

The evolving management of HER2 low and ultralow breast cancer

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First-line cytotoxic treatment for endocrine-refractory HER2 low/ultralow metastatic breast cancer

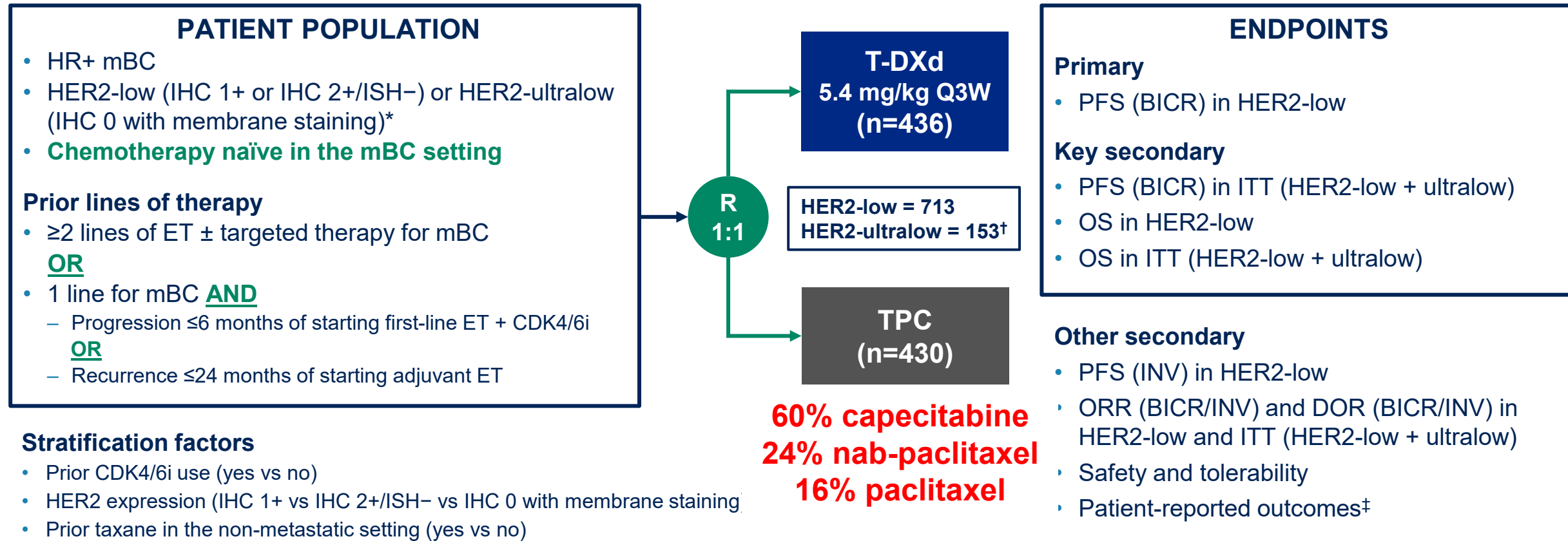
January 27, 2025:

**FDA approves fam-trastuzumab deruxtecan-nxki
for unresectable or metastatic HR-positive,
HER2-low or HER2-ultralow breast cancer**

- For HR+ metastatic breast cancer that is:
 - **HER2 low** or **HER2 ultralow (0+)**
 - Progressed following one or more lines of endocrine therapy

Study design

DESTINY-Breast06: a Phase 3, randomized, multicenter, open-label study (NCT04494425)



*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization. HER2-ultralow was defined as faint, partial membrane staining in ≤10% of tumor cells (also known as IHC >0<1+); [†]HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n=152 as determined per central laboratory testing data); [‡]to be presented separately BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor-positive; IHC, immunohistochemistry; INV, investigator assessed; IRT, interactive response technology; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice NCT04494425. Updated. April 12, 2024. Available from: <https://clinicaltrials.gov/study/NCT04494425> (Accessed May 13, 2024)

Modified from G Curigliano et al ASCO 2024

Destiny-Breast06: Important differences from prior trials

- HR+ patients only (no TNBC)
- First-line chemotherapy population (all endocrine pre-treated)
- Incorporation of HER2 low **AND ultralow** (IHC 0 with 1-10% staining)

Targeting 'low' and 'ultralow' HER2-expressing tumors in mBC

HER2 IHC categories within HR+, HER2-negative (HER2-) mBC (per ASCO/CAP¹)

DESTINY-Breast06
patient population:

~85% of HR+, HER2- mBC

HER2-low

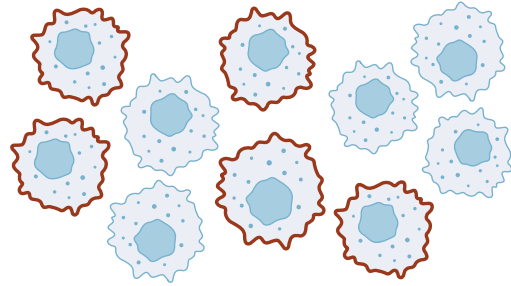
~60–65%^{2,3}

HER2-ultralow

~20–25%²⁻⁴

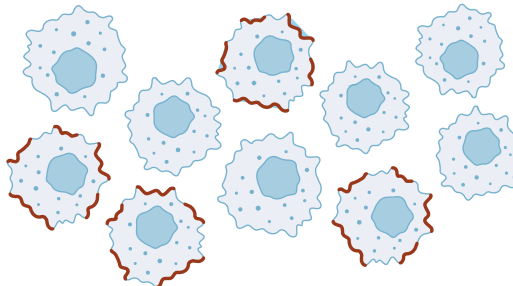
HER2 null

~10-20%



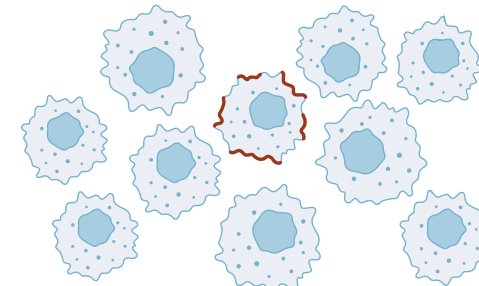
IHC 2+/ISH-

Weak-to-moderate complete membrane staining in >10% tumor cells



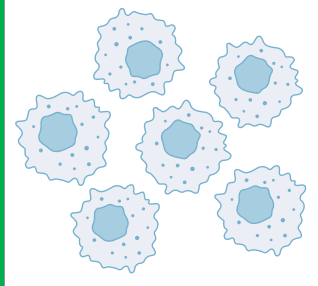
IHC 1+

Faint, incomplete membrane staining in >10% tumor cells



IHC 0

Faint, incomplete membrane staining in ≤10% tumor cells



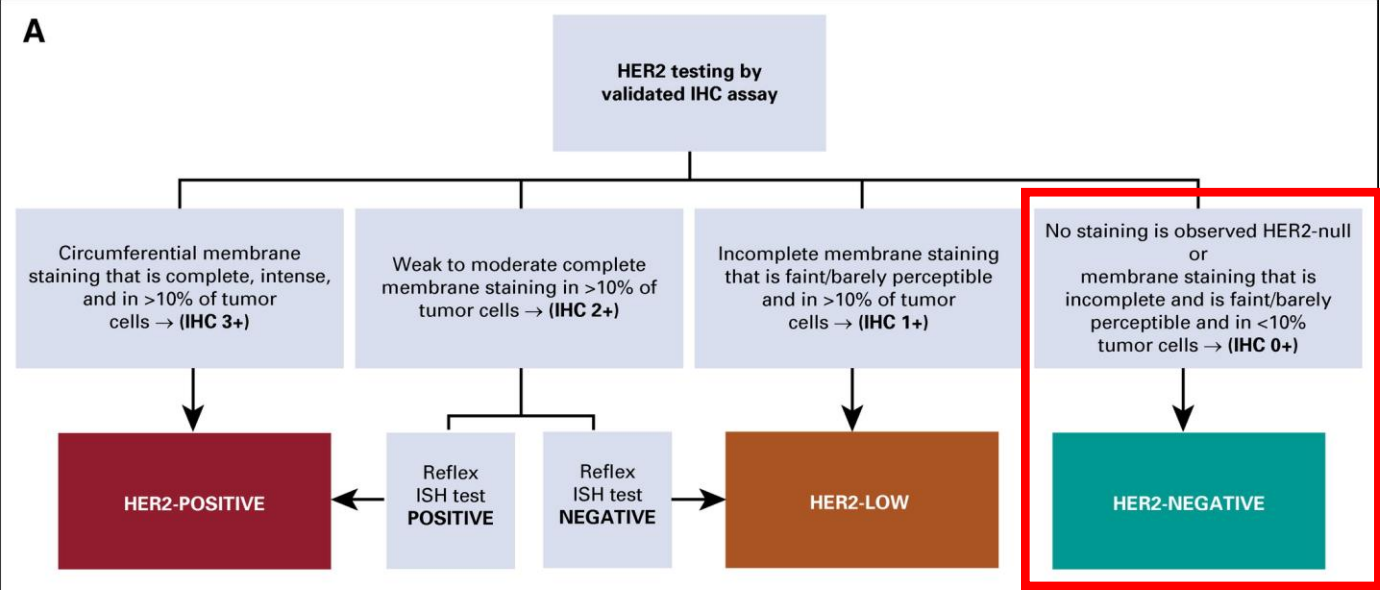
Absent / no observable membrane staining

ASCO/CAP, American Society of Clinical Oncology / College of American Pathologists; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor-positive; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan

Images adapted from Venetis K, et al. *Front Mol Biosci.* 2022;9:834651. CC BY 4.0 license available from: <https://creativecommons.org/licenses/by/4.0/>

1. Wolff AC, et al. *J Clin Oncol.* 2023;41:3867–3872; 2. Denkert C, et al. *Lancet Oncol.* 2021;22:1151–1161; 3. Chen Z, et al. *Breast Cancer Res Treat.* 2023;202:313–323; 4. Mehta S, et al. *J Clin Oncol.* 2024;42(Suppl. 16):Abstract e13156

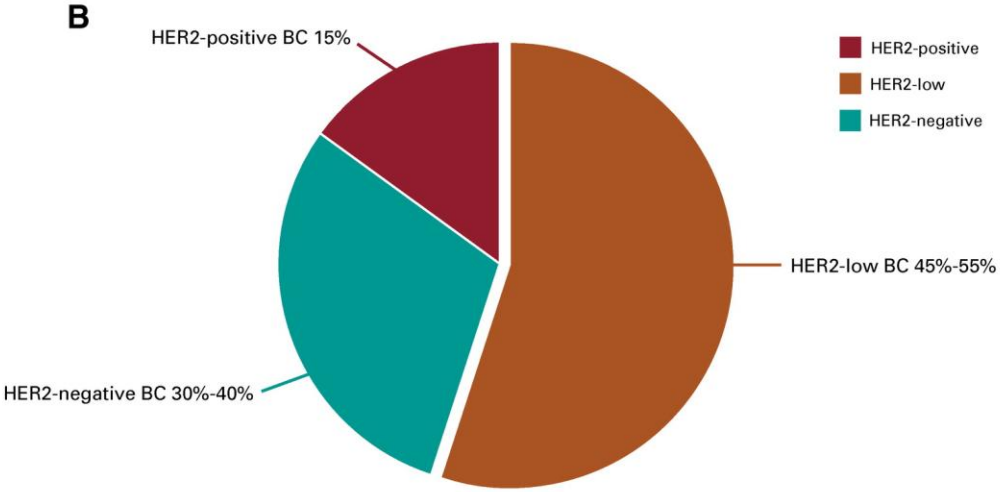
Expanding HER2 categories: positive, low, ultralow (0+), null (0)



2025:

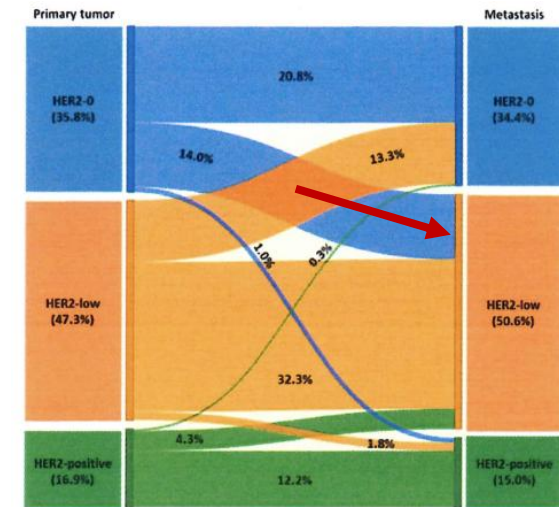
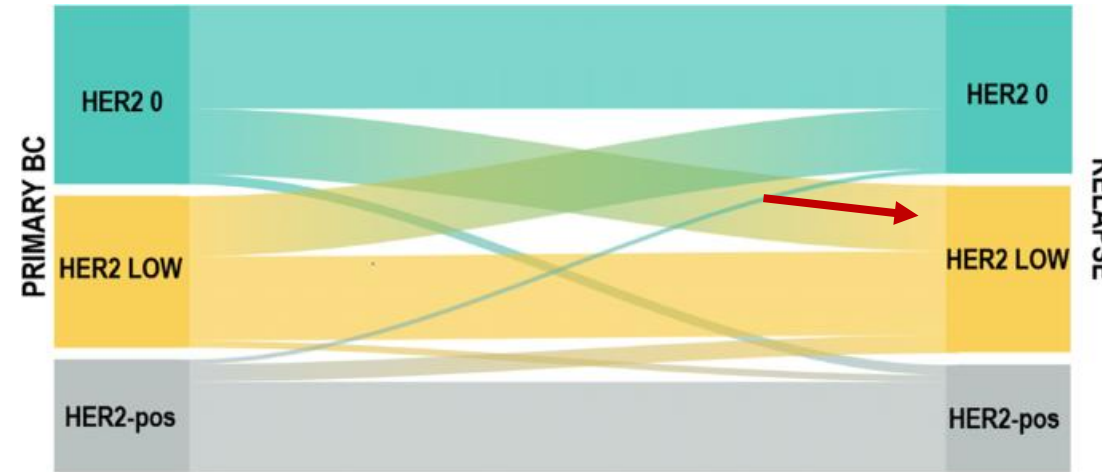
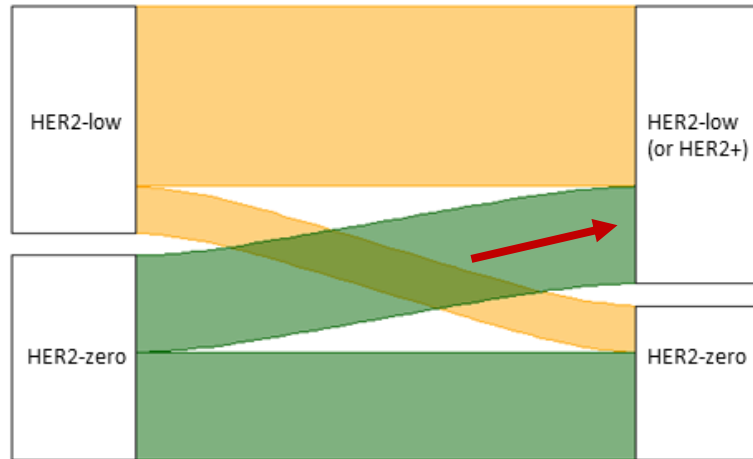
**HER2 null:
IHC 0 (0% expression)**

**HER2 ultralow:
IHC 0+ (1-10% expression)**

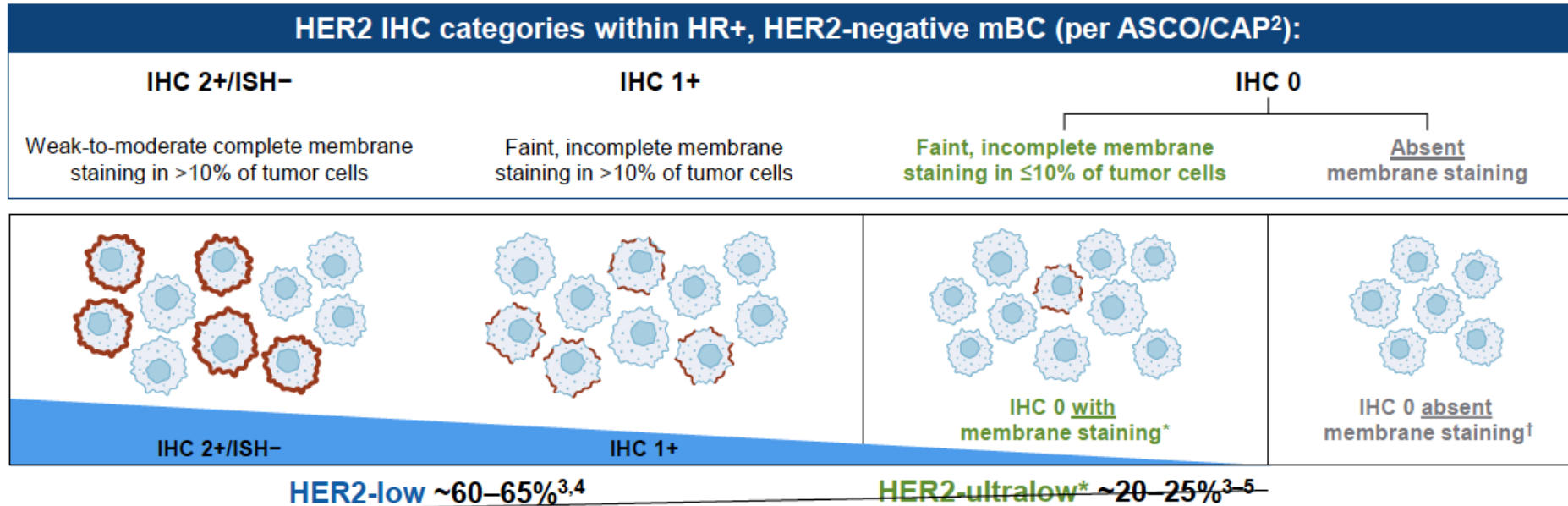


HER2-low (and ultralow) status is unstable – it changes over time

Multiple studies have confirmed the instability of HER2-low expression. The reason is unclear, but may be multifactorial: (pre)analytical factors, HER2 expression heterogeneity, biologic evolution of the disease

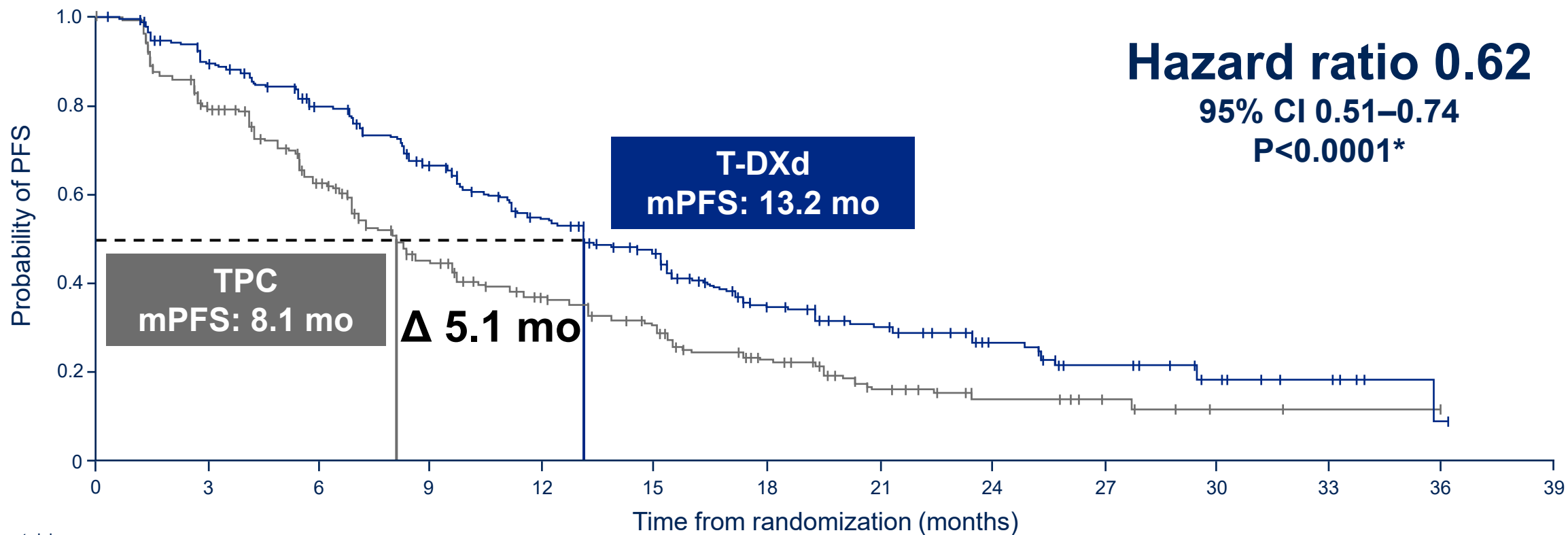


Targeting 'low' and 'ultralow' HER2-expressing tumors in mBC



- **78% overall agreement** between central vs local testing for **HER2 low status**
- Of pts with locally assessed HER2 IHC 0: 64% were either HER2 low or ultralow on central review – and therefore eligible for the trial
- **Underscores the importance of going back to re-review patients' IHC 0 results in clinical practice.**

PFS (BICR) in HER2-low: primary endpoint

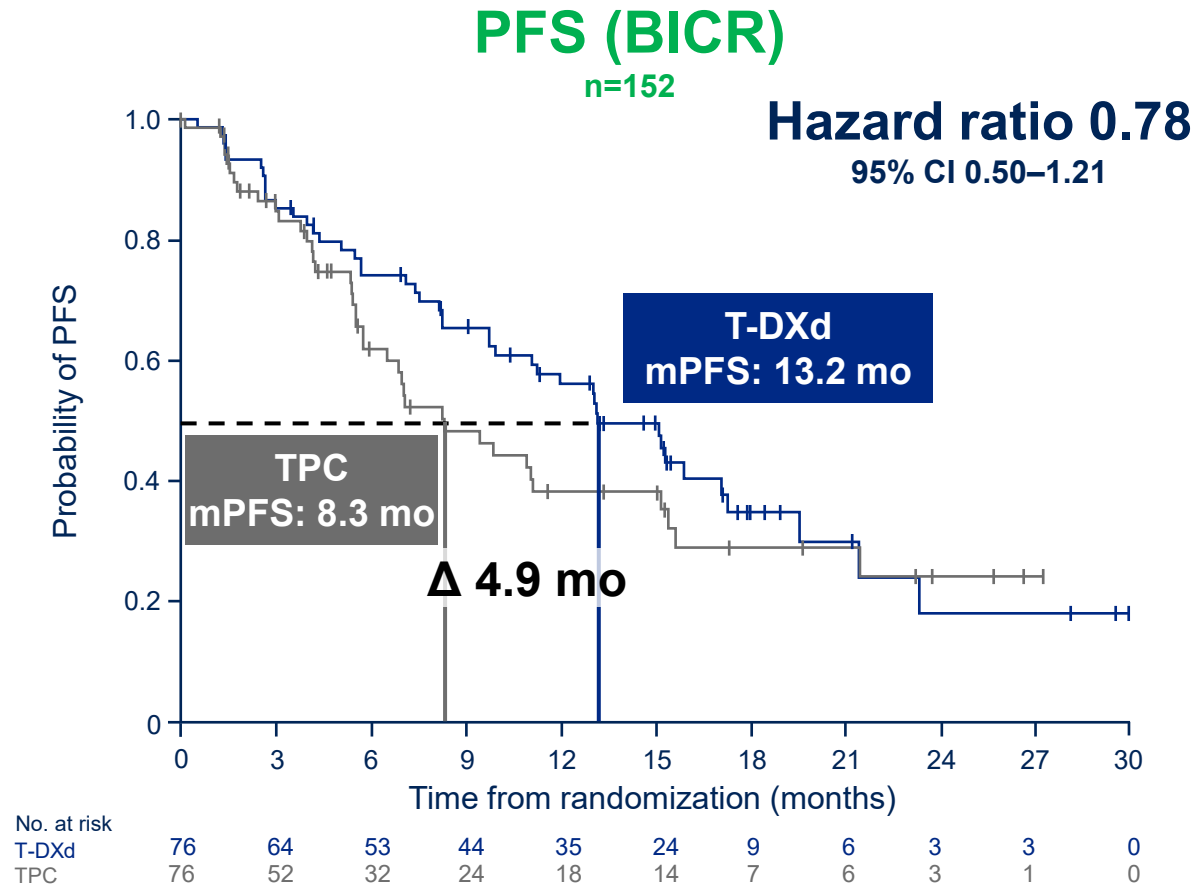


No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
T-DXd	359	310	265	213	163	131	72	49	28	17	10	6	1	0
TPC	354	254	192	118	85	65	37	19	10	6	2	1	1	0

T-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with standard-of-care chemotherapy in HER2-low

*P-value of <0.05 required for statistical significance
 BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

PFS in HER2-ultralow: prespecified exploratory analyses



PFS improvement with T-DXd vs TPC in HER2-ultralow was consistent with results in HER2-low

*34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months

BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; OS, overall survival; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan;

TPC, chemotherapy treatment of physician's choice

OS in HER2-low and ITT: key secondary endpoints (~40% maturity)

HER2-low*

n=713

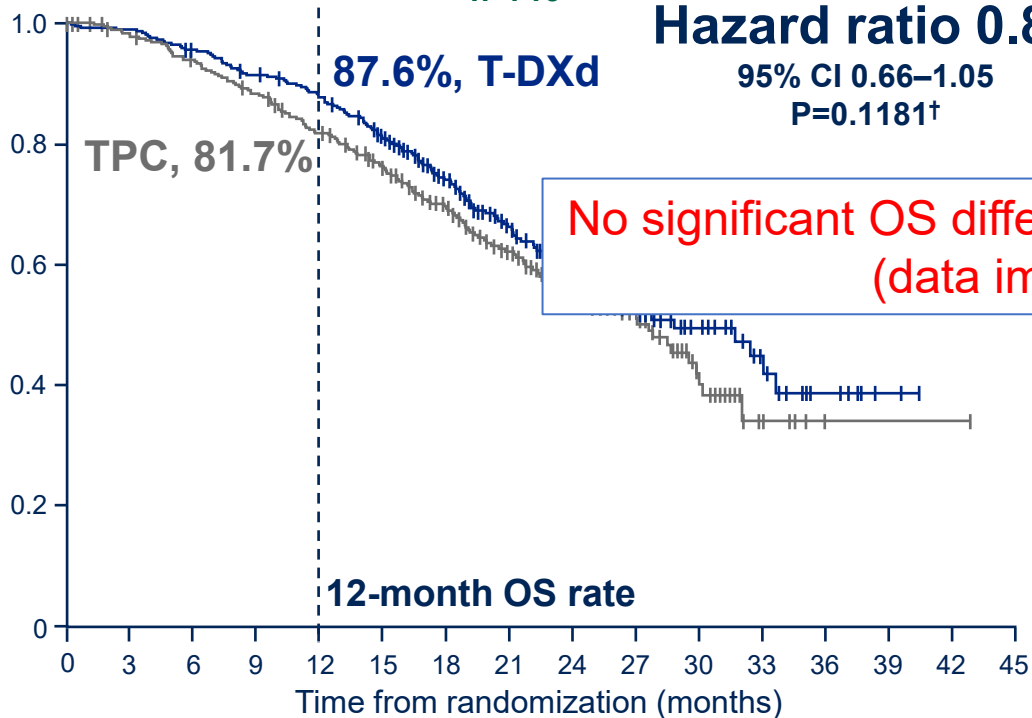
Hazard ratio 0.83

95% CI 0.66–1.05
P=0.1181†

87.6%, T-DXd

TPC, 81.7%

Probability of OS



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
T-DXd	359	354	341	324	309	279	198	140	96	53	32	16	7	2	0	0
TPC	354	333	319	298	273	247	185	126	86	53	23	6	2	1	1	0

20.1% of patients in the TPC group received T-DXd post treatment discontinuation (HER2-low)

ITT (HER2-low + HER2-ultralow)

N=866

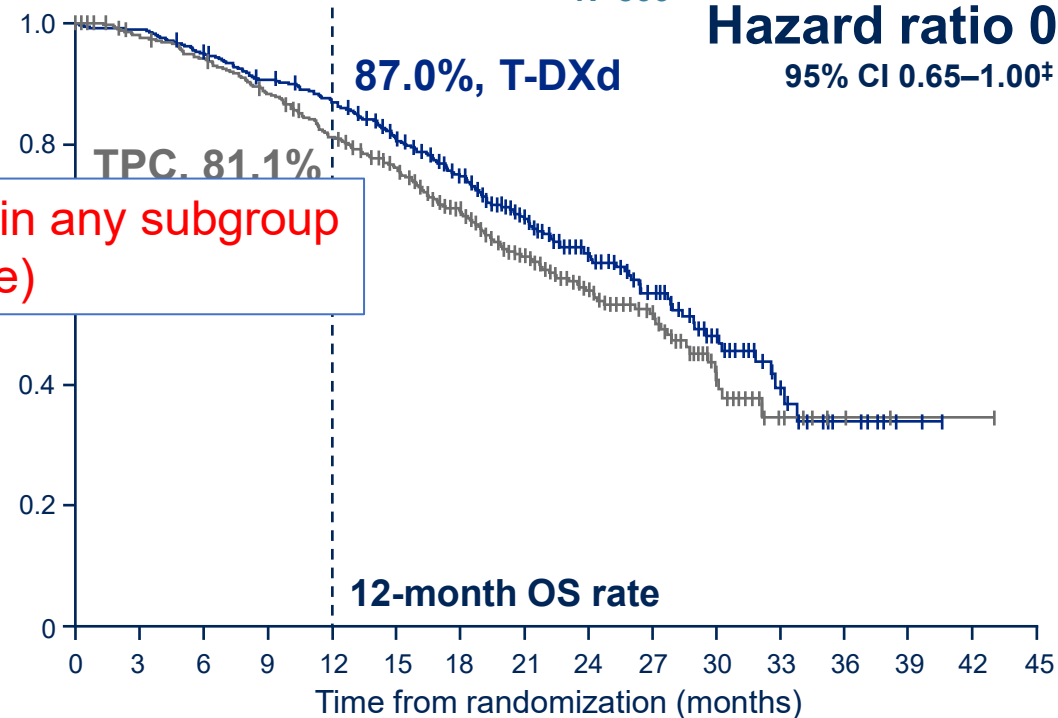
Hazard ratio 0.81

95% CI 0.65–1.00‡

87.0%, T-DXd

TPC, 81.1%

Probability of OS



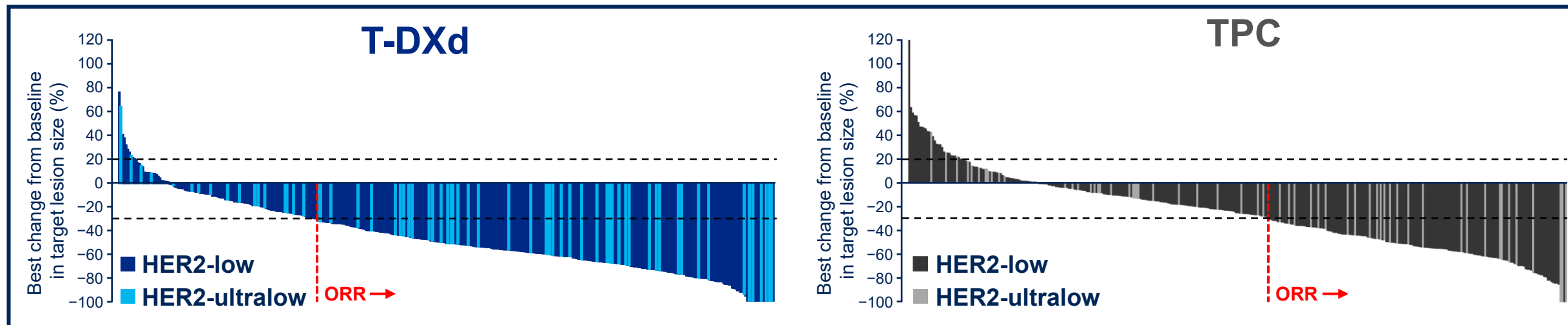
No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
T-DXd	436	431	412	391	373	329	235	169	120	69	39	16	7	2	0	0
TPC	430	402	387	360	328	292	210	143	101	62	27	9	3	1	1	0

17.9% of patients in the TPC group received T-DXd post treatment discontinuation (ITT)

*39.6% maturity (of total N for population) at this first interim analysis; median duration of follow up was 18.6 months (HER2-low); †P-value of <0.0046 required for statistical significance; ‡no test of significance was performed in line with the multiple testing procedure; median duration of follow up was 18.2 months (ITT)

CI, confidence interval; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Antitumor activity



	HER2-low*		ITT		HER2-ultralow*	
	T-DXd (n=359)	TPC (n=354)	T-DXd (n=436)	TPC (n=430)	T-DXd (n=76)	TPC (n=76)
Confirmed ORR, n (%)	203 (56.5)	114 (32.2)	250 (57.3)	134 (31.2)	47 (61.8)	20 (26.3)
Best overall response, n (%)						
Complete response	9 (2.5)	0	13 (3.0)	0	4 (5.3)	0
Partial response	194 (54.0)	114 (32.2)	237 (54.4)	134 (31.2)	43 (56.6)	20 (26.3)
Stable disease	125 (34.8)	170 (48.0)	148 (33.9)	212 (49.3)	22 (28.9)	42 (55.3)
Clinical benefit rate, n (%)[†]	275 (76.6)	190 (53.7)	334 (76.6)	223 (51.9)	58 (76.3)	33 (43.4)
Median duration of response, mo	14.1	8.6	14.3	8.6	14.3	14.1

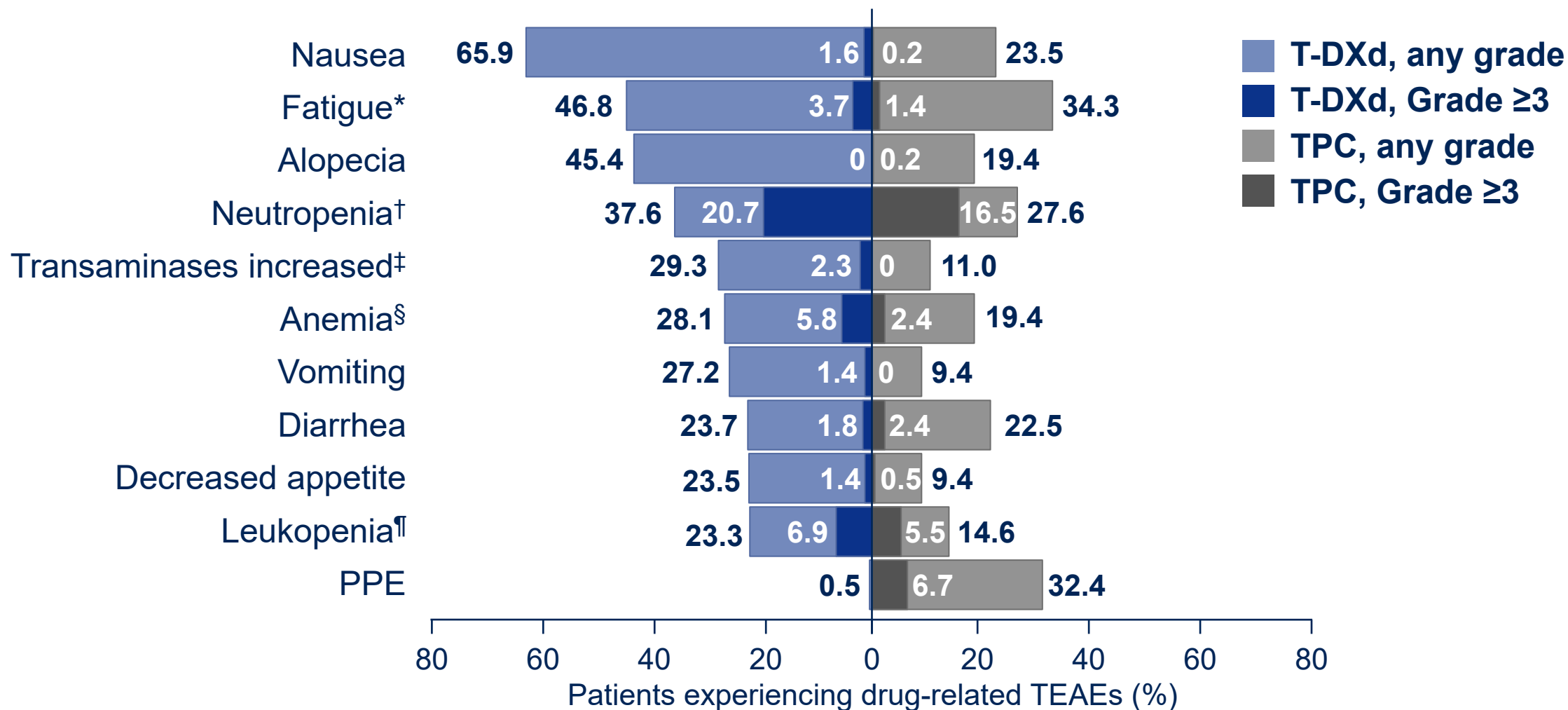
ORR based on RECIST v1.1; response required confirmation after 4 weeks

*HER2-low status defined at randomization per IRT data, and HER2-ultralow status defined by central laboratory testing data; [†]defined as complete response + partial response + stable disease at Week 24, by blinded independent central review

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IRT, interactive response technology; ITT, intent-to-treat; mo, months; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors;

T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Drug-related TEAEs in ≥20% of patients (either treatment group)



*Includes the preferred terms fatigue, asthenia, malaise, and lethargy; †includes the preferred terms neutrophil count decreased and neutropenia; ‡includes the preferred terms transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, liver function test abnormal, hepatic function abnormal, and liver function test increased; §includes the preferred terms hemoglobin decreased, red blood cell count decreased, anemia, and hematocrit decreased; ¶includes the preferred terms white blood cell count decreased and leukopenia
 PPE, palmar-plantar erythrodysesthesia; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; TPC, chemotherapy treatment of physician's choice

Adverse events of special interest

Adjudicated as drug-related interstitial lung disease / pneumonitis*

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n=434)	7 (1.6)	36 (8.3)	3 (0.7)	0	3 (0.7)	49 (11.3)
TPC (n=417)	0	1 (0.2)	0	0	0	1 (0.2)

Left ventricular dysfunction†

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
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Ejection fraction decreased

T-DXd (n=434)	1 (0.2)	31 (7.1)	3 (0.7)	0	0	35 (8.1)
TPC (n=417)	0	11 (2.6)	1 (0.2)	0	0	12 (2.9)

Cardiac failure

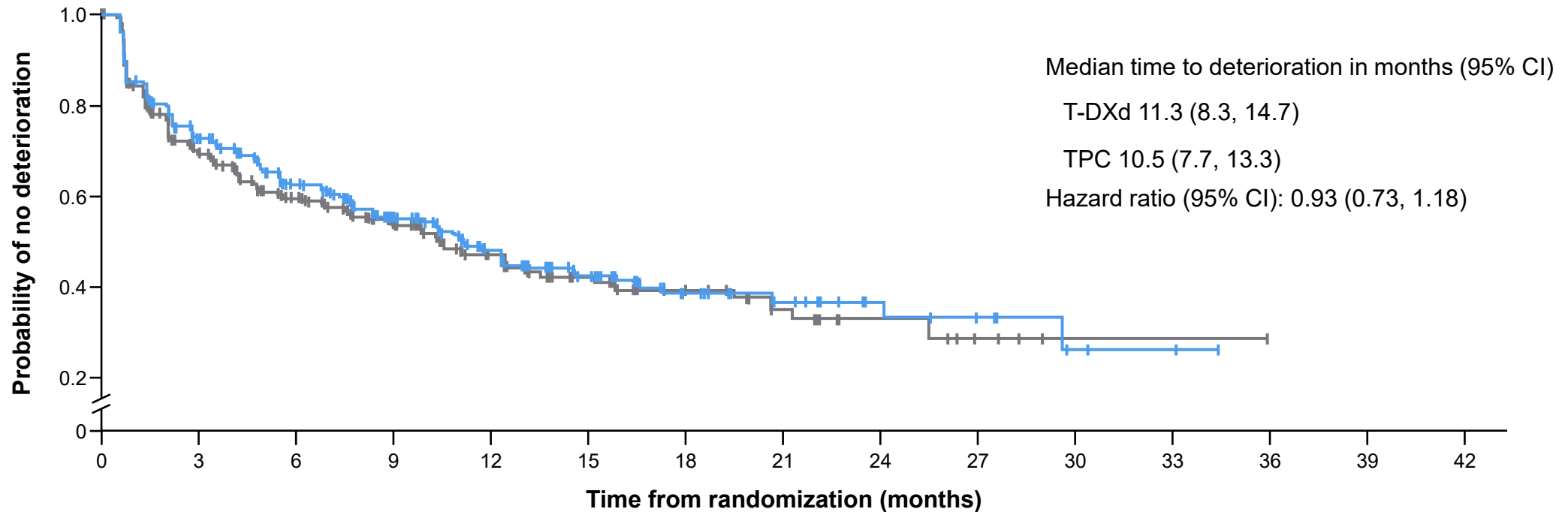
T-DXd (n=434)	0	0	0	0	0	0
TPC (n=417)	0	1 (0.2)	1 (0.2)	1 (0.2)	0	3 (0.7)

*Grouped term. Median time to first onset of interstitial lung disease / pneumonitis for patients with T-DXd was 141 days (range 37–835). No pending cases of drug-related interstitial lung disease / pneumonitis to be adjudicated. One interstitial lung disease–related death per investigator assessment was upheld by the adjudication committee. An additional two deaths were adjudicated as interstitial lung disease–related by the adjudication committee; †data for the most common preferred terms are shown on the slide; additionally, one patient in each treatment group had the preferred term left ventricular dysfunction (Grade 3 with T-DXd, Grade 2 with TPC)

T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Time to deterioration in QLQ-C30 GHS/QOL was similar with T-DXd and TPC

Time to deterioration in QLQ-C30 GHS/QOL: ITT population



—	T-DXd (n=)	436	193	145	104	68	46	26	17	10	7	3	2	0	0	0
—	TPC (n=)	430	170	122	84	51	33	23	14	8	4	1	1	0	0	0

Vertical tick mark indicates a censored observation

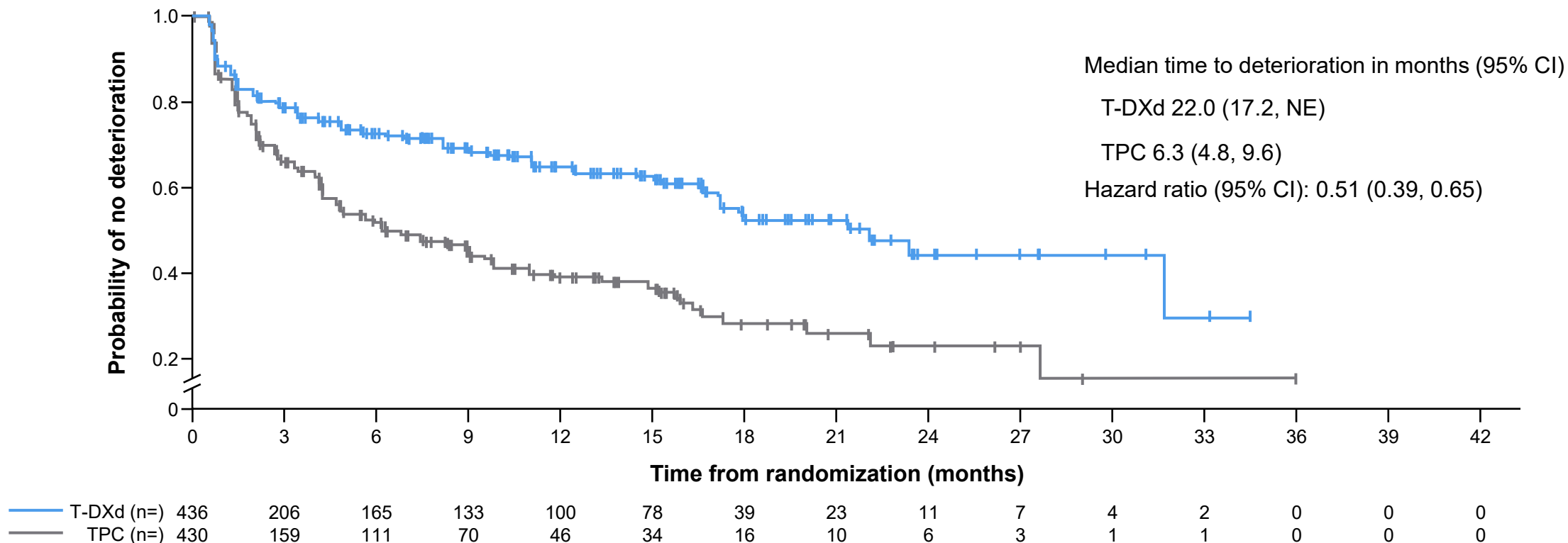
CI, confidence interval; GHS, Global Health Status; ITT, intent-to-treat; QLQ-C30, Quality of Life Core 30 questionnaire; QOL, quality of life; T-DXd, trastuzumab deruxtecan;

TPC, chemotherapy treatment of physician's choice

Presented by Xichun Hu ESMO 2024

T-DXd reduced the risk of clinically meaningful deterioration in pain by 49% vs TPC

Deterioration in QLQ-C30 pain: ITT



Vertical tick mark indicates a censored observation

CI, confidence interval; ITT, intent-to-treat; NE, not evaluable; QLQ-C30, Quality of Life Core 30 questionnaire; QOL, quality of life; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Presented by Xichun Hu ESMO 2024

NCCN 1/2025: Endocrine-refractory HR+ MBC

SYSTEMIC THERAPY FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE^a

HR-Positive and HER2-Negative with Visceral Crisis [†] or Endocrine Refractory		
See BINV-Q (1) for Considerations for Systemic Therapy.		
Setting	Subtype/Biomarker	Regimen
First Line	No germline <i>BRCA1/2</i> mutation ^b and/or IHC HER2 0+, 1+, or 2+/ISH negative ^d	Systemic chemotherapy ^e (category 1, preferred) BINV-Q (5) , or fam-trastuzumab deruxtecan-nxki ^{e,f} (other recommended regimen)
	Germline <i>BRCA1/2</i> mutation ^b	PARPi (olaparib, talazoparib) ^c (Category 1, preferred)
Second Line	HER2 IHC 0+, 1+, or 2+/ISH negative ^d	Fam-trastuzumab deruxtecan-nxki ^f (Category 1, preferred)
	Not a candidate for fam-trastuzumab deruxtecan-nxki	Sacituzumab govitecan ^g (Category 1, preferred)
		Systemic chemotherapy BINV-Q (5)
		Targeted therapy BINV-Q (6) and BINV-Q (7)
	For HER2 IHC 0, 1+, or 2+/ISH negative: ^d Datopotamab deruxtecan-dlnk ^h (other recommended regimen)	
Third Line and beyond	Any	Systemic chemotherapy BINV-Q (5)
	Biomarker positive (ie, MSI-H, NTRK, RET, TMB-H)	Targeted agents and emerging biomarker options BINV-Q (6) , BINV-Q (7) , and BINV-Q (8)

Second-line (and later) cytotoxic treatment
for endocrine-refractory HER2 low/ultralow
metastatic breast cancer

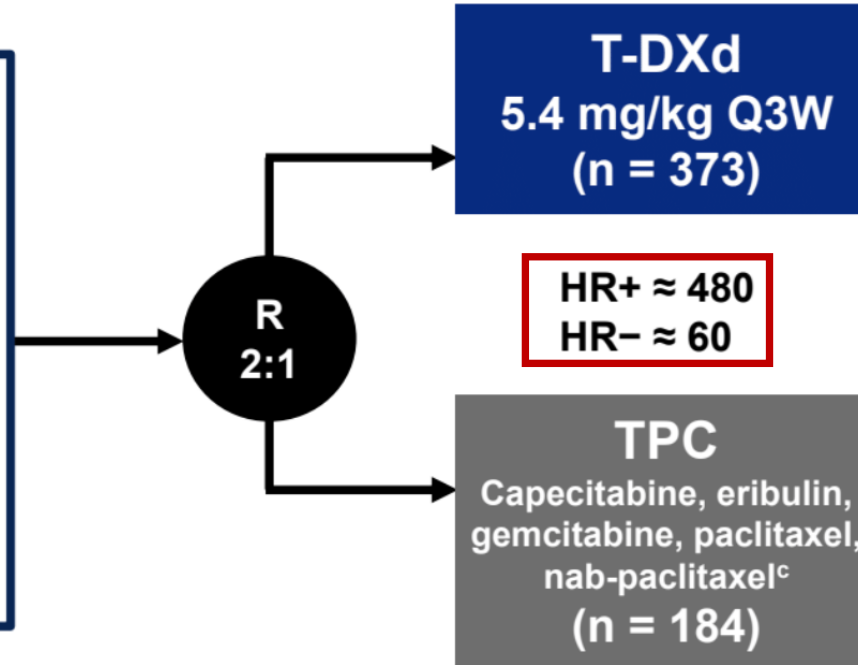
PHASE 3 trial: DESTINY-Breast04

Patients^a

- 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

Stratification factors

- Centrally assessed HER2 status^d (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-



Primary endpoint

- PFS by BICR (HR+)

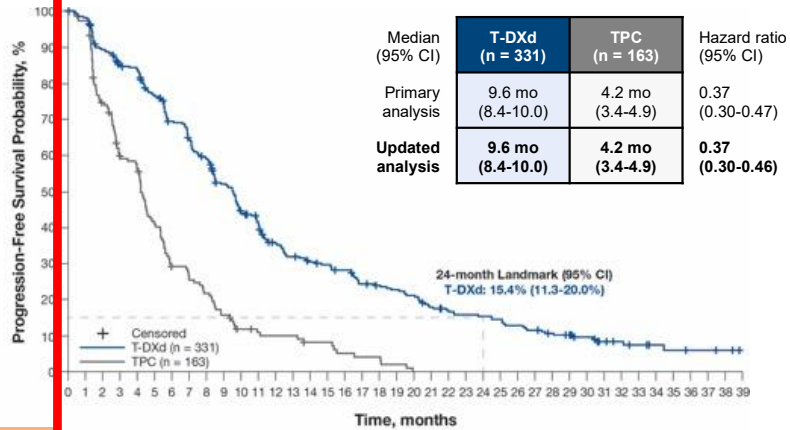
Key secondary endpoints^b

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

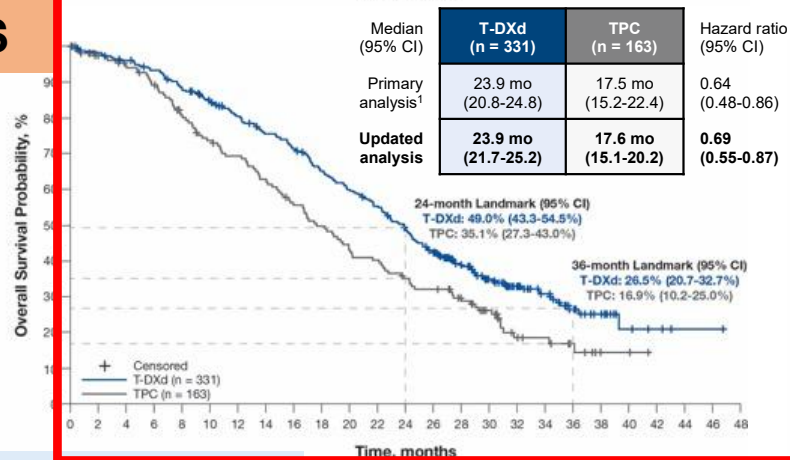
DB04: Trastuzumab deruxtecan in HER2-low MBC

PFS

Hormone Receptor-positive (n=494)

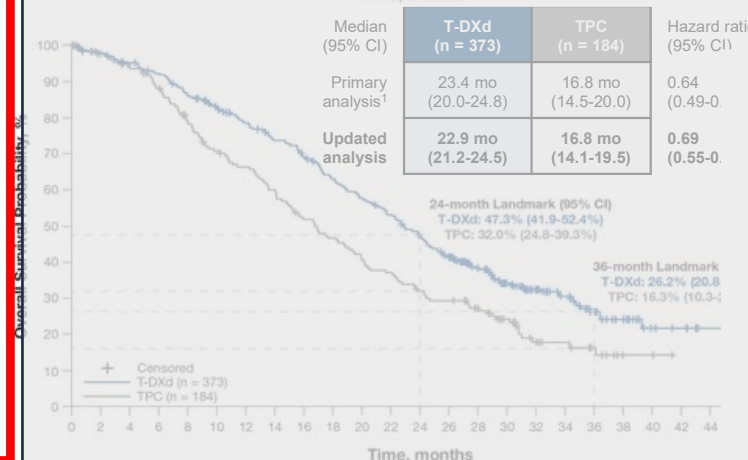
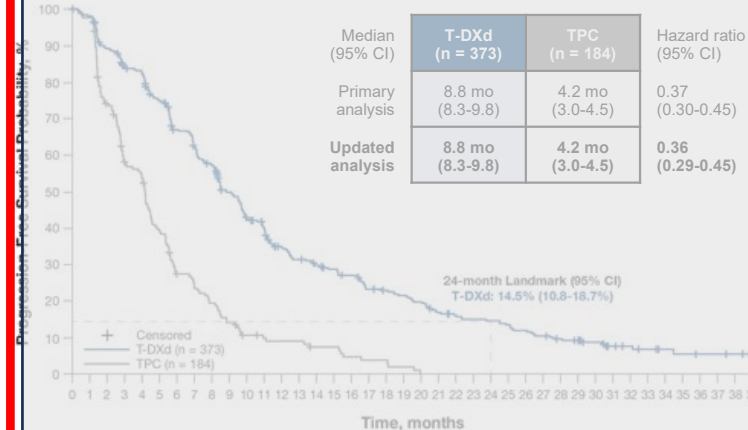


OS

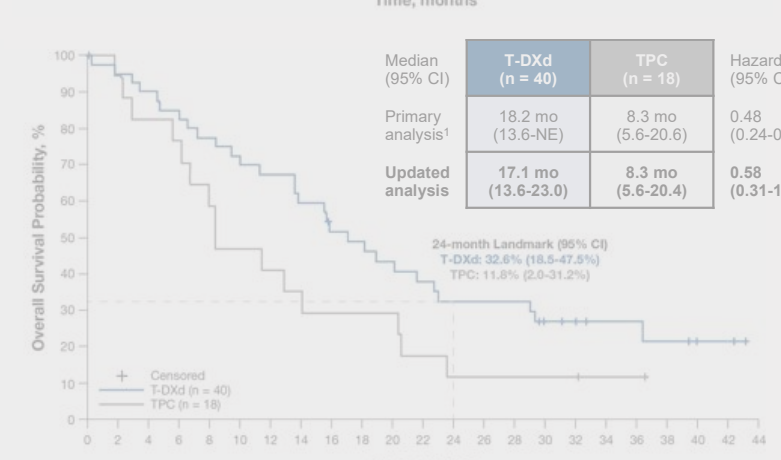
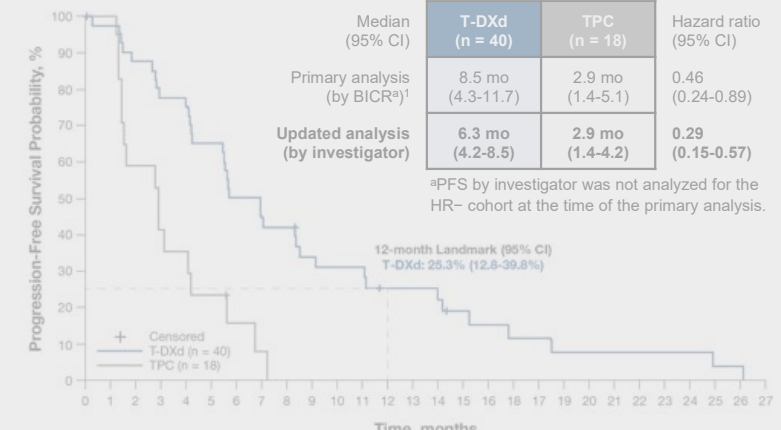


Median FU: 32.0 months

ALL Patients (n=557)



Hormone Receptor-negative (n=58)



Modi S et al. ESMO 2023.

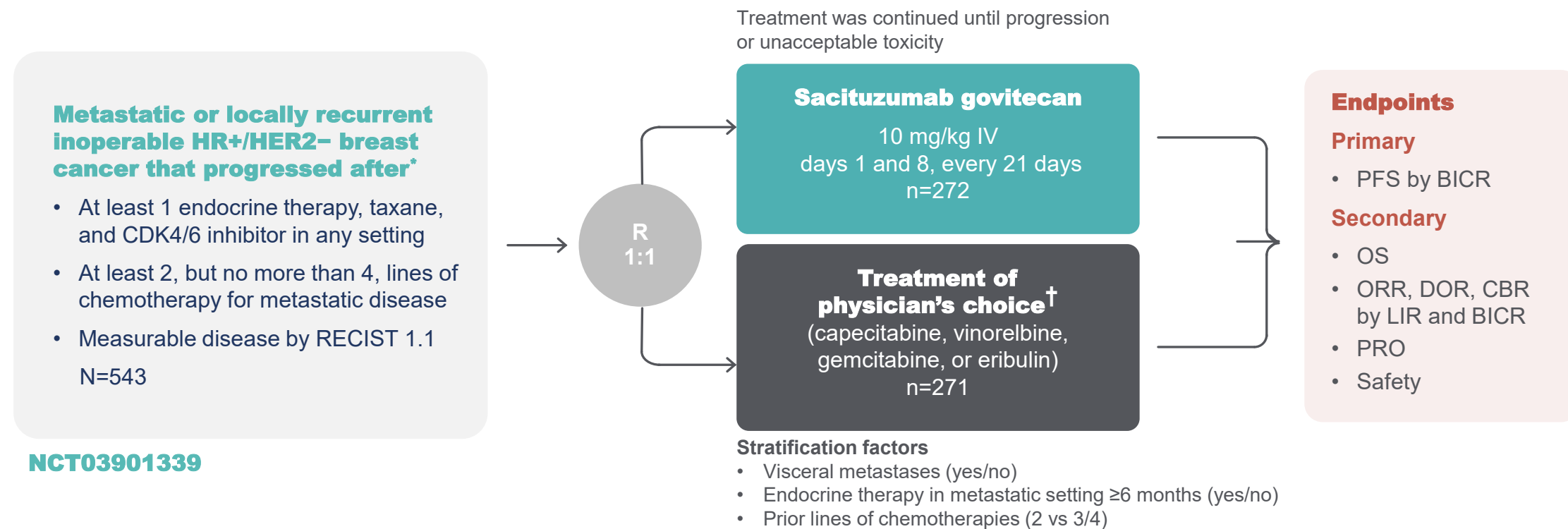
NCCN 1/2025: Endocrine-refractory HR+ MBC

SYSTEMIC THERAPY FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE^a

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	Germline <i>BRCA1/2</i> mutation ^b	PARPi (olaparib, talazoparib) ^c (Category 1, preferred)
Second Line	HER2 IHC 0+, 1+, or 2+/ISH negative ^d	Fam-trastuzumab deruxtecan-nxki ^f (Category 1, preferred)
	Not a candidate for fam-trastuzumab deruxtecan-nxki	Sacituzumab govitecan ^g (Category 1, preferred)
		Systemic chemotherapy BINV-Q (5)
		Targeted therapy BINV-Q (6) and BINV-Q (7)
	For HER2 IHC 0, 1+, or 2+/ISH negative: ^d Datopotamab deruxtecan-dlnk ^h (other recommended regimen)	
Third Line and beyond	Any	Systemic chemotherapy BINV-Q (5)
	Biomarker positive (ie, MSI-H, NTRK, RET, TMB-H)	Targeted agents and emerging biomarker options BINV-Q (6) , BINV-Q (7) , and BINV-Q (8)

TROPiCS-02:

A Phase 3 Study of SG in pre-treated HR+/HER2- (IHC0, IHC1+, IHC2+/ISH-) locally recurrent inoperable or metastatic breast cancer^{1,2}



*Disease histology based on the ASCO/CAP criteria. †Single-agent standard-of-care treatment of physician's choice was specified prior to randomisation by the investigator.

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CBR, clinical benefit rate; CDK, cyclin-dependent kinase; DOR, duration of response; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor-positive; IV, intravenously; LIR, local investigator review; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; R, randomised; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Adapted from Rugo H, et al. ESMO 2022. Oral LBA76; 2. Rugo HS, et al. J Clin Oncol. 2022;40:3365-3376.

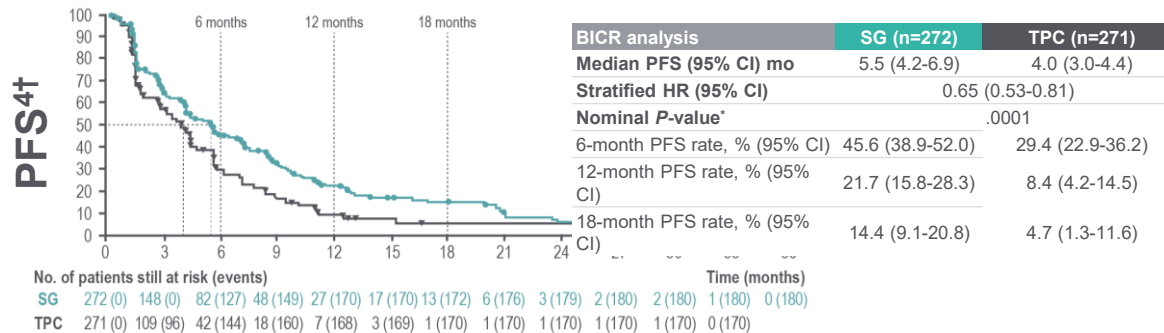
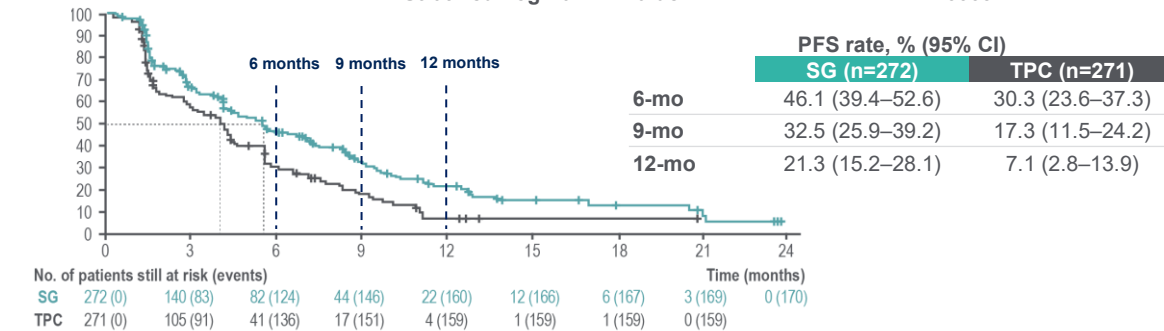
TROPiCS-02:

Sacituzumab govitecan demonstrated a statistically significant and clinically meaningful improvement in PFS and OS vs chemotherapy, with continued improvement confirmed with longer follow-up¹⁻⁴

ORR: 21% vs. 14%
p=0.035

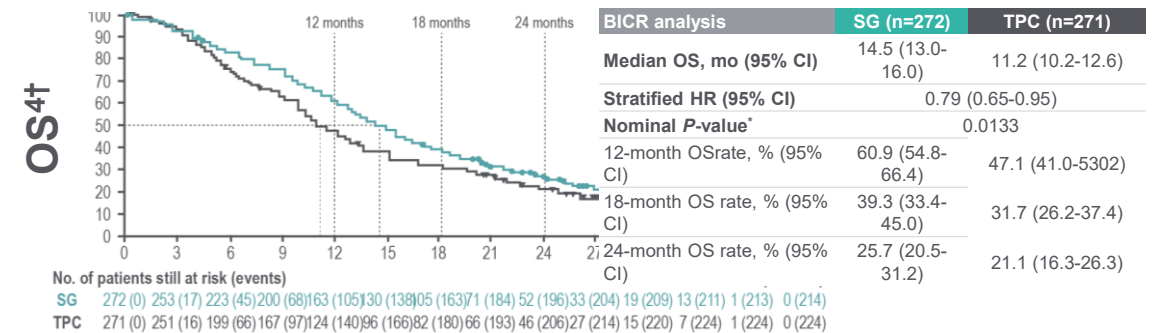
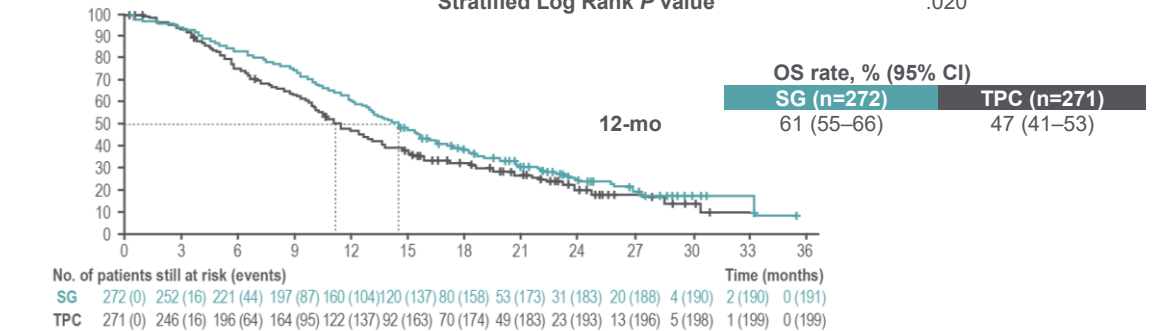
PFS_{1,2} #

BICR analysis	SG (n=272)	TPC (n=271)
Median PFS, mo (95% CI)	5.5 (4.2-7.0)	4.0 (3.1-4.4)
Stratified HR (95% CI)	0.66 (0.53-0.83)	
Stratified Log Rank P value	.0003	



OS₃ #

	SG (n=272)	TPC (n=271)
Median OS, mo (95% CI)	14.4 (13.0-15.7)	11.2 (10.1-12.7)
Stratified HR (95% CI)	0.79 (0.65-0.96)	
Stratified Log Rank P value	.020	



*Stratified log rank P-value. # Primary endpoint (PFS) assessed by blinded independent central review in the ITT study population, as predefined in the study protocol. Secondary endpoint (OS). † PFS and OS exploratory analysis with an extended follow-up of ~13 months. BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice, ITT, intent-to-treat.

1. Adapted from Rugo HS, et al. *J Clin Oncol*. 2022;40:3365-3376; 2. Adapted from Rugo H, et al. ESMO 2022. Oral LBA76; 3. Adapted from Rugo H, et al. *Lancet*. 2023;S0140-6736(23)01245-X. 4. Tolaney S, et al. ASCO 2023. Abstract #1003.

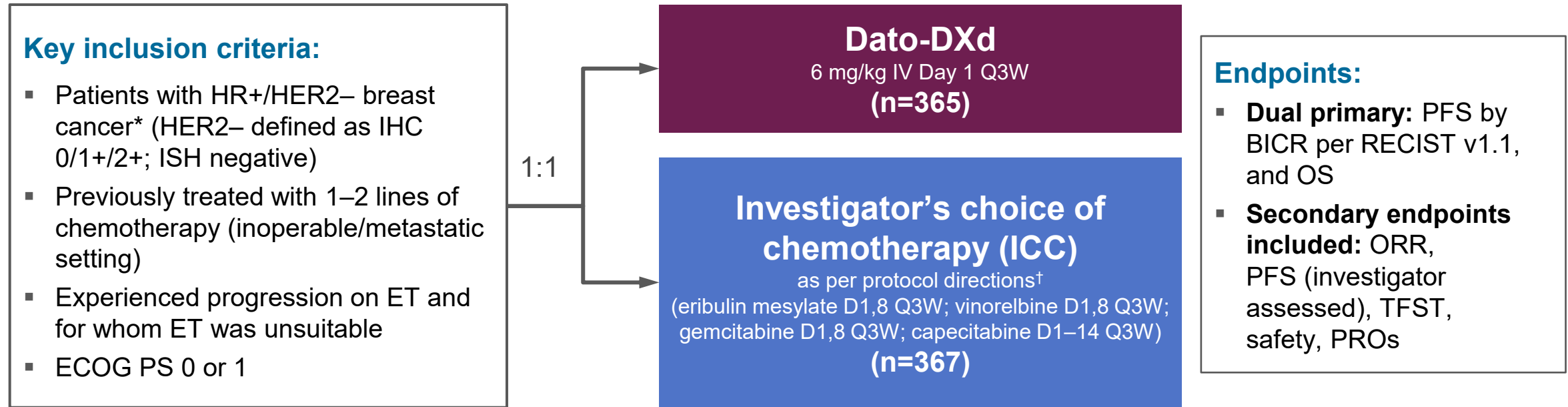
NCCN 1/2025: Endocrine-refractory HR+ MBC

SYSTEMIC THERAPY FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE^a

HR-Positive and HER2-Negative with Visceral Crisis [†] or Endocrine Refractory		
See BINV-Q (1) for Considerations for Systemic Therapy.		
Setting	Subtype/Biomarker	Regimen
First Line	No germline <i>BRCA1/2</i> mutation ^b and/or IHC HER2 0+, 1+, or 2+/ISH negative ^d	Systemic chemotherapy ^e (category 1, preferred) BINV-Q (5) , or fam-trastuzumab deruxtecan-nxki ^{e,f} (other recommended regimen)
	Germline <i>BRCA1/2</i> mutation ^b	PARPi (olaparib, talazoparib) ^c (Category 1, preferred)
Second Line	HER2 IHC 0+, 1+, or 2+/ISH negative ^d	Fam-trastuzumab deruxtecan-nxki ^f (Category 1, preferred)
	Not a candidate for fam-trastuzumab deruxtecan-nxki	Sacituzumab govitecan ^g (Category 1, preferred)
		Systemic chemotherapy BINV-Q (5)
		Targeted therapy BINV-Q (6) and BINV-Q (7)
		For HER2 IHC 0, 1+, or 2+/ISH negative: ^d Datopotamab deruxtecan-dlnk ^h (other recommended regimen)
Third Line and beyond	Any	Systemic chemotherapy BINV-Q (5)
	Biomarker positive (ie, MSI-H, NTRK, RET, TMB-H)	Targeted agents and emerging biomarker options BINV-Q (6) , BINV-Q (7) , and BINV-Q (8)

TROPION-Breast01 Study Design¹

Randomized, phase 3, open-label, global study (NCT05104866)



Randomization stratified by:

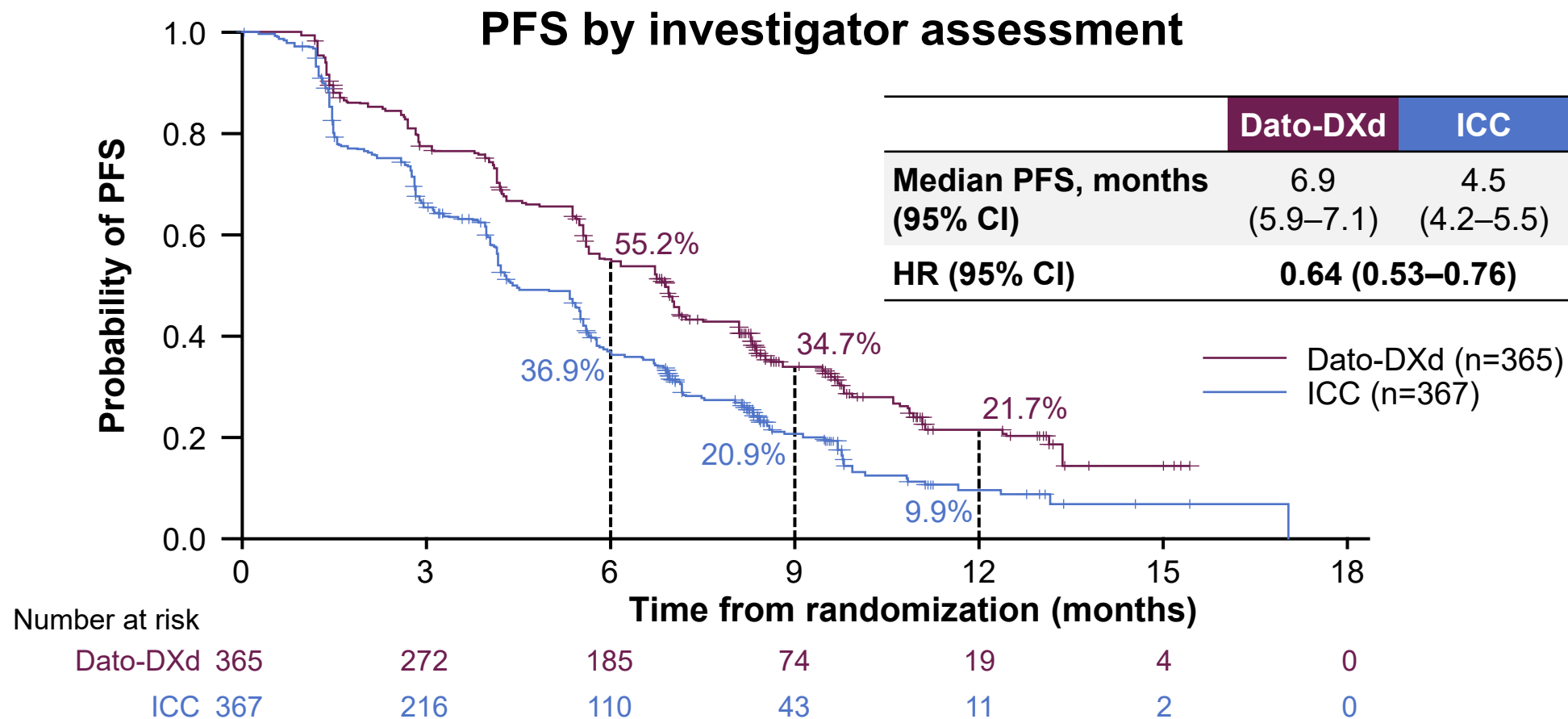
- **Lines of chemotherapy** in unresectable/metastatic setting (1 vs 2)
- **Geographic location** (US/Canada/Europe vs ROW)
- **Previous CDK4/6 inhibitor** (yes vs no)

- Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Detailed description of the statistical methods published previously.¹ *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines. †ICC was administered as follows: eribulin mesylate, 1.4 mg/m² IV on Days 1 and 8, Q3W; vinorelbine, 25 mg/m² IV on Days 1 and 8, Q3W; or gemcitabine, 1000 mg/m² IV on Days 1 and 8, Q3W; capecitabine, 1000 or 1250 mg/m² orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice). CDK4/6, cyclin-dependent kinase 4/6; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; IHC, immunohistochemistry; ISH, in-situ hybridization; IV, intravenous; PD, progressive disease; PROs, patient-reported outcomes; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; ROW, rest of world; TFST, time to first subsequent therapy.

1. Bardia A, et al.
Future Oncol 2023;
doi: 10.2217/fon-2023-0188.

Progression-Free Survival



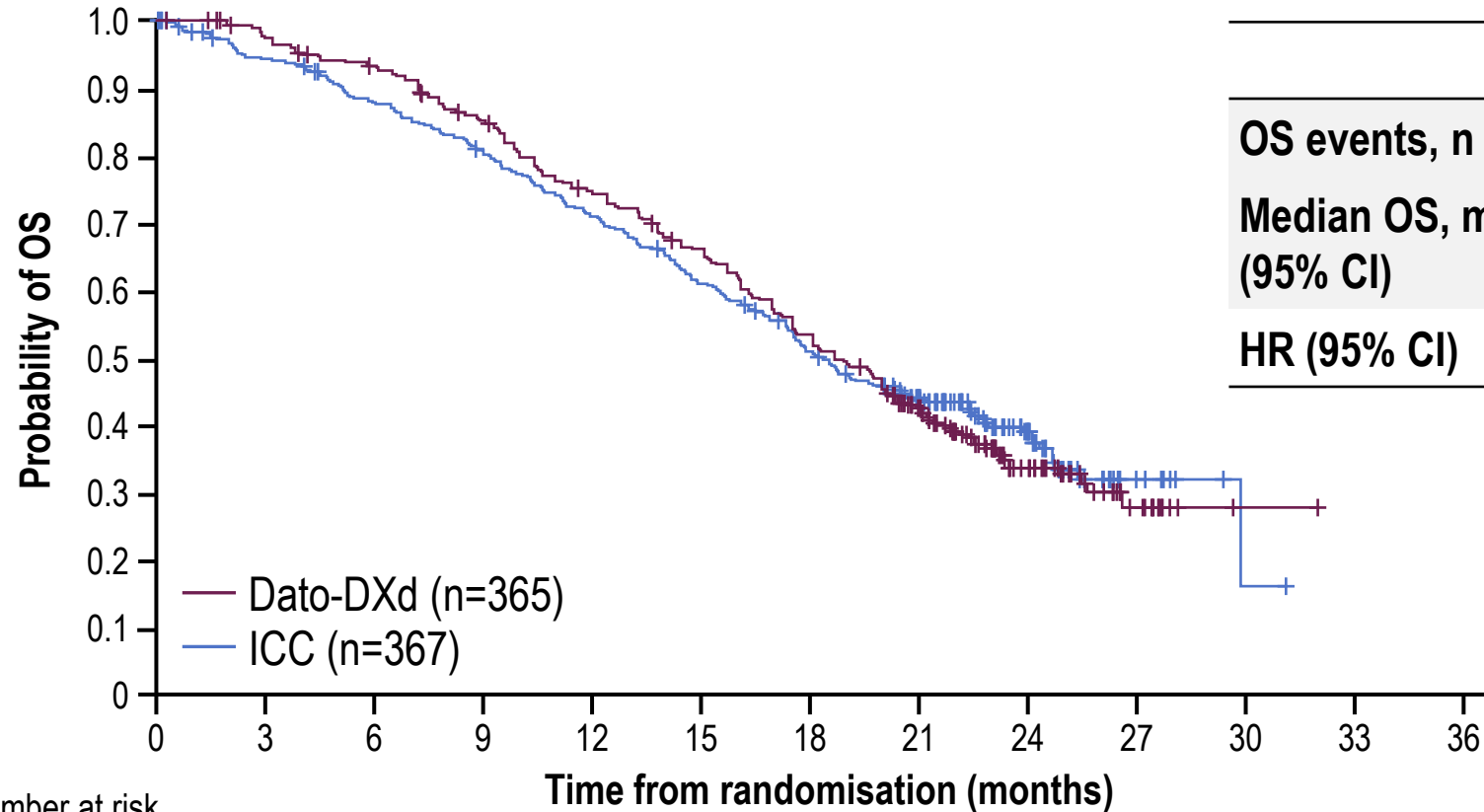
PFS by BICR (primary endpoint)¹: Median 6.9 vs 4.9 months; HR 0.63 (95% CI 0.52–0.76); P<0.0001

Data cut-off: 17 July 2023.

1. Bardia A, et al. Oral Presentation at ESMO 2023; Abstract LBA11.

Overall Survival

Dato arm: **12% crossover** to subsequent ADC
 ICC arm: **24% crossover** to subsequent ADC



Number at risk		Time from randomisation (months)										
		0	3	6	9	12	15	18	21	24	27	30
Dato-DXd	365	349	331	299	259	227	180	118	49	12	1	
ICC	367	335	309	283	249	213	175	123	51	9	1	

	Dato-DXd	ICC
OS events, n (%)	223 (61)	213 (58)
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
HR (95% CI)	1.01 (0.83–1.22)	

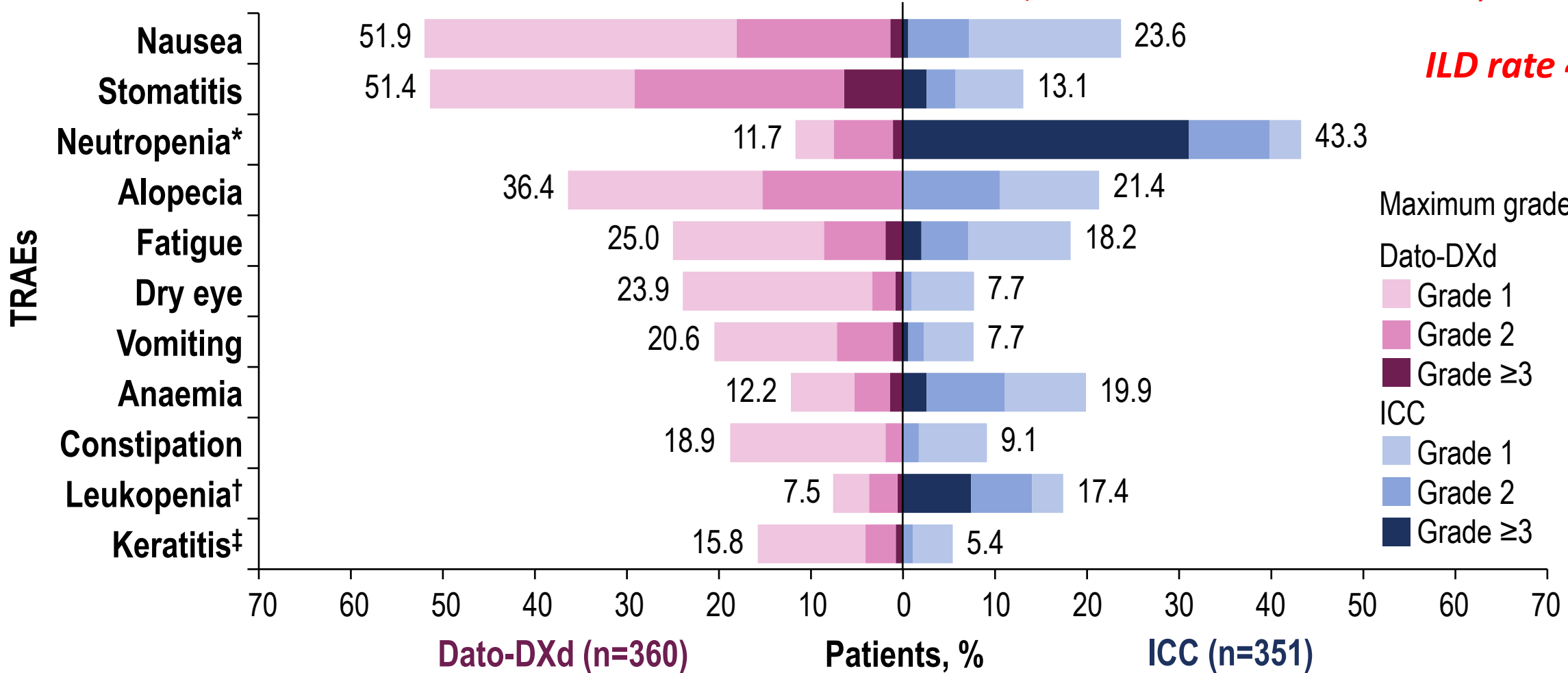
- Maturity: 59.6%
- Median follow-up: 22.8 months
- Protocol prespecified OS sensitivity analysis based on the stratification factors according to the eCRF*: **HR 0.99 (95% CI: 0.82–1.20)**

Data cutoff: 24 July 2024. Pre-specified P-value boundary for OS analysis: $\alpha=0.0427$.

*Mis-stratification between interactive response technology and eCRF <5%.
 eCRF, electronic case report form.

TRAEs Occurring in $\geq 15\%$ of Patients

*Recommend use of preventive dexamethasone mouthwash and preservative-free artificial tears during tx
(FDA label recommends baseline eye exam)*



Data cutoff: 24 July 2024. Data are ordered according to frequency in either the Dato-DXd or ICC arms.

*Grouped term comprising neutropenia and neutrophil count decreased. †Grouped term comprising white blood cell count decreased and leukopenia. ‡Grouped term comprising keratitis, punctate keratitis, ulcerative keratitis.

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Case

- 58 yo F with metastatic HR+/HER2 ultralow breast cancer and *PIK3CA* mutation
- No relevant comorbidities, labs WNL, compliant with all recommended treatments
- Treatment so far:
 - Letrozole + ribociclib – 24 mos, stopped for progression
 - Fulvestrant + capivasertib – 7 mos, stopped for progression
- Current disease burden = “innumerable” bony mets, two 1.5 cm liver lesions (all asymptomatic)
- ***What is the next therapy you recommend for this patient?***

Case

- 58 yo F with metastatic HR+/HER2 ultralow breast cancer and *PIK3CA* mutation
- No relevant comorbidities, labs WNL, compliant with all recommended treatments
- Treatment so far:
 - Letrozole + ribociclib – 24 mos, stopped for progression
 - Fulvestrant + capivasertib – 7 mos, stopped for progression
- Current disease burden = “innumerable” bony mets, two 1.5 cm liver lesions + low back and hip pain due to mets
- ***What is the next therapy you recommend for this patient?***

Case

- 58 yo F with metastatic HR+/HER2 ultralow breast cancer and *PIK3CA* mutation
- relevant comorbidities, labs WNL, compliant with all recommended treatments
- Treatment so far:
 - Letrozole + ribociclib – 24 mos, stopped for progression
 - Fulvestrant + capivasertib – 7 mos, stopped for progression
- Current disease burden = “innumerable” bony mets, + GI tract serosal involvement – uncertain absorption of oral medications
- ***What is the next therapy you recommend for this patient?***

THANK YOU!

