A single-arm, open-label, multicenter study of enfortumab vedotin (ASG-22CE) for treatment of patients with locally advanced or metastatic urothelial cancer who previously received immune checkpoint inhibitor (CPI) therapy.

Published: 15-06-2018
Last updated: 10-01-2025

Primary:* * To determine the antitumor activity of single-agent enfortumab vedotin as measured by confirmed objective response rate (ORR) in patients with locally advanced or metastatic urothelial cancer who have previously received systemic therapy...

Ethical review	Approved WMO
Status	Completed
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON50360

Source
ToetsingOnline

Brief title
EV-201

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
Transitional cell carcinoma, Urothelial cancer

Research involving

Human

Sponsors and support

Primary sponsor: Seattle Genetics, Inc.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Enfortumab Vedotin, ORR, Phase 2, Urothelial Cancer

Outcome measures

Primary outcome

Primary Endpoint

* The primary efficacy endpoint of this study is ORR (confirmed CR or PR per Response Evaluation Criteria in Solid Tumors [RECIST] Version 1.1) as determined by an independent review facility (IRF)

Secondary outcome

Secondary Endpoints

* DOR (confirmed CR or PR) per IRF

* DCR16 (disease control rate [CR, PR or SD] at 16 weeks) per IRF

* PFS per IRF

* ORR per investigator assessment

* DOR per investigator assessment

* DCR16 per investigator assessment

* PFS per investigator assessment

* OS

* Type, incidence, severity, seriousness, and relatedness of AEs

* Laboratory abnormalities

* Selected plasma or serum PK parameters of enfortumab vedotin, MMAE and total antibody (TAb)

* Incidence of ATA to enfortumab vedotin

Additional Endpoints

* Biomarkers of biological and clinical activity, including Nectin-4 expression

* Patient reported outcomes (PRO) per the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ-C30)

* PRO per EuroQol 5-dimensions (EQ-5D), including health utility values, and visual analog scale

Study description

Background summary

Enfortumab vedotin is a type of drug called an antibody drug conjugate or ADC. ADCs usually have 2 parts:
• The antibody, which finds the cancer cells in your body. Antibodies are part of the immune system. They can stick to and attack specific targets on cells. The antibody part of enfortumab vedotin is designed to stick to a target called Nectin-4. Nectin-4 is an important part of some cancer cells and some normal cells.
• The chemotherapy, which is the cell-killing medicine. The cell-killing part of enfortumab vedotin is a chemotherapy called MMAE. It can kill the cells that the antibody sticks to in your body.
More than 830 people with cancer have already been given enfortumab vedotin in other clinical studies. These clinical studies were done to test the safety of different doses of enfortumab vedotin. They were also done to find out if enfortumab vedotin works to treat cancer.

Study objective

Primary:
* * To determine the antitumor activity of single-agent enfortumab vedotin as measured by confirmed objective response rate (ORR) in patients with locally

advanced or metastatic urothelial cancer who have previously received systemic therapy with a CPI and either previously received platinum-containing chemotherapy or are platinum-naïve and cisplatin-ineligible

Secondary:
* To assess duration of response (DOR)
* To assess disease control rate (DCR)
* To assess progression-free survival (PFS)
* To assess overall survival (OS)
* To assess the safety and tolerability of enfortumab vedotin
* To assess the pharmacokinetics (PK) of enfortumab vedotin
* To assess the incidence of antitherapeutic antibodies (ATA)

Additional:
* To explore potential correlations between biomarkers and clinical outcomes
* To evaluate the treatment effect of enfortumab vedotin on quality of life (QoL)

Study design

This is a single-arm, open-label, multicenter trial designed to assess the efficacy and safety of enfortumab vedotin as a single agent in locally advanced or metastatic urothelial cancer patients who have previously received systemic therapy with a CPI. For the purpose of this study a CPI is defined as a programmed cell death protein 1 (PD-1) inhibitor or programmed death-ligand 1 (PD L1) inhibitor (including, but not limited to: atezolizumab, pembrolizumab, durvalumab, avelumab, and nivolumab). Patients must either have received prior treatment with platinum-containing chemotherapy (Cohort 1) or received no prior treatment with platinum-containing or other chemotherapy and are ineligible for treatment with cisplatin at time of enrollment (Cohort 2).
Enfortumab vedotin at a dose of 1.25 mg/kg will be administered as an intravenous (IV) infusion over approximately 30 minutes on Days 1, 8, and 15 of each 28-day cycle. Patients will continue to receive study treatment until disease progression, unacceptable toxicity, investigator decision, consent withdrawal, start of a subsequent anticancer therapy, pregnancy, or study termination by the sponsor. After discontinuation of study treatment, patients will be followed every 8 weeks (±1 week) for response assessments, ECOG performance status, and physical exams. After 1 year of on study, the frequency of follow-up exams including response assessments will be reduced to every 12 weeks (±1 week). Patients that have progressed or begun subsequent anticancer therapy will be contacted every 8 weeks (±1 week) up to 1 year on study, and every 12 weeks (±1 week) thereafter to obtain information on subsequent anticancer therapy, and survival status until death, study closure, or withdrawal of consent, whichever occurs first. The study will be closed 5 years after enrollment of the last patient, or when no patients remain in long-term follow-up, whichever occurs first. Additionally, the sponsor may terminate the study at any time.

On a periodic basis, an independent data monitoring committee (IDMC) will monitor the safety of patients participating in this trial. The IDMC will be responsible for evaluating the results of safety analyses and will make recommendations to the sponsor.
An ongoing real-time review of patient safety and serious adverse events (SAEs) will also be conducted by the sponsor*s Drug Safety Department.

Intervention

Enfortumab vedotin 1.25 mg/kg will be administered as an IV infusion over approximately 30 minutes on
Day 1, 8, and 15 of each 28-day cycle.

Study burden and risks

- Blood collection (See E6 and additional information)
- Study visits
- Questionnaires: EORTC and QLQ-C30
- Scans: CT or MRI scan of chest, abdomen and pelvis (every 8 weeks).
- Side effects (see question E9)
- Risks related to the study procedures:

Blood Samples: Blood draws may cause local pain, bleeding and/or bruising, and dizziness. You may faint and/or get an infection with redness and irritation at the place where the needle enters your vein. In very rare cases, nerve damage may occur.

Heart monitoring: When you have your heart monitored, you may have itching or get bruising of the skin where the machine patches are placed. ECG patch adhesive may also be cold and sticky. Sometimes a small area needs to be shaved to help the patch stick.
Intravenous infusion (IV dosing): Medications administered into veins (intravenously) can sometimes cause pain, swelling and redness of the vein and surrounding tissues, which may not go away quickly, even if the medication is stopped.

CT/MRI scans: A CT scan or MRI scan may cause you to feel *closed in* while lying in the scanner. However, the scanner is open at both ends and an intercom allows you to talk with doctors and staff. If you feel ill or anxious during scanning, doctors and/or technicians will give comfort or the scanning will be stopped.

CT scans: CT scans expose your body to radiation. While the dose is small (about the same as 3 years of natural background radiation that you would normally receive going about your daily life), all radiation adds up over a lifetime. The study doctor can provide more information.

MRI scans: There are no known risks or side effects resulting directly from exposure to MRI scans. However, subjects who have a pacemaker or metal objects in their body should not have the scan performed. If you have kidney disease, there is a small risk that the contrast agent used for the MRI scan may cause stiffening of the skin (nephrogenic systemic fibrosis). The study doctor can provide more information.

Tumor biopsy (if needed): If you do not have a tumor tissue sample available for this study, this sample will be obtained by a biopsy. Risks related to tumor biopsies include bleeding from the biopsy site, pain, local reaction to the anesthesia, infection, and scarring. Your study doctor will further discuss the risks involved with these biopsies if you are providing a sample of your tumor tissue.

Bone scans: Before the scan, we will inject a tiny amount of radioactive dye into your vein. There is a small risk of allergic reaction or radiation exposure with this material. Nearly all of the radioactivity from the dye will be gone from your body in 2 or 3 days. Your study doctor can provide more information.

Eye exam: An eye doctor will test the health of your eyes. Some parts of the test involve bright lights which can be dazzling, and other tests may be uncomfortable. In addition, the eye doctor may need to give you eye drops. These can cause blurry vision and you should not drive for about 4 hours afterwards.

Unknown risks
Because the number of patients who have received enfortumab vedotin to date is small, we do not know all the risks of this study drug. It*s possible that side effects we don*t know about yet could happen. The side effect may be a minor inconvenience or could be severe enough to be life-threatening or cause death. We will watch you closely for side effects. The study drug will be stopped if unwanted or serious side effects develop.
We haven*t studied enfortumab vedotin in many patients with liver problems. We don*t know if people with liver problems will have side effects that we don*t know about yet.
We have only studied enfortumab vedotin in a few patients with serious kidney problems. We don*t know if people with serious kidney problems will have side effects that we don*t know about yet.
There may also be other unknown effects that could harm you during the time you take part in the study or after the study is finished. These side effects could also harm your unborn child, if you become pregnant or father a child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Histologically documented urothelial (previously known as transitional cell) carcinoma (squamous differentiation or mixed cell types allowed). , • Metastatic disease or locally advanced disease that is not resectable., • Must have received prior treatment with a CPI in the locally advanced or metastatic urothelial cancer setting. Patients who received CPI therapy in the neoadjuvant/adjuvant setting and had recurrent or progressive disease either during therapy or within 3 months of therapy completion are eligible. A CPI is defined as a programmed cell death protein 1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor., • Must be one of the following:
a. Platinum-treated (Cohort 1): Patients who received prior treatment with platinumcontaining chemotherapy defined as those who received platinum in the adjuvant/neoadjuvant setting and had recurrent or progressive disease within 12

months of completion OR received treatment with platinum in the locally advanced (defined as unresectable with curative intent) or metastatic setting;
OR
b.Platinum-naïve and cisplatin ineligible (Cohort 2): Patients who have not received prior treatment with platinum-containing or other chemotherapy in the locally advanced or metastatic setting and are ineligible for treatment with cisplatin at time of enrollment due to one of the following: ECOG performance status score of 2; impaired renal function (defined as creatinine clearance [CrCl] >=30 and <60 mL/min), or a >= Grade 2 hearing loss. Patients who received platinum in the adjuvant/neoadjuvant setting and did not progress within12 months of completion will be considered platinum-naïve., • Must have had progression or recurrence of urothelial cancer during or following receipt of most recent therapy., • Tumor tissue samples must be available for submission to the sponsor prior to study treatment., • Must have measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) (Version 1.1). , • An Eastern Cooperative Oncology Group (ECOG) PerformanceStatus score of <=1 for Cohort 1, or <=2 for Cohort 2.

Exclusion criteria

• Ongoing sensory or motor neuropathy Grade >=2., • Active central nervous system (CNS) metastases., • Immunotherapy related myocarditis, colitis, uveitis, or pneumonitis., • Prior enrollment in an enfortumab vedotin study or prior treatment with monomethyl auristatin E (MMAE)-based antibody-drug conjugates (ADCs).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Completed

Start date (anticipated):	14-01-2019
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ASG-22ME
Generic name:	Enfortumab Vedotin

Ethics review

Approved WMO Date:	15-06-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-11-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-01-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2019
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	19-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-05-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-07-2021
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-003479-78-NL
ClinicalTrials.gov	NCT03219333
CCMO	NL64755.031.18

Study results

Date completed:	17-03-2021
Results posted:	13-05-2024
Actual enrolment:	5

First publication
29-01-2024