP B-18

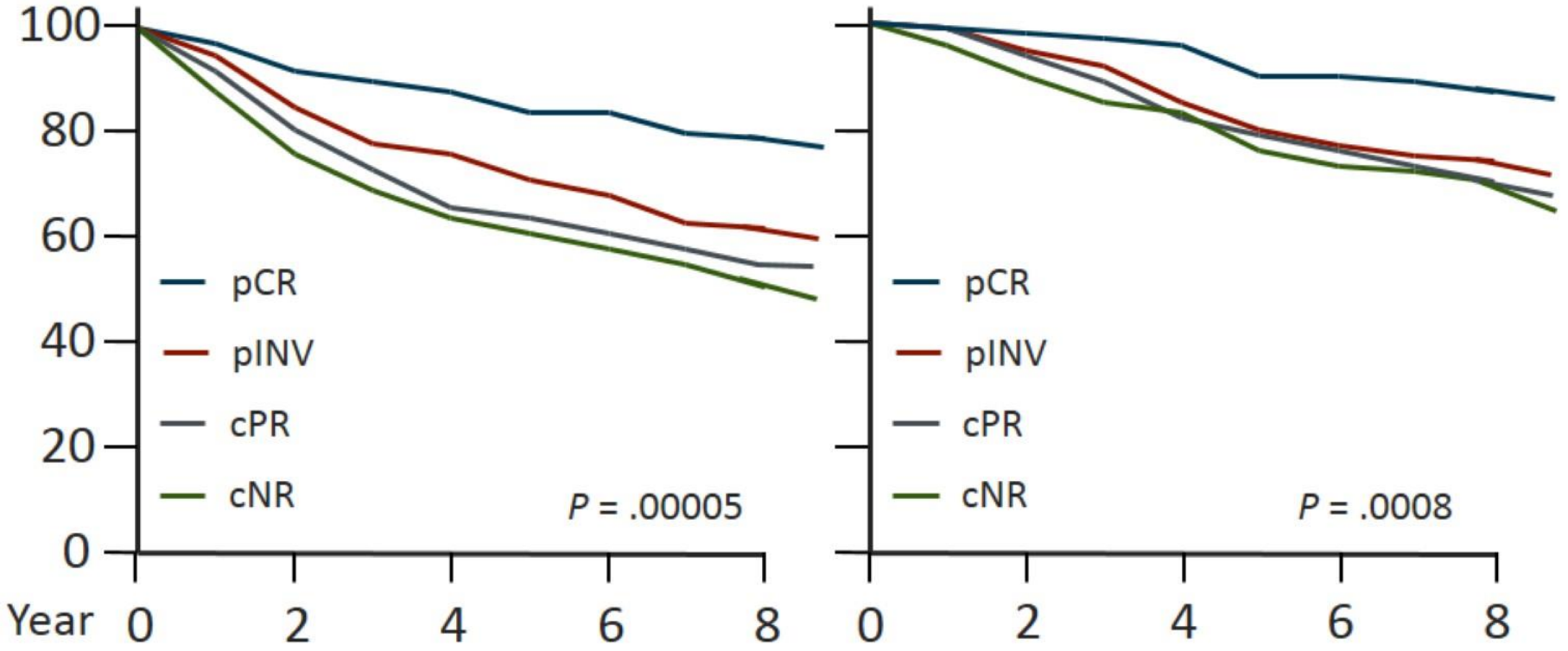
Disease-Free and Overall Survival Rates



Wolmark N, et al. *J Natl Cancer Inst Monogr* 2001;30:96-102. By permission of Oxford University Press.

NSABP B-18

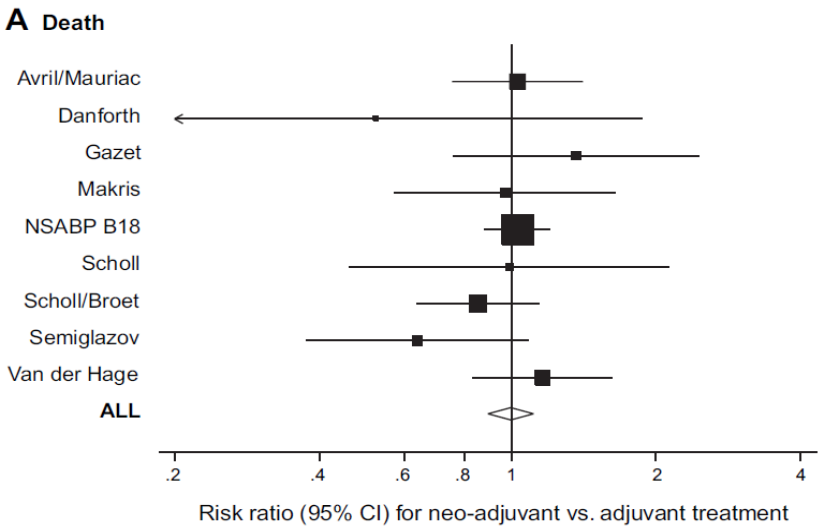
Disease-Free and Overall Survival Rates According to Response

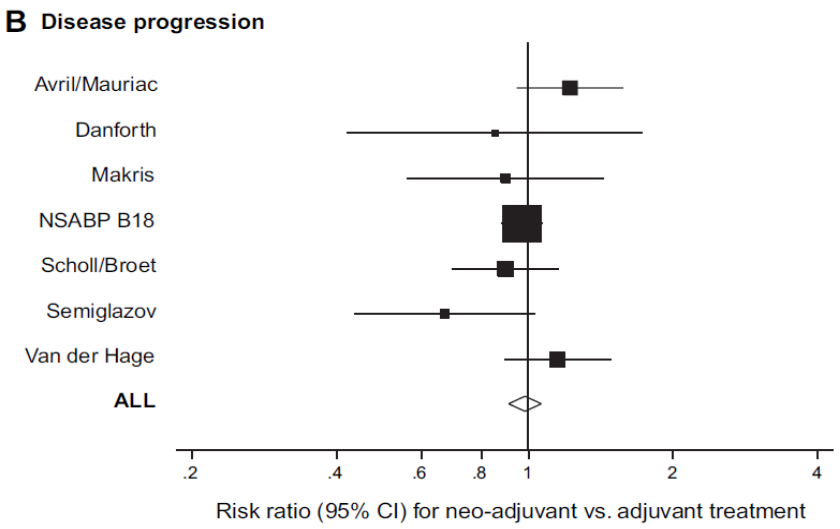


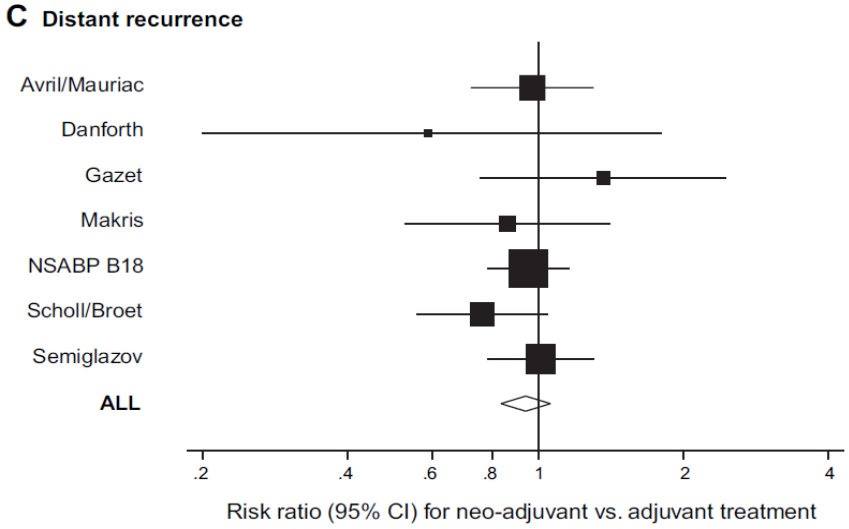
Wolmark N, et al. *J Natl Cancer Inst Monogr* 2001;30:96-102. By permission of Oxford University Press.

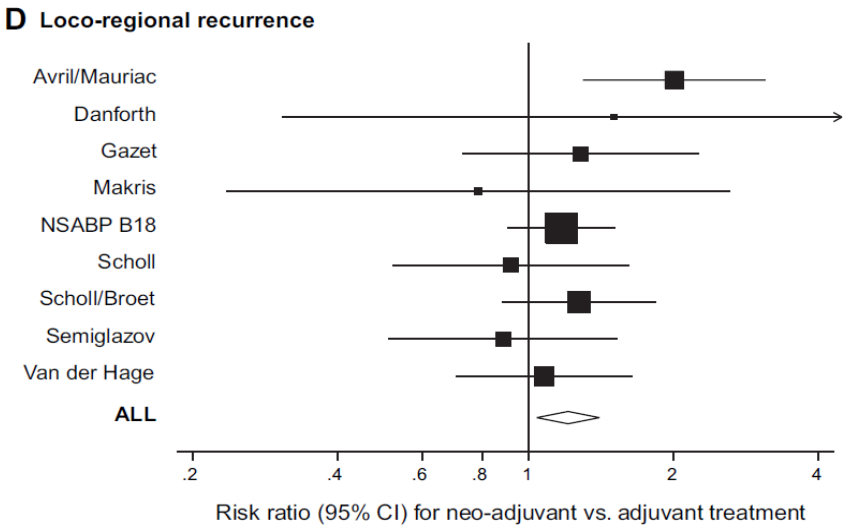
Neoadjuvant Versus Adjuvant Systemic Treatment in Breast Cancer: A Meta-Analysis

Davide Mauri, Nicholas Pavlidis, John P. A. Ioannidis









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- Direnç ve duyarlılık için prediktif belirteçlerin belirlenmesi

Conversion to BCT With NAC
Early Clinical Trials

Trial	Chemotherapy	Mastectomy → BCT
NSABP B18	AC x 4	27%
EORTC 10902	FEC x 4	23%

Fisher B, et al. *J Clin Oncol.* 1997;15(7):2483-2493. van der Hage JA, et al. *J Clin Oncol.* 2001;19(22):4224-4237.

NSABP B-18
Axillary Node Downstaging

	Surgery first (n = 743)	Chemo first (n = 735)
Overall node +	57%	41%
1-3 nodes +	30%	24%
4-9 nodes +	17%	12%
>10 nodes +	10%	4%
		P<.001

Fisher B, et al. *J Clin Oncol*. 1997;15(7):2483-2493.

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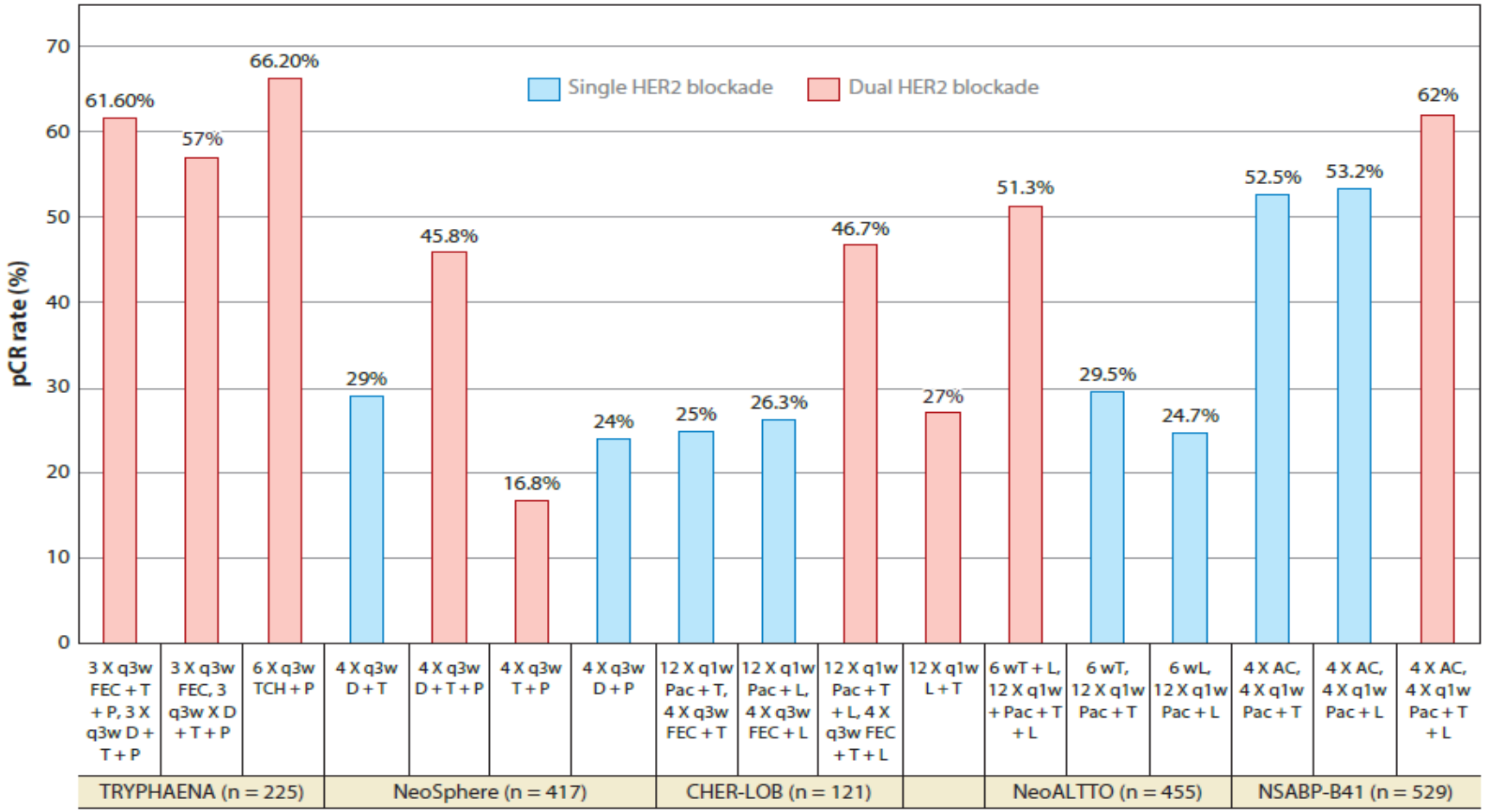
PATOLOJİK TAM CEVAP?



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Pathological Complete Response and Accelerated Drug Approval in Early Breast Cancer

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

N Engl J Med 2012; 366:2438-2441 | June 28, 2012 | DOI: 10.1056/NEJMp1205737

Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis

Patricia Cortazar, Lijun Zhang, Michael Untch, Keyur Mehta, Joseph P Costantino, Norman Wolmark, Hervé Bonnefoi, David Cameron, Luca Gianni, Pinuccia Valagussa, Sandra M Swain, Tatiana Prowell, Sibylle Loibl, D Lawrence Wickerham, Jan Bogaerts, Jose Baselga, Charles Perou, Gideon Blumenthal, Jens Blohmer, Eleftherios P Mamounas, Jonas Bergh, Vladimir Semiglazov, Robert Justice, Holger Eidtmann, Soonmyung Paik, Martine Piccart, Rajeshwari Sridhara, Peter A Fasching, Leen Slaets, Shenghui Tang, Bernd Gerber, Charles E Geyer Jr, Richard Pazdur, Nina Ditsch, Priya Rastogi, Wolfgang Eiermann, Gunter von Minckwitz

- 12 çalışma 11955 hasta
- 4 önemli soru…
  - pCR ile EFS ve OS arasında ilişki var mı ? (Hasta seviyesinde)
  - pCR en iyi şekilde nasıl tanımlanmalıdır?
  - Hangi meme kanseri alt grubunda pCR ile OS arasındaki ilişki güçlüdür?
  - pCR deki artış EFS ve OS artışına neden olmakta mıdır? (Çalışma seviyesinde)

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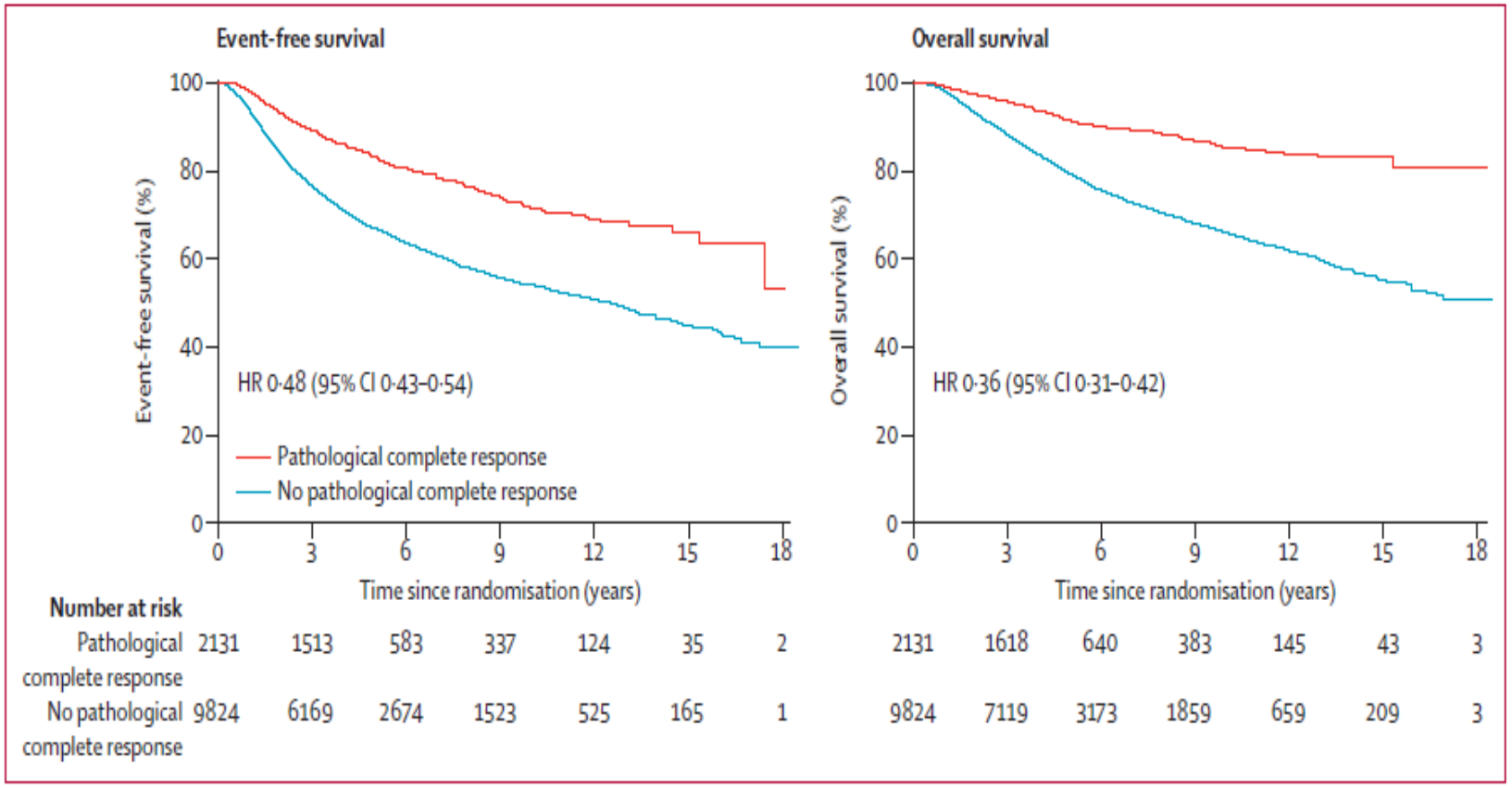

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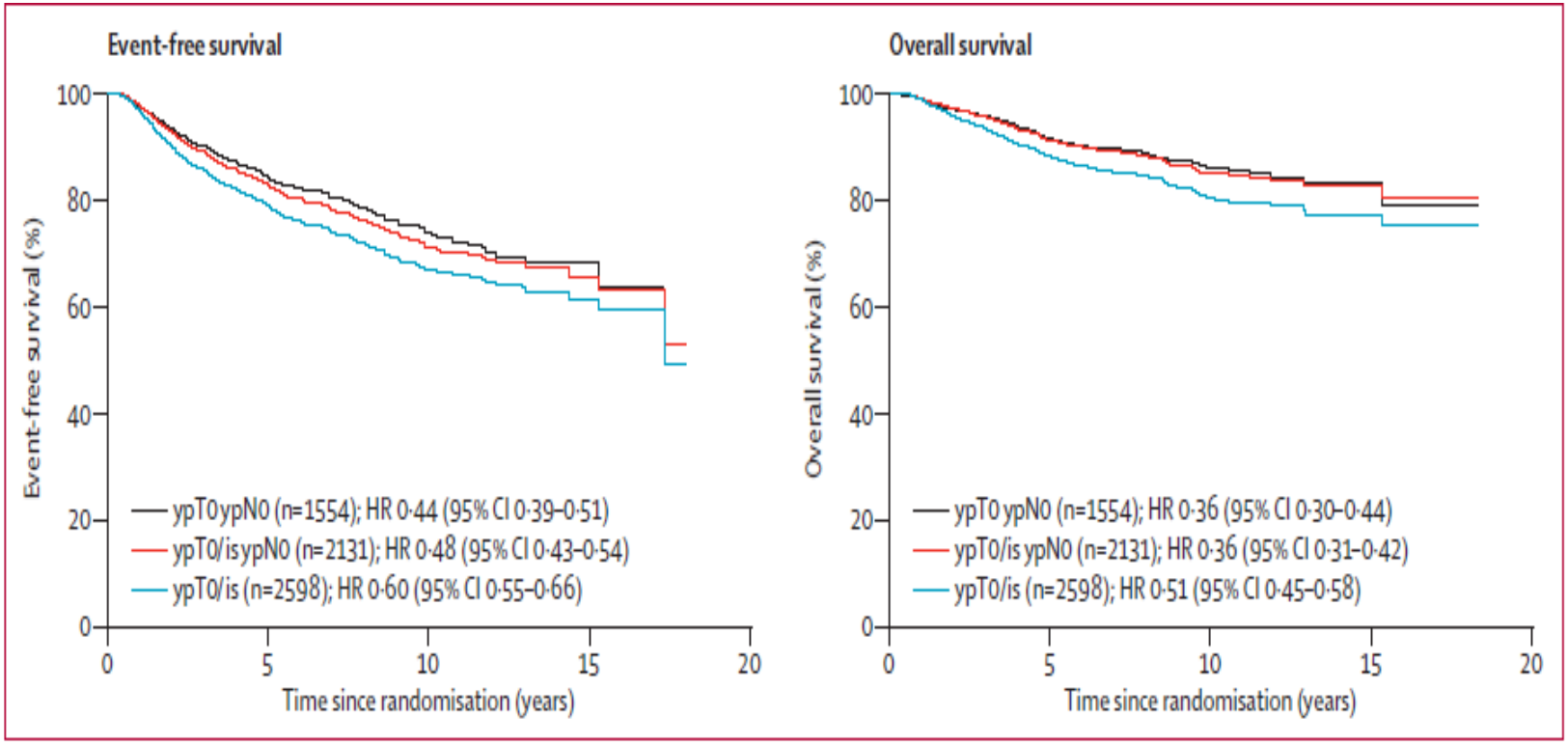

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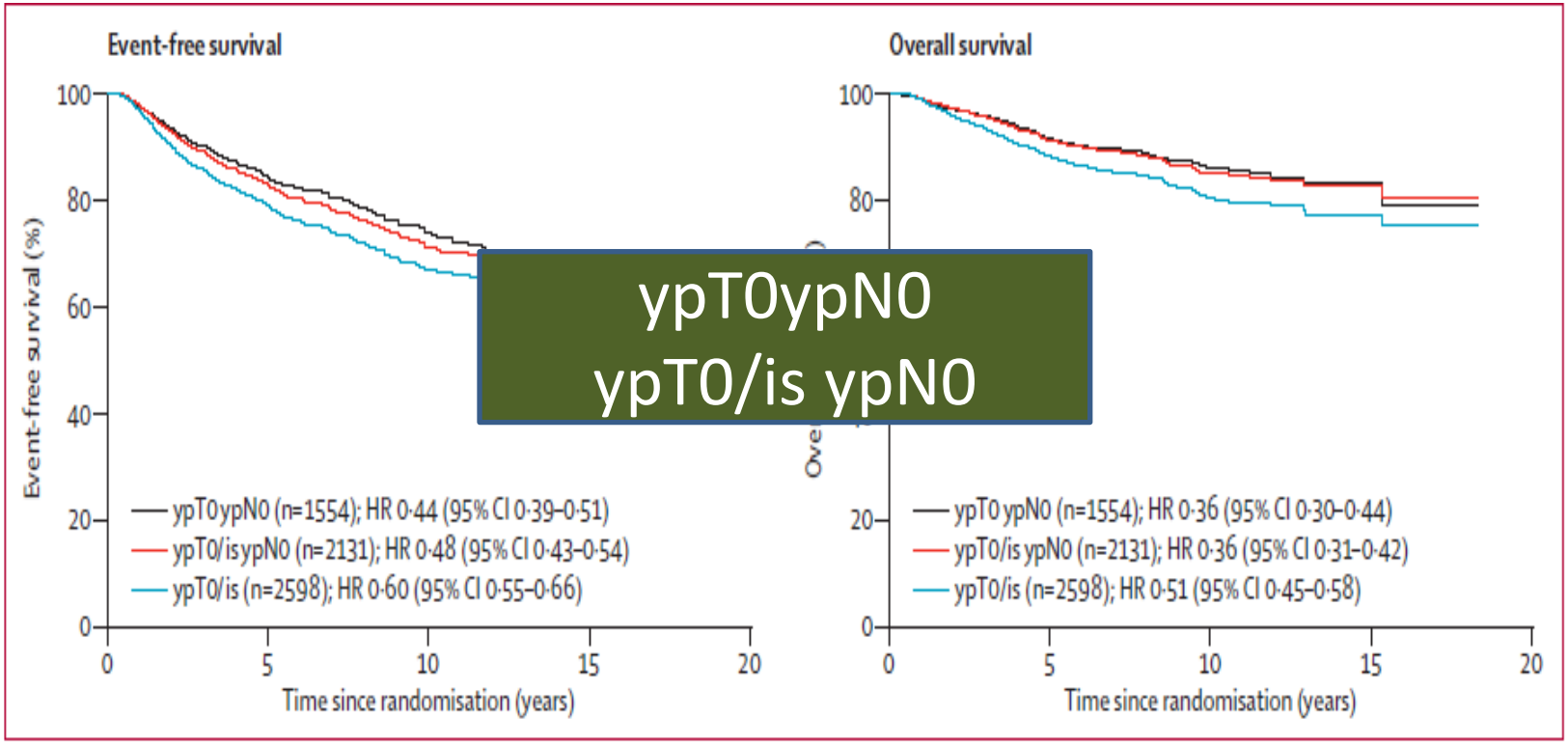

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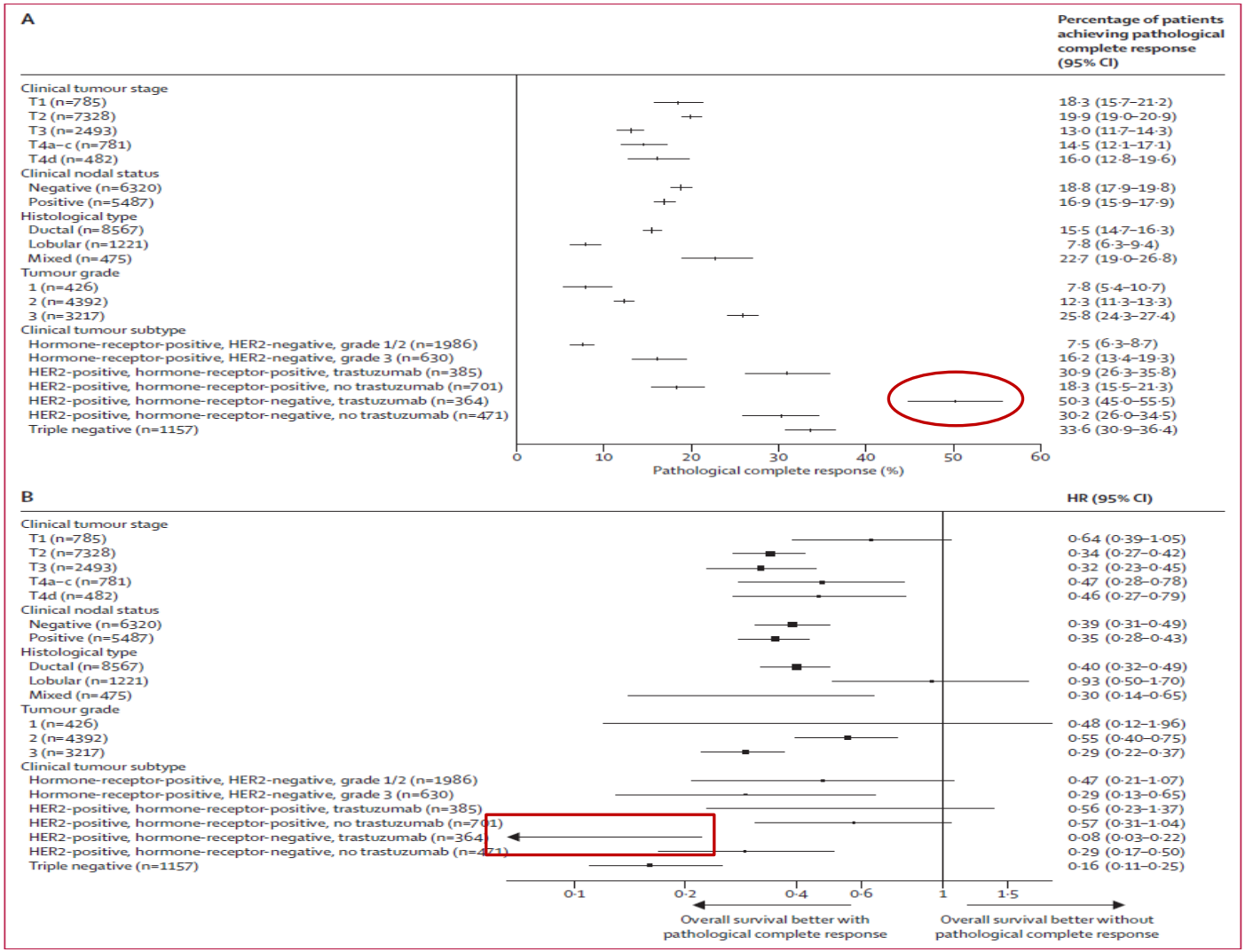

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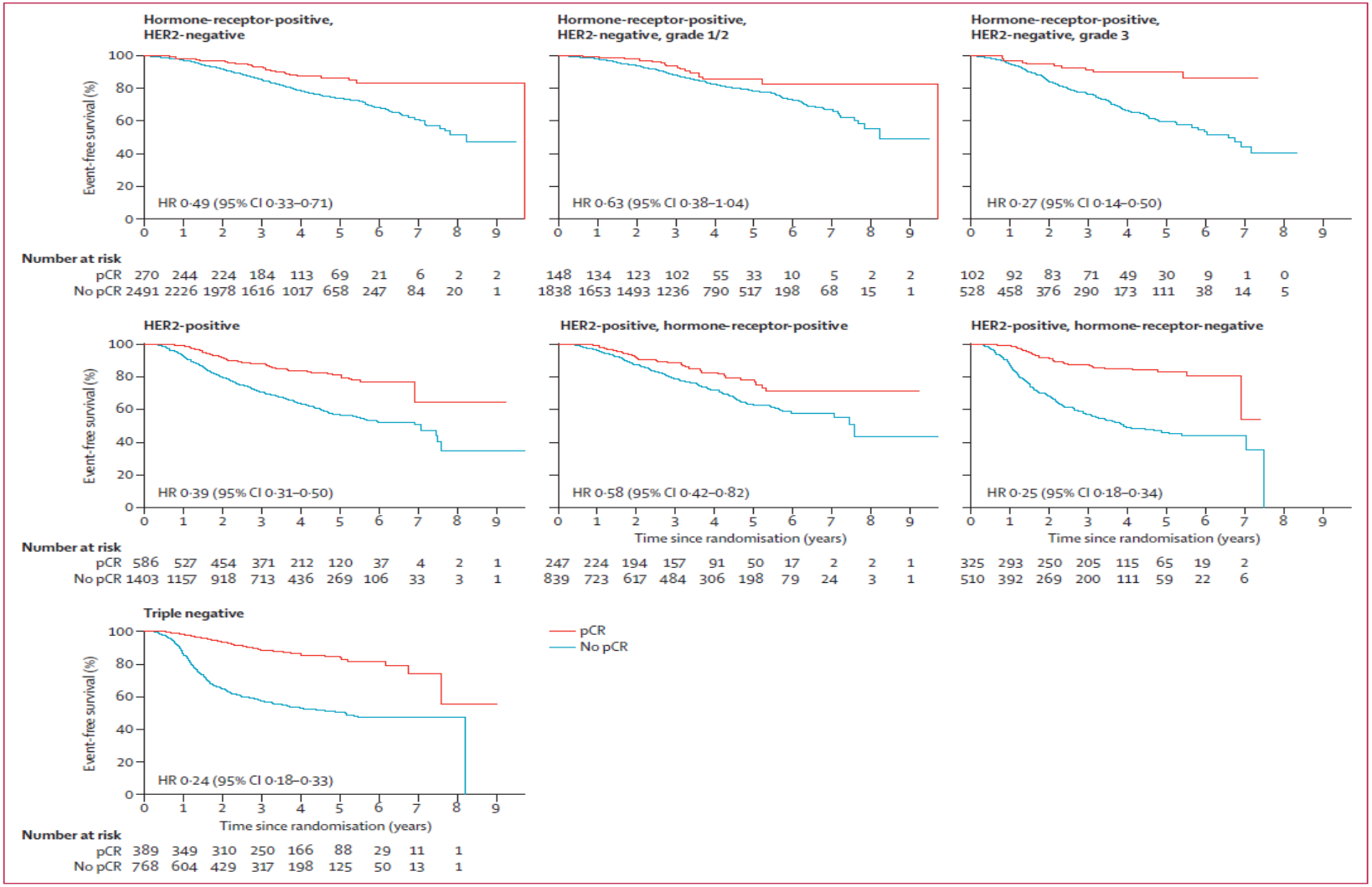
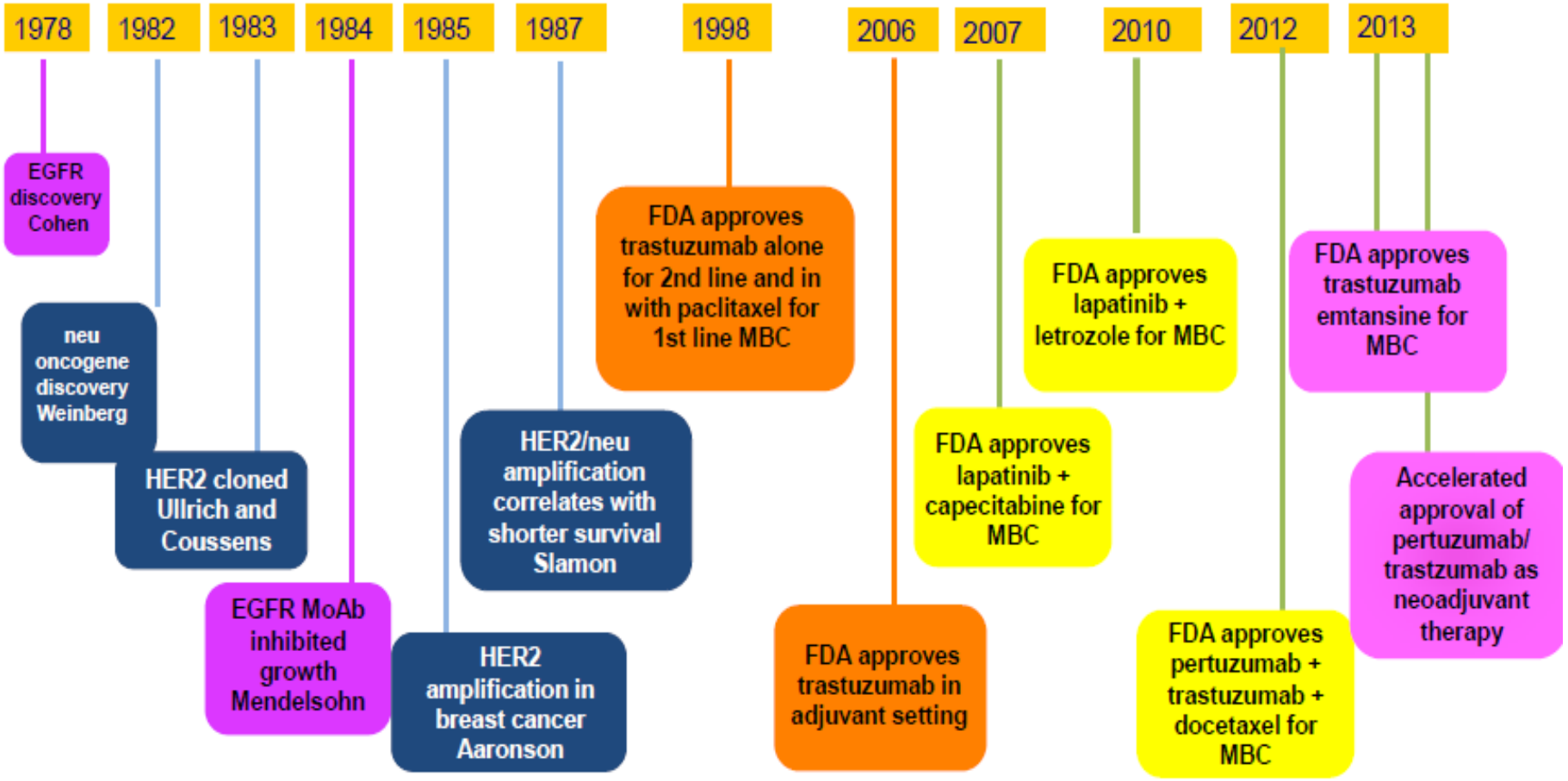


SONUÇ…


1978
EGFR discovery Cohen
1982
neu oncogene discovery Weinberg
1983
HER2 cloned Ullrich and Coussens
1984
EGFR MoAb inhibited growth Mendelsohn
1985
HER2 amplification in breast cancer Aaronson
1987
HER2/neu amplification correlates with shorter survival Slamon
1998
FDA approves trastuzumab alone for 2nd line and in with paclitaxel for 1st line MBC
2006
FDA approves trastuzumab in adjuvant setting
2007
FDA approves lapatinib + capecitabine for MBC
2010
FDA approves lapatinib + letrozole for MBC
2012
FDA approves pertuzumab + trastuzumab + docetaxel for MBC
2013
FDA approves trastuzumab emtansine for MBC
Accelerated approval of pertuzumab/ trastzumab as neoadjuvant therapy

VOLUME 34 · NUMBER 33 · NOVEMBER 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Perils of the Pathologic Complete Response

Brent S. Rose, *Harvard Radiation Oncology Program, Boston, MA*
Eric P. Winer, *Dana-Farber Cancer Institute, Boston, MA*
Harvey J. Mamon, *Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA*

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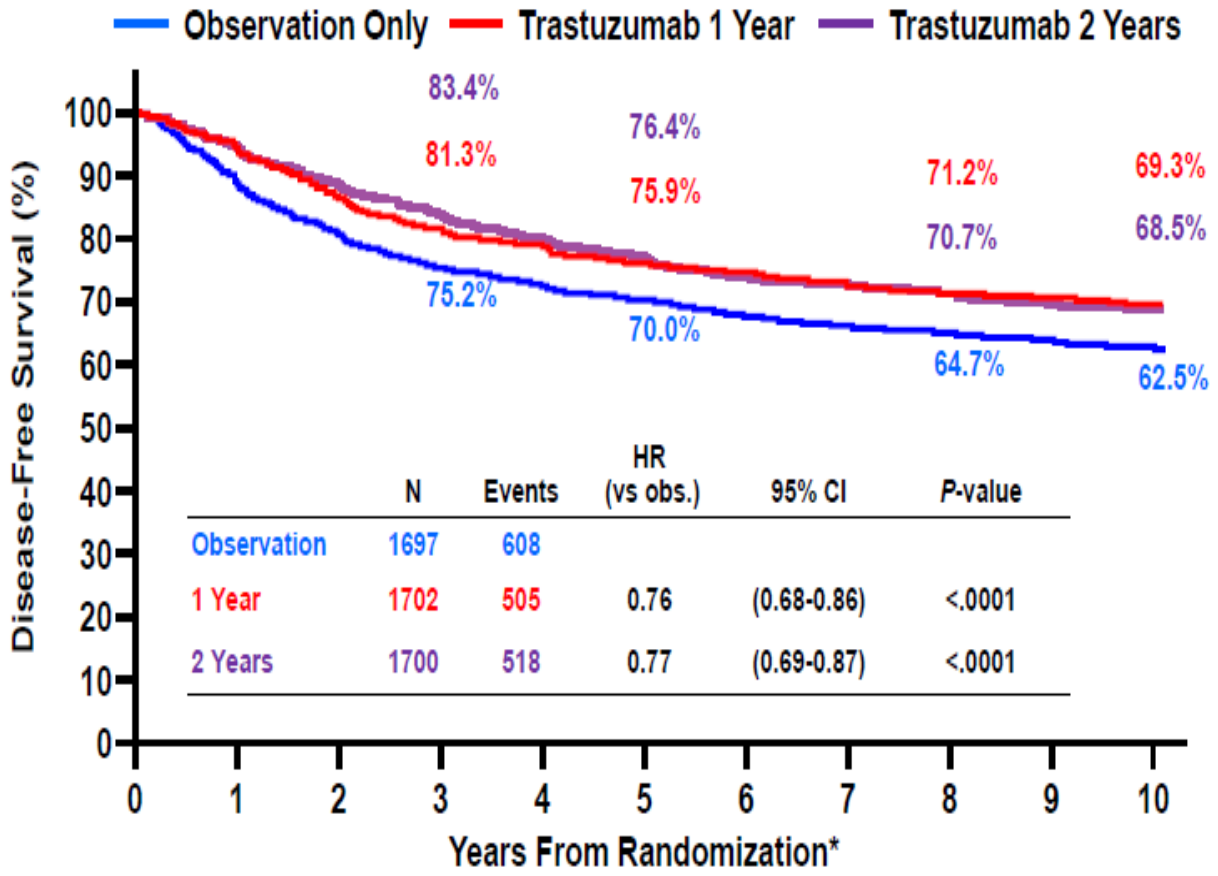
HERA Trial: 10-Year Follow-Up of Trastuzumab After Adjuvant Chemotherapy in HER2-Positive Early Breast Cancer–Final Analysis



	N	Events	HR (vs obs.)	95% CI	*P*-value
Observation	1697	608			
1 Year	1702	505	0.76	(0.68-0.86)	<.0001
2 Years	1700	518	0.77	(0.69-0.87)	<.0001

Number at Risk

Observation Only	1697	1201	1095	946	831
Trastuzumab 1 Year	1702	1319	1213	1099	996
Trastuzumab 2 Years	1700	1361	1222	1087	965

*Plotting area truncated to 0 – 120 months

Jackisch C, et al. *Cancer Res.* 2016;76(4 Suppl): Abstract PD5-01

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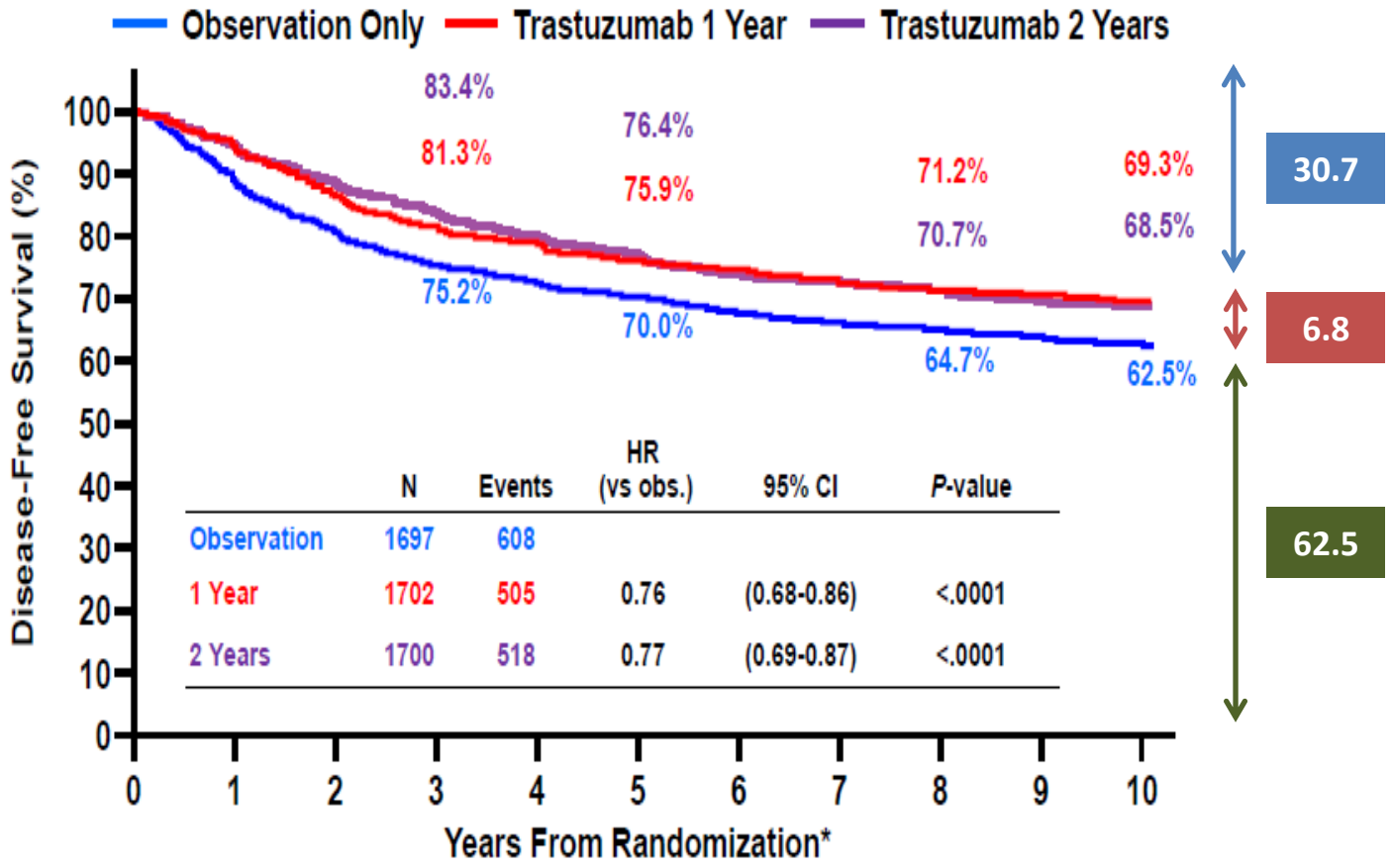

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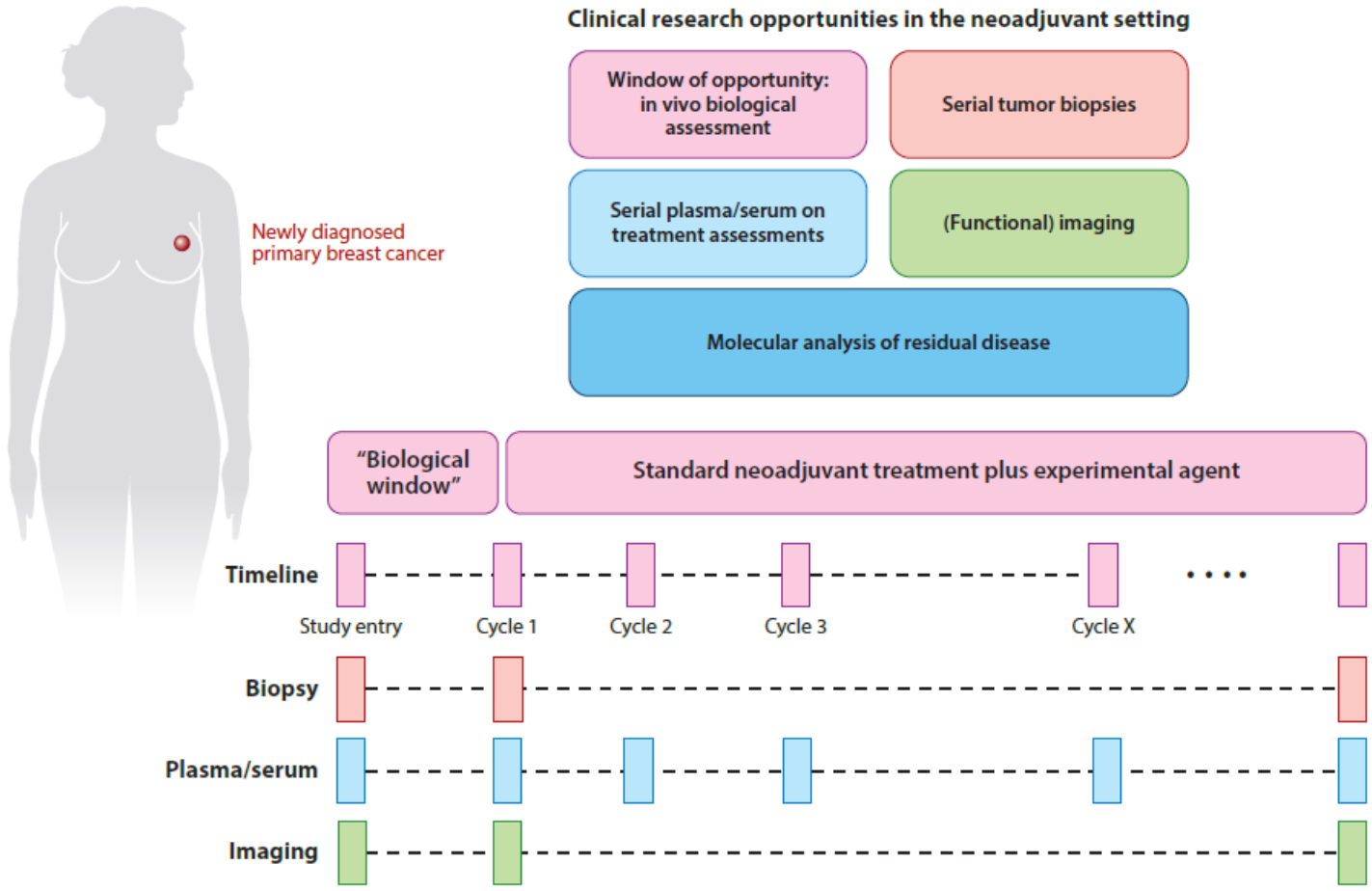
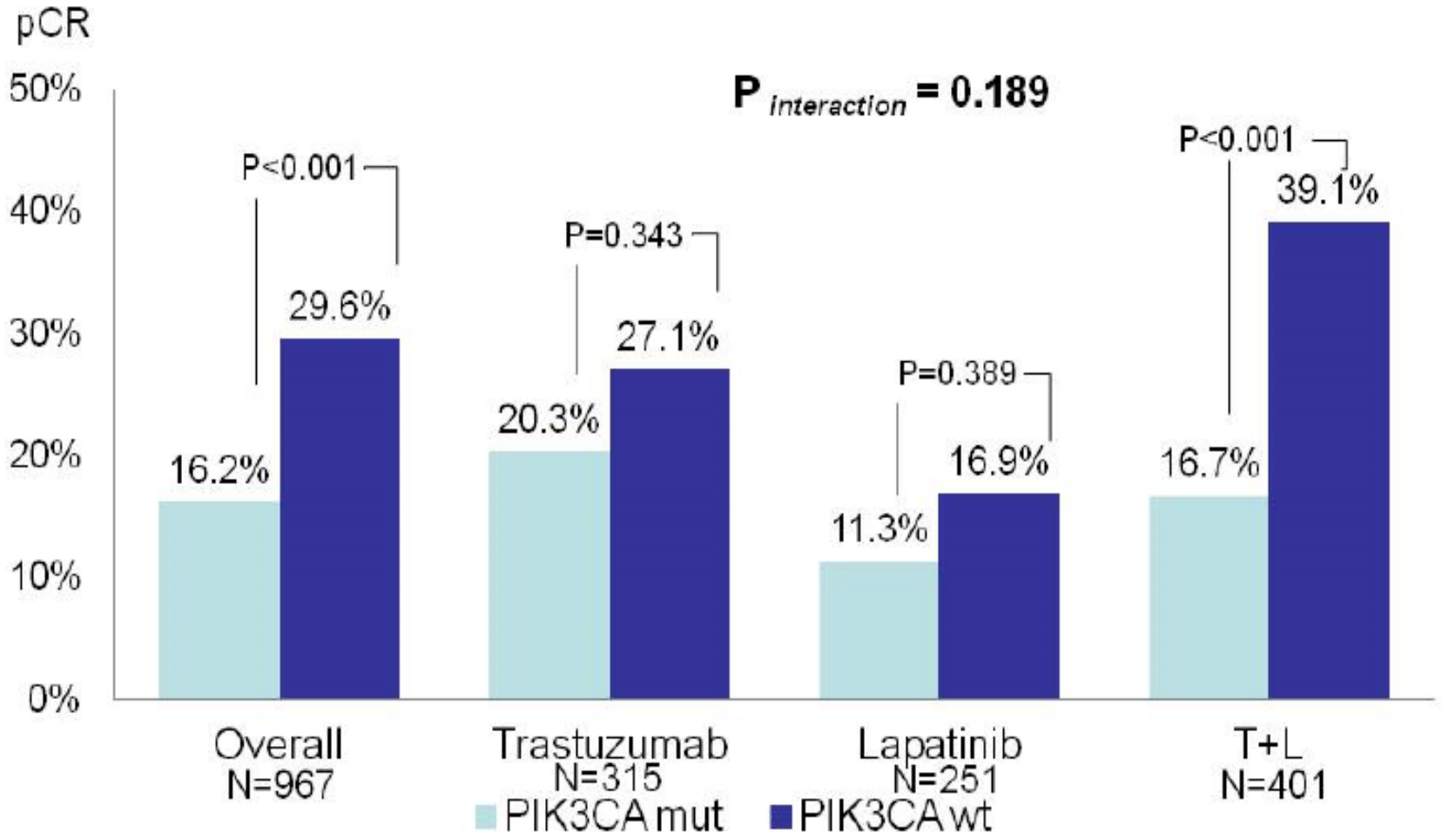
Neoadjuvant Therapy for Breast Cancer

Dimitrios Zardavas[1,2] and Martine Piccart[1,2]



pCR Rates According to PIK3CA Mutation Status Overall and by Anti-HER2 Treatment

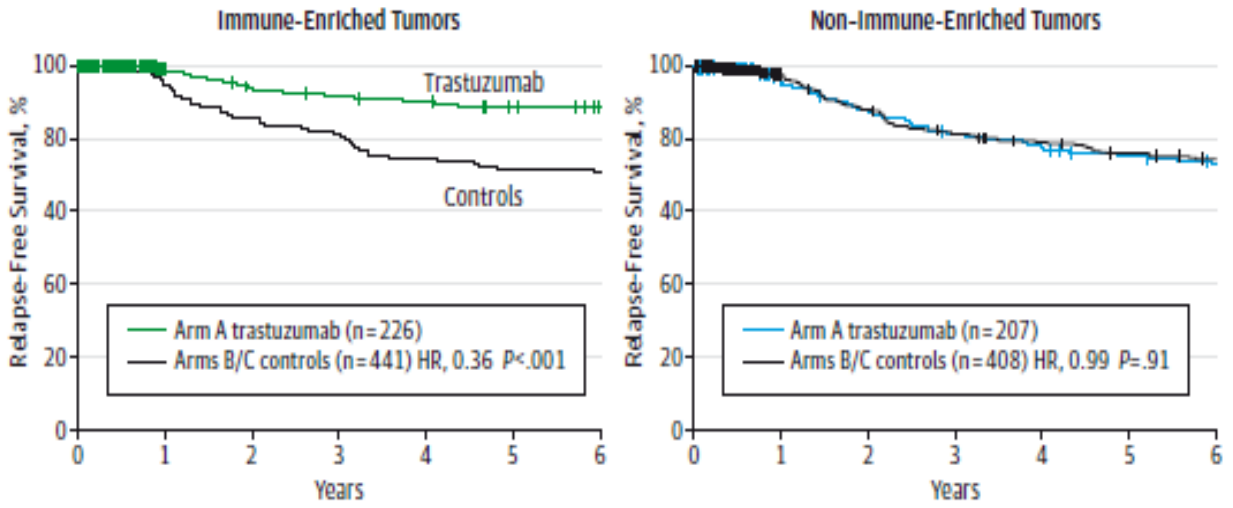


Loibl S, et al. *J Clin Oncol.* 2015;33(suppl): Abstract 511.

Review

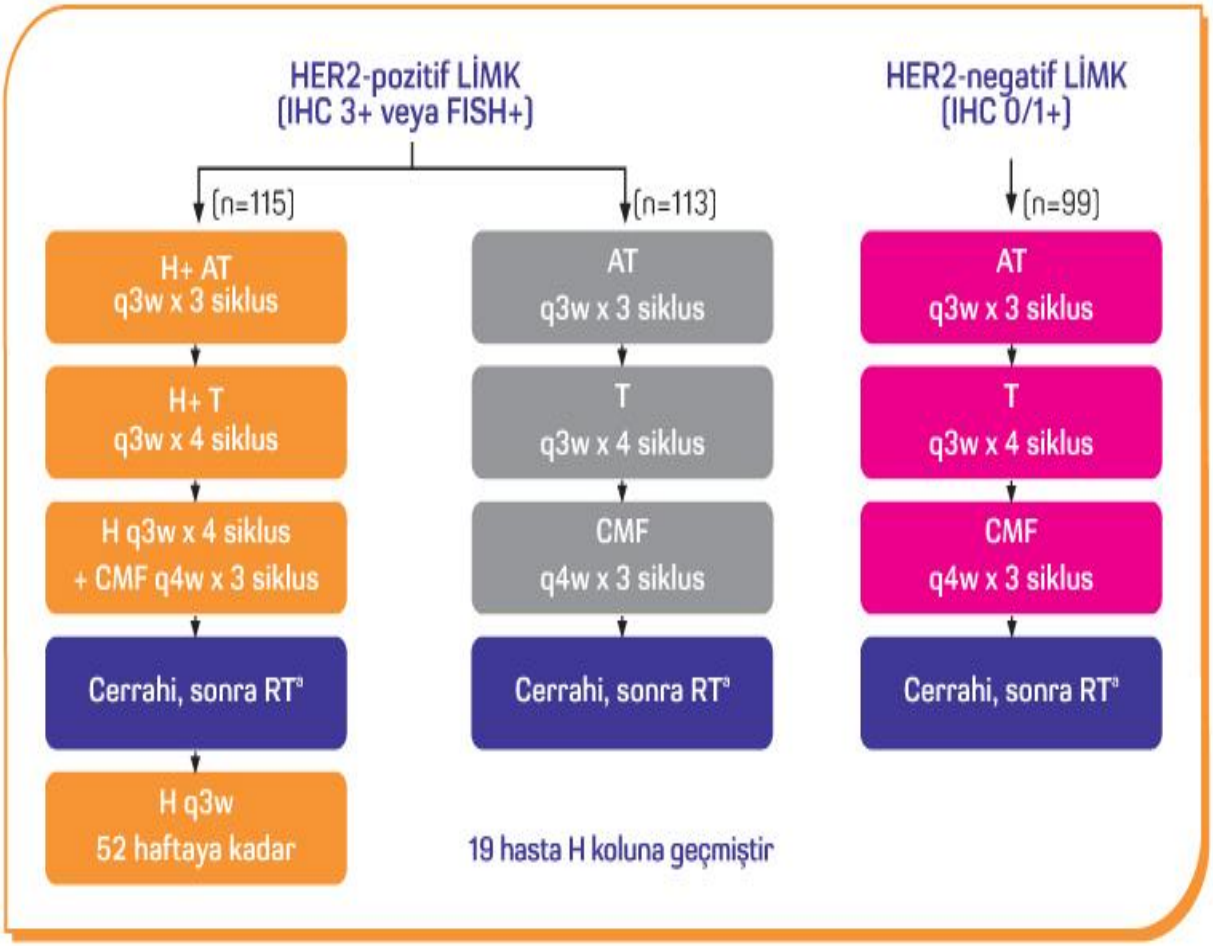
The Evolving Landscape of HER2 Targeting in Breast Cancer

Mark M. Moasser, MD; Ian E. Krop, MD, PhD



A 14-gene biomarker of immune enrichment was applied to tumor tissue from 1282 patients in a phase 3 randomized adjuvant trastuzumab study. Roughly half of the cohort was found to have immune-enriched tumors, and half non–immune-enriched tumors. The benefit of trastuzumab was seen entirely in the cohort with immune-enriched tumors. Figure adapted from Perez et al[83] with permission.

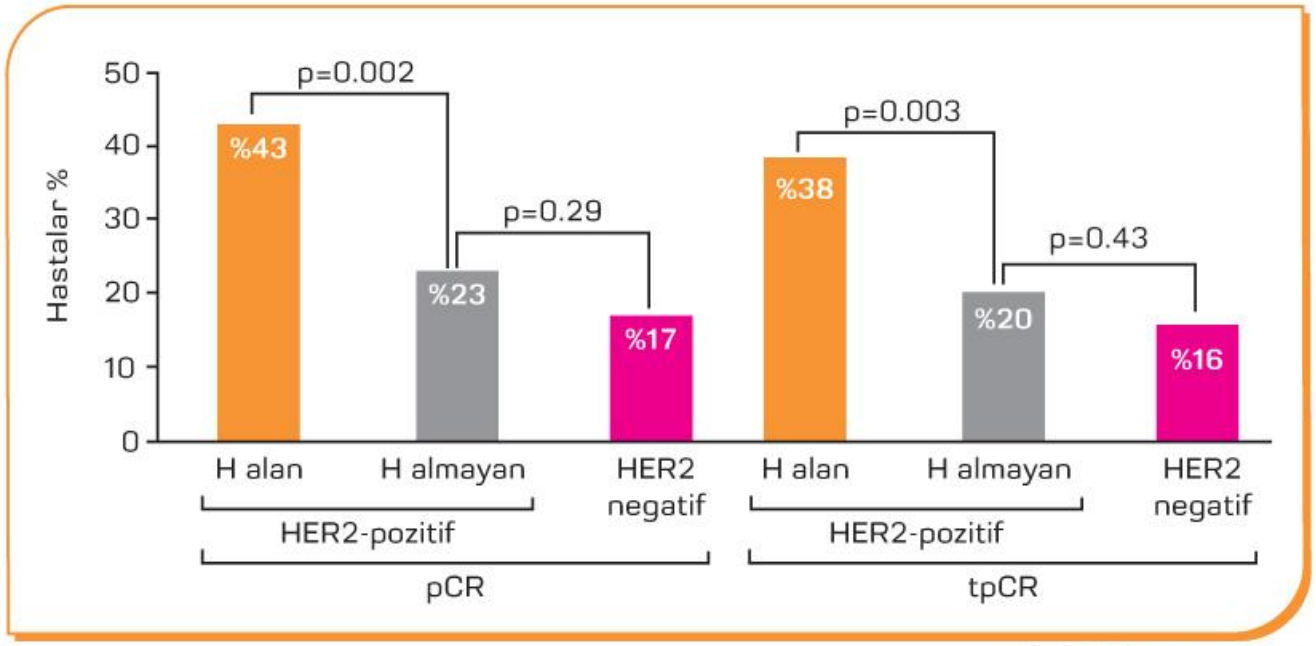
NOAH çalışma düzeni[1]



Sonlanma noktaları[1]

- **Primer (final analiz)[1]**
  - EFS: tedavi sırasında progresyon veya cerrahi sonrası relaps veya herhangi bir sebebe bağlı ölüm.
- **Sekonder[1]**
  - pCR oranı
  - ORR
  - Güvenlilik ve tolerabilite

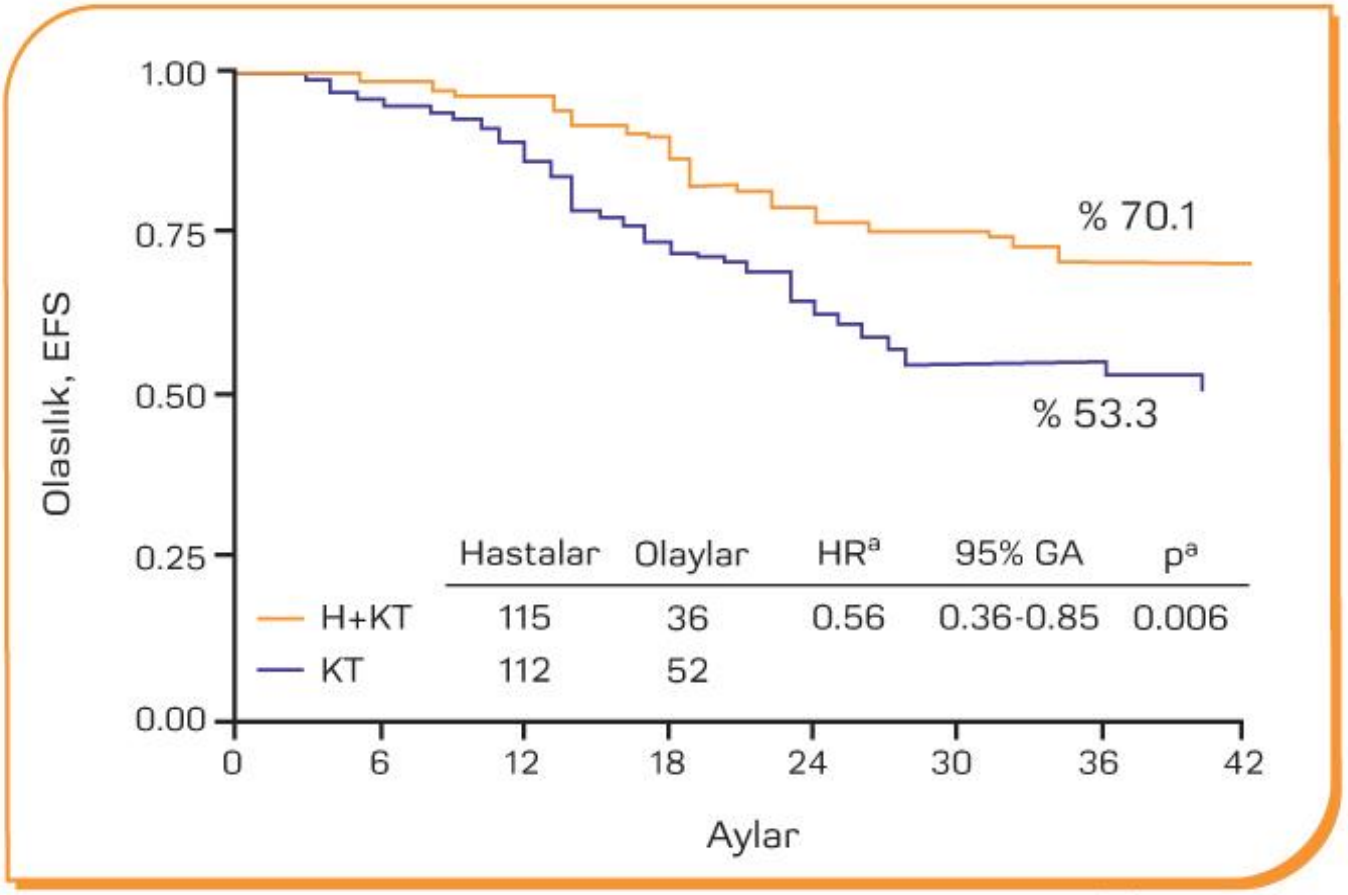
Primer tümörde pCR: ITT popülasyon[1,2,3]



1, 2 ve 3 no'lu referanslardan uyarlanmıştır.

tpCR: Meme ve nodlarda total patolojik tam yanıt (total pathologic complete response in breast and nodes)

EFS: HER2-pozitif popülasyon[1]



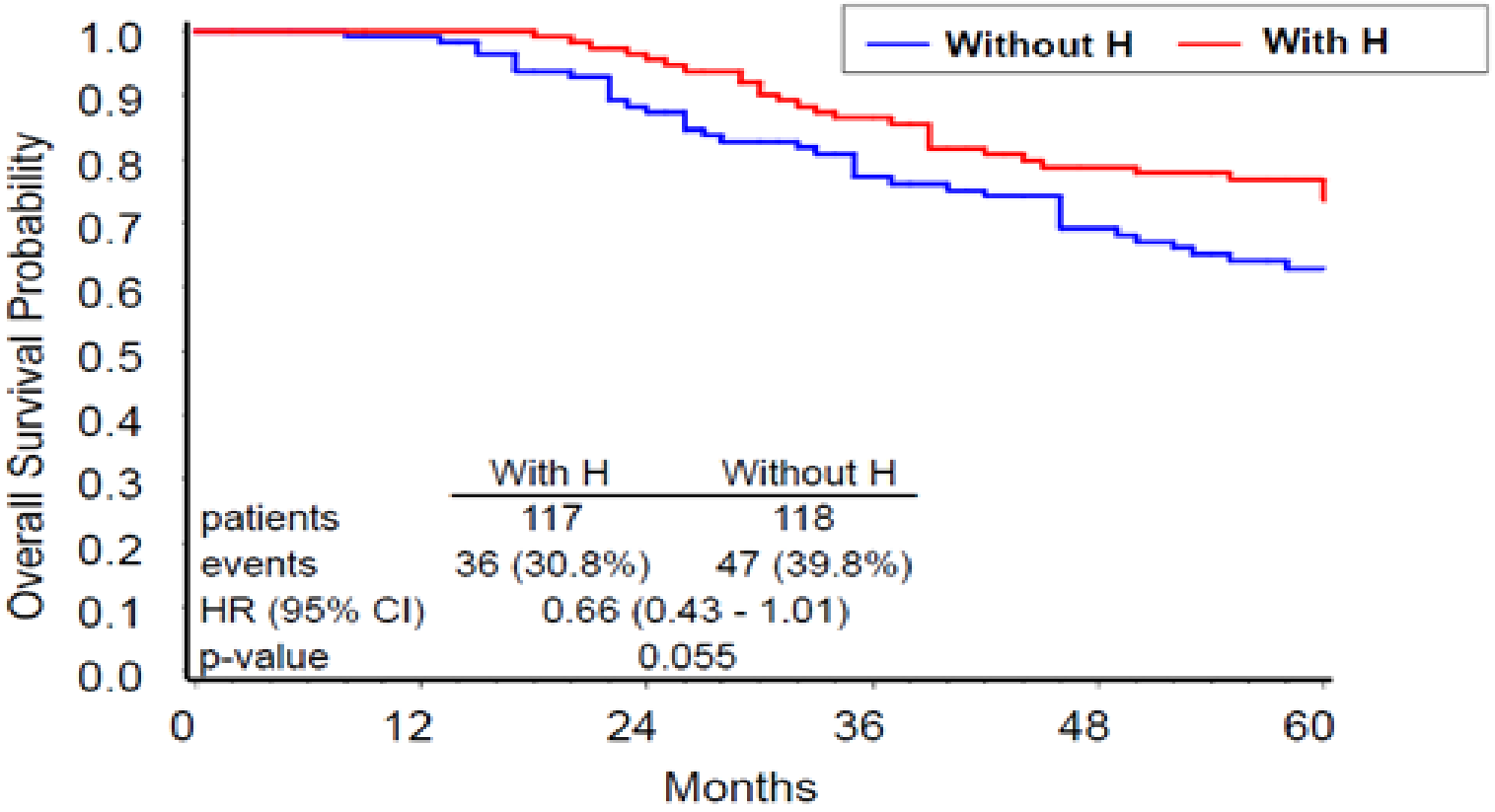
1 no'lu referanstan uyarlanmıştır.

Medyan izlem 3 yıl

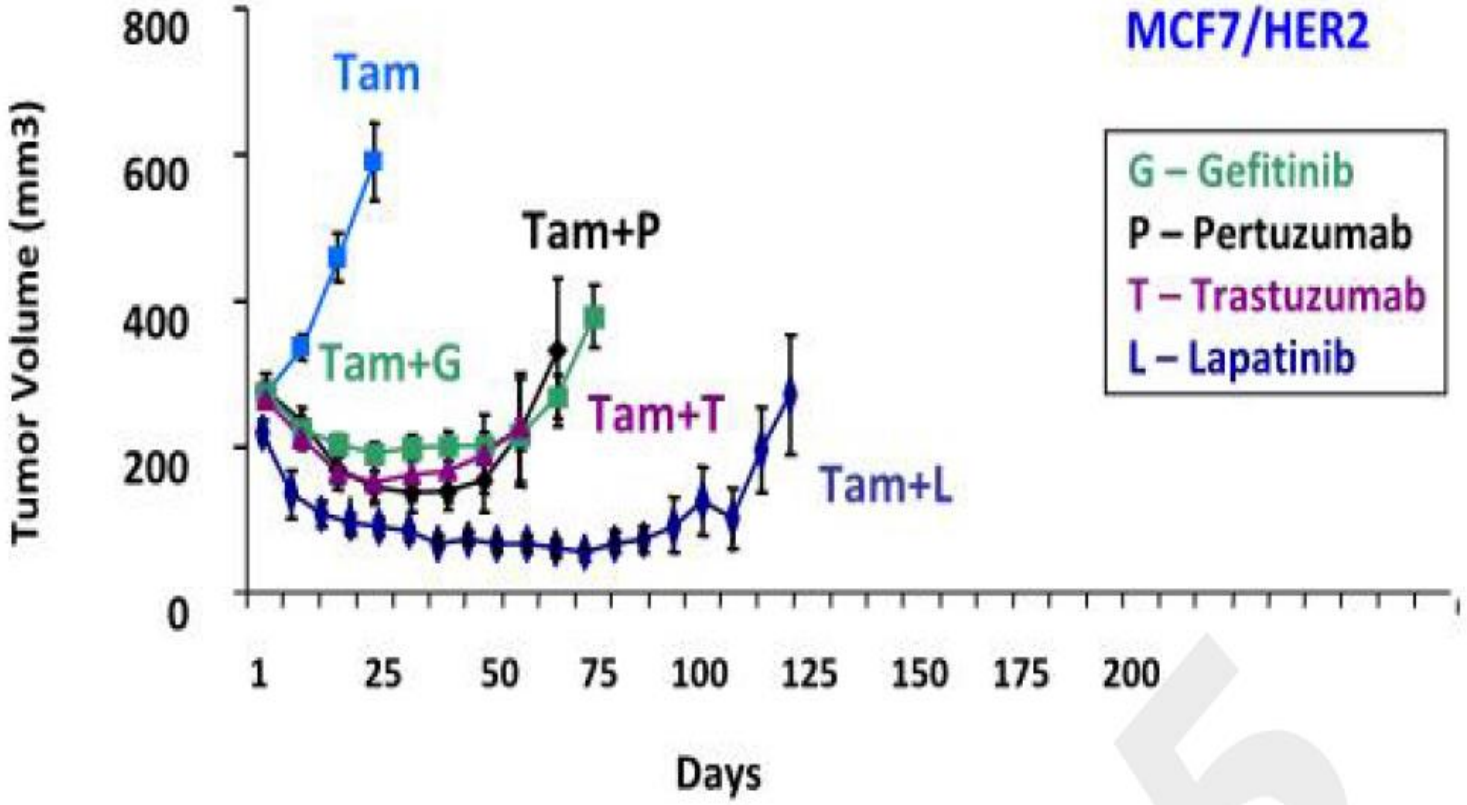
[a]Stratifikasyon değişkenlerine göre düzeltilmemiş: düzeltilmiş HR=0.55, p=0.0062

HR, hazard ratio; GA, güvenlik aralığı; KT, kemoterapi

OS : HER2-pozitif popülasyon[1]

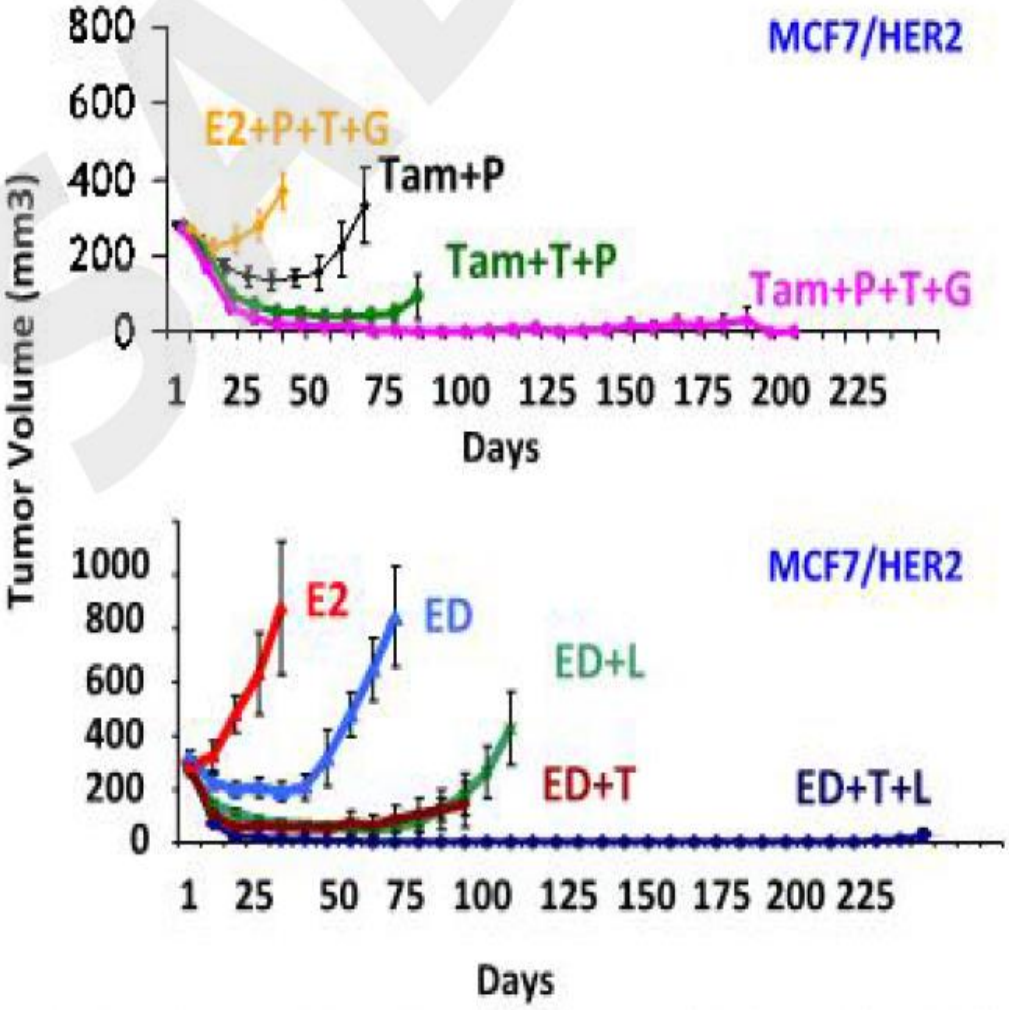


Single agent anti-HER therapy in HER2+ Xenograft



Arpino et al, JNCI 2007
Rimawi et al, CCR 2011

Multiagent anti-HER therapy in HER2+ Xenografts



E2 - Estrogen
ED - Estrogen deprivation
Tam- Tamoxifen
T - Trastuzumab
L - Lapatinib
P- Pertuzumab
G- Gefitinib

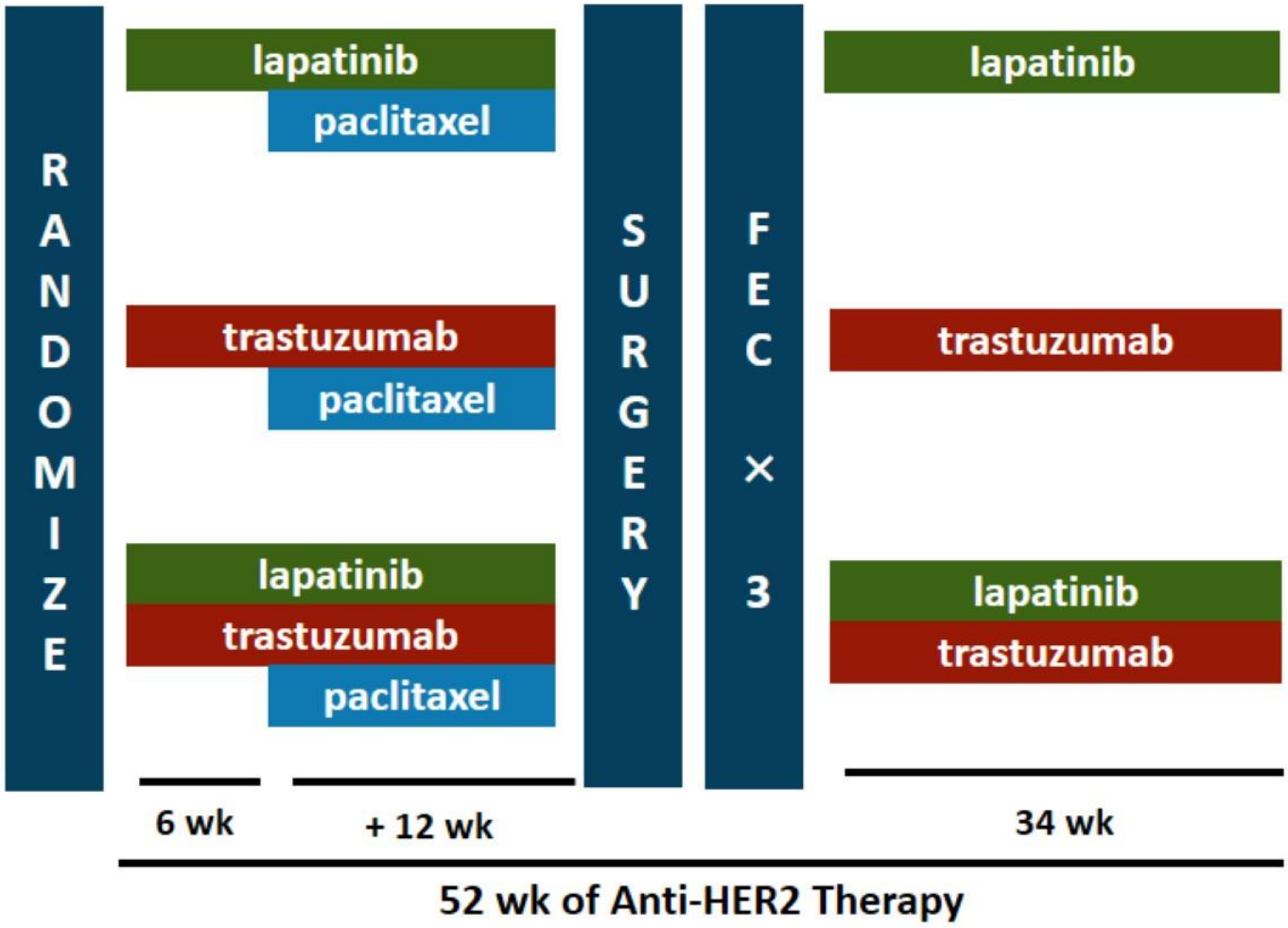
Arpino, JNCI, 2007
Rimawi, CCR, 2011

Neo ALTTO

Invasive operable
HER2+ BC
Tumor > 2 cm
(inflammatory BC excluded)
LVEF ≥ 50%
N = 450

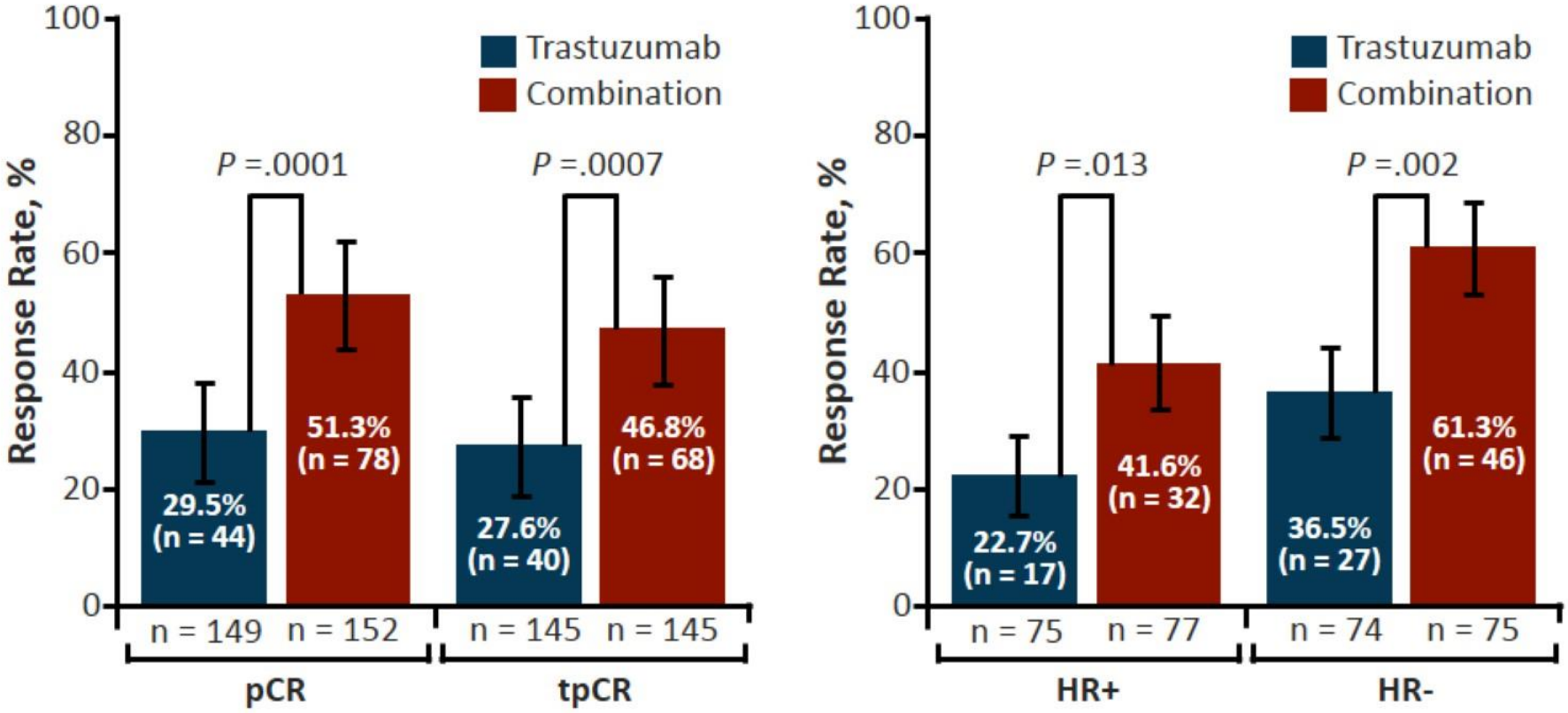
Stratification

- Tumor ≤ 5 cm vs Tumor > 5 cm
- ER- or PgR+ vs ER- and PgR-
- N 0-1 vs N ≥ 2
- Conservative surgery or not



Baselga J, et al. *Lancet*. 2012;379:633-640.[12]

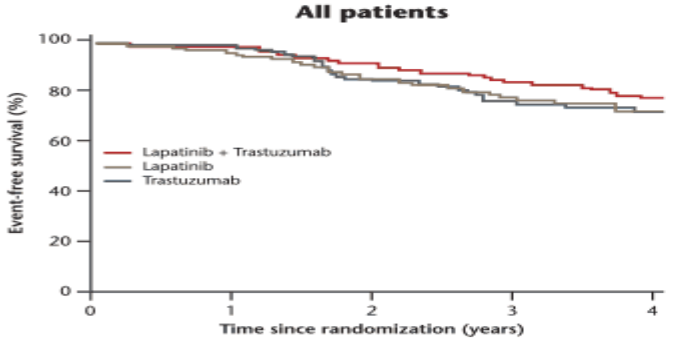
NeoALTTO: Total pCR and by HR Status



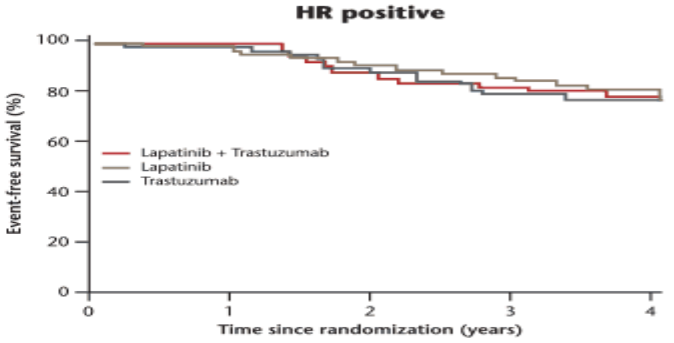
Baselga J, et al. *Lancet*. 2012;379:633-640.[12]

Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): survival outcomes of a randomised, open-label, multicentre, phase 3 trial and their association with pathological complete response

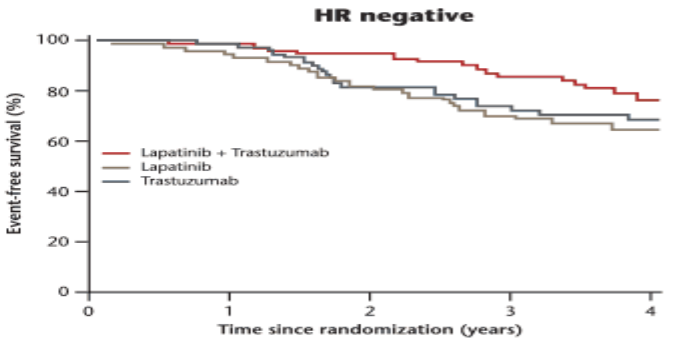
Evandro de Azambuja, Andrew P Holmes, Martine Piccart-Gebhart, Eileen Holmes, Serena Di Cosimo, Ramona F Swaby, Michael Untch, Christian Jackisch, Istvan Lang, Ian Smith, Frances Boyle, Binghe Xu, Carlos H Barrios, Edith A Perez, Hatem A Azim Jr, Sung-Bae Kim, Sherko Kuemmel, Chiun-Sheng Huang, Peter Vuylsteke, Ruey-Kuen Hsieh, Vera Gorbunova, Alexandru Eniu, Lydia Dreosti, Natalia Tavartkiladze, Richard D Gelber, Holger Eidtmann, José Baselga



Arm	Patients, n	Events, n	3-yr EFS rate, %	Hazard ratio compared with trastuzumab (95% CI)	p-value
Lapatinib + Trastuzumab	152	30	84	0.78 (0.47–1.28)	0.33
Lapatinib	154	38	78	1.06 (0.66–1.69)	0.81
Trastuzumab	149	37	76		



Arm	Patients, n	Events, n	3-yr EFS rate, %	Hazard ratio compared with trastuzumab (95% CI)	p-value
Lapatinib + Trastuzumab	77	15	83	0.96 (0.46–2.01)	0.92
Lapatinib	80	13	86	0.92 (0.43–1.95)	0.83
Trastuzumab	75	15	80		



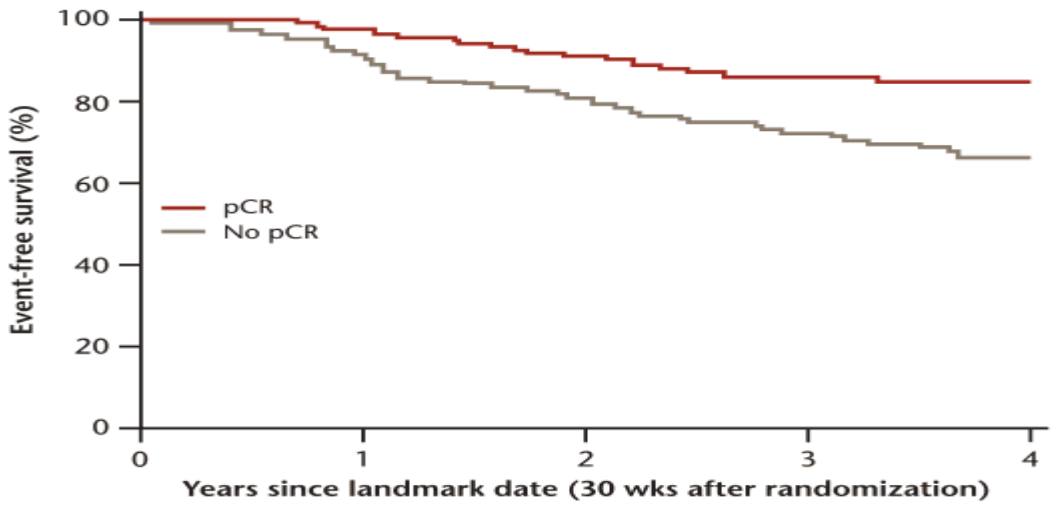
Arm	Patients, n	Events, n	3-yr EFS rate, %	Hazard ratio compared with trastuzumab (95% CI)	p-value
Lapatinib + Trastuzumab	75	15	86	0.65 (0.32–1.28)	0.22
Lapatinib	74	25	70	1.16 (0.63–2.11)	0.64
Trastuzumab	74	22	72		

CI = confidence interval; EFS = event-free survival; HR = hormone receptor; yr = year

**Tests for interaction according to HR status: lapatinib + trastuzumab vs. trastuzumab, p = 0.48; lapatinib vs. trastuzumab, p = 0.56.*

Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): survival outcomes of a randomised, open-label, multicentre, phase 3 trial and their association with pathological complete response

Evandro de Azambuja, Andrew P Holmes, Martine Piccart-Gebhart, Eileen Holmes, Serena Di Cosimo, Ramona F Swaby, Michael Untch, Christian Jackisch, Istvan Lang, Ian Smith, Frances Boyle, Binghe Xu, Carlos H Barrios, Edith A Perez, Hatem A Azim Jr, Sung-Bae Kim, Sherko Kuemmel, Chiun-Sheng Huang, Peter Vuylsteke, Ruey-Kuen Hsieh, Vera Gorbunova, Alexandru Eniu, Lydia Dreosti, Natalia Tavartkiladze, Richard D Gelber, Holger Eidtmann, José Baselga



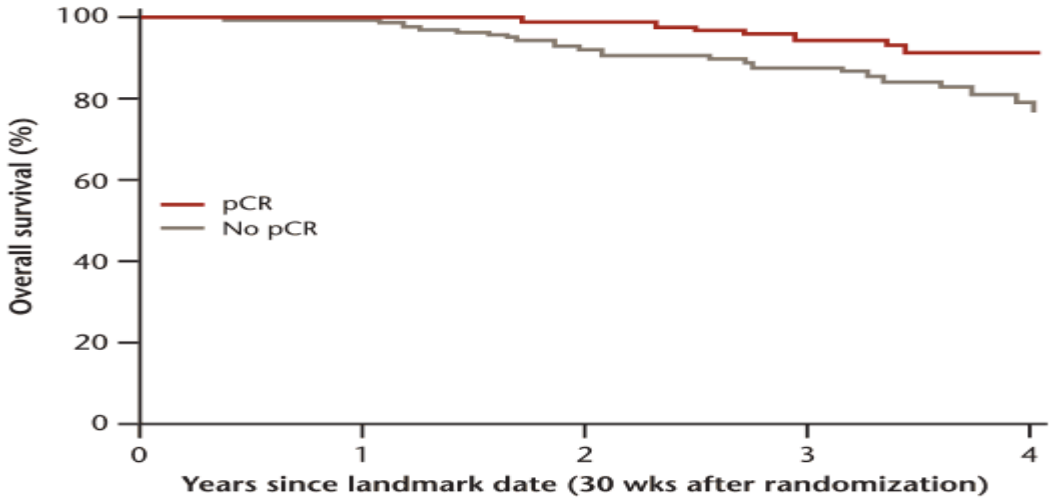
pCR status	Patients, n	Events, n	3-yr EFS rate, %	Hazard ratio (95% CI)	*p*-value
pCR	137	19	86	0.38 (0.22–0.63)	0.0003
No pCR	274	79	72		

CI = confidence interval; EFS = event-free survival; HR = hormone receptor; pCR = pathological complete response; wks = weeks; yr = year

**Test for interaction: pCR x HR, p = 0.34.*

Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): survival outcomes of a randomised, open-label, multicentre, phase 3 trial and their association with pathological complete response

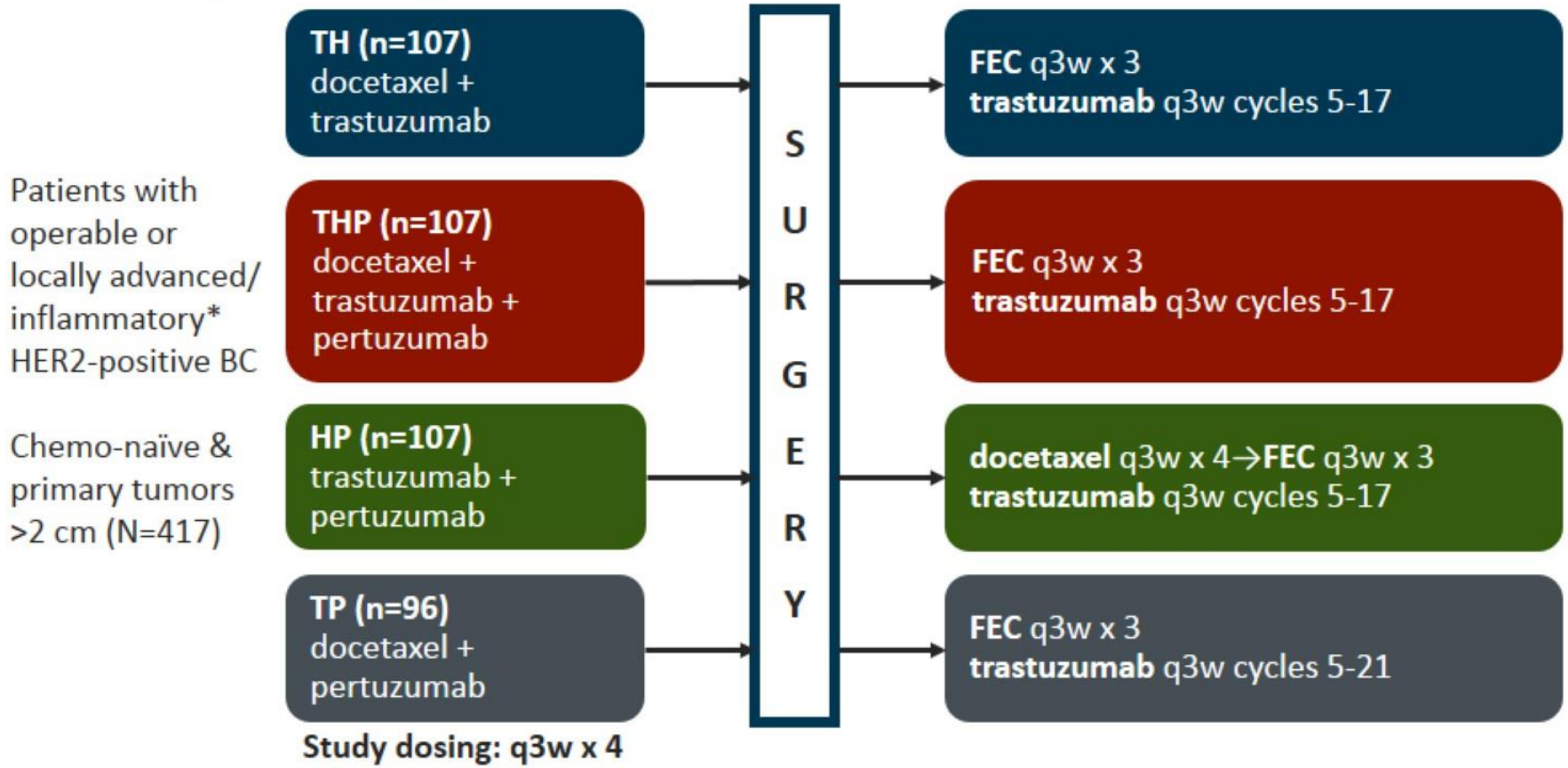
Evandro de Azambuja, Andrew P Holmes, Martine Piccart-Gebhart, Eileen Holmes, Serena Di Cosimo, Ramona F Swaby, Michael Untch, Christian Jackisch, Istvan Lang, Ian Smith, Frances Boyle, Binghe Xu, Carlos H Barrios, Edith A Perez, Hatem A Azim Jr, Sung-Bae Kim, Sherko Kuemmel, Chiun-Sheng Huang, Peter Vuylsteke, Ruey-Kuen Hsieh, Vera Gorbunova, Alexandru Eniu, Lydia Dreosti, Natalia Tavartkiladze, Richard D Gelber, Holger Eidtmann, José Baselga



pCR status	Patients, n	Deaths, n	3-yr OS rate, %	Hazard ratio (95% CI)	*p*-value
pCR	137	9	94	0.35 (0.15–0.70)	0.005
No pCR	282	42	87		

CI = confidence interval; OS = overall survival; pCR = pathological complete response; wks = weeks; yr = year

NeoSphere
Study Design



Study dosing: q3w x 4

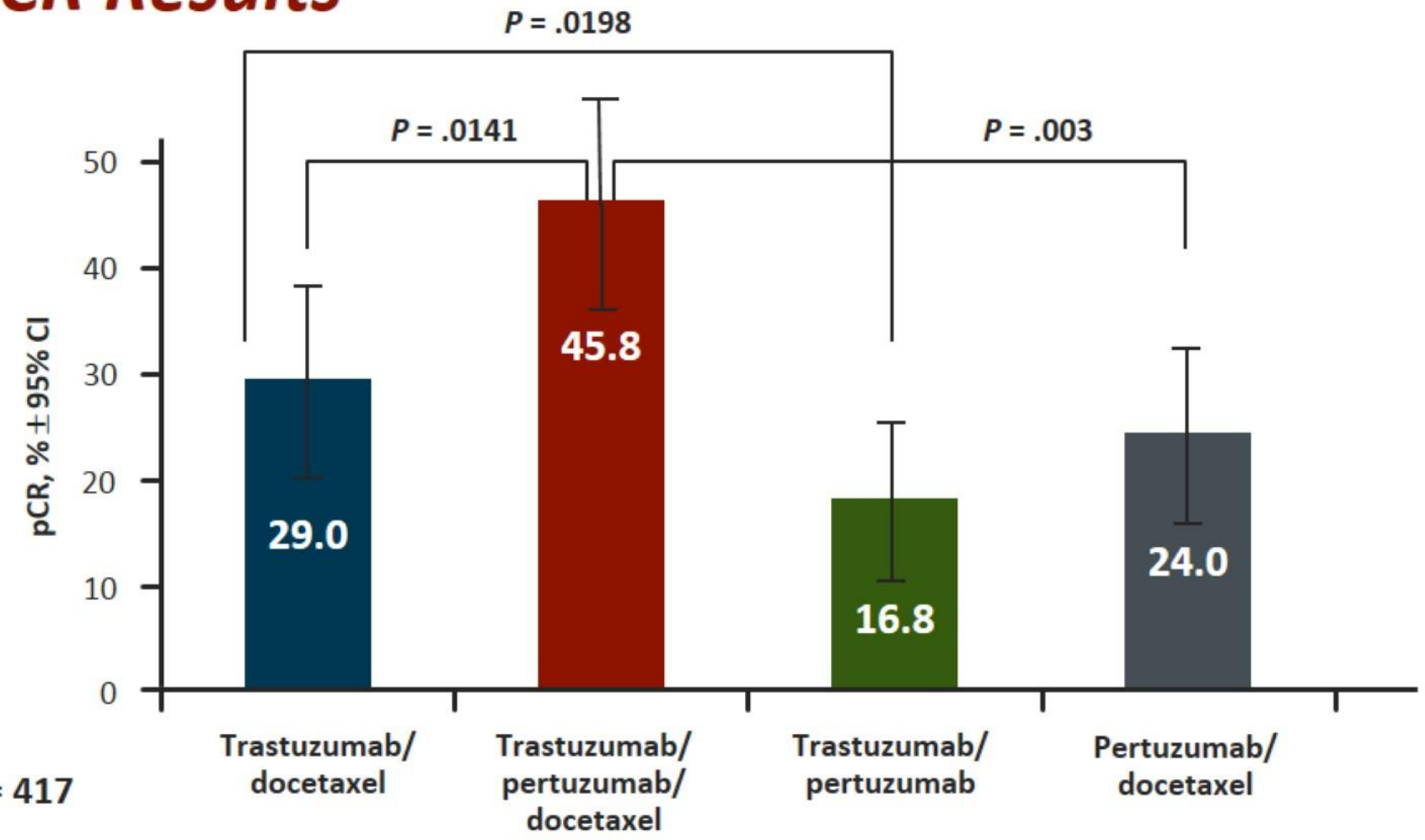
Planned sample size of 400 patients provides about 80% power to detect an absolute difference in pCR of 15% between groups.

*Locally advanced = T2–3, N2–3, M0 or T4a–c, any N, M0; operable=T2–3, N0–1, M0; inflammatory = T4d, any N, M0.

Gianni L, et al. *Lancet Oncol*. 2012;13:25-32.

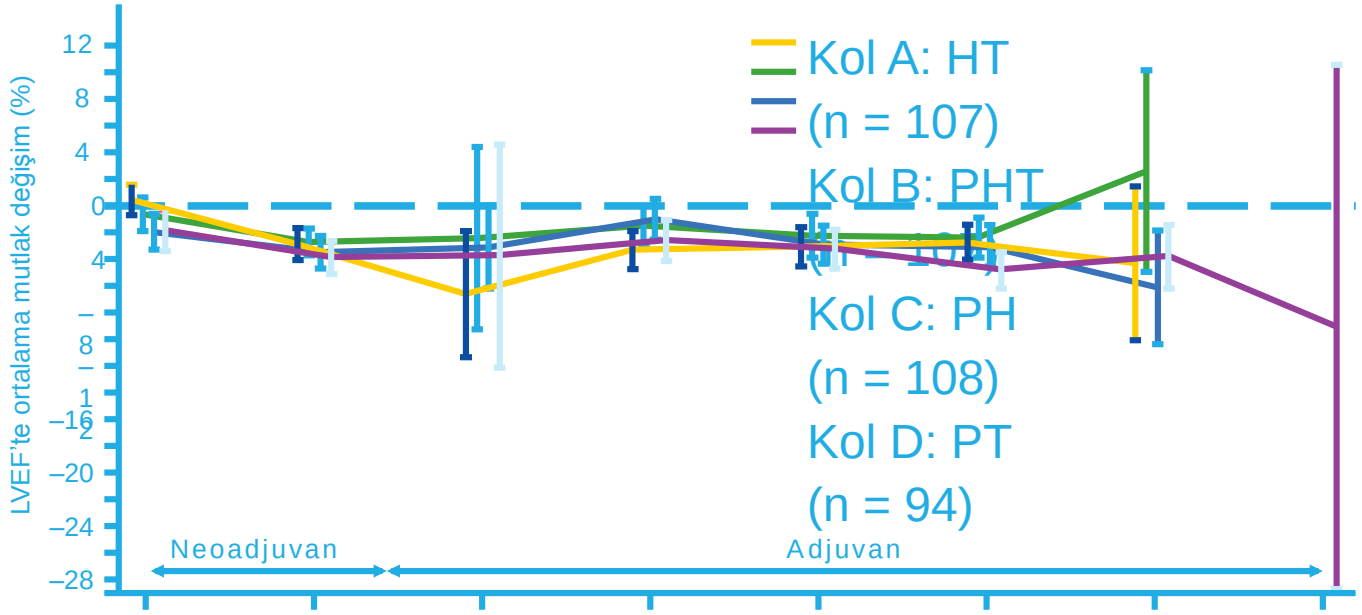
NeoSphere

Neoadjuvant Therapy in HER2+ BC: pCR Results



Gianni L, et al. *Lancet Oncol*. 2012;13:25-32.

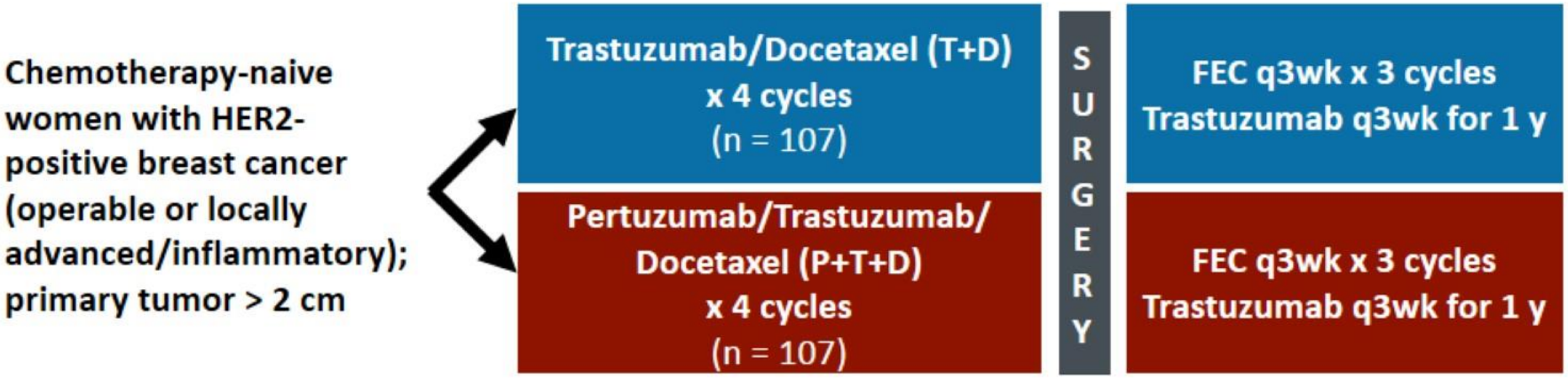
NeoSphere: Yerel değerlendirmelere göre LVEF değerinde başlangıca kıyasla ortalama mutlak değişim



Siklus	2	4	5	8	11	15	17		
Değerlendirilen hastalar n	86	103	6	74	88	87	5		HT
	92	101	6	72	79	73	3		PHT
	91	92	10	77	80	76	4		PH
	77	89	3	65	70	70	30	2	PT

H, trastuzumab; LVEF, sol ventriküler ejeksiyon fraksiyonu; P, pertuzumab; T, dosetaksel Gianni L, et al. St. Gallen BCC 2013 (Abstract 250; poster presentation).

NeoSphere Trial 2015 Update

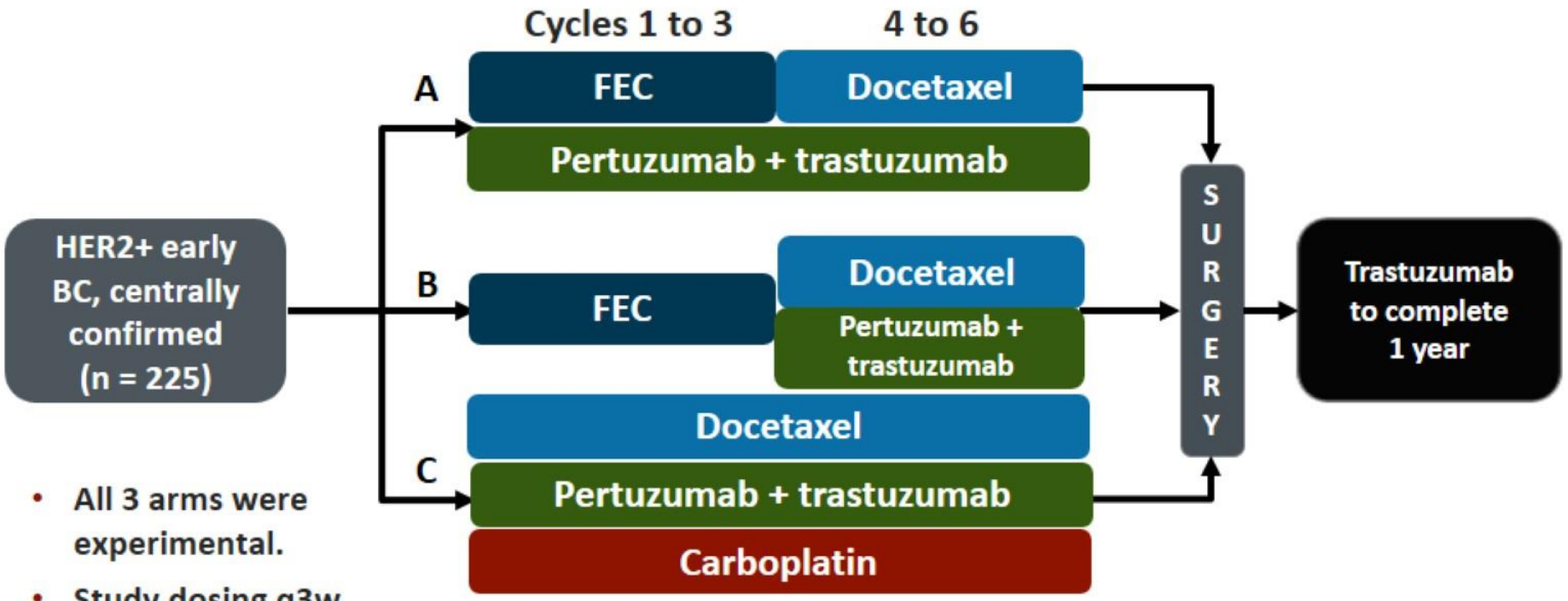


- Preplanned, 5-y analysis again strongly supports the association between pCR and improvement in long-term outcomes

		T+D	P+T+D
DFS	3-y estimate	85%	92%
	HR (95% CI)	0.6 (0.28-1.27)	
PFS	3-y estimate	86%	90%
	HR (95% CI)	0.69 (0.34-1.40)	

Gianni L, et al. *J Clin Oncol*. 2015;33. Abstract 505.[10]

TRYPHAENA: Neoadjuvant Trastuzumab and Pertuzumab in HER2+ Early BC: Study Design (Phase 2)

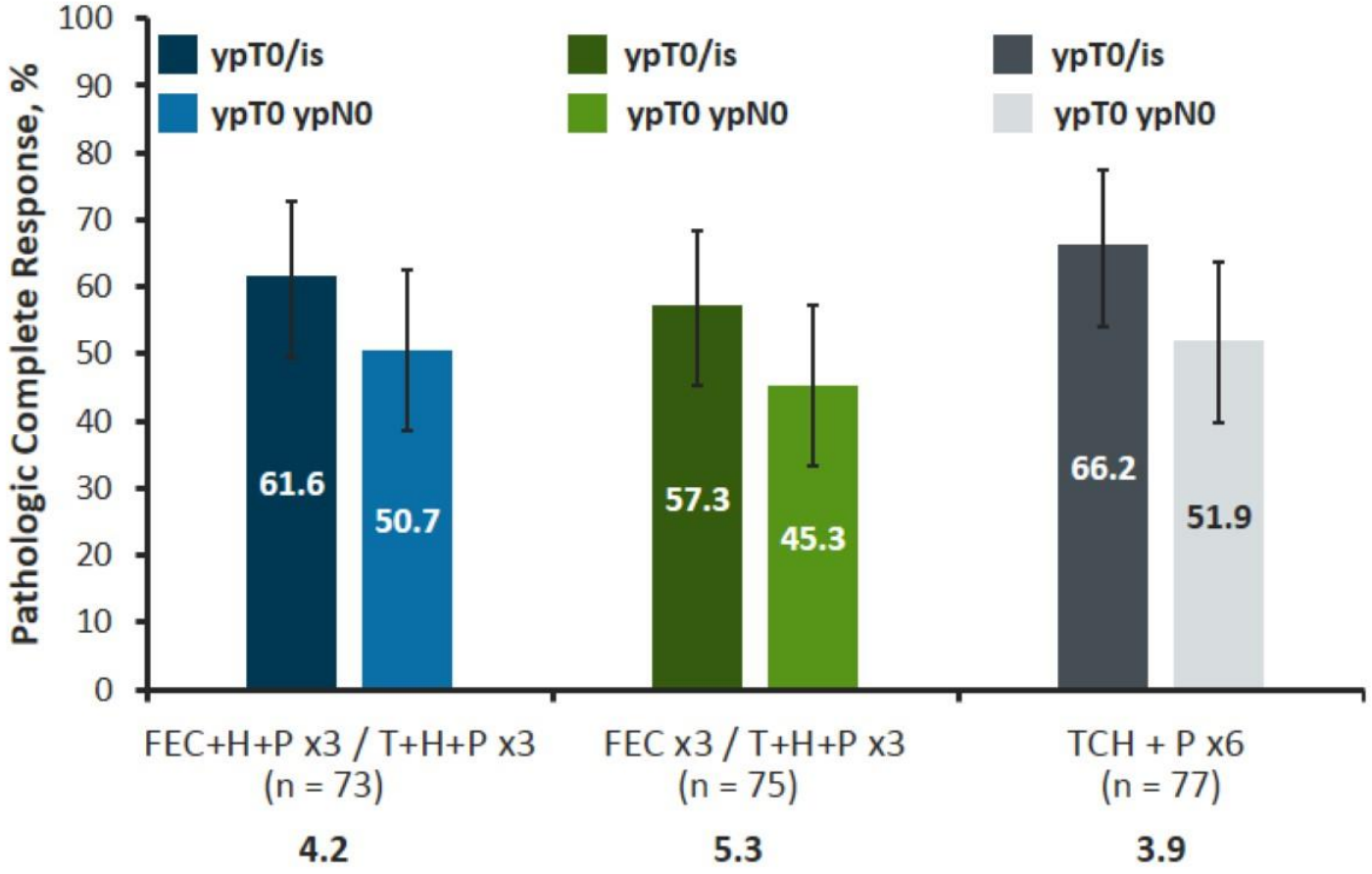


- All 3 arms were experimental.
- Study dosing q3w
  - FEC: 500 mg/m^2, 100 mg/m^2, 600 mg/m^2
  - Carboplatin: AUC 6
  - Trastuzumab: 8 mg/kg loading dose, 6 mg/kg maintenance
  - Pertuzumab: 840 mg loading dose, 420 mg maintenance
  - Docetaxel: 75 mg/m^2 (escalating to 100 mg/m^2 if tolerated, in arms A and B only)
- Stratification
  - Operable, locally advanced, and inflammatory BC
  - HR positivity

Schneeweiss A, et al. *Ann Oncol*. 2013;24:2278-2284.[19]

TRYPHAENA

Cardiac Safety (Randomized Phase 2 Study)



LVEF decline ≥10% points and below 50%, n (%)

Schneeweiss A, et al. Presented at SABCS 2011. Abstract S5-6.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Pathological Complete Response and Accelerated Drug Approval in Early Breast Cancer

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

N Engl J Med 2012; 366:2438-2441 | June 28, 2012 | DOI: 10.1056/NEJMp1205737

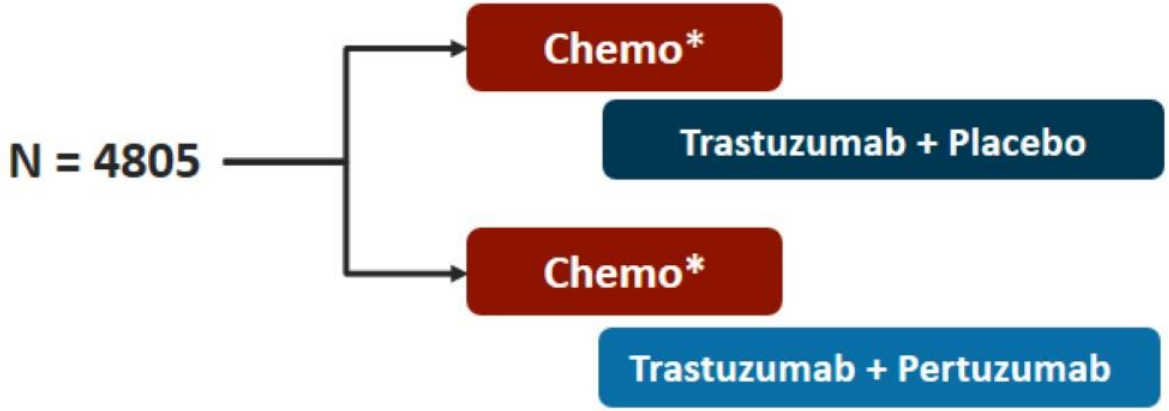
FDA NEWS RELEASE

For Immediate Release: Sept. 30, 2013
Media Inquiries: Stephanie Yao, 301-796-0394, stephanie.yao@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves Perjeta for neoadjuvant breast cancer treatment
First drug approved for use in preoperative breast cancer

The U.S. Food and Drug Administration today granted accelerated approval to Perjeta (pertuzumab) as part of a complete treatment regimen for patients with early stage breast cancer before surgery (neoadjuvant setting). Perjeta is the first FDA-approved drug for the neoadjuvant treatment of breast cancer.

APHINITY
Study Schema



- HER2+ *centrally confirmed*
  - Node + or node – (tumor >1 cm or 0.5-1 cm with high risk feature)
- Stratification factors:
  - Nodal status, ER/PR ±; geographic region;
  - Anthracycline vs non-anthracycline regimen

***Chemo: FEC or FAC x 3 or 4 →TH x 3-4 OR AC x 4 → TH x 4 OR TCH x 6**

Clinicaltrials.gov.

Neoadjuvan tedavi sonrası cerrahide karşılaşılan sorunlar?

NEOADJUVAN TEDAVİ SONRASI CERRAHİ NE KADAR GÜVENİLİR…

	Post-op Chemotherapy (n = 91)	Pre-op Chemotherapy (n = 150)	*P* value
T2 and T3 tumors			
Median tumor size (cm)	3.0	3.45	.13
Volume resected (cm^3)	213	113	.004
% Re-excision	14%	14%	1
# IBTR	1	1	

Median f/u 33 months

Boughey JC, et al. *Ann Surg*. 2006;244(3):464-470.

SUBTİPLERE GÖRE MEME KORUYUCU CERRAHİ ORANLARI

ACOSOG Z1071
n = 694

Subtype	n	Rate of BCT	Rate of breast pCR
HR+, HER2-	317	35%	16%
HER2+	207	43%	50%
Triple negative	170	47%	48%

Boughey JC, et al. *Ann Surg*. 2014;260(4):608-614.

pCR MEME KORUYUCU CERRAHİ ORANLARINI NEDEN ETKİLEMİYOR

	pCR (%)	BCS (%)
NSABP B27		
AC x 4	13.7	62
ACT x 4	26.1	64
GeparQuinto		
ECT + lapatinib	30.2	59
ECT + trastuzumab	44.6	64
NeoALTTO		
Lapatinib + paclitaxel	24.7	43
Trastuzumab + paclitaxel	29.5	35
Lapatinib + trastuzumab+ paclitaxel	51.3	41

King TA, et al. *Nat Rev Clin Oncol*. 2015;12(6):335-343.

Neoadjuvan tedavi sonrası SLNB ne kadar güvenilir ?

Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy

Tari A. King and Monica Morrow

Trial	SLN-identification rate	False-negative rate*
Before adjuvant chemotherapy		
McMasters *et al.* (2000)[48‡]	Single-agent injection: 86% Dual-agent injection: 90%	Single-agent injection: 11.8% Dual-agent injection: 5.8%
Veronesi *et al.* (2003)[50]	NR	8.8%
ALMANAC trial (2006)[45]	96.1%	6.7%
Kim *et al.* (2006)[47§]	96% (range 41–100%)	7.3% (range 0–29%)
NSABP B-32 (2007)[59]	97.2%	9.8%
After NACT		
Tafra *et al.* (2001)[49]	93%	0
NSABP B-27 (2005)[40]	85%	10.7%
Xing *et al.* (2006)[43‖]	90% (range 72–100%)	12% (range 0–33%)
Hunt *et al.* (2009)[41]	97.4%	5.9%
Classe *et al.* (2009)[44]	90%	11.5%
Kelly *et al.* (2009)[46¶]	89.6% (95% CI 86.0–92.3)	8.4% (95% CI 6.4–10.9)

Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy

Tari A. King and Monica Morrow

Table 3 | False-negative rates for SLNB after conversion to clinically node-negative disease following NACT

Prospective trial	Overall false-negative rate	Stratified by number of SLNs			Stratified by SLN-detection technique	
		1 (%)	2 (%)	≥3 (%)	Single agent (%)	Dual agent (%)
SENTINA (treatment arm C)[58]	14.2 (95% CI 9.9–19.4)	24.3	18.5	7.3	16.0*	8.6
ACOSOG Z1071[57]	12.6% (95% CI 9.9–16.1)	31.5	21	9.1	20.3‡	10.8
SN FNAC[56]	8.4% (95% CI 2.4–14.4)	18.2	4.9§	NR	16.0*	5.2

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minckwitz, Valentina Nekljudova, Sabine Schmatloch, Peter Schrenk, Annette Staebler, Michael Untch

	Arms A and B	Arm B	Arm C	p
Hot spot on lymphoscintigraphy	1014/1022 (99%)	236/360 (66%)	476/592 (80%)	<0·0001
Overall surgical detection rate (n/N; 95% CI)	99·1% (1013/1022; 98·3–99·6)	60·8% (219/360; 55·6–65·9)	80·1% (474/592; 76·6–83·2)	<0·0001
Overall surgical detection rate with radiocolloid alone	98·8% (573/580; 97·5–99·5)	52·9% (126/238; 46·4–59·4)	77·4% (301/389; 72·9–81·4)	--
Overall surgical detection rate with radiocolloid and blue dye	99·5% (399/401; 98·2–99·9)	76·2% (80/105; 66·9–84·0)	87·8% (144/164; 81·8–92·4)	--
Sentinel lymph nodes removed				
0	9/1022 (1%)	141/360 (39%)	118/592 (20%)	--
1	284/1022 (28%)	96/360 (27%)	142/592 (24%)	--
2	294/1022 (29%)	56/360 (16%)	131/592 (22%)	--
3	186/1022 (18%)	22/360 (6%)	81/592 (14%)	--
4	114/1022 (11%)	20/360 (6%)	59/592 (10%)	--
>4	135/1022 (13%)	25/360 (7%)	61/592 (10%)	--
At least one sentinel node removed				
All patients	Mean 2·7, median 2·0	Mean 2·4, median 2·0	Mean 2·7, median 2·0	<0·0001
Radiocolloid alone	Mean 2·6, median 2·0	Mean 2·3, median 2·0	Mean 2·6, median 2·0	0·012
Radiocolloid and blue dye	Mean 2·8, median 2·0	Mean 2·6, median 2·0	Mean 2·9, median 3·0	0·059

Data are n/N (%), unless otherwise stated.

Table 3: **Detection of sentinel lymph nodes, according to selected factors**

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minckwitz, Valentina Nekljudova, Sabine Schmatloch, Peter Schrenk, Annette Staebler, Michael Untch

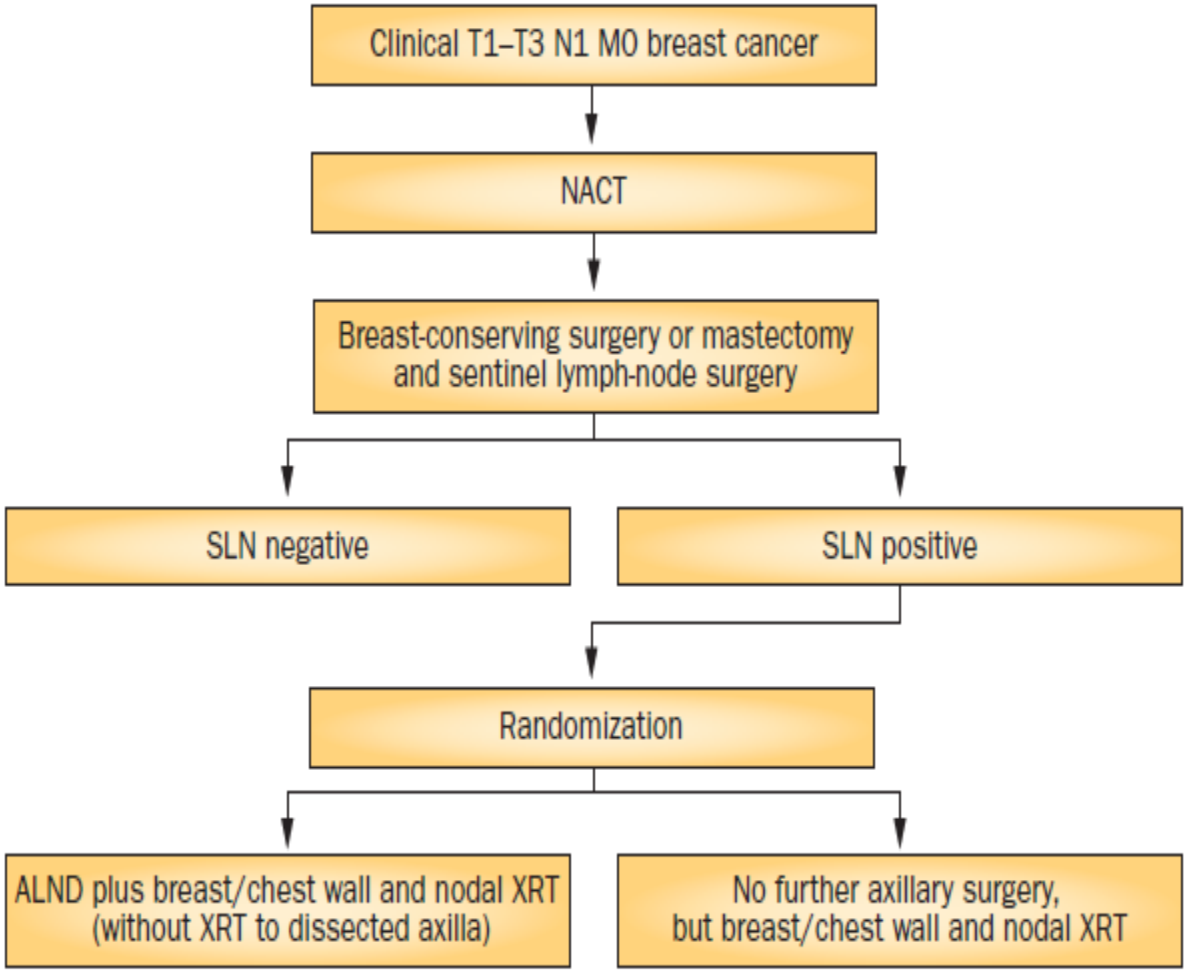
	Arm B (n=64)	Arm C (n=226)
Overall false-negative rate (n/N; 95% CI)	51·6% (33/64; 38·7–64·2)	14·2% (32/226; 9·9–19·4)
False-negative rate, according to number of sentinel nodes removed		
1	66·7% (16/24)	24·3% (17/70)
2	53·8% (7/13)	18·5% (10/54)
3	50·0% (5/10)	7·3% (3/41)
4	50·0% (3/6)	0·0% (0/28)
5	18·2% (2/11)	6·1% (2/33)
False-negative rate, according to detection technique		
Radiocolloid alone	46·2% (18/39)	16·0% (23/144)
Radiocolloid and blue dye	60·9% (14/25)	8·6% (6/70)

Data are rate (number of patients), unless otherwise stated.

Table 4: **False-negative rate of sentinel-lymph-node resection in patients with positive nodes, according to selected factors**

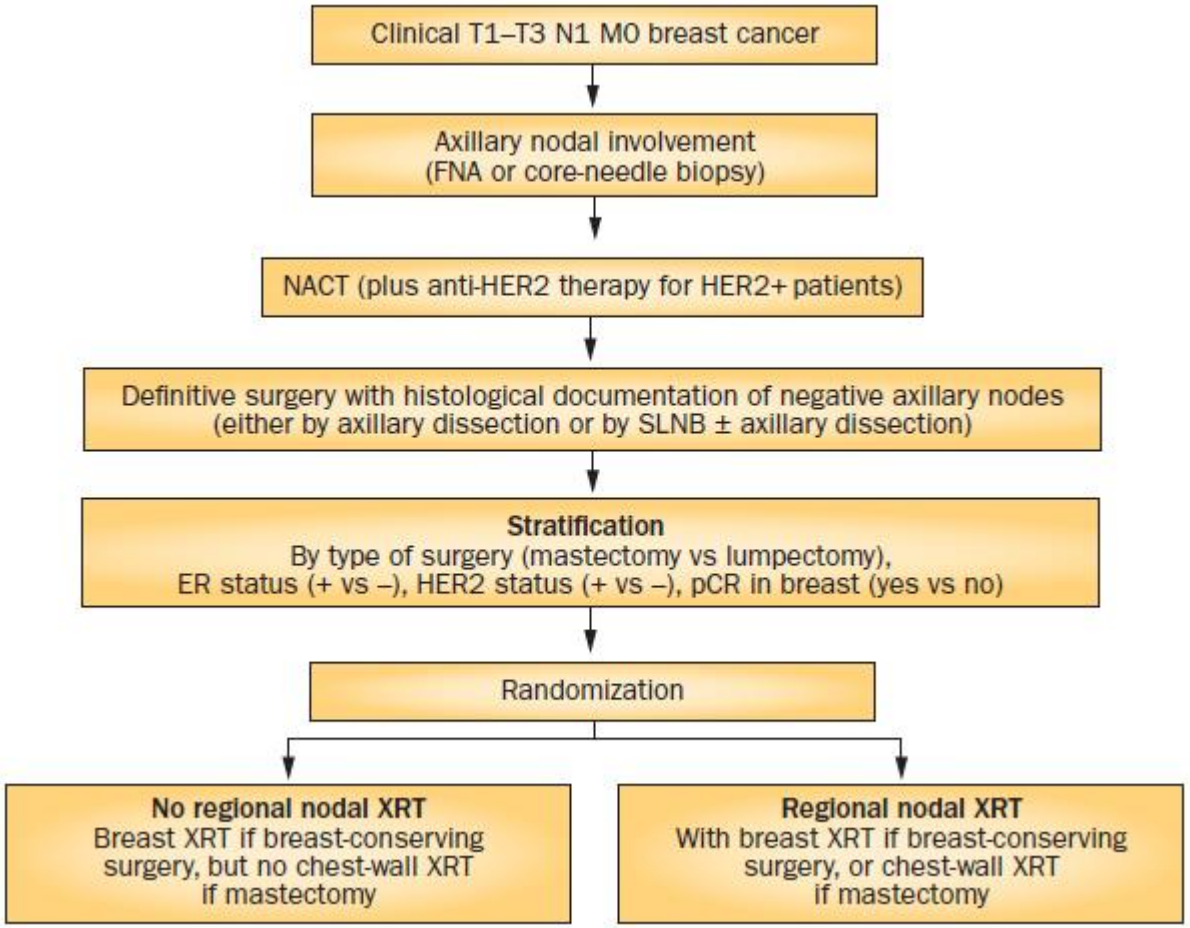
Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy

Tari A. King and Monica Morrow



Surgical issues in patients with breast cancer receiving neoadjuvant chemotherapy

Tari A. King and Monica Morrow



SONUÇ…

- Neoadjuvan kemoterapi özellikle Her 2 + hastalarda oldukça etkin….
- pCR ile sağ kalım arasında güçlü bir ilişki söz konusudur…
- Trastuzumab + pertuzumab kombinasyonu içeren protokoller güncel tedavide yerini…
- Sağ kalım sonuçları açısından güçlendirilmiş çalışma sonuçlarına ihtiyaç vardır.