HER2+ Breast Cancer in Elderly

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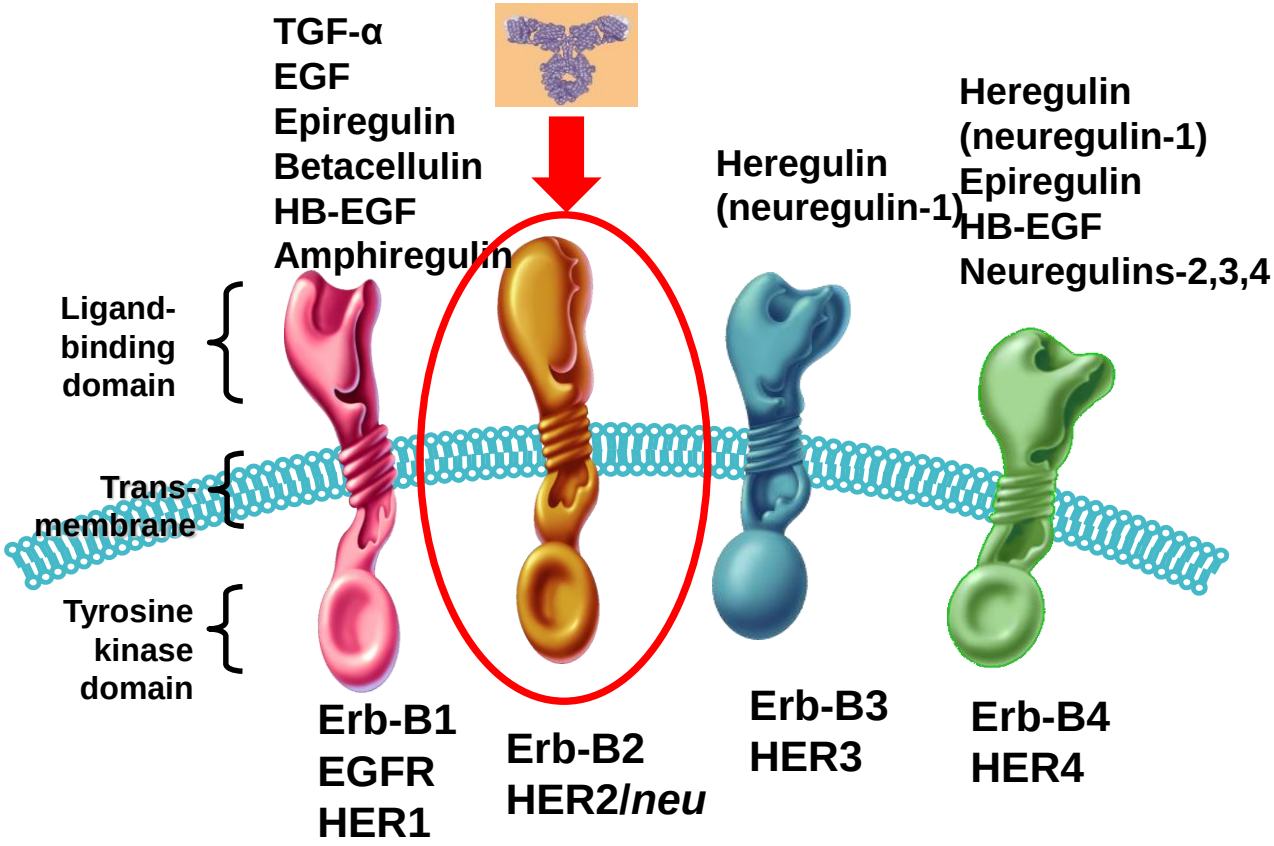
institutCurie

SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

EORTC
The future of cancer therapy

1990 = trastuzumab (Herceptin®)

1st humanized (95%) antibody anti-HER2



VOLUME 25 · NUMBER 6 · FEBRUARY 20 2007

JOURNAL OF CLINICAL ONCOLOGY

EDITORIAL

Do the Large Benefits Justify the Large Costs of Adjuvant Breast Cancer Trastuzumab?

Bruce E. Hillner and Thomas J. Smith, *Department of Internal Medicine and the Massey Cancer Center, Virginia Commonwealth University, Richmond, VA*

We should all be rejoicing that the breast cancer death rates will fall further in Western countries with trastuzumab. We must remember that everyone is not as affluent as us and/or as willing to devote increasingly amounts of their economic resources to health care. Let's hope that the translational scientific community will hit more home runs. In our opinion, there have been only two walk-off home run oncology products or strategies in the last 20 years—ones that provided relative reductions exceeding 50% compared with the best current care—imatinib and trastuzumab. Unless we want to bankrupt future generations, cost-effectiveness assessments will have an increasing role in determining value and how we spend or allocate our precious health care dollars.[15-17]

DFS & OS w/ trastuzumab 1 year

			DFS		OS	
Study	**Follow-up (years)**	**N**	**HR**	**p value**	**HR**	**p value**
HERA[1–4] CT+/–RT→H vs. CT+/–RT	1	3387	0.54	< 0.0001	0.76	0.26
	2	3401	0.64	< 0.0001	0.66	0.0115
	4	3401	0.76	< 0.0001	0.85	0.1087
	8	3401	0.76	< 0.0001	0.76	0.0005
NCCTG N9831/ NSABP B-31[5–7] AC→TH→H vs. AC→T	2	3351	0.48	< 0.0001	–	–
	4	4045	0.52	< 0.001	0.61	< 0.001
	8.4	4046	0.60	< 0.0001	0.63	< 0.0001
BCIRG 006[8]						
AC→TH→H vs. AC→T	5.5	3222	0.64	< 0.001	0.63	< 0.001
TCH vs. AC→T			0.75	0.04	0.77	0.04

AMM FDA/EMA 2006

CT, chemotherapy; DFS, disease-free survival; H, trastuzumab; HR, hazard ratio; OS, overall survival; RT, radiotherapy; T, taxane.

1. Piccart-Gebhart MJ, *et al*; *N Engl J Med* 2005; **353:**1659-1672;
2. Smith I, *et al*. *Lancet* 2007; **369:**29-36;
3. Gianni L, *et al*; *Lancet Oncol* 2011; **12:**236-244;
4. Goldhirsch A, *et al*. *Lancet* 2013 [Epub ahead of print];
5. Romond EH, *et al*. *N Engl J Med* 2005; **353:**1673-1684;
6. Perez EA, *et al*. *J Clin Oncol* 2011; **29:**3366-3373;
7. Romond EH, *et al*. SABCS 2012 (abstract S5-5; oral presentation);
8. Slamon D, *et al*. *N Engl J Med* 2011; **365:**1273-1283.

Trastuzumab adjuvant & DFS

	HR all	(95%CI)	HR 60+	(95%CI)
HERA	0.64	0.54-0.76	0.91	0.59-1.41
NSABP-B31/N9831	0.48	0.39-0.59	0.41	0.24-0.68
BCIRG 006	0.61	0.37-0.65	NR	NR
FinHER	0.42	0.21-0.83	NR	NR
PACS-04	0.86	0.61-1.22	NR	NR

> 60 yo ≤ 16% in HERA for ex!

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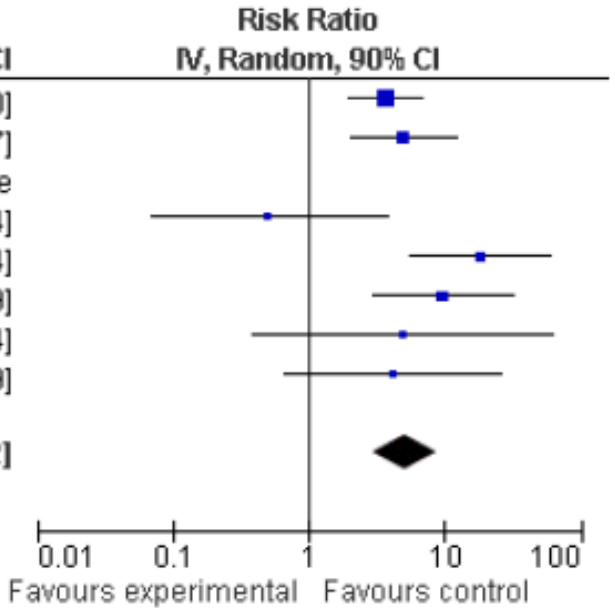
Figure 8. Congestive heart failure (CHF): all studies.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 90% CI
B31	35	932	9	872	31.7%	3.64 [1.98, 6.70]
BCIRG006	20	1068	4	1050	21.4%	4.92 [2.00, 12.07]
Buzdar	0	23	0	19		Not estimable
FinHer	1	115	2	116	6.3%	0.50 [0.07, 3.74]
HERA	36	1678	2	1708	14.6%	18.32 [5.55, 60.44]
N9831	37	1280	2	664	14.6%	9.60 [2.92, 31.59]
NOAH	2	115	0	113	4.1%	4.91 [0.39, 62.24]
PACS-04	4	260	1	268	7.3%	4.12 [0.66, 25.79]
Total (90% CI)		**5471**		**4810**	**100.0%**	**5.11 [3.00, 8.72]**
Total events	135		20			

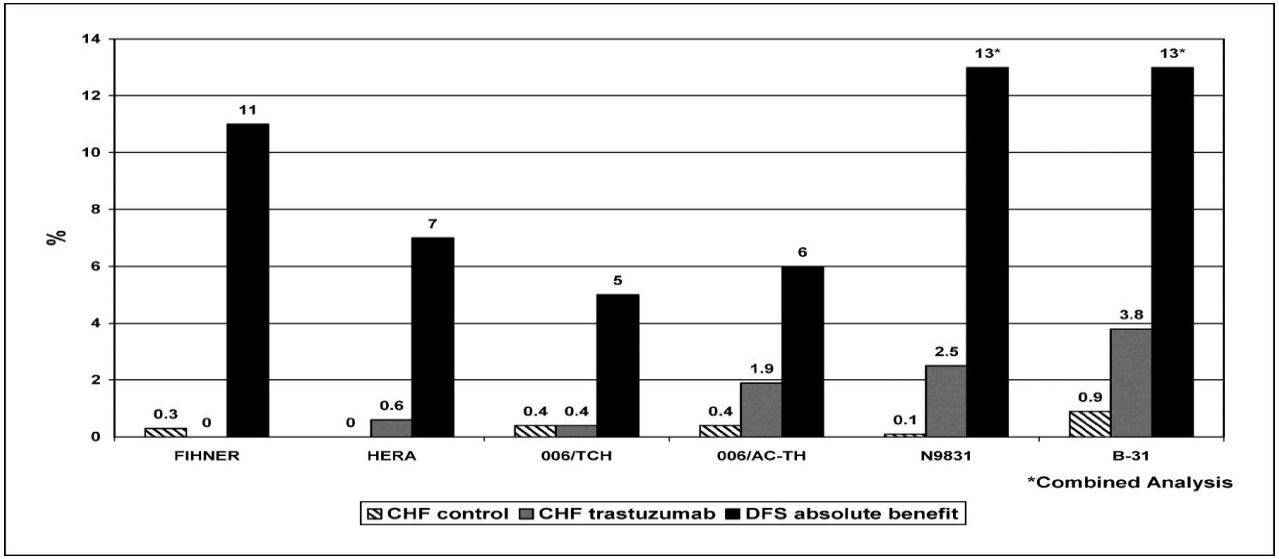
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 8.32$, $df = 6$ ($P = 0.22$); $I^2 = 28\%$

Test for overall effect: $Z = 5.02$ ($P < 0.00001$)



Moja. Cochrane Database Syst Rev 2012

The incidence of CHF from the Finnish Herceptin Study (FINHER), Herceptin Adjuvant trial (HERA), Breast Cancer International Collaborative Group trial 006 (006) with TCH and AC-TH analyzed separately, the North Central Cancer Treatment Group trial 9831 (N9831), and NSABP B-31 (B-31).



Bird B R H , Swain S M Clin Cancer Res 2008;14:14-24

- NSABP B31
  - **Age**
    - **2% < 50 yo vs 5.4% > 60 yo**
  - LVEF > 4 AC
    - 12% if LVEF < 55%)
  - Concomitant > sequential
  - **Hypertension comedications**
- B31/N9831
  - 6.7% pts who had completed AC had a lower LVEF or developed cardiac symptoms preventing the initiation of TZT
  - 1/3 pts who started TZT discontinued it: 4.7% with symptomatic CHF, 14.2% with confirmed asymptomatic decline in LVEF, and the rest for noncardiac reasons

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

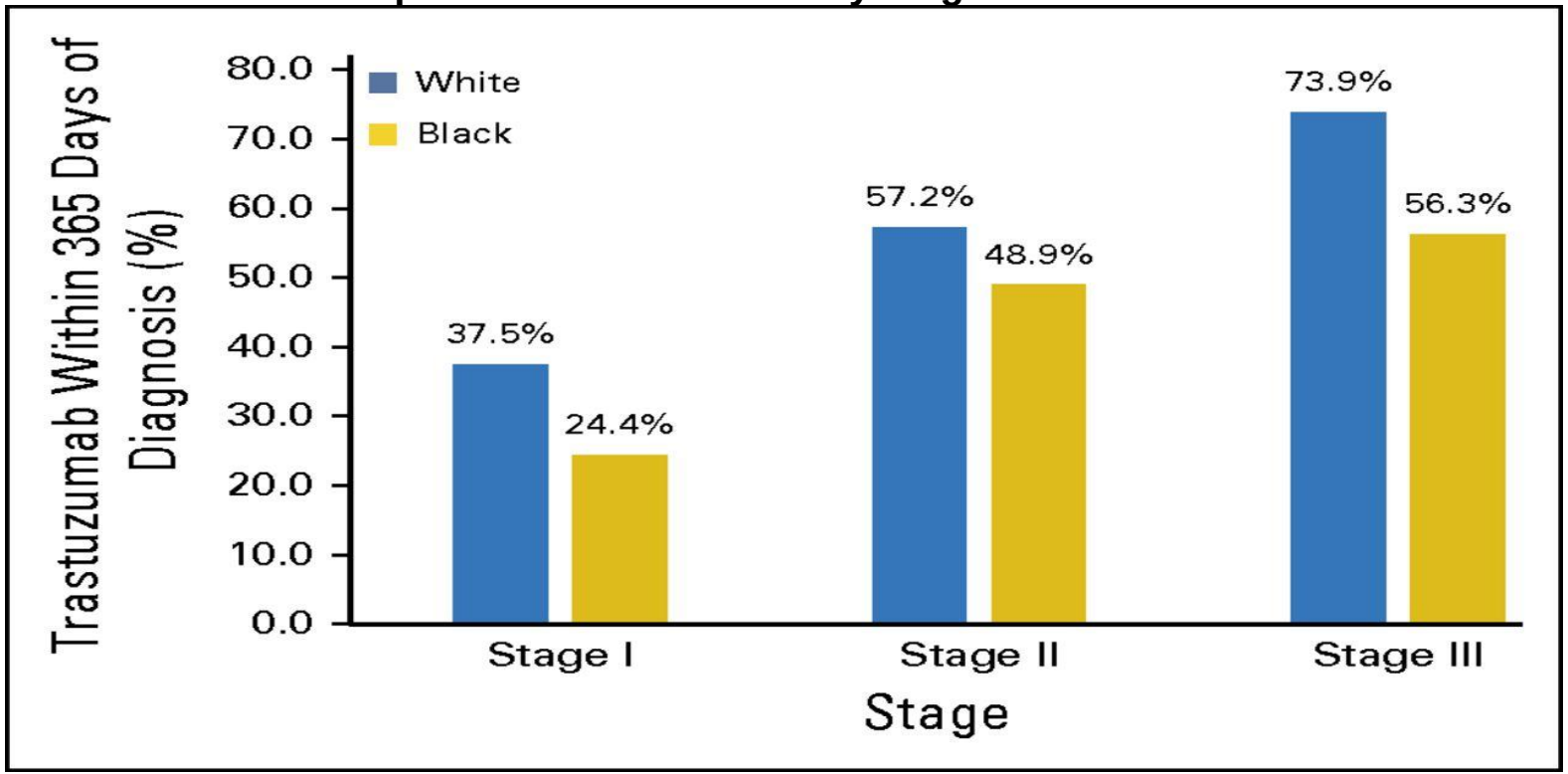
Duration and Toxicity of Adjuvant Trastuzumab in Older Patients With Early-Stage Breast Cancer: A Population-Based Study

Ines Vaz-Luis, Nancy L. Keating, Nancy U. Lin, Huichuan Lii, Eric P. Winer, and Rachel A. Freedman

- SEER database
- 2,028 patients ≥ 66, stage I-III, 2005-2009, trastuzumab
  - 71.2% < 76
  - 66.8% w/o comorbidities (Charlson)
  - 85.2% w/ chemotherapy
  - 81.7% w/ complete trastuzumab treatment (> 9 months)
  - Factors correlated w/ incomplete treatment
    - Age 80+ vs 66-70 OR 0.40 (0.30-0.55)
    - Comorbidities 2 vs 0 OR 0.65 (0.49-0.88)

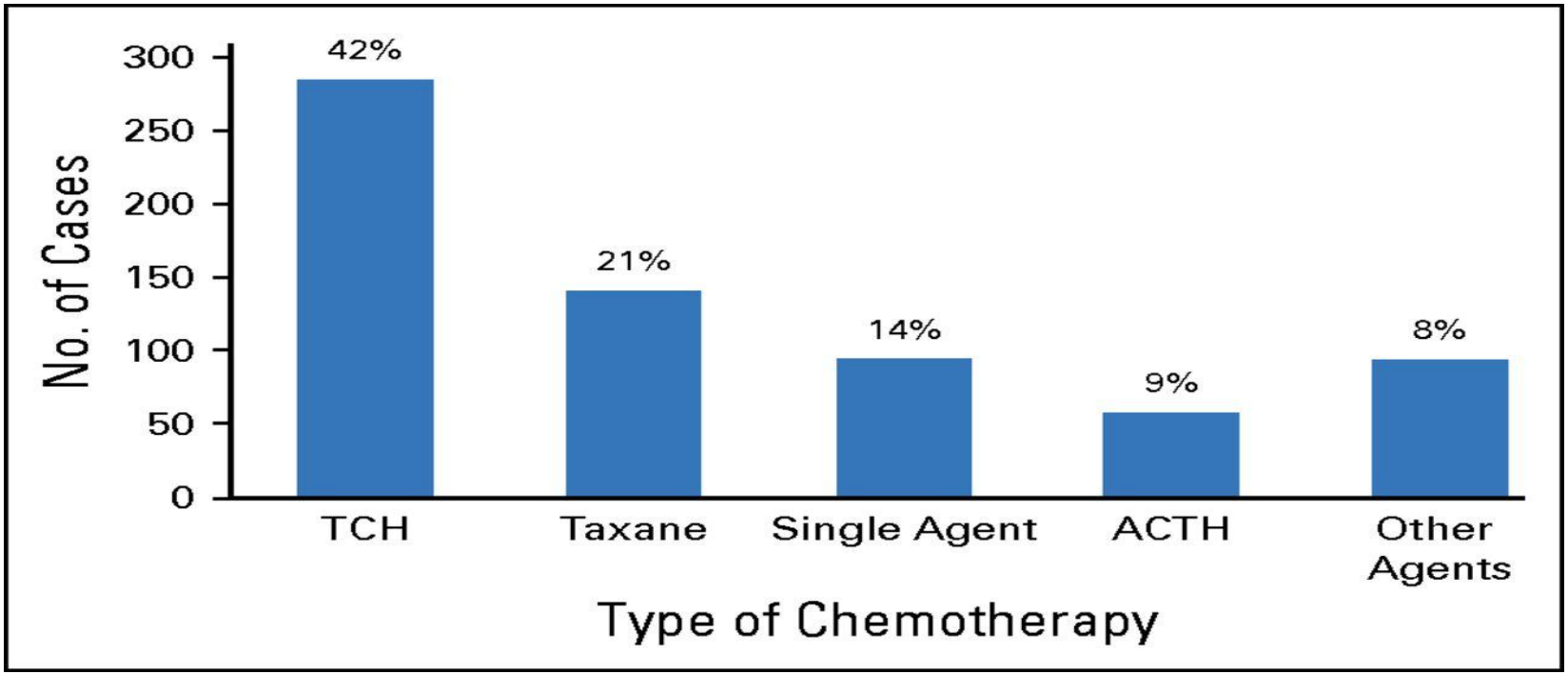
Vaz-Luiz. J Clin Oncol 2014

Receipt of trastuzumab among women with human epidermal growth factor receptor 2–positive breast cancer by stage and race.



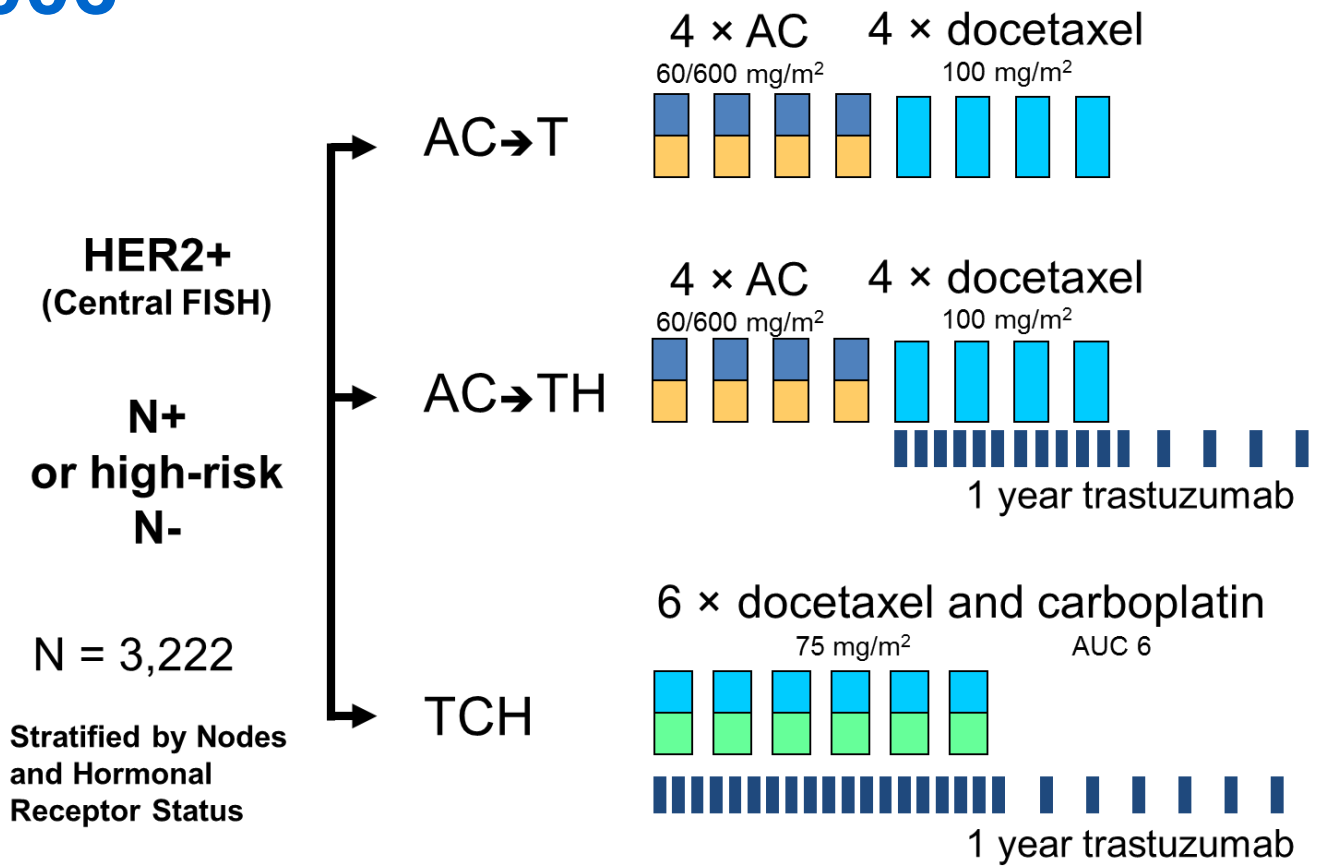
Katherine Reeder-Hayes et al. JCO 2016;34:2003-2009

Chemotherapies received with trastuzumab (n = 672).



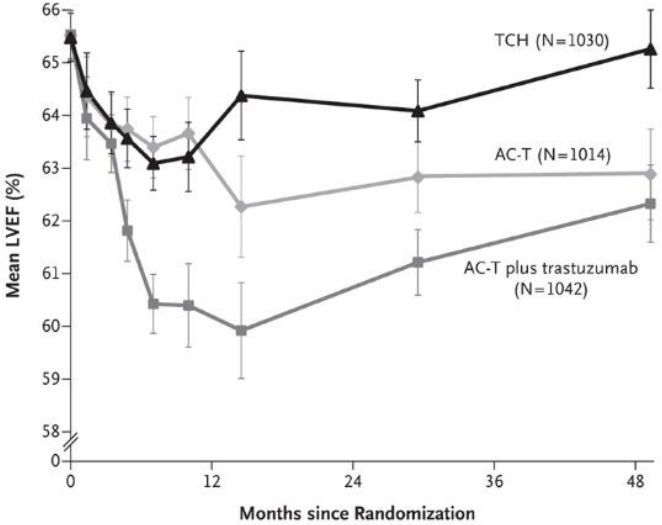
Katherine Reeder-Hayes et al. JCO 2016;34:2003-2009

BCIRG 006



Slamon. NEJM 2011

Cardiac events



	ACTH	TCH
Disease-free survival events	269	279
Grade 3/4 CHF	21 (2%)	4 (0.4%)
Treatment-related leukemia	7	0

Trial	Severe cardiac dysfunction (class III-IV CHF)	Significant asx LVEF decline (≥10% to below LLN or ≥ 16% from BL)	Discontinued trastuzumab for cardiac toxicity
Intergroup Trials (included anthracycline)	4.1%	18%	14%
BCIRG 006	0.4%	7%	n/a

Slamon. NEJM 2011, SABCS 2009 & 2015

Romond. NEJM 2005 & JCO 2012; Piccart-Gebhart. NEJM 2005; Joensuu. NEJM 2006

Adjuvant docetaxel and cyclophosphamide plus trastuzumab in patients with *HER2*-amplified early stage breast cancer: a single-group, open-label, phase 2 study

Stephen E Jones, Rufus Collea, Devchand Paul, Scot Sedlacek, Anne M Fawret, Ira Gore Jr, Deborah L Lindquist, Frankie Ann Holmes, Mary Ann K Allison, Barry D Brooks, Raul M Portillo, Svetislava J Vukelja, Michael S Steinberg, Christopher Stokoe, Maria W Crockett, Yunfei Wang, Lina Asmar, Nicholas J Robert, Joyce O'Shaughnessy

Lancet Oncol 2013; 14: 1121–28
Published Online
September 3, 2013

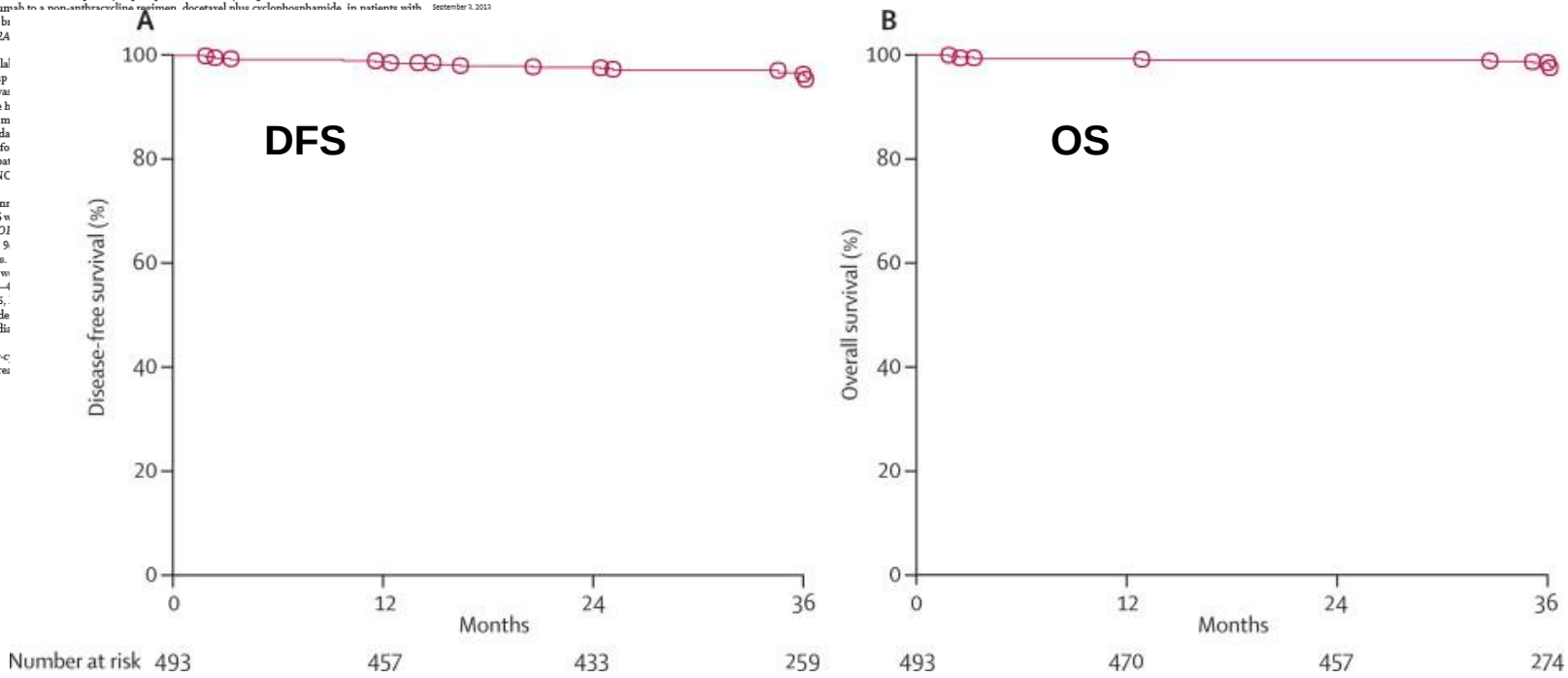
Summary

Background Previous results suggest that docetaxel plus cyclophosphamide improves disease-free survival (DFS) and overall survival compared with doxorubicin plus cyclophosphamide in early stage breast cancer. We assessed the addition of 1 year of trastuzumab to a non-anthracycline regimen, docetaxel plus cyclophosphamide, in patients with *HER2*-amplified early stage br
TOP2A-amplified and *TOP2A*

Methods This was an open-la
Cooperative Oncology Group
histologically confirmed, inva
TOP2A status; and adequate h
of intravenous docetaxel 75 m
4 mg/kg (loading dose) on da
6 mg/kg every three weeks fo
and *TOP2A*-non-amplified pat
ClinicalTrials.gov, number NC

Findings 493 patients were enr
(IQR 35·5–36·7), 2-year DFS w
for the 190 patients with *TO1*
survival was 98·8% (95% CI 9
assessable for *TOP2A* status.
adverse events of any grade w
The most common grade 3–4
(21, 4·3%), and diarrhoea (16,
grade 2, and two [0·4%] grade
trastuzumab because of cardia

Interpretation A short, four-c
be an option for adjuvant tre
TOP2A status.



Follow up 36 mos

Jones. Lancet Oncol 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Paclitaxel and Trastuzumab for Node-Negative, HER2-Positive Breast Cancer

Sara M. Tolaney, M.D., M.P.H., William T. Barry, Ph.D., Chau T. Dang, M.D., Denise A. Yardley, M.D., Beverly Moy, M.D., M.P.H., P. Kelly Marcom, M.D., Kathy S. Albain, M.D., Hope S. Rugo, M.D., Matthew Ellis, M.B., B.Chir., Ph.D., Iuliana Shapira, M.D., Antonio C. Wolff, M.D., Lisa A. Carey, M.D., Beth A. Overmoyer, M.D., Ann H. Partridge, M.D., M.P.H., Hao Guo, M.S., Clifford A. Hudis, M.D., Ian E. Krop, M.D., Ph.D., Harold J. Burstein, M.D., Ph.D., and Eric P. Winer, M.D.

ABSTRACT

BACKGROUND

No single standard treatment exists for patients with small, node-negative, human epidermal growth factor receptor type 2 (HER2)–positive breast cancers, because most of these patients have been ineligible for the pivotal trials of adjuvant trastuzumab.

METHODS

We performed an uncontrolled, single-group, multicenter, investigator-initiated study of adjuvant paclitaxel and trastuzumab in 406 patients with tumors measuring up to 3 cm in greatest dimension. Patients received weekly treatment with paclitaxel and trastuzumab for 12 weeks, followed by 9 months of trastuzumab monotherapy. The primary end point was survival free from invasive disease.

RESULTS

The median follow-up period was 4.0 years. The 3-year rate of survival free from invasive disease was 98.7% (95% confidence interval [CI], 97.6 to 99.8). Among the 12 relapses seen, 2 were due to distant metastatic breast cancer. Excluding contralateral HER2-negative breast cancers and nonbreast cancers, 7 disease-specific events were noted. A total of 13 patients (3.2%; 95% CI, 1.7 to 5.4) reported at least one episode of grade 3 neuropathy, and 2 had symptomatic congestive heart failure (0.5%; 95% CI, 0.1 to 1.8), both of whom had normalization of the left ventricular ejection fraction after discontinuation of trastuzumab. A total of 13 patients had significant asymptomatic declines in ejection fraction (3.2%; 95% CI, 1.7 to 5.4), as defined by the study, but 11 of these patients were able to resume trastuzumab therapy after a brief interruption.

CONCLUSIONS

Among women with predominantly stage I HER2-positive breast cancer, treatment with adjuvant paclitaxel plus trastuzumab was associated with a risk of early recurrence of about 2%; 6% of patients withdrew from the study because of protocol-specified adverse events. (Funded by Genentech; ClinicalTrials.gov number, NCT00542451.)

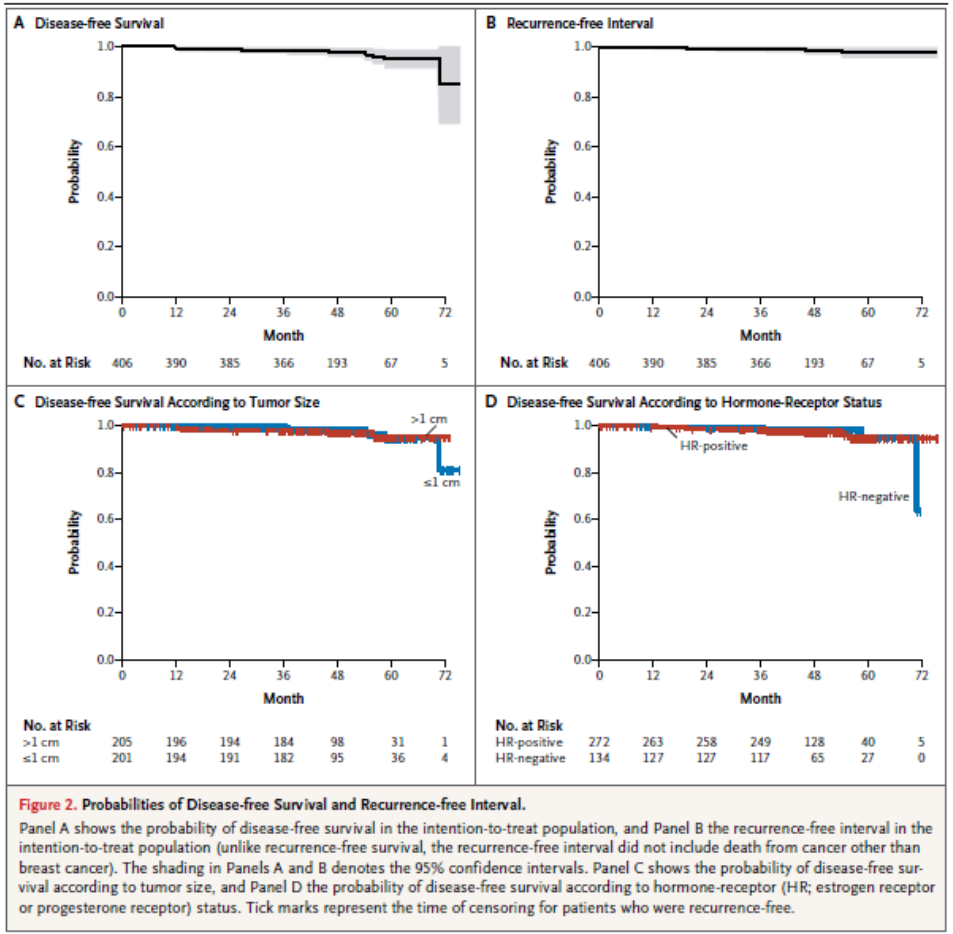


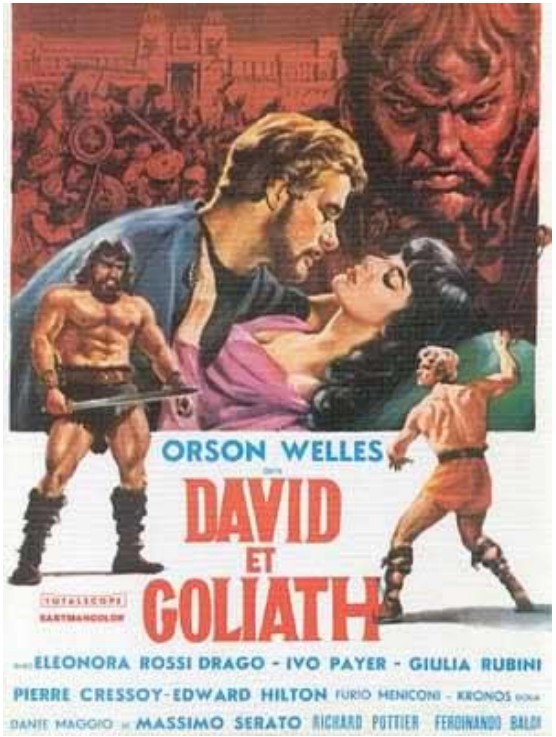
Figure 2. Probabilities of Disease-free Survival and Recurrence-free Interval.

Panel A shows the probability of disease-free survival in the intention-to-treat population, and Panel B the recurrence-free interval in the intention-to-treat population (unlike recurrence-free survival, the recurrence-free interval did not include death from cancer other than breast cancer). The shading in Panels A and B denotes the 95% confidence intervals. Panel C shows the probability of disease-free survival according to tumor size, and Panel D the probability of disease-free survival according to hormone-receptor (HR; estrogen receptor or progesterone receptor) status. Tick marks represent the time of censoring for patients who were recurrence-free.

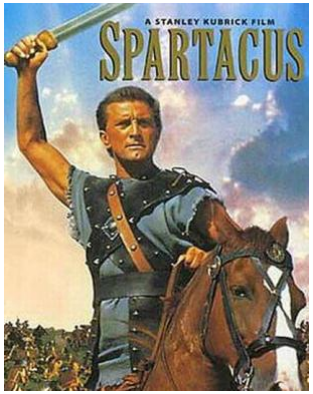
Tolaney. NEJM 2015

"Anti-HER2 match"

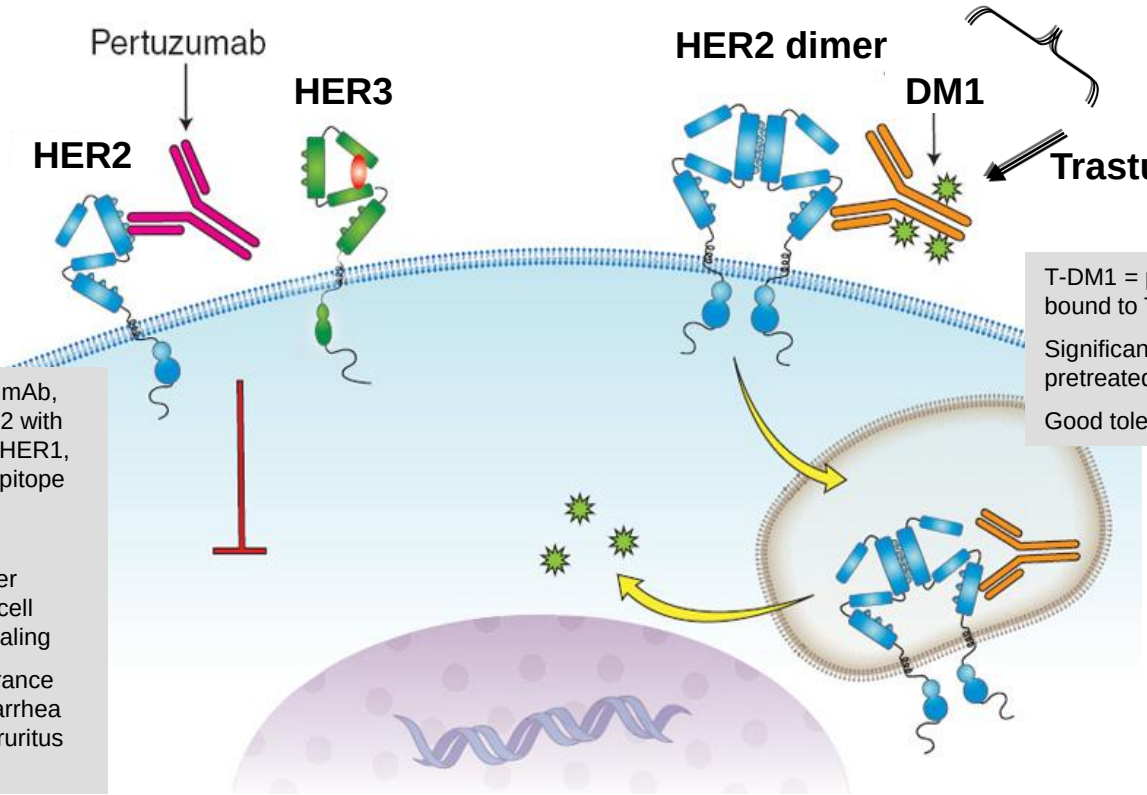
trastuzumab



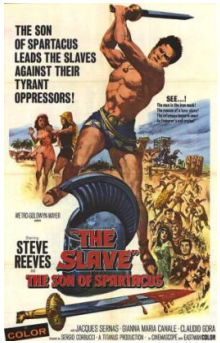
lapatinib



Pertuzumab



T-DM1



P = recombinant humanized mAb, prevents dimerization of HER2 with other HER receptors (HER3, HER1, and HER4) (different HER2 epitope than TZT)

TZT and P complementary mechanisms of action: broader blockade of the HER tumour cell proliferation and survival signaling

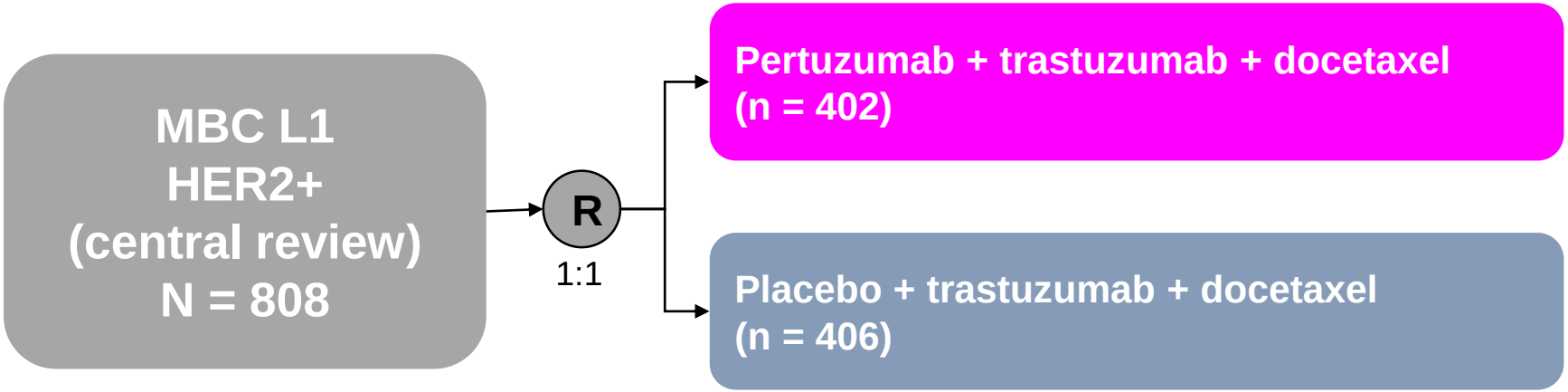
P+TZT: CB 50% w/good tolerance (only noted grade 3-4 was diarrhea 3%; asthenia 2%, rash 3%, pruritus 2%), NEOSPHERE

T-DM1 = µtubule blocking agent DM1 bound to TZT = targeted delivery of DM1

Significant single agent activity in pretreated HER2+ MBC (RR 30-50%)

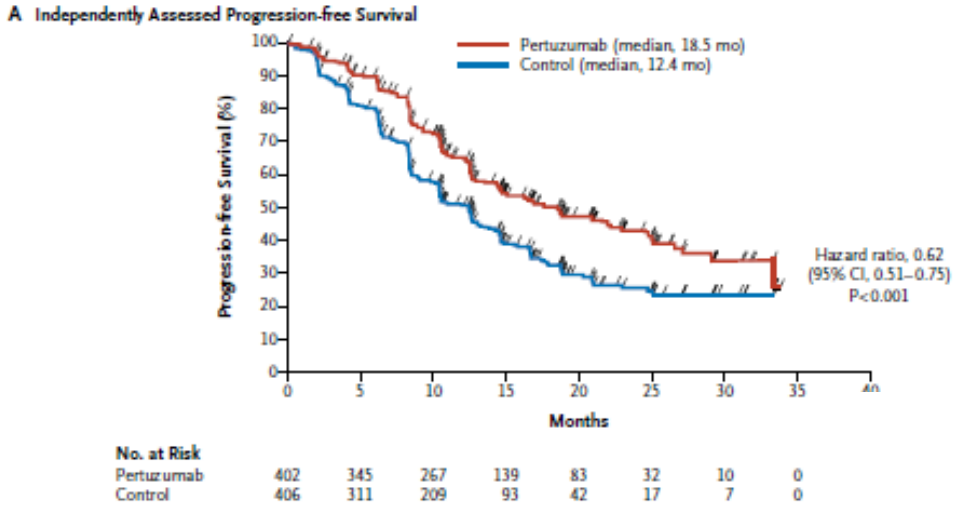
Good tolerance (moderate thrombopenia)

Cleopatra double-blinded phase III trial



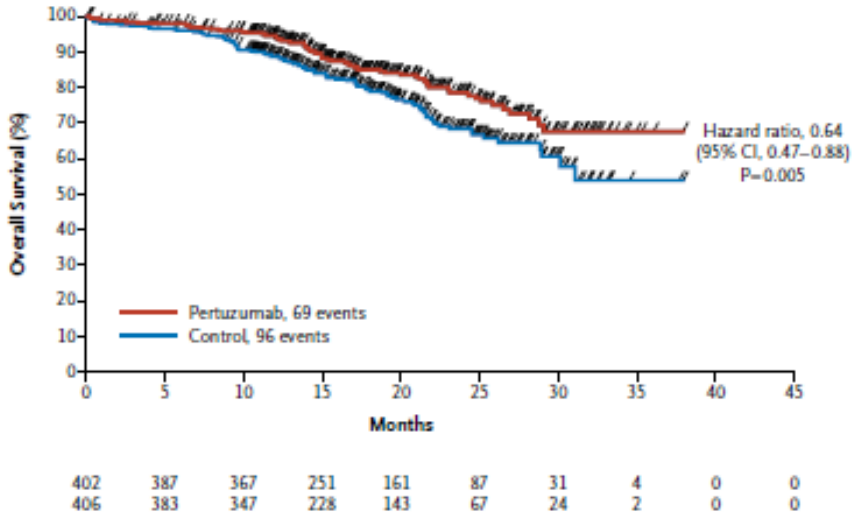
- Pertuzumab: 840 mg loading dose → 420 mg
- Trastuzumab: 8 mg/kg loading dose → 6 mg/kg
- Docetaxel: 75 mg/m^2 → 100 mg/m^2 depending on tolerance
- Primary objective: PFS
- Secondary objectives: OS, ORR, tolerance
- Stratification: geography, (neo)adjuvant treatment

Baselga. N Engl J Med 2012



Pertuzumab plus Trastuzumab plus Docetaxel for Metastatic Breast Cancer

José Baselga, M.D., Ph.D., Javier Cortés, M.D., Sung-Bae Kim, M.D., Seock-Ah Im, M.D., Roberto Hegg, M.D., Young-Hyuck Im, M.D., Laslo Roman, M.D., José Luiz Pedrini, M.D., Tadeusz Pienkowski, M.D., Adam Knott, Ph.D., Emma Clark, M.Sc., Mark C. Benyunes, M.D., Graham Ross, F.F.P.M., and Sandra M. Swain, M.D., for the CLEOPATRA Study Group*



Cleopatra

docetaxel + trastuzumab ± pertuzumab

~6 mos BENEFIT IN PFS

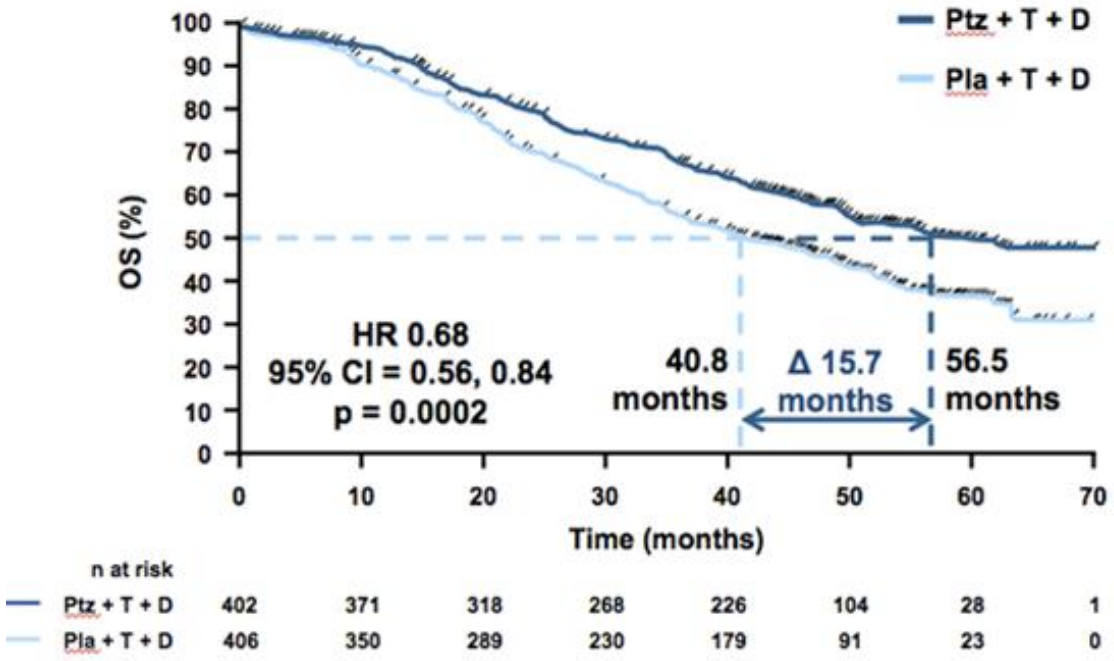
A new standard of care

Baselga. N Engl J Med 2012

Cleopatra

Final OS Analysis

Median follow-up 50 months (range 0–70 months)

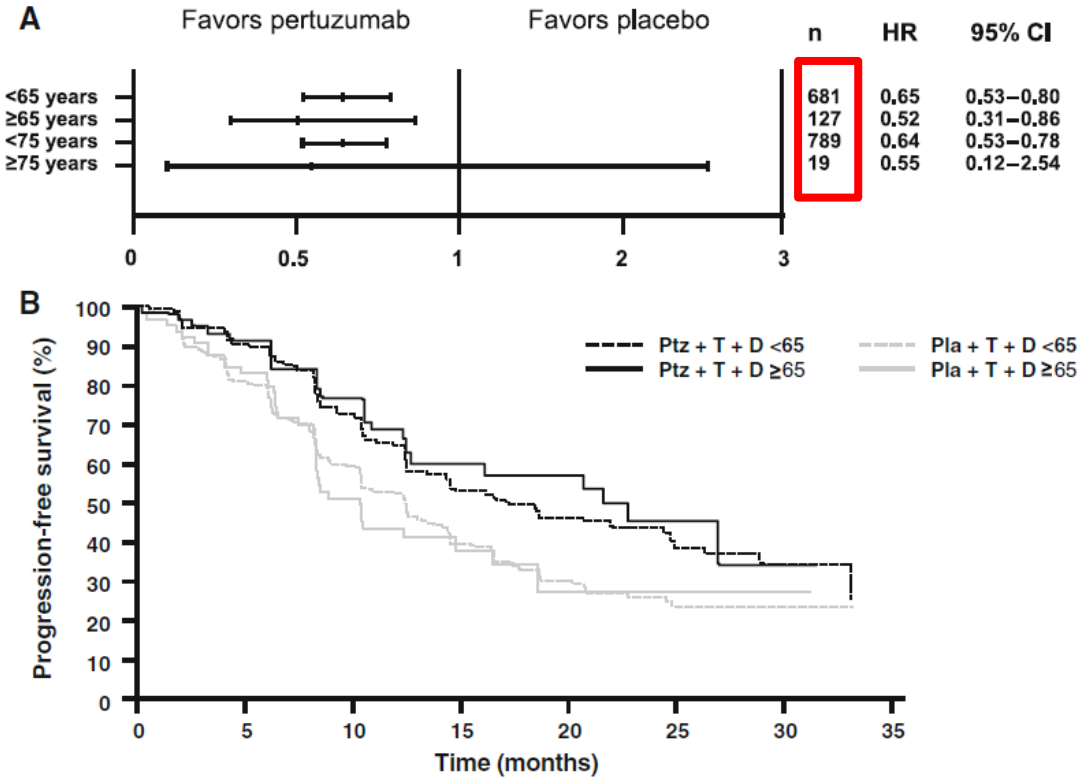


ITT population. Stratified by geographic region and neo/adjuvant chemotherapy.

CI, confidence interval; D, docetaxel; HR, hazard ratio; OS, overall survival; Pla, placebo; Ptz, pertuzumab; T, trastuzumab.

Swain. ESMO 2014; Swain. NEJM 2015

Pertuzumab



CLEOPATRA

808 patients

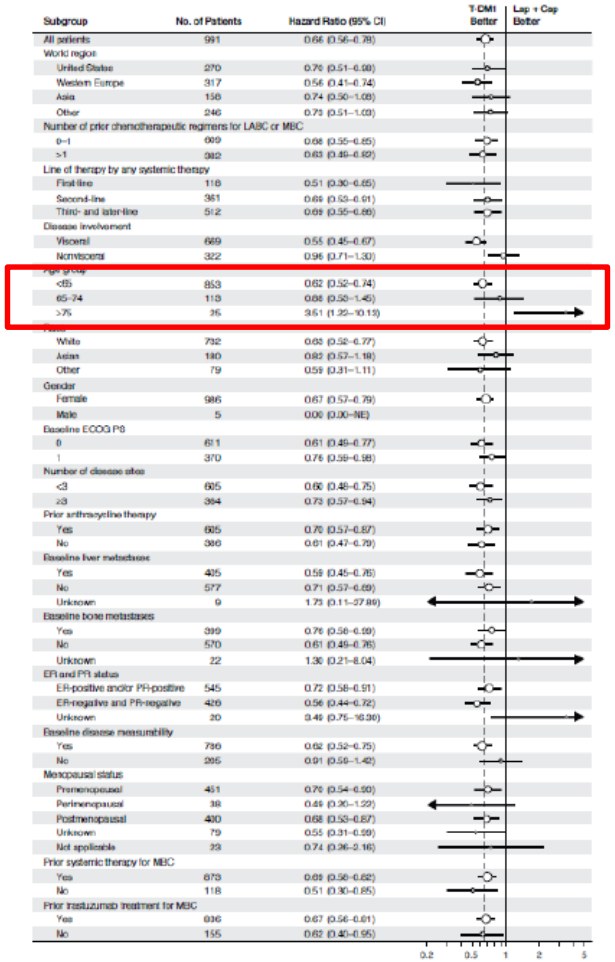
→ 127 (16%) 65+

→ 19 (2%) 75+

Diarrhea, asthenia, fatigue, decreased appetite, vomiting and dysgeusia (any grade) more frequent in elderly patients

Miles. Breast Cancer Res Treat 2013

T-DM1



EMILIA

991 patients

→ 113 (11%) 65-74

→ 25 (3%) 75+

Table 4. Incidence of Grade ≥ 3 AEs by Patient Subgroup in T-DM1–Exposed Patients

Subgroup	Total No. of Patients (N = 884)	Grade ≥ 3 AE	
		No. of Patients	%
Age, years			
< 65	762	335	44.0
≥ 65	122	63	51.6
≥ 65 to < 75	93	49	52.7
≥ 75	29	14	48.3
Race			
White	692	288	41.6
Asian	99	63	63.6
Other	93	47	50.5
Previous systemic therapy for MBC			
Yes	722	336	46.5
No	162	62	38.3
Previous anthracycline use			
Yes	586	267	45.6
No	298	131	44.0

Abbreviations: AE, adverse event; MBC, metastatic breast cancer; T-DM1, trastuzumab emtansine.

Kamilla 2220 patients

194 (9%) 65-69, 78 (4%) 70-74, 120 (5%) 75+

Verma. N Engl J Med 2013; Dieras. J Clin Oncol 2014; Barrios ASCO 2015

NeoSphere

Phase II

417 EBC HER2+, randomisation 4 groups 1:1:1:1

1. Taxotere + trastuzumab
2. Taxotere + trastuzumab + pertuzumab
3. Trastuzumab + pertuzumab
4. Taxotere + pertuzumab

Accelerated FDA approval 2013

pCR increased if dual blockade (trastuzumab + pertuzumab)

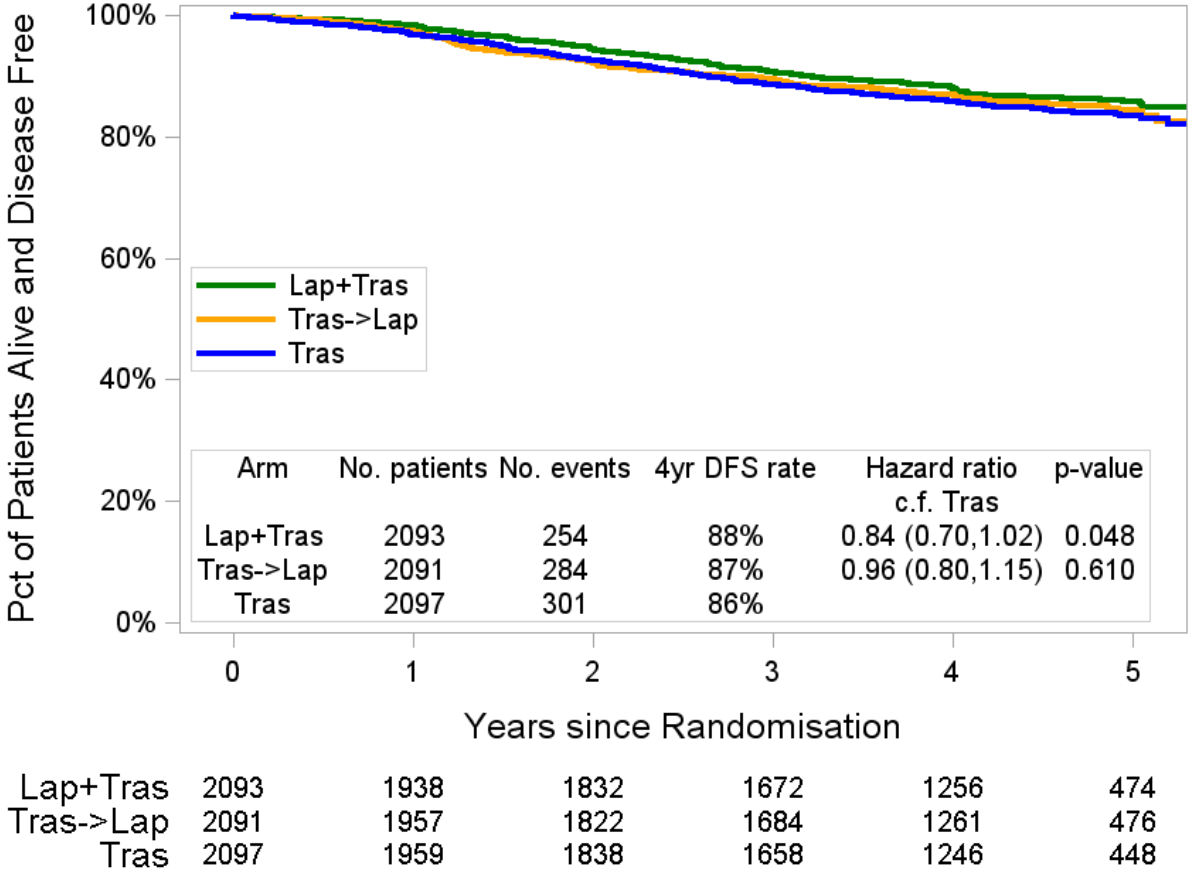
	Trastuzumab plus docetaxel (group A; n=107)	Pertuzumab, trastuzumab, and docetaxel (group B; n=107)	Pertuzumab plus trastuzumab (group C; n=107)	Pertuzumab plus docetaxel (group D; n=96)
Pathological complete response in ITT population	31 (29·0%, 20·6–38·5)	49 (45·8%, 36·1–55·7)*	18 (16·8%, 10·3–25·3)†	23 (24·0%, 15·8–33·7)‡
Pathological complete response and N– at surgery	23 (21·5%, 14·1–30·5)	42 (39·3%, 30·0–49·2)	12 (11·2%, 5·9–18·8)	17 (17·7%, 10·7–26·8)
Pathological complete response and N+ at surgery	8 (7·5%, 3·3–14·2)	7 (6·5%, 2·7–13·0)	6 (5·6%, 2·1–11·8)	6 (6·3%, 2·3–13·1)
Pathological complete response in ER positive or PR positive, or both, women	10/50 (20·0%, 10·0–33·7)	13/50 (26·0%, 14·6–40·3)	3/51 (5·9%, 1·2–16·2)	8/46 (17·4%, 7·8–31·4)
Pathological complete response in ER negative and PR negative women	21/57 (36·8%, 24·4–50·7)	36/57 (63·2%, 49·3–75·6)	15/55 (27·3%, 16·1–41·0)	15/50 (30·0%, 17·9–44·6)

Data are n (%, 95% CI) or n/N (%, 95% CI). ITT=intention-to-treat. N–=lymph-node negative. N+=lymph-node positive. ER=oestrogen receptor. PR=progesterone receptor. *p=0·0141 *vs* group A. †p=0·0198 *vs* group A. ‡p=0·003 *vs* group B.

Table 2: **Pathological complete responses in the ITT population, by hormone-receptor status, and by axillary lymph node status at surgery**

Gianni. Lancet Oncol 2012

ALTTO DFS



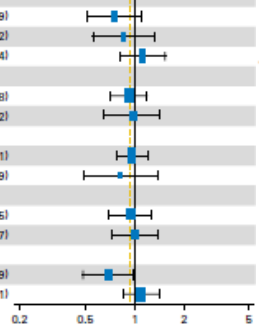
Arm	No. patients	No. events	4yr DFS rate	Hazard ratio c.f. Tras	p-value
Lap+Tras	2093	254	88%	0.84 (0.70,1.02)	0.048
Tras->Lap	2091	284	87%	0.96 (0.80,1.15)	0.610
Tras	2097	301	86%		

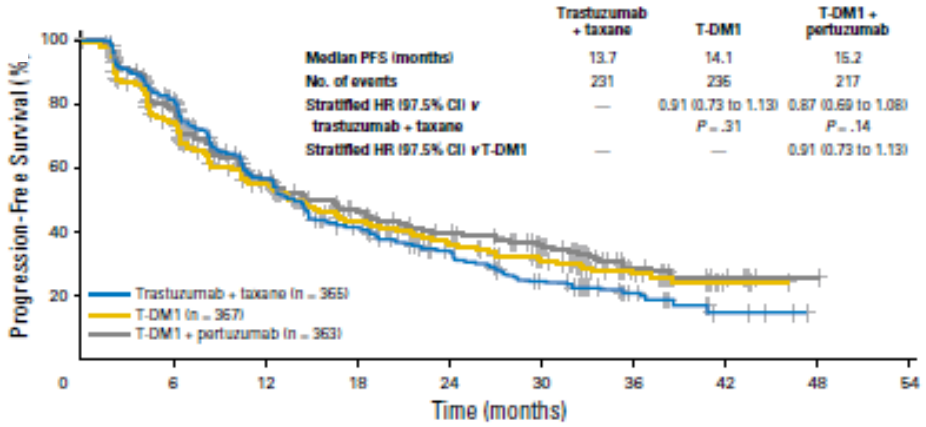
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Trastuzumab Emtansine With or Without Pertuzumab Versus Trastuzumab Plus Taxane for Human Epidermal Growth Factor Receptor 2–Positive, Advanced Breast Cancer: Primary Results From the Phase III MARIANNE Study

Edith A. Perez, Carlos Barrios, Wolfgang Eiermann, Masakazu Toi, Young-Hyuck Im, Pierfranco Conte, Miguel Martin, Tadeusz Pienkowski, Xavier Pivot, Howard Burris III, Jennifer A. Petersen, Sven Stanzel, Alexander Strasak, Monika Patre, and Paul Ellis

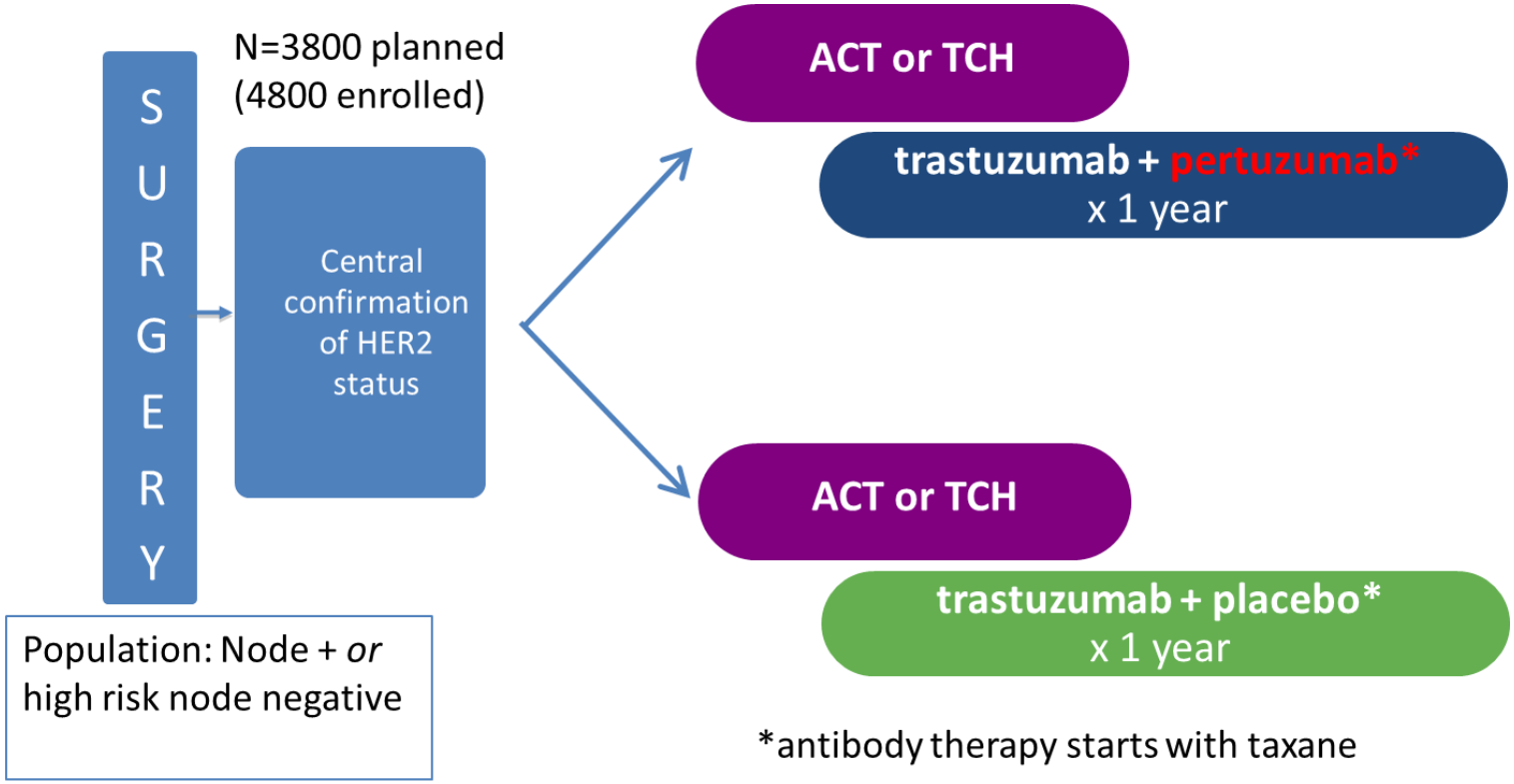
Baseline Risk Factors	Total No.	Trastuzumab + Taxane (n = 365) Median, Mo	T-DM1 (n = 367) Median, Mo	HR (97.5% CI)
All patients	732	13.7	14.1	0.94 (0.76 to 1.16)
World region*				
Asia	153	17.2	11.9	1.16 (0.72 to 1.85)
E. Europe	115	12.4	12.4	1.00 (0.59 to 1.69)
W. Europe, Canada, Australia/Pacific	271	14.0	15.9	0.89 (0.63 to 1.25)
United States	89	12.9	12.6	0.82 (0.45 to 1.49)
Others	104	10.5	14.6	0.75 (0.44 to 1.29)
Neoadjuvant/adjuvant therapy*				
Yes, trastuzumab or lapatanib	226	10.3	15.2	0.75 (0.52 to 1.09)
Yes, not trastuzumab or lapatanib	182	16.5	18.0	0.86 (0.56 to 1.32)
No	324	14.8	12.4	1.12 (0.82 to 1.54)
Visceral involvement*				
Yes	492	12.5	12.4	0.92 (0.72 to 1.18)
No	240	18.1	19.5	0.96 (0.64 to 1.42)
Age group, years				
< 65	609	13.2	13.3	0.96 (0.77 to 1.21)
≥ 65	123	14.6	19.5	0.82 (0.49 to 1.39)
Hormonal status				
ER+ and/or PR+	402	13.7	13.4	0.94 (0.71 to 1.25)
ER- and PR-	314	14.0	13.3	1.00 (0.73 to 1.37)
Prior taxane				
Yes	233	10.8	15.2	0.69 (0.48 to 0.99)
No	499	14.9	12.6	1.10 (0.85 to 1.41)





No. at risk:								
Trastuzumab + taxane	365	265	163	107	75	50	21	5
T-DM1	367	257	176	133	104	67	28	3
T-DM1 + pertuzumab	363	261	177	135	109	75	25	5	1

APHINITY



A=doxorubicin, E=epirubicin, C=cyclophosphamide, T=taxane (paclitaxel or docetaxel),
F=5-fluorouracil, H=trastuzumab, P=pertuzumab

Phase III APHINITY Study: Adjuvant Pertuzumab/Trastuzumab/Chemotherapy Increased Invasive Disease–Free Survival in HER2-Positive Breast Cancer

By The ASCO Post

Posted: 3/2/2017 10:55:14 AM

Last Updated: 3/2/2017 10:55:14 AM

EORTC 75111-10114

(Co-PI Hans Wildiers & Etienne Brain)

EORTC
The future of cancer therapy

80 pts HER2+ MBC
≥ 70 Years
(≥65/≥60y with co-morbidity)

® **1:1**

Pertuzumab + Trastuzumab

Pertuzumab + Trastuzumab + metronomic CT

→ **PD** → **T-DM1**

Primary endpoint
PFS at 6 months of PH or PHM

Secondary endpoints
OS, BCSS, toxicity, RR (RECIST v1.1), HRQoL, evolution of GA during treatment

Stratification: ER/PgR, previous HER2 treatment, G8

Pertuzumab	**840 mg loading dose, further 420 mg q3w iv**
Trastuzumab	**8 mg/kg loading dose, further 6 mg/kg q3w iv**
Chemotherapy	**Metronomic chemotherapy: cyclophosphamide 50 mg/d po continuously**
On progression	**Option to have T-DM1** *(3.6 mg/kg iv q3w)* **till progression**

Task Force HER2+

Laura Biganzoli (*Italy*), Etienne Brain *(France),* Philippe Caillet *(France),*
Karis Cheng *(Singapore),* Nienke de Glas *(The Netherlands),* Hans Wildiers *(Belgium)*

March 26th, 2015

Submitted

Cost!

VOLUME 34 · NUMBER 9 · MARCH 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Cost-Effectiveness of Pertuzumab in Human Epidermal Growth Factor Receptor 2–Positive Metastatic Breast Cancer

Ben Y. Durkee, Yushen Qian, Erqi L. Pollom, Martin T. King, Sara A. Dudley, Jenny L. Shaffer, Daniel T. Chang, Iris C. Gibbs, Jeremy D. Goldhaber-Fiebert, and Kathleen C. Horst

See accompanying editorial on page 889

Ben Y. Durkee, Yushen Qian, Erqi L. Pollom, Martin T. King, Sara A. Dudley, Jenny L. Shaffer, Daniel T. Chang, Iris C. Gibbs, and Kathleen C. Horst, Stanford University School of Medicine; and Jeremy D. Goldhaber-Fiebert, Stanford University, Stanford CA.

Published online ahead of print at www.jco.org on September 8, 2015.

Processed as a Rapid Communication manuscript.

Supported in part by the Henry S. Kaplan Research Fund, Department of Radiation Oncology, Stanford University (to B.Y.D.), and by Career Development Award No. K01AG037593-01A1, National Institute on Aging of the National Institutes of Health (to J.D.G.-F.).

Both B.Y.D. and Y.Q. contributed equally to this work and are co-first authors.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

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A B S T R A C T

Purpose

The Clinical Evaluation of Pertuzumab and Trastuzumab (CLEOPATRA) study showed a 15.7-month survival benefit with the addition of pertuzumab to docetaxel and trastuzumab (THP) as first-line treatment for patients with human epidermal growth factor receptor 2 (HER2) –overexpressing metastatic breast cancer. We performed a cost-effectiveness analysis to assess the value of adding pertuzumab.

Patient and Methods

We developed a decision-analytic Markov model to evaluate the cost effectiveness of docetaxel plus trastuzumab (TH) with or without pertuzumab in US patients with metastatic breast cancer. The model followed patients weekly over their remaining lifetimes. Health states included stable disease, progressing disease, hospice, and death. Transition probabilities were based on the CLEOPATRA study. Costs reflected the 2014 Medicare rates. Health state utilities were the same as those used in other recent cost-effectiveness studies of trastuzumab and pertuzumab. Outcomes included health benefits expressed as discounted quality-adjusted life-years (QALYs), costs in US dollars, and cost effectiveness expressed as an incremental cost-effectiveness ratio. One- and multiway deterministic and probabilistic sensitivity analyses explored the effects of specific assumptions.

Results

Modeled median survival was 39.4 months for TH and 56.9 months for THP. The addition of pertuzumab resulted in an additional 1.81 life-years gained, or 0.62 QALYs, at a cost of $472,668 per QALY gained. Deterministic sensitivity analysis showed that THP is unlikely to be cost effective even under the most favorable assumptions, and probabilistic sensitivity analysis predicted 0% chance of cost effectiveness at a willingness to pay of $100,000 per QALY gained.

Conclusion

THP in patients with metastatic HER2-positive breast cancer is unlikely to be cost effective in the United States.

EDITORIAL

Scientific Evidence and Financial Obligations to Ensure Access to Biosimilars for Cancer Treatment

Howard Bauchner, MD; Phil B. Fontanarosa, MD, MBA; Robert M. Golub, MD

A Value-Based Approach to Treatment of HER2-Positive Breast Cancer: Examining the Evidence

Nancy Nixon, MD, FRCPC, and Sunil Verma, MD, MSEd, FRCPC

OVERVIEW

Over the past decade, treatment of HER2-positive breast cancer has been revolutionized with the introduction of targeted therapies. Survival in both early and advanced HER2-positive breast cancer has improved significantly. With evidence for major clinical benefit, it is imperative that health systems evaluate new treatments to maximize the value of health expenditures. Physicians, funding agencies, and policy makers are tasked with analyzing available evidence to ensure that each individual patient receives the optimal treatment in a resource-challenged environment.

Original Investigation

January 3, 2017

Effect of a Proposed Trastuzumab Biosimilar Compared With Trastuzumab on Overall Response Rate in Patients With ERBB2 (HER2)-Positive Metastatic Breast Cancer

A Randomized Clinical Trial

Hope S. Rugo, MD[1]; Abhijit Barve, MD, PhD, MBA[2,3]; Cornelius F. Waller, MD[4]; et al

» Author Affiliations

JAMA. 2017;317(1):37-47. doi:10.1001/jama.2016.18305

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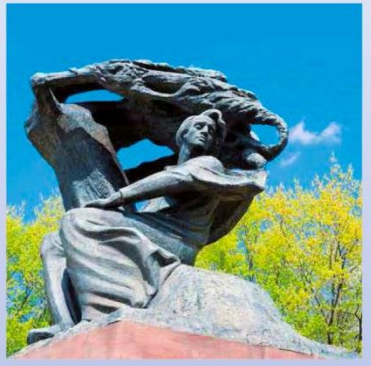


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