Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Urothelial Bladder Cancer

A CME-Accredited Virtual Event

Monday, May 6, 2024
5:00 PM – 6:00 PM ET

Faculty

Matthew D Galsky, MD
Ashish M Kamat, MD, MBBS

Moderator

Neil Love, MD

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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, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, 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 US Inc, Gilead Sciences Inc, Grail Inc, GSK, 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, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology 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, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, 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.

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Dr Kamat — Disclosures
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Contracted Research	Arquer Diagnostics, enGene, Ferring Pharmaceuticals, Photocure, Seagen Inc
Data and Safety Monitoring Board/Committee	Seagen Inc
Nonrelevant Financial Relationships	Patient-Centered Outcomes Research Institute, SWOG

Dr Hafron — Disclosures
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Consulting Agreements	Lilly, Lynx Dx, Myovant Sciences, Myriad Genetic Laboratories Inc, Photocure, Promaxo, Tolmar
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Speakers Bureaus	Amgen Inc, Bayer HealthCare Pharmaceuticals, Dendreon Pharmaceuticals Inc, Janssen Biotech Inc, Lantheus, Merck, Myriad Genetic Laboratories Inc, Pfizer Inc, PROCEPT BioRobotics, Tolmar

Dr Morris — Disclosures
Consulting Faculty

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Contracted Research	Bayer HealthCare Pharmaceuticals, Clovis Oncology, Janssen Biotech Inc, Merck, Pfizer Inc

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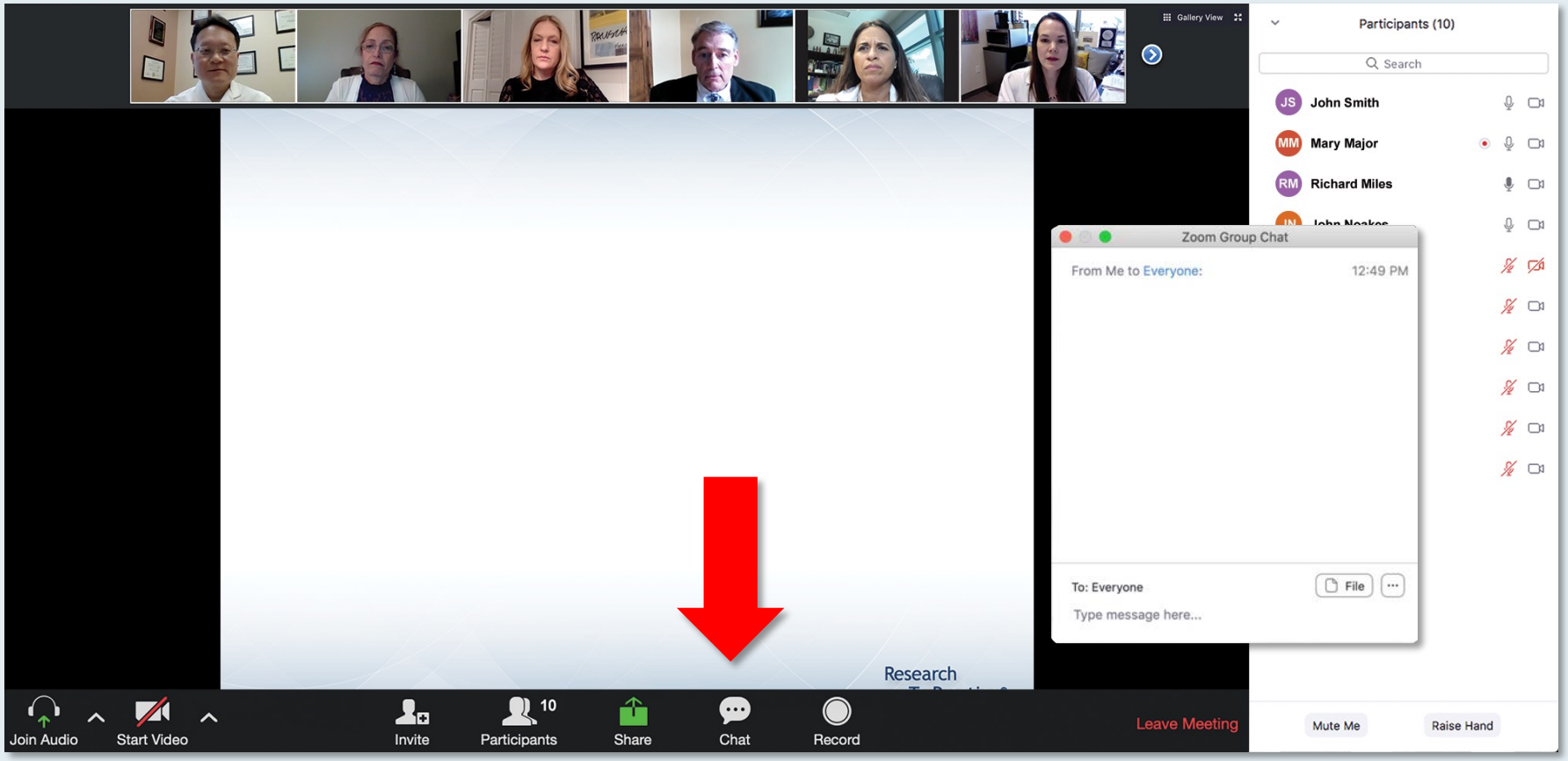

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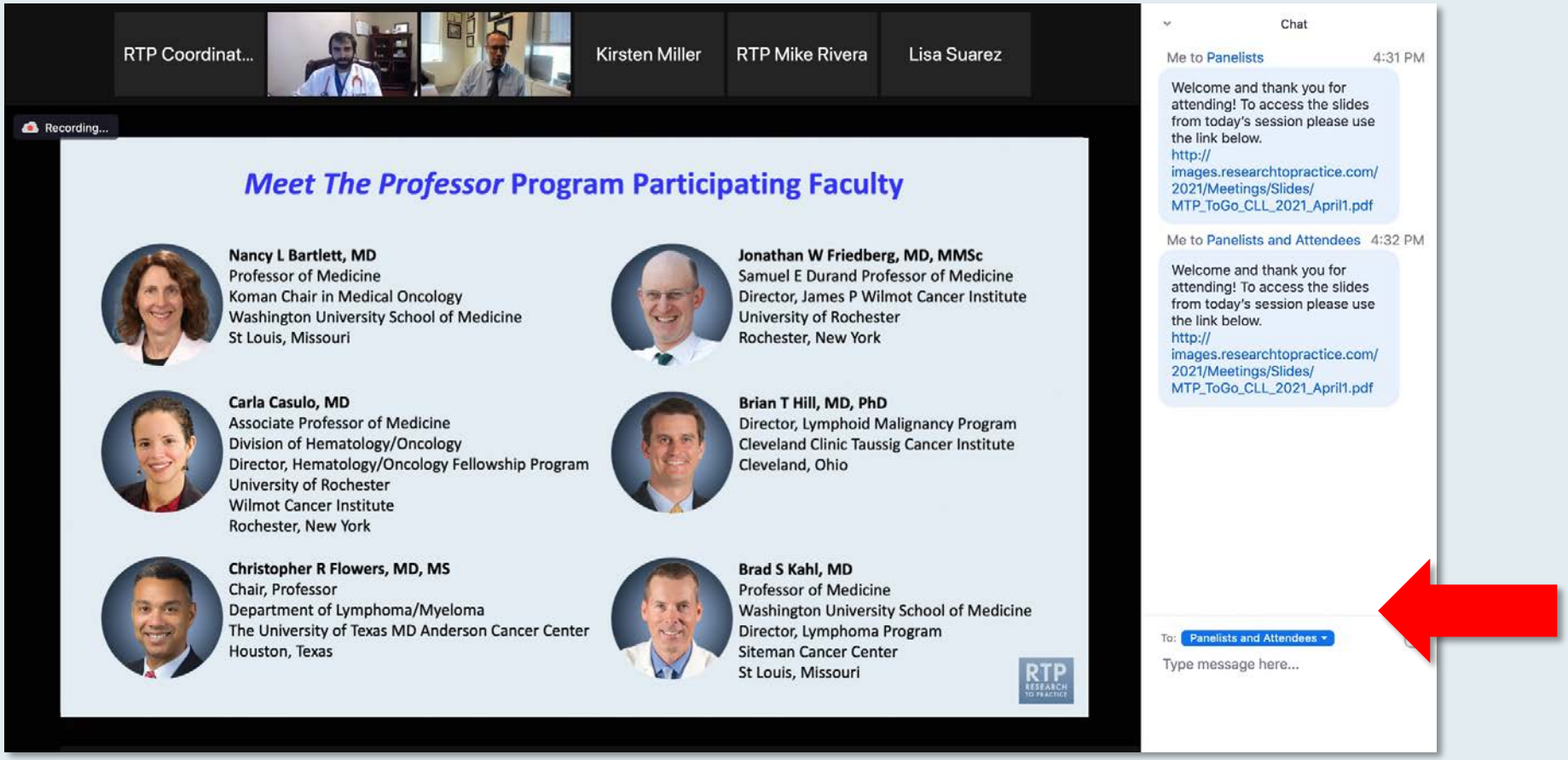

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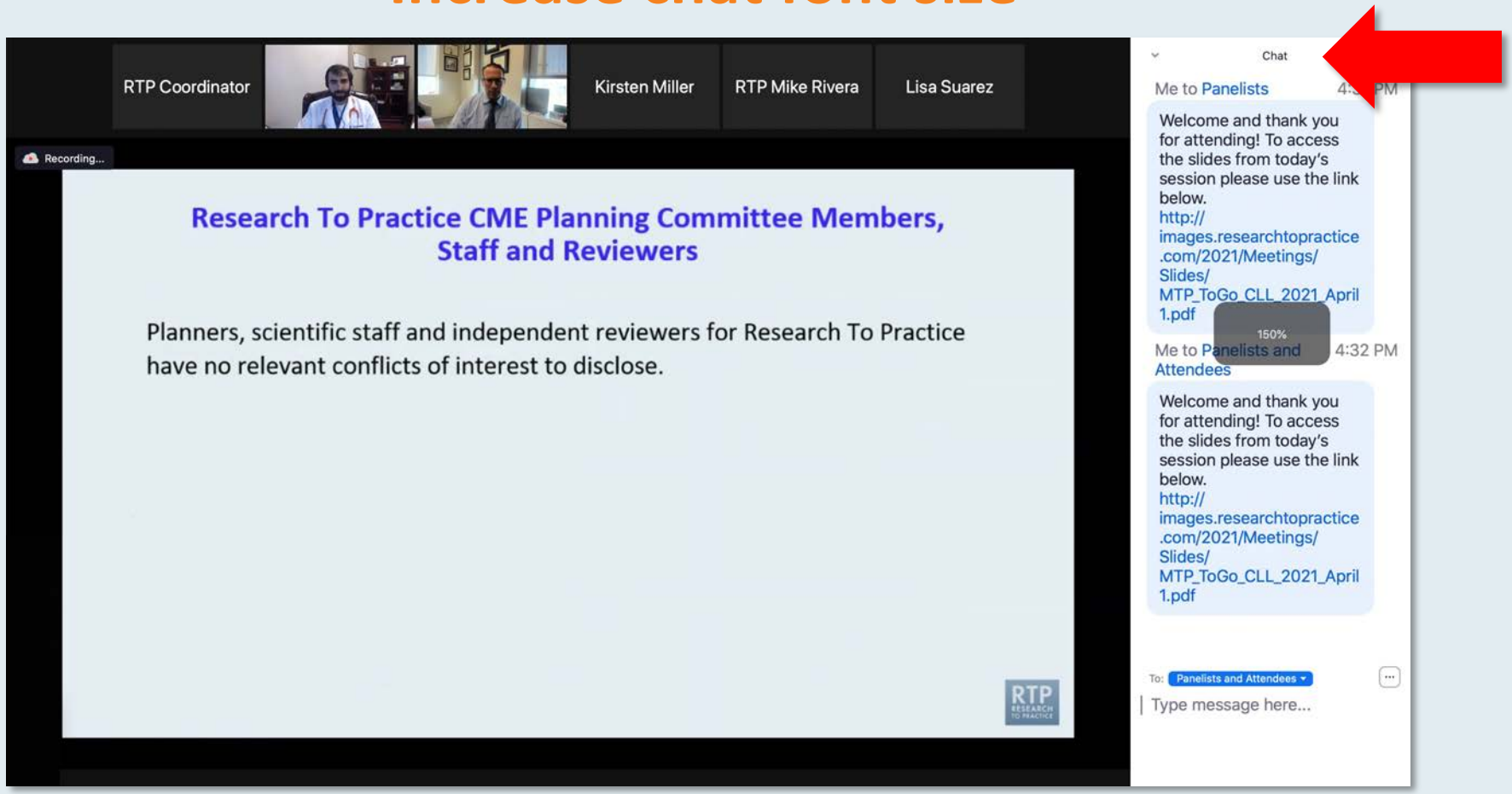

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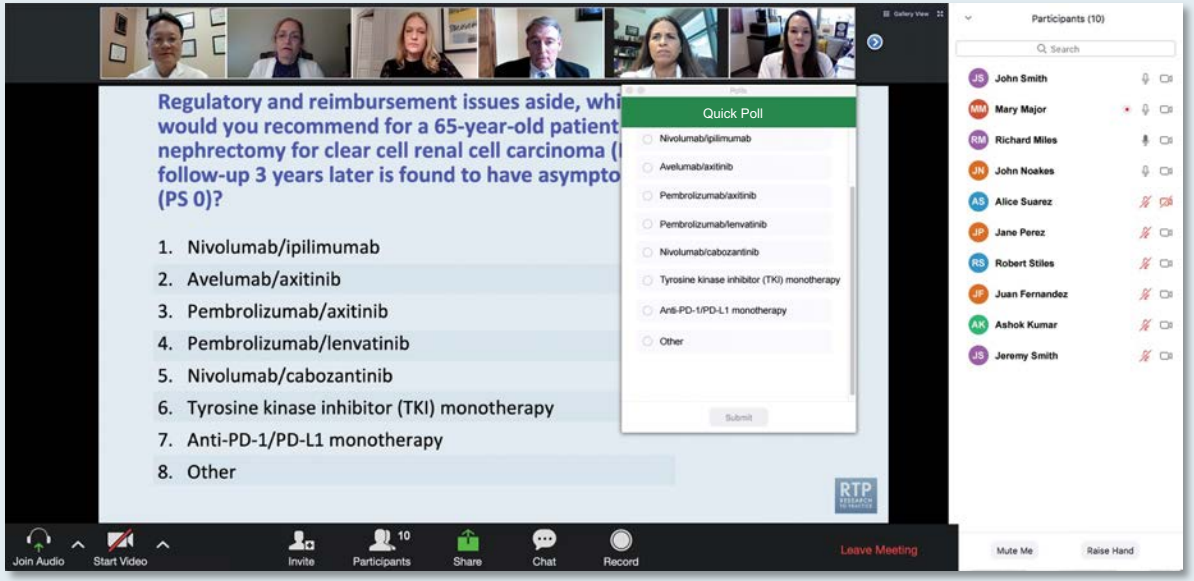

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WITH DR NEIL LOVE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Urothelial Bladder Cancer

DR SHILPA GUPTA
CLEVELAND CLINIC

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BARTS CANCER INSTITUTE, QUEEN MARY UNIVERSITY OF LONDON

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Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A Multitumor CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

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Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Year in Review: Myelofibrosis

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RTP Year in Review 2024

Exciting CME Events in Chicago You Do Not Want to Miss

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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

Additional faculty to be announced

Antibody-Drug Conjugates in Lung Cancer

Saturday, June 1, 2024

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

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Jacob Sands, MD

Non-Small Cell Lung Cancer with an EGFR Mutation

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Zofia Piotrowska, MD, MHS

Joshua K Sabari, MD

Helena Yu, MD

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LIVE WEBCAST

Colorectal Cancer

Monday, June 3, 2024

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Thank you for joining us!

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

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AUA Follow-Up: The Interface of Urology and Medical Oncology

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Faculty

Matthew D Galsky, MD
Professor of Medicine
Icahn School of Medicine at Mount Sinai
Co-Leader, Bladder Cancer Center of Excellence
Associate Director, Translational Research
The Tisch Cancer Institute
New York, New York

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Ashish M Kamat, MD, MBBS
Professor of Urologic Oncology (Surgery)
Wayne B Duddlesten Professor of Cancer Research
Department of Urology, Division of Surgery
The University of Texas
MD Anderson Cancer Center
Houston, Texas

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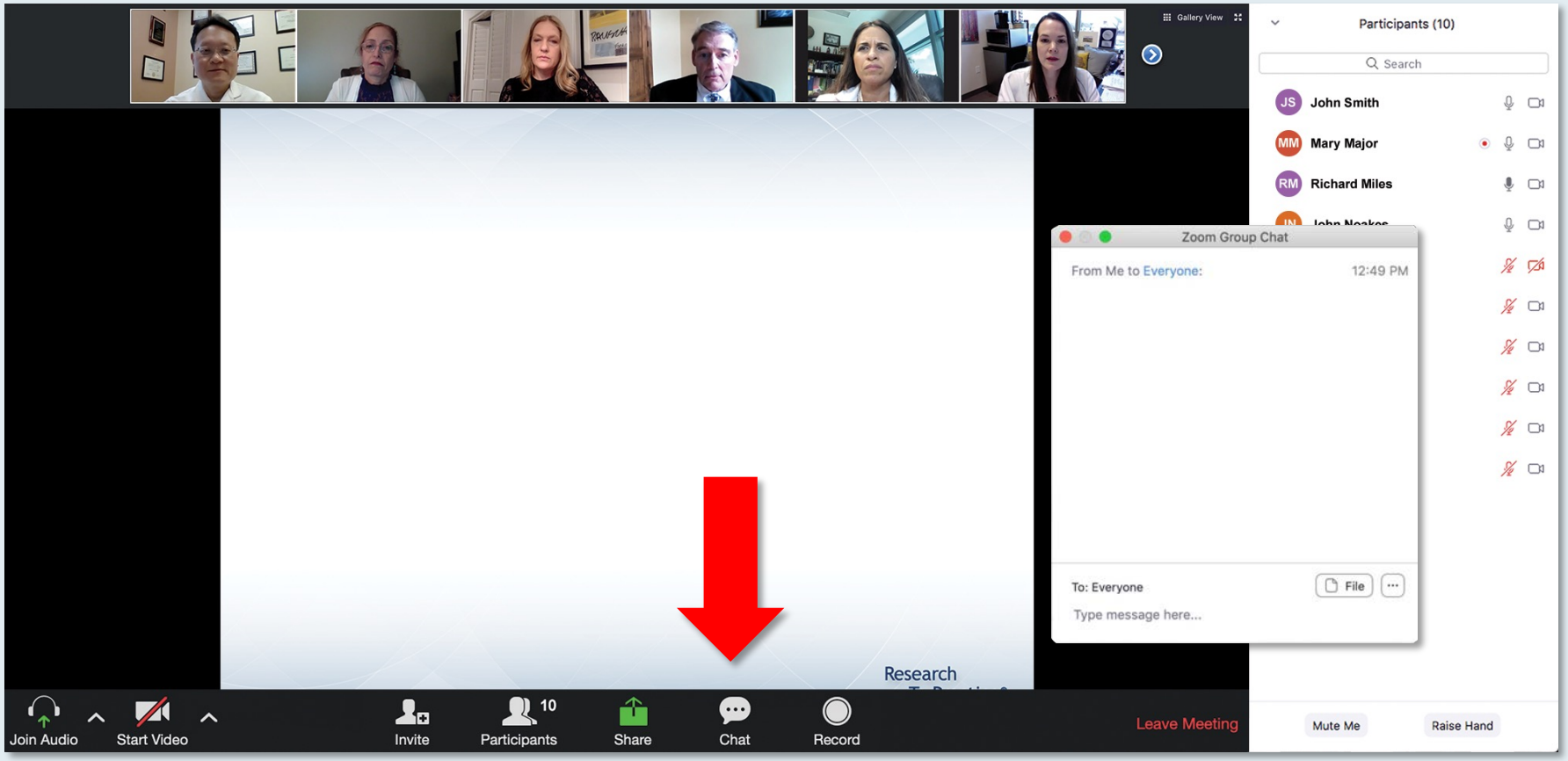

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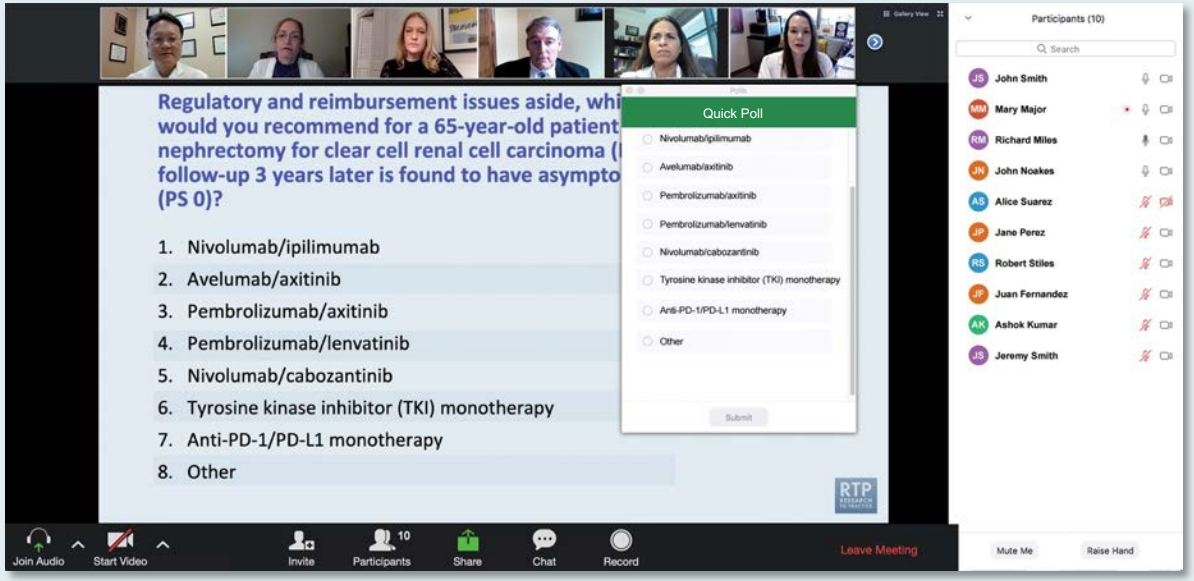

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Agenda

Introduction: Urologist for Life

Module 1: Non-Muscle-Invasive Urothelial Bladder Cancer (UBC) Update

Module 2: Enfortumab Vedotin/Pembrolizumab Now and in the Future

Module 3: HER2-Positive UBC

Module 4: Future Directions — ctDNA

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A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2024 (AUA2024)

Friday, May 3, 2024

8:00 AM – 10:00 AM CT (9:00 AM – 11:00 AM ET)

Faculty

Rahul Aggarwal, MD
Adam S Kibel, MD
Laurence Klotz, CM, MD
Sandy Srinivas, MD

Moderator

Elisabeth I Heath, MD

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Consulting Faculty

Jason Hafron, MD
Michigan Institute of Urology
West Bloomfield, Michigan

David S Morris, MD
Urology Associates
Nashville, Tennessee

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Consulting Faculty Comments

Urologist for life – Metastatic urothelial cancers and the urologist

Jason Hafron, MD

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Consulting Faculty Comments

Defining adequate levels of TURBT needed prior to therapy

David S Morris, MD

TURBT = transurethral resection of bladder tumor

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Consulting Faculty Comments

Approved treatment options for BCG-unresponsive non-muscle invasive bladder cancer

Jason Hafron, MD

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Consulting Faculty Comments

Novel intravesical therapy approaches under clinical investigation

David S Morris, MD

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Consulting Faculty Comments

Use of enfortumab vedotin/pembrolizumab for UBC

Jason Hafron, MD

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Consulting Faculty Comments

Toxicity profile of enfortumab vedotin/pembrolizumab in the neoadjuvant and perioperative settings

David S Morris, MD

Front-Line Treatment of Metastatic Urothelial Bladder Cancer

Cisplatin eligible

- Enfortumab vedotin + pembrolizumab (category 1)
- DDMVAC (dose-dense methotrexate/vinblastine/doxorubicin/cisplatin) and gemcitabine/cisplatin (category 1)
- Gemcitabine/cisplatin + nivolumab (category 1)

Cisplatin ineligible

- Enfortumab vedotin + pembrolizumab (category 1)
- Gemcitabine and carboplatin
- Atezolizumab or pembrolizumab
  - Those not eligible for any chemotherapy regardless of PD-L1 expression

Maintenance (in first response to platinum)

- Avelumab
  - Consider maintenance avelumab for patients with CR/PR or stable disease with platinum-based chemotherapy (category 1)

Content Courtesy of Arlene Siefker-Radtke, MD. NCCN clinical practice guidelines in oncology. Bladder cancer — Version 3.2024.

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FDA Approves Enfortumab Vedotin with Pembrolizumab for Previously Untreated Locally Advanced or Metastatic Urothelial Bladder Cancer

Press Release – December 15, 2023

"The Food and Drug Administration (FDA) approved enfortumab vedotin-ejfv in combination with pembrolizumab for patients with locally advanced or metastatic urothelial cancer (la/mUC). FDA previously granted accelerated approval to this combination for patients with la/mUC who are ineligible for cisplatin-containing chemotherapy.

Efficacy was evaluated in EV-302/KN-A39 (NCT04223856), an open-label, randomized trial of 886 patients with la/mUC and no prior systemic therapy for advanced disease.

Statistically significant improvements in both OS and PFS were demonstrated for enfortumab vedotin-ejfv with pembrolizumab compared with platinum-based chemotherapy."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-enfortumab-vedotin-ejfv-pembrolizumab-locally-advanced-or-metastatic-urothelial-cancer

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 7, 2024 VOL. 390 NO. 10

Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer

T. Powles, B.P. Valderrama, S. Gupta, J. Bedke, E. Kikuchi, J. Hoffman-Censits, G. Iyer, C. Vulsteke, S.H. Park, S.J. Shin, D. Castellano, G. Fornarini, J.-R. Li, M. Gümüş, N. Mar, Y. Loriot, A. Fléchon, I. Duran, A. Drakaki, S. Narayanan, X. Yu, S. Gorla, B. Homet Moreno, and M.S. van der Heijden, for the EV-302 Trial Investigators*

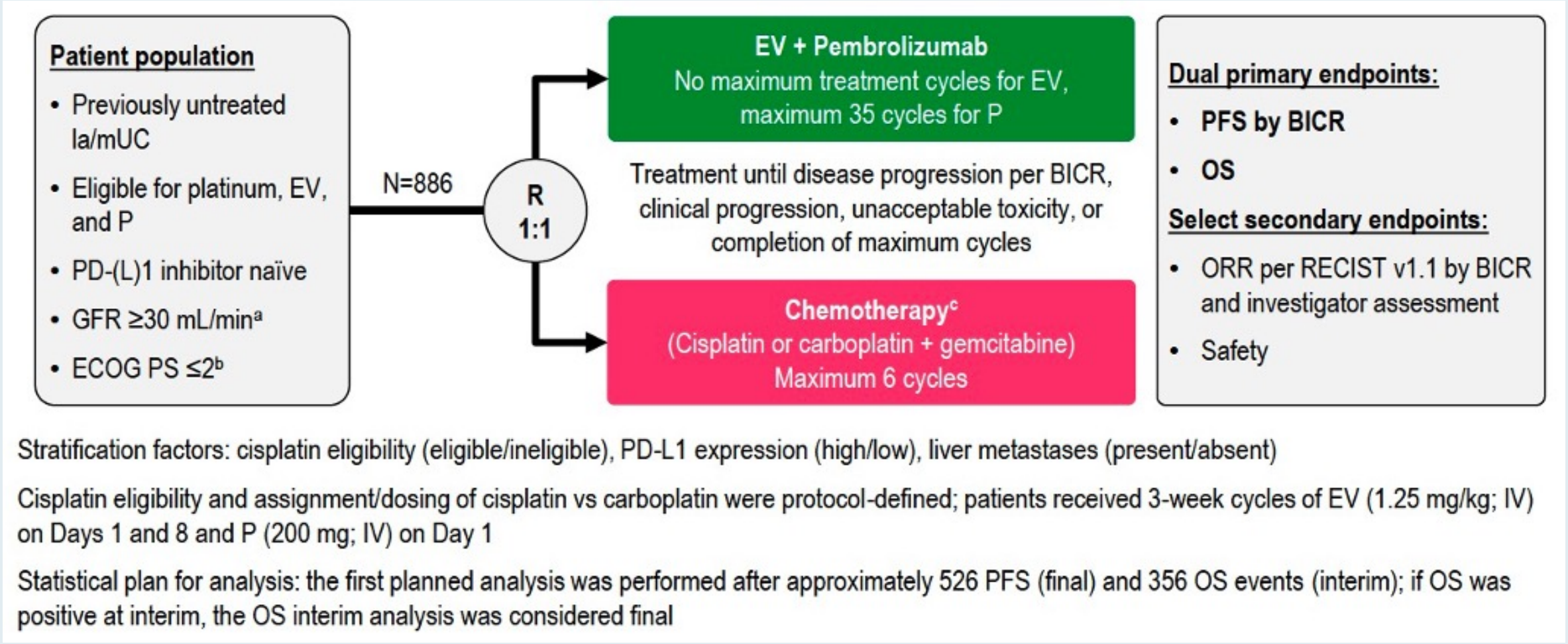
ASCO Genitourinary Cancers Symposium

Enfortumab vedotin (EV) in combination with pembrolizumab (P) versus chemotherapy in previously untreated locally advanced or metastatic urothelial carcinoma (la/mUC): Subgroup analyses from EV-302, a phase 3 global study

Michiel S. van der Heijden, Thomas Powles, Shilpa Gupta, Jens Bedke, Eiji Kikuchi, Ronald de Wit, Matt D. Galsky, Ignacio Duran, Andrea Necchi, Margitta Retz, Evan Y. Yu, Jean H. Hoffman-Censits, Gopa Iyer, Se Hoon Park, Wen-Pin Su, Hema Parmar, Xuesong Guan, Seema Rao Gorla, Blanca Homet Moreno, Begoña Pérez Valderrama

2024;Abstract LBA530

EV-302/KEYNOTE-A39 Phase III Study Design



Stratification factors: cisplatin eligibility (eligible/ineligible), PD-L1 expression (high/low), liver metastases (present/absent)

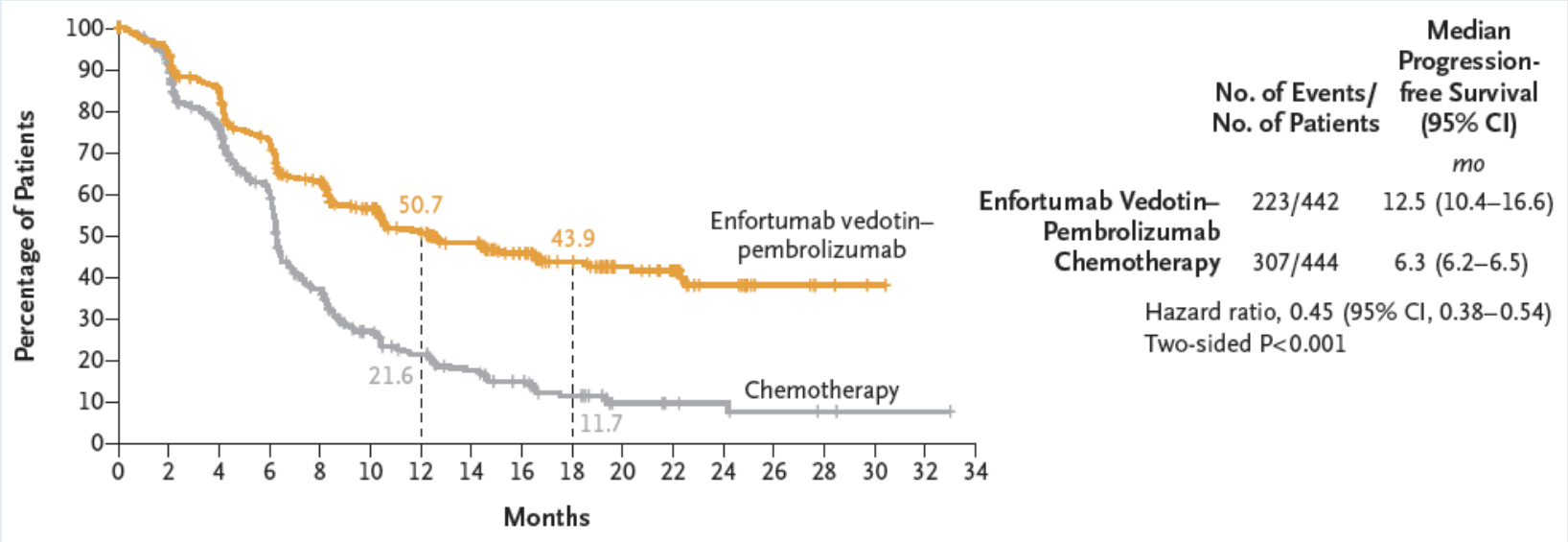
Cisplatin eligibility and assignment/dosing of cisplatin vs carboplatin were protocol-defined; patients received 3-week cycles of EV (1.25 mg/kg; IV) on Days 1 and 8 and P (200 mg; IV) on Day 1

Statistical plan for analysis: the first planned analysis was performed after approximately 526 PFS (final) and 356 OS events (interim); if OS was positive at interim, the OS interim analysis was considered final

PFS = progression-free survival; OS = overall survival; ORR = overall response rate

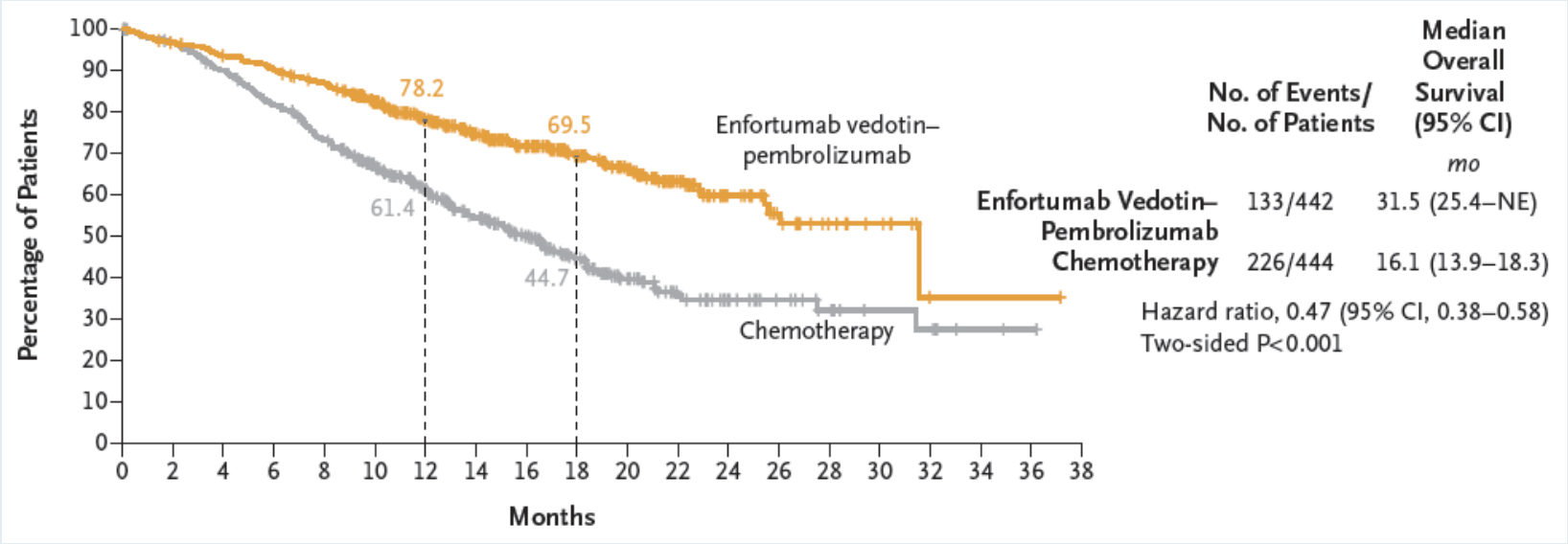
Kikuchi E et al. ESMO Asia 2023;Abstract 211MO; Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

EV-302/KEYNOTE-A39: Survival



	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)
		mo
Enfortumab Vedotin–Pembrolizumab	223/442	12.5 (10.4–16.6)
Chemotherapy	307/444	6.3 (6.2–6.5)

Hazard ratio, 0.45 (95% CI, 0.38–0.54)
Two-sided P<0.001

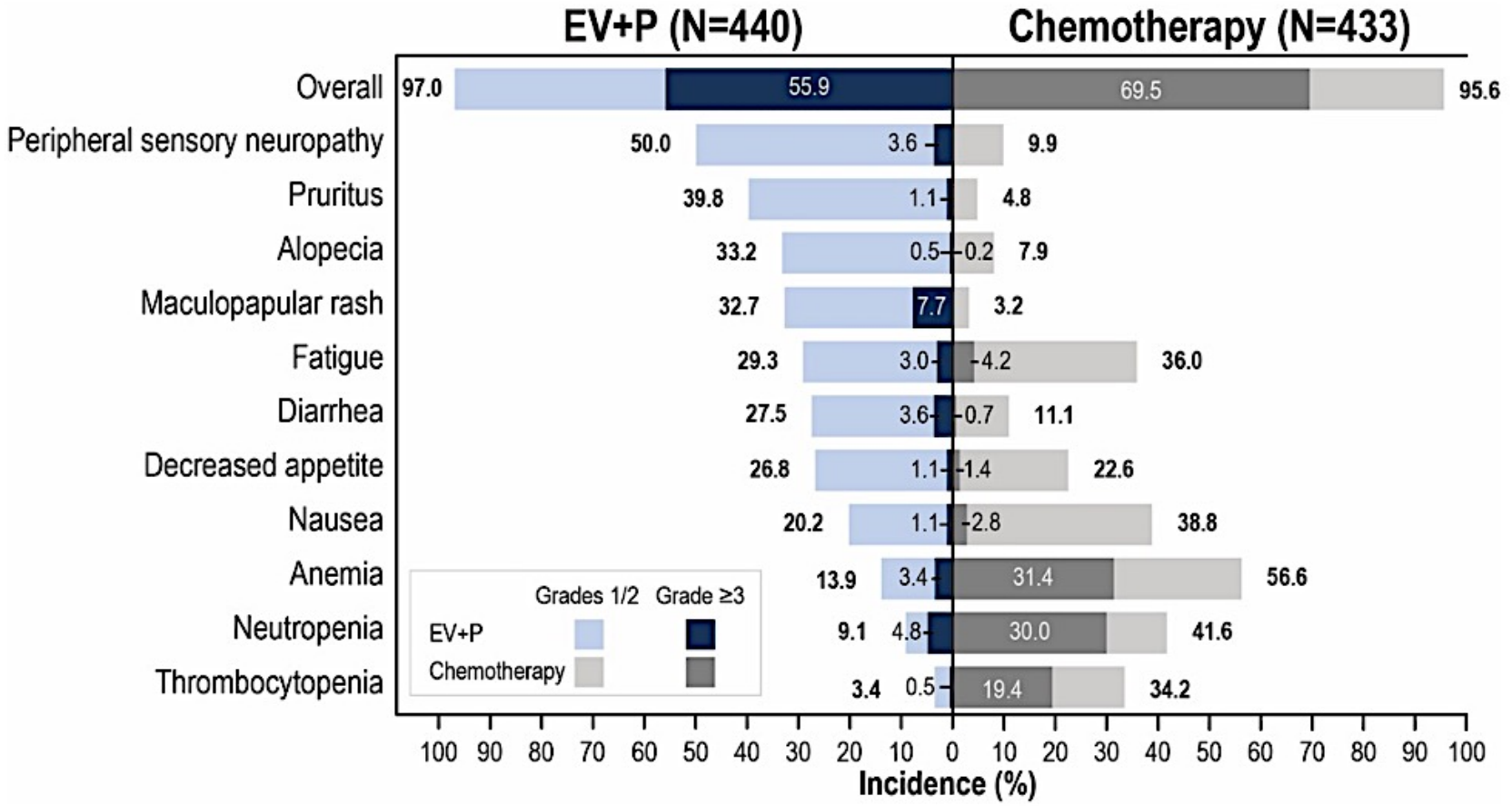


	No. of Events/ No. of Patients	Median Overall Survival (95% CI)
		mo
Enfortumab Vedotin–Pembrolizumab	133/442	31.5 (25.4–NE)
Chemotherapy	226/444	16.1 (13.9–18.3)

Hazard ratio, 0.47 (95% CI, 0.38–0.58)
Two-sided P<0.001

Powles T et al. *N Engl J Med* 2024 March 7;390(10):875-88; Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

EV-302/KEYNOTE-A39: Treatment-Related Adverse Events (TRAEs)



- Grade ≥3 events were observed in 56% in EV+P and 70% in chemotherapy
- No new safety signals were seen for EV AESIs or pembrolizumab AEOSIs

TRAEs leading to death (per investigator):

EV+P: 4 (0.9%)
- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

Chemotherapy: 4 (0.9%)
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

AESIs = adverse events of special interest; AEOSIs = AESIs with pembrolizumab

Powles T et al. *N Engl J Med* 2024 March 7;390(10):875-88; Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

FDA Approves Nivolumab in Combination with Cisplatin and Gemcitabine as First-Line Therapy for Unresectable or Metastatic Urothelial Carcinoma

Press Release – March 6, 2024

"On March 6, 2024, the Food and Drug Administration approved nivolumab in combination with cisplatin and gemcitabine for first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma (UC).

Efficacy was evaluated in CheckMate-901 (NCT03036098), a randomized, open-label trial enrolling 608 patients with previously untreated unresectable or metastatic UC. Patients were randomized (1:1) to receive either nivolumab in combination with cisplatin and gemcitabine (up to 6 cycles) followed by nivolumab alone for up to two years or cisplatin and gemcitabine (up to 6 cycles). On both arms, patients discontinuing cisplatin were permitted to receive carboplatin. Randomization was stratified by tumor PD-L1 expression and presence of liver metastasis.

The major efficacy outcome measures were overall survival (OS) and progression-free survival (PFS), assessed by blinded independent central review using RECIST v1.1."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-combination-cisplatin-and-gemcitabine-unresectable-or-metastatic-urothelial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab plus Gemcitabine–Cisplatin in Advanced Urothelial Carcinoma

M.S. van der Heijden, G. Sonpavde, T. Powles, A. Necchi, M. Burotto, M. Schenker, J.P. Sade, A. Bamias, P. Beuzeboc, J. Bedke, J. Oldenburg, G. Chatta, Y. Ürün, D. Ye, Z. He, B.P. Valderrama, J.H. Ku, Y. Tomita, J. Filian, L. Wang, D. Purcea, M.Y. Patel, F. Nasroulah, and M.D. Galsky, for the CheckMate 901 Trial Investigators*

MADRID 2023 ESMO congress

Nivolumab plus gemcitabine-cisplatin versus gemcitabine-cisplatin alone for previously untreated unresectable or metastatic urothelial carcinoma: results from the phase 3 CheckMate 901 trial

Michiel S. van der Heijden,[1] Guru Sonpavde,[2a] Thomas Powles,[3] Andrea Necchi,[4b] Mauricio Burotto,[5] Michael Schenker,[6] Juan Pablo Sade,[7] Aristotelis Bamias,[8] Philippe Beuzeboc,[9] Jens Bedke,[10c] Jan Oldenburg,[11] Yüksel Ürün,[12] Dingwei Ye,[13] Zhisong He,[14] Begoña P. Valderrama,[15] Yoshihiko Tomita,[16] Jeiry Filian,[17] Daniela Purcea,[18] Federico Nasroulah,[17] Matthew D. Galsky[19]

[1]Netherlands Cancer Institute, Amsterdam, the Netherlands; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]Barts Cancer Institute, Queen Mary University of London, London, UK; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [5]Bradford Hill Clinical Research Center, Santiago, Chile; [6]University of Medicine and Pharmacy, Craiova, Romania; [7]Alexander Fleming Institute, Buenos Aires, Argentina; [8]National and Kapodistrian University of Athens, ATTIKON University Hospital, Athens, Greece; [9]Hopital Foch, Suresnes, France; [10]Eberhard Karls University Tübingen, Tübingen, Germany; [11]Akershus University Hospital (Ahus), Lørenskog, Norway; [12]Ankara University, Ankara, Turkey; [13]Fudan University Shanghai Cancer Center, Shanghai, China; [14]Peking University First Hospital, Beijing, China; [15]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [16]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [17]Bristol Myers Squibb, Princeton, NJ, USA; [18]Bristol Myers Squibb, Boudry, Switzerland; [19]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA

[a]Current affiliation is AdventHealth Cancer Institute and University of Central Florida, Orlando, FL, USA. [b]Current affiliation is IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy. [c]Current affiliation is Klinikum Stuttgart, Katharinenhospital, Stuttgart, Germany.

Presentation number LBA7

van der Heijden MS et al. *N Engl J Med* 2023;389:1778-89; ESMO 2023;Abstract LBA7.

RTP RESEARCH TO PRACTICE

Agenda

Introduction: Urologist for Life

Module 1: Non-Muscle-Invasive Urothelial Bladder Cancer (UBC) Update

Module 2: Enfortumab Vedotin/Pembrolizumab Now and in the Future

Module 3: HER2-Positive UBC

Module 4: Future Directions — ctDNA

Consulting Faculty Comments

Evolving role of HER2 status in the management of UBC

David S Morris, MD

Jason Hafron, MD

Consulting Faculty Comments

Toxicity profiles of HER2-targeted agents

David S Morris, MD

Jason Hafron, MD

RTP RESEARCH TO PRACTICE

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

Press Release – April 5, 2024

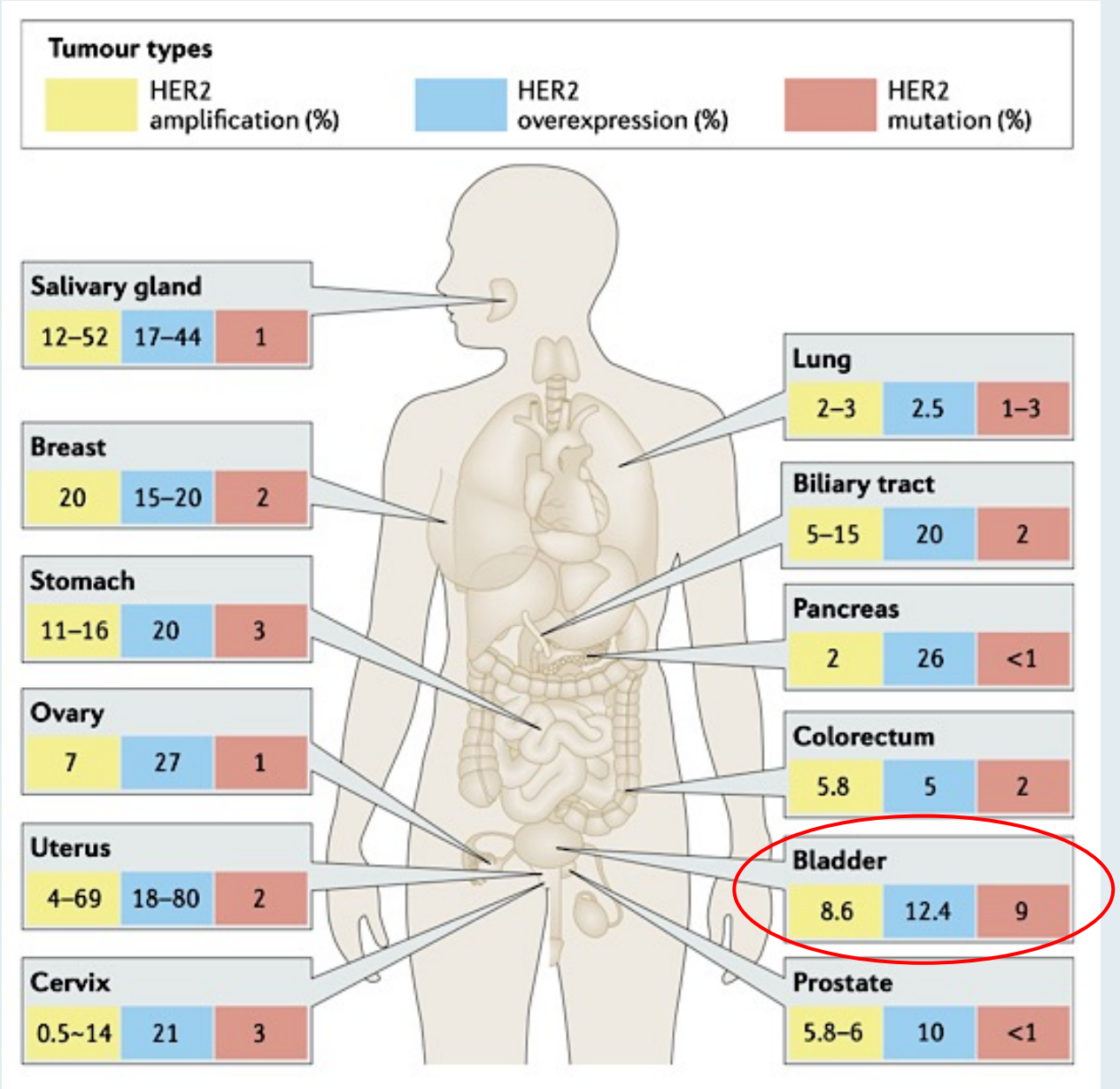
"…the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.

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

Incidence of HER2 Alterations in Solid Tumors

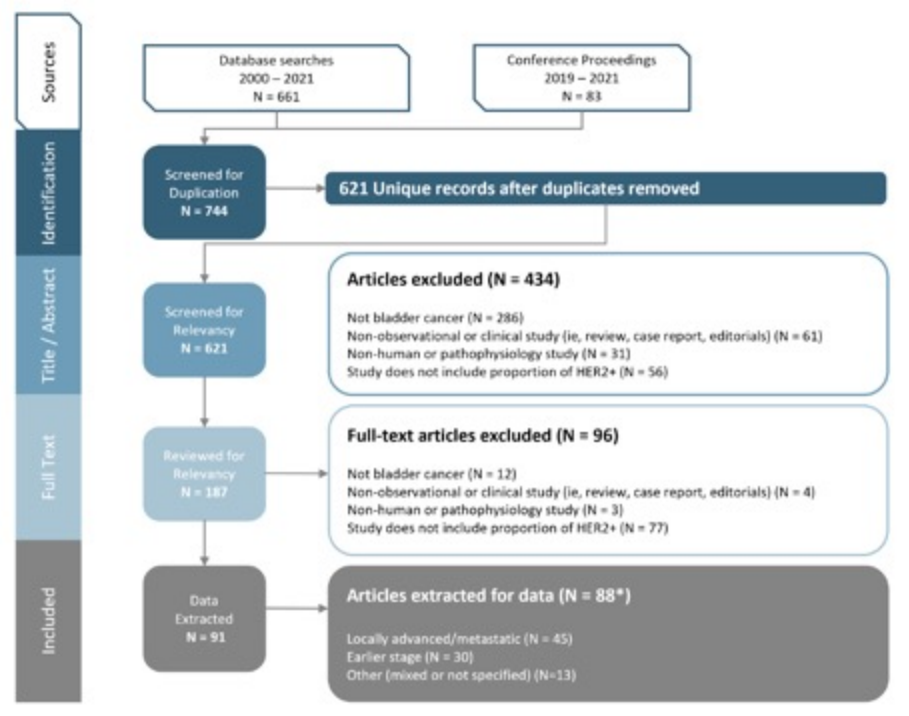


Oh DY, Bang YJ. *Nat Rev Clin Oncol* 2020;17:33-48.

RTP RESEARCH TO PRACTICE

HER2 Expression in Locally Advanced or Metastatic UBC

- HER2 IHC not typically assessed as part of standard clinical care
- No standardized criteria for defining HER2 expression
- Systematic literature review of reported HER2 status in locally advanced or metastatic UBC



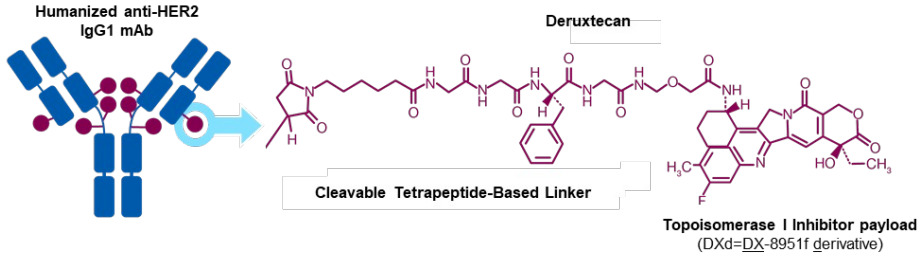
- A significant proportion of patients with locally advanced or metastatic UBC have tumors with HER2 expression based on predefined criteria
- **HER2+** (IHC 3+ OR IHC 2+ / ISH+): **12.3% weighted avg** (6 studies, N = 971 pts)
- **HER2 low** (IHC 2+/ISH- OR IHC 1+): **47.9% weighted avg** (4 studies, N = 275 pts)

Scherrer E et al. *Front Oncol* 2022 October 21:12:1011885.

Content Courtesy of Evan Y Yu, MD, adapted

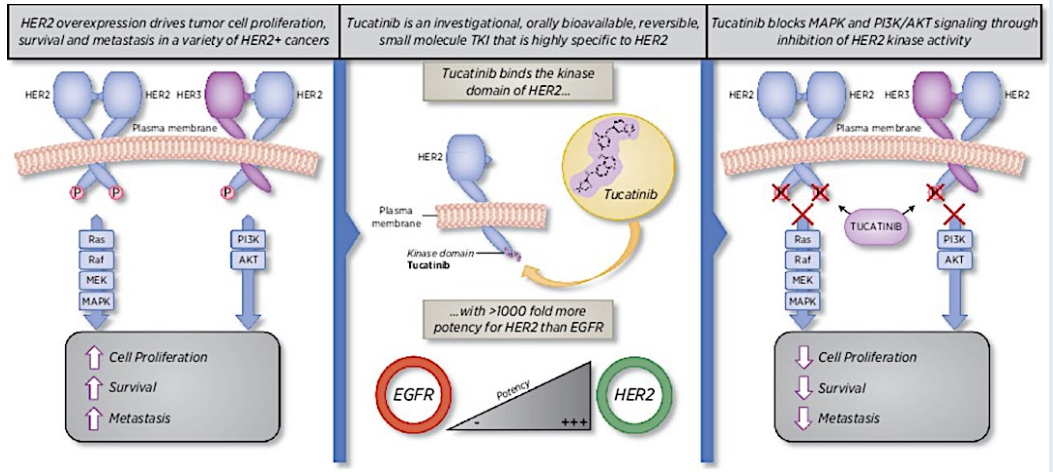
RTP RESEARCH TO PRACTICE

HER2 as a Therapeutic Target in UBC



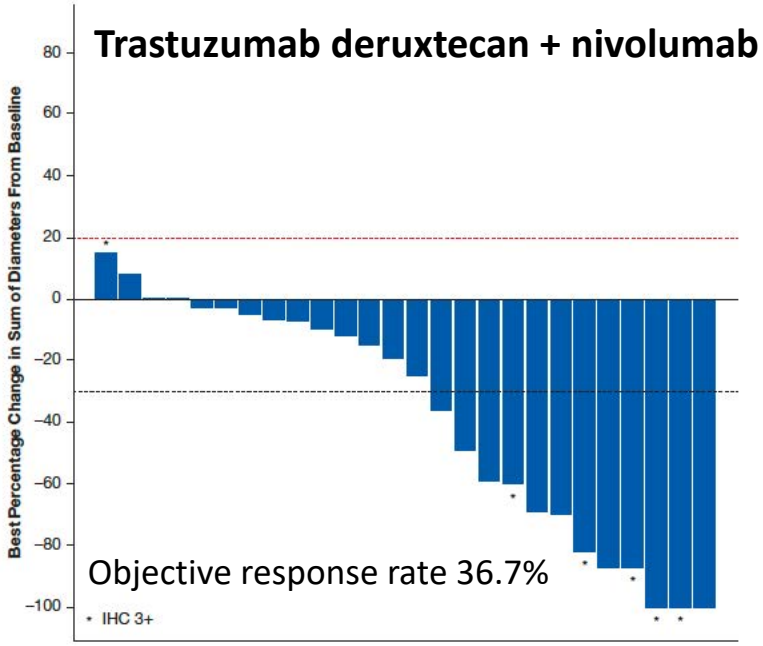
Conjugation chemistry
The tetrapeptide-based cleavable linker is connected to the humanized anti-HER2 IgG1 monoclonal antibody, with the same amino acid sequence as trastuzumab

Tucatinib basket trial with enough responses to go on to Stage 2 of design.



Tucatinib is an investigational agent and its efficacy and safety have not been established

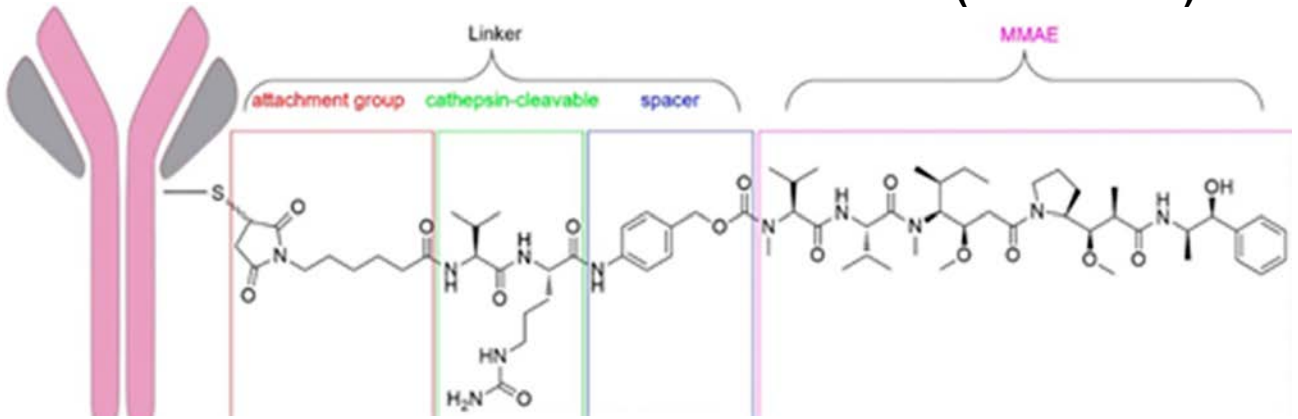
Trastuzumab deruxtecan + nivolumab



Cohort 3 IHC 3+/2+ (n = 30) (part 2: T-DXd 5.4 mg/kg and nivolumab 360 mg) Best (minimum) percentage change					
n	Mean	SD	Median	Min	Max
26	−37.8	38.52	−22.0	−100	15

*In cohort 3, 4 patients did not have best percentage change available, of whom 2 were IHC 3+.
The line at 20% indicates progressive disease, and the line at −30% indicates a partial response.

Disitamab vedotin (RC48-ADC)



Galsky MD et al. Genitourinary Cancers Symposium 2022;Abstract 438.

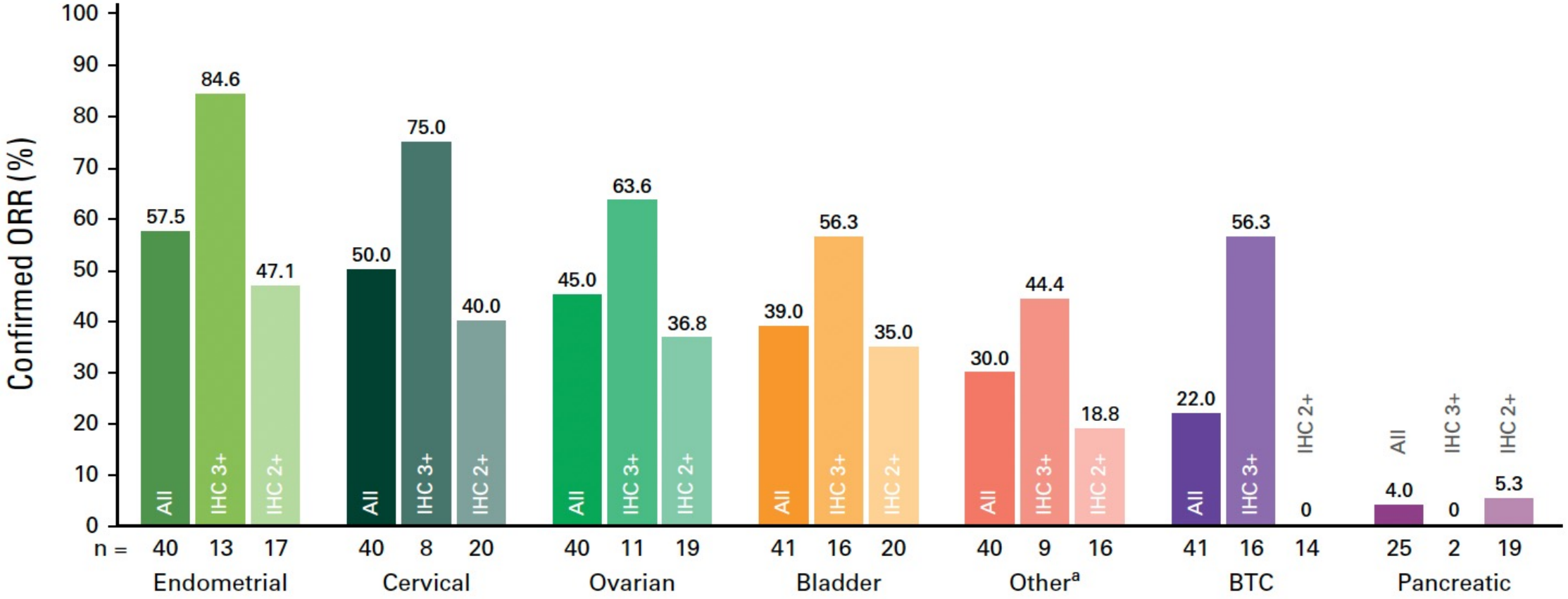
RTP RESEARCH TO PRACTICE

Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

Funda Meric-Bernstam, MD[1]; Vicky Makker, MD[2,3]; Ana Oaknin, MD[4]; Do-Youn Oh, MD[5]; Susana Banerjee, PhD[6]; Antonio González-Martín, MD[7]; Kyung Hae Jung, MD[8]; Iwona Ługowska, MD[9]; Luis Manso, MD[10]; Aránzazu Manzano, MD[11]; Bohuslav Melichar, MD[12]; Salvatore Siena, MD[13]; Daniil Stroyakovskiy, MD[14]; Anitra Fielding, MBChB[15]; Yan Ma, MSc[16]; Soham Puvvada, MD[15]; Norah Shire, PhD[15]; and Jung-Yun Lee, MD[17]

J Clin Oncol 2024;42(1):47-58.

DESTINY-PanTumor02: Response to Trastuzumab Deruxtecan in HER2-Expressing Solid Tumors



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

RTP RESEARCH TO PRACTICE

DESTINY-PanTumor02: Adverse Events in Patients with Bladder Cancer

Adverse Event	Bladder Cancer (n = 41)
Drug-related adverse events, No. (%)	38 (92.7)
Grade ≥3	17 (41.5)
Serious adverse events	4 (9.8)
Leading to discontinuation	4 (9.8)
Leading to dose modification[a]	15 (36.6)
Associated with death	1 (2.4)
Most common drug-related adverse events (>10% of total patients), No. (%)	
Nausea	21 (51.2)
Anemia	12 (29.3)
Diarrhea	13 (31.7)
Fatigue	11 (26.8)
Vomiting	6 (14.6)
Neutropenia	11 (26.8)
Decreased appetite	8 (19.5)
Asthenia	3 (7.3)
Alopecia	5 (12.2)
Thrombocytopenia	6 (14.6)

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

Reviews

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

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

JCO Oncol Pract 2023;19:539-46.

Editorials

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

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

JCO Oncol Pract 2023;19:526-7.

The Five "S" Rules: Strategies to Minimize the Risk and Impact of Insterstitial Lung Disease (ILD)

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

Tarantino P, Tolaney SM. *JCO Oncol Pract* 2023;19:526-7.

RTP RESEARCH TO PRACTICE

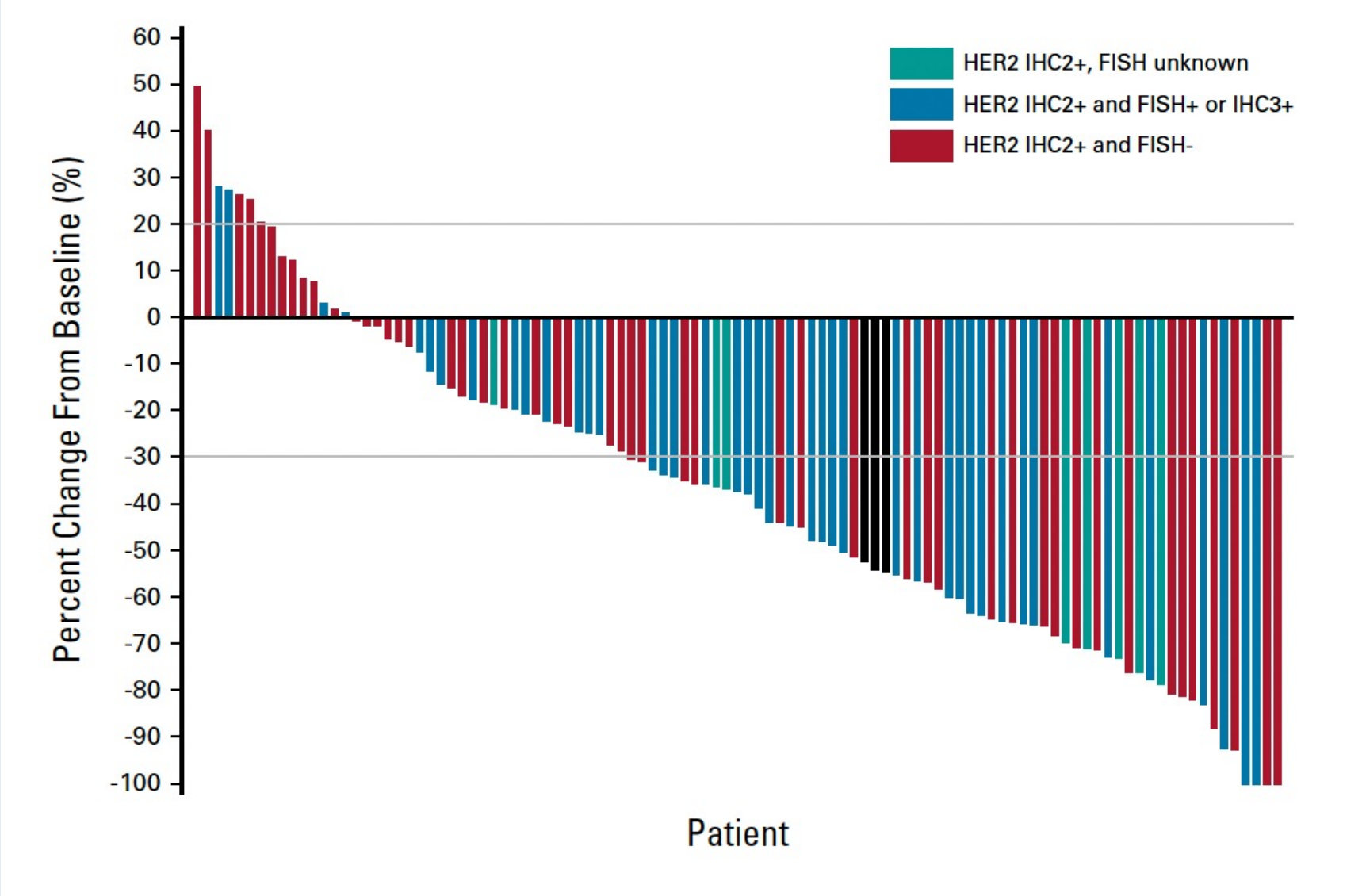
Efficacy and Safety of Disitamab Vedotin in Patients With Human Epidermal Growth Factor Receptor 2–Positive Locally Advanced or Metastatic Urothelial Carcinoma: A Combined Analysis of Two Phase II Clinical Trials (RC48-C005 and RC48-C009)

Xinan Sheng, MD[1]; Lin Wang, MD[2]; Zhisong He, MD[3]; Yanxia Shi, MD[4]; Hong Luo, MD[5]; Weiqing Han, MD[6]; Xin Yao, MD[7]; Benkang Shi, MD[8]; Jiyan Liu, MD[9]; Changlu Hu, MD[10]; Ziling Liu, MD[11]; Hongqian Guo, MD[12]; Guohua Yu, MD[13]; Zhigang Ji, MD[14]; Jianming Ying, MD[15]; Yun Ling, MD[15]; Shiying Yu, MD[16]; Yi Hu, MD[17]; Jianming Guo, MD[18]; Jianmin Fang, PhD[19,20]; Aiping Zhou, MD[2]; and Jun Guo, MD[1]

J Clin Oncol 2024 April 20;42(12):1391-402.

RTP RESEARCH TO PRACTICE

Disitamab Vedotin: Response in a Combined Analysis of 2 Phase II Trials



Sheng X et al. *J Clin Oncol* 2024 April 20;42(12):1391-402.

RTP RESEARCH TO PRACTICE

Disitamab Vedotin: Safety in a Combined Analysis of 2 Phase II Trials

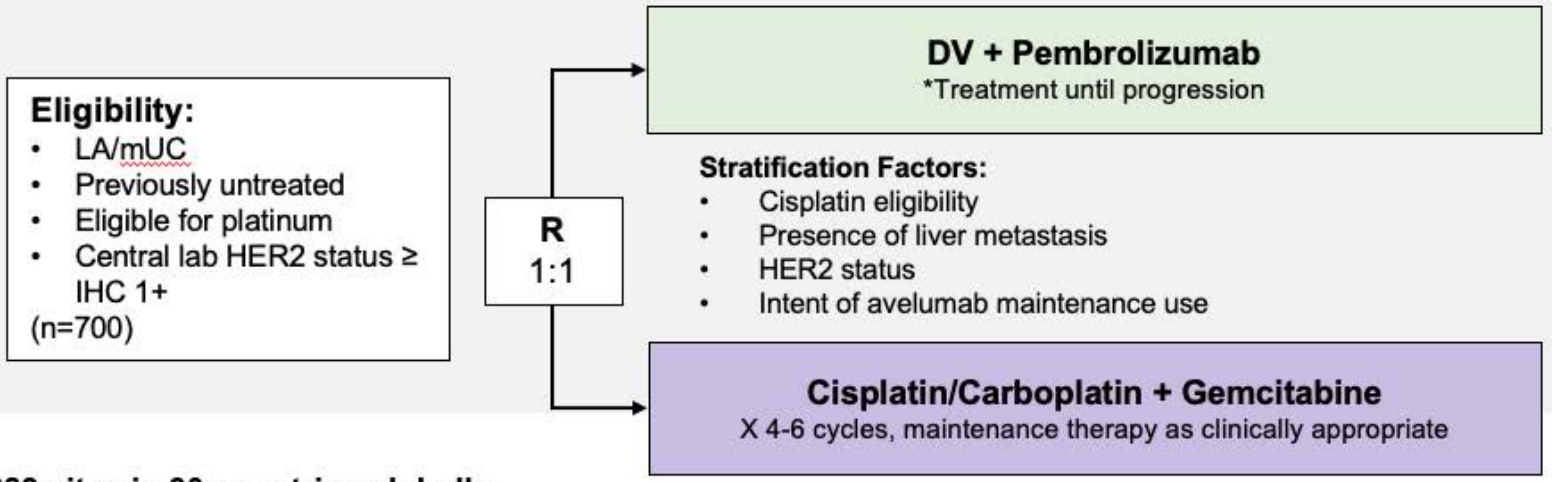
TRAE	Grade 1, No. (%)	Grade 2, No. (%)	Grade 3, No. (%)	Grade 4, No. (%)	Grade 5, No. (%)	Total (n = 107), n (%)
Any TRAE	13 (12.1)	36 (33.6)	55 (51.4)	3 (2.8)	0	107 (100.0)
Peripheral sensory neuropathy	35 (32.7)	18 (16.8)	20 (18.7)	0	0	73 (68.2)
Leukopenia	19 (17.8)	33 (30.8)	2 (1.9)	0	0	54 (50.5)
AST increased	39 (36.4)	5 (4.7)	1 (0.9)	0	0	45 (42.1)
Neutropenia	13 (12.1)	19 (17.8)	12 (11.2)	1 (0.9)	0	45 (42.1)
Alopecia	37 (34.6)	5 (4.7)	1 (0.9)	0	0	43 (40.2)
Asthenia	26 (24.3)	12 (11.2)	4 (3.7)	0	0	42 (39.3)
ALT increased	31 (29.0)	7 (6.5)	0	0	0	38 (35.5)
Decreased appetite	30 (28.0)	3 (2.8)	1 (0.9)	0	0	34 (31.8)
Nausea	27 (25.2)	4 (3.7)	0	0	0	31 (29.0)
Weight decreased	16 (15.0)	11 (10.3)	0	0	0	27 (25.2)
Platelet count decreased	14 (13.1)	12 (11.2)	0	0	0	26 (24.3)
Constipation	21 (19.6)	3 (2.8)	0	0	0	24 (22.4)
Blood triglycerides increased	17 (15.9)	5 (4.7)	1 (0.9)	1 (0.9)	0	24 (22.4)
Anemia	12 (11.2)	8 (7.5)	3 (2.8)	0	0	23 (21.5)
Gamma-glutamyltransferase increased	7 (6.5)	9 (8.4)	6 (5.6)	0	0	22 (20.6)
Pruritus	13 (12.1)	7 (6.5)	1 (0.9)	0	0	21 (19.6)
Vomiting	16 (15.0)	2 (1.9)	1 (0.9)	0	0	19 (17.8)
Blood creatine phosphokinase increased	11 (10.3)	2 (1.9)	2 (1.9)	1 (0.9)	0	16 (15.0)
Blood glucose increased	8 (7.5)	6 (5.6)	2 (1.9)	0	0	16 (15.0)
Hemoglobin decreased	7 (6.5)	5 (4.7)	1 (0.9)	0	0	13 (12.1)
Protein urine present	4 (3.7)	7 (6.5)	1 (0.9)	0	0	12 (11.2)
Rash	9 (8.4)	3 (2.8)	0	0	0	12 (11.2)
Pyrexia	6 (5.6)	5 (4.7)	0	0	0	11 (10.3)
Pain in extremity	8 (7.5)	3 (2.8)	0	0	0	11 (10.3)

TRAE = treatment-related adverse event

Sheng X et al. *J Clin Oncol* 2024 April 20;42(12):1391-402.

RTP RESEARCH TO PRACTICE

Ongoing Phase III Trial of Disitamab Vedotin/Pembrolizumab versus Chemotherapy for Previously Untreated Locally Advanced or Metastatic UBC (LA/mUC) That Expresses HER2



* DV 1.5 mg/kg Q2W until disease progression and pembrolizumab 400 mg Q6W for up to 18 cycles

Dual-Primary Endpoints

- **PFS by BICR**
- **OS**

289 sites in 30 countries globally

- US, Canada, LATAM, EU, Israel, Turkey, APAC
- Competitive enrollment – No site/country cap
- Estimated enrollment start & end date
  - FPI: Q3 2023
  - LPI: Q1 2026

Maintenance therapy in the 1L setting as clinically appropriate and locally approved is allowed.
Avelumab will not be provided by sponsor.

NCT05911295

www.clinicaltrials.gov; Accessed May 2024

Courtesy of Evan Yu, MD

Agenda

Introduction: Urologist for Life

Module 1: Non-Muscle-Invasive Urothelial Bladder Cancer (UBC) Update

Module 2: Enfortumab Vedotin/Pembrolizumab Now and in the Future

Module 3: HER2-Positive UBC

Module 4: Future Directions — ctDNA

Consulting Faculty Comments

Integration of tissue and ctDNA testing into the management of UBC

Jason Hafron, MD

ctDNA = circulating tumor DNA

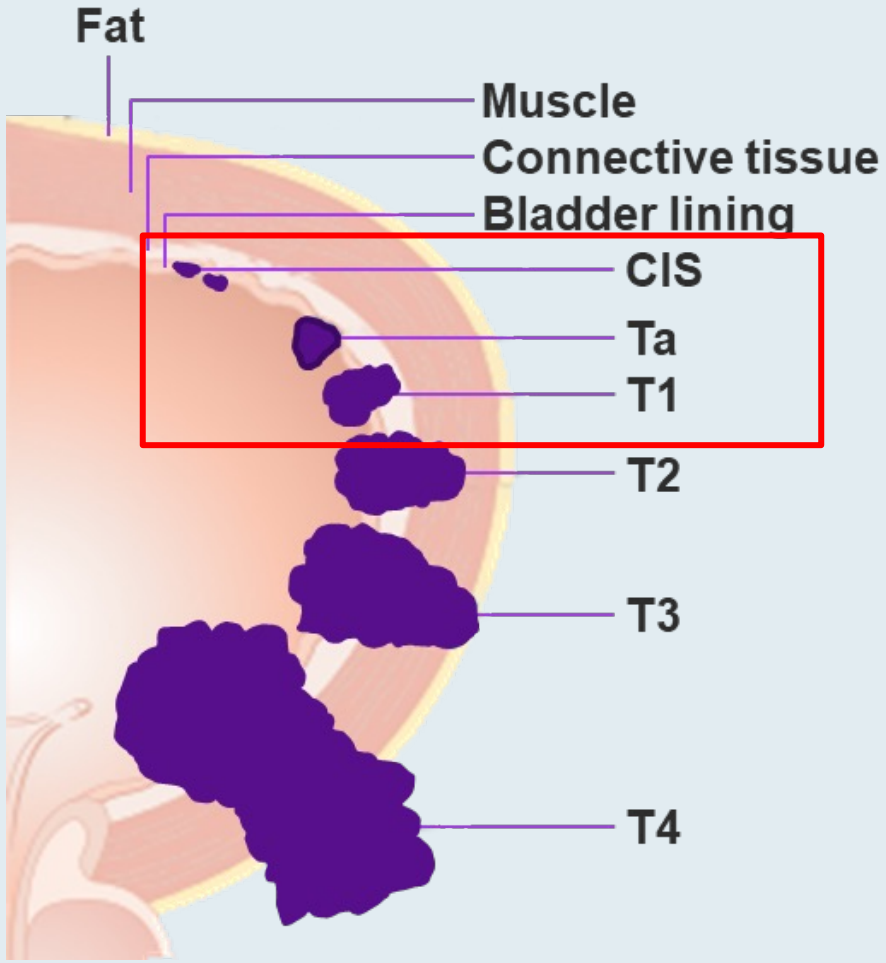
RTP RESEARCH TO PRACTICE

Appendix

Nonmetastatic UBC

High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC)

- High-risk (HR) NMIBC is defined as any carcinoma in situ (CIS), T1 tumor, and/or high-grade Ta tumor
- Standard-of-care therapy for HR NMIBC is TURBT and intravesical Bacillus Calmette-Guérin (BCG)
  - Although there is a high rate of complete response (70%) to initial therapy, most patients with high-risk disease do not maintain response
    - 30% of patients experience recurrence within 1 year
    - 40% of patients at high-risk progress to muscle-invasive disease
    - 20% - 30% of patients progress to metastatic disease
- BCG unresponsive disease – standard of care is cystectomy
- With the lack of a suitable comparator, single-arm designs testing novel agents are thought to be acceptable in the BCG-unresponsive population
- World-wide BCG shortage



Cumberbatch MGK et al. *Eur Urol* 2018;74:784-95. NCCN Guidelines: Bladder Cancer (Version 3.2024). Hemdan T et al. *J Urol* 2014;191:1244. Herr HW et al. *Urol Oncol* 2015;33:108.e1-4. Anastasiadis A et al. *Ther Adv Urol* 2012;4:13-32. Babjuk M et al. *Eur Urol* 2017;71:447-61.

Courtesy of Arjun V Balar, MD

Treatment Options for Nonmetastatic Bladder Cancer

Treatment options

~75% Of newly diagnosed bladder cancers are NMIBC

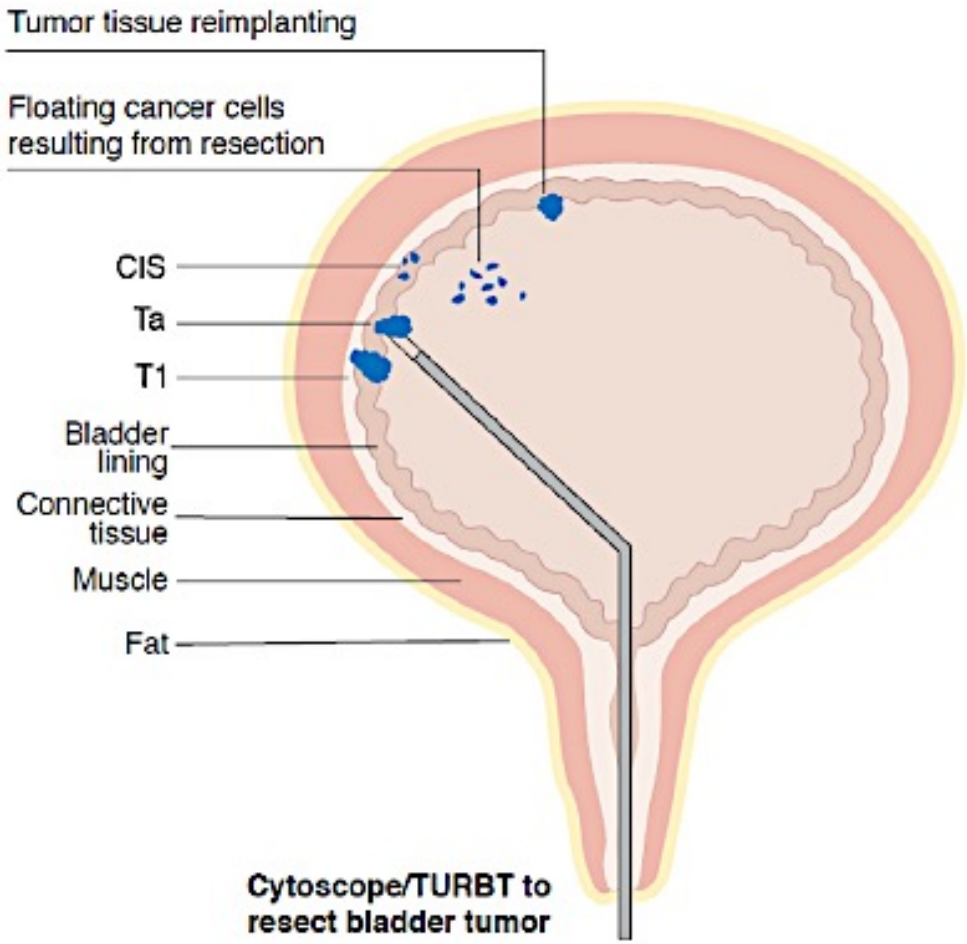
Current treatment options for patients with high-risk NMIBC include:

Preferred options per guidelines

- **TURBT** (also diagnostic)
- **BCG** following TURBT is the standard of care

- **Chemotherapy** is an alternative if BCG is not possible
- **Radical cystectomy** for very high-risk disease (associated with reduced quality of life)

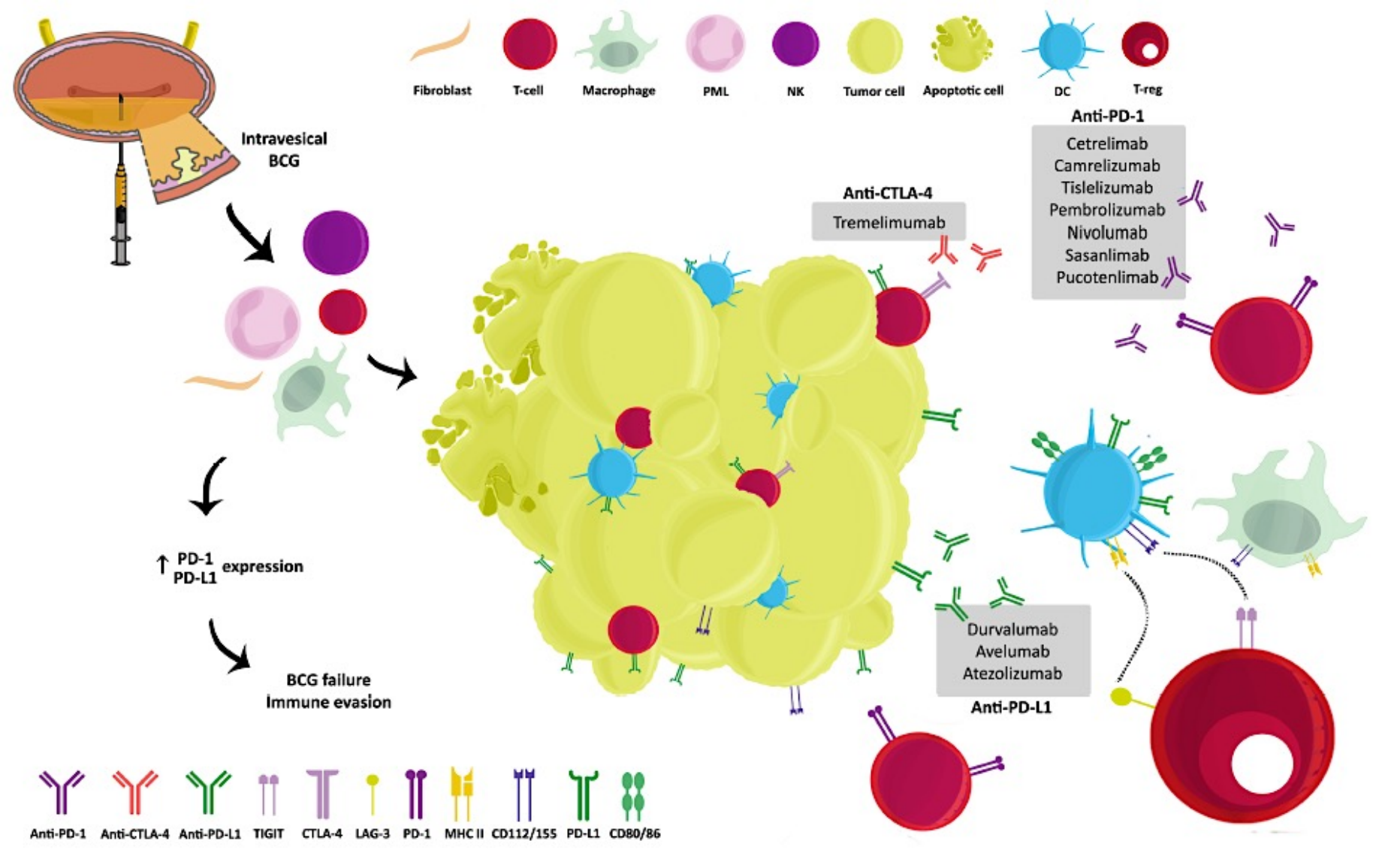
TURBT success is assessed by cytoscopy. There may still be residual disease and risk of tumor reimplantation



TURBT = transurethral resection of bladder tumor

Bedke J et al. *Urol Oncol* 2023 December;41(12):461-75.

Interplay Between Immune Checkpoint Inhibitors and BCG in NMIBC



Hannouneh ZA et al. *Cancer Med* 2023 December;12(24):21944-68.

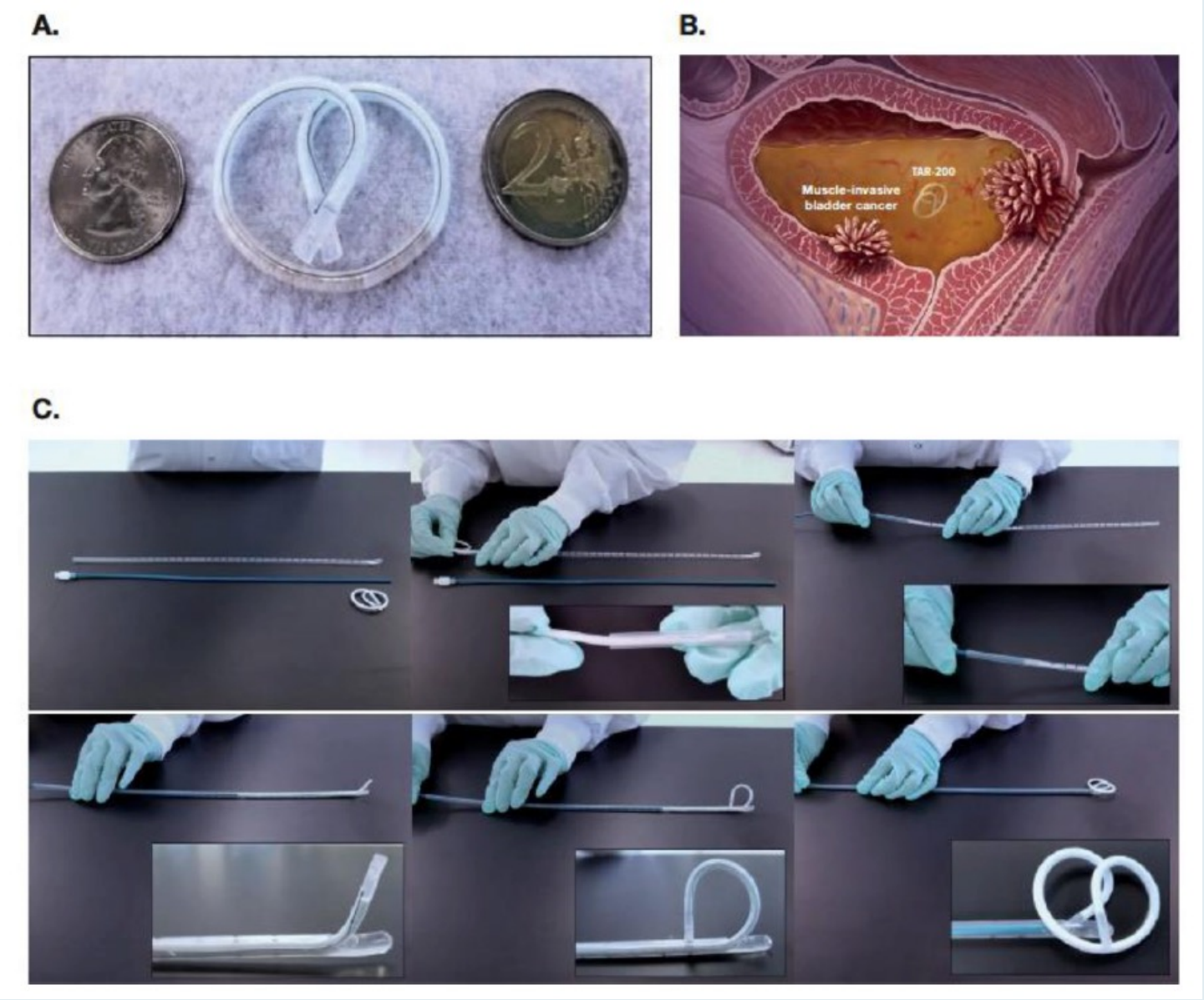
Key Ongoing Phase III Trials of Anti-PD-1/PD-L1 Antibodies for NMIBC

Protocol	n	Randomization	Estimated primary completion
ALBAN (NCT03799835)	516 (actual)	• **Atezolizumab + BCG** (induction and maintenance) • BCG alone (induction and maintenance)	April 2024
POTOMAC (NCT03528694)	1,018 (actual)	• **Durvalumab + BCG** (induction only) • **Durvalumab + BCG** (induction and maintenance) • BCG alone (induction and maintenance)	October 2024
KEYNOTE-676 (NCT03711032)	1,405 (estimated) A – 430 B – 975	<u>Cohort A – recurrent after BCG</u> • **Pembrolizumab + BCG** (induction and full maintenance) • BCG alone (induction and maintenance) <u>Cohort B – BCG-naïve</u> • **Pembrolizumab + BCG** (induction and reduced maintenance) • **Pembrolizumab + BCG** (induction and full maintenance) • BCG alone (induction and full maintenance)	December 2025

BCG = Bacillus Calmette-Guérin

www.clinicaltrials.gov. Accessed May 2024. Roupret M et al. ASCO 2019;Abstract TPS4589. DeSantis M et al. GU Cancers Symposium 2019;Abstract TPS500. Shore ND et al. GU Cancers Symposium 2024;Abstract TPS722. Kamat AM et al. GU Cancers Symposium 2022;Abstract TPS597.

Components of TAR-200



TAR-200, a gemcitabine-releasing intravesical system, is formed into a "pretzel"-like configuration within the bladder.

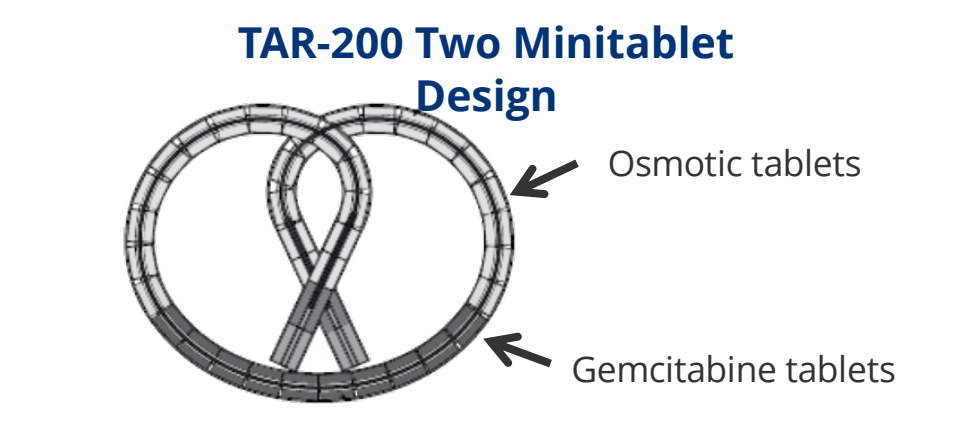
TAR-200 …

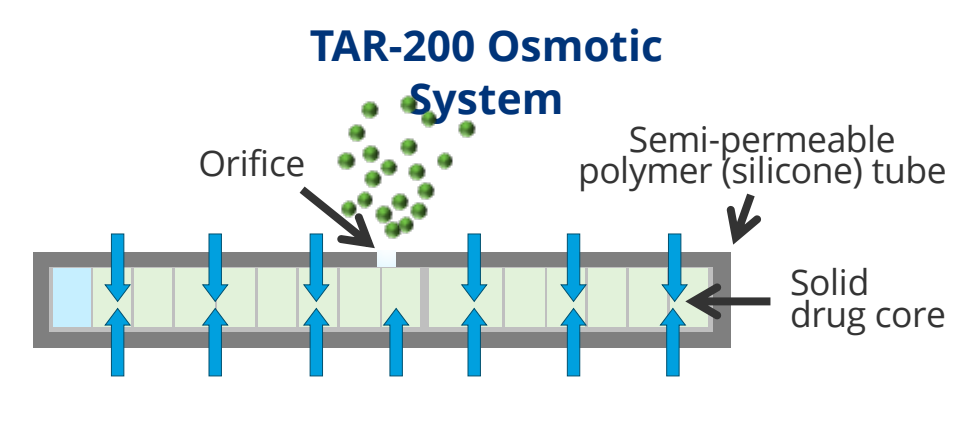
A. Consists of a small, flexible silicone tube filled with gemcitabine
B. Is designed to release drug directly inside the bladder over the indwelling period
C. Is inserted using a urinary placement catheter

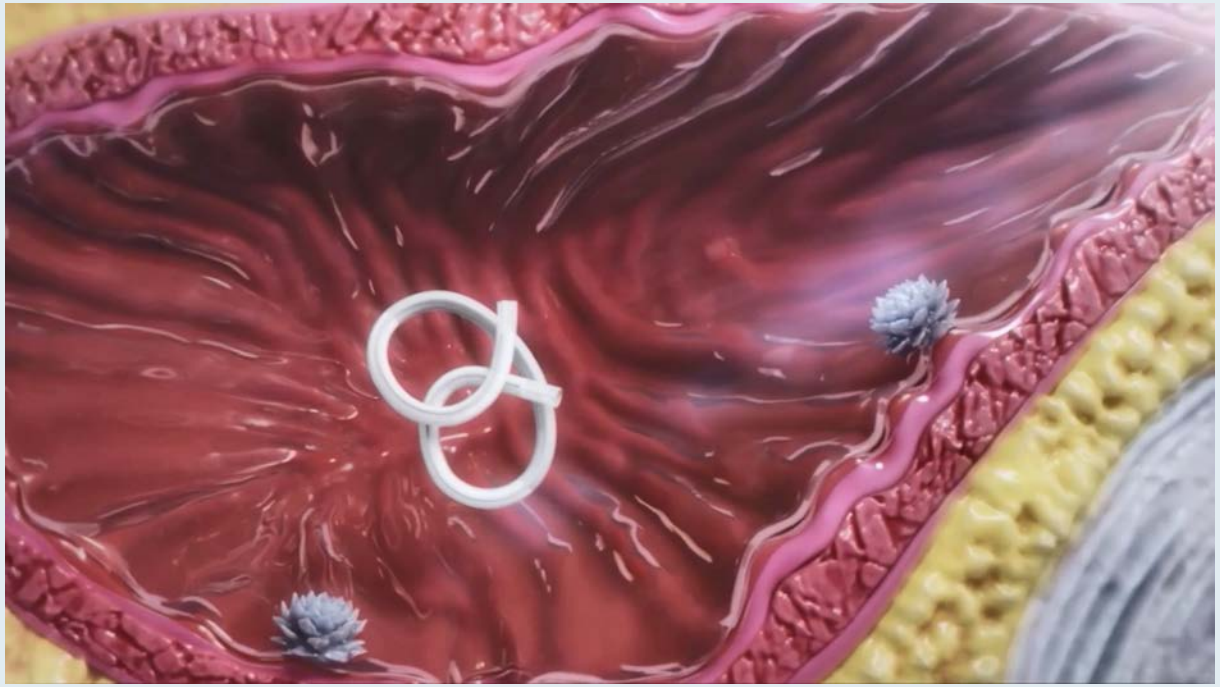
Daneshmand S et al. *Urol Oncol* 2022;40(7):344e1-9.

RTP RESEARCH TO PRACTICE

TAR-200: A Novel Drug Delivery System for Sustained Local Release of Gemcitabine in the Bladder







Grimberg DC, et al. *Eur Urol Focus* 2020;6:620-2; Daneshmand S, et al. *Urol Oncol* 2022;40:344.e1-344.e9; Tyson MD, et al. *J Urol* 2023:209:890-900.

Courtesy of Sia Daneshmand, MD

RTP RESEARCH TO PRACTICE

SunRISe: Ongoing Studies of TAR-200-Based Therapy for Bladder Cancer

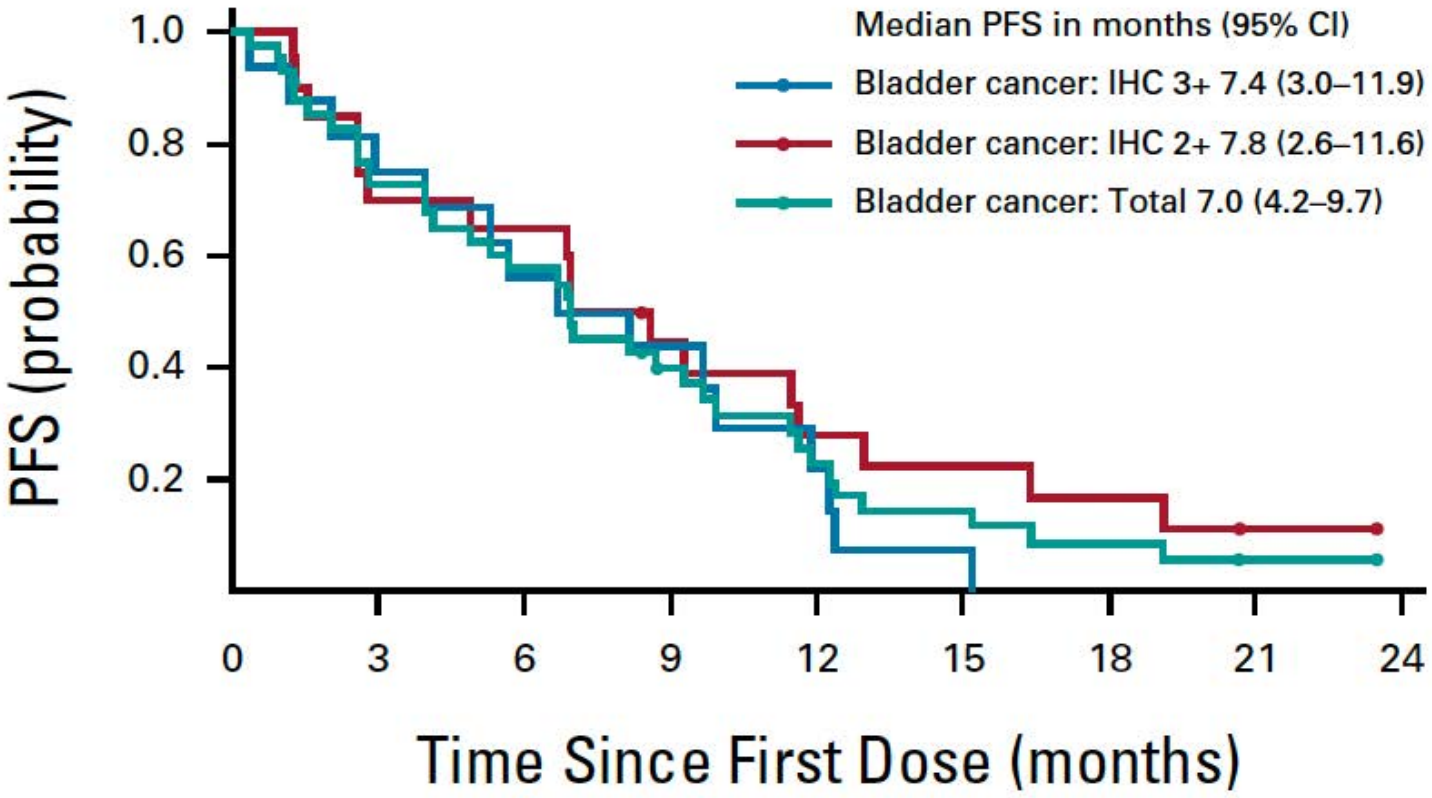
Protocol	Disease setting	n	Randomization	Primary endpoint	Estimated primary completion
SunRISe-1 (NCT04640623)	NMIBC unresponsive to BCG	200	• TAR-200 • TAR-200 + cetrelimab • Cetrelimab	CR	Nov 2026
SunRISe-2 (NCT04658862)	MIBC not receiving RC	550	• TAR-200 + cetrelimab • CRT	BI-EFS	Dec 2026
SunRISe-3 (NCT05714202)	BCG-naïve high-risk NMIBC	1,050	• TAR-200 • TAR-200 + cetrelimab • BCG	EFS	Sep 2029
SunRISe-4 (NCT04919512)	MIBC scheduled for RC	160	• TAR-200 + cetrelimab • Cetrelimab	pCR	Dec 2026

NMIBC = non-muscle-invasive bladder cancer; MIBC = muscle-invasive bladder cancer; BCG = Bacillus Calmette-Guérin; CR = complete response; RC = radical cystectomy; CRT = chemoradiation therapy; BI-EFS = bladder intact event-free survival; pCR = pathologic CR

www.clinicaltrials.gov. Accessed May 2024. Necchi A et al. ESMO 2023;Abstract LBA105. Williams SB et al. ASCO 2021;Abstract TPS4586. Necchi A et al. ESMO 2023;Abstract 2407TiP. Psutka SP et al. GU Cancers Symposium 2023;Abstract TPS584.

HER2-Positive UBC

DESTINY-PanTumor02: Progression-Free Survival (PFS) Outcomes in Bladder Cancer

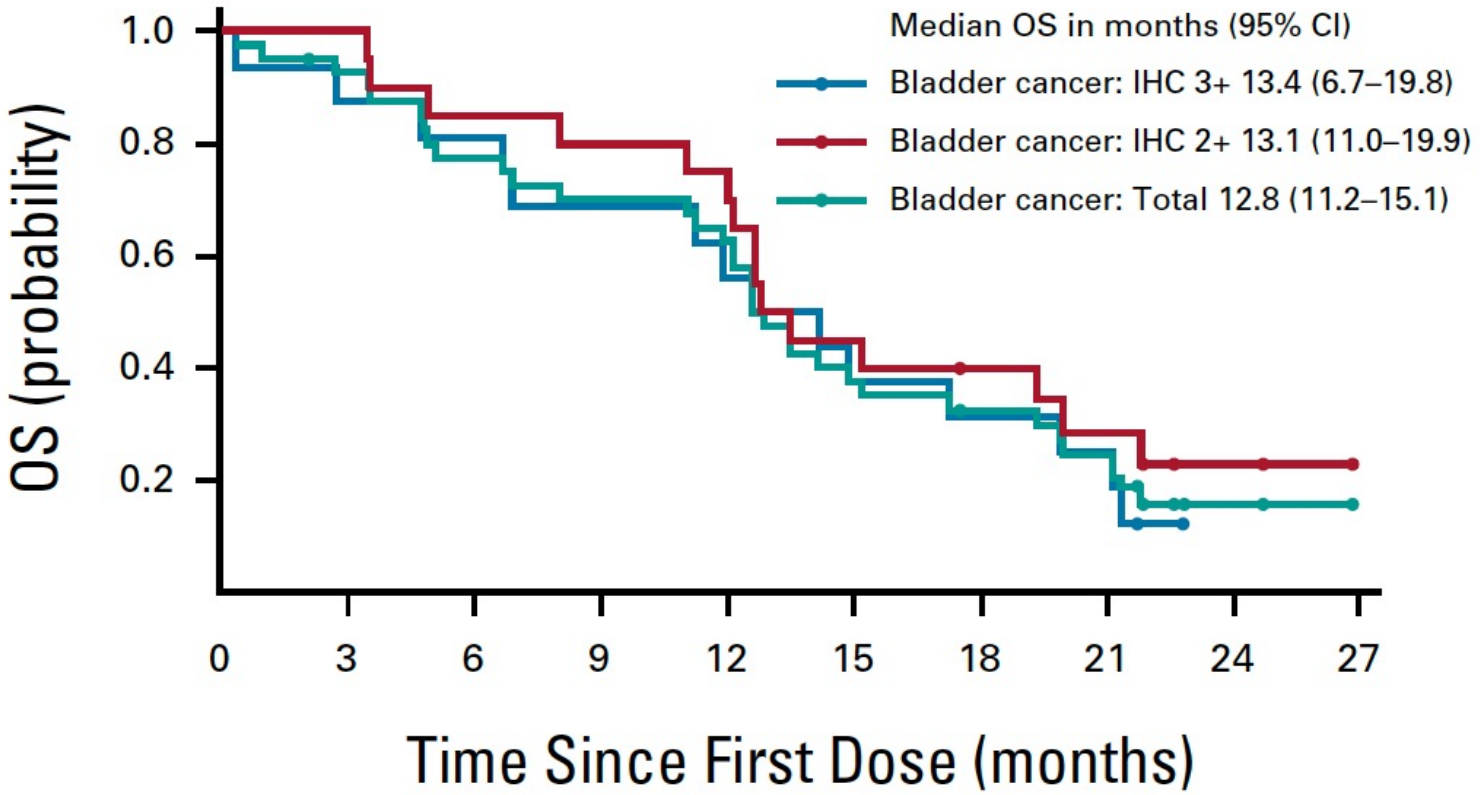


No. at risk:

Bladder cancer: IHC 3+	16	12	9	6	3	1	0		
Bladder cancer: IHC 2+	20	14	13	8	5	4	3	1	0
Bladder cancer: Total	41	29	23	14	8	5	3	1	0

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

DESTINY-PanTumor02: Overall Survival (OS) Outcomes in Bladder Cancer



No. at risk:										
Bladder cancer: IHC 3+	16	14	13	11	9	6	5	4	0	
Bladder cancer: IHC 2+	20	20	17	16	15	9	7	5	2	0
Bladder cancer: Total	41	37	31	28	25	15	12	9	2	0

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

Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A Multitumor CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Thank you for joining us!

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

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

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