

Clinical Updates From San Antonio

HER2+ and HER2-Low Breast Cancer

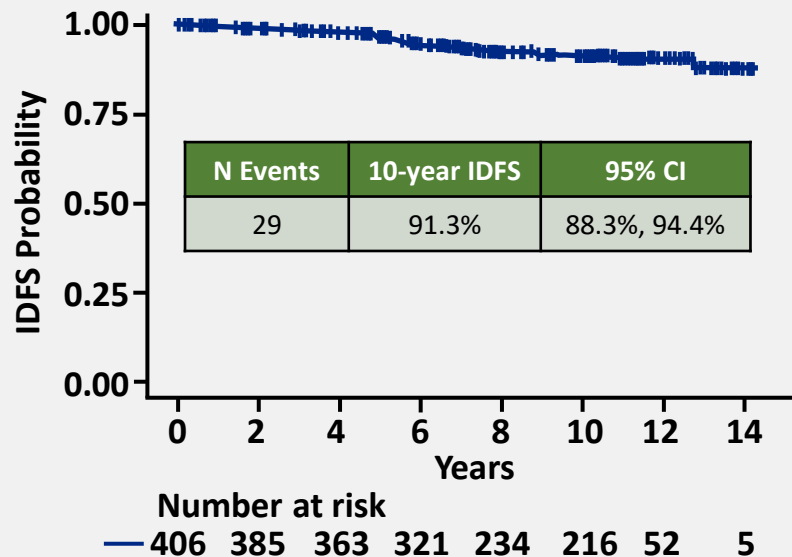
This activity is provided by Integrity Continuing Education, Inc.

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This activity is supported by an educational grant from Lilly.

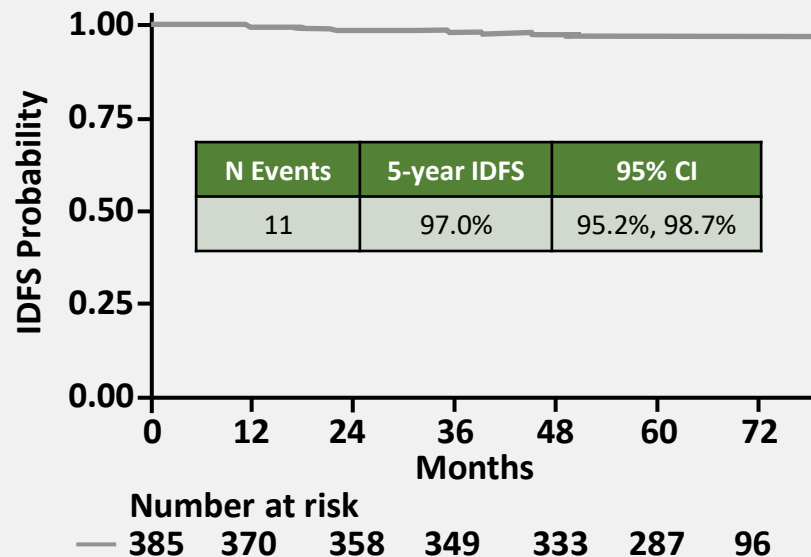
Adjuvant Therapy For HER2+ Breast Cancer

IDFS (APT*)



10-year OS: 94.3% (95% CI 91.8%, 96.8%)

IDFS With T-DM1 (ATEMPT[†])



5-year OS: 97.8% (95% CI 96.3%, 99.3%)

Weekly paclitaxel + trastuzumab for 12 weeks, followed by trastuzumab for 9 months; [†]T-DM1 vs TH regimen.

CI, confidence interval; IDFS, invasive disease-free survival; OS, overall survival; T-DM1, trastuzumab emtansine.

Tarantino P, et al. SABCs 2022. Abstract PD18-01; Tolaney SM, et al. SABCs 2022. Abstract PD18-02.

Phase 3 Outcomes With Second- and Subsequent-Line Anti-HER2 ADCs for Recurrent or Metastatic Breast Cancer

Trial	DESTINY-Breast03	DESTINY-Breast02	EMILIA
Intervention	T-DXd vs T-DM1	T-DXd vs capecitabine + trastuzumab or lapatinib	T-DM1 vs lapatinib + capecitabine
Population	HER2+ mBC previously treated with trastuzumab and a taxane N=524 (1:1)	HER2+ unresectable or metastatic BC previously treated with T-DM1 N=608 (2:1)	HER2+ aBC previously treated with trastuzumab and a taxane N=991 (1:1)
Median follow-up, months	28.4 vs 26.5	21.5 vs 18.6	24.1
mPFS, months (95% CI)	29.1 (23.7, NE) vs 7.2 (6.8, 8.3)* HR 0.30 (0.24, 0.38); <i>P</i> <.000001	17.8 (14.3, 20.8) vs 6.9 (5.5, 8.4)* HR 0.36 (0.28, 0.45); <i>P</i> <.000001	9.6 vs 6.4 [†] HR 0.65 (0.55, 0.77); <i>P</i> <.001
mOS, months (95% CI)	NR (40.5, NE) vs NR (34.0, NE) HR 0.64 (0.47, 0.87); <i>P</i> =.0037	39.2 (32.7, NE) vs 26.5 (21.0, NE) HR 0.66 (0.50, 0.86); <i>P</i> =.0021	29.9 (26.3, 34.1) vs 25.9 (22.7, 28.3) [†] HR 0.75 (0.64, 0.88); <i>P</i> <.0037
ORR, %	78.5 vs 34.2	69.7 vs 29.2	43.6 vs 30.8
AEs grade ≥3 (≥5%), %	Neutrophil count decreased (16 vs 3.1), anemia (9.3 vs 6.5), platelet count decreased (7.8 vs 19.9), nausea (7 vs 0.4), white blood cell count decreased (6.2 vs 0.8), fatigue (5.8, 0.8), AST increased (0.8 vs 5.4)	Neutrophil count decreased (10.6 vs 2.1), anemia (7.9 vs 3.1), neutropenia (7.7 vs 2.1), nausea (6.7 vs 2.6)	Thrombocytopenia (14 vs 0.41)

*Primary endpoint; [†]Copriprimary endpoint.

aBC, advanced breast cancer; AE, adverse event; AST, aspartate aminotransferase; HR, hazards ratio; mBC, metastatic breast cancer; mOS, median overall survival; mPFS, median progression-free survival; NE, not evaluable; NR, not reached; ORR, objective response rate; T-DXd, trastuzumab deruxtecan.

Cortes J, et al. *N Engl J Med*. 2022;386(12):1143-1154; Diéras V, et al. *Lancet Oncol*. 2017;18(6):732-742; Hurvitz SA, et al. SABCs 2022. Abstract GS2-02; Hurvitz SA, et al. *Lancet*. 2022; Krop I, et al. SABCs 2022. Abstract GS2-01; Verma S, et al. *N Engl J Med*. 2012;367(19):1783-1791.

GS2-02, Trastuzumab Deruxtecan Versus Trastuzumab Emtansine in Patients With HER2-Positive Metastatic Breast Cancer: Updated Survival Results of the Randomized, Phase 3 Study DESTINY-Breast03

Patients (N=524)

- Confirmed HER2+ unresectable or metastatic BC
- Prior trastuzumab and taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of completing adjuvant therapy

Randomization

1:1

Stratification

- History of visceral disease
- Hormone receptor status
- Prior pertuzumab

Primary Endpoint

- PFS

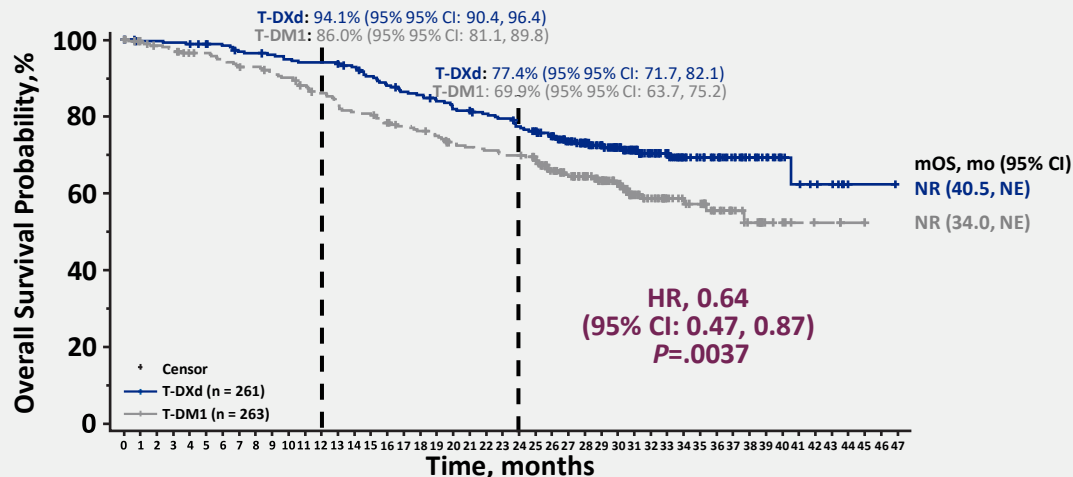
Secondary Endpoints

- OS
- ORR, DOR, Safety

T-DXd
5.4 mg/kg Q3W

T-DM1
3.6 mg/kg Q3W

Hurvitz SA, Hegg R, Chung W-P, Im S-A, Jacot W, Ganju V, Chiu JWY, Xu B, Hamilton E, Madhusudan S, Iwata H, Altintas S, Henning J-W, Curigliano G, Pérez-García JM, Egorov A, Liu Y, Cathcart J, Ashfaq S, Cortés J



DOR, duration of response; Q3W, every 3 weeks.

Cortes J, et al. *N Engl J Med*. 2022;386(12):1143-1154; Hurvitz SA, et al. SABCs 2022. Abstract GS2-02; Hurvitz SA, et al. *Lancet*. 2022.

P1-11-01, Trastuzumab Deruxtecan vs Treatment of Physician's Choice in Patients With HER2-Low Unresectable and/or Metastatic Breast Cancer: Subgroup Analyses From DESTINY-Breast04

Patients (N=557)

- HER2-low mBC
- HR+ n=494
- HR- n=63
- IHC 1+ or IHC 2+/ISH-

Randomization
2:1

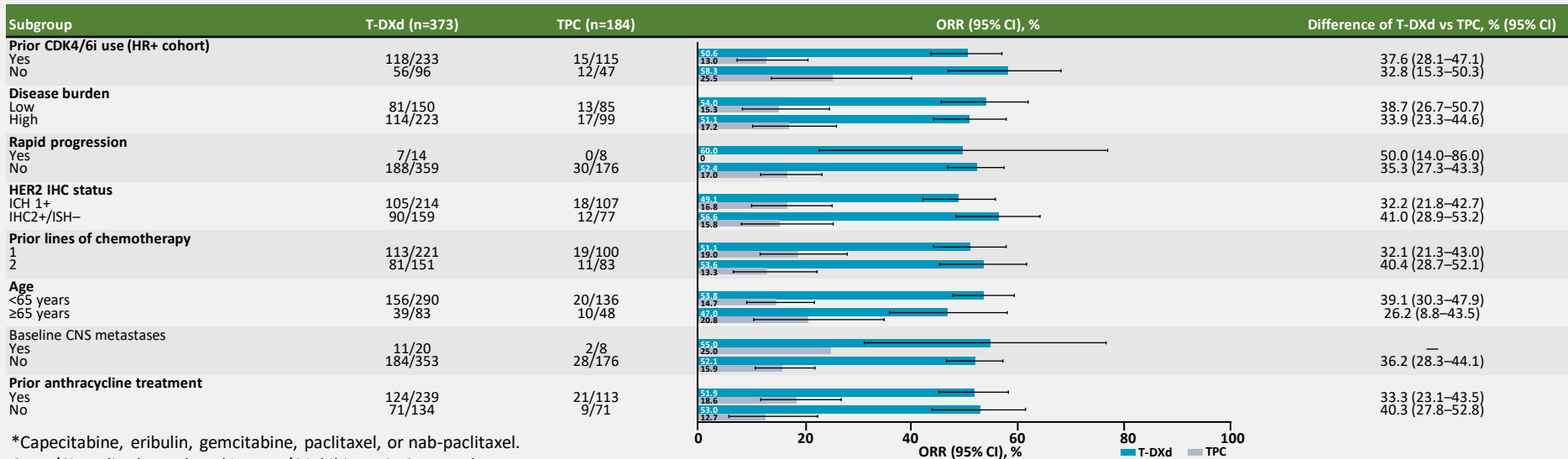
T-DXd mg/kg Q3W

(n=373: HR+ n=331; HR- n=42)

Physicians' choice*

(n=184: HR+ n=163; HR- n=21)

Harbeck N, Modi S, Jacot W, Yamashita T, Sohn JH, Vidal M, Tsurutani J, Ueno NT, Prat A, Niikura N, Xu B, Rugo HS, Papazisis K, Cortés J, Krop I, Gambhire D, Yung L, Wang Y, Singh J, Cameron D



*Capecitabine, eribulin, gemcitabine, paclitaxel, or nab-paclitaxel.

CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CNS, central nervous system;

HR+, hormone receptor positive; HR-, hormone receptor negative; IHC, immunohistochemistry; ISH, in situ hybridization; TPC, treatment of physician's choice.

Harbeck N, et al. SABCS 2022. Abstract P1-11-01; Modi S, et al. *N Engl J Med.* 2022;387(1):9-20.