
	CRITERES DE SELECTION FRESCO-2	Identité patient (coller étiquette patient)
Version 1.0 du 10/03/2015	Investigateur : Pr Ghiringhelli	Arc : Céline S 3427


VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion

1. Provide written informed consent	<input type="checkbox"/> oui <input type="checkbox"/> non
2. Age ≥18 years	<input type="checkbox"/> oui <input type="checkbox"/> non
3. Histologically and/or cytologically documented metastatic colorectal adenocarcinoma. RAS, BRAF, and microsatellite instability (MSI)/mismatch repair (MMR) status for each patient must be documented, according to country level guidelines;	<input type="checkbox"/> oui <input type="checkbox"/> non
Subjects must have progressed on or been intolerant to treatment with either trifluridine/tipiracil (TAS-102) or regorafenib. Subjects are considered intolerant to TAS-102 or regorafenib if they have received at least 1 dose of either agents and were discontinued from therapy for reasons other than disease progression. Subjects who have been treated with both TAS-102 and regorafenib are permitted. Subjects must also have been previously treated with standard approved therapies: fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if RAS wildtype, an anti-EGFR therapy;	<input type="checkbox"/> oui <input type="checkbox"/> non
Subjects with microsatellite-high (MSI-H) or mismatch repair deficient (dMMR) tumors must have been treated with immune checkpoint inhibitors if approved and available in the subject's country unless the patient is ineligible for treatment with a checkpoint inhibitor;	<input type="checkbox"/> oui <input type="checkbox"/> non
Subjects who received oxaliplatin in the adjuvant setting and developed metastatic disease during or within 6 months of completing adjuvant therapy are considered eligible without receiving oxaliplatin in the metastatic setting. Subjects who developed metastatic disease more than 6 months after completion of oxaliplatin-containing adjuvant treatment must be treated with oxaliplatin-based therapy in the metastatic setting	<input type="checkbox"/> oui <input type="checkbox"/> non
6. to be eligible; 7. Body weight ≥40kg;	<input type="checkbox"/> oui <input type="checkbox"/> non
8. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1;	<input type="checkbox"/> oui <input type="checkbox"/> non
Have measurable disease according to RECIST Version 1.1 (RECIST v1.1), assessed locally. Tumors that were treated with radiotherapy are not measurable per RECIST v1.1, unless there has been documented progression of those lesions;	<input type="checkbox"/> oui <input type="checkbox"/> non
9. v1.1, unless there has been documented progression of those lesions; 10. Expected survival >12 weeks	<input type="checkbox"/> oui <input type="checkbox"/> non


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<p>For female subjects of childbearing potential and male subjects with partners of childbearing potential, agreement to use a highly effective form(s) of contraception, that results in a low failure rate (<1% per year) when used consistently and correctly, starting during the screening period, continuing throughout the entire study period, and for 90 days after taking the last dose of study drug. Such methods include: oral hormonal contraception (combined estrogen/ progestogen, or progestogen-only) associated with inhibition of ovulation, intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal ligation, vasectomized partner, or true sexual abstinence in line with the preferred and usual lifestyle of the subject. Highly effective contraception should always be combined with an additional barrier method (eg, diaphragm, with a spermicide). The same criteria are applicable to male subjects involved in this clinical trial if they have a partner of childbirth potential, and male subjects must always use a</p> <p>11. condom;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>Subjects with BRAF-mutant tumors must have been treated with a BRAF inhibitor if approved and available in the subject's country unless the patient is ineligible for</p> <p>12. treatment with a BRAF inhibitor;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

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Critères de non inclusion

1. Absolute neutrophil count (ANC) $<1.5 \times 10^9/L$, platelet count $<100 \times 10^9/L$, or hemoglobin <9.0 g/dL. Blood transfusion within 1 week prior to enrollment for the purpose of increasing the likelihood of eligibility is not allowed;	<input type="checkbox"/> oui <input type="checkbox"/> non
Serum total bilirubin $>1.5 \times$ the upper limit of normal (ULN). Subjects with Gilbert syndrome, bilirubin $<2 \times$ ULN, and normal aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) are eligible	<input type="checkbox"/> oui <input type="checkbox"/> non
2. ALT or AST $>2.5 \times$ ULN in subjects without hepatic metastases; ALT or AST $>5 \times$ ULN in subjects with hepatic metastases;	<input type="checkbox"/> oui <input type="checkbox"/> non
Serum creatinine $>1.5 \times$ ULN or creatinine clearance <60 mL/min. Creatinine clearance can either be measured in a 24-hour urine collection or estimated by the Cockcroft-Gault equation;	<input type="checkbox"/> oui <input type="checkbox"/> non
Urine dipstick protein $\geq 2+$ or 24-hour urine protein ≥ 1.0 g/24-h. Subjects with greater than 2+ proteinuria by dipstick must undergo a 24-hour urine collection to assess urine protein level. For conversions between quantitative and qualitative results, please see Appendix 9 ;	<input type="checkbox"/> oui <input type="checkbox"/> non
6. Uncontrolled hypertension, defined as: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mm Hg despite optimal medical management;	<input type="checkbox"/> oui <input type="checkbox"/> non
7. International Normalized Ratio (INR) $>1.5 \times$ ULN or activated partial thromboplastin time (aPTT) $>1.5 \times$ ULN, unless the subject is currently receiving or intended to receive anticoagulants for prophylactic purposes;	<input type="checkbox"/> oui <input type="checkbox"/> non
History of, or active gastric/duodenal ulcer or ulcerative colitis, active hemorrhage of an unresected gastrointestinal tumor, history of perforation or fistulas; or any other condition that could, in the investigator's judgment, result in gastrointestinal hemorrhage or perforation; within the 6 months prior to screening;	<input type="checkbox"/> oui <input type="checkbox"/> non
History or presence of hemorrhage from any other site (eg, hemoptysis or hematemesis) within 2 months prior to screening;	<input type="checkbox"/> oui <input type="checkbox"/> non
History of a thromboembolic event, including deep vein thrombosis (DVT), pulmonary embolism (PE), or arterial embolism within 6 months prior to screening;	<input type="checkbox"/> oui <input type="checkbox"/> non
11. Stroke and/or transient ischemic attack within 12 months prior to screening;	<input type="checkbox"/> oui <input type="checkbox"/> non
Clinically significant cardiovascular disease, including but not limited to acute myocardial infarction or coronary artery bypass surgery within 6 months prior to enrollment, severe or unstable angina pectoris, New York Heart Association Class III/IV congestive heart failure, ventricular arrhythmias requiring treatment, or left ventricular ejection fraction (LVEF) $<50\%$ by echocardiogram;	<input type="checkbox"/> oui <input type="checkbox"/> non

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Mean corrected QT interval using the Fridericia method (QTcF) >480 msec or any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as hypokalemia, congenital long QT syndrome, family history of long QT syndrome, or 13. unexplained sudden death under 40 years of age in a first-degree relative;	<input type="checkbox"/> oui <input type="checkbox"/> non
Concomitant medications with a known risk of causing QT prolongation and/or Torsades de Pointes (See list in Appendix 4 ; source list is continuously updated online at 14. www.crediblemeds.org);	<input type="checkbox"/> oui <input type="checkbox"/> non
Systemic anti-neoplastic therapies (except for those described in Exclusion Criterion 18) or any investigational therapy within 4 weeks prior to the first dose of study drug, including chemotherapy, radical radiotherapy, hormonotherapy, biotherapy and 15. immunotherapy;	<input type="checkbox"/> oui <input type="checkbox"/> non
Systemic small molecule targeted therapies (eg, tyrosine kinase inhibitors) within 5 halflives 16. or 4 weeks (whichever is shorter) prior to the first dose of study drug;	<input type="checkbox"/> oui <input type="checkbox"/> non
Palliative radiotherapy for bone metastasis/lesion within 2 weeks prior to the initiation of 17. study drug;	<input type="checkbox"/> oui <input type="checkbox"/> non
Brachytherapy (ie, implantation of radioactive seeds) within 60 days prior to the first 18. dose of study drug;	<input type="checkbox"/> oui <input type="checkbox"/> non
Use of strong inducers or inhibitors of CYP3A4 within 2 weeks (or 5 half-lives, whichever is longer) before the first dose of study drug (see Appendix 4 for a list of 19. applicable drugs);	<input type="checkbox"/> oui <input type="checkbox"/> non
Surgery or invasive procedure (ie, a procedure that includes a biopsy; central venous catheter placement is allowed) within 60 days prior to the first dose of study drug or 20. unhealed surgical incision;	<input type="checkbox"/> oui <input type="checkbox"/> non
Any unresolved toxicities from a previous antitumor treatment greater than National Cancer Institute (NCI) Common Terminology Criteria for Adverse Event (CTCAE) v5.0 21. grade 1 (except for alopecia or neurotoxicity grade ≤2);	<input type="checkbox"/> oui <input type="checkbox"/> non
22. Known human immunodeficiency virus (HIV) infection;	<input type="checkbox"/> oui <input type="checkbox"/> non
23. Known history of active viral hepatitis. For subjects with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. Subjects with HCV infection who are currently on treatment are eligible if they have an undetectable HCV viral load;	<input type="checkbox"/> oui <input type="checkbox"/> non
24. Clinically uncontrolled active infection requiring IV antibiotics	<input type="checkbox"/> oui <input type="checkbox"/> non
25. Tumor invasion of a large vascular structure (eg, pulmonary artery, superior or inferior vena cava);	<input type="checkbox"/> oui <input type="checkbox"/> non
26. Women who are pregnant or lactating;	<input type="checkbox"/> oui <input type="checkbox"/> non

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<p>27. Brain metastases and/or spinal cord compression untreated with surgery and/or radiotherapy, and without clinical imaging evidence of stable disease for 14 days or longer; subjects requiring steroids within 4 weeks prior to start of study treatment are excluded;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>28. Other malignancy, except for non-melanoma skin cancer, in situ cervical ca or bladder ca (Tis and T1) that have been adequately treated during the 5 years prior to screening;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>29. Inability to take medication orally, dysphagia or an active gastric ulcer resulting from previous surgery (eg, gastric bypass) or a severe gastrointestinal disease, or any other condition that investigators believe may affect absorption of the investigational product;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>30. Other disease, metabolic disorder, physical examination anomaly, abnormal laboratory result, or any other condition (eg, current alcohol or drug abuse) that investigators suspect may prohibit use of the investigational product, affect interpretation of study results, or put the subject at undue risk of harm based on the investigator's assessment;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>31. Known hypersensitivity to fruquintinib or any of its (or placebo) inactive ingredients including the azo dyes Tartrazine - FD&C Yellow 5 and Sunset yellow FCF - FD&C Yellow 6;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>32. Subjects who have received prior fruquintinib;</p>	<input type="checkbox"/> oui <input type="checkbox"/> non
<p>33. Live vaccine ≤28 days before the first dose of study drug(s) Seasonal vaccines for influenza are generally inactivated vaccines and are allowed. Intranasal vaccines are live vaccines and are not allowed</p>	<input type="checkbox"/> oui <input type="checkbox"/> non

Date : _____

Signature de l'investigateur : _____