Emerging Role of Antibody-Drug Conjugates in the Management of Non-Small Cell Lung Cancer

A CME/MOC-Accredited Virtual Event

Thursday, December 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Alexander I Spira, MD, PhD
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Alexander I Spira, MD, PhD
CEO and Clinical Director, NEXT Virginia
Director, Virginia Cancer Specialists Research Program
Fairfax, Virginia

MODERATOR
Neil Love, MD
Research To Practice

Helena Yu, MD
Medical Oncologist
Associate Attending
Memorial Sloan Kettering Cancer Center
New York, New York

RTP RESEARCH TO PRACTICE

Commercial Support

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

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Spira — Disclosures

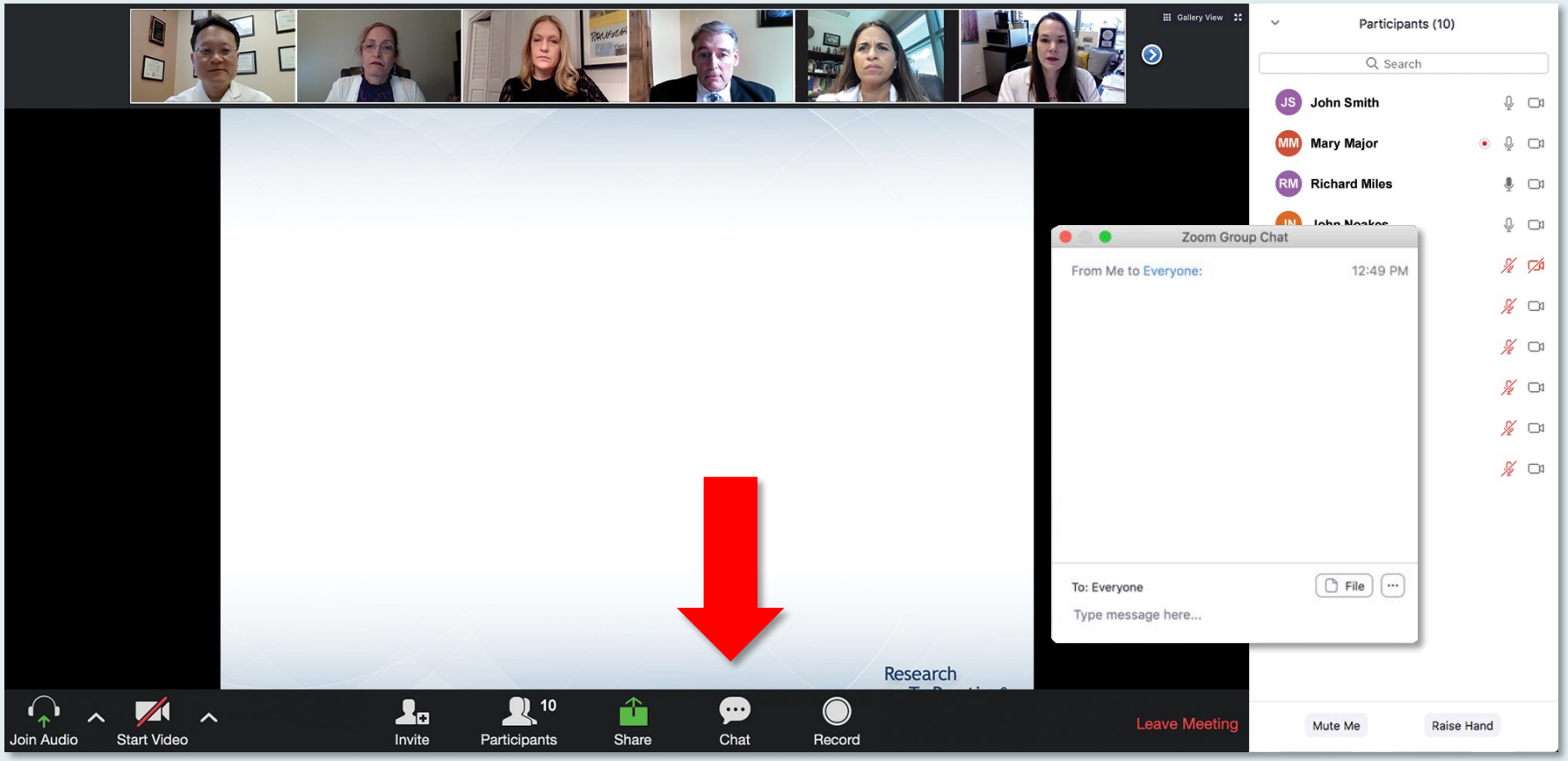
Consulting/Advisory Role	Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Gritstone bio, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Novartis, Regeneron Pharmaceuticals Inc, Takeda Pharmaceuticals USA Inc
Contracted Research	AbbVie Inc, ADC Therapeutics, AI Therapeutics, Alkermes, Amgen Inc, Arch Therapeutics Inc, Astellas, Astex Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Cardiff Oncology, CytomX Therapeutics, Daiichi Sankyo Inc, Gritstone bio, Ignyta Inc, Incyte Corporation, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Lumos Pharma, MacroGenics Inc, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Novartis, Plexxikon Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines, Roche Laboratories Inc, Rubius Therapeutics, Synthekine Inc, Takeda Pharmaceuticals USA Inc
Honoraria	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, CytomX Therapeutics, Janssen Biotech Inc, Merck, Novartis, Takeda Pharmaceuticals USA Inc
Stock Options/Ownership	Lilly

RTP RESEARCH TO PRACTICE

Dr Yu — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, C4 Therapeutics, Cullinan Oncology, Daiichi Sankyo Inc, Janssen Biotech Inc
Research Funding to My Institution	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, Cullinan Oncology, Daiichi Sankyo Inc, Erasca, Janssen Biotech Inc, Novartis, Pfizer Inc

We Encourage Clinicians in Practice to Submit Questions

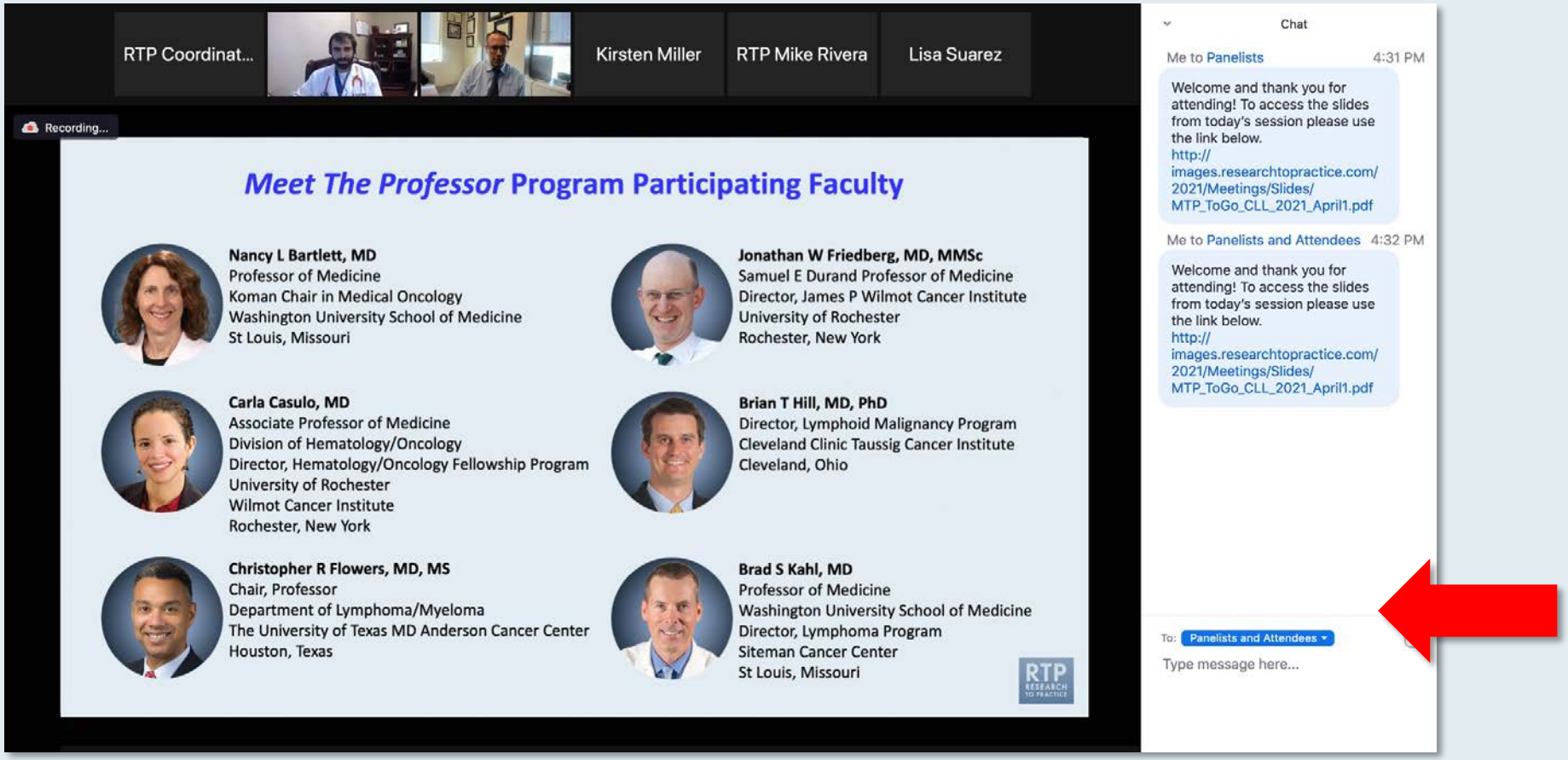


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

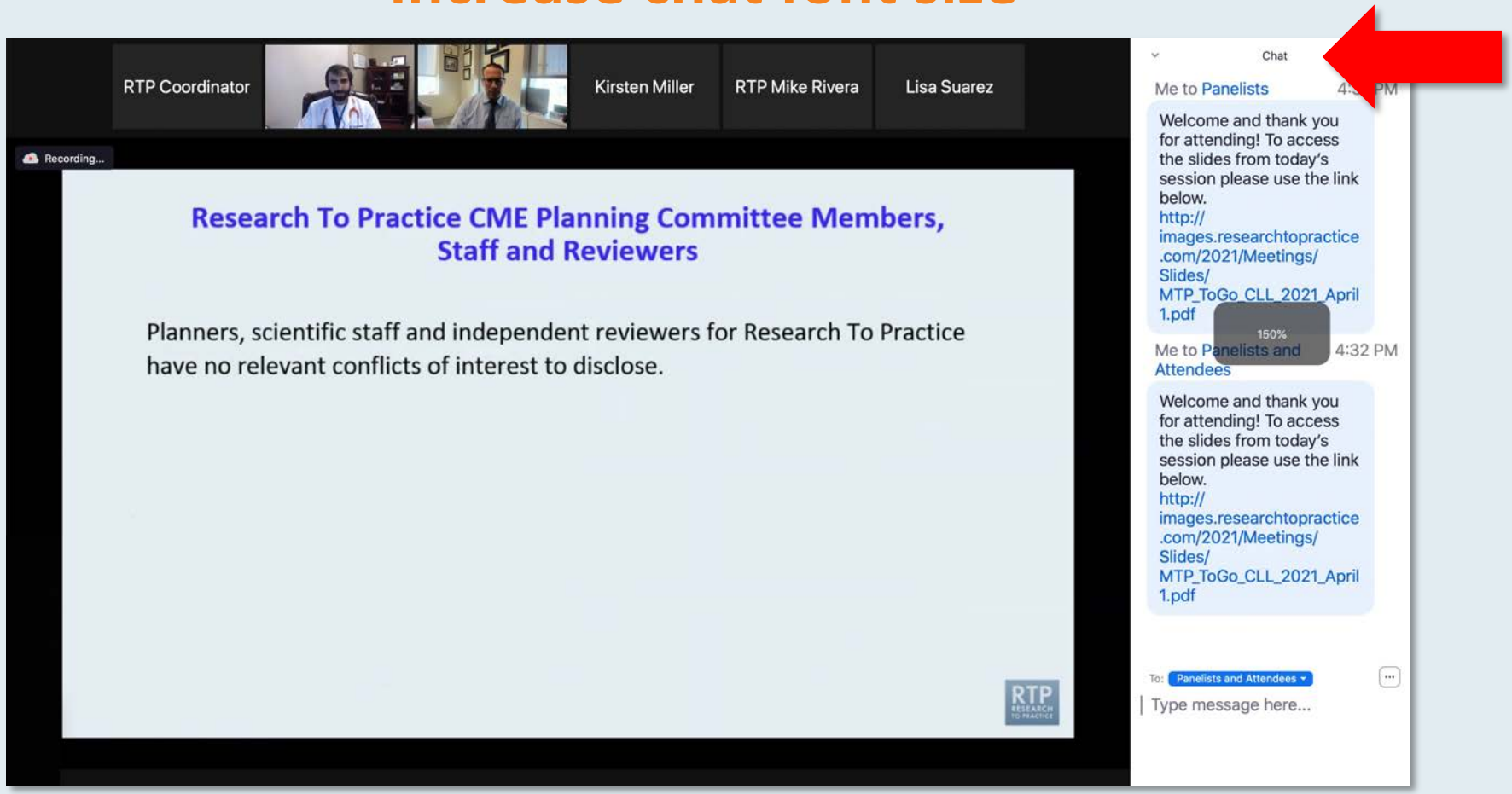


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

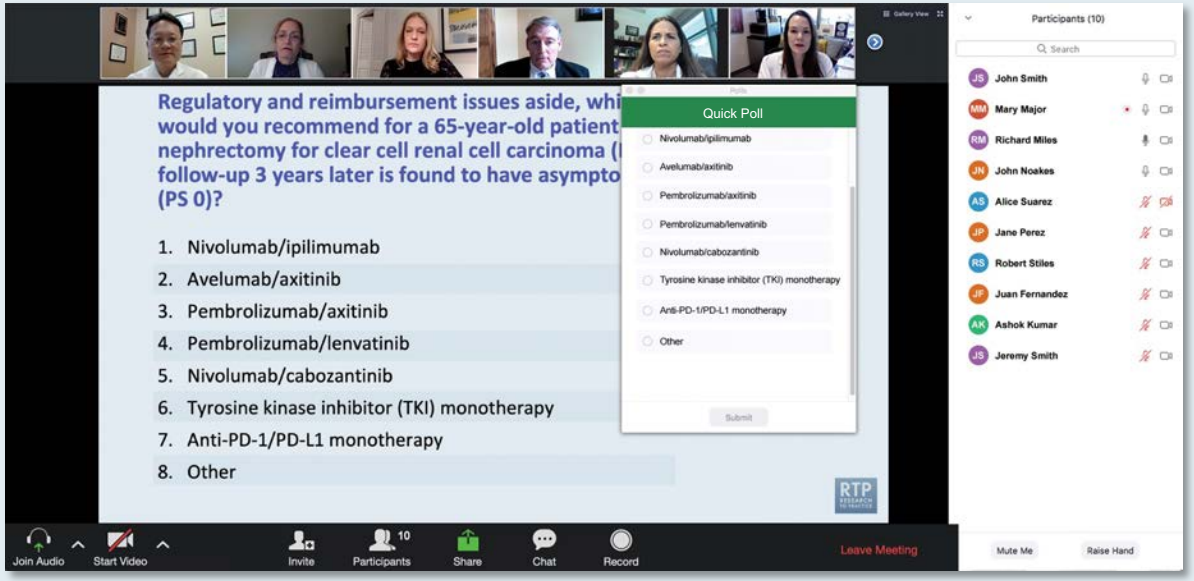
Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Management of MET-Altered Non-Small Cell Lung Cancer

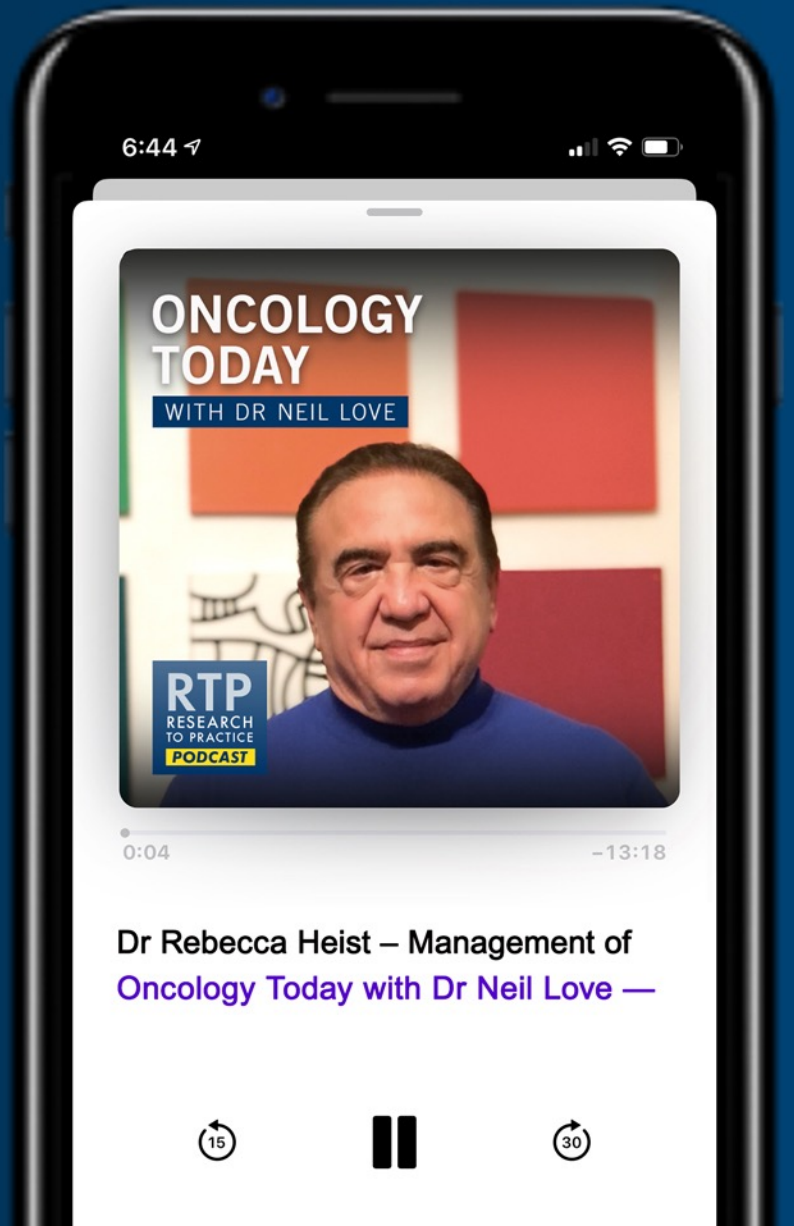
DR REBECCA HEIST

MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Wednesday, December 7, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Erika Hamilton, MD

Sara A Hurvitz, MD

Ian E Krop, MD, PhD

Shanu Modi, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of ER-Positive Breast Cancer

Part 2 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Thursday, December 8, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Aditya Bardia, MD, MPH

Matthew P Goetz, MD

Virginia Kaklamani, MD, DSc

Kevin Kalinsky, MD, MS

Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Chronic Lymphocytic Leukemia — What Clinicians Want to Know

Part 1 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
11:30 AM – 1:30 PM CT (12:30 PM – 2:30 PM ET)

Faculty

Alexey V Danilov, MD, PhD
Matthew S Davids, MD, MMSc
Professor Dr Arnon P Kater, MD, PhD
Lindsey Roeker, MD
Philip A Thompson, MB, BS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Hodgkin and Non-Hodgkin Lymphoma — What Clinicians Want to Know

Part 2 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
3:15 PM – 5:15 PM CT (4:15 PM – 6:15 PM ET)

Faculty

Jonathan W Friedberg, MD, MMSc
Brad S Kahl, MD
David G Maloney, MD, PhD
Loretta J Nastoupil, MD
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Multiple Myeloma — What Clinicians Want to Know

Part 3 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Jesús G Berdeja, MD
Rafael Fonseca, MD
Sagar Lonial, MD
Robert Z Orlowski, MD, PhD
Noopur Raje, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Acute Myeloid Leukemia

A CME/MOC-Accredited Virtual Event

Wednesday, December 14, 2022
5:00 PM – 6:00 PM ET

Faculty

Courtney D DiNardo, MD, MSCE
Mark Levis, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Multiple Myeloma

Thursday, December 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Shaji K Kumar, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP
RESEARCH
TO PRACTICE

Emerging Role of Antibody-Drug Conjugates in the Management of Non-Small Cell Lung Cancer

A CME/MOC-Accredited Virtual Event

Thursday, December 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Alexander I Spira, MD, PhD
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

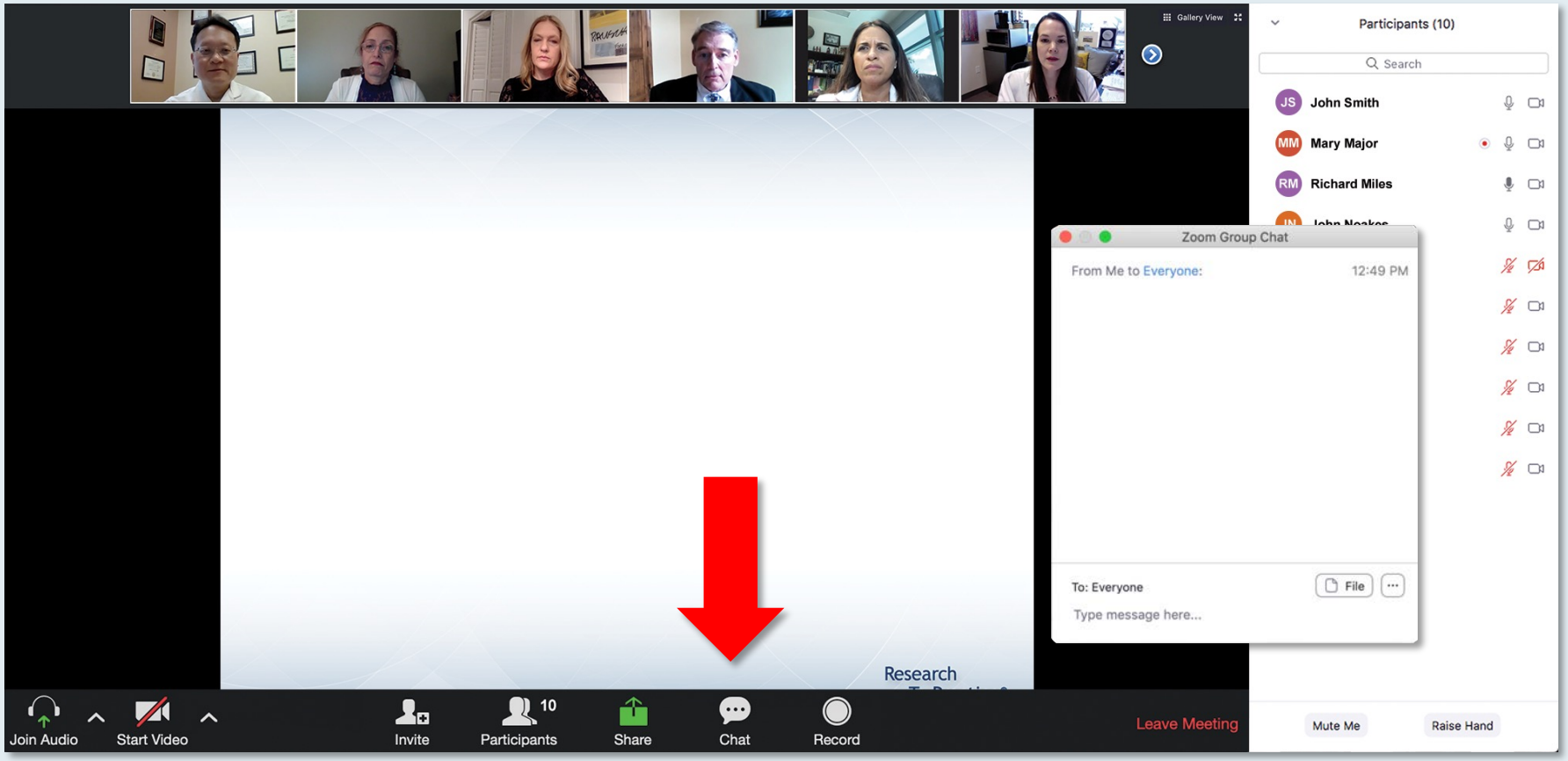
Alexander I Spira, MD, PhD
CEO and Clinical Director, NEXT Virginia
Director, Virginia Cancer Specialists Research Program
Fairfax, Virginia

MODERATOR
Neil Love, MD
Research To Practice

Helena Yu, MD
Medical Oncologist
Associate Attending
Memorial Sloan Kettering Cancer Center
New York, New York

RTP RESEARCH TO PRACTICE

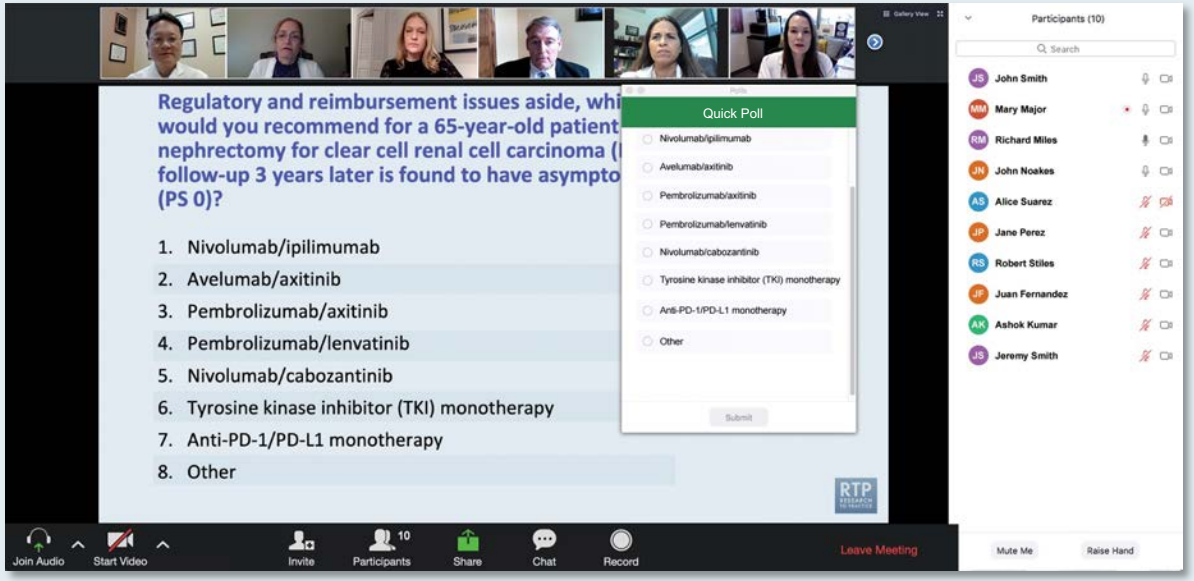
We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Management of MET-Altered Non-Small Cell Lung Cancer

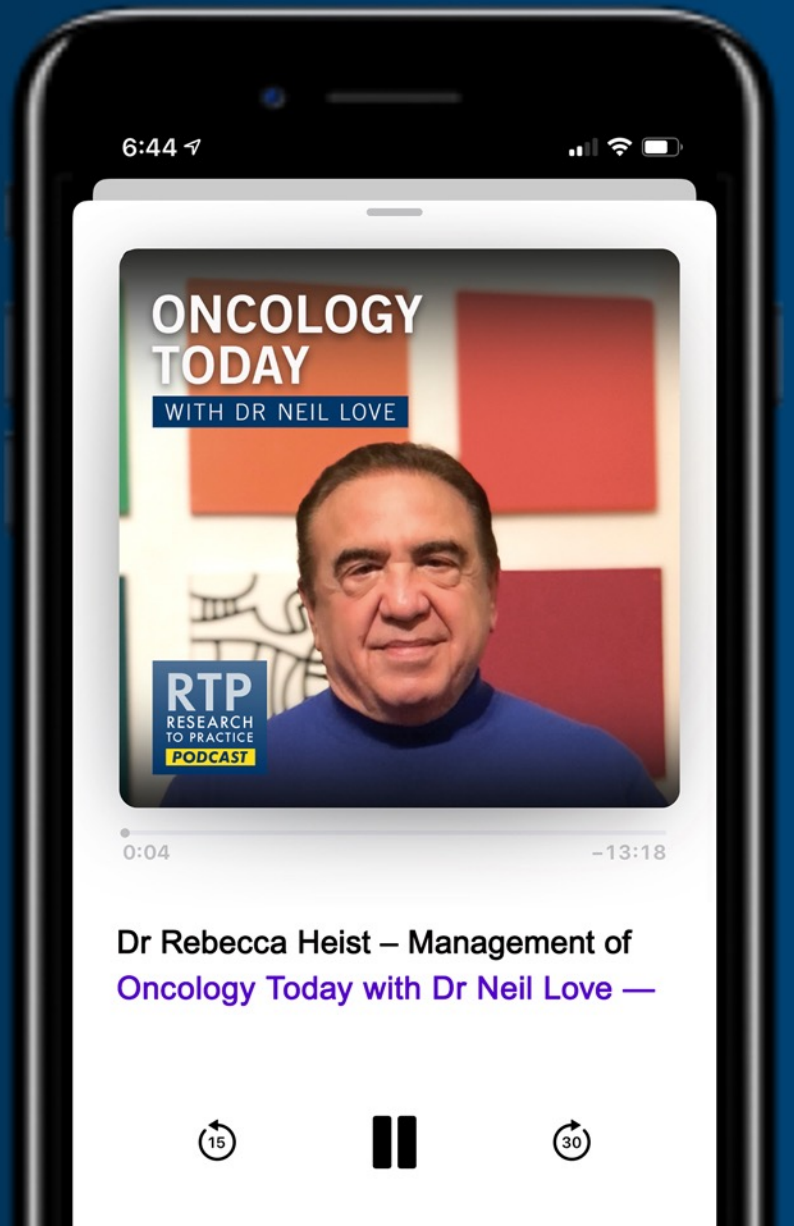
DR REBECCA HEIST

MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Wednesday, December 7, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Erika Hamilton, MD

Sara A Hurvitz, MD

Ian E Krop, MD, PhD

Shanu Modi, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of ER-Positive Breast Cancer

Part 2 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Thursday, December 8, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Aditya Bardia, MD, MPH

Matthew P Goetz, MD

Virginia Kaklamani, MD, DSc

Kevin Kalinsky, MD, MS

Hope S Rugo, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Chronic Lymphocytic Leukemia — What Clinicians Want to Know

Part 1 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
11:30 AM – 1:30 PM CT (12:30 PM – 2:30 PM ET)

Faculty

Alexey V Danilov, MD, PhD
Matthew S Davids, MD, MMSc
Professor Dr Arnon P Kater, MD, PhD
Lindsey Roeker, MD
Philip A Thompson, MB, BS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Hodgkin and Non-Hodgkin Lymphoma — What Clinicians Want to Know

Part 2 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
3:15 PM – 5:15 PM CT (4:15 PM – 6:15 PM ET)

Faculty

Jonathan W Friedberg, MD, MMSc
Brad S Kahl, MD
David G Maloney, MD, PhD
Loretta J Nastoupil, MD
Sonali M Smith, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Multiple Myeloma — What Clinicians Want to Know

Part 3 of a 3-Part CME Friday Satellite Symposium and Virtual Event Series
Preceding the 64th ASH Annual Meeting

Friday, December 9, 2022
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Jesús G Berdeja, MD
Rafael Fonseca, MD
Sagar Lonial, MD
Robert Z Orlowski, MD, PhD
Noopur Raje, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of Acute Myeloid Leukemia

A CME/MOC-Accredited Virtual Event

Wednesday, December 14, 2022
5:00 PM – 6:00 PM ET

Faculty

Courtney D DiNardo, MD, MSCE
Mark Levis, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Management of Multiple Myeloma

Thursday, December 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Shaji K Kumar, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Emerging Role of Antibody-Drug Conjugates in the Management of Non-Small Cell Lung Cancer

A CME/MOC-Accredited Virtual Event

Thursday, December 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Alexander I Spira, MD, PhD
Helena Yu, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Commercial Support

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

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Spira — Disclosures

Consulting/Advisory Role	Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Gritstone bio, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Novartis, Regeneron Pharmaceuticals Inc, Takeda Pharmaceuticals USA Inc
Contracted Research	AbbVie Inc, ADC Therapeutics, AI Therapeutics, Alkermes, Amgen Inc, Arch Therapeutics Inc, Astellas, Astex Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Cardiff Oncology, CytomX Therapeutics, Daiichi Sankyo Inc, Gritstone bio, Ignyta Inc, Incyte Corporation, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Lumos Pharma, MacroGenics Inc, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Novartis, Plexxikon Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines, Roche Laboratories Inc, Rubius Therapeutics, Synthekine Inc, Takeda Pharmaceuticals USA Inc
Honoraria	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, CytomX Therapeutics, Janssen Biotech Inc, Merck, Novartis, Takeda Pharmaceuticals USA Inc
Stock Options/Ownership	Lilly

RTP RESEARCH TO PRACTICE

Dr Yu — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, C4 Therapeutics, Cullinan Oncology, Daiichi Sankyo Inc, Janssen Biotech Inc
Research Funding to My Institution	AstraZeneca Pharmaceuticals LP, Black Diamond Therapeutics Inc, Blueprint Medicines, Cullinan Oncology, Daiichi Sankyo Inc, Erasca, Janssen Biotech Inc, Novartis, Pfizer Inc

Targeting HER2 and HER3 with Antibody Drug Conjugates in non-small cell lung cancer

Helena Yu
Associate Attending
Memorial Sloan Kettering Cancer Center

Antibody Drug Conjugates: TROP2 and Beyond

Alex Spira, MD PhD FACP
Virginia Cancer Specialists
Co Chair, US Oncology Thoracic Oncology Committee
CEO and Director, NEXT Oncology Virginia

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

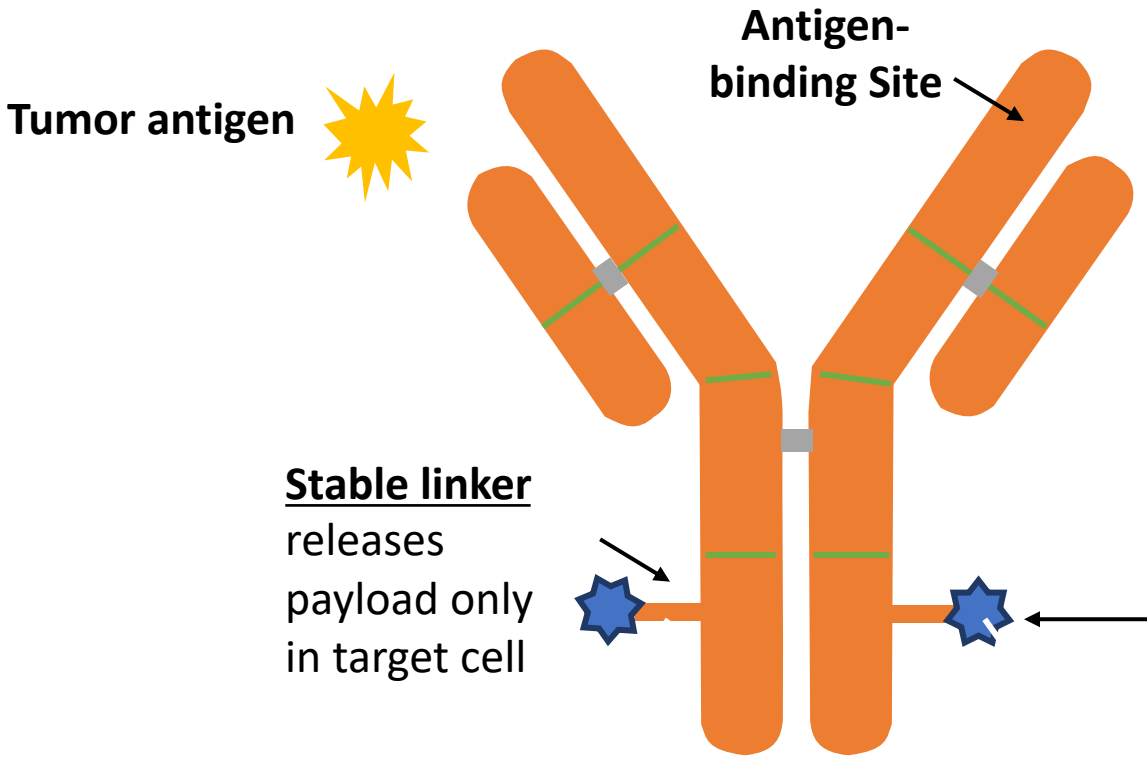
- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

Antibody–Drug Conjugates

Monoclonal antibody linked to a cytotoxic drug designed to widen the therapeutic window by focusing delivery to specific cells



Monoclonal antibody
selective for a cell surface protein (antigen) preferentially expressed on the tumor cell

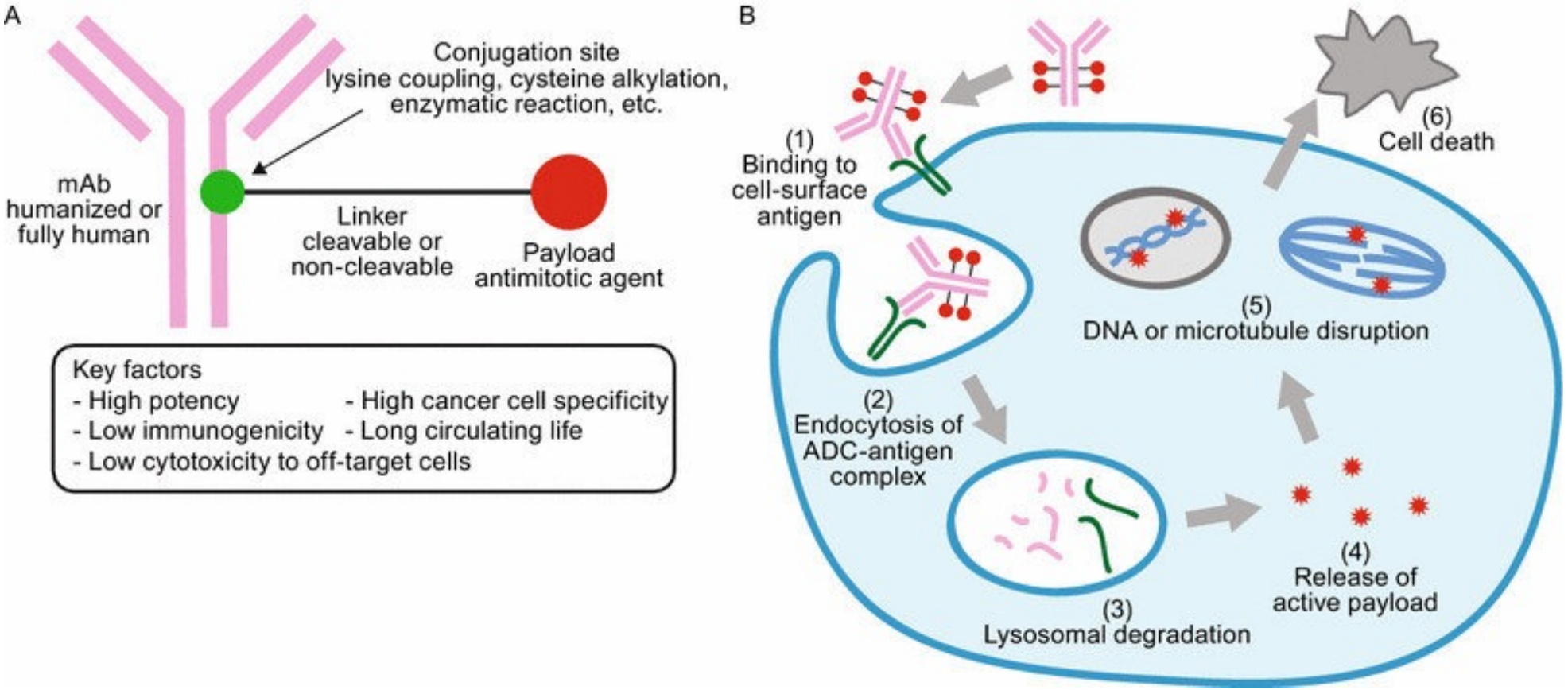
Payload
Cytotoxic drug with enhanced cytotoxicity, variable DAR (drug antibody ratio) affects efficacy and clearance

Drago. Nat Rev Clin Oncol. 2021;18:327.

Courtesy of Helena Yu, MD

Other ADCs

- How many combinations can we make ?



Courtesy of Alexander I Spira, MD, PhD

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

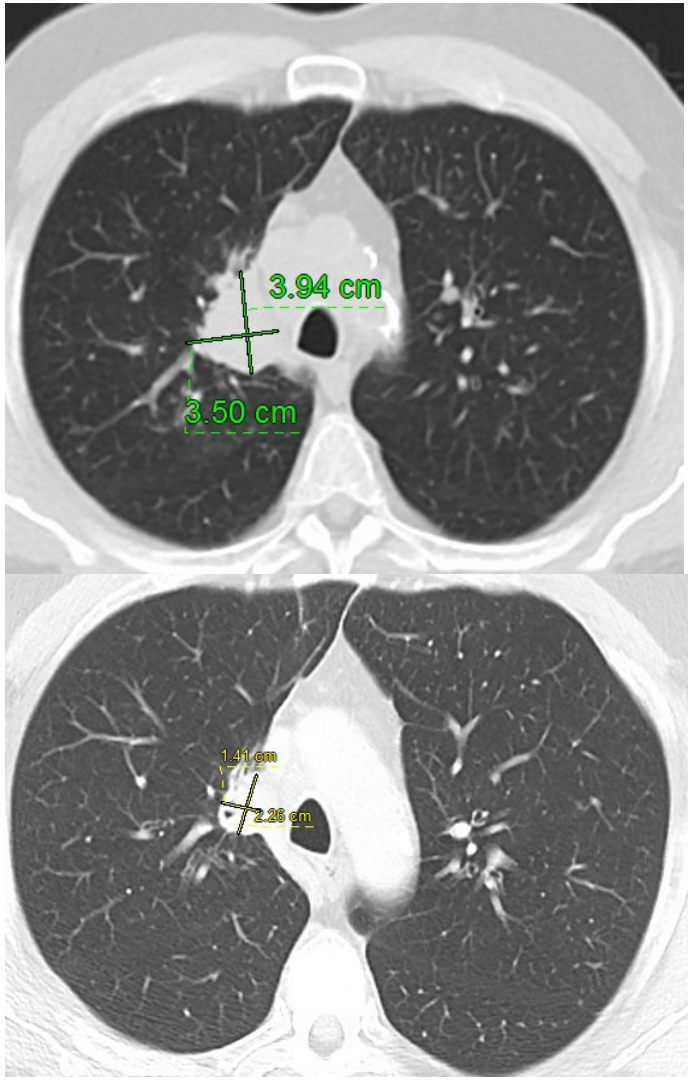
Case Presentation – Dr Yu: 55-year-old woman with HER2 positive lung cancer

55 yo never-smoker who initially presented with oligometastatic disease with involvement of the R lung (3.5cm RUL mass), R mediastinal lymph node (2cm) and isolated R humeral osseous met (1.5cm lytic lesion).

She got 4 cycles of carboplatin/pemetrexed/pembrolizumab with minor shrinkage followed by definitive radiation therapy to remaining sites of disease.

On a follow up scan after 3 months, she had a new R lung mass and additional osseous metastases.

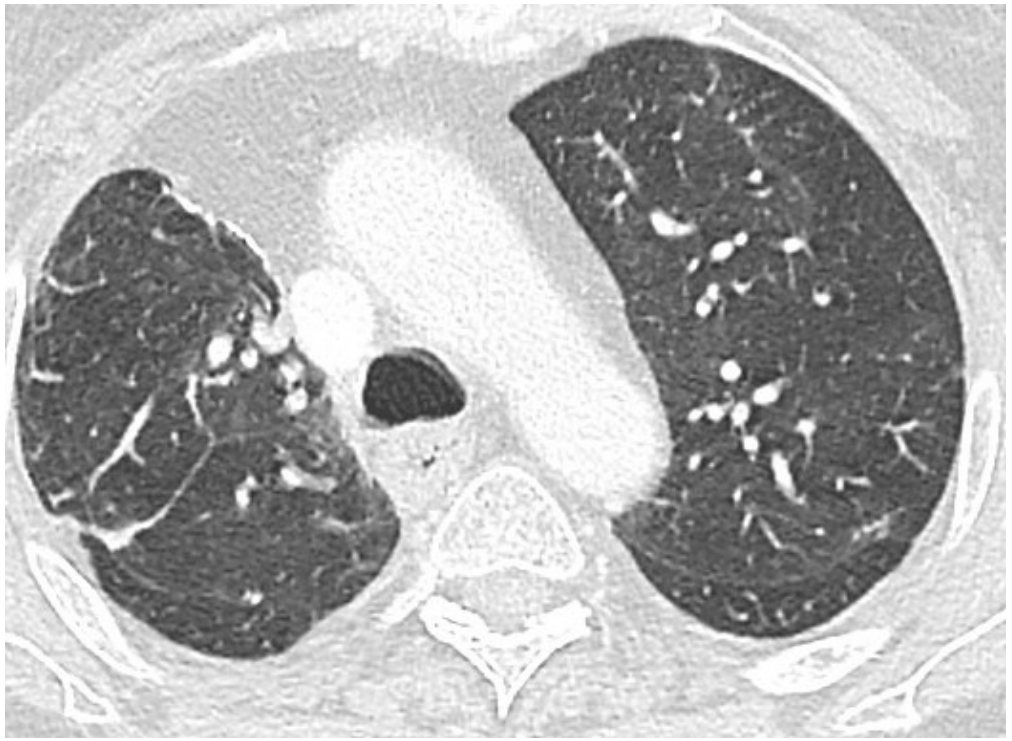
Case Presentation – Dr Yu: 55-year-old woman with HER2 positive lung cancer (continued)



She was started on trastuzumab deruxtecan which she tolerated well (grade 1 fatigue, grade 1 thrombocytopenia).

Repeat scans demonstrated improvement in her R hilar mass and sclerosis of osseous mets.

Case Presentation – Dr Yu: 55-year-old woman with HER2 positive lung cancer (continued)



Follow up 2 scan demonstrated incidental ground glass interstitial opacities bilaterally. She was asymptomatic.

T-DXd was held, she was started on prednisone 30mg and tapered over 3 weeks.

Repeat scan 4 weeks later showed resolution of infiltrates, she continued to be asymptomatic and T-DXd was restarted at the same dose with no recurrence of the radiographic findings. She has been on drug for 15 months with maintained partial response.

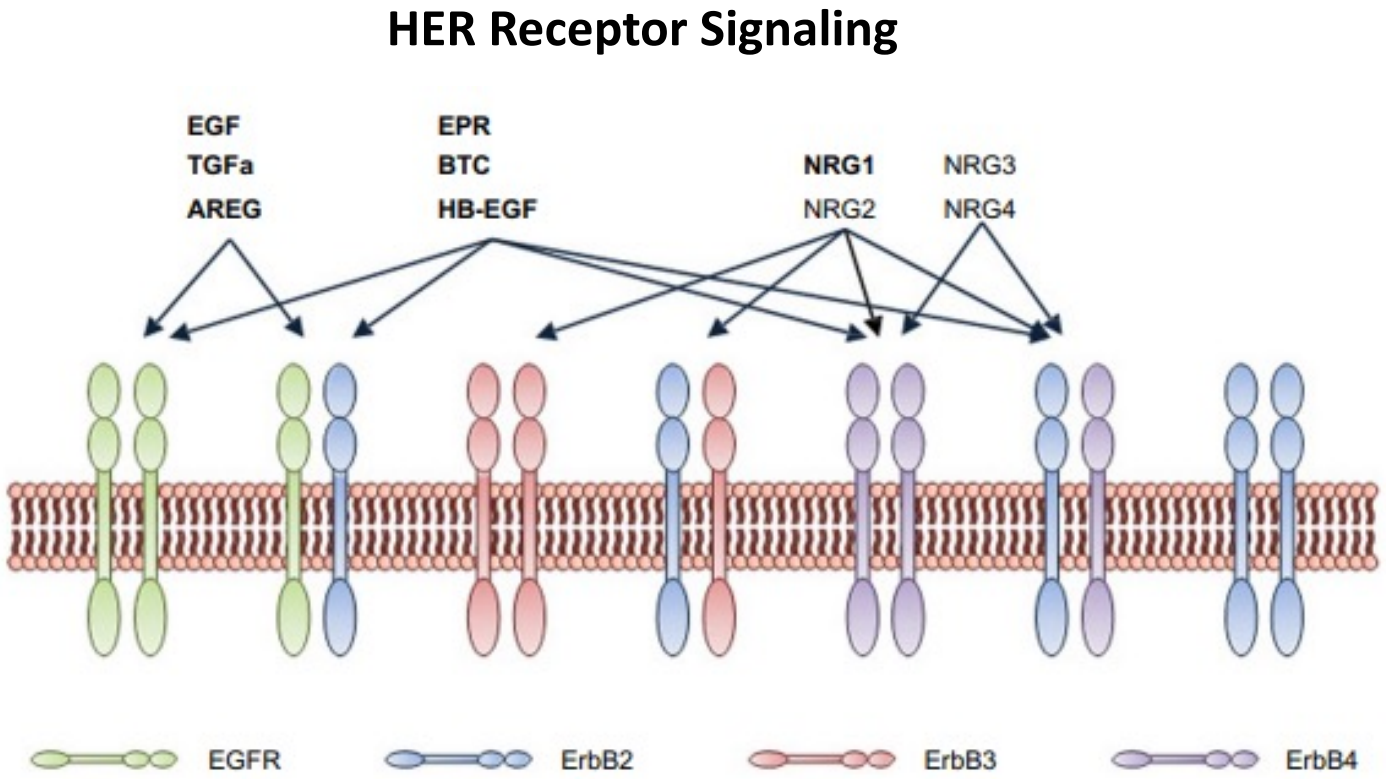
HER family

HER1 (EGFR) - Oncogene

HER2 - Oncogene

HER3

HER4



Cook GI Cancer: Targets and Therapy 2014

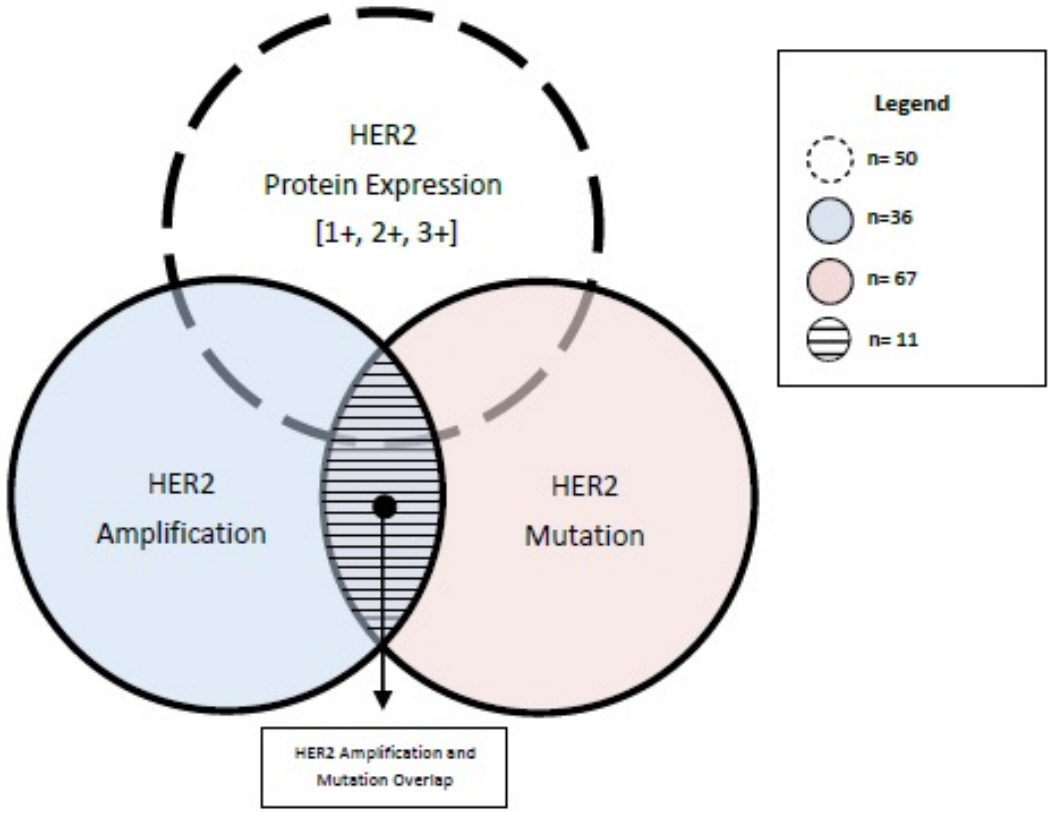
Courtesy of Helena Yu, MD

Spectrum of HER2 alterations in NSCLC

HER2 Mutant
- HER2 mutation in kinase domain (exon 20)
- 2-3% of all lung cancers
- Identified by NGS

HER amplified
- HER2 amp is increased gene copy number (≥2) compared to control gene
- 3-5% of all lung cancers
- Identified by NGS or FISH

HER2 overexpression
- Protein expression identified by IHC (2+, 3+ by HER2 antibody)
- Up to 20% of all lung cancers, high expression rare (<5%)
- Identified by IHC

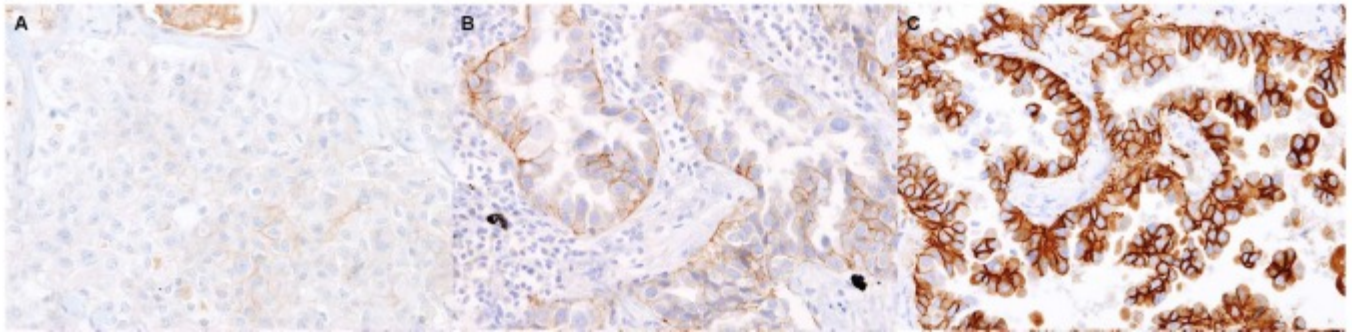


- HER2 amp is usually associated HER2 protein expression
- Not all tumors with HER2 expression have HER2 gene amplification
- HER2 amplification and mutation are distinct (only 10% overlap)

Courtesy of Helena Yu, MD

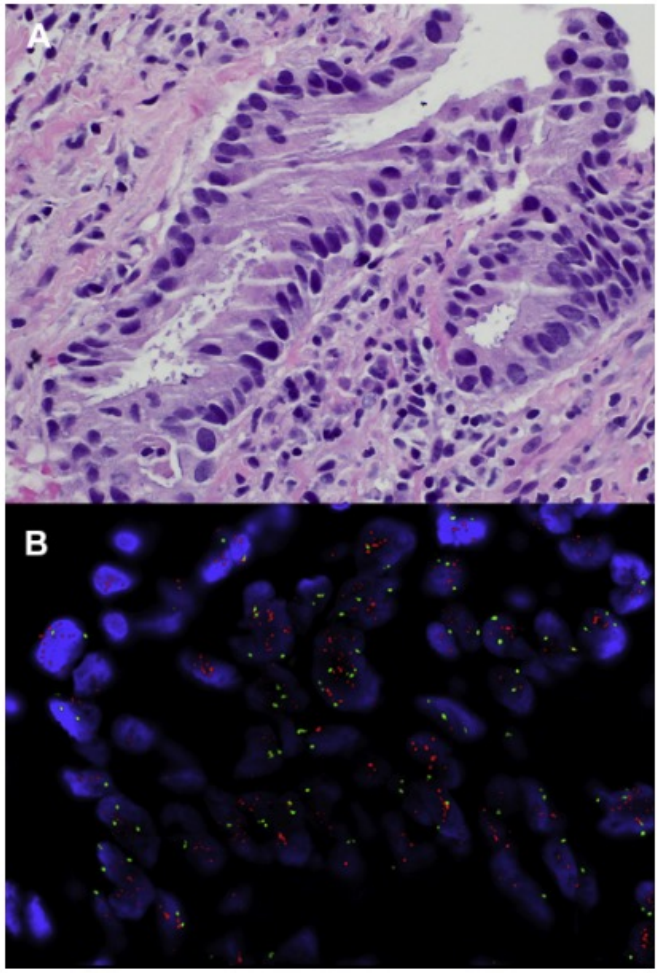
Spectrum of HER2 alterations in NSCLC

IHC 1+ **IHC 2+** **IHC 3+**



HER2 insertion on NGS

POSITIVE FOR THE FOLLOWING SOMATIC ALTERATIONS:
1. ERBB2 (NM_004448) exon20 p.Y772_A775dup (c.2313_2324dup)

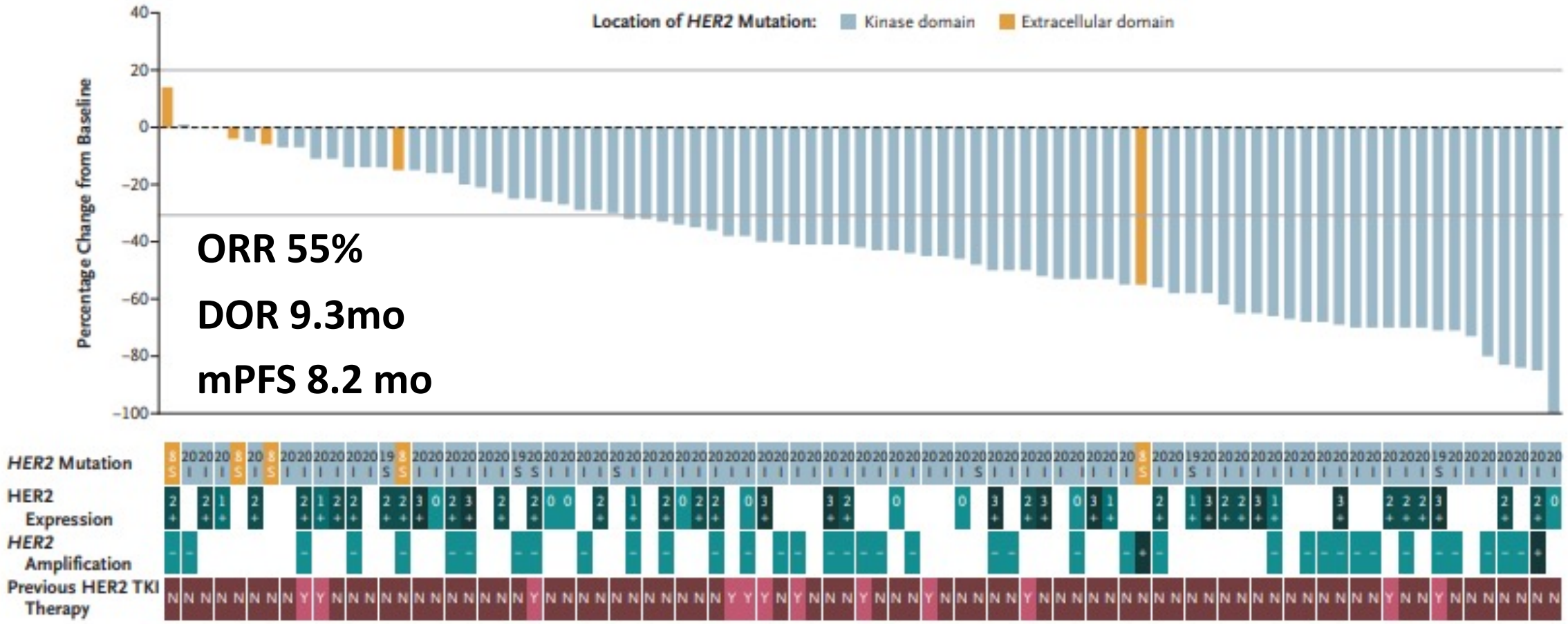


FISH pos for HER2 amplification

Li JTO 2015, Kim Plos One 2017

Courtesy of Helena Yu, MD

DESTINY-Lung01 – HER2 mutant

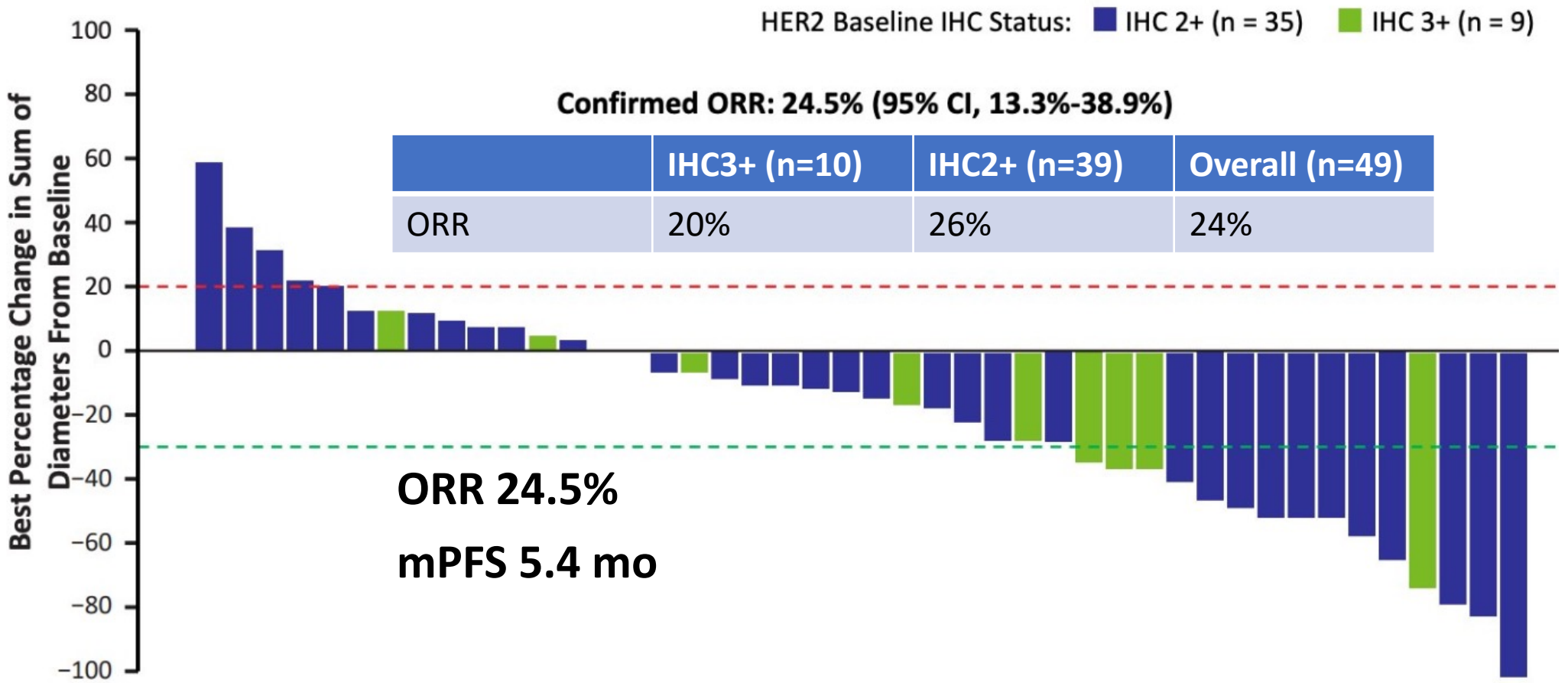


N=91 HER2 mutant

Li NEJM 2022

Courtesy of Helena Yu, MD

DESTINY-Lung01 – HER2 overexpressing



	IHC3+ (n=10)	IHC2+ (n=39)	Overall (n=49)
ORR	20%	26%	24%

Nakagawa WCLC 2020

Courtesy of Helena Yu, MD

Adverse events with T-DXd

Drug-related adverse events with ≥20% incidence

Nausea	66 (73)
Fatigue†	48 (53)
Alopecia	42 (46)
Vomiting	36 (40)
Neutropenia‡	32 (35)
Anemia§	30 (33)
Diarrhea	29 (32)
Decreased appetite	27 (30)
Leukopenia¶	21 (23)
Constipation	20 (22)

Any TEAE	49 (100.0%)	TEAE grade ≥3 (>15%)	
Drug related	44 (89.8%)	Decreased neutrophil count	10 (20.4%)
TEAE grade ≥3	36 (73.5%)	TEAE associated with dose discontinuation[b]	
Drug related	27 (55.1%)	Pneumonitis	5 (10.2%)
Serious TEAE	22 (44.9%)	TEAEs associated with dose reduction[b]	
Drug related	8 (16.3%)	Decreased neutrophil count	5 (10.2%)
TEAE associated with dose discontinuation	11 (22.4%)	Fatigue	4 (8.2%)
Drug related	6 (12.2%)	Nausea	3 (6.1%)
TEAE associated with dose reduction	17 (34.7%)	TEAEs associated with dose interruption[b]	
Drug related	16 (32.7%)	Decreased neutrophil count	5 (10.2%)
TEAE associated with dose interruption	26 (53.1%)	Nausea	3 (6.1%)
Drug related	17 (34.7%)	TEAE grade 5[c] | Drug related	7 (14.3%) | 1 (2.0%)

On-target, but off-tumor: target protein expressed in normal tissue

- Skin toxicity, cardiac toxicity

Off-target and off-tumor: more diffuse payload release, inadvertent cellular uptake

- Anemia, neutropenia seen with many ADCs

Unknown

- Pulmonary toxicity with T-DXd

Li NEJM 2022, Nakagawa WCLC 2020

Courtesy of Helena Yu, MD

Adverse events – ILD/Pneumonitis

AEs of Special Interest: ILD

All Patients (N = 49)						
n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Any Grade/Total**
Adjudicated drug-related ILD[a]	2 (4.1%)	3 (6.1%)	0	0	3 (6.1%)	8 (16.3%)

Adjudicated drug-related ILDs[b]

- Median time to onset was 64.5 days (range, 2-126 days)
- All patients had drug withdrawn
- Steroid treatment was used in patients who had grade 2 (n = 3) and those who had grade 5 ILDs (n = 3)
- 3 patients recovered (grade 1 [n = 1] and grade 2 [n = 2]) and 2 patients had not recovered by data cutoff (grade 1 [n = 1] and grade 2 [n = 1])
- 4 of 8 patients had immune checkpoint inhibitors included in their prior lines of therapy

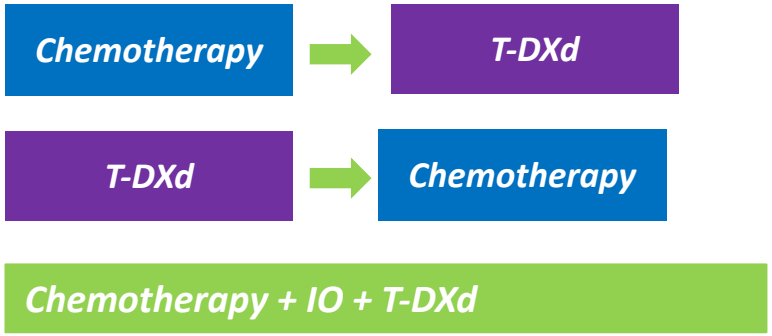
Grade 5 ILD[c] events

- Medical history of the 3 patients included
  1. Pulmonary embolism, productive cough, dyspnea, pleural effusion, and lobectomy; 4 prior lines of therapy
  2. Cough, dyspnea, pleural effusion, and pulmonary embolism; 5 prior lines of therapy
  3. Dyspnea, SLE without lung involvement, and TTP; 1 prior line of therapy
- Steroid treatment was initiated within 5 days after the event was reported by the investigator[d]
- All had previously received immune checkpoint inhibitors
- Primary cause of death was PD in 2 patients and pneumonitis in 1 patient

Li NEJM 2022

Courtesy of Helena Yu, MD

Trastuzumab Deruxtecan

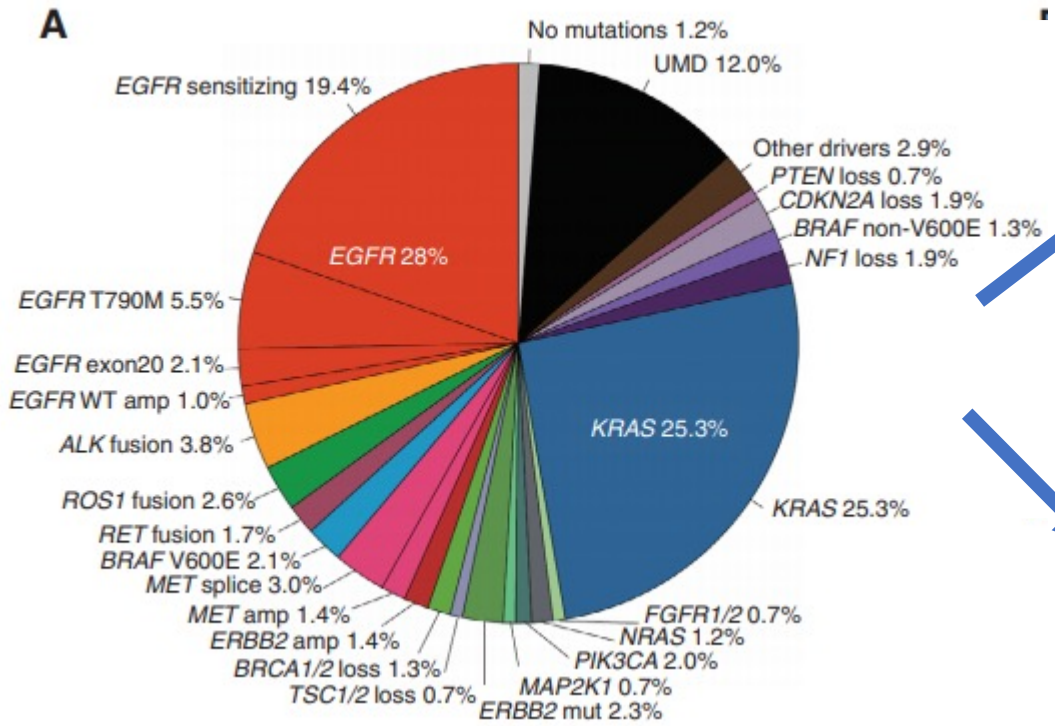


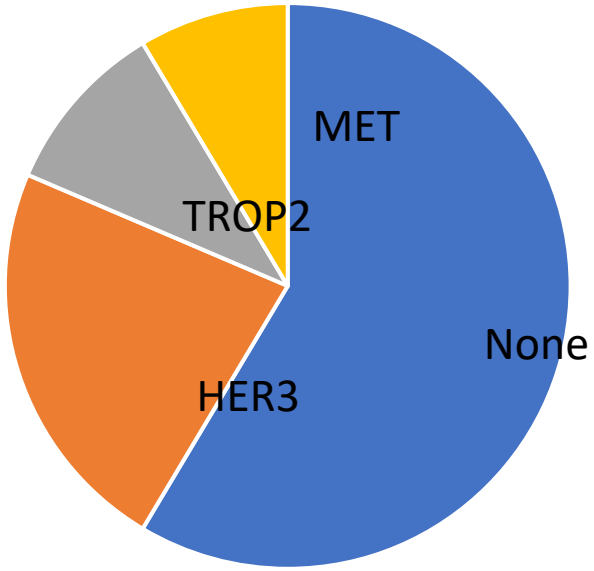
- Recent approval of trastuzumab deruxtecan after chemotherapy for HER2 mutant lung cancers
- Continued assessment of T-DXd in HER2 overexpressed lung cancers
- Assessment of T-DXd in first-line setting with chemo +/- IO

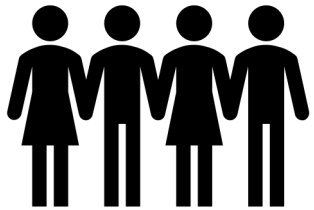
Phase	Indication/Setting	Treatment	Clinicaltrials.gov identifier
3	HER2-mutated NSCLC First-line	T-DXd vs platinum chemotherapy	DESTINY-Lung04 NCT05048797
1B	HER2-mutated NSCLC Later-line, First-line	T-DXd with durvalumab and chemotherapy	DESTINY-Lung02 NCT04686305

Courtesy of Helena Yu, MD

Biomarker selection







Urothelial Cancer

Why is response higher in HER2 mutant vs HER2 overexpressed NSCLC?

HER2 mutations may be a true driver, with HER2 expression more a passenger (cancer can adapt and use other signaling pathways)

Courtesy of Helena Yu, MD

<u>Protein expression as biomarker</u>

Measure presence of target antigen

Precedent exists: HER2 IHC in breast cancer, PDL1 in lung cancer

How much is enough?

Best method? IHC? H Score?

Challenge: Protein expression and driver mutations are not mutually exclusive – what is driving the cancer?

Select a patient population enriched for a certain target

Nectin 4, target of enfortumab vedotin, expressed in 83% of urothelial cancers

Rosenberg JCO 2019, Jordan Canc Disc 2017

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Yu: 63-year-old male with EGFR-mutant lung cancer

63 yo never-smoker who initially presented with metastatic EGFR-mutant lung cancer. He was on osimertinib for 15 months before he developed disease progression. Repeat biopsy showed an acquired BRAF fusion. He was symptomatic with pain from progressive liver metastases and he was started on carboplatin/pemetrexed/bevacizumab, followed by pemetrexed/bevacizumab maintenance for a total of 10 months before further disease progression.

Procedures/Addenda
MSK-IMPACT Solid Date Ordered: 1/13/2022 14:03 Status: Signed Out

Interpretation
Summary: 9 mutations, no copy number alterations, 2 structural variants detected.

MSI Status: MICROSATELLITE STABLE (MSS). The MSIsensor score is 0.78.

TUMOR MUTATION BURDEN: The estimated tumor mutation burden (TMB) for this sample is 7.4 mutations per megabase (mt/Mb).

POSITIVE FOR THE FOLLOWING SOMATIC ALTERATIONS:
1. EGFR (NM_005228) exon19 p.L747_P753delinsS (c.2240_2257del)
2. TP53 (NM_000546) exon5 p.P151S (c.451C>T)
3. CHEK1 (NM_001274) exon11 p.M409Yfs*10 (c.1224dupT)
4. DOT1L (NM_032482) exon27 p.S1264C (c.3790A>T)
5. FGFR2 (NM_000141) exon11 p.E499A (c.1496A>C)
6. FOXO1 (NM_002015) exon2 p.Q335E (c.1003C>G)
7. HLA-C (NM_002117) exon8 p.*367Wext*41 (c.1101A>G)
8. PIK3CG (NM_002649) exon2 p.P183L (c.548C>T)
9. PRKCI (NM_002740) exon15 p.R483H (c.1448G>A)
10. EPHA5 (NM_004439) rearrangement: c.182-5310_c.246+67dup (Note: 2)
11. WDR91 (NM_014149) - BRAF (NM_004333) fusion: c.891+1148:WDR91_c.1105:BRAFdup (Note: 3)

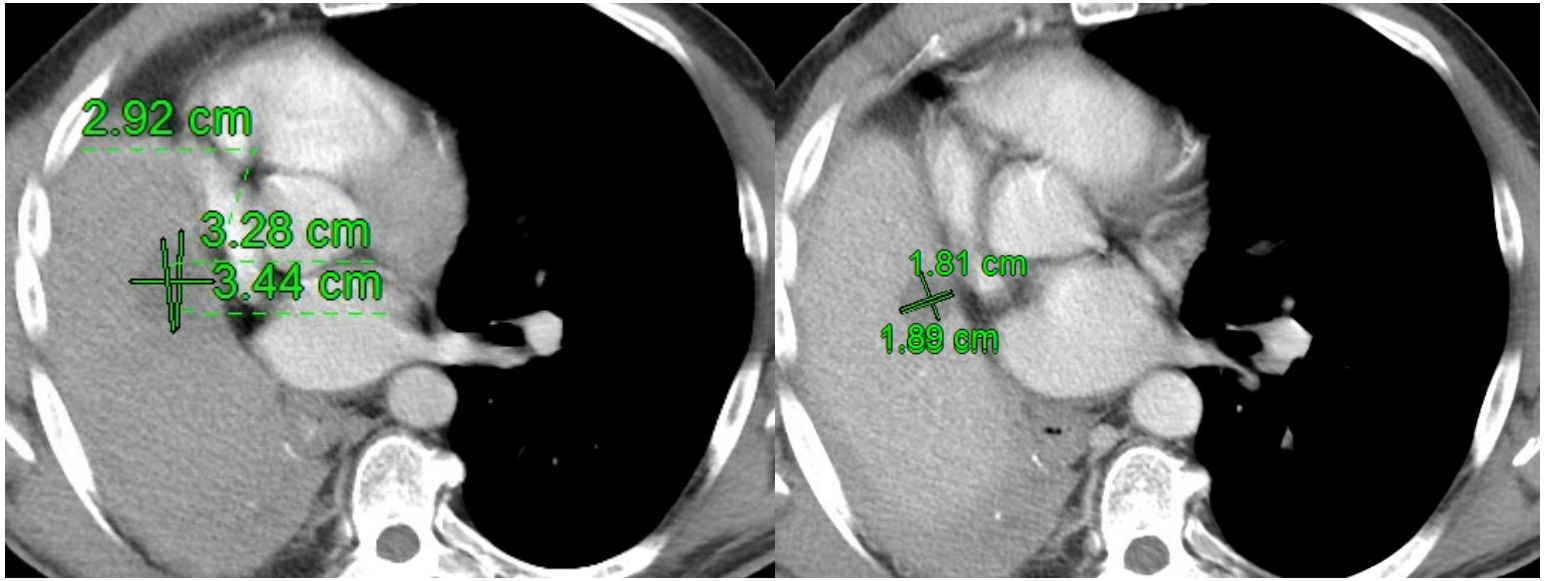
POSITIVE FOR THE FOLLOWING GENE FUSION IN THE CLINICALLY VALIDATED PANEL:

WDR91-BRAF fusion.

Note: The rearrangement is an in-frame fusion between genes WDR91 Exon6 (NM_014149) and BRAF Exon9 (NM_004333).

NEGATIVE FOR GENE FUSIONS IN THE INVESTIGATIONAL PANEL.

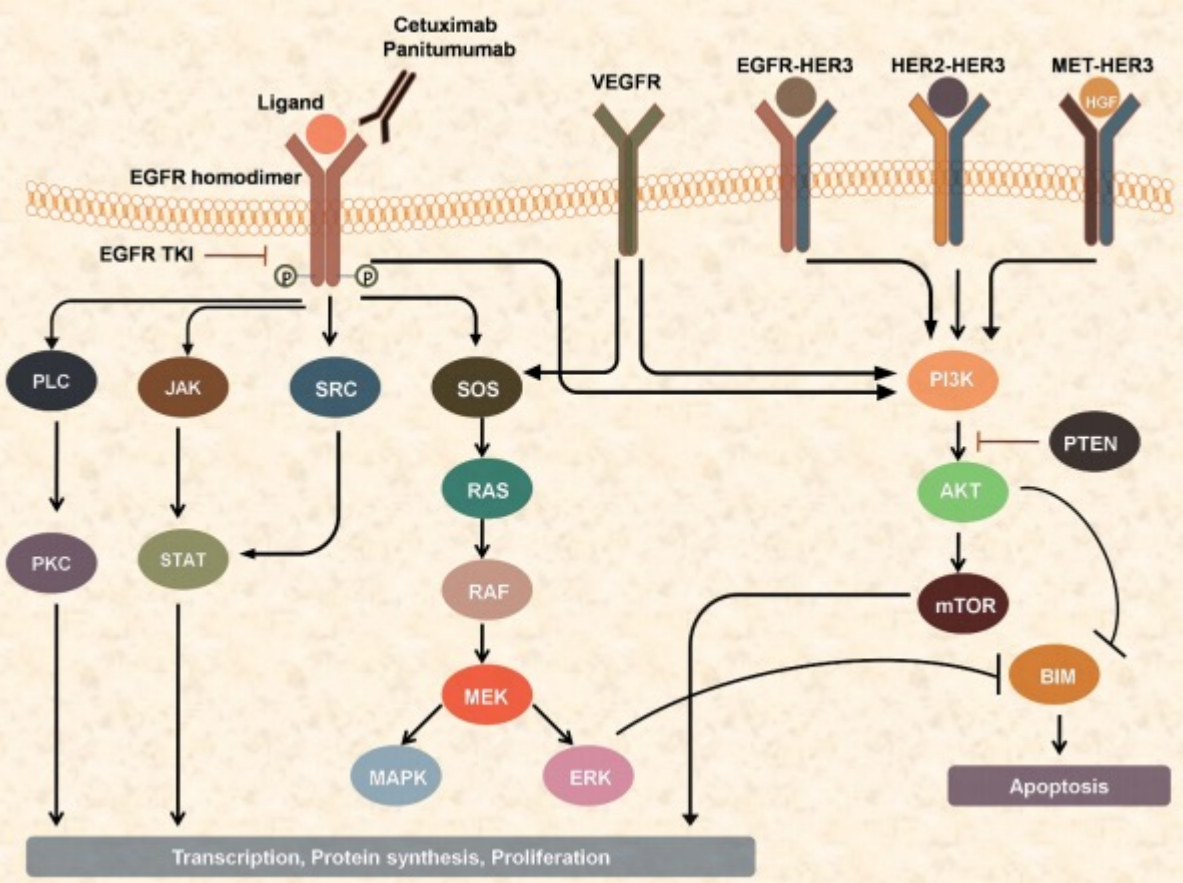
Case Presentation – Dr Yu: 63-year-old male with EGFR-mutant lung cancer (continued)



He was started on patritumab deruxtecan on a clinical trial. He had grade 1 nausea, fatigue and alopecia.

He had a confirmed partial response to treatment with response in his liver metastases, lung nodules and stable CNS metastases. He remained on treatment for 8 months.

HER3



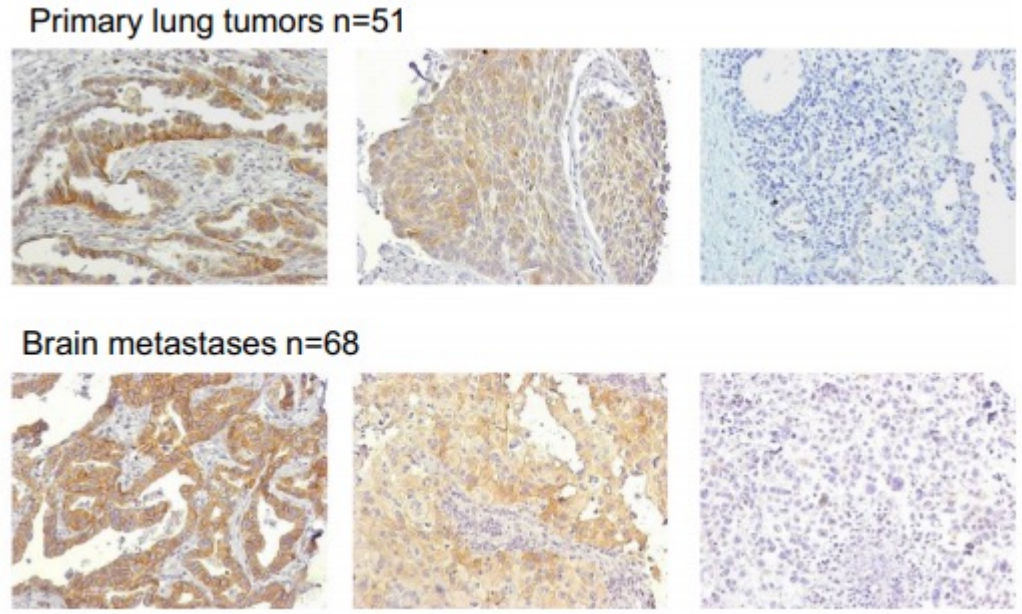
- HER3 is a member of the ErbB protein kinase family
- HER3 overexpressed in cancer, and associated with poorer prognosis
- Binds to neuregulins
- HER3 itself is not an oncogene but heterodimerizes with other RTKs activating oncogenic signaling (through PI3K and MAPK)
- HER3 expression can mediate resistance to targeted therapy (such as resistance to EGFR therapies in lung cancer)

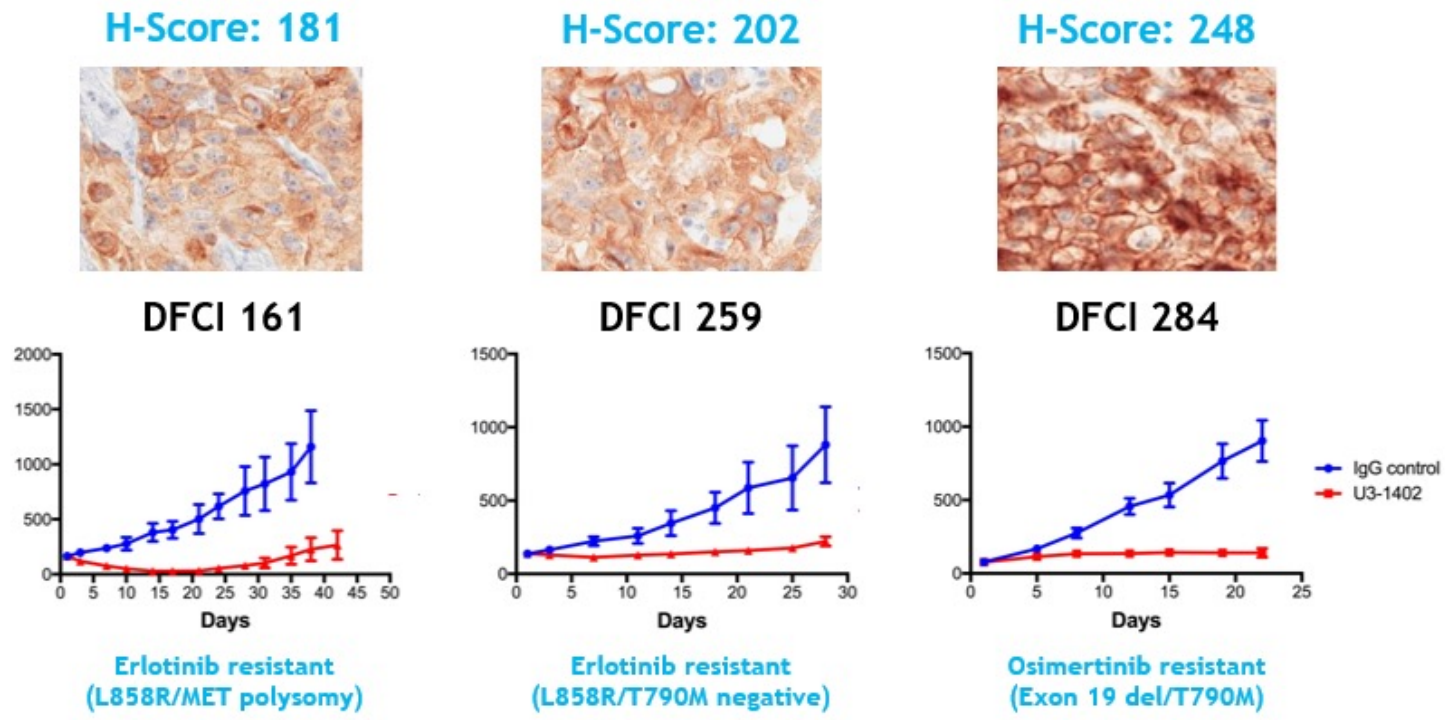
Dokola Oncogene 2017, Lyu Acta Pharma Sinica B, 2018, Mishra Onc Rev 2018, Jacob Cancer Treat Rev 2018

Courtesy of Helena Yu, MD

HER3 staining

- HER3 mutations or HER3 amplification not commonly seen
- HER3 expression by IHC seen in 83% of non-small cell lung cancers
- H-Score is a composite score that considers the predominant staining intensity seen in a given field
- Possible role in resistance to EGFR TKI therapy in NSCLC
  - In gefitinib-resistant cells, oncogenic MET phosphorylates HER3, leading to activation of the PI3K pathway
  - HER3 expression is strongly upregulated in osimertinib-resistant cancer cells



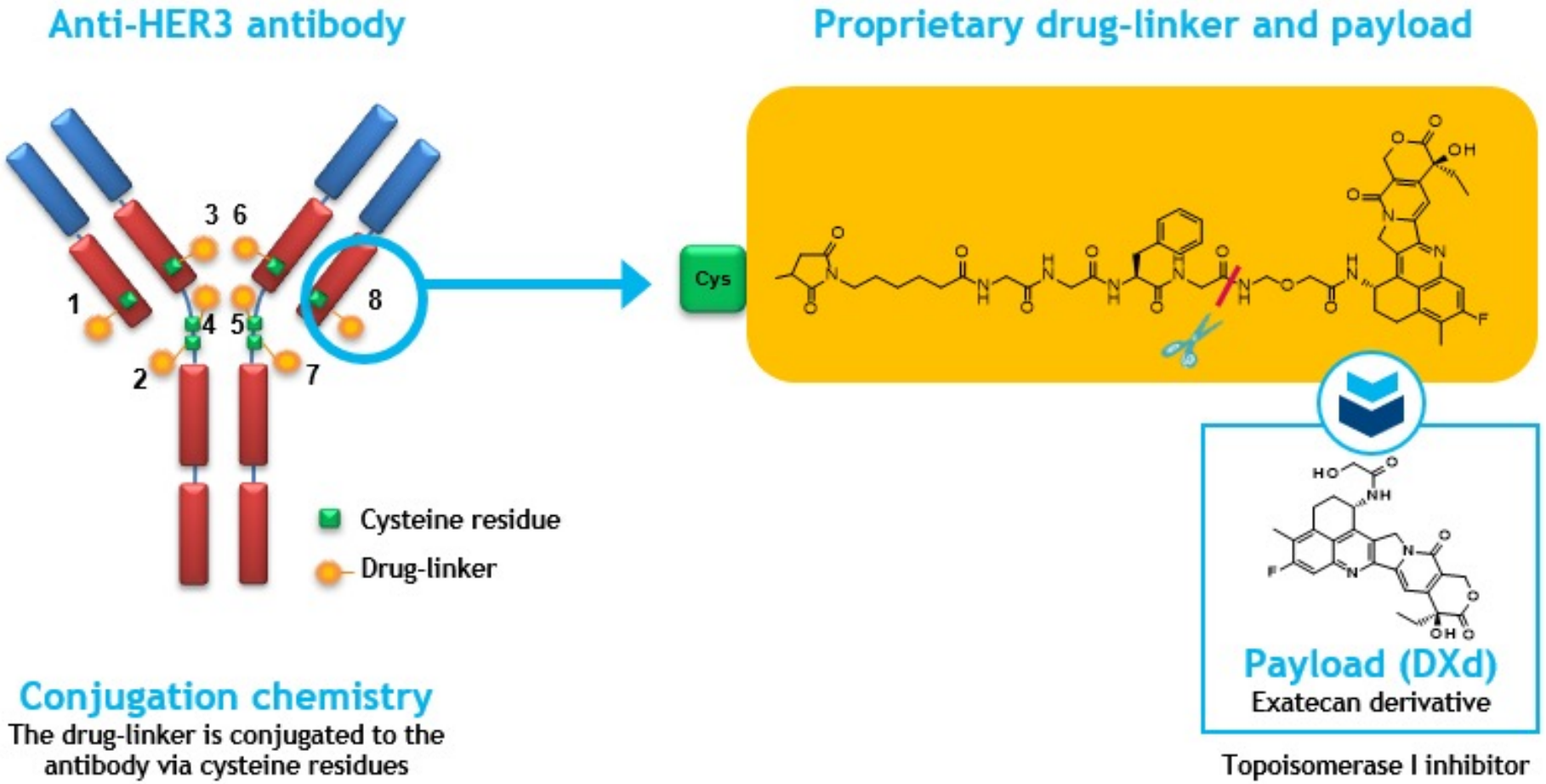


Janne PASCO 2019, Scharpenseel Sci Rep 2019
Engelman Science 2007, Romaniello Cancers 2020

Courtesy of Helena Yu, MD

Patritumab Deruxtecan

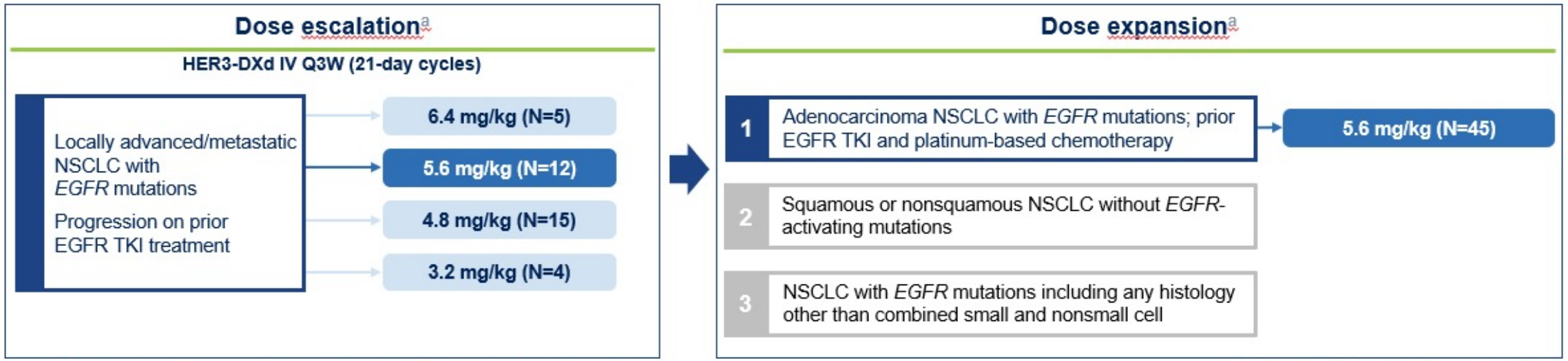
- Payload MOA; Topo I inhibitor
- High potency of payload
- High drug-to-antibody ratio (~8:1)
- Payload with short systemic half-life
- Stable linker-payload
- Tumor-selective cleavable linker
- Bystander effect



Courtesy of Helena Yu, MD

Janne PASCO 2019

Patritumab Deruxtecan



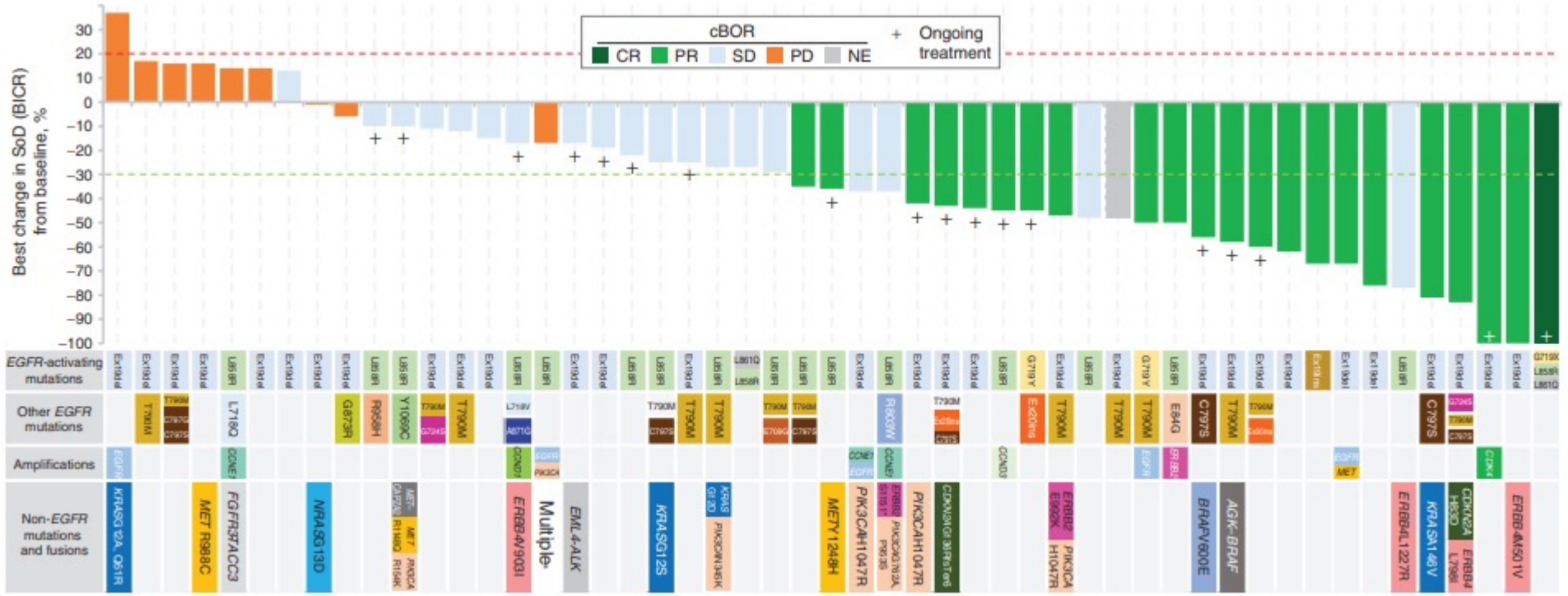
Patient Characteristics and Treatment History	5.6 mg/kg (N=57)
Age, median (range), years	65 (40-80)
Female, n (%)	36 (63)
ECOG performance status 0/1, n (%)	23 (40) / 34 (60)
Sum of diameters at baseline,[a] median (range), mm	54 (13-195)
History of CNS metastases, n (%)	27 (47)
Prior lines of systemic therapy, median (range)[b]	4 (1-9)
Prior cancer regimens	
Prior EGFR TKI therapy, n (%)	57 (100)
Prior osimertinib, n (%)	49 (86)
Prior platinum-based chemotherapy, n (%)	52 (91)
Prior immunotherapy, n (%)	23 (40)

Outcomes (BICR per RECIST 1.1) Median Follow Up: 10.2 (range, 5.2-19.9) mo[a]	Prior TKI ± PBC (N=57)
Confirmed ORR, % (95% CI)	39 (26-52)
Best overall response, n (%)	
CR	1 (2)
PR	21 (37)
SD, Non-CR/Non-PD	19 (33)
PD	9 (16)
Not evaluable	7 (12)
Disease control rate, % (95% CI)	72 (59-83)
Time to response, median (range), mo	2.6 (1.2-5.4)
Duration of response, median (95% CI), mo	6.9 (3.1-NE)
PFS, median (95% CI), mo	8.2 (4.4-8.3)

Courtesy of Helena Yu, MD

Janne PASCO 2021

Patritumab Deruxtecan

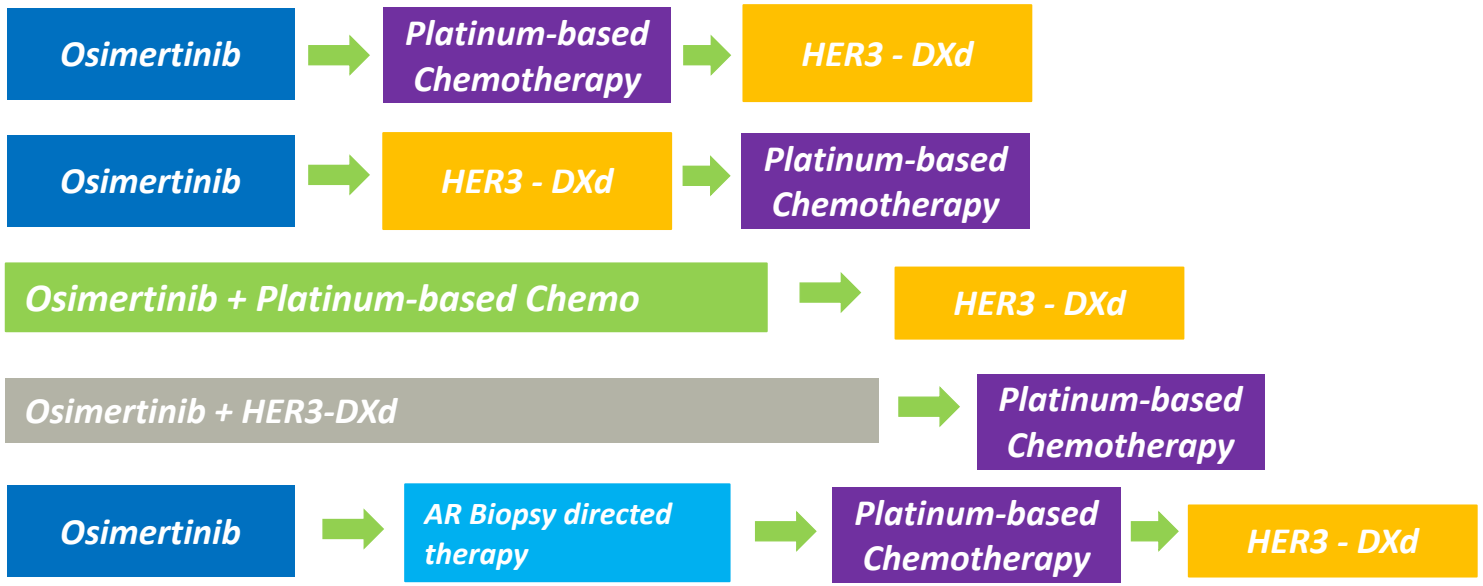


ORR 39%
DoR 6.9mo
mPFS 8.2mo
OS not reached

Janne PASCO 2021

Courtesy of Helena Yu, MD

Patritumab Deruxtecan



-Sequencing of therapy in flux in EGFR+ NSCLC

-Exploration in combination with osimertinib as well as first-line treatment

-Ideal targeted therapies post-osimertinib transcend mechanisms of resistance

Phase	Indication/Setting	Treatment	Clinicaltrials.gov identifier
2	EGFR-mutated NSCLC Post-TKI and chemotherapy	HER3-DXd	HERTHENA-Lung01 NCT04619004
1	EGFR-mutated NSCLC Post-osimertinib	HER3-DXd + osimertinib	NCT04676477
3	EGFR-mutated NSCLC Post-osimertinib	HER3-DXd vs Platinum doublet chemo	HERTHENA-Lung02 NCT045338970

Courtesy of Helena Yu, MD

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

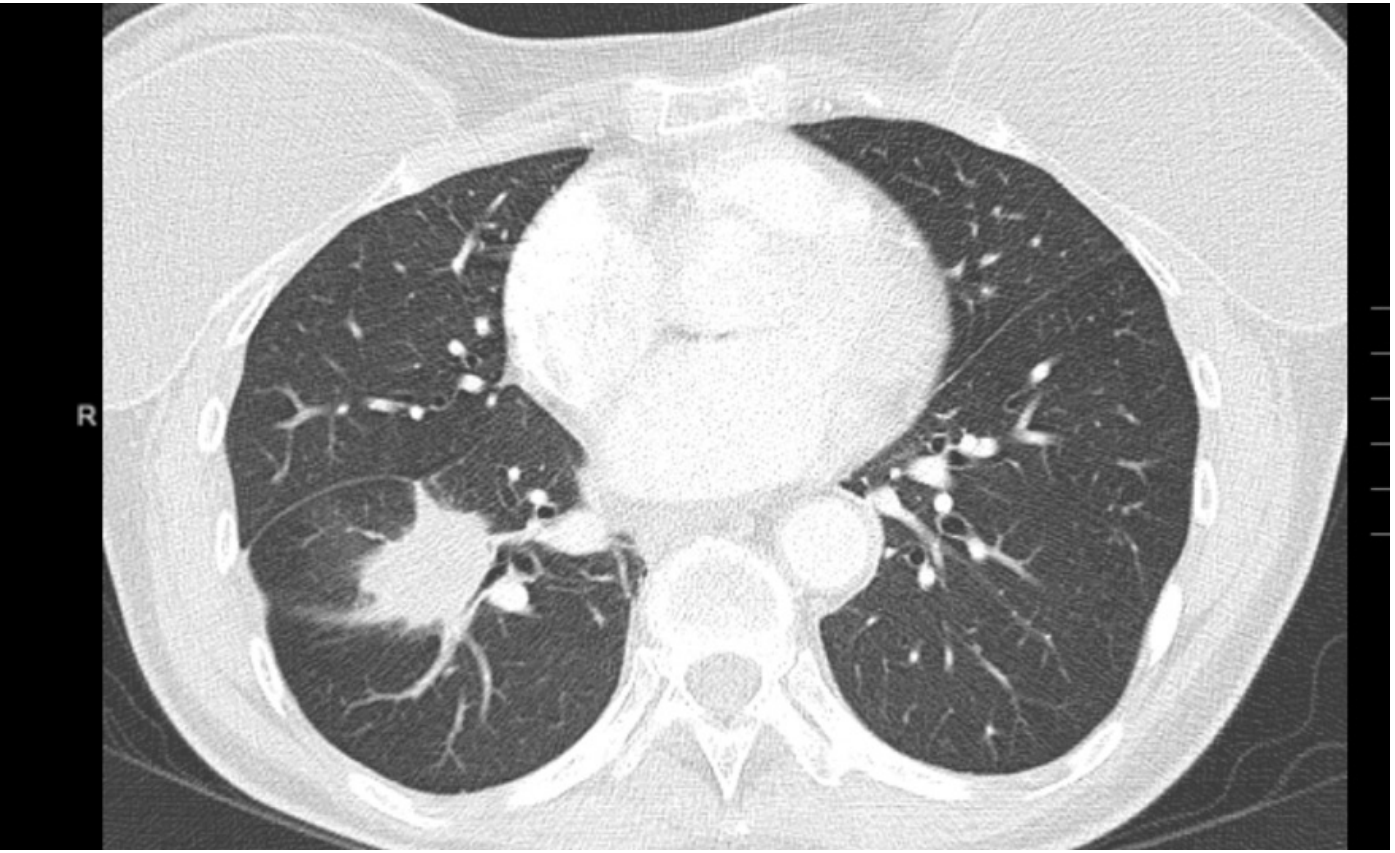
MODULE 5: Appendix

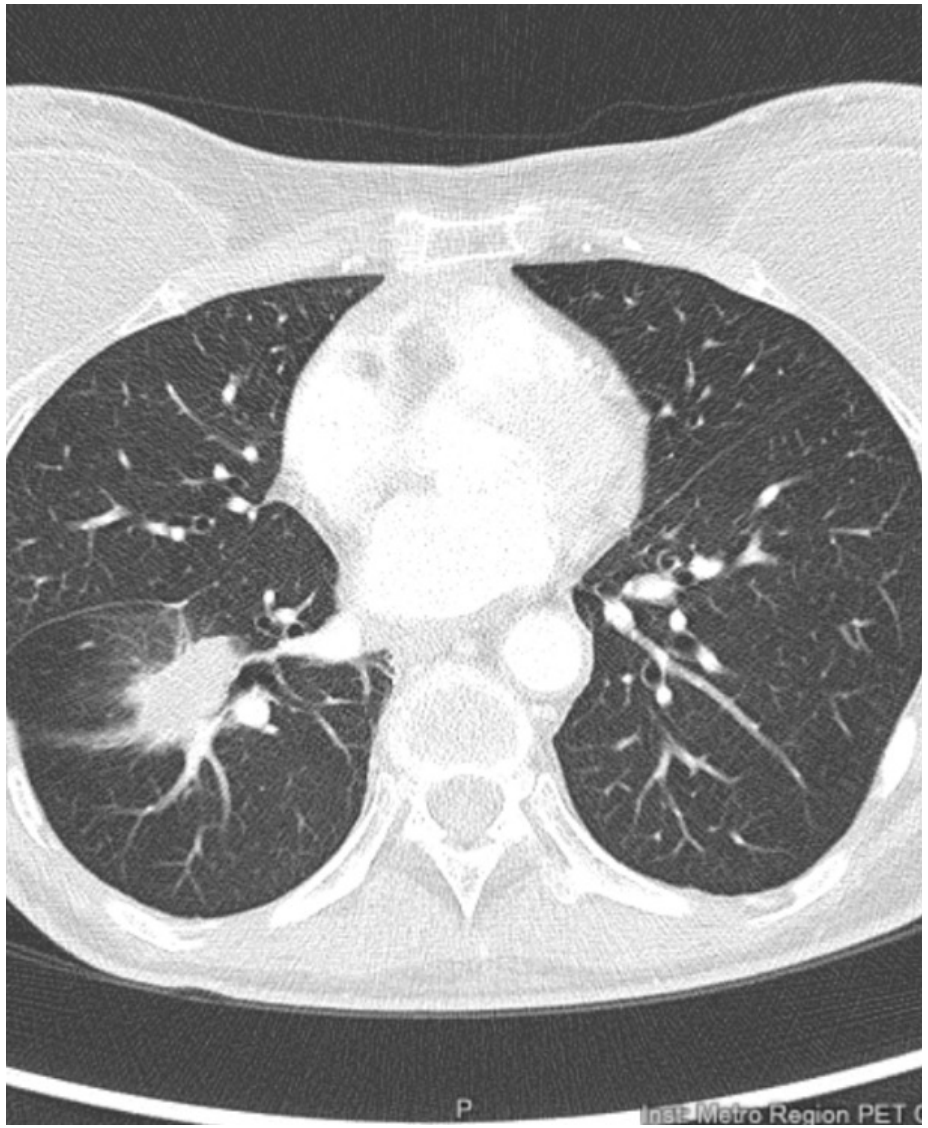
RTP RESEARCH TO PRACTICE

Case Presentation – Dr Spira

- 52-year-old woman with KRAS g12v m NSCLC
- Progressed on carbo/pem/pembro
- Options presented:
  - Docetaxel
  - IO combo trial
  - Dato-DXd trial

Case Presentation – Dr Spira (continued)





Case Presentation – Dr Spira

It's getting complicated.

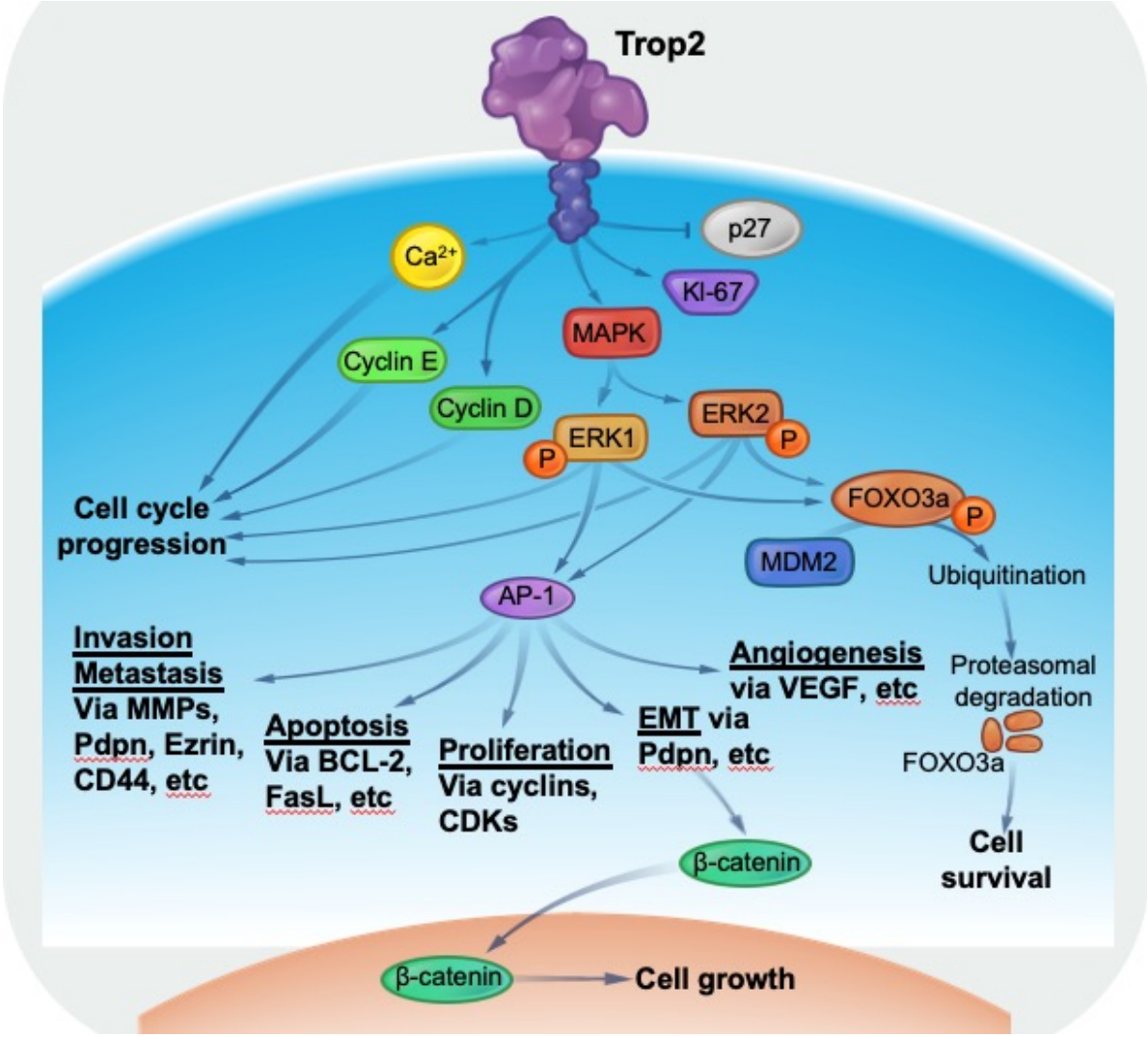
- 65 yo woman with met NSCLC, EGFR Exon 19 del
- Progressed on Osimertinib after 9 mos with new liver mets
- Options:
  - Carboplatin/pemetrexed
  - Carboplatin/pemetrexed/osi
  - Carboplatin/pemetrexed +/- amivantamab/lazertinib on trial
  - Osimertinib/Patritumab on trial
  - Patritumab vs Carboplatin/pemetrexed on trial
  - Osi/Telo-V if secondary c-met on trial
  - Other trial of new targeted RX (C797s)

TROP2 ADCs

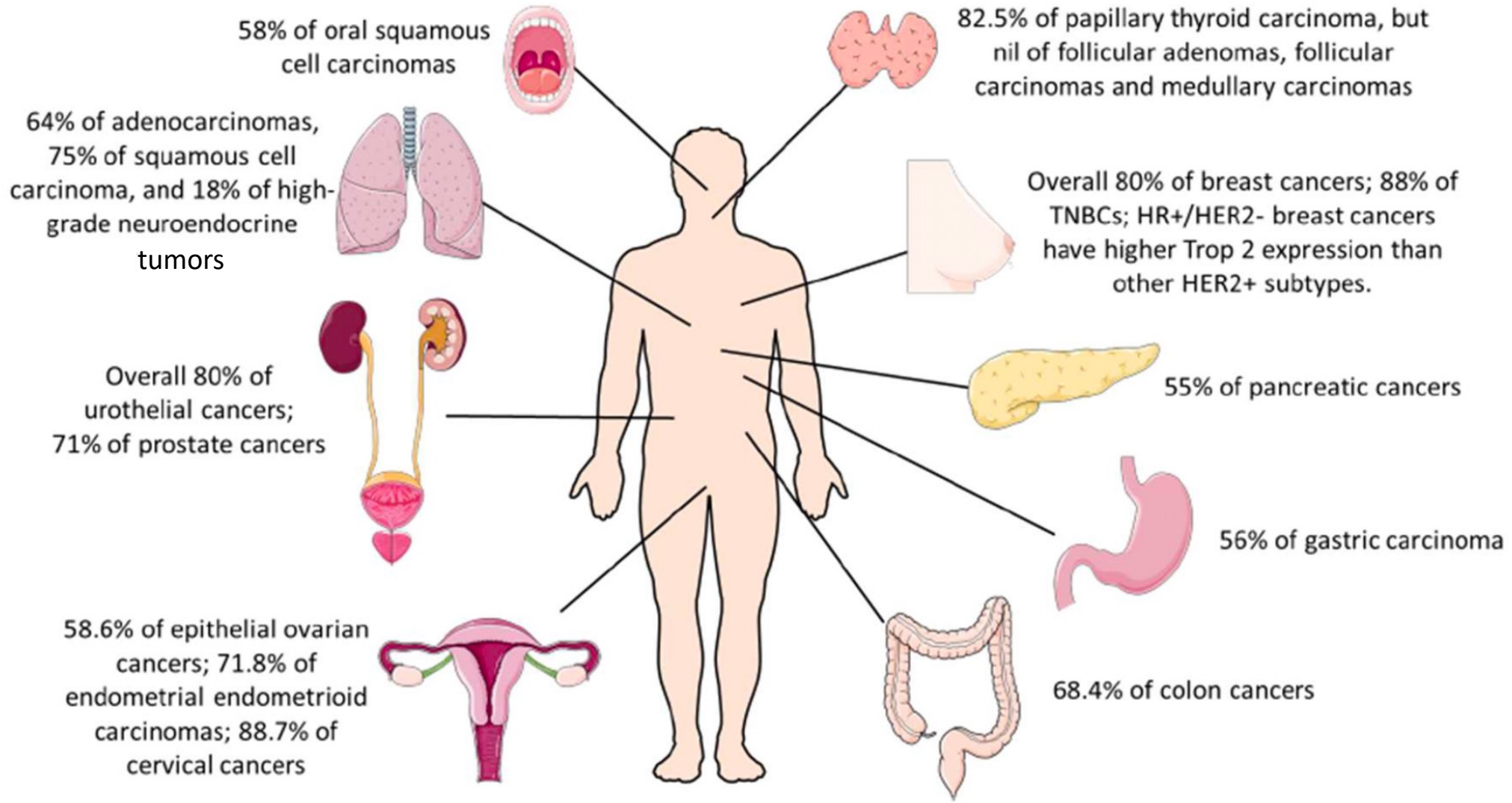
TROP2 is a transmembrane glycoprotein overexpressed in many solid tumors[1]

TNBC and NSCLC are associated with TROP2 overexpression

TROP2 is an epithelial adhesion molecule and stem cell marker associated with cell regeneration



Courtesy of Alexander I Spira, MD, PhD



http://proteinatlas.org (11/2022)

Courtesy of Alexander I Spira, MD, PhD

TROPION-PanTumor01: Updated Results From the NSCLC Cohort of the Phase 1 Study of Datopotamab Deruxtecan in Solid Tumors

Edward B. Garon,[1] Melissa Johnson,[2] Aaron E. Lisberg,[1] Alexander Spira,[3] Noboru Yamamoto,[4] Rebecca S. Heist,[5] Jacob M. Sands,[6] Kiyotaka Yoh,[7] Funda Meric-Bernstam,[8] Satoru Kitazono,[9] Jonathan Greenberg,[10] Fumiaki Kobayashi,[11] Ferdinand Guevara,[10] Yui Kawasaki,[11] Toshio Shimizu[4]

[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Sarah Cannon Research Institute, Tennessee Oncology, PLLC, OneOncology, Nashville, TN, USA; [3]Virginia Cancer Specialists and US Oncology Research, Fairfax, VA, USA; [4]National Cancer Center Hospital, Tokyo, Japan; [5]Massachusetts General Hospital, Boston, MA, USA; [6]Dana-Farber Cancer Institute, Boston, MA, USA; [7]National Cancer Center Hospital East, Chiba, Japan; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [9]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [10]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [11]Daiichi Sankyo Co, Ltd, Tokyo, Japan

IASLC 2021 World Conference on Lung Cancer
SEPTEMBER 8 - 14, 2021 I WORLDWIDE VIRTUAL EVENT

Courtesy of Alexander I Spira, MD, PhD

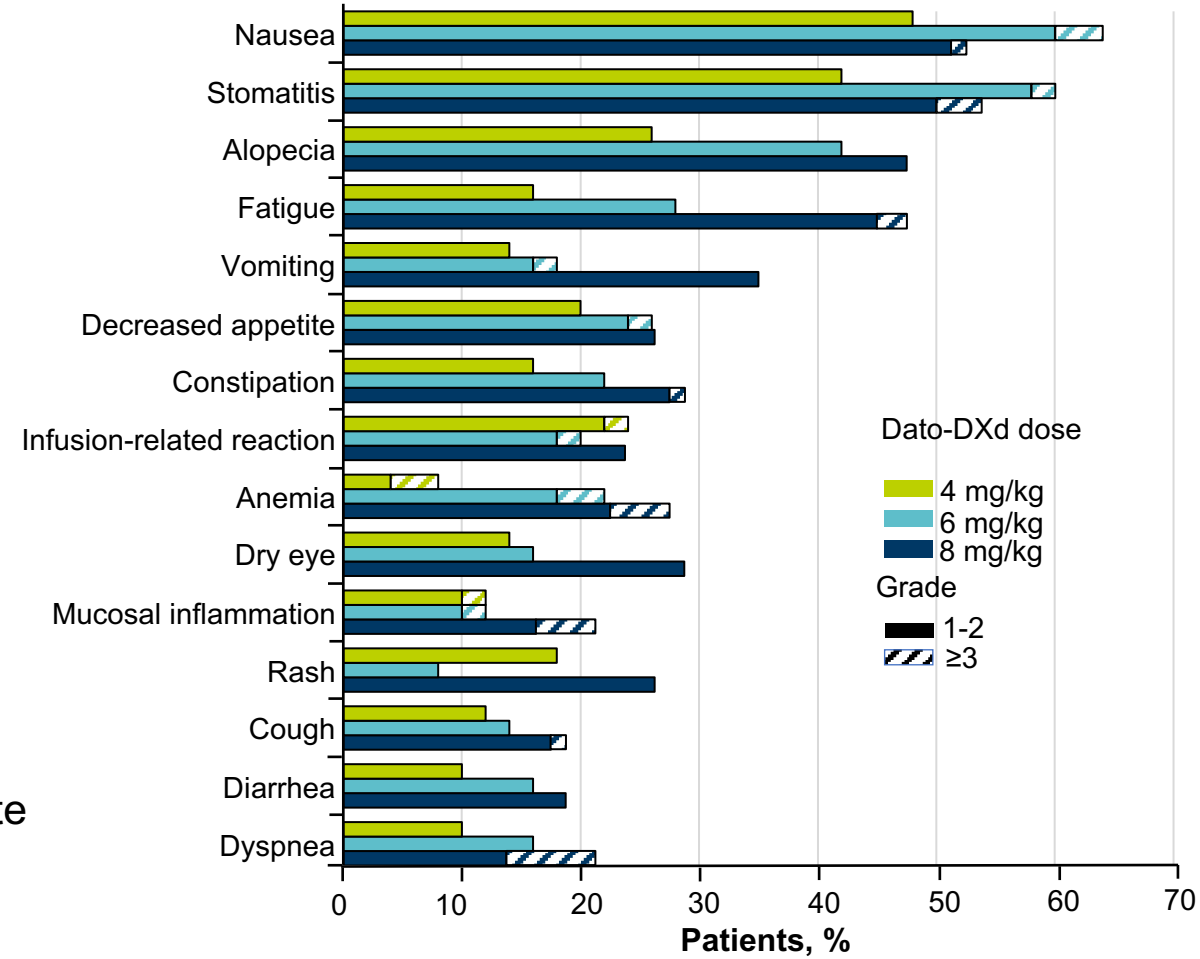
Safety

Overall Safety Summary

Patients, n (%)	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
TEAE	49 (98)	49 (98)	80 (100)
Grade ≥3	15 (30)	27 (54)	46 (58)
Drug-related TEAE	47 (94)	41 (82)	78 (98)
Grade ≥3	7 (14)	13 (26)	28 (35)
Serious TEAE	10 (20)	24 (48)	40 (50)
Grade ≥3	10 (20)	18 (36)	37 (46)
Dose adjustments			
TEAEs associated with discontinuation	8 (16)	7 (14)	19 (24)
TEAEs associated with dose interruption	4 (8)	15 (30)	29 (36)
TEAEs associated with dose reduction	1 (2)	5 (10)	23 (29)
ILD adjudicated as drug related[a]	5 (10)	3 (6)	11 (14)
Grade ≤2	4 (8)	2 (4)	7 (9)
Grades 3-4	1 (2)	1 (2)	1 (1)
Grade 5	0	0	3 (4)

- The safety profile was manageable with mainly mild/moderate toxicity; TEAEs were primarily nonhematologic

TEAEs in ≥15% of Patients[b]



Data cutoff: April 6, 2021.
ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.
[a] Cases of ILD adjudicated as drug related comprised 5 patients in the 4-mg/kg cohort (1 grade 1, 3 grade 2, 1 grade 3), 3 patients in the 6-mg/kg cohort (2 grade 2, 1 grade 4), and 11 patients in the 8-mg/kg cohort (2 grade 1, 5 grade 2, 1 grade 3, 3 grade 5). [b] Of 180 patients (4 mg/kg [n=50]; 6 mg/kg [n=50]; 8 mg/kg [n=80]).

Courtesy of Alexander I Spira, MD, PhD

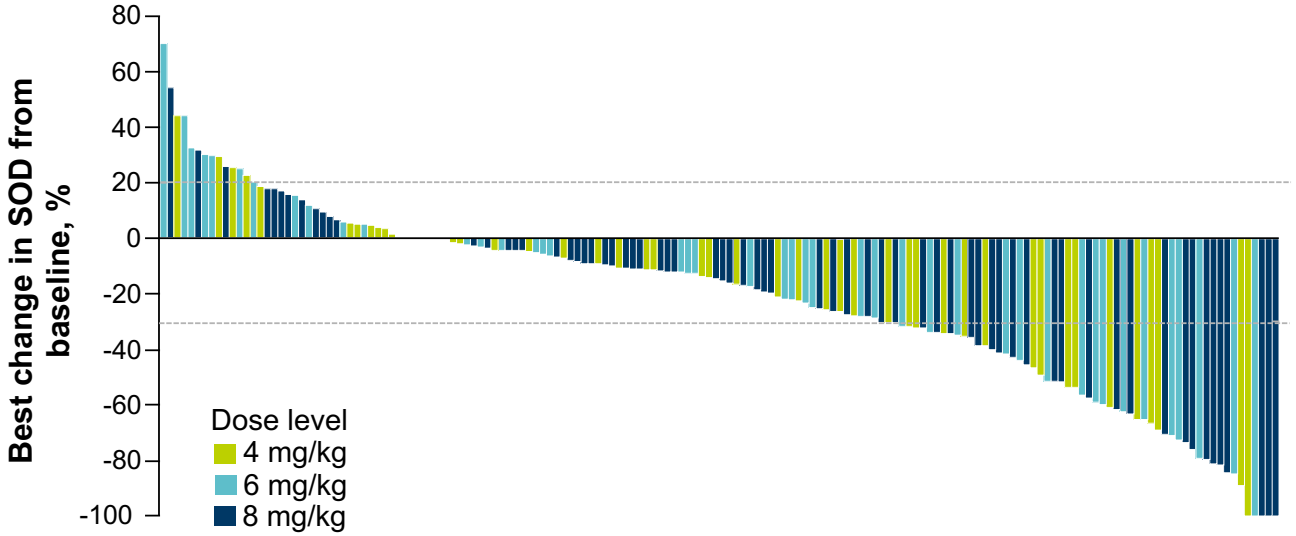
Antitumor Activity of Dato-DXd

Best Overall Response (BICR)

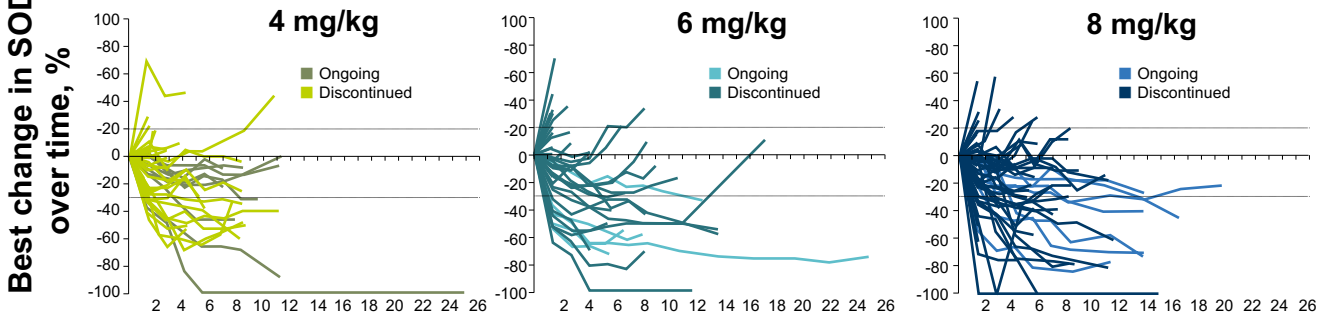
Patients[a]	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)[b]	12 (24)	14 (28)	19 (24)
CR, n (%)	0	0	1 (1)
PR, n (%)[b]	12 (24)	14 (28)	18 (23)
SD, n (%)	25 (50)	20 (40)	42 (53)
Non-CR/PD, n (%)	1 (2)	2 (4)	2 (3)
PD, n (%)	7 (14)	10 (20)	8 (10)
NE, n (%)	5 (10)	5 (10)	9 (11)
DOR, median (95% CI), mo	NE (2.8-NE)	10.5 (5.6-NE)	9.4 (5.8-NE)

- Antitumor activity was observed at 4-, 6-, and 8-mg/kg doses of Dato-DXd
- Most responses were durable over time, including a median duration of response of 10.5 months in the 6-mg/kg cohort

Best Change in Sum of Diameters (per BICR)



Change in Sum of Diameters of Target Lesion (per BICR) Over Time



Data cutoff: April 6, 2021.
BICR, blinded independent central review; CR, complete response; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SOD, sum of diameters; SD, stable disease.
[a] Includes response-evaluable patients who had ≥1 postbaseline tumor assessment or discontinued treatment. [b] ORR and CR/PR include 1 response in the 6-mg/kg cohort that is pending confirmation.

Courtesy of Alexander I Spira, MD, PhD

Tox Management of Dato DXd

TEAEs associated with dose reduction	1 (2)	5 (10)	23 (29)
ILD adjudicated as drug related[a]	5 (10)	3 (6)	11 (14)
Grade ≤2	4 (8)	2 (4)	7 (9)
Grades 3-4	1 (2)	1 (2)	1 (1)
Grade 5	0	0	3 (4)

Trastuzumab Deruxtecan-Induced Interstitial Lung Disease/Pneumonitis in ERBB2-Positive Advanced Solid Malignancies: A Systematic Review

Ziad Abuhelwa,[1] Abdurahman Alloghbi,[2,3] Ali Alqahtani,[4] and Misako Nagasaka[5,6]

Author information · Article notes · Copyright and License information Disclaimer

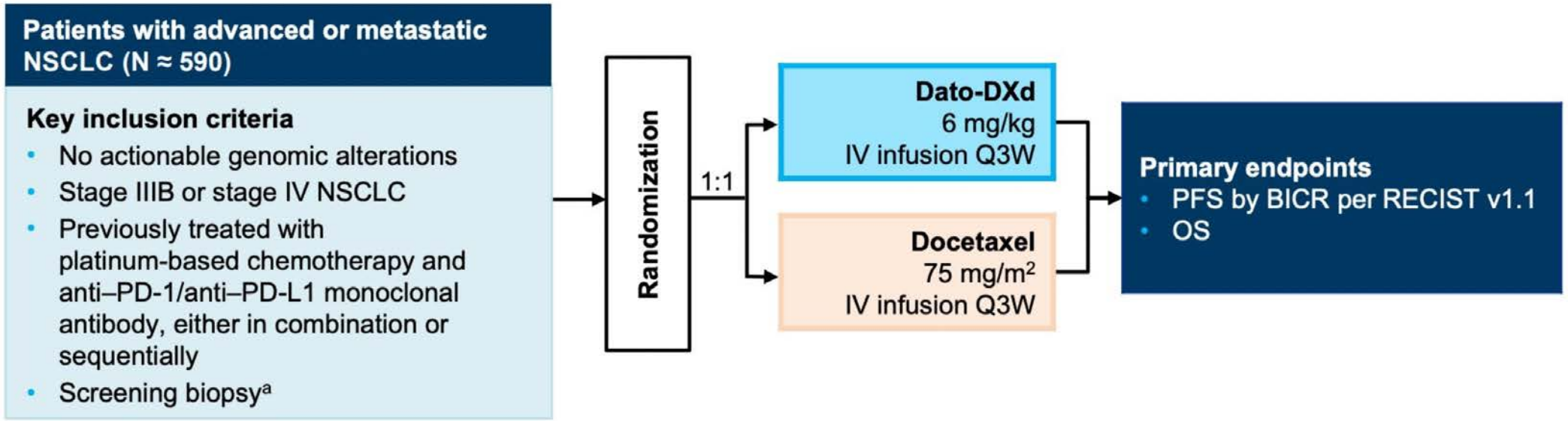
ILD: 11.5 % all comers
25% NSCLC
10% G5 Rate

Challenges: Recognition, Lack of Treatment and Improvement

Courtesy of Alexander I Spira, MD, PhD

Phase 3 TROPION-Lung01 (NCT04656652) Study Design

- This phase 3 study is open for enrollment



a cutoff: 4 September 2020.
date, no correlation between TROP2 expression and Dato-DXd clinical activity in NSCLC has been observed.
R, blinded independent central review; NSCLC, non–small cell lung cancer; OS, overall survival; PD-1, programmed cell death protein 1;
L1, programmed death ligand 1; PFS, progression-free survival; Q3W, once every 3 weeks; RECIST: Response Evaluation Criteria in Solid Tumors;
P2, trophoblast cell surface antigen 2.

Courtesy of Alexander I Spira, MD, PhD

TROPION-Lung02: Initial Results for Datopotamab Deruxtecan Plus Pembrolizumab and Platinum Chemotherapy in Advanced NSCLC

Benjamin Levy,[1] Luis Paz-Ares,[2] Olivier Rixe,[3,4] Wu-Chou Su,[5] Tsung-Ying Yang,[6] Anthony Tolcher,[7] Yanyan Lou,[8] Yoshitaka Zenke,[9] Panayiotis Savvides,[10] Enriqueta Felip,[11] Manuel Domine,[12] Konstantinos Leventakos,[13] Mariano Provencio Pulla,[14] Marianna Koczywas,[15] Atsushi Horiike,[16] Siddhartha Rawat,[4] Xiangfeng Wu,[4] Priyanka Basak,[4] Michael Chisamore,[17] Yasushi Goto[18]

[1]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Medicine, Baltimore, MD, USA; [2]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense & CiberOnc, Madrid, Spain; [3]Quantum Santa Fe, Santa Fe, NM, USA; [4]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [5]Department of Oncology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan [6]Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [7]NEXT Oncology, San Antonio, TX, USA; [8]Mayo Clinic, Jacksonville, FL, USA; [9]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [10]Mayo Clinic, Phoenix, AZ, USA; [11]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [12]Department of Oncology, Hospital Universitario Fundación Jiménez Díaz (IIS-FJD), Madrid, Spain; [13]Mayo Clinic, Rochester, MN, USA; [14]Department of Medical Oncology, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain; [15]Department of Medical Oncology & Therapeutic Research, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [16]Department of Thoracic Medical Oncology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]National Cancer Center Hospital, Tokyo, Japan

Courtesy of Alexander I Spira, MD, PhD

TROPION-Lung07 Phase III Trial Design

Estimated enrollment (N = 975)

Estimated primary completion: August 2027

- Previously untreated metastatic NSCLC or
- Stage IIIB or IIIC disease and not candidates for surgical resection or definitive chemoradiation therapy
- PD-L1 <50%

R

Dato-DXd + pembrolizumab + platinum chemotherapy

Dato-DXd + pembrolizumab

Pembrolizumab + pemetrexed + platinum chemotherapy

Primary endpoints: Progression-free and overall survival

www.clinicaltrials.gov. NCT05555732. Accessed November 2022.

RTP RESEARCH TO PRACTICE

Sacituzumab

- TROP2 ADC conjugated to irinotecan metabolite SN38
- Approved in US in bladder, TNBC
- D1, D8 q21D dosing
- Approx 20% RR in pretreated NSCLC (Heist et al 2017)
- Ongoing Ph III study (EVOKE1)

Courtesy of Alexander I Spira, MD, PhD

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

2021;32(6):746-56.

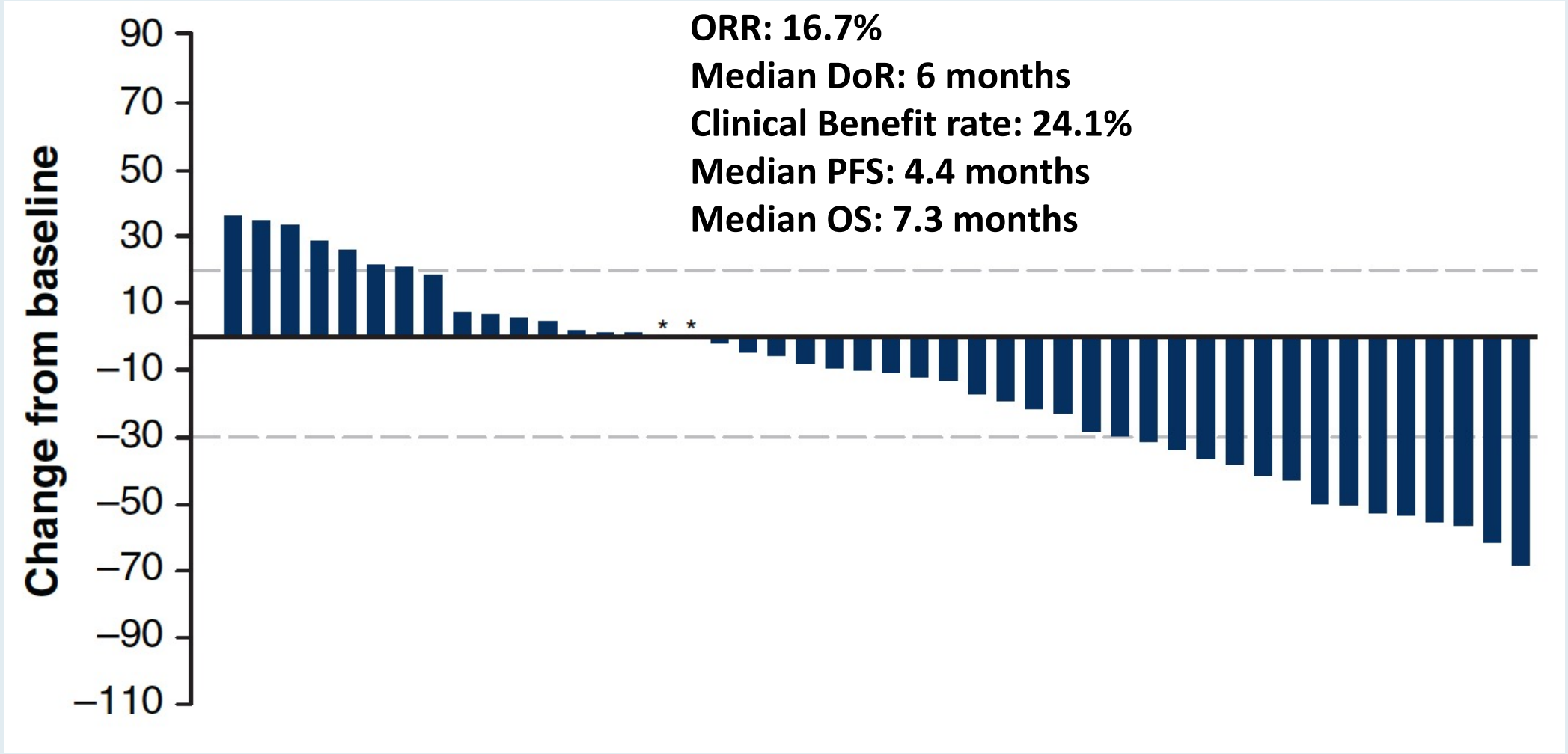
ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial

A. Bardia[1], W. A. Messersmith[2], E. A. Kio[3], J. D. Berlin[4], L. Vahdat[5†], G. A. Masters[6], R. Moroose[7], A. D. Santin[8], K. Kalinsky[9‡], V. Picozzi[10], J. O'Shaughnessy[11], J. E. Gray[12], T. Komiya[13], J. M. Lang[14], J. C. Chang[15], A. Starodub[16], D. M. Goldenberg[17§], R. M. Sharkey[17], P. Maliakal[17‖], Q. Hong[17], W. A. Wegener[17], T. Goswami[17] & A. J. Ocean[5*]

Phase I/II IMMU-132-01 Trial of Sacituzumab Govitecan: Efficacy in the Metastatic NSCLC Population



ORR = objective response rate; DoR = duration of response; PFS = progression-free survival; OS = overall survival

Bardia A et al. *Ann Oncol* 2021;32(6):746-56.

RTP RESEARCH TO PRACTICE

Key Ongoing Clinical Trials of Sacituzumab Govitecan for Metastatic NSCLC

Study (N)	Phase	Setting	Treatment	Est completion date
EVOKE-01 (N = 520)	III	• Metastatic NSCLC • Progression after platinum and CIP therapies • ≥1 previous targeted treatment for actionable alterations	• Sacituzumab govitecan • Docetaxel	May 2024
MK-3475-D46 (N = 614)	III	• Metastatic NSCLC • Previously untreated • PD-L1 ≥ 50%	• Sacituzumab govitecan • Pembrolizumab	January 2027
EVOKE-02 (N = 164)	II	• Metastatic NSCLC • Previously untreated • No actionable mutations	• Sacituzumab govitecan + pembrolizumab • Sacituzumab govitecan + pembrolizumab + carboplatin	May 2023

Garassino MC et al. ASCO 2022;Abstract TPS9149; Garon EB et al. ASCO 2022; Abstract TPS9146; www.clinicaltrials.gov. Accessed November 2022.

Where are we going?

- 2nd line ”approval” studies for Docetaxel (same old story)
- 1st line combos ?
  - Will this be better than Keynote 189 (carbo/pem/pembro)?
  - Will this be better tolerated than Keynote 189?
- NSCLC with actionable mutations (ph 2 studies completed)
- Concerns with ILD

Courtesy of Alexander I Spira, MD, PhD

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

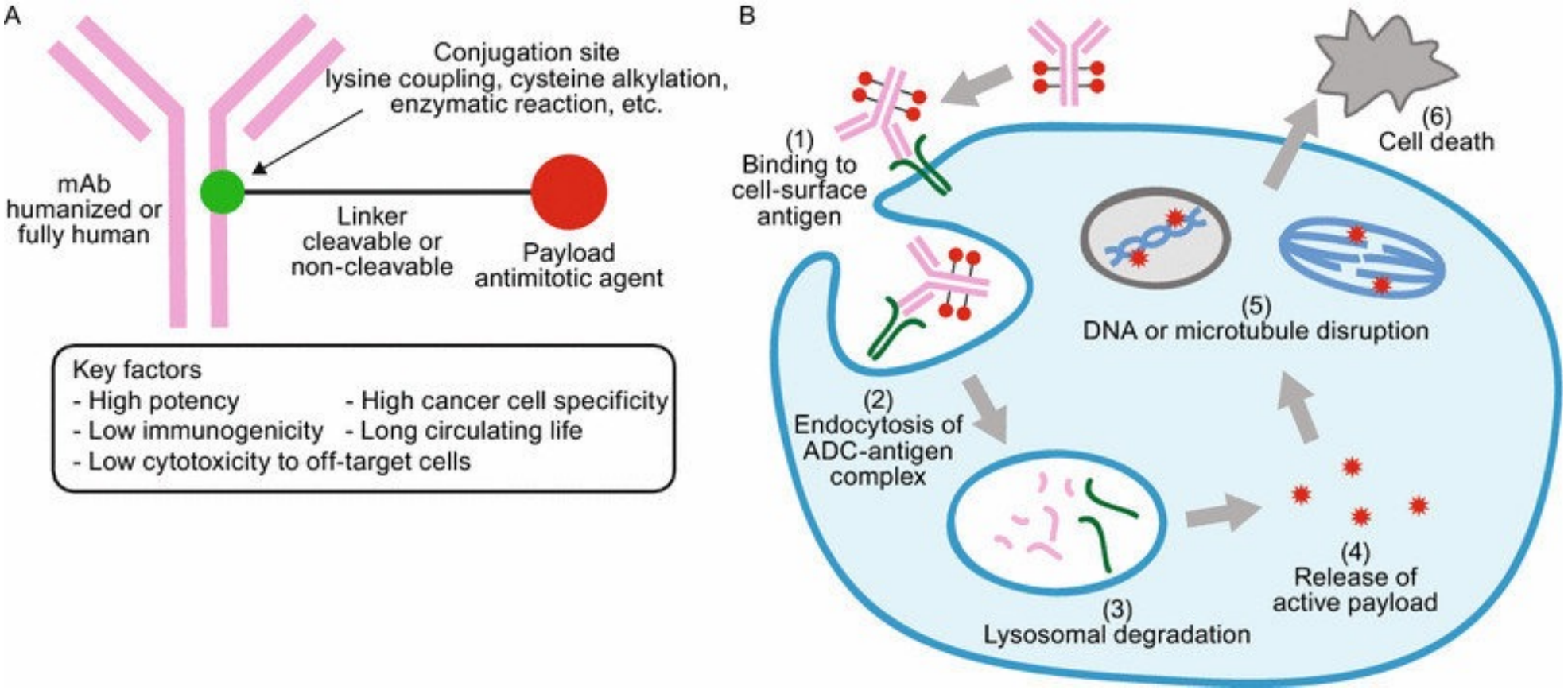
- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

Other ADCs

- How many combinations can we make ?



Courtesy of Alexander I Spira, MD, PhD

Other ADCs

- Tusamitamab ravtansine
  - Anti CEACAM5 ADC

- Telisotuzumab vedotin (Telo V)
  - Anti c-met ADC
  - C met overexpressing cancers (NSCLC)
  - C met overexpressing EGFR-m NSCLC

Courtesy of Alexander I Spira, MD, PhD

Agenda

INTRODUCTION: What is an antibody-drug conjugate (ADC)?

MODULE 1: "HER2-positive" NSCLC

- Clinical and pathological phenotypes; current and future role of trastuzumab deruxtecan
- Dr Yu: 55-year-old woman with HER2 insertion in exon 20

MODULE 2: Targeting HER3 in NSCLC

- Biologic rationale and clinical role of patritumab deruxtecan
- Dr Yu: 63-year-old man with EGFR-mutant lung cancer

MODULE 3: TROP2-directed treatment

- Biologic rationale and clinical role of datopotamab deruxtecan and sacituzumab govitecan
- Dr Spira: 52-year-old woman with KRAS G12V-mutant lung cancer
- Dr Spira: 65-year-old woman with metastatic NSCLC and an EGFR exon 19 deletion

MODULE 4: Novel agents

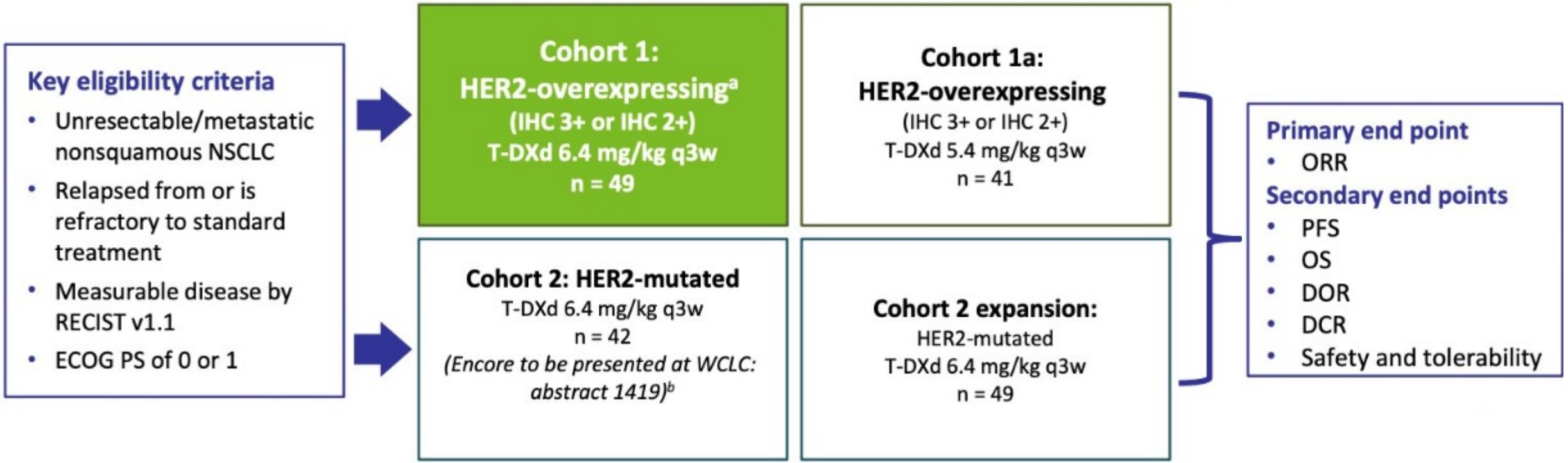
- Mechanism of action of tusamitamab ravtansine and telisotuzumab vedotin

MODULE 5: Appendix

RTP RESEARCH TO PRACTICE

HER2-directed treatments

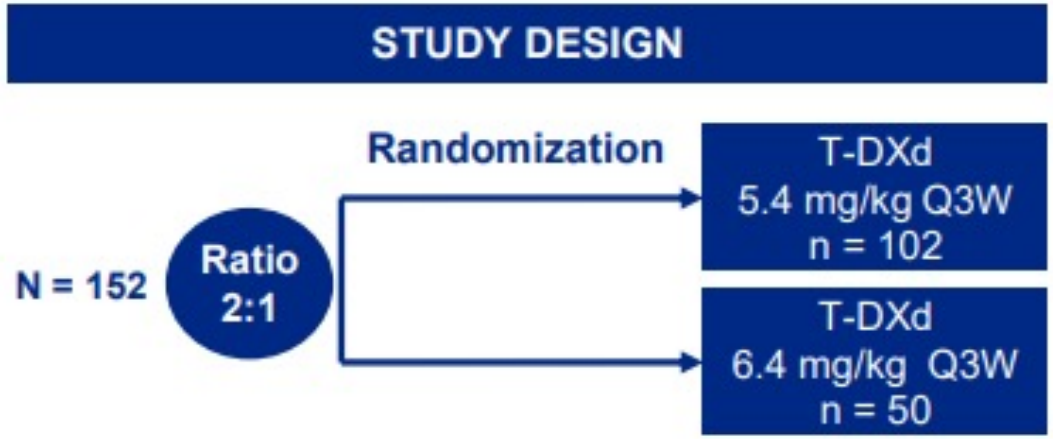
DESTINY-Lung01 study



Nakagawa WCLC 2020

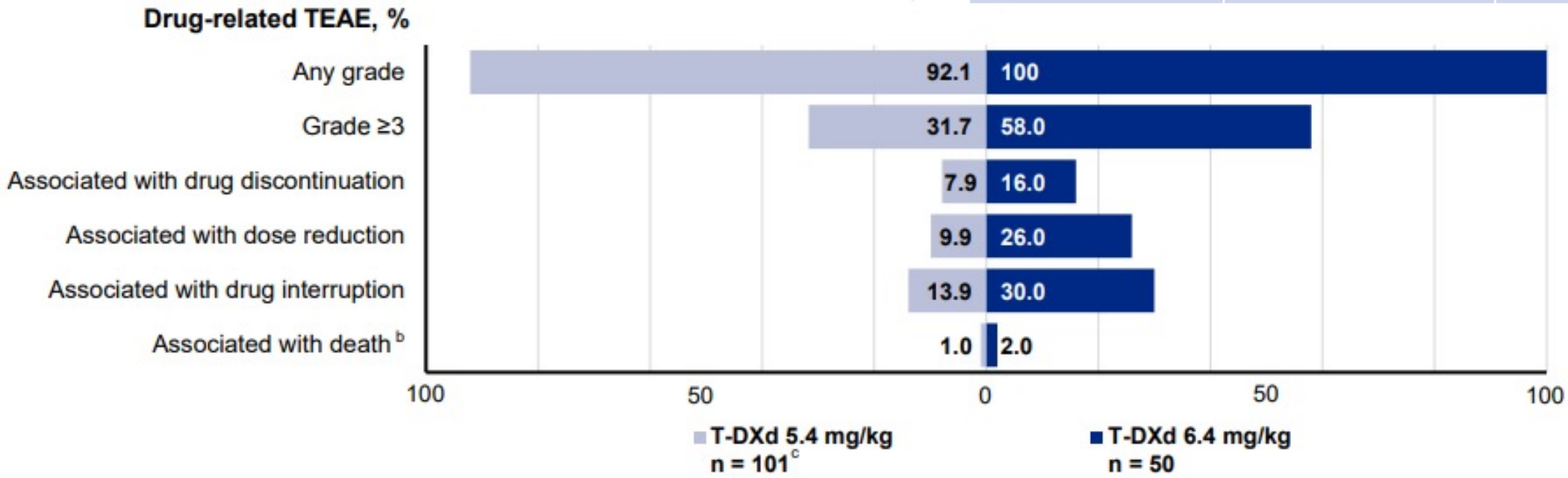
Courtesy of Helena Yu, MD

DESTINY-Lung02 – HER2 mutant



	TDXd 5.4mg/kg N=52	TDXd 6.4mg/kg n-=28
ORR	53.8%	42.9%

	TDXd 5.4mg/kg N=101	TDXd 6.4mg/kg n-=50
ILD (any grade)	5.9%	14.0%



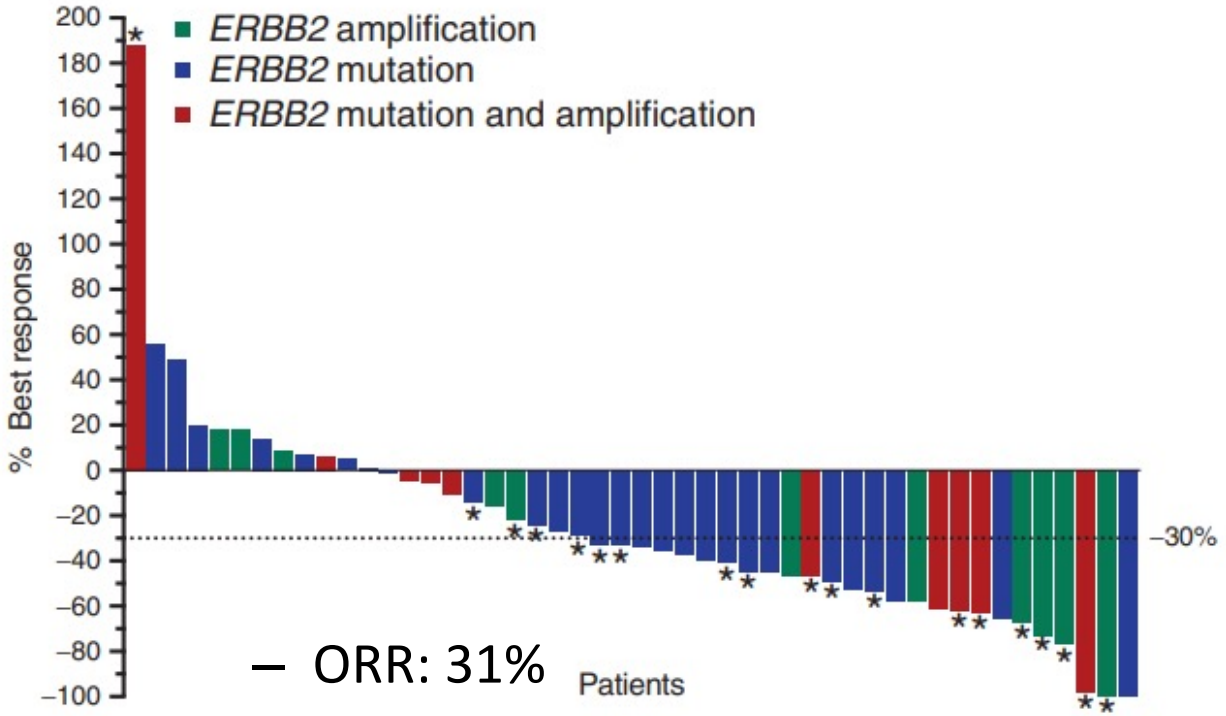
FDA approval of T-DXd at 5.4mg/kg

Goto ESMO 2022

Courtesy of Helena Yu, MD

Other HER2 targeting agents

T-DM1 (Trastuzumab emtansine)



- ORR: 31%
- RECIST/PERCIST: 51%
- Median PFS: 5 mos

PERCIST ORR similar for HER2 amplified (55%), mutant (50%), both (50%)

Trastuzumab + docetaxel

Table 3 HER2 Overexpression by Immunohistochemistry

Immunohistochemistry Score	Number of Patients
0	30
1+	13
2+	9
3+	4
Not assessable/inadequate tissue	13

HER 2 amplification by FISH 2/12 pos

N=13 with 2 or 3+ HER IHC
ORR 8%
mPFS 4.3mo, mOS 5.7mo

Why the differences in efficacy?

- Naked antibody limited efficacy
- T-DM1 and T-DXd different payloads
- Different therapeutic indexes? Bystander effect?

Li Canc Disc 2020, Lara Clinical Lung Cancer 2004

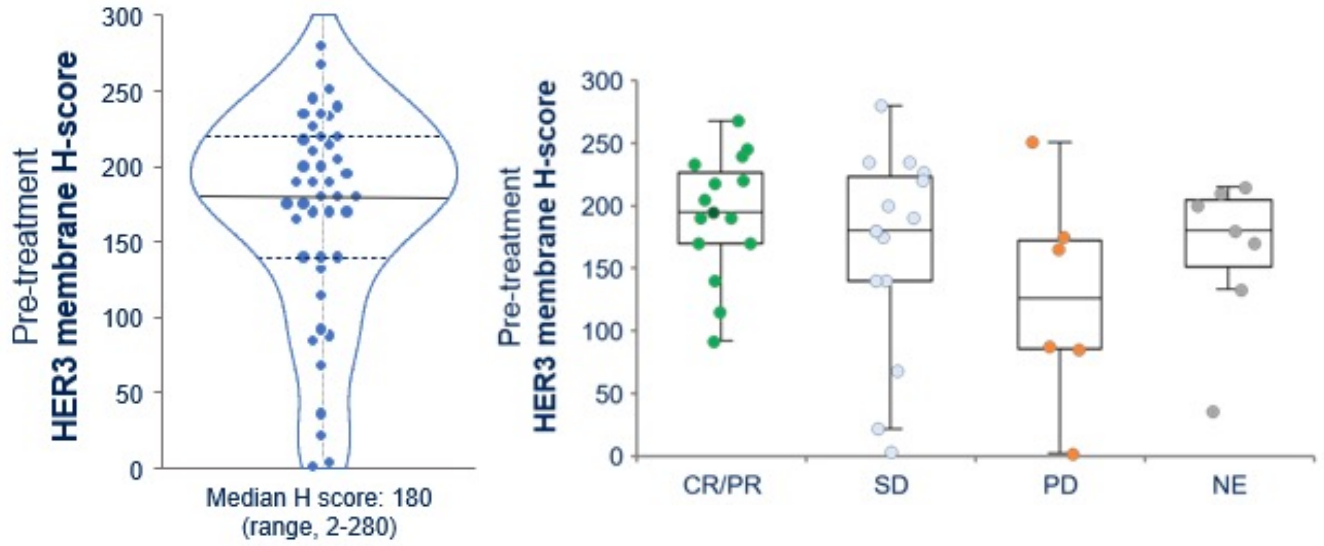
Courtesy of Helena Yu, MD

HER3-directed treatments

Patritumab Deruxtecan

TEAEs	Pooled RDE 5.6 mg/kg (*n* = 57), *n* (%)
Any TEAE	57 (100)
Grade ≥3 TEAEs	42 (74)
Serious TEAEs	25 (44)
TEAEs associated with treatment discontinuation	6 (11)[a]
TEAEs associated with dose reduction	12 (21)
TEAEs associated with dose interruption	21 (37)
TEAEs associated with death	4 (7)[c]
Treatment-related TEAEs	55 (96)
Grade ≥3 treatment-related TEAEs	31 (54)
Treatment-related TEAEs associated with death	0
Serious treatment-related TEAEs	12 (21)
Grade ≥3 TEAEs occurring in ≥5% of patients	
Platelet count decrease/thrombocytopenia	17 (30)
Neutrophil count decrease/neutropenia	11 (19)
Fatigue	8 (14)
Anemia/hemoglobin decrease	5 (9)
Dyspnea	5 (9)
Febrile neutropenia	5 (9)
Hypoxia	4 (7)
White blood cell count decrease/leukopenia	4 (7)
Hypokalemia	3 (5)
Lymphocyte count decrease/lymphopenia	3 (5)
Adjudicated ILD	5 (9)[e]
Adjudicated treatment-related ILD	4 (7)[f]

- 11% treatment related discontinuation, 21% dose reduction
- Thrombocytopenia/neutropenia relatively common
- 7% treatment related ILD



- HER3 was expressed in all evaluable patients (43/57 on study)
- HER3 expression was not correlated with time of last EGFR TKI dose
- Responses were observed in patients with a range of HER3 expression
- HER3 expression levels did not clearly distinguish responders vs non-responders
- Unclear what will be the appropriate biomarker for HER3-directed treatment

Courtesy of Helena Yu, MD

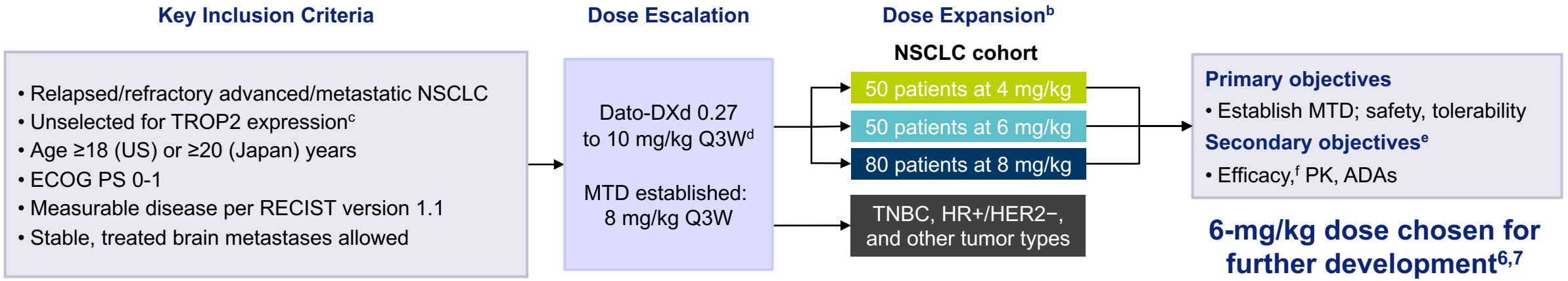
Janne Canc Disc 2022

TROP2-directed treatments

Introduction and Methods

- Patients with advanced or metastatic NSCLC represent a high unmet need[1]
- TROP2 is highly expressed in NSCLC and has been associated with poor prognosis[2-4]
- Datopotamab deruxtecan (Dato-DXd) is an antibody drug conjugate composed of a humanized anti-TROP2 monoclonal antibody conjugated to a potent topoisomerase I inhibitor payload via a stable tetrapeptide-based cleavable linker; this enables a bystander tumor effect resulting in elimination of both target tumor cells and surrounding cells[5,6]
- Previous results from the TROPION-PanTumor01 first-in-human study of Dato-DXd (NCT03401385) demonstrated highly encouraging antitumor activity with a manageable safety profile in patients with NSCLC.[6,7] Here we present updated results from the NSCLC cohort, with a data cutoff of April 6, 2021[a]

TROPION-PanTumor01 Study Design



ADA, antidrug antibody; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PK, pharmacokinetics; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TNBC, triple-negative breast cancer; TROP2, trophoblast cell-surface antigen 2.

[a] This analysis in the NSCLC cohort was performed 6 months after the last patient received their first dose of study drug on October 6, 2020. [b] Includes patients treated in the dose-escalation and dose-expansion portions. [c] Pretreatment tumor tissue was required for retrospective analysis of TROP2 expression. [d] The 4-, 6-, and 8-mg/kg dose levels are being further evaluated for safety and efficacy. [e] Additional exploratory objectives include analyses of biomarkers associated with response. [f] Response assessments are based on RECIST v1.1.

1. Simeone JC, et al. *Future Oncol.* 2019;15(30):3491-3502. 2. Mito R, et al. *Pathol Int.* 2020;70(5):287-294. 3. Inamura K, et al. *Oncotarget.* 2017;8(17):28725-28735. 4. Jiang A, et al. *Oncol Lett.* 2013;6(2):375-380. 5. Okajima D, et al. AACR-NCI-EORTC 2019. Abstract C026. 6. Meric-Bernstam F, et al. ASCO 2021. Abstract 9058. 7. Spira A, et al. WCLC 2020. Abstract 3407.

Baseline Characteristics and Patient Disposition

Characteristic	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
Age, median (range), years	61 (35-82)	63 (38-76)	64 (31-84)
Age ≥65 years, %	36	40	46
Weight, median (range), kg	72 (38-156)	66 (39-104)	70 (38-115)
Male, %	54	56	51
Country, %			
United States	58	76	79
Japan	42	24	21
Histology, %			
Nonsquamous	82	90	88
Squamous	18	10	13
≥3 Prior lines of therapy, %	54	62	64
Previous systemic treatment, %			
Immunotherapy	88	74	88
Platinum-based chemotherapy	96	96	98
Tyrosine kinase inhibitor	20	18	19
***EGFR* mutations, %**	14	16	19
History of brain metastases, %	36	34	41

Treatment status	Dato-DXd dose		
	4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
Ongoing study treatment, n (%)[a]	9 (18)	5 (10)	7 (9)
Discontinued from study treatment, n (%)	41 (82)	45 (90)	73 (91)
Progression[b]	31 (62)	34 (68)	43 (54)
Adverse events	8 (16)	6 (12)	20 (25)
Death	0	1 (2)	1 (1)
Other[c]	2 (4)	4 (8)	9 (11)
Duration on study, median (range), mo	12.1 (7-29)	9.5 (6-27)	16.8 (10-25)
Exposure, median (range), mo	4.1 (0.7-27.6)	3.5 (0.7-26.2)	3.3 (0.7-20.4)

- Patients were heavily pretreated, with 74%-88% having received prior immunotherapy and 96%-98% having received prior platinum-based chemotherapy across dose cohorts

Data cutoff: April 6, 2021.
EGFR, epidermal growth factor receptor.
[a] Due to a later time of enrollment, follow-up was shorter for patients treated with the 4- and 6-mg/kg doses than for those treated with the 8-mg/kg dose. [b] Includes progressive disease per RECIST v1.1 and clinical progression. [c] Includes physician decision, withdrawal by subject, and other.

Courtesy of Alexander I Spira, MD, PhD

Summary

- In the updated data cutoff for the NSCLC cohort, Dato-DXd continued to demonstrate highly encouraging antitumor activity and a manageable safety profile at the 4-, 6-, and 8-mg/kg doses in this heavily pretreated population
- The 6-mg/kg dose has been selected for further development
  - The 6-mg/kg dose was better tolerated than the 8-mg/kg dose, with low rates of discontinuation due to adverse events
  - 28% of patients achieved an ORR, and the median DOR was 10.5 months
- TROPION-PanTumor01 is also investigating Dato-DXd in other tumor types. Promising antitumor activity and a similar safety profile have been observed in the TNBC cohort[1]
- Dato-DXd is currently being evaluated in the phase 3 TROPION-Lung01 trial (NCT04656652)[2] and additional phase 1 and 2 trials in NSCLC[3-5]

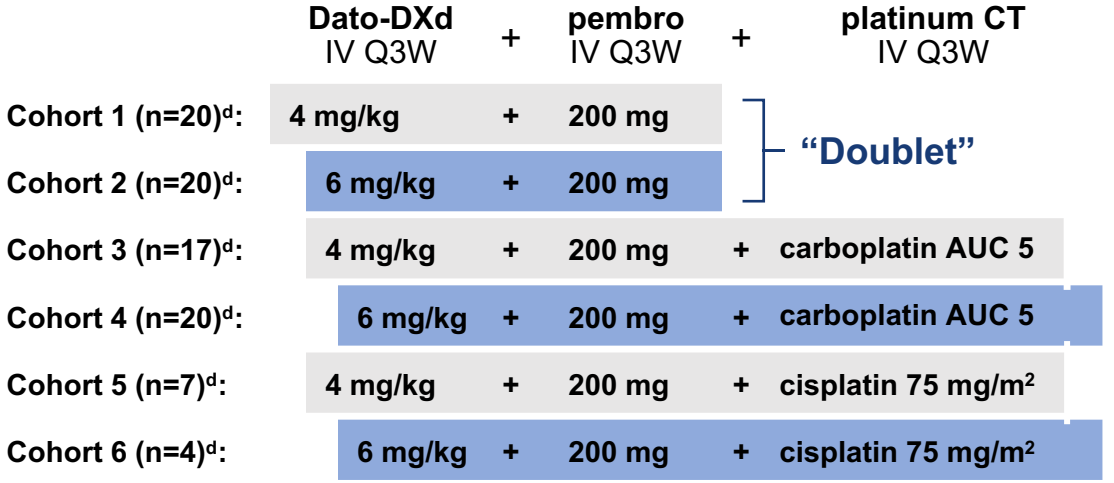
1. Bardia A, et al. ESMO Breast Cancer 2021. Abstract LBA4. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04656652. 3. Levy B, et al. WCLC 2021. Abstract 564. 4. Borghaei H, et al. WCLC 2021. Abstract 588. 5. Johnson M, et al. WCLC 2021. Abstract 653.

Background

- Dato-DXd is an ADC composed of a humanized TROP2 IgG1 mAb covalently linked to a topoisomerase I inhibitor payload via a stable tetrapeptide-based cleavable linker
- TROPION-Lung02 is a phase 1b study evaluating Dato-DXd + pembrolizumab (pembro) ± platinum CT[a] in advanced NSCLC without actionable genomic alterations (NCT04526691)
- Study approach: safety of Dato-DXd + pembro "doublets" was established prior to evaluation of platinum-containing "triplets"
  - Safety of Dato-DXd 4-mg/kg combinations was established prior to evaluation of 6-mg/kg combinations

Key eligibility

- Advanced/metastatic NSCLC
- Dose confirmation[b]: ≤2 lines of prior therapy[c]
- Dose expansion
  - ≤1 line of platinum-based CT (cohorts 1 and 2)[c]
  - No prior therapy (cohorts 3-6)[c]



- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and anti-drug antibodies

ADC, antibody-drug conjugate; AUC, area under the curve; CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DLT, dose-limiting toxicity; IgG1, immunoglobulin G1; IV, intravenous; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; pembro, pembrolizumab; Q3W, every 3 weeks; TROP2, trophoblast cell-surface antigen 2.
[a] Administered sequentially at the same visit. [b] The first 3-6 patients in each cohort were enrolled to confirm acceptable safety/DLT rate; the remaining patients are considered part of "dose expansion" (for which enrollment was ongoing at time of data cutoff). [c] Prior therapy requirements are for treatment in the advanced/metastatic setting. [d] As of the May 2, 2022, data cutoff.

Courtesy of Alexander I Spira, MD, PhD

Baseline Characteristics and Patient Disposition

Characteristic		Doublet (n=40)	Triplet (n=48)
Age, median (range), years		68 (44-77)	64 (33-84)
Male, n (%)		28 (70%)	33 (69%)
Histology, n (%)[a]	Non-squamous	28 (70%)	41 (85%)
	Squamous	11 (28%)	7 (15%)
History of brain metastases, n (%)		8 (20%)	10 (21%)
PD-L1 expression, n (%)[b]	<1%	13 (33%)	21 (44%)
	1-49%	13 (33%)	14 (29%)
	≥50%	12 (30%)	11 (23%)
Prior lines of therapy, median[c]		1	0
Previous systemic treatment, n (%)	Immunotherapy	12 (30%)	18 (38%)
	Platinum CT	24 (60%)	17 (35%)
Dato-DXd combination line of therapy, n (%)	1L	13 (33%)[d]	30 (63%)[d]
	2L+	27 (68%)[d]	18 (38%)[d]

At the time of data cutoff for doublet and triplet therapy, respectively:

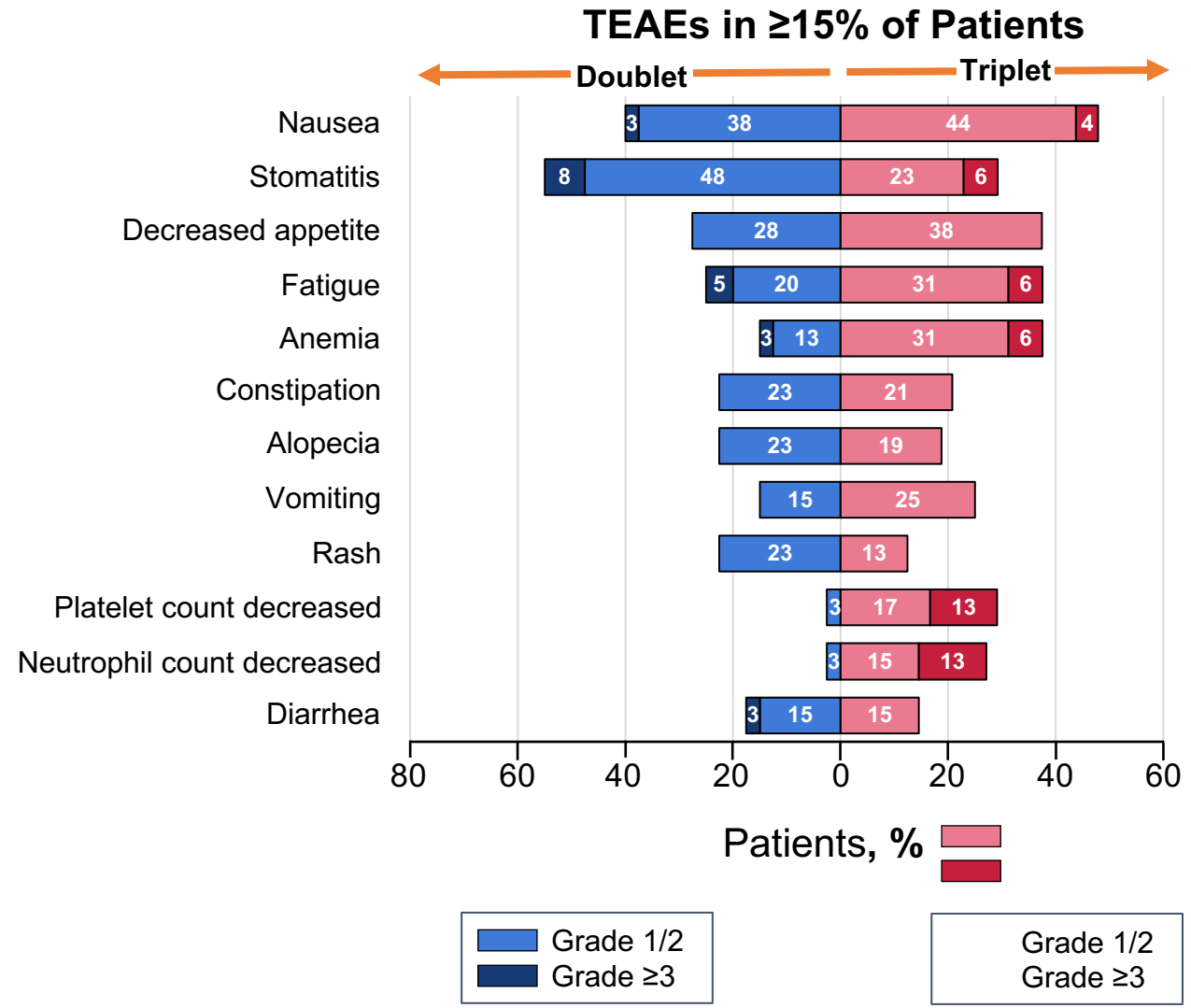
- Study treatment was ongoing in 53% and 77% of patients
- Median treatment duration was 4.1 months and 3.0 months
- Median follow-up was 6.5 months and 4.4 months

Data cutoff: May 2, 2022.
1L, first line; 2L, second line; PD-L1, programmed cell death 1 ligand 1.
[a] One patient (3%) received doublet therapy and had unknown histology. [b] PD-L1 expression was unknown in 2 patients (5%) receiving doublet therapy and 2 patients (4%) receiving triplet therapy. [c] Prior therapy for advanced/metastatic disease. [d] Percentages totaling >100% are due to rounding.

Courtesy of Alexander I Spira, MD, PhD

Safety

Events, n (%)	Doublet (n=40)	Triplet (n=48)
TEAEs	37 (93%)	47 (98%)
Study treatment-related[a]	33 (83%)	46 (96%)
Grade ≥3 TEAEs	16 (40%)	29 (60%)
Study treatment-related[a]	14 (35%)	26 (54%)
Serious TEAEs	9 (23%)	13 (27%)
Study treatment-related	4 (10%)	7 (15%)
TEAEs associated with		
Death[b]	2 (5%)	1 (2%)
Discontinuation due to any drug	9 (22%)	9 (19%)
Discontinuation due to Dato-DXd	6 (15%)	5 (10%)
ILD adjudicated as drug related[c]		
Grade 1/2	2 (5%)	0
Grade 3	1 (3%)	1 (2%)



Data cutoff: May 2, 2022.
ILD, interstitial lung disease. TEAE, treatment emergent adverse event.
[a] Drug related TEAEs may be associated with any component of the study treatment: Dato-DXd, pembro, cisplatin, or carboplatin. [b] TEAEs associated with death (encephalopathy, respiratory failure, and death) were considered unrelated to study treatment. [c] Three ILD cases (1 grade 1, 1 grade 3, and 1 grade 5), are pending adjudication.

Courtesy of Alexander I Spira, MD, PhD

Antitumor Activity

In the overall population:

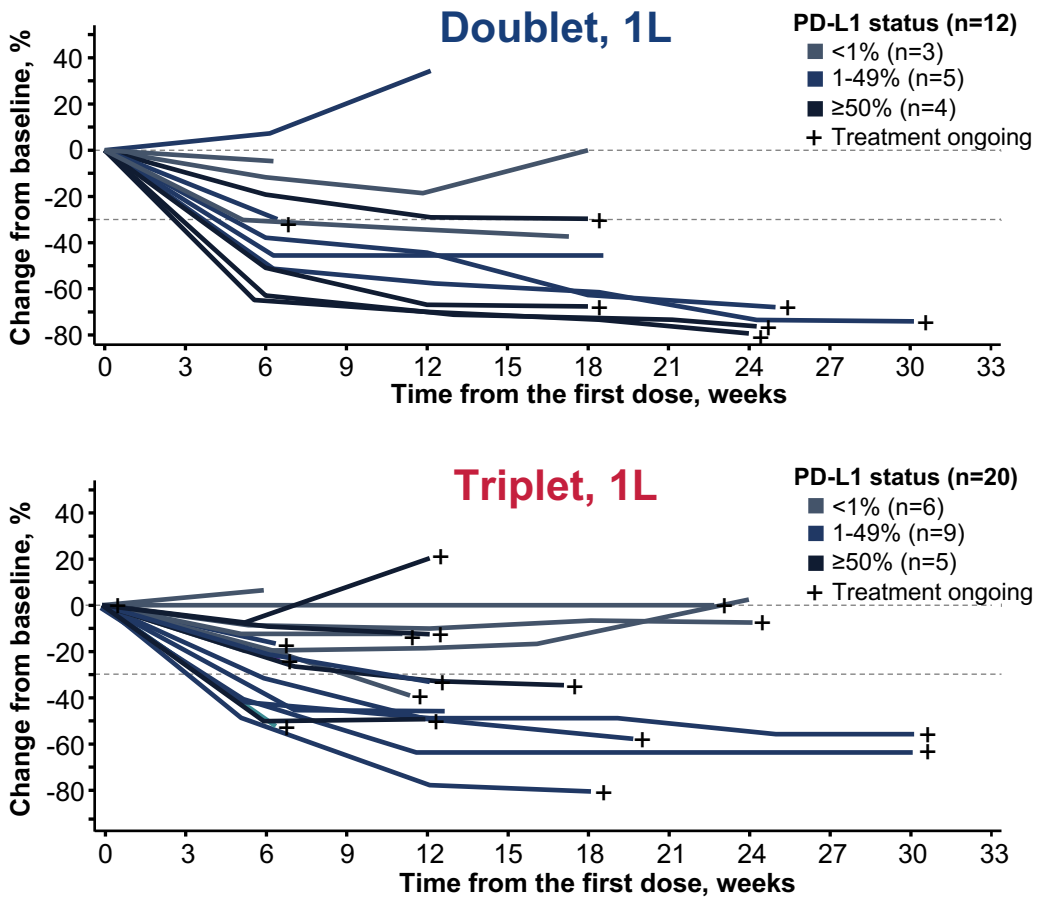
ORRs (confirmed + pending) of 37% and 41% were seen with doublet (n=38) and triplet (n=37) therapy, respectively; both groups had 84% DCR

BOR With 1L Therapy For Advanced NSCLC[a,b]

Response, n (%)	Doublet (n=13)	Triplet (n=20)
ORR confirmed + pending	**8 (62%)**	**10 (50%)**
CR	0	0
PR confirmed	8 (62%)	7 (35%)
PR pending	0	3 (15%)
SD	5 (39%)	8 (40%)
DCR	13 (100%)	18 (90%)

- As 1L therapy, the doublet and triplet yielded ORRs (confirmed + pending) of 62% and 50%, respectively
- As 2L+ therapy, respective ORRs (confirmed + pending) were 24% and 29%

Percent Change in Sum of Diameters[a]



Data cutoff: May 2, 2022.
BOR, best overall response; CR, complete response; DCR, disease control rate; ORR, overall response rate; PR, partial response; SD, stable disease.
[a] By investigator. [b] BOR is based on response evaluable patients who have ≥1 postbaseline tumor assessment or discontinued.

Courtesy of Alexander I Spira, MD, PhD

Summary

- This first reported clinical experience of a TROP2 ADC + a checkpoint inhibitor ± platinum CT in metastatic NSCLC demonstrated a tolerable safety profile and supported further evaluation of the 6-mg/kg dose of Dato-DXd in immunotherapy combination regimens[a]
- Stomatitis and nausea, mostly grade 1/2, were the most frequent TEAEs in patients receiving doublet and triplet therapy, respectively
- Interim efficacy results in the overall population and in patients receiving 1L therapy are encouraging
  - Responses were observed across all PD-L1 expression levels
  - The study is ongoing, and additional analyses with longer follow-up and more patients are pending
- The phase 3 TROPION-Lung08 trial (NCT05215340) is evaluating Dato-DXd + pembro vs pembro alone as 1L therapy in advanced/metastatic NSCLC with PD-L1 TPS >50%[1]

TPS, tumor proportion score.
[a] The Dato-DXd 6-mg/kg dose is also being evaluated as monotherapy in ongoing, global, phase 3 studies.
1. Levy B, et al. Poster presented at: American Society for Clinical Oncology; June 3-7, 2022. Abstract TPS3162.

Courtesy of Alexander I Spira, MD, PhD

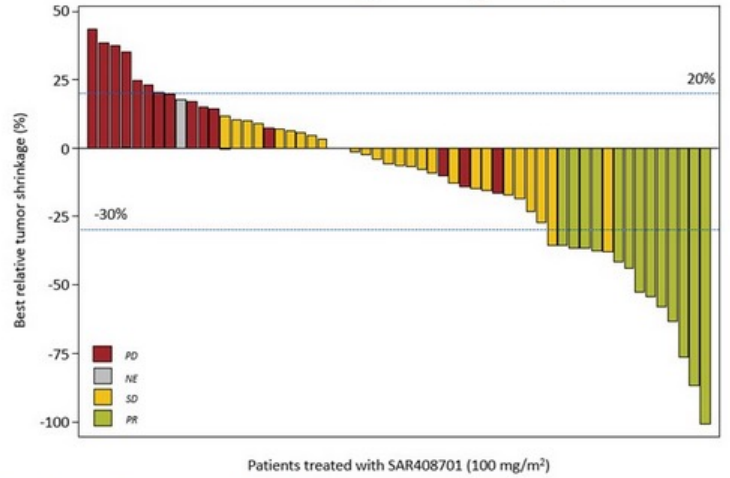
Novel ADCs

Best Overall Response with Tusamitamab Ravtansine in a Phase I/II Study for Patients with Nonsquamous NSCLC Expressing CEACAM5

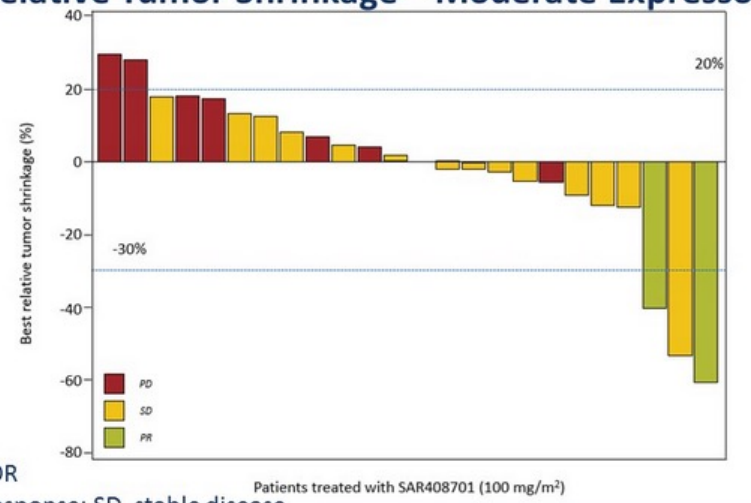
Overall Population

Response, n (%)	High expressors (n = 64)	Moderate expressors (n = 28)
ORR [95% CI]	13 (20.3%) [12.27-31.71]	2 (7.1%) [1.98-22.65]
Confirmed PR	13 (20.3%)	2 (7.1%)
SD	28 (43.8%)	15 (53.6%)
DCR	41 (64.1%)	17 (60.7%)
PD	21 (32.8%)	10 (35.7%)
NE	2 (3.1%)	1 (3.6%)

Best relative tumor shrinkage – High Expressor Cohort



Best Relative Tumor Shrinkage – Moderate Expressor Cohort

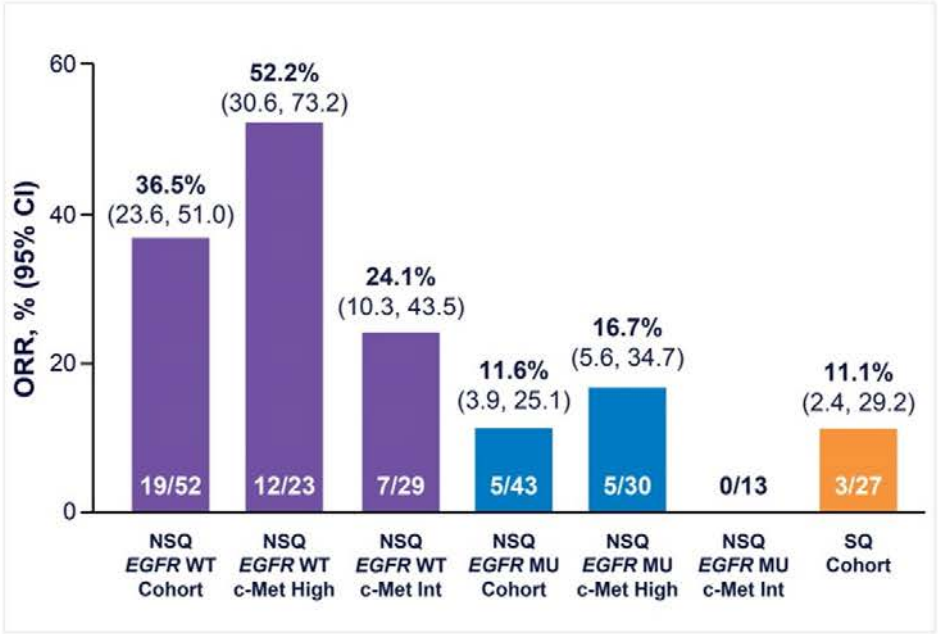


Best relative tumor shrinkage: Patients who had unconfirmed PR (>30% decrease) were counted as SD for BOR
DCR, disease control rate; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Gazzah A et al. ASCO 2020;Abstract 9505.

LUMINOSITY: Phase II Study of Telisotuzumab Vedotin Monotherapy for Patients with Previously Treated c-MET–Overexpressing Advanced NSCLC

ORR per Central Review by Cohort/Group



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

DOR per Central Review by Cohort/Group

Cohort/Group	mDOR by ICR, No. of Events/No. of Responders, Months [95% CI]
NSQ *EGFR* WT	8/19, 6.9 [4.1, NR]
c-Met high	5/12, 6.9 [2.4, NR]
c-Met int	3/7, NR [4.1, NR]
NSQ *EGFR* MU	2/5, NR [3.0, NR]
c-Met high	2/5, NR [3.0, NR]
c-Met int	NA
SQ	2/3, 4.4 [3.0, NR]

CI, confidence interval; DOR, duration of response; *EGFR*, epidermal growth factor receptor; ICR, independent central review; int, intermediate; mDOR, median duration of response; MU, mutant; NA, not available; NR, not reached; NSQ, non-squamous; SQ, squamous; WT, wild-type.

Objective Response Rate per Central Review for Subgroups Defined by Prior Therapies: NSQ *EGFR* WT Cohort

Cohort/Group	Prior Platinum, n/N (%)	Prior Platinum and Immune Checkpoint Inhibitor, n/N (%)
NSQ *EGFR* WT	18/50 (36.0)	15/37 (40.5)
c-Met high	11/21 (52.4)	9/16 (56.3)
c-Met int	7/29 (24.1)	6/21 (28.6)

EGFR, epidermal growth factor receptor; int, intermediate; NSQ, non-squamous; WT, wild-type.

Molecular oncogene analyses in tumors of patients with available tissue are underway.

Camidge DR et al. ASCO 2022;Abstract 9016.

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

Wednesday, December 7, 2022

7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

Faculty

Erika Hamilton, MD

Sara A Hurvitz, MD

Ian E Krop, MD, PhD

Shanu Modi, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP
RESEARCH
TO PRACTICE