Acsé NIVOLUMAB - Cohorte carcinome non à cellules claires du rein (dernière mise à jour : 06/08/2019)

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Informations générales

Titre de l'étude : Secured access to Nivolumab for adult patients with selected rare cancer types

Traitement : Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : II **Stade** : NA **Ligne(s)** : 1, 2, 3, 4

Schéma : This is a Phase 2, non-randomised, open-label, multicentric study to investigate the efficacy and safety of nivolumab monotherapy (Nivolumab 240 mg IV over 60 minutes every 14 days) in 5 cohorts of patients with specific rare cancers who have unresectable locally advanced or metastatic disease, which is resistant or refractory to standard therapy, or for which standard therapy does not exist, or is not considered appropriate, and for which no other experimental treatment options are available.

The study plans to enrol up to 250 patients in total with between 20 and 50 patients assigned to each cohort according to indication, as follows:

Cohort 1: Non-clear cell RCC
Cohort 2: Rare head and neck cancer
Cohort 3: Rare skin cancer
Cohort 4: MSI-nonCRC
Cohort 5: Penile cancer
The study will use a two-stage Bayesian enrichment design. The first stage treats all patients from the different cohorts with the investigational product and identifies possibly sensitive indications. The second stage will compare outcomes among subsets of patients in the identified cohorts to distinguish between subpopulations of patients who may benefit from the treatment and patients for whom there is no evidence of efficacy.

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 : 1. Patient information sheet and written informed consent form signed.
2. Histologically confirmed diagnosis of a pathology corresponding to one of the following selected cancer types:
a. Non-clear cell renal-cell carcinomas (RCC): papillary renal cell carcinoma (pRCC, type I, type II and non-classified pRCC), chromophobe RCC (ChRCC), renal medullary carcinoma (RMC), collecting duct/Bellini duct carcinoma (CDC), microphthalmia-associated transcription (MiT) family translocation renal cell carcinoma (tRCC), renal cell carcinoma with a prominent sarcomatoid component (sarcRCC).
b. Rare head and neck cancers: principal and accessory salivary gland tumours, facial tissue tumours.
c. Rare skin cancers: adnexal carcinomas, basal cell carcinoma resistant to vismodegib.
d. Non-colorectal cancers with microsatellite instability determined locally by immunohistochemistry or polymerase chain-

reaction.
e. Squamous cell carcinoma of penis.
3. Metastatic disease or unresectable locally advanced malignancy that is resistant or refractory to standard therapy or for which standard therapy does not exist or is not considered appropriate by the Investigator.
4. Aged >= 18 years old.
5. Measurable disease according to RECIST v1.1 guidelines for solid tumours (Eisenhauer,2009).
6. Able to provide a formalin-fixed, and paraffin-embedded biopsy sample of a metastatic site or primitive tumour tissue.
Note: Patients for whom suitable archived biopsy material is not available must be willing to undergo a biopsy of a tumour lesion prior to study entry, unless this is medically contraindicated (e.g. site inaccessible or patient safety concerns).
7. Patients must have a mandatory treatment-free interval of at least 21 days following previous systemic anti-cancer treatments.
8. Patients who have received previous systemic anticancer treatment and/or radiotherapy should have recovered from any treatment related toxicity, to a level of <= grade 1 (according to National Cancer Institute [NCI] common terminology criteria for adverse events, version 4 (CTCAE v4)) with the exception of Grade 2 alopecia.
9. Adequate hematologic function (absolute neutrophil count >= 1.0 x109/L, platelets >= 100 x109/L, haemoglobin >= 9 g/L) measured within 14 days of treatment initiation.
10. Adequate renal function (creatinine clearance >= 50 mL/min using the MDRD or CKI EPI method) measured within 14 days of treatment initiation.
11. Adequate hepatic function (serum bilirubin <= 1.5 xULN unless due to Gilbert's syndrome; aspartate aminotransferase [ASAT] and alanine aminotransferase [ALAT] <= 3 xULN) measured within 14 days of treatment initiation. For patients with documented liver metastasis, ASAT/ALAT <= 5x ULN is acceptable.
12. Strictly normal blood levels of calcium and magnesium, measured within 14 days of treatment initiation.
13. Eastern Cooperative Oncology Group Performance Status of <= 1.
14. Estimated life expectancy >= 90 days.
15. Patients who are sexually active must agree to use a medically accepted method of contraception (e.g. implants, injectables, combined oral contraceptives, some intrauterine devices or vasectomized partner, for participating women; condoms for participating men) or practice complete abstinence, beginning 14 days before the first administration of IP, while on treatment and for at least 5 months after the last administration of IP for female patients, and 7 months after the last administration of IP for male patients.
16. Women of childbearing potential must have a negative urine or serum pregnancy test within 72 hours prior to the first administration of IP. If urine test results are positive or cannot be confirmed as negative, a serum pregnancy test will be required.
17. Women who are breastfeeding should discontinue nursing prior to the first administration of IP and for at least 90 days after the last administration of IP.
18. Patients must be affiliated to a Social Security System or equivalent.

Critères de non-inclusion : 1. Prior treatment with an anti-PD1 or anti-PD-L1 antibody
2. Eligible, and willing, to participate in a clinical trial of an alternative anticancer therapy targeting their disease, which is open to accrual in France.
3. Concurrent steroid medication at a dose greater than prednisone 10 mg/day or equivalent.
4. Has active autoimmune disease that has required systemic treatment in the past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
5. History of (non-infectious) pneumonitis that required steroids, or current pneumonitis.
6. History of severe hypersensitivity reaction to any monoclonal antibody therapy
7. Radiotherapy (except for brain and extremities) within 21 days prior to the first administration of IP.
8. Treatment with other investigational drugs or participation in another clinical trial within 21 days prior to the first administration of IP or concomitantly with the trial.
9. Has known symptomatic central nervous system (CNS) metastases. Patients with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least 7 days prior to trial treatment.
10. Has known carcinomatous meningitisor a history of leptomeningeal disease.
11. Serum creatinine > 1.5 xULN or glomerular filtration rate < 50 ml/min.
12. Lymphocytes count below 1,000/mm3 and CD4+ count below 500/mm3 as assessed by routine blood phenotyping.
13. Other malignancies within the past 5 years other than basal cell skin cancer or carcinoma in situ of the cervix.
14. Active serious infections in particular if requiring systemic antibiotic or antimicrobial therapy.
15. Active or chronic hepatitis B, hepatitis C and/or human immunodeficiency virus infection (HIV 1/2 antibodies) or a known history of active Tuberculosis bacillus.
16. Live vaccine received within 30 days of planned start of study treatment.
Note: Seasonal influenza vaccines for injection are generally inactivated vaccines and are allowed; however intranasal influenza

vaccines (e.g. Flu-Mist®) are live attenuated vaccines, and are not allowed.
17. Active alcohol or drug abuse.
18. Psychological, familial, sociological or geographical factors potentially hampering compliance with the study protocol and follow-up schedule.
19. Any condition which in the Investigator's opinion makes it undesirable for the subject to participate in the trial or which would jeopardize compliance with the protocol.

Informations promoteur

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Ouverture de l'essai : CLOS

Liens utiles

ClinicalTrials :
https://clinicaltrials.gov/ct2/show/NCT03012581?term=Secured+access+to+nivolumab+for+adult+patients+with+selected+rare+

cancer+types&cntry1=EU%3AFR&rank=1