Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Strategies to Safely and Effectively Implement Antibody-Drug Conjugates

Wednesday, May 13, 2026,

11:15 AM – 12:45 PM

Faculty

Courtney Arn, CNP
Jamie Carroll, APRN, MSN, CNP
Edward B Garon, MD, MS
Heather McArthur, MD, MPH, FASCO

Moderator

Kathleen N Moore, MD, MS

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Faculty

Courtney Arn, CNP
The James Cancer Hospital and Solove Research Institute
The Ohio State University
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Heather McArthur, MD, MPH, FASCO
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Komen Distinguished Chair in Clinical Breast Cancer Research
UT Southwestern Medical Center
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Moderator

Kathleen N Moore, MD, MS
Deputy Director and Director, Phase 1 Clinical Trials
Fred and Pamela Buffett Cancer Center at the University of Nebraska
Omaha, Nebraska

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Ms Arn — Disclosures

Speakers Bureaus	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Eisai Inc, Genmab US Inc, GSK, Merck, Pfizer Inc

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Ms Carroll — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Lilly, Novartis

Dr Garon — Disclosures

Consulting Agreements	AbbVie Inc, ArriVent Biopharma, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Black Diamond Therapeutics Inc, BridgeBio, Bristol Myers Squibb, Daiichi Sankyo Inc, Gilead Sciences Inc, GSK, Hexagon Bio, I-Mab Biopharma, IO Biotech, iTeos Therapeutics, LianBio, Merck, Novartis, Oxford BioTherapeutics, Pfizer Inc, Regeneron Pharmaceuticals Inc, Samsung Bioepis, Sanofi, Servier Pharmaceuticals LLC, Strata Oncology, Synthekine, TransCode Therapeutics, Verastem Inc
Contracted Research	ABL Bio, ArriVent Biopharma, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, BridgeBio, Bristol Myers Squibb, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Iovance Biotherapeutics, Lilly, Merck, Novartis, Prelude Therapeutics, Regeneron Pharmaceuticals Inc, Synthekine, TILT Biotherapeutics
Data and Safety Monitoring Boards/Committees	Bicycle Therapeutics, Nuvalent, Servier Pharmaceuticals LLC

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Dr McArthur — Disclosures

Advisory Committees	Arvinas, AstraZeneca Pharmaceuticals LP, Boston Scientific Corporation, Celcuity, Daiichi Sankyo Inc, Delcath Systems Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Lilly, Merck, Novartis, Pfizer Inc
Consulting Agreements	ALX Oncology

Dr Moore — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, Corcept Therapeutics Inc, GSK, Mersana Therapeutics Inc
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Contracted Research	Accent Therapeutics, Advaxis Inc, Allarity Therapeutics, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, GSK, Immunocore, Iovance Biotherapeutics, Regeneron Pharmaceuticals Inc, Schrödinger, Verastem Inc
Data and Safety Monitoring Boards/Committees	Bicycle Therapeutics
Nonrelevant Financial Relationships	ASCO, GOG Partners, NRG Oncology

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Commercial Support

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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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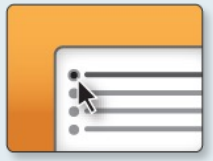
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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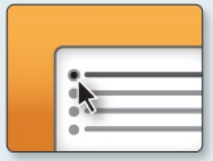
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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RTP RESEARCH TO PRACTICE ONCOLOGY NURSING UPDATE WITH NEIL LOVE, MD

NONMELANOMA SKIN CANCERS
Check out our recent program with Dr Nikhil I Khushalni from Moffitt Cancer Center in Tampa, Florida. Published May 7, 2026.

Overview of nonmelanoma skin cancers (12 min)

Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)

Hedgehog inhibitors for basal cell carcinoma (6 min)

New developments in therapy for nonmelanoma skin cancers (5 min)

CASE: A man in his early 70s with cutaneous squamous cell carcinoma receives cemiplimab (8 min)

CASE: A man in his mid 70s with a history of basal cell carcinoma presents with disease of the ocular surface and receives immunotherapy (6 min)

CASE: A man in his early 70s with recurrent metastatic basal cell carcinoma receives vismodegib followed by cemiplimab on disease progression (6 min)

Subscribe to our Oncology Nursing Update podcast

Feedback (Please!)

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“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”
Eighteenth Annual RTP-ONS NCPD Symposium Series

Wednesday May 13	**Antibody-Drug Conjugates** 11:15 AM – 12:45 PM CT
	Ovarian Cancer 6:00 PM – 7:30 PM CT
Thursday May 14	**Immunotherapeutic Approaches for Endometrial Cancer** 6:00 AM – 7:30 AM CT
	Prostate Cancer 12:15 PM – 1:45 PM CT
	Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer 6:00 PM – 7:30 PM CT
Friday May 15	**Pancreatic Cancer** 6:00 AM – 7:30 AM CT
	Targeting the PI3K/AKT/mTOR Pathway in HR-Positive Metastatic BC 12:15 PM – 1:45 PM CT
	Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia 6:00 PM – 8:00 PM CT
Saturday May 16	**CDK4/6 Inhibitors for HR-Positive Breast Cancer** 6:00 AM – 7:30 AM CT
	Relapsed/Refractory Multiple Myeloma 12:15 PM – 1:45 PM CT
	Oral SERDs for Breast Cancer 6:00 PM – 7:30 PM CT

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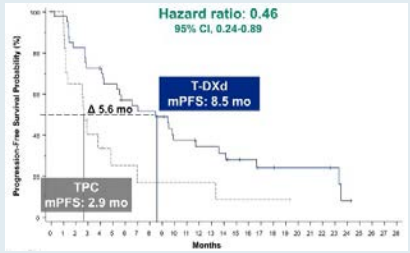
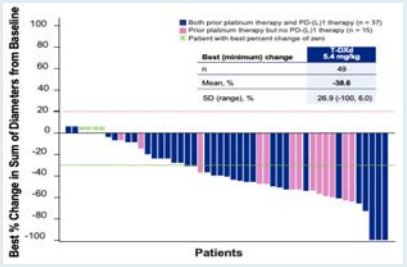
Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

- When should it be used, for whom and why?
- How to prevent and manage side effects: dose holds and reductions
  - Kaplan Meier curves — HR and absolute benefit



  - Waterfall plots



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Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

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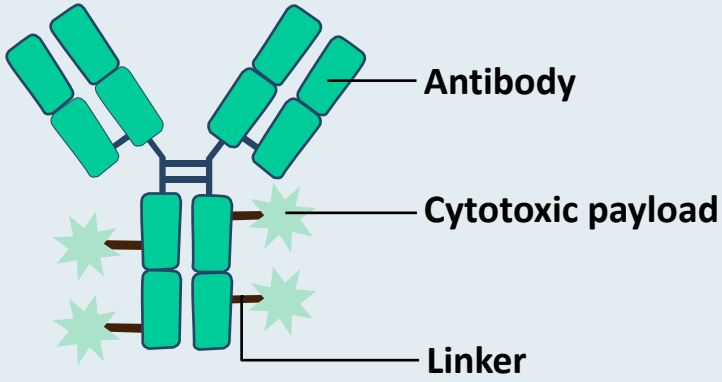
Discussion Questions

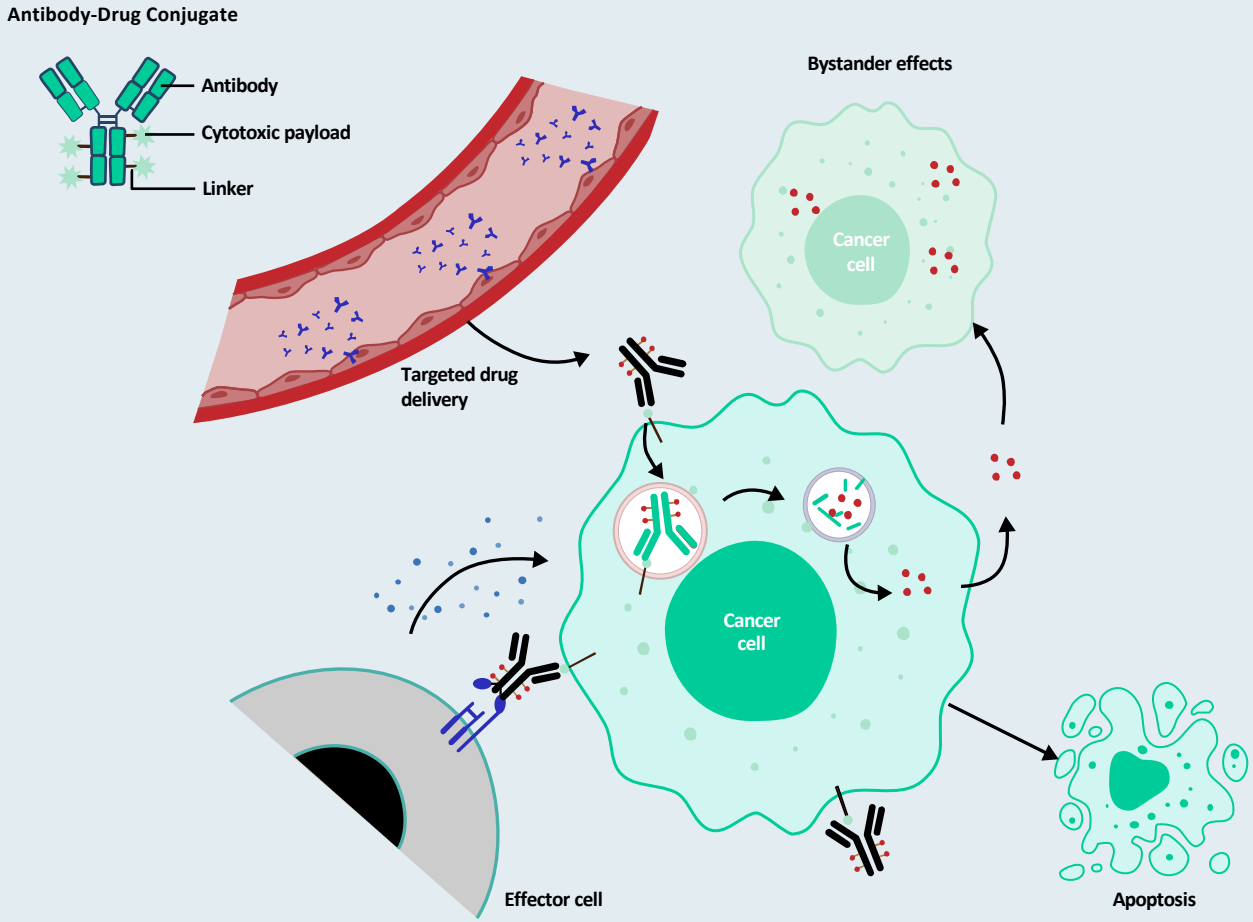
How do you explain to your patients how an antibody-drug conjugate works?

Mechanism of Action: ADCs



ADC Components

- **Antibody** specific for target antigen on cancer cells
- High-potency **cytotoxic payload**
- Cleavable or noncleavable **linker** between antibody and payload



Courtesy of Marianne J Davies, DNP, ACNP, AOCNP, FAAN

Current Approved ADCs in Oncology

Name	Year approved	Tumor type
Trastuzumab emtansine (T-DM1)	Adjuvant: 2019 Metastatic: 2013	Breast
Sacituzumab govitecan	HR-positive: 2023 Triple-negative: 2021 (Traditional) Triple-negative: 2020 (Accelerated)	Breast
Datopotamab deruxtecan	2025 (Traditional) 2025 (Accelerated)	Breast Non-small cell lung
Trastuzumab deruxtecan	2025 (Traditional) 2025 2024 2022 2022 2021 2019 (Accelerated) 2022 (Traditional)	HER2-positive breast (first-line) HER2-low/ultralow breast HER2-positive solid tumors HER2-mutant lung HER2-low breast HER2-positive gastric HER2-positive metastatic breast

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

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Current Approved ADCs in Oncology (Continued)

Name	Year approved	Tumor type
Mirvetuximab soravtansine	2024 (Traditional) 2022 (Accelerated)	Ovarian
Tisotumab vedotin	2024 (Traditional) 2021 (Accelerated)	Cervical
Enfortumab vedotin (monotherapy)	2021 (Traditional) 2019 (Accelerated)	Urothelial
Enfortumab vedotin (with pembrolizumab)	2025 (Traditional) 2023 (Accelerated/Traditional)	Muscle-invasive bladder Urothelial
Telisotuzumab vedotin	2025 (Accelerated)	Non-small cell lung
Gemtuzumab ozogamicin	2017 (Traditional) 2000 (Accelerated)	Acute myeloid leukemia
Brentuximab vedotin	2011 (Accelerated) 2015 (Traditional) 2017 (Traditional) 2018 (Traditional) 2018 (Traditional) 2025 (Traditional)	Hodgkin lymphoma (HL), systemic anaplastic large cell lymphoma (ALCL) HL (consolidation) ALCL, mycosis fungoides HL (front line) Peripheral T-cell lymphoma Large B-cell lymphoma (LBCL), diffuse LBCL

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

Current Approved ADCs in Oncology (Continued)

Name	Year approved	Tumor type
Inotuzumab ozogamicin	2017 (Traditional)	Acute lymphoblastic leukemia
Polatuzumab vedotin	2023 (Traditional) 2019 (Accelerated)	DLBCL
Loncastuximab tesirine	2021 (Accelerated)	LBCL
Belantamab mafodotin	2020 (Accelerated) 2022 (Withdrawn) 2025 (Traditional)	Multiple myeloma

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

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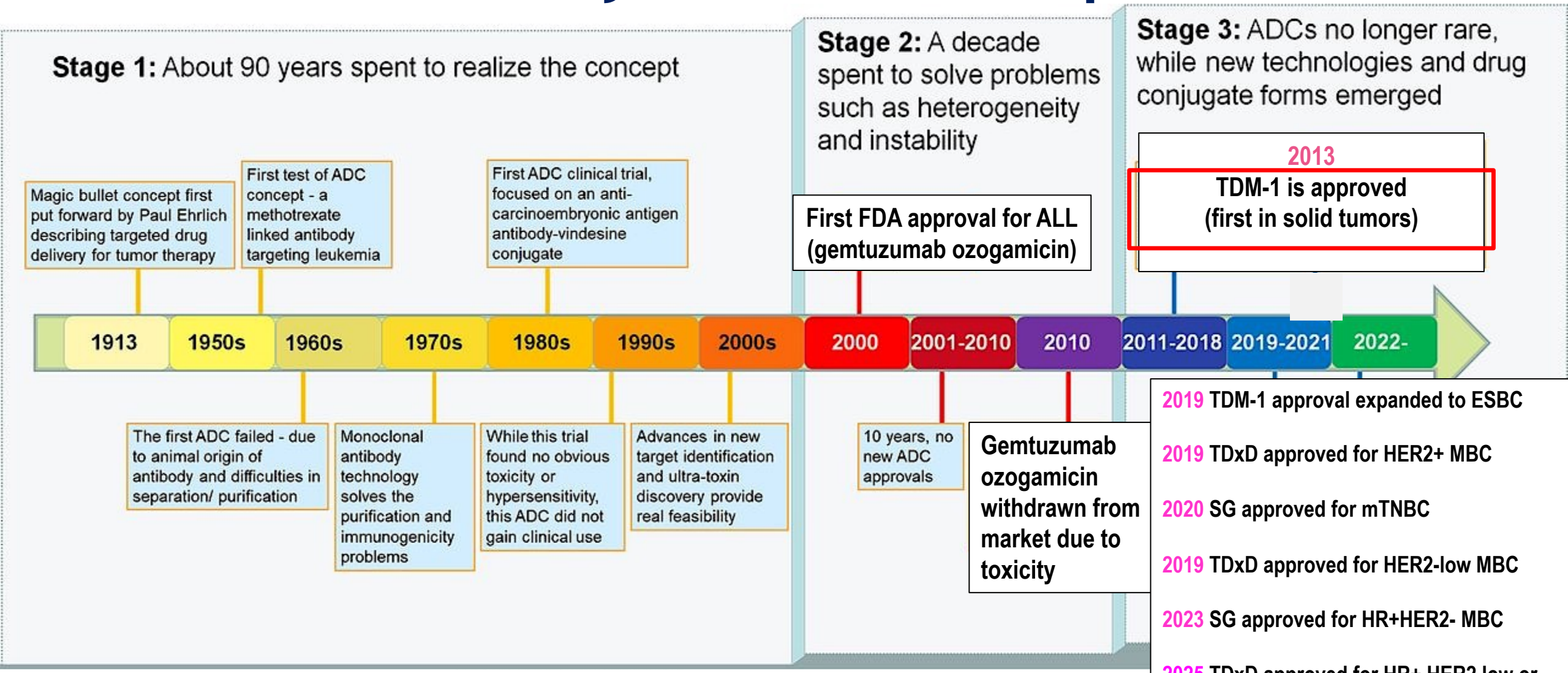
Current and Future Role of HER2-Targeted Antibody-Drug Conjugates (ADCs) in Breast Cancer

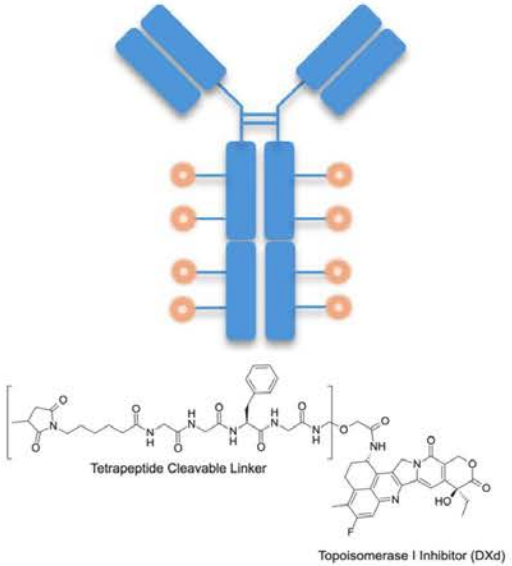
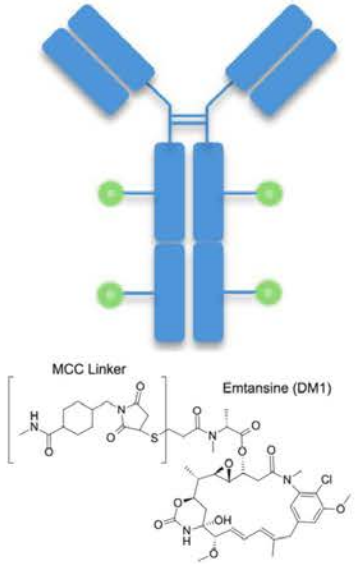
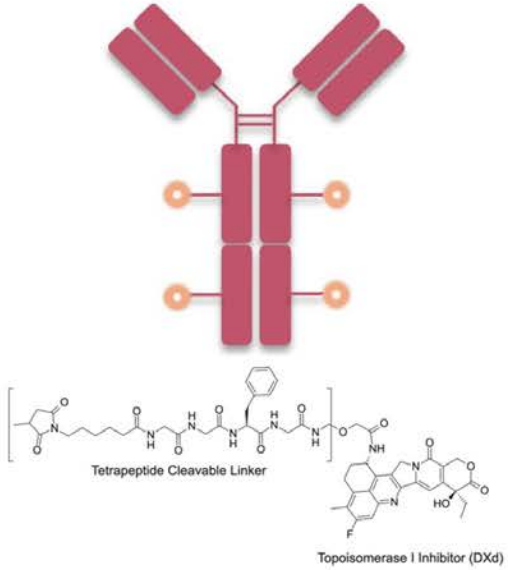
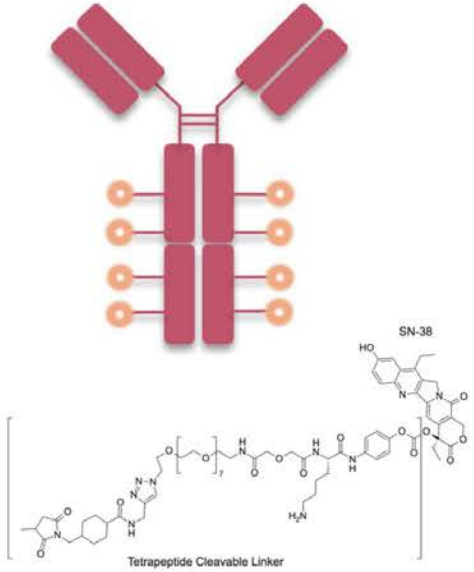
Heather McArthur, MD, MPH, FASCO
Professor, Department of Internal Medicine
Clinical Director, Breast Cancer Program
Komen Distinguished Chair in Clinical Breast Cancer Research
UT Southwestern Medical Center
Dallas, Texas

The History of ADC Development



Adapted from Jin et al. Pharmacological Reviews 2022;74(3):680-713.

Available ADCs in Breast Cancer

	Trastuzumab deruxtecan (T-DXd)	Trastuzumab emtansine (T-DM1)	Datopotamab deruxtecan (Dato-DXd)	Sacituzumab govitecan (SG)
				
Target	HER2	HER2	TROP2	TROP2
Payload	TOP1 inhibitor	Microtubule inhibitor	TOP1 inhibitor	TOP1 inhibitor
Linker Type	Cleavable	Non-cleavable	Cleavable	Cleavable
Bystander Effect	Very strong	Limited	Strong	Medium/Strong
Toxicity Profile				
All Grades	Any >95-99% Grade ≥3 50-57%	Any >95-99% Grade ≥3 40-48%	Any >95-99% Grade ≥3 36-52%	Any >95-99% Grade ≥3 51-74%
Grade ≥3	Neutropenia 14-24%, Anemia 8-10%, Nausea 2-8%, Fatigue 4-8%, ILD <3%	Thrombocytopenia 4-14%, Hepatotoxicity 3-9%, Anemia 3-4%, Fatigue 2-11%	Stomatitis 6-11%, Fatigue 4%, Vomiting 1.4%	Neutropenia 51-59%, Leukopenia 10-38%, Anemia 8-27%, Diarrhea 10%, Fatigue 6-8%
Discontinuation Rate due to Toxicity	14-20%	6-21%	2-8%	3-6%

[1] ILD= interstitial lung disease

Newman AB et al. Cell Rep Med. 2026 Apr 7:102742.

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	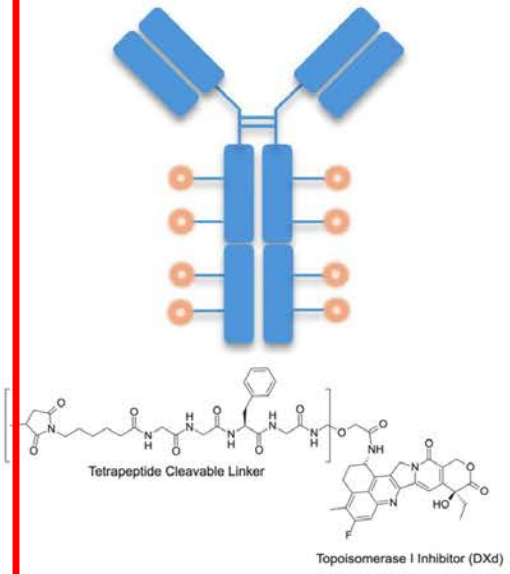	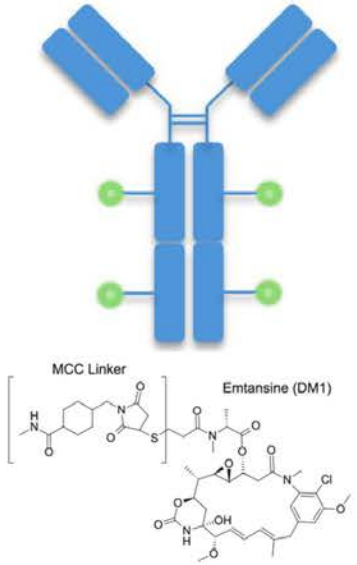	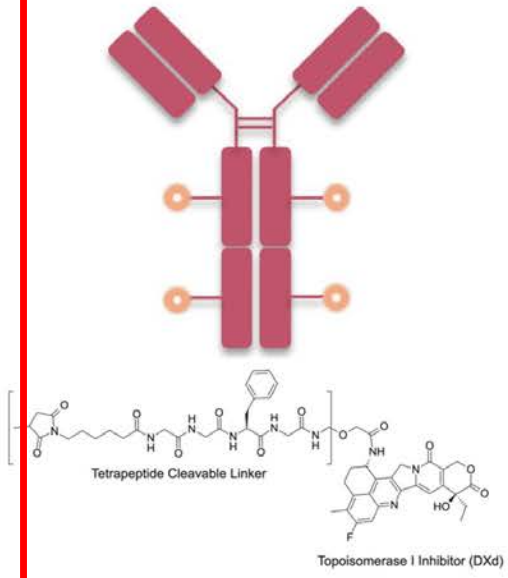	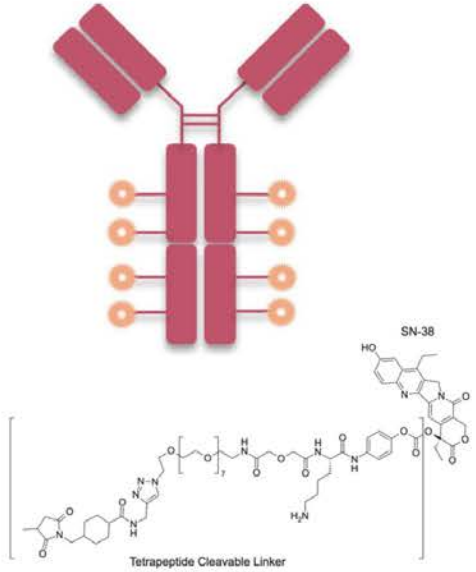
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DESTINY-Breast09 Study Design

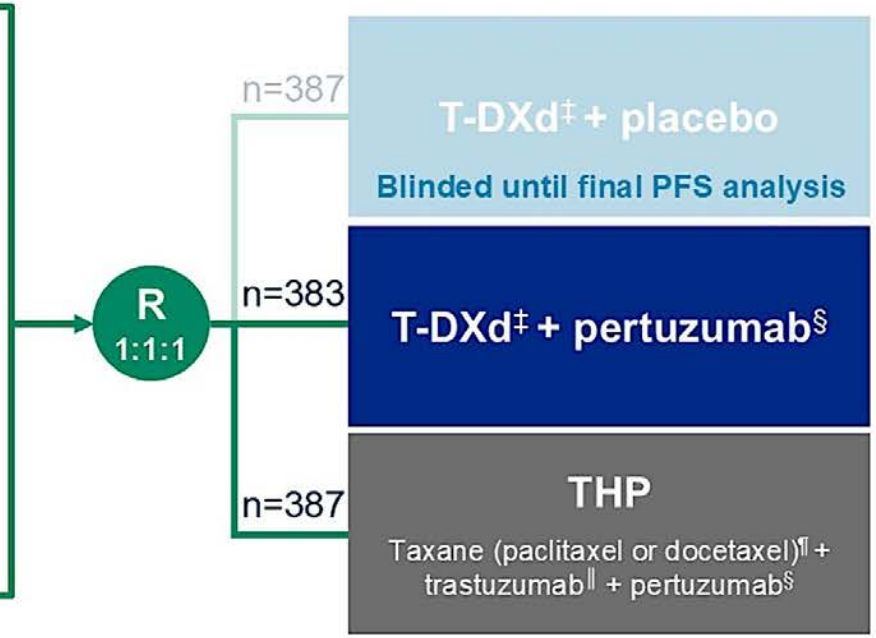
A randomized, multicenter, open-label,* Phase 3 study (NCT04784715)

Eligibility criteria

- HER2+ a/mBC
- Asymptomatic/inactive brain mets allowed
- DFI >6 mo from last chemotherapy or HER2-targeted therapy in neoadjuvant/adjuvant setting
- One prior line of ET for mBC permitted
- **No other prior systemic treatment for mBC†**

Stratification factors

- De-novo vs recurrent mBC
- HR+ or HR−
- *PIK3CA*m (detected vs non-detected)



Endpoints

Primary

- PFS (BICR)

Key secondary

- OS

Secondary

- PFS (INV)
- ORR (BICR/INV)
- DOR (BICR/INV)
- PFS2 (INV)
- Safety and tolerability

At this planned interim analysis (DCO Feb 26, 2025), results are reported for the T-DXd + P and THP arms

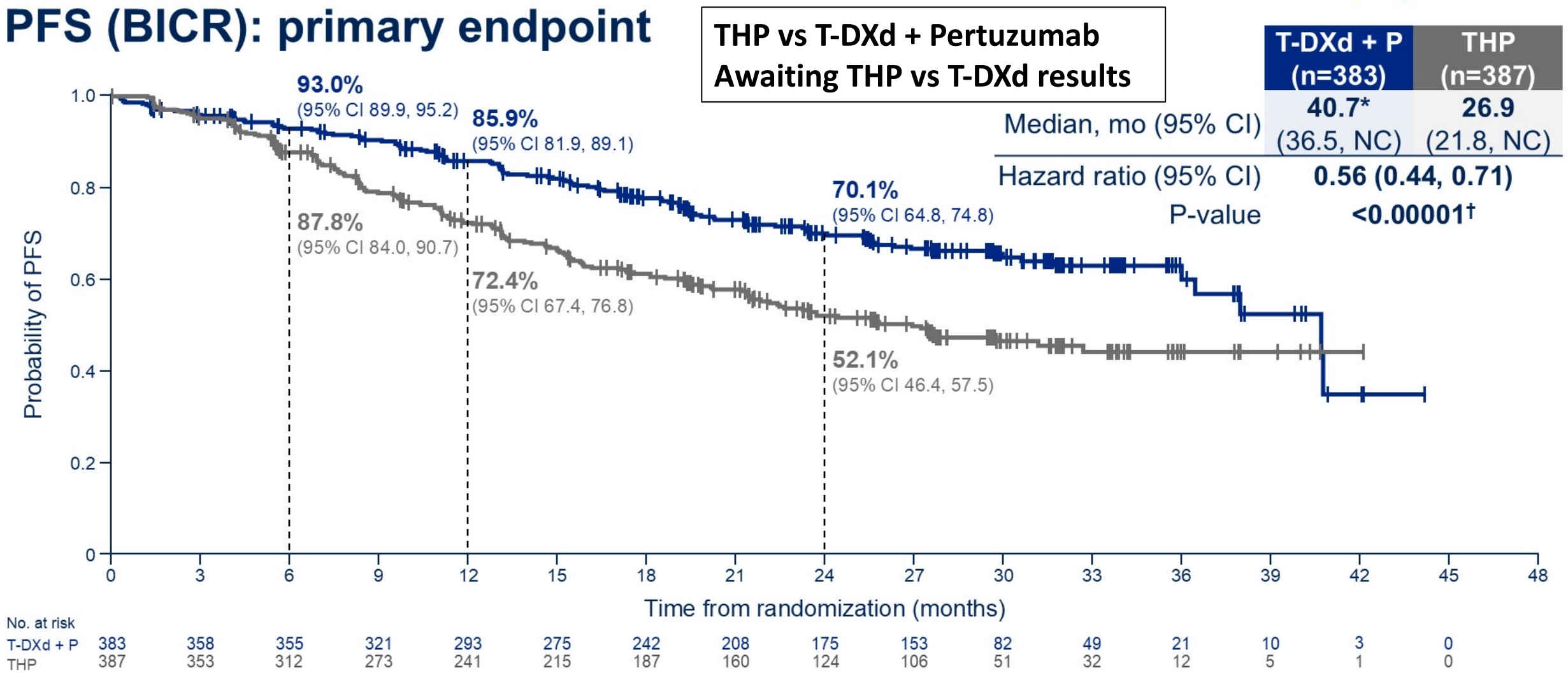
*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W

a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DCO, data cutoff; DFI, disease-free interval; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; INV, investigator; mBC, metastatic breast cancer; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; P, pertuzumab; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

NCT04784715. Updated. May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

Tolaney SM et al. 2025 ASCO Annual Meeting. Abstract LBA 1008.

DESTINY-Breast09: 1L HER2+ mBC Clinical Trial

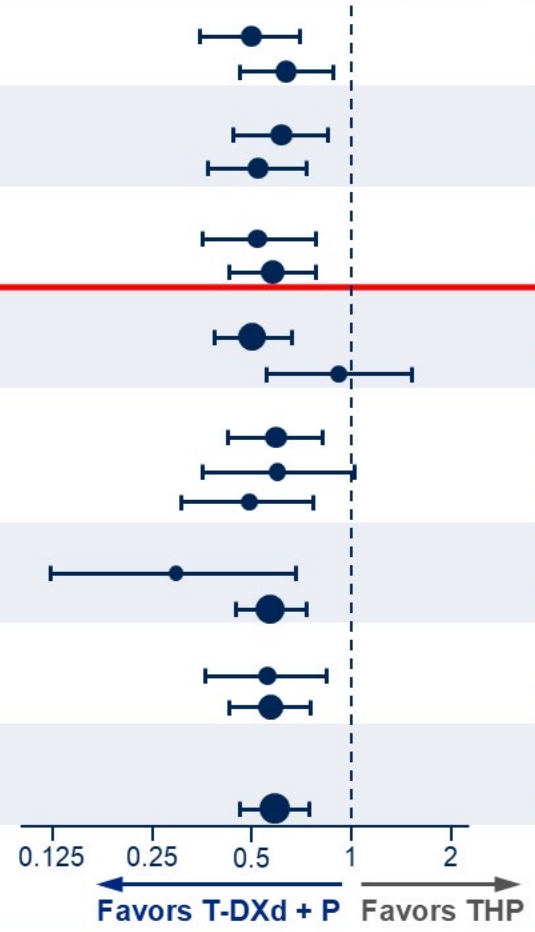


*T-DXd arm not reported

Tolaney SM et al. 2025 ASCO Annual Meeting. Abstract LBA 1008.

DESTINY-Breast09: PFS benefit across Subgroups

	No. of events / no. of patients		mPFS, months (95% CI)		Hazard ratio (95% CI)
	T-DXd + P	THP	T-DXd + P	THP	
Prior treatment status					
De novo	52/200	85/200	NC (36.5, NC)	31.2 (23.5, NC)	0.49 (0.35, 0.70)
Recurrent	66/183	87/187	38.0 (26.9, NC)	22.5 (18.1, NC)	0.63 (0.46, 0.87)
HR status					
Positive	65/207	87/209	38.0 (36.0, NC)	27.7 (22.4, NC)	0.61 (0.44, 0.84)
Negative	53/176	85/178	40.7 (40.7, NC)	22.6 (17.3, 32.7)	0.52 (0.37, 0.73)
***PIK3CA* mutation status**					
Detected	41/116	64/121	36.0 (29.7, NC)	18.1 (15.1, 25.6)	0.52 (0.35, 0.77)
Not detected	76/266	108/266	40.7 (38.0, NC)	32.7 (24.4, NC)	0.57 (0.43, 0.77)
Age at randomization					
<65 years	90/315	139/315	40.7 (36.5, NC)	27.4 (22.4, NC)	0.50 (0.38, 0.65)
≥65 years	28/68	33/72	27.6 (14.9, NC)	21.5 (13.9, NC)	0.92 (0.55, 1.51)
Geographical region					
Asia	62/188	87/191	40.7 (36.5, NC)	27.2 (21.5, NC)	0.60 (0.43, 0.83)
Western Europe and North America	27/87	31/78	36.0 (30.6, NC)	31.2 (15.8, NC)	0.60 (0.35, 1.01)
Rest of World	29/108	54/118	NC (38.0, NC)	24.4 (14.8, NC)	0.48 (0.30, 0.76)
Brain metastases at baseline					
Present	10/25	15/22	31.8 (18.5, NC)	9.5 (5.6, 13.3)	0.30 (0.12, 0.68)
Not present	108/358	157/365	40.7 (36.5, NC)	27.6 (22.6, NC)	0.58 (0.45, 0.74)
Prior exposure to anti-HER2 therapies					
Yes	39/115	51/112	38.0 (26.9, NC)	21.5 (15.3, NC)	0.55 (0.36, 0.83)
No	79/268	121/275	40.7 (36.5, NC)	27.6 (22.5, NC)	0.56 (0.42, 0.74)
Prior exposure to pertuzumab					
Yes	5/31	12/26	40.8 (25.4, NC)	19.8 (7.5, NC)	NC
No	113/352	160/361	40.7 (36.0, NC)	27.4 (22.4, NC)	0.61 (0.48, 0.77)



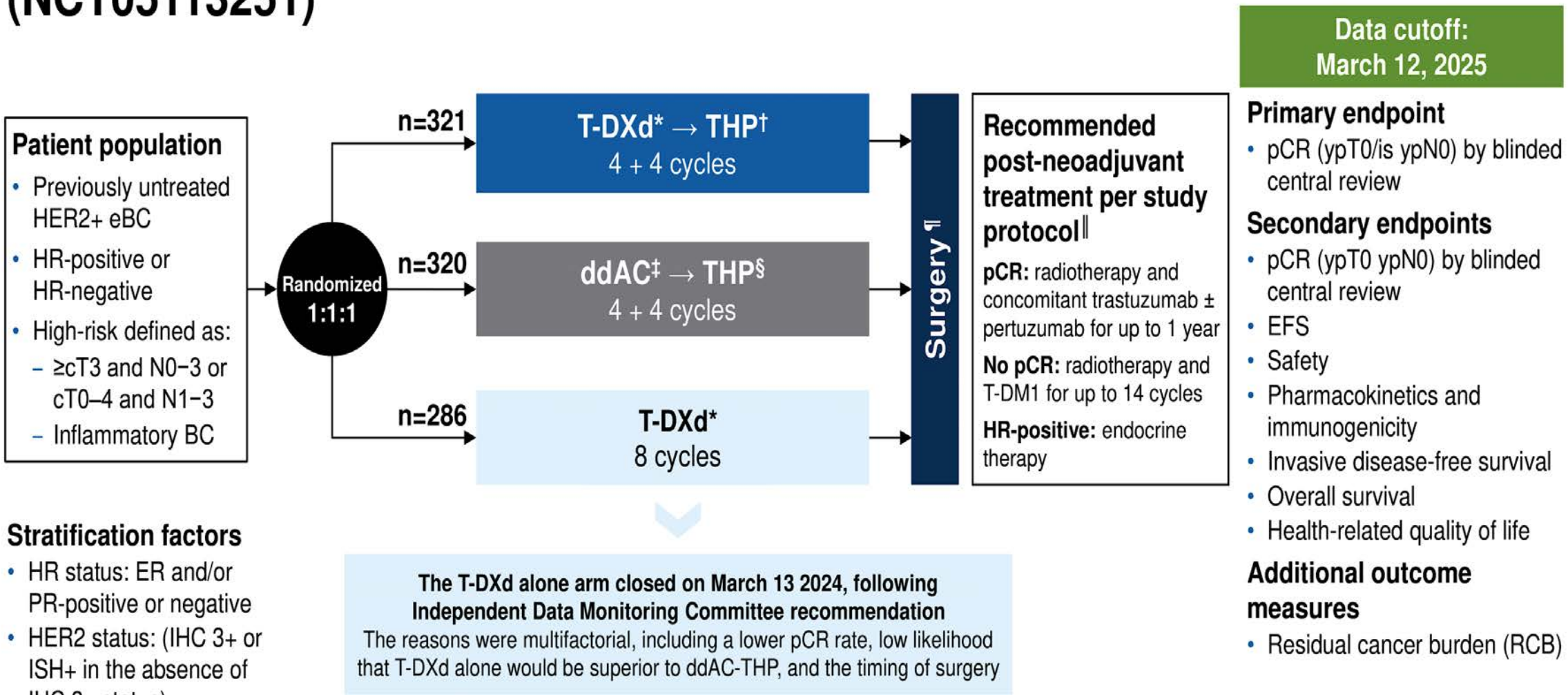
Size of circle is proportional to the number of events
BICR, blinded independent central review;
CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hormone receptor;
NC, not calculable; P, pertuzumab;
(m)PFS, (median) progression-free survival;
T-DXd, trastuzumab deruxtecan;
THP, taxane + trastuzumab + pertuzumab

PFS benefit with T-DXd + P vs THP was consistently observed across prespecified subgroups, including stratification factors

Tolaney SM et al. 2025 ASCO Annual Meeting. Abstract LBA 1008.

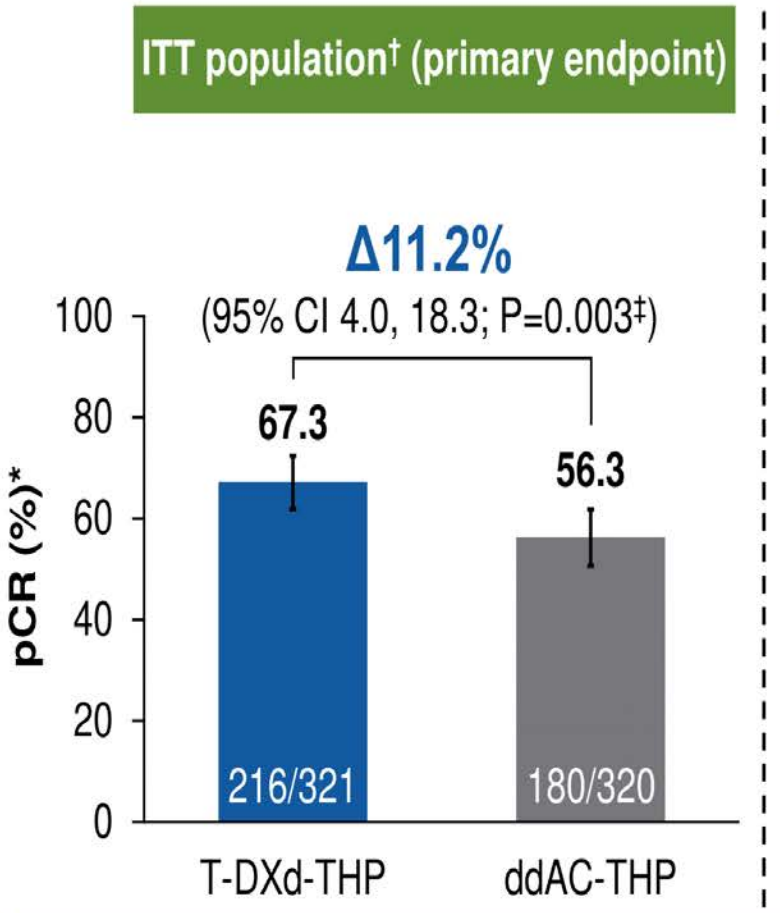
DESTINY-Breast11 study design

A randomized, global, multicenter, open-label, Phase 3 study (NCT05113251)



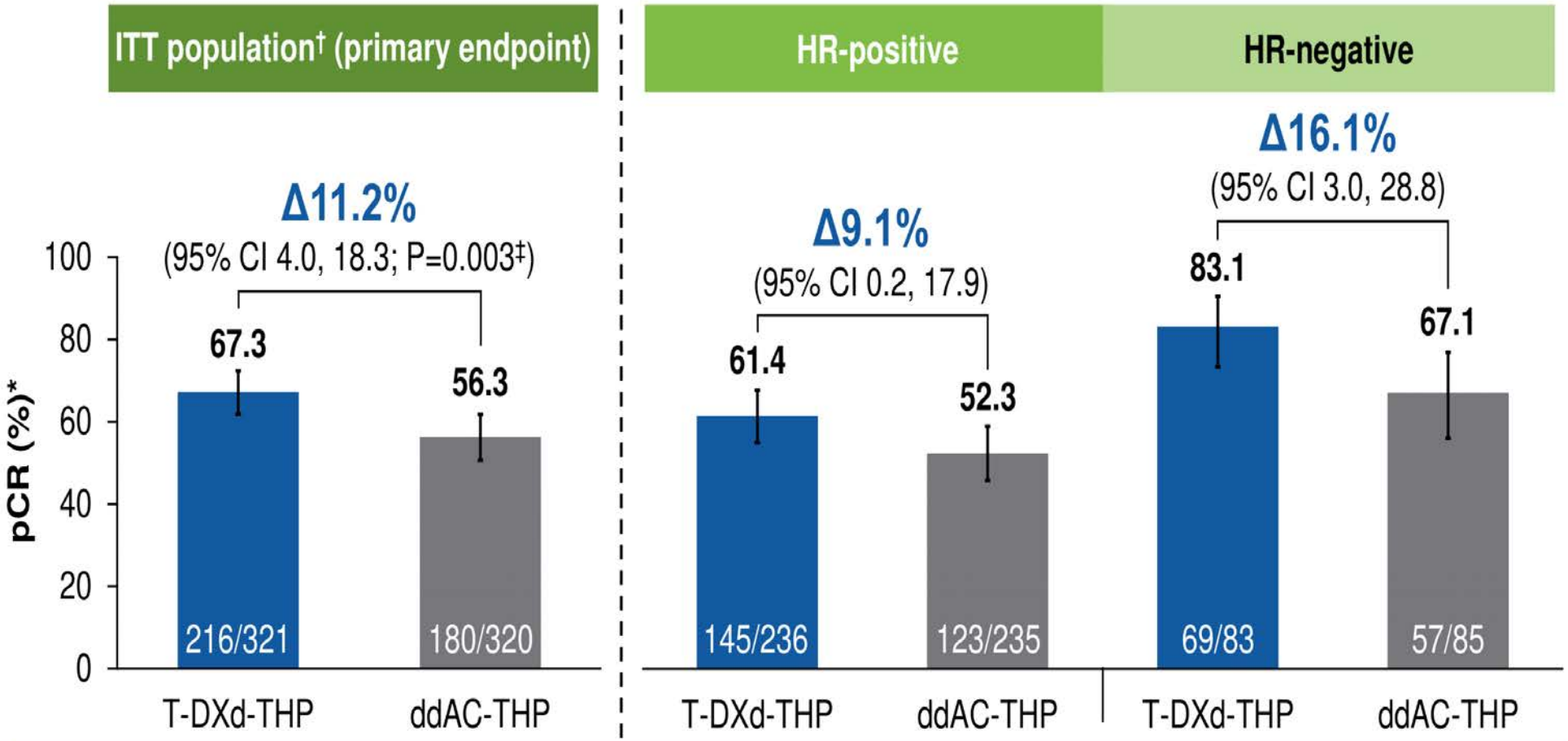
Harbeck et al. ESMO 2025

pCR (ypT0/is ypN0): primary endpoint



Harbeck et al. ESMO 2025

pCR (ypT0/is ypN0): primary endpoint



Neoadjuvant T-DXd-THP demonstrated a statistically significant and clinically meaningful improvement in pCR vs ddAC-THP

Improvement was observed in both the HR-positive and HR-negative subgroups

Harbeck et al. ESMO 2025

DESTINY-Breast05 study design

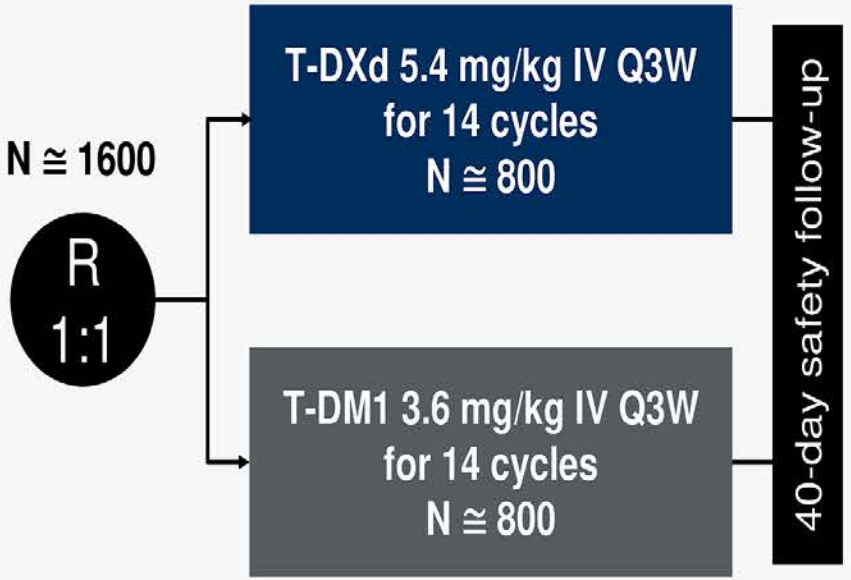
A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)

Key Eligibility Criteria

- **Residual invasive disease in the breast and/or axillary lymph nodes** after neoadjuvant chemotherapy with HER2-directed therapy (NAT)[a]
- **High-risk defined as presentation prior to NAT with:**
  - **Inoperable eBC (cT4,N0-3,M0 or cT1-3,N2-3,M0) OR**
  - **Operable eBC (cT1-3,N0-1,M0) with axillary node–positive disease (ypN1-3) after NAT**
- **Centrally confirmed HER2+** (IHC 3+ or ISH+) eBC
- ECOG PS 0 or 1

Stratification factors

- Extent of disease at presentation (inoperable, operable)
- HER2-targeted NAT (single, dual)
- Hormone receptor status (positive, negative)
- Post-NAT pathologic nodal status (positive, negative)



Primary endpoint

- IDFS

Key secondary endpoint

- DFS

Other secondary endpoints

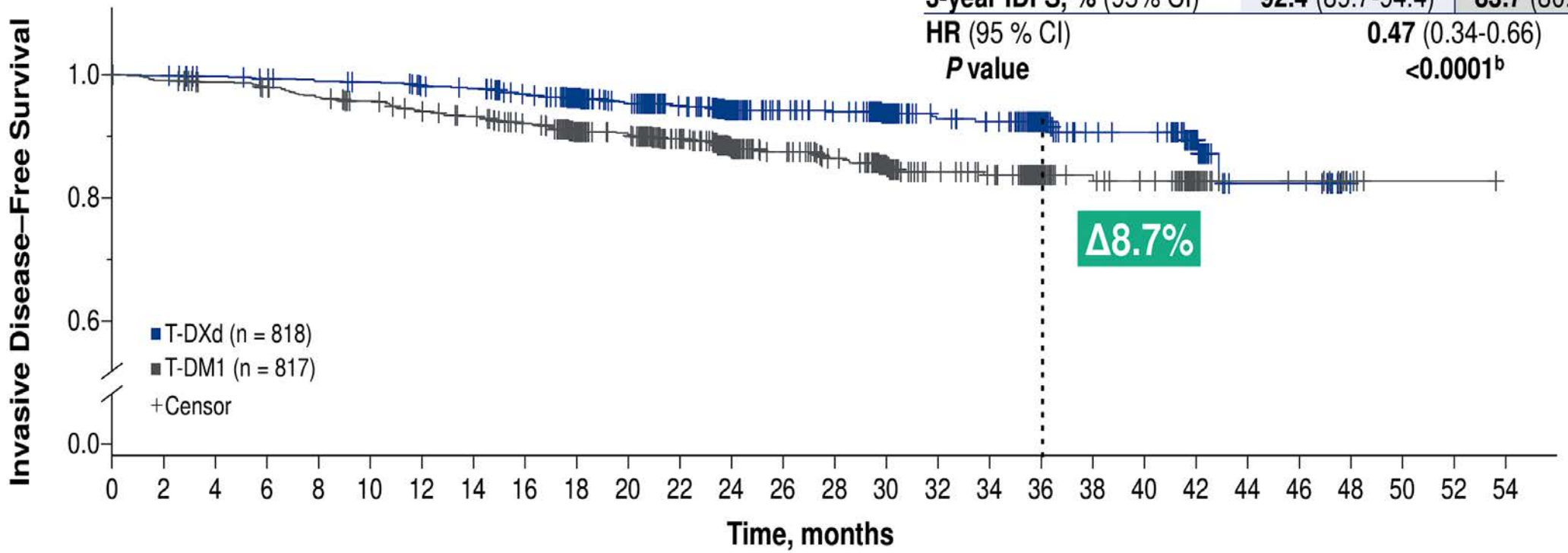
- OS
- DRFI
- BMFI
- Safety

- **Concomitant adjuvant ET was allowed per local practices**
- **If administered, RT could be initiated concurrent with study therapy or completed prior to initiation of study therapy (sequential) per investigator**
- **ILD monitoring program for patients treated with RT**
  - All patients had baseline non-contrast, low dose (LD) chest CT during screening
  - All RT patients (concurrent and sequential) had LD chest CT 6 weeks after start of study therapy, then every 12 weeks while on therapy, and at 40-day follow-up
  - Sequential RT patients had additional LD chest CT after completion of RT prior to start of study therapy

Geyer et al. ESMO 2025;Abstract LBA1

Primary endpoint: IDFS[a]

	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	**51** (6.2)	**102** (12.5)
3-year IDFS, % (95% CI)	**92.4** (89.7-94.4)	**83.7** (80.2-86.7)
HR (95 % CI)	**0.47** (0.34-0.66)	
***P* value**	**<0.0001[b]**	



Number at Risk:

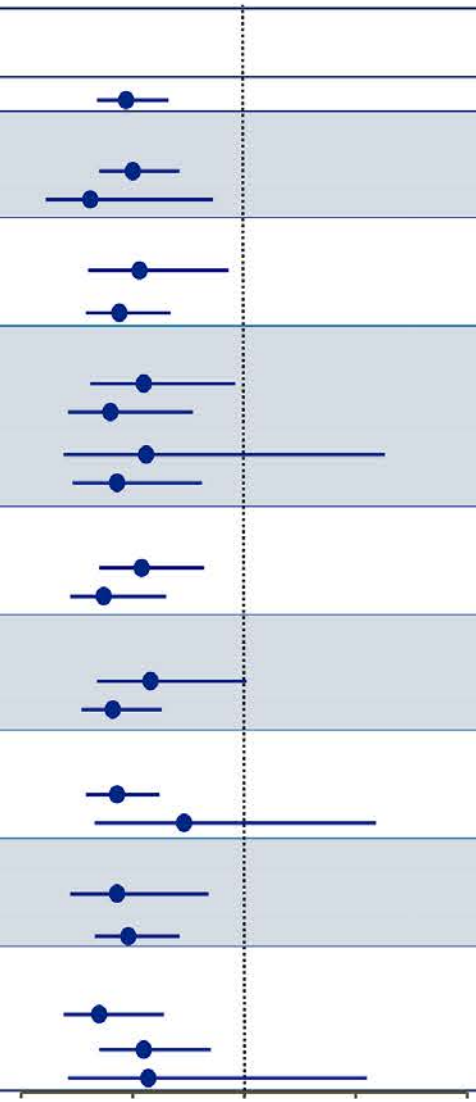
T-DXd	818	788	781	776	771	768	758	753	731	684	634	544	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	781	769	760	745	734	719	708	687	632	599	527	417	355	337	233	186	177	120	84	79	38	14	13	4	1	1	0

53% reduction in the risk of invasive disease recurrence or death for T-DXd compared with T-DM1

Geyer et al. ESMO 2025;Abstract LBA1

Primary endpoint subgroup analysis: IDFS

	No. events/patients		3-year IDFS, % (95% CI)		
	T-DXd	T-DM1	T-DXd n = 818	T-DM1 n = 817	HR (95% CI)[b]
All patients	**51/818**	**102/817**	**92.4 (89.7-94.4)**	**83.7 (80.2-86.7)**	**0.47 (0.34-0.66)**
Age					
<65 years	46/735	87/736	92.1 (89.2-94.3)	84.1 (80.2-87.2)	0.50 (0.35-0.71)
≥65 years	5/83	15/81	94.9 (87.0-98.1)	79.2 (67.9-87.0)	0.31 (0.11-0.86)
Race					
Asian	19/399	34/386	95.1 (91.9-97.0)	89.5 (85.3-92.6)	0.53 (0.30-0.93)
Non-Asian	32/419	68/431	89.5 (84.5-93.0)	77.9 (72.1-82.7)	0.44 (0.29-0.67)
Region					
Asia	19/392	33/380	95.0 (91.9-97.0)	89.7 (85.4-92.7)	0.55 (0.31-0.96)
Europe	13/222	30/223	93.1 (86.9-96.4)	82.9 (75.8-88.1)	0.40 (0.21-0.77)
North America + Australia	5/57	10/72	85.8 (63.9-94.9)	80.7 (65.3-89.7)	0.56 (0.19-1.63)
Rest of world	14/147	29/142	85.1 (73.6-91.8)	69.2 (56.3-79.0)	0.43 (0.23-0.81)
Hormone receptor status					
Postive	33/581	59/583	93.5 (90.6-95.6)	86.8 (82.9-89.9)	0.54 (0.35-0.82)
Negative	18/237	43/234	89.4 (82.0-93.9)	75.6 (67.6-81.9)	0.37 (0.22-0.65)
Disease status at presentation before NAT					
Operable (cT1-3, N0-1, M0)	21/387	34/393	92.8 (88.0-95.7)	88.4 (83.8-91.8)	0.58 (0.34-1.01)
Inoperable (cT4, N0-3, M0 or cT1-3, N2-3, M0)	30/431	68/424	92.0 (88.5-94.5)	79.4 (73.9-83.8)	0.41 (0.27-0.63)
Post-NAT pathologic nodal status					
Positive[a]	40/660	87/658	92.5 (89.3-94.8)	82.5 (78.4-85.9)	0.43 (0.29-0.62)
Negative[a]	11/158	15/159	91.6 (85.3-95.3)	88.3 (80.6-93.0)	0.73 (0.33-1.59)
HER2-targeted NAT					
Single	13/176	27/171	87.5 (77.6-93.3)	77.9 (67.7-85.2)	0.43 (0.22-0.84)
Dual	38/642	75/646	93.6 (90.9-95.5)	85.2 (81.4-88.2)	0.48 (0.33-0.71)
Radiotherapy treatment					
Sequential radiotherapy	15/326	34/279	93.8 (88.4-96.7)	83.2 (76.4-88.2)	0.35 (0.19-0.64)
Concurrent radiotherapy	30/438	57/480	92.8 (89.7-95.0)	85.1 (80.6-88.6)	0.55 (0.35-0.85)
No radiotherapy	6/54	11/58	81.0 (61.0-91.4)	73.4 (56.4-84.6)	0.57 (0.21-1.55)



Geyer et al. ESMO 2025;Abstract LBA1

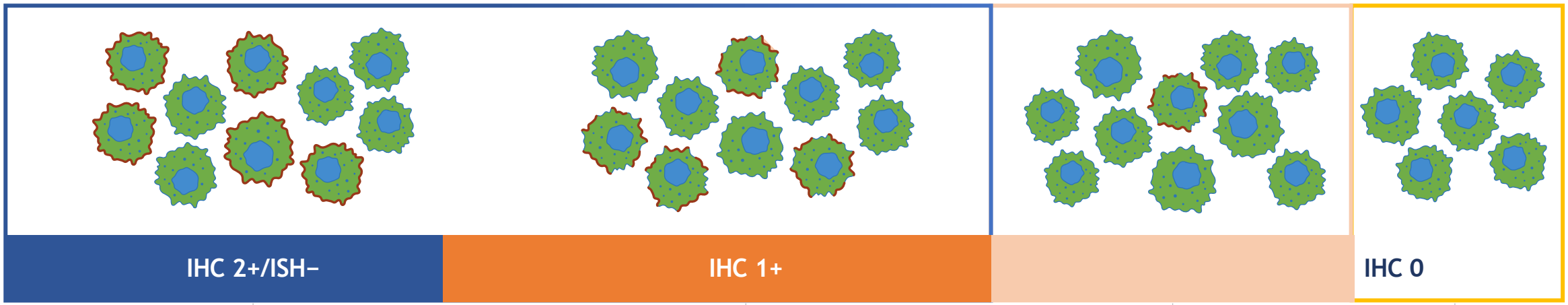
Targeting "Low" and "Ultralow" HER2-Expressing Tumors in mBC

HER2 IHC categories within HR+, HER2-negative (HER2−) mBC (per ASCO/CAP[1])

DESTINY-Breast06 patient population: ~85% of HR+, HER2− mBC

HER2-low ~60-65%[2,3]

HER2-ultralow ~20-25%[2-4]



Adapted from: 1. Schettini F, et al. NPJ Breast Cancer. 2021;7:1; 2. Wolff AC, et al. Arch Pathol Lab Med. 2018;142:1364-1382; 3. Wolff AC, et al. J Clin Oncol. 2023;41:3867-3872; 4. Ahn S, et al. J Pathol Transl Med. 2020;54:34-44.

DESTINY-Breast06: T-DXd in HR+/HER2-Low or -Ultralow mBC

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

PATIENT POPULATION

- HR+ mBC
- HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining)*
- **Chemotherapy naïve in the mBC setting**

Prior lines of therapy

- ≥2 lines of ET ± targeted therapy for mBC
  OR
- 1 line for mBC **AND**
  - Progression ≤6 months of starting first-line ET + CDK4/6i
    OR
  - Recurrence ≤24 months of starting adjuvant ET

Stratification factors

- Prior CDK4/6i use (yes vs no)
- HER2 expression (IHC 1+ vs IHC 2+/ISH− vs IHC 0 with membrane staining)
- Prior taxane in the non-metastatic setting (yes vs no)

R 1:1

T-DXd
5.4 mg/kg Q3W
(n=436)

HER2-low = 713
HER2-ultralow = 153†

TPC
(n=430)

Options: capecitabine, nab-paclitaxel, paclitaxel

ENDPOINTS

Primary

- PFS (BICR) in HER2-low

Key secondary

- PFS (BICR) in ITT (HER2-low + ultralow)
- OS in HER2-low
- OS in ITT (HER2-low + ultralow)

Other secondary

- PFS (INV) in HER2-low
- ORR (BICR/INV) and DOR (BICR/INV) in HER2-low and ITT (HER2-low + ultralow)
- Safety and tolerability
- Patient-reported outcomes‡

	HER2-low		HER2-ultralow	
	T-DXd (N=331)	TPC (N=163)	T-DXd (N=331)	TPC (N=163)
Median PFS	13.2 months	8.1 months	13.2 months	8.3 months
	HR 0.62 (95% CI 0.51, 0.74); *P*<.0001		HR 0.78 (95% CI 0.50, 1.21)	
12-month OS	87.6%	81.7%	84.0%	78.7%
	HR 0.83 (95% CI 0.66, 1.05); *P*=.1181		HR 0.75 (95% CI 0.43, 1.29)	
ORR	56.5%	32.2%	61.8%	26.3%

Curigliano G et al. ASCO 2024;Abstract LBA1000

DESTINY-Breast04: First Randomized Phase 3 Study of T-DXD for HER2-low mBC

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[b]

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

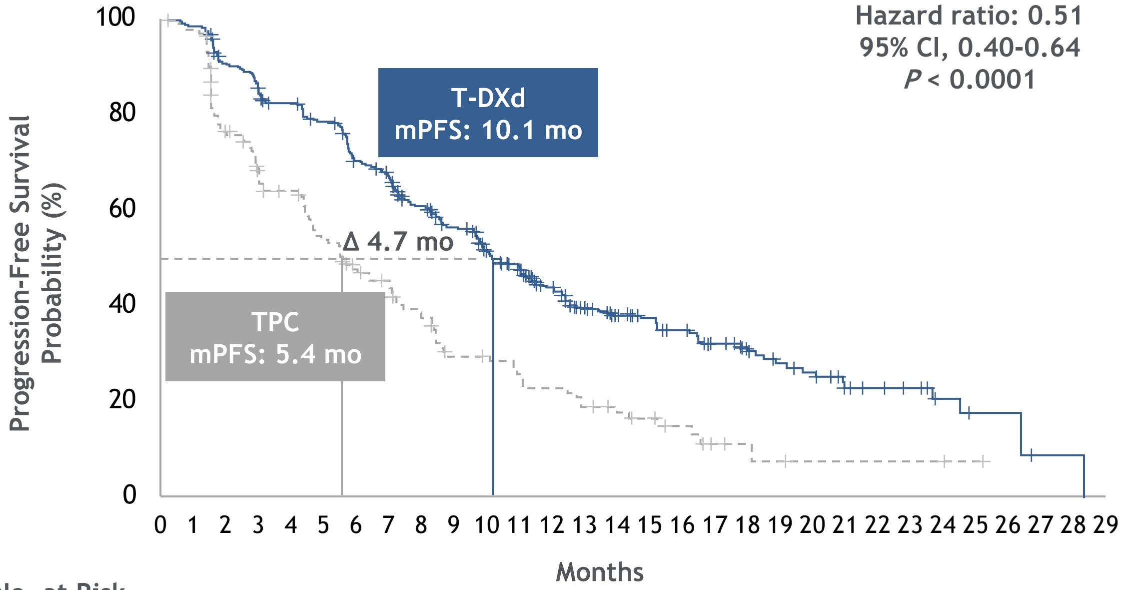
Stratification factors

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

Modi. ASCO 2022. Abstr LBA3

DESTINY-Breast04: PFS and OS in HR+ Patients

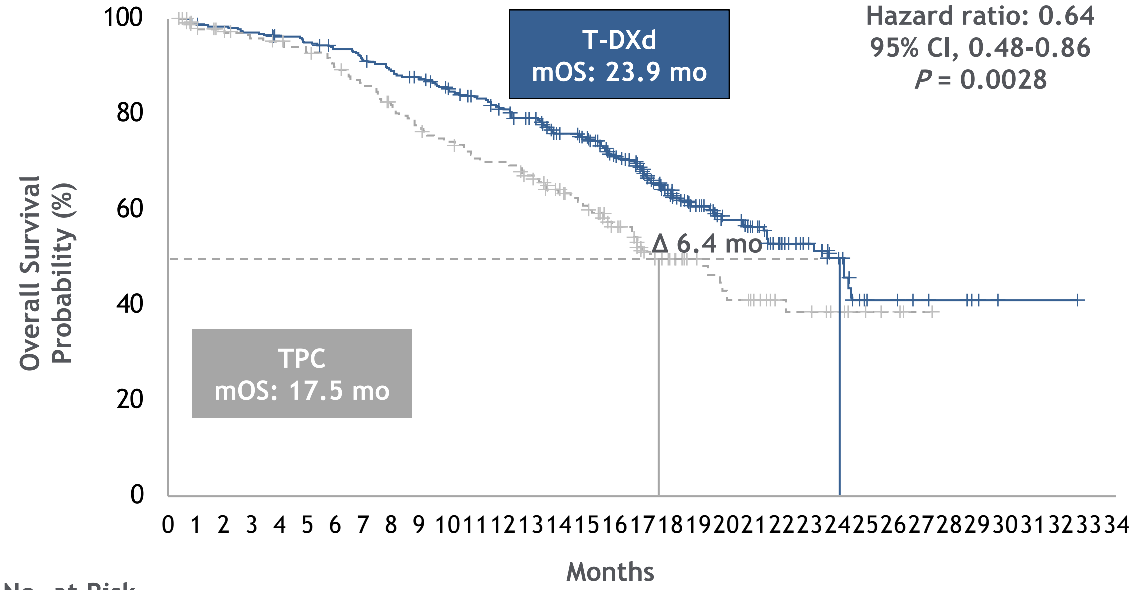
Progression Free Survival



No. at Risk

T-DXd (n=331):	331	324	290	265	262	248	218	198	182	165	142	128	107	89	78	73	64	48	37	31	28	17	14	12	7	4	4	1	1	0
TPC (n=163):	163	146	105	85	84	69	57	48	43	32	30	27	24	20	14	12	8	4	3	2	1	1	1	1	1	1	0			

Overall Survival



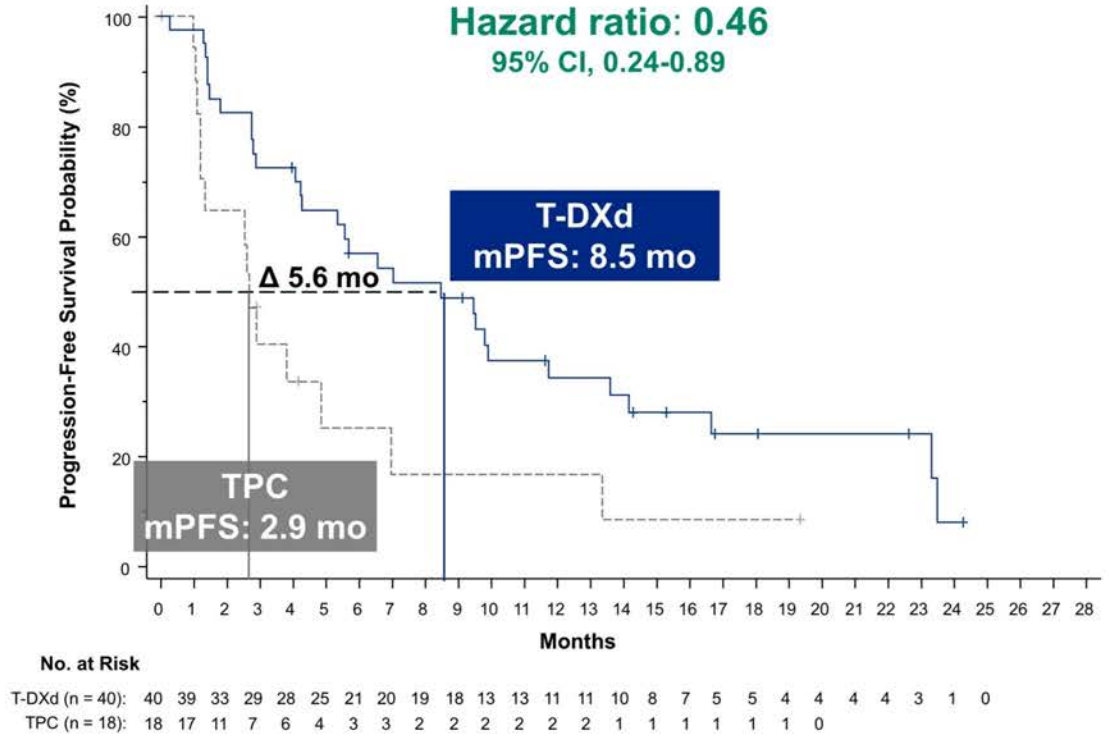
No. at Risk

T-DXd (n=331):	331	325	323	319	314	309	303	293	285	280	268	260	250	228	199	190	168	144	116	95	81	70	51	40	26	14	9	8	6	6	2	1	1	1	0
TPC(n=163):	163	151	145	143	139	135	130	124	115	109	104	98	96	89	80	71	56	45	37	29	25	23	16	14	7	5	3	1	0						

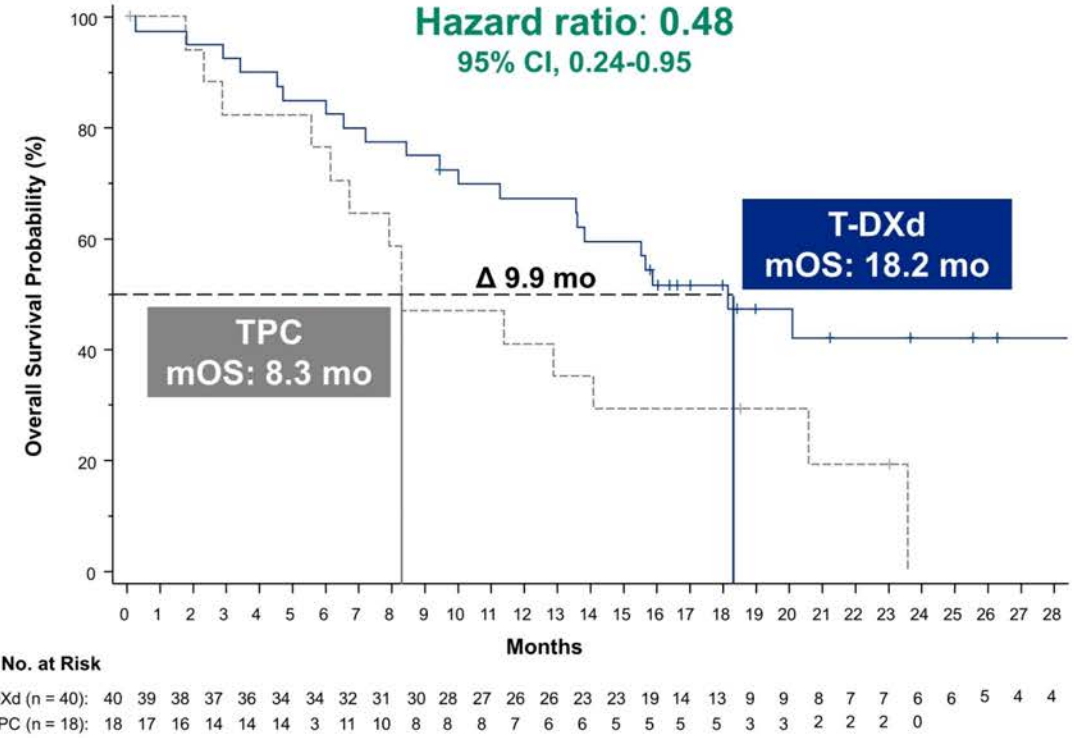
Modi. ASCO 2022. Abstr LBA3

DESTINY-Breast04: PFS and OS in HR- Patients

Progression Free Survival

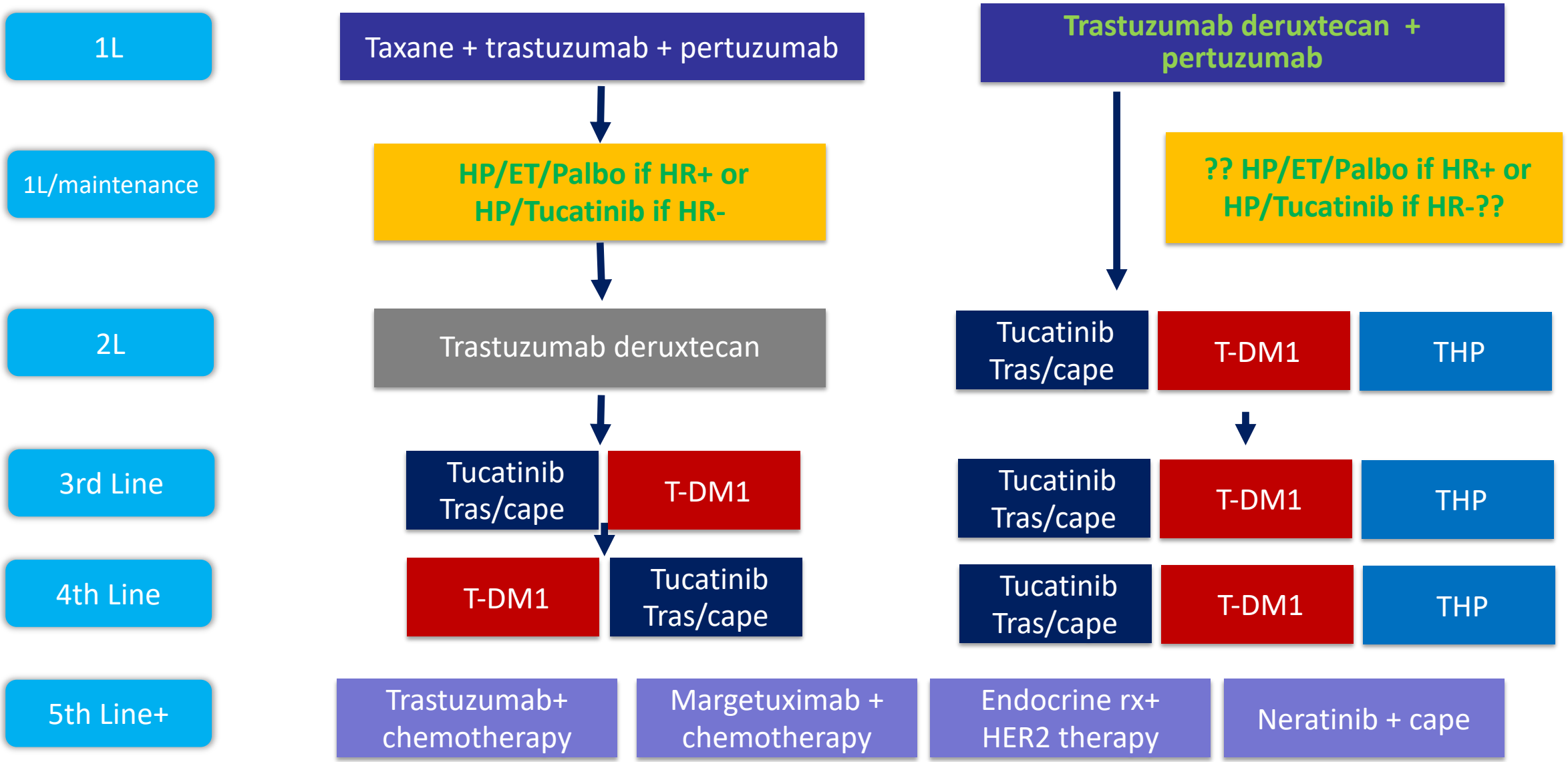


Overall Survival



Modi. ASCO 2022. Abstr LBA3

A patient with HER2-positive mBC who received first-line T-DXd/pertuzumab



Discussion Questions

Are most patients with metastatic HER2-positive breast cancer for whom you are going to start first-line therapy receiving T-DXd/pertuzumab? Which ones, if any, are not?

How do you explain to a patient the potential role of T-DXd in localized breast cancer?

What side effects can occur with T-DXd? What are the top things that you would tell a patient who is to going receive T-DXd about potential toxicities?

Cardiovascular toxicity with HER2 + ADC

Jamie Carroll, CNP, MSN

How common is LVEF dysfunction?

- Clinical trial data show that HER2-targeted ADCs are associated with a low but clinically relevant incidence of left ventricular ejection fraction (LVEF) decline.
- Reported incidence of LVEF decrease ranges:
- ~1% with T-DM1 to
- ~4–5% with T-DXd, with most events being asymptomatic and reversible following treatment interruption.

Baseline Cardiac Assessment

- Baseline LVEF (either Echo or MUGA) prior to initiating ADC
- Review patient history for cardiac risk factors:

-Age >60

-HTN

-Diabetes

-Prior anthracycline

-Baseline LVEF <60%

Identify concerning findings

- LVEF decline meeting institutional or trial-informed thresholds for concern (e.g., ≥10% decline to below the lower limit of normal)
- Symptoms suggestive of cardiac dysfunction, including:

-New or worsening dyspnea

-Fatigue not attributable to other causes

-Peripheral edema

-Orthopnea or chest discomfort

- Most patients are asymptomatic. Monitor for every 3 month LVEF.

Patient counseling

- Educate patients: Cardiac monitoring is routine and evidence-based.
- Many LVEF changes detected in trials were asymptomatic and reversible.
- Instruct patients to report new cardiac or respiratory symptoms promptly.
- Reinforce adherence to scheduled cardiac imaging appointments, as timely monitoring was integral to safety in all major trials.

I held treatment, now what?

- Understanding when to restart is important too!

-LVEF >50% or returned to baseline.

-Patient is asymptomatic

-Generally dose reduction not indicated.

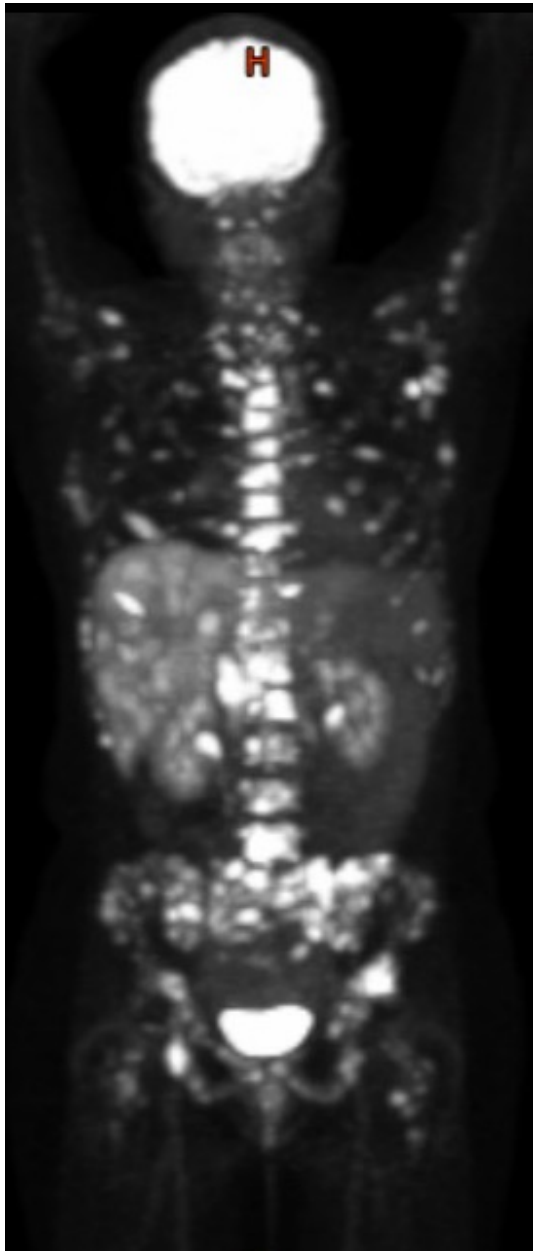
-Repeat LVEF at shorter intervals after rechallenge (6-8 weeks).

-Utilize Multi-disciplinary team.

Case Study - Cardiovascular AE’s

- 2023: 40 yo female, screen mammogram revealed spiculated mass 2 cm. US 1.6 x 1.6 cm in breast with enlarged LN.
- Biopsy: IDC, Grade III, ER/PR Negative, HER2 3+, LN +
- PET: Hypermetabolic focus in left breast, LN, hepatic and osseous metastases.
- MRI Brain: Negative

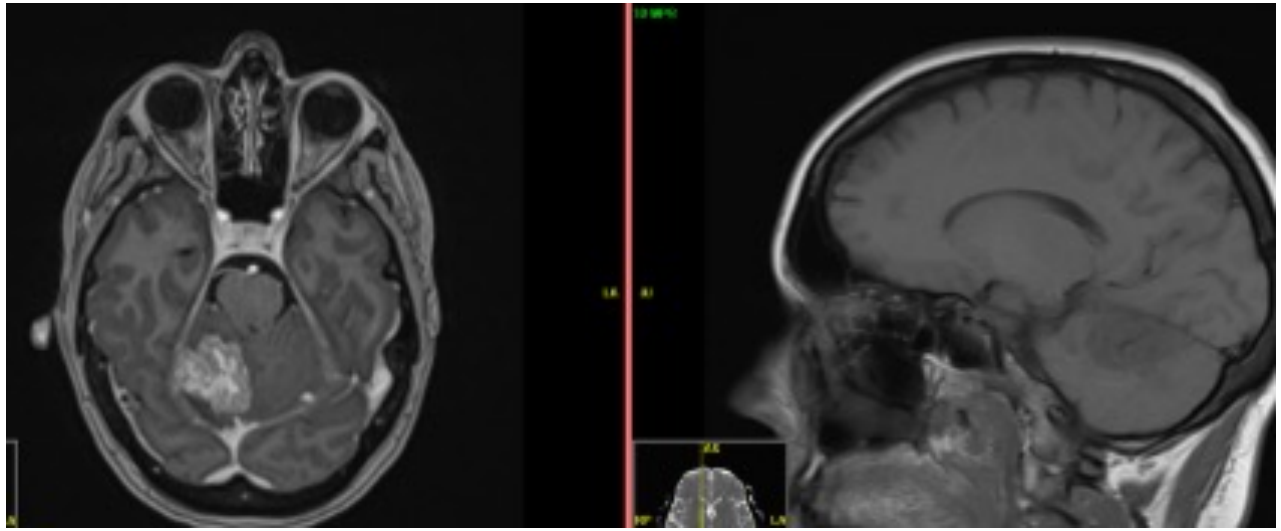
Staging PET

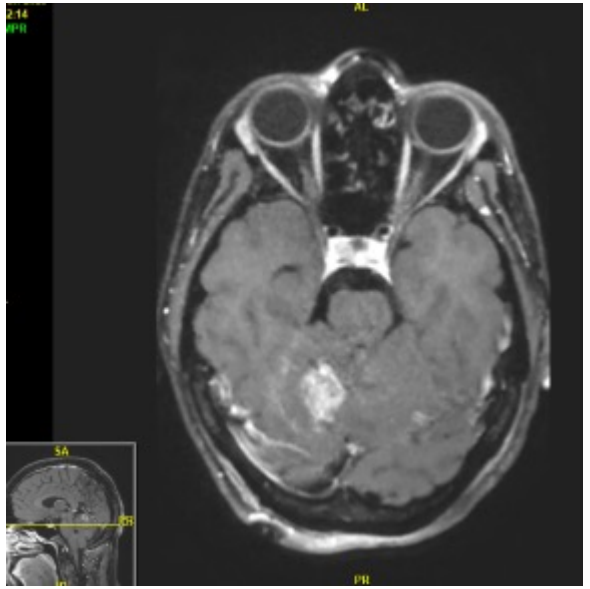


Onc history cont.

- Germline genetics-Negative
- 3/2023: Started Docetaxel, Trastuzumab and Pertuzumab
- Initial Echo: Ejection Fraction 65%, Strain -18%
- 7/2023: Maintenance H/P
- 1/2025: New brain metastases 3.5 cm (weakness, loss of motor control in hand). Underwent resection and XRT to surgical cavity.

MRI Brain





Onc history cont.

- 2/2025: Began T-Dxd. Baseline Echo: EF 60%, Strain -20%.
- 7/2025: Repeat Echo: EF 50%, Strain -16%.
- E-Consult to Cardio Oncology for recommendations-

-Continue T-Dxd

-Start Carvedilol 3.125 mg BID slowly titrate up every 2 weeks by increments of 3.125 mg BID to max dose of 25 mg BID as tolerated.

-Obtain Blood pressure cuff at home.

-Repeat Echo in 3 months.

Onc history cont.

- Repeat Echo: EF 57%, Strain -18%. Patient taking Carvedilol 12.5 mg BID, mild occasional dizziness, normal BP/pulse.
- Cardio-Oncology consult: Decrease Carvedilol to 6.25 mg BID.

-Recommend alternating Echo with NT pro BNP every 3 months.

- Echo: EF 57%, Strain -20%.

Discussion Questions

Do other HER2-targeted therapies (eg, trastuzumab, pertuzumab) cause cardiac toxicity? Is the likelihood of this adverse event greater with T-DXd?

What preexisting cardiac conditions are absolute contraindications to receiving T-DXd?

Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

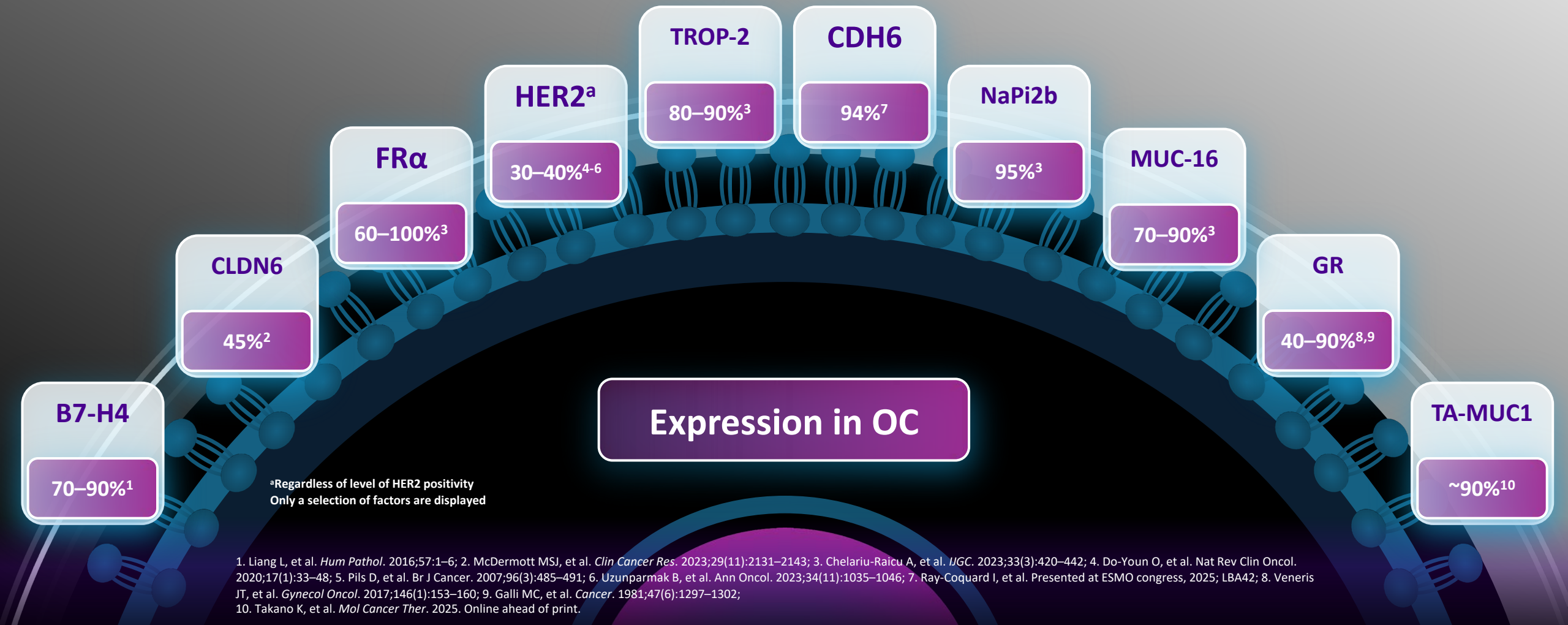
Currently Available ADCs in Gynecologic Cancer Management

Kathleen N. Moore, MD, MS, FASCO
Deputy Director, Fred & Pamela Buffett Cancer Center at the University of Nebraska
Director, Phase 1 Clinical Trials
Professor, Gynecologic Oncology
ASCO BOD
GOG F BOD

FRED & PAMELA BUFFETT CANCER CENTER

@DrKatyMoore

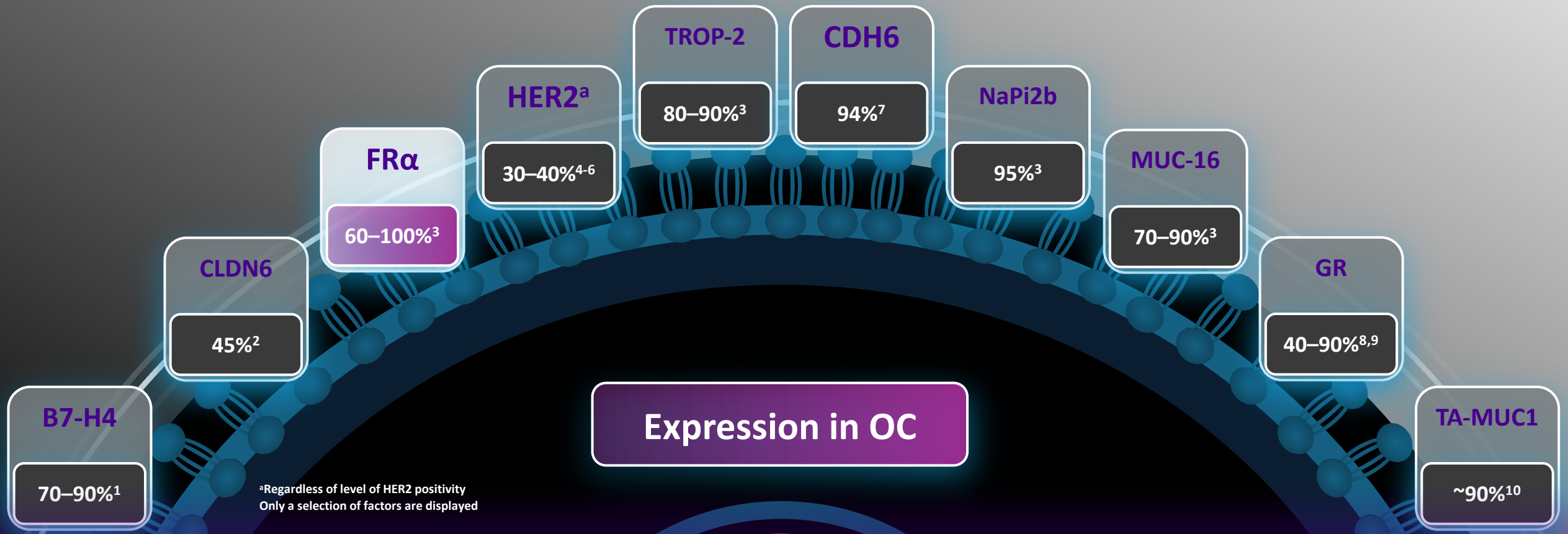
Many targets are under evaluation in PROC…



[a]Regardless of level of HER2 positivity
Only a selection of factors are displayed

1. Liang L, et al. *Hum Pathol*. 2016;57:1–6; 2. McDermott MSJ, et al. *Clin Cancer Res*. 2023;29(11):2131–2143; 3. Chelariu-Raicu A, et al. *IJGC*. 2023;33(3):420–442; 4. Do-Youn O, et al. Nat Rev Clin Oncol. 2020;17(1):33–48; 5. Pils D, et al. Br J Cancer. 2007;96(3):485–491; 6. Uzunparmak B, et al. Ann Oncol. 2023;34(11):1035–1046; 7. Ray-Coquard I, et al. Presented at ESMO congress, 2025; LBA42; 8. Veneris JT, et al. *Gynecol Oncol*. 2017;146(1):153–160; 9. Galli MC, et al. *Cancer*. 1981;47(6):1297–1302;
10. Takano K, et al. *Mol Cancer Ther*. 2025. Online ahead of print.

Many targets are under evaluation in PROC…

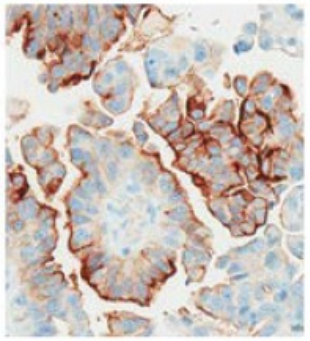


[a]Regardless of level of HER2 positivity
Only a selection of factors are displayed

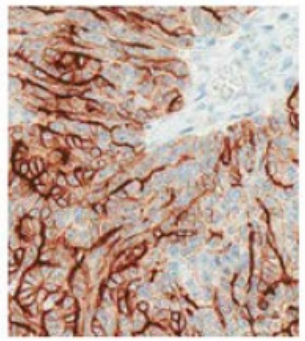
1. Liang L, et al. *Hum Pathol*. 2016;57:1–6; 2. McDermott MSJ, et al. *Clin Cancer Res*. 2023;29(11):2131–2143; 3. Chelariu-Raicu A, et al. *IJGC*. 2023;33(3):420–442; 4. Do-Youn O, et al. Nat Rev Clin Oncol. 2020;17(1):33–48; 5. Pils D, et al. Br J Cancer. 2007;96(3):485–491; 6. Uzunparmak B, et al. Ann Oncol. 2023;34(11):1035–1046; 7. Ray-Coquard I, et al. Presented at ESMO congress, 2025; LBA42; 8. Veneris JT, et al. *Gynecol Oncol*. 2017;146(1):153–160; 9. Galli MC, et al. *Cancer*. 1981;47(6):1297–1302;
10. Takano K, et al. *Mol Cancer Ther*. 2025. Online ahead of print.

High FRα expression found in ~35% of patients

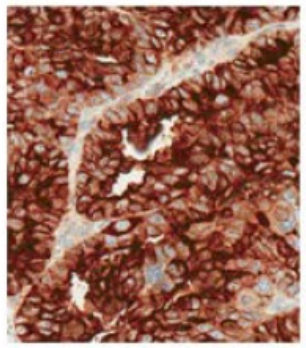
Staining patterns for FRα from archival tumour specimens[1]



Low
25–49% of cells with ≥2+ intensity



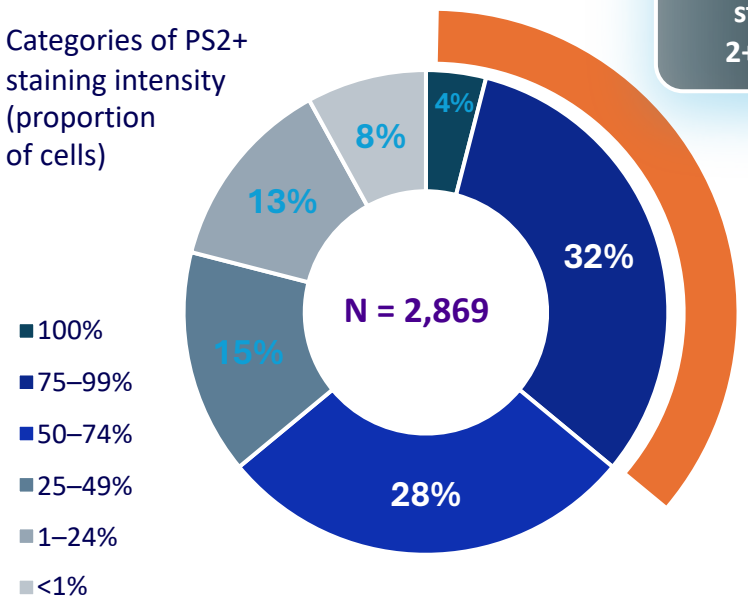
Medium
50–74% of cells with ≥2+ intensity



High
≥75% of cells with ≥2+ intensity

Prevalence of PS2+ FRα expression in 2,869 pooled samples from patients with HGSOC[2]

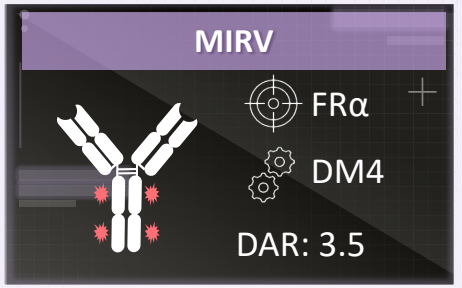
36% had positive staining intensity 2+ in ≥75% of cells



FRα, folate receptor alpha; HGSOC, high-grade serous ovarian cancer; PS2, positive staining 2+.
Figures adapted from 1. Martin LP, et al. *Gynecol Oncol*. 2017;147(2):402–407; 2. Speaker's own based on Deutschman E, et al. *Arch Pathol Lab Med*. 2025; 149:930–937.

MIRASOL: Study design

An open-label, phase 3 randomised trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high PROC



Patient Population

(n=453)

- Platinum-resistant disease
- (PFI ≤6 mo)
- FRα detected by IHC with PS2+ intensity among ≥75% of viable tumour cells
- High-grade serous histology
- Primary platinum-refractory disease excluded (primary PFI <3 months)
- 1–3 prior lines of therapy
- Prior BEV and PARPi allowed
- Patients with BRCA mutations allowed

1:1 Randomisation

Treatment Regimen-Experimental

MIRV
(6mg/kg AIBW Q3W)

Treatment Regimen-Control

Investigator's Choice Chemotherapy
(Paclitaxel, PLD, or Topotecan)

Stratification Factors
- IC chemotherapy: paclitaxel, PLD, or topotecan
- Prior lines of therapy: 1 *vs* 2 *vs* 3

Primary Endpoint
PFS by INV
BICR Sensitivity analysis

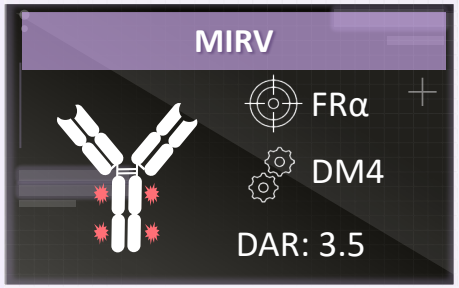
Key Secondary Endpoints
ORR by INV
OS
PROs

Secondary Endpoints
Safety and tolerability
DOR
CA-125 response
PFS2

AIBW, adjusted ideal body weight; BEV, bevacizumab; BICR, blinded independent central review; BRCA1, breast cancer gene 1; DAR, drug-to-antibody ratio; DM4, ravtansine; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab Soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly-ADP ribose polymerase inhibitor; PFI, platinum-free interval; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; PRO, patient reported outcome; PROC, platinum-resistant ovarian cancer; PS2, positive staining 2+; Q3W, every 3 weeks.

Moore KN, et al. *NEJM*. 2023;389:2162–2174.

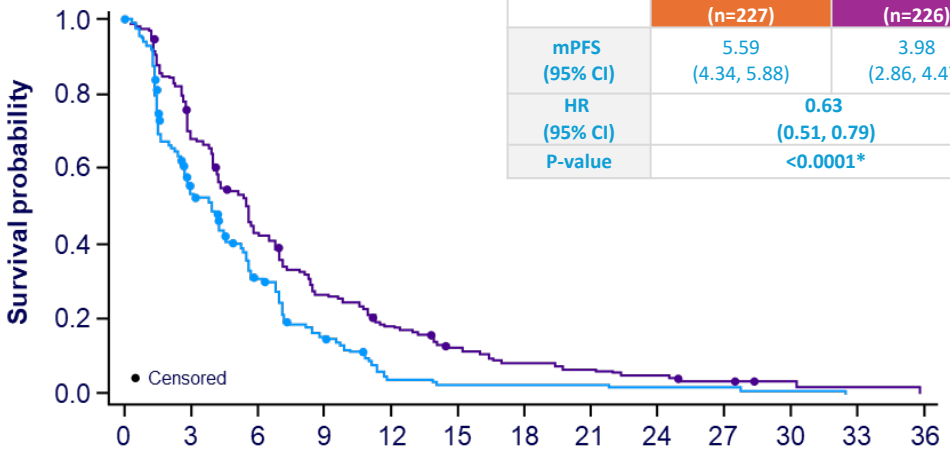
MIRASOL: PFS and OS results



ORR (by INV)[a] with MIRV was 41.9%, compared with 15.9% with ICC

PFS by INV

	Final analysis[1,a]	
	MIRV (n=227)	ICC (n=226)
mPFS (95% CI)	5.59 (4.34, 5.88)	3.98 (2.86, 4.47)
HR (95% CI)	0.63 (0.51, 0.79)	
P-value	<0.0001*	

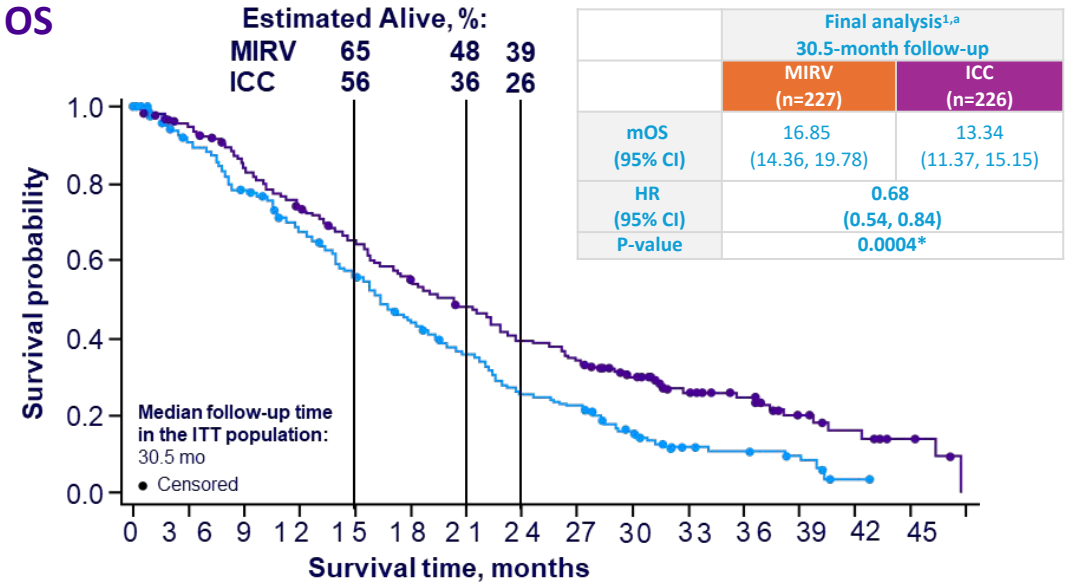


Number of patients at risk:

MIRV	227	151	89	54	36	23	15	12	9	5	2	1	0
ICC	226	98	49	22	5	3	3	3	2	2	1	0	

OS

	Final analysis[1,a] 30.5-month follow-up	
	MIRV (n=227)	ICC (n=226)
mOS (95% CI)	16.85 (14.36, 19.78)	13.34 (11.37, 15.15)
HR (95% CI)	0.68 (0.54, 0.84)	
P-value	0.0004*	



Number of patients at risk:

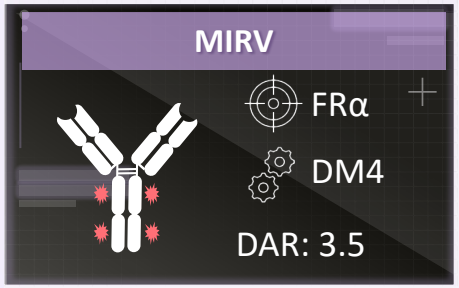
MIRV	227	204	178	156	135	114	98	80	70	50	33	25	12	8
ICC	226	186	159	134	110	85	67	48	42	25	13	11	7	1

[a]An objective response was defined as a complete or partial response.

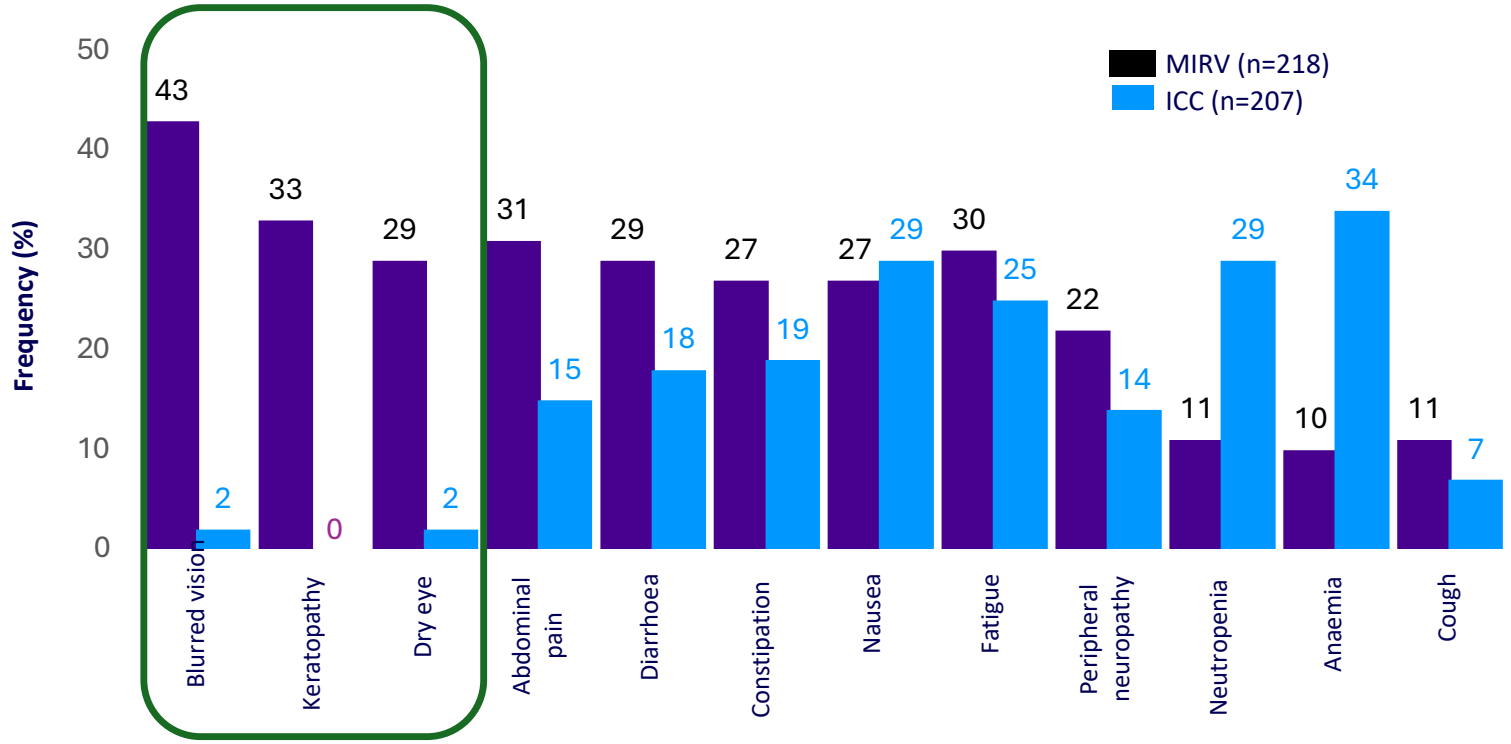
CI, confidence interval; DAR, drug-to-antibody ratio; DM4, ravtansine; FRα, folate receptor alpha; HR, hazard ratio; ICC, investigators choice chemotherapy; INV, investigator; ITT, intent-to-treat; MIRV, mirvetuximab soravtansine; mOS, median overall survival; mPFS, median progression-free survival; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer.

1. Van Gorp T, et al. Presented at SGO Annual Meeting on Women's Cancer, 2025.

MIRASOL: Safety profile of MIRV



- **Ocular toxicities with MIRV** included **blurred vision** (43%), **keratopathy** (33%), and **dry eye** (29%)
- **MIRV displayed lower rates** of **grade ≥3 TEAEs** (44%) *vs* ICC (55%)
- **TEAEs leading to discontinuation** were reported in 6% of patients treated with MIRV *vs* 11% with ICC
- **No TRAEs** leading to **death** were reported with MIRV



[a]An objective response was defined as a complete or partial response.

AE, adverse event; CI, confidence interval; DAR, drug-to-antibody ratio; DM4, ravtansine; FRα, folate receptor alpha; ICC, investigator's choice chemotherapy; ILD, interstitial lung disease; INV, investigator; MIRV, mirvetuximab soravtansine; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; PROC, platinum-resistant ovarian cancer; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

1. Van Gorp T, et al. Presented at SGO Annual Meeting on Women's Cancer, 2025.

Background (1): Evolution of treatment for recurrent cervical cancer

	First line therapy			Second line therapy	
	GOG-204 [1]	**GOG-240** [2]	**KN-826** [3]	**EMPOWER** [4]	**Innova TV 301** [5]
Treatment	CDDP + Paclitaxel	Doublet + Bevacizumab	CTx + Pembrolizumab +/- Bevacizumab	Cemiplimab	Tisotumab Vedotin
Median OS	12.0 mo	17.0 mo , HR 0.71	24.4 mo, HR 0.64	12.0mo, HR 0.69	11.5mo, HR 0.70
Median PFS				2.8 mo	4.2 mo
ORR	29.1%	48.0%	68.1% in PD-L1 ≥1	18.0% in PD-L1 ≥1	17.8%

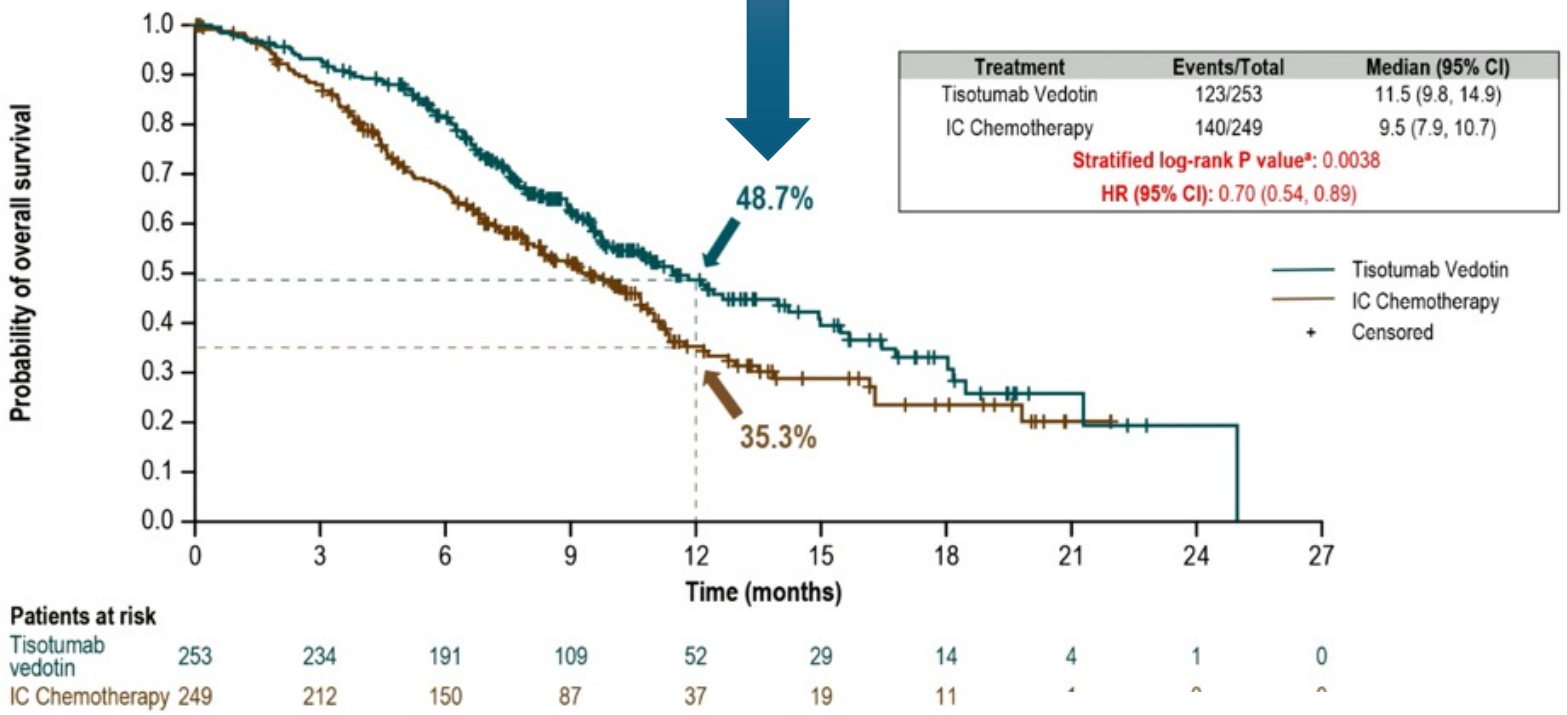
[1] Monk BJ, et al. JCO 2009; [2] Tewari KS, et al. NEJM 2014; [3] Colombo N, et al. NEJM 2021; [4] Tewari KS, et al. NEJM 2022; [5] Vergote I, et al. ESMO 2023

Tisotumab – while not studied specifically in a "post CPI" setting has become a preferred SOC based on modest improvements in OS

	Tisotumab Vedotin (N=253)	IC Chemotherapy (N=249)
ORR, % (95% CI)	17.8 (13.3-23.1)	5.2 (2.8-8.8)
Odds ratio (95% CI)	4.0 (2.1-7.6)	
P value	p<0.0001	
Best Overall Response, n (%)		
CR	6 (2.4)	0
PR	39 (15.4)	13 (5.2)
SD	147 (58.1)	132 (53.0)
PD	46 (18.2)	74 (29.7)
Not evaluable/Not available	15 (5.9)	30 (12.0)
DCR[a], % (95% CI)	75.9 (70.1-81.0)	58.2 (51.8-64.4)
Median DOR (95% CI)	5.3 (4.2-8.3)	5.7 (2.8-NR)

We can agree here that IC chemotherapy is just insufficient for our patients

innovaTV 301
ORR 17.8 vs. 5.2%
mOS 11.5 vs. 9.5 months



[a]The threshold for statistical significance is 0.0226 (2-sided), based on the actual number of OS events at interim analysis.

Vergote et al. 2024

@DrKatyMoore

STUDY DESIGN

DESTINY-PanTumor02: Study Design in Recurrent Solid Tumors

Phase 2 study of T-DXd for HER2-expressing solid tumors

Key eligibility criteria

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer scoring)[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0-1

T-DXd
5.4 mg/kg q3w

40 per cohort[b]

- Endometrial cancer
- Cervical cancer
- Ovarian cancer
- Bladder cancer
- Other tumors[c]
- Biliary tract cancer
- Pancreatic cancer

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analysis

- Subgroup analyses by HER2 status

[a] Patients were eligible for either test. All patients were centrally confirmed; [b] Planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed; [c] Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.

2L, second-line; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.

Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42(1):47-58.

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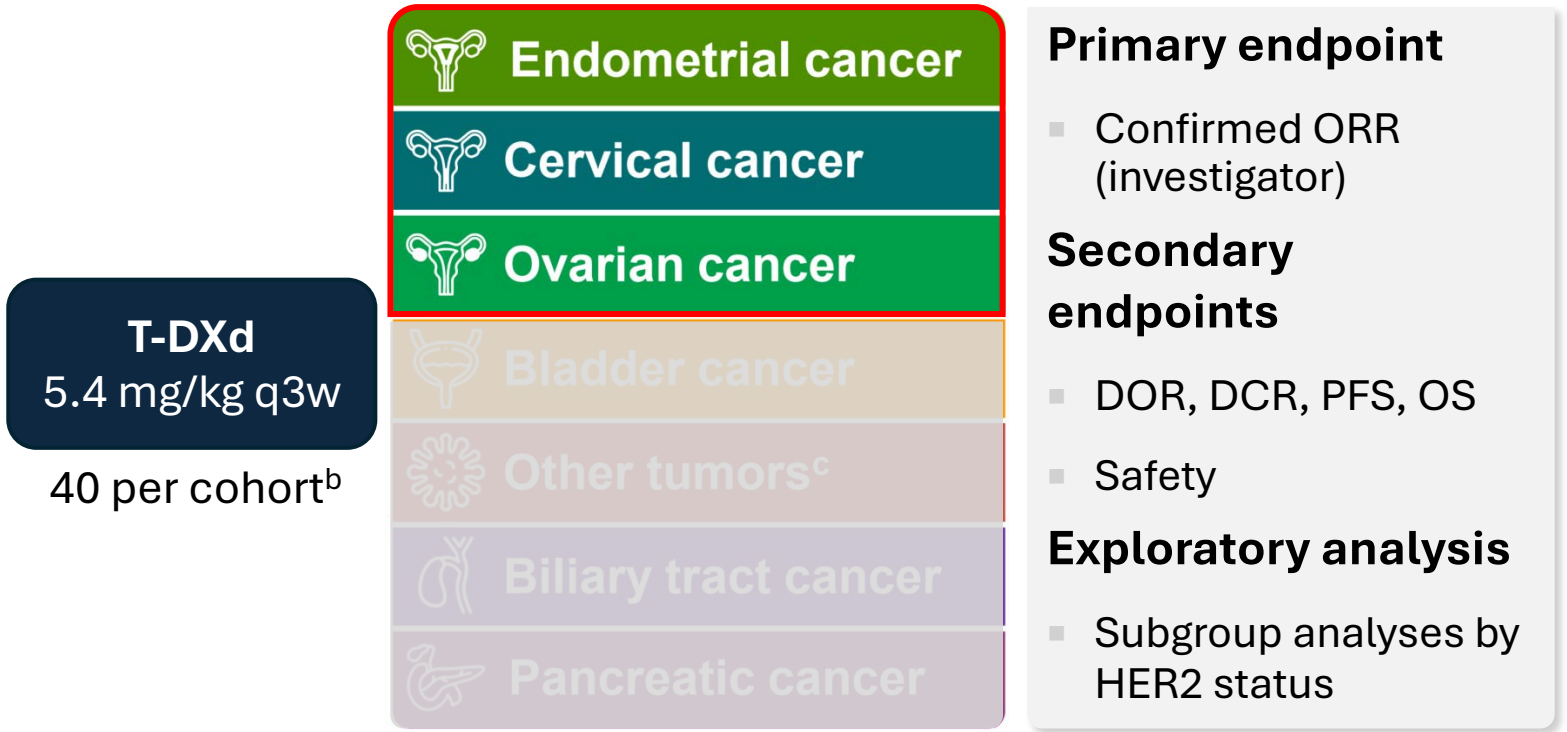


[a] Patients were eligible for either test. All patients were centrally confirmed; [b] Planned recruitment, cohorts with no objective responses in the first 15 patients were to be closed; [c] Patients with tumors that express HER2, excluding tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer.

2L, second-line; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organization.

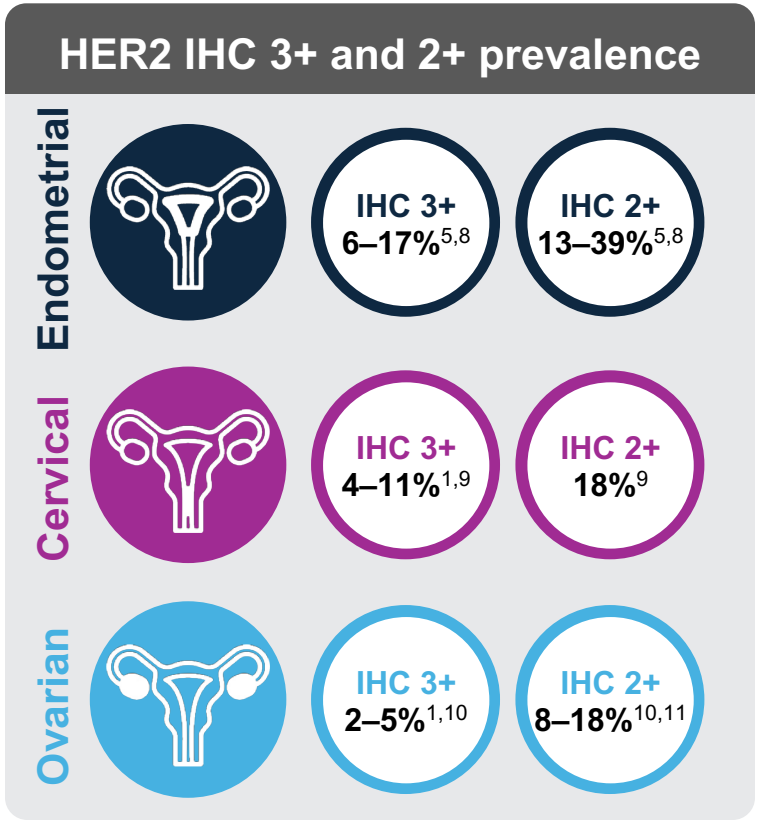
Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42(1):47-58.

Unmet need in HER2-expressing tumors

- **HER2 expression is seen in a wide range of solid tumors, including gynecological tumors**, and is associated with a biologically aggressive phenotype[1–5]

- In DESTINY-PanTumor02, **T-DXd demonstrated clinically meaningful response rates, progression-free survival, and overall survival** in HER2-expressing tumors, with particular benefit in gynecological tumors[6]
  - **Antitumor activity was observed with T-DXd** in heavily pre-treated patients with **endometrial, cervical, and ovarian tumors across HER2 IHC expression levels, and in ISH+ or plasma *ERBB2*-amplified subgroups**[7]

- Today's presentation reports further subgroup and biomarker analyses from the DESTINY-PanTumor02 **endometrial, cervical, and ovarian cancer cohorts**



ERBB2, erb-b2 receptor tyrosine kinase 2; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; T-DXd, trastuzumab deruxtecan

1. Yan M, et al. *Cancer Metastasis Rev*. 2015;34:157–164; 2. Li Z, et al. *EBioMedicine*. 2020;62:103074; 3. Uzunparmak B, et al. *Ann Oncol*. 2023;34:1035–1046;
4. Xing F, et al. *Mol Cancer*. 2023;22:6; 5. Halle MK, et al. *Br J Cancer*. 2018;118:378–387;
6. Meric-Bernstam F, et al. *J Clin Oncol*. 2024;42:47–58; 7. Lee J-Y, et al. Oral presentation at IGCS 2023 (Abstract 1550);
8. Vermij L, et al. *Cancers*. 2021;13:44; 9. Shi J, et al. *J Pathol Clin Res*. 2021;7:86–95;
10. Tuefferd M, et al. *PLoS One*. 2007;2:e1138. doi:10.1371/journal.pone.0001138; 11. Ersoy E, et al. *Int J Gynecol Pathol*. 2022;41:313–319

Makker et al. SGO 2024

Discussion Questions

What are the most common toxicities observed with mirvetuximab soravtansine? What about tisotumab vedotin?

Does the side-effect profile of T-DXd differ when the agent is employed in gynecologic cancers versus breast cancer?

OCULAR TOXICITIES WITH ADCS

Courtney Arn, APRN-CNP

The Ohio State University

PATIENT EDUCATION

- Expected ocular toxicities
- Signs/symptoms to report immediately
- Eye exams/Monitoring
- Eye drops

PROPHYLACTIC MEASURES

- Baseline Ophthalmologic Evaluation
- Preservative-Free Artificial Tears / Lubricating Drops
- Topical Corticosteroid Eye Drops?
- Vasoconstrictor Eye Drops
- Cooling Eye Pads / Cold Compresses
- Avoidance of Contact Lenses

SUPPORTIVE CARE

- Frequent Monitoring During Therapy
- Dose Modification
- Management of Dry Eye and Surface Disease
- Multidisciplinary Care

INTERDISCIPLINARY COORDINATION WITH EYE-CARE PROFESSIONALS

- Baseline exams to identify pre-existing conditions / risk factors
- Early Detection
- Management
- Dose Modification / Discontinuation
- Long-Term follow-up if needed
- Improved Patient Education / Communication

CASE STUDY

- 68 y.o with recurrent, platinum resistant high grade serous ovarian cancer; initially diagnosed in 2024
- **Medical History:** CKD, HTN
- **Genetics:** No pathogenic mutations, somatic BRCA/HRD negative
- **IHC:** FOLR 100%, HER2 2+

11/2024: 6 cycles of Paclitaxel 175 mg/m2, Carboplatin AUC 5 and Bev 15 mg/kg every 3 weeks

12/12/24-10/23/25: Received 16 cycles of maintenance Bev

11/21/25: Liver lesion biopsy - Metastatic adenocarcinoma involving liver

11/25/25-1/6/26: 3 cycles of Gem 1000 mg/m2, Carboplatin AUC 3 + Bev with progression of disease

2/2026: Started Mirvetuximab 6 mg/kg every 3 weeks

CASE STUDY

- Presented for Cycle 3 Mirvetuximab, reported blurred vision
- Eye Exam: confluent superficial keratitis
- Treatment held one week with resolution of blurred vision
- Repeat eye exam: improved to nonconfluent superficial keratitis
- Restarted Mirvetuximab at same dose level
- Imaging after 3 cycles showed decrease in disease
- No changes in vision or evidence of keratitis on exam

DOSE MODIFICATION FOR MIRV OCULAR TOXICITIES

Adverse reaction	Severity of adverse reaction†	Dosage modification
Keratitis/keratopathy	Nonconfluent superficial keratitis	Monitor
	Confluent superficial keratitis, a corneal epithelial defect, or 3-line or more loss in best-corrected visual acuity	Withhold until improved or resolved, then maintain at same dose level or consider dose reduction
	Corneal ulcer or stromal opacity or best-corrected distance visual acuity 20/200 or worse	Withhold until improved or resolved, then reduce by 1 dose level
	Corneal perforation	Permanently discontinue
Uveitis	Grade 1: Rare cell in anterior chamber	Monitor
	Grade 2: 1 to 2+ cell or flare in anterior chamber	Withhold until Grade 1 or less, then maintain dose at same dose level
	Grade 3: 3+ cell or flare in anterior chamber	Withhold until Grade 1 or less, then reduce dose by 1 dose level
	Grade 4: Hypopyon	Permanently discontinue

Discussion Questions

How do the frequency and severity of ocular toxicities compare between tisotumab vedotin versus mirvetuximab soravtansine versus datopotamab deruxtecan?

How do you respond if a patient asks, “Can I go blind from one of these agents?”

In general, do ADC-associated ocular toxicities completely resolve when the treatment is discontinued?

Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

Currently Available ADCs in Lung Cancer Management

Edward B. Garon, MD, MS

Professor

David Geffen School of Medicine at UCLA

Los Angeles, CA

Case

- 57-year-old woman for whom I have cared for several years
- Originally diagnosed 7 years earlier with “stage 3” disease with an EGFR mutation. She received chemoradiotherapy followed by durvalumab, but a brain met was discovered during therapy
- Received stereotactic radiotherapy
- At progression received osimertinib. Developed pneumonitis managed by steroids, but was able to wean and continue
- Eventually added carboplatin/pemetrexed and also received radiation therapy to several areas
- Experienced progression on maintenance pemetrexed/osimertinib

TROPION-Lung01 Study Design

Randomized, Phase 3, Open-Label, Global Study (NCT04656652)

Key Eligibility Criteria

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS of 0 or 1
- No prior docetaxel

Without actionable genomic alterations[a]

- 1 or 2 prior lines, including platinum CT and anti–PD-(L)1 mAb therapy

With actionable genomic alterations

- Positive for *EGFR*, *ALK*, *NTRK*, *BRAF*, *ROS1*, *MET* exon 14 skipping, or *RET*
- 1 or 2 prior approved targeted therapies + platinum-based CT, and ≤1 anti–PD-(L)1 mAb

R 1:1

Dato-DXd
6 mg/kg Q3W
(N=299)

Docetaxel
75 mg/m² Q3W
(N=305)

Dual Primary Endpoints

- PFS by BICR
- OS

Secondary Endpoints

- ORR by BICR
- DOR by BICR
- Safety

Stratified by: histology,[b] actionable genomic alteration,[c] anti–PD-(L)1 mAb included in most recent prior therapy, geography[d]

Enrollment period: 19 February 2021 to 7 November 2022.
BICR, blinded independent central review; CT, chemotherapy; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed cell death 1 (ligand 1); PFS, progression-free survival; Q3W, every 3 weeks; R, randomized.
[a]Patients with *KRAS* mutations in the absence of known actionable genomic alterations are eligible; must meet prior therapy requirements for patients without actionable genomic alterations. [b]Squamous vs non-squamous. [c]Presence vs absence. [d]United States/Japan/Western Europe vs rest of world.

Adverse Events of Special Interest

AESI, n (%)	Dato-DXd N=297	Docetaxel N=290
Stomatitis/oral mucositis[a]		
All grades	160 (54)	59 (20)
Grade ≥3	19 (6)	4 (1)
Ocular events[b]		
All grades	57 (19)	27 (9)
Grade ≥3	5 (2)[c]	0
Adjudicated drug-related ILD[d]		
All grades	25 (8)	12 (4)
Grade ≥3	10 (3)	4 (1)
Grade 5	7 (2)	1 (0.3)

- Stomatitis/oral mucositis associated with Dato-DXd resulted in a low rate of discontinuation (0.7%)
- Dry eye was the most common ocular event seen with Dato-DXd (6.1%; primarily grade ≤2), followed by increased lacrimation (5.4%)
- Seven adjudicated drug-related grade 5 ILD events
  - Primary cause of death in 4 out of 7 was attributed to disease progression by investigator
  - Non-squamous: 4 of 232 patients (1.7%); Squamous: 3 of 65 patients (4.6%)[e]
- IRRs were observed in 8% of patients in each arm, all were grade ≤2 with the exception of 1 grade 3 event with Dato-DXd

AESI, adverse event of special interest; ILD, interstitial lung disease; IRR, infusion-related reaction; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SMQ, standardized MedDRA query; SOC, system organ class. AESIs listed in this slide are treatment emergent and include all PTs that define the medical concept.

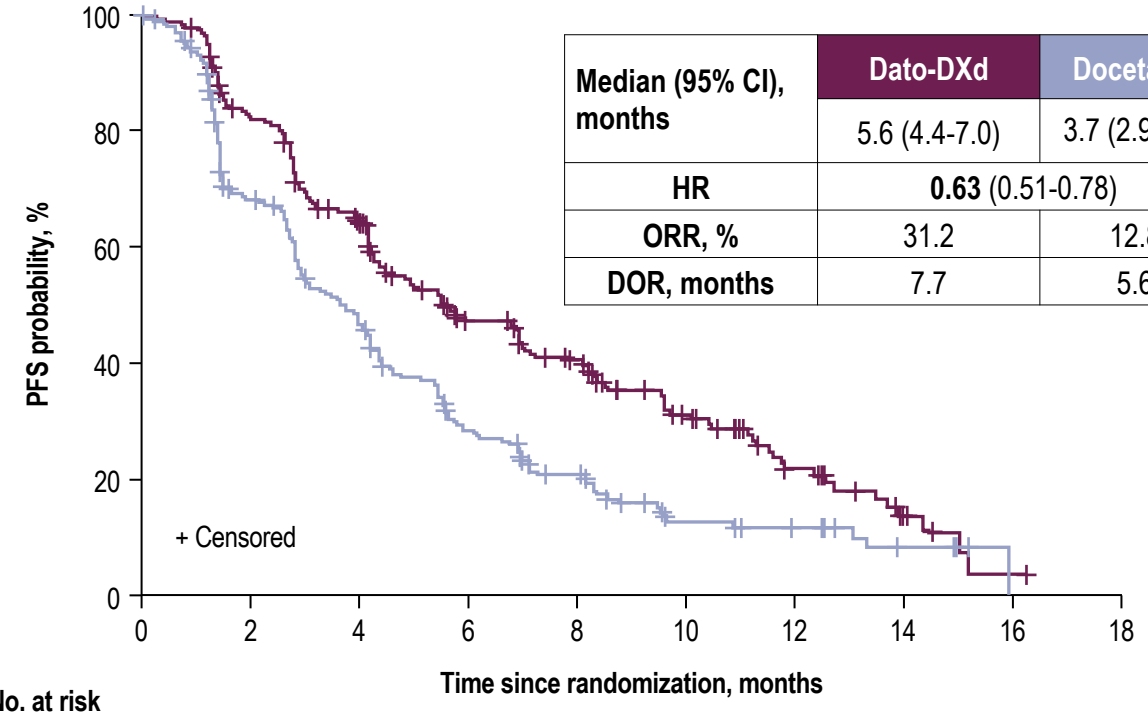
[a]Events included the selected PTs oral mucositis/stomatitis, oropharyngeal pain, mouth ulceration, odynophagia, dysphagia, oral pain, glossitis, pharyngeal inflammation, aphthous ulcer, and oral mucosa erosion. [b]Ocular events included selected PTs from the corneal disorder SMQ and selected relevant PTs from the eye disorder SOC. [c]Included 4 cases of keratitis and 1 case of ulcerative keratitis. [d]ILD includes events that were adjudicated as ILD and related to use of Dato-DXd or docetaxel (includes cases of potential ILD/pneumonitis based on MedDRA v26.0 for the narrow ILD SMQ, selected terms from the broad ILD SMQ, and PTs of respiratory failure and acute respiratory failure). [e]Among treated patients, histology information per the case report form.

PFS by Histology

Non-squamous

(with and without AGAs)

Median (95% CI), months	Dato-DXd	Docetaxel
	5.6 (4.4-7.0)	3.7 (2.9-4.2)
HR	**0.63** (0.51-0.78)	
ORR, %	31.2	12.8
DOR, months	7.7	5.6

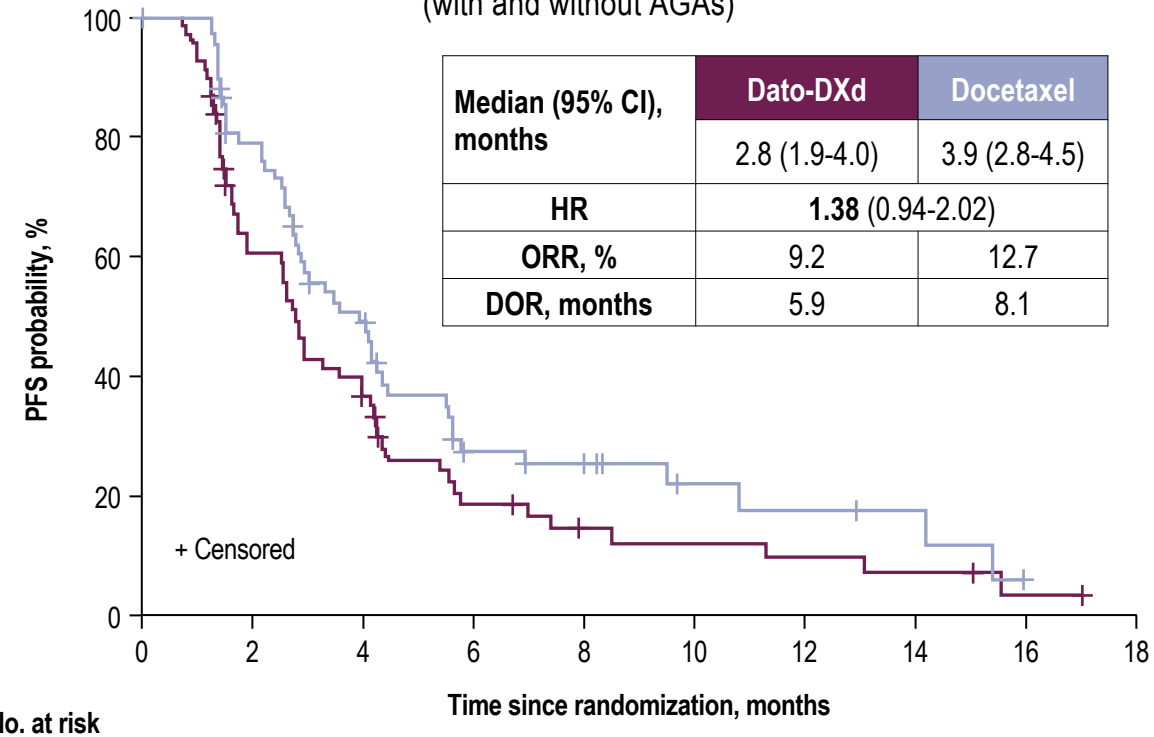


No. at risk										
Dato-DXd	229	178	134	86	68	41	20	7	1	0
Docetaxel	232	135	90	50	32	14	10	4	0	0

Squamous

(with and without AGAs)

Median (95% CI), months	Dato-DXd	Docetaxel
	2.8 (1.9-4.0)	3.9 (2.8-4.5)
HR	**1.38** (0.94-2.02)	
ORR, %	9.2	12.7
DOR, months	5.9	8.1

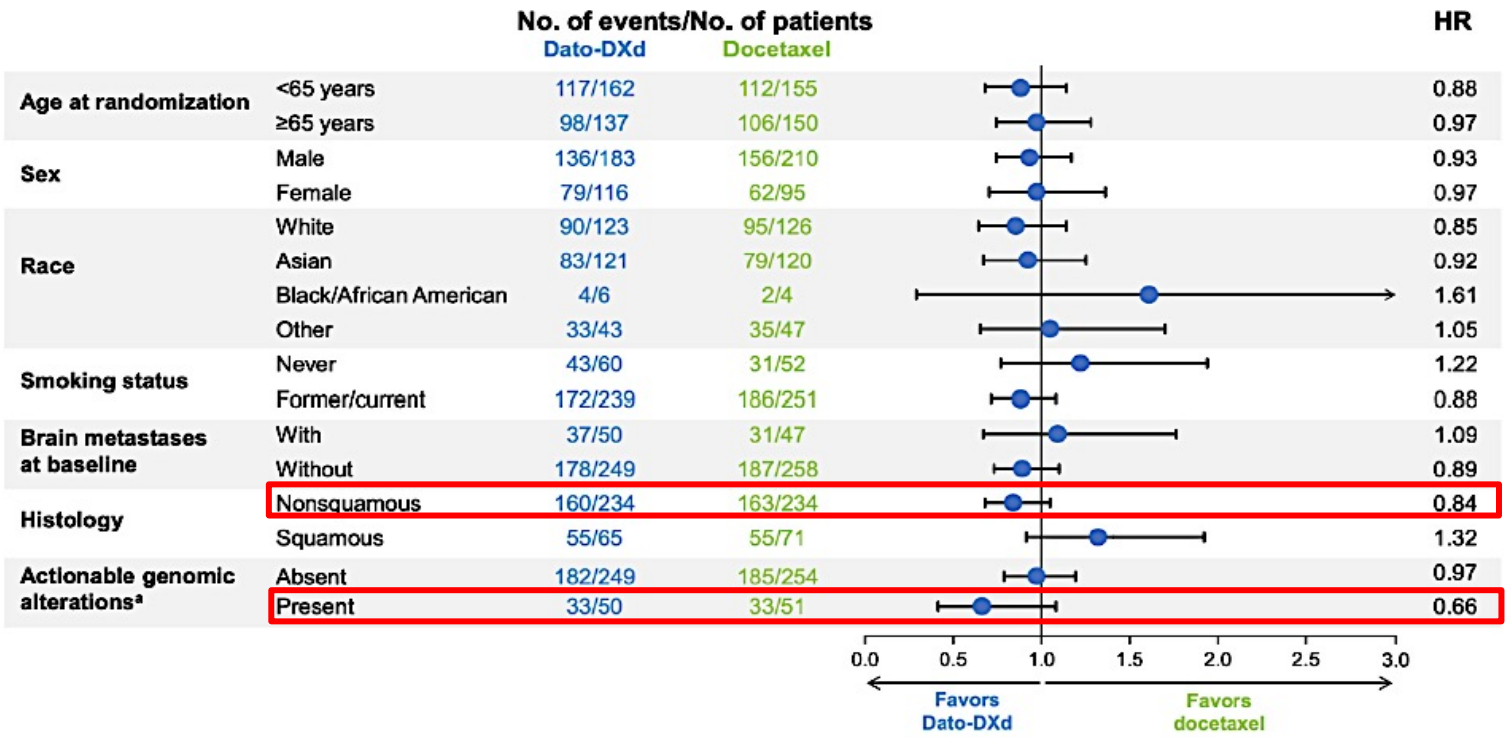


No. at risk										
Dato-DXd	70	38	22	10	6	5	4	3	1	0
Docetaxel	73	51	30	13	10	5	4	3	0	0

PFS HR for non-squamous without AGAs: 0.71 (0.56, 0.91)

AGA, actionable genomic alteration; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival.
Squamous subset included 3 patients with AGAs.

Final Overall Survival from TROPION-Lung01

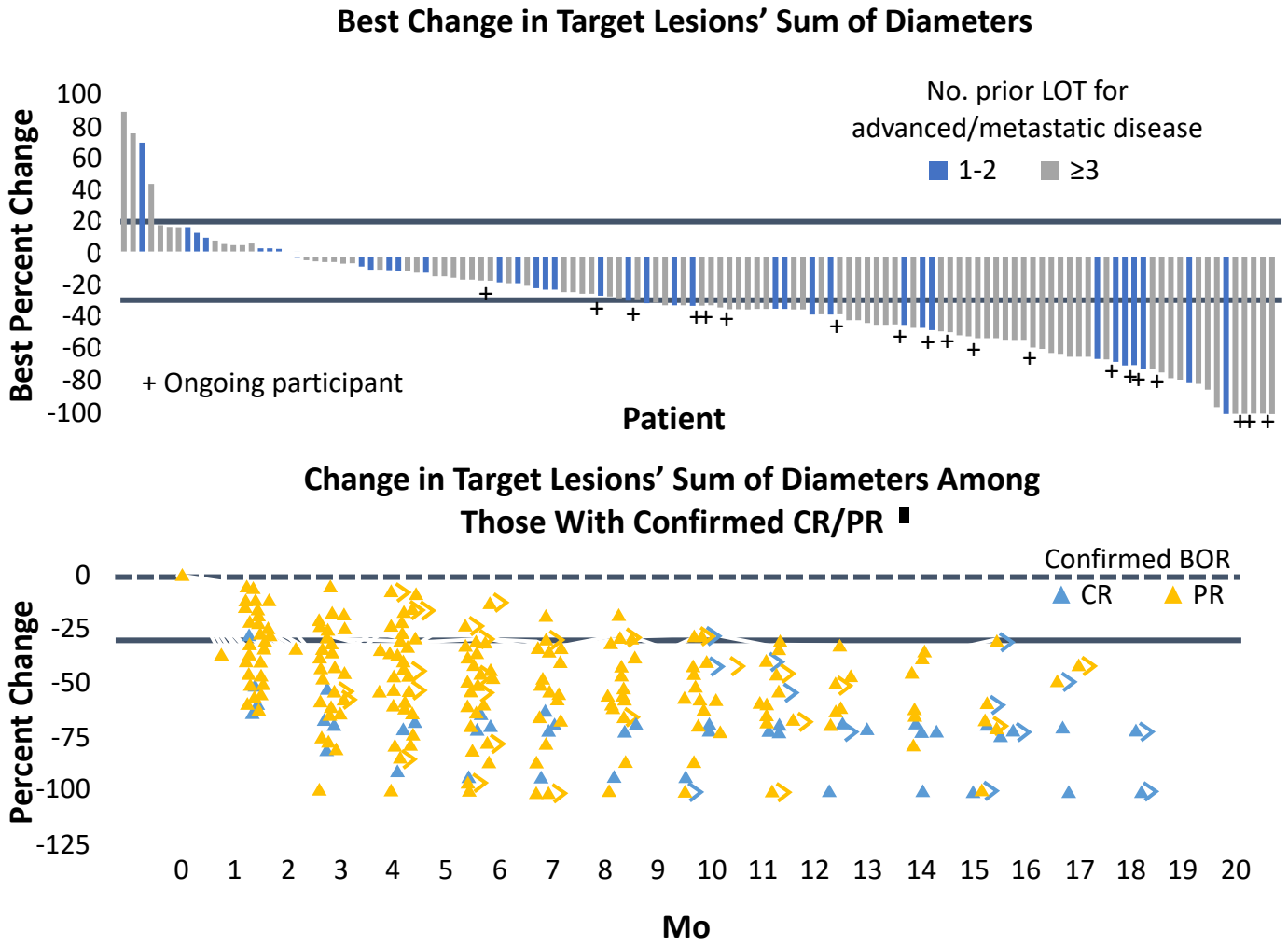


The dual primary endpoint of OS showed a numerical improvement but was not statistically significant

Sands et al, WCLC 2024

Phase II TROPION-Lung05: Dato-DXd in Previously Treated Advanced NSCLC With AGAs

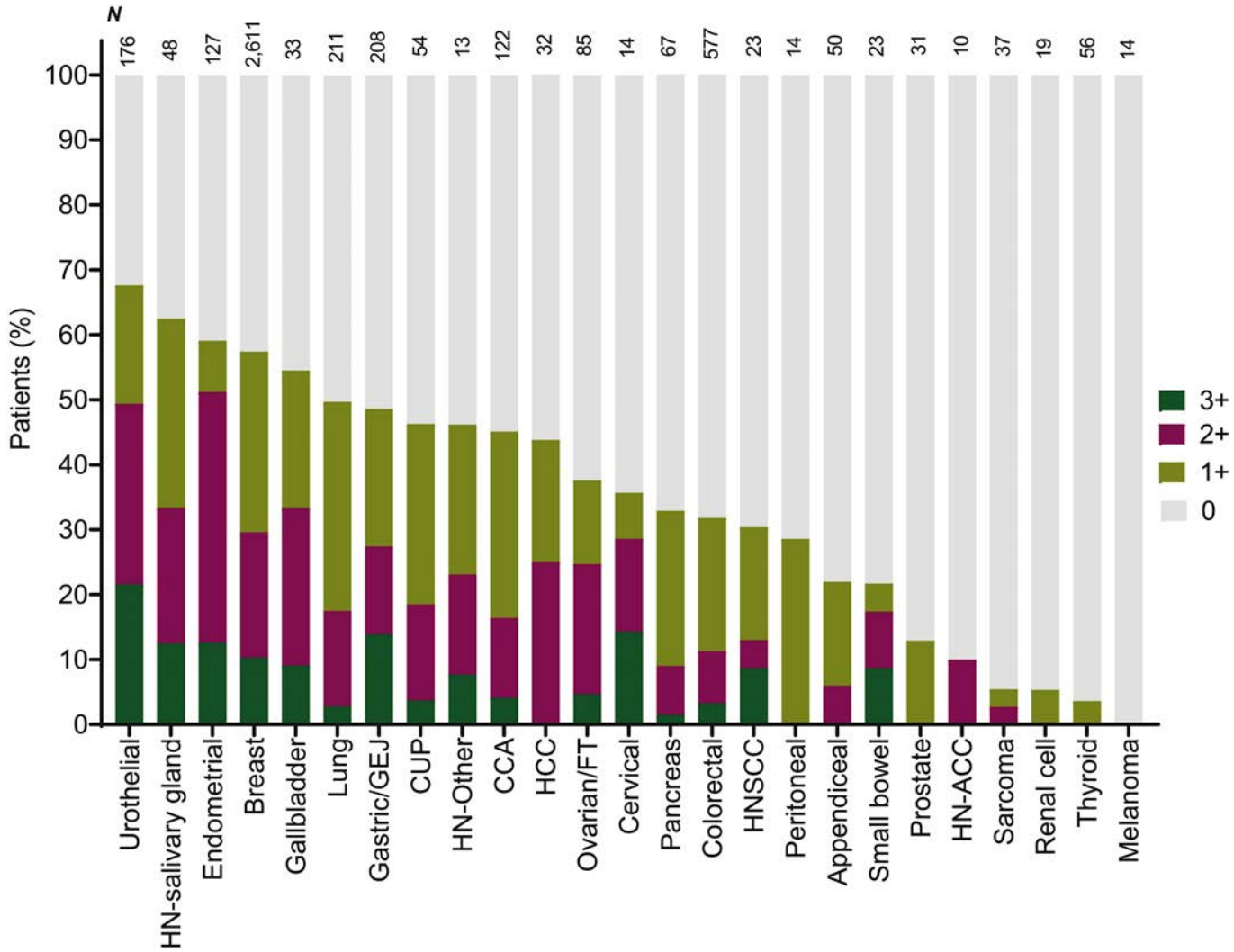
Outcome	All Patients (N = 137)	*EGFR*m (n = 78)	*ALK*+ (n = 34)
Confirmed ORR, n (%)	49 (35.8)	34 (43.6)	8 (23.5)
mDoR, mo (95% CI)	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
Confirmed DCR, n (%)	108 (78.8)	64 (82.1)	25 (73.5)
mPFS, mo (95% CI)	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)



Paz-Ares. ESMO 2023. Abstr 1314MO.

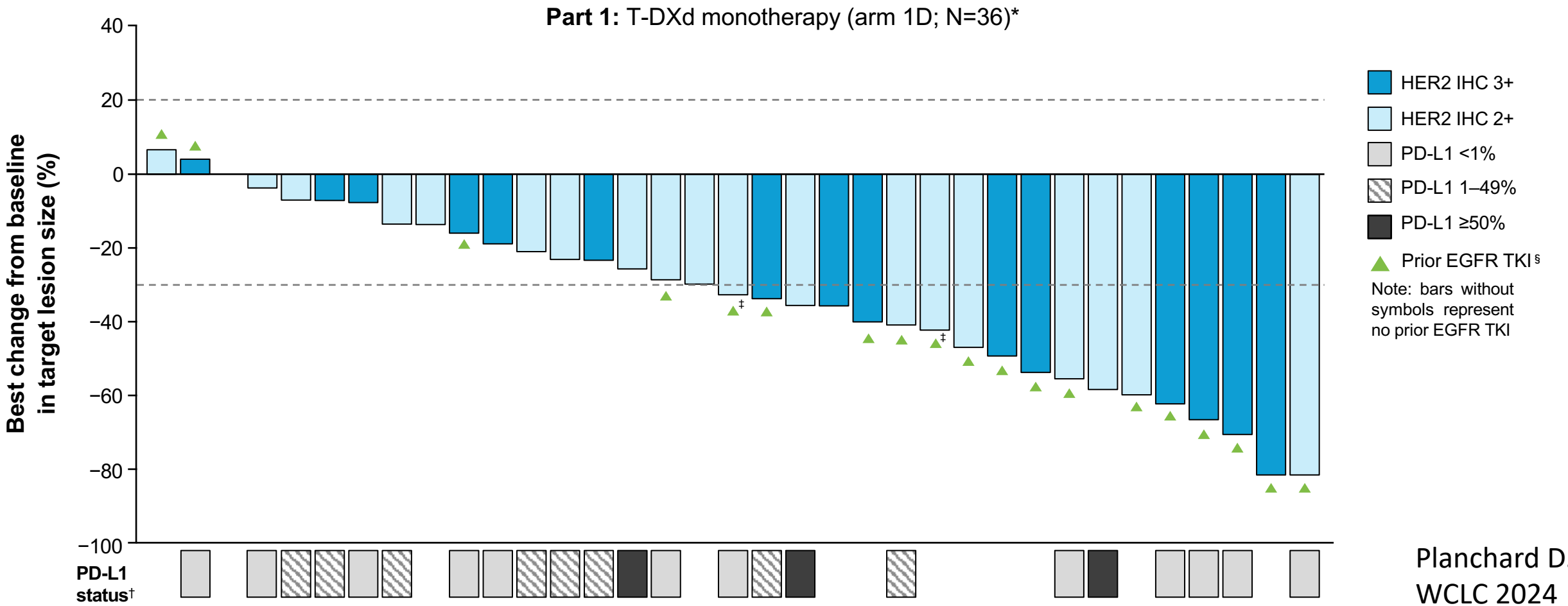
HER2 Abnormalities in NSCLC

- HER2 mutations are seen in nearly 2% of NSCLC cases in US
- HER2 3+ is seen in nearly 3% of NSCLC
- High level HER2 amplification is seen in nearly 1% of NSCLC



Uzunparnak B. Annals of Oncology 2023
Waliany S. Cancer Med 2024
Odintsov I. Journal of Thoracic Oncology 2024

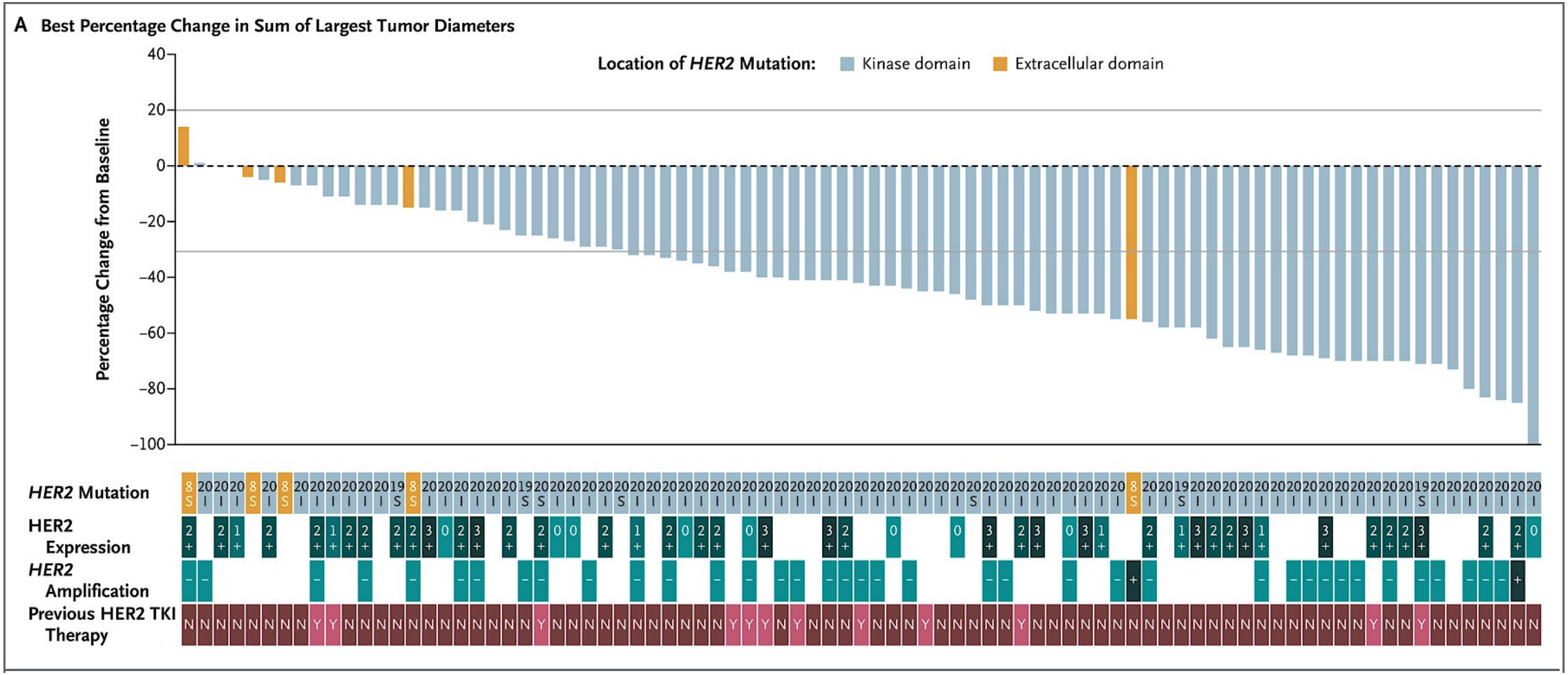
Best percentage change from baseline in target lesion size



Planchard D. WCLC 2024

Investigator assessed per RECIST v1.1. Best percentage change is the maximum reduction or minimum increase from baseline in the target lesion size; the dashed lines at −30% and 20% change in target lesion size indicate the thresholds for partial response and progressive disease, respectively. The study was not designed/powered to compare efficacy between subgroups.
*One patient was not evaluable; †patients with unknown PD-L1 status (n=12) are represented by white spaces; ‡unconfirmed response; § patients had HER2-OE (IHC 3+/2+) NSCLC.
EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; HER2-OE, HER2-overexpressing; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor.

Trastuzumab Deruxtecan in HER2 Mutation Positive NSCLC

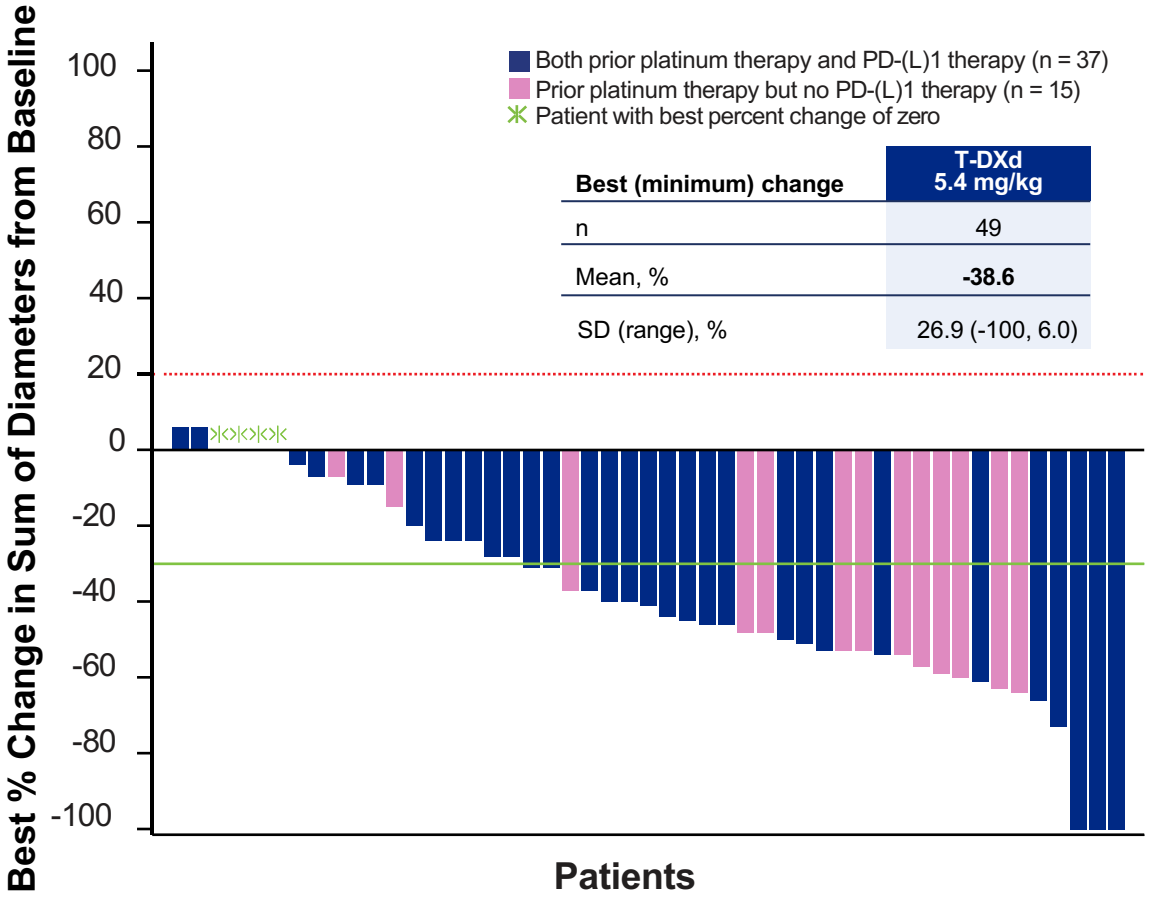


Li BT et al. N Engl J Med. 2022 Jan 20;386(3):241-251.

DESTINY-Lung02

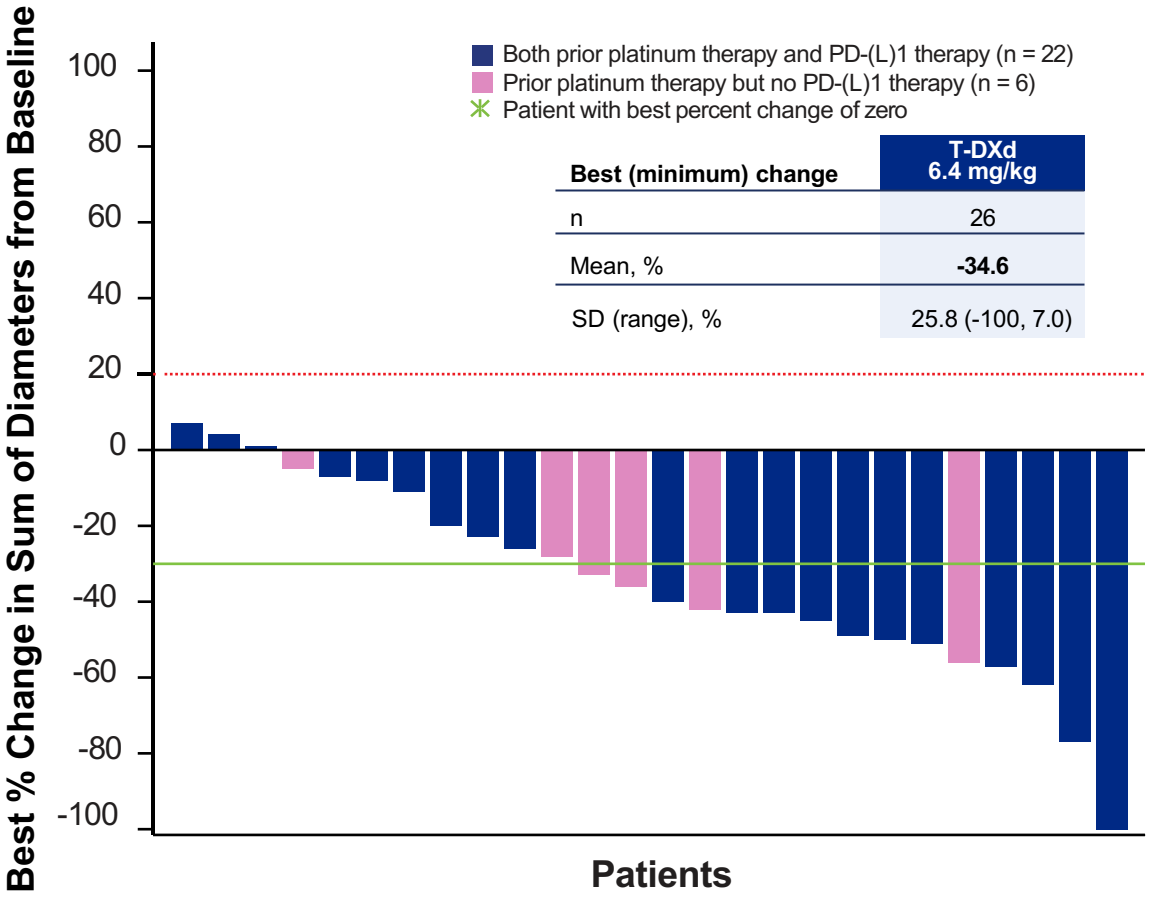
Best Percent Change in Tumor Size by BICR

T-DXd 5.4 mg/kg (n = 52)



Best (minimum) change	T-DXd 5.4 mg/kg
n	49
Mean, %	**-38.6**
SD (range), %	26.9 (-100, 6.0)

T-DXd 6.4 mg/kg (n = 28)



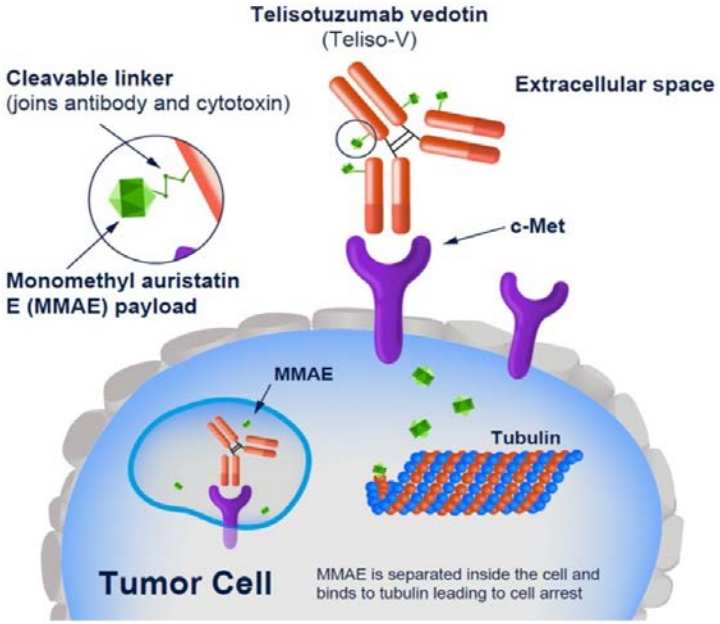
Best (minimum) change	T-DXd 6.4 mg/kg
n	26
Mean, %	**-34.6**
SD (range), %	25.8 (-100, 7.0)

Goto K. ESMO 2022

Data cutoff: Mar 24, 2022.

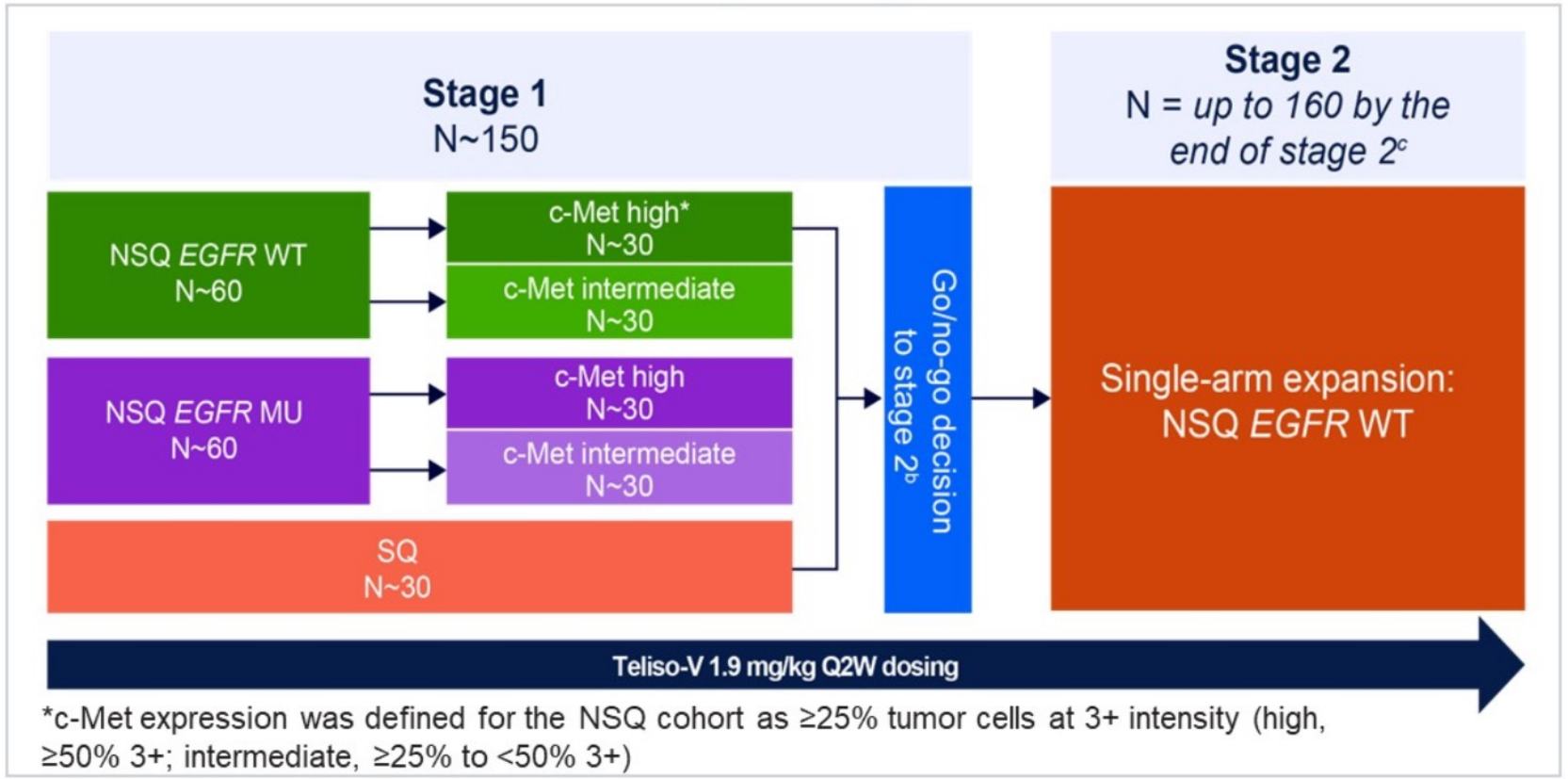
The red line at 20% indicates progressive disease, and the green line at −30% indicates a partial response.

LUMINOSITY: Phase II Study of Telisotuzumab Vedotin in Previously Treated c-Met–Overexpressing Nonsquamous EGFR Wild-Type NSCLC



Eligible Patients

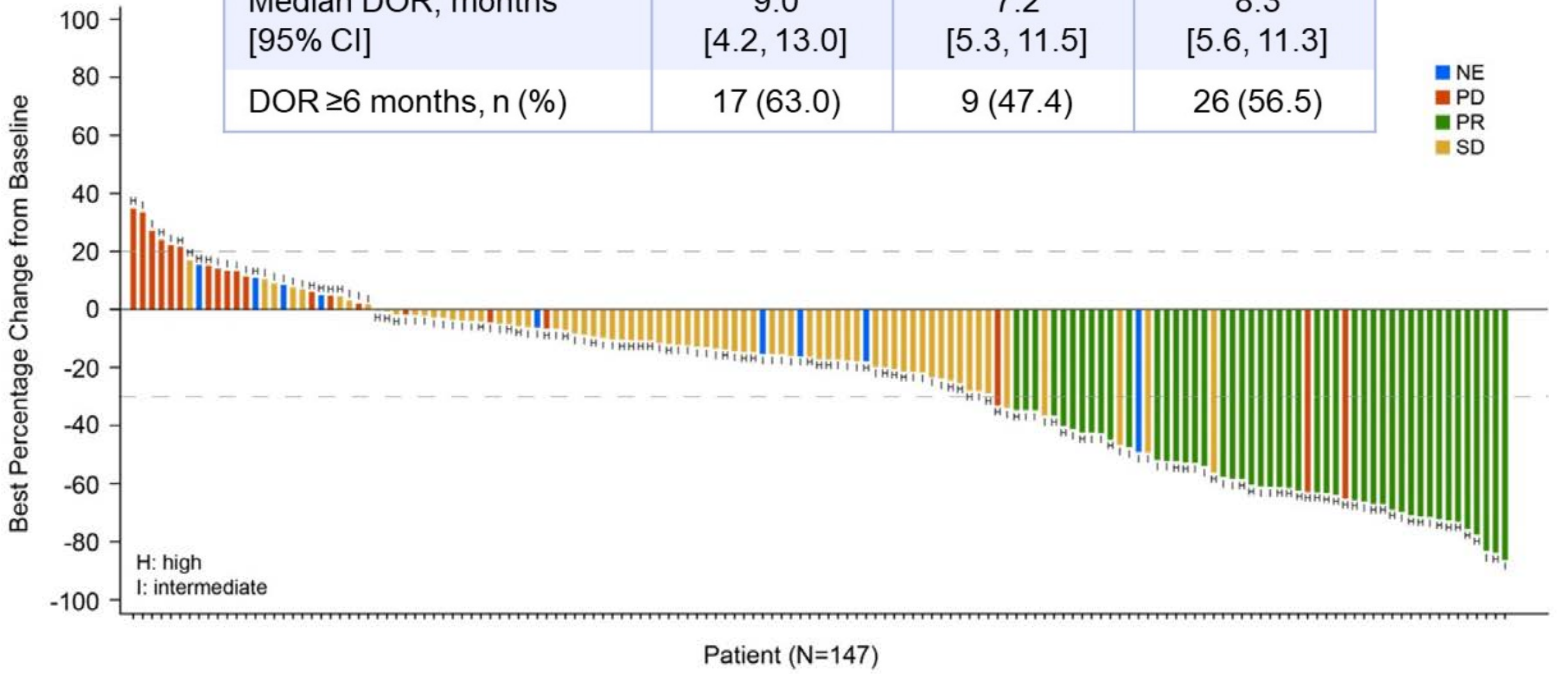
- ≥18 years
- Advanced/metastatic NSCLC
- c-Met OE by IHC[a]
- Received ≤2 prior lines of systemic therapy in the advanced/metastatic setting, including cytotoxic CTx (≤1 line), immunotherapy (sequential or combined with CTx), and therapy targeting driver gene alterations (if eligible)

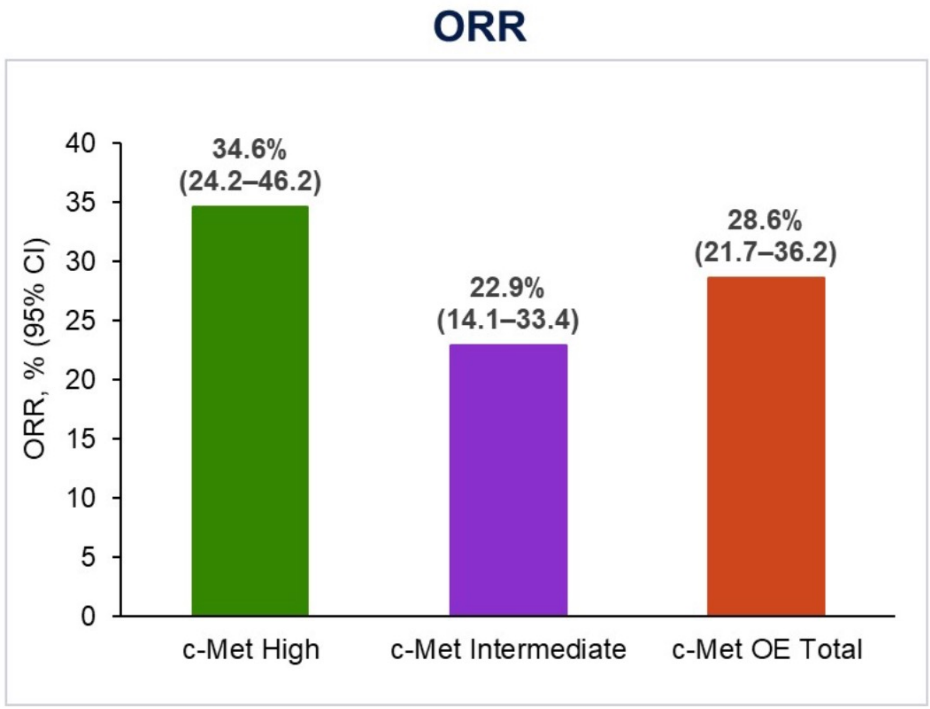


Camidge DR et al. ASCO 2024;Abstract 103.

LUMINOSITY: Telisotuzumab Vedotin in c-Met–Overexpressing NSCLC – Efficacy

	c-Met High (n=78)	c-Met Intermediate (n=83)	c-Met OE Total (N=161)
Number of responders	27	19	46
Median DOR, months [95% CI]	9.0 [4.2, 13.0]	7.2 [5.3, 11.5]	8.3 [5.6, 11.3]
DOR ≥6 months, n (%)	17 (63.0)	9 (47.4)	26 (56.5)

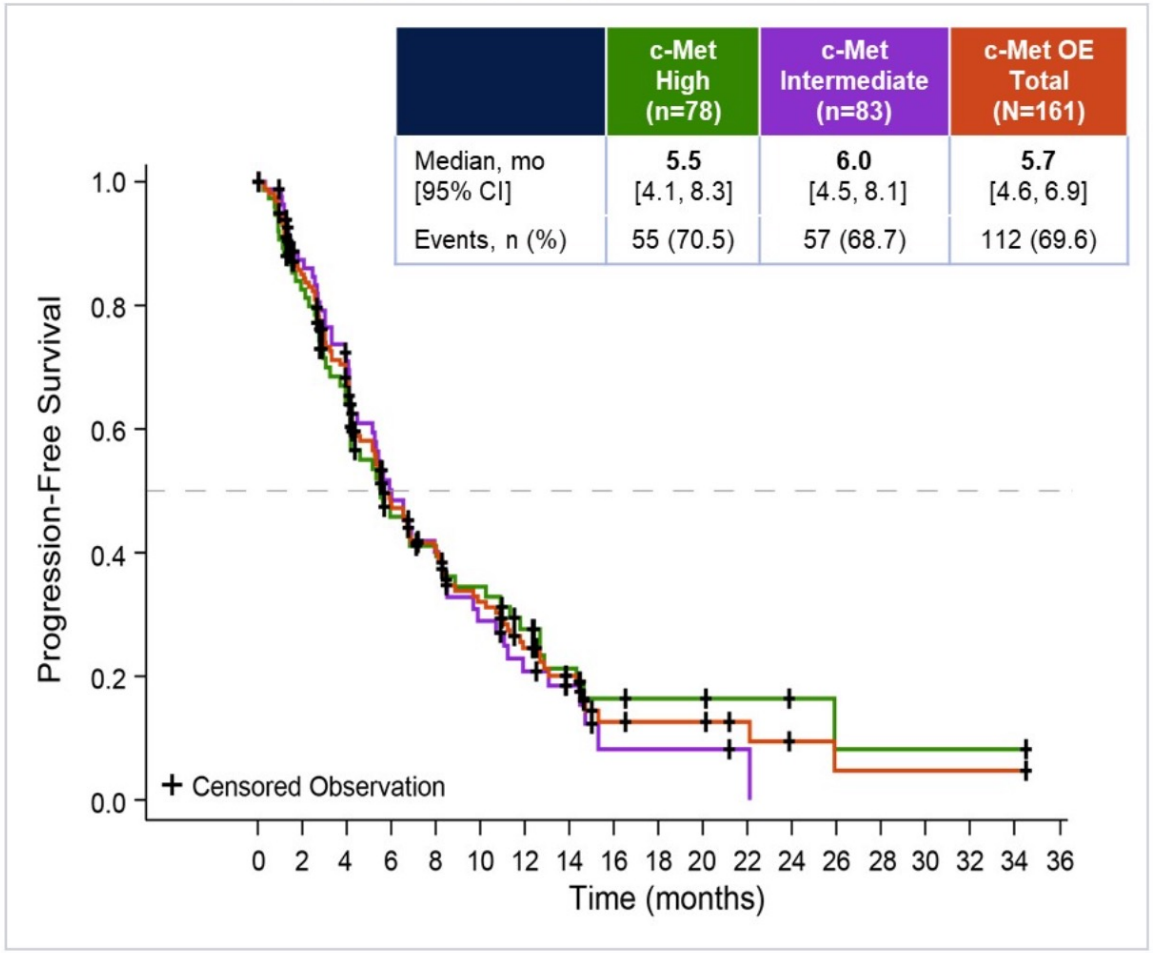




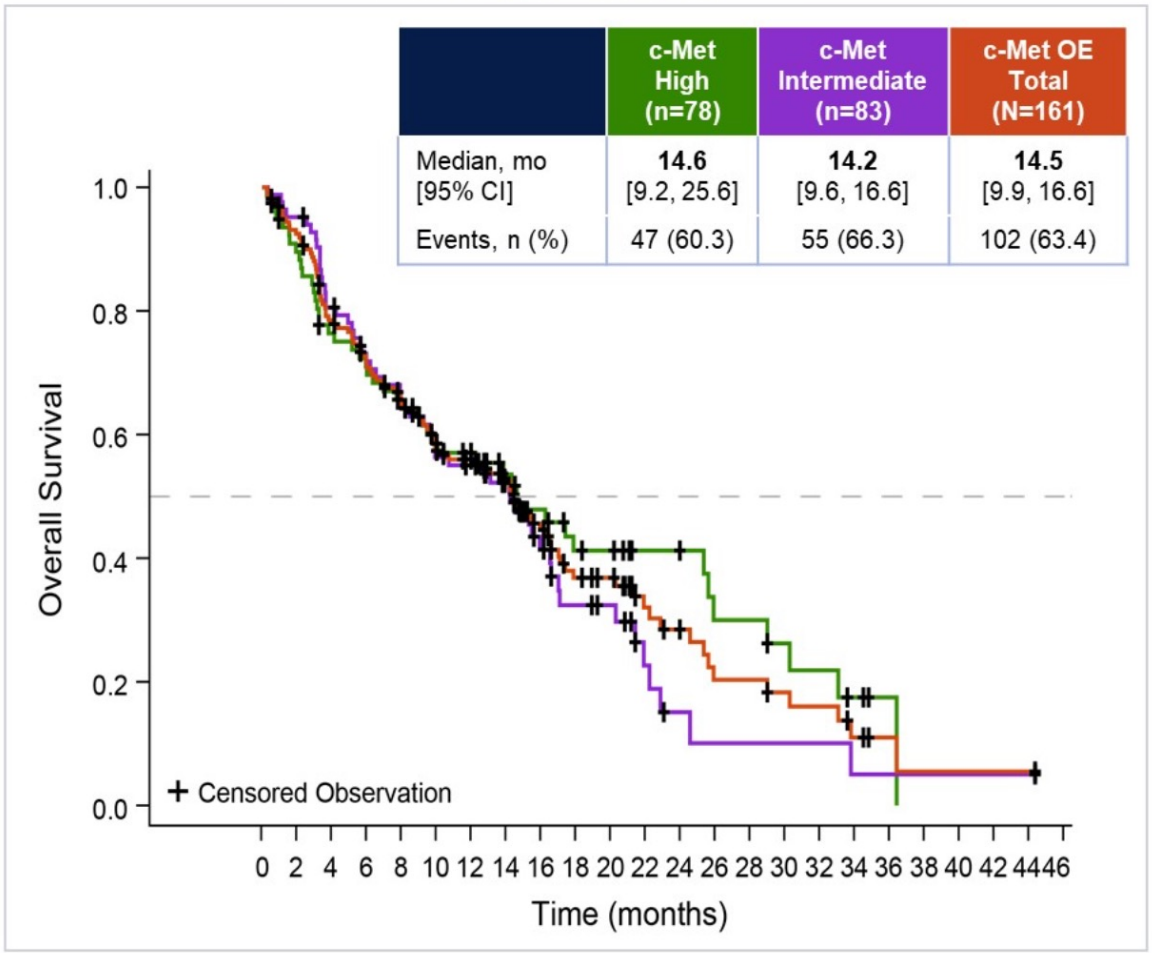
Camidge DR et al. ASCO 2024;Abstract 103.

LUMINOSITY: Telisotuzumab Vedotin in c-Met–Overexpressing NSCLC – Survival

Progression-Free Survival



Overall Survival



Camidge DR et al. ASCO 2024;Abstract 103.

Case Continued

- Last summer the patient chose to initiate datopotamab deruxtecan
- She has tolerated it well with very little mucositis, and no problems with pneumonitis (clinical or radiographic)
- She did not have a robust reduction in tumor volume, but disease did stabilize
- She did receive SBRT to a single brain lesion during treatment
- She continues on therapy at this time

Discussion Questions

To which patients with EGFR-mutated NSCLC are you currently administering Dato-DXd?

What toxicities are most common with Dato-DXd? What about telisotuzumab vedotin?

Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

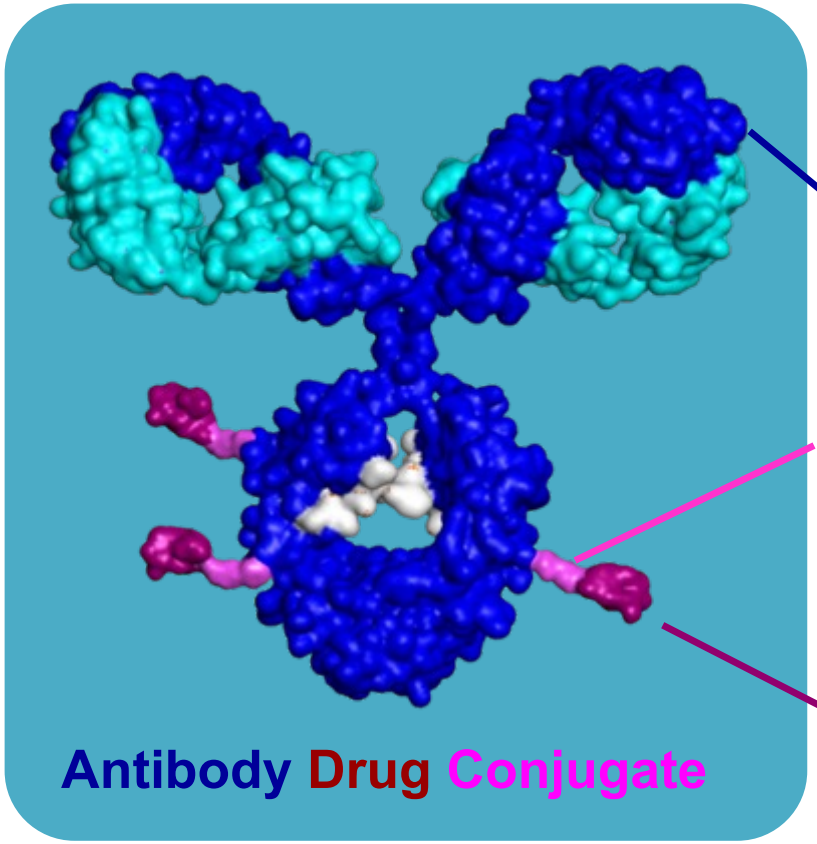
Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

Current and Future Role of TROP2-Targeted ADCs in mBC

Heather McArthur, MD, MPH, FASCO
Professor, Department of Internal Medicine
Clinical Director, Breast Cancer Program
Komen Distinguished Chair in Clinical Breast Cancer Research
UT Southwestern Medical Center
Dallas, Texas

ADCs Have Different Antibodies, Linkers and Payloads

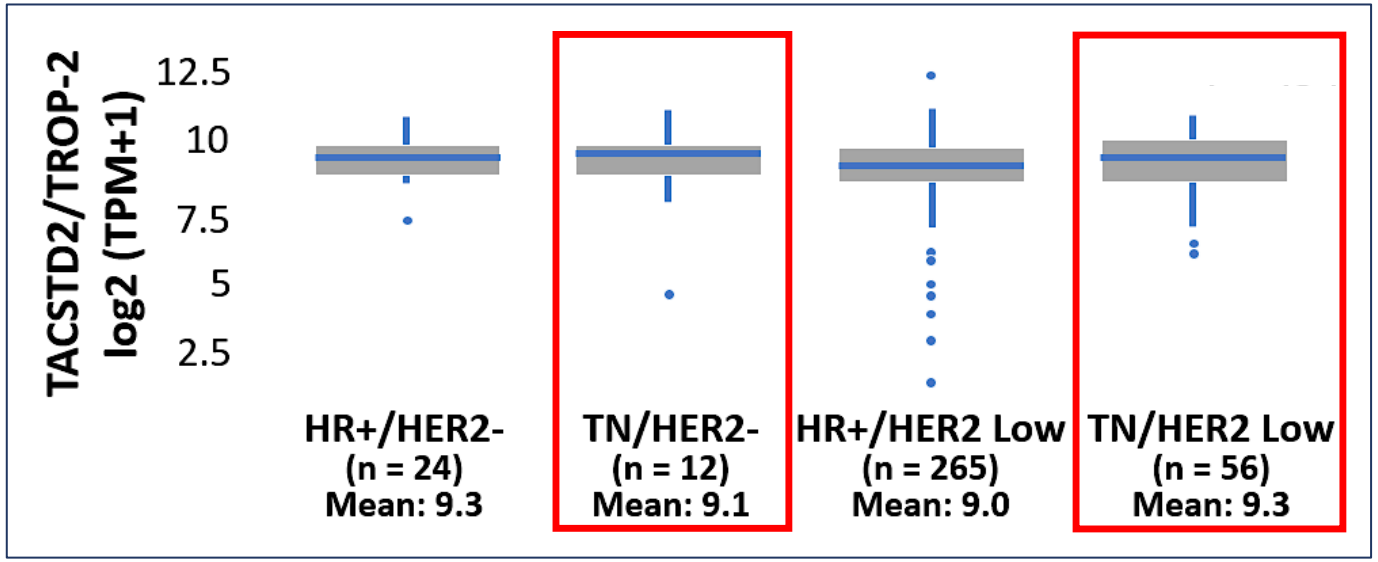


	ADC Attributes	Sacituzumab govitecan (SG)	Datopotamab deruxtecan (Dato-DXd)	Sacituzumab tirumotecan (sac-TMT)
Antibody	Target	TROP2	TROP2	TROP2
	Antibody	hRS7 IgG1k	Datopotamab	hRS7 IgG1
	DAR	~7.6:1	~4:1	~7.4:1
Linker	Linker	Hydrolysable	Tetrapeptide-based	2-methylsulfonyl pyrimidine
	Cleavable linker?	Yes	Yes	Yes
Payload	Payload	SN-38	DXd	KL610023 (T030)
	Payload MoA	Topo1 inhibitor	Topo1 inhibitor	Topo1 inhibitor
	Membrane permeable?	Yes	Yes	Yes

ADC, antibody-drug conjugate; DAR, drug to antibody ratio; Dato-DXd, datopotamab deruxtecan; HER2/3, human epidermal growth factor receptor 2/3; IgG, immunoglobulin; MMAE, monomethyl auristatin E; MoA, mechanism of action; SG, sacituzumab govitecan; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TROP, trophoblast cell surface antigen.

TROP-2 as a Therapeutic Target

- Targeting broadly expressed markers allows for the selective delivery of potent agents
- TROP-2 is a pan-epithelial cancer antigen
  - Overexpressed in all breast cancer subtypes
  - Less expression on normal tissues
  - Excellent target for ADC
  - Marker of poor prognosis: larger tumor size, higher risk of recurrence
  - High TROP-2 levels: aggressive tumor, resistance to chemotherapy



Medford AJ et al. 2023 AACR. Abstract 960. Yao L et al. *Front Oncol*. 2023;13:1292211. Sakach E et al. *Cancers (Basel)*. 2022;14(23):5936.

ASCENT-03: Study Design

Patients with previously untreated, locally advanced inoperable or metastatic TNBC[a]:

- Not candidates for PD-(L)1 inhibitors:
  - PD-L1 negative[b] tumors (CPS < 10)
  - PD-L1 positive[b] tumors (CPS ≥ 10) and previously treated with a PD-(L)1 inhibitor in curative setting
  - Ineligible for a PD-(L)1 inhibitor due to a comorbidity
- ≥ 6 months since treatment in curative setting
- Previously treated, stable CNS metastases were allowed

Treatment was continued until BICR-verified progression or unacceptable toxicity

N = 558

R 1:1

Sacituzumab govitecan
10 mg/kg IV
(days 1 and 8 of 21-day cycles)
n = 279

Chemotherapy
Paclitaxel 90 mg/m^2 OR nab-Paclitaxel 100 mg/m^2
(days 1, 8, and 15 of 28-day cycles) OR
Gemcitabine 1000 mg/m^2 + Carboplatin AUC2
(days 1 and 8 of 21-day cycles)
n = 279

Eligible patients were offered crossover to 2L SG, provided through the study, following BICR-verified disease progression

End points

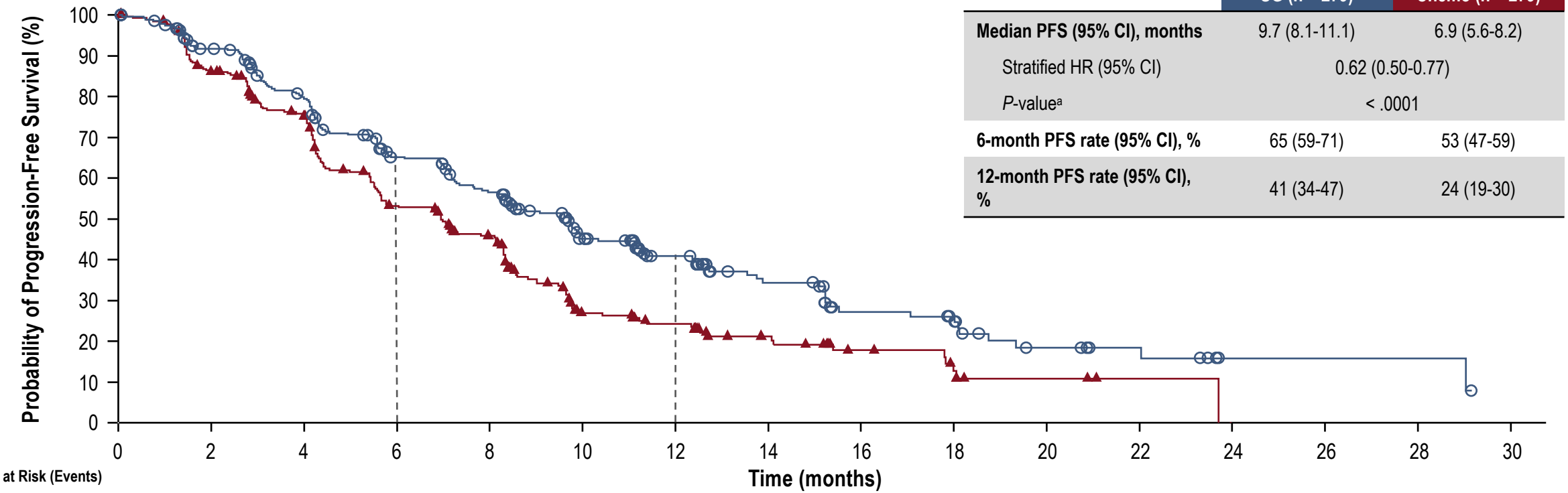
Primary
- PFS by BICR[d]

Secondary
- OS
- ORR, DOR, TTR by BICR[d]
- Safety
- QOL

Stratification factors:
- US/Canada/Western Europe vs rest of the world
- De novo mTNBC[c] vs recurrent within 6 to 12 months of treatment vs recurrent after > 12 months from treatment in curative setting

Cortes et al. ESMO 2025;Abstract LBA20

Progression-Free Survival by BICR



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-month PFS rate (95% CI), %	41 (34-47)	24 (19-30)

SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo by BICR analysis, with a 38% reduction in risk of disease progression or death

Cortes et al. ESMO 2025;Abstract LBA20

TROPION-Breast02: Study Design

Randomised, phase 3, open-label, global study (NCT05374512)

Key inclusion criteria:

- Patients with histologically or cytologically documented locally recurrent inoperable or metastatic TNBC*
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy not an option†
- ECOG PS 0 or 1
- No minimum DFI‡

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=323)

Investigator's choice of chemotherapy (ICC)#
Paclitaxel, nab-paclitaxel, capecitabine, eribulin mesylate/eribulin, carboplatin
(n=321)

Endpoints

Dual primary:

- OS
- PFS by BICR per RECIST v1.1

Secondary included:

- PFS (investigator-assessed)
- ORR, DoR
- Safety

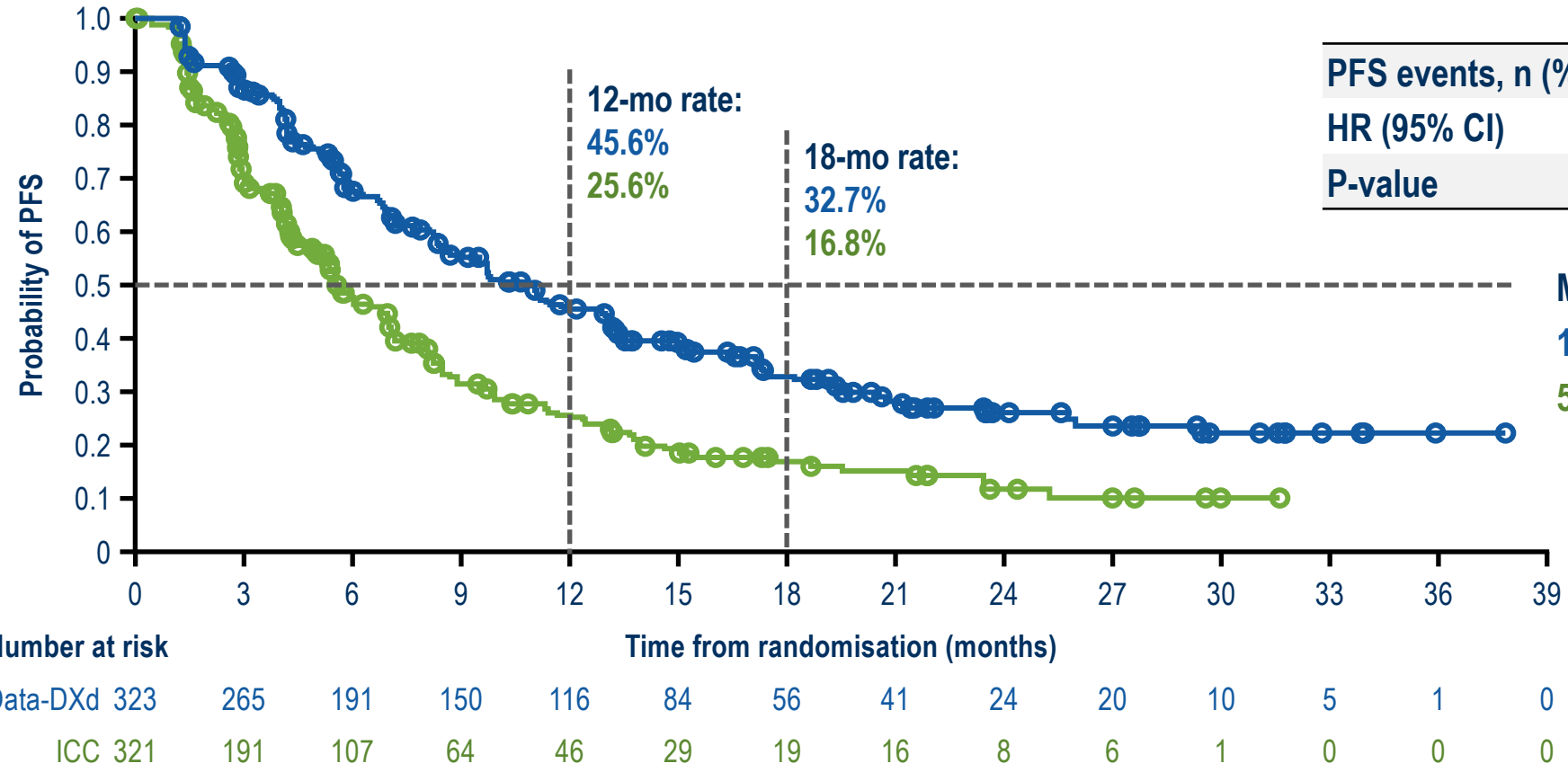
Randomisation stratified by:

- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10]) §
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)¶

- Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met
- Following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion‖

Dent et al. ESMO 2025;Abstract LBA21

Progression-Free Survival by BICR



Number at risk														
Data-DXd	323	265	191	150	116	84	56	41	24	20	10	5	1	0
ICC	321	191	107	64	46	29	19	16	8	6	1	0	0	0

	Dato-DXd	ICC
PFS events, n (%)	199 (62)	209 (65)
HR (95% CI)	0.57 (0.47–0.69)	
P-value	<0.0001	

Median PFS (95% CI)

10.8 mo (8.6–13.0)

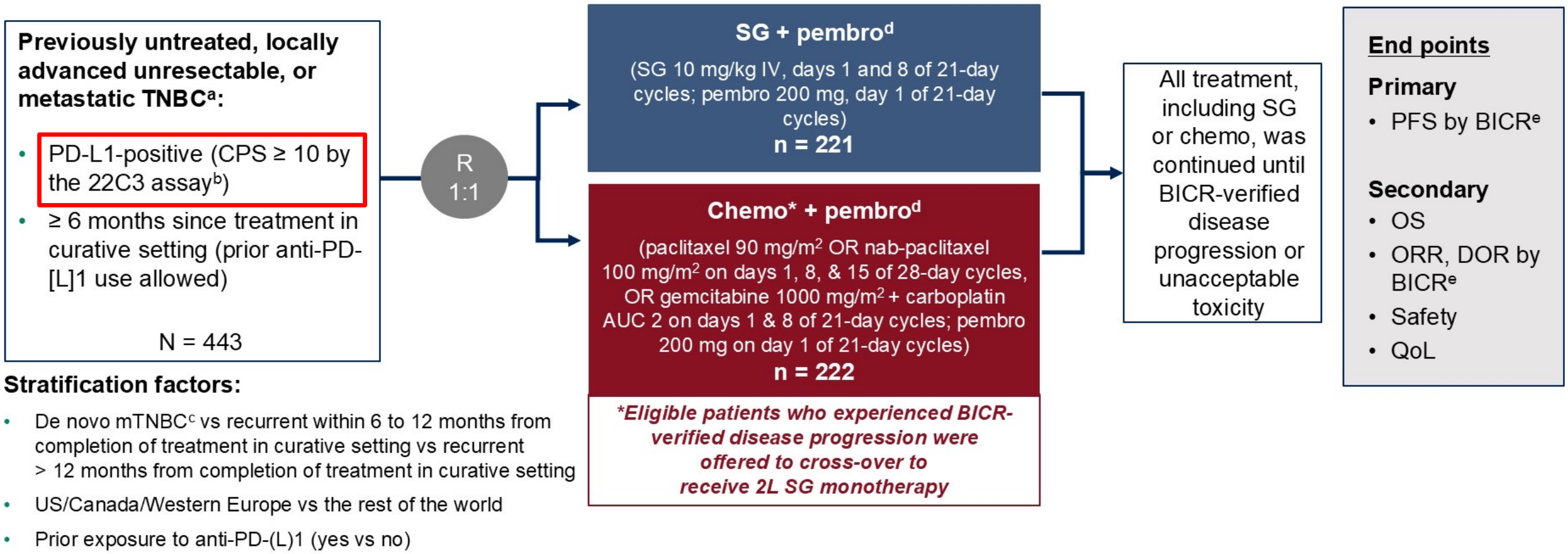
5.6 mo (5.0–7.0)

Δ 5.3 mo*

Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with ICC, reducing the risk of progression or death by 43%

Dent et al. ESMO 2025;Abstract LBA21

ASCENT-04/KEYNOTE-D19 Study Design

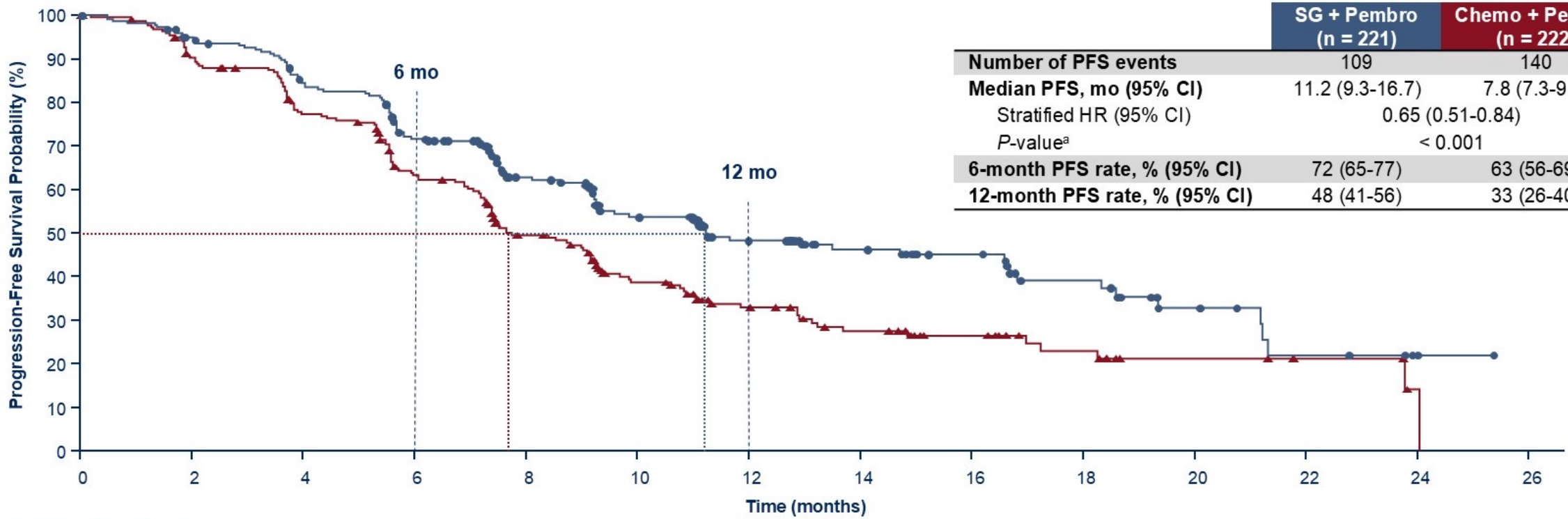


Stratification factors:

- De novo mTNBC[c] vs recurrent within 6 to 12 months from completion of treatment in curative setting vs recurrent > 12 months from completion of treatment in curative setting
- US/Canada/Western Europe vs the rest of the world
- Prior exposure to anti-PD-(L)1 (yes vs no)

Tolaney et al. ASCO 2025;Abstract LBA109

Progression-Free Survival by BICR



	SG + Pembro (n = 221)	Chemo + Pembro (n = 222)
Number of PFS events	109	140
Median PFS, mo (95% CI)	11.2 (9.3-16.7)	7.8 (7.3-9.3)
Stratified HR (95% CI)	0.65 (0.51-0.84)	
P-value[a]	< 0.001	
6-month PFS rate, % (95% CI)	72 (65-77)	63 (56-69)
12-month PFS rate, % (95% CI)	48 (41-56)	33 (26-40)

No. of Patients Still at Risk (Events)

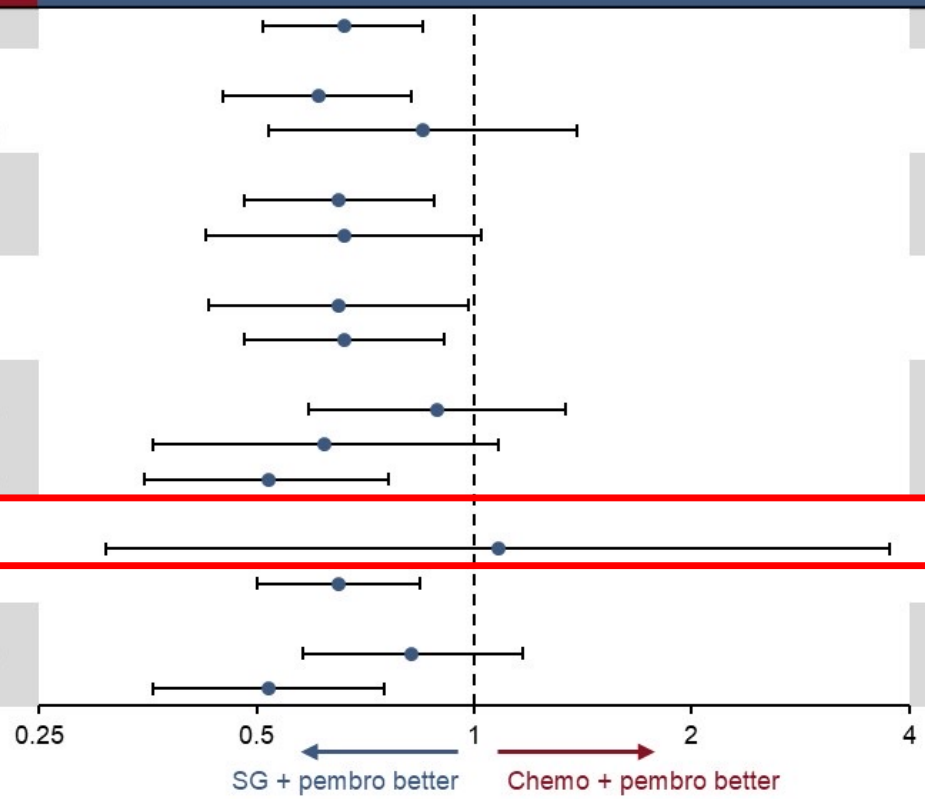
SG + Pembro	221 (0)	202 (11)	174 (33)	142 (59)	105 (75)	78 (89)	58 (96)	42 (98)	34 (99)	22 (103)	11 (106)	6 (109)	2 (109)	0 (109)
Chemo + Pembro	222 (0)	191 (21)	159 (48)	123 (76)	88 (102)	59 (120)	40 (128)	29 (134)	21 (135)	13 (137)	7 (138)	4 (138)	1 (139)	0 (140)

SG + pembro demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo + pembro by BICR analysis, with a 35% reduction in risk of disease progression or death

Tolaney et al. ASCO 2025;Abstract LBA109

Subgroup Analysis of Progression-Free Survival by BICR

	SG + Pembro		Chemo + Pembro		Unstratified HR (95% CI)	Unstratified HR (95% CI)
	n	Median PFS, mo (95% CI)	n	Median PFS, mo (95% CI)		
ITT population	221	**11.2** (9.3-16.7)	222	**7.8** (7.3-9.3)		0.66 (0.51-0.85)
Age group						
< 65 yr	163	**11.3** (9.3-16.8)	165	**7.5** (7.0-9.2)		0.61 (0.45-0.82)
≥ 65 yr	58	**11.1** (7.5-NR)	57	**9.3** (7.3-13.2)		0.85 (0.52-1.39)
ECOG PS						
0	156	**12.9** (9.3-16.8)	154	**8.7** (7.3-9.9)		0.65 (0.48-0.88)
≥ 1	65	**9.2** (7.5-18.3)	67	**7.5** (5.6-9.3)		0.66 (0.43-1.03)
Geographic region						
US/Canada/Western Europe	85	**11.7** (7.5-19.4)	85	**7.4** (5.7-9.9)		0.65 (0.43-0.98)
Rest of the world	136	**11.2** (9.3-16.7)	137	**8.4** (7.4-9.3)		0.66 (0.48-0.91)
Curative treatment-free interval						
De novo	75	**8.1** (7.3-18.6)	75	**7.7** (6.1-11.9)		0.89 (0.59-1.34)
Recurrent 6-12 mo	40	**9.9** (5.7-16.8)	40	**7.2** (4.4-9.1)		0.62 (0.36-1.08)
Recurrent > 12 mo	106	**16.6** (11.0-NR)	107	**8.7** (7.3-10.8)		0.52 (0.35-0.76)
Prior (neo)adjuvant anti-PD-(L)1 therapy						
Yes	9	**7.5** (0.9-NR)	11	**6.6** (2.1-NR)		1.08 (0.31-3.75)
No	212	**11.7** (9.3-16.8)	211	**7.8** (7.4-9.3)		0.65 (0.50-0.84)
Chemo selected prior to randomization						
Taxane	116	**11.1** (8.6-16.7)	114	**9.2** (7.2-12.9)		0.82 (0.58-1.17)
Gemcitabine/Carboplatin	105	**11.3** (9.2-21.2)	108	**7.4** (6.9-9.0)		0.52 (0.36-0.75)



PFS benefit was observed for SG + pembro vs chemo + pembro across prespecified subgroups

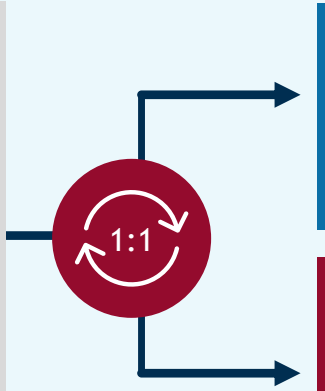
Tolaney et al. ASCO 2025;Abstract LBA109

ASCENT: A Phase 3 Confirmatory Study of Sacituzumab Govitecan in 2L and Later mTNBC[1-3*]

Metastatic TNBC

- ≥2 chemotherapies – one of which could be in neo/adjuvant setting provided progression occurred within a 12-month period
- Patients with stable brain metastases were allowed

(N=529)



Sacituzumab govitecan 10 mg/kg IV days 1 and 8, every 21 days (n=267)

Treatment of physician's choice† (n=262)

Continue treatment until progression or unacceptable toxicity

Endpoints

Primary

- PFS‡

Secondary

- PFS for the ITT population, § OS, ORR, DOR, TTR, QoL, safety

Stratification Factors

- Number of prior chemotherapies (2 or 3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (Yes/No)

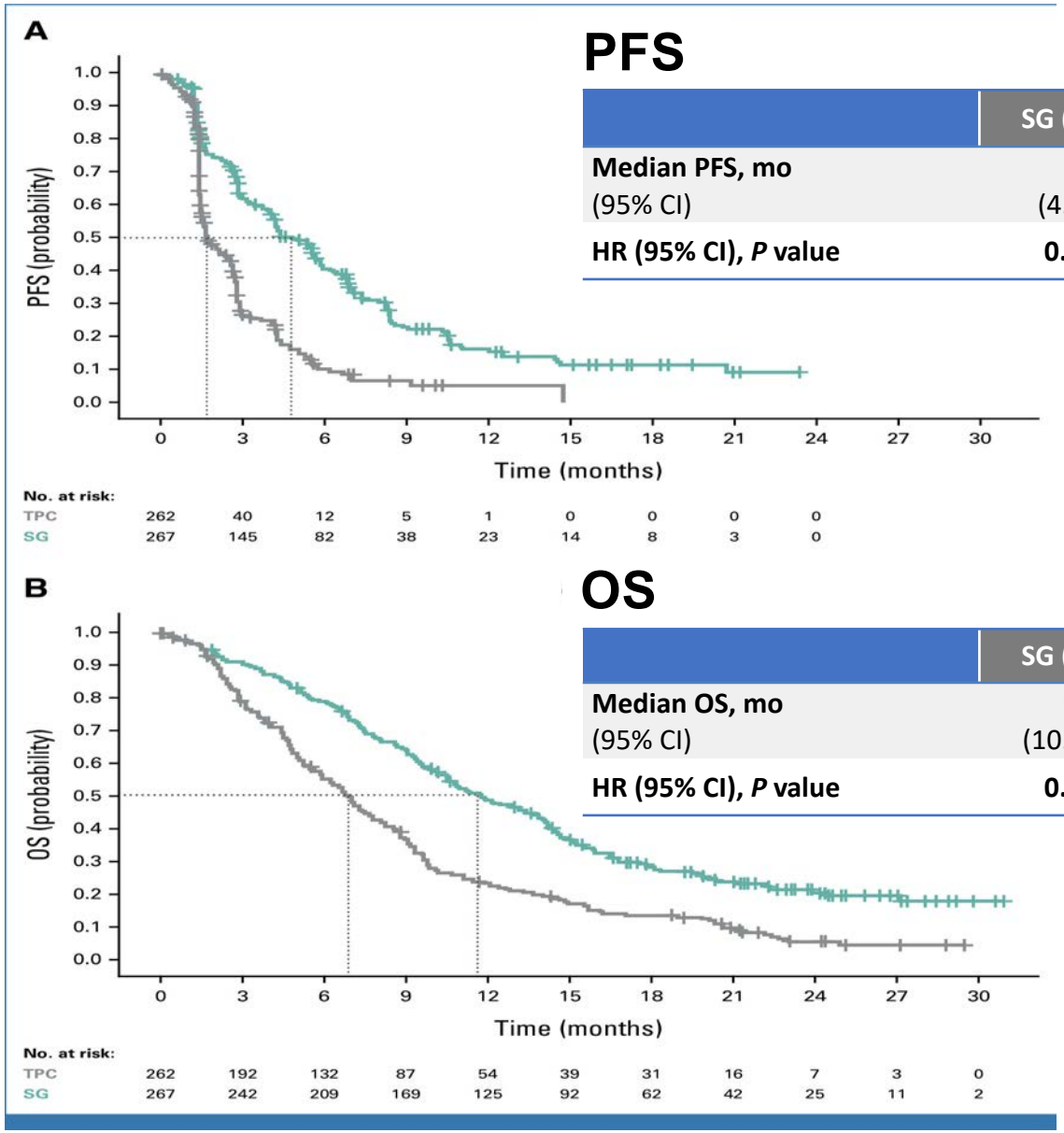
NCT02574455

***ASCENT was an international, Phase 3, multicentre, open-label, randomised trial of patients with unresectable locally advanced or metastatic TNBC (N=529). †Treatment of physician's choice: eribulin, vinorelbine, gemcitabine, or capecitabine; ‡PFS measured by an independent centralised and blinded group of radiology experts who assessed tumour response using RECIST 1.1 criteria in patients without brain metastasis; §The full population or intention-to-treat population includes all randomised patients (with and without brain metastases).**

DOR, duration of response; IV, intravenous; ITT, intention-to-treat; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumours; TNBC, triple-negative breast cancer; TTR, time to response; QoL, quality of life.

1. Bardia A, et al. *N Engl J Med.* 2021;384(16):1529-1541; 2. Bardia A, et al. ESMO 2020. Abstract LBA17; 3. ClinicalTrials.gov website. Available at: https://clinicaltrials.gov/ct2/show/NCT02574455. Accessed March 2022.

ASCENT: PFS and OS in the ITT Population



PFS

	SG (n=267)	TPC (n=262)
Median PFS, mo (95% CI)	**4.8** (4.1-5.8)	**1.7** (1.5-2.5)
HR (95% CI), *P* value	**0.41** (0.33-0.51), ***P*<.0001**	

OS

	SG (n=267)	TPC (n=262)
Median OS, mo (95% CI)	**11.8** (10.5-13.8)	**6.9** (5.9-7.7)
HR (95% CI), *P* value	**0.51** (0.42-0.62), ***P*<.0001**	

Bardia A et al. *N Engl J Med*. 2021;384(16):1529-1541.
Bardia A et al. *J Clin Oncol.* 2024:JCO2301409.

TROPiCS-02 Study Design[1]

A Phase 3 Study of SG in HR+/HER2- Locally Recurrent Inoperable or Metastatic Breast Cancer[1]

Metastatic or locally recurrent inoperable HR+/HER2− breast cancer that progressed after[a]:

- At least 1 endocrine therapy, taxane, and CDK4/6i in any setting
- 2-4 lines of chemotherapy for metastatic disease
  - (Neo)adjuvant therapy for early-stage disease qualified as a prior line of chemotherapy if disease recurred within 12 months
- Measurable disease by RECIST 1.1

N=543

NCT03901339

R
1:1

Treatment was continued until progression or unacceptable toxicity

Sacituzumab govitecan
10 mg/kg IV
days 1 and 8, every 21 days
n=272

Treatment of physician's choice[b]
(capecitabine, vinorelbine, gemcitabine or eribulin)
n=271

Stratification:
- Visceral metastases (yes/no)
- Endocrine therapy in metastatic setting ≥6 months (yes/no)
- Prior lines of chemotherapies (2 vs 3/4)

Endpoints

Primary
- PFS by BICR

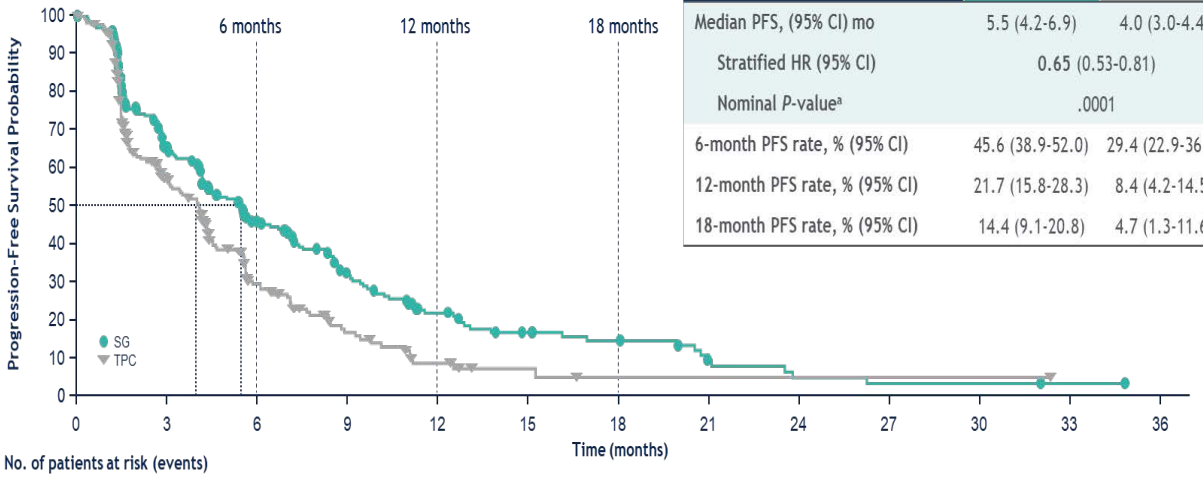
Secondary
- OS
- ORR, DOR, CBR by LIR and BICR
- PRO
- Safety

Tolaney et al. ASCO 2023;Abstract 1003

TROPiCS-02: Progression-Free and Overall Survival

Median 3 prior lines of chemo 98%: Prior CDK4/6i

Progression-Free Survival

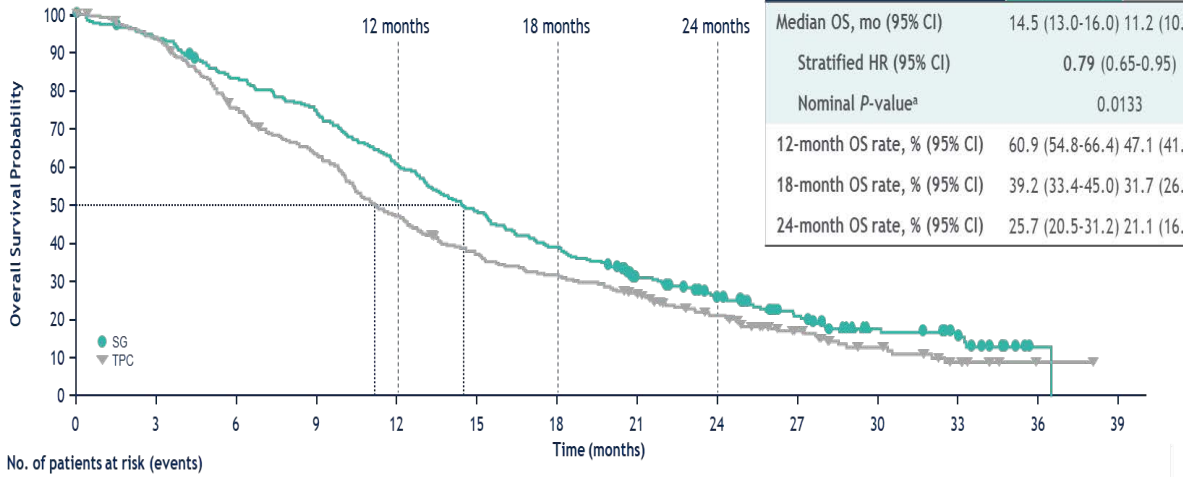


BICR analysis	SG (n = 272)	TPC (n = 271)
Median PFS, (95% CI) mo	5.5 (4.2-6.9)	4.0 (3.0-4.4)
Stratified HR (95% CI)	0.65 (0.53-0.81)	
Nominal *P*-value[a]	.0001	
6-month PFS rate, % (95% CI)	45.6 (38.9-52.0)	29.4 (22.9-36.2)
12-month PFS rate, % (95% CI)	21.7 (15.8-28.3)	8.4 (4.2-14.5)
18-month PFS rate, % (95% CI)	14.4 (9.1-20.8)	4.7 (1.3-11.6)

No. of patients at risk (events)

SG	272 (0)	148 (86)	82 (127)	48 (149)	27 (164)	17 (170)	13 (172)	6 (176)	3 (179)	2 (180)	2 (180)	1 (180)	0 (180)
TPC	271 (0)	109 (96)	42 (144)	18 (160)	7 (168)	3 (169)	1 (170)	1 (170)	1 (170)	1 (170)	1 (170)	0 (170)	

Overall Survival



	SG (n = 272)	TPC (n = 271)
Median OS, mo (95% CI)	14.5 (13.0-16.0)	11.2 (10.2-12.6)
Stratified HR (95% CI)	0.79 (0.65-0.95)	
Nominal *P*-value[a]	0.0133	
12-month OS rate, % (95% CI)	60.9 (54.8-66.4)	47.1 (41.0-53.0)
18-month OS rate, % (95% CI)	39.2 (33.4-45.0)	31.7 (26.2-37.4)
24-month OS rate, % (95% CI)	25.7 (20.5-31.2)	21.1 (16.3-26.3)

No. of patients at risk (events)

SG	272 (0)	253 (17)	223 (45)	200 (68)	163 (105)	130 (138)	105 (163)	71 (184)	52 (196)	33 (204)	19 (209)	13 (211)	1 (213)	0 (214)
TPC	271 (0)	251 (16)	199 (66)	167 (97)	124 (140)	96 (166)	82 (180)	66 (193)	46 (206)	27 (214)	15 (220)	7 (224)	1 (224)	0 (224)

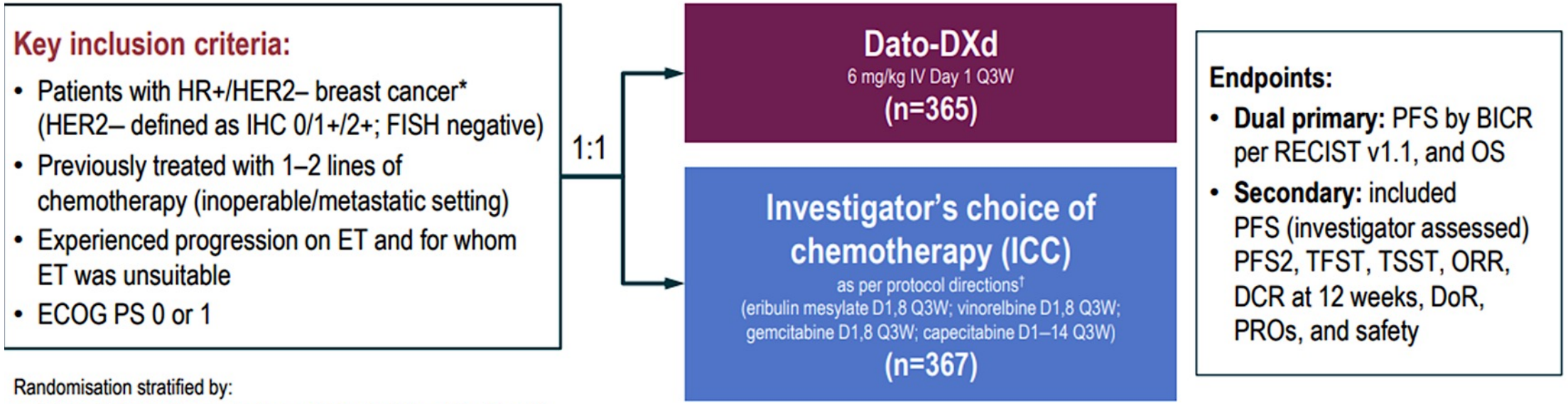
SG continued to demonstrate improvement in PFS and OS vs TPC at longer follow-up, with 35% and 21% reduction in risk of disease progression or death, and a higher proportion of patients remained alive and progression-free at each landmark

A Stratified log rank P-value.BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice. Study of Sacituzumab Govitecan-hziy Versus Treatment of Physician's Choice in Participants With HR+/HER2- Metastatic Breast Cancer (TROPiCS-02) (NCT03901339): https://classic.clinicaltrials.gov/ct2/show/NCT03901339

1. Tolaney S, et al. Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor-positive/HER2-negative (HR+/HER2-) metastatic breast cancer (mBC). Presented at ASCO 2023 Abstract #1003.

GILEAD | Oncology

TROPION-Breast01 Study Design



Randomisation stratified by:
- **Lines of chemotherapy** in inoperable/metastatic setting (1 vs 2)
- **Geographic location** (USA/Canada/Europe vs other geographic regions)
- **Previous CDK4/6 inhibitor** (yes vs no)

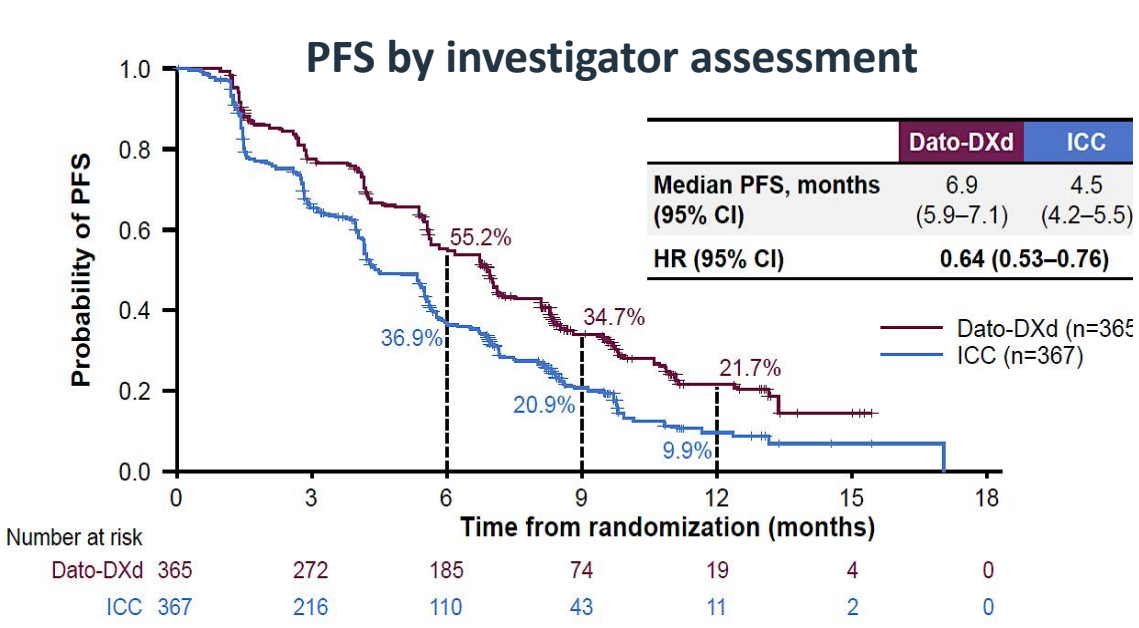
- Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Statistical considerations: Study deemed positive if either of the dual primary endpoints (PFS by BICR or OS) were statistically significant

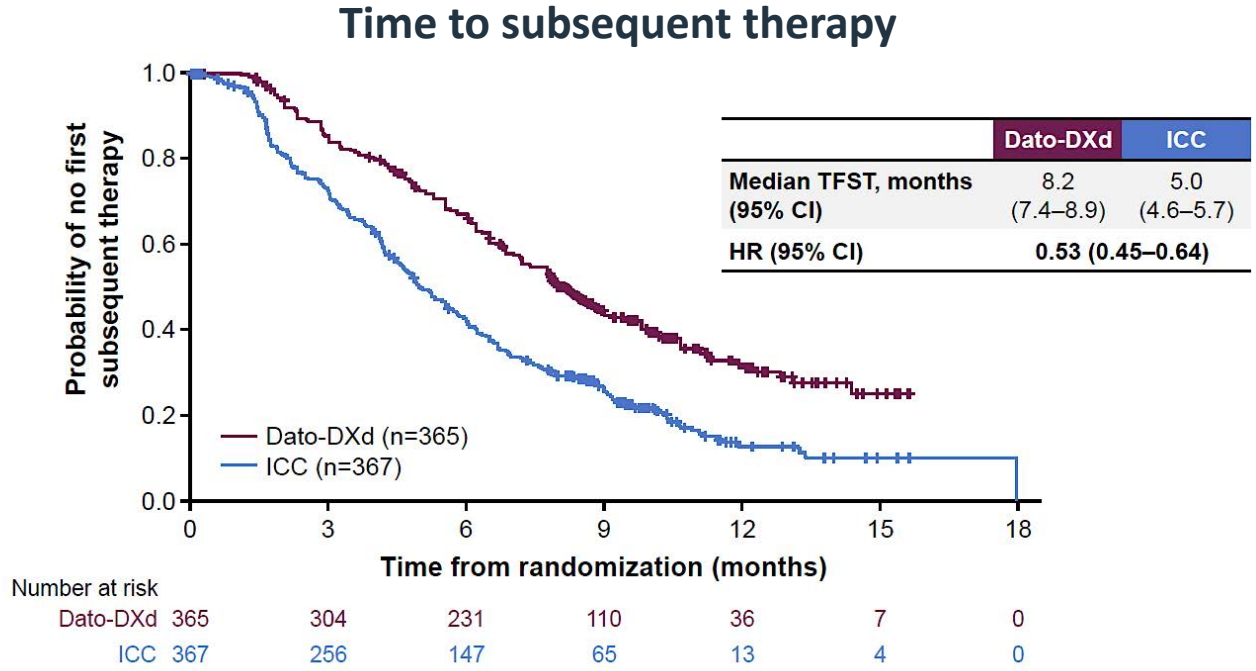
Detailed description of the statistical methods published previously.[1] *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines.
†ICC was administered as follows: eribulin mesylate, 1.4 mg/m^2 IV on Days 1 and 8, Q3W; capecitabine, 1000 or 1250 mg/m^2 orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice); vinorelbine, 25 mg/m^2 IV on Days 1 and 8, Q3W; or gemcitabine, 1000 mg/m^2 IV on Days 1 and 8, Q3W.
CDK4/6, cyclin-dependent kinase 4/6; D, day; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; FISH, fluorescent in-situ hybridisation; IHC, immunohistochemistry; IV, intravenous; PD, progressive disease; PFS2, time to second progression or death; PRO, patient-reported outcome; RECIST, Response Evaluation Criteria in Solid Tumors; TFST, time to first subsequent therapy; TSST, time to second subsequent therapy.

Adapted from Bardia 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. Journal of Clinical Oncology 2025 43:3, 285-296

TROPION-Breast01: PFS and Time to Subsequent Therapy



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.9–7.1)	4.5 (4.2–5.5)
HR (95% CI)	0.64 (0.53–0.76)	



	Dato-DXd	ICC
Median TFST, months (95% CI)	8.2 (7.4–8.9)	5.0 (4.6–5.7)
HR (95% CI)	0.53 (0.45–0.64)	

PFS by BICR (primary endpoint)

- Median 6.9 vs 4.9 months
- HR 0.63 (95% CI, 0.52-0)

Adapted from Bardia 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. Journal of Clinical Oncology 2025 43:3, 285-296

Discussion Questions

How do you explain to a patient the similarities and differences in tolerability among the TROP2-directed ADCs for metastatic breast cancer — sacituzumab govitecan, datopotamab deruxtecan and sacituzumab tirumotecan (sac-TMT)?

Gastrointestinal and Other AEs with ADCs

Jamie Carroll, CNP, MSN

GI side effects for each ADC

ADC	Key Trials	N/V	D/C	Abdominal Pain
Trastuzumab Deruxtecan (HER2/Dxd)	Pooled DESTINY analyses	Nausea 70-75% Vomiting 40-45%	Diarrhea 25-30% Constipation uncommon	10-15%
Sacituzumab govitecan (TROP2/SN-38)	ASCENT; TROPICS-02	Nausea 60-65% Vomiting 40-45%	Diarrhea 60%, Gr-3 7-10%	10%
Datopotamab deruxtecan (TROP2/Dxd)	TROPION-Breast01	Nausea 45-55%	Diarrhea 20-30% Constipation infrequent	<10%
Trastuzumab Emtansine (HER2/DM1)	EMILIA, KATHERINE	Nausea 40-45% Vomiting 20-25%	Diarrhea 20% Constipation <10%	<10%

Anti-emetics

Anti-emetics	T-Dxd	Sacituzumab	TDM-1	Datopotamab
Olanzapine 5 mg x 5 days at HS	X	X	X	X
Dexamethasone 8 mg x 3 days	X	X		X
Prochlorperazine 10 mg every 6 hrs PRN	X	X	X	X
Ondansetron 8 mg every 8 hours PRN	X	X	X	X

** If nausea persistent: Add Aprepitant 125 mg Day 1, 80 mg Day 2,3

Symptom specific interventions: N/V

- Encourage scheduled anti-emetics
- Reinforce initial around the clock dosing for 48-72 hours
- Encourage small, frequent meals
- Avoid trigger foods such as: High fat or greasy foods, strong smelling foods, spicy or highly seasoned, acidic food/beverage and very sweet foods
- Natural remedies: Ginger, acupuncture/pressure

Symptom specific interventions: Diarrhea

- Start anti-diarrheals (Loperamide 2 mg) at first loose stool
- If ≥ 4 stools/day or overnight diarrhea, call.
- Monitor for signs of dehydration
- Review hydration strategies
- Patient maximizing anti-diarrheals, high volume stools, then what?

-Obtain GI pathogen panel

-Consider starting 5 mg diphenoxylate/0.05 mg atropine taken 4x/day, max 8 tablets per day.

Symptom specific interventions: Constipation

- Medication reconciliation
- Consider past medical history
- Exercise
- Hydration
- Consider: Bowel regimen (Stool softener + osmotic daily)
- If not effective, add stimulant but continue above.
- Red flag symptoms: No BM >4 days, abdominal pain, vomiting, hard stool with diarrhea, rectal bleeding.

Symptom specific interventions: Stomatitis

- Most common treatment related AE with Datopotamab.
- Occurs in 50% of patients
- Prophylaxis is KEY!
- Recommend:

-Dexamethasone mouth rinse 0.5 mg/5 ml Use 4x/day

-Magic mouthwash preparation (Diphenhydramine, Lido, Dex)

-Lidocaine viscous gel 2%

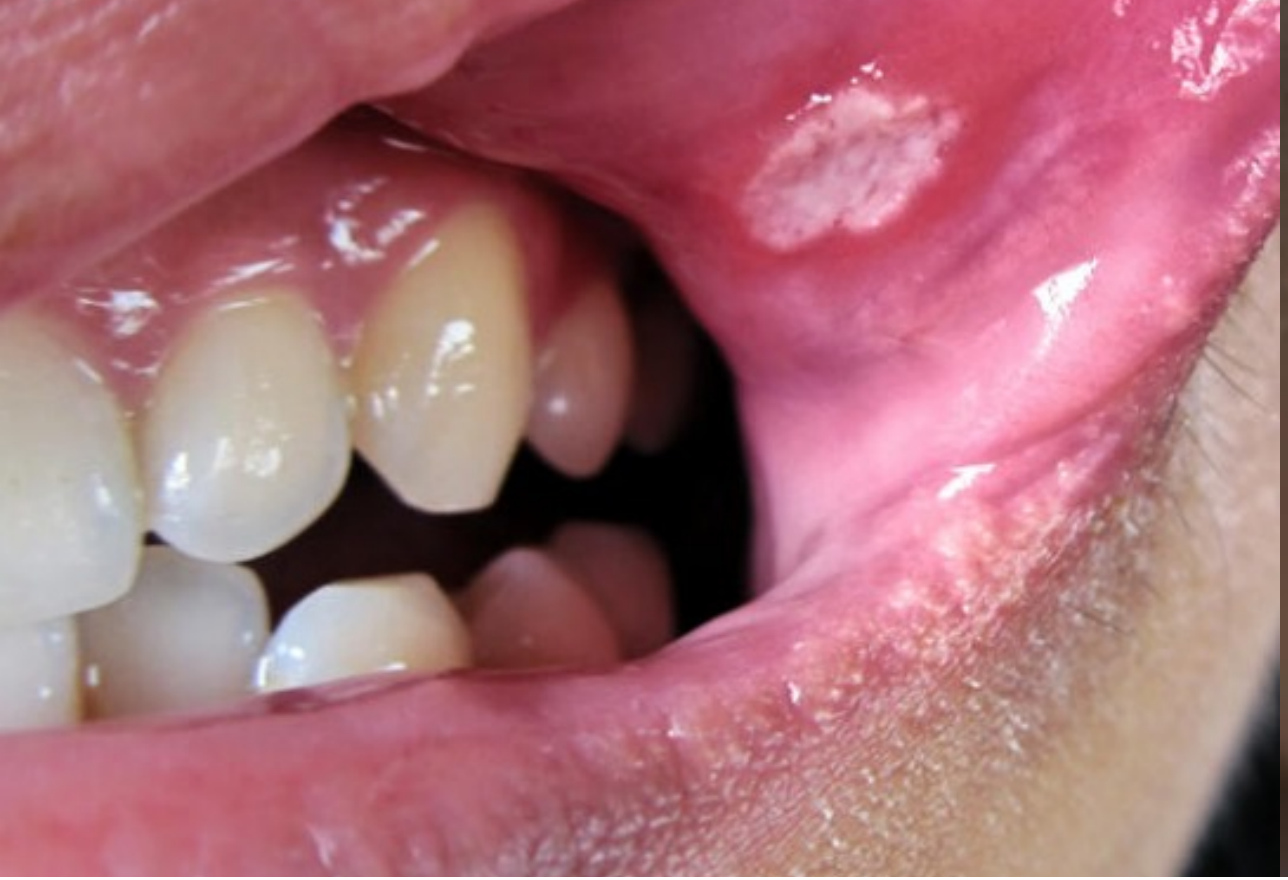
-Baking soda and salt rinse

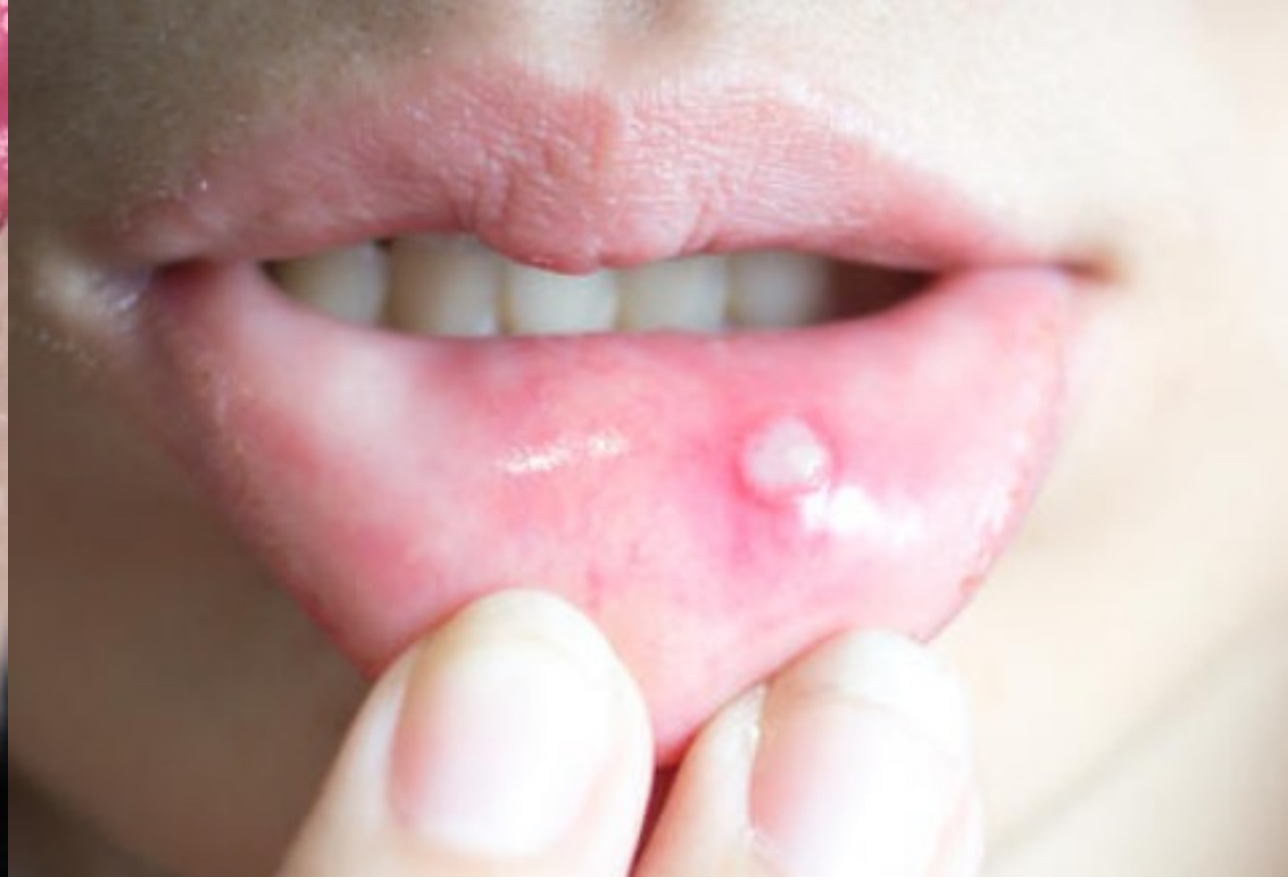
Case Study - Gastrointestinal and Other AE's

- 33 yo woman, diagnosed with early stage ER pos, HER2 neg breast cancer in 2006. Upfront mastectomy, pT2N1. AC/T, XRT, Tamoxifen
- 2008-Imaging revealed bony mets. Anastrozole
- 2017-PD in bones, added Palbociclib
- Over the years, received SERD, PIK3CA, oral chemo, multiple clinical trials, Trastuzumab deruxtecan, Sacituzumab, IV chemo, immunotherapy
- 4/2026-PD in bones, liver, lungs, lymph node. Started on Datopotamab

Stomatitis

- Prescribed Dexamethasone mouth rinse.
  -National shortage
- Patient informed team one week in that she was unable to pick up.
- Team prescribed Magic mouthwash.
  -Insurance would not cover compound.
- Development of stomatitis.





Stomatitis photos

Discussion Questions

What is the typical time course for the emergence of GI toxicities with T-DXd? What about sacituzumab govitecan?

What, if anything, is known about the use of dose escalation strategies to mitigate GI and other toxicities?

What is your typical approach to the management of ADC-associated mucositis/stomatitis?

Have you used the Chemo Mouthpiece®? If so, do you find it effective?

CHEMO MOUTHPIECE®

Contact Our Team

Financial Assistance Available

How to Prescribe

Prescription Only

About the Chemo Mouthpiece®

The Chemo Mouthpiece® is an FDA-cleared oral cooling device used during chemo infusion and at home afterwards.

Developed by a cancer survivor **(see David's story)** who experienced firsthand the severe effects of oral mucositis, the device is easy to use and delivers consistent cooling to help reduce the risk of painful mouth sores.

Patients using the Chemo Mouthpiece experienced significantly **less pain** and used significantly **less analgesics and opioids**.

The Chemo Mouthpiece requires a prescription from a healthcare provider. The device is shipped directly to patients from a specialty pharmacy.

Questions about access or cost?
Submit the form and a member of our U.S.-based team will follow up promptly.

CHEMO MOUTHPIECE®

Contact Our Team

Financial Assistance Available

How to Prescribe

Prescription Only

Each Chemo Mouthpiece device contains prefilled internal chambers that are frozen before use.

When placed in the mouth, the device is designed to deliver **consistent cooling** in the oral cavity. Each kit includes:

- Six prefilled oral cooling devices
- Cooler, insulated sleeves & cold packs
- Cleaning tools
- Simple instructions for use

Patients typically use a frozen device immediately before, during, and after their chemotherapy infusion, based on guidance from their care team.

Questions about access or cost?

Contact Our Team

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

Antibody Drug Conjugate in Ovarian Cancer: Selection, Sequencing and Strategy

Tumor Associated Antigens Including CDH6, TROP2 and FRα

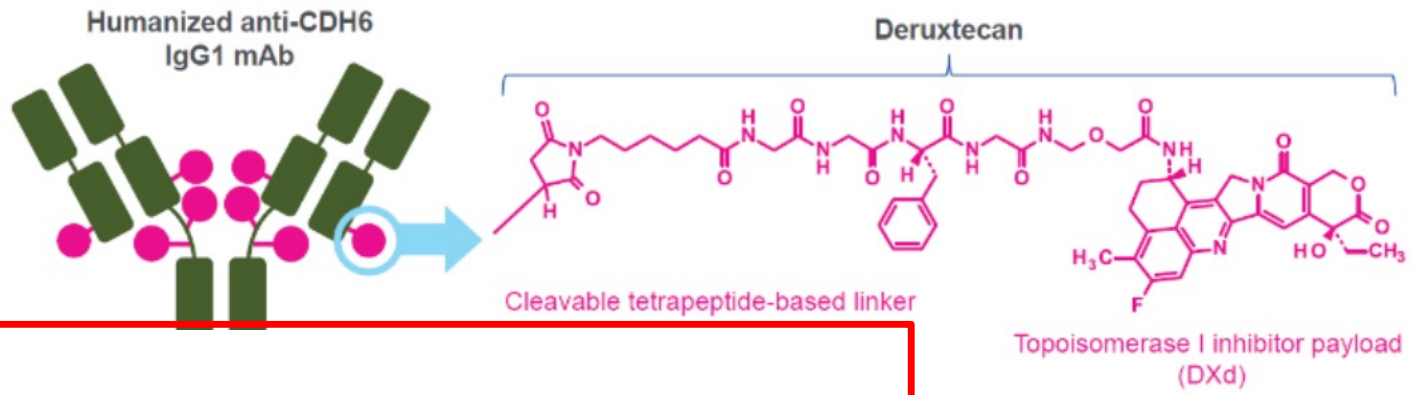
Kathleen N. Moore, MD, MS, FASCO
Deputy Director, Buffett Cancer Center at the University of Nebraska Medical Center
Professor, Gynecologic Oncology
ASCO BOD
GOG F BOD

FRED & PAMELA BUFFETT CANCER CENTER

@DrKatyMoore

Targeting Cadherin 6 (CDH6): Raludotatug deruxtecan

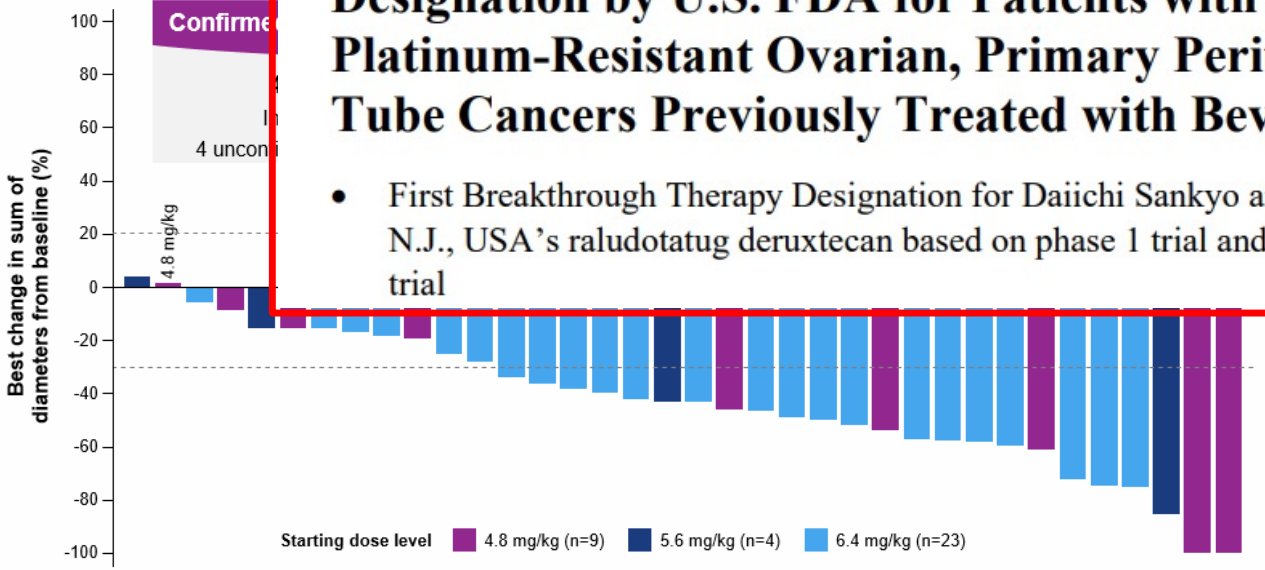
	Raludotatug deruxtecan (DS-6000)[1,2]
Payload	Topoisomerase 1 inhibitor (DXd)
DAR	8
Linker	
Trial	



Press Release

Raludotatug Deruxtecan Granted Breakthrough Therapy Designation by U.S. FDA for Patients with CDH6 Expressing Platinum-Resistant Ovarian, Primary Peritoneal or Fallopian Tube Cancers Previously Treated with Bevacizumab

- First Breakthrough Therapy Designation for Daiichi Sankyo and Merck & Co., Inc., Rahway, N.J., USA's raludotatug deruxtecan based on phase 1 trial and REJOICE-Ovarian01 phase 2/3 trial



(95% CI: 3.1–NE)
6.7 months (1.4–16.8)

5% CI: 5.3–11.4)

Median PFS:[b]

8.1 months (95% CI: 5.3–NE)
Median (range) FU: 4.0 months (0–25.1)

1. Moore K, et al. Presented at European Society for Medical Oncology (ESMO) Annual Meeting; 20-24 October 2023; Madrid, Spain.;
2. NCT04707248. Accessed from: https://clinicaltrials.gov/study/NCT04707248?cond=NCT04707248&rank=1.

@DrKatyMoore

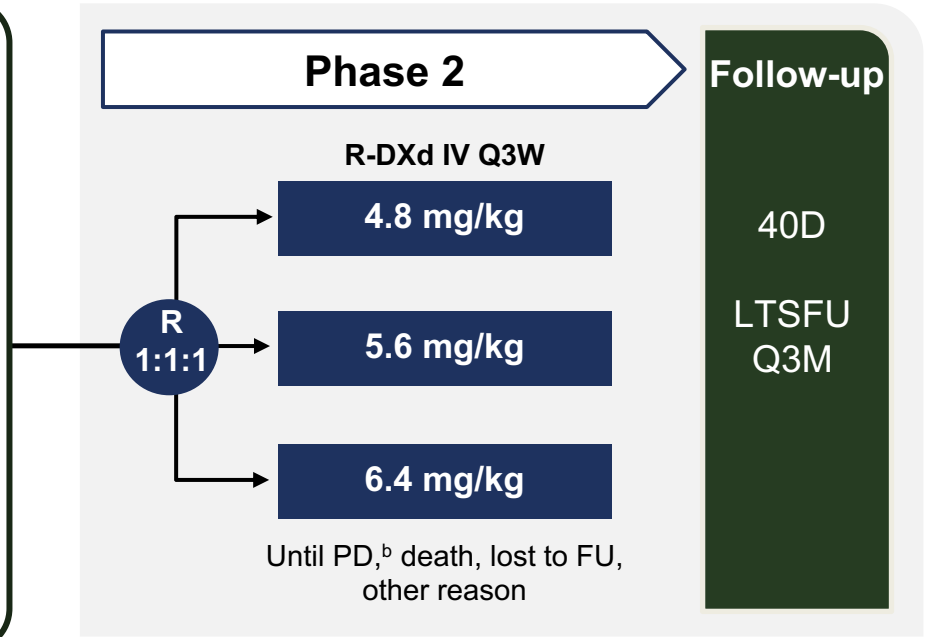
REJOICE-Ovarian01/GOG-3096: Phase 2/3 Randomized Study of R-DXd in Platinum-Resistant EOC

Key eligibility criteria:

- High-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer
- 1−3 prior LOT (inc. bevacizumab)
- Platinum-resistant disease
- Prior MIRV if high FRα[a]
- ECOG PS 0−1
- No prior CDH6-targeting agents or ADCs with linked TOPO I inhibitor
- Patients with primary platinum-refractory disease are not eligible

Stratification:

- Number of prior LOT (1 vs 2/3)
- CDH6 expression (high vs low)
- TPC (paclitaxel vs others; *Ph 3 only*)

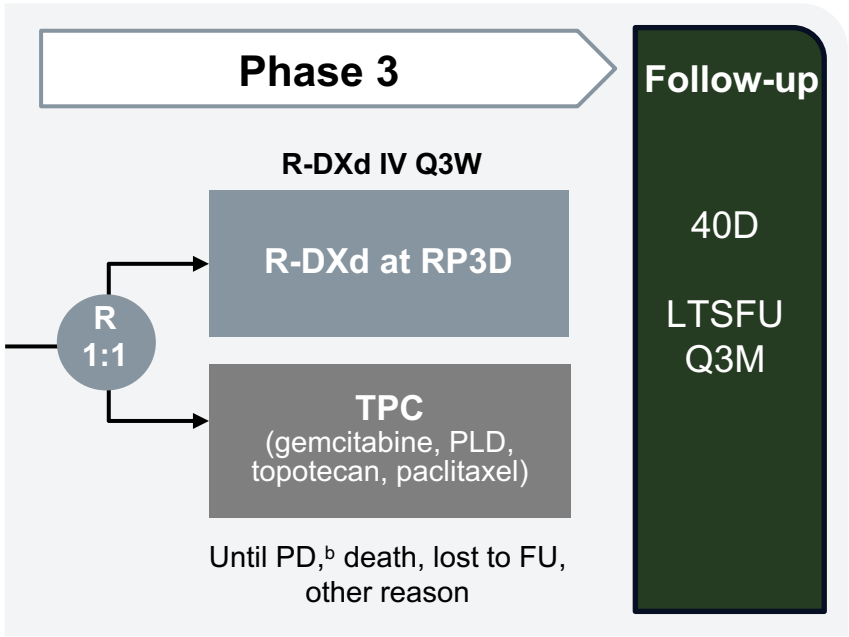


Primary endpoints:

- ORR per BICR[b]

Key secondary endpoints:

- ORR per inv[b]
- DOR



Primary endpoints:

- ORR per BICR[b]
- PFS per BICR[b]

Key secondary endpoints:

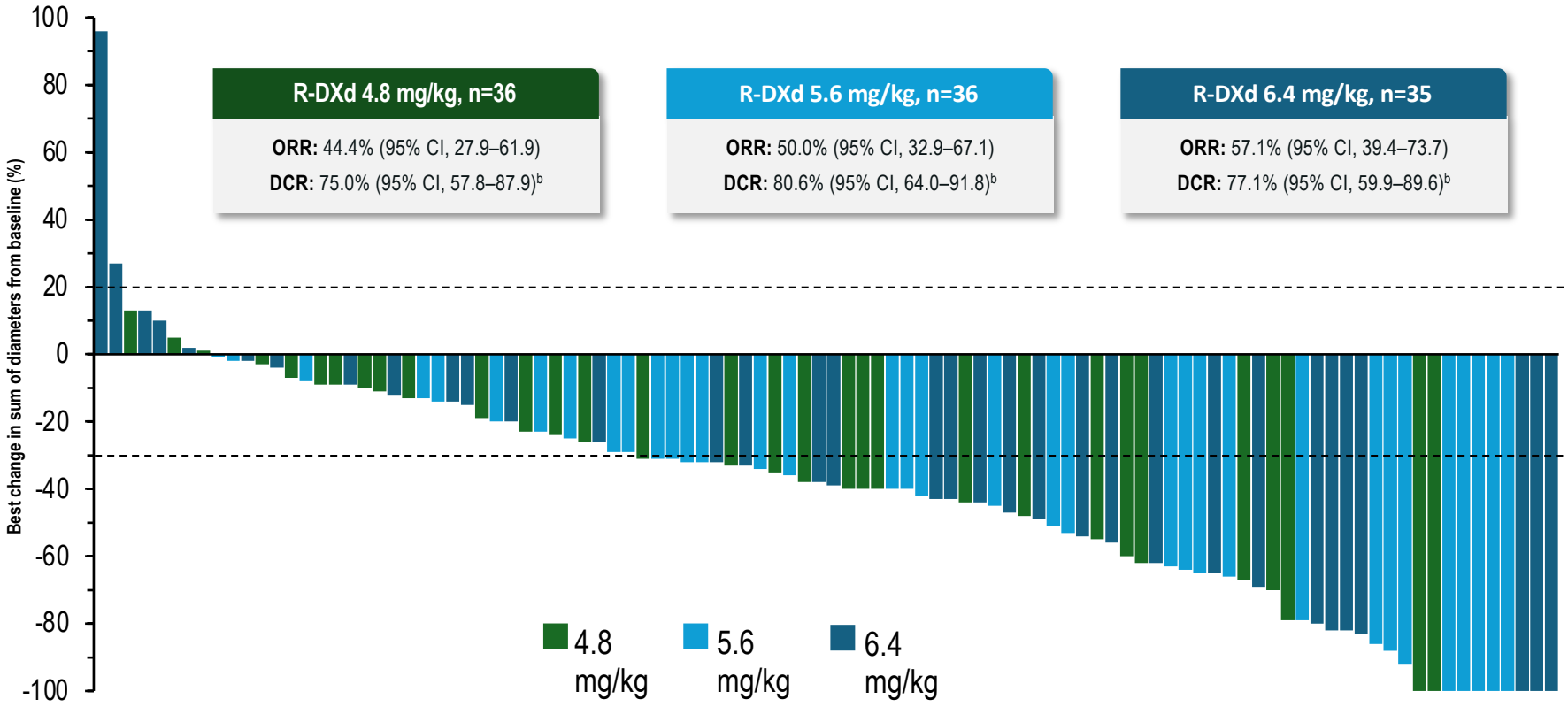
- OS
- QOL

NCT06161025

NCT06161025. Accessed from: https://clinicaltrials.gov/study/NCT06161025?term=NCT06161025&rank=1.

REJOICE 01: Phase 2

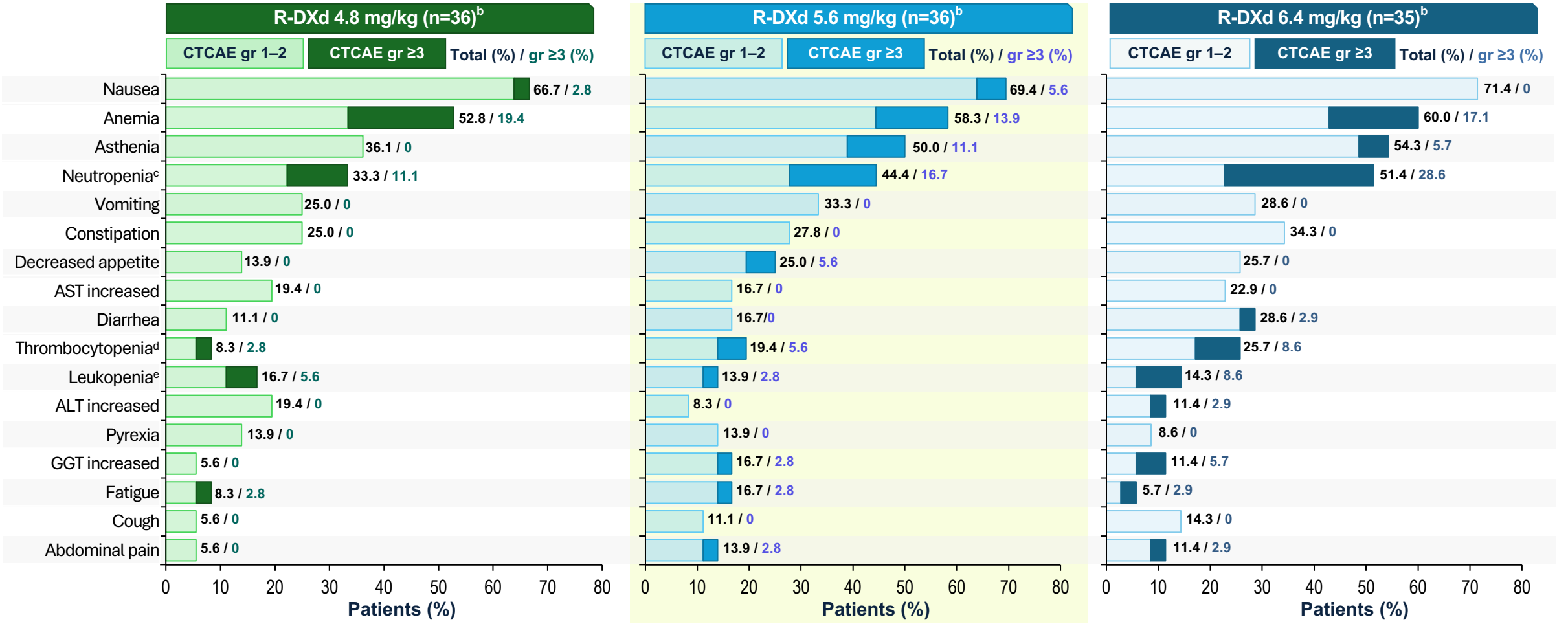
Raludotatug deruxtecan



Ray Couquad et al. ESMO 2025.

@DrKatyMoore

REJOICE-Ovarian01: Most common TEAEs (≥10%)



Nausea, anemia, asthenia and neutropenia were the most common TEAEs across all doses.

[a]TEAEs reported in ≥10% of all patients who received R-DXd 4.8–6.4 mg/kg. Reported safety events are defined by MedDRA preferred terminology. [b]Grade 4 hematologic TEAEs reported at 4.8 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1); at 5.6 mg/kg: neutropenia[c] (n=2), thrombocytopenia[d] (n=1), leukopenia[e] (n=1); at 6.4 mg/kg: neutropenia[c] (n=3), thrombocytopenia[d] (n=1), lymphopenia (n=1). No grade 5 hematologic TEAEs were reported at any dose. Grade 3 febrile neutropenia was reported in 2 patients, one each in the R-DXd 5.6 and 6.4 mg/kg cohorts. [c]Neutropenia was defined as the grouped incidence of events reported under the preferred terms '*neutropenia*' and '*neutrophil count decreased*', with a maximum of one event per patient per grouped preferred term. [d]Thrombocytopenia was defined as the grouped incidence of events reported under the preferred terms '*thrombocytopenia*' and '*platelet count decreased*', with a maximum of one event per patient per grouped preferred term. [e]Leukopenia was defined as the preferred term '*white blood cell count decreased.*'

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyltransferase; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

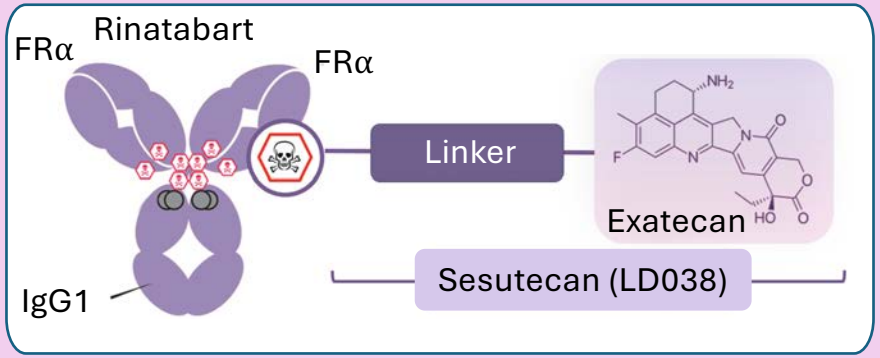
1. Ray-Coquard I et al. Presented at ESMO Congress 2025; October 17–21, 2025; Berlin, Germany; Oral LBA42

Targeting FRα

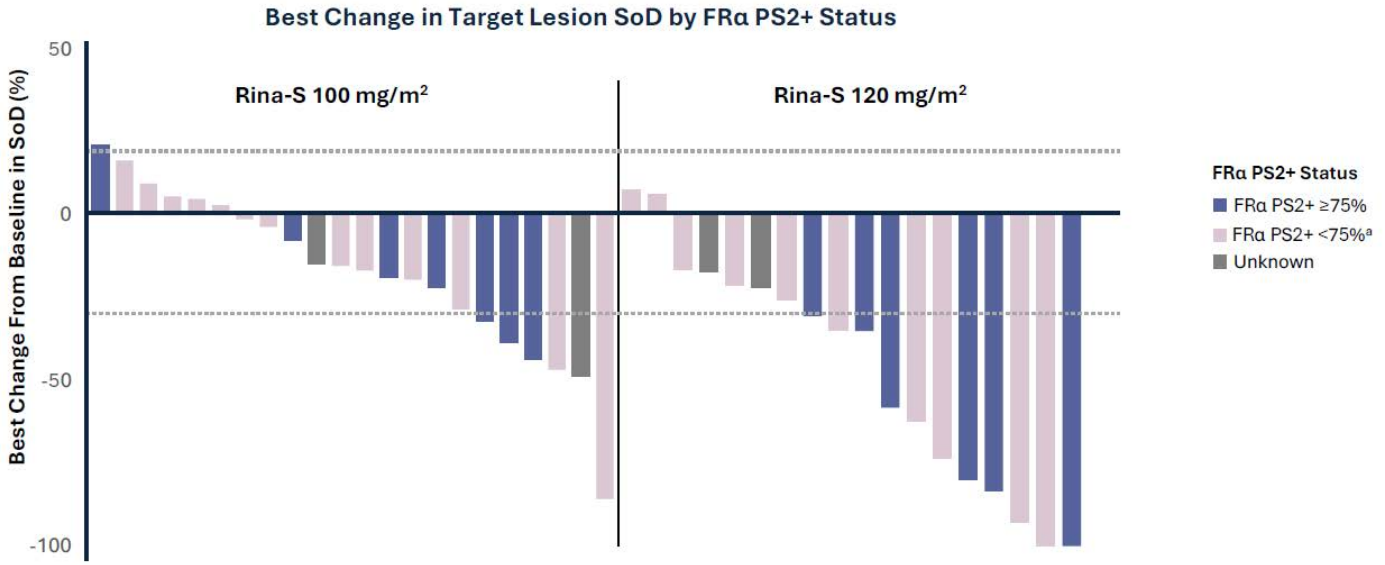
Rinatabart Sesutecan (Rina-S)

Novel FRα-directed ADC

- Highly hydrophilic linker, sesutecan
- Topoisomerase 1 inhibitor payload



	Rina-S 100 mg/m² (n=22)[a]	Rina-S 120 mg/m² (n=18)[a]
Median on-study follow-up, weeks (range)	46.4 (6.6, 65.3)	48.1 (10.9-65.9)
Confirmed ORR[b], % (95% CI)	22.7 (7.8-45.4)	55.6 (30.8-78.5)
Confirmed response, n (%)		
CR	1 (4.5)	2 (11.1)
PR	4 (18.2)	8 (44.4)
SD	14 (63.6)	6 (33.3)
NE	0	1 (5.6)
Disease control rate, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)



Deep responses observed regardless of FRα expression levels with Rina-S 120 mg/m²

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1. https://clinicaltrials.gov/study/NCT05579366. 2. Lee EK et al. ESMO 2024 Abstract 719MO, Lee EK et al.SGO 2025

@DrKatyMoore

RainFol: Efficacy of Rina-S for Relapsed PROC

Phase 3 RainFol/GCT1184-02/ENGOT-OV86/GOG3107

Key Eligibility Criteria[a]

- Histologically or cytologically confirmed high-grade serous or endometrioid epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer
- Prior treatment with the following
  - Platinum-based therapy
  - Bevacizumab (unless contraindicated)
  - PARP inhibitor (if known *BRCA* mutation)
  - Mirvetuximab (if positive FRα expression and available in the region
- Platinum-resistant disease
- No prior ADC therapy containing a topoisomerase 1 inhibitor
- No known active central nervous system metastases or carcinomatous meningitis

N = 530

Phase 3
Platinum-resistant ovarian cancer

R

1:1

RINA-S IV

Investigator's choice of chemotherapy
Paclitaxel IV
Topotecan IV
Pegylated liposomal doxorubicin IV
Gemcitabine IV

Evaluation of Study Objectives[a]

- **Primary outcome measure:** PFS
- **Secondary outcome measures:** OS, ORR, DOR, CA-125 response by GCIG criteria, AEs, and GHS/QOL (EORTC-QLQ-C30)

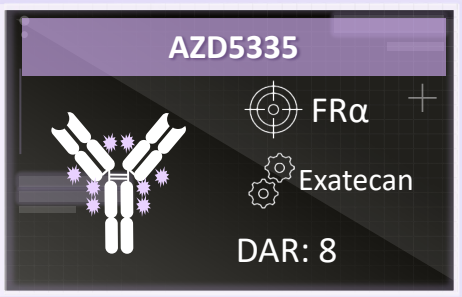
Currently enrolling

[a] Not comprehensive.

1. https://clinicaltrials.gov/study/NCT06619236.

@DrKatyMoore

FONTANA: Phase 1/2a study of Torvutatug samrotecan (AZD5335) in patients with PROC



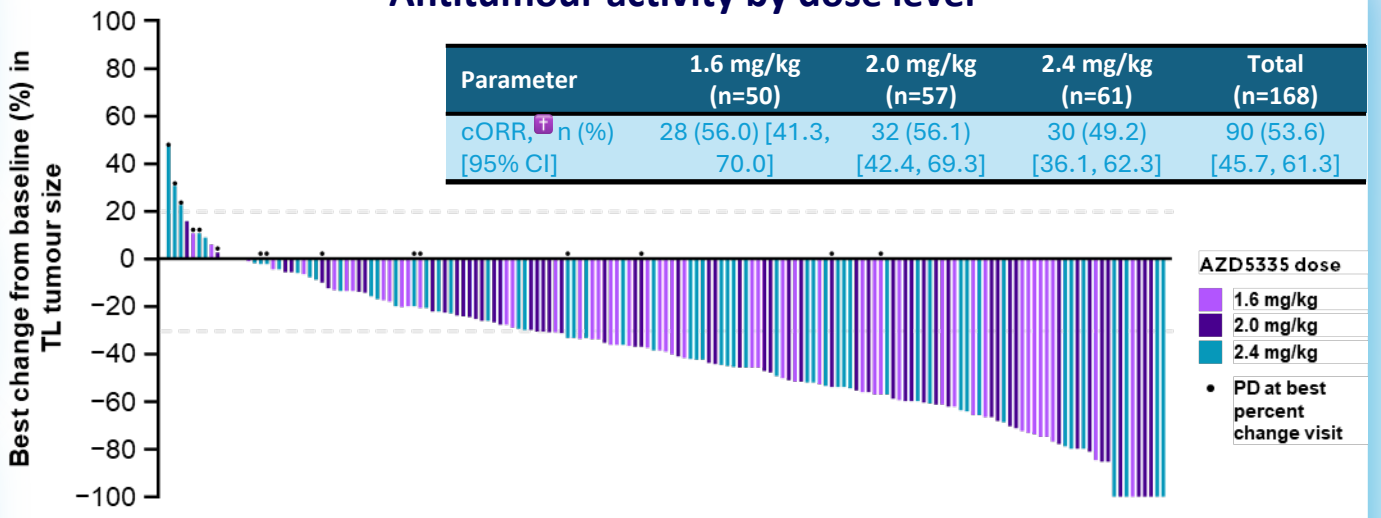
With a median follow-up of **7.8 months** (range 1.0–19.2), **56.2%** of patients remained **PFS event-free** across 1.6, 2.0 and 2.4 mg/kg dose levels

Across doses, the most common TEAEs were nausea (**81.1%**), fatigue (**56.2%**) and neutropenia (**54.4%**)

The most common grade ≥3 TEAEs were neutropenia (**26.0%**) and anaemia (**16.0%**)

Antitumour activity by dose level

Parameter	1.6 mg/kg (n=50)	2.0 mg/kg (n=57)	2.4 mg/kg (n=61)	Total (n=168)
cORR,† n (%) [95% CI]	28 (56.0) [41.3, 70.0]	32 (56.1) [42.4, 69.3]	30 (49.2) [36.1, 62.3]	90 (53.6) [45.7, 61.3]



Activity was observed **across all dose levels** and in both **FRα-high** and **low-expressing tumours**

Interim response evaluable set, defined as all dosed patients with measurable disease at baseline who have ≥15 weeks follow-up or 2 post-baseline scans ≥4 weeks apart, according to RECIST 1.1 criteria. Data cutoff: 11 July 2025.
CI, confidence interval; cORR, confirmed objective response rate; DAR, drug-to-antibody ratio; FRα, folate receptor alpha; PD, progressive disease; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; RECIST 1.1, Response evaluation criteria in solid tumours, version 1.1; TOPO1, topoisomerase 1; TEAE, treatment-emergent adverse event.
Oaknin A, et al. Presented at ESMO Congress, 2025.

Targeting Trop2 in Ovarian Cancer: ESMO 2024

	Sacituzumab tirumotecan (MK-2870) 5mg/kg D1, D15 N=35 (PROC)	Datopotamab deruxtecan N=26 (PROC)	SHR A1921[2] Q 21 day dosing 3.0mg/kg (N=26) Day 1, 8 2.0mg/kg (N=20)
Payload	Belotecan derivative Topoisomerase I	Topoisomerase 1- deruxtecan	Topoisomerase 1 (proprietary SHR9265)
DAR	7.4	4	4
Linker	Sulfonyl pyrimidine CL2A-carbonate linker	Cleavable tetrapeptide based linker	Cleavable linker
Trial	NCT06049212	NCT05489211	NCT05765032
Prior PARPi	NR	51.4%	65.4% 50.0%
Prior Bev	NR	71.4%	76% 60.0%
ORR (PROC)	37.1% (PROC)	34.6% (95% CI 17.2- 55.7)	42.3% (95% CI 23.4-63.1) 58.8% (95% CI 32.9-81.6)
DOR (PROC)	5.3 months (2.1, 24.4+)	5.6 months (2.9-NC)	9.9 months (4.5-NC) 6.3 months (3.0-NC)
mPFS	6.0 months (95% CI 3.9-7.3) (inclusive of PSOC)	5.6 months (inclusive of PSOC)	7.9 (4.2-NR) 6.9 (4.2- 9.6)

Wang et al. ESMO 2024, Oaknin A et al. ESMO 2024, He N et al. AACR 2023 LB030

Conclusions

- In the past 1-2 years we have seen a panoply of new ADCs – many with very promising efficacy signals in patients with limited options. Now the hard work begins
    - Dose Optimization will be key for each disease type and agent - how much and how often to maximize benefit and minimize toxicity
    - Regimen Optimization is upon us – where do we use these assets? All in R/M? or moving up to PSOC, maintenance – what data do we need to get the timing right?
    - Sequencing is a huge opportunity for our patients. The biomarkers have to be evaluated and validated and built into trials.
    - New constructs will have to be evaluated carefully – all comer studies may not give us the information we need to really craft scientifically based directions for drug development with these exciting agents.

Discussion Questions

How does the toxicity profile of raludotatug deruxtecan compare to that of other ADCs with DXd payloads?

Do any of the investigational FRα-targeted ADCs potentially offer advantages from a tolerability standpoint?

RECOGNITION AND MANAGEMENT OF INTERSTITIAL LUNG DISEASE (ILD)/PNEUMONITIS WITH THE USE OF ADCS

Courtney Arn, APRN-CNP

The Ohio State University

RISK FACTORS

- Environmental and occupational factors
- Autoimmune and inflammatory diseases
- Pre-existing lung diseases (COPD, asthma, ILD)
- Smoking
- Radiation Therapy
- Medications
  - Anti-cancer therapy, antibiotics, antiarrhythmics, immune suppressing agents

DIAGNOSIS

- Clinical Assessment
  - History
  - Physical Examination
- Diagnostic Workup
  - CT Chest
  - Rule out infection
  - Pulmonology consult +/- Bronchoscopy (if indicated)
  - Distinguishing Factors: Timing, Imaging, Response

MANAGEMENT

- Depends on severity
- **Hold treatment** for any suspected ILD/pneumonitis pending evaluation.
- Corticosteroids depending on severity of symptoms/imaging.
- Symptom management
- Serial imaging
- Hospitalization Criteria
  - New oxygen requirement, progressive symptoms, significant radiographic involvement

MANAGEMENT

ILD/Pneumonitis Grade	Recommended Action
Grade 1 (asymptomatic radiographic findings only)	Hold ADC therapy; consider prednisone ≥0.5 mg/kg/day (or equivalent); monitor closely.
Grade 2 or higher (symptomatic)	Consider discontinuing ADC; initiate systemic corticosteroids promptly (typically prednisone ≥1 mg/kg/day or IV equivalent).
Grade 3–4	Permanent discontinuation; escalate supportive care (IV methylprednisolone 1–2 mg/kg/day)/hospitalization as needed.

RESTARTING ADC THERAPY

- Consider restarting after complete resolution (grade 0)
- Dose reduction depending on severity
- Permanently discontinue if persistent/recurrent
- Things to Consider: Severity of symptoms/imaging, risk of recurrence

SUPPORTIVE CARE

- Corticosteroids (usually tapered gradually over ≥ 4 weeks)
- Oxygen supplementation
- Long Term Pulmonary Follow-up/Pulmonary Rehab if needed

KEY TAKEAWAYS

- Patient education
- Rapid recognition
- Immediate interruption
- Early corticosteroid initiation
- Multidisciplinary approach/supportive care

CASE STUDY

- 54 year old with recurrent endometrial cancer; initially diagnosed with IIIA grade 3 (>50% myometrial invasion, +LVSI, 8 negative lymph nodes, MMRp) in 2023
- **Social History:** Raising her grandson, smoker
- **Medical History:** Diabetes, Hypertension, Anxiety
- **NGS:** MSS, Her2 2+, ARID1A

2/28/24: Robotic hysterectomy with bilateral salpingo-oophorectomy with sentinel lymphadenectomy

4/13/24-7/27/24: 6 cycles Paclitaxel 135 mg/m2 (reduced Cycle 6 for neuropathy) + Carboplatin AUC 5

9/12/24-10/24/24: EBRT + VcBT

2/15/25: CT with new liver lesion, biopsy confirmed disease recurrence

4/11/25-12/2025: 11 cycles of Len/Pem with progression

12/8/25-current: T-DXd

CASE STUDY

- Imaging after 6 cycles (decrease in disease, no evidence of pneumonitis)
- 4/13/26: Received cycle 7 T-DXd
- 4/29/26: Called with dry cough x 2 weeks, O2 95%
- 5/1/26: CT Chest: Interval ground glass opacities and subpleural reticulations throughout the left greater than right lungs likely representing an infectious/inflammatory process such as treatment-related pneumonitis.
- 5/3/26: Worsening cough, home pulse ox 79%; presented to ED.

CASE STUDY

- Started on IV steroids which she received for 48 hrs with clinical improvement and was transitioned to PO prednisone 1 mg/kg with plan to taper over 4 weeks
- Initially required 4L NC oxygen supplementation, was weaned to room air. By day of discharge.
- Provided with a prescription for sliding scale lispro in the setting of her T2DM and anticipated elevated blood sugars due to steroids.
- Discontinue T-DXd and repeat imaging after completion of steroids

Discussion Questions

What symptoms prompt suspicion of ILD/pneumonitis? How do you distinguish drug-related pulmonary toxicity from other potential causes?

In general, why does T-DXd need to be discontinued in patients with Grade 2 ILD? Is this the same for other ADCs, such as mirvetuximab soravtansine?

Agenda

Module 1: Overview of Antibody-Drug Conjugates (ADCs)

Module 2: Current and Future Role of HER2-Targeted ADCs for Breast Cancer

Module 3: Currently Available ADCs for Gynecologic Cancer Management

Module 4: Currently Available ADCs for Lung Cancer Management

Module 5: Current and Future Role of TROP2-Targeted ADCs for Metastatic Breast Cancer

Module 6: Other ADCs That May Soon Reach the Clinic for Advanced Gynecologic Cancers

Module 7: Promising Investigational Strategies Employing ADCs for Lung Cancer

RTP RESEARCH TO PRACTICE

Promising Investigational Strategies Employing ADCs in Lung Cancer

Edward B. Garon, MD, MS

Professor

David Geffen School of Medicine at UCLA

Los Angeles, CA

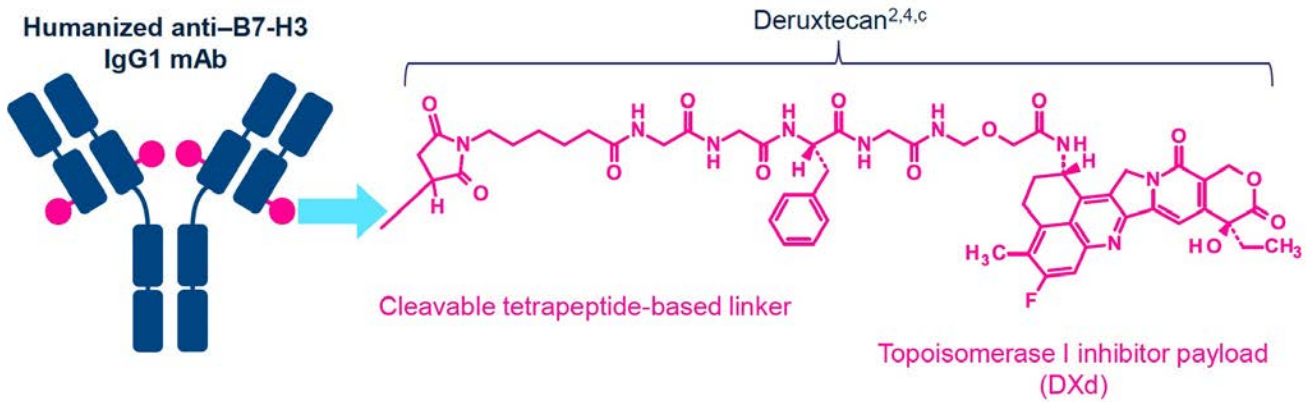
Case

- 63-year-old man diagnosed with SCLC based on screening CT
- Original staging at an outside institution treated the patient as limited stage disease, although an MRI was omitted
- In second opinion after much of the radiation was completed, an MRI was ordered and was suspicious for malignancy
- There was benefit, so atezolizumab was added to complete 4 cycles of chemotherapy and maintenance atezolizumab (preceded lurbinectedin maintenance data) and SRS was performed
- After progression, tarlatamab was started
- Patient did well on tarlatamab for 8 months, but progressed

IDeate-Lung01: Phase II Study of Ifinatamab Deruxtecan (I-DXd) in ES-SCLC

I-DXd is a B7-H3 (CD276)–directed ADC with 3 components[1–4]:

- A humanized anti–B7-H3 IgG1 mAb
- A tetrapeptide-based cleavable linker that covalently bonds antibody and payload
- A topoisomerase I inhibitor payload (an exatecan derivative, DXd)



Patient eligibility:

- Histologically or cytologically documented ES-SCLC
- Age ≥18 years[a]
- ≥1 prior line of PBC and ≤3 prior lines of systemic therapy
- Radiologically documented PD on or after most recent prior systemic therapy
- ECOG PS 0–1
- ≥1 measurable lesion per RECIST 1.1[b]
- Patients with asymptomatic brain metastases (untreated or previously treated) are eligible

R 1:1

Arm 1: I-DXd 8 mg/kg Q3W (n≈40)

Arm 2: I-DXd 12 mg/kg Q3W (n≈40)

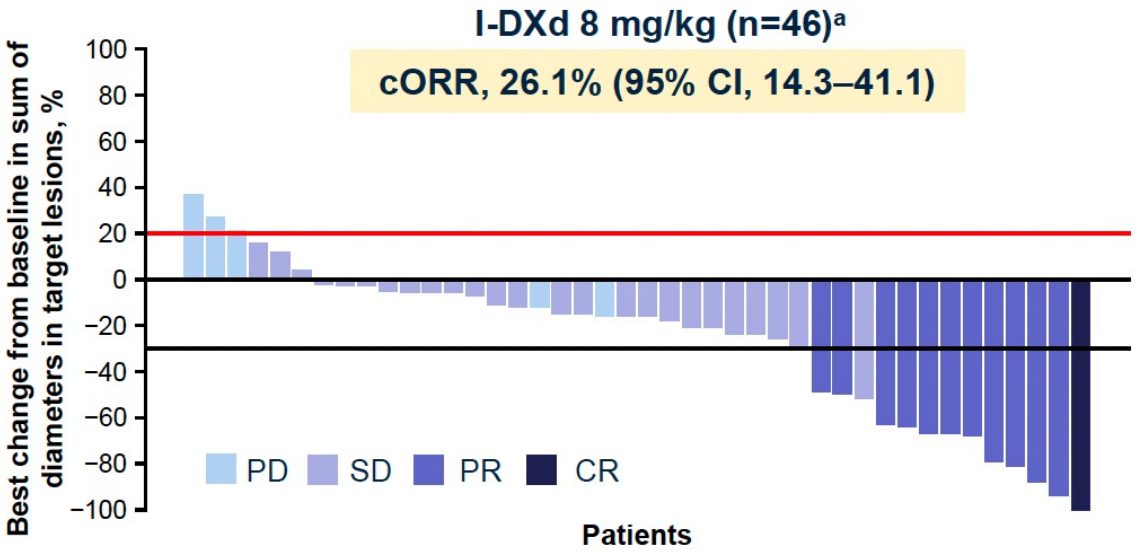
Extended enrollment at RP3D (n≈70 3L+)

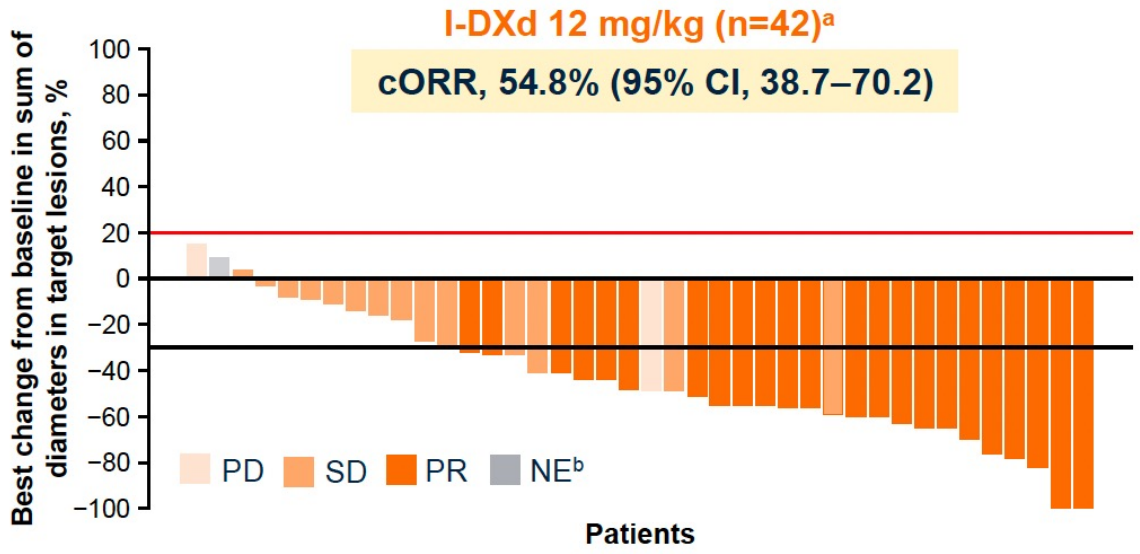
Stratification:

- 2L CTFI <90 days, 2L CTFI ≥90 days, 3L or 4L
- Prior anti–PD-(L)1 treatment (yes or no)

Rudin CM et al. WCLC 2024;Abstract OA04.03.

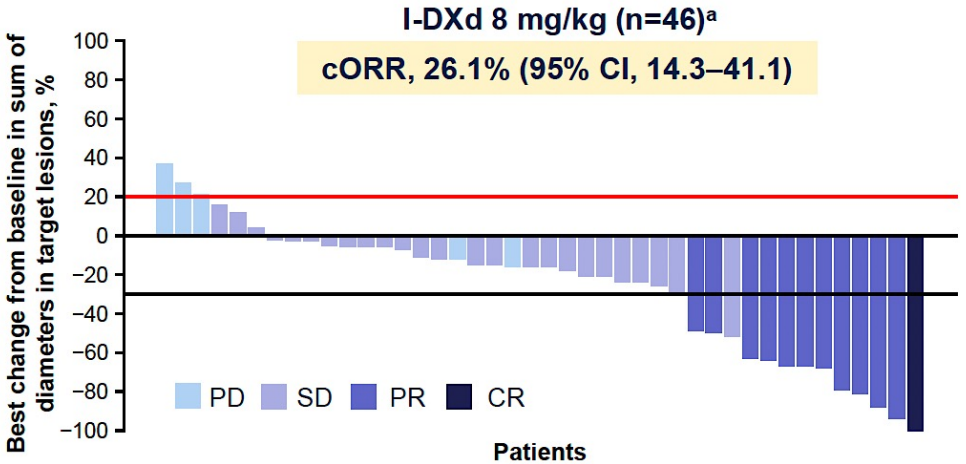
IDeate-Lung01: Phase II Study of Ifinatamab Deruxtecan (I-DXd) in ES-SCLC – Safety

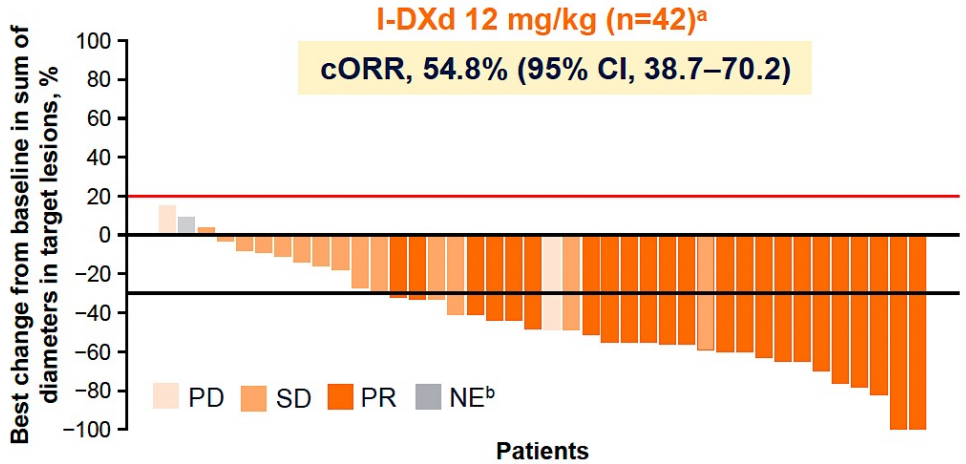




Confirmed response by BICR[c]	I-DXd 8 mg/kg n=46	I-DXd 12 mg/kg n=42
ORR, % (95% CI)	26.1 (14.3–41.1)	54.8 (38.7–70.2)
CR, n (%)	1 (2.2)	0
PR, n (%)	11 (23.9)	23 (54.8)
DCR, % (95% CI)	80.4 (66.1–90.6)	90.5 (77.4–97.3)

Rudin CM et al. WCLC 2024;Abstract OA04.03; Hayashi H et al. JSMO 2025;Abstract O12-4.





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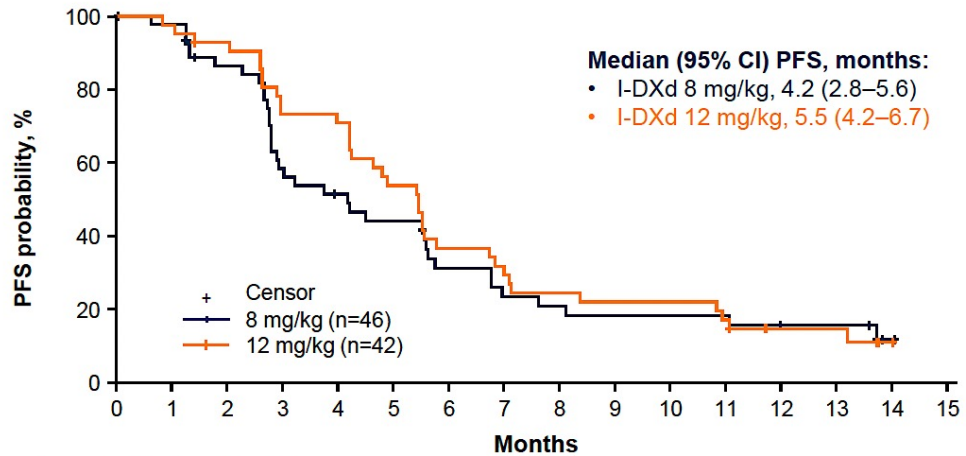
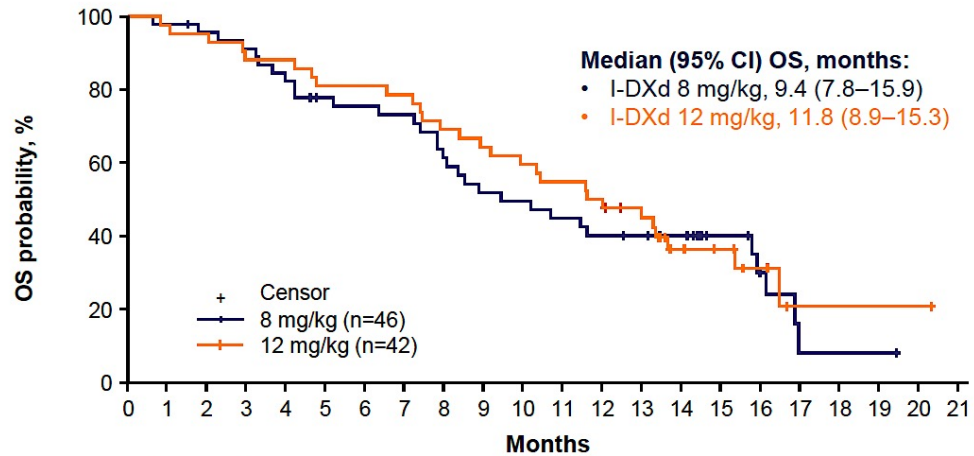
ORR, % (95% CI)	26.1 (14.3–41.1)	54.8 (38.7–70.2)
CR, n (%)	1 (2.2)	0
PR, n (%)	11 (23.9)	23 (54.8)
DCR, % (95% CI)	80.4 (66.1–90.6)	90.5 (77.4–97.3)



Number of patients still at risk

8 mg/kg	46	44	37	25	21	18	12	9	8	7	7	7	5	5	1	0
12 mg/kg	42	41	38	30	29	22	15	12	10	9	9	7	4	4	1	0

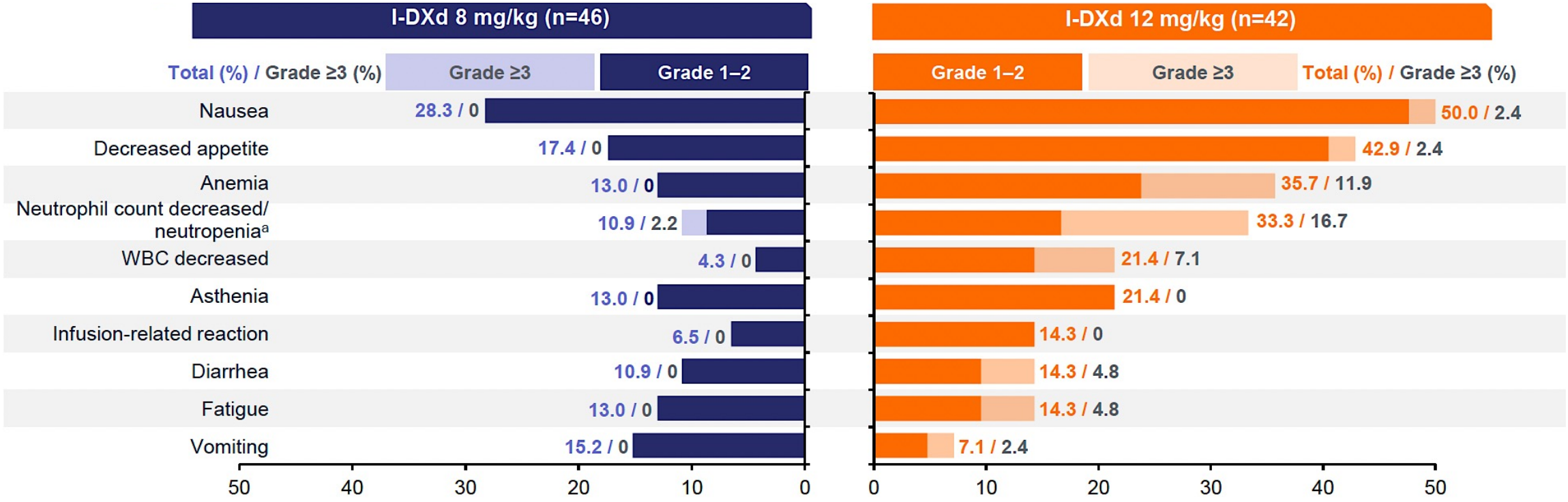


Number of patients still at risk

8 mg/kg	46	45	43	41	37	33	32	31	26	22	21	19	17	16	14	9	5	1	1	1	0	0
12 mg/kg	42	41	40	37	37	34	34	33	29	27	25	23	20	17	10	8	5	1	1	1	1	0

Rudin CM et al. WCLC 2024;Abstract OA04.03; Hayashi H et al. JSMO 2025;Abstract O12-4.

IDeate-Lung01: Phase II Study of Ifinatamab Deruxtecan (I-DXd) in ES-SCLC – Safety



ILD/pneumonitis adjudicated as treatment-related was reported in:

- Four (8.7%) patients in the 8-mg/kg cohort (Grade 2, n=3; Grade 5, n=1)
- Five (11.9%) patients in the 12-mg/kg cohort (Grade, 1 n=1; Grade 2, n=3; Grade 3, n=1)
- No ILD events were pending adjudication at the time of data cutoff

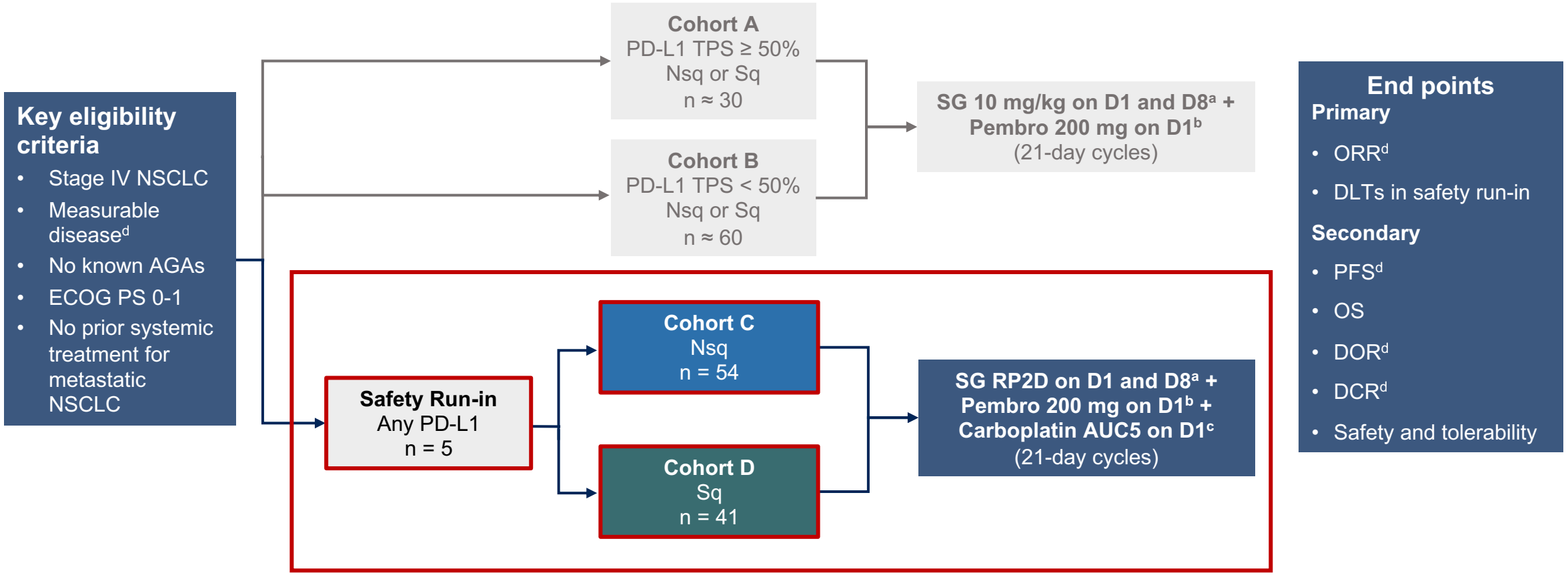
Rudin CM et al. WCLC 2024;Abstract OA04.03; Hayashi H et al. JSMO 2025;Abstract O12-4.

Further IDeate Studies

- IDeate-Lung02- Randomized clinical trial of I-DXd vs standard of care (topotecan, amrubicin or lurbinectedin) for previously treated Extensive Stage Small Cell Lung Cancer

- IDeate-Lung03- Dose findings study of I-DXd substituting for either etoposide or etoposide plus carboplatin in induction therapy along with atezolizumab followed by maintenance I-DXd plus atezolizumab

EVOKE-02: A Global, Open-Label, Multi-Cohort Phase 2 Study



Data cutoff: 01 December 2023

Median (range) follow-up for patients with nonsquamous and squamous histologies were 8.4 (6.1–16.2) months and 8.1 (4.9–16.9) months, respectively

[a]SG IV until progressive disease or unacceptable toxicity. [b]Pembro IV up to 35 cycles. [c]Carboplatin up to 4 cycles. [d]Assessed by IRC per RECIST v1.1. AGA, actionable genetic alterations; AUC, area under the concentration by time curve 5; D, day; DCR, disease control rate; DLT, dose-limiting toxicities; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; Nsq, nonsquamous; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed death (ligand) 1; Pembro, pembrolizumab; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; RP2D, recommended phase II dose; SG, sacituzumab govitecan; Sq, squamous; TPS, tumor proportion score.

EVOKE-02 Safety Run-In: Efficacy by Histology and PD-L1 Levels

	Cohort C (NSQ) SG + CP (n = 51)[b]	Cohort D (SQ) SG + CP (n = 41)
Follow-up, median (range), months	14.5 (12.2–22.3)	14.2 (11.0–23.0)
ORR, % (95% CI)	45.1 (31.1–59.7)	39.0 (24.2–55.5)
Partial response, n (%)	23 (45.1)	16 (39.0)
Stable disease, n (%)	16 (31.4)	17 (41.5)
Progressive disease, n (%)	5 (9.8)	3 (7.3)
Not evaluable, n (%)	7 (13.7)	5 (12.2)
Time to response, median (range), months	2.7 (1.2–7.2)	1.5 (1.2–5.8)
DOR, median (95% CI), months	NR (3.2–NR)	11.5 (5.6–NR)
PFS, median (95% CI), months	8.1 (5.2–15.0)	8.3 (4.3–11.2)
PFS rate at 6 months, % (95% CI)	53.7 (37.8–67.2)	64.6 (46.0–78.2)

	PD-L1 TPS < 1% SG + CP (n = 44)	PD-L1 TPS 1–49% SG + CP (n = 36)	PD-L1 TPS ≥ 50% SG + CP (n = 12)
ORR, % (95% CI)	43.2 (28.3–59.0)	33.3 (18.6–51.0)	66.7 (34.9–90.1)
Partial response, n (%)	19 (43.2)	12 (33.3)	8 (66.7)
Stable disease, n (%)	15 (34.1)	16 (44.4)	2 (16.7)
Progressive disease, n (%)	3 (6.8)	4 (11.1)	1 (8.3)
Not evaluable, n (%)	7 (15.9)	4 (11.1)	1 (8.3)
PFS, median (95% CI), months	8.3 (5.2–15.0)	6.8 (4.0–10.7)	NR (1.9–NR)

Gray et al. WCLC 2024;Abstract OA-08-07.

Phase III Trial of Sacituzumab Tirumotecan in Combination with Pembrolizumab as First-Line Treatment for PD-L1-Positive NSCLC Met the Primary Endpoint

Press Release: November 24, 2025

The Phase III OptiTROP-Lung05 clinical study of the TROP2 ADC sacituzumab tirumotecan (sac-TMT, also known as SKB264/MK-2870) in combination with pembrolizumab as a first-line treatment for PD-L1-positive advanced non-small cell lung cancer (NSCLC) has demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS), the study's primary endpoint. A positive trend in overall survival was also observed. This is the first Phase III clinical trial of ADC combined with immune checkpoint inhibitor to achieve its primary endpoint in the first-line treatment of NSCLC.

OptiTROP-Lung05 is a randomized, open-label, multicenter Phase III clinical study evaluating the efficacy and safety profile of sac-TMT in combination with pembrolizumab versus pembrolizumab monotherapy as first-line treatment for PD-L1-positive locally advanced or metastatic NSCLC with PD-L1 TPS ≥ 1%. At a prespecified interim analysis, the sac-TMT combination therapy demonstrated a statistically significant and clinically meaningful improvement in PFS. Based on the results from the interim analysis, the Company plans to communicate with the Center for Drug Evaluation of the National Medical Products Administration of China regarding the submission of a supplemental new drug application of sac-TMT.

https://www.prnewswire.com/news-releases/kelun-biotech-announces-phase-iii-trial-of-sac-tmt-in-combination-with-keytruda-pembrolizumab-as-first-line-treatment-for-pd-l1-positive-nsclc-met-primary-endpoint-302624279.html

Case Continued

- He was quite disappointed that now two different immunotherapies failed to control his tumor
- After discussion, he was not willing to go on a randomized trial vs. lurbinectedin, but was willing to go on a single arm trial of an investigational B7-H3 directed ADC with a topoisomerase 1 payload

Discussion Questions

If ifinatamab deruxtecan (I-DXd) were to become available, for which patients with extensive-stage small cell lung cancer would you prioritize its use?

How does the toxicity profile of I-DXd compare to that of other ADCs with DXd payloads?

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Ovarian Cancer

Wednesday, May 13, 2026

6:00 PM – 7:30 PM

Faculty

Bradley J Monk, MD
Kathryn M Schlenker, MSN, WHNP-BC, AGNP-C
Jaclyn Shaver, MS, APRN, CNP, WHNP

Moderator

David M O'Malley, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

Virtual attendees: The NCPD credit link is posted in the chat room.

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