HER2-LOW:
THINK DIFFERENT

Explore >>>

Daiichi-Sankyo | AstraZeneca

ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

HER2-LOW:

THINK DIFFERENT

- The Newly Identified Patients
- Primary Endpoint
- Exploratory Endpoints
- Study Design
- Overall Survival
- Summary

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HER2-LOW:

THINK DIFFERENT

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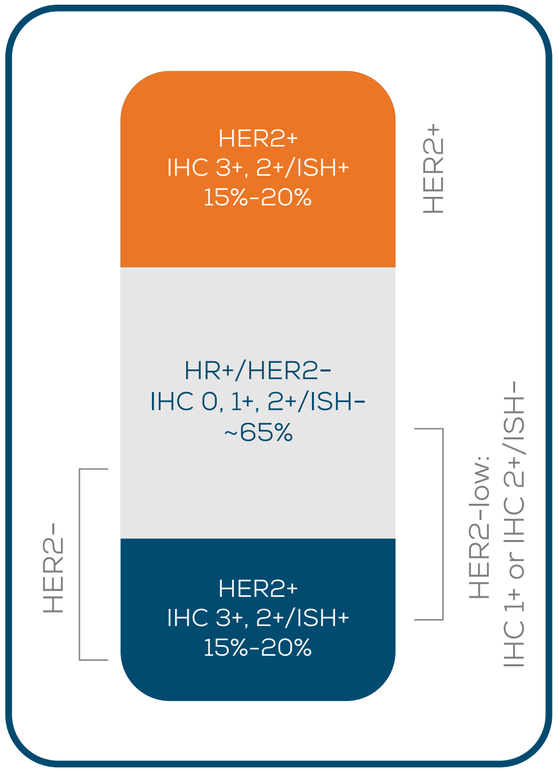
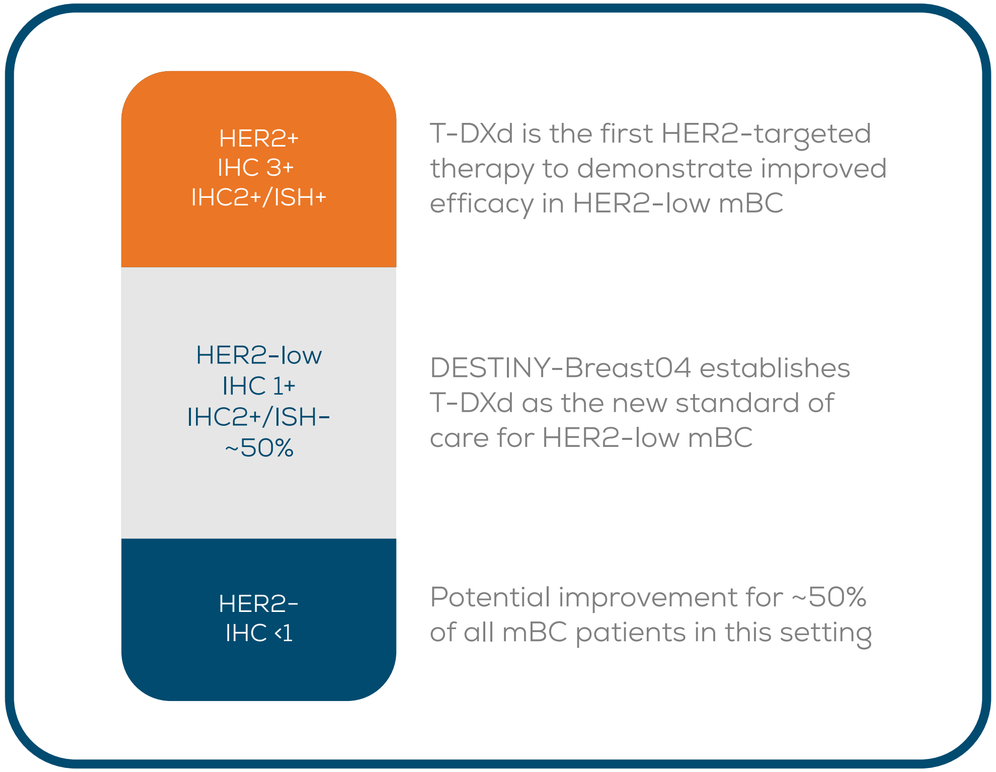
T-DXd treatment showed unprecedented improvement in efficacy for patients with HER2-low mBC

Current mBC Paradigm[1,2]



The New mBC Paradigm



T-DXd is the first HER2-targeted therapy to demonstrate improved efficacy in HER2-low mBC

DESTINY-Breast04 establishes T-DXd as the new standard of care for HER2-low mBC

Potential improvement for ~50% of all mBC patients in this setting

HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice. 1. Schettini F, et al. NPJ Breast Cancer. 2021;7(1):1. 2. Tarantino P, et al. J Clin Oncol. 2020;38(17):1951-1962.

DESTINY-Breast04: First Randomized Phase 3 Study of T-DXd for HER2-low mBC

An open-label, multicenter study (NCT03734029)

Patientsa

HER2-low (IHC 1+ vs IHC 2+/ISH−), unresectable, and/or mBC treated with 1-2 prior lines of chemotherapy in the metastatic setting
HR+ disease considered endocrine refractory

R
2:1

T-DXd
5.4 mg/kg Q3W
(n = 373)

HR+ ≈ 480
HR− ≈ 60

TPC
Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxelc
(n = 184)

Primary endpoint
- PFS by BICR (HR+)

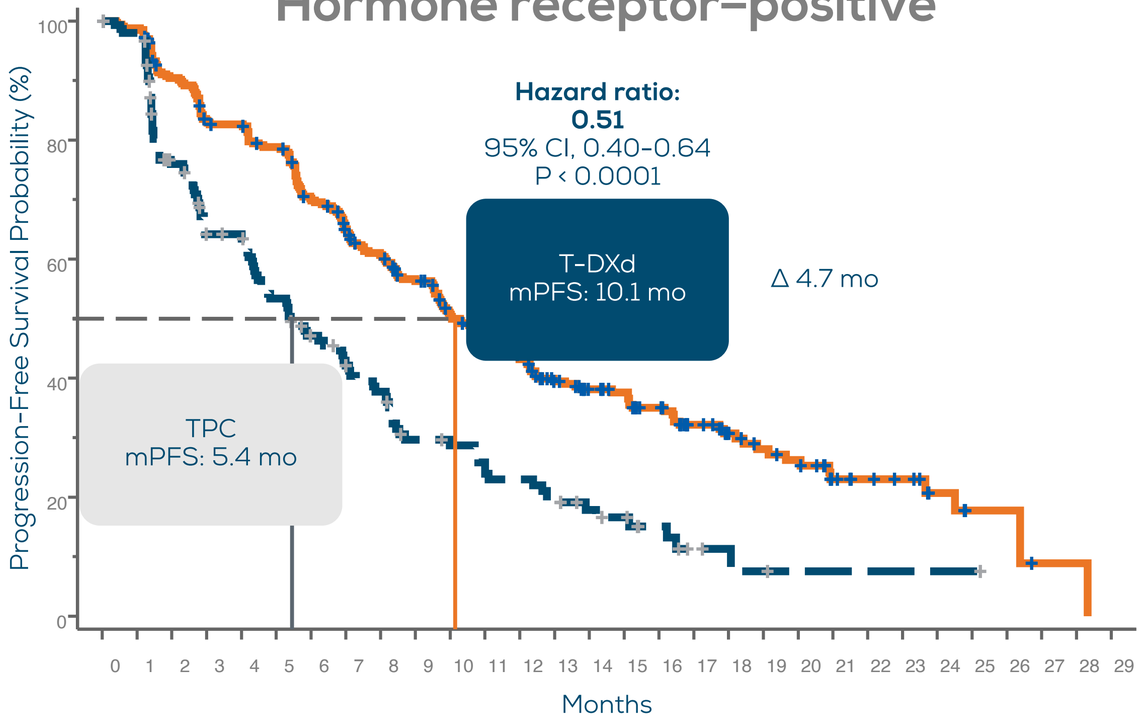
Key secondary endpointsb
- PFS by BICR (all patients)
- OS (HR+ and all patients)

Stratification factors
- Centrally assessed HER2 statusd (IHC 1+ vs IHC 2+/ISH−)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR−

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CDK, cyclin-dependent kinase; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
aIf patients had HR+ mBC, prior endocrine therapy was required. bOther secondary endpoints included ORR (BICR and investigator), DOR (BICR), PFS (investigator), and safety; efficacy in the HR− cohort was an exploratory endpoint. cTPC was administered accordingly to the label. dPerformed on adequate archived or recent tumor biopsy per ASCO/CAP guidelines using the VENTANA HER2/neu (4B5) investigational use only [IUO] Assay system.

PFS in HR+ and All Patients

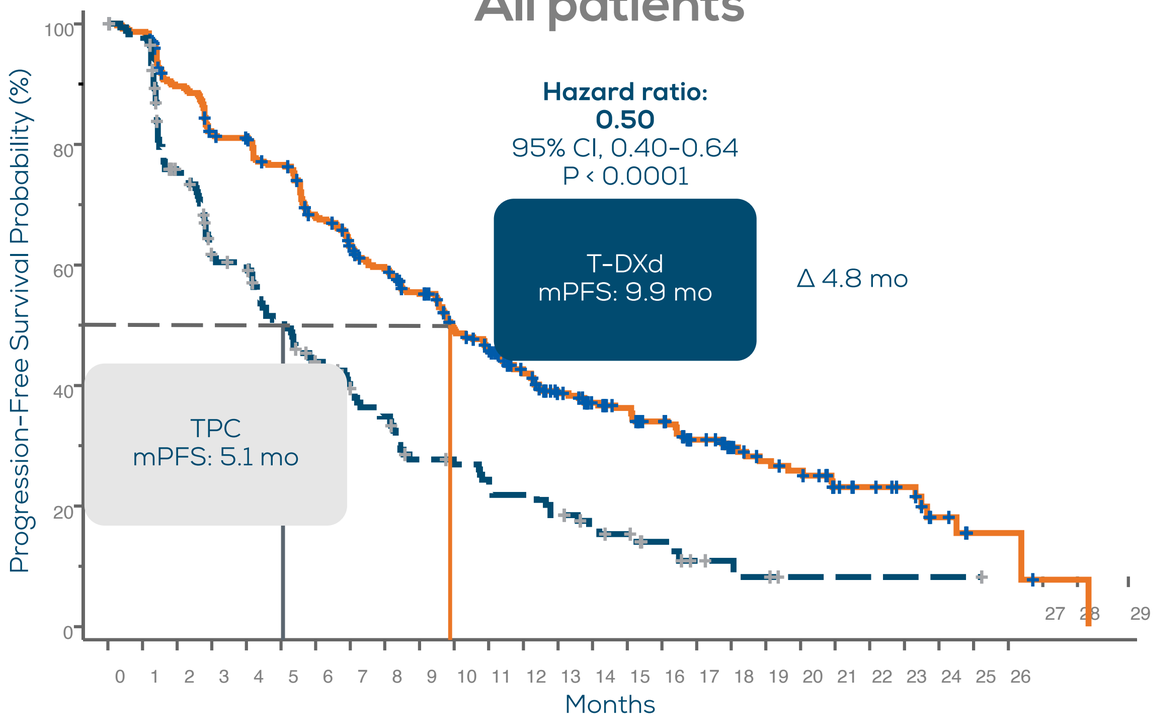
Hormone receptor–positive



No. at Risk

T-DXd (n = 331):	331	324	290	265	262	248	218	198	182	165	142	128	107	89	78	73	64	48	37	31	28	17	14	12	7	4	4	1	1	0
TPC (n = 163):	163	146	105	85	84	69	57	48	43	32	30	27	24	20	14	12	8	4	3	2	1	1	1	1	1	1	0			

All patients



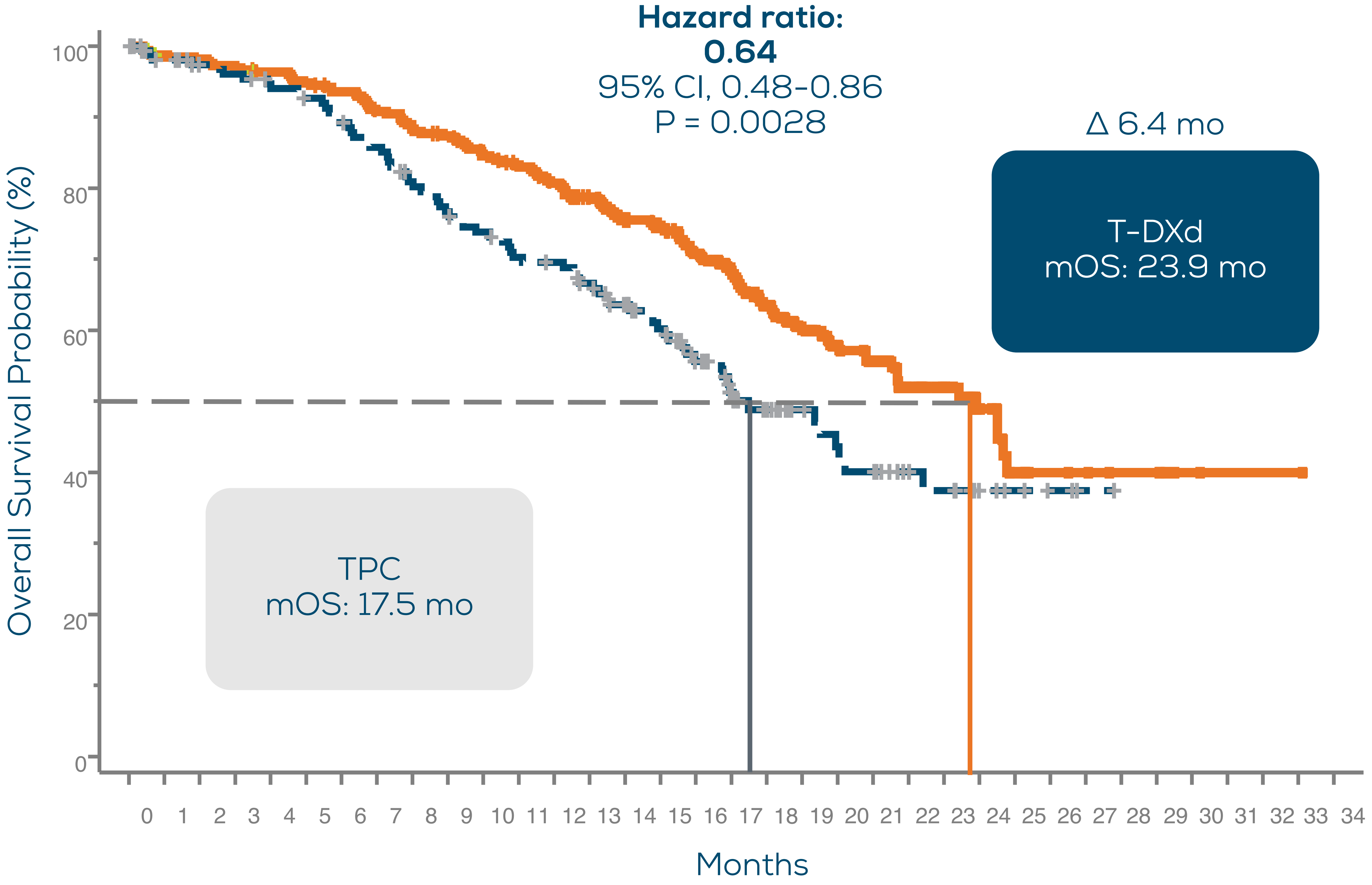
No. at Risk

T-DXd (n = 373):	373	365	325	295	290	272	238	217	201	183	156	142	118	100	88	81	71	53	42	35	32	21	18	15	8	4	4	1	1	0
TPC (n = 184):	184	166	119	93	90	73	60	51	45	34	32	29	26	22	15	13	9	5	4	3	1	1	1	1	1	1	0			

PFS by blinded independent central review.
HR, hormone receptor; mPFS, median progression-free survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

OS in HR+ and All Patients

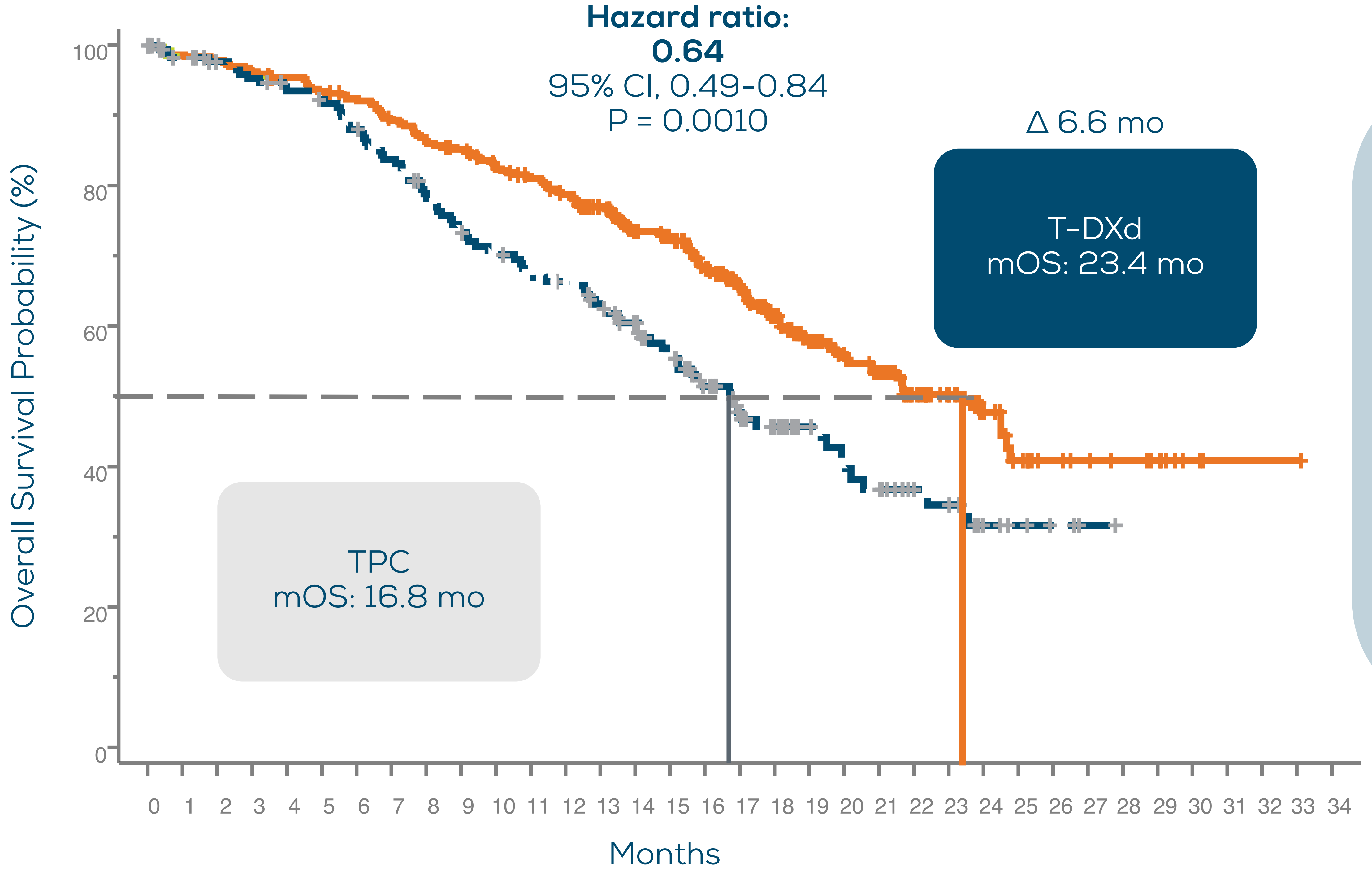
Hormone receptor–positive



No. at Risk

T-DXd (n = 331):	331	325	323	319	314	309	303	293	285	280	268	260	250	228	199	190	168	144	116	95	81	70	51	40	26	14	9	8	6	6	2	1	1	1	0
TPC (n = 163):	163	151	145	143	139	135	130	124	115	109	104	98	96	89	80	71	56	45	37	29	25	23	16	14	7	5	3	1	0						

All patients



No. at Risk

T-DXd (n = 331):	373	366	363	357	351	344	338	326	315	309	296	287	276	254	223	214	188	158	129	104	90	78	59	48	32	20	14	12	10	8	3	1	1	1	0
TPC (n = 163):	184	171	165	161	157	153	146	138	128	120	114	108	105	97	88	77	61	50	42	32	28	25	18	16	7	5	3	1	0						

HR, hormone receptor; mOS, median overall survival; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

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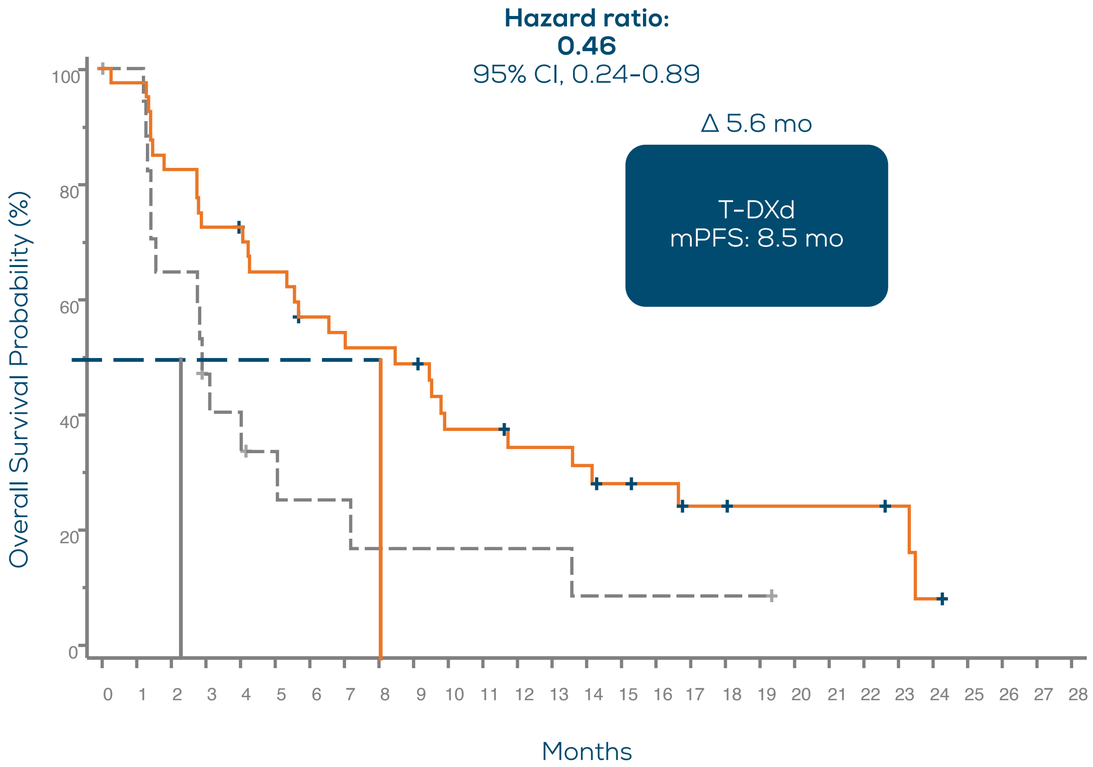
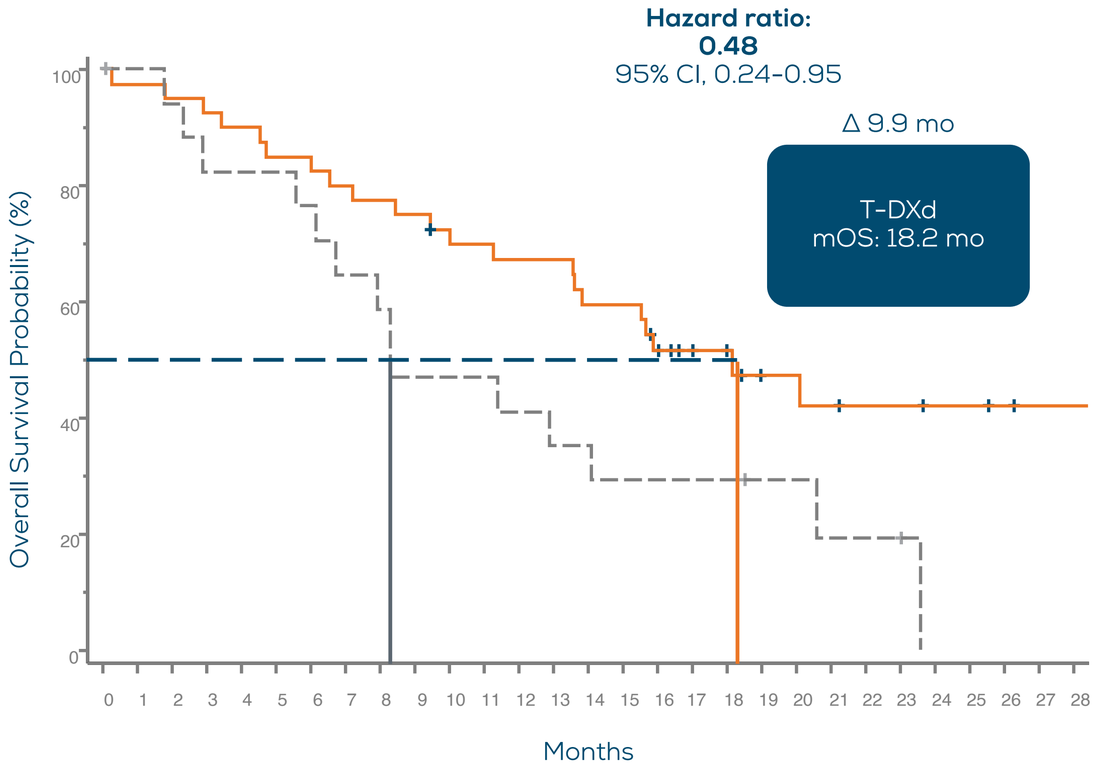
Hormone receptor–negative



No. at Risk

T-DXd (n = 331):	40	39	33	29	28	25	21	20	19	18	13	13	11	11	10	8	7	5	5	4	4	4	4	3	1	0
TPC (n = 163):	18	17	11	7	6	4	3	3	2	2	2	2	2	2	1	1	1	1	1	1	0					

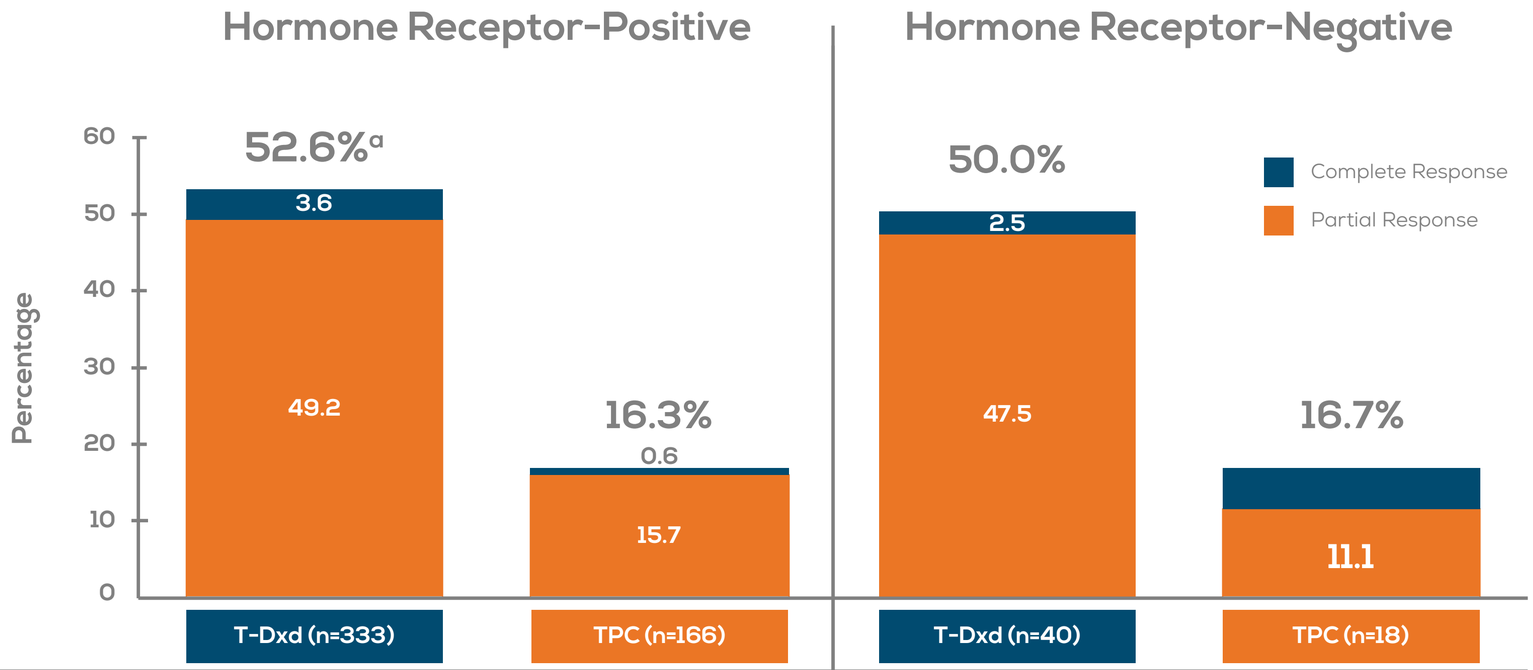


No. at Risk

T-DXd (n = 331):	40	39	38	37	36	34	34	32	31	30	28	27	26	26	23	23	19	14	13	9	9	8	7	7	6	6	5	4	4
TPC (n = 163):	18	17	16	14	14	14	3	11	10	8	8	8	7	6	6	5	5	5	5	3	3	2	2	2	0				

HR, hormone receptor; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice. For efficacy in the hormone receptor–negative cohort, hormone receptor status is based on data from the electronic data capture corrected for misstratification.

Confirmed Objective Response Rate

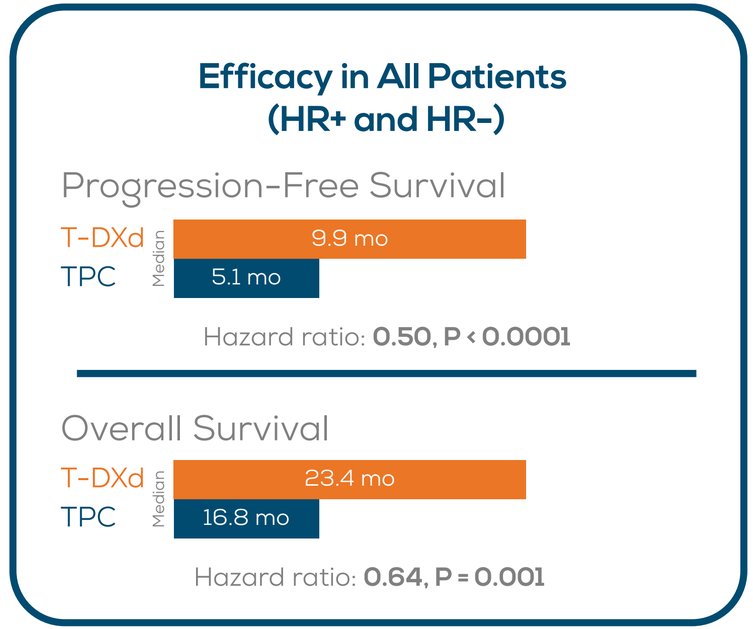


Progressive Disease, %	7.8	21.1	12.5	33.3
Not Evaluable, %	4.2	12.7	7.5	5.6
Clinical Benefit Rate,[b] %	71.2	34.3	62.5	27.8
Duration of Rresponse, Months	10.7	6.8	8.6	4.9

Hormone receptor status is based on data from the electronic data capture corrected for misstratification
ORR, objective respone rate: T-Dxd, Trastuzmab Deruxtecan: TPC, Treatment of Physcivian's Choice.
*The respone of 1 patient was not confirmed. [b]Clinical benefit rate is defined as the sum of complete response rate, partial response rate, and more than 6 months' stable disease rate, based on blinded independent cntral review.

DESTINY-Breast04 establishes T-DXd as the new standard of care in HER2-low, HR+/HR- mBC

- T-DXd is the first HER2-targeted therapy to demonstrate unprecedented statistically significant and clinically meaningful improvement in PFS and OS versus TPC.
- Similar magnitude of benefit across all subgroups, including HER2 IHC status and prior CDK4/6i use.
- Safety is consistent with the known safety profile and showed an overall positive benefit-risk.
- DESTINY-Breast04 establishes HER2-low (IHC 1+, IHC 2+/ISH-) mBC as a new targetable patient population, with T-DXd as a new standard of care.



CDK4/6i, cyclin-dependent kinase 4/6 inhibitors; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.