Essai Clinique

Généré le 29 avr. 2024 à partir de

Titre	A Single Arm, Multicenter, Phase 2 Trial to Evaluate the Efficacy of Lenvatinib (LEN) in Combination With Pembrolizumab (KEYtruda) in Subjects With Locally Advanced or Metastatic Non-clear Cell Renal Cell Carcinoma
Protocole ID	The LENKYN Trial
ClinicalTrials.gov ID	NCT04267120
Type(s) de cancer	Rein
Phase	Phase II
Stade	Maladie avancée ou métastatique
Type étude	Clinique
Médicament	Lenvatinib en association avec le pembrolizumab
Institution	CHU DE QUEBEC – UNIVERSITE LAVAL L'HOTEL-DIEU DE QUEBEC ET CRCEO 11 Côte du Palais, Québec, QC, G1R 2J6
Ville	
Investigateur principal	Dr Louis Lacombe
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Statut	Actif en recrutement
But étude	This is a single-arm, multicenter, phase 2 study of lenvatinib in combination with pembrolizumab (lenvatinib 20 mg/day + pembrolizumab 200mg q3weeks) in subjects with unresectable advanced or metastatic non-clear cell renal carcinoma who have not received any chemotherapy for advanced disease.

Critères d'éligibilité	• Locally advanced or metastatic histologically confirmed nccRCC (2, 7). Must have one of the following subtypes of nccRCC:
	  • papillary RCC
	  • chromophobe RCC
	  • TFE-3/B translocation RCC
	  • SDHB-loss RCC
	  • TSC1-loss RCC
	  • sarcomatoid RCC without clear cell component
	  • unclassified RCC
	• Has not received any prior lines of systemic therapy except adjuvant or neoadjuvant treatments.
	• Radiologically measurable disease meeting the following criteria:
	  • At least 1 lesion of ≥ 10 mm in the longest diameter for a non-lymph node or ≥ 15 mm in the short axis diameter for a lymph node which is serially measurable according to iRECIST (Section 12) using computerized tomography (CT) or magnetic resonance imaging (MRI).
	  • Lesions that have had external beam radiotherapy (EBRT) or locoregional therapies such as radiofrequency (RF) ablation must show evidence of subsequent progressive disease (substantial size increase of ≥20%) to be deemed a target lesion. Patients who received EBRT must be at least 2 weeks out from last RT treatment.
	• At least 18 years of age.
	• Karnofsky performance status ≥ 70%
	• Blood pressure (BP) ≤ 150/90 mmHg at screening with or without antihypertensive medications and no change in antihypertensive medications within 1 week prior to Cycle 1 Day 1.
	• Adequate renal function defined as creatinine <1.5 x ULN or calculated creatinine clearance

	≥40 mL/min per the Cockcroft and Gault formula with creatinine levels >1.5 x ULN.
	• Adequate bone marrow function:
	  • Absolute neutrophil count (ANC) ≥1500/mm3 (≥1.5 x 103/L)
	  • Platelets ≥100,000/mm3 (≥100 x 109/L)
	  • Hemoglobin ≥9.0 g/dL
	• Adequate blood coagulation function as evidenced by an International Normalized Ratio (INR) ≤1.5
	• Adequate liver function as evidenced by:
	  • bilirubin ≤1.5 times the upper limit of normal (ULN)
	  • alkaline phosphatase (ALP) ≤3×ULN (in the case of liver metastases ≤5×ULN)
	  • alanine aminotransferase (ALT) ≤3×ULN (in the case of liver metastases ≤5×ULN)
	  • aspartate aminotransferase (AST) ≤3×ULN (in the case of liver metastases ≤5×ULN).
	
	In case ALP is >3×ULN (in the absence of liver metastases) or >5×ULN (in the presence of liver metastases) AND the subject also is known to have bone metastases, the liver specific ALP isoenzyme must be separated from the total and used to assess the liver function instead of the total ALP.
	
	• Subjects with known brain metastases will be eligible if they have completed the primary brain therapy (such as whole brain radiotherapy, stereotactic radiosurgery, or complete surgical resection) and if they have remained clinically stable, asymptomatic, and off steroids for at least 2 months before starting study treatment.
	• All females of childbearing potential must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of beta-human chorionic gonadotropin [β-hCG]) at the screening visit. Females of childbearing potential* must agree to use a highly effective method of contraception for the entire study period and for 120 days after study discontinuation
	• Male subjects who are partners of women of childbearing potential must follow one of the methods of contraception described in Section 6.5 beginning at least 1 menstrual cycle prior to starting study drugs, throughout the entire study period, and for 120 days after the last dose of study drug, unless the male subjects are totally sexually abstinent or have undergone a successful vasectomy with confirmed azoospermia or unless the female partners have been sterilized surgically or are otherwise proven sterile.
	• Archival tumor tissue from within 3 months (preferred) or up to 6 months (acceptable) must be available prior to the first dose of study drug for biomarker analysis. If no biopsy has been performed in the prior 6 months, a standard of care biopsy is requested if safe and feasible. In the case tissue cannot be provided, patients can be enrolled upon consultation and agreement by the trial PI.
	Note: In case of submitting unstained cut slides, freshly cut slides should be submitted to the testing laboratory within 14 days from when the slides are cut.-Ability to understand and willingness to sign an IRB approved written informed consent document (or that of legally authorized representative, if applicable).

Critères d'exclusion	• Predominant clear cell renal cell carcinoma (RCC) • Uncontrolled or untreated brain metastasis • Major surgery performed within 4 weeks prior to the first dose of study drugs or scheduled for major surgery during the study. Subjects must have recovered adequately from any toxicity and/or complications from major surgery prior to starting therapy. • Subjects having >1+ proteinuria on urinalysis will undergo 24-h urine collection for quantitative assessment of proteinuria. Subjects with urine protein ≥1 g/24-hour will be ineligible. • Gastrointestinal malabsorption, gastrointestinal anastomosis, or any other condition that might affect the absorption of lenvatinib. • New York Heart Association congestive heart failure of grade II or above, unstable angina, myocardial infarction within the past 6 months, or serious cardiac arrhythmia associated with significant cardiovascular impairment within the past 6 months. • Prolongation of QTc interval to >480 msec. • Active hemoptysis (bright red blood of at least 0.5 teaspoon) within 3 weeks prior to the first dose of study drug. • Active infection (any infection requiring systemic treatment). • Subject is known to be positive for Human Immunodeficiency Virus (HIV), Hepatitis B, or Hepatitis C • Serious nonhealing wound, ulcer, or bone fracture. • Known intolerance to either of the study drugs (or any of the excipients). • History of organ allograft (subject has had an allogenic tissue/solid organ transplant). • Biologic response modifiers (e.g., granulocyte colony-stimulating factor) within 4 weeks before study entry. Chronic erythropoietin therapy is permitted provided that no dose adjustments were made within 2 months before first dose of study treatment. • Any medical or other condition which, in the opinion of the investigator, would preclude participation in a clinical trial. • Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the pre-screening or screening visit through 120 days after the last dose of trial treatment. If the required urine pregnancy test is positive (or cannot be confirmed as negative) within 72 hours prior to start of treatment, a serum pregnancy test will be required. • Excluding the primary tumor leading to enrollment in this study, any other active malignancy (except for definitively treated melanoma in-situ, basal or squamous cell carcinoma of the skin, or carcinoma in-situ of the bladder or cervix) within the past 36 months. • Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form

of immunosuppressive therapy within 7 days prior to the first dose of study treatment. The use of up to 10 mg/day of prednisone or equivalent is approved and does not exclude the patient from the trial.

- Active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease modifying agents, > 10 mg of prednisone per day, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment. The use of up to 10 mg/day of prednisone or equivalent is approved and does not exclude the patient from the trial.
- Has a history of (non-infectious) pneumonitis/interstitial lung disease that required maintenance steroids (>10 mg of prednisone) or current pneumonitis/interstitial lung disease.
- Has received a live-virus vaccination or live-attenuated vaccine within 30 days of planned treatment start. Administration of killed vaccines is allowed.