IN 2L HER2+ mBC[1]

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

In DESTINY-Breast03, a head-to-head study vs ado-trastuzumab emtansine (T-DM1),

UNPARALLELED PFS
THE STANDARD OF CARE IN 2L HER2+ mBC[1-3]

	ENHERTU	T-DM1
Primary mPFS (BICR)	**NR** (n=261; 95% CI: 18.5, NE)	**6.8** months (n=263; 95% CI: 5.6, 8.2)
Secondary ORR[a] (BICR)	**82.7%** (n=205/248; 95% CI: 77.4, 87.2) 15.7% CR (n=39) + 66.9% PR (n=166)	**36.1%** (n=87/241; 95% CI: 30.0, 42.5) 8.3% CR (n=20) + 27.8% PR (n=67)
Secondary mPFS (investigator)	**25.1** months (n=261; 95% CI: 22.1, NE)	**7.2** months (n=263; 95% CI: 6.8, 8.3)

72% reduction in risk of disease progression or death
HR: 0.28 (95% CI: 0.22, 0.37; *P*<0.0001)

~83% confirmed ORR

25.1 months mPFS
HR: 0.26 (95% CI: 0.20, 0.35)

DESTINY-Breast03 is a Phase 3, multicenter, open-label, randomized, head-to-head study to compare efficacy and safety of ENHERTU vs T-DM1 of 524 adults with HER2+ unresectable and/or mBC who received prior trastuzumab and taxane therapy for metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy. ENHERTU patients received 5.4 mg/kg IV Q3W until unacceptable toxicity or disease progression. Primary endpoint was PFS (BICR) according to RECIST v1.1. Secondary endpoints included OS, ORR, and PFS (investigator).[1,2]

Secondary endpoints (ORR and mPFS by investigator) were not tested for statistical significance and not powered to show differences between treatment arms.

NCCN CATEGORY 1, Preferred 2L Option—NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommends fam-trastuzumab deruxtecan-nxki (ENHERTU) as Category 1 preferred option as second-line therapy for recurrent unresectable (local or regional) or stage IV HER2+ disease[3,b]

[a]Analysis was performed based on the patients with measurable disease assessed by BICR at baseline (n=248 patients randomized to receive ENHERTU; n=241 for T-DM1).[1]
[b]Fam-trastuzumab deruxtecan-nxki may be considered in the first-line metastatic setting as an option for select patients (ie, those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens]). Regimen may also be used as an option for third-line and beyond; the optimal sequence for third-line therapy and beyond is not known.[3]

Important Safety Information

Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:

- In the metastatic setting, or
- In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including 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.**

Please see Important Safety Information on pages 6-7, and click here for full Prescribing Information, including Boxed WARNINGS, and click here for Medication Guide.

In DESTINY-Breast03, a head-to-head study vs T-DM1,

ENHERTU delivered groundbreaking progression-free survival in 2L to patients with HER2+ mBC[1,a]

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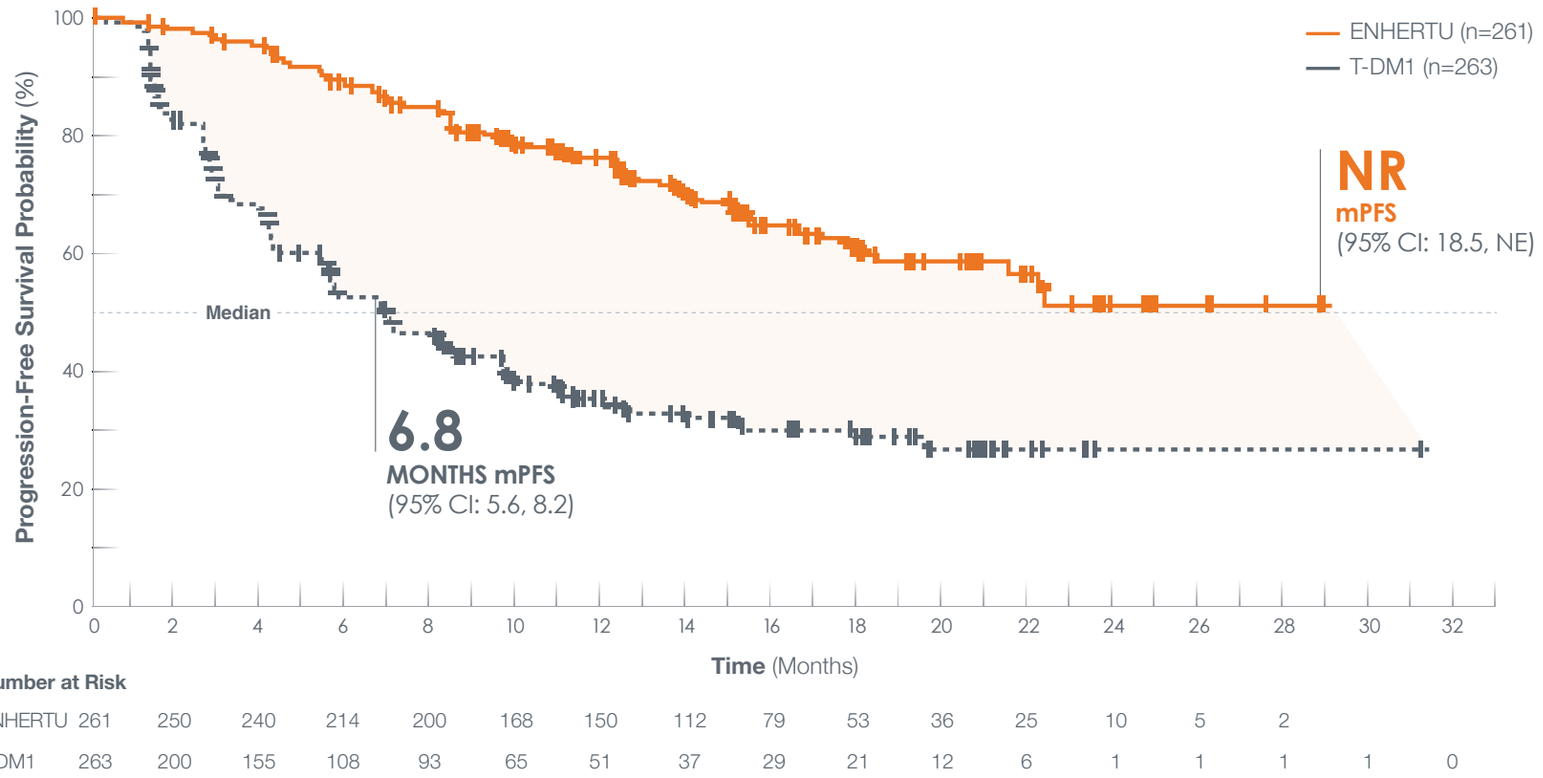
Primary endpoint: Progression-free survival as assessed by BICR



72% reduction **in risk of disease progression or death** vs T-DM1 (HR: 0.28; 95% CI: 0.22, 0.37; *P*<0.0001)

Efficacy endpoint	ENHERTU (n=261)	T-DM1 (n=263)
Secondary: mPFS (investigator), months (95% CI)[2]	**25.1** (22.1, NE)	**7.2** (6.8, 8.3)
	HR: 0.26 (0.20, 0.35)	

- PFS (investigator) was not tested for statistical significance and not powered to show a difference between treatment arms

[a]PFS (BICR) based on a median duration of follow-up of 15.5 months (range: 15.1-16.6) for ENHERTU and 13.9 months (range: 11.8-15.1) for T-DM1.[4]

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. 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 one 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.

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In DESTINY-Breast03, a head-to-head study vs T-DM1,

ENHERTU delivered nearly 83% confirmed ORR, more than double the 36.1% T-DM1 response[1,4,a]

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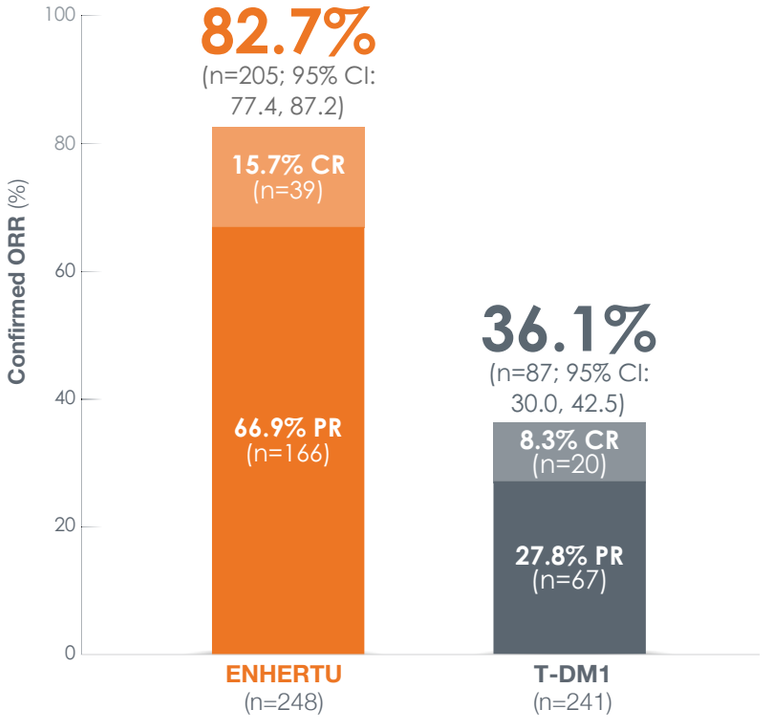
Secondary endpoint: Confirmed objective response rate per BICR



	ENHERTU (n=248)	T-DM1 (n=241)
CR, % (n)	**15.7** (39)	**8.3** (20)
PR, % (n)	**66.9** (166)	**27.8** (67)
SD, % (n)	**14.9** (37)	**40.2** (97)
PD, % (n)	**1.2** (3)	**17.8** (43)
NE, % (n)	**1.2** (3)	**5.8** (14)
DCR (CR+ PR+SD), % (n)	**97.5** (242)	**76.3** (184)

- 99% of patients did not progress on treatment
- ~98% of patients had disease control (CR+PR+SD)

- ORR was not tested for statistical significance and not powered to show differences between treatment arms

Nearly every patient (~98%) in the ENHERTU arm experienced a response from treatment

[a]Analysis was performed based on the patients with measurable disease assessed by BICR at baseline (n=248 patients randomized to receive ENHERTU; n=241 for T-DM1).[1]

Important Safety Information (cont'd)

Warnings and Precautions

Interstitial Lung Disease / Pneumonitis (cont'd)

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.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)
In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, ILD occurred in 12% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 1.0% of patients treated with ENHERTU. Median time to first onset was 5 months (range: 0.9 to 23).

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.

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Safety data from DESTINY-Breast03 confirmed the benefit-risk profile of ENHERTU for HER2+ mBC (5.4 mg/kg) demonstrated in prior studies[1,a]

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The majority of adverse reactions were Grade 1 or 2

- Median duration of treatment was 14 months (range: 0.7 to 30) with ENHERTU and 7 months (range: 0.7 to 25) with T-DM1[1]
- Prophylactic or supportive treatment of ENHERTU or T-DM1–induced adverse reactions was at the discretion of the treating physician and institutional guidelines[4]

Common adverse reactions (≥10% All Grades or ≥2% Grades 3-4) in patients treated with ENHERTU in DESTINY-Breast03[1]

Adverse reactions		ENHERTU 5.4 mg/kg (n=257)		T-DM1 3.6 mg/kg (n=261)	
		All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Gastrointestinal disorders	Nausea	76	7	30	0.4
	Vomiting	49	1.6	10	0.8
	Constipation	34	0	20	0
	Diarrhea	29	1.2	7	0.4
	Abdominal pain[b]	21	0.8	8	0.4
	Stomatitis[c]	20	0.8	5	0
	Dyspepsia	11	0	6	0
General disorders and administration site conditions	Fatigue[d]	49	6	35	0.8
Blood and lymphatic system disorders	Anemia[e]	33	7	17	6
Skin and subcutaneous tissue disorders	Alopecia[f]	37	0.4	3.1	0
Musculoskeletal and connective tissue disorders	Musculoskeletal pain[g]	31	1.2	25	0.4
Metabolism and nutrition disorders	Decreased appetite	29	1.6	17	0.4
Investigations	Decreased weight	17	1.2	6	0.4
Respiratory, thoracic, and mediastinal disorders	Respiratory infection[h]	22	0.8	12	1.1
	Epistaxis	11	0	16	0.4
	Cough	11	0.4	10	0
	Interstitial lung disease[i]	11	0.8	1.9	0
Nervous system disorders	Headache[j]	22	0.4	16	0
	Peripheral neuropathy[k]	13	0.4	14	0.4
	Dizziness	13	0.4	8	0

- **The most common (≥20%) laboratory abnormalities for ENHERTU** were decreased white blood cell count (74%), decreased neutrophil count (70%), increased aspartate aminotransferase (67%), decreased hemoglobin (64%), decreased lymphocyte count (55%), increased alanine aminotransferase (53%), decreased platelet count (52%), increased blood alkaline phosphatase (49%), hypokalemia (35%), and increased blood bilirubin (20%)

Events were graded using NCI-CTCAE v.5.0.
[a]Prior ENHERTU HER2+ mBC studies: Phase 2 DESTINY-Breast01 and Phase 1 DS8201-A-J101. [b]Grouped term of abdominal pain includes PTs of abdominal pain, abdominal discomfort, lower abdominal pain, and upper abdominal pain. [c]Grouped term of stomatitis includes PTs of stomatitis, aphthous ulcer, mouth ulceration, oral mucosa erosion, and oral mucosal eruption. [d]Grouped term of fatigue includes PTs of fatigue, asthenia, malaise, and lethargy. [e]Grouped term of anemia includes PTs of anemia, decreased hemoglobin, and decreased red blood cell count. [f]This Grade 3 event was reported by the investigator. Per NCI-CTCAE v.5.0, the highest NCI-CTCAE grade for alopecia is Grade 2. [g]Grouped term of musculoskeletal pain includes PTs of back pain, myalgia, pain in extremity, musculoskeletal pain, muscle spasms, bone pain, neck pain, musculoskeletal chest pain, and limb discomfort. [h]Grouped term of respiratory infection includes PTs of respiratory tract infection, lower and upper respiratory tract infection, pneumonia, influenza, influenza-like illness, viral upper respiratory infection, bronchitis, and respiratory syncytial virus infection. [i]Interstitial lung disease includes events that were adjudicated as ILD for ENHERTU: pneumonitis, interstitial lung disease, organizing pneumonia, pneumonia, and pulmonary mass. For T-DM1: pneumonitis, interstitial lung disease, organizing pneumonia, and pulmonary embolism. [j]Grouped term of headache includes PTs of headache and migraine. [k]Grouped term of peripheral neuropathy includes PTs of peripheral neuropathy, peripheral sensory neuropathy, and paresthesia.

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Safety data from DESTINY-Breast03 confirmed the benefit-risk profile of ENHERTU for HER2+ mBC (5.4 mg/kg) demonstrated in prior studies[1,2,4,a]

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- Median duration of treatment was 14 months (range: 0.7 to 30) with ENHERTU and 7 months (range: 0.7 to 25) with T-DM1

	ENHERTU 5.4 mg/kg (n=257)	T-DM1 3.6 mg/kg (n=261)	
Serious adverse reactions	19.1%	18.0%	• For ENHERTU, serious ARs in >1% of patients were vomiting, ILD, pneumonia, pyrexia, and urinary tract infection. Fatalities occurred in 2 patients (1 due to COVID-19 and 1 due to sudden death)
Discontinuations due to adverse reactions	14%	7%	• For ENHERTU, most frequent (>2%) was ILD/pneumonitis (8%). Permanently discontinue ENHERTU in patients who are diagnosed with any symptomatic ILD (Grade ≥2)
Dose interruptions due to adverse reactions	44%	23%	• For ENHERTU, most frequent (>2%) were neutropenia, leukopenia, anemia, thrombocytopenia, pneumonia, nausea, fatigue, and ILD/pneumonitis
Dose reductions due to adverse reactions	21%	13%	• For ENHERTU, most frequent (>2%) were nausea, neutropenia, and fatigue

ILD and pneumonitis, including Grade 5 cases, have been reported with ENHERTU 5.4 mg/kg (pooled clinical studies; N=984); the majority were Grade 1 or 2 in the ENHERTU arm (n=98/118)[1,4,b]

- In patients with mBC and other solid tumors, ILD occurred in 12% of patients (n=118/984); fatal outcomes due to ILD and/or pneumonitis occurred in 1% of patients (n=10/984)
- Median time to first onset was 5 months (range: 0.9-23)

In DESTINY-Breast03, no Grade 4 or 5 adjudicated drug-related ILD/pneumonitis events were observed[4]

Adjudicated as drug-related ILD, n (%)	ENHERTU 5.4 mg/kg (n=257)	T-DM1 3.6 mg/kg (n=261)
Grade 1	7 (2.7)	4 (1.5)
Grade 2	18 (7.0)	1 (0.4)
Grade 3	2 (0.8)	0
Grade 4	0	0
Grade 5	0	0
All Grades	27 (10.5)	5 (1.9)

- In patients treated with ENHERTU, the majority of ILD/pneumonitis events were Grade 1 or 2 (n=25/27)
- Symptom identification is key to diagnosis; monitor patients and initiate management at first sign of ILD

[a]Prior ENHERTU HER2+ mBC studies: Phase 2 DESTINY-Breast01 and Phase 1 DS8201-A-J101.
[b]Grade 5=fatal cases.[4]

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Important Safety Information

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Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:

- In the metastatic setting, or
- In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including 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 one 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.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, ILD occurred in 12% of patients. Fatal outcomes due to ILD and/or pneumonitis occurred in 1.0% of patients treated with ENHERTU. Median time to first onset was 5 months (range: 0.9 to 23).

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 one 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 one level.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, a decrease in neutrophil count was reported in 65% of patients. Sixteen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 2 to 664). Febrile neutropenia was reported in 1.1% of patients.

Left Ventricular Dysfunction

Patients treated with ENHERTU may be at increased risk of developing left ventricular dysfunction. Left ventricular ejection fraction (LVEF) decrease has been observed with anti-HER2 therapies, including ENHERTU. Assess LVEF prior to initiation of ENHERTU and at regular intervals during treatment as clinically indicated. Manage LVEF decrease 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.

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

In patients with metastatic breast cancer and other solid tumors treated with ENHERTU 5.4 mg/kg, LVEF decrease was reported in 3.6% of patients, of which 0.4% 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

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Important Safety Information (cont'd)

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Warnings and Precautions

Embryo-Fetal Toxicity (cont'd)

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 one level.

Adverse Reactions

Metastatic Breast Cancer and Other Solid Tumors (5.4 mg/kg)

The pooled safety population reflects exposure to ENHERTU 5.4 mg/kg intravenously every 3 weeks in 984 patients in Study DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast03, DESTINY-Breast04, and another clinical trial. Among these patients 65% were exposed for >6 months and 39% were exposed for >1 year. In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (71%), decreased hemoglobin (66%), decreased neutrophil count (65%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (47%), increased aspartate aminotransferase (48%), vomiting (44%), increased alanine aminotransferase (42%), alopecia (39%), increased blood alkaline phosphatase (39%), constipation (34%), musculoskeletal pain (32%), decreased appetite (32%), hypokalemia (28%), diarrhea (28%), and respiratory infection (24%).

HER2-Positive Metastatic Breast Cancer

DESTINY-Breast03

The safety of ENHERTU was evaluated in 257 patients with unresectable or metastatic HER2-positive breast cancer who received at least one dose of ENHERTU 5.4 mg/kg intravenously every three weeks in DESTINY-Breast03. The median duration of treatment was 14 months (range: 0.7 to 30).

Serious adverse reactions occurred in 19% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were vomiting, interstitial lung disease, pneumonia, pyrexia, and urinary tract infection. Fatalities due to adverse reactions occurred in 0.8% of patients including COVID-19 and sudden death (one patient each).

ENHERTU was permanently discontinued in 14% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 44% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, leukopenia, anemia, thrombocytopenia, pneumonia, nausea, fatigue, and ILD/pneumonitis. Dose reductions occurred in 21% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were nausea, neutropenia, and fatigue.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (74%), decreased neutrophil count (70%), increased aspartate aminotransferase (67%), decreased hemoglobin (64%), decreased lymphocyte count (55%), increased alanine aminotransferase (53%), decreased platelet count (52%), fatigue (49%), vomiting (49%), increased blood alkaline phosphatase (49%), alopecia (37%), hypokalemia (35%), constipation (34%), musculoskeletal pain (31%), diarrhea (29%), decreased appetite (29%), respiratory infection (22%), headache (22%), abdominal pain (21%), increased blood bilirubin (20%), and stomatitis (20%).

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.
- **Geriatric Use:** Of the 883 patients with breast cancer treated with ENHERTU 5.4 mg/kg, 22% were ≥65 years and 3.6% were ≥75 years. No overall differences in efficacy within clinical studies were observed between patients ≥65 years of age compared to younger patients. There was a higher incidence of Grade 3-4 adverse reactions observed in patients aged ≥65 years (60%) as compared to younger patients (48%).
- **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, closely monitor for increased toxicities related to the topoisomerase inhibitor. 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 click here for full Prescribing Information, including Boxed WARNINGS, and click here for Medication Guide.

ENHERTU is the Standard of Care in 2L HER2+ mBC[1,3]

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20 mg/mL INJECTION FOR INTRAVENOUS USE

Most common (≥20%) ARs, including laboratory abnormalities, in the pooled safety population of patients with mBC and other solid tumors treated with ENHERTU 5.4 mg/kg (N=984)[1]

- Nausea (76%), decreased white blood cell count (71%), decreased hemoglobin (66%), decreased neutrophil count (65%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (47%), increased aspartate aminotransferase (48%), vomiting (44%), increased alanine aminotransferase (42%), alopecia (39%), increased blood alkaline phosphatase (39%), constipation (34%), musculoskeletal pain (32%), decreased appetite (32%), hypokalemia (28%), diarrhea (28%), and respiratory infection (24%)

Abbreviations

2L, second line
AE, adverse event
AR, adverse reaction
BICR, blinded independent central review
CI, confidence interval
CR, complete response
DCR, disease control rate
HER2, human epidermal growth factor receptor 2
HR, hazard ratio
ILD, interstitial lung disease
IV, intravenous
mBC, metastatic breast cancer
mPFS, median progression-free survival
MedDRA, Medical Dictionary for Regulatory Activities
NCCN, National Comprehensive Cancer Network
NCI-CTCAE, National Cancer Institute–Common Terminology Criteria for Adverse Events
NE, not evaluable
NR, not reached
ORR, objective response rate
OS, overall survival
PD, progressive disease
PFS, progression-free survival
PR, partial response
PT, preferred term
Q3W, every 3 weeks
RECIST, Response Evaluation Criteria in Solid Tumors
SAE, serious adverse event
SD, stable disease
SMQ, Standardised MedDRA Query
T-DM1, ado-trastuzumab emtansine

References: 1. ENHERTU [prescribing information]. Daiichi Sankyo Inc., Basking Ridge, NJ and AstraZeneca Pharmaceuticals LP, Wilmington, DE, 2022. **2.** Cortés J, Kim SB, Chung WP, et al; DESTINY-Breast03 Trial Investigators. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. *N Engl J Med*. 2022;386(12):1143-1154. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V4.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed June 21, 2022. 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. **4.** Data on file. Daiichi Sankyo Inc., Basking Ridge, NJ.

Please see Important Safety Information on pages 6-7, and click here for full Prescribing Information, including Boxed WARNINGS, and click here for Medication Guide.

Daiichi-Sankyo | AstraZeneca

Important Safety Information

Indication

ENHERTU is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:

- In the metastatic setting, or
- In the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy

WARNING: INTERSTITIAL LUNG DISEASE and EMBRYO-FETAL TOXICITY

- **Interstitial lung disease (ILD) and pneumonitis, including 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.**