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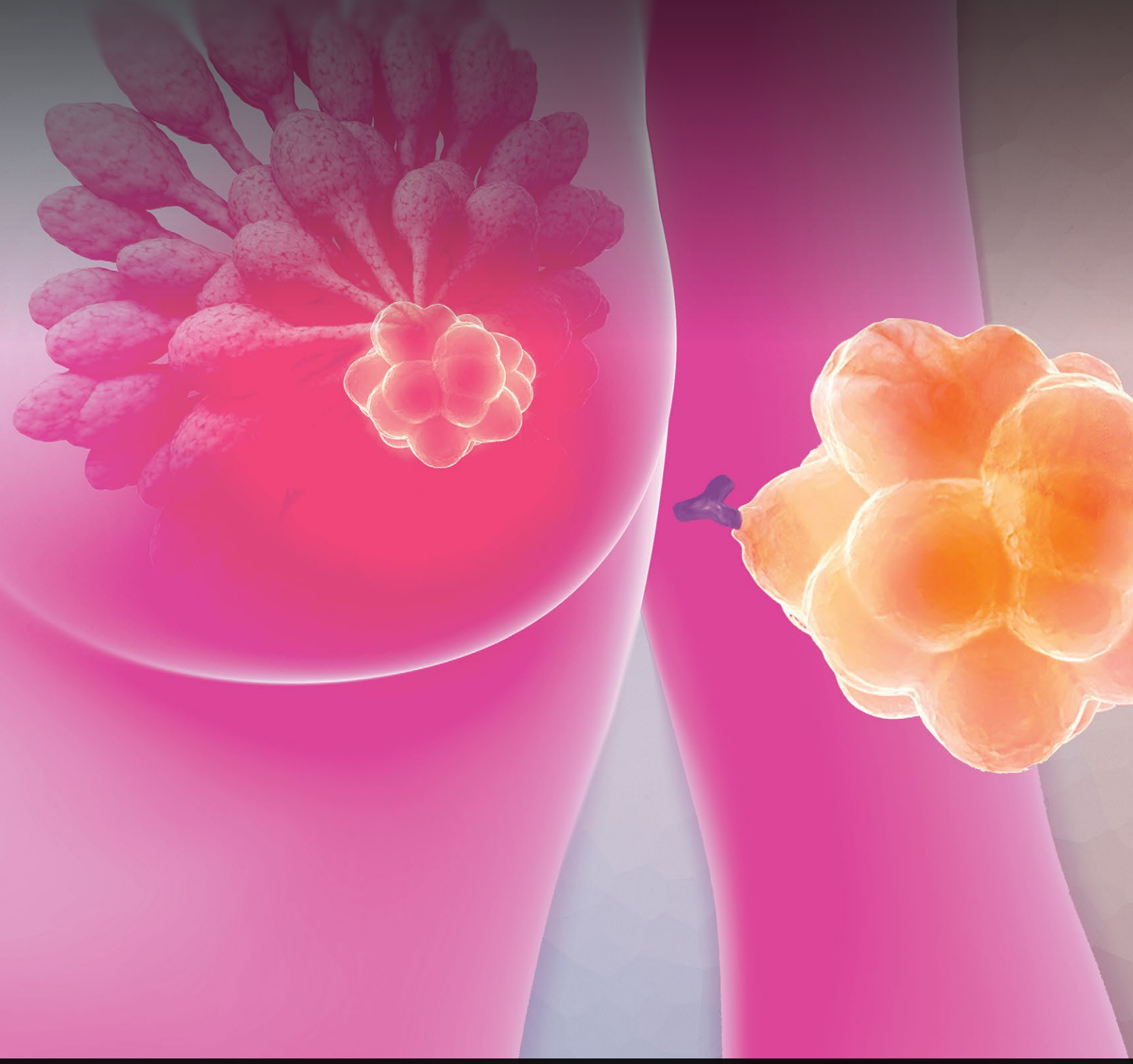
CHAIRPERSON'S PERSPECTIVE

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

Improving HR+/HER2- Breast Cancer Outcomes with TROP2 Antibody-Drug Conjugates



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AXIS Medical Education

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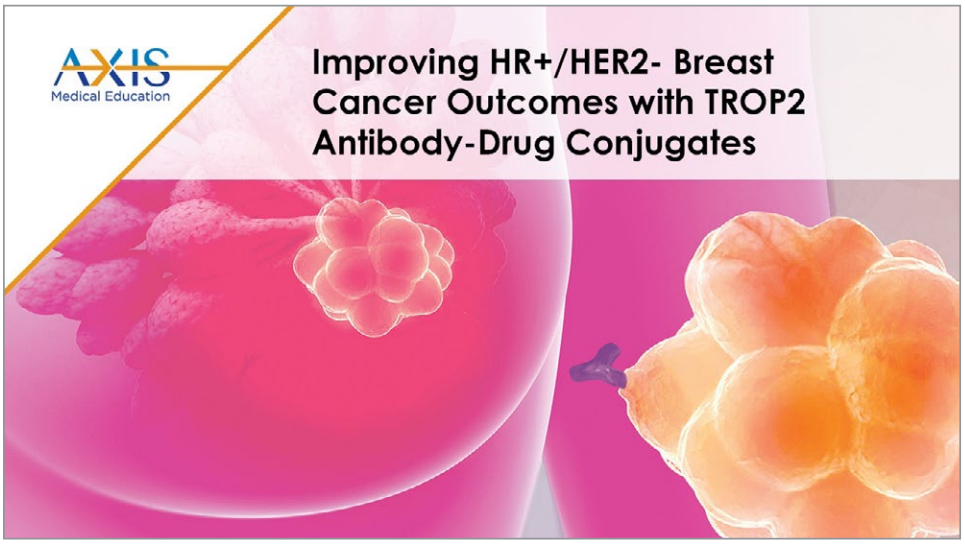
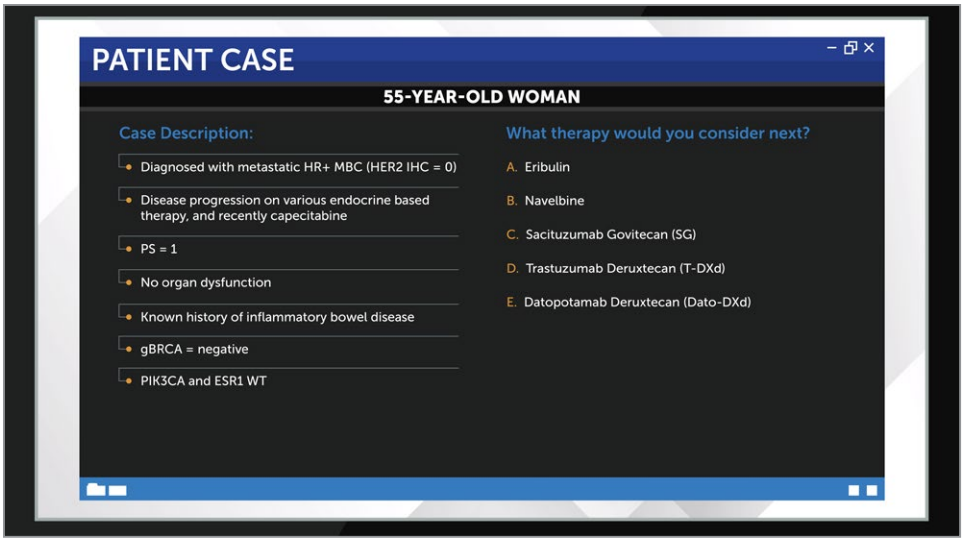
CHAIRPERSON'S PERSPECTIVE
Improving HR+/HER2- Breast Cancer Outcomes with TROP2 Antibody-Drug Conjugates

Aditya Bardia, MD



Aditya Bardia, MD: Hello. I'm Aditya Bardia, Medical Oncologist at UCLA, and I'm excited to talk about this important topic, which is improving the outcomes of patients with hormone receptive-positive, HER2-negative metastatic breast cancer with TROP2-directed antibody-drug conjugates.



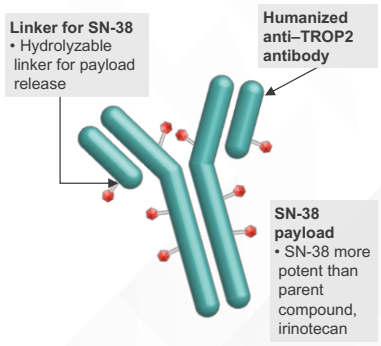
Let's start with a case, a common scenario we see in clinic. A 55-year-old female with metastatic hormone receptor-positive, HER2 IHC 0 metastatic breast cancer, who's had disease progression on various endocrine-based regimens, also received one line of chemotherapy with capecitabine, good performance status, no actionable genomic alterations, germline BRCA-negative, has a history of inflammatory bowel disease. And the question is, after capecitabine, what would you consider for this patient? Eribulin, navelbine, sacituzumab govitecan, or trastuzumab deruxtecan, or datopotamab deruxtecan.

So it's a common scenario we are faced with the clinic. We have all these drugs that are FDA approved now, so I'll review how to select these agents and how to sequence these agents.

Sacituzumab Govitecan: First-in-Class TROP2 ADC

SG is distinct from other ADCs

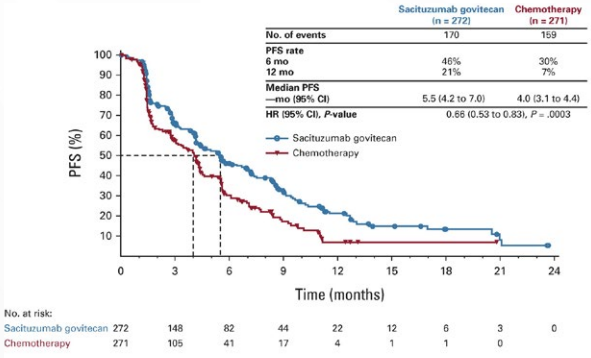
- Antibody highly specific for Trop-2
- High drug-to-antibody ratio (7.6:1)
- Internalization and enzymatic cleavage by tumor cell not required for the liberation of SN-38 from the antibody
- Hydrolysis of the linker also releases the SN-38 cytotoxic extracellularly in the tumor microenvironment, providing a bystander effect



ADC, antibody-drug conjugate; SG, sacituzumab govitecan; TROP2, trophoblast cell-surface antigen 2.
Nagayama A, et al. *Ther Adv Med Oncol*. 2020;12:1758835920915980.
Cardillo TM, et al. *Bioconjugate Chem*. 2015;26(5):919-931.

- Let's start with sacituzumab govitecan. It was the first in class TROP2-directed ADC. It targets TROP2. It has SN38, the active metabolite of irinotecan as the payload, also has a bystander effect, so it can even impact cells with low or no expression of TROP2.

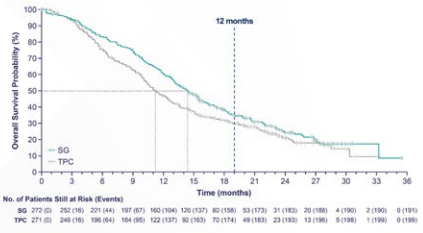
Sacituzumab Govitecan vs TPC: PFS (HR+ MBC)



HR, hormone receptor; MBC, metastatic breast cancer; PFS, progression-free survival; TPC, treatment of physician's choice.
Rugo HS, et al. *J Clin Oncol*. 2022;40(20):3365-3376.

- This was evaluated in the TROPiCS-02 study, a pivotal phase 3 trial that demonstrated that sacituzumab govitecan was superior to standard chemotherapy for patients with hormone receptor-positive, HER2-negative breast cancer, so that was both HER2-low as well as HER2 IHC 0 metastatic breast cancer. There was improvement in progression-free survival.

Sacituzumab Govitecan vs TPC: OS (HR+ MBC)



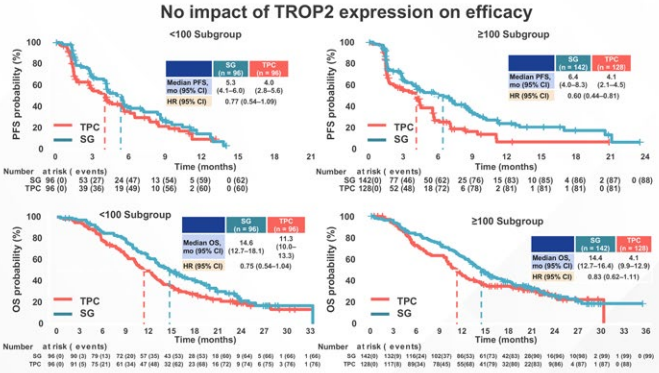
- SG demonstrated a statistically significant improvement in OS vs TPC with 21% reduction in the risk of death; having met statistical significance, no further formal statistical testing of OS will occur
- Patients who received SG survived a median of 3.2 months longer than those who received TPC

	SG (n=272)	TPC (n=271)
Number of events	191	199
Median OS, mo (95% CI)	14.4 (13.0–15.7)	11.2 (10.1–12.7)
Stratified HR (95% CI)	0.79 (0.65–0.96)	
Stratified Log Rank *P* value	*P*=0.020	
12-month OS rate, % (95% CI)	61 (55–66)	47 (41–53)

Median follow-up was 12.5 months.
HR, hormone receptor; MBC, metastatic breast cancer; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
Rugo HS, et al. ESMO 2022. Abstract 15530.

- And impressively, there was improvement in overall survival as well the median overall survival 14.5 months with sacituzumab govitecan versus 11 months or so with standard chemotherapy. So this led to the FDA approval for sacituzumab govitecan. And as per label, it was for patients who've received at least two prior lines of systemic therapy in this setting.

Efficacy by TROP2 Expression in the TROPiCS-02 Study of Patients With HR+/HER2– Metastatic Breast Cancer



HER2, human epidermal growth factor receptor 2; HR, hormone receptor; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TROP2, trophoblast cell-surface antigen 2.
Rugo HS, et al. *Lancet*. 2023;402(10411):1423-1433.

- Now, how about biomarkers? Should we look for TROP2, the drug targets TROP2? Should we measure for TROP2? And the answer in clinic is no. We do not look at TROP2 expression for selection of sacituzumab govitecan at this time based on the FDA label. In TROPiCS-02, as well as other trials like ASCENT, the team looked at the correlation between TROP2 and outcomes, and even in patients with low expression of TROP2, the benefit with SG was maintained, so the outcomes were better with SG as compared to standard chemotherapy. So measurement of TROP2 does not influence clinical decision-making, and that's why we don't use it in clinic at this time.

Treatment Related Adverse Effects: Sacituzumab Govitecan (vs TPC)

		SG (n=258)			TPC (n=224)		
TRAE		All grade %	Grade 3, %	Grade 4, %	All grade, %	Grade 3, %	Grade 4, %
Hematologic	Neutropenia	63	46	17	43	27	13
	Anemia	34	8	0	24	5	0
	Leukopenia	16	10	1	11	5	1
	Febrile neutropenia	6	5	1	2	2	<1
Gastrointestinal	Diarrhea	59	10	0	12	<1	0
	Nausea	57	2	<1	26	<1	0
	Vomiting	29	1	<1	10	<1	0
Other	Fatigue	45	3	0	30	5	0
	Alopecia	46	0	0	16	0	0

- Key grade ≥3 TRAEs (SG vs TPC): neutropenia (51% vs 33%), diarrhea (10% vs <1%), leukopenia (10% vs 5%), anemia (8% vs 5%), and febrile neutropenia (6% vs 2%)
- No severe cardiovascular toxicity, no grade >2 neuropathy or grade >3 interstitial lung disease with SG

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SG, sacituzumab govitecan; TPC, treatment of physician's choice; TRAE, treatment-related adverse event.
Bardia A, et al; ASCENT Clinical Trial Investigators. *N Engl J Med.* 2021;384(16):1529-1541.

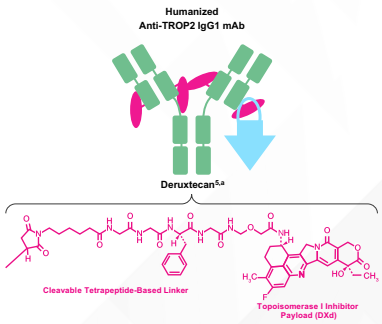
How about AEs? Three common AEs seen with sacituzumab govitecan; the first one is neutropenia, close to 50% so 1 in 2 patients will have grade 3 or grade 4 neutropenia. Generally recommend secondary prophylaxis, although for certain patients, such as elderly, you could consider primary prophylaxis as well. The second side effect is diarrhea, generally grade 1/ grade 2, although you can see grade 3/4 diarrhea as well. Generally recommend prophylactic antidiarrheal, secondary prophylaxis with the use of loperamide. And the third side effect is alopecia. The drug uniformly causes alopecia, so it's important to counsel patients regarding this side effect.

The AEs we do not see with sacituzumab govitecan include cardiovascular toxicity, neuropathy, or interstitial lung disease. And this becomes important as we have multiple agents in this setting. And how do we select between the different agents? The AE profile can be an important factor to consider when selecting the ADC.

The other point to note is sacituzumab govitecan is given Day 1, Day 8, every 21 days in terms of schedule.

Datopotamab Deruxtecan

- Patients with relapsed/refractory advanced or metastatic TNBC have poor clinical outcomes[1]
- Dato-DXd is a differentiated TROP2-directed ADC designed with 3 components[2,3]:
  - A humanized anti-TROP2 IgG1 mAb
  - A topoisomerase I inhibitor payload (exatecan derivative, DXd)
  - A tetrapeptide-based cleavable linker
- Dato-DXd has demonstrated highly encouraging antitumor activity and manageable AEs in the NSCLC cohort[4]
  - 6 mg/kg has been selected as the dose for expansion into other advanced tumor types

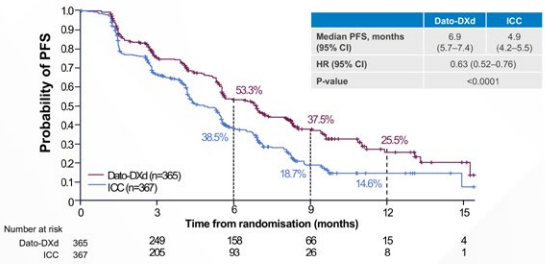


[a]Actual drug positions may vary.
ADC, antibody drug conjugate; AE, adverse event; IgG1, immunoglobulin G1; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; TNBC, triple-negative breast cancer; TROP2, trophoblast cell-surface antigen 2.
1. Bardia A, et al; ASCENT Clinical Trial Investigators. *N Engl J Med.* 2021;384(16):1529-1541. 2. Okajima D, et al. AACR-NCI-EORTC 2019. Abstract C026. 3. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. 4. Spira A, et al. WCLC 2020. Abstract 3407. 5. Krop I, et al. SABCS 2019. Abstract GS1-03.

The second ADC, that's now FDA approved, is datopotamab deruxtecan, which targets TROP2. It's a different antibody than sacituzumab govitecan. It's datopotamab. It's a different payload as well, deruxtecan as opposed to SN38 which is much more potent in terms of TOP1 inhibition. And the linker is different as well. It's a tetrapeptide-based cleavable linker. The drug is given every 3 weeks, so it has a different schedule as well, as compared to sacituzumab govitecan.

Dato-DXd in HR+ MBC (TROPION-Breast01)

PFS by BICR: primary endpoint



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.7–7.4)	4.9 (4.2–5.5)
HR (95% CI)	0.63 (0.52–0.76)	
P-value	<0.0001	

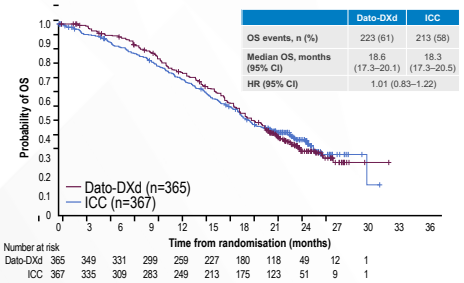
PFS by investigator assessment: Median 6.9 vs 4.5 months; HR 0.64 (95% CI 0.53–0.76)

PFS by BICR was consistent across subgroups

BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; HR, hormone receptor; ICC, investigator's choice of chemotherapy; MBC, metastatic breast cancer; PFS, progression-free survival.
Bardia A, et al. ESMO 2023. Abstract LBA11.

In terms of efficacy, this was evaluated in the phase 3 TROPION-Breast01 study, where there was improvement in progression-free survival, median PFS of about 7 months with Dato-DXd versus about 5 months with standard chemotherapy. Hazard ratio of 0.63. So improvement in progression-free survival was seen with this agent. Statistically significant, clinically meaningful as well.

Dato-DXd in HR+ MBC: Overall Survival (Tropion-B01)



	Dato-DXd	ICC
OS events, n (%)	223 (61)	213 (58)
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
HR (95% CI)	1.01 (0.83–1.22)	

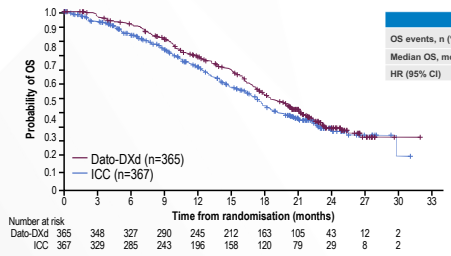
- Maturity: 59.6%
- Median follow-up: 22.8 months
- Protocol prespecified OS sensitivity analysis based on the stratification factors according to the eCRF*: HR 0.99 (95% CI: 0.82–1.20)

Data cutoff: July 24, 2024. Pre-specified *P*-value boundary for OS analysis: α=0.0427.
*Mis-stratification between interactive response technology (where data entered could not be changed by the site) and eCRF (where data could be corrected by sites) was <5%. Dato-DXd, datopotamab deruxtecan; eCRF, electronic case report form; HR, hormone receptor; ICC, investigator's choice of chemotherapy; MBC, metastatic breast cancer; OS, overall survival. Pistilli B, et al. ESMO Virtual Plenary 2025. Abstract VP1-2025.

- In terms of overall survival, the team did not see an improvement in overall survival in this clinical trial with a hazard ratio of 1.

Overall Survival Adjusted for Subsequent ADC Therapy

Post-hoc Sensitivity Analysis Using IPCW Method



	Dato-DXd	ICC
OS events, n (%)	195 (53)	177 (48)
Median OS, months	19.1	17.5
HR (95% CI)	0.86 (0.70–1.06)	

Data cutoff: July 24, 2024.
ADC, antibody-drug conjugate; Dato-DXd, datopotamab deruxtecan; ICC, investigator's choice of chemotherapy; IPCW, inverse probability censoring weighting; OS, overall survival.
Pistilli B, et al. ESMO Virtual Plenary 2025. Abstract VP1-2025.
1. Robins JM. American Statistical Association; 1993:24-33.
2. Robins JM, Finkelstein DM. *Biometrics*. 2000;56(3):779-788.
3. Sherry AD, et al. *BMJ Oncology*. 2024;3:e000322.

- However, this study was done in an era where trastuzumab deruxtecan was also approved, and so the team did additional sensitivity analysis, adjusting for the use of T-DXd, or balancing the use of T-DXd in both the arms so there was no imbalance. And then you could see a trend towards improvement in overall survival with Dato-DXd, a hazard ratio 0.86, 19 months of median OS with Dato-DXd was a 17.5 with investigator's choice of chemotherapy. So it appears that at least some of the difference in OS was because of imbalance in the use of subsequent ADC like T-DXd. And also speaks to the challenge in interpreting overall survival in the current era, when there are multiple effective agents.

Adverse Events of Clinical Interest

Neutropenia*	Dato-DXd (n=360)	ICC (n=351)
Treatment-related neutropenia*, n (%)		
Any grade	39 (11)	149 (42)
Grade ≥3	4 (1)	108 (31)
Leading to dose interruption	0	60 (17)
Leading to dose reduction	1 (0.3)	45 (13)
Leading to dose discontinuation	0	1 (0.3)
G-CSF usage, n (%)		
On treatment	10 (3)	81 (22)
Post-treatment†	1 (0.3)	30 (8)

Stomatitis‡	Dato-DXd (n=360)	ICC (n=351)
Treatment-related stomatitis‡, n (%)		
Any grade	180 (50)	46 (13)
Grade 3	23 (6)	9 (3)
Leading to dose interruption	5 (1)	3 (1)
Leading to dose reduction	44 (12)	5 (1)
Leading to dose discontinuation	1 (0.3)	0

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*Neutropenia includes the preferred terms neutropenia and neutrophil count decreased. Treatment-related febrile neutropenia occurred in 0 patients in the Dato-DXd arm and 8 patients (2.3%; all grade ≥3) in the ICC arm. †Administered after discontinuation of study treatment. ‡As part of the Oral Care Protocol specified in the study protocol, daily use of prophylaxis with a steroid-containing mouthwash (e.g., dexamethasone oral solution or a similar mouthwash regimen using an alternative steroid advocated by institutional/local guidelines) was highly recommended.
Dato-DXd, datopotamab deruxtecan; G-CSF, granulocyte colony stimulating factor; ICC, investigator's choice of chemotherapy.
Bardia A, et al. ESMO 2023. Abstract LBA11.

- In terms of side effects, the side effect of Dato-DXd, while it targets TROP2, is different from sacituzumab govitecan. In the clinical trial, the incidence of grade 3/grade 4 AEs were actually lower with Dato-DXd as compared to standard chemotherapy. So overall, it's well tolerated. The percentage of dose reduction interruptions were lower with Dato-DXd as compared to standard chemo. Generally does not cause much neutropenia, unlike sacituzumab govitecan. And the rate of neutropenia with Dato-DXd is lower as compared to standard chemo as well. But the drug does have side effects. Two important side effects to note; one is stomatitis, or mucositis, which can be seen with Dato-DXd, usually grade 1/grade 2, recommend primary prophylaxis with the use of a steroid mouthwash, and usually with that, you can manage the mucositis. The second side effect is pneumonitis, not to the degree as seen with T-DXd, but it is a side effect that can be seen with Dato-DXd, so it does require monitoring as well.

Management of AESIs with Datopotamab Deruxtecan

Ocular surface toxicity

- Median time to onset: 2.1 months
- Recommend primary prophylaxis with preservative-free lubricant eye drops several times daily; Avoid use of contact lenses if possible
- Ophthalmology visit for baseline ophthalmic exam at treatment initiation, annually while on treatment, at end of treatment, and as clinically indicated
- Monitor for ocular adverse events during treatment and prompt referral to ophthalmologist for any new or worsening ocular adverse reactions

AESI, adverse event of special interest.
DATROWAY (datopotamab deruxtecan-dlnk). Prescribing information. Daiichi Sankyo, Inc.; 2025.

- How do you manage these side effects? Let's talk about ocular toxicity. The median onset of ocular toxicity is about 2 months from the start of Dato-DXd. Generally recommend primary prophylaxis with a preservative-free lubricant eye drop and ophthalmology visit as well. If it's severe, you can hold the drug. In very severe cases, discontinue Dato-DXd.

Management of AESIs with Datopotamab Deruxtecan

Mucositis/Stomatitis

- Median time to onset: 0.7 months
- Recommend corticosteroid containing mouth wash 3-4 times/day, both for primary prophylaxis as well as treatment
- Ice-chips or ice-water during infusion could be considered
- Monitor for signs and symptoms of stomatitis; If stomatitis increases, consider increasing frequency of mouthwash, adding other topical treatment, and/or withholding Dato-DXd treatment to help reduce severity

AESI, adverse event of special interest.
DATROWAY (datopotamab deruxtecan-dlnk). Prescribing information. Daiichi Sankyo, Inc.; 2025.

- In terms of mucositis, as I mentioned, this is a side effect seen with Dato-DXd. Usually the first cycle, you'll see the side effect. Recommend steroid mouthwash three to four times a day, ice chips or ice water during infusion can also be considered. Again if it becomes severe, grade 3/grade 4, hold Dato-DXd, which would then allow this AE to recover, and then you can resume generally at a lower dose.

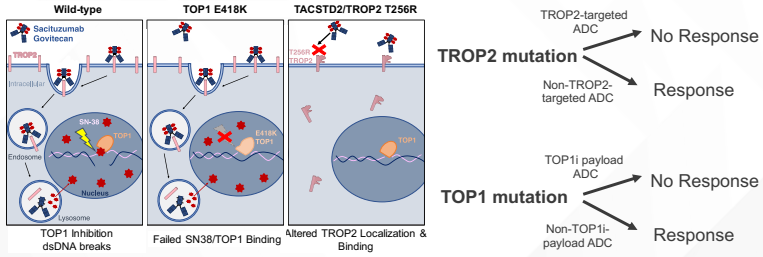
ADCs to Target MBC: Multiple Agents in Development

Antibody-Drug Conjugate	Target	Payload
Trastuzumab deruxtecan (DS-8201a)	HER2	Topo-1 inhibitor
Sacituzumab govitecan (IMMU-132)	TROP2	Topo-1 inhibitor
Datopotamab deruxtecan (DS-1062)	TROP2	Topo-1 inhibitor
Sacituzumab Tirumotecan	TROP2	Topo-1 inhibitor
Patritumab deruxtecan (U3-1402)	HER3	Topo-1 inhibitor
NBE-002	ROR1	Topo-2 inhibitor
Praluzatamab ravtansine	CD166	Microtubule inhibitor

ADC, antibody-drug conjugate; CD166, activated leukocyte cell adhesion molecule; HER2/3, human epidermal growth factor receptor 2/3; MBC, metastatic breast cancer; ROR1, receptor tyrosine kinase–like orphan receptor 1; TROP2, trophoblast cell-surface antigen 2.

- Now, besides this, there are other drugs that are in development or even approved. For example, T-DXd is another drug that's approved for HER2-low and ultralow metastatic breast cancer that's hormone receptor-positive. There are other drugs in development, like sacituzumab tirumotecan, patritumab deruxtecan. So multiple ADCs in development.

Implications of Resistance Mechanisms for ADC Sequencing

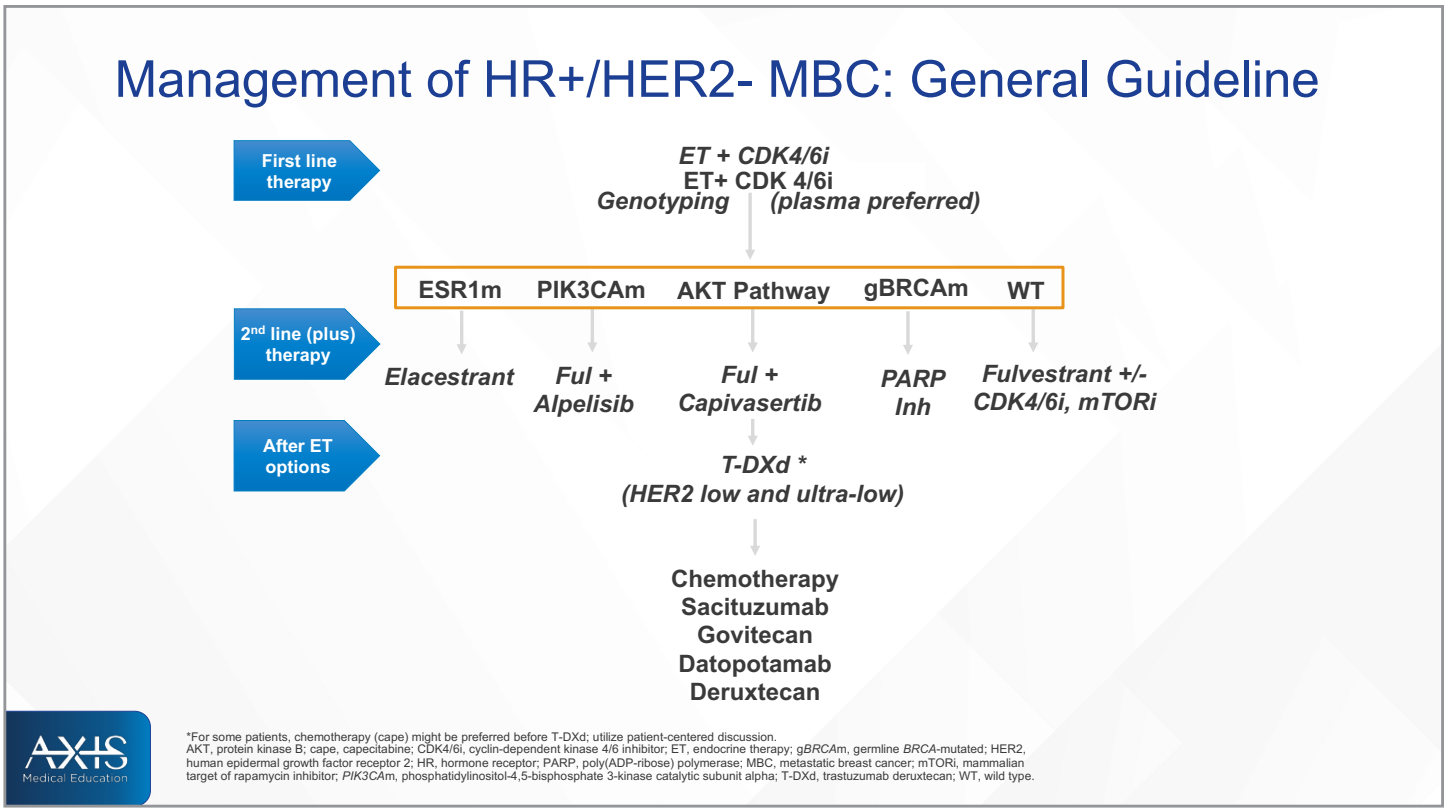


ADC, antibody-drug conjugate; *TACSTD2*, tumor associated calcium signal transducer 2; TOP1i, topoisomerase I inhibitor; TROP2, trophoblast cell-surface antigen 2.
Coates JT, et al. *Cancer Discov*. 2021;11(10):2436-2445.

- And a question for the field is, how do we sequence the different ADCs? At this time, we don't have any biomarkers to guide sequencing of ADCs, but conceptually it'll be based on resistance. So for example, we know that some tumors develop mutations in TOP1, which is the target of the payload, both sacituzumab govitecan and datopotamab deruxtecan. And if you have emergence of TOP1 mutation, that'll cross resistance between SG and Dato-DXd and even T-DXd. All these three ADCs that are FDA approved have TOP1 payload, so there's TOP1 mutation that could result in cross resistance.

  On the other hand, if the resistance is more because of the antigen, then you can use T-DXd and then Dato-DXd. Because one targets HER2, the other targets TROP2.

  So better understanding of resistance could help with sequencing. It's not ready for prime time yet because we need the clinical assays, but conceptually as a field, that's where we are going.



So what's the current guideline? This is my recommendation for management of hormone receptor-positive HER2-negative metastatic breast cancer. In the first-line setting, I would recommend endocrine therapy, plus a CDK4/6 inhibitor, ribociclib, palbociclib, abemaciclib, those are the three ones that are FDA approved. In the second-line setting, strongly recommend genotyping, because it's actionable. If a patient has ESR1-mutant breast cancer or detection of ESR1 mutations, generally by a blood-based assay, elacestrant is the drug that's approved for a patient who has PIK3CA mutation. Fulvestrant plus alpelisib, or fulvestrant plus capivasertib would be an option for a patient who has detectable alterations in the AKT pathway. So that's PIK3CA mutation, or PTEN mutation, or AKT mutation, then you can use fulvestrant plus capivasertib as well. For patients with germline BRCA mutations, PARP inhibitors, olaparib and talazoparib, would be options to consider. If a patient does not have any actionable genomic alteration that's detectable, you can use fulvestrant with/without switching the CDK4/6 inhibitor. So if in the first-line setting, ribociclib was used; in the second-line setting, you could consider abemaciclib or consider the use of everolimus. The approval of everolimus is not linked to any genomic alteration. So certainly something you can use in this setting. In the second-line, third-line setting, usually we sequence these endocrine-based options. So if you've started with fulvestrant/capicitabine, then after that, you could consider everolimus or abemaciclib. Or if a patient has both ESR1/PIK3CA mutation, you could consider elacestrant as well. So generally, we use endocrine-based options.

Once endocrine-based options have been exhausted, that's when we go to ADCs and chemo. Based on DESTINY-Breast06, T-DXd, or trastuzumab deruxtecan, is an option to consider in this setting for both HER2-low or ultralow metastatic breast cancer. For some patients, capecitabine could be an option before T-DXd, it's an older drug. If you use T-DXd first, then you can use capecitabine after that. If you use capecitabine first, then you can use T-DXd after that. Generally, that's the preferred regimen to consider for a patient with HER2-low or ultralow disease. And then after that, we consider sacituzumab govitecan. And now we have datopotamab deruxtecan as well. For a patient who has HER2 IHC 0 disease, two or three biopsies, all HER2 IHC 0, 00, not even ultralow, then as per label, the option would be sacituzumab govitecan or datopotamab deruxtecan. You cannot use T-DXd as per the label.

So that's my algorithm. I generally sequence these ADCs. I prioritize ADCs over chemo based on what we've seen from the clinical trials. If there's a good clinical trial option available, that's always something to consider.

Shared Decision-Making (SDM)

- SDM is a fundamental method of care that is central to individualizing treatment[1]
- It involves an MDT approach to ensure optimal care for and communication with the patient and their family[1]
- The initial step involves promoting productive dialogues that encourage active patient-clinician collaboration, facilitating the process of care plan development, and supporting the cocreation of a comprehensive care plan[1]
- Person-centered decision-making (PCDM)[2]
  - A person-centered orientation throughout the care continuum is fundamental to PCDM
  - The patient and the clinician share values and preferences, comprehensively discuss options, and then arrive collaboratively at treatment decisions that are preference-aligned

MDT, multi-disciplinary team; SDM, shared decision-making.
1. Shickh S, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e389516. 2. Rocque GB, et al. *J Natl Compr Cancer Netw*. 2024;22(1):e237113.

- It's good to do shared decision-making with the patient based on their priorities based on the comorbid conditions they have. Sometimes it requires multidisciplinary management as well. So if a patient has history of pneumonitis with T-DXd, involving a pulmonologist. Or like the case we reviewed a patient with inflammatory bowel disease, working with a GI specialist. So having a multidisciplinary team and involving the patient as well. So more of a patient-centered, person-centered decision-making, is critical when there are multiple options.

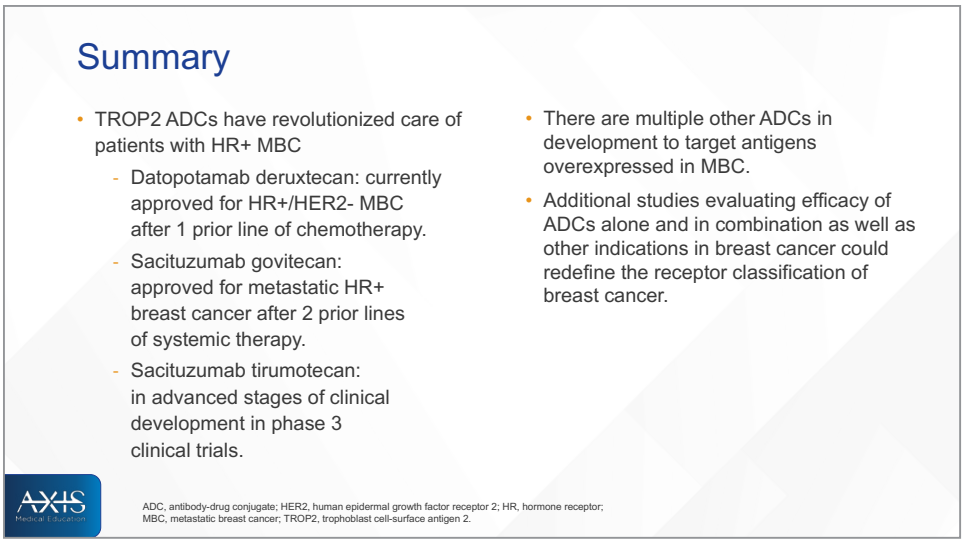
  Schedule. SG is Day 1, Day 8 every 21 days, while Dato-DXd is every 3 weeks. So all of those factors come into picture in terms of looking at these drugs.

Key Components of Patient-Centered Decision-Making

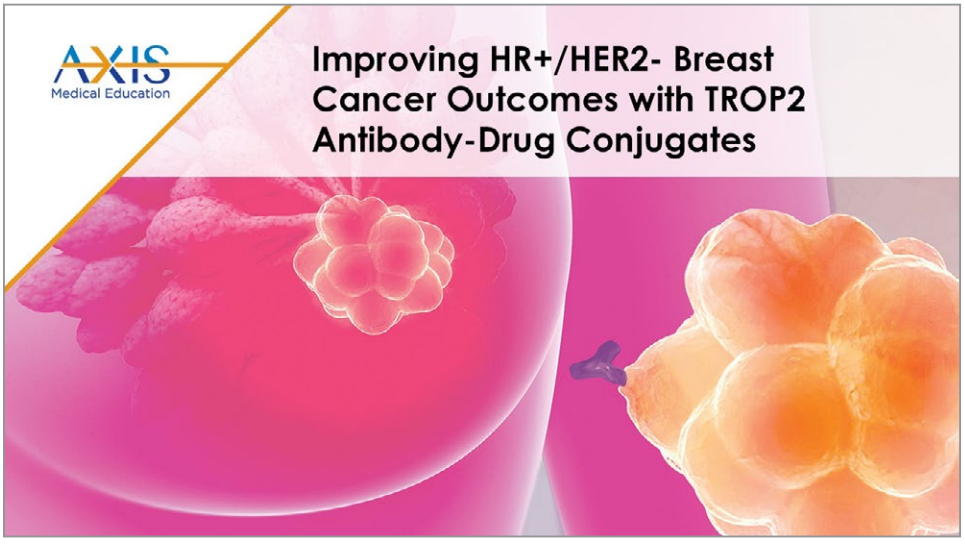
Component	Description
Fostering the patient–clinician relationship	• Both the patient and the clinician are recognized as key partners within the clinical encounter, contributing perspectives, experiences, knowledge, and expertise to the decision-making process. • Both parties collaborate to foster a trusting, respectful, empathetic, and open patient–clinician relationship.
Engaging in patient-centered communication	• Bidirectional communication underscores patient-centered discourse and is fundamental to PCDM. • The clinician's conversational approach includes open-ended questions, active listening, curiosity, and acknowledging emotion to better understand how the patient's experiences and perspectives may influence treatment decision-making. • PCDM emphasizes the clinician's critical role in gathering information and ensuring that the patient has been heard and understood. • During the bidirectional information exchange, the clinician shares their expertise, experiences, and perspectives and the patient is encouraged to ask questions to better understand the clinician's perspectives.
Understanding individual and contextual factors	• The patient–clinician partnership includes exploring the unique individual characteristics of the patient and clinician, as well as the medical and nonmedical contextual circumstances that may influence treatment decisions. • The clinician learns more about the patient's demographic, individual, and clinical characteristics; preferred level of engagement; desired level of and access to information; treatment preferences; skills and willingness to manage their health care; social support system; and access to and engagement in health resources and programs. The clinician likewise shares their expertise, experiences, and recommended treatment approaches, while encouraging the patient to ask questions. • Understanding personal and contextual factors ensures that the treatment decision-making process is adapted to the individual patient's needs and preferences (ie, contextualized care), and helps the clinician to understand how patients' preferences may evolve over time (eg, due to clinical course, age) or in different contexts. • The clinician communicates a treatment recommendation, contextualized by patient preferences and values and inclusive of the clinician's experience and clinical knowledge.

PCDM, person-centered decision-making .
Rocque GB, et al. *J Natl Compr Cancer Netw*. 2024;22(1):e237113.

- And the key components are to foster the patient-clinician relationship, ensuring that we are engaged in a patient-centered communication, understanding their preferences, understanding the different comorbid conditions, and providing the right drug.



So to summarize, TROP2 ADCs have revolutionized the care for patients with hormone receptor-positive metastatic breast cancer. Datopotamab deruxtecan is now approved for hormone receptor-positive HER2-negative metastatic breast cancer after one prior line of chemo, as per label. Sacituzumab govitecan also approved for hormone receptor-positive breast cancer after two prior lines of systemic therapy. And sacituzumab tirumotecan, not approved yet, is being evaluated in phase 3 clinical trials. Besides this, there are other drugs and development as well. So for the field, the question is going to be, how do we sequence these agents? How do we move them to earlier lines? As well as, how do we build with combinations that are ADC based?



Thanks so much for joining today. Hope this was helpful.

REFERENCES

Bardia A, Hurvitz SA, Tolaney SM, et al; ASCENT Clinical Trial Investigators. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med.* 2021;384(16):1529-1541.

Bardia A, Jhaveri K, Im S, et al. Datopotamab deruxtecan (Dato-DXd) vs chemotherapy in previously-treated inoperable or metastatic hormone receptor-positive, HER2-negative (HR+/HER2–) breast cancer (BC): Primary results from the randomised phase III TROPION-Breast01 trial. Abstract presented at: European Society of Medical Oncology Congress; Madrid, Spain; October 20-24, 2023. Abstract LBA11.

Cardillo TM, Govindan SV, Sharkey RM, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2/SN-38 antibody-drug conjugate: characterization and efficacy in pancreatic, gastric, and other cancers. *Bioconjugate Chem*. 2015;26(5):919-931.

Coates JT, Sun S, Leshchiner I, et al. Parallel genomic alterations of antigen and payload targets mediate polyclonal acquired clinical resistance to sacituzumab govitecan in triple-negative breast cancer. *Cancer Discov*. 2021;11(10):2436-2445.

DATROWAY (datopotamab deruxtecan-dlnk). Prescribing information. Daiichi Sankyo, Inc.; 2025.

Krop I, Saura C, Yamashita T, et al. [Fam-] trastuzumab deruxtecan (T-DXd; DS-8201a) in subjects with HER2-positive metastatic breast cancer previously treated with T-DM1: A phase 2, multicenter, open-label study (DESTINY-Breast01. Abstract presented at: San Antonio Breast Cancer Symposium; San Antonio, Texas; December 10-14, 2019. Abstract GS1-03.

Nagayama A, Vidula N, Ellisen L, Bardia A. Novel antibody-drug conjugates for triple negative breast cancer. *Ther Adv Med Oncol.* 2020;12:1758835920915980.

Nakada T, Sugihara K, Jikoh T, Abe Y, Agatsuma T. The latest research and development into the antibody-drug conjugate, [fam-] trastuzumab deruxtecan (DS-8201a), for HER2 cancer therapy. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185.

Okajima D, Yamaguchi J, Kitamura M, et al. DS-1062a, a novel TROP2-targeting antibody-drug conjugate with a novel DNA topoisomerase I inhibitor DXd, demonstrates potent antitumor activity in preclinical models. Abstract presented at: AACR-NCI-EORTC International Conference; Boston, Massachusetts; October 26-30, 2019. Abstract C026.

Pistilli B, Jhaveri K, Im S-A, et al. Datopotamab deruxtecan (Dato-DXd) vs chemotherapy (CT) in previously-treated inoperable or metastatic hormone receptor-positive, HER2-negative (HR+/HER2–) breast cancer (BC): Final overall survival (OS) from the phase III TROPION-Breast01 trial. Abstract presented at: ESMO Virtual Plenary; February 12, 2025. Abstract VP1-2025.

Robins JM, Finkelstein DM. Correcting for noncompliance and dependent censoring in an AIDS Clinical Trial with inverse probability of censoring weighted (IPCW) log-rank tests. *Biometrics*. 2000;56(3):779-788.

Robins JM. Information recovery and bias adjustment in proportional hazards regression analysis of randomized trials using surrogate markers. In: Proceedings of the Biopharmaceutical Section, American Statistical Association. American Statistical Association; 1993:24-33.

Rocque GB, Patel MI, Wallner LP, et al. Patient-centered decision-making in metastatic breast cancer care delivery: a call to action. *J Natl Compr Canc Netw*. 2024;22(1):e237113.

Rugo HS, Bardia A, Marmé F, 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):1423-1433.

Rugo HS, Bardia A, Marmé F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol.* 2022;40(20):3365-3376.

Rugo HS, Schmid P, Tolaney SM, et al. Health-related quality of life (HRQoL) in the phase III TROPiCS-02 trial of sacituzumab govitecan (SG) vs chemotherapy in HR+/HER2- metastatic breast cancer (MBC). Abstract presented at: European Society of Medical Oncology Congress; Paris, France; September 9-13, 2022. Abstract 15530.

Sherry AD, Msaouel P, Lin TA, et al. Postprogression therapy and confounding for the estimated treatment effect on overall survival in phase III oncology trials. *BMJ Oncology*. 2024;3:e000322.

Shickh S, Leventakos K, Lewis MA, et al. Shared decision making in the care of patients with cancer. *Am Soc Clin Oncol Educ Book*. 2023;43:e389516.

Spira A, Lisberg A, Sands J, et al. Datopotamab deruxtecan (Dato-DXd; DS-1062), a TROP2 ADC, in patients with advanced NSCLC: updated results of TROPION-PanTumor01 phase 1 study. Abstract presented at: World Conference on Lung Cancer; Virtual; January 28-31, 2021. Abstract 3407.

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