Essai Clinique

Généré le 08 mai 2024 à partir de

Titre	Étude de l'enfortumab védotine (ASG-22CE) en monothérapie ou en association avec d'autres thérapies anticancéreuses pour le traitement du cancer urothélial
Protocole ID	SGN22E-002 (MK-3475-869/KEYNOTE KN-869)
ClinicalTrials.gov ID	NCT03288545
Type(s) de cancer	Vessie/urothélial
Phase	Phase I-II
Type étude	Clinique
Médicament	Enfortumab védotine seul ou en association avec d'autres thérapies
Institution	CIUSSS DE L'ESTRIE – CENTRE HOSP. UNIV. DE SHERBROOKE HOPITAL FLEURIMONT 3001 12e Avenue Nord, Sherbrooke, QC, J1H 5N4
Ville	
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Statut	Fermé
But étude	This study will test an experimental drug (enfortumab vedotin) alone and with different combinations of anticancer therapies. Pembrolizumab is an immune checkpoint inhibitor (CPI) that is used to treat patients with cancer of the urinary system (urothelial cancer). This type of cancer includes cancer of the bladder, renal pelvis, ureter or urethra. Some parts of the study will look at locally-advanced and metastatic urothelial cancer, which means the cancer has spread to nearby tissues or to other areas of the body. Other parts of the study will look at muscle-invasive bladder cancer (MIBC), which is cancer at an earlier stage that has spread into the muscle wall of the bladder. This study will look at the side effects of enfortumab vedotin alone and with other anticancer therapies. A side effect is a response to a drug that is not part of the treatment effect. This study will also test if the cancer shrinks with the different treatment combinations.

Critères d'éligibilité	• Locally advanced or metastatic urothelial cancer (la/mUC) - Cohorts A, B, D, E, F, G and K.
	  • Histologically documented la/mUC, including squamous differentiation or mixed cell types.
	  • An Eastern Cooperative Oncology Group (ECOG) Performance Status score of 0, 1 or 2: Participants with ECOG performance status of 2 must meet the following additional criteria: hemoglobin ≥10 g/dL, GFR ≥50 mL/min, may not have NYHA Class III heart failure.
	  • Eligible for pembrolizumab (Dose-escalation cohorts, Cohorts A, B, G and K Combination Arm).
	  • Dose-escalation cohorts: Ineligible for first-line cisplatin-based chemotherapy and no prior treatment for la/mUC, or have disease progression following at least 1 platinum-containing treatment.
	  • Cohort A: Ineligible for cisplatin-based chemotherapy and no prior treatment for la/mUC. No prior adjuvant/neoadjuvant platinum-based therapy in at least 12 months.
	  • Cohort B: Must have disease progression during/following treatment with at least 1 platinum-containing regimen for la/mUC or disease recurrence.
	  • Cohort D: Eligible for cisplatin-based chemotherapy and no prior treatment for la/mUC. No prior adjuvant/neoadjuvant platinum-based therapy in at least 12 months.
	  • Cohort E: Ineligible for cisplatin-based chemotherapy, eligible for carboplatin, and no prior treatment for la/mUC. No prior adjuvant/neoadjuvant platinum-based therapy in at least 12 months.

	• Cohort F: Ineligible for platinum-based chemotherapy, or disease progression during/following at least 1 prior treatment for la/mUC. Eligible for gemcitabine. • Cohort G: Eligible for platinum-based chemotherapy (either cisplatin or carboplatin) and no prior treatment for la/mUC. No prior adjuvant/neoadjuvant platinum-based therapy in at least 12 months. • Cohort K: Ineligible for cisplatin-based chemotherapy due to at least 1 of the following: Glomerular filtration rate (GFR) <60 mL/min and ≥30 mL/min, ECOG performance status of 2, NCI CTCAE Version 4.03 Grade ≥2 hearing loss, New York Heart Association (NYHA) Class III heart failure. No prior systemic treatment for locally advanced or metastatic disease. No adjuvant/neoadjuvant platinum-based therapy within 12 months prior to randomization. • Muscle Invasive Bladder Cancer (MIBC)- Cohorts H, J and L. • Histologically confirmed MIBC with predominant >50% urothelial histology:Cohorts H and J: Clinical stage cT2-T4aN0M0; Cohort L: Clinical stage cT2-T4aN0M0 or cT1-T4aN1M0: Participants with pT1 disease are eligible only if they have N1 disease on imaging. Mixed cell types are eligible if urothelial cancer is predominant (>50%); Participants with plasmacytoid and/or neuroendocrine tumors are ineligible regardless of component percentage. • Must be cisplatin-ineligible. • Cohort-specific eligibility: Cohort J, H, and L: No prior systemic treatment, chemoradiation, or radiation therapy for MIBC. May have received prior intravesical Bacillus Calmette-Guerin (BCG) or intravesical chemotherapy for non-MIBC; Cohort J: Eligible for pembrolizumab. • ECOG performance status of 0, 1, or 2. • Anticipated life expectancy of ≥3 months. • Tumor samples with an associated pathology report from the diagnostic transurethral resection of a bladder tumor done 90 days prior to the first dose of study treatment must be available prior to enrollment and determined to be sufficient for pathology review and biomarker analysis. • Participants must be deemed eligible for radical cystectomy and pelvic lymph node dissection.
Critères d'exclusion	• la/mUC - Cohorts A, B, D, E, F, G, and K • Received any prior treatment with a PD-1 inhibitor, PD-L1 inhibitor, or PD-L2 inhibitor, except Cohort F. • Received any prior treatment with stimulatory or co-inhibitory T-cell receptor agents, such as CD137 agonists, OX-40 agonists, or cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) inhibitors (except Cohort F). • Ongoing sensory or motor neuropathy Grade 2 or higher. • Active central nervous system (CNS) metastases. • Ongoing clinically significant toxicity (Grade 2 or greater) associated with prior treatment (including radiotherapy or surgery). • Conditions requiring high doses of steroids or other immunosuppressive medications. • Prior treatment with enfortumab vedotin or other monomethyl auristatin E (MMAE)-based antibody-drug conjugates (ADCs). • Uncontrolled diabetes mellitus. • MIBC - Cohorts H, J, and L • Received prior systemic treatment, chemoradiation, and/or radiation therapy of muscle invasive bladder cancer. • Received any prior treatment with a CPI. • Received any prior treatment with stimulatory or co-inhibitory T-cell receptor agents, such as CD137 agonists, CTLA-4 inhibitors, or OX-40 agonists. • Evidence of nodal or metastatic disease on imaging per local assessment. Participants in Cohort L with pT1 disease may not have ≥N2 nodal disease on imaging. • Ongoing sensory or motor neuropathy Grade 2 or higher. • Conditions requiring high doses of steroids or other immunosuppressive medications. • Prior treatment with enfortumab vedotin or other MMAE-based ADCs for urothelial cancer. • History of another malignancy within 3 years before first dose of study drug.