What I Tell My Patients:
New Treatments and Clinical Trial Options

An NCPD Hybrid Symposium Series
Held During the 47th Annual ONS Congress

Bladder Cancer

Saturday, April 30, 2022
12:15 PM – 1:45 PM PT

Faculty

Monica Averia, MSN, AOCNP, NP-C
Shilpa Gupta, MD
Brenda Martone, MSN, NP-BC, AOCNP
Sumanta Kumar Pal, MD

Moderator

Neil Love, MD

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Faculty

Monica Averia, MSN, AOCNP, NP-C
Oncology Nurse Practitioner
USC Norris Cancer Center
Los Angeles, California

Shilpa Gupta, MD
Associate Professor
Director, Genitourinary Oncology Program
Taussig Cancer Institute, Cleveland Clinic
Cleveland, Ohio

Brenda Martone, MSN, NP-BC, AOCNP
Northwestern Medicine
Northwestern Memorial Hospital
Chicago, Illinois

Sumanta Kumar Pal, MD
Professor, Department of Medical Oncology and Therapeutics Research
City of Hope
Duarte, California

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Ms Averia — Disclosures

No relevant conflicts of interest to disclose

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Dr Gupta — Disclosures

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Ms Martone — Disclosures

No relevant conflicts of interest to disclose

Dr Pal — Disclosures

No relevant conflicts of interest to disclose

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

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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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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"What I Tell My Patients"
14th Annual RTP-ONS NCPD Symposium Series
ONS Congress, Anaheim, California — April 27 - May 1, 2022

Thursday April 28	**Prostate Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Ovarian Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Non–Small Cell Lung Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Hepatobiliary Cancers 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Friday April 29	**Small Cell Lung Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Chronic Lymphocytic Leukemia 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)
	Breast Cancer 6:00 PM – 8:00 PM PT (9:00 PM – 11:00 PM ET)
	Acute Myeloid Leukemia and Myelodysplastic Syndromes 8:20 PM – 9:20 PM PT (11:20 PM – 12:20 AM ET)
Saturday April 30	**Cervical and Endometrial Cancer** 6:00 AM – 7:30 AM PT (9:00 AM – 10:30 AM ET)
	Bladder Cancer 12:15 PM – 1:45 PM PT (3:15 PM – 4:45 PM ET)

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Join Us After ONS for Our Series Continuation

What I Tell My Patients —
A 2-Part NCPD Webinar Series

Hodgkin and Non-Hodgkin Lymphomas

Date and time to be announced

Gastroesophageal Cancers

Wednesday, May 18, 2022

5:00 PM – 6:00 PM ET

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Ten years from now, what will the death rate from cancer be compared to today?

1. Increased
2. Decreased modestly (<20% reduction)
3. Decreased substantially (20%-50% reduction)
4. Eliminated (>90% reduction)

Agenda

Module 1 – Management of Localized Urothelial Bladder Cancer (UBC): Adjuvant Treatment, TAR-200

Module 2 – Management of Metastatic UBC: Antibody-Drug Conjugates, Checkpoint Inhibitors

Module 3 – Management of FGFR-Mutant UBC

Module 4 – Oncology/UBC 2032 and Crystal Ball: Part 2

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Agenda

Module 1 – Management of Localized Urothelial Bladder Cancer (UBC): Adjuvant Treatment, TAR-200

Module 2 – Management of Metastatic UBC: Antibody-Drug Conjugates, Checkpoint Inhibitors

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Module 4 – Oncology/UBC 2032 and Crystal Ball: Part 2

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SELF-ASSESSMENT QUIZ

Usual initial treatment for non-muscle invasive bladder cancer is…

1. Observation
2. Bacillus Calmette-Guérin (BCG)
3. Cystectomy
4. Immune checkpoint inhibitor
5. I don’t know

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SELF-ASSESSMENT QUIZ

What is the mechanism of action of TAR-200?

1. Antibody-drug conjugate
2. FGFR inhibitor
3. PD-1/PD-L1 inhibitor
4. Intravesicular gemcitabine
5. I don’t know

SELF-ASSESSMENT QUIZ

Most patients with muscle-invasive bladder cancer are initially treated with cystectomy followed by adjuvant therapy.

1. Agree
2. Disagree
3. I don't know

SELF-ASSESSMENT QUIZ

Which of the following is FDA approved as adjuvant therapy for bladder cancer?

1. Enfortumab vedotin
2. Erdafitinib
3. Pembrolizumab
4. Nivolumab
5. I don’t know

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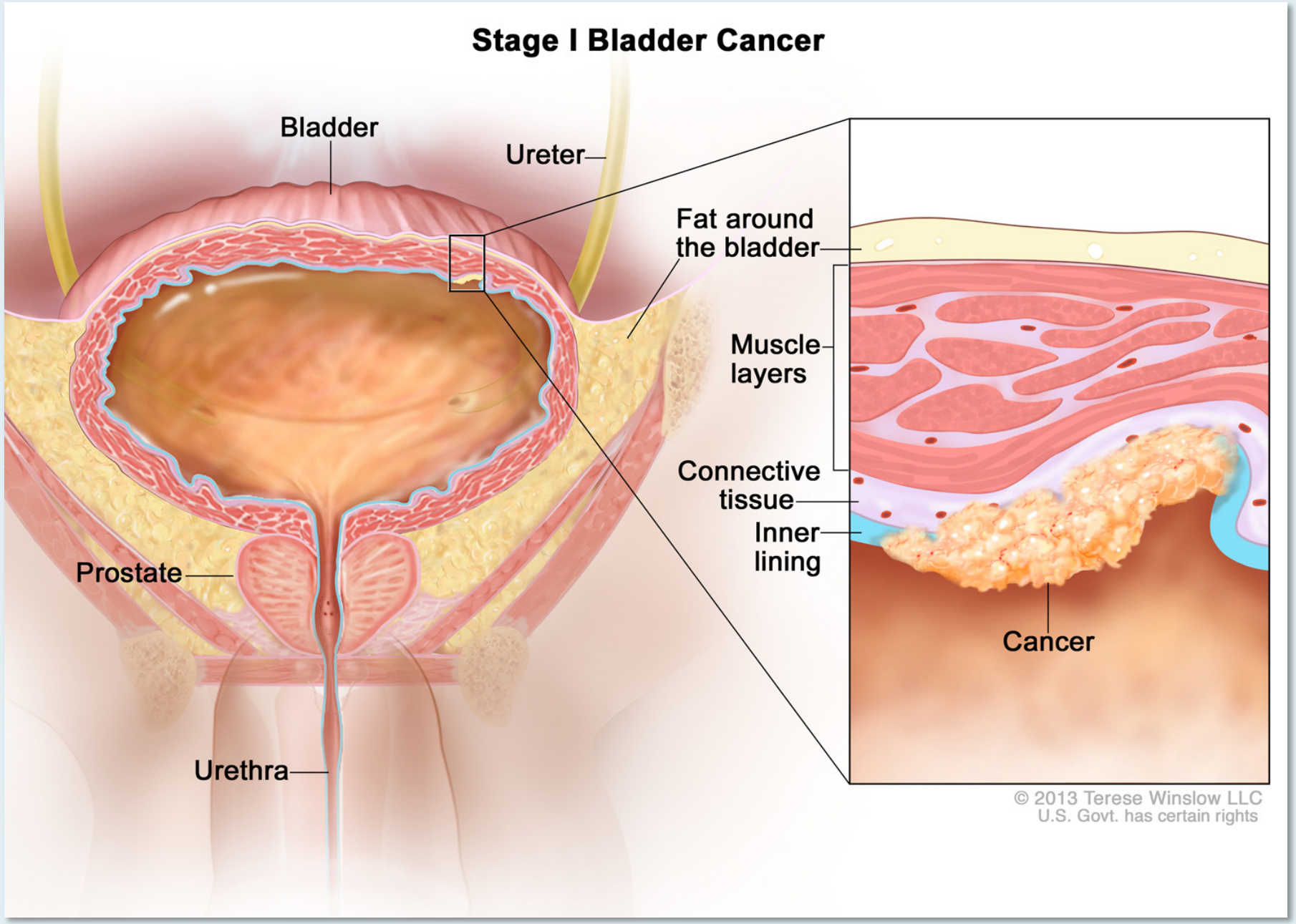
Overview of Bladder Cancer

- Patient profile
  - Median age at diagnosis: 73 years
  - 76% male
  - Smoking is the most well-established risk factor (47% of all cases in the US)
- Natural history
  - Non-muscle-invasive
  - Muscle-invasive
  - Metastatic
- Cystectomy and ileal conduit/stoma management
- Neoadjuvant and adjuvant chemotherapy

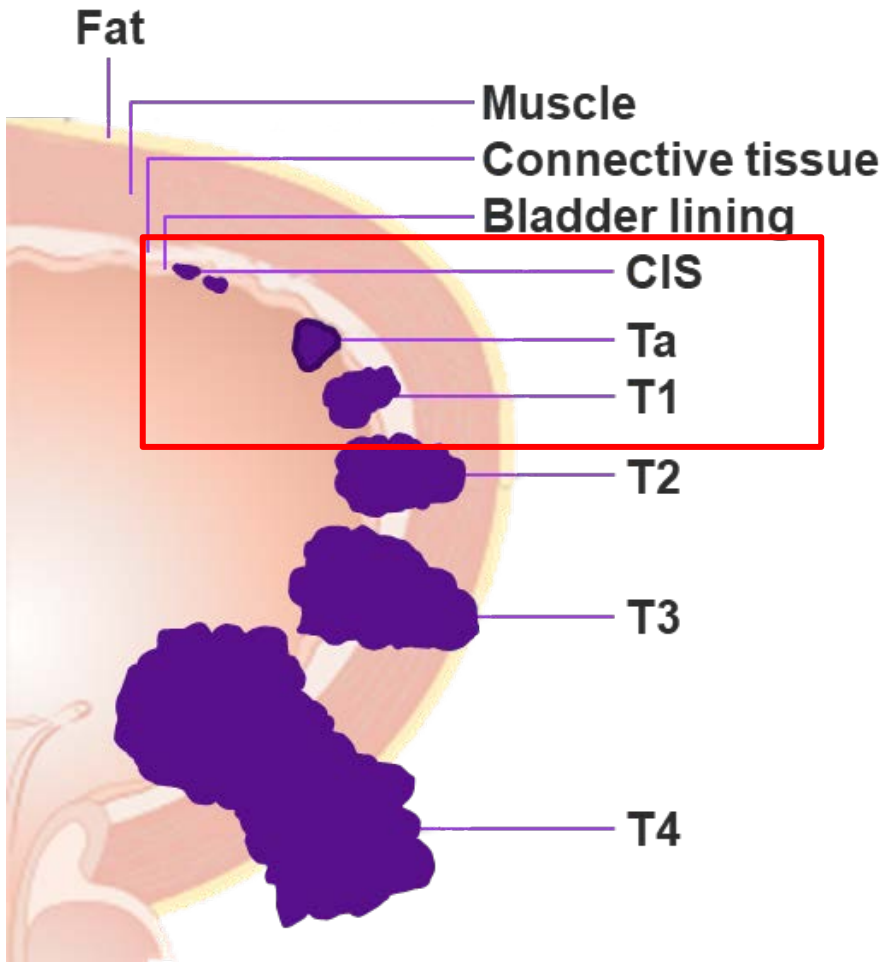
ACS Cancer Facts & Figures 2020; www.cancer.org.



With permission from Terese Winslow LLC

High-Risk Non–Muscle-Invasive BC

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



Cumberbatch MGK et al. *Eur Urol.* 2018;74:784-795. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN guidelines): bladder cancer (Version 1.2019). https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed January 7, 2019. Hemdan T et al. *J Urol*. 2014;191:1244. Herr HW et al. *Urol Oncol.* 2015;33:108.e1-4. 5. Anastasiadis A et al. *Ther Adv Urol.* 2012;4:13-32. US Department of Health and Human Services. BCG-unresponsive nonmuscle invasive bladder cancer: developing drugs and biologics for treatment—Guidance for industry. February 2018. https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm529600.pdf. Accessed February 5, 2019. Babjuk M et al. *Eur Urol.* 2017;71:447-461.

NYU Langone Health

Courtesy of Arjun V. Balar, MD

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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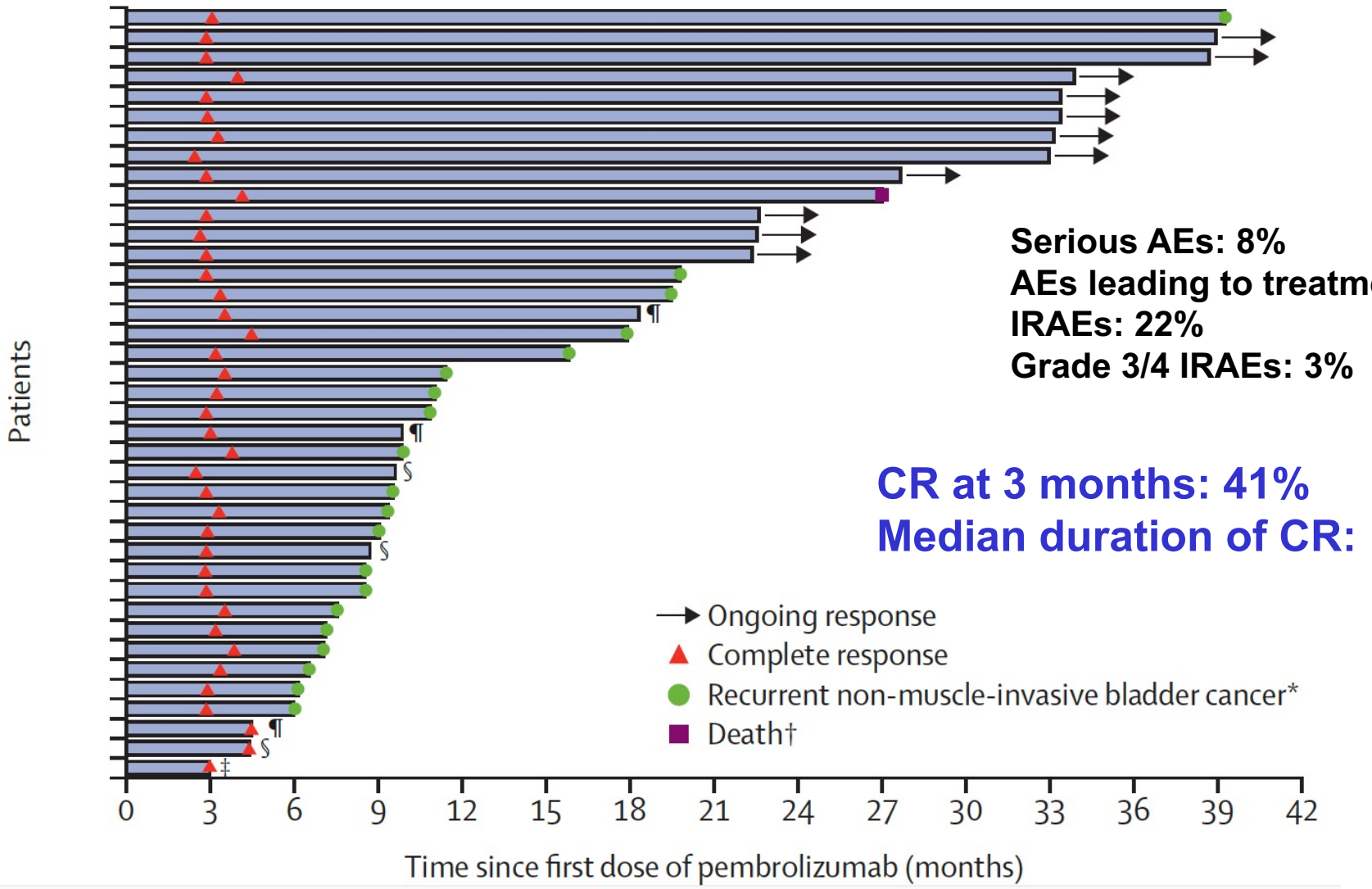
KEYNOTE-057: Pembrolizumab for High-Risk NMIBC

Response, Duration of Response and Summary of Adverse Events



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

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

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

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

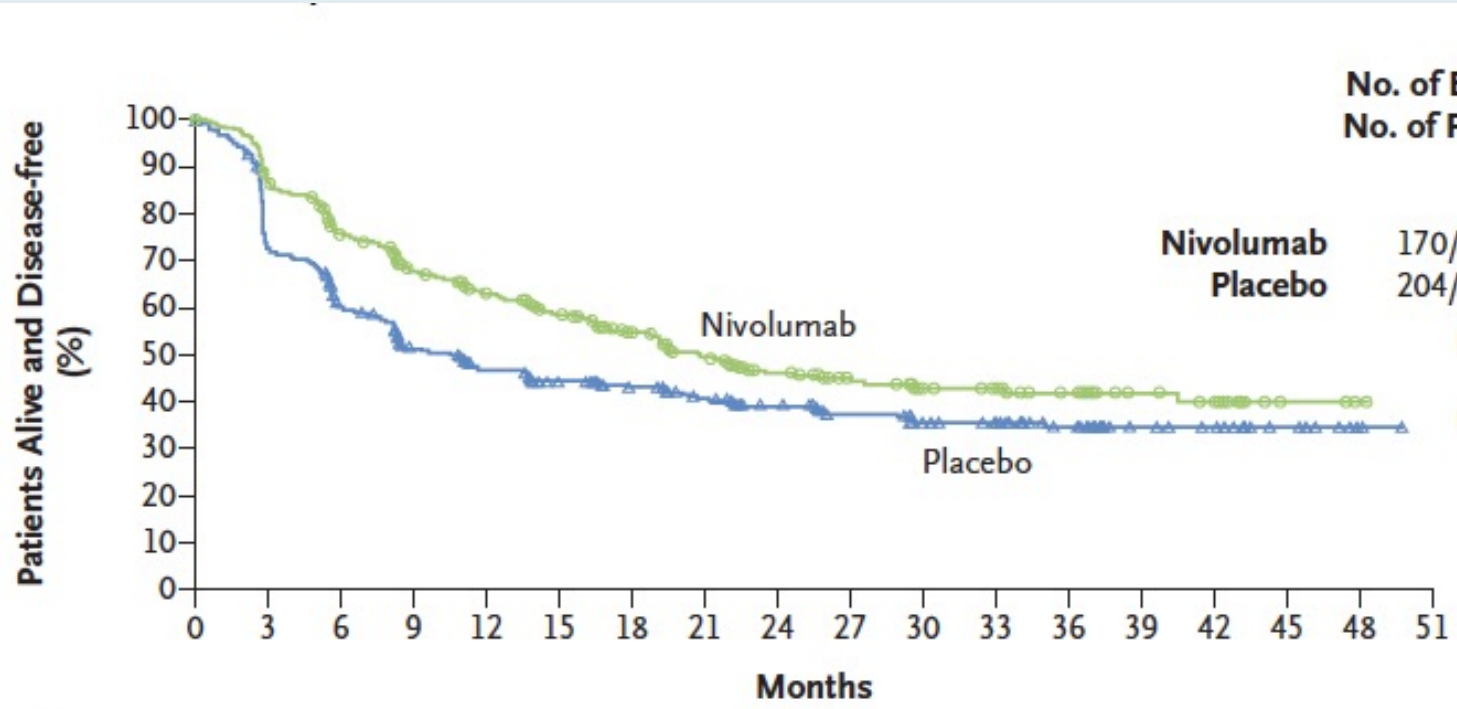
Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

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.

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)

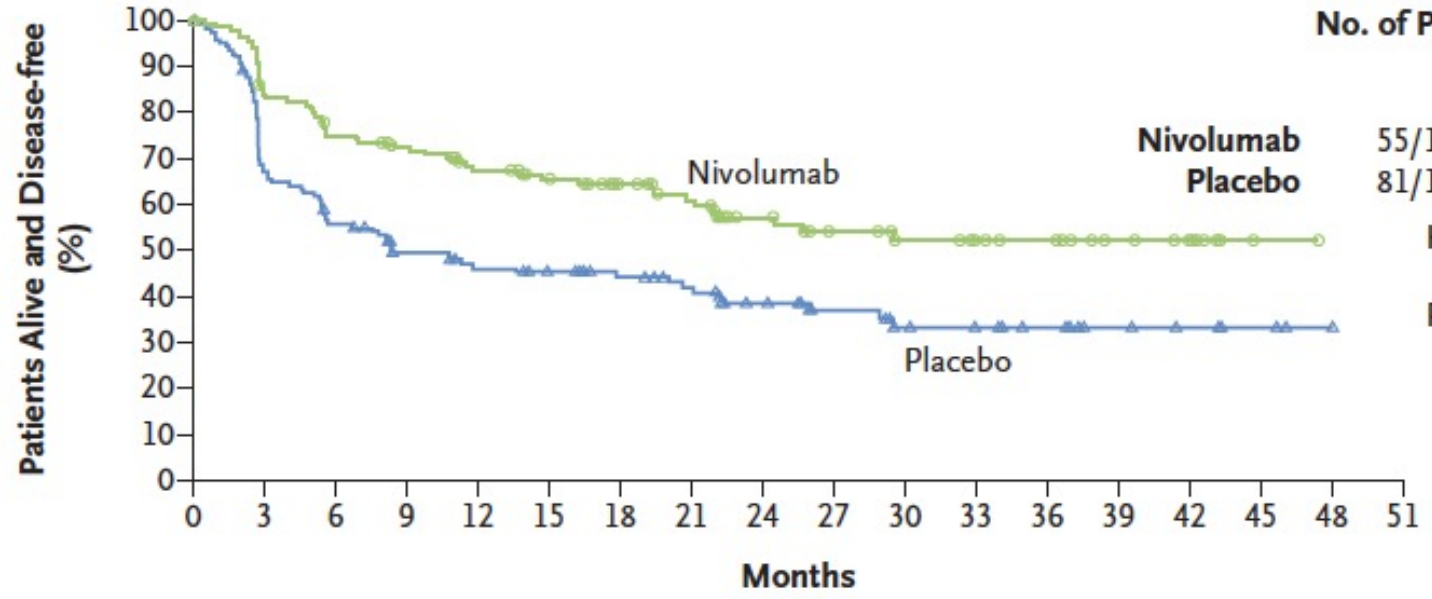
Hazard ratio for disease recurrence or death, 0.70 (98.22% CI, 0.55–0.90)
P<0.001

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 in Patients with PD-L1 Expression Level 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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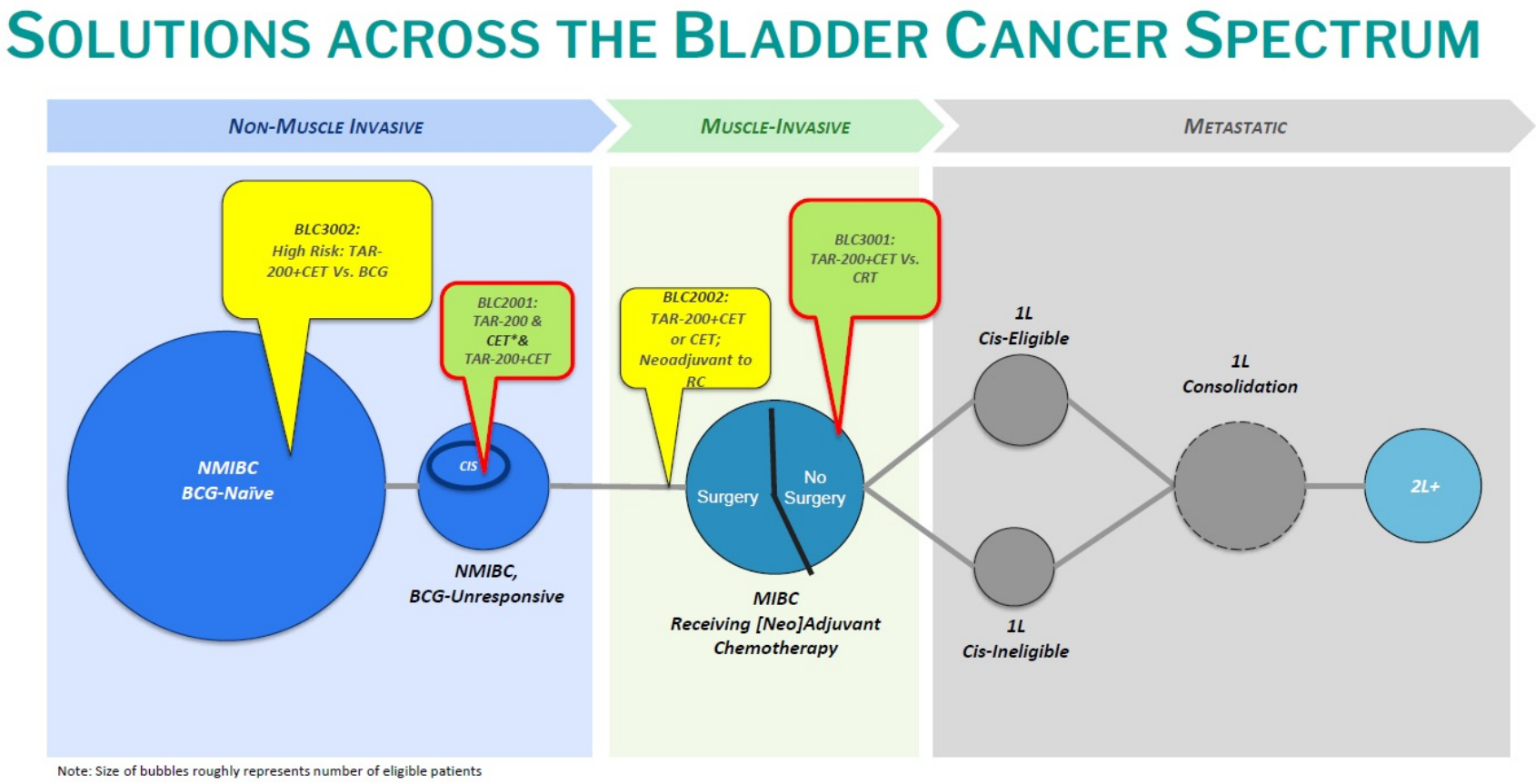
PARADIGM SHIFT: DELIVERY SYSTEMS ENTER THE ROOM…

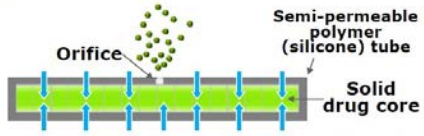


Courtesy of Stephen B Williams, MD

PARADIGM SHIFT: DELIVERY SYSTEMS ENTER THE ROOM…

TAR-200 System Allows Controlled Drug Delivery

Example of Delivery: Osmotic Engine

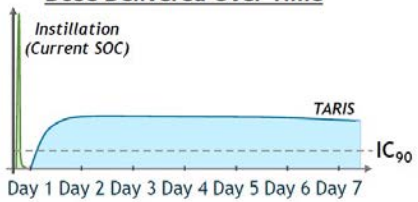


Osmotic pump modulates drug release from internal reservoir

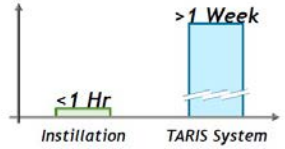
Dose and duration tailored to specific disease states

Rational dosing maximizes intracellular drug potency

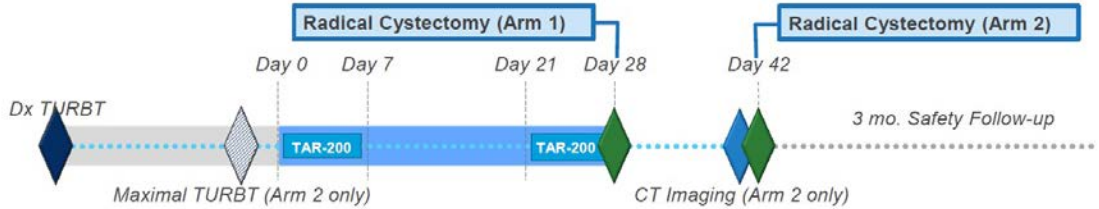
Dose Delivered Over Time



Time of Drug Exposure >IC90



Proof of Principle: TAR-200-101 in MIBC Neoadjuvant to RC



- Organ-confined, non-metastatic MIBC patients
  - Clinical Staging: cT_2-cT_3 N_{0-1} M_0
- TAR-200 administered neoadjuvant to radical cystectomy
- Status: Complete, 20 patients through cystectomy (10/Arm)

TABLE 3: Pathologic Response in the ITT Population

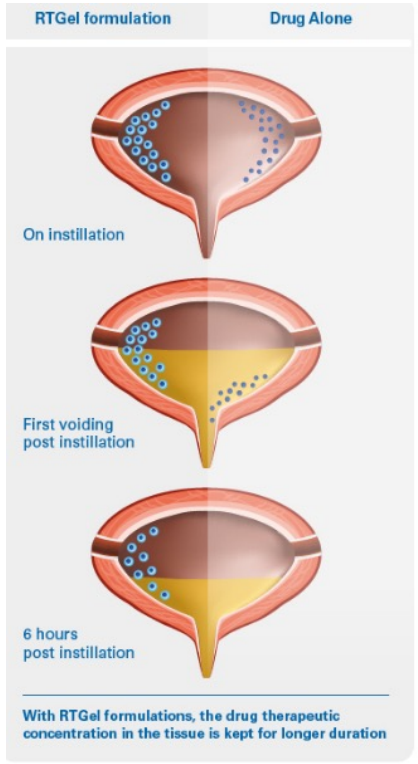
Response, n/N (%)	Arm 1 (> 3 cm)	Arm 2 (< 3 cm)
Underwent pathology at RC	10/11 (91)[a]	10/12 (83)[b]
Pathologic response	4/10 (40)	6/10 (60)
pCR	1/10 (10)	3/10 (30)
pPR	3/10 (30)	3/10 (30)

[a]1 patient in Arm 1 did not receive either dosing cycle due to an initial unsuccessful insertion attempt. [b]2 patients in Arm 2 discontinued study treatment before the second dosing cycle (1 consent withdrawal, 1 local disease progression).

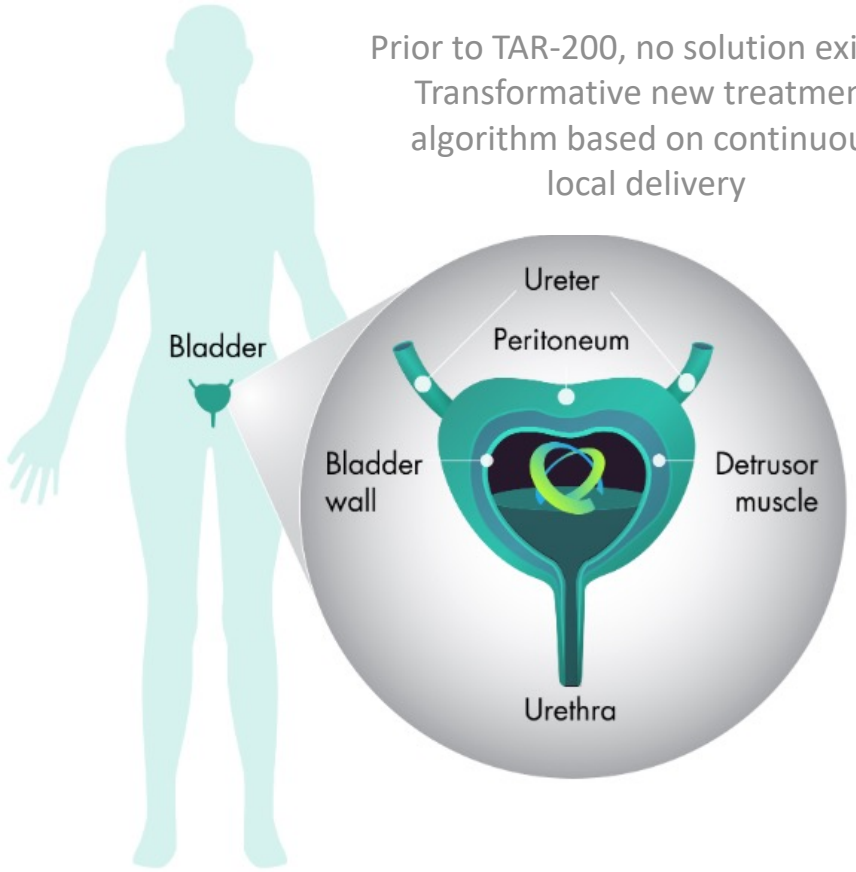
TAR-200 is safe, well tolerated, 50% pCR or pPR

Courtesy of Stephen B Williams, MD

TAR-200



Prior to TAR-200, no solution existed
Transformative new treatment algorithm based on continuous local delivery



Courtesy of Ashish M Kamat, MD

ELSEVIER

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

UROLOGIC ONCOLOGY

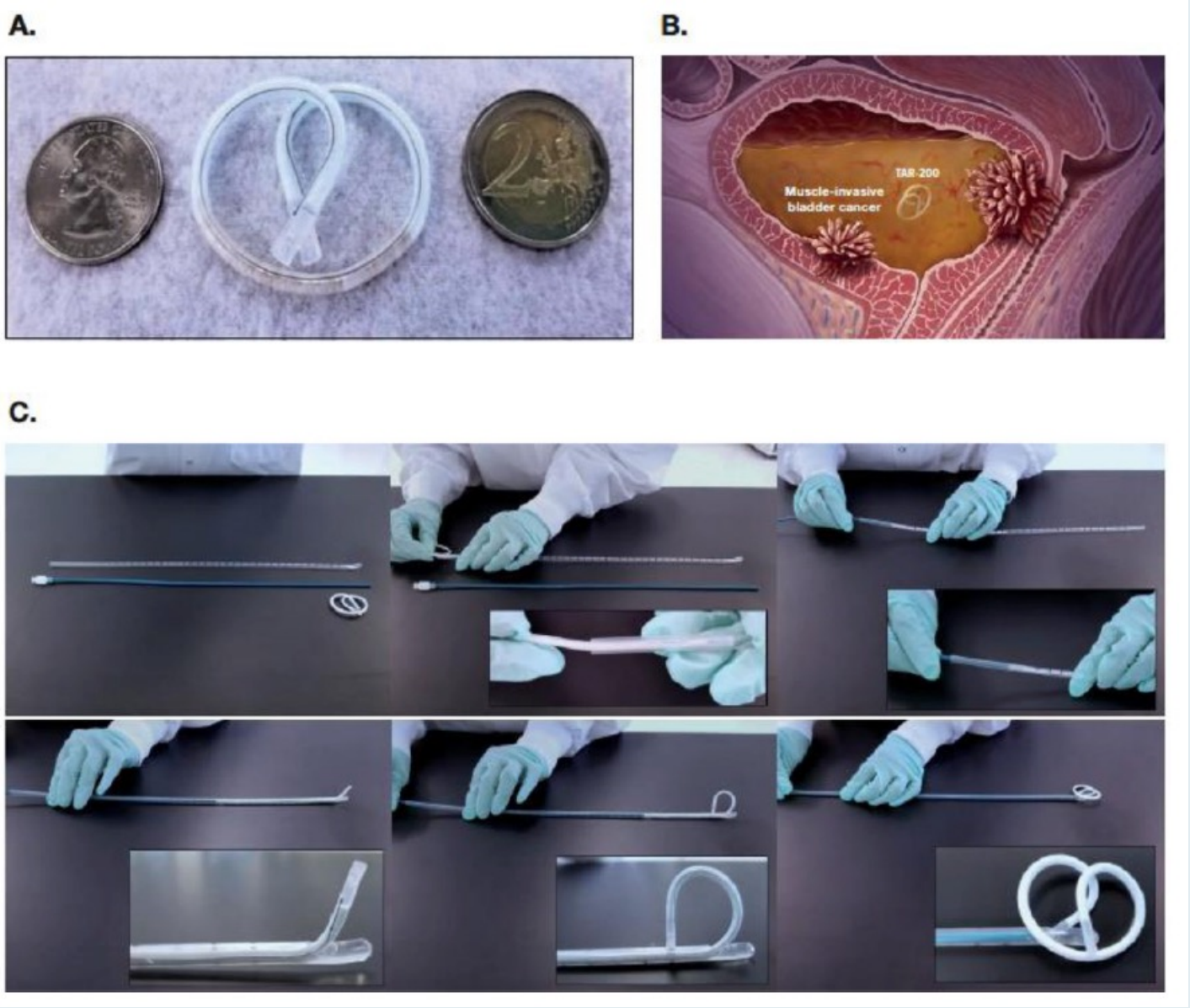
Clinical-Bladder cancer

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].**

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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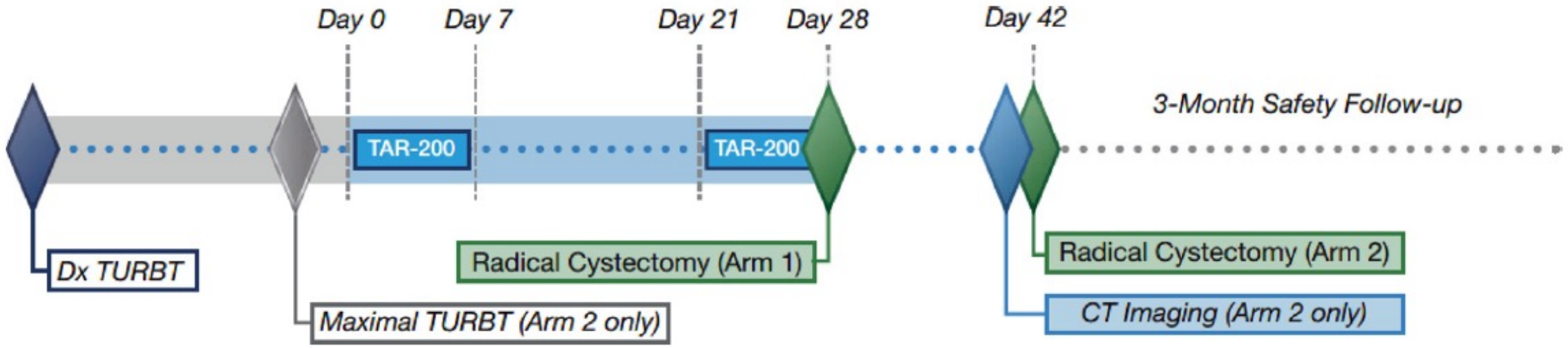
TAR-200-101: Study Design and Outcomes



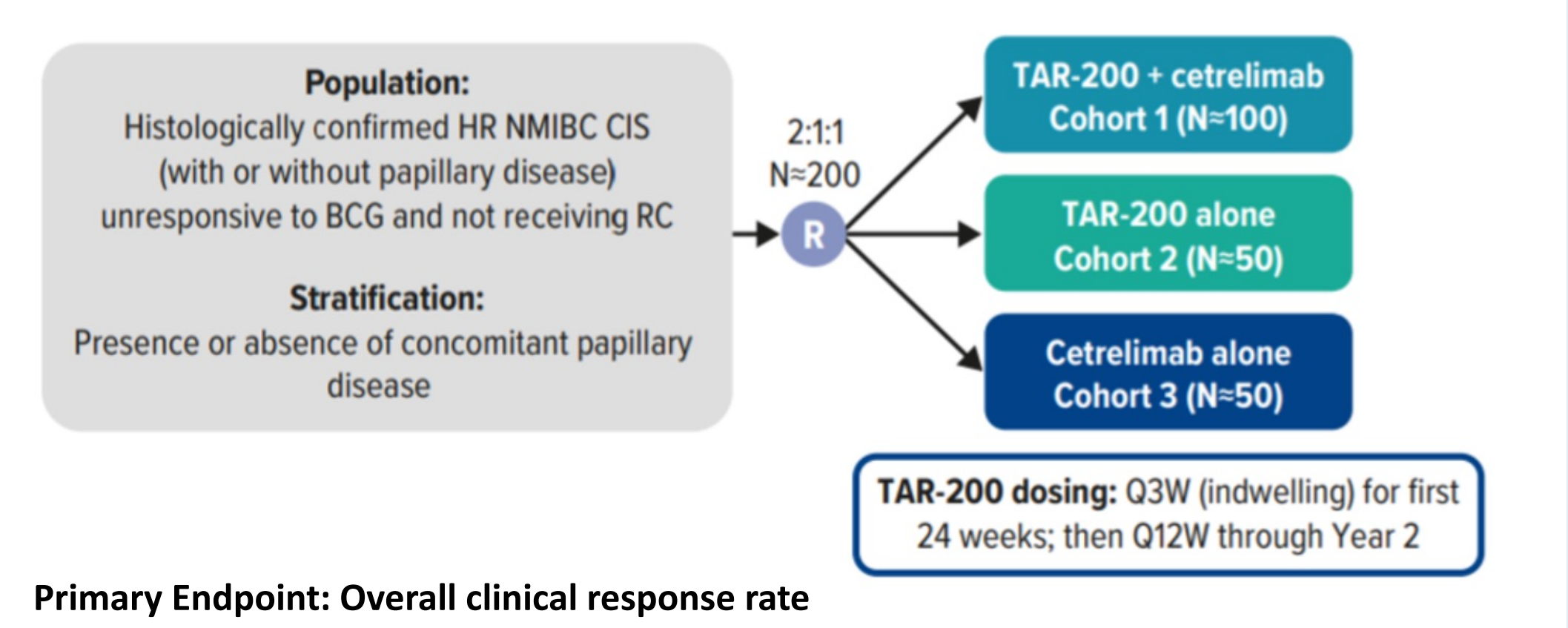
Response	Arm 1 (>3 cm)	Arm 2 (max TURBT)
Underwent pathology at RC, *n/N* (%)	10/11 (90.9)	10/12 (83.3)
Pathologic response, *n/N* (%)	4/10 (40.0)	6/10 (60.0)
Complete response, *n/N* (%)	1/10 (10.0)	3/10 (30.0)
Partial response, *n/N* (%)	3/10 (30.0)	3/10 (30.0)

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 Alone, Cetrelimab Alone, or the Combination for BCG-Unresponsive, High-Risk Non-Muscle-Invasive Bladder Cancer

Clinical Trial Identifier: NCT04640623



Primary Endpoint: Overall clinical response rate

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

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Questions — Shilpa Gupta, MD

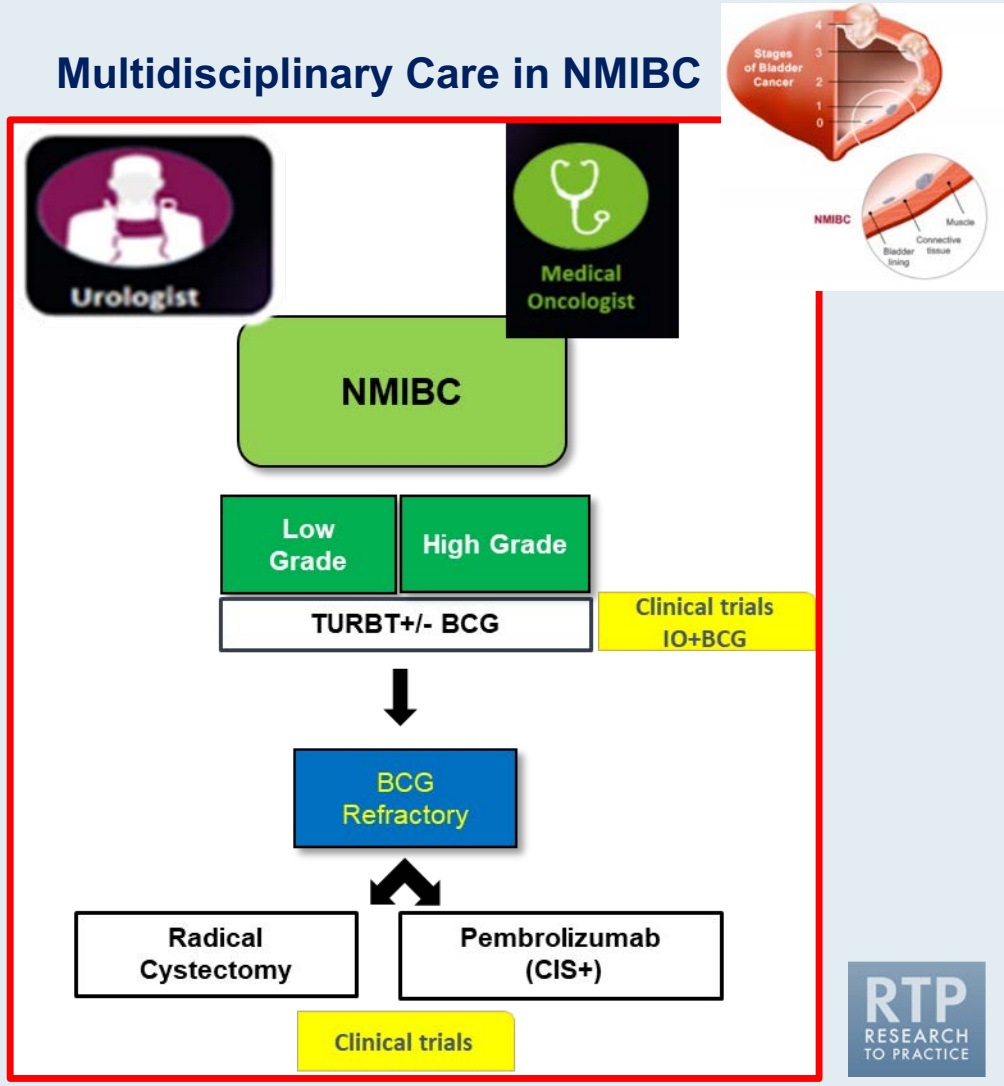
Patients with non-muscle-invasive bladder cancer (NMIBC)

- **How is NMIBC typically diagnosed and managed?**
- **How do you explain to patients how the available therapies for NMIBC work?**

Commentary — Shilpa Gupta, MD

Patients with non-muscle-invasive bladder cancer (NMIBC)

- **Presentation:**
  - **Hematuria, frequent/painful urination, pain**
- **Diagnosis:**
  - **Need timely referral to Urology**
  - **Urine cytology, Imaging, Cystoscopy, TURBT**
- **Treatment:**
  - **TURBT +/- Intravesical BCG**
  - **Immunotherapy in select cases**
  - **Novel intravesical therapy/immunotherapy trials**
  - **Radical cystectomy**
  - **Patients prefer bladder preservation approaches**



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Questions — Monica Averia, MSN, AOCNP, NP-C

Patients with non-muscle-invasive bladder cancer (NMIBC)

- **What are some of the clinical and support issues that arise for patients undergoing cystectomy and urinary diversion?**
- **What are some of the clinical and support issues that arise for patients who have received chemoradiation and are now eligible for surgery?**
- **What are some of the psychosocial issues that arise in these situations?**

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Commentary — Monica Averia, MSN, AOCNP, NP-C

Patients with non-muscle-invasive bladder cancer (NMIBC)

What are some of the clinical and support issues that arise for pts undergoing cystectomy and urinary diversion?

- **RC and UD pts require tremendous support.**

a. **Preoperative period**

b. **Self-care challenges**

c. **Postoperative period**

Commentary — Monica Averia, MSN, AOCNP, NP-C

What are some of the clinical and support issues that arise for pts who have received chemoradiation and are now eligible for surgery?

- **Chemoradiation patients tend to have already gone through the SE profile of both regimens:**
- **Fatigue, nausea, vomiting, diarrhea, neuropathy, decreased counts, and reduced QOL.**

Presenting surgery as an option in some pts can be viewed as:

A. Welcomed option

B. Challenging option

Commentary — Monica Averia, MSN, AOCNP, NP-C

Cite brief instructive examples of actual clinical experiences with pts in your practice.

Med onc

- **Post op pts referred for adjuvant Tx**
- **Fear, uncertainty, and knowledge deficit**
- **Empower pts with correct info to help them decide on life changing treatment options**

What are some of the PSYCHOSOCIAL issues that arise in these situations?

- **Radical cystectomy and urinary diversion**
- **Often associated with permanent alteration of body image and function**
- **Poses a serious threat to the patient's psychological well-being**

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Commentary — Monica Averia, MSN, AOCNP, NP-C

Life after cystectomy and urinary diversion:

1. **Body function changes**
2. **Financial impact**
3. **Loss of independence and control**
4. **Lifestyle changes**
5. **Effects on sexuality and intimacy**
6. **Feelings of anxiety and depression over cancer recurrence**
7. **Pain management**

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Agenda

Module 1 – Management of Localized Urothelial Bladder Cancer (UBC): Adjuvant Treatment, TAR-200

Module 2 – Management of Metastatic UBC: Antibody-Drug Conjugates, Checkpoint Inhibitors

Module 3 – Management of FGFR-Mutant UBC

Module 4 – Oncology/UBC 2032 and Crystal Ball: Part 2

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SELF-ASSESSMENT QUIZ

Patients with metastatic urothelial bladder cancer (mUBC) may be designated as “platinum-ineligible” due to…

1. Renal dysfunction
2. Poor performance status
3. Peripheral neuropathy
4. All of the above
5. Only 1 and 2
6. Only 2 and 3
7. Only 1 and 3
8. I don’t know

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Platinum Ineligibility

- Eastern Cooperative Oncology Group PS 2
- CrCl , 60 mL/min
- Grade ≥2 hearing loss
- Grade ≥2 neuropathy
- New York Heart Association Class III heart failure

Probability of cisplatin ineligibility increases with age. More than 40% of patients with MIBC age ≥70 years are ineligible.

Relief of ureteric obstruction and hydronephrosis using a stent or nephrostomy may convert cisplatin-ineligible patients to cisplatin-eligible.

SELF-ASSESSMENT QUIZ

What is the mechanism of action of enfortumab vedotin?

1. Antibody-drug conjugate
2. FGFR inhibitor
3. PD-1/PD-L1 inhibitor
4. Intravesicular gemcitabine
5. I don’t know

SELF-ASSESSMENT QUIZ

Enfortumab vedotin is showing encouraging results in the initial treatment of mUBC when combined with…

1. Erdafitinib
2. Chemotherapy
3. Anti-PD-1/PD-L1 agents
4. Trastuzumab deruxtecan
5. I don’t know

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ASCO Genitourinary Cancers Symposium 2022;Abstract 487

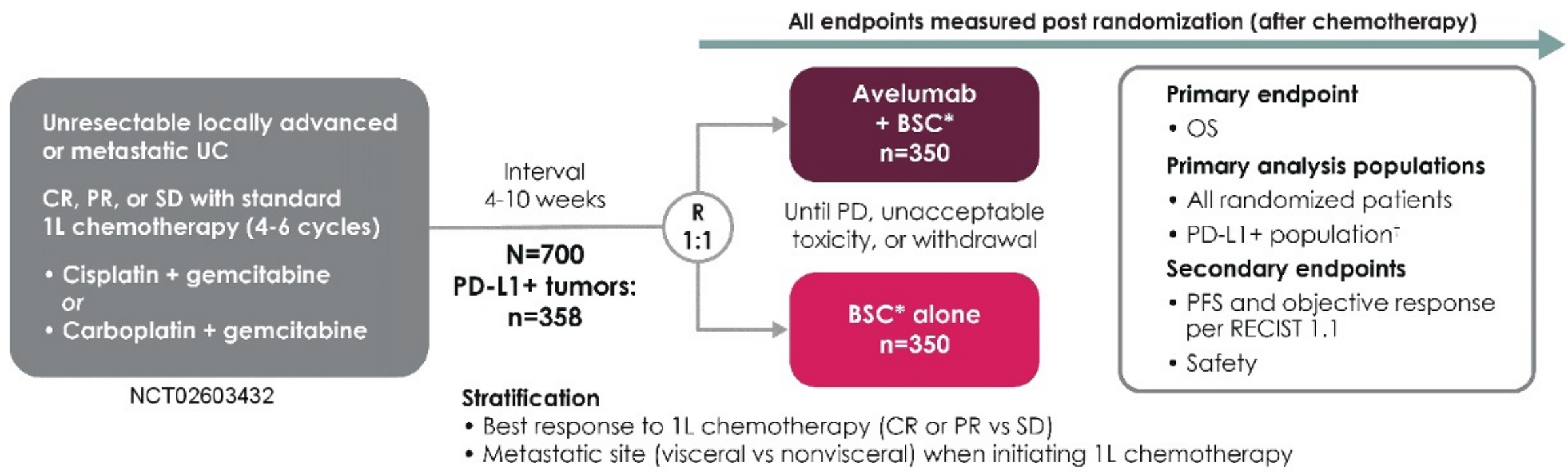
Avelumab first-line maintenance for advanced urothelial carcinoma: long-term follow-up results from the JAVELIN Bladder 100 trial

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

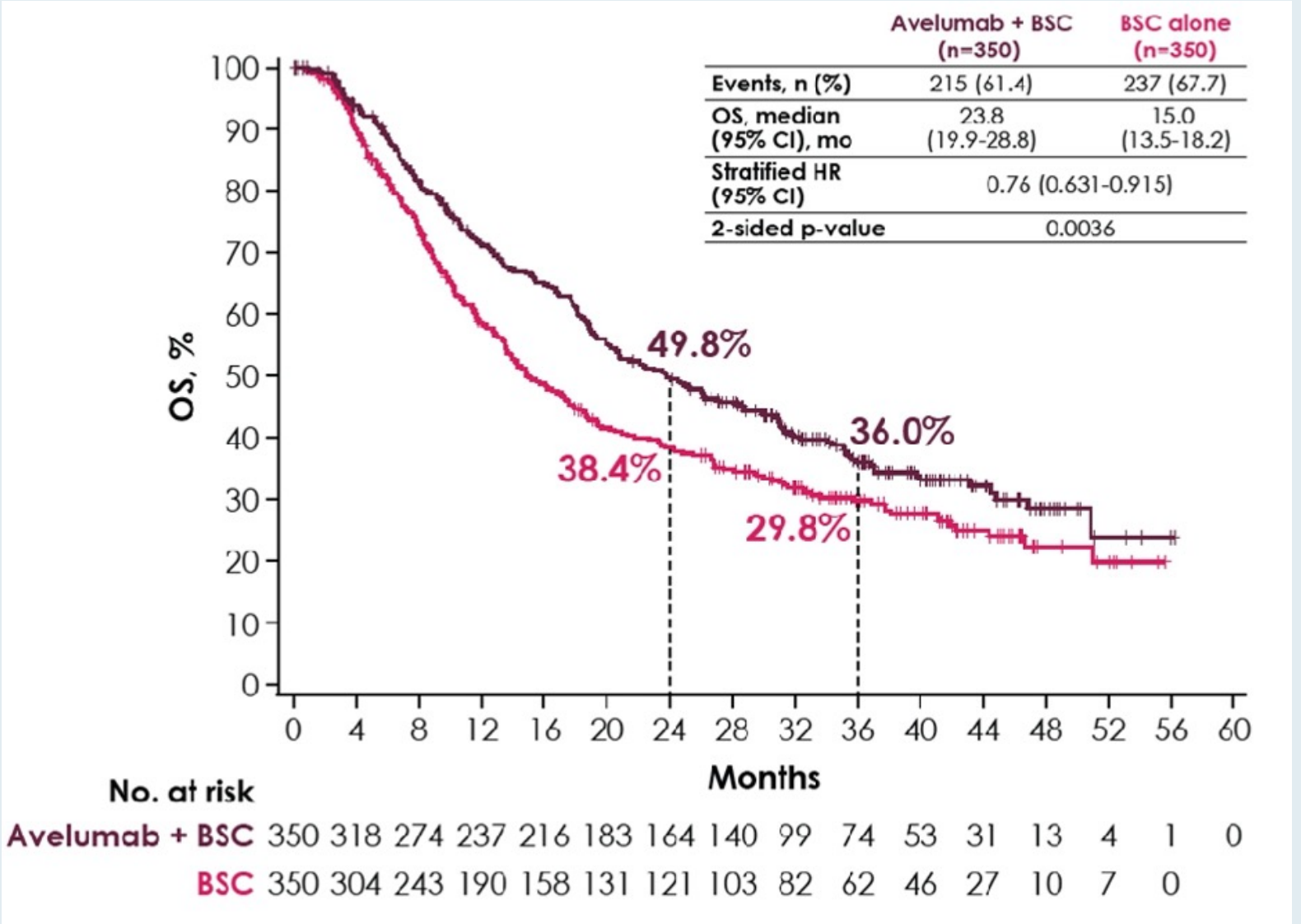
PRESENTED BY: Thomas Powles, MD

JAVELIN-100 Study Design



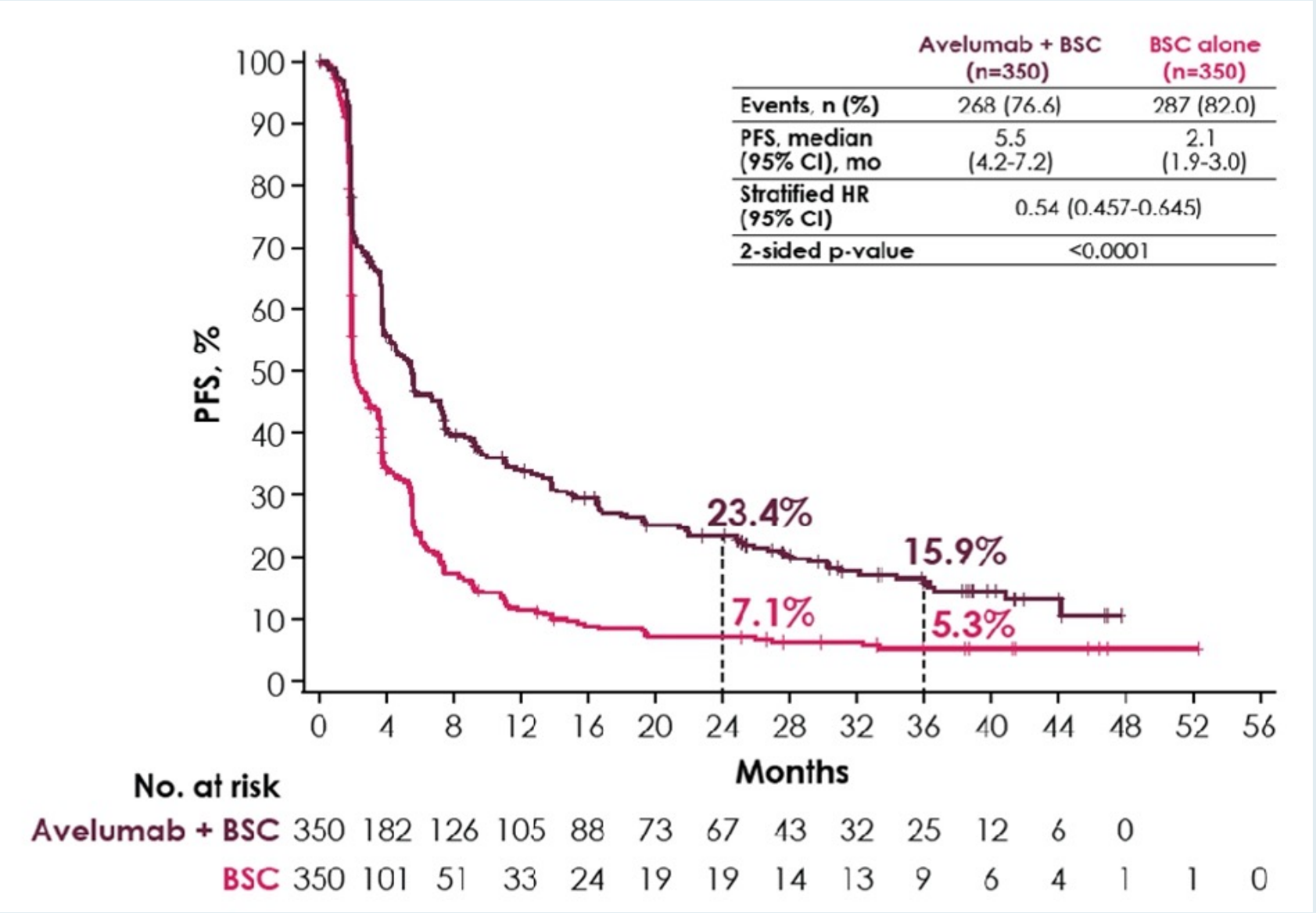
Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

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



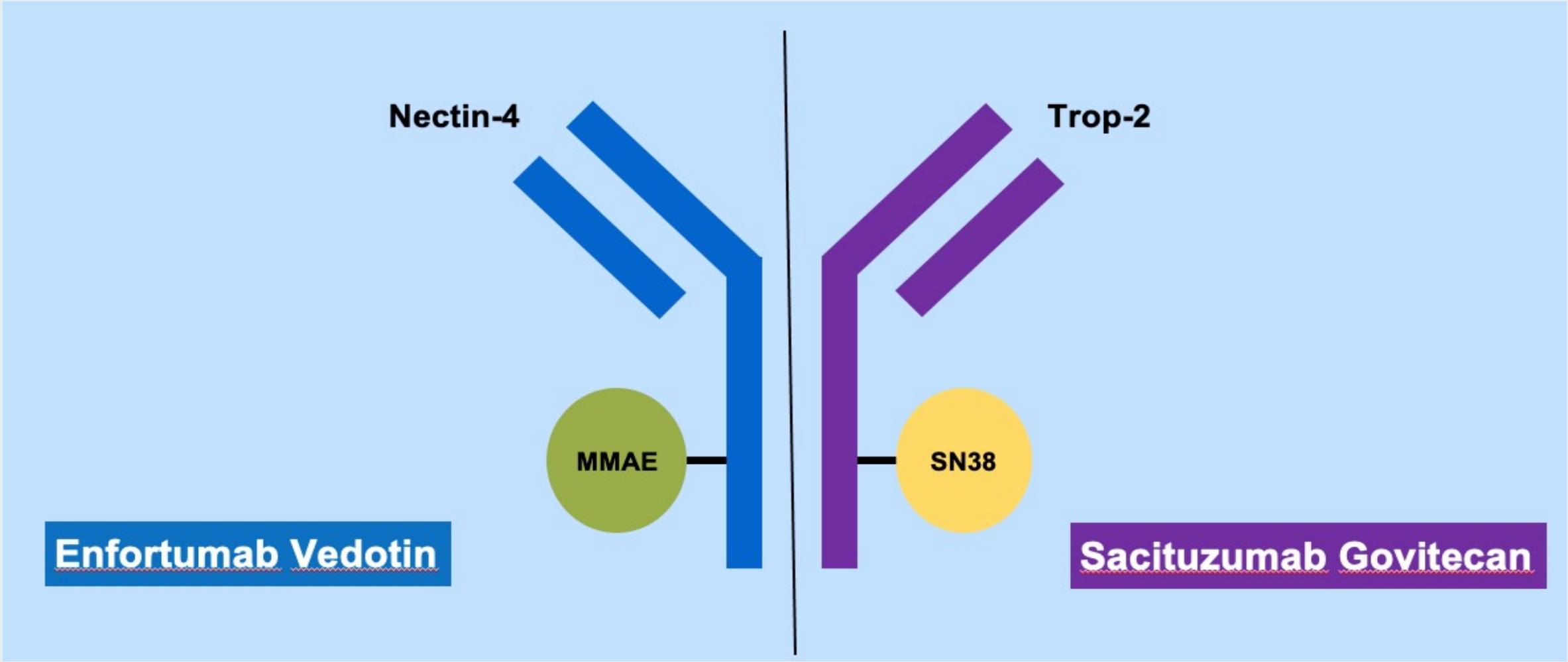
Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

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



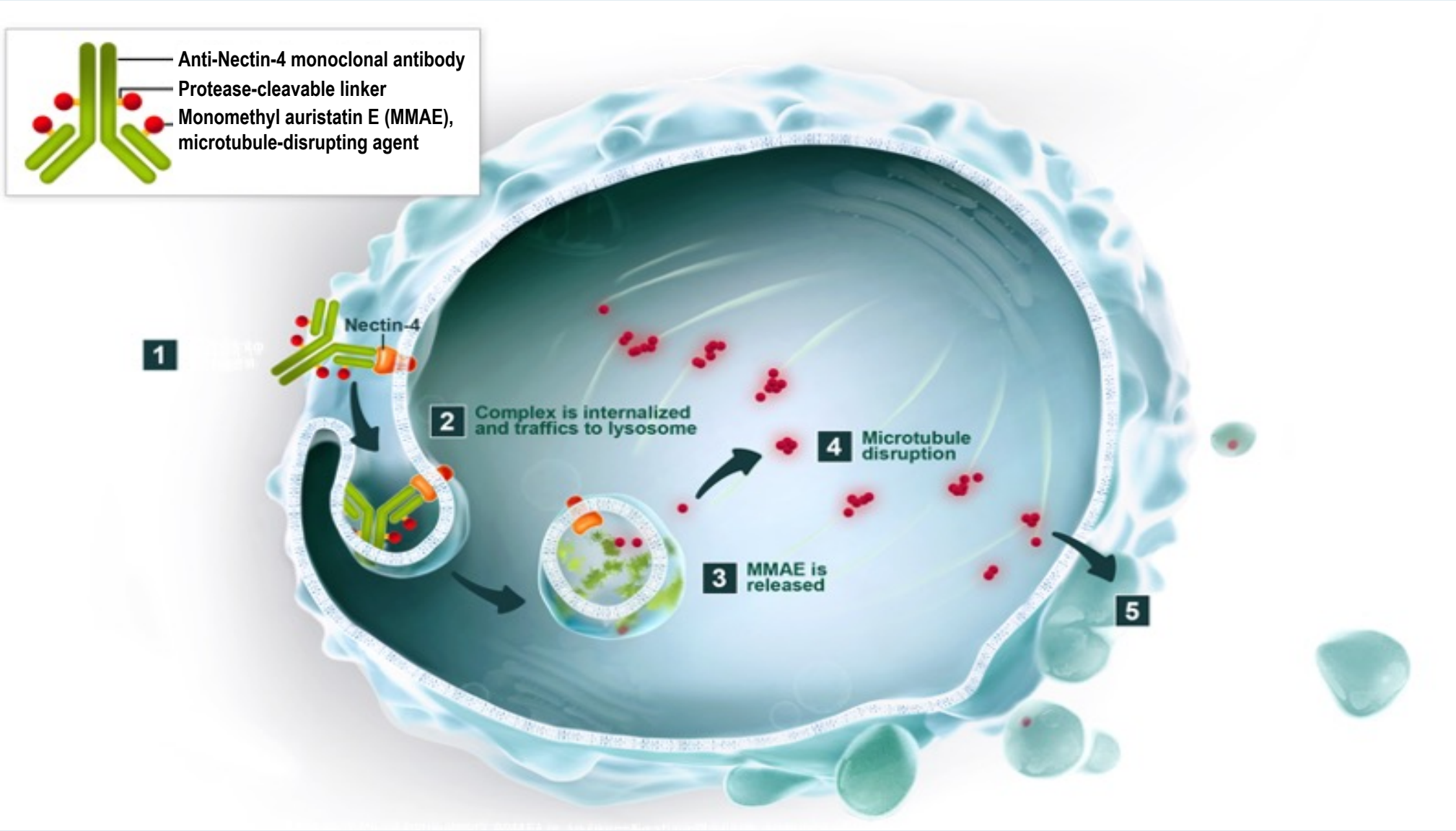
Powles T et al. Genitourinary Cancers Symposium 2022;Abstract 487.

Antibody-Drug Conjugates in UBC



Courtesy of Matthew Galsky, MD

Enfortumab Vedotin: Nectin-4 Targeted Therapy



Courtesy of Jonathan Rosenberg, MD

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

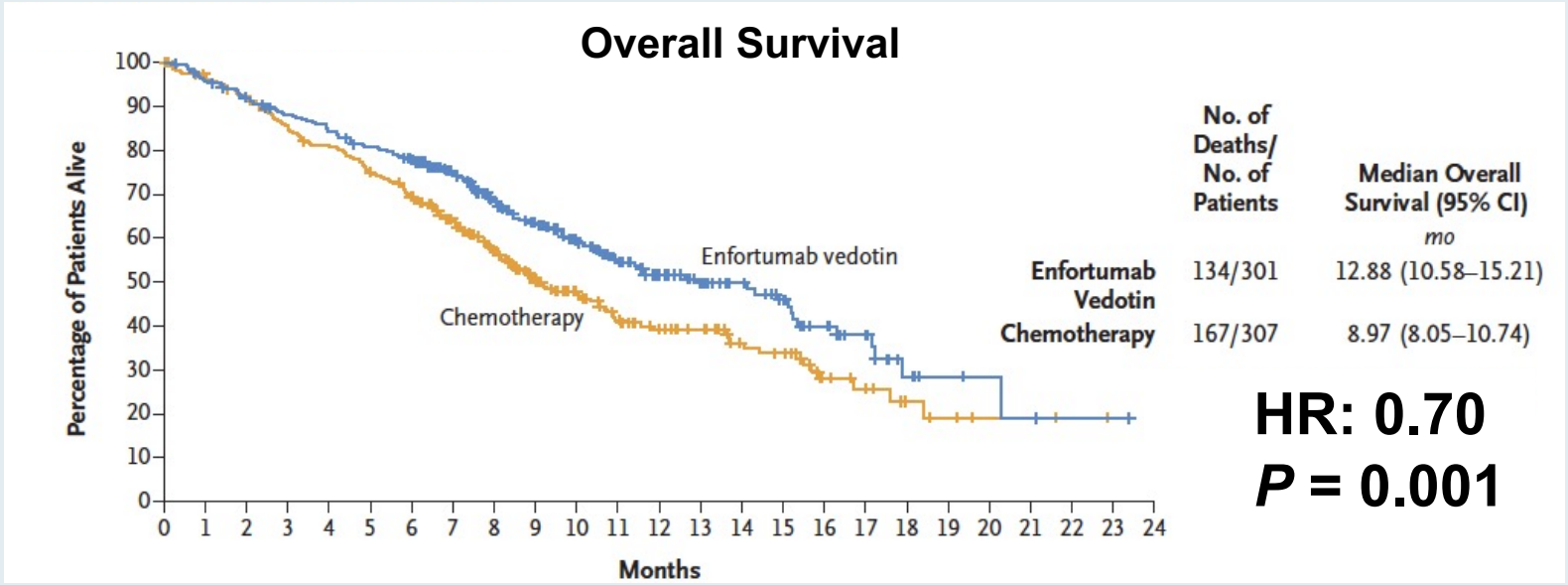
Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

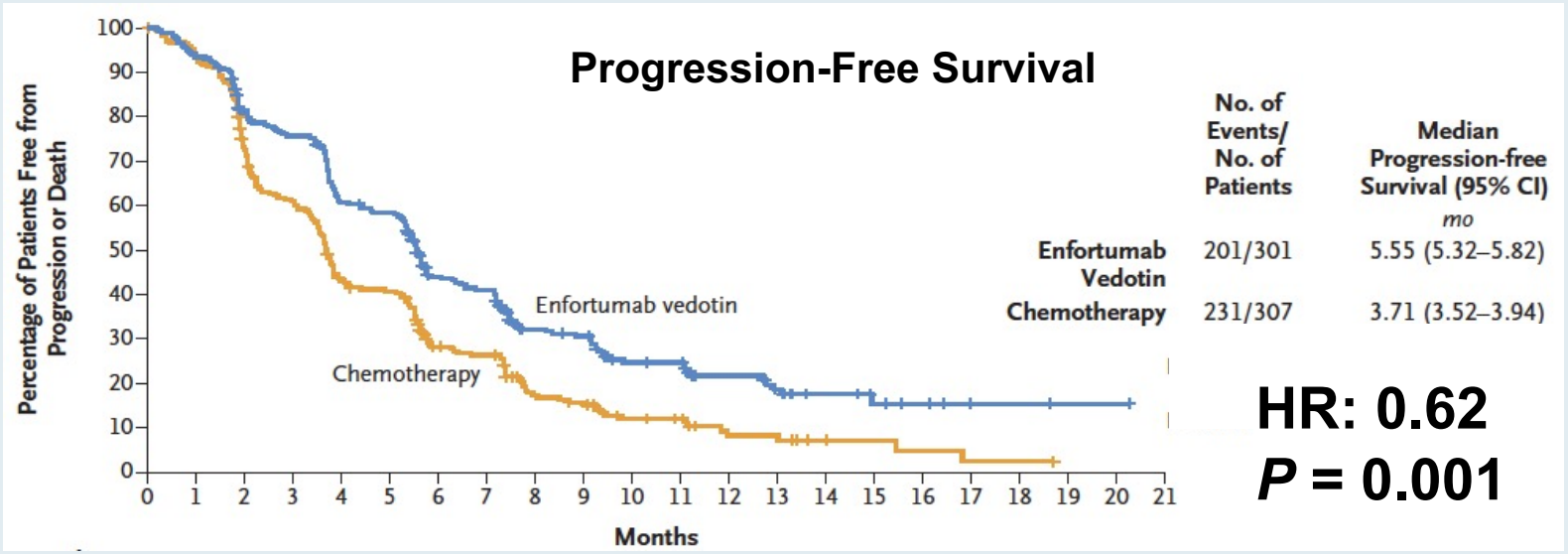
Thomas Powles, M.D., Jonathan E. Rosenberg, M.D., Guru P. Sonpavde, M.D., Yohann Loriot, M.D., Ph.D., Ignacio Durán, M.D., Ph.D., Jae-Lyun Lee, M.D., Ph.D., Nobuaki Matsubara, M.D., Christof Vulsteke, M.D., Ph.D., Daniel Castellano, M.D., Chunzhang Wu, Ph.D., Mary Campbell, M.D., Maria Matsangou, M.B.,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

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

EV-301: Enfortumab Vedotin for Previously-Treated Advanced UC

Survival Analyses





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

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EV-301: Antitumor Response

	EV (n = 288)	Chemo (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.

EV-301: Treatment-Related Adverse Events of Special Interest

Treatment-related adverse event (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%	

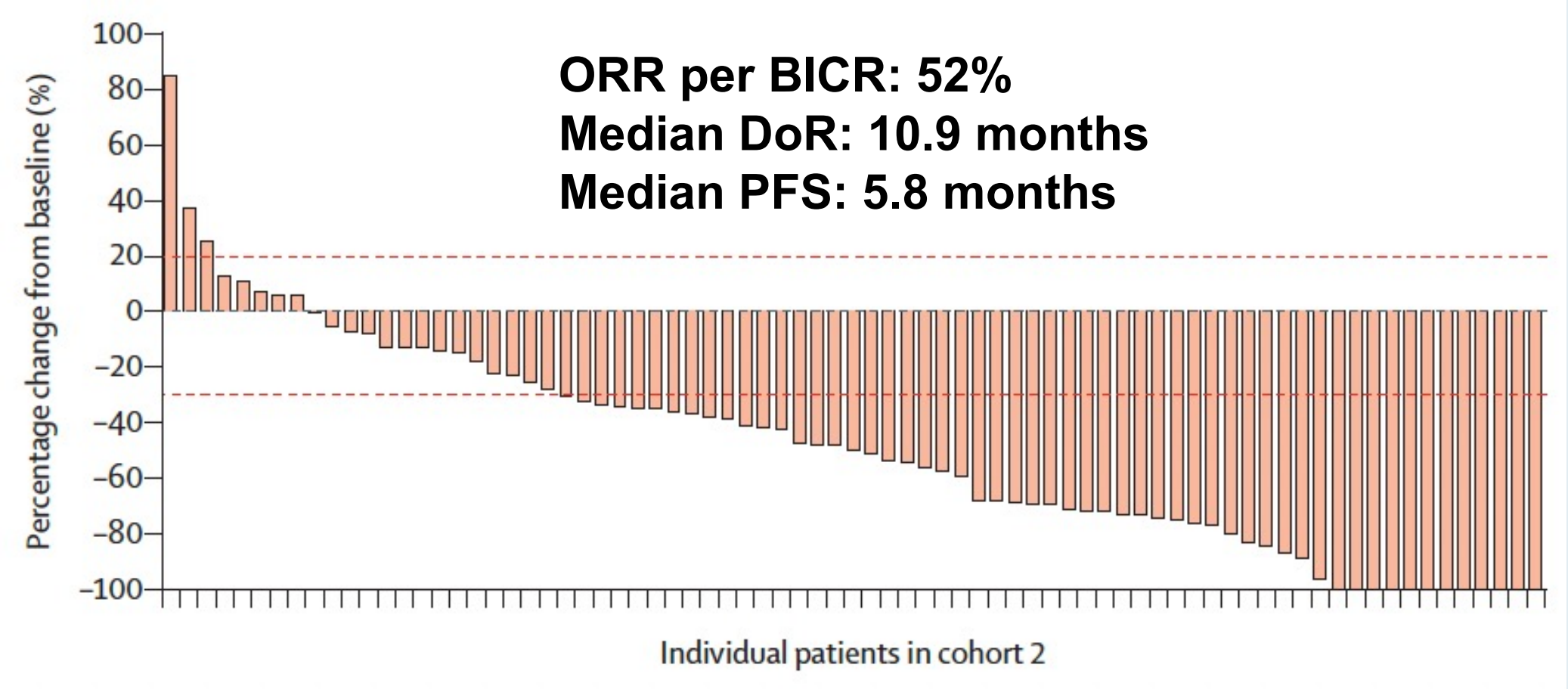
Powles T et al. *N Engl J Med* 2021;384(12):1125-35.

Lancet Oncol 2021;22(6):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: Enfortumab Vedotin for Cisplatin-Ineligible Patients with Advanced UC Previously Treated with PD-1 or PD-L1 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(6):872-82.

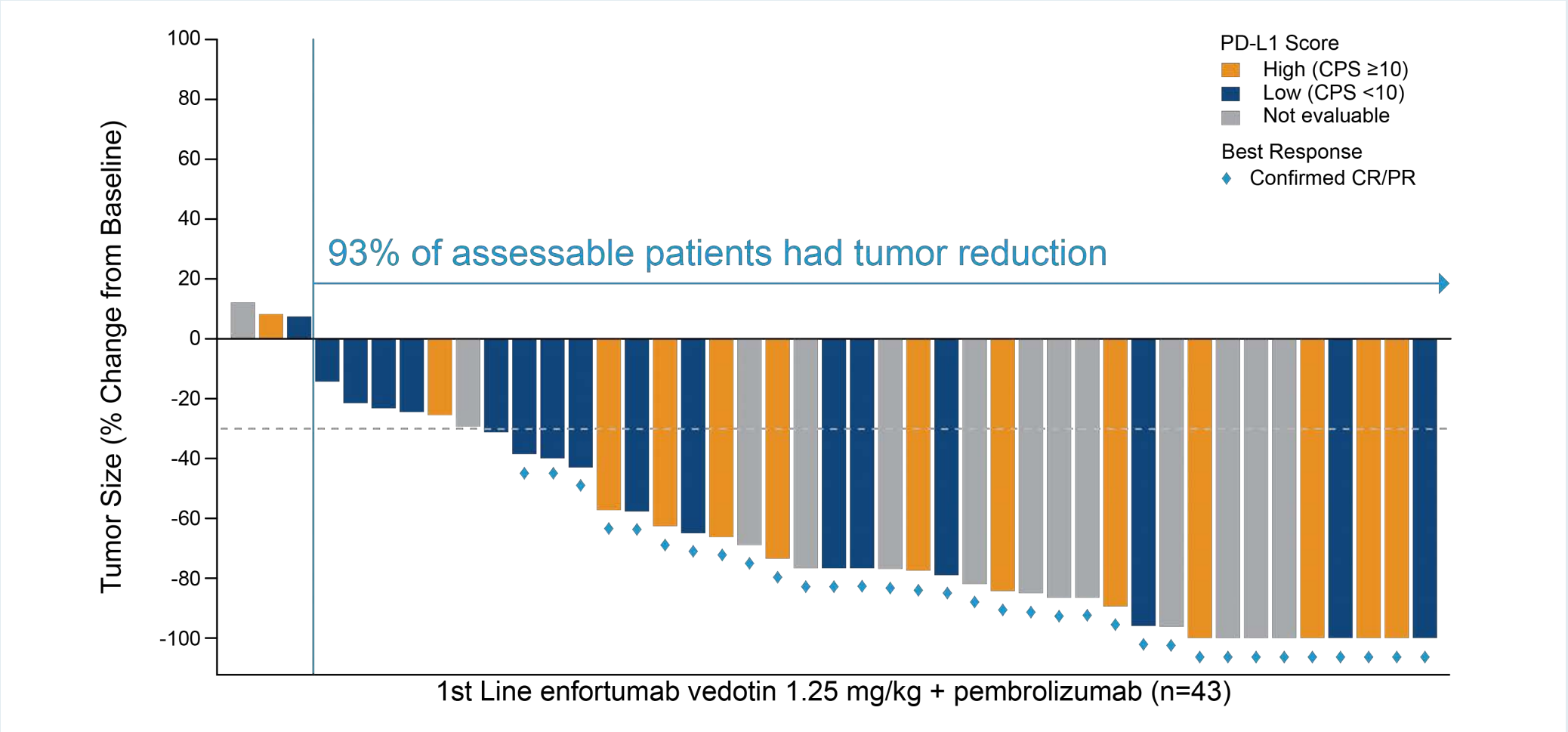
RTP RESEARCH TO PRACTICE

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

Friedlander TW et al.

ASCO 2021;Abstract 4528.

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



Friedlander TW et al. ASCO 2021;Abstract 4528.

RTP RESEARCH TO PRACTICE

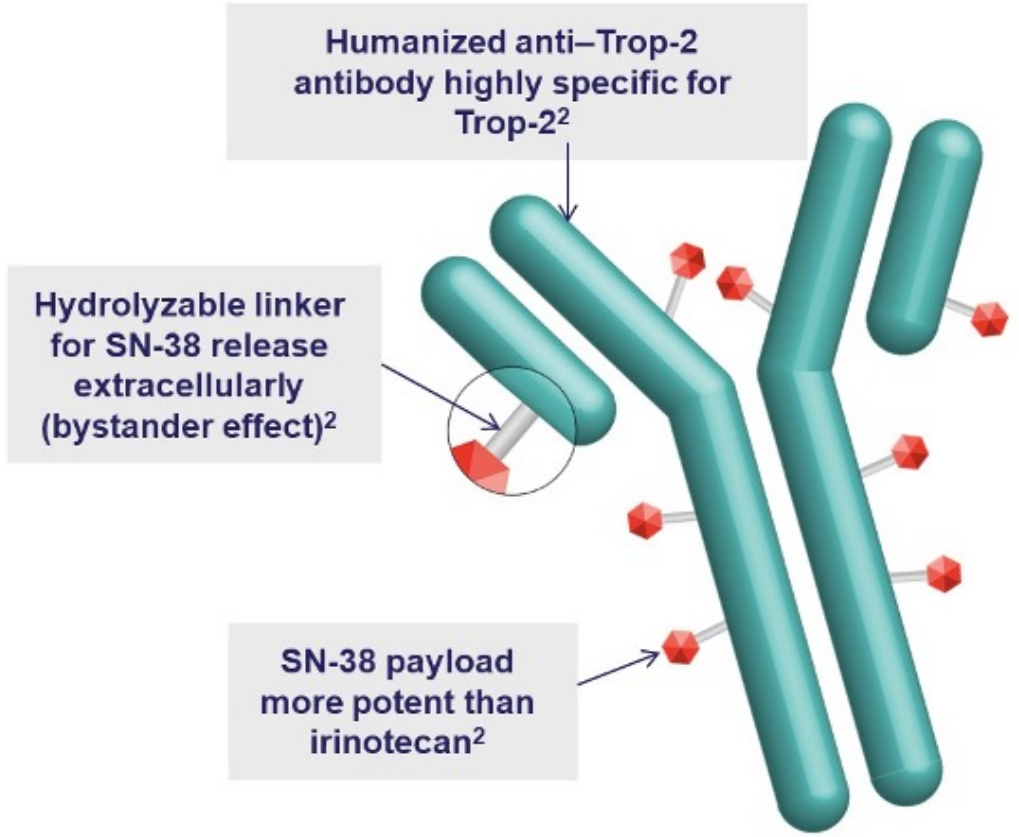
TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors

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.

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]



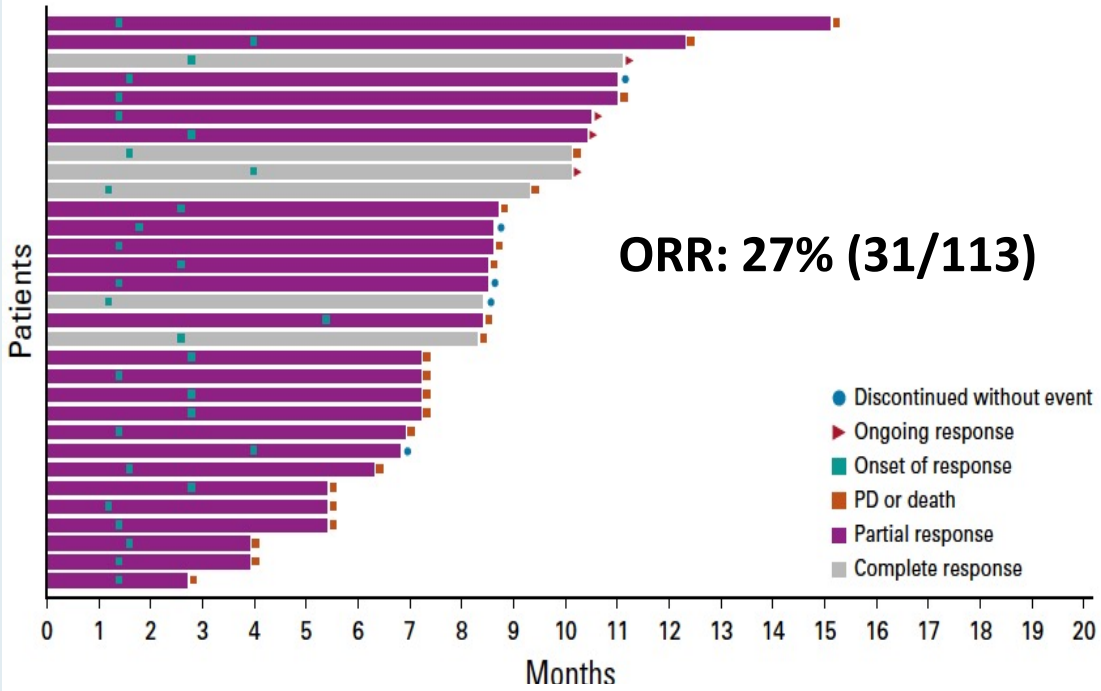
Grivas P et al. Genitourinary Cancers Symposium 2022;Abstract 434.

RTP RESEARCH TO PRACTICE

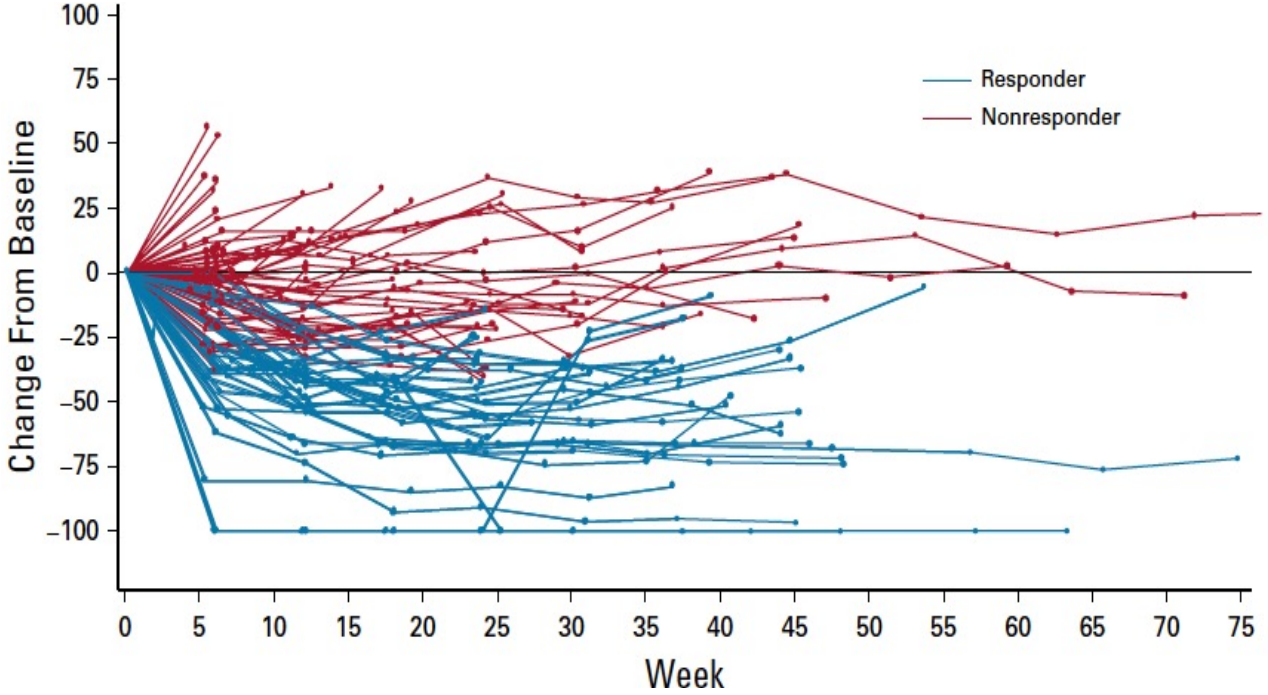
TROPHY U-01 (Cohort 1): ORR, Duration of Response and Survival

Median DOR: 7.2 mo

Median time to onset of response: 1.6 mo



ORR: 27% (31/113)



Median PFS: 5.4 mo

Median OS: 10.9 mo

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

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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

Questions — Sumanta Kumar Pal, MD

Patients with FGFR wild-type metastatic urothelial bladder cancer (FGFR-WT UBC)

- **What are the common clinical histories of patients with mUBC?**
- **What are the usual first- and second-line systemic treatments administered to patient with FGFR-WT UBC?**
- **How do you explain to patients the mechanism of action enfortumab vedotin and its potential benefits?**

Commentary — Sumanta Kumar Pal, MD

Patients with FGFR wild-type metastatic urothelial bladder cancer (FGFR-WT UBC)

- **Cisplatin-based neoadjuvant chemotherapy remains a gold-standard for those patients with muscle-invasive bladder cancer who are cisplatin-eligible**
- **Adjuvant nivolumab is a consideration for patients with ypT2-ypT4a or ypN+ didsease or pT3-pT4a or pN+ disease**
- **Adjuvant FGFR3-directed therapy with infigratinib is being explored in clinical trials, as is adjuvant atezolizumab based on ctDNA**
- **Cisplatin-based chemotherapy followed by maintenance avelumab is a gold standard front-line approach for patients with metastatic urothelial cancer**

Commentary — Sumanta Kumar Pal, MD

- **Carboplatin-based chemotherapy followed by maintenance avelumab is a gold standard for patients with metastatic urothelial cancer who are cisplatin-ineligible, but immunotherapy can be considered in selected circumstances**
- **Enfortumab has demonstrated level 1 evidence following platinum-based chemotherapy and checkpoint inhibitor for metastatic urothelial cancer**
- **FGFR3 mutations should be assessed early in the course of treatment to determine eligibility for agents such as erdafitinib**
- **Sacituzumab has shown compelling response rates in patients with prior platinum-based chemotherapy and immunotherapy**

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Questions — Brenda Martone, MSN, NP-BC, AOCNP

Patients with FGFR wild-type metastatic urothelial bladder cancer (FGFR-WT UBC)

- **What do you say to patients who are about to receive enfortumab vedotin in terms of what they should expect with this treatment?**
- **What are some of the psychosocial issues that arise in this situation?**

Commentary —Brenda Martone, MSN, NP-BC, AOCNP

Patients with FGFR wild-type metastatic urothelial bladder cancer (FGFR-WT UBC)

- **Explain how Enfortumab vedotin is different from their previous treatments.**
  - **Conjugated antibody that attaches to protein receptors on the surface bladder cancer cells, and then inserts the medication directly into the bladder cancer cells.**
  - **It can also cause harm to normal cells**
- **What you can expect while on treatment. These side effects are somewhat unique to this treatment.**
  - **Peripheral neuropathies**
  - **Skin rash**
  - **Changes in the sense of smell**
  - **Dry eyes**
  - **Elevated glucose readings**

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Commentary —Brenda Martone, MSN, NP-BC, AOCNP

- **Actual patient cases**
  - **49 y/o female with metastatic bladder cancer and a history of spina bifida. S/p 7 cycles of treatment with persistence of bothersome rash despite dose reduction and interventions. Coming for treatment created anxiety and worsening of her baseline depression. FYI, her last treatment was May 2021 and she remains in CR.**
  - **68 y/o male s/p 7 cycles who developed grade 2-3 peripheral neuropathies. Currently remodeling a house in Wisconsin with plans to move there.**
- **Psychosocial issues to consider during treatment**
  - **Anxiety**
  - **Changes to physical appearance**
  - **Impact of side effects on ADLs**
  - **Treatment schedule**
  - **Access to transportation: cost of parking in downtown Chicago**

RTP RESEARCH TO PRACTICE

Agenda

Module 1 – Management of Localized Urothelial Bladder Cancer (UBC): Adjuvant Treatment, TAR-200

Module 2 – Management of Metastatic UBC: Antibody-Drug Conjugates, Checkpoint Inhibitors

Module 3 – Management of FGFR-Mutant UBC

Module 4 – Oncology/UBC 2032 and Crystal Ball: Part 2

RTP RESEARCH TO PRACTICE

SELF-ASSESSMENT QUIZ

What is the mechanism of action of erdafitinib?

1. Antibody-drug conjugate
2. Tyrosine kinase inhibitor
3. PD-1/PD-L1 inhibitor
4. Intravesicular gemcitabine
5. I don’t know

SELF-ASSESSMENT QUIZ

Erdafitinib targets…

1. FGFR2
2. Nectin-4
3. TROP2
4. I don’t know

SELF-ASSESSMENT QUIZ

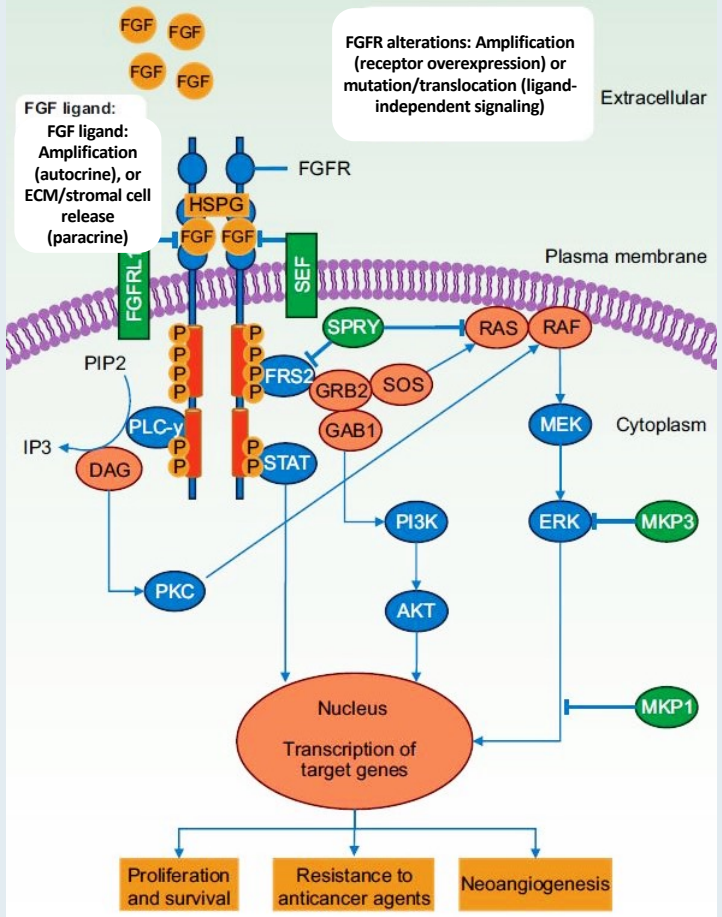
Which of the following is a potential unique side effect of erdafitinib that requires monitoring?

1. Atrial fibrillation
2. Ocular disorders
3. Peripheral neuropathy
4. I don’t know

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

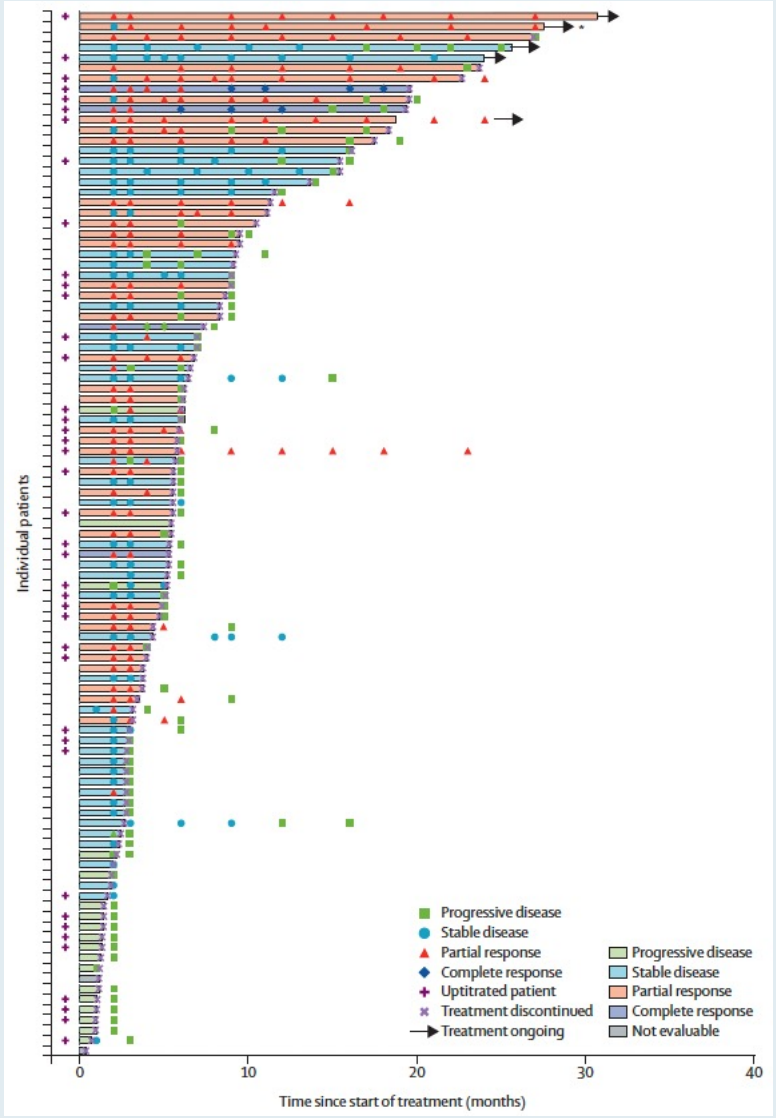
Lancet Oncol 2022;23(2):248-58.

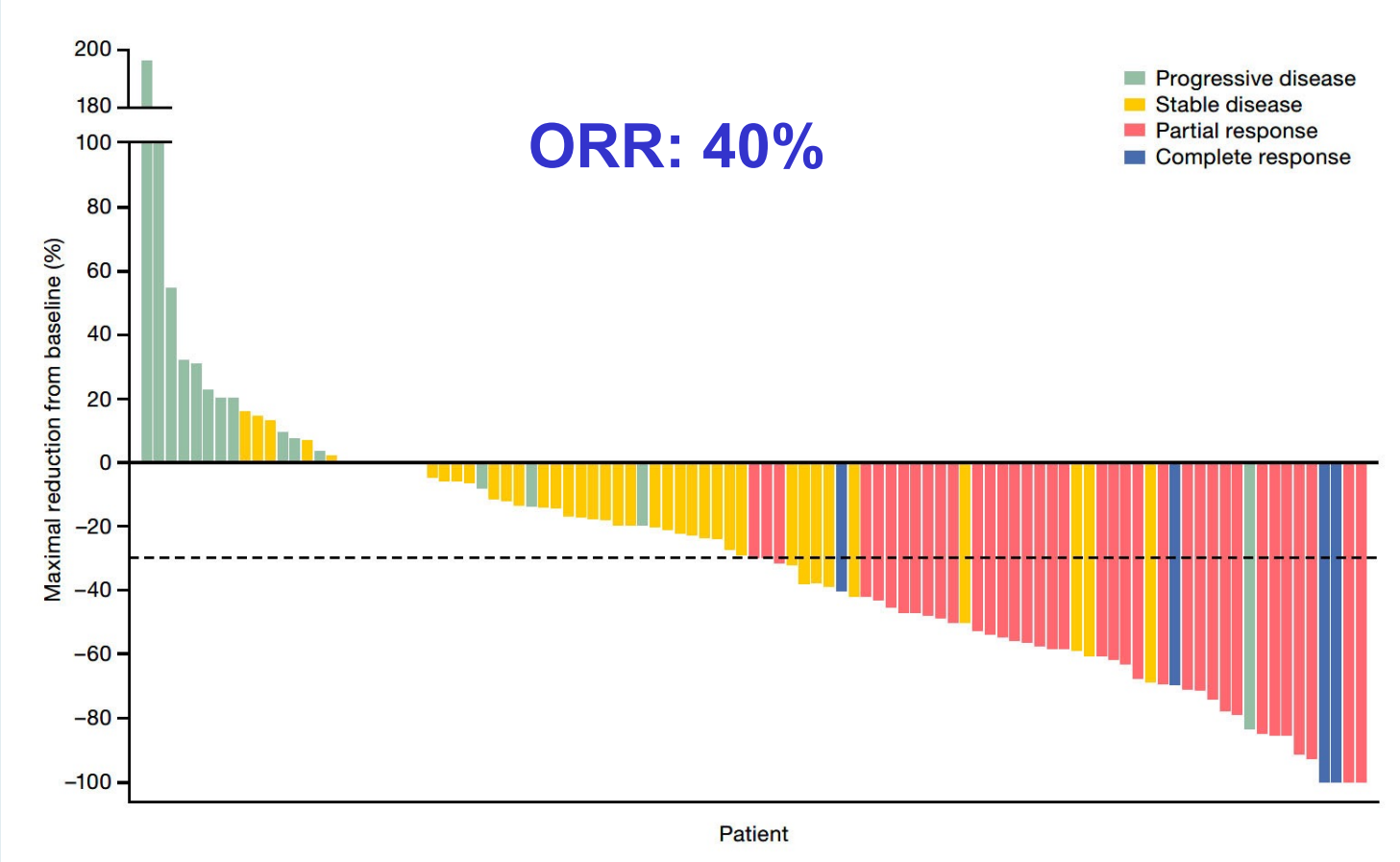
Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study

*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: Erdafitinib for Locally Advanced or Metastatic UBC

Responses in Patients Treated with the Selected 8 mg/day Erdafitinib UpT Regimen

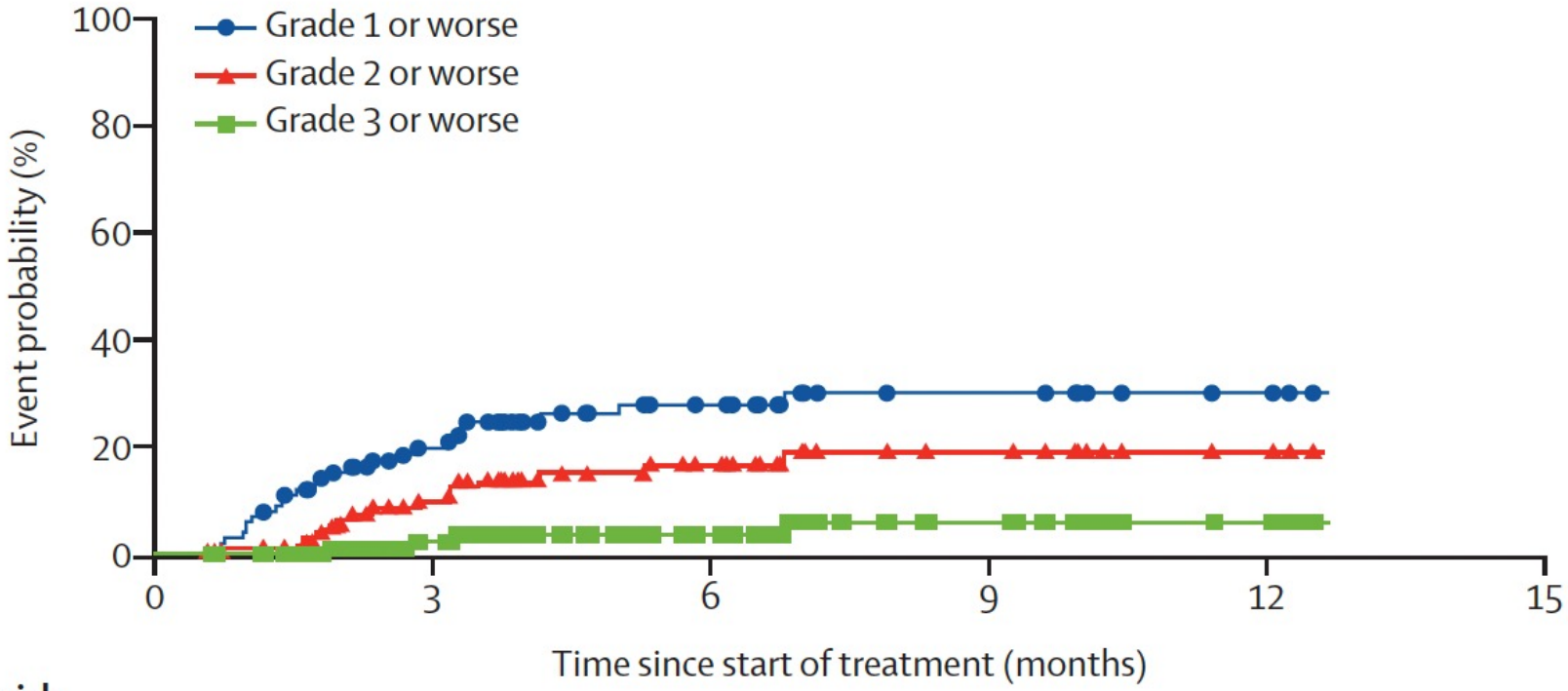




Siefker-Radtke A et al. *Lancet Oncol* 2022;23(2):248-58.

RTP RESEARCH TO PRACTICE

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 A et al. *Lancet Oncol* 2022;23(2):248-58.

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 A et al. *Lancet Oncol* 2022;23(2):248-58.

Questions — Shilpa Gupta, MD

Patients with mUBC and an FGFR mutation

- **How do you explain FGFR mutations and how erdafitinib works to patients?**
- **What are the potential benefits with this treatment?**

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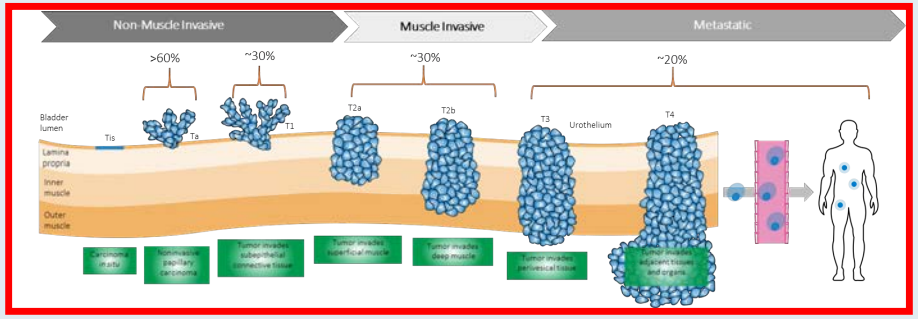
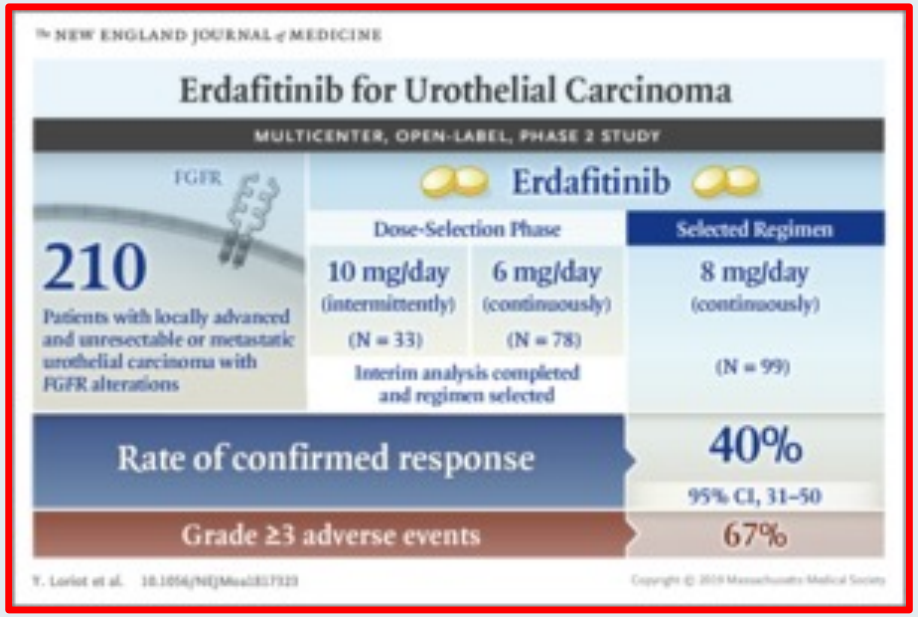
Commentary — Shilpa Gupta, MD

Patients with mUBC and an FGFR mutation

- FGFR mutations occur in ~ 20% mUBC patients
- Erdafitinib is an oral targeted therapy that inhibits FGFR pathway to block cancer growth
- It results in tumor shrinkage in ~ 40% patients and median overall survival ~ 11 months
- Significant toxicity, needs monitoring
  - Skin and nail toxicity
  - Eye toxicity- regular ophthalmologic evals
  - Hyperphosphatemia- regular lab monitoring





Knowles MA et al. *Nat Rev Cancer*. 2015, Loriot Y et al. NEJM 2019

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Questions — Monica Averia, MSN, AOCNP, NP-C

Patients with mUBC and an FGFR mutation

- **What do you say to patients who are about to receive erdafitinib in terms of what they should expect with this treatment?**
- **What are some of the psychosocial issues that arise in this situation?**

Commentary — Monica Averia, MSN, AOCNP, NP-C

Patients with mUBC and an FGFR mutation

What do you say to pts who are abt to receive Erdafitinib in terms of what to EXPECT with the treatment?

- **Erdafitinib is used to treat patients with metastatic urothelial carcinoma**
- **FGFR gene alterations**
- **Decreased the tumors of some patients whose cancers did not respond to other treatments**

Common side effects:

- **Fatigue, Nausea, Vomiting, Diarrhea, Dry mouth, Changes to nails, Hand-foot syndrome**

Commentary — Monica Averia, MSN, AOCNP, NP-C

Cite brief instructive examples of actual clinical experiences with pts in your practice

65 y/o male from Guatemala case study

- **ddMVAC chemo**
- **Radical cystectomy with ileal conduit**
- **>1 yr: DP with new LN met, Bx proven**
- **Option: immunotherapy or chemo. Cisplatin/Gemcitabine chemo**
- **COVID-19: intubated, hospitalized, lost to follow-up**
- **Presented with DP: liver, lungs, LN**
- **Tumor Profiling: FGFR gene alteration**
- **Cycle 1: CT showed dec in lesions. Cycle 2: CT pending**

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Commentary — Monica Averia, MSN, AOCNP, NP-C

What are some of the psychosocial issues that arise in this situation?

Side effects experienced:

- **Self limiting**
- **Reinforce ways to manage SE profile of the medication**

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Agenda

Module 1 – Management of Localized Urothelial Bladder Cancer (UBC): Adjuvant Treatment, TAR-200

Module 2 – Management of Metastatic UBC: Antibody-Drug Conjugates, Checkpoint Inhibitors

Module 3 – Management of FGFR-Mutant UBC

Module 4 – Oncology/UBC 2032 and Crystal Ball: Part 2

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Questions — Sumanta Kumar Pal, MD

Fantasies for the future… Oncology 2032?

- **UBC now has immunotherapy, chemotherapy, antibody-drug conjugates and targeted treatment options approved. How do you see these treatment modalities and others being incorporated into the next generation of therapies?**

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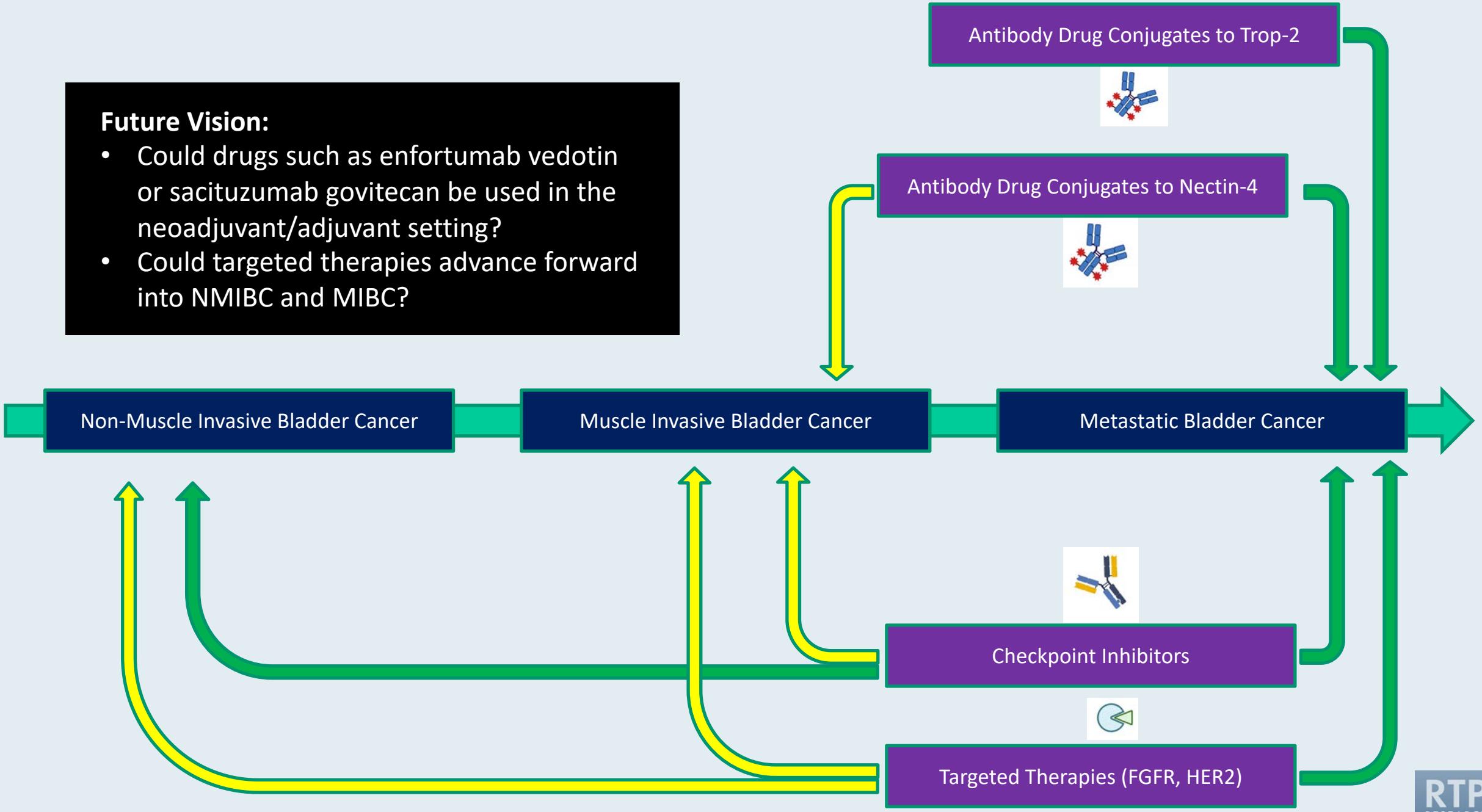
Future Vision:

- Could drugs such as enfortumab vedotin or sacituzumab govitecan be used in the neoadjuvant/adjuvant setting?
- Could targeted therapies advance forward into NMIBC and MIBC?



Questions — Brenda Martone, MSN, NP-BC, AOCNP

Fantasies for the future… Oncology 2032?

- **What is your vision for oncology nursing in 2032?**
- **How can advances in technology be harnessed to provide better patient care?**

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Commentary —Brenda Martone, MSN, NP-BC, AOCNP

Fantasies for the future… Oncology 2032?

- **Oncology nurses and APP's will practice at the top of their license.**
- **Better understanding and appreciation of the role of all oncology nurses**
- **All oncology nurses will hold OCN or AOCN**
- **Advances to in technology to be harnessed**
- **Detection of NMIBC and multifocal bladder cancer by imaging**
- **Non-invasive screening for patients globally.**
- **Circulating tumor DNA for cancer monitoring**

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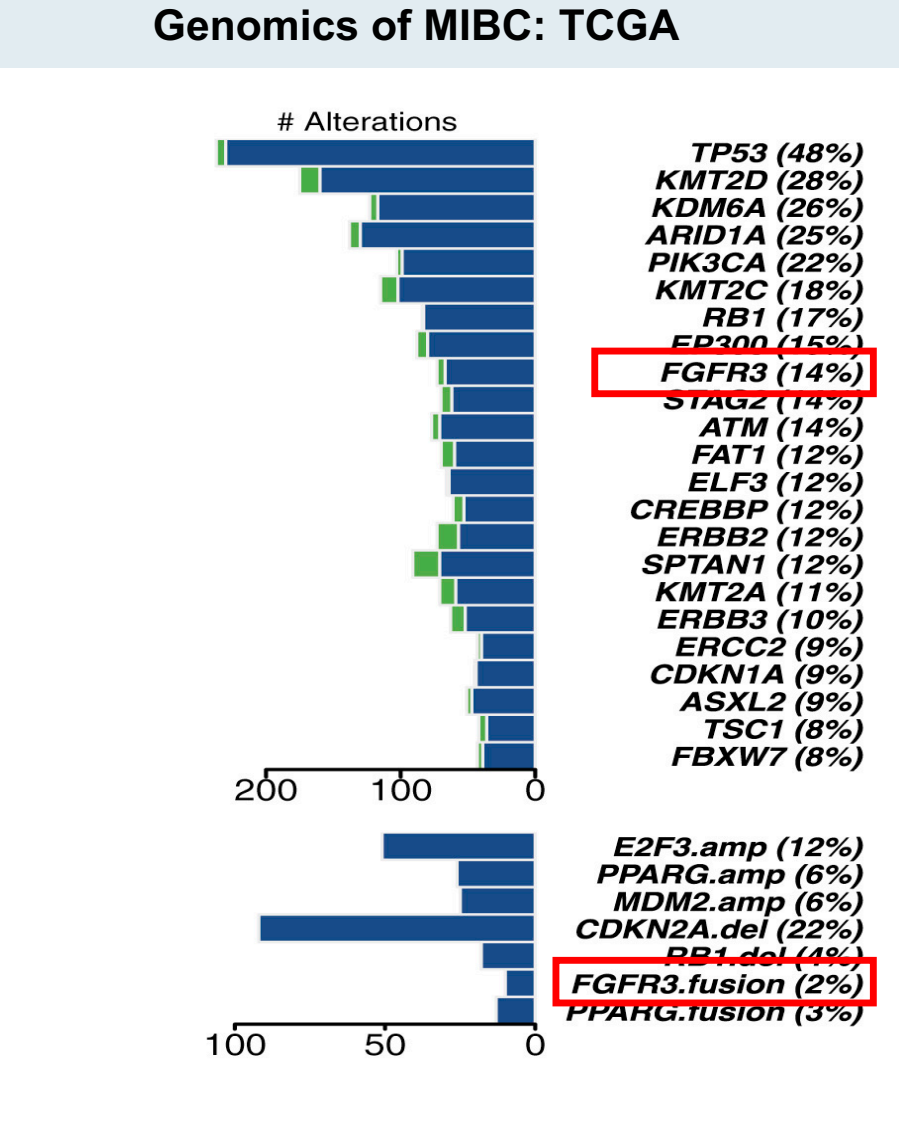
Appendix of Recent Data Sets

FGFR3 Genomic Alterations in Muscle-Invasive Bladder Cancer



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

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

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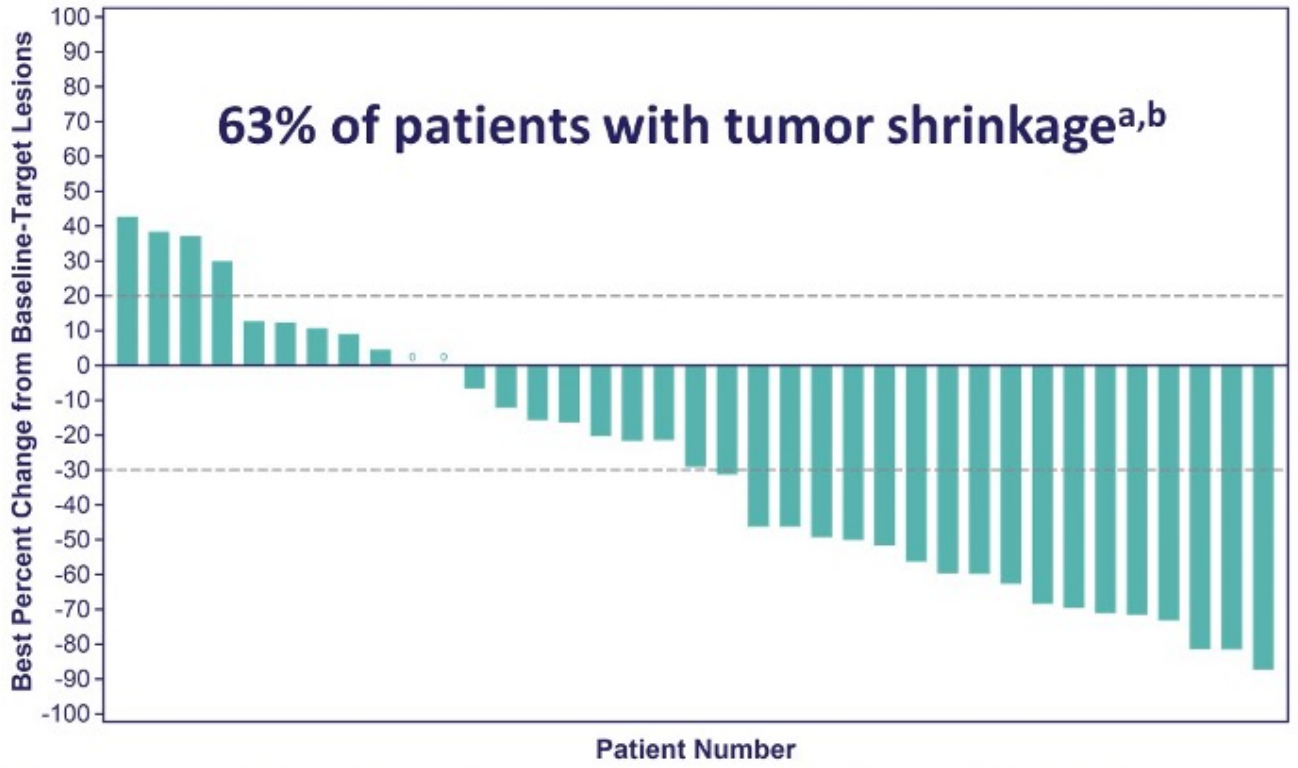
TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors

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

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

TROPHY-U-01: 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.

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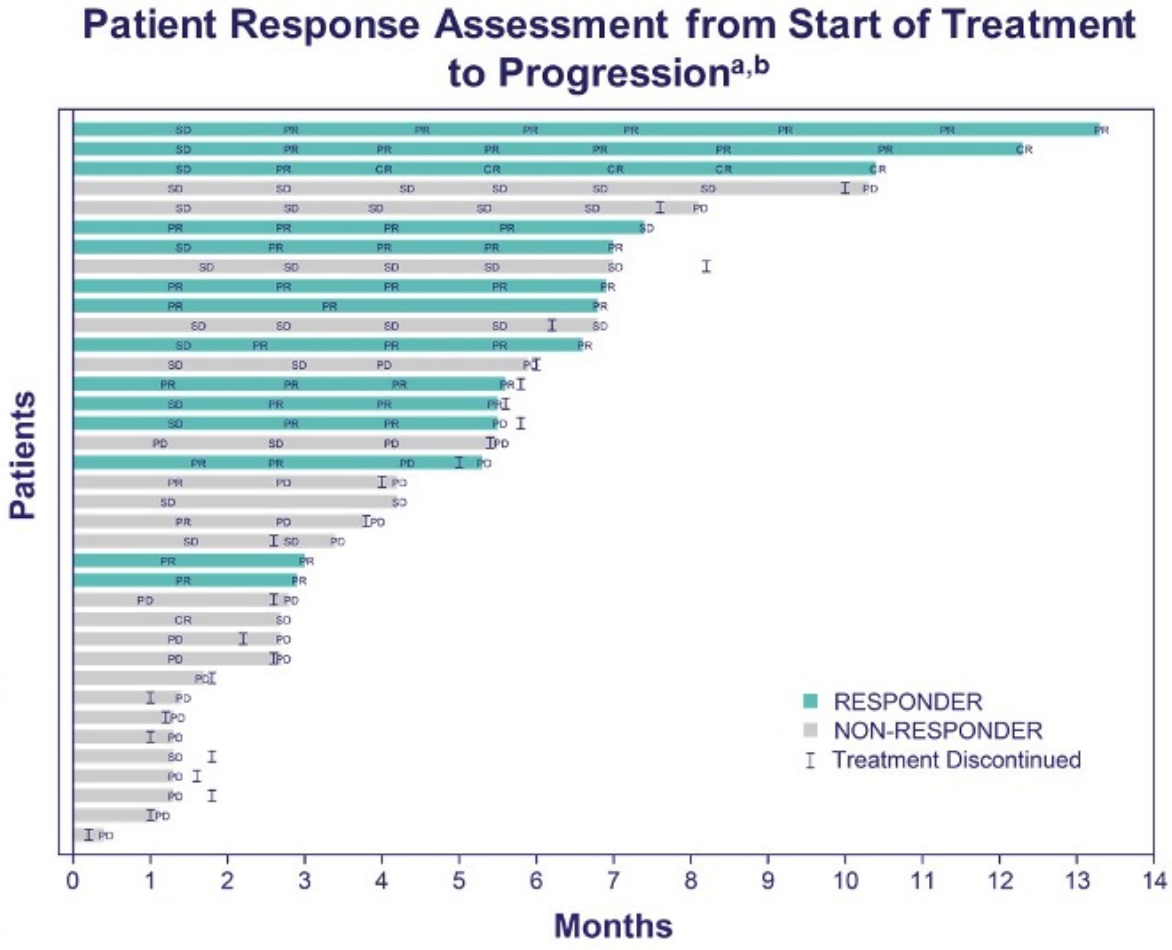
TROPHY-U-01: ORR by Subgroup and Individual Response Assessment

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.

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TROPHY-U-01: Most Common Treatment-Emergent Adverse Events (TEAEs) for All Patients

	Cohort 3 (N=41)	
TEAEs Occurring in >20% of Patients, n (%)	All Grade	Grade ≥3
Diarrhea	31 (76)	10 (24)
Nausea	24 (59)	2 (5)
Anemia	23 (56)	8 (20)
Neutropenia	18 (44)	11 (27)
Asthenia	17 (41)	2 (5)
Alopecia	16 (39)	0
Fatigue	14 (34)	3 (7)
Decreased appetite	13 (32)	1 (2)
Leukopenia	12 (29)	8 (20)
Vomiting	12 (29)	0
Constipation	10 (24)	0
Hypomagnesaemia	10 (24)	0
Pruritus	10 (24)	0
Lymphopenia	9 (22)	1 (2)

	Cohort 3 (N=41)
Median duration of treatment, months (range)	
SG	4 (0-15)
Pembrolizumab	3.5 (0-14)
Patients remaining on therapy at data cutoff, n (%)	13 (32)
Permanently discontinued treatment, n (%)	28 (68)
Progressive disease	21 (51)
Withdrawal of consent	2 (5)
Adverse event	1 (3)
Gr 2 altered general condition, n	1
Treatment delay >5 weeks	3 (7)
Other	1 (2)

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

TROPHY-U-01: Most Common Treatment-Related Adverse Events (TRAEs) 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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Online attendees: NCPD credit information will be emailed to each participant within 3 business days.

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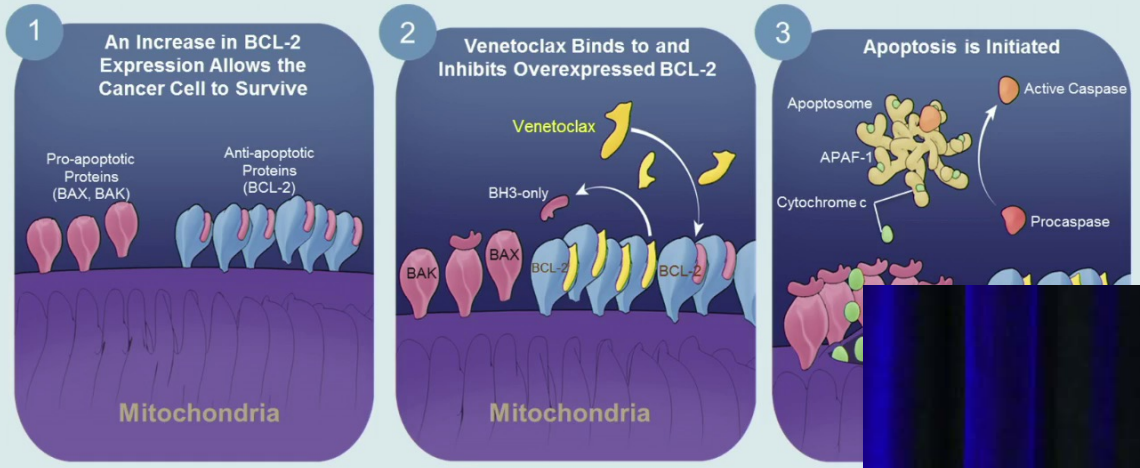
Venetoclax Mechanism of Action



- Cancer cells increase the expression of anti-apoptotic proteins to offset the increase in p
  tipping the balance toward cell survival
- The large # of pro-apoptotic proteins bound and sequestered by Bcl-2 in AML make ther

Kumar et al. ASCO 2015;Abstract 8576.