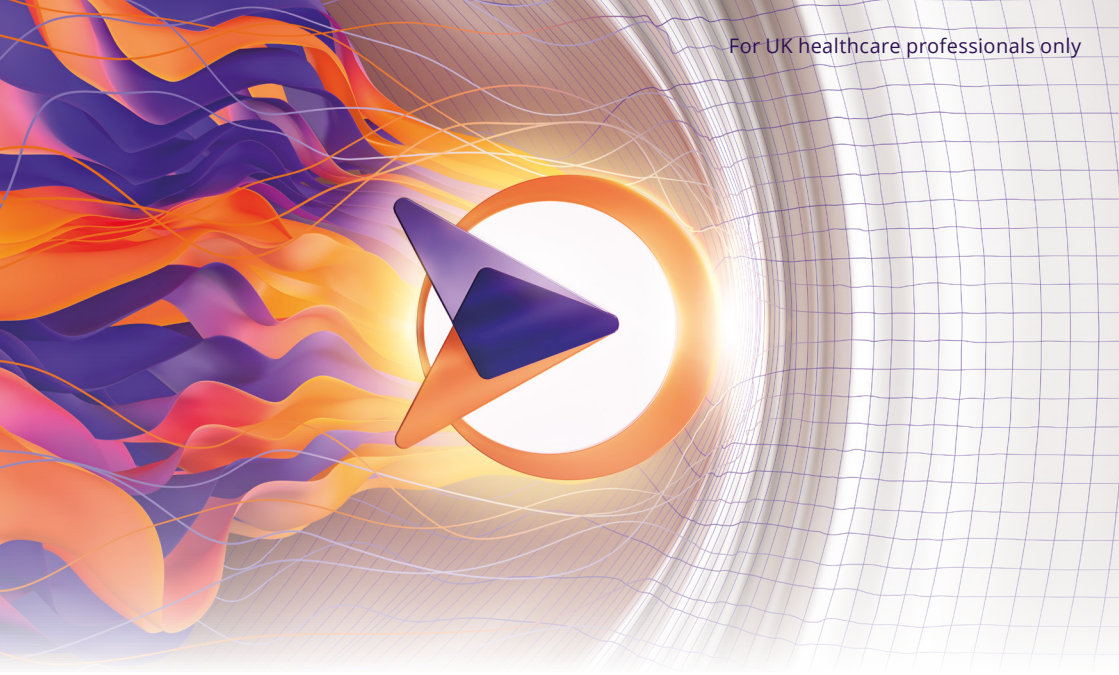




ENHERTU[▼]

(trastuzumab deruxtecan):

defining expectations in HER2-low (IHC 1+ or IHC 2+/ISH-) mBC

Efficacy and safety profile from DESTINY-Breast04

This material has been developed and funded by Daiichi Sankyo and AstraZeneca, and is intended for personal use only, not for distribution. This medicinal product has a Conditional Marketing Authorisation. This means that further evidence on this medicinal product is awaited.

Relevant Therapeutic Indication:

ENHERTU as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.¹



Click or scan the QR code to access
Enhertu Prescribing Information and
Adverse Event Reporting.

The DESTINY-Breast04 study was designed to assess treatment options for patients with HER2-low (IHC 1+ or IHC 2+/ISH-) mBC¹

A Phase III, international, open-label, multicentre study to evaluate ENHERTU vs physicians' choice of single-agent chemotherapy in patients with HER2-low (IHC 1+ or IHC 2+/ISH-) mBC.¹⁻⁴

Patients^{2,4}

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

R 2:1

Chemotherapy

Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel[†]

(n=184; HR+ n=163; HR- n=18)

ENHERTU

5.4 mg/kg Q3W

(n=373; HR+ n=331; HR- n=40)

Primary Endpoint:

- PFS by BICR (HR+)

Secondary Endpoints Included:

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

Exploratory:

- PFS and OS in HR-

STRATIFICATION FACTORS^{1,3}

- Centrally assessed HER2 status[‡] (IHC 1+ vs IHC 2+/ISH-)
- 1 vs 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6i) vs HR-

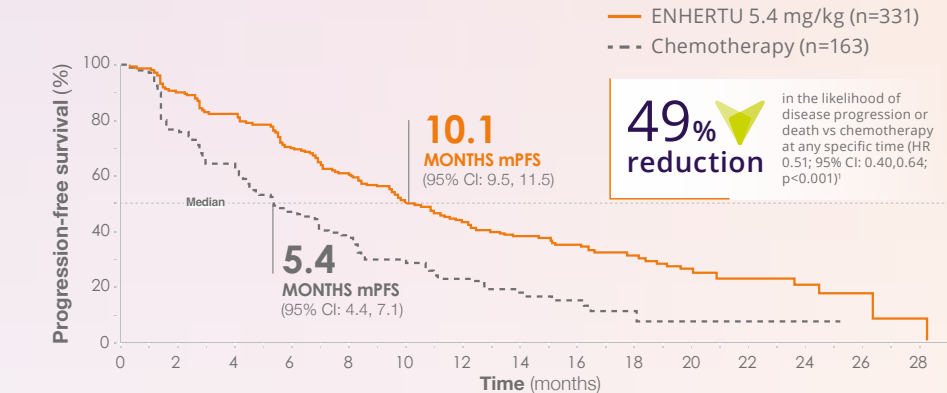
*If patients had HR+ mBC, prior endocrine therapy was required.² [†]Chemotherapy was administered according to the label. [‡]Performed on adequate archived or recent tumour biopsy per ASCO/CAP guidelines using the VENTANA HER2/neu (4B5) investigational use-only assay system.²

ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CAP, College of American Pathologists; CDK4/6i, cyclin-dependent kinases 4 and 6 inhibitor; HR-, hormone receptor-negative; HR+, hormone receptor-positive; ORR, objective response rate; OS, overall survival; PFS, progression free survival; Q3W, once every 3 weeks.

References: **1.** Modi S, et al. N Engl J Med 2022;387:9-20. **2.** Harbeck N, et al. Presented at 2022 San Antonio Breast Cancer Symposium (SABCS), 6-10 December 2022; San Antonio, TX. Poster P1-11-0. **3.** Modi S, et al. N Engl J Med 2022;387:9-20. Protocol. **4.** Modi S, et al. Presented at 2023 European Society for Medical Oncology (ESMO) Congress, 20-24 October 2023; Madrid, Spain. Presentation 376O.

With ENHERTU your patients have the potential of nearly doubling their mPFS vs chemotherapy¹

Primary endpoint: mPFS in the HR+/HER2-low population (by BICR)¹

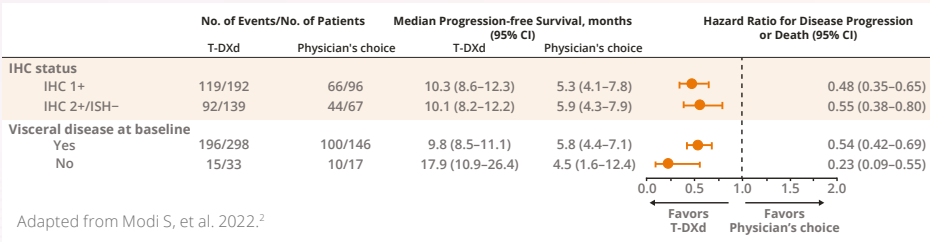


Number at risk	331	290	262	218	182	142	107	78	64	37	28	14	7	4	1
ENHERTU	331	290	262	218	182	142	107	78	64	37	28	14	7	4	1
Chemotherapy	163	105	84	57	43	30	24	14	8	3	1	1	1	0	

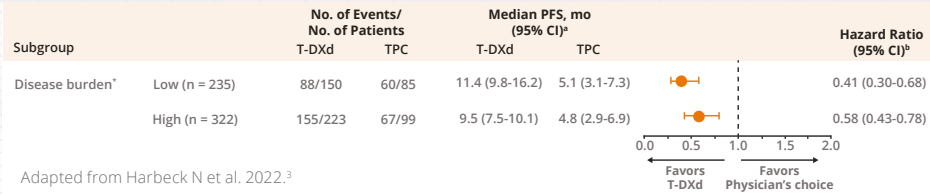
Adapted from Modi S, et al. 2022.¹

Enhertu demonstrated a similar PFS benefit across analysed subgroups^{2,3}

Prespecified PFS subgroup analysis in HR+ cohort²



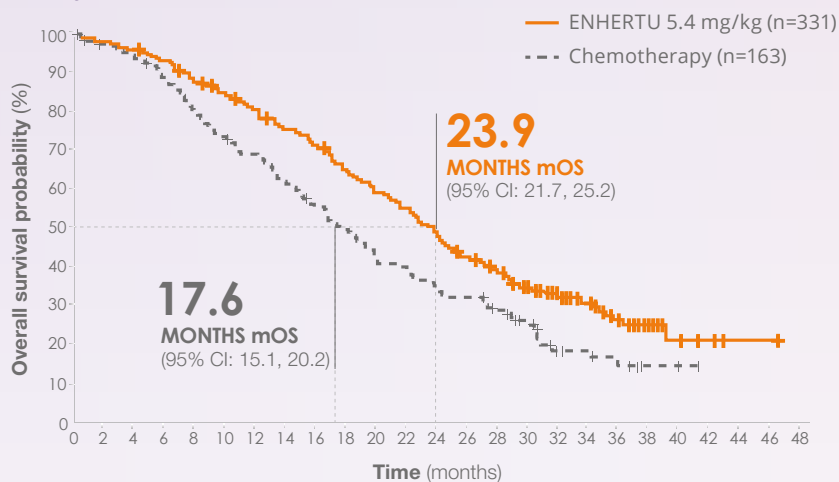
Retrospective, exploratory subgroup analysis in all patients³



Study was not powered for subgroup analyses; statistical significance testing was not undertaken. All data on this page is based on the primary data cut-off: January 2022. *Disease burden (low = 0–2, high = 3+ sites)
CI, confidence interval; HR, hazard ratio; mPFS, median progression-free survival; T-DXd, Trastuzumab Deruxtecan; TPC, treatment of physician's choice.
References: 1. Modi S, et al. N Engl J Med 2022;387:9–20. 2. Modi S, et al. 2022;387:9-20 Supplementary Appendix. 3. Harbeck N, et al. Presented at 2022 San Antonio Breast Cancer Symposium (SABCS), 6–10 December 2022; San Antonio, TX. Poster P1-11-0

ENHERTU could offer your patients the prospect of 6 more months of life vs chemotherapy¹

Key secondary endpoint: overall survival in the HR+/HER2-low population (updated analysis)¹



Patients still at risk

ENHERTU	331	323	313	302	284	267	250	233	220	199	183	168	147	124	94	72	54	42	23	14	5	3	1	1
Chemotherapy	163	144	138	129	114	103	96	87	76	68	59	55	47	43	35	25	13	11	7	2	2	0		

Adapted from Modi S, et al. 2025.¹

Descriptive analysis only; statistical significance testing was not undertaken.

- **Data cut-off at updated analysis: 1 March 2023; median follow-up: 32.0 months** (95% CI: 31.0, 32.8)¹

31%
reduction

in the likelihood of death
vs chemotherapy at any
specific time
(HR 0.69; 95% CI: 0.55, 0.87)¹

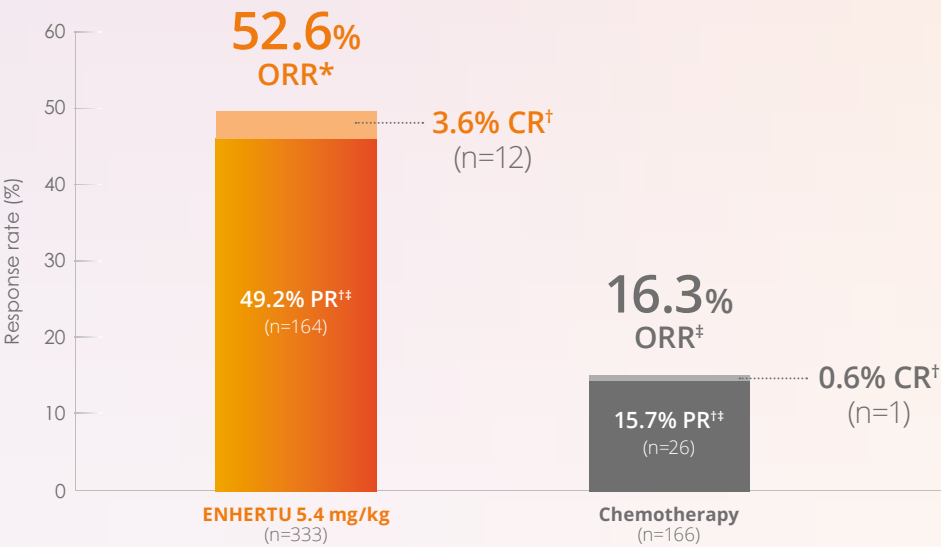
- **Data cut-off at primary analysis was January 2022, with a median follow-up of 18.4 months**
The longer follow-up in the updated analysis for DESTINY-Breast04 confirms a sustained clinically-meaningful improvement in OS with ENHERTU vs chemotherapy in HER2-low patients^{1,2}

mOS, median overall survival.

References: 1. Modi S, et al. Nat Med 2025; 31: 4205-4213 2. Modi S, et al. N Engl J Med 2022;387:9-20.

The objective response rate was over three times higher in patients receiving ENHERTU vs chemotherapy¹

Secondary endpoint: response rates by BICR in the HR+/HER2-low population (primary analysis)



Adapted from Modi S, et al. 2022.¹

Nearly 90%

of patients experienced **disease control**[§] with **ENHERTU** compared to ~66% with chemotherapy¹

mDOR was 10.7 months

with **ENHERTU** and 6.8 months with chemotherapy¹

ORR and DOR were not tested for statistical significance, and the study was not powered to show differences between treatment arms.

*n=175/333; 95% CI: 47.0–58.0.¹ [†]A complete response (CR) is defined as the disappearance of all target lesions, and partial response (PR) is defined as at least a 30% decrease in the sum of the target lesions.² ^{††}n=27/166; 95% CI: 11.0, 22.8.¹

[‡]DCR=CR+PR+SD.¹

CR, complete response; DCR, disease control rate; mDOR, median duration of response; PR, partial response; SD, stable disease.

References: 1. Modi S, et al. N Engl J Med 2022;387:9–20. 2. Ruchalski K, et al. Eur J Radiol Open 2022;9:100426.

DESTINY-Breast04: efficacy in the HR-/HER2-low population (exploratory analysis)^{1,2*}

Exploratory analyses: mOS and mPFS in patients with HR- mBC^{1,2}

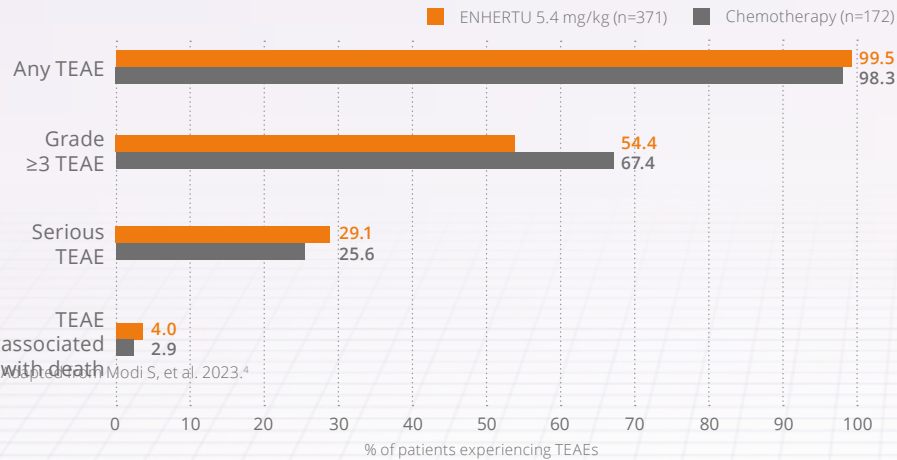
	ENHERTU 5.4 mg/kg (n=40)	Chemotherapy (n=18)
mOS (updated analysis) ¹	17.1 months (95% CI: 13.6, 23.0)	8.3 months (95% CI: 5.6, 20.4)
	HR 0.58 (95% CI: 0.31, 1.08)	
mPFS (by BICR, primary analysis) ²	8.5 months (95% CI: 4.3, 11.7)	2.9 months (95% CI: 1.4, 5.1)
	HR 0.46 (95% CI: 0.24, 0.89)	

Adapted from Modi S, et al. 2025¹ and Modi S, et al. 2022.²

- Following a similar trend to HR+ patients, 50% of HR-/HER2-low patients treated with ENHERTU achieved an objective response vs 16.7% with chemotherapy²

ENHERTU’s safety profile in DB04 was similar to the established safety profile in HER2+ studies³⁻⁷

Proportion of patients experiencing TEAEs (any grade and grade ≥3)⁴



***The HR- cohort was an exploratory population. The data are descriptive and were not tested for statistical significance, nor powered to show a difference between treatment arms.¹**

DBO4, DESTINY-Breast04; NE, not estimable; TEAE, treatment emergent adverse event.

References: 1. Modi S, et al. Nat Med 2025; 31: 4205-4213. 2. Modi S, et al. N Engl J Med 2022;387:9-20. 3. ENHERTU (trastuzumab deruxtecan). Summary of Product Characteristics. 4. Modi S, et al. Presented at 2023 European Society for Medical Oncology (ESMO) Congress, 20-24 October 2023. 5. Cortes J, et al. Nature Med 2024; 30: 2208-15. 6. Andre F, et al. Lancet 2023; 401: 1773-85. 7. Modi S, et al. New Engl J Med 2020; 382: 610-21.

ENHERTU's safety profile in DB04 was similar to the established safety profile in HER2+ studies¹⁻⁴

Most common drug-related TEAEs (in ≥20% of patients)¹

Adverse reactions	ENHERTU 5.4 mg/kg (n=371)		Chemotherapy (n=172)	
	All grades (%)	Grade ≥ 3 (%)	All grades (%)	Grade ≥ 3 (%)
Nausea	73	5	24	0
Fatigue*	52	8	44	5
Transaminases increased†	42	4	40	11
Alopecia	38	0	32	0
Neutropenia‡	35	14	53	42
Anaemia§	34	9	24	5
Vomiting	34	1	10	0
Decreased appetite	29	2	16	1
Thrombocytopenia¶	25	6	9	1
Leukopenia#	24	7	31	19
Diarrhoea	22	1	18	2
Constipation	22	0	13	0

Adapted from Modi S, et al. 2023.1 (March 2023 data cut-off)

- **Patients and HCPs need to be aware of the risk of ILD and to promptly identify and report symptoms in order to initiate appropriate management⁵**
- **Incidence of ILD/pneumonitis in DESTINY-Breast04¹**

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5 (fatal)	Any grade
ENHERTU (n=371)	13 (3.5%)	24 (6.5%)	4 (1.1%) ¹	0	4 (1.1%) ²	45 (12.1%)
Chemotherapy (n=172)	1 (0.6%)	0	0	0	0	1 (0.6%)

Adapted from Modi S, et al. 2023.1 (March 2023 data cut-off)

- **Most ILD events were Grade 1 or 2¹**
- **After an additional ~14 months of follow-up since the primary analysis⁶ (January 2022), no new cases of ILD and/or pneumonitis were reported¹**
- **ILD/pneumonitis is part of a risk management plan (see RMM)⁵**

For a full list of adverse events, please refer to the ENHERTU SmPC and RMM^{5,7}

*Includes the preferred terms fatigue, asthenia and malaise.† Includes the preferred terms aspartate aminotransferase increased, alanine aminotransferase increased, gamma glutamyltransferase increased and hepatic function abnormal. ‡Includes the preferred terms neutrophil count decreased and neutropenia.1 †Includes the preferred terms haemoglobin decreased, red cell count decreased, anaemia and haematocrit decreased.1 †Includes the preferred terms platelet count decreased and thrombocytopenia.1 †Includes the preferred terms white cell count decreased and leukopenia.1

ILD, interstitial lung disease; RMM, Risk Minimisation Materials

References: 1. Modi S, et al. Presented at 2023 European Society for Medical Oncology (ESMO) Congress, 20–24 October 2023; 2. Cortes J, et al. Nature Med 2024; 30: 2208-15. 3. Andre F, et al. Lancet 2023; 401: 1773-85. 4. Modi S, et al. New Engl J Med 2020; 382: 610-21. 5. ENHERTU (trastuzumab deruxtecan). Risk Minimisation Materials. 6. Modi S, et al. N Engl J Med 2022;387:9–20. 7. ENHERTU (trastuzumab deruxtecan) Summary of Product Characteristics.

Consider Enhertu in the treatment journey for your HER2-low mBC patients

As demonstrated in the DESTINY-Breast04 study, ENHERTU is the first HER2-directed therapy to bring significant survival benefit to patients with HER2-low (IHC 1+ or IHC 2+/ISH-) mBC after progression on standard therapies.^{1,2}

 in HR+/HER2-low mBC	 in HR+/HER2-low mBC	
~2 times longer mPFS vs chemotherapy² • 10.1 months with ENHERTU vs 5.4 months with chemotherapy (HR 0.51 [95% CI: 0.40-0.64])	>6-month increase in mOS vs chemotherapy¹ • 23.9 months with ENHERTU vs 17.6 months with chemotherapy (HR 0.69 [95% CI: 0.55-0.87])*	Safety profile consistent with HER2- positive mBC studies^{1,2} • The overall rate of grade ≥3 TEAEs was 54.4% with ENHERTU vs 67.4% with chemotherapy

~60% of your patients classified as HER2-negative could be reclassified as HER2-low and may be eligible for treatment with ENHERTU²

Knowing your patient's IHC score could help set them on an appropriate treatment pathway. If their score has not been recorded or previously classified as HER2-negative, ask your pathologist for their IHC score



ENHERTU website

Click or scan this QR code for more information on clinical trials, helpful resources and more

This is a promotional website developed by Daiichi Sankyo and AstraZeneca, intended for UK HCPs only.

*Updated analysis.

References: **1.** Modi S, et al. Presented at 2023 European Society for Medical Oncology (ESMO) Congress, 20–24 October 2023; Madrid, Spain. Presentation 376O. **2.** Modi S, et al. N Engl J Med 2022;387:9–20.



UK/ADC/07/26/0011 | August 2026