Breakfast with the Investigators: Urothelial Bladder Cancer

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Monday, June 5, 2023

6:45 AM – 7:45 AM CT

Faculty

Matthew D Galsky, MD

Andrea Necchi, MD

Scott T Tagawa, MD, MS

Moderator

Neil Love, MD

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Faculty

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Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Galsky — Disclosures

Consulting Agreements	AbbVie Inc, Alligator Bioscience, Analog Devices Inc, Asieris Pharmaceuticals, AstraZeneca Pharmaceuticals LP, Basilea Pharmaceutica Ltd, Bicycle Therapeutics, Bristol Myers Squibb, Curis Inc, Dragonfly Therapeutics, EMD Serono Inc, FUJIFILM Pharmaceuticals USA Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, GSK, Janssen Biotech Inc, Merck, Numab Therapeutics AG, Rappta Therapeutics, Pfizer Inc, Seagen Inc, Silverback Therapeutics, UroGen Pharma
Contracted Research	AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Dendreon Pharmaceuticals Inc, Genentech, a member of the Roche Group, Merck, Novartis

Prof Necchi — Disclosures

No relevant conflicts of interest to disclose

Dr Tagawa — Disclosures

Consulting Agreements	AbbVie Inc, AIkido Pharma Inc, Amgen Inc, Astellas, Bayer HealthCare Pharmaceuticals, Blue Earth Therapeutics, Clarity Pharmaceuticals, Clovis Oncology, Convergent Therapeutics Inc, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Exact Sciences Corporation, Genentech, a member of the Roche Group, Gilead Sciences Inc, Janssen Biotech Inc, Karyopharm Therapeutics, Merck, Myovant Sciences, Novartis, Pfizer Inc, POINT Biopharma, QED Therapeutics, Sanofi, Seagen Inc, Telix Pharmaceuticals Limited, Tolmar
Contracted Research	AbbVie Inc, Ambrx, Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Clovis Oncology, Genentech, a member of the Roche Group, Gilead Sciences Inc, Inovio Pharmaceuticals Inc, Janssen Biotech Inc, Karyopharm Therapeutics, Lumos Pharma, Medivation Inc, a Pfizer Company, Merck, Novartis, Ocuphire Pharma Inc, POINT Biopharma, Sanofi, Seagen Inc, Takeda Pharmaceuticals USA Inc
Patent	Gilead Sciences Inc (biomarkers for sacituzumab govitecan therapy)
Stock Options/Ownership — Public Company	AIkido Pharma Inc

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Commercial Support

This activity is supported by educational grants from Astellas and Seagen Inc, AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, 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.

Friday June 2	**Gastroesophageal Cancers** 11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)
	Non-Small Cell Lung Cancer 6:30 PM – 9:00 PM CT (7:30 PM – 10:00 PM ET)
Saturday June 3	**Hepatobiliary Cancers** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Prostate Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday June 4	**Ovarian Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Lymphoma, Chronic Lymphocytic Leukemia and Multiple Myeloma 7:00 PM – 9:30 PM CT (8:00 PM – 10:30 PM ET)
Monday June 5	**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 6	**Renal Cell Carcinoma (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

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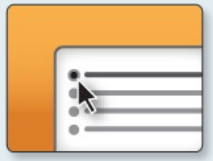
Clinicians in the Meeting Room

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 pre- and postmeeting surveys.

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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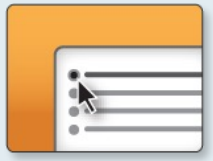
Clinicians Attending via Zoom

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 pre- and postmeeting surveys.

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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PREMEETING SURVEY – Available Now

Clinicians in Attendance: If you have not already done so, please take a moment to complete the premeeting survey on the iPads for attendees in the room and on Zoom for those attending virtually. Your input on this survey will be integral to the program today.

A postmeeting survey will be posted toward the end of the session.

Thank you for your input.

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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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- Management of non-muscle-invasive bladder cancer
- Neoadjuvant and adjuvant therapy for muscle-invasive bladder cancer
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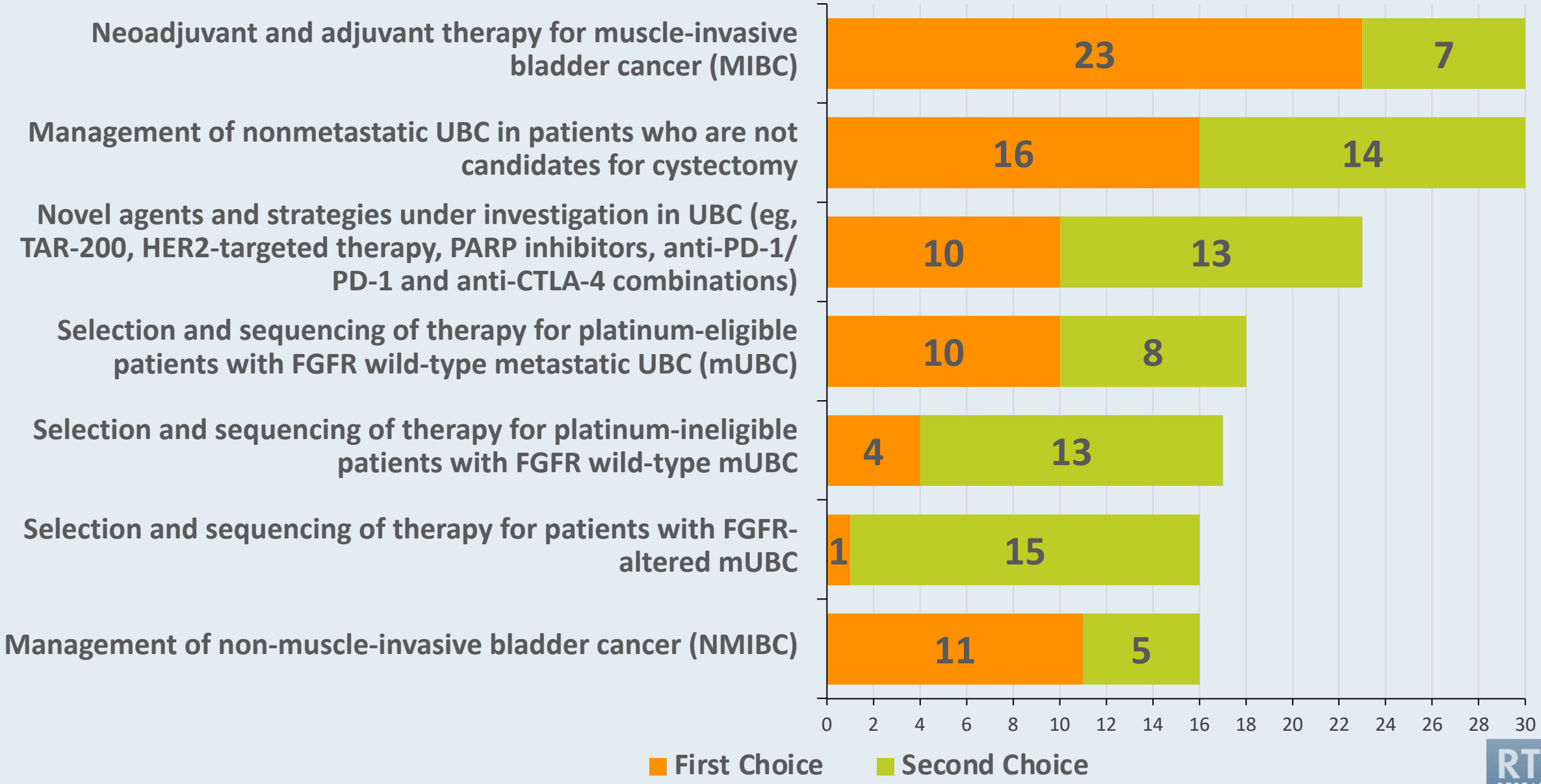
- Selection and sequencing of therapy for platinum-ineligible patients with FGFR wild-type mUBC
- Selection and sequencing of therapy for patients with FGFR-altered mUBC
- Novel agents and strategies under investigation in UBC

Topics of Interest for Future CME Programs



Survey of US-based general medical oncologists, May 2023. N = 75

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How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the management of NMIBC?

39% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

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Management of non-muscle-invasive bladder cancer

- Kulkarni GS et al. **Pembrolizumab in participants with bacillus Calmette-Geurin-unresponsive non-muscle-invasive bladder cancer: 5-year follow-up from cohort A of the phase 2 KEYNOTE-057 trial.** Society of Urologic Oncology 2022;Poster 188.
- Neechi A et al. **Pembrolizumab monotherapy for patients with high-risk non-muscle-invasive bladder cancer unresponsive to bacillus Calmette-Guerin: Results from cohort B of the phase 2 KEYNOTE-057 trial.** Genitourinary Cancers Symposium 2023;Abstract LBA442.
- Daneshmand S et al. **First results from SunRISe-1 in patients with BCG unresponsive high-risk non–muscle-invasive bladder cancer receiving TAR-200 in combination with cetrelimab, TAR-200, or cetrelimab alone.** AUA 2023;Abstract LBA02-03.

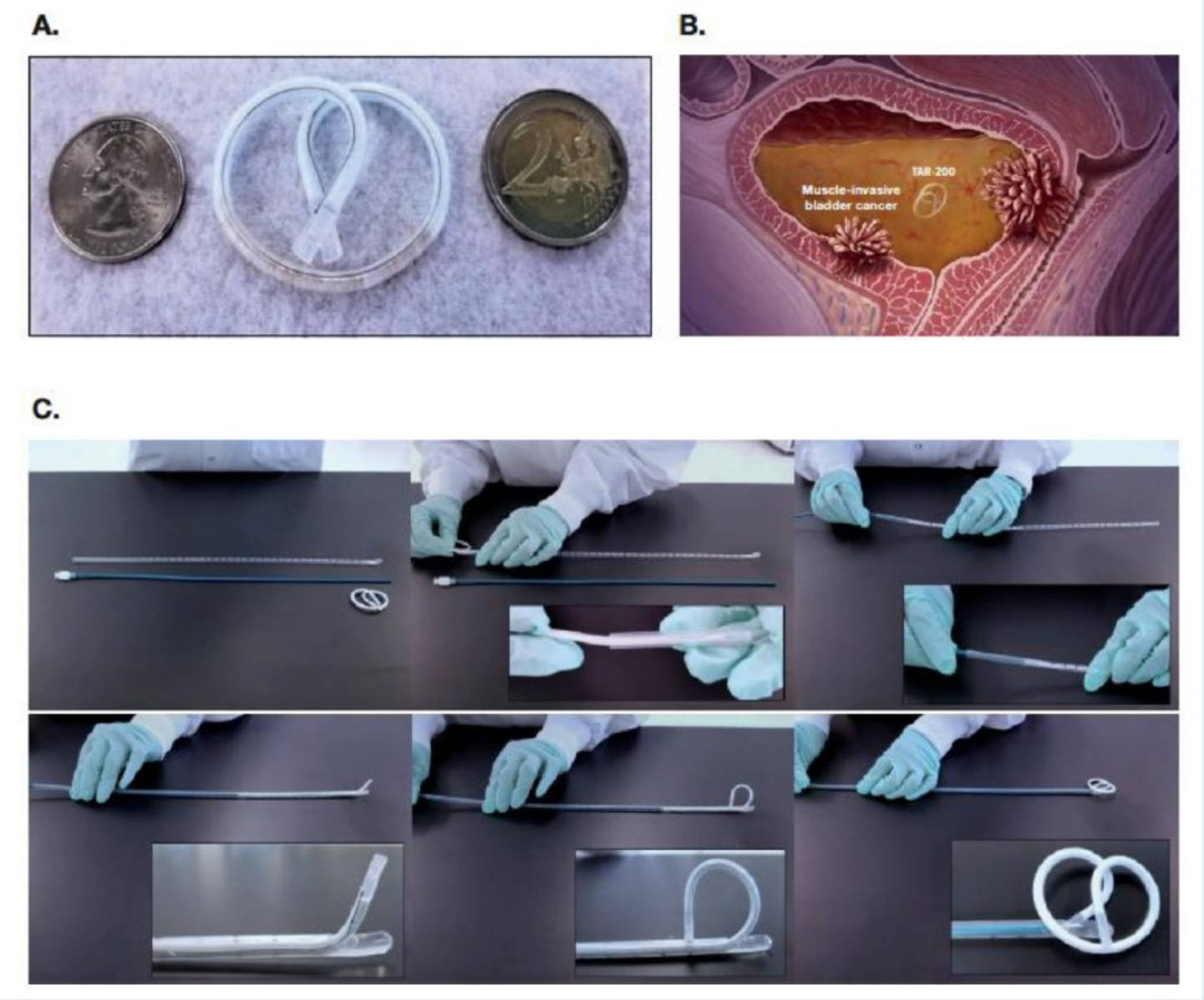
Key Ongoing Phase III Trials of Anti-PD-1/PD-L1 Antibodies for NMIBC

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.

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 urinary placement catheter

Daneshmand S et al. *Urol Oncol* 2022;40(7):344e1-9.

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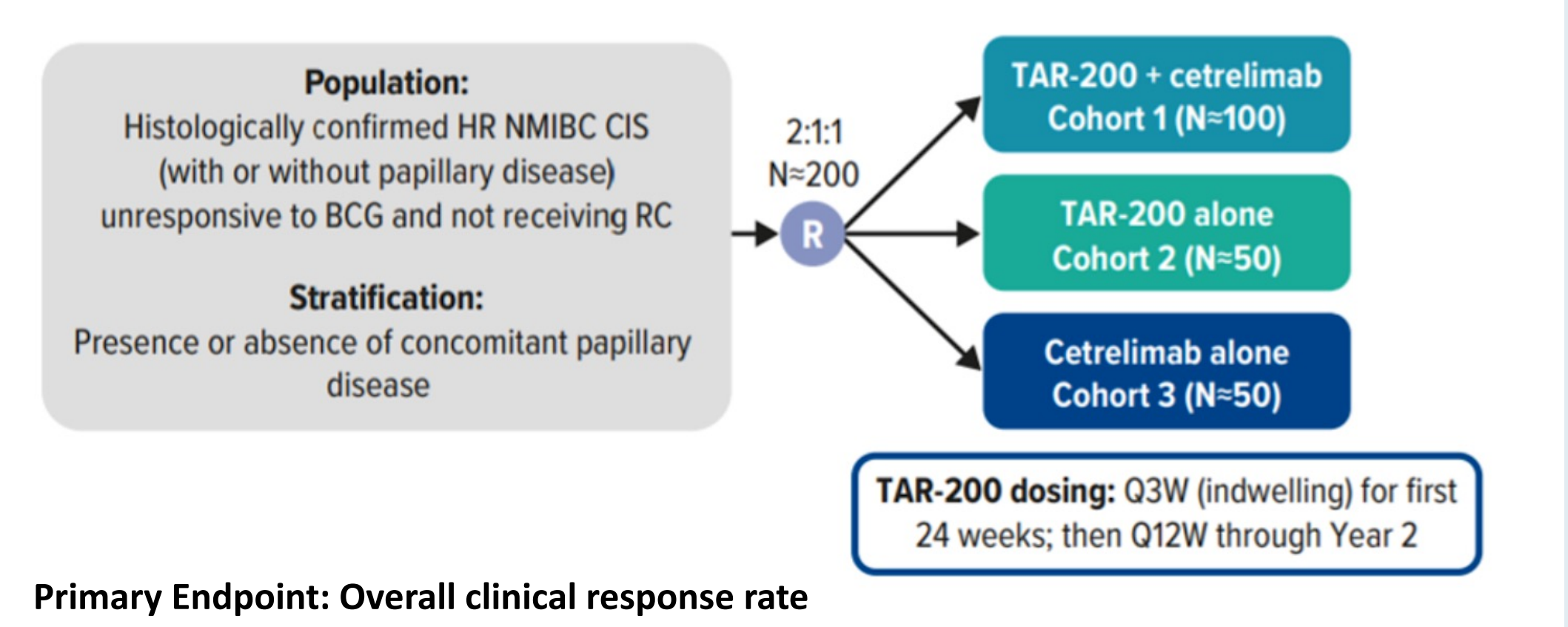
SunRISe-1: Ongoing Phase IIb Trial of TAR-200 Alone, Cetrelimab Alone or in Combination for BCG-Unresponsive, High-Risk NMIBC

Clinical Trial Identifier: NCT04640623



Primary Endpoint: Overall clinical response rate

BCG = bacillus Calmette-Guérin; HR = high-risk; RC = radical cystectomy

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

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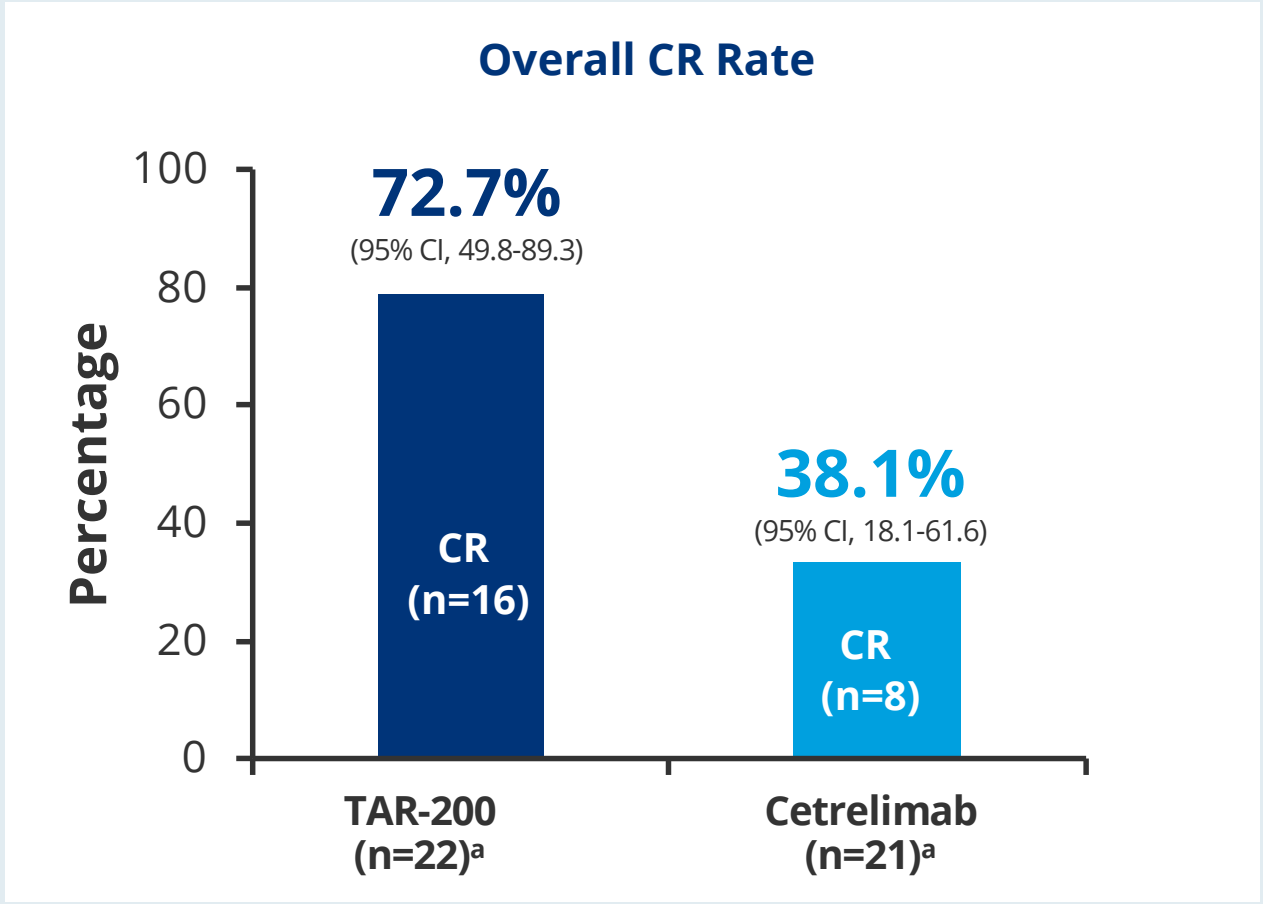
SunRISe-1: Efficacy of TAR-200 and Cetrelimab Monotherapies — 73% of Evaluable Patients Achieved CR With TAR-200



CR is based on cystoscopy and centrally assessed urine cytology and biopsy at Weeks 24 and 48

Daneshmand S et al. AUA 2023;Abstract LBA02-03.

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Questions from General Medical Oncologists

- **What has been your experience with pembrolizumab in patients who are BCG refractory? Any biomarkers that predict response to pembrolizumab in this setting?**
- **What are your management strategy recommendations for NMIBC patients with the continuing BCG shortage?**
- **TAR 200 vs intravesical vaccine therapy in bladder CA after BCG failure**
- **I have used pembrolizumab several times for NMIBC. How about upper urothelial cancer, which is more difficult to determine if it's invasive or not?**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **How do you determine whom to treat with pembro vs nadofaragene in high-risk NMIBC? How long do you give pembro in such cases?**

Survey of US-based general medical oncologists, May 2023. N = 75

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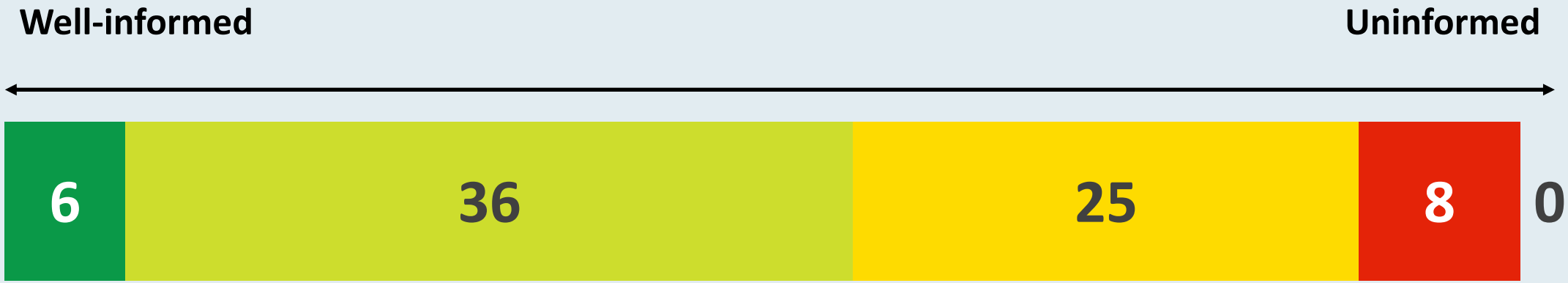
- Novel agents and strategies under investigation in UBC

How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to neoadjuvant and adjuvant therapy for MIBC?



60% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

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Neoadjuvant and adjuvant therapy for muscle-invasive bladder cancer

- Basile G et al. **Neoadjuvant pembrolizumab and radical cystectomy in patients with muscle-invasive urothelial bladder cancer: 3-year median follow-up update of PURE-01 trial.** *Clin Can Res* 2022;28(23):5107-14.
- Szabados B et al. **Final results of neoadjuvant atezolizumab in cisplatin-ineligible patients with muscle-invasive urothelial cancer of the bladder.** *Eur Urol* 2022;82(2):212-22.
- Galsky MD et al. **Extended follow-up results from the CheckMate 274 trial.** Genitourinary Cancers Symposium 2023;Abstract LBA443.
- Daneshmand S et al. **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.** *Urol Oncol* 2022;40(7):344.e1-344.e9.

ASCO Genitourinary Cancers Symposium 2023;Abstract LBA443.

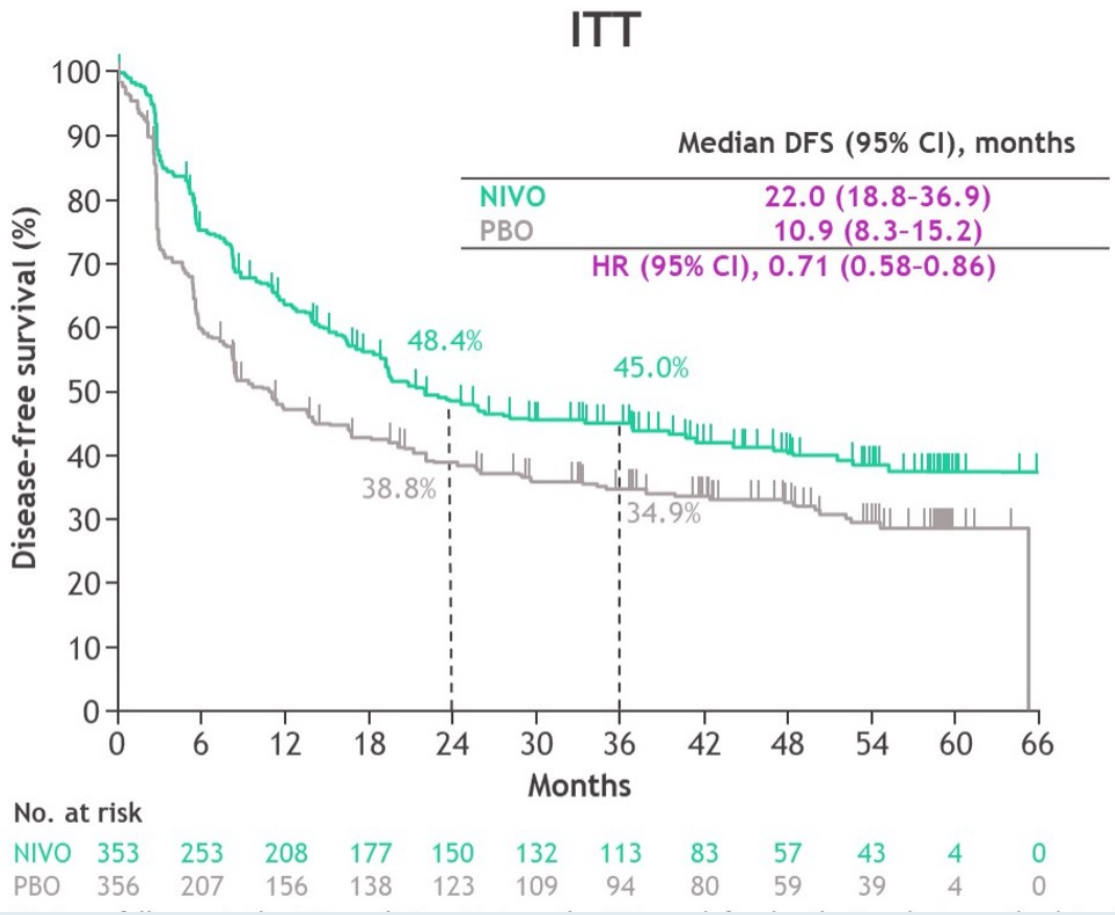
Extended follow-up results from the CheckMate 274 trial

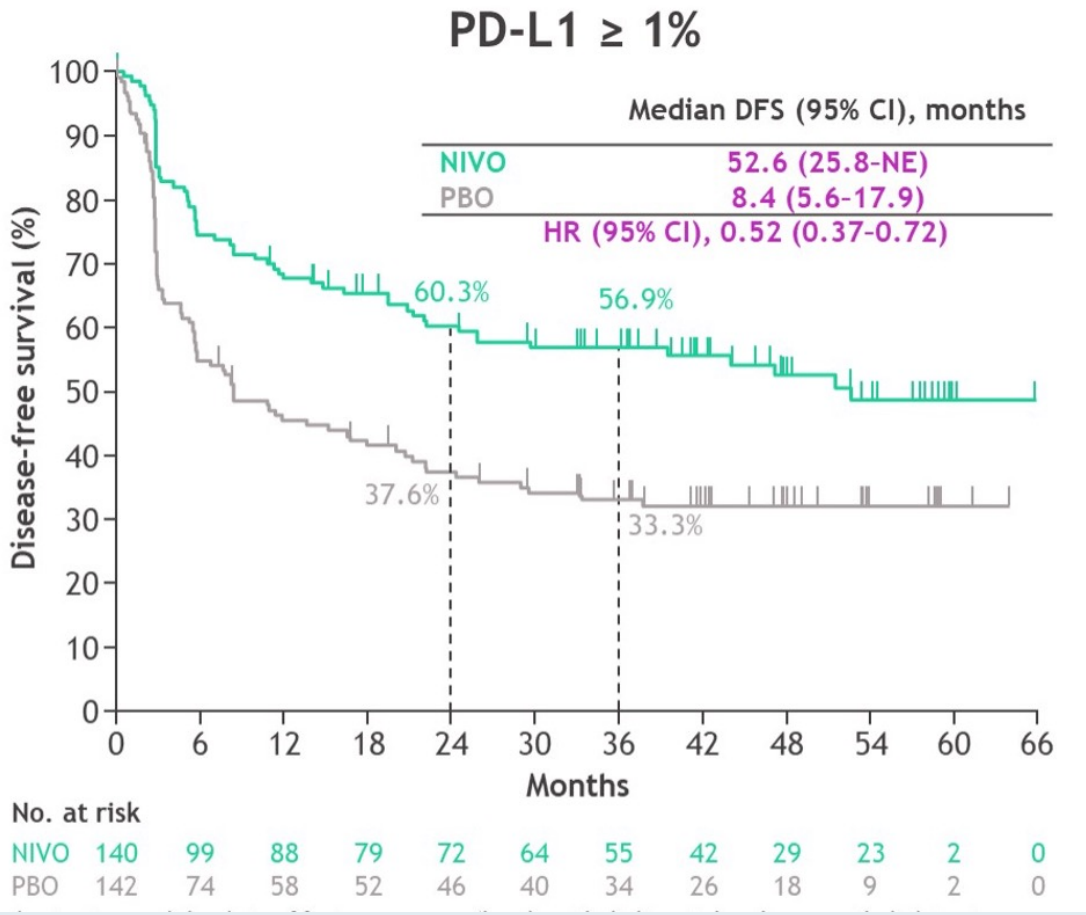
Matthew D. Galsky,[1] Johannes Alfred Witjes,[2] Jürgen E. Gschwend,[3] Michael Schenker,[4] Begoña P. Valderrama,[5] Yoshihiko Tomita,[6] Aristotelis Bamias,[7] Thierry Lebret,[8] Shahrokh F. Shariat,[9] Se Hoon Park,[10] Mads Agerbaek,[11] Gautam Jha,[12] Frank Stenner,[13] Santanu Dutta,[14] Federico Nasroulah,[14] Joshua Zhang,[14] Lynne Brophy,[14] Dean F. Bajorin[15]

[1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Radboud University, Nijmegen, the Netherlands; [3]Technical University Munich, Munich, Germany; [4]Sf. Nectarie Oncology Center, Craiova, Romania; [5]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [6]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [7]National and Kapodistrian University of Athens, Athens, Greece; [8]Hôpital Foch, Paris-Saclay University UVSQ, Versailles, France; [9]Medical University of Vienna, Vienna General Hospital, Vienna, Austria; [10]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [11]Aarhus University Hospital, Aarhus, Denmark; [12]M Health Fairview Clinics and Surgery Center, Minneapolis, MN; [13]University Hospital Basel, Basel, Switzerland; [14]Bristol Myers Squibb, Princeton, NJ; [15]Memorial Sloan Kettering Cancer Center, New York, NY

CheckMate 274 Extended Follow-Up: Disease-Free Survival (Primary Endpoint)

- Continued DFS benefit was observed with NIVO versus PBO both in the ITT and tumor PD-L1 expression ≥ 1% populations





DFS = disease-free survival; NIVO = nivolumab; PBO = placebo; ITT = intent to treat

Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA443.

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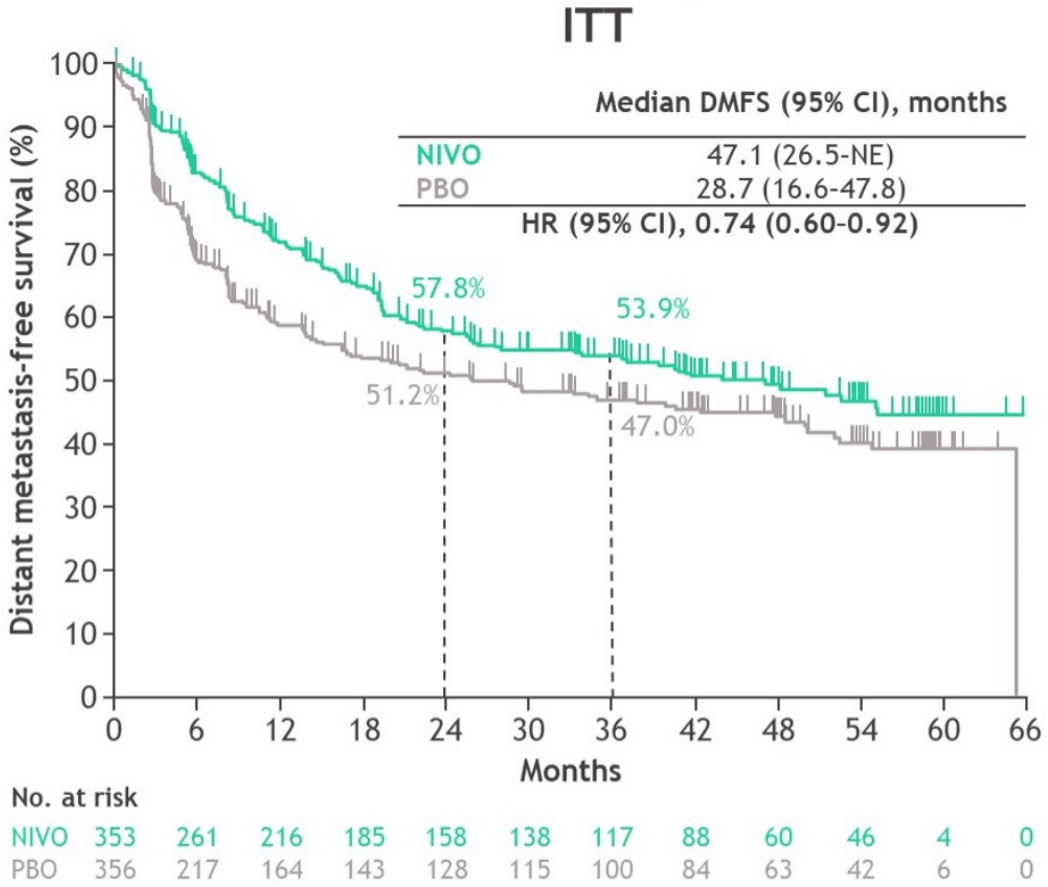
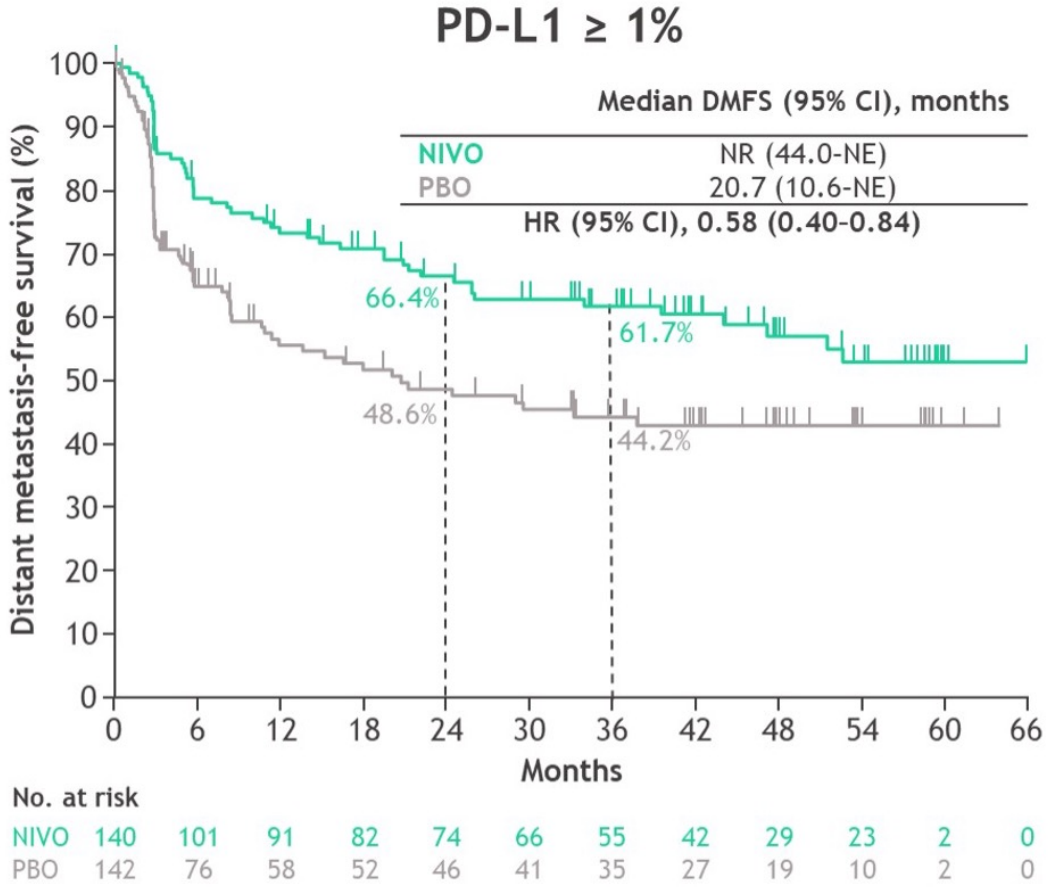
CheckMate 274 Extended Follow-Up: Distant Metastasis-Free Survival (DMFS)

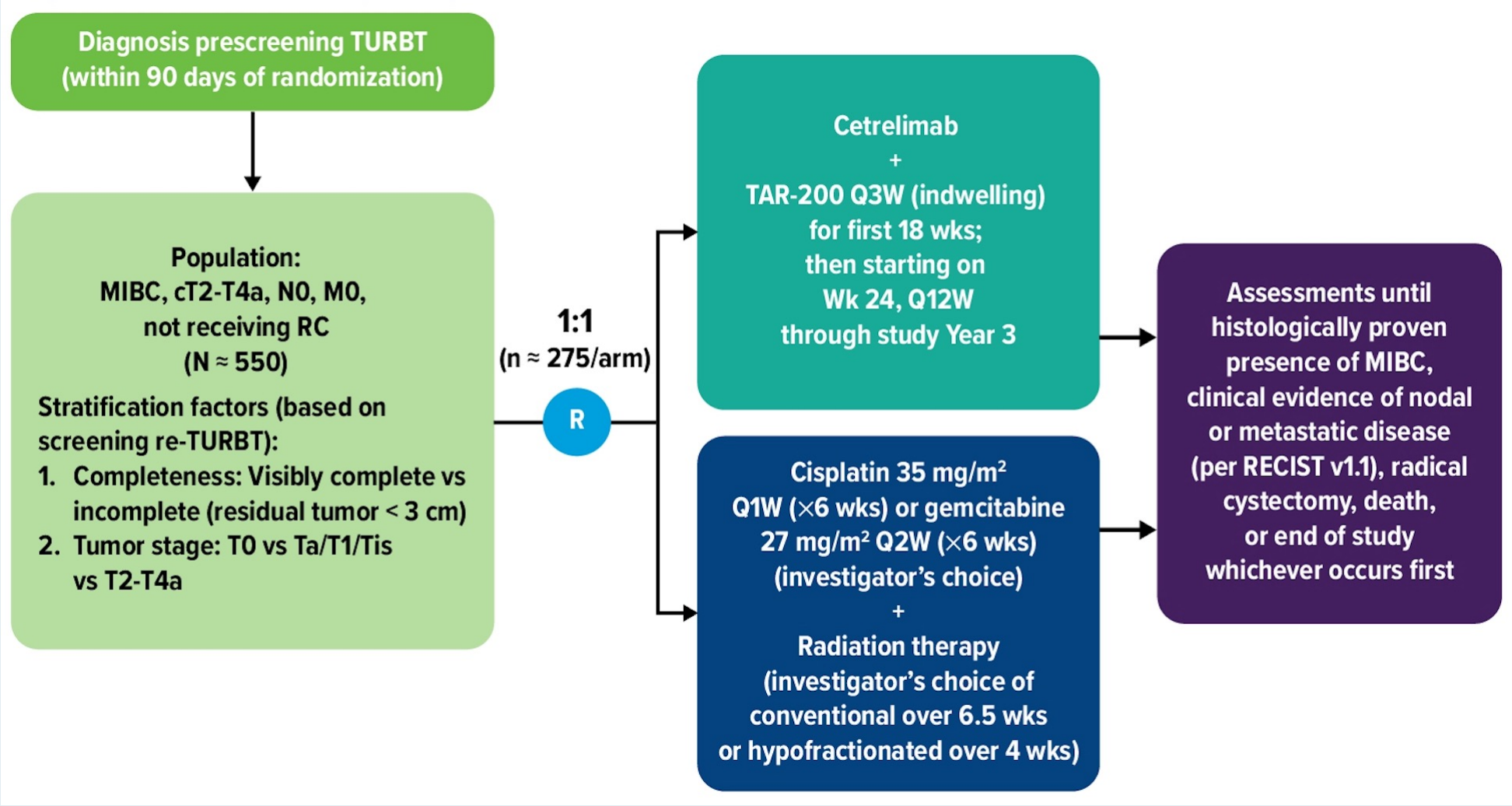
- Continued DMFS benefit was observed with NIVO versus PBO both in the ITT population and in patients with tumor PD-L1 expression ≥ 1%





Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA443.

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



Williams SB et al. ASCO 2021;Abstract TPS4586.

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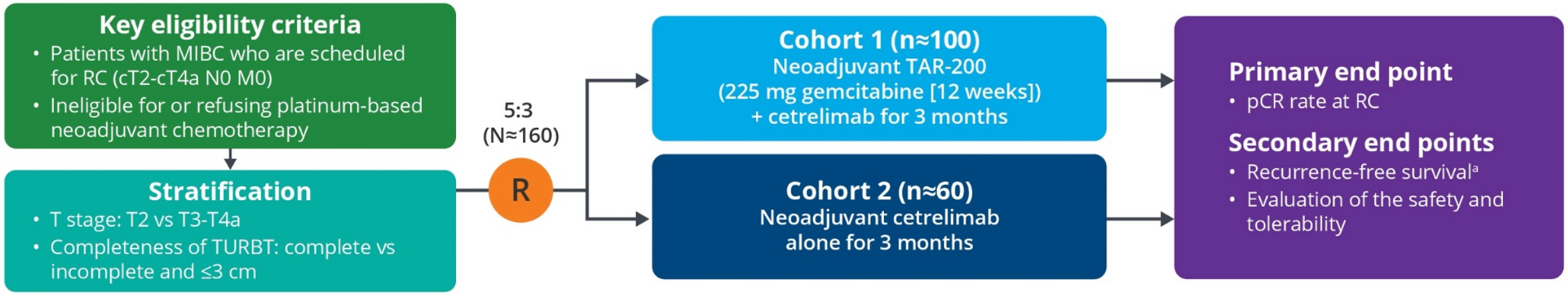
Ongoing Multicenter Randomized Phase II SunRISe-4 Study Design



pCR, pathologic complete response; TURBT, transurethral resection of bladder tumor.
[a]Per Response Evaluation Criteria In Solid Tumors 1.1 or histologic evidence.

Psutka SP et al. Genitourinary Cancers Symposium 2023;Abstract 584.

Questions from General Medical Oncologists

- **How do you choose between MVAC, dd MVAC and gem/cis neoadjuvantly?**
- **Is dd MVAC dead?**
- **For patients who underwent neoadjuvant treatment and still have residual disease, what should we do?**
- **I had a 51 yo chronic smoker with Stage IIIB bladder Ca who started neoadjuvant chemo XRT but halfway through decided to not proceed with chemotherapy due to tolerability issues. He had a PR, and we proceeded with surgery and started him on nivolumab maintenance. What would be your strategy for such patients?**

Survey of US-based general medical oncologists, May 2023. N = 75

Questions from General Medical Oncologists (Continued)

- **Is there a role of PD-1 adjuvant Tx in pts who achieved pCR after neoadjuvant Tx?**
- **How do you go about the current chemo shortage in this setting?**
- **Using ctDNA in selecting patients for adjuvant immunotherapy**

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How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to the management of nonmetastatic UBC in patients who are not candidates for cystectomy?

37% feel well informed

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Questions from General Medical Oncologists

- **What, if any, role does immunotherapy play in managing these patients?**
- **Can we use adjuvant IO after definitive chemoRT?**
- **60 yo with ESRD presents with locally advanced bladder cancer. What neoadjuvant regimen would you recommend?**
- **78 yo man w/past prostate cancer s/p pelvic RT who now has MIBC and declines cystectomy; cancer is PD-L1-positive**
- **Can TAR 200 be used?**

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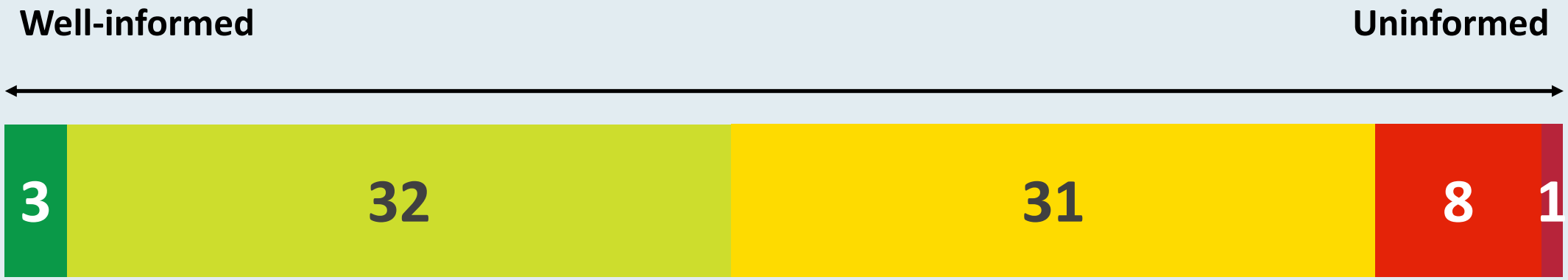

47% feel well informed

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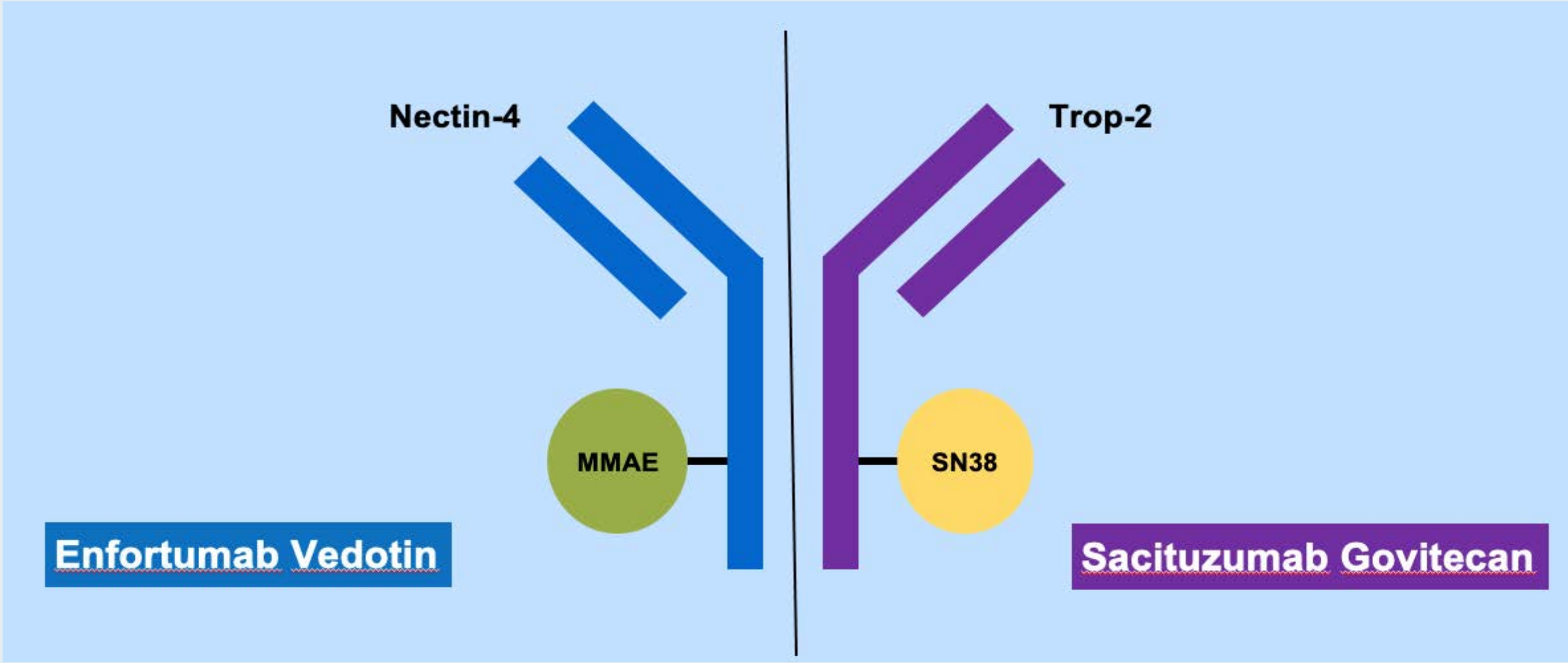
Selection and sequencing of therapy for platinum-eligible patients with FGFR wild-type mUBC

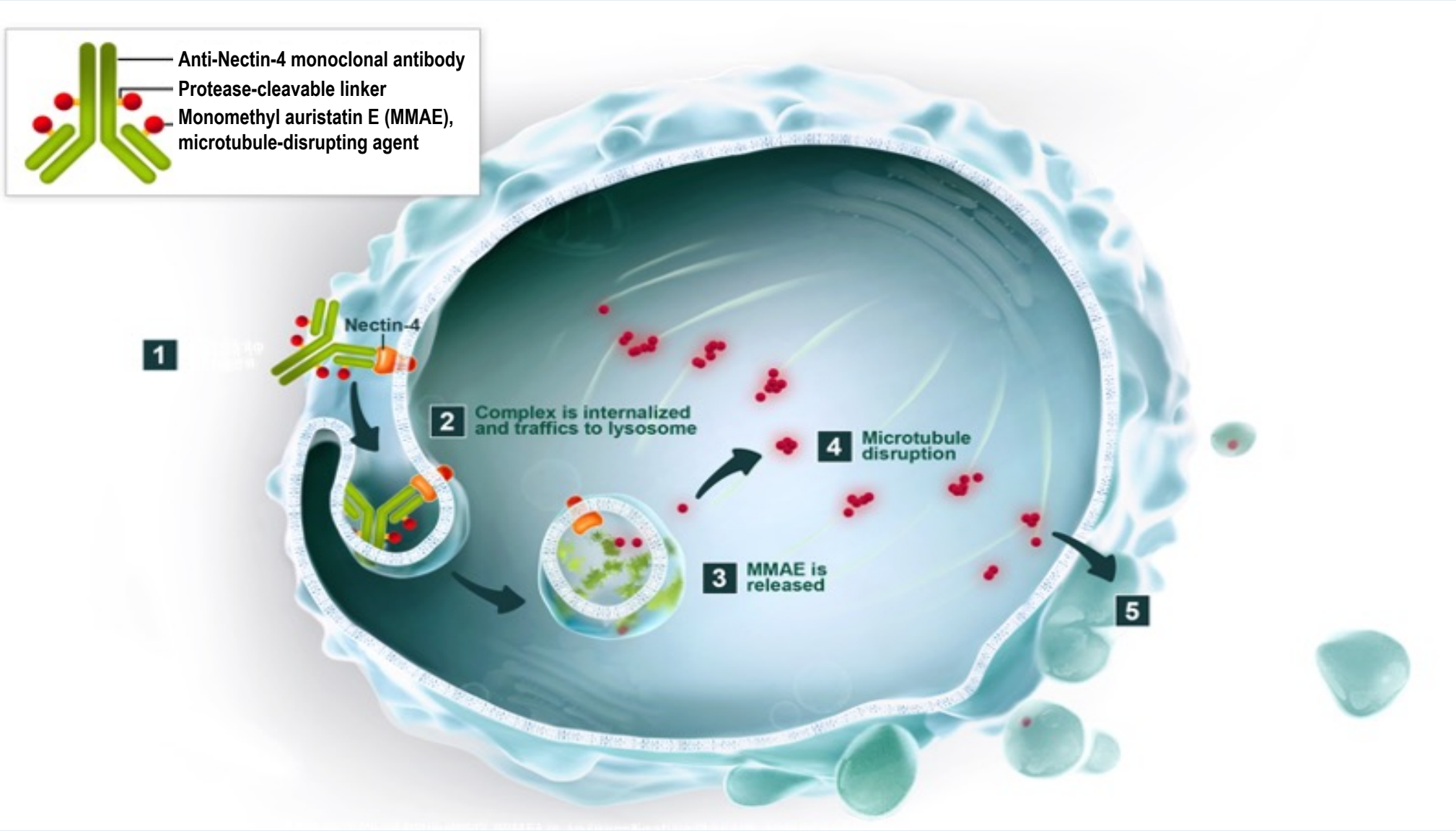
- Powles T et al. **Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC): Long-term follow-up results from the JAVELIN Bladder 100 trial.** Genitourinary Cancers Symposium 2022;Abstract 487.
- Rosenberg JE et al. **Long-term outcomes in EV-301: 24-month findings from the phase 3 trial of enfortumab vedotin vs chemotherapy in patients with previously treated advanced urothelial carcinoma.** ASCO 2023;Abstract 4516.
- Tagawa ST et al. **Updated outcomes in TROPHY-U-01 cohort 1, a phase 2 study of sacituzumab govitecan in patients with metastatic urothelial cancer who progressed after platinum-based chemotherapy and a checkpoint inhibitor.** Genitourinary Cancers Symposium 2023;Abstract 526.

Antibody-Drug Conjugates in UBC



Courtesy of Matthew Galsky, MD

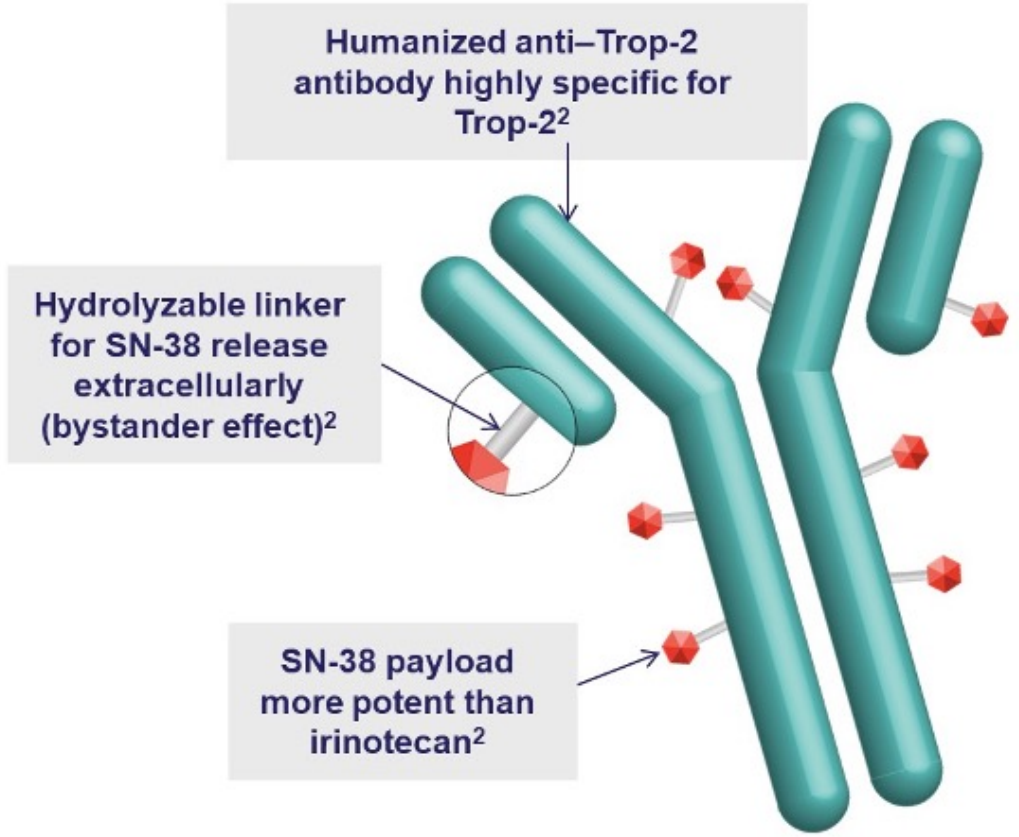
Enfortumab Vedotin: Nectin-4 Targeted Therapy



Courtesy of Jonathan Rosenberg, MD

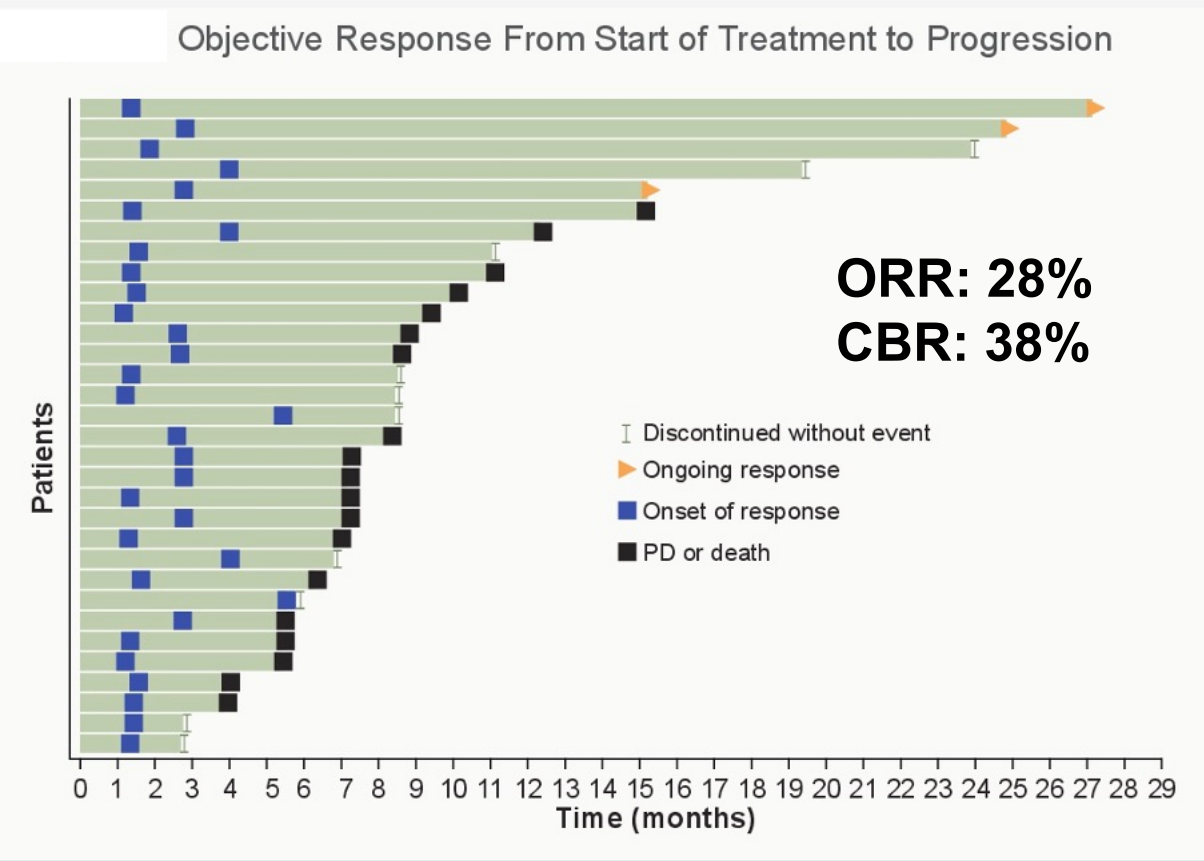
Sacituzumab Govitecan: A First-in-Class TROP2-Directed Antibody-Drug Conjugate

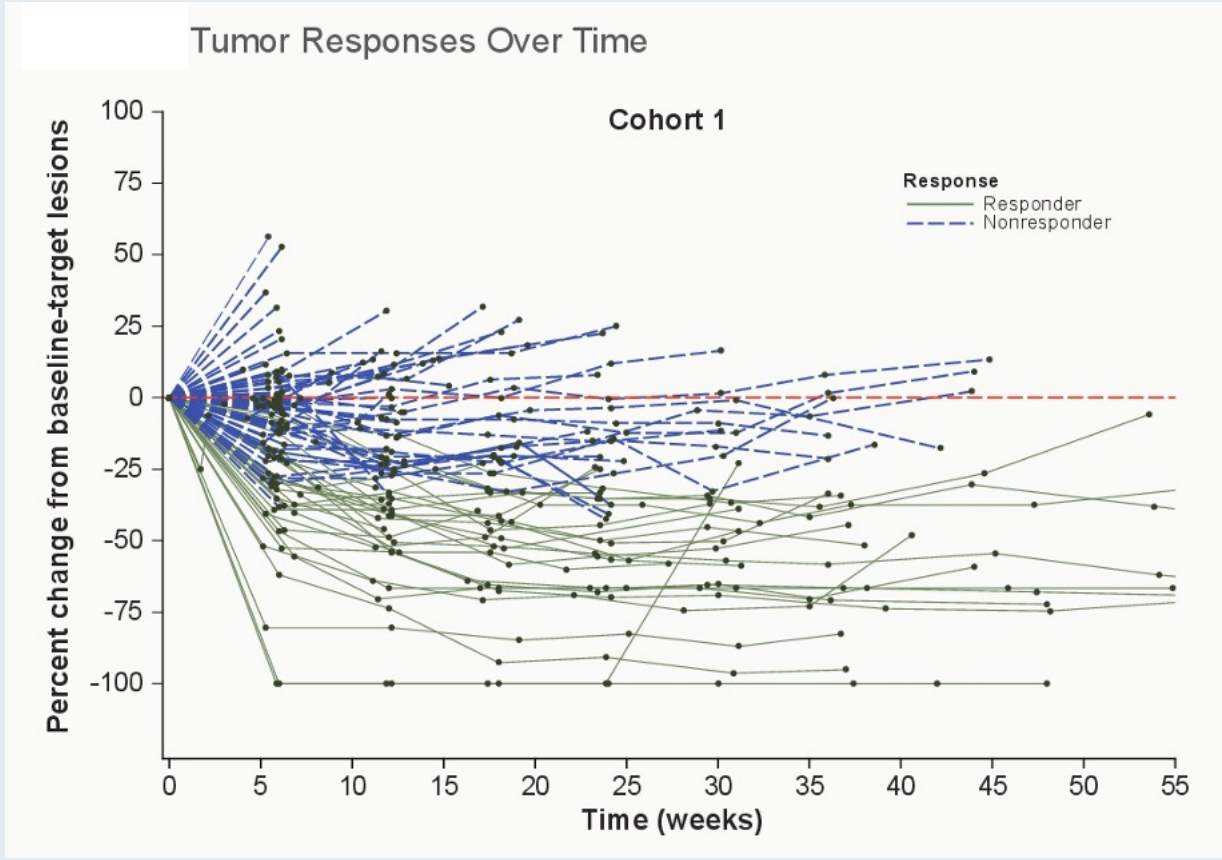
- Trop-2 is an epithelial cell surface antigen highly expressed in many solid tumors including invasive bladder cancer[1]
- SG is distinct from other ADCs[2-6]
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and enzymatic cleavage by tumor cell not required for SN-38 (active metabolite of 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.

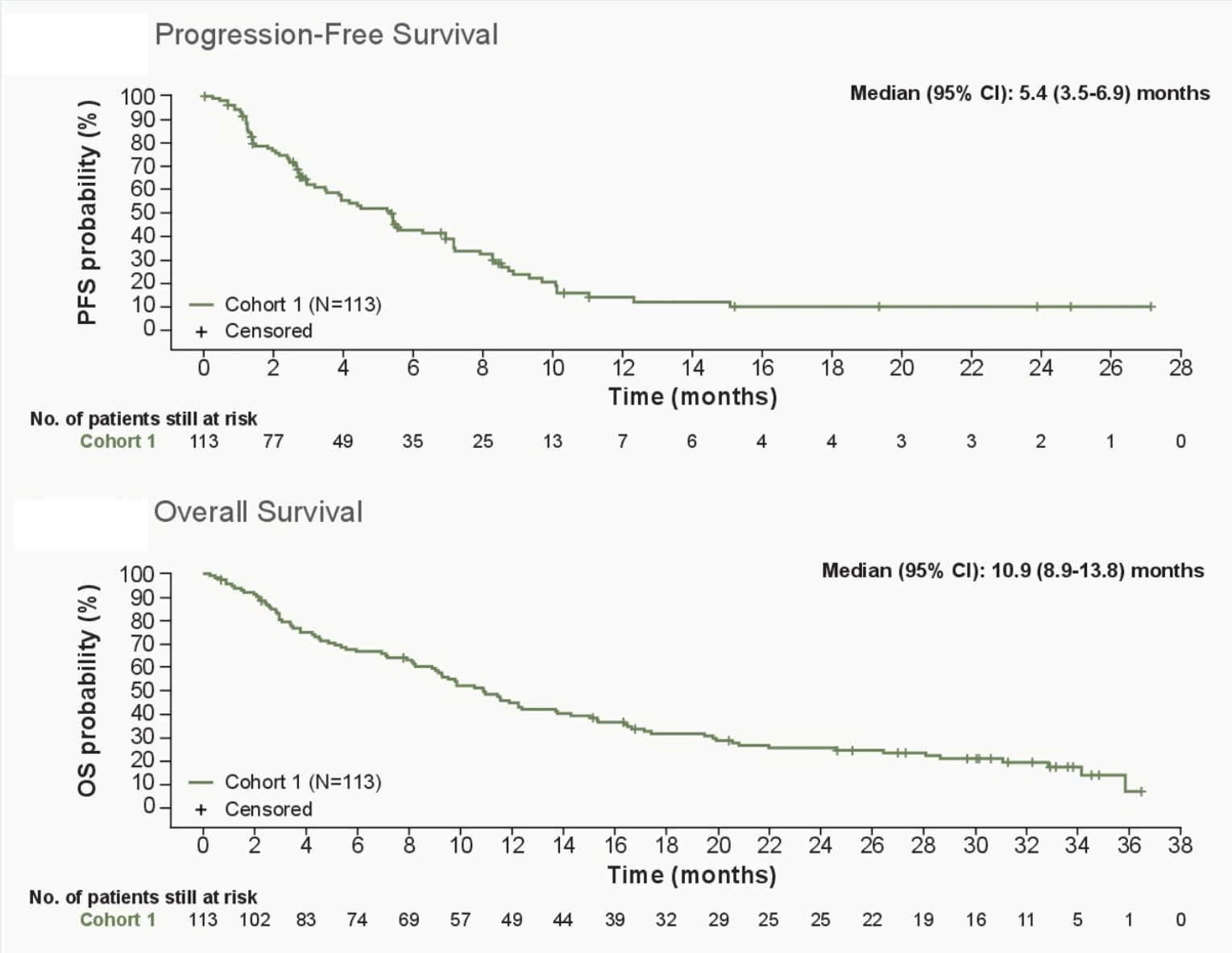
TROPHY U-01 (Cohort 1): Response





Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.

TROPHY U-01 (Cohort 1): Survival Analyses



Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.

TROPHY U-01 (Cohort 1): Safety Outcomes

- Grade ≥3 treatment-related adverse events (TRAE) occurred in 65% of patients and were consistent with the previous data cut (**Table 2**)
  - The most common grade ≥3 TRAEs were neutropenia, leukopenia, anemia, diarrhea, and febrile neutropenia
- TRAEs led to SG dose reductions in 40% of patients and SG dose discontinuations in 7% of patients
- One treatment-related death occurred due to febrile neutropenia–related sepsis, which was previously reported[2]
- In total, 42% of patients received G-CSF (22% for prophylaxis and 23% for AE treatment)
- No new treatment-related deaths occurred since the prior data cutoff

	Cohort 1 (N=113)		
Most Common Grade ≥3 TRAEs[a]	All Grades, n (%)	Grade 3, n (%)	Grade 4, n (%)
Neutropenia	53 (47)	25 (22)	14 (12)
Leukopenia	29 (26)	14 (12)	6 (5)
Anemia	38 (34)	16 (14)	0
Diarrhea	73 (65)	10 (9)	1 (1)
Febrile neutropenia	11 (10)	8 (7)	3 (3)

Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.

Questions from General Medical Oncologists

- **Does immunotherapy have any role if patients have already received maintenance avelumab?**
- **Saci before or after EV based on QoL considerations**
- **Now with carboplatin shortage, any recs for cisplatin-ineligible patients?**
- **What are your thoughts on the use enfortumab and pembrolizumab in the first-line metastatic setting as opposed to platinum combo followed by avelumab?**
- **When should NGS panel be obtained?**
- **What to do in elderly frail patients who fail IO**

Survey of US-based general medical oncologists, May 2023. N = 75

Agenda

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

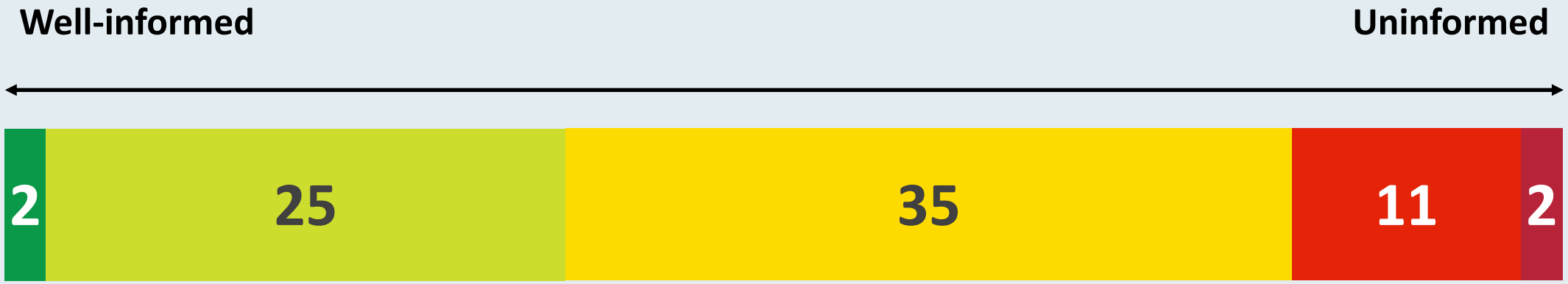
- Management of non-muscle-invasive bladder cancer
- Neoadjuvant and adjuvant therapy for muscle-invasive bladder cancer
- Management of nonmetastatic UBC in patients who are not candidates for cystectomy

Module 2 – Recent Advances in the Treatment of Metastatic UBC (mUBC)

- Selection and sequencing of therapy for platinum-eligible patients with FGFR wild-type mUBC
- Selection and sequencing of therapy for platinum-ineligible patients with FGFR wild-type mUBC
- Selection and sequencing of therapy for patients with FGFR-altered mUBC
- Novel agents and strategies under investigation in UBC

RTP RESEARCH TO PRACTICE

How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to selection and sequencing of therapy for platinum-ineligible patients with FGFR wild-type mUBC?



36% feel well informed

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Selection and sequencing of therapy for platinum-ineligible patients with FGFR wild-type mUBC

- Hoimes CJ et al. **Enfortumab vedotin plus pembrolizumab in previously untreated advanced urothelial cancer.** *J Clin Oncol* 2023;41(1):22-31.
- Gupta S et al. **Study EV-103 dose escalation/cohort A: Long-term outcome of enfortumab vedotin + pembrolizumab in first-line (1L) cisplatin-ineligible locally advanced or metastatic urothelial carcinoma (la/mUC) with nearly 4 years of follow-up.** ASCO 2023;Abstract 4505.

FDA Grants Accelerated Approval to Enfortumab Vedotin with Pembrolizumab as First-Line Therapy for Locally Advanced or Metastatic Urothelial Carcinoma

Press Release: April 3, 2023

"The Food and Drug Administration granted accelerated approval to enfortumab vedotin-ejfv with pembrolizumab for patients with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing chemotherapy.

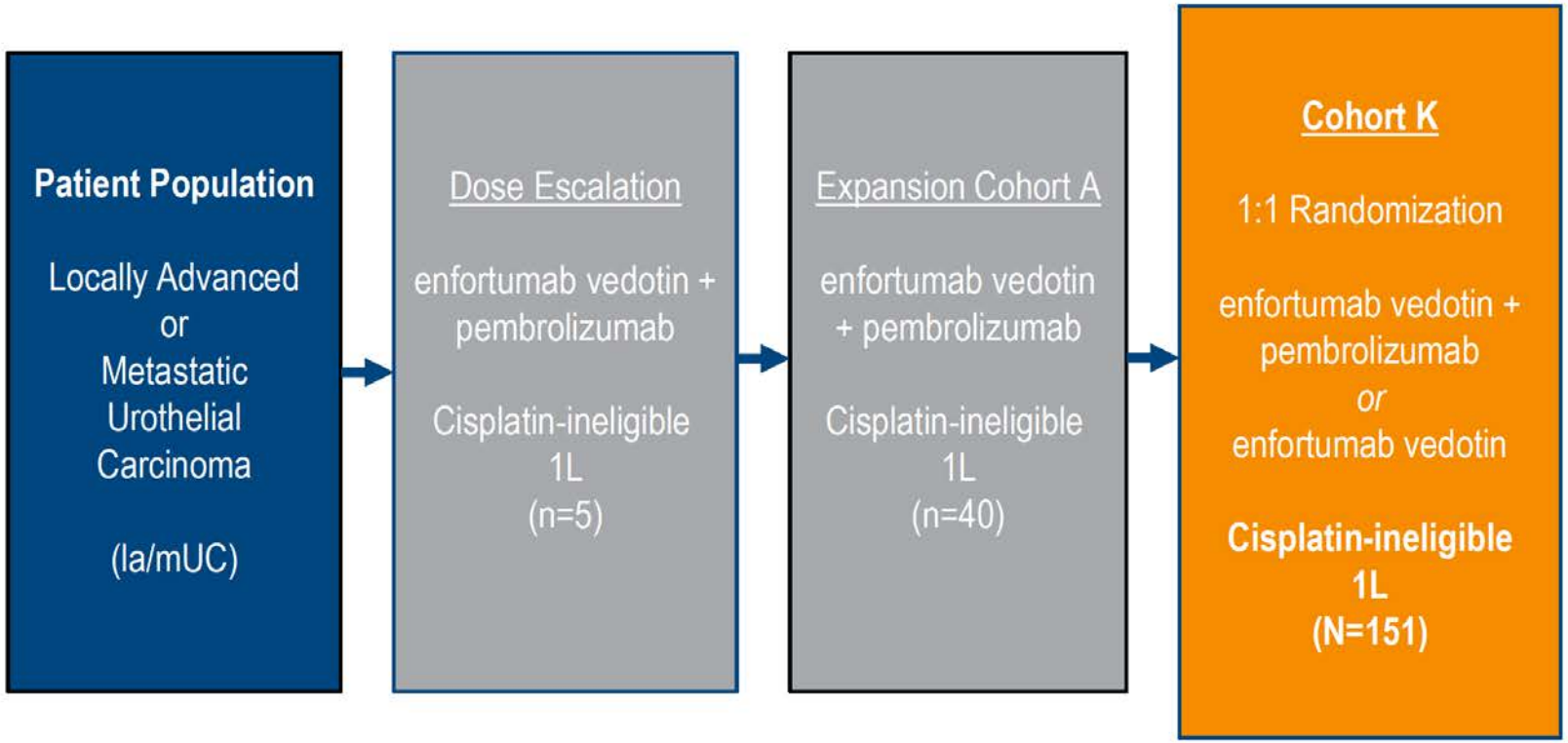
Efficacy was evaluated in EV-103/KEYNOTE-869 (NCT03288545), a multi-cohort (dose escalation cohort, Cohort A, Cohort K) study. The dose escalation cohort and Cohort A were single-arm cohorts treating patients with enfortumab vedotin-ejfv plus pembrolizumab while patients on Cohort K were randomized to either the combination or to enfortumab vedotin-ejfv alone. Patients had not received prior systemic therapy for locally advanced or metastatic disease and were ineligible for cisplatin-containing chemotherapy. A total of 121 patients received enfortumab vedotin-ejfv plus pembrolizumab.

The major efficacy outcome measures were objective response rate (ORR) and duration of response (DoR) determined by blinded independent central review using RECIST v1.1. The confirmed ORR in 121 patients was 68%, including 12% with complete responses. The median DoR for the dose escalation cohort + Cohort A was 22 months and for Cohort K was not reached."

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

EV-103 Cohort K

Part of an open-label, multiple cohort, phase 1b/2 study in patients with urothelial carcinoma



- **Dosing:** EV 1.25 mg/kg IV on days 1 and 8, and P 200 mg IV on day 1 of every 3-week cycle
- **Primary endpoint:** confirmed ORR by RECIST v1.1 per BICR
- **Key secondary endpoints:** confirmed ORR per RECIST v1.1 by investigator, DOR, DCR, PFS, OS, safety/ tolerability, and lab abnormalities

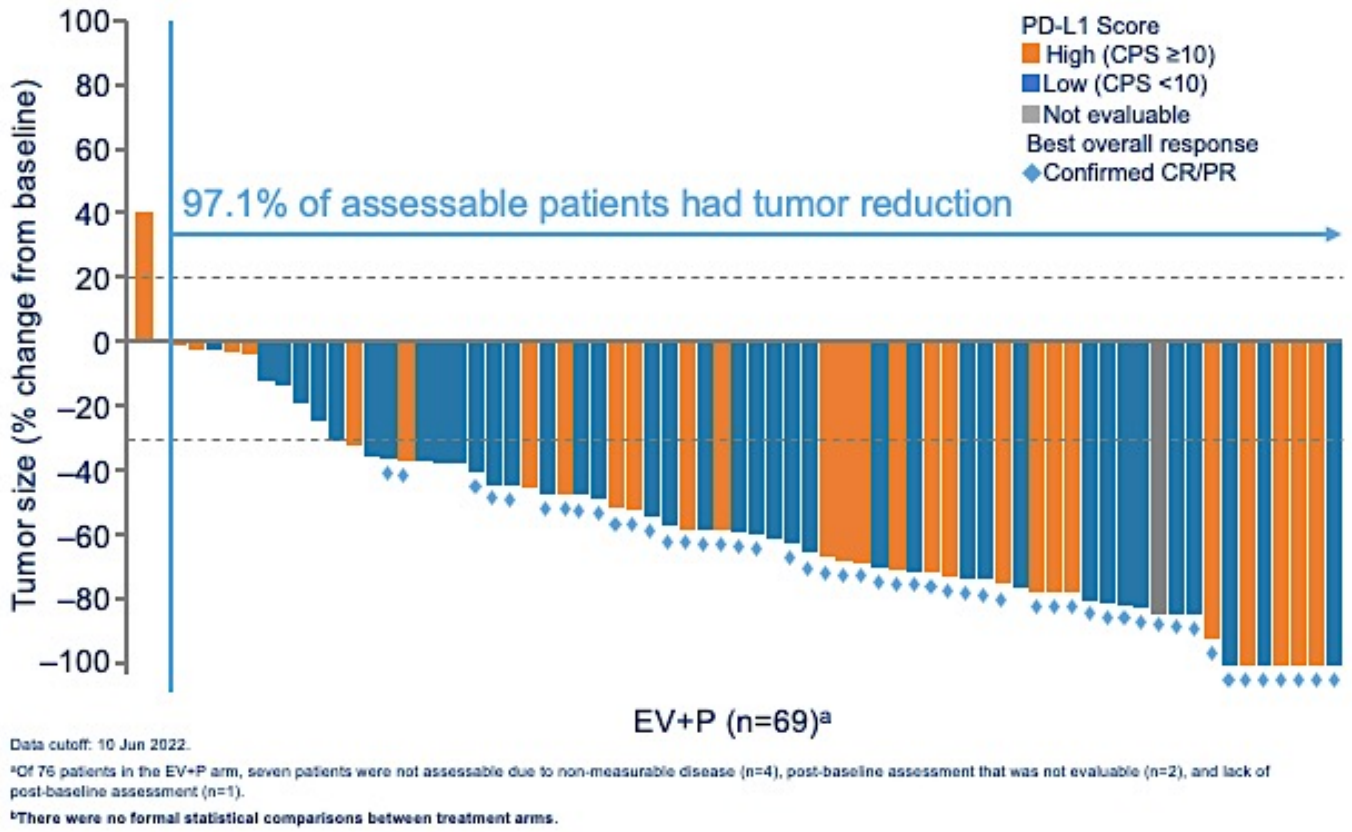
Statistical considerations

- The sample size was based on precision of the estimate for ORR characterized by 95%CIs
- No formal statistical comparisons between the 2 treatment arms

Stratification factors: Liver metastases (present/absent) and ECOG PS (0 or 1/2); **Exploratory endpoints**: pharmacokinetics, antitherapeutic antibody, biomarkers of activity including baseline PD-L1 status and Nectin-4 expression, progression-free survival on subsequent therapy by investigator, patient reported outcomes; **Cohort K** completed enrollment on 11 Oct 2021; **Data cutoff was 10 Jun 2022**

Rosenberg JE et al. ESMO 2022;Abstract LBA73.

EV-103 Cohort K: Efficacy and Safety



Data cutoff: 10 Jun 2022.

[a]Of 76 patients in the EV+P arm, seven patients were not assessable due to non-measurable disease (n=4), post-baseline assessment that was not evaluable (n=2), and lack of post-baseline assessment (n=1).

[b]There were no formal statistical comparisons between treatment arms.

	EV+P[b] (n=76)	EV mono[b] (n=73)
cORR, n (%) (95% CI)	49 (64.5) (52.7-75.1)	33 (45.2) (33.5-57.3)
Median time to objective response (range), mo	2.07 (1.1-6.6)	2.07 (1.9-15.4)
Median number of treatment cycles (range)	11.0 (1-29)	8.0 (1-33)

EV+P

- 42/49 (85.7%) of responses observed at first assessment (week 9±1 week)
- Most common AEs were fatigue, peripheral sensory neuropathy, alopecia, and maculopapular rash

EV mono

- Activity is consistent with prior results in 2L+ la/mUC
- Safety profile consistent with previous studies

Rosenberg JE et al. ESMO 2022;Abstract LBA73.

EV-103 Cohort K: Treatment-Related Adverse Events of Special Interest (AESIs)

The majority of treatment-related AESIs were grade ≤2

	EV+P (N=76)		EV Mono (N=73)	
	Any Grade n (%)	Grade ≥3 n (%)	Any Grade n (%)	Grade ≥3 n (%)
Skin reactions	51 (67.1)	16 (21.1)	33 (45.2)	6 (8.2)
Peripheral neuropathy	46 (60.5)	2 (2.6)	40 (54.8)	2 (2.7)
Ocular disorders	20 (26.3)	0	21 (28.8)	0
Dry eye	18 (23.7)	0	9 (12.3)	0
Blurred vision	9 (11.8)	0	10 (13.7)	0
Corneal disorders	0	0	4 (5.5)	0
Hyperglycemia	11 (14.5)	5 (6.6)	8 (11.0)	7 (9.6)
Infusion-related reactions	3 (3.9)	0	4 (5.5)	0

- Skin reactions were observed more frequently with EV+P
  - No serious skin reactions occurred with EV+P
- Peripheral neuropathy remains the most common reason for treatment-related discontinuations

*There are differences in the rates of skin reactions reported for EV treatment-related AESIs and pembro TEAEs of special interest because these adverse events were reported via different methodologies developed for EV and pembro monotherapies, respectively

Rosenberg JE et al. ESMO 2022;Abstract LBA73.

Questions from General Medical Oncologists

- **How should we think about therapy sequencing now that there are strong data for enfortumab + pembrolizumab?**
- **Should carbo/gem/ICI be used if EV/pembro is approved?**
- **Role of avelumab in patients who did not/could not receive platinum-based chemo**
- **Please review management of toxicity from enfortumab vedotin**
- **Is one immunotherapy better than another one? From data**
- **Can sequential ctDNA be used to assess disease response and duration of therapy?**
- **How should we classify platinum ineligible?**

Survey of US-based general medical oncologists, May 2023. N = 75

Agenda

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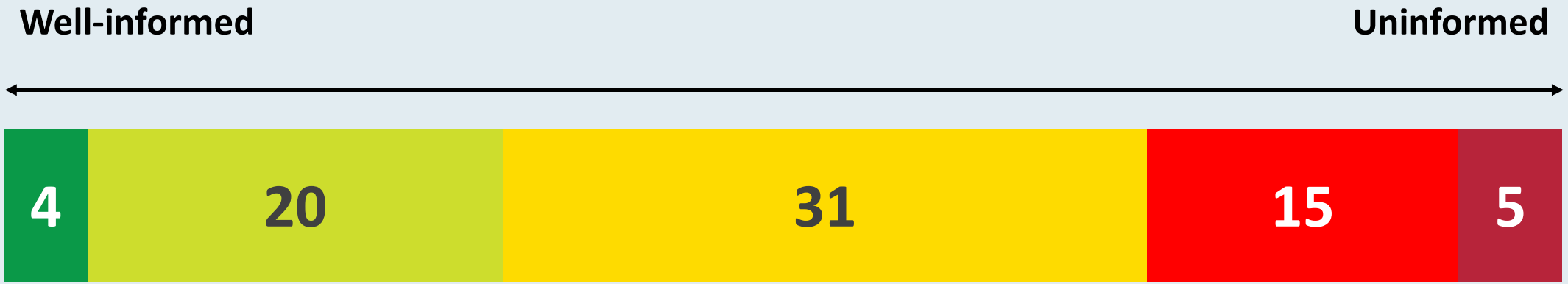
- Novel agents and strategies under investigation in UBC

RTP RESEARCH TO PRACTICE

How comfortable/familiar are you with the published data sets, available guidelines, investigator perspectives and ongoing research studies pertaining to selection and sequencing of therapy for patients with FGFR-altered mUBC?



32% feel well informed

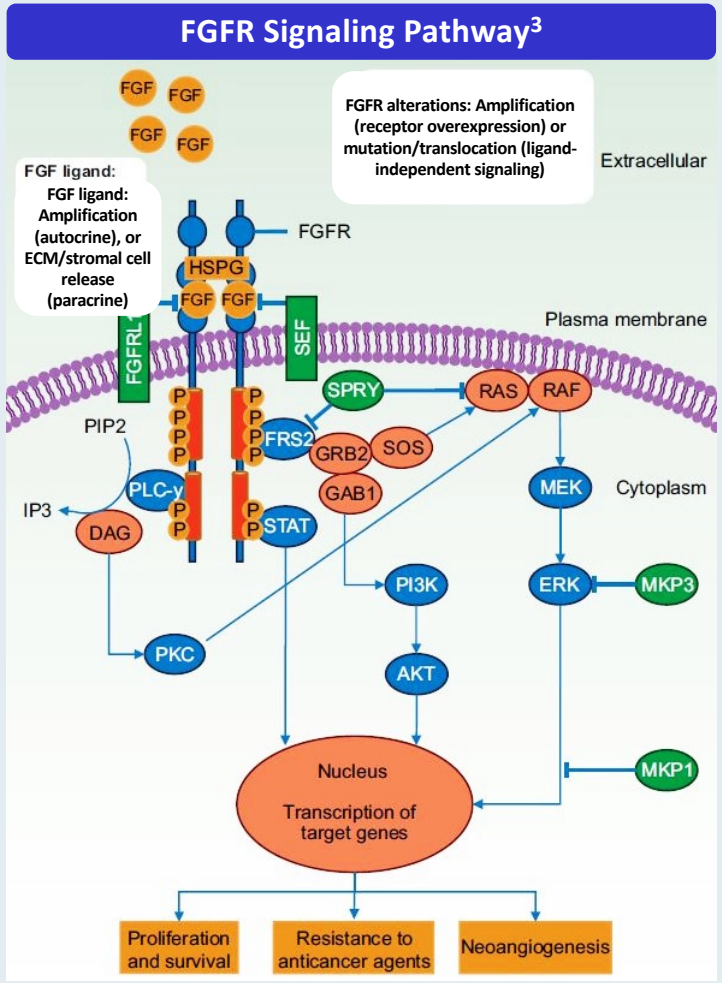
Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Selection and sequencing of therapy for patients with FGFR-altered mUBC

- Siefker-Radtke AO et al. **Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: Long-term follow-up of a phase 2 study.** *Lancet Oncol* 2022;23(2):248-58.
- Loriot Y et al. **Phase 3 THOR study: Results of erdafitinib (erda) versus chemotherapy (chemo) in patients (pts) with advanced or metastatic urothelial cancer (mUC) with select fibroblast growth factor receptor alterations (FGFRalt).** ASCO 2023;Abstract LBA4619.
- Siefker-Radtke AO et al. **Erdafitinib (ERDA) vs ERDA plus cetrelimab (ERDA+CET) for patients (pts) with metastatic urothelial carcinoma (mUC) and fibroblast growth factor receptor alterations (FGFRa): Final results from the phase 2 Norse study.** ASCO 2023;Abstract 4504.

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



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

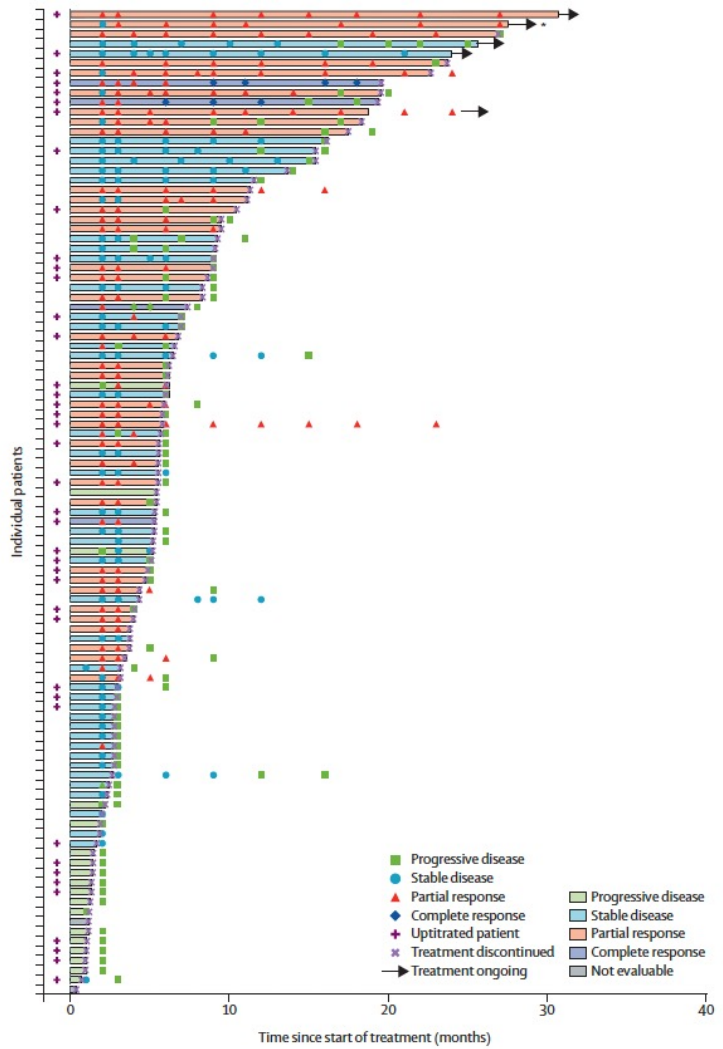
Cancer Type	Frequency of FGFR Alterations[1]
Metastatic UC	15%-20%
NMIBC	40%-70%
Cholangiocarcinoma	14%-22%
NSCLC	4%
HCC (FGF19 amp by FISH)	21%
Glioblastoma	23%
Breast cancer	3%-5%
Ovarian cancer	7%
Head and neck cancer	9%-17%

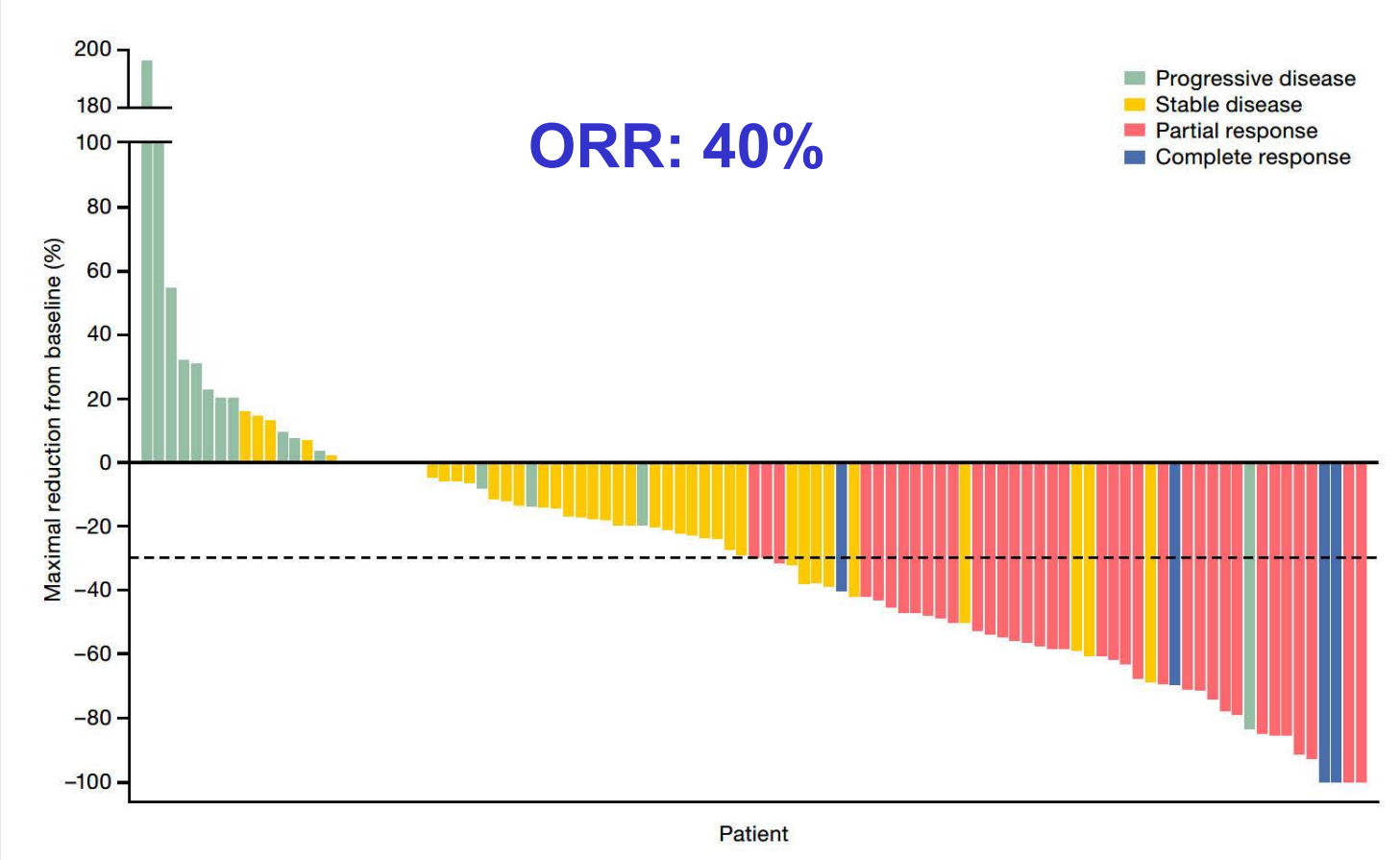
1. The Cancer Genome Atlas (TCGA) genomic alteration database: https://tcga-data.nci.nih.gov/docs/publications/tcga/. Accessed February 6, 2020.
2. Genomics Evidence Neoplasia Information Exchange (GENIE) genomic alteration database: https://www.aacr.org/Research/Research/pages/aacr-project-genie.aspx. 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

BLC2001: Erdafitinib for Locally Advanced or Metastatic UBC

Responses in Patients Who Received the Selected 8 mg/day Erdafitinib UpT* Regimen



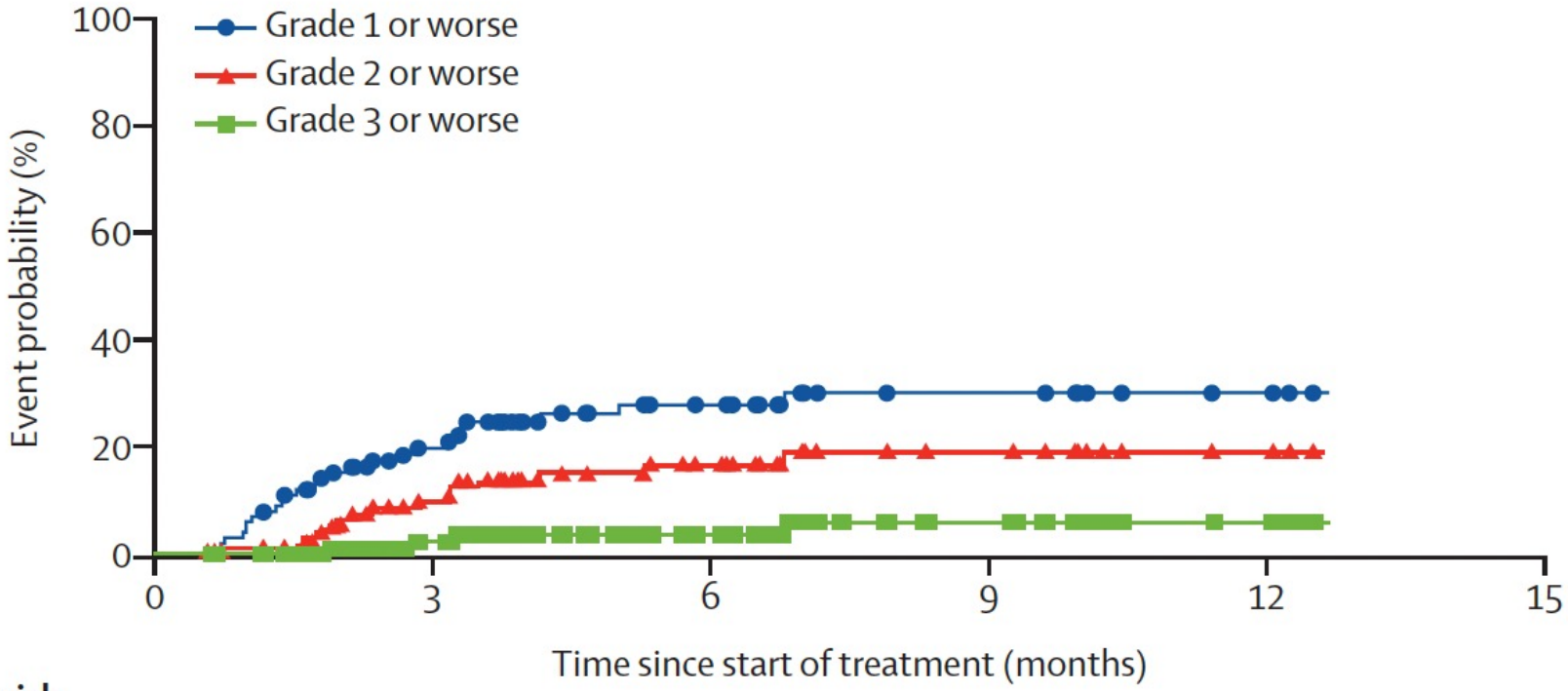


* Continuous once-daily 8 mg/day oral erdafitinib in 28-day cycles, with provision for pharmacodynamically guided uptitration to 9 mg/day

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

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;23:248-58.

Randomized Phase III Erdafitinib THOR Trial Schema

Key Inclusion Criteria:

- Locally advanced, unresectable or metastatic UC (minority component histologies allowed)
- FGFR inhibitor Clinical Trial Assay to determine molecular eligibility
- Only one line of prior systemic therapy
- ECOG PS 0, 1 or 2

Cohort 1 – Prior PD-1/PD-L1 treatment

1:1 RANDOMIZE

- Erdafitinib 8 mg po qd, N =140
- Docetaxel or Vinflunine IV Day 1 of a 21-day cycle, N =140

Cohort 2 – No prior PD-1/PD-L1 treatment

1:1 RANDOMIZE

- Erdafitinib 8 mg po qd, N =175
- Pembrolizumab IV Day 1 of a 21-day cycle, N =175

Primary Endpoint: Overall survival

Secondary Endpoints: Progression-free survival, overall response rate, duration of response, safety, patient-reported outcomes, pharmacokinetics.

www.clinicaltrials.gov. NCT03390504. Accessed May 2023.

Phase 3 THOR Study: Results Of Erdafitinib (Erda) versus Chemotherapy (Chemo) in Patients (Pts) with Advanced or Metastatic Urothelial Cancer (mUC) with Select Fibroblast Growth Factor Receptor Alterations (FGFRalt)

Loriot Y et al.

ASCO 2023;Abstract LBA4619.

Monday, June 5th, 7:30 AM CDT

RTP RESEARCH TO PRACTICE

Erdafitinib (ERDA) vs ERDA plus Cetrelimab (ERDA+CET) for Patients (Pts) with Metastatic Urothelial Carcinoma (Muc) and Fibroblast Growth Factor Receptor Alterations (Fgfra): Final Results from the Phase 2 Norse Study

Siefker-Radtke AO et al.

ASCO 2023;Abstract 4504.
Monday, June 5th, 12:42 PM CDT

Questions from General Medical Oncologists

- **What advice would you give when starting a patient on erdafitinib regarding toxicities, dosing, prophylactic use of symptomatic medications, follow-up?**
- **How would you sequence erdafitinib in an 83 yo male with metastatic urothelial cancer who is technically platinum eligible?**
- **65 yo female bladder cancer with FGFR alteration, progressed on first-line chemotherapy. Should I give erdafitinib or checkpoint inhibitor?**
- **Which FGFR mutations confer sensitivity to erdafitinib, and what toxicities have you most commonly seen?**
- **I am concerned about the eye toxicity of erdafitinib. I cannot find an enthusiastic ophthalmologist to monitor its toxicity. I have not used it.**

Survey of US-based general medical oncologists, May 2023. N = 75

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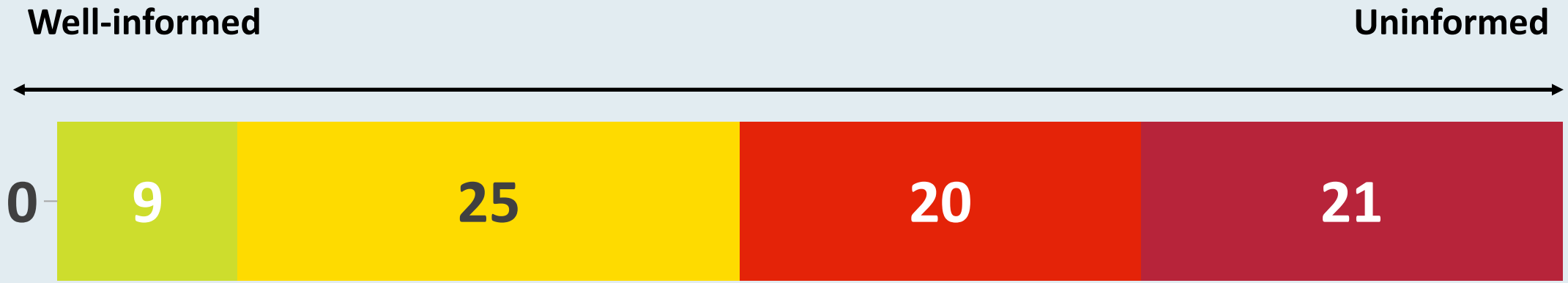
How comfortable/familiar are you with the published data sets, investigator perspectives and ongoing research studies pertaining to novel agents and strategies under investigation in UBC (eg, TAR-200, HER2-targeted therapy, PARP inhibitors, anti-PD-1/PD-L1 and anti-CTLA-4 combinations)?



12% feel well informed

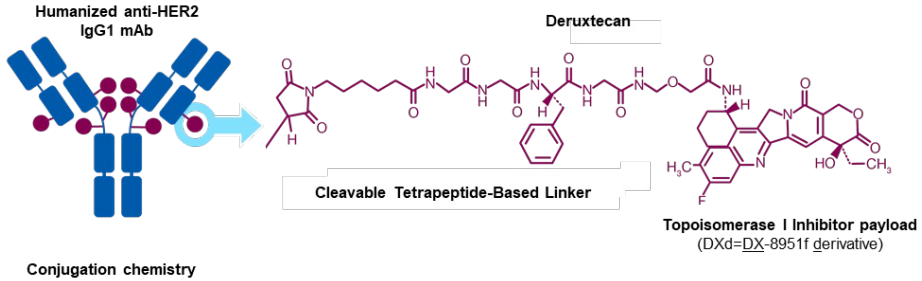
Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

Novel agents and strategies under investigation in UBC

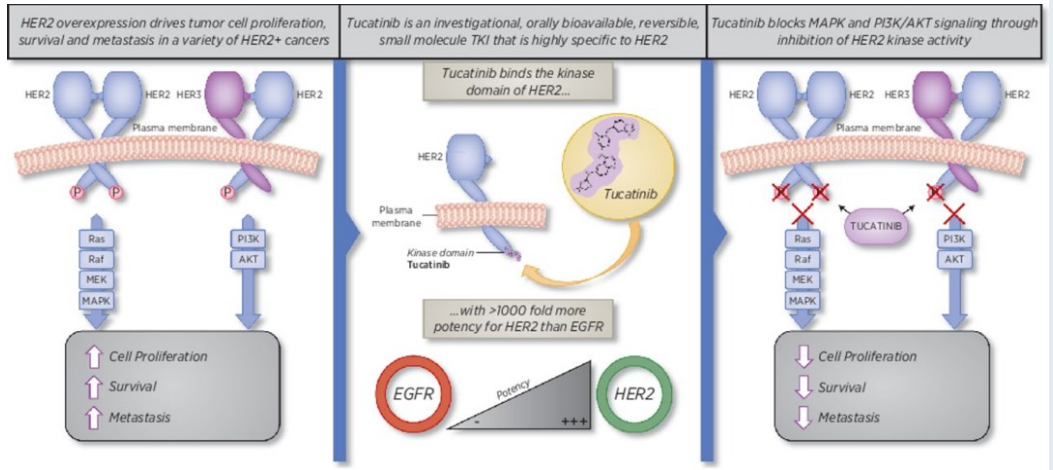
- Sheng X et al. **RC48-ADC for metastatic urothelial carcinoma with HER2-positive: Combined analysis of RC48-C005 and RC48-C009 trials.** ASCO 2022;Abstract 4520.
- Sheng X et al. **Primary results of a phase Ib/II combination study of RC48-ADCV, a novel humanized anti-HER2 antibody-drug conjugate (ADC) with toripalimab, a humanized IgG4 mAb against programmed death-1 (PD-1) in patients with locally advanced or metastatic urothelial carcinoma (LA/mUC).** ASCO 2023;Abstract 4518.
- Galsky MD et al. **Primary analysis from DS8201-A-U105: A phase 1b, 2-part, open-label study of trastuzumab deruxtecan (T-DXd) with nivolumab in patients with HER2-expressing urothelial carcinoma (UC).** ASCO 2022;Abstract 438.
- Meric-Bernstam F et al. **Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results.** ASCO 2023;Abstract LBA3000.
- Rosenberg JE et al. **Durvalumab plus olaparib in previously unthreatened, platinum-ineligible patients with nmetastatic urothelial carcinoma: A multicenter, randomized, phase II trial (BAYOU).** *J Clin Oncol* 2023;41(1):43-53.

HER2 as a Bladder Cancer Target



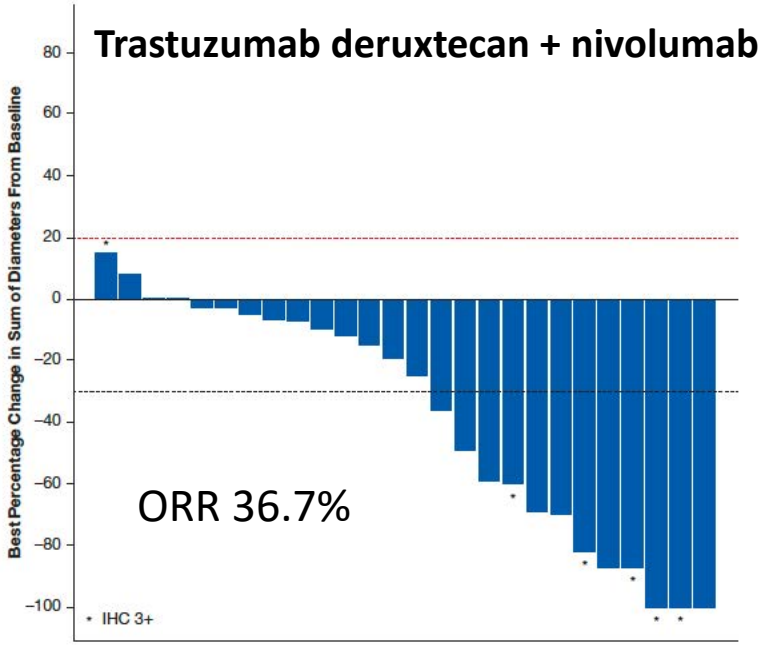
Conjugation chemistry
The tetrapeptide-based cleavable linker is connected to the humanized anti-HER2 IgG1 monoclonal antibody, with the same amino acid sequence as trastuzumab

Tucatinib basket trial with enough responses to go on to Stage 2 of design.



Tucatinib is an investigational agent and its efficacy and safety have not been established

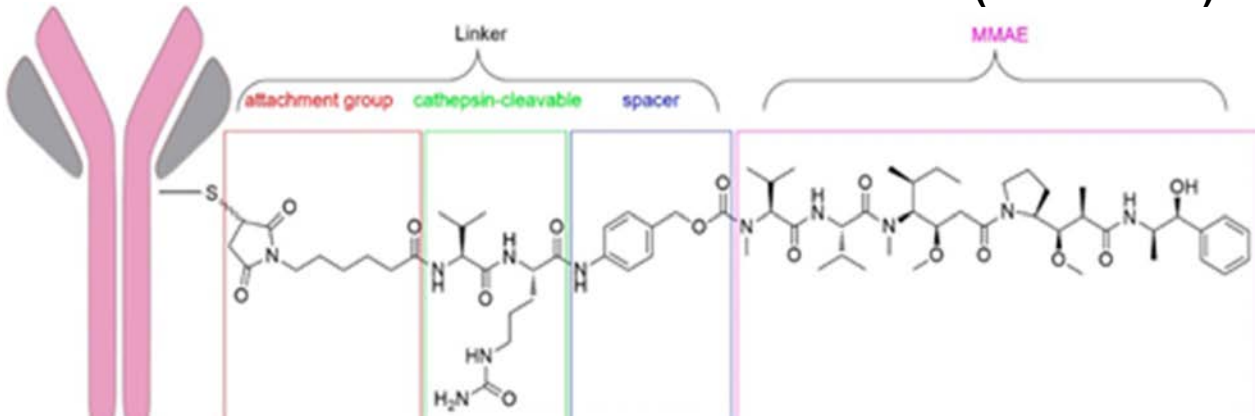
Trastuzumab deruxtecan + nivolumab



Cohort 3 IHC 3+/2+ (n = 30) (part 2: T-DXd 5.4 mg/kg and nivolumab 360 mg) Best (minimum) percentage change					
n	Mean	SD	Median	Min	Max
26	−37.8	38.52	−22.0	−100	15

[a]In cohort 3, 4 patients did not have best percentage change available, of whom 2 were IHC 3+.
The line at 20% indicates progressive disease, and the line at −30% indicates a partial response.

Disitamab vedotin (RC48-ADC)



Hertuzumab

RTP RESEARCH TO PRACTICE

2022 ASCO® ANNUAL MEETING

Abstract 4520

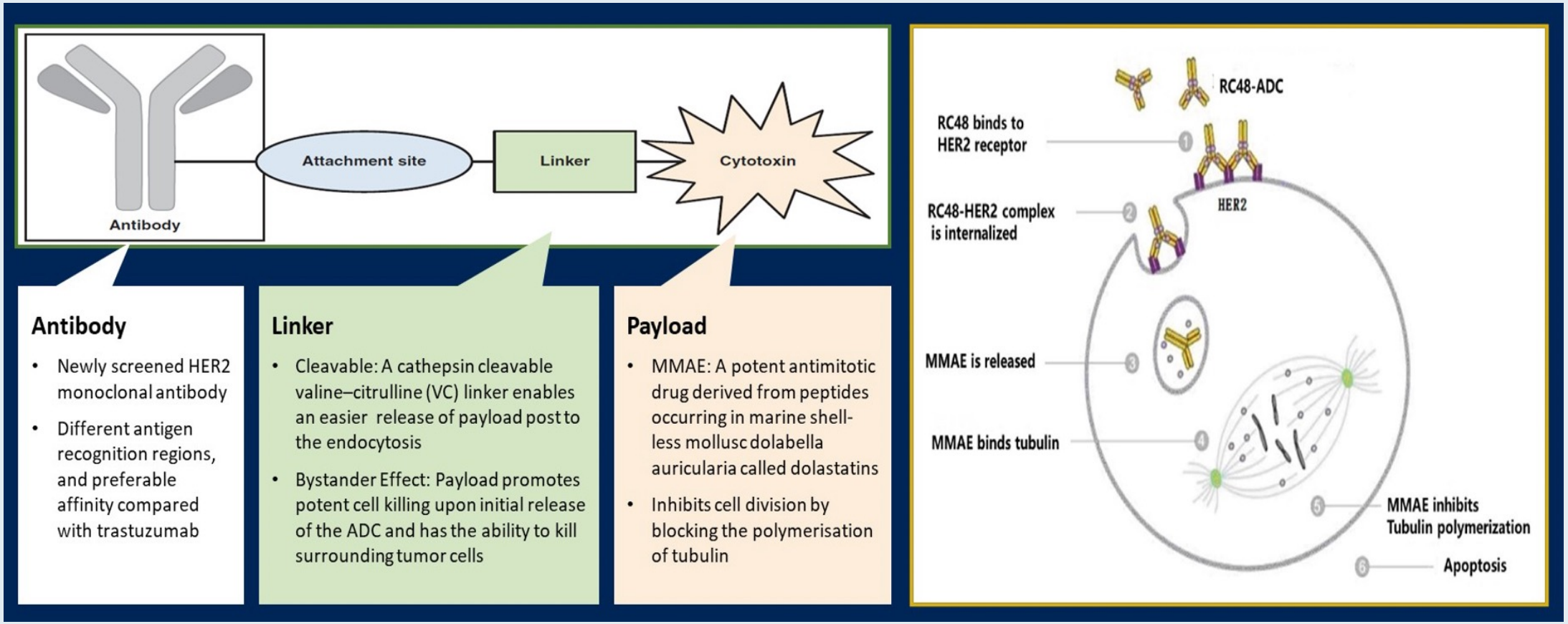
RC48-ADC for Metastatic Urothelial Carcinoma with HER2-positive: combined analysis of RC48-C005 and RC48-C009 trials

Xinan Sheng[1]*, Zhisong He[3], Yan-Xia Shi[4], Hong Luo[5],Weiqing Han[6], Xin Yao[7], Benkang Shi[8], Jiyan Liu[9], Changlu Hu[10] Ziling Liu[11], Hongqian Guo[12], Guohua Yu[13], Zhigang Ji[14] , Shi Ying Yu[15], Yi Hu[16], Jianming Guo[17], Jianmin Fang[18] , Ai-Ping Zhou[2] **, Jun Guo[1]**

1.Department of Renal Cancer and Melanoma, Peking University Cancer Hospital & Institute, Beijing, China; 2.Peking University Cancer Hospital and Institute, Beijing, China Department of Medical Oncology, Cancer Hospital, CAMS, Beijing, China; 3.Department of Urology, Peking university First Hospital, Institute of Urology, Peking University, Beijing, China; 4.Department of Medical Oncology, Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; 5.Chongqing Cancer Hospital, Chongqing, China; 6.Hunan Cancer Hospital, Changsha, China; 7.Tianjin Cancer Hospital, Tianjin, China; 8.Qilu Hospital of Shandong University, Jinan, China; 9.West China Hospital, Sichuan University, Chengdu,China;10. Anhui Provincial Cancer Hospital, Hefei, China; 11. Department of Cancer Centre, First Hospital of Jilin University, Changchun, China; 12. Nanjing Drum Tower Hospital, Nanjing, China; 13.Weifang People's Hospital, Weifang, China; 14. Peking Union Medical College Hospital, Beijing, China; 15. Tongji Hospital, Wuhan, China; 16. Chinese PLA General Hospital, Beijing, China; 17. Zhongshan Hospital, Fudan University, Shanghai, China; 18. Remegen, Ltd

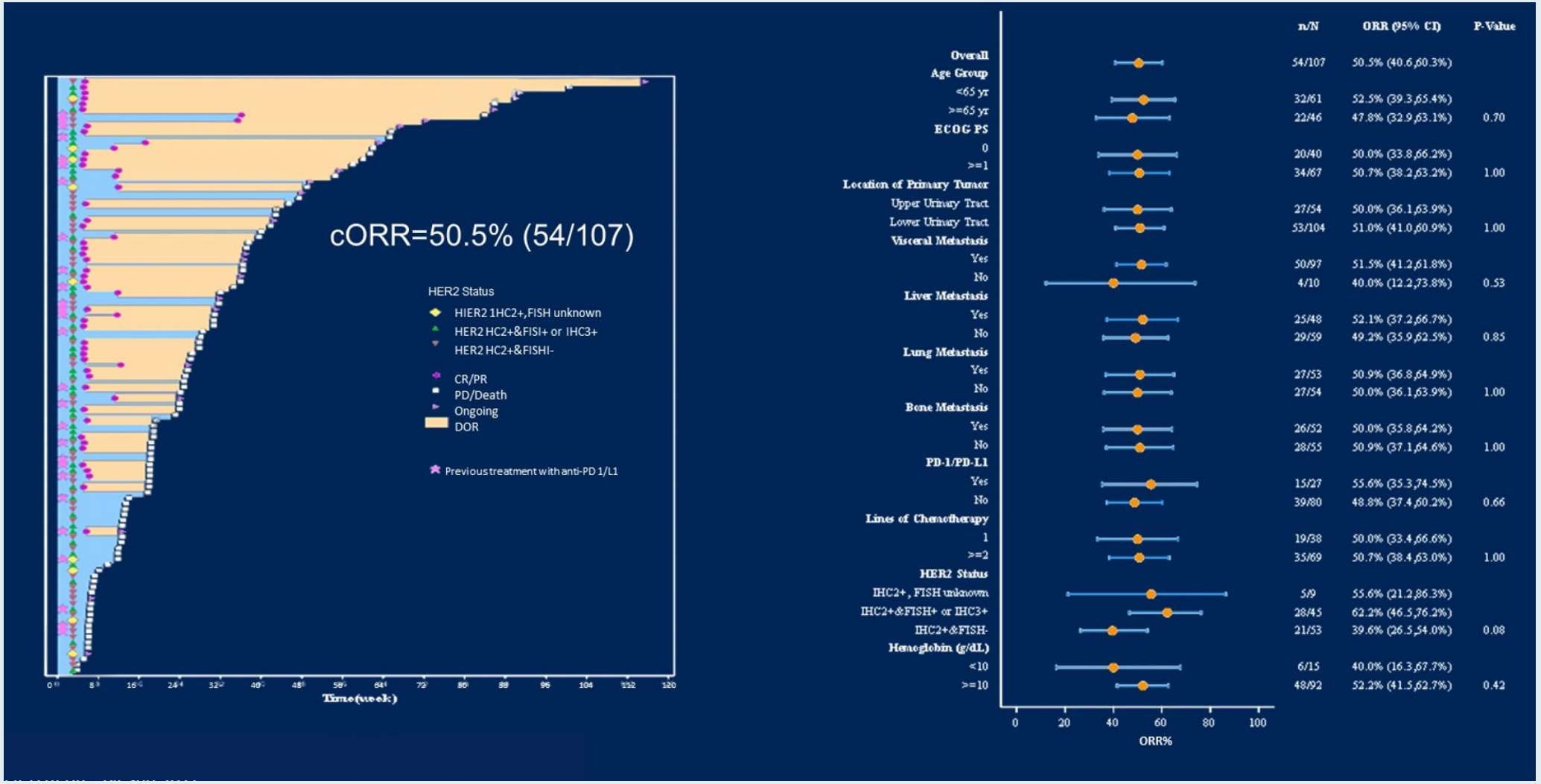
*Presenting author * * Corresponding author

Disitamab Vedotin (RC48-ADC) Structure and Mechanisms of Action



Sheng X et al. ASCO 2022;Abstract 4520.

Pooled Efficacy Results of RC48-C005 and RC48-C009

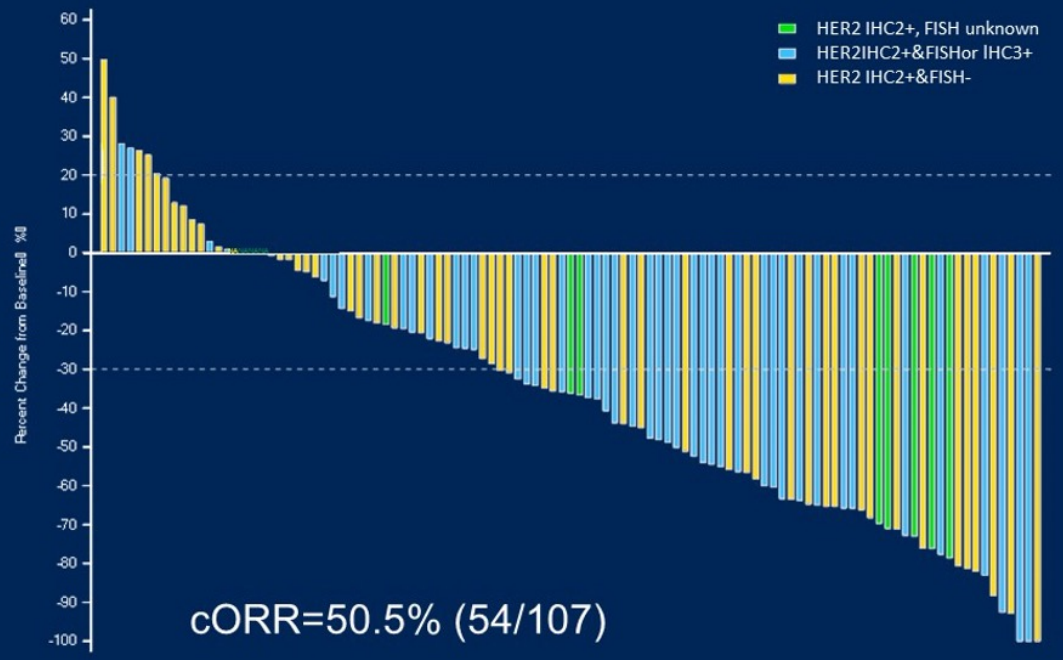


cORR = confirmed objective response rate

Sheng X et al. ASCO 2022;Abstract 4520.

Pooled Efficacy Results of RC48-C005 and RC48-C009

Target Lesion Change from Baseline



Patients were enrolled between December 28, 2017 and September 4, 2020
Data cut off : 04-Sep-2021

Subgroup Analysis for cORR

Subgroups	cORR (%, 95% CI)
HER2 status	
IHC2+FISH+ or IHC3+ (n=45)	62.2% (46.5%, 76.2%)
IHC2+FISH- (n=53)	39.6% (26.5%, 54.0%)
metastasis site	
Visceral Metastasis (n=97)	51.5% (41.2%, 61.8%)
Metastasis to Liver (n=48)	52.1% (37.2%, 66.7%)
Prior therapies	
Post PD1/PDL1 Treatments (n=27)	55.6% (35.3%, 74.5%)
Post 1 line of Chemotherapy (n=38)	50.0% (33.4%, 66.6%)
Post ≥2 Lines of Chemotherapy (n=69)	50.7% (38.4%, 63.0%)

Sheng X et al. ASCO 2022;Abstract 4520.

Trastuzumab Deruxtecan Meets Prespecified Criteria of Objective Response Rate and Duration of Response in the Phase II DESTINY-PanTumor02 Trial

Press Release – March 6, 2023

"Positive high-level results from an analysis of the ongoing DESTINY-PanTumor02 Phase II trial showed trastuzumab deruxtecan met the prespecified target for objective response rate (ORR) and demonstrated durable response across multiple HER2-expressing advanced solid tumours in heavily pretreated patients.

The DESTINY-PanTumor02 Phase II trial is evaluating the efficacy and safety of trastuzumab deruxtecan in patients with locally advanced, unresectable, or metastatic previously treated, HER2-expressing solid tumours not eligible for curative therapy, including biliary tract, bladder, cervical, endometrial, ovarian, pancreatic, and rare cancers. The primary endpoint of the trial is investigator-assessed confirmed ORR and investigator-assessed duration of response (DoR) is a key secondary endpoint.

The data will be presented at an upcoming medical meeting and shared with global regulatory authorities."

https://www.astrazeneca.com/media-centre/press-releases/2023/enhertu-destiny-pantumor02-shows-positive-results.html

Efficacy and Safety of Trastuzumab Deruxtecan (T-DXd) in Patients (Pts) with HER2-Expressing Solid Tumors: DESTINY-PanTumor02 (DP-02) Interim Results

Meric-Bernstam F et al.

ASCO 2023;Abstract LBA3000.
Monday, June 5th, 8:00 AM CDT

original reports

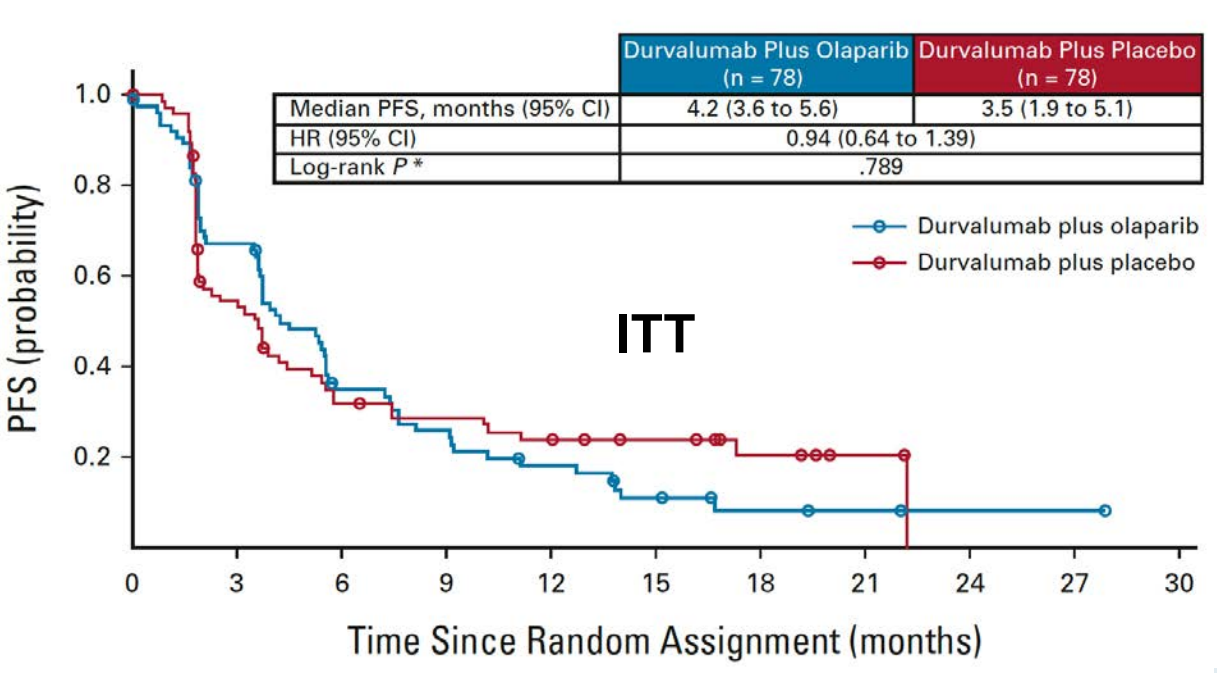
Durvalumab Plus Olaparib in Previously Untreated, Platinum-Ineligible Patients With Metastatic Urothelial Carcinoma: A Multicenter, Randomized, Phase II Trial (BAYOU)

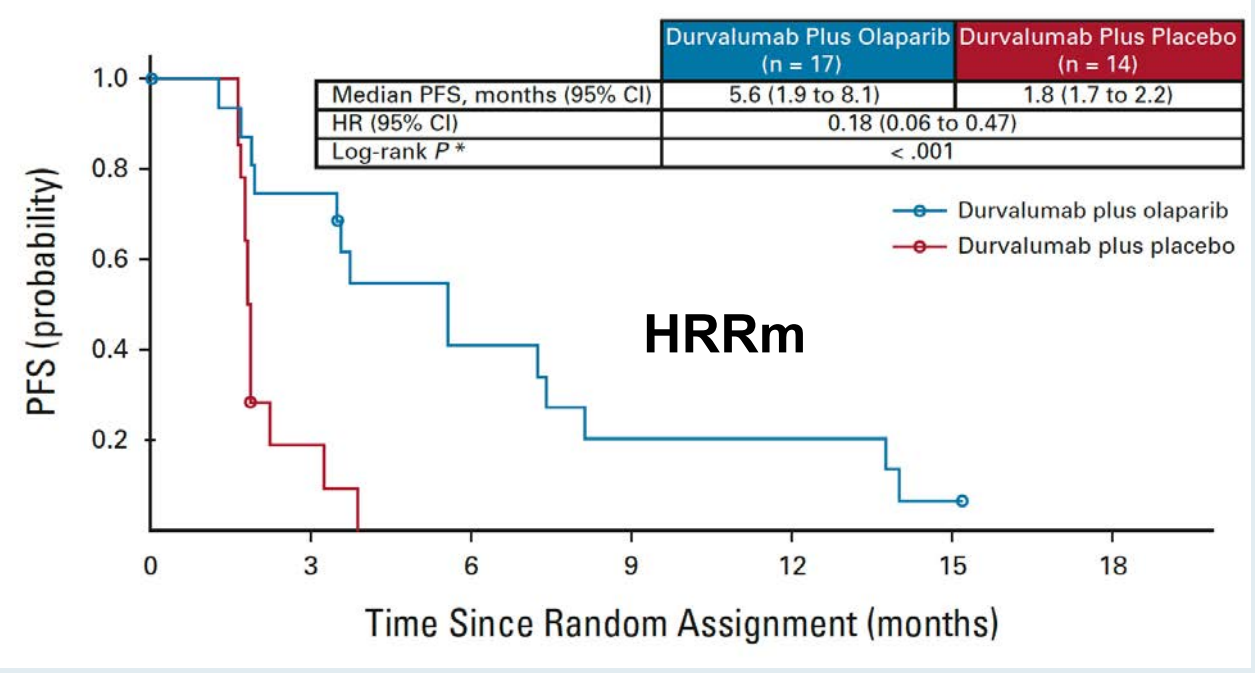
Jonathan E. Rosenberg, MD[1]; Se Hoon Park, MD, PhD[2]; Vadim Kozlov, MD[3]; Tu V. Dao, MD, PhD[4]; Daniel Castellano, MD[5]; Jian-Ri Li, MD, PhD[6]; Som D. Mukherjee, MD[7]; Kathryn Howells, MSc[8]; Hannah Dry, BSc[9]; Mark C. Lanasa, MD, PhD[9]; Ross Stewart, PhD[8]; and Dean F. Bajorin, MD[1]

J Clin Oncol 2023 January 1;41(1):43-53.

RTP RESEARCH TO PRACTICE

BAYOU: PFS in the Intent-to-Treat (ITT) and Homologous Recombination Repair Gene Mutation (HRRm) Populations

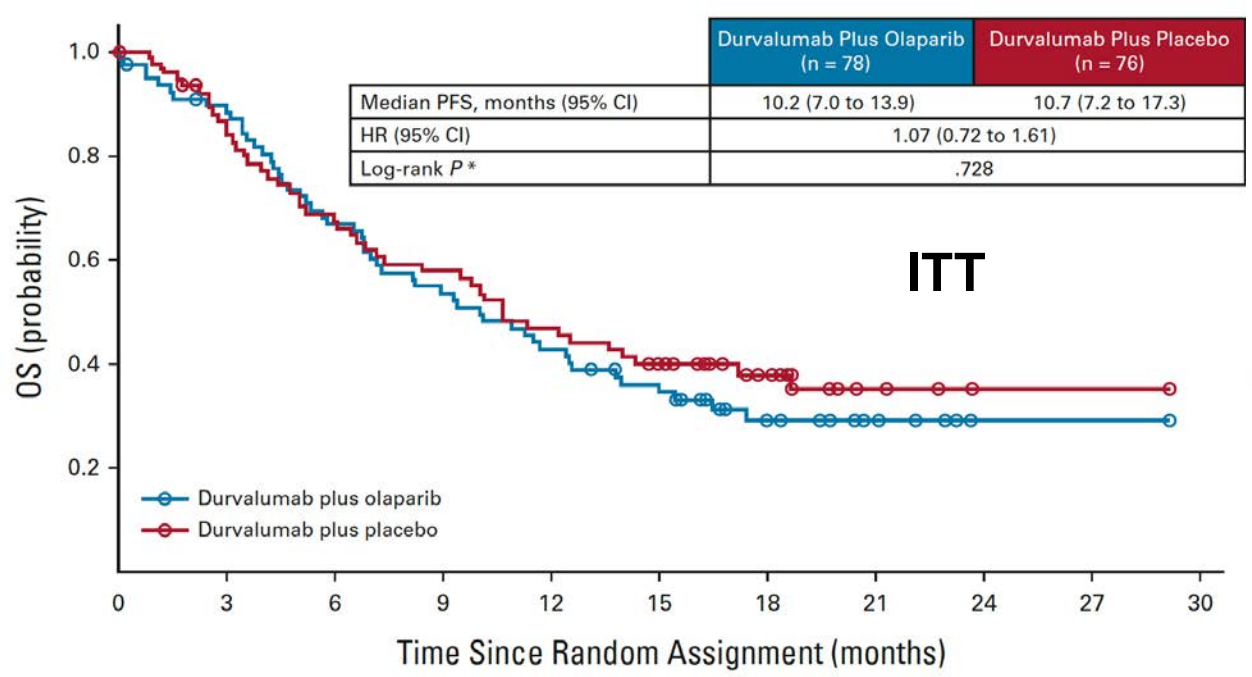


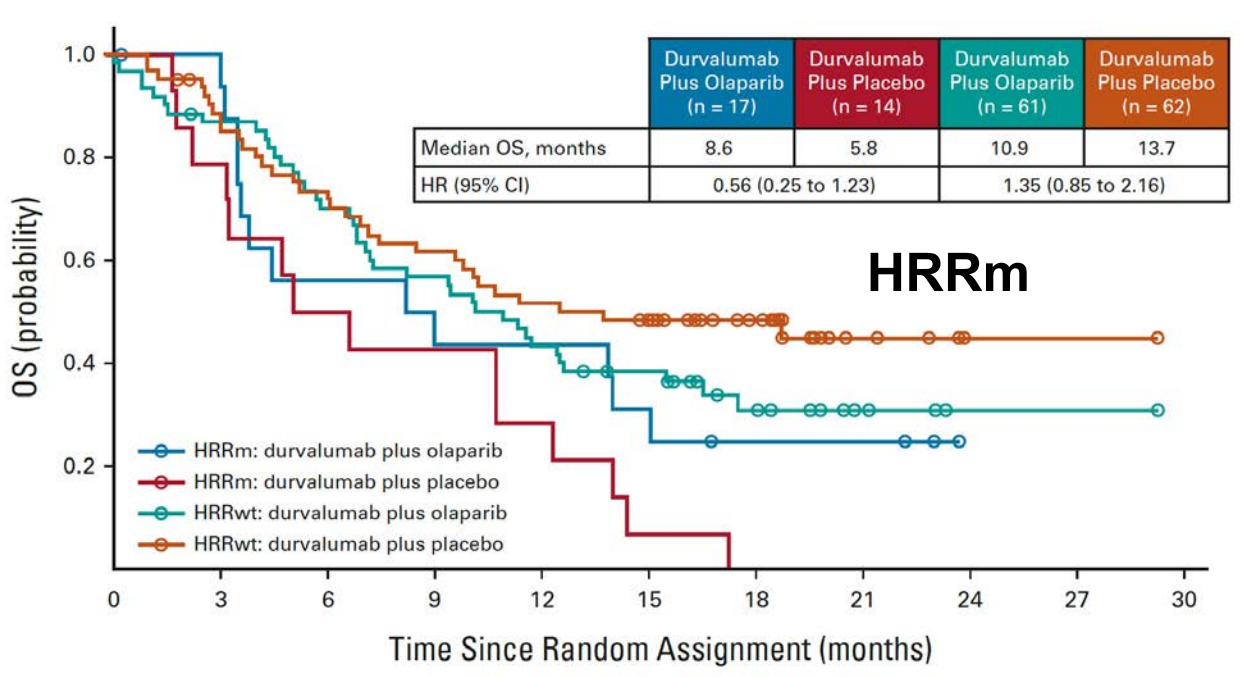


Rosenberg JE et al. *J Clin Oncol* 2023 January 1;41(1):43-53.

RTP RESEARCH TO PRACTICE

BAYOU: OS in the Intent-to-Treat (ITT) and Homologous Recombination Repair Gene Mutation (HRRm) Populations





Rosenberg JE et al. *J Clin Oncol* 2023 January 1;41(1):43-53.

RTP RESEARCH TO PRACTICE

Questions from General Medical Oncologists

- **In which patients would you use anti-PD-1/PD-L1 and CTLA-4 vs single-agent immunotherapy?**
- **What to do when pt has BRCA mutation: Is PARP inhibitor relevant in first line?**
- **What is the role of HER2-targeted therapy in this space?**
- **Trastuzumab deruxtecan in HER2 mutation or amplification?**

Survey of US-based general medical oncologists, May 2023. N = 75

Impediments you have encountered in delivering high-quality care to patients with urothelial bladder cancer

- **The main barrier in my clinical experience is rapid deterioration for patients who progress after first-line therapy**
- **Longer approval times for oral targeted agents, due to high cost**
- **The patients tend to be elderly males, former smokers with poorer protoplasm so balancing their performance status in light of treatment. Many of these patients understandably are concerned about side effects of treatment.**
- **The lack of urological oncology in small towns — accessibility**
- **Overwhelming number of treatments now available and real-world advice on dosing, prophylaxis for toxicity, follow-up, support**

Survey of US-based general medical oncologists, May 2023. N = 75

RTP RESEARCH TO PRACTICE

APPENDIX

ASCO 2023 Bladder Orals

RTP
RESEARCH
TO PRACTICE

Multicenter Randomized Phase III Trial of Dose-Dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (Dd-MVAC) or Gemcitabine and Cisplatin (GC) as Perioperative Chemotherapy for Muscle-Invasive Bladder Cancer (MIBC): Overall Survival (OS) Data at 5 Years in the GETUG/AFU V05 VESPER Trial

Pfister C et al.

ASCO 2023;Abstract LBA4507.

Monday, June 5th, 1:42 PM CDT

SWOG S1011: A Phase III Surgical Trial to Evaluate the Benefit of a Standard versus an Extended Lymphadenectomy Performed at Time of Radical Cystectomy for Muscle Invasive Urothelial Cancer

Lerner SP et al.

ASCO 2023;Abstract 4508.

Monday, June 5th, 1:54 PM CDT

RTP
RESEARCH
TO PRACTICE

Overall Survival (OS) by Response to First-Line (1L) Induction Treatment with Atezolizumab (Atezo) + Platinum/Gemcitabine (Plt/Gem) vs Placebo + Plt/Gem in Patients (Pts) with Metastatic Urothelial Carcinoma (Muc): Updated Data from the Imvigor130 OS Final Analysis

Grande E et al.

ASCO 2023;Abstract 4503.

Monday, June 5th, 12:30 PM CDT

Study EV-103 Dose Escalation/Cohort A: Long-Term Outcome of Enfortumab Vedotin + Pembrolizumab in First-Line (1L) Cisplatin-Ineligible Locally Advanced or Metastatic Urothelial Carcinoma (La/Muc) with Nearly 4 Years of Follow-Up

Gupta S et al.

ASCO 2023;Abstract 4505.
Monday, June 5th, 12:54 PM CDT

Non-Muscle-Invasive Bladder Cancer (NMIBC)

ASCO Genitourinary Cancers Symposium

2023;Abstract LBA442

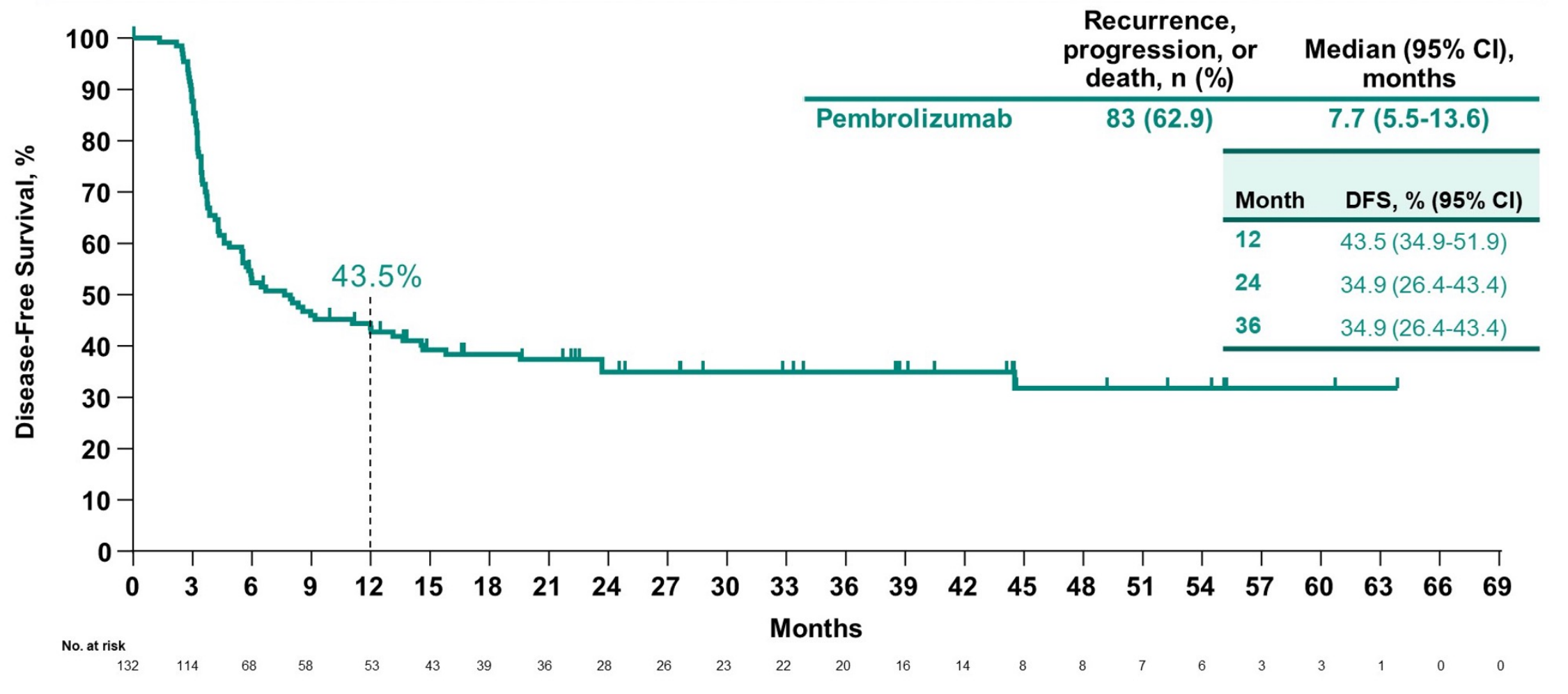
Pembrolizumab Monotherapy for Patients With High-Risk Non–Muscle-Invasive Bladder Cancer Unresponsive to Bacillus Calmette-Guérin: Results From Cohort B of the Phase 2 KEYNOTE-057 Trial

Andrea Necchi[1]; Mathieu Roumiguié[2]; Ahmet Adil Esen[3]; Thierry Lebret[4]; Ronald de Wit[5]; Neal D. Shore[6]; Dean F. Bajorin[7]; Laurence E. M. Krieger[8]; Shuya Kandori[9]; Edward M. Uchio[10]; Ho Kyung Seo[11]; Joost Boormans[5] ; Ashish M. Kamat[12]; Eric A. Singer[13]; Petros Grivas[14]; Hiroyuki Nishiyama[9]; Kijoeng Nam[15]; Ekta Kapadia[15]; Margot Van den Sigtenhorst-Fijlstra[16]; Girish S. Kulkarni[17]

[1]Vita-Salute San Raffaele University, IRCCS San Raffaele Hospital and Scientific Institute, Milan, Italy; [2]Institut Universitaire du Cancer Toulouse–Oncopole CHU, Toulouse, France; [3]Dokuz Eylül University, Izmir, Turkey; [4]Hôpital Foch, Université Paris-Saclay, Université Versailles Saint-Quentin-en-Yvelines, Suresnes, France; [5]Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, Netherlands; [6]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [8]GenesisCare and Royal North Shore Hospital, Sydney, NSW, Australia; [9]University of Tsukuba, Tsukuba, Japan; [10]UCI Health, Orange, CA, USA; [11]National Cancer Center, Goyang, South Korea; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [13]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [14]University of Washington and Fred Hutchinson Cancer Center, Seattle, WA, USA; [15]Merck & Co., Inc., Rahway, NJ, USA; [16]MSD Netherlands, Haarlem, Netherlands; [17]University Health Network, UHN Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

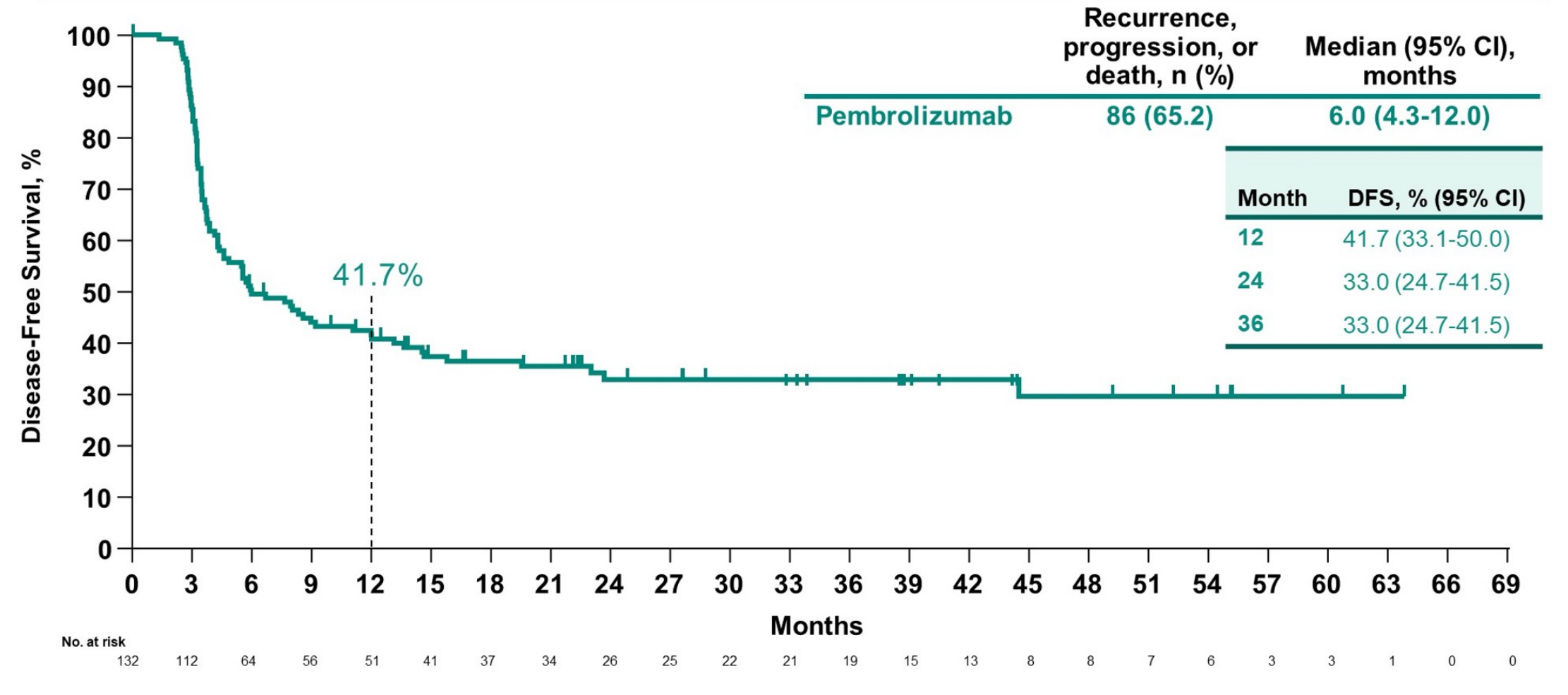
RTP RESEARCH TO PRACTICE

KEYNOTE-057 (Cohort B): Disease-Free Survival (DFS) for High-Risk NMIBC



Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract LBA442.

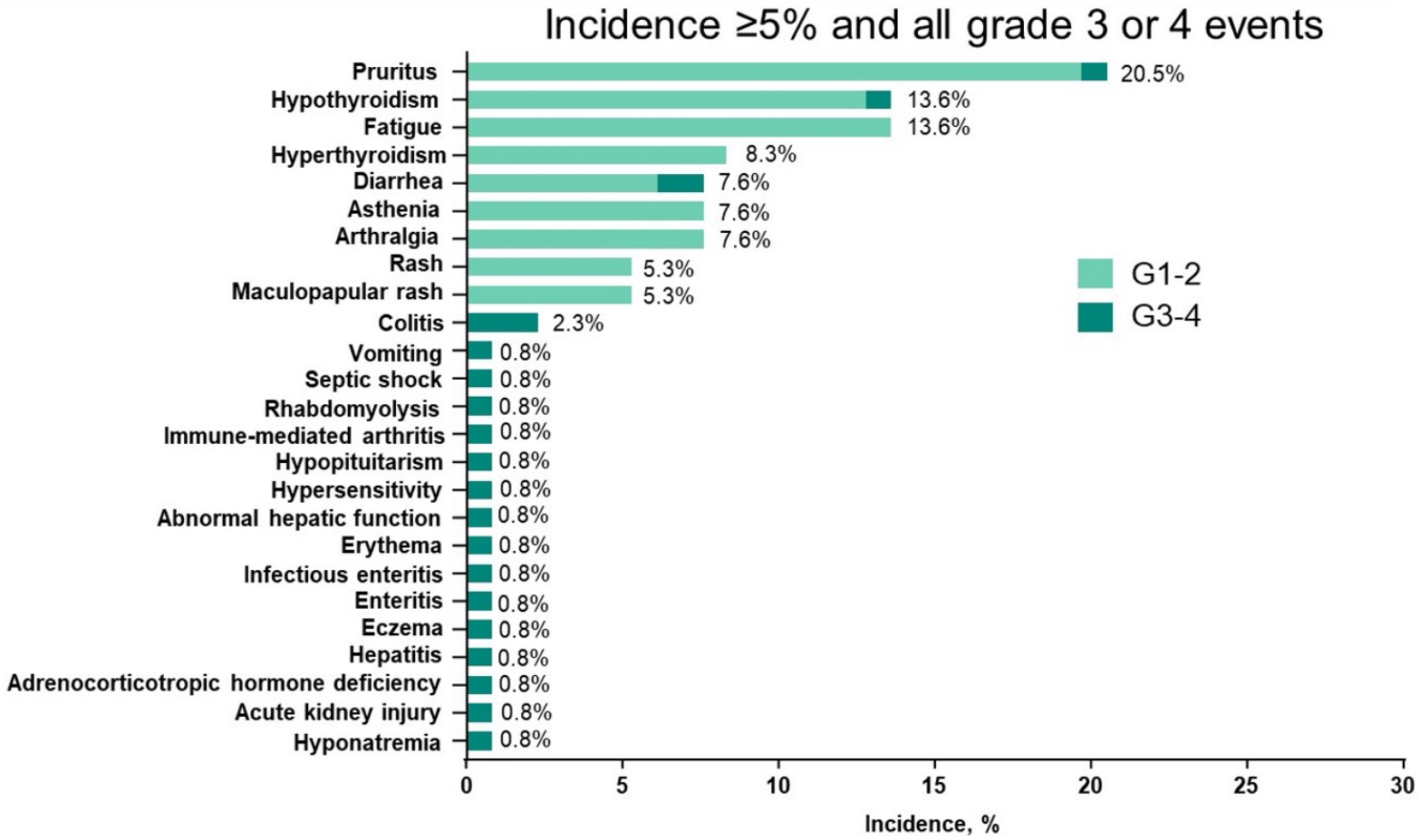
KEYNOTE-057 (Cohort B): Disease-Free Survival for Any Disease



Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract LBA442.

KEYNOTE-057 (Cohort B): Summary of Treatment-Related Adverse Events

Summary	Cohort B N = 132
Treatment-related AEs	97 (73.5)
Grade 3 or 4	19 (14.4)
Serious	17 (12.9)
Discontinuations	14 (10.6)
Deaths	0 (0)



- Median duration of treatment: 6.3 months (range, 0-26.9)

Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract LBA442.

Safety, Tolerability, and Preliminary Efficacy of TAR-200 in Intermediate-Risk Non–Muscle-Invasive Bladder Cancer Patients: a Phase 1 Study

F. Johannes P. van Valenberg,[1] Antoine G. van der Heijden,[1] Christopher J. Cutie,[2] Sumeet Bhanvadia,[2] Kirk A. Keegan,[2] Shalaka Hampras,[3] Hussein Sweiti,[4] John C. Maffeo,[2] Shu Jin,[2] Albert Chau,[5] Donald L. Reynolds,[2] Crysti Iarossi,[2] April Kelley,[3] Xiang Li,[3] Katharine Stromberg,[3] Michiel Sedelaar,[1] Jessica J.O. Steenbruggen,[6] Diederik M. Somford,[6] J. Alfred Witjes[1]

Genitourinary Cancers Symposium 2023;Abstract 505.

RTP RESEARCH TO PRACTICE

Phase Ib Study of TAR-200 in Intermediate-Risk NMIBC: Methods and Safety

- In this phase 1b open-label, prospective study, patients with papillary recurrence after prior histologically proven IR NMIBC received two 1-week TAR-200 dosing cycles over a 4- to 6-week period (Figure 2)
- The study used a marker lesion/ablation design with cystoscopy to assess for recurrent papillary disease and for complete transurethral resection of the residual bladder tumor (TURBT) after treatment
- The primary outcome was TAR-200 safety; secondary outcomes were tolerability, pharmacokinetics, preliminary efficacy, and immunohistochemistry

FIGURE 2: TAR-200 dosing schedule[a]

[a]Dosing schedule shown for Arm 1 of the study (n=11 patients). Arm 2 was initiated to evaluate a longer TAR-200 dwell time (n=1 patient). Arm 2 was terminated early for nonclinical reasons at the sponsor's discretion.

Overview of treatment-emergent adverse events (TEAEs)

Patients with events, n (%)	N=12
TEAE (any grade)	11 (92)
Grade ≥3 TEAE	0
Serious TEAE	0
TEAE leading to study discontinuation	0
TEAE leading to death	0
TEAE related to TAR-200 (any grade)	9 (75)

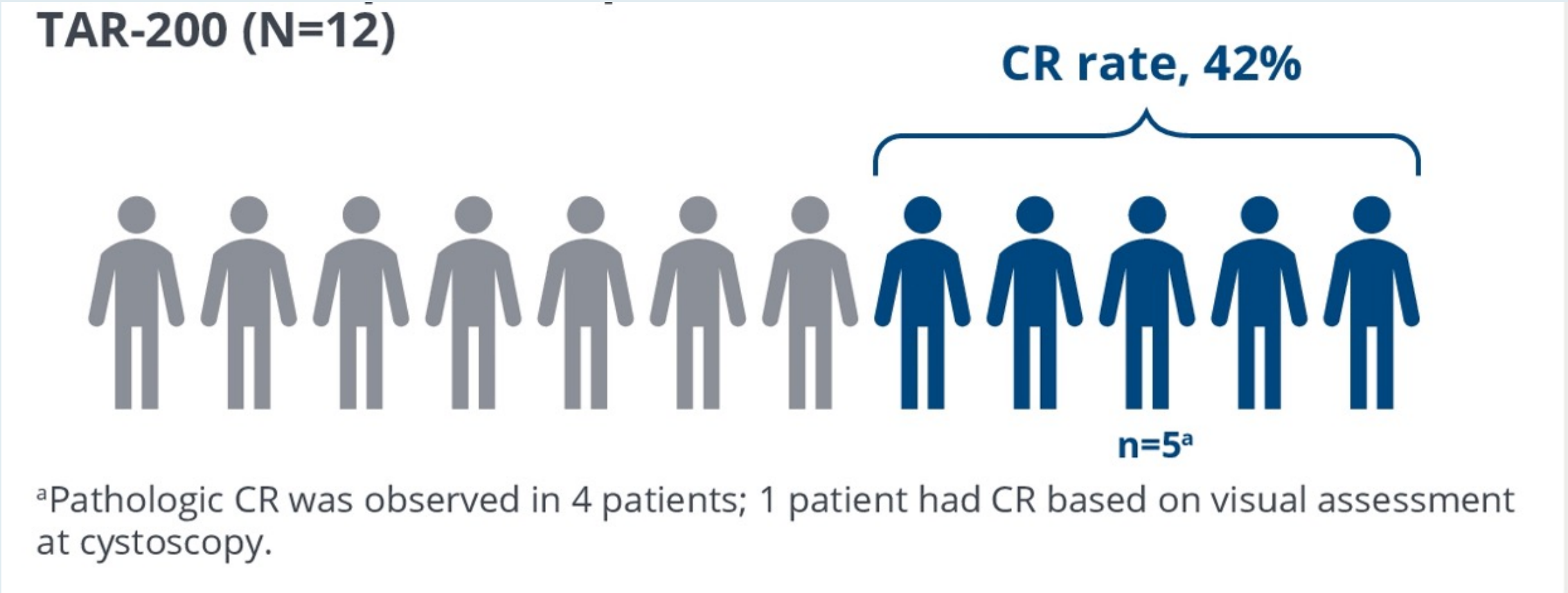
Most frequent TEAEs by preferred term and grade

Patients with events, n (%)[a]	N=12		
	All	Grade 1	Grade 2
Pollakiuria	7 (58)	5 (42)	2 (17)
Dysuria	5 (42)	4 (33)	1 (8)
Hematuria	5 (42)	5 (42)	0
Constipation	4 (33)	4 (33)	0
Penile pain	3 (25)	3 (25)	0

[a]TEAEs reported in ≥25% of patients.

Van Valenberg FJP et al. Genitourinary Cancers Symposium 2023;Abstract 505.

Phase Ib Study of TAR-200 in Intermediate-Risk NMIBC: Response



CR = complete response

Van Valenberg FJP et al. Genitourinary Cancers Symposium 2023;Abstract 505.

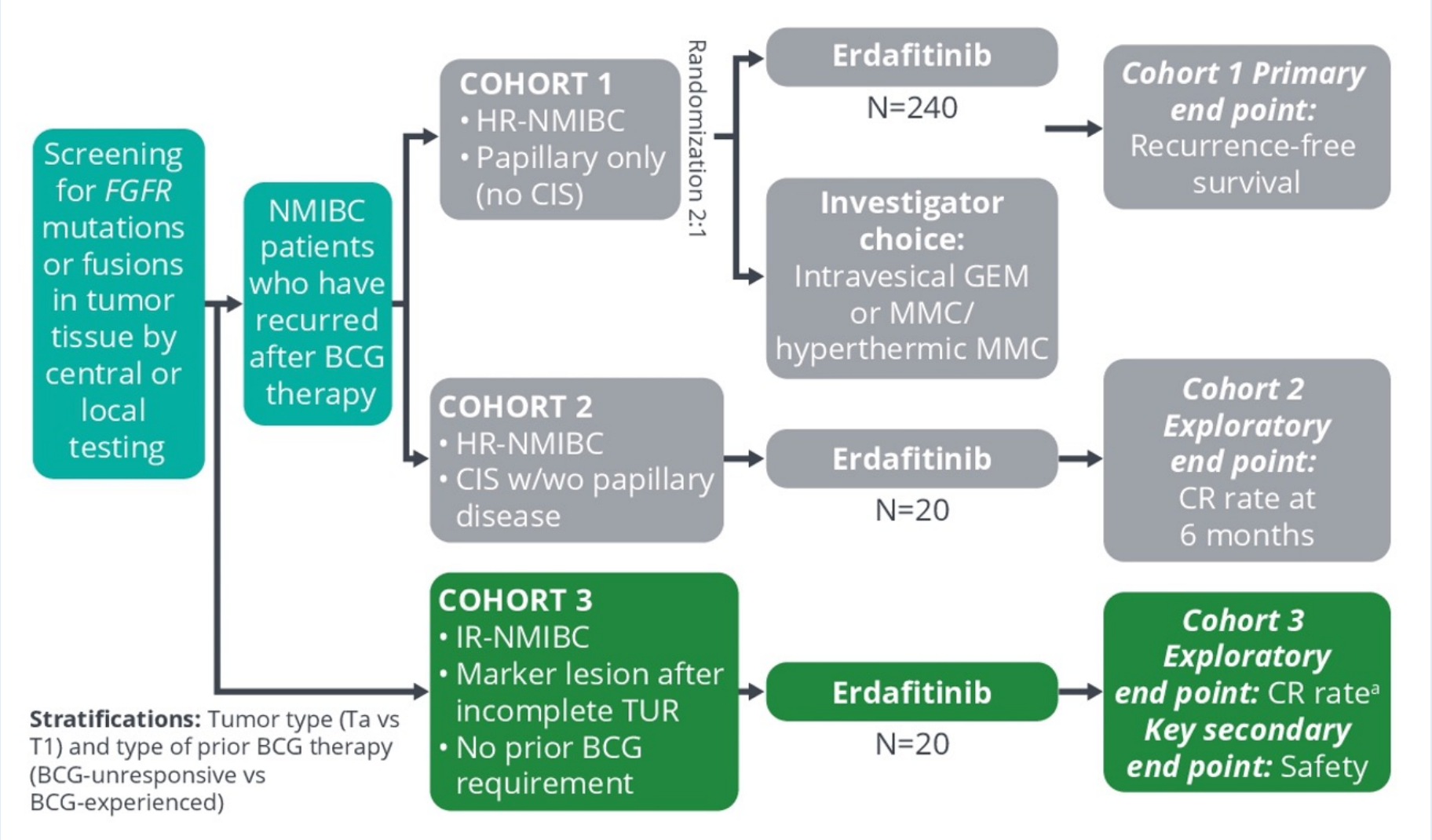
Phase 2 Study of the Efficacy and Safety of Erdafitinib in Patients With Intermediate-Risk Non–Muscle-Invasive Bladder Cancer (IR-NMIBC) With *FGFR3/2* Alterations (*alt*) in THOR-2: Cohort 3 Interim Analysis

Siamak Daneshmand,[1] Renata Zaucha,[2] Benjamin A. Gartrell,[3] Yair Lotan,[4] Syed A. Hussain,[5] Eugene K. Lee,[6] Giuseppe Procopio,[7] Fernando Galanternik,[8] Vahid Naini,[9] Jenna Cody Carcione,[10] Spyros Triantos,[10] Mahadi Baig,[10] Jodi K. Maranchie[11]

Genitourinary Cancers Symposium 2023;Abstract 504.

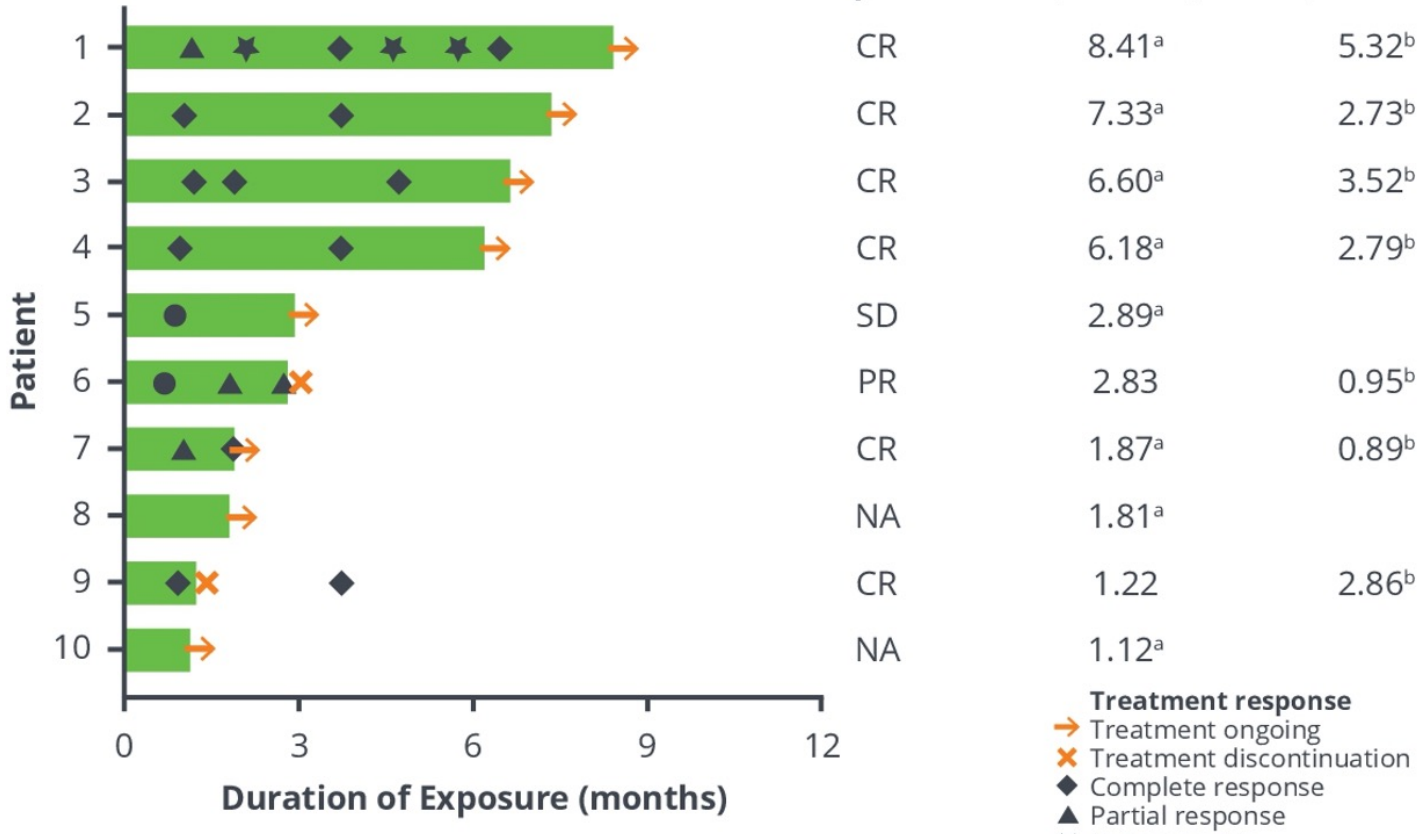
RTP RESEARCH TO PRACTICE

THOR-2 (Cohort 3) Study Design



Daneshmand S et al. Genitourinary Cancers Symposium 2023;Abstract 504.

THOR-2 (Cohort 3): Response Duration in Evaluable Patients



Patient	Best overall response	Total duration of exposure (months)	DOR (months)
1	CR	8.41[a]	5.32[b]
2	CR	7.33[a]	2.73[b]
3	CR	6.60[a]	3.52[b]
4	CR	6.18[a]	2.79[b]
5	SD	2.89[a]	
6	PR	2.83	0.95[b]
7	CR	1.87[a]	0.89[b]
8	NA	1.81[a]	
9	CR	1.22	2.86[b]
10	NA	1.12[a]	

NA, not assessed.
[a]Patient is still on treatment. [b]DOR for patient is currently censored.

Daneshmand S et al. Genitourinary Cancers Symposium 2023;Abstract 504.

THOR-2 (Cohort 3): Safety Summary and Most Common Treatment-Emergent Adverse Events (TEAEs)

TEAEs summary	n (%)
Any grade TEAEs Treatment related	9 (90) 9 (90)
Grade ≥3 TEAEs Treatment related	2 (20) 1 (10)
Serious TEAEs	0
TEAEs leading to treatment discontinuation	0
Deaths on study	0

TEAE by preferred term	Any grade (≥30%) n (%)	Grade ≥3 (all events) n (%)
Hyperphosphatemia	9 (90)	0
Diarrhea	5 (50)	1 (10)
Dry mouth	5 (50)	0
Dysgeusia	3 (30)	0

Daneshmand S et al. Genitourinary Cancers Symposium 2023;Abstract 504.

Muscle-Invasive Bladder Cancer (MIBC)

CheckMate 274 Phase III Study Design

- CheckMate 274 is a phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab versus placebo in patients with high-risk MIUC[a]

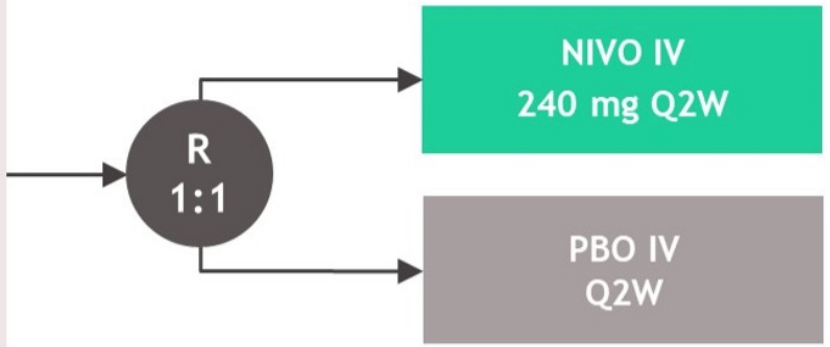
N = 709

Key inclusion criteria

- Patients with ypT2-ypT4a or ypN+ MIUC who had neoadjuvant cisplatin chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior neoadjuvant cisplatin chemotherapy and not eligible/refuse adjuvant cisplatin chemotherapy
- Radical surgery within the past 120 days
- Disease-free status within 4 weeks of randomization

Stratification factors

- Tumor PD-L1 status (≥ 1% vs < 1% or indeterminate)[b]
- Prior neoadjuvant cisplatin-based chemotherapy
- Nodal status



Treat for up to 1 year of adjuvant therapy

Median (range) follow-up[c] (ITT population),
36.1 (0.0-75.3) months (37.4 months for NIVO, 33.9 months for PBO)
Minimum follow-up[d] (ITT population), 31.6 months
Median (range) follow-up[c] (PD-L1 ≥ 1% population),
37.1 (0.0-75.3) months (39.8 months for NIVO, 33.3 months for PBO)

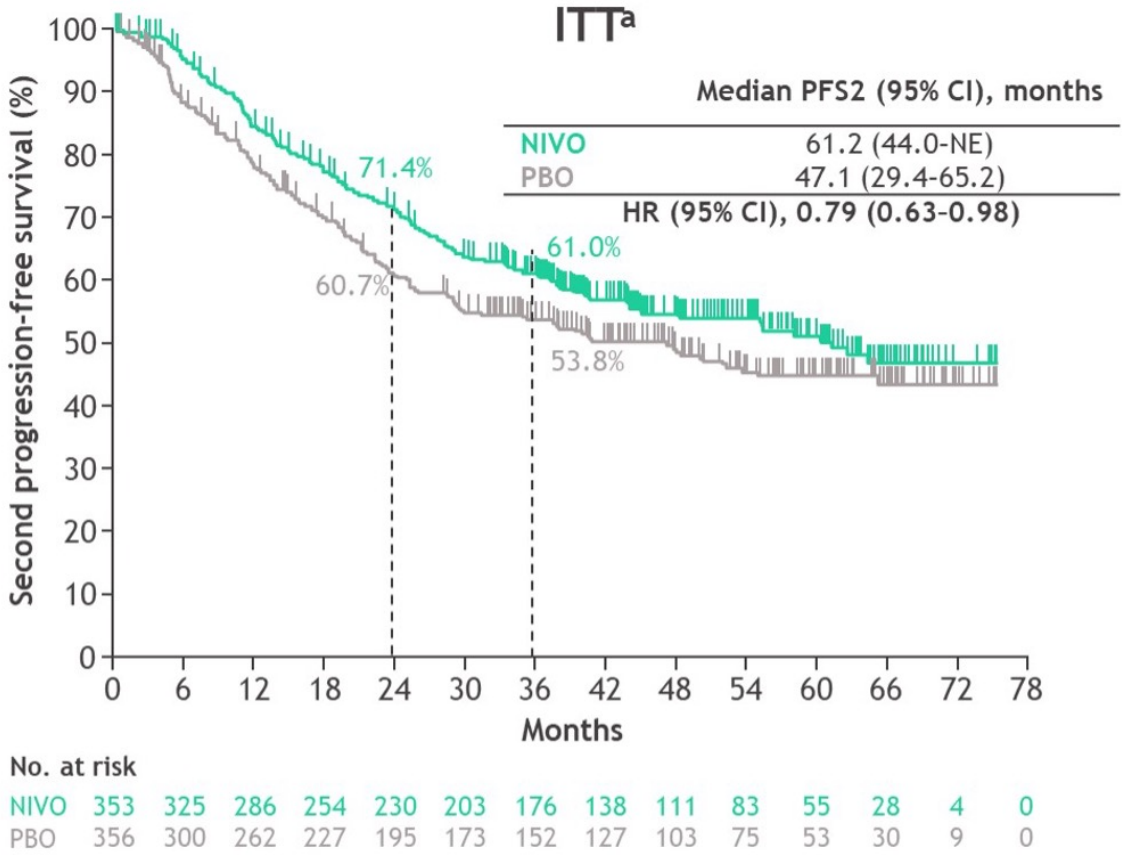
Primary endpoints: DFS in all randomized patients (ITT population) and DFS in all randomized patients with tumor PD-L1 ≥ 1%
Secondary endpoints: NUTRFS, DSS, and OS[e]
Exploratory endpoints included: DMFS, PFS2, safety, HRQoL

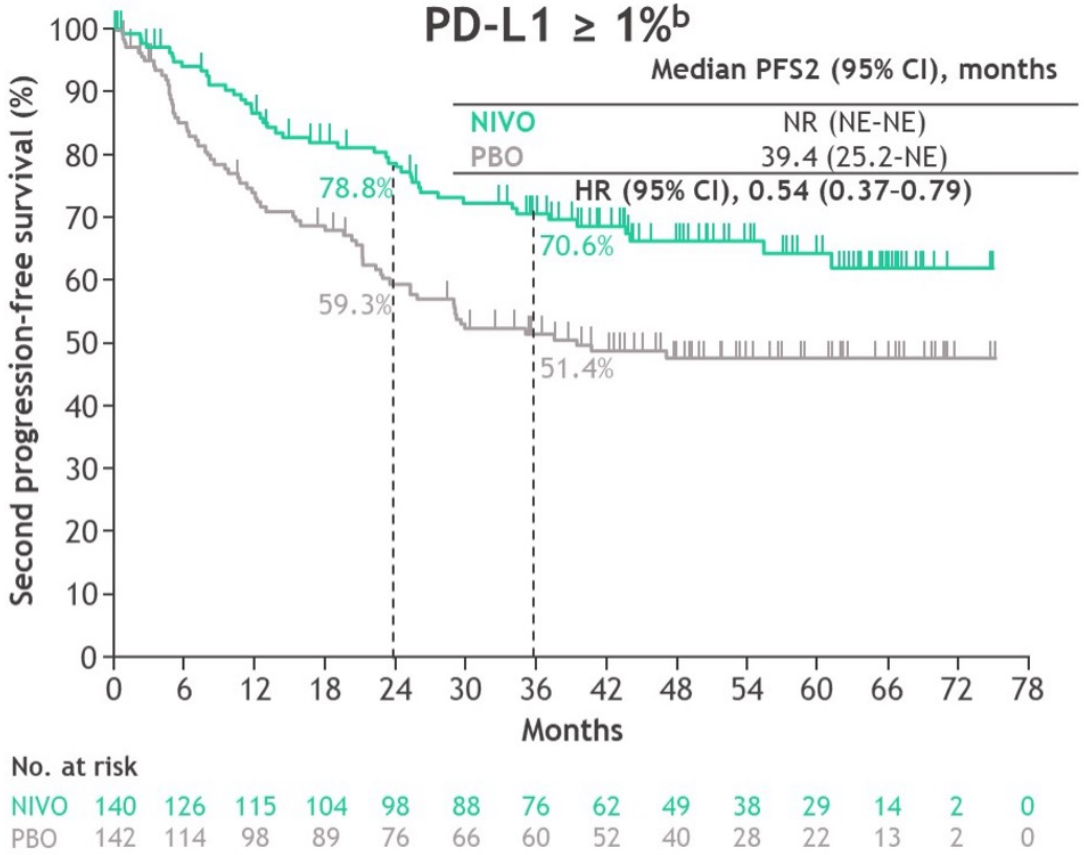
MIUC = muscle-invasive urothelial carcinoma; ITT = intent-to-treat; NIVO = nivolumab; PBO = placebo; DFS = disease-free survival; NUTRFS = non-urothelial tract recurrence-free survival; DSS = disease-specific survival; OS = overall survival; DMFS = distant metastasis-free survival; PFS2 = progression-free survival with first subsequent therapy; HRQoL = health-related quality of life

Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA443.

CheckMate 274 Extended Follow-Up: Second Progression-Free Survival

- PFS2 (time from randomization to disease progression after subsequent next-line systemic anticancer therapy, start of second subsequent next-line systemic anticancer therapy, or death) was improved with NIVO versus PBO in both study populations



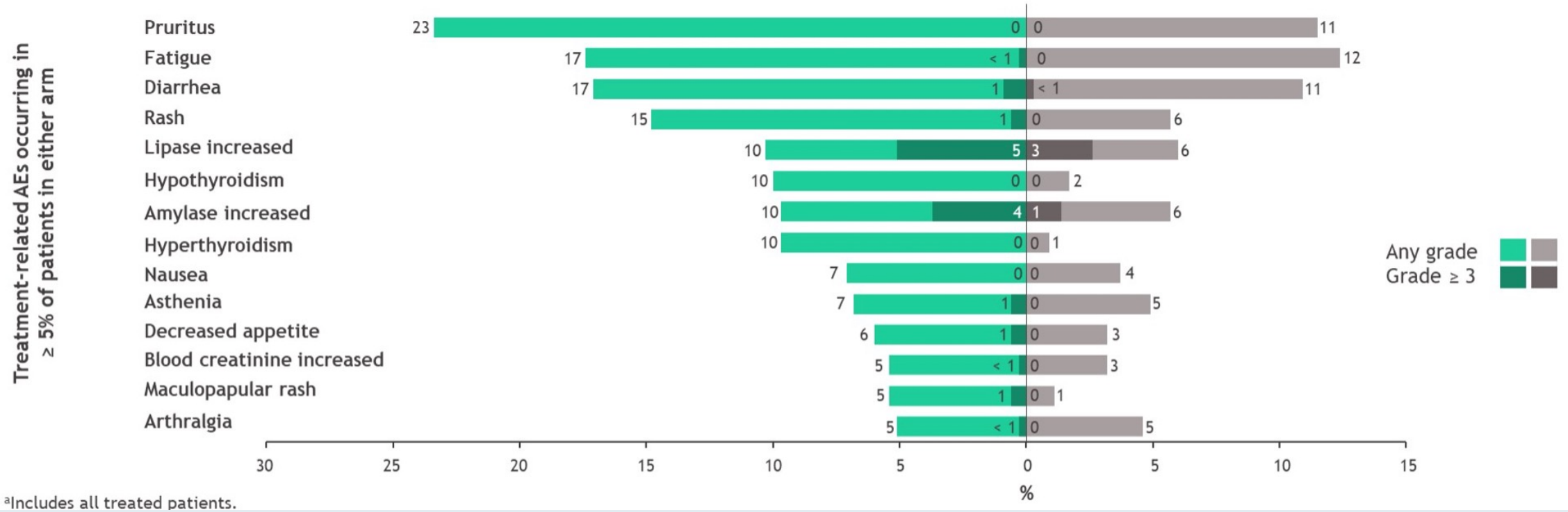


Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA443.

RTP RESEARCH TO PRACTICE

CheckMate 274 Extended Follow-Up: Safety Summary

	NIVO (n = 351)[a]		PBO (n = 348)[a]	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Treatment-related AEs, %	79	18	56	7
Treatment-related AEs leading to discontinuation, %	14	7	2	1



[a]Includes all treated patients.

Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA443.

RTP RESEARCH TO PRACTICE

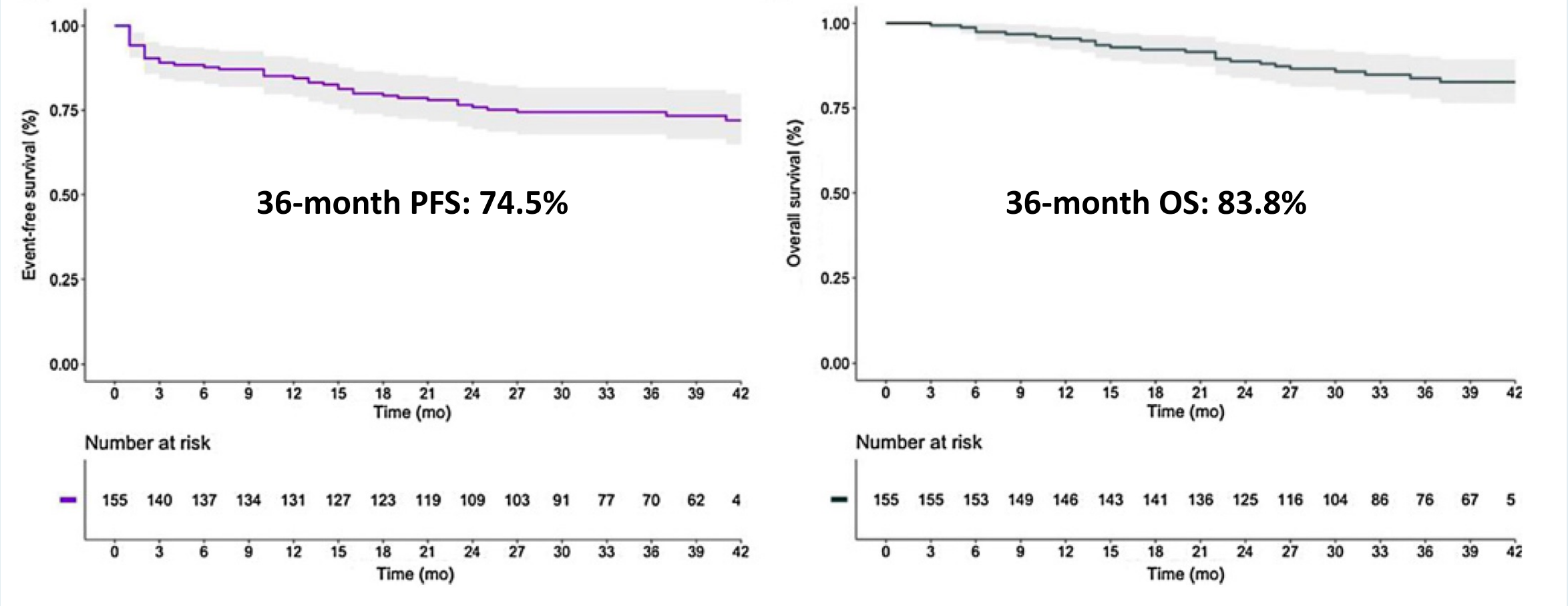
2022 December 1;28(23):5107-14.

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Neoadjuvant Pembrolizumab and Radical Cystectomy in Patients with Muscle-Invasive Urothelial Bladder Cancer: 3-Year Median Follow-Up Update of PURE-01 Trial

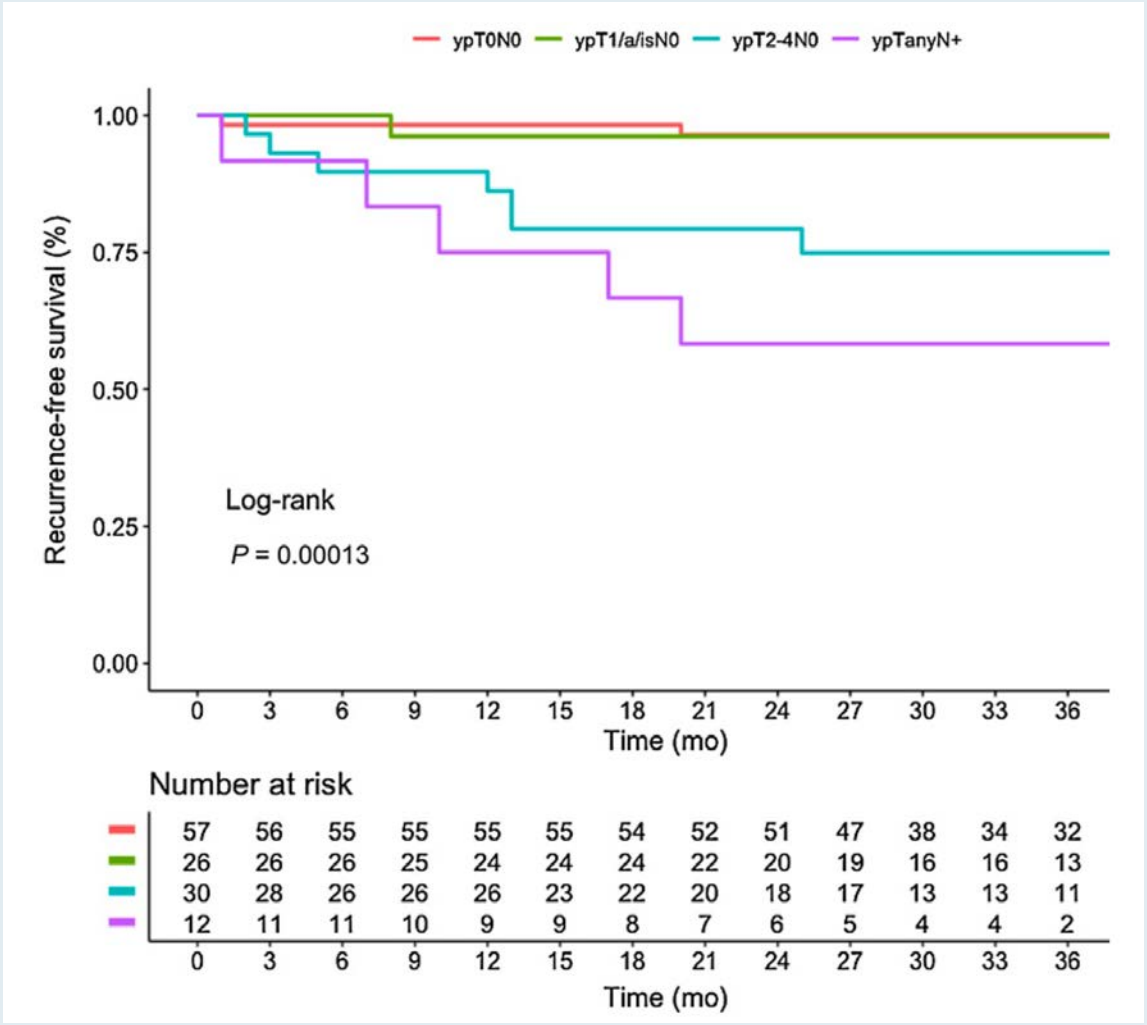
Giuseppe Basile[1], Marco Bandini[1], Ewan A. Gibb[2], Jeffrey S. Ross[3,4], Daniele Raggi[5], Laura Marandino[5], Tiago Costa de Padua[5], Emanuele Crupi[5], Renzo Colombo[1], Maurizio Colecchia[6,7], Roberta Lucianò[6], Luigi Nocera[1], Marco Moschini[1], Alberto Briganti[1,7], Francesco Montorsi[1,7], and Andrea Necchi[5,7]

PURE-01: Survival Analyses (ITT Population)



Basile G et al. *Clin Cancer Res* 2022 December 1;28(23):5107-14.

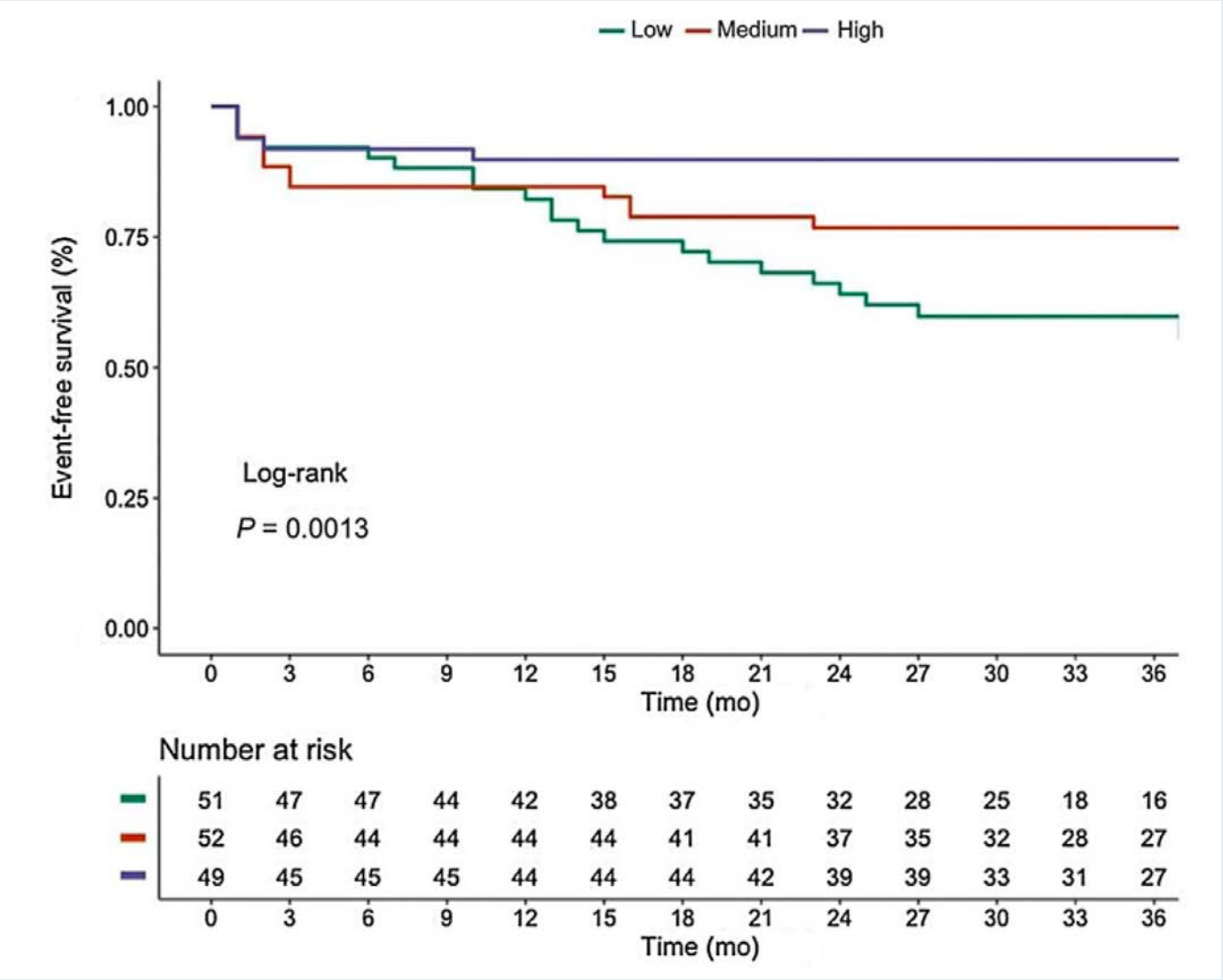
PURE-01: Recurrence-Free Survival in Patients Treated with Radical Cystectomy without Additional Chemotherapy According to Pathologic Response Category



Basile G et al. *Clin Cancer Res* 2022 December 1;28(23):5107-14.

RTP RESEARCH TO PRACTICE

PURE-01: 36-Month Event-Free Survival Rates According to PD-L1 CPS Score Tertile Distribution



Basile G et al. *Clin Cancer Res* 2022 December 1;28(23):5107-14.

original reports

Neoadjuvant Atezolizumab With Gemcitabine and Cisplatin in Patients With Muscle-Invasive Bladder Cancer: A Multicenter, Single-Arm, Phase II Trial

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J Clin Oncol 2022;40:1312-22.

Pathologic Response at the Time of Radical Cystectomy (<pT2N0: Primary Endpoint)

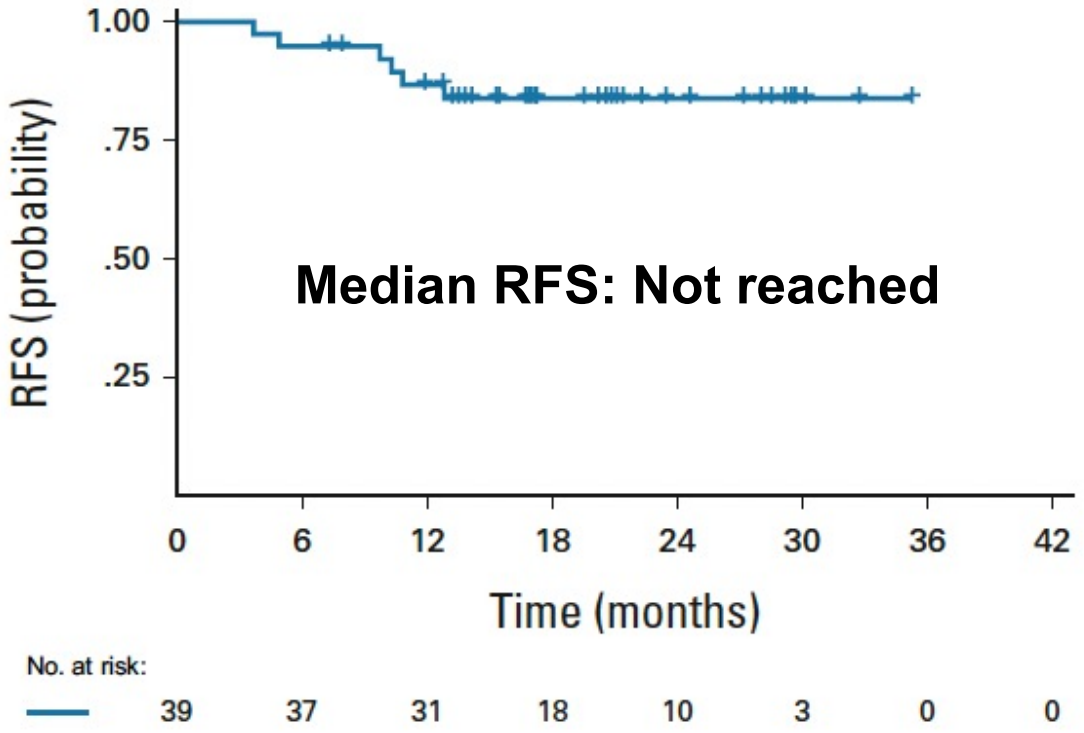
Pathologic Response	No. (%)
Responders (< pT2N0)	27 (69.2; 95% CI, 55.0 to 79.0)
pT0N0/pT0NX[a]	16 (41.0)
pTaN0	2 (5.1)
pTisN0	7 (17.9)
pT1N0	2 (5.1)
Nonresponders (≥ pT2N0)	9 (23.1)
pT2N0	2 (5.1)
pTxN1	3 (7.7)
pTxN2	3 (7.7)
pTxN3	1 (2.6)
No surgery	3 (7.7)
Refused surgery	1 (2.6)
Developed metastatic disease before surgery	2 (5.1)

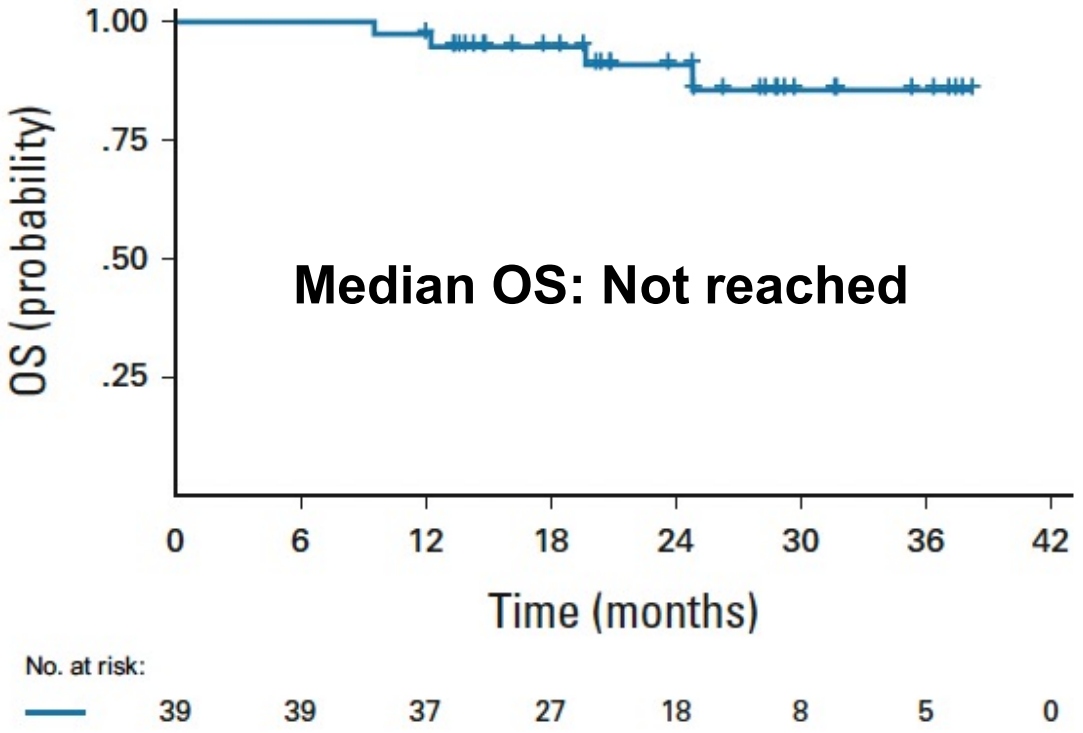
Abbreviation: RC, radical cystectomy.

[a]One patient was unable to have a lymph node dissection because of adhesions from prior abdominal surgeries.

Funt SA et al. *J Clin Oncol* 2022;40:1312-22.

RFS and OS in 39 Response-Evaluable Patients Treated with Neoadjuvant Gemcitabine/Cisplatin and Atezolizumab

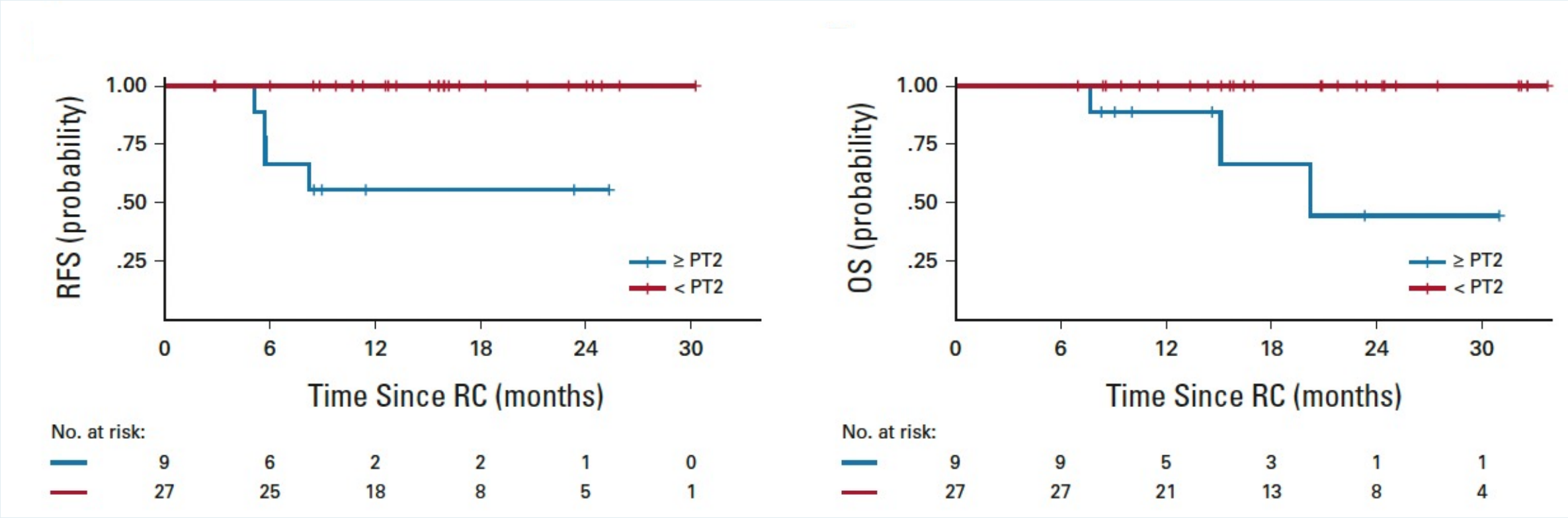




RFS = recurrence-free survival; OS = overall survival

Funt SA et al. *J Clin Oncol* 2022;40:1312-22.

RFS and OS Stratified by Pathologic Response (<pT2 versus ≥pT2N0)



Funt SA et al. *J Clin Oncol* 2022;40:1312-22.

RTP RESEARCH TO PRACTICE

ELSEVIER

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

UROLOGIC ONCOLOGY

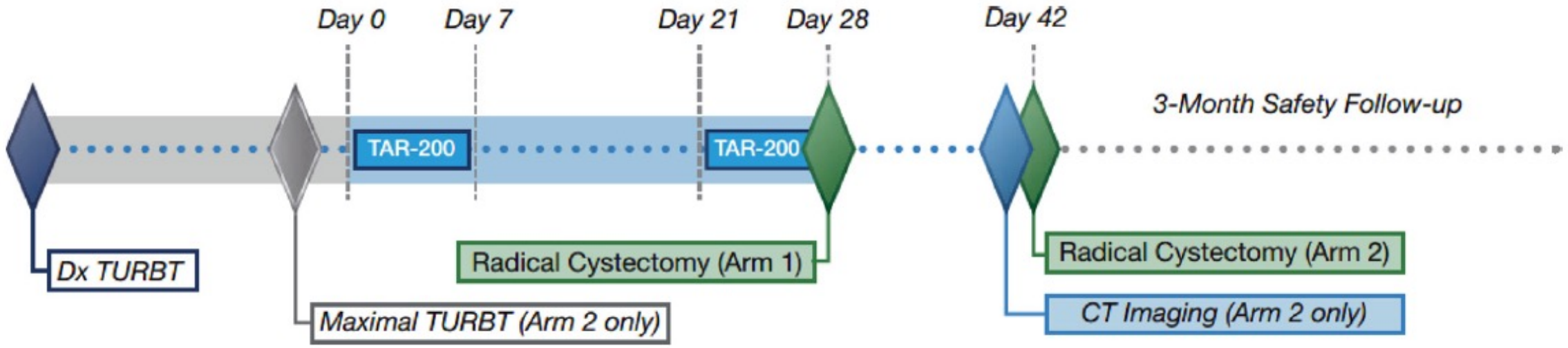
Clinical-Bladder cancer

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]

2022 July;40(7):344e1-9.

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;40(7):344e1-9.

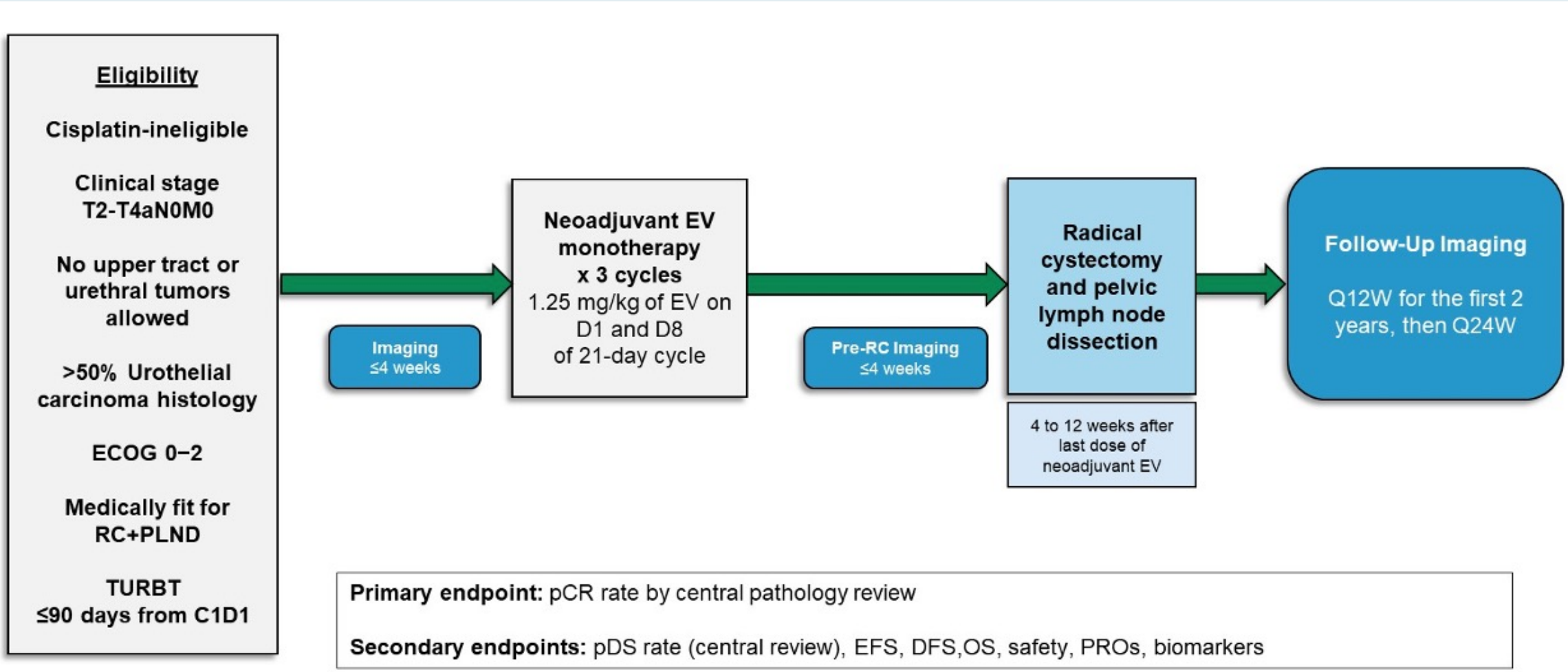
ASCO Genitourinary Cancers Symposium 2022;Abstract 435

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

EV-103 Cohort H Study Schema



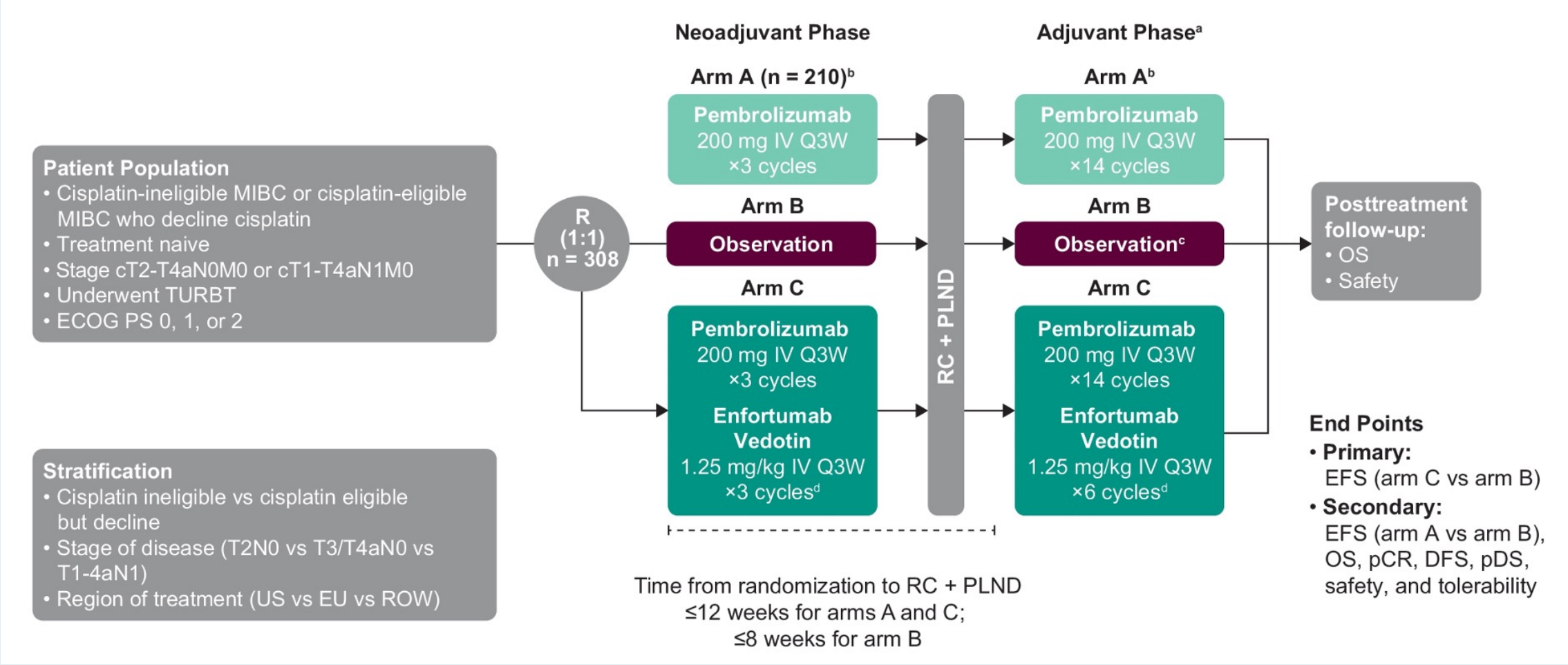
Petrylak DP et al. Genitourinary Cancers Symposium 2022;Abstract 435.

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.

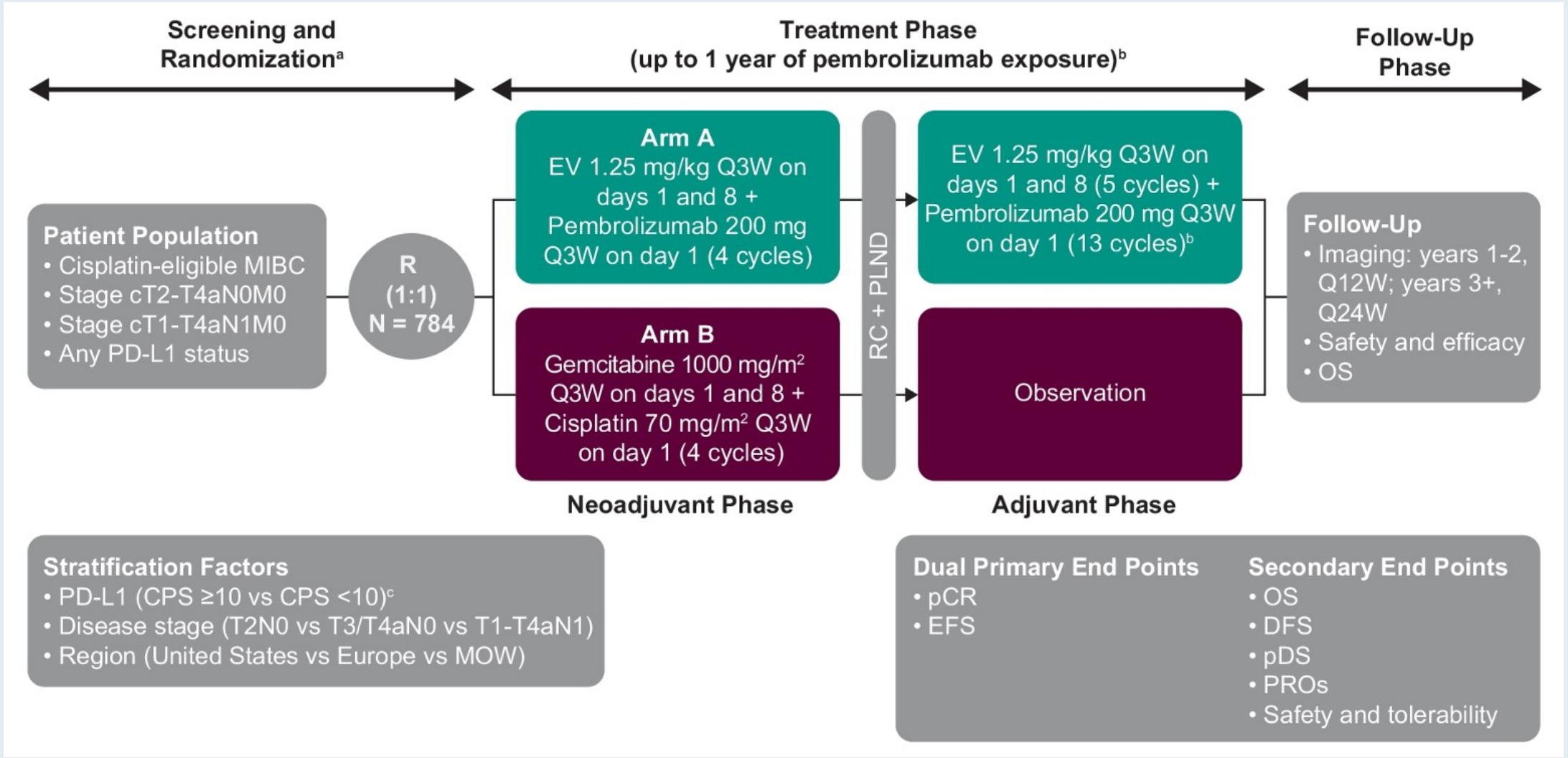
Ongoing Phase III KEYNOTE-905/EV-303 Study Design



RC = radical cystectomy; PLND = pelvic lymph node dissection; OS = overall survival; EFS = event-free survival; pCR = pathologic complete response; DFS = disease-free survival; pDS = pathologic downstaging

Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract TPS585.

Ongoing Phase III KEYNOTE-B15/EV-304 Study Design



OS = overall survival; pCR = pathologic complete response; EFS = event-free survival; DFS = disease-free survival; pDS = pathologic downstaging; PROs = patient-reported outcomes

Hoimes C et al. Genitourinary Cancers Symposium 2023;Abstract TPS588.

Metastatic Urothelial Bladder Cancer: Immunotherapy

RTP
RESEARCH
TO PRACTICE

ASCO Genitourinary Cancers Symposium

2023;Abstract LBA440.

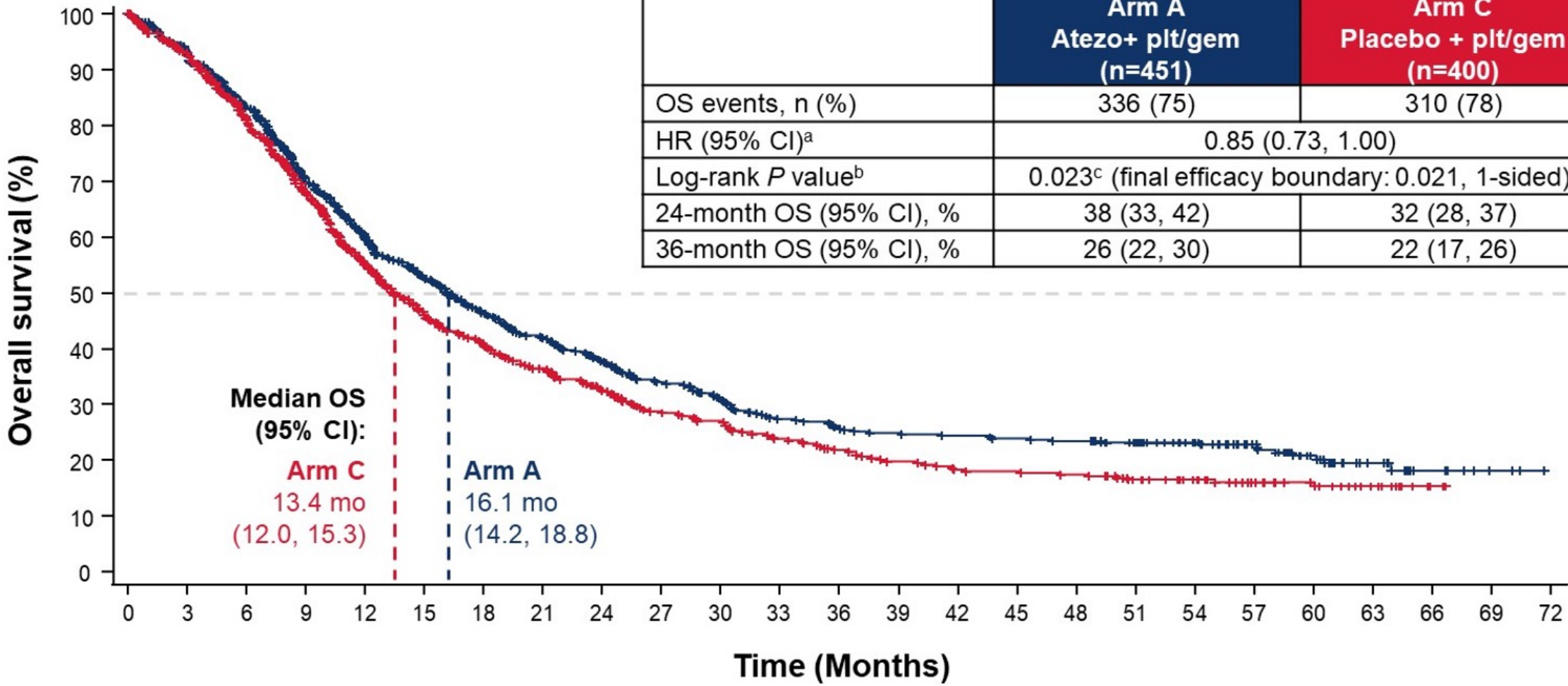
Atezolizumab + Platinum/Gemcitabine vs Placebo + Platinum/Gemcitabine for First-Line Treatment of Locally Advanced or Metastatic Urothelial Carcinoma: Final Overall Survival Analysis From the Phase III IMvigor130 Study

Matthew D. Galsky,[1] José Ángel Arranz,[2] Maria De Santis,[3] Ian D. Davis,[4] Aristotelis Bamias,[5] Eiji Kikuchi,[6] Xavier Garcia del Muro,[7] Se Hoon Park,[8] Ugo De Giorgi,[9] Boris Alekseev,[10] Marina Mencinger,[11] Kouji Izumi,[12] Javier Puente Vázquez,[13] Jian-Ri Li,[14] Peter H. O'Donnell,[15] Sandrine Bernhard,[16] Chooi Lee,[16] Fabiola Bene-Tchaleu,[17] Sanjeev Mariathasan,[18] Enrique Grande[19]

[1]Icahn School of Medicine at Mount Sinai/Tisch Cancer Institute, New York, NY; [2]Gregorio Maranon Hospital, Madrid, Spain; [3]Charité University Hospital, Department of Urology, Berlin, Germany, and Medical University, Department of Urology, Vienna, Austria; [4]Eastern Health Clinical School, Monash University and Eastern Health, Melbourne, Australia; [5]National & Kapodistrian University of Athens, Athens, Greece; [6]St. Marianna University School of Medicine, Kawasaki, Japan; [7]Catalan Institute of Oncology, IDIBELL, University of Barcelona, Barcelona, Spain; [8]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [9]IRCCS Istituto Romagnolo per lo Studiodei Tumori (IRST), Dino Amadori, Meldola, Italy; [10]Research Oncology Institute, Tomsk, Russia; [11]Institute of Oncology Ljubljana, Ljubljana, Slovenia; [12]Kanazawa University Hospital, Kanazawa, Japan; [13]Medical Oncology Department, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), CIBERONC, Madrid, Spain; [14]Taichung Veterans General Hospital, Taichung, Taiwan; [15]University of Chicago, Chicago, IL; [16]Roche Products Limited, Welwyn Garden City, UK; [17]F. Hoffmann-La Roche Ltd, Mississauga, ON, Canada; [18]Genentech, Inc, South San Francisco, CA; [19]MD Anderson Cancer Center Madrid, Madrid, Spain

IMvigor130: Final OS (ITT Population)

	Arm A Atezo+ plt/gem (n=451)	Arm C Placebo + plt/gem (n=400)
OS events, n (%)	336 (75)	310 (78)
HR (95% CI)[a]	0.85 (0.73, 1.00)	
Log-rank *P* value[b]	0.023[c] (final efficacy boundary: 0.021, 1-sided)	
24-month OS (95% CI), %	38 (33, 42)	32 (28, 37)
36-month OS (95% CI), %	26 (22, 30)	22 (17, 26)



Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA440.

IMvigor130: ORR per Investigator Assessment

	ITT[a]		Cisplatin[a]		Carboplatin[a]	
	Arm A Atezo + plt/gem (n=447)	Arm C Placebo + plt/gem (n=397)	Arm A Atezo + plt/gem (n=136)	Arm C Placebo + plt/gem (n=135)	Arm A Atezo + plt/gem (n=311)	Arm C Placebo + plt/gem (n=262)
Responders, n	215	178	66	68	149	110
ORR (95% CI), %	48.1 (43.4, 52.8)	44.8 (39.9, 49.9)	48.5 (39.9, 57.3)	50.4 (41.6, 59.1)	47.9 (42.2, 53.6)	42.0 (35.9, 48.2)
CR, n (%)	63 (14)	31 (8)	25 (18)	14 (10)	38 (12)	17 (6)
PR, n (%)	152 (34)	147 (37)	41 (30)	54 (40)	111 (36)	93 (35)
SD, n (%)	129 (29)	135 (34)	43 (32)	43 (32)	86 (28)	92 (35)
PD, n (%)	54 (12)	53 (13)	13 (10)	19 (14)	41 (13)	34 (13)
DCR (95% CI), %[b]	64.9 (60.3, 69.3)	60.2 (55.2, 65.1)	–	–	–	–
DOR events, %[c]	76.3	84.8	63.6	76.5	81.9	90.0
Median DOR (95% CI), mo[c]	9.1 (8.0, 10.6)	8.2 (6.3, 8.6)	13.2 (10.3, 24.3)	8.3 (6.3, 14.4)	8.1 (6.5, 10.2)	8.1 (6.2, 8.6)

Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA440.

IMvigor130: Overall Safety Profile

Patients with ≥1 AE, n (%)	Arm A Atezo + plt/gem (n=454)	Arm C Placebo + plt/gem (n=389)
All-grade AE	452 (>99)	385 (99)
Treatment-related AE	435 (96)	372 (96)
Grade 3/4 AE	382 (84)	330 (85)
Treatment-related Grade 3/4 AE	370 (81)	312 (80)
Grade 5 AE	34 (7)	21 (5)
Treatment-related Grade 5 AE	9 (2)	4 (1)
AESI of any grade	242 (53)	138 (35)
Grade 3/4 AESI	41 (9)	17 (4)
Grade 5 AESI	4 (1)	1 (<1)
Serious AE	243 (54)	196 (50)
Treatment-related serious AE	145 (32)	101 (26)
AE leading to withdrawal from any treatment	165 (36)	132 (34)
AE leading to withdrawal from atezo/placebo	61 (13)	31 (8)
AE leading to dose modification or interruption[a]	370 (81)	303 (78)

Galsky MD et al. Genitourinary Cancers Symposium 2023;Abstract LBA440.

ASCO Genitourinary Cancers Symposium 2023;Abstract LBA441.

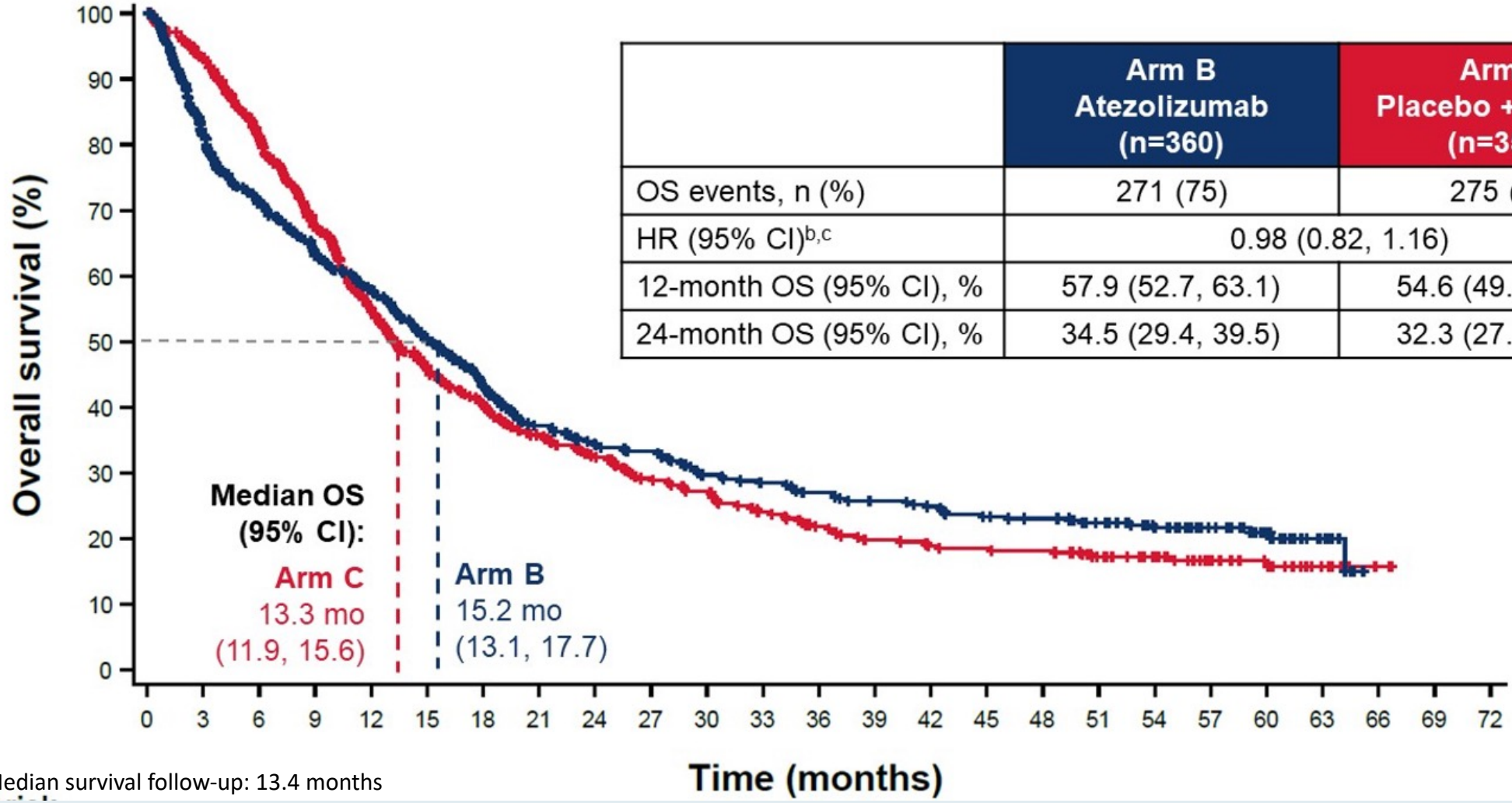
Final Overall Survival Analysis of Atezolizumab Monotherapy vs Chemotherapy in Untreated Locally Advanced or Metastatic Urothelial Carcinoma From the Phase III IMvigor130 Study

Aristotelis Bamias,[1] Ian D. Davis,[2] Matthew Galsky,[3] José Ángel Arranz Arija,[4] Eiji Kikuchi,[5] Enrique Grande,[6] Xavier Garcia del Muro,[7] Se Hoon Park,[8] Ugo De Giorgi,[9] Boris Alekseev,[10] Marina Mencinger,[11] Kouji Izumi,[12] Javier Puente Vazquez,[13] Jian-Ri Li,[14] Fabiola Bene-Tchaleu,[15] Sanjeev Mariathasan,[16] Chooi Lee,[17] Sandrine Bernhard,[17] Maria De Santis[18]

[1]National and Kapodistrian University of Athens, Athens, Greece; 2. Eastern Health Clinical School, Monash University and Eastern Health, Melbourne, Australia; 3. Icahn School of Medicine at Mount Sinai/Tisch Cancer Institute, New York, NY; 4. Gregorio Marañón Hospital, Madrid, Spain; 5. St. Marianna University School of Medicine, Kawasaki, Japan; 6. MD Anderson Cancer Center Madrid, Madrid, Spain; 7. Catalan Institute of Oncology, IDIBELL, University of Barcelona, Barcelona, Spain; 8. Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 9. IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST), Dino Amadori, Meldola, Italy; 10. Research Oncology Institute, Tomsk, Russia; 11. Institute of Oncology Ljubljana, Ljubljana, Slovenia; 12. Kanazawa University Hospital, Kanazawa, Japan; 13. Medical Oncology Department, Hospital Clínico San Carlos, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), CIBERONC, Madrid, Spain; 14. Taichung Veterans General Hospital, Taichung, Taiwan; 15. F. Hoffmann-La Roche Ltd, Mississauga, ON, Canada; 16. Genentech, Inc, South San Francisco, CA; 17. Roche Products Limited, Welwyn Garden City, UK; 18. Charité University Hospital, Department of Urology, Berlin, Germany, and Medical University, Department of Urology, Vienna, Austria

IMvigor130: Final OS Analysis (ITT Population)

	Arm B Atezolizumab (n=360)	Arm C Placebo + plt/gem (n=359)[a]
OS events, n (%)	271 (75)	275 (77)
HR (95% CI)[b,c]	0.98 (0.82, 1.16)	
12-month OS (95% CI), %	57.9 (52.7, 63.1)	54.6 (49.2, 59.9)
24-month OS (95% CI), %	34.5 (29.4, 39.5)	32.3 (27.3, 37.4)



Median survival follow-up: 13.4 months

Bamias A et al. Genitourinary Cancers Symposium 2023;Abstract LBA441.

IMvigor130: Investigator-Assessed ORR

	ITT		Cisplatin ineligible IC2/3	
	Arm B Atezolizumab (n=359)[a]	Arm C Placebo + plt/gem (n=356)[a,b]	Arm B Atezolizumab (n=50)[a]	Arm C Placebo + plt/gem (n=43)[a,b]
Responders, n	87	158	20	14
ORR (95% CI), %	24.2 (19.9, 29.0)	44.4 (39.2, 49.7)	40.0 (26.4, 54.8)	32.6 (19.1, 48.5)
CR, n (%)	29 (8)	28 (8)	6 (12)	4 (9)
PR, n (%)	58 (16)	130 (37)	14 (28)	10 (23)
SD, n (%)	86 (24)	123 (35)	11 (22)	19 (44)
PD, n (%)	135 (38)	47 (13)	14 (28)	4 (9)
DCR, n (%)[c] [95% CI]	137 (38) [33, 43]	211 (59) [54, 64]	–	–
DOR event proportion, %[d]	57	84	45	86
Median DOR (95% CI), mo[d]	29.6 (15.9, NE)	8.1 (6.3, 8.5)	NE (7.2, NE)	6.2 (4.2, 10.9)

Bamias A et al. Genitourinary Cancers Symposium 2023;Abstract LBA441.

IMvigor130: Overall Safety Profile

Patients with ≥1 AE, n (%)	Arm B Atezolizumab (n=354)	Arm C Placebo + plt/gem (n=389)[a]
All-grade AE	331 (94)	385 (99)
Treatment-related all-grade AE	217 (61)	372 (96)
Grade 3/4 AE	162 (46)	330 (85)
Treatment-related Grade 3/4 AE	57 (16)	312 (80)
Grade 5 AE	29 (8)	21 (5)
Treatment-related Grade 5 AE	3 (1)	4 (1)
Serious AE	163 (46)	196 (50)
Treatment-related serious AE	44 (12)	101 (26)
All-grade AESI	139 (39)	138 (35)
Grade 3/4 AESI	36 (10)	17 (4)
Grade 5 AESI	2 (1)	1 (<1)
AE leading to withdrawal from any treatment	31 (9)	132 (34)
AE leading to withdrawal from atezolizumab or placebo	30 (8)	31 (8)
AE leading to dose modification or interruption[b]	129 (36)	303 (78)

Bamias A et al. Genitourinary Cancers Symposium 2023;Abstract LBA441.

2023 March;34(3):289-99.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY
driving innovation in oncology

ORIGINAL ARTICLE

Efficacy and safety of pembrolizumab in metastatic urothelial carcinoma: results from KEYNOTE-045 and KEYNOTE-052 after up to 5 years of follow-up☆

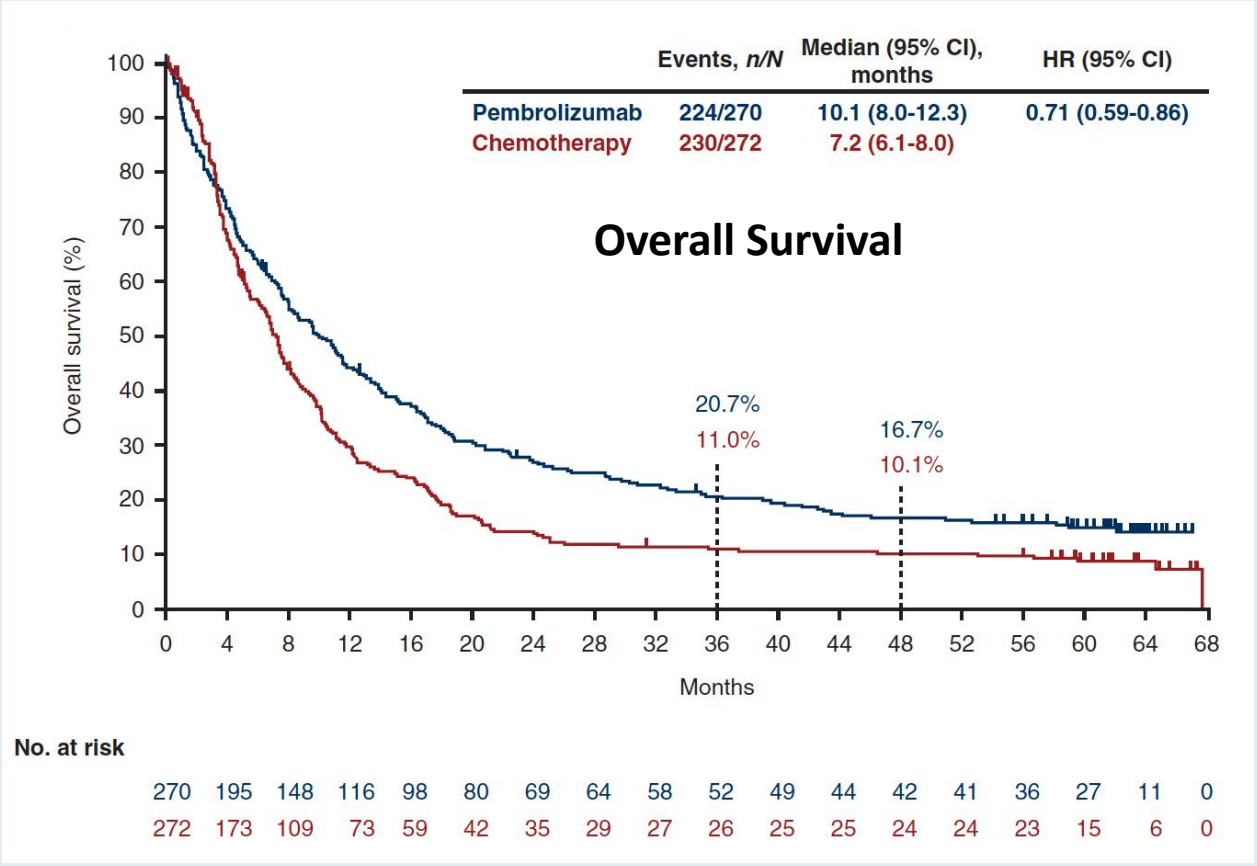
A. V. Balar[1], D. E. Castellano[2], P. Grivas[3], D. J. Vaughn[4], T. Powles[5], J. Vuky[6], Y. Fradet[7], J.-L. Lee[8], L. Fong[9], N. J. Vogelzang[10†], M. A. Climent[11], A. Necchi[12], D. P. Petrylak[13], E. R. Plimack[14], J. Z. Xu[15], K. Imai[15], B. H. Moreno[15], J. Bellmunt[16], R. de Wit[17*] & P. H. O'Donnell[18*]

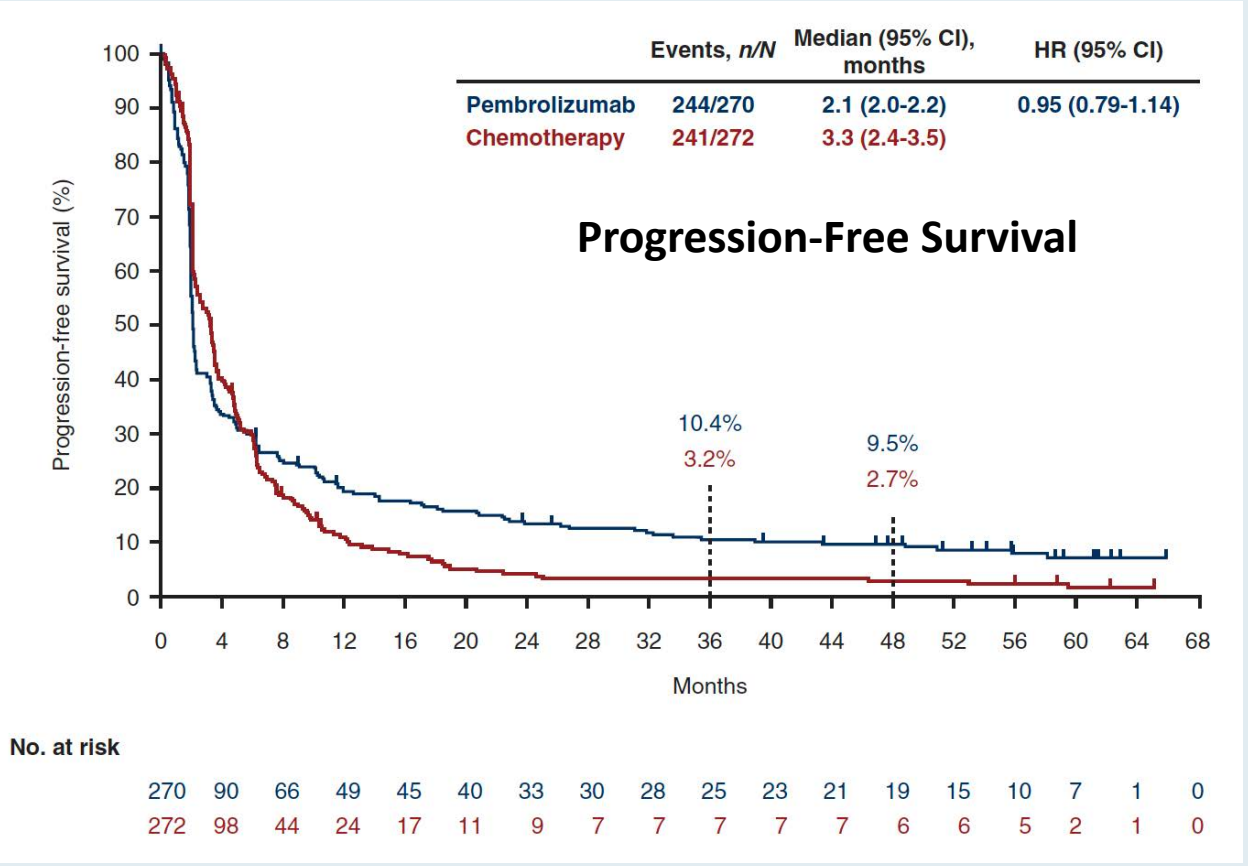
ORR and DOR in KEYNOTE-045 and KEYNOTE-052

	KEYNOTE-045		KEYNOTE-052		
	Pembrolizumab ($n = 270$)	Chemotherapy[a] ($n = 272$)	PD-L1 CPS <10 ($n = 251$)	PD-L1 CPS ≥10 ($n = 110$)	Total ($N = 370$)
ORR (CR + PR), % (95% CI)	21.9 (17.1-27.3)	11.0 (7.6-15.4)	20.7 (15.9-26.3)	47.3 (37.7-57.0)	28.9 (24.3-33.8)
Difference (95% CI)	10.8 (4.6-17.0)		N/A	N/A	N/A
Best response, *n* (%)					
CR	27 (10.0)	8 (2.9)	10 (4.0)	23 (20.9)	35 (9.5)
PR	32 (11.9)	22 (8.1)	42 (16.7)	29 (26.4)	72 (19.5)
SD	47 (17.4)	92 (33.8)	44 (17.5)	22 (20.0)	67 (18.1)
PD	129 (47.8)	90 (33.1)	121 (48.2)	30 (27.3)	155 (41.9)
Not evaluable[b]	4 (1.5)	9 (3.3)	9 (3.6)	0 (0)	9 (2.4)
No assessment[c]	31 (11.5)	51 (18.8)	25 (10.0)	6 (5.5)	32 (8.6)
Time to response, median (range), months	2.1 (1.4-6.3)	2.1 (1.7-4.9)	2.1 (1.6-9.0)	2.1 (1.3-4.7)	2.1 (1.3-9.0)
DOR, median (range), months	29.7 (1.6+ to 60.5+)	4.4 (1.4+ to 63.1+)	21.2 (1.6+ to 59.7+)	NR (1.4+ to 60.7+)	33.4 (1.4+ to 60.7+)
Responders at ≥36 months, %	44.4	28.3	34.4	57.6	44.8
Responders at ≥48 months, %	40.9	28.3	27.4	57.6	39.4

Balar AV et al. *Ann Oncol* 2023 March;34(3):289-99.

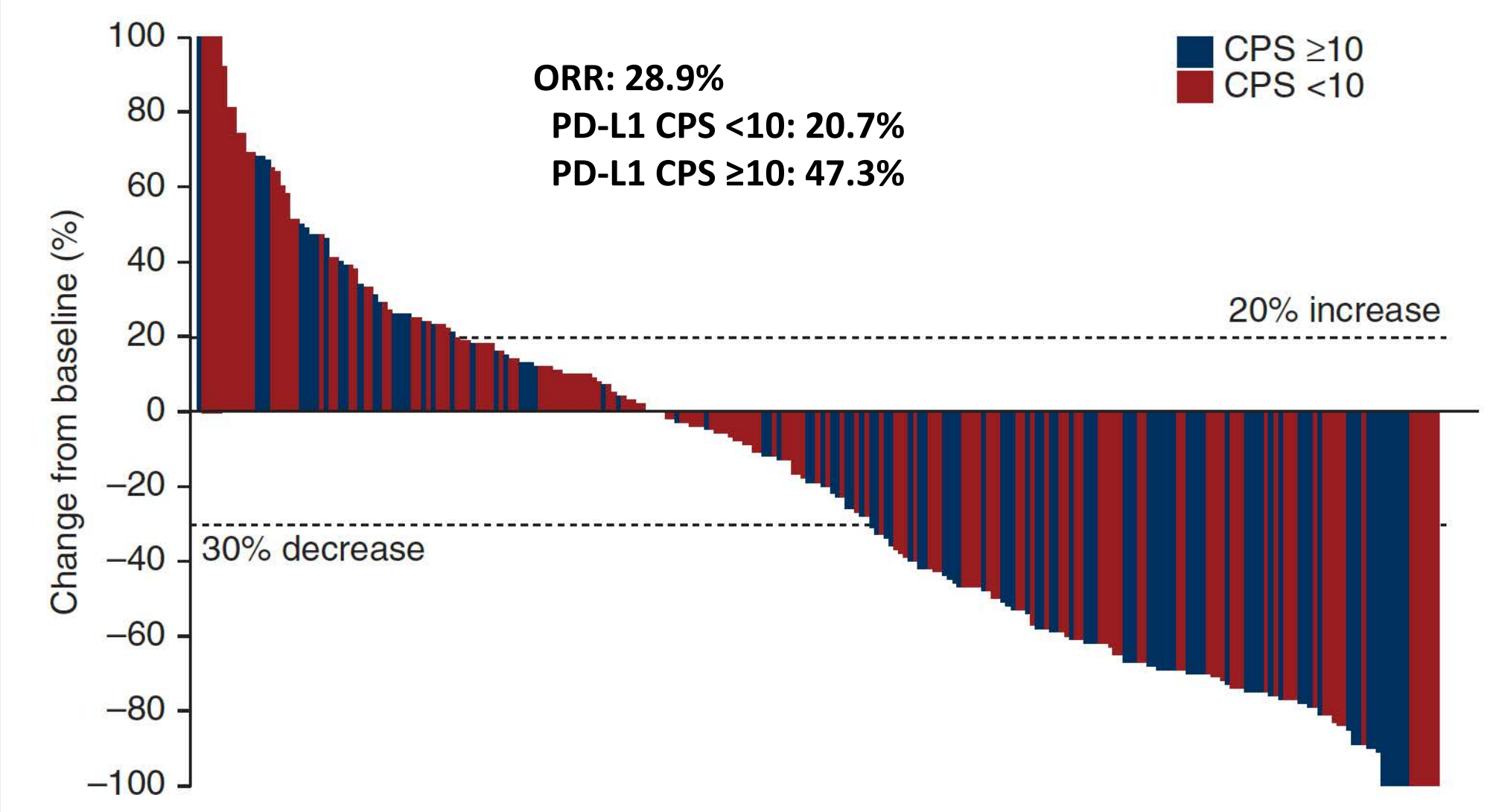
KEYNOTE-045: Survival Analyses After 5 Years





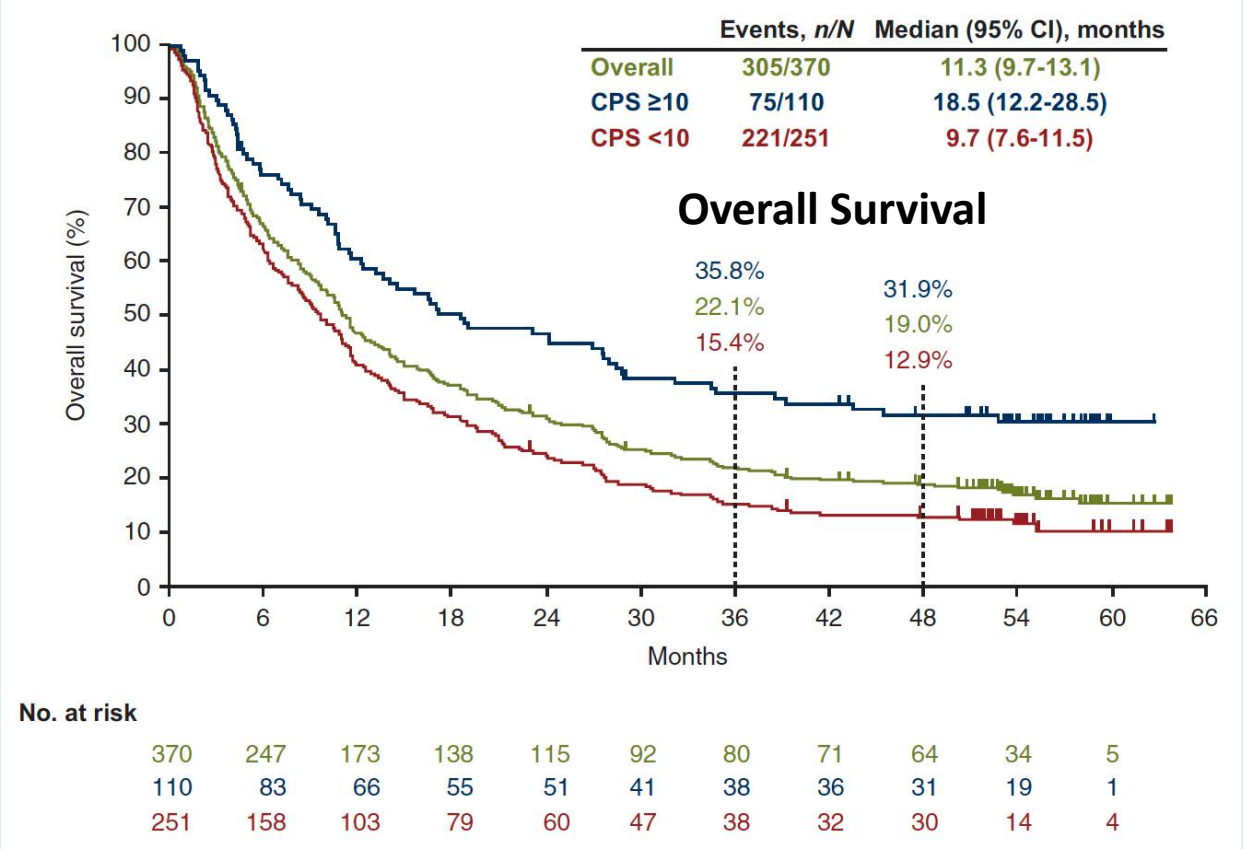
Balar AV et al. *Ann Oncol* 2023 March;34(3):289-99.

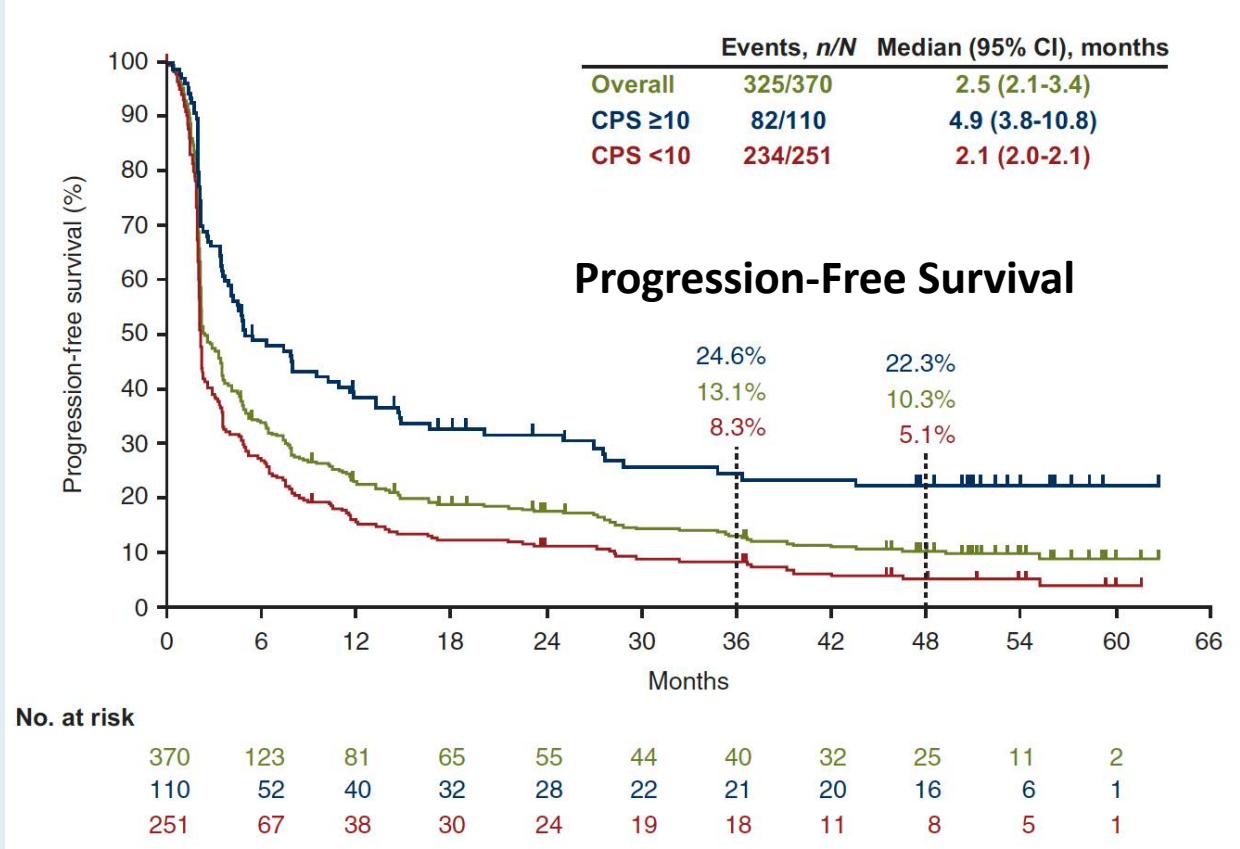
KEYNOTE-052: Response



Balar AV et al. *Ann Oncol* 2023 March;34(3):289-99.

KEYNOTE-052: Survival Analyses After 5 Years





Balar AV et al. *Ann Oncol* 2023 March;34(3):289-99.

Adverse Event (AE) Summary for KEYNOTE-045 and KEYNOTE-052

	KEYNOTE-045 Pembrolizumab (n = 266)	KEYNOTE-045 Chemotherapy (n = 255)	KEYNOTE-052 Pembrolizumab CPS <10 (n = 251)	KEYNOTE-052 Pembrolizumab CPS ≥10 (n = 110)	KEYNOTE-052 Pembrolizumab Total (N = 370)
Any AE	250 (94.0)	250 (98.0)	243 (96.8)	109 (99.1)	361 (97.6)
Grade 3-5 AEs	147 (55.3)	166 (65.1)	166 (66.1)	68 (61.8)	236 (63.8)
Any treatment-related AE[a]	165 (62.0)	231 (90.6)	162 (64.5)	81 (73.6)	249 (67.3)
Grade 3-5 treatment-related AEs	45 (16.9)	128 (50.2)	51 (20.3)	26 (23.6)	78 (21.1)
Serious AEs	105 (39.5)	104 (40.8)	127 (50.6)	60 (54.5)	190 (51.4)
Serious treatment-related AEs	34 (12.8)	57 (22.4)	28 (11.2)	14 (12.7)	43 (11.6)
Discontinued any drug due to treatment-related AEs	19 (7.1)	32 (12.5)	17 (6.8)	18 (16.4)	35 (9.5)
Death	13 (4.9)	10 (3.9)	17 (6.8)	9 (8.2)	26 (7.0)
Death due to treatment-related AEs	4 (1.5)	4 (1.6)	0 (0)	1 (0.9)	1 (0.3)

Balar AV et al. *Ann Oncol* 2023 March;34(3):289-99.

Antibody-Drug Conjugates

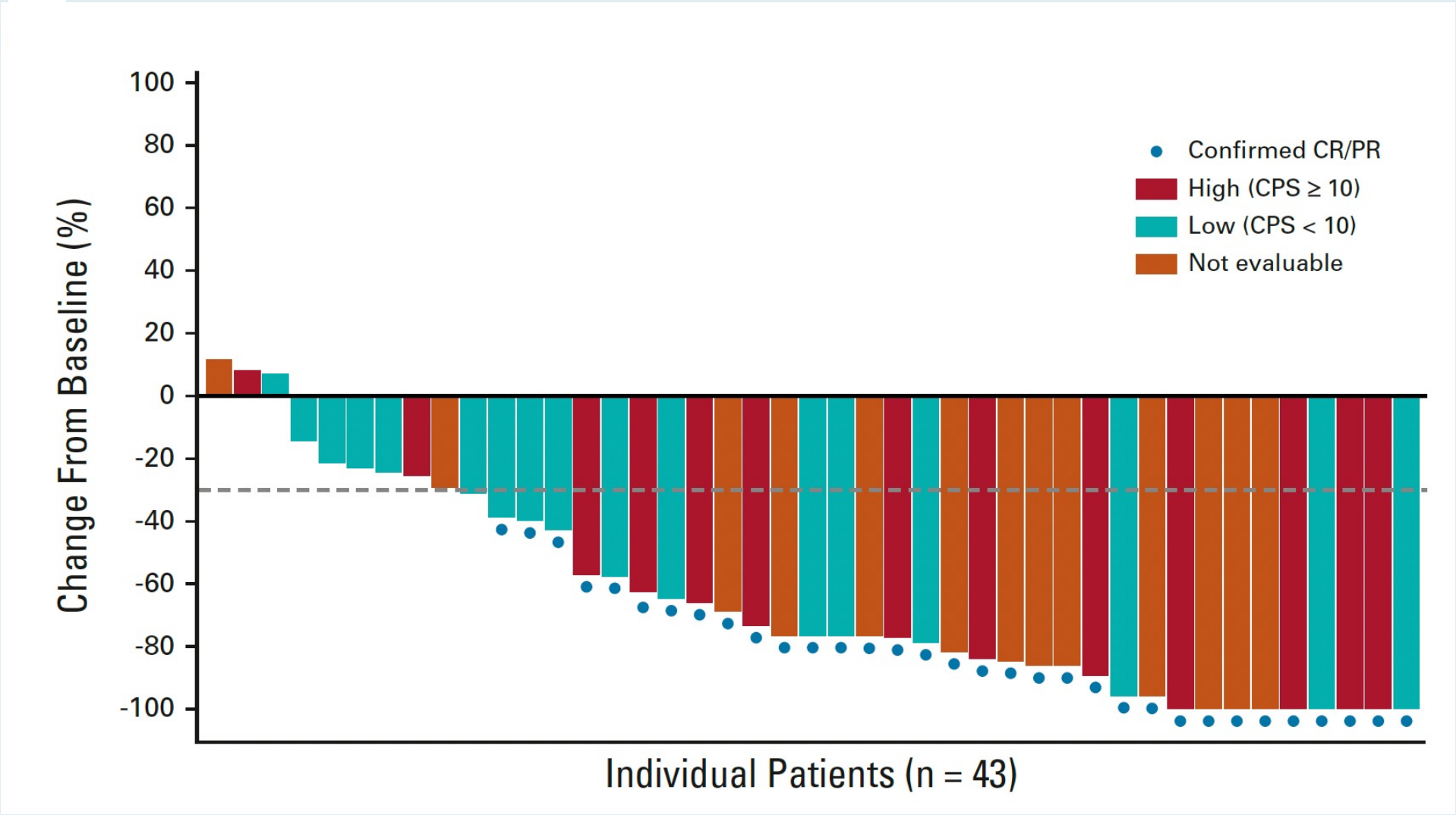
Enfortumab Vedotin

Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer

Christopher J. Hoimes, DO[1,2]; Thomas W. Flaig, MD[3]; Matthew I. Milowsky, MD[4]; Terence W. Friedlander, MD[5]; Mehmet Asim Bilen, MD[6]; Shilpa Gupta, MD[7]; Sandy Srinivas, MD[8]; Jaime R. Merchan, MD[9]; Rana R. McKay, MD[10]; Daniel P. Petrylak, MD[11]; Carolyn Sasse, BS[12]; Blanca Homet Moreno, MD, PhD[13]; Yao Yu, PhD[14]; Anne-Sophie Carret, MD[14]; and Jonathan E. Rosenberg, MD[15]

J Clin Oncol 2023 January 1;41(1):22-31.

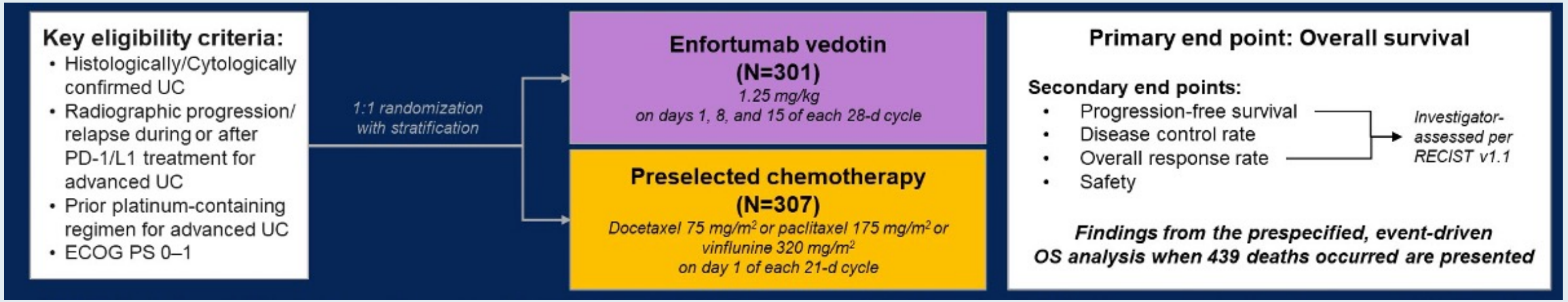
EV-103 Cohort A: Enfortumab Vedotin with Pembrolizumab for Previously Untreated Advanced Urothelial Cancer



Hoimes CJ et al. *J Clin Oncol* 2023:41:22-31.

RTP RESEARCH TO PRACTICE

EV-301 Study Design



Rosenberg JE et al. ASCO 2022;Abstract 4516.

2022 ASCO® ANNUAL MEETING

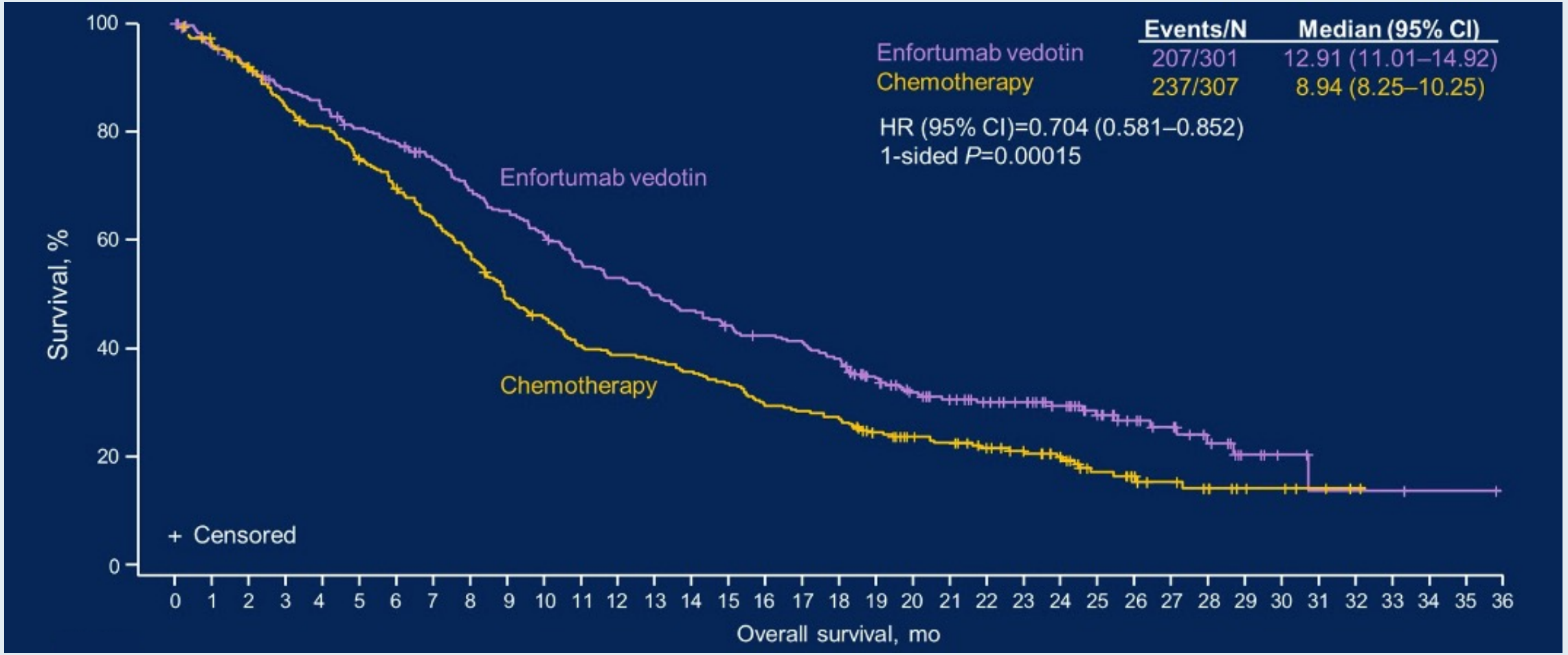
Abstract 4516

Long-Term Outcomes in EV-301: 24-Month Findings From the Phase 3 Trial of Enfortumab Vedotin vs Chemotherapy in Patients With Previously Treated Advanced Urothelial Carcinoma

Jonathan E. Rosenberg, MD[1]; Thomas Powles, MD[2]; Guru P. Sonpavde, MD[3]; Yohann Loriot, MD, PhD[4]; Ignacio Duran, MD, PhD[5]; Jae-Lyun Lee, MD, PhD[6]; Nobuaki Matsubara, MD[7]; Christof Vulsteke, MD, PhD[8]; Daniel Castellano, MD[9]; Ronac Mamtani, MD[10]; Chunzhang Wu, PhD[11]; Maria Matsangou, MD[11]; Mary Campbell, MD[12]; Daniel P. Petrylak, MD[13]

[1]Department of Medicine, Division of Solid Tumor Oncology, Genitourinary Oncology Service, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Barts Cancer Institute, CRUK Experimental Cancer Medicine Centre, London, UK; [3]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [4]Gustave Roussy, Université Paris-Saclay, Villejuif, France; [5]Hospital Universitario Marques de Valdecilla, IDIVAL, Cantabria, Spain; [6]Asan Medical Center and University of Ulsan College of Medicine, Seoul, South Korea; [7]National Cancer Center Hospital East, Chiba, Japan; [8]Center for Oncological Research (CORE), University of Antwerp, Integrated Cancer Center Ghent, Ghent, Belgium; [9]Hospital Universitario 12 de Octubre, Madrid, Spain; [10]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [11]Astellas Pharma, Inc., Northbrook, IL; [12]Seagen Inc., Bothell, WA; [13]Yale Cancer Center, New Haven, CT

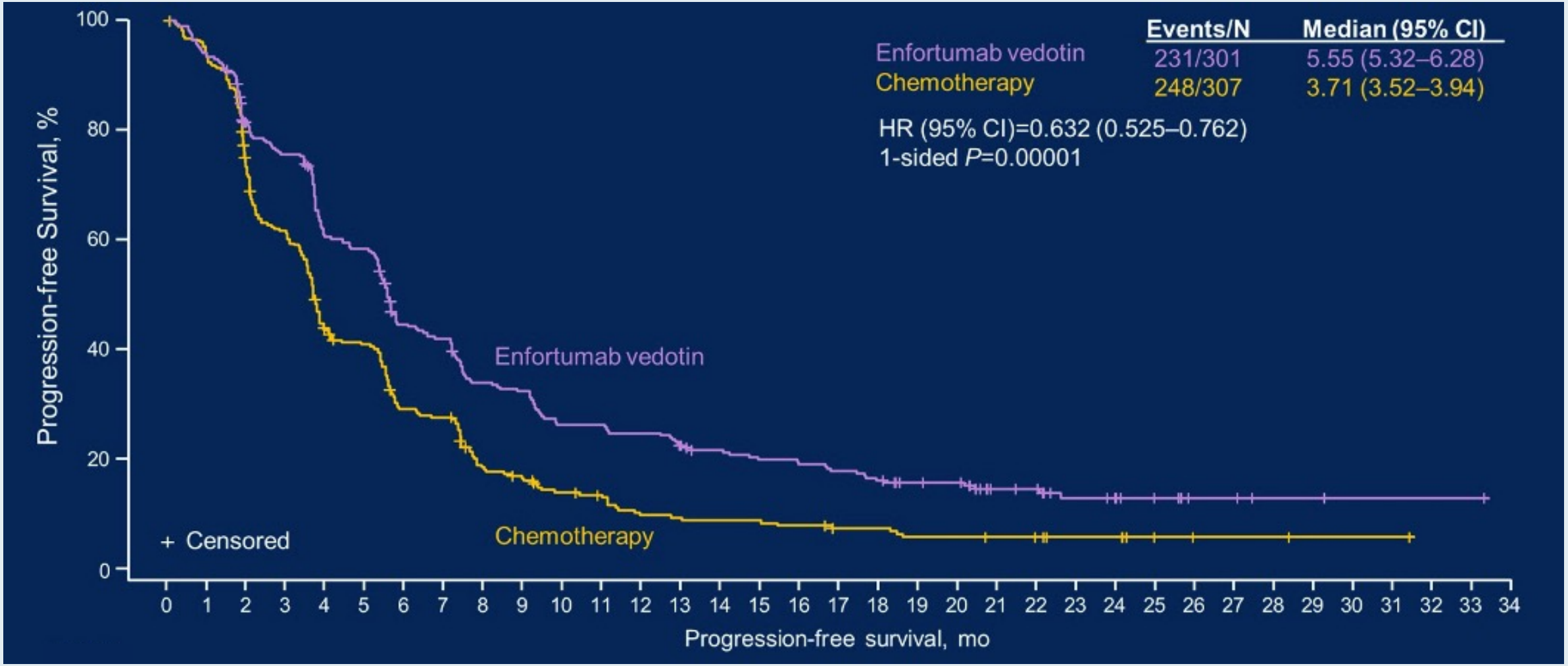
EV-301: Overall Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

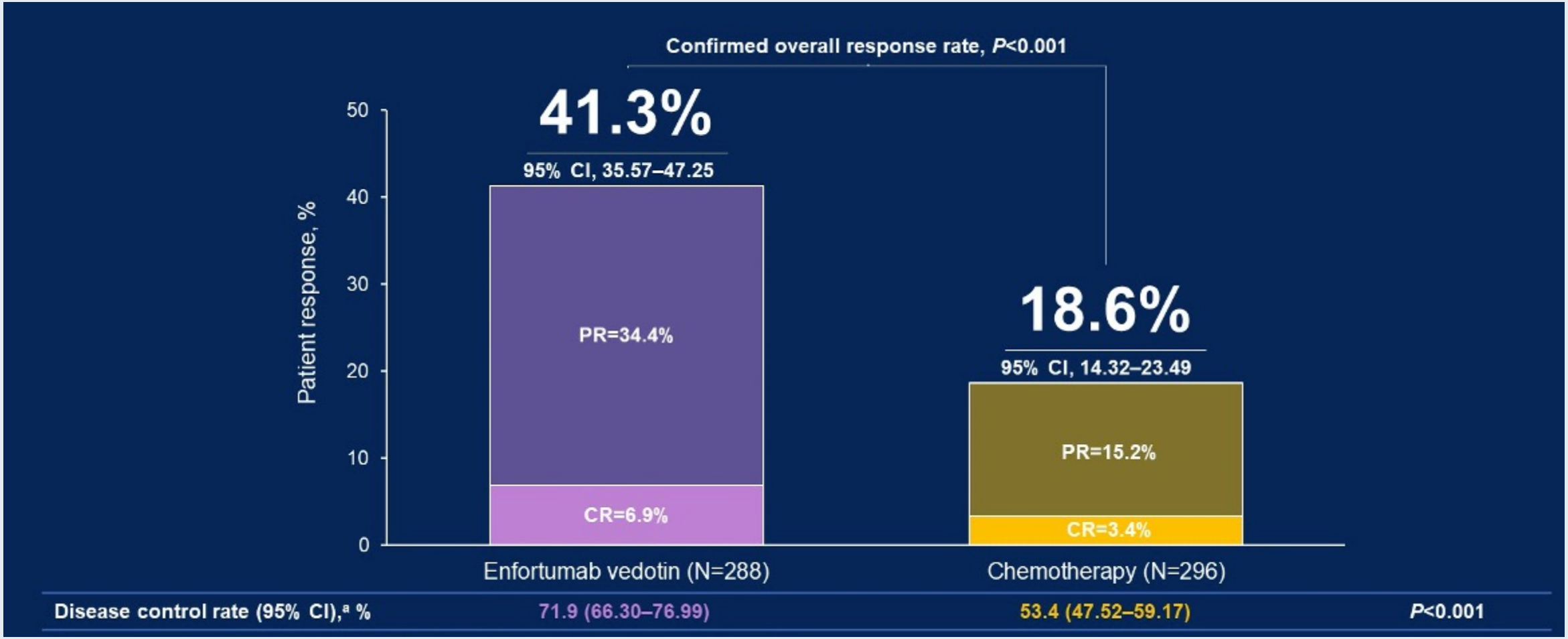
RTP RESEARCH TO PRACTICE

EV-301: Progression-Free Survival



Rosenberg JE et al. ASCO 2022;Abstract 4516.

EV-301: Investigator-Assessed Clinical Response



Rosenberg JE et al. ASCO 2022;Abstract 4516.

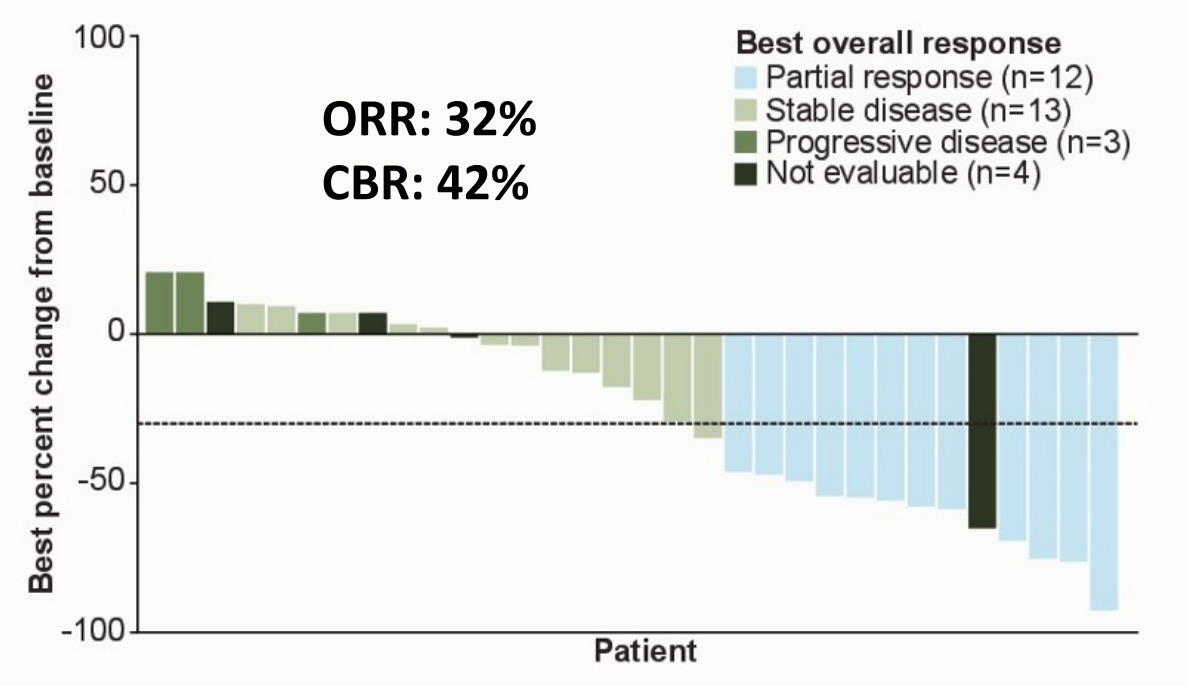
EV-301: Adverse Events of Special Interest (Safety Population)

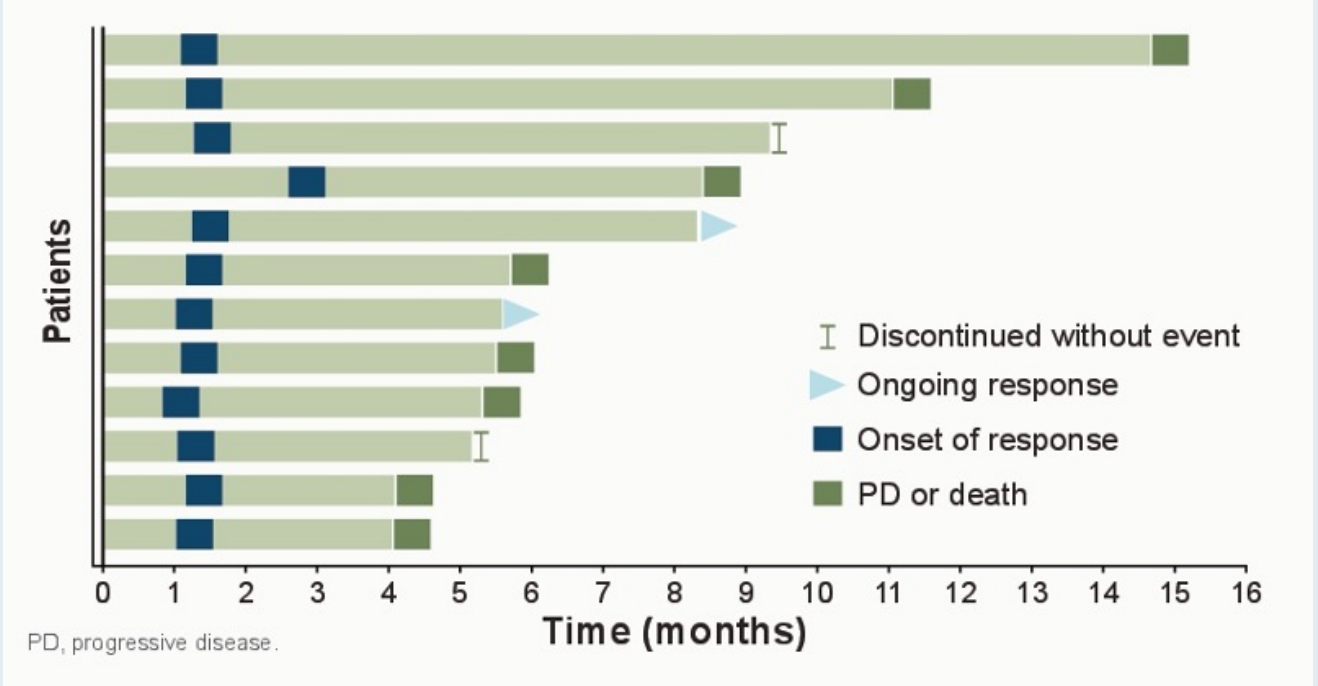
Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)						Chemotherapy (N=291)					
	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Rash	133 (44.9)	41 (13.9)	48 (16.2)	43 (14.5)	1 (0.3)	NR	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	NR
Severe cutaneous adverse reaction	60 (20.3)	20 (6.8)	25 (8.4)	14 (4.7)	1 (0.3)	NR	22 (7.6)	12 (4.1)	8 (2.7)	2 (0.7)	0	NR
Peripheral neuropathy	142 (48.0)	36 (12.2)	84 (28.4)	22 (7.4)	NR	NR	92 (31.6)	43 (14.8)	41 (14.1)	8 (2.7)	NR	NR
Peripheral neuropathy sensory events	135 (45.6)	35 (11.8)	82 (27.7)	18 (6.1)	NR	NR	89 (30.6)	42 (14.4)	39 (13.4)	8 (2.7)	NR	NR
Peripheral neuropathy motor events	23 (7.8)	6 (2.0)	11 (3.7)	6 (2.0)	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Dry eye	48 (16.2)	34 (11.5)	12 (4.1)	2 (0.7)	NR	NR	9 (3.1)	6 (2.1)	2 (0.7)	1 (0.3)	NR	NR
Blurred vision	13 (4.4)	11 (3.7)	2 (0.7)	0	NR	NR	6 (2.1)	5 (1.7)	0	1 (0.3)	NR	NR
Corneal disorders	2 (0.7)	2 (0.7)	NR	NR	NR	NR	0	0	NR	NR	NR	NR
Infusion-related reaction	27 (9.1)	12 (4.1)	11 (3.7)	4 (1.4)	NR	NR	14 (4.8)	7 (2.4)	7(2.4)	0	NR	NR
Systemic infusion-related reaction event	24 (8.1)	11 (3.7)	9 (3.0)	4 (1.4)	NR	NR	9 (3.1)	4 (1.4)	5 (1.7)	0	NR	NR
Local infusion-related reaction event	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Infusion-site reaction	2 (0.7)	0	2 (0.7)	0	NR	NR	5 (1.7)	4 (1.4)	1 (0.3)	0	NR	NR
Extravasation-site reaction	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR
Hyperglycemia	20 (6.8)	3 (1.0)	4 (1.4)	12 (4.1)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0	0	0

Rosenberg JE et al. ASCO 2022;Abstract 4516.

Sacituzumab Govitecan

TROPHY U-01 (Cohort 2): Response

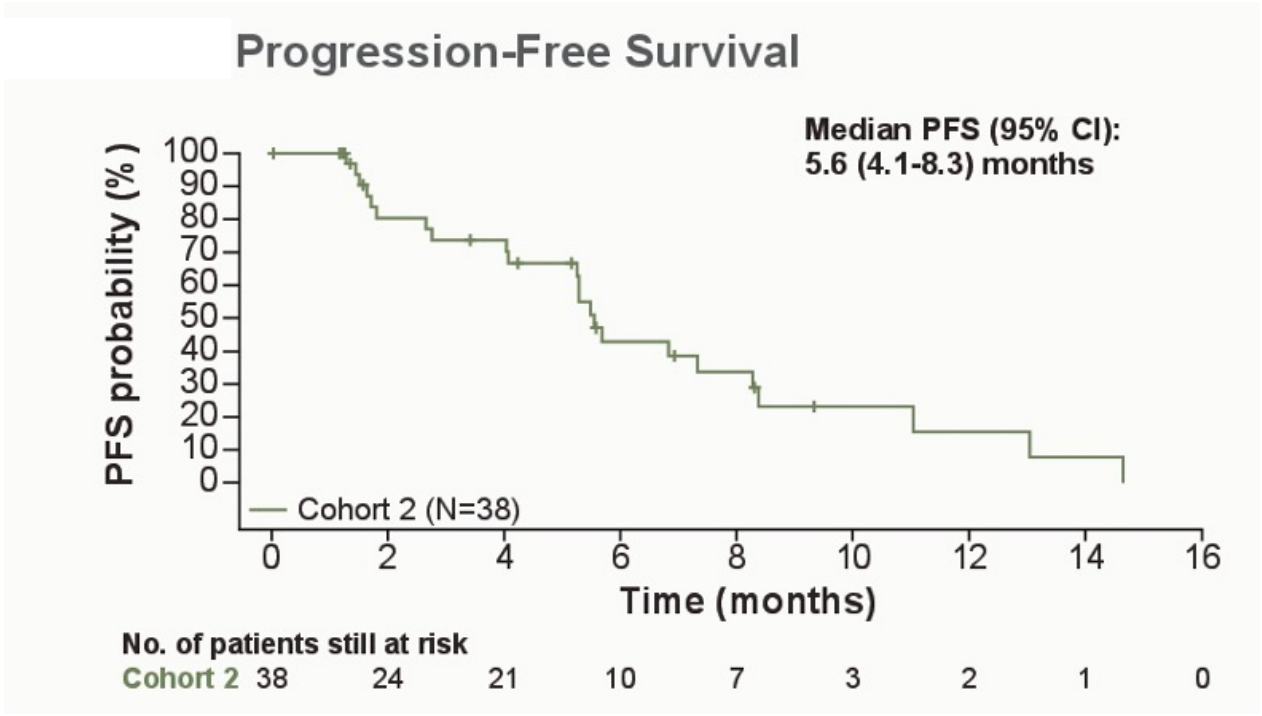


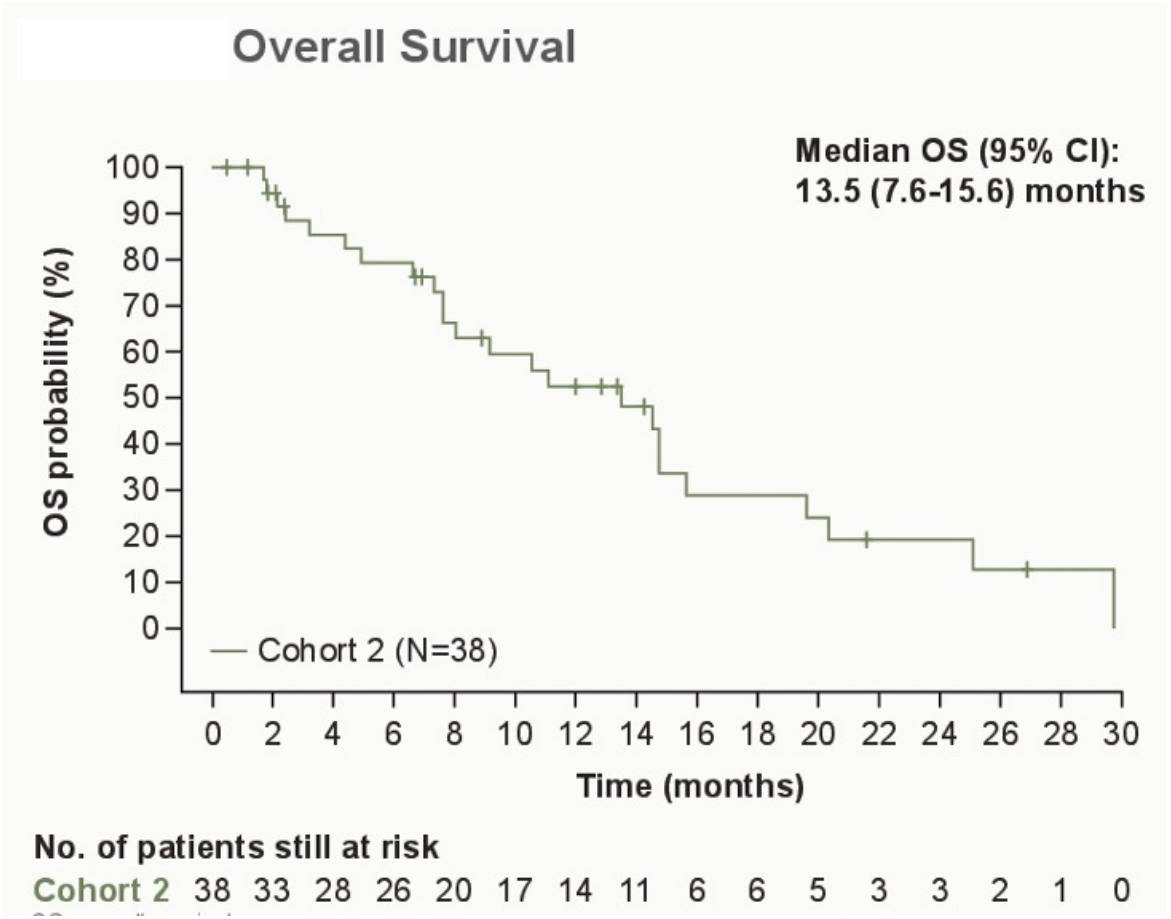


Petrylak DP et al. Genitourinary Cancers Symposium 2023;Abstract 520.

RTP RESEARCH TO PRACTICE

TROPHY U-01 (Cohort 2): Survival Analyses





Petrylak DP et al. Genitourinary Cancers Symposium 2023;Abstract 520.

RTP RESEARCH TO PRACTICE

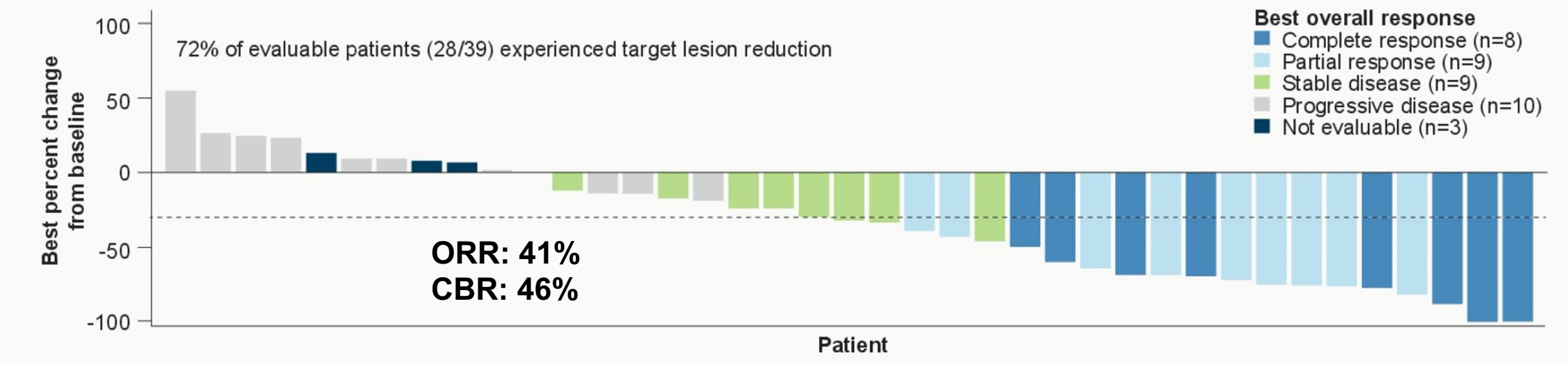
TROPHY U-01 (Cohort 2): Safety Outcomes

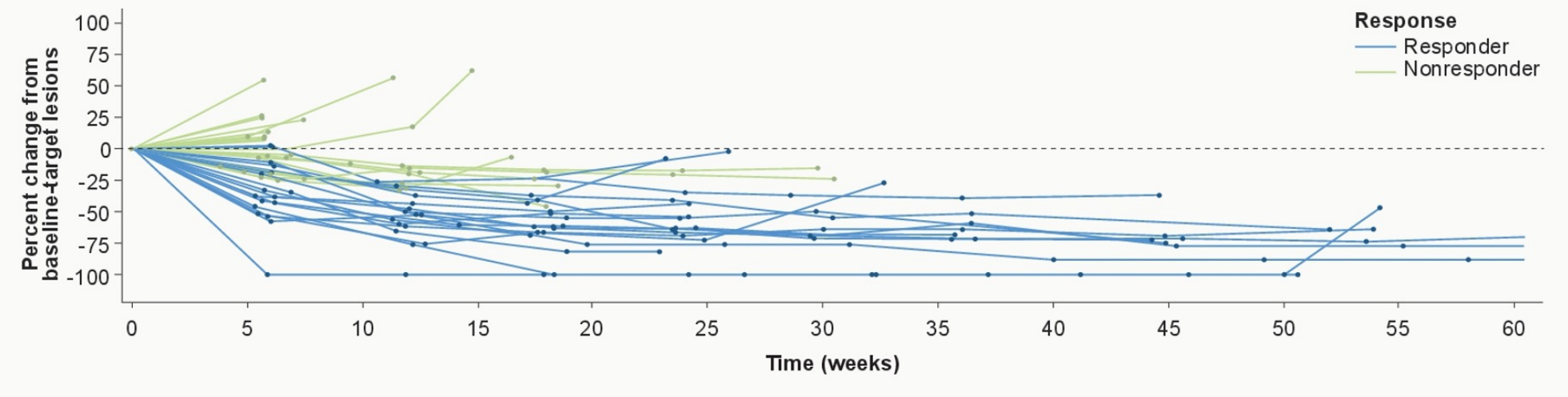
- 68% of patients experienced a grade ≥3 treatment-related adverse events (TRAEs) , with the most common being neutropenia (34%), anemia (21%), leukopenia (18%), fatigue (18%), diarrhea (16%; **Table 4**)
- 3 (8%) patients experienced treatment-related febrile neutropenia (2 [5%] patients with grade 3 and 1 patient [3%] with grade 4)
- 14 (37%) patients had SG dose reduction due to TRAEs
- 7 (18%) patients discontinued treatment due to TRAEs
- No treatment-related death occurred
- Granulocyte colony-stimulating factor was received by 7 patients (18%) for prophylactic use and 10 patients (26%) for treatment of an AE

TRAEs Occurring in >20% of Patients, n (%)	Cohort 2(N=38)	
	All Grade	Grade ≥3
Diarrhea	24 (63)	6 (16)
Alopecia	19 (50)	0
Nausea	18 (47)	0
Neutropenia	17 (45)	13 (34)
Fatigue	16 (42)	7 (18)
Anemia	14 (37)	8 (21)
Leukopenia	13 (34)	7 (18)
Decreased appetite	10 (26)	0

Petrylak DP et al. Genitourinary Cancers Symposium 2023;Abstract 520.

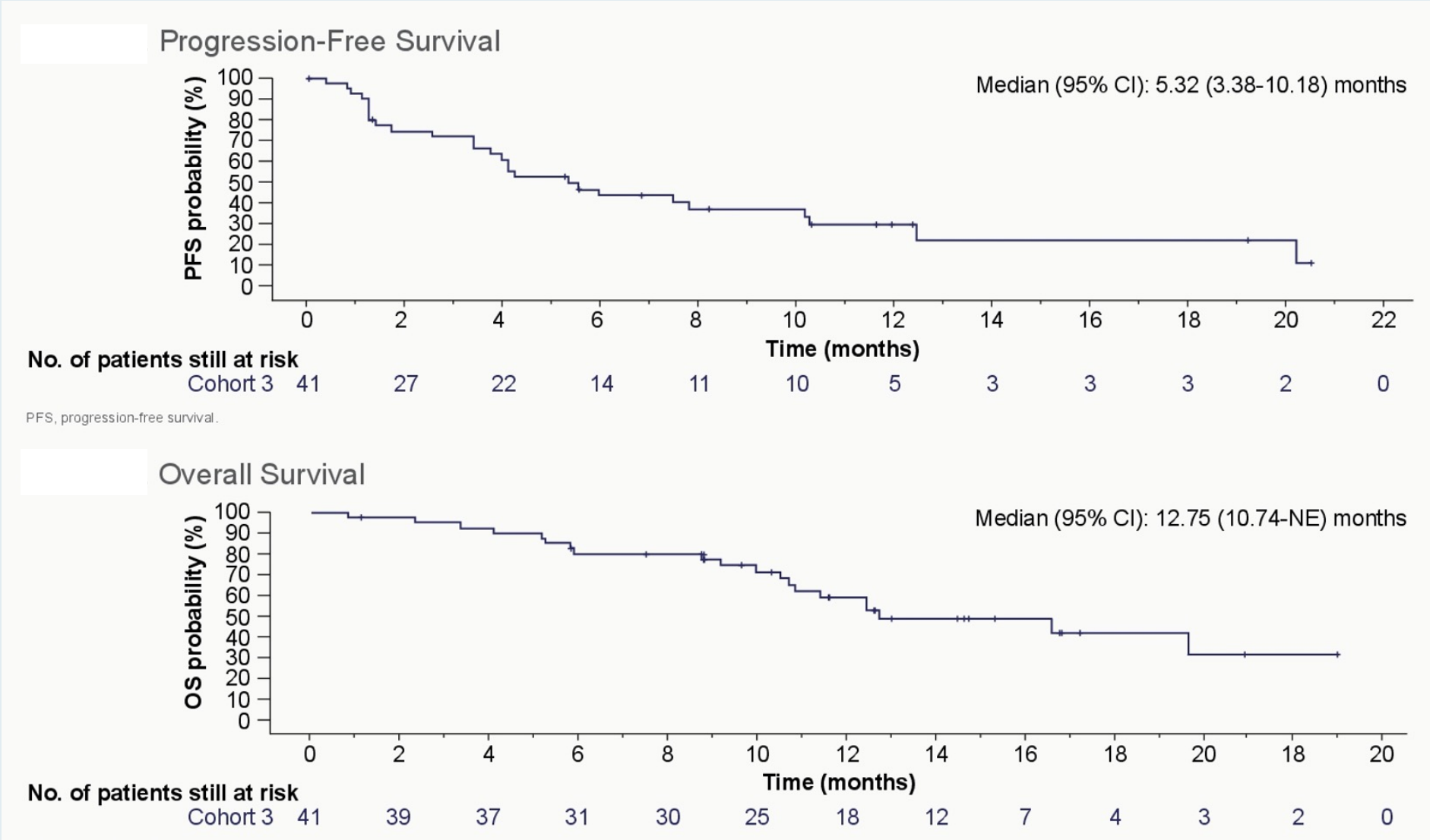
TROPHY U-01 (Cohort 3): Response





Grivas P et al. Genitourinary Cancers Symposium 2023;Abstract 518.

TROPHY U-01 (Cohort 3): Survival Analyses



Grivas P et al. Genitourinary Cancers Symposium 2023;Abstract 518.

RTP RESEARCH TO PRACTICE

TROPHY U-01 (Cohort 3): Safety Outcomes and Common TRAEs

Safety Outcomes

- All 41 patients experienced at least 1 treatment-related adverse event (TRAE)
- 61% of patients experienced a grade ≥3 TRAE, with the most common being neutropenia (37%), leukopenia (20%), and diarrhea (20%; **Table 4**)
- TRAEs led to SG dose reductions in 39% of patients and SG discontinuations in 15% of patients
- No treatment-related death occurred
- The most common pembrolizumab-related AEs of any grade were diarrhea (24%), asthenia (22%), pruritus (20%), and fatigue (17%)
  - 5 patients received systemic steroids (oral [4] or intravenous [IV; 1]) due to pembrolizumab-related AEs including diarrhea (3 patients), pruritus (1 patient), and pneumonitis (1 patient)
- Granulocyte colony-stimulating factor was received by 9 patients (22%) for prophylactic use and 8 patients (20%) for treatment of an AE

	Cohort 3 (N=41)	
TRAE[a]	All Grades Reported by ≥15% of Patients, n (%)	Grade ≥3 Reported by ≥5% of Patients, n (%)
Diarrhea	29 (71)	8 (20)
Nausea	23 (56)	3 (7)
Neutropenia	21 (51)	15 (37)
Anemia	20 (49)	7 (17)
Asthenia	17 (41)	3 (7)
Alopecia	16 (39)	0
Fatigue	13 (32)	3 (7)
Decreased appetite	12 (29)	2 (5)
Vomiting	12 (29)	0
Leukopenia	11 (27)	8 (20)
Pruritus	10 (24)	0
Stomatitis	7 (17)	0
Hypomagnesemia	7 (17)	0
Febrile neutropenia[b]	4 (10)	4 (10)
Pneumonitis	2 (5)	2 (5)

Grivas P et al. Genitourinary Cancers Symposium 2023;Abstract 518.

TROPiCS-04 Phase III Study Design

Study Population

- Locally advanced unresectable or mUC
- Upper/lower tract tumors
- Mixed histologic types are allowed if urothelial is predominant
- Progression after platinum-based **and** anti–PD-1/PD-L1 therapy

OR

- Platinum in neo/adj setting if progression within 12 months and subsequent CPI

N = 482

Sacituzumab govitecan

Sacituzumab govitecan
10 mg/kg
D1/8 of 21-day cycle

Treatment of physician's choice

- Docetaxel @ 75 mg/m^2

OR

- Paclitaxel @ 175 mg/m^2

OR

- Vinflunine @ 320 mg/m^2 on D1 of 21-day cycle

Continue treatment until loss of clinical benefit or unacceptable toxicity

Endpoints

Primary Endpoints:

- OS

Secondary Endpoints:

- PFS by PI assessment using RECIST 1.1
- ORR, DOR, and CBR by PI assessment using RECIST 1.1
- EORTC QLQ C30 score and EuroQOL EQ-5D-5L QOL score

www.clinicaltrials.gov. NCT04527991. Accessed May 2023.

RTP RESEARCH TO PRACTICE

Erdafitinib

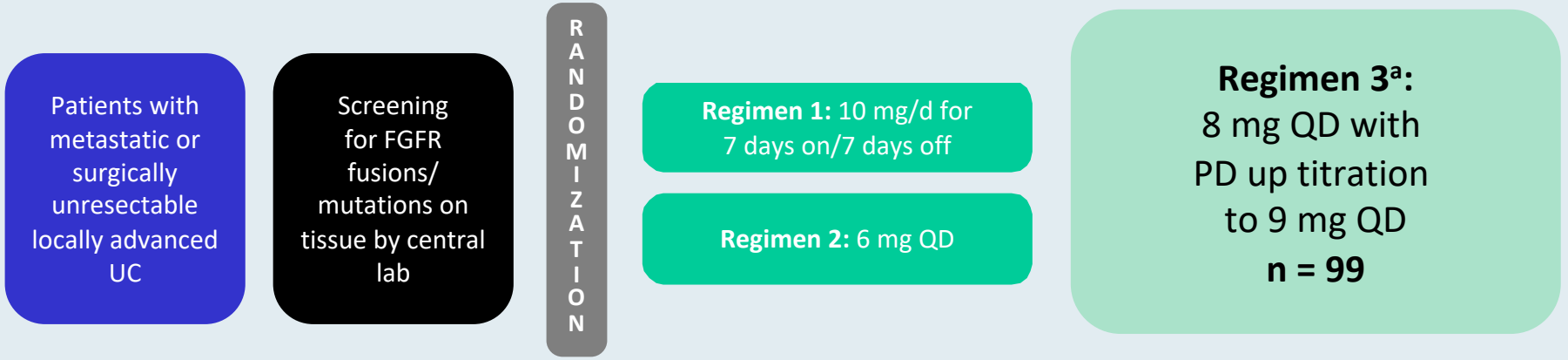
RTP
RESEARCH
TO PRACTICE

Lancet Oncol 2022 February;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: Phase II Trial of Erdafitinib



Endpoints

ORR (primary)

PFS, DoR, OS, safety, predictive biomarker evaluation, and PK (secondary)

Eligibility Criteria

- Progression on ≥1 line prior systemic chemo or within 12 months of (neo)adjuvant chemo

OR

- Chemotherapy-naïve: cisplatin-ineligible per protocol criteria[b]
- Prior immunotherapy was allowed

[a]Dose uptitration if ≥5.5 mg/dL target serum phosphate not reached by Day 14 and if no treatment-related adverse events.
[b]Ineligibility for cisplatin: impaired renal function or peripheral neuropathy.

ORR = objective response rate; PFS = progression-free survival; DoR = duration of response; OS = overall survival; PK = pharmacokinetics

Siefker-Radtke A et al. ASCO 2018;Abstract 4503.

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;23:248-58.

HER2-Targeted Therapy

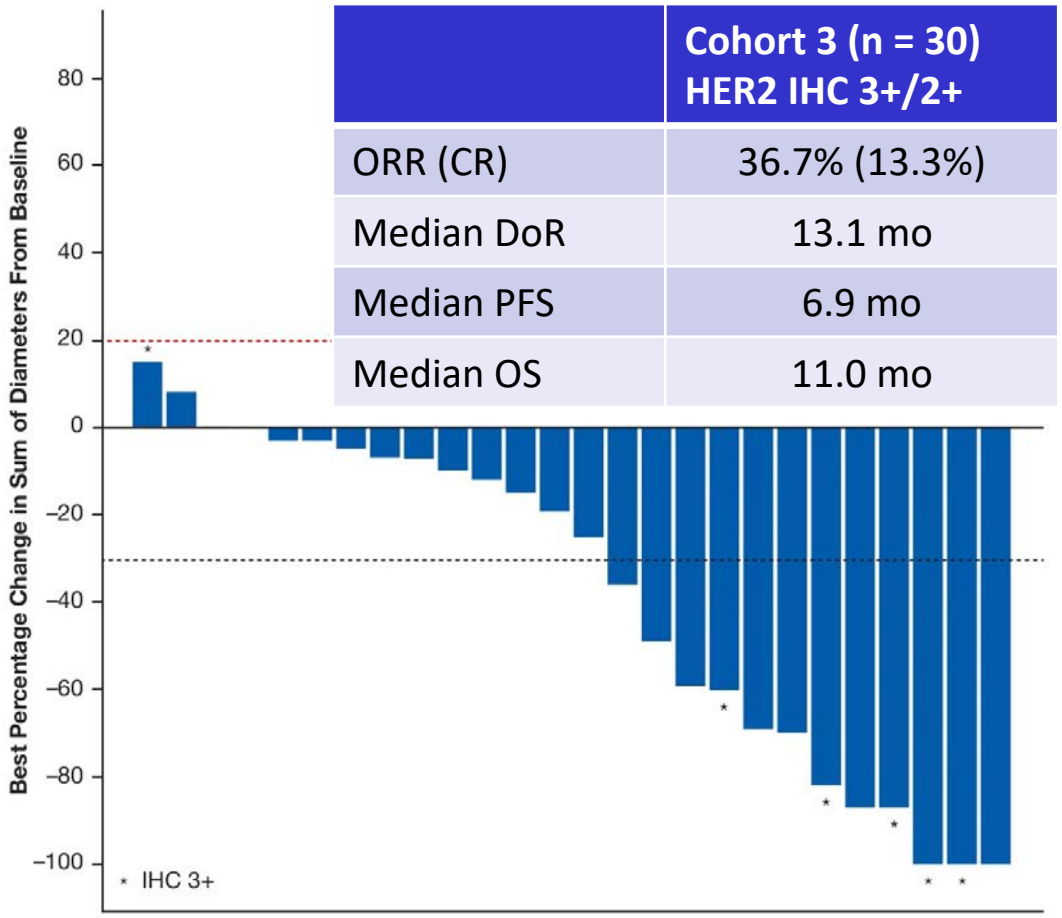
ASCO 2022 | Abstract 438

Primary Analysis From DS8201-A-U105: A Phase 1b, 2-Part, Open-Label Study of Trastuzumab Deruxtecan (T-DXd) With Nivolumab in Patients With HER2-Expressing Urothelial Carcinoma (UC)

Matthew D. Galsky,[1] Gianluca Del Conte,[2] Silvia Foti,[2] Evan Y. Yu,[3] Jean-Pascal H. Machiels,[4] Bernard Doger,[5] Andrea Necchi,[2,6] Filippo G. De Braud,[7] Erika P. Hamilton,[8] Audrey Hennequin,[9] Tom Van den Mooter,[10] Philip R. Debruyne,[11] Irene Moreno,[12] Hendrik-Tobias Arkenau,[13] Zenta Tsuchihashi,[14] Fu-Chih Cheng,[14] Bincy Augustine,[14] Ben Cheng,[14] Daniel Barrios,[14] Diana Lüftner[15]

DS8201-A-U105: Efficacy

	Cohort 3 (n = 30) HER2 IHC 3+/2+
ORR (CR)	36.7% (13.3%)
Median DoR	13.1 mo
Median PFS	6.9 mo
Median OS	11.0 mo



Cohort 3 IHC 3+/2+ (n = 30) (part 2: T-DXd 5.4 mg/kg and nivolumab 360 mg)
Best (minimum) percentage change

n	Mean	SD	Median	Min	Max
26	−37.8	38.52	−22.0	−100	15

Galsky MD et al. ASCO 2022;Abstract 438.

DS8201-A-U105: Safety Summary

n (%)	Cohort 3 HER2 IHC 3+/2+ n = 30	Cohort 4 HER2 IHC 1+ n = 4	Overall N = 34
TEAEs	**30 (100)**	**4 (100)**	**34 (100)**
Related to T-DXd	30 (100)	4 (100)	34 (100)
Related to nivolumab	26 (86.7)	4 (100)	30 (88.2)
Grade ≥3 TEAEs	**21 (70.0)**	**4 (100)**	**25 (73.5)[a]**
Related to T-DXd	12 (40.0)	3 (75.0)	15 (44.1)
Related to nivolumab	9 (30.0)	0	9 (26.5)
Serious TEAEs	**17 (56.7)**	**3 (75.0)**	**20 (58.8)**
Related to T-DXd	5 (16.7)	2 (50.0)	7 (20.6)
Related to nivolumab	5 (16.7)	0	5 (14.7)
TEAEs leading to any study drug discontinuation[b]	**9 (30.0)**	**2 (50.0)**	**11 (32.4)**
Related to T-DXd	6 (20.0)	2 (50.0)	8 (23.5)
Related to nivolumab	9 (30.0)	0	9 (26.5)
TEAEs leading to T-DXd discontinuation[b]	**5 (16.7)**	**2 (50.0)**	**7 (20.6)**
Related to and leading to T-DXd discontinuation	4 (13.3)[c]	2 (50.0)[d]	6 (17.6)
TEAEs leading to nivolumab discontinuation[b]	**8 (26.7)**	**1 (25.0)**	**9 (26.5)**
Related to and leading to nivolumab discontinuation	8 (26.7)[e]	0	8 (23.5)
TEAEs leading to T-DXd dose reduction and related to T-DXd	**4 (13.3)**	**1 (25.0)**	**5 (14.7)**
TEAEs leading to any study drug interruption	**18 (60.0)**	**2 (50.0)**	**20 (58.8)**
Related to T-DXd	10 (33.3)	2 (50.0)	12 (35.3)
Related to nivolumab	7 (23.3)	0	7 (20.6)
TEAEs associated with death	**7 (23.3)**	**0**	**7 (20.6)**
Drug-related[f]	1 (3.3)	0	1 (2.9)

Galsky MD et al. ASCO 2022;Abstract 438.

DS8201-A-U105: Adjudicated Drug-Related Interstitial Lung Disease/Pneumonitis

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/Total
Cohort 3 HER2 IHC 3+/2+ (n = 30)	0	4 (13.3)	1 (3.3)	0	1 (3.3)	6 (20.0)
Cohort 4 HER2 IHC 1+ (n = 4)	2 (50.0)	0	0	0	0	2 (50.0)
Overall (N = 34)	2 (5.9)	4 (11.8)[c]	1 (2.9)	0	1 (2.9)	8 (23.5)

Galsky MD et al. ASCO 2022;Abstract 438.

Pooled Efficacy Results of RC48-C005 and RC48-C009: Safety

Table1 AE summary

AE	RC48-ADC(N=107)
Treatment-Emergent Adverse Event (TEAE)	107(100%)
Treatment-Related Adverse Event (TRAE)	107 (100%)
Serious Adverse Event (SAE)	31(29.0%)
Treatment Related SAE	12 (11.2%)
TEAE leading to death	1（0.9%）
Grade ≥3 TEAE	72(67.3%)
Grade ≥3 TRAE	58 (54.2%)
TEAE leading to discontinuation	20 (18.7%)
TEAE leading to dose reduction	32 (29.9%)
TEAE leading to delayed infusion	62(57.9%)

Patients were enrolled between December 28, 2017 and September 4, 2020
Data cut off : 04-Sep-2021

Table2 TRAEs≥10% in all patients

TRAE	All grades(N = 107)	Grade≥3
	107 (100.0)	**58 (54.2)**
Hypoaesthesia	54 (50.5)	16 (15.0)
White blood cell count decreased	53 (49.5)	2 (1.9)
Aspartate aminotransferase increased	45 (42.1)	1 (0.9)
Neutrophil count decreased	45 (42.1)	13 (12.1)
Alopecia	43 (40.2)	1 (0.9)
Asthenia	42 (39.3)	4 (3.7)
Alanine aminotransferase increased	38 (35.5)	0
Decreased appetite	34 (31.8)	1 (0.9)
Nausea	31 (29.0)	0
Weight decreased	27 (25.2)	0
Platelet count decreased	26 (24.3)	0
Blood triglycerides increased	24 (22.4)	2 (1.9)
Constipation	24 (22.4)	0
Anaemia	23 (21.5)	3 (2.8)
Gamma-glutamyltransferase increased	22 (20.6)	6 (5.6)
Peripheral sensory neuropathy	22 (20.6)	5 (4.7)
Pruritus	21 (19.6)	1 (0.9)
Vomiting	19 (17.8)	1 (0.9)
Blood creatine phosphokinase increased	16 (15.0)	3 (2.8)
Blood glucose increased	16 (15.0)	2 (1.9)
Haemoglobin decreased	13 (12.1)	1 (0.9)
Protein urine present	12 (11.2)	1 (0.9)
Rash	12 (11.2)	0
Pyrexia	11 (10.3)	0
Pain in extremity	11 (10.3)	0

Sheng X et al. ASCO 2022;Abstract 4520.

Pooled Efficacy Results of RC48-C005 and RC48-C009: Conclusions

- RC48-ADC(DV) can substantially improve the response rate and show long-term survival benefit in patients with locally advanced or metastatic UC who have received prior systemic chemotherapy/immunotherapy with HER2 expression of mUC.
- Similar responses were observed in prespecified subgroups, including those with visceral metastasis, previously treated with I-O agents.
- RC48-ADC(DV) also showed continuously a manageable safety profile in HER2-postive mUC patients who had failed at least one line systemic chemotherapy.

Sheng X et al. ASCO 2022;Abstract 4520.

2022 ASCO ANNUAL MEETING

Abstract 4518

Preliminary results of a phase Ib/II combination study of RC48-ADC, a novel humanized anti-HER2 antibody-drug conjugate (ADC) with toripalimab, a humanized IgG4 mAb against programmed death-1 (PD-1) in patients with locally advanced or metastatic urothelial carcinoma(La/mUC)

Xinan Sheng*[1], Li Zhou[1], Zhisong He[3], Hongqian Guo[2], Xieqiao Yan[1], Siming Li[1], Huayan Xu[1], Juan Li[1],Zhihong Chi[1], Lili Mao[1], Bin Lian[1], Bixia Tang[1], Xuan Wang[1],Xue Bai[1], Jun Guo**[1];

1. Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Genitourinary Oncology, Peking University Cancer Hospital & Institute

2. Nanjing Drum Tower Hospital ,The Affiliated Hospital of Nanjing University Medical school.

3.Peking University First Hospital, Institute of Urology ,Peking University

*Presenting author * * Corresponding author

2022 ASCO ANNUAL MEETING **Abstract 4519**

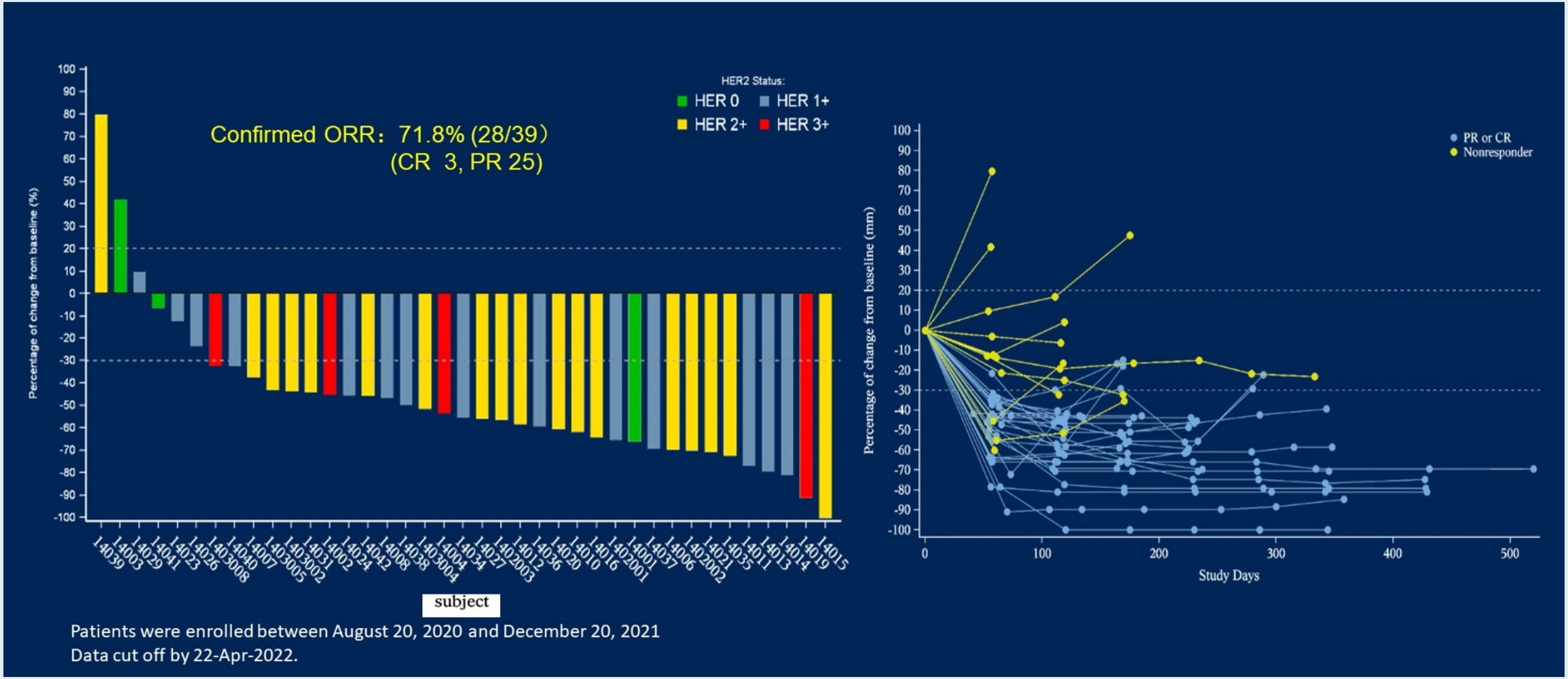
A phase II study of RC48-ADC in HER2-negative patients with locally advanced or metastatic urothelial carcinoma.

Huayan Xu*, Xinan Sheng, Li Zhou, Xieqiao Yan, Siming Li, Zhihong Chi, Chuanliang Cui, Lu Si, Bixia Tang, Lili Mao, Bin Lian, Xuan Wang, Xue Bai, Juan Li, Jun Guo**

Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Genitourinary Oncology, Peking University Cancer Hospital & Institute

*Presenting author * * Corresponding author

RC48-C014: ORR and Percent Change from Baseline by ORR



Sheng X et al. ASCO 2022;Abstract 4518.

RC48-C014: Adverse Events

	RC48-ADC + JS001 (N=41)	
Adverse Events	All grades n (%)	Grade ≥ 3 n (%)
Overall	41 (100)	15 (36.59)
Aspartate aminotransferase increase	27 (65.85)	2 (4.88)
Alanine aminotransferase increase	26 (63.41)	3 (7.32)
Peripheral sensory neuropathy	26(63.41)	0
Asthenia	24(58.54)	3(7.32)
Appetite decrease	23(56.1)	0
Hypertriglyceridaemia	23(56.1)	3(7.32)
γ -glutamyltransferase increase	21(51.22)	5(12.2)
Alopecia	17(41.46)	0
Nausea	16(39.02)	0
Hypercholesterolaemia	15(36.59)	0
White blood cell count decrease	14(34.15)	1(2.44)
Blood creatine phosphokinase increase	14(34.15)	1(2.44)
Anaemia	14(34.15)	0

Patients were enrolled between August 20, 2020 and December 20, 2021
Data cut off by 22-Apr-2022.

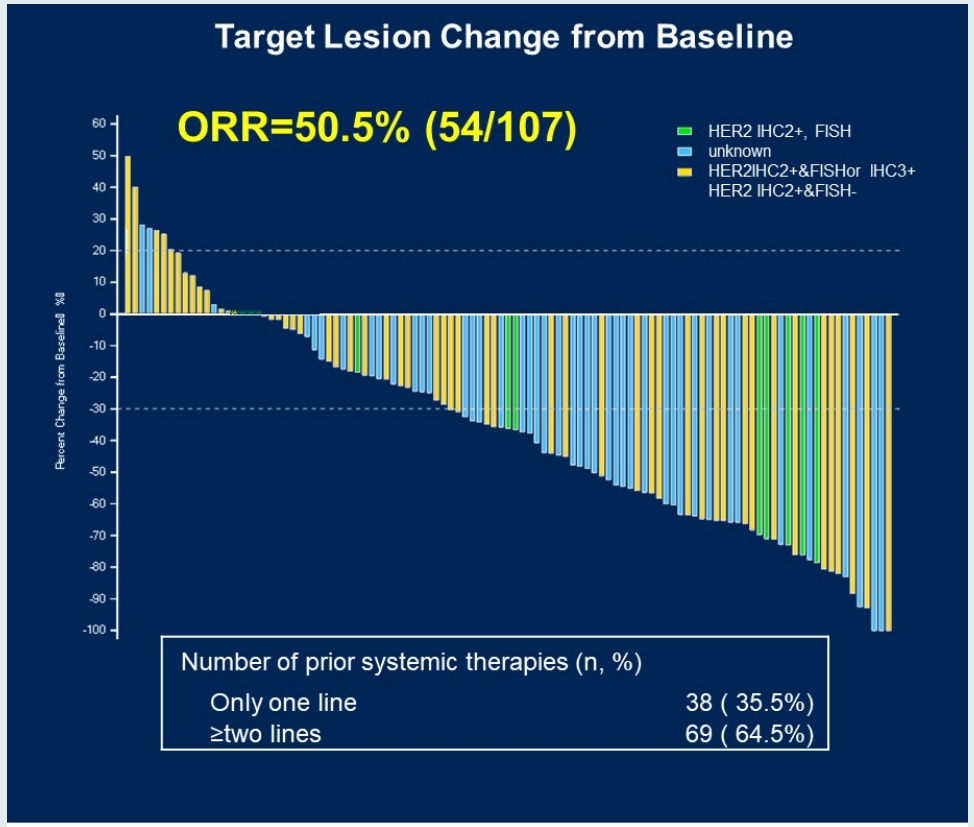
	RC48-ADC + JS001 (N=41)	
TRAE	All grades n (%)	Grade ≥ 3 n (%)
Overall	41 (100)	15 (36.59)
Blood glucose increase	12(29.27)	2(4.88)
Neutrophil count decrease	10(24.39)	2(4.88)
Pruritus	10(24.39)	0
Bilirubin conjugated increase	9(21.95)	2(4.88)
Blood thyroid stimulating hormone increase	9(21.95)	0
Vomitting	9(21.95)	0

	RC48-ADC + JS001 (N=41)
irAE	All grades n (%)
Overall	16(39.02)
Interstitial lung disease	3(7.32)
Immune-related pneumonitis	5(12.2)
Rash	8(19.51)
Hyperglycaemia	1(2.44)
Immune-related hepatic	1(2.44)
Immune-related myositis	1(2.44)

Sheng X et al. ASCO 2022;Abstract 4518.

Disitamab Vedotin (RC48) at ASCO 2022

Activity in HER2 2-3+



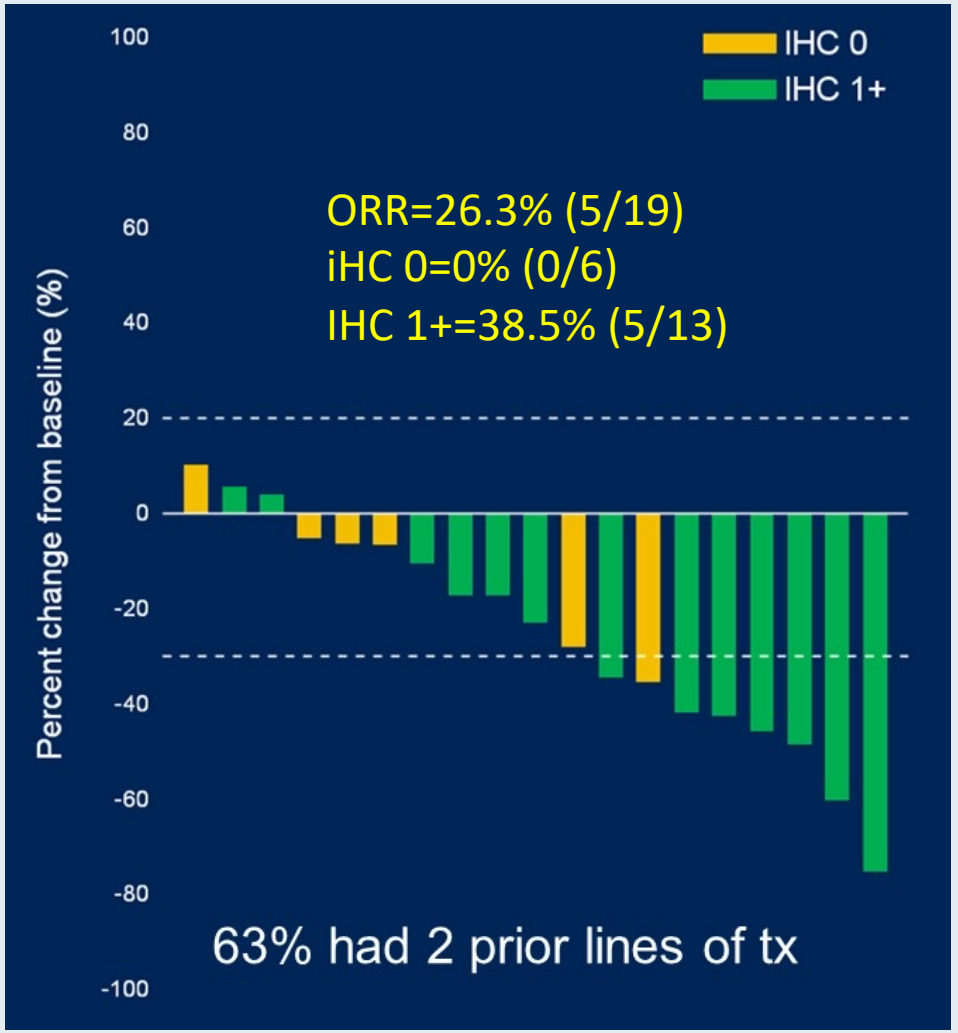
ORR

IHC2+FISH+ or IHC3+ (n=45) = 62.2%

IHC2+FISH- (n=53) = 39.6%

Sheng X et al. ASCO 2022;Abstract 4518.

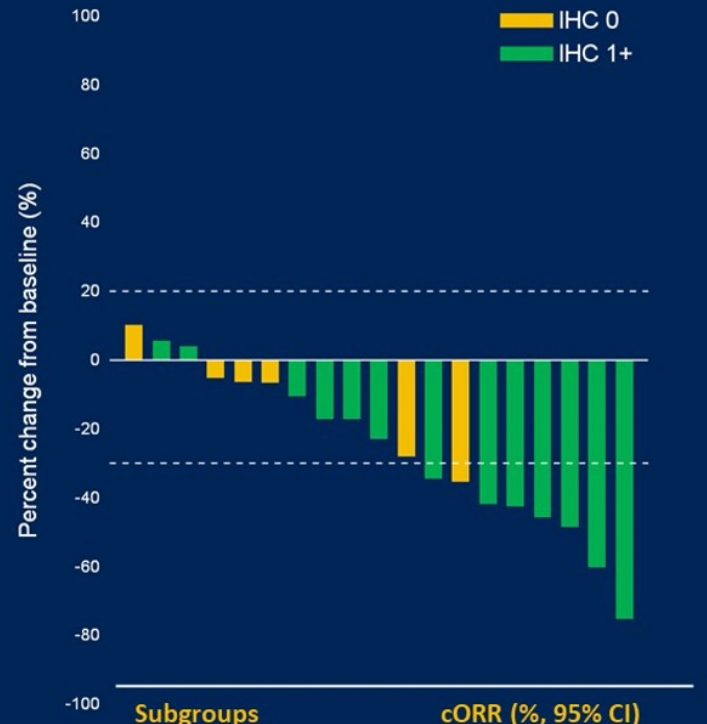
Activity in HER2 1+



Xu H et al. ASCO 2022;Abstract 4519.

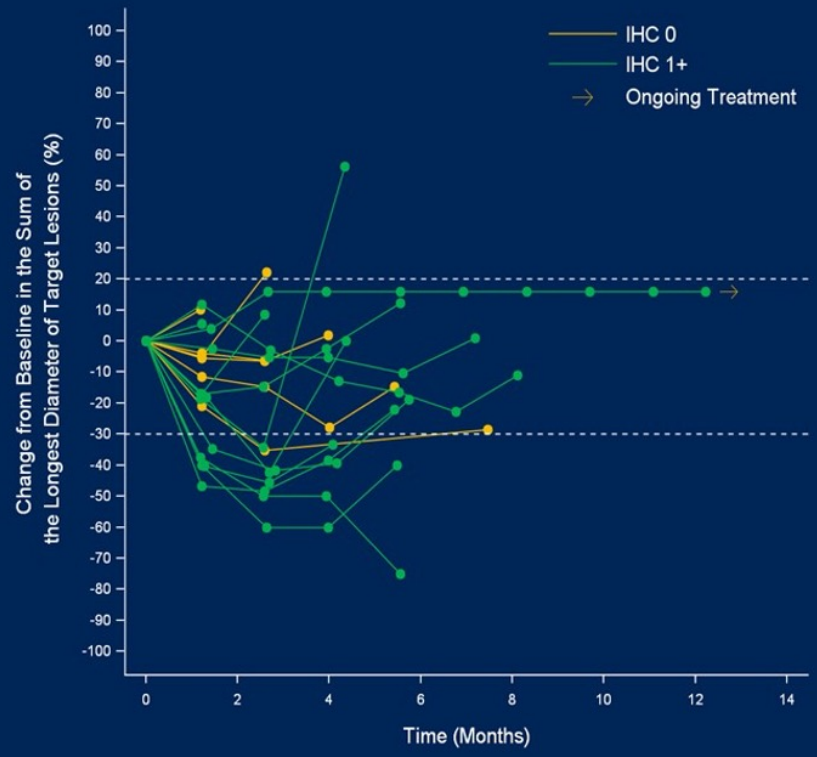
RTP RESEARCH TO PRACTICE

RC48-C011: Change from Baseline by HER2 Status and ORR Results



Subgroups	cORR (%, 95% CI)
IHC 0 (n=6)	0
IHC 1+ (n=13)	38.5 (13.9, 68.4)

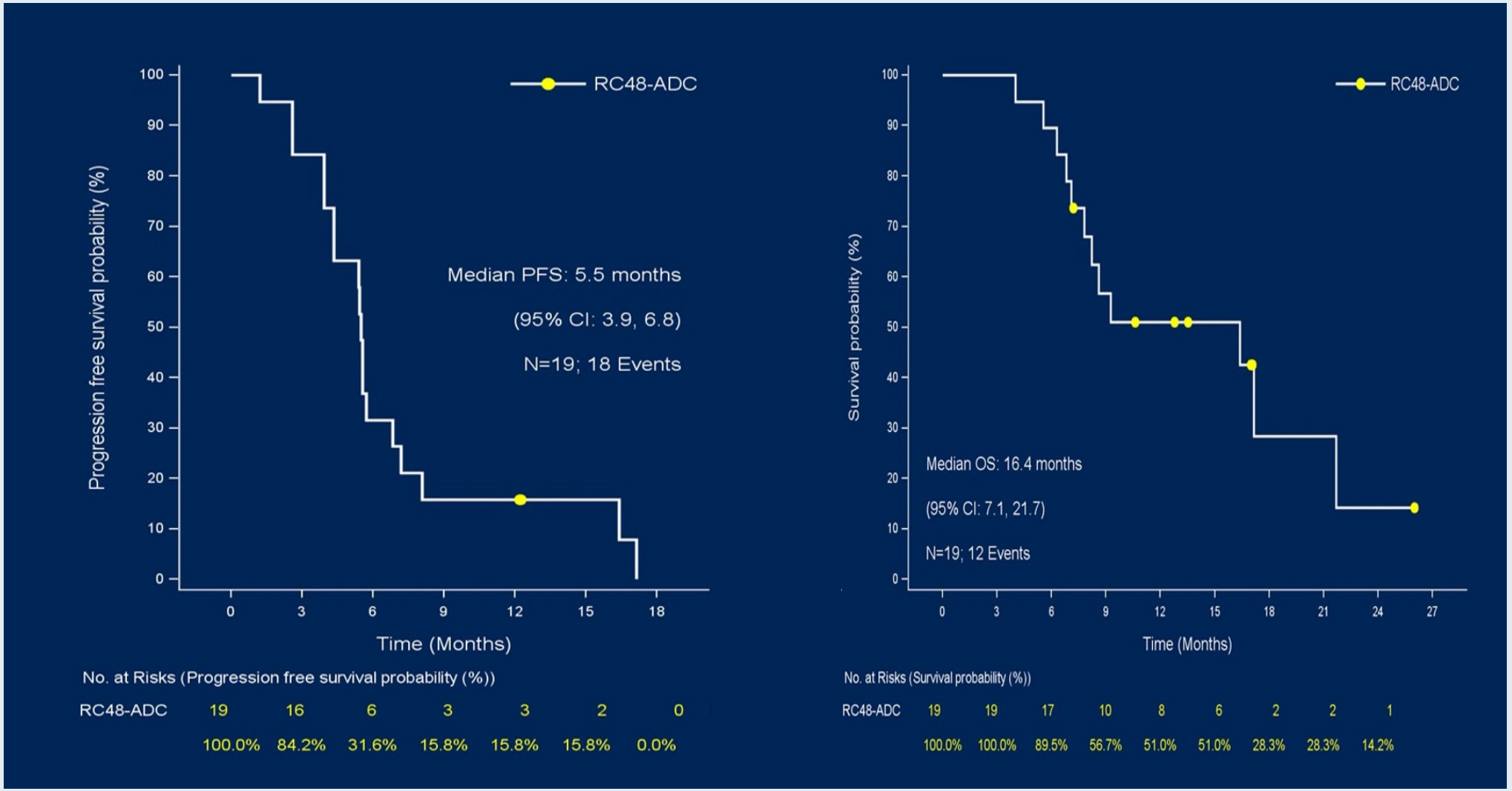
Confirmed ORR	
n (%)	5 (26.3%)
95%CI	9.1%, 51.2%
Best overall response, n (%)	
CR	0
PR	5 (26.3%)
SD	13 (68.4%)
PD	1 (5.3%)
DCR	
n (%)	18 (94.7%)
95%CI	74.0%, 99.9%



Patients were enrolled between August 19, 2019 and June 28, 2021
Data cut off by May-2022.

Xu H et al. ASCO 2022;Abstract 4519.

RC48-C011: PFS and OS



Xu H et al. ASCO 2022;Abstract 4519.

RC48-C011: Adverse Events

Adverse Events	RC48-ADC (N=19)
Treatment-Emergent Adverse Event (TEAE)	19 (100%)
Treatment-Related Adverse Event (TRAE)	19 (100%)
Serious Adverse Event (SAE)	1(5.3%)
Treatment Related SAE	1 (5.3%)
TEAE leading to death	0
Grade ≥3 TEAE	7 (36.8%)
Grade ≥3 TRAE	3 (15.8%)
TEAE leading to discontinuation	2 (10.5%)
TEAE leading to dose reduction	5 (26.3%)
TEAE leading to delayed infusion	8 (42.1%)

TRAEs	RC48 -ADC (N=19)	
	All grades n (%)	Grade ≥ 3 n (%)
Overall	19 (100.0)	3 (15.8)
White blood cell count decreased	10 (52.6)	1 (5.3)
Hypoesthesia	9 (47.4)	0
Alopecia	9 (47.4)	0
Neutropenia	8 (42.1)	2 (10.5)
Alanine aminotransferase increase	8 (42.1)	0
Aspartate aminotransferase increase	8 (42.1)	0
Fatigue	8 (42.1)	0
Weight loss	5 (26.3)	0
Nausea	5 (26.3)	0
Decreased appetite	5 (26.3)	0
Platelet count decreased	5 (26.3)	0
Abdominal disccomfort	4 (21.1)	0
Hypertriglyceridemia	4 (21.1)	0

Xu H et al. ASCO 2022;Abstract 4519.

Breakfast with the Investigators: Urothelial Bladder Cancer

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Monday, June 5, 2023

6:45 AM – 7:45 AM CT

Faculty

Matthew D Galsky, MD

Andrea Necchi, MD

Scott T Tagawa, MD, MS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Video Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Management of Breast Cancer

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Monday, June 5, 2023

7:00 PM – 9:30 PM CT

Faculty

Komal Jhaveri, MD
Kevin Kalinsky, MD, MS
Ian E Krop, MD, PhD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Prof Peter Schmid, FRCP, MD, PhD

Moderator

Neil Love, MD

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