CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**CRITERES DE SELECTION** **ETUDE TAS-117-201**	Identité patient (coller étiquette patient)
Version 2.0 du 27/04/2021	Investigateur en charge du patient : …….. PI : AHervieu@cgfl.fr *A contacter pour adresser/inclure patient externe au CGFL*	Arc : *Valérie Boyeau* ***poste*** *3494*

A Phase 2 Study of TAS-117 in Patients with Advanced Solid Tumors Harboring Germline *PTEN* Inactivating Mutations

Study Design:
This is an open-label, single-arm Phase 2 study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and antitumor activity of TAS-117 in patients with advanced or metastatic solid tumors harboring germline PTEN inactivating mutations. The study will be conducted in two parts:

- Part A: Safety lead-in (Dose Escalation and Dose and Regimen Confirmation)
- Part B: Single-arm Phase 2 study

VALIDATION DES CRITERES DE SELECTION

(TAS-117-201 Protocol Amendment 1 9 December 2020)

Critères d'inclusion

1. Provide written informed consent.	☐ oui ☐ non
2. Life expectancy of at least 12 weeks.	☐ oui ☐ non
3. Dose escalation in Part A: a. ≥18 years of age b. ECOG performance status 0 or 1. c. Histologically or cytologically confirmed advanced or metastatic solid tumors (patients with primary brain tumors are not eligible). d. Has progressed after all standard treatment for advanced or metastatic disease known to provide clinical benefit, or was intolerant to or ineligible for such available standard therapies. e. Patients with solid tumors irrespective of gene alterations. f. Patients with at least one measurable or non-measurable lesion per RECIST 1.1.	☐ oui ☐ non
4. Dose and Regimen Confirmation in Part A and Phase 2 (Part B): a. ≥12 years of age. Patients age ≥12 and <18 years must have a body weight of ≥40 kg. b. ECOG performance status 0 or 1 (for patients ≥18 years of age) or KPS of ≥70% (for patients age ≥12 and <18 years of age). Patients who are unable to walk because of paralysis or stable	☐ oui ☐ non

neurological disability, but who are up in a wheelchair, will be considered ambulatory for the purpose of KPS. c. Histologically confirmed advanced or metastatic solid tumors (patients with primary brain tumors are not eligible). d. Has progressed after standard treatment for advanced or metastatic disease or was intolerant to or ineligible for available standard therapies. e. Patients with locally confirmed germline PTEN inactivating mutations determined from a blood sample (in case that germline PTEN mutation is predicted by local tumor tissue sample testing, it must be confirmed by blood sample germline testing at a local laboratory or a laboratory designated by the Sponsor). f. Patients with at least one measurable lesion per RECIST 1.1.	
5. Has cancerous tumor tissue available from archival tumor tissue samples or newly obtained core or excisional biopsy (preferably a tumor lesion not previously irradiated). Formalin-fixed, paraffin-embedded tissue blocks are preferable to slides. Newly obtained biopsies are preferable to archived tissue.	☐ oui ☐ non
6. Adequate organ function as defined by the following criteria: a. ANC ≥1.5 × 109/L (At least a 7-day washout is required if G-CSF is administered). b. Platelet count ≥75,000/mm3 (≥75 × 109/L) (At least a 14-day washout is required if platelet transfusion is performed). c. Hemoglobin ≥8.5 g/dL (At least a 14-day washout is required if blood transfusion is performed). d. ALT and AST ≤3.0 × ULN; if liver function abnormalities are due to underlying liver metastasis, AST and ALT ≤5.0 × ULN. e. Total bilirubin ≤1.5 × ULN, or ≤3.0 × ULN for patients with Gilbert's syndrome. f. Glycosylated hemoglobin (HbA1c) ≤7.0%. g. Creatinine clearance (CrCl) (calculated or measured value): ≥50 mL/min. For calculated CrCl, use the Cockcroft-Gault formula.	☐ oui ☐ non
7. WOCBP must have a negative serum pregnancy test prior to administration of the first dose of study treatment. Female patients are not considered to be of child-bearing potential if they are post-menopausal (no menses for 12 months without an alternative medical cause) or permanently sterile (hysterectomy, bilateral salpingectomy, or bilateral oophorectomy).	☐ oui ☐ non
8. Both males and females of reproductive potential must agree to use effective birth control (prior to the first dose, during the study, for 180 days after the last dose of study treatment, or longer) based on local requirements.	☐ oui ☐ non
9. Patients are willing and able to comply with scheduled visits and study procedures.	☐ oui ☐ non

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Critères de non inclusion

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1. Currently receiving an investigational drug in a clinical trial or participating in anyother type of medical research judged not to be scientifically or medically compatible with this study.	□ oui □ non
2. History of or current evidence of active interstitial lung disease or pneumonitis.	□ oui □ non
3. Current evidence of diabetes mellitus that requires insulin therapy.	□ oui □ non
4. Prior treatment with PI3K/AKT/mTOR pathway inhibitors.	□ oui □ non
5. Patients with primary brain tumor.	□ oui □ non
6. Corrected QT interval using Fridericia's formula (QTcF) >470 msec.	□ oui □ non
7. Any unresolved acute toxicity CTCAE Grade ≥2 from previous anticancer therapy with the exception of alopecia, vitiligo, skin pigmentation, and the laboratory values defined in the inclusion criteria (for example, anemia). *Note: Patients with Grade ≥2 neuropathy may be included on a case-by-case basis after consultation with the Sponsor.*	□ oui □ non
8. Prior treatment with any of the following within the specific time frame prior to the first dose of study treatment: a. Major surgery/surgical therapy for any cause within 4 weeks; the patient must have recovered adequately from the toxicity and/or complications of the intervention prior to starting study treatment. b. Any noninvestigational anticancer therapy (chemotherapy, biologic therapy, targeted therapy, or immunotherapy) within 5 half-lives or within 3 weeks (whichever is shorter) prior to the first dose of study treatment. c. Any investigational agent within 5 half-lives or within 4 weeks (whichever is shorter) prior to the first dose of study treatment. d. Radiotherapy within 4 weeks prior to the first dose of study treatment. A 2-week washout is permitted for palliative radiation (≤4 weeks of radiotherapy) to non-CNS disease.	□ oui □ non
9. Patients with prior active malignancies must be excluded unless a complete remission was achieved at least 2 years prior to enrollment and no additional therapy is required or anticipated to be required during the study. Patients with nonmelanoma skin cancers or carcinoma in situ (for example, bladder, prostate, cervical, breast cancers) who have undergone potentially curative therapy are not excluded.	□ oui □ non

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10. Patients with meningeal carcinomatosis, leptomeningeal carcinomatosis, spinal cord compression, or symptomatic or unstable brain metastasis. *Note: patients with stable brain metastasis (defined as asymptomatic or no requirement for high-dose or increasing dose of systemic corticosteroids) and without imminent need of radiation therapy are eligible (including those with untreated brain metastasis).* *If applicable, patients must have completed brain radiation therapy and recovered adequately from any associated toxicity and/or complications prior to eligibility assessment. For patients who have received prior radiation therapy, post-treatment MRI scan should show no increase in brain lesion size/volume.*	□ oui □ non
11. Currently receiving chronic corticosteroid therapy of ≥10 mg/day of prednisone or its equivalent.	□ oui □ non
12. Patients unable to swallow orally administered medication (feeding tube is not permitted).	□ oui □ non
13. Pregnant or breastfeeding women.	□ oui □ non
14. A serious illness or medical condition(s) including (but not limited to) the following: a. Known acute systemic infection. b. History of severe myocardial infarction within 6 months of screening. c. Any New York Heart Association Classification of Heart Failure ≥ Class II (Appendix A). d. History or current evidence of uncontrolled ventricular arrhythmia. e. Congenital long QT syndrome, or any known history of torsade de pointes, or family history of unexplained sudden death. f. Other clinically significant acute or chronic medical or psychiatric condition that may increase the risk associated with study drug administration, or may interfere with the interpretation of study results (based on Investigator decision). This may include (but is not limited to) chronic nausea, vomiting, or diarrhea considered to be clinically significant (≥ Grade 2).	□ oui □ non

Date : _____

Signature de l'investigateur : _____