Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Urothelial Bladder Carcinoma

Andrea Apolo, MD
Genitourinary Medical Oncologist
Specialist, Bladder Cancer Research
Bethesda, Maryland

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Commercial Support

This activity is supported by an educational grant from Astellas and Seagen Inc.

Dr Love — Disclosures

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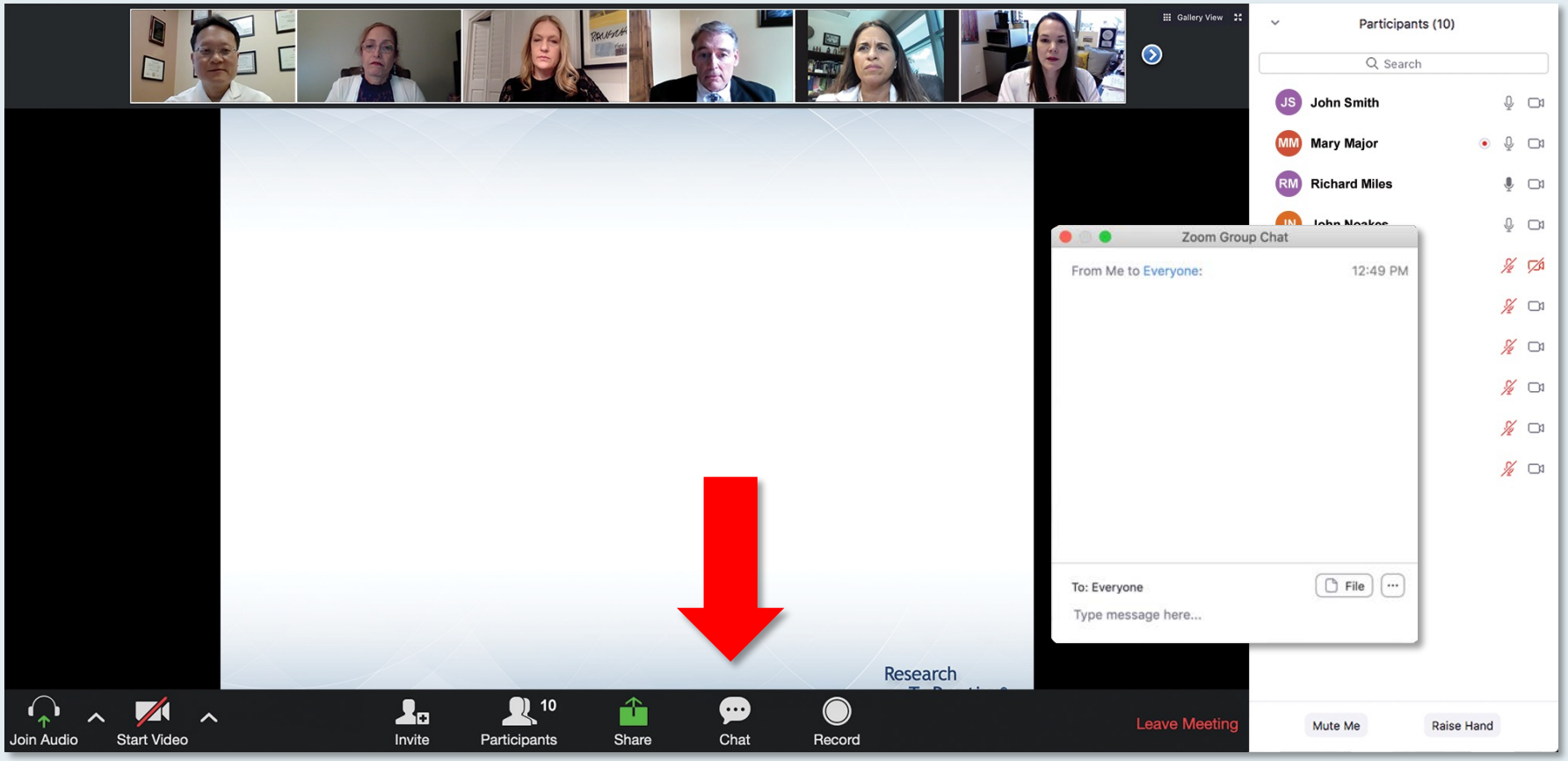
Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Apolo — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



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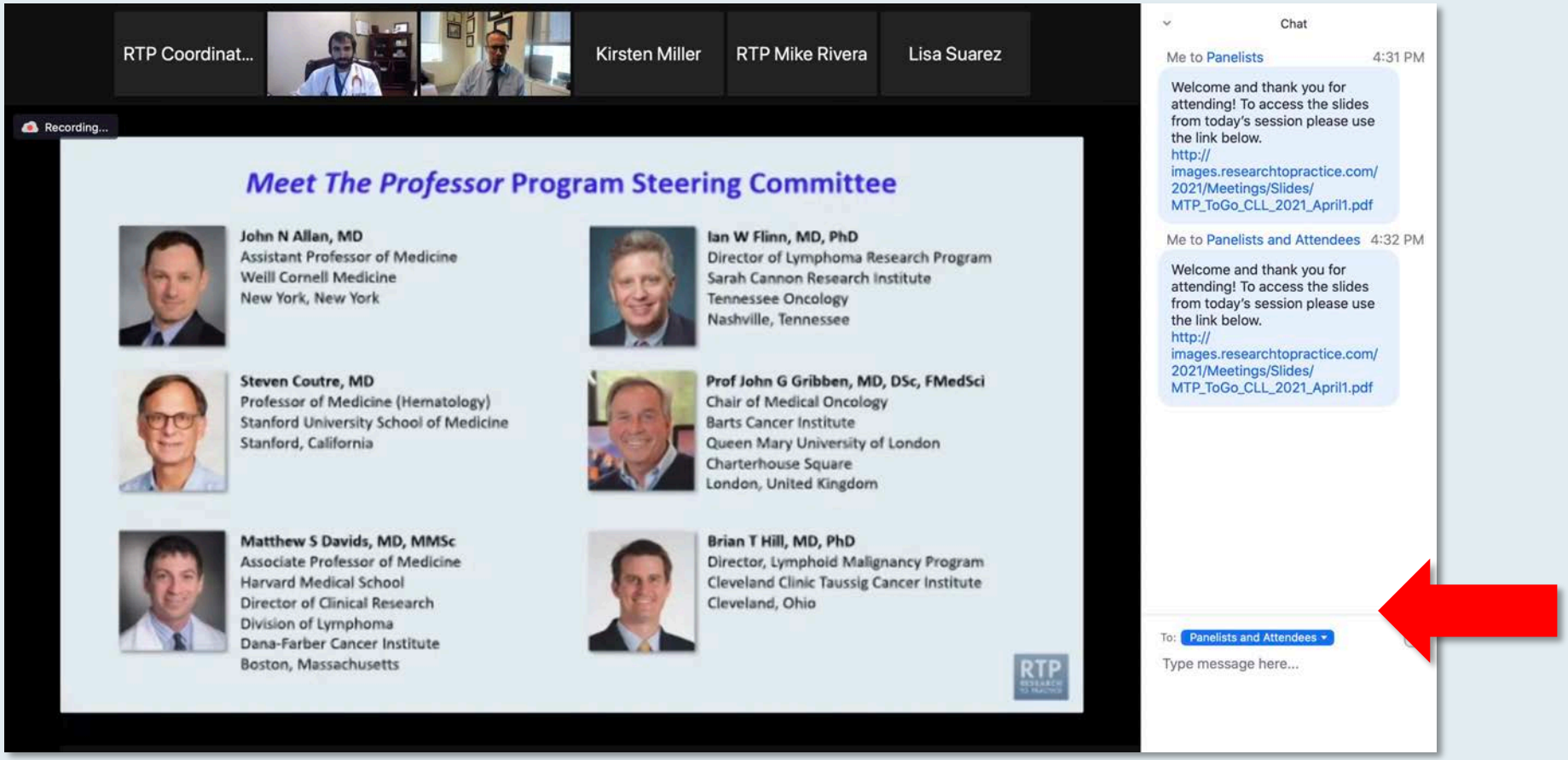

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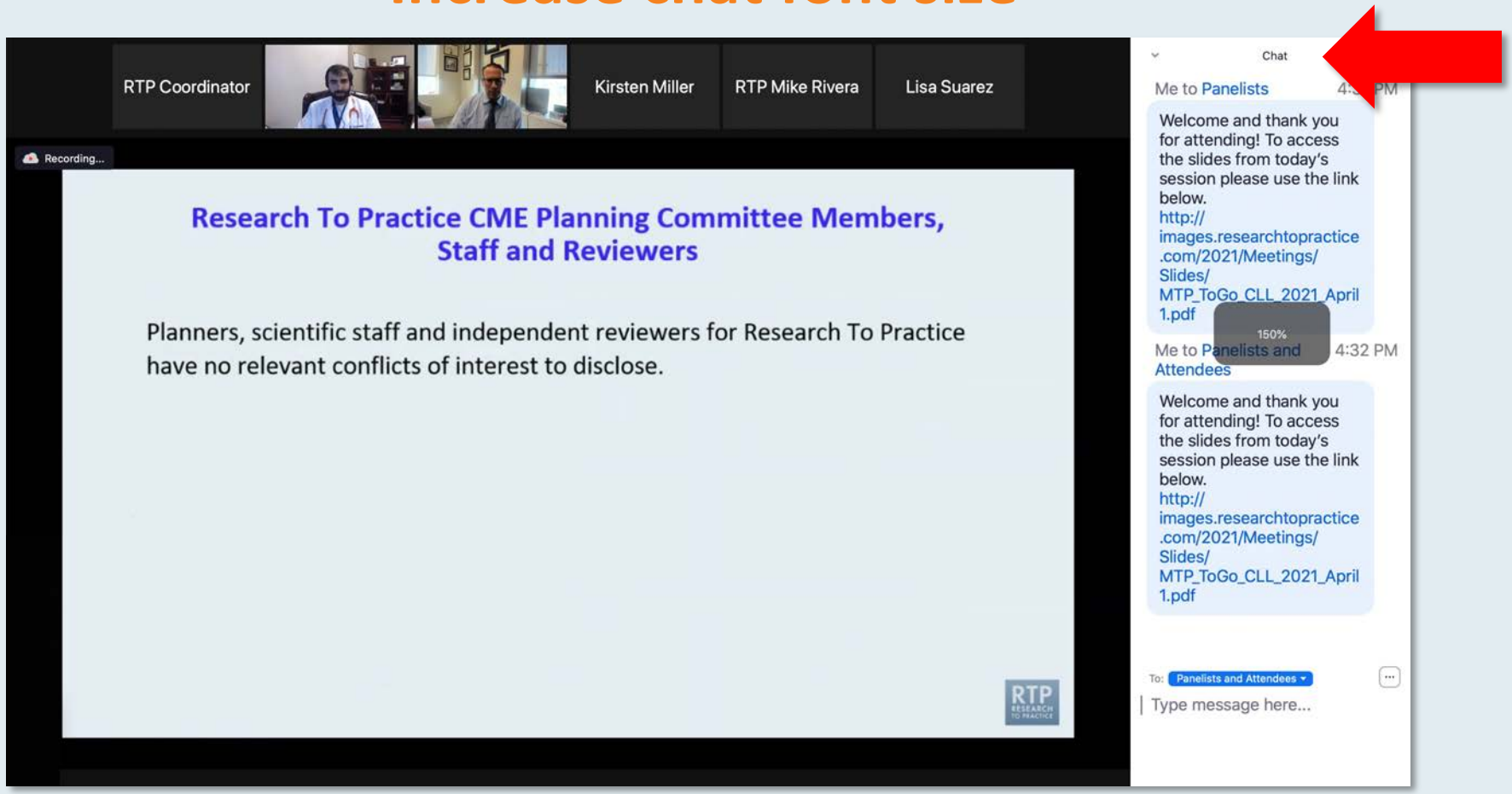

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You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Genitourinary Cancers from the 2021 ASCO Annual Meeting

DR ARJUN BALAR

NYU PERLMUTTER CANCER CENTER

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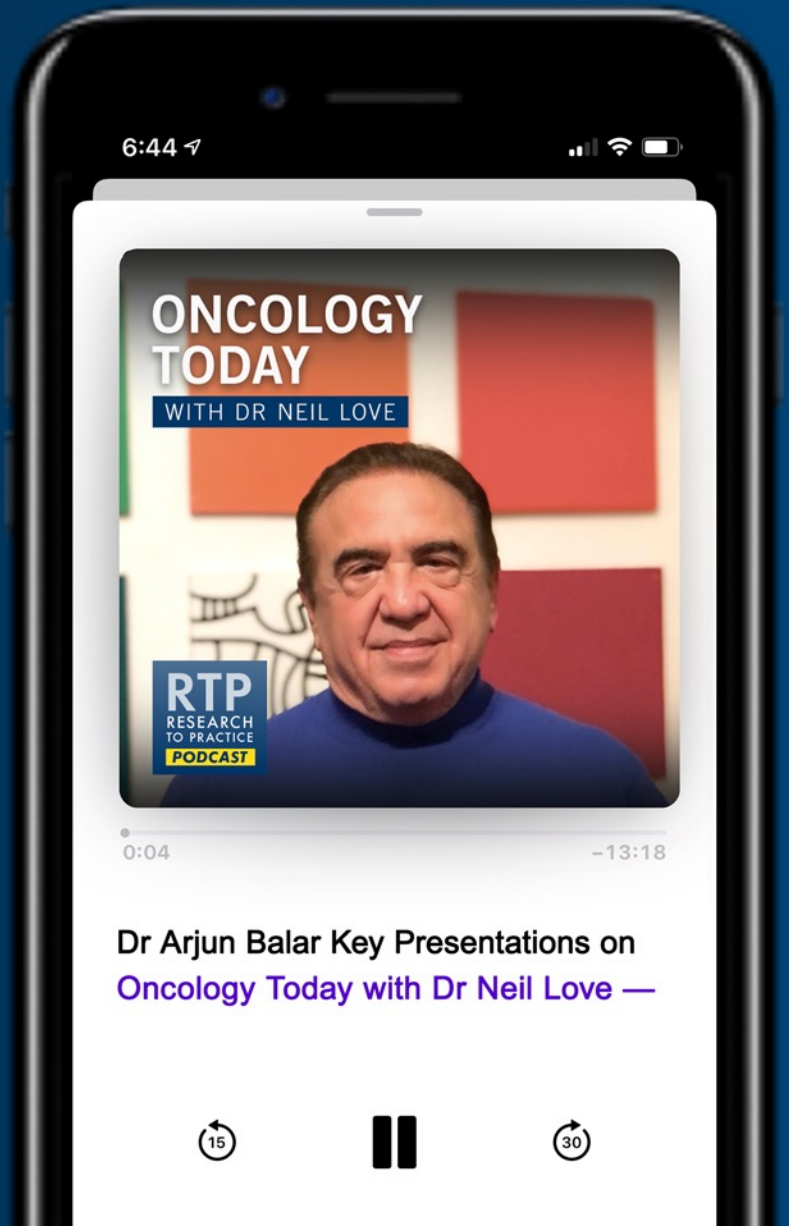

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, November 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Adam M Brufsky, MD, PhD

Moderator

Neil Love, MD

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Key Considerations in the Optimal Clinical Care of Patients with Small Cell Lung Cancer

A CME/MOC-Accredited Virtual Event

Thursday, November 4, 2021
5:00 PM – 6:00 PM ET

Faculty

Anne Chiang, MD, PhD
David R Spigel, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Monday, November 8, 2021
5:00 PM – 6:00 PM ET

Faculty
Keith W Pratz, MD

Moderator
Neil Love, MD

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Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Tuesday, November 9, 2021
5:00 PM – 6:00 PM ET

Faculty

Simon Chowdhury, MD, PhD

Moderator

Neil Love, MD

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VIRTUAL MOLECULAR TUMOR BOARD
Optimizing Biomarker-Based Decision-Making for Patients with Non-Small Cell Lung Cancer with EGFR Mutations or with Other Oncogene-Addicted Lung Cancers

A 2-Part CME/MOC-Accredited Webinar Series

Thursday, November 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Marc Ladanyi, MD
Andrew J McKenzie, PhD
Helena Yu, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Monday, November 15, 2021
5:00 PM – 6:00 PM ET

Faculty

Christopher R Flowers, MD, MS

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Wednesday, November 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Kevin Kalinsky, MD, MS

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

Andrea Apolo, MD
Genitourinary Medical Oncologist
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Associate Professor
Director, Genitourinary
Oncology Program
Taussig Cancer Institute, Cleveland Clinic
Cleveland, Ohio

Jonathan E Rosenberg, MD
Chief, Genitourinary Medical Oncology Service
Division of Solid Tumor Oncology
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Memorial Sloan Kettering Cancer Center
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Guru Sonpavde, MD
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Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Moderator
Neil Love, MD
Research To Practice
Miami, Florida

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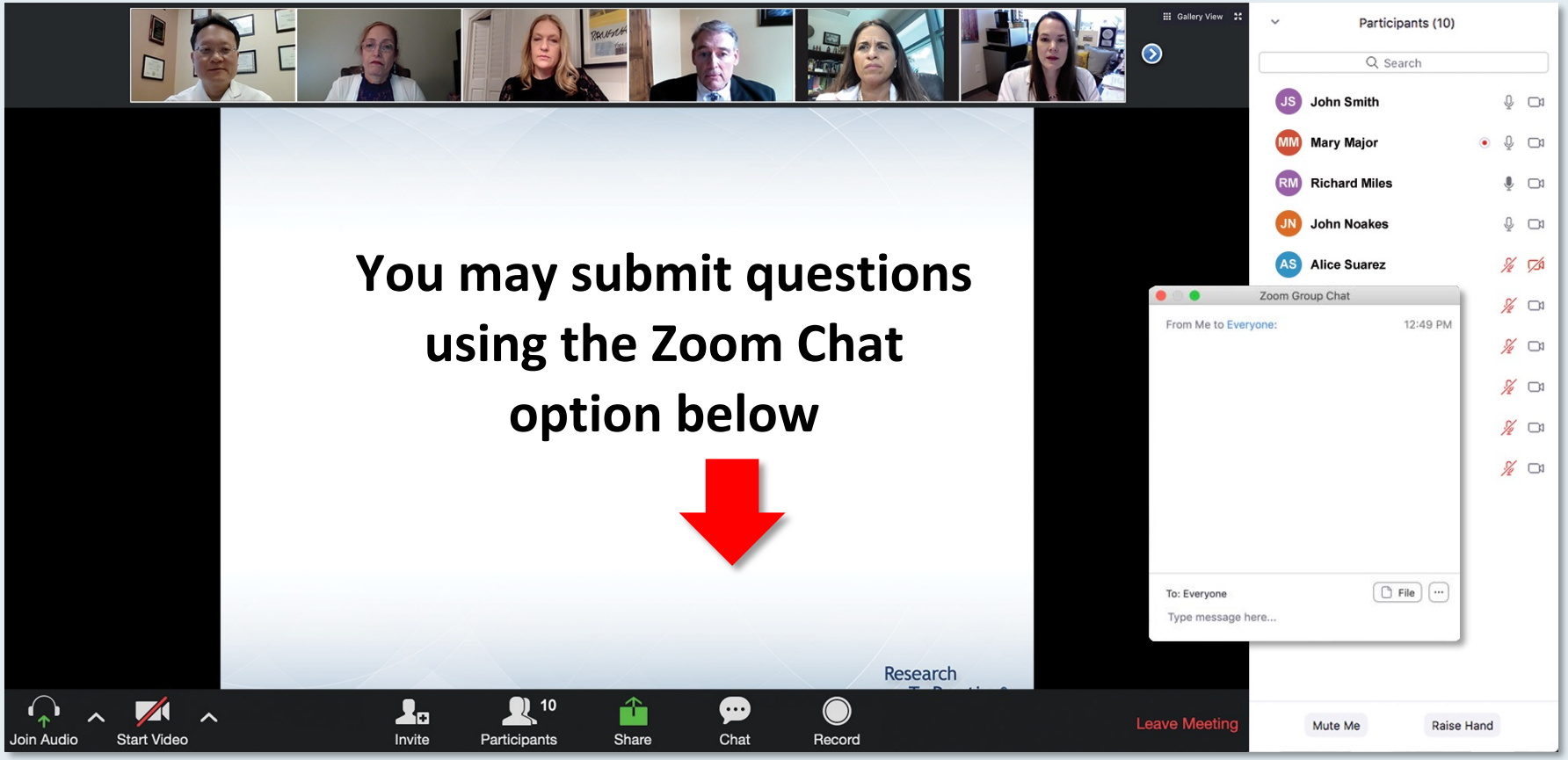

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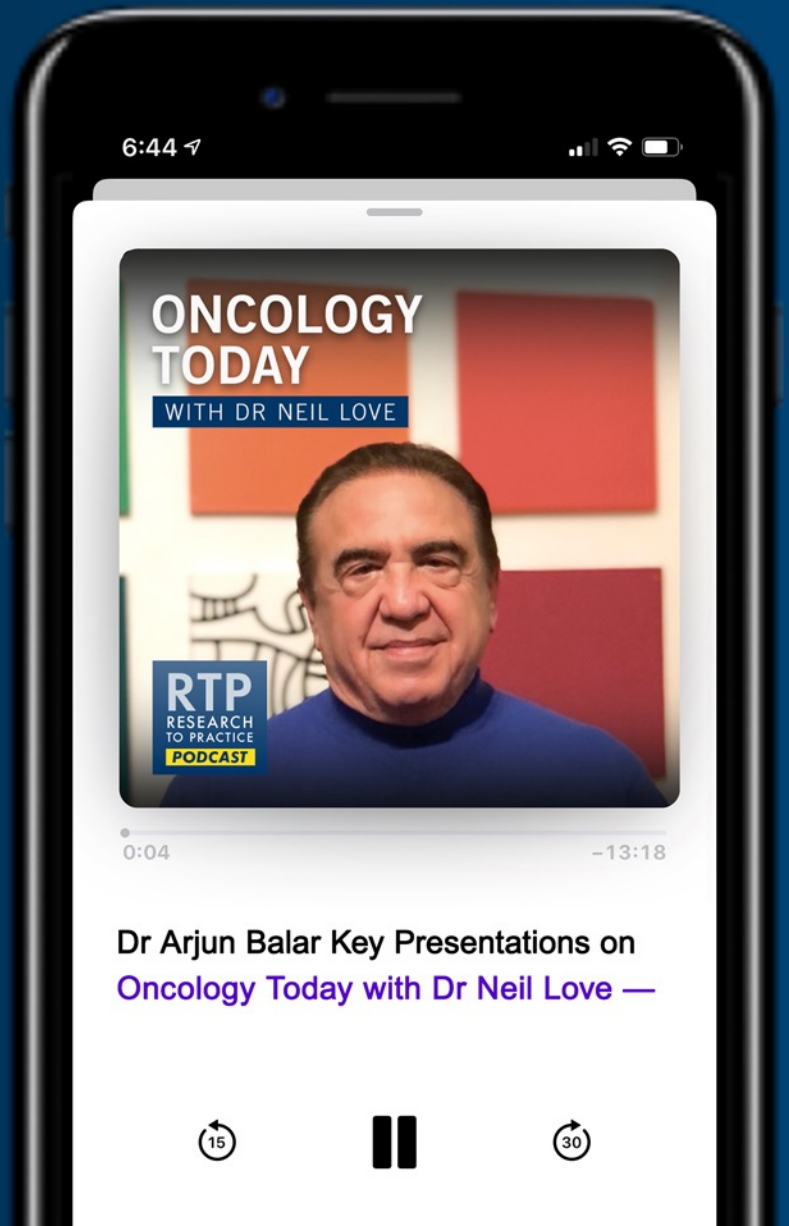

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Mamta Choksi, MD
Florida Cancer Specialists and Research Institute
New Port Richey, Florida

Ranju Gupta, MD
Attending Physician
LVPG Hematology Oncology Associates
Lehigh Valley Health Network
Bethlehem, Pennsylvania

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

Nataliya Mar, MD
Assistant Clinical Professor
Division of Hematology/Oncology
University of California, Irvine
Irvine, California

Elizabeth Guancial, MD
Florida Cancer Specialists and Research Institute
Sarasota, Florida

Ferdy Santiago, MD
Florida Cancer Specialists and Research Institute
Naples, Florida

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Meet The Professor with Dr Apolo

MODULE 1: Timing and Sequencing of Therapies for Metastatic Disease

MODULE 2: PET and MRI Imaging

MODULE 3: Case Presentations

- Dr Mar: A 64-year-old woman with muscle-invasive bladder cancer
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Uncertainties in the Timing and Sequencing of Therapies for Metastatic Disease

Andrea B. Apolo, MD
Investigator and Lasker Scholar
Chief, Bladder Cancer Section
Genitourinary Malignancies Branch
Center for Cancer Research
National Cancer Institute
National Institutes of Health
February 12, 2021

Presented By Andrea Apolo at 2021 Genitourinary Cancers Symposium

Advanced/Metastatic Bladder Cancer

Genitourinary Cancers Symposium #GU21

Summary of Timing and Sequencing of Therapies

First-Line

Cisplatin-eligible

- Cisplatin + gemcitabine
- Dose-dense methotrexate + vinblastine + doxorubicin + cisplatin (ddMVAC)

Cisplatin-ineligible

- Carboplatin + gemcitabine

PD-L1 High

- Atezolizumab
- Pembrolizumab

Consider tumor sequencing for actionable mutations such as FGF 2/3 alterations

Maintenance

May be considered in patients who achieve a response to platinum-based chemotherapy

- Avelumab
- Pembrolizumab
- Atezolizumab
- Nivolumab
- Durvalumab

or Second-Line

- Atezolizumab
- Nivolumab
- Durvalumab
- Avelumab
- Pembrolizumab

FGFR3 2/3 genetic alterations

- Erdafitinib

Third-Line

FGFR3 2/3 genetic alterations

- Erdafitinib
- Enfortumab Vedotin

Fourth-Line

- Sacituzumab govitecan (when FDA approved)
- Clinical trial
- Paclitaxel or docetaxel

Presented by Andrea B. Apolo, MD

Presented By Andrea Apolo at 2021 Genitourinary Cancers Symposium

Advanced/Metastatic Bladder Cancer

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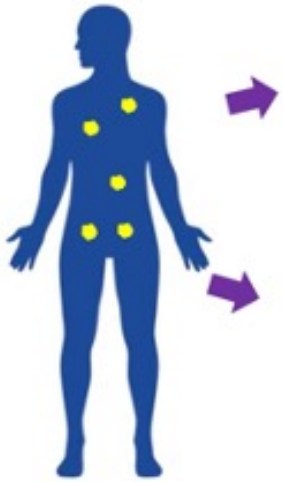

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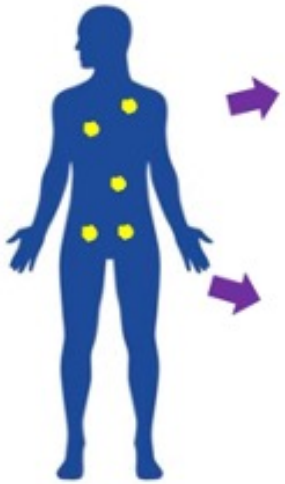

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JAMA Network Open

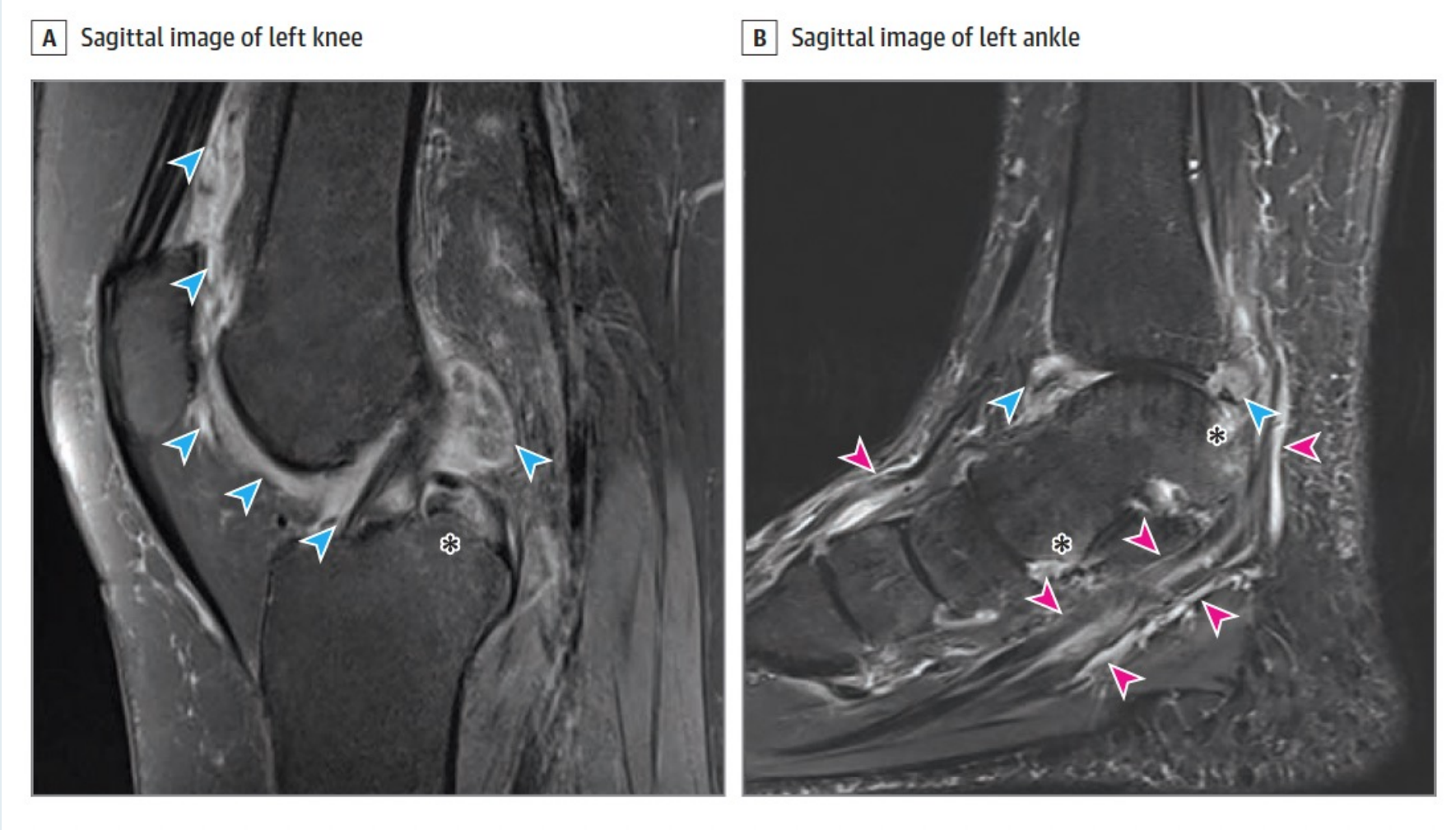
JAMA Netw Open 2020;3(2):e200032

Original Investigation | Oncology

Use of Magnetic Resonance Imaging to Identify Immune Checkpoint Inhibitor–Induced Inflammatory Arthritis

Ananta Subedi, MD; Sandra G. Williams, MD, PhD; Lawrence Yao, MD; Suresh Maharjan, MD; Julius Strauss, MD; Elad Sharon, MD; Anish Thomas, MD; Andrea B. Apolo, MD; Pravitt Gourh, MD; Sarfaraz A. Hasni, MD; James L. Gulley, MD, PhD; Mariana J. Kaplan, MD; James D. Katz, MD; Sarthak Gupta, MD

Magnetic Resonance Image of the Knee and Ankle of an Individual with Cervical Cancer and Immune Checkpoint Inhibitor–Induced Inflammatory Arthritis



Subedi A et al. *JAMA Netw Open* 2020;3(2):e200032

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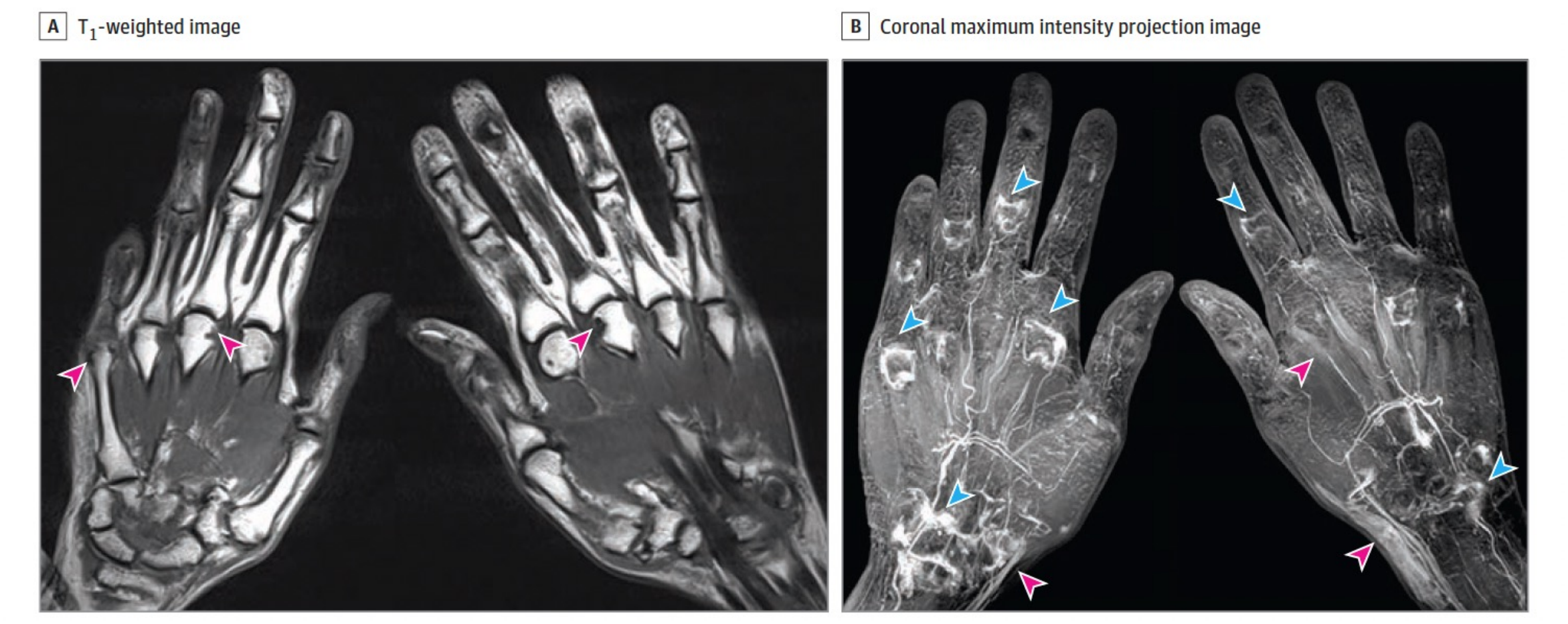
Magnetic Resonance Image of Bilateral Hands of an Individual with Thyroid Cancer and Inhibitor–Induced Inflammatory Arthritis



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ELSEVIER

Urologic Oncology: Seminars and Original Investigations 39 (2021) 787.e17–787.e21

UROLOGIC ONCOLOGY

Original Article

Clinical value of ^{18}FDG PET/MRI in muscle-invasive, locally advanced, and metastatic bladder cancer

Ali Cahid Civelek, M.D.[a,#], Scot A. Niglio, M.D., M.S.[b,#], Ashkan A. Malayeri, M.D., M.S.[a,b], Jeffrey Lin, M.D.[b], Sandeep Gurram, M.D.[c], Heather J. Chalfin, M.D.[c], Baris Turkbey, M.D.[a], Vladimir Valera, M.D. Ph.D.[c], Seth M. Steinberg, Ph.D.[d], Andrea B. Apolo, M.D.[b,*]

[a] *Radiology and Imaging Sciences Department, Nuclear Medicine Division, National Institutes of Health, Bethesda, MD*
[b] *Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD*
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Received 31 December 2020; received in revised form 16 March 2021; accepted 13 April 2021

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Case Presentation – Dr Mar: A 64-year-old woman with muscle-invasive bladder cancer

Dr Nataliya Mar

- Presented with intermittent, painless gross hematuria
- CT A/P: Masses near right UVJ and bladder neck
- Cystoscopy and TURBT: High-grade urothelelial carcinoma invasive into the muscularis propria
- PET: Negative for adenopathy, distant metastases; GFR > 60
- Neoadjuvant cisplatin-based chemotherapy → Radical cystectomy (pT2pN2) → Close surveillance

Questions

- What is the best next step in her management?
- Would using PD-1/PD-L1 inhibitor therapy be appropriate for this patient?
- In the third-line setting for patients with metastatic urothelial carcinoma and an FGFR mutation, what treatment would you choose?

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Case Presentation – Dr Gandhi: A 69-year-old man with muscle-invasive UBC

Dr Sunil Gandhi

- Presented with hematuria and TURBT revealed 8-10-cm muscle-invasive bladder cancer
- Neoadjuvant gemcitabine/cisplatin
- Patient is scheduled for radical cystectomy

Questions

- Is adjuvant nivolumab worth the cost and toxicities?
- What are your thoughts as to why a recent trial of adjuvant atezolizumab for muscle-invasive bladder cancer did not meet its primary endpoint while the trial of adjuvant nivolumab was positive?

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Case Presentation – Dr Gupta: A 67-year-old man with metastatic bladder cancer

Dr Ranju Gupta

- 2017: Muscle-invasive bladder cancer, s/p gemcitabine/cisplatin and radical cystectomy
- 2019: Metastatic disease
- Patient intolerant to gemcitabine/cisplatin
- Pembrolizumab x 2 years → PD
- Enfortumab vedotin → PD within 6 months
- Sacituzumab govitecan, with grade 3 hypersensitivity reaction requiring EpiPen®, oxygen, steroids

Questions

- Have you seen hypersensitivity reactions to sacituzumab govitecan? Have you rechallenged patients with premedication, steroids, etc?

Case Presentation – Dr Guancial: A 69-year-old man with metastatic UBC – FGFR3 mutation, MSS, TMB low, PD-L1 negative

Dr Elizabeth Guancial

- Diagnosed with stage IV (pT3 cN2 cM0) right upper tract urothelial carcinoma with extensive retroperitoneal, retrocrural and left supraclavicular lymphadenopathy, and hepatic metastases
- Molecular analyses: FGFR3 mutation, PD-L1-negative, MSS, TMB-low
- Cisplatin/gemcitabine → 50% response
- Avelumab maintenance

Question

- Would you expect this patient to have less of a response to maintenance immune therapy given his next-generation sequencing profile?

Case Presentation – Dr Guancial: An 82-year-old man with metastatic UBC – FGFR mutation

Dr Elizabeth Guancial

- PMH: immune-related ulcerative colitis
- Presented with widespread metastatic disease, FGFR mutation-positive
- Carboplatin/gemcitabine → good response
- Rapid progression in the liver 3 months later
- Erdafitinib → 40% shrinkage in all tumors after 2 months of treatment
  - Issues with high phosphorus levels and working with a nutritionist to keep levels within range

Question

- For patients with a partial response on erdafitinib, how far do you push it with the hyperphosphatemia before dose reducing the drug?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Choksi: A 61-year-old woman with metastatic urothelial carcinoma – PD-L1 positive

Dr Mamta Choksi

- Followed by urologists for superficial bladder cancer since 2011
- 8/2021: Hematuria and blood clots → PET: Multiple lung, liver and osseous metastases, LAD
- Patient not interested in treatment with chemotherapy
- NGS: PD-L1-positive, TMB-low, MSS, FGFR wildtype, ATM and NTRAK negative
- Palliative RT to bladder for hematuria
- Hypercalcemia of malignancy → Zoledronic acid
- Single-agent atezolizumab, but hospitalized after 2 weeks with immunotherapy-related pneumonitis
  - High-dose steroids, with clinical improvement

Questions

- Would you consider rechallenging her with immunotherapy after she recovers from the pneumonitis?

Case Presentation – Dr Santiago: A 56-year-old man with metastatic urothelial carcinoma – PD-L1 negative

Dr Ferdy Santiago

- 1/2019 TURP: Invasive high-grade UBC, PD-L1-negative → palliative RT
- PET: Metastases to lung, LN, and bones
- Gemcitabine/cisplatin x 8 and zoledronic acid, with excellent response
- 12/2019 re-staging: Widespread PD
- Atezolizumab, with PD
- 3/2020: Enfortumab vedotin x 6 months, with improvement in disease, but developed rash
- 10/2020: Paclitaxel on PD → improvement in disease
- 3/2021: Worsening of sacral mass → gemcitabine/cisplatin + palliative RT

Questions

- How do you differentiate the rash associated with enfortumab vedotin versus some other type of paraneoplastic rash? How do you mitigate this rash?
- Are there any trials looking at enfortumab or other later-line therapies before the use of immunotherapy?

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Apolo

MODULE 1: Timing and Sequencing of Therapies for Metastatic Disease

MODULE 2: PET and MRI Imaging

MODULE 3: Case Presentations

- Dr Mar: A 64-year-old woman with muscle-invasive bladder cancer
- Dr Gandhi: A 69-year-old man with muscle-invasive urothelial bladder carcinoma (UBC)
- Dr Gupta: A 67-year-old man with metastatic bladder cancer
- Dr Guancial: A 69-year-old man with metastatic UBC – FGFR3 mutation, MSS, TMB low, PD-L1 negative
- Dr Guancial: An 82-year-old man with metastatic UBC – FGFR mutation
- Dr Choksi: A 61-year-old woman with metastatic urothelial carcinoma – PD-L1 positive
- Dr Santiago: A 56-year-old man with metastatic urothelial carcinoma – PD-L1 negative

MODULE 4: Journal Club with Dr Apolo

MODULE 5: Faculty Survey

MODULE 6: Reference Appendix

RTP
RESEARCH
TO PRACTICE

Journal Club with Dr Apolo

Giannarini G et al. **Urologists, you'll never walk alone! How novel immunotherapy and modern imaging may change the management of non-muscle-invasive bladder cancer.** *Eur Urol Oncol* 2021;[Online ahead of print].

Girardi DM et al. **Systemic therapy in bladder preservation.** *Urol Oncol* 2020;[Online ahead of print].

Kelly K et al. **Efficacy and immune-related adverse event associations in avelumab-treated patients.** *J Immunother Cancer* 2020;8(2):e001427.

Cordes LM et al. **Neurotoxicities associated with checkpoint inhibitors: Two case reports and a review of the literature.** *Clin Case Rep* 2019;8(1):24-32.

Noble CW et al. **Ocular adverse events following use of immune checkpoint inhibitors for metastatic malignancies.** *Ocul Immunol Inflamm* 2020;28(6):854-9.

RTP RESEARCH TO PRACTICE

Journal Club with Dr Apolo (Continued)

Saoud R et al. **Rapidly progressing urothelial carcinoma due to a rare TP53 (p.arg110pro) mutation: A case report and review of the literature.** *Res Rep Urol* 2021;13:181-4.

Sonpavde G et al. **Five-factor prognostic model for survival of post-platinum patients with metastatic urothelial carcinoma receiving PD-L1 inhibitors.** *J Urol* 2020;204(6):1173-9.

Meet The Professor with Dr Apolo

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RTP
RESEARCH
TO PRACTICE

Current and Emerging Treatment Strategies for Patients with Nonmetastatic Urothelial Bladder Cancer (UBC)

In general, would you recommend pembrolizumab to a 65-year-old patient with BCG-unresponsive non-muscle-invasive UBC who is otherwise healthy and prefers not to undergo cystectomy?

 Dr Apolo	No
 Dr Gupta	Yes
 Dr Rosenberg	No
 Dr Sonpavde	Yes

RTP
RESEARCH
TO PRACTICE

In general, would you recommend pembrolizumab to a 65-year-old patient with BCG-unresponsive non-muscle-invasive UBC who has significant comorbidities and is not a candidate for cystectomy?

 Dr Apolo	Yes
 Dr Gupta	Yes
 Dr Rosenberg	Yes
 Dr Sonpavde	No

RTP
RESEARCH
TO PRACTICE

A 65-year-old man receives neoadjuvant dose-dense MVAC for muscle-invasive UBC and undergoes cystectomy, which reveals significant residual disease and a positive pelvic lymph node. PD-L1 = 80%. Regulatory and reimbursement issues aside, what adjuvant systemic therapy, if any, would you recommend?

 Dr Apolo	Nivolumab
 Dr Gupta	Nivolumab
 Dr Rosenberg	Nivolumab
 Dr Sonpavde	Nivolumab

MVAC = methotrexate/vinblastine/doxorubicin/cisplatin

RTP RESEARCH TO PRACTICE

A 65-year-old man receives neoadjuvant dose-dense MVAC for muscle-invasive UBC and undergoes cystectomy, which reveals small amounts of residual disease and negative pelvic lymph nodes. PD-L1 = 80%. Regulatory and reimbursement issues aside, what adjuvant systemic therapy, if any, would you recommend?

 Dr Apolo	Nivolumab
 Dr Gupta	None
 Dr Rosenberg	None
 Dr Sonpavde	Nivolumab

RTP RESEARCH TO PRACTICE

Optimizing the Selection and Sequencing of Therapy for Patients with Metastatic UBC

RTP
RESEARCH
TO PRACTICE

What would be your preferred first-line treatment regimen for a 65-year-old patient with de novo metastatic UBC?

 Dr Apolo	Cisplatin/gemcitabine → maintenance avelumab
 Dr Gupta	Cisplatin/gemcitabine → maintenance avelumab
 Dr Rosenberg	Cisplatin/gemcitabine
 Dr Sonpavde	Cisplatin/gemcitabine → maintenance avelumab

RTP RESEARCH TO PRACTICE

What would be your preferred first-line treatment regimen for an 80-year-old patient with de novo metastatic UBC who is not a candidate for cisplatin-based chemotherapy?

 Dr Apolo	Carboplatin/gemcitabine → maintenance avelumab
 Dr Gupta	Carboplatin/gemcitabine → maintenance avelumab
 Dr Rosenberg	Carboplatin/gemcitabine → maintenance avelumab
 Dr Sonpavde	Carboplatin/gemcitabine → maintenance avelumab

RTP RESEARCH TO PRACTICE

What would you generally recommend for a 65-year-old patient who experiences disease recurrence in the liver 9 months after cystectomy and adjuvant gemcitabine/cisplatin for muscle-invasive FGFR wild-type UBC?

 Dr Apolo	Pembrolizumab
 Dr Gupta	Pembrolizumab
 Dr Rosenberg	Enfortumab vedotin
 Dr Sonpavde	Pembrolizumab

RTP RESEARCH TO PRACTICE

What would you generally recommend for a 65-year-old patient who experiences disease recurrence in the liver 9 months after cystectomy and adjuvant nivolumab for muscle-invasive FGFR wild-type UBC?

 Dr Apolo	Gemcitabine/cisplatin
 Dr Gupta	Enfortumab vedotin
 Dr Rosenberg	Enfortumab vedotin
 Dr Sonpavde	Enfortumab vedotin

RTP RESEARCH TO PRACTICE

What would you generally recommend for a 65-year-old patient who experiences disease recurrence in the liver 9 months after cystectomy and adjuvant gemcitabine/cisplatin for muscle-invasive UBC who is found to have an FGFR3 mutation?

 Dr Apolo	Pembrolizumab
 Dr Gupta	Pembrolizumab
 Dr Rosenberg	Erdafitinib
 Dr Sonpavde	Erdafitinib

RTP RESEARCH TO PRACTICE

What would you generally recommend for a 65-year-old patient who experiences disease recurrence in the liver 9 months after cystectomy and adjuvant nivolumab for muscle-invasive UBC who is found to have an FGFR3 mutation?

 Dr Apolo	Cisplatin/gemcitabine
 Dr Gupta	Erdafitinib
 Dr Rosenberg	Cisplatin/gemcitabine
 Dr Sonpavde	Erdafitinib

RTP RESEARCH TO PRACTICE

What would you generally recommend as second-line therapy for a 65-year-old patient with FGFR wild-type UBC metastatic to the liver whose disease progresses on first-line cisplatin/gemcitabine?

 Dr Apolo	Pembrolizumab
 Dr Gupta	Pembrolizumab
 Dr Rosenberg	Pembrolizumab
 Dr Sonpavde	Pembrolizumab

RTP RESEARCH TO PRACTICE

What would you generally recommend as second-line therapy for a 65-year-old patient with metastatic FGFR wild-type UBC to the liver whose disease progresses on first-line cisplatin/gemcitabine followed by avelumab maintenance?


Dr Apolo

Enfortumab vedotin


Dr Gupta

Enfortumab vedotin


Dr Rosenberg

Enfortumab vedotin


Dr Sonpavde

Enfortumab vedotin

RTP RESEARCH TO PRACTICE

What would you generally recommend as second-line therapy for a 65-year-old patient with FGFR3 mutation-positive UBC metastatic to the liver whose disease progressed on first-line cisplatin/gemcitabine?

 Dr Apolo	Pembrolizumab
 Dr Gupta	Erdafitinib
 Dr Rosenberg	Pembrolizumab
 Dr Sonpavde	Erdafitinib

RTP RESEARCH TO PRACTICE

What would you generally recommend as second-line therapy for a 65-year-old patient with FGFR3 mutation-positive UBC metastatic to the liver whose disease progressed on first-line cisplatin/gemcitabine followed by avelumab maintenance?

 Dr Apolo	Erdafitinib
 Dr Gupta	Enfortumab vedotin
 Dr Rosenberg	Enfortumab vedotin
 Dr Sonpavde	Erdafitinib

RTP RESEARCH TO PRACTICE

Of enfortumab vedotin, erdafitinib and sacituzumab govitecan, which would you generally recommend first for a patient with metastatic UBC who is eligible to receive all 3 agents?

 Dr Apolo	Erdafitinib
 Dr Gupta	Enfortumab vedotin
 Dr Rosenberg	Enfortumab vedotin
 Dr Sonpavde	Enfortumab vedotin

RTP
RESEARCH
TO PRACTICE

How frequently do you monitor blood glucose levels in your patients receiving enfortumab vedotin?

 Dr Apolo	Weekly
 Dr Gupta	I do not routinely monitor blood glucose levels in these patients
 Dr Rosenberg	Prior to each dose
 Dr Sonpavde	Weekly

RTP
RESEARCH
TO PRACTICE

Based on available evidence and your own clinical experience, please list common clinically relevant adverse side effects associated with sacituzumab govitecan:

 Dr Apolo	Neutropenia, diarrhea, fatigue
 Dr Gupta	Neutropenia, diarrhea, anemia
 Dr Rosenberg	Neutropenia, diarrhea, abdominal cramping
 Dr Sonpavde	Neutropenia, diarrhea

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

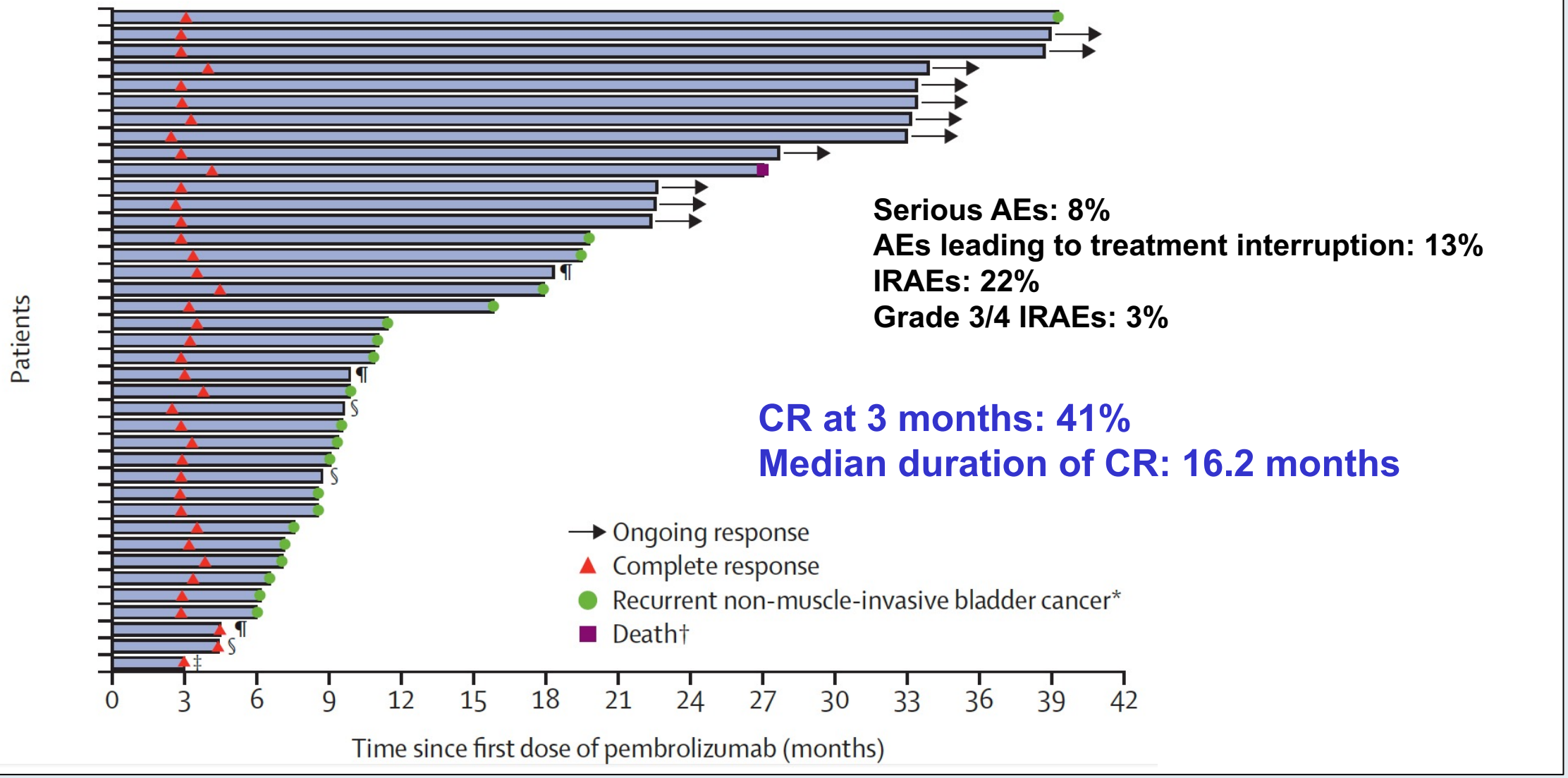
Nonmetastatic UBC

Lancet Oncol 2021;22:919-30

Pembrolizumab monotherapy for the treatment of high-risk non-muscle-invasive bladder cancer unresponsive to BCG (KEYNOTE-057): an open-label, single-arm, multicentre, phase 2 study

Arjun V Balar, Ashish M Kamat, Girish S Kulkarni, Edward M Uchio, Joost L Boormans, Mathieu Roumiguié, Laurence E M Krieger, Eric A Singer, Dean F Bajorin, Petros Grivas, Ho Kyung Seo, Hiroyuki Nishiyama, Badrinath R Konety, Haojie Li, Kijoeng Nam, Ekta Kapadia, Tara Frenkl, Ronald de Wit

KEYNOTE-057: Response, Duration of Response and Summary of Adverse Events



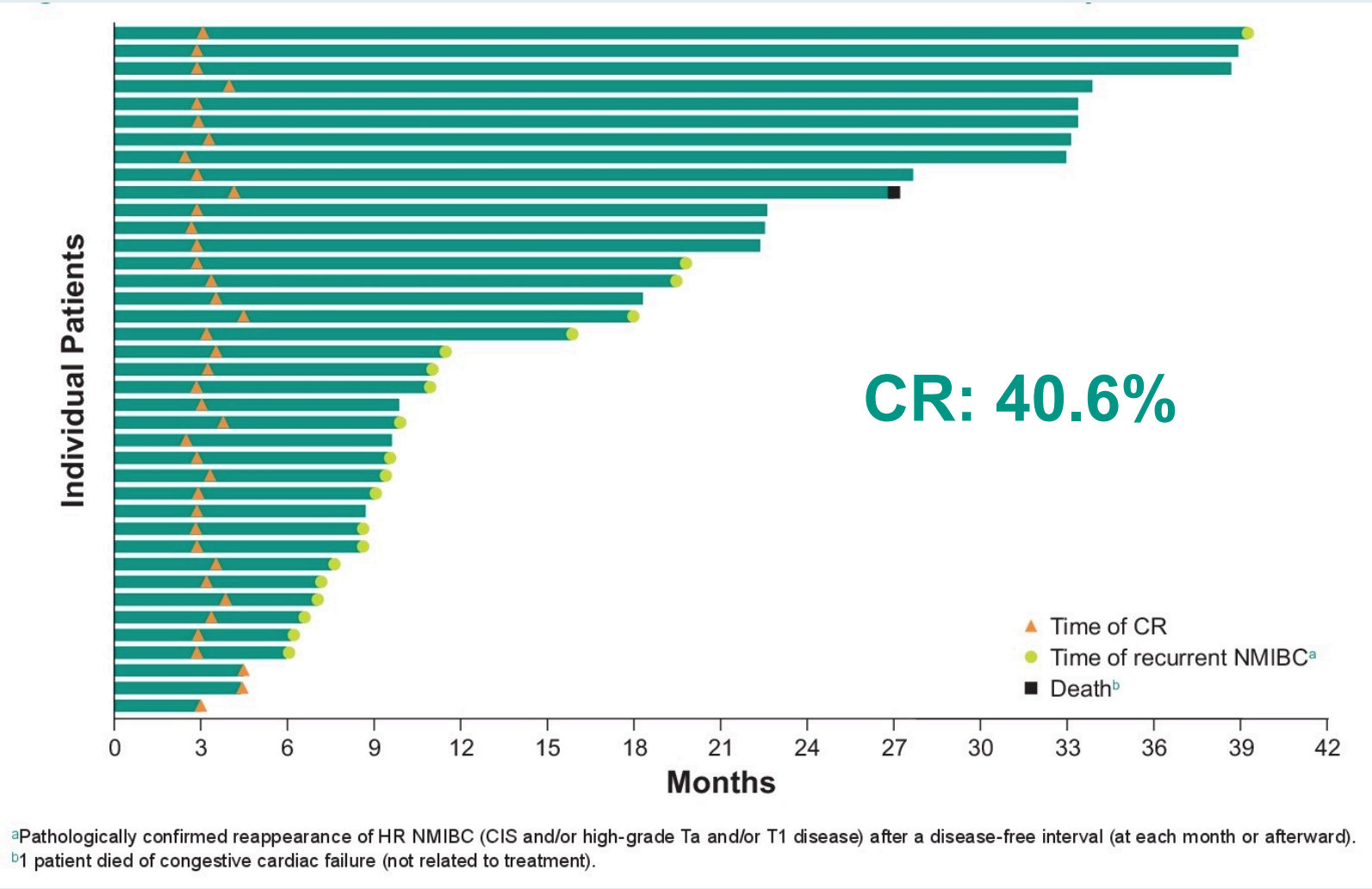
Balar AV et al. *Lancet Oncol* 2021;22:919-30.

Pembrolizumab for the Treatment of Patients with High-Risk (HR) Non-Muscle-Invasive Bladder Cancer (NMIBC) Unresponsive to Bacillus Calmette-Guérin: Extended Follow-Up of KEYNOTE-057 Cohort A

Balar AV et al.

Genitourinary Cancers Symposium 2021;Abstract 451.

Extended Follow-Up of KEYNOTE-057: Response, Time to Response and Recurrence of High-Risk NMIBC in Patients Who Experienced CR



[a]Pathologically confirmed reappearance of HR NMIBC (CIS and/or high-grade Ta and/or T1 disease) after a disease-free interval (at each month or afterward).
[b]1 patient died of congestive cardiac failure (not related to treatment).

Balar AV et al. Genitourinary Cancers Symposium 2021;Abstract 451.

RTP RESEARCH TO PRACTICE

FDA Approves Nivolumab for Adjuvant Treatment of Urothelial Carcinoma

Press Release – August 19, 2021

"The Food and Drug Administration approved nivolumab for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection.

This is the first FDA approval for adjuvant treatment of patients with high-risk UC. The results supporting this approval also supported the conversion of nivolumab's accelerated approval for advanced/metastatic UC to a regular approval.

Nivolumab was investigated in CHECKMATE-274 (NCT02632409), a randomized, double-blind, placebo-controlled trial in patients who were within 120 days of radical resection of UC of the bladder or upper urinary tract (renal pelvis or ureter) at high risk of recurrence. Patients were randomized (1:1) to receive nivolumab 240 mg or placebo by intravenous infusion every 2 weeks until recurrence or until unacceptable toxicity for a maximum treatment duration of 1 year."

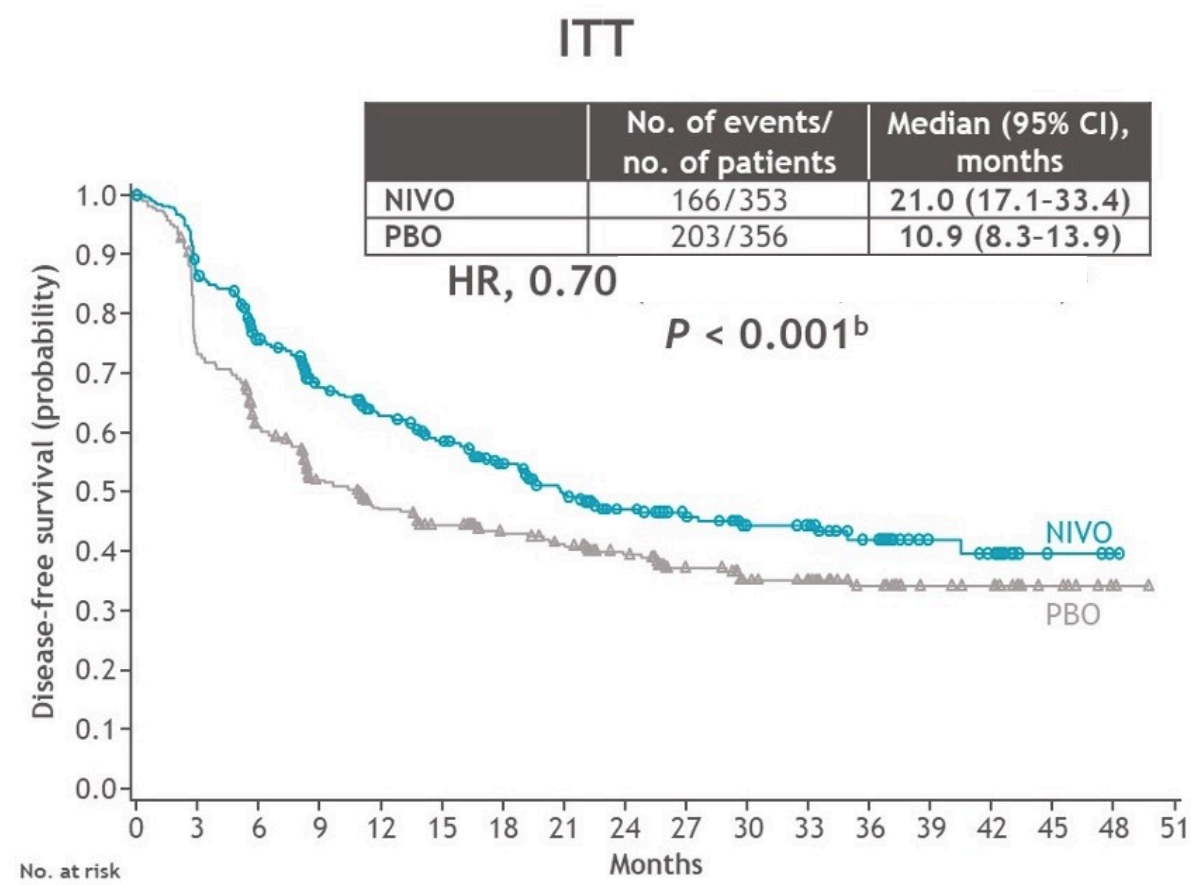
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-adjuvant-treatment-urothelial-carcinoma

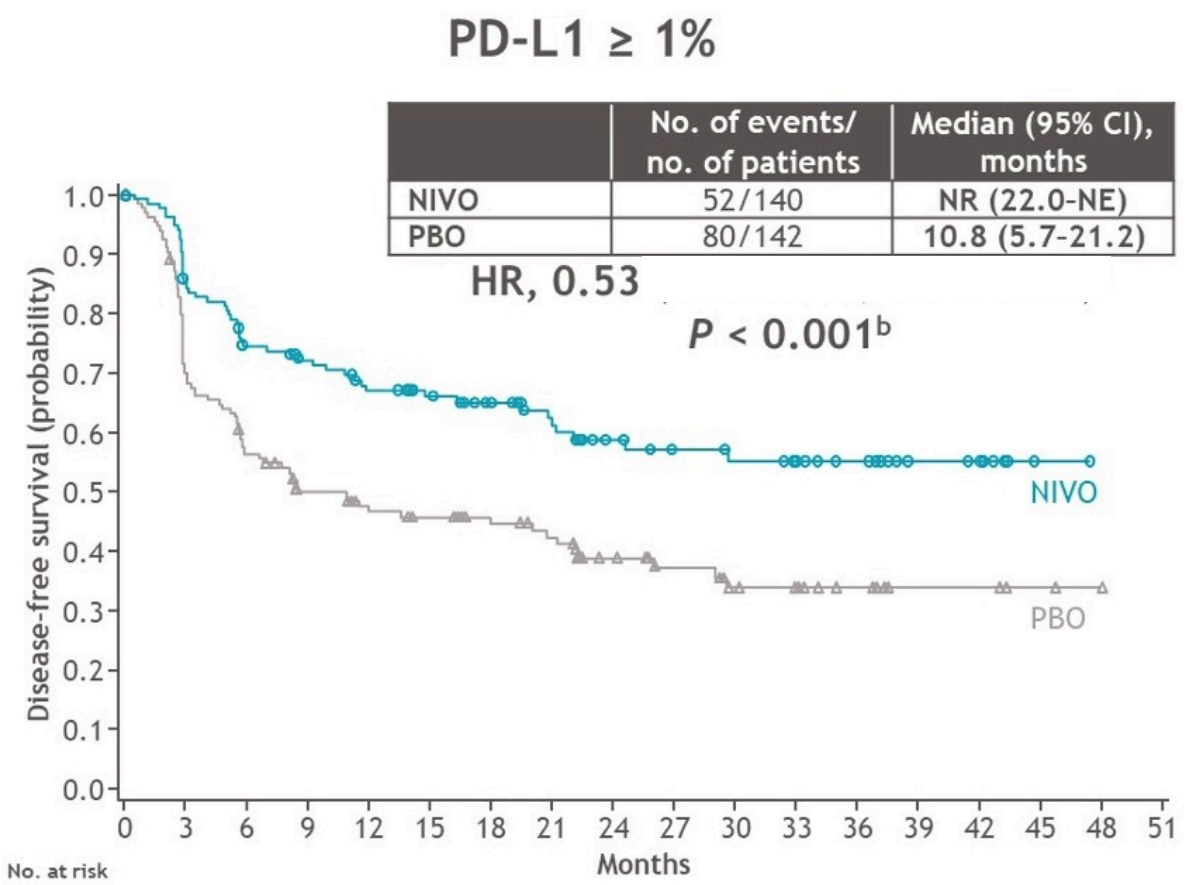
First Results from the Phase 3 CheckMate 274 Trial of Adjuvant Nivolumab vs Placebo in Patients Who Underwent Radical Surgery for High-Risk Muscle-Invasive Urothelial Carcinoma (MIUC)

Bajorin DF et al.

Genitourinary Cancers Symposium 2021;Abstract 391.

CheckMate 274: Disease-Free Survival in the ITT and PD-L1 ≥1% Populations





Bajorin DF et al. Genitourinary Cancers Symposium 2021;Abstract 391.

RTP RESEARCH TO PRACTICE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

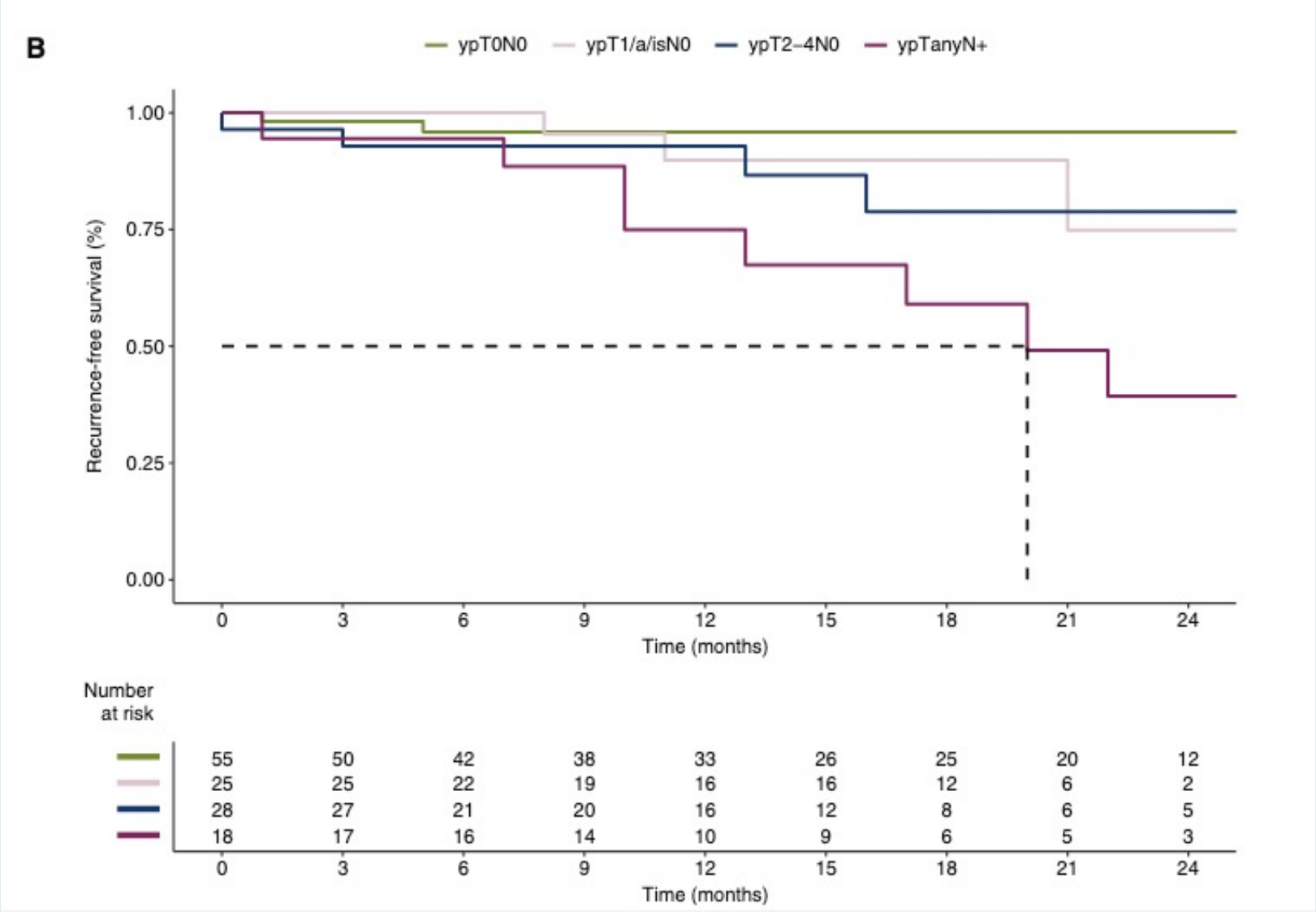
Does the administration of preoperative pembrolizumab lead to sustained remission post-cystectomy? First survival outcomes from the PURE-01 study☆

M. Bandini[1], E. A. Gibb[2], A. Gallina[1], D. Raggi[3], L. Marandino[3], M. Bianchi[1], J. S. Ross[4,5], M. Colecchia[3], G. Gandaglia[1], N. Fossati[1], F. Pederzoli[1], R. Lucianò[6], R. Colombo[1], A. Salonia[1], A. Briganti[1], F. Montorsi[1] & A. Necchi[3*]

[1]Urological Research Institute (URI), Unit of Urology, IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy; [2]Decipher Biosciences Inc., Vancouver, Canada; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [4]Foundation Medicine Inc., Cambridge; [5]Upstate Medical University, Syracuse, United States; [6]Department of Pathology, IRCCS Ospedale San Raffaele, Milan, Italy

Available online 23 September 2020

PURE-01: Recurrence-Free Survival (RFS) by ypTypN Stage



RFS	12-mo	24-mo
Overall (n = 126)	90.5%	78.3%
ypT0ypN0 (n = 55)	95.9%	95.9%
$ypT_{1/a/is}ypN0$ (n = 25)	89.8%	74.9%
ypT2-4 ypN0 (n = 28)	92.9%	78.8%
ypTanyN+ (n = 18)	74.9%	39.3%

Bandini M et al. *Ann Oncol* 2020;31(12):1755-63.

RTP RESEARCH TO PRACTICE

Avelumab (A) as the Basis of Neoadjuvant Chemotherapy (NAC) Regimen in Platinum Eligible and Ineligible Patients (pts) with Non-metastatic Muscle Invasive Bladder Cancer (NM-MIBC)

Martinez Chanza N et al.

ESMO 2021;Abstract 659MO.

Mini Oral Session – Genitourinary Tumors – Nonprostate

Saturday September 18, 2021

Optimizing the Selection and Sequencing of Therapy for Patients with Metastatic UBC

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TO PRACTICE

N Engl J Med 2020;383:1218-30.

The NEW ENGLAND JOURNAL of MEDICINE

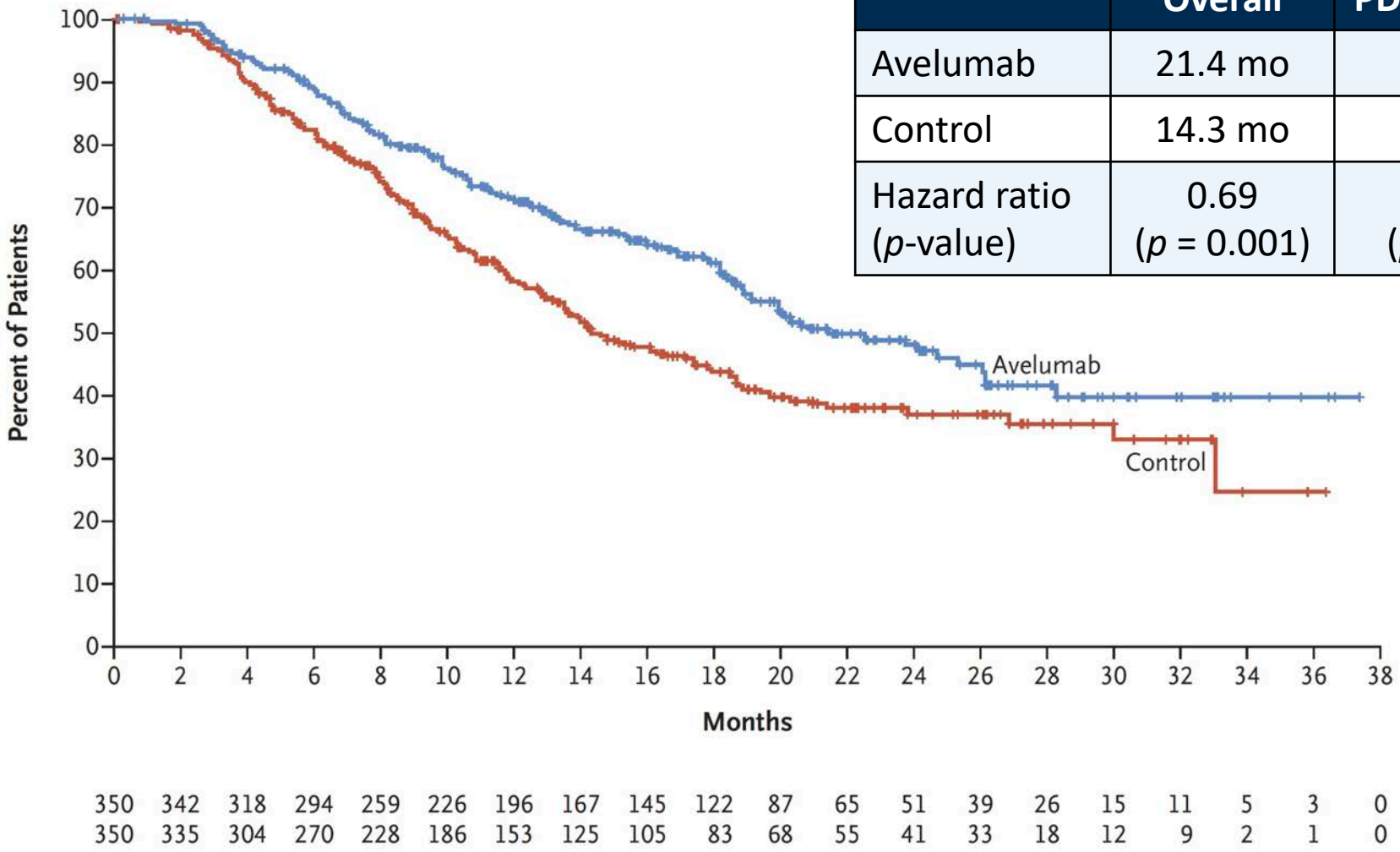
ORIGINAL ARTICLE

Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma

T. Powles, S.H. Park, E. Voog, C. Caserta, B.P. Valderrama, H. Gurney, H. Kalofonos, S. Radulović, W. Demey, A. Ullén, Y. Loriot, S.S. Sridhar, N. Tsuchiya, E. Kopyltsov, C.N. Sternberg, J. Bellmunt, J.B. Aragon-Ching, D.P. Petrylak, R. Laliberte, J. Wang, B. Huang, C. Davis, C. Fowst, N. Costa, J.A. Blake-Haskins, A. di Pietro, and P. Grivas

JAVELIN Bladder 100 Primary Endpoint: Overall Survival

	Overall	PD-L1-positive
Avelumab	21.4 mo	NE
Control	14.3 mo	17.1 mo
Hazard ratio (*p*-value)	0.69 ($p = 0.001$)	0.56 ($p < 0.001$)



Powles T et al. *N Engl J Med* 2020;383:1218-30.

Voluntary Withdrawal of Durvalumab Indication for Advanced Bladder Cancer in the United States

Press Release – February 22, 2021

"The voluntary withdrawal of the durvalumab indication in the US for previously treated adult patients with locally advanced or metastatic bladder cancer [was announced today]. This decision was made in consultation with the Food and Drug Administration (FDA).

In May 2017, durvalumab was granted accelerated approval in the US based on promising tumor response rates and duration of response data from Study 1108, a Phase I/II trial that evaluated the safety and efficacy of durvalumab in advanced solid tumors, including previously treated bladder cancer. Continued approval was contingent on results from the DANUBE Phase III trial in the 1st-line metastatic bladder cancer setting, which did not meet its primary endpoints in 2020. The withdrawal is aligned with FDA guidance for evaluating indications with accelerated approvals that did not meet post-marketing requirements, as part of a broader industry-wide evaluation. This withdrawal does not impact the indication outside the US and does not impact other approved durvalumab indications within or outside the US."

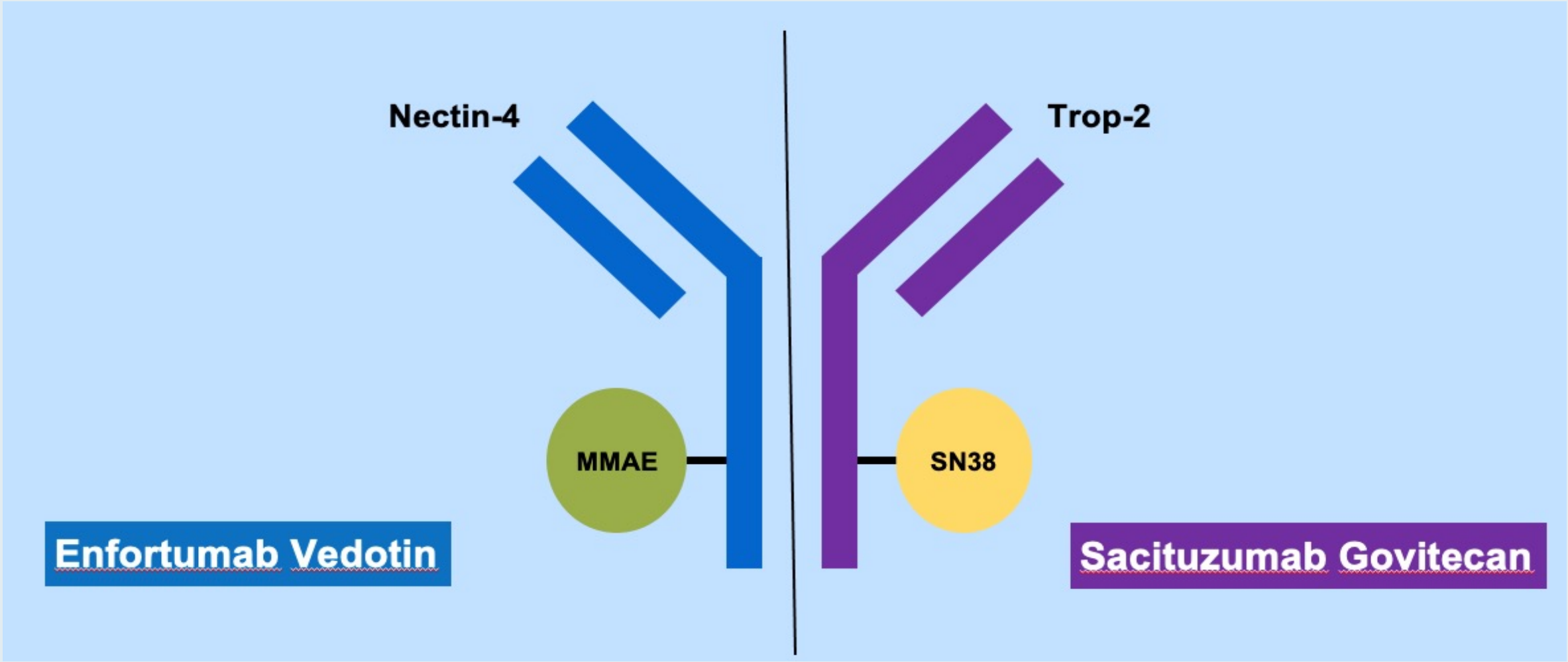
https://www.astrazeneca.com/media-centre/press-releases/2021/voluntary-withdrawal-imfinzi-us-bladder-indication.html

Ongoing Phase III Trials of Immunotherapy Combinations for UBC

Trial identifier	N	Setting	Treatment arms
POTOMAC (NCT03528694)	1,019	High-risk, BCG-naïve, non-muscle invasive	• Durvalumab + BCG (induction + maintenance) • Durvalumab + BCG (induction only) • BCG
NIAGARA (NCT03732677)	1,050	Neoadjuvant/ adjuvant, muscle invasive	• Chemotherapy + durvalumab → surgery → durvalumab • Chemotherapy alone → surgery
NILE (NCT03682068)	1,292	Unresectable, first line	• Durvalumab + standard chemotherapy • Durvalumab + tremelimumab + standard therapy • Standard chemotherapy

www.clinicaltrials.gov. Accessed September 2021.

Antibody-Drug Conjugates in UBC



Courtesy of Matthew Galsky, MD.

FDA Grants Regular Approval to Enfortumab Vedotin-ejfv for Locally Advanced or Metastatic Urothelial Cancer

Press Release – July 9, 2021

"The Food and Drug Administration approved enfortumab vedotin-ejfv, a Nectin-4-directed antibody and microtubule inhibitor conjugate, for adult patients with locally advanced or metastatic urothelial cancer who

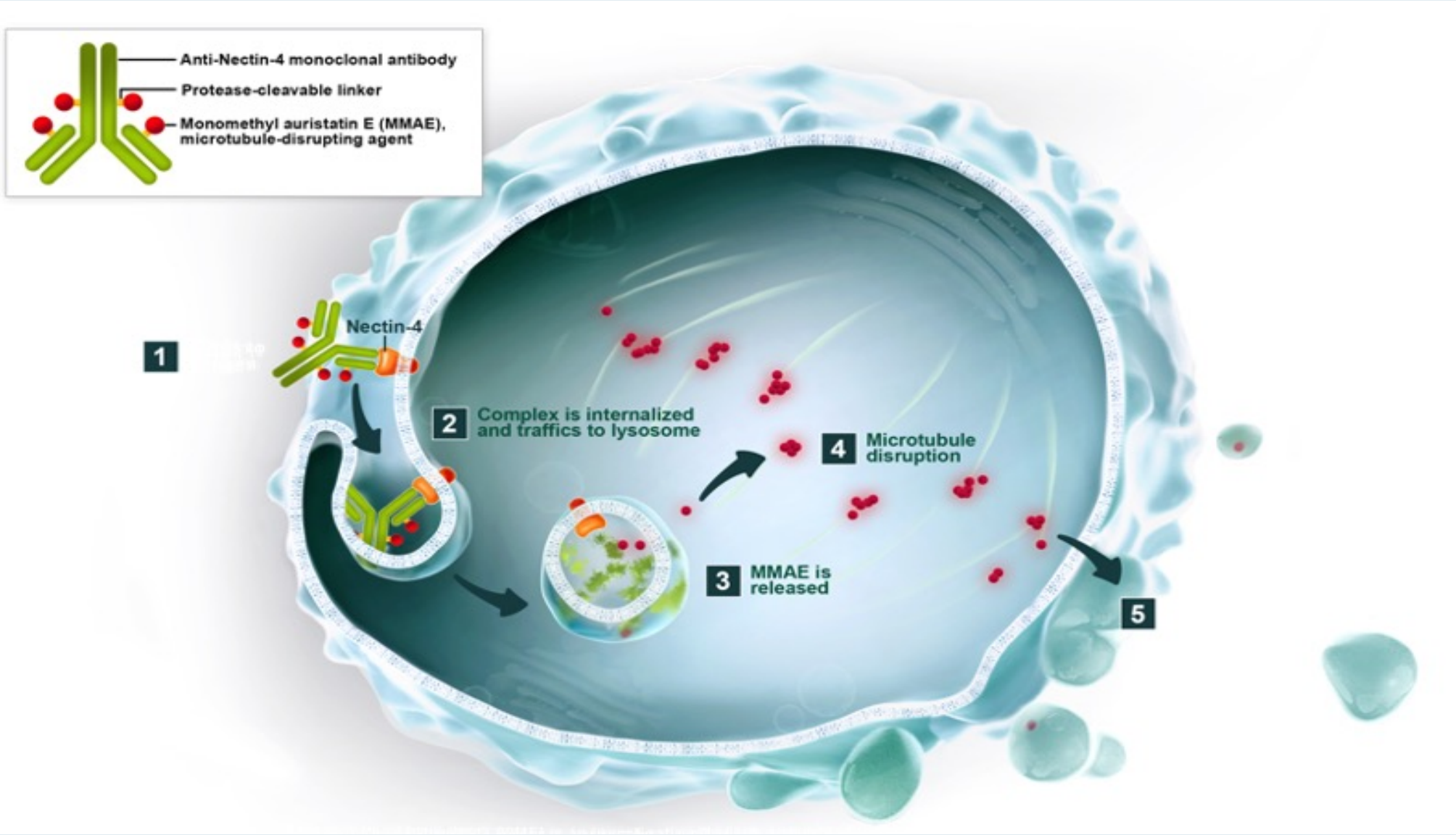
- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

Trial EV-301 was an open-label, randomized, multicenter trial required to confirm the clinical benefit of the 2019 accelerated approval.

Efficacy for patients ineligible for cisplatin-containing chemotherapy was evaluated in Cohort 2 of EV-201, a single-arm, multi-cohort, international trial in 89 patients with locally advanced or metastatic urothelial cancer who received a prior PD-1 or PD-L1 inhibitor and were ineligible for cisplatin-containing chemotherapy."

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

Enfortumab Vedotin: Nectin-4-Targeted Therapy



Courtesy of Jonathan Rosenberg, MD

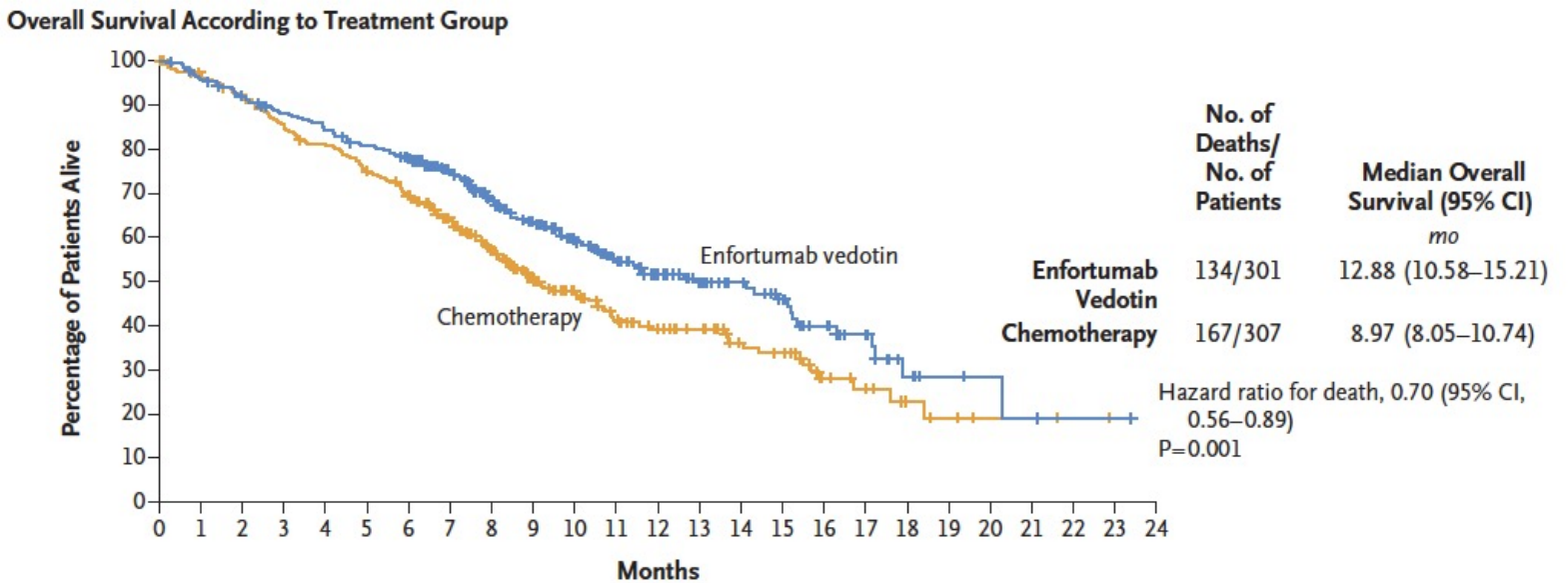
ORIGINAL ARTICLE

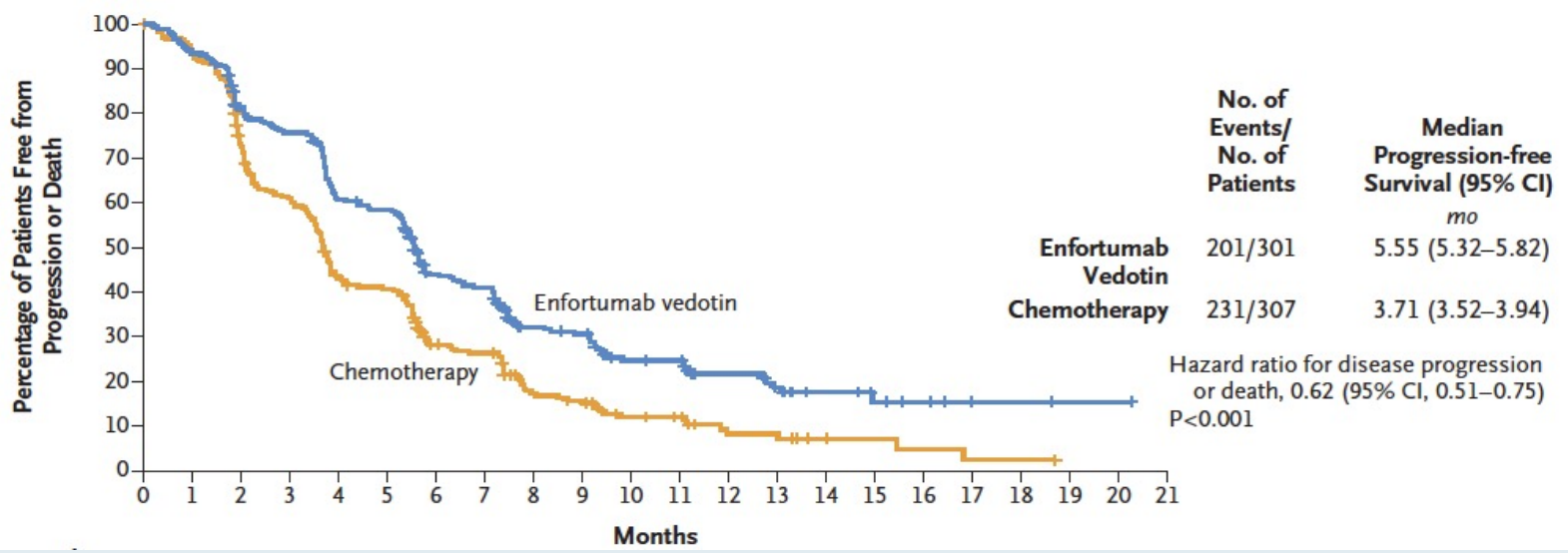
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

Thomas Powles, M.D., Jonathan E. Rosenberg, M.D., Guru P. Sonpavde, M.D., Yohann Loriot, M.D., Ph.D., Ignacio Durán, M.D., Ph.D., Jae-Lyun Lee, M.D., Ph.D., Nobuaki Matsubara, M.D., Christof Vulsteke, M.D., Ph.D., Daniel Castellano, M.D., Chunzhang Wu, Ph.D., Mary Campbell, M.D., Maria Matsangou, M.B., Ch.B., M.D., and Daniel P. Petrylak, M.D.

N Engl J Med 2021;384(12):1125-35.

EV-301: Survival and Response Analyses





	EV (n = 301)	Chemo (n = 307)
ORR	40.6%	17.9%
DCR	71.9%	53.4%

Incidence of treatment-related adverse events was similar in the 2 groups:

- 93.9% versus 91.8%

Incidence of events of Grade 3 or higher was also similar in the 2 groups:

- 51.4% versus 49.8%

Powles T et al. *N Engl J Med* 2021;384(12):1125-35.

EV-301: Enfortumab Vedotin Safety Analysis

Adverse Event	Enfortumab Vedotin Group (N=296)		Chemotherapy Group (N=291)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Any adverse event	278 (93.9)	152 (51.4)	267 (91.8)	145 (49.8)
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy†	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Maculopapular rash	48 (16.2)	22 (7.4)	5 (1.7)	0
Anemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Decreased neutrophil count	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
Decreased white-cell count	16 (5.4)	4 (1.4)	31 (10.7)	20 (6.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

Powles T et al. *N Engl J Med* 2021;384(12):1125-35.

Research Letter

ONLINE FIRST

September 8, 2021

Postmarketing Cases of Enfortumab Vedotin-Associated Skin Reactions Reported as Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis

Michelle Nadeau Nguyen, PharmD, BCOP, BCPS[1]; Melissa Reyes, MD, MPH, DTMH[1]; S. Christopher Jones, PharmD, MS, MPH[1]

» Author Affiliations

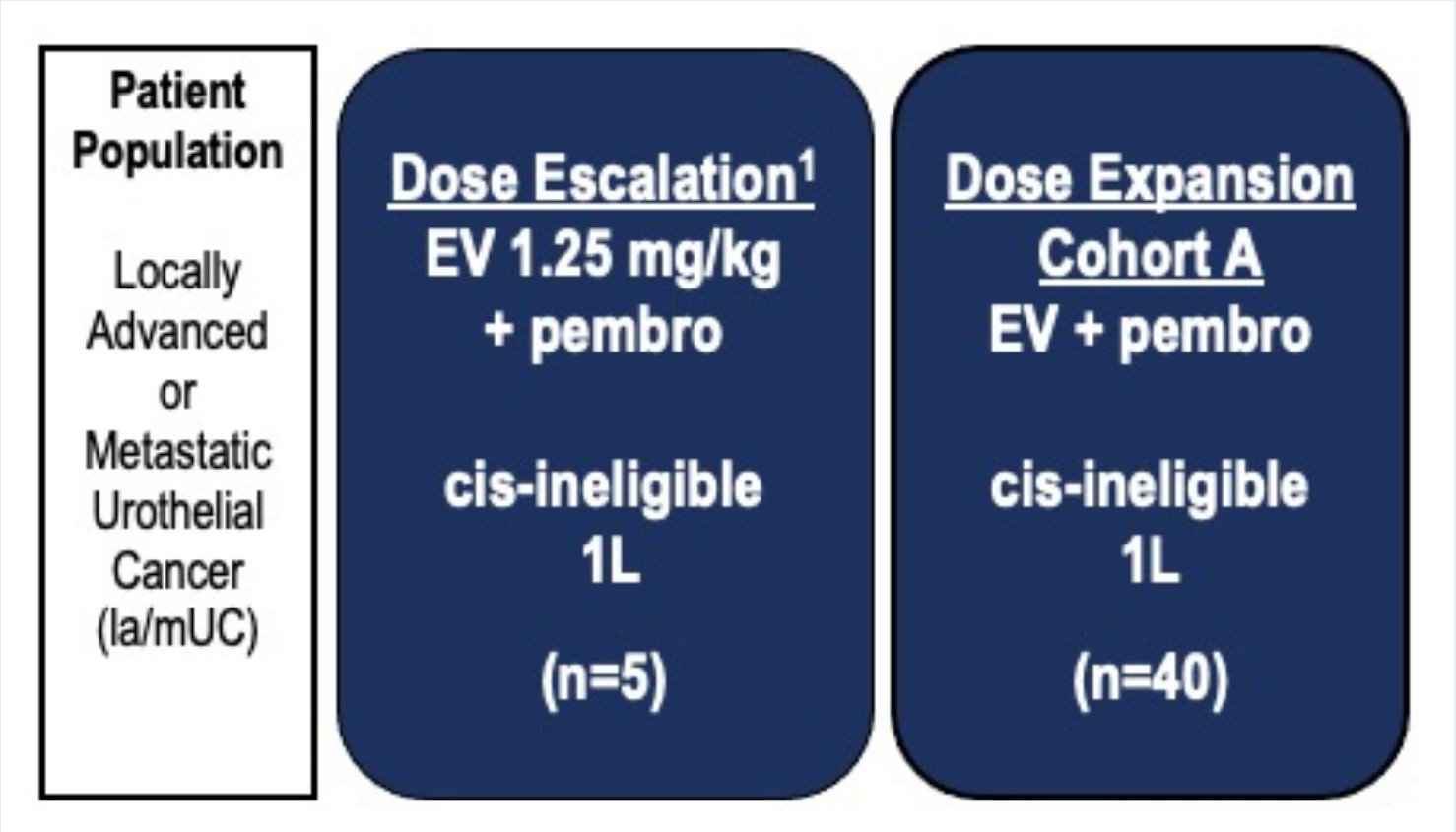
JAMA Dermatol. Published online September 8, 2021. doi:10.1001/jamadermatol.2021.3450

Study EV-103: Update on Durability Results and Long Term Outcome of Enfortumab Vedotin + Pembrolizumab in First Line Locally Advanced or Metastatic Urothelial Carcinoma (la/mUC)

Friedlander TW et al.

ASCO 2021;Abstract 4528.

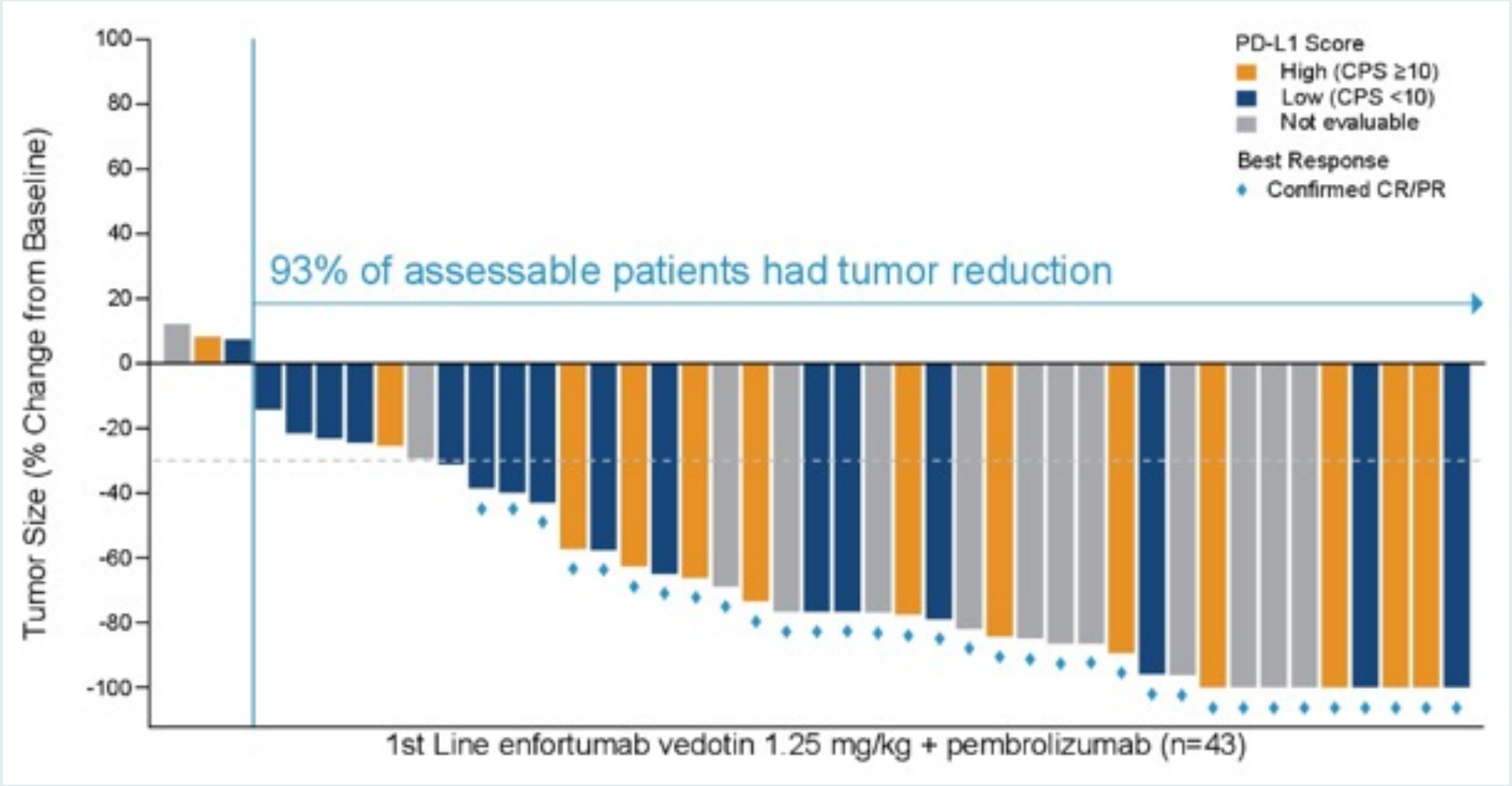
EV-103: Enfortumab Vedotin + Pembrolizumab Cohorts



- **Dosing:** Enfortumab vedotin on days 1 and 8 and pembrolizumab on day 1 of every 3-week cycle
- **Primary endpoints:** Adverse events, laboratory abnormalities
- **Key secondary endpoints:** Dose-limiting toxicities, ORR, duration of response, progression-free survival, OS

Friedlander TW et al. ASCO 2021;Abstract 4528.

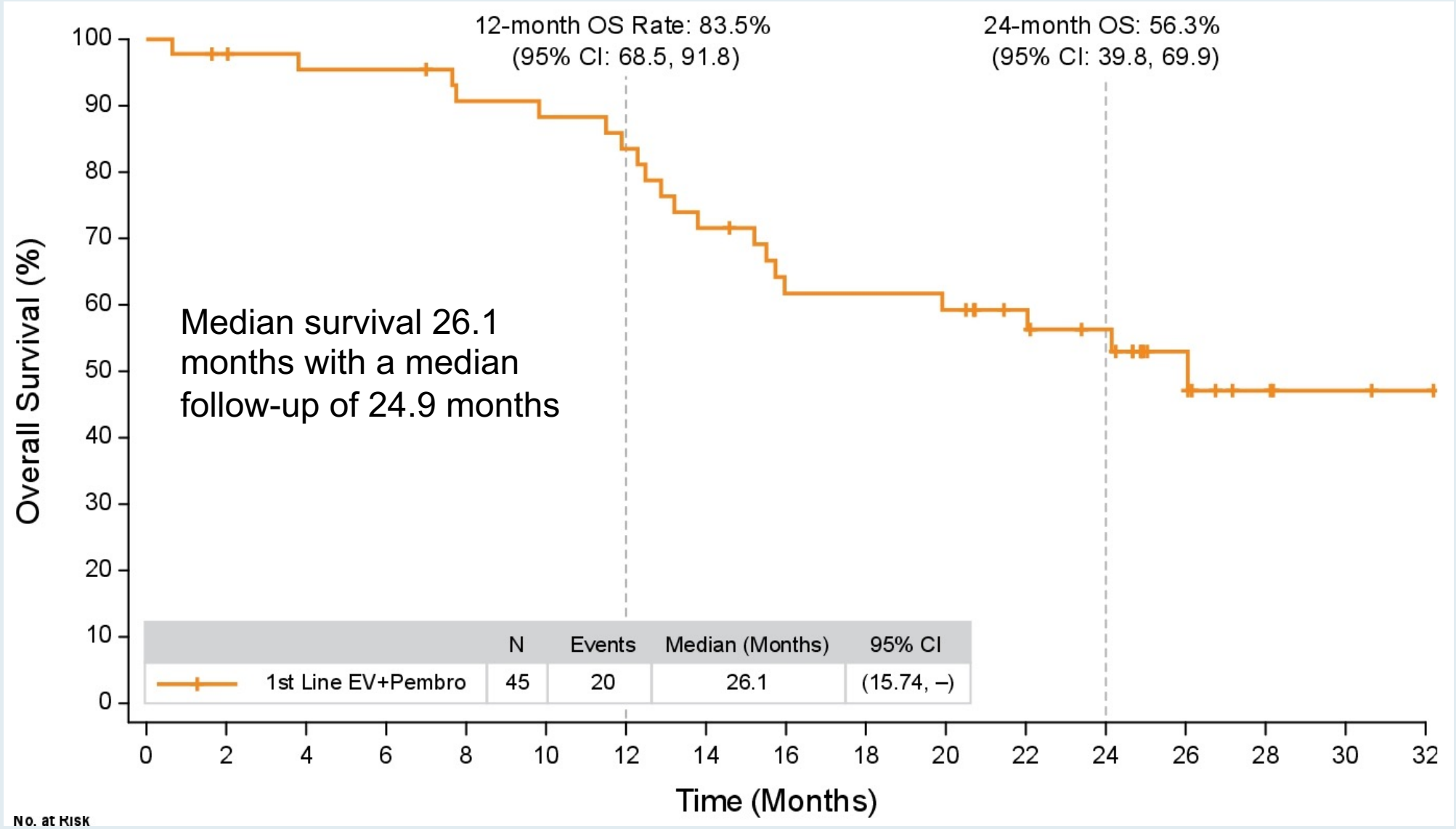
EV-103: Best Overall Response per RECIST



Friedlander TW et al. ASCO 2021;Abstract 4528.

RTP RESEARCH TO PRACTICE

EV-103: Updated Overall Survival



Friedlander TW et al. ASCO 2021;Abstract 4528.

FDA Grants Accelerated Approval to Sacituzumab Govitecan for Advanced Urothelial Cancer

Press Release – April 13, 2021

"The Food and Drug Administration granted accelerated approval to sacituzumab govitecan for patients with locally advanced or metastatic urothelial cancer (mUC) who previously received a platinum-containing chemotherapy and either a programmed death receptor-1 (PD-1) or a programmed death-ligand 1 (PD-L1) inhibitor.

Efficacy and safety were evaluated in TROPHY (IMMU-132-06; NCT03547973), a single-arm, multicenter trial that enrolled 112 patients with locally advanced or mUC who received prior treatment with a platinum-containing chemotherapy and either a PD-1 or PD-L1 inhibitor. Patients received sacituzumab govitecan, 10 mg/kg intravenously, on days 1 and 8 of a 21-day treatment cycle."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sacituzumab-govitecan-advanced-urothelial-cancer

TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors

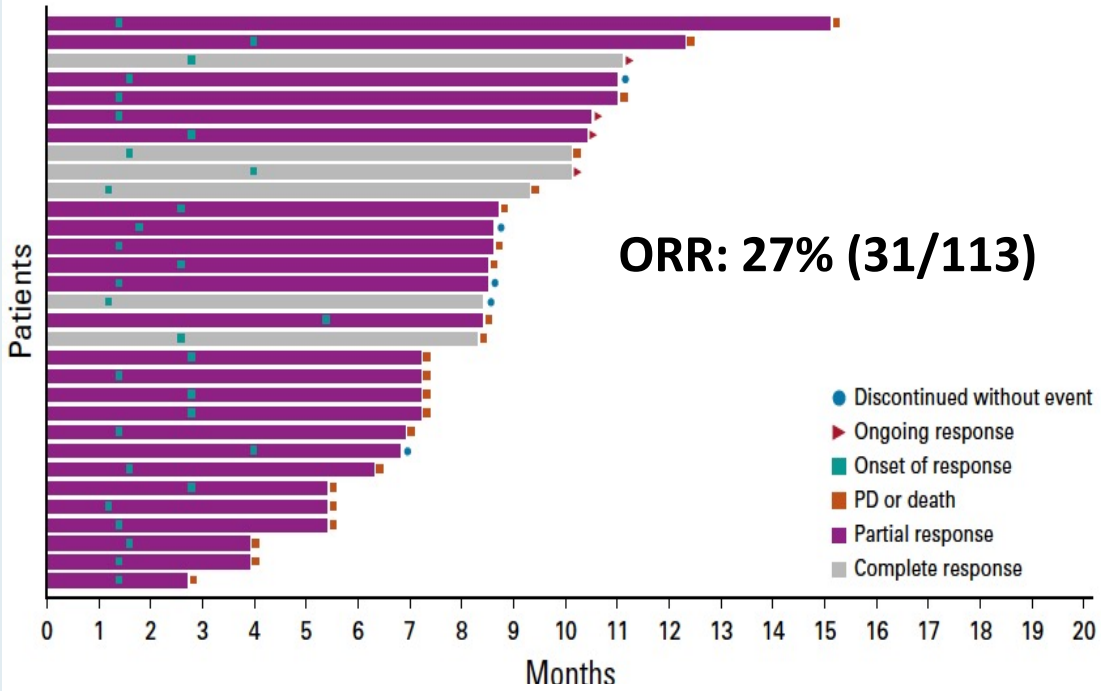
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11]; Phillip Palmbos, MD, PhD[12]; Christos E. Kyriakopoulos, MD[13]; Damien Pouessel, MD, PhD[14]; Cora N. Sternberg, MD[1]; Quan Hong, MD[15]; Trishna Goswami, MD[15]; Loretta M. Itri, MD[15]; and Petros Grivas, MD, PhD[16]

J Clin Oncol 2021;39(22):2474-85.

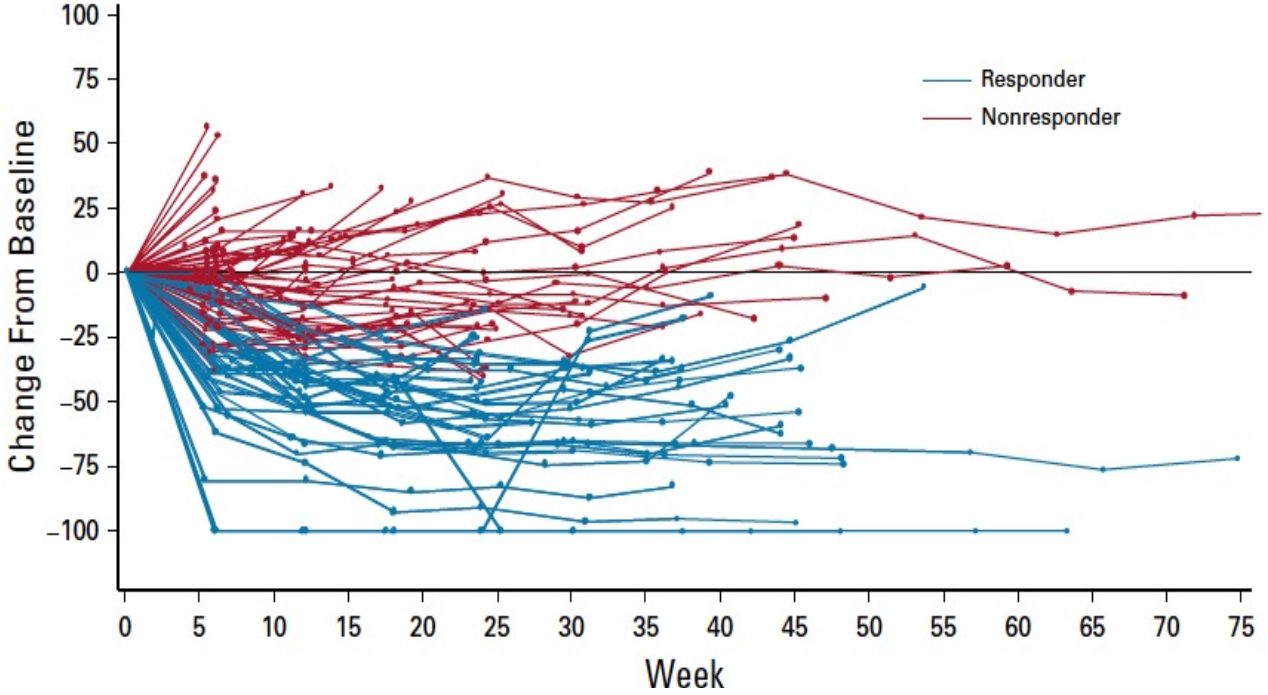
TROPHY U-01 (Cohort 1): ORR, Duration of Response and Survival

Median DOR: 7.2 mo

Median time to onset of response: 1.6 mo



ORR: 27% (31/113)



Median PFS: 5.4 mo

Median OS: 10.9 mo

Tagawa ST et al. *J Clin Oncol* 2021;39(22):2474-85; Loriot Y et al. ESMO 2020;Abstract LBA24.

RTP RESEARCH TO PRACTICE

FDA Grants Breakthrough Therapy Designation to Disitamab Vedotin for HER2-Positive Locally Advanced or Metastatic Urothelial Carcinoma

Press Release – September 30, 2020

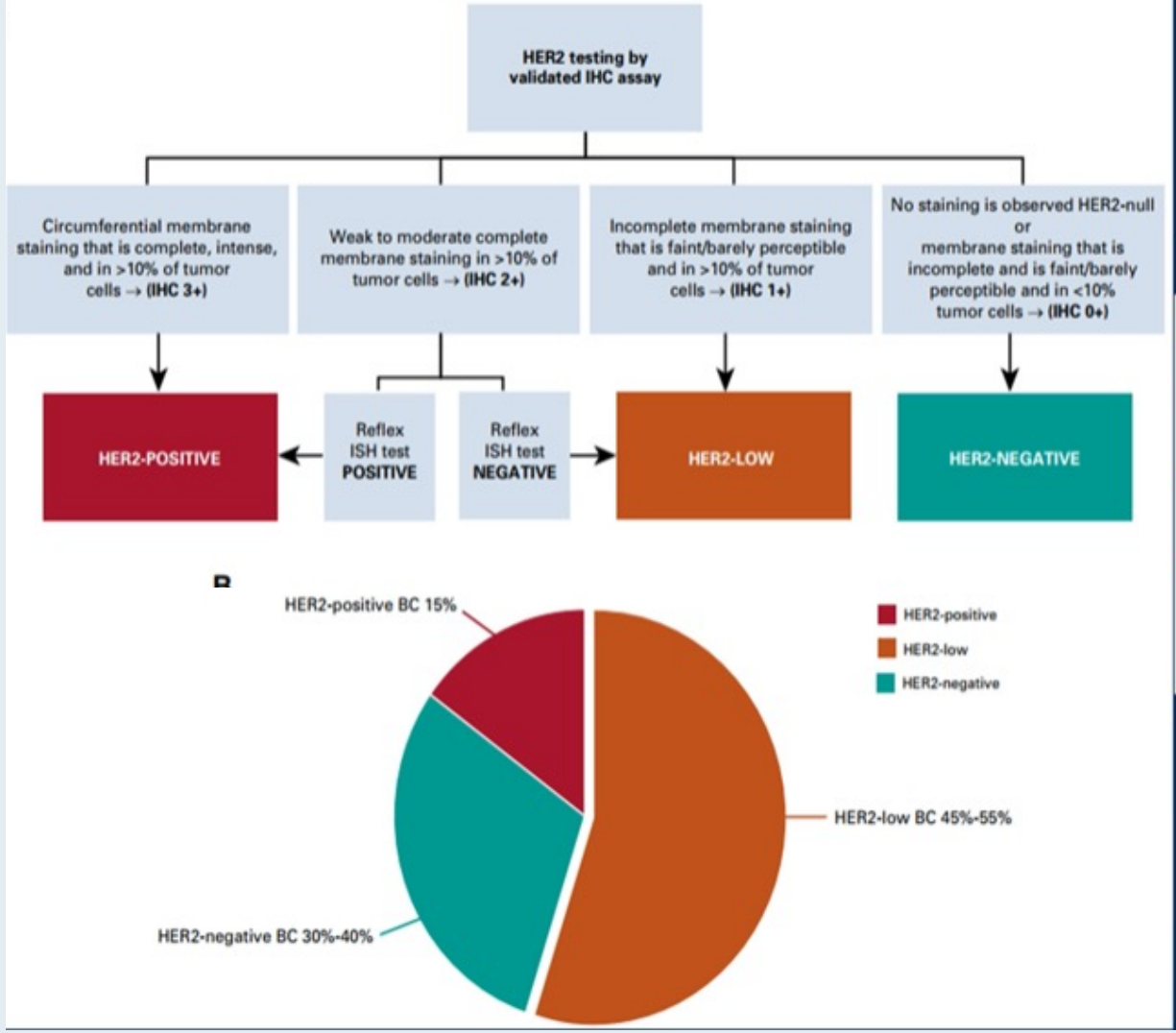
"The FDA has granted disitamab vedotin (RC48) a breakthrough therapy designation for the treatment of patients with HER2-positive locally advanced or metastatic urothelial carcinoma following treatment with platinum-based chemotherapy, according to the company developing the antibody-drug conjugate (ADC).

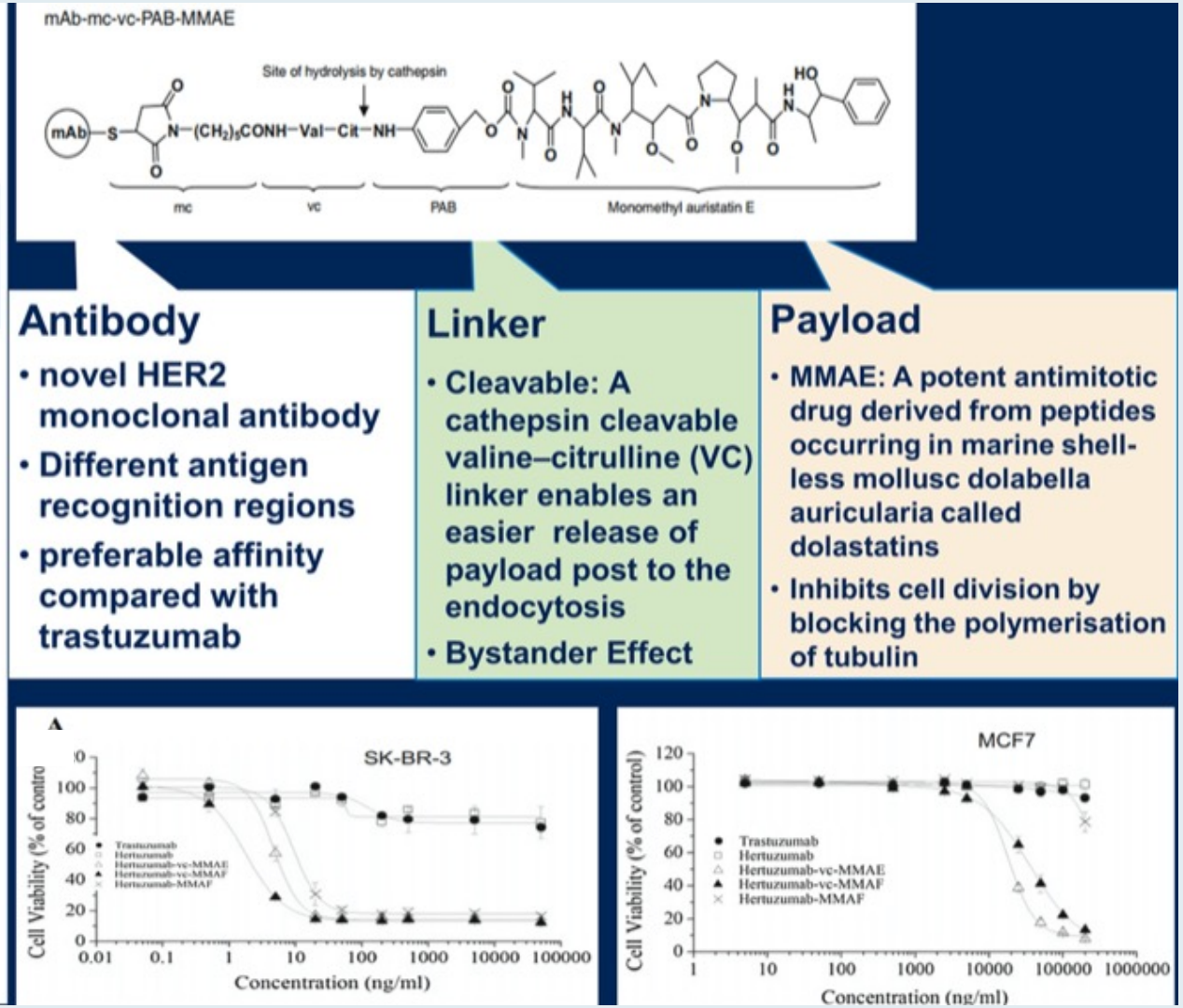
The designation will expedite the development and review of disitamab vedotin in this setting. Phase 2 data presented at the 2019 ASCO Annual Meeting showed that the ADC achieved a confirmed objective response rate of 51.2%, with confirmed responses reported in 22 of 43 patients. The best overall response was a partial response in 26 patients. An additional 13 patients reached stable disease for a disease control rate of 90.7%.

The median progression-free survival (PFS) was 6.9 months, with a 6-month PFS rate of 56.9%. The 6- and 12-month overall survival rates were 85.2% and 59.6%, respectively. Of note, the confirmed objective response rate was 62.5% in patients with prior anti–PD-1/PD-L1 treatment and 56.8% in patients with visceral metastases."

https://www.urologytimes.com/view/disitamab-vedotin-granted-fda-breakthrough-therapy-designation-in-bladder-cancer

Disitamab Vedotin: A Novel HER2-Targeted ADC

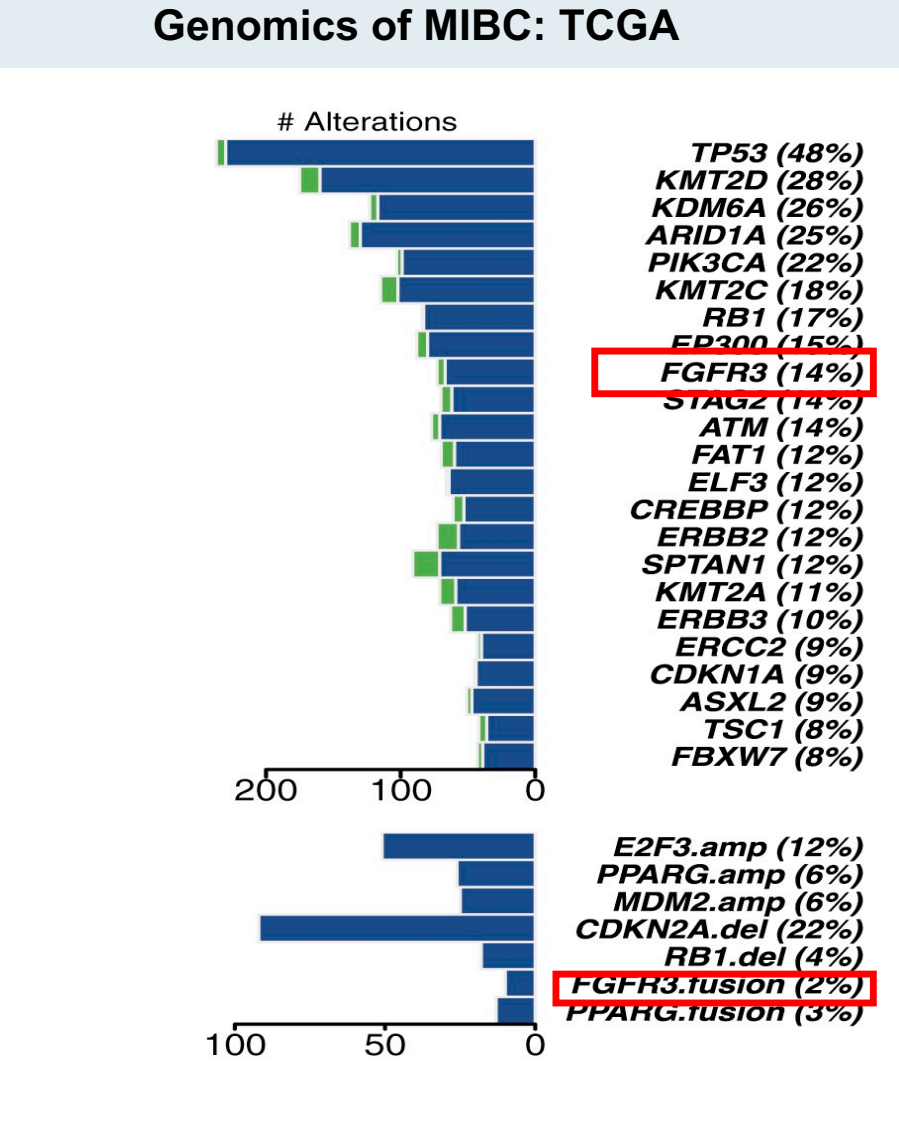




Wang J et al. ASCO 2021;Abstract 1022.

RTP RESEARCH TO PRACTICE

FGFR3 Genomic Alterations in Muscle-Invasive Bladder Cancer



- In muscle-invasive disease, *FGFR3* mutations in ~20% of tumors, but protein and/or gene overexpression in ~50%.
- Activating mutations of *FGFR3* in ~75% of low-grade papillary bladder tumors.
- FGFR3-TACC3 fusions enriched in young, Asian, non-smokers, upper tract tumors (invasive, high grade)
- Preclinical evidence for activity of FGFR inhibitors in selected cells with FGFR alterations

Courtesy of Guru Sonpavde, MD

Robertson AG et al. *Cell* 2017;171(3):540-56; Cappellen D et al. *Nat Genet* 1999;23:18-20; Nassar A et al. *JCO Precis Oncol* 2018; Gust KM et al. *Mol Cancer Ther* 2013;12:1245-54; Grünewald S et al. *Int J Cancer* 2019; Sfakianos JP Eur Urol 2015;68(6):970-7.

Erdafitinib or Erdafitinib plus Cetrelimab for Patients with Metastatic or Locally Advanced Urothelial Carcinoma and Fibroblast Growth Factor Receptor Alterations: First Results from the Phase 2 NORSE Study

Powles TB et al.

ESMO 2021;Abstract LBA27

NORSE: Trial Design

NORSE Phase 2 Study Design

Key eligibility criteria

- Age ≥ 18 years
- mUC diagnosis
- Ineligible for cisplatin
- Select *FGFRa* (mutation/fusion)
- Measurable disease
- No prior systemic therapy for mUC

Patients with any PD-L1 status could be enrolled

Target enrollment, N = 90
1:1 randomization

Erdafitinib
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

Erdafitinib + cetrelimab
Once-daily erdafitinib 8 mg + IV cetrelimab 240 mg every 2 weeks at Cycles 1-4 and 480 mg every 4 weeks thereafter

Primary end points

- ORR
- Safety

Key secondary end points

- DCR
- DOR
- Time to response

No formal statistical comparisons between arms are prespecified

Point estimates along with 95% CI will be presented for each arm.

- *Sample size determination:* Assuming a true ORR of 45% in the erdafitinib arm and 55% in the erdafitinib + cetrelimab arm, n ≈ 45 patients in each arm would result in an estimated ORR that is above a 95% CI lower bound of 30% and 40%, respectively
- A review of safety and efficacy data was planned per the data review committee charter when ~40 patients were response-evaluable

Powles TB et al. ESMO 2021;Abstract LBA27.

NORSE: Efficacy

	Erdafitinib (n = 18)	Erdafitinib + Cetrelimab (n = 19)
ORR[a], n (%) [95% CI]	6 (33%) [13%-59%]	13 (68%) [43%-87%]
Complete response, n (%)	1 (6%)	4 (21%)
Partial response, n (%)	5 (28%)	9 (47%)
DOR, median, months [95% CI]	NE [4.4-NE]	6.9 [1.6-NE]
Responses ongoing, n (%)	5 (28%)	10 (53%)
Time to response, median (range), months	2.3 (1-6)	1.8 (1-4)
DCR, n (%) [95% CI]	18 (100%) [82%-100%]	17 (90%) [67%-99%]

Powles TB et al. ESMO 2021;Abstract LBA27.

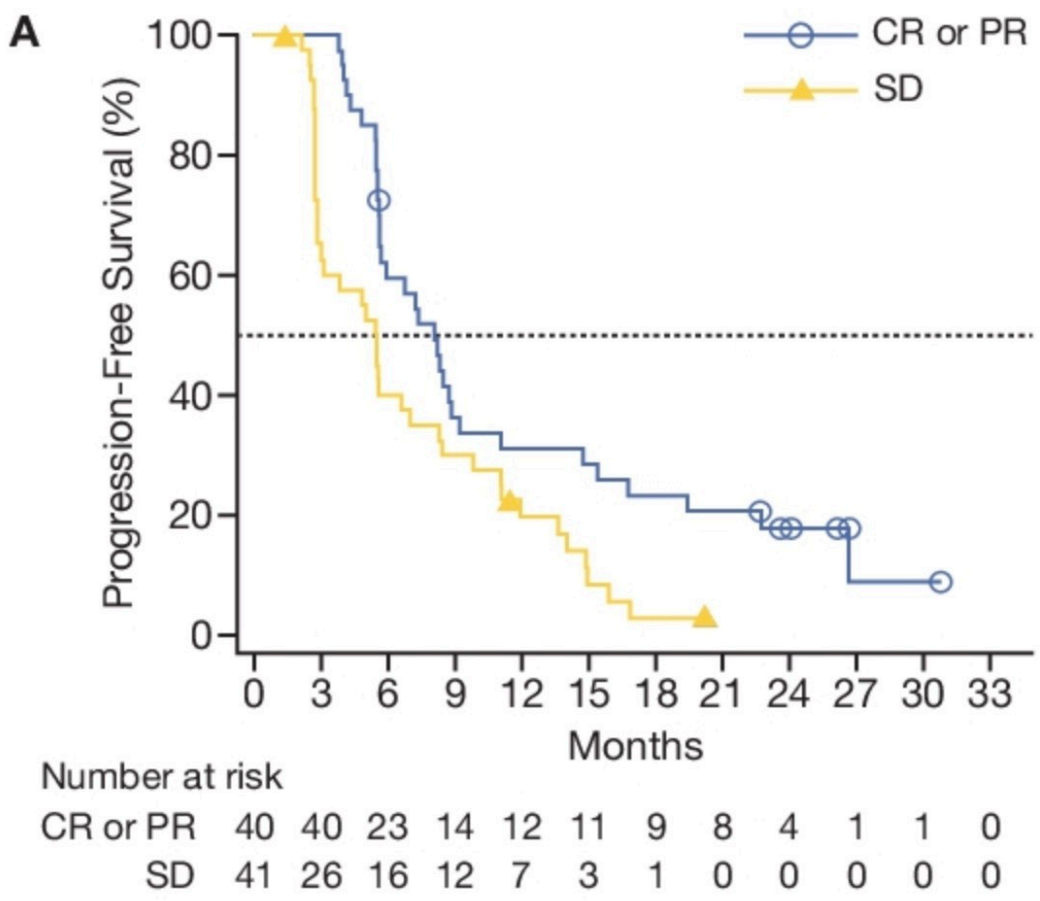
Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma (mUC): Long-Term Outcomes in BLC2001

Siefker-Radtke AO et al.

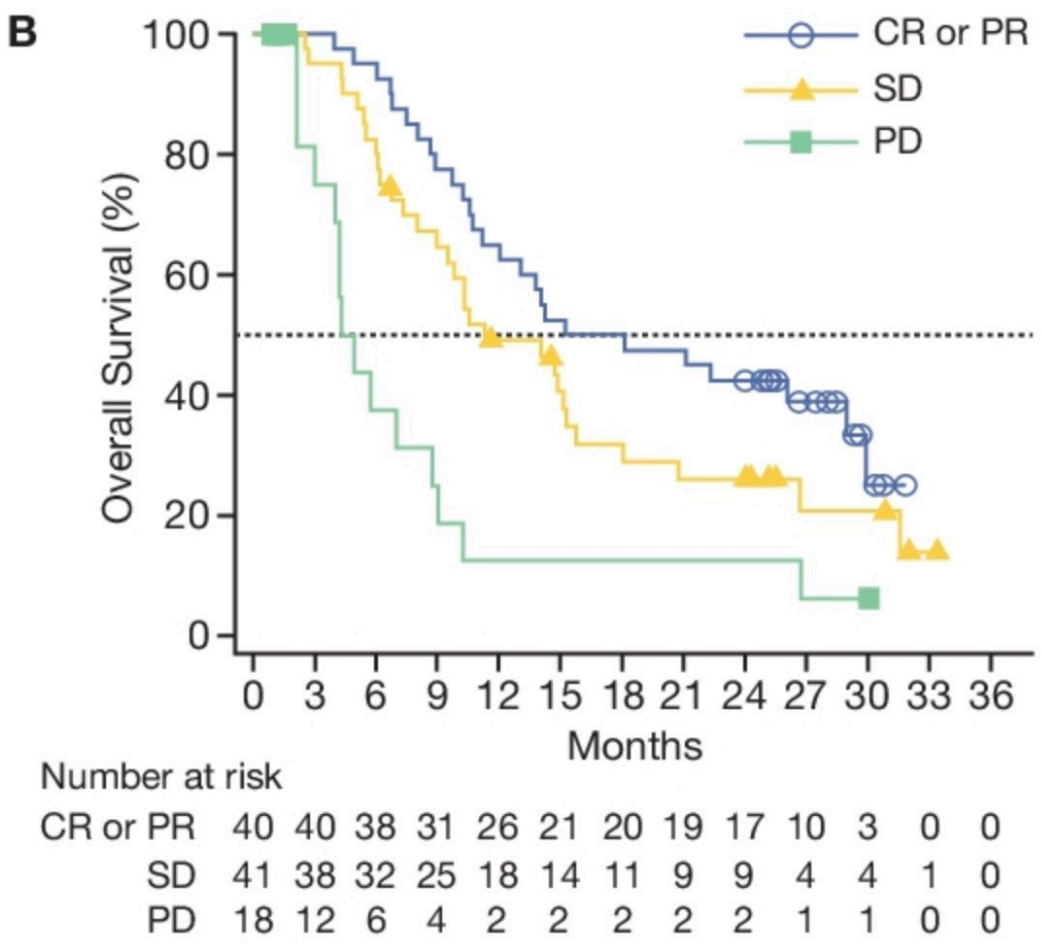
ASCO 2020;Abstract 5015.

BLC2001: Survival

Median PFS: 5.5 months



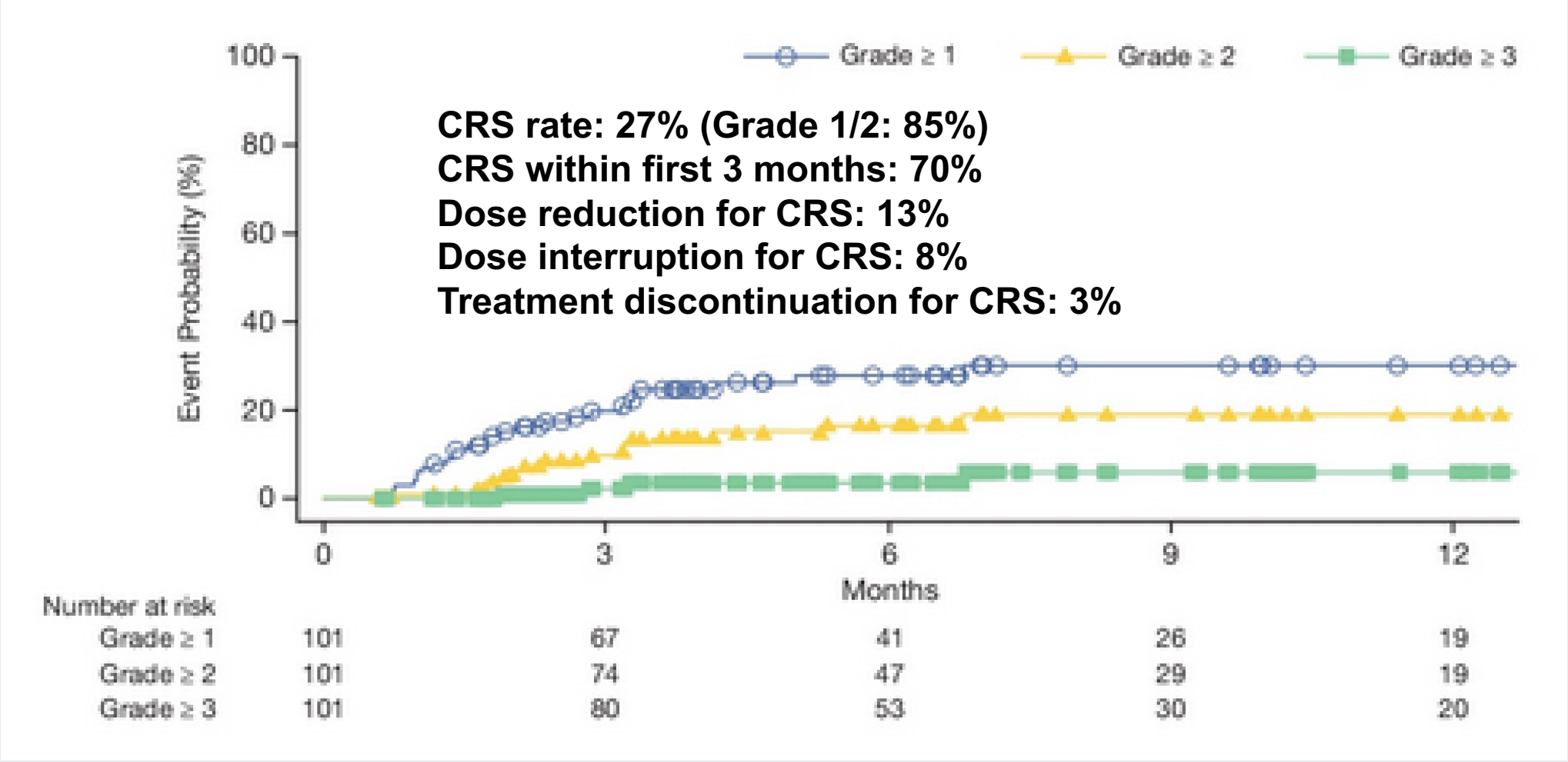
Median OS: 11.3 months



Siefker-Radtke AO et al. ASCO 2020;Abstract 5015.

RTP RESEARCH TO PRACTICE

BLC2001: Central Serous Retinopathy (CRS)



Siefker-Radtke AO et al. ASCO 2020;Abstract 5015.

RTP RESEARCH TO PRACTICE

Are FGFR3 Alterations Associated with Resistance to PD-1/PD-L1 Blockade in Large Clinical Trial Cohorts?

Phase 2
(IMvigor 210)

N = 274

18% mFGFR

Objective Response Rate

Wild type	**21% (95% CI: 16%, 27%)**
Mutant	**24% (95% CI: 14%, 39%)**

Phase 2
(*Checkmate 275*)

N = 139

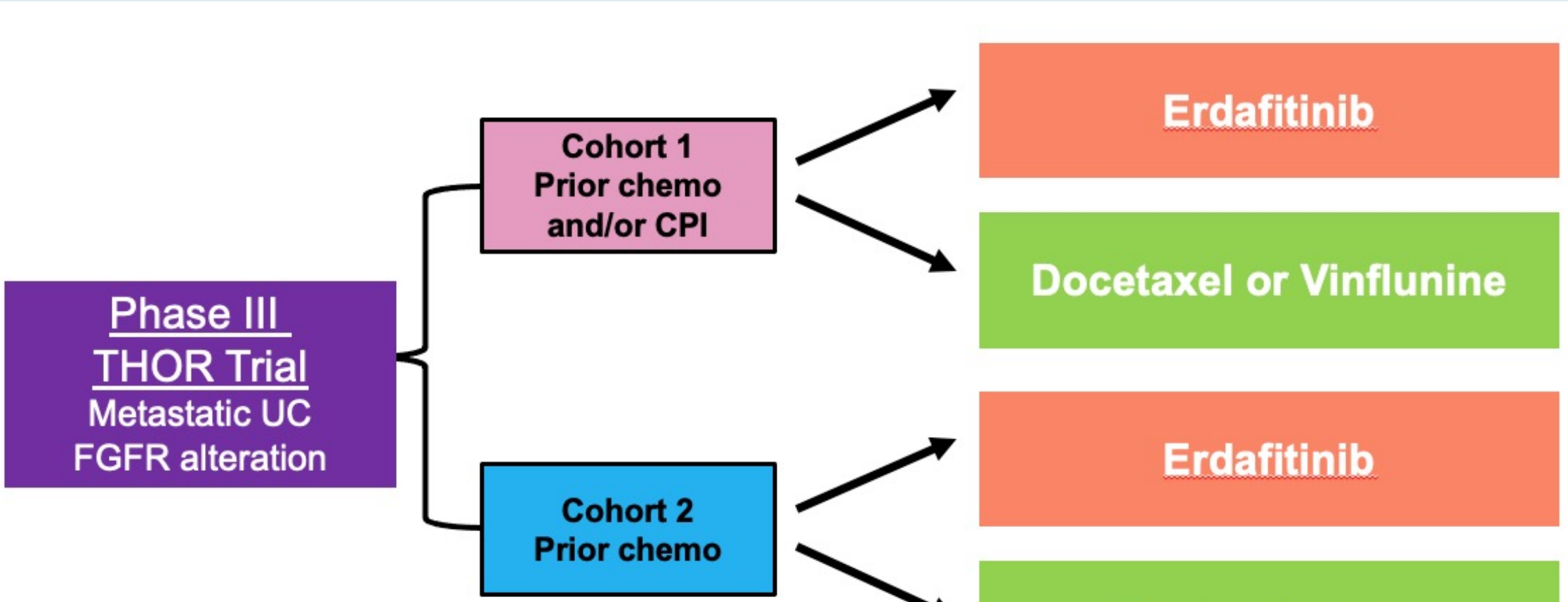
11% mFGFR

Wild type	**21% (95% CI: 15%, 29%)**
Mutant	**21% (95% CI: 15%, 29%)**

Wang, European Urology, 2019

Courtesy of Matthew Galsky, MD.

Ongoing Phase III THOR Trial Design



Primary endpoint: Overall survival
Secondary endpoints include progression-free survival, response, safety, change in disease severity and quality of life

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, November 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Adam M Brufsky, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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