EV-201 COHORT 2: ENFORTUMAB VEDOTIN IN CISPLATIN-INELIGIBLE PATIENTS WITH LOCALLY ADVANCED OR METASTATIC UROTHELIAL CANCER WHO RECEIVED PRIOR PD-1/PD-L1 INHIBITORS (NCT03219333)

Arjun V. Balar, Bradley McGregor, Jonathan Rosenberg, Michiel S. van der Heijden, Se Hoon Park, Jae Lyun Lee, Michael R. Harrison, Elisabeth I. Heath, Mark N. Stein, Yohann Loriot, Andrea Necchi, Joyce Steinberg, Shang-Ying Liang, Eric Kim, Janet Trowbridge, Mary Campbell, Daniel P. Petrylak, and Evan Y. Yu

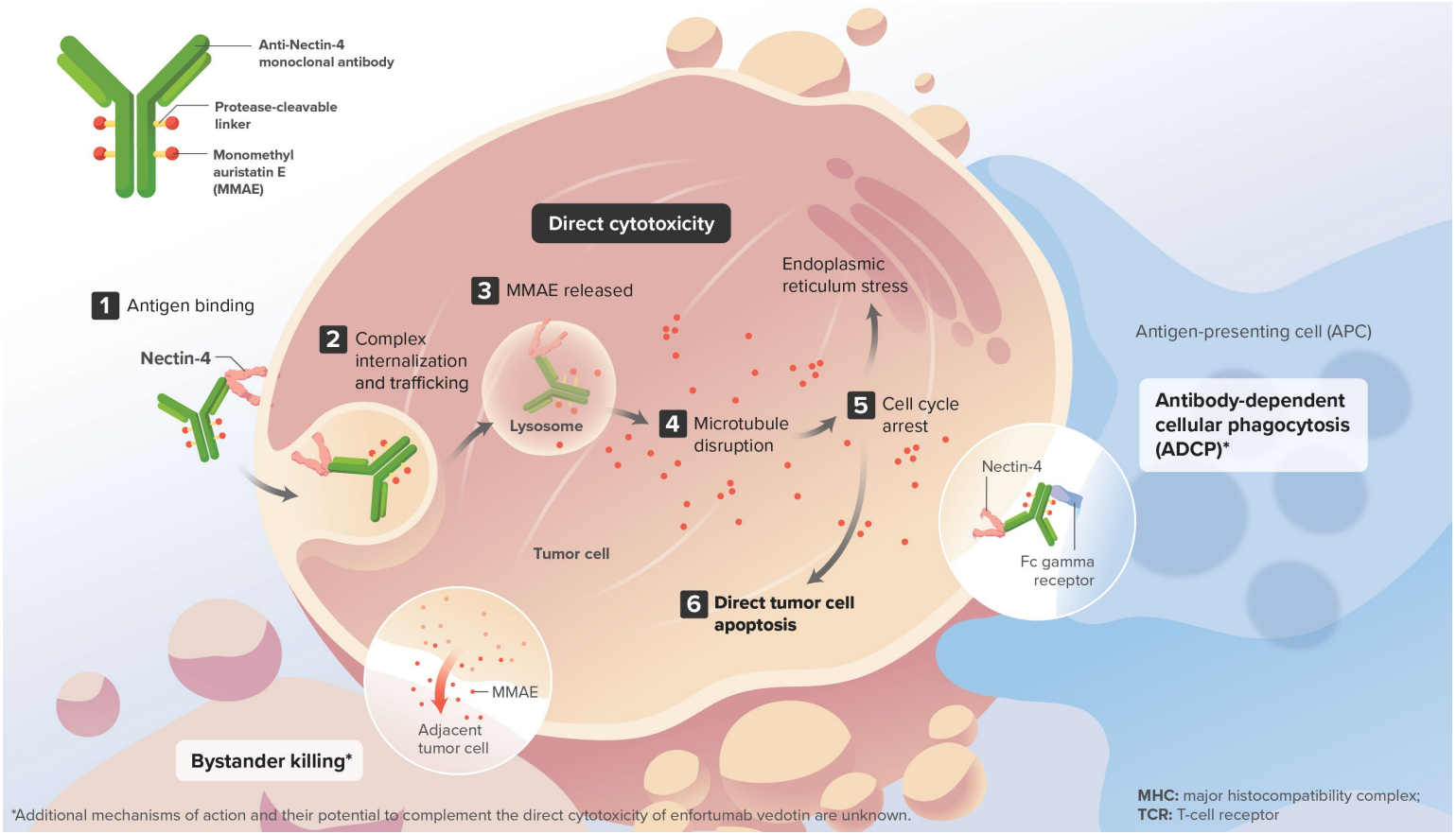
ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

Cisplatin-Ineligible Patients with Advanced Urothelial Carcinoma have Limited Treatment Options

- Cisplatin-based chemotherapy is the first-line standard of care for advanced urothelial carcinoma and is associated with an overall survival benefit[1]
- Approximately half of patients with advanced urothelial carcinoma in the United States are cisplatin-ineligible[2]
- PD-1/PD-L1 inhibitors are approved in first line for cisplatin-ineligible patients with advanced urothelial carcinoma whose tumors express PD-L1[3,4]
  - Objective responses occur in ~20-30% of patients unselected for PD-L1 expression
- Cisplatin-ineligible patients progressing on first-line immunotherapy have limited treatment options
  - EV has demonstrated survival benefit in patients who have received both platinum-containing chemotherapy and immunotherapy[5]
  - EV-201 Cohort 2 evaluated EV in the post-immunotherapy setting in cisplatin-ineligible patients

[1]von der Maase H, et al. J Clin Oncol. 2005;23(21):4602-8; [2]Galsky MD, et al. J Clin Oncol. 2011;29(17):2432-8; [3]Vuky J, et al. J Clin Oncol. 2020;38(23):2658-66; [4]Balar AV, et al. Lancet. 2017;389(10064):67-76; [5]Seagen Inc., Press release, Sep 18, 2020.

Enfortumab Vedotin: Nectin-4 Directed Therapy Mechanism of Action

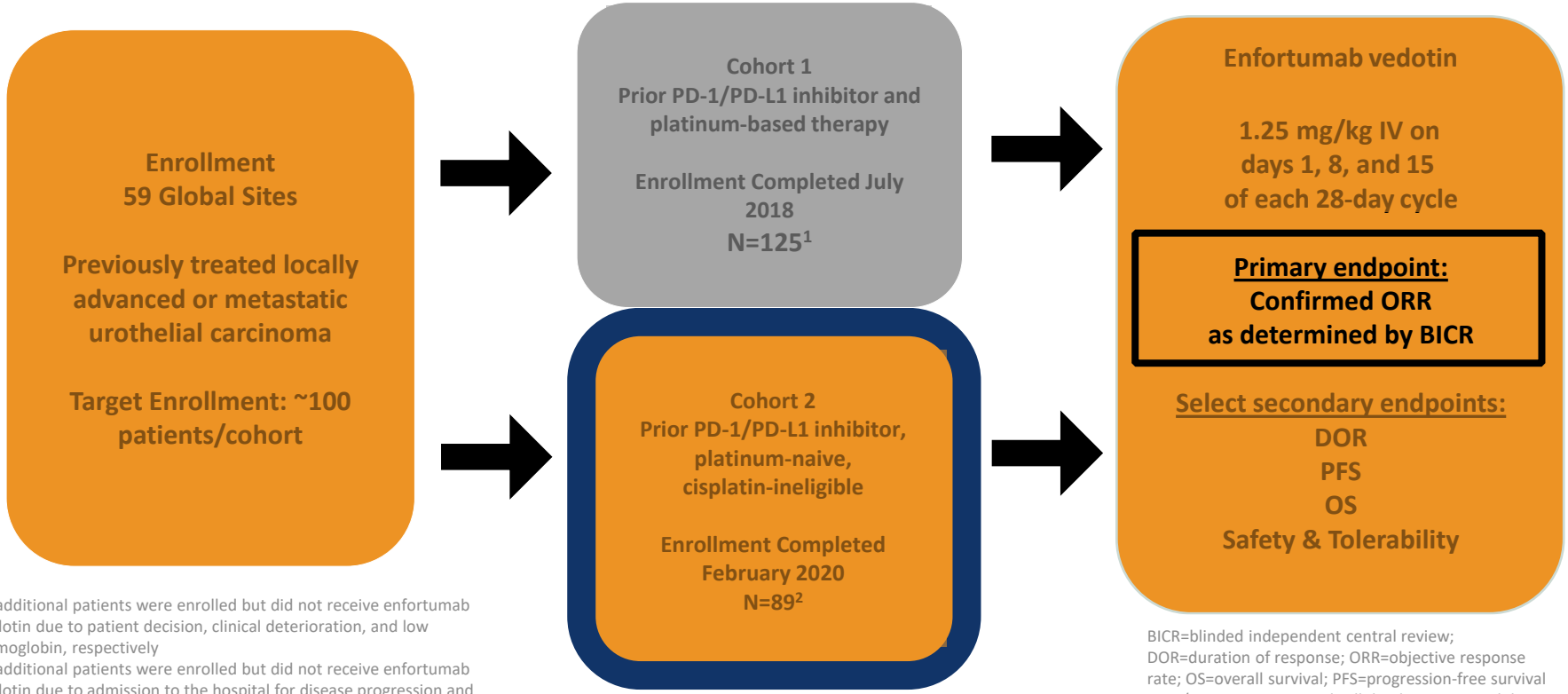


Enfortumab vedotin is an investigational agent in some settings, and its safety and efficacy have not been established.

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201: Non-Comparative, Pivotal Phase 2 Trial



[1]3 additional patients were enrolled but did not receive enfortumab vedotin due to patient decision, clinical deterioration, and low hemoglobin, respectively

[2]2 additional patients were enrolled but did not receive enfortumab vedotin due to admission to the hospital for disease progression and hospice care, respectively

BICR=blinded independent central review; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival PD-1/PD-L1=programmed cell death protein 1 inhibitor, programmed death-ligand 1 inhibitor

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

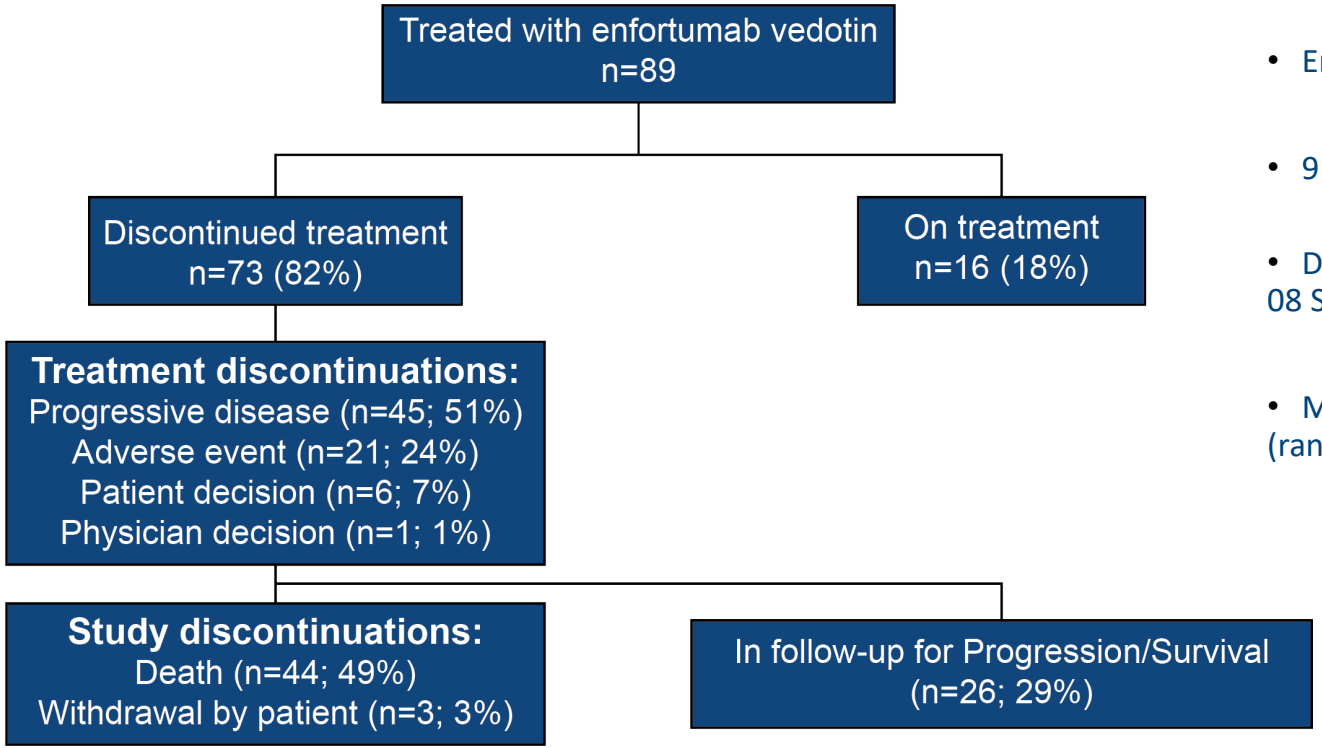
EV-201 Cohort 2: Key Eligibility Criteria

- Key inclusion criteria:
  - Locally advanced unresectable or metastatic urothelial carcinoma (including divergent differentiation)
  - Previously treated with a PD-1/PD-L1 inhibitor
  - Ineligible for cisplatin-containing chemotherapy[1] and no prior exposure to platinum-containing chemotherapy in the locally advanced or metastatic setting
  - Progression during or following most recent treatment
- Key exclusion criteria:
  - Ongoing sensory or motor neuropathy ≥Grade 2
  - Active CNS metastases
  - Uncontrolled diabetes mellitus[2]

[1] Defined as meeting any of the following criteria: impaired renal function ([CrCl] ≥30 and <60 mL/min), hearing loss ≥Grade 2, ECOG performance status score >2
[2] Hemoglobin A1C (HbA1c) ≥8% or HbA1c of 7% to <8% with associated diabetes symptoms, polyuria or polydipsia, that were not otherwise explained

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201 Cohort 2: Patient Disposition



- Enrollment from Oct 2017 to Feb 2020
- 91 enrolled[1]
- Data Cutoff date for Primary Analysis: 08 Sept 2020
- Median time on treatment: 6 months (range 0.3-24.6 months)

[1]2 patients did not receive enfortumab vedotin treatment due to admission to the hospital for disease progression and pursuing hospice care, respectively

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%)

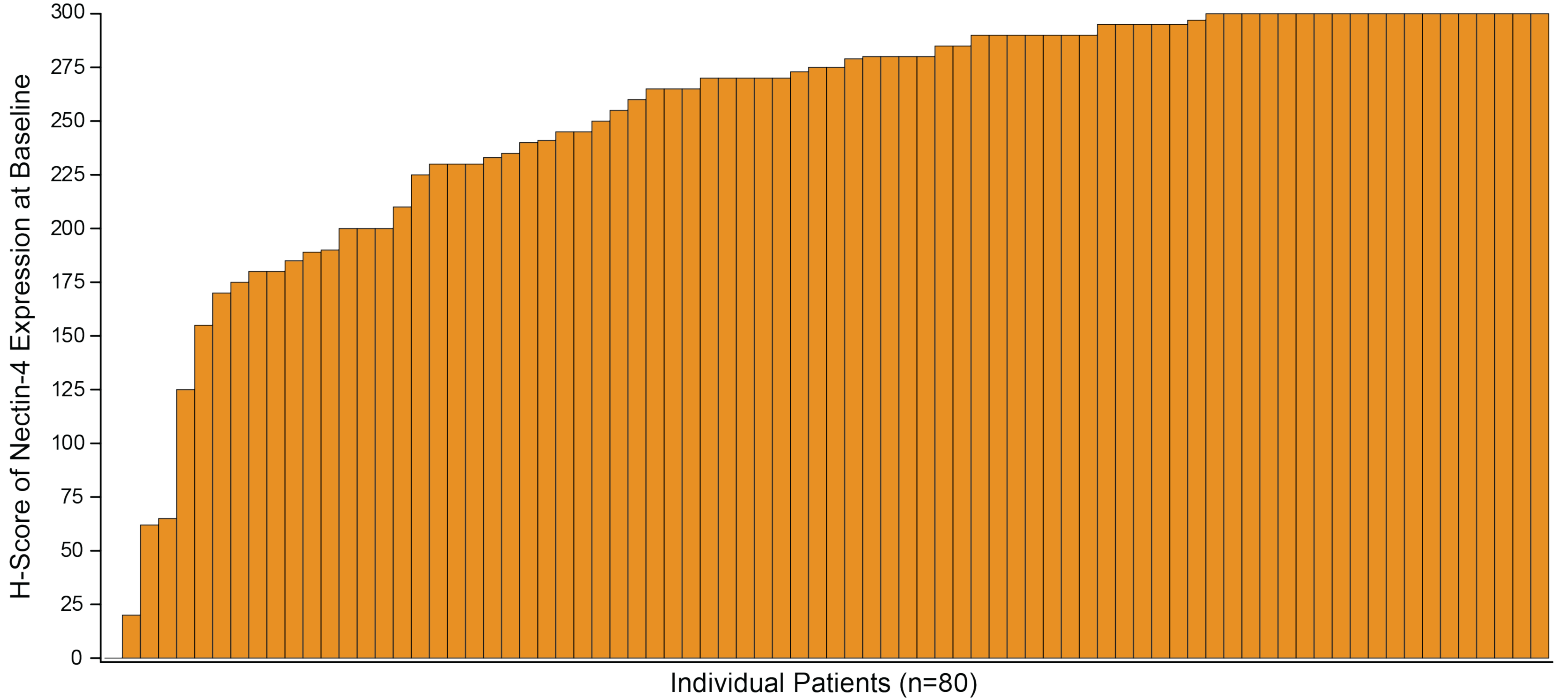
Characteristic	Patients (N=89)
Primary tumor location	
Upper tract[1]	38 (43%)
Bladder/other	51 (57%)
Metastasis sites	
Lymph nodes only	18 (20%)
Visceral disease[2]	70 (79%)
Liver	21 (24%)
Received prior PD-1/PD-L1 therapy in first line	87 (98%)
Responder[3] to PD-1/PD-L1-containing therapy	22 (25%)

[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.

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

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.

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

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

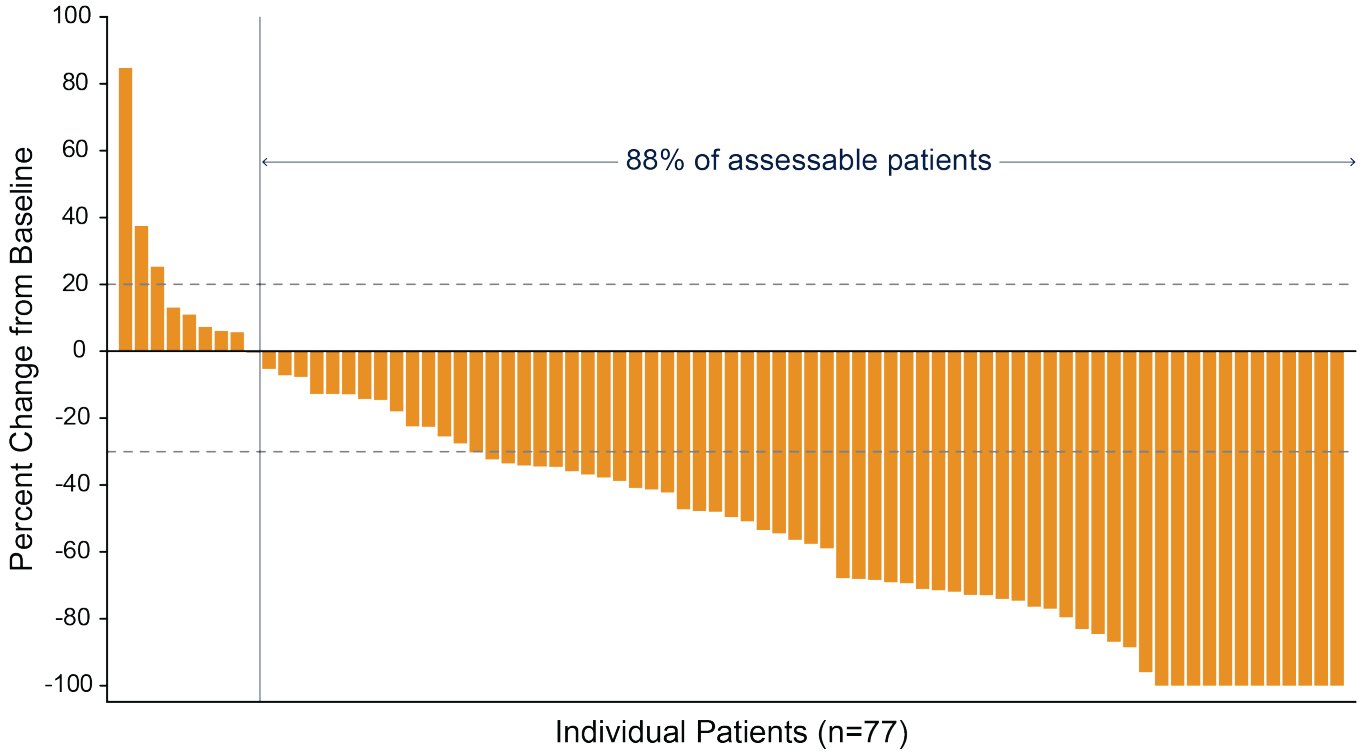
[2]Best overall response according to RECIST v1.1. Complete response and partial response were confirmed with repeat scans ≥28 days after initial response.

[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.

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

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

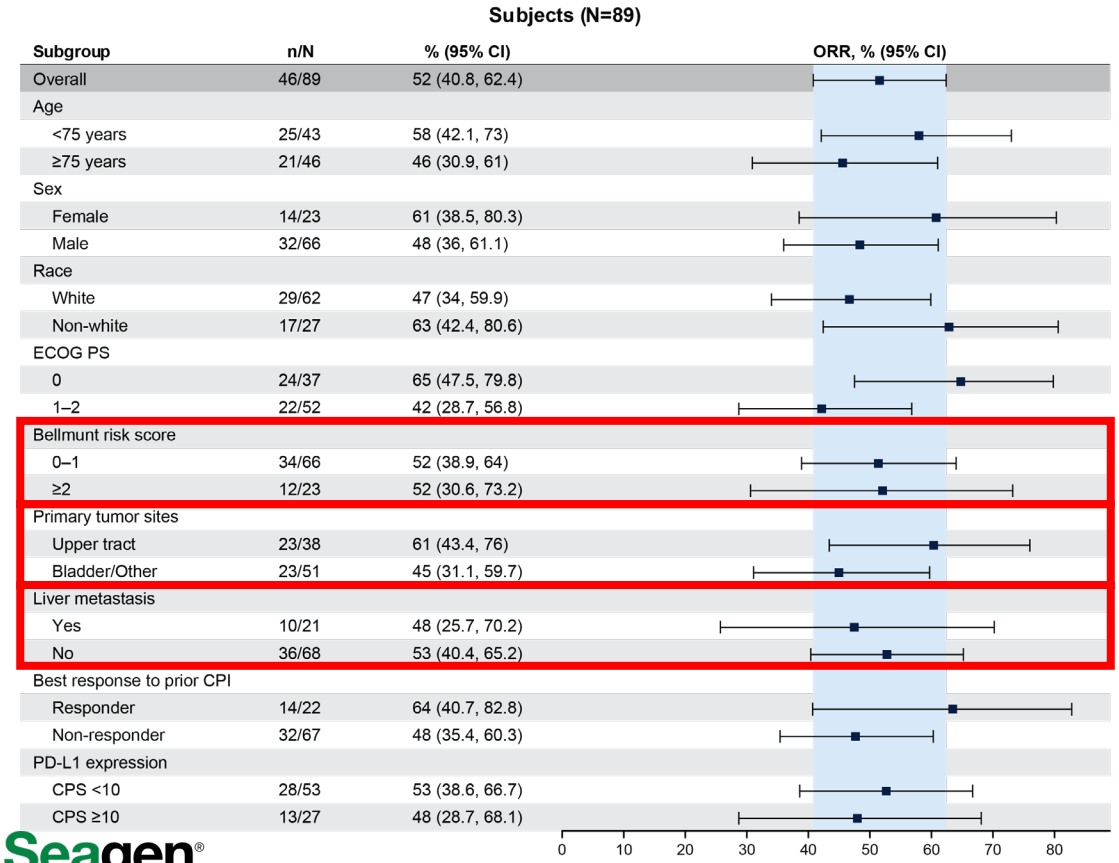


Data are not available for 12 subjects due to no response assessment post-baseline (n=5), incomplete assessment of target lesions post-baseline (n=1), or no measurable disease at baseline per BICR (n=6).

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201 Cohort 2: Responses by Subgroup per BICR



Responses were observed across all subgroups, including patients:

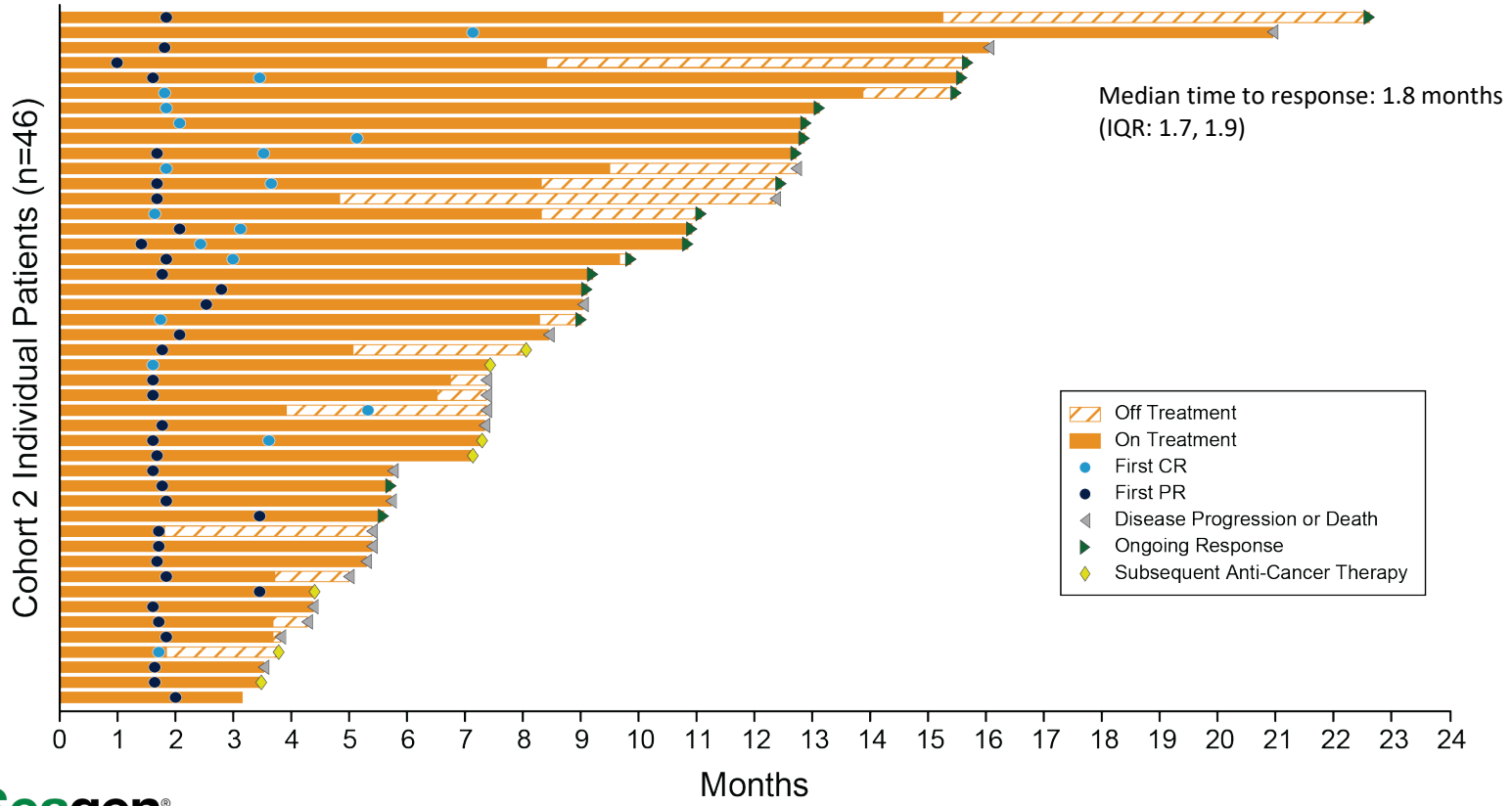
- with primary tumor sites in the upper tract (ORR=61%)
- with liver metastasis (ORR=48%)
- who did not respond to prior PD-1/PD-L1 inhibitors (ORR=48%)

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

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

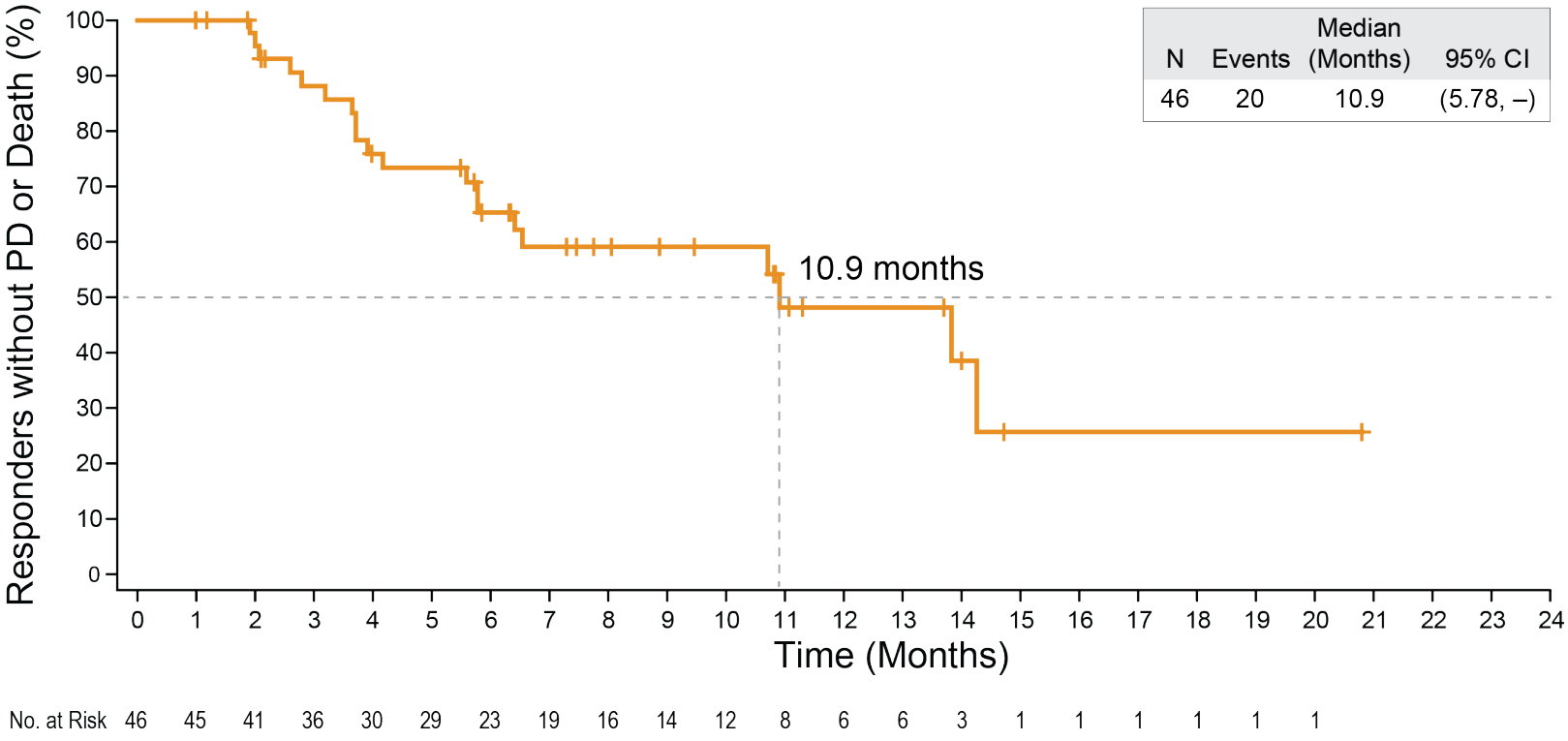
EV-201 Cohort 2: Time to Response per BICR



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

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201 Cohort 2: Duration of Response per BICR



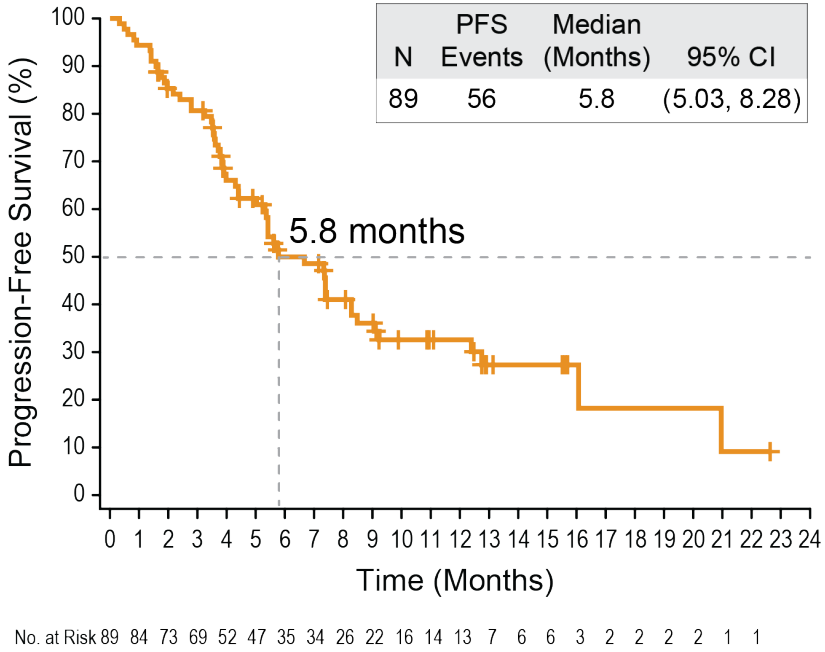
N	Events	Median (Months)	95% CI
46	20	10.9	(5.78, –)

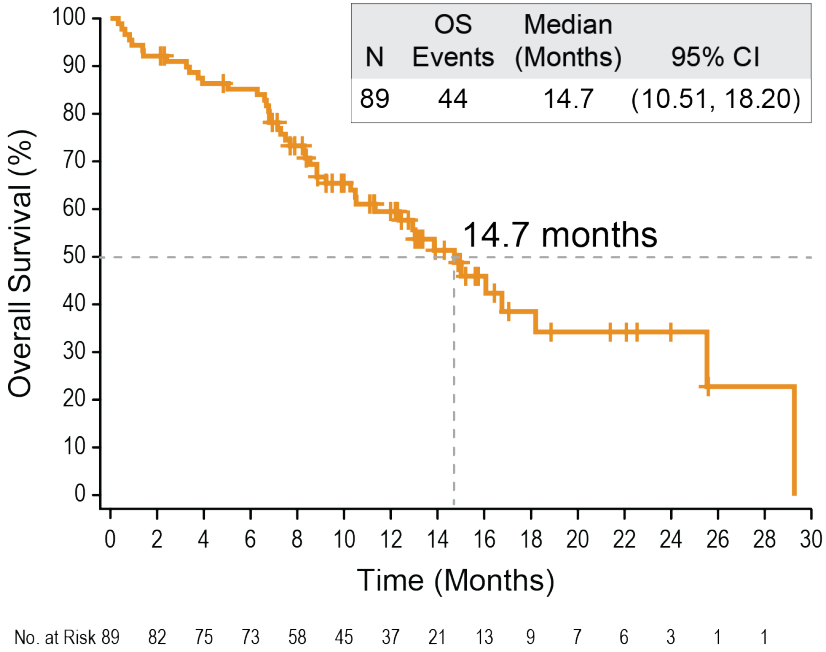
BICR = Blinded Independent Central Review; PD = Progressive Disease; CI = Confidence Interval

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

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

Median follow-up: 13.4 months





Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

14

EV-201 Cohort 2: Treatment-Related Adverse Events

TRAEs[1] in ≥20% of patients (any Grade) or ≥5% (≥Grade 3)	Patients (N=89) n (%)	
	Any Grade	≥Grade 3
Overall TRAEs	86 (97)	49 (55)
Alopecia	45 (51)	–
Peripheral sensory neuropathy	42 (47)	3 (3)
Fatigue	30 (34)	6 (7)
Decreased appetite	29 (33)	5 (6)
Pruritus	27 (30)	3 (3)
Rash maculo-papular	27 (30)	7 (8)
Dysgeusia	24 (27)	–
Weight decreased	23 (26)	1 (1)
Anemia	22 (25)	5 (6)
Diarrhea	20 (22)	5 (6)
Nausea	20 (22)	1 (1)
Neutropenia	11 (12)	8 (9)
Hyperglycemia	8 (9)	5 (6)
Lipase increased	7 (8)	5 (6)

TRAEs led to discontinuations in 16% of patients

- Peripheral sensory neuropathy was the most common reason (4%)

4 deaths considered to be treatment related by the investigator:

- acute kidney injury
- metabolic acidosis
- multiple organ dysfunction syndrome
- pneumonitis (occurred >30 days of last dose)

3 of these deaths occurred within 30 days of first dose of EV occurred in patients with BMI ≥30 kg/m^2

All 4 deaths: confounded by age (≥75 years) and other comorbidities

TRAEs = Treatment-related Adverse Events

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201 Cohort 2: Treatment-Related Adverse Events of Special Interest

Events categorized based on queries for related MedDRA[1] terms

Skin Reactions
61% any grade, 17% ≥Grade 3
Median Onset = 0.5 months[2]
% resolution/improvement[3] = 80%

- No Grade 5 events, 1 Grade 4 event
- 13 patients with severe cutaneous adverse reactions[4]
  - Most ≤Grade 2, no Grade 4 or 5 events
  - 4 patients with Grade 3 events: stomatitis, skin exfoliation, dermatitis bullous, dermatitis exfoliative generalised
  - 1 discontinuation due to severe cutaneous adverse reaction

Peripheral Neuropathy
54% any grade, 8% ≥Grade 3
Median Onset = 2.4 months
% resolution/improvement[3] = 56%

- PN rate was similar in patients with and without pre-existing PN (53% vs 54%)

Hyperglycemia
10% any grade, 6% ≥Grade 3
Median Onset = 0.5 months[2]
% resolution/improvement[3] = 89%

- Higher rate of HG in patients with pre-existing HG than those without pre-existing HG (20% vs. 7%)
- Higher rate of HG in patients with BMI ≥30 kg/m^2 than those with BMI <30 kg/m^2 (23% vs. 8%)

PN = Peripheral Neuropathy; HG = Hyperglycemia; BMI = Body Mass Index

[1]Medical Dictionary for Regulatory Activities

[2]Most occurred in Cycle 1

[3]Resolution/Improvement as of last follow-up

[4]A range of skin reaction preferred terms, irrespective of grade

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

EV-201 Cohort 2: Summary and Conclusions

- Following immunotherapy, cisplatin-ineligible patients need effective treatment options
- The response rates to EV in this study are numerically the highest observed for any regimen in cisplatin-ineligible patients with advanced urothelial carcinoma
  - 52% ORR, with 20% CR rate
  - 10.9 months median duration of response
  - Response rates were consistent across all subgroups
- Tolerable safety profile in an elderly patient population ineligible for cisplatin
- Activity demonstrated in EV-201 Cohort 2 builds upon the benefit shown in PD-1/PD-L1 inhibitor and platinum-treated patients in EV-301
- These data support continued investigation of EV across the spectrum of urothelial carcinoma and may support a new standard of care for this population with unmet need

ORR = Objective Response Rate; CR = Complete Response
Ongoing enfortumab vedotin trials: **EV-103:** EV alone or in combination with pembrolizumab and/or chemotherapy (NCT03288545) **EV-302:** EV in combination with pembrolizumab vs. chemotherapy alone (NCT04223856)

Seagen®

ASCO GU 2021 Virtual Congress. Presented February 12, 2021; Abstract No. 394

Acknowledgments

Thank you to our patients and their families for their participation in the study, and to all research personnel for their support of this important trial.