Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Urothelial Update

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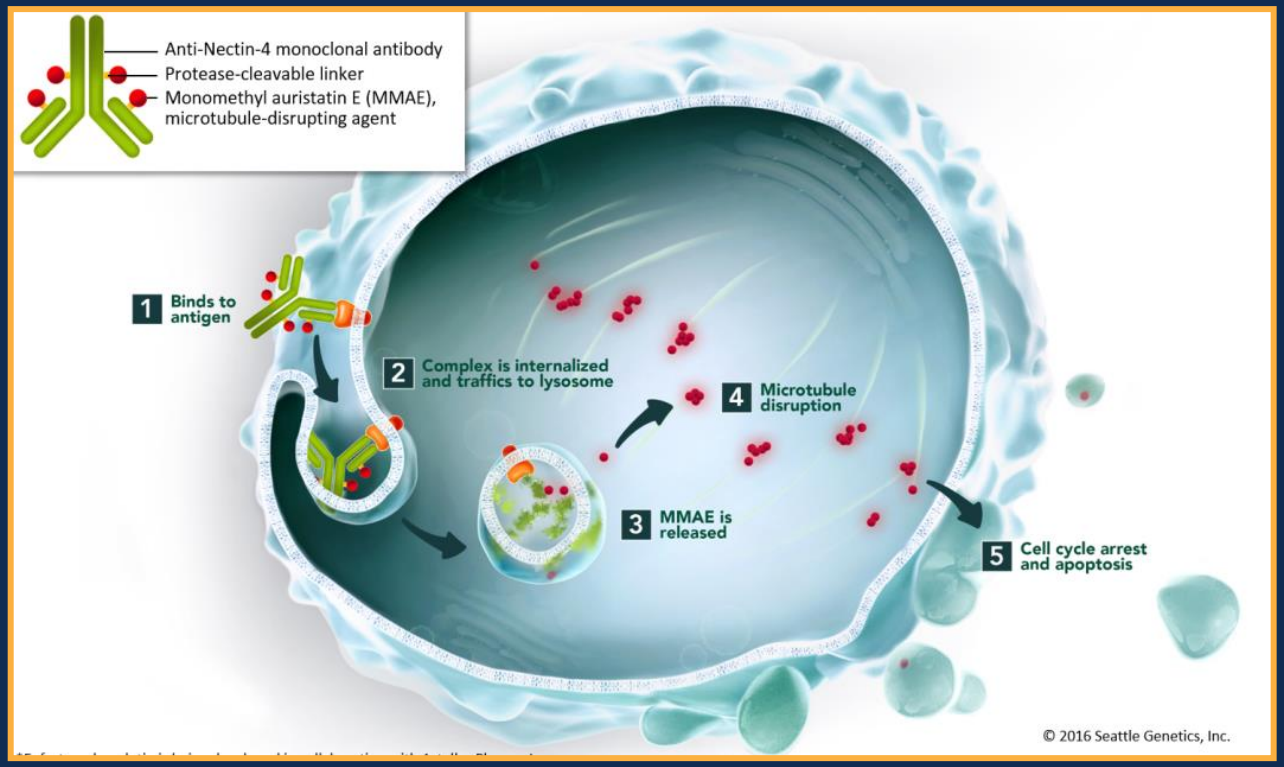
Disclosures

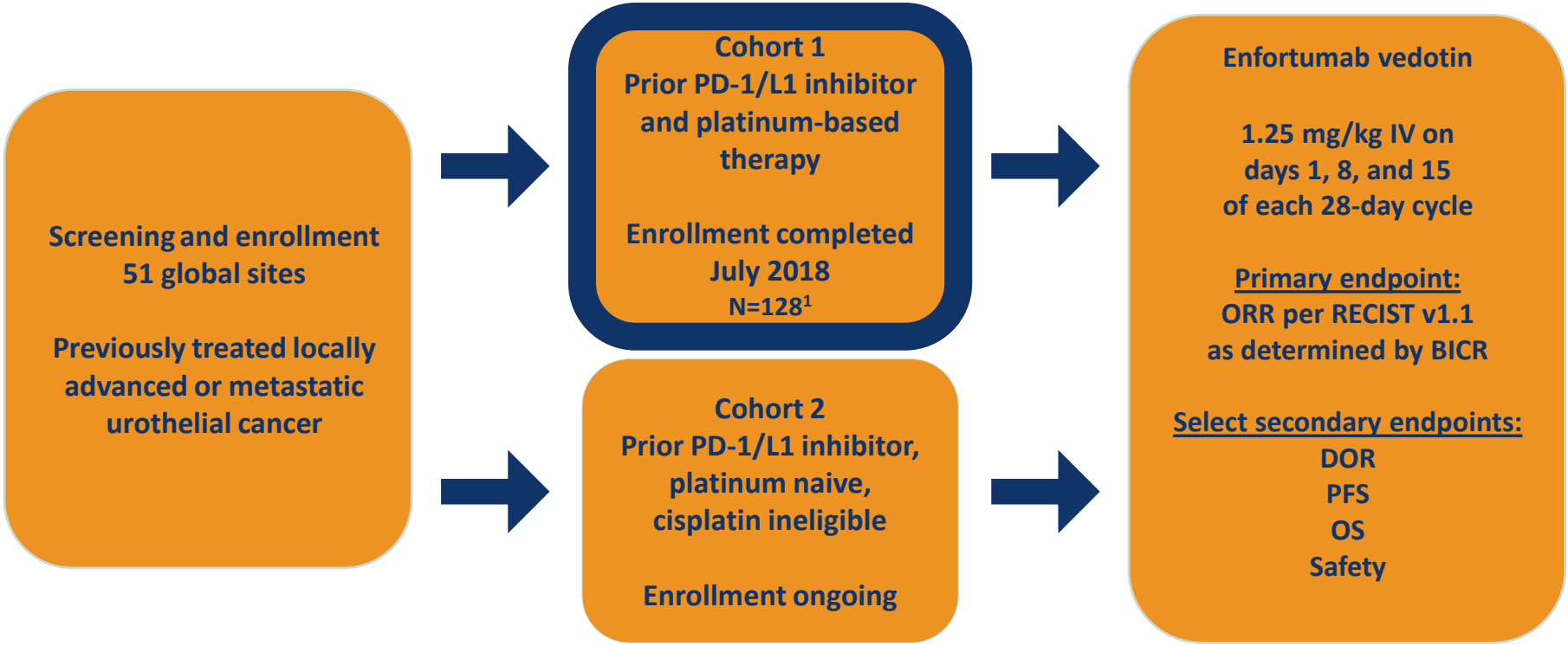
- **Consulting Fees:** Ada Cap (Advanced Accelerator Applications) Amgen, Astellas, AstraZeneca, Bayer, Bicycle Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Clovis Oncology, Eli Lilly, Exelixis, Gilead Sciences, Incyte, Ipsen, Janssen, Mirati, Monopteros, Pfizer, Pharmacyclics, Regeneron, Roche, Seattle Genetics, Urogen
- **Contracted Research:** Ada Cap (Advanced Accelerator Applications), Agensys Inc, *Astellas, AstraZeneca, *Bayer, BioXcel Therapeutics, Bristol Myers Squibb, Clovis Oncology, Eisai, *Eli Lilly, *Endocyte, Genentech, Gilead Sciences, *Innocrin, MedImmune, Medivation, Merck, Mirati, *Novartis, Pfizer, *Progenics, Replimune, Roche, *Sanofi Aventis, Seattle Genetics
- *Denotes study trials that have terminated
- **Ownership Interest Less Than 5%**: Bellicum (Sold 7/2020), Tyme (sold 10/2019)

Enfortumab Vedotin: Proposed Mechanism of Action



Enfortumab Vedotin is being co-developed by Seattle Genetics, Inc. and Astellas Pharma Inc.

EV-201: Single-Arm, Pivotal Phase 2 Trial



[1] 3 patients did not receive enfortumab vedotin treatment:
one each due to clinical deterioration, patient decision, and low hemoglobin after enrollment

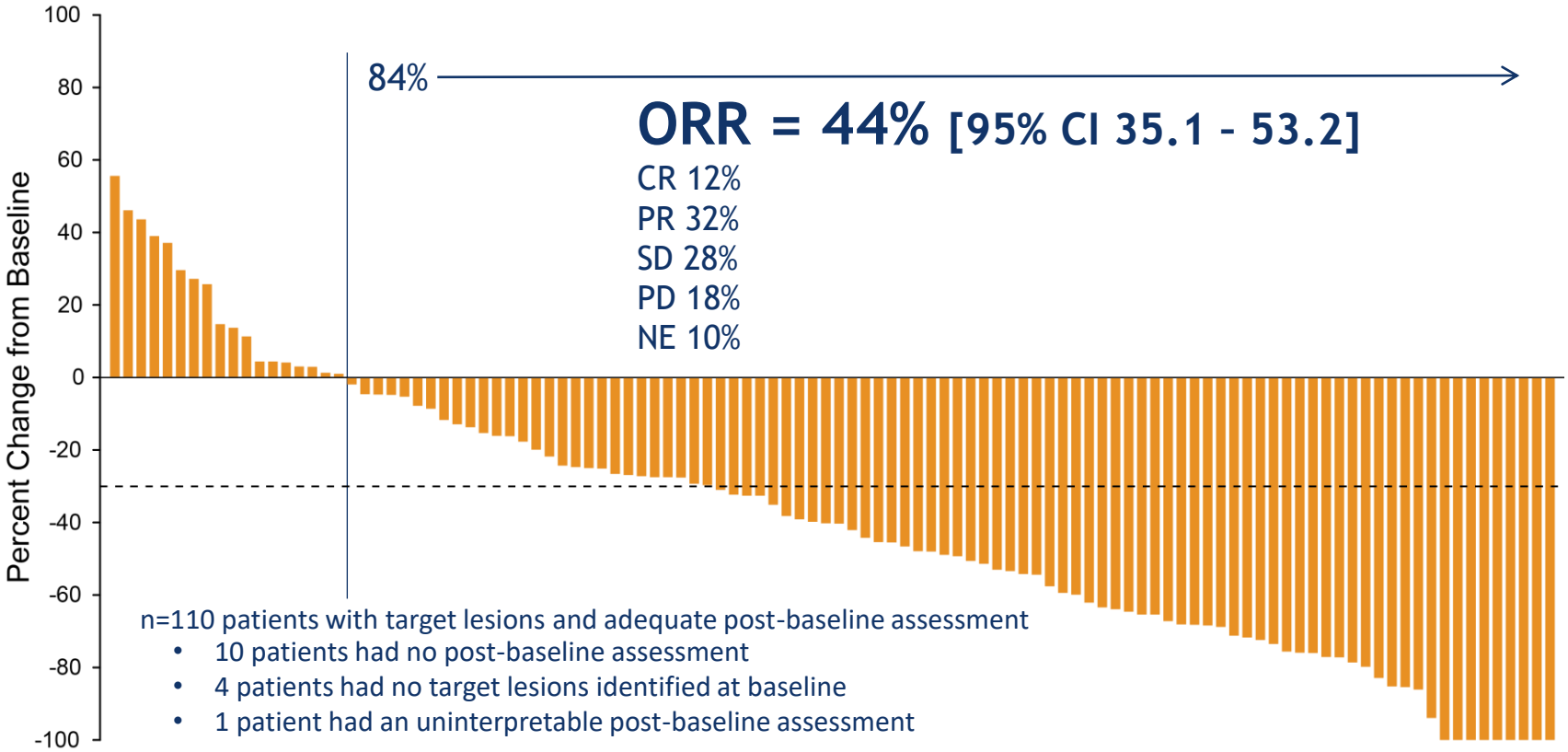
BICR=blinded independent central review; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival

EV-201: Cohort 1 Demographics and Disease Characteristics

	Patients (N=125)
Male sex, n (%)	88 (70)
Age, years	
Median (min, max)	69 (40, 84)
≥75 years, n (%)	34 (27)
ECOG PS of 1, n (%)	85 (68)
Primary tumor location, n (%)	
Bladder/other	81 (65)
Upper tract	44 (35)
Number of prior systemic therapies[1], median (range)	3 (1, 6)
≥2 Bellmunt adverse prognostic factors	52 (42)
Metastasis sites, n (%)	
Lymph nodes only	13 (10)
Visceral disease	112 (90)
Liver	50 (40)
PD-L1 status by combined positive score[2]	
<10	78/120 (65)
≥10	42/120 (35)

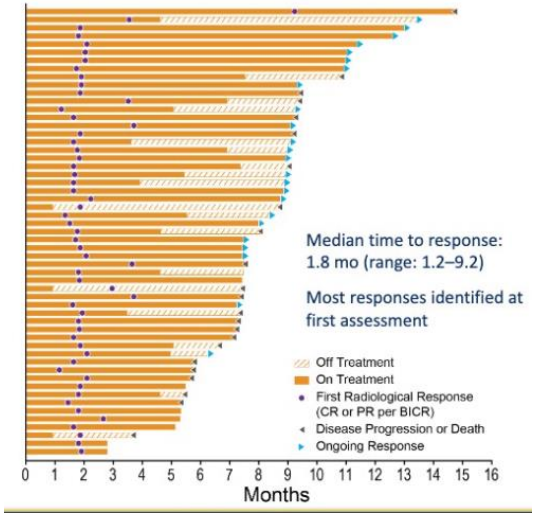
[1] Patients with 1 prior therapy had platinum and a PD-1/L1 inhibitor in combination; [2] Five patients were not evaluable for PD-L1

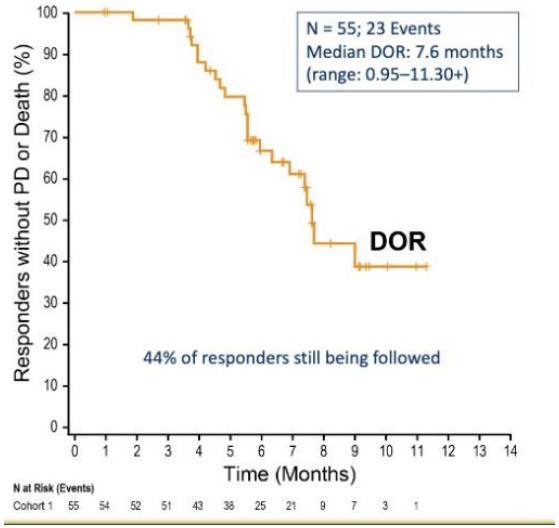
EV-201: Cohort 1 Change in Tumor Measurements per BICR



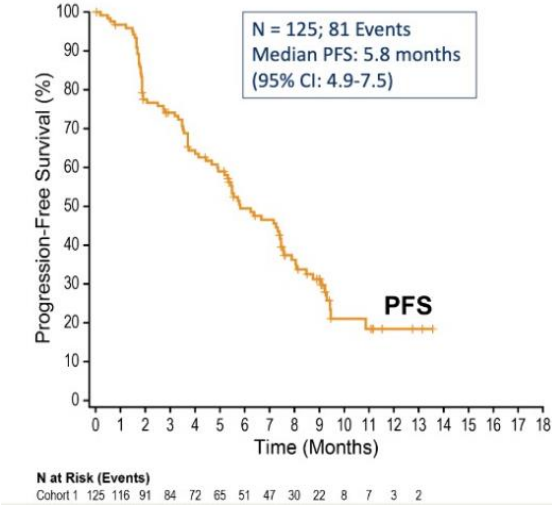
n=110 patients with target lesions and adequate post-baseline assessment

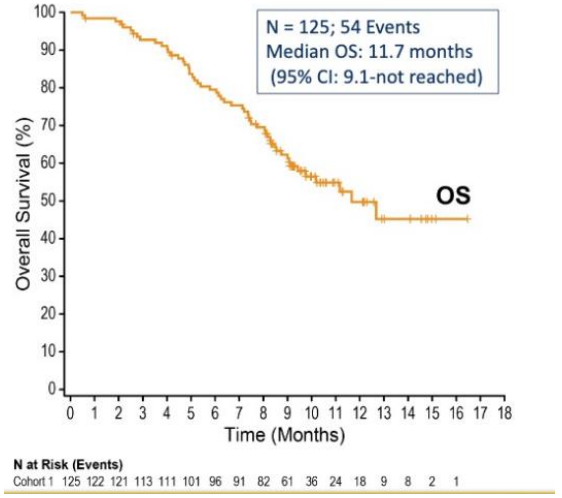
- 10 patients had no post-baseline assessment
- 4 patients had no target lesions identified at baseline
- 1 patient had an uninterpretable post-baseline assessment





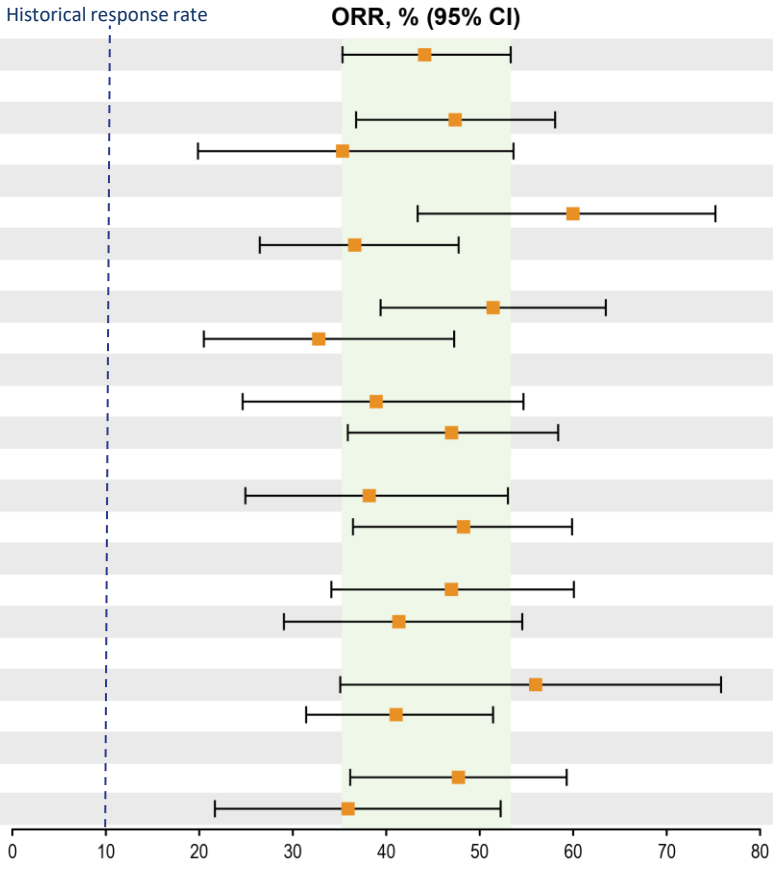
- Short time to response
- Median DOR 7.6 mo
- PFS 5.8 mo
- OS 11.7 mo





EV-201: Cohort 1 Responses by Subgroup per BICR

Subgroup	n/N	% (95% CI)
Overall	55/125	44 (35.1, 53.2)
Age		
<75	43/91	47 (36.7, 58.0)
≥75	12/34	35 (19.7, 53.5)
ECOG performance status, n (%)		
Grade 0	24/40	60 (43.3, 75.1)
Grade 1	31/85	36 (26.3, 47.6)
Bellmunt risk score[1]		
0–1	37/72	51 (39.3, 63.3)
≥2	17/52	33 (20.3, 47.1)
Primary tumor sites		
Upper tract	17/44	39 (24.4, 54.5)
Bladder/Other	38/81	47 (35.7, 58.3)
Liver metastasis		
Yes	19/50	38 (24.7, 52.8)
No	36/75	48 (36.3, 59.8)
Number of prior therapies in metastatic UC setting		
1–2	29/62	47 (34.0, 59.9)
≥3	26/63	41 (29.0, 54.4)
Best response to prior PD-1/L1[2]		
Responder	14/25	56 (34.9, 75.6)
Non-responder	41/100	41 (31.3, 51.3)
PD-L1 expression[3]		
CPS <10	37/78	47 (36.0, 59.1)
CPS ≥10	15/42	36 (21.6, 52.0)



[1] Bellmunt risk score was not available for 1 patient; [2] Anti-PD-1 or anti-PD-L1 therapy;
[3] Five patients were not evaluable for PD-L1 expression levels.

Clinical Response With Enfortumab Vedotin in mUC Patients With or Without Prior CPI or Liver Metastases

	Prior CPI Treatment[a]	CPI-Naïve[a]	Liver Metastases[a]
	1.25 mg/kg (n=89)	1.25 mg/kg (n=23)	1.25 mg/kg (n=33)
Confirmed CR	**3.4%**	9%	0
Confirmed PR	**37%**	35%	39%
Confirmed ORR[b] (95% CI)	**40% (30.2, 51.4)**	44% (23.2, 65.5)	39% (22.9, 57.9)
SD	**34%**	17%	21%
DCR[b] (95% CI)	**74% (63.8, 82.9)**	61% (38.5, 80.3)	60% (42.1, 77.1)

Data cut-off date is April 9, 2018.
Data presented as n (%), unless otherwise indicated.
CR, complete response; CPI, checkpoint inhibitor, DCR, disease control rate (DCR=CR+PR+SD); PR, partial response; ORR, overall response rate (ORR=CR+PR); SD, stable disease.
[a]Evaluable patients must have at least one post-baseline assessment; responses assessed per RECIST 1.1.
[b]Data presented as % (95% CI); 95% CI based on the Clopper-Pearson method.

Jonathan E. Rosenberg

EV-201: Cohort 1 Treatment-Related Adverse Events

Treatment-related AEs by preferred term in ≥20% of patients (any Grade) or ≥5% (≥Grade 3)	Patients (N=125) n (%)	
	Any Grade	≥Grade 3
Fatigue	62 (50)	7 (6)
Alopecia	61 (49)	–
Decreased appetite	55 (44)	1 (1)
Dysgeusia	50 (40)	–
Peripheral sensory neuropathy	50 (40)	2 (2)
Nausea	49 (39)	3 (2)
Diarrhea	40 (32)	3 (2)
Dry skin	28 (22)	0
Weight decreased	28 (22)	1 (1)
Rash maculo-papular	27 (22)	5 (4)
Anemia	22 (18)	9 (7)
Neutropenia	13 (10)	10 (8)

- Treatment-related AEs led to few discontinuations (12%)
  - Peripheral sensory neuropathy was the most common (6%)
- **Peripheral neuropathy** = 50% (3% Gr ≥ 3)
  - Mostly sensory
  - 52% of pre-existing neuropathy worsened
  - 76% improved at follow up
- **Rash** = 48% (12% Gr ≥ 3)
  - 93% improved at follow up
- **Hyperglycemia** = 11% (6% Gr ≥ 3)
  - 32% pre-existing worsened
  - 71% improved at follow up

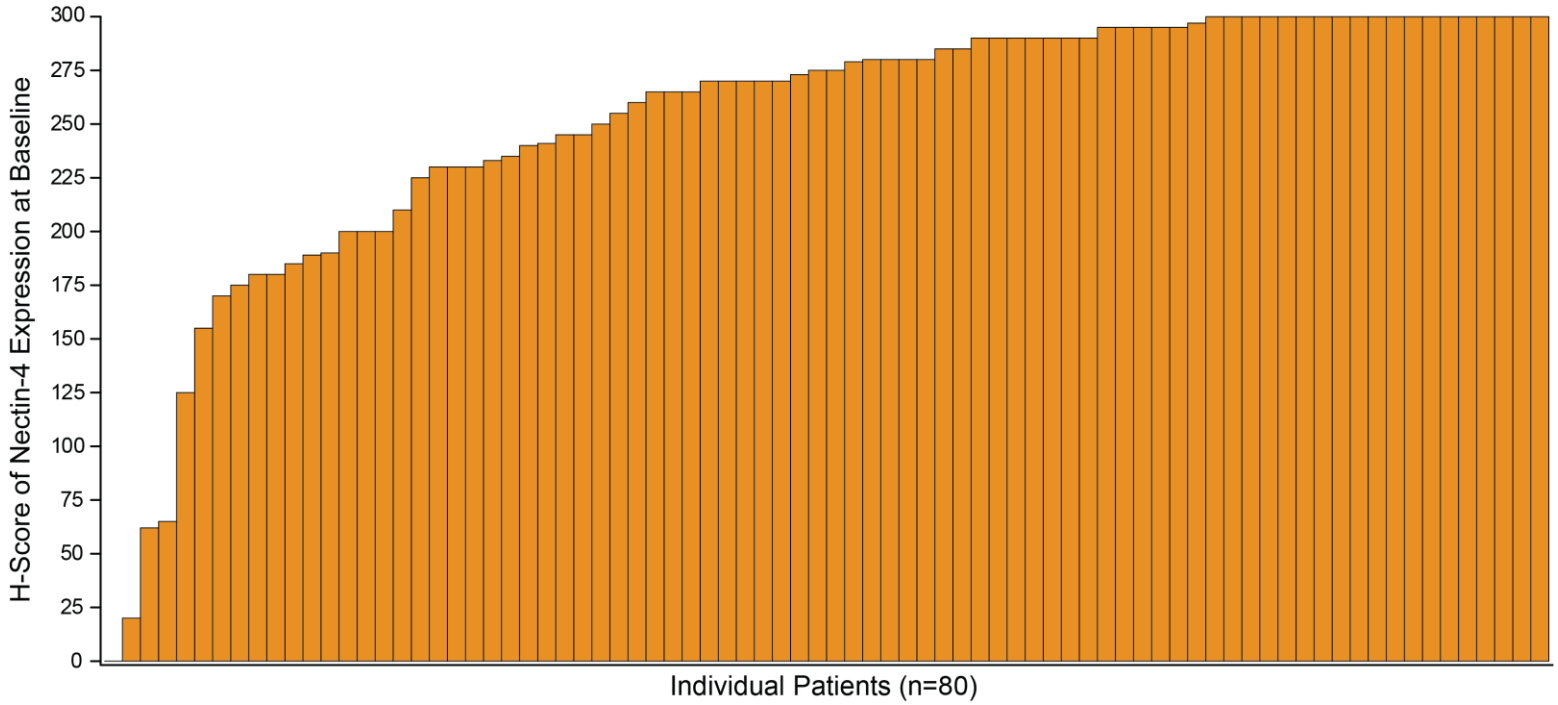
EV-201 Cohort 2: Key Demographics and Disease Characteristics

Characteristic	Patients (N=89)
Median age (range), years	75 (49, 90)
Male sex	66 (74%)
ECOG performance status	
0 or 1	78 (88%)
2	11 (12%)
Body mass index ≥30 kg/m^2	13 (15%)
Renal function based on creatinine clearance	
Normal/Mild decrease ≥60 mL/min	27 (30%)
Moderate decrease: ≥30 and <60 mL/min	60 (67%)
Severe decrease: ≥15 and <30 mL/min	2 (2%)

Characteristic	Patients (N=89)
Primary tumor location	
Upper tract[1]	38 (43%)
Bladder/other	51 (57%)
Metastasis sites	
Lymph nodes only	18 (20%)
Visceral disease[2]	70 (79%)
Liver	21 (24%)
Received prior PD-1/PD-L1 therapy in first line	87 (98%)
Responder[3] to PD-1/PD-L1-containing therapy	22 (25%)

[1]Includes renal pelvis and ureter.
[2]Sites of visceral disease include liver, lung, intra-thoracic or intra-abdominal soft tissue, kidney, spleen, ovary, adrenal glands, and bone.
[3]Responses were investigator reported.

EV-201 Cohort 2: Nectin-4 Expression



Median H-score 275 (range: 0-300)

Nectin-4 levels in tumor tissue were assessed by IHC.[1]

[1]IHC images were scored by a pathologist using the H-score method. (H-score = [percentage of strongly positive tumour cells x 3] + [percentage of moderately positive tumor cells x 2] + [percentage of weakly positive tumor cells x 1]). A score of 0 indicates no expression and a score of 300 indicates the maximum possible expression with this assay.
9 patients did not have adequate tissue for Nectin-4 testing.

EV-201 Cohort 2: Best Overall Response per BICR

ORR per RECIST v 1.1 assessed by BICR	Patients (N=89) %
Confirmed ORR, 95% CI[1]	52 (40.8, 62.4)
Best overall response[2]	
Confirmed complete response	20
Confirmed partial response	31
Stable disease	30
Progressive disease	9
Not evaluable[3]	9

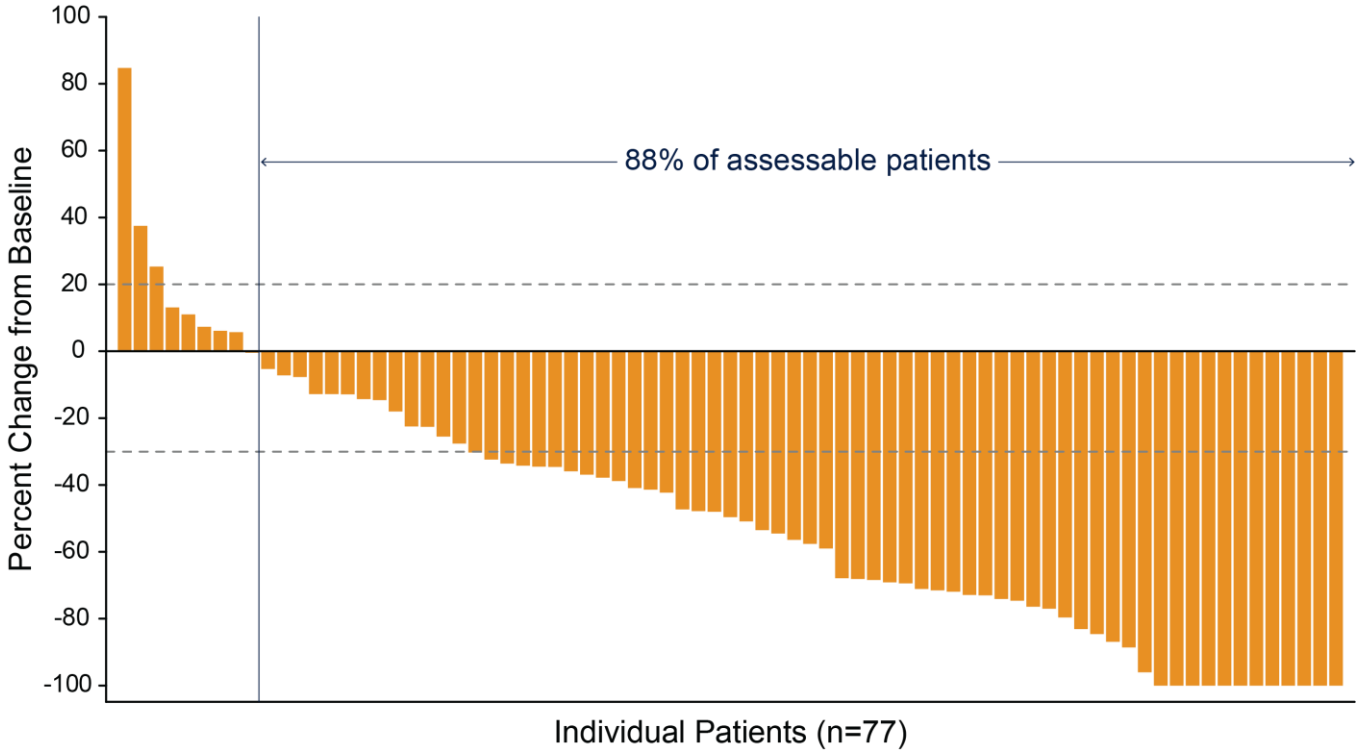
ORR = Objective Response Rate; RECIST = Response Evaluation Criteria in Solid Tumors; BICR = Blinded Independent Central Review

[1]CI = Confidence Interval, Computed using the Clopper-Pearson method

[2]Best overall response according to RECIST v1.1. Complete response and partial response were confirmed with repeat scans ≥28 days after initial response.

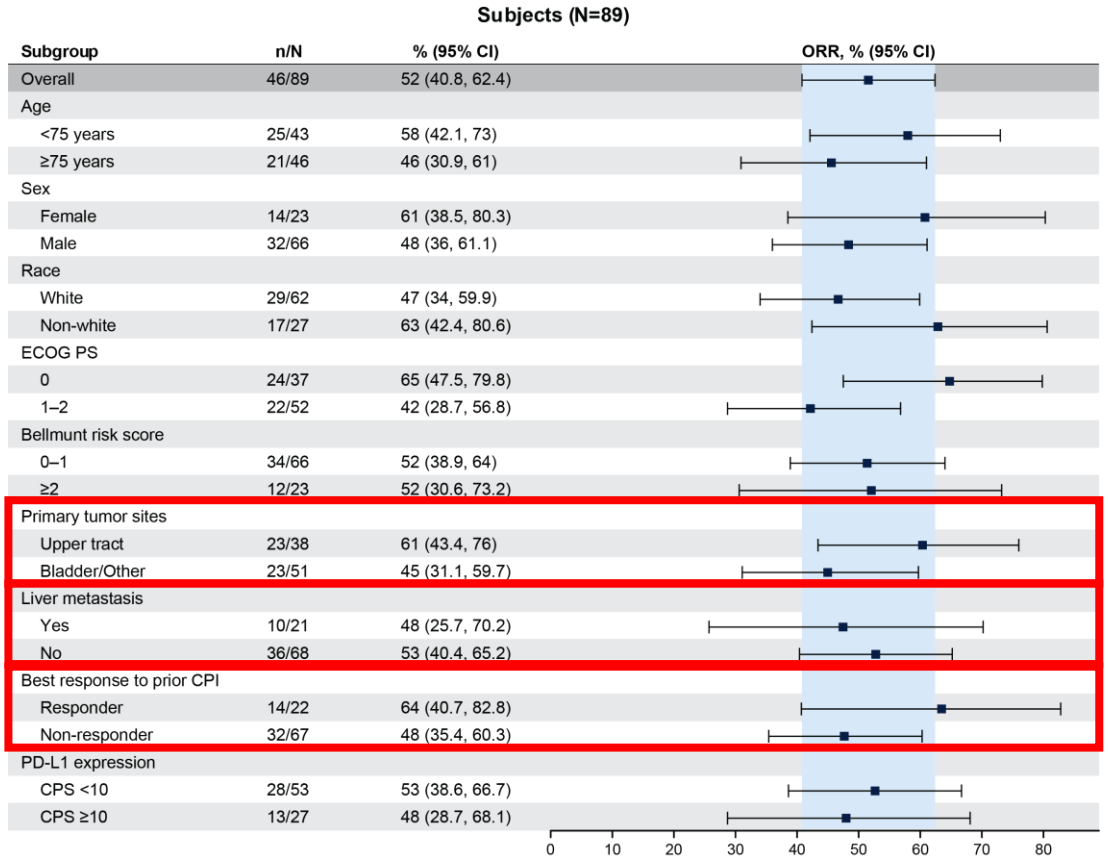
[3]Includes five subjects who did not have response assessment post-baseline, two subjects whose post-baseline assessment did not meet the minimum interval requirement for stable disease, and one subject whose response cannot be assessed due to incomplete anatomy.

EV-201 Cohort 2: Change in Tumor Measurements per BICR



Data are not available for 12 subjects due to no response assessment post-baseline (n=5), incomplete assessment of target lesions post-baseline (n=1), or no measurable disease at baseline per BICR (n=6).

EV-201 Cohort 2: Responses by Subgroup per BICR

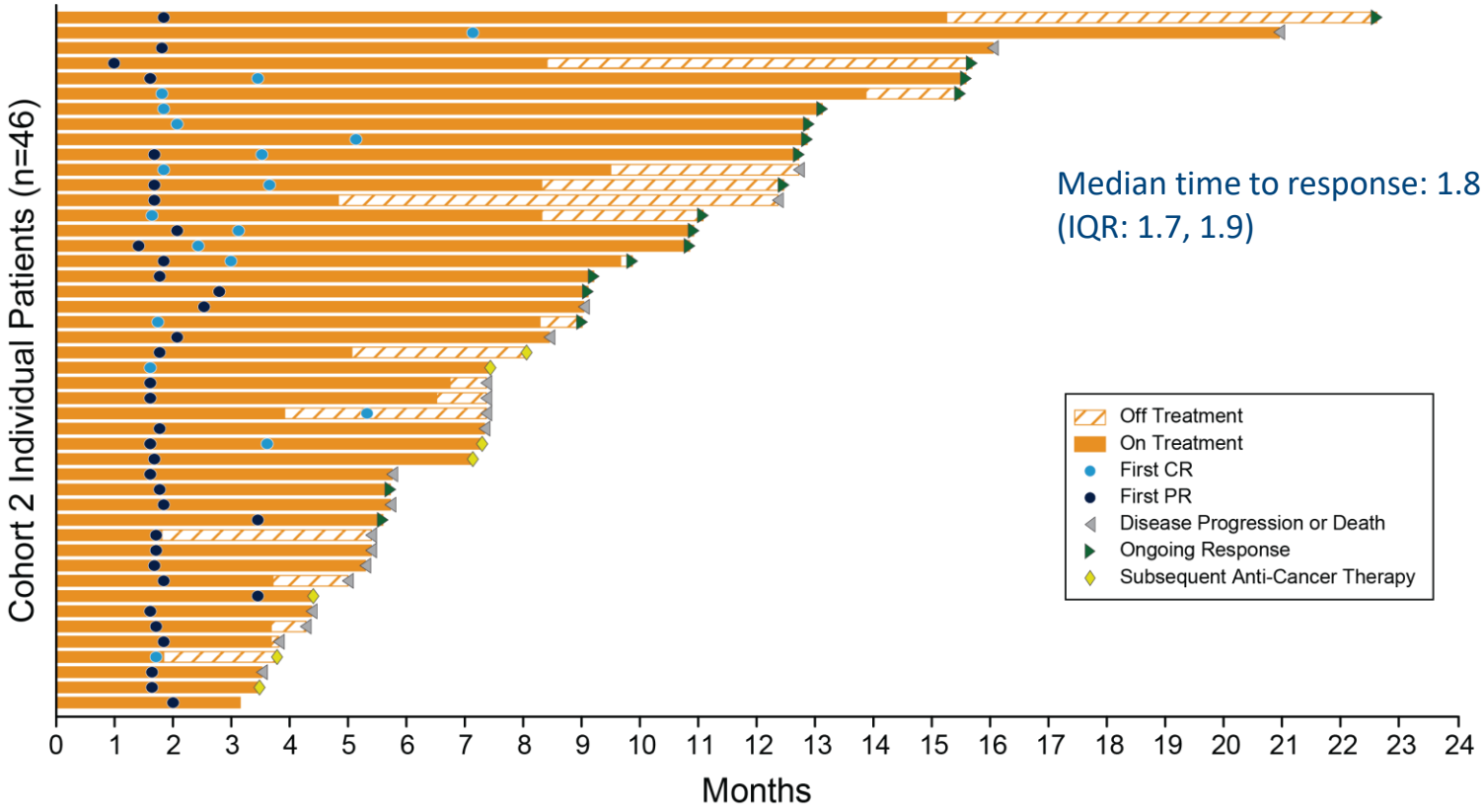


Responses were observed across all subgroups, including patients:

- with primary tumor sites in the upper tract (ORR=61%)
- with liver metastasis (ORR=48%)
- who did not respond to prior PD-1/PD-L1 inhibitors (ORR=48%)

BICR = Blinded Independent Central Review; ORR = Objective Response Rate; ECOG PS= Eastern Cooperative Oncology Group Performance Score; CPI = Checkpoint Inhibitor; PD-1 = programmed cell death protein 1 inhibitor; PD-L1 = programmed death-ligand 1; CPS = combined positive score

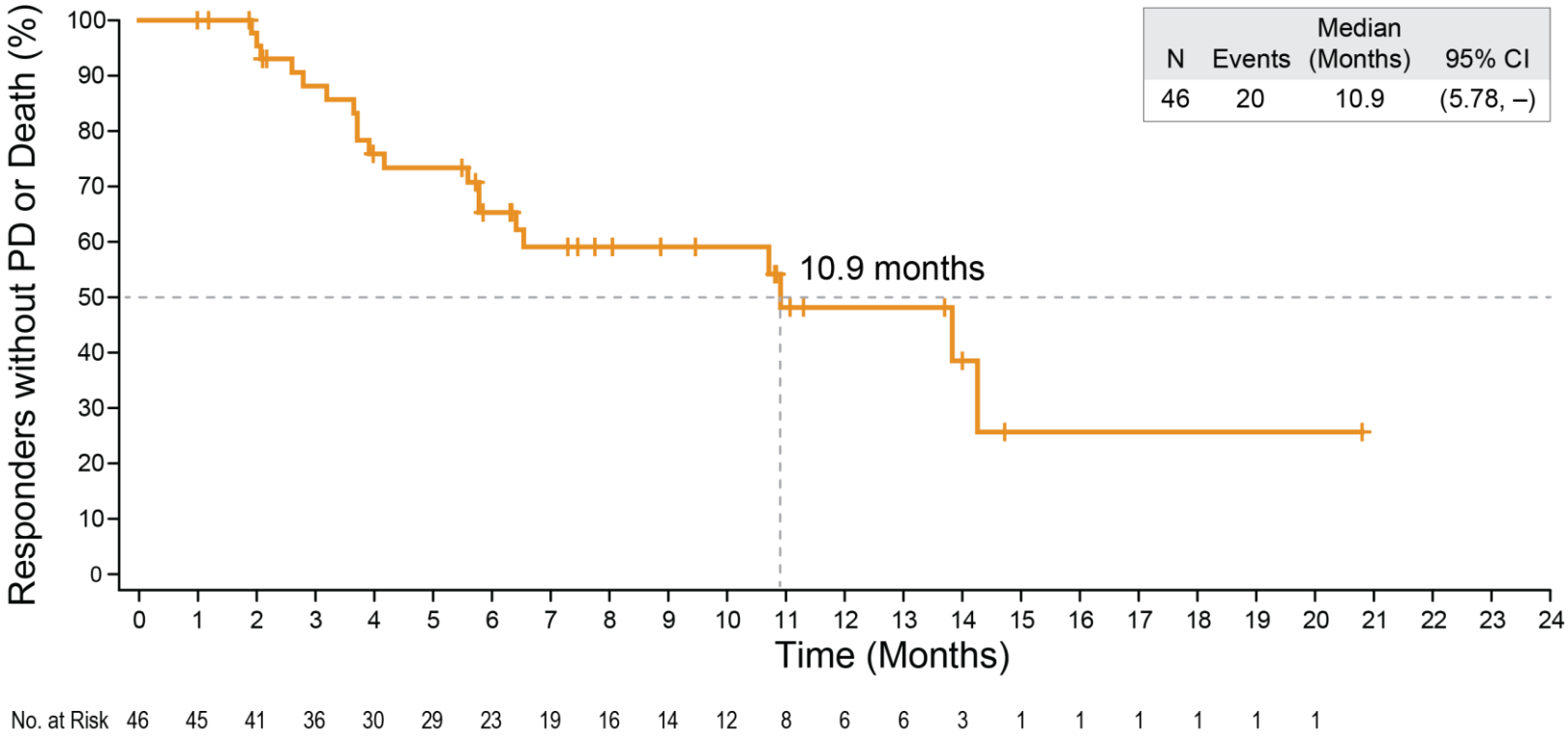
EV-201 Cohort 2: Time to Response per BICR



Median time to response: 1.8 months
(IQR: 1.7, 1.9)

BICR = Blinded Independent Central Review; CR = Complete Response; PR = Partial Response; IQR = Interquartile Range

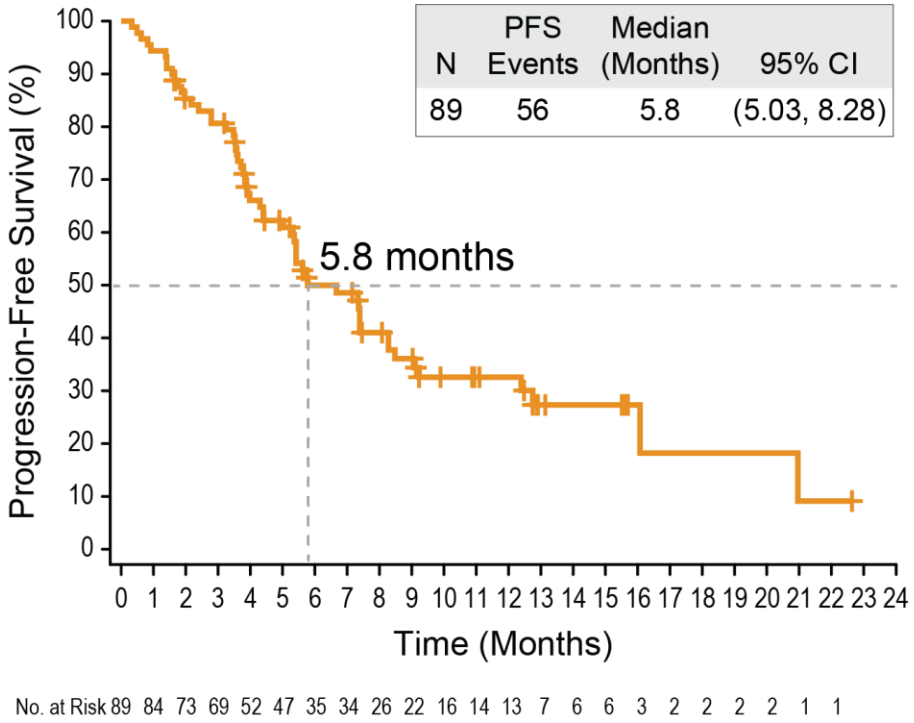
EV-201 Cohort 2: Duration of Response per BICR

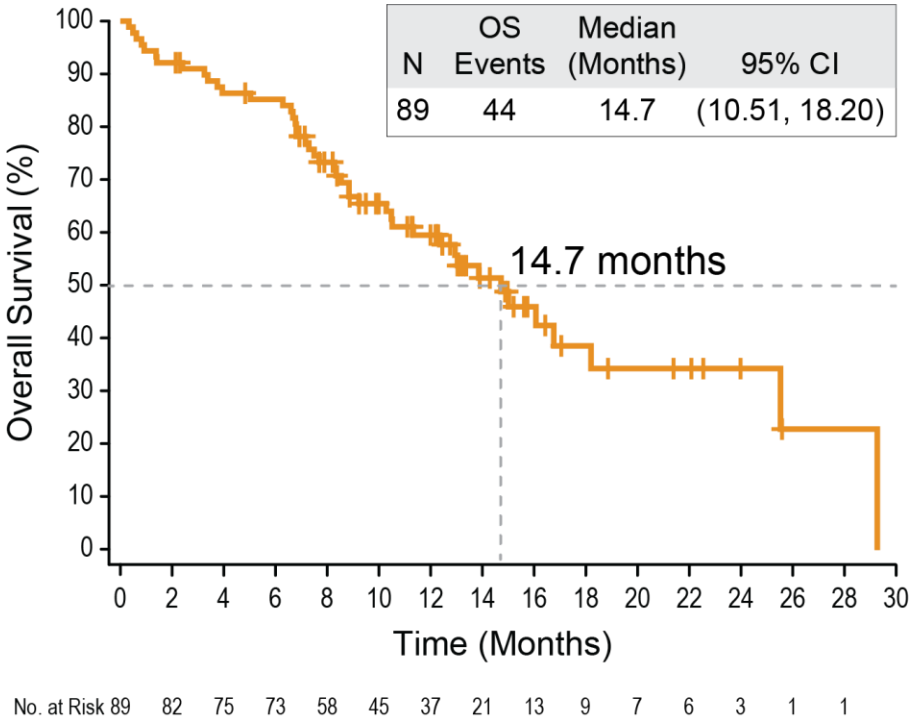


N	Events	Median (Months)	95% CI
46	20	10.9	(5.78, –)

BICR = Blinded Independent Central Review; PD = Progressive Disease; CI = Confidence Interval

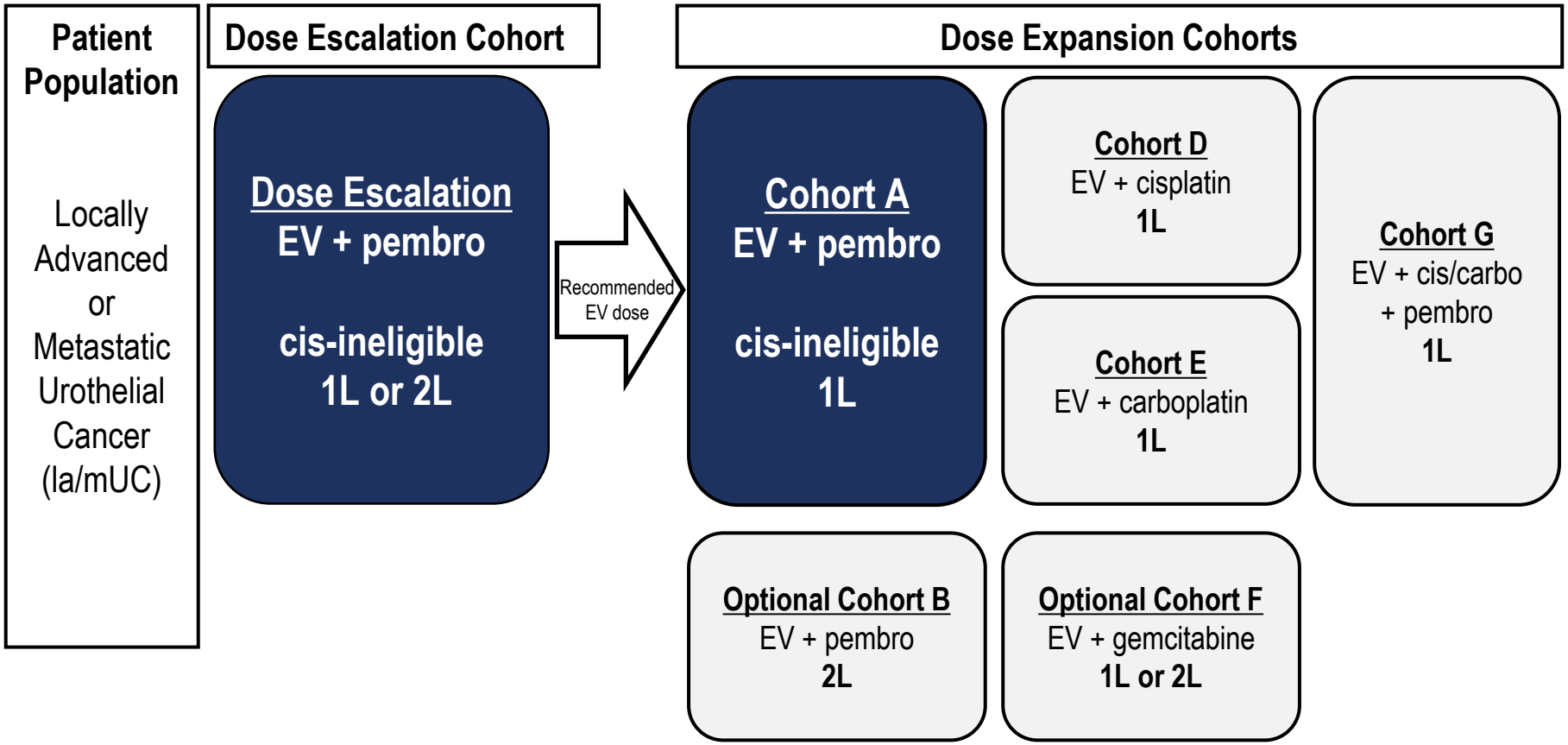
EV-201 Cohort 2: Progression-Free Survival and Overall Survival





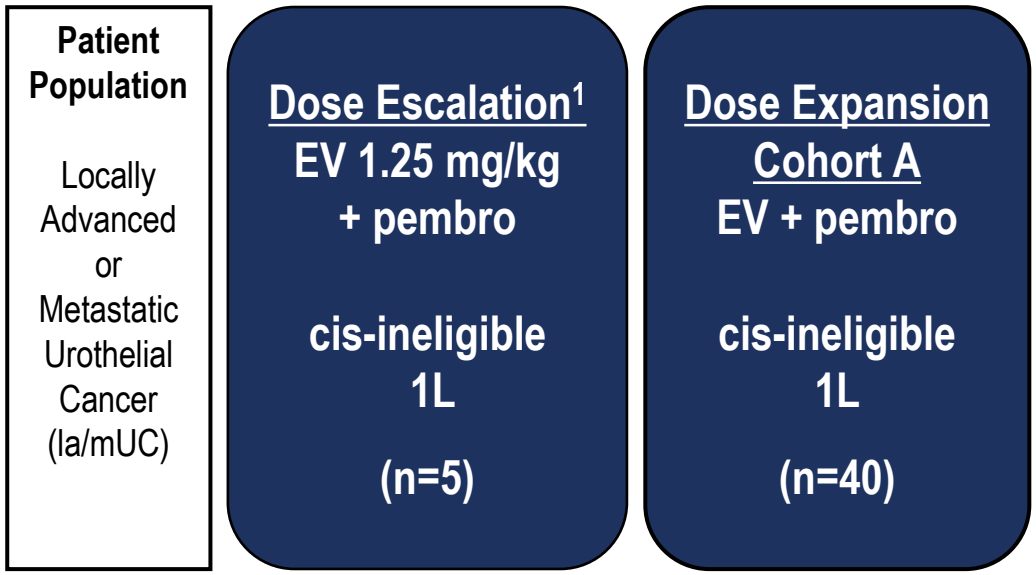
Median follow-up: 13.4 months

STUDY DESIGN: EV-103 (NCT03288545)



ENFORTUMAB VEDOTIN + PEMBROLIZUMAB COHORTS

EV 1.25 mg/kg + pembrolizumab (200 mg) in 1L la/mUC patients



Dosing: EV days 1 and 8 of 3-wk cycle to align with pembro (day 1 of 3-wk cycle)

EV exposure: Similar to EV monotherapy on 4-wk schedule (EV Days 1, 8, and 15)[2]

Primary endpoints: AEs, lab abnormalities

Key secondary endpoints: DLTs, ORR, DCR, DOR, OS

[1] Not included in the current analysis: three 1L patients treated with EV 1 mg/kg + pembro 200 mg and two 2L patients treated with EV 1.25 mg/kg + pembro 200 mg

[2] Rosenberg et al. *J Clin Oncol. Epub July* 2019

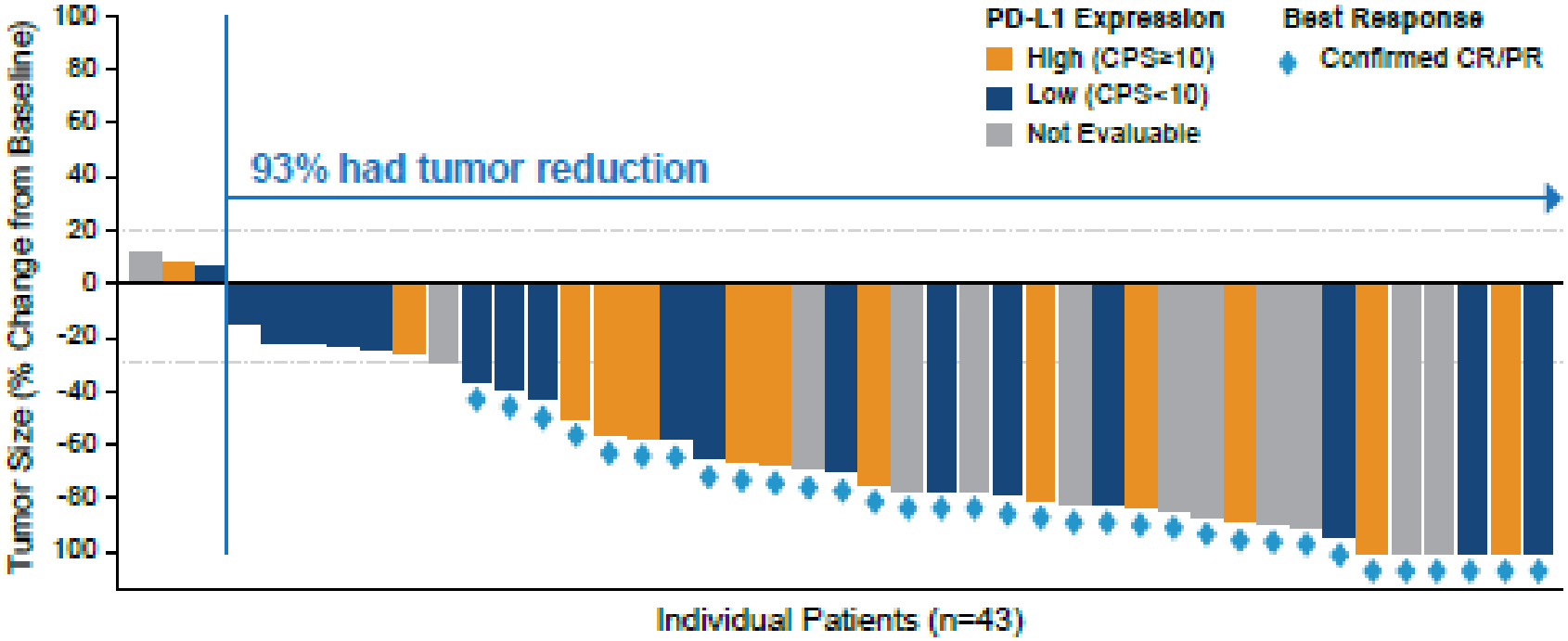
Efficacy

Best Overall Response Per RECIST v 1.1 by investigator (N=45)

Confirmed ORR	73.3% (33)
95% CI	(58.1, 85.4)
Complete response	15.6% (7)
Partial response	57.8% (26)
Stable disease	20.0% (9)
Progressive disease	2.2% (1)
Not evaluable	4.4% (2)
ORR in patients with liver metastasis	53.3% (8/15)
ORR by PD-L1 Expression	
High expression:	78.6% (11/14)
Low expression:	63.2% (12/19)

- Enfortumab vedotin + pembrolizumab demonstrated an ORR of of 73.3% in 1L cisplatin-ineligible la/mUC patients, per investigator
- Responses observed regardless of PD-L1 expression level

Maximum Percent Reduction from Baseline in Sum of Diameters of Target Lesions Per Investigator by PD-L1 Status

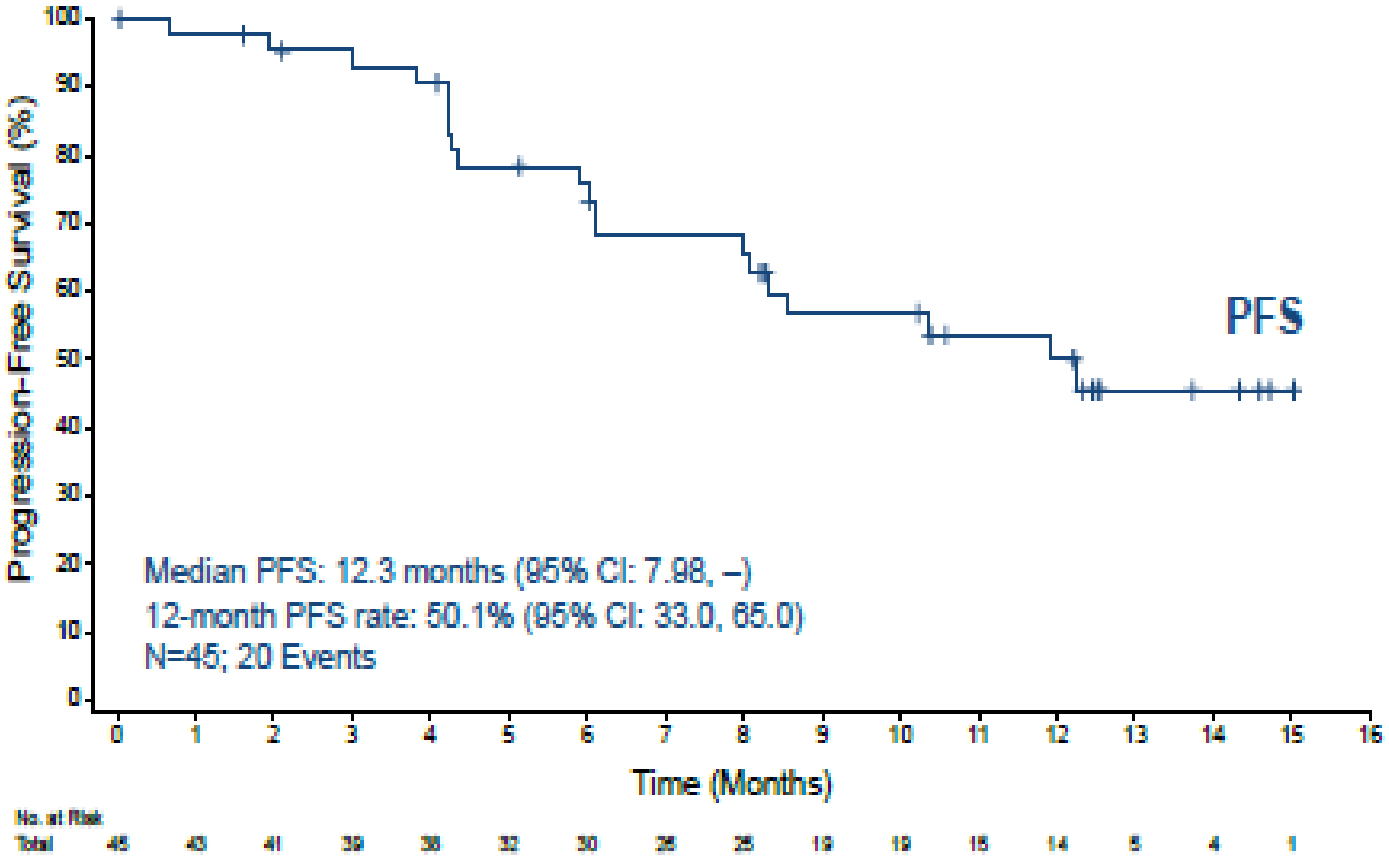


CPS = combined positive score

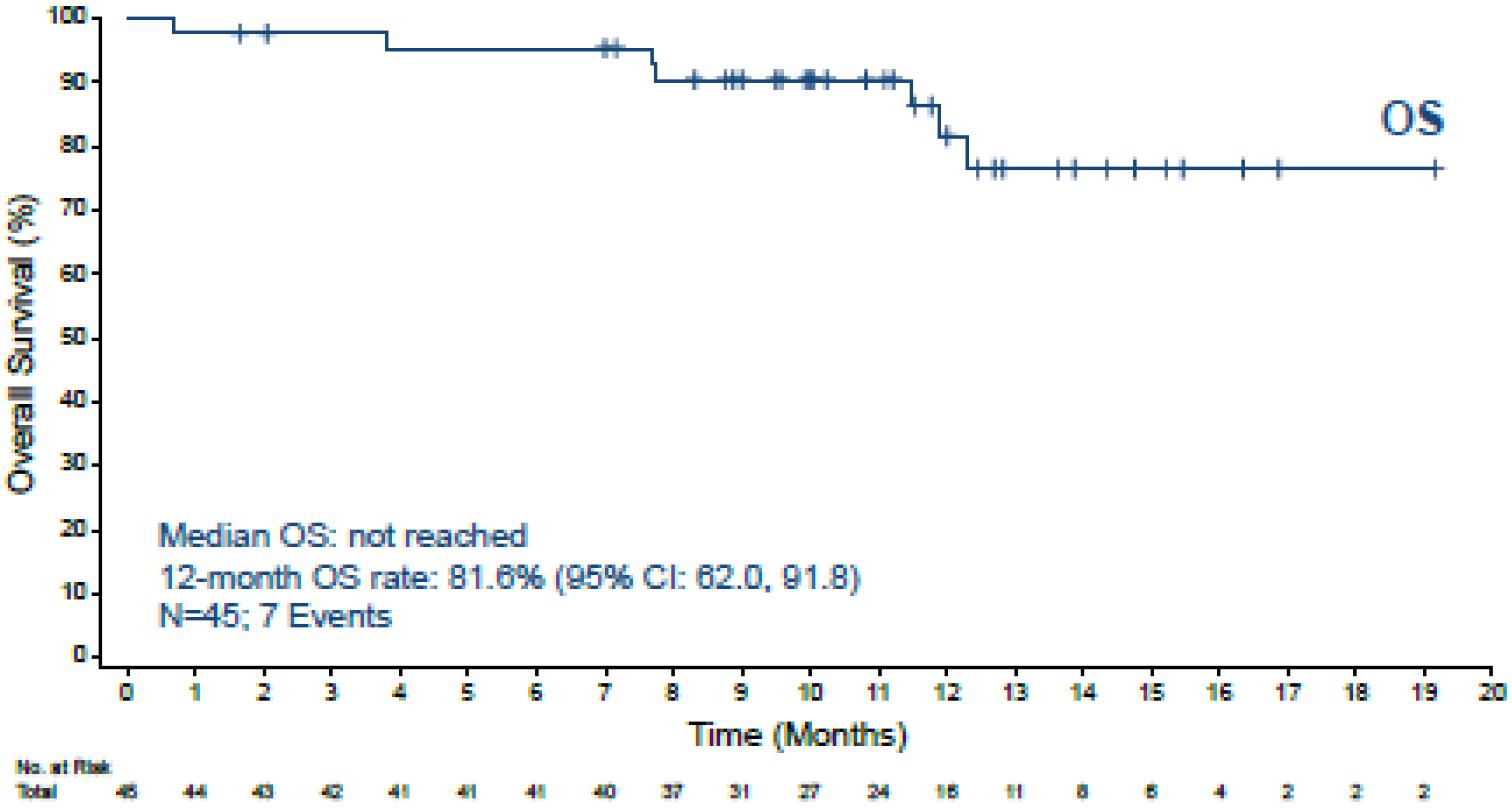
Two patients did not have post-baseline response assessments before end-of-treatment: 1 withdrew consent and 1 died before any post-baseline response assessment.

Horizontal lines at positive 20% and negative 30% denote thresholds for target lesions for disease progression and response, respectively.

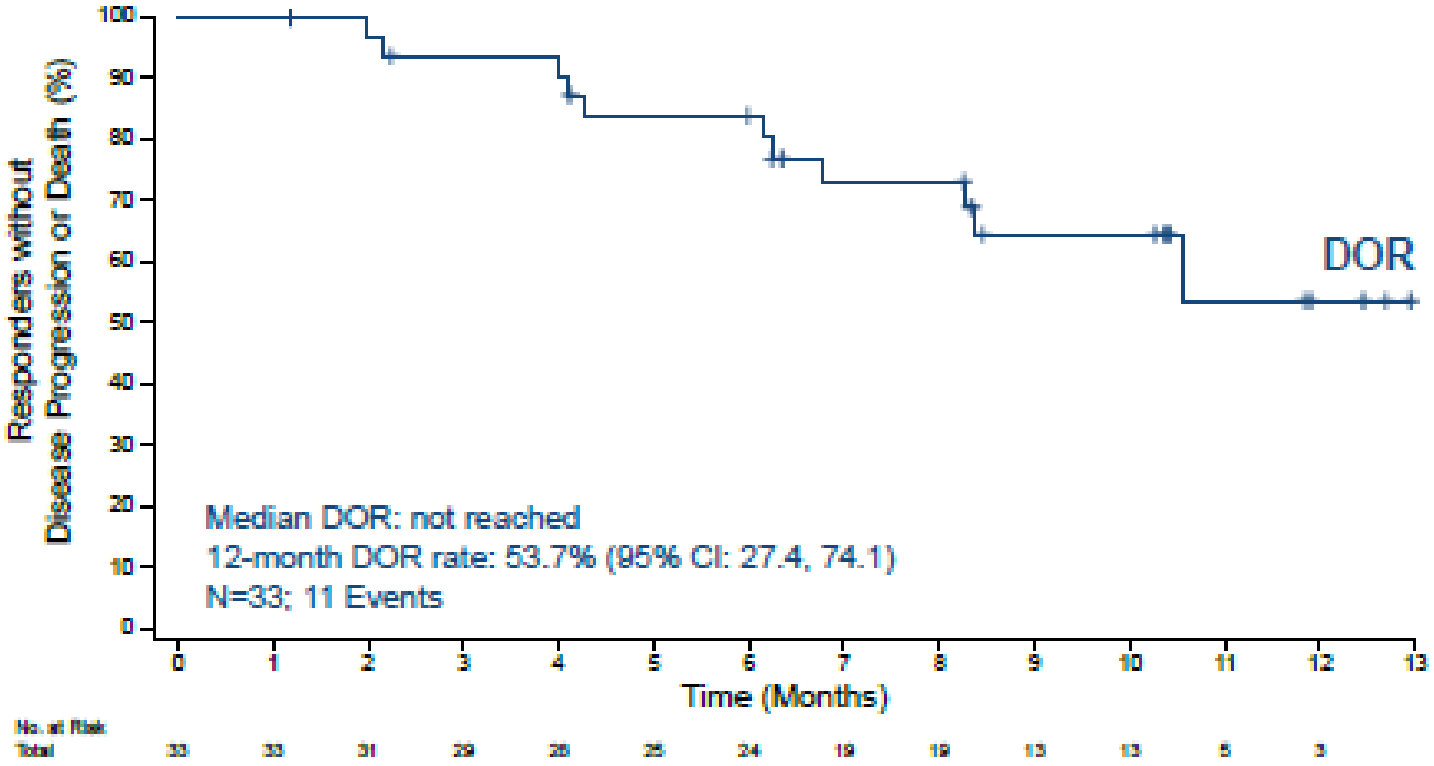
Progression-Free Survival



Overall Survival



Duration of Response



- Median DOR has not been reached with a median follow-up of 10.4 months
  - DOR (range: 1.2, 12.9+ months)
- Out of the 33 responders,
  - 18 (55%) had an ongoing response
  - 11 (33%) had progressed or died
  - 4 (12%) had started a new antitumor treatment before progressive disease

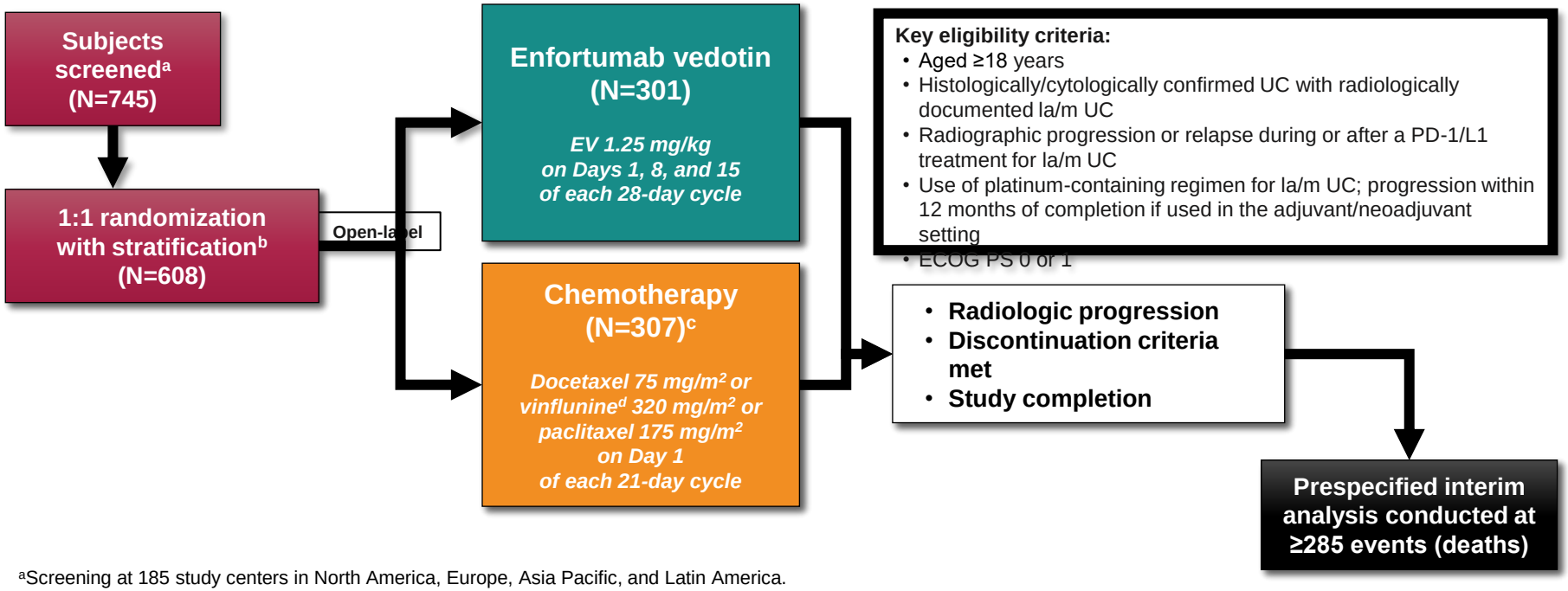
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enfortumab Vedotin in Previously Treated Advanced Urothelial Carcinoma

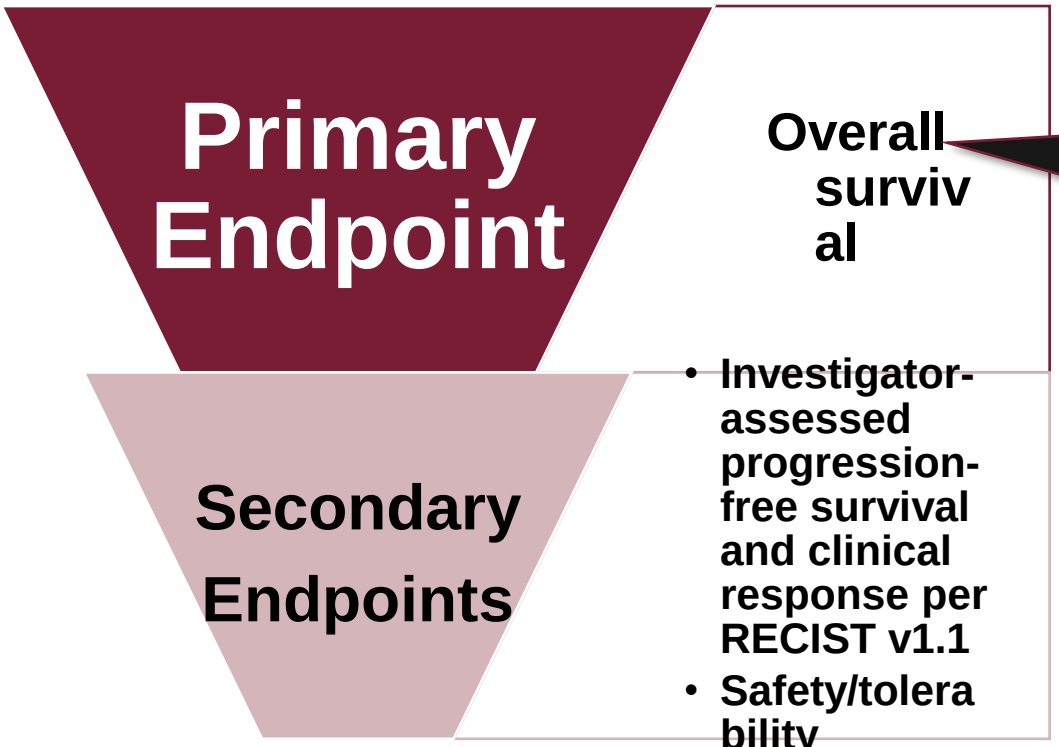
Thomas Powles, M.D., Jonathan E. Rosenberg, M.D., Guru P. Sonpavde, M.D., Yohann Loriot, M.D., Ph.D., Ignacio Durán, M.D., Ph.D., Jae-Lyun Lee, M.D., Ph.D., Nobuaki Matsubara, M.D., Christof Vulsteke, M.D., Ph.D., Daniel Castellano, M.D., Chunzhang Wu, Ph.D., Mary Campbell, M.D., Maria Matsangou, M.B.,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

Methods – EV-301 Phase 3 Trial Design



[a]Screening at 185 study centers in North America, Europe, Asia Pacific, and Latin America.
[b]Stratification variables were ECOG performance status (0 or 1), regions of the world (US, western Europe, or rest of world), liver metastasis (yes or no).
[c]Investigator selected prior to randomization.
[d]In countries where approved; overall proportion of patients receiving vinflunine will be capped at 35%.
Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; la/m, locally advanced or metastatic; PD-1/L1, programmed cell death protein-1/programmed death-ligand 1; UC, urothelial carcinoma.

Methods – Trial Endpoints and Statistical Analyses



Interim analysis
Tested at a 1-sided significance level of 0.00541 for efficacy according to the O'Brien-Fleming stopping boundary, as implemented by Lan-DeMets alpha spending function

Adjusted to 0.00679 based on 301 observed deaths

Statistical analyses

- Kaplan-Meier methodology to estimate survival
- Stratified log-rank test to compare survival between groups
- Stratified Cochran-Mantel-Haenszel test to compare response and disease control rates between groups
- Stratified Cox proportional hazard model to estimate hazard ratios

Abbreviation: RECIST, Response Evaluation Criteria in Solid Tumors.

Results – Patient and Disease Characteristics at Baseline

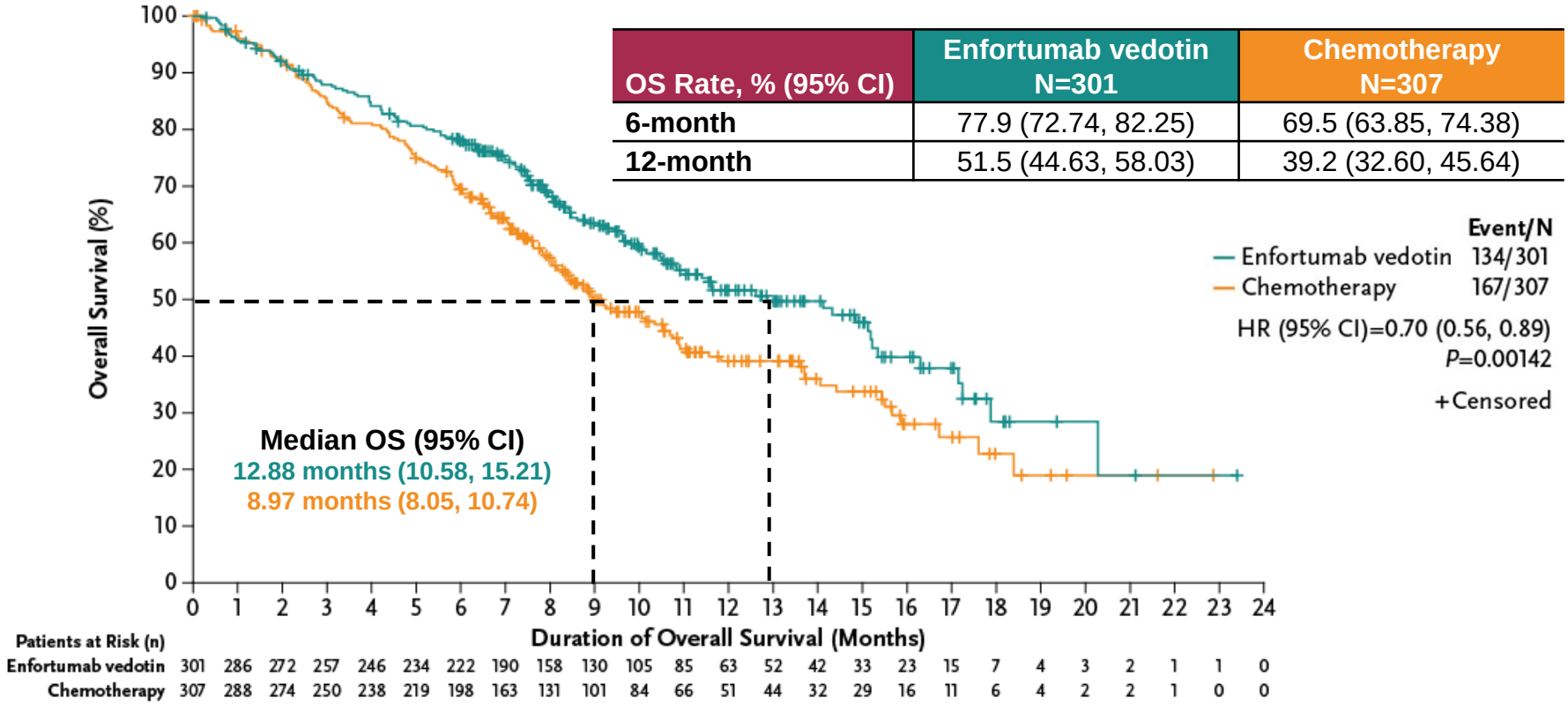
Parameter, n (%)*	Enfortumab vedotin N=301	Chemotherapy N=307
Age (years), median (range)	68.0 (34.0-85.0)	68.0 (30.0-88.0)
Male sex	238 (79.1)	232 (75.6)
Tobacco history		
Former/current user	196 (65.1)	195 (63.5)
Never used	91 (30.2)	102 (33.2)
ECOG performance status		
0	120 (39.9)	124 (40.4)
1	181 (60.1)	183 (59.6)
Bellmunt risk score		
0-1	201 (66.8)	208 (67.8)
≥2	90 (29.9)	96 (31.3)
Liver metastasis	93 (30.9)	95 (30.9)
Prior lines of systemic therapy		
1-2	262 (87.0)	270 (87.9)
≥3	39 (13.0)	37 (12.1)
Response to prior CPI	61 (20.3)	50 (16.3)

*Values are expressed as n (%), unless otherwise specified.
Abbreviations: CPI, checkpoint inhibitor; ECOG, Eastern Cooperative Oncology Group.

Data cut-off: July 15, 2020

Overall Survival (Intention-to-Treat Population)

OS Rate, % (95% CI)	Enfortumab vedotin N=301	Chemotherapy N=307
6-month	77.9 (72.74, 82.25)	69.5 (63.85, 74.38)
12-month	51.5 (44.63, 58.03)	39.2 (32.60, 45.64)

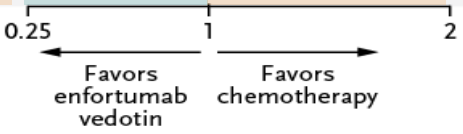


Abbreviations: CI, confidence interval; HR, hazard ratio; OS, overall survival.

Data cut-off: July 15, 2020

Overall Survival: Subgroup Analyses

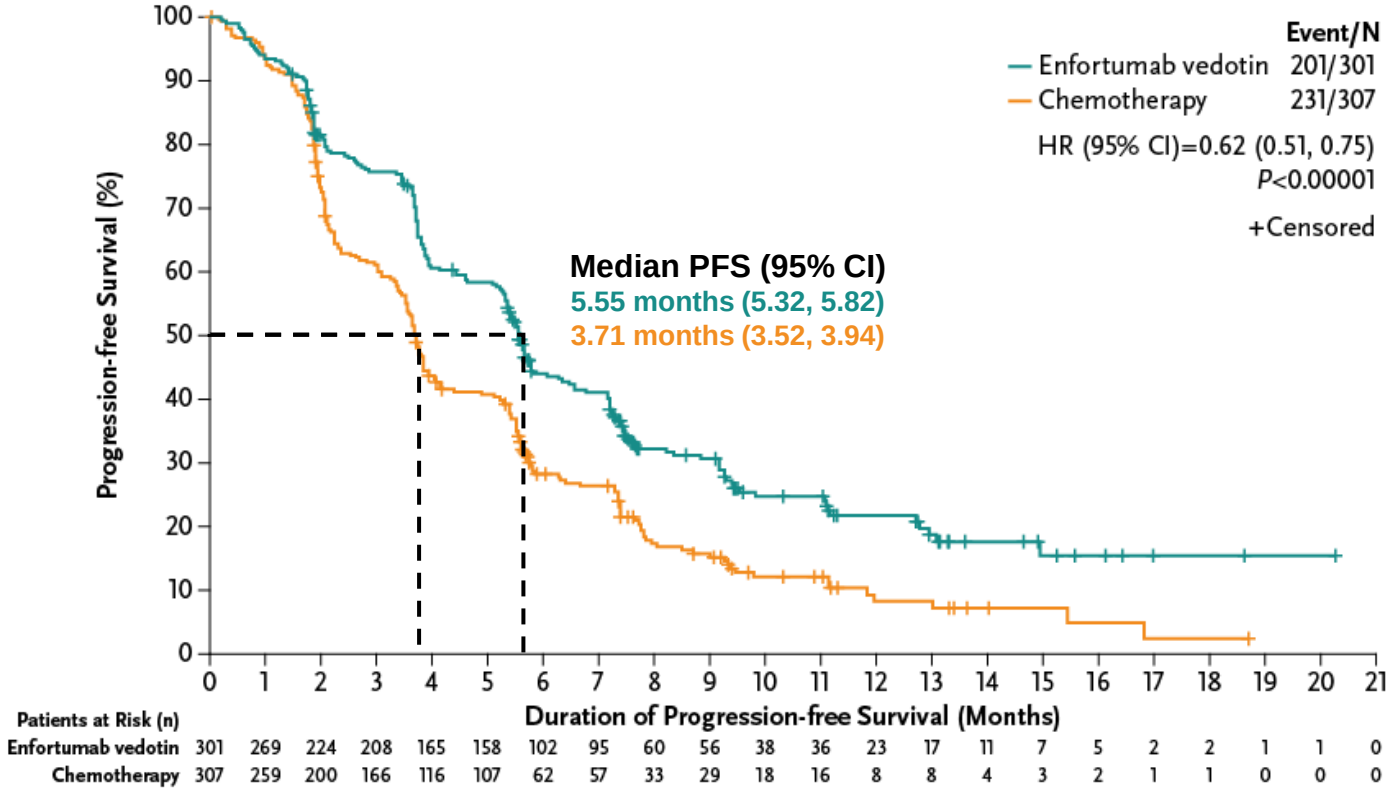
		Enfortumab vedotin Event/N	Chemotherapy Event/N	HR (95% CI)
All subjects		134/301	167/307	0.70 (0.56, 0.89)
Age, group 1	<65 years	49/108	66/111	0.68 (0.47, 0.99)
	≥65 years	85/193	101/196	0.75 (0.56, 1.00)
Age, group 2	<75 years	109/249	128/239	0.69 (0.53, 0.89)
	≥75 years	25/52	39/68	0.91 (0.55, 1.51)
Sex	Male	101/238	132/232	0.61 (0.47, 0.79)
	Female	33/63	35/75	1.17 (0.72, 1.89)
Region	W Europe	57/126	72/129	0.76 (0.53, 1.07)
	US	25/43	25/44	0.88 (0.51, 1.54)
	Rest of World	52/132	70/134	0.64 (0.45, 0.92)
ECOG PS	0	40/120	46/124	0.81 (0.53, 1.24)
	1	94/181	121/183	0.67 (0.51, 0.87)
Liver metastasis	Yes	53/93	63/95	0.66 (0.46, 0.96)
	No	81/208	104/212	0.73 (0.55, 0.98)
Pre-selected control therapy	Paclitaxel	63/141	59/112	0.71 (0.49, 1.01)
	Docetaxel	41/87	67/117	0.71 (0.48, 1.04)
	Vinflunine	30/73	41/78	0.77 (0.48, 1.24)
Primary site of tumor	Upper tract	44/98	52/107	0.85 (0.57, 1.27)
	Bladder/other	90/203	115/200	0.67 (0.51, 0.88)
Prior lines of systemic therapy	1-2	115/262	147/270	0.69 (0.54, 0.88)
	≥3	19/39	20/37	0.88 (0.47, 1.64)
Best response to prior CPI	Responder	18/61	23/50	0.63 (0.34, 1.17)
	Non-responder	100/207	120/215	0.76 (0.58, 0.99)



Abbreviations: CI, confidence interval, CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio, US, United States; W, western.

Data cut-off: July 15, 2020

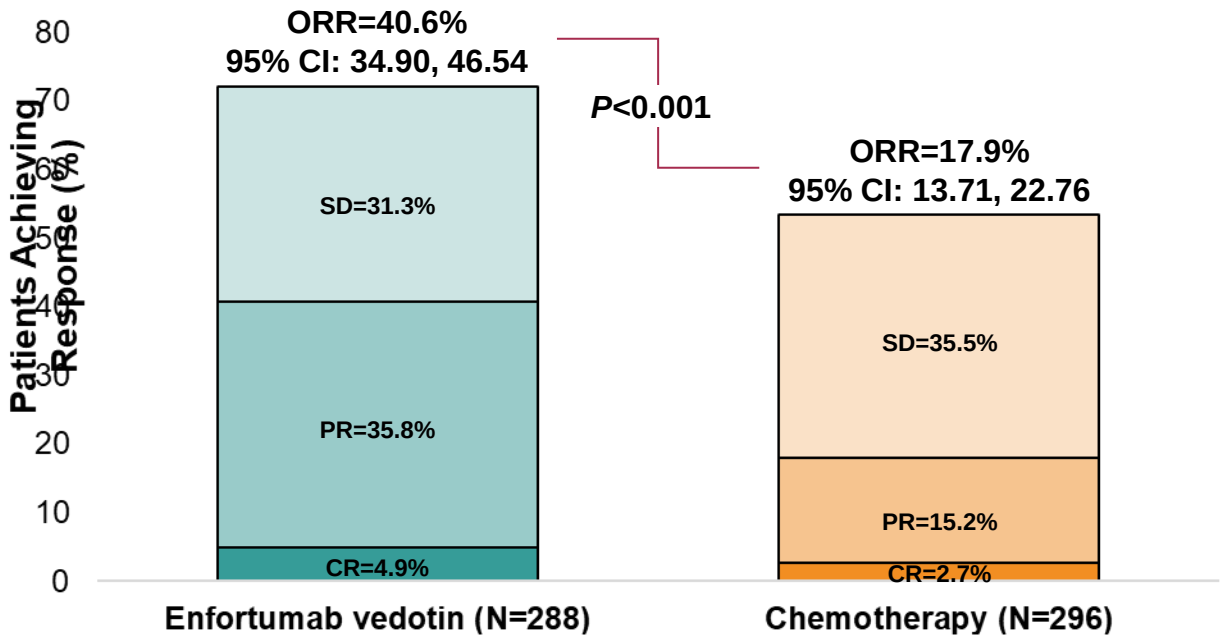
Progression-Free Survival (Intention-to-Treat Population)



Abbreviations: CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

Data cut-off: July 15, 2020

Best Overall Response (Response-Evaluable Population)



Disease control rate, % (95% CI)	**71.9 (66.30, 76.99)**	**53.4 (47.52, 59.17)**	***P*<0.001**

*Disease control rate is defined as the proportion of patients who had a best overall response of confirmed CR, PR, or SD (at least 7 weeks).
Abbreviations: CR, complete response; ORR, objective response rate; PR, partial response; SD, stable disease.

Data cut-off: July 15, 2020

Treatment-Related Adverse Events (Safety Population)

Adverse Event, n (%)*	Enfortumab vedotin N=296		Chemotherapy N=291	
	All Grade	Grade ≥3	All Grade	Grade ≥3
Any adverse event	**278 (93.9)**	**152 (51.4)**	**267 (91.8)**	**145 (49.8)**
Serious adverse events[†]	67 (22.6)	-	68 (23.4)	-
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy[†]	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Rash maculopapular	48 (16.2)	22 (7.4)	5 (1.7)	0
Anemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Neutrophil count decreased	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
White blood cell decreased	16 (5.4)	4 (1.4)	31 (10.7)	26 (8.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

*TRAEs occurring in ≥20% of patients in either treatment group or grade ≥3 TRAEs occurring in ≥5% of patients in either treatment group.

[†]TRAEs that were deemed "serious" in the view of the investigator or sponsor and based upon predefined criteria.

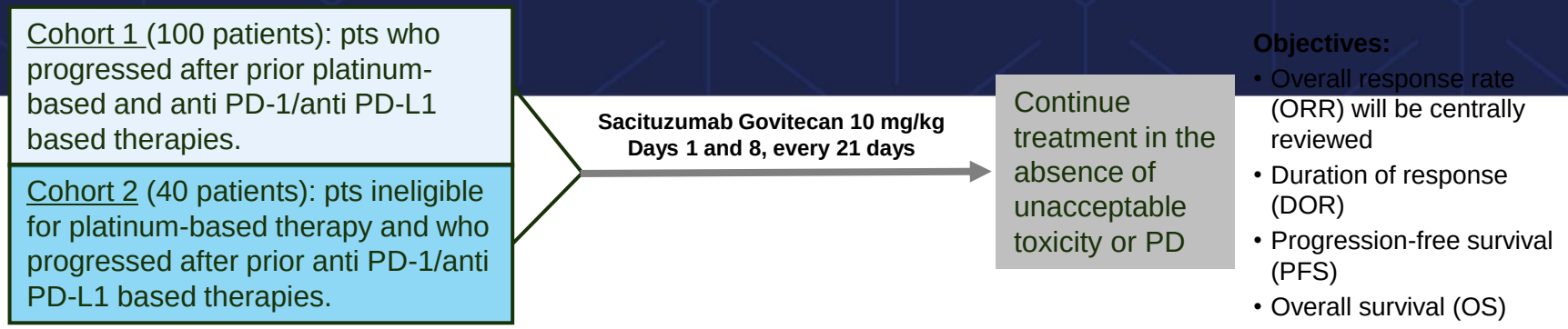
Abbreviation: TRAE, treatment-related adverse event.

Data cut-off: July 15, 2020

TROPHY-U-01 (IMMU-132-06) Study

A Phase II Open Label, Study of IMMU-132 in Metastatic Urothelial Cancer After Failure of Platinum-based Regimen or Anti-PD-1/ PD-L1 Based Immunotherapy

- Results from the Study-01 basket trial warranted further investigation in a dedicated phase 2 trial.
- TROPHY-U-01 (NCT03547973) is an international, single-arm, open-label, phase 2 trial evaluating the antitumor activity and safety of sacituzumab govitecan in 140 pts with advanced UC.



NCT Trial Number: 03547973
PD-1, programmed cell death-1; PD-L1, programmed death ligand-1.

View TROPHY-U-01 Poster on Feb 15th TPS #495; Poster Board #N5

Treatment-Related Adverse Events ≥20% Any grade or ≥5% Grade ≥3 (N=35)

Category	Event	All Grades (%)	Grades 3 (%)	Grade 4 (%)
Hematologic[a,b]	Neutropenia[c]	66	29	26
	Leukopenia[d]	40	20	9
	Anemia	34	17	0
	Febrile neutropenia	11	9	3
	Lymphocyte count decreased	11	6	3
Gastrointestinal	Diarrhea	57	6	3
	Nausea	43	0	0
	Abdominal pain	20	3	0
General disorders and administrative site conditions	Fatigue	54	6	0
Infections and infestations	Urinary Tract infection	14	11	0
Skin & subcutaneous tissue	Alopecia	74	0	0
Metabolism and nutrition	Decreased appetite	20	0	0

Median treatment cycles: 5 (range: 1-11); worst grade CTCAE reported; data cut-off for the interim analysis: 05Aug2019

[a]Prophylactic growth factor support was permitted per protocol, at the discretion of the investigator; [b]included SOC terms Blood and lymphatic system disorders and Investigations; [c]combined term includes neutropenia and neutrophil count decreased; [d]combined term includes leukopenia and WBC count decreased; [e]discontinuations due to TRAEs: G3 febrile neutropenia, G3 neutrophil count decreased; G4 leukopenia/G3 anemia/G3 thrombocytopenia. CTCAE, Common Toxicity Criteria for Adverse Events; G, grade; ILD, interstitial lung disease; SOC, system organ class; TRAE, treatment-related adverse event; WBC, white blood cell.

- 3 patients discontinued due to TRAEs[e]
- Other key TRAEs:
  - 5 pts with rash (≤G2)
  - No cases of ILD, ocular toxicities, or hyperglycemia
  - No G >2 peripheral neuropathy
- **No treatment-related deaths**

Patients With Objective Responses

Response Outcomes

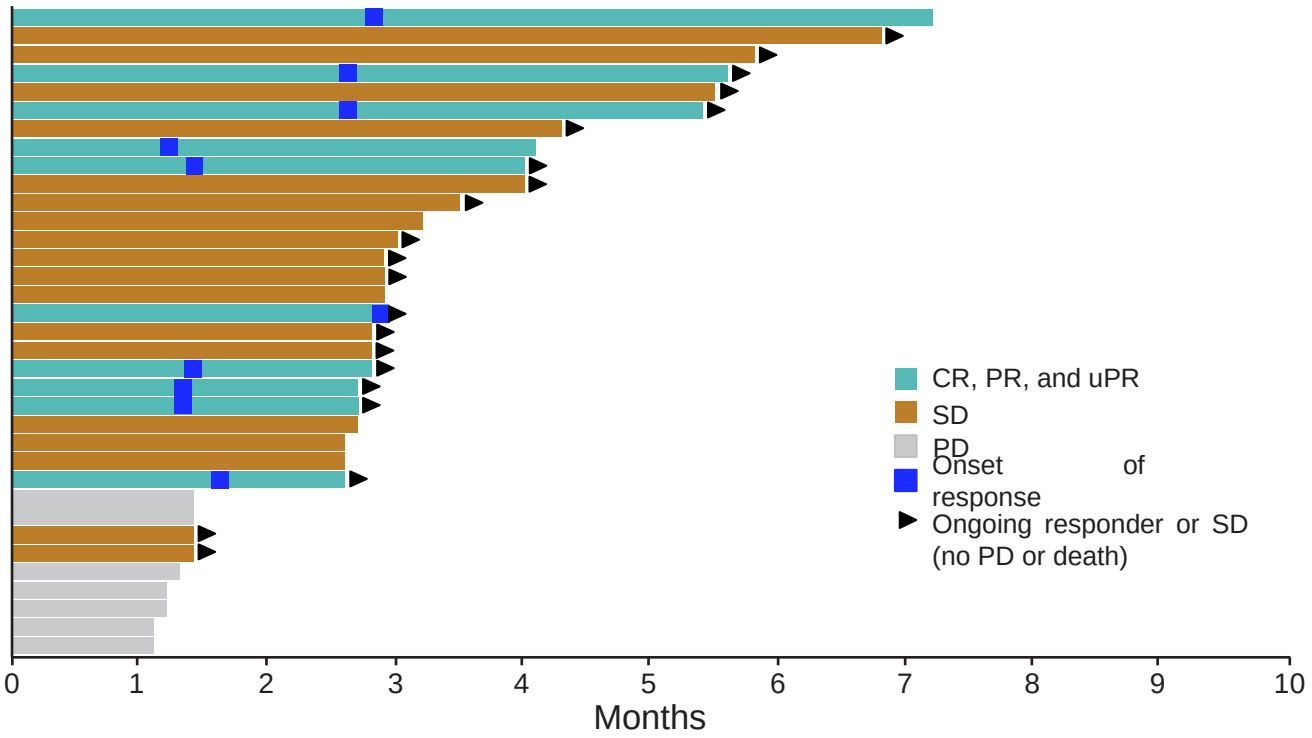
Endpoint	Cohort 1 (N=35)
Median follow-up, mon	**4.1**
Patients continuing treatment, n (%)	20 (57)
ORR, n (%) [95% CI]	10 (29) [15, 46]
CR, n (%)	2 (6)
PR, n (%)	6 (17)
uPR pending confirmation,[a] n (%)	2 (6)
Median time to onset of response, mon (range)	1.5 (1.2, 2.8)

ORR in Patient Subgroups

Category	Subgroup	ORR, % (n/N)
Overall	**N/A**	**29 (10/35)**
Age	<75	29 (8/28)
	≥75	29 (2/7)
ECOG PS	0	33 (5/15)
	1	25 (5/20)
No. prior anticancer regimens	2	18 (2/11)
	≥3	33 (8/24)
Visceral involvement at study entry	Yes	23 (5/22)
	Liver	25 (2/8)
	No	39 (5/13)
Bellmunt risk factors	0-1	35 (10/29)
	2-3	0 (0/6)

[a]Follow-up scan is pending.
CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ORR, objective response rate; PR, partial response; uPR, unconfirmed partial response.

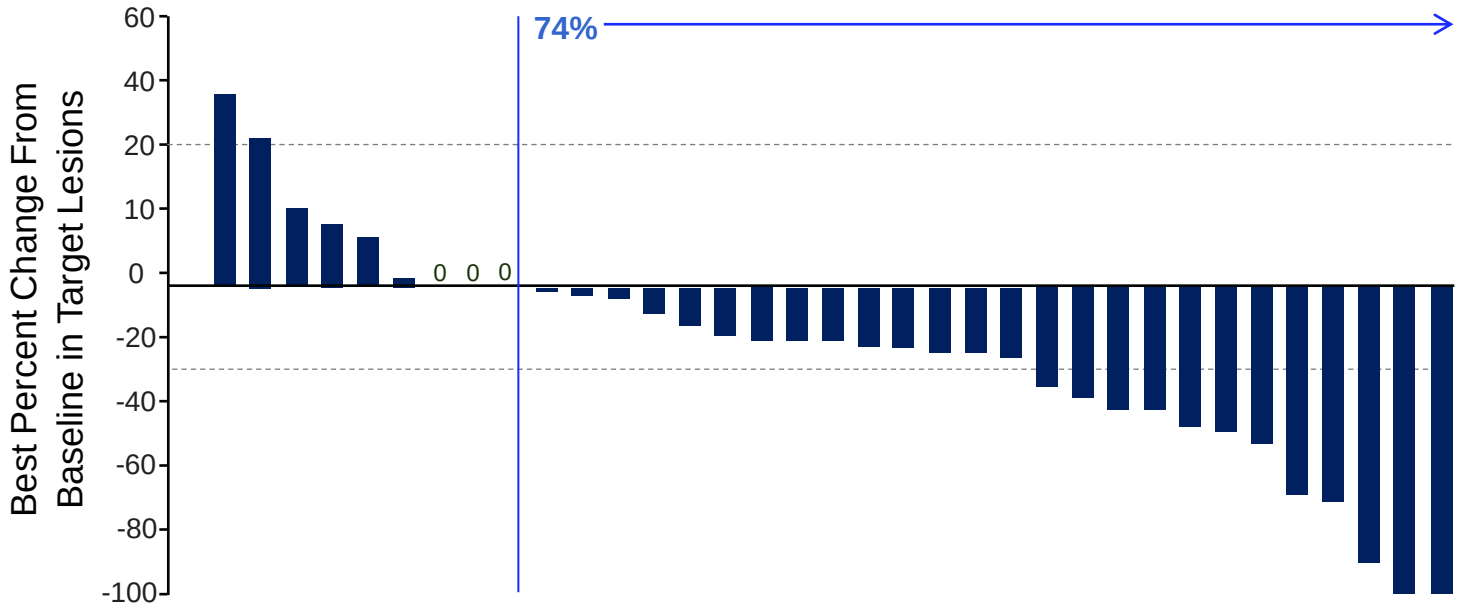
Treatment Duration and Response (N=35)



- 8 of 10 responders have ongoing response at data cutoff

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; uPR, unconfirmed partial response.

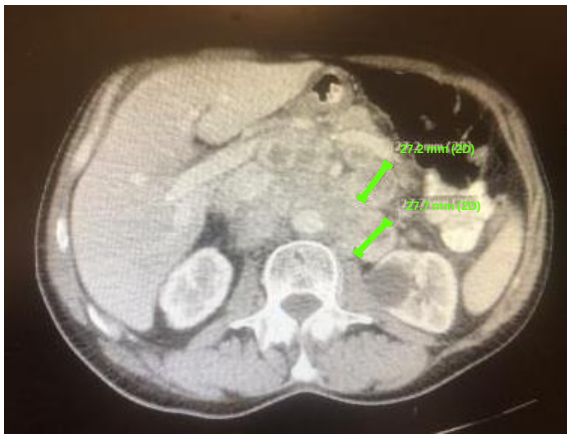
74% of Patients Demonstrated a Reduction in Tumor Size



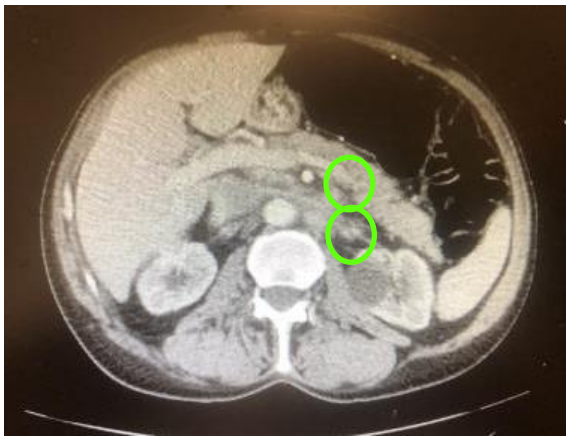
- 61 year-old male with past medical history of G1 neuropathy and RLE edema, with target lesions consisting of periportal, retroperitoneal, and mesenteric adenopathy
- Refractory to adjuvant tx: Cisplatin/gemcitabine
- Prior metastatic regimens:
  - Atezolizumab (24 mon)
  - Enfortumab vedotin (8 mon)
  - Pemetrexed (3 mon)
- **Confirmation of PR after cycle 4 with SG treatment[a]**
  - **No worsening of neuropathy reported**
  - **Significant reduction in lower extremity edema**
  - **On treatment for 7 mon and ongoing at time of data cut-off**

Please provide high res images

Images provided by Daniel P. Petrylak from the Yale School of Medicine, New Haven, CT



Baseline CT



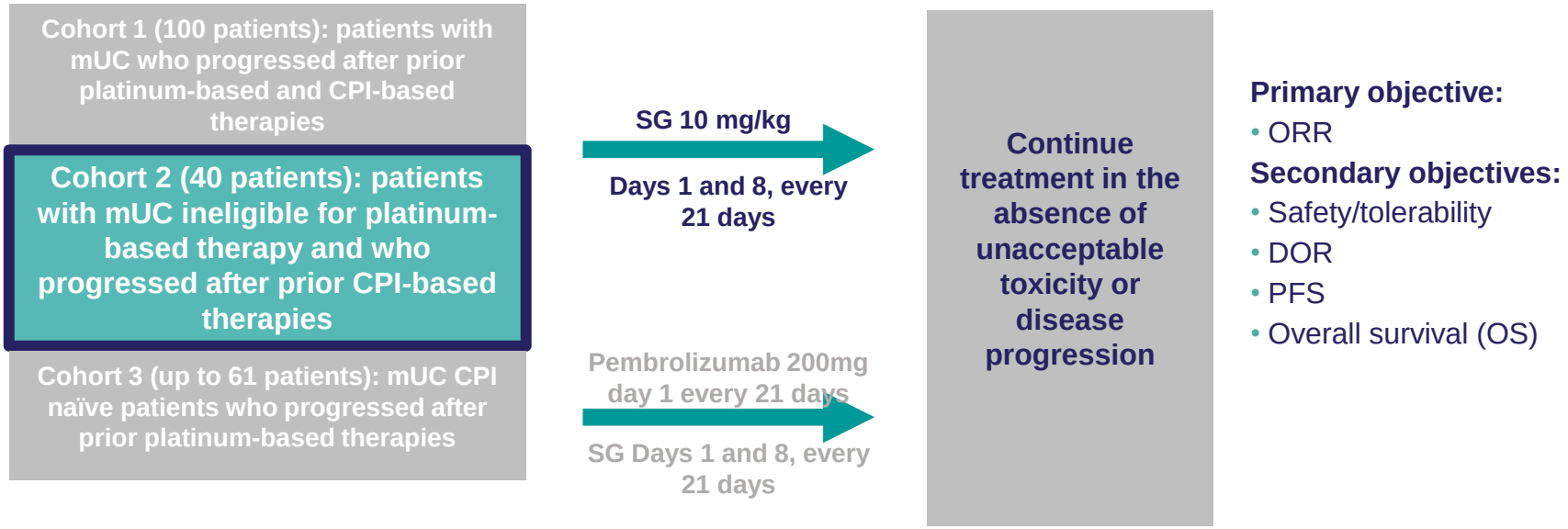
Follow-up CT
(after 10 cycles of SG)

70% reduction of target lesions

[a]Assessed by investigator using RECIST v1.1

CT, computed tomography; G1, grade 1; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors; RLE, right leg extremity; SG, sacituzumab govitecan.

Figure 3. TROPHY-U-01: Phase II trial of SG in stage IV urothelial cancer after failure of a platinum-based regimen and/or anti-PD-1/PD-L1-based therapies



CPI therapy (includes anti-PD-1/anti-PD-L1–based therapies).
CPI, checkpoint inhibitor; DOR, duration of response; mUC, metastatic urothelial cancer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival.
EudraCT Number: 2018-001167-23; ClinicalTrials.gov Number: NCT03547973; IMMU-132-06 study.

Cohort 2 Results: Demographics

Characteristic	N=21
Age, median (range), y	76 (57–87)
≥75 y, n (%)	12 (57)
Male, n (%)	11 (52)
Race, n (%)	
White	19 (90)
Black	1 (5)
Missing	1 (5)
ECOG PS 0, n (%)	10 (48)
ECOG PS 1, n (%)	10 (48)
ECOG PS 2, n (%)	1 (5)[a]
Visceral metastatic sites, n (%) [b]	14 (67)
Lung/Pleura	9 (43)
Liver	5 (24)
Other	4 (19)

Characteristic	N=21
Prior anticancer regimens, median (range), n	2 (1–5)
Median duration of last anticancer regimen (range), mon	1.6 (0.7–4.9)
Lines of prior therapies, n (%)	
1	5 (24)
2	10 (48)
≥3	6 (29)
Bellmunt risk factors[c], n (%)	
0	6 (29)
1	10 (48)
2	5 (24)

[a]Patient was screened and had ECOG of 1, but prior to the first dose the patient became ECOG 2. [b]Visceral metastases included only target and non-target lesions (metastatic sites are not mutually exclusive). [c]Risk factors are ECOG PS >0, presence of liver metastases, and hemoglobin <10 g/dL.
ECOG PS, Eastern Cooperative Oncology Group Performance Status; mon, months.

Exposure and Response Outcomes

Suggested for center column content

- Median treatment cycles (range): 5 (1-15)
- Median duration of treatment (range): 4.5 months (0.3 – 15.6)
- Median Dose intensity: 92%

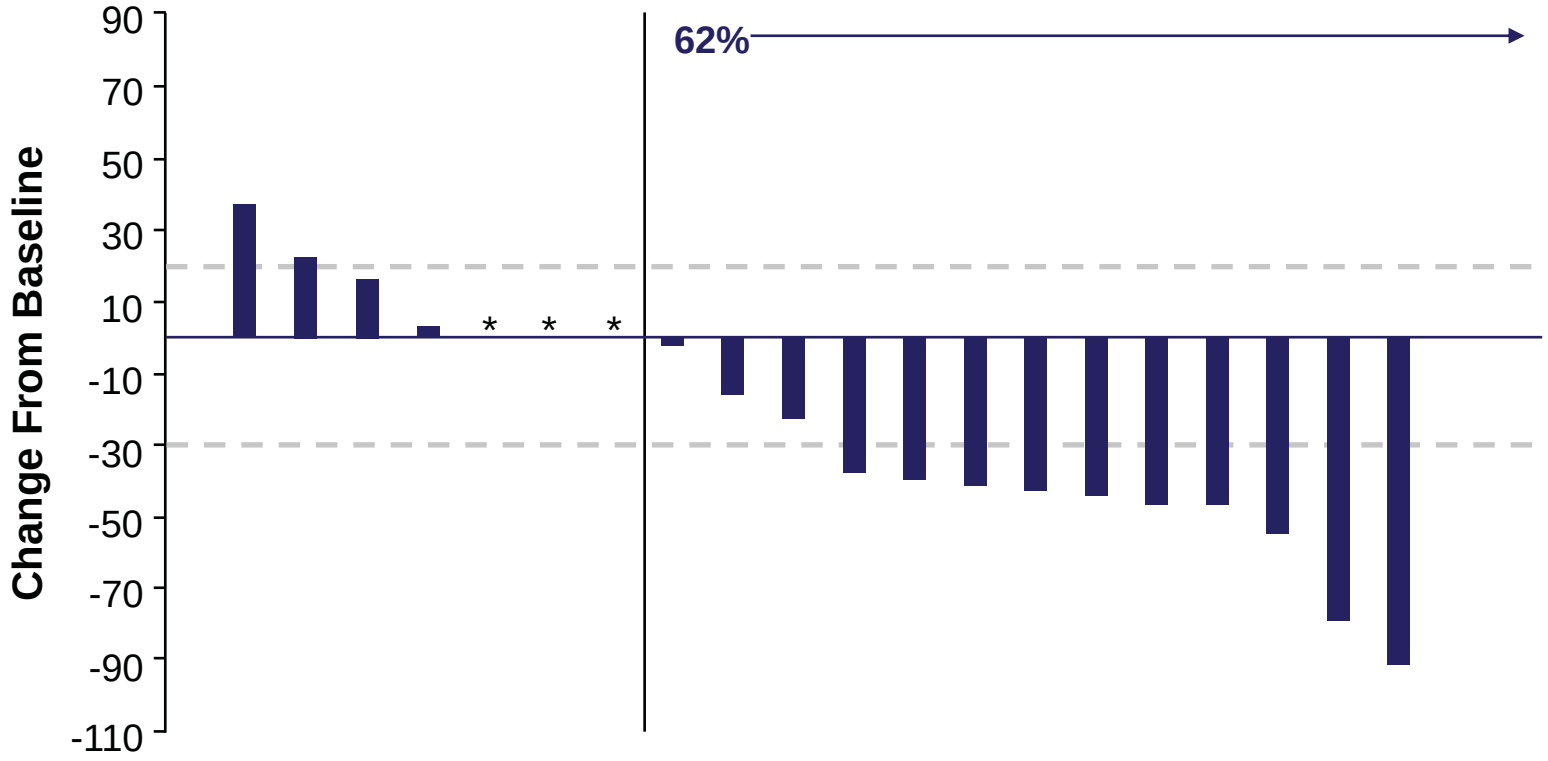
- At a median follow-up of 6.8 months, ORR was 29% (6/21) with 6 confirmed PRs

Response Outcomes

Endpoint	N=21
Median (range) follow-up, mon	6.8 (1.6–18.9)
Patients continuing treatment, n (%)	9 (43)
ORR, n (%) [95% CI]	6 (29) [12–54]
CR, n (%)	0 (0)
PR, n (%)	6 (29)
SD, n (%)	10 (48)
Median TTR, (range), mon	1.3 (1.1–1.5)
CBR, n (%) [95% CI]	7 (33) [15–59]
Median DOR (95% CI), mon	NR (4.3–NR)

CBR, clinical benefit rate defined as CR + uCR + PR + uPR or (SD >= 6 months); CI, confidence interval; DOR, duration of response; mon, month; NR, not reached; ORR, objective response; PR, partial response; SD, stable disease; TTR, time to response

62% (13/21) of Patients Demonstrated a Reduction in Tumor Size

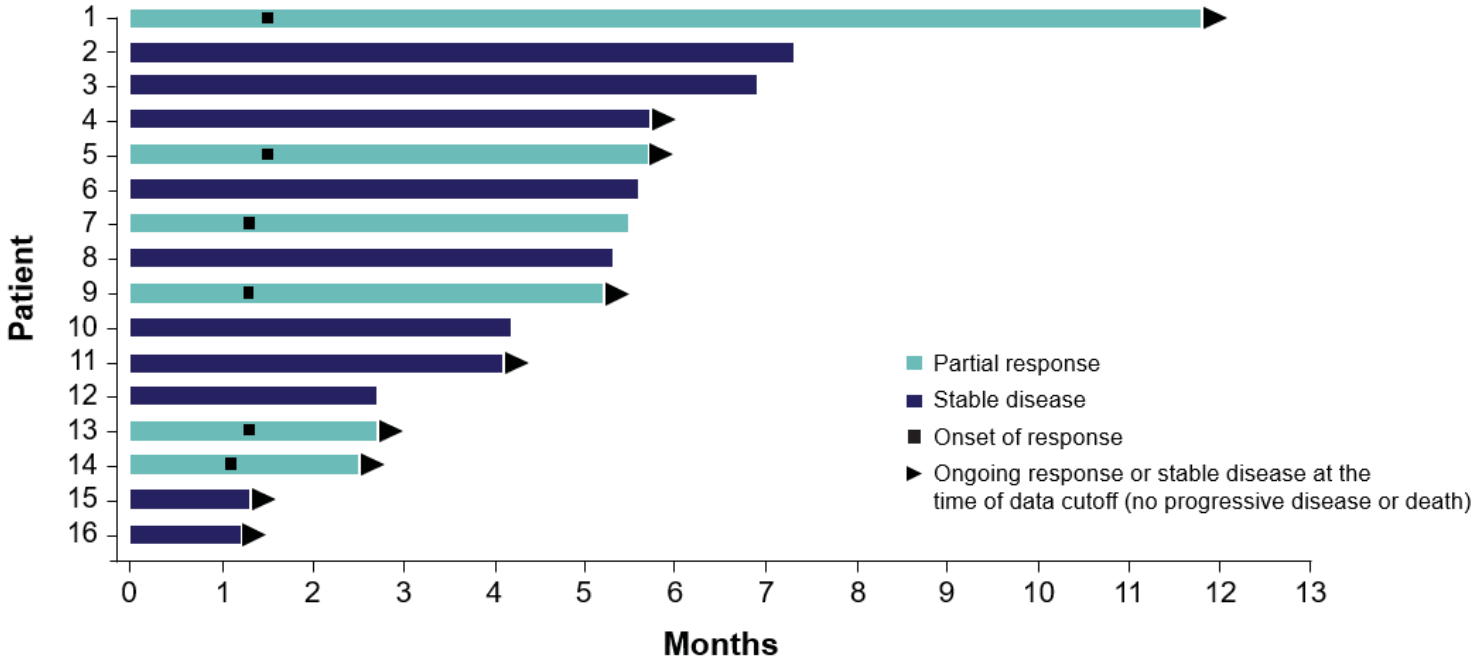


*Denotes patients who had a 0% change from baseline in tumor size.
One patient had only screening data and thus is not represented.

Duration of Response (Local Assessment)

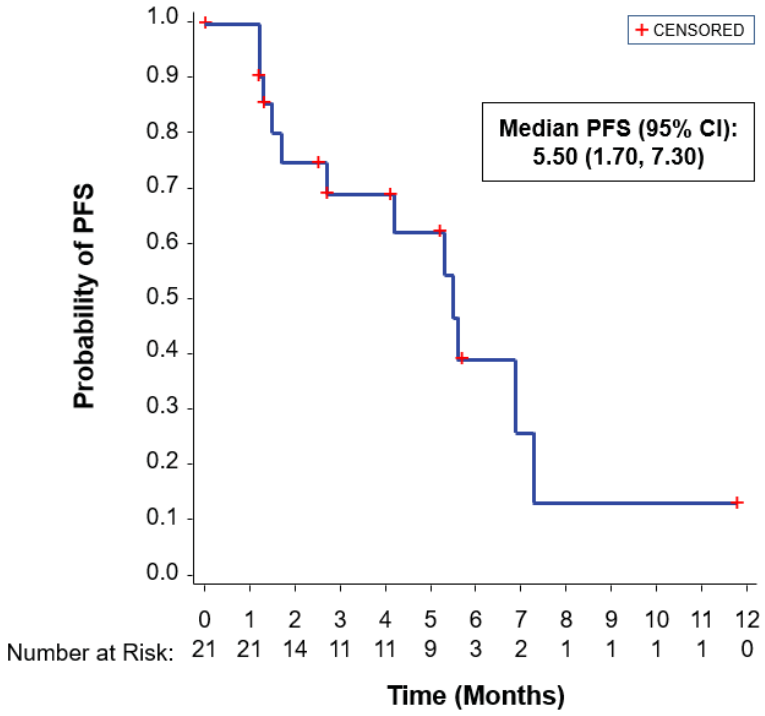
Suggested for center column content

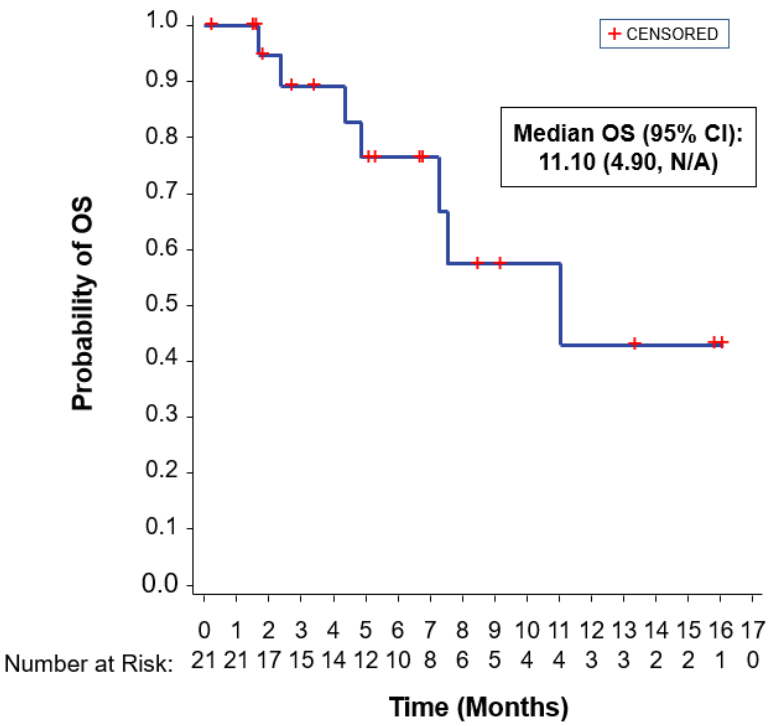
- Median DOR not reached
- The DOR of responders ranged from 1.4+ to 10.4+ months, with 3 of 6 responders having a duration of ≥4 months
- Five of 6 responders have an ongoing response



DOR, duration of response.

Survival Outcomes





- At this early follow-up, the median PFS and OS compare favorably to current standards of care for platinum-ineligible patients with mUC who have progressed after CPI therapy
- The OS rate (95% CI) at 6 months and 12 months was: 76.4% (48.4–90.5) and 43.0% (13.1–70.4), respectively

Treatment-Related Adverse Events ≥15% Any Grade (N=21)

Category	Event	All Grades (%)	Grade 3 (%)	Grade 4 (%)
Hematologic	**Neutropenia[a]**	**10 (48)**	**5 (24)**	**4 (19)**
	Leukopenia[b]	**8 (38)**	**2 (9)**	**2 (9)**
	Anemia	7 (33)	4 (19)	0 (0)
Gastrointestinal	**Diarrhea**	**14 (67)**	**3 (14)**	**1 (5)**
	Nausea	**9 (43)**	**0 (0)**	**0 (0)**
	Abdominal pain	5 (24)	0 (0)	0 (0)
General disorders & administrative site conditions	Fatigue	12 (57)	7 (33)	0 (0)
Skin & subcutaneous tissue	**Alopecia**	**11 (52)**	**0 (0)**	**0 (0)**
Metabolism & nutrition	Decreased appetite	5 (24)	0 (0)	0 (0)
	Hyponatremia	5 (24)	1 (5)	0 (0)

Median treatment cycles: 5 (range: 1–15); worst grade CTCAE reported; data cut-off : 03Feb2020
[a]Combined term includes neutropenia and neutrophil count decreased; [b]Combined term includes leukopenia and white blood cell count decreased
CTCAE, Common Toxicity Criteria for Adverse Events; pts, patients; TRAE, treatment-related adverse event.

- Most common TRAEs were: diarrhea, fatigue, alopecia, neutropenia, and nausea
- Key grade ≥3 TRAEs were: fatigue, neutropenia, anemia, diarrhea, and febrile neutropenia [n=2, all grade 3]
- Other key TRAEs:
  - 1 event of grade 3 pneumonitis that resolved and required drug withdrawal in a patient who was previously treated with a CPI and then Enfortumab vedotin
  - No cases of ocular toxicities

Conclusions: Treatment of Metastatic Urothelial Cancer

- Enfortumab Vedotin is FDA approved as third line therapy in patients who have progressed on chemotherapy and checkpoint inhibition therapy
- Enfortumab Vedotin has accelerated approved in patient who cisplatin ineligible and have progressed on 1 prior treatment
- IMU132 (phase 2) have promising activity in patients who have failed 2 or more prior therapies
- Studies are evaluating the combination of checkpoint inhibition with targeted therapies