CANCÉROLOGIE

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Portail d'information
des acteurs de santé ville-hôpital

PAXIPEM

Etude de phase II, multicentrique évaluant l'axitinib +/- le pembrolizumab en première ligne de traitement chez des patients ayant un carcinome rénal papillaire localement avancé ou métastatique

Phase : II

Type d'essai : Académique / Institutionnel

Etat de l'essai : Ouvert

Objectif principal

Efficacité d'axitinib + pembrolizumab versus axitinib chez les patients atteints d'un carcinome rénal papillaire de type 2 localement avancé ou métastatique en traitement de première ligne.

Résumé / Schéma de l'étude

Bras A - Experimental : axitinib + pembrolizumab.
Bras B - Contrôle : axitinib alone.

Critères d'inclusion

1. Age ≥ 18 years on the day of signing informed consent.
2. Metastatic or locally advanced (inoperable) type 2 or mixed PRCC, histologically confirmed by central review: FFPE blocks (or all HES and IHC slides) with the initial histology report must be sent for central reading before confirmation of inclusion in the study.
3. No prior systemic treatment for renal cancer (chemotherapy, immunotherapy, anti-angiogenic drugs, or treatment under evaluation) even in adjuvant setting.
4. At least one measurable site of disease according to RECIST v1.1.
5. Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) ≤ 1 evaluated within 7 days prior to the date of inclusion.
6. In case of prior radiation therapy, discontinuation of irradiation for at least 3 weeks before first dose of study treatment, with at least 1 site kept/preserved for evaluation. Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (≤ 2 weeks - limited field (<10% of the whole body)) to non-CNS disease.

7. Adequate bone-marrow, hepatic, and renal functions within 14 days prior to the inclusion, with :
   1. Hemoglobin ≥ 9.0 g/dl ou ≥ 5.6 mmol/l. Neutrophils ≥ 1 000/mm^3 (1.0 G/l). Platelets ≥ 100 000/mm^3 (100 G/l).
   2. Serum creatinine ≤ 2 x LSN OR creatinine clearance ≥ 50 ml/min/1.73m^2 (calculated using either MDRD or CKD-EPI formula).
   3. AST and ALT ≤ 2.5 x LSN (or ≤ 5 x ULN in case of liver metastasis).
   4. Total serum bilirubin ≤ 1.5 x LSN(or direct bilirubin ≤ LSN for participants with total bilirubin levels >1.5 × LSN).
8. Absence of significant proteinuria (<0.5 g/24h) confirmed by urinary dipstick test. If the dipstick test is ≥ 2+, proteinuria will be quantitated on a complete 24h urine sample (< 1 g/l of protein/24h sample).
9. Covered by a medical/health insurance.
10. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures.
11. Patients of childbearing potential accepting to use effective contraception or abstain from heterosexual activity during study treatment and within 4 months after final dose of study therapy or being surgically sterile. Refer to Appendix 1 for approved methods of contraception.
12. Signed and dated approved informed consent form before any study specific procedures or assessments.

Critères de non-inclusion

1. Presence of brain metastases on Magnetic Resonance Imaging (MRI) or Computed Tomography-scan (CT-scan) performed within 28 days prior to inclusion. Patients with a history of brain metastases treated by surgery or stereotactic surgery, with normal brain MRI or CT-scan are allowed to participate.
2. Metastases with high risk of nervous compression or bone lesion with high risk of fracture.
3. Prior history of other malignancies other than PRCC (except for curatively treated basal cell or squamous cell carcinoma of the skin or in situ uterine cervix carcinoma) unless the subjects has been free of the disease for at least 5 years.
4. Major surgical procedure, open biopsy, or serious none healing wound within 28 days prior to inclusion.
5. Significant cardiovascular disease, including :
   1. Disorder of left ventricular function with a left ventricular ejection fraction (LVEF) < 50%.
   2. Uncontrolled arterial hypertension under adapted medication: systolic blood pressure ≥ 150 mmHg or diastolic blood pressure ≥ 90 mmHg or both despite appropriate therapy, blood pressure must be monitored and controlled before inclusion, or patients under 3 antihypertensive therapies at screening.
   3. Myocardial infarction, severe angina, or unstable angina within 6 months prior to inclusion.
   4. History of serious ventricular arrhythmia (ie ventricular tachycardia or ventricular fibrillation).
   5. Cardiac arrhythmias requiring anti-arrhythmic medications (except for atrial fibrillation that is well controlled with anti-arrhythmic medication).
   6. Coronary or peripheral artery bypass graft or active coronary stent within 6 months prior to inclusion.
   7. Veinous thrombosis or pulmonary embolism within 6 months prior to inclusion.
6. Any anti-coagulation therapy except prophylactic low dose.
7. History of auto-immune disease except thyroiditis more than 6 months ago.
8. History of any allograft.
9. HIV, HBV, HCV active infections.
10. Any active acute or chronic or uncontrolled infection/disorder that would impair the ability to evaluate the patient or the ability for the patient to complete the study.
11. Known history of active TB (Bacillus Tuberculosis).
12. Interstitial lung disease, respiratory insuffisancy whatever the cause.
13. Prior (non-infectious) pneumonitis requiring systemic corticosteroid therapy or current pneumonitis.
14. Inability to swallow oral medications, or presence of active inflammatory bowel disease, partial or complete bowel obstruction or chronic diarrhea.
15. History of severe hypersensitivity to another monoclonal antibody.
16. Known hypersensitivity to the active substances or to any of the excipients.

17 Receiving or having received immunosuppressive therapy or corticosteroids within 1 month prior to inclusion (except for hydrocortisone for substitution purposes).

18 Live vaccine within 30 days prior to the 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, Bacillus Calmette-Guérin (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. COVID-19 vaccine is allowed if non-living/inactivated.

19 Psychological, familial, sociological, or geographical conditions that would limit compliance with study protocol requirements or known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the study.

20 Inclusion in another clinical trial, except for supportive care trials.

21 Pregnant or breastfeeding woman or patient expecting to conceive or father children within the projected duration of the study, starting with the screening visit through 4 months after the last dose of study treatment (mandatory negative serum or urinary pregnancy test at study entry for all women of childbearing potential).

22 Under or requiring tutorship or curatorship.

Calendrier prévisionnel

Lancement de l'étude : Janvier 2022
Fin estimée des inclusions : Juillet 2024
Nombre de patients à inclure : 72

Etablissement(s) participant(s)

> Centre Antoine Lacassagne (CAL)

(06) ALPES-MARITIMES

Dr. Delphine BORCHIELLINI
Investigateur principal

> Institut Paoli-Calmettes (IPC)

(13) BOUCHES-DU-RHÔNE

Dr. Gwenaelle GRAVIS-MESCAM
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