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

ENHERTU is FDA-approved as a post-neoadjuvant treatment for patients with HER2+ (IHC 3+ or ISH+) early breast cancer who have residual invasive disease[1]

The approval of this indication for ENHERTU was based on the results of the DESTINY-Breast05 trial

RECOMMENDED IN
NCCN GUIDELINES®

Fam-trastuzumab deruxtecan-nxki (ENHERTU) is an NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Category 1, Preferred Treatment Option[2]

- for patients with high risk of recurrence defined as inoperable cancer (cT4, N0–3, M0 or cT1–3, N2–3, M0) at presentation prior to neoadjuvant therapy or operable cancer (cT1–3, N0–1, M0) with axillary node–positive disease (ypN1–3) following preoperative therapy

Indication and Important Safety Information

Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for:

- HER2-Positive Early Breast Cancer
  - As neoadjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) Stage II or III breast cancer, as determined by an FDA-authorized test followed by a taxane, trastuzumab, and pertuzumab (THP)
  - As adjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) breast cancer who have residual invasive disease following neoadjuvant trastuzumab (with or without pertuzumab) and taxane-based treatment

Important Safety Information

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including severe, life-threatening, and fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms.**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.**

Contraindications

None.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Abbreviations: FDA, US Food and Drug Administration; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, *in situ* hybridization.

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In HER2+ eBC,

Post-neoadjuvant treatment is a critical opportunity to treat patients with residual disease and reduce metastatic recurrence[3,4]

Despite the established HER2+ eBC treatment paradigm, some patients remain at risk for poor outcomes

DIAGNOSIS → NEOADJUVANT TREATMENT → SURGERY → **POST-NEOADJUVANT TREATMENT**

Patients who **do not achieve pCR** have a

49% **increased risk of disease progression, recurrence, or death[5,a,b]**

HR: 0.67 (95% CI: 0.60, 0.74)

Among patients with residual disease

24% **will experience recurrence or death within 3 years with the current SOC[5,b]**

In patients who **have invasive residual disease** and then receive post-neoadjuvant therapy, up to

23% **did not achieve 3-year iDFS[3,c,d]**

The post-neoadjuvant setting provides a critical opportunity to address residual disease and reduce the risk of recurrence

[a]HR: 0.67 (95% CI: 0.60, 0.74). Risk is calculated using the reciprocal of the HR to evaluate risk between negative and positive directions (1/0.67=1.49).

[b]Based on 51 studies of 12,535 patients that reported outcomes relating to pCR as an indicator of EFS, from a systematic review and meta-analysis of 78 observational HER2+ neoadjuvant breast cancer clinical trials published between 2009 and 2020. Data from 25,150 patients were included in the trial-level analysis. pCR was defined as no evidence of invasive and/or *in situ* disease in the breast and/or axillary lymph nodes.[5]

[c]Included patients with inoperable disease at presentation (T4/N0-3/M0 or T1-4/N2-3/M0) and operable disease (T1-3/N0-1/M0) with residual invasive disease in breast or axillary lymph nodes. Based on the KATHERINE study evaluating adjuvant T-DM1 vs trastuzumab in patients with residual invasive eBC after neoadjuvant chemotherapy + HER2-targeted therapy.[3]

[d]3-year IDFS based on Kaplan-Meier estimates. iDFS defined as time from randomization to occurrence of one of the following: recurrence of ipsilateral locoregional invasive breast cancer; contralateral invasive breast cancer; distant disease recurrence; and death of any cause.[3]

Abbreviations: BMFI, brain metastases–free interval; CI, confidence interval; DFS, disease-free survival; DRFI, distant recurrent-free interval; eBC, early breast cancer; EFS, event-free survival; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; iDFS, invasive disease-free survival; pCR, pathological complete response; SOC, standard of care; T-DM1, ado-trastuzumab emtansine.

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DESTINY-Breast05 is a Phase 3 global superiority trial evaluating post-neoadjuvant ENHERTU vs T-DM1 in HER2+ eBC[1,6]

DESTINY-Breast05: open-label, multicenter, randomized clinical trial

Patients with HER2+ residual invasive early breast cancer (N=1635)

Key eligibility criteria:
- ≥18 years of age
- ECOG performance status 0-1
- Completed neoadjuvant systemic chemotherapy, including taxane and HER2-directed treatment
- Either:
  - Inoperable at disease presentation (T4/N0-3/M0 or T1-3/N2-3/M0) with residual invasive disease in breast or axillary lymph nodes

  OR
  - Operable at disease presentation (T1-3/N0-1/M0) with residual invasive disease in axillary lymph nodes (ypN1-3)
- LVEF ≥50%

RANDOMIZED 1:1[a]

Post-neoadjuvant treatment

- **ENHERTU Q3W**
  14 cycles (n=818)
- **T-DM1 Q3W**
  14 cycles (n=817)

Primary Efficacy Endpoint	• iDFS[b]	
Secondary Efficacy Endpoints	• DFS	• BMFI
	• DRFI	• OS

Stratification factors

- Operative status at disease presentation, prior to neoadjuvant therapy (operable vs inoperable)
- Post-neoadjuvant therapy pathologic nodal status (positive vs negative)
- Tumor hormone receptor status (positive vs negative)
- HER2-targeted neoadjuvant therapy approach (single vs dual)

Select exclusion criteria

- History of ILD/pneumonitis requiring treatment with steroids
- ILD/pneumonitis at screening
- ECOG performance status >1

[a]Included patients with a high risk of recurrence. In DESTINY-Breast05, high-risk characteristics were defined as inoperable (T4/N0-N3/M0 or T1-3/N2-3/M0) or operable (cT1-3/N0-1/M0) disease followed by axillary node–positive disease (ypN1-3) after neoadjuvant therapy.[6]

[b]iDFS defined as time from randomization to occurrence of one of the following: recurrence of ipsilateral locoregional invasive breast cancer; contralateral invasive breast cancer; distant disease recurrence; and death of any cause.[1]

Abbreviations: BMFI, brain metastases-free interval; DFS, disease-free survival; DRFI, distant recurrent-free interval; eBC, early breast cancer; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; iDFS, invasive disease-free survival; LVEF, left ventricular ejection fraction; OS, overall survival; Q3W, every 3 weeks; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)

Warnings and Precautions

Interstitial Lung Disease / Pneumonitis

Severe, life-threatening, or fatal interstitial lung disease (ILD), including pneumonitis, can occur in patients treated with ENHERTU. A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Monitor patients for signs and symptoms of ILD. Promptly investigate evidence of ILD. Evaluate patients with suspected ILD by radiographic imaging.

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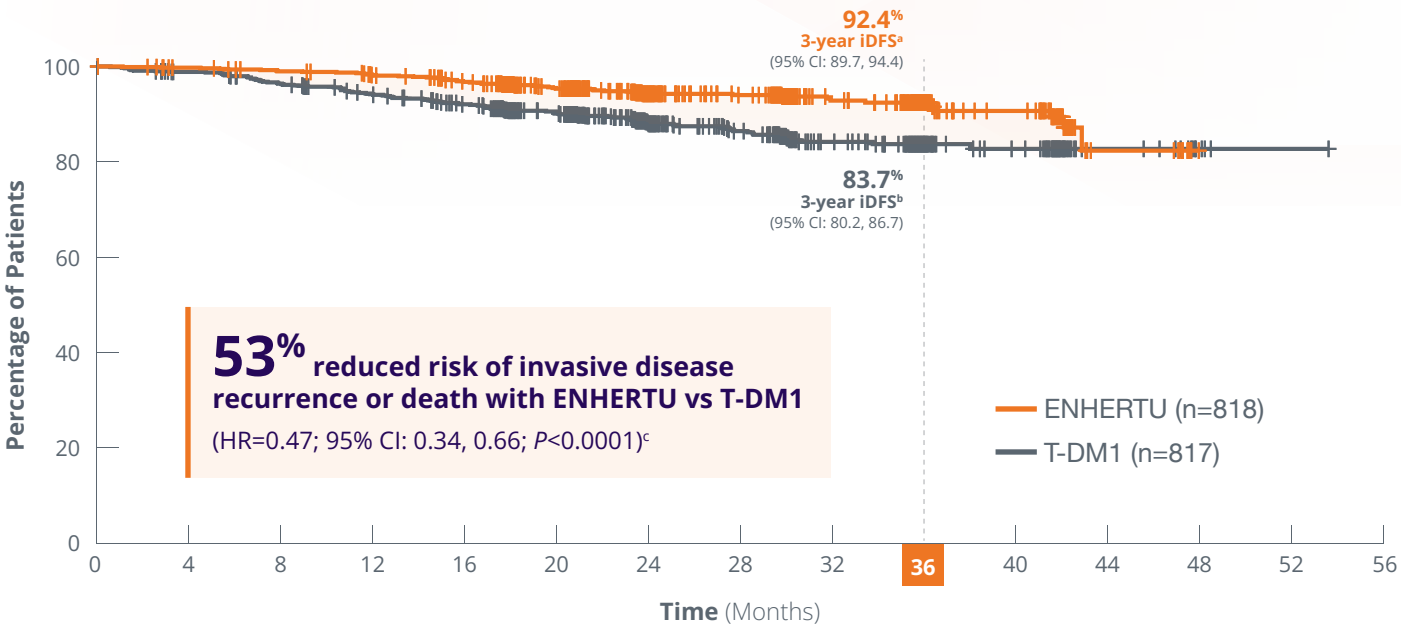
In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

Superior iDFS with ENHERTU vs T-DM1 in a head-to-head trial in the curative-intent setting[1]

Primary endpoint: iDFS



Number at Risk

ENHERTU	818	781	771	758	731	634	440	370	218	129	90	14	0	0	0
T-DM1	817	769	745	719	687	599	417	337	186	120	79	14	4	1	0

- Interim analysis (data cutoff July 2, 2025). Median duration of follow-up: 29.9 months[6]
- **The analysis at 3 years is based on Kaplan-Meier estimates and is descriptive only; DESTINY-Breast05 was not powered to assess a statistical difference between treatment groups at this time point**

ENHERTU delivered statistically significant iDFS[1]

[a]Number of events in the ENHERTU arm at 3 years: 51/818 (6%).[1]
[b]Number of events in the T-DM1 arm at 3 years: 102/817 (12%).[1]
[c]The stratified log-rank test *P* value is compared with the allocated alpha of 0.0183 for this interim analysis (with 74% of the planned number of events for final analysis).[1]
Abbreviations: BC, breast cancer; CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; iDFS, invasive disease-free survival; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Interstitial Lung Disease / Pneumonitis (cont'd)

Consider consultation with a pulmonologist. For asymptomatic ILD/pneumonitis (Grade 1), interrupt ENHERTU until resolved to Grade 0, then if resolved in ≤28 days from date of onset, maintain dose. If resolved in >28 days from date of onset, reduce dose 1 level. Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥0.5 mg/kg/day prednisolone or equivalent).

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In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

iDFS rates measured in prespecified subgroups[6]

	ENHERTU 3-year iDFS rate, % (95% CI)	T-DM1 3-year iDFS rate, % (95% CI)	Hazard Ratio (95% CI)
All patients (N=1635)	**92.4** (89.7, 94.4) (n=51/818)	**83.7** (80.2, 86.7) (n=102/817)	**0.47** (0.34, 0.66)
Operative status at disease presentation, before neoadjuvant therapy			
Operable disease	**92.8** (88.0, 95.7) (n=21/387)	**88.4** (83.8, 91.8) (n=34/393)	**0.58** (0.34, 1.01)
Inoperable disease	**92.0** (88.5, 94.5) (n=30/431)	**79.4** (73.9, 83.8) (n=68/424)	**0.41** (0.27, 0.63)
Pathological nodal status after neoadjuvant therapy			
Positive	**92.5** (89.3, 94.8) (n=40/660)	**82.5** (78.4, 85.9) (n=87/658)	**0.43** (0.29, 0.62)
Negative	**91.6** (85.3, 95.3) (n=11/158)	**88.3** (80.6, 93.0) (n=15/159)	**0.73** (0.33, 1.59)
Hormone receptor status			
Positive	**93.5** (90.6, 95.6) (n=33/581)	**86.8** (82.9, 89.9) (n=59/583)	**0.54** (0.35, 0.82)
Negative	**89.4** (82.0, 93.9) (n=18/237)	**75.6** (67.6, 81.9) (n=43/234)	**0.37** (0.22, 0.65)
HER2-targeted neoadjuvant therapy			
Single	**87.5** (77.6, 93.3) (n=13/176)	**77.9** (67.7, 85.2) (n=27/171)	**0.43** (0.22, 0.84)
Dual	**93.6** (90.9, 95.5) (n=38/642)	**85.2** (81.4, 88.2) (n=75/646)	**0.48** (0.33, 0.71)
Previous neoadjuvant therapy			
Anthracycline	**90.6** (86.1, 93.6) (n=32/423)	**80.3** (74.8, 84.8) (n=61/399)	**0.45** (0.29, 0.69)
Platinum compound	**93.9** (90.4, 96.1) (n=20/386)	**87.3** (82.4, 90.9) (n=37/392)	**0.54** (0.31, 0.93)

- **The DESTINY-Breast05 study protocol did not power the prespecified exploratory patient subgroup analysis to detect treatment effect differences between subgroups. Therefore, the clinical significance of these data cannot be determined**

Abbreviations: BC, breast cancer; CI, confidence interval; HER2, human epidermal growth factor receptor 2; iDFS, invasive disease-free survival; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Interstitial Lung Disease / Pneumonitis (cont'd)

For symptomatic ILD/pneumonitis (Grade 2 or greater), permanently discontinue ENHERTU. Promptly initiate systemic corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks.

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In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

iDFS rates measured in prespecified subgroups[6] (cont'd)

	ENHERTU 3-year iDFS rate, % (95% CI)	T-DM1 3-year iDFS rate, % (95% CI)	Hazard Ratio (95% CI)
Radiotherapy treatment			
Sequential radiotherapy	**93.8** (88.4, 96.7) (n=15/326)	**83.2** (76.4, 88.2) (n=34/279)	**0.35** (0.19, 0.64)
Concurrent radiotherapy	**92.8** (89.7, 95.0) (n=30/438)	**85.1** (80.6, 88.6) (n=57/480)	**0.55** (0.35, 0.85)
No radiotherapy	**81.0** (61.0, 91.4) (n=6/54)	**73.4** (56.4, 84.6) (n=11/58)	**0.57** (0.21, 1.55)
Central HER2 status			
IHC 3+	**91.8** (88.7, 94.1) (n=46/676)	**83.2** (79.2, 86.5) (n=86/670)	**0.49** (0.34, 0.70)
ISH+	**96.2** (91.0, 98.4) (n=5/140)	**86.5** (78.1, 91.8) (n=16/147)	**0.35** (0.13, 0.97)
Age			
<65 yr	**92.1** (89.2, 94.3) (n=46/735)	**84.1** (80.2, 87.2) (n=87/736)	**0.50** (0.35, 0.71)
≥65 yr	**94.9** (87.0, 98.1) (n=5/83)	**79.2** (67.9, 87.0) (n=15/81)	**0.31** (0.11, 0.86)
Race			
Asian	**95.1** (91.9, 97.0) (n=19/399)	**89.5** (85.3, 92.6) (n=34/386)	**0.53** (0.30, 0.93)
Non-Asian	**89.5** (84.5, 93.0) (n=32/419)	**77.9** (72.1, 82.7) (n=68/431)	**0.44** (0.29, 0.67)
Geographic region			
Asia	**95.0** (91.9, 97.0) (n=19/392)	**89.7** (85.4, 92.7) (n=33/380)	**0.55** (0.31, 0.96)
Europe	**93.1** (86.9, 96.4) (n=13/222)	**82.9** (75.8, 88.1) (n=30/223)	**0.40** (0.21, 0.77)
North America and Australia	**85.8** (63.9, 94.9) (n=5/57)	**80.7** (65.3, 89.7) (n=10/72)	**0.56** (0.19, 1.63)
Rest of the world	**85.1** (73.6, 91.8) (n=14/147)	**69.2** (56.3, 79.0) (n=29/142)	**0.43** (0.23, 0.81)

- **The DESTINY-Breast05 study protocol did not power the prespecified exploratory patient subgroup analysis to detect treatment effect differences between subgroups. Therefore, the clinical significance of these data cannot be determined**

Abbreviations: BC, breast cancer; CI, confidence interval; HER2, human epidermal growth factor receptor 2; iDFS, invasive disease-free survival; IHC, immunohistochemistry; ISH, *in situ* hybridization; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Interstitial Lung Disease / Pneumonitis (cont'd)

In the adjuvant HER2+ breast cancer setting, if drug-induced ILD is suspected, rule out radiotherapy-related pneumonitis. If only radiotherapy-related pneumonitis is suspected, consider interruption of ENHERTU for Grade 2 and permanently discontinue ENHERTU for Grade ≥3.

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In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

ENHERTU was assessed across additional efficacy endpoints

	ENHERTU (n=818)	**T-DM1** (n=817)
DFS[1,a]		
Number of events, n (%)	52 (6)	103 (13)
DFS rate at 3 years, % (95% CI)	92.3 (89.5, 94.3)	83.5 (79.9, 86.4)
Hazard ratio (95% CI)	**0.47** (0.34, 0.66); *P*<0.0001[b]	

	ENHERTU (n=818)	**T-DM1** (n=817)
BMFI[6,c]		
Number of events, n (%)	17 (2.1)	26 (3.2)
BMFI rate at 3 years, % (95% CI)	97.6 (96.2, 98.5)	95.8 (93.6, 97.2)
Hazard ratio (95% CI)	**0.64** (0.35, 1.17)	
DRFI[6,d]		
Number of events, n (%)	42 (5.1)	81 (9.9)
DRFI rate at 3 years, % (95% CI)	93.9 (91.4, 95.7)	86.1 (82.5, 89.1)
Hazard ratio (95% CI)	**0.49** (0.34, 0.71)	
OS[6,e]		
Number of events, n (%)	18 (2.2)	29 (3.5)
Maturity	2.9%	
Hazard ratio (95% CI)	**0.61** (0.34, 1.10)	

Although DFS was powered for statistical significance, the DFS rate at 3 years is based on Kaplan-Meier estimates and are descriptive only; DESTINY-Breast05 was not powered to assess a statistical difference between treatment groups at this time point. The DESTINY-Breast05 protocol did not power BMFI, DRFI, and OS (secondary endpoints) to detect differences between treatment arms. Therefore, no statistical conclusions can be made and the clinical significance of these data cannot be determined.

[a]DFS was defined as the time between randomization and the date of the first occurrence of an iDFS event (including death from any cause), including a second primary non-breast invasive cancer event or contralateral or ipsilateral ductal carcinoma *in situ*.[6]

[b]The stratified log-rank test *P* value is compared with the allocated alpha of 0.0144 for this interim analysis (with 70% of the planned number of events for final analysis).[1]

[c]BMFI was defined as the time between randomization and the date of documentation of brain metastases or leptomeningeal disease. BMFI was determined based on disease recurrence per investigator.[6]

[d]DRFI was defined as the time between randomization and the date of distant breast cancer recurrence. DRFI was determined based on disease recurrence per investigator.[6]

[e]OS was defined as the time from the date of randomization to the date of death from any cause. If death is not reported for a patient before data cutoff for the OS analysis, OS will be censored at the last contact date at which the patient is known to be alive.[6]

Abbreviations: BC, breast cancer; BMFI, brain metastases–free interval; CI, confidence interval; DRFI, distant recurrent-free interval; HER2, human epidermal growth factor receptor 2; OS, overall survival; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Interstitial Lung Disease / Pneumonitis (cont'd)

HER2-Positive Breast Cancer and Other Solid Tumors (5.4 mg/kg)

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, ILD occurred in 4.4% of patients. Median time to first onset was 2.7 months (range: 1.1 to 6.0). Fatal outcomes due to ILD and/or pneumonitis occurred in 1 patient (0.3%) treated with ENHERTU followed by THP.

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In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

The majority of ARs were Grade 1 or 2 in the ENHERTU arm[1]

Common adverse reactions (≥10% all Grades or ≥2% Grade 3-4) in DESTINY-Breast05

Adverse reactions		ENHERTU (n=806)		T-DM1 (n=801)	
		All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Gastrointestinal disorders	Nausea	71	4.5	29	0.1
	Constipation	32	0	16	0.1
	Vomiting	31	1.1	9	0.1
	Diarrhea	23	1.2	9	0.4
	Abdominal Pain[a]	15	0.2	9	0.1
	Stomatitis[b]	10	0.2	6	0.1
General disorders and administration site conditions	Fatigue[c]	54	6	37	1.0
	Pyrexia	10	0.1	12	0.2
Musculoskeletal and connective tissue disorders	Musculoskeletal pain[d]	23	0.7	32	0.6
Metabolism and nutrition disorders	Decreased appetite	20	0.9	10	0
Infections and infestations	Upper respiratory tract infection[e]	18	0.1	17	0.5
	COVID-19	17	0.5	20	0.4
Respiratory, thoracic, and mediastinal disorders	Interstitial lung disease[f]	17	1.1	3.7	0.2
	Cough	13	0	11	0
Nervous system disorders	Headache[g]	16	0.2	21	0.1
	Peripheral neuropathy[h]	13	0.4	20	1.1
	Dizziness[i]	11	0.4	7	0.1
Skin and subcutaneous tissue disorders	Alopecia	16	0	1.2	0
	Rash[j]	10	0.4	14	0.1
Investigations	Decreased weight	12	0.2	7	0.1

Events were graded using NCI-CTCAE v.5.0.
[a]Including abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, and gastrointestinal pain.[1]
[b]Including aphthous ulcer, cheilitis, mouth ulceration, mucosal inflammation, pharyngeal inflammation, and stomatitis.[1]
[c]Including asthenia, fatigue, lethargy, and malaise.[1]
[d]Including arthralgia, back pain, bone pain, limb discomfort, muscle spasms, musculoskeletal chest pain, musculoskeletal pain, myalgia, neck pain, and pain in extremity.[1]
[e]Including influenza, influenza like illness, laryngitis, nasopharyngitis, pharyngitis, rhinitis, sinusitis, and upper respiratory tract infection.[1]
[f]Including COVID-19 pneumonia, interstitial lung disease, lung opacity, organizing pneumonia, pneumocystis jirovecii pneumonia, pneumonia, and pneumonitis which was adjudicated as ILD (irrespective of causality). Adjudicated drug-related ILD for ENHERTU was 10% for all Grades and 0.9% for Grade 3 or 4 and for T-DM1, 1.6% for all Grades and 0% for Grades 3 or 4.[1]
[g]Including headache, migraine, and sinus headache.[1]
[h]Including dysesthesia, hyperesthesia, hypoesthesia, neuralgia, neuropathy peripheral, paresthesia, peripheral motor neuropathy, peripheral sensory neuropathy, and polyneuropathy.[1]
[i]Including dizziness, dizziness postural, vertigo, and vertigo positional.[1]
[j]Including dermatitis, dermatitis acneiform, dermatitis exfoliative generalized, drug eruption, dyshidrotic eczema, eczema, eczema asteatotic, erythema multiforme, palmar-plantar erythrodysesthesia syndrome, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, skin exfoliation, and Stevens-Johnson syndrome.[1]
Abbreviations: AR, adverse reaction; BC, breast cancer; HER2, human epidermal growth factor receptor 2; NCI-CTCAE, National Cancer Institute–Common Terminology Criteria for Adverse Events; T-DM1, ado-trastuzumab emtansine.

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In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

Benefit-risk profile of ENHERTU was demonstrated in DESTINY-Breast05[1,6]

No new safety signals were identified in the ENHERTU arm

- Median duration of post-neoadjuvant treatment: 10 months (range: 0.7-16) with ENHERTU

Clinically relevant AR considerations	**ENHERTU** (n=806)	**T-DM1** (n=801)	
Serious ARs	17%	13.6%	• Serious adverse reactions in ≥1% of patients who received ENHERTU were ILD/pneumonitis, radiation pneumonitis, pneumonia, and platelet count decreased. Fatal ARs occurred in 0.4% of patients including ILD/pneumonitis (2 patients) and respiratory tract infection (1 patient)
Permanent discontinuations due to ARs	18%	12.9%	• AR which resulted in permanent discontinuation of ENHERTU >2% included ILD/pneumonitis
Dose interruptions due to ARs	50%	41.1%	• ARs which required dosage interruptions in >2% included radiation pneumonitis, neutrophil count decreased, COVID-19, white blood cell count decreased, ILD/pneumonitis, platelet count decreased, upper respiratory tract infection, fatigue, cough, and pyrexia
Dose reductions due to ARs	26%	26.6%	• ARs which required dose reductions in >2% of patients included nausea, fatigue, platelet count decreased, ILD/pneumonitis, and neutrophil count decreased

- Interim analysis (data cutoff July 2, 2025). Median duration of follow-up for ENHERTU: 29.9 months[6]
- At data cutoff, 51 iDFS events were reported with ENHERTU, and 102 events were reported with T-DM1[6]

72.3% **of patients completed all 14 ENHERTU treatment cycles[6]**
- 76.3% completion rate with T-DM1

Abbreviations: AR, adverse reaction; BC, breast cancer; HER2, human epidermal growth factor receptor 2; iDFS, invasive disease-free survival; ILD, interstitial lung disease; T-DM1, ado-trastuzumab emtansine.

In patients with HER2+ residual invasive BC in the post-neoadjuvant setting

Early identification of ILD/pneumonitis is key to appropriate management

Incidence of adjudicated drug-related ILD/pneumonitis in DESTINY-Breast05[6]	ENHERTU (n=806)	T-DM1 (n=801)
All Grades, n (%)	77 (9.6)	13 (1.6)
Grade 1, n (%)	16 (2.0)	8 (1.0)
Grade 2, n (%)	52 (6.5)	5 (0.6)
Grade 3, n (%)	7 (0.9)	0 (0)
Grade 4, n (%)	0 (0)	0 (0)
Grade 5, n (%)[a]	2 (0.2)	0 (0)

In the post-neoadjuvant setting, drug-related ILD/pneumonitis occurred in 9.6% of patients, with less than 1% experiencing Grade ≥3 events with ENHERTU

Radiation pneumonitis was observed in both arms of DESTINY-Breast05 since most[b] patients received sequential or concurrent radiotherapy[1,6]

Radiation pneumonitis is an AE associated with radiation therapy[7]

- Per DESTINY-Breast05 study protocol, all patients received low-dose, non-contrast chest CT at screening[6]
- All patients who received adjuvant radiotherapy received low-dose chest CT at 6 weeks after the start of treatment, then every 12 weeks while on treatment, and again at a 40-day follow-up[6]
- Patients who received sequential radiotherapy had an additional low-dose chest CT after completing radiotherapy, prior to initiating treatment[6]
- Among patients receiving sequential or concurrent adjuvant radiotherapy in DESTINY-Breast05, radiation pneumonitis occurred in[1]:
  - 31% of patients receiving ENHERTU (N=757; all cases Grade 1 [27%] or Grade 2 [4.9%])
  - 31% of patients receiving T-DM1 (N=750; all cases Grade 1 [24%] or Grade 2 [7%])
- A higher incidence of radiation pneumonitis was reported for patients who received sequential vs concurrent adjuvant radiotherapy[1]:
  - ENHERTU arm: 34% sequential; 29% concurrent
  - T-DM1 arm: 37% sequential; 27% concurrent
- For patients treated with ENHERTU, median time to onset of first event of radiation pneumonitis was 4.1 months (range: 1.3–11.6)[1]
- Management of ENHERTU with radiotherapy-related pneumonitis differs from management of ENHERTU with ILD/pneumonitis

[a]Grade 5=fatal cases.[6]

[b]In DESTINY-Breast05, 93.4% of patients in the ENHERTU arm (n=764) and 92.9% of patients in the T-DM1 arm (n=759) received adjuvant radiotherapy.[6]

Abbreviations: AE, adverse event; BC, breast cancer; CT, computed tomography; HER2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; T-DM1, ado-trastuzumab emtansine.

Please see Important Safety Information throughout as well as on pages 14-17, and accompanying full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

AR management strategies can support patients' experience while receiving ENHERTU

Nausea & Vomiting

- ENHERTU is highly emetogenic which includes delayed nausea and/or vomiting[1]
- Premedication: Antiemetics may be administered in accordance with standard medical practice and patient tolerance for prophylaxis or management[1]

The NCCN Guidelines® for Antiemesis[8]

- Recommends **3-4-drug prophylactic antiemetic** regimens for **high emetic risk** agents, including fam-trastuzumab deruxtecan-nxki (ENHERTU), to prevent or decrease anticancer agent–induced acute and delayed emesis
- **Premedicate** with an antiemetic regimen for high emetic risk agents before infusion on Day 1, then **continue** for at least 3 days **(4 days total)** during every cycle, as it is harder to control nausea and/or vomiting once it has started

Management of ARs may require temporary interruption, dose reduction, or treatment discontinuation of ENHERTU

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Abbreviations: AR, adverse reaction; NCCN, National Comprehensive Cancer Network.

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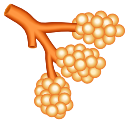
Monitoring for potential symptoms of ILD/pneumonitis is critical for early identification and proper management

Signs and symptoms of ILD/pneumonitis[1,9]

- Cough
- Dyspnea
- Fever
- New or worsening respiratory symptoms

Promptly investigate evidence of ILD/pneumonitis[10,11]



- Diagnosis of ILD/pneumonitis requires exclusion of other causes
- All events of ILD/pneumonitis, regardless of severity or seriousness, should be followed until resolution, including after drug discontinuation
- Advise patients of the potential risks of treatment and to contact their HCP immediately to report any of these symptoms

Patients and HCPs should be aware of ILD risk; regular monitoring and quickly identifying and reporting symptoms are needed for appropriate management[9,11]

- Frequency of CT scans was determined by the DESTINY-Breast05 study protocols (see ILD data on page 10 for more information)

Conduct routine reviews of scans to determine the presence of asymptomatic or symptomatic ILD/pneumonitis; identification based on scans, along with reporting of potential symptoms, may lead to modifying or discontinuing treatment[1,9,a]

For asymptomatic ILD (Grade 1)

- Interrupt ENHERTU until resolved to Grade 0, then:
  - If resolved in 28 days or less from date of onset, maintain dose
  - If resolved in greater than 28 days from date of onset, reduce dose one level
- Consider corticosteroid treatment (eg, ≥0.5 mg/kg/day prednisolone or equivalent)

For symptomatic ILD (Grade 2 or greater)

- Promptly initiate systemic corticosteroid treatment (eg, ≥1 mg/kg/day prednisolone or equivalent)
  - Continue for at least 14 days followed by gradual taper for at least 4 weeks
- Permanently discontinue ENHERTU in patients who are diagnosed with any symptomatic ILD/pneumonitis

Abbreviations: CT, computed tomography; HCP, healthcare provider; ILD, interstitial lung disease.

[a]In the adjuvant setting, if drug-induced ILD is suspected, rule out radiotherapy-related pneumonitis. If only radiotherapy-related pneumonitis is suspected, consider interruption of ENHERTU for Grade 2 and permanently discontinue ENHERTU for Grade ≥3.[1]

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ENHERTU defines the next era in HER2+ eBC in the post-neoadjuvant setting[1,6]

53%
reduced risk of invasive disease recurrence or death

53% reduced risk of invasive disease recurrence or death with ENHERTU vs T-DM1
(HR=0.47; 95% CI: 0.34, 0.66; *P*<0.0001)
- iDFS rates measured in prespecified subgroups

DEMONSTRATED
BENEFIT-RISK PROFILE

DESTINY-Breast05 established the benefit-risk profile for ENHERTU
- 72.3% of patients completed treatment with ENHERTU vs 76.3% with T-DM1

NO NEW SAFETY SIGNALS IDENTIFIED

The majority of ARs were Grade 1 or 2 in the ENHERTU arm, with no new safety signals identified
- Serious ARs with ENHERTU was 17% with ENHERTU vs 13.6% with T-DM1
- Radiation pneumonitis occurred in 31% of patients receiving ENHERTU and 31% of patients receiving T-DM1 who received adjuvant radiotherapy

Safety data from DESTINY-Breast05[1]

- The most common (≥20%) adverse reactions, including laboratory abnormalities, in patients receiving ENHERTU were decreased white blood cell count (80%), decreased lymphocyte count (72%), decreased neutrophil count (72%), nausea (71%), decreased hemoglobin (61%), increased aspartate aminotransferase (60%), fatigue (54%), increased alanine aminotransferase (53%), decreased platelet count (46%), increased blood alkaline phosphatase (39%), constipation (32%), vomiting (31%), decreased blood potassium (27%), diarrhea (23%), musculoskeletal pain (23%), and decreased appetite (20%)

ENHERTU is FDA-approved for certain patients with HER2+ eBC in the post-neoadjuvant setting. Click here to learn more

Abbreviations: AR, adverse reaction; CI, confidence interval; eBC, early breast cancer; FDA, US Food and Drug Administration; HER2, human epidermal growth factor receptor 2; HR, hazard ration; iDFS, invasive disease-free survival; NCCN, National Comprehensive Cancer Network; T-DM1, ado-trastuzumab emtansine.

Important Safety Information (cont'd)
Warnings and Precautions (cont'd)
Neutropenia
Severe neutropenia, including febrile neutropenia, can occur in patients treated with ENHERTU. Monitor complete blood counts prior to initiation of ENHERTU and prior to each dose, and as clinically indicated. For Grade 3 neutropenia (Absolute Neutrophil Count [ANC] <1.0 to 0.5 x 10^9/L), interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC <0.5 x 10^9/L), interrupt ENHERTU until resolved to Grade 2 or less, then reduce dose by 1 level.

Please see Important Safety Information throughout as well as on pages 14-17, and accompanying full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

Indication and Important Safety Information

Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for:

- HER2-Positive Early Breast Cancer
  - As neoadjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) Stage II or III breast cancer, as determined by an FDA-authorized test followed by a taxane, trastuzumab, and pertuzumab (THP)
  - As adjuvant treatment of adult patients with HER2-positive (IHC 3+ or ISH+) breast cancer who have residual invasive disease following neoadjuvant trastuzumab (with or without pertuzumab) and taxane-based treatment

Important Safety Information

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including severe, life-threatening, and fatal cases, have been reported with ENHERTU. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue ENHERTU in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms.**
- **Exposure to ENHERTU during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.**

Contraindications

None.

Warnings and Precautions

Interstitial Lung Disease / Pneumonitis

Severe, life-threatening, or fatal interstitial lung disease (ILD), including pneumonitis, can occur in patients treated with ENHERTU. A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Monitor patients for signs and symptoms of ILD. Promptly investigate evidence of ILD. Evaluate patients with suspected ILD by radiographic imaging. Consider consultation with a pulmonologist. For asymptomatic ILD/pneumonitis (Grade 1), interrupt ENHERTU until resolved to Grade 0, then if resolved in ≤28 days from date of onset, maintain dose. If resolved in >28 days from date of onset, reduce dose 1 level. Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥0.5 mg/kg/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), permanently discontinue ENHERTU. Promptly initiate systemic corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks. In the adjuvant HER2+ breast cancer setting, if drug-induced ILD is suspected, rule out radiotherapy-related pneumonitis. If only radiotherapy-related pneumonitis is suspected, consider interruption of ENHERTU for Grade 2 and permanently discontinue ENHERTU for Grade ≥3.

HER2-Positive Breast Cancer and Other Solid Tumors (5.4 mg/kg)

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, ILD occurred in 4.4% of patients. Median time to first onset was 2.7 months (range: 1.1 to 6.0). Fatal outcomes due to ILD and/or pneumonitis occurred in 1 patient (0.3%) treated with ENHERTU followed by THP.

Neutropenia

Severe neutropenia, including febrile neutropenia, can occur in patients treated with ENHERTU. Monitor complete blood counts prior to initiation of ENHERTU and prior to each dose, and as clinically indicated. For Grade 3 neutropenia (Absolute Neutrophil Count [ANC] <1.0 to 0.5 x 10^9/L), interrupt ENHERTU until resolved to Grade 2 or less, then maintain dose. For Grade 4 neutropenia (ANC <0.5 x 10^9/L), interrupt ENHERTU until resolved to Grade 2 or less, then reduce dose by 1 level. For febrile neutropenia (ANC <1.0 x 10^9/L and temperature >38.3° C or a sustained temperature of ≥38° C for more than 1 hour), interrupt ENHERTU until resolved, then reduce dose by 1 level.

HER2-Positive Breast Cancer and Other Solid Tumors (5.4 mg/kg)

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, a decrease in neutrophil count was reported in 58% of patients. Seventeen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 42 days (range: 11 to 165). Febrile neutropenia was reported in 0.9% of patients.

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

Left Ventricular Dysfunction

Patients treated with ENHERTU may be at increased risk of developing left ventricular dysfunction. Left ventricular dysfunction (LVD) has been observed with anti-HER2 therapies, including ENHERTU. Assess left ventricular ejection fraction (LVEF) prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVD through treatment interruption. When LVEF is >45% and absolute decrease from baseline is 10-20%, continue treatment with ENHERTU. When LVEF is 40-45% and absolute decrease from baseline is <10%, continue treatment with ENHERTU and repeat LVEF assessment within 3 weeks. When LVEF is 40-45% and absolute decrease from baseline is 10-20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF has not recovered to within 10% from baseline, permanently discontinue ENHERTU. If LVEF recovers to within 10% from baseline, resume treatment with ENHERTU at the same dose. When LVEF is <40% or absolute decrease from baseline is >20%, interrupt ENHERTU and repeat LVEF assessment within 3 weeks. If LVEF of <40% or absolute decrease from baseline of >20% is confirmed, permanently discontinue ENHERTU. Permanently discontinue ENHERTU in patients with symptomatic congestive heart failure. Treatment with ENHERTU has not been studied in patients with a history of clinically significant cardiac disease or LVEF <50% prior to initiation of treatment.

HER2-Positive Breast Cancer and Other Solid Tumors (5.4 mg/kg)

ENHERTU followed by THP

In patients treated with ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11, LVD was reported in 1.3% of patients, of which 0.3% were Grade 3.

Embryo-Fetal Toxicity

ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. Verify the pregnancy status of females of reproductive potential prior to the initiation of ENHERTU. Advise females of reproductive potential to use effective contraception during treatment and for 7 months after the last dose of ENHERTU. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after the last dose of ENHERTU.

Additional Dose Modifications

Thrombocytopenia

For Grade 3 thrombocytopenia (platelets <50 to 25 x 10^9/L) interrupt ENHERTU until resolved to Grade 1 or less, then maintain dose. For Grade 4 thrombocytopenia (platelets <25 x 10^9/L) interrupt ENHERTU until resolved to Grade 1 or less, then reduce dose by 1 level.

Adverse Reactions

HER2-Positive Early Breast Cancer

DESTINY-Breast11

The safety of ENHERTU followed by THP was evaluated in 320 patients with HER2-positive (IHC 3+ or ISH+) early breast cancer who received at least 1 dose of ENHERTU 5.4 mg/kg followed by THP in DESTINY-Breast11. ENHERTU was administered by intravenous infusion once every three weeks for 4 cycles followed by THP for 4 cycles. The median duration of treatment was 5.6 months (range: 0.7 to 9.1) for patients who received ENHERTU followed by THP.

Serious adverse reactions occurred in 11% of patients receiving ENHERTU followed by THP, including COVID-19 (0.9%) and ILD/pneumonitis (0.6%). Fatal adverse reactions occurred in 0.6% of patients, including ILD/pneumonitis and death not otherwise specified (1 patient each).

In patients treated with ENHERTU followed by THP, the permanent discontinuation of ENHERTU due to adverse reactions occurred in 1.3%, of which ILD/pneumonitis accounted for 0.6%. Dose interruptions of ENHERTU due to adverse reactions occurred in 11% of patients. The most frequent adverse reactions (>2%) associated with dose interruption were decreased neutrophil count and COVID-19. Dose reductions of ENHERTU occurred in 2.5% of patients treated with ENHERTU.

The most common (≥20%) adverse reactions in patients treated with ENHERTU followed by THP, including laboratory abnormalities, were decreased hemoglobin (83%), increased alanine aminotransferase (79%), increased aspartate aminotransferase (74%), decreased white blood cell count (67%), nausea (65%), peripheral neuropathy (59%), diarrhea (59%), decreased neutrophil count (58%), alopecia (48%), fatigue (41%), decreased lymphocyte count (40%), rash (31%), musculoskeletal pain (30%), decreased blood potassium (29%), constipation (29%), vomiting (29%), stomatitis (23%), and decreased appetite (20%).

Important Safety Information (cont'd)

Adverse Reactions (cont'd)

DESTINY-Breast05

The safety of ENHERTU was evaluated in 806 patients with HER2-positive breast cancer with residual invasive disease following neoadjuvant HER2-targeted therapy who then received at least one dose of ENHERTU 5.4 mg/kg. ENHERTU was administered by intravenous infusion once every three weeks for 14 cycles. The median duration of treatment was 10 months (range: 0.7 to 16) for patients who received ENHERTU.

Serious adverse reactions occurred in 17% of patients receiving ENHERTU. Serious adverse reactions in ≥1% of patients who received ENHERTU were ILD/pneumonitis, radiation pneumonitis, pneumonia, and platelet count decreased. Fatal adverse reactions occurred in 0.4% of patients including ILD/pneumonitis (2 patients) and respiratory tract infection (1 patient).

Permanent discontinuation of ENHERTU due to an adverse reaction occurred in 18% of patients. The adverse reaction which resulted in permanent discontinuation of ENHERTU >2% included ILD/pneumonitis. Dose interruptions of ENHERTU due to an adverse reaction occurred in 50% of patients. Adverse reactions which required dosage interruptions in >2% included radiation pneumonitis, neutrophil count decreased, COVID-19, white blood cell count decreased, ILD/pneumonitis, platelet count decreased, upper respiratory tract infection, fatigue, cough, and pyrexia. Dose reductions of ENHERTU due to an adverse reaction occurred in 26% of patients. Adverse reactions which required dose reductions in >2% of patients included nausea, fatigue, platelet count decreased, ILD/pneumonitis, and neutrophil count decreased.

The most common (≥20%) adverse reactions, including laboratory abnormalities, in patients receiving ENHERTU were decreased white blood cell count (80%), decreased lymphocyte count (72%), decreased neutrophil count (72%), nausea (71%), decreased hemoglobin (61%), increased aspartate aminotransferase (60%), fatigue (54%), increased alanine aminotransferase (53%), decreased platelet count (46%), increased blood alkaline phosphatase (39%), constipation (32%), vomiting (31%), decreased blood potassium (27%), diarrhea (23%), musculoskeletal pain (23%), and decreased appetite (20%).

ILD was reported in 17% of patients receiving ENHERTU, which included COVID-19 pneumonia, interstitial lung disease, lung opacity, organizing pneumonia, pneumocystis jirovecii pneumonia, pneumonia, and pneumonitis which was adjudicated as ILD (irrespective of causality). Adjudicated drug-related ILD for ENHERTU was 10% for all Grades and 0.9% for Grades 3 or 4.

Use in Specific Populations

- **Pregnancy:** ENHERTU can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risks to a fetus. There are clinical considerations if ENHERTU is used in pregnant women, or if a patient becomes pregnant within 7 months after the last dose of ENHERTU.
- **Lactation:** There are no data regarding the presence of ENHERTU in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with ENHERTU and for 7 months after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy testing: Verify pregnancy status of females of reproductive potential prior to initiation of ENHERTU. Contraception: *Females*: ENHERTU can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with ENHERTU and for 7 months after the last dose. *Males*: Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ENHERTU and for 4 months after the last dose. Infertility: ENHERTU may impair male reproductive function and fertility.
- **Pediatric Use:** Safety and effectiveness of ENHERTU have not been established in pediatric patients.

Important Safety Information (cont'd)

Use in Specific Populations (cont'd)

- **Geriatric Use:** *ENHERTU followed by THP*: Of the 320 patients with HER2-positive early breast cancer treated with ENHERTU 5.4 mg/kg followed by THP, 12% were ≥65 years and 1.6% were ≥75 years. No overall differences in efficacy were observed between patients ≥65 years compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients ≥65 years (38%) as compared to younger patients (30%).
- **Renal Impairment:** A higher incidence of Grade 1 and 2 ILD/pneumonitis has been observed in patients with moderate renal impairment. Monitor patients with moderate renal impairment more frequently. The recommended dosage of ENHERTU has not been established for patients with severe renal impairment (CLcr <30 mL/min).
- **Hepatic Impairment:** In patients with moderate hepatic impairment, due to potentially increased exposure, monitor for increased adverse reactions related to the topoisomerase inhibitor, DXd. The recommended dosage of ENHERTU has not been established for patients with severe hepatic impairment (total bilirubin >3 times ULN and any AST).

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see accompanying full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

References: 1. ENHERTU. Prescribing Information. Daiichi Sankyo, Inc.; 2026. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.3.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. Accessed May 12, 2026. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** von Minckwitz G , et al. *N Engl J Med*. 2019;380(7):617-628. doi:10.1056/NEJMoa1814017 **4.** Mahtani R, et al. *Cancers (Basel)*. 2025;17(11):1848. doi:10.3390/cancers17111848 **5.** Davey MG, et al. *BJS Open*. 2022;6(3):zrac028. doi:10.1093/bjsopen/zrac028 **6.** Loibl S, et al. *N Engl J Med*. 2026;394(9):845-857. **7.** Rahi MS, et al. *Clin Pract*. 2021;11(3):410-429. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. Accessed May 11, 2026. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **9.** Data on file. Daiichi Sankyo, Inc. Basking Ridge, NJ. **10.** Harbeck, et al. *Ann Oncol*. 2026;37(2):166-179. doi:10.1016/j.annonc.2025.10.019 **11.** Swain, et al. *Cancer Treat Rev*. 2022;106:102378. doi:10.1016/j.ctrv.2022.102378

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