What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Optimal Implementation of Antibody-Drug Conjugates

Thursday, April 25, 2024
12:15 PM – 1:45 PM

Faculty

Jamie Carroll, APRN, MSN, CNP
Kelly EH Goodwin, MSN, RN, ANP-BC
Erika Hamilton, MD
Hope S Rugo, MD

Moderator

Neil Love, MD

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Faculty

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Ms Carroll — Disclosures

Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Lilly, Novartis

Ms Goodwin — Disclosures

No relevant conflicts of interest to disclose

Dr Hamilton — Disclosures

Consulting Agreements — Payment Made to Institution	Accutar Biotechnology Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Ellipses Pharma, Entos Pharmaceuticals, Fosun Pharma, Genentech, a member of the Roche Group, Gilead Sciences Inc, Greenwich LifeSciences Inc, Jazz Pharmaceuticals Inc, Lilly, Mersana Therapeutics Inc, MphaR, Novartis, Olema Oncology, Orum Therapeutics, Pfizer Inc, Stemline Therapeutics Inc, Theratechnologies, Tubulis, Zentalis Pharmaceuticals
Contracted Research — Payment Made to Institution	AbbVie Inc, Accutar Biotechnology Inc, Acerta Pharma — A member of the AstraZeneca Group, ADC Therapeutics, Akesobio Australia Pty Ltd, Amgen Inc, Aravive Inc, ArQule Inc, Artios, Arvinas, AstraZeneca Pharmaceuticals LP, AtlasMedx Inc, BeiGene Ltd, Black Diamond Therapeutics Inc, Bliss Biopharmaceutical, Boehringer Ingelheim Pharmaceuticals Inc, Clovis Oncology, Compugen, Context Therapeutics, Cullinan Oncology, Curis Inc, CytomX Therapeutics, Daiichi Sankyo Inc, Dantari, Deciphera Pharmaceuticals Inc, Duality Biologics, eFFECTOR Therapeutics Inc, Ellipses Pharma, Elucida Oncology Inc, EMD Serono Inc, FUJIFILM Pharmaceuticals USA Inc, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, H3 Biomedicine, Harpoon Therapeutics, Hutchison MediPharma, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Inspirna, InventisBio, Jacobio Pharmaceuticals Group Co Ltd, Karyopharm Therapeutics, K-Group Beta, Kind Pharmaceuticals LLC, Leap Therapeutics Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Lycera, MacroGenics Inc, Marker Therapeutics Inc, Mersana Therapeutics Inc, Merus, Molecular Templates, Myriad Genetic Laboratories Inc, Novartis, NuCana, Olema Oncology, OncoMed Pharmaceuticals Inc, Onconova Therapeutics Inc, Oncothyreon, ORIC Pharmaceuticals, Orinove Inc, Orum Therapeutics, Pfizer Inc, PharmaMar, Pieris Pharmaceuticals Inc, Pionyr Immunotherapeutics, Plexxikon Inc, Prelude Therapeutics, ProfoundBio, Radius Health Inc, Regeneron Pharmaceuticals Inc, Relay Therapeutics, Repertoire Immune Medicines, Seagen Inc, Sermonix Pharmaceuticals, Shattuck Labs, Stemcentrx, Sutro Biopharma, Syndax Pharmaceuticals, Syros Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, Tolmar, Transcenta, Treadwell Therapeutics, Verastem Inc, Zenith Epigenetics, Zymeworks Inc
Nonrelevant Financial Relationship	Verascity Science

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Dr Rugo — Disclosures

Consulting Agreements	Daiichi Sankyo Inc, Eisai Inc, Napo Pharmaceuticals Inc, Viatris
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Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP and Daiichi Sankyo Inc.

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

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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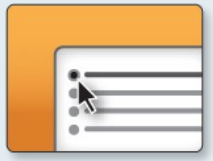
Clinicians in the Meeting Room

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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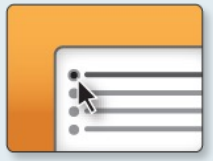
Clinicians Attending via Zoom

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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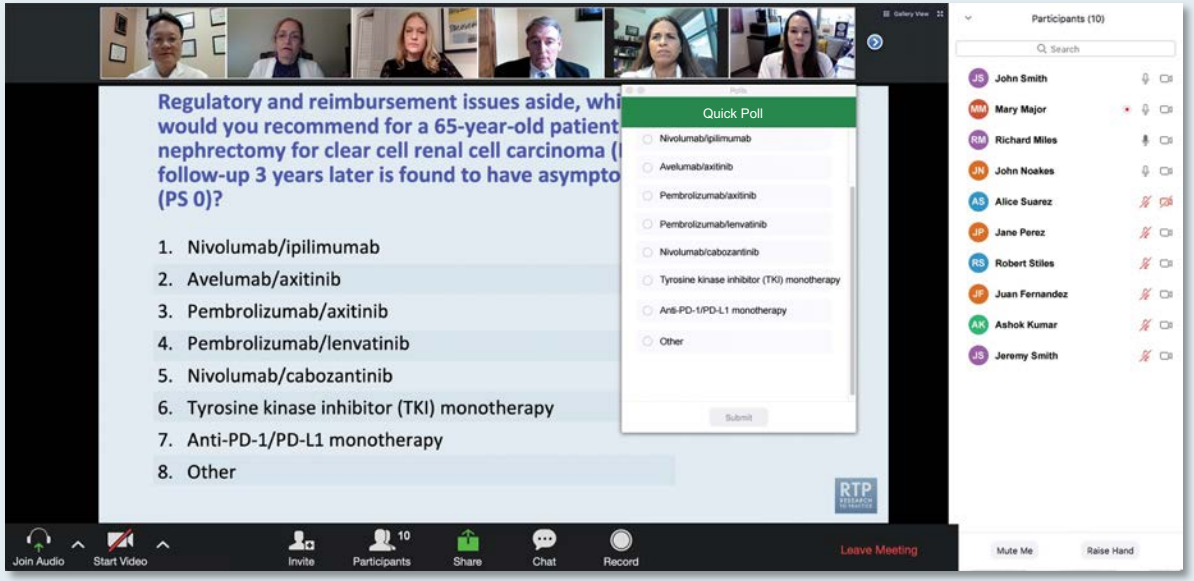
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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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 video/PowerPoint 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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“What I Tell My Patients”
Sixteenth Annual RTP-ONS NCPD Symposium Series

Wednesday April 24	**Hormone Receptor–Positive Breast Cancer** 6:00 PM – 8:00 PM ET
Thursday April 25	**Endometrial Cancer** 6:00 AM – 7:30 AM ET
	Antibody–Drug Conjugates 12:15 PM – 1:45 PM ET
	Chronic Lymphocytic Leukemia and Bispecific Antibodies in Lymphoma 6:00 PM – 8:00 PM ET
Friday April 26	**Head and Neck Cancer** 6:00 AM – 7:30 AM ET
	Non–Small Cell Lung Cancer with an EGFR Mutation 12:15 PM – 1:45 PM ET
	Ovarian Cancer 6:00 PM – 7:30 PM ET
Saturday April 27	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM ET
	Myelofibrosis 12:15 PM – 1:45 PM ET
	Gastroesophageal and Colorectal Cancers 6:00 PM – 8:00 PM ET
Wednesday, May 1	**LIVE WEBINAR — Prostate Cancer** 7:00 PM – 8:00 PM ET

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How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Consulting Nurse Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
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https://www.ResearchToPractice.com/ONS2024Clips

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Introduction

Module 1: Overview of Antibody-Drug Conjugates (ADCs); HER2-Targeted ADCs for Breast Cancer — T-DM1, Trastuzumab Deruxtecan

Module 2: The Incidence and Management of Interstitial Lung Disease (ILD) with ADCs

Module 3: ADCs Targeting Other Signaling Pathways in Breast Cancer — Sacituzumab Govitecan, Datopotamab Deruxtecan, Patritumab Deruxtecan

Module 4: Other Side Effects Associated with ADCs

Module 5: ADCs for Other Tumor Types

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Module 5: ADCs for Other Tumor Types

Consulting Nursing Faculty Comments

Listening versus talking

Jessica Mitchell, APRN, CNP, MPH

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Panel Discussion

The Current and Future Role of ADCs in Cancer Therapy

- FDA-approved indications for ADCs for various tumor types
- Other promising ADCs in clinical development as anticancer therapy
- Counseling patients regarding reasonable expectations about ADC efficacy and tolerability; customizing communication strategies based on individual preferences, educational background, cultural and linguistic background, et cetera
- Suitability of ADCs for various patient populations, including those who are older or frail and those with preexisting comorbidities

FDA Grants Accelerated Approval to Fam-Trastuzumab-Deruxtecan-Nxki for Unresectable or Metastatic HER2-Positive Solid Tumors

Press Release – April 5, 2024

"…the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.

Efficacy was evaluated in 192 adult patients with previously treated unresectable or metastatic HER2-positive (IHC 3+) solid tumors who were enrolled in one of three multicenter trials: DESTINY-PanTumor02 (NCT04482309), DESTINY-Lung01 (NCT03505710), and DESTINY-CRC02 (NCT04744831)."

"The major efficacy outcome measure in all three trials was confirmed objective response rate (ORR), and an additional efficacy outcome was duration of response (DOR). All outcomes were assessed by independent central review (ICR) based on RECIST v1.1. In DESTINY-PanTumor02, ORR was 51.4% (95% CI: 41.7, 61.0) and median DOR was 19.4 months (range 1.3, 27.9+). In DESTINY-Lung01, ORR was 52.9% (95% CI: 27.8, 77.0) and median DOR was 6.9 months (range 4.0, 11.7+). In DESTINY-CRC02, ORR was 46.9% (95% CI: 34.3, 59.8), and DOR was 5.5 months (range 1.3+, 9.7+)."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-fam-trastuzumab-deruxtecan-nxki-unresectable-or-metastatic-her2

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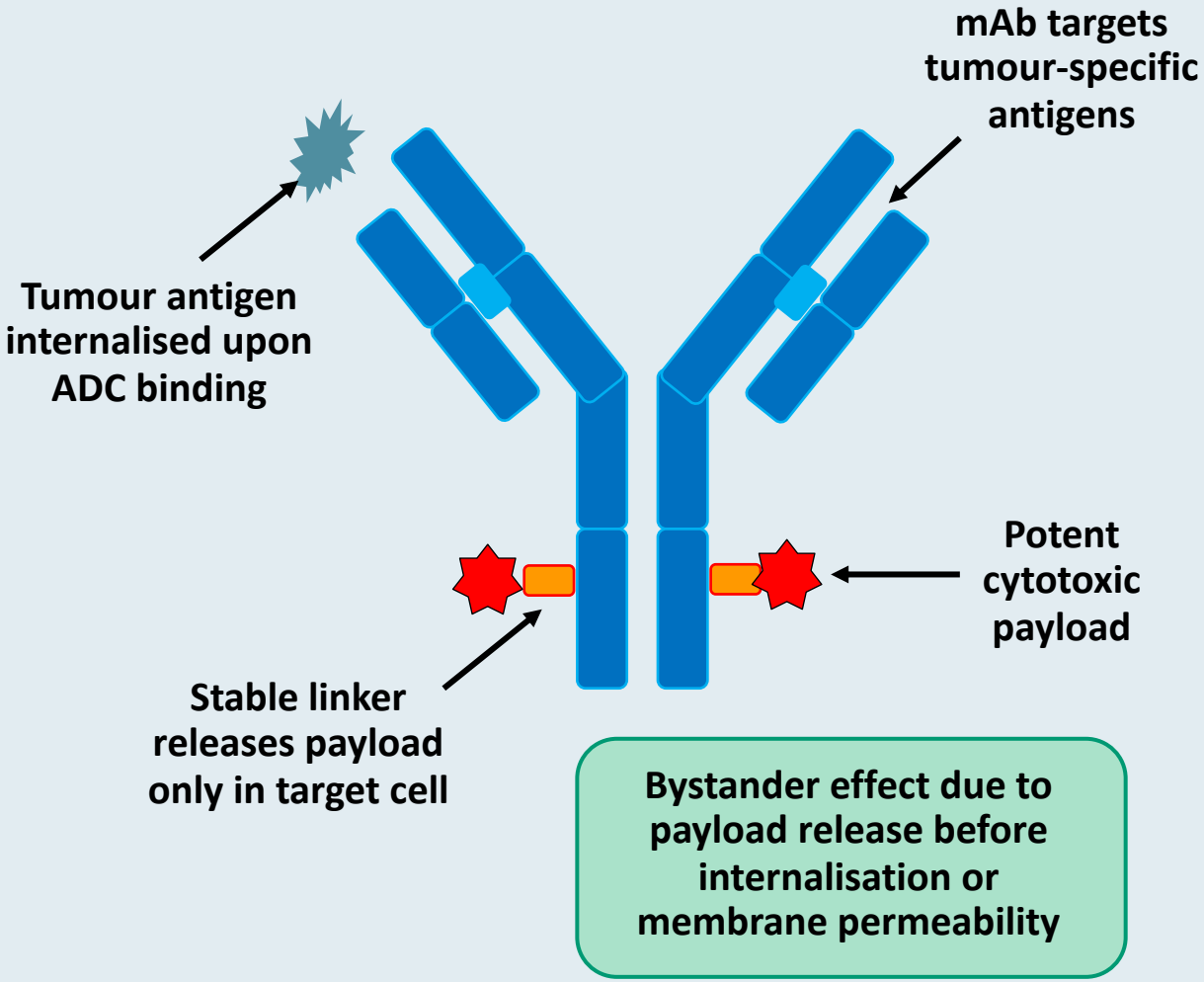
HER2-Targeting Antibody-Drug Conjugates (ADCs)



ADC Attributes	T-DM1	T-DXd
Payload MoA	Antimicrotubule	Topoisomerase I inhibitor
Drug-to-antibody ratio	~3.5:1	~8:1
Tumor-selective cleavable linker?	No	Yes
Evidence of bystander antitumor effect?	No	Yes

Schmid P et al. San Antonio Breast Cancer Symposium 2021.

Trastuzumab Deruxtecan

Mechanism of action

- **Antibody-drug conjugate directed against HER2**

Indications in other tumor types

- **For patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy**
- **For patients with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.**
- **For patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic therapy and have no satisfactory alternative therapeutic options**

Recommended dose

- **5.4 mg/kg IV infusion q3wk until disease progression or unacceptable toxicity**
- **6.4 mg/kg IV infusion q3wk until disease progression or unacceptable toxicity (gastric cancer)**

Trastuzumab deruxtecan package insert, April 2024.

FDA-Approved Indications for Select ADCs for Solid Tumors

Agent	Initial indication	Approval date
Enfortumab vedotin (monotherapy)	Patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy	Accelerated: 12/18/2019 Traditional: 7/9/2021
Enfortumab vedotin (plus pembrolizumab)	In combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer	Accelerated: 4/3/2023 Traditional: 12/15/2023
Mirvetuximab soravtansine	Patients with folate receptor alpha (FRα)-positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received 1 to 3 prior systemic therapy regimens	Accelerated: 11/14/2022 Traditional: 3/22/2024
Tisotumab vedotin	Patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy	Accelerated: 9/20/2021

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

FDA-Approved Indications for Select ADCs for Heme Malignancies

Agent	Initial indication	Approval date
Gemtuzumab ozogamicin	Newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults and pediatric patients 1 month and older and in relapsed or refractory CD33-positive AML in adults and pediatric patients 2 years and older	Accelerated: 5/17/2000 Traditional: 9/1/2017
Brentuximab vedotin	Patients with Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates	Accelerated: 8/19/2011 Traditional: 8/18/2015
Inotuzumab ozogamicin	Adult patients with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukemia (ALL)	Traditional: 8/17/2017
Polatuzumab vedotin	In combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies	Accelerated: 6/10/2019 Traditional: 4/19/2023
Loncastuximab tesirine	Patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, DLBCL arising from low-grade lymphoma, and high-grade B-cell lymphoma	Accelerated: 4/23/2021

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

Antibody-Drug Conjugates (ADCs) as Cancer Treatment; Overview of HER2-Targeted ADCs for Breast Cancer — T-DM1, Trastuzumab Deruxtecan

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Specificity of monoclonal antibodies and ability to target cancer while avoiding normal tissues**
- **Rationale for conjugating monoclonal antibodies with cytotoxic drugs; theoretical improvement of chemotherapy efficacy while reducing systemic exposure and toxicity**
- **Structural components of commercially available and investigational ADCs**
- **Direct mechanism of antitumor activity of ADCs**
- **Other means by which ADCs can elicit an antitumor effect, such as bystander killing, antibody-dependent cellular toxicity and complement-dependent cytotoxicity**
- **Optimal timing for approved ADCs or consideration of a clinical trial with one of these agents**
- **Mode of administration, dose and schedule of various ADCs**
- **Recommended premedications for patients about to begin therapy with an ADC**
- **Known drug-drug interactions between ADCs and other classes of agents**

Ado-Trastuzumab Emtansine (T-DM1)

Mechanism of action

- **Antibody-drug conjugate directed against HER2**

Indication in breast cancer

- **For patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease or experienced disease recurrence during or within 6 months of completing adjuvant therapy**
- **For patients with HER2-positive localized breast cancer who have residual invasive disease after receiving neoadjuvant taxane and trastuzumab-based therapy**

Recommended dose for breast cancer

- **3.6 mg/kg IV infusion q3wk (21-day cycle) until disease progression or unacceptable toxicity, or a total of 14 cycles for patients with localized breast cancer**

Ado-trastuzumab emtansine package insert, February 2022.

Trastuzumab Deruxtecan (T-DXd)

Mechanism of action

- **Antibody-drug conjugate directed against HER2**

Indication in breast cancer

- **For patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting or in the (neo)adjuvant setting and have experienced disease recurrence during or within 6 months of completing therapy**
- **For patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH negative) breast cancer who have received a prior chemotherapy in the metastatic setting or have experienced disease recurrence during or within 6 months of completing adjuvant chemotherapy**

Recommended dose for breast cancer

- **5.4 mg/kg IV infusion q3wk until disease progression or unacceptable toxicity**

Trastuzumab deruxtecan package insert, April 2024.

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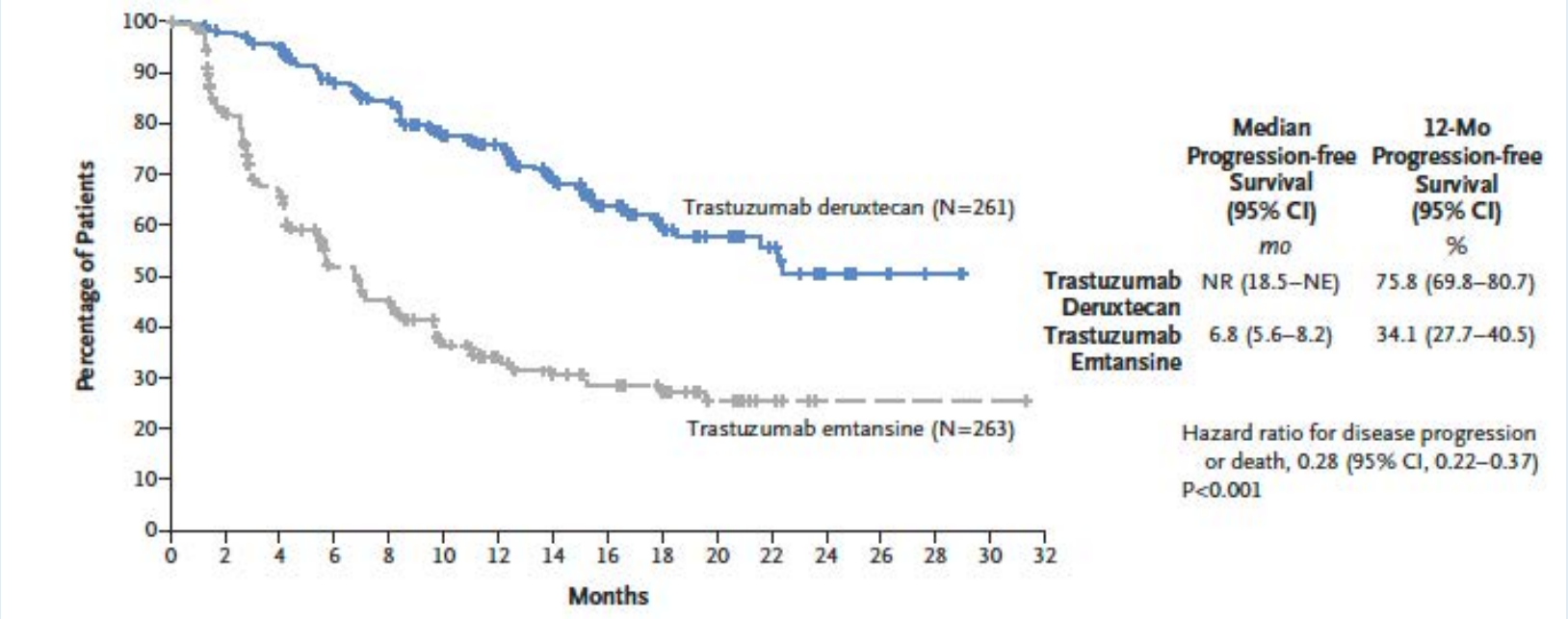
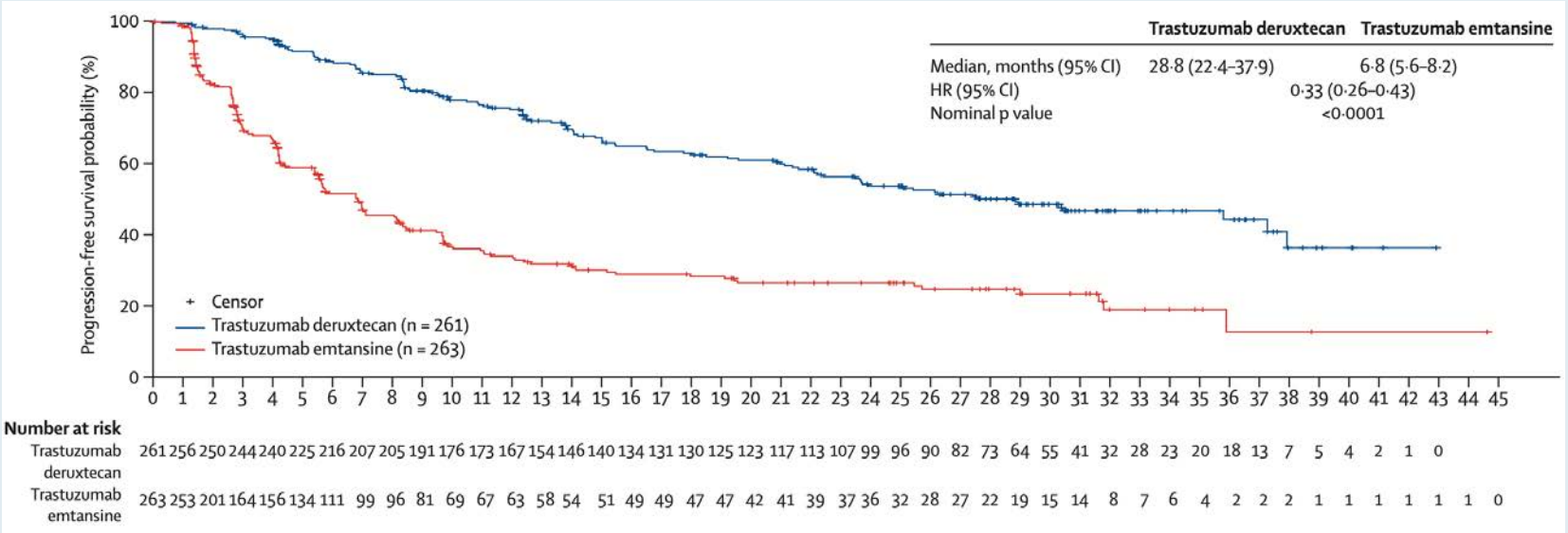
DESTINY-Breast03: Progression-Free Survival by BICR

First Interim Analysis



Updated Results



Cortes J et al. *N Engl J Med* 2022;386:1143-54; Hurvitz SA et al. *Lancet* 2023;401:105-17.

BICR = blinded independent central review

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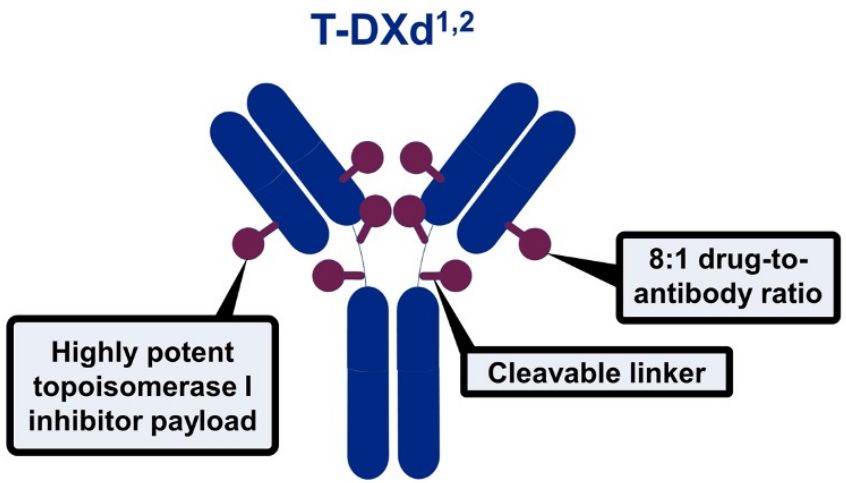
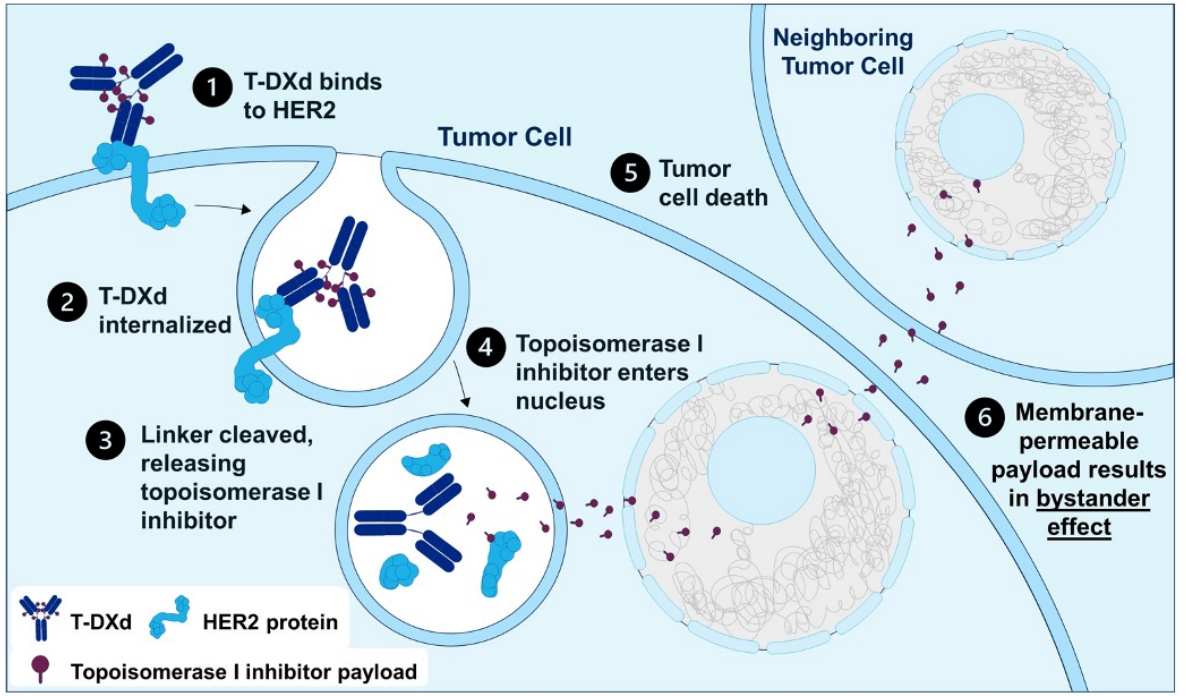
T-DXd Mechanism of Action, Bystander Effect and Rationale for Targeting HER2-Low Breast Cancer



Internalization of T-DXd leads to release of the DXd payload and subsequent cell death in the target tumor cell and neighboring tumor cells through the bystander effect[1,2]



Adapted with permission from Modi S, et al. *J Clin Oncol* 2020;38:1887-96. CC BY ND 4.0.

- **Results from a phase 1b study have reported efficacy of T-DXd in heavily pretreated patients (N = 54) with HER2-low mBC, with a mPFS of 11.1 months and an ORR of 37.0%[3]**

ORR = objective response rate

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022;387(1):9-20.

Jamie Carroll, APRN, MSN, CNP

What I tell my patients with HER2-positive and HER2-low breast cancer about the mechanism of action of and acute side effects associated with trastuzumab deruxtecan

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Kelly EH Goodwin, MSN, RN, ANP-BC

What I tell my patients with lung cancer and HER2 mutations about the mechanism of action of and acute side effects associated with trastuzumab deruxtecan

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Module 4: Other Side Effects Associated with ADCs

Module 5: ADCs for Other Tumor Types

The Incidence and Management of Interstitial Lung Disease (ILD) with ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Pathophysiology of ILD associated with ADCs; baseline risk factors for the development of ILD**
- **Rates, severity and timing of ILD in clinical trials of various ADCs**
- **Appropriate workup for patients suspected of experiencing therapy-related ILD; strategies to distinguish drug-related pulmonary toxicity from other potential causes**
- **Guidelines for treatment modifications and discontinuation for patients experiencing complications from ILD; indications for restarting ADC therapy after resolution of symptoms**
- **Utility of other supportive care measures for patients experiencing ILD, such as corticosteroids and oxygen supplementation**

DESTINY-Breast02: Adjudicated Drug-Related ILD/Pneumonitis

	Adjudicated as drug-related ILD					
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 404)	11 (2.7)	26 (6.4)	3 (0.7)	0	2 (0.5)	42 (10.4)
TPC (n = 195)	0	0	1 (0.5)	0	0	1 (0.5)

- Median time to onset of adjudicated drug-related ILD was 209.5 days (41-628 days) with T-DXd

Left ventricular (LV) dysfunction

- T-DXd arm, 18 (4.5%) patients experienced an LV dysfunction event
  - 2 (0.5%) patients had a Grade ≥3 event
- TPC arm, 3 (1.5%) patients experienced an LV dysfunction event
  - 1 (0.5%) patient had a Grade ≥3 event

Andre F et al. *Lancet* 2023;401(10390):1773-85; Krop I et al. San Antonio Breast Cancer Symposium 2022;Abstract GS2-01.

Reviews

Real-World Perspectives and Practices for Pneumonitis/ Interstitial Lung Disease Associated With Trastuzumab Deruxtecan Use in Human Epidermal Growth Factor Receptor 2–Expressing Metastatic Breast Cancer

Hope S. Rugo, MD[1]; Christine L. Crossno, PharmD[2]; Yaron B. Gesthalter, MD[3]; Kristen Kelley, MD[2]; Heather B. Moore, PharmD[4]; Mothaffar F. Rimawi, MD[5]; Kelly E. Westbrook, MD[4]; and Saundra S. Buys, MD[2]

JCO Oncol Pract 2023;19:539-46.

Editorials

Detecting and Managing T-DXd–Related Interstitial Lung Disease: The Five "S" Rules

Paolo Tarantino, MD[1,2,3] and Sara M. Tolaney, MD, MPH[1,2]

JCO Oncol Pract 2023;19:526-27.

The Five "S" Rules: Strategies to Minimize the Risk and Impact of ILD

1. Screen: Careful patient selection is warranted before initiating T-DXd to optimize the monitoring strategies based on the baseline risk. Screening continues during treatment, with regular clinical assessments to exclude signs/symptoms of ILD.
2. Scan: The fundamental diagnostic tools for ILD remain radiological scans, with preference for high-resolution CT scans of the chest. A baseline scan is recommended, with repeat scans to be performed every 6-12 weeks.
3. Synergy: Minimizing the risk of ILD involves a teamwork, which includes educating patients and all the care team, as well as multidisciplinary management once ILD is suspected.
4. Suspend treatment: T-DXd should always be interrupted if ILD is suspected; it can only be restarted in the case of asymptomatic ILD that fully resolves.
5. Steroids: The mainstay for treating T-DXd–induced ILD remains corticosteroids, with the dose to be adapted to the toxicity grade.

Tarantino P and SM Tolaney. *JCO Oncol Pract* 2023;19:526-27.

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Jamie Carroll, APRN, MSN, CNP

What I tell my patients with breast cancer about to begin therapy with trastuzumab deruxtecan about screening for and management of ILD

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Kelly EH Goodwin, MSN, RN, ANP-BC

What I tell my patients with lung cancer about to begin therapy with trastuzumab deruxtecan about screening for and management of ILD

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Module 4: Other Side Effects Associated with ADCs

Module 5: ADCs for Other Tumor Types

Other ADCs for Breast Cancer; Sacituzumab Govitecan, Datopotamab Deruxtecan, Patritumab Deruxtecan

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Optimal timing for initiation of approved ADCs or consideration of a clinical trial evaluating one of these agents**
- **Mode of administration, dose and schedule of various ADCs**
- **Recommended premedications for patients about to begin therapy with an ADC**
- **Known drug-drug interactions between ADCs and other classes of agents**
- **Sequencing of ADCs for patients with HER2-low and HER2-negative breast cancer**

Sacituzumab Govitecan

Mechanism of action

- **Antibody-drug conjugate directed against TROP2**

Indication in breast cancer

- **For patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior systemic therapies, at least 1 of them for metastatic disease**
- **For patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH negative) breast cancer who have received endocrine-based therapy and at least 2 additional systemic therapies in the metastatic setting**

Recommended dose for breast cancer

- **10 mg/kg IV infusion once weekly on days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity**

Sacituzumab govitecan package insert, February 2023.

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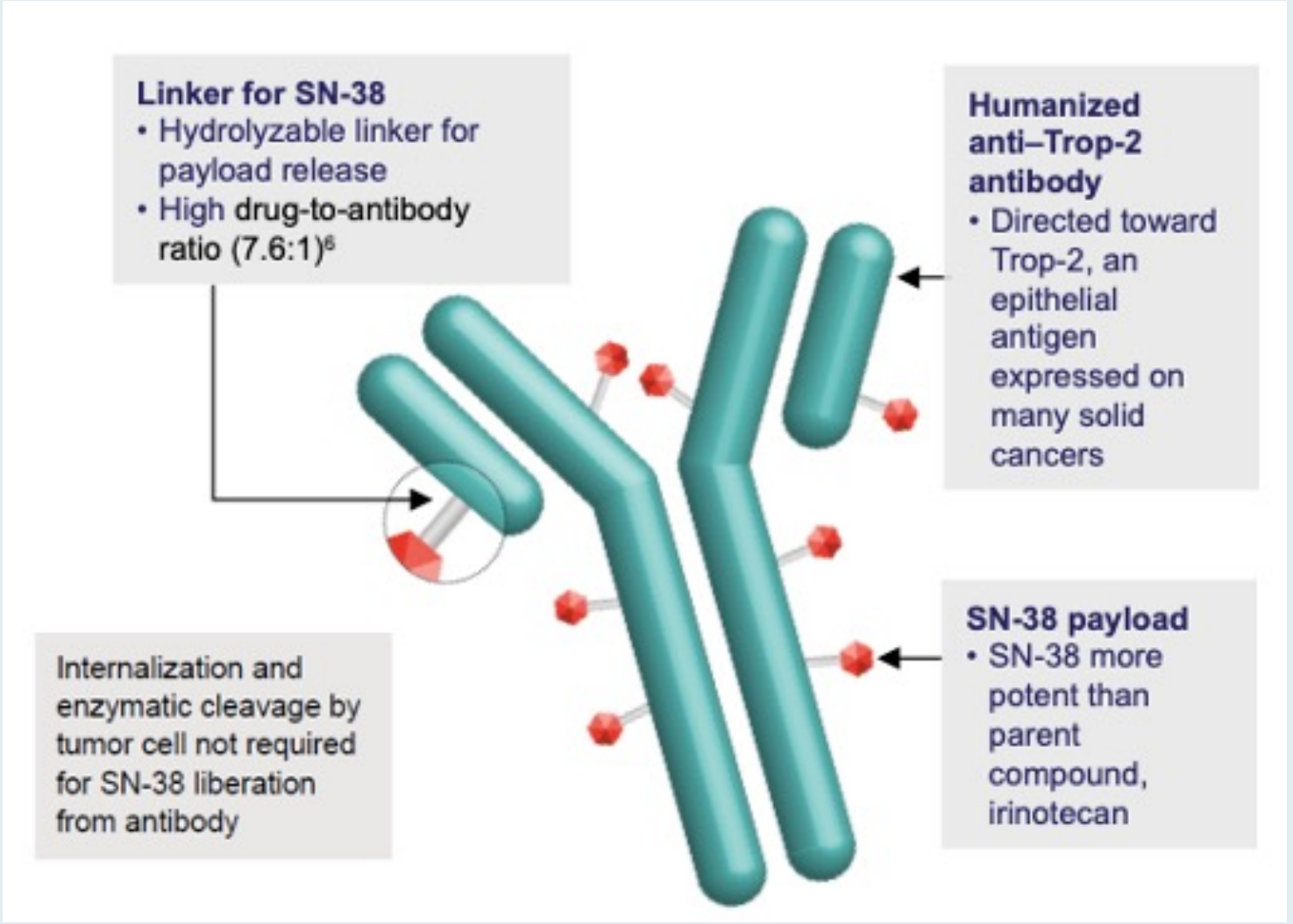
Sacituzumab Govitecan



Courtesy of Hope S Rugo, MD.

Sacituzumab Govitecan: Safety Profile in the TROPiCS-02 Trial

TRAEs, n (%)		SG (n=268)		TPC (n=249)	
		All grade	Grade ≥3	All grade	Grade ≥3
Hematologic	**Neutropenia[b]**	188 (70)	**136 (51)**	134 (54)	**94 (38)**
	Anemia[c]	91 (34)	17 (6)	62 (25)	8 (3)
	Leukopenia[d]	37 (14)	23 (9)	23 (9)	13 (5)
	Lymphopenia[e]	31 (12)	10 (4)	25 (10)	8 (3)
	Febrile neutropenia	**14 (5)**	**14 (5)**	**11 (4)**	**11 (4)**
Gastrointestinal	**Diarrhea**	152 (57)	**25 (9)**	41 (16)	**3 (1)**
	Nausea	148 (55)	3 (1)	77 (31)	7 (3)
	Vomiting	50 (19)	1 (<1)	30 (12)	4 (2)
	Constipation	49 (18)	0	36 (14)	0
	Abdominal pain	34 (13)	2 (1)	17 (7)	0
Other	Alopecia	123 (46)	0	41 (16)	0
	Fatigue	100 (37)	15 (6)	73 (29)	6 (2)
	Asthenia	53 (20)	5 (2)	37 (15)	2 (1)
	Decreased appetite	41 (15)	1 (<1)	34 (14)	1 (<1)
	Neuropathy[f]	23 (9)	3 (1)	38 (15)	6 (2)

There were no events of interstitial lung disease in the SG arm (vs 1% in the TPC arm) and no TRAEs of cardiac failure or left ventricular dysfunction in either arm

SG = sacituzumab govitecan; TPC = treatment of physician's choice; TRAEs = treatment-related adverse events

Rugo HS et al. *Lancet* 2023;402(10411):1423-33. Rugo HS et al. ASCO 2022;Abstract LBA1001.

Datopotamab Deruxtecan (Dato-DXd)

Mechanism of action

- **Antibody-drug conjugate directed against TROP2**

Indication

- **Investigational**

Key clinical trial in breast cancer

- **Phase III TROPION-Breast01 trial of datopotamab deruxtecan versus investigator's choice of chemotherapy for patients with inoperable or metastatic HR-positive, HER2-negative breast cancer who have received 1 or 2 prior lines of systemic chemotherapy**

Bardia A et al. San Antonio Breast Cancer Symposium 2023;Abstract GS02-01.

Datopotamab Deruxtecan (Dato-DXd)

- **Dato-DXd** is a **TROP2-directed ADC**, that selectively delivers a potent Topo-I inhibitor payload directly into tumor cells,[1] and has several unique properties*:
  - Optimised drug to antibody ratio ≈ 4
  - Stable linker-payload
  - Tumour-selective cleavable linker
  - Bystander antitumour effect
- Dato-DXd previously demonstrated **promising antitumour activity** and a **manageable safety profile** with a convenient Q3W schedule in pre-treated patients with **metastatic HR+/HER2– BC**[2]

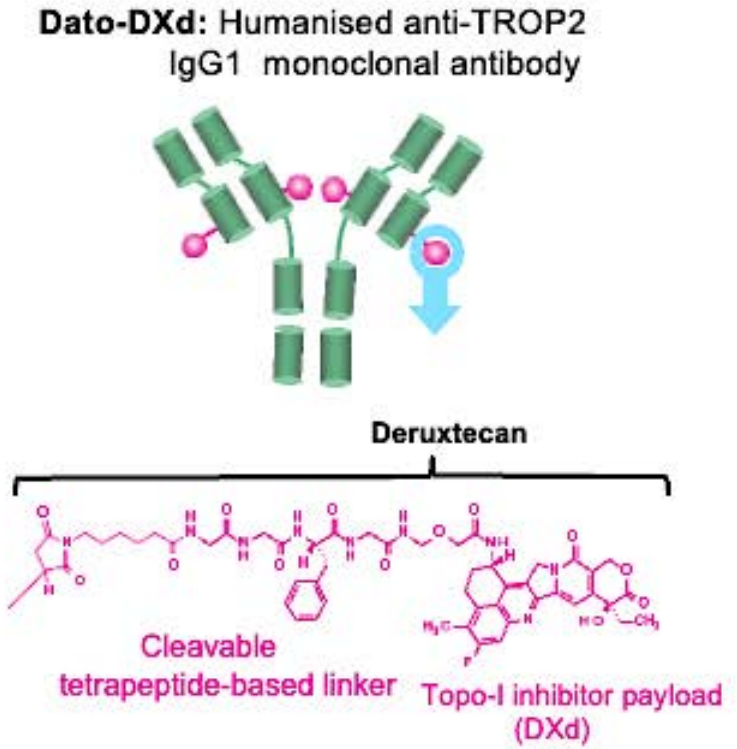


Image is for illustrative purposes only; actual drug positions may vary.

1. Okajima D, et al. *Mol Cancer Ther* 2021;20:2329–40;

2. Meric-Bernstam F, et al. Poster presentation at SABCS 2022: abstract PD13-08.

*The clinical relevance of these features is under investigation. Based on animal data.

Dato-DXd, datopotamab deruxtecan; IgG1, immunoglobulin G1; Q3W, every 3 weeks; Topo-I, topoisomerase I.

Bardia A et al. ESMO 2023;Abstract LBA11.

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TROPION-Breast01: Adverse Events of Clinical Interest

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

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

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

Bardia A et al. San Antonio Breast Cancer Symposium 2023;Abstract GS02-01.

Datopotamab Deruxtecan Biologics License Application Accepted in the US for Patients with Previously Treated Metastatic HR-Positive, HER2-Negative Breast Cancer

Press Release – April 2, 2024

"…the Biologics License Application (BLA) for datopotamab deruxtecan (Dato-DXd) has been accepted in the US for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior systemic therapy for unresectable or metastatic disease. The Prescription Drug User Fee Act date, the US Food and Drug Administration (FDA) action date for its regulatory decision, is during the first quarter of 2025.

The BLA is based on results from the pivotal TROPION-Breast01 Phase III trial in which datopotamab deruxtecan demonstrated a statistically significant and clinically meaningful improvement for the dual primary endpoint of progression-free survival (PFS) compared to investigator's choice of chemotherapy in patients with unresectable or metastatic HR-positive, HER2-negative breast cancer previously treated with endocrine-based therapy and at least one systemic therapy. For the dual primary endpoint of overall survival (OS), interim results numerically favoured datopotamab deruxtecan over chemotherapy but were not mature at the time of data cut-off. The trial is ongoing and OS will be assessed at future analyses."

https://www.astrazeneca.com/media-centre/press-releases/2024/fda-accepts-dato-dxd-bla-for-breast-cancer.html

Patritumab Deruxtecan (HER3-DXd)

Mechanism of action

- Antibody-drug conjugate directed against HER3

Indication

- Investigational (breast cancer, lung cancer)

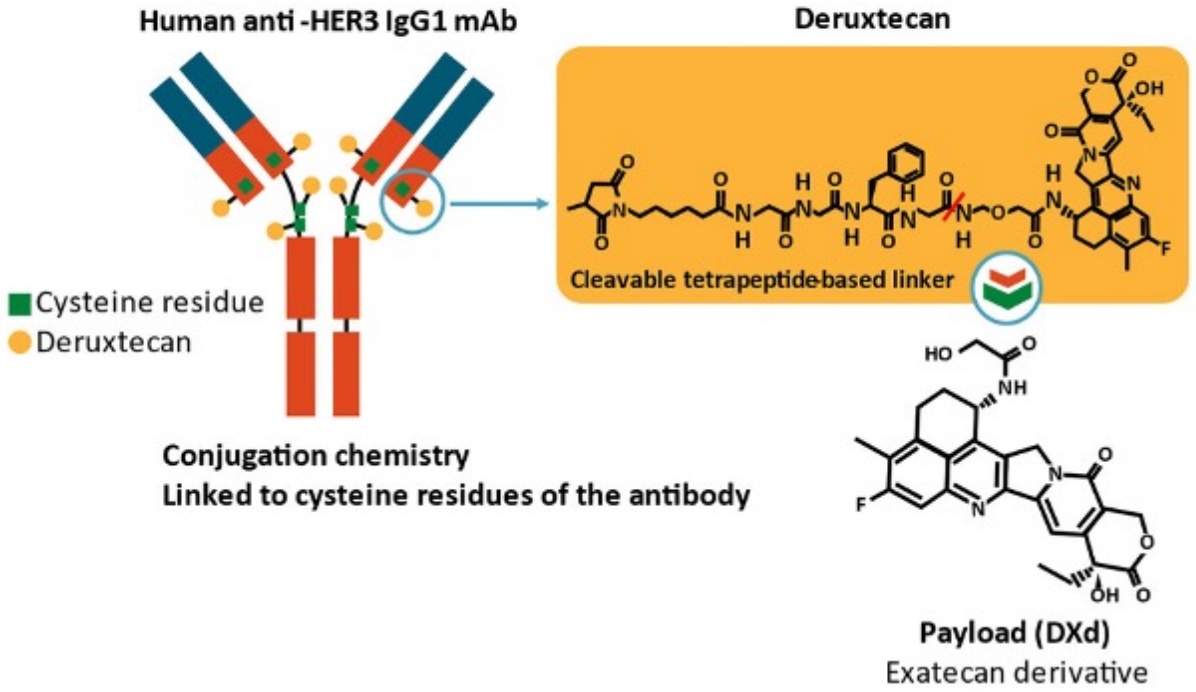
Key clinical trials

- Phase I/II multicenter trial of patritumab deruxtecan for previously treated HER3-expressing metastatic breast cancer
- Multiple ongoing Phase II studies to evaluate patritumab deruxtecan in the metastatic setting (ICARUS-BREAST01, BRE 354)
- Ongoing studies to evaluate patritumab deruxtecan as neoadjuvant therapy (TOT-HER3, VALENTINE)
- Phase II HERTHENA-Lung01 study demonstrating efficacy for EGFR-mutated NSCLC
- Ongoing Phase III HERTHENA-Lung02 study for EGFR-mutated NSCLC after a third-generation EGFR tyrosine kinase inhibitor

Krop IE et al. *J Clin Oncol* 2023;41:5550-60.

Patritumab Deruxtecan (HER3-DXd)

Patritumab deruxtecan (U3-1402) is a novel ADC coupling an anti-HER3 mAb to DXd with a high DAR (8:1)



Krop IE et al. ASCO 2022;Abstract 1002.

Adverse Events in a Phase I/II Study of Patritumab Deruxtecan for Previously Treated HER3-Positive Metastatic Breast Cancer

	4.8 mg/kg (n = 48)			6.4 mg/kg (n = 98)			All Doses (N = 182)		
Patients	All Grade	Grade 3	Grade 4	All Grade	Grade 3	Grade 4	All Grade	Grade 3	Grade 4
TEAEs (≥20% of all patients), %[d]	97.9	45.8	16.7	100	41.8	33.7	99.5	42.3	25.3
Nausea	68.8	4.2	0	80.6	5.1	0	79.7	5.5	0
Platelet count decreased[e]	60.4	10.4	16.7	71.4	14.3	24.5	62.1	12.1	18.7
Neutrophil count decreased[e]	62.5	25.0	2.1	66.3	32.7	19.4	61.0	26.9	12.6
Decreased appetite	56.3	6.3	0	53.1	6.1	0	52.7	4.9	0
Vomiting	47.9	4.2	0	46.9	1.0	0	46.2	3.8	0
WBC count decreased[e]	45.8	10.4	0	45.9	19.4	4.1	42.3	15.9	2.2
Diarrhea	41.7	4.2	0	43.9	3.1	0	41.2	3.8	0
Anemia[e]	43.8	20.8	0	43.9	20.4	1.0	40.1	18.1	0.5
AST increased	43.8	4.2	0	34.7	6.1	0	34.6	6.0	0
ALT increased	41.7	2.1	0	31.6	6.1	1.3	31.9	5.5	0.5
Fatigue	31.3	0	0	33.7	3.1	0	31.9	2.2	0
Stomatitis	25.0	0	0	34.7	1.0	0	30.2	0.5	0
Constipation	22.9	0	0	29.6	0	0	26.9	0	0
Malaise	22.9	0	0	26.5	1.0	0	24.2	1.1	0
Alopecia	20.8	NA	NA	28.6	NA	NA	23.6	NA	NA

Krop IE et al. *J Clin Oncol* 2023;41:5550-60.

Treatment-Related ILD in a Phase I/II Study of Patritumab Deruxtecan for Previously Treated HER3-Positive Metastatic Breast Cancer

Patients	4.8 mg/kg (n = 48)	6.4 mg/kg (n = 98)	All Doses (N = 182)
Adjudicated treatment-related ILD, No. (%)			
Grade 1	0	2 (2.0)	3 (1.6)
Grade 2	1 (2.1)	2 (2.0)	5 (2.7)
Grade 3	0	2 (2.0)	3 (1.6)
Grade 4	0	0	0
Grade 5	0	1 (1.0)[f]	1 (0.5)[f]
Total	1 (2.1)	7 (7.1)	12 (6.6)

Krop IE et al. *J Clin Oncol* 2023;41:5550-60.

Jamie Carroll, APRN, MSN, CNP

What I tell my patients with breast cancer about the mechanism of action of and side effects associated with sacituzumab govitecan

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Kelly EH Goodwin, MSN, RN, ANP-BC

What I tell my patients with lung cancer about the mechanisms of action of and side effects associated with datopotamab deruxtecan and patritumab deruxtecan

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Agenda

Introduction

Module 1: Overview of Antibody-Drug Conjugates (ADCs); HER2-Targeted ADCs for Breast Cancer — T-DM1, Trastuzumab Deruxtecan

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Module 4: Other Side Effects Associated with ADCs

Module 5: ADCs for Other Tumor Types

Cytopenias Associated with ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Educating patients regarding the capacity of ADCs to cause acute chemotherapy-like side effects**
- **Incidence and severity of neutropenia, thrombocytopenia and anemia with approved and investigational ADCs**
- **Appropriate monitoring of complete blood counts during therapy**
- **Thresholds for dose modification, treatment interruption or treatment discontinuation for patients experiencing cytopenias**

Mucositis/Stomatitis Associated with Certain ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Incidence and severity of mucositis/stomatitis with various approved and investigational ADCs**
- **Educating patients about the importance of oral hygiene during treatment with ADCs known to cause mucositis/stomatitis**
- **Role of prescription steroid mouthwash or homemade mouth rinses, prophylactic antibiotics/antifungals and pain medications for patients at risk for or experiencing mucositis/stomatitis**
- **Dietary recommendations for patients experiencing mucositis/stomatitis; utility of meal replacement shakes or protein powders for those not receiving adequate nutrition**

Rare Cardiac Toxicities with HER2-Targeted ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Pathophysiology of the cardiotoxicity associated with anti-HER2 therapies, including ADCs**
- **Incidence of left ventricular dysfunction noted with HER2-targeted ADCs in clinical trial experiences**
- **Appropriate monitoring of left ventricular ejection fraction (LVEF) at baseline and during treatment with HER2-targeted ADCs**
- **Threshold for treatment interruption for patients experiencing LVEF decrease; indications for restarting HER2-targeted ADC therapy after recovery**
- **Role of interdisciplinary coordination with cardiologists when monitoring for and managing cardiac toxicities associated with HER2-targeted ADCs**

Ocular Toxicities of ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Pathophysiology of ocular adverse events associated with certain ADCs; spectrum, incidence and severity of ocular toxicities with different agents**
- **Optimal patient counseling and education regarding signs of ocular toxicity and the importance of early reporting of symptoms**
- **Guidelines for treatment modification for patients experiencing ocular complications of ADCs**
- **Utility of other prophylactic and supportive care measures to mitigate and/or manage ocular toxicities**
- **Importance of interdisciplinary coordination with eye-care professionals in the identification and management of treatment-related ocular events**

Gastrointestinal and Other Side Effects of ADCs

Dr Hamilton
Nashville, Tennessee

Dr Rugo
San Francisco, California

- **Rates of various gastrointestinal issues, such as nausea/vomiting, diarrhea, decreased appetite and constipation, among patients receiving ADC therapy**
- **Role of prophylactic antiemetics and/or antidiarrheals for patients about to begin treatment with an ADC**
- **Educating patients regarding strategies to maintain proper nutrition during treatment**
- **Role of complementary therapies such as acupuncture in managing gastrointestinal side effects of ADCs**
- **Incidence and management of peripheral neuropathy associated with various ADCs**
- **Strategies to mitigate the potential psychosocial ramifications of visible side effects of ADC treatment, such as alopecia**
- **Spectrum of other toxicities associated with 1 or more ADCs used in the treatment of cancer, such as fatigue, cutaneous reactions, hemorrhage, effusion/edema and hyperglycemia**
- **Collaborative role of oncology nurses in comprehensive biopsychosocial care for patients with cancer; capacity to optimize clinical and quality-of-life outcomes with anticancer therapies, including ADCs**

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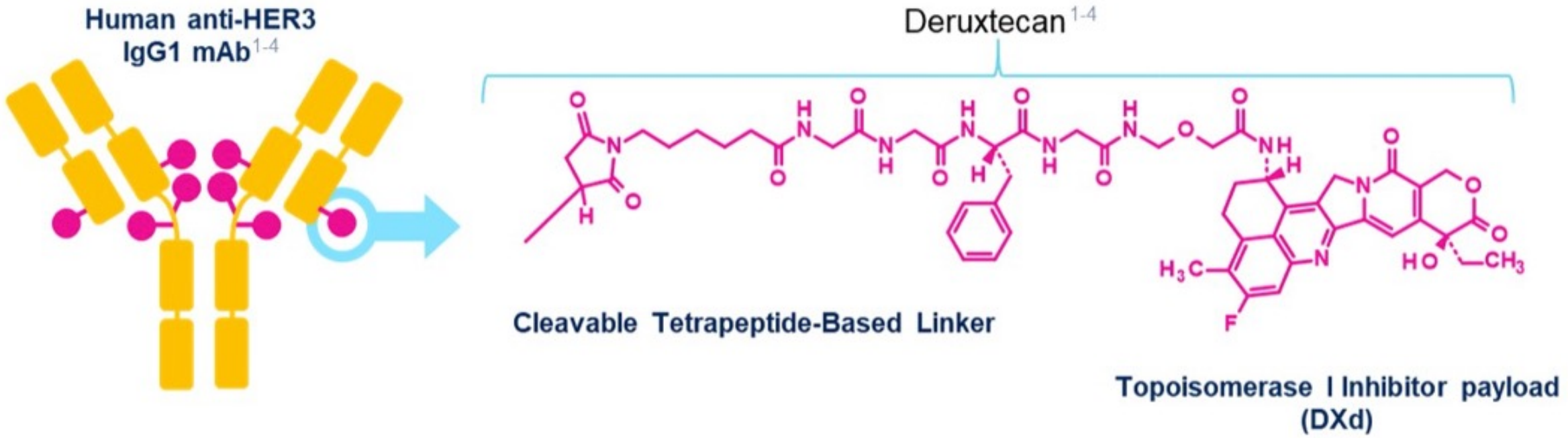
Patritumab Deruxtecan (HER3-DXd) Targeting HER3 May Address Multiple EGFR TKI Resistance Mechanisms in NSCLC

HER3-DXd is an antibody-drug conjugate with 3 components:

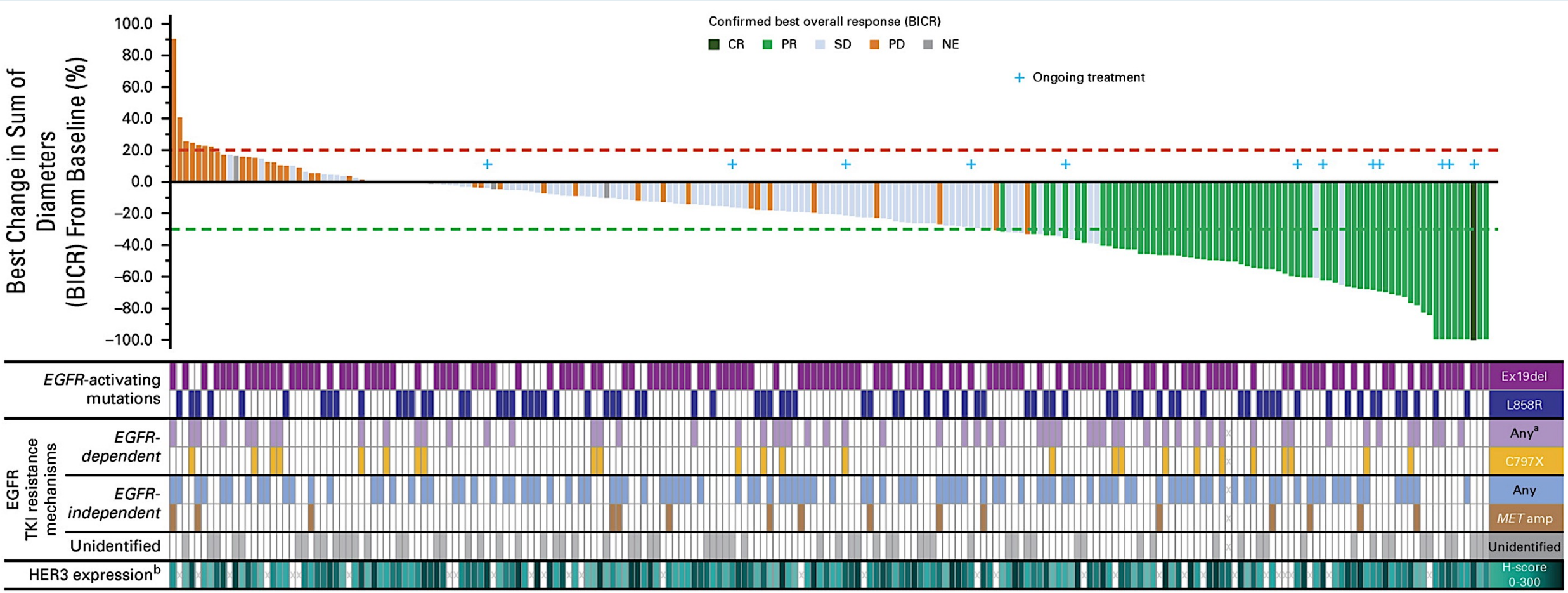
- A fully human anti-HER3 IgG1 mAb (patritumab), covalently linked to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleaver linker



TKI = tyrosine kinase inhibitor

Janne PA et al. ASCO 2021;Abstract 9007.

Patritumab Deruxtecan Demonstrated Efficacy for NSCLC with EGFR Mutations in the Phase II HERTHENA-Lung01 Study



CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = not evaluated

Yu HA et al. *J Clin Oncol* 2023;41(35):5363-75.

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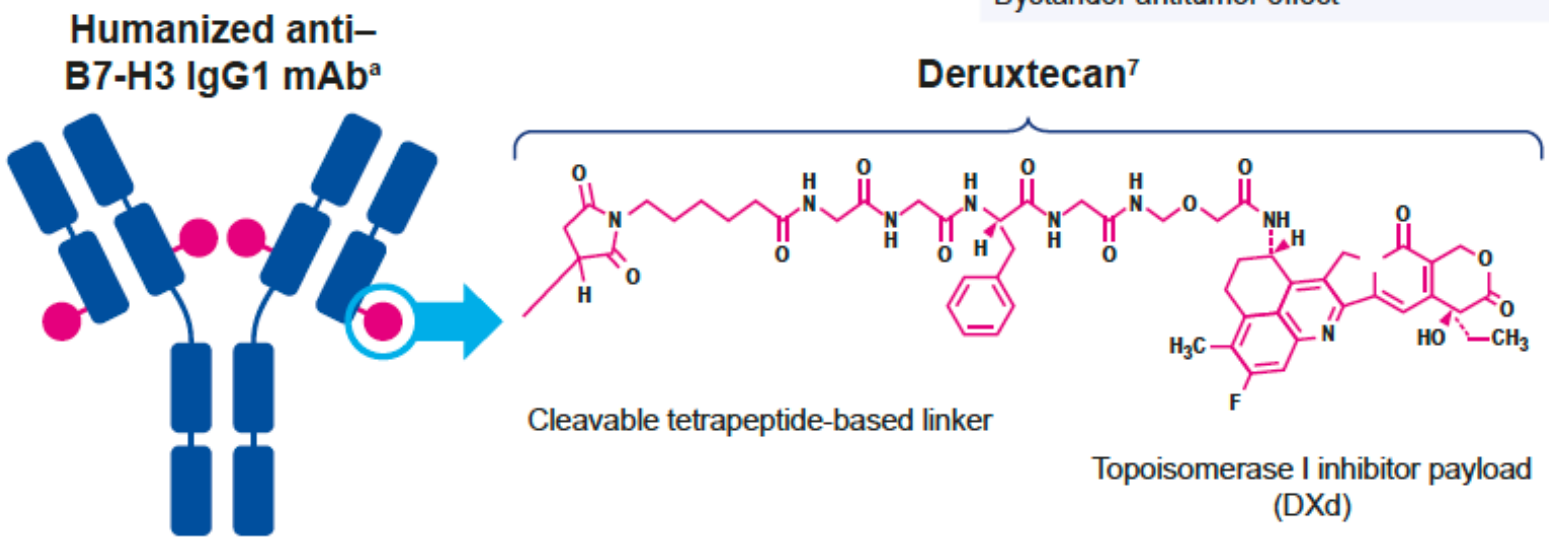
Ifinatamab Deruxtecan (I-DXd)

Figure 1: I-DXd was Designed with 7 Key Attributes

- I-DXd is a B7-H3–directed ADC composed of three parts[7–11]:
  - A humanized anti–B7-H3 IgG1 mAb
  - A topoisomerase I inhibitor payload (an exatecan derivative, DXd)
  - A tetrapeptide-based cleavable linker that covalently bonds the other two components

Payload mechanism of action: topoisomerase I inhibitor[7,9,11,b]
High potency of payload[7,11,b]
Optimized drug-to-antibody ratio ≈4[7–10,12,b]
Payload with short systemic half-life[7,11,b,c]
Stable linker-payload[7,11,b]
Tumor-selective cleavable linker[7,11,b]
Bystander antitumor effect[7,9,11,12,b]

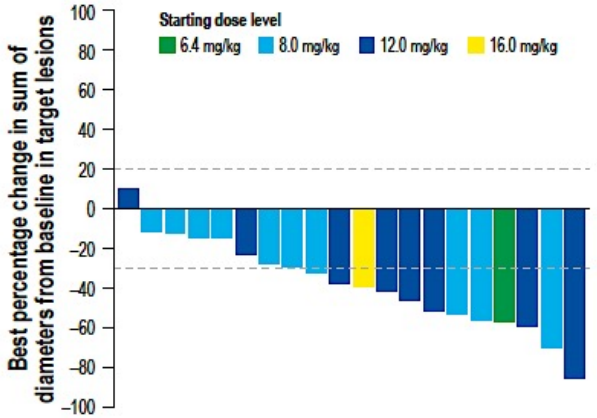


[a]Image is for illustrative purposes only; actual drug positions may vary. [b]The clinical relevance of these features is under investigation. [c]Based on animal data.

Patel MR et al. ESMO 2023;Abstract 690P.

Phase I/II Study of Ifinatamab Deruxtecan for Advanced Solid Tumors

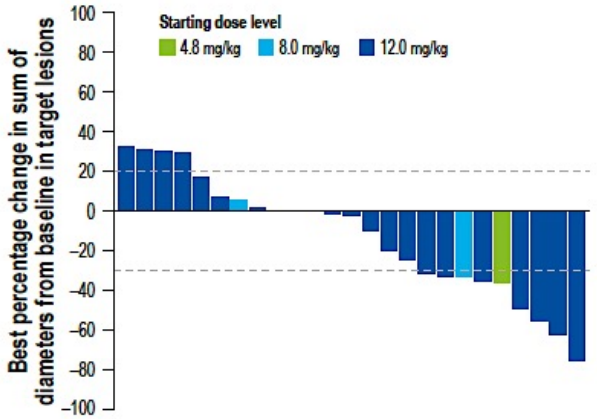
A) SCLC[3]



	SCLC
Efficacy population (≥4.8 mg/kg)	**n=21**
Confirmed ORR, n (%; 95% CI)	11 (52.4; 29.8–74.3)
Confirmed CR, n (%)	1 (4.8)
Confirmed PR, n (%)	10 (47.6)
TTR, median (95% CI), months	1.2 (1.2–1.4)
DOR, median (95% CI), months	5.9 (2.8–7.5)
Median PFS, months (95% CI)	5.6 (3.9–8.1)
Median OS, months (95% CI)	12.2 (6.4–NE)
Follow-up, median (95% CI), months	11.7 (4.6–12.9)
Safety population (all doses)	**n=22**
Number of prior systemic regimens, median (range)	2 (1–7)
Platinum-based chemotherapy, n (%)	22 (100)
Immunotherapy, n (%)	18 (81.8)
Irinotecan or topotecan, n (%)	5 (22.7)[a]
Topotecan, n (%)	3 (13.6)

[a]One patient received both.
Change from baseline in target lesions was assessed per RECIST v1.1. All 21 patients were evaluable at baseline, but one did not have any post-baseline tumor assessments, and so was not included in the waterfall plot.

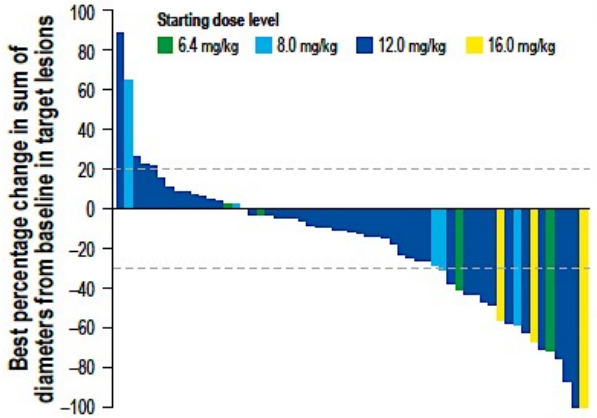
B) ESCC



	ESCC
Efficacy population (≥4.8 mg/kg)	**n=28**
Confirmed ORR, n (%; 95% CI)	6 (21.4; 8.3–41.0)
Confirmed PR, n (%)	6 (21.4)
TTR, median (95% CI), months	1.4 (1.2–NE)
DOR, median (95% CI), months	3.5 (2.4–NE)
Median PFS, months (95% CI)	2.8 (2.1–5.5)
Median OS, months (95% CI)	7.0 (4.8–12.2)
Follow-up, median (95% CI), months	14.9 (6.3–NE)
Safety population (all doses)	**n=29**
Number of prior systemic regimens, median (range)	4 (1–7)
Cisplatin/carboplatin/oxaliplatin, n (%)	29 (100)
Taxane, n (%)	21 (72.4)
Immunotherapy, n (%)	27 (93.1)

Change from baseline in target lesions was assessed per RECIST v1.1. Of 28 patients with measurable disease at baseline, three did not have post-baseline tumor assessments, and so were not included in the waterfall plot.

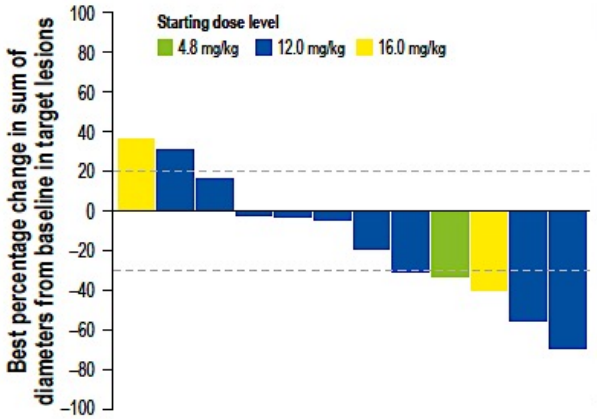
C) mCRPC



	mCRPC
Efficacy population (≥4.8 mg/kg)	**n=73**
Confirmed ORR, n (%; 95% CI)[a]	15 (25.4; 15.0–38.4)
Confirmed PR, n (%)	15 (25.4)
Confirmed ORR in patients with liver mets at baseline (27/59, 45.8% of mCPRC efficacy population ≥4.8 mg/kg), n (%)	9 (33.3)
TTR, median (95% CI), months[a]	1.4 (1.2–2.6)
DOR, median (95% CI), months[a]	6.4 (3.0–10.0)
Median PFS, months (95% CI)[b]	5.3 (4.1–6.9)
Median OS, months (95% CI)[b]	13.0 (10.3–16.0)
Follow-up, median (95% CI), months[b]	16.6 (14.5–18.6)
Safety population (all doses)	**n=75**
Number of prior systemic regimens, median (range)	6 (1–11)
Taxane, n (%)	61 (81.3)
NHA, n (%)	72 (96.0)

[a]The ORR is calculated based on 59 patients who received ≥1 dose ≥4.8 mg/kg, had measurable disease at baseline, ≥2 postbaseline scans, and/or discontinued treatment for any reason at data cutoff. [b]n=73, including patients with bone metastases who were not evaluable for ORR.
Change from baseline in target lesions was assessed per RECIST v1.1. Two patients did not have any post-baseline tumor assessments and were not included in the waterfall plot.

D) sqNSCLC



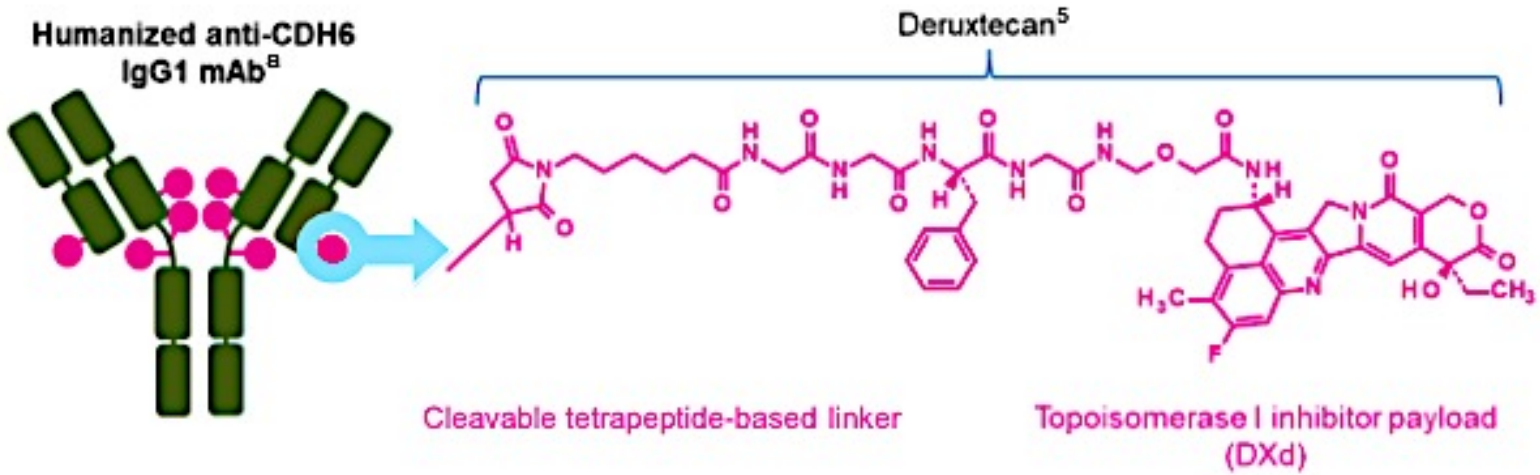
	sqNSCLC
Efficacy population (≥4.8 mg/kg)	**n=13**
Confirmed ORR, n (%; 95% CI)	4 (30.8, 9.1–61.4)
Confirmed PR, n (%)	4 (30.8)
TTR, median (95% CI), months	1.3 (0.7–NE)
DOR, median (95% CI), months	4.1 (2.8–NE)
Follow-up, median (95% CI), months	5.2 (1.7–NE)
Safety population (all doses)	**n=18**
Number of prior systemic regimens, median (range)	3 (1–12)
Platinum-based chemotherapy, n (%)	18 (100)
Immunotherapy, n (%)	18 (100)
Taxane, n (%)	16 (88.9)

Change from baseline in target lesions was assessed per RECIST v1.1. One patient did not have any post-baseline tumor assessments and was not included in the waterfall plot. Since enrollment in the sqNSCLC cohort is ongoing, analyses of PFS and OS in this cohort are not yet mature.

Patel MR et al. ESMO 2023;Abstract 690P.

RTP RESEARCH TO PRACTICE

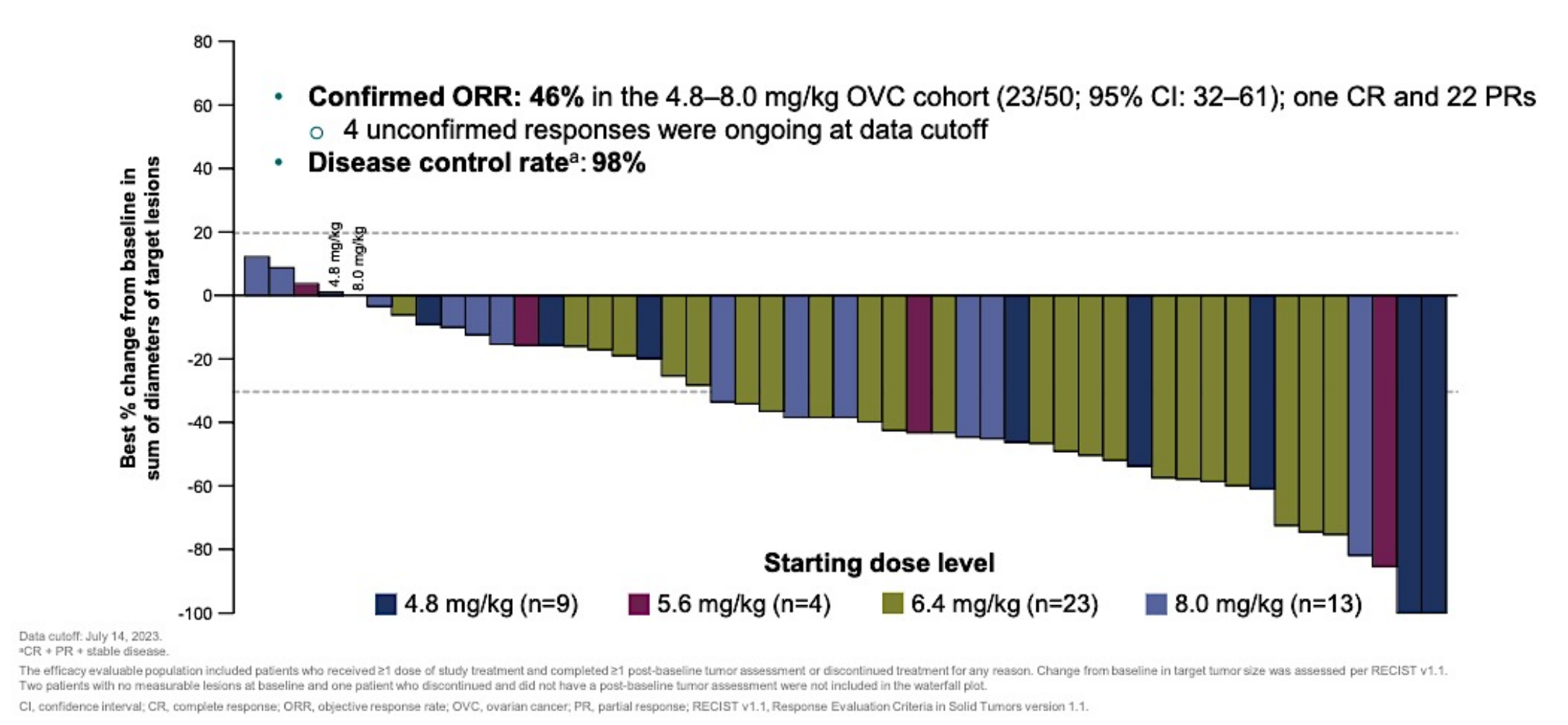
Raludotatug Deruxtecan (R-DXd)



- Payload mechanism of action: topoisomerase I inhibitor[5,b]
- High potency of payload[5,b]
- High drug-to-antibody ratio ≈8[5,b]
- Payload with short systemic half-life[6,b,c]
- Stable linker-payload[5,b]
- Tumor-selective cleavable linker[5,b]
- Bystander antitumor effect[5,b]

Moore K et al. ESMO 2023;Abstract 745MO.

Phase I Study of Raludotatug Deruxtecan for Pretreated Ovarian Cancer



Data cutoff: July 14, 2023.
[a]CR + PR + stable disease.

The efficacy evaluable population included patients who received ≥1 dose of study treatment and completed ≥1 post-baseline tumor assessment or discontinued treatment for any reason. Change from baseline in target tumor size was assessed per RECIST v1.1. Two patients with no measurable lesions at baseline and one patient who discontinued and did not have a post-baseline tumor assessment were not included in the waterfall plot.

CI, confidence interval; CR, complete response; ORR, objective response rate; OVC, ovarian cancer; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Moore K et al. ESMO 2023;Abstract 745MO.

Consulting Nursing Faculty Comments

Importance of mentorship and giving back

Ronald Stein, JD, MSN, NP-C, AOCNP

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Consulting Nursing Faculty Comments

Humor in oncology

Kathleen D Burns, RN, MSN, AGACNP-BC, OCN

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APPENDIX

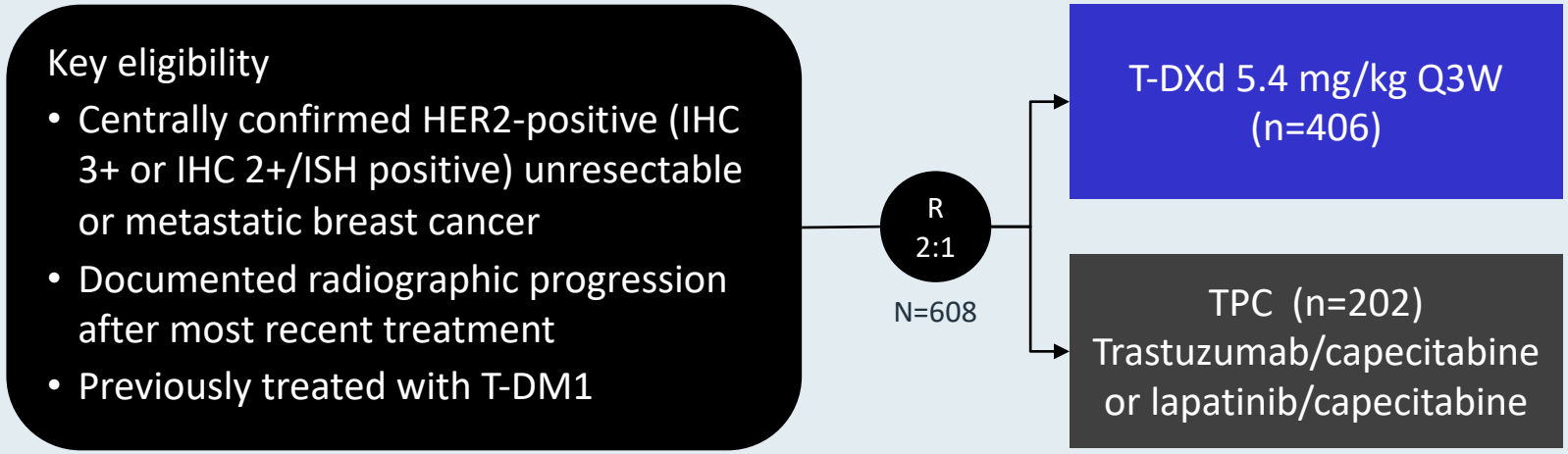
HER2-Targeted ADCs for Breast Cancer

Trastuzumab deruxtecan versus treatment of physician's choice in patients with HER2-positive metastatic breast cancer (DESTINY-Breast02): a randomised, open-label, multicentre, phase 3 trial

Fabrice André, Yeon Hee Park, Sung-Bae Kim, Toshimi Takano, Seock-Ah Im, Giuliano Borges, Joao Paulo Lima, Sercan Aksoy, Joaquin Gavila Gregori, Michelino De Laurentiis, Giampaolo Bianchini, Rebecca Roylance, Yasuo Miyoshi, Anne Armstrong, Rajni Sinha, Manuel Ruiz Borrego, Elgene Lim, Johannes Ettl, Rinat Yerushalmi, Flora Zagouri, Francois P Duhoux, Tanja Fehm, Dhiraj Gambhire, Jillian Cathcart, Cai Wu, Changan Chu, Anton Egorov, Ian Krop

***Lancet* 2023;401(10390):1773-85**

DESTINY-Breast02: Phase III Trial Schema



Primary endpoint:
- PFS (BICR)

Key secondary endpoint:
- OS

Secondary endpoints:
- ORR (BICR)
- DOR (BICR)
- PFS (investigator)
- Safety

Exploratory endpoints:
- CBR (BICR)
- PFS2 (investigator)

Median (range) follow-up duration at data cutoff (June 30, 2022):
- **T-DXd: 21.5 months (range, 0.1-45.6 months)**
- **TPC: 18.6 months (range, 0-45.7 months)**

Protocol-prespecified statistical analysis plan:
- Primary analysis planned for ~372 BICR PFS events observed or 18 months from the last patient randomized (whichever came first)
- Group sequential testing used to compare OS between treatment groups hierarchically, provided PFS was significant

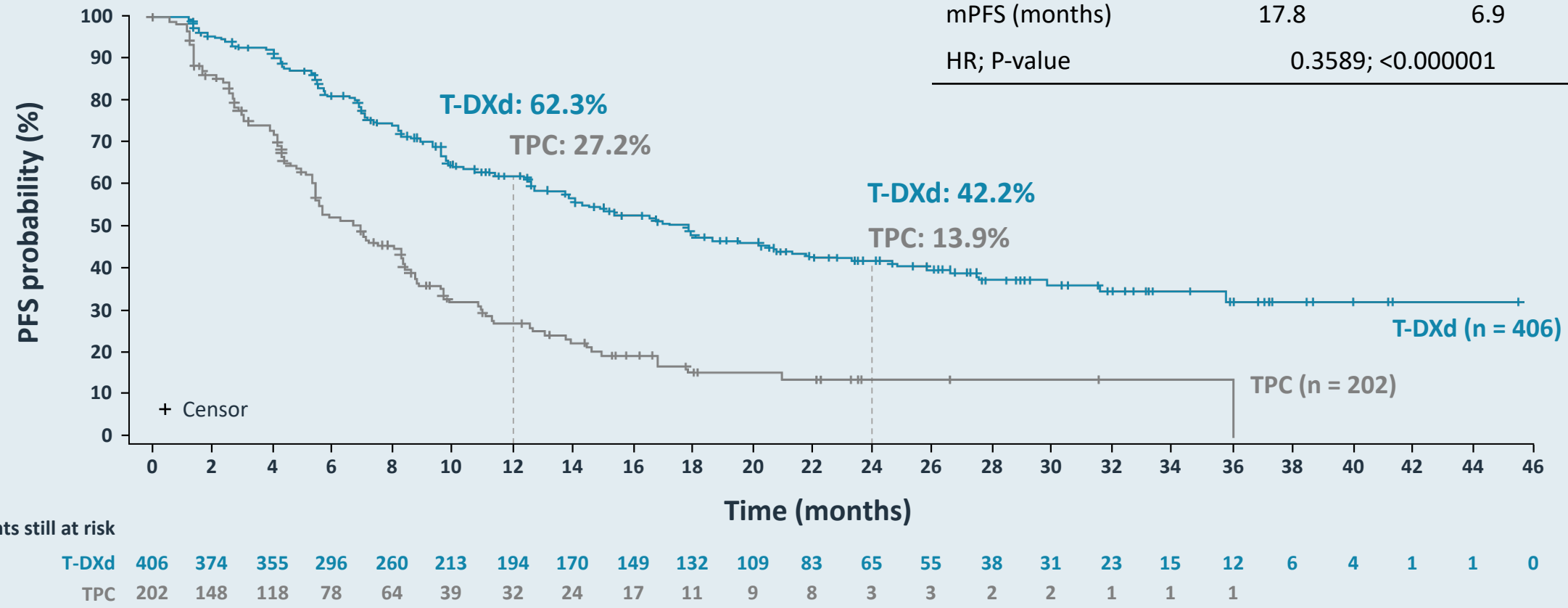
BICR = blinded independent central review; CBR = clinical benefit rate; DOR = duration of response; ORR = objective response rate; T-DXd = trastuzumab deruxtecan; T-DM1 = trastuzumab emtansine; TPC = treatment of physician's choice

Krop I et al. San Antonio Breast Cancer Symposium 2022;Abstract GS2-01.

Courtesy of Giuseppe Curigliano, MD, PhD

DESTINY-Breast02: Progression-Free Survival

	T-DXd	TPC
mPFS (months)	17.8	6.9
HR; P-value	0.3589; <0.000001	

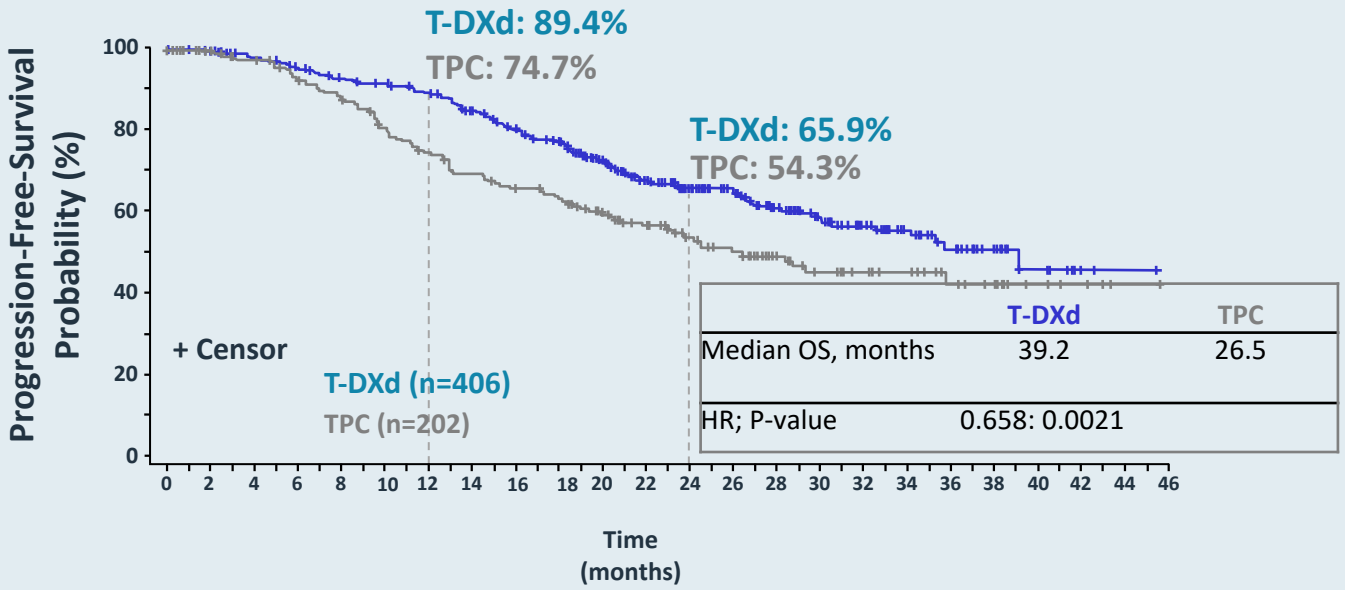


T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice

Andre F et al. *Lancet* 2023;401(10390):1773-85; Krop I et al. San Antonio Breast Cancer Symposium 2022;Abstract GS2-01.

RTP RESEARCH TO PRACTICE

DESTINY-Breast02: Overall Survival and Objective Response Rate



Data are n (%) or months (95% CI)	T-DXd (n = 406)	TPC (n = 202)
Confirmed ORR by BICR [95% CI]	283 (69.7) [65.0, 74.1]	59 (29.2) [23.0, 36.0]
	P <0.0001	
Confirmed best overall response		
CR	57 (14.0)	10 (5.0)
PR	226 (55.7)	49 (24.3)
SD	95 (23.4)	94 (46.5)
PD	19 (4.7)	26 (12.9)
Not evaluable	9 (2.2)	23 (11.4)
mDOR by BICR, months	19.6 (15.9, NE)	8.3 (5.8, 9.5)
CBR by BICR	82.3 (78.2, 85.9)	46.0 (39.0, 53.2)
mPFS by investigator, months	16.7 (14.3, 19.6)	5.5 (4.4, 7.0)
mPFS, months	35.8 (28.4, NE)	15.8 (13.5, 21.0)

In the TPC arm:

- 69.3% of patients received a new systemic therapy
- 25.7% of patients received T-DXd in the post-trial setting

TPC = treatment of physician's choice

Andre F et al. *Lancet* 2023;401(10390):1773-85; Krop I et al. San Antonio Breast Cancer Symposium 2022;Abstract GS2-01.

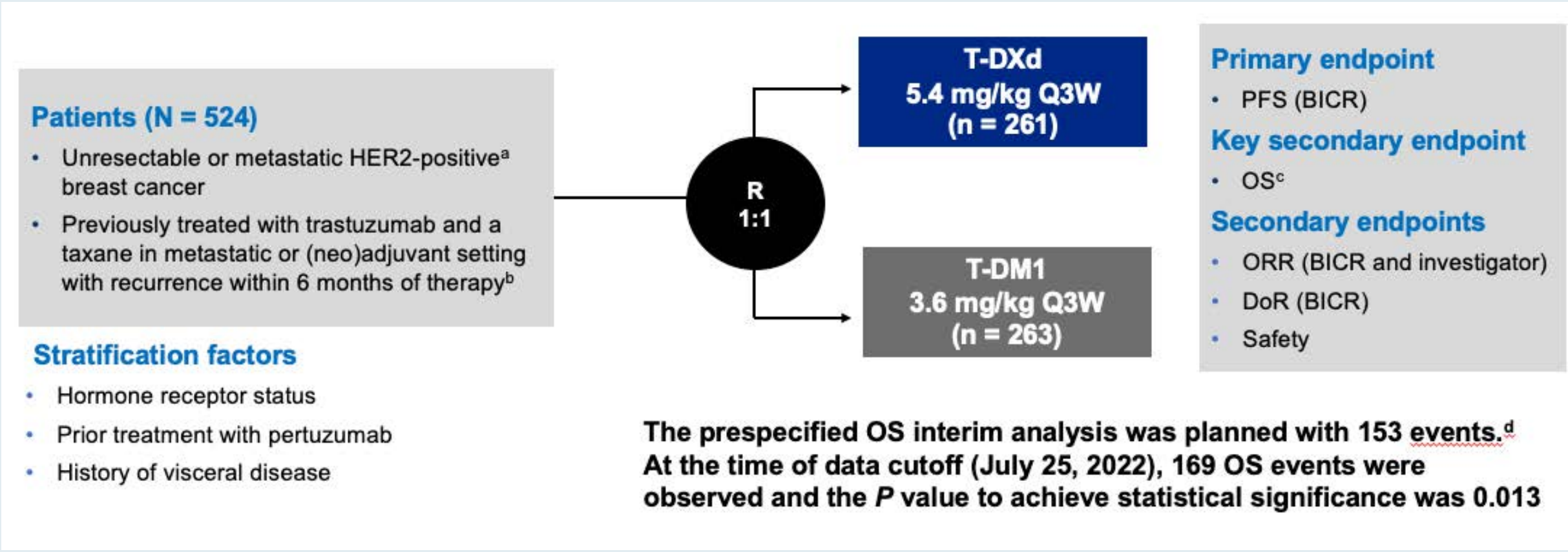
Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial

Sara A Hurvitz, Roberto Hegg, Wei-Pang Chung, Seock-Ah Im, William Jacot, Vinod Ganju, Joanne Wing Yan Chiu, Binghe Xu, Erika Hamilton, Srinivasan Madhusudan, Hiroji Iwata, Sevilay Altintas, Jan-Willem Henning, Giuseppe Curigliano, José Manuel Perez-Garcia, Sung-Bae Kim, Vanessa Petry, Chiun-Sheng Huang, Wei Li, Jean-Sebastien Frenel, Silvia Antolin, Winnie Yeo, Giampaolo Bianchini, Sherene Loi, Junji Tsurutani, Anton Egorov, Yali Liu, Jillian Cathcart, Shahid Ashfaque, Javier Cortés

***Lancet* 2023;401:105-17.**

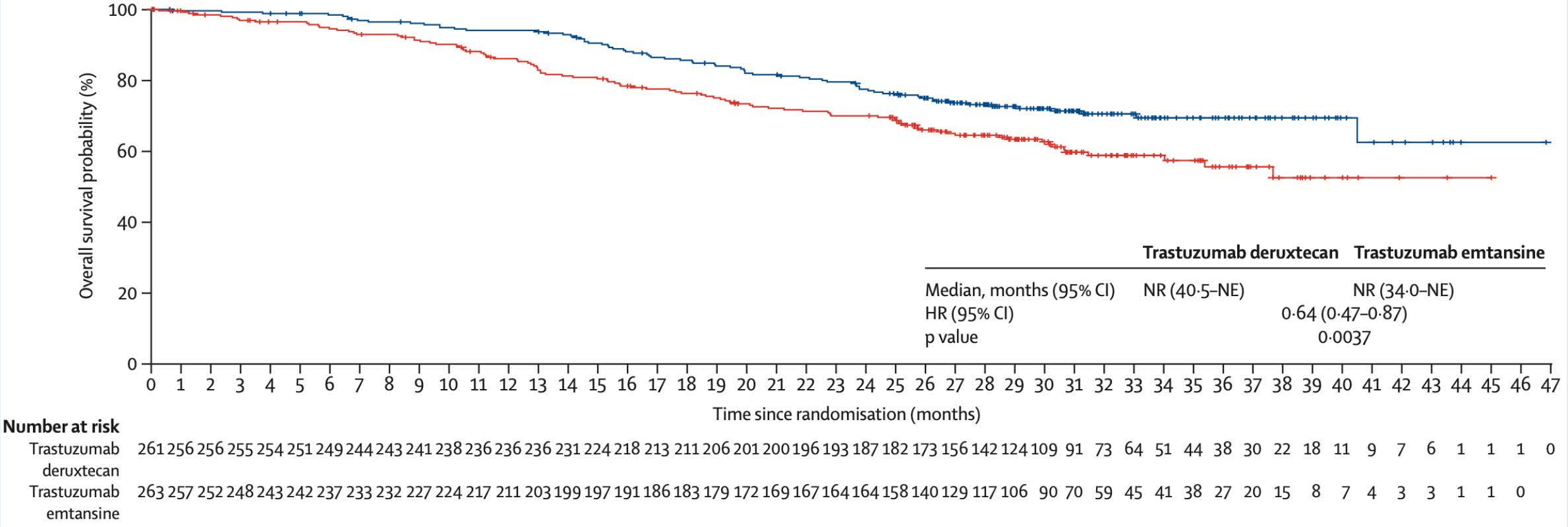
RTP RESEARCH TO PRACTICE

DESTINY-Breast03: Phase III Trial Schema



Hurvitz SA et al. San Antonio Breast Cancer Symposium 2022;Abstract GS2-02.

DESTINY-Breast03: Overall Survival



Hurvitz SA et al. *Lancet* 2023;401:105-17.

The Incidence and Management of Interstitial Lung Disease (ILD) with ADCs

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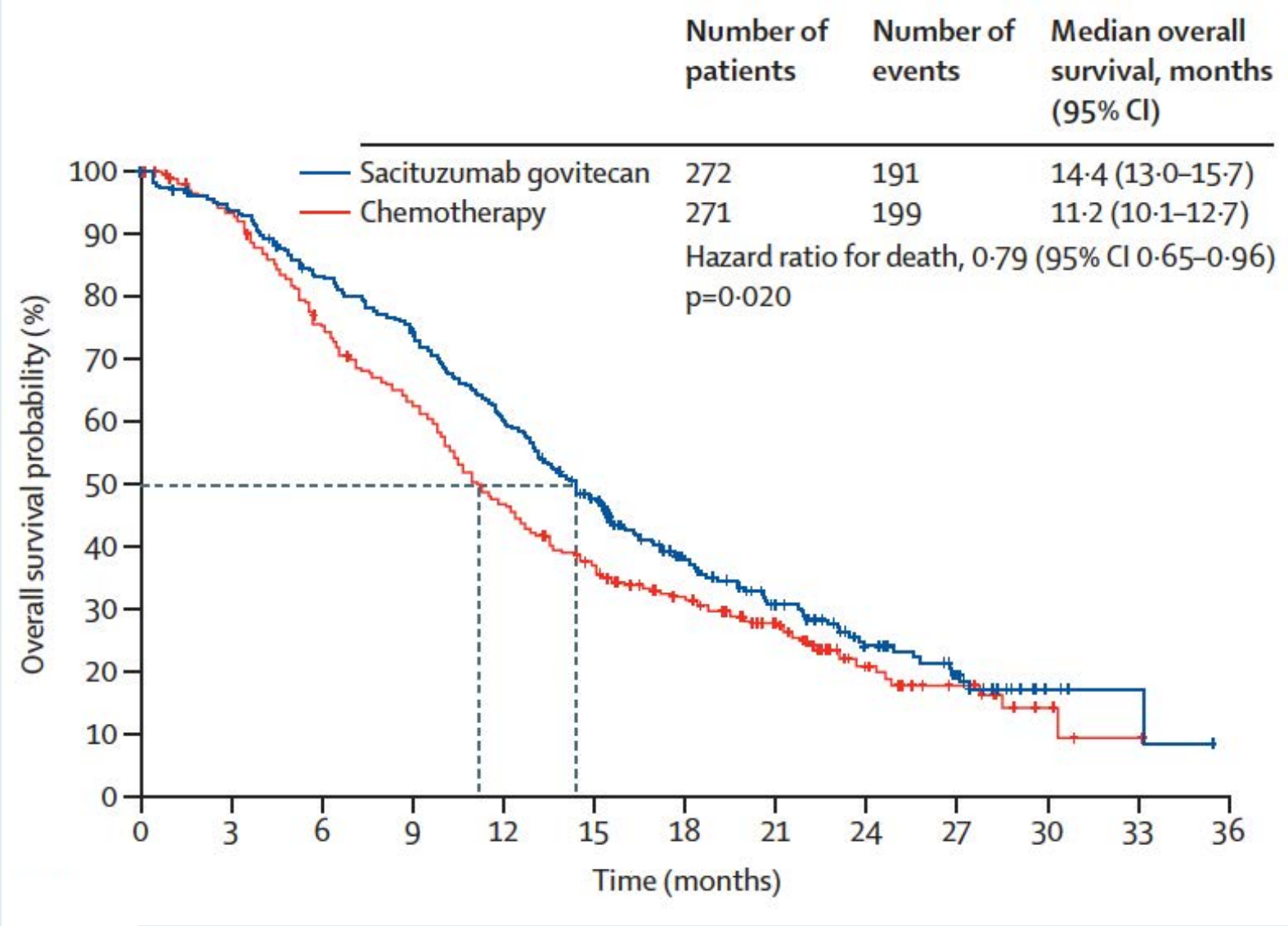
ADCs Targeting Other Signaling Pathways in Breast Cancer — Sacituzumab Govitecan, Datopotamab Deruxtecan, Patritumab Deruxtecan

Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial

Hope S Rugo, Aditya Bardia*, Frederik Marmé, Javier Cortés, Peter Schmid, Delphine Loirat, Olivier Trédan, Eva Ciruelos, Florence Dalenc, Patricia Gómez Pardo, Komal L Jhaveri, Rosemary Delaney, Theresa Valdez, Hao Wang, Monica Motwani, Oh Kyu Yoon, Wendy Verret, Sara M Tolaney*

***Lancet* 2023;402(10411):1423-33.**

TROPiCS-02: Overall Survival in the Intention-to-Treat Population



Rugo HS et al. *Lancet* 2023;402(10411):1423-33.

Safety Profile in TROPiCS-02

TRAEs, n (%)		SG (n=268)		TPC (n=249)	
		All grade	Grade ≥3	All grade	Grade ≥3
Hematologic	**Neutropenia[b]**	188 (70)	**136 (51)**	134 (54)	**94 (38)**
	Anemia[c]	91 (34)	17 (6)	62 (25)	8 (3)
	Leukopenia[d]	37 (14)	23 (9)	23 (9)	13 (5)
	Lymphopenia[e]	31 (12)	10 (4)	25 (10)	8 (3)
	Febrile neutropenia	**14 (5)**	**14 (5)**	**11 (4)**	**11 (4)**
Gastrointestinal	**Diarrhea**	152 (57)	**25 (9)**	41 (16)	**3 (1)**
	Nausea	148 (55)	3 (1)	77 (31)	7 (3)
	Vomiting	50 (19)	1 (<1)	30 (12)	4 (2)
	Constipation	49 (18)	0	36 (14)	0
	Abdominal pain	34 (13)	2 (1)	17 (7)	0
Other	Alopecia	123 (46)	0	41 (16)	0
	Fatigue	100 (37)	15 (6)	73 (29)	6 (2)
	Asthenia	53 (20)	5 (2)	37 (15)	2 (1)
	Decreased appetite	41 (15)	1 (<1)	34 (14)	1 (<1)
	Neuropathy[f]	23 (9)	3 (1)	38 (15)	6 (2)

There were no events of interstitial lung disease in the SG arm (vs 1% in the TPC arm) and no TRAEs of cardiac failure or left ventricular dysfunction in either arm

Rugo HS et al. *Lancet* 2023;402(10411):1423-33. Rugo HS et al. ASCO 2022;Abstract LBA1001.

Randomized phase 3 study of datopotamab deruxtecan vs chemotherapy for patients with previously-treated inoperable or metastatic hormone receptor-positive, HER2-negative breast cancer: Results from TROPION-Breast01

Aditya Bardia,[1] Komal Jhaveri,[2] Seock-Ah Im,[3] Michelino De Laurentiis,[4] Binghe Xu,[5] Sonia Pernas,[6] Giuliano Borges,[7] David W. Cescon,[8] Masaya Hattori,[9] Yen-Shen Lu,[10] Noelia Martínez Jañez,[11] Erika Hamilton,[12] Shusen Wang,[13] Junji Tsurutani,[14] Kevin Kalinsky,[15] Lu Xu,[16] Sabrina Khan,[17] Neelima Denduluri,[17] Hope S. Rugo,[18*] Barbara Pistilli[19*]

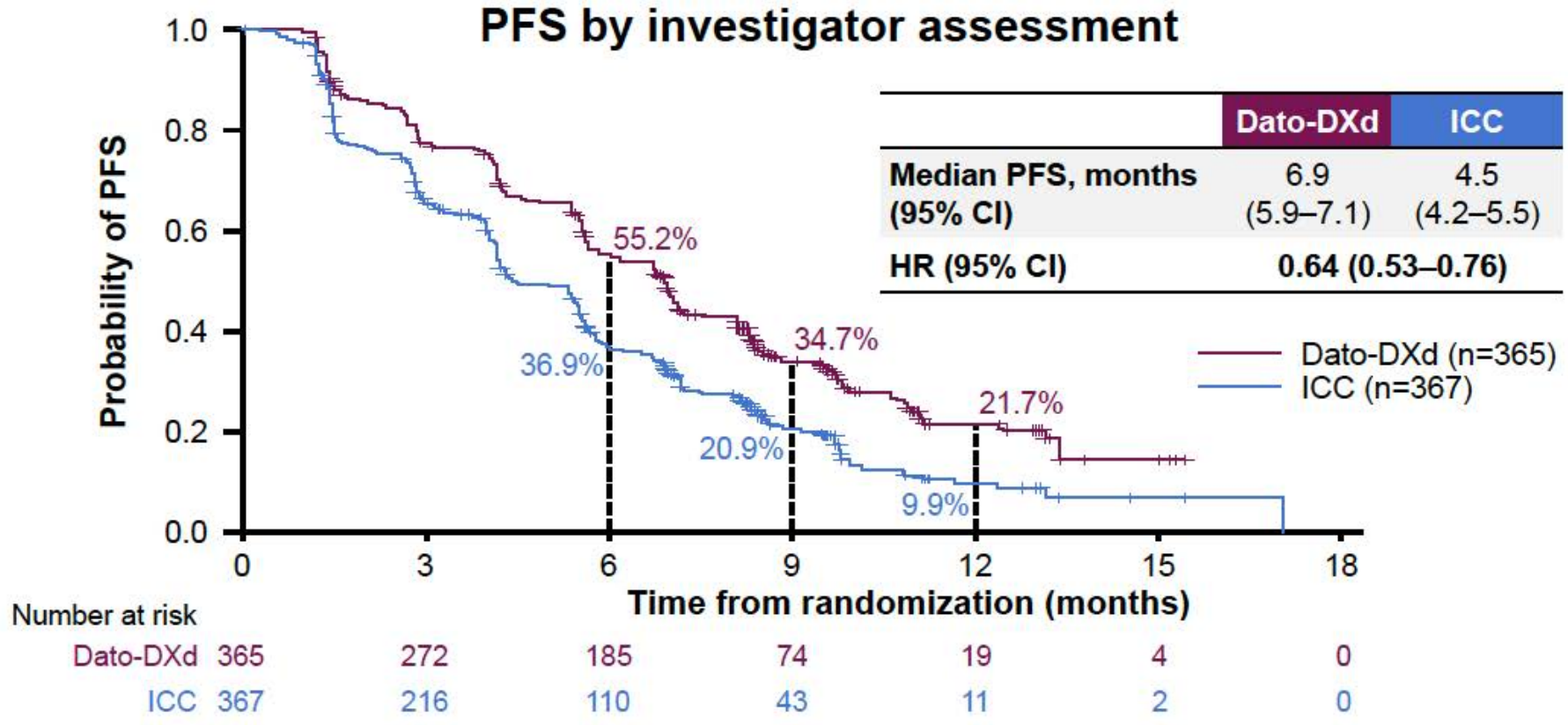
*Contributed equally.

[1]Mass General Cancer Center, Harvard Medical School, Boston, MA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA, and Weill Cornell Medical College, New York, NY, USA; [3]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; [4]Istituto Nazionale Tumori Napoli IRCCS "Fondazione Pascale", Napoli, Italy; [5]National Cancer Center / National Clinical Research Center for Cancer / Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [6]Institut Català d'Oncologia, IDIBELL, L'Hospitalet, Barcelona, Spain; [7]Catarina Pesquisa Clínica, Santa Catarina, Brazil; [8]Princess Margaret Cancer Centre/UHN, Toronto, ON, Canada; [9]Aichi Cancer Center, Nagoya, Japan; [10]National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan; [11]Ramón y Cajal University Hospital, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain; [12]Sarah Cannon Research Institute / Tennessee Oncology, Nashville, TN, USA; [13]Cancer Center of Sun Yet-sen University, Guangzhou, China; [14]Showa University Hospital, Tokyo, Japan; [15]Winship Cancer Institute at Emory University, Atlanta, GA, USA; [16]AstraZeneca, New York, NY, USA; [17]AstraZeneca, Gaithersburg, MD, USA; [18]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; [19]Gustave Roussy Cancer Center, Villejuif, France.

San Antonio Breast Cancer Symposium 2023;Abstract GS02-01.

RTP RESEARCH TO PRACTICE

TROPION-Breast01: Progression-Free Survival



	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)**	

PFS by BICR (primary endpoint)[1]: Median 6.9 vs 4.9 months; HR 0.63 (95% CI 0.52–0.76); P<0.0001

Data cut-off: 17 July 2023.

1. Bardia A, et al. Oral Presentation at ESMO 2023; Abstract LBA11.

Bardia A et al. San Antonio Breast Cancer Symposium 2023;Abstract GS02-01.

Original Reports | Breast Cancer

Patritumab Deruxtecan (HER3-DXd), a Human Epidermal Growth Factor Receptor 3–Directed Antibody-Drug Conjugate, in Patients With Previously Treated Human Epidermal Growth Factor Receptor 3–Expressing Metastatic Breast Cancer: A Multicenter, Phase I/II Trial

Ian E. Krop, MD, PhD[1]; Norikazu Masuda, MD, PhD[2]; Toru Mukohara, MD, DMedSci[3]; Shunji Takahashi, MD, PhD[4]; Takahiro Nakayama, MD, PhD[5]; Kenichi Inoue, MD, PhD[6]; Hiroji Iwata, MD, PhD[7]; Yutaka Yamamoto, MD, PhD[8]; Ricardo H. Alvarez, MD, MSc[9]; Tatsuya Toyama, MD, PhD[10]; Masato Takahashi, MD[11]; Akihiko Osaki, MD, PhD[12]; Shigehira Saji, MD, PhD[13]; Yasuaki Sagara, MD, MPH[14]; Joyce O'Shaughnessy, MD[15]; Shoichi Ohwada, PhD[16]; Kumiko Koyama, PhD[16]; Tatsuya Inoue, MD, PhD[17]; Li Li, PhD[18]; Parul Patel, MS[18]; Joseph Mostillo, PharmD[18]; Yoshimi Tanaka, MA[18]; David W. Sternberg, MD, PhD[18]; Dalila Sellami, MD[18]; and Kan Yonemori, MD, PhD[19]

J Clin Oncol 2023;41:5550-60.

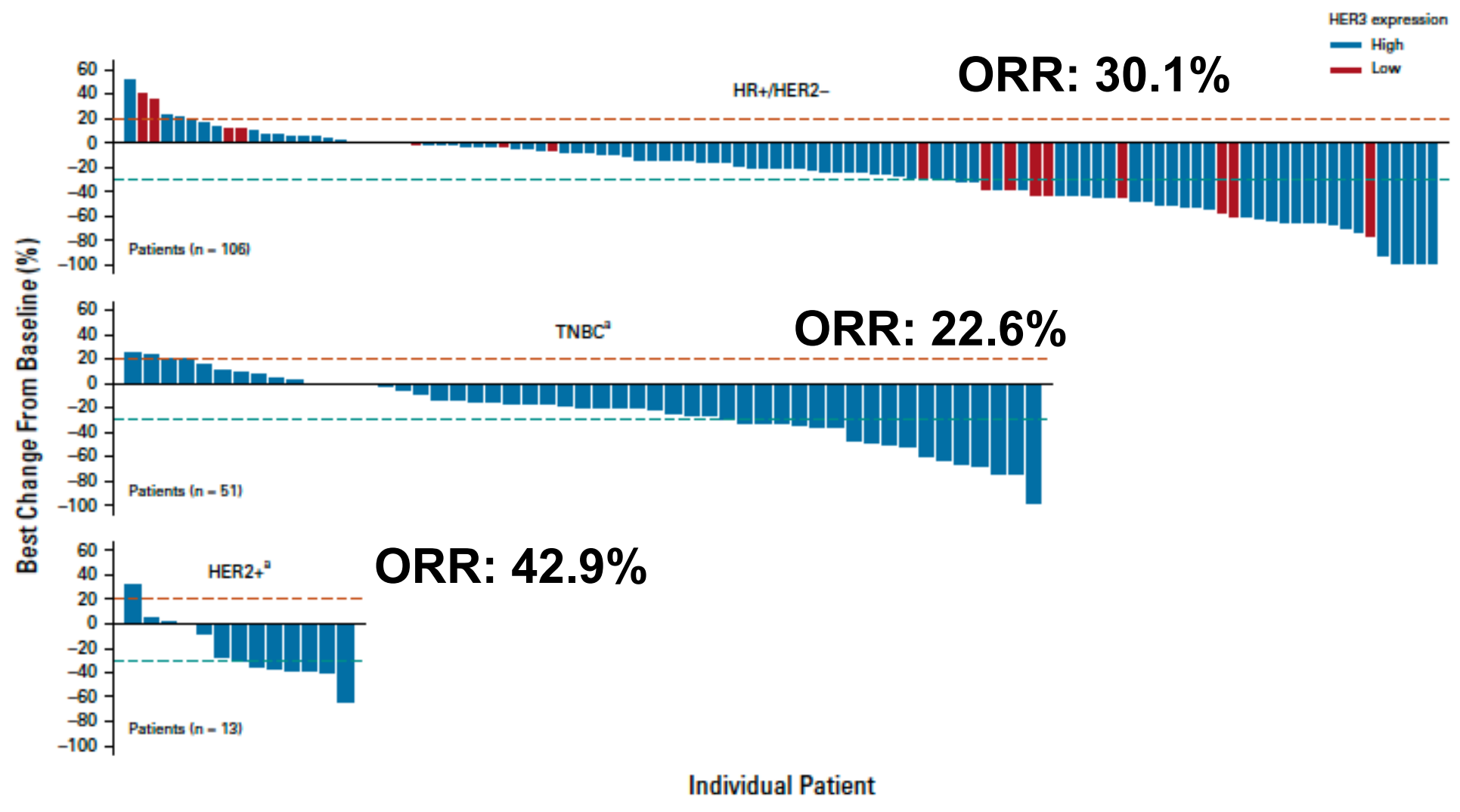
Phase I/II Efficacy of Patritumab Deruxtecan by Breast Cancer Subtype

Outcome (BICR per RECIST 1.1)	HR+/HER2− (n = 113) HER3-High[a] and HER3-Low	TNBC (n = 53) HER3-High[a]	HER2+ (n = 14) HER3-High[a]
Confirmed ORR (95% CI), %[b]	30.1 (21.8 to 39.4)	22.6 (12.3 to 36.2)	42.9 (17.7 to 71.1)
Best overall response, %[c]			
PR	30.1	22.6	42.9
SD	50.4	56.6	50.0
PD	11.5	17.0	7.1
NE	8.0	3.8	0
DCR (95% CI), %	80.5 (72.0 to 87.4)	79.2 (65.9 to 89.2)	92.9 (66.1 to 99.8)
CBR (95% CI), %	43.4 (34.1 to 53.0)	35.8 (23.1 to 50.2)	50.0 (23.0 to 77.0)
DOR, median (95% CI), months	7.2 (5.3 to NE)	5.9 (3.0 to 8.4)	8.3 (2.8 to 26.4)
PFS, median (95% CI), months	7.4 (4.7 to 8.4)	5.5 (3.9 to 6.8)	11.0 (4.4 to 16.4)
Six-month PFS rate (95% CI), %	53.5 (43.4 to 62.6)	38.2 (24.2 to 52.0)	51.6 (22.1 to 74.8)
OS, median (95% CI), months	14.6 (11.3 to 19.5)	14.6 (11.2 to 17.2)	19.5 (12.2 to NE)

Krop IE et al. *J Clin Oncol* 2023;41:5550-60.

RTP RESEARCH TO PRACTICE

Best Percent Change in Tumor Size with Patritumab Deruxtecan for Previously Treated HER3-Positive Metastatic Breast Cancer



Krop IE et al. *J Clin Oncol* 2023;41:5550-60.

RTP RESEARCH TO PRACTICE

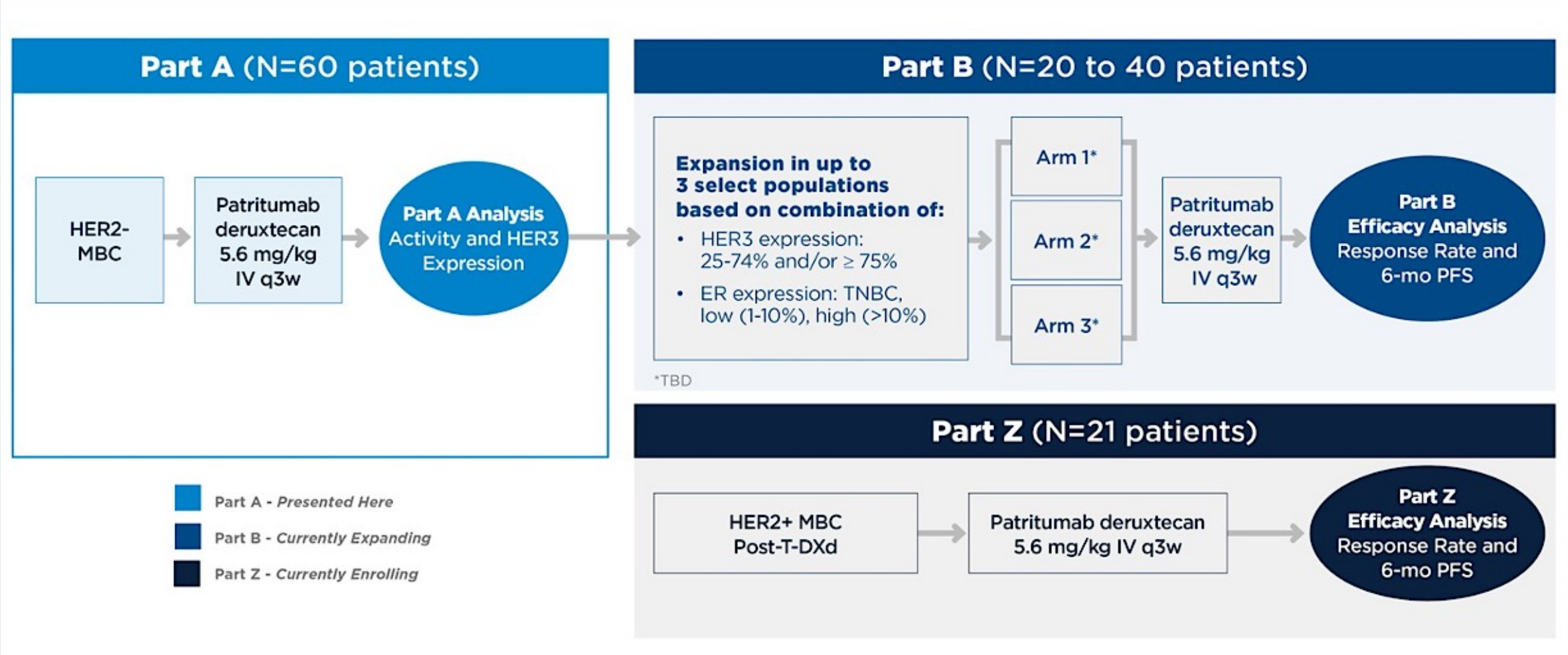
2023 ASCO ANNUAL MEETING

Abstract 1004

A Phase II Study of HER3-DXd in Patients with Metastatic Breast Cancer

Erika P. Hamilton, MD[1,2]; Ololade Dosunmu, MD, MPH[1]; Mythili Shastry, PhD[1]; Lindsey Finney, MS[1]; Dalila Sellami, MD[3]; David Sternberg, MD, PhD[3]; Vance Wright-Browne, MD[4]; Deborah Toppmeyer, MD[5]; William R. Gwin III, MD[6]; J. Thaddeus Beck, MD, FACP[7]; Jennifer Cultrera, MD[8]; Nusayba A. Bagegni, MD[9]; Katia Khoury, MD[10]; Arielle Heeke, MD[11]; Yuan Yuan, MD, PhD[12]

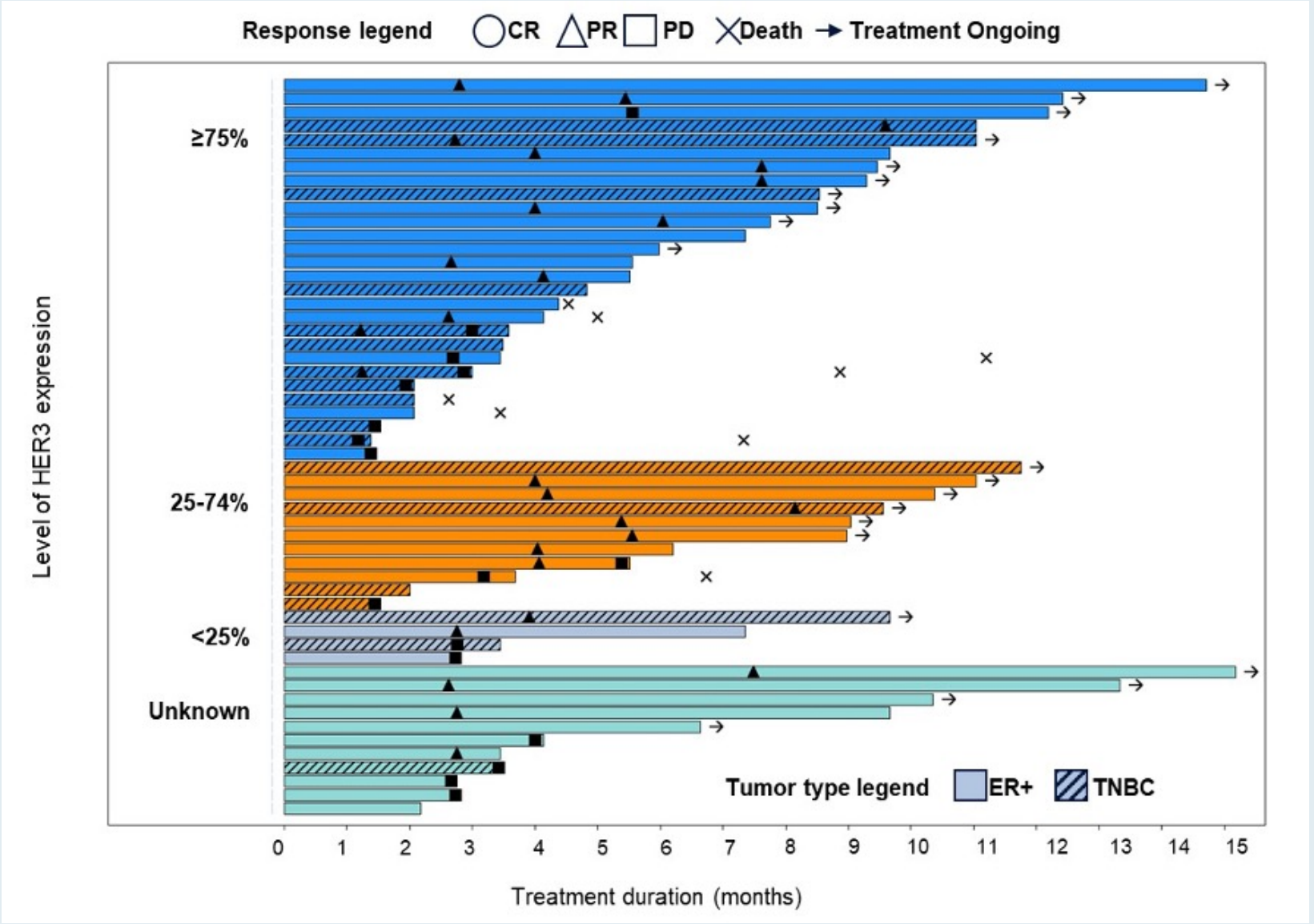
BRE-354: A Phase II Study of Patritumab Deruxtecan (HER3-DXd)



HER3 expression was not an enrollment criterion for Part A; HER3 expression was retrospectively assessed using immunohistochemistry.

Hamilton EP et al. ASCO 2023;Abstract 1004.

BRE-354: Duration on Study Treatment by HER3 Membrane Expression



Hamilton EP et al. ASCO 2023;Abstract 1004.

BRE-354: Author Conclusions

- Clinical activity of patritumab deruxtecan was observed across a broad range of HER3 membrane expression levels in patients with heavily pretreated ER+ and TN metastatic breast cancers.
  - This is consistent with emerging data:
    - SOLTI-TOT-HER3 reported an ORR of 30% to a *single dose* irrespective of HR status in patients with early HER2-negative BC (Oliviera M et al. ESMO BC 2023)
    - ICARUS-Breast01 reported an ORR of 29% in patients with HR+ MBC irrespective of level of HER3 expression (preliminary data) (Pistilli B et al. ESMO BC 2023)
- The safety profile of patritumab deruxtecan was manageable, with very low rates of Grade 3/4 adverse events.
- Data from this analysis supports the potential entry of patritumab deruxtecan into the therapeutic paradigm across MBC subtypes.
- Part B (currently expanding) and Part Z (HER2+ MBC after progression on T-DXd) are both enrolling patients irrespective of HER3 expression.

Hamilton EP et al. ASCO 2023;Abstract 1004.

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Optimal Implementation of Antibody-Drug Conjugates

Thursday, April 25, 2024
12:15 PM – 1:45 PM

Faculty

Jamie Carroll, APRN, MSN, CNP
Kelly EH Goodwin, MSN, RN, ANP-BC
Erika Hamilton, MD
Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Integrating New Research Information into Current Clinical Care

A Complimentary NCPD Hybrid Symposium Series Held During the 49th Annual ONS Congress

Chronic Lymphocytic Leukemia and Bispecific Antibodies in the Management of Lymphoma

Thursday, April 25, 2024

6:00 PM – 8:00 PM

Faculty

John N Allan, MD
Brad S Kahl, MD
Robin Klebig, MSN, APRN, CNP, AOCNP
Mollie Moran, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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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.

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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.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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