CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**CRITERES DE SELECTION** **ETUDE PROOF**	Identité patient (coller étiquette patient)
Version 1.0 du 10/03/2015	Investigateur :	Arc : Kevin L.

VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion

1. Have histologically or cytologically confirmed unresectable locally advanced or metastatic cholangiocarcinoma. Subjects with gallbladder cancer or ampulla of Vater carcinoma are not eligible.	☐ oui ☐ non
2. Have written documentation of local laboratory or central laboratory determination of a known or likely activating FGFR2 fusion/rearrangement from a sample collected before randomization (refer to Section 10.3.1 for the definition of a known or likely activating FGFR2 fusion/rearrangement). Note: All subjects enrolled based on local molecular test results must have sufficient tumor tissue for confirmation of FGFR2 fusion/rearrangement by the central laboratory, but this central confirmation is not required prior to enrollment in the study.	☐ oui ☐ non
3. Have an archival tumor tissue sample available with sufficient tumor content for FGFR2 fusion/rearrangement molecular testing by the central laboratory. However, if an archival tumor tissue sample is not available or does not meet requirements for central testing, a newly obtained (before randomization) tumor biopsy may be submitted instead. If a prestudy written documentation of FGFR2 fusion/rearrangement in tumor tissue is available from the central laboratory, an additional tumor sample does not need to be submitted.	☐ oui ☐ non
4. Have full recovery from the following permitted prior treatments (as applicable) such that the subject is reasonably expected to tolerate study treatment (gemcitabine/cisplatin or infigratinib) according to the investigator's assessment: a. A non-curative operation (ie, R2 resection [with macroscopic residual disease] or palliative bypass surgery only) b. Curative surgery with evidence of unresectable disease relapse requiring systemic chemotherapy c. Adjuvant radiotherapy (with or without radio-sensitizing low-dose chemotherapy) for localized disease provided there has been clear evidence of disease progression before inclusion in this study d. Adjuvant or neoadjuvant chemotherapy, provided recurrence occurred >6 months after the date of the last dose of adjuvant or neoadjuvant therapy and before randomization e. Gemcitabine-based chemotherapy (specified in Appendix 5 [Section 17.5]) for advanced/unresectable or metastatic cholangiocarcinoma (≤1 cycle) i. Recovery from acute toxicities to the extent that would allow initiation of cisplatin-gemcitabine (absolute neutrophil count	☐ oui ☐ non

(ANC) ≥1,000/mm3 (≥1.0 × 109/L); platelets ≥100,000/mm3 (≥100× 109/L) ii. Baseline tumor assessment at least 7 days after the last dose of chemotherapy and before randomization iii. The window between the last dose of chemotherapy and the start of randomized study treatment must be ≥14 days and ≤5 weeks f. Photodynamic treatment provided there is clear evidence of disease progression at the local site or at a new metastatic site	
5. Are ≥18 years of age of either gender.	☐ oui ☐ non
6. Have an Eastern Cooperative Oncology Group (ECOG) performance status ≤1.	☐ oui ☐ non
7. Have a life expectancy >3 months.	☐ oui ☐ non
8. Are able to read and/or understand the details of the study and provide written evidence of informed consent as approved by IRB/IEC.	☐ oui ☐ non
9. Are able to swallow and retain oral medication.	☐ oui ☐ non
10. Are willing and able to comply with scheduled visits, treatment plan and laboratory tests.	☐ oui ☐ non
11. If a woman of childbearing potential (WOCBP), must have a negative pregnancy test within 7 days of the first dose of study drug. A woman is not of childbearing potential if she has undergone surgical sterilization (total hysterectomy, or bilateral tubal ligation or bilateral oophorectomy at least 6 weeks before taking study drug) or if she is postmenopausal and has had no menstrual bleeding of any kind including menstrual period, irregular bleeding, spotting, etc., for at least 12 months, with an appropriate clinical profile, and there is no other cause of amenorrhea (eg, hormonal therapy, prior chemotherapy). WOCBP and males whose sexual partners are WOCBP must agree to use barrier contraception and a second form of highly effective contraception (Clinical Trials Facilitation Group 2014; see Appendix 3 [Section 17.3]) while receiving study drug and for 1 month following their last dose of infigratinib or 6 months following their last dose of gemcitabine/cisplatin (or according to local labeling and standard institutional practice). Alternatively, total abstinence is also considered a highly effective contraception method when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception. Sexually active males must use a condom during intercourse while taking drug and for 1 month after the last dose of infigratinib or 6 months after their last dose of gemcitabine/cisplatin (or according to local labeling and standard institutional practice) and should not father a child during this period. A condom is required to be used by vasectomized men and by men having intercourse with a male partner, to prevent delivery of the drug via seminal fluid.	☐ oui ☐ non

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Critères de non inclusion

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1. Have received treatment with any systemic anti-cancer therapy for unresectable locally advanced or metastatic cholangiocarcinoma, with the following exceptions: a. Prior neoadjuvant or adjuvant therapy is permitted if documented disease recurrence occurred ≥6 months after the last date of neoadjuvant or adjuvant therapy b. One cycle of gemcitabine-based chemotherapy (specified in Appendix 5 [Section 17.5]) for locally advanced or metastatic cholangiocarcinoma is permitted before randomization	☐ oui ☐ non
2. Have history of a liver transplant.	☐ oui ☐ non
3. Have previously or currently is receiving treatment with a mitogen-activated protein kinase (MEK) or selective FGFR inhibitor.	☐ oui ☐ non
4. Have neurological symptoms related to underlying disease requiring increasing doses of corticosteroids. Note: Steroid use for management of central nervous system tumors is allowed but must be at a stable or decreasing dose of corticosteroids for at least 2 weeks preceding randomization.	☐ oui ☐ non
5. Have a history of another primary malignancy within 3 years except adequately treated in situ carcinoma of the cervix or non-melanoma carcinoma of the skin or any other curatively treated or surveilled malignancy (eg, localized low-risk prostate cancer) that is not expected to require treatment for recurrence during the course of the study.	☐ oui ☐ non
6. Have any other medical condition that would, in the investigator's judgment, prevent the subject's participation in the clinical study due to safety concerns or compliance with clinical study procedures.	☐ oui ☐ non
7. Have current evidence of corneal or retinal disorder/keratopathy including, but not limited to, bullous/band keratopathy, inflammation or ulceration, keratoconjunctivitis, or diabetic retinopathy, confirmed by ophthalmic examination. Subjects with asymptomatic ophthalmic conditions assessed by the investigator to pose minimal risk for study participation may be enrolled in the study.	☐ oui ☐ non
8. Have a history and/or current evidence of extensive tissue calcification including, but not limited to, the soft tissue, kidneys, intestine, myocardium, vascular system, and lung with the exception of calcified lymph nodes, minor pulmonary parenchymal calcifications, and asymptomatic coronary calcification.	☐ oui ☐ non
9. Have impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of oral infigratinib (eg, ulcerative diseases, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection).	☐ oui ☐ non

10. Have current evidence of endocrine alterations of calcium/phosphate homeostasis, eg, parathyroid disorders, history of parathyroidectomy, tumor lysis, tumoral calcinosis, etc.	☐ oui ☐ non
11. Are currently receiving or are planning to receive during participation in this study, treatment with agents that are known moderate or strong inducers or inhibitors of CYP3A4 and medications which increase serum phosphorus and/or calcium concentration. Subjects are not permitted to receive enzyme-inducing anti-epileptic drugs, including carbamazepine, phenytoin, phenobarbital, and primidone. See Appendix 2 (Section 17.2) for details.	☐ oui ☐ non
12. Have consumed grapefruit, grapefruit juice, grapefruit hybrids, pomegranates, star fruits, pomelos, Seville oranges or products containing juice of these fruits within 7 days prior to first dose of study drug.	☐ oui ☐ non
13. Have insufficient bone marrow function: a. Absolute neutrophil count (ANC) <1,000/mm3 (1.0 × 109/L) b. Platelets <100,000/mm3 (<100× 109/L) c. Hemoglobin <8.5 g/dL; transfusion support is allowed if >1 week before randomization and hemoglobin remains stable	☐ oui ☐ non
14. Have insufficient hepatic and renal function: a. Total bilirubin >1.5 × upper limit of normal (ULN) (for patients with documented Gilbert syndrome, direct bilirubin ≤1.5 × ULN and enrollment requires approval by the medical monitor) b. AST/ serum glutamic-oxaloacetic transaminase (SGOT) and ALT/ serum glutamic-pyruvic transaminase (SGPT) >2.5 × ULN (AST and ALT >5 × ULN in the presence of liver involvement of cholangiocarcinoma) c. Calculated (using the Cockcroft-Gault formula [Cockcroft and Gault 1976]) or measured creatinine clearance of <45 mL/min (or value ≥45 mL/min that excludes administration of cisplatin per local label and institutional guidelines)	☐ oui ☐ non
15. Have amylase or lipase >2.0 × ULN	☐ oui ☐ non
16. Have elevated phosphorus or abnormal serum calcium, or calcium-phosphorus product ≥55 mg2/dL2 (refer to Section 9.3 for guidance on calculation): a. Inorganic phosphorus >1.1 × ULN b. Total corrected serum calcium >11 mg/dL or <8 mg/dL	☐ oui ☐ non
17. Have clinically significant cardiac disease including any of the following: a. Congestive heart failure requiring treatment (New York Heart	☐ oui ☐ non

Association Grade ≥2B) or uncontrolled hypertension (refer to the European Society of Cardiology and European Society of Hypertension guidelines [Williams et al 2018]) b. Presence of Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Grade ≥2 ventricular arrhythmias, atrial fibrillation, bradycardia, or conduction abnormality c. Unstable angina pectoris or acute myocardial infarction ≤3 months prior to first dose of study drug d. QTcF >470 msec (males and females). Note: If the QTcF is >470 msec in the first ECG, a total of 3 ECGs separated by at least 5 minutes should be performed. If the average of these 3 consecutive results for QTcF is ≤470 msec, the subject meets eligibility in this regard e. Known history of congenital long QT syndrome	
18. Have had a recent (≤3 months prior to first dose of study drug) transient ischemic attack or stroke	☐ oui ☐ non
19. CTCAE (v5.0) Grade ≥2 hearing loss	☐ oui ☐ non
20. CTCAE (v5.0) Grade ≥2 neuropathy	☐ oui ☐ non
21. If female, is pregnant or nursing (lactating), where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive human chorionic gonadotrophin urine or blood laboratory test.	☐ oui ☐ non
22. Have known microsatellite instability-high (MSI-H) disease and the decision is made by the treating investigator that an alternative, non-study therapy is warranted according to standard of care.	☐ oui ☐ non
23. Have any known hypersensitivity to gemcitabine, cisplatin, calcium-lowering agents, infigratinib, or their excipients.	☐ oui ☐ non
24. Have any contraindication to cisplatin or gemcitabine treatment according to local labeling or standard institutional practice.	☐ oui ☐ non
25. Have taken any Chinese herbal medicine or Chinese patent medicine treatments with anticancer activity within 14 days of the first dose of study drug.	☐ oui ☐ non
26. Have received a live vaccine within 30 days before the first dose of study drug or are planning to receive a live vaccine during participation in this study.	☐ oui ☐ non

Date : _____

Signature de l'investigateur : _____