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Enfortumab Vedotin Plus Pembrolizumab in Previously Untreated Advanced Urothelial Cancer

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abstract

PURPOSE Cisplatin-based combination chemotherapy remains the standard of care for locally advanced or metastatic urothelial cancer (la/mUC); however, toxicity is substantial, responses are rarely durable, and many patients with la/mUC are ineligible. Each enfortumab vedotin and pembrolizumab have shown a survival benefit versus chemotherapy in UC, are not restricted by cisplatin eligibility, and warrant investigation as a first-line (1L) combination therapy in patients ineligible for cisplatin.

METHODS In this ongoing phase Ib/II, multicenter, open-label study, 1L cisplatin-ineligible patients with la/mUC received enfortumab vedotin 1.25 mg/kg once daily on days 1 and 8 and pembrolizumab 200 mg (day 1) intravenously once daily in 3-week cycles. The primary end point was safety. Key secondary end points included confirmed objective response rate, duration of response (DOR), and overall survival (OS).

RESULTS Forty-five patients received enfortumab vedotin plus pembrolizumab. The most common treatment-related adverse events (TRAEs) were peripheral sensory neuropathy (55.6%), fatigue (51.1%), and alopecia (48.9%). Twenty-nine patients (64.4%) had grade 3 or higher TRAEs; the most common were increased lipase (17.8%), maculopapular rash (11.1%), and fatigue (11.1%). One death (2.2%) was classified as a TRAE. The confirmed objective response rate after a median of nine cycles was 73.3% with a complete response rate of 15.6%. The median DOR and median OS were 25.6 months and 26.1 months, respectively.

CONCLUSION Enfortumab vedotin plus pembrolizumab showed a manageable safety profile. Most patients experienced tumor shrinkage. The median DOR and median OS exceeding 2 years in a cisplatin-ineligible patient population make this a promising combination currently under investigation in a phase III study (ClinicalTrials.gov identifier: NCT04223856).

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ASSOCIATED CONTENT

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Data Supplement

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

Locally advanced or metastatic urothelial carcinoma (la/mUC) is a lethal malignancy. Approximately half of all patients with la/mUC are ineligible for cisplatin chemotherapy because of impaired renal function, poor performance status, and other comorbidities.[1-6] Historically, first-line (1L) carboplatin-based regimens have shown limited activity and have been poorly tolerated.[7,8] Programmed cell death protein 1/programmed death-ligand 1 (PD-1/PD-L1) inhibitors are restricted to a limited number of patients who are either cisplatin-ineligible with a high level of PD-L1 expression or are not eligible for any platinum-based therapy. Although maintenance therapy with avelumab after 1L platinum-gemcitabine treatment has shown a survival benefit, only patients who did not progress with 1L therapy were eligible. These limitations highlight the continuous unmet need for more effective and tolerable 1L treatment options for cisplatin-ineligible patients.

Both enfortumab vedotin and pembrolizumab are effective monotherapy treatments in patients with la/mUC.[9-12] Preclinical studies of vedotin antibody–drug conjugates (ADCs), including enfortumab vedotin, show that these ADCs induce hallmarks of immunogenic cell death, including the release of damage-associated molecular patterns.[13-16] Damage-associated molecular patterns are recognized by innate and adaptive immune cells, which ultimately leads to engulfment of tumor cells by antigen-presenting cells and subsequent

CONTEXT

Key Objective

To assess the safety and tolerability of first-line enfortumab vedotin in combination with pembrolizumab in patients with advanced urothelial cancer (aUC) who are cisplatin-ineligible.

Knowledge Generated

Enfortumab vedotin plus pembrolizumab showed a tolerable and manageable safety profile and a confirmed objective response rate of 73.3%. With the median duration of response and the overall survival exceeding 2 years, this combination offers a potential first-line treatment option for patients with aUC.

Relevance

The antitumor activity of enfortumab vedotin plus pembrolizumab appears to be higher than that of conventional carboplatin-based chemotherapy in patients with aUC. Given this potential clinical benefit, enfortumab vedotin plus pembrolizumab received Breakthrough Therapy designation by the US Food and Drug Administration and is under further investigation in phase II and III studies.

cross-presentation of tumor antigens to cytotoxic T cells. These T cells mount antigen-specific responses that are further augmented by PD-1/PD-L1 inhibitors, such as pembrolizumab. Thus, combining enfortumab vedotin with pembrolizumab may enhance antitumor activity versus either agent alone on the basis of their distinct and complementary engagement of the immune system. Here, we present safety and efficacy results from the EV-103 Dose Escalation Phase and Dose Expansion Cohort A to evaluate enfortumab vedotin plus pembrolizumab in 1L cisplatin-ineligible patients with la/mUC.

METHODS

Trial Participants

Eligible patients (age ≥ 18 years) had histologically documented la/mUC (including squamous differentiation and mixed cell types), an Eastern Cooperative Oncology Group performance status score of 0 or 1 (on a 5-point scale; higher scores indicate greater disability), and an investigator-assessed life expectancy of 3 or more months. Patients had measurable disease according to RECIST v1.1[17] and adequate organ function and were eligible for pembrolizumab therapy. Patients with pre-existing grade 2 or higher sensory or motor neuropathy, active CNS metastases, or uncontrolled diabetes (defined as hemoglobin A1c [HbA1c] ≥ 8% or HbA1c 7% to < 8% with associated diabetes symptoms) were excluded.

During the Dose Escalation Phase, investigators determined if patients were either ineligible for 1L cisplatin-based chemotherapy and had not received prior systemic therapy for la/mUC or had disease progression during or after treatment with at least one platinum-containing regimen in the neoadjuvant or adjuvant setting. Patients in Dose Expansion Cohort A were all ineligible for cisplatin-based chemotherapy at enrollment on the basis of investigator assessment or if they had an Eastern Cooperative Oncology Group performance status of 2, impaired renal function (defined as creatinine clearance, calculated or measured) ≥ 30 and <60 mL/min, hearing loss/dysfunction, age, and/or allergy to cisplatin. Previous adjuvant or neoadjuvant platinum-based therapy was not permitted within 12 months of the study. Full eligibility criteria are provided in the trial protocol, available with the full text of this article in the Protocol (online only).

Treatment

The recommended doses of enfortumab vedotin were determined in the Dose Escalation phase. The enfortumab vedotin dose was escalated from 1 mg/kg to 1.25 mg/kg (maximum total dose 125 mg) intravenously (IV) over 30 minutes once on days 1 and 8 of every 3-week cycle in cohorts of three patients. Pembrolizumab was given as 200 mg IV once on day 1 of each 3-week cycle and was administered 30 minutes after enfortumab vedotin. Patients were permitted to continue study treatment until radiographically confirmed disease progression, unacceptable toxicity, investigator decision, consent withdrawal, the start of subsequent anticancer therapy, or pregnancy.

Trial Oversight

This study was designed by the sponsors in collaboration with an advisory committee. The study protocol was approved by independent review boards or ethics committees, and the trial was conducted in agreement with the Declaration of Helsinki and International Council for Harmonisation Good Clinical Practice Guidelines. Written informed consent was obtained from patients before any study procedures. Aggregated safety data were generated by the sponsor biostatisticians and analyzed by sponsors and authors. Safety parameters were evaluated throughout the treatment cycle and study by the safety monitoring committee.

The authors attest to the accuracy and completeness of the data and the fidelity of the study to the protocol. All the

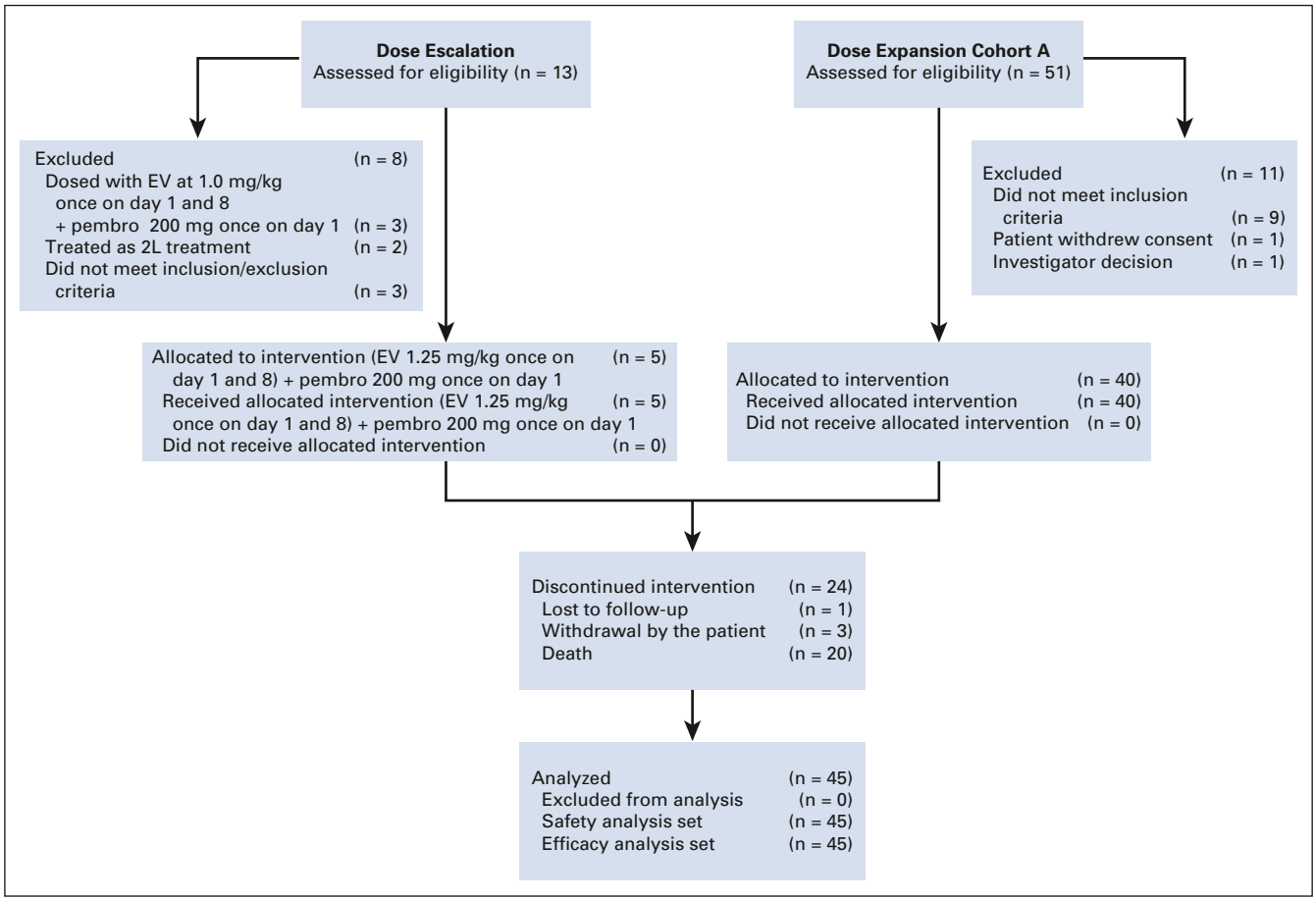

FIG 1. Screening, allocation, follow-up, and analyses. 2L, second-line; EV, enfortumab vedotin; pembro, pembrolizumab.

authors had access to the data used in the preparation of the manuscript. The authors, with writing and editorial support funded by the trial sponsors, developed and approved the manuscript.

End Points and Assessments

The primary end point was safety as assessed by adverse events (AEs), laboratory abnormalities, and dose-limiting toxicities (only during the Dose Escalation Phase). Adverse events, including AEs of special interest (AESIs; preidentified on the basis of enfortumab vedotin), were classified by the system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA Version 23.0; Data Supplement, online only) and graded according to the National Cancer Institute common terminology criteria for AEs version 4.03. Treatment-related adverse events (TRAEs) were determined by the investigator and assessed for the treatment combination. Immune-mediated (im) AEs were evaluated using previously described criteria for pembrolizumab monotherapy.[9]

Key secondary end points included disease control rate, confirmed objective response rate, duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Investigators assessed and confirmed antitumor efficacy by reviewing computed tomography (CT) scans with IV contrast of the chest, abdomen, and pelvis. CT without contrast or magnetic resonance imaging was permitted if contrast was contraindicated; the same imaging modality was recommended throughout the study. Response assessment time points were calculated from cycle 1 day 1, and objective response rates were confirmed by the investigators per RECIST v1.1, with repeat scans 4-5 weeks after the first documented response. Subsequent response assessments after confirmation of response were performed every 9 weeks (± 7 days) until 1 year after the first dose and then every 12 weeks (± 7 days).

In addition, Nectin-4 and PD-L1 expression levels were assessed retrospectively on baseline archival or fresh tumor specimens. Briefly, formalin-fixed, paraffin-embedded tumor biopsies were collected at screening and assessed centrally for Nectin-4 protein expression levels. Immunostained slides were scored by a pathologist to generate an H-score (range, 0-300). PD-L1 expression status was assessed using the combined positive score (low, < 10; high, ≥ 10).

Statistical Analysis

Safety and efficacy end points were assessed in all patients who received any dose of enfortumab vedotin or

TABLE 1. Patient Demographics and Disease Characteristics at Baseline

Characteristic	Patients (N = 45)
Sex, No. (%)	
Male	36 (80.0)
Female	9 (20.0)
Age, years	
Median (range)	69.0 (51-90)
Age group, years, No. (%)	
< 75	29 (64.4)
≥ 75	16 (35.6)
ECOG PS, No. (%)	
0	15 (33.3)
1	22 (48.9)
2	8 (17.8)
BMI, kg/m^2, No. (%)	
< 25	16 (35.6)
25 to < 30	19 (42.2)
≥ 30	10 (22.2)
HbA1c, %, No. (%)	
< 6.5	42 (93.3)
≥ 6.5	3 (6.7)
Primary tumor location, No. (%)	
Bladder/others	30 (66.7)
Upper tract	15 (33.3)
Histology type	
Transitional cell carcinoma (or UC) only	15 (33.3)
With squamous differentiation	8 (17.8)
With other histologic variants	22 (48.9)
Baseline metastatic site(s), No. (%)[a]	
Visceral disease	38 (84.4)
Liver	14 (31.1)
Lymph node only	7 (15.6)
Prior surgeries	
Prior cystectomy[b]	21 (46.7)
Prior nephrectomy[c]	13 (28.9)
Prior metastasectomy	2 (4.4)
Baseline PD-L1 expression, No. (%)	
CPS ≥ 10	14 (31.1)
CPS < 10	18 (40.0)
CPS not available	13 (28.9)

Abbreviations: BMI, body mass index; CPS, Combined Positive Score; ECOG PS, Eastern Cooperative Oncology Group performance status; HbA1c, hemoglobin A1c; PD-L1, programmed death-ligand 1; UC, urothelial cancer.

[a]A patient might have metastatic disease in more than one location.

[b]Cystectomy includes partial and total cystectomy/cystoprostatectomy.

[c]Nephrectomy includes partial and total nephrectomy/nephroureterectomy.

pembrolizumab. Patients who received the recommended dose of enfortumab vedotin in combination with pembrolizumab in the 1L setting in the Dose Escalation Phase (N = 5) were pooled for analysis with Dose Expansion Cohort A (N = 40). Time-to-event end points, such as DOR, PFS, and OS, were estimated using the Kaplan-Meier method, with 95% CIs by the complementary log-log transformation. Objective response rate and disease control rate were summarized with 95% CIs using the Clopper-Pearson method. The sample size of Dose Expansion Cohort A was determined using Simon's two-stage minimax design. With a target sample size of 39 patients and assuming at least a 55% objective response rate, Dose Expansion Cohort A had a power of 80% to detect a historical objective response rate of ≥ 35% for the corresponding population.

RESULTS

Patient Disposition and Baseline Characteristics

We report data on 45 cisplatin-ineligible patients with la/mUC who received enfortumab vedotin 1.25 mg/kg IV once daily on days 1 and 8 and pembrolizumab 200 mg IV once on day 1 in the 1L setting at 18 US clinical sites. At data cutoff (October 13, 2020), 21 (46.7%) patients remained on study, with 7 (15.6%) patients still receiving treatment and 14 (31.1%) patients in long-term follow-up (Fig 1). Patients received a median of 9 (range, 1-34) cycles of study treatment.

At baseline, patients were predominately male (80.0%) and the median age was 69 years; 35.6% were age ≥ 75 years. Visceral metastases were present in 84.4% of patients, including 31.1% with liver metastases. Disease originated in upper tract in 33.3% of patients (Table 1).

Safety

The most common TRAEs were peripheral sensory neuropathy, fatigue, and alopecia; the most common grade 3 or higher events were asymptomatic lipase elevation, fatigue, and maculopapular rash (Table 2). Seven patients (15.6%) experienced a serious TRAE, with no serious TRAE occurring more than once. TRAEs led to dose reductions in 14 (31.1%) patients and discontinuations in 11 (24.4%) patients and were not mutually exclusive. Peripheral sensory neuropathy was the most common TRAE leading to either dose reduction (six patients, 13.3%) or treatment discontinuation (four patients, 8.9%). No patients discontinued therapy because of a skin reaction or hyperglycemia. One patient (2.2%) died because of a TRAE (multiple organ dysfunction syndrome).

Treatment-related AESIs prespecified for analysis (as composite terms defined by MedDRA) were peripheral neuropathy, skin reactions, and hyperglycemia (Data Supplement). Treatment-related peripheral neuropathy occurred in 28 (62.2%) patients, and the median time to

TABLE 2. TRAEs by Any Grade (≥ 20%) or Grade 3 (≥ 5%)

TRAE	Any Grade, No. (%)	Grade ≥ 3, No. (%)
Peripheral sensory neuropathy	25 (55.6)	2 (4.4)
Fatigue	23 (51.1)	5 (11.1)
Alopecia	22 (48.9)	—
Diarrhea	21 (46.7)	2 (4.4)
Decreased appetite	18 (40.0)	1 (2.2)
Rash maculopapular	16 (35.6)	5 (11.1)
Dysgeusia	15 (33.3)	—
Pruritus	15 (33.3)	1 (2.2)
Nausea	13 (28.9)	—
Weight decreased	11 (24.4)	1 (2.2)
Dry skin	10 (22.2)	—
ALT increased	9 (20.0)	—
Anemia	9 (20.0)	4 (8.9)
AST increased	9 (20.0)	—
Lipase increased	8 (17.8)	8 (17.8)
Amylase increased	7 (15.6)	4 (8.9)
Hyperglycemia	5 (11.1)	4 (8.9)
Neutropenia	5 (11.1)	4 (8.9)
Transaminases increased	3 (6.7)	3 (6.7)

Abbreviations: AE, adverse event; TRAE, treatment-related adverse event.

first onset was 2.4 (interquartile range [IQR], 1.9-4.6) months. The median time (IQR) to resolution for peripheral neuropathy was 5.2 (3.5-8.6) months. Most peripheral neuropathies (57.8%) were grade ≤ 2 (53.3%). Seven of eight (87.5%) patients who had peripheral neuropathy at baseline developed treatment-related peripheral neuropathy. Of the 37 patients without peripheral neuropathy at baseline, 21 (56.8%) developed treatment-related peripheral neuropathy. Among patients who had treatment-related peripheral neuropathy, 19 (67.8%) resolved or improved at last follow-up.

Ten of 45 (22.2%) patients had baseline hyperglycemia/diabetes mellitus. Hyperglycemia occurred in five (11.1%) patients (one grade 2; four grade 3) with a median time to first onset of 0.5 months (IQR, 0.5-0.5), of which three (30%) were considered treatment-related (grade 3). The median (IQR) time to resolution was 1.6 (0.7-1.6) months. At last follow-up, treatment-related hyperglycemia experienced by three patients had resolved; the two remaining patients with hyperglycemia unrelated to treatment improved to grade 2. Hyperglycemia occurred more frequently in patients with a body mass index of ≥ 30 kg/m^2 or with baseline hyperglycemia or diabetes mellitus.

Skin reactions occurred in 30 (66.7%) patients with a median time to first onset of 0.7 (IQR: 0.33-4.1) months. Twenty-eight (62.2%) patients experienced grade ≤ 3, and two (4.4%) grade 4 (dermatitis bullous and toxic epidermal necrolysis), and there were no grade 5 events. Twenty-two (73.3%) patients had all events resolved, and five (16.7%) patients showed improvement at last follow-up. The median time to resolution was 1.0 (0.4, 2.2) months. Eight (26.7%) patients had ongoing skin reactions at last follow-up; seven (23.3%) patients had a grade 1 event, and one (3.3%) patient had a grade 4 event.

Twenty (44.4%) patients had treatment-emergent imAEs of any grade: eight (17.8%) grade 1-2, 12 (26.7%) grade 3-4, and no grade 5 events. Treatment-emergent imAEs and the most common imAEs requiring systemic steroids are described in the Data Supplement.

Efficacy

The disease control rate was 93.3% with an investigator-confirmed objective response rate (RECIST version 1.1) of 73.3% (95% CI, 58.1 to 85.4; 33 of 45 patients); seven patients (15.6%) achieved a complete response; 26 patients (57.8%) achieved a partial response (Fig 2A and Data Supplement). Twenty-nine of the 33 (87.9%) responses were observed at the first tumor assessment (week 9 ± 1 week; Fig 2B), and the median time to response was 2.1 months (Fig 2C). The median DOR was 25.6 months with a median follow-up of 20.0 months (Fig 3A). The median PFS was 12.3 months (Fig 3B); the median OS was 26.1 months with a median follow-up of 24.9 months (Fig 3C).

Responses were observed to be independent of Nectin-4 and PD-L1 expression levels. Thirty-eight of 39 patients had detectable Nectin-4 expression (H-score ≥ 0). The distribution of expression was similar among responders and nonresponders (Data Supplement). The confirmed objective response rate in PD-L1 High (combined positive score ≥ 10; n = 14 patients) and PD-L1 Low (combined positive score < 10; n = 18 patients) subgroups was 78.6% (95% CI, 49.2 to 95.3) and 61.1% (95% CI, 35.7 to 82.7), respectively (Data Supplement). The confirmed objective response rate in the PD-L1–not evaluable subgroup (n = 13) was 84.6% (95% CI, 54.6 to 98.1). The objective response rate was 57.1% (95% CI, 28.9 to 82.3) in eight patients with liver metastases and 73.3% (95% CI, 44.9 to 92.2) in 11 patients with primary upper tract disease. Two of six (18.2%) patients were censored because starting a new antitumor treatment achieved complete response and they went on to receive potentially curative therapy (see the Data Supplement for pharmacokinetic/pharmacodynamic data).

DISCUSSION

Enfortumab vedotin plus pembrolizumab is a 1L platinum-free regimen that showed promising antitumor activity and a manageable safety profile in cisplatin-ineligible patients, including those with impaired performance status and/or liver metastases. Most patients experienced rapid responses to the combination. Our results suggest that responses were durable with both the median DOR and the median OS exceeding 2 years. This activity was

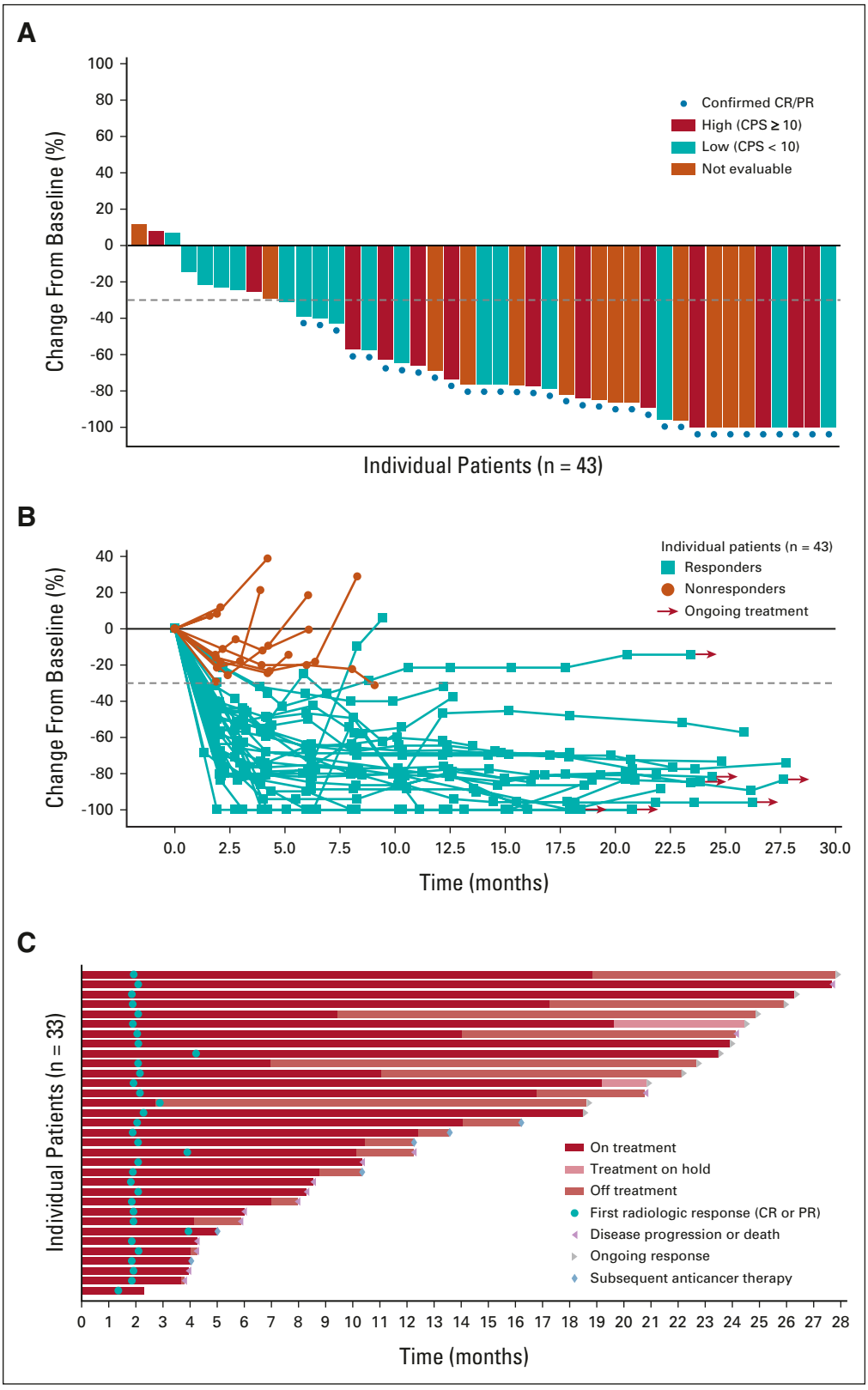

FIG 2. Change in target lesions from baseline. (A) Waterfall plot of change from baseline in the sum of the diameters of target lesions by investigator per RECIST v1.1. (B) Change from baseline of the sum of diameters of target lesions (the dotted horizontal line indicates threshold for partial response (–30%) but is not necessarily indicative of response) and (C) Swimmer plot of time to response and duration of response in patients achieving confirmed objective response per RECIST v1.1. PD-L1 expression status was assessed using the (continued on following page)

FIG 2. (Continued). combined positive score (low, < 10; high ≥ 10) with a validated PD-L1 IHC assay using the 22C3 antibody. Two patients did not have any post-baseline response assessments before the end of the study and did not have change from baseline in sum of the diameters of target lesions. CPS, combined positive score; CR, complete response; IHC, immunohistochemistry; PR, partial response.

observed independent of the PD-L1 expression level and disease site of origin (upper or lower tract) and in prespecified patient subgroups with poor prognostic characteristics, including those with liver metastases. The safety profile of the combination, including AESIs, was manageable and consistent with enfortumab vedotin or pembrolizumab as monotherapy.[9,10,12,18,19]

Approximately 50% of la/mUC patients never receive any 1L treatment.[20] Recent data suggest that treatment rates may be increasing.[21] Among patients who receive treatment, platinum-based regimens, particularly cisplatin/carboplatin plus gemcitabine, have been common 1L options in la/mUC.[1,22] Recent analyses suggest that many patients with la/mUC never receive additional therapy after initial treatment, further emphasizing the importance of achieving disease control with 1L therapy.[23,24] Moreover, half of all patients with la/mUC are ineligible to receive cisplatin because of comorbidities,[3,25,26] and survival is poor among cisplatin-ineligible patients who receive 1L therapy, likely because of the activity of carboplatin and underlying patient comorbidities. Some improvements in outcomes with carboplatin/gemcitabine have been observed likely because of better experience and supportive care measures. However, survival in more contemporary trials has been significantly influenced by the use of checkpoint inhibitors in later lines. Furthermore, fewer patients who receive carboplatin/gemcitabine may be eligible to benefit from avelumab because of lower response rates and decreased durability compared with cisplatin/gemcitabine.[27,28] This finding, combined with the historically lower rate of disease control seen with carboplatin-gemcitabine, underscores the need for effective 1L treatment options. To our knowledge, the confirmed response and disease control rates observed with the combination of enfortumab vedotin plus pembrolizumab, the median DOR, and OS exceeding 2 years are the highest reported to date for 1L treatment in la/mUC. Results suggest that enfortumab vedotin plus pembrolizumab is an active and durable treatment option that does not require the use of 1L platinum therapy.

Enfortumab vedotin plus pembrolizumab had a manageable safety profile, and no new or unexpected safety concerns were identified. Most treatment-related peripheral neuropathies were grade ≤ 2 in severity and had resolved or improved at the time of last follow-up, consistent with longer-term clinical experience with other vedotin ADCs, such as brentuximab vedotin.[29-32] Peripheral neuropathy can often be managed via dose reductions and/or interruptions. Skin reactions, including severe skin reactions, are known AEs for enfortumab vedotin and pembrolizumab. A total of three (7%) patients experienced serious skin reactions, which did not result in treatment discontinuation. These adverse events were captured in the analyses for both imAEs and AESIs. The contributions of each agent are unknown for skin toxicity at this time. In this study, overall skin events were primarily grade ≤ 2 and the majority completely resolved at last follow-up. Management of skin reactions included dose modifications or the use of topical or systemic steroids per protocol, as well as previously published guidance.[33,34] The rate of treatment-related hyperglycemia was low and resolved in all patients by last follow-up. Hyperglycemia was more prevalent in patients with preexisting hyperglycemia or diabetes mellitus and/or a body mass index ≥ 30 kg/m^2. These findings are not entirely unexpected given that la/mUC disproportionately affects older adults who have a history of comorbidities, including diabetes.[3,11,22,23] However, no patients in this trial discontinued therapy because of a skin reaction or hyperglycemia.

In addition to the limitations inherent to the single-arm design and a modest sample size, the study was not designed to determine the individual effects of enfortumab vedotin or pembrolizumab on efficacy and safety. There was no central radiology review in the current analysis, and no quality-of-life/patient-reported outcomes were collected. Although comparisons with historical data must be interpreted with caution, the antitumor activity of enfortumab vedotin plus pembrolizumab reported here appears to be higher than that of conventional carboplatin-based chemotherapy in this patient population. Given the potential clinical benefits, this combination received Breakthrough Therapy Designation by the US Food and Drug Administration and is undergoing further evaluation in cisplatin-ineligible patients versus enfortumab vedotin alone in a randomized part of this study (Cohort K). Furthermore, a randomized, phase III study is enrolling an unselected 1L population evaluating this combination compared with cisplatin or carboplatin plus gemcitabine (EV-302/KN-A39, ClinicalTrials.gov identifier: NCT04223856). In addition, enfortumab vedotin plus pembrolizumab is currently under investigation in two randomized phase III studies in muscle-invasive bladder cancer (EV-303/KN-905, ClinicalTrials.gov identifier: NCT03924895 and EV-304/KN-B15, ClinicalTrials.gov identifier: NCT04700124).[35,36]

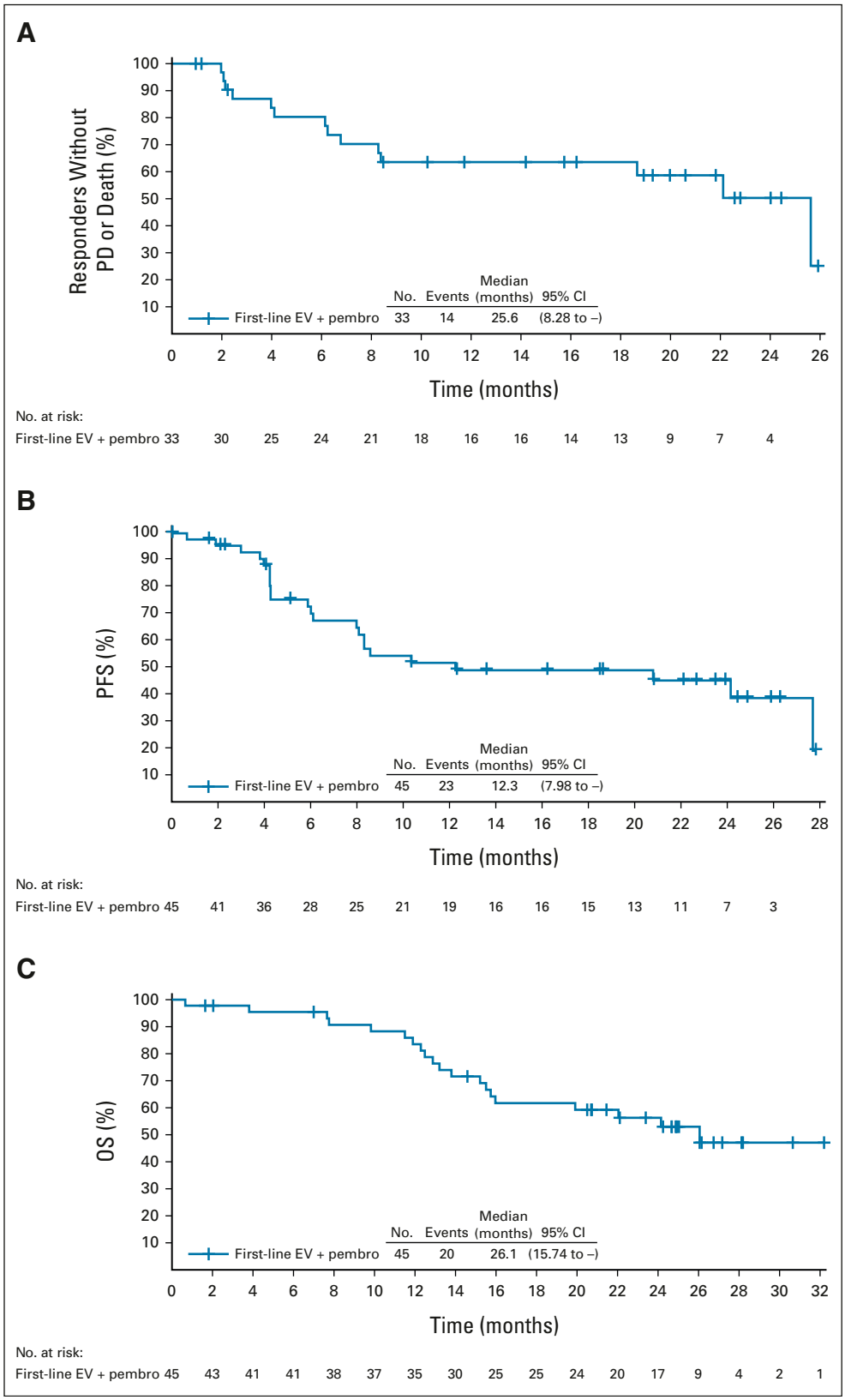

FIG 3. (A) DOR, (B) PFS, and (C) OS by the investigator per RECIST v1.1. DOR, duration of response; EV, enfortumab vedotin; OS, overall survival; PD, progressive disease; pembro, pembrolizumab; PFS, progression-free survival.

On the basis of data from these EV-103 cohorts, enfortumab vedotin plus pembrolizumab could provide a highly active and durable 1L platinum-free option for patients whose disease may not be suitable for treatment with a cisplatin-based chemotherapy, pending prospective validation in randomized studies.

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CLINICAL TRIAL INFORMATION

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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DATA SHARING STATEMENT

Deidentified patient-level trial data that underlie the results reported in this publication will be made available on a case-by-case basis to researchers who provide a methodologically sound proposal. Additional documentation may also be made available. Data availability will begin after approval of the qualified request and end 30 days after receipt of data sets. All requests can be submitted to CTDR@seagen.com and will be reviewed by an internal review committee.
Please note that the data sharing policy of this clinical study's sponsor, Seagen Inc, requires all requests for clinical trial data be reviewed to determine the qualification of the specific request. This policy is available at https://www.seagen.com/healthcare-professionals/clinical-data-requests and is aligned with BIO's Principles on Clinical Trial Data Sharing (available at https://www.bio.org/blogs/principles-clinical-trial-data-sharing-reaffirm-commitment).

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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