ESMO 2022 INDUSTRY SATELLITE SYMPOSIUM

FROM LANDMARK DATA TO CLINICAL EXCELLENCE: IMPROVING OUTCOMES IN LA/mUC

Sunday 11 September 2022, 18:30–20:00 CEST

7.2.F – Fécamp Auditorium, Hall 7, Level 7.2, Paris Expo Porte de Versailles, Paris, France

Join us to engage in debate and discussion with leading oncologists and urologists on the latest developments in the management of locally advanced/metastatic urothelial carcinoma (LA/mUC).

Learn more about the role of Nectin-4 as a clinically relevant and viable target for the treatment of urothelial carcinoma, hear expert opinions on the role of enfortumab vedotin (EV) in the LA/mUC treatment pathway, and share your perspectives on the evolving treatment landscape during this industry session.

Meeting Chair

Professor Ignacio Durán, Spain

Faculty

Dr María José Juan Fita, Spain

Dr Yohann Loriot, France

Professor Rob Jones, United Kingdom

Professor Axel Merseburger, Germany

Agenda

Time	Session
18:30–18:40	**Making milestones: The evolving treatment landscape in LA/mUC**
18:40–18:55	**Discovering the data: MoA and core clinical evidence**
18:55–19:15	**Defining the direction: Enfortumab vedotin eligibility and treatment initiation**
19:15–19:35	**Practical tips for treatment: Optimising outcomes and managing adverse events**
19:35–19:45	**Prioritising patients in practice: Evidence-driven care in the clinic**
19:45–20:00	**Pinpoints of interest: Panel discussion and Q&A**

For prescribing information please download the invitation.

Prescribing information may vary. Please refer to your local prescribing information.

ASTELLAS-SPONSORED INDUSTRY SESSION

Intended for an international audience

Date of preparation: August 2022 | ENF_2022_0042_FR

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Prescribing Information: PADCEV™ ▼ (enfortumab vedotin) 20 mg and 30 mg powder for concentrate for solution for infusion

For full prescribing information refer to the Summary of Product Characteristics (SPC). **Presentation:** One vial of PADCEV powder for concentrate for solution for infusion contains either 20 mg or 30 mg enfortumab vedotin. After reconstitution, each ml of solution contains 10 mg of enfortumab vedotin. Enfortumab vedotin is comprised of a fully human IgG1 kappa antibody, conjugated to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable maleimidocaproyl valine-citrulline linker. **Indications:** PADCEV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and a programmed death receptor-1 or programmed death-ligand 1 inhibitor (see section 5.1 of the SPC). **Posology and method of administration:** Treatment with PADCEV should be initiated and supervised by a physician experienced in the use of anti-cancer therapies. PADCEV is for intravenous use. Good venous access prior to starting treatment should be ensured (see section 4.4 of the SPC). The recommended dose of enfortumab vedotin is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg). It must be administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. It must not be administered as an intravenous push or bolus injection. For information on recommended dose reductions for adverse reactions as well as instructions on dose modifications (interruption, reduction and discontinuation) in patients experiencing adverse reactions refer to section 4.2 of the SPC. Special Populations. *Elderly:* No dose adjustment is necessary in patients ≥65 years of age (see section 5.2 of the SPC). *Renal impairment:* No dose adjustment is necessary in patients with mild [creatinine clearance (CrCL) >60-90 mL/min], moderate (CrCL 30–60 mL/min) or severe (CrCL 15–<30 mL/min) renal impairment. Enfortumab vedotin has not been evaluated in patients with end stage renal disease (CrCL <15 mL/min) (see section 5.2 of the SPC). *Hepatic impairment:* No dose adjustment is necessary in patients with mild hepatic impairment [total bilirubin of 1 to 1.5 × upper limit of normal (ULN) and aspartate transaminase (AST) any, or total bilirubin ≤ ULN and AST > ULN]. Enfortumab vedotin has only been evaluated in a limited number of patients with moderate hepatic impairment and has not been evaluated in patients with severe hepatic impairment (see section 5.2 of the SPC). *Paediatric population:* There is no relevant use of enfortumab vedotin in the paediatric population for the indication of locally advanced or metastatic urothelial cancer. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SPC. **Special warnings and precautions for use:** Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Skin reactions: Skin reactions are associated with enfortumab vedotin as a result of enfortumab vedotin binding to Nectin-4 expressed in the skin. Fever or flu-like symptoms may be the first sign of a severe skin reaction, and patients should be observed, if this occurs. Mild to moderate skin reactions, predominantly maculopapular rash, have been reported (see section 4.8 of the SPC). Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), with fatal outcome have also occurred in patients treated with enfortumab vedotin, predominantly during the first cycle of treatment. In clinical trials, the median time to onset of severe skin reactions was 0.6 months (range: 0.1 to 6.4). Patients should be monitored starting with the first cycle and throughout treatment for skin reactions. Appropriate treatment such as topical corticosteroids and antihistamines can be considered for mild to moderate skin reactions. For suspected SJS or TEN, or in case of bullous lesions onset, withhold treatment immediately and refer to specialised care; histologic confirmation, including consideration of multiple biopsies, is critical to early recognition, as diagnosis and intervention can improve prognosis Permanently discontinue PADCEV for confirmed SJS or TEN, Grade 4 or recurrent severe skin reactions. For Grade 2 worsening, Grade 2 with fever or Grade 3 skin reactions, treatment should be withheld until Grade ≤1 and referral for specialised care should be considered. Treatment should be resumed at the same dose level or consider dose reduction by one dose level (see section 4.2 of the SPC). Hyperglycaemia: Hyperglycaemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with enfortumab vedotin (see section 4.8 of the SPC). Hyperglycaemia occurred more frequently in patients with pre-existing hyperglycaemia or a high body mass index (≥30 kg/m^2). Patients with baseline HbA1c ≥8% were excluded from clinical trials. Blood glucose levels should be monitored prior to dosing and periodically throughout the course of treatment as clinically indicated in patients with or at risk for diabetes mellitus or hyperglycaemia. If blood glucose is elevated >13.9 mmol/L (>250 mg/dL), PADCEV should be withheld until blood glucose is ≤13.9 mmol/L (≤250 mg/dL) and treat as appropriate (see section 4.2 of the SPC). Peripheral neuropathy: Peripheral neuropathy, predominantly peripheral sensory neuropathy, has occurred with enfortumab vedotin, including Grade ≥3 reactions (see section 4.8 of the SPC). Patients with pre-existing peripheral neuropathy Grade ≥2 were excluded from clinical trials. Patients should be monitored for symptoms of new or worsening peripheral neuropathy as these patients may require a delay, dose reduction or discontinuation of enfortumab vedotin. PADCEV should be permanently discontinued for Grade ≥3 peripheral neuropathy (see section 4.2 of the SPC). Ocular disorders: Ocular disorders, predominantly dry eye, have occurred in patients treated with enfortumab vedotin (see section 4.8 of the SPC). Patients should be monitored for ocular disorders. Consider artificial tears for prophylaxis of dry eye and referral for ophthalmologic evaluation if ocular symptoms do not resolve or worsen. Infusion site extravasation: Skin and soft tissue injury following enfortumab vedotin administration has been observed when extravasation occurred (see section 4.8 of the SPC). Ensure good venous access prior to starting PADCEV and monitor for possible infusion site extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions. Embryo-foetal toxicity and contraception: Pregnant women should be informed of the potential risk to a foetus (see sections 4.6 and 5.3 of the SPC). Females of reproductive potential should be advised to have a pregnancy test within 7 days prior to starting treatment with enfortumab vedotin, to use effective contraception during treatment and for at least 12 months after stopping treatment. Men being treated with enfortumab vedotin are advised not to father a child during treatment and for up to 9 months following the last dose of PADCEV. **Effects on ability to drive and use machines:** PADCEV has no or negligible influence on the ability to drive and use machines. **Interactions:** Formal drug-drug interaction studies with enfortumab vedotin have not been conducted. Caution is advised in case of concomitant treatment with CYP3A4 inhibitors. Patients receiving concomitant strong CYP3A4 inhibitors (e.g. boceprevir, clarithromycin, cobicistat, indinavir, itraconazole, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole) should be monitored more closely for signs of toxicities. Strong CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin, St John's wort [Hypericum perforatum]) may decrease the exposure of unconjugated MMAE with moderate effect (see section 5.2 of the SPC). **Fertility, pregnancy and lactation:** Women of childbearing potential/ Contraception in males and females: Refer to 'Special warnings and precautions for use' section above. Pregnancy: PADCEV can cause foetal harm when administered to pregnant women based upon findings from animal studies. PADCEV is not recommended during pregnancy and in women of childbearing potential not using effective contraception. Breast-feeding: Breast-feeding should be discontinued during PADCEV treatment and for at least 6 months after the last dose. Fertility: Men being treated with this medicinal product are advised to have sperm samples frozen and stored before treatment. There are no data on the effect of PADCEV on human fertility. **Undesirable effects:** Summary of the safety profile: The most common adverse reactions with enfortumab vedotin were alopecia (48.8%), fatigue (46.8%), decreased appetite (44.9%), peripheral sensory neuropathy (38.7%), diarrhoea (37.6%), nausea (36%), pruritus (33.4%), dysgeusia (29.9%), anaemia (26.5%), weight decreased (23.4%), rash maculo-papular (22.9%), dry skin (21.6%), vomiting (18.4%), aspartate aminotransferase increased (15.3%), hyperglycaemia, (13.1%), dry eye (12.8%), alanine aminotransferase increased (12.1%) and rash (10.4%). The most common serious adverse reactions were diarrhoea (2%) and hyperglycaemia (2%). Nine percent of patients permanently discontinued enfortumab vedotin for adverse reactions; the most common adverse reaction (≥2%) leading to dose discontinuation was peripheral sensory neuropathy (4%). Adverse reactions leading to dose interruption occurred in 44% of patients; the most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (15%), fatigue (7%), rash maculo-papular (4%), aspartate aminotransferase increased (4%), alanine aminotransferase increased (4%), anaemia (3%), diarrhoea (3%) and hyperglycaemia (3%). Thirty percent of patients required a dose reduction due to an adverse reaction; the most common adverse reactions (≥2%) leading to a dose reduction were peripheral sensory neuropathy (10%), fatigue (5%), rash maculo-papular (4%) and decreased appetite (2%). Summary of adverse reactions: The safety of enfortumab vedotin as monotherapy has been evaluated in 680 patients with locally advanced or metastatic urothelial cancer receiving 1.25 mg/kg on Days 1, 8 and 15 of a 28-day cycle in clinical studies). Patients were exposed to enfortumab vedotin for a median duration of 4.7 months (range: 0.3 to 34.8 months). Adverse reactions observed during clinical studies are listed in this section according to Medical Dictionary for Regulatory Activities (MedDRA) system organ classification by frequency category. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequency categories are defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). *Blood and lymphatic system disorders* Very common: Anaemia, Not known[1]: Neutropenia, febrile neutropenia, neutrophil count decreased. *Metabolism and nutrition disorders:* Very common: Hyperglycaemia, decreased appetite. *Nervous system disorders:* Very common: Peripheral sensory neuropathy, dysgeusia, Common: Neuropathy peripheral, peripheral motor neuropathy, peripheral sensorimotor neuropathy, paraesthesia, hypoaesthesia, gait disturbance, muscular weakness, Uncommon: Demyelinating polyneuropathy, polyneuropathy, neurotoxicity, motor dysfunction, dysaesthesia, muscle atrophy, neuralgia, peroneal nerve palsy, sensory loss, skin burning sensation, burning sensation. *Eye disorders:* Very common: Dry eye. *Gastrointestinal disorders:* Very common: Diarrhoea, vomiting, nausea. *Skin and subcutaneous tissue disorders:* Very common: Alopecia, pruritus, rash, rash maculo-papular, dry skin, Common: Drug eruption, skin exfoliation, conjunctivitis, dermatitis bullous, blister, stomatitis, palmar-plantar erythrodysesthesia syndrome, eczema, erythaema, rash erythaematous, rash macular, rash papular, rash pruritic, rash vesicular, Uncommon: Dermatitis exfoliative generalised, erythaema multiforme, exfoliative rash, pemphigoid, rash maculovesicular, dermatitis, dermatitis allergic, dermatitis contact, intertrigo, skin irritation, stasis dermatitis, blood blister, Not known[1]: TEN, SJS, epidermal necrosis, symmetrical drug-related intertriginous and flexural exanthaema. *General disorders and administration site conditions:* Very common: Fatigue, Common: Infusion site extravasation. *Investigations:* Very common: Alanine aminotransferase increased, aspartate aminotransferase increased, weight decreased. [1]Based on global post-marketing experience. Description of selected adverse reactions. *Immunogenicity:* A total of 590 patients were tested for immunogenicity to enfortumab vedotin 1.25 mg/kg; 15 patients were confirmed to be positive at baseline for anti-drug antibody (ADA), and in patients that were negative at baseline (N=575), a total of 16 (2.8%) were positive postbaseline (13 transiently and 3 persistently). Due to the limited number of patients with antibodies against PADCEV, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy, safety or pharmacokinetics. *Skin reactions:* In clinical studies, skin reactions occurred in 55% (375) of the 680 patients treated with enfortumab vedotin 1.25 mg/kg. Severe (Grade 3 or 4) skin reactions occurred in 13% (85) of patients and a majority of these reactions included maculo-papular rash, rash erythematous, rash or drug eruption. The median time to onset of severe skin reactions was 0.62 months (range: 0.1 to 6.4 months). Serious skin reactions occurred in 3.8% (26) of patients. In the EV-201 (N=214) clinical study, of the patients who experienced skin reactions, 75% had complete resolution and 14% had partial improvement (see section 4.4 of the SPC). *Hyperglycaemia:* In clinical studies, hyperglycaemia (blood glucose >13.9 mmol/L) occurred in 14% (98) of the 680 patients treated with enfortumab vedotin 1.25 mg/kg. Serious events of hyperglycaemia occurred in 2.2% of patients, 7% of patients developed severe (Grade 3-4) hyperglycaemia and 0.3% of patients experienced fatal events, one event each of hyperglycaemia and diabetic ketoacidosis. The incidence of Grade 3-4 hyperglycaemia increased consistently in patients with higher body mass index and in patients with higher baseline haemoglobin A1C (HbA1c). The median time to onset of hyperglycemia was 0.6 months (range: 0.1 to 20.3). In the EV-201 (N=214) clinical study, at the time of their last evaluation, 61% of patients had complete resolution, and 19% of patients had partial improvement (see section 4.4 of the SPC). *Peripheral neuropathy:* In clinical studies peripheral neuropathy occurred in 52% (352) of the 680 patients treated with enfortumab vedotin 1.25 mg/kg. Four percent of patients experienced severe (Grade 3-4) peripheral neuropathy including sensory and motor events. The median time to onset of Grade ≥2 was 4.6 months (range: 0.1 to 15.8). In the EV-201 (N=214) clinical study, at the time of their last evaluation, 19% of patients had complete resolution, and 39% of patients had partial improvement (see section 4.4 of the SPC). *Ocular disorders:* In clinical studies, 30% of patients experienced dry eye during treatment with enfortumab vedotin 1.25 mg/kg. Treatment was interrupted in 1.3% of patients and 0.1% of patients permanently discontinued treatment due to dry eye. Severe (Grade 3) dry eye only occurred in 3 patients (0.4%). The median time to onset of dry eye was 1.7 months (range: 0 to 19.1 months) (see section 4.4). Prescribers should consult the full SPC in relation to other adverse reactions. **Overdose:** There is no known antidote for overdosage with enfortumab vedotin. In case of overdosage, the patient should be closely monitored for adverse reactions, and supportive treatment should be administered as appropriate taking into consideration the half-life of 3.6 days (ADC) and 2.6 days (MMAE). **Legal classification:** POM. **Marketing Authorisation numbers:** PADCEV 20 mg powder for concentrate for solution for infusion EU/1/21/1615/001 (Northern Ireland) and PLGB 00166/0432 (Great Britain). PADCEV 30 mg powder for concentrate for solution for infusion EU/1/21/1615/002 (Northern Ireland) and PLGB 00166/0433 (Great Britain). **Marketing Authorisation Holders:** Astellas Pharma Europe B.V. Sylviusweg 62, 2333 BE Leiden, The Netherlands (Northern Ireland); Astellas Pharma Ltd, SPACE, 68 Chertsey Road, Woking, GU21 5BJ, UK (Great Britain).

Adverse events should be reported.
Report adverse events to regulatory bodies. Also report to Astellas Pharma Inc by email to safety-eu@astellas.com, by facsimile to +31 (0)71-545 5208, or contact your local Astellas office (www.astellas.com/eu/worldwide).

▼ This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions. Please consult the SmPC for full information.

This product was reviewed and approved based on the European Federation of Pharmaceutical Industries and Associations (EFPIA) code and the European Medicines Agency (EMA) label; the EU Summary of Product Characteristics (SmPC) can be provided upon request.

Date of preparation: August 2022 | ENF_2022_0042_FR