

Year ⁱⁿ Review

Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Novel Agents and Treatment Strategies for HER2-Positive Breast Cancer — Kimberly L Blackwell, MD

Select Publications

Chan A et al. Invasive disease-free survival benefit following neratinib as extended adjuvant therapy in centrally-confirmed HER2+ early-stage breast cancer: The ExteNET phase III randomized placebo-controlled trial. *Breast Cancer Symposium 2015;Abstract 117.*

Ellis PA et al. Phase III, randomized study of trastuzumab emtansine (T-DM1) ± pertuzumab (P) vs trastuzumab + taxane (HT) for first-line treatment of HER2-positive MBC: Primary results from the MARIANNE study. *Proc ASCO 2015;Abstract 507.*

Gianni L et al. Five-year analysis of the phase II NeoSphere trial evaluating four cycles of neoadjuvant docetaxel (D) and/or trastuzumab (T) and/or pertuzumab (P). *Proc ASCO 2015;Abstract 505.*

Harbeck N et al. Efficacy of 12-weeks of neoadjuvant TDM1 with or without endocrine therapy in HER2-positive hormone-receptor-positive early breast cancer: WSG-ADAPT HER2+/HR+ phase II trial. *Proc ASCO 2015;Abstract 506.*

Novel Agents and Treatment Strategies for HER2-Positive Breast Cancers



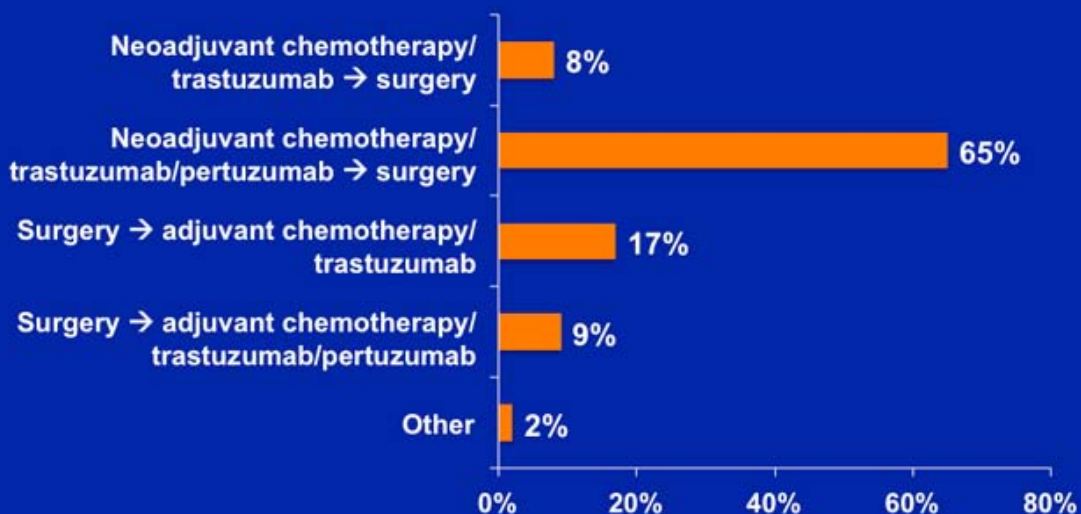
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Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Celgene Corporation, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche Laboratories Inc, Sandoz
Contracted Research	Celgene Corporation, Genentech BioOncology, Pfizer Inc

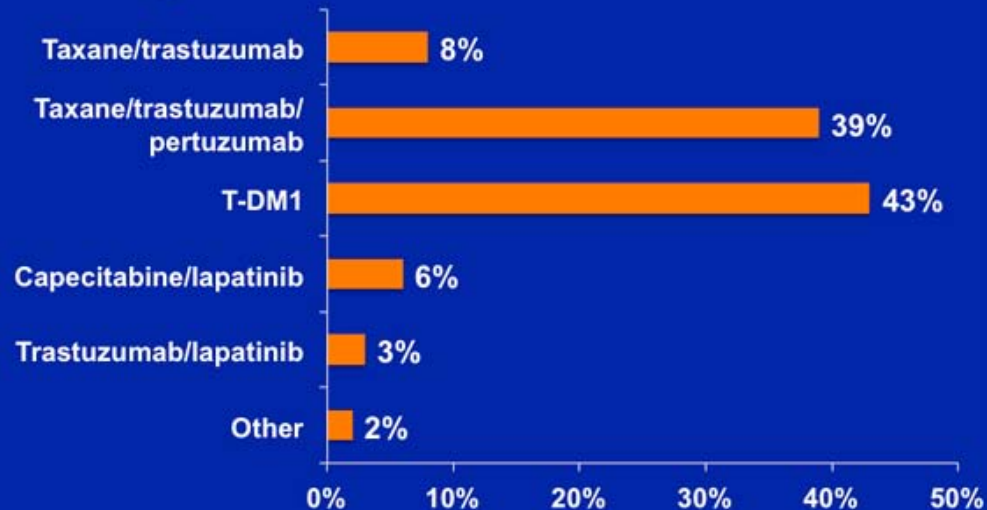
AUDIENCE POLL

A 60-year-old woman is diagnosed by core biopsy with a 2.2-cm, ER-negative/HER2-positive IDC and clinically negative axilla. The patient is a candidate for breast conservation. What treatment approach would you most likely recommend?



AUDIENCE POLL

A 60-year-old woman with a 6-cm, ER-negative/HER2-positive tumor and palpable nodes receives TCH/pertuzumab with good response but residual disease at surgery. The patient completes 1 year of trastuzumab and 6 months later develops metastatic disease. What would you most likely recommend?

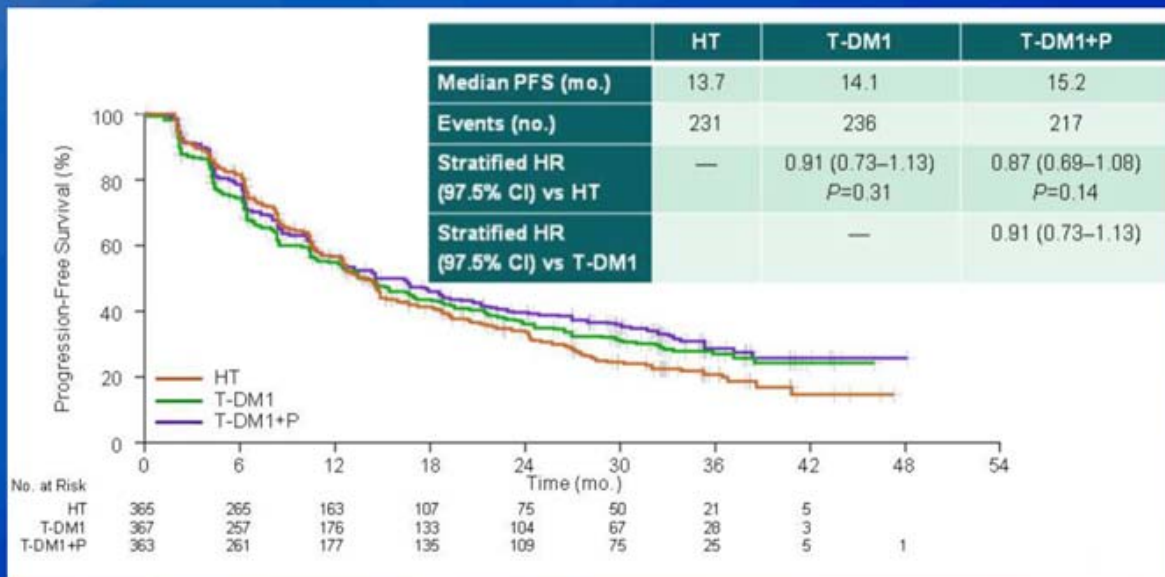


Phase III, Randomized Study of Trastuzumab Emtansine ± Pertuzumab vs Trastuzumab + Taxane for First-line Treatment of HER2-positive MBC: Primary Results from the MARIANNE Study

Ellis PA et al.

Proc ASCO 2015; Abstract 507

MARIANNE: PFS (Primary Endpoint) and OS



At time of interim analysis, median OS had not been reached for any of the treatment arms.

Ellis PA et al. *Proc ASCO* 2015;Abstract 507.

Conclusions

Critical finding(s): In first-line HER2+ MBC, there were no efficacy differences between taxane + trastuzumab, T-DM1 alone and T-DM1 + pertuzumab. T-DM1 was better tolerated than taxane + trastuzumab.

Clinical implication(s): Taxane + pertuzumab + trastuzumab remains the standard therapy for first-line HER2+ MBC.

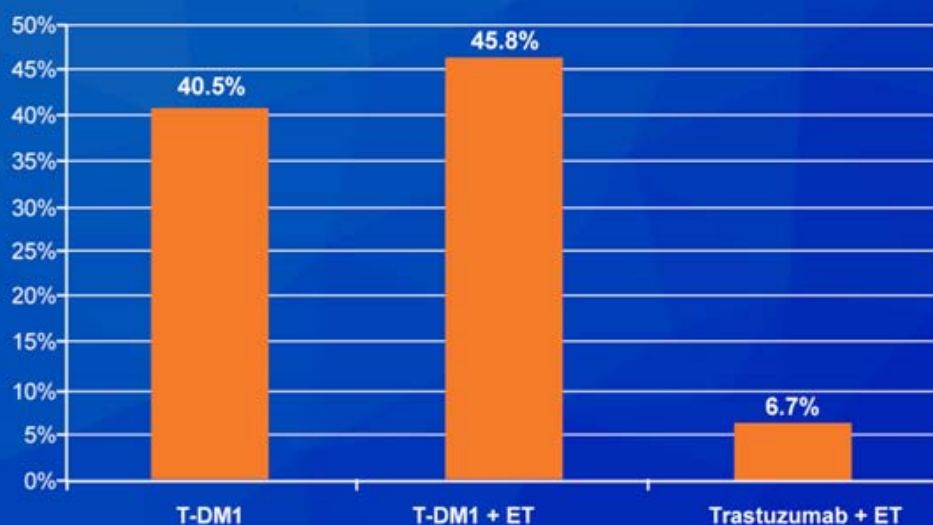
Research relevance: Trials are already under way to evaluate these combinations in the adjuvant setting.

Efficacy of 12-Weeks of Neoadjuvant TDM1 with or without Endocrine Therapy in HER2-Positive Hormone-Receptor-Positive Early Breast Cancer: WSG-ADAPT HER2+/HR+ Phase II Trial

Harbeck N et al.

Proc ASCO 2015; Abstract 506

ADAPT HER2+/HR+: pCR (No invasive tumor in breast and nodes)



pCR rates were substantially higher in T-DM1-containing arms ($p < 0.001$ for T-DM1 or T-DM1+ET versus Trastuzumab+ET)

Harbeck N et al. *Proc ASCO 2015; Abstract 506.*

Conclusions

Critical finding(s): T-DM1 was extremely active in the neoadjuvant treatment of ER+, HER2+ breast cancer. The addition of endocrine therapy to T-DM1 did not result in a higher pCR.

Clinical implication(s): T-DM1 is active and well tolerated.

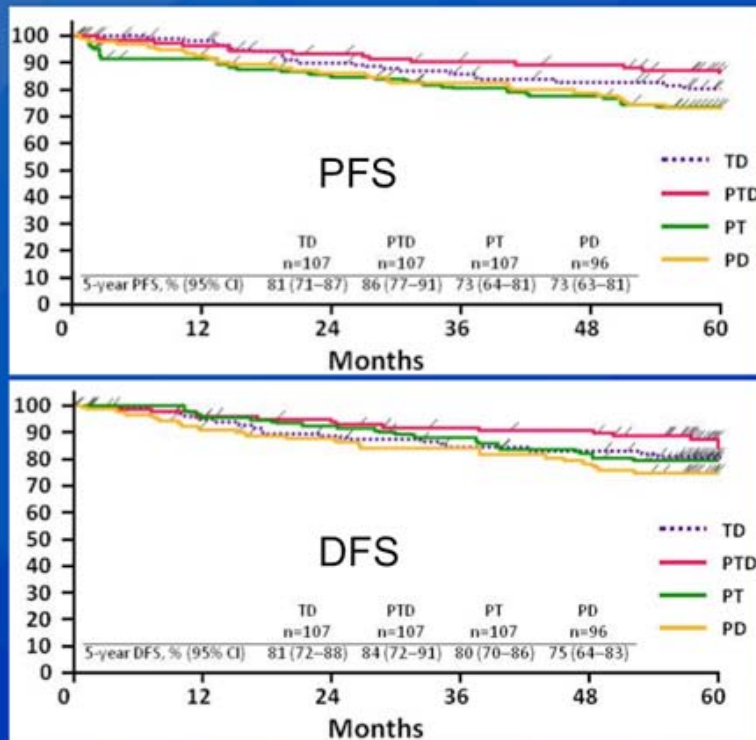
Research relevance: Clinical trials evaluating the use of T-DM1 versus taxane + trastuzumab (standard) are well supported by this trial.

Five-Year Analysis of the Phase II NeoSphere Trial Evaluating Four Cycles of Neoadjuvant Docetaxel (D) and/or Trastuzumab (T) and/or Pertuzumab (P)

Gianni L et al.

Proc ASCO 2015; Abstract 505

Progression-Free and Disease-Free Survival (ITT)



5-year PFS

PTD: 86%

TD: 81%

HR = 0.69

5-year DFS

PTD: 84%

TD: 81%

HR = 0.60

Gianni L et al. *Proc ASCO* 2015; Abstract 505.

Conclusions

Critical finding(s): Taxane + trastuzumab + pertuzumab is very active in the neoadjuvant setting — this did not result in statistically significant differences in DFS.

Clinical implication(s): Taxane + trastuzumab + pertuzumab remains an approved choice for the neoadjuvant treatment of HER2+ breast cancer.

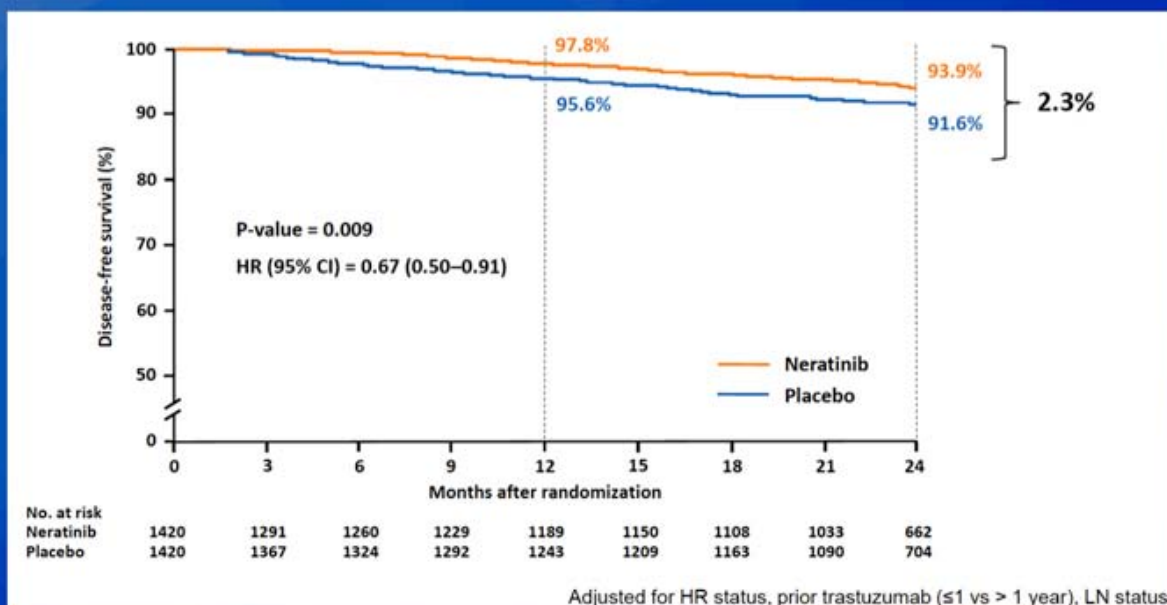
Research relevance: The pending results of APHINITY will be important in helping to determine the impact of pertuzumab on the treatment of HER2+ early-stage breast cancer.

Invasive Disease-Free Survival Benefit Following Neratinib as Extended Adjuvant Therapy in Centrally-Confirmed HER2+ Early-Stage Breast Cancer: The ExteNET Phase III Randomized Placebo-Controlled Trial

Chan A et al.

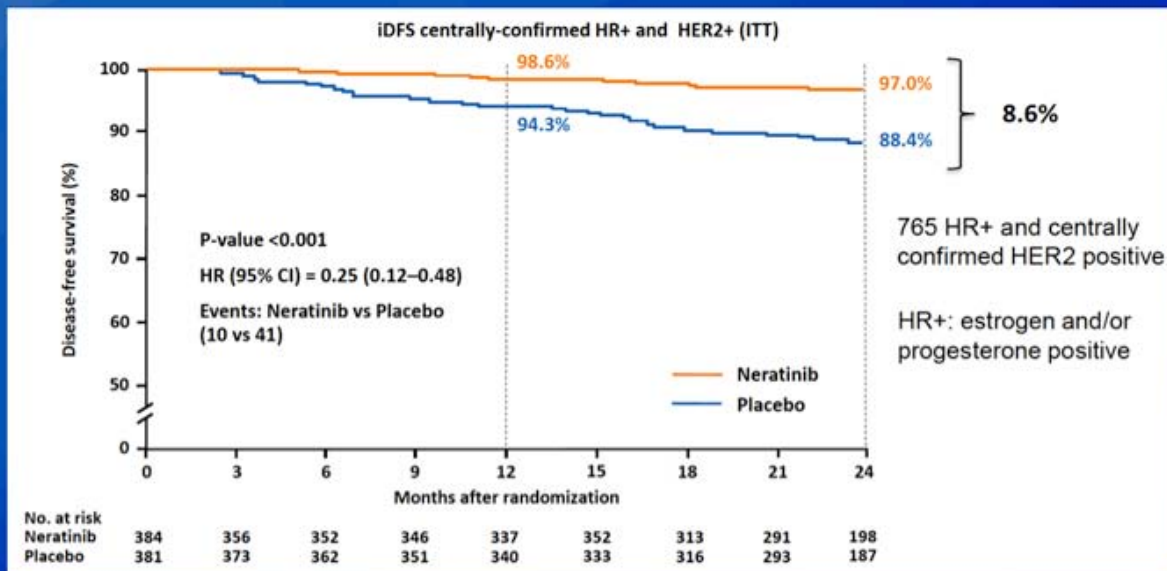
Breast Cancer Symposium 2015;Abstract 117.

ExteNET: Invasive DFS (ITT; Primary Endpoint)



Chan A et al. Breast Cancer Symposium 2015;Abstract 117.

ExteNET: Centrally-Confirmed Invasive DFS (Primary Endpoint) in HER2-Positive and HR-Positive



Chan A et al. Breast Cancer Symposium 2015;Abstract 117.

Conclusions

Critical finding(s): The addition of neratinib for 1 year after a year of trastuzumab results in an improvement in DFS at 2 years. This was most pronounced in the ER+ subgroup, and the majority of recurrences were local-regional ones.

Clinical implication(s): None at this point; additional follow-up is necessary.

Research relevance: Longer follow-up of this very large study population will help define the role of extended HER2-targeted therapy with neratinib.