EIFFEL - (dernière mise à jour : 05/08/2019)

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Informations générales

Titre de l'étude : Etude de phase I/II de recherche de dose, d'évaluation de la tolérance et de l'efficacité d'un traitement par radium-223 dichlorure (XOFIGO®) chez des patients avec un carcinome rénal (RCC) avec métastases osseuses

Traitement : Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : I/II **Stade** : Métastatique **Ligne(s)** : 1, 2, 3

Schéma : This is a prospective, multicentre, open-label, phase I/II study to evaluate the maximum tolerated dose (MTD), and the most successful dose (MSD) of XOFIGO®, in renal cancer patients with metastases to bone, without (Group A) or with (Group B) visceral metastases.

Dose-finding will be performed according to the Continual Reassessment Method (CRM) using either toxicity (escalation cohort) or joined toxicity-efficacy (expansion cohort) endpoints.

Two groups of patients will be evaluated:

Group A: patients with bone disease mainly will be treated with XOFIGO® alone. (node and/or adrenal metastases and/or ?5 lung metastases ?1cm each are allowed in Group A).
Group B: patients already treated with an ongoing approved Tyrosine Kinase Inhibitor (TKI) for their visceral metastases will be treated with XOFIGO® for bone disease.
XOFIGO® will be administered intravenously as a bolus injection every 4 weeks with a maximum of 6 administrations per patient. Four dose levels are available for evaluation : 27.5 kBq/kg, 55 kBq/kg, 88 kBq/kg and 110 kBq/kg.

Starting dose for phase I will be 55 kBq/kg.

Visit schedule:

Selection Patients will come to the hospital at baseline, and screening assessments must be performed within 28 days prior to first XOFIGO® administration.

XOFIGO® period Patients will receive an injection of XOFIGO® on Day 1 of each 4 weeks-cycle for a maximum of 6 cycles. Patients will be subject to physical examination, blood sampling and pain evaluation prior to each injection. Scintigraphy of biodistribution of radium-223 dichloride will be realised on C1D1 after the 1st injection of XOFIGO® On C1D15, patients will also come for physical examination and blood sampling. On C2D15 (end of DLT period for phase I), patients will also come for end of DLT period evaluation and will be subject to physical examination and blood sampling.

Prior to C3D1 and C5D1, patients will undergo WB-IRM and FNa-PET. End of treatment visit (EOT) will take place 4 weeks after the last administration of XOFIGO®.

In the absence of confirmed bone progression at XOFIGO® discontinuation time, patients will continue to undergo WB-IRM and FNa-PET every 2 months until confirmed bone progression or end of follow-up.

Confirmation of bone progression upon WB-IRM will be performed 4 weeks after the initial progression is observed.

Follow-up Patients will be followed-up for a maximum of 12 months from the 1st administration of XOFIGO®.

Number of subjects:

Maximum number of patients to be enrolled in the escalation cohort is 21. Maximum number of patients to be enrolled in the expansion cohort is 21. Group A: 2-4 patients; Group B: 38-40 patients.

Spécialités / Localisations

Spécialité n°1 : Voies urinaires

CIM10 - Localisation n°1 : **C64** - Tumeur maligne du rein, à l'exception du bassinet

Critères

Critères d'inclusion : - Histologically confirmed metastatic renal cell carcinoma with a clear cell component.
- Bone metastases upon bone scan with no CT and MRI performed any time within period of 4 weeks prior to study entry, with at least one evaluable unidimensional bone lesion (i.e., >=1 malignant tumour mass that can be accurately measured in at least 1 dimension >= 10 mm on T1-weighted Magnetic Resonance Imaging [MRI]).
Group A: bone metastases (lymph nodes and/or adrenal metastases, and/or <= 5 lung metastases of less than 1 cm each, are allowed).
Group B: bone metastases AND visceral metastases upon MRI (according to revised RECIST 1.1 criteria).
- Patient in a) first (naïve), or b) second or third line setting receiving or about to receive an approved Tyrosine Kinase Inhibitor (patients on mTOR inhibitors are not eligible).
- Male or female, age >=18 years at ICF signature time.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.
- Good or Intermediate prognostic group according to the International Metastatic Database Consortium (IMDC).
- At least 4 weeks from the end of a previous systemic treatment, if any, with resolution of all treatment-related toxicity according to NCI CTCAE Version 4.03 grade <= 1 except for alopecia.
- Palliative local treatment allowed if performed >= 2 weeks prior to study entry for radiotherapy, cementoplasty or minor surgery; >= 4 weeks prior to study entry for major surgery.
- Adequate organ function defined by the following criteria:
1) Absolute Neutrophils count (ANC) >=1 500 cells/mm3
2) Platelets >=100 000 cells/mm3
3) Haemoglobin >= 9.0 g/dL
4) AST and ALT <= 2.5 x upper limit of normal (ULN), unless there are liver metastases in which case AST and ALT <=5.0 x ULN
5) Total bilirubin <= 1.5 x ULN
6) Estimated glomerular filtration rate upon MDRD >= 50 mL/min
7) Urinary protein < 2+ by urine dipstick. If dipstick is >= 2+ then a 24-hour urine collection can be done and the patient may enter only if urinary protein is < 2 g per 24 hours
8) Corrected calcium <= 2.8 mmol/L.
- Women of childbearing potential must have a negative serum pregnancy test within 7days prior to treatment initiation.
- Signed and dated informed consent document indicating that the patient (or legally acceptable representative) has been informed of all pertinent aspects of the trial prior to enrolment.
- Willingness, for men and women,to use effective contraception during study treatment and for 6 months after last dose of study drug.
- Willingness to comply with protocol requirements.

Critères de non-inclusion : - Poor prognostic group according to the IMDC. 2. Prior radiotherapy to >= 40% of bone marrow, whole pelvic irradiation and/or prior isotope therapy whatever the isotope (any ?- or ?-emitters).
- Active secondary cancer including prior malignancy from which the subject has been disease-free for <= 3 years (however, adequately treated superficial basal cell skin or cervical carcinoma in situ before 4 weeks prior to entry are eligible to the study).
- Known brain or leptomeningeal involvement.
- Any other concurrent serious illness or medical conditions including:
1) Crohn?s disease or ulcerative colitis
2) Bone marrow dysplasia
3) Known presence of osteonecrosis of the jaw
4) Uncontrolled hypertension.
5) Uncontrolled cardiac arrhythmias, angina pectoris, and/or hypertension. History of congestive heart failure, or myocardial infarction within the last 6 months.

- QTc interval (QTc) assessed by local device > 500ms in the 7 days prior to inclusion.
- Ongoing biphosphonates, denosumab and/or vitamin D supplementation.
- Active infection requiring systemic antibiotic or anti-fungal medication.
- Any contra-indication to MRI, including:
1) Carrying a metallic medical device (e.g. pacemaker) or foreign body prohibiting use of MRI
2) Known allergy to gadolinium or iodine
3) Dysthyroidism precluding usage of iodine contrast agent
- Pregnant or breast feeding.
- Participation in another clinical trial with any investigational drug within 30 days prior to study enrolment.

Informations promoteur

Nom du promoteur : Association Pour La Recherche des Thérapeutiques Innovantes en Cancérologie

Type de promoteur : Institutionnel

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Ouverture de l'essai : OUVERT

Liens utiles

Clinicaltrials : https://clinicaltrials.gov/ct2/show/NCT02880943?term=EIFFEL&rank=1

INCa : http://www.e-cancer.fr/Professionnels-de-sante/Le-registre-des-essais-cliniques/Le-registre-des-essais-cliniques/Etudes-cliniques/Etude-EIFFEL-Etude-de-phase-1-2-en-escalade-de-dose-evaluant-l-efficacite-et-la-tolerance-d-un-traitement-par-le-radium-223-dichlorure-XOFIGO-R-chez-des-patients-ayant-un-carcinome-renal-RCC-avec-metastases-osseuses.-essai-en-attente-d-ouverture