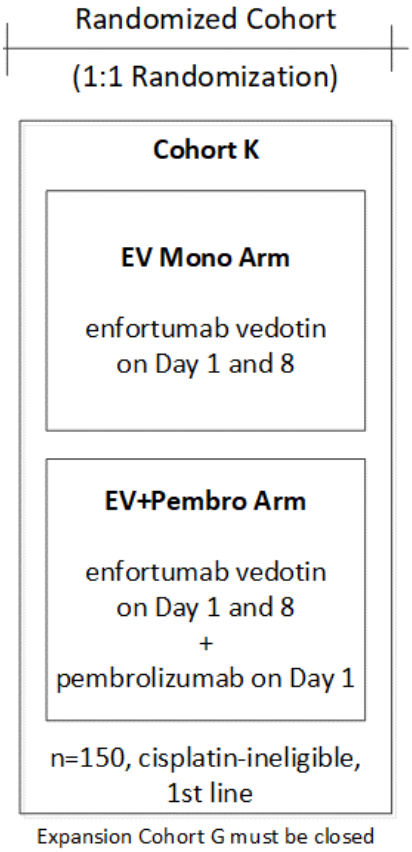
CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**CRITERES DE SELECTION** **ETUDE EV103 (SGN22E-002)**	Identité patient (coller étiquette patient)
Version 2.0 du 27/04/2021	Investigateur en charge du patient : …….. PI : **Pr LADOIRE** *(sladoire@cgfl.fr)*	Arc : Serife Poste : 3740

Étude sur l'enfortumab védotine (ASG-22CE) en monothérapie ou en association à d'autres traitements anticancéreux pour le traitement du cancer urothélial



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VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion

1. *Locally Advanced or Metastatic Urothelial Cancer* Patients must have histologically documented locally advanced or metastatic urothelial (previously known as transitional cell) cancer (ie, cancer of the bladder, renal pelvis, ureter, or urethra). Patients with squamous differentiation or mixed cell types are eligible. Patients with locally advanced disease that is resectable with curative intent are ineligible.	☐ oui ☐ non
2. Patients in dose-escalation cohorts, cohort A, optinal Cohort B, Cohort G, and Cohort K must be eligible for CPI therapy	☐ oui ☐ non
3. Randomized Cohort K (EV Mono arm and EV+Pembro arm): Patients must be ineligible for cisplatin-based chemotherapy at the time of enrollment due to at least 1 of the following criteria: i. Glomerular filtration rate (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) ii. ECOG performance status of 2 (refer to inclusion criterion #6 for additional criteria for subjects with ECOG 2) iii. NCI CTCAE Version 4.03 Grade ≥2 hearing loss iv. NYHA Class III heart failure Patients must not have received prior systemic treatment for locally advanced or metastatic disease. Patients may not have previously received adjuvant/neoadjuvant platinum-based therapy within 12 months prior to randomization.	☐ oui ☐ non
4. Minimum age of 18 years	☐ oui ☐ non
5. Patients must have measurable disease according to RECIST Version 1.1 (Eisenhauer 2009) (Appendix B). Lesions in a prior irradiated field must have progressed to be considered measurable.	☐ oui ☐ non
6. An ECOG performance status of 0, 1, or 2 (Appendix D). 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	☐ oui ☐ non

7. Anticipated life expectancy of ≥3 months as assessed by the investigator.

☐ oui
☐ non

8. Have adequate organ function as defined in the following table. Specimens must be collected within 7 days prior to the start of study treatment.

System	Laboratory Value
Hematological	
ANC	≥1500/µL
Platelets	≥100,000/µL
Hemoglobin	≥9.0 g/dL or ≥5.6 mmol/L[a]
Renal	
Measured or calculated[b] CrCl AND/OR creatinine ≤1.5 × ULN. Both creatinine level and creatinine clearance will be applicable when local guidelines require both assessments. (GFR can also be used in place of CrCl)	≥30 mL/min for participants with creatinine levels (required for Cohort K; see Inclusion Criterion 3) >1.5× institutional ULN, AND/OR ≤1.5× upper limit of normal (ULN)
Hepatic	
Serum Total bilirubin	≤1.5× ULN OR direct bilirubin ≤ ULN for participants with total bilirubin levels >1.5× ULN ≤3× ULN for patients with Gilbert's disease
AST (SGOT) and ALT (SGPT)	≤3× ULN
Coagulation	
International normalized ratio (INR) OR prothrombin time (PT) Activated partial thromboplastin time (aPTT) OR Partial thromboplastin time (PTT)	≤1.5× ULN unless participant is receiving anticoagulant therapy as long as PT or aPTT is within therapeutic range of intended use of anticoagulants

Note: This table includes eligibility-defining laboratory value requirements for treatment; laboratory value requirements should be adapted according to local regulations and guidelines for the administration of specific chemotherapies.
ALT (SGPT)=alanine aminotransferase (serum glutamic pyruvic transaminase); ANC=absolute neutrophil count; AST (SGOT)=aspartate aminotransferase (serum glutamic oxaloacetic transaminase); CrCl=creatinine clearance; GFR=glomerular filtration rate

a Criteria must be met without erythropoietin dependency and without packed red blood cell (pRBC) transfusion within last 2 weeks.

b Creatinine Clearance should be calculated using the Cockcroft-Gault method, Modification of Diet in Renal Disease equations (MDRD), or by 24-hour urine collection.

☐ oui
☐ non

9. A female subject of childbearing potential is anyone born female who has experienced menarche and who has not undergone surgical sterilization (eg, hysterectomy, bilateral salpingectomy, bilateral oophorectomy) or has not completed menopause. Menopause is defined clinically as 12 months of amenorrhea in a person over age 45 in the absence of other biological, physiological, or pharmacological causes. 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 3 days prior to Day 1. Female subjects with false positive results and documented verification of negative pregnancy status are eligible for participation.

☐ oui
☐ non

• If heterosexually active, must consistently use highly effective methods of birth control, with a failure rate of less than 1% (as described in Appendix M) 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. A male subject who can father children is anyone born male who has testes and who has not undergone surgical sterilization (eg, vasectomy followed by a clinical test proving that the procedure was effective). 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. Male subjects will be informed about the negative risk to reproductive function and fertility from the study treatment. Prior to treatment male subjects should be advised to seek information on fertility preservation and sperm cryoconservation. □ Must consistently use highly effective methods of birth control, with a failure rate of less than 1% (as described in Appendix M) starting at screening and continue throughout study period and for at least 6 months after the final dose of study drug. □ Male subjects with a pregnant or breastfeeding partner(s) must consistently use one of 2 contraception options for preventing secondary exposure to seminal fluid (as described in Appendix M) 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.	☐ oui ☐ non
11. The patient must provide written informed consent.	☐ oui ☐ non

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Critères de non inclusion

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1. Received any prior treatment with a CPI. A CPI is defined as a PD-1 inhibitor, PD-L1 inhibitor, or PD-L2 inhibitor (including, but not limited to, atezolizumab, pembrolizumab, nivolumab, durvalumab, or avelumab).	□ oui □ non
2. Received any prior treatment with an agent directed to another stimulatory or co-inhibitory T-cell receptor (including but not limited to CD137 agonists, CTLA-4 inhibitors, or OX-40 agonists).	□ oui □ non
3. Ongoing sensory or motor neuropathy Grade 2 or higher.	□ oui □ non
4. Active central nervous system [CNS] metastases. Patients with treated CNS metastases are permitted on study if all the following are true: a. CNS metastases have been clinically stable for at least 6 weeks prior to screening and baseline scans show no evidence of new or enlarged metastasis. b. If requiring steroid treatment for CNS metastases, the patient is on a stable dose <10 mg/day of prednisone or equivalent for at least 2 weeks. c. Patient does not have leptomeningeal disease.	□ oui □ non
5. Ongoing clinically significant toxicity (Grade 2 or greater) associated with prior treatment (including radiotherapy or surgery).	□ oui □ non
6. Patients 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.	□ oui □ non
7. Prior treatment with enfortumab vedotin or other MMAE-based ADCs for urothelial cancer.	□ oui □ non
8. History of another malignancy within 3 years before the first dose of study drug, or any evidence of residual disease from a previously diagnosed malignancy. Patients with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ (eg, breast carcinoma, cervical cancer) who have undergone potentially curative therapy are not excluded. Patients with low-risk prostate cancer (T1-T2a, Gleason score ≤6, and prostate specific antigen [PSA] <10 ng/mL) either treated with definite intent any time prior to screening or untreated in active surveillance are not excluded.	□ oui □ non
9. Currently receiving systemic antimicrobial treatment for active infection (viral, bacterial, or fungal) at the time of first dose of enfortumab vedotin. Routine antimicrobial prophylaxis is permitted.	□ oui □ non

10. Patients with a positive hepatitis B surface antigen and/or antihepatitis B core antibody; patients with a negative polymerase chain reaction (PCR) assay are permitted with either universal prophylaxis or the use of a pre-emptive approach. The approach will be selected in accordance with regional or national guidelines for patients who receive anticancer therapies.	□ oui □ non
11. Active hepatitis C infection or known human immunodeficiency virus (HIV) infection. Patients who have been curatively treated for hepatitis C infection are permitted if they have documented sustained virologic response of 12 weeks. No HIV testing is required unless mandated by local health authority.	□ oui □ non
12. Patients with active tuberculosis.	□ oui □ non
13. Documented history of a cerebral vascular event (stroke or transient ischemic attack), unstable angina, myocardial infarction, or cardiac symptoms (including congestive heart failure) consistent with NYHA Class III–IV (see Appendix E) within 6 months prior to the first dose of enfortumab vedotin. Patients with NYHA Class III are permitted in Cohort K.	□ oui □ non
14. Radiotherapy or major surgery within 2 weeks prior to first dose of study drug. Patient must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study treatment.	□ oui □ non
15. Treatment with chemotherapy, biologics, or investigational agents not otherwise prohibited by exclusion criterion No. 2 that is not completed 4 weeks prior to first dose of study drug.	□ oui □ non
16. Known severe (≥ Grade 3) hypersensitivity to enfortumab vedotin or to any excipient contained in the drug formulation of enfortumab vedotin (including histidine, trehalose dihydrate, and polysorbate 20). Known severe (≥ Grade 3) hypersensitivity to pembrolizumab or to any excipient contained in the drug formulations of pembrolizumab.	□ oui □ non
17. Patients with active keratitis or corneal ulcerations. Patients with superficial punctate keratitis are allowed if the disorder is being adequately treated in the opinion of the investigator.	□ oui □ non
18. For Cohort K only: Has an active autoimmune disease that has required systemic treatment in past 2 years (ie, use of disease modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.	□ oui □ non

19. History of idiopathic pulmonary fibrosis; organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan.	□ oui □ non
20. Prior allogeneic stem cell or solid organ transplant.	□ oui □ non
21. Administration of a live, attenuated vaccine within 30 days prior to first dose of study drug. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, BCG, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed.	□ oui □ non
22. Other underlying medical condition that, in the opinion of the investigator, would impair the ability of the patient 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.	□ oui □ non
23. Patients with uncontrolled diabetes. Uncontrolled diabetes is defined as hemoglobin A1c (HbA1c) ≥8% or HbA1c 7% to <8% with associated diabetes symptoms (polyuria or polydipsia) that are not otherwise explained.	□ oui □ non

Date : _____

Signature de l'investigateur : _____