Thank you for joining us.
The program will commence momentarily.

Recent Advances in Medical Oncology: Urothelial Bladder Carcinoma

Monday, August 3, 2020

5:00 PM – 6:00 PM ET

Faculty

Arjun Balar, MD

Thomas Powles, MBBS, MRCP, MD

Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

Co-provided by USF Health
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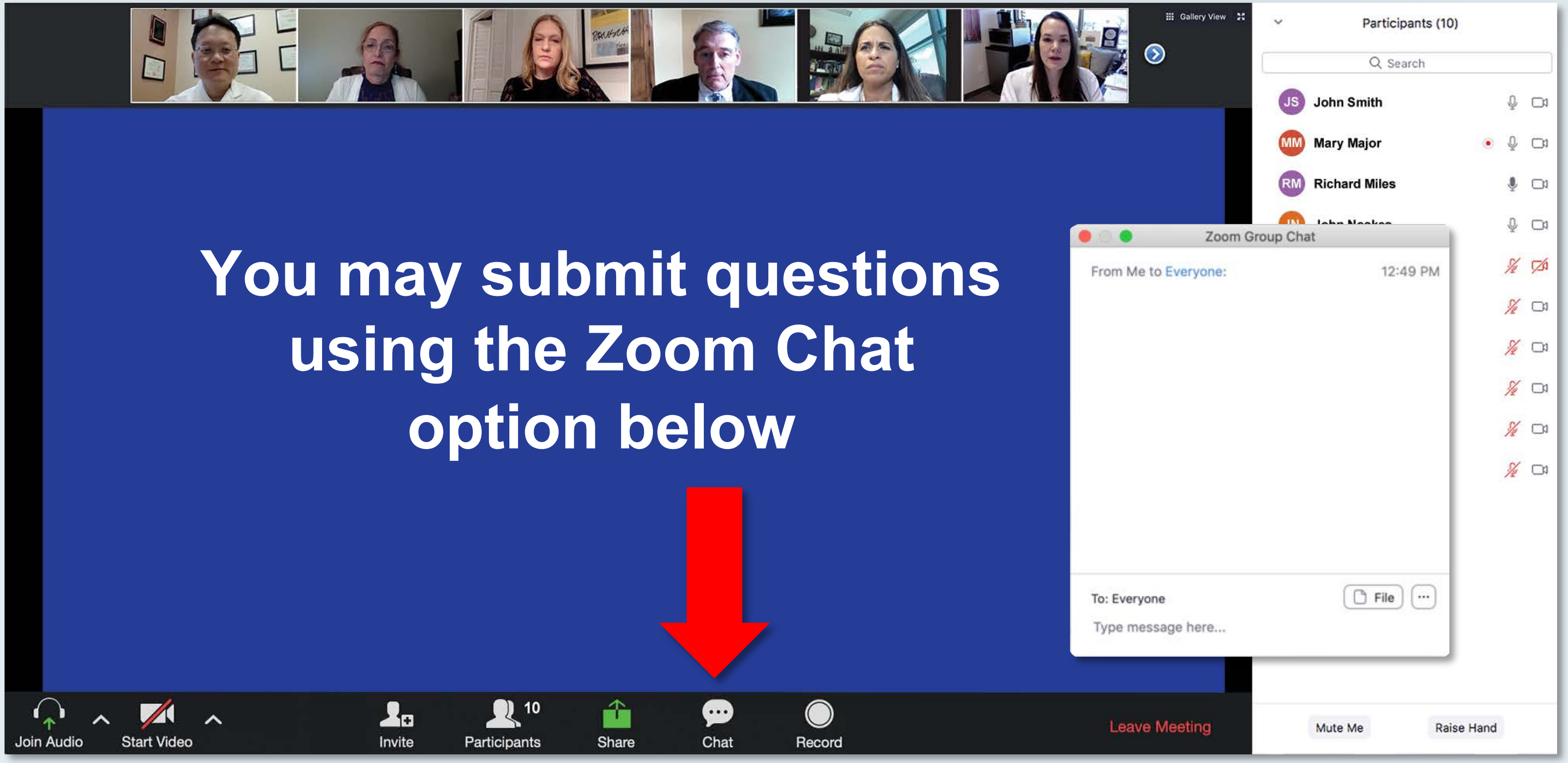
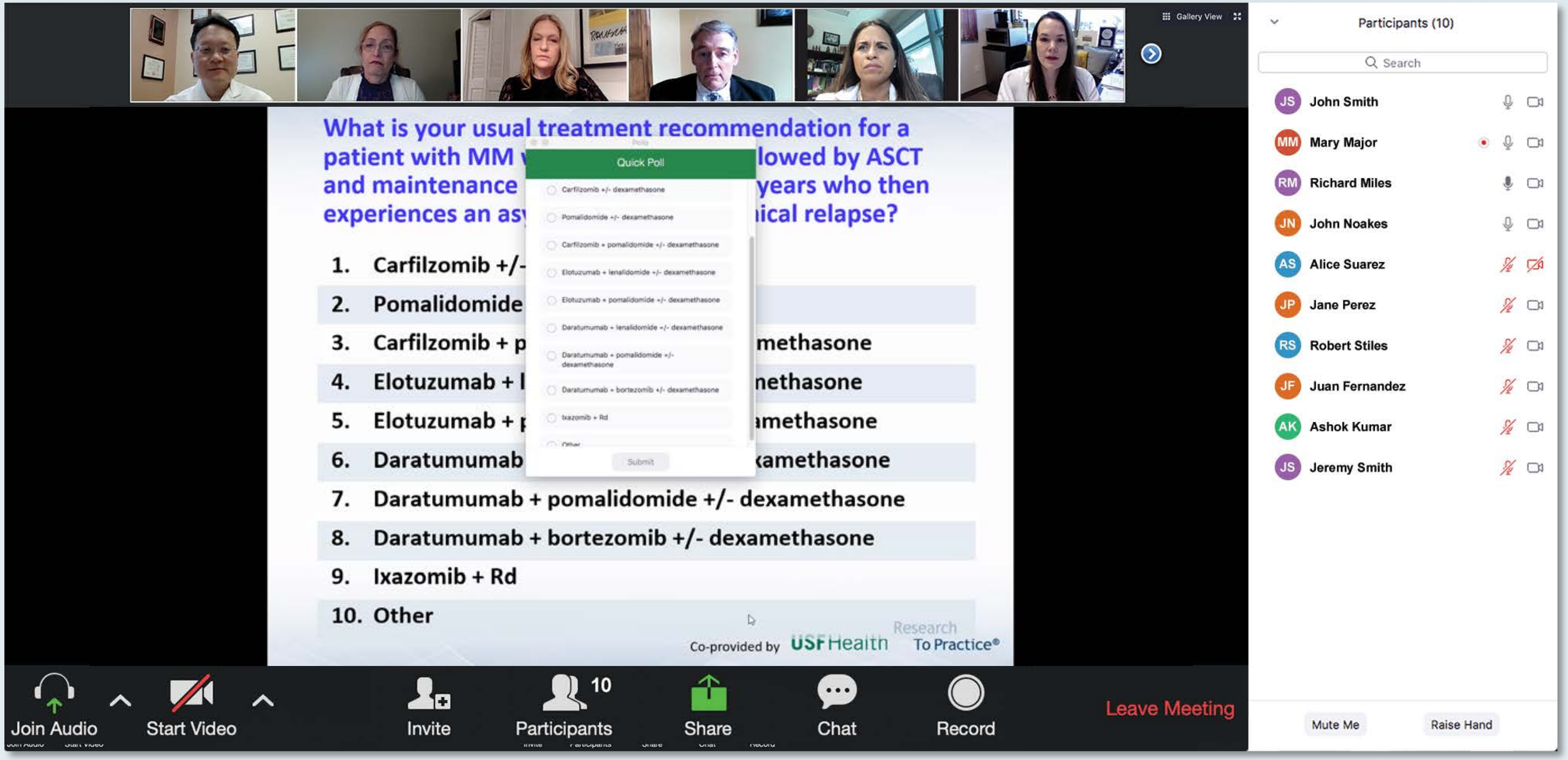
Dr Love and Faculty Encourage You to Ask Questions



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

Familiarizing yourself with the Zoom interface
How to answer poll questions



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

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Please note, this program has been specifically designed for the following ABIM specialty: medical oncology.

ABIM CME MOC ACCREDITED

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc, Tolero Pharmaceuticals and Verastem Inc.

Dr Balar — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, Janssen Biotech Inc, Merck, Nektar, Pfizer Inc, Seattle Genetics
Contracted Research	AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, Immunomedics Inc, Janssen Biotech Inc, Merck, Nektar, Pfizer Inc, Seattle Genetics

Prof Powles — Disclosures

Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Eisai Inc, Exelixis Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Johnson & Johnson Pharmaceuticals, Merck Serono, Merck Sharp & Dohme Corp, Novartis, Pfizer Inc, Roche Laboratories Inc, Seattle Genetics
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Dr Siefker-Radtke — Disclosures

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Contracted Research	Janssen Biotech Inc
Speakers Bureau	Janssen Biotech Inc

Upcoming Live Webinars

Tuesday, August 4, 2020
1:00 PM – 2:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
Shaji K Kumar, MD

Moderator
Neil Love, MD

Wednesday, August 5, 2020
5:00 PM – 6:30 PM ET

Recent Advances in Medical Oncology: Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Faculty
Edward B Garon, MD, MS
Stephen V Liu, MD, PhD
David R Spigel, MD

Moderator
Neil Love, MD

Upcoming Live Webinars

Thursday, August 6, 2020
12:00 PM – 1:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
John V Heymach, MD, PhD

Moderator
Neil Love, MD

Virtual Molecular Tumor Board: Optimizing Biomarker-Based Decision-Making for Patients with Solid Tumors

Identification of New and Emerging Genomic Alterations in Metastatic Non-Small Cell Lung Cancer

Friday, August 7, 2020
9:00 AM – 10:00 AM ET

Alexander E Drilon, MD

Recognition and Management of Targetable Tumor Mutations in Less Common Cancer Types

Friday, August 14, 2020
9:00 AM – 10:00 AM ET

Marcia S Brose, MD, PhD

All sessions moderated by Neil Love, MD and featuring Bryan Schneider, MD and Milan Radovich, PhD of the Indiana University Health Precision Genomics Program

Upcoming Live Webinars

Monday, August 10, 2020
5:00 PM – 6:00 PM ET

Recent Advances in Medical Oncology: Hodgkin and Non-Hodgkin Lymphomas

Faculty
Jeremy Abramson, MD
Christopher R Flowers, MD, MS

Moderator
Neil Love, MD

Wednesday, August 12, 2020
1:00 PM – 2:00 PM ET

Meet The Professors
Clinical Investigators Discuss Existing and Emerging Treatment Strategies for Patients with Ovarian, Cervical and Endometrial Cancer

Faculty
Stephanie Lheureux, MD, PhD
Professor Ignace Vergote

Moderator
Neil Love, MD

Upcoming Live Webinars

Wednesday, August 12, 2020
5:00 PM – 6:30 PM ET

Recent Advances in Medical Oncology: Hepatocellular Carcinoma and Pancreatic Cancer

Faculty
Tanios Bekaii-Saab, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP
Alan P Venook, MD

Moderator
Neil Love, MD

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Moderator

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Co-provided by USF Health RTP RESEARCH TO PRACTICE

Faculty

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

Arlene Siefker-Radtke, MD
Professor
Department of Genitourinary Medical Oncology
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Thomas Powles, MBBS, MRCP, MD
Professor of Genitourinary Oncology
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Director of Barts Cancer Centre
Queen Mary University of London
London, United Kingdom

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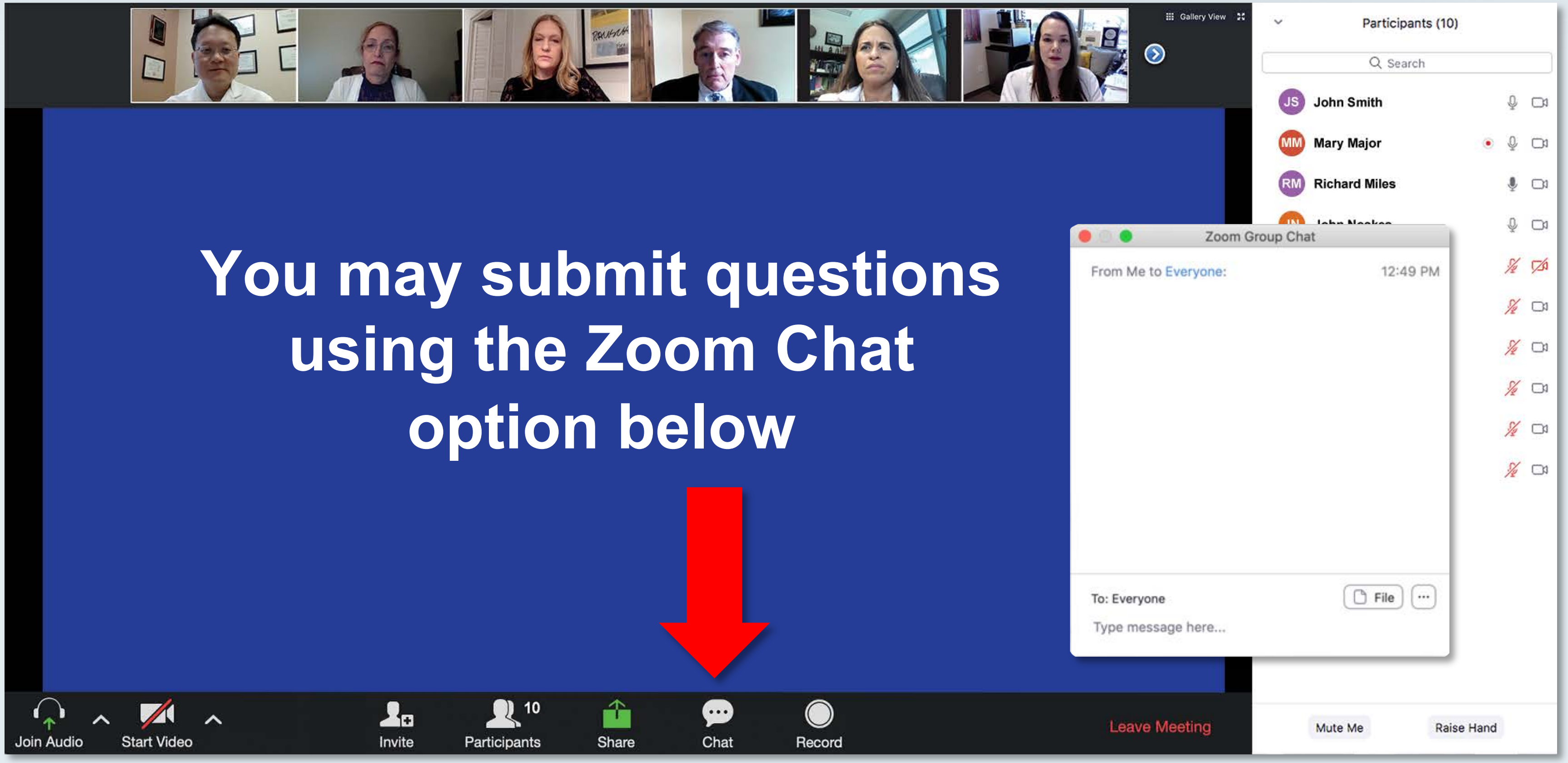

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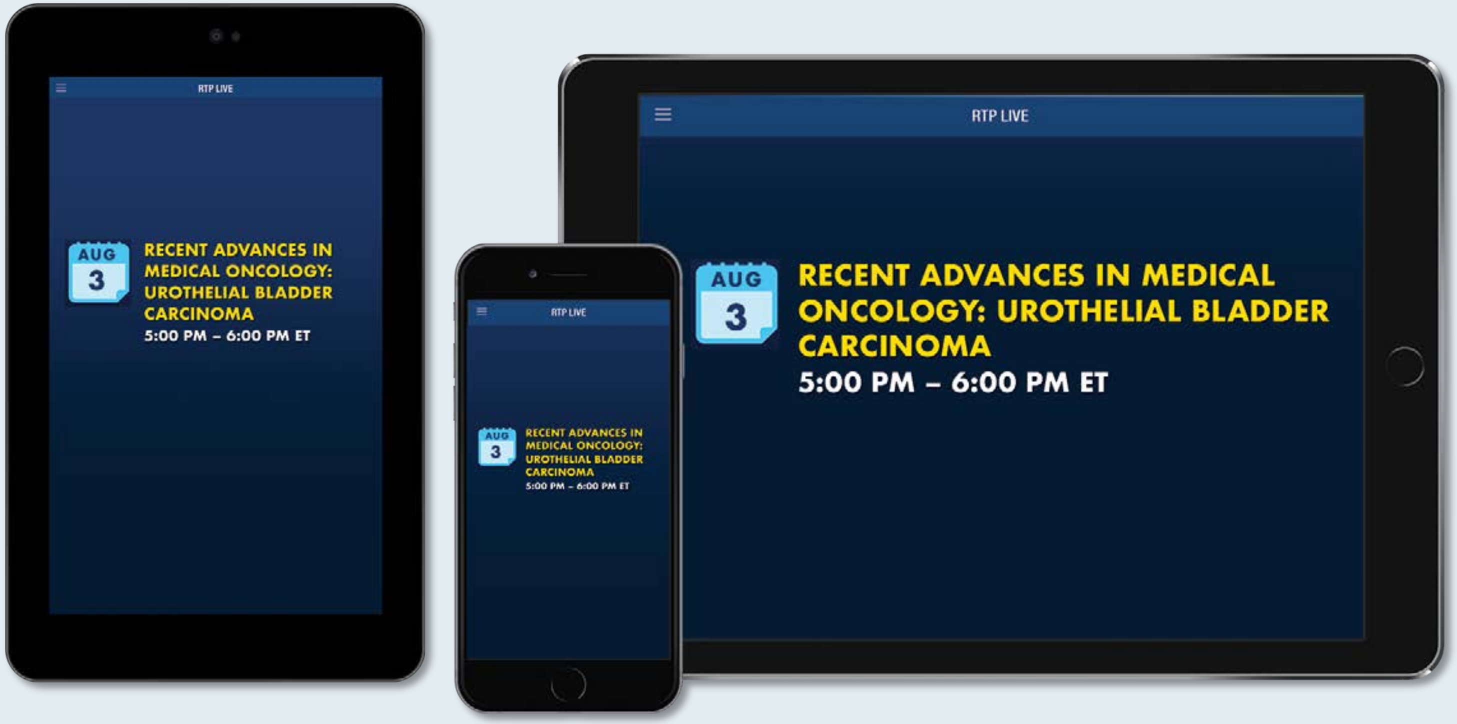

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Recent Developments in the Management of Urothelial Bladder Cancer (UBC)

Module 1: Immune Checkpoint Inhibitors — Dr Balar

- Key Recent Data Sets
  - Avelumab as maintenance therapy after induction chemotherapy for metastatic disease
  - Pembrolizumab for high-risk non-muscle-invasive bladder cancer (NMIBC)
- Faculty Case Discussion: 73-year-old woman with NMIBC

Module 2: Antibody-Drug Conjugates — Prof Powles

- Key Recent Data Sets
  - Enfortumab vedotin (EV) after platinum-based chemotherapy and immunotherapy (IO)
  - First-line EV in combination with pembrolizumab (chemotherapy)
  - Sacituzumab govitecan-hziy
- Faculty Case Discussion: 74-year-old man with metastatic UBC — Progression on chemotherapy, IO

Module 3: Erdafitinib — Dr Siefker-Radtke

- Key Recent Data Sets
  - Erdafitinib for metastatic FGFR-positive tumors after chemotherapies
- Faculty Case Discussion: 65-year-old man with metastatic UBC with FGFR3 S249C mutation and disease progression on chemotherapy

Module 1: Immune Checkpoint Inhibitors — Dr Balar

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  - Avelumab as maintenance therapy after induction chemotherapy for metastatic disease
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Regulatory Updates for Anti-PD-1/PD-L1 Therapy in Advanced Cis-Ineligible UC

Requires the use of an FDA-approved companion diagnostic test to determine PD-L1 levels in tumor tissue

- **Pembrolizumab is indicated for the treatment of patients with locally advanced or metastatic UC who are not eligible for cisplatin-containing chemotherapy and *<u>whose tumors express PD-L1 (CPS ≥10)</u>* as determined by an FDA-approved test, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status**

- **Atezolizumab is indicated for the treatment of patients with locally advanced or metastatic UC who are not eligible for cisplatin-containing chemotherapy and *<u>whose tumors express PD-L1 (PD-L1–stained tumor-infiltrating immune cells covering ≥5% of the tumor area),</u>* as determined by an FDA-approved test, or are not eligible for any platinum-containing therapy regardless of PD-L1 status**

Courtesy of Arjun V. Balar, MD

IMvigor130: a phase III study of atezolizumab with or without platinum-based chemotherapy in previously untreated metastatic urothelial carcinoma

Enrique Grande,[1] Matthew D Galsky,[2] José Ángel Arranz Arija,[3] Maria De Santis,[4] Ian D Davis,[5] Ugo De Giorgi,[6] Marina Mencinger,[7] Eiji Kikuchi,[8] Xavier García-del-Muro,[9] Mahmut Gumus,[10] Mustafa Özgüroğlu,[11] Arash Rezazadeh Kalebasty,[12] Se Hoon Park,[13] Boris Alekseev,[14] Fabio Augusto Schutz,[15] Jian-Ri Li,[16] Almut Mecke,[17] Sanjeev Mariathasan,[18] AnnChristine Thåström,[18] Aristotelis Bamias[19]

[1]MD Anderson Cancer Center Madrid, Madrid, Spain; [2]Icahn School of Medicine at Mount Sinai/Tisch Cancer Institute, New York, NY, USA; [3]Hospital General Universitario Gregorio Marañón, Madrid, Spain; [4]Charité University Hospital, Berlin, Germany, and Department of Urology, Medical University, Vienna, Austria; [5]Eastern Health/Monash University, Melbourne, Australia; [6]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), IRCCS, Meldola, Italy; [7]Institute of Oncology Ljubljana, Ljubljana, Slovenia; [8]Keio University, Tokyo, Japan; [9]Catalan Institute of Oncology, IDIBELL, University of Barcelona, Barcelona, Spain; [10]Istanbul Medeniyet University, Goztepe Research Hospital, Istanbul, Turkey; [11]Istanbul University-Cerrahpaşa, Cerrahpasa School of Medicine, Istanbul, Turkey; [12]Norton Cancer Institute, Louisville, KY, USA; [13]Sungkyunkwan University Samsung Medical Center, Seoul, Korea; [14]P. Herzen Oncology Research Institute, Moscow, Russia; [15] Beneficência Portuguesa de São Paulo, São Paulo, Brazil; [16]Taichung Veterans General Hospital/Hungkuang University, Taichung, Taiwan; [17]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [18]Genentech, Inc., South San Francisco, CA, USA; [19]National and Kapodistrian University of Athens, Athens, Greece

Courtesy of Arjun V. Balar, MD

IMvigor130 baseline characteristics

Characteristic	Atezo + plt/gem (n = 451)	Placebo + plt/gem (n = 400)[a]	Atezo (n = 362)
Median age (range), y	69 (31-87)	67 (33-89)	67 (36-87)
ECOG PS, n (%)			
0	182 (40)	173 (43)	157 (43)
1	209 (46)	187 (47)	174 (48)
2	60 (13)	40 (10)	31 (9)
Bajorin risk factor score, n (%)			
0	176 (39)	162 (41)	151 (42)
1	169 (37)	149 (37)	134 (37)
2 and/or liver mets	106 (24)	89 (22)	77 (21)
PD-L1 status on IC, n (%)			
IC2/3	108 (24)	91 (23)	88 (24)
IC1	195 (43)	179 (45)	160 (44)
IC0	148 (33)	130 (33)	114 (31)
Cisplatin ineligibility[b]	204 (45)	140 (35)	107 (30)
Renal impairment	113 (25)	94 (24)	65 (18)
Investigator choice of chemotherapy[c]			
Carboplatin	314 (70)	264 (66)	227 (63)
Cisplatin	137 (30)	136 (34)	135 (37)

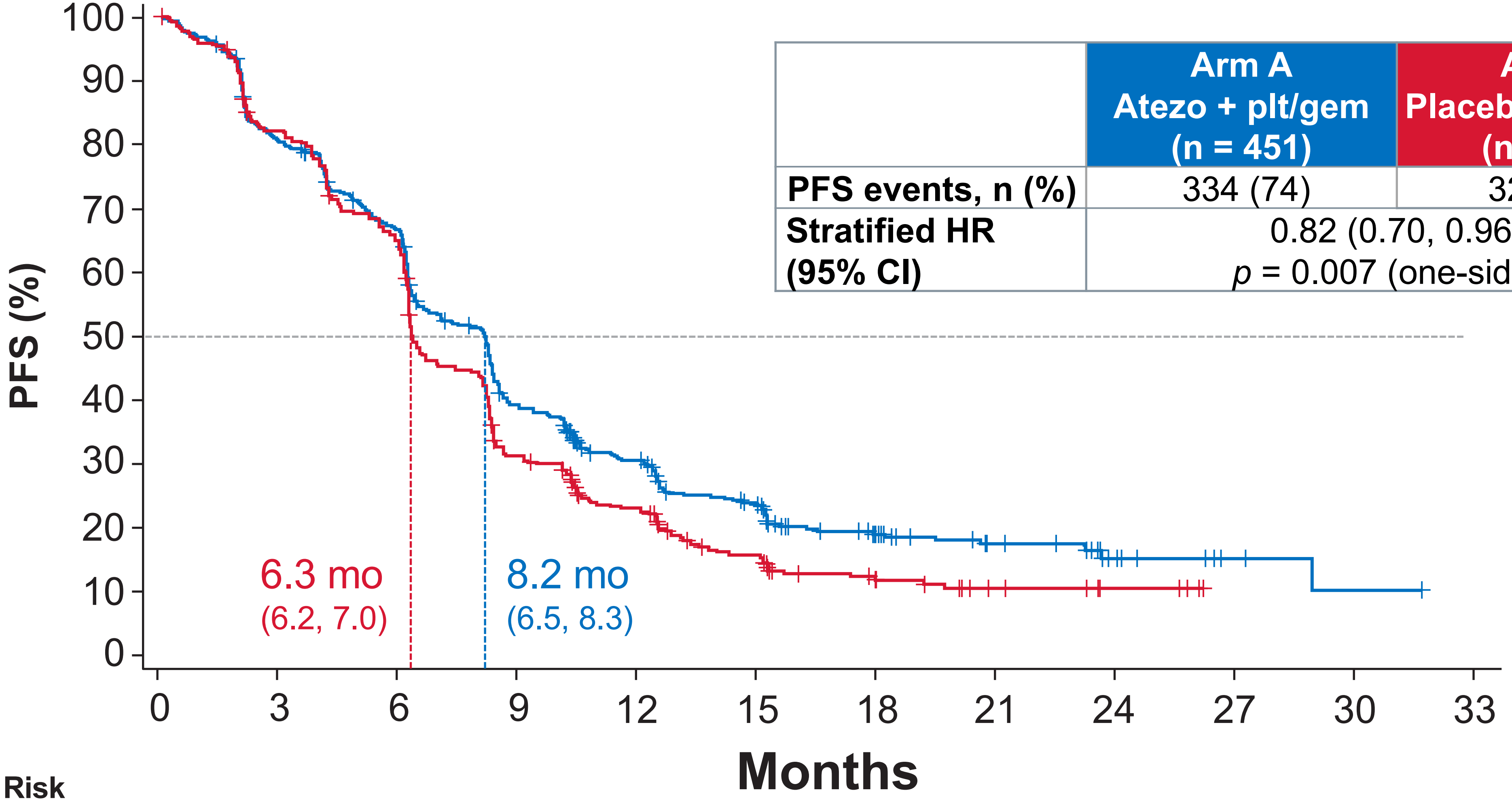
[a] n = 359 for comparisons to atezo monotherapy arm. [b] Per Galsky criteria per protocol, excluding New York Heart Association functional classification.
[c] Of the patients considered cisplatin eligible at study entry, 52% received carboplatin, while 10% of patients who were cisplatin ineligible received cisplatin.

Courtesy of Arjun V. Balar, MD

Grande E et al. ESMO 2019;Abstract LBA14_PR.

http://bit.ly/2Z1bPbD

IMvigor130 Final PFS: ITT (Arm A vs Arm C)



	Arm A Atezo + plt/gem (n = 451)	Arm C Placebo + plt/gem (n = 400)
PFS events, n (%)	334 (74)	326 (82)
Stratified HR (95% CI)	0.82 (0.70, 0.96) *p* = 0.007 (one-sided)	

No. at Risk												
Atezo + plt/gem	451	345	282	160	111	74	42	22	10	4	2	NE
Placebo + plt/gem	400	317	246	116	73	40	18	11	4	NE	NE	NE

NE, not estimable. Data cutoff 31 May 2019; median survival follow-up 11.8 months (all patients).

Grande E et al. ESMO 2019;Abstract LBA14_PR.

IMvigor130—ESMO 2019 (LBA14): presented by Dr Enrique Grande

Courtesy of Arjun V. Balar, MD

http://bit.ly/2Z1bPbD

KEYNOTE-361: BREAKING NEWS!

Update on Phase 3 KEYNOTE-361 Trial Evaluating Pembrolizumab as Monotherapy and in Combination with Chemotherapy in Patients with Advanced or Metastatic Urothelial Carcinoma

June 09, 2020

KENILWORTH, N.J. --(BUSINESS WIRE)-- The Phase 3 KEYNOTE-361 trial evaluating pembrolizumab, an anti-PD-1 therapy, in combination with chemotherapy for the first-line treatment of patients with advanced or metastatic urothelial carcinoma (bladder cancer) did not meet its pre-specified dual primary endpoints of overall survival (OS) or progression-free survival (PFS), compared with standard of care chemotherapy. In the final analysis of the study, there was an improvement in OS and PFS for patients treated with pembrolizumab in combination with chemotherapy (cisplatin or carboplatin plus gemcitabine) compared to chemotherapy alone; however, these results did not meet statistical significance per the pre-specified statistical plan. The monotherapy arm of the study was not formally tested, since superiority was not reached for OS or PFS in the pembrolizumab combination arm. The safety profile of pembrolizumab in this trial was consistent with previously reported studies, and no new safety were identified. Results will be presented at an upcoming medical meeting and will be discussed with regulatory authorities.

Courtesy of Arjun V. Balar, MD

JAVELIN Bladder 100 study design (NCT02603432)

All endpoints measured post randomization (after chemotherapy)

- **CR, PR, or SD with standard 1st-line chemotherapy (4-6 cycles)**
  - **– Cisplatin + gemcitabine or**
  - **– Carboplatin + gemcitabine**
- **Unresectable locally advanced or metastatic UC**

Treatment-free interval 4-10 weeks

N=700

R 1:1

Avelumab
10 mg/kg IV Q2W
+ BSC*
n=350

Until PD, unacceptable toxicity, or withdrawal

BSC alone*
n=350

Stratification

- Best response to 1st-line chemo (CR or PR vs SD)
- Metastatic site (visceral vs non-visceral)

Primary endpoint

- OS

Primary analysis populations

- All randomized patients
- PD-L1+ population

Secondary endpoints

- PFS and objective response per RECIST 1.1
- Safety and tolerability
- PROs

PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively, using the SP263 assay; 358 patients (51%) had a PD-L1–positive tumor

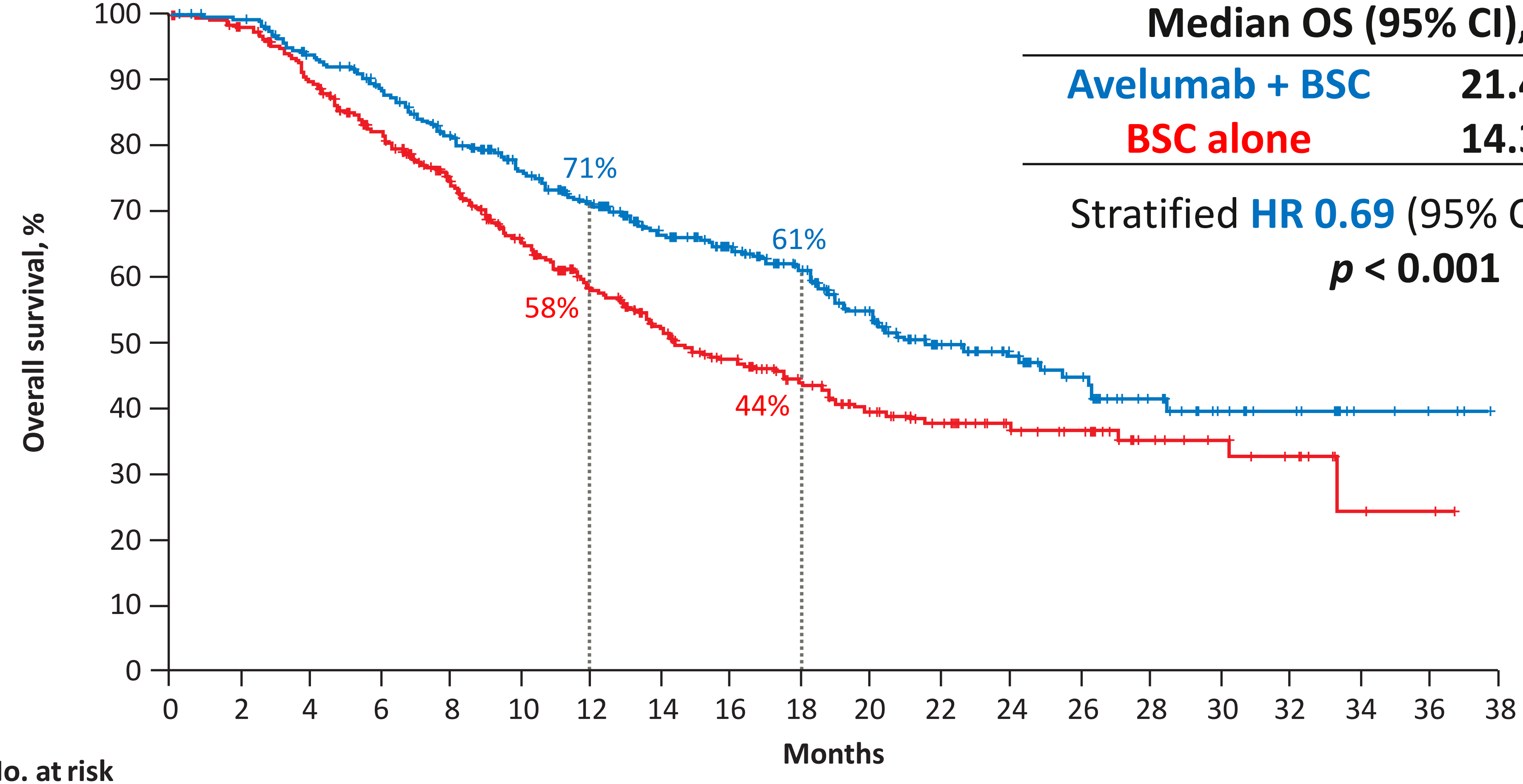
BSC, best supportive care; **CR,** complete response; **IV,** intravenous; **PR**, partial response; **PRO**, patient reported outcome; **Q2W,** every 2 weeks; **R**, randomization; **RECIST 1.1,** Response Evaluation Criteria in Solid Tumors version 1.1; **SD**, stable disease

*BSC (eg, antibiotics, nutritional support, hydration, or pain management) was administered per local practice based on patient needs and clinical judgment; other systemic antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable

Powles T et al. ASCO 2020;Abstract LBA1.

Courtesy of Arjun V. Balar, MD

OS in the overall population



Median OS (95% CI), months	
Avelumab + BSC	**21.4** (18.9, 26.1)
BSC alone	**14.3** (12.9, 17.9)

Stratified **HR 0.69** (95% CI, 0.56, 0.86)

***p* < 0.001**

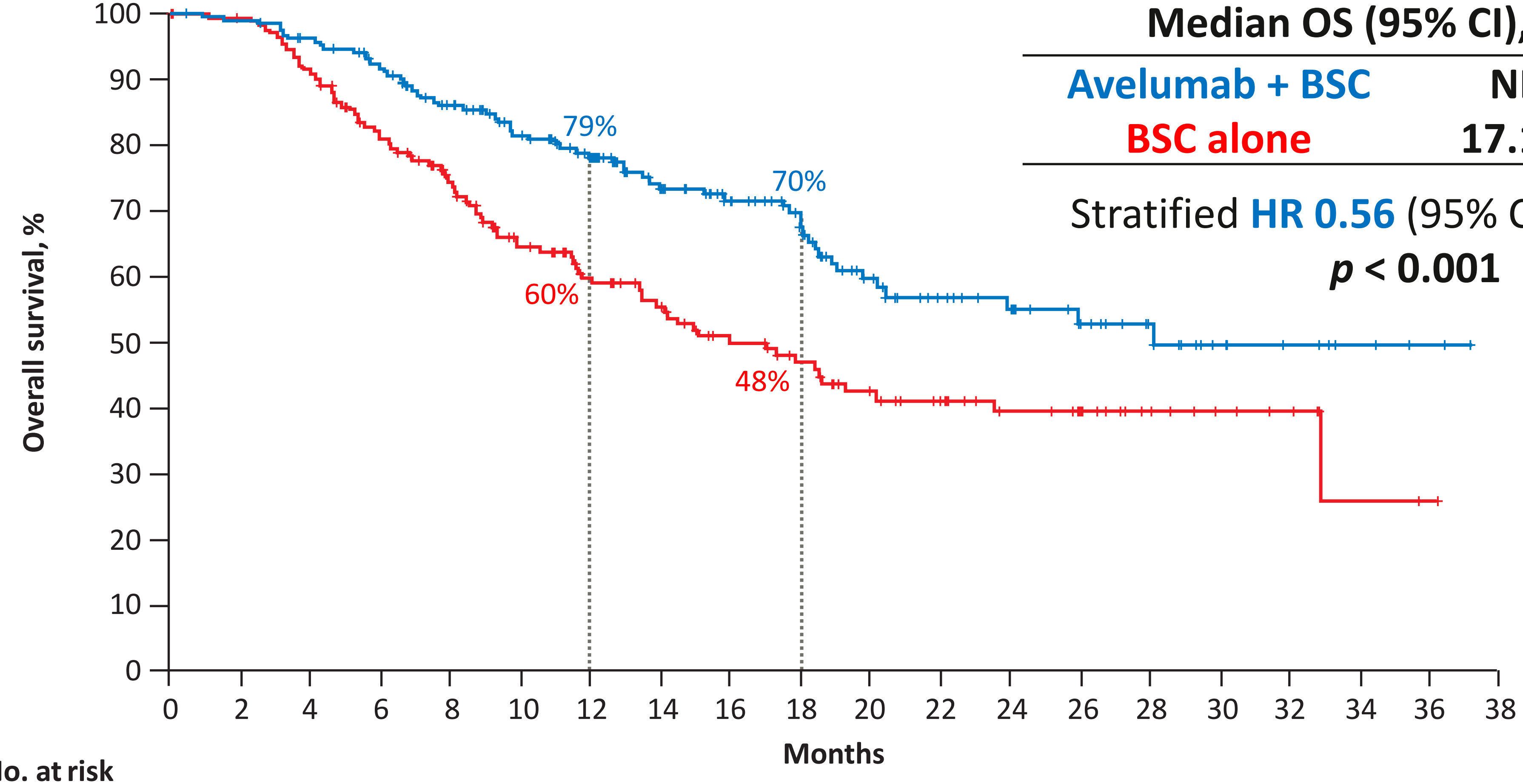
No. at risk																				
Avelumab + BSC	350	342	318	294	259	226	196	167	145	122	87	65	51	39	26	15	11	5	3	0
BSC	350	335	304	270	228	186	153	125	105	83	68	55	41	33	18	12	9	2	1	0

OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (P<0.0053)

Powles T et al. ASCO 2020;Abstract LBA1.

Courtesy of Arjun V. Balar, MD

OS in the PD-L1+ population



Median OS (95% CI), months	
Avelumab + BSC	**NE** (20.3, NE)
BSC alone	**17.1** (13.5, 23.7)

Stratified **HR 0.56** (95% CI, 0.40, 0.79)
***p* < 0.001**

No. at risk																				
Avelumab + BSC	189	185	177	165	146	129	114	95	81	70	49	38	32	26	18	9	8	4	2	0
BSC	169	165	152	132	113	89	76	67	54	45	37	30	23	21	12	8	6	2	1	0

OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (P<0.0014). **NE**, not estimable

Powles T et al. ASCO 2020;Abstract LBA1.

Courtesy of Arjun V. Balar, MD

FDA approves avelumab for urothelial carcinoma maintenance treatment

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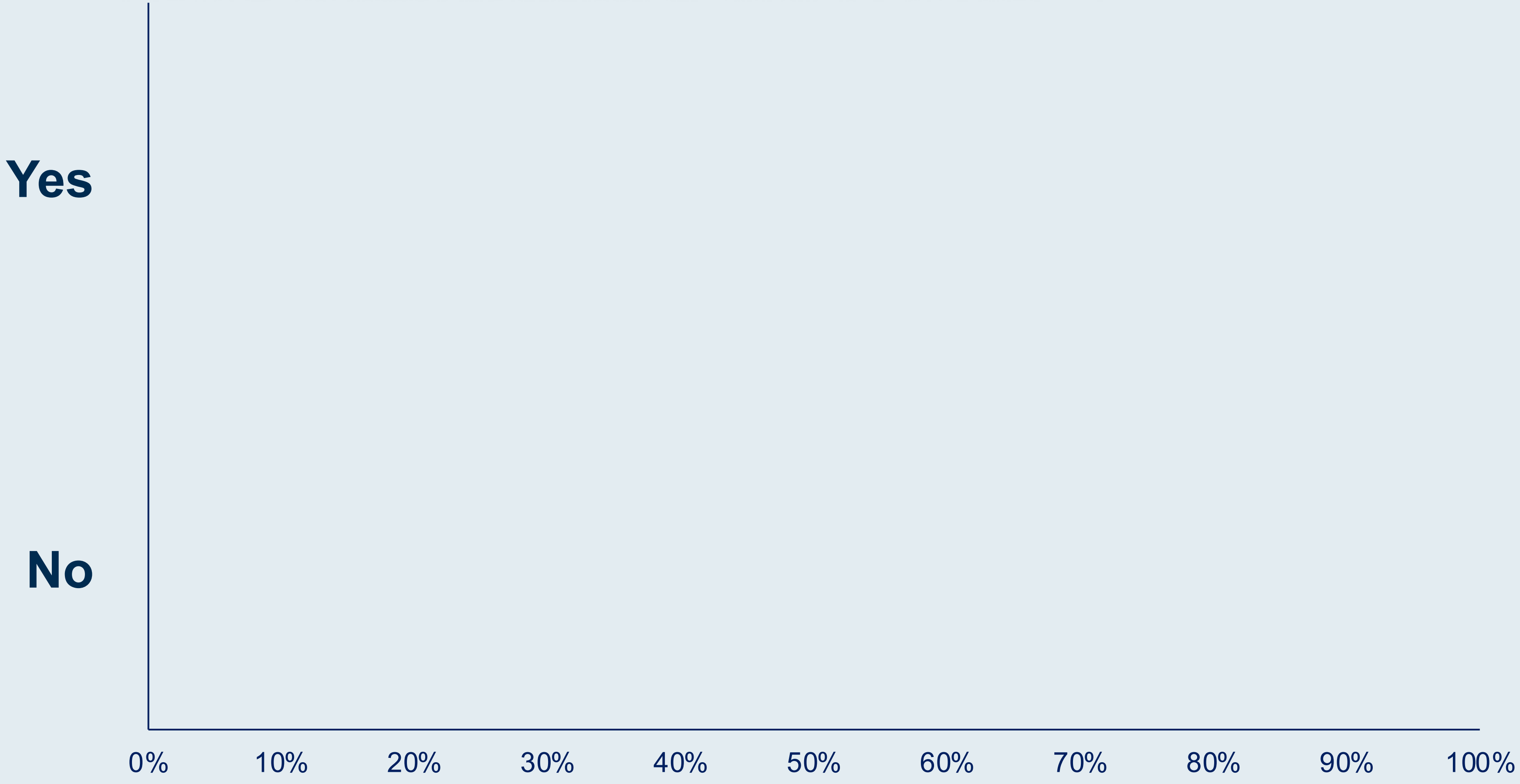
On June 30, 2020, the Food and Drug Administration approved avelumab for maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line-platinum containing chemotherapy.

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-avelumab-urothelial-carcinoma-maintenance-treatment

Courtesy of Arjun V Balar, MD

Regulatory and reimbursement issues aside, would you administer maintenance avelumab to a patient with metastatic UBC who received first-line platinum-based chemotherapy?



Survey of 50 US-based medical oncologists

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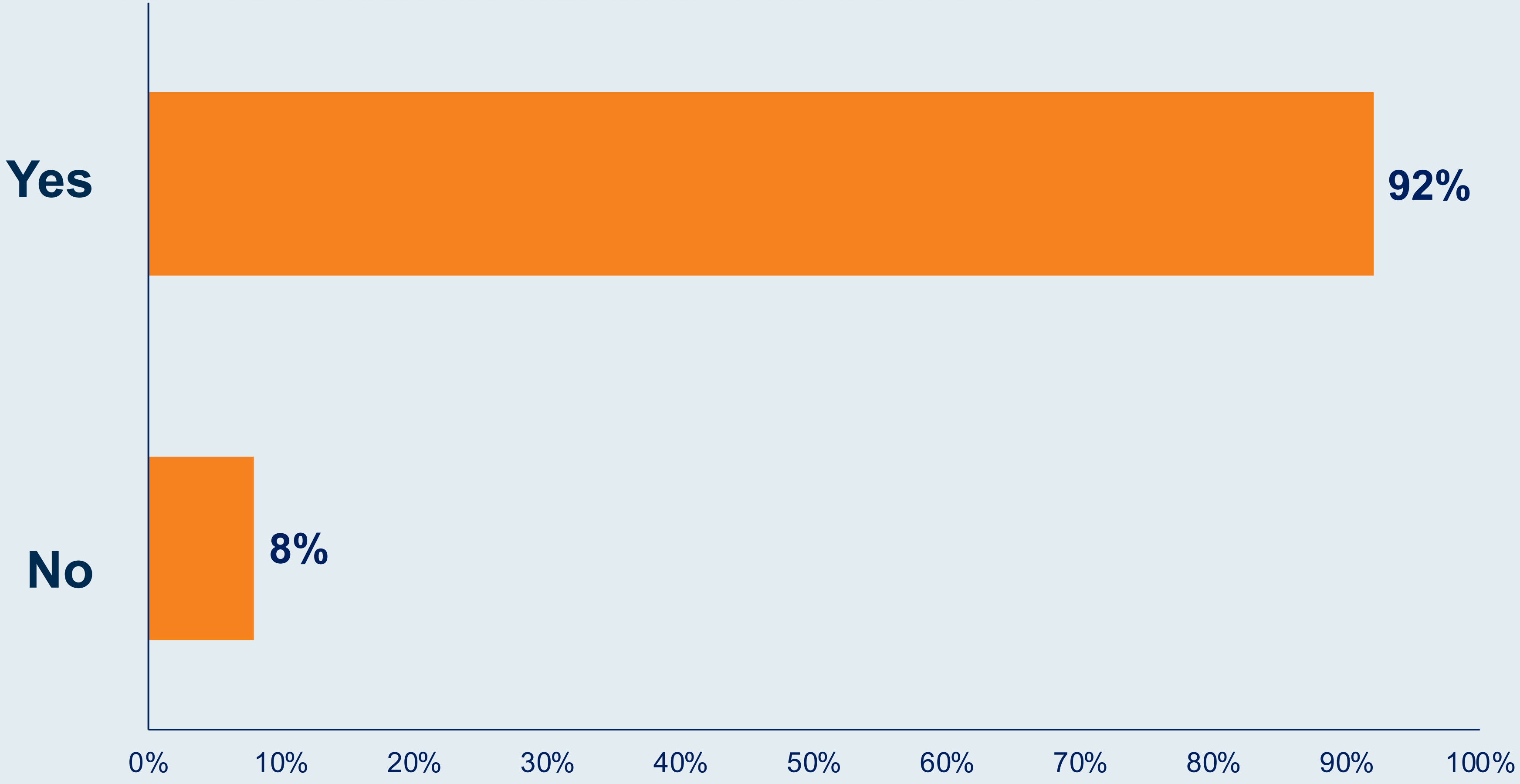
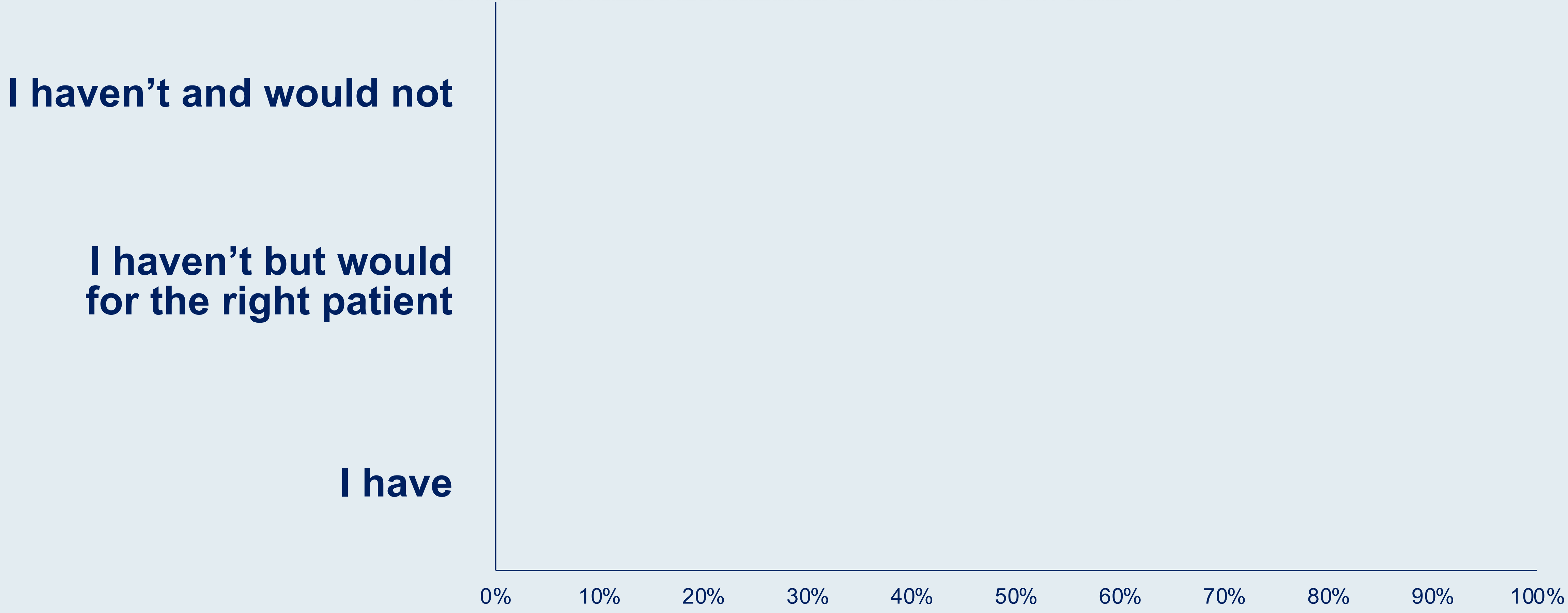


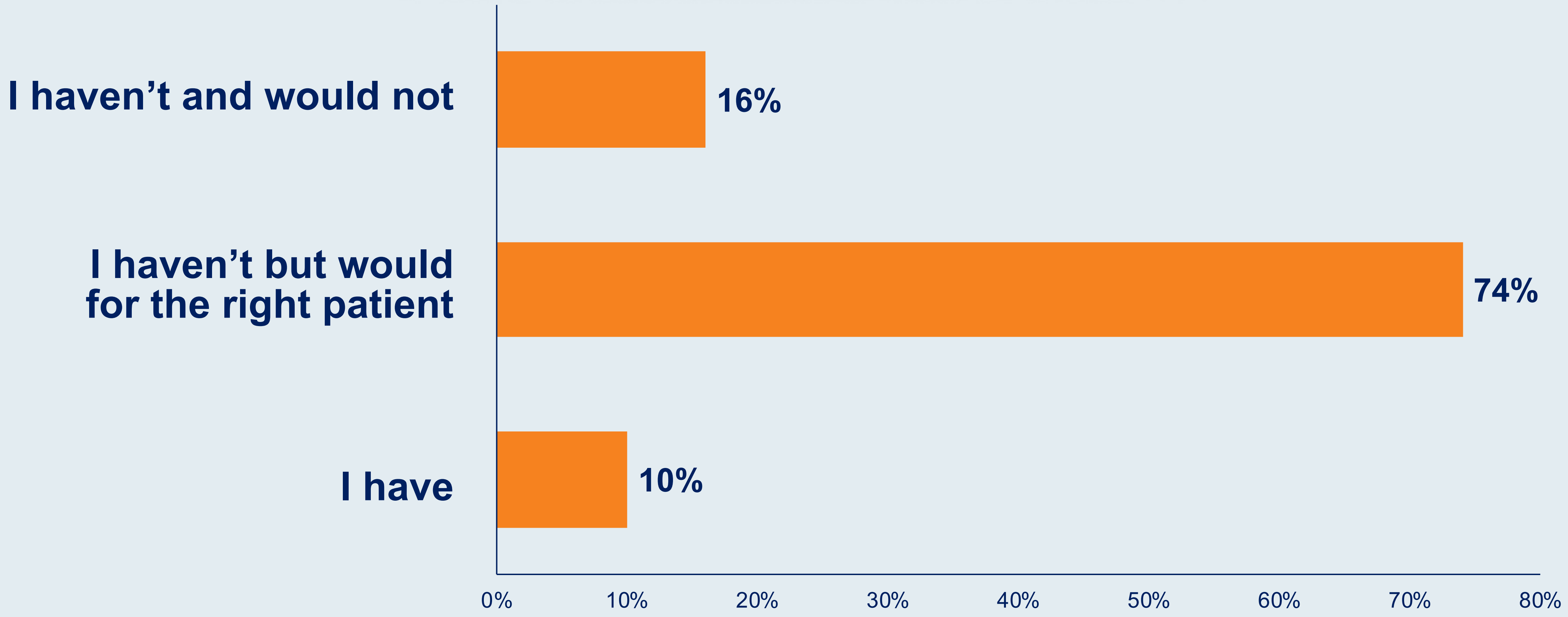
Survey of 50 US-based medical oncologists

Have you administered or would you administer maintenance therapy with an anti-PD-1/PD-L1 antibody other than avelumab to a patient with metastatic UBC who has recently completed first-line platinum-based chemotherapy?



Survey of 50 US-based medical oncologists

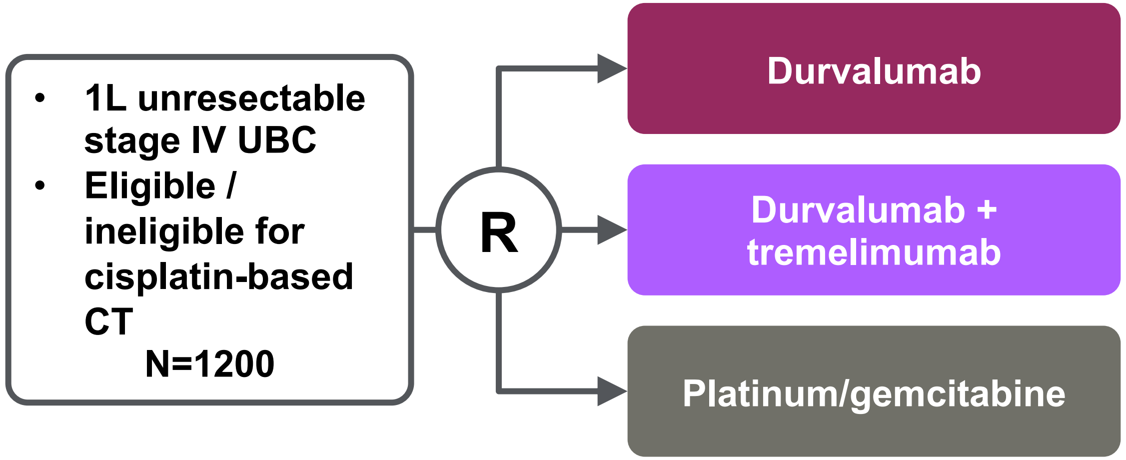
Have you administered or would you administer maintenance therapy with an anti-PD-1/PD-L1 antibody other than avelumab to a patient with metastatic UBC who has recently completed first-line platinum-based chemotherapy?



Survey of 50 US-based medical oncologists

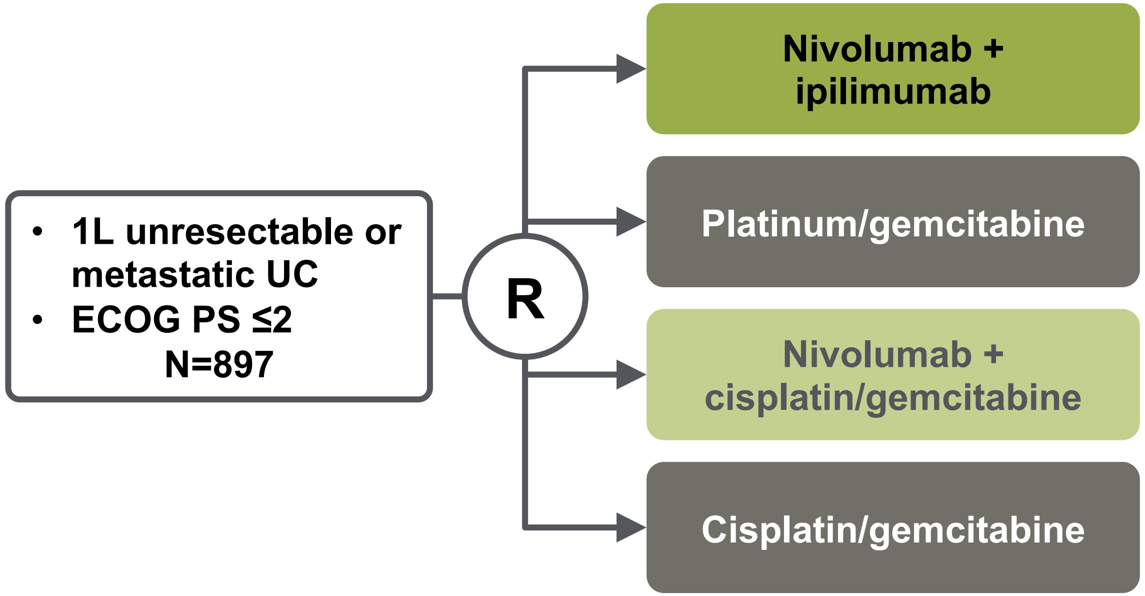
What’s next for PD-L1/PD-1 inhibitors in 1L mUC?

DANUBE (NCT02516241)[1]



Primary endpoint: OS (ITT and PD-L1+ populations)
Estimated primary completion date: 23 September 2019

CheckMate 901 (NCT03036098)[2]



Co-primary endpoints: PFS and OS (cisplatin-ineligible)
Estimated primary completion date: 26 April 2020

1. https://clinicaltrials.gov/ct2/show/NCT02516241
2. https://clinicaltrials.gov/ct2/show/record/NCT03036098

Courtesy of Arjun V. Balar, MD

KEYNOTE-057 Phase 2 Trial: Pembrolizumab in High-Risk NMIBC—Study Design[1,2]

- High-risk NMIBC unresponsive to BCG; patients refuse or are ineligible for cystectomy
- Patients with papillary disease must have fully resected disease at study entry
- Two cohorts
  - Cohort A (n = 130): CIS ± papillary disease (high-grade Ta or T1)
  - Cohort B (n = 130): papillary disease (high-grade Ta or any T1) without CIS

→ **Pembrolizumab** 200 mg every 3 wk

→ **Cystoscopy, cytology, ± biopsy** every 12 wk × 2 y, then every 24 wk × 2 y and once yearly thereafter *and* **extravesical disease on CTU** every 24 wk × 2 y or more frequently as clinically indicated

If no persistence or recurrence of high-risk NMIBC at any assessment → **Continue assessments and pembrolizumab until recurrence of high-risk NMIBC, PD, or 24-mo treatment complete**

If high-risk NMIBC present at any assessment → **Discontinue treatment; enter survival follow-up**

Primary endpoints

- Cohort A: CR (absence of high-risk NMIBC)
- Cohort B: DFS

Secondary endpoints

- Cohort A: CR (absence of any disease [high- or low-risk NMIBC])
- Cohort A: DOR and safety/tolerability

1. https://clinicaltrials.gov/ct2/show/NCT02625961. Accessed February 7, 2020.
2. Balar A et al. ASCO GU 2019. Abstract 350.

Courtesy of Arjun V. Balar, MD

The CR Rate Exceeds the Success Criterion for the Primary Hypothesis Test[1,2]

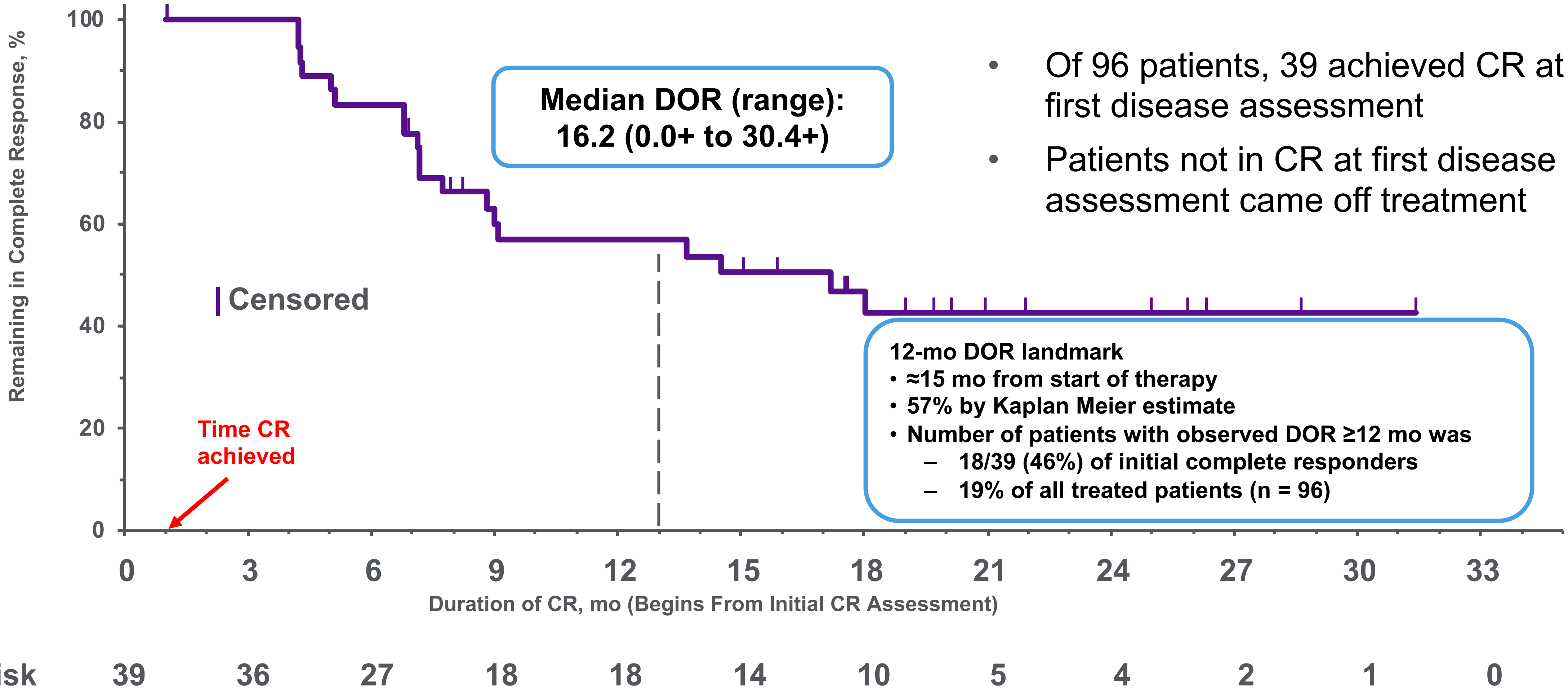
- Statistically significant CRR: lower bound of 95% CI exceeds the 20% success criterion for the primary hypothesis test (ASCO 2020)

Best Response	N = 96	
	n (%)	95% CI
CR	39 (40.6)	30.7-51.1
Non-CR	56 (58.3)	47.8-68.3
Persistent	40 (41.7)	31.7-52.2
Recurrent	6 (6.3)	2.3-13.1
NMIBC stage progression to T1	9 (9.4)	4.4-17.1
Non-bladder malignancy	1 (1.0)	0.0-5.7
Progression to T2	0 (0)	NA
Nonevaluable	1 (1.0)	0.0-5.7

[a] Extravesical disease is defined as the presence of lesions suspicious for locally advanced or metastatic bladder cancer on imaging. The one patient included in this category developed new liver lesions on imaging and was later found to have a second primary malignancy of pancreatic cancer. Subsequent review of the baseline scan showed subtle findings that, in retrospect, could be attributed to pancreatic cancer, and later scans showed metastases that were most likely from the pancreatic cancer. Clinical course and laboratory values further supported the diagnosis of metastatic pancreatic cancer.

Balar A et al. ASCO GU 2019. Abstract 350. Balar A, et al. ASCO 2020. Abstract 5041.

Duration of Complete Response Is Clinically Meaningful[1,2]



Median DOR (range): 16.2 (0.0+ to 30.4+)

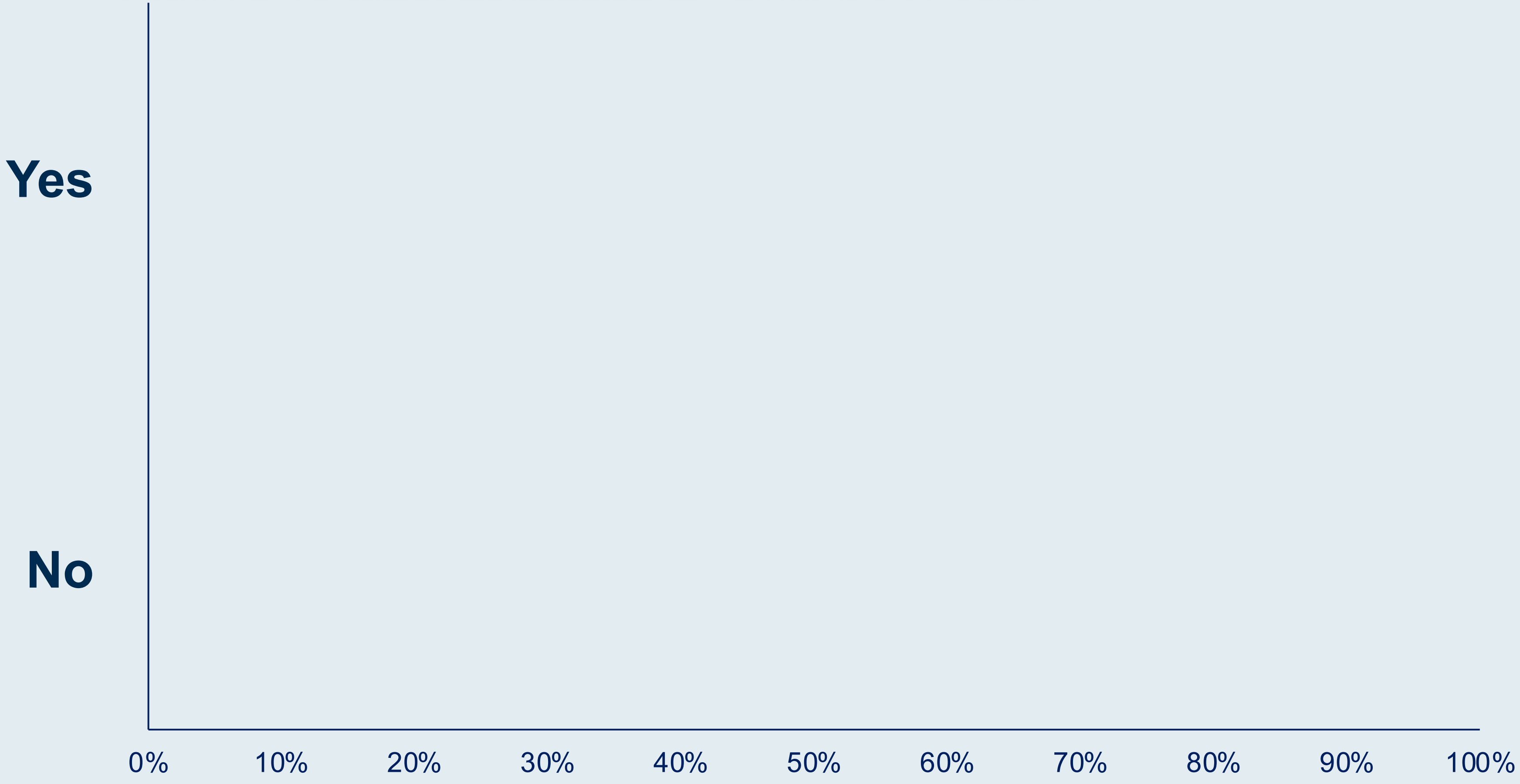
- Of 96 patients, 39 achieved CR at first disease assessment
- Patients not in CR at first disease assessment came off treatment

12-mo DOR landmark
- ≈15 mo from start of therapy
- 57% by Kaplan Meier estimate
- Number of patients with observed DOR ≥12 mo was
  - 18/39 (46%) of initial complete responders
  - 19% of all treated patients (n = 96)

1. Balar A et al. ASCO GU 2019. Abstract 350. 2. Balar A. FDA ODAC submission 2019.

Courtesy of Arjun V. Balar, MD

Would you generally recommend pembrolizumab to an 80-year-old patient with BCG-unresponsive non-muscle-invasive UBC and significant comorbidities?



Survey of 50 US-based medical oncologists

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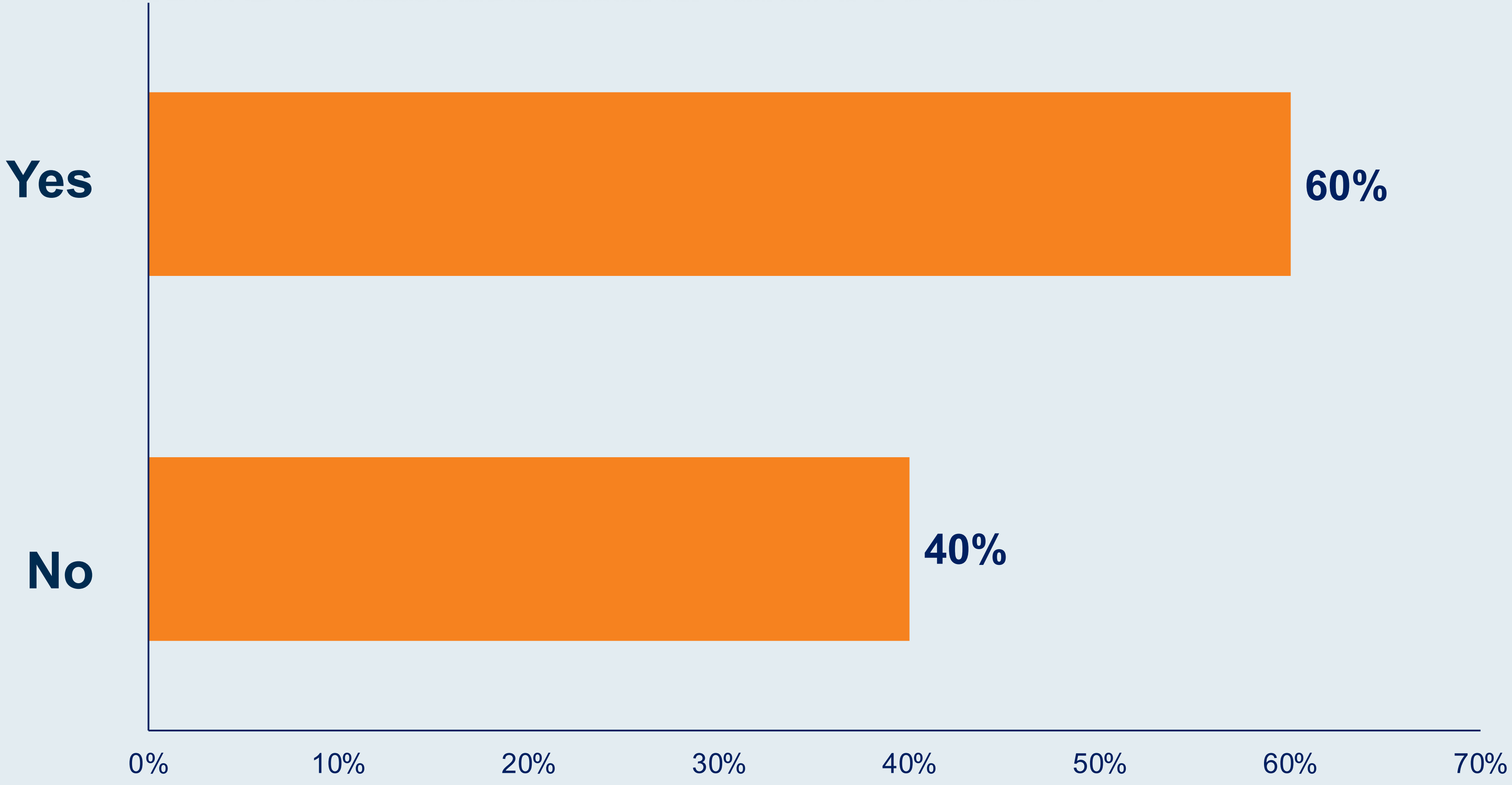


Survey of 50 US-based medical oncologists

Phase 3 Trials of PD-1/PD-L1 Inhibitors in NMIBC

Primary endpoint: CR

KEYNOTE-676 (NCT03711032)[1]; N = ≈550
- High-risk NMIBC persistent or recurrent after BCG induction and following cytoscopy/ transurethral resection
- ECOG PS ≤2

R
- Pembrolizumab + BCG
- BCG

Primary endpoint: DFS

POTOMAC (NCT03528694)[2]; N = ≈975
- High-risk NMIBC previously resected and naïve to BCG and cancer immunotherapy

R
- Durvalumab + BCG (induction and maintenance)
- Durvalumab + BCG (induction only)
- BCG

Primary endpoint: RFS

ALBAN (NCT03799835)[3]; N = 614
- High-risk NMIBC previously resected and naïve to BCG
- Tumor tissue available for PD-L1 assay

R
- BCG × 1 y
- BCG + atezolizumab every 3 wk × 1 y

1. https://clinicaltrials.gov/ct2/show/NCT03711032. Accessed February 7, 2020. 2. https://clinicaltrials.gov/ct2/show/NCT03528694. Accessed February 7, 2020.
3. https://clinicaltrials.gov/ct2/show/NCT03799835. Accessed February 7, 2020.

Courtesy of Arjun V. Balar, MD

Recent Developments in the Management of Urothelial Bladder Cancer

Module 1: Immune Checkpoint Inhibitors — Dr Balar

- Key Recent Data Sets
  - Avelumab as maintenance therapy after induction chemotherapy for metastatic disease
  - Pembrolizumab for high-risk non-muscle-invasive bladder cancer (NMIBC)
- Faculty Case Discussion: 73-year-old woman with NMIBC

Case Presentation – Dr Balar: A 73-Year-Old Woman with BCG Unresponsive NMIBC

- 73 year old woman, retired school teacher
- PMH: High Cholesterol, Former 36 pack-year smoker
- Presented in 2014 with LUTS thought to be due to overactive bladder s/p multiple opinions
- 2018 cystoscopy: bladder erythema and subsequent fulguration/biopsy showed CIS and urine cytology was positive for HG UC.
- 7/9/2018 TURBT showed CIS.
  - Induction BCG from 8/21/2018 through 9/25/2018 full strength BCG for 6 of 6 instillations, tolerated well.
- 11/2018 cystoscopy showed positive cytology, biopsy negative but suspicious on appearance.
- 12/14/2018 TURBT with bluelight showed HG UC with LP invasion
  - Counseled about cystectomy, refused

Case Presentation – Dr Balar: A 73-Year-Old Woman with BCG Unresponsive NMIBC (Continued)

- 1/28/2019 re-TURBT showed CIS only, no papillary disease
  - Re-induction BCG 2/25/2019 through 4/1/2019 full-strength 6 of 6 doses.
- Cystoscopy in 7/9/2019 was suspicious and biopsy was negative, cytology atypical. She did not receive maintenance due to the BCG shortage.
- 11/5/2019 cystoscopy showed inflamed/erythematous bladder. Cytology positive for HG UC.
- 12/9/2019 re-TURBT which showed CIS and no papillary disease
- She was referred for an opinion re: investigational management options for BCG unresponsive HR NMIBC.
- 2/18/2020 started anti-PD-1 immunotherapy on protocol, now s/p 3 cycles
- 5/21/2020 cystoscopy with biopsy and urine cytology
  - Complete response; urine cytology: atypical cells

Module 2: Antibody-Drug Conjugates — Prof Powles

- **Key Recent Data Sets**
  - Enfortumab vedotin (EV) after platinum-based chemotherapy and immunotherapy (IO)
  - First-line EV in combination with pembrolizumab (chemotherapy)
  - Sacituzumab govitecan-hziy
- Faculty Case Discussion: 74-year-old man with metastatic UBC — Progression on chemotherapy, IO

Summary

Enfortumab vedotin is active in treatment refractory advanced UC. This includes patients who have not responded to other treatments

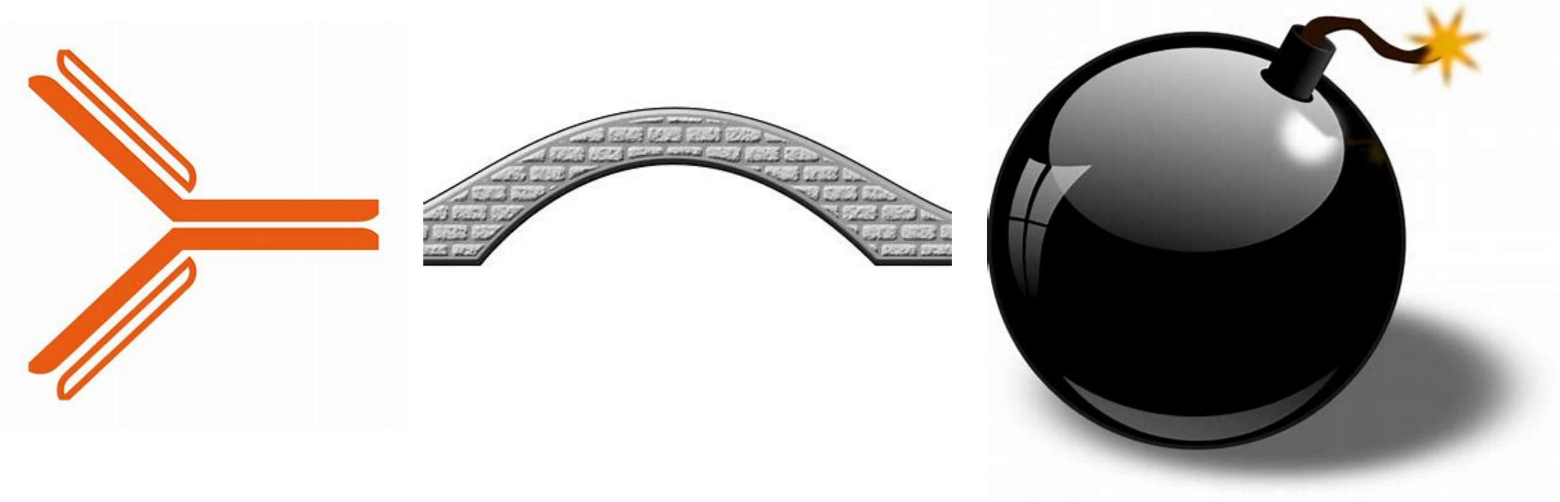
It is associated with rapid responses. Its toxicity profile is distinct from other agents used in UC.

The combination with pembrolizumab in first-line disease is very promising

Courtesy of Thomas Powles, MBBS, MRCP, MD

Antibody-drug conjugates (ADC) in Urothelial Cancer.

Targeted antibody | Linker molecule | cytotoxic



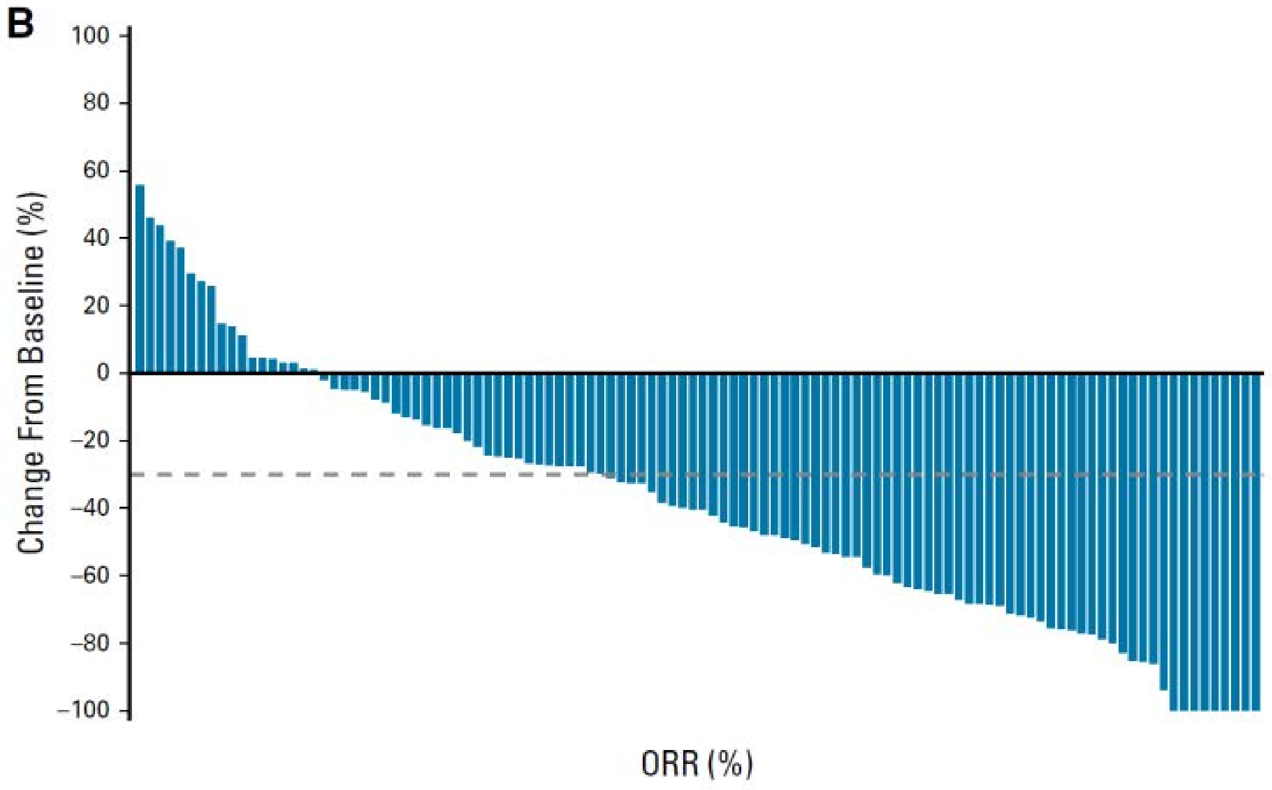
Nectin-4 (IgG1) | **SGD-1006** | **Monomethyl auristatin E (MMAE) = Enfortumab vedotin**

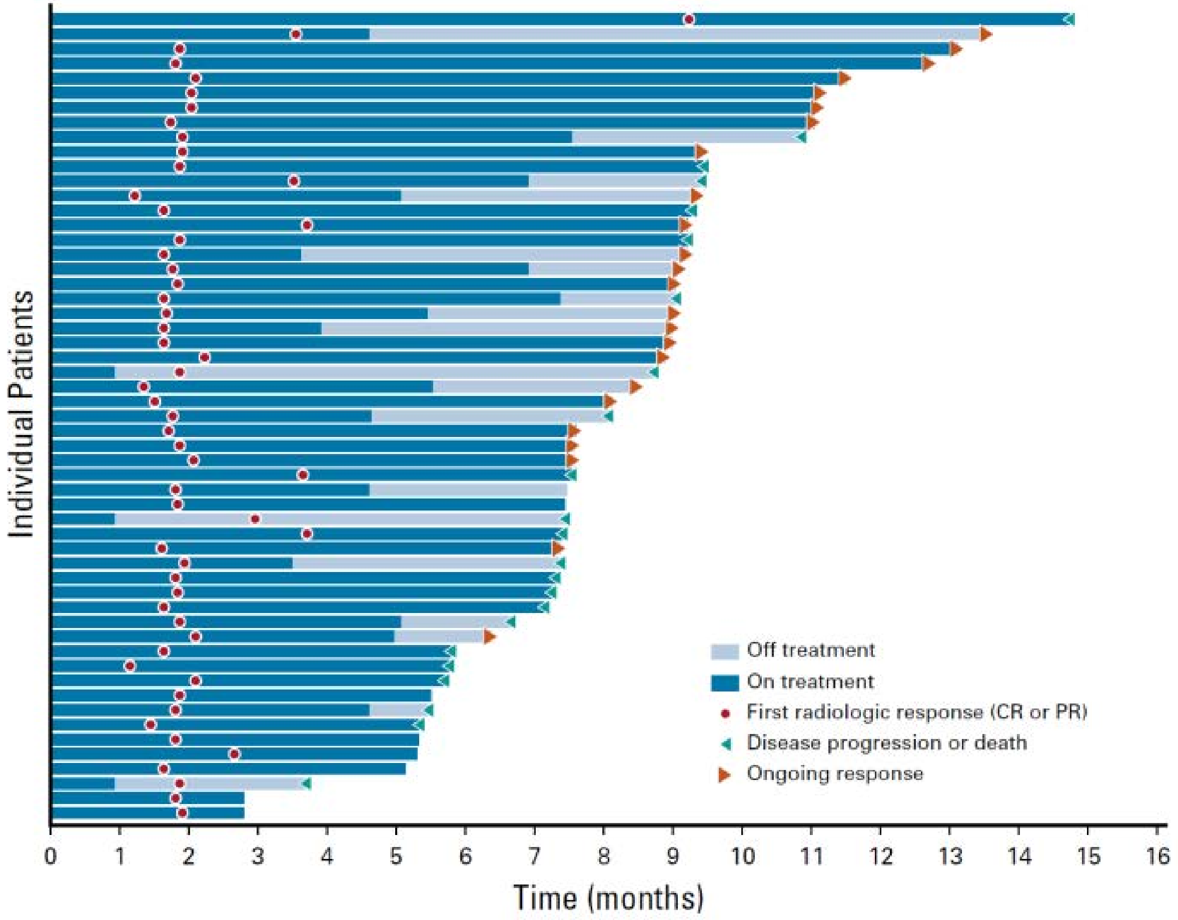
Courtesy of Thomas Powles, MBBS, MRCP, MD

Pivotal Trial of Enfortumab Vedotin in Urothelial Carcinoma After Platinum and Anti-Programmed Death 1/Programmed Death Ligand 1 Therapy

EV-201 Phase II Trial

Jonathan E. Rosenberg, MD[1,2]; Peter H. O'Donnell, MD[3]; Arjun V. Balar, MD[4]; Bradley A. McGregor, MD[5]; Elisabeth I. Heath, MD[6]; Evan Y. Yu, MD[7,8]; Matthew D. Galsky, MD[9]; Noah M. Hahn, MD[10]; Elaina M. Gartner, MD[11]; Juan M. Pinelli, PA-C, MMSc[11]; Shang-Ying Liang, PhD[11]; Amal Melhem-Bertrandt, MD[12]; and Daniel P. Petrylak, MD[13]



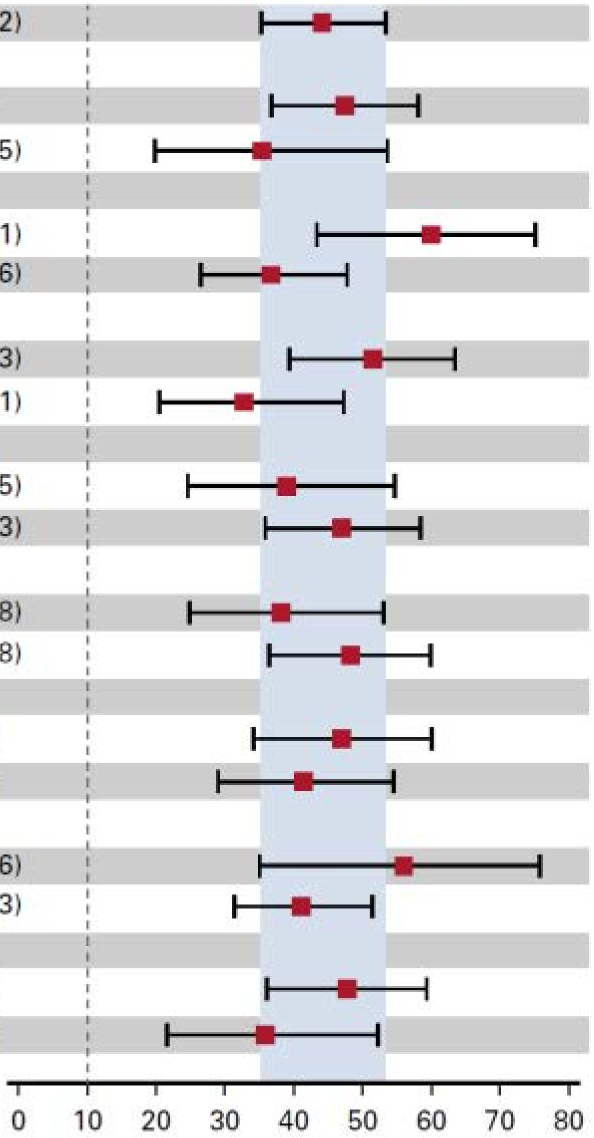


Rosenberg 2019

Courtesy of Thomas Powles, MBBS, MRCP, MD

Subset analysis from EV 201 study.

Subgroup	No. of Events/ No. of Patients	% (95% CI)	ORR, % (95% CI)
Overall	55/125	44 (35.1 to 53.2)	
Age, years			
< 75	43/91	47 (36.7 to 58)	
≥ 75	12/34	35 (19.7 to 53.5)	
ECOG performance status			
Grade 0	24/40	60 (43.3 to 75.1)	
Grade 1	31/85	36 (26.3 to 47.6)	
Bellmunt risk score†			
0-1	37/72	51 (39.3 to 63.3)	
≥ 2	17/52	33 (20.3 to 47.1)	
Primary tumor sites			
Upper tract	17/44	39 (24.4 to 54.5)	
Bladder/other	38/81	47 (35.7 to 58.3)	
Liver metastasis			
Yes	19/50	38 (24.7 to 52.8)	
No	36/75	48 (36.3 to 59.8)	
No. of prior therapies in metastatic UC setting			
1-2	29/62	47 (34 to 59.9)	
≥ 3	26/63	41 (29 to 54.4)	
Best response to prior anti-PD-1/L1‡			
Responder	14/25	56 (34.9 to 75.6)	
Nonresponder	41/100	41 (31.3 to 51.3)	
PD-L1 expression§			
CPS < 10	37/78	47 (36 to 59.1)	
CPS ≥ 10	15/42	36 (21.6 to 52)	



Rosenberg JE et al. *J Clin Oncol* 2019;37(29):2592-600.

Courtesy of Thomas Powles, MBBS, MRCP, MD

EV-201: Summary of adverse events.

Variable	Patients (N = 125)
Any adverse event	125 (100)
Treatment-related adverse events	117 (94)
Grade ≥ 3 treatment-related adverse events	68 (54)
Treatment-related serious adverse events	24 (19)
Treatment-related adverse events resulting in treatment discontinuation	15 (12)
Treatment-related adverse events leading to death*	0 (0)

* There were no treatment-related deaths during the 30-day safety reporting period. One death as a result of ILD that occurred outside the safety reporting period was reported as treatment related.

Rosenberg JE et al. *J Clin Oncol* 2019;37(29):2592-600.

EV-201: Summary of specific adverse events.

	Any Grade	Grade ≥ 3
Fatigue	62 (50)	7 (6)
Alopecia	61 (49)	0
Decreased appetite	55 (44)	1 (1)
Dysgeusia	50 (40)	0
Peripheral sensory neuropathy	50 (40)	2 (2)
Nausea	49 (39)	3 (2)
Diarrhea	40 (32)	3 (2)
Rash maculopapular	27 (22)	5 (4)

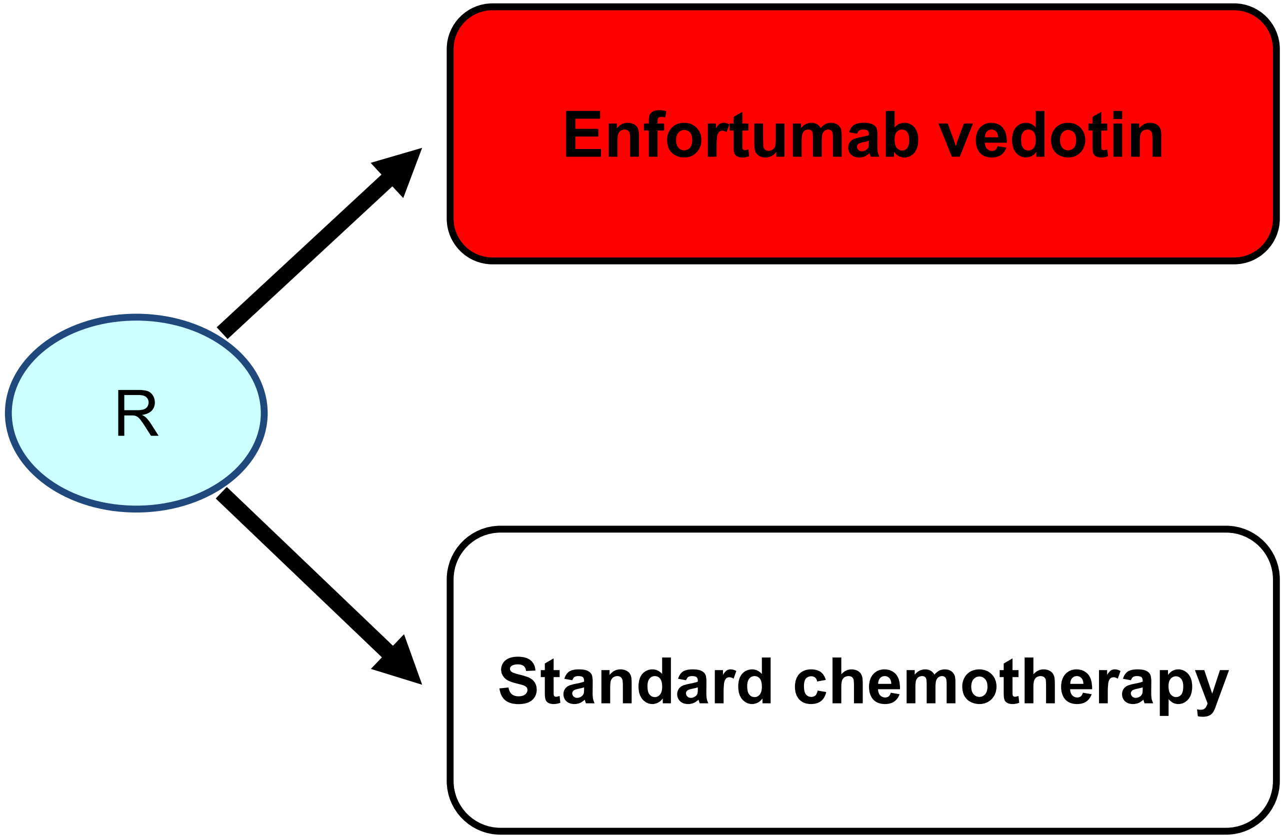
Rosenberg JE et al. *J Clin Oncol* 2019;37(29):2592-600.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Enfortumab vedotin vs chemotherapy alone in advanced chemotherapy and immune refractory urothelial cancer (EV-301).

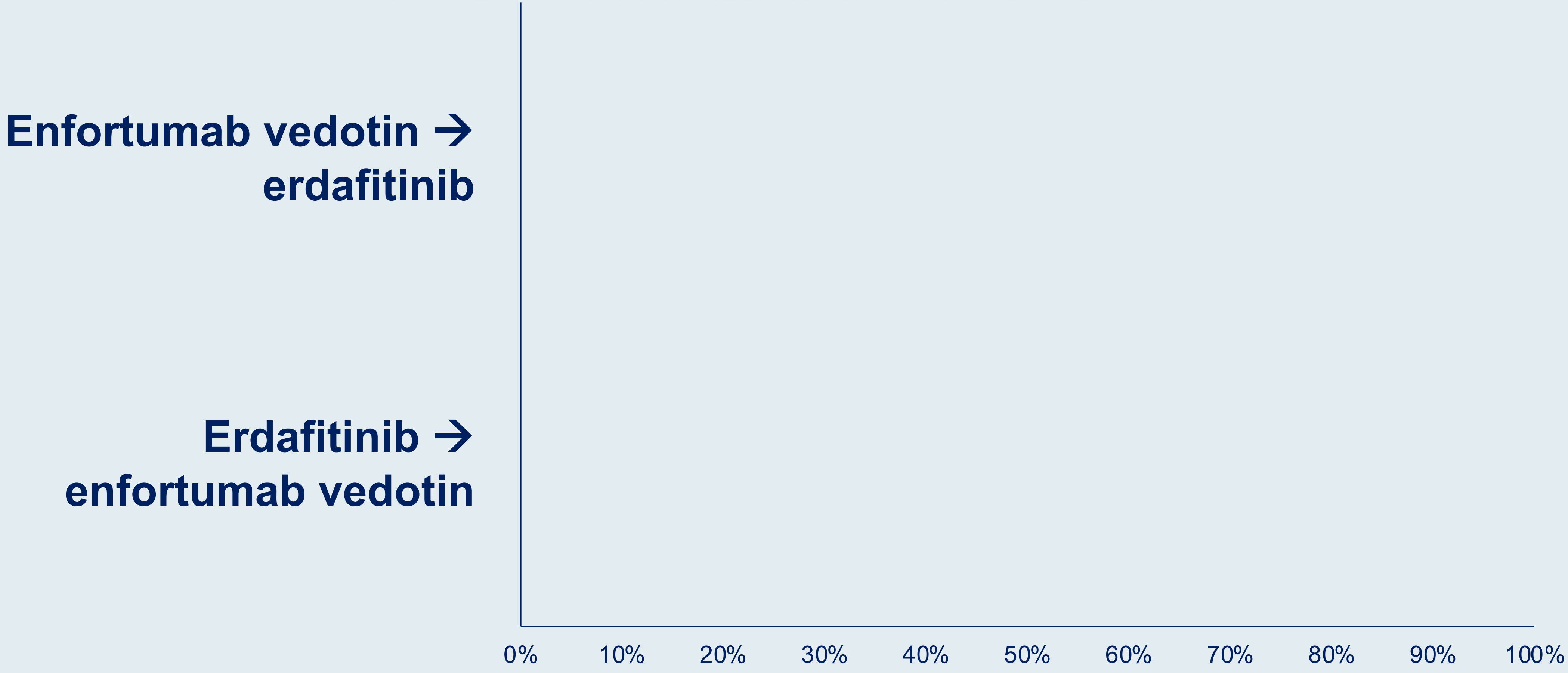
NCT03474107

- **Previously treated advanced UC**
- **Performance status 0-1**
- **N=608**
- **Endpoints=OS**
- **Open label**
- **Start date: March 2018**



Courtesy of Thomas Powles, MBBS, MRCP, MD

How would you generally sequence enfortumab vedotin and erdafitinib for a patient with metastatic UBC who is eligible to receive both agents?



Survey of 50 US-based medical oncologists

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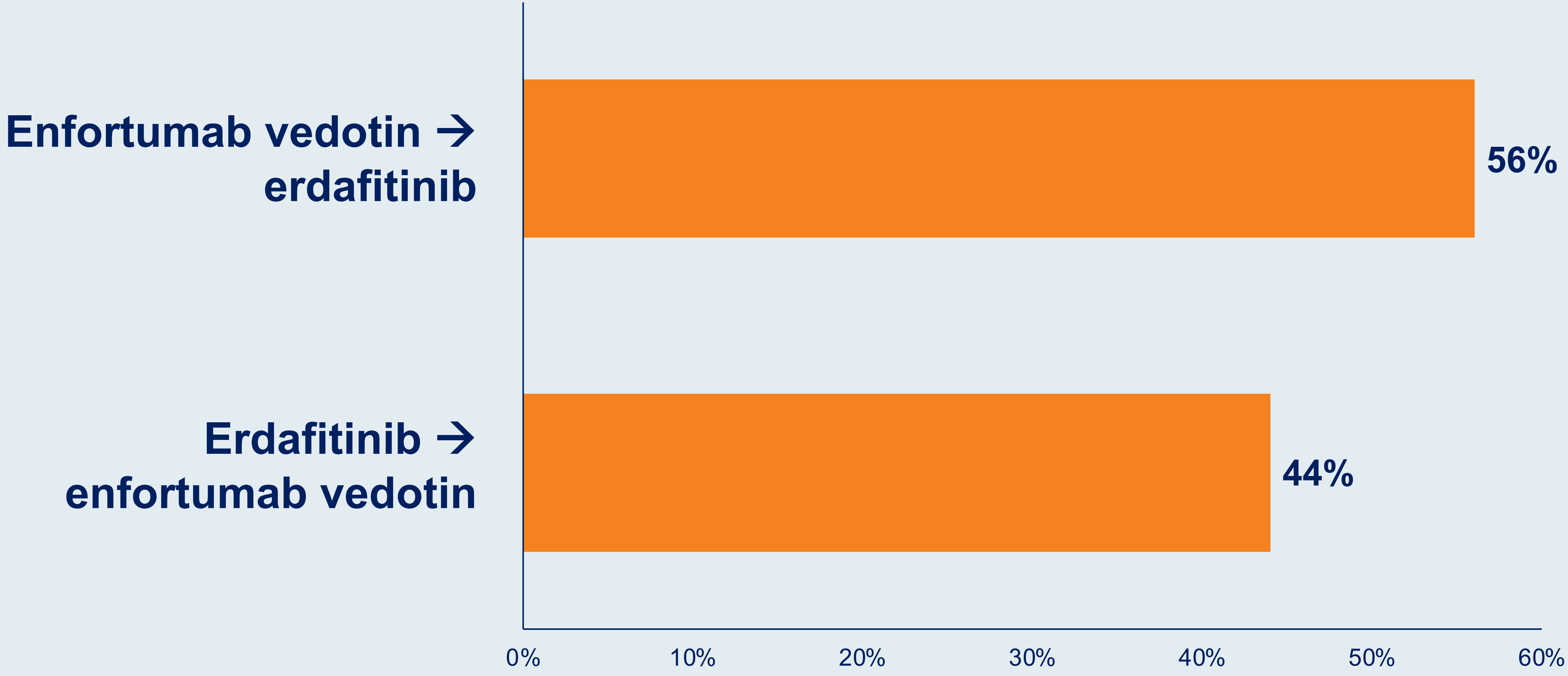
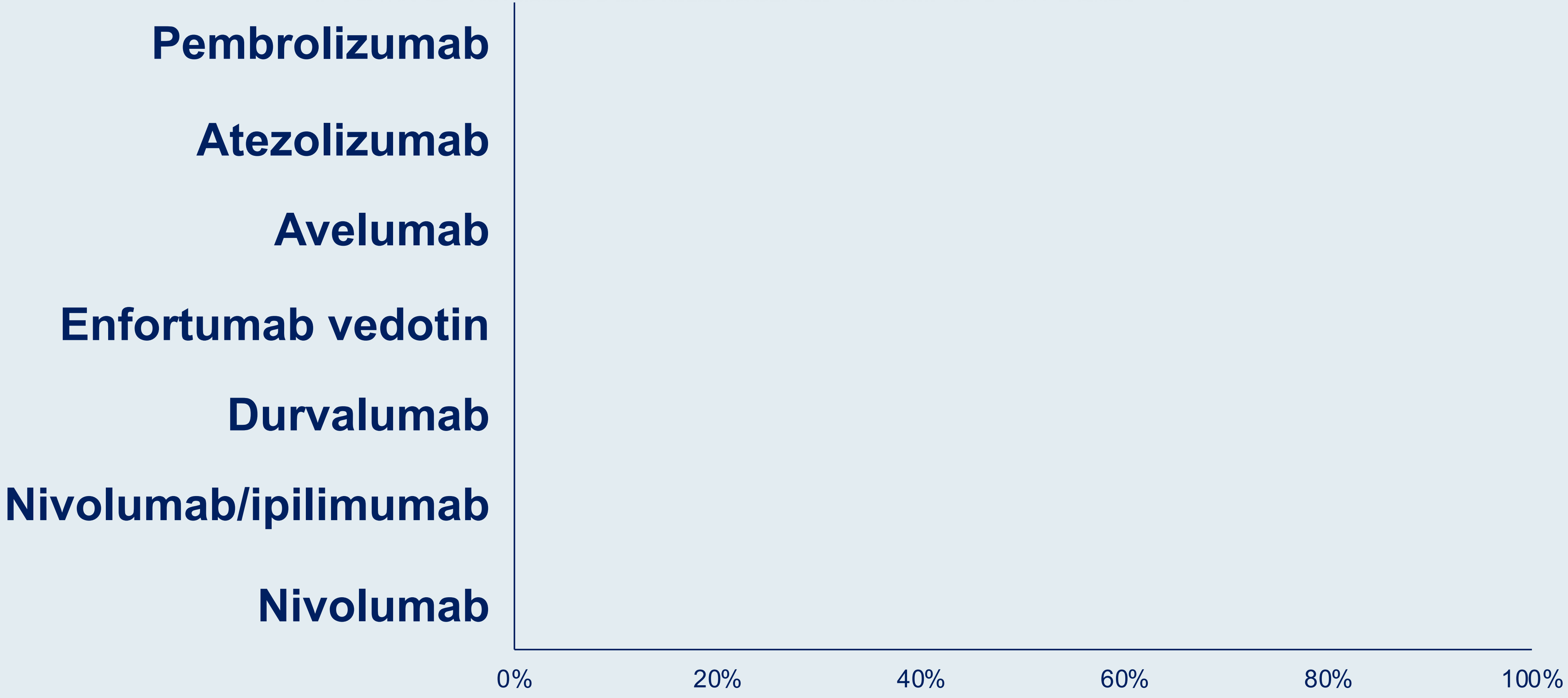


Survey of 50 US-based medical oncologists

What would you generally recommend as second-line therapy for a patient with FGFR wild-type UBC metastatic to the liver whose disease progresses on first-line cisplatin/gemcitabine?



Survey of 50 US-based medical oncologists

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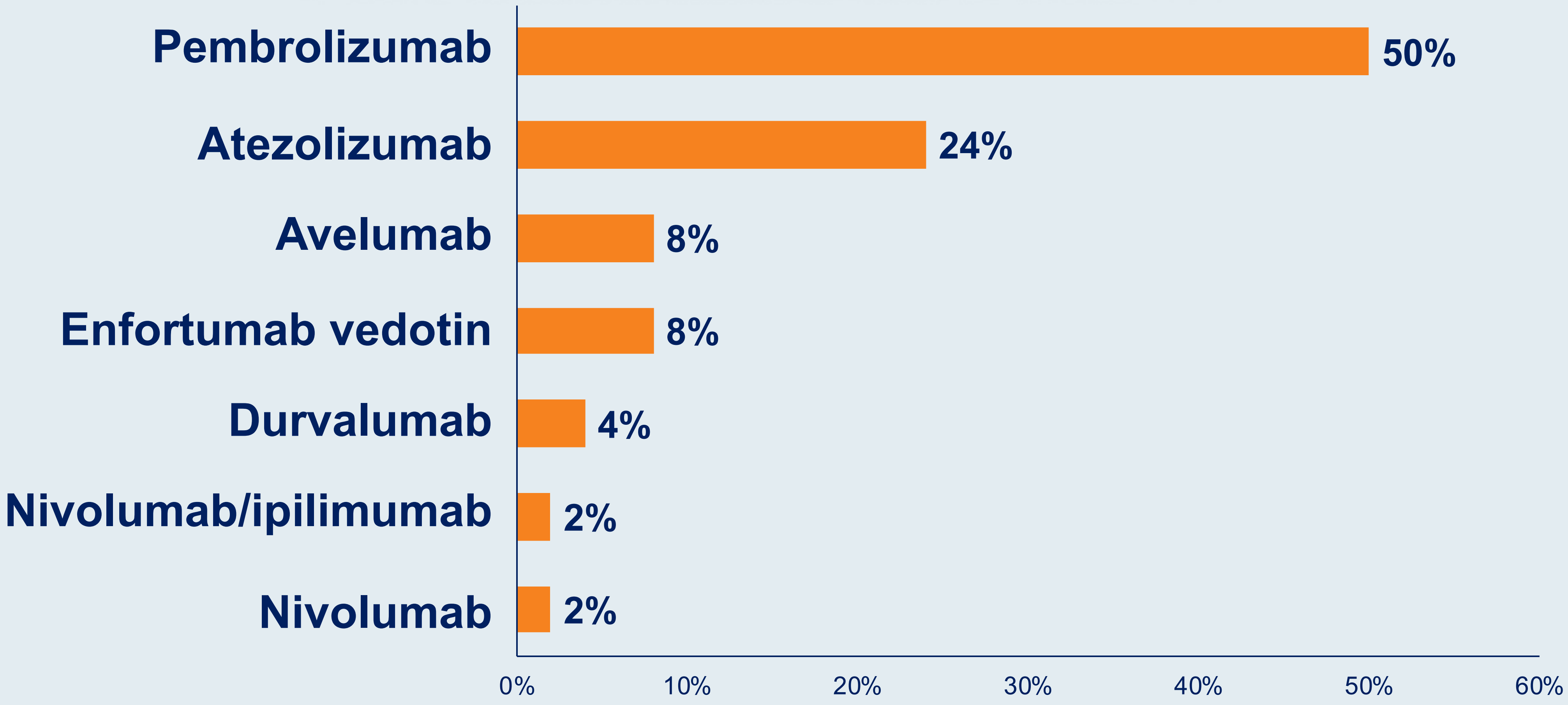
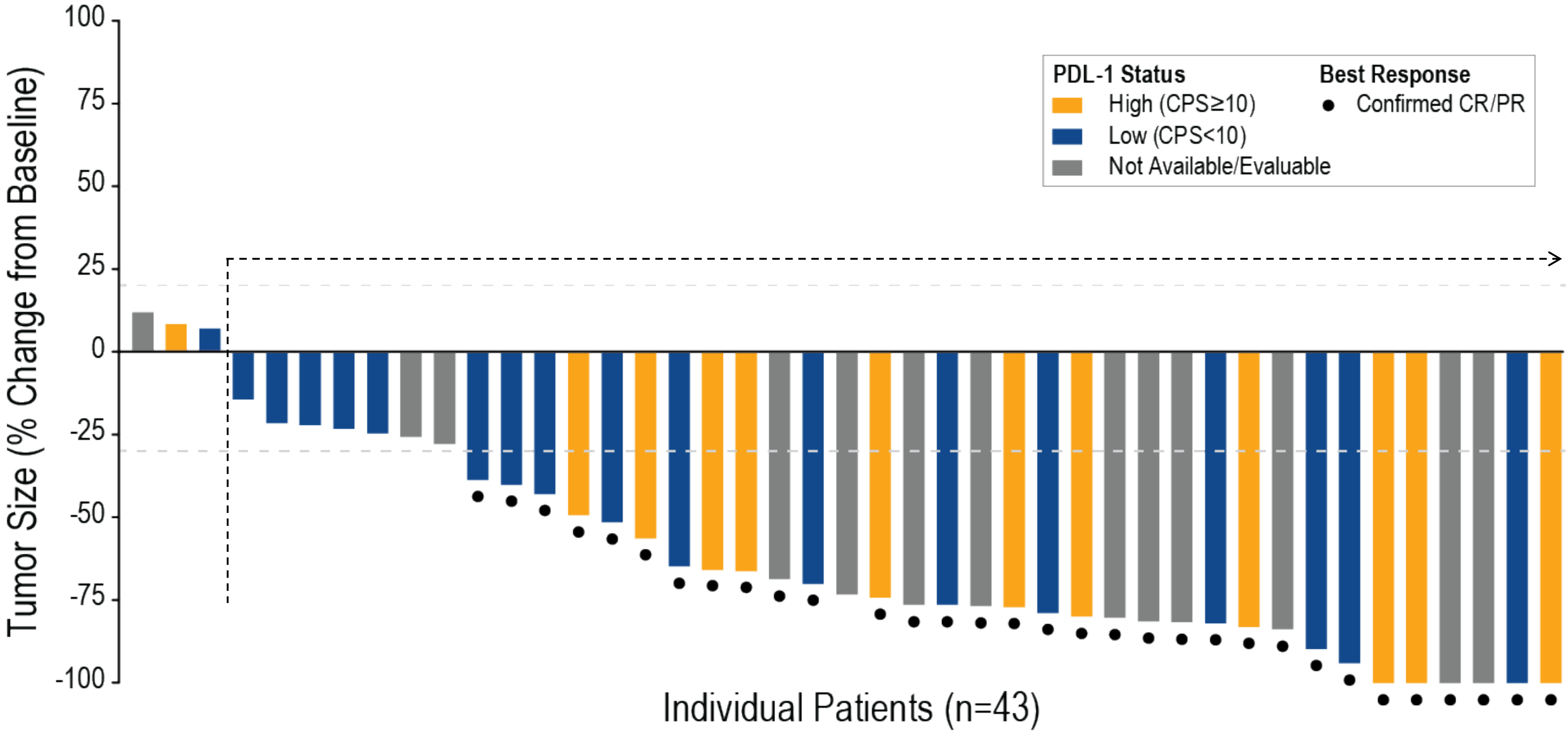


Survey of 50 US-based medical oncologists

EV-103: PEMBROLIZUMAB + ENFORTUMAB VEDOTIN IN FIRST LINE PLATINUM INELIGIBLE DISEASE



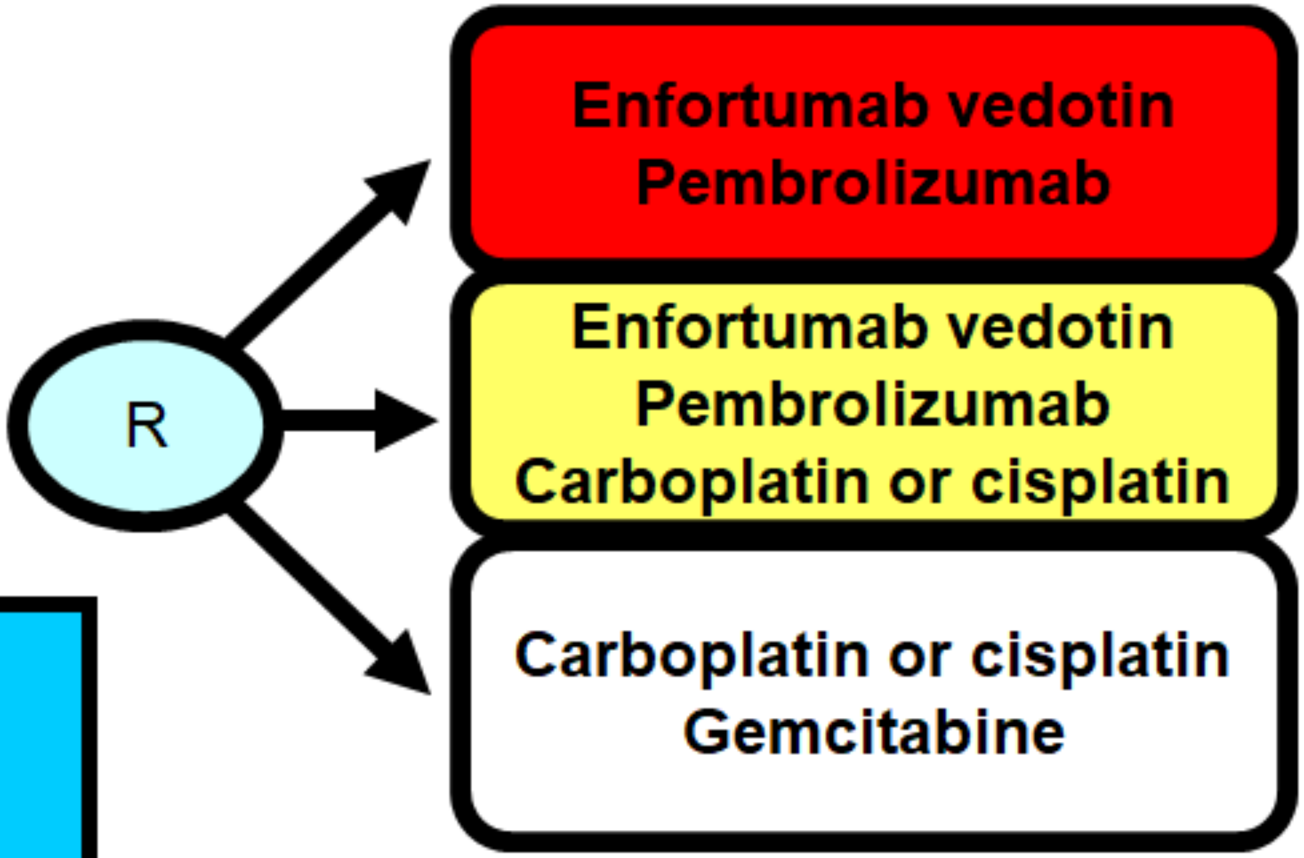
PD-L1 tested using the 22C3 PharmDx assay

Rosenberg et al. ASCO GU 2020;Abstract 441.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Enfortumab vedotin and pembrolizumb with or without chemotherapy vs chemotherapy alone in advanced urothelial cancer (EV-302).

NCT04223856



- **First-line advanced UC**
- **Performance status 0-2**
- **N=1095**
- **Endpoints=PFS and OS**
- **Open label**
- **Start date: March 2020**

Courtesy of Thomas Powles, MBBS, MRCP, MD

Sacituzumab govitecan for mUC: Efficacy

Sacituzumab govitecan (SG): Humanised ADC comprised of an anti-Trop-2 glycoprotein linked with SN-38, an active metabolite of irinotecan

NCT01631552: Phase I/II study of SG in patients with epithelial cancers (PS 0–1)

ORR in patients with previously treated mUC (N=45)		
ORR by subgroup	**ORR, % (n/N)**	**95% CI**
Overall	31 (14/45)	18–47
Lines of prior therapy		
≤2 prior lines	39 (11/28)	22–59
≥3 prior lines	18 (3/17)	4–43
Prior checkpoint inhibitors	24 (4/17)	7–50
Prior platinum and checkpoint inhibitors	27 (4/15)	8–55

Best percent change in tumour size from baseline in patients with mUC

*0% change with best overall response of PD; †Shrinkage of target lesions of >30%, but unconfirmed, hence classified as SD; ‡CR based on shrinkage of lymph node target lesions to <10 mm; §100% reduction of target lesions, but stable persistence of a non-target lesion, hence classified as PR

Tagawa ST et al. ASCO GU 2019;Abstract 354.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Recent Developments in the Management of Urothelial Bladder Cancer

Module 2: Antibody-Drug Conjugates — Prof Powles

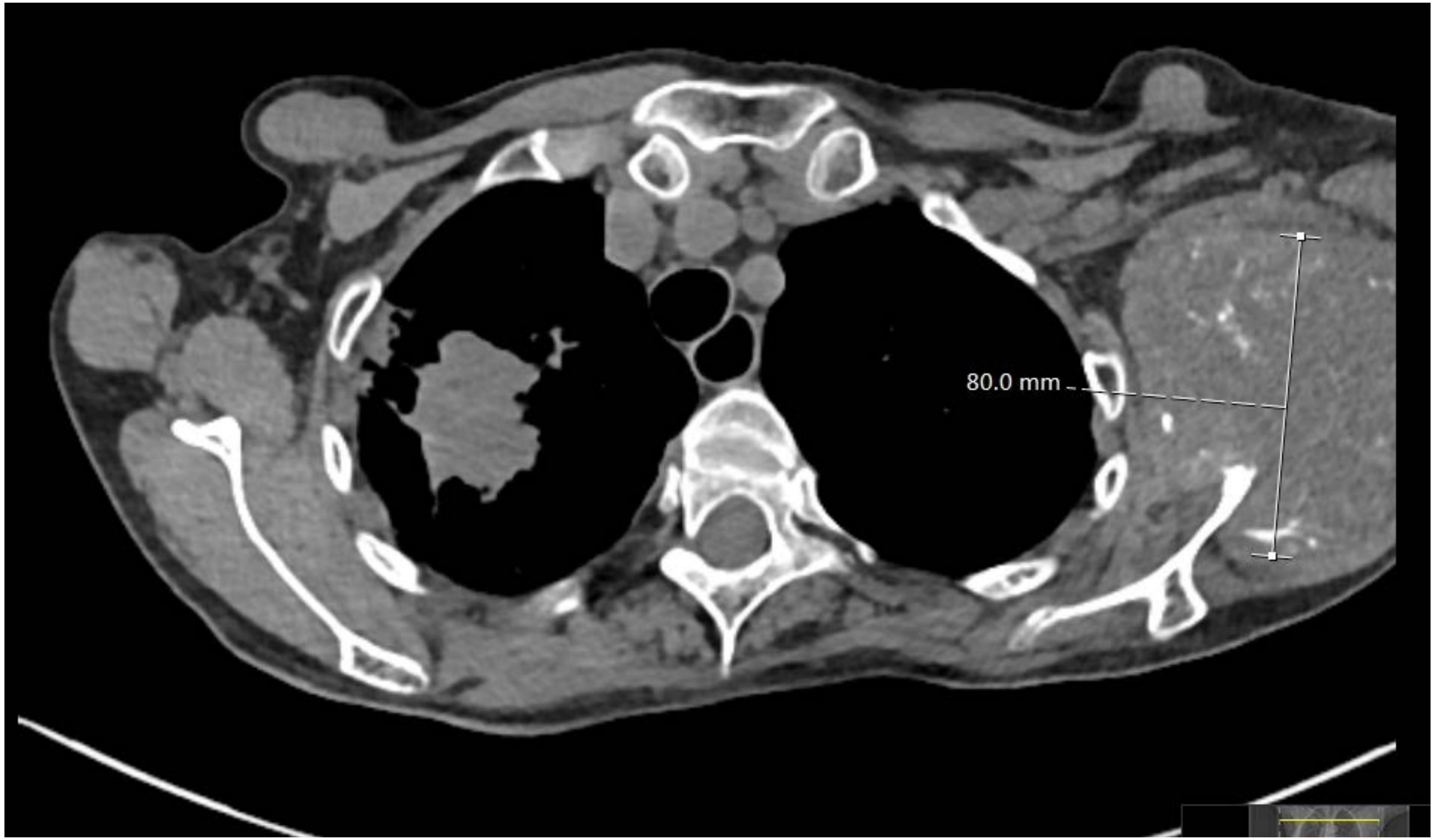
- Key Recent Data Sets
  - Enfortumab vedotin (EV) after platinum-based chemotherapy and immunotherapy (IO)
  - First-line EV in combination with pembrolizumab (chemotherapy)
  - Sacituzumab govitecan-hziy
- Faculty Case Discussion: 74-year-old man with metastatic UBC — Progression on chemotherapy, IO

Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC

Patient characteristics	74 year old male Performance status 1 Past medical history: heavy smoker, diet controlled diabetes and hypertension.
Tumor characteristics	FEB 2017 Neoadjuvant chemotherapy and cystectomy for T2N1M0 TCC bladder (Gem/cis x3). NOV 2018: CT scan shows 1.4 cm lung mets. Creatinine clearance 45ml/min
Options	Treated with gemcitabine and carboplatin chemotherapy X6 Grade 3 haematological toxicity, Grade 2 fatigue and diarrhoea. CT scan shows progressive disease 3 months after completion of treatment.

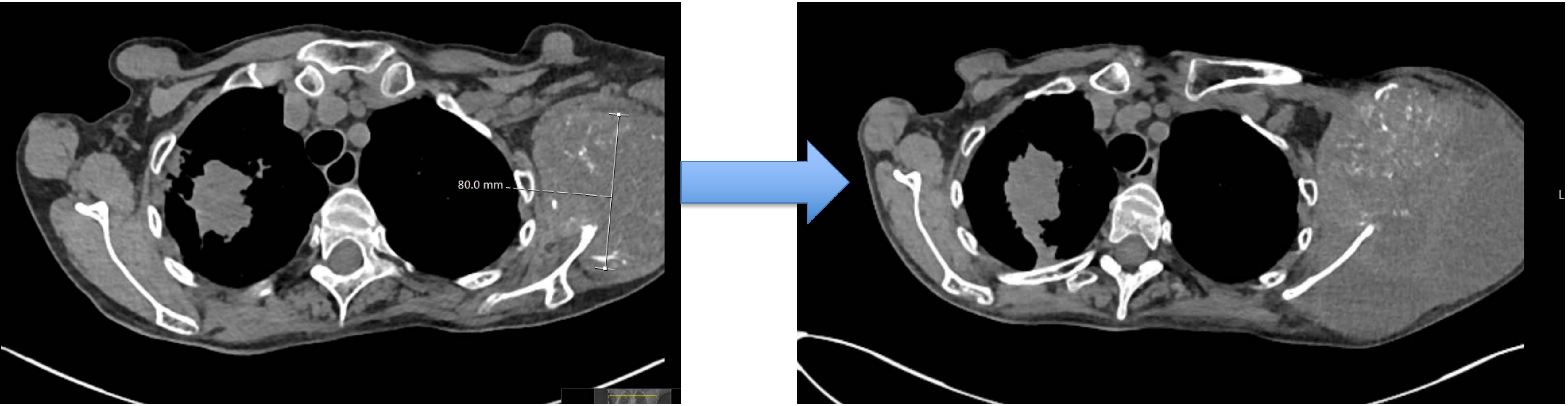
Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

Started immune checkpoint inhibition.



Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

Rapid progression of disease after 2 cycles.



More pain and symptoms.

Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

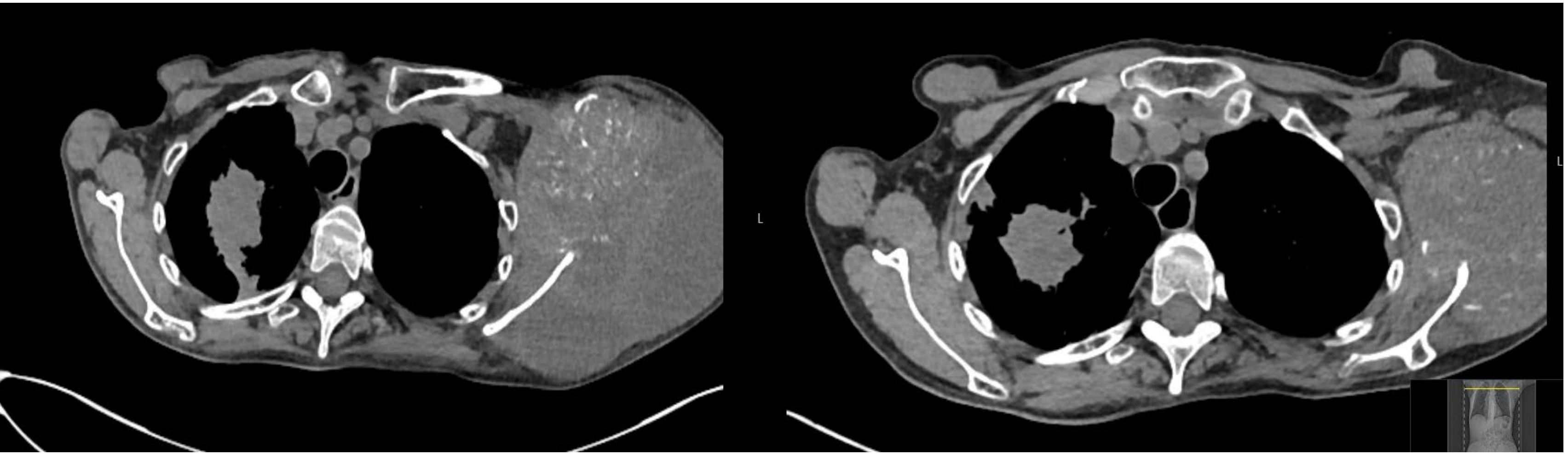
Enfortumab vedotin: Day 1, 8, 15 on 28 day cycles.

Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

Enfortumab vedotin: Day 1, 8, 15 on 28 day cycles.

CT at 8 weeks= 45% reduction in target lesions. Rapid improvement in symptoms

Fatigue G2
Rash G1
Neuropathy G1

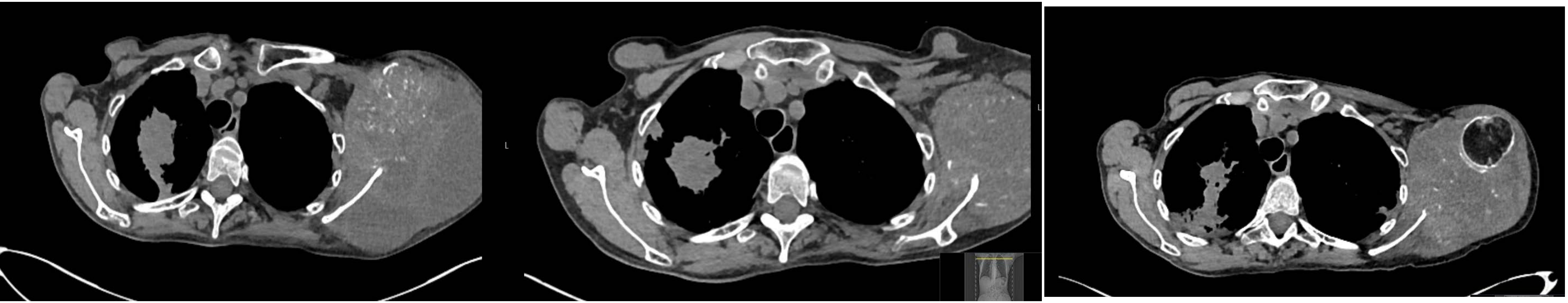


Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

Enfortumab vedotin: Day 1, 8, 15 on 28 day cycles.

CT at 16 weeks= 65% reduction in target lesions.

Fatigue G2
Rash G1
Neuropathy G2: dose reduction

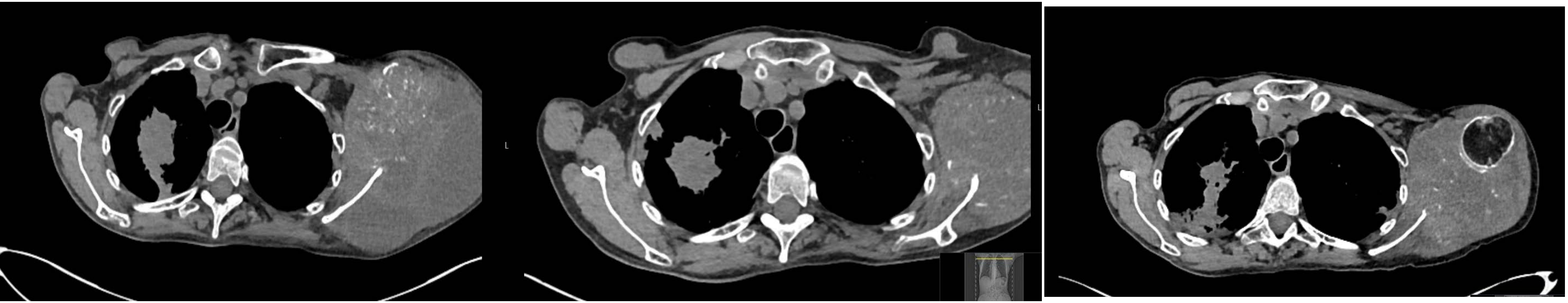


Case Presentation - Prof Powles: A 74-Year-Old Man with Metastatic UBC (continued)

Enfortumab vedotin: Day 1, 8, 15 on 28 day cycles.

CT at 16 weeks= 65% reduction in target lesions.

Fatigue G2
Rash G1
Neuropathy G2: dose reduction



Currently: Well on reduced dose, CT at 32 weeks shows SD (10% increase from nadir)

Recent Developments in the Management of Urothelial Bladder Cancer

Module 3: Erdafitinib — Dr Siefker-Radtke

- Key Recent Data Sets
  - Erdafitinib for metastatic FGFR-positive tumors after chemotherapy
- Faculty Case Discussion: 65-year-old man with metastatic UBC with FGFR3 S249C mutation and disease progression on chemotherapy

Paradigm shift in urothelial cancer

- Urothelial cancer is no longer just one disease

"Basal"

- Chemosensitive
- Immune signature
- Angiogenesis

Classification

- CK5/6+

Therapies

- GCb/DD-MVAC
- Immunotherapy
- Angiogenesis

"Basal-Claudin Low"

- Immune signature
- MDSC?
- Does autocrine FGFR signalling play a role?

Classification

- CK5/6+

Therapies

- IDO-IO?
- FGFR inhibitor + IO

"Luminal-P53-like"

- Stromal enrichment
- Chemoresistance
- Immune signature
- Bone metastases

Classification

- CK20+ or GATA3+
- Lack *FGFR* mutations or translocations
- ERBB2-

Therapies

- Immunotherapy
- Bone-targeting agents

"Luminal"

- FGFR-PPAR-ɣ
- Intermediate chemosensitive
- Immunoquiescent

Classification

- *FGFR3* mutations
- *FGFR* translocations
- CK20+ or GATA3+
- ERBB2-

Therapies

- FGFR inhibitors (+IO)
- TUR, initial surgery

"Luminal"

- ERBB2+
- Chemosensitive

Classification

- ERBB2+
- CK20+ or GATA3+
- WT FGFR

Therapies

- Chemotherapy
- HER2-targeted therapies

CK, cytokeratin; HER2, human epidermal growth factor receptor 2; IDO-IO; indoleamine 2,3-dioxygenase immuno-oncology; MDSC, myeloid-derived suppressor cells; WT, wild type.

Siefker-Radtke AO, et al. ASCO 2018

Courtesy of Arlene O. Siefker-Radtke, MD

Bladder cancer is composed of multiple tumors: Subtypes within subtypes

	Luminal Papillary	Luminal Non-Specified	Luminal Unstable	Stroma-rich	Basal/Squamous	Neuroendocrine-like
	24%	8%	15%	15%	35%	3%
Differentiation	Urothelial / Luminal				Basal	Neuroendocrine
Oncogenic mechanisms	FGFR3 ++ CDKN2A -	PPAR-γ ++	PPAR-γ ++ E2F3 +, ERBB2 + Genomic instability		EGFR +	TP53 --, RB1 --, Cell cycle +
Mutations	*FGFR3* (40%), *KDM6A* (38%), *STAG2* (22%)	*ELF3* (35%)	*TP53* (76%), *ERCC2* (22%) TMB +, APOBEC +		*TP53* (61%), *RB1* (25%)	*TP53* (94%) *RB1* (39%)
Stromal infiltrate		Fibroblasts		Smooth muscle Fibroblasts Myofibroblasts	Fibroblasts Myofibroblasts	
Immune infiltrate				B cells	CD8 T cells NK cells	
Histology	Papillary morphology	Micropapillary variants			Squamous differentiation	Neuroendocrine differentiation
Clinical	T2 stage +	Older patients + (80+)			Women + T3/T4 stage +	
Median overall survival (years)	4	1.8	2.9	3.8	1.2	1

APOBEC, apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like; CDKN2A, cyclin-dependent kinase Inhibitor 2A; E2F3, E2F transcription factor 3; NK, natural killer; TMB, tumour mutation burden.

Kamoun A, et al. 2019. Epub ahead of print date.

Courtesy of Arlene O. Siefker-Radtke, MD

FGFR as a target:
The immunologically “cold” tumour

Courtesy of Arlene O. Siefker-Radtke, MD

Abstract 4503

First Results From the Primary Analysis Population of the Phase 2 Study of Erdafitinib (JNJ-42756493) in Patients With Metastatic or Surgically Unresectable Urothelial Carcinoma and *FGFR* Alterations

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on behalf of the BLC2001 Study Group sponsored by Janssen Research & Development

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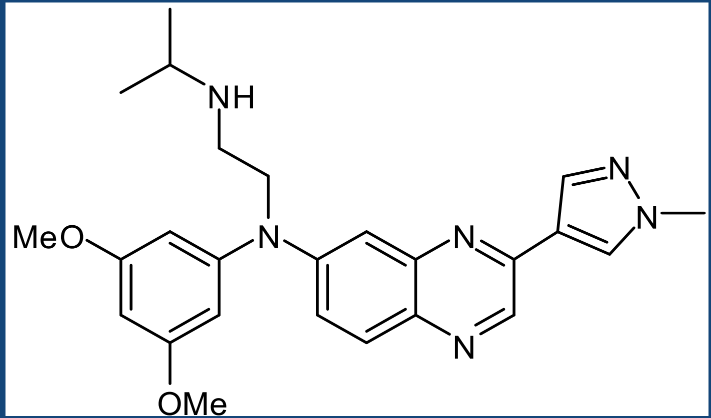
Erdafitinib Is a Potent FGFR Inhibitor

- Erdafitinib* is an oral pan-FGFR (1-4) inhibitor with IC_{50} in the single-digit nanomolar range[1]
- Erdafitinib is taken up by lysosomes, resulting in sustained intracellular release, which may contribute to its long-lasting activity[1]
- Erdafitinib has demonstrated promising activity in patients with metastatic or unresectable UC and other histologies (eg, cholangiocarcinoma) with *FGFR* alterations[2-5]



**Investigational compound erdafitinib (JNJ-42756493) was discovered in collaboration with Astex Pharmaceuticals.*

Abbreviation: IC_{50}, drug concentration at which 50% of target enzyme activity is inhibited.

1. Perera TPS, et al. *Mol Cancer Ther*. 2017;16:1010-1020.
2. Tabernero J, et al. *J Clin Oncol*. 2015;33:3401-3408.
3. Soria J-C, et al. ESMO 2016. Abstract 781PD.
4. Loriot Y, et al. ASCO GU 2018. Abstract 411.
5. Siefker-Radtke A, et al. ASCO GU 2018. Abstract 450.

Phase 2 BLC2001 Study Design

Patients with metastatic or surgically unresectable locally advanced UC → Screening for *FGFR* fusions/ mutations on tissue by central lab → RANDOMIZATION

→ Regimen 1: 10 mg/d for 7 days on/7 days off

→ Regimen 2: 6 mg QD

Regimen 3[a]:
8 mg QD with PD
Uptitration to 9 mg QD
n = 99

Primary end point
ORR
Secondary end points
PFS, DoR, OS, safety, predictive biomarker evaluation, and PK

Patients
• Progression on ≥ 1 line prior systemic chemo or within 12 months of (neo)adjuvant chemo OR • Chemo-naïve: cisplatin ineligible per protocol criteria[b]
• Prior immunotherapy was allowed

Primary hypothesis:

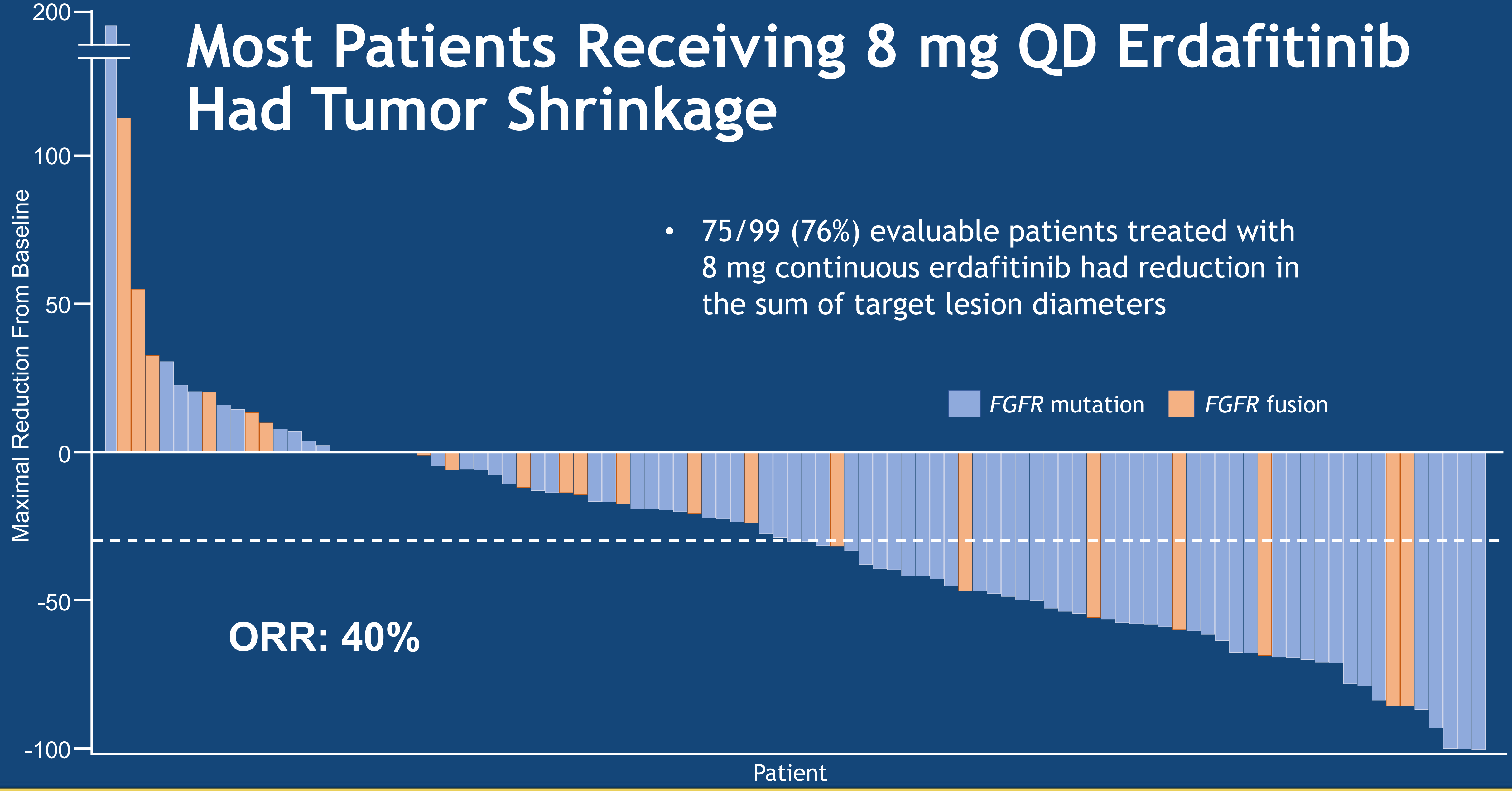
- ORR in Regimen 3 is > 25%
- One-sided α = 0.025
- 85% power

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

Abbreviations: DoR, duration of response; PD, pharmacodynamics; PFS, progression-free survival; PK, pharmacokinetics; QD, daily; TRAEs, treatment-related adverse events.

Most Patients Receiving 8 mg QD Erdafitinib Had Tumor Shrinkage

- 75/99 (76%) evaluable patients treated with 8 mg continuous erdafitinib had reduction in the sum of target lesion diameters



Response to Erdafitinib in a Patient With Liver Metastases

Baseline

First Restaging (6 weeks)

Second Restaging (12 weeks)

Percentage changes in sum of longest diameters:	-53%	-82%

Images provided by Dr. Arlene Siefker-Radtke

Most Common Treatment-Related AEs (TRAEs)

Reported in >20% of patients	8 mg continuous dose (n = 99)	
Patients with TRAEs, n (%)	Any grade	Grade 3
Hyperphosphatemia	72 (73)	2 (2)
Stomatitis	54 (55)	9 (9)
Dry mouth	43 (43)	0
Diarrhea	37 (37)	4 (4)
Dysgeusia	35 (35)	1 (1)
Dry skin	32 (32)	0
Alopecia	27 (27)	0
Decreased appetite	25 (25)	0
Hand-foot syndrome	22 (22)	5 (5)
Fatigue	21 (21)	2 (2)

Most were grade 1 or 2

There were no grade 4 or 5 TRAEs

Serious TRAEs were reported in 9 patients (9%); none was reported in more than 1 patient

Conclusions

FDA Accelerated Approval 4/2019

- The trial met its primary end point, with a 40% ORR
- Median PFS was 5.5 months and median OS was 13.8 months
- Erdafitinib 8 mg/d was well tolerated, with a safety profile that allows continuous dosing and uptitration to 9 mg/d in patients whose serum phosphate remained < 5.5 mg/dL
- On the basis of the results from the Phase II BLC2001 trial, the FDA has granted accelerated approval to erdafitinib for patients with previously treated locally advanced or metastatic urothelial carcinoma with susceptible FGFR3 or FGFR2 genetic alterations (April 2019)
- Patients with *FGFR* alterations responded poorly to prior IO (5% ORR)
- Erdafitinib is being investigated further in patients with UC
  - Phase 3 THOR trial of erdafitinib versus chemotherapy or pembrolizumab (NCT03390504)
  - Phase 1b/2 NORSE trial of erdafitinib plus PD-1 inhibitor cetrelimab (JNJ-63723283) (NCT03473743)

Do mutFGFR3 UC have greater benefit from IO or erdafitinib?

Courtesy of Arlene O. Siefker-Radtke, MD

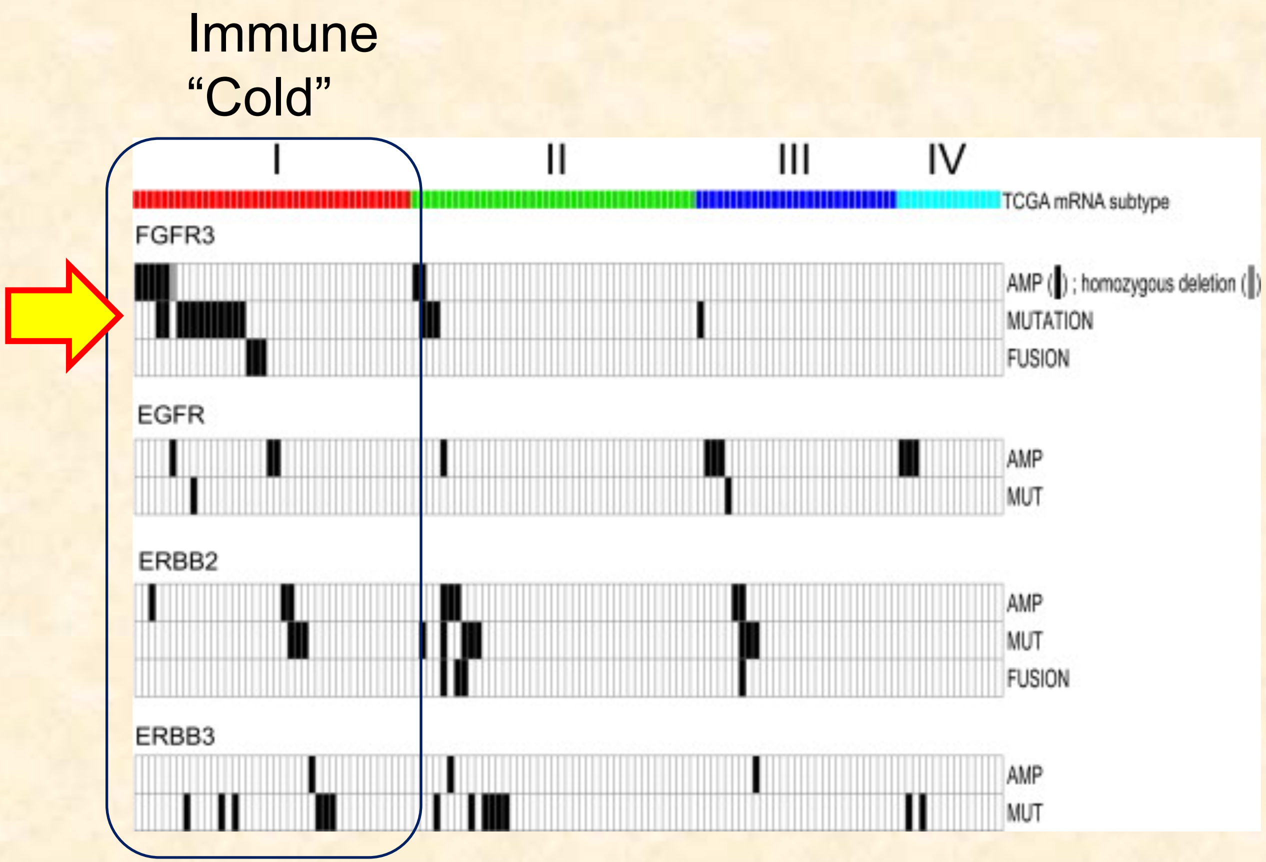


Fig. 3. Distribution of clinically actionable mutations in receptor tyrosine kinases in the intrinsic subtypes in the TCGA cohort. Clusters I and II correspond to the luminal tumors, and clusters III and IV are basal; cluster IV contains tumors that have under...

David J. McConkey, Woonyoung Choi, Andrea Ochoa, Arlene Siefker-Radtke, Bogdan Czerniak, Colin P.N. Dinney

Therapeutic Opportunities in the Intrinsic Subtypes of Muscle-Invasive Bladder Cancer

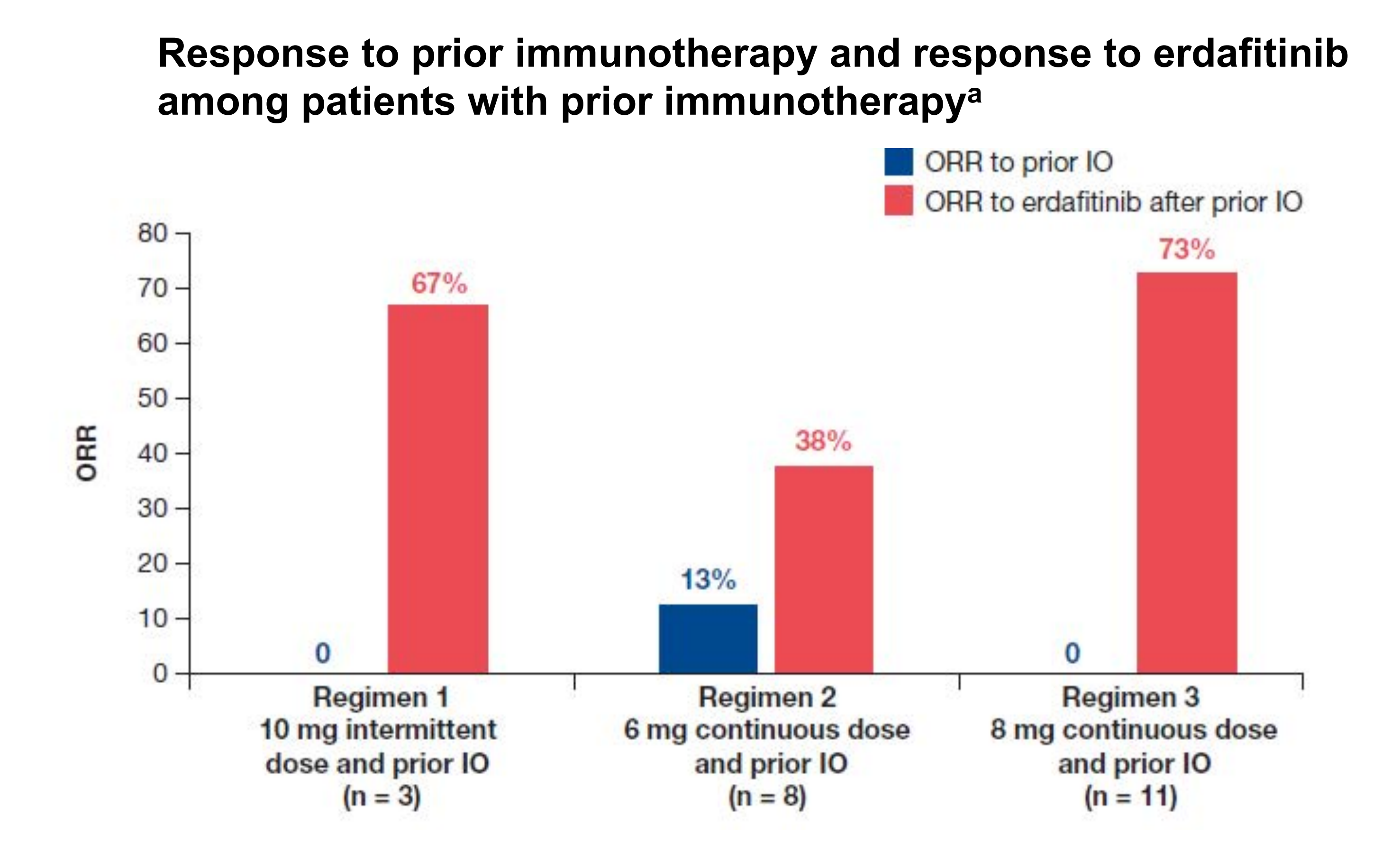
Hematology/Oncology Clinics of North America, Volume 29, Issue 2, 2015, 377–394

http://dx.doi.org/10.1016/j.hoc.2014.11.003

Courtesy of Arlene O. Siefker-Radtke, MD

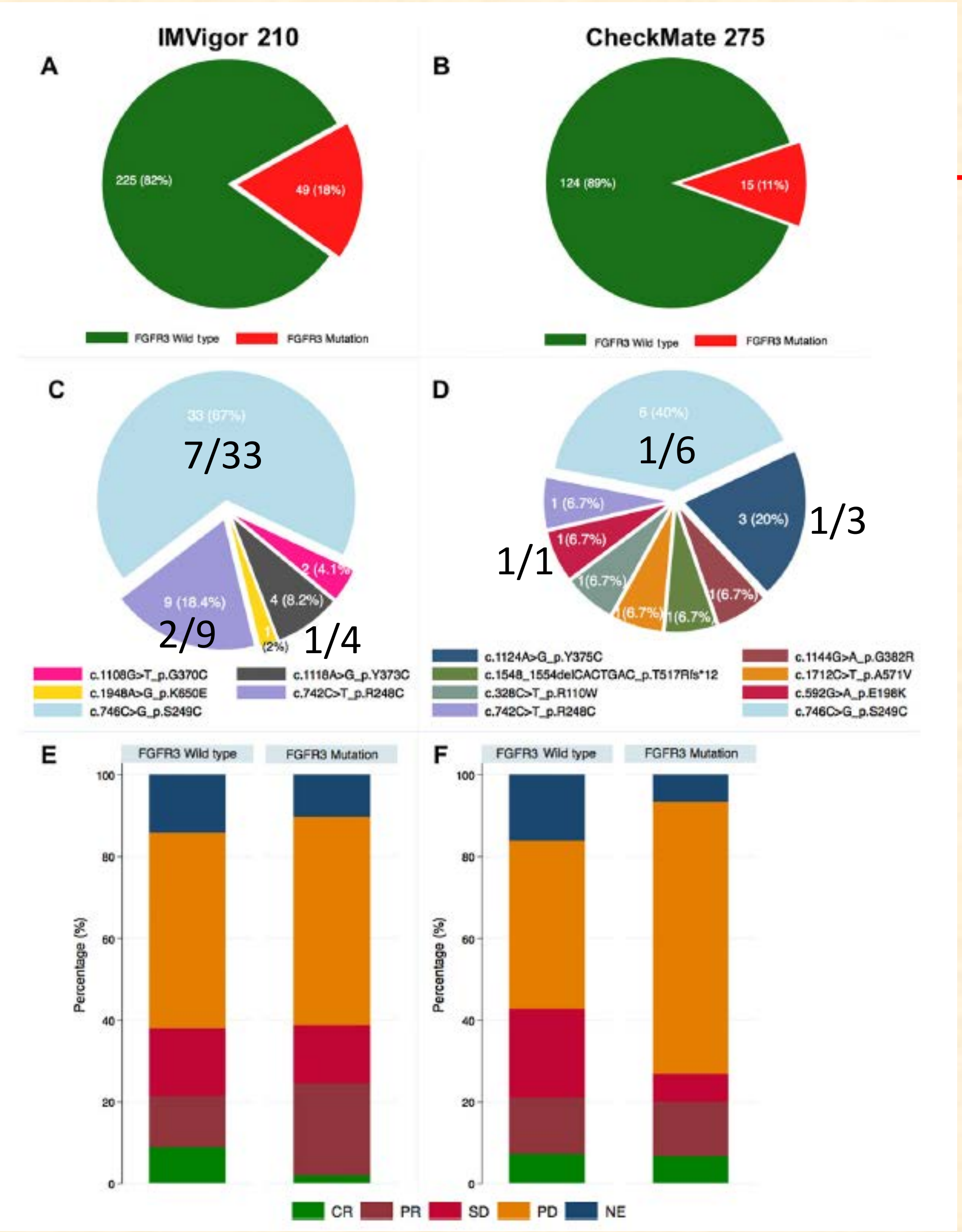
Patients with FGFR alterations may respond to FGFR inhibition better than to immuno-oncology therapy

- ORR prior to IO therapy: 1/22 (5%)
- Response was not durable
    - TTNT 10 months following PR to IO therapy
- Median TTNT following IO: 3.2 months (range 2–10 months, 95% CI 4.8)
- ORR with erdafitinib: 59%
- Limitations: small numbers, excellent responders to IO may not have progressed



Siefker-Radtke AO, et al. Abstract presented at ASCO 2018; abstract 450; NEJM 2019

Courtesy of Arlene O. Siefker-Radtke, MD



Do FGFR3 mutations respond to IO?

- Patients from 2nd line Atezolizumab and nivolumab trials
- Mutation (any) FGFR3
    - Nivo N = 15
        - ORR (PR/CR) 3/15 (20%)
        - “Known hotspot” n=12 (20%)
    - Atezo N = 49
        - ORR : 10/49 (21%)

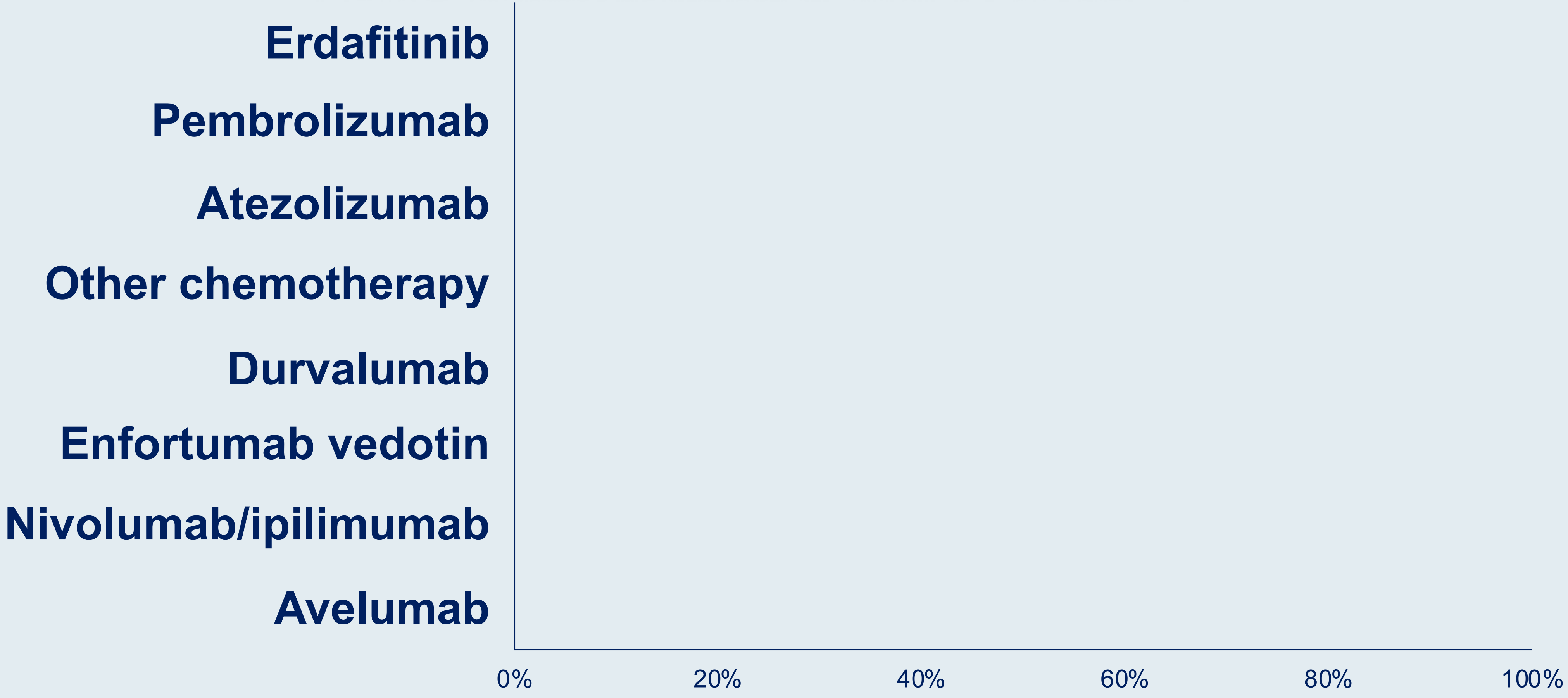
- CD8 T-cell signature: lower in mutant FGFR3 (P<0.001)
- No difference in TMB
- Lower TGF-B signature p<0.001
- Stromal signature lower in FGFR3 mutant (p=0.01)

- Limitations include small numbers, enrichment for PD-L1+ cohorts
- Information on durability of response, other driver mutations N/A

Galsky et al. Brief Correspondence Eur Urol 2019

Courtesy of Arlene O. Siefker-Radtke, MD

What would you generally recommend for a patient who experiences disease recurrence in the liver 18 months after neoadjuvant chemotherapy and cystectomy for muscle-invasive UBC and is found to have an FGFR3 mutation?



Survey of 50 US-based medical oncologists

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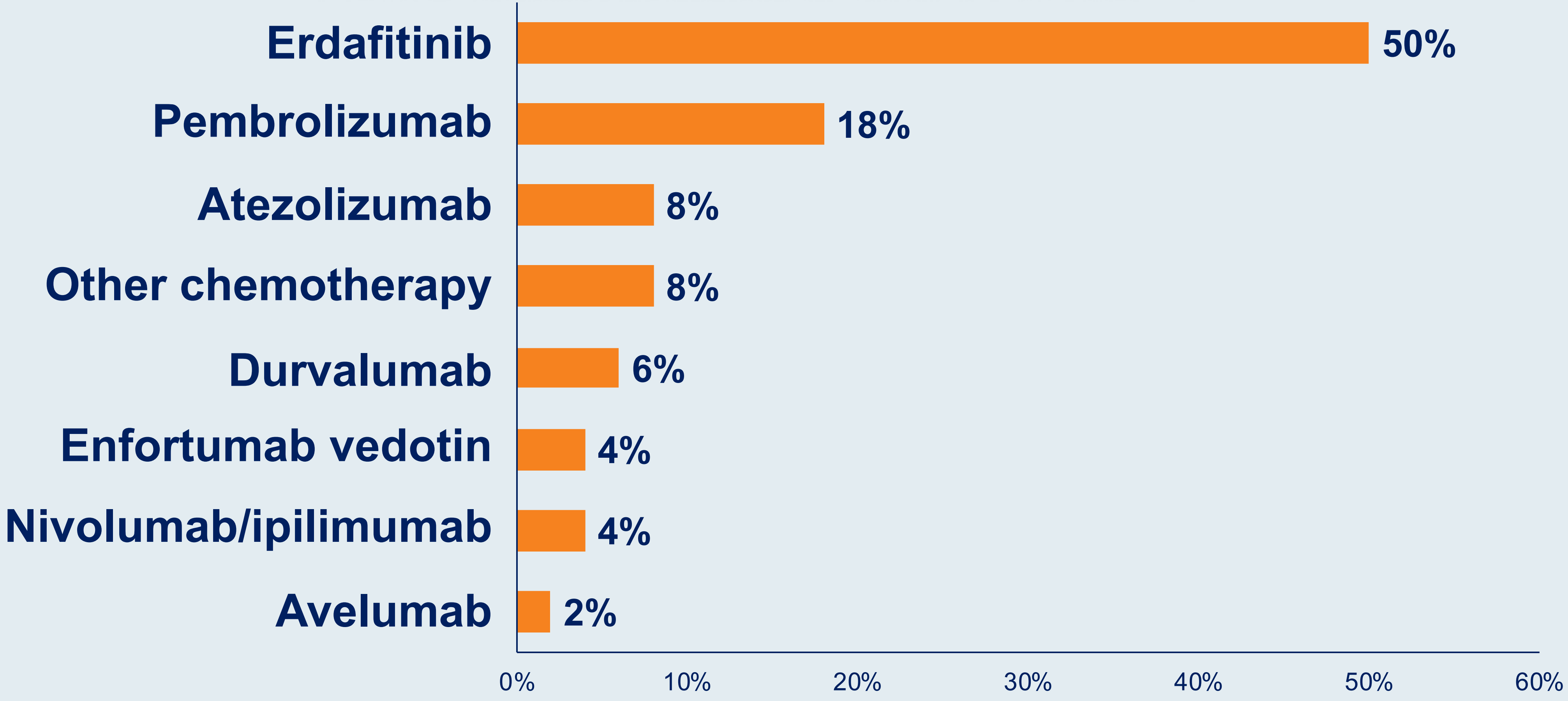
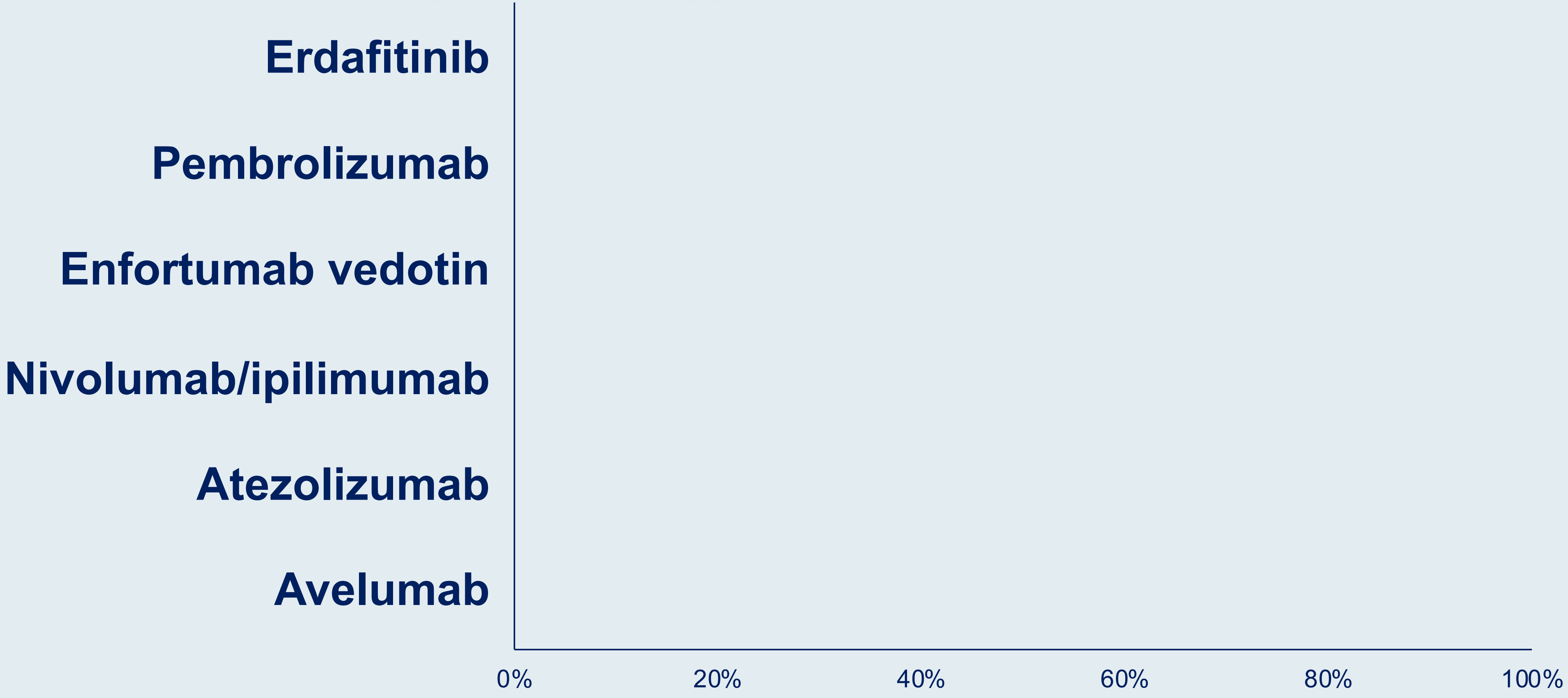


Survey of 50 US-based medical oncologists

What would you generally recommend as second-line therapy for a patient with UBC metastatic to the liver whose disease progresses on first-line cisplatin/gemcitabine and who is found to have an FGFR3 mutation?



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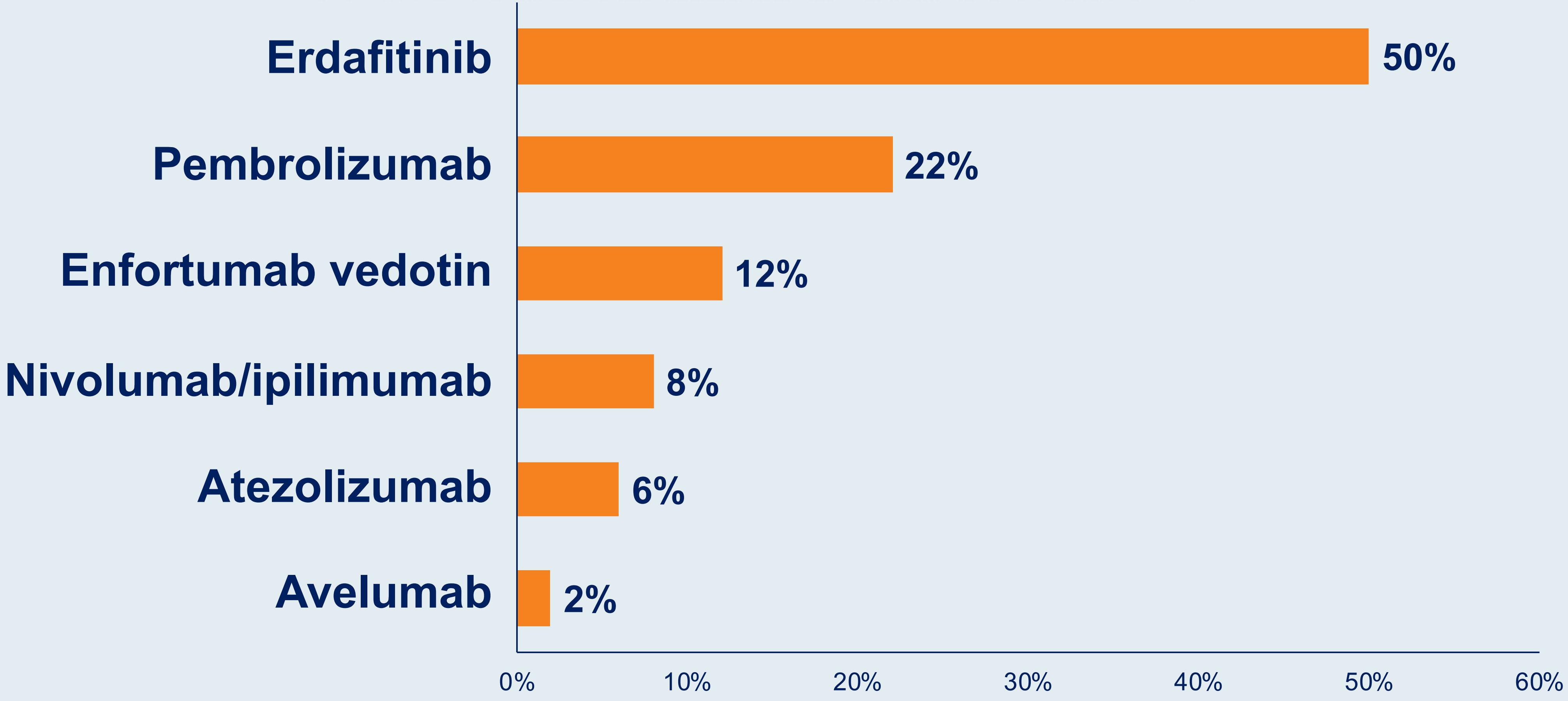

Survey of 50 US-based medical oncologists

Recent Developments in the Management of Urothelial Bladder Cancer

Module 3: Erdafitinib — Dr Siefker-Radtke

- Key Recent Data Sets
  - Erdafitinib for metastatic FGFR-positive tumors after chemotherapy
- Faculty Case Discussion: 65-year-old man with metastatic UBC with FGFR3 S249C mutation and disease progression on chemotherapy

Case Presentation – Dr Siefker-Radtke: A 65-Year-Old Man with Metastatic UBC and an FGFR3 S249C mutation

A 65 year old man was diagnosed with a cT2N0 bladder cancer, treated with neoadjuvant chemotherapy with DDMVAC in 12/2018, and had pT3bN+ disease at surgery. In 7/2019, his CT images show evidence of rapidly progressive disease with extensive liver metastases. His creatinine clearance is 45 ml/min. Mutation testing confirms an FGFR3 S249C mutation.

Case Presentation – Dr Siefker-Radtke: A 65-Year-Old Man with Metastatic UBC and an FGFR3 S249C mutation (continued)

You would recommend:

a. Front-line systemic chemotherapy for metastatic disease with gemcitabine/cisplatin.
b. Front-line systemic chemotherapy for metastatic disease with gemcitabine/carboplatin.
c. Second-line therapy with an immune checkpoint inhibitor.
d. Second-line therapy with erdafitinib.
e. Second-line systemic chemotherapy with gemcitabine and cisplatin since liver metastases do not respond well to immunotherapy or erdafitinib.

Case Presentation – Dr Siefker-Radtke: A 65-Year-Old Man with Metastatic UBC and an FGFR3 S249C mutation (continued)

D is the correct answer.

Patients who relapse within 12 months of their neoadjuvant or adjuvant chemotherapy are eligible for second-line therapies. Immune checkpoint inhibitors have a lower response rate in patients with liver metastases. Erdafitinib has been approved for second-line treatment of metastatic urothelial cancer with an FGFR3 mutation. Similar response rates were observed in visceral and non-visceral and liver metastases in patients treated with erdafitinib.

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

A Meet The Professor Series

Tuesday, August 4, 2020
1:00 PM – 2:00 PM ET

Faculty

Shaji K Kumar, MD

Moderator

Neil Love, MD

Co-provided by USF Health RTP Research To Practice

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