Breakfast with the Investigators: Current and Emerging Role of Antibody-Drug Conjugates in the Treatment of Lung Cancer

Saturday, June 1, 2024
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rebecca S Heist, MD, MPH
Luis Paz-Ares, MD, PhD

Moderator

Jacob Sands, MD

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Faculty

Rebecca S Heist, MD, MPH
Associate Professor of Medicine
Harvard Medical School
Thoracic Oncology
Massachusetts General Hospital Cancer Center
Boston, Massachusetts

Moderator
Jacob Sands, MD
Physician
Dana-Farber Cancer Institute
Assistant Professor
Harvard Medical School
Boston, Massachusetts

Luis Paz-Ares, MD, PhD
Chair of the Medical Oncology Department at the Hospital Universitario 12 de Octubre
Associate Professor at the Universidad Complutense
Head of the Lung Cancer Unit at the National Oncology Research Center
Madrid, Spain

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Dr Heist — Disclosures
Faculty

Consulting Agreements	AbbVie Inc, AstraZeneca Pharmaceuticals LP, Biohaven, Claim Therapeutics, Daiichi Sankyo Inc, Lilly, Merck, Novartis, Regeneron Pharmaceuticals Inc, Sanofi
Contracted Research	Agios Pharmaceuticals Inc, Corvus Pharmaceuticals, Daiichi Sankyo Inc, Erasca, Lilly, Mirati Therapeutics Inc, Mythic Therapeutics, Novartis, Turning Point Therapeutics Inc

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Dr Paz-Ares — Disclosures
Faculty

Advisory Committees	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Daiichi Sankyo Inc, GSK, Janssen Biotech Inc, Lilly, Merck, Mirati Therapeutics Inc, MSD, Novartis, Pfizer Inc, PharmaMar, Roche Laboratories Inc, Sanofi, Servier Pharmaceuticals LLC, Takeda Pharmaceuticals USA Inc
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Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, GSK, Janssen Biotech Inc, Lilly, Mirati Therapeutics Inc, MSD, PharmaMar, Sanofi

Dr Sands — Disclosures
Moderator

Advisory Committee	Curadev
Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Daiichi Sankyo Inc, Gilead Sciences Inc, Lilly, Medtronic Inc, Pfizer Inc, PharmaMar, Sanofi
Contracted Research	Amgen Inc, Harpoon Therapeutics
Data and Safety MonitoringBoard/Committee	Johnson & Johnson Pharmaceuticals

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Dr Love — Disclosures

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Friday May 31	**Hepatobiliary Cancers** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Non-Small Cell Lung Cancer with an EGFR Mutation 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
Saturday June 1	**Antibody-Drug Conjugates in the Treatment of Lung Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Prostate Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday June 2	**Multiple Myeloma** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Ovarian and Endometrial Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Monday June 3	**Colorectal Cancer (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)
	Metastatic Breast Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Tuesday June 4	**Bispecific Antibodies in the Management of Lymphoma (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

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Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Hepatobiliary Cancers

Friday, May 31, 2024

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

Faculty

Robin K (Katie) Kelley, MD
Edward Kim, MD
Arndt Vogel, MD, PhD

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rebecca S Heist, MD, MPH
Luis Paz-Ares, MD, PhD
Jacob Sands, MD

Non-Small Cell Lung Cancer with an EGFR Mutation

Friday, May 31, 2024

6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)

Faculty

Jonathan W Goldman, MD
Corey J Langer, MD
Joel W Neal, MD, PhD
Zofia Piotrowska, MD, MHS
Joshua K Sabari, MD
Helena Yu, MD

Prostate Cancer

Saturday, June 1, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO
Emmanuel S Antonarakis, MD
Andrew J Armstrong, MD, ScM
Tanya B Dorff, MD
Matthew R Smith, MD, PhD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

Multiple Myeloma

Sunday, June 2, 2024

6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Rafael Fonseca, MD
María-Victoria Mateos, MD, PhD
Elizabeth O'Donnell, MD

LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

Faculty

Scott Kopetz, MD, PhD
John Strickler, MD

Ovarian and Endometrial Cancer

Sunday, June 2, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Floor J Backes, MD
Mansoor Raza Mirza, MD
Ritu Salani, MD, MBA
Angeles Alvarez Secord, MD, MHSc
Brian M Slomovitz, MD

Metastatic Breast Cancer

Monday, June 3, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Aditya Bardia, MD, MPH
Harold J Burstein, MD, PhD
Professor Giuseppe Curigliano, MD, PhD
Sara A Hurvitz, MD, FACP
Joyce O'Shaughnessy, MD
Hope S Rugo, MD

Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2024 ASCO® Annual Meeting

LIVE WEBCAST

Bispecific Antibodies in Lymphoma

Tuesday, June 4, 2024

7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

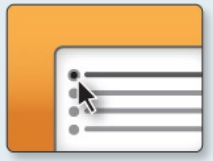
Faculty

Joshua Brody, MD
Ian W Flinn, MD, PhD
Tycel Phillips, MD

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.

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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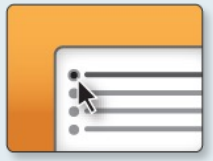
Clinicians Attending via Zoom

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.

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

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

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
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Breakfast with the Investigators: Current and Emerging Role of Antibody-Drug Conjugates in the Treatment of Lung Cancer

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Rebecca S Heist, MD, MPH
Luis Paz-Ares, MD, PhD

Moderator

Jacob Sands, MD

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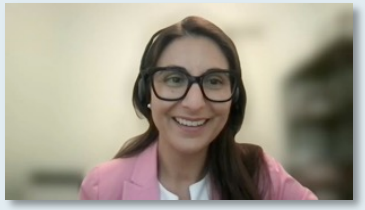
Consulting Oncologists

Neil Love, MD
Research To Practice
Miami, Florida



Laila Agrawal, MD
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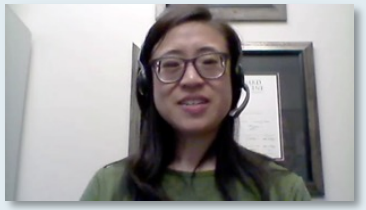
Lynn Cancer Institute
Boca Raton, Florida

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida

Gigi Chen, MD
John Muir Health
Pleasant Hill, California

Sunil Gandhi, MD
Florida Cancer Specialists
& Research Institute
Lecanto, Florida

Shaachi Gupta, MD, MPH
Florida Cancer Specialists
& Research Institute
Lake Worth, Florida



Kimberly Ku, MD
Bloomington, Illinois

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Estelamari Rodriguez, MD, MPH
Sylvester Comprehensive Cancer Center
Miami, Florida

Erik Rupard, MD
Intermountain Health
St George, Utah

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Agenda

Module 1: Integration of Antibody-Drug Conjugates (ADCs) into the Care of Patients with Non-Small Cell Lung Cancer (NSCLC) and HER2 Alterations — Dr Paz-Ares

Module 2: Emerging Role of TROP2-Targeted ADCs for NSCLC — Dr Sands

Module 3: Other Promising Targets for ADCs for Lung Cancer — Dr Heist

Agenda

Module 1: Integration of Antibody-Drug Conjugates (ADCs) into the Care of Patients with Non-Small Cell Lung Cancer (NSCLC) and HER2 Alterations — Dr Paz-Ares

Module 2: Emerging Role of TROP2-Targeted ADCs for NSCLC — Dr Sands

Module 3: Other Promising Targets for ADCs for Lung Cancer — Dr Heist

Consulting Faculty Comments

Trastuzumab deruxtecan as first-line therapy for NSCLC with a HER2 mutation; approach to HER2 testing

Dr Gigi Chen (Pleasant Hill, California)

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QUESTIONS FOR THE FACULTY

For patients with NSCLC with a HER2 mutation, where in the treatment sequence are you typically offering trastuzumab deruxtecan (T-DXd)?

Does the response rate with this agent justify its use as a first-line approach?

QUESTIONS FOR THE FACULTY

Are you generally assessing HER2 overexpression in your patients with NSCLC?

Are you now offering T-DXd to all of your patients with HER2-positive (IHC 3+) NSCLC?

Where in the treatment course are you integrating this agent?

Consulting Faculty Comments

Identification and management of interstitial lung disease (ILD) and other adverse events associated with trastuzumab deruxtecan

Dr Shaachi Gupta
(Lake Worth, Florida)

Dr Erik Rupard
(St George, Utah)

Dr Kimberly Ku
(Bloomington, Illinois)

Dr Estelamari Rodriguez
(Miami, Florida)

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QUESTIONS FOR THE FACULTY

What are the most common toxicities that have been noted with T-DXd?

Which of these do you find most challenging to manage?

Which of these do you believe are most detrimental to patient quality of life?

QUESTIONS FOR THE FACULTY

How specifically are you monitoring for ILD in your patients receiving T-DXd?

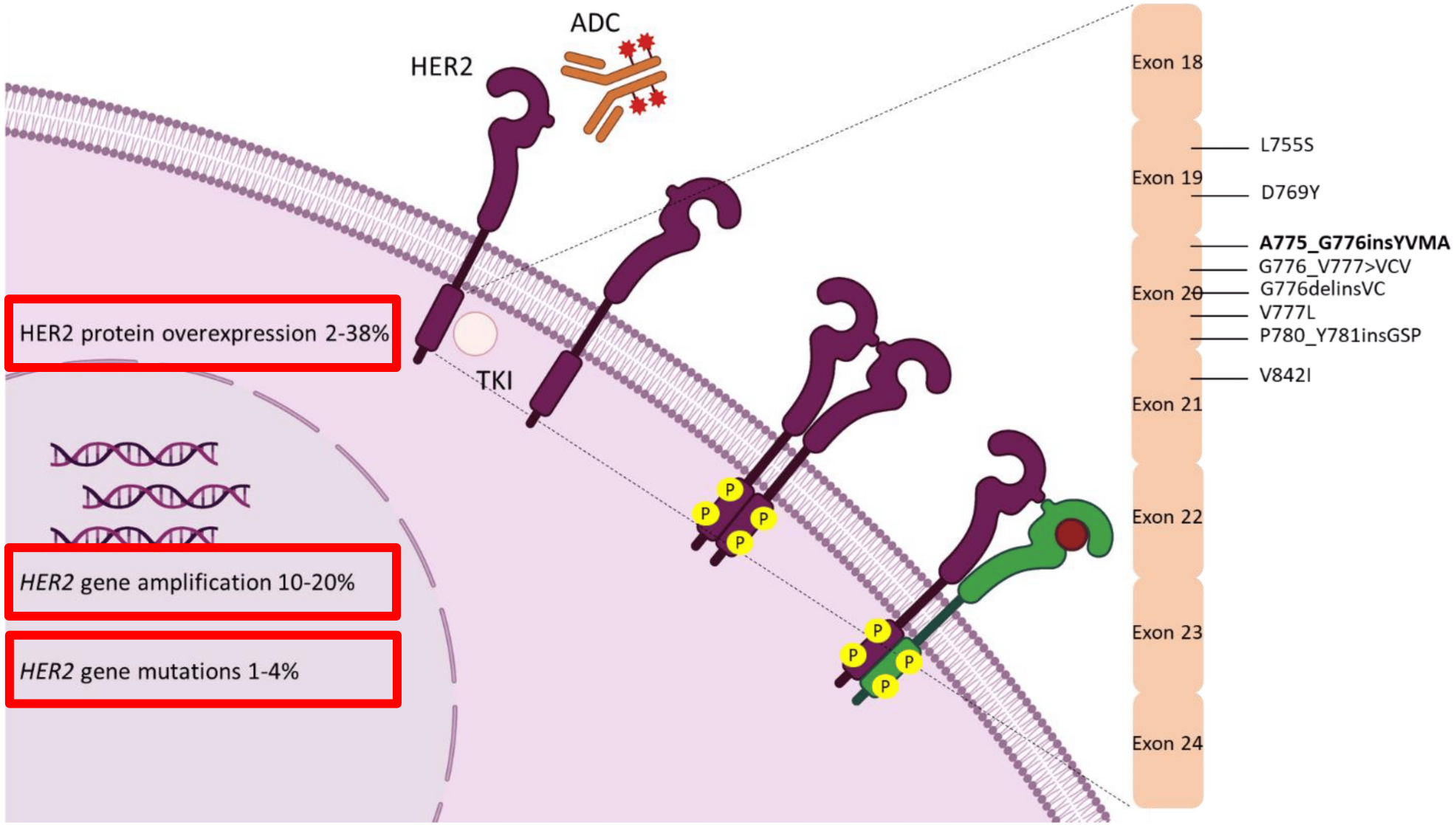
At what level of ILD are you permanently discontinuing treatment, even after resolution of symptoms?

Should these approaches be employed for other deruxtecan-based ADCs, such as datopotamab deruxtecan (Dato-DXd) and patritumab deruxtecan?

Integration of Antibody-Drug Conjugates into the Care of Patients with Non-Small Cell Lung Cancer and HER2 Alterations

Luis Paz-Ares, MD, PhD
Hospital Universitario 12 de Octubre
Madrid, Spain

HER2 as a Targetable Biomarker in NSCLC

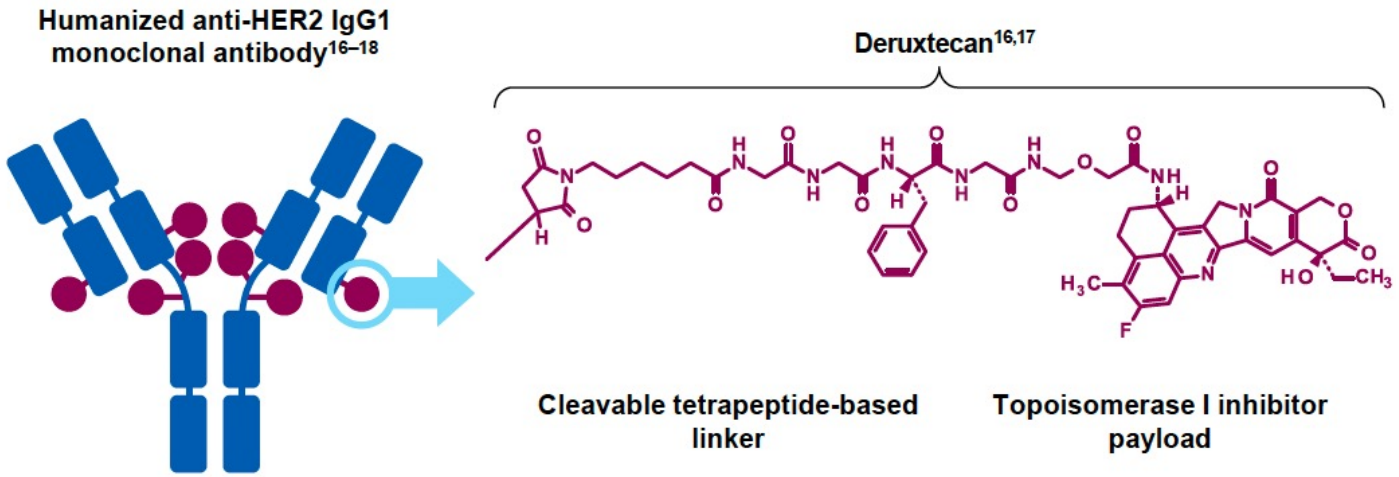


Vathiotis IA et al. Pharmaceuticals 2021, 14(12), 1300

Antibody-Drug Conjugate
Trastuzumab Deruxtecan (T-DXd)

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



HER2, human epidermal growth factor receptor 2; IgG1; immunoglobulin 1

- Payload mechanism of action: topoisomerase I inhibitor
- High potency of payload
- High drug to antibody ratio ≈ 8
- Payload with short systemic half-life
- Stable linker-payload
- Tumor-selective cleavable linker
- Membrane-permeable payload

Smit EF et al. ASCO 2020;Abstract 9504.
Planchard D et al. ESMO 2023. Abstract 1507TiP.

The NEW ENGLAND JOURNAL of MEDICINE

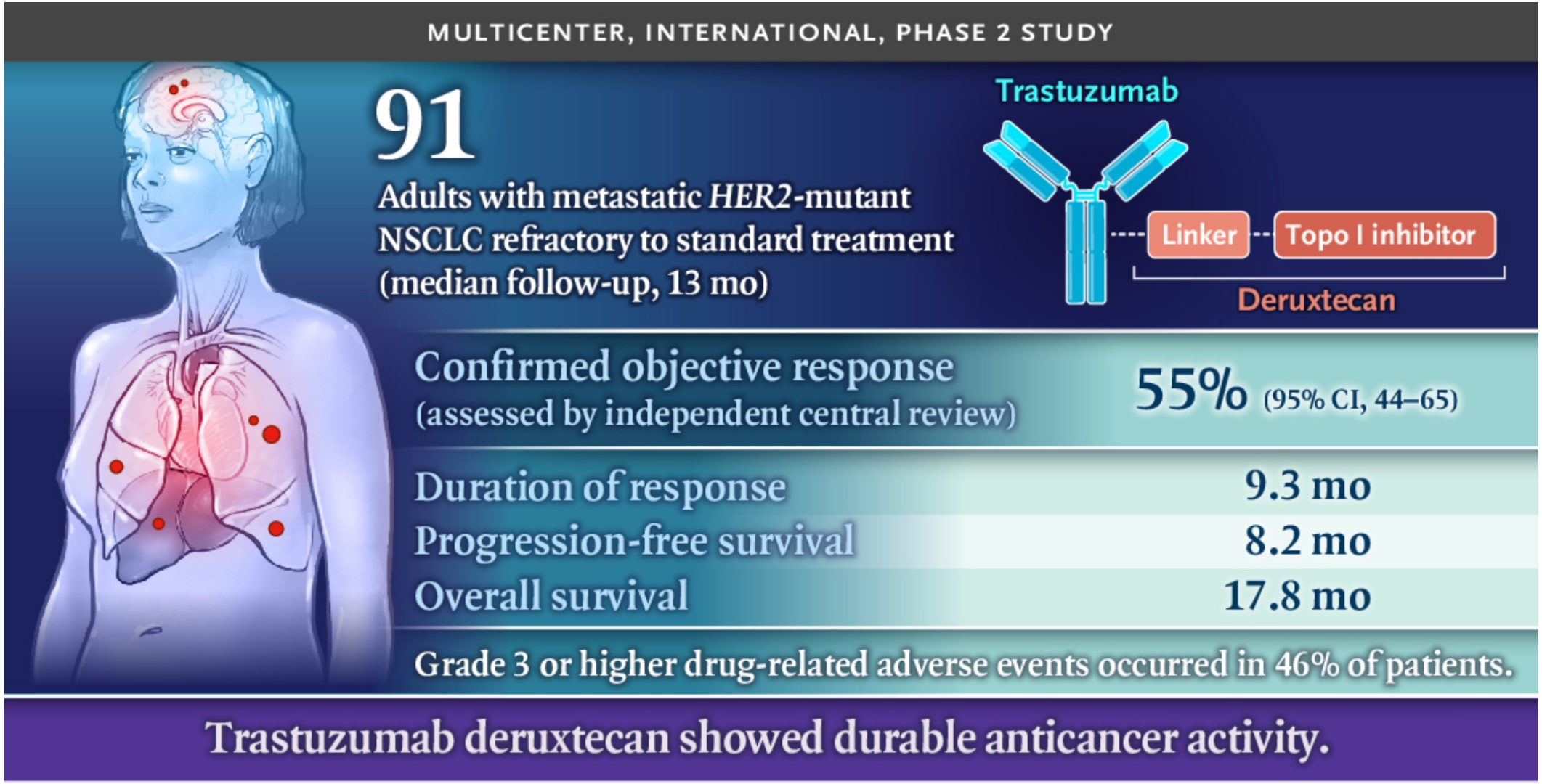
2022;386:241-51

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

Bob T. Li, M.D., Ph.D., M.P.H., Egbert F. Smit, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Hibiki Udagawa, M.D., Julien Mazières, M.D., Misako Nagasaka, M.D., Ph.D., Lyudmila Bazhenova, M.D., Andreas N. Saltos, M.D., Enriqueta Felip, M.D., Ph.D., Jose M. Pacheco, M.D., Maurice Pérol, M.D., Luis Paz-Ares, M.D., Kapil Saxena, M.D., Ryota Shiga, B.Sc., Yingkai Cheng, M.D., Ph.D., Suddhasatta Acharyya, Ph.D., Patrik Vitazka, M.D., Ph.D., Javad Shahidi, M.D., David Planchard, M.D., Ph.D., and Pasi A. Jänne, M.D., Ph.D., for the DESTINY-Lung01 Trial Investigators*

Phase II DESTINY-Lung01 Study



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

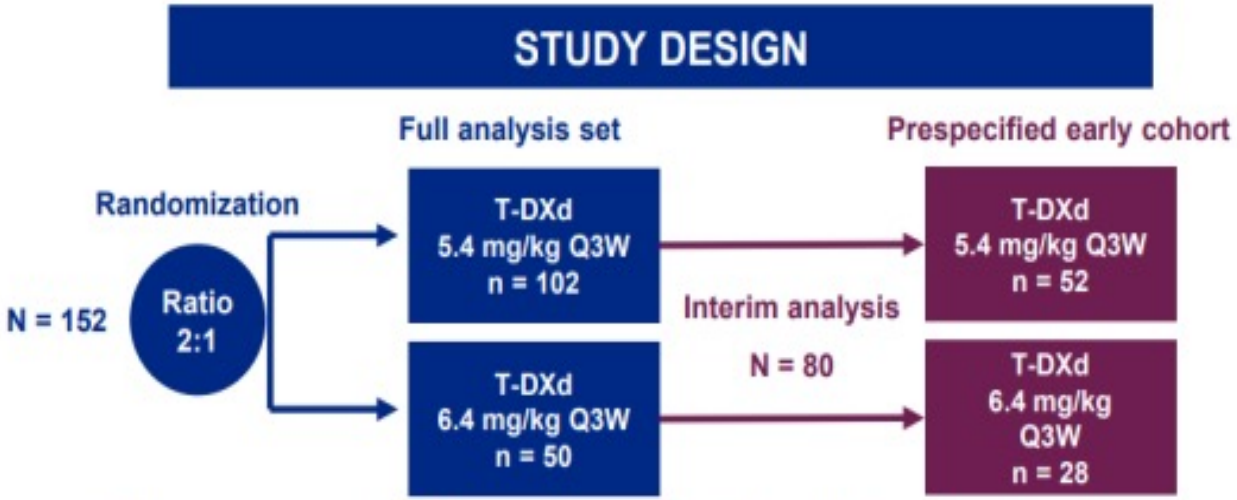
Phase II DESTINY-Lung02 Study

Key eligibility criteria

- Metastatic *HER2*m NSCLC
- Activating *HER2* mutation
- ≥1 prior anti-cancer therapy (2L+), including platinum-based chemotherapy
- Measurable disease by BICR based on RECIST v1.1
- ECOG PS of 0 or 1

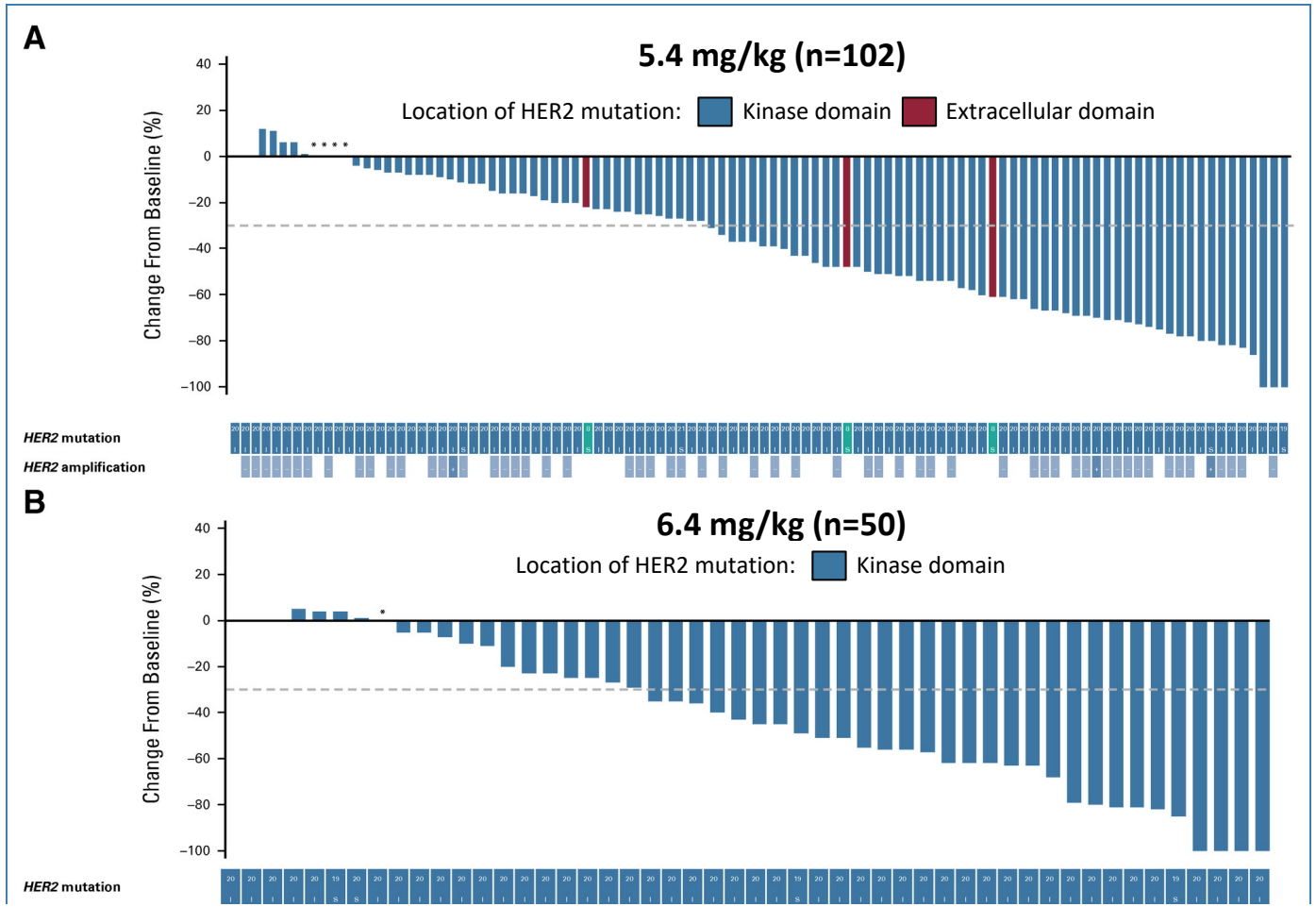
Stratification factor:

- Previous use of anti-PD-(L)1



Data cutoff: Mar 24, 2022
Median follow-up: 5.54 months (range 0.6-12.1 months)

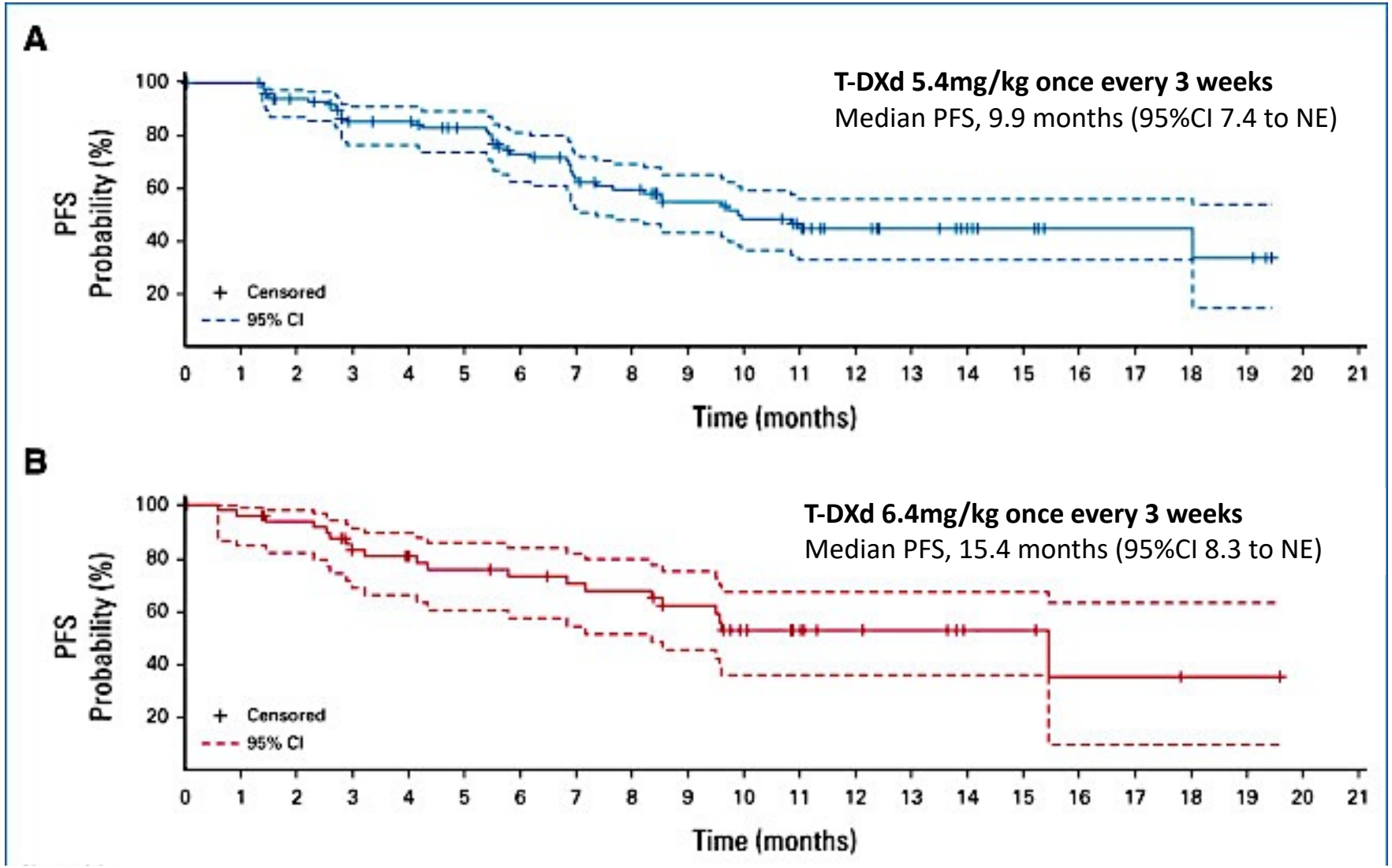
DESTINY-Lung02: Responses by Dose



Response Assessment by BICR	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 102)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 50)
Confirmed ORR, No. (%)	50 (49.0)	28 (56.0)
95% CI	39.0 to 59.1	41.3 to 70.0
Best confirmed overall response, No. (%)		
CR	1 (1.0)	2 (4.0)
PR	49 (48.0)	26 (52.0)
SD	45 (44.1)	18 (36.0)
PD	4 (3.9)	2 (4.0)
Nonevaluable[a]	3 (2.9)	2 (4.0)
DCR, No. (%)	95 (93.1)	46 (92.0)
95% CI	86.4 to 97.2	80.8 to 97.8
DoR, months, median (95% CI)	16.8 (6.4 to NE)	NE (8.3 to NE)
TTIR, months, median (range)	1.8 (1.2-7.0)	1.6 (1.2-11.2)
Follow-up, months, median (range)	11.5 (1.1-20.6)	11.8 (0.6-21.0)

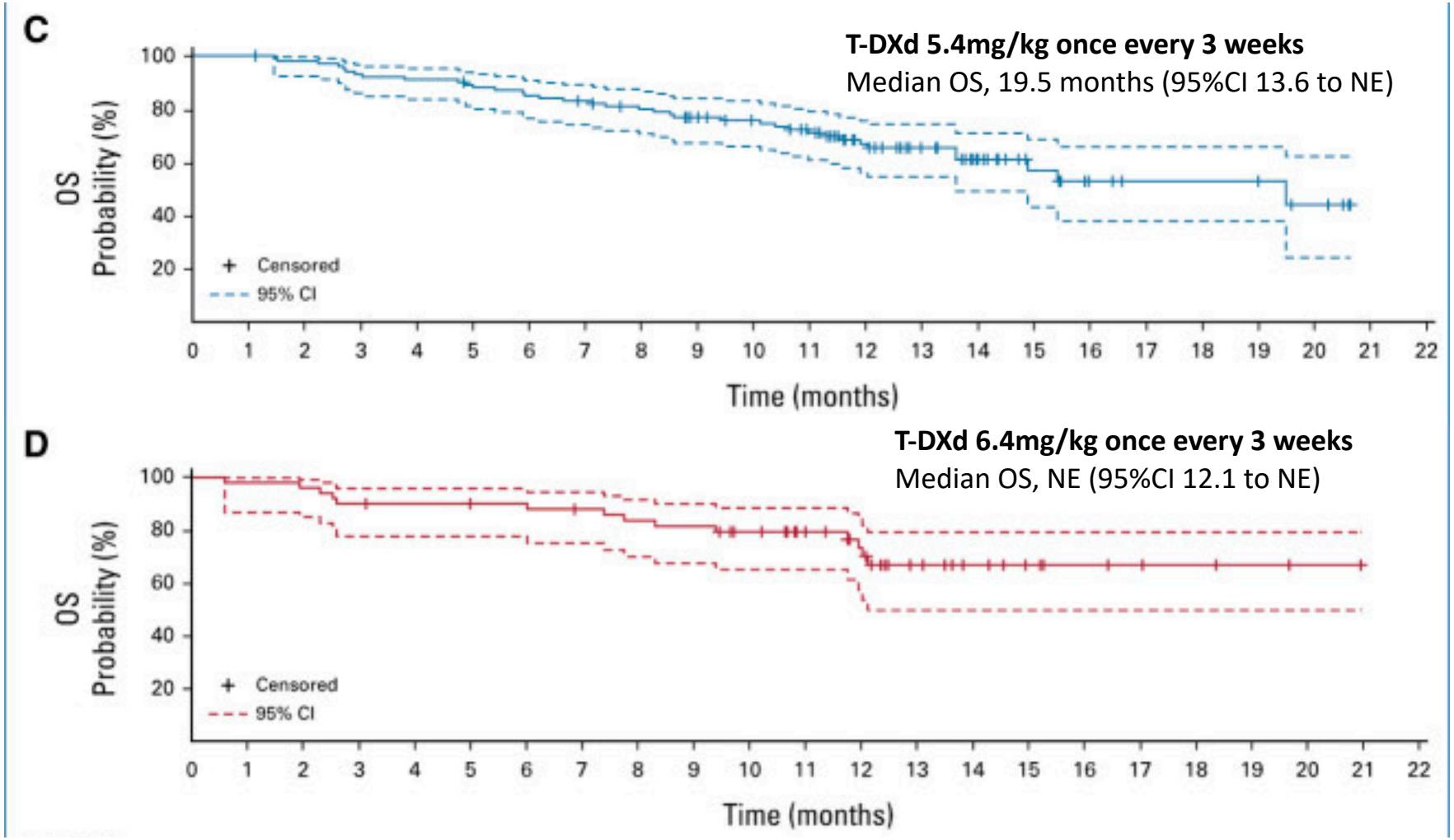
Goto K et al. *J Clin Oncol* 2023 Nov 1; 41(31): 4852–4863.

DESTINY-Lung02: PFS by Dose



Goto K et al. *J Clin Oncol* 2023 Nov 1; 41(31): 4852–4863.

DESTINY-Lung02: OS by Dose



Goto K et al. *J Clin Oncol* 2023 Nov 1; 41(31): 4852–4863.

DESTINY-Lung02: Final Analysis Results

Efficacy Summary		
	T-DXd 5.4 mg/kg (n=102)	**T-DXd 6.4 mg/kg (n=50)**
cORR,[a] % (95% CI)	50.0 (39.9-60.1)	56.0 (41.3-70.0)
Median DoR, mo (95% CI)	12.6 (6.4-NE)	12.2 (7.0-NE)
Median PFS, mo (95% CI)	10.0 (7.7-15.2)	12.9 (7.2-16.7)
Median OS, mo (95% CI)	19.0 (14.7-NE)	17.3 (13.8-NE)

Adjudicated drug-related interstitial lung disease (ILD)/pneumonitis was reported in 14.9% (15/101) and 32.0% (16/50) of patients in the T-DXd 5.4 and 6.4 mg/kg arms, respectively; most events were grade 1 or 2 (1 grade 5 event in each arm).

NE; not estimable

[a]By BICR

Janne PA et al. ASCO 2024. Abstract 8543.

DESTINY-Lung02: Common TRAEs

	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 101),[a] No. (%)		T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 50),[a] No. (%)	
Preferred Term	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Nausea	68 (67.3)	4 (4.0)	41 (82.0)	3 (6.0)
Neutropenia[b]	43 (42.6)	19 (18.8)	28 (56.0)	18 (36.0)
Fatigue[b]	45 (44.6)	8 (7.9)	25 (50.0)	5 (10.0)
Decreased appetite	40 (39.6)	2 (2.0)	25 (50.0)	2 (4.0)
Anemia[b]	37 (36.6)	11 (10.9)	26 (52.0)	8 (16.0)
Vomiting	32 (31.7)	3 (3.0)	22 (44.0)	1 (2.0)
Constipation	37 (36.6)	1 (1.0)	16 (32.0)	0
Leukopenia[b]	29 (28.7)	5 (5.0)	17 (34.0)	8 (16.0)
Thrombocytopenia[b]	28 (27.7)	6 (5.9)	14 (28.0)	5 (10.0)
Diarrhea	23 (22.8)	1 (1.0)	18 (36.0)	2 (4.0)
Alopecia	22 (21.8)	0	17 (34.0)	0
Transaminases increased[b]	22 (21.8)	3 (3.0)	10 (20.0)	0

Goto K et al. *J Clin Oncol* 2023 Nov 1; 41(31): 4852–4863.

DESTINY-Lung02: Adjudicated Drug-Related ILD

Adjudicated Drug-Related ILD in Patients With Prior Anti–PD-(L)1 Therapy	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 74), No. (%)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 39), No. (%)
Grade 1	4 (5.4)	2 (5.1)
Grade 2	5 (6.8)	9 (23.1)
Grade 3	1 (1.4)	0
Grade 4	0	0
Grade 5	1 (1.4)	0
Total	11 (14.9)	11 (28.2)

Adjudicated Drug-Related ILD in Patients Without Prior Anti–PD-(L)1 Therapy	T-DXd 5.4 mg/kg Once Every 3 Weeks (n = 27), No. (%)	T-DXd 6.4 mg/kg Once Every 3 Weeks (n = 11), No. (%)
Grade 1	0	2 (18.2)
Grade 2	2 (7.4)	0
Grade 3	0	0
Grade 4	0	0
Grade 5	0	1 (9.1)
Total	2 (7.4)	3 (27.3)

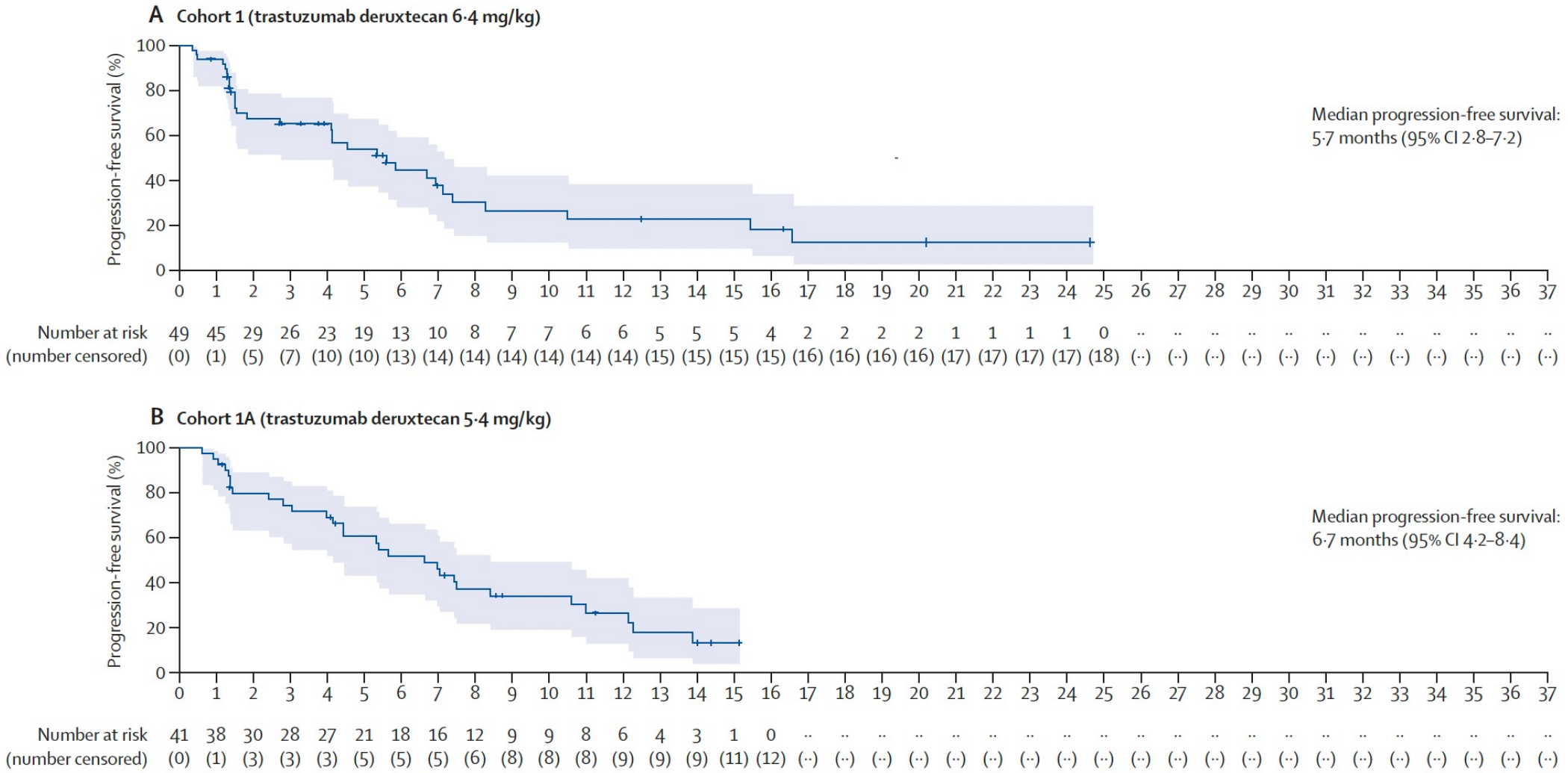
*Two of the three patients with grade 1 ILD in the 6.4 mg/kg arm were retreated with T-DXd, both with negative rechallenge (no recurrence of ILD/pneumonitis after retreatment with T-DXd).

Goto K et al. *J Clin Oncol* 2023 Nov 1; 41(31): 4852–4863.

Trastuzumab deruxtecan in patients with metastatic non-small-cell lung cancer (DESTINY-Lung01): primary results of the HER2-overexpressing cohorts from a single-arm, phase 2 trial

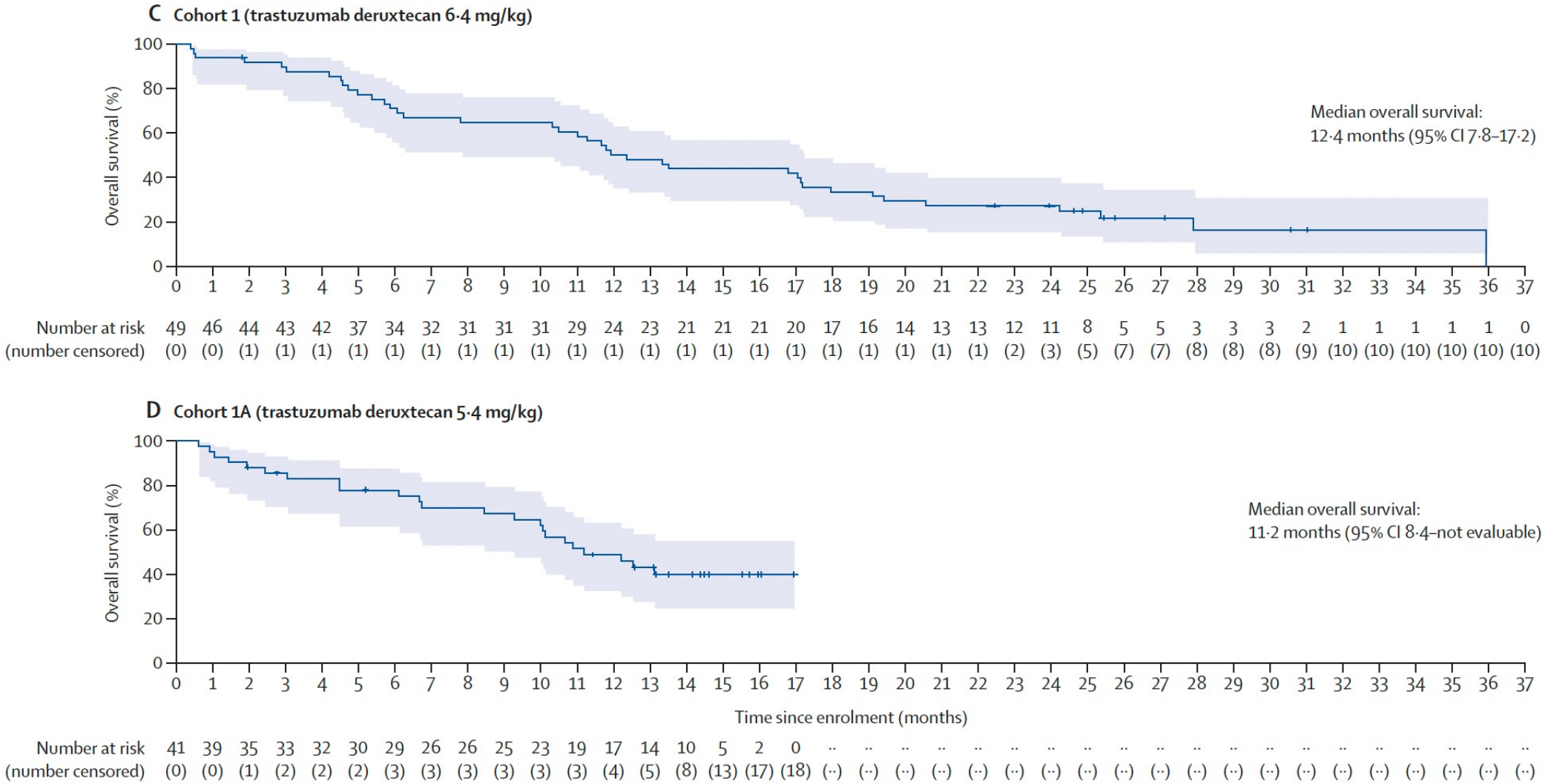
Egbert F Smit, Enriqueta Felip, Dipesh Uprety, Misako Nagasaka, Kazuhiko Nakagawa, Luis Paz-Ares Rodríguez, Jose M Pacheco, Bob T Li, David Planchard, Christina Baik, Yasushi Goto, Haruyasu Murakami, Andreas Saltos, Kaline Pereira, Ayumi Taguchi, Yingkai Cheng, Qi Yan, Wenqin Feng, Zenta Tsuchihashi, Pasi A Jänne

DESTINY-Lung01: PFS by T-DXd Dose — HER2 Overexpression Cohort Data



Smit EF et al. *Lancet Oncol* 2024; 25: 439–54

DESTINY-Lung01: OS by T-DXd Dose — HER2 Overexpression Cohort Data



Smit EF et al. *Lancet Oncol* 2024; 25: 439–54

DESTINY-Lung01: Most Common Adverse Events — HER2 Overexpression Cohort Data

	Cohort 1 (6·4 mg/kg); N=49				Cohort 1A (5·4 mg/kg); N=41			
	Grades 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Nausea	26 (53%)	3 (6%)	0	0	28 (68%)	2 (5%)	0	0
Fatigue	23 (47%)	6 (12%)	0	0	26 (63%)	3 (7%)	0	0
Decreased appetite	20 (41%)	2 (4%)	0	0	19 (46%)	0	0	0
Constipation	15 (31%)	0	0	0	10 (24%)	0	0	0
Vomiting	13 (27%)	2 (4%)	0	0	12 (29%)	1 (2%)	0	0
Diarrhoea	12 (24%)	2 (4%)	0	0	13 (32%)	2 (5%)	0	0
Weight decreased	12 (24%)	0	0	0	7 (17%)	1 (2%)	0	0
Anaemia	10 (20%)	3 (6%)	1 (2%)	0	8 (20%)	3 (7%)	0	0
Alopecia	10 (20%)	0	0	0	5 (12%)	0	0	0
Dyspnoea	8 (16%)	5 (10%)	0	0	10 (24%)	1 (2%)	0	1 (2%)
Dizziness	8 (16%)	2 (4%)	0	0	3 (7%)	0	0	0
Thrombocytopenia	7 (14%)	1 (2%)	1 (2%)	0	3 (7%)	0	0	0
Hypokalaemia	6 (12%)	2 (4%)	0	0	1 (2%)	2 (5%)	0	0
Stomatitis	6 (12%)	0	0	0	2 (5%)	0	0	0
Cough	6 (12%)	0	0	0	12 (29%)	0	0	0
Pneumonitis	5 (10%)	1 (2%)	1 (2%)	1 (2%)†	2 (5%)	0	0	0
Blood creatinine increased	5 (10%)	0	0	0	3 (7%)	0	0	0
Upper respiratory tract infection	5 (10%)	0	0	0	1 (2%)	0	0	0

Smit EF et al. *Lancet Oncol* 2024; 25: 439–54

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).

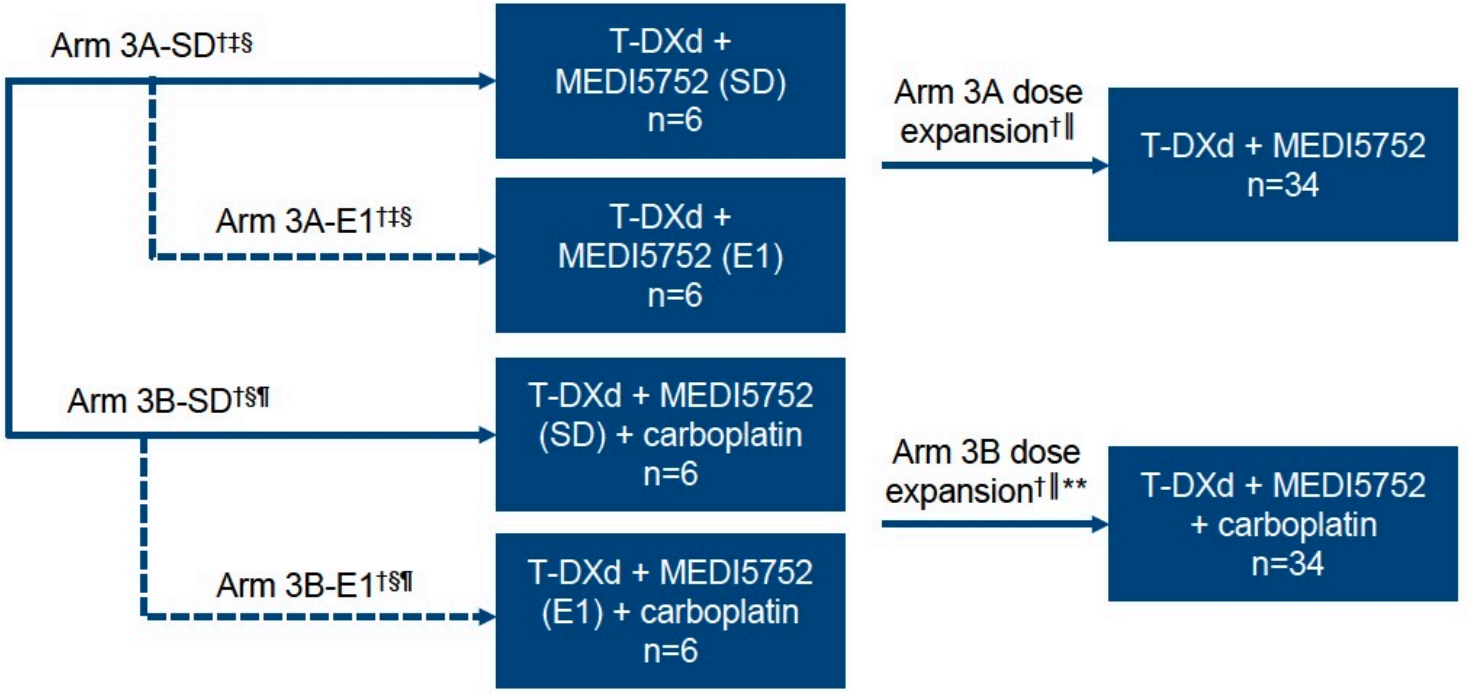
The major efficacy outcome measure in all three trials was confirmed objective response rate (ORR), and an additional efficacy outcome was duration of response (DOR). All outcomes were assessed by independent central review (ICR) based on RECIST v1.1. In DESTINY-PanTumor02, ORR was 51.4% (95% CI: 41.7, 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

Phase Ib DESTINY-Lung03: Study Design

Patient population for Part 3

- Unresectable, locally advanced or metastatic HER2-OE* nonsquamous NSCLC
- Naïve for non-curative treatment for locally advanced or metastatic NSCLC
- No *EGFR* mutations, *EML4-ALK* fusion, or other targetable alterations for which a targeted therapy is available
- WHO/ECOG performance status of 0 or 1



Primary Endpoint:
Frequency of AEs and SAEs

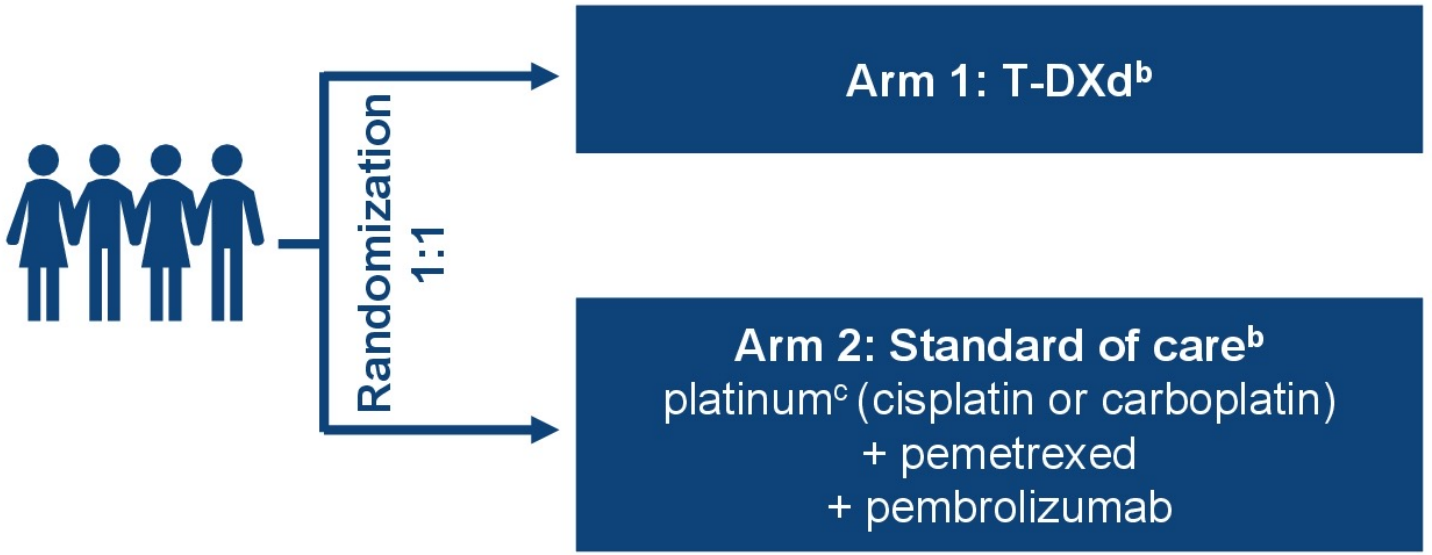
Planchard D et al. ESMO 2023. Abstract 1507TiP.

Phase III DESTINY-Lung04: Study Design

Patient population (N≈264)

- Unresectable, locally advanced (not amenable to curative therapy), or metastatic nonsquamous NSCLC with *HER2* exon 19 or 20 mutations[a]
- Naive to systemic therapy in the locally advanced or metastatic setting
- No known other targetable oncogenic mutations/alterations

[a] *HER2* mutations may be detected in tissue or ctDNA.
[b] Crossover is not permitted.
[c] Investigator's choice of cisplatin or carboplatin.



Primary Endpoint:
PFS (by RECIST v1.1 per BICR)

Li BT et al. ASCO 2022. Abstract TPS9137.

Agenda

Module 1: Integration of Antibody-Drug Conjugates (ADCs) into the Care of Patients with Non-Small Cell Lung Cancer (NSCLC) and HER2 Alterations — Dr Paz-Ares

Module 2: Emerging Role of TROP2-Targeted ADCs for NSCLC — Dr Sands

Module 3: Other Promising Targets for ADCs for Lung Cancer — Dr Heist

RTP
RESEARCH
TO PRACTICE

Consulting Faculty Comments

Integrating TROP2-directed ADCs into the management of lung cancer

Dr Gigi Chen (Pleasant Hill, California)

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

From a risk/benefit standpoint, how do you believe Dato-DXd compares to currently available therapies such as docetaxel?

Given what we currently know about Dato-DXd, would you like to have access to this agent for your patients with progressive NSCLC?

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Is there a biological rationale as to why Dato-DXd would be more effective in patients with nonsquamous histology?

QUESTIONS FOR THE FACULTY

What are the most common toxicities that have been noted with Dato-DXd?

Which of these do you find most challenging to manage?

Which of these do you believe are most detrimental to patient quality of life?

QUESTIONS FOR THE FACULTY

What strategies do you employ to prevent stomatitis/ oral mucositis in patients receiving Dato-DXd?

For patients who develop stomatitis/oral mucositis while receiving the drug, what can be done to manage it?

Dana-Farber
Cancer Institute

Trop2 Antibody-Drug Conjugates

Jacob Sands, MD

June 2024

Trophoblast-Cell Surface Antigen 2 (TROP 2)

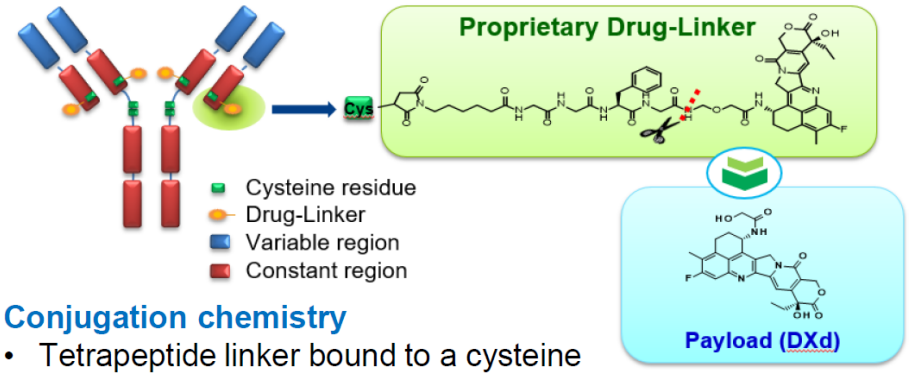
- Initially discovered in human trophoblast and choriocarcinoma cells
- An intracellular calcium signal transducer overexpressed in various epithelial cancers
- Associated with poor prognosis in some data sets
- Not expressed in normal tissue
- Encoded by TACSTD2
- Role is not fully understood but thought to have a role in growth and proliferation of carcinoma cells
- Thought to be an oncogene with a role in initiating signaling mechanisms that can increase tumorigenicity, aggressiveness, and metastasis

Basu A, et al. Int J Cancer. 1995
Lipinski M, et al. Proc Natl Acad Sci U S A. 1981
Shvartsur A, et al. Genes Cancer. 2015
Wang J, et al. Mol Cancer Ther. 2008
Ohmachi, et al. Clin Cancer Res. 2006;12:3057

TROP2 Antibody-Drug Conjugates

Datopotamab Deruxtecan (DS-1062)

DS-1062a structure: TROP2-targeting antibody-drug conjugate[1] with a novel topoisomerase I inhibitor (DXd)[2,3]

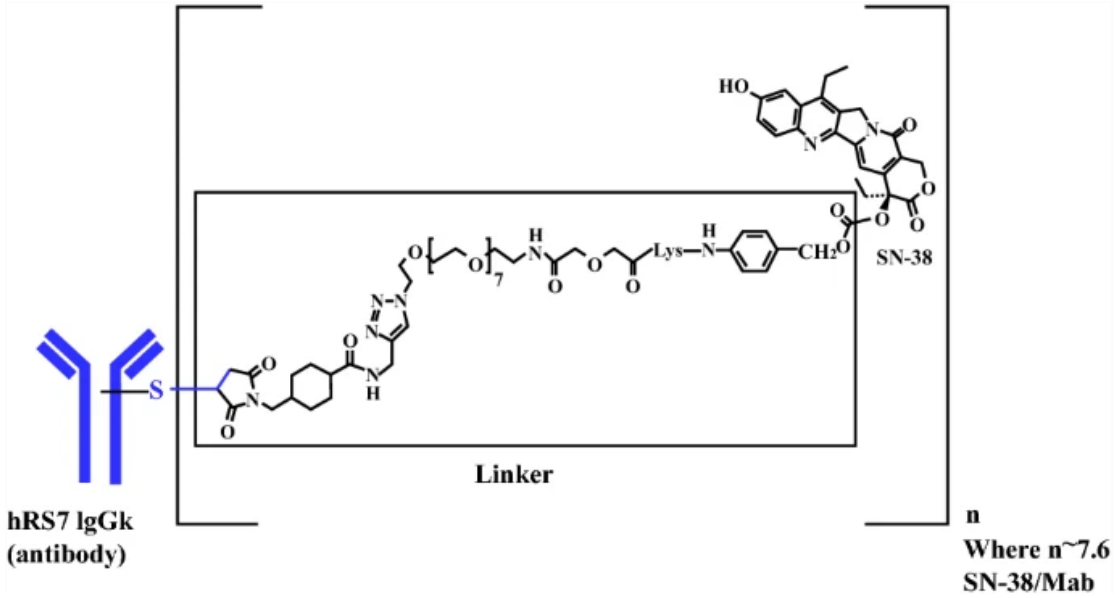


Conjugation chemistry

- Tetrapeptide linker bound to a cysteine residue of the antibody
- DS-1062a is a selective DAR4 conjugate

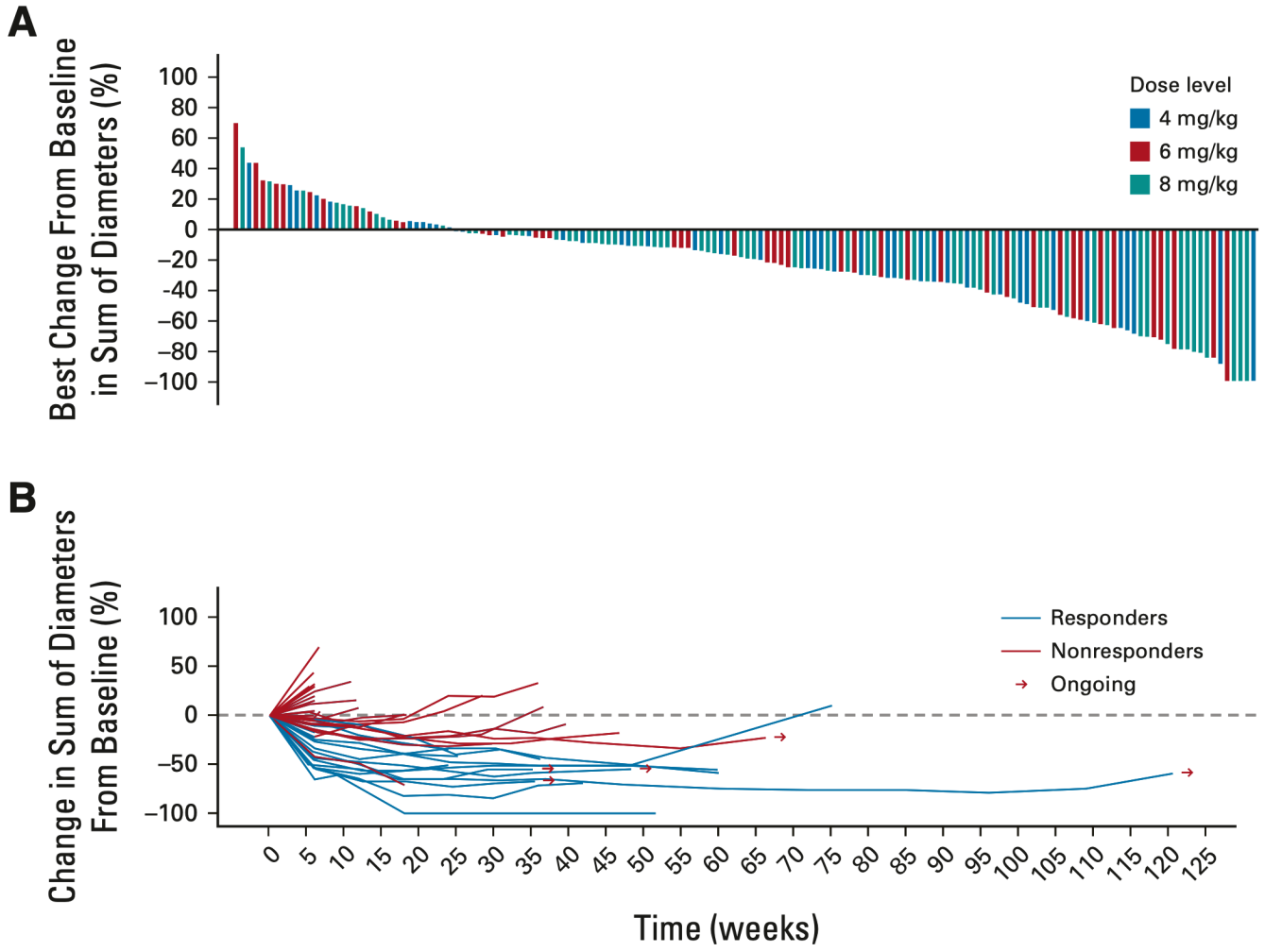
Sands et al. ASCO 2018

Sacituzumab govitecan



Syed YY. Drugs 2020;80:1019-1025

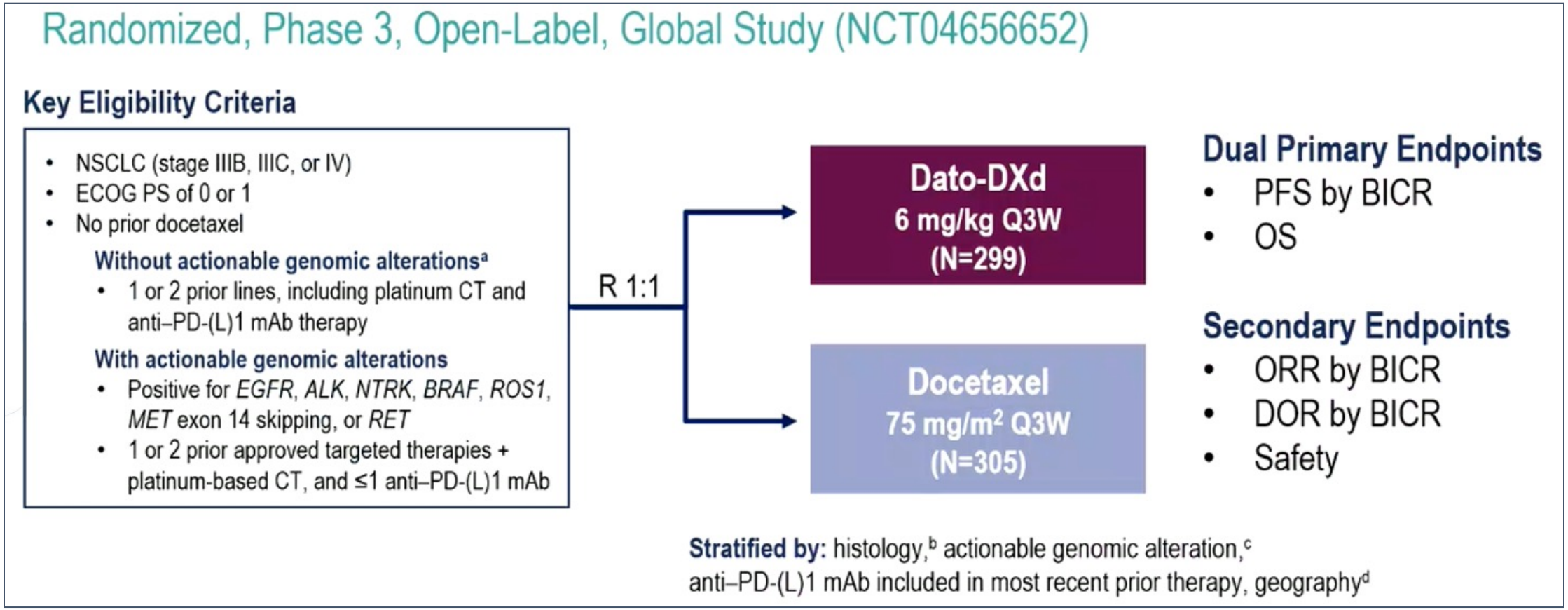
Datopotamab Deruxtecan (Dato-DXd): TROPION-PanTumor01 (NSCLC)



Response	Dato-DXd Dose 4 mg/kg (n = 50)	6 mg/kg (n = 50)	8 mg/kg (n = 80)
Confirmed ORR, No. (%)	11 (22)	13 (26)	19 (23.8)
95% CI	11.5 to 36.0	14.6 to 40.3	14.9 to 34.6
CR	0	0	1 (1.3)
PR	11 (22)	13 (26)	18 (22.5)
ORR confirmed and pending confirmation, No. (%)	15 (30)	16 (32)	25 (31.3)
PR pending confirmation	4 (8)	3 (6)	6 (7.5)
DCR, No. (%)	38 (76)	35 (70)	63 (78.8)
95% CI	61.8 to 86.9	55.4 to 82.1	68.2 to 87.1
SD, No. (%)	26 (52)	20 (40)	42 (52.5)
Non-CR/PD, No. (%)	1 (2)	2 (4)	2 (2.5)
PD, No. (%)	7 (14)	10 (20)	8 (10)
NE, No. (%)	5 (10)	5 (10)	9 (11.3)
TTR, months, median (range)	1.4 (1.2-8.2)	1.4 (1.2 to 5.7)	1.4 (1.2 to 13.7)
DOR, months, median (95% CI)	12.7 (2.8 to NE)	10.5 (5.6 to 26.5)	9.6 (5.8 to NE)
PFS, months, median (95% CI)	4.3 (2.9 to 6.9)	6.9 (2.7 to 8.8)	5.2 (4.1 to 7.1)
OS, months, median (95% CI)	12.9 (9.4 to NE)	11.4 (7.1 to 20.6)	10.5 (8.0 to 12.0)

Shimizu T, Sands J, Yoh K, et al. J Clin Oncol. 2023;41(29):4678-4687.

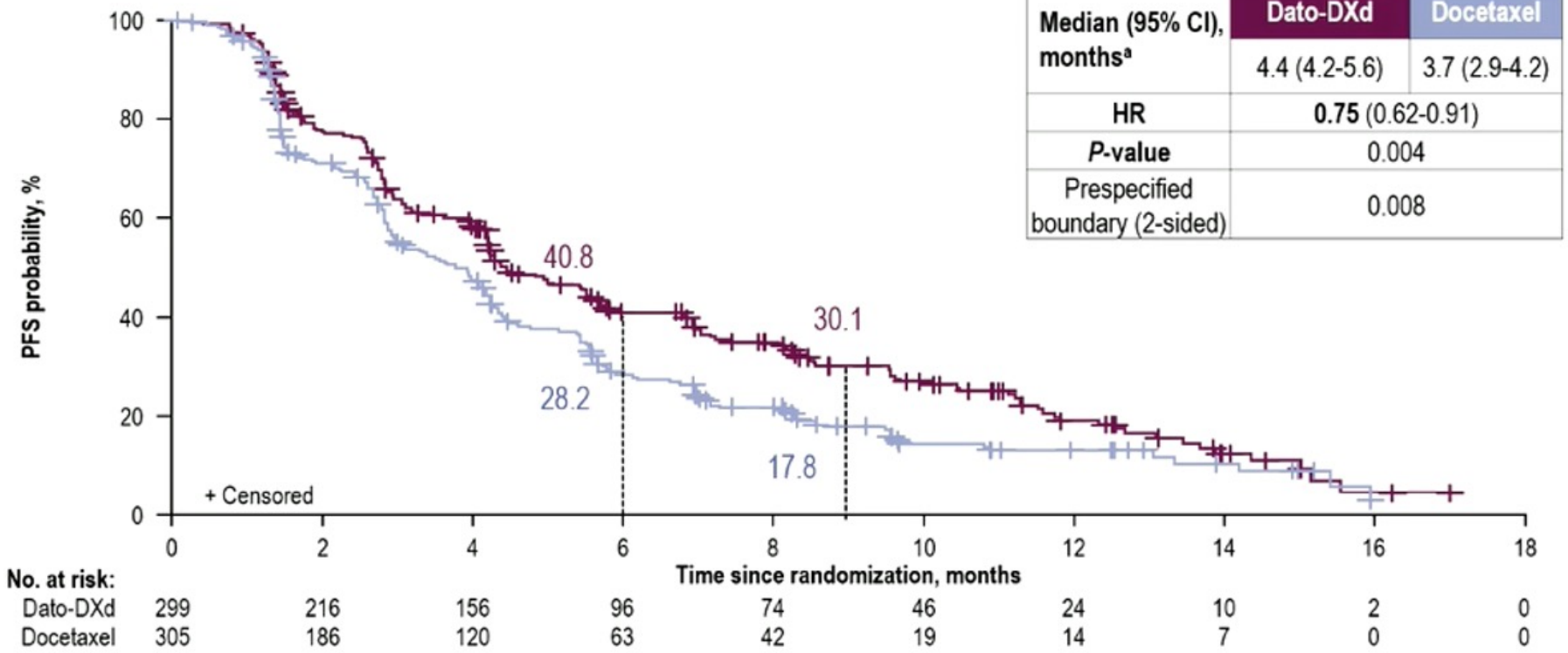
TROPION-Lung01



Lisberg et al. ESMO 2023

Datopotamab Deruxtecan (Dato-DXd)

Progression-Free Survival: ITT

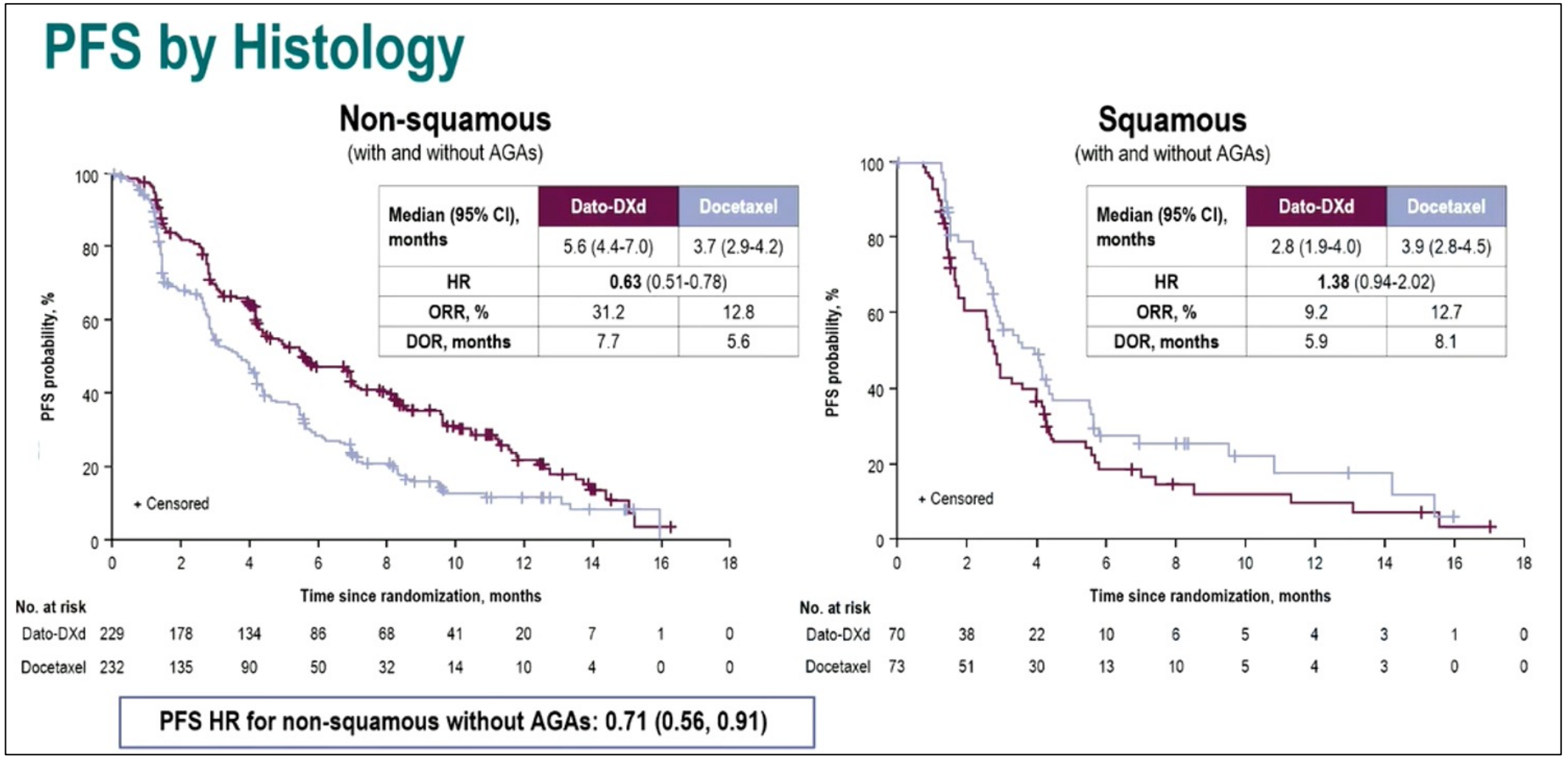


Median (95% CI), months[a]	Dato-DXd	Docetaxel
	4.4 (4.2-5.6)	3.7 (2.9-4.2)
HR	**0.75** (0.62-0.91)	
P-value	0.004	
Prespecified boundary (2-sided)	0.008	

	Dato-DXd	Docetaxel
ORR (95% CI), %[b]	**26.4** (21.5-31.8)	**12.8** (9.3-17.1)
DOR (95% CI), mo	**7.1** (5.6-10.9)	**5.6** (5.4-8.1)

Lisberg et al. ESMO 2023

Datopotamab Deruxtecan (Dato-DXd)



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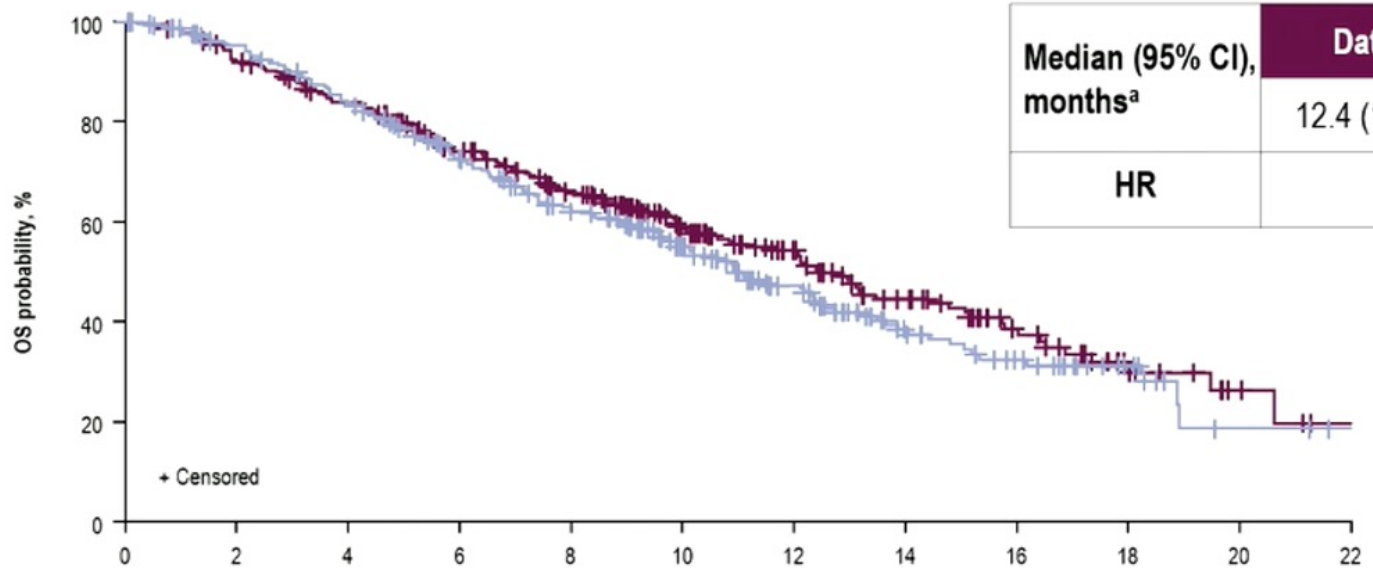
Datopotamab Deruxtecan (Dato-DXd)

Interim Overall Survival: ITT



Median (95% CI), months[a]	Dato-DXd	Docetaxel
	12.4 (10.8-14.8)	11.0 (9.8-12.5)
HR	**0.90** (0.72-1.13)	

Information fraction at interim analysis (events/total events required): **74%.**

No. at risk												
Dato-DXd	299	273	243	201	166	121	85	56	33	14	6	1
Docetaxel	305	273	239	193	156	115	76	42	29	13	4	1

Non-squamous HR (95% CI): **0.77** (0.59-1.01); **Squamous HR** (95% CI): **1.32** (0.87-2.00)

Trial is continuing to final OS analysis

HR, hazard ratio; ITT, intention to treat; OS, overall survival.
[a]Median OS follow-up was 11.8 (95% CI, 11.3-12.7) and 11.7 (95% CI, 10.9-12.9) months for Dato-DXd and docetaxel, respectively.

Lisberg et al. ESMO 2023

TROPION-Lung01

TRAEs Occurring in ≥10% of Patients

System organ class Preferred term, n (%)	Dato-DXd N=297		Docetaxel N=290	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Blood and lymphatic system				
Anemia	43 (15)	11 (4)	59 (20)	11 (4)
Neutropenia[a]	12 (4)	2 (1)	76 (26)	68 (23)
Gastrointestinal				
Stomatitis	140 (47)	19 (6)	45 (16)	3 (1)
Nausea	100 (34)	7 (2)	48 (17)	3 (1)
Vomiting	38 (13)	3 (1)	22 (8)	1 (0.3)
Constipation	29 (10)	0	30 (10)	0
Diarrhea	28 (9)	1 (0.3)	55 (19)	4 (1)
General				
Asthenia	55 (19)	8 (3)	55 (19)	5 (2)
Fatigue	34 (11)	2 (1)	40 (14)	6 (2)
Metabolism and nutrition				
Decreased appetite	68 (23)	1 (0.3)	45 (16)	1 (0.3)
Skin and subcutaneous				
Alopecia	95 (32)	0	101 (35)	1 (0.3)[b]
Rash	36 (12)	0	18 (6)	0
Pruritus	30 (10)	0	12 (4)	0

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Datopotamab Deruxtecan (Dato-DXd)

Adverse Events of Special Interest

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

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

Lisberg et al. ESMO 2023

TROPION-Lung05 (Dato-DXd – actionable genomic alterations)

Screening

Key inclusion criteria

- Stage IIIB, IIIC, or IV NSCLC
- Presence of ≥1 actionable genomic alteration (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
- ECOG PS of 0 or 1
- ≥1 line of targeted therapy
- 1 or 2 prior cytotoxic agent–containing therapies including platinum-based therapy in the metastatic setting
- Radiographic disease progression after targeted therapy

Treatment

Dato-DXd
6 mg/kg
Q3W

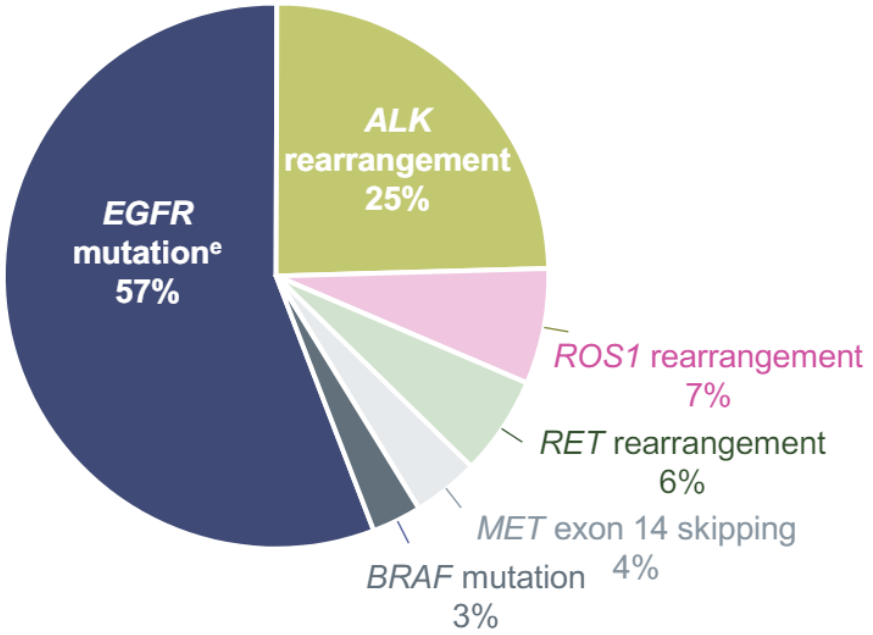
Endpoints[a]

Primary: ORR by BICR

Secondary:

- By BICR and investigator: DOR, DCR, CBR, PFS, TTR
- By investigator: ORR
- OS, safety, PK, immunogenicity

Relative Frequency of Genomic Alterations[b-d]



Disposition

At the time of data cutoff (December 14, 2022):

- Median (range) treatment duration was 4 (1-21) months
- 60 participants (44%) were ongoing in study
- 20 participants (15%) were ongoing on study treatment

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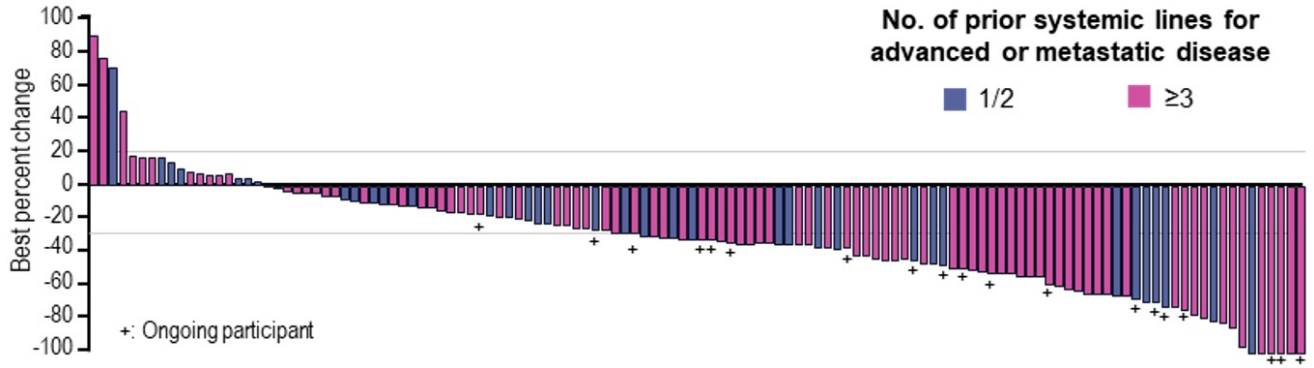
TROPION-Lung05 (Dato-DXd – actionable genomic alterations)

Response per BICR	All treated patients (N=137)	Patients with *EGFR* mutations (N=78)	Patients with *ALK* rearrangement (N=34)
ORR confirmed, n (%) [95% CI][a]	49 (35.8) [27.8-44.4]	34 (43.6) [32.4-55.3]	8 (23.5) [10.7-41.2]
Median DOR (95% CI), months	7.0 (4.2-9.8)	7.0 (4.2-10.2)	7.0 (2.8-8.4)
DCR confirmed, n (%) [95% CI][a]	108 (78.8) [71.0-85.3]	64 (82.1) [71.7-89.8]	25 (73.5) [55.6-87.1]
Median PFS, (95% CI), months[b]	5.4 (4.7-7.0)	5.8 (5.4-8.3)	4.3 (2.6-6.9)

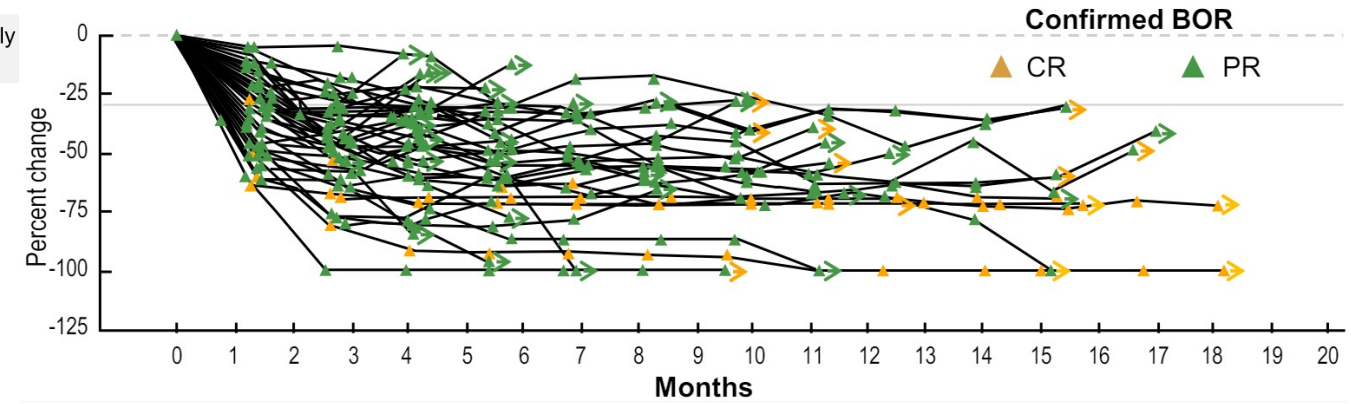
BOR: In the overall population (N=137), 4 patients (3%) achieved a CR and 45 (33%) achieved a PR

***EGFR* subset:** Among patients with sensitizing or T790M mutations (N=68), the ORR was 49.1% in those previously treated with osimertinib

Best Percentage Change From Baseline in Sum of Diameters in Target Lesions



Percent Change From Baseline in Sum of Diameters of Target Lesions in Patients With Confirmed CR/PR[c]



Paz-Ares et al. ESMO 2023

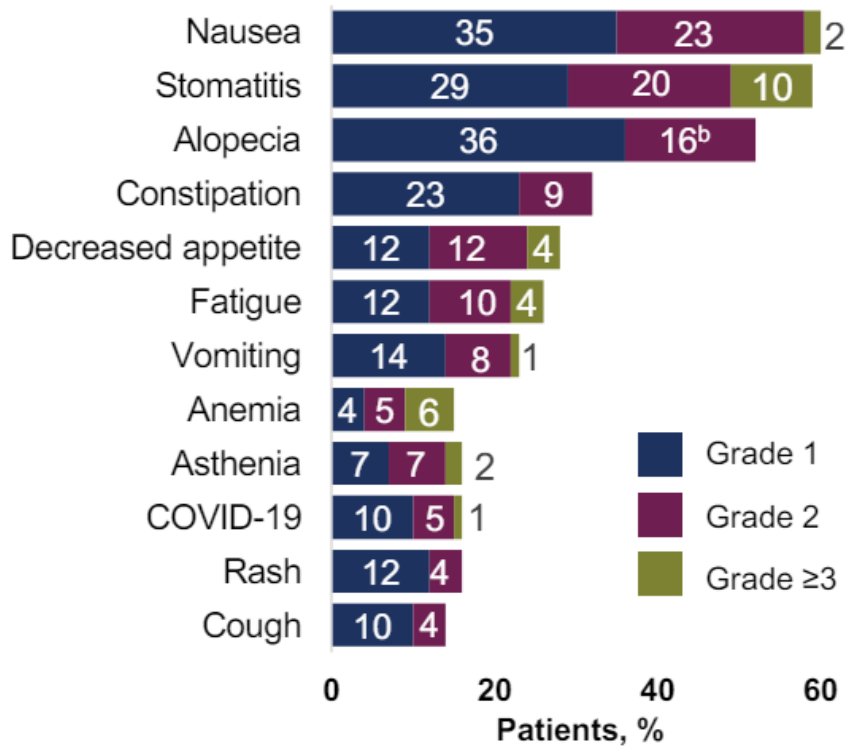
Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

TROPION-Lung05 (Dato-DXd – actionable genomic alterations)

Safety Summary

TEAEs Occurring in ≥15% of Patients; All Grades (N=137)[a]



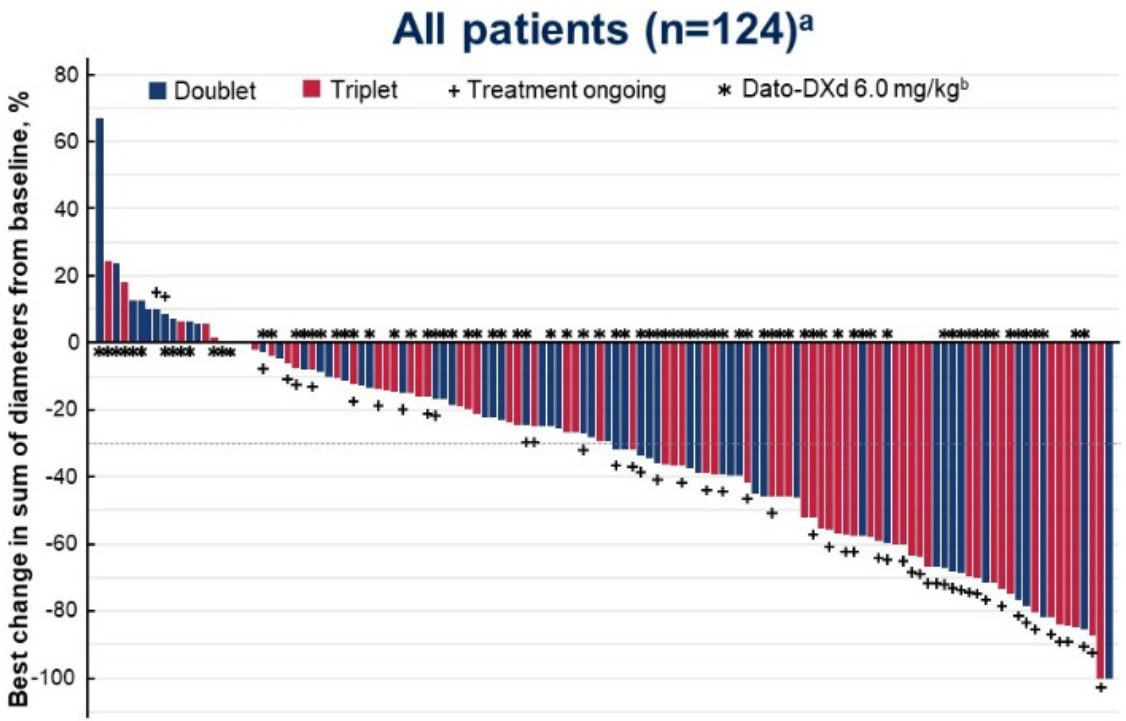
- 137 patients (100%) experienced **TEAEs** (grade ≥3, 47%)
  - 129 (94%) experienced **treatment-related TEAEs** (grade ≥3, 29%)
  - 34 (25%) experienced **serious AEs** (grade ≥3, 5%)
- 30 (22%), 13 (10%), and 2 (2%) patients experienced TEAEs associated with **dose reduction**, **dose withdrawal**, and **death**,[c] respectively

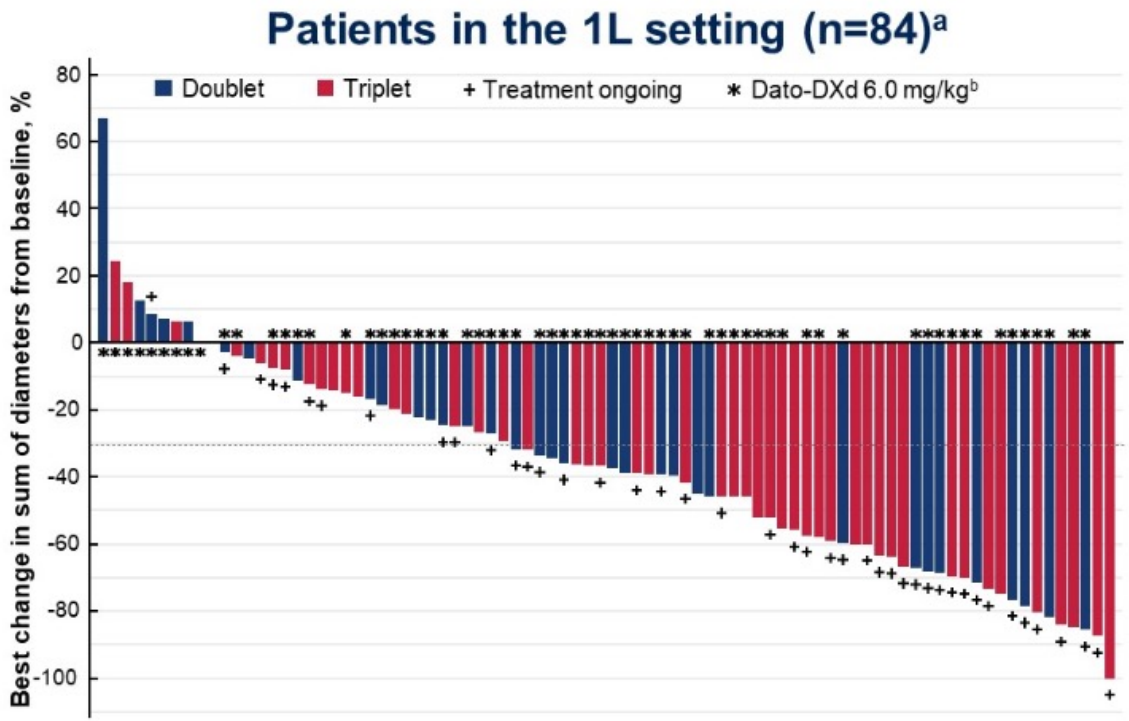
AESI Incidence by Grade[d]

n (%)	Total	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis	90 (66)	45 (33)	30 (22)	15 (11)
Ocular surface toxicity[e]	36 (26)	26 (19)	7 (5)	3 (2)[f]
IRR	22 (16)	15 (11)	7 (5)	0
Adjudicated drug-related ILD	5 (4)	1 (1)	3 (2)	1 (1)[g]

Paz-Ares et al. ESMO 2023

TROPION-Lung02: Dato-DXd + Pembro





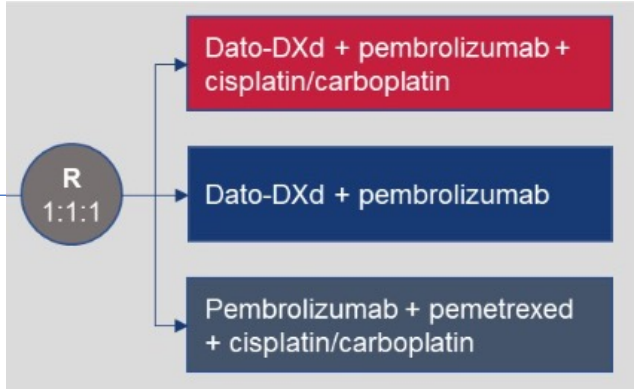
Dana-Farber Cancer Institute

Goto et al. ASCO 2023

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Multiple TROP2 Trials Underway

- **<u>Dato-DXd</u>**
- **First-Line:**
  - TROPION-Lung04: Dato-DXd in combo with durva +/- carboplatin in NSCLC
  - TROPION-Lung07: Dato-DXd in 1st line non-squam NSCLC, PD-L1 <50%
  - TROPION-Lung08: Dato-DXd in 1st line non-squam NSCLC, Pembro +/- Dato-DXd

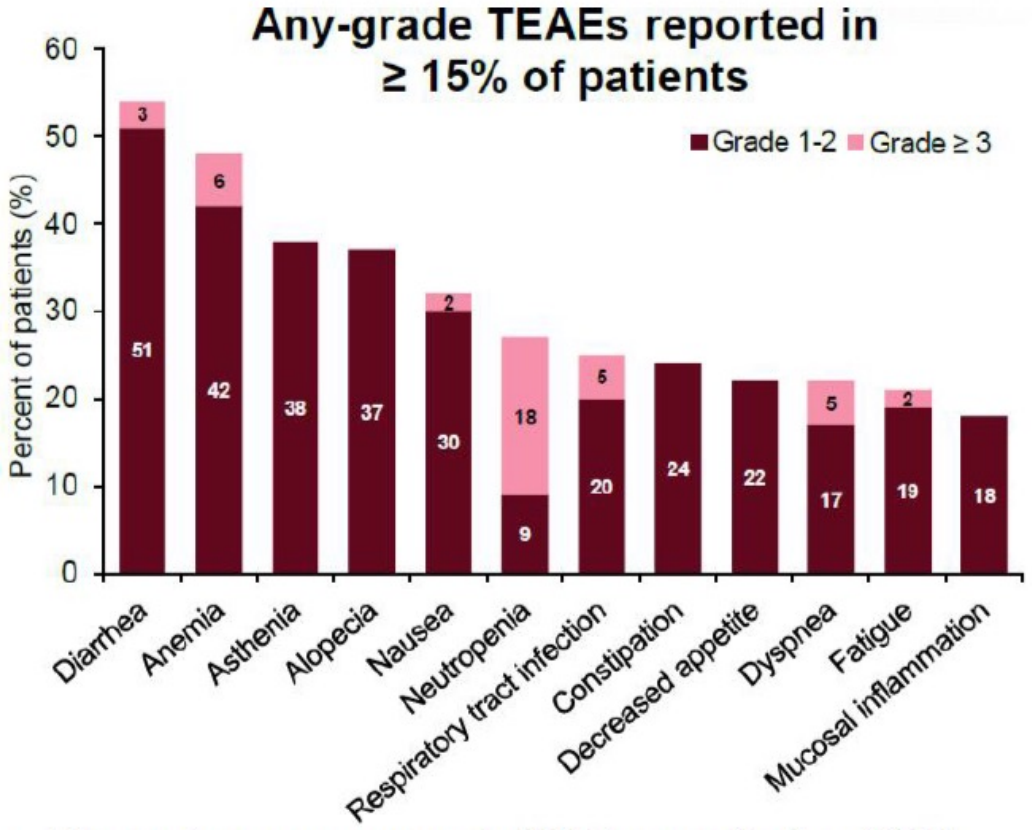


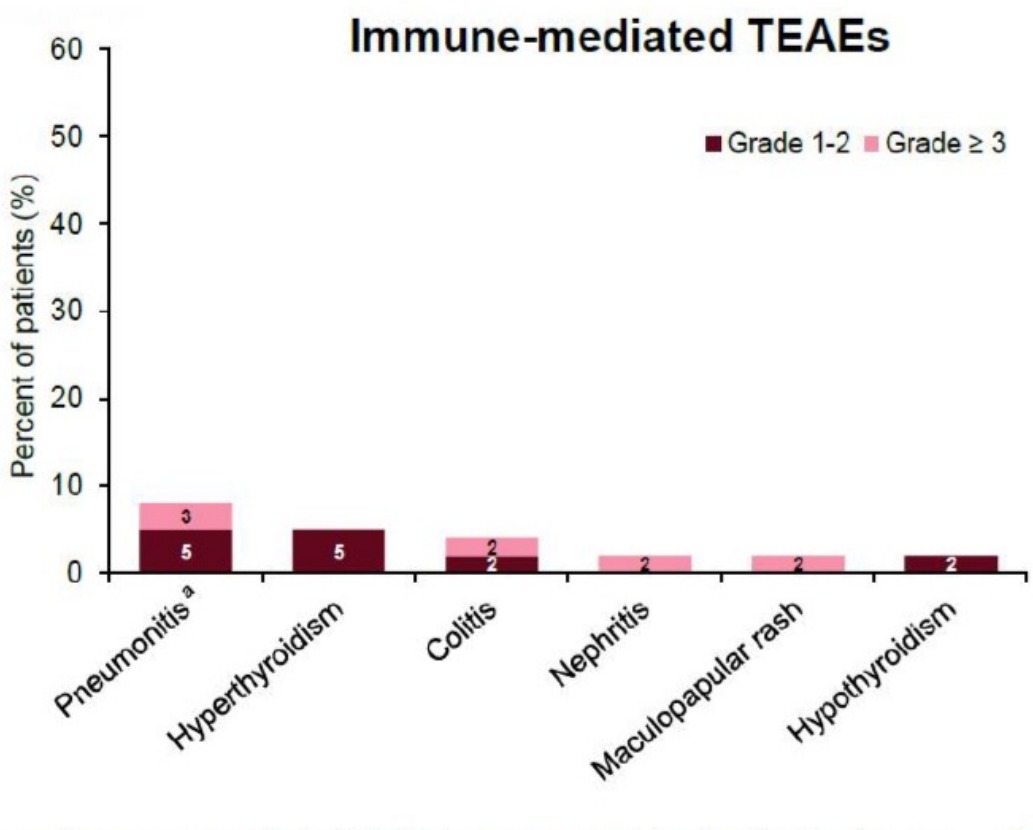
- **<u>Sacituzumab Govitecan</u>**
- **First-Line:**
  - EVOKE-03: Pembro +/- Sacituzumab Govitecan in NSCLC, PD-L1 ≥50%

Sacituzumab Govitecan – EVOKE-01

- **Per press release:** "Did not meet its primary endpoint of overall survival… vs docetaxel in patients with metastatic or advanced NSCLC that had progressed on or after platinum-based chemotherapy and checkpoint inhibitor."
- "A numerical improvement in OS favoring SG was observed in this study including in patients with both squamous and non-squamous histology."

EVOKE-02





- The most common any-grade TEAEs were diarrhea (54%), anemia (48%), and asthenia (38%)
- Immune-mediated TEAEs were consistent with the known safety profile of Pembro

All patients who received ≥ 1 dose of study treatment were included in the safety analysis. [a]Grade 3 pneumonitis was the highest grade observed to date (n = 2). Pembro, pembrolizumab; TEAE, treatment-emergent adverse event.

Still a lot to discover…

Datopotamab Deruxtecan (DS-1062)

- Trop2 antibody
- Cleavable linker
- Topoisomerase I inhibitor payload
- DAR: 4:1

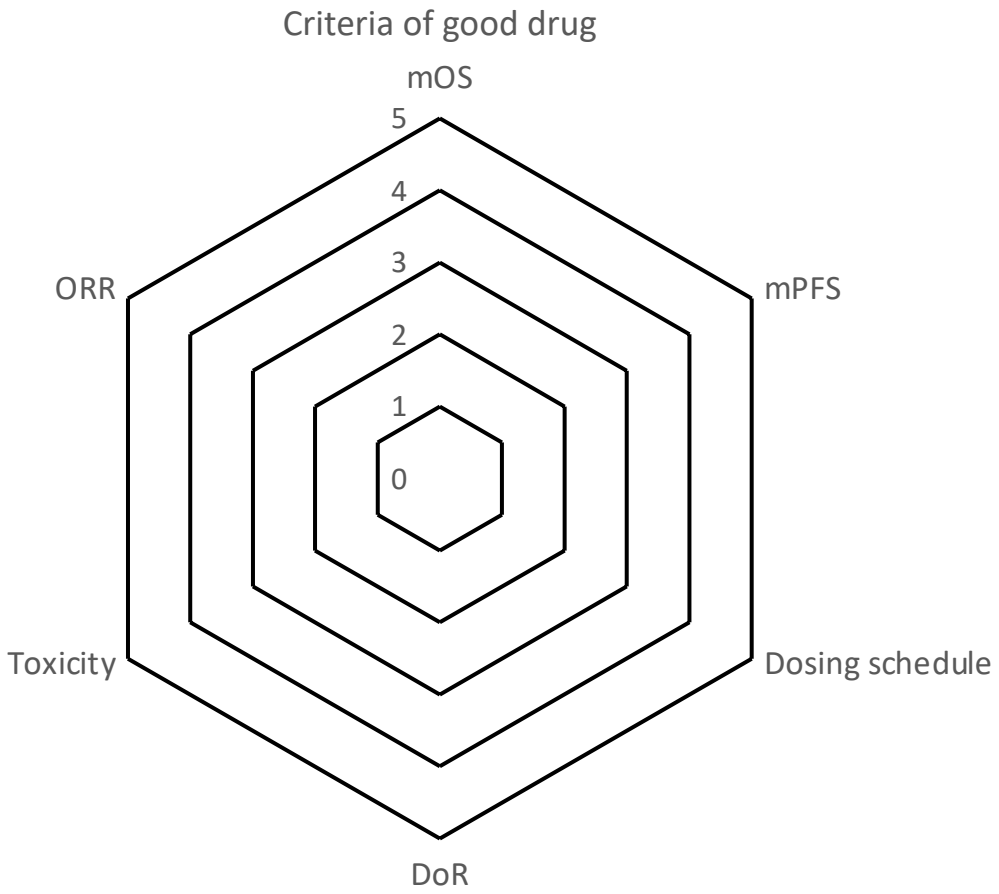
- mPFS difference non-squam and squam
- OS pending
- Tox: eye surface, stomatitis, ILD

Sacituzumab govitecan

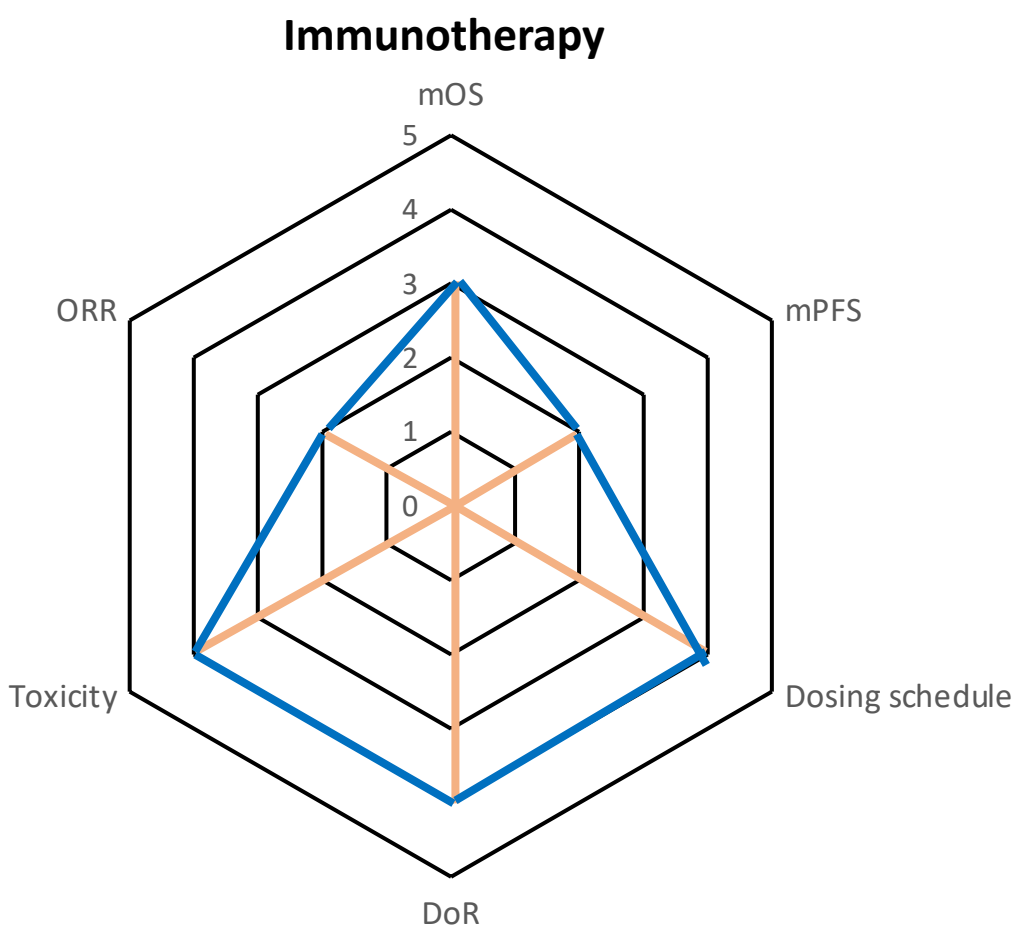
- Trop2 antibody
- Cleavable linker
- Topoisomerase I inhibitor payload
- DAR: 8:1

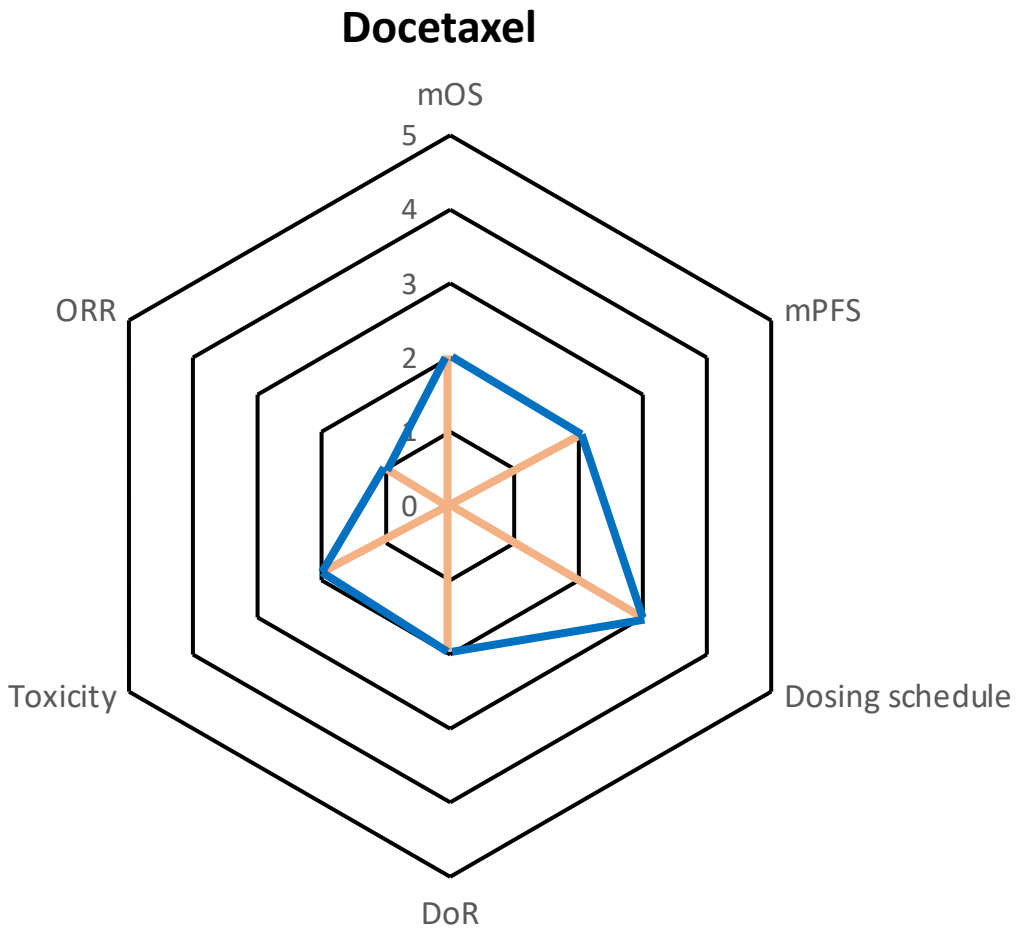
- mPFS reported similarity non-squam and squam (data pending)
- OS negative (data pending)
- Tox: nausea, diarrhea, cytopenias

Criteria of a “good drug”



Criteria of a “good drug”





The Road Ahead in TROP2

Photo credit: Steven Schild

Agenda

Module 1: Integration of Antibody-Drug Conjugates (ADCs) into the Care of Patients with Non-Small Cell Lung Cancer (NSCLC) and HER2 Alterations — Dr Paz-Ares

Module 2: Emerging Role of TROP2-Targeted ADCs for NSCLC — Dr Sands

Module 3: Other Promising Targets for ADCs for Lung Cancer — Dr Heist

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TO PRACTICE

Consulting Faculty Comments

Toxicity profile of patritumab deruxtecan; ADCs after progression on chemotherapy and EGFR tyrosine kinase inhibitors

Dr Neil Morganstein (Summit, New Jersey)

Dr Estelamari Rodriguez (Miami, Florida)

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

Would you like to have access to patritumab deruxtecan at the current time?

If this agent were available, where in the treatment sequence do you envision employing it for your patients with EGFR mutation-positive disease?

QUESTIONS FOR THE FACULTY

Should community-based oncologists be testing for c-Met overexpression in their patients with metastatic NSCLC?

If yes, what testing methodology should be used and how should the results be interpreted?

QUESTIONS FOR THE FACULTY

From a risk/benefit standpoint, how do you believe telisotuzumab vedotin (Teliso-V) compares to currently available therapies such as docetaxel?

Given what we currently know about Teliso-V, would you like to have access to this agent for your patients with progressive NSCLC?

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TO PRACTICE

QUESTIONS FOR THE FACULTY

What are the most common toxicities that have been noted with Teliso-V?

Which of these do you find most challenging to manage?

Which of these do you believe are most detrimental to patient quality of life?

QUESTIONS FOR THE FACULTY

What other novel ADCs in development do you believe are most promising for patients with lung cancer?

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TO PRACTICE

Other Promising Targets for ADCs in Lung Cancer

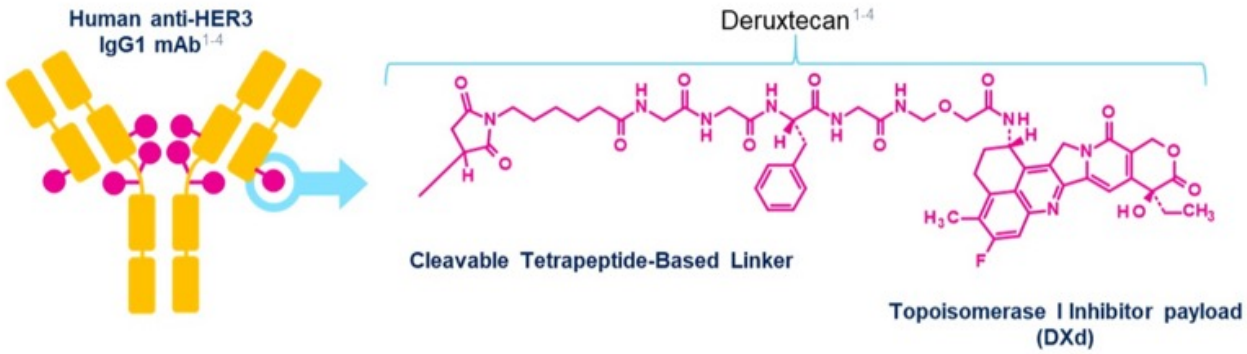
Rebecca S Heist, MD, MPH

HER3 in lung cancer

- Member of ERBB/HER family of receptor tyrosine kinases
- Forms heterodimers; has minimal intrinsic kinase activity
- Expressed in over 80% of NSCLCs
- HER3 overexpression is associated with metastatic progression and poor prognosis NSCLC
- HER3 overexpression implicated in resistance to multiple types of treatment, including EGFR

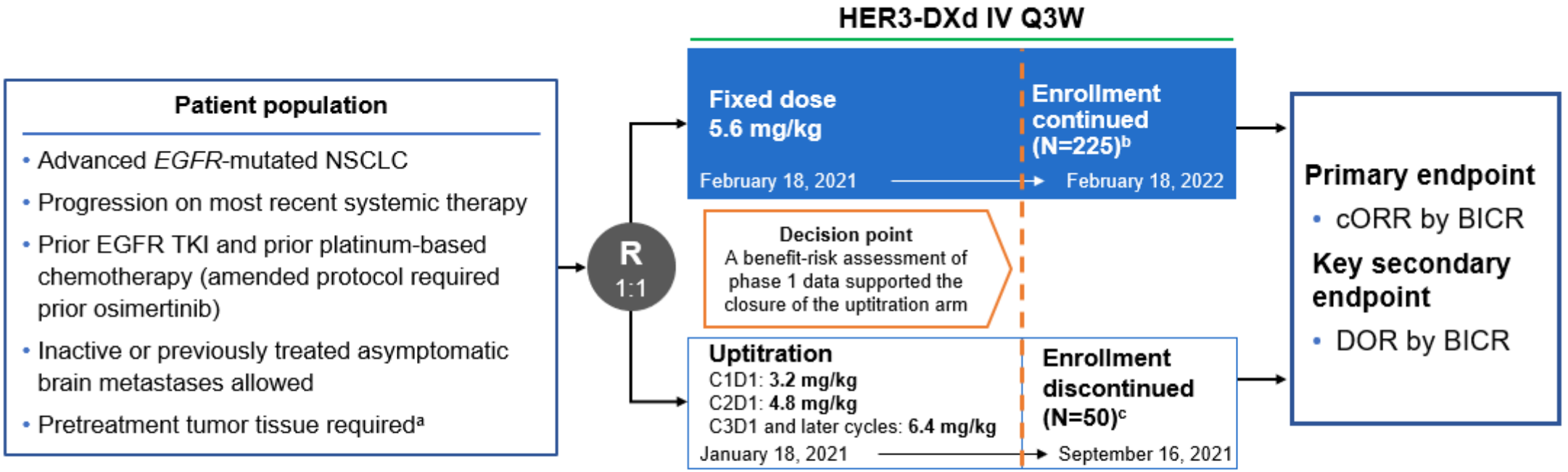
Patritumab deruxtecan (HER3-DXd)

- Antibody drug conjugate
- Fully human anti-HER3 IgG1 mAb (patritumab), covalently linked via a tetrapeptide based cleavable linker to deruxtecan, a topoisomerase 1 inhibitor payload



Uliano et al ESMO Open 2023; Janne et al ASCO 2021

HERTHENA-Lung01 Study Schema



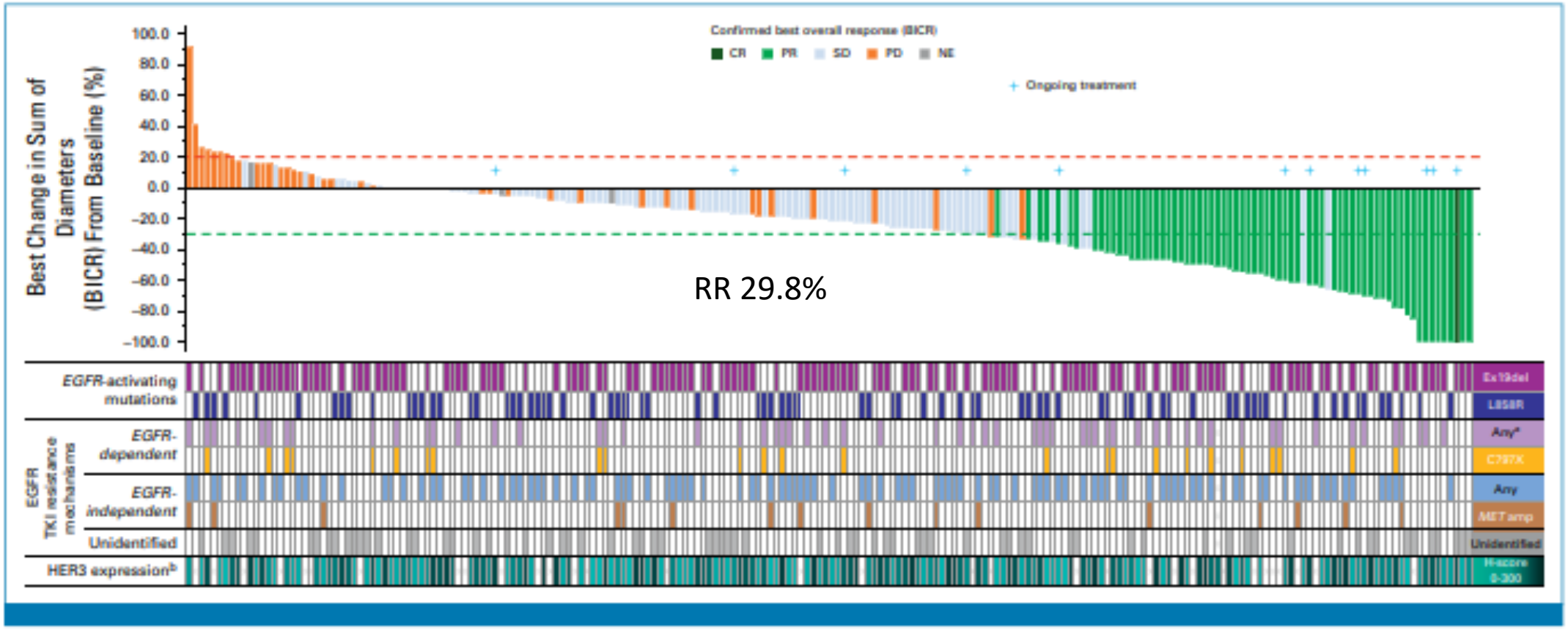
Primary data cutoff, 21 Nov 2022[d]
Snapshot data cutoff, 18 May 2023 (additional 6 months follow-up)
Data are presented for the 5.6-mg/kg fixed-dose arm

- Efficacy from snapshot data cutoff—median study follow-up, 18.9 (range, 14.9-27.5) months
- Safety from primary data cutoff—median treatment duration, 5.5 (range, 0.7-18.2) months

BICR, blinded independent central review; C, cycle; cORR, confirmed objective response rate (complete or partial response confirmed ≥4 weeks after initial response [RECIST version 1.1]); D, day; DOR, duration of response; HER, human epidermal growth factor receptor; IV, intravenous; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor.
[a] Inclusion not based on detection of HER3 expression. [b] 226 patients were enrolled; 225 received ≥1 dose. [c] 51 patients were enrolled; 50 received ≥1 dose. [d] Data cutoff for the primary analysis occurred when all enrolled patients had either ≥9 months of follow-up or had discontinued from the study earlier.
1. Yu HA, et al. *Future Oncol*. 2023;19:1319-1329.

Yu et al WCLC 2023

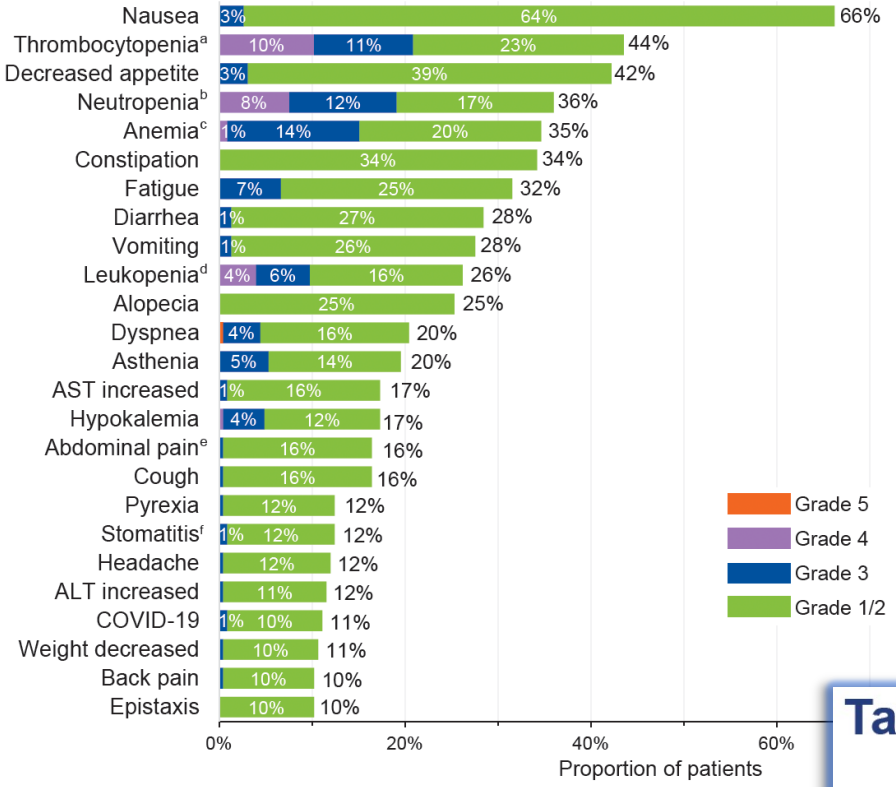
HERTHENA-Lung01 Response



Yu et al JCO 2023

HERTHENA-Lung01 Updated Safety

Figure 3 Most Common TEAEs Occurring in ≥10% of Patients



Safety summary	HER3-DXd 5.6 mg/kg (N=225)
Study drug exposure	
Treatment duration, median (range), months	5.5 (0.7-23.7)
Dose intensity, median (range), mg/kg/cycle	5.45 (3.2-6.0)
Relative dose intensity, median (range), %	97.4 (57.1-107.8)
TEAEs	
Any TEAE, n (%)	224 (99.6)
Associated with treatment discontinuation	19 (8.4)
Associated with treatment dose reduction	50 (22.2)
Associated with treatment dose interruption	93 (41.3)
Grade ≥3 TEAE, n (%)	147 (65.3)
Treatment-related TEAE, n (%)	215 (95.6)
Associated with death[a]	4 (1.8)
Grade ≥3	104 (46.2)
Serious TEAE	36 (16.0)

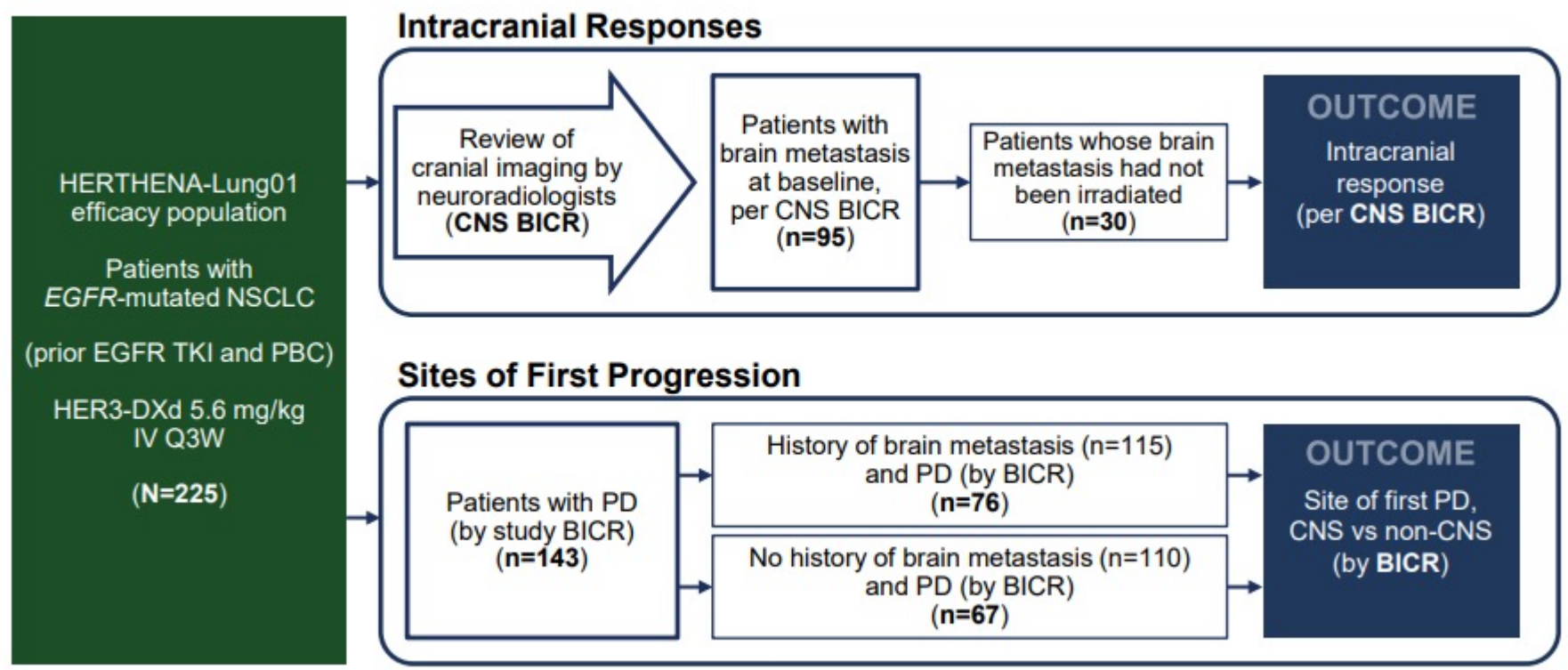
[a] Pneumonitis, GI perforation, pneumonia, respiratory failure (n=1 each)

Table 3 ILD Adjudication for HER3-DXd 5.6 mg/kg (N=225)

Worst ILD grade per investigator	Patients with suspected ILD	Adjudicated not ILD	Grade after adjudication (all adjudicated ILD were treatment related) Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total ILD
Any grade, n	22							
Grade 1	8	2	1	4	0	0	1	6
Grade 2	3	0	0	2	1	0	0	3
Grade 3	5	1	0	2	2	0	0	4
Grade 4	3	2	0	0	1	0	0	1
Grade 5	3	3	0	0	0	0	0	0
Total adjudicated ILD, n (%)			**1 (0.4)**	**8 (3.6)**	**4 (1.8)**	**0**	**1 (0.4)**	**14 (6.2)**

Hayashi H et al. ESMO Lung 2024;Abstract 11P.

Additional analyses of CNS activity of patritumab deruxtecan



BICR, blinded independent central review; CNS, central nervous system; IV, intravenous; NSCLC, non–small cell lung cancer; PBC, platinum-based chemotherapy; PD, progressive disease; RT, radiotherapy; Q3W, every 3 weeks; TKI, tyrosine kinase inhibitor.

Johnson et al ESMO 2023

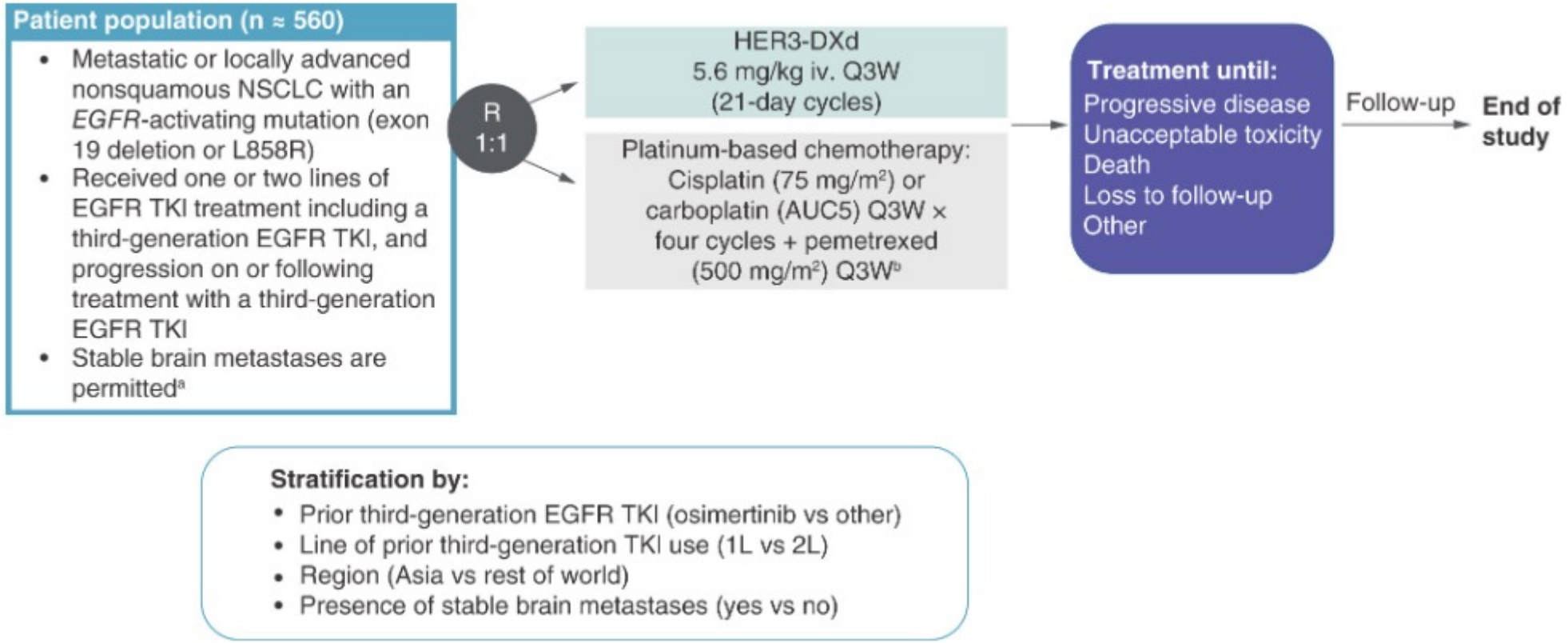
CNS activity of patritumab deruxtecan

Responses by CNS BICR[a]	All patients with baseline BM by CNS BICR (n=95)	Patients whose baseline BM had not been irradiated (n=30)[b]
CNS cORR, n (%) [95% CI]	19 (20.0) [12.5, 29.5]	10 (33.3) [17.3-52.8]
CR, n (%)	15 (15.8)	9 (30.0)[c]
PR, n (%)	4 (4.2)	1 (3.3)
SD/non-CR/non-PD, n (%)	57 (60.0)	13 (43.3)
PD, n (%)	13 (13.7)	4 (13.3)
NE, n (%)	6 (6.3)	3 (10.0)
CNS DCR (95% CI), %	80.0 (70.5, 87.5)	76.7 (57.7-90.1)
CNS DOR, median (95% CI), mo	9.2 (8.1-11.1)	8.4 (5.8-9.2)

Snapshot data cutoff, 18 May 2023.
Median study follow-up, 18.9 (range, 14.9-27.5) months.

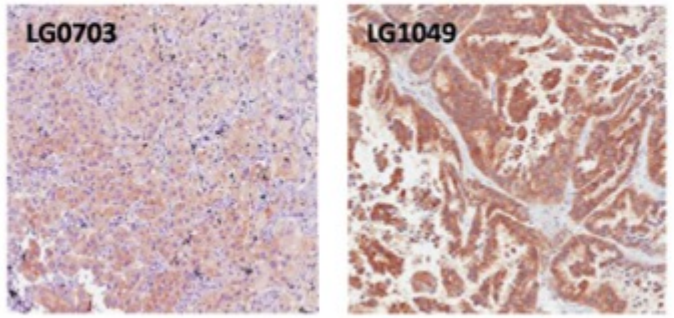
Johnson et al ESMO 2023

Phase III HERTHENA-Lung02 Study Design NCT05338970



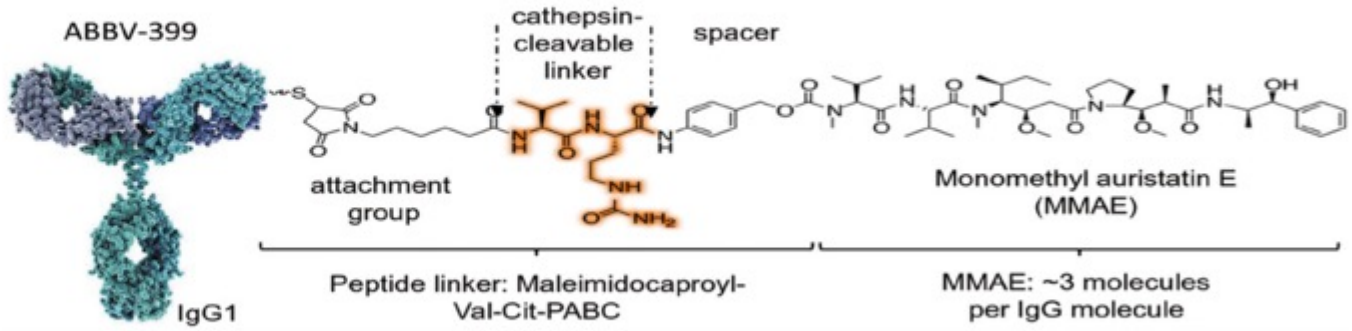
Mok et al Future Oncology 2024

c-MET overexpression



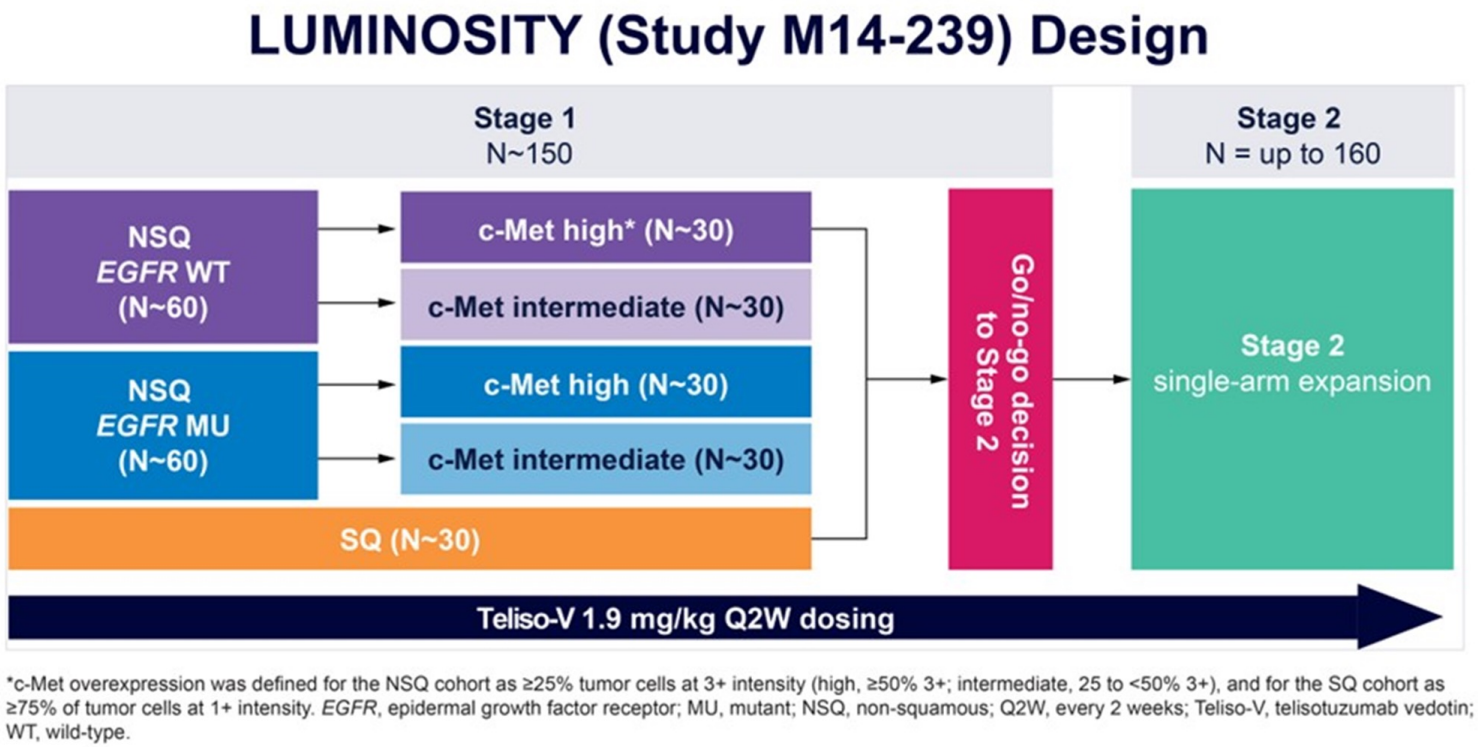
Telisotuzumab vedotin (ABBV-399)

Antibody-drug conjugate composed of a c-Met-targeting antibody (telisotuzumab), a cleavable valine-citrulline (dipeptide) linker, and a microtubule polymerization inhibitor (cytotoxin monomethyl auristatin E [MMAE])



Wang Y et al Clin Cancer Res 2017; Yao HP et al J Exp Clin Cancer Res 2020

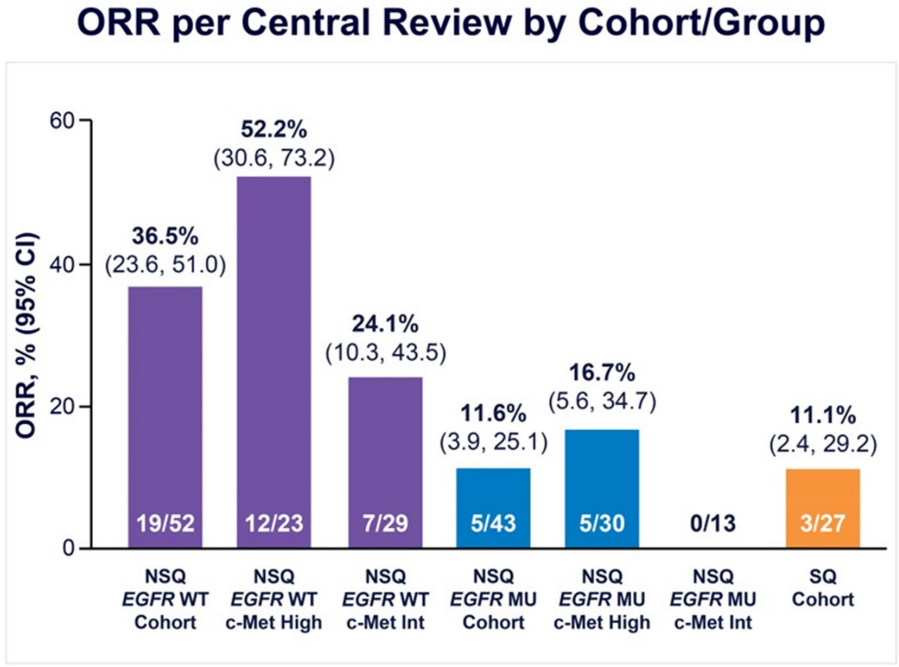
Phase II LUMINOSITY Study Design



*c-Met overexpression was defined for the NSQ cohort as ≥25% tumor cells at 3+ intensity (high, ≥50% 3+; intermediate, 25 to <50% 3+), and for the SQ cohort as ≥75% of tumor cells at 1+ intensity. *EGFR*, epidermal growth factor receptor; MU, mutant; NSQ, non-squamous; Q2W, every 2 weeks; Teliso-V, telisotuzumab vedotin; WT, wild-type.

Camidge et al ASCO 2022

Phase II LUMINOSITY: Response rates by cohort



CI, confidence interval; *EGFR*, epidermal growth factor receptor; Int, intermediate; MU, mutant; NSQ, non-squamous; ORR, overall response rate; SQ, squamous; WT, wild-type.

- The NSQ *EGFR* WT NSCLC cohort met protocol-specified criteria for expansion in Stage 2 at interim analysis 3. Updated data at the time of interim analysis 4 are shown
- The NSQ *EGFR* MU NSCLC cohort met protocol-specified criteria for futility at interim analysis 4. The SQ cohort met criteria for futility at the previous interim analysis; final data shown

Press release Nov 2023:

	RR	DOR	mOS
c-MET high	35%	9 mo	14.6 mo
c-MET intermediate	23%	7.2 mo	14.2 mo

2024 ASCO Annual Meeting

Add to Agenda

Clinical Science Symposium

Next-Generation Antibody–Drug Conjugates: The Revolution Continues

Primary Track: Special Sessions

June 2 – 9:45 AM CDT Hall D1 | Live Stream

Telisotuzumab vedotin monotherapy in patients with previously treated c-Met–overexpressing non-squamous *EGFR* wildtype advanced NSCLC: Primary analysis of the LUMINOSITY trial.

10:01 AM CDT David Ross Camidge, MD, PhD Abstract 103

Camidge et al ASCO 2022

Phase II LUMINOSITY: AEs

Summary of Treatment-Emergent Adverse Events

TEAEs, n (%)	Total N=136	
	Any Grade	Grade ≥3
Any TEAE	131 (96)	65 (48)
Most common any-grade TEAEs (≥10%)		
Peripheral sensory neuropathy	34 (25)	6 (4)
Nausea	30 (22)	1 (1)
Hypoalbuminemia	28 (21)	1 (1)
Peripheral edema	25 (18)	0
Blurred vision	25 (18)	1 (1)
Decreased appetite	24 (18)	0
Fatigue	22 (16)	5 (4)
Anemia	19 (14)	3 (2)
Dyspnea	19 (14)	4 (3)
Asthenia	18 (13)	3 (2)
Increased gamma-glutamyl transferase	18 (13)	3 (2)
Keratitis	18 (13)	0
Constipation	16 (12)	1 (1)
Cough	14 (10)	0
Diarrhea	14 (10)	0
Dizziness	14 (10)	0
Malignant neoplasm progression	14 (10)	11 (8)
Vomiting	14 (10)	1 (1)

*Per investigator assessment. TEAEs, treatment-emergent adverse events; Teliso-V, telisotuzumab vedotin.

Any TEAE related to Teliso-V*	104 (76)
Any serious TEAE	41 (30)
Any TEAE leading to Teliso-V discontinuation	45 (33)
Any TEAE leading to Teliso-V discontinuation possibly related to Teliso-V*	18 (13)
Any TEAE leading to death possibly related to Teliso-V*	2 (1)

*Per investigator assessment.
TEAEs, treatment-emergent adverse events; Teliso-V, telisotuzumab vedotin.

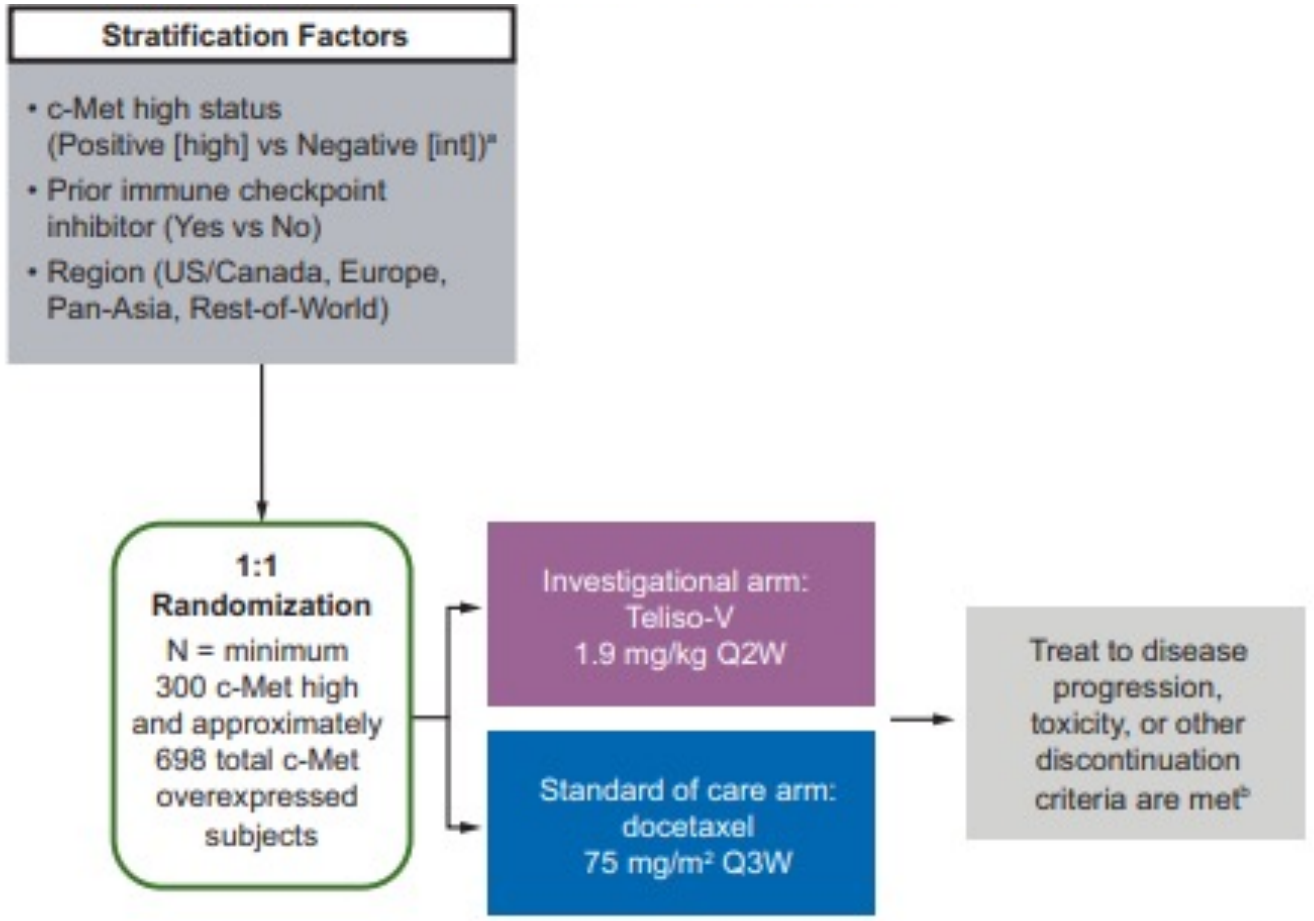
- Treatment-emergent adverse events leading to death assessed by investigator as possibly related to Teliso-V were sudden death and pneumonitis, in 1 patient each. Both were in the squamous cohort
- Any-grade pneumonitis was reported in 9 patients (6.6%) and grade ≥3 pneumonitis was reported in 3 patients (2.2%)

Camidge et al ASCO 2022

Phase III TeliMET NSCLC-01 Study Design NCT04928846

c-MET overexpressing NSCLC (≥25% tumor cells at 3+ intensity by central testing)

EGFR WT NonSquamous



Primary Endpoints: PFS, OS

Secondary Endpoints: RR, DOR, PROs, PFS by inv

Safety, tolerability, PK, PD

Lugini et al ESMO 2023

B7-H3 in Small Cell

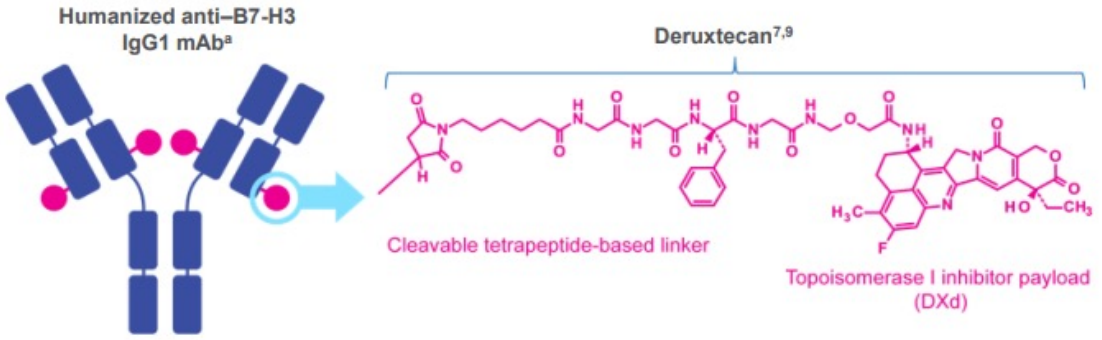
B7-H3 overexpressed in broad range of cancer types

Immunomodulatory role

Associated with cancer progression and poor survival

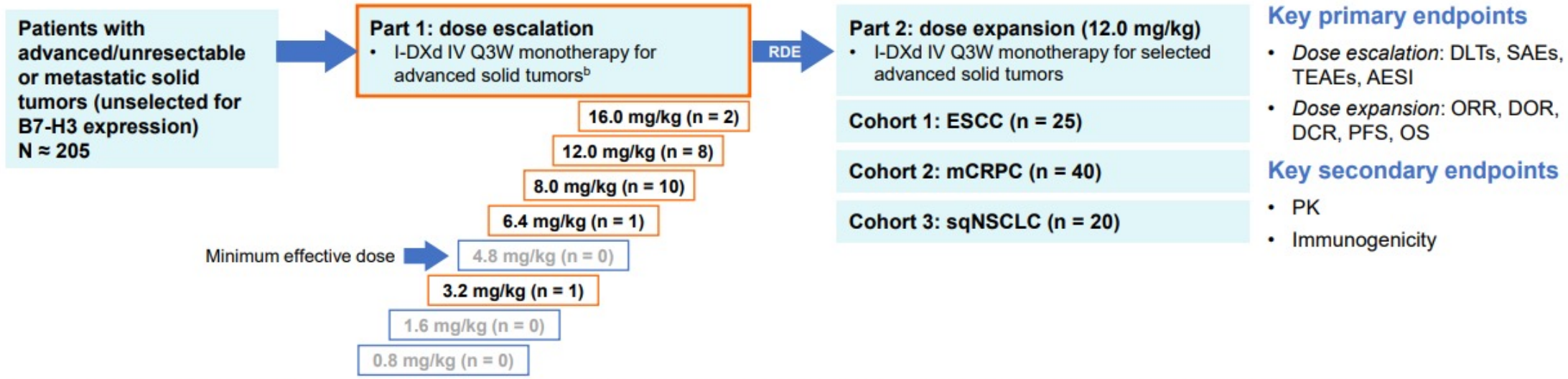
Ifinatamab deruxtecan (I-DXd, DS-7300)

Antibody-drug conjugate composed of anti-B7=H3 IgG1 monoclonal antibody, linked via a tetrapeptide based cleavable linker to topoisomerase inhibitor payload deruxtecan
DAR ~4



Yang et al Int J Biol Sci 2020; Johnson et al WCLC 2023

DS7300-A-J101 Study Design NCT04145622

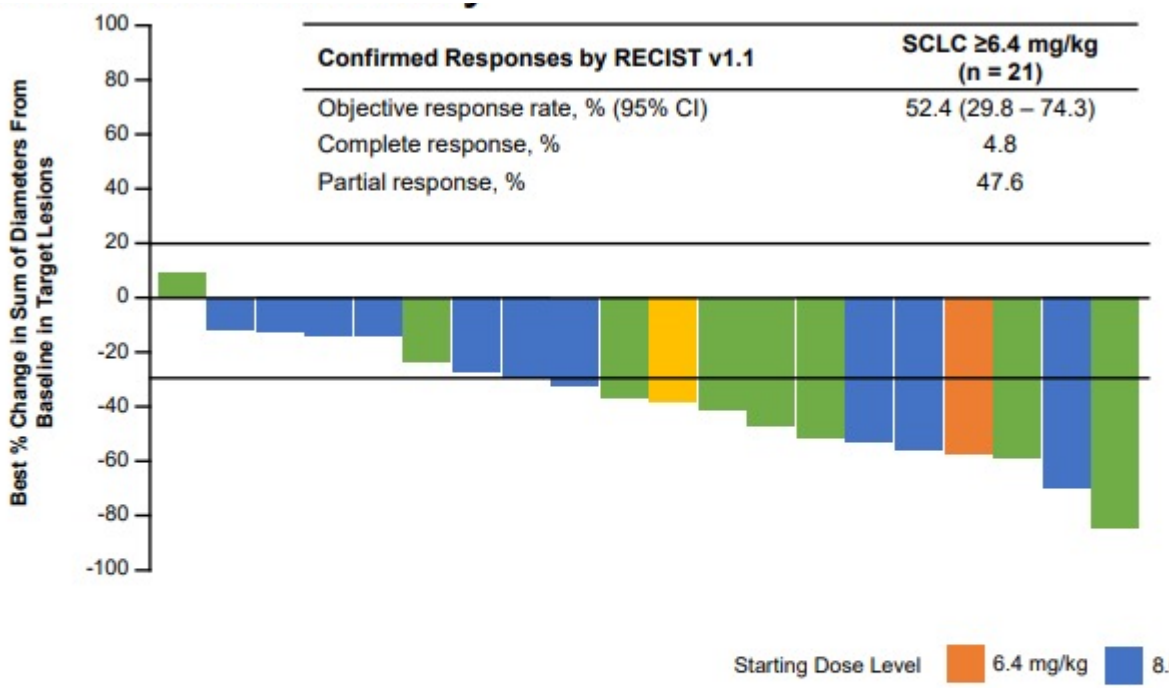


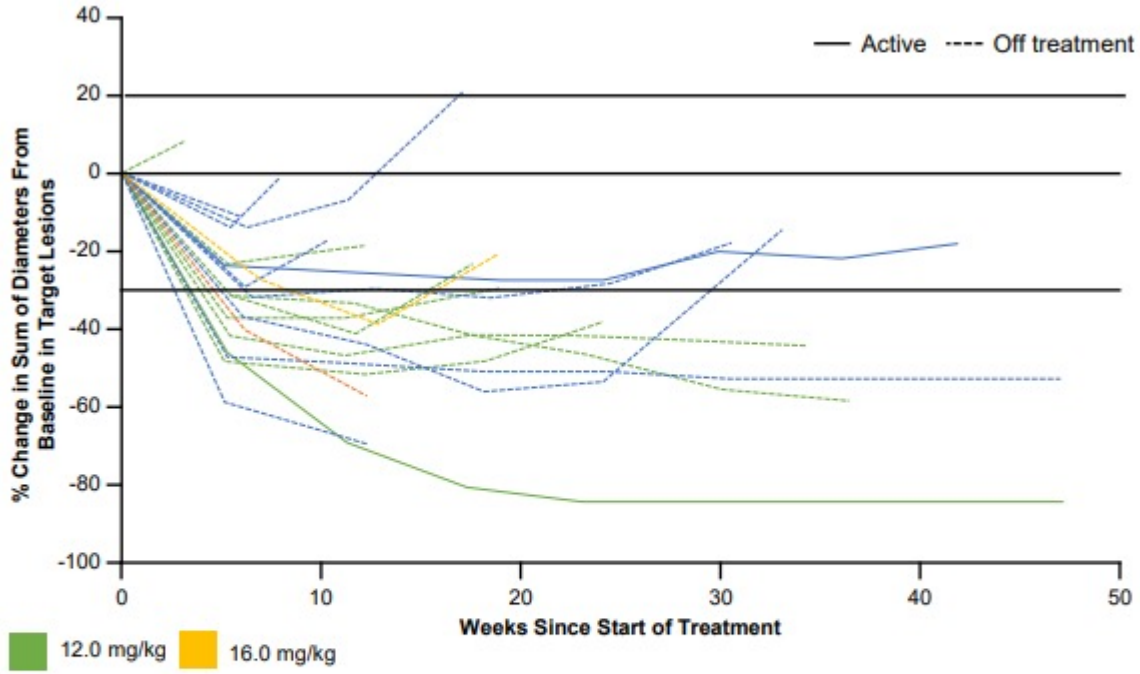
Subgroup analysis of patients with Small Cell Lung Cancer (n = 22) from Part 1 dose escalation
Patients dosed at ≥ 6.4 mg/kg (n = 21) evaluable for efficacy

Johnson et al WCLC 2023

DS7300-A-J101 Small Cell Response Rate

Confirmed Responses by RECIST v1.1	SCLC ≥6.4 mg/kg (n = 21)
Objective response rate, % (95% CI)	52.4 (29.8 – 74.3)
Complete response, %	4.8
Partial response, %	47.6





- Nearly all patients with post-baseline scans had a reduction in target lesions
- Median time to response was 1.2 months (95% CI, 1.2 – 1.4)

- Median duration of response was 5.9 months (95% CI, 2.8 – 7.5); two patients remain on treatment
- Median follow-up was 11.7 months (95% CI, 4.63 – 12.88)

Johnson et al WCLC 2023

DS7300-A-J101 Small Cell AEs

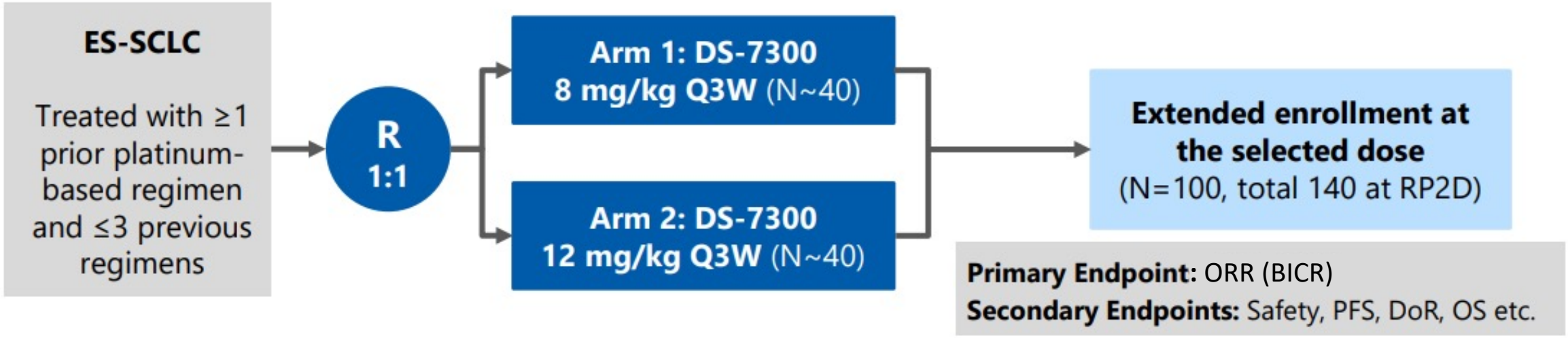
System Organ Class Preferred Term, n (%)	SCLC (N = 22)	
	Any Grade	Grade ≥3
Nausea	13 (59.1)	1 (4.5)
Fatigue	11 (50.0)	0 (0.0)
Anemia	6 (27.3)	1 (4.5)
Vomiting	6 (27.3)	0 (0.0)
Decreased appetite	5 (22.7)	1 (4.5)
Pyrexia	4 (18.2)	0 (0.0)
Constipation	4 (18.2)	1 (4.5)
IRR	3 (13.6)	0 (0.0)
Diarrhea	3 (13.6)	0 (0.0)
Dehydration	3 (13.6)	0 (0.0)
Dyspnea	3 (13.6)	0 (0.0)
Platelet count decreased	3 (13.6)	0 (0.0)
Arthralgia	3 (13.6)	0 (0.0)
Hyponatremia	3 (13.6)	0 (0.0)

- A total of three patients (13.6%) experienced an ILD or pneumonitis event (two Gr 1, one Gr 2)
  - All events were adjudicated by the ILD adjudication committee, of which one was adjudicated as drug-related ILD (Gr 2, 8.0 mg/kg) and discontinued treatment per protocol[a]
- Prophylactic premedication for nausea, vomiting, and IRR were not permitted for primary prophylaxis during cycle 1 of dose escalation

TEAEs
≥ Grade 3: 36.4%
Dose discontinuation: 22.7%
Dose reduction: 13.6%
Dose delay: 13.6%

Johnson et al WCLC 2023

Phase II IDeate-01 Study Design NCT05280470



IDeate-Lung02: A Phase III Study of Ifinatamab Deruxtecan versus Treatment of Physician's Choice for Relapsed SCLC

Key inclusion criteria

- Histologically confirmed SCLC
- ≥1 prior therapy, including ≥2 cycles of platinum-based therapy
- ECOG PS 0-1

N = 468

- I-DXd at 12 mg/kg Day 1 of each 21-day cycle
- Topotecan, lurbinectedin or amrubicin

Key exclusion criteria

- Prior orlotamab, enoblituzumab or other B7-H3-targeted agents (including I-DXd)
- Prior ADC that consists of an exatecan derivative (eg, T-DXd)
- Received the study comparators or any topoisomerase I inhibitor
- Any history of ILD/pneumonitis

Outcomes

- Primary endpoints: ORR and OS (up to 4.5 years)
- Key secondary endpoints: PFS, DOR, safety (up to 4.5 years)

ADC = antibody-drug conjugate; ILD = interstitial lung disease; ORR = overall response rate

www.clinicaltrials.gov. NCT06203210. Accessed May 2024.

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Prostate Cancer

A CME Symposium Held in Conjunction with the 2024 ASCO® Annual Meeting

Saturday, June 1, 2024

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO

Emmanuel S Antonarakis, MD

Tanya B Dorff, MD

Matthew R Smith, MD, PhD

Moderator

Andrew J Armstrong, MD, ScM

RTP RESEARCH TO PRACTICE

Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. 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 CME credit link or QR code. Online/Zoom attendees: The CME credit link is posted in the chat room.

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