An open-label, randomized, controlled phase 3 study of enfortumab vedotin in combination with pembrolizumab, versus chemotherapy alone in previously untreated locally advanced or metastatic urothelial cancer

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This study has been transitioned to CTIS with ID 2023-503421-19-00 check the CTIS register for the current data. This study will evaluate the efficacy, safety, and PK of enfortumab vedotin in combination with pembrolizumab, with or without platinum-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON55964

Source
ToetsingOnline

Brief title
EV-302

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
Urothelial cancer / Bladder cancer

Research involving

Human

Sponsors and support

Primary sponsor: Seagen, Inc.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Enfortumab Vedotin, phase 3, Urothelial cancer

Outcome measures

Primary outcome

Dual Primary Endpoints

* PFS per RECIST v1.1 by BICR

* OS

Secondary outcome

Corresponding Secondary Endpoints

* ORR per RECIST v1.1 by BICR

* TTPP

* Mean change from baseline in worst pain at Week 26

* PFS per RECIST v1.1 by investigator assessment

* ORR per RECIST v1.1 by investigator assessment

* DOR per RECIST v1.1 by BICR

* DOR per RECIST v1.1 by investigator assessment

* DCR per RECIST v1.1 by BICR

* DCR per RECIST v1.1 by investigator assessment

* Mean scores and change from baseline of the European Organisation for

Research and Treatment of Cancer (EORTC) Quality of Life Core 30 (QLQ-C30), and

EuroQOL 5-dimensions (EQ-5D-5L) visual analogue scale (VAS), and utility scores

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

* Type, incidence and severity of laboratory abnormalities

* Treatment discontinuation rate due to AEs

Corresponding Exploratory Endpoints

* PFS, ORR, and DOR per iRECIST by investigator assessment in Arm A

* Cumulative incidence of HRU as reported by subject

* Plasma or serum of enfortumab vedotin, MMAE

* Incidence of ATA to enfortumab vedotin

* Exploratory biomarkers of clinical activity

Study description

Background summary

Urothelial Cancer
Urothelial cancer is estimated to kill nearly 200,000 patients globally on an annual basis, including more than 65,000 in Europe and 33,000 in the United States (US) (Bray 2018; Ferlay 2018; Siegel 2019). Annual diagnoses of new cases of urothelial cancer (UC) are estimated to be more than 549,000 worldwide, including more than 197,000 in Europe and 158,000 in the US (Bray 2018; Ferlay 2018; Siegel 2019).Those patients with metastatic UC represent a population with significant unmet medical need, as the 5-year mortality rate for this disease exceeds 85% (von der Maase 2005).

Metastatic Urothelial Cancer
First-line therapy for locally advanced and metastatic UC in patients with sufficient renal function consists of cisplatin-based combinations, like methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) or gemcitabine plus cisplatin, which demonstrate an objective response rate (ORR) of up to 55%, including approximately 12% complete responses (CRs) (von der Maase 2000). Despite initial chemosensitivity, most patients are not cured and the outcome of metastatic UC after these regimens is poor: median time to progression is 7

months and median overall survival (mOS) is 14 months. Long-term survival is poor (approximately 15%) and the prognosis is particularly grim for patients with visceral metastases, for whom the 5 year survival rate is 7% (Bellmunt 2011; von der Maase 2000; von der Maase 2005).
Unfortunately, more than 50% of patients with UC are cisplatin-ineligible due to poor renal function, poor performance status, or co-morbidities (De Santis 2012). An even higher unmet need exists in this population. For these cisplatin-ineligible patients, carboplatin is the platinum-containing therapy of choice. Carboplatin is also an alkylating agent, similar to cisplatin, but with less nephrotoxicity, neurotoxicity, and ototoxicity (Dogliotti 2007). In first line therapy for cisplatin-ineligible metastatic UC in patients, response rates to treatment with carboplatin monotherapy range from 8%-18% (Bamias 2006). In the European Organisation for Research and Treatment of Cancer (EORTC) 30986 trial, carboplatin combined with gemcitabine in a cisplatin-ineligible patient population resulted in a confirmed ORR of 36.1%. Median progression-free survival (mPFS) was 5.8 months and median OS was 9.3 months (De Santis 2012). The modest efficacy reported for available platinum-containing therapies highlights the need for additional treatment options for patients with metastatic UC.
Programmed cell death protein-1 (PD-1)/programmed cell death ligand-1 (PD-L1) inhibitors have demonstrated a survival benefit compared to chemotherapy in the management of late line metastatic UC. Randomized phase 3 trials have been reported for both atezolizumab (Tecentriq®) and pembrolizumab (Keytruda®) in the second-line (2L+) metastatic UC setting. In the IMvigor211 trial, median OS was not significantly different between the 2 arms (11.1 months vs. 10.6 months, respectively) (Powles 2018). KEYNOTE 045 studied pembrolizumab vs. investigator's choice of chemotherapy in metastatic UC patients who had recurred or progressed following platinum-containing chemotherapy. This study demonstrated a statistically significant improvement in OS (10.3 months vs. 7.4 months) when comparing the pembrolizumab arm to the chemotherapy arm (Bellmunt 2017).
In the US, both atezolizumab(Tecentriq®) and pembrolizumab (Keytruda®) have also received accelerated approvals for first-line use in cisplatin-ineligible UC patients based on open label, single-arm studies that showed ORRs of 24% and 29%, respectively (Tecentriq® Prescribing Information, Genentech, Apr 2017) (Keytruda® Prescribing Information, Merck, May 2017). This was followed by European Union approval in September 2017. In May 2018, the Food and Drug Administration (FDA) issued an alert regarding decreased survival in patients with low expression of PD-L1 being treated in the first-line setting with pembrolizumab or atezolizumab monotherapy, compared with platinum-containing chemotherapy. Subsequent prescribing information for pembrolizumab and atezolizumab were revised to require high PD-L1 expression in first-line metastatic UC patients who are not eligible for cisplatin containing chemotherapy. This development has further limited the options for metastatic UC patients with low expression of PD-L1.

Pharmaceutical and Therapeutic Background

The PD-1 receptor-ligand interaction is a major pathway hijacked by tumors to suppress immune control. The normal function of PD-1, expressed on the cell surface of activated T cells under healthy conditions, is to down-modulate unwanted or excessive immune responses, including autoimmune reactions. PD-1 (encoded by the gene Pdcd1) is an Ig superfamily member related to cluster of differentiation 28 (CD28) and cytotoxic T lymphocyte-associated protein 4 (CTLA-4) that has been shown to negatively regulate antigen receptor signaling upon engagement of its ligands (PD-L1 and/or PD-L2) (Greenwald 2005; Okazaki 2001).
The structure of murine PD-1 has been resolved (Zhang 2004). PD-1 and its family members are type I transmembrane glycoproteins containing an Ig-variable-type domain responsible for ligand binding and a cytoplasmic tail responsible for the binding of signaling molecules. The cytoplasmic tail of PD-1 contains 2 tyrosine-based signaling motifs, an immunoreceptor tyrosine-based inhibition motif, and an immunoreceptor tyrosine-based switch motif. Following T-cell stimulation, PD-1 recruits the tyrosine phosphatases, SHP-1 and SHP-2, to the immunoreceptor tyrosine-based switch motif within its cytoplasmic tail, leading to the dephosphorylation of effector molecules such as CD3 zeta (CD3*), protein kinase C-theta (PKC*), and zeta-chain-associated protein kinase (ZAP70), which are involved in the CD3 T-cell signaling cascade (Chemnitz 2004; Okazaki 2001; Riley 2009; Sheppard 2004). The mechanism by which PD-1 down-modulates T cell responses is similar to, but distinct from, that of CTLA-4, because both molecules regulate an overlapping set of signaling proteins (Francisco 2010; Parry 2005). As a consequence, the PD-1/PD-L1 pathway is an attractive target for therapeutic intervention in locally advanced or metastatic UC.

Enfortumab Vedotin and Pembrolizumab in Combination
PD-1/PD-L1 inhibitors unleash the antitumor activity of T-lymphocytes by targeting the T cell inhibition pathway (Sonpavde 2017), and have shown effective antitumor activity as a single agent in locally advanced or metastatic UC. Although these agents are able to induce durable responses, most patients do not respond to PD-1/PD-L1 monotherapy. Combining PD-1/PD L1 inhibitors with a novel therapy, such as enfortumab vedotin, may be beneficial. Data from preclinical studies of brentuximab vedotin (a CD30-directed ADC comprising the same linker and MMAE payload as enfortumab vedotin), shows potential to induce immunogenic cell death (ICD), antigen presentation, and tumor immune infiltration (Gardai 2015). These results suggest that the effects are due to MMAE. Treatment with brentuximab vedotin in vitro and in preclinical models has been shown to induce hallmarks of ICD. ICD is characterized by induction of the endoplasmic reticulum stress response and subsequent surface presentation of danger-associated molecular patterns immune stimulatory molecules. These danger-associated molecular patterns induce innate immune migration and activation into the tumor cell activation (Cao 2018; Cao 2017). Based on the potential enhancement of immune response, it is hypothesized that combining enfortumab vedotin with a PD-(L)-1 inhibitor will result in improved response leading to prolonged progression-free survival (PFS) and OS in patients with locally advanced or metastatic UC.

Common AEs associated with enfortumab vedotin are reviewe

Study objective

This study has been transitioned to CTIS with ID 2023-503421-19-00 check the CTIS register for the current data.

This study will evaluate the efficacy, safety, and PK of enfortumab vedotin in combination with pembrolizumab, with or without platinum-containing chemotherapy, versus standard of care gemcitabine plus platinum-containing chemotherapy in subjects with previously untreated locally advanced or metastatic UC. Specific objectives and corresponding endpoints for the study are summarized below.

Objectives

Primary Objectives
* To compare PFS between experimental arm (enfortumab vedotin + pembrolizumab [Arm A] and the control arm (gemcitabine + cisplatin or carboplatin [Arm B]) by blinded independent central review (BICR)
* To compare overall survival (OS) between experimental arm (Arm A) and the control arm (Arm B)

Secondary Objectives
* To compare the objective response rate (ORR) between the experimental arm (Arm A) and the control arm (Arm B) by BICR
* To compare time to pain progression (TTPP) from the subject perspective between the experimental arm (Arm A) and the control arm (Arm B)
* To compare average change in pain from the subject perspective between the experimental arm (Arm A) and the control arm (Arm B)
* To evaluate PFS between the experimental arm (Arm A) and the control arm (Arm B) by investigator assessment
* To evaluate the ORR between the experimental arm (Arm A) and the control arm (Arm B) by investigator assessment
* To evaluate the DOR between the experimental arm (Arm A) and the control arm (Arm B)
* To evaluate the disease control rate (DCR) between the experimental arm (Arm A) and the control arm (Arm B)
* To evaluate the impact of study treatment on quality of life (QOL), functioning, and symptoms from the subject perspective
* To evaluate the safety profile of each treatment regimen

Exploratory Objectives
* To assess PFS, ORR, and DOR per the modified RECIST v1.1 for immune based therapeutics (iRECIST) in Arm A
* To assess subject reported health resource utilization (HRU)
* To assess the pharmacokinetics of enfortumab vedotin, and MMAE

* To assess the development of ATA to enfortumab vedotin
* To assess biomarkers of biological activity, resistance and predictive biomarkers of response

Study design

This is a phase 3 open-label, 2-arm randomized, controlled multicenter study to evaluate the combination of enfortumab vedotin + pembrolizumab, versus standard of care gemcitabine + platinum-containing chemotherapy, in subjects with previously untreated locally advanced or metastatic urothelial cancer. The study is designed to assess the dual primary endpoints of progression-free survival (PFS) and overall survival (OS) of experimental Arm A (enfortumab vedotin + pembrolizumab) compared to control Arm B (gemcitabine + cisplatin or carboplatin), and experimental Arm C (enfortumab vedotin + pembrolizumab + cisplatin or carboplatin) compared to control Arm B. Subjects will be randomized in a 1:1 manner to one of the study arms with the following stratification factors: cisplatin eligibility (eligible or ineligible), PD-L1 expression (high or low), and liver metastases (present or absent).

Subjects in Arm A will receive enfortumab vedotin at 1.25 mg/kg, administered as an IV infusion on Days 1 and 8 of every 3-week cycle, and pembrolizumab 200 mg as an IV infusion on Day 1 of every 3-week cycle, after completion of the enfortumab vedotin infusion.

Subjects in Arm B will receive gemcitabine at 1000 mg/m2 as an IV infusion on Days 1 and 8 of every 3 week cycle. Cisplatin (70 mg/m2) or carboplatin (area under the curve [AUC] 4.5, or AUC of 5 according to local guidelines) will be administered on Day 1 of every 3-week cycle, with adequate pre- and post-hydration, by IV infusion per institutional standards.

Pembrolizumab 200 mg will be administered as an IV infusion on Day 1 of every 3-week cycle after completion of the platinum containing chemotherapy infusion. Response will be assessed by computed tomography (CT) scans with contrast (unless contraindicated) every 9 weeks (±1-week) timed from the randomization date. For subjects who cannot receive CT scans with contrast, other protocol-specified imaging methods may be used Appendix C). Brain scans should be repeated at this time point in subjects with a history of CNS metastasis or signs/symptoms of CNS metastasis. Bone imaging should also be repeated at this time point in subjects with a history of skeletal metastasis or suspicion of skeletal metastases based on imaging or symptoms. Objective responses will be confirmed per RECIST v1.1 with repeat scans done at the next scheduled response assessment per protocol after first documentation of response. Subsequent response assessments should be performed every 9 weeks (±1-week) until 18 months after randomization, then every 12 weeks (±1-week). Tumor imaging should also be performed, and blinded independent central review (BICR) evaluation triggered, whenever disease progression is suspected.

Subjects may continue on study treatment until progressive disease (BICR-confirmed or clinical progression [see Section 7.3]), an adverse event (AE), pregnancy, investigator decision, start of a subsequent anticancer therapy, subject decision (non-AE), study termination by the sponsor, completion of the maximum number of drug cycles allowed, or other reason unrelated to an AE (see Section 4.3). Treatment beyond disease progression per RECIST v1.1 may be considered in subjects in study Arm A (enfortumab vedotin [EV] + pembrolizumab) who are deriving clinical benefit as defined in Section 5.7. Subjects treated beyond disease progression per RECIST v1.1 may continue until confirmed disease progression per iRECIST as assessed by the investigator (Seymour 2017) (Appendix K). Confirmatory scans must be performed 4 to 9 weeks after disease progression per RECIST v1.1 by BICR. Treatment with gemcitabine and treatment with platinum-containing chemotherapy may be given up to 6 cycles. Treatment with pembrolizumab will be discontinued once the subject has received a maximum of 35 administrations (approximately 2 years). There is no upper limit to the number of cycles of enfortumab vedotin permitted. Palliative radiotherapy on a nontarget bone lesion that is not progressing is permitted and will not be considered a subsequent anticancer therapy; however, radiotherapy on any new or progressing (per BICR-assessed RECIST v1.1) lesion will be considered a subsequent anticancer therapy and subjects will not be permitted to resume study treatment. Surgical resection for curative intent during study treatment may be permitted in subjects with favorable tumor response after discussion with the medical monitor.

Subjects who discontinue treatment for reasons other than disease progression or consent withdrawal will continue to receive response assessments every 9 weeks (±1-week) for the first 18 months timed from the randomization date, and every 12 weeks (±1-week) thereafter, until the subject has radiologically-confirmed disease progression per RECIST v1.1 guidelines as determined by BICR, initiates a subsequent anticancer therapy, dies, withdraws consent, or the study closes, whichever occurs first. After progression and discontinuation of study treatment, subjects will be followed every 12 weeks (±1-week) to obtain information on subsequent anticancer therapy, and to assess survival status until death, study closure, or subject withdraws consent, whichever occurs first.
Safety will be monitored over the course of the study by an Independent Data Monitoring Committee (IDMC).

Study burden and risks

Protocol amendment 7 includes all this information

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

1. Subjects must have histologically documented, unresectable locally advanced or metastatic urothelial carcinoma (i.e., cancer of the bladder, renal pelvis, ureter, or urethra). Subjects with squamous or sarcomatoid differentiation or mixed cell types are eligible.

2. Subjects must have measurable disease by investigator assessment according to RECIST v1.1.
a. Subjects with prior definitive radiation therapy must have measurable disease per RECIST v1.1 that is outside the radiation field or has demonstrated unequivocal progression since completion of radiation therapy

3. Subjects must not have received prior systemic therapy for locally advanced or metastatic urothelial carcinoma with the following exceptions:
a. Subjects that received neoadjuvant chemotherapy with recurrence >12 months from completion of therapy are permitted

b. Subjects that received adjuvant chemotherapy following cystectomy with recurrence >12 months from completion of therapy are permitted

4. Subjects must be considered eligible to receive cisplatin- or carboplatin-containing chemotherapy, in the investigator*s judgement.
a. Subjects will be considered cisplatin-ineligible, and will receive carboplatin, if they meet at least one of the following criteria:
i. GFR <60 mL/min but >=30 mL/min (measured by the Cockcroft-Gault formula, Modification of Diet in Renal Disease [MDRD] or 24-hour urine)
· Subjects with a GFR >=50 mL/min and no other cisplatin ineligibility criteria may be considered cisplatin-eligible based on the investigator*s clinical judgement
ii. ECOG or WHO performance status of 2 (refer to Inclusion 7 for additional criteria for ECOG 2 subjects)
iii. NCI CTCAE Grade >=2 audiometric hearing loss
iv. NYHA Class III heart failure

5. Subjects must be age 18 years or older or considered an adult by local regulations.

6. Archival tumor tissue comprising muscle-invasive urothelial carcinoma or a biopsy of metastatic urothelial carcinoma must be provided for PD-L1 testing prior to randomization. If adequate archival tumor sample is not available, or evaluable, a new biopsy sample may be performed.

7. Subjects must have an ECOG Performance Status score of 0, 1, or 2.
a. Subjects with ECOG performance status of 2 must additionally meet the following criteria:
i. Hemoglobin >=10 g/dL
ii. GFR >=50 mL/min
iii. May not have NYHA Class III heart failure

8. Subjects must have adequate hematologic and organ function as defined by the baseline laboratory values in Table 5 (see protocol)

9. Female subjects of childbearing potential must meet the following conditions:
· Agree not to try to become pregnant during the study and for at least 6 months after the final dose of study drug.
· Must have a negative urine or serum pregnancy test (minimum sensitivity of 25 mIU/mL or equivalent units of beta human chorionic gonadotropin [β-hCG]) within 1 day prior to administration of the drug. Female subjects with false positive results and documented verification of negative pregnancy status are eligible for participation.
· If heterosexually active, agree to abstinence (if in line with the usual preferred lifestyle of the subject) or consistently use a condom plus 1 form of highly effective birth control per locally accepted standards starting at screening, throughout the study period, and for at least 6 months after the

final dose of study drug.
· Female subjects must agree not to breastfeed or donate ova starting at screening and throughout the study period, and for at least 6 months after the final dose of study drug.

10. Male subjects who can father children, must meet the following conditions:
· Must not donate sperm starting at screening and throughout the study period, and for at least 6 months after the final dose of study drug.
· Agree to abstinence (if in line with the usual preferred lifestyle of the subject) or to use a male condom starting at screening and continue throughout study period and for at least 6 months after the final dose of study drug. If the male subject has not had a vasectomy or is not sterile as defined below their female partner(s) is utilizing 1 form of highly effective birth control per locally accepted standards starting at screening and continuing throughout study treatment and for at least 6 months after the male subject receives their final dose of study drug.
· Male subjects with a pregnant or breastfeeding partner(s) must agree to abstinence or use a condom for the duration of the pregnancy or time partner is breastfeeding throughout the study period and for at least 6 months after the final dose of study drug.

Exclusion criteria

1. Subjects who have previously received enfortumab vedotin or other MMAE-based ADCs.
2. Subjects who have received prior treatment with a PD-(L)-1 inhibitor for any malignancy, including earlier stage UC, defined as a PD-1 inhibitor or PD-L1 inhibitor.
3. Subjects who have previously received any prior treatment with an agent directed to another stimulatory or co inhibitory T-cell receptor.
4. Subjects who have received anti-cancer treatment with chemotherapy, biologics, or investigational agents not otherwise prohibited by exclusion criterion 1-3 that is not completed 4 weeks prior to first dose of study treatment.
5. Subjects with uncontrolled diabetes.
6. Subjects with an estimated life expectancy <12 weeks
7. Subjects with ongoing sensory or motor neuropathy Grade 2 or higher.
8. Subjects with active CNS metastases. Subjects with treated CNS metastases are permitted on study if all of the following are true: a) CNS metastases have been clinically stable for at least 4 weeks prior to screening and baseline scans show no evidence of new or enlarged metastasis; b) the subject is on a stable dose of <=10 mg/day of prednisone or equivalent for at least 2 weeks (if requiring steroid treatment); c) subject does not have leptomeningeal disease.
9. Subjects with ongoing clinically significant toxicity associated with prior treatment (including radiotherapy or surgery) that has not resolved to <= Grade

1 or returned to baseline.
10. Currently receiving systemic antimicrobial treatment for active infection (viral, bacterial, or fungal) at the time of randomization. Routine antimicrobial prophylaxis is permitted.
11. Subjects who have a known history of hepatitis B (defined as HBsAg reactive) or known active hepatitis C virus (defined as HCV RNA [qualitative] is detected) infection. No testing for hepatitis B and hepatitis C is required unless mandated by local health authority. Subjects who have been curatively treated for hepatitis C infection are permitted if they have documented sustained virologic response of 12 weeks.
12. Has a known history of human immunodeficiency virus (HIV) infection. Testing is not required unless mandated by the local health authority.
13. Subjects with conditions requiring high doses of steroids (>10 mg/day of prednisone or equivalent) or other immunosuppressive medications are excluded. Inhaled or topical steroids are permitted in the absence of active autoimmune disease. Physiologic replacement doses of corticosteroids are permitted for subjects with adrenal insufficiency.
14. Subjects with a history of another invasive malignancy within 3 years before the first dose of study drug, or any evidence of residual disease from a previously diagnosed malignancy (eligible exceptions see protocol).
15. Subjects with a documented history of a cerebral vascular event (stroke or transient ischemic attack), unstable angina, myocardial infarction, or cardiac symptoms consistent with NYHA Class IV within 6 months prior to randomization.
16. Subjects who have received radiotherapy within 2 weeks prior to randomization.
17. Subjects who have received major surgery (defined as requiring general anesthesia and >24-hour inpatient hospitalization) within 3 weeks prior to randomization.
18. Subjects with known severe (>= Grade 3) hypersensitivity to any excipient contained in the drug formulations of enfortumab vedotin, pembrolizumab, the platinum agent selected by the investigator or gemcitabine.
19. Subjects with active keratitis or corneal ulcerations.
20. History of autoimmune disease that has required systemic treatment in the past 2 years.
a. Replacement therapy (e.g., thyroxine, insulin, physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.
b. Brief (<7 days) use of systemic corticosteroids is allowed when use is considered standard of care.
c. Subjects with vitiligo, psoriasis, type 1 diabetes mellitus, hypothyroidism, or resolved childhood asthma/atopy will not be excluded.
d. Subjects requiring intermittent use of bronchodilators, inhaled steroids, or local steroid injections will not be excluded.
e. Subjects with hypothyroidism that is stable with hormone replacement or Sjögren's syndrome will not be excluded.
21. Subjects with a history of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of

active pneumonitis on screening chest CT scan.
22. Subjects who have received a prior allogeneic stem cell or solid organ transplant.
23. Subjects who have received a live attenuated vaccine within 30 days prior to randomization.
24. Subjects with active tuberculosis.
25. Subjects with another underlying medical condition that, in the opinion of the investigator, would impair the ability of the subject to receive or tolerate the planned treatment and follow-up; any known psychiatric or substance abuse disorders that would interfere with cooperating with the requirements of the study.

Study design

Design

Study phase:	3
Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-06-2021
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Enfortumab Vedotin
Generic name:	Balversa
Product type:	Medicine

Brand name:	Pembrolizumab
Generic name:	Keytruda
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	02-07-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	12-03-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	27-05-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-11-2021
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Approved WMO Date:	01-02-2022
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Approved WMO Date:	15-02-2022

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-10-2022
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Review commission:	METC NedMec
Approved WMO Date:	18-11-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-02-2023

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Approved WMO Date:	25-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-06-2023
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
EU-CTR	CTIS2023-503421-19-00
EudraCT	EUCTR2019-004542-15-NL
ClinicalTrials.gov	NCT04223856
CCMO	NL73925.031.20