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Antibody-Drug Conjugates in Breast Cancer: Current Landscape and Future Targets

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Antibody-drug conjugates (ADCs) have transformed therapeutic options for patients with breast cancer, delivering targeted cytotoxic agents with enhanced efficacy, albeit with systemic toxicity. Since the approval of trastuzumab emtansine in 2012, the ADC landscape has rapidly expanded to include agents targeting HER2, TROP-2, and other novel targets. Currently, four ADCs are approved in breast cancer, showing clinical benefit across HER2-positive, HER2-low, hormone receptor (HR)-positive and triple-negative subtypes. Trastuzumab deruxtecan has demonstrated superior outcomes compared to earlier HER2-targeted ADCs and is the preferred treatment in multiple settings. Anti-TROP-2 ADCs, such as sacituzumab govitecan and datopotamab deruxtecan, have provided improvements in progression-free survival in both triple-negative and HR-positive/HER2-negative disease. Ongoing research is exploring additional targets, such as HER3, Nectin-4, B7-H4, and CD166, with several promising candidates showing efficacy in early phase trials. As ADCs move into earlier lines of therapy and combination regimens, understanding optimal sequencing, toxicity management, and cost considerations will be essential. This review summarizes the current ADC landscape in breast cancer and highlights future directions for this rapidly evolving therapeutic class.

Introduction

Antibody-drug conjugates (ADCs) first entered the breast cancer (BC) treatment paradigm in 2012. In the last few years, ADCs have dramatically changed the treatment landscape in both the curative and advanced setting, leading to significantly improved clinical outcomes for patients with BC.^{1,2} ADCs are composed of a monoclonal antibody (mAb), a linker, and a cytotoxic payload.² Ideally, the mAb utilized in the ADC targets an antigen highly expressed on tumour cells, with limited expression on normal tissue. The linkers can be cleavable or non-cleavable, and keep the cytotoxic payload attached to the mAb while the ADC is in circulation, and then release a dose of the cytotoxic payload close to the target cells resulting in direct, bystander, and immune-mediated cell killing.² In this review, we conducted a search of OVID Medline® from January 1, 1946, to February 25, 2025, along with abstracts from Embase and Cochrane over the last 3 years which

retrieved 1,840 unique citations. Using these, we discuss the current landscape of ADC use in BC and highlight future targets and agents under investigation. Currently, four different ADCs are approved by the Food and Drug Administration (FDA) for use in BC (**Figure 1A**), and many novel agents are under investigation as monotherapies or as combinations (**Figure 1B**).³⁻⁶

Currently Approved ADCs

HER2-positive BC

HER2-positive (HER2+) BC was the first subtype to be targeted by ADCs. Ado-trastuzumab-emtansine (T-DM1) targets HER2 with a non-cleavable linker and anti-microtubule cytotoxic payload, and was first approved for use in the metastatic setting in patients who had prior treatment with taxane and trastuzumab (**Table 1**). This was based on the EMILIA trial comparing T-DM1 to lapatinib + capecitabine (LC), which found both

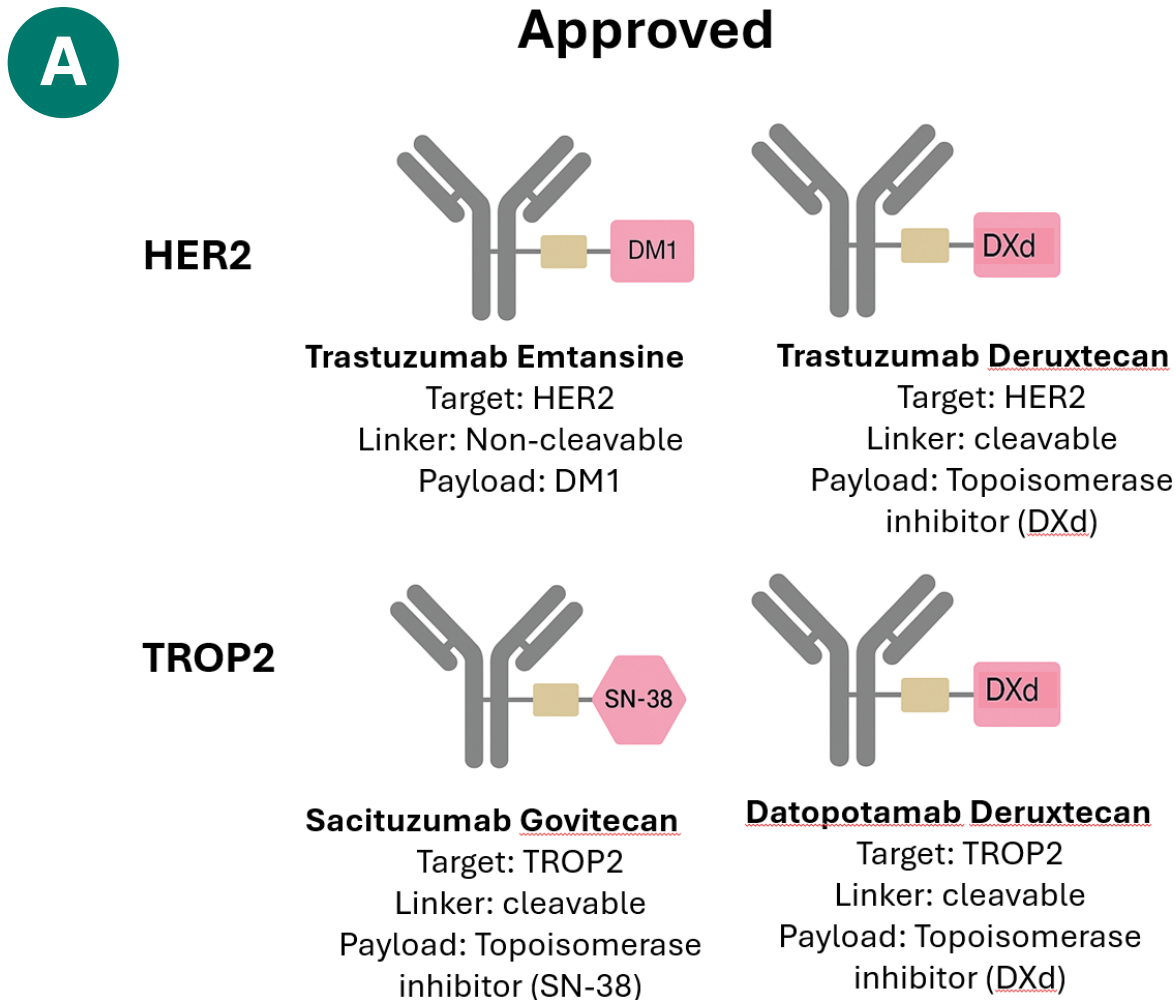


Figure 1A. Approved ADCs for patients with breast cancer; courtesy of Jennifer Leigh, MD and Arif Ali Awan, MD.

Abbreviations: ADC: antibody-drug conjugate

improved median progression-free survival (mPFS, 9.6 vs. 6.4 months, HR: 0.65, 95% confidence interval [CI]: 0.55-0.77) and median overall survival (mOS, 29.9 vs. 25.9 months, HR: 0.75, 95% CI: 0.64-0.88).⁷ The most common toxicities in this trial were thrombocytopenia and elevated liver enzymes, and rare cardiac dysfunction.⁷ The benefit of this therapy was confirmed with the TH3RESA trial, which compared T-DM1 to physician's choice chemotherapy (PCC) in patients who had received prior taxane, trastuzumab, and lapatinib.^{8,9} Finally, T-DM1 was shown to be non-inferior to trastuzumab plus a taxane in the first-line setting in the MARIANNE trial; however, the CLEOPATRA regimen of pertuzumab,

trastuzumab, and a taxane remains standard of care in this setting.^{10,11}

T-DM1 has also been incorporated in the curative setting. The KATHERINE trial compared adjuvant use of T-DM1 with trastuzumab in patients with residual disease after neoadjuvant therapy.¹² This demonstrated improved invasive disease-free survival (iDFS) with 13.7% at 7 years (80.8% vs. 67.1%), and a 4.7% improvement in OS at 7 years (89.1% vs. 84.4%, **Table 1**).¹² Based on these positive results, T-DM1 use has become the standard of care in this setting. T-DM1 has also been studied in patients with stage I HER2+ BC and compared to taxane and trastuzumab. While T-DM1 had a 3-year iDFS of 97.8%

B

Investigational

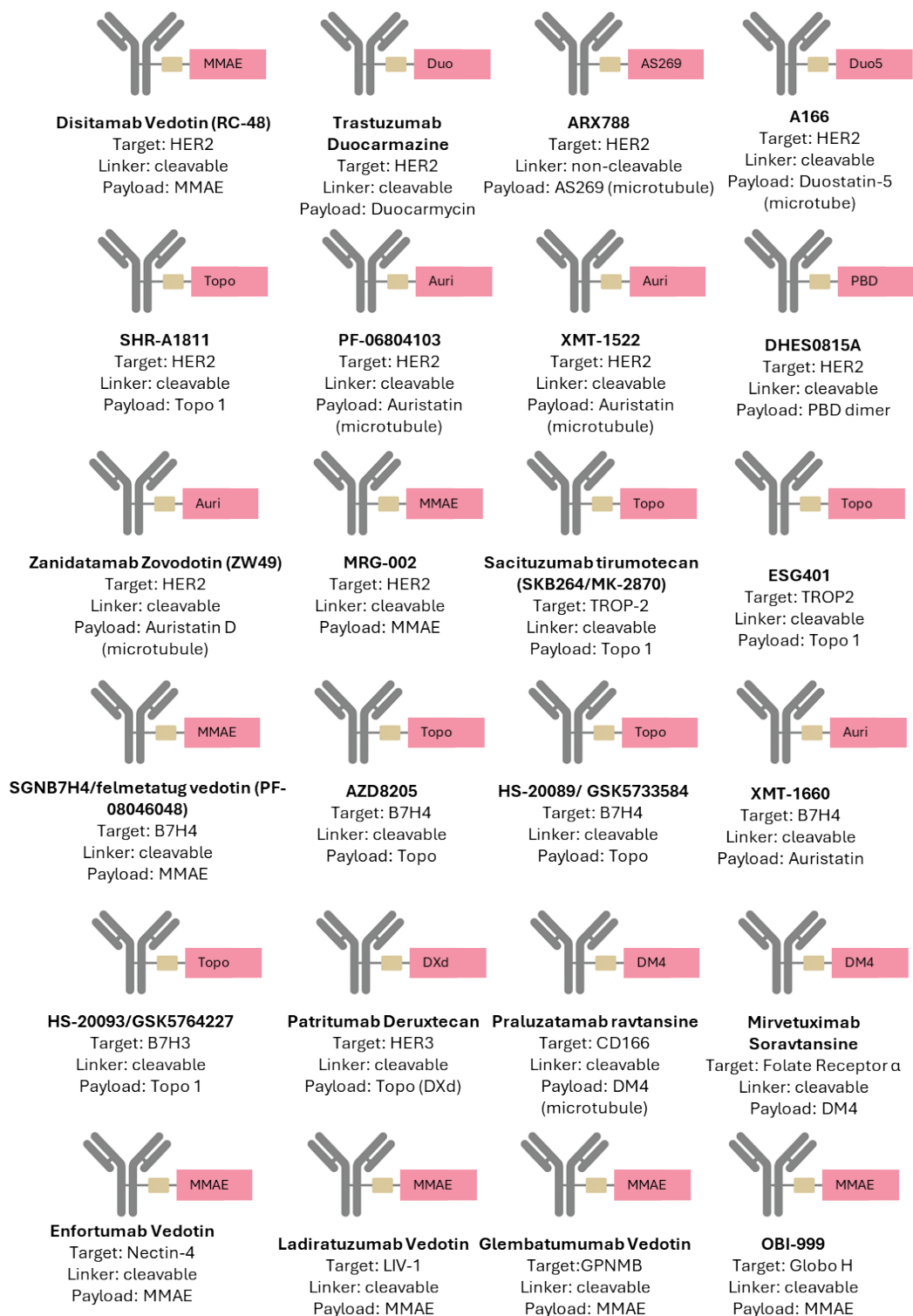


Figure 1B. Investigational ADCs for patients with breast cancer; *courtesy of Jennifer Leigh, MD and Arif Ali Awan, MD.*

Abbreviations: ADC: antibody-drug conjugate

Subtype	ADC	Target	Trial	Setting	Comparator	DFS or PFS	OS	Experimental ADC ORR (%)
HER2+	T-DM1	HER2	KATHERINE	Early BC with residual disease	Trastuzumab	7-year DFS 79.8% (T-DM1) vs 66.2%	7-year 89.1% T-DM1 vs 84.4% Trastuzumab	N/A
			EMILIA	Advanced BC, prior trastuzumab and taxane	Lapatinib + capecitabine	mPFS 9.6 (T-DM1) vs 6.4 months (HR 0.65, 95% CI 0.55-0.77)	mOS 29.9 months (T-DM1) vs 25.9 months (HR 0.75, 95% CI 0.64-0.88)	43.6
			TH3RESA	Advanced BC, prior taxane, trastuzumab and lapatinib	Physician's choice of treatment	mPFS 6.2 (T-DM1) vs. 3.3 months (HR 0.53, 95% CI 0.42-0.66)	mOS 22.7 months (T-DM1) vs. 15.8 months (HR: 0.68, 95% CI: 0.54-0.85)	31.0
	T-DXd	HER2	DESTINY BREAST 01	Advanced BC, prior TDM1	N/A	mPFS 19.4 months	mOS 29.1 months	62.0
			DESTINY BREAST 02	Advanced BC, prior TDM1	Physician's choice of treatment	mPFS 17.8 (T-DXd) vs. 6.9 months (HR: 0.36, 95% CI: 0.28-0.45)	mOS 39.2 (T-DXd) vs. 26.5 months (HR: 0.66, 95% CI: 0.50-0.86)	70.0
			DESTINY BREAST 03	Advanced BC, prior taxane and trastuzumab	TDM1	mPFS 29.0 (T-DXd) vs. 7.2 months (HR: 0.30, 95% CI: 0.24-0.38)	mOS 52.6 (T-DXd) vs. 42.7 months (HR: 0.73, 95% CI: 0.56-0.94)	78.9
HR+	T-DXd	HER2	DESTINY BREAST 04	Advanced HER2 low BC, one or two prior lines of chemotherapy	Physician's choice of treatment	mPFS 10.1 (T-DXd) vs. 5.4 months (HR: 0.51, 95% CI: 0.4-0.64)*	mOS 23.9 (T-DXd) vs. 17.5 months (HR: 0.64, 95% CI: 0.48-0.86)*	52.6*
			DESTINY-BREAST 06	Advanced HR+, HER2 low BC with progression on endocrine therapy but no chemotherapy	Physician's choice of treatment	mPFS 13.2 (T-DXd) vs. 8.1 months (HR: 0.62, 95% CI: 0.52-0.75)	Data remains immature	56.5
			TROPICS-02	Advanced HR+/HER2- BC, at least one prior BC, ET, taxane, and CDK 4/6 inhibitor, and two to four prior lines of chemotherapy	Physician's choice of treatment	mPFS 5.5 (SG) vs. 4.0 months (HR: 0.66, 95% CI: 0.53-0.83)	mOS 14.4 (SG) vs. 11.2 months (HR: 0.79, 95% CI: 0.65-0.96)	21
	SG	TROP-2	TROPION-Breast01	Advanced HR+/HER2-, prior ET, one to two lines of chemotherapy	Physician's choice of treatment	mPFS 6.9 (Dato-DXd) vs. 4.9 months, (HR: 0.63, 95% CI: 0.52-0.76)	Data immature, (HR: 0.84, 95% CI: 0.62-1.14)	36.4
			ASCENT	Advanced TNBC with ≥2 prior lines of therapy	Physician's choice of treatment	mPFS 4.8 (SG) vs. 1.7 months (HR: 0.41, 95% CI: 0.33-0.63)	mOS 11.8 (SG) vs. 6.9 months (HR: 0.51, 95% CI: 0.33-0.52)	31.0
			DESTINY BREAST 04	Advanced HER2 low BC, one or two prior lines of chemotherapy	Physician's choice of treatment	mPFS 8.5 (T-DXd) vs. 2.9 months (HR: 0.46, 95% CI: 0.24-0.89)**	mOS 18.2 (T-DXd) vs. 8.3 months (HR: 0.48, 95% CI: 0.24-0.95)**	50.0**
TNBC	T-DXd	HER2	DESTINY BREAST 04	Advanced HER2 low BC, one or two prior lines of chemotherapy	Physician's choice of treatment	mPFS 8.5 (T-DXd) vs. 2.9 months (HR: 0.46, 95% CI: 0.24-0.89)**	mOS 18.2 (T-DXd) vs. 8.3 months (HR: 0.48, 95% CI: 0.24-0.95)**	50.0**

Table 1. Antibody-drug conjugates currently approved for use in breast cancer courtesy of Jennifer Leigh, MD and Arif Ali Awan, MD.

* = HR+ group only.
** = TNBC group only.

Abbreviations: **ADC:** antibody-drug conjugate, **BC:** breast cancer, **CI:** confidence interval, **Dato-DXd:** datopotamab deruxtecan, **DFS:** disease-free survival, **ET:** endocrine therapy, **HR:** hazard ratio, **HR+:** hormone receptor-positive, **mOS:** median overall survival, **mPFS:** median progression-free survival, **SG:** sacituzumab govitecan, **T-DXd:** trastuzumab deruxtecan, **T-DM1:** ado-trastuzumab-emtansine, **TNBC:** triple-negative breast cancer

(95% CI: 96.3–99.3), it was not associated with fewer clinically relevant toxicities than taxane + trastuzumab.¹³

The second ADC that changed the treatment landscape for HER2+ BC is trastuzumab deruxtecan (T-DXd), which targets HER2 using a cleavable linker and a topoisomerase I cytotoxic payload. The DESTINY-BREAST 01 trial demonstrated activity in patients with advanced HER2+ BC who had previously received T-DM1, with a mPFS of 19.4 months and mOS of 29.1 months, and the most common toxicities were nausea, vomiting, fatigue, myelosuppression, alopecia, and a 2.2% risk of fatal pneumonitis, which is reported as closer to 1% in more recent trials (**Table 1**).^{14,15} T-DXd has since been compared to T-DM1 in the Phase III trial DESTINY-BREAST 03, and demonstrated improved mPFS (29.0 vs. 7.2 months, HR: 0.30, 95% CI: 0.24–0.38) and mOS (52.6 vs. 42.7 months, HR: 0.73, 95% CI: 0.56–0.94) as compared to T-DM1, and is now considered the preferred second-line option (**Table 1**).⁴ Furthermore, T-DXd has also shown remarkable intracranial activity, challenging the traditional paradigm that these large molecules may not have significant intracranial activity, with 60.7% (95% CI: 50.5–70.8%) of patients with active brain metastases obtaining a confirmed intracranial objective response in the DESTINY-BREAST 12 trial.¹⁶ Several ongoing trials are exploring other indications for T-DXd, including the DESTINY-BREAST 09 trial exploring first-line use (NCT04784715), and the DESTINY-BREAST 05 (NCT04622319) trial exploring adjuvant use in patients with residual disease after neoadjuvant therapy versus T-DM1.

HER2-low/ultralow BC

HER2-low BC is defined as an immunohistochemistry (IHC) score of 1+ or 2+ and negative *in situ* hybridization (ISH), and includes both hormone receptor positive (HR+) and negative (HR-) disease. T-DXd was first approved by the FDA for HER2-low disease following progression on chemotherapy in 2022 (**Table 1**).² This was based on results from the DESTINY-BREAST 04 trial, which demonstrated improved mPFS and mOS in comparison to PCC (eribulin, capecitabine, paclitaxel, nab-paclitaxel, and gemcitabine).¹⁷ The trial explored outcomes for patients with HR+ disease and triple-negative BC (TNBC), in addition to the overall cohort. In HR+ patients, mPFS was improved to 10.1 months compared to 5.4 months following PCC treatment (HR: 0.51, 95% CI: 0.4–0.64, **Table 2**). mOS was

also improved with T-DXd (23.9 vs. 17.5 months, HR: 0.64, 95% CI: 0.48–0.86). In the subgroup of patients with TNBC, both outcomes demonstrated improvement (mPFS 8.5 vs. 2.9 months, HR: 0.46, 95% CI: 0.24–0.89, and mOS 18.2 vs. 8.3 months, HR: 0.48, 95% CI: 0.24–0.95, **Table 1**). Use of T-DXd in HR+/HER2-low and HER2-ultralow (defined as faint HER2 membrane staining in ≤10% of cells, IHC >0 and <1+) patients who have progressed on endocrine therapy (ET) and have not received chemotherapy in the advanced setting, was also recently approved based on improved mPFS in the DESTINY-BREAST 06 trial showing a similar magnitude of mPFS benefit as the DESTINY BREAST 04 trial (**Table 1**).¹⁸

TNBC

Sacituzumab govitecan (SG) is the first ADC approved for the treatment of metastatic TNBC (mTNBC). It targets TROP-2 and has a cleavable linker and a topoisomerase I cytotoxic payload (**Table 1**). The Phase III trial ASCENT compared SG to PCC (eribulin, capecitabine, vinorelbine, or gemcitabine) in patients who had received ≥2 lines of treatment.⁶ This demonstrated improvement in mPFS (4.8 vs. 1.7 months, HR: 0.41, 95% CI: 0.33–0.63) and mOS (11.8 vs. 6.9 months, HR: 0.51, 95% CI: 0.33–0.52) with neutropenia, diarrhea, nausea, and alopecia being the common side effects. Ongoing trials are exploring the use of SG and datopotomab deruxtecan (Dato-DXd), which also targets TROP-2 and has a cleavable linker and a topoisomerase I cytotoxic payload, in the first-line setting as monotherapy (NCT05382299, NCT05374512) and in addition to pembrolizumab or durvalumab in those with a programmed cell death ligand 1 (PD-L1) combined positive score (CPS) ≥10 (NCT05382286, NCT06103864). Currently, no ADCs are approved for the curative setting, although their use is being explored in Phase III trials in the neoadjuvant setting and in patients with residual disease after neoadjuvant treatment (NCT06112379, NCT05629585, NCT05633654).¹⁹

HR+/HER2- BC

SG and Dato-DXd are also used for metastatic HR+/HER2- BC, the most common subtype of BC (**Table 1**). SG is approved in this setting by the US Food and Drug Administration (FDA) and Health Canada in patients who have progressed on endocrine therapy (ET) and two other lines of treatment.²⁰ Benefit in this setting was demonstrated in the TROPICS-02 trial, which

Target	Drug	Payload	Breast Cancer Subtype	Phase	Design	Sample Size (n)	Efficacy	Safety
CD166	Praluzatamab ravtansine	Maytansine	Advanced HR+/HER2 and TNBC	Phase II	Evaluate praluzatamab ravtansine monotherapy in cohort A (HR+/HER2-) and cohort B (TNBC)	60 (HR+/HER2 arm) and 55 (TNBC)	• ORR HR+/HER2- 14.9%, and mPFS 11.4 weeks • ORR TNBC <10%	• Blurred vision (42%), nausea (35%), fatigue (35%), diarrhea (25%), peripheral neuropathy (27%), infusion-related reaction (23%)
HER3	Patritumab Deruxtecan (HER3-DXd)	Deruxtecan	HER-3 expressing advanced BC	Phase I/II	Dose escalation followed by dose expansion with both 4.8 mg/kg and 6.4 mg/kg doses	182	• HR+/HER2- : ORR 30.1%, mPFS 7.4 months • HER2+: ORR 42.9%, mPFS 11.0 months • TNBC: ORR 22.6%, mPFS 5.5 months	• Grade ≥3 TEAEs were observed in 71.4% of patients • Most common TEAEs were nausea (79.7%), thrombocytopenia (62.1%), neutropenia (61.0%)
HER2	ARX788	Amberstatin 269	Advanced BC who have progressed on CDK 4/6 inhibitor and one line of chemotherapy	Phase II	All patients received HER3-DXd 5.6 mg/kg IV every 3 weeks	99	• ORR 53.5% • mPFS 9.4 months	• Grade ≥3 AEs occurred in 55.6%. Most frequent AEs were nausea (75%), and diarrhea (53%). Six patients developed ILD.
HER2	Disitamab vedotin	MMAE	HER2+ and HER2-low metastatic mBC with at least one prior line of chemotherapy, and PAM pathway activation	Phase II/III	Randomized to ARX788 vs lapatinib + capecitabine	441	• ORR 70.0% (HER3-DXd) vs 81.3% (HER3-DXd + letrozole) vs 70.8% (chemotherapy) • pCR rate 4.0% (HER3-DXd) vs 2.1% (HER3-DXd) vs 4.2% (chemotherapy)	• Grade ≥3 TEAEs 18.0% (HER3-DXd) vs. 16.7% (HER3-DXd + letrozole) vs 54.2% (chemotherapy)
HER2	DP303c	MMAE	HER2+ advanced solid tumours	Phase I	Patients received Disitamab vedotin 2 mg/kg IV every 2 weeks	62	• ORR: 42.9% HER2+ and 33.3% HER2 low • mPFS: 5.7 months HER2+ and 5.1 months HER2 low	• Most common Grade ≥3 TRAEs were blurred vision, dry eye, keratopathy, ILD • Most common Grade ≥3 TRAEs were neutropenia (17.6%), GGT increase (13.2%), asthenia (11.0%), peripheral neuropathy (5.9%), and neurotoxicity (0.7%)
HER2	DP303c	MMAE	HER2+ advanced solid tumours	Phase I	Dose escalation followed by dose expansion of DP303c every 3 weeks	94 (68 breast cancer)	• ORR: 51.5% for patients with BC • mPFS: 6.4 months for patients with BC	• Most common TRAEs were corneal disease (87.2%), blurred vision (61.7%), dry eye (57.4%), peripheral neuropathy (46.8%), hypertriglyceridemia (44.7%)

Target	Drug	Payload	Breast Cancer Subtype	Phase	Design	Sample Size (n)	Efficacy	Safety
	MRG002	MMAE	Advanced HER2-low BC	Phase II	Patients received MRG002 2.6 mg/kg every 3 weeks	56	• ORR: 34.7%	• Most common TRAEs were neutropenia (53.6%), leukopenia (48.2%), AST increase (46.4%), alopecia and ALT increase (39.3%)
	SHR-A1811	Topoisomerase inhibitor	HER2+ mBC with brain metastases	Phase II	Patients received SHR-A1811 monotherapy or in combination with pyrotinib (Arm 2) or bevacizumab (Arm 3)	25	• ORR: 76% • Intracranial ORR: 84%	• Grade ≥3 TRAEs occurred in 76%. Most common were neutropenia (64%), leukopenia (48%), thrombocytopenia (28%), anemia (28%), nausea (8%)
			Stage II-III HER2+ BC	Phase II	Randomization to neoadjuvant SHR-A1811, SHR-A1811 + pyrotinib, or nab-paclitaxel + carboplatin + trastuzumab + pertuzumab (PCbHP)	265	• pCR: 63.2% monotherapy, 62.5% SHR-A1811 + pyrotinib, and 64.4% PCbHP	• Grade ≥3 TRAEs were 44.8% with monotherapy, 71.6% SHR-A1811 + pyrotinib, and 38.8% PCbHP
	Trastuzumab duocarmazine (T-Duo)	Duocarmycin	HER2+ advanced BC	Phase III	Patients randomized to T-Duo every 3 weeks or physician's choice of chemotherapy	437	• mPFS: 7.0 (T-Duo) vs. 4.9 months (HR: 0.64, 95% CI: 0.49-0.84) • mOS: 20.4 (T-Duo) vs. 16.3 months (HR: 0.83, 95% CI: 0.62-1.09) • ORR: 27.8% (T-Duo) vs. 29.5%	• Grade ≥3 TEAEs 52.8%. Most common AEs conjunctivitis, keratitis, fatigue, dry eye, nausea, alopecia, diarrhea, asthenia, decreased appetite
Nectin-4	Enfortumab vedotin	MMAE	Advanced TNBC and HR+/HER2 BC	Phase II	Patients received EV 1.25 mg/kg day 1, 8, and 15 of a 28 day cycle	87 (42 TNBC, 45 HR+/HER2-)	• ORR TNBC: 19.0% • ORR HR+/HER2-: 15.6%	• Special interest TRAEs included skin reactions, peripheral neuropathy, and hyperglycemia
TROP-2	Datopotomab deruxtecan	Deruxtecan	TNBC with active brain metastases	Phase II	Patients received Dato-DXd 6.0 mg/kg every 3 weeks	8	• Intracranial ORR 37.5%	• Main toxicity: fatigue
	Datopotamab deruxtecan	Deruxtecan	Advanced TNBC eligible for first line treatment	Phase I/II	Patients received Dato-DXd plus Durvalumab	62	• ORR: 79% • mPFS: 13.8 months	• Most common AEs nausea (65%) and stomatitis (65%). Grade 3 or 4 AEs occurred in 57%. ILD rate 5%.

Target	Drug	Payload	Breast Cancer Subtype	Phase	Design	Sample Size (n)	Efficacy	Safety
B7-H4	ESG401	SN-38	First-line advanced TNBC	Phase IB	Patients received ESG401 1 6 mg/kg IV day 1, 8, and 15 of 28 day cycle	23	• ORR 78.6% • Intracranial disease control rate 73%	• Most common TRAEs were leukopenia (65.2%), neutropenia (69.6%), anemia (43.5%), fatigue (21.7%), nausea (43.5%), and vomiting (34.8%)
	ESG401	SN-38	mBC	Phase IA/B	Dose escalation followed by dose expansion of ESG401	141 (74 TNBC, 65 HR+/HER2-, HER2+)	• ORR • HR+/HER2-: 34.5% • ORR TNBC: first-line: 85.0%, later line: 35.1% • ORR HER2+: 0% • mPFS HR+/HER2-: 7.6 months • mPFS TNBC: 3.9 months later line patients • mPFS HER2+: 3.8 months	• Most common Grade ≥3 TRAE was neutropenia and leukopenia. No new safety signals
	Sacituzumab tirumotecan (SKB264.MK-2870)	Belotecan-derivative	Advanced TNBC, receipt of two or more prior lines of therapy	Phase III	Patients randomized to SKB264 or physician's choice of chemotherapy	263	• mPFS by BICR 5.7 (SKB264) vs 2.3 months (HR 0.31, 95% CI 0.22-0.45) • mOS: NR for SKB264 vs 9.4 months (HR: 0.53, 95% CI: 0.36-0.78) • ORR by BICR 43.8% (SKB264) vs 12.8%	• Most common Grade ≥3 TRAE with SKB264 were neutropenia (32.3%), anemia (27.7%), and leukopenia (25.4%)
	SGNB7H4	MMAE	Metastatic breast cancer, at least 1 cytotoxic prior treatment, including taxane	Phase I	Dose escalation	25 patients with breast cancer	• ORR 28% (7/25)	• Most common TRAE Grade ≥3 Neutropenia (17%), Fatigue (4.9%), No Grade 3 sensory neuropathy
B7-H4	HS-20089/GSK5733584	Topoisomerase inhibitor	Metastatic breast cancer, at least 1 cytotoxic prior treatment	Phase I	Dose escalation	28 patients with TNBC	• ORR 28.6% in 28 patients	• Most common TRAE Grade ≥3 WBC decreased (36%), Anemia (24%), nausea/vomiting (<5)

Table 2. Novel ADC targets being explored for breast cancer; courtesy of Jennifer Leigh, MD and Arif Ali Awan, MD.

Abbreviations: ADC: antibody-drug conjugate, AE: adverse event, BC: breast cancer, BICR: blinded independent central reviews, CI: confidence interval, Dato-Dxd: datopotamab deruxitecan, ET: endocrine therapy, EV: enfortumab vedotin, GGT: gamma-glutamyl transferase, HR: hazard ratio, HR+: hormone receptor-positive, ILD: interstitial lung disease, IV: intravenous, mBC: metastatic breast cancer, mOS: median overall survival, mPFS: median progression-free survival, NR: not reached, ORR: objective response rate, PAM: phosphoinositide 3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR), PCR: pathological complete response, TNBC: triple-negative breast cancer, TEAE: treatment-emergent adverse events, TRAE: treatment-related adverse events, WBC: white blood cell

demonstrated statistically significant improvement in both mPFS (5.5 vs. 4.0 months, HR: 0.66, 95% CI: 0.53-0.83) and mOS (14.4 vs. 11.2 months, HR: 0.79, 95% CI: 0.65-0.96) compared to PCC.²⁰ Use of Dato-DXd after progression on both ET and chemotherapy was explored in the TROPION-Breast01 study, which compared Dato-DXd to PCC, and demonstrated improved mPFS for Dato-DXd (mPFS 6.9 vs. 4.9 months, HR: 0.63, 95% CI: 0.52-0.76); however, OS data remain immature. Common or pertinent side effects of this therapy are mucositis, nausea/vomiting, fatigue, alopecia, and ocular toxicity. Approval by the FDA for use in metastatic HR+/HER2 BC after progression on ET and chemotherapy was granted in early 2025; however, it is not yet approved by Health Canada.

The Future of ADCs in BC – Novel Drugs and Targets

Human Epidermal Growth Factor Receptor 3 (HER3/ErbB3)

A promising target in BC is HER3, a tyrosine kinase receptor belonging to the HER family. HER3 can form heterodimers with HER2 and/or epidermal growth factor receptor (EGFR), and activate critical pathways including the PI3K/AKT pathway and mitogen-activated protein kinase (MAPK) signaling.^{21,22} Patritumab deruxtecan (HER3-DXd) is a first-in-class ADC targeting HER3 with a cleavable linker and a topoisomerase I cytotoxic payload (DXd). HER3-DXd's activity in HER3-expressing advanced BC was explored in the Phase I/II trial U31402-A-J101 in patients who had received ≥ 2 lines of prior cytotoxic therapy. The study demonstrated an objective response rate (ORR) of 30.1% in HR+/HER2-, 42.9% in HER2+, and 22.6% in TNBC (**Table 2**).²³ The most common adverse events (AEs) were nausea and cytopenias. ICARUS-BREAST01 is an ongoing Phase II trial exploring the use of HER3-DXd in advanced HR+/HER2- disease that was previously treated by a CDK 4/6 inhibitor and ≥ 1 line of chemotherapy, and found an ORR of 53.5% and mPFS 9.4 months.²⁴ Finally, SOLTI VALENTINE is an ongoing Phase II neoadjuvant study exploring the use of HER3-DXd +/- letrozole compared to standard of care chemotherapy in HR+/HER2-operable BC with Ki67 $\geq 20\%$ and/or high genomic risk. Preliminary results demonstrate activity (ORR: 70.0% HER3-DXd vs. 81.3% HER3-DXd + letrozole vs. 70.8% chemotherapy, **Table 2**).^{25,26}

HER2

Several novel ADCs targeting HER2 are currently under investigation (**Table 2**). Trastuzumab duocarmazine (T-Duo) targets HER2 and has a cleavable linker with a DNA alkylating agent as the cytotoxic payload, and was studied in the Phase III TULIP trial in patients with advanced HER2+ BC after ≥ 2 HER2-targeted therapies in comparison to PCC (**Table 2**).²⁷ The mPFS was improved by 2.1 months with T-Duo (7.0 vs. 4.9 months, HR: 0.64, 95% CI: 0.49-0.84), although clinically significant ocular toxicity limits its use.

ARX788 targets HER2 and has a tubulin inhibitor as the cytotoxic payload connected to the mAb with a non-cleavable linker, and has demonstrated activity in advanced HER2+ BC (**Table 2**). The ACE-Breast 02 study evaluated use in patients with HER2+ BC who had been treated with prior trastuzumab and taxane, and demonstrated mPFS of 11.3 months vs. 8.3 months for patients treated with LC (HR: 0.64, 95% CI: 0.49-0.82).²⁸ The mOS has not yet been reached in this study. Grade 3 or higher treatment-related adverse events (TRAEs) were similar in both groups (41.4% for ARX788 and 40.0% for LC). Multiple ongoing trials explore the use of ARX788 in HER2-low disease and in patients with brain metastases.

Disitamab vedotin (RC48) targets HER2 and has a cleavable linker attached to a microtubule inhibitor as the cytotoxic payload. It has demonstrated efficacy in HER2+/HER2-low pre-treated metastatic BC (mBC). A Phase I/II trial demonstrated ORRs of 42.9% (HER2+) and 33.3% (HER2-low), and mPFS of 5.7 (HER2+) and 5.1 months (HER2-low).²⁹

Three other HER2-targeted ADCs in development are DP303c, MRG002, and SHR-A1811. DP303c is an ADC being studied and developed in China, and studies showed an ORR of 51.5% in patients with mBC.³⁰ MRG002 has demonstrated an ORR of 34.7% in advanced HER2-low BC that has progressed on standard therapies.³¹ Finally, SHR-A1811 is being studied in an ongoing Phase II trial of pre-treated HER2+ BC with radiotherapy-naïve brain metastases not requiring immediate treatment. This study showed an intracranial-ORR (IC-ORR) of 84% and ORR of 76%. Grade 3 or 4 TRAEs occurred in 76% of patients, and were predominantly cytopenias and nausea.³² There is also evidence for the efficacy of SHR-A1811 in the neoadjuvant setting in stage II/III HER2+ BC, with an impressive

63.2% pathological complete response (pCR) rate when used as monotherapy.³³ A summary of novel HER2-targeting ADCs can be found in **Table 2**.

TROP-2

Dato-DXd has also been studied in TNBC. The Phase Ib/II BEGONIA trial exploring treatment options for first-line mTNBC includes an arm of durvalumab + Dato-DXd, and has identified an ORR of 79% with mPFS of 13.8 months (**Table 2**).³⁴ Sacituzumab tirumotecan (SKB264/MK-2870) targets TROP-2 and has a topoisomerase I inhibitor as cytotoxic payload connected using a cleavable linker. In previously treated mTNBC, it demonstrated an ORR of 42.4% and a mOS of 16.8 months in a Phase II trial. In patients with high TROP-2 expression, the ORR was 53.1% and mOS was not reached.³⁵ A Phase III trial exploring its use in the third-line or later is underway, as well as a Phase II study exploring first-line use with an anti-PD-L1 mAb, and in the curative setting for patients with TNBC with residual disease (NCT06393374). Finally, ESG401 also targets TROP-2 and has a topoisomerase I inhibitor as the cytotoxic payload, and is being explored in advanced BC of all subtypes. In the pre-treated setting, ORRs of 34.5%, 35.1%, and 0% were detected for HR+/HER2-, TNBC, and HER2+ subtypes, respectively.³⁶ In the first-line treatment of TNBC, the ORR was 78.6% with evidence of central nervous system (CNS) activity (**Table 2**).³⁷

Nectin-4

Nectins are important mediators for cell-cell adhesion, and Nectin-4 gene amplification has been observed in BC.³⁸ Enfortumab vedotin (EV) targets Nectin-4 with a mAb that is connected to a microtubule inhibitor payload with a cleavable linker. Its use is currently being explored in the ongoing Phase II trial EV-202, which has two BC-specific cohorts (HR+/HER2- and TNBC) who have previously received a taxane or anthracycline.³⁹ Preliminary results demonstrate activity, with an ORR of 19.0% in patients with TNBC and 15.6% in those with HR+/HER2- disease. Toxicities are in line with those previously observed with EV, and include rash, peripheral neuropathy, and hyperglycemia.

B7-H4

B7-H4 is an immune checkpoint ligand upregulated in breast cancer and expressed at low levels in normal tissue. SGNB7H4/felmetatug vedotin (PF-08046048) targets B7-H4 and has a microtubule inhibitor cytotoxic payload.⁴⁰ The ORR for patients with BC was 28% (7/25) with common toxicities being fatigue, nausea, and neuropathy. HS-20089/GSK5733584 targets B7-H4 and has a topoisomerase I inhibitor cytotoxic payload, and has demonstrated an ORR of 28.6% in 28 patients with TNBC, with myelosuppression and nausea being the most common toxicities.⁴¹ Other ADCs targeting B7-H4, such as AZD8205 and XMT-1660, and an ADC targeting B7-H3, another checkpoint from the same family (HS-20093/GSK5764227), are being assessed in Phase I trials.

CD166

CD166 is a transmembrane type-1 glycoprotein involved in cell adhesion and migration that is present in healthy and tumour tissue.⁴² Praluzatamab ravtansine (CX-2009) is a CD166 targeting proboddy drug conjugate which uses a cleavable linker to connect a microtubule inhibitor cytotoxic payload, in which the antigen-binding site is masked, thus reducing healthy tissue binding.⁴³ An ongoing Phase II trial evaluating its use in pre-treated advanced HR+/HER2 and TNBC has demonstrated an ORR of 14.9% in the HR+/HER2- cohort with a mPFS of 11.4 months, and an ORR of <10% for TNBC (**Table 2**).⁴⁴ Common toxicities included blurred vision, nausea, fatigue, diarrhea, peripheral neuropathy, and infusion-related reactions.

Conclusions

ADCs have dramatically changed the landscape of BC treatment, and have led to significant gains in clinical outcomes. All four currently approved ADCs are utilized in the metastatic setting, and T-DM1 is also approved for curative intent use. Several novel drugs are under development targeting HER2 and TROP-2, as well as exciting novel targets, including HER3, nectin-4, B7-H4, and CD166. It is anticipated that the indication and use of ADCs in BC will continue to expand in metastatic and curative settings as single-agent and in combinations with increasing need for evidence-based guiding of ADC sequencing, rationale combinations, toxicity management, and cost implications for the healthcare systems.

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References

- Dumontet C, Reichert JM, Senter PD, Lambert JM, Beck A. Antibody–drug conjugates come of age in oncology. *Nat Rev Drug Discov.* 2023;22(8):641–61.
- Monteiro M, Nunes N, Junior A, Fêde A, Bretas G, Souza C, et al. Antibody–drug conjugates in breast cancer: a comprehensive review of how to selectively deliver payloads. *Breast Cancer Targets Ther.* 2024; 16:51–70.
- Bardia A, Jhaveri K, Im SA, Pernas S, De Laurentiis M, Wang S, et al. Datopotamab deruxtecan versus chemotherapy in previously treated inoperable/ metastatic hormone receptor–positive human epidermal growth factor receptor 2–negative breast cancer: primary results from TROPION-Breast01. *J Clin Oncol.* 2025;43(3):285–96.
- Cortés J, Hurvitz SA, Im SA, Iwata H, Curigliano G, Kim SB, et al. Trastuzumab deruxtecan versus trastuzumab emtansine in HER2-positive metastatic breast cancer: long-term survival analysis of the DESTINY-Breast03 trial. *Nat Med.* 2024;30(8):2208–15.
- Verma S, Miles D, Gianni L, Krop IE, Welslau M, Baselga J, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med.* 2012;367(19):1783–91.
- Bardia A, Rugo HS, Tolaney SM, Loirat D, Punie K, Oliveira M, et al. Final results from the randomized Phase III ASCENT clinical trial in metastatic triple-negative breast cancer and association of outcomes by human epidermal growth factor receptor 2 and trophoblast cell surface antigen 2 expression. *J Clin Oncol.* 2024;42(15):1738–44.
- Diéras V, Miles D, Verma S, Pegram M, Welslau M, Baselga J, et al. Trastuzumab emtansine versus capecitabine plus lapatinib in patients with previously treated HER2-positive advanced breast cancer (EMILIA): a descriptive analysis of final overall survival results from a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2017;18(6):732–42.
- Krop IE, Kim SB, González-Martín A, LoRusso PM, Ferrero JM, Smitt M, et al. Trastuzumab emtansine versus treatment of physician's choice for pretreated HER2-positive advanced breast cancer (TH3RESA): a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2014;15(7):689–99.
- Krop IE, Kim SB, Martin AG, LoRusso PM, Ferrero JM, Badovinac-Crnjevic T, et al. Trastuzumab emtansine versus treatment of physician's choice in patients with previously treated HER2-positive metastatic breast cancer (TH3RESA): final overall survival results from a randomised open-label phase 3 trial. *Lancet Oncol.* 2017;18(6):743–54.
- Perez EA, Barrios C, Eiermann W, Toi M, Im Y, Conte P, et al. Trastuzumab emtansine with or without pertuzumab versus trastuzumab with taxane for human epidermal growth factor receptor 2–positive advanced breast cancer: Final results from MARIANNE. *Cancer.* 2019;125(22):3974–84.
- Swain SM, Miles D, Kim SB, Im YH, Im SA, Semiglazov V, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. *Lancet Oncol.* 2020;21(4):519–30.
- Geyer CE, Untch M, Huang CS, Mano MS, Mamounas EP, Wolmark N, et al. Survival with Trastuzumab Emtansine in Residual HER2-Positive Breast Cancer. *N Engl J Med.* 2025;392(3):249–57.

13. Tolaney SM, Tayob N, Dang C, Yardley DA, Isakoff SJ, Valero V, et al. Adjuvant trastuzumab emtansine versus paclitaxel in combination with trastuzumab for stage I HER2-positive breast cancer (ATEMPT): A randomized clinical trial. *J Clin Oncol*. 2021;39(21):2375–85.
14. Modi S, Saura C, Yamashita T, Park YH, Kim SB, Tamura K, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer. *N Engl J Med*. 2020;382(7):610–21.
15. Saura C, Modi S, Krop I, Park YH, Kim SB, Tamura K, et al. Trastuzumab deruxtecan in previously treated patients with HER2-positive metastatic breast cancer: updated survival results from a phase II trial (DESTINY-Breast01). *Ann Oncol*. 2024;35(3):302–7.
16. Harbeck N, Ciruelos E, Jerusalem G, Müller V, Niikura N, Viale G, et al. Publisher Correction: Trastuzumab deruxtecan in HER2-positive advanced breast cancer with or without brain metastases: a phase 3b/4 trial. *Nat Med*. 2024;30(12):3780.
17. Modi S, Jacot W, Yamashita T, Sohn J, Vidal M, Tokunaga E, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. *N Engl J Med*. 2022;387(1):9–20.
18. Bardia A, Hu X, Dent R, Yonemori K, Barrios CH, O'Shaughnessy JA, et al. Trastuzumab deruxtecan after endocrine therapy in metastatic breast cancer. *N Engl J Med*. 2024;391(22):2110–22.
19. Spring LM, Tolaney SM, Fell G, Bossuyt V, Abelman RO, Wu B, et al. Response-guided neoadjuvant sacituzumab govitecan for localized triple-negative breast cancer: results from the NeoSTAR trial. *Ann Oncol*. 2024;35(3):293–301.
20. Rugo HS, Bardia A, Marmé F, Cortés J, Schmid P, Loirat D, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. *Lancet*. 2023;402(10411):1423–33.
21. Uliano J, Corvaja C, Curigliano G, Tarantino P. Targeting HER3 for cancer treatment: a new horizon for an old target. *ESMO Open*. 2023;8(1):100790.
22. Suenaga A, Takada N, Hatakeyama M, Ichikawa M, Yu X, Tomii K, et al. Novel mechanism of interaction of p85 subunit of phosphatidylinositol 3-kinase and ErbB3 receptor-derived phosphotyrosyl peptides. *J Biol Chem*. 2005;280(2):1321–6.
23. Krop IE, Masuda N, Mukohara T, Takahashi S, Nakayama T, Inoue K, et al. Patritumab deruxtecan (HER3-DXd), a human epidermal growth factor receptor 3-directed antibody-drug conjugate, in patients with previously treated human epidermal growth factor receptor 3-expressing metastatic breast cancer: a multicenter, Phase I/II trial. *J Clin Oncol*. 2023;41(36):5550–60.
24. Pistilli B, Pierotti L, Lacroix-Triki M, Vicier C, Frenel JS, D'Hondt V, et al. 3400 Efficacy, safety and biomarker analysis of ICARUS-BREAST01: A phase II study of patritumab deruxtecan (HER3-DXd) in patients (pts) with HR+/HER2- advanced breast cancer (ABC). *Ann Oncol*. 2024;35:S357.
25. Oliveira M, Pascual T, Villacampa G, Munoz M, Martorell AP, Lopez MEP, et al. 155TIP A randomised phase II trial of neoadjuvant multi-agent chemotherapy (CHT) OR patritumab deruxtecan (HER3-DXd; U3-1402) +/- endocrine therapy (ET) for high-risk hormone receptor-positive (HR+/HER2-) early breast cancer (EBC): SOLT1-2103 VALENTINE trial. *ESMO Open*. 2023;8(1):101494.
26. Oliveira M. LB1-06: Primary results of SOLT1 VALENTINE: neoadjuvant randomized phase II trial of HER3-DXd alone or in combination with letrozole for high-risk hormone receptor positive (HR+)/HER2-negative (neg) early breast cancer (EBC). In 2024.
27. Turner N, Saura C, Aftimos P, Van Den Tweel E, Oesterholt M, Koper N, et al. Trastuzumab duocarmazine in pretreated human epidermal growth factor receptor 2-positive advanced or metastatic breast cancer: an open-label, randomized, Phase III trial (TULIP). *J Clin Oncol*. 2025;43(5):513–23.
28. Hu X, Wang L, Zhang J, Zhang Q, Ouyang Q, Wang X, et al. ACE-Breast-02: A pivotal phase II/III trial of ARX788, a novel anti-HER2 antibody-drug conjugate (ADC), versus lapatinib plus capecitabine for HER2+ advanced breast cancer (ABC). *J Clin Oncol*. 2024;42(16_suppl):1020–1020.
29. Wang J, Liu Y, Zhang Q, Li W, Feng J, Wang X, et al. Disitamab vedotin, a HER2-directed antibody-drug conjugate, in patients with HER2-overexpression and HER2-low advanced breast cancer: a phase I/Ib study. *Cancer Commun*. 2024;44(7):833–51.
30. Zhang J, Du Y, Meng Y, Liu X, Mu Y, Liu Y, et al. First-in-human study of DP303c, a HER2-targeted antibody-drug conjugate in patients with HER2 positive solid tumors. *Npj Precis Oncol*. 2024;8(1):200.
31. Jiang Z, Sun T, Wang X, Liu Q, Yan M, Tong Z, et al. A multiple center, open-label, single-arm, phase II clinical trial of MRG002, an HER2-targeted antibody-drug conjugate, in patients with HER2-low expressing advanced or metastatic breast cancer. *J Clin Oncol*. 2022;40(16_suppl):1102–1102.
32. Yan M, Lv H, Niu L, Zhang M, Liu Z, Sun H, et al. Efficacy and safety of HER2-ADC SHR-A1811 in HER2-positive breast cancer with brain metastases. *J Clin Oncol*. 2024;42(16_suppl).

33. Li JJ, Wang ZH, Chen L, Zhang WJ, Ma LXX, Wu J, et al. Efficacy and safety of neoadjuvant SHR-A1811 with or without pyrotinib in women with locally advanced or early HER2-positive breast cancer: a randomized, open-label, phase 2 trial. *Ann Oncol*. 2025;S0923753425000821.
34. Schmid P, Wysocki PJ, Ma CX, Park YH, Fernandes R, Lord S, et al. 379MO Datopotamab deruxtecan (Dato-DXd) + durvalumab (D) as first-line (1L) treatment for unresectable locally advanced/metastatic triple-negative breast cancer (a/mTNBC): Updated results from BEGONIA, a phase Ib/II study. *Ann Oncol*. 2023;34:S337.
35. Xu B, Yin Y, Fan Y, Ouyang Q, Song L, Wang X, et al. Sacituzumab tirumotecan (SKB264/MK-2870) in patients (pts) with previously treated locally recurrent or metastatic triple-negative breast cancer (TNBC): Results from the phase III OptiTROP-Breast01 study. *J Clin Oncol*. 2024;42(16_suppl):104-104.
36. Ma F, Qiu F, Tong Z, Wang J, Shi Y, Zhang Y, et al. 349MO Results from a phase Ia/Ib Study of ESG401, a novel Trop2 antibody-drug conjugate, in patients with different subtypes of metastatic breast cancer. *Ann Oncol*. 2024;35:S361-2.
37. Ma F, Qiu F, Tong Z, Shi Y, Yu G, Wu X, et al. ESG401, a trophoblast cell-surface antigen 2 (TROP2) antibody drug conjugate (ADC), for the treatment of first-line metastatic triple negative breast cancer (mTNBC). *J Clin Oncol*. 2024 Jun 1;42(16_suppl):e13132-e13132.
38. Wang Y, Li G, Wang H, Qi Q, Wang X, Lu H. Targeted therapeutic strategies for Nectin-4 in breast cancer: Recent advances and future prospects. *The Breast*. 2025;79:103838.
39. Giordano A, Awan AAA, Yang Bruce J, Rugo HS, Diamond JR, Novik Y, et al. Enfortumab vedotin (EV) in triple-negative breast cancer (TNBC) and HR+/HER2- breast cancer (BC) cohorts of EV-202. *J Clin Oncol*. 2024;42(16_suppl):1005-1005.
40. Perez CA, Henry JT, Lakhani N, Call JA, Hamilton EP, Colon-Otero G, et al. 660MO First-in-human study of SGN-B7H4V, a B7-H4-directed vedotin ADC, in patients with advanced solid tumors: Preliminary results of a phase I study (SGNB7H4V-001). *Ann Oncol*. 2023;34:S464-5.
41. Wu J, Zhang J, Li H, Wang X, Zhang QY, Shi Y, et al. 381O First-in-human/phase I trial of HS-20089, a B7-H4 ADC, in patients with advanced solid tumors. *Ann Oncol*. 2023;34:S336.
42. Ferragut F, Vachetta VS, Troncoso MF, Rabinovich GA, Elola MT. ALCAM/CD166: A pleiotropic mediator of cell adhesion, stemness and cancer progression. *Cytokine Growth Factor Rev*. 2021;61:27-37.
43. Boni V, Fidler MJ, Arkenau HT, Spira A, Meric-Bernstam F, Uboha N, et al. Praluzatamab ravtansine, a CD166-targeting antibody-drug conjugate, in patients with advanced solid tumors: an open-label phase I/II trial. *Clin Cancer Res*. 2022;28(10):2020-9.
44. Miller K, Tolaney S, Emens LA, Kim SB, Hamilton E, Saura C, et al. Abstract P4-01-15: Preliminary results from a phase 2 study of praluzatamab ravtansine (CX-2009) in patients with advanced breast cancer (ABC). *Cancer Res*. 2023;83(5_Supplement):P4-01-15-P4-01-15.