Transcript Details
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Clinical Decision Making for HER2 Low Metastatic Breast Cancer

Announcer:
You're listening to ReachMD. This medical industry feature, titled "Clinical Decision Making for HER2 Low Metastatic Breast Cancer," is sponsored by Daiichi Sankyo and AstraZeneca.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I'm your host, Dr, Jennifer Caudle. And joining me to discuss the diagnosis and treatment of HER2-low metastatic breast cancer is Dr. Jules Cohen. He's a Clinical Associate Professor of Medicine at Stony Brook University in New York, and has been paid for his participation in today's program.

Dr. Cohen, welcome to the program today.

Dr. Cohen:
Thank you. I am pleased to be here.

Dr. Caudle:
Well, we're happy that you're here as well.

Dr. Caudle:
And now to begin, I think it's important to acknowledge that HER2 is a well-established biomarker in breast cancer. And while HER2-low is not a new breast cancer subtype, some oncologists may not be as familiar with it as they are with HER2-positive and HER2-negative subtypes.

So to start us off, Dr. Cohen, can you tell us how the HER2-low subtype was discovered and what it means for physicians and people living with metastatic breast cancer?

Dr. Cohen:
Sure, of course. So human epidermal growth factor receptor 2, or HER2, is one of the drivers of tumor growth in breast cancer. And when tumors have high amounts of HER2, we know that they can grow quickly and be difficult to treat.[1,2] This is one reason why the research and development of HER2-targeted therapies have been important in the breast cancer treatment landscape for 25 years.

Up until 2022, HER2-expressing breast cancers were clinically categorized as either HER2-positive or HER2-negative, even though there's a broad range of HER2 expression within these categories.[3] It is with this in mind that researchers began studying how different levels of HER2 expression may respond to HER2-directed therapies to further inform treatment approaches. It turns out that more than half of patients historically classified and diagnosed as having HER2-negative disease actually have low levels of HER2 expression and could potentially benefit from HER2-targeted therapy.[3] This is significant because for many years, patients with HER2-negative metastatic breast cancer whose disease had progressed through endocrine therapy or who had triple negative breast cancer to start with had limited treatment options apart from conventional chemotherapy.[1,3]

Dr. Caudle:
Thank you for that. And next, let's further discuss how HER2-low is measured and assessed. When do you recommend pathologists test for HER2? What tests are used? And what scores are they looking for to identify HER2-low?

Dr. Cohen:
Of course. HER2 immunohistochemistry, or IHC, may be performed on any biopsy in breast cancer patients, whether the biopsy is from a primary breast lesion or a metastatic site.[3] Generally, we recommend a biopsy of a metastatic site at initial recurrence or at presentation of de novo metastatic disease in a patient who was never treated in the early-stage setting.[5] This metastatic biopsy will demonstrate, one, breast cancer recurrence and, two, spread of disease, typically to the liver, lungs, or bone.[4] These findings put patients in the incurable category, but if they qualify as having HER2-low disease, they may be eligible for other treatment options.[5]

If the patient tests HER2 0 on their initial biopsy, on progression of disease it is reasonable to repeat HER2 testing on a new biopsy site, as metastatic breast cancer can dedifferentiate and new clones may express higher levels of HER2.[5] Although bone metastases are common in breast cancer, and bone is often the site of biopsy, the laboratory preparation of bone samples may affect the HER2 test results and interpretation. Due to this, it is recommended that metastatic sites other than bone are biopsied in a patient whose disease has progressed.[4]

To measure HER2 expression, we use IHC to measure the amount of HER2 protein on a cancer cell as well as a confirmatory in situ hybridization, or ISH, test, which counts the copies of the HER2 gene in cancer cells.[1] Results from an IHC assay will report scores as 0, 1+, 2+ or 3+ based on the percentage of cells positive for HER2 and the intensity of HER2 staining on the cell membrane.[1]

IHC 3+ is conventionally considered HER2-positive, while IHC 0 or 1+ is conventionally considered HER2-negative. IHC 2+ is considered equivocal and reflexes to an ISH test, which determines whether the biopsy is HER2-positive if the HER2 copy number is high or HER2-negative if the HER2 copy number is low.[1]

IHC 3+ or IHC 2+ ISH positive is currently classified as HER2-positive.[1] Conventionally, HER2-negative would include IHC 0 as well as IHC 1+ or IHC 2+ with a negative ISH.[1] With the release of the DESTINY-Breast04 clinical trial results, however, a result of IHC 1+ or IHC 2+ ISH negative indicates low levels of HER2 expression, and is classified as HER2-low.[1] And a result of IHC 0 indicates no or very low levels of HER2 expression.[7] Notably, the American Society of Clinical Oncology and the College of American Pathologists codified guidelines for HER2 testing in 2007. These guidelines have since been updated in 2013, 2018, and most recently in 2023. The ASCO-CAP 2023 update retains the same guidance for IHC categorization as the 2018 guidelines, although they now state the clinical relevance of HER2-low.[5]

Dr. Caudle:
Thank you for that. And with this in mind, let's dive deeper on an earlier point you made about treatment. Can you tell us about the treatment challenges that existed for patients before the introduction of HER2-low?

Dr. Cohen:
Sure. An ongoing challenge for many patients with metastatic breast cancer was that even though they presented with low levels of HER2 expression, the majority of patients, were classified as HER2-negative and deemed ineligible for HER2-directed therapy.[3]

Allow me to explain what I mean by that. To assess existing HER2 levels, breast cancer patients will undergo a biopsy, or preferably a biopsy from a metastatic site, and that sample will be tested using an IHC and/or ISH test.[1,4] By definition, HER2-positive is an IHC score of 3+ or 2+ with a positive ISH test.[1] What that means is that patients with lower levels of HER2 like IHC 1+ or 2+ with a negative ISH test haven't qualified for HER2-targeted therapies in the past, and therefore had fewer treatment options.[1]

Of note, low HER2 expression occurs in both hormone receptor-positive, also known as HR-positive, and hormone receptor-negative metastatic breast cancer and had previously not been actionable.[8] For patients classified with HR-positive, HER2-negative metastatic breast cancer, outcomes worsen after they develop endocrine-resistant disease.[9] For patients classified with HR-negative, HER2-negative metastatic breast cancer, also known as triple-negative breast cancer, the mainstay of treatment was conventional chemotherapy.[10]

Dr. Caudle:
Thank you for that. And for those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Jules Cohen about diagnosing and treating HER2-low metastatic breast cancer.

Now, we spoke about diagnosing HER2-low breast cancer and the kinds of treatment challenges that the medical community looked to solve for, particularly if the disease metastasizes. Can you tell us about how the treatment landscape has evolved?

Dr. Cohen:
Prior to June 2022, no HER2-directed therapy was shown to be effective in certain people with metastatic breast cancer who had low levels of HER2 expression.[11] At the 2022 ASCO annual meeting, data from DESTINY-Breast04, a global, randomized, open-label, phase 3 clinical trial, were presented and showed for the first time that this patient group could benefit from this type of treatment. The

medicine, ENHERTU®, or fam-trastuzumab deruxtecan-nxki, was quickly granted breakthrough therapy designation, priority review status, and was approved by the US Food and Drug Administration about 2 months later as the first HER2-directed treatment for HER2-low metastatic breast cancer in patients who have been previously treated with chemotherapy.[12]

Announcer:

In January 2025, ENHERTU® was approved in the U.S. for the treatment of adult patients with unresectable or metastatic hormone receptor (HR) positive, HER2 low (IHC 1+ or IHC 2+/ISH-) or HER2 ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting.

ENHERTU® is the first HER2 directed therapy to be approved in this setting. The approval brings ENHERTU to an earlier HR-positive treatment setting and broadens the patient population that may be eligible for treatment with a HER2-directed therapy to those with HER2-ultralow disease.

Dr. Caudle:
Thank you so much for that, Dr. Cohen. And now we're going to pause here for a moment to share some important safety information on Enhertu.

Announcer:
ENHERTU carries **Boxed WARNINGS** for Interstitial Lung Disease/Pneumonitis and Embryo-Fetal Toxicity and risks of Neutropenia and Left Ventricular Dysfunction. The most common adverse reactions (frequency greater than or equal to 20 percent), including laboratory abnormalities, in patients with HER2-low metastatic breast cancer were nausea, decreased white blood cell count, decreased hemoglobin, decreased neutrophil count, decreased lymphocyte count, fatigue, decreased platelet count, alopecia, vomiting, increased aspartate aminotransferase, increased alanine aminotransferase, constipation, increased blood alkaline phosphatase, decreased appetite, musculoskeletal pain, diarrhea, and decreased blood potassium.

Please stay tuned for additional Important Safety Information at the end of this segment.

Dr. Caudle:
Now, in terms of treatment you previously mentioned Enhertu as an option for certain people living with HER2-low metastatic breast cancer. What advice do you have for healthcare providers treating patients with Enhertu?

Dr. Cohen:
So the FDA approval allowed clinicians to offer Enhertu as a potential treatment option to a broader range of eligible patients with metastatic breast cancer, or MBC, depending on their level of HER2 expression.[12] Enhertu is designed to work differently than traditional chemotherapies.[12] It's specifically made up of an anti-HER2 monoclonal antibody covalently linked to a topoisomerase inhibitor via a tetrapeptide-based cleavable linker.[12]

How it is thought to work within the body is that the antibody portion of Enhertu targets and attaches to HER2 on cancer cells. Upon release, membrane permeable payload causes DNA damage and cell death, resulting in destruction of targeted tumor cells and neighboring cells present in the tumor microenvironment known as the bystander anti-tumor effect. Although Enhertu is designed to target HER2, it may affect some healthy nearby cells as well.[12]

If your patient is diagnosed with MBC, it's important to discuss the role that IHC testing can play in their treatment journey, and if treatment with Enhertu may be right for them. Enhertu is also featured in practice-setting guidelines as a preferred regimen for indicated patients.

It's important to know that interstitial lung disease, or ILD, and pneumonitis, including fatal cases, have been reported with Enhertu.[12] Healthcare providers should monitor for and promptly investigate signs and symptoms, including cough, dyspnea, fever, and other new or worsening respiratory symptoms.[13] It's advised to permanently discontinue Enhertu in all patients with grade 2 or higher ILD or pneumonitis, and advise patients of the risk and to immediately report symptoms. Additionally, exposure to Enhertu during pregnancy can cause embryo fetal harm. Advise patients of these risks and the need for effective contraception.

More information for healthcare providers on Enhertu and HER2-low MBC is available atwww.EnhertuHCP.com.

Dr. Caudle:
Thank you so much for sharing that, Dr. Cohen. And now let's review some important safety information for Enhertu.

Announcer:
Indication and 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:

- Hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting
- HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

Important Safety Information
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 1 level. Consider corticosteroid treatment as soon as ILD/pneumonitis is suspected (e.g., ≥0.5mg/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. Median time to first onset was 5.5 months (range: 0.9 to 31.5). Fatal outcomes due to ILD and/or pneumonitis occurred in 0.9% of patients treated with ENHERTU.

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.

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. Nineteen percent had Grade 3 or 4 decreased neutrophil count. Median time to first onset of decreased neutrophil count was 22 days (range: 2 to 939). Febrile neutropenia was reported in 1.2% 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 4.6% of patients, of which 0.6% were Grade 3 or 4.

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
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 2233 patients in Study DS8201-A-J101 (NCT02564900), DESTINY-Breast01, DESTINY-Breast02, DESTINY-Breast03, DESTINY-Breast04, DESTINY-Breast06, and other clinical trials. Among these patients, 67% were exposed for >6 months and 38% were exposed for >1 year. In this pooled safety population, the most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (73%), nausea (72%), decreased hemoglobin (67%), decreased neutrophil count (65%), decreased lymphocyte count (60%), fatigue (55%), decreased platelet count (48%), increased aspartate aminotransferase (46%), increased alanine aminotransferase (44%), increased blood alkaline phosphatase (39%), vomiting (38%), alopecia (37%), constipation (32%), decreased blood potassium (32%), decreased appetite (31%), diarrhea (30%), and musculoskeletal pain (24%).

HER2-Low and HER2-Ultralow Metastatic Breast Cancer
DESTINY-Breast06
The safety of ENHERTU was evaluated in 434 patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast06. The median duration of treatment was 11 months (range: 0.4 to 39.6) for patients who received ENHERTU.

Serious adverse reactions occurred in 20% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, COVID-19, febrile neutropenia, and hypokalemia. Fatalities due to adverse reactions occurred in 2.8% of patients including ILD (0.7%); sepsis (0.5%); and COVID-19 pneumonia, bacterial meningoencephalitis, neutropenic sepsis, peritonitis, cerebrovascular accident, general physical health deterioration (0.2% each).

ENHERTU was permanently discontinued in 14% of patients. The most frequent adverse reaction (>2%) associated with permanent discontinuation was ILD/pneumonitis. Dose interruptions due to adverse reactions occurred in 48% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were COVID-19, decreased neutrophil count, anemia, pyrexia, pneumonia, decreased white blood cell count, and ILD. Dose reductions occurred in 25% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were nausea, fatigue, decreased platelet count, and decreased neutrophil count.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased white blood cell count (86%), decreased neutrophil count (75%), nausea (70%), decreased hemoglobin (69%), decreased lymphocyte

count (66%), fatigue (53%), decreased platelet count (48%), alopecia (48%), increased alanine aminotransferase (44%), increased blood alkaline phosphatase (43%), increased aspartate aminotransferase (41%), decreased blood potassium (35%), diarrhea (34%), vomiting (34%), constipation (32%), decreased appetite (26%), COVID-19 (26%), and musculoskeletal pain (24%).

DESTINY-Breast04
The safety of ENHERTU was evaluated in 371 patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who received ENHERTU 5.4 mg/kg intravenously once every 3 weeks in DESTINY-Breast04. The median duration of treatment was 8 months (range: 0.2 to 33) for patients who received ENHERTU.

Serious adverse reactions occurred in 28% of patients receiving ENHERTU. Serious adverse reactions in >1% of patients who received ENHERTU were ILD/pneumonitis, pneumonia, dyspnea, musculoskeletal pain, sepsis, anemia, febrile neutropenia, hypercalcemia, nausea, pyrexia, and vomiting. Fatalities due to adverse reactions occurred in 4% of patients including ILD/pneumonitis (3 patients); sepsis (2 patients); and ischemic colitis, disseminated intravascular coagulation, dyspnea, febrile neutropenia, general physical health deterioration, pleural effusion, and respiratory failure (1 patient each).

ENHERTU was permanently discontinued in 16% of patients, of which ILD/pneumonitis accounted for 8%. Dose interruptions due to adverse reactions occurred in 39% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose interruption were neutropenia, fatigue, anemia, leukopenia, COVID-19, ILD/pneumonitis, increased transaminases, and hyperbilirubinemia. Dose reductions occurred in 23% of patients treated with ENHERTU. The most frequent adverse reactions (>2%) associated with dose reduction were fatigue, nausea, thrombocytopenia, and neutropenia.

The most common (≥20%) adverse reactions, including laboratory abnormalities, were nausea (76%), decreased white blood cell count (70%), decreased hemoglobin (64%), decreased neutrophil count (64%), decreased lymphocyte count (55%), fatigue (54%), decreased platelet count (44%), alopecia (40%), vomiting (40%), increased aspartate aminotransferase (38%), increased alanine aminotransferase (36%), constipation (34%), increased blood alkaline phosphatase (34%), decreased appetite (32%), musculoskeletal pain (32%), diarrhea (27%), and decreased blood potassium (25%).

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 1741 patients with breast cancer treated with ENHERTU 5.4 mg/kg, 24% were ≥65 years and 4.9% 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 (61%) as compared to younger patients (52%).
- **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, 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.

Dr. Caudle:
Now, unfortunately, that's all the time that we have for today. I'd like to thank my guest, Dr. Jules Cohen, for helping us better understand the diagnosis and treatment of HER2-low metastatic breast cancer. Dr. Cohen, it was great speaking with you today.

Dr. Cohen:
Thank you for having me.

Announcer:
This program was sponsored by Daiichi Sankyo and AstraZeneca. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

References

1. American Cancer Society. Breast Cancer HER2 Status. Accessed April 2025.
2. Tapia M, et al. Cancers. 2023;15(18):4522.
3. Tarantino P, et al. J Clin Oncol. 2020;38(17):1951-1962.
4. American Cancer Society. How Is a Biopsy Done?. Accessed April 2025.
5. Wolff AC, et al. Arch Pathol Lab Med. 2023;147(9): 993–1000
6. American Cancer Society. What Information Is Included in a Pathology Report?. Accessed April 2025.
7. Sajjadi E, et al. Cancer Drug Resist. 2022;5:882-8.10.20517/cdr.2022.29.
8. Modi S, et al. N Engl J Med. 2022;387(1):9-20.
9. Magno E, Bussard KM. Int J Mol Sci. 2024 Mar 17;25(6):3407.
10. Cabel L, et al. Breast. 2021;56:18-25.
11. National Cancer Institute. Enhertu Improves Survival for Metastatic “HER2-Low” Breast Cancer. Accessed April 2025.
12. ENHERTU Prescribing Information. Accessed April 2025.
13. NCCN Clinical Practice Guidelines in Oncology for Breast Cancer V2.2022. Accessed April 2025.