What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Management of HER2-Expressing Cancers Across the Oncology Spectrum: The Role of Antibody-Drug Conjugates

Thursday, April 27, 2023
6:00 PM – 7:30 PM

Faculty

Lyudmila A Bazhenova, MD
Kelly EH Goodwin, MSN, RN, ANP-BC
Virginia Kaklamani, MD, DSc
Caroline Kuhlman, MSN, APRN-BC
Alexis N McKinney, MSN, AGNP-BC
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Faculty

Lyudmila A Bazhenova, MD
Professor of Medicine
Lung Cancer Unit Leader
Director, Hematology and Oncology Fellowship Training Program
UC San Diego Moores Cancer Center
San Diego, California

Kelly EH Goodwin, MSN, RN, ANP-BC
Thoracic Cancer Center
Massachusetts General Hospital
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Virginia Kaklamani, MD, DSc
Professor of Medicine
Ruth McLean Bowman Bowers Chair in Breast Cancer Research and Treatment
AB Alexander Distinguished Chair in Oncology
Leader, Breast Oncology Program
UT Health San Antonio
MD Anderson Cancer Center
San Antonio, Texas

Caroline Kuhlman, MSN, APRN-BC
Nurse Practitioner
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Massachusetts General Hospital
Boston, Massachusetts

Alexis N McKinney, MSN, AGNP-BC
Adult-Gerontology Nurse Practitioner
Mays Cancer Center
UT Health San Antonio
MD Anderson Cancer Center
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Zev Wainberg, MD, MSc
Co-Director, GI Oncology Program
Director of Early Phase Clinical Research
Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Bazhenova — Disclosures

Consulting Agreements	AbbVie Inc, AnHeart Therapeutics, Bayer HealthCare Pharmaceuticals, Daiichi Sankyo Inc, Elevation Oncology, Genentech, a member of the Roche Group, Gilead Sciences Inc, InterVenn Biosciences, Janssen Biotech Inc, Merck, Mirati Therapeutics Inc, NEUVOGEN Inc, Novocure Inc, Regeneron Pharmaceuticals Inc, Sanofi, Turning Point Therapeutics Inc
Data and Safety Monitoring Board/Committee	ORIC Pharmaceuticals (completed)

Ms Goodwin — Disclosures

No relevant conflicts of interest to disclose

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Dr Kaklamani — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc, Puma Biotechnology Inc, TerSera Therapeutics LLC
Contracted Research	Eisai Inc
Data and Safety Monitoring Board/Committee	Bristol-Myers Squibb Company
Speakers Bureau	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Exact Sciences Corporation, Genentech, a member of the Roche Group, Gilead Sciences Inc, Novartis, Pfizer Inc, Seagen Inc

Ms Kuhlman — Disclosures

Nonrelevant Financial Relationship	Clinical Care Options

Ms McKinney — Disclosures

No relevant conflicts of interest to disclose

Dr Wainberg — Disclosures

Advisory Committee and Consulting Agreements	Arcus Biosciences, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc, Seagen Inc
Contracted Research	Arcus Biosciences, Bristol-Myers Squibb Company, Plexxikon Inc
Data and Safety Monitoring Board/Committee	Daiichi Sankyo Inc, Pfizer Inc

Commercial Support

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

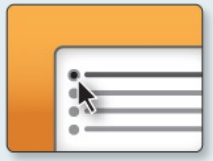
Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

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.

Complete Your Evaluation: Tap the NCPD Evaluation button to complete your evaluation electronically to receive credit for your participation.

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

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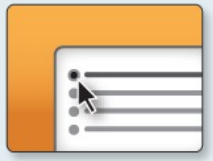
Clinicians Attending via Zoom

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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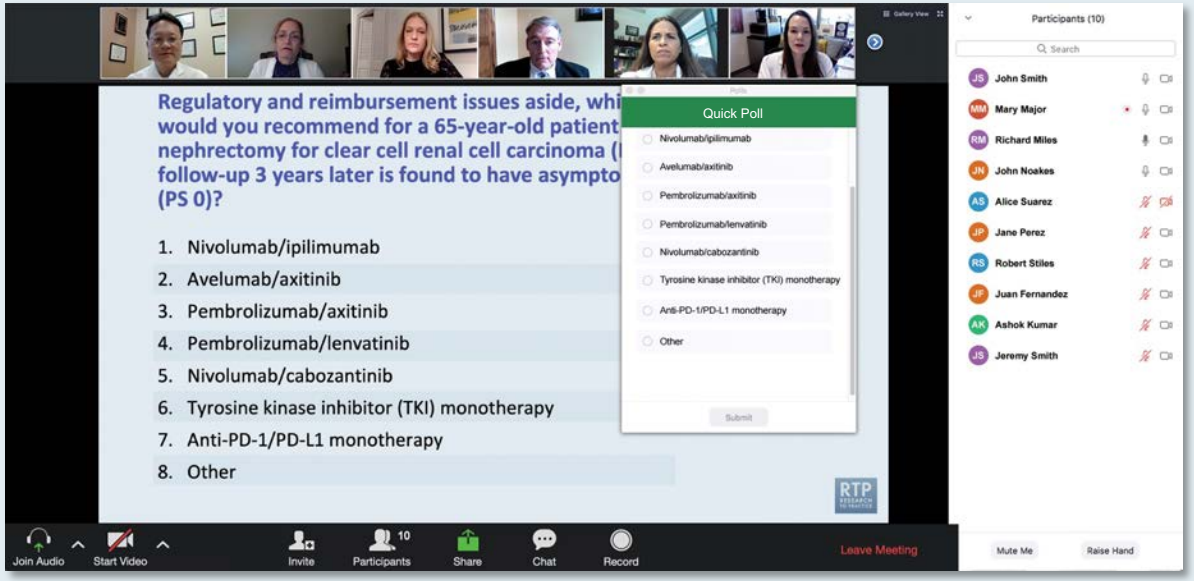
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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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”
Fifteenth Annual RTP-ONS NCPD Symposium Series
ONS Congress, San Antonio, Texas — April 26 to 29, 2023

Wednesday April 26	**Cervical and Endometrial Cancer** 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Thursday April 27	**Diffuse Large B-Cell Lymphoma** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	HER2-Targeted Antibody-Drug Conjugates 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET)
Friday April 28	**Hepatobiliary Cancers** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)
	Lung Cancer 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)
Saturday April 29	**Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)
	Prostate Cancer 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

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What I Tell My Patients

2023 ONS Congress

San Antonio, Texas

Symposia Themes

- New agents and therapies; ongoing trials related to specific clinical scenarios
- Patient education: Preparing to receive new therapies
- The bond that heals
- THANKS! (Great job)

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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?

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Agenda

Module 1: HER2 as a Therapeutic Target; Antibody-Drug Conjugates

Module 2: HER2-Positive Breast Cancer

Module 3: HER2-Positive Gastrointestinal Cancers

Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Agenda

Module 1: HER2 as a Therapeutic Target; Antibody-Drug Conjugates

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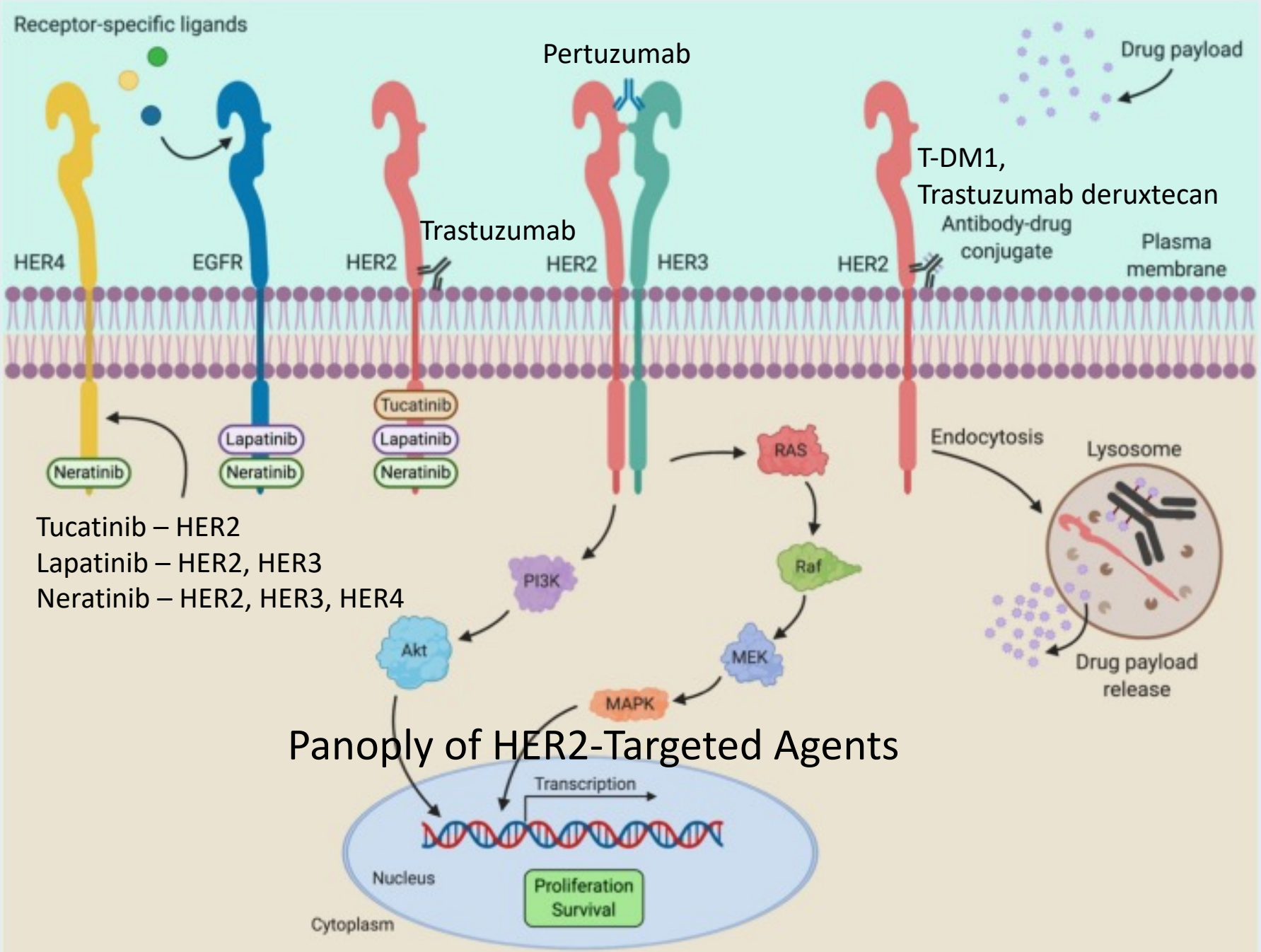
Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Clinical Research Background

- What is HER2, and what are the mechanisms of action of approved targeted therapies? What is an antibody-drug conjugate?
  - Trastuzumab
  - Pertuzumab
  - Neratinib
  - Tucatinib
  - Lapatinib
  - T-DM1
  - Trastuzumab deruxtecan
- Bystander effect in HER2-low disease

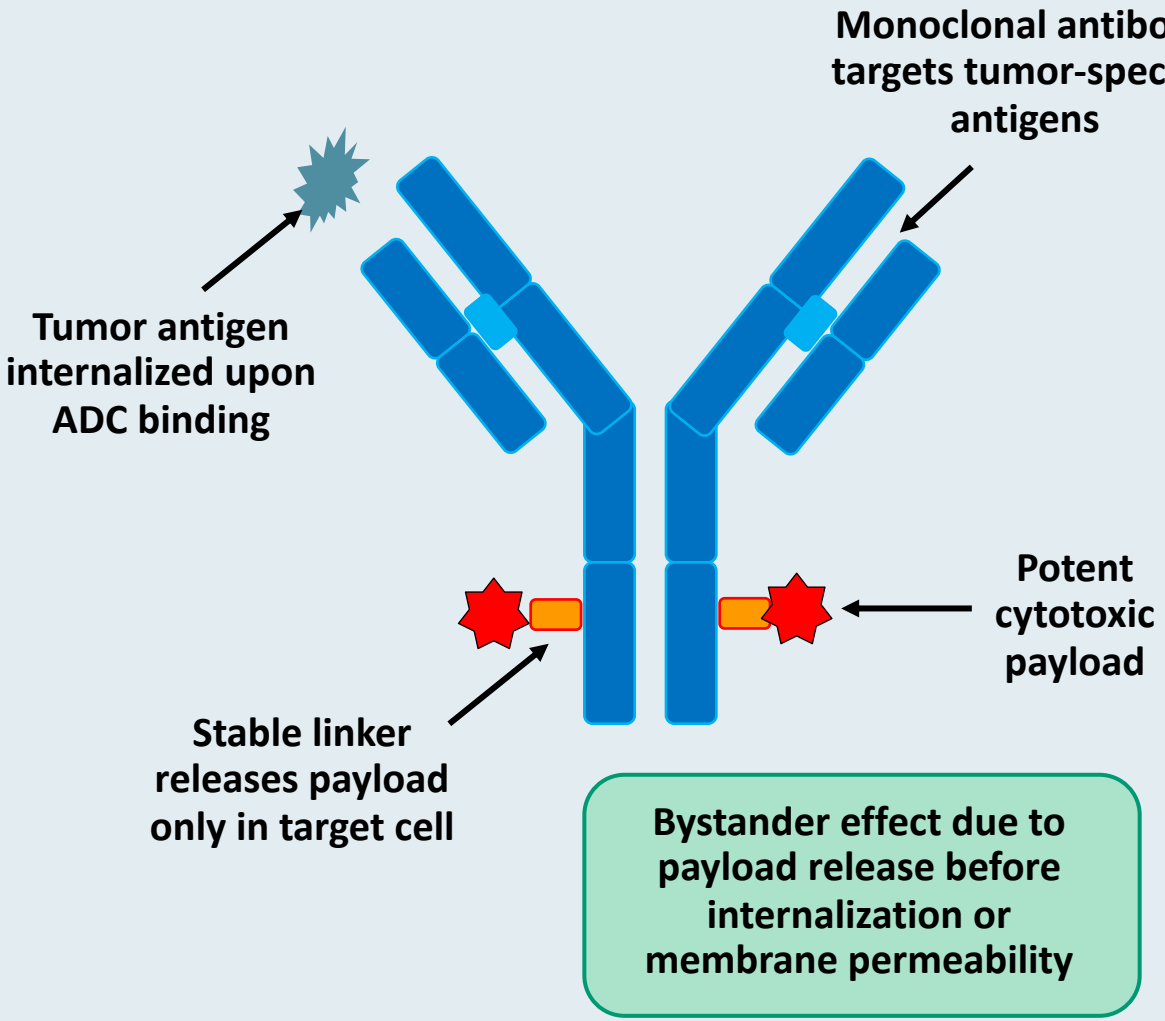
Panoply of HER2-Targeted Agents



Tucatinib – HER2
Lapatinib – HER2, HER3
Neratinib – HER2, HER3, HER4

Tesch ME, Gelmon KA. *Drugs* 2020;80:1811-30.

HER2-Targeting Antibody-Drug Conjugates (ADCs)



ADC attributes	T-DM1	T-DXd
Payload mechanism of action	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. SABCS 2021.

Agenda

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Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Alexis N McKinney, MSN, AGNP-BC

48-year-old woman with metastatic HER2-positive inflammatory breast cancer who received first-line THP → second-line trastuzumab deruxtecan

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Dr Kaklamani
San Antonio, Texas

Clinical Research Background

- **HER2-positive metastatic disease**
- **HER2-low metastatic disease (HR-positive and HR-negative)**

Alexis N McKinney, MSN, AGNP-BC

72-year-old woman with metastatic HER2-low breast cancer who received trastuzumab deruxtecan

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Dr Kaklamani
San Antonio, Texas

Clinical Research Background

- **HER2-positive metastatic disease**
- **HER2-low metastatic disease (HR-positive and HR-negative)**

Trastuzumab Deruxtecan: Breast Cancer

Mechanism of action

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

Indication

- **For patients with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either in the metastatic setting or in the (neo)adjuvant setting and 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-) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy**

Recommended dose

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

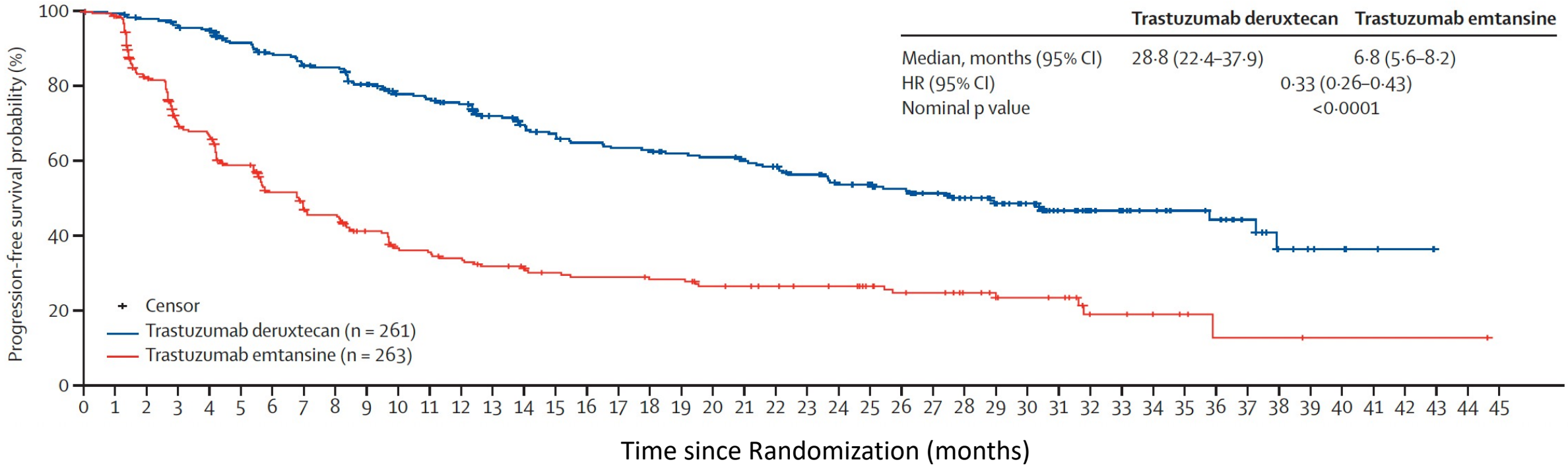
Trastuzumab deruxtecan package insert, 11/2022.

Lancet 2023 January 14;401:105-17.

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

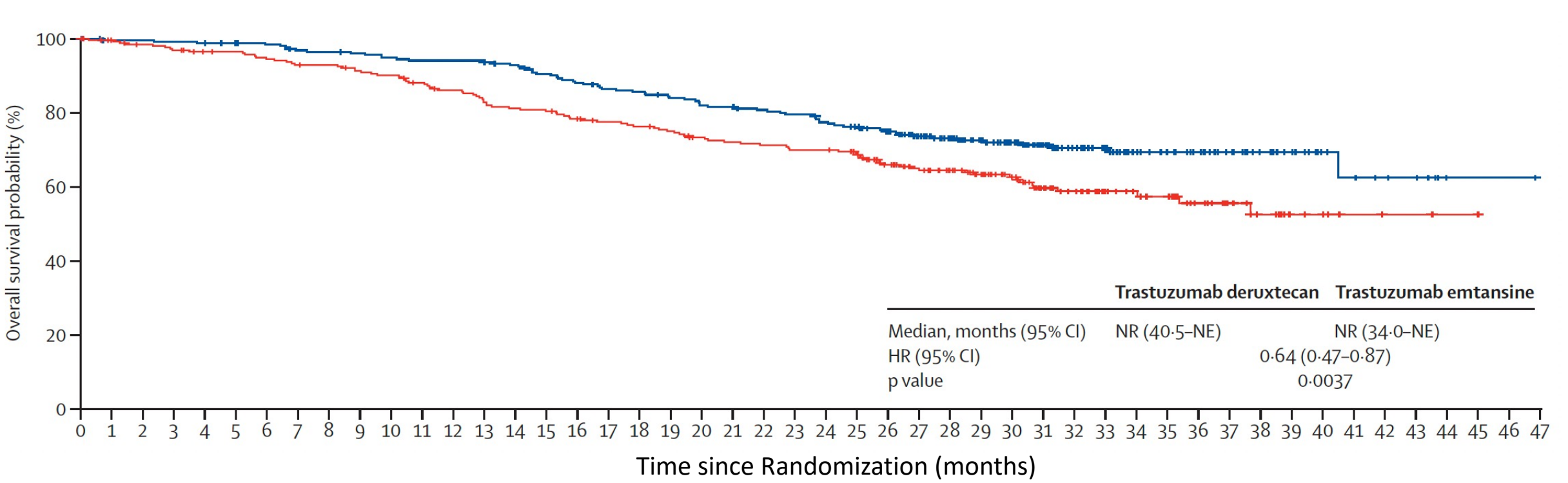
Sara A Hurvitz, Roberto Hegg, Wei-Pang Chung, Seock-Ah Im, William Jacot, Vinod Ganju, Joanne Wing Yan Chiu, Binghe Xu, Erika Hamilton, Srinivasan Madhusudan, Hiroji Iwata, Sevilay Altintas, Jan-Willem Henning, Giuseppe Curigliano, José Manuel Perez-Garcia, Sung-Bae Kim, Vanessa Petry, Chiun-Sheng Huang, 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

DESTINY-Breast03: Progression-Free Survival



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

DESTINY-Breast03: Overall Survival



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

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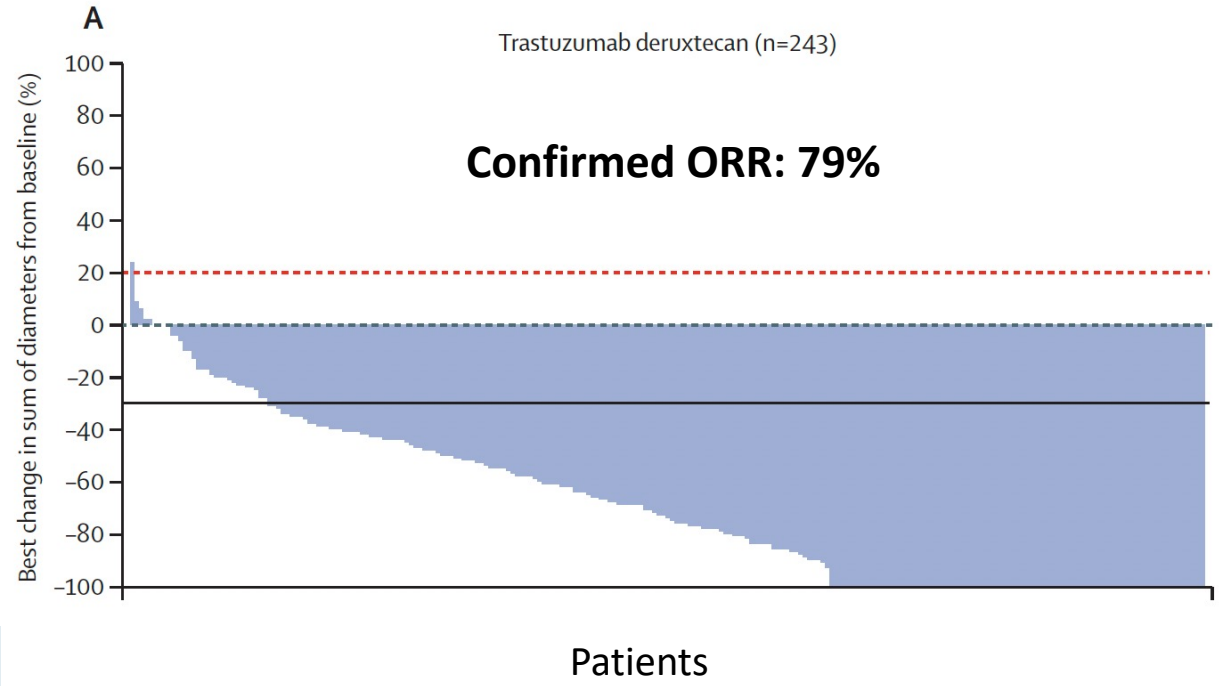
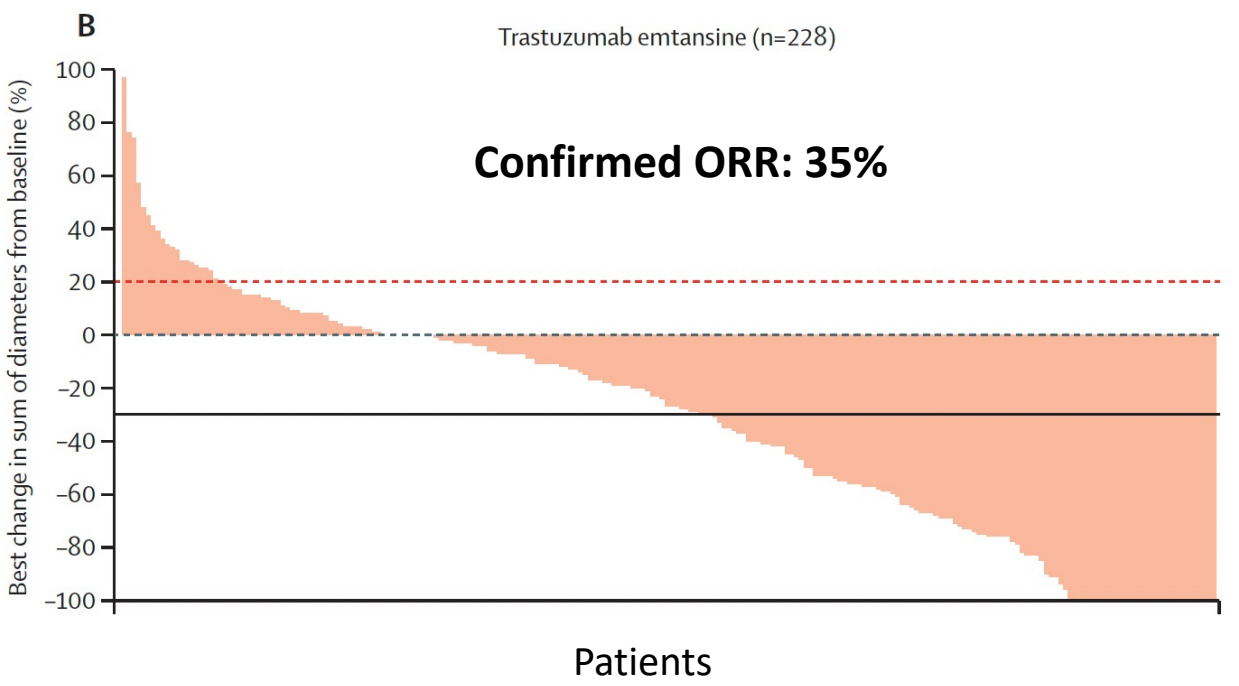
DESTINY-Breast03: Antitumor Activity





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

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Trastuzumab Deruxtecan Granted FDA Approval for HER2-Low Breast Cancer

Press Release: August 5, 2022

"Today, the US Food and Drug Administration approved fam-trastuzumab-deruxtecan-nxki, an IV infusion for the treatment of patients with unresectable (unable to be removed) or metastatic (spread to other parts of the body) HER2-low breast cancer. This is the first approved therapy targeted to patients with the HER2-low breast cancer subtype, which is a newly defined subset of HER2-negative breast cancer.

Patients with HER2-low breast cancer are eligible for fam-trastuzumab-deruxtecan-nxki if they have received a prior chemotherapy in the metastatic setting, or their cancer returned during, or within 6 months of completing, adjuvant chemotherapy.

This approval is based on DESTINY-Breast04, a randomized, multicenter, open label clinical trial that enrolled 557 adult patients with unresectable or metastatic HER2-low breast cancer."

https://www.fda.gov/news-events/press-announcements/fda-approves-first-targeted-therapy-her2-low-breast-cancer

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2022 ASCO ANNUAL MEETING **Abstract LBA3** DESTINY-Breast04

Trastuzumab deruxtecan (T-DXd) vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Results of DESTINY-Breast04, a randomized, phase 3 study

Shanu Modi Memorial Sloan Kettering Cancer Center, Memorial Hospital, New York, NY, USA

June 5, 2022

Additional authors: William Jacot, Toshinari Yamashita, Joo Hyuk Sohn, Maria Vidal, Eriko Tokunaga, Junji Tsurutani, Naoto Ueno, Yee Soo Chae, Keun Seok Lee, Naoki Niikura, Yeon Hee Park, Xiaojia Wang, Binghe Xu, Dhiraj Gambhire, Lotus Yung, Gerold Meinhardt, Yibin Wang, Nadia Harbeck, David Cameron

On behalf of the DESTINY-Breast04 investigators

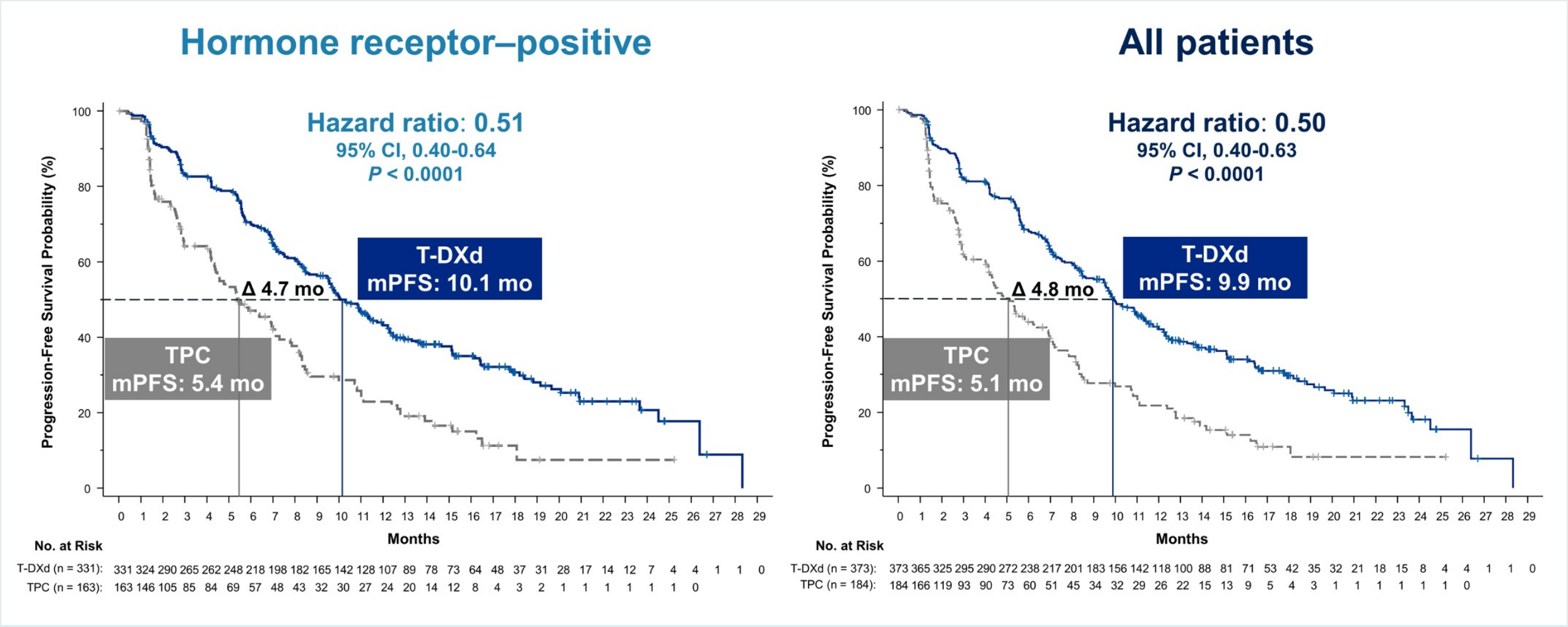
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 7, 2022 VOL. 387 NO. 1

Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

S. Modi, W. Jacot, T. Yamashita, J. Sohn, M. Vidal, E. Tokunaga, J. Tsurutani, N.T. Ueno, A. Prat, Y.S. Chae, K.S. Lee, N. Niikura, Y.H. Park, B. Xu, X. Wang, M. Gil-Gil, W. Li, J.-Y. Pierga, S.-A. Im, H.C.F. Moore, H.S. Rugo, R. Yerushalmi, F. Zagouri, A. Gombos, S.-B. Kim, Q. Liu, T. Luo, C. Saura, P. Schmid, T. Sun, D. Gambhire, L. Yung, Y. Wang, J. Singh, P. Vitazka, G. Meinhardt, N. Harbeck, and D.A. Cameron, for the DESTINY-Breast04 Trial Investigators*

DESTINY-Breast04: PFS for HR-Positive Population (Primary Endpoint) and All Patients



TPC = treatment of physician's choice; mPFS = median progression-free survival

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022 July 7;387(1):9-20.

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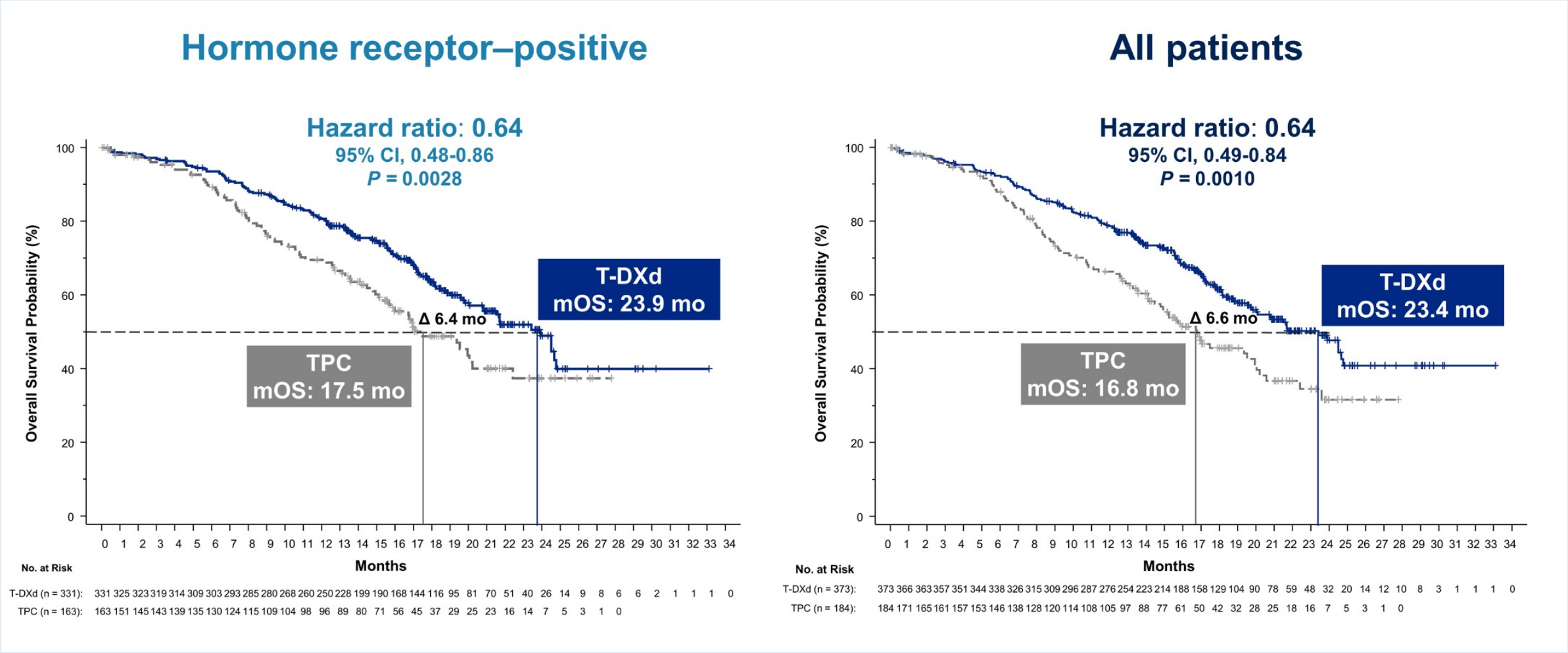
DESTINY-Breast04: OS for HR-Positive Population and All Patients



mOS = median overall survival

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022 July 7;387(1):9-20.

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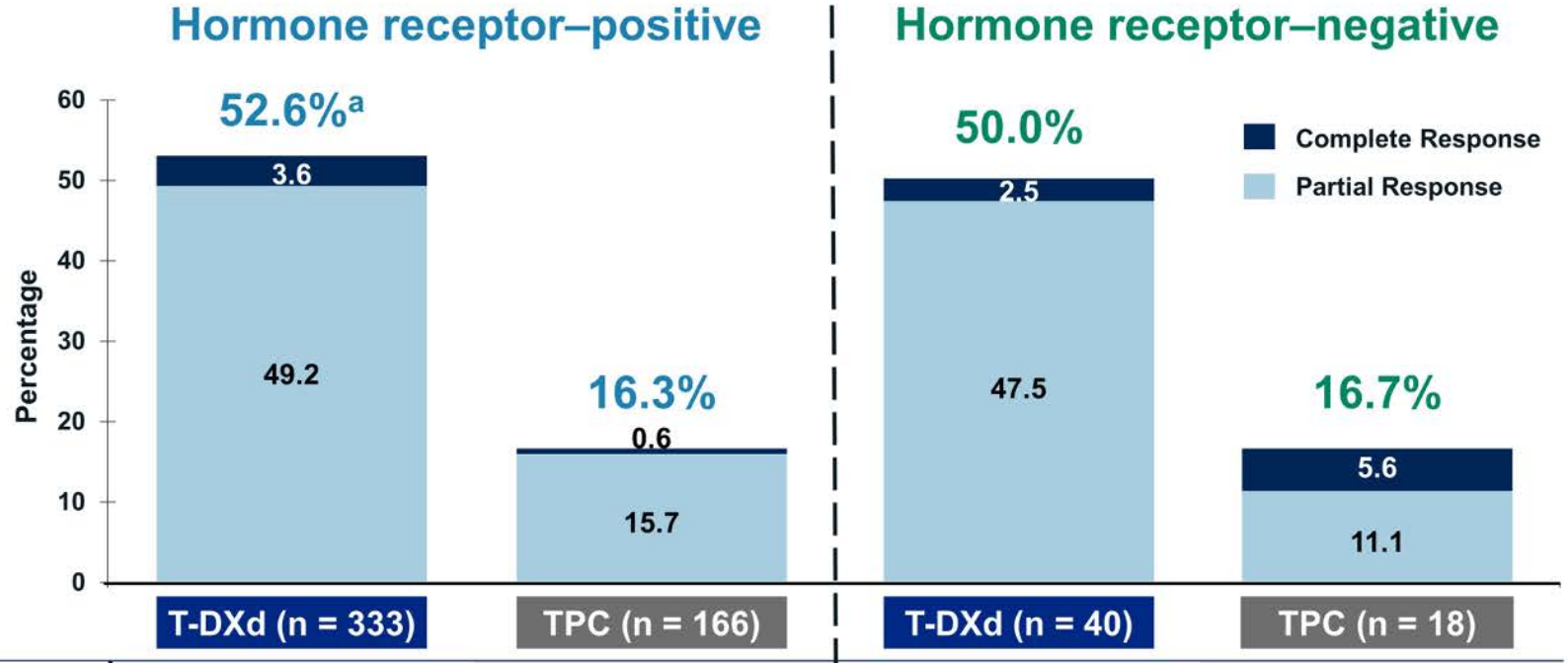
DESTINY-Breast04: Confirmed Objective Response Rate



	T-DXd (n = 333)	TPC (n = 166)	T-DXd (n = 40)	TPC (n = 18)
Progressive disease, %	7.8	21.1	12.5	33.3
Not evaluable, %	4.2	12.7	7.5	5.6
Clinical benefit rate,[b] %	71.2	34.3	62.5	27.8
Duration of response, months	10.7	6.8	8.6	4.9

Modi S et al. ASCO 2022;Abstract LBA3. Modi S et al. *N Engl J Med* 2022 July 7;387(1):9-20.

DESTINY-Breast04: Response and Survival with T-DXd in the HR-Negative Population

	All patients			Hormone receptor-negative		
	T-DXd (N = 373)	TPC (N = 184)	HR (*p*-value)	T-DXd (N = 40)	TPC (N = 18)	Hazard ratio
Median PFS	9.9 mo	5.1 mo	0.5 (<0.001)	8.5 mo	2.9 mo	0.46
Median OS	23.4 mo	16.8 mo	0.64 (0.001)	18.2 mo	8.3 mo	0.48
Objective response rate	52.3%	16.3%	—	50.0%	16.7%	—

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

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Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Caroline Kuhlman, MSN, APRN-BC

77-year-old man with HER2-positive gastroesophageal adenocarcinoma and brain metastases who received first-line chemotherapy/trastuzumab → second-line trastuzumab deruxtecan with decreased EF

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Dr Wainberg
Los Angeles, California

Clinical Research Background

- **First- and second-line therapy for HER2-positive gastroesophageal cancer**
- **HER2-positive colorectal cancer**

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Caroline Kuhlman, MSN, APRN-BC

42-year-old man with metastatic HER2-positive esophageal cancer who received first-line chemotherapy/trastuzumab → second-line trastuzumab deruxtecan and developed pneumonitis

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Dr Wainberg
Los Angeles, California

Clinical Research Background

- **First- and second-line therapy for HER2-positive gastroesophageal cancer**
- **HER2-positive colorectal cancer**

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Trastuzumab Deruxtecan: Gastroesophageal Cancer

Mechanism of action

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

Indication

- **For patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen**

Recommended dose

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

Trastuzumab deruxtecan package insert, 11/2022.

PARIS 2022 ESMO congress

Updated Analysis of DESTINY-Gastric02: a Phase 2 Single-Arm Trial of Trastuzumab Deruxtecan (T-DXd) in Western Patients with HER2-Positive Unresectable/Metastatic Gastric/Gastroesophageal Junction (GEJ) Cancer Who Progressed on or After Trastuzumab-Containing Regimen

Presentation 1205MO

Geoffrey Ku,[a] Maria di Bartolomeo, Elizabeth Smyth, Ian Chau, Haeseong Park, Salvatore Siena, Sara Lonardi, Zev A. Wainberg, Jaffer Ajani, Joseph Chao, Ferdous Barlaskar, Yoshinori Kawaguchi, Amy Qin, Jasmeet Singh, Aashima Puri, Gerold Meinhardt, Eric Van Cutsem

On behalf of the DESTINY-Gastric02 investigators

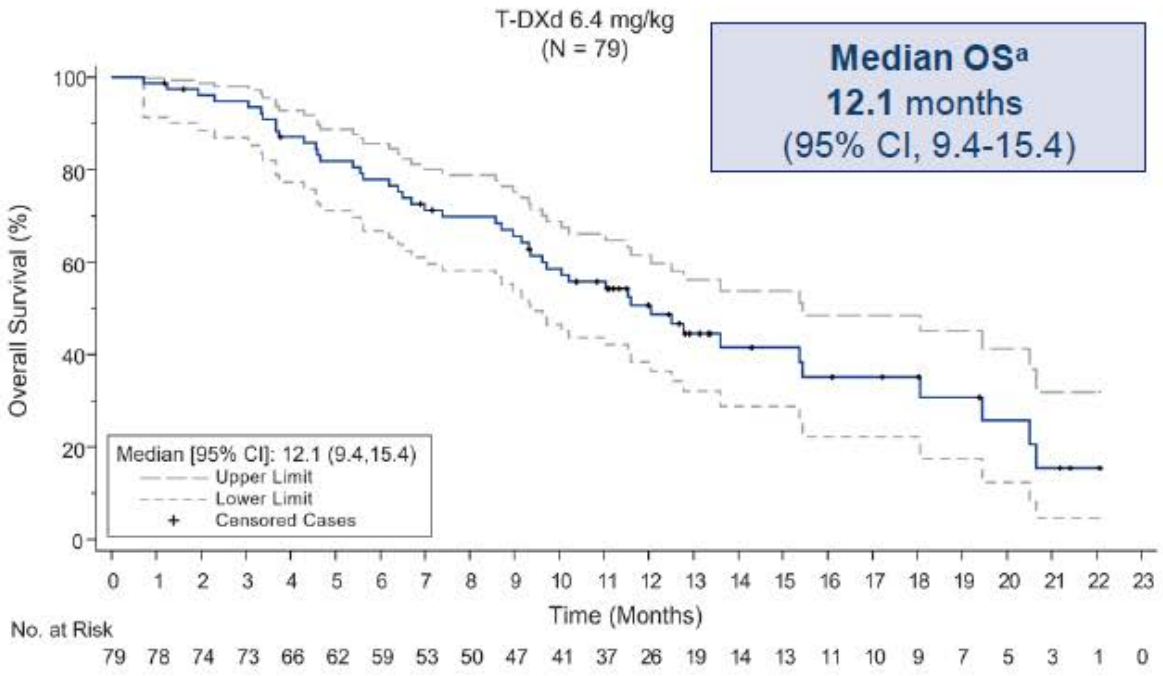
[a]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Paris, France, September 9-13, 2022

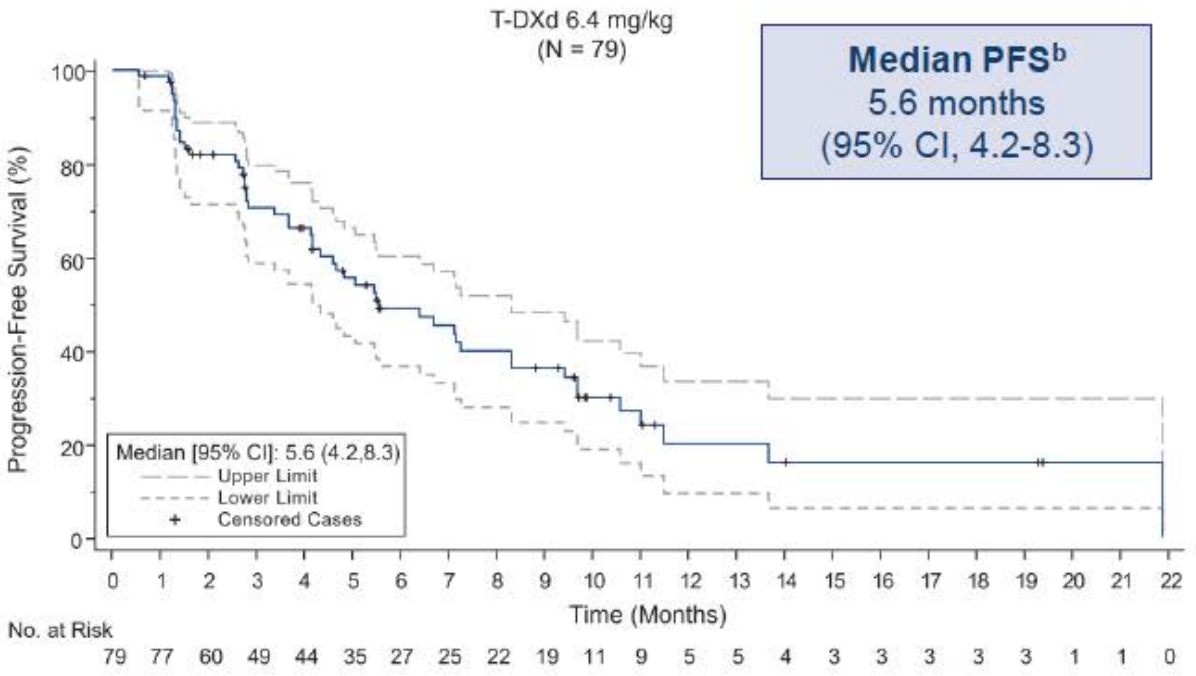
Abstract 1205MO

DESTINY-Gastric02: PFS and OS

Kaplan-Meier Plot of OS



Kaplan-Meier Plot of PFS by ICR



Ku G et al. ESMO 2022;Abstract 1205MO.

DESTINY-Gastric02: Overall Safety Summary and ILD/Pneumonitis

% (n)	Patients (N = 79)
Any TEAE	100 (79)
Drug-related	94.9 (75)
TEAE grade ≥3	55.7 (44)
Drug-related	30.4 (24)
Serious TEAE	41.8 (33)
Drug-related	12.7 (10)
TEAE associated with study drug discontinuation	19.0 (15)
Drug-related	12.7 (10)
TEAE associated with dose reduction	21.5 (17)
Drug-related	17.7 (14)
TEAE associated with an outcome of death	13.9 (11)
Drug-related	2.5 (2)
Adjudicated drug-related ILD/pneumonitis	10.1 (8)[a]
Adjudicated drug-related ILD/pneumonitis grade 5	2.5 (2)

- Median treatment duration was 4.3 months (range, 0.7-22.1 months)
- The most common TEAEs were nausea (67.1%), vomiting (44.3%), and fatigue (41.8%)
- Grade 1 adjudicated drug-related ILD/pneumonitis occurred in 2 patients (2.5%), grade 2 in 4 patients (5.1%), and grade 5 in 2 patients (2.5%)
- Median time to onset of adjudicated drug-related ILD/pneumonitis was 80.5 days (range, 42-344 days), with a median duration of 36.0 days (range, 15-142 days)
- Of the 2 fatal ILD/pneumonitis cases, 1 occurred 171 days after drug initiation and the second after 353 days

ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.
Cutoff date: November 8, 2021.
[a]Of the 6 grade 1/2 ILD/pneumonitis cases, 3 patients had recovered or were recovering at the time of data cutoff, 1 had recovered with sequelae, 1 had not recovered, and 1 had an outcome that was unknown.

Ku G et al. ESMO 2022;Abstract 1205MO.

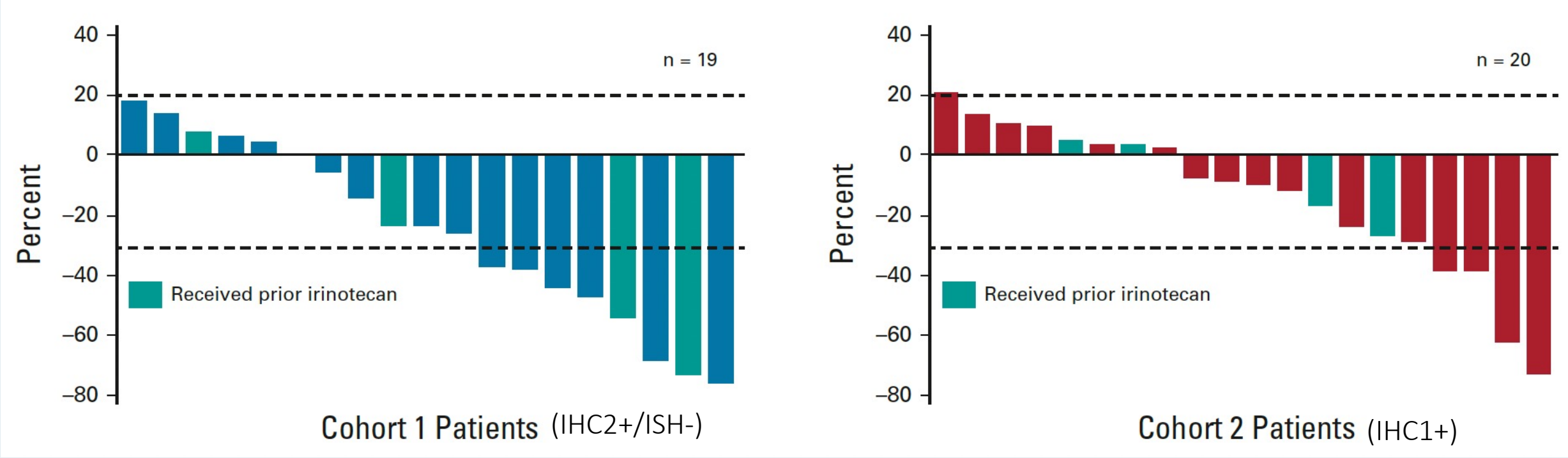
original reports

Trastuzumab Deruxtecan in Anti–Human Epidermal Growth Factor Receptor 2 Treatment–Naive Patients With Human Epidermal Growth Factor Receptor 2–Low Gastric or Gastroesophageal Junction Adenocarcinoma: Exploratory Cohort Results in a Phase II Trial

Kensei Yamaguchi, MD[1]; Yung-Jue Bang, MD, PhD[2]; Satoru Iwasa, MD[3]; Naotoshi Sugimoto, MD[4]; Min-Hee Ryu, MD, PhD[5]; Daisuke Sakai, MD[6]; Hyun Cheol Chung, MD, PhD[7]; Hisato Kawakami, MD, PhD[8]; Hiroshi Yabusaki, MD[9]; Jeeyun Lee, MD[10]; Tatsu Shimoyama, MD[11]; Keun-Wook Lee, MD, PhD[12]; Kaku Saito, MSc, MBA[13]; Yoshinori Kawaguchi, MSc, MBA[13]; Takahiro Kamio, MD[13]; Akihito Kojima, MSc[14]; Masahiro Sugihara, PhD[14]; and Kohei Shitara, MD[15]

J Clin Oncol 2023 February 1;41(4):816-25

DESTINY-Gastric01: Antitumor Activity of Trastuzumab Deruxtecan in Patients with Untreated HER2-Low Gastric or Gastroesophageal Cancer



Yamaguchi K et al. *J Clin Oncol* 2023 February 1;41(4):816-25.

Agenda

Module 1: HER2 as a Therapeutic Target; Antibody-Drug Conjugates

Module 2: HER2-Positive Breast Cancer

Module 3: HER2-Positive Gastrointestinal Cancers

Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Kelly EH Goodwin, MSN, RN, ANP-BC

67-year-old man with metastatic NSCLC with a HER2 L755P mutation who received first-line carboplatin/pemetrexed/ pembrolizumab → second-line trastuzumab deruxtecan

RTP
RESEARCH
TO PRACTICE

Dr Bazhenova
San Diego, California

Clinical Research Background

- **HER2 mutation versus amplification**
- **ILD in lung cancer population**

Kelly EH Goodwin, MSN, RN, ANP-BC

69-year-old man with a PMH of chordoma who was diagnosed with metastatic HER2-positive NSCLC and received trastuzumab deruxtecan

RTP
RESEARCH
TO PRACTICE

Dr Bazhenova
San Diego, California

Clinical Research Background

- **HER2 mutation versus amplification**
- **ILD in lung cancer population**

Trastuzumab Deruxtecan: NSCLC

Mechanism of action

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

Indication

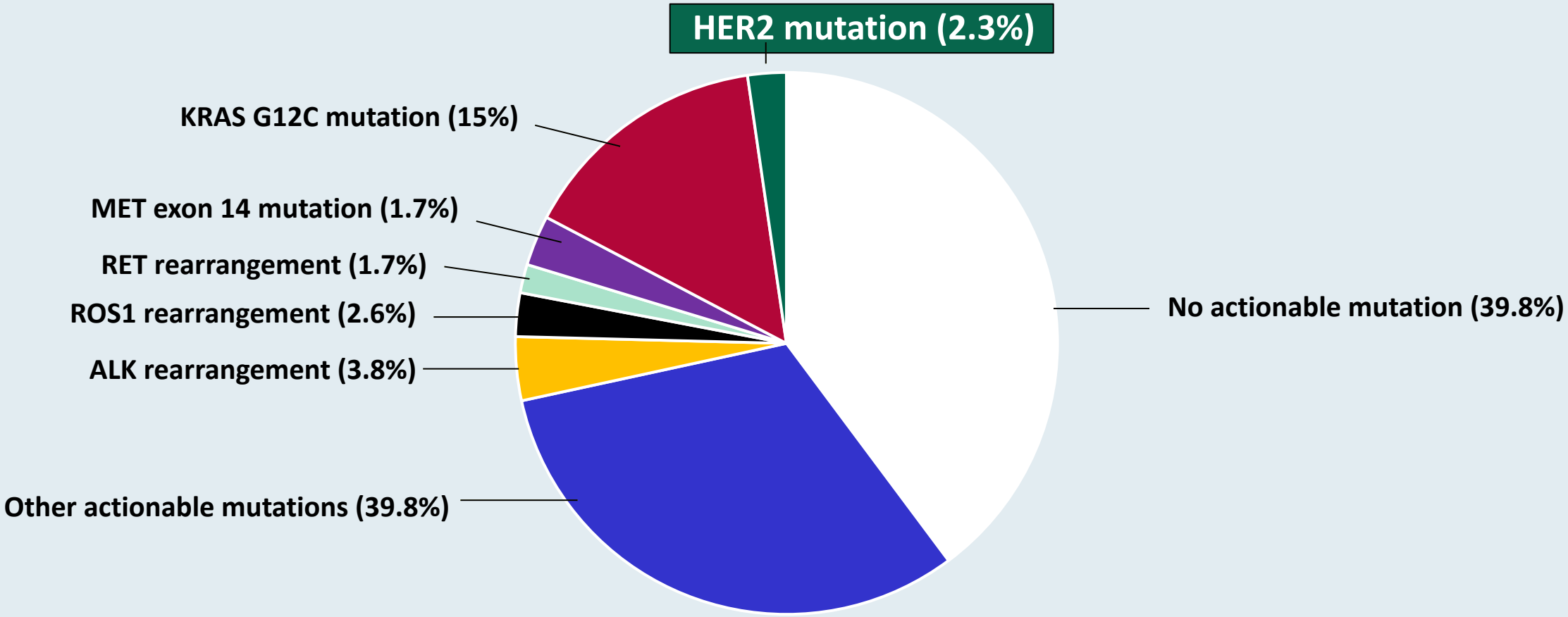
- **For patients with unresectable or metastatic NSCLC whose tumors have activating HER2 mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy**

Recommended dose

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

Trastuzumab deruxtecan package insert, 11/2022.

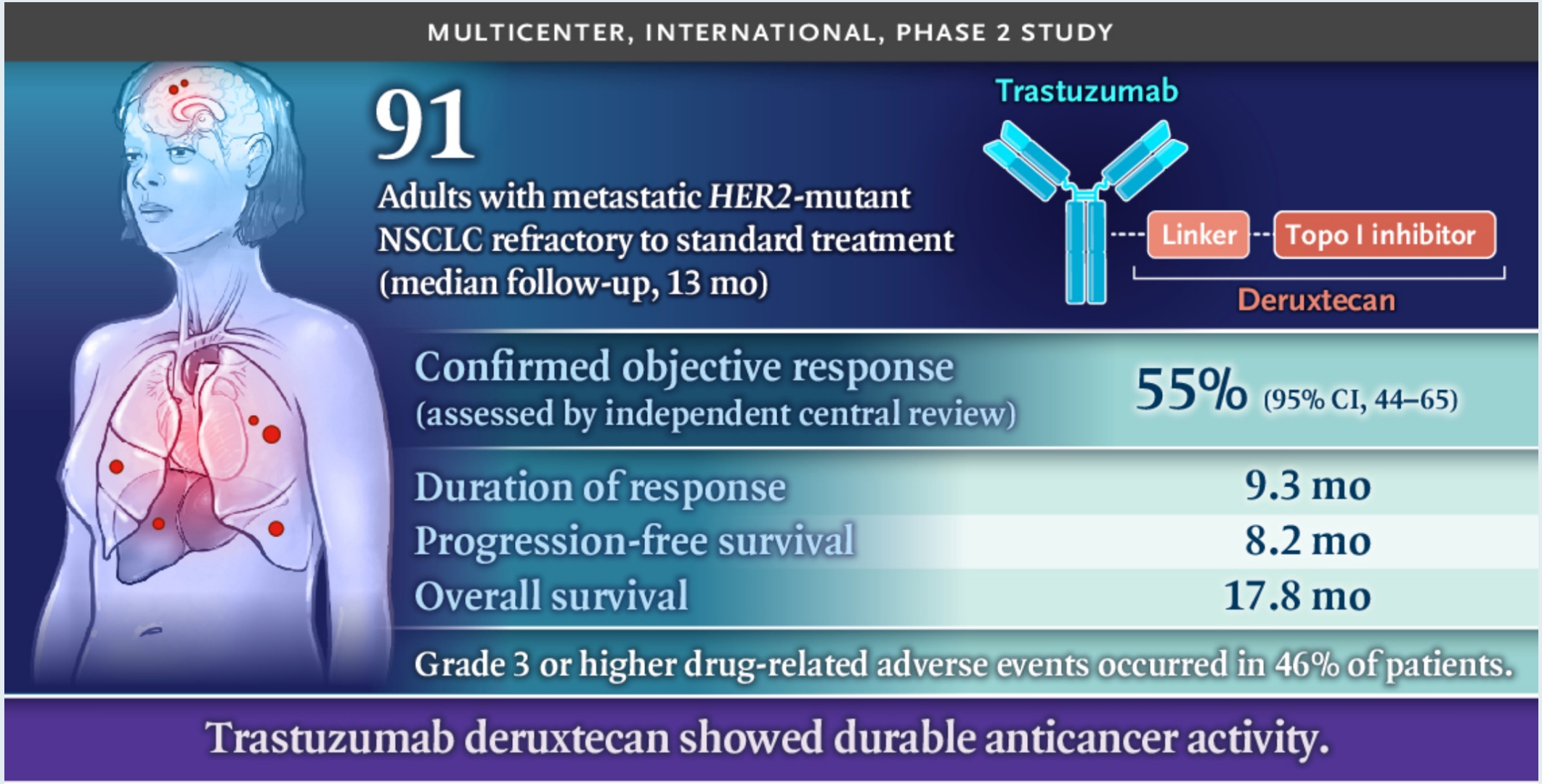
Frequency of Targetable Oncogenic Driver Molecular Alterations in Adenocarcinoma of the Lung



Derived from Tan AC et al. *J Clin Oncol* 2022;40:611-25.

RTP RESEARCH TO PRACTICE

DESTINY-Lung01: Activity of Trastuzumab Deruxtecan in Patients with Advanced NSCLC with HER2 Mutations



Li BT et al. *N Engl J Med* 2022;386(3):241-51.

PARIS 2022 ESMO congress

Trastuzumab Deruxtecan in Patients With *HER2* Mutant Metastatic Non–Small-Cell Lung Cancer: Interim Results From the Phase 2 DESTINY-Lung02 Trial

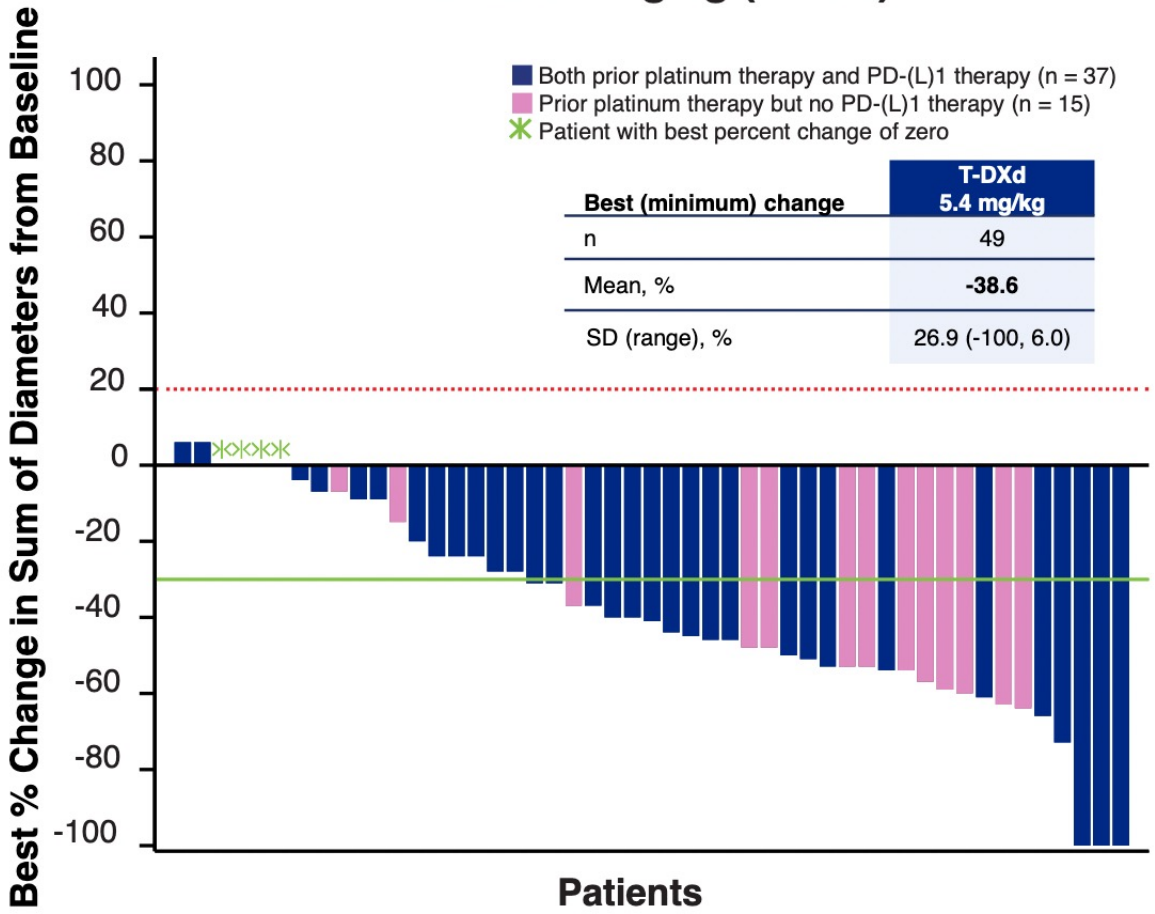
Koichi Goto, MD, PhD,[a] Sang-We Kim, Toshio Kubo, Yasushi Goto, Myung-Ju Ahn, David Planchard, Dong-Wan Kim, James Chih-Hsin Yang, Tsung-Ying Yang, Kaline Pereira, Kapil Saxena, Ryota Shiga, Yingkai Cheng, Mehreteab Aregay, Pasi A. Jänne

On behalf of the DESTINY-Lung02 investigators

[a]National Cancer Center Hospital East, Kashiwa, Japan

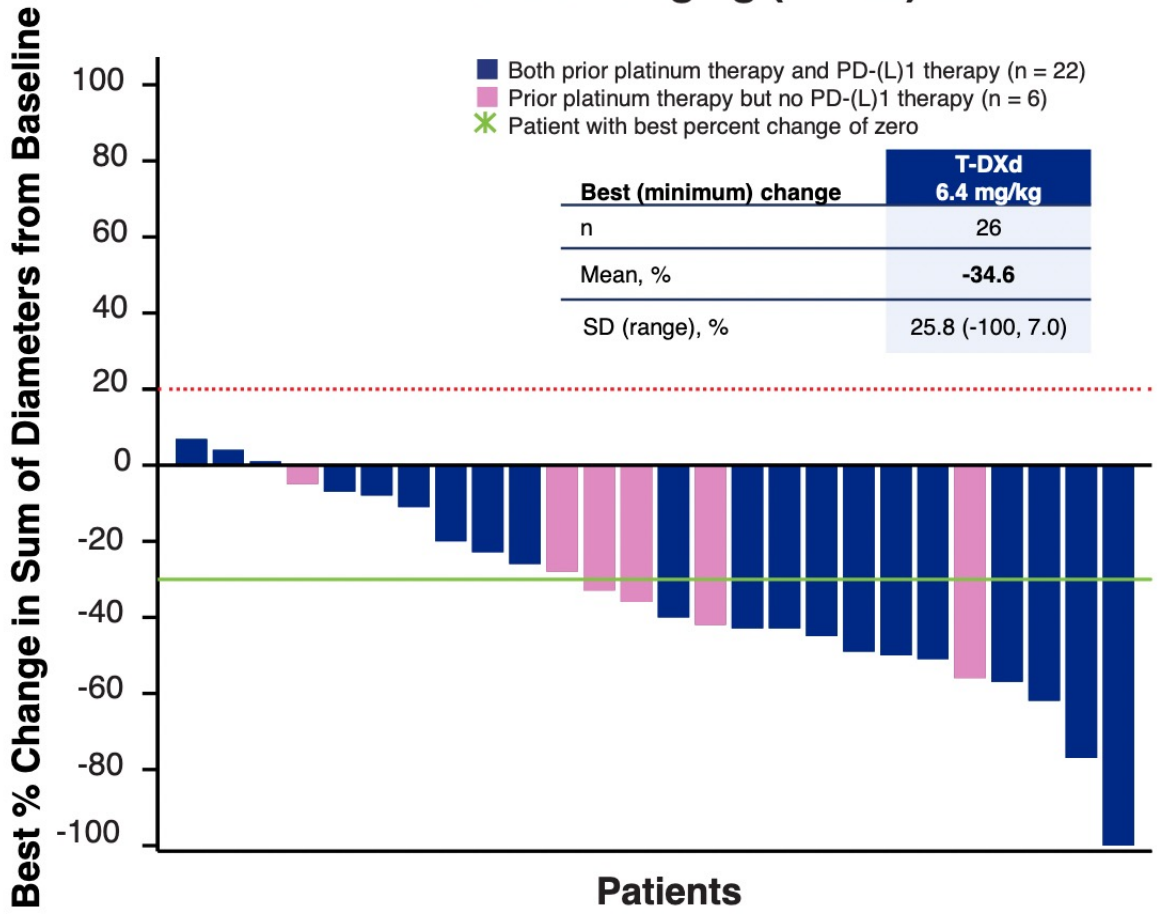
Best Percent Change in Tumor Size by BICR

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)

PARIS 2022 ESMO congress

Data cutoff: Mar 24, 2022.

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

Agenda

Module 1: HER2 as a Therapeutic Target; Antibody-Drug Conjugates

Module 2: HER2-Positive Breast Cancer

Module 3: HER2-Positive Gastrointestinal Cancers

Module 4: HER2-Positive Non-Small Cell Lung Cancer

Module 5: Toxicities of Trastuzumab Deruxtecan

Clinical Research Background

- Toxicities associated with trastuzumab deruxtecan
  - Acute chemotherapy-related toxicity (GI, alopecia)
  - ILD
  - Cytopenias
  - Cardiotoxicity
  - Other toxicities
- Role of premedication
- Identification and management of ILD
- Imaging and clinical screening forr ILD

APPENDIX

DESTINY-Breast03: Adjudicated Drug-Related ILD/Pneumonitis

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 257)	11 (4.3)	26 (10.1)	2 (0.8)	0	0	39 (15.2)
T-DM1 (n = 261)	4 (1.5)	3 (1.1)	1 (0.4)	0	0	8 (3.1)

- Adjudicated drug-related ILD/pneumonitis rates were similar to other mBC trials with T-DXd[1,2]
- With longer treatment exposure and follow-up, the ILD/pneumonitis rate increased from 10.5% in the PFS interim analysis[3] to 15.2%
  - There were 4 additional grade 1, 8 additional grade 2, and no additional grade 3 events
- The overall incidence of grade 3 events (0.8%) was the same as in the PFS interim analysis[3]
- There were no adjudicated drug-related grade 4 or 5 events

Hurvitz SA et al. SABCS 2022;Abstract GS2-02

DESTINY-Breast03: Most Common Drug-Related Adverse Events

	Trastuzumab deruxtecan group (n=257)		Trastuzumab emtansine group (n=261)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood and lymphatic system disorders				
Anaemia	95 (37%)	24 (9%)	51 (20%)	17 (7%)
Platelet count decreased*	64 (25%)	20 (8%)	114 (44%)	52 (20%)
White blood cell count decreased	60 (23%)	16 (6%)	16 (6%)	2 (<1%)
Gastrointestinal disorders				
Nausea	198 (77%)	18 (7%)	79 (30%)	1 (<1%)
Vomiting	133 (52%)	4 (2%)	28 (11%)	2 (<1%)
Constipation	96 (37%)	0	51 (20%)	0
Diarrhoea	83 (32%)	3 (1%)	21 (8%)	2 (<1%)
General disorders				
Fatigue	79 (31%)	15 (6%)	53 (20%)	2 (<1%)
Headache	61 (24%)	1 (<1%)	40 (15%)	0
Investigations				
Neutrophil count decreased†	79 (31%)	41 (16%)	30 (11%)	8 (3%)
Aspartate aminotransferase increased	72 (28%)	2 (<1%)	108 (41%)	14 (5%)
Alanine aminotransferase increased	59 (23%)	4 (2%)	83 (32%)	12 (5%)
Metabolism and nutrition disorders				
Decreased appetite	78 (30%)	4 (2%)	46 (18%)	1 (<1%)
Bodyweight decreased	58 (23%)	6 (2%)	23 (9%)	2 (<1%)
Skin and subcutaneous disorders				
Alopecia	102 (40%)	1 (<1%)‡	9 (3%)	0

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

RTP RESEARCH TO PRACTICE

DESTINY-Breast04: Adverse Events of Special Interest

Adjudicated as drug-related ILD/pneumonitis

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n = 371)	13 (3.5)	24 (6.5)	5 (1.3)	0	3 (0.8)	45 (12.1)
TPC (n = 172)	1 (0.6)	0	0	0	0	1 (0.6)

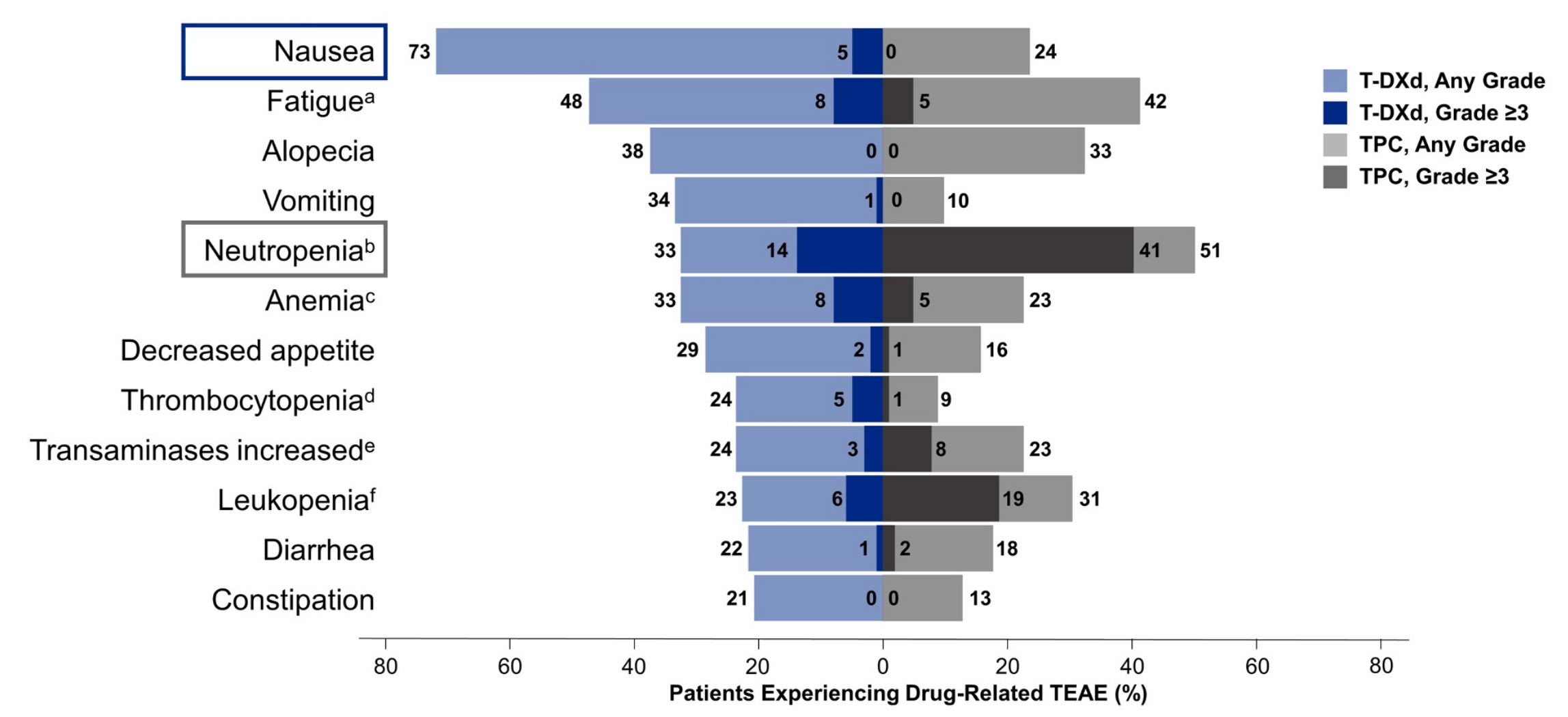
Left ventricular dysfuctions

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
Ejection fraction decreased						
T-DXd (n = 371)	1 (0.3)	12 (3.8)	1 (0.3)	0	0	16 (4.3)
TPC (n = 172)	0	0	0	0	0	0
Cardiac failure						
T-DXd (n = 371)	0	1 (0.3)	1 (0.3)	0	0	2 (0.5)
TPC (n = 172)	0	0	0	0	0	0

ILD = interstitial lung disease; TPC = treatment of physician's choice

Modi S et al. ASCO 2022;Abstract LBA3.

DESTINY-Breast04: Common Drug-Related TEAEs



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

ESMO Open 2022 Aug 10;7(4):100554.

ORIGINAL RESEARCH

Pooled analysis of drug-related interstitial lung disease and/or pneumonitis in nine trastuzumab deruxtecan monotherapy studies☆

C. A. Powell[1*], S. Modi[2], H. Iwata[3], S. Takahashi[4], E. F. Smit[5], S. Siena[6,7], D.-Y. Chang[8], E. Macpherson[9], A. Qin[10], J. Singh[10], C. Taitt[10], N. Shire[9] & D. Ross Camidge[11]

[1]Catherine and Henry J. Gaisman Division of Pulmonary Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York; [2]Memorial Sloan Kettering Cancer Center, New York, USA; [3]Aichi Cancer Center Hospital, Nagoya, Aichi; [4]Medical Oncology, The Cancer Institute Hospital of JFCR, Koto, Tokyo, Japan; [5]Department of Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, the Netherlands; [6]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan; [7]Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy; [8]National Taiwan University Hospital, Taipei City, Taiwan; [9]AstraZeneca Pharmaceuticals, Gaithersburg; [10]Daiichi Sankyo Inc., Basking Ridge; [11]University of Colorado Cancer Center, Aurora, USA

DESTINY-Lung01: Summary of Adverse Events and AEs of Clinical Interest

Event	N = 91
Discontinued due to AEs	25%
Dose reduction due to AEs	34%
Dose interruption due to AEs	32%
Drug-related interstitial lung disease (ILD)	26% (N = 24)
Grade 1	3 pts
Grade 2	15 pts
Grade 3	4 pts
Grade 5	2 pts
Median time to onset of ILD	141 days
Median duration of ILD	43 days

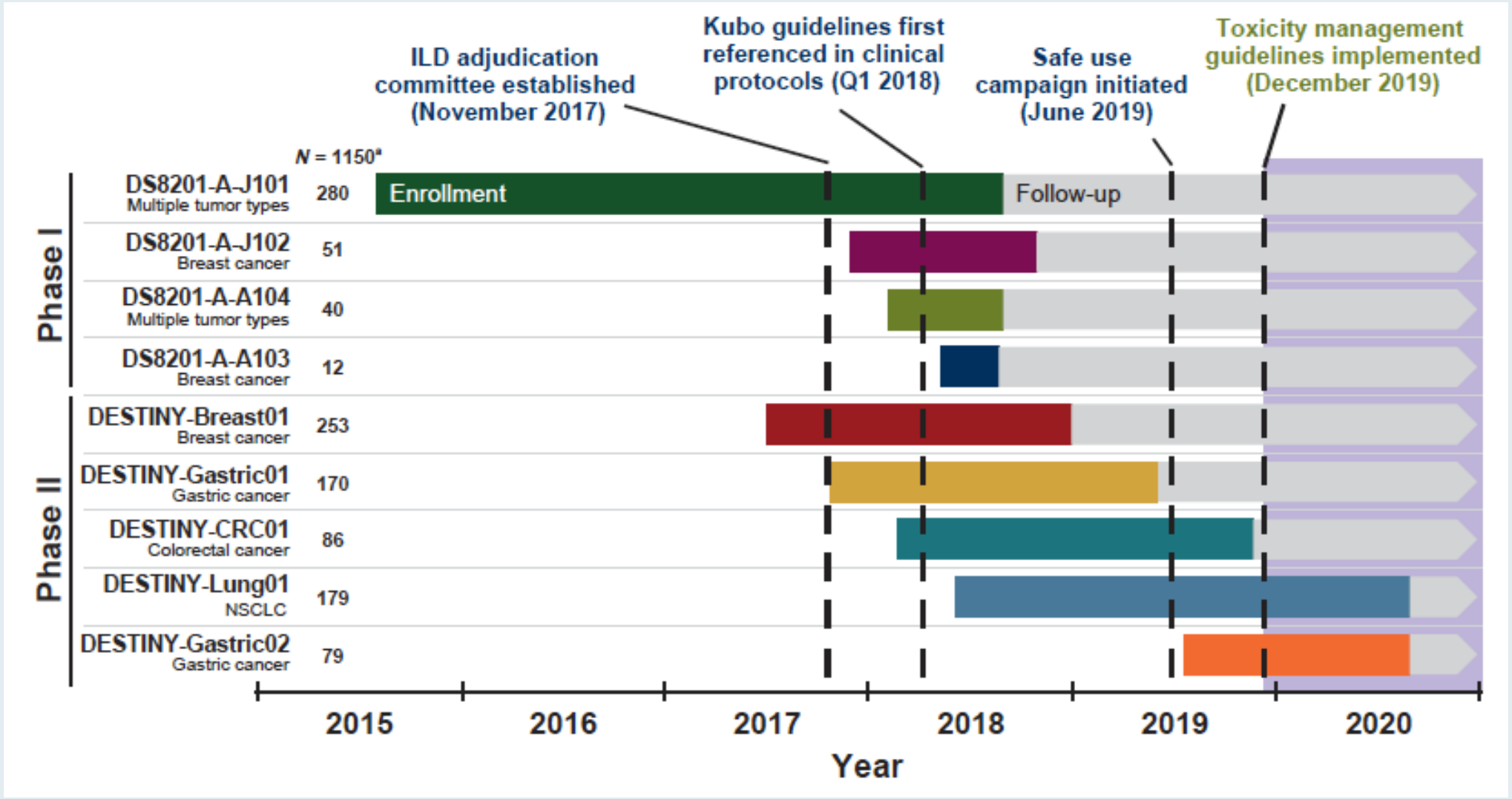
Li BT et al. *N Engl J Med* 2022;386(3):241-51.

DESTINY-Lung01: Common Adverse Events (N = 91)

Event	Any grade	Grade ≥3
Nausea	73%	9%
Fatigue	53%	7%
Alopecia	46%	0
Vomiting	40%	3%
Neutropenia	35%	18%
Anemia	33%	10%
Diarrhea	32%	3%
Decreased appetite	30%	0
Leukopenia	23%	4%
Constipation	22%	0

Li BT et al. *N Engl J Med* 2022;386(3):241-51.

Analysis of ILD Across Multiple Tumor Types



Powell CA et al. ESMO Open 2022;7(4):100554.

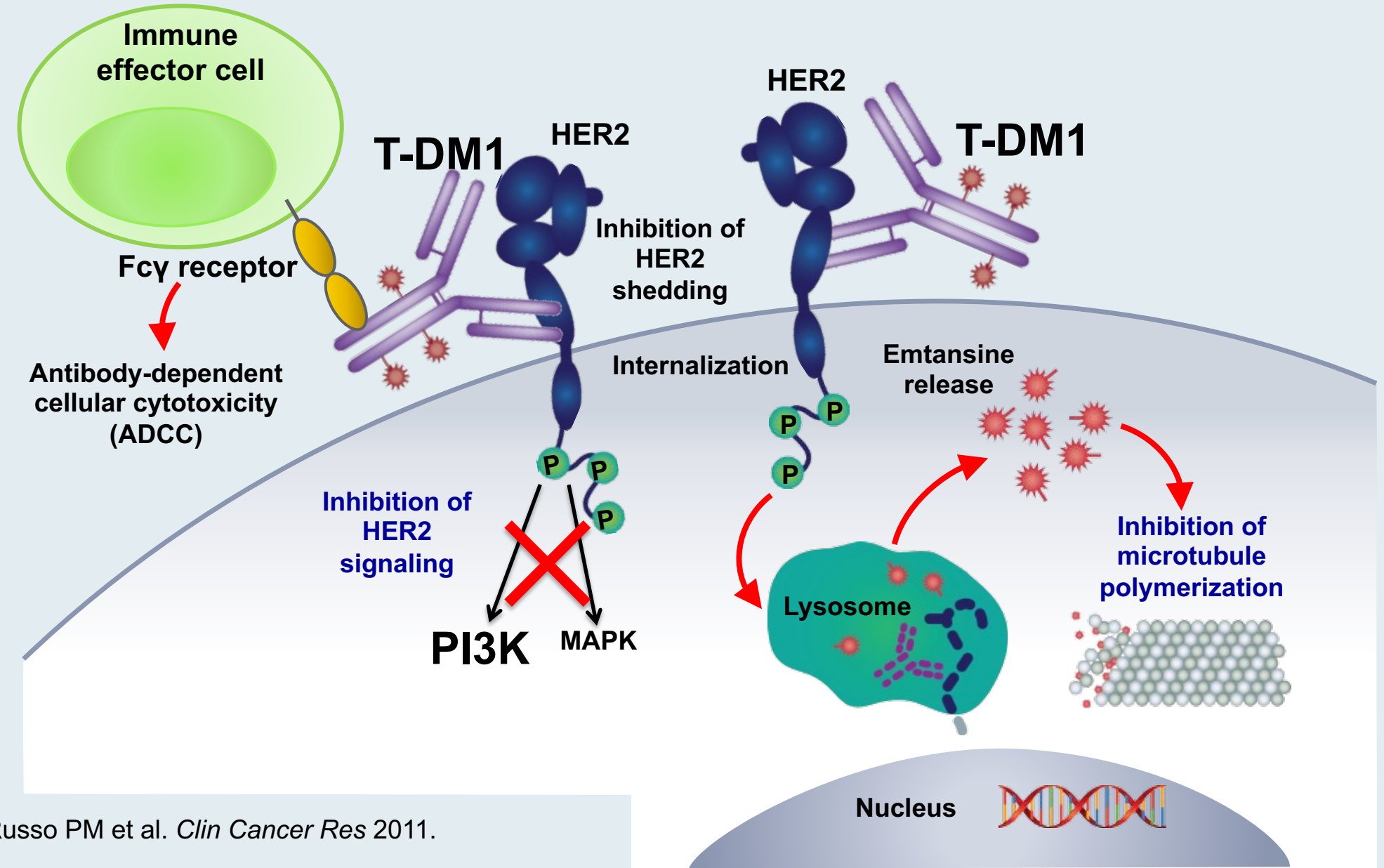
Adjudicated Drug-related ILD/Pneumonitis By Tumor Type And Grade

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
All patients ($N = 1150$)	48 (4.2)	89 (7.7)	14 (1.2)	1 (0.1)	25 (2.2)	177 (15.4)
Breast cancer ($n = 510$)	32 (6.3)	51 (10.0)	7 (1.4)	0	15 (2.9)	105 (20.6)
HER2-positive breast cancer treated with T-DXd 5.4 mg/kg q3w ($n = 245$)[b]	9 (3.7)	22 (9.0)	2 (0.8)	0	7 (2.9)	40 (16.3)
Gastric cancer ($n = 294$)	5 (1.7)	15 (5.1)	3 (1.0)	1 (0.3)	1 (0.3)	25 (8.5)
Lung cancer ($n = 203$)[c]	7 (3.4)	16 (7.9)	2 (1.0)	0	6 (3.0)	31 (15.3)
Colorectal cancer ($n = 107$)	0	5 (4.7)	1 (0.9)	0	3 (2.8)	9 (8.4)
Other cancer ($n = 34$)	4 (11.8)	2 (5.9)	1 (2.9)	0	0	7 (20.6)

- Most of these patients with ILD/pneumonitis [137/177 (77.4%); 11.9% (137/1150) of patients overall] had low-grade (worst grade of 1 or 2) ILD/pneumonitis

Powell CA et al. ESMO Open 2022;7(4):100554.

Trastuzumab Emtansine (T-DM1): Mechanisms of Action



Adapted from LoRusso PM et al. *Clin Cancer Res* 2011.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

2021 Aug;32(8):1005-1014

ANNALS OF ONCOLOGY driving innovation in oncology

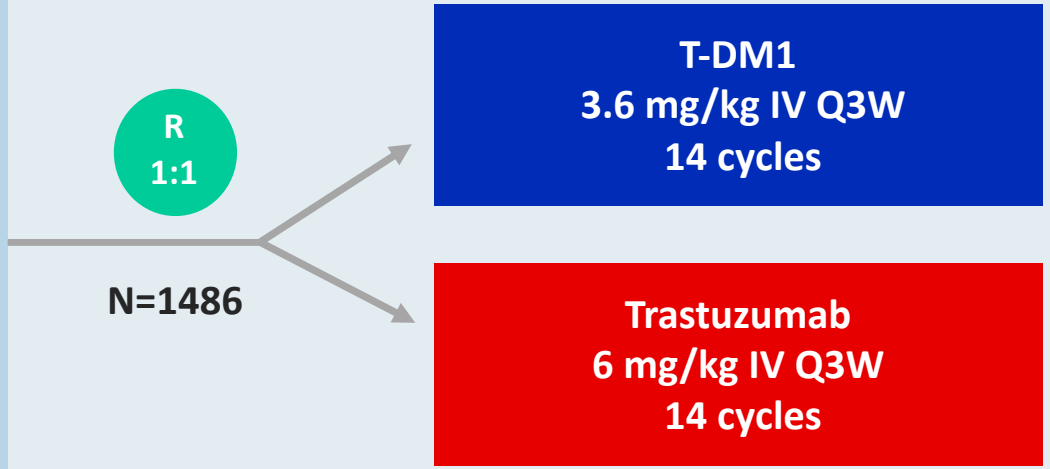
ORIGINAL ARTICLE

Adjuvant T-DM1 versus trastuzumab in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer: subgroup analyses from KATHERINE

E. P. Mamounas[1,2*], M. Untch[3], M. S. Mano[4], C.-S. Huang[5], C. E. Geyer Jr[1,6], G. von Minckwitz[7], N. Wolmark[1,8], X. Pivot[9], S. Kuemmel[10,11], M. P. DiGiovanna[12], B. Kaufman[13], G. Kunz[7,14], A. K. Conlin[1,15], J. C. Alcedo[16], T. Kuehn[17], I. Wapnir[1,18], A. Fontana[19], J. Hackmann[7,20], J. Polikoff[1,21], M. Saghatchian[22], A. Brufsky[1,23], Y. Yang[24], M. Zimovjanova[25], T. Boulet[26], H. Liu[27], D. Tesarowski[28], L. H. Lam[28], C. Song[28], M. Smitt[28,29] & S. Loibl[7,30]

KATHERINE: STUDY DESIGN

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
  - Minimum of 6 cycles of chemotherapy
    - Minimum of 9 weeks of taxane
    - Anthracyclines and alkylating agents allowed
    - All chemotherapy prior to surgery
  - Minimum of 9 weeks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



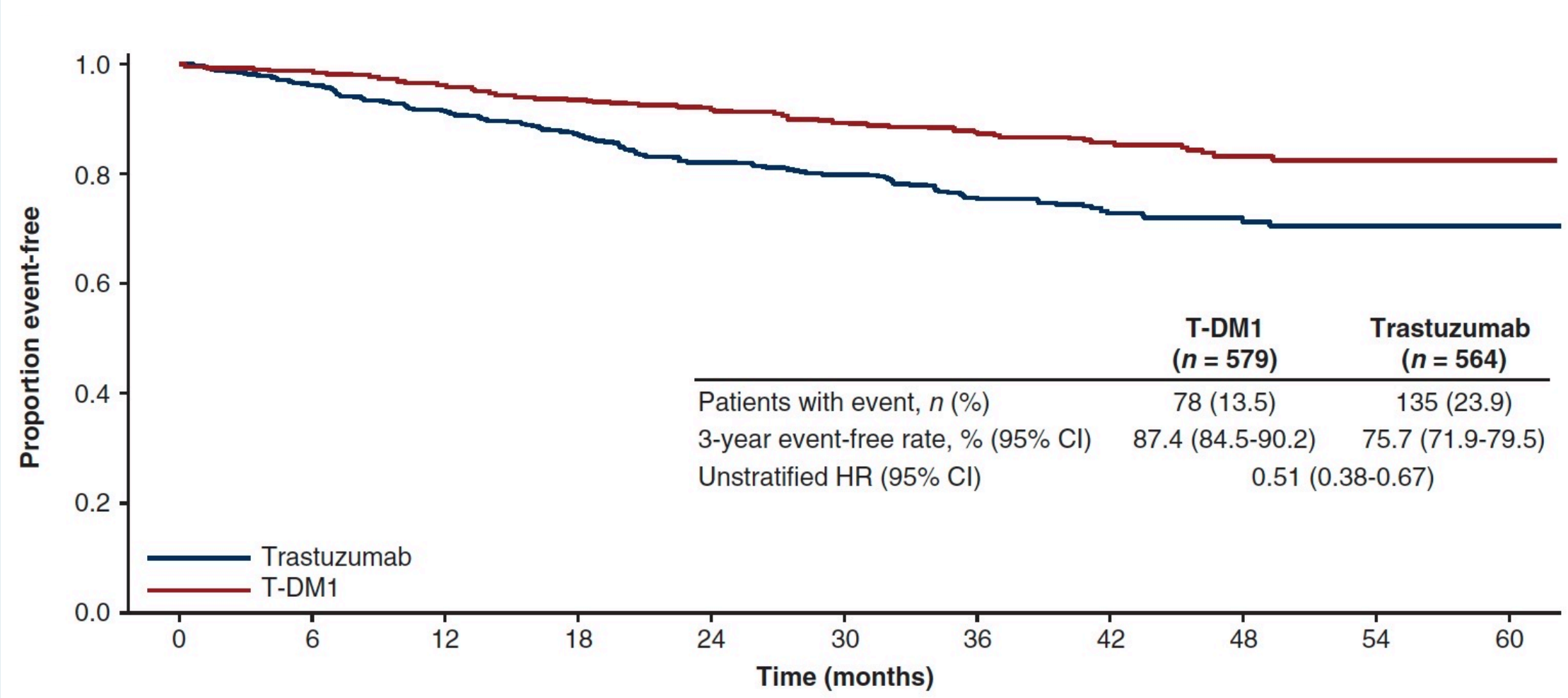
Radiation and endocrine therapy per protocol and local guidelines

Stratification factors:
- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs operable (stages cT1-3N0-1)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs negative/not done

Geyer C et al. SABCS 2018;Abstract GS1-10. von Minckwitz G et al. *N Engl J Med* 2019;380(7) 617-628.

Courtesy of Sara Tolaney, MD, MPH

Time to First Invasive Disease-Free Survival Event for Patients Who Received Anthracycline-Based Neoadjuvant Therapy



	T-DM1 (*n* = 579)	Trastuzumab (*n* = 564)
Patients with event, *n* (%)	78 (13.5)	135 (23.9)
3-year event-free rate, % (95% CI)	87.4 (84.5-90.2)	75.7 (71.9-79.5)
Unstratified HR (95% CI)	0.51 (0.38-0.67)	

Mamounas EP et al. *Ann Oncol* 2021;32(8):1005-1014.

RTP RESEARCH TO PRACTICE

DESTINY-Gastric01: HER2-Low Disease

original reports

Trastuzumab Deruxtecan in Anti–Human Epidermal Growth Factor Receptor 2 Treatment–Naive Patients With Human Epidermal Growth Factor Receptor 2–Low Gastric or Gastroesophageal Junction Adenocarcinoma: Exploratory Cohort Results in a Phase II Trial

Kensei Yamaguchi, MD[1]; Yung-Jue Bang, MD, PhD[2]; Satoru Iwasa, MD[3]; Naotoshi Sugimoto, MD[4]; Min-Hee Ryu, MD, PhD[5]; Daisuke Sakai, MD[6]; Hyun Cheol Chung, MD, PhD[7]; Hisato Kawakami, MD, PhD[8]; Hiroshi Yabusaki, MD[9]; Jeeyun Lee, MD[10]; Tatsu Shimoyama, MD[11]; Keun-Wook Lee, MD, PhD[12]; Kaku Saito, MSc, MBA[13]; Yoshinori Kawaguchi, MSc, MBA[13]; Takahiro Kamio, MD[13]; Akihito Kojima, MSc[14]; Masahiro Sugihara, PhD[14]; and Kohei Shitara, MD[15]

J Clin Oncol 2023 February 1;41(4):816-25

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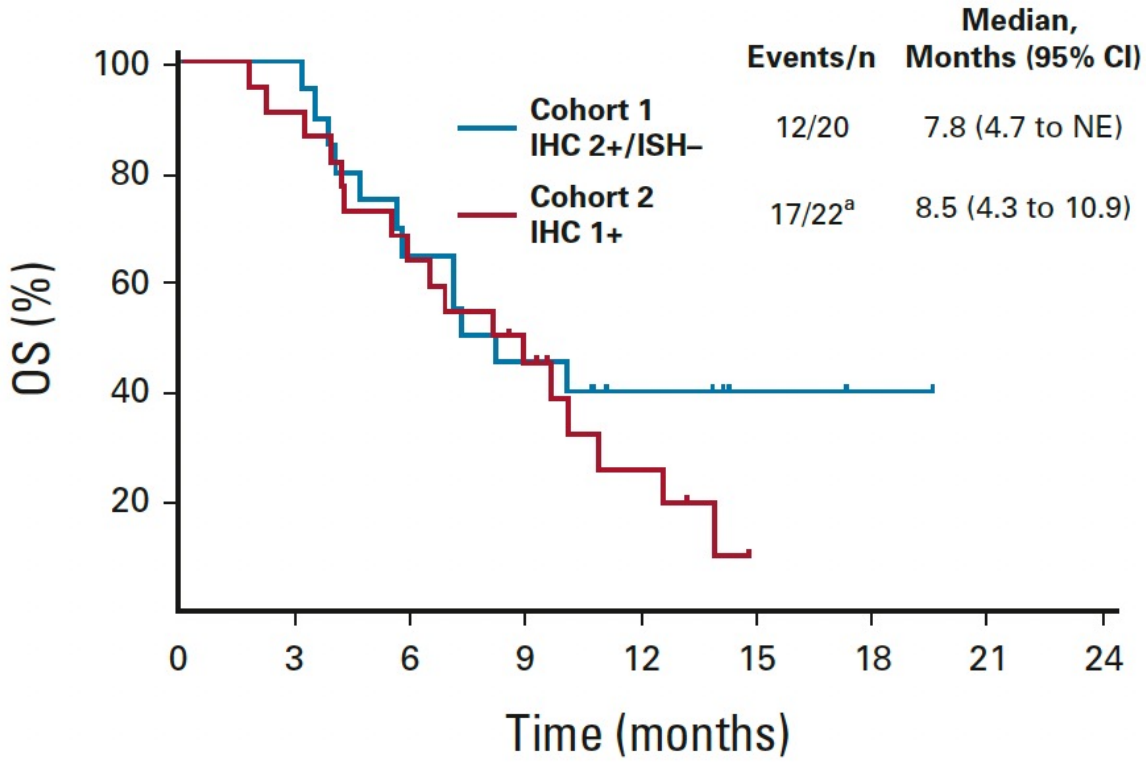
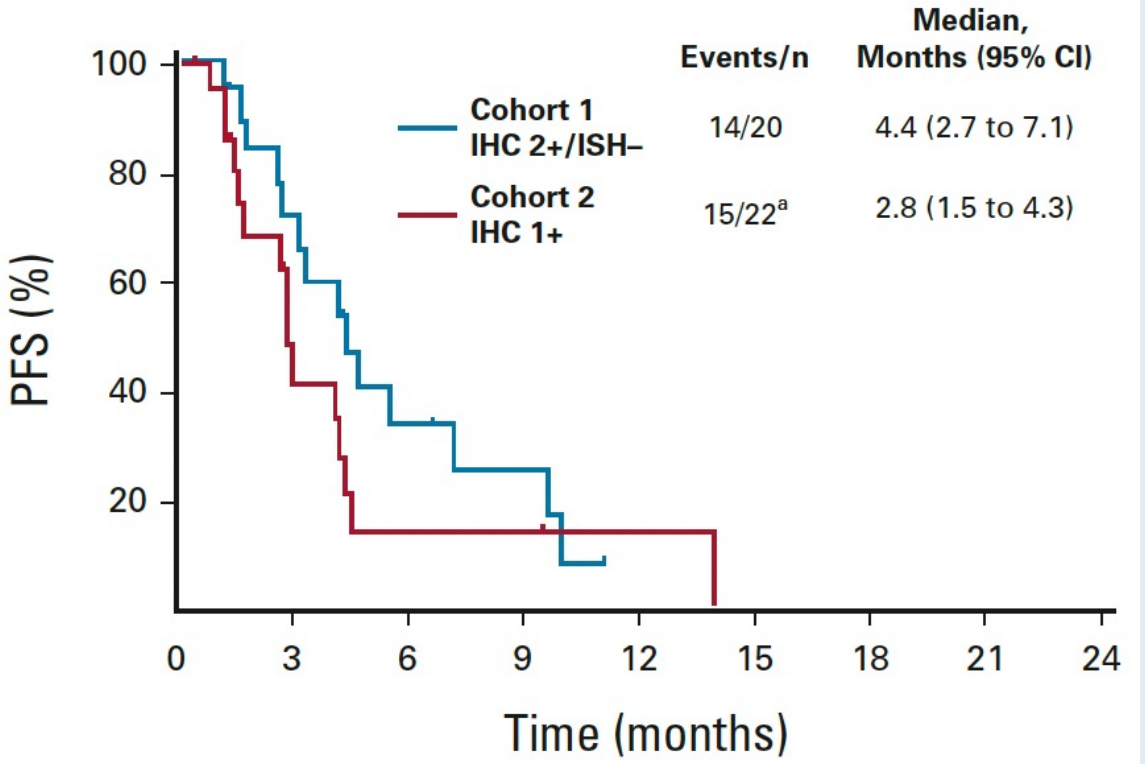




Yamaguchi K et al. *J Clin Oncol* 2023 February 1;41(4):816-25.

RTP RESEARCH TO PRACTICE

DESTINY-Lung01: HER2-Overexpressing Disease

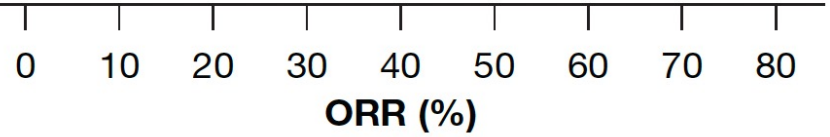
975P ESMO 2022

Trastuzumab Deruxtecan in Patients With HER2-Overexpressing Metastatic Non–Small Cell Lung Cancer: Results From the DESTINY-Lung01 Trial

Egbert F. Smit,[1] Enriqueta Felip,[2] Dipesh Uprety,[3] Kazuhiko Nakagawa,[4] Luis Paz-Ares Rodríguez,[5] Jose M. Pacheco,[6*] Bob T. Li,[7] David Planchard,[8] Christina Baik,[9] Yasushi Goto,[10] Haruyasu Murakami,[11] Andreas Saltos,[12] Kapil Saxena,[13*] Ryota Shiga,[13] Yingkai Cheng,[13] Qi Yan,[13] Wenqin Feng,[13] Pasi A. Jänne[14]

DESTINY-Lung01: Responses to T-DXd by HER2 IHC Status

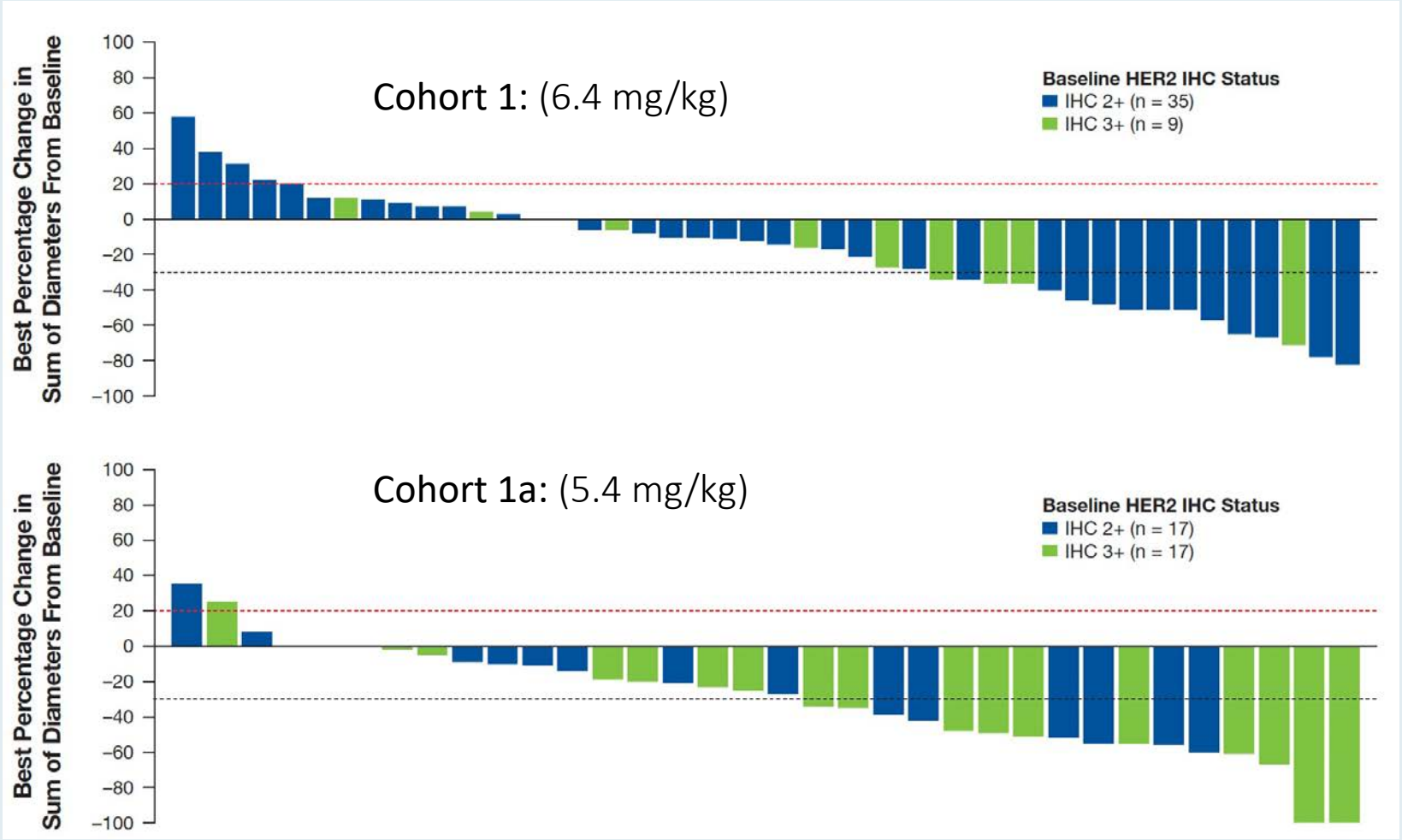
	No. of responders	Confirmed ORR (95% CI)	Confirmed ORR (95% CI)
Cohort 1 (all patients)	13/49	26.5 (15.0-41.1)	
(6.4 mg/kg)			
HER2 IHC 3+	2/10	20.0 (2.5-55.6)	
HER2 IHC 2+	11/39	28.2 (15.0-44.9)	
Cohort 1a (all patients)	14/41	34.1 (20.1-50.6)	
(5.4 mg/kg)			
HER2 IHC 3+	9/17	52.9 (27.8-77.0)	
HER2 IHC 2+	5/24	20.8 (7.1-42.2)	



IHC = immunohistochemistry

Smit EF et al. ESMO 2022;Abstract 975P.

DESTINY-Lung01: Responses to T-DXd by HER2 IHC Status



Smit EF et al. ESMO 2022;Abstract 975P.

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Management of HER2-Expressing Cancers Across the Oncology Spectrum: The Role of Antibody-Drug Conjugates

Thursday, April 27, 2023
6:00 PM – 7:30 PM

Faculty

Lyudmila A Bazhenova, MD
Kelly EH Goodwin, MSN, RN, ANP-BC
Virginia Kaklamani, MD, DSc
Caroline Kuhlman, MSN, APRN-BC
Alexis N McKinney, MSN, AGNP-BC
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What I Tell My Patients:
Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Hepatobiliary Cancers

Friday, April 28, 2023
6:00 AM – 7:30 AM

Faculty

Ahmed Omar Kaseb, MD, CMQ
Blanca Ledezma, MSN, NP, AOCNP
Daneng Li, MD
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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.

In-person attendees can use the networked iPads® to claim NCPD credit or use the QR code as instructed in the program syllabus.

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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