

Virtual Case Clinic: ADCs Across the Spectrum of HER2 Expression in Metastatic Breast Cancer

This transcript has been edited for style and clarity and includes all slides from the presentation.



Virtual Case Clinic: ADCs Across the Spectrum of HER2 Expression in Metastatic Breast Cancer

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► **Reshma L. Mahtani, DO:**

Hello, and welcome to this educational activity. My name is Dr. Reshma Mahtani, and I'm Chief of Breast Medical Oncology at Miami Cancer Institute, Baptist Health, South Florida.

Case Studies in Metastatic Breast Cancer

Case 1

**ER-/HER2-Positive
Metastatic Breast
Cancer**

Case 2

**HR+/HER2-Low
Metastatic Breast
Cancer**

Case 3

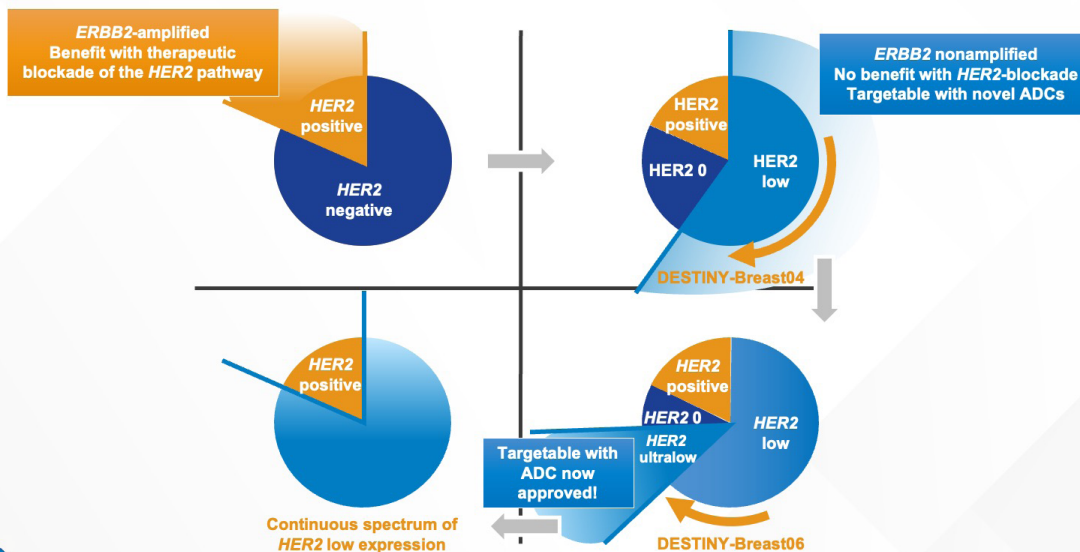
**HR+/HER2-Ultralow
Metastatic Breast
Cancer**



ER-, estrogen receptor negative; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor positive.

- ▶ Today, I will be reviewing three cases to demonstrate the application of antibody-drug conjugates across the spectrum of HER2 expression in metastatic breast cancer. Let's begin.

The Past, Present, and Future of HER2 Low



ADC, antibody-drug conjugate; ERBB, erythroblastic leukemia viral oncogene homolog; HER2, human epidermal growth factor receptor 2. Tarantino P, et al. Cancer Discov. 2022;12(9):2026-2030.

► It's always great to start with a general overview of the past, present, and future of HER2 testing and how we classify these tumors. We used to consider tumors as either HER2-positive or HER2-negative. HER2-positive being those that are HER2 amplified or with HER2 protein overexpression, really trying to identify these tumors that can benefit with

therapeutic blockade of the HER2 pathway.

And it was initially the intent of our assays to identify these tumors that were going to benefit from these targeted treatments. And then with more recent data sets, we've started to segment the HER2-negative tumors into HER2-low and even now HER2-ultralow tumors, recognizing that we now have an a

ntibody-drug conjugate that can target these lower levels of HER2 expression.

And so with that, we still have tumors that are clearly HER2-positive, but the rest are at a varying expression, or continuous spectrum of HER2-low expression. And the cases that we'll go through will nicely highlight these nuances.

Case 1: *HER2*-Positive Metastatic Breast Cancer



- ▶ So let's start with the first case, a *HER2*-positive metastatic breast cancer case.

Patient Presentation and History

– □ ×

62-Year-Old Woman

Presentation

- 62-year-old woman with history of stage II ER-/HER2+ right breast cancer
- Declined neoadjuvant therapy and underwent lumpectomy and radiation; declined adjuvant therapy
- 2 years after completion of adjuvant radiation, presented with abdominal pain, bloating, and a cough with exertional SOB
- CT scan identifies multiple liver lesions, largest 3 cm, with mildly elevated transaminases; innumerable lung lesions
- Biopsy of liver: ER-/HER2+ breast cancer, consistent with original diagnosis

Medical History

- **PMHx:** Anxiety, depression, HTN, and hyperlipidemia
- **PSHx:** Negative
- **SocHx:** Lives alone, works as a piano teacher
- **FamHx:** Negative

ER-, estrogen receptor negative; HER2+, human epidermal growth factor receptor 2 positive; HTN, hypertension; SOB, shortness of breath.

► This is a 62-year-old woman with a history of stage II ER-negative, HER2-positive right breast cancer. She declined neoadjuvant therapy and underwent upfront surgery with lumpectomy and radiation, and then she declined adjuvant systemic therapy.

Two years after completion of local treatment, she presents with abdominal pain, bloating,

and a cough associated with exertional shortness of breath. On imaging, there are multiple lesions in the liver. The largest is 3 cm. Transaminases are mildly elevated, and there are innumerable lung lesions on imaging. Biopsy of a liver lesion confirms the diagnosis of metastatic breast cancer with those same markers, ER-negative, HER2-positive. These were consistent with the original diagnosis.

And in terms of her past medical history, she has anxiety, hypertension, depression, and hyperlipidemia. These are common comorbidities that we see in our patients in clinic. Negative surgical history. She lives alone. She works as a piano teacher. And her family history is negative.

Clinical Course

62-Year-Old Woman

- Treatment initiated with paclitaxel, trastuzumab, and pertuzumab with significant improvement in cough and abdominal pain after 3 cycles
- Imaging after 6 cycles identifies small scattered lung nodules (subcm) and complete response in the liver
- Patient starts to develop mild neuropathy interfering with her work as a piano teacher; paclitaxel discontinued
- Continues HP alone, with continued response noted on serial imaging for 2.5 years; subsequently, tumor markers start to rise, patient remains asymptomatic
- Imaging documents progression of disease with new suspicious liver lesions and multiple scattered bone lesions
- Patient reports occasional headaches, but brain MRI negative

HP, trastuzumab and pertuzumab.

► In terms of her clinical course, she initiates treatment with first-line paclitaxel, trastuzumab, and pertuzumab. And at the time that she was treated, this was considered the standard of care as first-line therapy based on the CLEOPATRA trial. Of course, we heard the exciting new data at ASCO this year, the DESTINY-Breast09 trial, where we saw the remarkable median PFS associated with T-DXd and pertuzumab in combination. But in any case, this patient received what had been standard at that time, the CLEOPATRA regimen, and she reported significant

improvement in cough and abdominal pain after three cycles of therapy. And after six cycles, imaging identified small, scattered lung nodules that were all subcentimeter. She had a complete response in the liver. And I would say that this is not unusual, as we see these ER-negative, HER2-positive tumors responding remarkably well to our chemotherapy and targeted therapy options, as shown here.

So after that induction chemotherapy time period that she was on the taxane, she then stops after a period of time and continues on dual

antibody therapy alone, and has a continued response noted on serial imaging lasting 2.5 years. And then subsequently she develops asymptomatic progression. She has tumor markers that are rising, and imaging documents progression of disease with new suspicious liver lesions and multiple scattered bone lesions. She does report occasional headaches. And on that basis, an MRI is ordered. As we know, patients with HER2-positive breast cancer are not infrequently diagnosed with brain metastases. Fortunately, her brain MRI is negative.

Case Study Question

What would you recommend for this patient?

- A. Trastuzumab emtansine
- B. Tucatinib, capecitabine, trastuzumab
- C. Trastuzumab deruxtecan
- D. Vinorelbine + trastuzumab
- E. Unsure

► What would you recommend for this patient?

Conclusion and Rationale

What would you recommend for this patient?

- a) Trastuzumab emtansine
- b) Tucatinib, capecitabine, trastuzumab
- c) Trastuzumab deruxtecan
- d) Vinorelbine + trastuzumab
- e) Unsure

Correct answer:
Trastuzumab deruxtecan

- The DESTINY-Breast03 trial directly compared T-DXd to T-DM1
- T-DXd demonstrated improvements in PFS and OS compared to T-DM1
- The tucatinib regimen could be considered 2nd line, but would be considered in the presence of significant CNS progression
- Given the OS benefit demonstrated with T-DXd, it would be preferred over single agent chemo (vinorelbine) and trastuzumab



CNS, central nervous system; OS, overall survival; PFS, progression-free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

▶ So the correct answer with this case is trastuzumab deruxtecan. And this is on the basis of the DESTINY-Breast03 trial, which directly head-to-head compared the two antibody-drug conjugates, T-DXd and T-DM1. As you may recall, prior to this trial, T-DM1 had been our standard second-line therapy based on the EMILIA trial, where T-DM1 was compared against capecitabine and lapatinib, and shown to be superior in terms

of progression-free and overall survival.

And in the DESTINY-Breast03 trial, these two ADCs were compared head-to-head, and T-DXd demonstrated improvements in progression-free and overall survival compared to T-DM1, quickly becoming our go-to second-line regimen.

It should be mentioned that the tucatinib regimen, meaning tucatinib, trastuzumab, and

capecitabine, per guidelines, can be considered in the second-line therapy, but we would usually consider this triplet regimen in the presence of significant CNS progression, and this patient did not have progression in the brain. Given the overall survival benefit demonstrated with T-DXd, again, it would be preferred over single-agent chemotherapy with vinorelbine and trastuzumab.

DESTINY-Breast03: Study Design

Randomized, Open-Label, Multicenter Study (NCT03529110)

Patients (N = 524)

- Unresectable or metastatic *HER2*-positive breast cancer
- Previously treated with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of therapy

R

1:1

T-DXd

5.4 mg/kg Q3W
(n = 261)

T-DM1

3.6 mg/kg Q3W
(n = 263)

Primary endpoint

- PFS (BICR)

Key secondary endpoint

- OS

Secondary endpoints

- ORR (BICR and investigator)
- DoR (BICR)
- Safety

Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

	T-DXd	T-DM1
Median PFS, months	29.0	7.2
HR	0.30	



BICR, blinded independent central review; DoR, duration of response; *HER2*, human epidermal growth factor receptor 2; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan. Cortés J, et al. *Nat Med*. 2024;30(8):2208-2215.

► So as a reminder, the study design for the DESTINY-Breast03 trial. This was a randomized, open-label, multicenter trial in which patients with *HER2*-positive metastatic breast cancer who were previously treated with trastuzumab and a taxane in the metastatic or early stage setting and developed

recurrence within 6 months, were randomized 1:1 to T-DXd versus T-DM1. And you see that remarkable improvement in median PFS, 29 months versus only 7.2 months with T-DM1. And subsequently a survival benefit was also reported. So our second-line therapy of choice.

Case 2: *HER2*-Low Metastatic Breast Cancer



- ▶ Now, let's move to a case that is demonstrating the activity of ADCs in *HER2*-low metastatic breast cancer, as we continue the discussion of *HER2* expression across the continuum.

Patient Presentation and History

53-Year-Old Woman

Presentation

- 53-year-old woman diagnosed with stage III ER+/PR-/HER2 1+ breast cancer, s/p adjuvant chemotherapy with AC→T, radiation, and 10 planned years of adjuvant endocrine therapy with AI
- While on year 3 of AI, develops severe back pain leading to imaging that identifies multiple bone mets and adenopathy, no visceral disease
- Bone biopsy: ER+/PR-/HER2 0
- First-line fulvestrant + abemaciclib (+ zoledronic acid): responds for 12 months and then develops recurrent back pain; imaging identifies progression in bone with new suspicious lung nodules

Medical History

- **PMHx:** No chronic medical issues
- **SocHx:** Married, works as a pharmacist, no toxic habits
- **FamHx:** Multiple family members with breast cancer but germline genetic testing negative

AC-T, adriamycin + cytoxan + taxol; AI, aromatase inhibitor; ER+, estrogen receptor positive; HER2, human epidermal growth factor receptor 2; PR-, progesterone receptor negative.

▶ This is a 53-year-old woman who's diagnosed with stage III, ER-positive, PR-negative, HER2 1+ breast cancer, so HER2-low. She undergoes adjuvant chemo with anthracycline and taxane-based treatment, along with radiation, and had planned 10 years of adjuvant endocrine therapy with an aromatase inhibitor.

While on year 3 of adjuvant AI therapy, she becomes symptomatic with back pain that then leads to imaging, unfortunately identifying

multiple bone metastases and malignant adenopathy, no visceral disease. The bone biopsy is done and shows invasive ductal cancer consistent with breast cancer, ER-positive, PR-negative. HER2 is reported simply as 0. She is started on first-line endocrine therapy and a CDK4/6 inhibitor, along with supportive therapy to reduce the risk of skeletal-related events with zoledronic acid, and responds for 12 months, and then develops recurrent back pain and imaging

identifies progression in bone with new suspicious lung nodules.

In terms of her other medical issues, she has no chronic medical conditions. She's married, works as a pharmacist, has no toxic habits, and does undergo germline genetic testing as she has multiple family members with breast cancer. And even if she didn't, per guidelines, any patient with metastatic breast cancer should be undergoing germline genetic testing.

Clinical Course



53-Year-Old Woman

- Repeat biopsy of lung nodule: ER+/PR-/HER2 2+, FISH not amplified; ctDNA identifies no mutations
- Start capecitabine with response noted on imaging for 6 months
- Follow-up imaging identifies enlarging lung nodules, and patient is now symptomatic with cough; bone is overall stable with some areas appearing slightly progressive; 2 new liver lesions, largest 1.8 cm; LFTs are normal



ctDNA, circulating tumor DNA; ER+, estrogen receptor positive; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; LFT, liver function test; PR-, progesterone receptor negative.



► So repeat biopsy of the lung nodule after progression on fulvestrant and abemaciclib for 12 months again shows evidence of carcinoma. This time, the tumor is HER2 2+, FISH not amplified, again, HER2-low. And ctDNA testing is done to identify any further mutations that could be helpful in identifying

biomarker-directed therapy, such as a PIK3CA inhibitor or the AKT inhibitor, capivasertib. But no mutations or alterations are identified.

So she then goes on to receive capecitabine with response noted on imaging for 6 months, but then, unfortunately, afterwards, has follow-up imaging that

shows further enlarging lung nodules. She's now symptomatic with cough. Bone disease is overall stable, with some areas appearing slightly progressive, and there are two new liver lesions, the largest 1.8 cm. LFTs are again normal.

Case Study Question

What would be the next best treatment option?

- a) Paclitaxel
- b) Trastuzumab deruxtecan
- c) Sacituzumab govitecan
- d) Eribulin
- e) Unsure

- So what would the next best treatment option be? Again, to summarize, this patient had fulvestrant and abemaciclib for about a year, then went on to get capecitabine, and is now progressing.

Conclusion and Rationale

What would be the next best treatment option?

- a) Paclitaxel
- b) Trastuzumab deruxtecan
- c) Sacituzumab govitecan
- d) Eribulin
- e) Unsure

Correct answer:
Trastuzumab deruxtecan

- The DESTINY-Breast04 trial randomized patients with HR+/*HER2*-low mBC to T-DXd or treatment of physician's choice chemotherapy, and demonstrated improvements in PFS and OS
- Most patients in the DESTINY-Breast04 trial were treated with 1-2 lines of chemotherapy in the metastatic setting whereas patients who received SG in the TROPICS 2 trial were more heavily pre-treated (2-4 prior lines of chemotherapy)
- T-DXd is the preferred ADC in patients with *HER2*-low disease per guidelines



ADC, antibody-drug conjugates; *HER2*, human epidermal growth factor receptor 2; HR, hormone receptor; mBC metastatic breast cancer; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; T-DXd, trastuzumab deruxtecan.

► So here, the correct answer would be trastuzumab deruxtecan, on the basis of the DESTINY-Breast04 trial, which randomized patients with hormone receptor-positive *HER2*-low metastatic breast cancer to treatment of physician's choice or the antibody-drug conjugate, T-DXd. And showed improvements in progression-free and overall survival favoring the use of the ADC.

Most of these patients were treated with one to two prior lines of chemotherapy in the metastatic setting, whereas patients who received sacituzumab govitecan in the TROPICS-02 trial (which was also an option in terms of the ADCs that you could have selected), these were more heavily pretreated patients who had received at least two to four prior lines of therapy. And as such, T-DXd is the

preferred ADC in patients with *HER2*-low disease, per guidelines. And again, this patient has hormone receptor-positive, *HER2*-low disease, not hormone receptor-negative, *HER2*-low or triple-negative, where one might consider utilizing sacituzumab before T-DXd.

DESTINY-Breast04: Study Design

An Open-Label, Multicenter, Phase 3 Study (NCT03734029)

Patients^a

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

R

2:1

T-DXd

5.4 mg/kg Q3W
(n = 373)

HR+ ≈ 480
HR- ≈ 60

TPC

Capecitabine, eribulin,
gemcitabine, paclitaxel,
nab-paclitaxel^c
(n = 184)

Primary endpoint

- PFS by BICR (HR+)

Key secondary endpoints^d

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

Stratification factors

- Centrally assessed HER2 status^b (IHC 1+ vs IHC 2+/ISH-)
- 1 vs 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) vs HR-

	T-DXd	TPC
Median PFS, months	9.6	4.2
HR	0.37	

^aIf patients had HR+ mBC, prior endocrine therapy was required. ^bPerformed on adequate archived or recent tumor biopsy per ASCO/CAP guidelines using the VENTANA HER2/neu (4B5) investigational use only [IUO] Assay system. ^cTPC was administered according to the label. ^dOther secondary endpoints included ORR (BICR and investigator), DOR (BICR), PFS (investigator), and safety; efficacy in the HR- cohort was an exploratory endpoint. ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CDK, cyclin-dependent kinase; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
Modi S, et al. *N Engl J Med*. 2022;387(1):9-20; Modi S, et al. ESMO 2023. Abstract 3760.



► So in any case, here we see the schema for the DBO4 trial. Again, these patients had HER2-low disease, defined as 1+ or 2+, and FISH not amplified, having been treated with one to two prior lines of chemo in the metastatic setting.

Notice the majority of these patients, as I mentioned a

moment ago, had hormone receptor-positive HER2-low disease. Only 60 patients had hormone receptor-negative HER2-low disease. The randomization was to T-DXd versus treatment of physician's choice. And the primary endpoint was progression-free survival. Again, as we see summarized in the box on

the right part of the slide, the median PFS favored the use of T-DXd, 9.6 months versus 4.2 months. And not shown is also the data that's documented in overall survival benefit as well.

Case 3: *HER2*-Ultralow Metastatic Breast Cancer



- ▶ And then finally, let's finish with a case of *HER2*-ultralow metastatic breast cancer.

Patient Presentation and History

65-Year-Old Woman

Presentation

- 65-year-old woman presents to her PCP with reports of several months of back pain, abdominal pain, and fatigue
- Had not seen a PCP in many years; on physical exam a palpable breast mass is noted with several axillary and cervical nodes
- Imaging identifies multiple liver, bone, and nodal suspicious lesions
- Liver biopsy: IDC consistent with breast primary, ER+/PR-/HER2 0
- Diagnosis: de novo mBC

Medical History

- **PMHx:** HTN, high cholesterol, GERD; germline genetic testing negative
- **SocHx:** No toxic habits, retired executive; has 1 daughter, 1 son, and 2 grandchildren
- **FamHx:** Negative

ER+, estrogen receptor positive; GERD, gastroesophageal reflux disease; HER2, human epidermal growth factor receptor 2; HTN, hypertension; IDC, invasive ductal carcinoma; mBC, metastatic breast cancer; PCP, primary care physician; PR-, progesterone receptor negative.

► This is a 65-year-old woman who is symptomatic with back pain and abdominal pain and fatigue, and goes to her primary medical physician who she had not seen in many years. And on physical exam, there's a palpable mass, several areas of adenopathy. On

imaging, there's widespread metastatic disease involving bone, liver, and nodal lesions. A liver lesion is biopsied and does show metastatic breast cancer, ER-positive, HER2-0. This patient has de novo metastatic breast cancer. As

far as other medical issues, she has hypertension, high cholesterol, GERD, undergoes germline genetic testing and it is negative. She has no toxic habits, no pertinent family history.

Clinical Course



65-Year-Old Woman

- First-line: AI + CDK4/6i; patient improved clinically and response noted for 1 year; subsequent slight progression in all areas; patient remained asymptomatic
- ctDNA identifies AKT mutation, no *ESR1m*
- Second-line: fulvestrant + capivasertib with response for 5 months, followed by extensive progression noted in liver
- Now symptomatic with abdominal pain and rising transaminases
- Patient indicates her daughter is getting married in 4 months

AI, aromatase inhibitor; ctDNA, circulating tumor DNA; *ESR1m*, estrogen receptor 1 mutation.

► In the first-line setting, she receives an AI and a CDK4/6 inhibitor, and has a response for a year, but then develops progression. She's asymptomatic. There is an AKT mutation noted on

ctDNA, no *ESR1* mutation. And on this basis, she receives fulvestrant and capivasertib, with a response lasting for 5 months, but then develops pretty widespread progression in the liver, and she's now very

symptomatic. LFTs are rising, and she says, 'I really want to feel well and be around for my daughter who's getting married in 4 months.'

Case Study Question

What would be the next best option?

- A. Rebiopsy a metastatic site, and if HER2-low, T-DXd
- B. Ask pathologist to quantify any faint HER2 expression, and if present, T-DXd
- C. Refer to hospice
- D. Eribulin
- E. Unsure



HER2, human epidermal growth factor receptor 2; T-DXd, trastuzumab deruxtecan.

► So what would the next best option be?

Conclusion and Rationale

What would be the next best option?

- a) Re-biopsy a metastatic site, and if *HER2*-low, T-DXd
- b) Ask pathologist to quantify any faint *HER2* expression, and if present, T-DXd
- c) Refer to hospice
- d) Eribulin
- e) Unsure

Correct answer:

*Ask pathologist to quantify any faint *HER2* expression, and if present, T-DXd*

- T-DXd is now approved as first line chemotherapy in patients with *HER2* ultralow as well as *HER2*-low MBC; Once pathology documents there is *HER2* expression, this patient is a candidate for T-DXd
- First-line treatment with T-DXd is a good treatment option for highly symptomatic patients with visceral disease who need a quick response

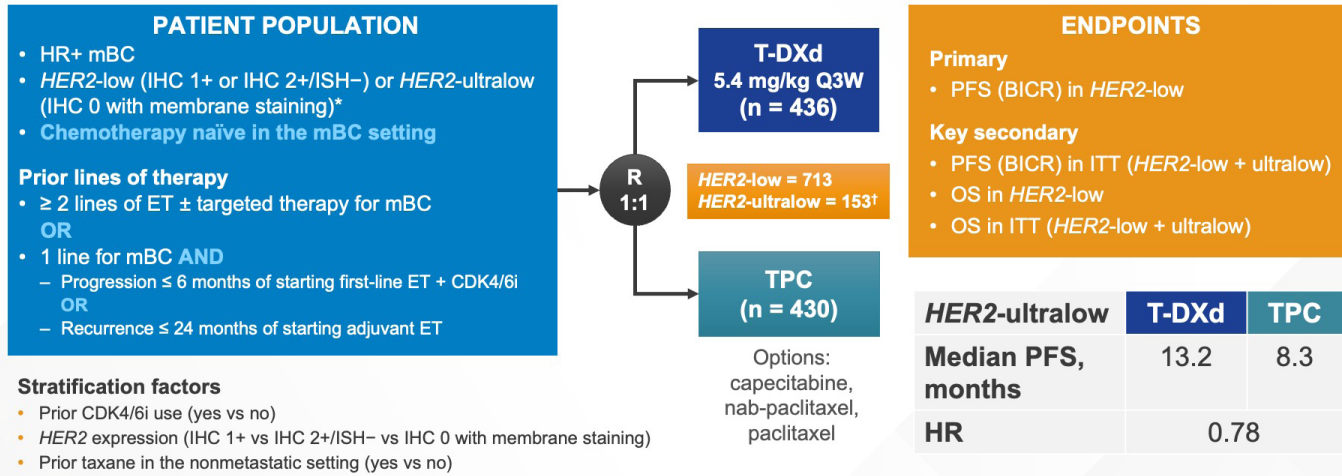
► So here, remember we had a liver biopsy that showed IHC simply reported as 0, and we now know that a certain subsegment of these IHC-0 tumors will be considered *HER2*-ultralow, meaning faint staining up to 10%. These were patients that were treated with T-DXd in

the first-line setting as part of the DESTINY-Breast06 trial; 150 of these patients were enrolled on this trial. And T-DXd is now available as a first-line chemotherapy option, not only for *HER2*-low, but now also *HER2*-ultralow. Once pathology documents that there is *HER2* expression

up to 10%, we would then be able to offer this patient T-DXd. And I would say that this is an excellent treatment option for her, as she's highly symptomatic and she needs a quick response.

DESTINY-Breast06: Study Design

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



*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization. HER2-ultralow was defined as faint, partial membrane staining in ≤ 10% of tumor cells (also known as IHC >0<1+). †HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n = 152 as determined per central laboratory testing data). ‡To be presented separately. BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; INV, investigator assessed; IRT, interactive response technology; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice. ClinicalTrials.gov identifier: NCT04494425. Curigliano G, et al. ASCO 2024. Abstract LBA1000. Bardia A, et al. *N Engl J Med*. 2024;391(22):2110-2122.

► Here you see the study schema of the DBO6 trial. Notable differences as compared to the DBO4 trial that we reviewed earlier is that these are patients that are receiving T-DXd or treatment

of physician's choice as first-line chemotherapy in the metastatic setting. And again, HER2-low tumors, as well as 150 or so HER2-ultralow tumors, IHC-0 with faint staining up to 10%, were

allowed on this trial. And the primary endpoint was progression-free survival, again favoring T-DXd, 13.2 months versus 8.3 months. And we await overall survival data to be reported.

FDA Approval Summary: ADCs in mBC

ADC	HER2-positive (IHC 3+ or ISH positive)	HER2-low (IHC 1+ or IHC 2+/ISH-)	HER2-ultralow (IHC 0 with membrane staining)	HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)
Trastuzumab emtansine (T-DM1)	EMILIA: patients who previously received trastuzumab and a taxane, separately or in combination			
Trastuzumab deruxtecan (T-DXd)	DESTINY-Breast03: patients who have received a prior anti-HER2-based regimen	DESTINY-Breast04: patients who have received a prior chemotherapy		
		DESTINY-Breast06: HR+ patients that have progressed on one or more endocrine therapies (chemotherapy-naïve in mBC)		
Sacituzumab govitecan (SG)				TROPICS-02: HR+ patients who have received endocrine-based therapy and at least two additional systemic therapies
Datopotamab deruxtecan (Dato-DXd)				TROPION-Breast01: HR+ patients who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease



ADC, antibody-drug conjugate; Dato-DXd, datopotamab deruxtecan; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; SG, sacituzumab govitecan; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Kadcyla. Prescribing information. Genentech, Inc; 2022. Enhertu. Prescribing information. Daiichi Sankyo, Inc; 2025. Trodelvy. Prescribing information. Gilead Sciences, Inc; 2025. Datroway. Prescribing information. Daiichi Sankyo, Inc; 2025.

► Here you see an FDA approval summary of ADCs in metastatic breast cancer. This is not meant to be comparative. Remember, these trials all enrolled somewhat different populations. But just to summarize the data,

we have T-DM1 for HER2-positive tumors. We have T-DXd across a broad range of HER2 expression, HER2-positive, HER2-low, HER2-ultralow. And then we have sacituzumab govitecan. And more recently, datopotamab

deruxtecan in patients that are hormone receptor-positive, HER2-negative as well, with sacituzumab govitecan being available in the triple-negative setting as well.

Thank you so much.

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About AXIS Medical Education, Inc.

AXIS Medical Education, Inc. is a full-service continuing education company that designs and implements live, web-based, and print-based educational activities for healthcare professionals. AXIS provides convenient opportunities to engage learners based on their individual learning preferences through a full spectrum of educational offerings.

The executive leadership of AXIS combines 75 years of experience in adult learning theory, curriculum design/implementation/assessment, continuing education accreditation standards, and medical meeting planning and logistics. Our team has a deep understanding of the governing guidelines overseeing the medical education industry to ensure compliant delivery of all activities.

AXIS employs an experienced team of medical and scientific experts, medical writers, project managers, meeting planners, and logistics professionals. This team is dedicated to meeting the unmet educational needs of healthcare professionals, with the goal of improving patient outcomes.

AXIS believes that partnerships are crucial in our mission to deliver timely, relevant, and high-quality medical education to healthcare professionals. To that end, AXIS partners with other organizations and accredited providers to offer added expertise and assist in expanding access to our educational interventions. AXIS also partners with numerous patient advocacy organizations to provide recommended patient education and caregiver resources in specific disease areas. AXIS finds value in these partnerships because they complement our core clinical curriculum with validated and relevant supplemental resources for busy clinicians and their patients.

The mission of AXIS is to enhance the knowledge, skills, competence, and performance of the interprofessional healthcare team to ensure patients receive quality care, resulting in improved patient outcomes. We engage healthcare professionals in fair-balanced, scientifically rigorous, expert-led certified educational activities designed to foster lifelong learning that is applicable to clinical practice and patient-centered care.

To learn more and to see our current educational offerings, visit us online at www.AXISMedEd.com.

