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EV-201 Cohort 1: Long-term Results of Enfortumab Vedotin Monotherapy for Locally Advanced or Metastatic Urothelial Cancer Previously Treated with Platinum and a PD-1 or PD-L1 Inhibitor (NCT03219333)

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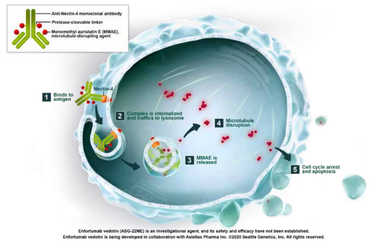
Advanced Urothelial Carcinoma Has a High Unmet Need

- Locally advanced and metastatic urothelial carcinoma is incurable with poor overall survival (OS), particularly in patients who progress on or after platinum-containing chemotherapy
  - Taxanes/vinflunine showed a median OS of 7.4 months and a 12-month OS rate of 30.7% in patients who previously received platinum-containing therapy[1]. OS data following PD-1/PD-L1 inhibitors and platinum-containing chemotherapy are limited.
- In the EV-201 study (NCT03219333; EudraCT Number 2017-003479-78), enfortumab vedotin, an antibody-drug conjugate, showed an objective response rate (ORR) of 44% in Cohort 1, which enrolled patients who previously received both a prior PD-1/PD-L1 inhibitor and platinum-containing chemotherapy in the neoadjuvant/adjuvant or locally-advanced/metastatic setting[2]
  - In Dec 2019, the US FDA granted accelerated approval to enfortumab vedotin based on the data from EV-201 Cohort 1 (01 Mar 2019 data cutoff)
- Herein, we present updated OS and safety data from EV-201 Cohort 1 with an additional year of follow-up (15 Mar 2020 data cutoff)

Enfortumab Vedotin: A Nectin-4 Directed Antibody-Drug Conjugate

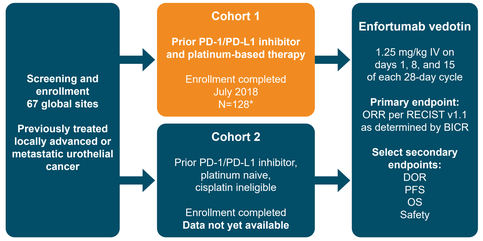
Proposed Mechanism of Action of Enfortumab Vedotin

- Enfortumab vedotin is directed against Nectin-4, a cell surface adhesion protein on target cells, and upon internalization releases monomethyl auristatin E, resulting in cell cycle arrest and apoptotic cell death



Enfortumab vedotin (ASG-22ME) is an investigational agent, and its safety and efficacy have not been established.
Enfortumab vedotin is being developed in collaboration with Astellas Pharma Inc. ©2020 Seattle Genetics, Inc. All rights reserved.

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



* 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

Based on this long-term follow-up of EV-201 Cohort 1:

- The median OS was 12.4 months (95% CI: 9.46, 15.57), with a median follow-up of 22.3 months
- At key milestones of 12 and 18 months, one-half and approximately one-third of patients, respectively, were alive
- Enfortumab vedotin was tolerable with a manageable safety profile consistent with previous reports

EV-201: Cohort 1 Key Eligibility Criteria

- Histologically documented urothelial carcinoma, including squamous differentiation or mixed cell types
- Metastatic disease or locally advanced disease that is not resectable
- Previous treatment with platinum-containing chemotherapy and a PD-1/PD-L1 inhibitor
- Progression during or following most recent treatment
- Measurable disease by RECIST v1.1
- ECOG ≤1
- No ongoing sensory or motor neuropathy ≥Grade 2
- No active CNS metastases
- No uncontrolled diabetes mellitus*

* Hemoglobin A1C (HbA1c) ≥8% or HbA1c of 7% to <8% with associated diabetes symptoms, polyuria or polydipsia, that were not otherwise explained

EV-201: Cohort 1 Patient Disposition

6 subjects remain on treatment; disease progression is the most common reason for treatment discontinuation

Patients with metastatic urothelial cancer who received enfortumab vedotin	Cohort 1 (N=125) n (%)
Patients continuing treatment	6 (4.8)
Patients in follow-up for progression/survival	25 (20)
Patients off study	94 (75.2)
Reason for treatment discontinuation	
Progressive disease	77 (61.6)
Progression by RECIST	71 (56.8)
Progression by clinical symptoms	6 (4.8)
Any adverse event	24 (19.2)
Patient decision	14 (11.2)
Physician decision	4 (3.2)
Median time on treatment (min, max)	**4.6 months (0.5, 27.3)**

- Enrollment from Oct 2017 to July 2018
- 128 enrolled; 125 treated
  - 3 withdrew prior to treatment
  - Analyses based on 125 treated patients (Full Analysis Set)
- Max time on treatment: 27.3 months and ongoing

EV-201: Cohort 1 Demographics and Disease Characteristics[2]

	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*, median (range)	3 (1, 6)
≥1 Bellmunt adverse prognostic factors**	101/124 (81)
≥2 Bellmunt adverse prognostic factors**	52/124 (42)
Metastasis sites, n (%)	
Lymph nodes only	13 (10)
Visceral disease	112 (90)
Liver	50 (40)
PD-L1 status by combined positive score†	
<10	78/120 (65)
≥10	42/120 (35)

* Patients with 1 prior therapy had platinum and a PD-1 or PD-L1 inhibitor in combination
** Bellmunt risk score was not available for 1 patient
† 5 patients were not evaluable for PD-L1

- Study subjects are representative of the advanced urothelial carcinoma population, predominantly older males with the majority ECOG 1, primary site of disease in the lower urinary tract, and median 3 lines of prior therapy
- Most had poor prognostic factors, 81% had at least 1 Bellmunt risk factor, 90% had visceral disease, and 40% had liver metastases

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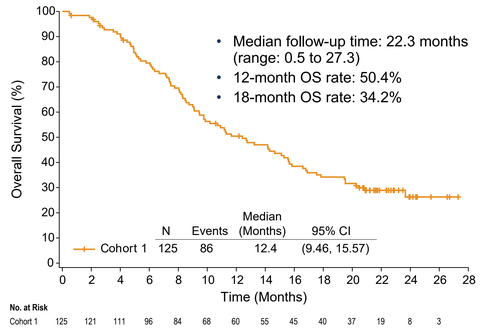
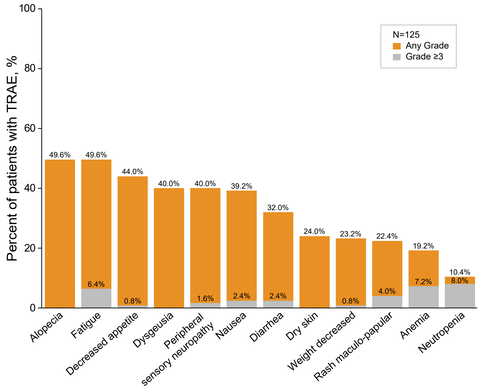
EV-201: Cohort 1 Kaplan-Meier Estimates of Survival



EV-201: Cohort 1 Treatment-Related Adverse Events by Preferred Term in ≥20% of Patients (Any Grade) or ≥5% (≥Grade 3)



- Few discontinuations due to treatment-related AEs (12%)
  - Peripheral sensory neuropathy was the most common (6%)
- 1 treatment-related death reported by the investigator
  - Interstitial lung disease
  - Confounded by high-dose corticosteroid use and suspected *Pneumocystis jiroveci* pneumonia

Acknowledgements

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.

EV-201: Cohort 1 Treatment-Related Adverse Events of Interest (AEOI)

Events categorized based on standardized MedDRA queries or sponsor-specific queries

- Peripheral neuropathy: 50% any grade, 3% ≥Grade 3
  - No Grade 4 events
  - Sensory events most common (44%, all patients)
  - Of patients with peripheral neuropathy at enrollment, 47% did not worsen
  - 76% had resolution or events ongoing at Grade 1 at last follow-up
- Skin reactions: 51% any grade, 13% ≥Grade 3
  - No Grade 4 events
  - 95% had resolution or improvement at last follow-up
  - Of those with ongoing skin reactions, most (80%) were Grade 1
- Hyperglycemia: 11% any grade, 6% ≥Grade 3
  - 52% of patients with pre-existing hyperglycemia did not worsen
  - 1 Grade 4 event, resolved, no need for ongoing medication
  - 79% had resolution or improvement at last follow-up

Data cutoff: 15 March 2020

EV-201: Cohort 1 Long-term Follow-up Summary and Conclusions

- Enfortumab vedotin: First in class ADC demonstrating substantial clinical activity in patients who progressed after a PD-1/PD-L1 inhibitor and platinum-containing chemotherapy
  - Previously presented ORR of 44% (CR 12%) and median DOR of 7.6 months supported US FDA accelerated approval
- Long-term follow-up from EV-201 Cohort 1 continues to demonstrate favorable benefit-risk profile
  - With median follow-up time of 22.3 months:
    - Median OS is 12.4 months (95% CI: 9.46, 15.57) with one-third being alive at 18 months
    - Safety profile remains tolerable and manageable
    - Rates of hyperglycemia, peripheral neuropathy, and skin reactions were consistent with prior reports and the USPI
- **EV-301** (NCT03474107), the confirmatory phase 3 trial evaluating OS (EV versus taxanes/vinflunine) in a similar population, has completed enrollment
- Other active enfortumab vedotin trials include:
  - **EV-103** (NCT03288545) **Cohort K** (Enfortumab vedotin ± pembrolizumab) currently enrolling 1L la/mUC patients who are ineligible for cisplatin
  - **EV-302** (NCT04223856) in untreated locally advanced/metastatic urothelial cancer treated with enfortumab vedotin and pembrolizumab, or chemotherapy (see ESMO ePoster 2065)
  - **EV-303/KEYNOTE-905** (NCT03924895) in cisplatin-ineligible patients with MIBC treated with perioperative pembrolizumab and enfortumab vedotin plus cystectomy, versus pembrolizumab plus cystectomy, versus cystectomy alone
  - **EV-202** (NCT04225117) in patients with previously treated locally advanced or metastatic solid tumors treated with enfortumab vedotin

References

1 Bellmunt J, et al. N Engl J Med. 2017;376:1015-26.
2 Rosenberg JE, et al. J Clin Oncol. 2019;37:2592-2600.