Essai Clinique

Généré le 04 mai 2024 à partir de

Titre	Étude de phase III, ouverte, multicentrique et à répartition aléatoire comparant le NUC-1031 en association avec le cisplatine à la gemcitabine en association avec le cisplatine chez des patients atteints d'un cancer des voies biliaires localement avancé ou métastatique n'ayant jamais été traités
Protocole ID	NuTide 121
ClinicalTrials.gov ID	NCT04163900
Type(s) de cancer	Voies biliaires
Phase	Phase III
Stade	Maladie avancée ou métastatique
Type étude	Traitement
Médicament	NUC-1031 + Cisplatine versus Gemcitabine + Cisplatine
Institution	CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL
Ville	
Investigateur principal	Dr Richard Létourneau
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Statut	Fermé
But étude	NuTide:121 compares NUC-1031 with gemcitabine, both in combination with cisplatin, in patients with previously untreated advanced biliary tract cancer. The primary hypotheses are: • The combination of NUC-1031 plus cisplatin prolongs overall survival compared to the gemcitabine plus cisplatin standard of care • The combination of NUC-1031 plus cisplatin increases overall response rate compared to the gemcitabine plus cisplatin standard of care
Critères d'éligibilité	1. Written informed consent and authorization to use and disclose health information. 2. Ability to comprehend and willingness to comply with the requirements of this protocol, including the QoL questionnaires. 3. Female or male patients aged ≥18 years. 4. Histologically- or cytologically-confirmed adenocarcinoma of the biliary tract (including gallbladder, intra and extra-hepatic biliary ducts and ampullary cancers) that is locally advanced, unresectable or metastatic (AJCC edition 8, 2018). Patients with measurable (as per RECIST v1.1 criteria) or non-measurable disease are permitted. 5. Life expectancy ≥16 weeks. 6. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. 7. Adequate biliary drainage with no evidence of ongoing infection. If applicable, treatable and clinically-relevant biliary duct obstruction has been relieved by internal endoscopic drainage/stenting at least 2 weeks previously or by palliative bypass surgery or percutaneous drainage prior to study treatment, and the patient has no active or suspected uncontrolled infection. Patients fitted with a biliary stent should be clinically stable and free of signs of infection for ≥2 weeks prior to study treatment. Patients with improving biliary function who meet all other inclusion criteria may be re-tested during the screening window. 8. Adequate bone marrow, hepatic, and renal function, as evidenced by: • Absolute neutrophil count (ANC) ≥1,500/µL without colony-stimulating factor support • Platelet count ≥100,000/µL • Haemoglobin ≥9 g/dL without need for haematopoietic growth factor or transfusion support in prior 2 weeks • Total bilirubin <2 × upper limit of normal (ULN); does not apply to patients with Gilbert's

	syndrome. Consistent with inclusion criterion 7, patients whose whole bilirubin and biliary function is recovering may be re-tested during the screening period. • Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) <5 × ULN • Creatinine clearance ≥45 mL/min actual or calculated by the Cockcroft-Gault method • International normalized ratio (INR) <1.5 and activated partial thromboplastin time (aPTT) <1.5 × ULN; does not apply to patients on an anti-coagulant with stable dose 28 days prior to first dose. 9. QTc interval <450 msec (males) or <470 msec (females), in the absence of bundle branch block. In the presence of bundle branch block with consequent QTc prolongation, patients may be enrolled based on a careful risk-benefit assessment. 10. Human Immunodeficiency Virus-infected patients who are healthy and have a low risk of Acquired Immunodeficiency Syndrome-related outcomes may be included in this study. 11. Female patients of child-bearing potential (i.e., all women except those who are post-menopausal for ≥1 year or who have a history of hysterectomy or surgical sterilization) must have a negative pregnancy test within 3 days prior to the first study drug administration. All patients of child-bearing potential must agree to practice true abstinence or to use two highly effective forms of contraception, one of which must be a barrier method of contraception, from the time of screening until 6 months after the last dose of study medication. 12. Male patients with a female partner must either have had a successful vasectomy or they and their female partner meet the criteria above (not of childbearing potential or practicing highly effective contraceptive methods).
Critères d'exclusion	1. Combined or mixed hepatocellular/cholangiocarcinoma. 2. Prior systemic therapy for advanced or metastatic biliary tract cancer. However, prior chemotherapy in the adjuvant setting or low-dose chemotherapy given in conjunction with radiotherapy in the adjuvant setting and completed at least 6 months prior to enrolment is permitted. The following prior interventions are allowed provided the patient has fully recovered: • Surgery: non-curative resection with macroscopic residual disease or palliative bypass surgery. Patients who have previously undergone curative surgery must now have evidence of non-resectable disease requiring systemic chemotherapy. • Radiotherapy: prior radiotherapy (with or without radio-sensitizing low-dose chemotherapy) for localized disease and there is now clear evidence of disease progression requiring systemic chemotherapy. • Photodynamic therapy: prior photodynamic therapy for localized disease with no evidence of metastatic disease or for localized disease to relieve biliary obstruction in the presence of metastatic disease provided there is now clear evidence of disease progression requiring systemic chemotherapy. • Palliative radiotherapy: palliative radiotherapy provided that all adverse events have resolved and the patient has measurable disease outside the field of radiation. 3. Prior treatment with or known hypersensitivity to NUC-1031, gemcitabine, cisplatin or other platinum-based agents or history of allergic reactions attributed to any parenteral excipients (e.g. dimethylacetamide [DMA], Cremophor EL, Polysorbate 80, Solutol HS 15). 4. Symptomatic central nervous system or leptomeningeal metastases. 5. History of other malignancies, except adequately treated non-melanoma skin cancer, curatively treated in situ cancer of the cervix, surgically excised or potentially curatively treated ductal carcinoma in situ of the breast, or low grade prostate cancer or patients after prostatectomy not requiring treatment. Patients with previous invasive cancers are eligible if treatment was completed more than 3 years prior to initiating the current study treatment, and the patient has had no evidence of recurrence since then. 6. Concurrent serious (as deemed by the Investigator) medical conditions, including, but not limited to, New York Heart Association class III or IV congestive heart failure, history of congenital prolonged QT syndrome, uncontrolled infection, active hepatitis B or C, or other co-morbid conditions that in the opinion of the Investigator would impair study participation or cooperation. 7. Congenital or acquired immunodeficiency (e.g., serious active infection with HIV). As per inclusion criterion 10, patients with HIV who are healthy and have a low risk of AIDS related outcomes are eligible. 8. Other acute or chronic medical, neurological, or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the Investigator, would make the patient inappropriate for entry into this study. 9. Prior exposure to another investigational agent within 28 days prior to randomization. 10. Major surgery within 28 days prior to randomization; patient must have completely recovered from any prior surgical or other procedures. 11. Pregnant or breastfeeding. 12. Residual toxicities from prior treatments or procedures which have not regressed to Grade ≤1 severity (CTCAE v5.0), except for alopecia or ≤ Grade 2 peripheral neuropathy. 13. Concomitant use of drugs at doses known to cause clinically relevant prolongation of QT/QTc interval. 14. Administration of a live vaccination within 28 days prior to randomization. 15. Ongoing or recent (≤6 months) hepatorenal syndrome.