Meet The Professor

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

Jonathan E Rosenberg, MD
Chief, Genitourinary Medical Oncology Service
Division of Solid Tumor Oncology
Enno W Ercklentz Chair
Memorial Sloan Kettering Cancer Center
New York, New York

Commercial Support

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Dr Love — Disclosures

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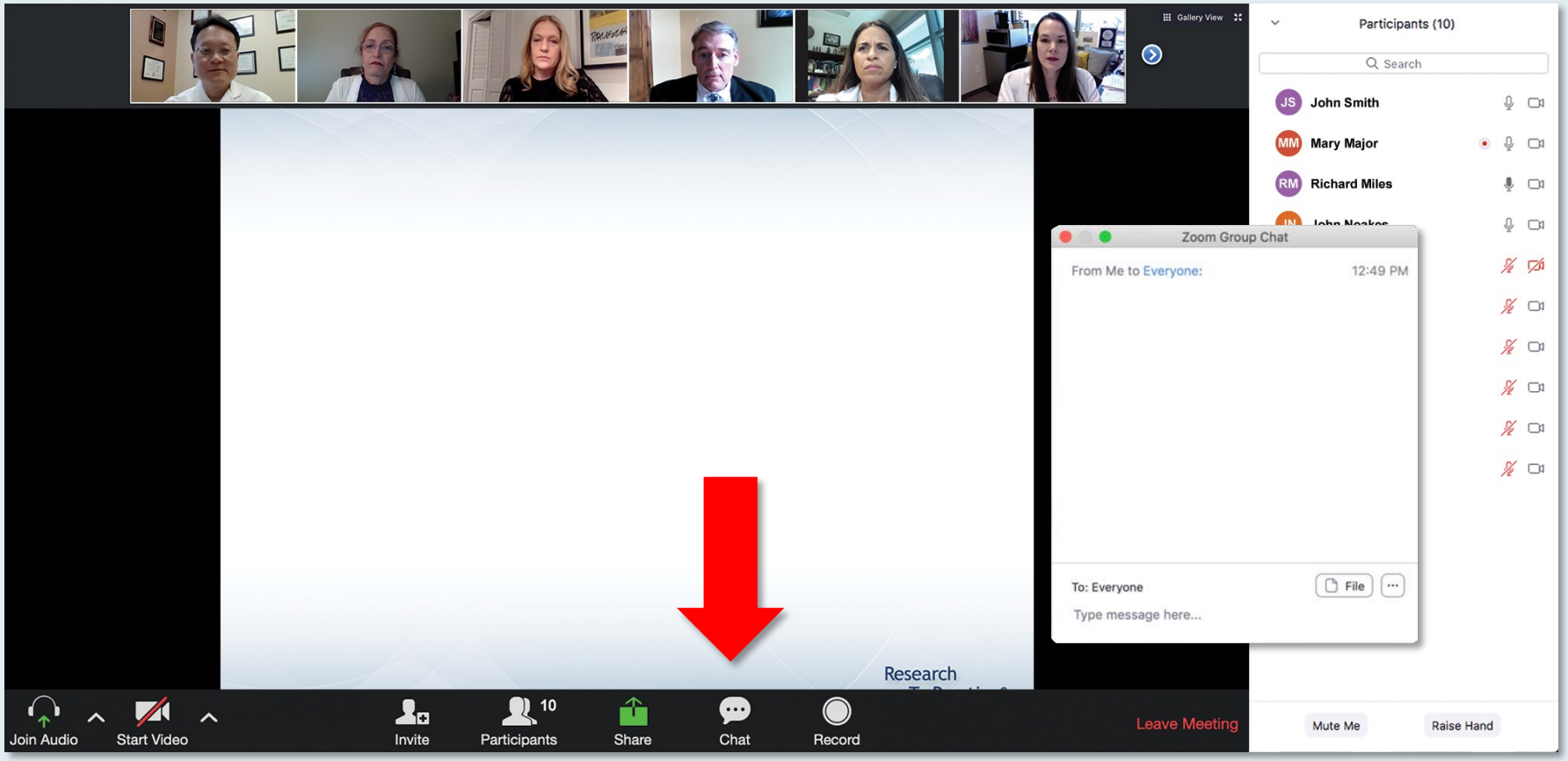

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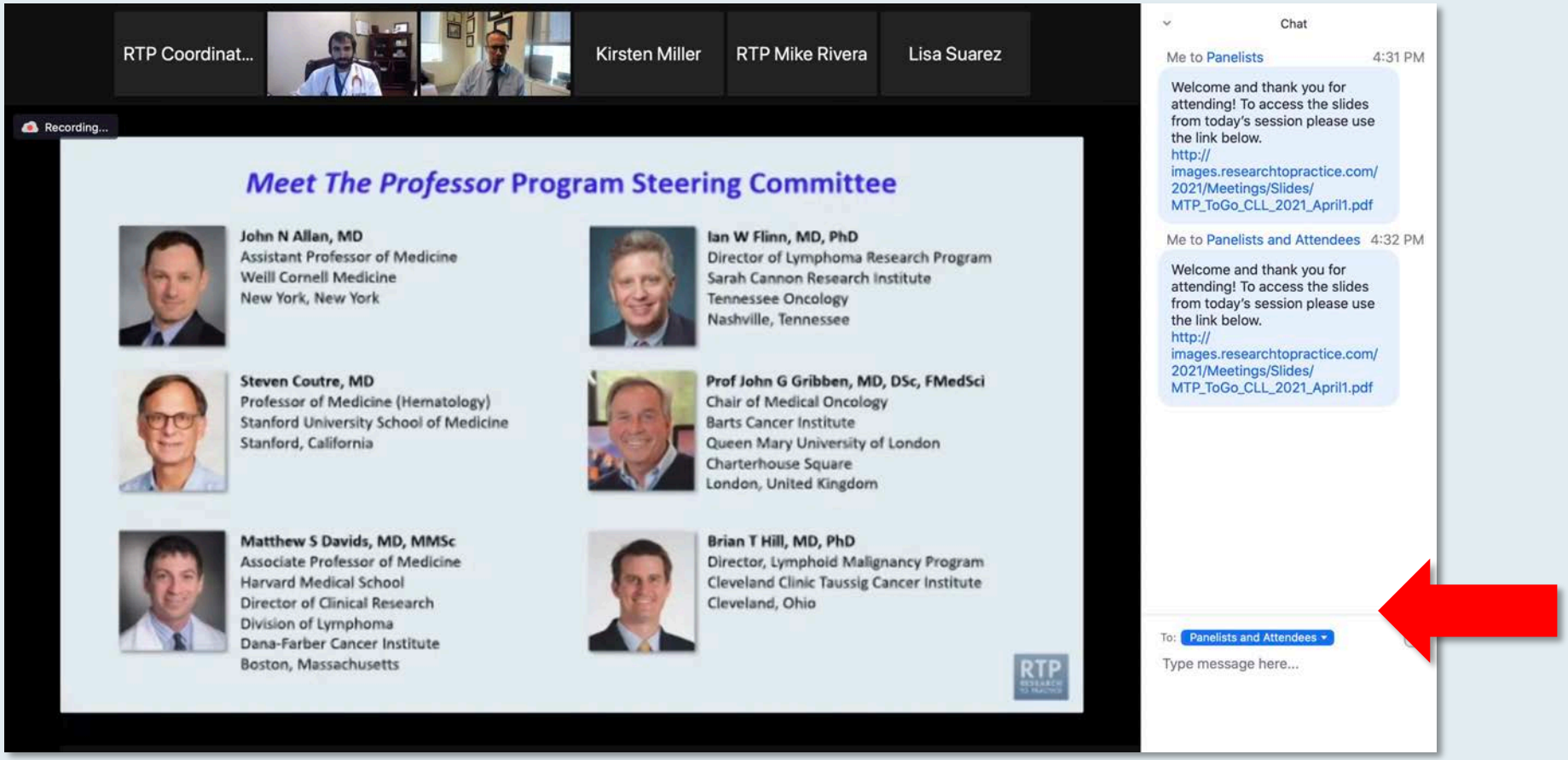

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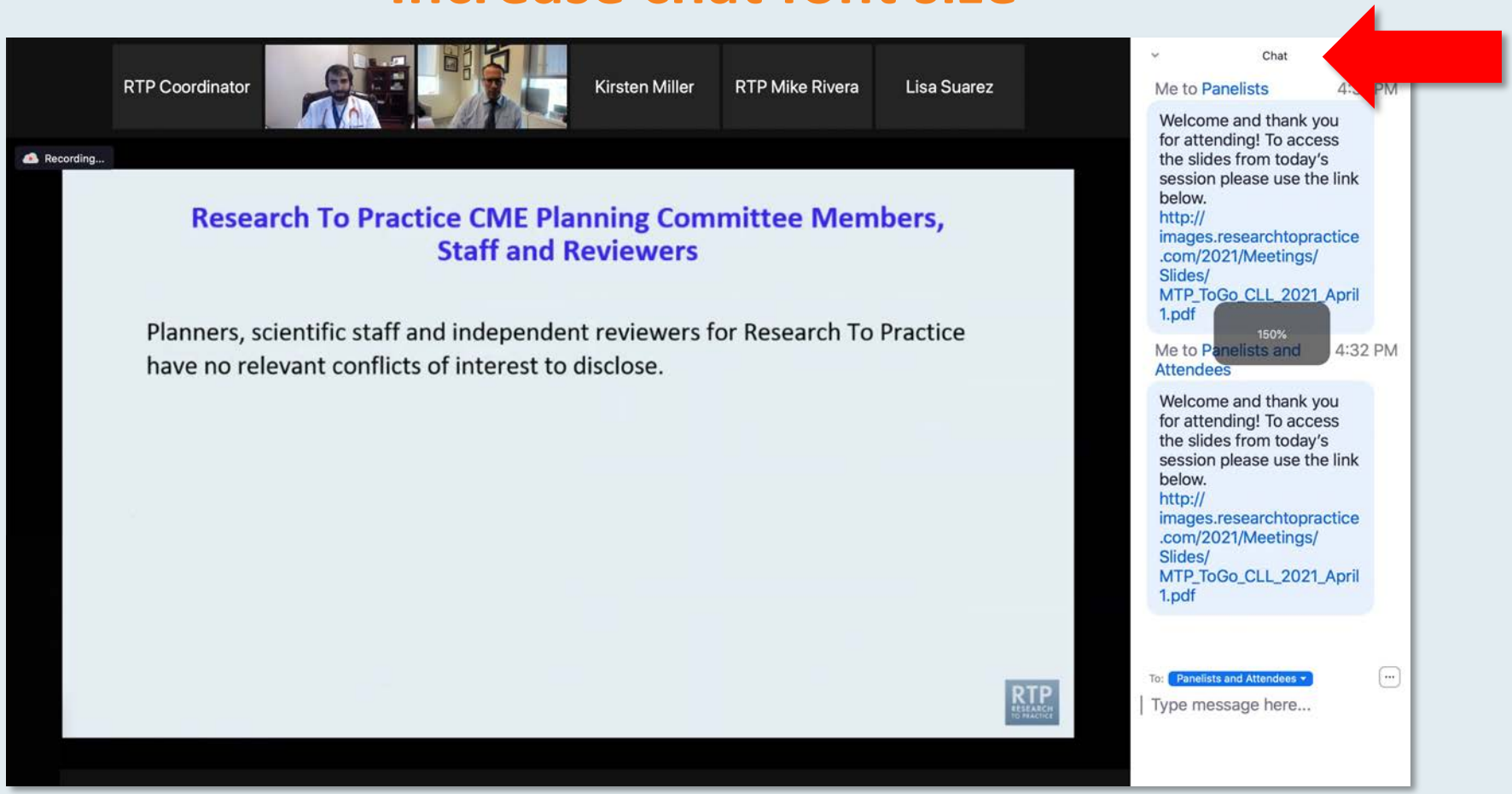

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Key Presentations on Genitourinary Cancers from the 2021 ASCO Annual Meeting

DR ARJUN BALAR

NYU PERLMUTTER CANCER CENTER

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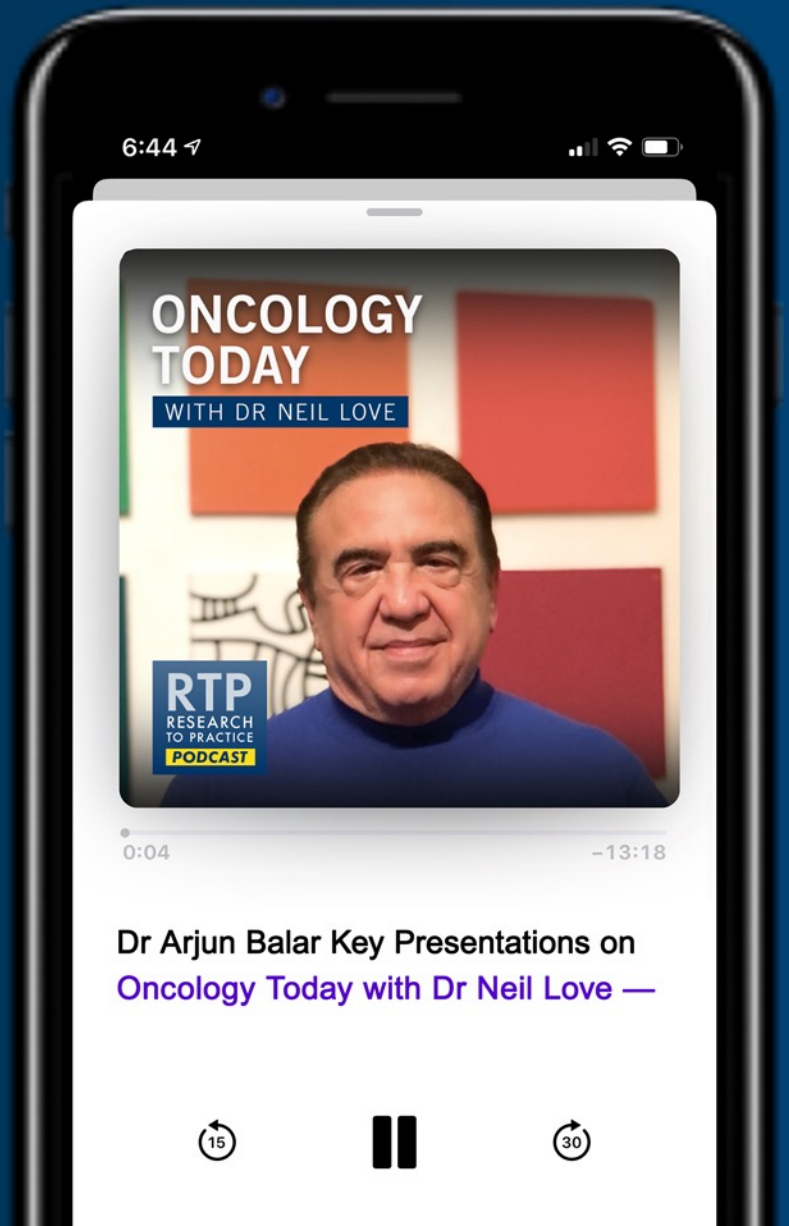

Meet The Professor

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

Wednesday, September 22, 2021
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Fall Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 23, 2021
5:00 PM – 6:00 PM ET

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John P Leonard, MD
Amy Goodrich, CRNP

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Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Friday, September 24, 2021
12:00 PM – 1:00 PM ET

Faculty

Martee L Hensley, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, September 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

Tuesday, September 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Peter Schmid, MD, PhD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Wednesday, September 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Brad S Kahl, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Friday, October 1, 2021
12:00 PM – 1:00 PM ET

Faculty

Hans Hammers, MD, PhD

Moderator

Neil Love, MD

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

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Enno W Ercklentz Chair
Memorial Sloan Kettering Cancer Center
New York, New York

Meet The Professor Program Participating Faculty

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

Shilpa Gupta, MD
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
Enno W Ercklentz Chair
Memorial Sloan Kettering Cancer Center
New York, New York

Guru Sonpavde, MD
Bladder Cancer Director
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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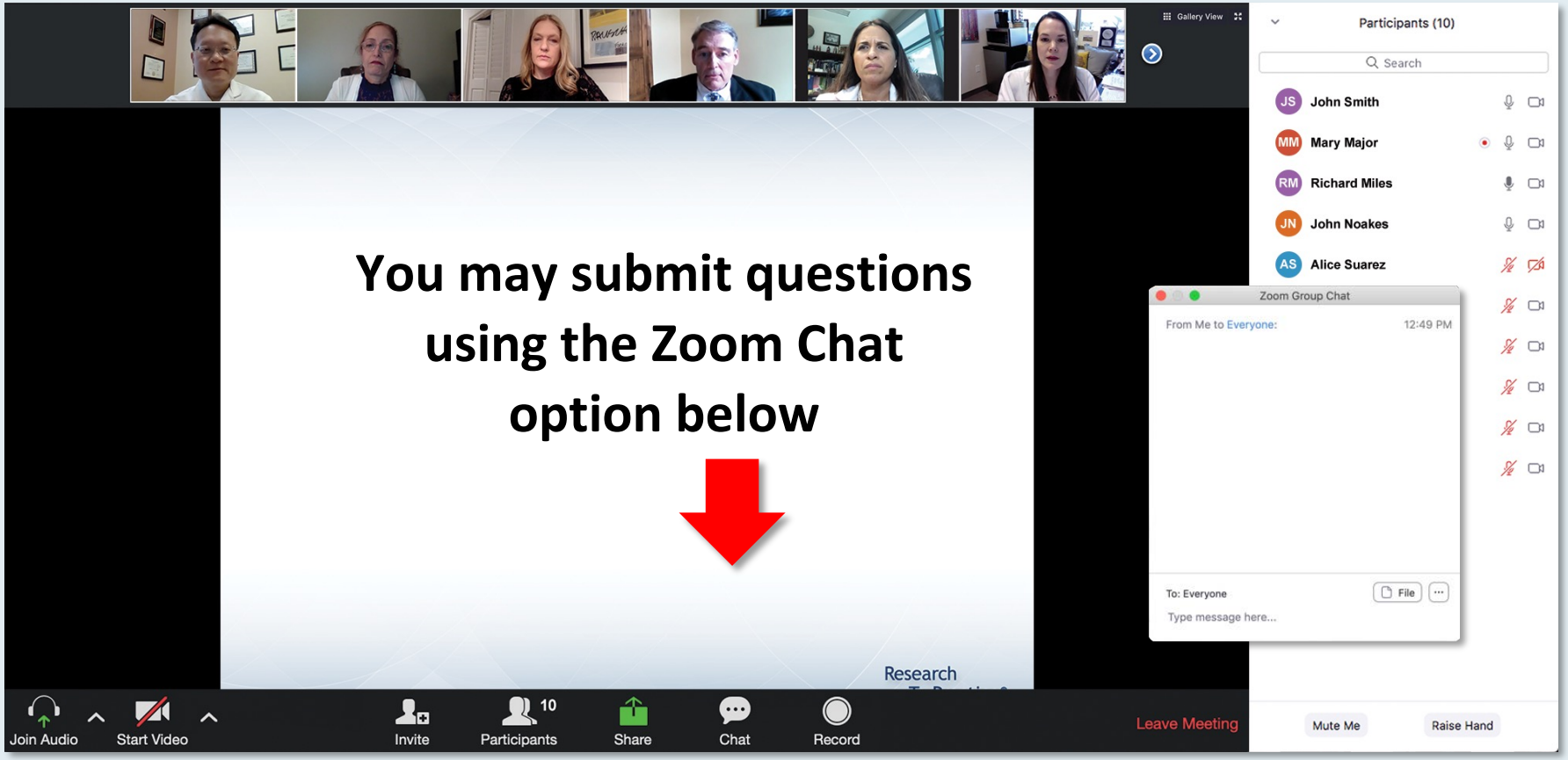

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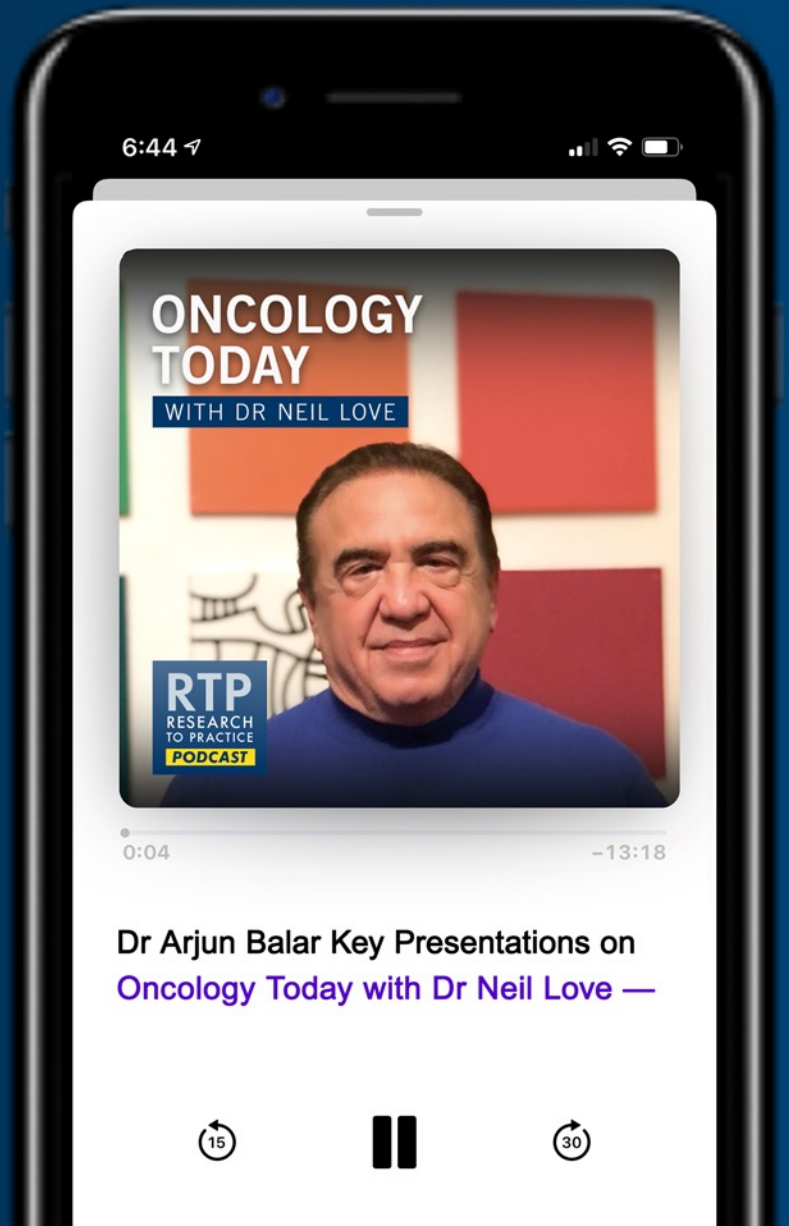

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New York, New York

Gordon A Brown, DO
Associate Professor of Urology
Rowan University SOM
Medical Director of Advanced Therapeutics
New Jersey Urology
Director of Robotic Surgery
Jefferson Health New Jersey
Sewell, New Jersey

Sulfi Ibrahim, MD
Hematology/Oncology
Reid Health
Richmond, Indiana

Jason Hafron, MD
Chief Medical Officer
Director of Clinical Research
Michigan Institute of Urology
Professor of Urology
Oakland University William Beaumont School of Medicine
Bloomfield, Michigan

Helen H Moon, MD
Medical Oncologist
Southern California Permanente Medical Group
Riverside, California

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Henna Malik, MD
Site Leader of Clinical Research Trials
Texas Oncology
North Houston, Willowbrook/Cypress
Houston, Texas

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

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Meet The Professor with Dr Rosenberg

Introduction: ADCs in the News!!

MODULE 1: Case Presentations

- Dr Moon: A 73-year-old man with metastatic UBC
- Dr Malik: An 84-year-old woman with non-muscle-invasive UBC and an FGFR2 tumor mutation
- Dr Ibrahim: A 72-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Santiago: A 56-year-old man with metastatic UBC – PD-L1-negative
- Dr Hafron: A 76-year-old woman with BCG-refractory non-muscle-invasive bladder cancer carcinoma in situ
- Dr Ibrahim: A 60-year-old man with BCG-refractory non-muscle-invasive UBC

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Rosenberg

MODULE 4: Key Data Sets

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Case Presentation – Dr Moon: A 73-year-old man with metastatic UBC

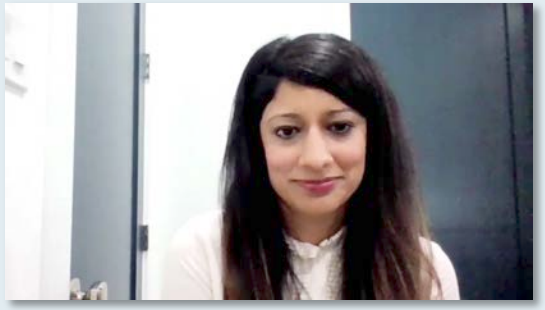
Dr Helen Moon

- PMH: DM, HTN, Peripheral neuropathy (grade 1), CAD and ECOG 0-1
- Presents with cough x 3 months
- CT chest: Bilateral lung nodules varying between 1-2.5 cm
  - Biopsy: Urothelial carcinoma
- Gemcitabine/cisplatin x 3, with PD → Platinum-refractory
- Pembrolizumab, with PR and grade 1 pneumonitis managed with inhaled steroids

Questions

- With COVID, what are the schedules that you feel most comfortable with for these medications? Do you think that there is any difference in efficacy and toxicity between different schedules?

Case Presentation – Dr Malik: An 84-year-old woman with non-muscle-invasive UBC and an FGFR2 tumor mutation



Dr Henna Malik

- PMH: Diabetes mellitus, hypertension and hyperlipidemia
- Presented with hematuria intermittent over the past 1 year and treated for UTI with antibiotics that continued to recur
- Cystoscopy: High-grade, non-muscle-invasive urothelial cell carcinoma, approximately 2 cm in the posterior bladder wall
- CT abdomen/pelvis: No metastatic disease. Labs normal, except creatinine 1.2
- Pembrolizumab 200 mg IV q3 weeks
- NGS: FGFR2 mutation
- Erdafitinib → decrease in disease burden and patient tolerating treatment well with some mucositis

Questions

- How do you sequence erdafitinib and enfortumab vedotin? Where does sacituzumab govitecan fit in?
- How do your diabetic patients tolerate erdafitinib? How frequently should we schedule their eye exams? Can it worsen their retinopathy? How would you dose-modify this drug?

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Case Presentation – Dr Ibrahim: A 72-year-old woman with metastatic UBC – PD-L1 30%

Dr Sulfi Ibrahim

- Metastatic UBC, PD-L1 30%
- Cisplatin/gemcitabine
- Clinical trial of nivolumab and sitravatinib → PD
- Enfortumab vedotin, with response
  - Ocular toxicity, with conjunctiva erythema
  - Skin toxicity, with pruritic rash on upper and lower extremities, that is not responding to methylprednisolone dose pack and dose reduction

Questions

- If a patient has disease progression on platinum-based therapy and has a low PD-L1 level, would you consider giving the enfortumab prior to immune checkpoint inhibitor therapy?
- What is the status of the clinical trial evaluating enfortumab vedotin and immune checkpoint inhibitor therapy in the front-line setting? Are the results expected relatively soon?
- How do you sequence enfortumab vedotin, erdafitinib, and sacituzumab govitecan for patients with metastatic disease who progress on platinum-based therapy?

Case Presentation – Dr Brown: A 74-year-old woman with metastatic UBC

Dr Gordon Brown

- Initial diagnosis of muscle-invasive UBC → cystectomy and anterior vaginectomy with urethrectomy
  - EBRT and cisplatin/gemcitabine followed by surveillance
- 5 years later develops metastases to pubic bone and femur
- Pembrolizumab → dose interrupted due to development of myositis → PD
- Enfortumab vedotin → lower extremity discomfort but stable disease

Questions

- What are your thoughts about the tolerability of the antibody-drug conjugates in patients with advanced bladder cancer compared to the historical tolerability of additional systemic chemotherapy in that same patient population?
- What is your opinion of the tolerability of erdafitinib in patients with metastatic muscle-invasive bladder cancer? How do you manage the associated toxicity issues?

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

Dr Ferdy Santiago

- 1/2019 TURP: Invasive high-grade urothelial carcinoma, with RAF fusion, 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 followed by PD
  - Developed a significant skin rash 3 to 4 months into treatment that was managed by steroids

Questions

- With enfortumab vedotin, how do you go about differentiating between a drug-related rash and some other type of paraneoplastic rash?
- What are some strategies that can be employed to help mitigate the rash?

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Case Presentation – Dr Hafron: A 76-year-old woman with BCG-refractory non-muscle-invasive bladder cancer carcinoma in situ

Dr Jason Hafron

- BCG unresponsive carcinoma in situ
- Elected to start treatment with pembrolizumab
- Initial labs for TSH were normal (TSH 1.2)
- After 3 infusions she began to have severe fatigue, constipation and joint weakness
  - TSH found to be 20.7 – immune mediated hypothyroidism
  - Managed with levothyroxine and short course of steroids
- Patient responded and is doing well

Question

- Do you routinely monitor thyroid studies for patients on pembrolizumab?

Case Presentation – Dr Ibrahim: A 60-year-old man with BCG-refractory non-muscle-invasive UBC

Dr Sulfi Ibrahim

- Diagnosed with non-muscle-invasive UBC
- Received intravesical BCG and intravesical mitomycin
- Disease recurrence
- Discussed clinical trial of atezolizumab in combination with intravesical gemcitabine therapy

Questions

- Would you offer this patient pembrolizumab?
- Are there evolving strategies evaluating combining intravesical treatment along with immunotherapy?

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Current and Emerging Treatment Strategies for Patients with Non-Metastatic Urothelial Bladder Cancer (UBC)

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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

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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

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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

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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

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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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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

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Meet The Professor with Dr Rosenberg

Introduction: ADCs in the News!!

MODULE 1: Case Presentations

- Dr Moon: A 73-year-old man with metastatic UBC
- Dr Malik: An 84-year-old woman with non-muscle-invasive UBC and an FGFR2 tumor mutation
- Dr Ibrahim: A 72-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Santiago: A 56-year-old man with metastatic UBC – PD-L1-negative
- Dr Hafron: A 76-year-old woman with BCG-refractory non-muscle-invasive bladder cancer carcinoma in situ
- Dr Ibrahim: A 60-year-old man with BCG-refractory non-muscle-invasive UBC

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Rosenberg

MODULE 4: Key Data Sets

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Journal Club with Dr Rosenberg – Part 1

- Teo MY et al. **Clinicogenomic predictors of extreme responses to anti-PD1/PDL1 checkpoint inhibitors (CPI) in metastatic urothelial cancer (mUC).** ASCO 2020;Abstract 5050.
- Guercio BJ, Iyer G, Rosenberg JE. **Developing precision medicine for bladder cancer.** *Hematol Oncol Clin North Am* 2021;35(3):633-53.
- Do MH et al. **Dermatologic infections in cancer patients treated with checkpoint inhibitors.** *J Am Acad Dermatol* 2021;[Online ahead of print].
- Francis JH et al. **Clinical and morphologic characteristics of fibroblast growth factor receptor inhibitor-associated retinopathy.** *JAMA Ophthalmol* 2021;[Online ahead of print].
- Powles T et al. **Beyond chemotherapy and checkpoint inhibitors: Weighing the risks and benefits of the novel therapies for metastatic urothelial carcinoma.** *J Clin Oncol* 2021;[Online ahead of print].

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Journal Club with Dr Rosenberg – Part 2

- Lyou Y et al. **Relationship between hyperphosphatemia with infigratinib (BGJ398) and efficacy in FGFR3-altered advanced/metastatic urothelial carcinoma (aUC).** Genitourinary Cancers Symposium 2021;Abstract 576.
- Balar AV et al. **Pembrolizumab (pembro) in combination with gemcitabine (Gem) and concurrent hypofractionated radiation therapy (RT) as bladder sparing treatment for muscle-invasive urothelial cancer of the bladder (MIBC): A multicenter phase 2 trial.** ASCO 2021;Abstract 4504.
- Bellmunt J et al; IMvigor010 Study Group. **Adjuvant atezolizumab versus observation in muscle-invasive urothelial carcinoma (IMvigor010): A multicentre, open-label, randomised, phase 3 trial.** *Lancet Oncol* 2021;22(4):525-37.
- Funt SA et al. **Neoadjuvant atezolizumab (A) with gemcitabine and cisplatin (GC) in patients (pts) with muscle-invasive bladder cancer (MIBC): A multicenter, single-arm, phase 2 trial.** ASCO 2021;Abstract 4517.

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Journal Club with Dr Rosenberg – Part 3

- Hussain MHA et al. **IMvigor010: Primary analysis from a phase III randomized study of adjuvant atezolizumab (atezo) versus observation (obs) in high-risk muscle-invasive urothelial carcinoma (MIUC).** ASCO 2020;Abstract 5000.
- Heath EI, Rosenberg JE. **The biology and rationale of targeting nectin-4 in urothelial carcinoma.** *Nat Rev Urol* 2021;18(2):93-103.
- Powles T et al. **Enfortumab vedotin in previously treated advanced urothelial carcinoma.** *N Engl J Med* 2021;384(12):1125-35.
- Rosenberg JE et al. **Analysis of hard-to-treat subgroups from EV-301: A phase III trial of enfortumab vedotin (EV) vs chemotherapy for previously treated advanced urothelial carcinoma.** ESMO 2021; Abstract 698P.
- Sarfaty M et al. **Detection of FGFR3 alt in plasma cfDNA in metastatic UC patients receiving Erda therapy.** ASCO 2021;Abstract e16519.
- Wong JL, Rosenberg JE. **Targeting nectin-4 by antibody-drug conjugates for the treatment of urothelial carcinoma.** *Expert Opin Biol Ther* 2021;21(7):863-73.

RTP RESEARCH TO PRACTICE

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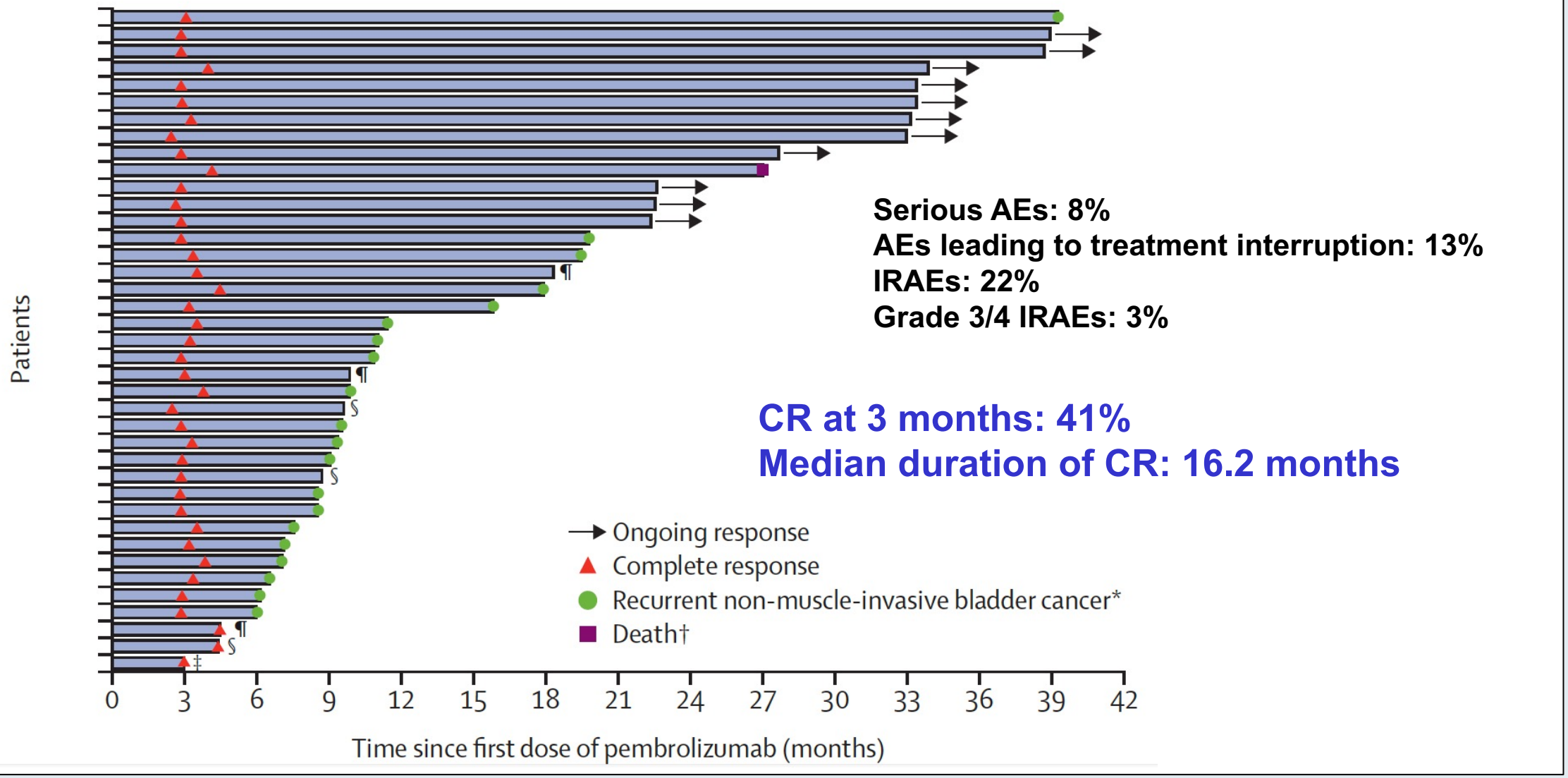
Nonmetastatic Urothelial Bladder Cancer (UBC)

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



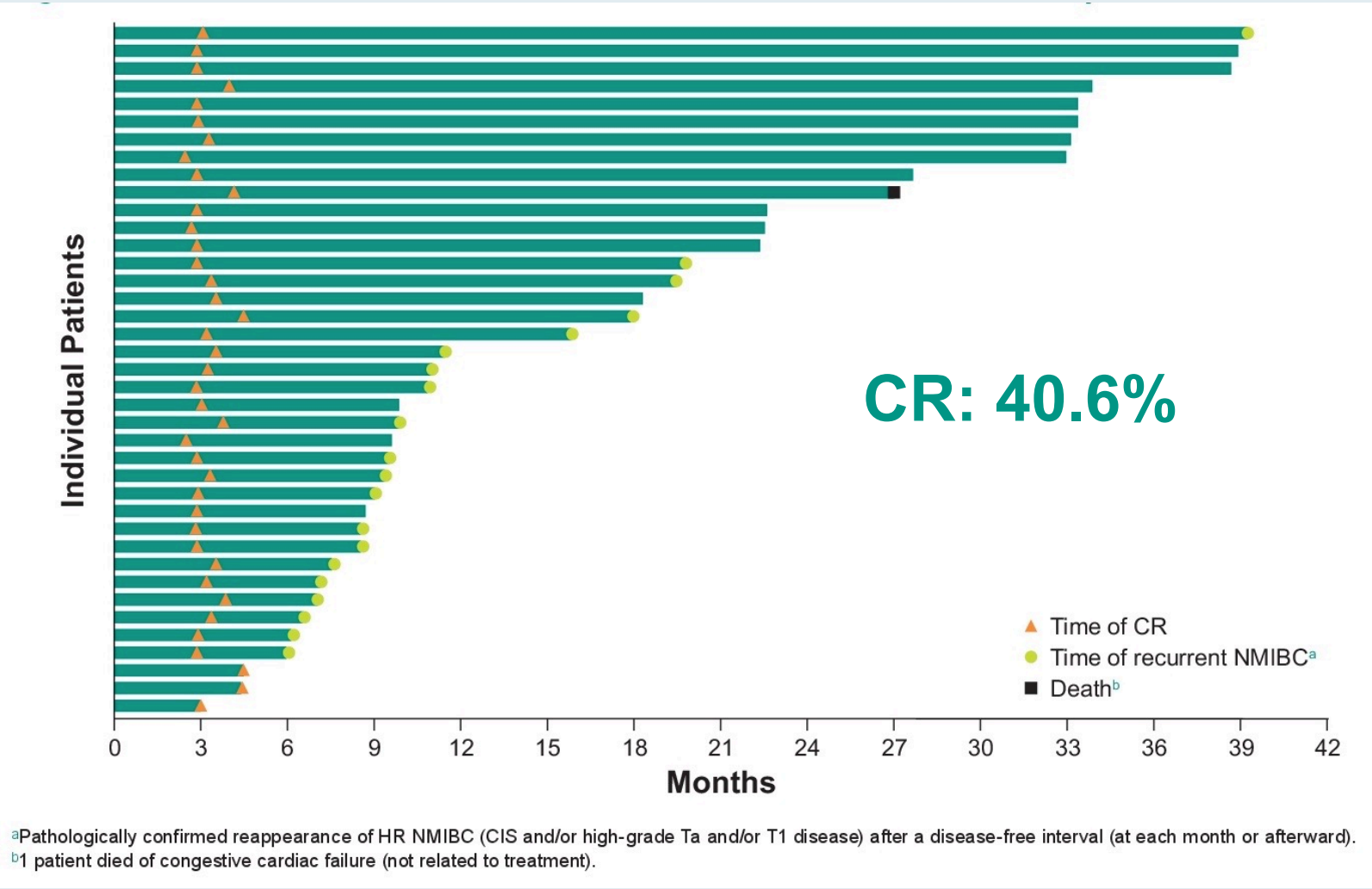
Balar AV et al. *Lancet Oncol* 2021;22:919-30.

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.

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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."

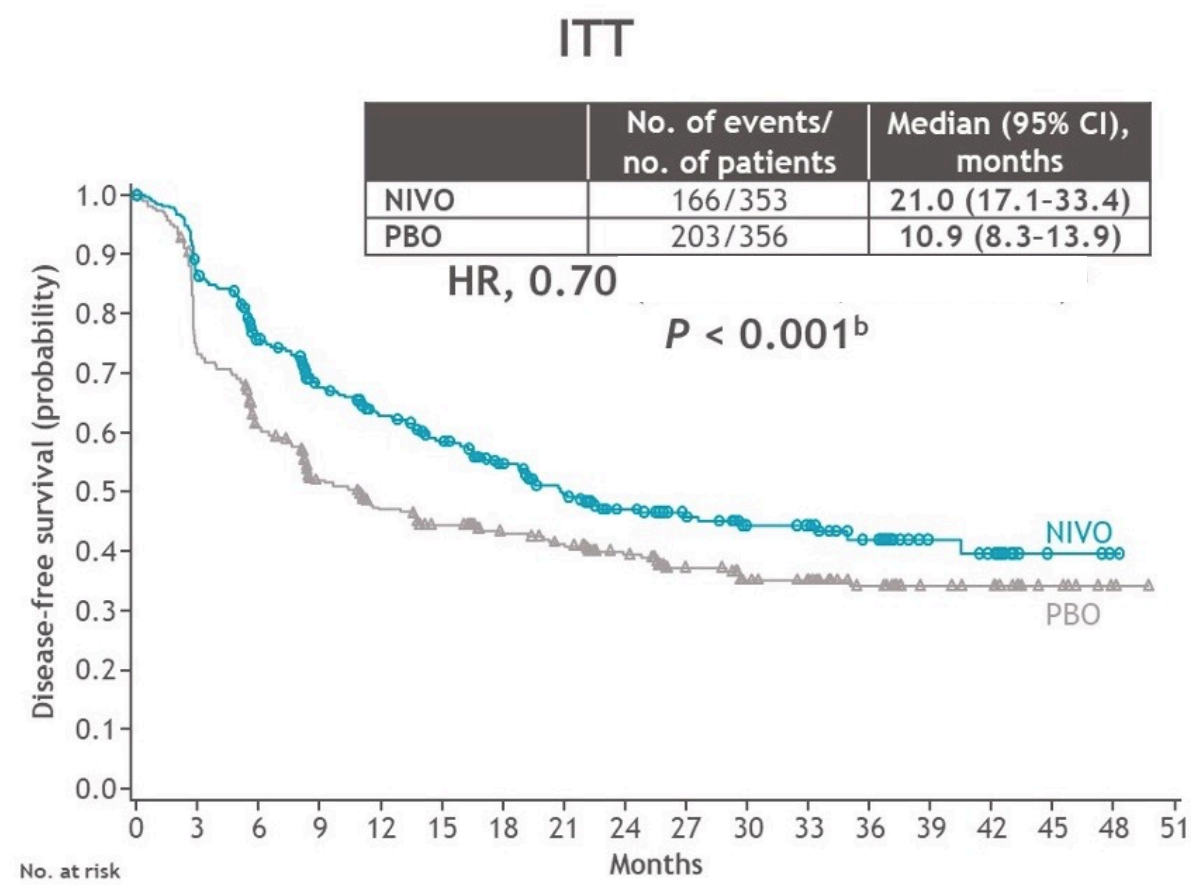
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-adjuvant-treatment-urothelial-carcinoma

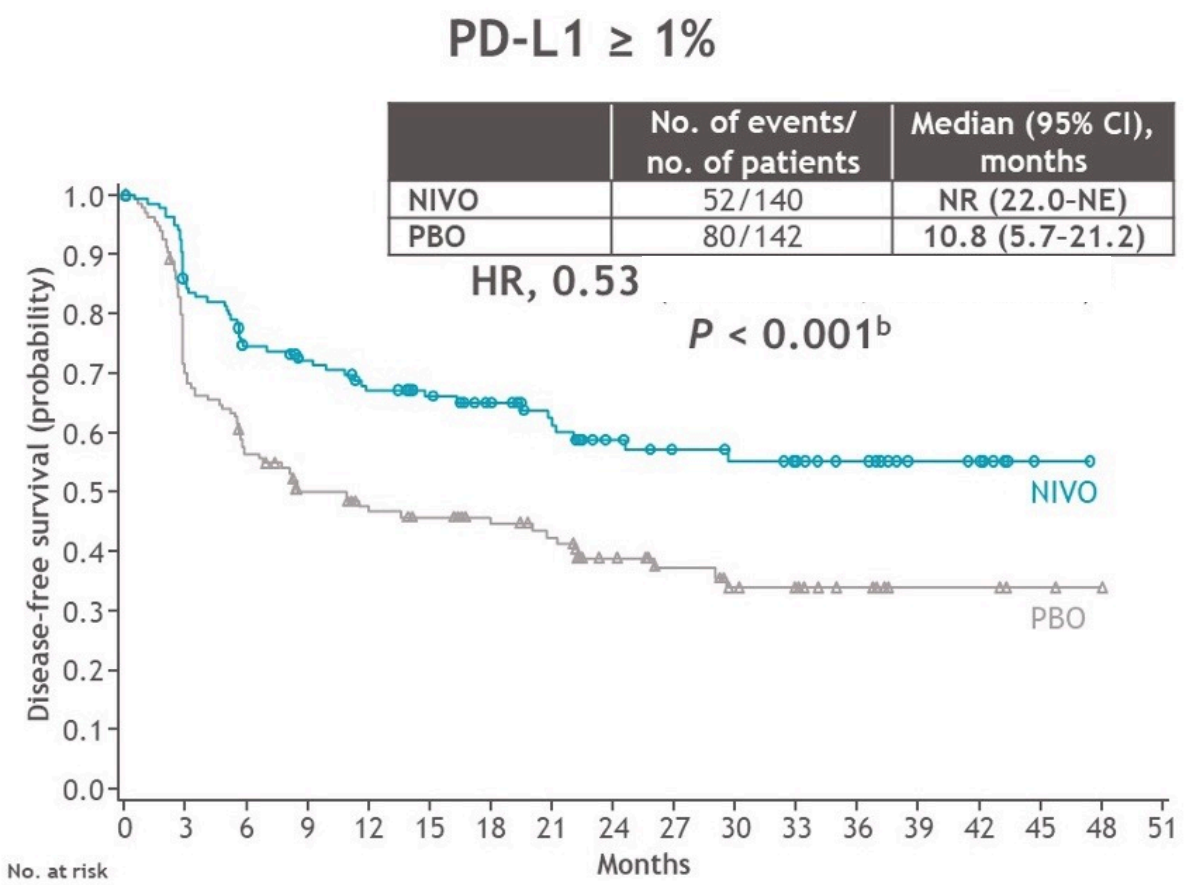
First Results from the Phase 3 CheckMate 274 Trial of Adjuvant Nivolumab vs Placebo in Patients Who Underwent Radical Surgery for High-Risk Muscle-Invasive Urothelial Carcinoma (MIUC)

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

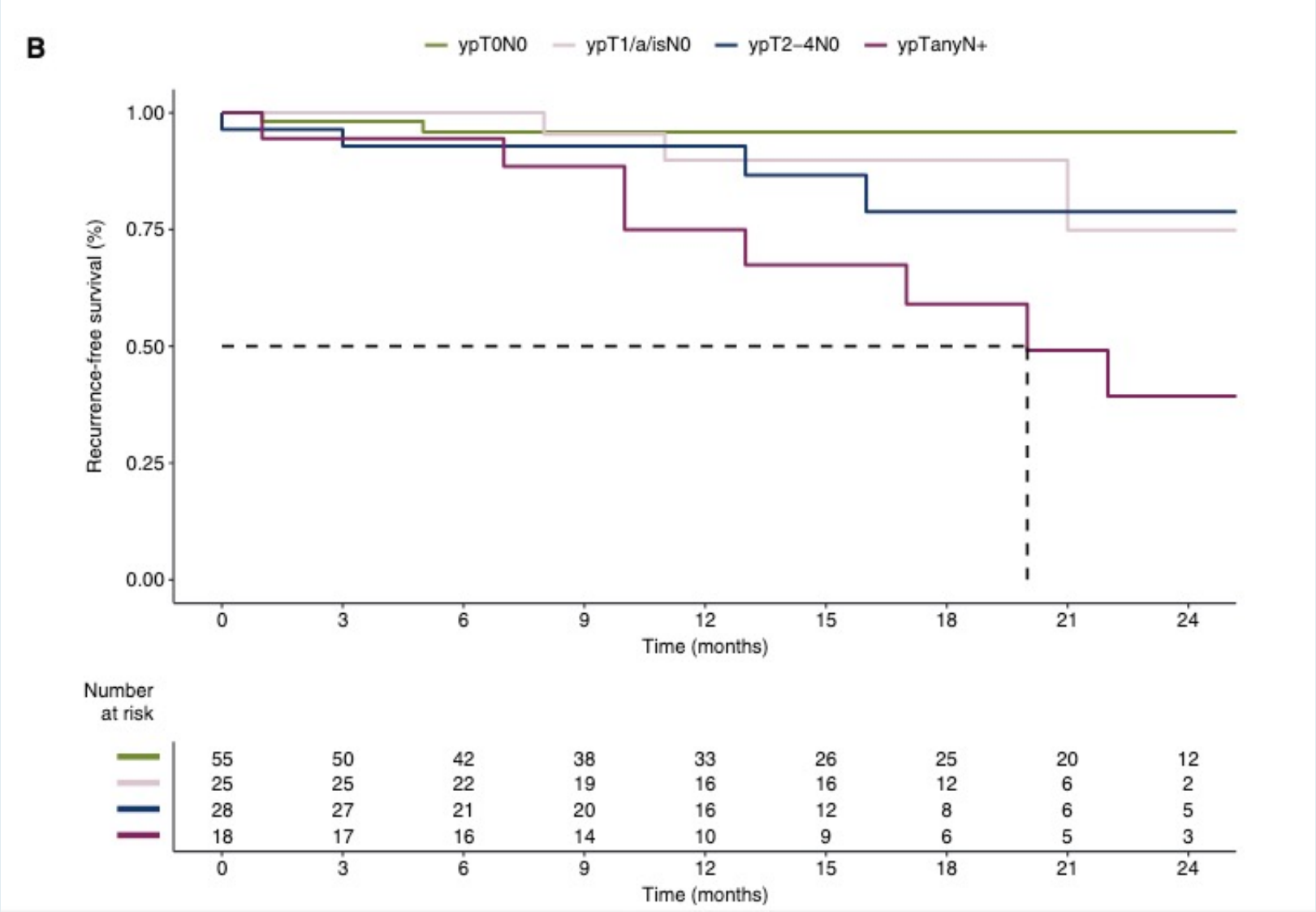
Does the administration of preoperative pembrolizumab lead to sustained remission post-cystectomy? First survival outcomes from the PURE-01 study☆

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

The NEW ENGLAND JOURNAL of MEDICINE

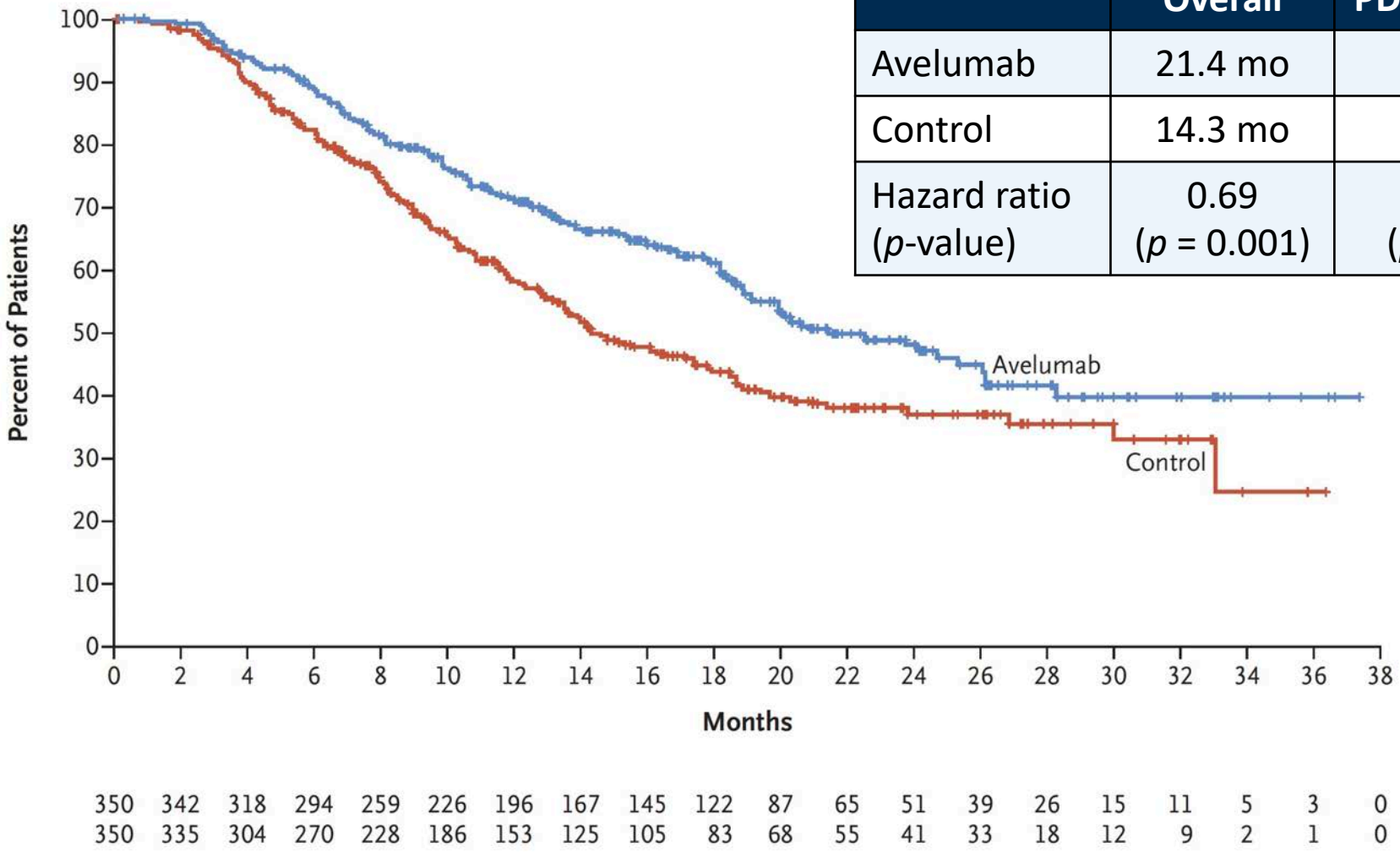
ORIGINAL ARTICLE

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."

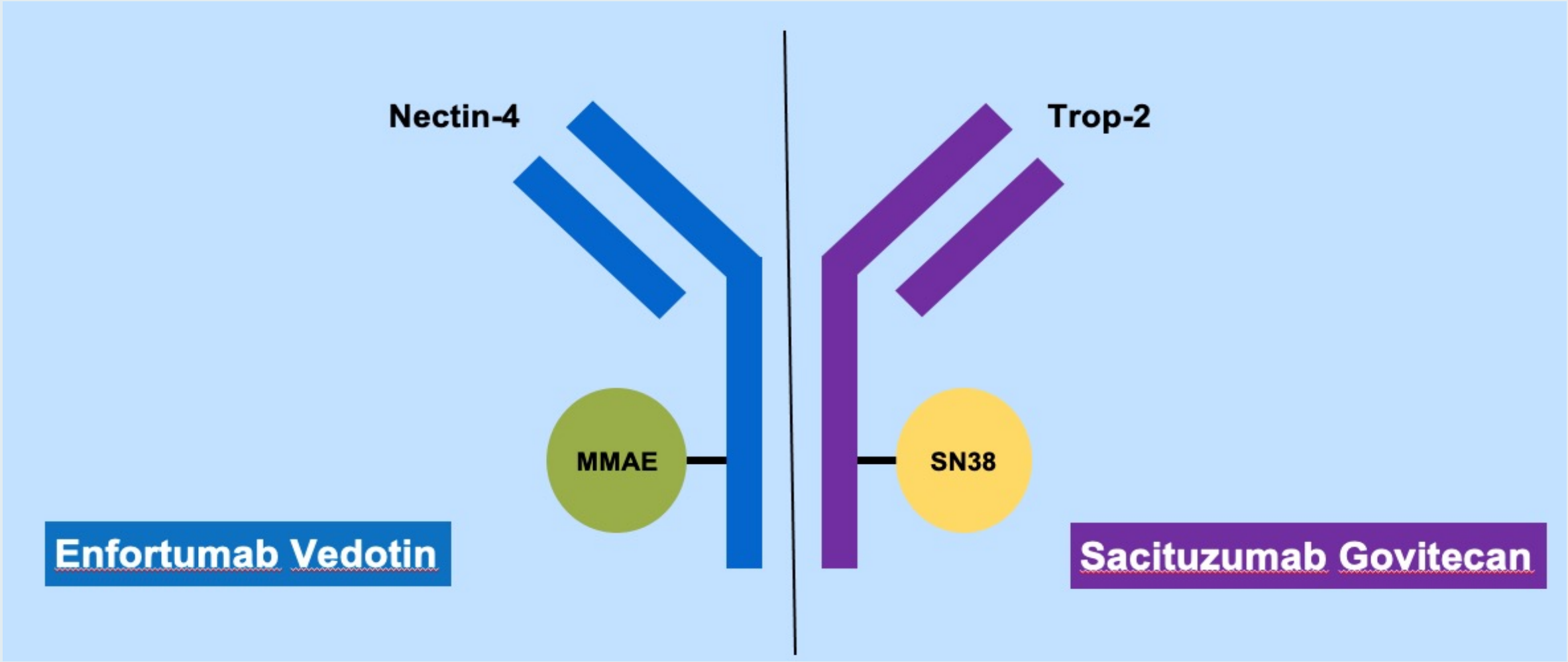
https://www.astrazeneca.com/media-centre/press-releases/2021/voluntary-withdrawal-imfinzi-us-bladder-indication.html

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

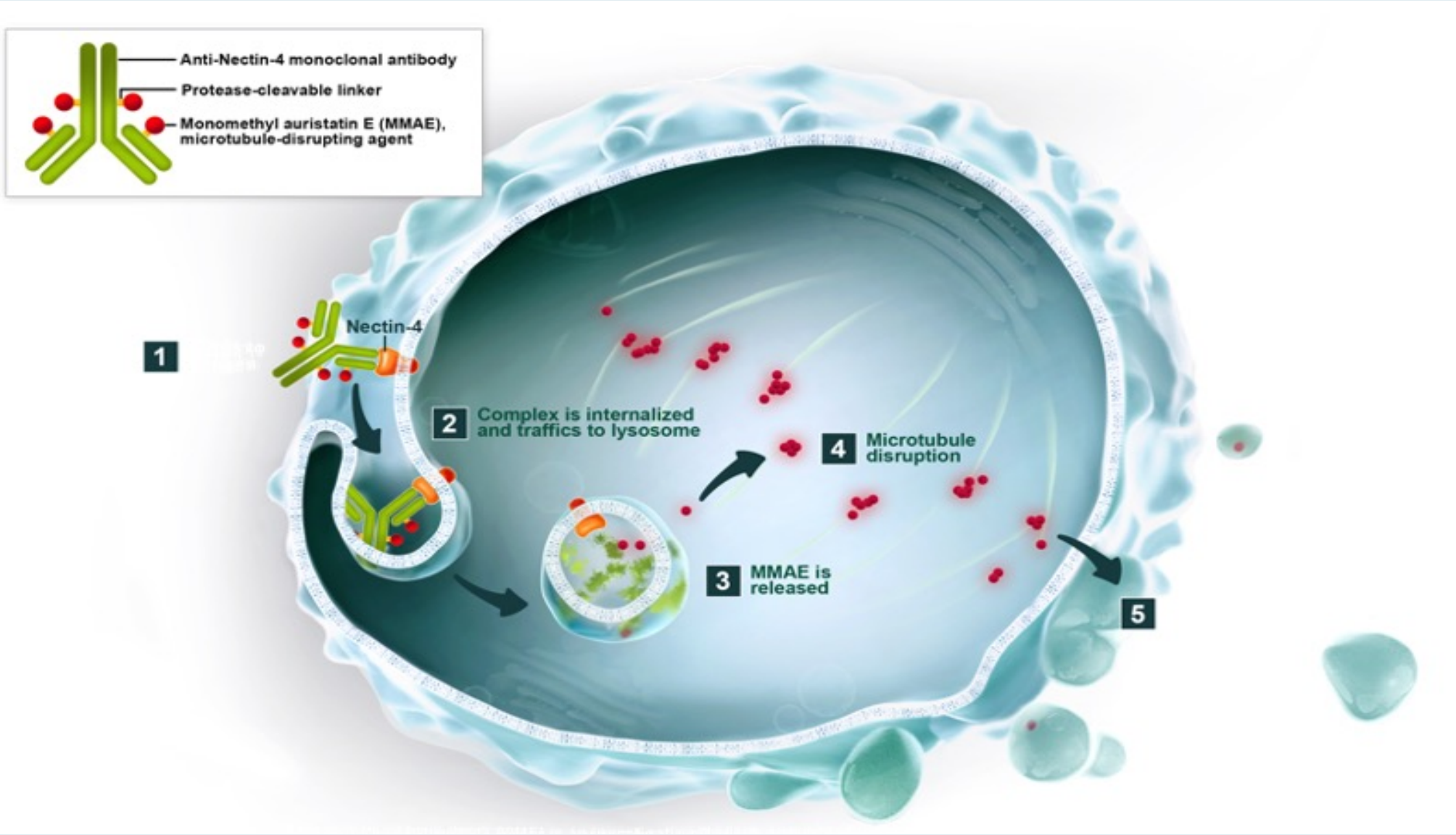
- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

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

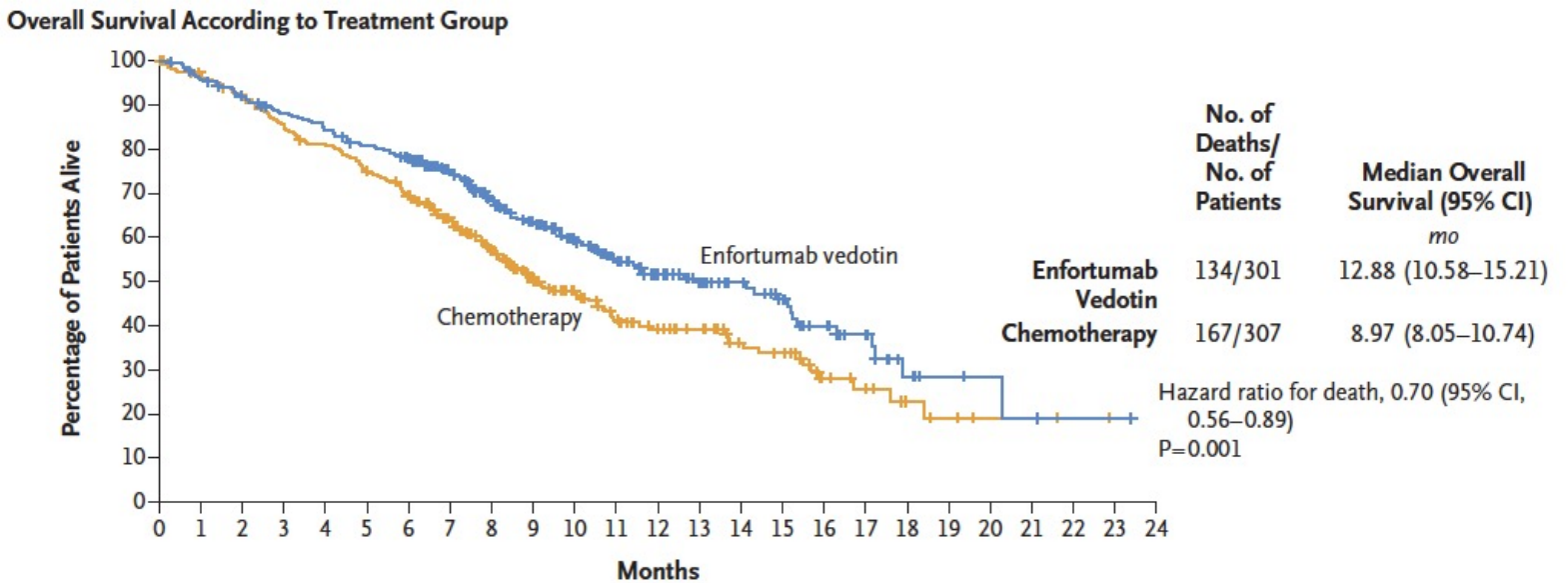
ORIGINAL ARTICLE

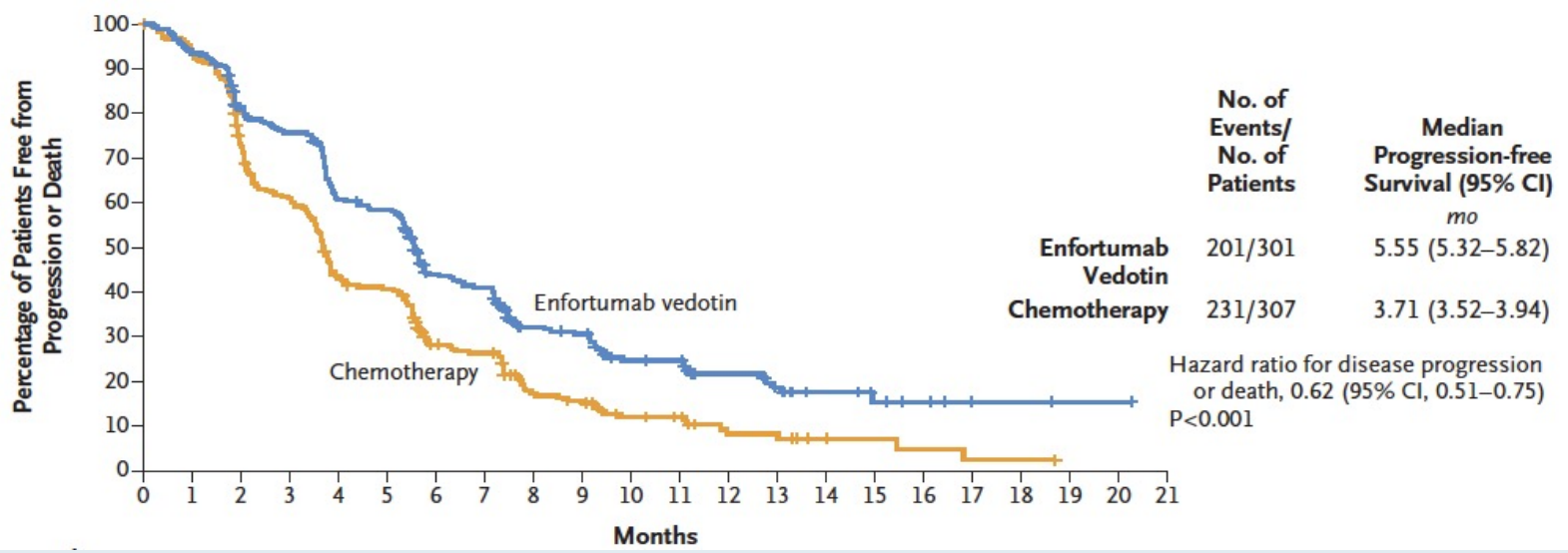
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

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

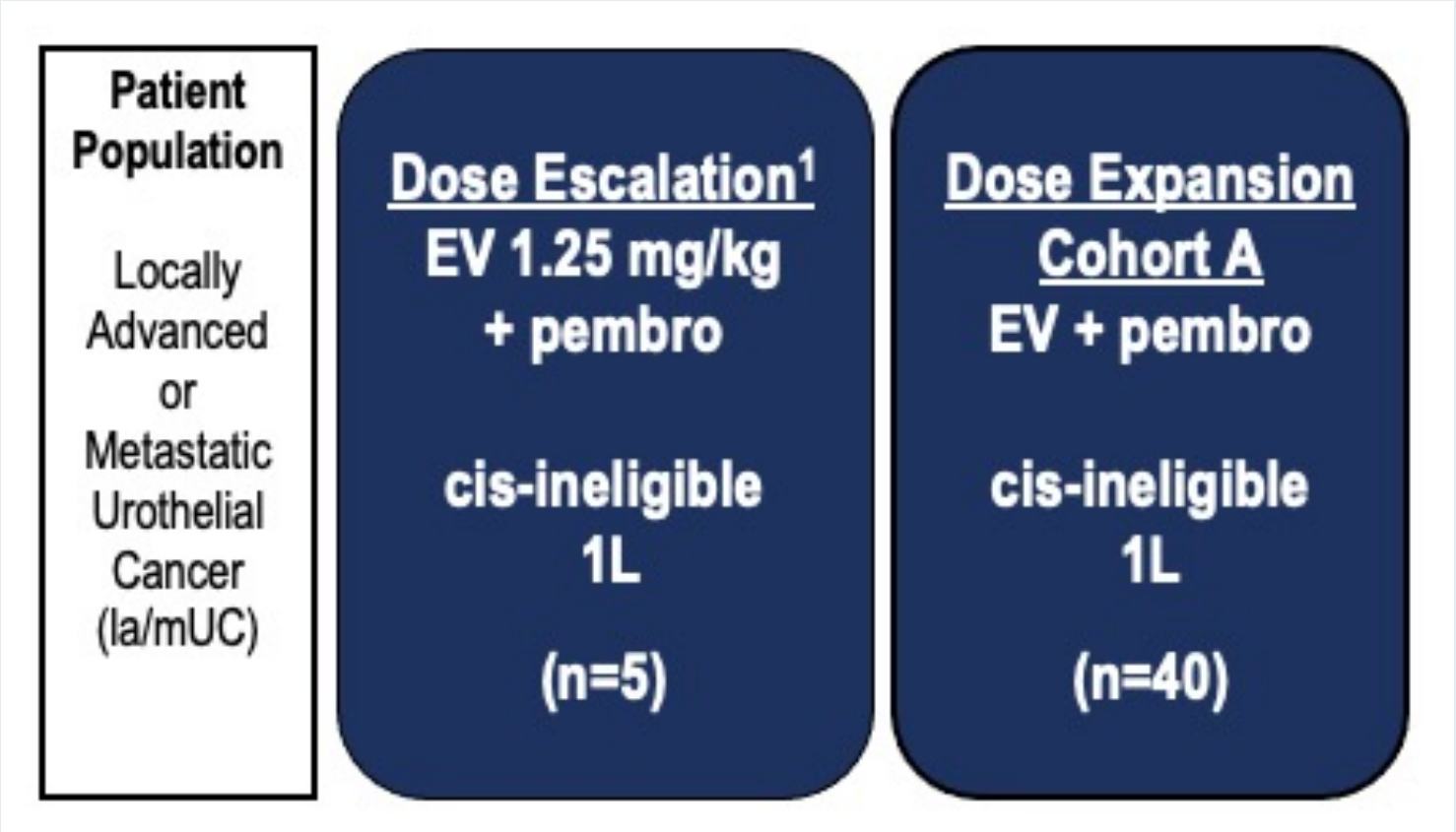
JAMA Dermatol. Published online September 8, 2021. doi:10.1001/jamadermatol.2021.3450

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.

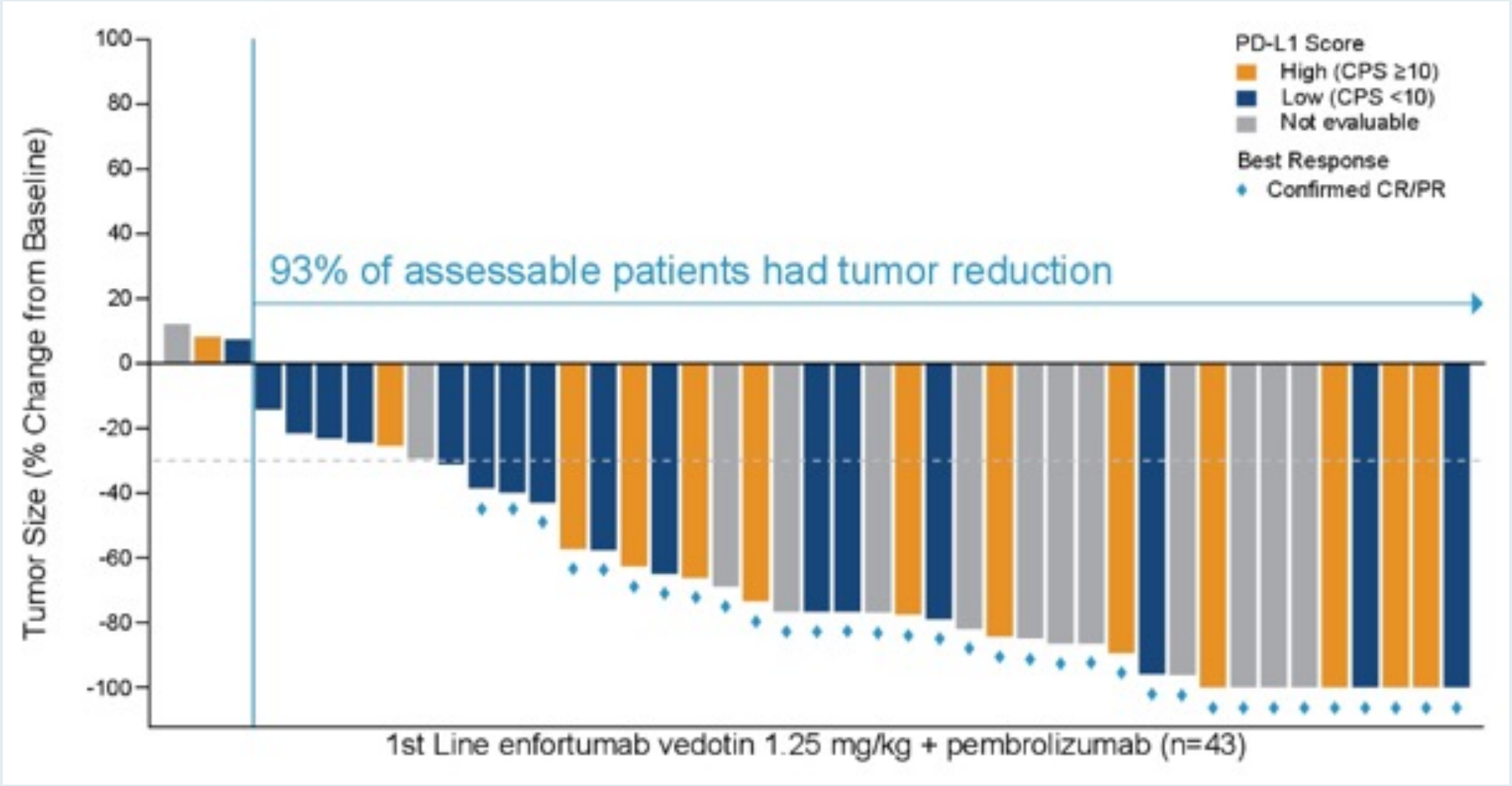
EV-103: Enfortumab Vedotin + Pembrolizumab Cohorts



- **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.

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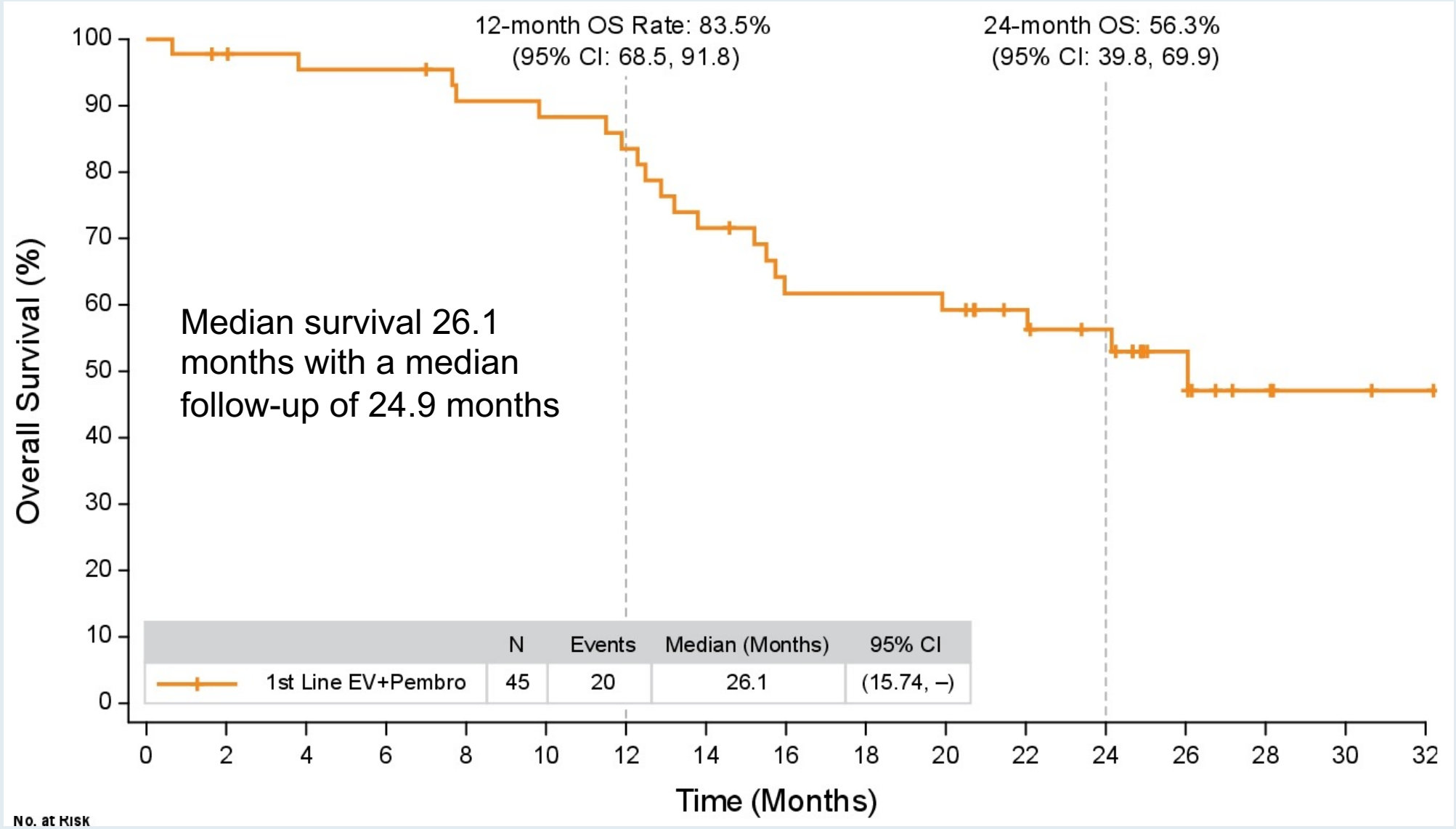
EV-103: Updated Overall Survival



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

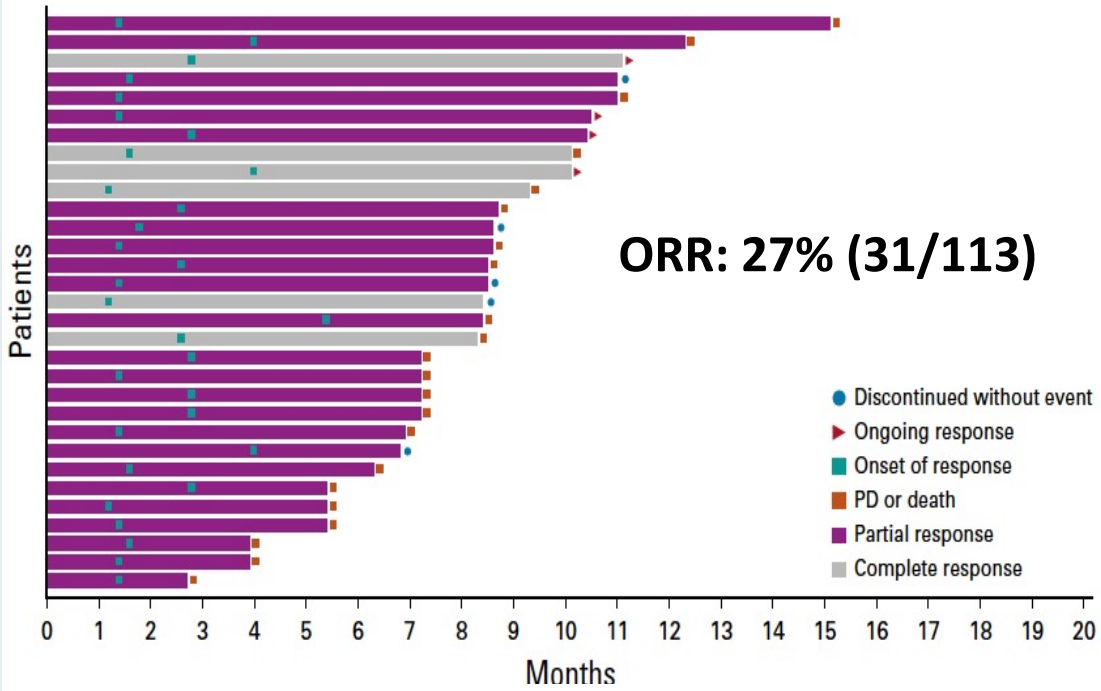
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11]; 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.

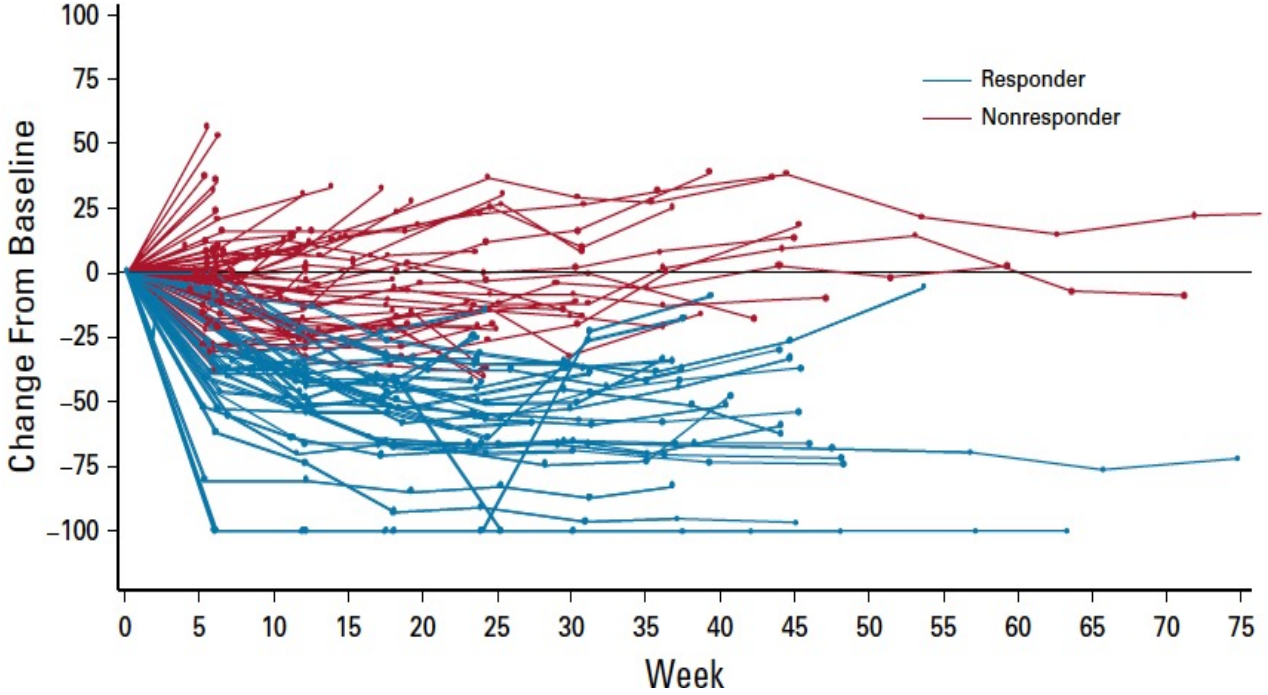
TROPHY U-01 (Cohort 1): ORR, Duration of Response and Survival

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

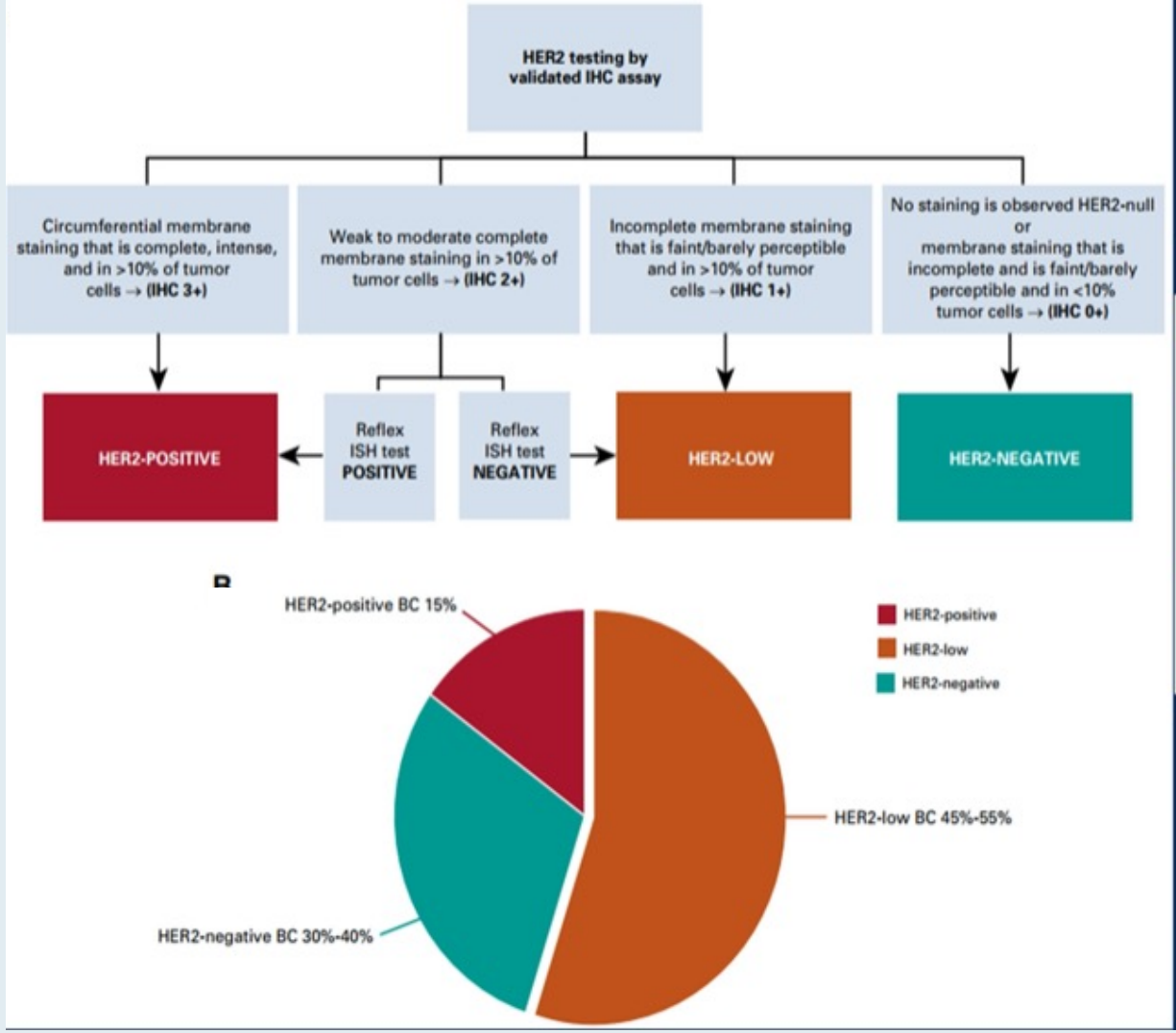
"The FDA has granted disitamab vedotin (RC48) a breakthrough therapy designation for the treatment of patients with HER2-positive locally advanced or metastatic urothelial carcinoma following treatment with platinum-based chemotherapy, according to the company developing the antibody-drug conjugate (ADC).

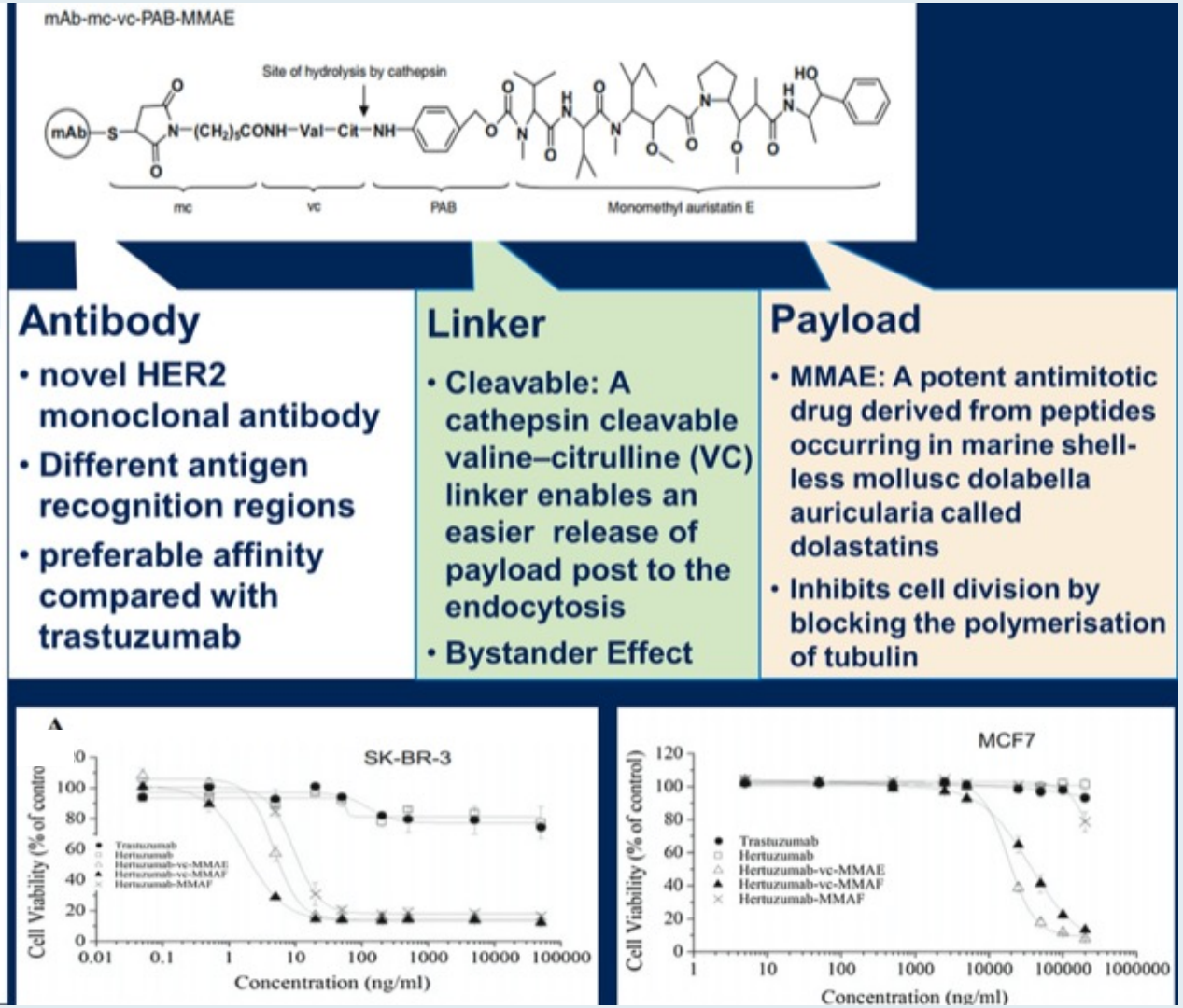
The designation will expedite the development and review of disitamab vedotin in this setting. Phase 2 data presented at the 2019 ASCO Annual Meeting showed that the ADC achieved a confirmed objective response rate of 51.2%, with confirmed responses reported in 22 of 43 patients. The best overall response 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

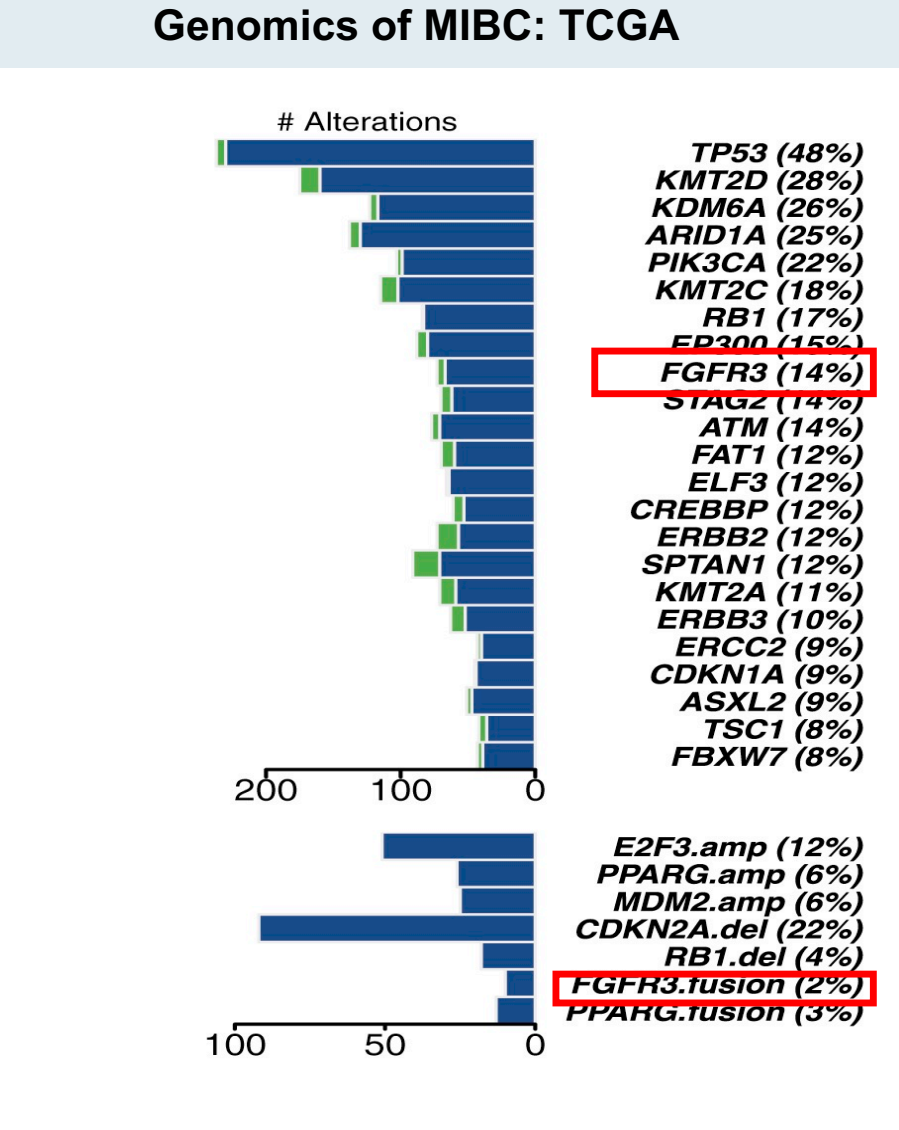




Wang J et al. ASCO 2021;Abstract 1022.

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.

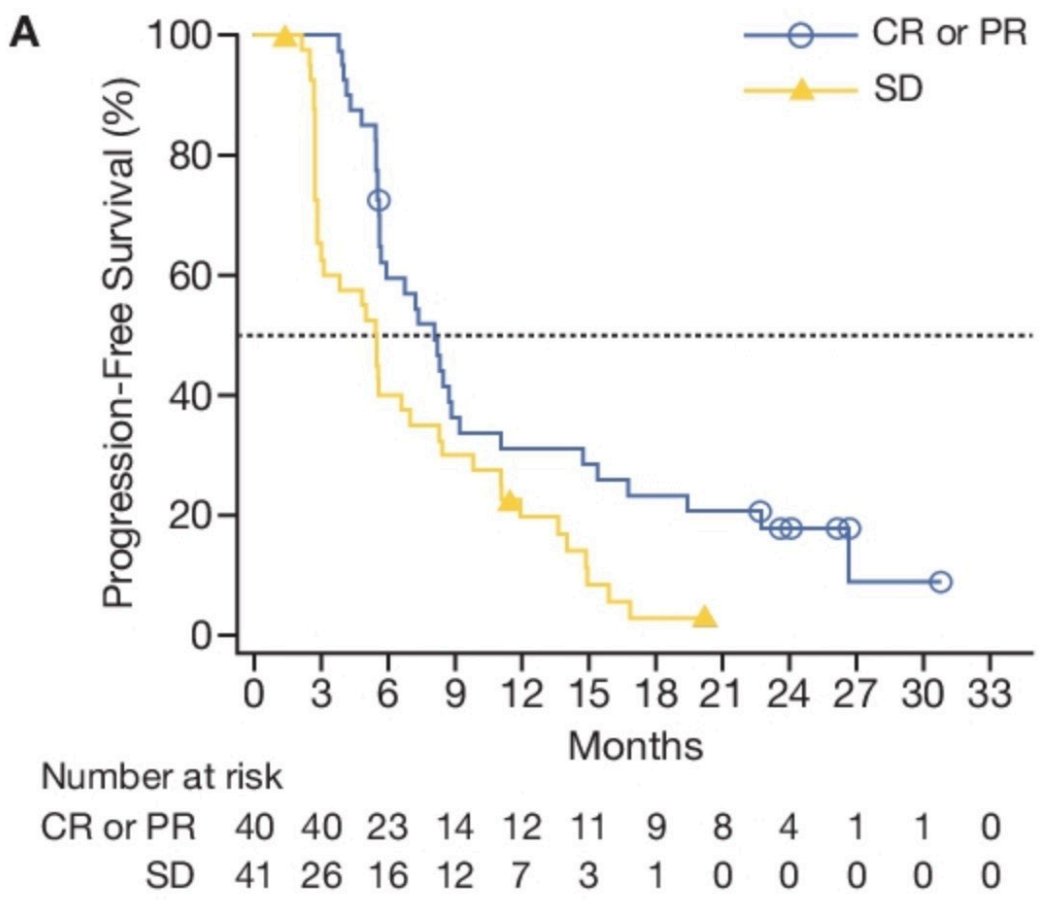
Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma (mUC): Long-Term Outcomes in BLC2001

Siefker-Radtke AO et al.

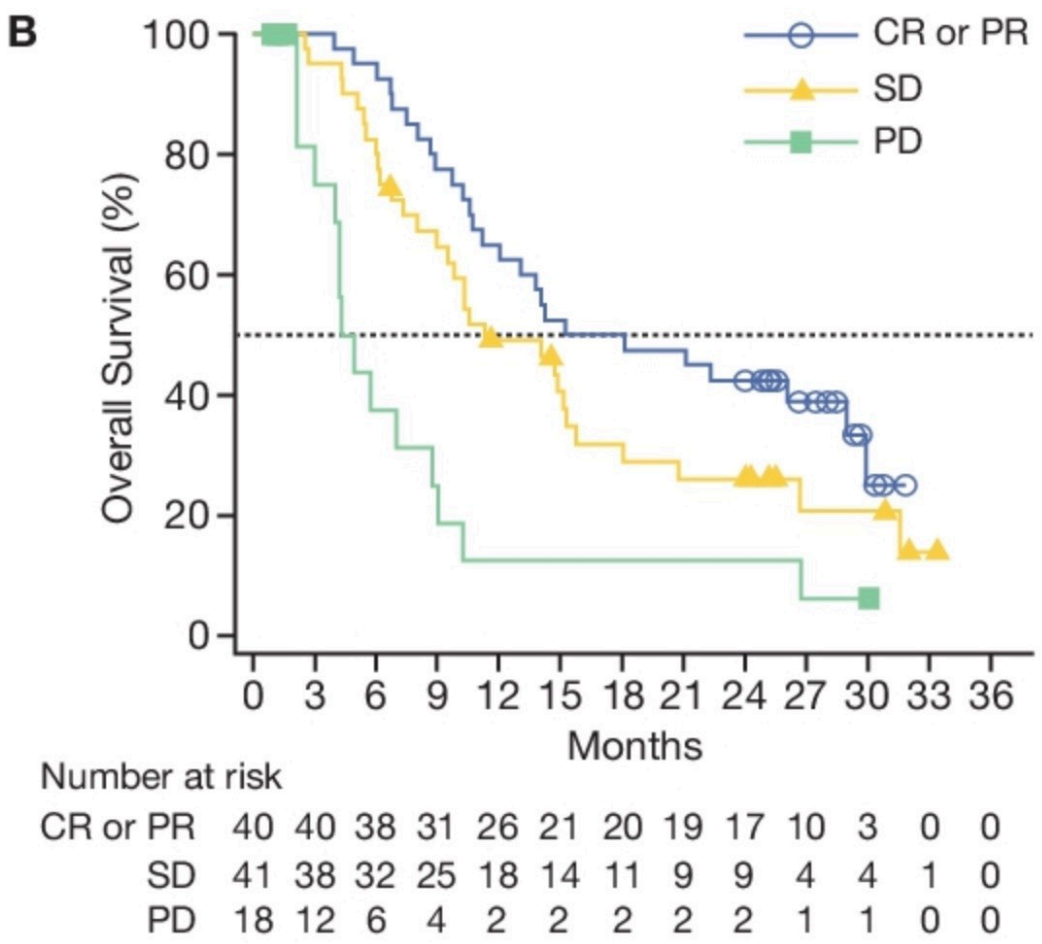
ASCO 2020;Abstract 5015.

BLC2001: Survival

Median PFS: 5.5 months



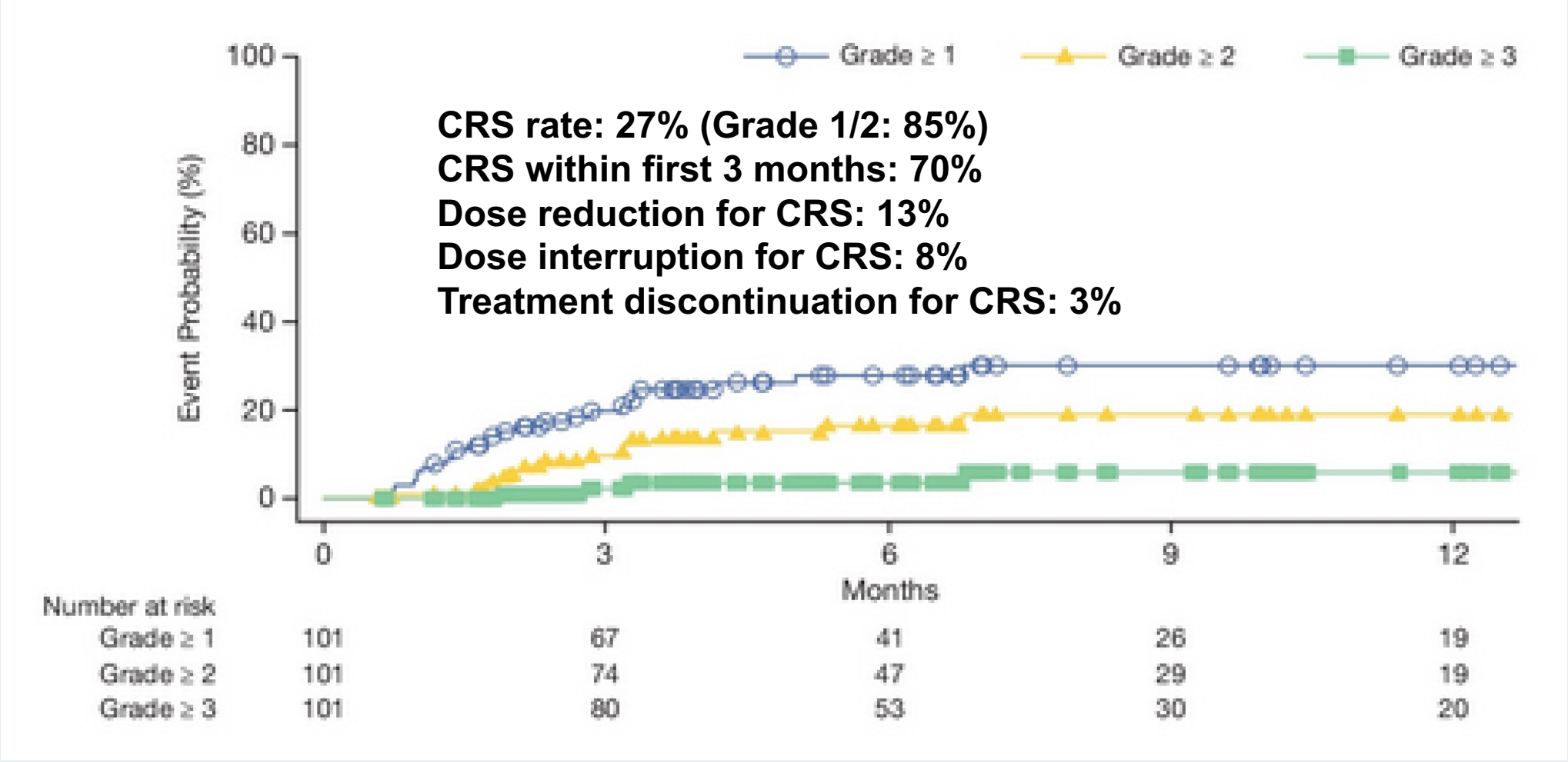
Median OS: 11.3 months



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

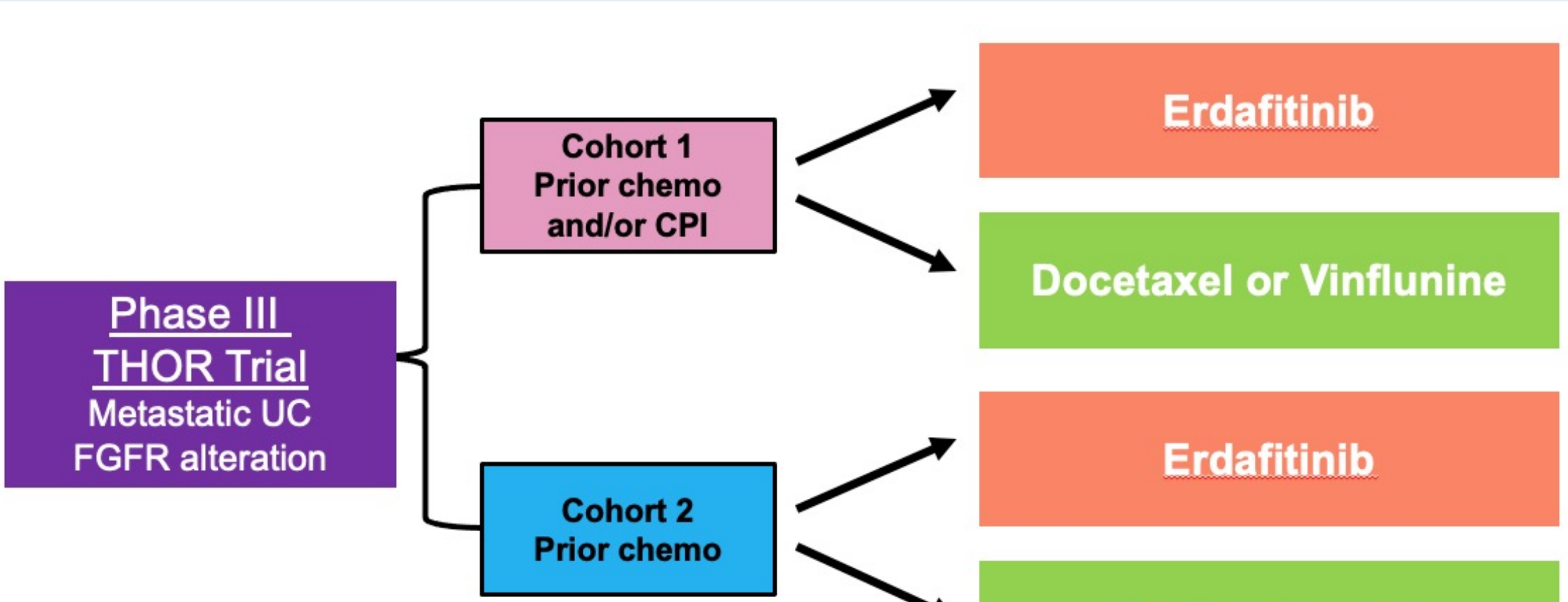
11% mFGFR

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, September 22, 2021
5:00 PM – 6:00 PM ET

Faculty

Sara M Tolaney, MD, MPH

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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