Acsé VEMURAFENIB - Cohorte "Pathologie diverses - Altération de BRAF activatrice" (dernière mise à jour : 30/08/2019)

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Informations générales

Titre de l'étude : Secured access to vemurafenib for patients with tumors harboring BRAF genomic alterations

Traitement : Adjuvant / Métastasique ou localement avancé

Type d'étude : Ciblage moléculaire / Innovation thérapeutique

Phase : II **Stade** : NA **Ligne(s)** :

Schéma : This is a biology driven, trans-tumoral, multicentric phase II trial assessing the efficacy and the safety of the targeted agent vemurafenib as a monotherapy in cohorts of patients with identified activating molecular alterations in BRAF gene. A cohort is defined by a pathology and a BRAF- alteration (eg ovarian cancer with BRAF V600 mutation).

To explore the efficacy of vemurafenib per pathology and per target. To assess the safety profile of vemurafenib. To explore whether molecularly driven, high quality multi-tumor screening phase II trials are feasible in the French multiinstitutional, multidisciplinary setting.

To investigate the additional molecular mechanisms in patients with tumor response versus patients without tumor response within the same cohort.

The study will include 11 cohorts of adult patients with the following cancers and alterations:

-> NSCLC V600 mutated
-> Ovarian cancer V600 mutated
-> Cholangiocarcinoma V600 mutated
-> Thyroid cancer V600 mutated
-> Prostatic cancer V600 mutated
-> Bladder cancer V600 mutated
-> Sarcoma/GIST V600 mutated
-> Multiple myeloma V600 mutated
-> Chronic Lymphocytic Leukemia (CLL) V600 mutated
-> Hairy cell leukaemia (HCL) V600 mutated (this excludes Hairy Cell Leukemia variant types, marginal zone splenic lymphoma (MZL), splenic red pulp lymphoma (SRPL) patients)
-> Other pathology / other alteration than those pre-defined above.
The cohort named "Other" will include adult patients with tumor harboring BRAF genomic alterations only tested via emerging biomarkers programs or molecular pangenomic programs:
- with any other non-predefined pathology harboring a V600 mutation
- Same or other non-predefined pathology harboring non V600 activating mutations
- Same or other non-predefined pathology harboring BRAF amplifications.

Spécialités / Localisations

Spécialité n°1 : Toutes tumeurs solides

CIM10 - Localisation n°1 : **C** - Toutes localisations

Critères

Critères d'inclusion : 1. Male and female >= 18 years of age
2. Unresectable locally advanced or metastatic histologically confirmed malignancy (excluding melanoma V600 mutation) resistant or refractory to standard therapy or for which standard therapy does not exist or is not considered appropriate by the Investigator and are not eligible to an appropriate ongoing clinical trial. For Hairy Cell Leukemia: .patients must have relapsed and/or be refractory HCL candidate for treatment after 2 lines of purine analogues treatment.
3. Patient with BRAF V600 mutation determined by the INCa platforms on the primary and/or metastatic lesion in the following pathologies:
. NSCLC
. Ovarian cancer
. Cholangiocarcinoma
. Thyroid cancer
. Prostatic cancer
. Bladder cancer
. Sarcoma/GIST
. Multiple myeloma
. Chronic Lymphocytic Leukemia (CLL)
. Hairy cell leukaemia (HCL) (this excludes Hairy Cell Leukemia variant types, marginal zone splenic lymphoma (MZL), splenic red pulp lymphoma (SRPL) patients)
Or patient with the same or another pre-listed pathology harboring any type of activating BRAF alteration determined from outside the INCa platforms network..
4. Measurable disease according to RECIST 1.1 guidelines for solid tumors with target lesion of at least 10 mm and presence of at least one RECIST-measurable lesion outside of a previously radiated field or potential palliative irradiation fields, International Myeloma Working group Response Criteria for myeloma, IWCLL Chronic Lymphocytic Leukemia and clinical/biological parameters for Hairy cell leukaemia (Serum M-protein > 0.5 g/dL; Urine M-protein > 200 mg per 24 hours; Involved FLC level > 10 mg/dL (> 100 mg/L) provided serum FLC ratio is abnormal).
5. Patients who had received any previous systemic anticancer treatment and/or radiotherapy should have recovered from any treatment related toxicity, i.e. <= grade1, with a mandatory free interval of at least 3 weeks for systemic or radiotherapy treatments and at least 5 half-lives for targeted drugs.
6. Patients who had received any investigational drug are eligible after a 4-week wash-out period or a wash-out period equivalent to 5 half-lives of the product, depending on the longest period
7. Adequate hematologic*, renal* and liver function*, as defined by the following laboratory values; test performed within 7 days prior to the first dose of vemurafenib:
. Hemoglobin >= 9 g/dL
. Absolute neutrophil count (ANC) >= 1.5 x 109/L
. Platelet count >= 100 x 109/L
. Serum creatinine <= 1.5 times upper limit of normal (ULN) or creatine clearance (CrCl) > 50 mL/min by Cockroft–Gault formula (Protocol Appendix 1)
. Aspartate aminotransferase (AST [SGOT]) and alanine aminotransferase (ALT [SGPT]) <= 2.5 times ULN (<= 5 times ULN if considered due to primary or metastatic liver involvement)
. Serum bilirubin <= 1.5 times ULN
. Alkaline phosphatase <= 2.5 times ULN (<= 5 times ULN if considered due to tumor)
* not applicable if biological abnormality(ies) is (are) fully related to the malignant disease itself.
8. Normal values for calcium, magnesium and potassium levels
9. Patients able to swallow and retain oral medication (tablet size: 19 mm. Can not be chewed or crushed)
10. ECOG Performance Status of 0 to 2, or Karnofsky scale > 50 %
11. Life expectancy >= 3 months
12. Potentially reproductive patients must agree to use an effective contraceptive method, practice adequate methods of birth control or practice complete abstinence while on treatment, beginning 2 weeks before the first dose of investigational product and for at least 6 months after the last dose of study drug
13. Women of childbearing potential must have a negative serum pregnancy test within 14 days of enrollment and/or urine pregnancy test 72 hours prior to the administration of the study drug
14. Women who are breastfeeding should discontinue nursing prior to the first day of study drug and permanently after the last dose
15. Patients must be affiliated to a Social Security System.
16. Patient information and written informed consent form signed.

Critères de non-inclusion : 1) V600 BRAF mutated melanoma patients or colorectal cancer patients

2) Patient eligible to a clinical trial with an anticancer drug (including vemurafenib) targeting the same BRAF molecular alteration in the same type/localization as the patient's cancer presentation open to accrual in France. Patient not eligible in this trial are still eligible for the AcSé study.
3) Prior treatment with a BRAF or MEK inhibitor
4) Major surgery or tumor embolization within 4 weeks and minor surgery within 2 weeks prior to the initiation of the study drug
5) Patients with other concurrent severe and/or uncontrolled medical disease which could compromise participation in the study, such as, but not limited to:
a) Any of the following within the 6 months prior to starting study treatment: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, or cerebrovascular accident including transient ischemic attack. Ongoing congestive heart failure.
b) Pulmonary embolism within 30 days prior to first vemurafenib administration
c) Hypertension not adequately controlled by current medications within 30 days prior to first vemurafenib administration
d) Congenital long QT syndrome
e) Ongoing cardiac dysrhythmias of NCI CTCAE Grade >= 2, uncontrolled atrial fibrillation of any grade, or machine-read ECG with QTc interval > 460 msec
f) Spinal cord compression unless treated with the patient attaining good pain control and stable or recovered neurologic function
g) Carcinomatous meningitis or leptomeningeal disease
h) Any uncontrolled infection
i) Other severe acute or chronic medical (including severe gastrointestinal conditions such as diarrhea or ulcer) or psychiatric conditions, or end stage renal disease on hemodialysis or laboratory abnormalities that would impart, in the judgment of the investigator and/or sponsor, excess risk associated with study participation or study drug administration, and which would, therefore, make the patient inappropriate for study entry
6) For MM, solitary bone or solitary extramedullary plasmacytoma as the only evidence of plasma cell dyscrasia
7) Known hypersensitivity to vemurafenib or another BRAF inhibitor
8) Concurrent administration of any anti-cancer therapies (e.g., chemotherapy, other targeted therapy, experimental drug, etc.) other than those administered in this study
9) Refractory nausea and vomiting, malabsorption, external biliary shunt or significant bowel resection that would preclude adequate absorption.
10) Patients with significantly altered mental status prohibiting the understanding of the study or with psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial
11) Individual deprived of liberty or placed under the authority of a tutor.
12) Unwillingness to practice effective birth control. Pregnant or lactating women.

Informations promoteur

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Ouverture de l'essai : OUVERT

Liens utiles

ClinicalTrials : https://clinicaltrials.gov/ct2/show/NCT02304809?term=NCT02304812