Enfortumab Vedotin in the Previously Treated Advanced Head and Neck Cancer Cohort of EV-202

Paul L. Swiecicki, MD[1]; Emrullah Yilmaz, MD, PhD[2]; Ari J. Rosenberg, MD[3]; Takao Fujisawa, MD[4]; Justine Yang Bruce, MD[5]; Changting Meng, MD[6]; Michele A. Wozniak, PhD[7]; Lu Wang, MS[7]; Seema Gorla, MD[7,*]; Jessica L. Geiger, MD[2]

[1]Department of Internal Medicine, Division of Hematology/Oncology, University of Michigan Medical School, Ann Arbor, MI; [2]Department of Hematology and Medical Oncology, Taussig Cancer Center, Cleveland Clinic, Cleveland, OH; [3]Department of Medicine, Section of Hematology/Oncology, University of Chicago, Chicago, IL; [4]Head and Neck Medical Oncology, National Cancer Center Hospital East, Chiba, Japan; [5]University of Wisconsin Carbone Cancer Center, Madison, WI; [6]Seagen, Bothell, WA; [7]Astellas Pharma, Northbrook, IL

*Corresponding author

Objective

- To assess antitumor activity and safety of enfortumab vedotin in adults with locally advanced or metastatic head and neck cancer who have received prior treatment with platinum-based chemotherapy and PD-1/L1 inhibitors

Conclusions

- Enfortumab vedotin monotherapy demonstrated promising efficacy with clinically meaningful responses in patients with head and neck cancers whose disease had progressed on prior anticancer therapies
- A manageable safety profile was observed, consistent with that identified in previously studied populations with advanced urothelial carcinoma[9]
  - No new safety signals were noted
- A new cohort 9 of the EV-202 study will investigate the effects of enfortumab vedotin in combination with pembrolizumab in head and neck squamous cell carcinoma (NCT04225117)

References

1. Ferlay J, et al. Global cancer observatory: cancer today. Published 2020. https://gco.iarc.fr/today.
2. Mody MD, et al. *Lancet*. 2021;18;398:2289-99.
3. Vermorken JB, et al. *N Engl J Med*. 2008;359:1116-27.
4. Challita-Eid PM, et al. *Cancer Res*. 2016;76:3003-13.
5. Sanders C, et al. *Oncotarget*. 2022;13:1166-73.
6. Enfortumab vedotin [package insert]. Northbrook, IL: 2023.
7. Enfortumab vedotin [summary of product characteristics]. Published 2022. https://www.ema.europa.eu/en/documents/product-information/padcev-epar-product-information_en.pdf.
8. Zhou H, et al. *Stat Med*. 2017;36:3302-14.
9. Powles T, et al. *N Engl J Med*. 2021;384:1125-35.

Disclosures

Paul L. Swiecicki reports honoraria from Elevar Therapeutics and Seagen Inc., as well as research funding from Ascentage Pharma Group. **Emrullah Yilmaz** reports advisory board payments from Astellas Pharma, Inc. **Ari J. Rosenberg** reports consulting fees from Astellas Pharma, Inc., Eisai, EMD-Serono, Novartis, and Vaccitech; and honoraria from Coherus. Dr Rosenberg also reports stock/stock options from Galectin, and Privo. **Takao Fujisawa** has no relationships to disclose. **Justine Yang Bruce** has no relationships to disclose. **Changting Meng** is an employee of Seagen Inc. **Michele A. Wozniak** is an employee of Astellas Pharma, Inc. **Lu Wang** is an employee of Astellas Pharma, Inc. **Seema Gorla** is an employee of Astellas Pharma, Inc. **Jessica L. Geiger** reports Advisory Board consulting fees from Astellas Pharma, Inc. (2022), Exelixis (2022), Merck (2022), and Regeneron (2019, 2022).

Funding

This study was funded by Astellas Pharma, Inc. and Seagen Inc.

Acknowledgements

This study was funded by Astellas Pharma, Inc. and Seagen Inc. Medical writing/editorial support was provided by Arpita Kulshrestha, PhD, and Sherri Damlo, MS, ELS, from Peloton Advantage, LLC, an OPEN Health company, Parsippany, NJ, and funded by the study sponsor.

Please direct any questions or comments regarding this poster to Biplob Dass, PhD (biplob.dass@astellas.com).

Presented at the American Society of Clinical Oncology Annual Meeting; June 2–6, 2023; Chicago, IL, and virtual; Poster No. 6017

Background

- Globally, head and neck cancers accounted for an estimated 932,000 new cases and 467,000 deaths in 2020[1]
- Most (≥90%) head and neck cancers are squamous cell carcinomas[2]
- Given the poor prognosis (median survival of <1 year) of recurrent or metastatic disease among individuals with head and neck squamous cell carcinoma,[3] effective treatments are needed
- Nectin-4, a cell-adhesion molecule, is expressed in the majority of head and neck cancers[4,5]
  - Targeting Nectin-4 with an antibody–drug conjugate may provide a novel treatment approach
- Enfortumab vedotin is an antibody–drug conjugate comprised of a fully human monoclonal antibody directed against Nectin-4 attached to the microtubule disrupting agent, monomethyl auristatin E, by a protease-cleavable linker[6]
- Enfortumab vedotin is approved in more than 40 countries:
  - As monotherapy in adults with locally advanced or metastatic urothelial carcinoma who previously received platinum-containing chemotherapy and a programmed cell death protein 1/ligand 1 (PD-1/L1) inhibitor or are ineligible for cisplatin-containing chemotherapy and have received 1 or more prior lines of therapy[6,7]
  - In combination with pembrolizumab for treatment of adults with locally advanced or metastatic urothelial carcinoma who are ineligible for cisplatin-containing therapy (accelerated approval in the United States)[6]

Methods

- EV-202 (NCT04225117) is a multicohort, open-label, phase 2 study of patients with previously treated locally advanced or metastatic solid tumors enrolled into tumor-specific cohorts (**Figure 1**)
  - Data from the head and neck cancer cohort (cohort 5) are presented
- A 2-stage Bayesian optimal design for a phase 2 study[8] was used to guide the decision for the interim decision rule wherein the head and neck cohort would:
  - Include 20 evaluable patients at the interim analysis (stage 1)
    - Proceed to stage 2 when a minimum of 2 patients with confirmed response (complete or partial response) per investigator assessment from stage 1 were observed
    - Be closed to further enrollment if the minimum number of responders was not met
  - Include 40 evaluable patients at the final analysis (stage 2)
    - Be required to have a minimum of 7 responders to claim promising antitumor activity

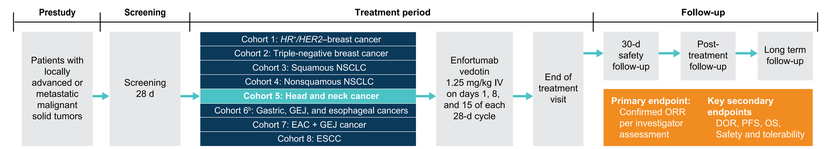
Statistical Analysis

- Data were summarized with descriptive statistics for continuous endpoints and frequency/percentage for categorical endpoints
- Kaplan–Meier estimates were provided for time-to-event endpoints, including duration of response, progression-free survival (PFS), and overall survival (OS)
- Analysis populations
  - Response-related efficacy analyses were evaluated in the response evaluable population, which included patients receiving any amount of study drug who have measurable disease at baseline per investigator assessment and at least 2 postbaseline scans or are no longer in the follow-up of response at the time of analysis
  - OS and PFS were assessed in the full analysis population, which included all enrolled patients receiving any amount of study drug
  - Safety was assessed in the safety population, which included patients who received any amount of study drug

Figure 1. EV-202 Study Design[a]

Key Eligibility Criteria

- Measurable disease per RECIST v1.1
- Histologically or cytologically confirmed head and neck cancer
  - Primary tumor sites arising from oral cavity, oropharynx, hypopharynx, and larynx; tumors arising from the nasopharynx and salivary and/or parotid gland tumors were excluded
- Locally advanced or metastatic head and neck cancer not amenable to curative-intent treatment
- ECOG PS 0–1
- Evidence of radiographic progression on/after last regimen received
- Disease that has progressed/relapsed or patient has discontinued treatment due to toxicity after 1 platinum-based therapy (≤2 prior lines of cytotoxic anticancer treatment) for locally advanced or metastatic disease
- Disease that has progressed/relapsed or patient has discontinued treatment due to toxicity with prior use of a PD-1/L1 inhibitor (based on tumor PD-1/L1 expression), unless contraindicated
- No active CNS metastases
- Nectin-4 expression was not an eligibility criterion



Data cutoff: April 11, 2022.
CNS, central nervous system; DOR, duration of response; EAC, esophageal adenocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; GEJ, gastroesophageal junction; IV, intravenous; NSCLC, non–small-cell lung cancer; PD-1/L1, programmed cell death protein 1/ligand 1; PFS, progression-free survival; ORR, objective response rate; OS, overall survival; RECIST, Response Evaluation Criteria in Solid Tumours.
[a]Disease assessment performed at screening/baseline and repeated every 8 wk (56 ± 7 d) from the first dose of study drug until radiologically confirmed disease progression, a new subsequent anticancer therapy is initiated, death, consent is withdrawn, patient is lost to follow-up, or study end, whichever comes first. Confirmatory imaging was required 4 wk (28 + 7-d window) after first response. After 1 y of study treatment, frequency of response assessments was reduced to every 12 wk (84 ± 7 d). [b]Patients initially enrolled in cohort 6 were reallocated to cohort 7 or 8 based on tumor type/histology.

Results

- As of April 11, 2022, a total of 46 patients in the head and neck cancer cohort received enfortumab vedotin and were included in the full analysis, response evaluable, and safety populations (**Table 1**)
  - The majority of patients (n=45) had squamous cell carcinoma; 1 patient had adenocarcinoma of the oropharynx
  - 1 patient had brain metastasis
- Median follow-up was 9.33 months

Table 1. Patient Demographics and Disease Characteristics

Characteristic	Patients (N=46)
Median age (range), y	65 (33–81)
Male sex	40 (87)
Primary tumor location	
Oral cavity	15 (32.6)
Pharynx	14 (30.4)
Larynx	10 (21.7)
Other	7 (15.2)
Human papillomavirus status	
Negative	6 (13.0)
Positive	20 (43.5)
Unknown	20 (43.5)
≥3 prior lines of systemic therapy[a]	31 (67.4)
Median time since initial diagnosis (range),[b] mo	28.7 (8.4–161.8)
Type of prior systemic therapy	
PD-1/L1 inhibitor	46 (100)
Platinum-based chemotherapy	46 (100)
Taxane	34 (73.9)
Cetuximab	26 (56.5)
Progressive disease on prior systemic therapy	
PD-1/L1 inhibitor	20 (43.5)
Platinum-based chemotherapy	8 (17.4)
Taxane	8 (17.4)
Cetuximab	10 (21.7)
Nectin-4 immunohistochemistry H score (tissue),[c,d] median (range)	180 (20–300)
PD-L1 immunohistochemistry (tissue)[d]	
Low (CPS <1)	6 (15.4)
High (CPS ≥1)	33 (84.6)
Missing	7
Body mass index ≥25 kg/m²[e]	7 (15.9)
Race	
White	27 (58.7)
Asian	15 (32.6)
Black or African American	1 (2.2)
Not reported	3 (6.5)

Values are n (%) unless otherwise indicated. Some proportions were calculated based on nonmissing data.
CPS, combined positive score; PD-1/L1, programmed cell death receptor 1/ligand 1.
[a]Includes prior systemic therapy in the locally advanced or metastatic setting or prior platinum-based therapy for the head and neck cohort received in the neoadjuvant/adjuvant setting if disease progression occurred ≤6 mo of therapy completion. [b]Time from initial diagnosis to date of first dose. [c]n=43 patients with evaluable tumor tissue. H-score range, 0–300. [d]Assessed using validated immunohistochemical assays (Nectin-4, M22-321b41.1; PD-L1, 22C3 antibody clones). [e]Data missing for 2 patients (n=44).

Antitumor Activity

- Objective response rate was 23.9%, and disease control rate was 56.5% (**Table 2**)
- Median time to response was 1.74 months

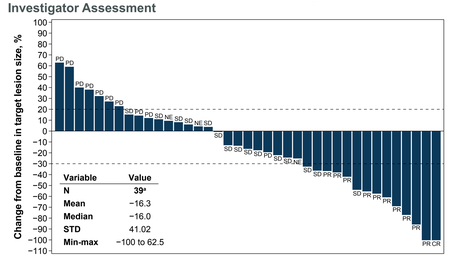
Table 2. Summary of Response by Investigator Assessment

Parameter/Variable	Patients (N=46)
Confirmed ORR[a]	11 (23.9)
95% CI,[b] %	12.6–38.8
Confirmed DCR[c]	26 (56.5)
95% CI,[b] %	41.1–71.1
BOR	
Confirmed CR	1 (2.2)
Confirmed PR	10 (21.7)
SD	15 (32.6)
Progressive disease	10 (21.7)
Not evaluable[d]	10 (21.7)

Values are n (%) unless otherwise indicated.
BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; ORR, objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.
[a]Patients whose BOR is confirmed CR or PR according to RECIST v1.1. [b]Using exact method based on binomial distribution (Clopper–Pearson). [c]Patients with BOR of confirmed CR, confirmed PR, or SD (≥7 wk). [d]Seven of these patients were considered not evaluable due to discontinuation from the study before a postbaseline response assessment was performed.

- Of 39 patients with postbaseline tumor assessments, 23 had tumor reduction from baseline and 14 had reductions of 30% or more from baseline (**Figure 2**)

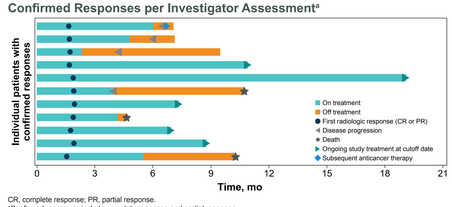
Figure 2. Best Change From Baseline in Size of Target Lesion per Investigator Assessment



CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease; STD, standard deviation.
[a]A total of 39 patients with postbaseline tumor assessments were included. Three patients were considered NE due to a postbaseline scan before day 49 with tumor assessment of SD.

- Eleven patients showed confirmed responses, including 5 patients who were receiving study treatment at the data cutoff date (**Figure 3**)

Figure 3. Time to Response and Duration of Response in Patients With Confirmed Responses per Investigator Assessment[a]

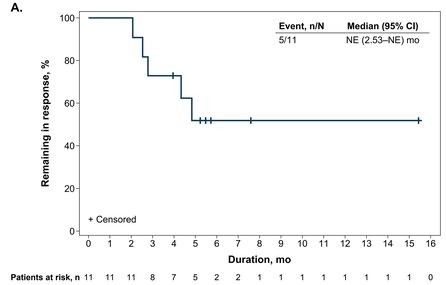


CR, complete response; PR, partial response.
[a]Confirmed responses include complete response and partial response.

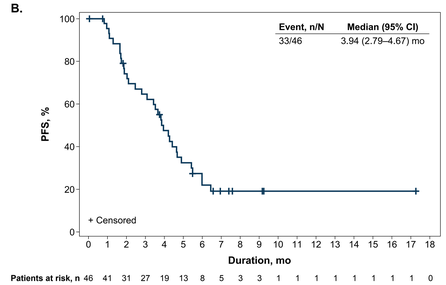
- Median duration of response per investigator assessment was not evaluable (**Figure 4A**), median PFS per investigator assessment was 3.94 months (**Figure 4B**), and median OS was 5.98 months (**Figure 4C**)

Figure 4. Kaplan–Meier Plots of (A) DOR,[a] (B) PFS,[a] and (C) OS

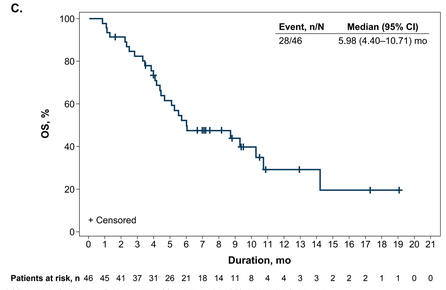
A.



B.



C.



DOR, duration of response; NE, not evaluable; OS, overall survival; PFS, progression-free survival.
[a]Per investigator assessment.

Safety/Tolerability

- Overall, 45 patients experienced a treatment-emergent adverse event (TEAE) and 41 patients experienced a treatment-related adverse event (TRAE; **Table 3**)
- The most common TEAEs and TRAEs of any grade were fatigue (28.3% and 26.1%, respectively), alopecia (both 28.3%), and peripheral sensory neuropathy (28.3% and 23.9%, respectively)
- Grade 3 or higher TEAEs occurring in more than 1 patient were anemia (n=3), decreased neutrophil count (n=2), and malignant neoplasm progression (disease progression of head and neck cancer; n=2); grade 3 or higher TRAEs occurring in more than 1 patient were anemia (n=2) and decreased neutrophil count (n=2)
- TRAEs led to dose reduction in 19.6% and withdrawal of treatment in 13.0% of patients

Table 3. Treatment-Related AEs in the Safety Population[a]

	Cohort (N=46)	
AE,[b,c] n (%)	Any grade	Grade ≥3
Overall	41 (89.1)	16 (34.8)
Alopecia	13 (28.3)	NR
Fatigue	12 (26.1)	1 (2.2)
Peripheral sensory neuropathy	11 (23.9)	1 (2.2)
Dysgeusia	9 (19.6)	NR
Maculopapular rash	8 (17.4)	0
Decreased appetite	7 (15.2)	1 (2.2)
Diarrhea	7 (15.2)	0
Decreased neutrophil count	3 (6.5)	2 (4.3)
Anemia	6 (13.0)	2 (4.3)

AE, adverse event; NR, not reported.
[a]All patients who were enrolled and received the study treatment were included in the safety population. [b]Any-grade AE occurring in ≥15% of patients or grade ≥3 AE occurring in >1 patient. [c]AEs are reported based on Preferred Term.

- The most common TRAEs of special interest for enfortumab vedotin were skin reactions and peripheral neuropathy (**Table 4**)

Table 4. Treatment-Related AEs of Interest for Enfortumab Vedotin

	Cohort (N=46)	
AE,[a] n (%)	Any grade	Grade ≥3
Skin reaction[b]	21 (45.7)	1 (2.2)
Peripheral neuropathy	15 (32.6)	2 (4.3)
Hyperglycemia	2 (4.3)	0
Ocular disorder		
Dry eye	3 (6.5)	0
Corneal disorder	0	0
Blurred vision	0	0
Infusion-related reaction	0	0

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities.
[a]AEs are composite terms and reported by standard MedDRA query or sponsor-specific query/customized medical query. [b]Includes rash or severe cutaneous adverse reaction.