What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Arjun Balar, MD
Associate Professor, Department of Medicine
Director, Genitourinary Medical Oncology Program
Medical Director, Clinical Trials Office
NYU Perlmutter Cancer Center
New York, New York

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

Guru Sonpavde, MD
Bladder Cancer Director
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Robert Svatek, MD
Associate Professor
Department of Urology
UT Health Science Center
San Antonio, Texas

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by educational grants from Astellas and Seagen Inc, AstraZeneca Pharmaceuticals LP and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

RTP
RESEARCH
TO PRACTICE

Dr Love — Disclosures

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

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Balar — Disclosures

Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, EMD Serono Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Immunomedics Inc, Incyte Corporation, Janssen Biotech Inc, Merck, Pfizer Inc, Seagen Inc
Contracted Research	Astellas, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Clovis Oncology, Genentech, a member of the Roche Group, Gilead Sciences Inc, Immunomedics Inc, Incyte Corporation, Janssen Biotech Inc, Merck, Pfizer Inc, Seagen Inc
Ownership Interest	GT Biopharma Inc

Dr Kamat — Disclosures

No relevant conflicts of interest to disclose.

RTP
RESEARCH
TO PRACTICE

Dr Sonpavde — Disclosures

Advisory Committee	Astellas, AstraZeneca Pharmaceuticals LP, Bicycle Therapeutics, Bristol-Myers Squibb Company, EMD Serono Inc, Exelixis Inc, G1 Therapeutics, Genentech, a member of the Roche Group, Gilead Sciences Inc, Immunomedics Inc, Infinity Pharmaceuticals Inc, Janssen Biotech Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Pfizer Inc, Sanofi Genzyme, Scholar Rock, Seagen Inc
Consulting Agreements (Paid)	AstraZeneca Pharmaceuticals LP, Debiopharm Group, EMD Serono Inc
Consulting Agreements (Unpaid)	Bavarian Nordic, Bristol-Myers Squibb Company, G1 Therapeutics, QED Therapeutics, Seagen Inc
Travel Cost	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company
Writing/Editor Fees	Elsevier Practice Update Bladder Cancer Center of Excellence

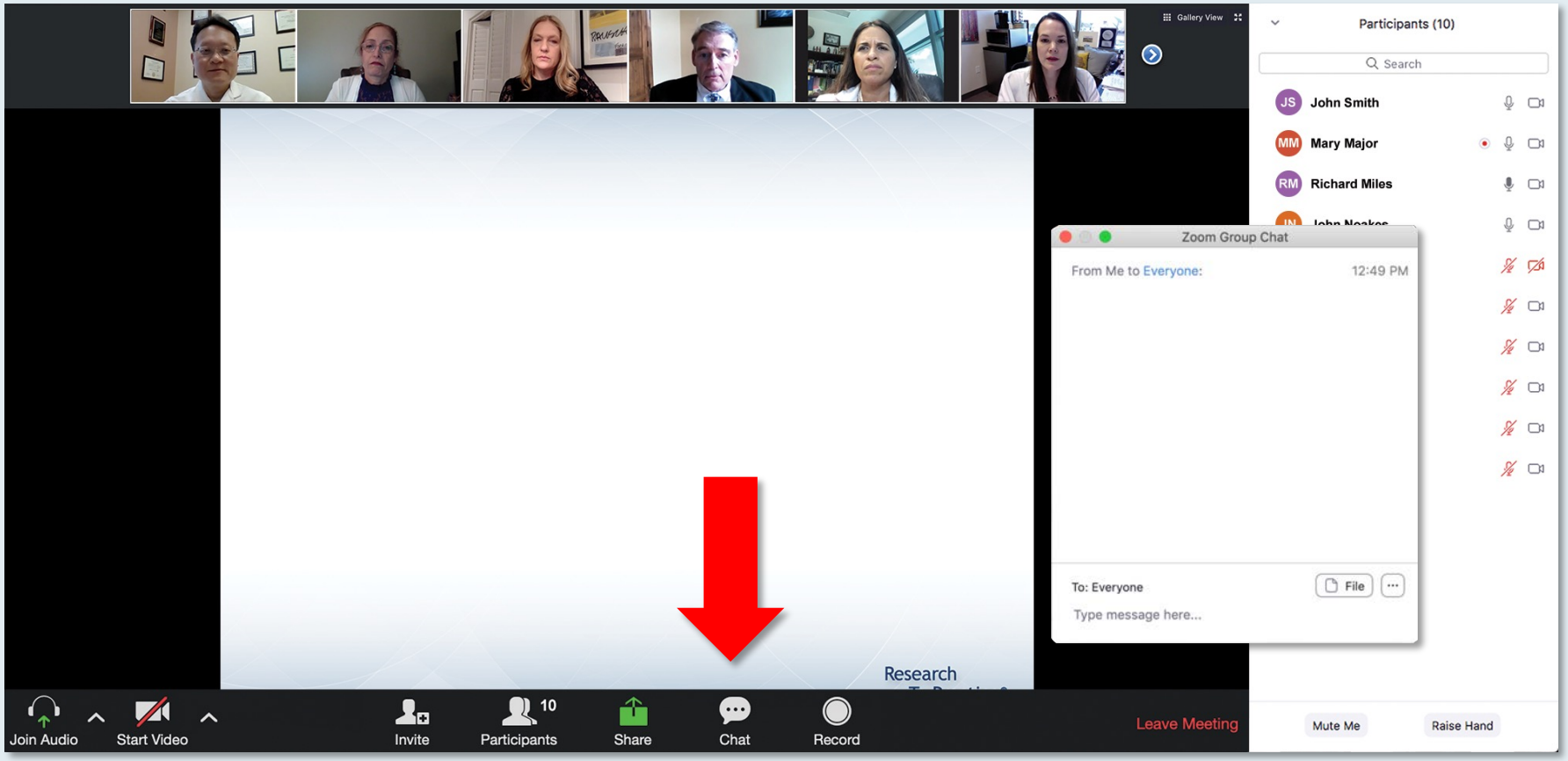
RTP
RESEARCH
TO PRACTICE

Dr Svatek — Disclosures

Consulting Agreement	Ferring Pharmaceuticals
Contracted Research	Japan BCG Laboratory, Rapamycin Holdings

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

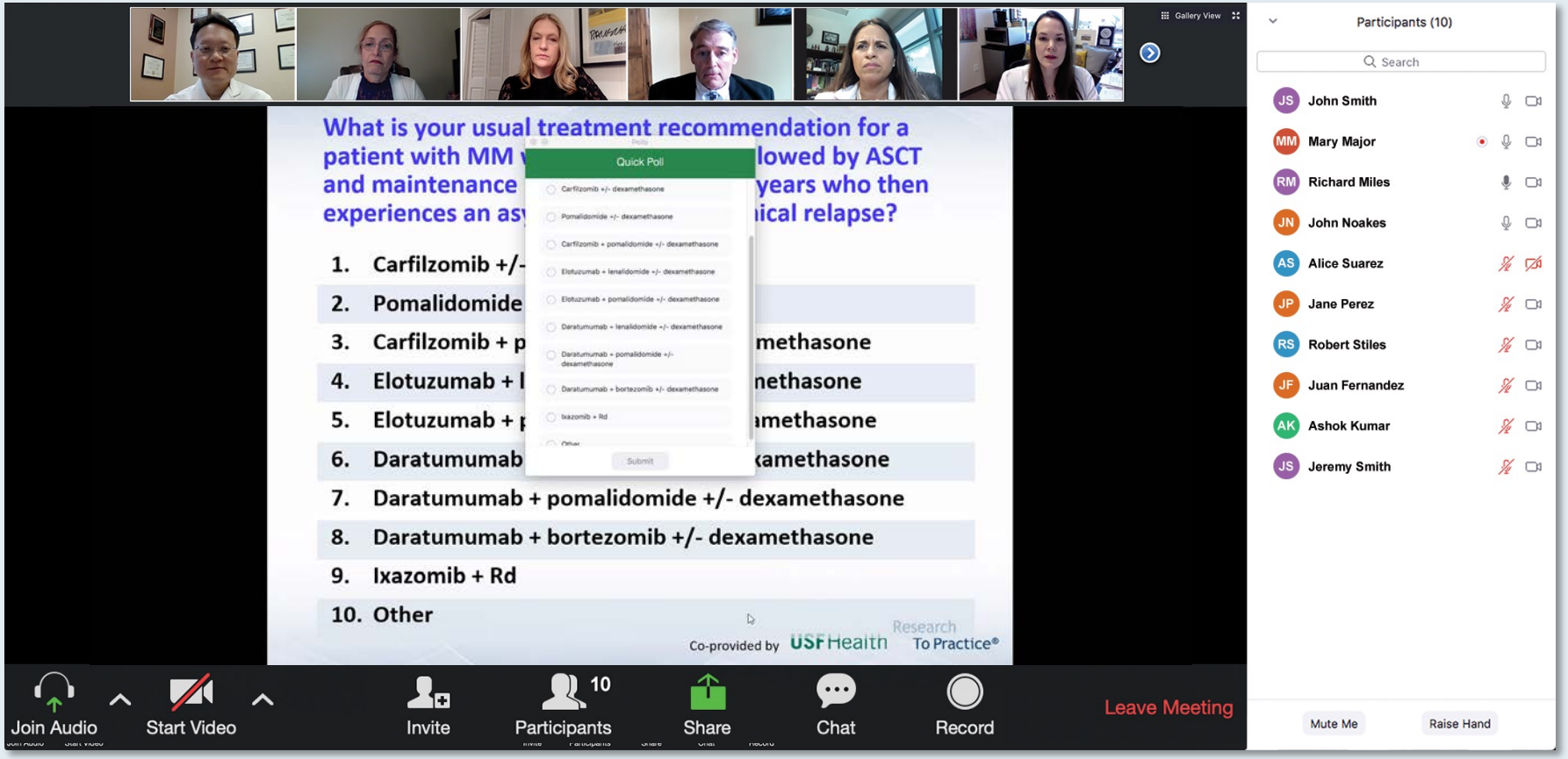


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

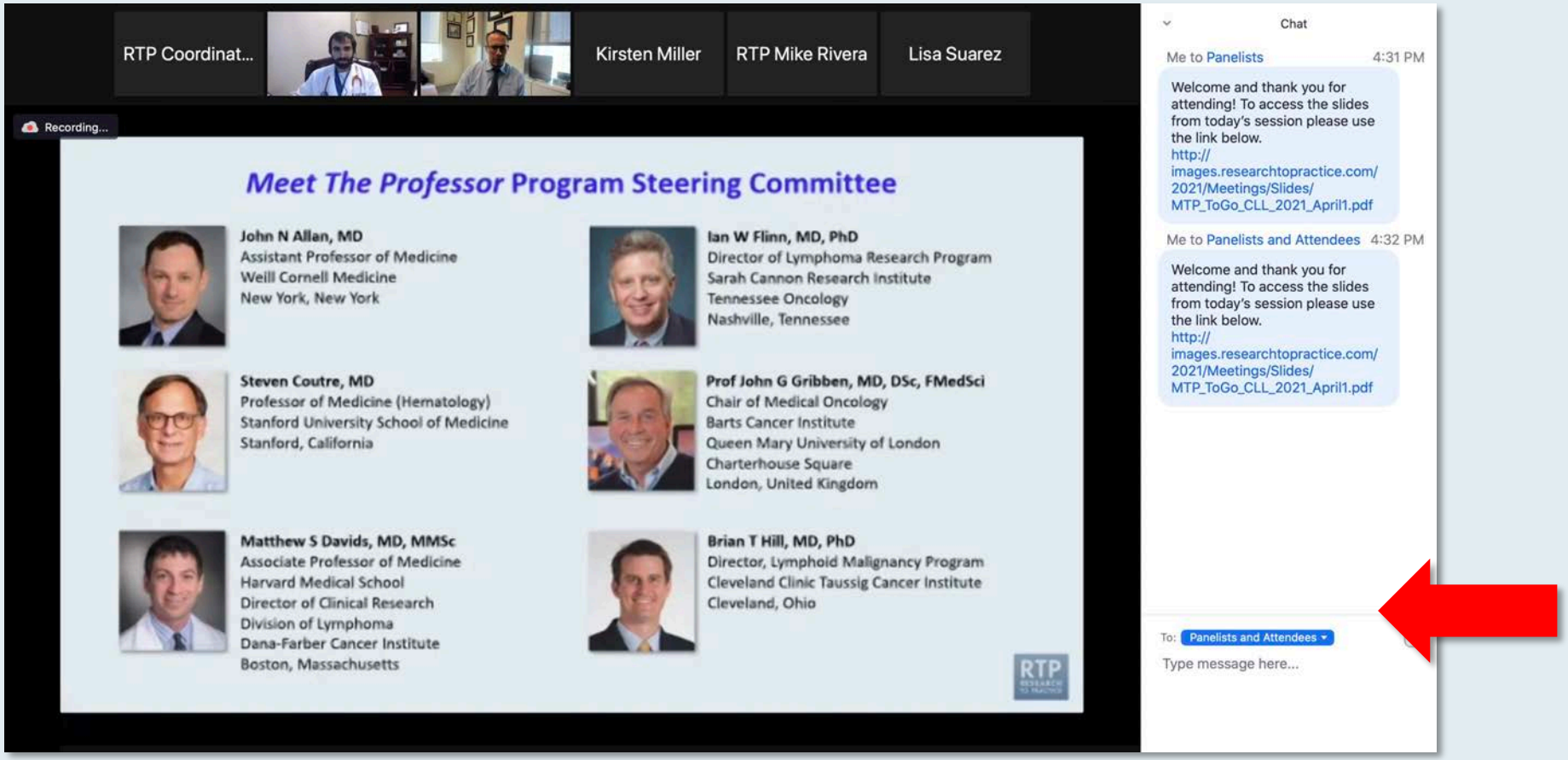
How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

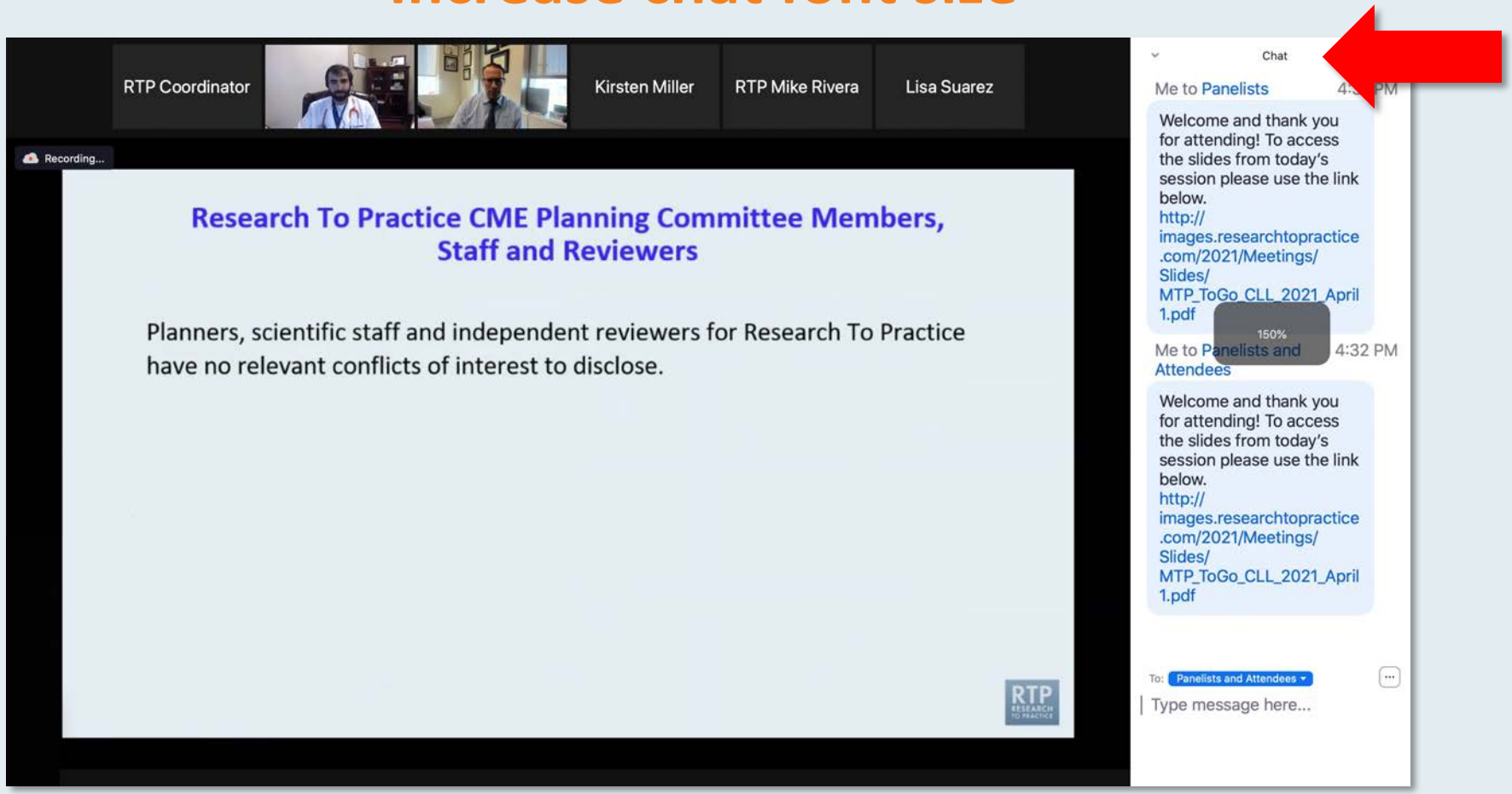


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

ONCOLOGY TODAY

WITH DR NEIL LOVE

Newly Approved Agents in the Management of Urothelial Bladder Carcinoma

DR MATTHEW GALSKY
ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Prostate Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
5:00 PM – 6:30 PM ET

Faculty

Leonard G Gomella, MD
Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

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

Tuesday, September 14, 2021
5:00 PM – 6:00 PM ET

Faculty

Neeraj Agarwal, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Loretta J Nastoupil, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

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

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

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

RTP
RESEARCH
TO PRACTICE

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

RTP
RESEARCH TO PRACTICE

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

Arjun Balar, MD
Associate Professor, Department of Medicine
Director, Genitourinary Medical Oncology Program
Medical Director, Clinical Trials Office
NYU Perlmutter Cancer Center
New York, New York

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

Guru Sonpavde, MD
Bladder Cancer Director
Dana-Farber Cancer Institute
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

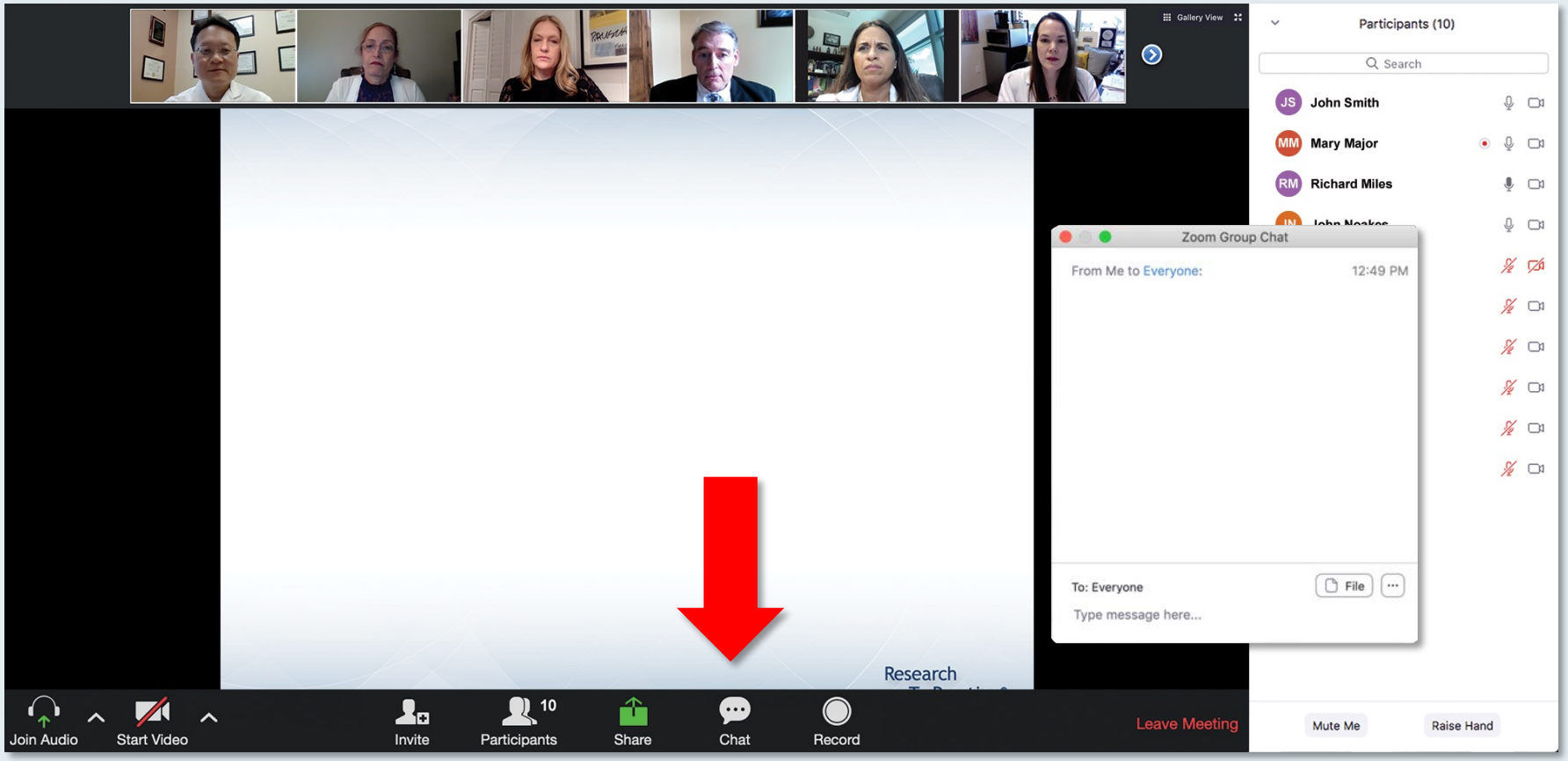
Robert Svatek, MD
Associate Professor
Department of Urology
UT Health Science Center
San Antonio, Texas

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

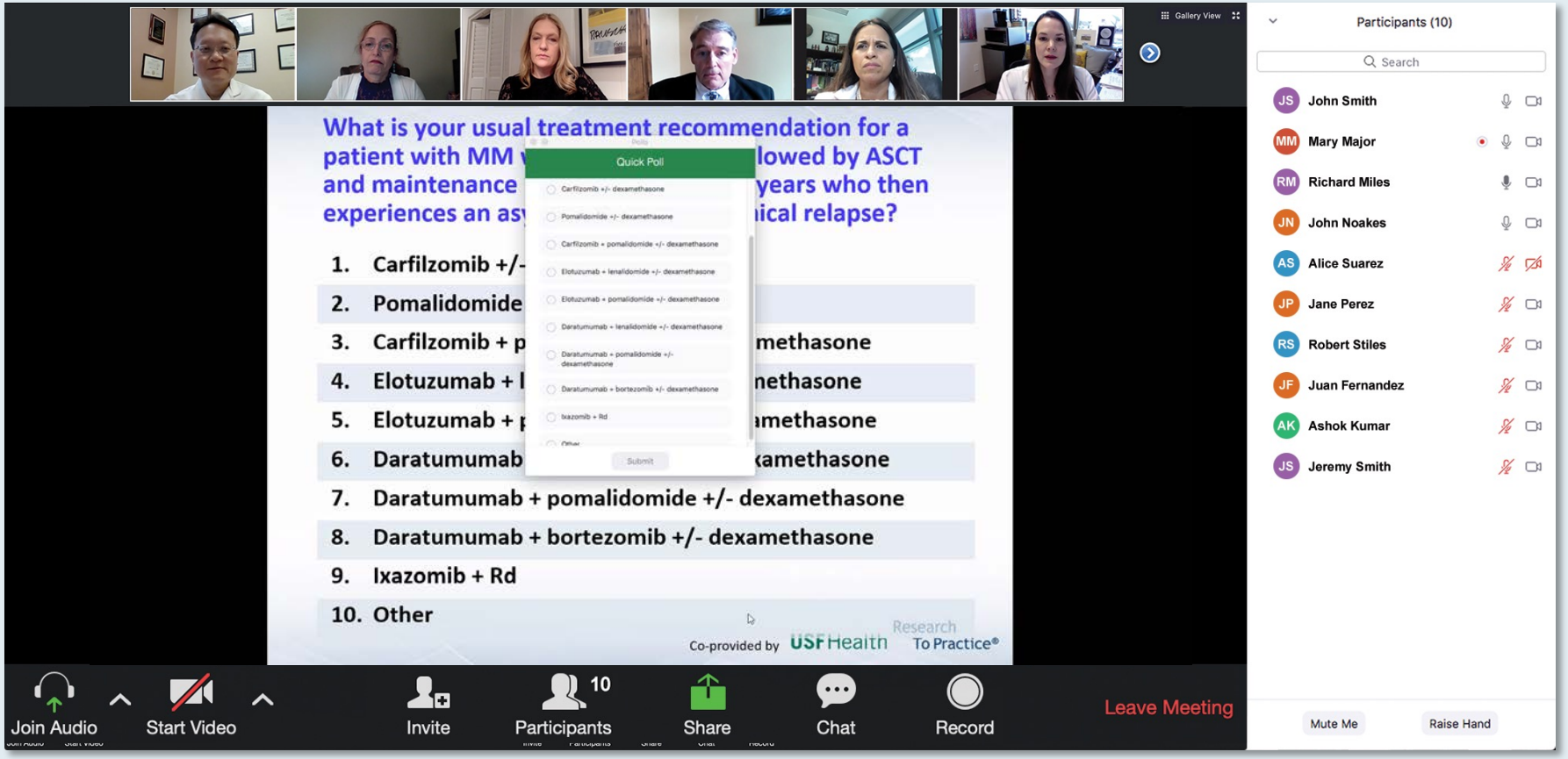


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

ONCOLOGY TODAY

WITH DR NEIL LOVE

Newly Approved Agents in the Management of Urothelial Bladder Carcinoma

DR MATTHEW GALSKY
ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Prostate Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
5:00 PM – 6:30 PM ET

Faculty

Leonard G Gomella, MD
Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

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

Tuesday, September 14, 2021
5:00 PM – 6:00 PM ET

Faculty

Neeraj Agarwal, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Thursday, September 16, 2021
5:00 PM – 6:00 PM ET

Faculty

Loretta J Nastoupil, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Meet The Professor

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

Friday, September 17, 2021
12:00 PM – 1:00 PM ET

Faculty

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

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

RTP
RESEARCH
TO PRACTICE

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

RTP
RESEARCH TO PRACTICE

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Bladder Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
11:00 AM – 12:30 PM ET

Faculty

Arjun Balar, MD
Ashish M Kamat, MD, MBBS
Guru Sonpavde, MD
Robert Svatek, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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

David S Morris, MD
President and Co-Director of Advanced Therapeutics Center
Urology Associates
Nashville, Tennessee

RTP
RESEARCH TO PRACTICE

Agenda

Introduction: Personalized Continuing Medical Education

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

- Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer
- Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC
- Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer
- Dr Morris: An 86-year-old man with recurrent high-grade noninvasive papillary carcinoma

Module 2: Neoadjuvant and Adjuvant Treatment of Muscle-Invasive UBC

- Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer who declines cystectomy
- Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Module 3: Treatment of Metastatic UBC

- Dr Ibrahim: A 70-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

Agenda

Introduction: Personalized Continuing Medical Education

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

- Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer
- Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC
- Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer
- Dr Morris: An 86-year-old man with recurrent high-grade noninvasive papillary carcinoma

Module 2: Neoadjuvant and Adjuvant Treatment of Muscle-Invasive UBC

- Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer who declines cystectomy
- Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Module 3: Treatment of Metastatic UBC

- Dr Ibrahim: A 70-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

At what point in your oncology career were you in 2007?

1. Clinical practice
2. Residency or fellowship
3. Medical school
4. College
5. High school
6. Before high school
7. Other

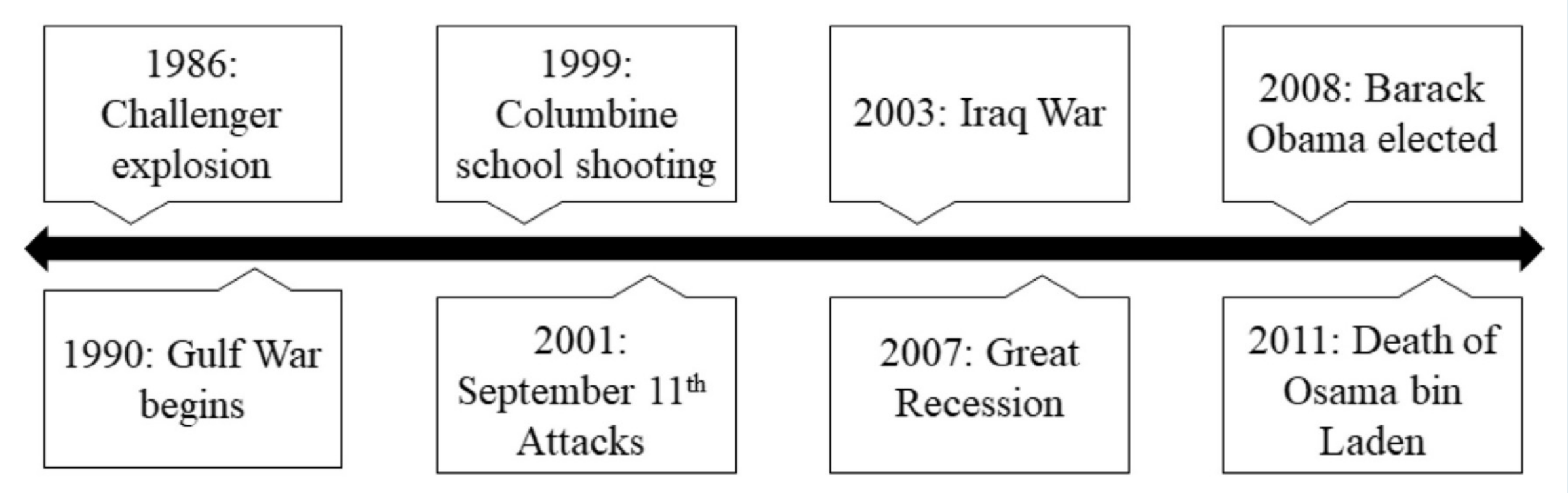
RTP
RESEARCH
TO PRACTICE

Urol Clin N Am 48 (2021) 195-202

Understanding the Millennial Physician

Jake Quarles[a], Jason Hafron, MD[b,*]

Key Events in Their Upbringing That Have Shaped the Lives of Millennials



Quarles J, Hafron J. *Urol Clin N Am* 48 (2021) 195-202.

Understanding the millennial physician

Dr Jason Hafron

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Personalized Continuing Medical Education

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

- Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer
- Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC
- Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer
- Dr Morris: An 86-year-old man with recurrent high-grade noninvasive papillary carcinoma

Module 2: Neoadjuvant and Adjuvant Treatment of Muscle-Invasive UBC

- Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer who declines cystectomy
- Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Module 3: Treatment of Metastatic UBC

- Dr Ibrahim: A 70-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

Case Presentation – Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer

Dr David Morris

- 2009: Robot-assisted laparoscopy for Gleason 3+4 prostate cancer
- 2011: Gross hematuria → TURBT: High-grade T1 → BCG induction
- 2013: Recurrence with CIS → Re-induction BCG → Maintenance BCG intermittently until 2017
- 8/2017: Recurrence on biopsy → Valrubicin
- 12/2018: Recurrence on biopsy → Patient declines cystectomy
- Re-induction BCG → NED until 1/2021: CIS recurrence
- Patient refuses cystectomy due to heart disease
- 4/2021: Pembrolizumab
  - After 2 treatments: Jaundice, with abnormal labs (total bilirubin: 11, AST: 850, ALT: 727) → High-dose steroids

Questions

- Do you have any suggestions about how to monitor and manage side effects of early induction therapy with immune checkpoint inhibitors (ICIs)? How rare is immune-related hepatic toxicity with ICIs?
- How do you counsel patients who are receiving ICIs about which side effects should prompt them to call?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC

Dr Gordon Brown

- Initial diagnosis of T1 disease → complete resection
- BCG induction plus maintenance therapy → recurrence of carcinoma in situ within bladder within 6 months
- Offered participation in a clinical trial, pembrolizumab or additional intravesical therapies such as docetaxel and gemcitabine
- Elected pembrolizumab therapy → discontinued after 4th dose due to development of hypothyroidism
- Intravesicle therapy with docetaxel and gemcitabine
- Currently NED

Questions

- What are your thoughts in terms of the side effect profile and management of immunotherapy in patients with high-risk non-muscle-invasive bladder cancers?
- How can we operationalize more consistently the use of immunotherapy in our bladder cancer clinics amongst urology practices across the country?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer

Dr Jason Hafron

- Presents with asymptomatic gross hematuria
- Cystoscopy: Erythematous area, right lateral wall of bladder and papillary tumor
- Transurethral resection: CIS and pTa high-grade urothelial carcinoma
- BCG x 6 → Cystoscopy 6 weeks later: Persistent CIS → BCG x 6 → Maintenance BCG x 3
- Cystoscopy 12 months later: CIS
- Patient declines cystectomy
- Pembrolizumab q3w x 4, but develops pneumonia x 2

Questions

- Would you stop the pembrolizumab for this recurrent pneumonia? Is this a true side effect of pembrolizumab?
- Would you consider changing him from q 3 week dosing of pembrolizumab to q 6 weeks? Would that reduce his risk of pulmonary issues?
- If the patient were to fail pembrolizumab and still refuse cystectomy, what else is there to offer this patient?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Morris: An 86-year-old man with recurrent high-grade non-invasive papillary carcinoma

Dr David Morris

- 5/2019: Presents with hematuria and diagnosed with low-grade noninvasive papillary carcinoma (Ta) in the left ureter
- Distal ureterectomy and reimplant, with negative margins
- Six months later, surveillance cystoscopy: High-grade Ta bladder lesion → Resected
- BCG induction not completed due to unplanned heart event and surgery
- After recovery, cystoscopy revealed numerous new high-grade Ta recurrences
- Re-induction BCG x 6 and Blue-Light cystoscopy, confirming high-grade Ta → Resected
- FGFR mutation identified and enrolled on a clinical trial of erdafitinib for localized disease

Questions

- Is Blue Light technology worth the extra cost for all populations or just those who may have a CIS history? Is it something that should be exclusionary only in the most complex situations just because of the added cost for potential delay and progression down the road?

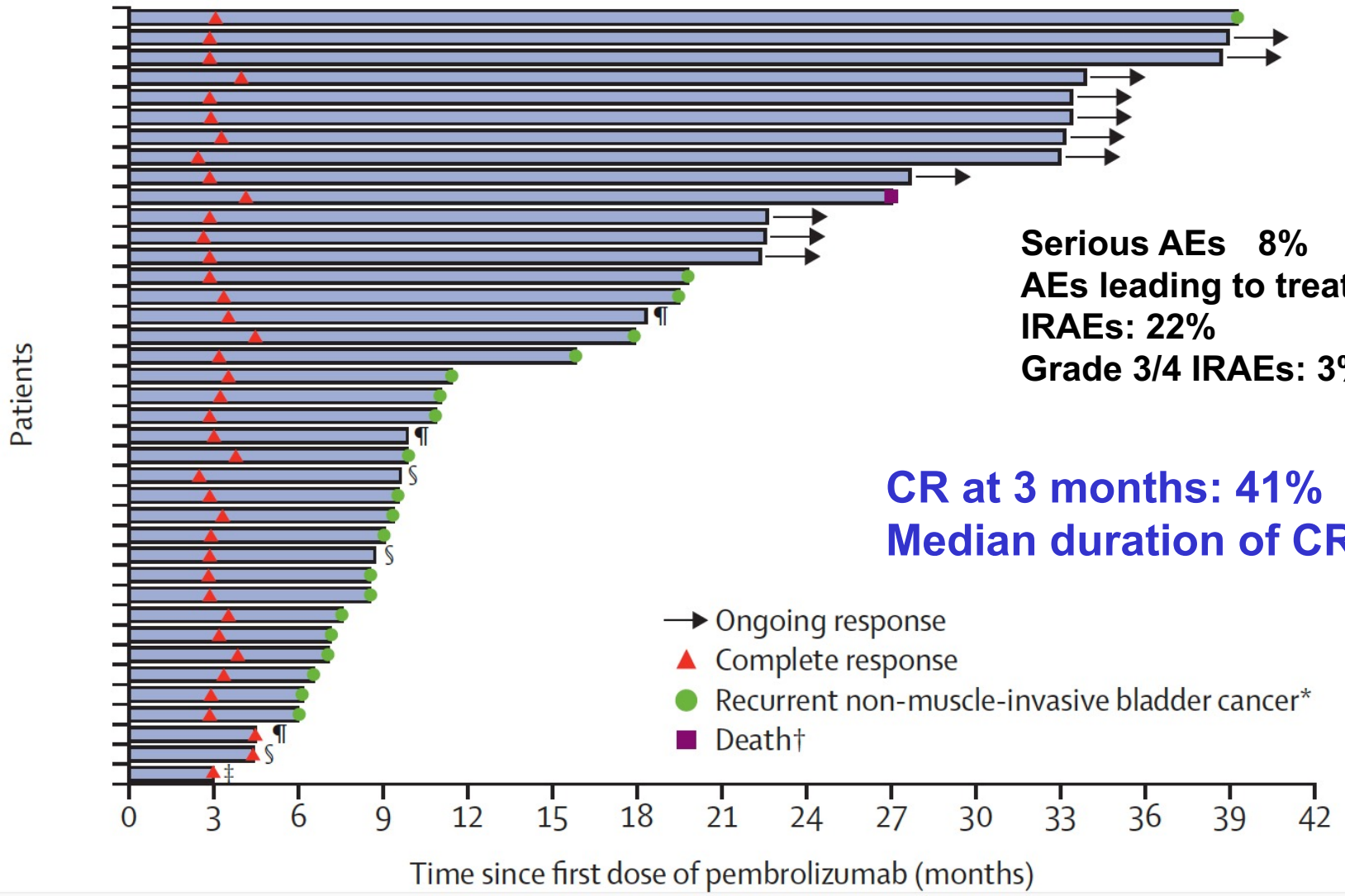
RTP RESEARCH TO PRACTICE

Lancet Oncol 2021;22:919-30 Articles

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



Serious AEs 8%
AEs leading to treatment interruption: 13%
IRAEs: 22%
Grade 3/4 IRAEs: 3%

CR at 3 months: 41%
Median duration of CR: 16.2 mo

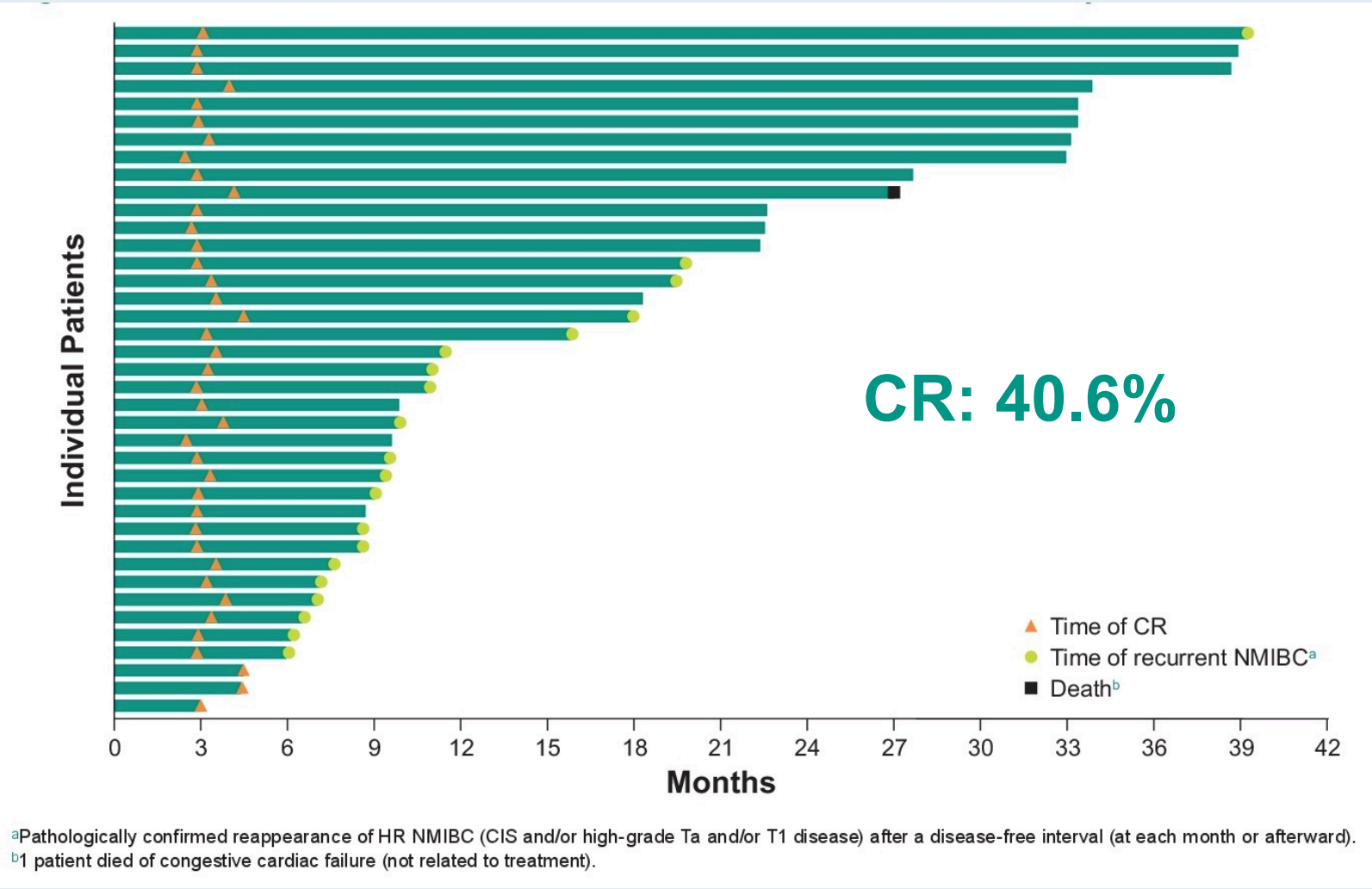
Balar AV et al. *Lancet Oncol* 2021;22:919-30.

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 HR NMIBC in Patients Who Experienced a 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.

Agenda

Introduction: Personalized Continuing Medical Education

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

- Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer
- Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC
- Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer
- Dr Morris: An 86-year-old man with recurrent high-grade noninvasive papillary carcinoma

Module 2: Neoadjuvant and Adjuvant Treatment of Muscle-Invasive UBC

- Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer who declines cystectomy
- Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Module 3: Treatment of Metastatic UBC

- Dr Ibrahim: A 70-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

Case Presentation – Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer (MIBC) who declines cystectomy

Dr Sulfi Ibrahim

- Diagnosed with MIBC, declines cystectomy
- Clinical trial of concurrent chemoradiation therapy with gemcitabine twice weekly and atezolizumab
  - Completed therapy 6 months ago, NED

Selection of patients for neoadjuvant therapy

Dr David Morris

RTP
RESEARCH
TO PRACTICE

Case Presentation – Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Dr Jason Hafron

- Presented with urinary frequency, urgency and elevated PSA
- Prostate biopsy: Gleason 4 + 3 adenocarcinoma of the prostate
- Cystoscopy: Papillary bladder cancer
- Transurethral resection: T2 high-grade transitional cell carcinoma of the bladder with angiolymphatic invasion
- Neoadjuvant cisplatin/gemcitabine x 4 → robotic cystoprostatectomy, bilateral lymph node dissection
  - PT3a adenocarcinoma of the prostate, Gleason 4 + 3, 1/18 nodes positive
  - Bladder pathology: T0

Questions

- Since he has already received cisplatin/gemcitabine x 4, would you consider adjuvant chemotherapy or immunotherapy, or would you just observe this patient with N1 disease following resection?
- What are the indications for adjuvant treatment with immune checkpoint inhibitors (ICIs) today? What is the duration of adjuvant ICI treatment?
- What is the best interval for using pembrolizumab – q3wks or q6wks? Is the q6wks interval associated with less symptoms?

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."

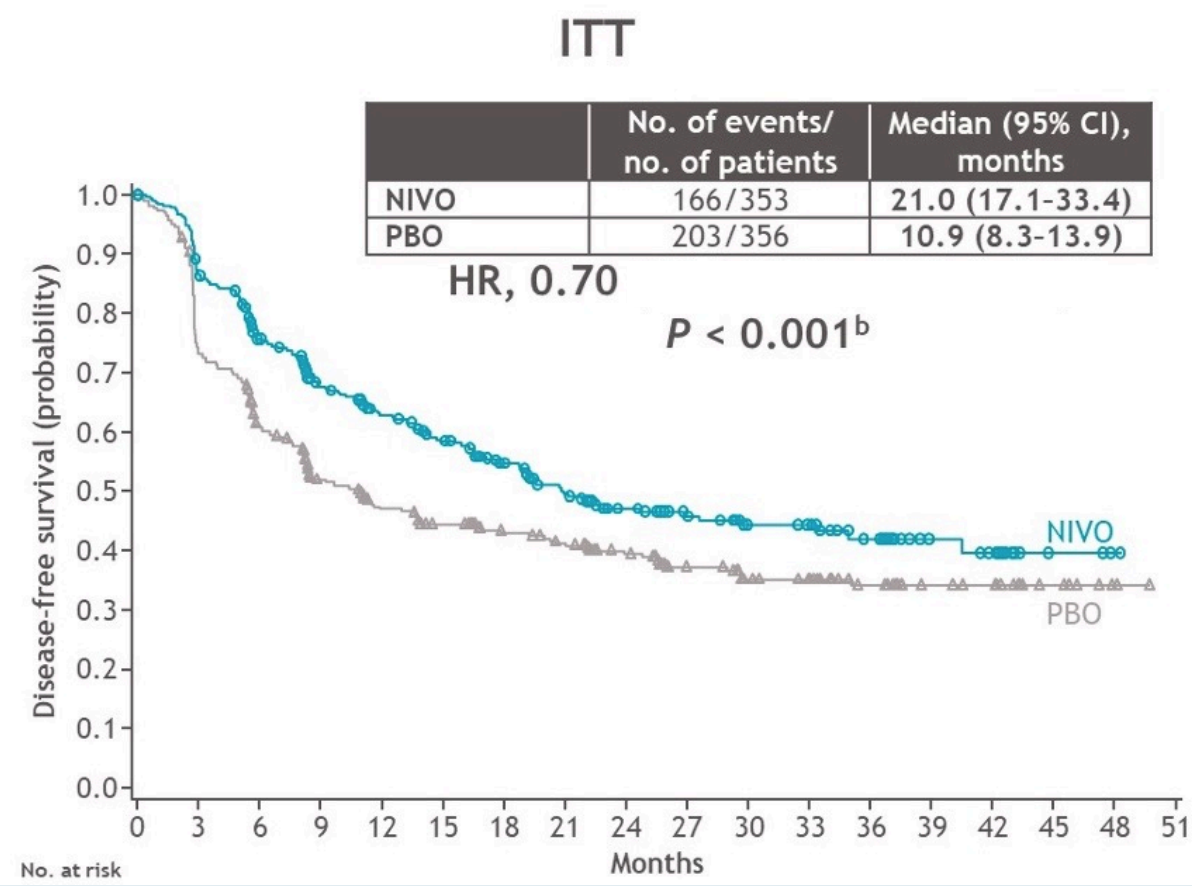
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-adjuvant-treatment-urothelial-carcinoma

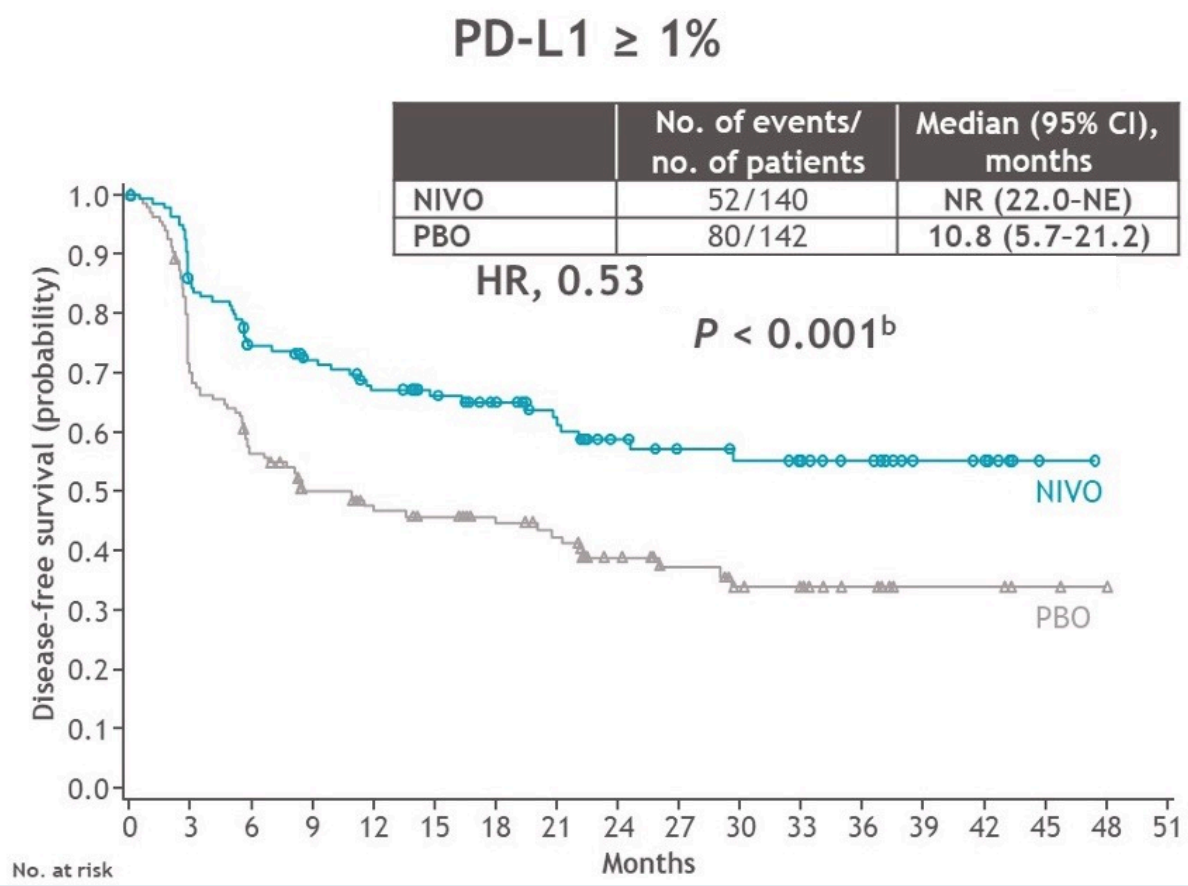
First Results from the Phase 3 CheckMate 274 Trial of Adjuvant Nivolumab vs Placebo in Patients Who Underwent Radical Surgery for High-Risk Muscle-Invasive Urothelial Carcinoma (MIUC)

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

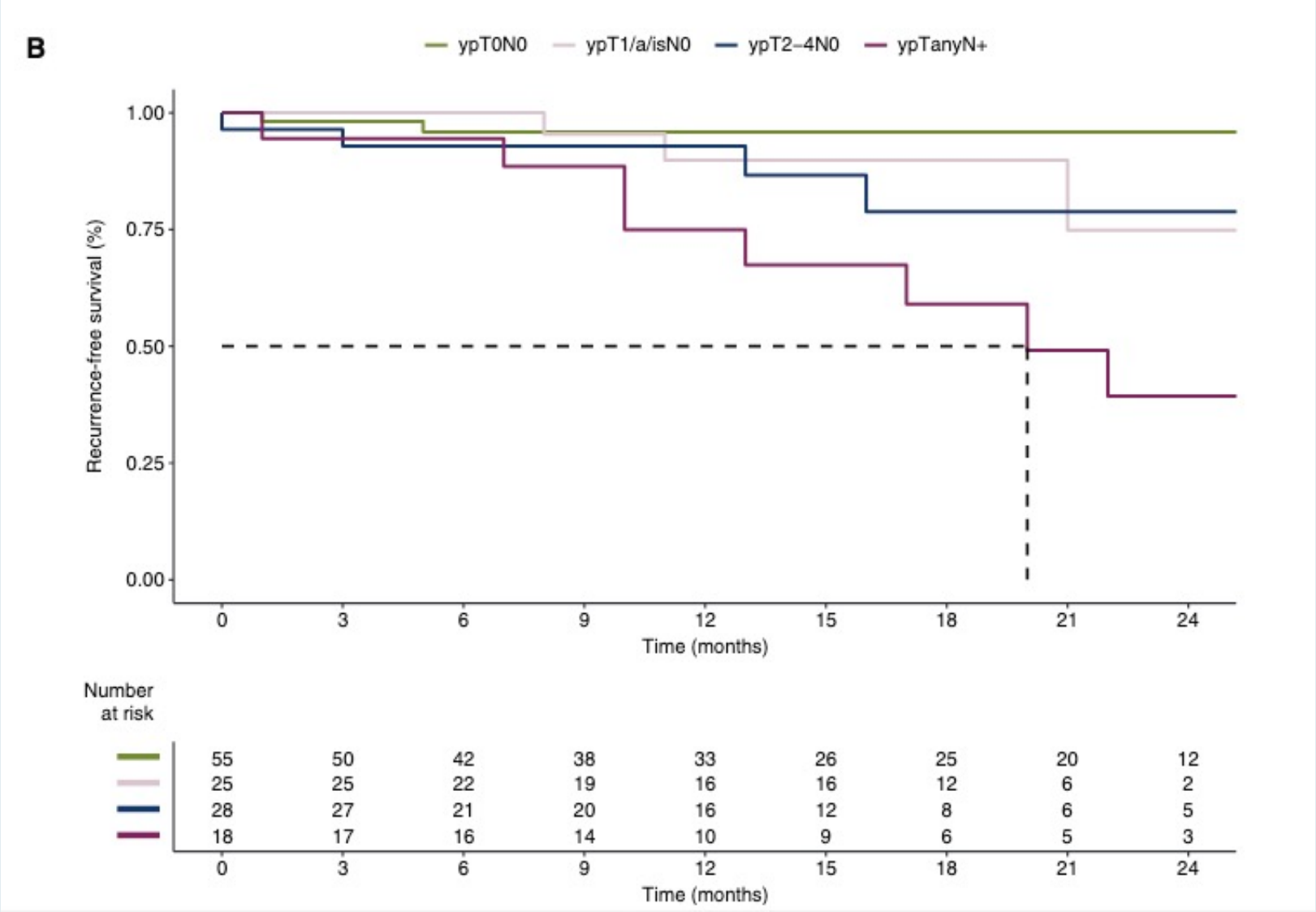
Does the administration of preoperative pembrolizumab lead to sustained remission post-cystectomy? First survival outcomes from the PURE-01 study☆

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

Agenda

Introduction: Personalized Continuing Medical Education

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

- Dr Morris: A 79-year-old man with BCG-refractory non-muscle-invasive bladder cancer
- Dr Brown: A 65-year-old man with high-risk non-muscle-invasive UBC
- Dr Hafron: A 58-year-old man with high-risk, BCG-refractory non-muscle-invasive bladder cancer
- Dr Morris: An 86-year-old man with recurrent high-grade noninvasive papillary carcinoma

Module 2: Neoadjuvant and Adjuvant Treatment of Muscle-Invasive UBC

- Dr Ibrahim: An 84-year-old man with muscle-invasive bladder cancer who declines cystectomy
- Dr Hafron: A 77-year-old man with Gleason 4 + 3 adenocarcinoma of the prostate and urothelial carcinoma

Module 3: Treatment of Metastatic UBC

- Dr Ibrahim: A 70-year-old woman with metastatic UBC – PD-L1 30%
- Dr Brown: A 74-year-old woman with metastatic UBC
- Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

Urologists' questions about second- and later-line therapies and management of side effects

Dr David Morris

RTP
RESEARCH
TO PRACTICE

Case Presentation – Dr Ibrahim: A 70-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

- What is the optimal management of the dermatologic toxicity with enfortumab vedotin? Is it dose holds? Is it a higher dose of corticosteroids?
- If the dermatologic toxicity continues to be a significant quality of life issue for her, is that a reason to consider switching therapy now that sacituzumab is also approved for urothelial carcinoma so I have another option that I can use to treat her?

RTP RESEARCH TO PRACTICE

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

- How would you characterize the tolerability of the antibody-drug conjugates in patients with advanced bladder cancer compared to the historical tolerability of additional systemic chemotherapy?
- What is your experience with the tolerability of erdafitinib, and how do you manage its side effects?
- What is your approach to the selection of second- and third-line therapy in patients who fail checkpoint inhibitors for the management of patients with metastatic muscle-invasive bladder cancer? How do you sequence the available therapies?

Sequencing of immune checkpoint inhibitor therapy, enfortumab vedotin, erdafitinib and sacituzumab govitecan

Dr Sulfi Ibrahim

RTP
RESEARCH
TO PRACTICE

Case Presentation – Dr Brown: A 55-year-old woman with muscle-invasive bladder cancer

Dr Gordon Brown

- High-grade T2 bladder cancer s/p nephroureterectomy
- Recurrent disease with muscle-invasive disease
- Currently, receiving neoadjuvant chemotherapy, with plans for cystectomy and urinary diversion

Questions

- In the setting of patients who have a solitary kidney disease with a recently diagnosed muscle-invasive bladder cancer, how do you approach the use of neoadjuvant therapy? Is there a role for immunotherapy in lieu of their reduced GFR?
- What is your opinion on the choice of urinary diversion in solitary kidney disease? She's desiring of a continent diversion, either Indiana pouch or Studer versus ileal loop. Would there be any thoughts as to concerns around a continent diversion in a patient with a solitary functional renal unit?

RTP RESEARCH TO PRACTICE

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

The NEW ENGLAND JOURNAL of MEDICINE

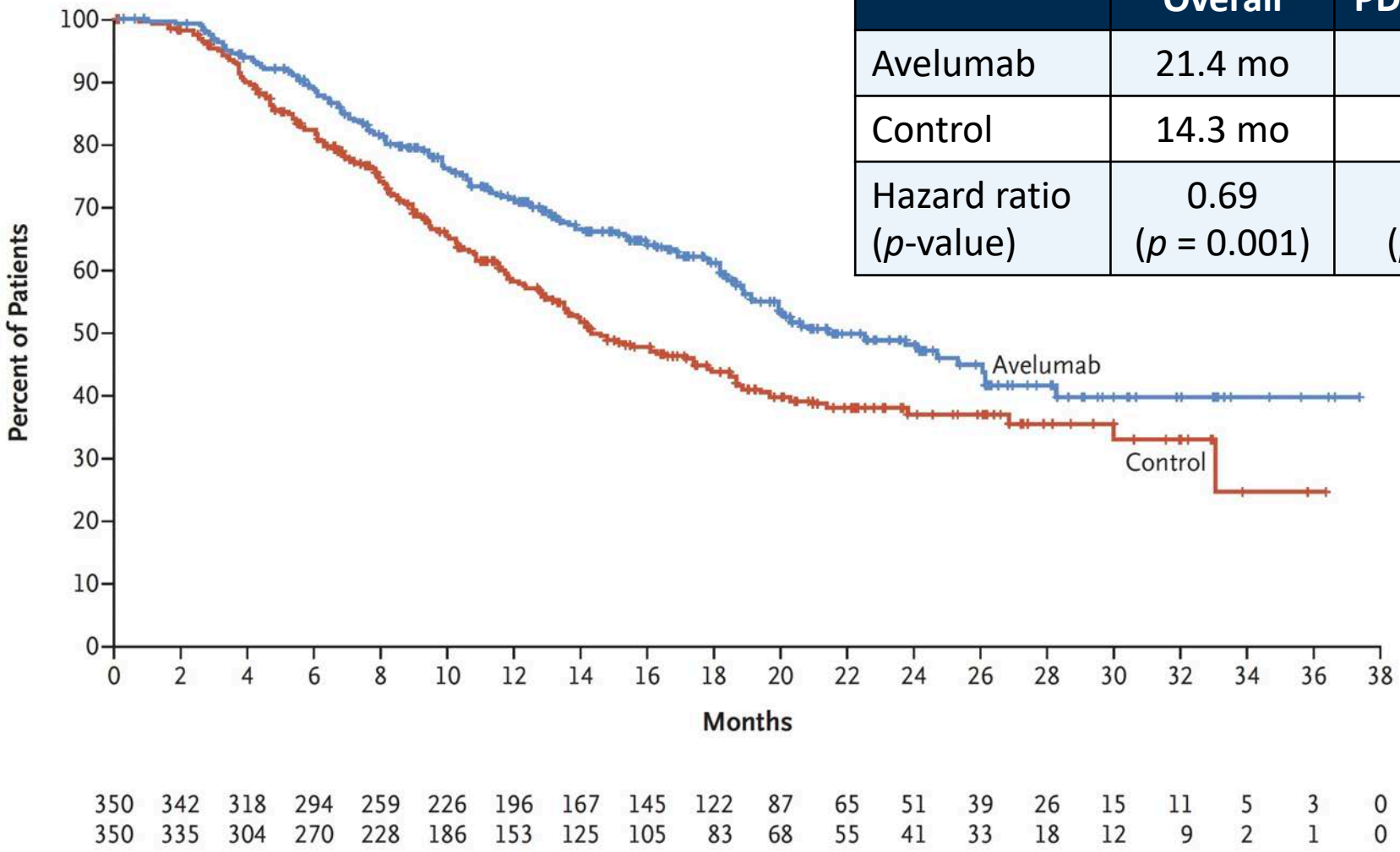
ORIGINAL ARTICLE

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.

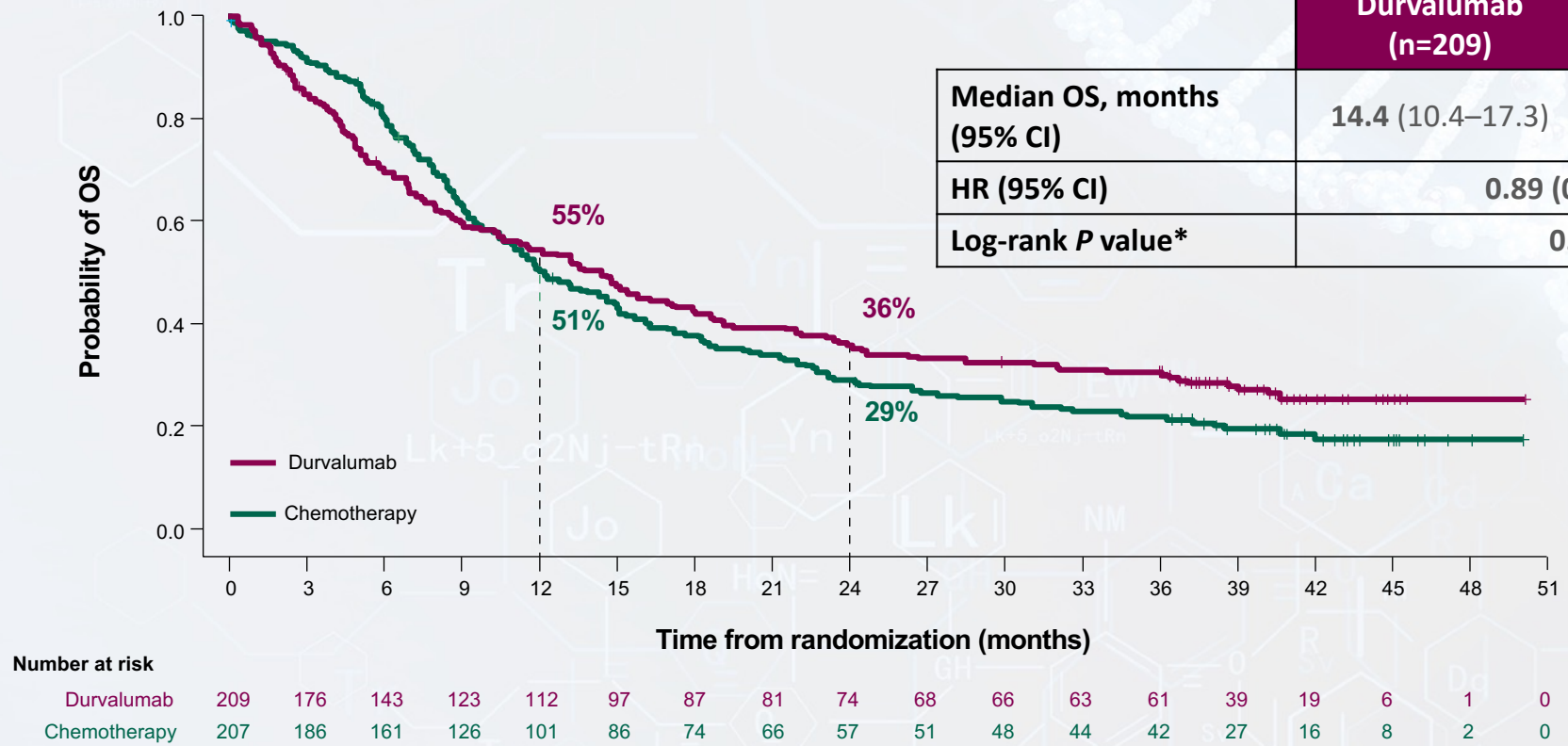
VIRTUAL 2020 ESMO congress

A phase 3, randomised, open-label study of first-line durvalumab with or without tremelimumab versus standard of care chemotherapy in patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE)

Thomas Powles, on behalf of the DANUBE Study Investigators
Professor
Barts Cancer Institute
Queen Mary University of London
London, UK

DANUBE Coprimary Endpoint: OS with durvalumab vs chemotherapy in the PD-L1-high population

	Durvalumab (n=209)	Chemotherapy (n=207)
Median OS, months (95% CI)	**14.4** (10.4–17.3)	**12.1** (10.4–15.0)
HR (95% CI)	0.89 (0.71–1.11)	
Log-rank *P* value*	0.3039	



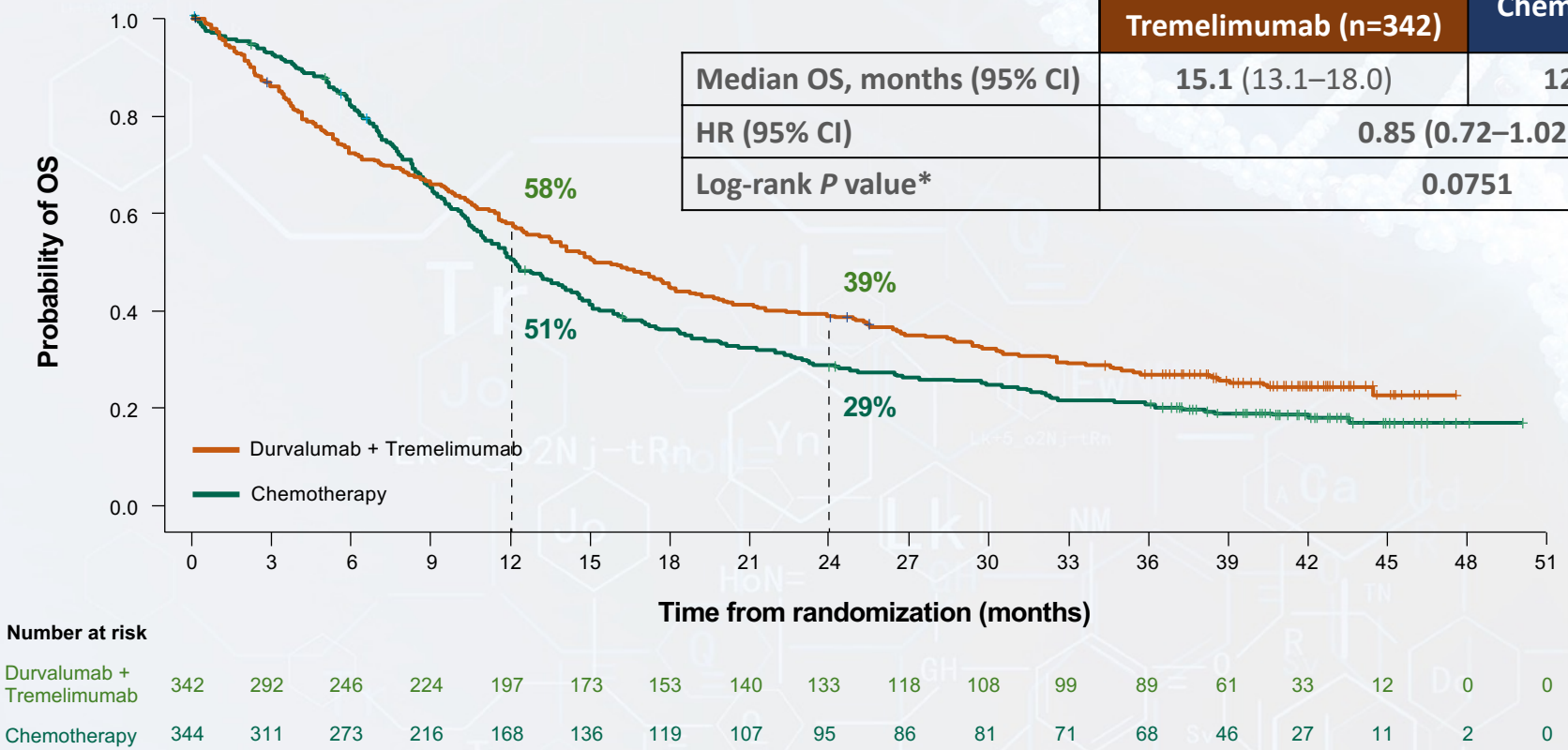
*Considered statistically significant if p<0.0301.

CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1.

Powles T et al. ESMO 2020;Abstract 6970.

DANUBE Coprimary Endpoint: OS with durvalumab + tremelimumab vs chemotherapy in the ITT population

	Durvalumab + Tremelimumab (n=342)	Chemotherapy (n=344)
Median OS, months (95% CI)	**15.1** (13.1–18.0)	**12.1** (10.9–14.0)
HR (95% CI)	0.85 (0.72–1.02)	
Log-rank *P* value*	0.0751	



*Considered statistically significant if p<0.0301.
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival.

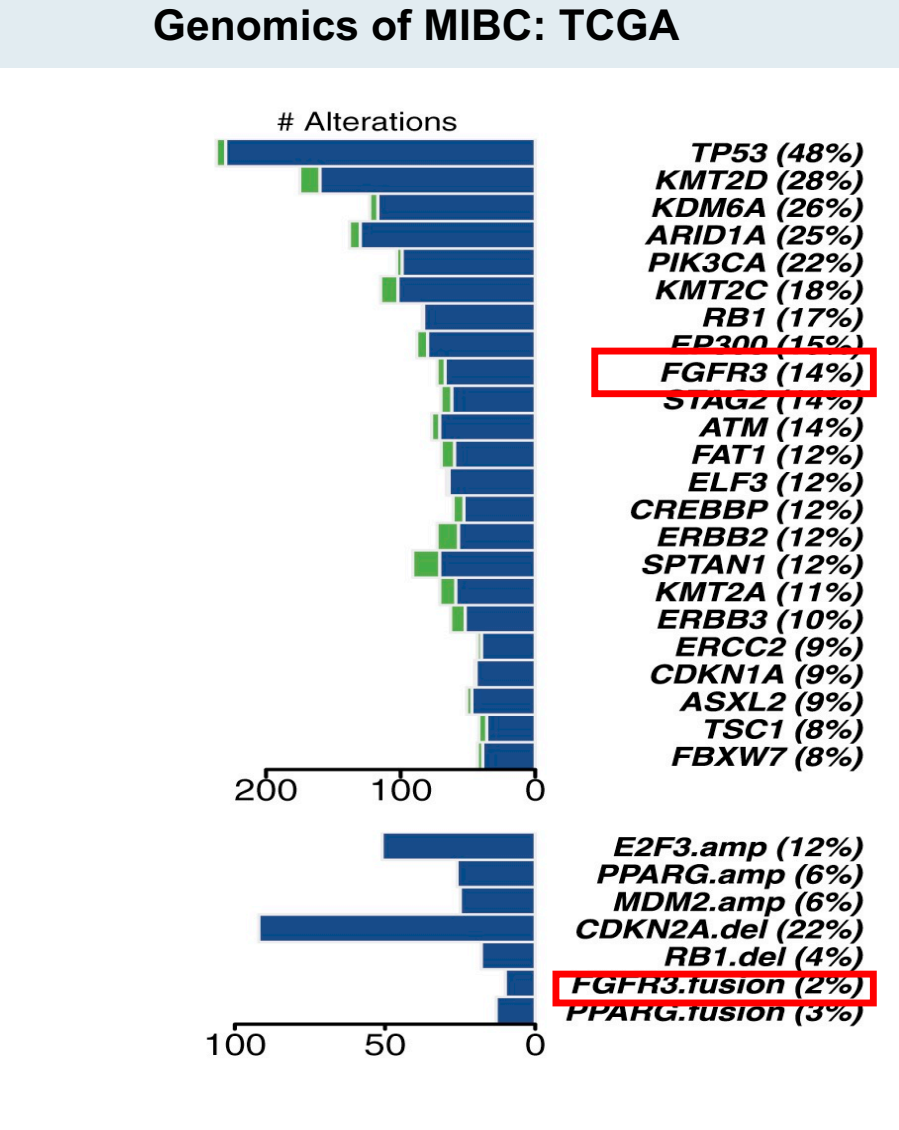
Powles T et al. ESMO 2020;Abstract 6970.

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.

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 et al. *Eur Urol* 2015;68(6):970-7.

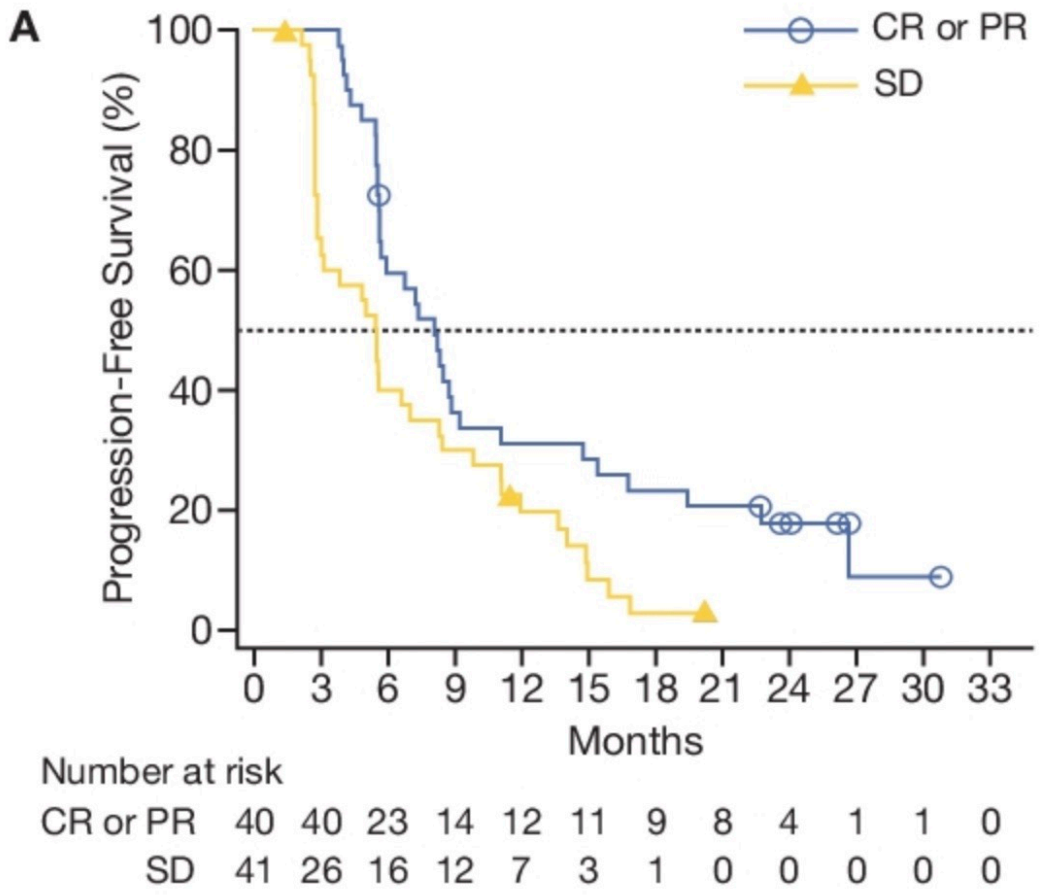
Erdafitinib in Locally Advanced or Metastatic Urothelial Carcinoma (mUC): Long-Term Outcomes in BLC2001

Siefker-Radtke AO et al.

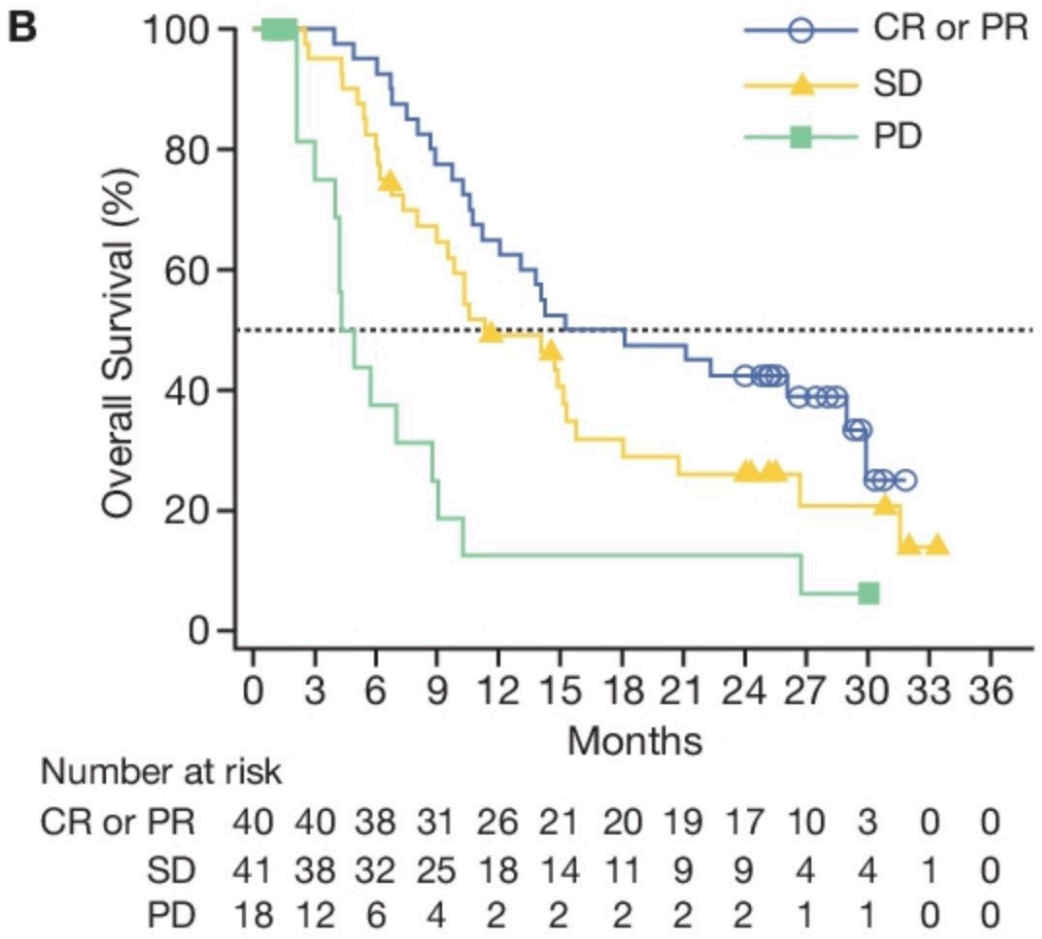
ASCO 2020;Abstract 5015.

BLC2001: Survival with Erdafitinib

Median PFS: 5.5 months



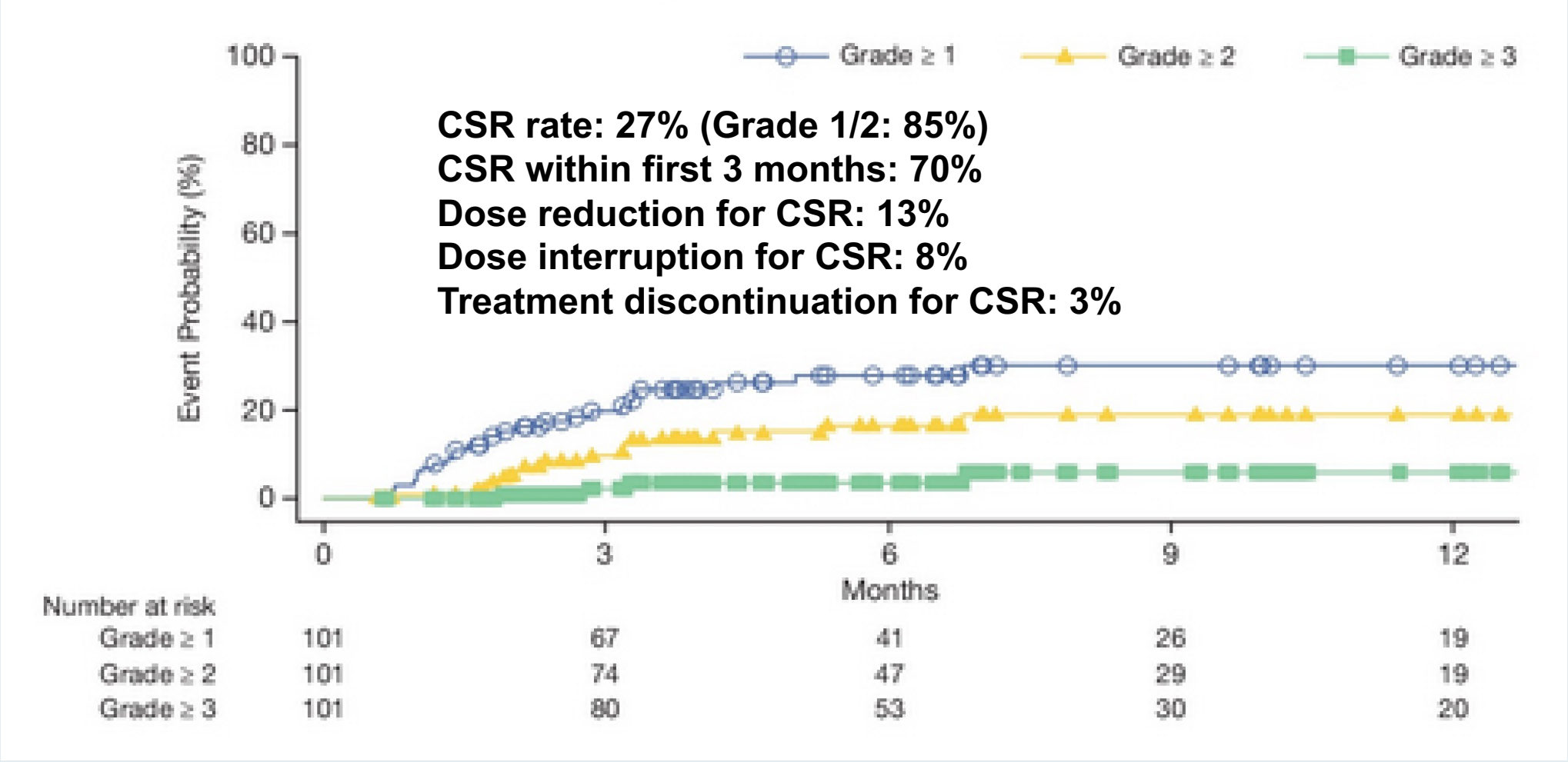
Median OS: 11.3 months



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

RTP RESEARCH TO PRACTICE

BLC2001: Central Serous Retinopathy (CSR)



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

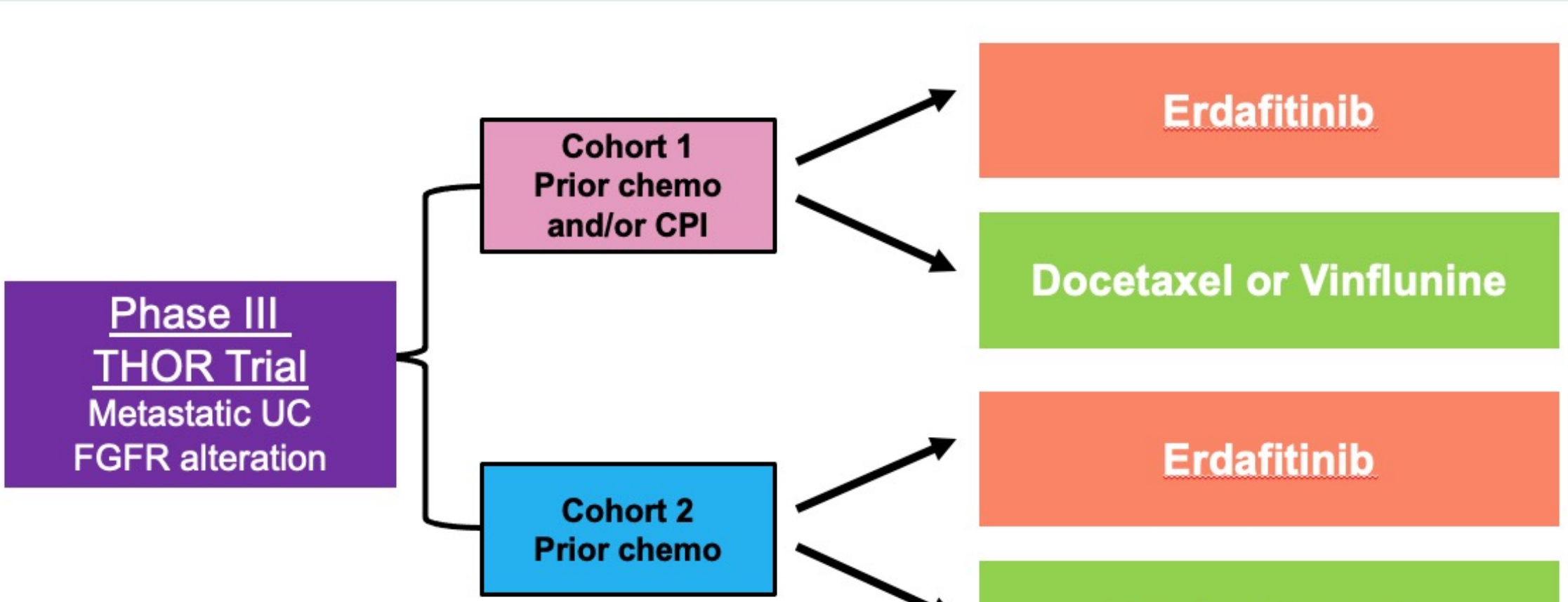
11% mFGFR

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

Wang, European Urology, 2019

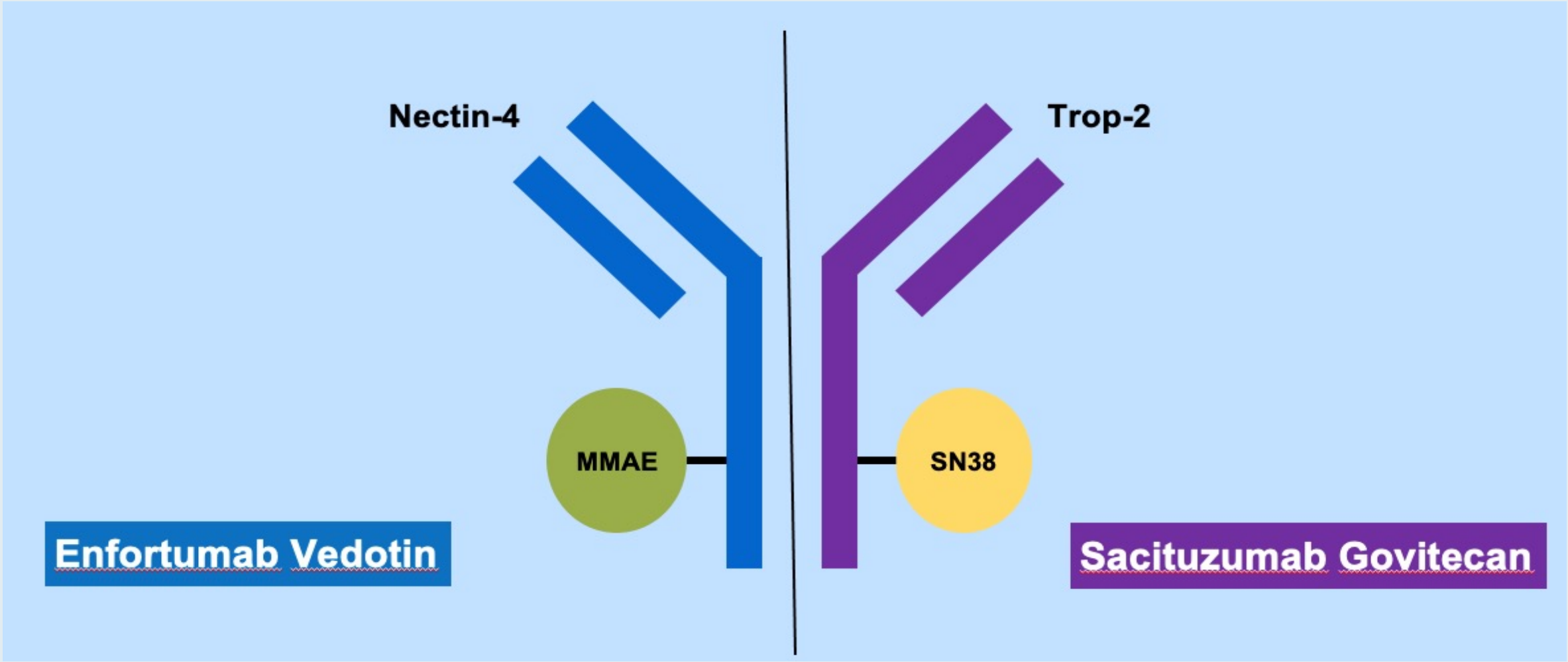
Courtesy of Matthew D Galsky, MD.

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

Antibody-Drug Conjugates in UBC



Courtesy of Matthew D 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

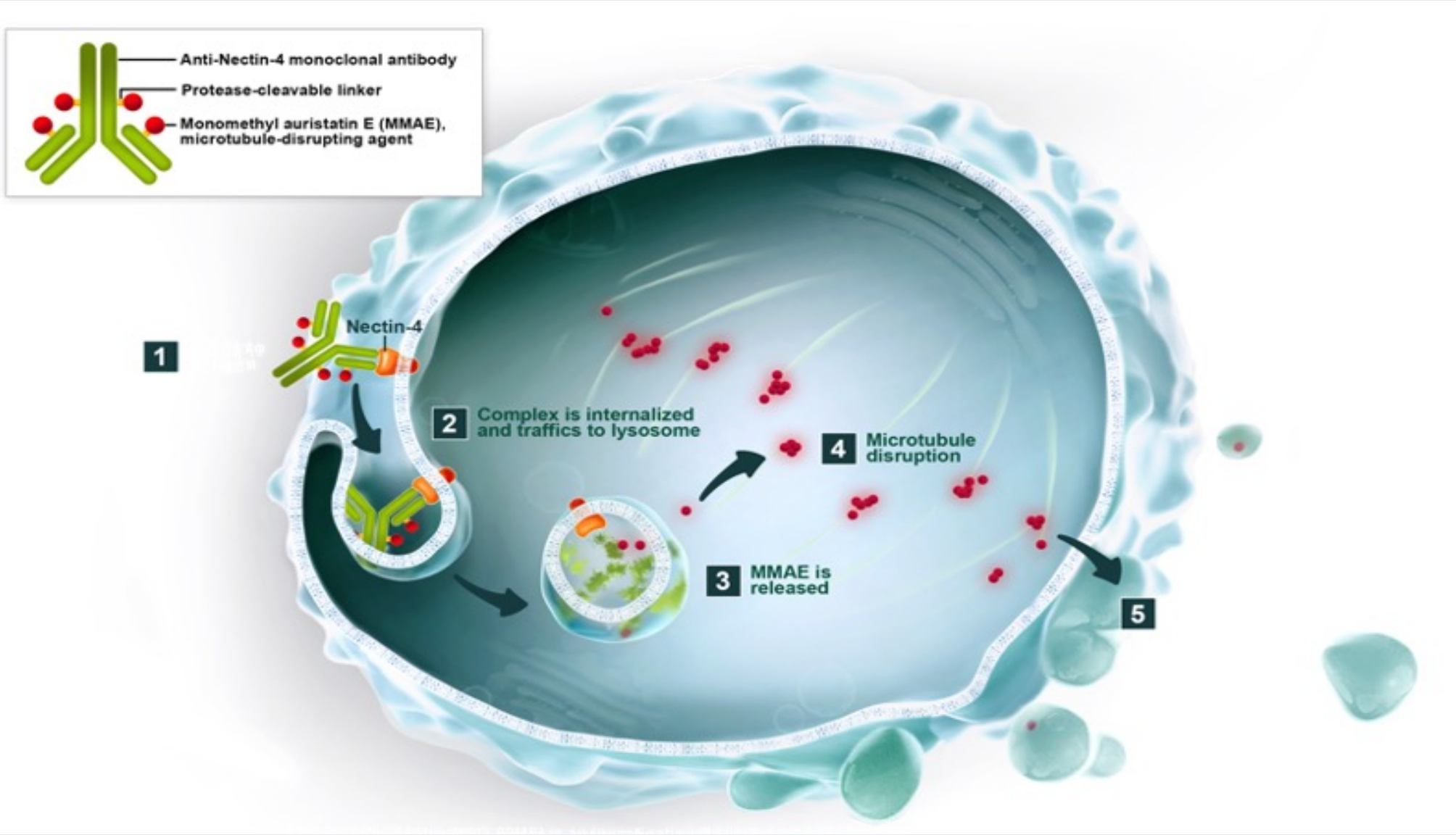
- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

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 E Rosenberg, MD

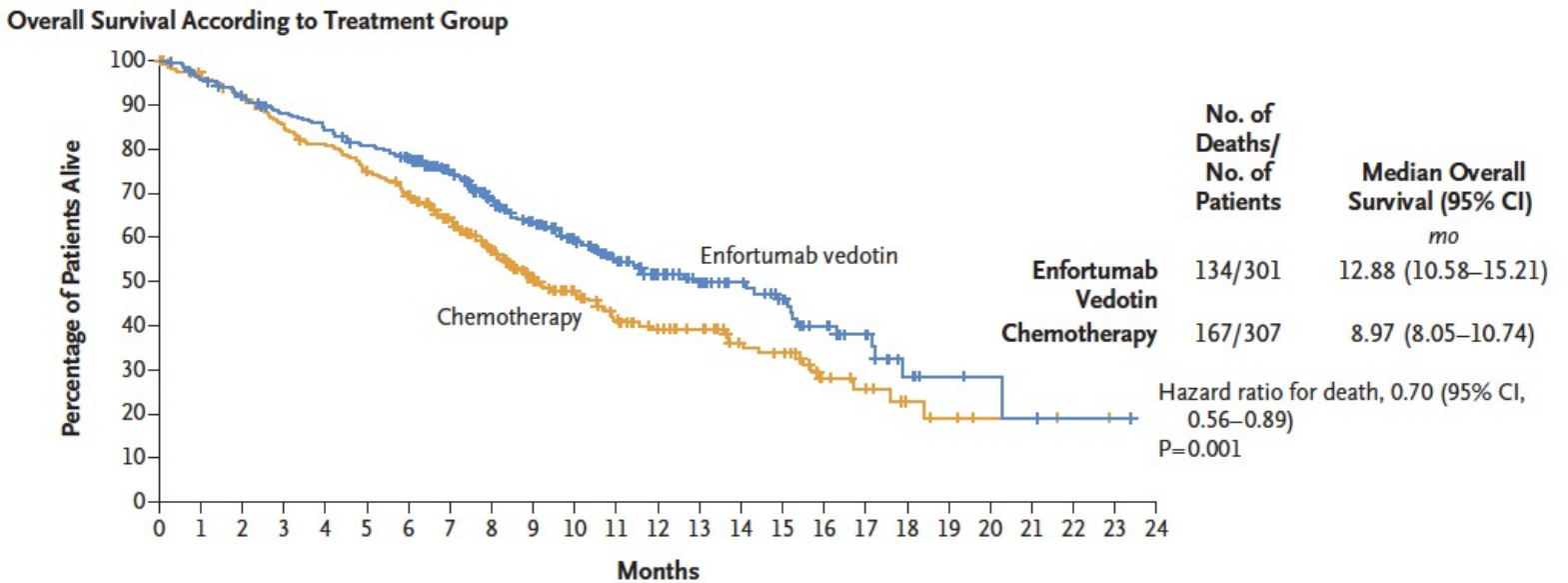
ORIGINAL ARTICLE

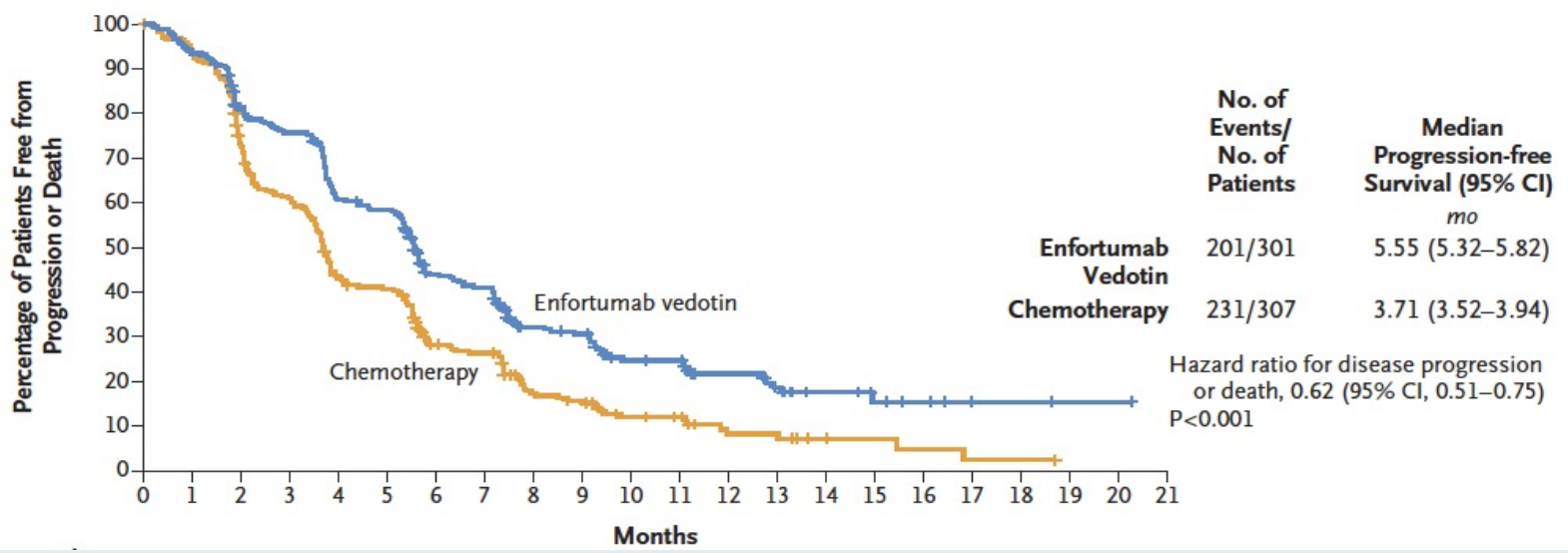
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

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.

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

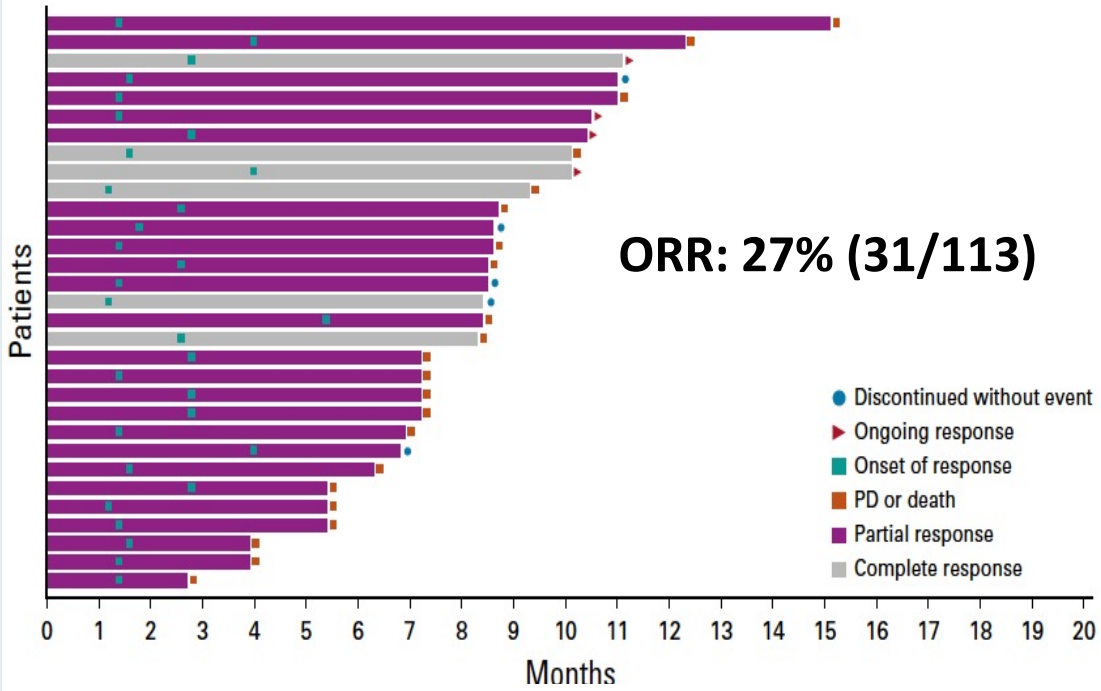
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11];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

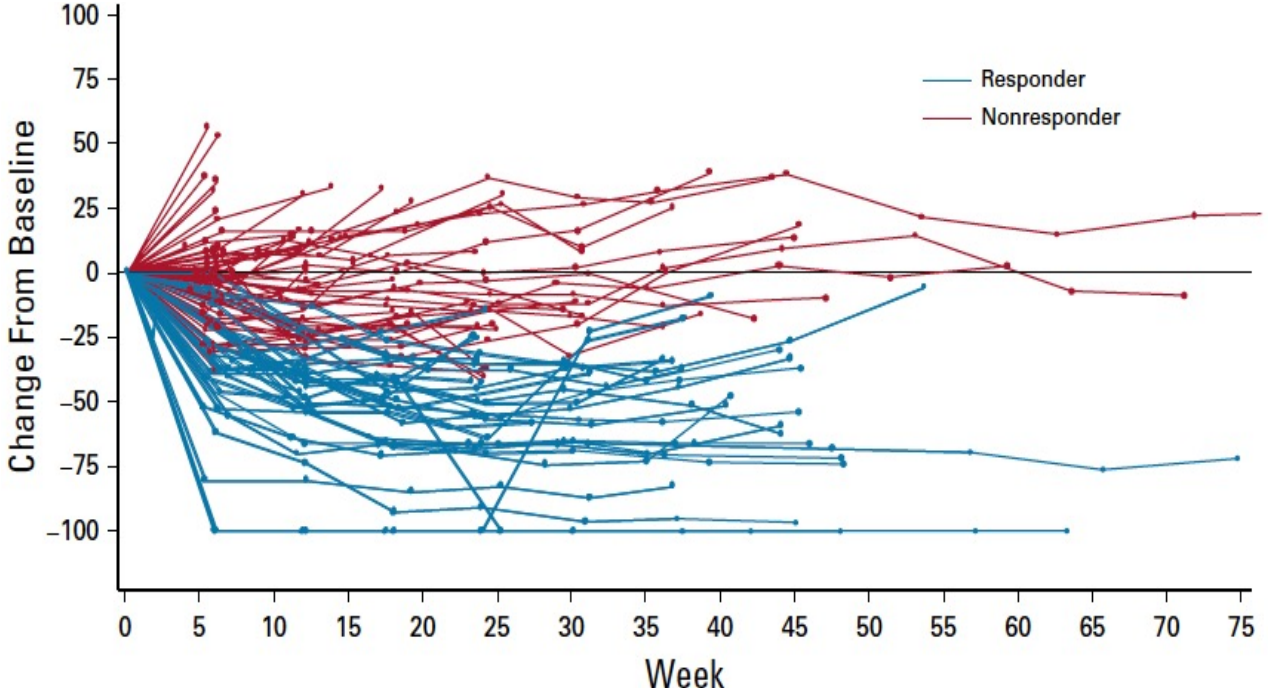
TROPHY U-01 (Cohort 1): ORR, Duration of Response and Survival

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;[Online ahead of print]; Loriot Y et al. ESMO 2020;Abstract LBA24.

RTP RESEARCH TO PRACTICE

What Urologists Want To Know: Addressing Current Questions and Controversies in the Management of Prostate Cancer

A Virtual CME Satellite Symposium During the American Urological Association (AUA) 2021 Annual Meeting

Monday, September 13, 2021
5:00 PM – 6:30 PM ET

Faculty

Leonard G Gomella, MD
Maha Hussain, MD, FACP, FASCO
A Oliver Sartor, MD
Neal D Shore, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.