NIPINEC - Cohorte carcinome neuroendocrine gastroentéropancréatique (dernière mise à jour : 29/07/2019)

http://archimaid.fr/index.php?action=show&id=728

Informations générales

Titre de l'étude : Etude GCO étudiant l'efficacité et la tolérance du nivolumab en monothérapie ou de l'association nivolumab – ipilimumab chez les patients pré-traités présentant un carcinome neuroendocrine (CNE) peu différencié de stade avancé pulmonaire ou gastroentéropancréatique.

Traitement : Métastatique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : II **Stade** : Localement avancé à Métastatique **Ligne(s)** : 2, 3

Schéma : Neuroendocrine tumors of the lung include the small cell carcinoma (SCLC), and large cell neuroendocrine carcinoma (LCNEC) and represent 20% of lung cancer. One of the only studies reported to date is reporting on a progression-free survival (PFS) and overall survival (OS) of 5.2 months and 7.7 months, respectively.

Poorly differentiated gastroentero-pancreatic neuroendocrine carcinomas (GEP-NEC) represent a small sub-group of digestive NENs, according to the studies, 7 to 21% of patients. However, their prognosis is more negative, with the 5-year survival at less than 20%.

Many Phase III trials showed superiority in terms of efficacy and tolerance of nivolumab+/-ipilimumab versus standard chemotherapy in second-line treatment in metastatic solid tumors. Neuroendocrine tumors are considered as rare disease without therapeutic guidelines in this setting. The French academic oncology groups (IFCT, FFCD and GERCOR) have the opportunity to recruit a sufficient number of patients, in a reasonable period of time, to provide a proof-of-concept of the safety and efficacy of nivolumab+/-ipilimumab in this population.

2 treatment arms:
- Experimental: Arm A : monotherapy arm
Nivolumab administered IV
- Experimental: Arm B : combination arm
Nivolumab administered IV followed by ipilimumab administered IV

Spécialités / Localisations

Spécialité n°1 : Organes digestifs

CIM10 - Localisation n°1 : **C16** - Tumeur maligne de l'estomac

Spécialité n°2 : Organes digestifs

CIM10 - Localisation n°2 : **C17** - Tumeur maligne de l'intestin grêle

Spécialité n°3 : Organes digestifs

CIM10 - Localisation n°3 : **C18** - Tumeur maligne du côlon

Spécialité n°4 : Organes digestifs

CIM10 - Localisation n°4 : **C20** - Tumeur maligne du rectum

Spécialité n°5 : Organes digestifs

CIM10 - Localisation n°5 : **C25** - Tumeur maligne du pancréas

Critères

Critères d'inclusion : - Age >= 18 years.
- WHO Performance status 0 - 2
- Life expectancy > 12 weeks
- Poorly differentiated neuroendocrine carcinoma (NEC): large and small cells for gastroenteropancreatic NEC (WHO 2010 classification) and only large cells for lung NEC (WHO 2015 classification), independently from PD-L1 expression status by tumor cells; mixed tumors with a prominent (>70%) NEC component are eligible
- Tumor progression after one or two lines of treatment, including at least one line of platin-based chemotherapy
- Unresectable locally advanced or metastatic stage
- Measurable disease according to RECIST 1.1 guidelines for solid tumors
- Patients must have adequate organ function: creatinine clearance > 50 mL/min (Cockcroft formula), Neutrophiles count >= 1500/mm3; Platelets > 100 000/mm3 ; Hemoglobin > 9 g/dL; hepatic enzymes < 3 x ULN (upper limit of normal) with total bilirubin <= 2 × ULN except subjects with documented Gilbert's syndrome (<= 5 × ULN) or liver metastasis, who must have a baseline total bilirubin <= 3.0 mg/dL
- Patients must have recovered from all toxicities associated with prior treatment, to acceptable baseline status, or a National Cancer Institute Common Terminology Criteria for Adverse Events(NCI CTCAE v4.0) Grade of 0 or 1, except for toxicities not considered a safety risk, such as alopecia or vitiligo
- Availability of tumor material for central review processes and translational research projects
- Absence of any unstable systemic disease and any psychological, familial, sociological or geographical factors potentially hampering compliance with the study protocol and follow-up schedule.
- Before patient inclusion, written informed consent must be given according to ICH/GCP, and national/local regulations.
- Females of childbearing potential who are sexually active with a non-sterilized male partner must use a highly effective method of contraception for 28 days prior to the first dose of investigational product, and must agree to continue using such precautions for 6 months after the final dose of investigational product; cessation of contraception after this point should be discussed with a responsible physician. Periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception. They must also refrain from egg cell donation for 6 months after the final dose of investigational product. Men receiving nivolumab and who are sexually active with women of childbearing potential will be instructed to adhere to contraception for a period of 31 weeks after the last dose of nivolumab.
- Patient must be affiliated to or a beneficiary of social security insurance.

Critères de non-inclusion : - Patients <18 years old
- Well-differentiated neuroendocrine tumor (NET G1 and G2 according to digestive WHO 2010 classification or typical/atypical carcinoid tumor according to lung WHO 2015 classification)
- Small cell lung NEC (except as a minor <30% component in mixed tumors)
- Known EGFR activating mutation or ALK or ROS1 rearrangement for lung NEC
- Brain metastasis, except if surgically resected or treated with stereotaxic radiotherapy with no evolution within the 3 months before inclusion, and asymptomatic patient
- Patients with a recent history of other malignancies except adequately treated non-melanoma skin cancer, and curatively treated in-situ cancer. Patients with history of solid tumors, including adenocarcinoma, treated in a curative way with or without chemotherapy and without any evidence of disease >2 years before randomisation can be included as well.
- History of primary immunodeficiency, history of organ transplant that requires therapeutic immunosuppression and the use of immunosuppressive agents within 28 days of randomization or a prior history of severe (grade 3 or 4) immune mediated toxicity from other immune therapy.
- Subjects with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of randomization. Intranasal/inhaled or topical steroids, and adrenal replacement steroid doses <= 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
- Live attenuated vaccination administered within 30 days prior to randomization.
- Known history of interstitial lung disease or CT-scan signs of interstitial lung disease.
- Subjects with an active, known or suspected autoimmune disease, including systemic lupus erythematosis or Wegener's granulomatosis. Subjects with type I diabetes mellitis, or hypothyroidism only requiring hormone replacement, or skin disorders

(such as vitiligo, psoriasis, or alopecia) not requiring systemic treatment, are permitted to enroll.
- Active or history of inflammatory or irritable bowel disease (eg, diverticulitis, colitis, Crohn's), irritable bowel disease, celiac disease or other serious gastrointestinal chronic conditions associated with diarrhea. Note that diverticulosis is permitted.
- Patients with active or uncontrolled infections or with serious illnesses or medical conditions which would not permit the patient to be managed according to the protocol. This includes but is not limited to:
-> known prior history of active tuberculosis-disease;
-> known acute or chronic B or C hepatitis by serological evaluation. Patients with serological sequelae of hepatitis (antibodies test serologically positive for virus) without hepatitis could be included.
-> known Human immunodeficiency virus infection.
- Concurrent administration of any anti-cancer therapies (e.g., chemotherapy, other targeted therapy, experimental drug, etc.) other than those administered in this study
- Prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways
- The last dose of prior chemotherapy or radiation therapy (with the exception of palliative radiotherapy) was received less than 3 weeks prior to randomization;
- Patients with a psychiatric history that hinders the comprehension of the information leaflet
- Individual deprived of liberty or placed under the authority of a tutor.
- Unwillingness to practice effective birth control. Pregnant or lactating women.
- Patients with other concurrent severe and/or uncontrolled medical disease which could compromise participation in the study

Informations promoteur

Nom du promoteur : INTERGROUPE FRANCOPHONE DE CANCEROLOGIE THORACIQUE

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Statut de l'essai : OUVERT

Liens utiles

ClinicalTrials : https://clinicaltrials.gov/ct2/show/NCT03591731?titles=nipinec&cntry=FR&rank=1

IFCT : https://www.ifct.fr/index.php/fr/la-recherche/item/2106-gco-001-nipinec