Breakfast with the Investigators: Urothelial Bladder Cancer

A CME Hybrid Symposium Held in Conjunction with the 2022 ASCO Annual Meeting

Monday, June 6, 2022

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

Faculty

Yohann Loriot, MD, PhD

Elizabeth R Plimack, MD, MS

Jonathan E Rosenberg, MD

Moderator

Neil Love, MD

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Faculty

Yohann Loriot, MD, PhD
Deputy Chair, Early Drug Development (DITEP)
Chair, GU Oncology Group
Leader, Resistance to Innovative Drugs Program
Molecular Predictors and New Targets in Oncology, INSERM U981
Gustave Roussy
Villejuif, France

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

Elizabeth R Plimack, MD, MS
Chief, Division of Genitourinary Medical Oncology
Director, Genitourinary Clinical Research
Professor, Medical Oncology
Deputy Director, Fox Chase Cancer Center
Temple Health
Philadelphia, Pennsylvania

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

Complete Your Evaluation: Tap the CME Evaluation button to complete your evaluation electronically to receive credit for your participation.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.

Answer Survey Questions: Complete the premeeting survey before the meeting. Survey results will be presented and discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Friday June 3	**Acute Myeloid Leukemia and Myelodysplastic Syndromes** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Lung Cancer 6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)
Saturday June 4	**Prostate Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Gastrointestinal Cancers 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Sunday June 5	**Ovarian Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Chronic Lymphocytic Leukemia and Non-Hodgkin Lymphoma 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Monday June 6	**Urothelial Bladder Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Breast Cancer 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Tuesday June 7	**Multiple Myeloma** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

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Exciting CME Events in Chicago You Do Not Want to Miss

A CME Hybrid Symposium Series Held in Conjunction with the 2022 ASCO Annual Meeting

Urothelial Bladder Cancer

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

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Jonathan E Rosenberg, MD

Multiple Myeloma

Tuesday, June 7, 2022
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty
Ajai Chari, MD
Elizabeth O'Donnell, MD
Robert Z Orlowski, MD, PhD

Breast Cancer

Monday, June 6, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty
Javier Cortés, MD, PhD
Matthew P Goetz, MD
Erika Hamilton, MD
Ian E Krop, MD, PhD
Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Spencer H Bachow, MD
Lynn Cancer Institute
Boca Raton, Florida

Philip L Brooks, MD
Northern Light Eastern Maine Medical Center and Lafayette Family Cancer Institute
Brewer, Maine

Shams Bufalino, MD
Advocate Aurora Health
Park Ridge, Illinois

Lionel A Kankeu Fonkoua, MD
Mayo Clinic
Rochester, Minnesota

Shaachi Gupta, MD, MPH
Florida Cancer Specialists
Lake Worth, Florida

Zanetta S Lamar, MD
Florida Cancer Specialists
Naples, Florida

Neil Morganstein, MD
Atlantic Health System
Summit, New Jersey

Vignesh Narayanan, MD
Colorado Permanente Medical Group (CPMG)
Lone Tree, Colorado

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Namrata I Peswani, MD
Harold C Simmons
Comprehensive Cancer Center
Richardson, Texas

Matthew R Strickland, MD
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts

Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

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Commercial Support

This activity is supported by educational grants from Astellas and Seagen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Gilead Sciences Inc, and Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC.

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 Love — Disclosures

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

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Dr Loriot — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Astellas, Basilea Pharmaceutica Ltd, Bristol-Myers Squibb Company, Gilead Sciences Inc, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck KgaA, Merck Sharp & Dohme LLC, Pfizer Inc, Roche Laboratories Inc, Seagen Inc
Contracted Research	Celsius Therapeutics, Janssen Biotech Inc, Merck Sharp & Dohme LLC, Roche Laboratories Inc, Sanofi Genzyme

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Dr Plimack — Disclosures

Advisory Committee	Astellas, Aveo Pharmaceuticals, Bristol-Myers Squibb Company, Calithera Biosciences, Genentech, a member of the Roche Group, Janssen Biotech Inc, MEI Pharma Inc, Merck, Pfizer Inc, Regeneron Pharmaceuticals Inc, Seagen Inc
Contracted Research	Astellas, Bristol-Myers Squibb Company, Genentech, a member of the Roche Group, Merck
Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP, Infinity Pharmaceuticals Inc

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Dr Rosenberg — Disclosures

Advisory Committee	Astellas, Seagen Inc
Consulting Agreements	Alligator Bioscience, Astellas, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, EMD Serono Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Infinity Pharmaceuticals Inc, Lilly, Merck, Mirati Therapeutics, Pfizer Inc, QED Therapeutics, Seagen Inc, Tyra Biosciences
Contracted Research	Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Seagen Inc
Data and Safety Monitoring Board/Committee	Gilead Sciences Inc
Honorarium	EMD Serono Inc

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Moderator

Neil Love, MD

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Agenda

Module 1 – Current and Future Management of Localized Urothelial Bladder Cancer (UBC)

Module 2 – First-Line Treatment for Patients with Metastatic UBC (mUBC)

Module 3 – Later-Line Therapeutic Options for Patients with mUBC; Novel Investigational Strategies

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Agenda

Module 1 – Current and Future Management of Localized Urothelial Bladder Cancer (UBC)

Module 2 – First-Line Treatment for Patients with Metastatic UBC (mUBC)

Module 3 – Later-Line Therapeutic Options for Patients with mUBC; Novel Investigational Strategies

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Case — Yohann Loriot, MD, PhD

A 67 yo gentleman referred to the GU oncology clinics for NMIBC

Comorbidities:

- **History of psoriasis**
- **Hypertension**

Disease history

- **Haematuria in July 2020 -> US and CT-scan revealed mass of the left wall of the bladder**
- **TURBT performed in late August 2020 (summer vacation..)**
- **Pathological report: urothelial carcinoma, no variant, high grade tumor, T1 and CIS**
- **Second TURBT in early October: no tumor cells**

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Case — Yohann Loriot, MD, PhD

Clinical case: what would you recommend?

1- BCG 1 year

2- BCG 3 years

3- Up-front cystectomy

4- Other

PD-L1, programmed cell death protein ligand 1; TMB, tumor mutation burden.

Case — Yohann Loriot, MD, PhD

Clinical case

- **The patient started BCG, 6 weekly instillations**
- **TURBT at 8 weeks: no relapse**
- **The patient received 3 additional instillations at month 3 and month 6**
- **Endoscopy performed at month 9: flat lesion in the left part of the bladder**
- **Pathological report: CIS, no papillary tumor**

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Case — Yohann Loriot, MD, PhD

Clinical case: what would you recommend?

1- Intravesical chemotherapy

2- Cystectomy

3- Pembrolizumab

4- Other

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Case — Yohann Loriot, MD, PhD

Clinical case

- The patient started pembrolizumab IV 200 mg q3wk
- Endoscopy performed at 3 months showed no lesion
- Systemic biopsies were performed and no lesion was found
- At 6 months, patient complained of psoriasis-like rash
- Psoriasis patches cover 10% of his body
- Creams and other topical meds probably were not enough

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Case — Yohann Loriot, MD, PhD

Clinical case: what would you recommend?

1- Start phototherapy and continue pembrolizumab

2- Stop pembrolizumab until Grade 1 rash resolves and then resume

3- Stop pembrolizumab and proceed with surgery

4- Other

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Case 2 — Yohann Loriot, MD, PhD

Clinical case

- **Pembrolizumab was stopped and the patient recovered within 3 months**
- **No lesion was found during 9 months**
- **New lesion was observed 1.5 years after the first infusion**
- **Finally, the patient proceeded with surgery**

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Case — Elizabeth R Plimack, MD, MS

- 70 yo woman, in 2015 presented with hematuria. Workup revealed 4 cm UC of left renal pelvis. Nephroureterectomy revealed pT1N0M0 with extensive non-invasive spread throughout the collecting duct
- 2016 TURBT high grade UC, T1
- 2017 BCG induction #1
- 2018 BCG maintenance
- 2018 HG T1, persistent
- 2019 BCG induction #2
- 2019 HG T1, persistent
- 2019-2020: Clinical trial with low dose radiation x 3 fractions with durvalumab x 8 cycles
- Complicated by rash covering 90% of body surface area requiring prolonged steroid taper

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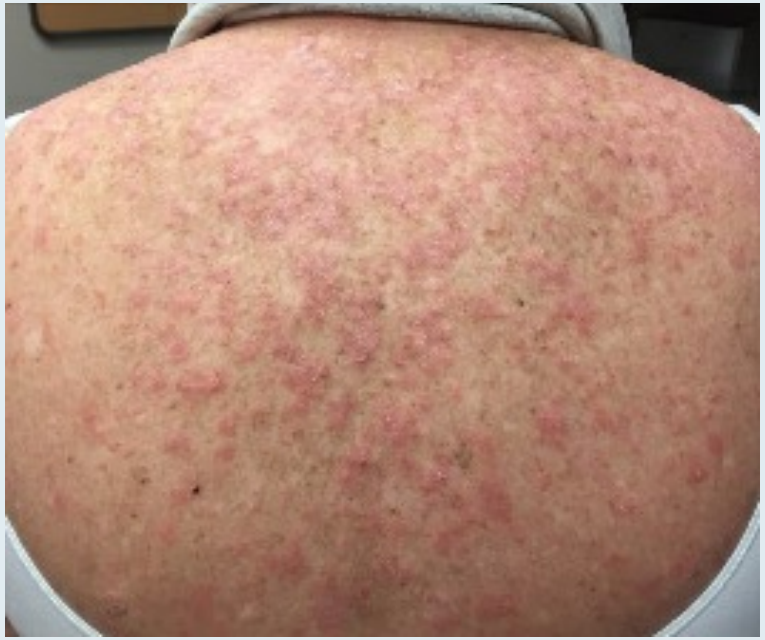
Case — Elizabeth R Plimack, MD, MS

- **Rash ultimately resolved. Q4 month cystoscopies – so far no recurrence of UC**
- **Rash – upper back:**



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Case — Jonathan E Rosenberg, MD

- **55-year-old man presented with gross hematuria in 2018**
- **Cystoscopy and TUR with CIS around L ureteral orifice**
- **Received induction BCG x 6, negative cytology at 3 months**
- **Received BCG maintenance x 3 doses**
- **3 months later, pt had suspicious cytology, negative cystoscopy**
- **3 months after, lateral wall erythema, TURBT showed CIS from left lateral wall**

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Case — Jonathan E Rosenberg, MD

- **Repeat induction BCG x 6**
- **3 months later, TURBT, ureteroscopy: atypia from bladder; left renal pelvis bx with atypia; bladder cytology positive**
- **3 months later, TURBT: CIS right anterior and left lateral wall; prostatic urethra with HG UCC with superficial lamina propria invasion**
- **Then received intravesical gemcitabine/docetaxel x 6**

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Case — Jonathan E Rosenberg, MD

- **3 months after intravesical chemotherapy, TURBT: left lateral wall with CIS**
- **Recommended for RC/diversion**
- **CT urogram + chest – no upper tract or metastatic disease**
- **Transferred care to tertiary center, TURBT showed CIS of posterior bladder wall**

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Case — Jonathan E Rosenberg, MD

- **Referred to medical oncology to discuss pembrolizumab**
- **RC recommended, but pt refused**
- **Started pembrolizumab**
- **After 3 months of pembrolizumab, cystoscopy was negative, but cytology positive**
- **CT urogram obtained, showed new urothelial thickening of proximal to mid right ureter concerning for tumor. No definite metastatic disease**
- **Right ureteroscopy with HG upper tract UC. Recommended for radical nephroureterectomy and is currently receiving preoperative chemotherapy**

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Case — Elizabeth R Plimack, MD, MS

- **74-year-old man, presented with gross hematuria, found to have muscle-invasive bladder cancer (MIBC) (cT2N0M0)**
- **Received 4 cycles of DDMVAC with a clinical complete response. He declined cystectomy**
- **Cystoscopic and CT surveillance every 3 months was NED x 2**

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Case — Elizabeth R Plimack, MD, MS

- **At 9 months biopsy proven recurrent disease was noted in the bladder and one iliac LN.**
- **His recurrent tumor was sequenced and compared to his primary. Mutations identified at diagnosis remained, additional mutations present.**
- **Given LN, he had NAC again – DDMVAC x 3. Developed peripheral neuropathy.**
- **Post-NAC imaging showed resolution of LAD, no distant disease.**
- **He went for cystoprostatectomy with LND**

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Case — Elizabeth R Plimack, MD, MS

- **Recovered well from surgery.**
- **Pathology showed no residual UC in the bladder, but occult nodal disease in the previously enlarged LN.**
- **Adjuvant therapy was discussed, and patient elected to pursue adjuvant immunotherapy with a checkpoint inhibitor.**

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Case — Elizabeth R Plimack, MD, MS

- **Adjuvant immunotherapy was well tolerated, only mild dry mouth noted.**
- **After completing 8 months of a 12 month planned course his imaging unfortunately showed a nodal recurrence.**
- **He discontinued adjuvant therapy and was presented options for treatment of metastatic disease.**

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Case — Elizabeth R Plimack, MD, MS

- **Patient elected enfortumab vedotin.**
- **He developed a pruritic rash:**
  - **Started after C1D8. C1D15 held. Resolved with 5d oral steroids.**
  - **Steroid premedication: Dex 4 mg day before, day of and day after each subsequent treatment helped but did not mitigate altogether.**
  - **Persistent and new skin toxicity required dose reduction and missed doses.**
- **Additional toxicities included dysguesia and poor appetite resulting in weight loss.**

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Case — Elizabeth R Plimack, MD, MS

- **Post-EV imaging showed radiographic complete response**
  - **Complete resolution of previously seen pelvic LAD**
  - **No evidence of metastatic disease**

- **Patient now enjoying a treatment break**

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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

***Lancet Oncol* 2021;22(7):919-30.**

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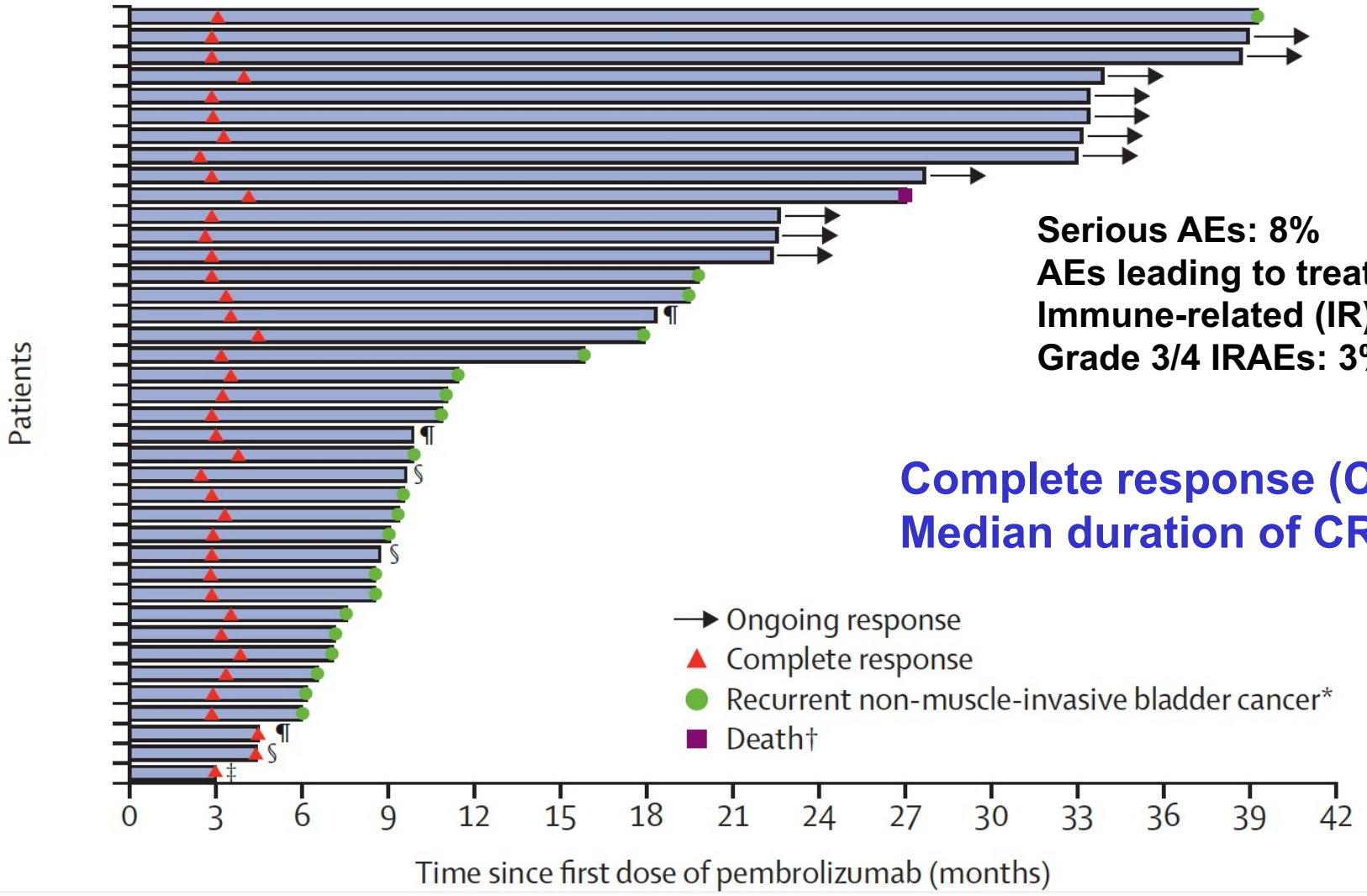
KEYNOTE-057: Pembrolizumab for High-Risk Non-Muscle-Invasive Bladder Cancer (NMIBC)

Response, Duration of Response and Summary of Adverse Events (AEs)



Serious AEs: 8%
AEs leading to treatment interruption: 13%
Immune-related (IR) AEs: 22%
Grade 3/4 IRAEs: 3%

Complete response (CR) at 3 months: 41%
Median duration of CR: 16.2 mo

Balar AV et al. *Lancet Oncol* 2021;22(7):919-30.

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

Protocol	n	Randomization
ALBAN (NCT03799835)	516	• Atezolizumab + BCG • BCG
POTOMAC (NCT03528694)	1,018	• Durvalumab + BCG • BCG
KEYNOTE-676 (NCT03711032)	1,405	• Pembrolizumab + BCG • BCG
CheckMate 7G8 (NCT04149574)	13	• Nivolumab + BCG • BCG

BCG = Bacillus Calmette-Guérin

www.clinicaltrials.gov; Accessed May 2022.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

D.F. Bajorin, J.A. Witjes, J.E. Gschwend, M. Schenker, B.P. Valderrama, Y. Tomita, A. Bamias, T. Lebret, S.F. Shariat, S.H. Park, D. Ye, M. Agerbaek, D. Enting, R. McDermott, P. Gajate, A. Peer, M.I. Milowsky, A. Nosov, J. Neif Antonio, Jr., K. Tupikowski, L. Toms, B.S. Fischer, A. Qureshi, S. Collette, K. Unsal-Kacmaz, E. Broughton, D. Zardavas, H.B. Koon, and M.D. Galsky

N Engl J Med 2021;384(22):2102-14.

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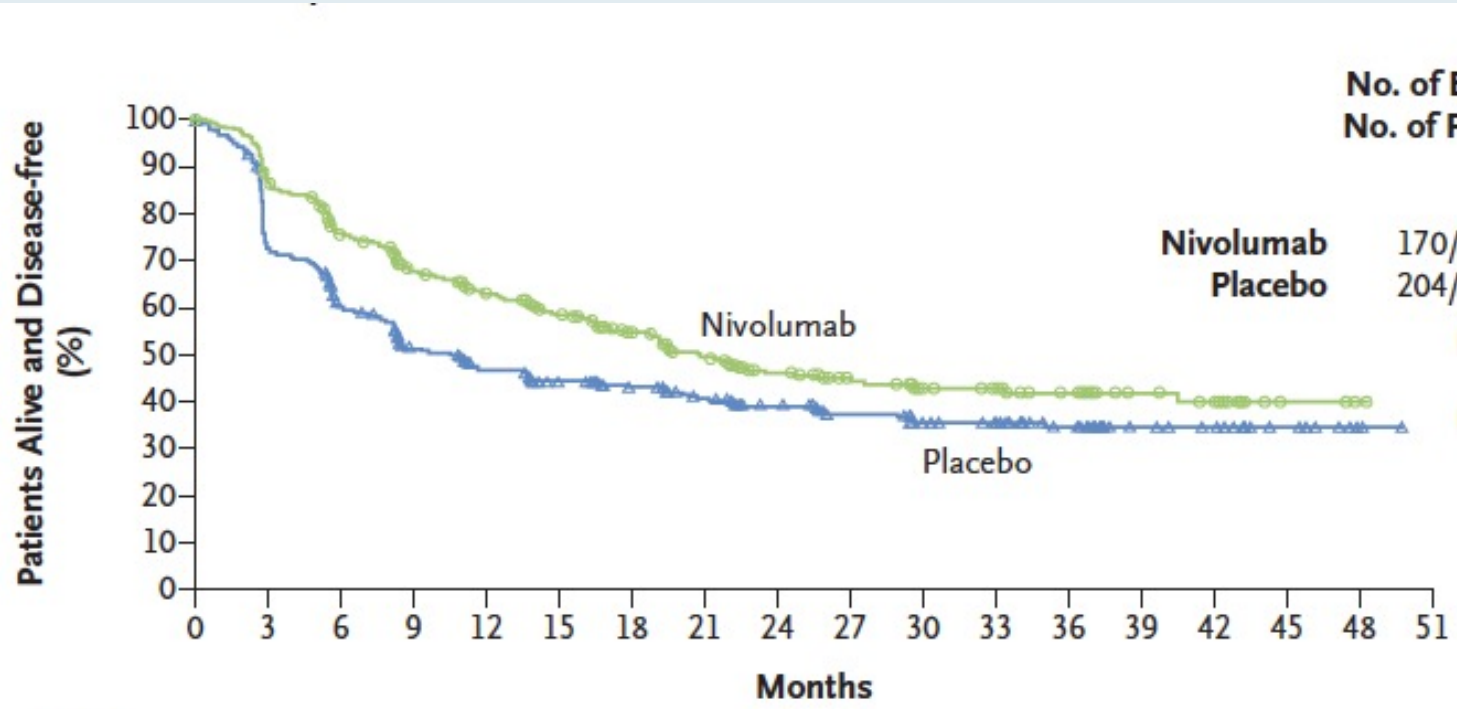
CheckMate 274: Adjuvant Nivolumab for High-Risk MIBC

Disease-Free Survival in the Intent-to-Treat Population



	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	170/353	74.9 (69.9–79.2)	62.8 (57.3–67.8)
Placebo	204/356	60.3 (54.9–65.3)	46.6 (41.1–51.9)

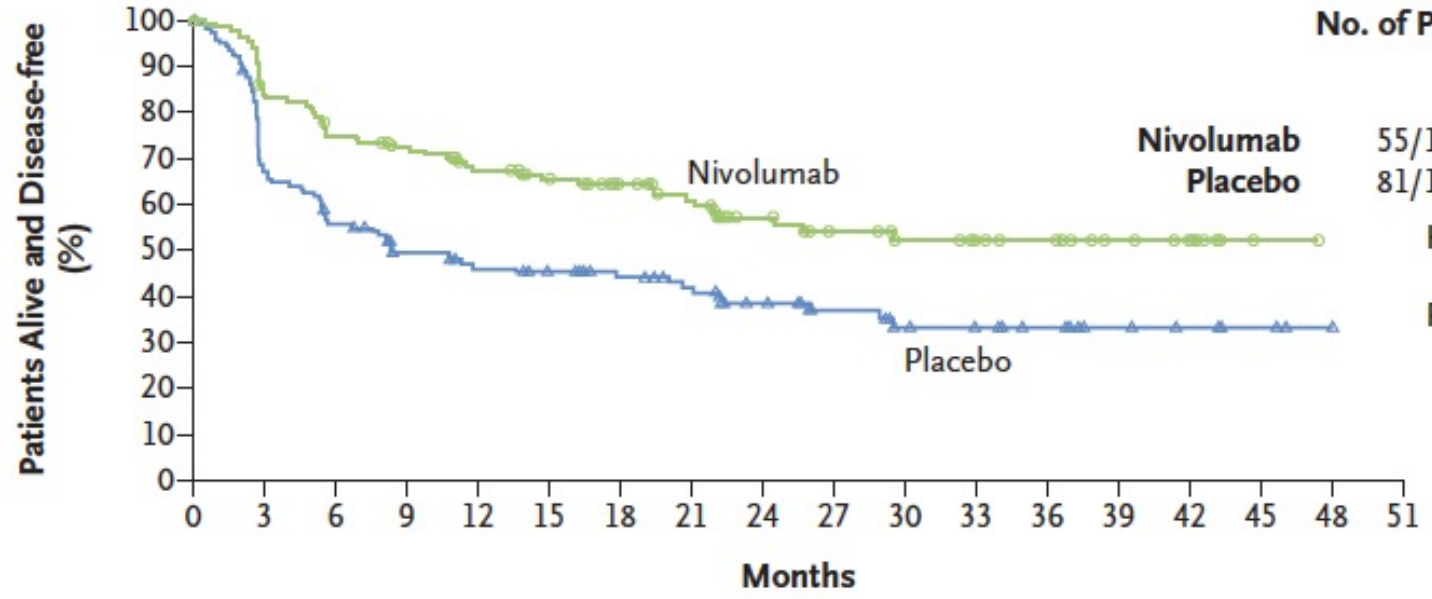
Hazard ratio for disease recurrence or death, 0.70 (98.22% CI, 0.55–0.90)
P<0.001

No. at Risk																		
Nivolumab	353	296	244	212	178	154	126	106	85	68	57	51	36	23	20	3	1	0
Placebo	356	248	198	157	134	121	105	94	80	65	54	50	37	22	19	10	2	0

Bajorin DF et al. *N Engl J Med* 2021;384(22):2102-14.

CheckMate 274: Adjuvant Nivolumab for High-Risk MIBC

Disease-Free Survival for Patients with PD-L1 Expression of 1% or More



	No. of Events/ No. of Patients	Disease-free Survival at 6 Mo (95% CI)	Disease-free Survival at 12 Mo (95% CI)
		%	
Nivolumab	55/140	74.5 (66.2–81.1)	67.2 (58.4–74.5)
Placebo	81/142	55.7 (46.8–63.6)	45.9 (37.1–54.2)

Hazard ratio for disease recurrence or death, 0.55 (98.72% CI, 0.35–0.85)
P<0.001

No. at Risk																	
Nivolumab	140	113	98	91	76	68	58	50	38	31	27	24	21	12	10	1	0	0
Placebo	142	90	73	59	53	49	42	37	28	22	17	16	12	7	5	3	1	0

Bajorin DF et al. *N Engl J Med* 2021;384(22):2102-14.

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ELSEVIER

Urologic Oncology: Seminars and Original Investigations 000 (2022) 1–9

UROLOGIC ONCOLOGY

Clinical-Bladder cancer

The safety, tolerability, and efficacy of a neoadjuvant gemcitabine intravesical drug delivery system (TAR-200) in muscle-invasive bladder cancer patients: a phase I trial

Siamak Daneshmand, M.D.[a,*], Iris S.G. Brummelhuis, M.D.[b], Kamal S. Pohar, M.D.[c], Gary D. Steinberg, M.D.[d], Manju Aron, M.D.[e], Christopher J. Cutie, M.D.[f], Kirk A. Keegan, M.D.[f], John C. Maffeo, M.S.H.S.[f], Donald L. Reynolds, Ph.D.[f], Bradley Raybold, M.S.[g], Albert Chau, M.Sc.[h], J. Alfred Witjes, M.D., Ph.D.[b]

Urol Oncol **2022;[Online ahead of print].**

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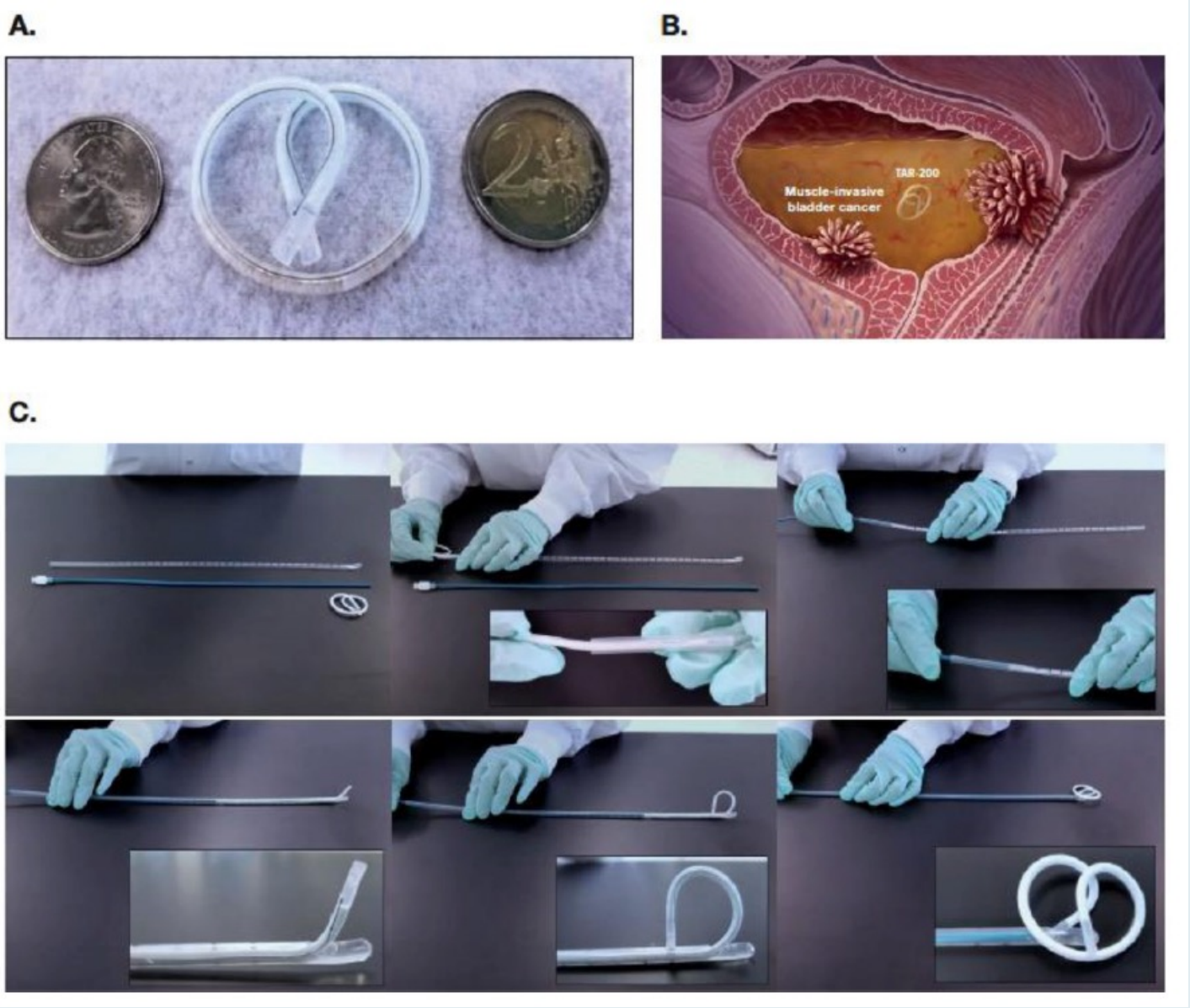
Components of TAR-200



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

TAR-200:

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

Daneshmand S et al. *Urol Oncol* 2022;[Online ahead of print].

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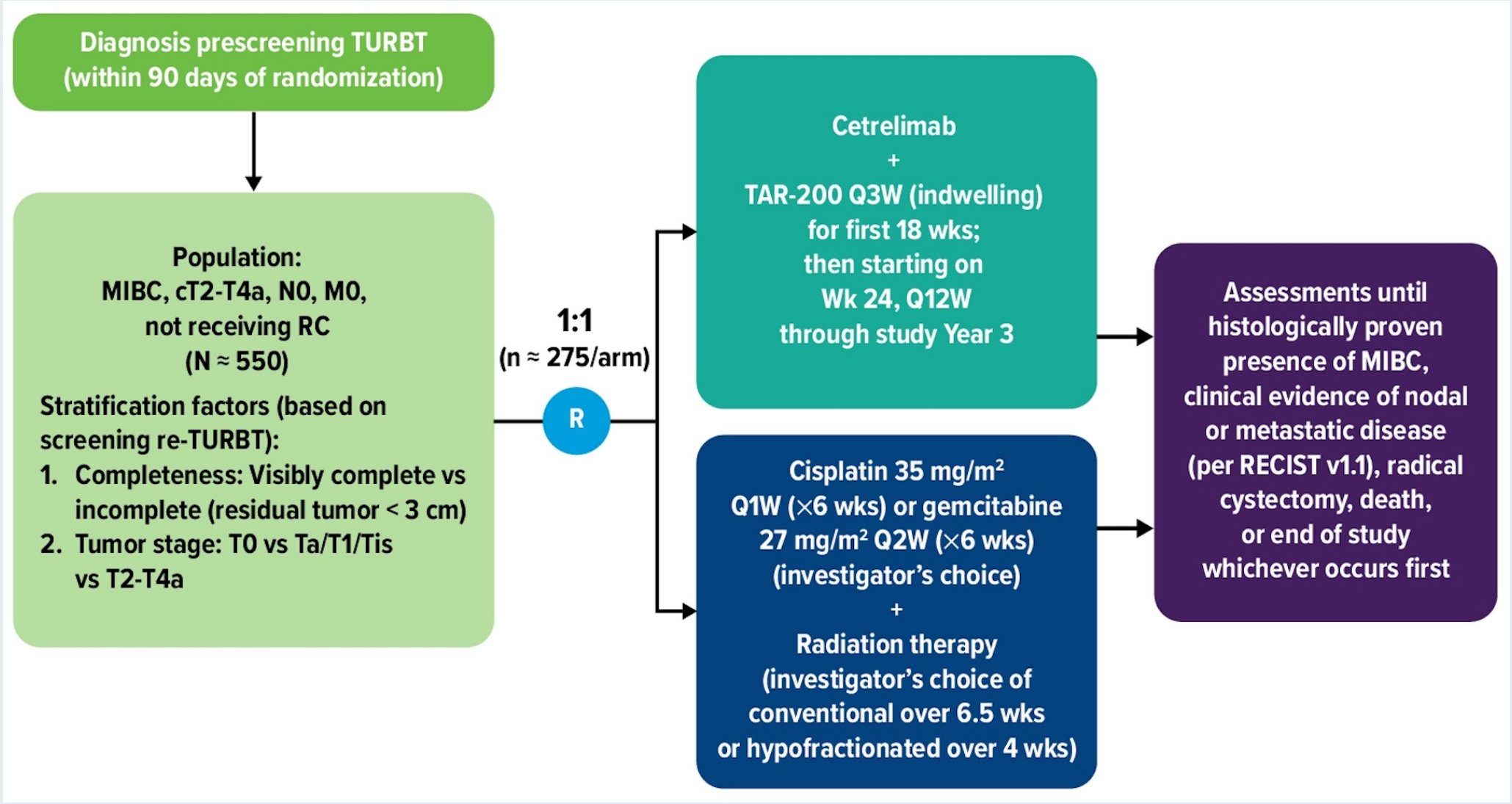
SunRISe-2: TAR-200 in Combination with Cetrelimab versus Concurrent Chemoradiation Therapy for Patients with MIBC



Williams SB et al. ASCO 2021;Abstract TPS4586.

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ASCO Genitourinary Cancers Symposium

2022 Abstract 435

Study EV-103 Cohort H: Antitumor activity of neoadjuvant treatment with enfortumab vedotin monotherapy in patients with muscle invasive bladder cancer (MIBC) who are cisplatin-ineligible

Daniel P. Petrylak, Yale University, New Haven, CT; Thomas W. Flaig, University of Colorado Comprehensive Cancer Center, Aurora, CO; Nataliya Mar, UC Irvine, Irvine, CA; Theodore S. Gourdin, Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; Sandy Srinivas, Stanford University Medical Center, Palo Alto, CA; Jonathan E. Rosenberg, Memorial Sloan Kettering Cancer Center, New York, NY; Maria Guseva, Astellas Pharma Inc., Northbrook, IL; Yao Yu, Seagen Inc., Bothell, WA; Sujata Narayanan, Seagen Inc., Bothell, WA; Christopher J. Hoimes, Duke University, Duke Cancer Institute, Durham, NC

Dr. Daniel P. Petrylak, Speaker

PRESENTED BY: Dr. Daniel P. Petrylak

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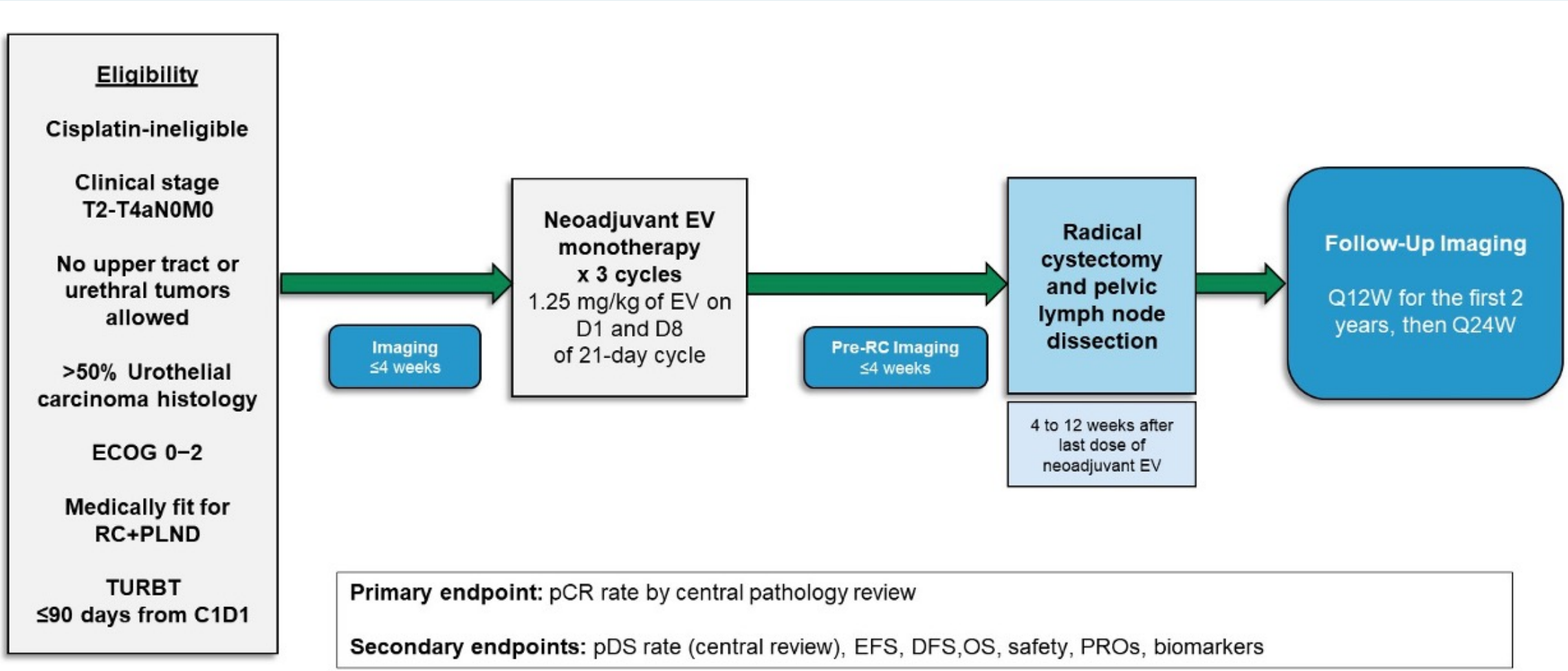
Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

EV-103 Cohort H Study Schema



Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

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EV-103 Cohort H: Efficacy by Central Pathology Review

Pathological Response	Central Pathology Results (N=22) n (%) [95% Confidence Interval]
Pathological Complete Response Rate (defined as absence of any viable tumor tissue: ypT0 and N0)	**8 (36.4%)** [17.2–59.3]
Pathological Downstaging Rate (defined as presence of ypT0, ypTis, ypTa, ypT1, and N0)	**11 (50.0%)** [28.2–71.8]

Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

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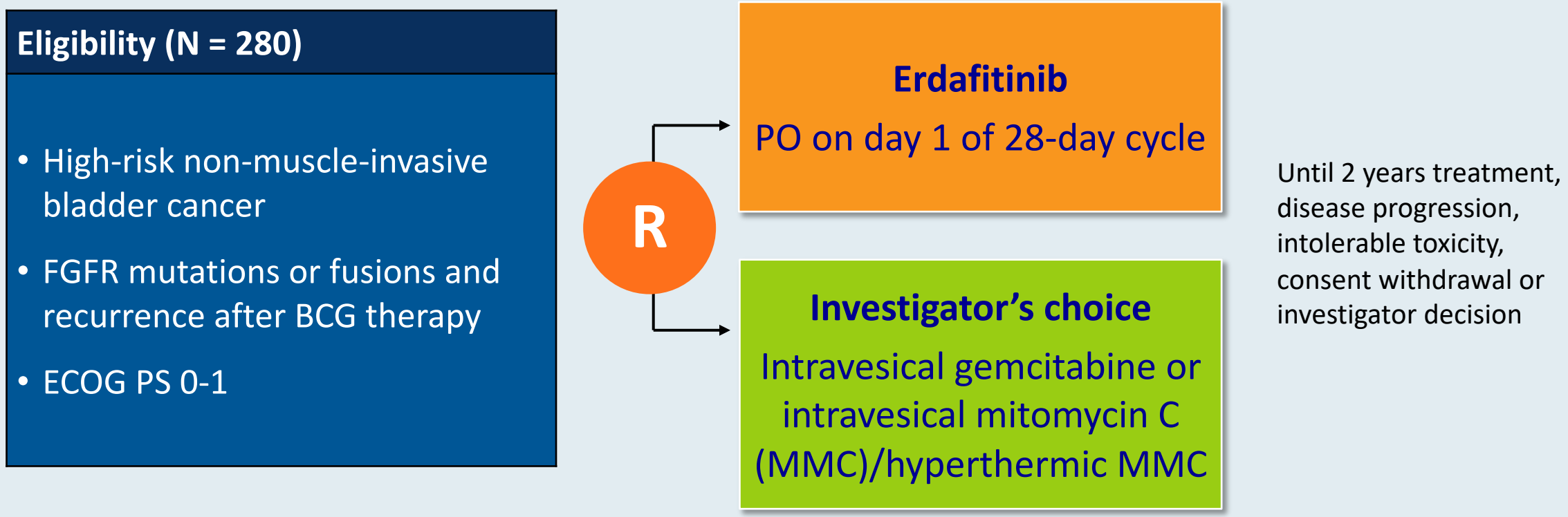
Phase II Study of Erdafitinib versus Investigator's Choice of Intravesical Chemotherapy for Patients with Recurrence of High-Risk NMIBC After BCG



Primary endpoint: Relapse-free survival (RFS)

Secondary endpoints: Time to progression/disease worsening, disease-specific survival, overall survival, RFS2, safety

www.clinicaltrials.gov. NCT04172675. Accessed May 2022.

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Agenda

Module 1 – Current and Future Management of Localized Urothelial Bladder Cancer (UBC)

Module 2 – First-Line Treatment for Patients with Metastatic UBC (mUBC)

Module 3 – Later-Line Therapeutic Options for Patients with mUBC; Novel Investigational Strategies

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Case — Yohann Loriot, MD, PhD

An 81 yo gentleman referred to the GU oncology clinic for metastatic urothelial carcinoma

Comorbidities:

- **Renal failure (creatinine clearance = 40 mL/min)**
- **Coronary heart disease**
- **Pacemaker insertion (atrial fibrillation)**

Disease history:

- **Haematuria in February 2020 → pathological mass in the right ureter**
- **Radical nephroureterectomy in June 2018 → urothelial carcinoma pT3pN0**
- **No perioperative systemic therapy**
- **October 2020: He's doing well (PS1) and he's asymptomatic but CT scan revealed retroperitoneum lymph nodes**

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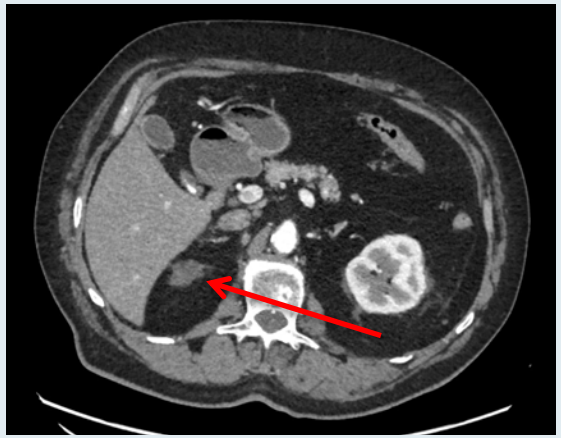
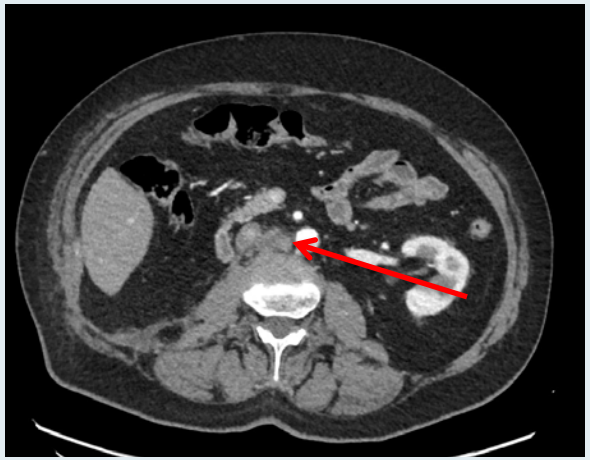
Case — Yohann Loriot, MD, PhD

Any additional work-up?





1- PD-L1 expression (CPS or IC)

2- FGFR2/3 mutation/fusion

3- TMB

4- Other

5- None

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Case — Yohann Loriot, MD, PhD

CPS = 20%, *FGFR3 S249C*

Clinical strategies discussed:

1- Carbo/gemcitabine first and switch maintenance with avelumab if no progression

2- Atezolizumab/pembrolizumab

3- Chemotherapy + atezolizumab

4- Erdafitinib

5- Other

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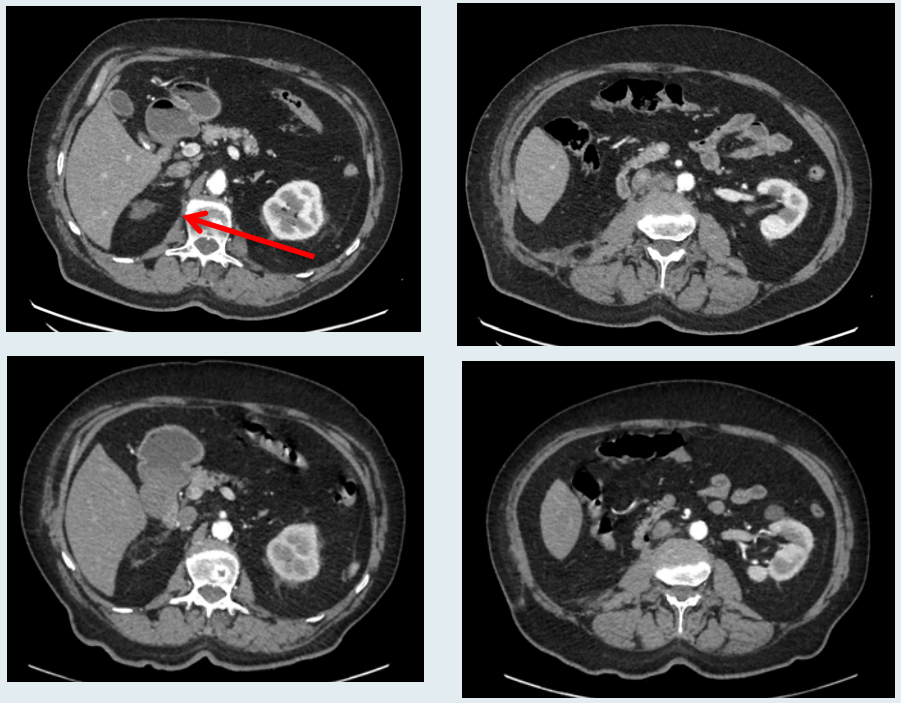
Case — Yohann Loriot, MD, PhD

Baseline

After 6 cycles



- **The patient declined the chemotherapy and received 6 cycles of atezolizumab**
- **Complete response of all LN except one in the mediastinum**

Which option would you select?

1- Continue atezolizumab

2- Stop and wait

3- Radiotherapy on residual lesion

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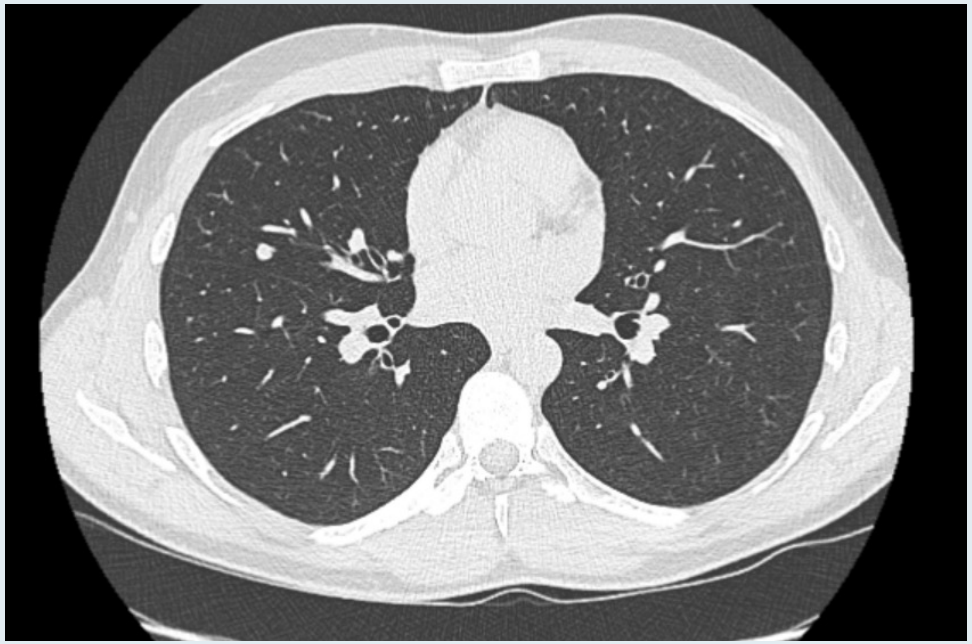
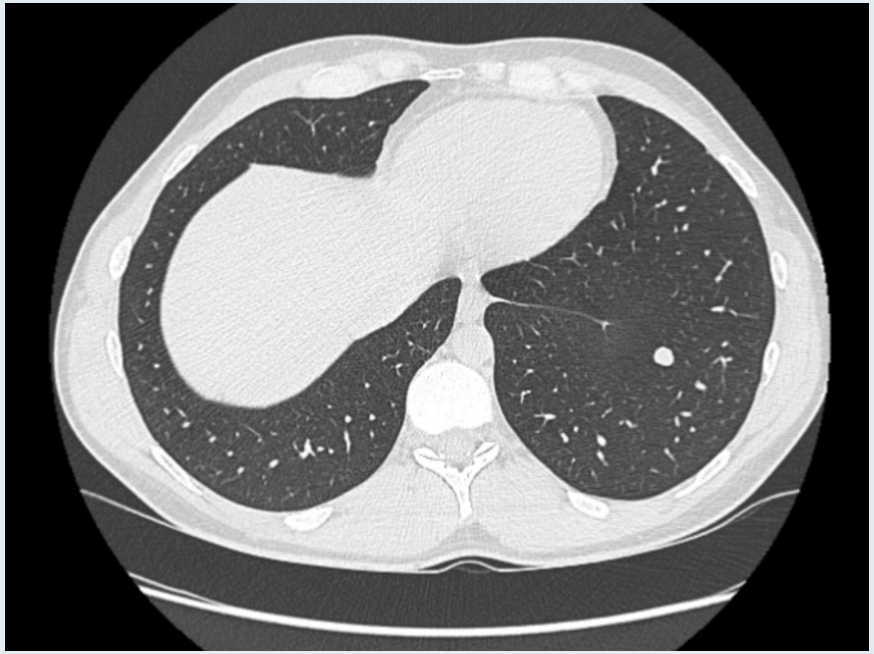
Case — Yohann Loriot, MD, PhD

- **Additional cycles of atezolizumab were given with excellent tolerance**
- **However, the new CT scan showed lung mets**





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Case — Yohann Loriot, MD, PhD

- **Again the patient declined the chemotherapy**
- **EV was not available in this setting**
- **Patient enrolled in a clinical trial with an FGFR inhibitor**
- **After three months, the patient achieved a complete response**

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Case — Jonathan E Rosenberg, MD

- 71 yo woman presented with hematuria, cystoscopy showed sessile tumor
- TURBT showed invasive urothelial carcinoma, NOS, involving the muscularis propria
- Imaging showed no extravesical disease or metastases
- Started gemcitabine and cisplatin neoadjuvant chemotherapy
- Chemotherapy was poorly tolerated
  - Required switch to split dosing for renal insufficiency
  - Required growth factor support and dose reduction for cytopenias
  - Stopped after 3.5 cycles of gemcitabine and cisplatin
- Post-chemo CT without metastases
- Radical cystectomy and TAH-BSO
  - 3.5 cm poorly differentiated UC with micropapillary and plasmacytoid features, pT3b, 7/20 LN involved, negative margins
- Refused enrollment to AMBASSADOR (A031501) trial (pembro vs observation)

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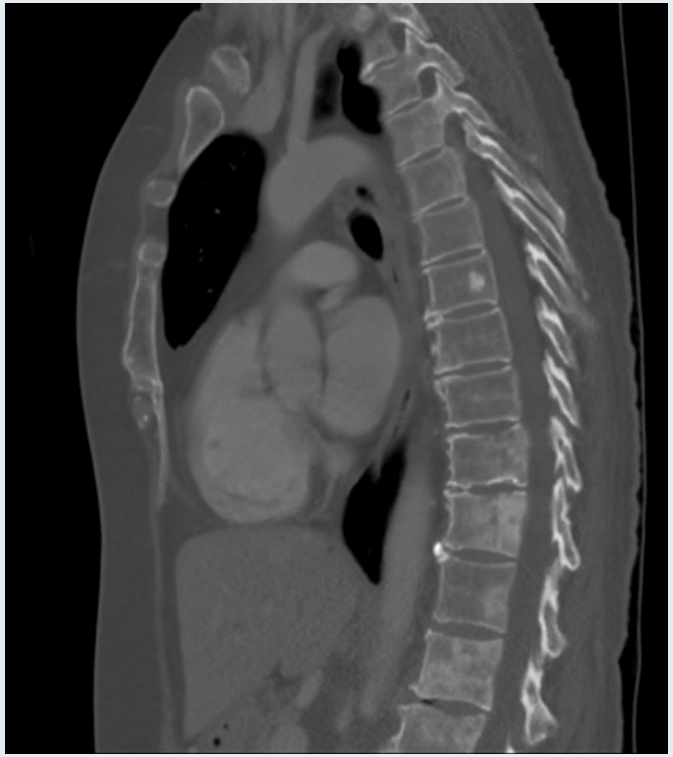
Case — Jonathan E Rosenberg, MD

- **CT just over 1 year following end of chemotherapy showed multiple mixed sclerotic and lytic lesions in the spine but no extraosseous tumors**
- **Biopsy showed metastatic poorly differentiated carcinoma positive for p63, CK20, GATA-3, and CK5/6, negative for TTF1, immunoprofile similar to prior specimens**
- **KPS 70% with fatigue and mild generalized back pain**
- **NGS sequencing showed no actionable alterations**
  - **TP53, ATM, KDM6A, RPTOR, TERT promoter**



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Case — Jonathan E Rosenberg, MD

- **No measurable disease and therefore not a trial candidate**
- **Poor tolerance to prior chemotherapy**
- **Bone-only disease has poor track record for IO therapy**
- **Relatively asymptomatic – mild pain, fatigue, MR without need for RT**
- **Reviewed data from EV-103 cohort A with 73% ORR, data from EV with bone pain palliation, and pt elected compassionate use for combination therapy enfortumab and pembrolizumab**

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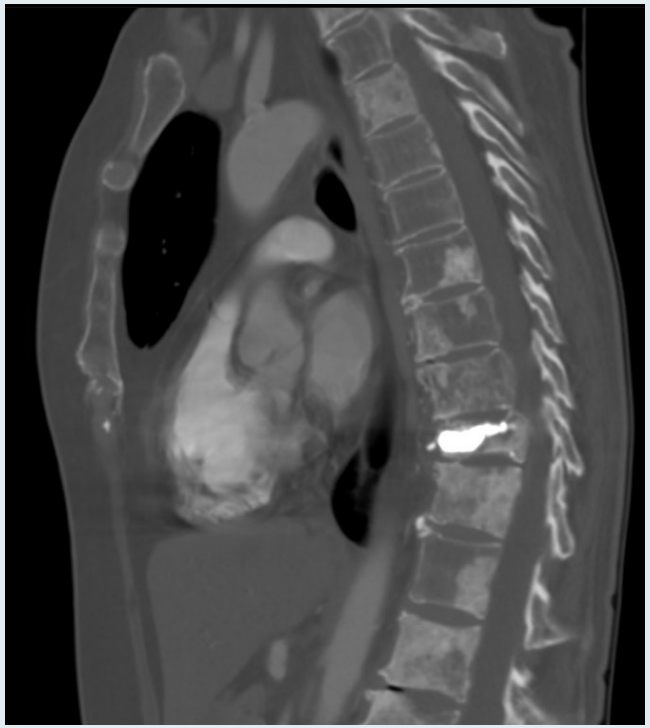
Case — Jonathan E Rosenberg, MD

- **Received enfortumab 1.25 mg/kg IV days 1 and 8 and pembrolizumab 200 mg IV day 1 every 21 days**
- **Developed acute back pain during cycle 1, found to have compression fracture and underwent kyphoplasty with relief**
- **Scans after cycle 2 showed sclerosis of bone lesions consistent with treatment effect, alkaline phosphatase went from 350 to 150, pain improved and KPS improved to 80%**

After cycle 2



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Case — Jonathan E Rosenberg, MD

- **Went on to receive 5 additional cycles of EV and pembrolizumab without significant complication except grade 1 neuropathy**
- **At cycle 6, presented with increasing back and pelvic bone pain**
- **Spinal MRI showed new epidural disease, and bone scan showed new pelvic metastases**
- **Palliative RT administered to spine and pelvis**
- **Performance status rapidly deteriorated, and pt decided for best supportive care and no further anticancer therapy**
- **Passed away 4 weeks after radiation completed**

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ASCO Genitourinary Cancers Symposium 2022 Abstract 487

Avelumab first-line maintenance for advanced urothelial carcinoma: long-term follow-up results from the JAVELIN Bladder 100 trial

T. Powles,[1] S. H. Park,[2] E. Voog,[3] C. Caserta,[4] B. P. Valderrama,[5] H. Gurney,[6] Y. Loriot,[7] S. S. Sridhar,[8] N. Tsuchiya,[9] C. N. Sternberg,[10] J. Bellmunt,[11] J. B. Aragon-Ching,[12] D. P. Petrylak,[13] J. A. Blake-Haskins,[14] R. J. Laliberte,[15] J. Wang,[15] N. Costa,[16] P. Grivas[17]

[1]Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK; [2]Sungkyunkwan University Samsung Medical Center, Seoul, Korea; [3]Centre Jean Bernard Clinique Victor Hugo, Le Mans, France; [4]Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy; [5]Department of Medical Oncology, Hospital Universitario Virgen del Rocío, Seville, Spain; [6]Department of Clinical Medicine, Macquarie University, Sydney, New South Wales, Australia; [7]Gustave Roussy, INSERMU981, Université Paris-Saclay, Villejuif, France; [8]Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada; [9]Department of Urology, Yamagata University Faculty of Medicine, Yamagata, Japan; [10]Englander Institute for Precision Medicine, Weill Cornell Medicine, Hematology/Oncology, New York, NY, USA; [11]Department of Medical Oncology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [12]Inova Schar Cancer Institute, Fairfax, VA, USA; [13]Yale Cancer Center, New Haven, CT, USA; [14]Pfizer, La Jolla, CA, USA; [15]Pfizer, Cambridge, MA, USA; [16]Pfizer, Porto Salvo, Portugal; [17]University of Washington, Fred Hutchinson Cancer Research Center, Seattle Cancer Care Alliance, Seattle, WA, USA

PRESENTED BY: Thomas Powles, MD

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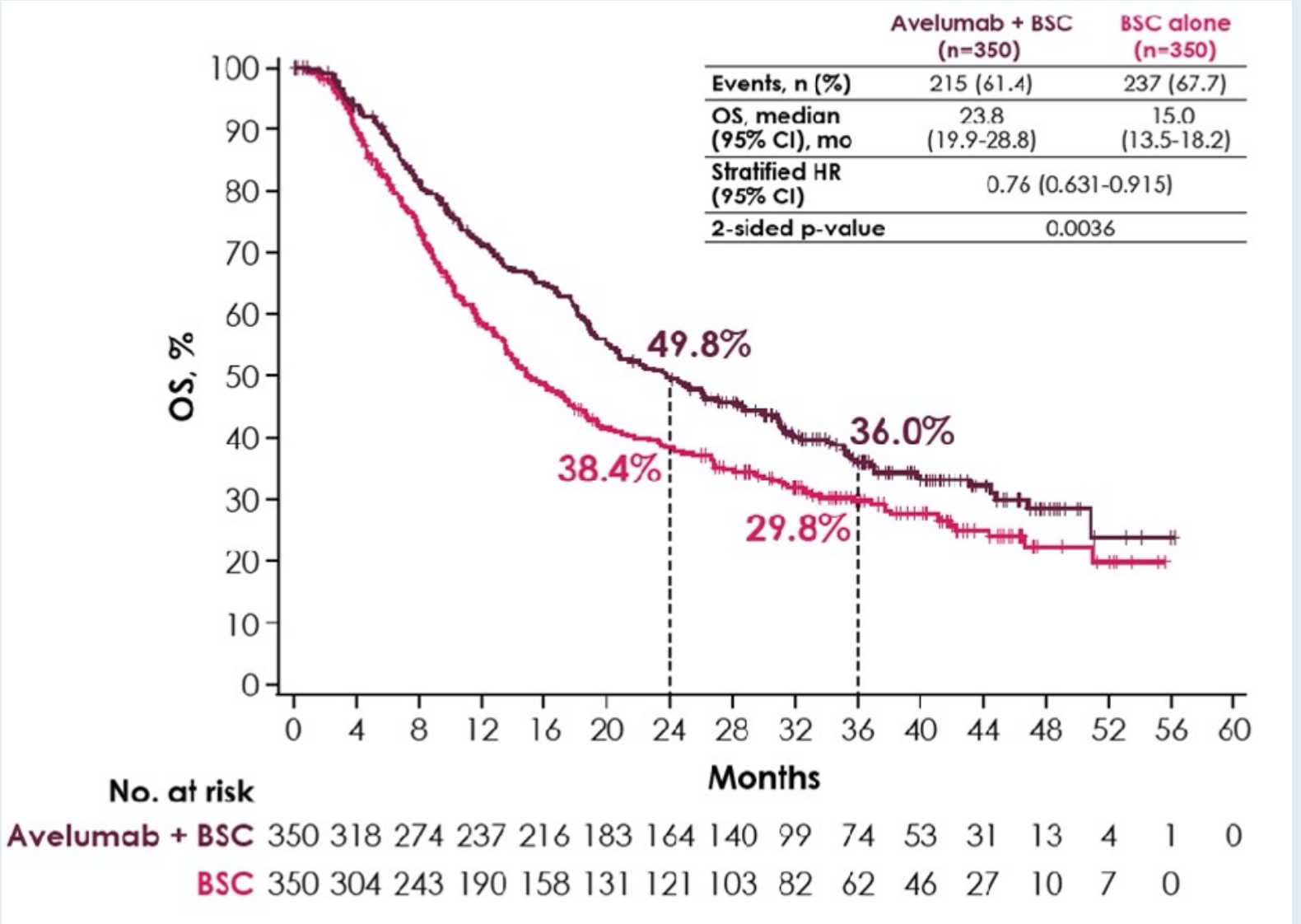
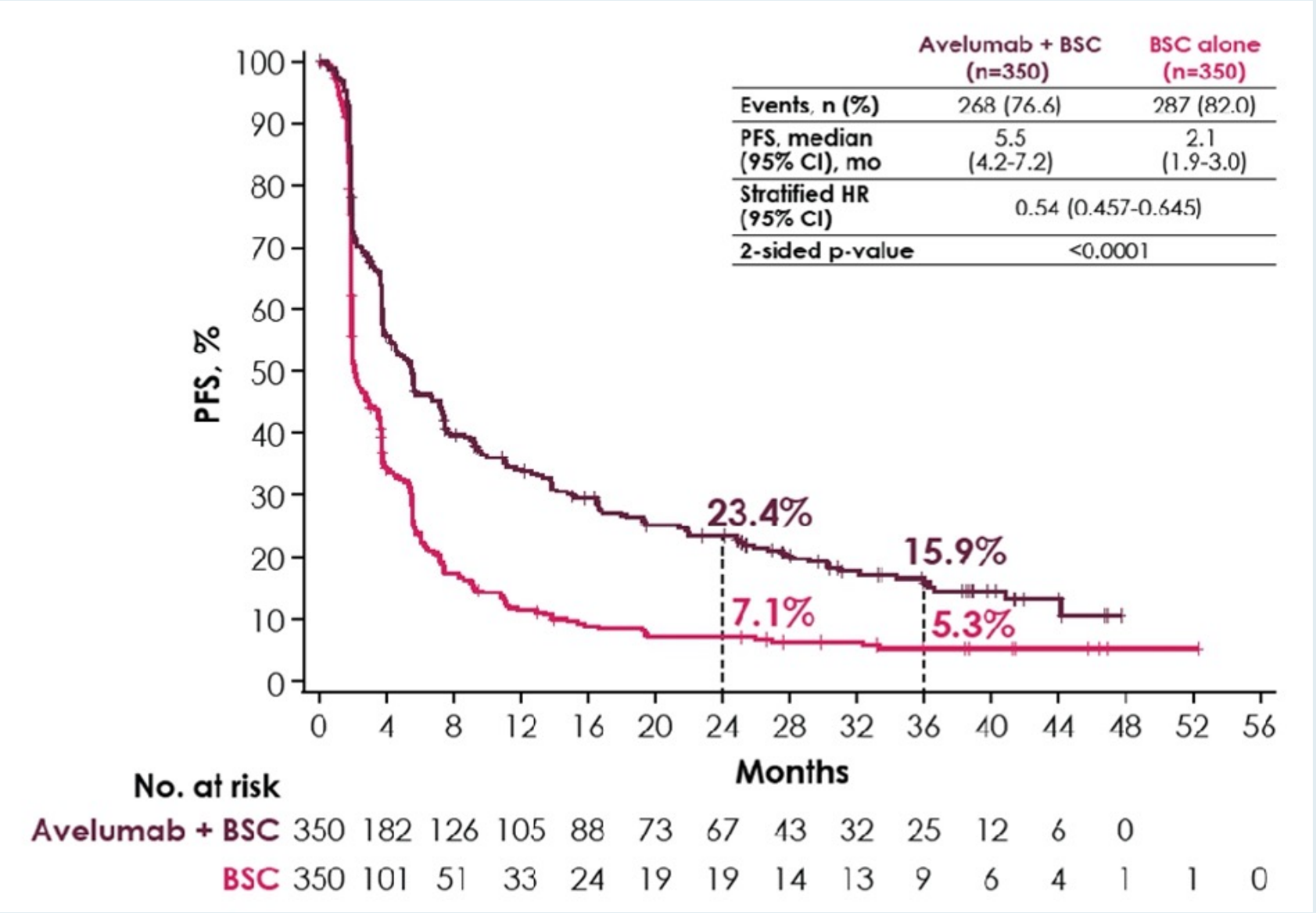
JAVELIN-100: Long-Term Overall Survival (OS)



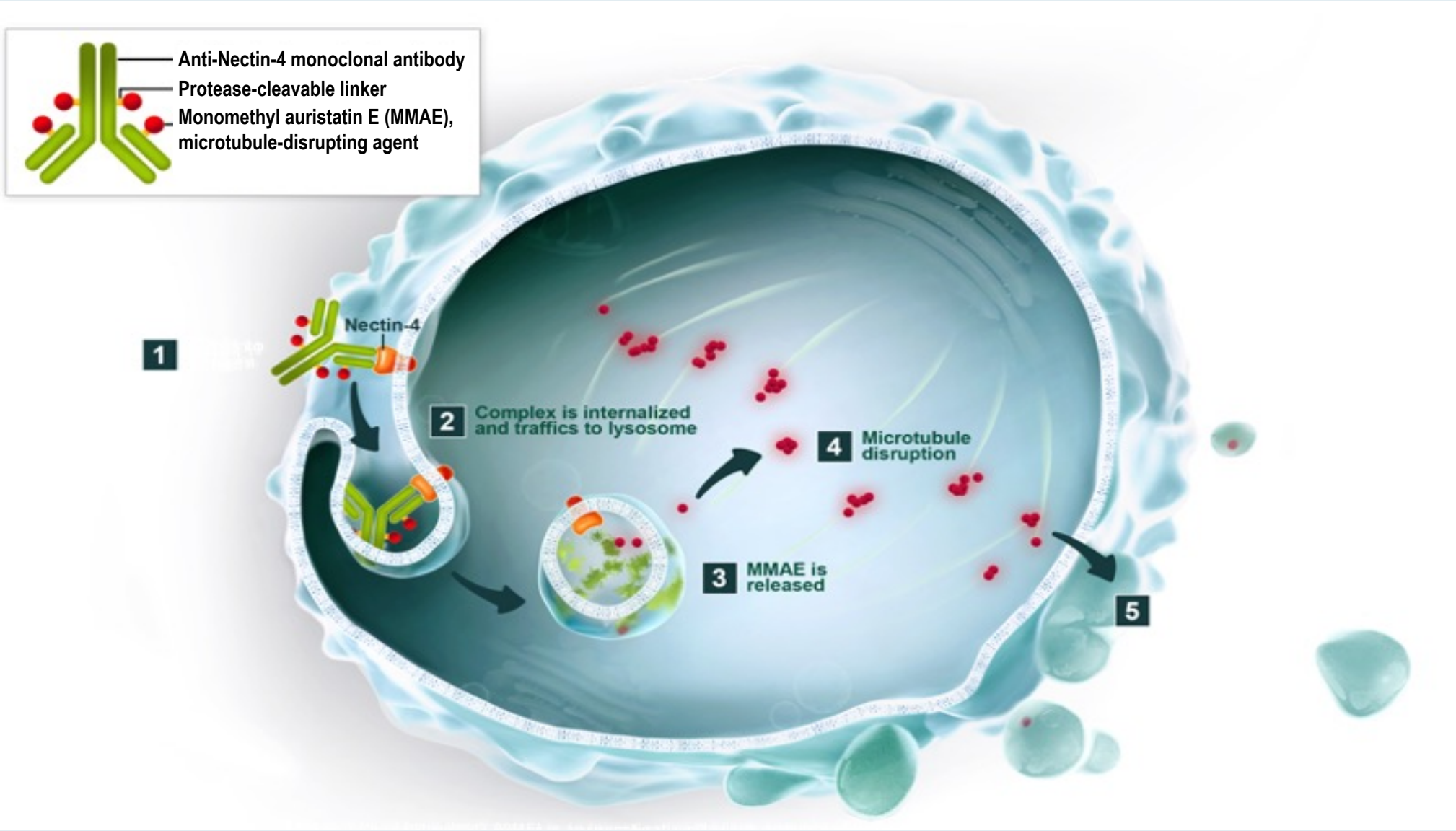
Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

JAVELIN-100: Investigator-Assessed Progression-Free Survival (PFS)



Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

Enfortumab Vedotin: Nectin-4 Targeted Therapy



Courtesy of Jonathan E Rosenberg, MD

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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.

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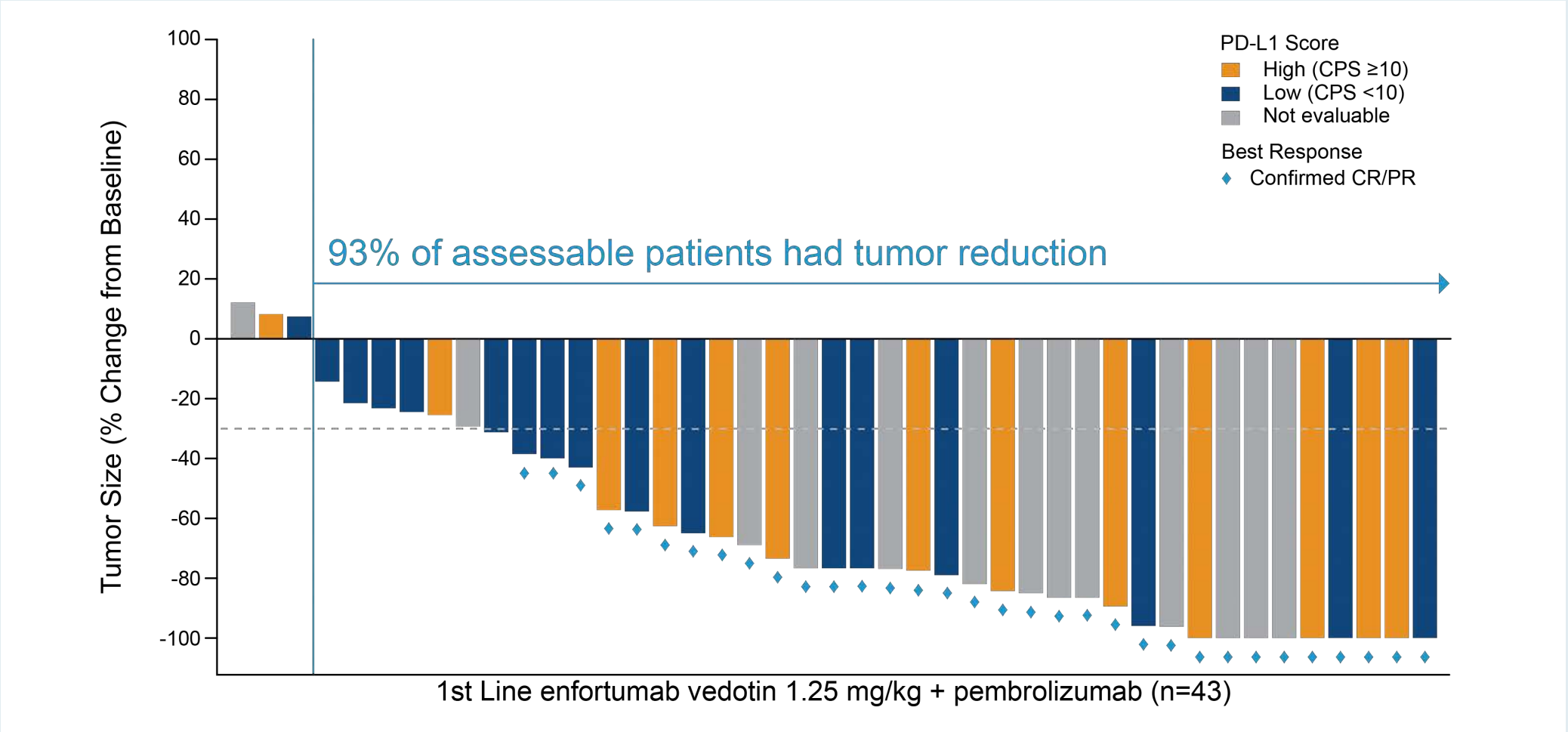
EV-103: Enfortumab Vedotin with Pembrolizumab as First-Line Therapy for Locally Advanced or Metastatic Urothelial Carcinoma



Friedlander TW et al. ASCO 2021;Abstract 4528.

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2021 ESMO congress

Abstract LBA27

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

Thomas Powles, Valeriy Chistyakov, Vasili Beliakouski, Andrey Semenov, Els Everaert, Yauheni Baranau, Victor Moreno, Begoña P. Valderrama, Yann Vano, Gianluca Del Conte, Yohann Loriot, Taek Won Kang, Meggan Tammaro, Anne O'Hagan, Mina Hosseini, Spyros Triantos, Harinder Chhabra, Ademi Santiago-Walker, Arlene Siefker-Radtke

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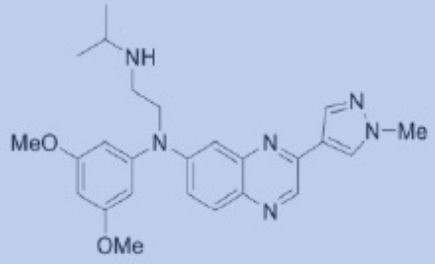
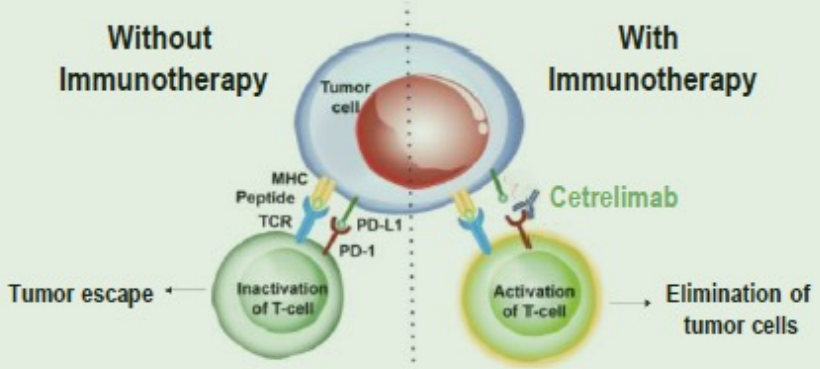
Rationale for Combining Erdafitinib and Cetrelimab

Erdafitinib: pan-FGFR inhibitor



- ~15%-20% of patients with mUC have *FGFRa*[1,2]
- FDA approved for adults with mUC with susceptible *FGFR3a/FGFR2a* who progressed during/after ≥ 1 prior line of platinum-based chemotherapy[3,4]
- Erdafitinib development is ongoing in bladder cancer and in the tumor agnostic setting

Cetrelimab: IgG4 monoclonal antibody PD-1 inhibitor[5]



- ~370 patients with cancer have been treated across clinical trials
- PK, PD, and safety profiles consistent with those of approved anti–PD-1s

- Neoantigen release by erdafitinib may prime the tumor microenvironment for response
- Combining **erdafitinib** with cetrelimab could expand treatment options for patients with newly diagnosed mUC with *FGFRa*
- We present the first phase 2 data from the NORSE study (NCT03473743) of erdafitinib alone or erdafitinib + cetrelimab in patients with newly diagnosed mUC with *FGFRa* who are ineligible for cisplatin

Powles T et al. ESMO 2021;Abstract LBA27.

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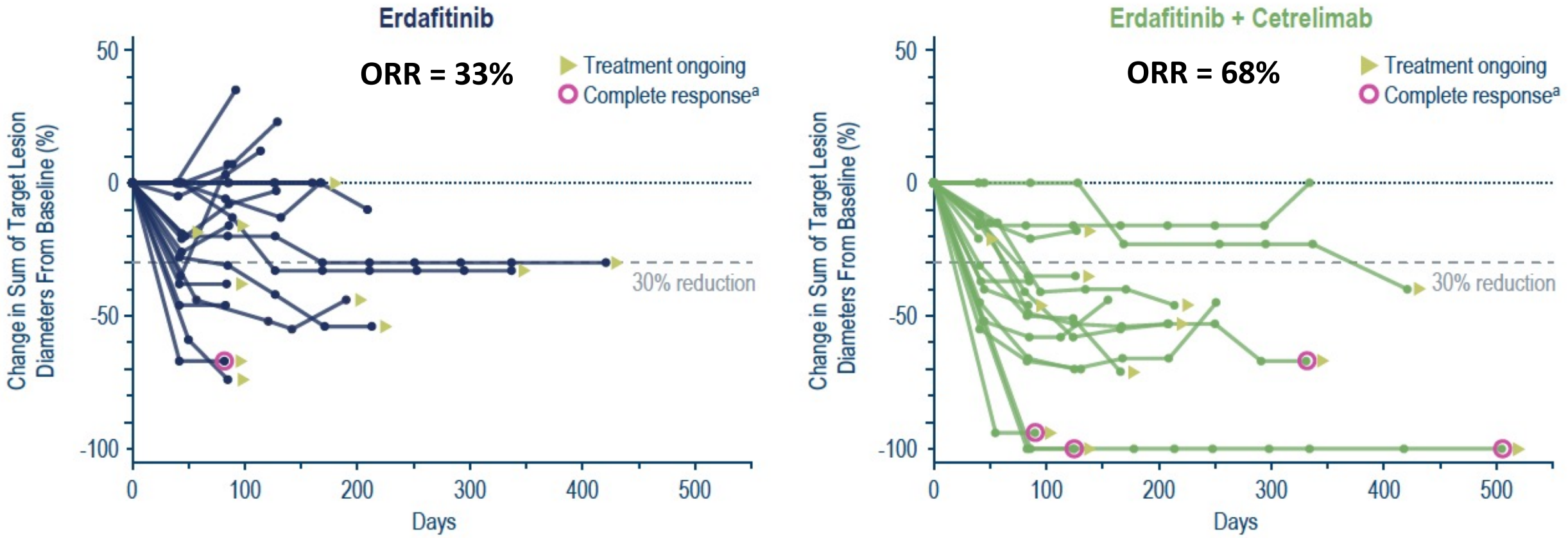
NORSE: Response and Antitumor Activity



- Patients in both treatment arms had a durable reduction in the sum of target lesion diameters over time
- Median of the maximum reduction in the sum of target lesion diameters was 28% in the erdafitinib arm and 51% in the erdafitinib + cetrelimab arm

Powles T et al. ESMO 2021;Abstract LBA27.

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Agenda

Module 1 – Current and Future Management of Localized Urothelial Bladder Cancer (UBC)

Module 2 – First-Line Treatment for Patients with Metastatic UBC (mUBC)

Module 3 – Later-Line Therapeutic Options for Patients with mUBC; Novel Investigational Strategies

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Case — Elizabeth R Plimack, MD, MS

79 yo former smoker, retired volunteer firefighter, motorcycle enthusiast

- **Presented with hematuria**
- **Treated with BCG for T1 urothelial carcinoma**
- **6 months later – lung metastases**
- **Pt had donated one of his kidneys 30 years ago. His current creatinine 0.96, EGFR >60**
- **PD-L1 testing was not performed**

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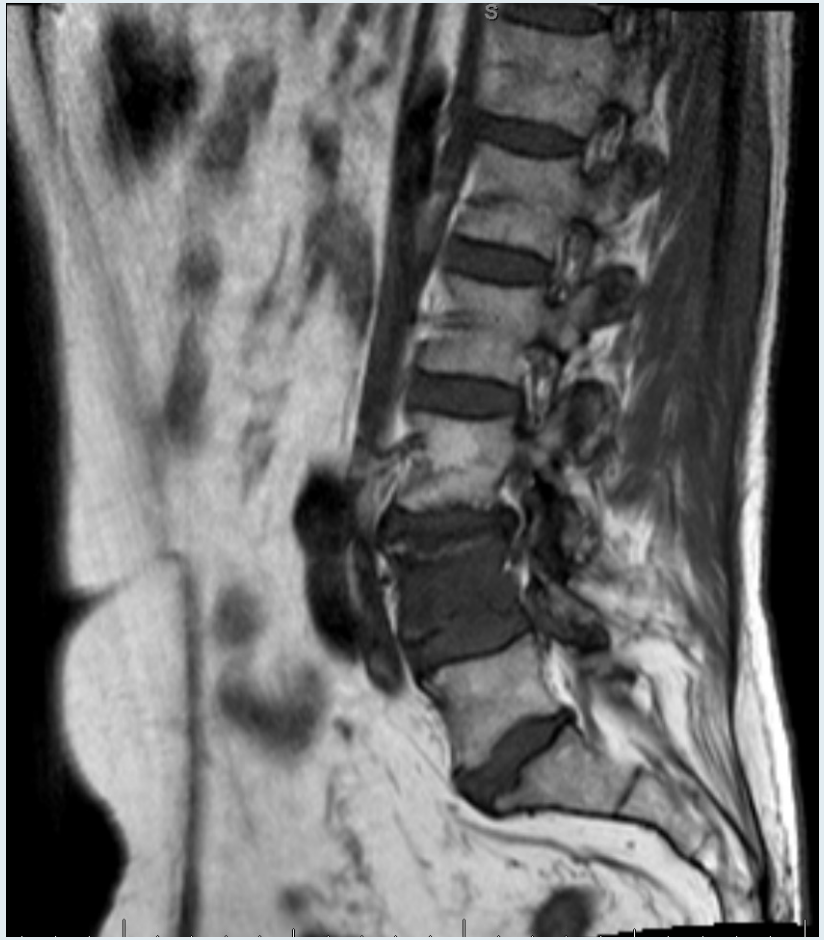
Case — Elizabeth R Plimack, MD, MS

- **Atezolizumab initiated**
- **Response in the lung**
- **At 9 months, PD with new lesion in the spine**
- **Radiation to spine**
- **Atezolizumab continued beyond PD**
- **Ultimately discontinued after 2 years for PD in the lungs**
- **Genomic testing not available**



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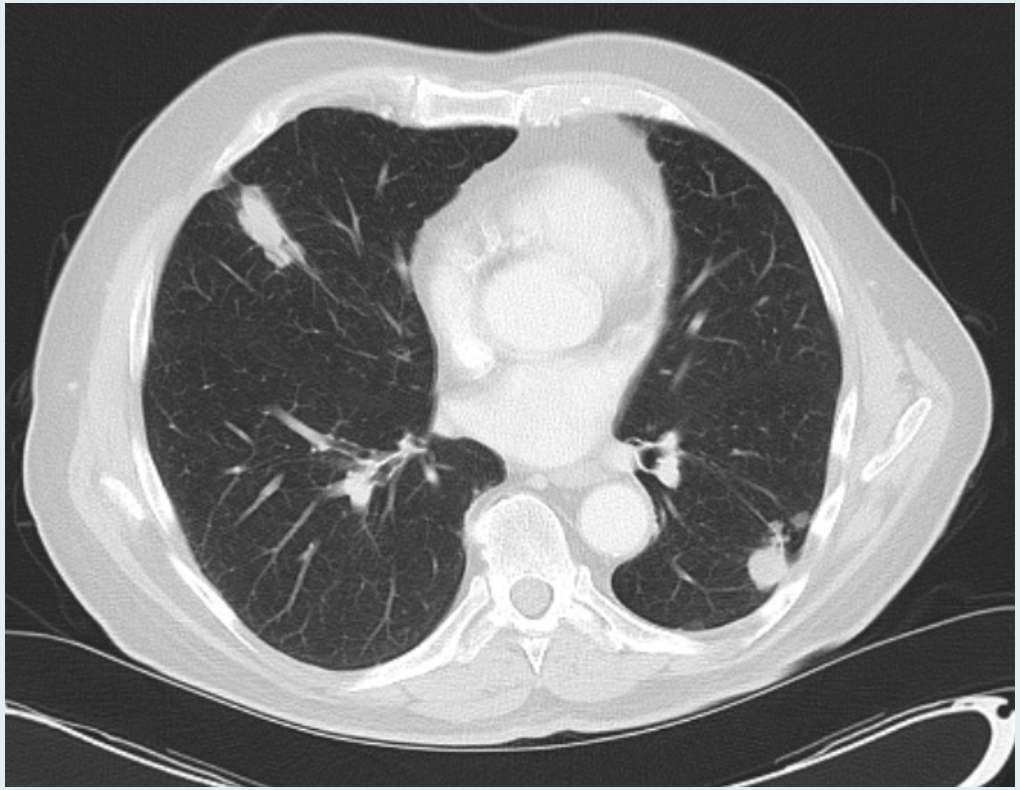
Case — Elizabeth R Plimack, MD, MS

Next-line therapy options

- **Pembrolizumab**
- **Gemcitabine**
- **Gemcitabine + carboplatin**
- **Paclitaxel**
- **Docetaxel**
- **Enfortumab vedotin**
- **Erdafitinib**



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Case — Elizabeth R Plimack, MD, MS

- **Started with gemcitabine**
- **PD in lung lesions after 9 months → carboplatin added**
- **At 18 months treatment stopped for chemo break in setting of response and cumulative toxicity**
- **Molecular testing sent**

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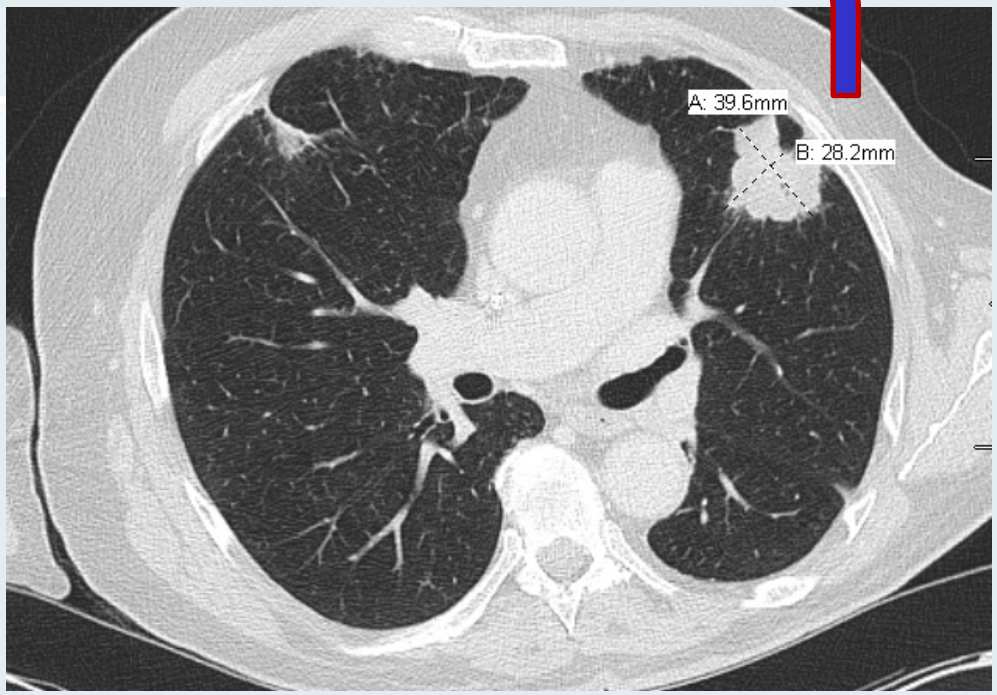
Case — Elizabeth R Plimack, MD, MS

High Impact Results

BIOMARKER	METHOD	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
FGFR3	NGS	Mutated, Pathogenic Exon 7 | p.S249C	BENEFIT	erdafitinib	Level 1
PD-L1 (22c3)	IHC	Negative, CPS: 0			
PD-L1 (SP142)	IHC	Negative, IC: 0%			



- Erdafitinib initiated at standard starting dose: 8 mg daily

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Case — Elizabeth R Plimack, MD, MS

Phase II erdafitinib: Oral pan-FGFR (1-4) inhibitor

- Notable AEs: Hyperphosphatemia, skin/nail changes, central retinopathy

	8 mg continuous dose (n = 99)	
Patients with AEs, n (%)	**Any grade**	**Grade ≥ 3**
Hyperphosphatemia	**72 (73)**	**2 (2)**
Skin events	**48 (49)**	**6 (6)**
Dry skin	32 (32)	0 (0)
Hand-foot syndrome	22 (22)	5 (5)
Nail events	**51 (52)**	**14 (14)**
Onycholysis	16 (16)	2 (2)
Paronychia	14 (14)	3 (3)
Nail Dystrophy	16 (16)	6 (6)
Central serous retinopathy (CSR)	**21 (21)**	**3 (3)**
Non-CSR ocular events[a]	**51 (52)**	**5 (5)**

[a]Most common non-CSR ocular events included dry eye (19%), blurry vision (16%), increased lacrimation (11%), and conjunctivitis (9%).

Siefker Radtke ASCO 2018
Loriot et al NEJM 2019

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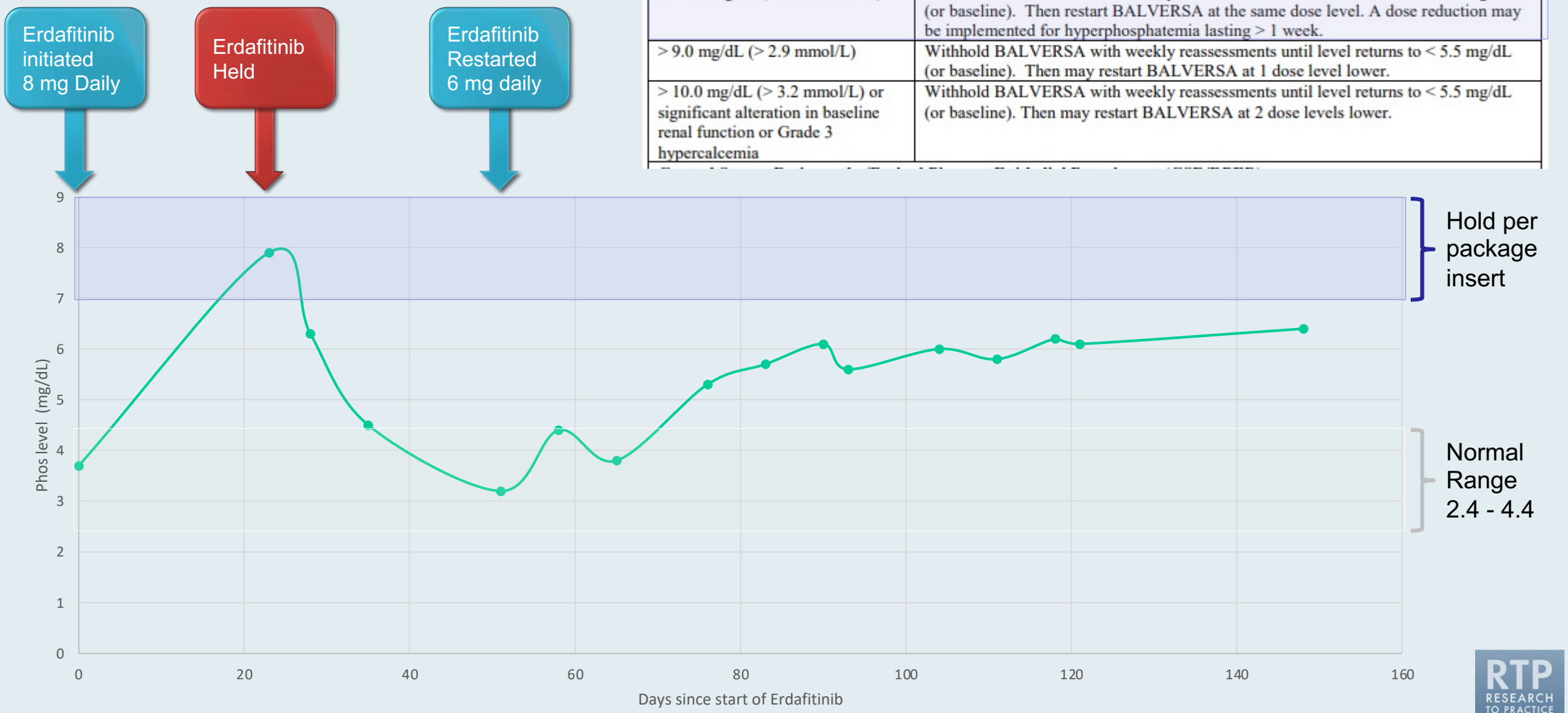
↑ Phosphorous

Hyperphosphatemia	
In all patients, restrict phosphate intake to 600-800 mg daily. If serum phosphate is above 7.0 mg/dL, consider adding an oral phosphate binder until serum phosphate level returns to < 5.5 mg/dL.	
5.6-6.9 mg/dL (1.8-2.3 mmol/L)	Continue BALVERSA at current dose.
7.0-9.0 mg/dL (2.3-2.9 mmol/L)	Withhold BALVERSA with weekly reassessments until level returns to < 5.5 mg/dL (or baseline). Then restart BALVERSA at the same dose level. A dose reduction may be implemented for hyperphosphatemia lasting > 1 week.
> 9.0 mg/dL (> 2.9 mmol/L)	Withhold BALVERSA with weekly reassessments until level returns to < 5.5 mg/dL (or baseline). Then may restart BALVERSA at 1 dose level lower.
> 10.0 mg/dL (> 3.2 mmol/L) or significant alteration in baseline renal function or Grade 3 hypercalcemia	Withhold BALVERSA with weekly reassessments until level returns to < 5.5 mg/dL (or baseline). Then may restart BALVERSA at 2 dose levels lower.



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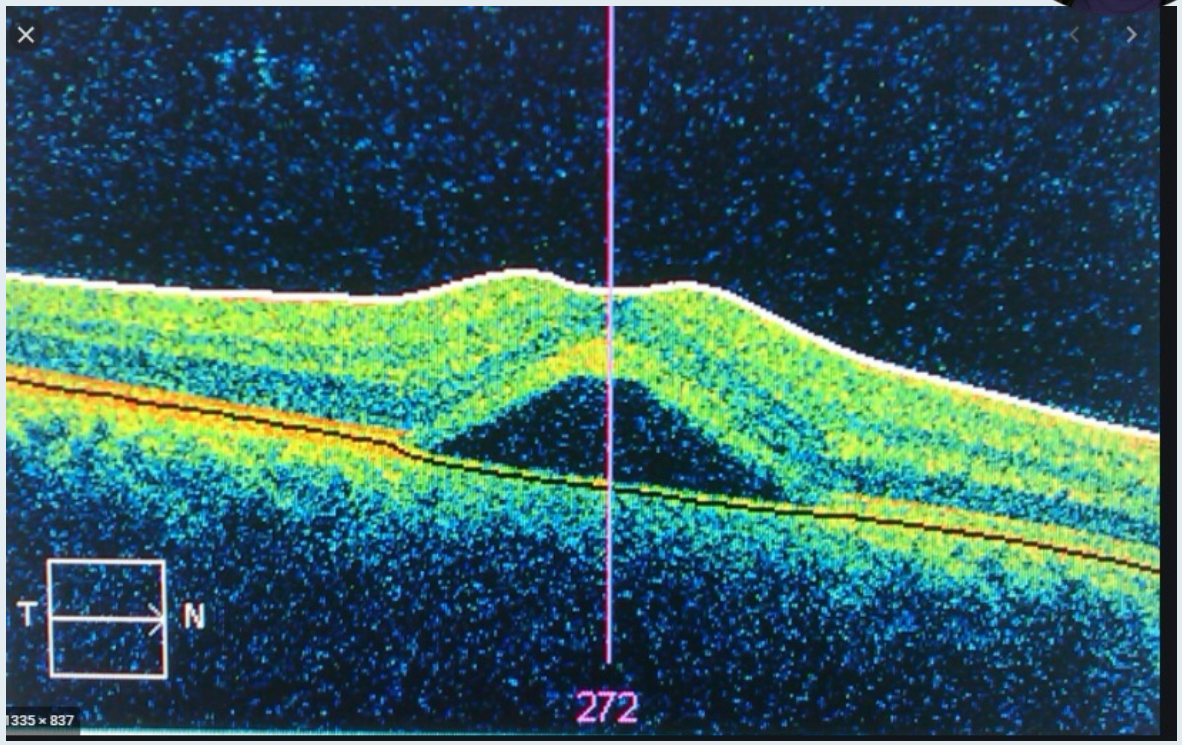
Case — Elizabeth R Plimack, MD, MS

Central serous retinopathy (CSR)

- **Routine monthly eye exams**
- **At month 2, retinal imaging showed CSR**
- **No changes in visual acuity**



Central Serous Retinopathy/Retinal Pigment Epithelial Detachment (CSR/RPED)	
Grade 1: Asymptomatic; clinical or diagnostic observations only	Withhold until resolution. If resolves within 4 weeks, resume at the next lower dose level. Then, if no recurrence for a month, consider re-escalation. If stable for 2 consecutive eye exams but not resolved, resume at the next lower dose level.
Grade 2: Visual acuity 20/40 or better or ≤ 3 lines of decreased vision from baseline	Withhold until resolution. If resolves within 4 weeks, may resume at the next lower dose level.
Grade 3: Visual acuity worse than 20/40 or > 3 lines of decreased vision from baseline	Withhold until resolution. If resolves within 4 weeks, may resume two dose levels lower. If recurs, consider permanent discontinuation.
Grade 4: Visual acuity 20/200 or worse in affected eye	Permanently discontinue.

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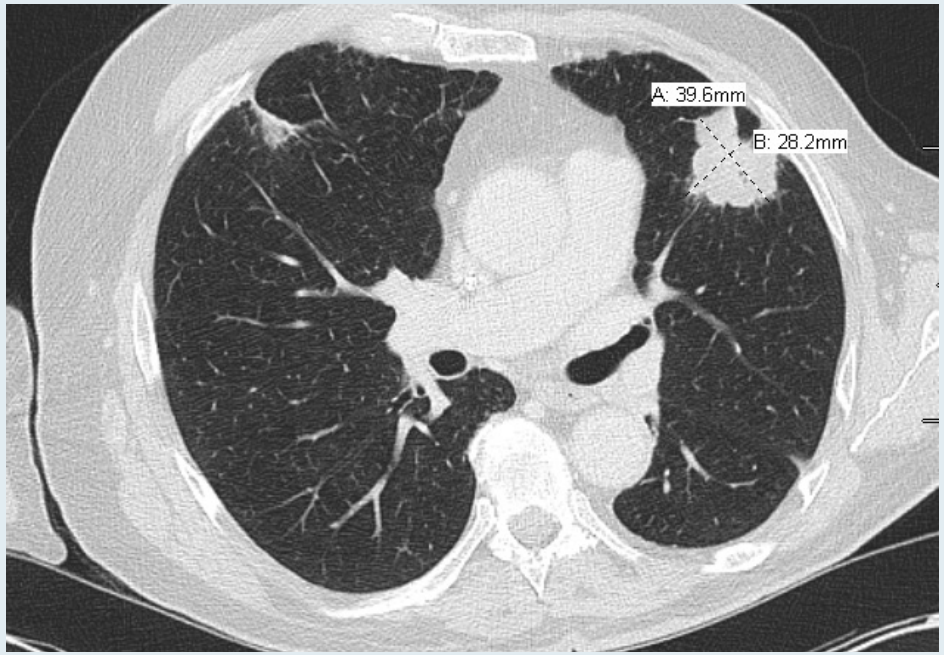
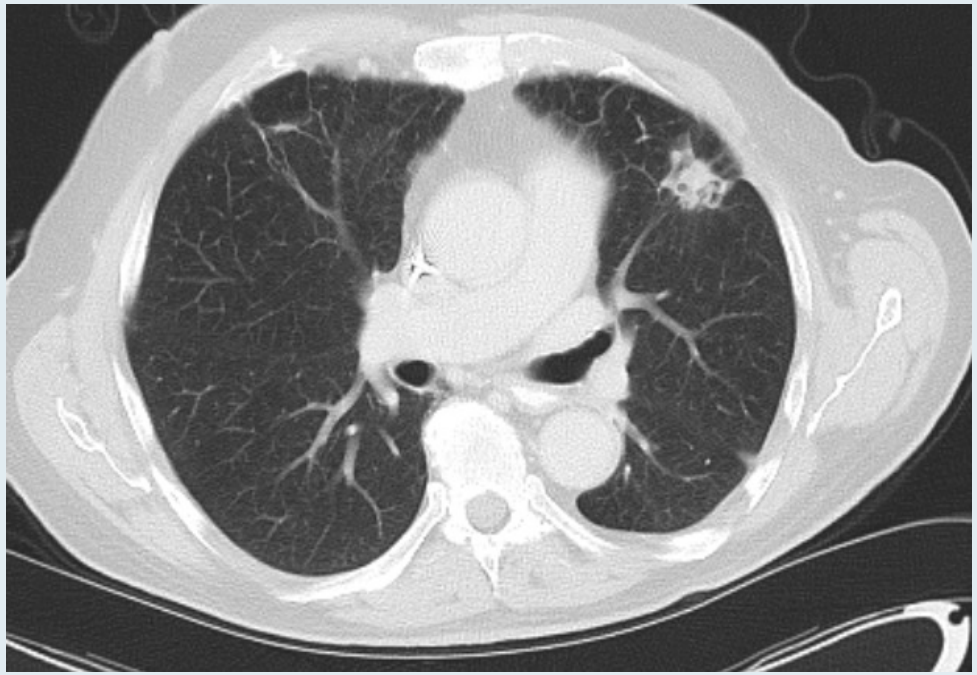
Case — Elizabeth R Plimack, MD, MS

Erdafitinib: Response at 6 mg daily





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Case — Jonathan E Rosenberg, MD

- 59-year-old man presented 10 years ago with NMIBC treated with BCG
- 8 years ago, had a high grade upper tract UC treated with cisplatin and gemcitabine followed by nephroureterectomy → pT0N0
- Subsequently developed bladder recurrence 1 year later with focus of high grade UC in background of low grade UC, cTa. Treated with BCG
- CT 1 year later with lung metastases, s/p wedge resection confirming metastatic UC
- Received atezolizumab with SD as best response, stopped after 1.5 years for progression, no autoimmune AEs
- Underwent RFA of selected growing lung metastases and was off systemic therapy for 1 year
- Subsequently was treated with enfortumab on EV-201 with partial response, continued therapy until progression at 1 year
- Went on clinical trial of PRMT5 inhibitor with prolonged stable disease, stopped for fatigue and hematologic toxicity

RTP
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TO PRACTICE

Case — Jonathan E Rosenberg, MD

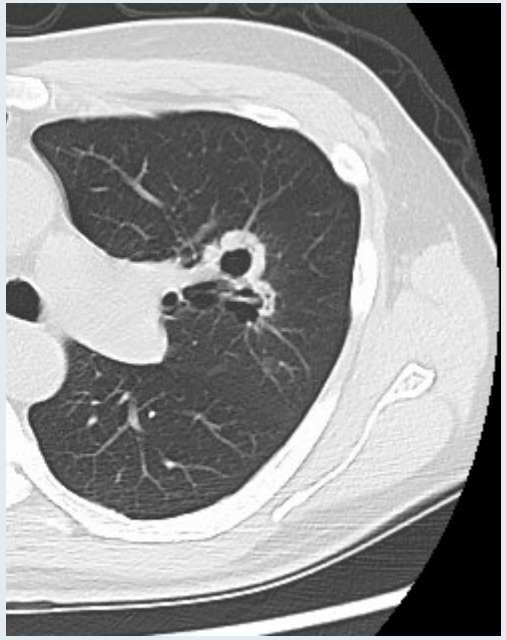
- **At progression, received gemcitabine/paclitaxel chemotherapy with partial response in lungs that lasted 1 year before having increasing size of lung tumors**
- **Molecular testing without any druggable alterations**
- **After sacituzumab govitecan was FDA approved, pt started on treatment**

RTP
RESEARCH
TO PRACTICE

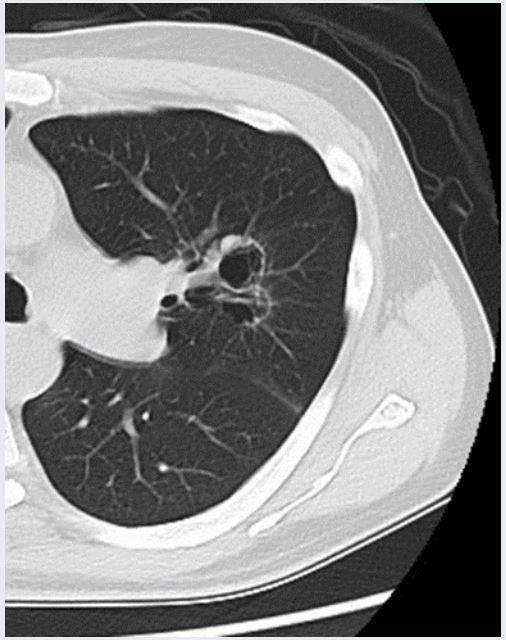
Case — Jonathan E Rosenberg, MD

- **In cycle 1, pt experienced neutropenic fever and was subsequently dose reduced to 7.5 mg/kg**
- **CT after cycle 3 showed decreased soft tissue component of cavitary metastasis, other pulmonary lesions stable**

Baseline



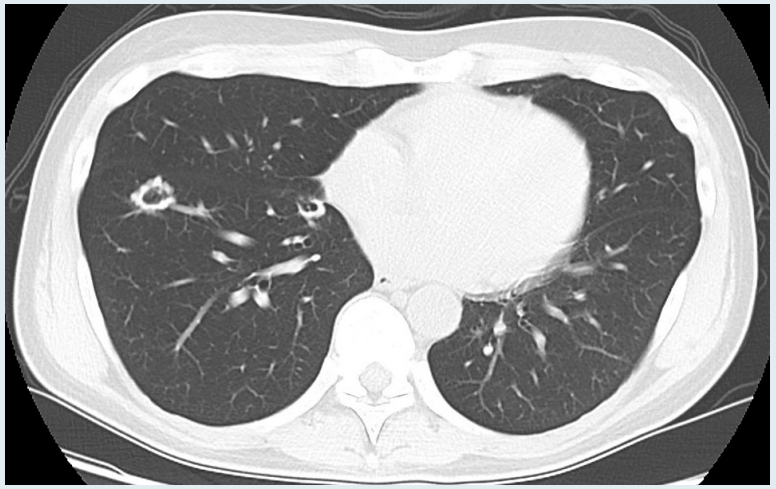
After cycle 3



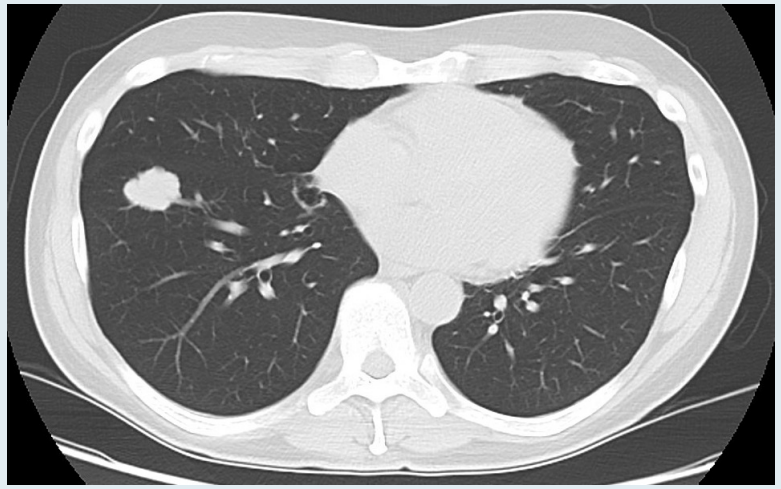
Case — Jonathan E Rosenberg, MD

- **Tolerated treatment well**
- **Restaging scan after cycle 6 showed unchanged response/stable disease**
- **After cycle 9, multiple pulmonary metastases increased in size and treatment was stopped**

Baseline



After cycle 9



RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

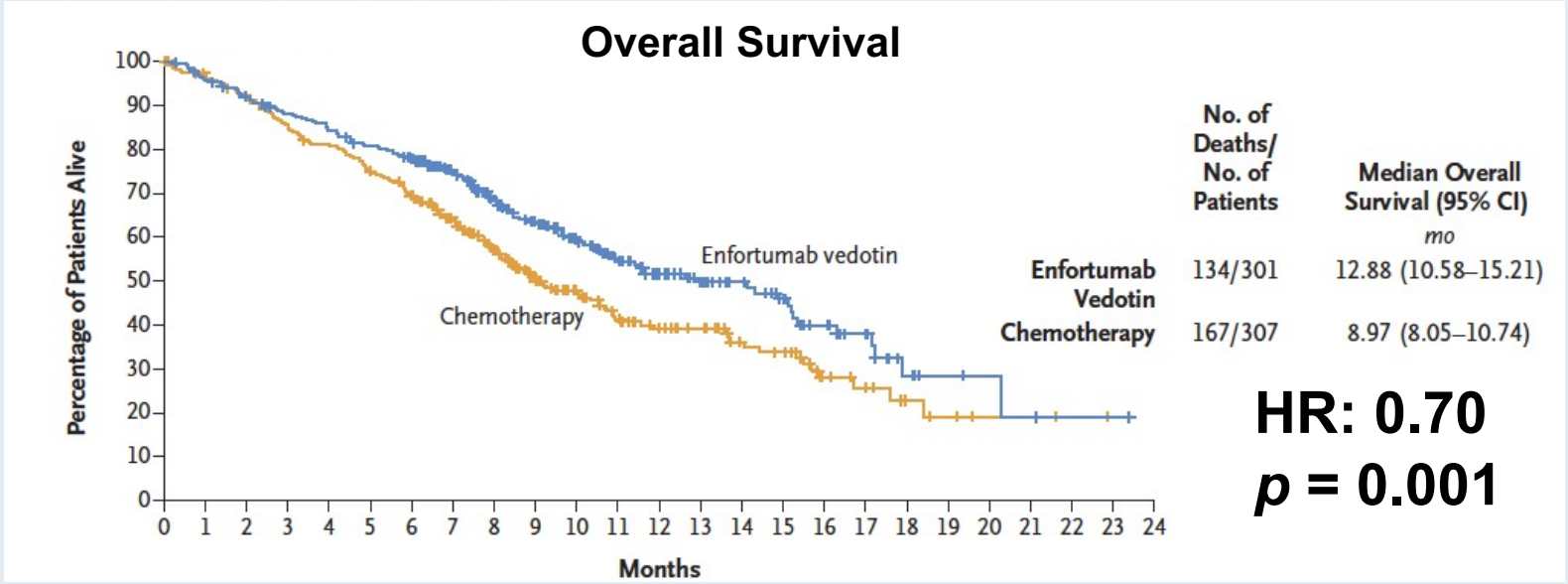
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

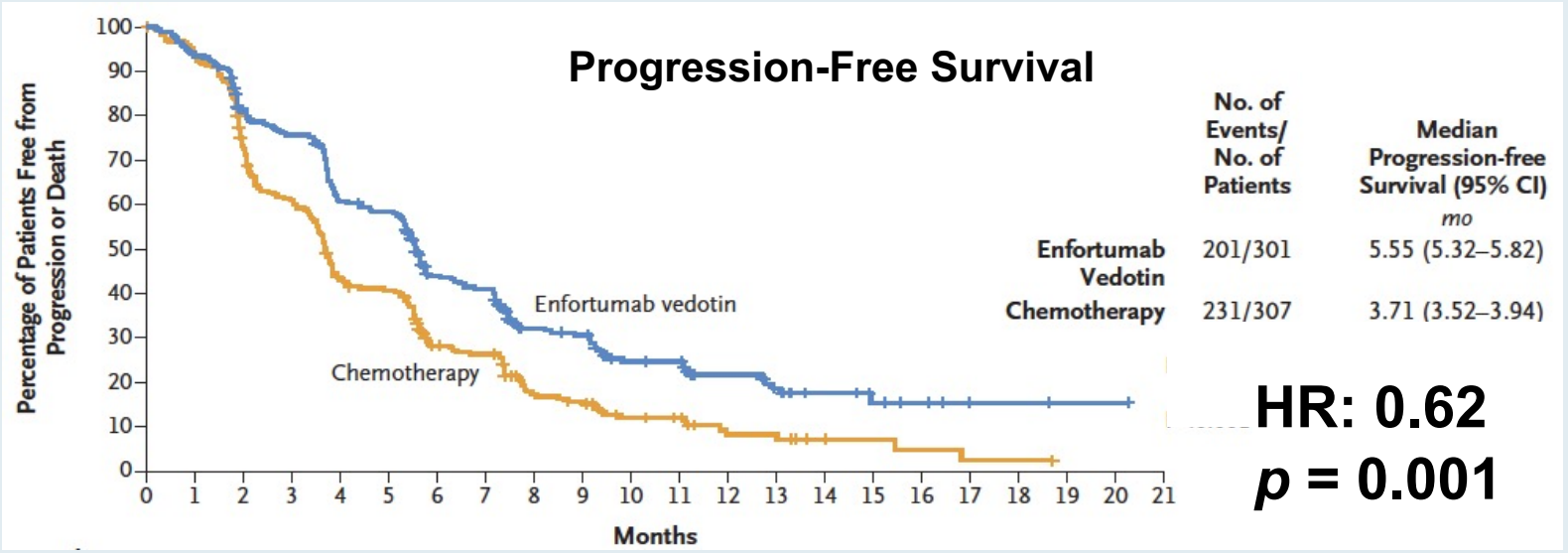
Thomas Powles, M.D., Jonathan E. Rosenberg, M.D., Guru P. Sonpavde, M.D., Yohann Loriot, M.D., Ph.D., Ignacio Durán, M.D., Ph.D., Jae-Lyun Lee, M.D., Ph.D., Nobuaki Matsubara, M.D., Christof Vulsteke, M.D., Ph.D., Daniel Castellano, M.D., Chunzhang Wu, Ph.D., Mary Campbell, M.D., Maria Matsangou, M.B.,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

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

RTP RESEARCH TO PRACTICE

EV-301: Survival and Response Analyses





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

ORR = overall response rate;
DCR = disease control rate

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.

RTP RESEARCH TO PRACTICE

EV-301: Antitumor Response

	EV (n = 288)	Chemotherapy (n = 296)	*p*-value
Overall response	40.6%	17.9%	<0.001
Complete response (CR)	49%	2.7%	
Partial response (PR)	35.8%	15.2%	
Stable disease (SD)	31.3%	35.5%	
Disease control rate*	71.9%	53.4%	<0.001
Duration of response at 12 months	27.7%	19.8%	
Time to response, median	1.87 mo	1.91 mo	

*Disease control rate: CR + PR + SD at least 7 weeks

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

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EV-301: Treatment-Related Adverse Events (TRAEs) of Special Interest

TRAE	Enfortumab vedotin (n = 296)		Chemotherapy (n = 291)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Skin reactions	47%	33%	16%	<1%
Peripheral neuropathy	46%	5%	31%	<1%
Ocular disorders	19%	<1%	5%	<1%
Infusion-related reactions	9%	1%	5%	0
Hyperglycemia	6%	4%	<1%	0
TRAE summary	**Any grade**		**Any grade**	
Leading to dose reduction	32%		28%	
Leading to dose interruption	51%		19%	
Leading to dose withdrawal	14%		11%	

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

RTP RESEARCH TO PRACTICE

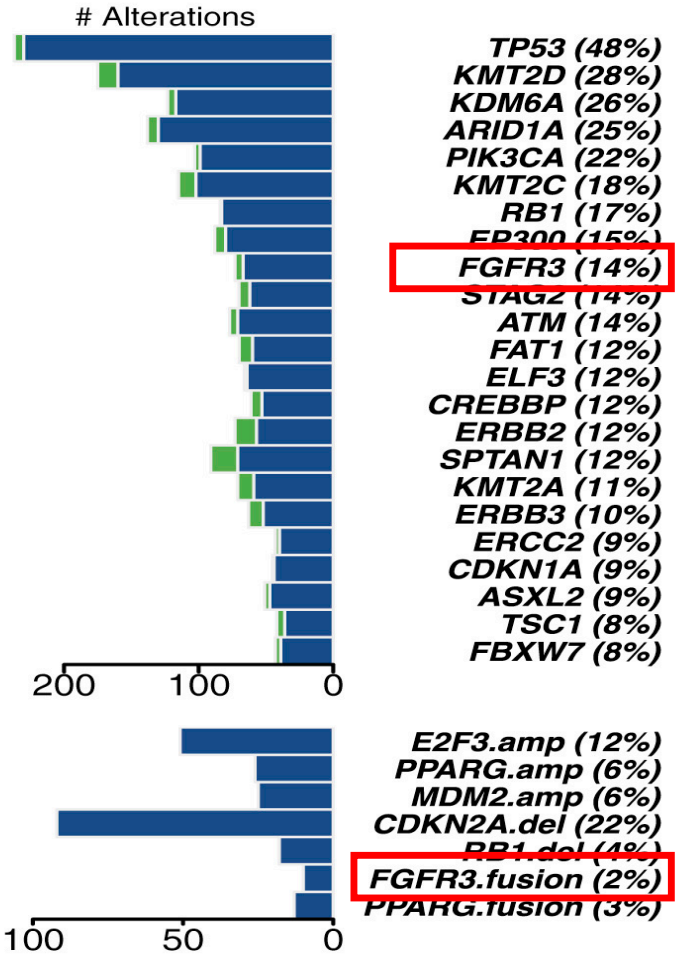
Lancet Oncol 2021;22:872-82.

Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV-201): a multicentre, single-arm, phase 2 trial

Evan Y Yu, Daniel P Petrylak*, Peter H O'Donnell, Jae-Lyun Lee, Michiel S van der Heijden, Yohann Loriot, Mark N Stein, Andrea Necchi, Takahiro Kojima, Michael R Harrison, Se Hoon Park, David I Quinn, Elisabeth I Heath, Jonathan E Rosenberg, Joyce Steinberg, Shang-Ying Liang, Janet Trowbridge, Mary Campbell, Bradley McGregor, Arjun V Balar*

FGFR3 Genomic Alterations in Muscle-Invasive Bladder Cancer

Genomics of MIBC: TCGA



- In muscle-invasive disease, FGFR3 mutations occur 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 are enriched in young, Asian, nonsmokers, upper tract tumors (invasive, high grade).
- Preclinical evidence exists for activity of FGFR inhibitors in selected cells with FGFR alterations.

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.

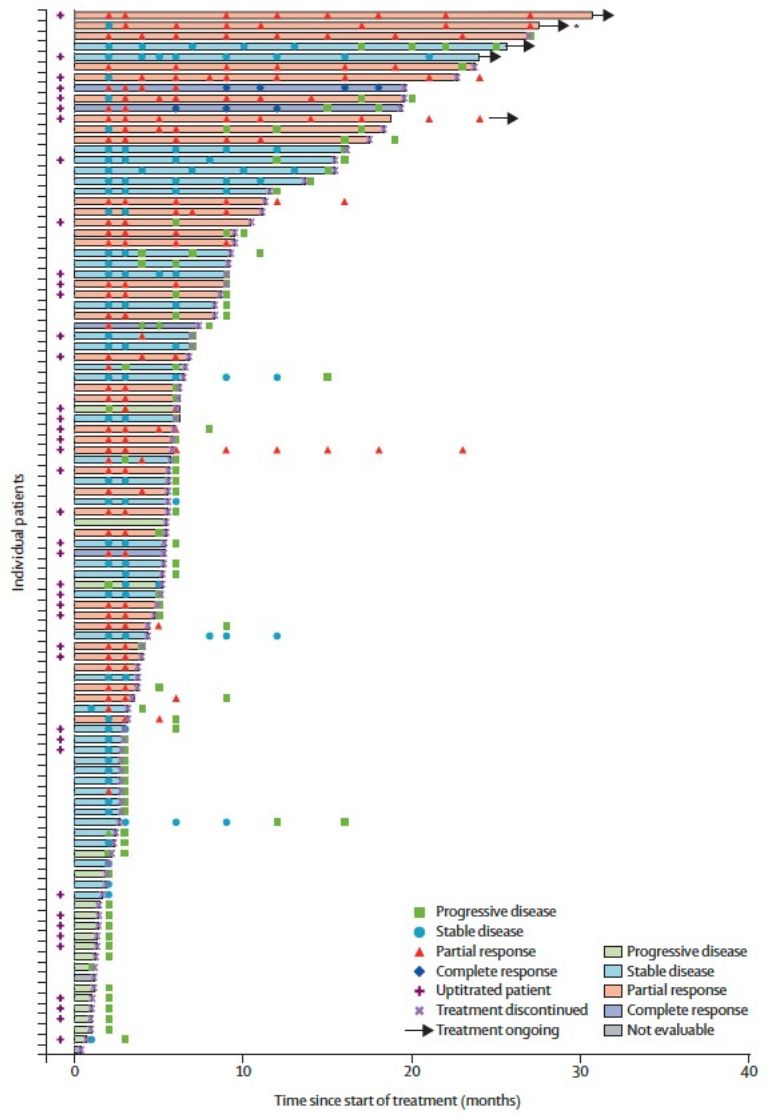
RTP RESEARCH TO PRACTICE

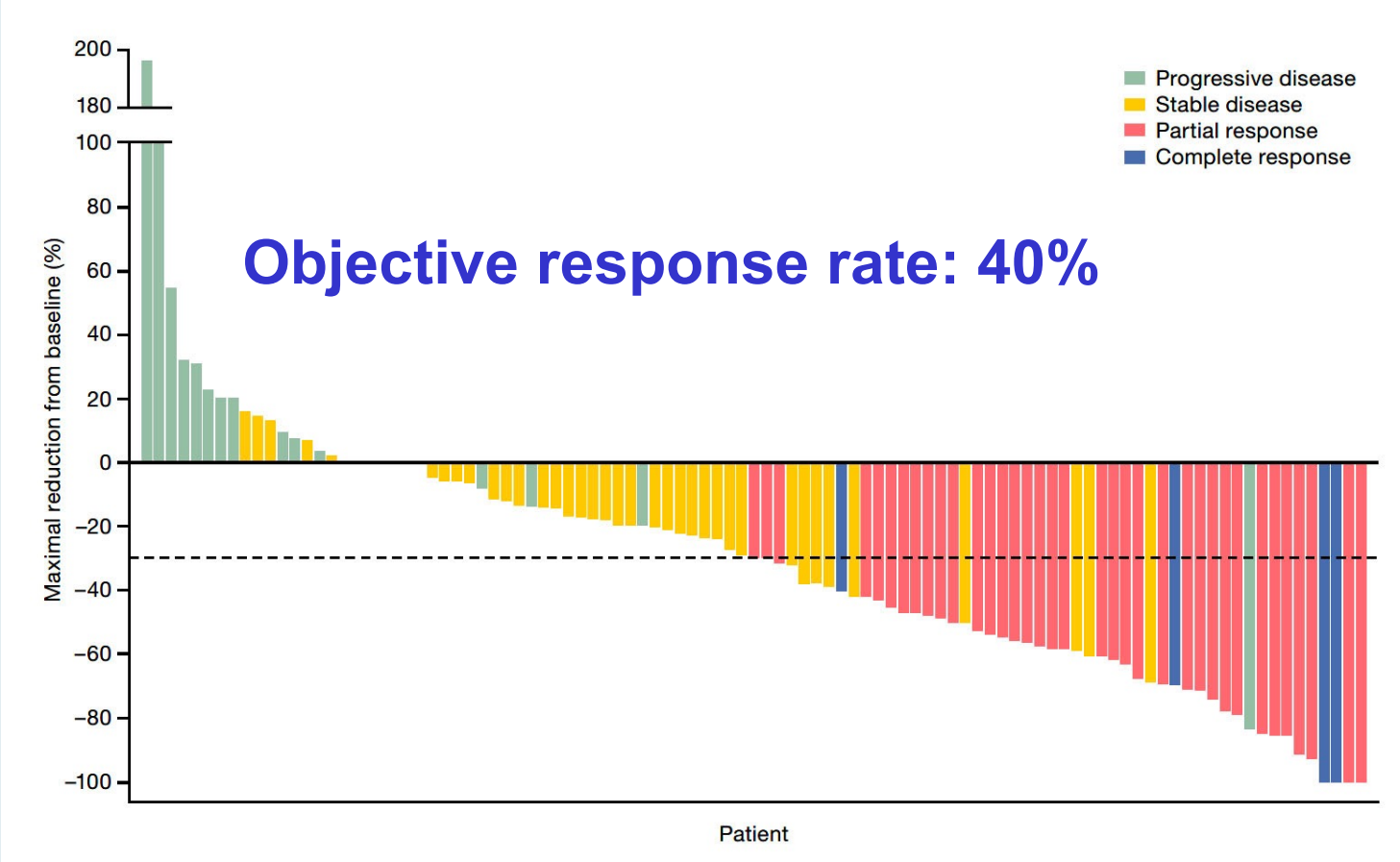
Lancet Oncol 2022;23:248-58.

Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study

*Arlene O Siefker-Radtke, Andrea Necchi, Se Hoon Park, Jesús García-Donas, Robert A Huddart, Earle F Burgess, Mark T Fleming, Arash Rezazadeh Kalebasty, Begoña Mellado, Sergei Varlamov, Monika Joshi, Ignacio Duran, Scott T Tagawa, Yousef Zakharia, Sydney Akapame, Ademi E Santiago-Walker, Manish Monga, Anne O'Hagan, Yohann Loriot, on behalf of the BLC2001 Study Group**

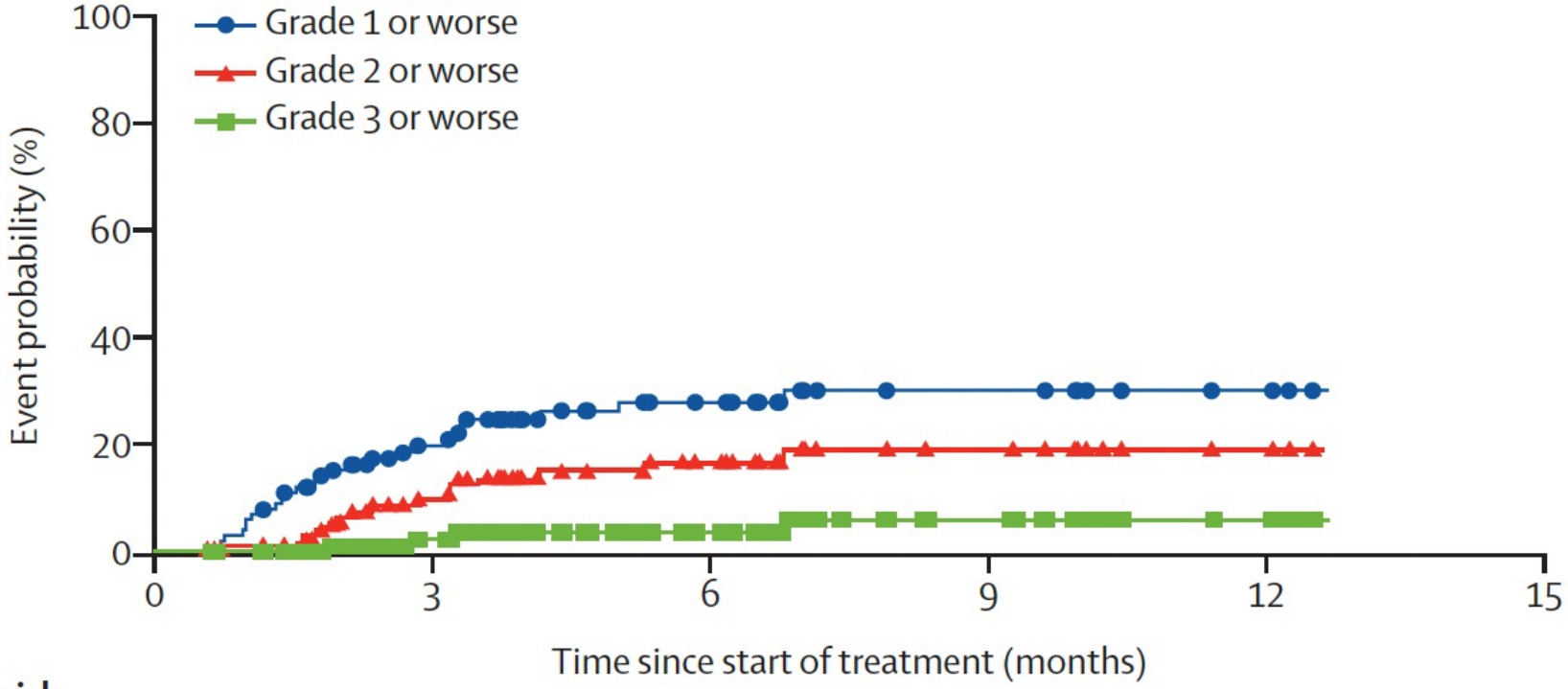
BLC2001: Responses in Patients Who Received the Selected 8 mg/Day Erdafitinib UpT Regimen





Siefker-Radtke AO et al. *Lancet Oncol* 2022;23:248-58.

BLC2001: Post-Hoc Analysis of the Cumulative Incidence of First-Onset Central Serous Retinopathy Events by Grade



Number at risk (number censored)						
Grade 1 or worse	101 (0)	67 (15)	41 (35)	26 (49)	19 (56)	..
Grade 2 or worse	101 (0)	74 (18)	47 (49)	29 (57)	19 (67)	..
Grade 3 or worse	101 (0)	80 (19)	53 (45)	30 (67)	20 (77)	..

Siefker-Radtke AO et al. *Lancet Oncol* 2022;23:248-58.

RTP RESEARCH TO PRACTICE

BLC2001: Select Treatment-Emergent Adverse Events

	Grade 1–2	Grade 3	Grade 4	Grade 5*
All treatment-emergent adverse events	29 (29%)	58 (57%)	6 (6%)	8 (8%)
Hyperphosphataemia†	77 (76%)	2 (2%)	0	0
Stomatitis	46 (21%)	14 (14%)	0	0
Diarrhoea	51 (50%)	4 (4%)	0	0
Dry mouth	45 (45%)	1 (1%)	0	0
Decreased appetite	40 (40%)	1 (1%)	0	0
Dysgeusia	39 (39%)	2 (2%)	0	0
Alopecia	34 (34%)	0	0	0
Dry skin	34 (34%)	0	0	0
Fatigue	31 (31%)	2 (2%)	0	0
Constipation	28 (28%)	1 (1%)	0	0
Dry eye	27 (27%)	1 (1%)	0	0
Palmar-plantar erythrodysaesthesia syndrome	20 (20%)	5 (5%)	0	0

Siefker-Radtke AO et al. *Lancet Oncol* 2022;23:248-58.

RTP RESEARCH TO PRACTICE

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

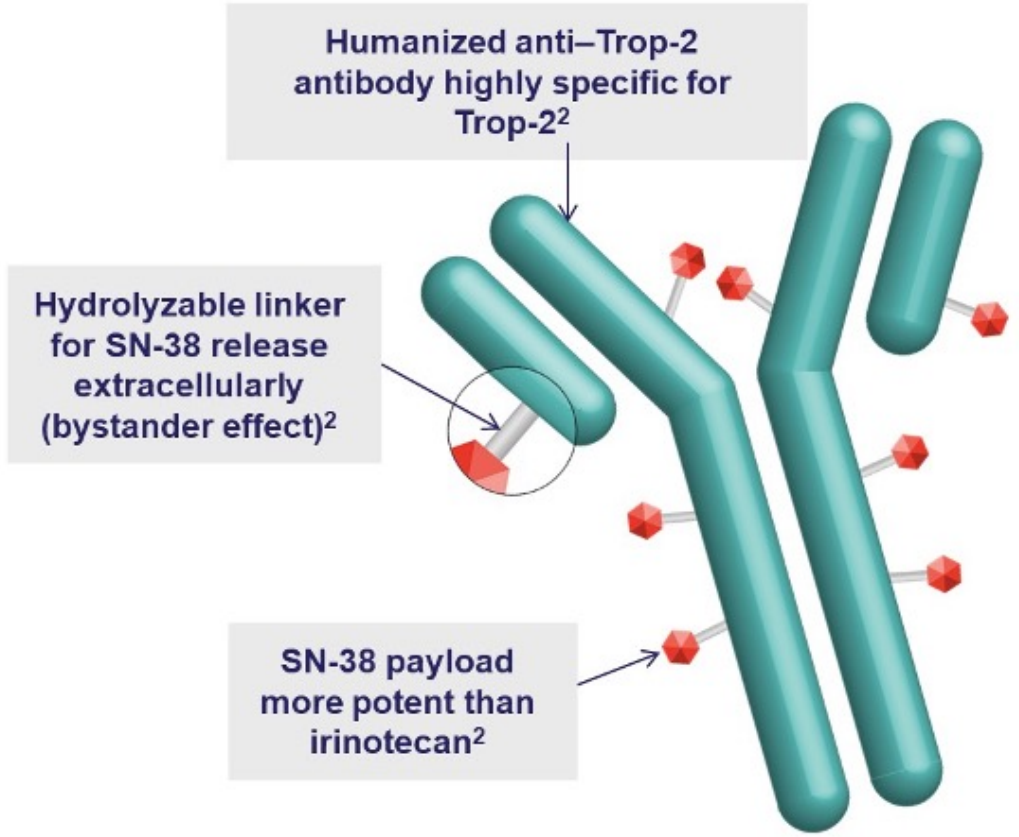
Scott T. Tagawa, MD, MS[1]; Arjun V. Balar, MD[2]; Daniel P. Petrylak, MD[3]; Arash Rezazadeh Kalebasty, MD[4]; Yohann Loriot, MD, PhD[5]; Aude Fléchon, MD, PhD[6]; Rohit K. Jain, MD[7]; Neeraj Agarwal, MD[8]; Manojkumar Bupathi, MD, MS[9]; Philippe Barthelemy, MD, PhD[10]; Philippe Beuzeboc, MD, PhD[11];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

RTP RESEARCH TO PRACTICE

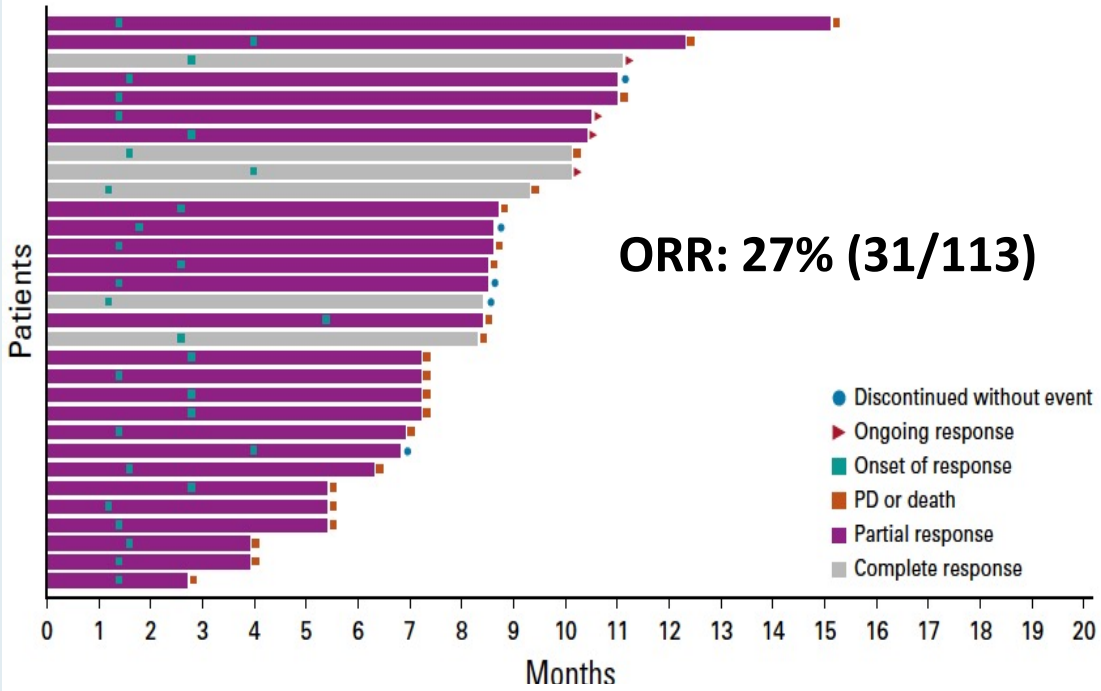
Sacituzumab Govitecan: A First-in-Class TROP2-Directed Antibody-Drug Conjugate

- Trop-2 is an epithelial cell surface antigen highly expressed in many solid tumors including invasive bladder cancer[1]
- SG is distinct from other ADCs[2-6]
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and enzymatic cleavage by tumor cell not required for SN-38 (active metabolite of irinotecan) liberation from antibody
- SG is FDA approved for the following:
  - Treatment of patients with mTNBC who received ≥2 prior chemotherapies (≥1 in metastatic setting)[7]
  - Treatment of patients with locally advanced or mUC who have previously received platinum-containing chemotherapy & PD-1/L1 inhibitor[a,7]



Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

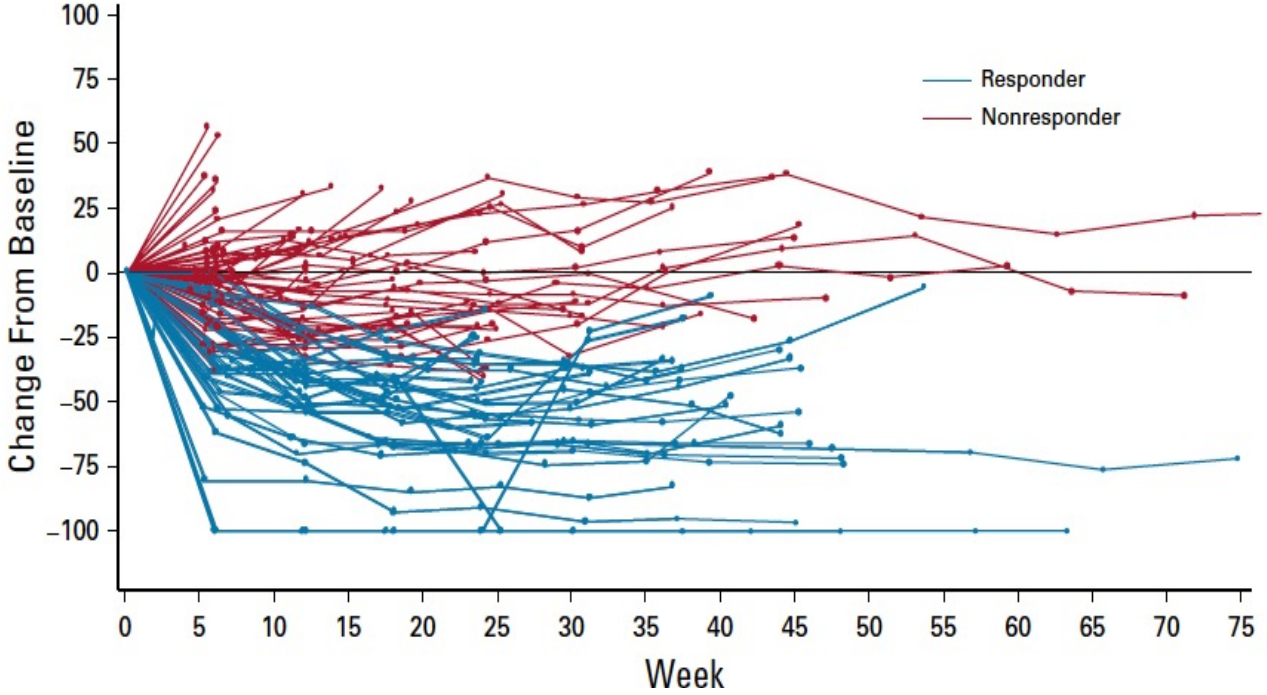
TROPHY U-01 (Cohort 1): Objective Response Rate, Duration of Response and Survival



ORR: 27% (31/113)

Median DOR: 7.2 mo

Median time to onset of response: 1.6 mo



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

ASCO Genitourinary Cancers Symposium

2022 Abstract 434

TROPHY-U-01 Cohort 3: Sacituzumab Govitecan (SG) in Combination With Pembrolizumab (Pembro) in Patients (pts) With Metastatic Urothelial Cancer (mUC) Who Progressed After Platinum (PLT)-Based Regimens

Petros Grivas,[1] Damien Pouessel,[2] Chandler H. Park,[3] Philippe Barthelemy,[4] Manojkumar Bupathi,[5] Daniel P. Petrylak,[6] Neeraj Agarwal,[7] Aude Fléchon,[8] Chethan Ramamurthy,[9] Nancy B. Davis,[10] Alejandro Recio-Boiles,[11] Scott T. Tagawa,[12] Cora N. Sternberg,[12] Astha Bhatia,[13] Cabilia Pichardo,[13] Trishna Goswami,[13] and Yohann Loriot[14]

[1]University of Washington, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [2]Department of Medical Oncology & Clinical Research Unit, Institut Claudius Regaud/Institut Universitaire du Cancer de Toulouse (IUCT-Oncopôle), Toulouse, France; [3]Norton Cancer Institute, Louisville, KY, USA; [4]Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [5]Rocky Mountain Cancer Centers, Littleton, CO, USA; [6]Yale School of Medicine, New Haven, CT, USA; [7]Huntsman Cancer Institute, Salt Lake City, UT, USA; [8]Centre Léon Bérard, Lyon, France; [9]University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; [10]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [11]University of Arizona Cancer Center, Tucson, AZ, USA; [12]Weill Cornell Medical College of Cornell University, New York, NY, USA; [13]Gilead Sciences, Inc, Morris Plains, NJ, USA; and [14]Institut de Cancérologie Gustave Roussy, Université Paris-Saclay, Villejuif, France

Abstract # 434
ClinicalTrials.gov Number: NCT03547973.

@PGrivasMDPhD

TROPHY U-01

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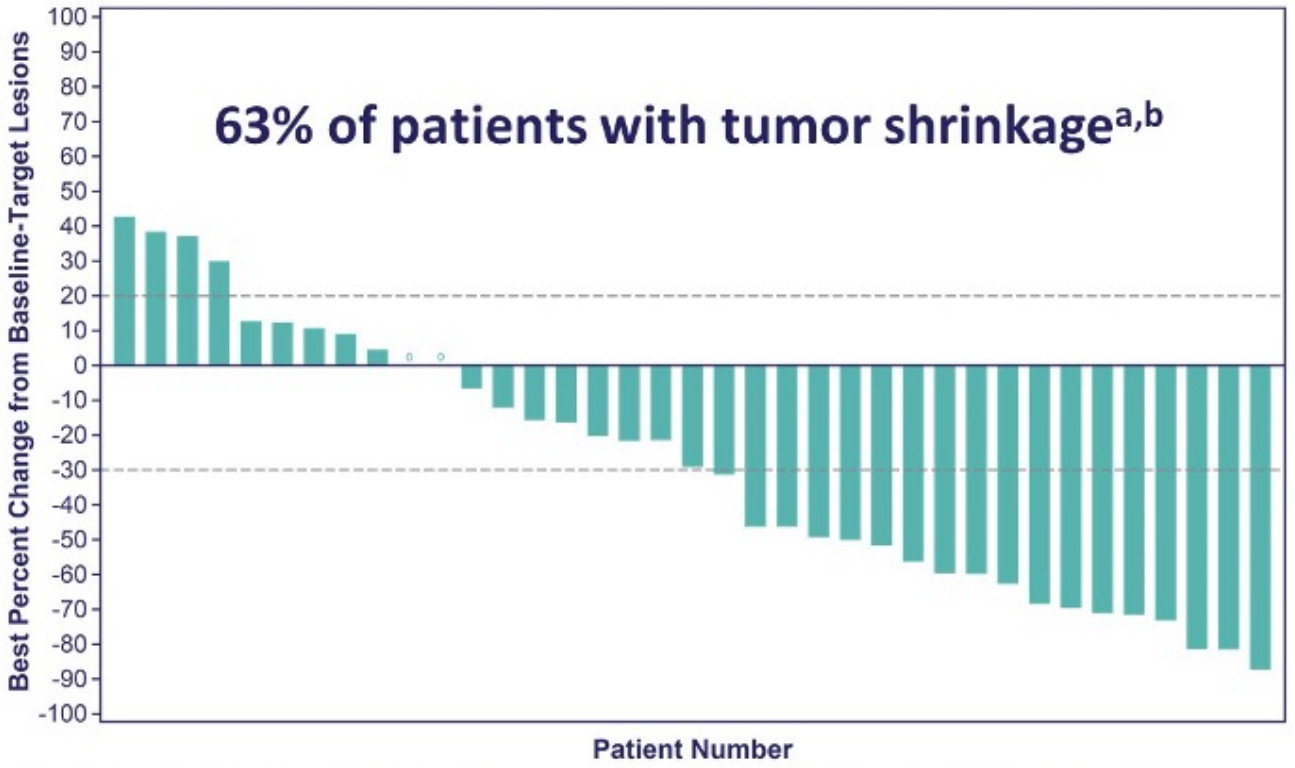
TROPHY U-01: Overall Response and Best Change from Baseline in Tumor Size

- Median follow-up: 5.8 months (data cutoff date: 2021-09-24)
- Median time to response: 2 months (1.3–2.8; n=14)
- Median DOR not yet reached: N/A (2.80-N/A)
- Median PFS (95% CI), 5.5 months (1.7–NR); median OS, not reached



	Cohort 3[a] (N=41)
Objective response rate (CR + PR), n (%) [95%CI]	14 (34) [20.1-50.6]
Objective response rate (CR + PR), evaluable patients, n (%)	14 (38)
Best overall response, n (%)	
CR	1 (2)
PR	13 (32)
SD	11 (27)
SD ≥ 6 months	*4 (10)*
PD	12 (29)
Not assessed	4 (10)
Clinical Benefit Rate (CR + PR + SD), n (%) [95%CI]	25 (61) [44.5-75.8]

Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: TARGETED THERAPY

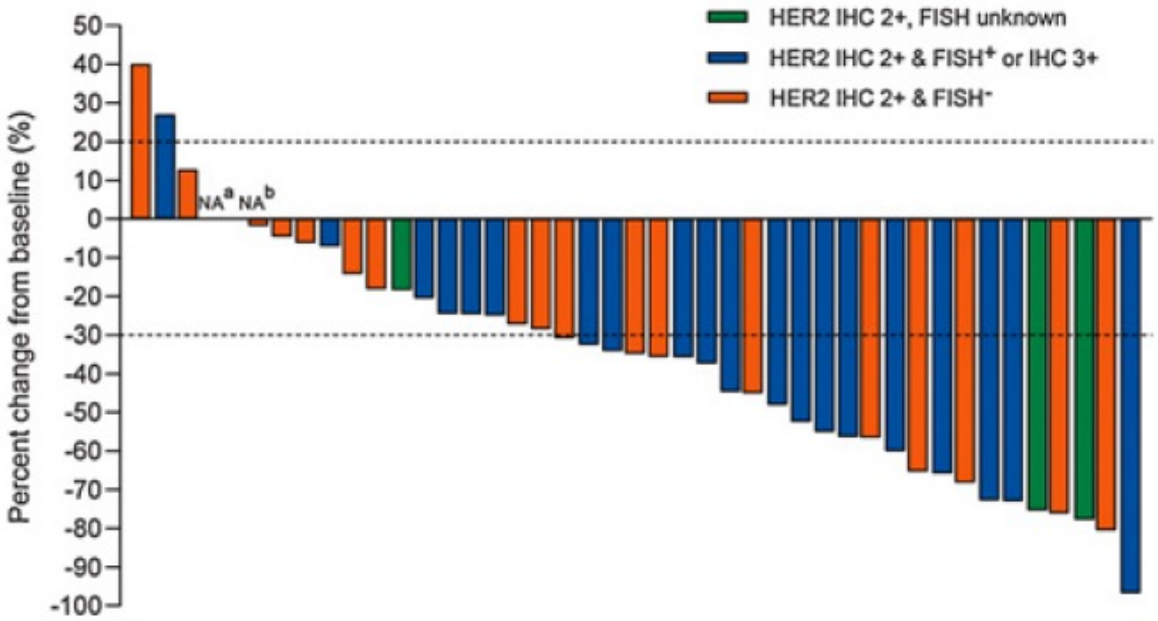
Open-label, Multicenter, Phase II Study of RC48-ADC, a HER2-Targeting Antibody–Drug Conjugate, in Patients with Locally Advanced or Metastatic Urothelial Carcinoma AC

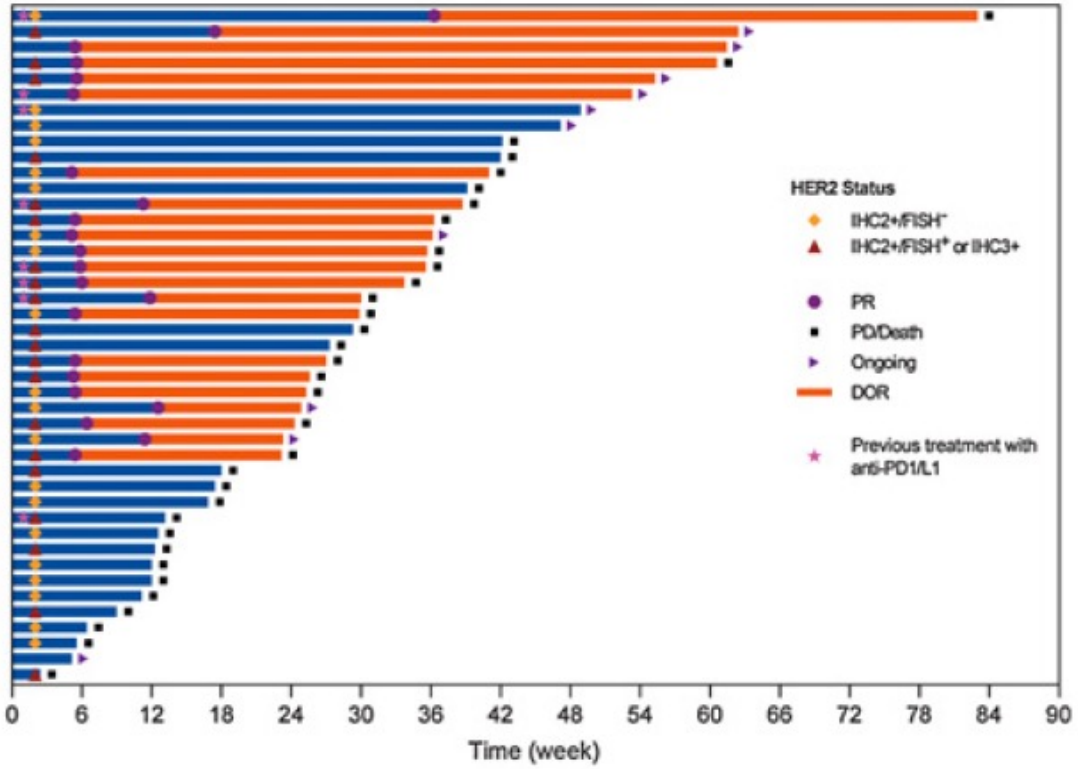
Xinan Sheng[1], Xieqiao Yan[1], Lin Wang[2], Yanxia Shi[3], Xin Yao[4], Hong Luo[5], Benkang Shi[6], Jiyan Liu[7], Zhisong He[8], Guohua Yu[9], Jianming Ying[10], Weiqing Han[11], Changlu Hu[12], Yun Ling[10], Zhihong Chi[1], Chuanliang Cui[1], Lu Si[1], Jianmin Fang[13,14], Aiping Zhou[2], and Jun Guo[1]

Clin Cancer Res 2021;27:43-51.

RTP RESEARCH TO PRACTICE

Phase II Study of Disitamab Vedotin (RC48) for HER2-Positive Locally Advanced or Metastatic Urothelial Carcinoma





Sheng X et al. *Clin Cancer Res* 2021;27:43-51.

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Appendix of Key Data Sets

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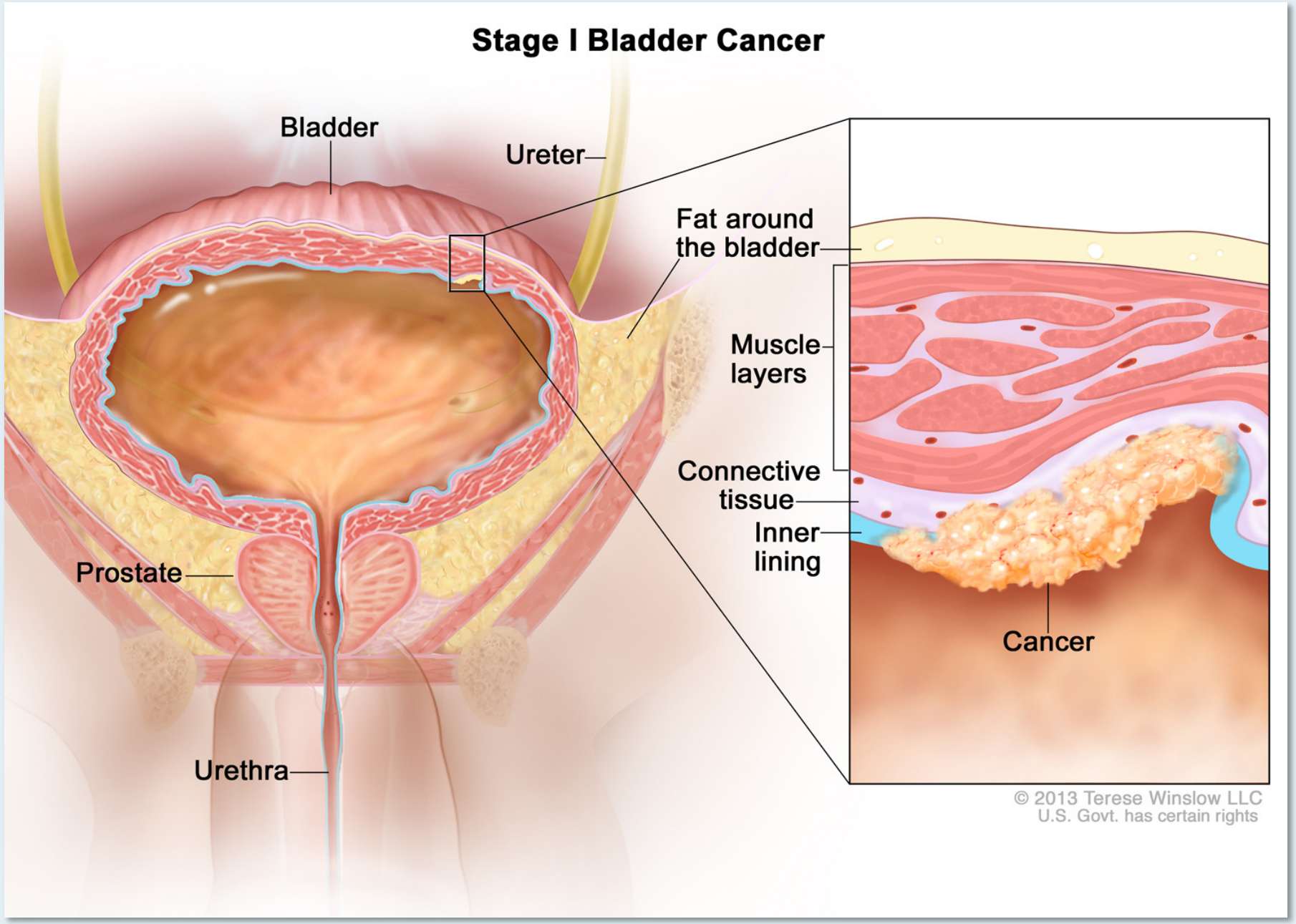
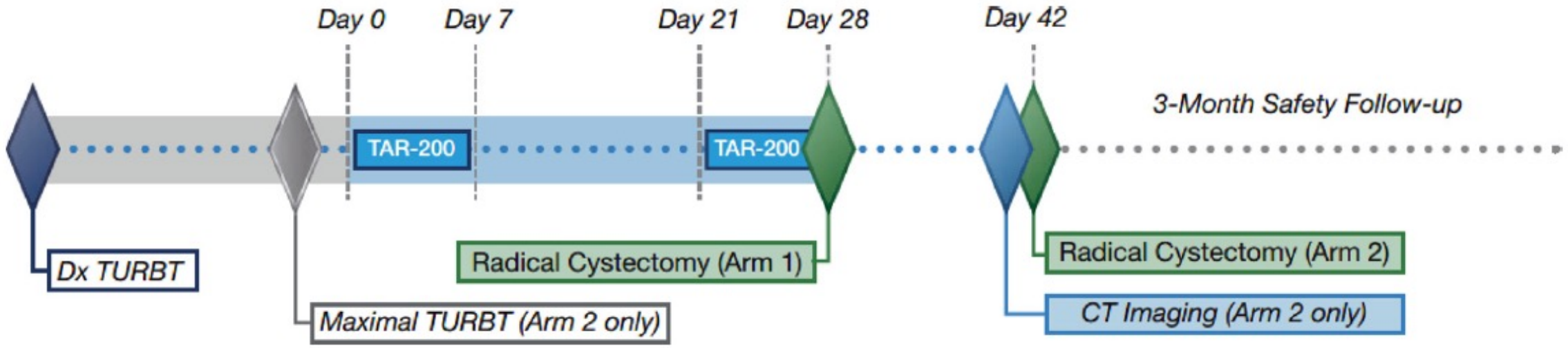


With permission from Terese Winslow LLC

TAR-200-101: Study Design and Outcomes



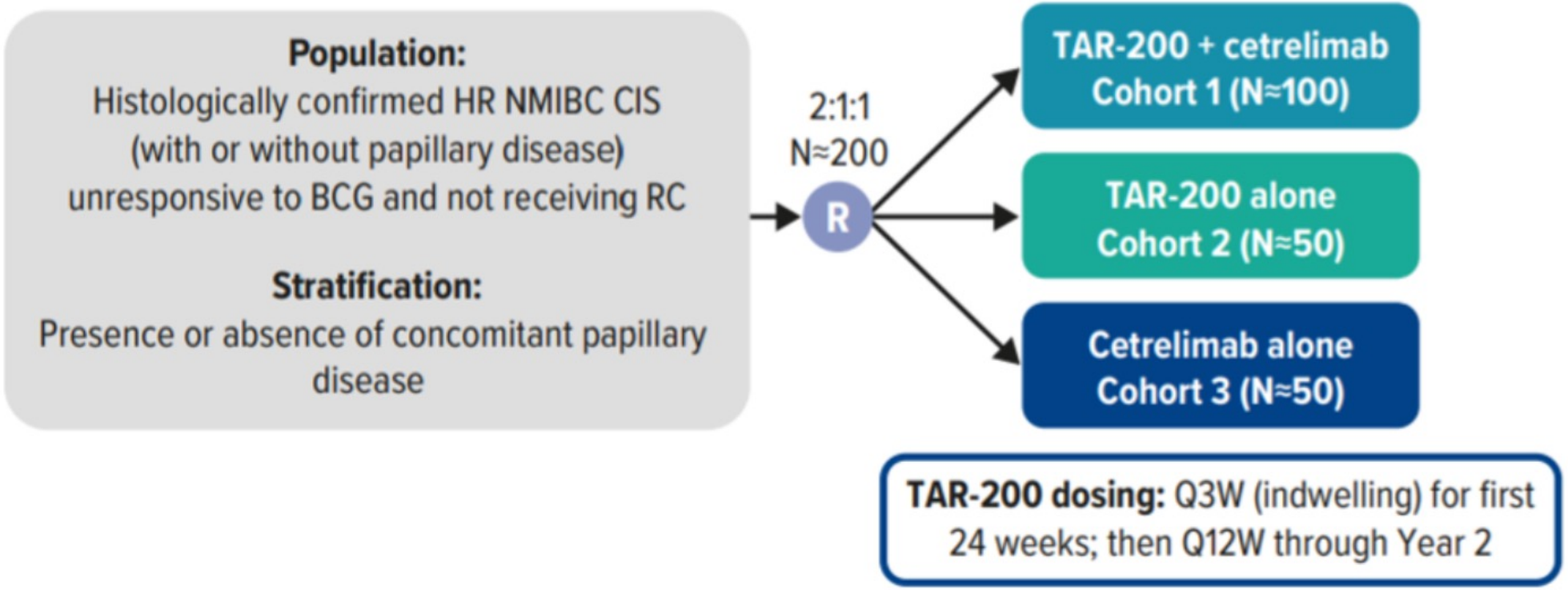
Response	Arm 1 (>3 cm)	Arm 2 (max TURBT)
Underwent pathology at RC, *n/N* (%)	10/11 (90.9)	10/12 (83.3)
Pathologic response, *n/N* (%)	4/10 (40.0)	6/10 (60.0)
Complete response, *n/N* (%)	1/10 (10.0)	3/10 (30.0)
Partial response, *n/N* (%)	3/10 (30.0)	3/10 (30.0)

Treatment-emergent adverse event, *n* (%)	TAR-200 related[a]	Procedure related[b]
Pollakiuria	3 (13)	2 (9)
Urinary incontinence	2 (9)	2 (9)
Micturation urgency	2 (9)	0
Urinary tract infection	1 (4)	2 (9)
Gross hematuria	0	1 (4)
Hematoma[c]	0	0

Daneshmand S et al. *Urol Oncol* 2022;[Online ahead of print].

SunRISe-1: Ongoing Phase IIb Trial of TAR-200, Cetrelimab, or the Combination for BCG-Unresponsive, High-Risk NMIBC

Clinical trial identifier: NCT04640623



Primary endpoint: Overall clinical response rate

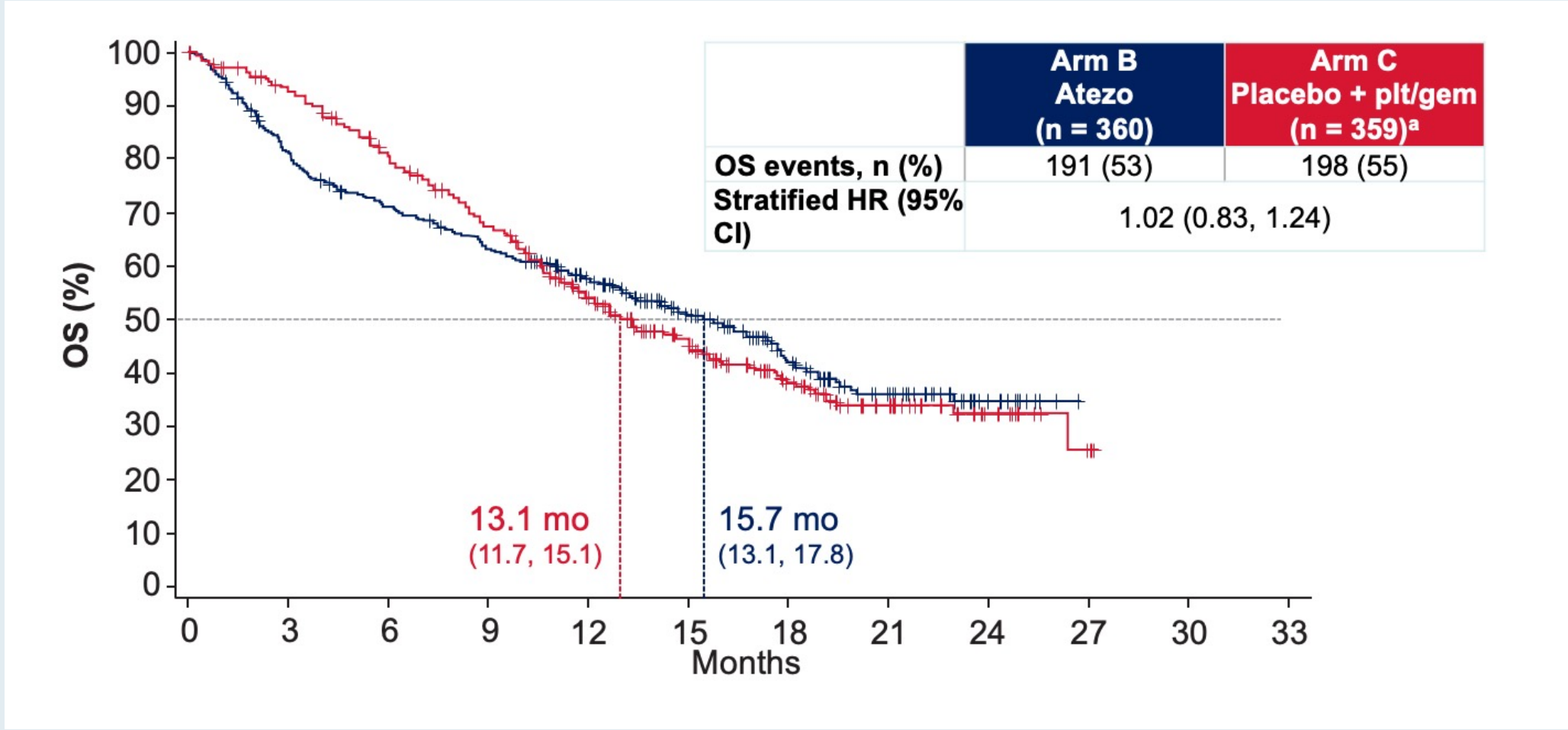
Van der Heijden SB et al. ESMO 2021;Abstract 719TiP.

Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomised, placebo-controlled phase 3 trial

Matthew D Galsky, José Ángel Arranz Arija, Aristotelis Bamias, Ian D Davis, Maria De Santis, Eiji Kikuchi, Xavier Garcia-del-Muro, Ugo De Giorgi, Marina Mencinger, Kouji Izumi, Stefano Panni, Mahmut Gumus, Mustafa Özgüroğlu, Arash Rezazadeh Kalebasty, Se Hoon Park, Boris Alekseev, Fabio A Schutz, Jian-Ri Li, Dingwei Ye, Nicholas J Vogelzang, Sandrine Bernhard, Darren Tayama, Sanjeev Mariathasan, Almut Mecke, AnnChristine Thåström, Enrique Grande, for the IMvigor130 Study Group†*

***Lancet* 2020;395:1547-57.**

IMvigor130: Overall Survival (OS) with Monotherapy (Arm B vs Arm C)

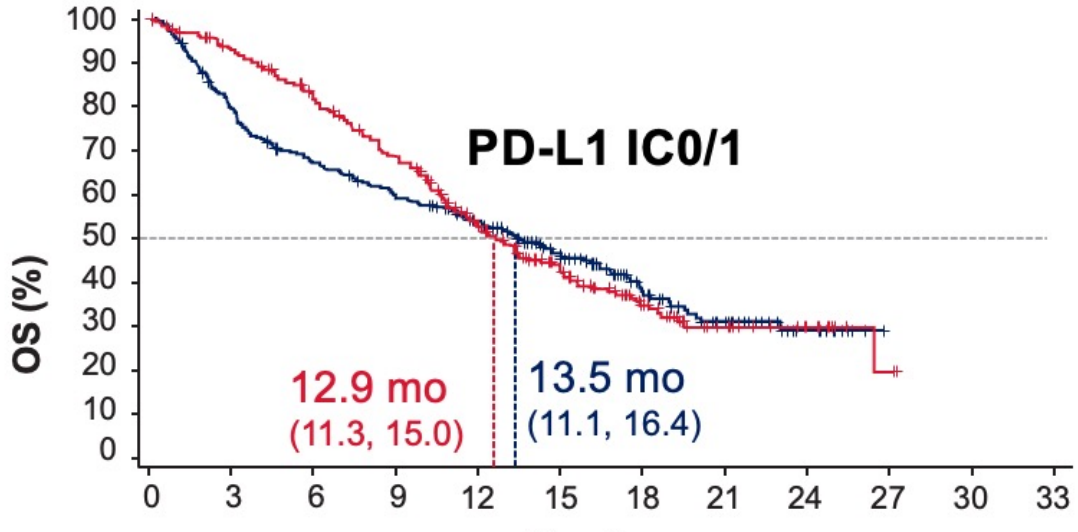


	Arm B Atezo (n = 360)	Arm C Placebo + plt/gem (n = 359)[a]
OS events, n (%)	191 (53)	198 (55)
Stratified HR (95% CI)	1.02 (0.83, 1.24)	

Galsky MD et al. *Lancet* 2020;395(10236):1547-57.

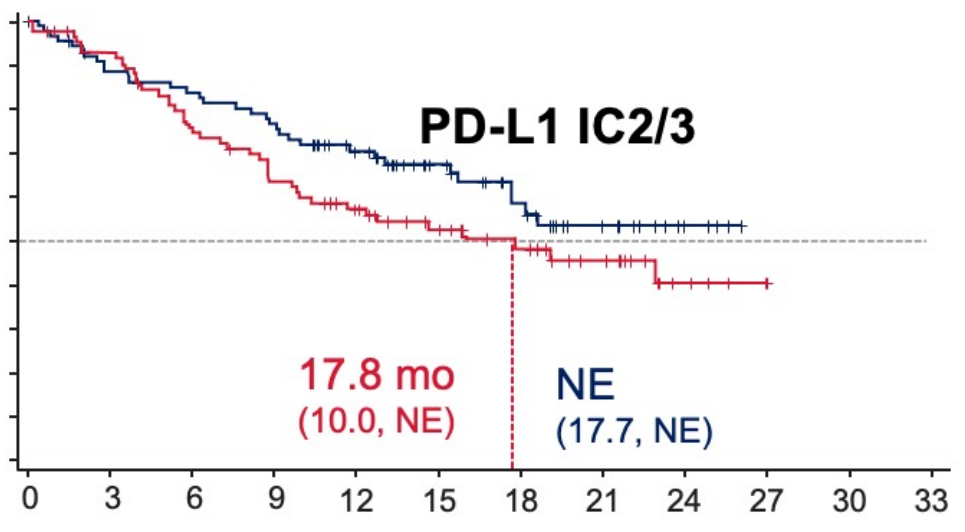
RTP RESEARCH TO PRACTICE

IMvigor130: OS by PD-L1 Status



No. at Risk												
Atezo	272	210	175	152	124	85	48	28	11	NE	NE	NE
Placebo + plt/gem	274	246	212	173	116	73	41	21	10	2	NE	NE

	Arm B Atezo (n = 272)	Arm C Placebo + plt/gem (n = 274)
OS events, n (%)	158 (58)	156 (57)
Unstratified HR (95% CI)	1.07 (0.86, 1.33)	



	88	75	70	64	49	35	24	14	5	NE	NE	NE
	85	76	62	51	42	30	21	14	5	1	NE	NE

	Arm B Atezo (n = 88)	Arm C Placebo + plt/gem (n = 85)
OS events, n (%)	33 (38)	42 (49)
Stratified HR (95% CI)	0.68 (0.43, 1.08)	

Galsky MD et al. *Lancet* 2020;395(10236):1547-57.

RTP RESEARCH TO PRACTICE

Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomised, open-label, phase 3 trial

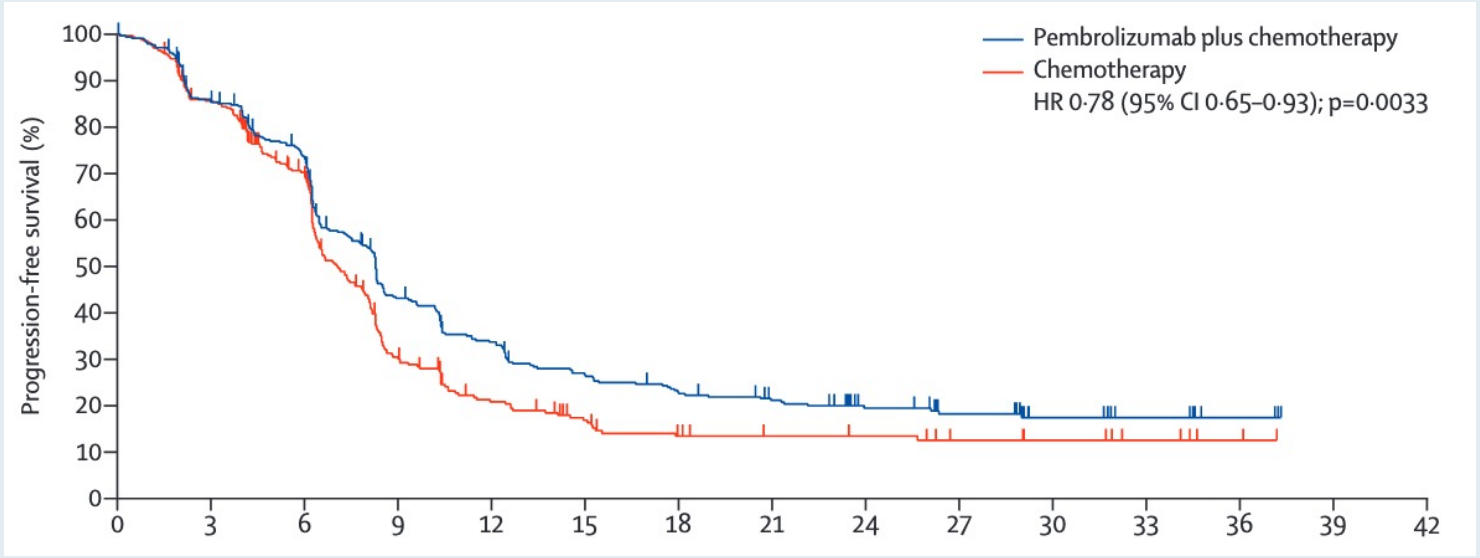
*Thomas Powles, Tibor Csőszi, Mustafa Özgüroğlu, Nobuaki Matsubara, Lajos Géczi, Susanna Y-S Cheng, Yves Fradet, Stephane Oudard, Christof Vulsteke, Rafael Morales Barrera, Aude Fléchon, Seyda Gunduz, Yohann Loriot, Alejo Rodriguez-Vida, Ronac Mamtani, Evan Y Yu, Kijoeng Nam, Kentaro Imai, Blanca Homet Moreno, Ajjai Alva, for the KEYNOTE-361 Investigators**

***Lancet Oncol* 2021;22:931-45.**

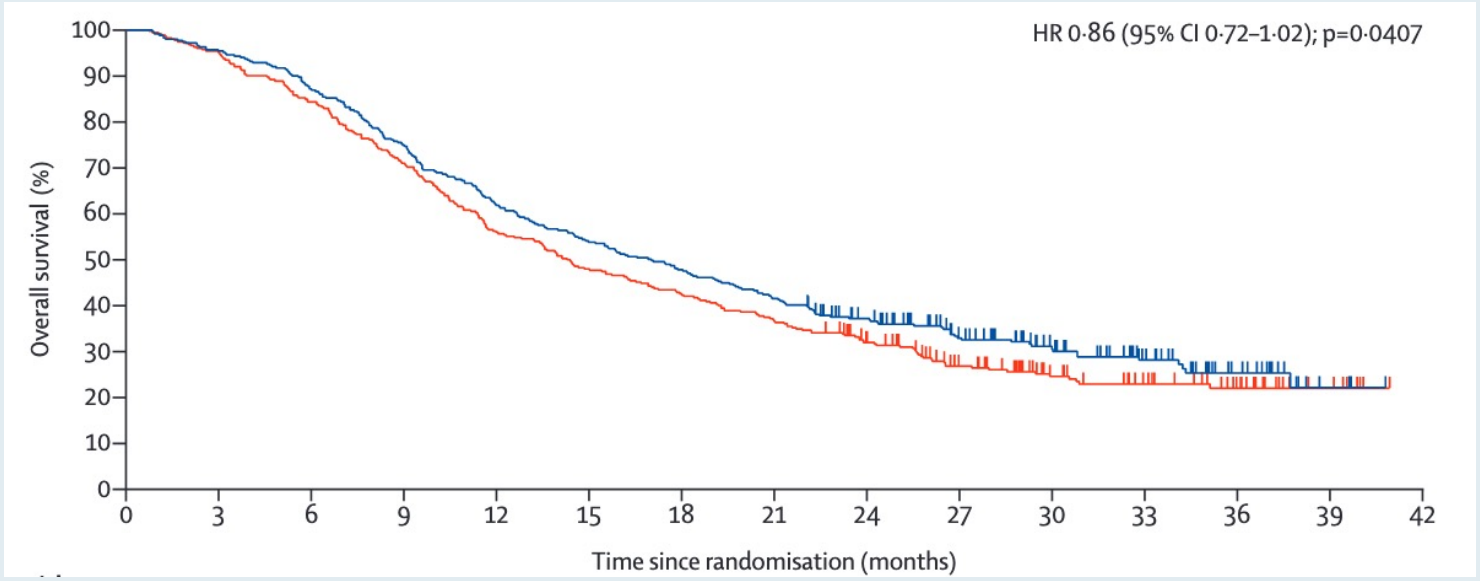
RTP RESEARCH TO PRACTICE

KEYNOTE-361: Progression-Free and Overall Survival with Pembrolizumab and Chemotherapy

PFS



OS

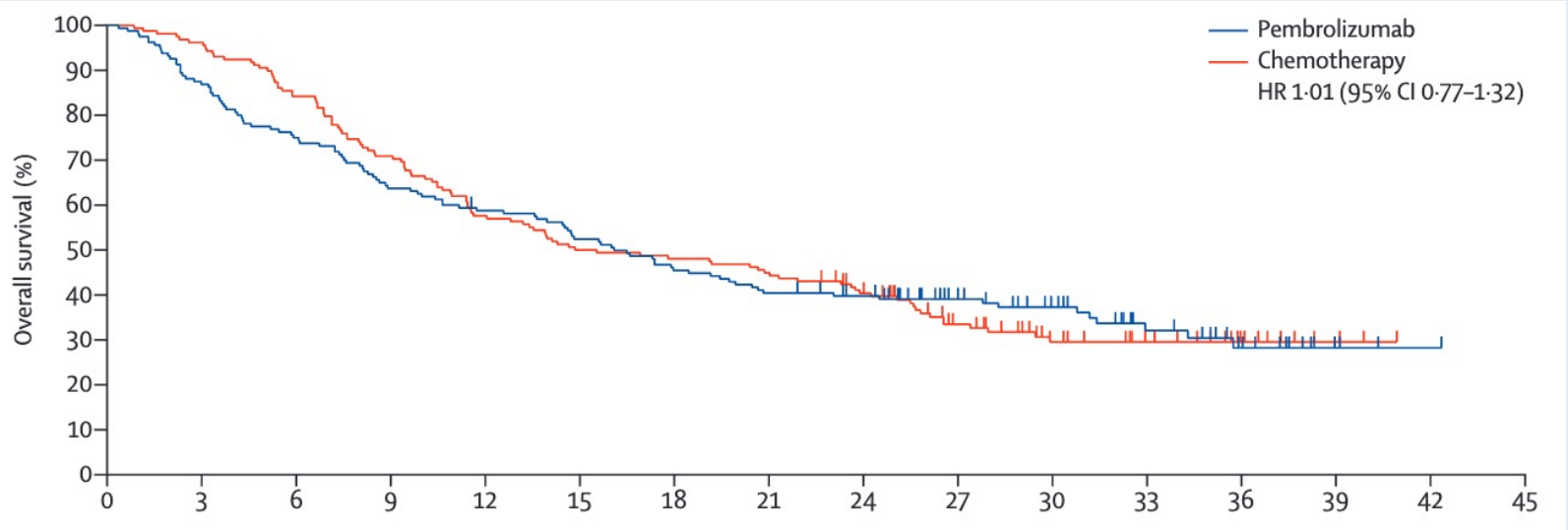


Powles T et al. *Lancet Oncol* 2021;22:931-45.

RTP RESEARCH TO PRACTICE

KEYNOTE-361: OS with Pembrolizumab Alone

PD-L1 CPS ≥10



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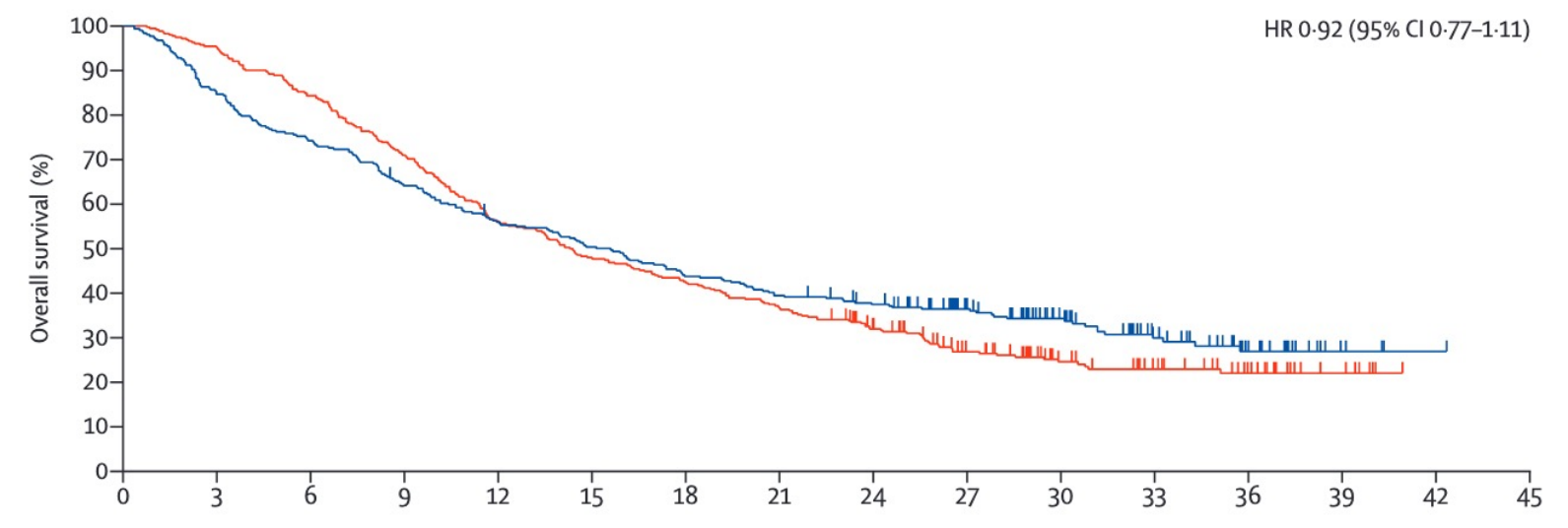


CPS = combined positive score

Powles T et al. *Lancet Oncol* 2021;22:931-45.

RTP RESEARCH TO PRACTICE

CheckMate 901 Evaluating Nivolumab with Ipilimumab as First-Line Treatment for Unresectable or Metastatic Urothelial Carcinoma Fails to Meet Primary Endpoint

Press Release: May 16, 2022

"The Phase 3 CheckMate-901 trial, comparing nivolumab plus ipilimumab to standard-of-care chemotherapy as a first-line treatment for patients with untreated unresectable or metastatic urothelial carcinoma, did not meet the primary endpoint of overall survival (OS) in patients whose tumor cells express PD-L1 ≥1% at final analysis. The company remains blinded to the data, and an independent Data Monitoring Committee recommended that the trial continue to assess other primary and secondary endpoints. No new safety signals were observed at the time of the analysis.

The CheckMate -901 trial is also assessing *nivolumab* plus *ipilimumab* in patients with unresectable or metastatic urothelial carcinoma who are ineligible for cisplatin-based chemotherapy. Additionally, a sub-study of CheckMate-901 with pivotal intent is evaluating *nivolumab* in combination with chemotherapy versus chemotherapy alone in patients who are eligible for cisplatin-based chemotherapy."

https://news.bms.com/news/corporate-financial/2022/Bristol-Myers-Squibb-Provides-Update-on-CheckMate--901-Trial-Evaluating-Opdivo-nivolumab-Plus-Yervoy-ipilimumab-as-First-Line-Treatment-for-Patients-with-Unresectable-or-Metastatic-Urothelial-Carcinoma/default.aspx

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Symposium 2022;Abstract 432

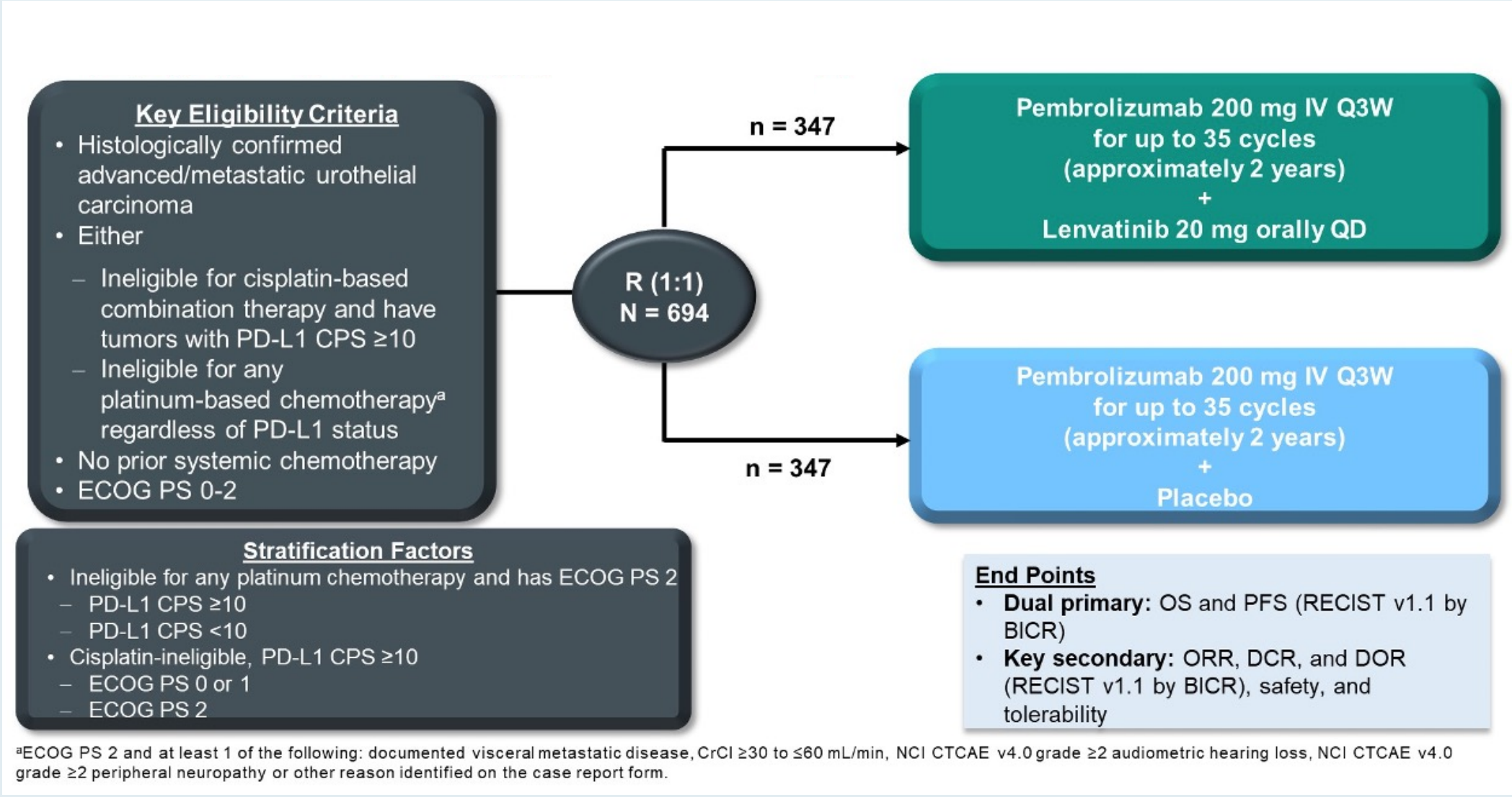
First-line pembrolizumab with or without lenvatinib in patients with advanced urothelial carcinoma (LEAP-011): A phase 3, randomized, double-blind study

Y. Loriot[1]; P. Grivas[2]; R. de Wit[3]; A. V. Balar[4]; A. O. Siefker-Radtke[5]; J. Zolnierek[6]; T. Csoszi[7]; S. J. Shin[8]; S. H. Park[9]; V. Atduev[10]; M. Gumus[11]; Y.-L. Su[12]; S. Burcak Karaca[13]; H. J. Cutuli[14]; M. N. Sendur[15]; K. O'Hara[16]; S. Franco[17]; B. Homet Moreno[17]; N. Matsubara[18]

[1]Gustave Roussy, Cancer Campus, and Université Paris-Saclay, Villejuif, France; [2]University of Washington, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Erasmus MC Cancer Institute, Rotterdam, Netherlands; [4]Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [6]LUXMED Oncology, Warsaw, Poland; [7]Jász-Nagykun-Szolnok County Hospital, Szolnok, Hungary; [8]Severance Hospital, Seoul, South Korea; [9]Samsung Medical Center, Seoul, South Korea; [10]Volga District Medical Center, Federal Medical-Biological Agency, Nizhny Novgorod, Russia; [11]Istanbul Medeniyet University, Istanbul, Turkey; [12]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan; [13]Tulay Aktas Onkoloji Hastanesi, Izmir Bornova, Turkey; [14]Institute for Metabolic Research (IDIM), Buenos Aires, Argentina; [15]Ankara Yildirim Beyazıt University Faculty of Medicine and Ankara City Hospital, Ankara, Turkey; [16]Eisai Inc., Nutley, NJ; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]National Cancer Center Hospital East, Chiba, Japan

RTP RESEARCH TO PRACTICE

LEAP-011 Study Design

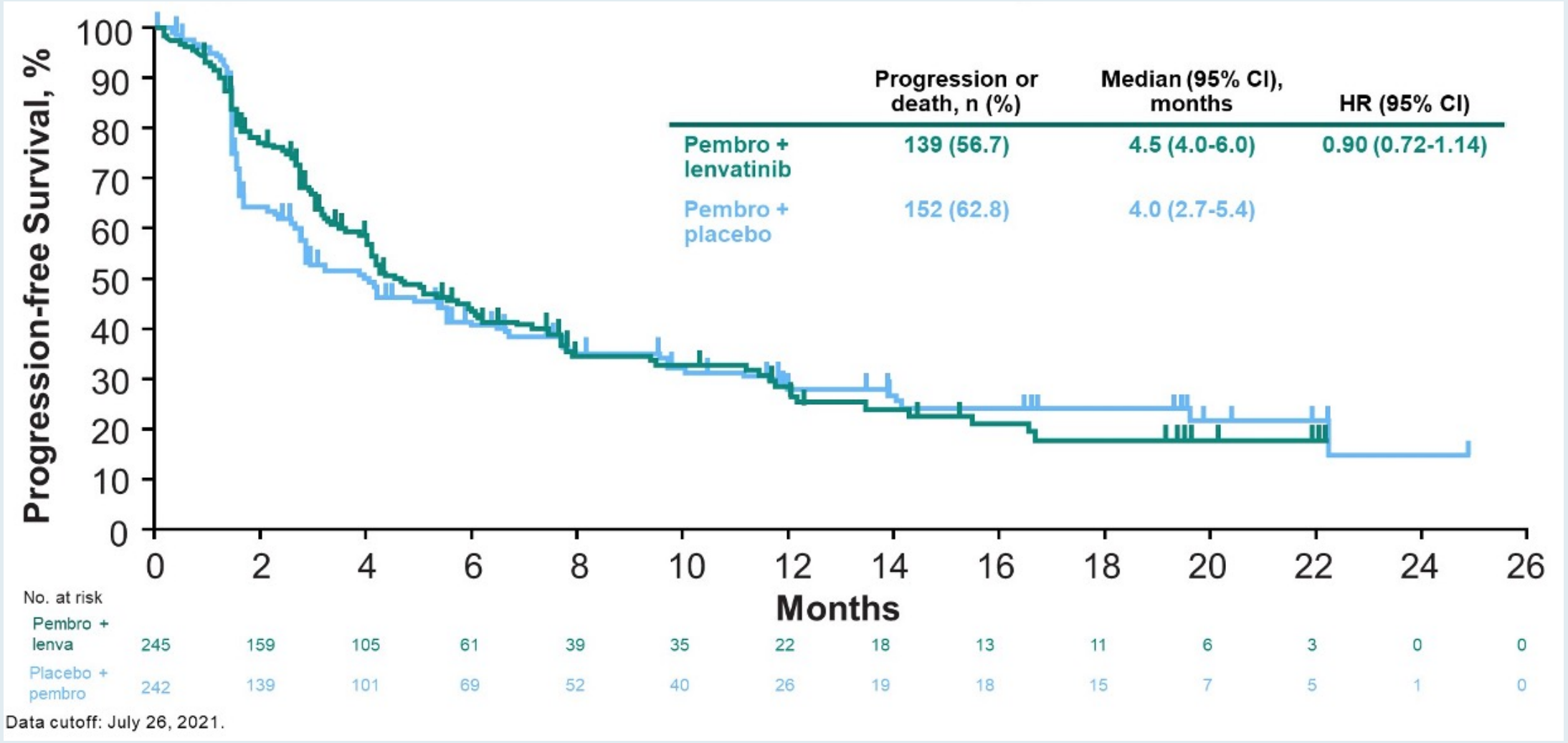


[a]ECOG PS 2 and at least 1 of the following: documented visceral metastatic disease, CrCl ≥30 to ≤60 mL/min, NCI CTCAE v4.0 grade ≥2 audiometric hearing loss, NCI CTCAE v4.0 grade ≥2 peripheral neuropathy or other reason identified on the case report form.

Loriot Y et al. Genitourinary Cancers Symposium 2022;Abstract 432.

RTP RESEARCH TO PRACTICE

LEAP-011: Progression-Free Survival by BICR

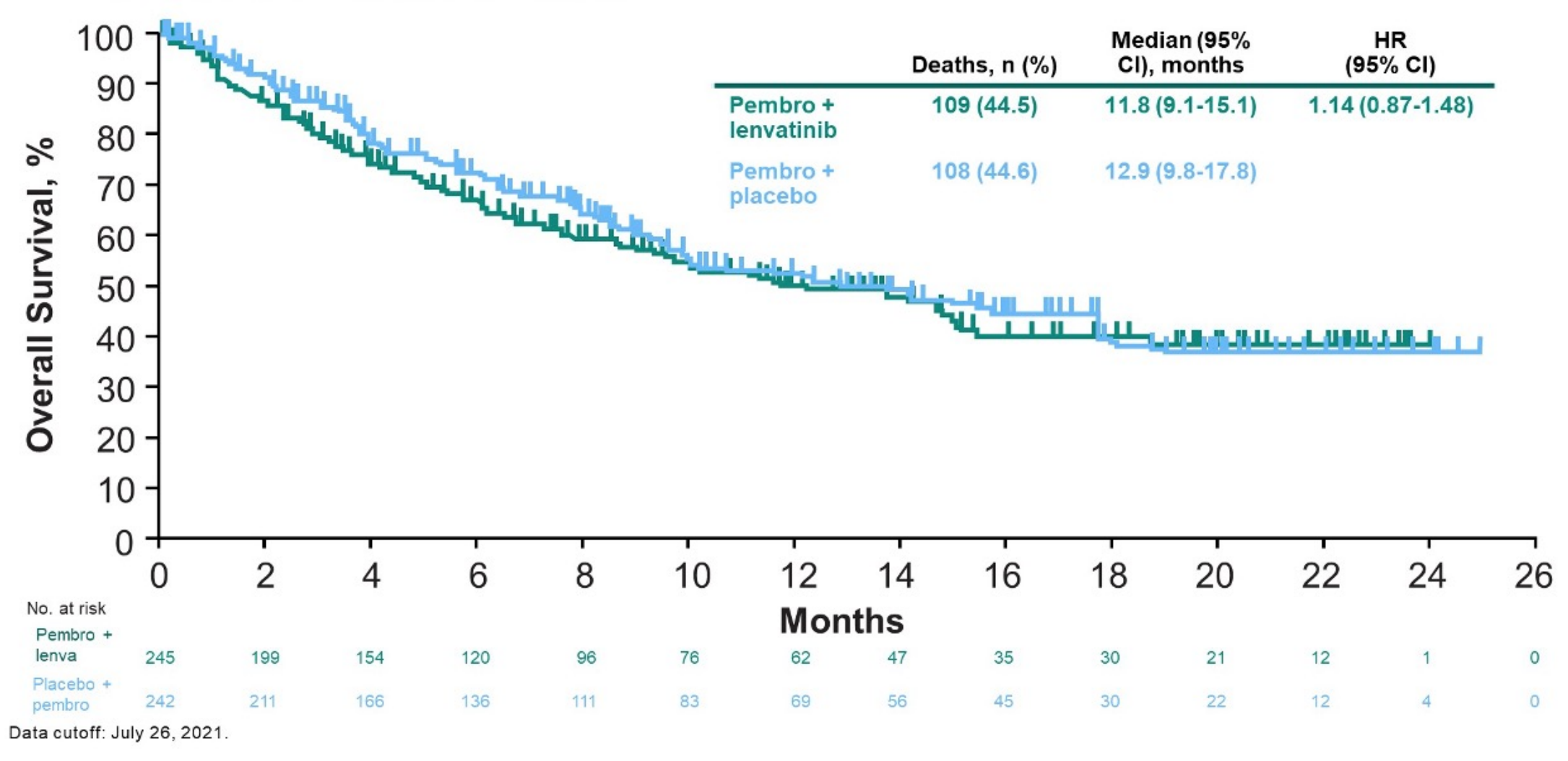


BICR = blinded independent central review

Loriot Y et al. Genitourinary Cancers Symposium 2022;Abstract 432.

RTP RESEARCH TO PRACTICE

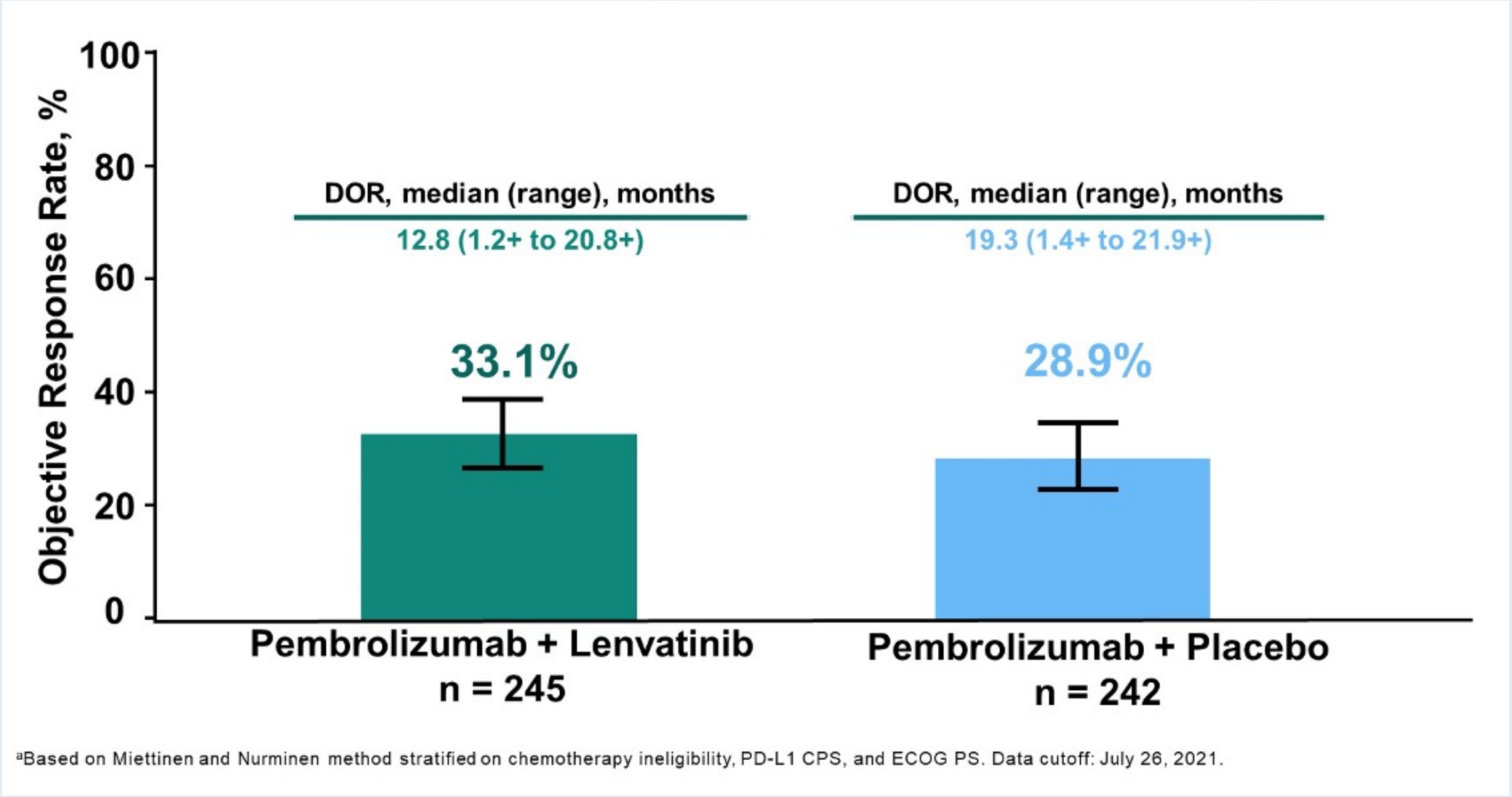
LEAP-011: Overall Survival



Loriot Y et al. Genitourinary Cancers Symposium 2022;Abstract 432.

RTP RESEARCH TO PRACTICE

LEAP-011: Confirmed ORR by BICR



[a]Based on Miettinen and Nurminen method stratified on chemotherapy ineligibility, PD-L1 CPS, and ECOG PS. Data cutoff: July 26, 2021.

Loriot Y et al. Genitourinary Cancers Symposium 2022;Abstract 432.

RTP RESEARCH TO PRACTICE

LEAP-011: Summary of Treatment-Related Adverse Events

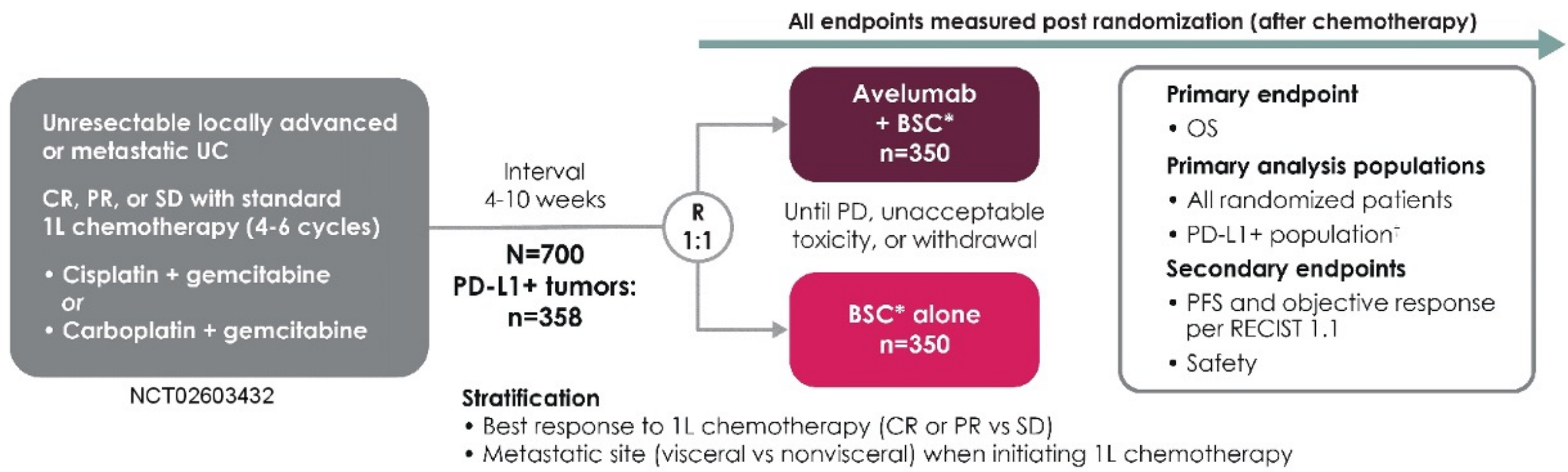
n (%)	Pembrolizumab + lenvatinib n = 241	Pembrolizumab + placebo n = 242
Any-grade treatment-related AE	211 (87.6)	167 (69.0)
Grade 3-5 treatment-related AEs	123 (51.0)	66 (27.3)
Discontinued any drug because of a treatment-related AE	48 (19.9)	22 (9.1)
Discontinued pembrolizumab	24 (10.0)	12 (5.0)
Discontinued lenvatinib/placebo	46 (19.1)	21 (8.7)
Discontinued both drugs	19 (7.9)	8 (3.3)
Serious treatment-related AEs	54 (22.4)	24 (9.9)
Death from a treatment-related AE	6 (2.5)[b]	1 (0.4)[c]
Duration of treatment (range), months	3.9 (0.0-23.4)	3.8 (0.0-25.0)

[a]All patients who received ≥1 dose of treatment. [b]Death due to sepsis (n = 1), cardiac failure (n = 1), pneumonitis (n = 2), cachexia (n = 1), and unknown cause (n = 1). [c]Death due to renal failure. Data cutoff: July 26, 2021.

Loriot Y et al. Genitourinary Cancers Symposium 2022;Abstract 432.

RTP RESEARCH TO PRACTICE

JAVELIN-100 Study Design



Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

ASCO Genitourinary Cancers Symposium

2022 Abstract 439

First line avelumab in PD-L1+ve metastatic or locally advanced urothelial cancer (aUC) patients unfit for cisplatin (cis): *The ARIES trial.*

Roberto Iacovelli[1], Chiara Ciccarese[1], Matteo Brunelli[2], Nicola Battelli[3], Consuelo Buttigliero[4], Claudia Caserta[5], Sebastiano Buti[6], Daniele Santini[7], Emanuele Naglieri[8], Luca Galli[9], Elena Verri[10], Paola Ermacora[11], Michele Milella[12], Cristina Masini[13], Giuseppe Aprile[14], Laura Milesi[15], Francesco Spina[16], Mimma Rizzo[17], Isabella Sperduti[18], Giuseppe Fornarini[19].

1.Oncology Unit, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Catholic University of Rome, Rome, Italy; 2.Department of Diagnostics and Public Health, Pathology Unit, Azienda Ospedaliera Universitaria Integrata di Verona, University of Verona, Verona, Italy; 3.Oncologia Medica, Ospedale Generale Provinciale di Macerata, Macerata, Italy; 4.Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Turin, Italy; 5.Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy; 6.Medical Oncology Unit, University Hospital of Parma, Parma, Italy and Department of Medicine and Surgery, University of Parma, Parma, Italy; 7.Department of Medical Oncology, Campus Bio-Medico University of Rome, Rome, Italy; 8.Istituto Oncologico Giovanni Paolo II, Bari, Italy; 9.Medical Oncology Unit 2, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; 10.Medical Oncology Division of Urogenital and Head and Neck Tumors, European Institute of Oncology, Milan, Italy; 11.Dipartimento di Oncologia, Azienda Ospedaliero-Universitaria, Udine, Italy; 12.Section of Oncology, Department of Medicine, University of Verona School of Medicine and Verona University Hospital Trust, Verona, Italy; 13.AUSL/IRCCS di Reggio Emilia, Reggio Emilia, Italy; 14.Department of Oncology, San Bortolo General Hospital, Vicenza, Italy; 15.Oncologia Medica Asst Papa Giovanni XXIII, Bergamo, Italy; 16.Department of Hematology & Oncology, Niguarda Cancer Center, Ospedale Niguarda Ca' Granda, Milan, Italy; 17.Division of Translational Oncology, IRCCS Istituti Clinici Scientifici Maugeri, Pavia, Italy; 18.Regina Elena National Cancer Institute IRCCS, Rome, Italy; 19.Medical Oncology Unit 1, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

PRESENTED BY: Roberto Iacovelli M.D., Ph.D. roberto.iacovelli@policlinicogemelli.it #DrIacovelli

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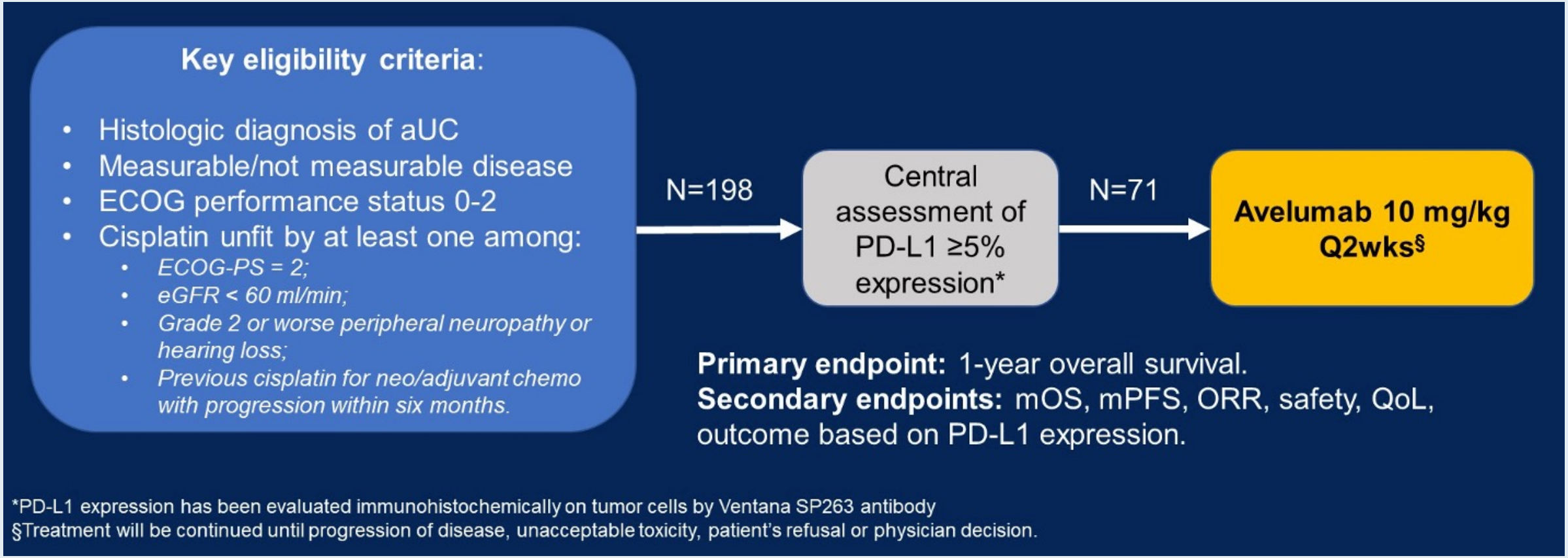
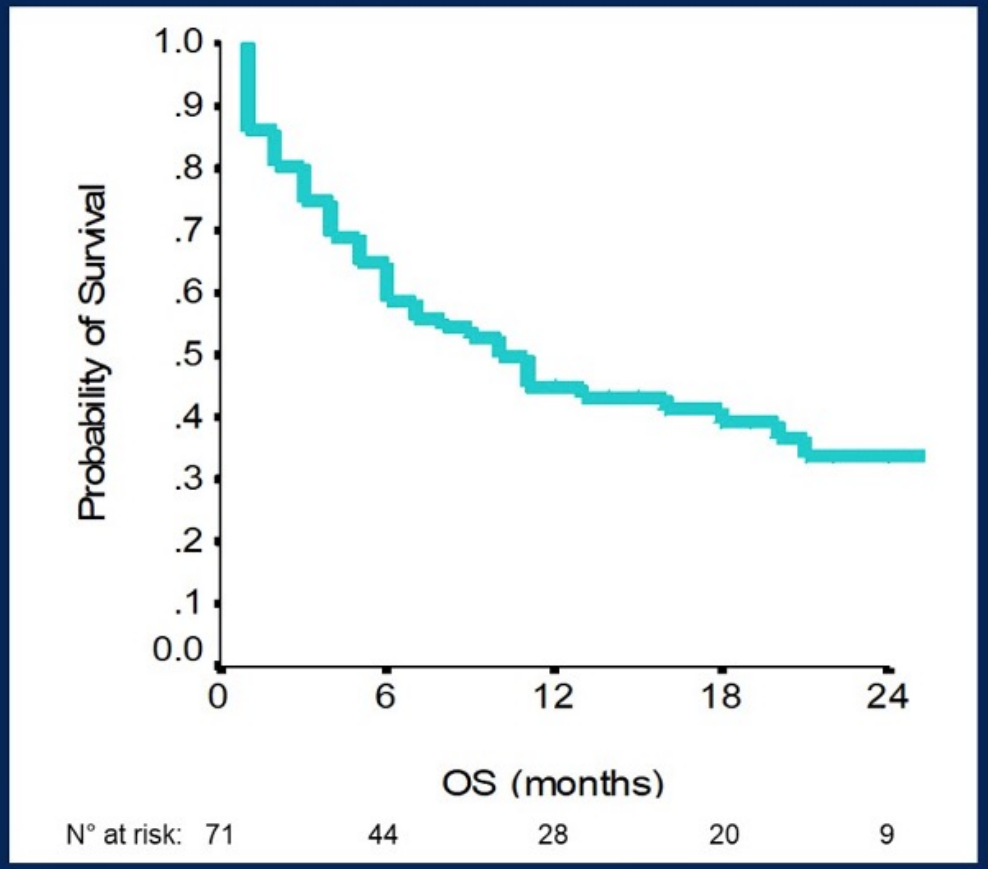
RTP RESEARCH TO PRACTICE

The ARIES Study Design



Iacovelli R et al. Genitourinary Cancers Symposium 2022;Abstract 439.

ARIES Primary Endpoint: 1-Year and Median Overall Survival



After a median follow up of 9.0 months,13 (19.4%) patients are still on treatment.

The median **OS** was 10.0 months (95%CI, 5.7-14.3) and the estimated 1-year OS was 44.9%

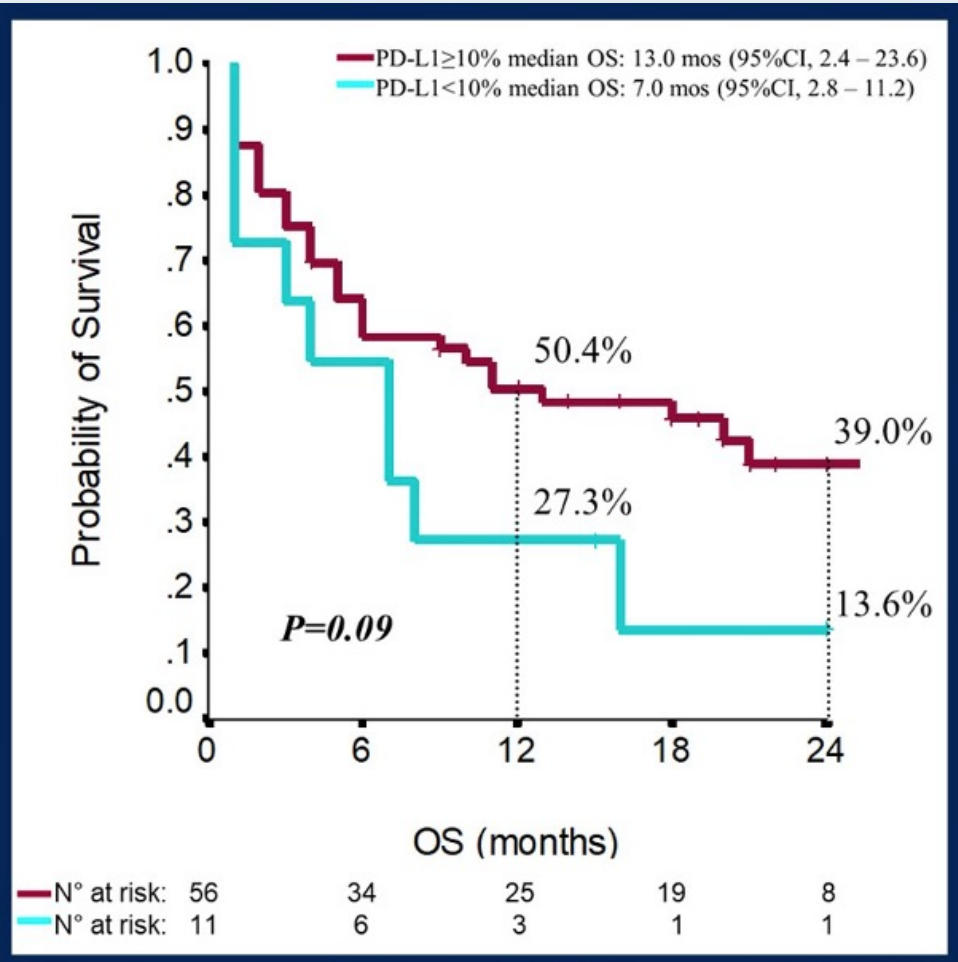
The rate of patients alive at 1 year was 40.8%.

The median **PFS** was 2.0 months (95% CI, 1.4-2.6).

Iacovelli R et al. Genitourinary Cancers Symposium 2022;Abstract 439.

RTP RESEARCH TO PRACTICE

ARIES Secondary Endpoint: Overall Survival by PD-L1 Expression



Among 71 PD-L1+ve patients, the differential PD-L1 expression has been evaluated by CPS.

56 had CPS≥10%, 11 had CPS<10%, 4 were not evaluable.

The **median OS** was 13.0 months (95%CI, 2.4 – 23.6) for patients with CPS≥10% compared to 7.0 (95%CI, 2.8 – 11.2) months for those with CPS<10% (p=0.09).

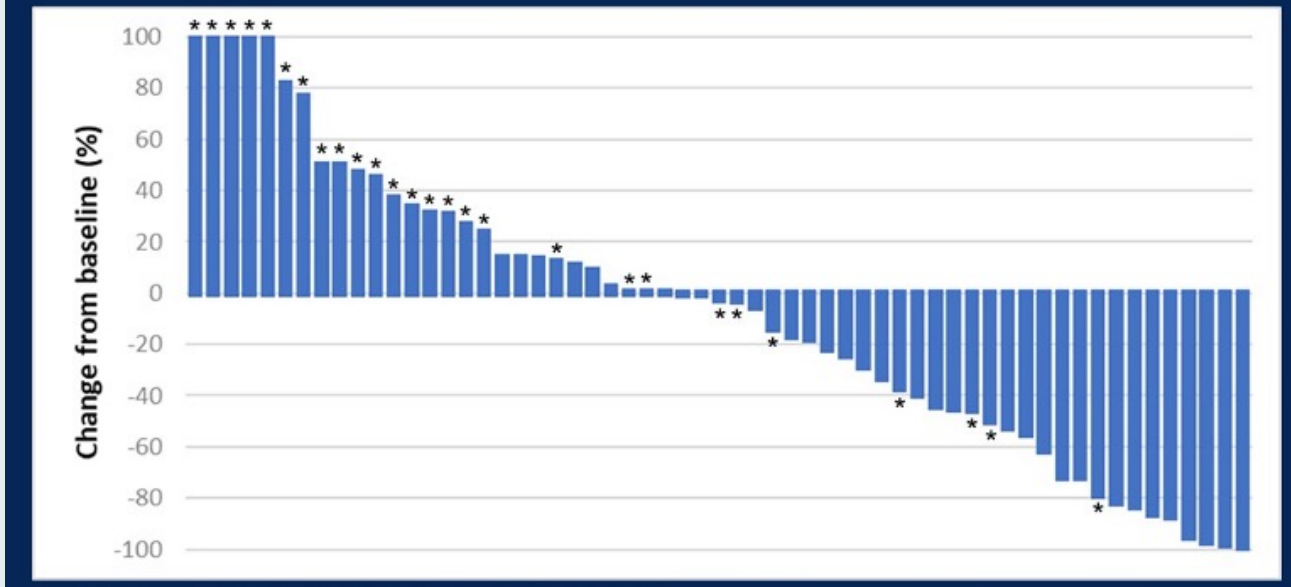
The **median PFS** was 2.0 months (95%CI, 1.2 – 2.8) for patients with CPS≥10% compared to 2.0 months (95%CI, 1.1 – 2.9) for those with CPS<10% (p=0.46).

CPS: combined positive score; mos: months; OS: overall survival; PD-L1: programmed death ligand 1, PFS: progression free survival.

Iacovelli R et al. Genitourinary Cancers Symposium 2022;Abstract 439.

RTP RESEARCH TO PRACTICE

ARIES Secondary Endpoint: Response Rate



* Progression of disease by RECIST Criteria

Best response*	N=71
Complete response	1 (1.4%)
Partial response	15 (21.1%)
Stable disease	15 (21.1%)
Progressive disease	28 (39.4%)
Not evaluable	12 (16.9%)

* Response rate has been locally evaluated by RECIST criteria v 1.1

Iacovelli R et al. Genitourinary Cancers Symposium 2022;Abstract 439.

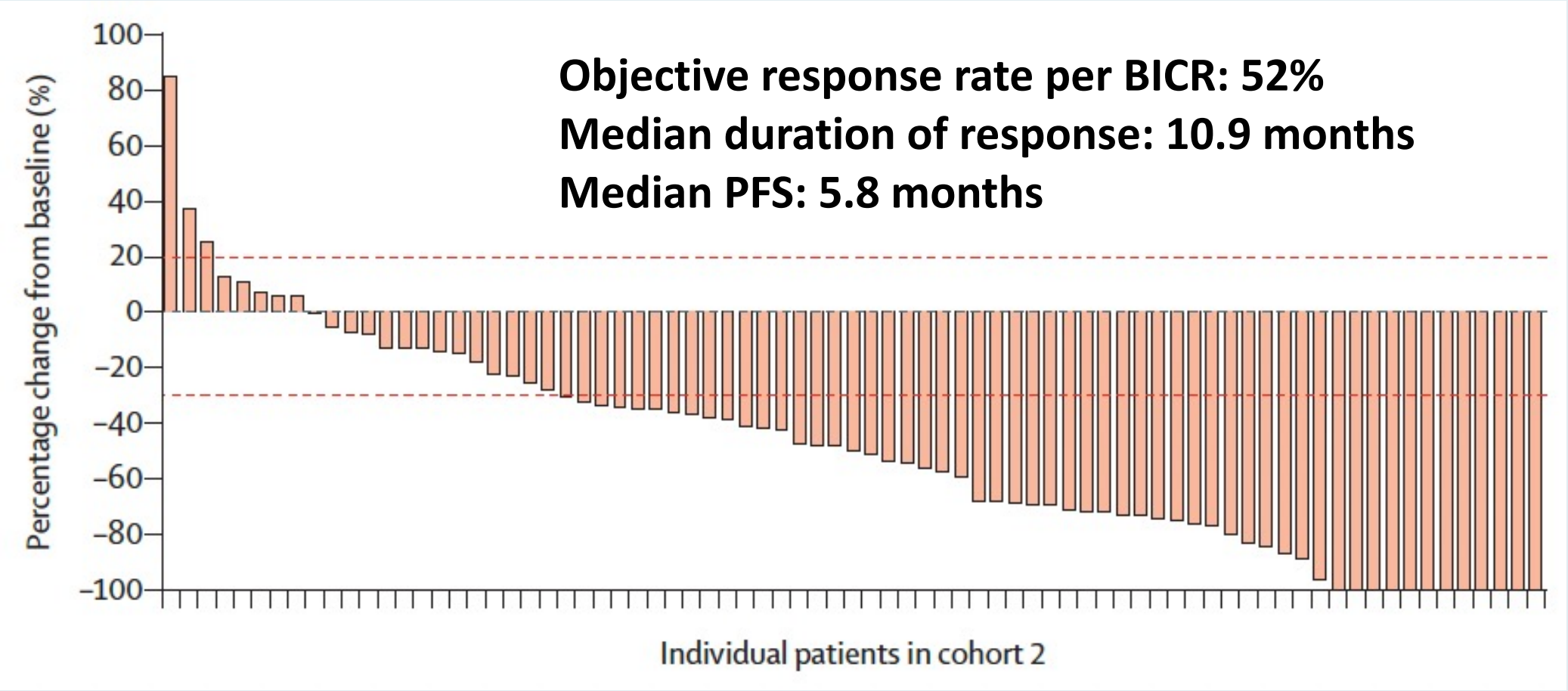
RTP RESEARCH TO PRACTICE

Lancet Oncol 2021;22:872-82.

Enfortumab vedotin after PD-1 or PD-L1 inhibitors in cisplatin-ineligible patients with advanced urothelial carcinoma (EV-201): a multicentre, single-arm, phase 2 trial

Evan Y Yu, Daniel P Petrylak*, Peter H O'Donnell, Jae-Lyun Lee, Michiel S van der Heijden, Yohann Loriot, Mark N Stein, Andrea Necchi, Takahiro Kojima, Michael R Harrison, Se Hoon Park, David I Quinn, Elisabeth I Heath, Jonathan E Rosenberg, Joyce Steinberg, Shang-Ying Liang, Janet Trowbridge, Mary Campbell, Bradley McGregor, Arjun V Balar*

EV-201: Efficacy in Cisplatin-Ineligible Patients with Advanced Urothelial Carcinoma Previously Treated with PD-1 or PD-L1 Inhibitor Therapy

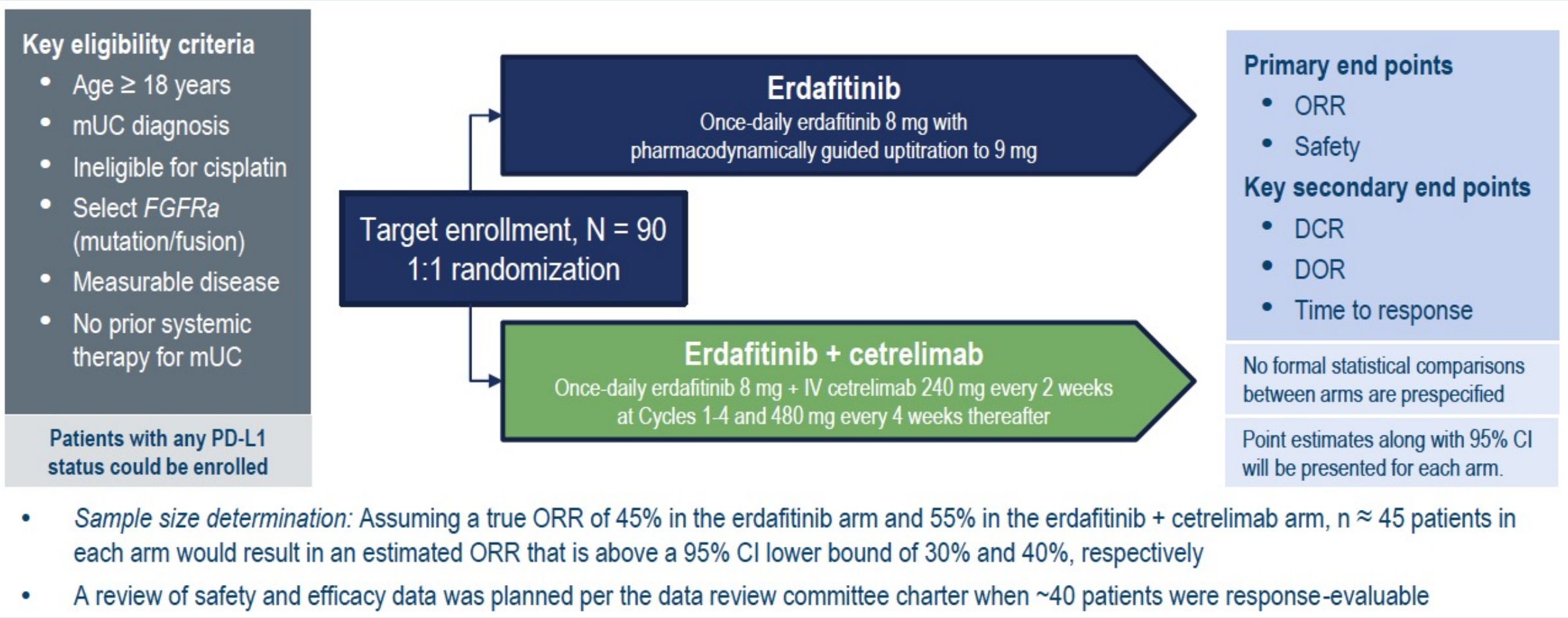


Cohort 2 included adults (aged ≥18 years) with an ECOG PS score of 2 or less who were considered ineligible for cisplatin at enrolment and who had not received platinum-containing chemotherapy in the locally advanced or metastatic setting.

Yu EY et al. *Lancet Oncol* 2021;22:872-82.

RTP RESEARCH TO PRACTICE

NORSE: Phase II Trial Design



- *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

ORR = overall response rate; DCR = disease control rate; DOR = duration of response

Powles T et al. ESMO 2021;Abstract LBA27.

RTP RESEARCH TO PRACTICE

NORSE: Safety

Patients with TEAE, n (%)	Erdafitinib (n = 24)	Erdafitinib + Cetrelimab (n = 24)
TEAE of any grade	23 (96%)	23 (96%)
Most frequent (≥ 25% of patients)		
Hyperphosphatemia	14 (58%)	14 (58%)
Stomatitis	15 (63%)	13 (54%)
Diarrhea	12 (50%)	10 (42%)
Dry mouth	5 (21%)	14 (58%)
Dry skin	5 (21%)	9 (38%)
Anemia	6 (25%)	6 (25%)
Drug-related TEAEs leading to treatment discontinuation[a]	2 (8%)	Erdafitinib and/or cetrelimab: 7 (29%)[b] Both erdafitinib and cetrelimab: 2 (8%)

- The safety profile of erdafitinib + cetrelimab was generally similar to that of erdafitinib alone
- Grade 3-4 TEAEs occurred in 9 patients (38%) in the erdafitinib arm and 12 patients (50%) in the erdafitinib + cetrelimab arm; most frequent were:
  - Erdafitinib arm: anemia (n = 3 patients [12.5%]) and general physical health deterioration (n = 3 [12.5%])
  - Erdafitinib + cetrelimab arm: stomatitis (n = 3 [12.5%]), lipase increased (n = 3 [12.5%]), and fatigue (n = 2 [8.3%])
- 1 death in the erdafitinib + cetrelimab arm was determined to be related to cetrelimab (respiratory failure)

TEAE = treatment-emergent adverse event

Powles T et al. ESMO 2021;Abstract LBA27.

RTP RESEARCH TO PRACTICE

NORSE: Treatment-Emergent Adverse Events

Patients with TEAE, n (%)	Erdafitinib (n = 24)		Erdafitinib + Cetrelimab (n = 24)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
TEAEs of interest				
Nail toxicity	12 (50%)	1 (4%)	8 (33%)	1 (4%)
Skin toxicity	9 (38%)	0	11 (46%)	0
Eye toxicity (excluding central serous retinopathy)	6 (25%)	1 (4%)	8 (33%)	0
Central serous retinopathy	4 (17%)	0	4 (17%)	0
Immune-related TEAEs[a]	1 (4%)[b]	0	12 (50%)	4 (17%)
Diarrhea	0	0	3 (13%)	0
Lipase increased	0	0	3 (13%)	2 (8%)
Stomatitis	0	0	2 (8%)	0
Anemia	0	0	2 (8%)	0

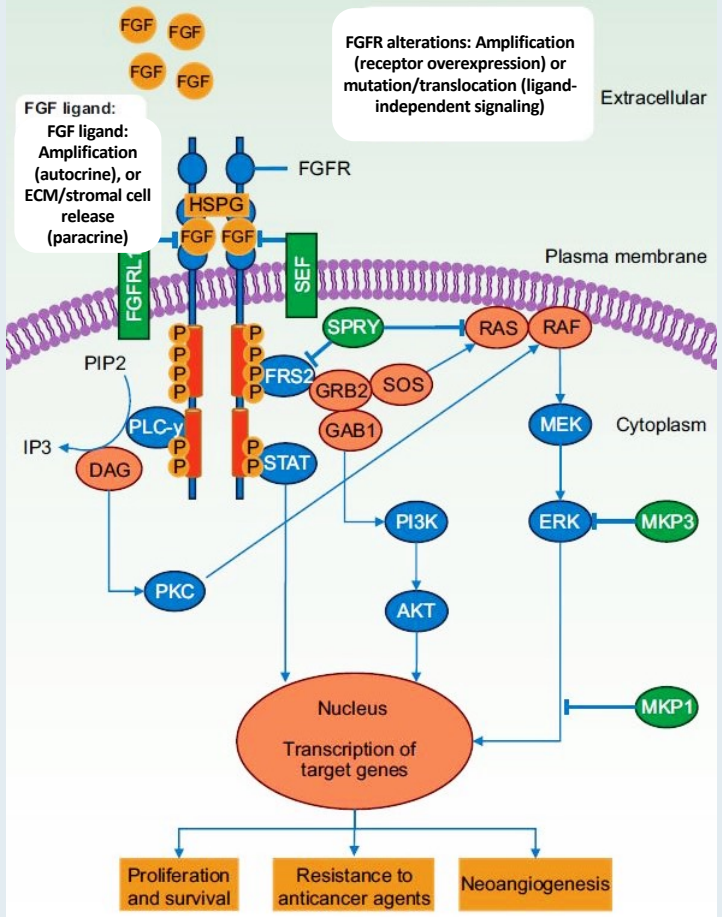
- The frequency of TEAEs of interest was mostly similar between arms, with the exception of immune-related TEAEs

Powles T et al. ESMO 2021;Abstract LBA27.

RTP RESEARCH TO PRACTICE

Rationale for Targeting FGFR in Urothelial Carcinoma (UC)[1,2]

FGFR Signaling Pathway[3]



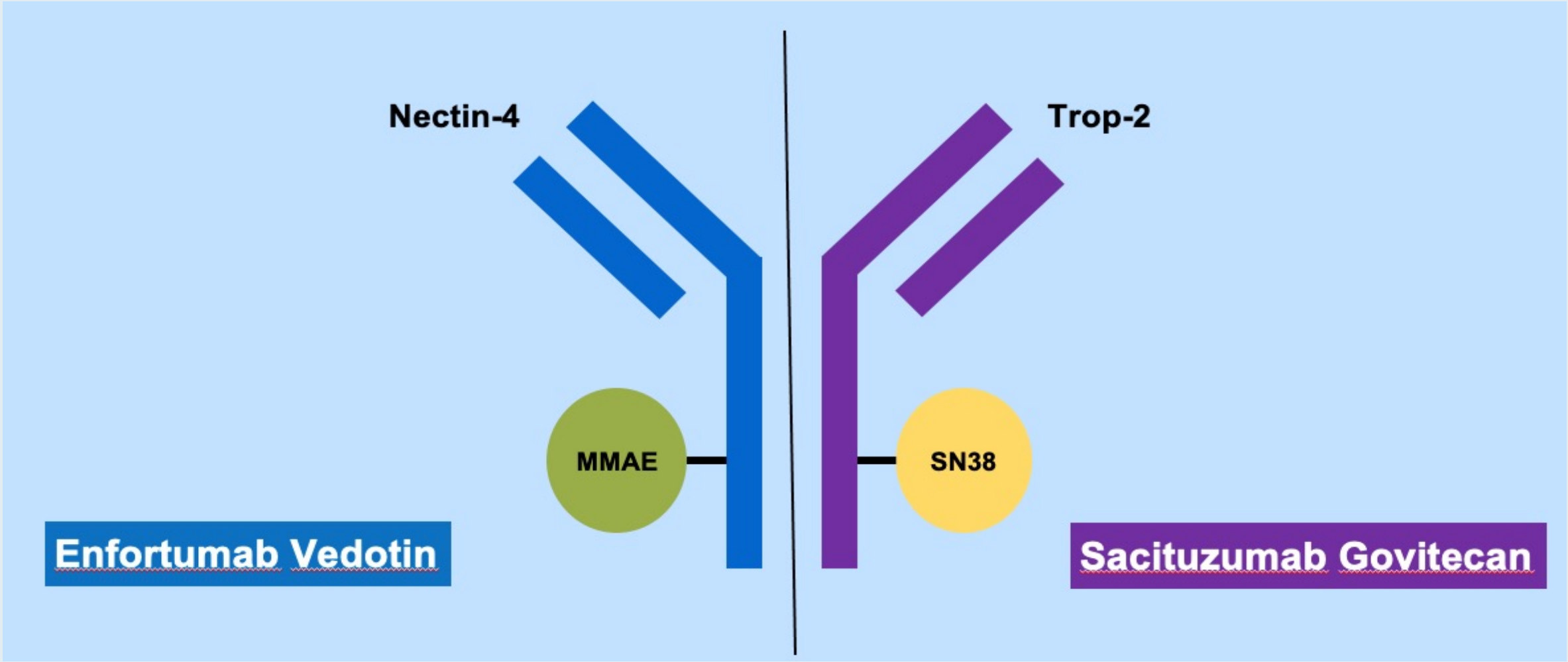
- *FGFR* is altered in 15%-20% of advanced UC[4]
  - Mutated *FGFR3* is present in 37% of upper-tract UC[5]

Cancer Type	Frequency of FGFR Alterations[1]
Metastatic UC	15%-20%
NMIBC	40%-70%
Cholangiocarcinoma	14%-22%
NSCLC	4%
HCC (FGF19 amp by FISH)	21%
Glioblastoma	23%
Breast cancer	3%-5%
Ovarian cancer	7%
Head and neck cancer	9%-17%

1. The Cancer Genome Atlas (TCGA) genomic alteration database: https://tcga-data.nci.nih.gov/docs/publications/tcga/. Accessed February 6, 2020.
2. Genomics Evidence Neoplasia Information Exchange (GENIE) genomic alteration database: https://www.aacr.org/Research/Research/pages/aacr-project-genie.aspx. Accessed February 6, 2020. 3. Touat M et al. *Clin Cancer Res*. 2015;21:2684-2694. 4. Rodriguez-Vida A et al. *J Hematol Oncol*. 2015;8:119. 5. Li Q et al. *Curr Urol Rep*. 2016;17:12.

Courtesy of Arjun Balar, MD

Antibody-Drug Conjugates in UBC



Courtesy of Matthew D Galsky, MD

RTP
RESEARCH
TO PRACTICE

ASCO Genitourinary Cancers Symposium

2022 Abstract 434

TROPHY-U-01 Cohort 3: Sacituzumab Govitecan (SG) in Combination With Pembrolizumab (Pembro) in Patients (pts) With Metastatic Urothelial Cancer (mUC) Who Progressed After Platinum (PLT)-Based Regimens

Petros Grivas,[1] Damien Pouessel,[2] Chandler H. Park,[3] Philippe Barthelemy,[4] Manojkumar Bupathi,[5] Daniel P. Petrylak,[6] Neeraj Agarwal,[7] Aude Fléchon,[8] Chethan Ramamurthy,[9] Nancy B. Davis,[10] Alejandro Recio-Boiles,[11] Scott T. Tagawa,[12] Cora N. Sternberg,[12] Astha Bhatia,[13] Cabilia Pichardo,[13] Trishna Goswami,[13] and Yohann Loriot[14]

[1]University of Washington, Seattle Cancer Care Alliance, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [2]Department of Medical Oncology & Clinical Research Unit, Institut Claudius Regaud/Institut Universitaire du Cancer de Toulouse (IUCT-Oncopôle), Toulouse, France; [3]Norton Cancer Institute, Louisville, KY, USA; [4]Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [5]Rocky Mountain Cancer Centers, Littleton, CO, USA; [6]Yale School of Medicine, New Haven, CT, USA; [7]Huntsman Cancer Institute, Salt Lake City, UT, USA; [8]Centre Léon Bérard, Lyon, France; [9]University of Texas Health Science Center at San Antonio, San Antonio, TX, USA; [10]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [11]University of Arizona Cancer Center, Tucson, AZ, USA; [12]Weill Cornell Medical College of Cornell University, New York, NY, USA; [13]Gilead Sciences, Inc, Morris Plains, NJ, USA; and [14]Institut de Cancérologie Gustave Roussy, Université Paris-Saclay, Villejuif, France

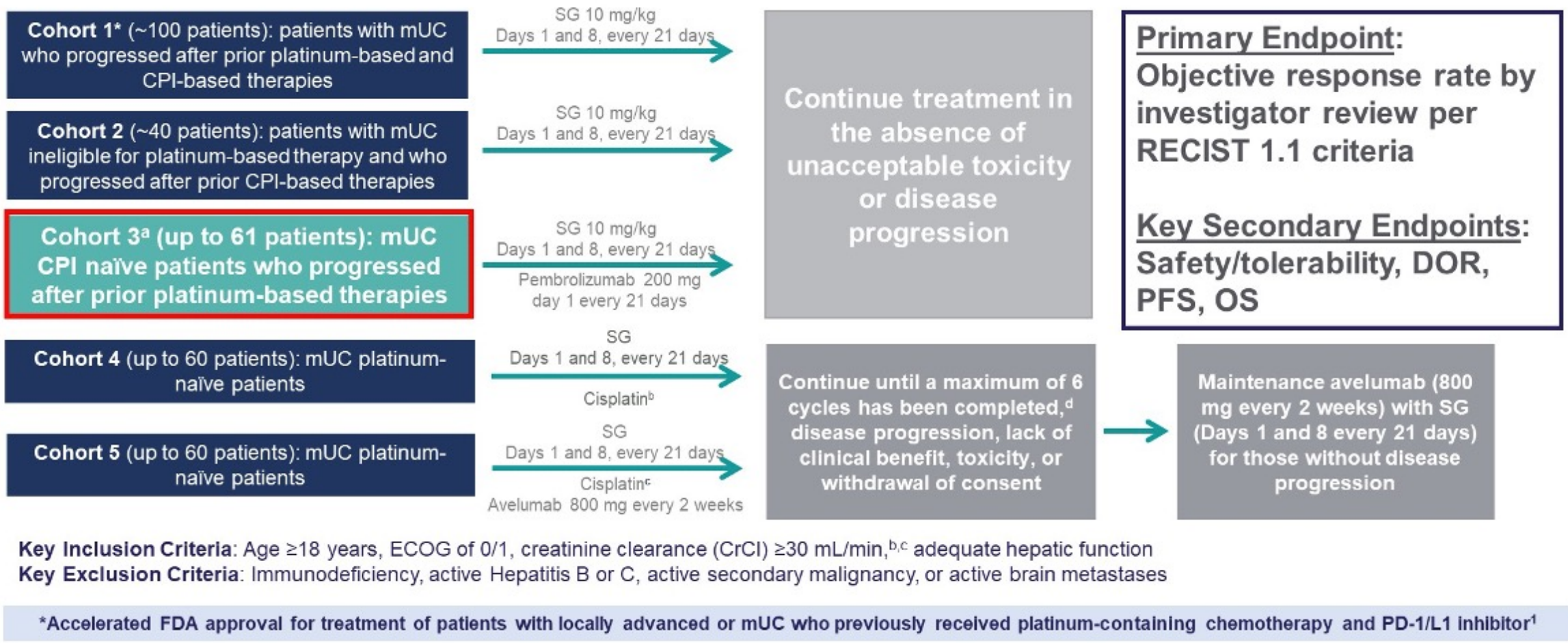
Abstract # 434
ClinicalTrials.gov Number: NCT03547973.

@PGrivasMDPhD

TROPHY U-01

RTP RESEARCH TO PRACTICE

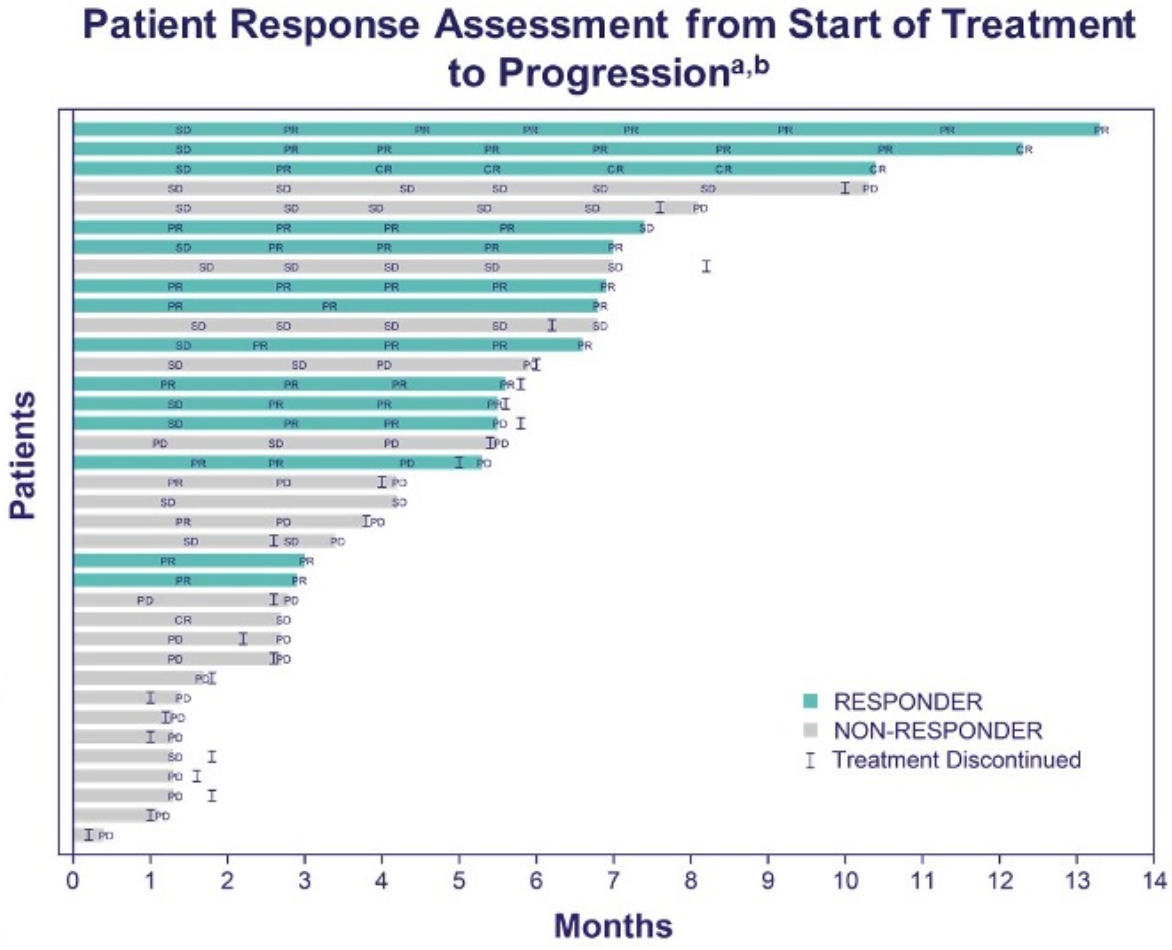
TROPHY U-01 Multicohort-Phase Trial in Metastatic Urothelial Carcinoma



Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

TROPHY U-01: Objective Response Rate by Subgroup and Individual Response Assessment

Subgroup[a]	n/N	Objective response rate, % (95% CI)
Overall	**14/41**	**34.1 (20.08–50.59)**
Age		
<50 Years	0/1	N/A (N/A–N/A)
50 to 64 Years	6/14	42.9 (17.66–71.14)
≥65 Years	8/26	30.8 (14.33–51.79)
Race		
White	8/22	36.4 (17.20–59.34)
Other	1/1	100.0 (2.50–100.00)
Not reported	5/18	27.8 (9.69–53.48)
Ethnicity		
Hispanic or Latino	2/2	100.0 (15.81–100.00)
Not Hispanic or Latino	8/22	36.4 (17.20–59.34)
Not reported	4/16	25.0 (7.27–52.38)
Missing	0/1	N/A (N/A–N/A)
ECOG PS		
0	7/16	43.8 (19.75–70.12)
1	7/25	28.0 (12.07–49.39)
Baseline visceral metastasis involvement		
Yes	10/28	35.7 (18.64–55.93)
No	4/13	30.8 (9.09–61.43)
Baseline visceral metastasis, involvement of liver		
Yes	5/12	41.7 (15.17–72.33)
No	9/29	31.0 (15.28–50.83)
Bellmunt risk factor groups		
0	4/10	40.0 (12.16–73.76)
1	7/20	35.0 (15.39–59.22)
2	3/11	27.3 (6.02–60.97)



Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

TROPHY U-01: Most Common Treatment-Related Adverse Events for All Patients

	Cohort 3 (N=41)
TRAEs Occurring in >20% of Patients, n (%)	All Grade
Diarrhea	29 (71)
Nausea	22 (54)
Vomiting	10 (24)
Neutropenia	18 (44)
Anemia	17 (41)
Leukopenia	12 (29)
Fatigue	12 (29)
Asthenia	16 (39)
Alopecia	14 (34)
Decreased appetite	11 (27)
Pruritus	9 (22)

- Treatment-related Gr 3-4 AEs in 59% of patients
- 16 (39%) patients had SG dose reduction due to TRAE
- No treatment-related death occurred
- 10 (25%) patients received steroids for iRAE[a]
  - Topical: 6 (15%) patients
  - Oral: 4 (10%) patients
    - diarrhea (2 patients)
    - pruritus (1 patient)
    - rash maculopapular (1 patient)
- 12 (29%) patients received G-CSF
- Gr ≥3 febrile neutropenia, 4 (10%) without prior G-CSF

Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

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Cabozantinib in Combination with Atezolizumab in Urothelial Carcinoma Previously Treated with Platinum-Containing Chemotherapy: Results from Cohort 2 of the COSMIC-021 Study

Pal SK et al.

ASCO 2020;Abstract 5013.

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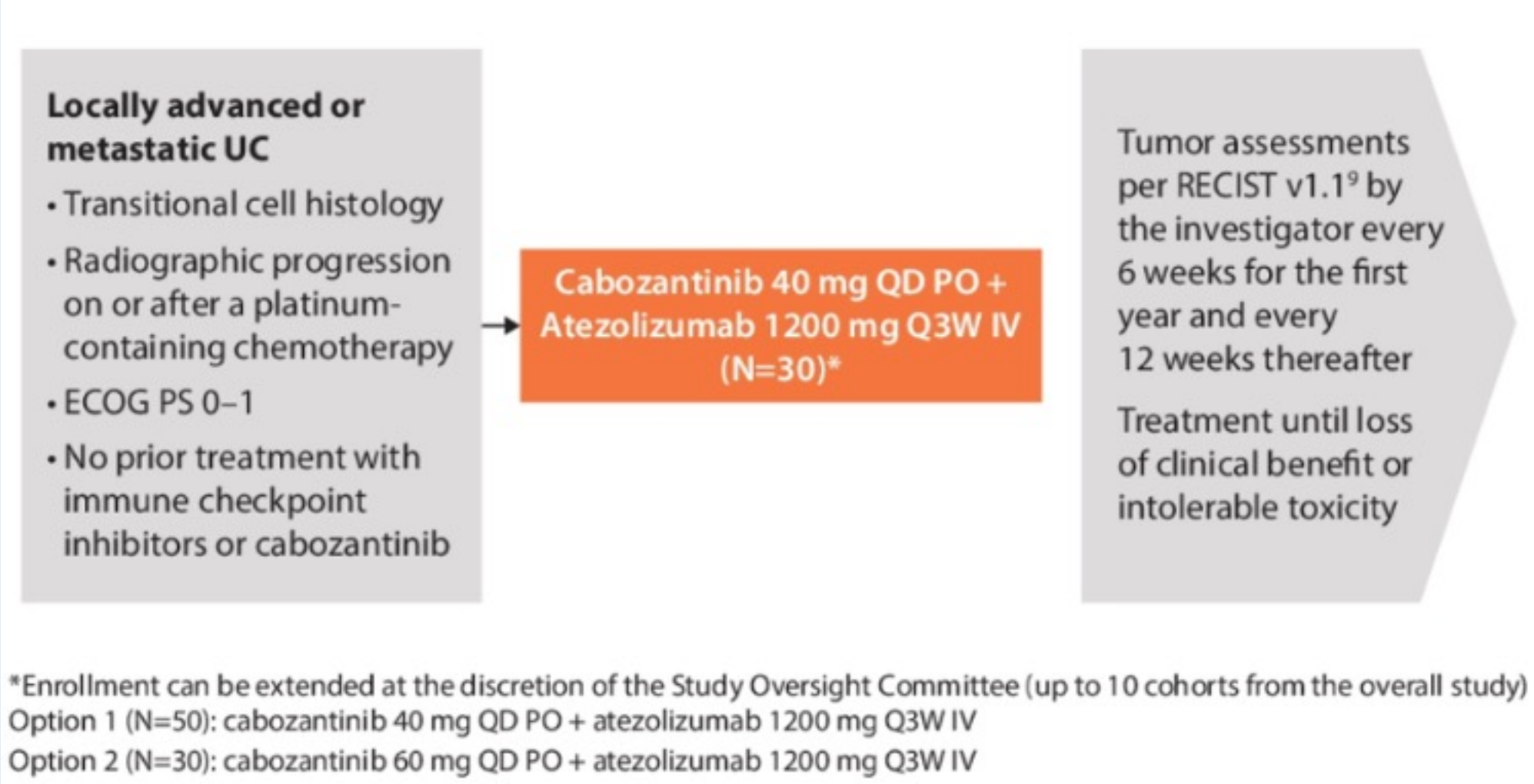
COSMIC-021: Study Design for UC Expansion Cohort 2



Pal SK et al. ASCO 2020;Abstract 5013.

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COSMIC-021: Immune-Related Adverse Events (AEs)

	UC Cohort 2 (N=30)		
	Any Grade	Grade 3	Grade 4
Any AE, n (%)	8 (27)	1 (3.3)	0
Hypothyroidism	3 (10)	0	0
Autoimmune thyroiditis	1 (3.3)	0	0
Chorioretinitis	1 (3.3)	1 (3.3)	0
Cytokine release syndrome	1 (3.3)	0	0
Infusion related reaction	1 (3.3)	0	0
Transaminases increased	1 (3.3)	0	0

Pal SK et al. ASCO 2020;Abstract 5013.

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COSMIC-021: Tumor Response by RECIST v1.1, Investigator Report

	UC Cohort 2 (N=30)
Objective response rate (80% CI), %	27 (16–40)
Best overall response, n (%)	
Complete response	2 (6.7)
Partial response	6 (20)
Stable disease	11 (37)
Progressive disease	7 (23)
Missing	4 (13)
Disease control rate, n (%)	19 (63)
Duration of objective response, median (range), months	NR (1.4+–15.6+)
Time to objective response, median (range), months	3.0 (1–6)

Pal SK et al. ASCO 2020;Abstract 5013.

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Cabozantinib (C) in Combination with Atezolizumab (A) in Urothelial Carcinoma (UC): Results from Cohorts 3, 4, 5 of the COSMIC-021 Study

Pal SK et al.

ASCO 2022;Abstract 4504.

June 3, 2022 – 5:09 PM EDT

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A Randomised, Double Blind, Phase II Clinical Trial of Maintenance Cabozantinib Following Chemotherapy for Metastatic Urothelial Carcinoma (mUC): Final Analysis of the ATLANTIS Cabozantinib Comparison

Jones RJ et al.

ASCO 2022;Abstract LBA4505.

June 3, 2022 – 5:21 PM EDT

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Breast Cancer

A CME Hybrid Symposium Held in Conjunction with the 2022 ASCO Annual Meeting

Monday, June 6, 2022
7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)

Faculty

Javier Cortés, MD, PhD
Matthew P Goetz, MD
Erika Hamilton, MD
Ian E Krop, MD, PhD
Hope S Rugo, MD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Thank you for joining us!

CME links will be posted in the chat (Zoom participants only) and emailed to all participants within 24 hours of the program.

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