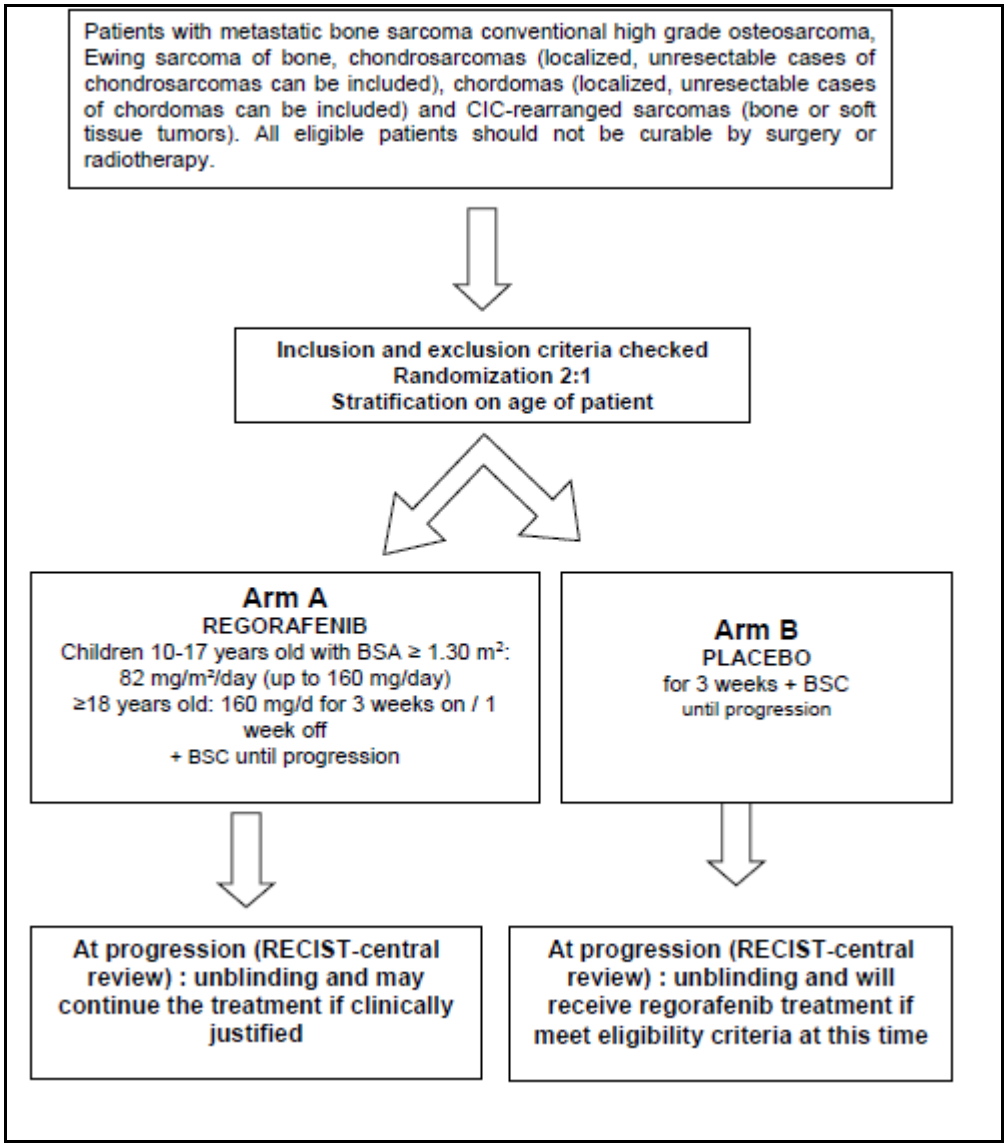
CGFL Centre Georges François Leclerc – Ensemble, dépassons le cancer	**CRITERES DE SELECTION DE L'ETUDE REGOBONE**	Identité patient (coller étiquette patient)
Version 1.0 du 01/11/2021	Investigateur en charge du patient : …….. PI : **Alice HERVIEU** Mail : ahervieu@cgfl.fr *A contacter pour adresser/inclure patient externe au CGFL*	Arc : **Sandra TURLOT** Poste : 3409

« REGOBONE »

Etude de phase II multicentrique, randomisée, contre placebo, évaluant l'efficacité et la tolérance du regorafenib chez des patients ayant un sarcome des os métastatique



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VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion :

1. Patients must have a histologically confirmed diagnosis of bone sarcoma (osteosarcoma, Ewing sarcoma of bone, chondrosarcoma, chordoma [adults patients only for chordomas]) or CIC-rearranged sarcoma (either bone or soft tissue) with available Formalin Fixed Paraffin Embedded (FFPE) blocks obtained for central review; **For CIC-rearranged sarcoma, diagnosis must be confirmed by molecular analysis.**	□ oui □ non
2. Patients with confirmed disease progression at study entry. The "baseline" radiological evaluation should demonstrate disease progression by RECIST V 1.1 for all cohorts (and CHOI criteria especially for chordoma), when compared to a prior disease assessment done within a prior period of 3 month for osteosarcomas, Ewing sarcomas and CIC-rearranged sarcomas, and within 6 months period for chondrosarcomas and chordomas prior to screening; Note: radiographic progression of disease will be based on at least 2 sets of scans (either MRI or CT) in the 3-months (for Osteosarcomas, Ewing sarcomas and and CICrearranged sarcomas) or 6-months period (for chondrosarcomas and chordomas) prior to or during screening in which radiographic progression of disease, as defined by RECIST for all cohorts(and CHOI criteria especially for chordoma) is demonstrated. No central review of scans (either MRIs or CTs) will be required for study eligibility; these scans must be sent for central review within 10 days after randomization;	□ oui □ non
3. Metastatic disease (and/or locally advanced disease for chondrosarcomas, CIC rearranged sarcomas, and chordomas) not amenable to surgical resection or radiation with curative intent;	□ oui □ non
4. Patients must have measurable disease (outside any previous irradiated field) defined as at least one unidimensionally lesion that can be accurately measured as ≥ 10 mm with CT scan according to RECIST V1.1 for all cohorts and CHOI criteria especially for chordoma; Locally advanced chordomas, with no distant metastatis, can be included only if MRI is done as the reference imaging exam in order to measure the disease according to RECIST 1.1 criteria.	□ oui □ non
5. Prior treatment : at least one, but no more than two prior (combination) chemotherapy regimen for metastatic disease (or locally advanced disease if applicable) for osteosarcoma, chondrosarcoma and Ewing sarcoma; at least one but no more than three prior chemotherapy regimen for metastatic disease or locally advanced disease for CIC-rearranged sarcoma; neo-adjuvant /maintenance therapy are not counted towards this requirement. Chordoma not pretreated or with 1 or 2 prior (combination)	□ oui □ non

chemotherapy regimen or with 1 or 2 molecularly targeted agent, but no more than 2 prior lines of treatment (whatever the indication) can be included. At least 4 weeks since last chemotherapy (6 weeks in case of nitrosoureas and mitomycin C), immunotherapy or any other pharmacological treatment and/or radiotherapy;	
6. Age ≥ 10 years for osteosarcomas, Ewing sarcomas, chondrosarcomas and CICrearranged sarcomas (for chordomas, patients must be ≥ 18 years old);	□ oui □ non
7. Body Surface Area ≥ 1.30 m²	□ oui □ non
8. Life expectancy of greater than 3 months;	□ oui □ non
9. ECOG performance status < 2 (Karnofsky ≥ 60%) for adults patients	□ oui □ non
10. Karnofsky scale ≥ 60 % for children aged > 12 years old / Lansky scale ≥ 60 % for children aged ≤ 12 years old	□ oui □ non
11. Patients must have adequate bone marrow, renal, and hepatic function, as evidenced by the following within 7 days of study treatment initiation : normal organ function as defined below : - Absolute neutrophil count ≥ 1.5 Giga/L - Platelets ≥ 100 Giga/L - Hemoglobin≥ 9 g/dL - Serum creatinin ≤ 1.5 x ULN - Glomerular filtration rate (GFR) ≥30 ml/min/1.73m2 according to the modified Diet in Renal Disease (MDRD) abbreviated formula - AST and ALT ≤2.5 x ULN (≤5.0 × ULN for patients with liver involvement of their cancer - Bilirubin ≤1.5 X ULN - Alkaline phosphatase ≤2.5 x ULN (≤5 x ULN with liver involvement of their cancer). If Alkaline phosphatase > 2.5 ULN, hepatic isoenzymes 5-nucleotidase or GGT tests must be performed; hepatic isoenzymes 5-nucleotidase must be within the normal range and/or GGT < 1.5 x ULN - lipase ≤1.5 x ULN - Spot urine must not show ≥ 1 "+"protein in urine or the patient will require a repeat urine analysis. If repeat urinalysis shows 1 "+" protein or more, a 24-hour urine collection will be required and must show total protein excretion <1000 mg/24 hours	□ oui □ non
12. INR/PTT ≤1.5 x ULN; Patients who are therapeutically treated with an agent such as warfarin or heparin will be allowed to participate provided that no prior evidence of underlying abnormality in coagulation parameters exists. Close monitoring of at least weekly evaluations will be performed until INR/PTT is stable based on a measurement that is pre-dose as defined by the local standard of care;	□ oui □ non
13. Recovery to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) v4.0 Grade 0 or 1 level or recovery to baseline preceding the prior treatment from any previous drug/procedure	□ oui □ non

related toxicity (except alopecia, anemia, and hypothyroidism);	
14. Women of childbearing potential and male patients must agree to use adequate contraception for the duration of study participation and up to 3 months following completion of therapy;	□ oui □ non
15. Women of childbearing potential must have a negative serum β-HCG pregnancy test within 7 days prior randomization and/or urine pregnancy test within 48 hours before the first administration of the study treatment;	□ oui □ non
16. Signed informed consent form by subjects and/or subjects' parents/legal representatives and age appropriate assent form by the subjects obtained before any study specific procedure	□ oui □ non
17. Patients must be willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures;	□ oui □ non
18. Patients affiliated to the Social Security System.	□ oui □ non

Critères de non inclusion :

1. Prior treatment with any VEGFR inhibitor (thus, any prior exposure to sunitinib, sorafenib, pazopanib, bevacizumab, or other VEGFR inhibitor would render the patient ineligible for this study);	□ oui □ non
2. Soft tissue sarcoma (including Ewing soft tissue sarcoma) except for CIC-rearranged sarcoma patients;	□ oui □ non
3. Other cancer (different histology) within 5 years prior to randomization	□ oui □ non
4. Major surgical procedure, open biopsy, significant trauma, within the last 28 days before randomization;	□ oui □ non
5. Cardiovascular dysfunction: - Left ventricular ejection fraction (LVEF) < 50% - Congestive heart failure (New York Heart Association [NYAH]) ≥ 2 - Myocardial infarction <6 months before study - Cardiac arrhythmias requiring therapy (beta blockers or digoxin are permitted) Uncontrolled hypertension (systolic blood pressure > 150mmHg or diastolic pressure > 90mmHg despite optimal treatment for adults patients, or for children SBP and/or DBP > 95th to the 99th percentile + 5 mmHg) - Unstable (angina symptoms at rest) or new-onset angina (begun within the last 3 months) ;	□ oui □ non
6. Arterial or venous thrombotic or embolic events such ascerebrovascular accident (including transient ischemic attacks), deep vein thrombosis, or pulmonary embolism within the last 6 months before randomization;	□ oui □ non
7. Severe hepatic impairment (Child-Pugh C);	□ oui □ non

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8. Ongoing infection > Grade 2 according to NCI-CTCAE v4.0;	□ oui □ non
9. Known history of human immunodeficiency virus (HIV) infection;	□ oui □ non
10. Active hepatitis B or C, or chronic hepatitis B or C requiring treatment with antiviral therapy;	□ oui □ non
11. Difficulties with swallowing study tablets;	□ oui □ non
12. Prior anticancer therapy, including radiotherapy, endocrine therapy, immunotherapy, chemotherapy (CT) within the last 4 weeks (6 weeks for nitrosoureas and mitomycin C), or other investigational agents ; concomitant antalgic palliative radiotherapy allowed;	□ oui □ non
13. Concurrent enrolment in another clinical trial in which investigational therapies are administered;	□ oui □ non
14. Known hypersensitivity to the active substance or to any of the excipients;	□ oui □ non
15. Pregnant women, women who are likely to become pregnant or are breast-feeding;	□ oui □ non
16. Individual deprived of liberty or placed under the authority of a tutor;	□ oui □ non
17. Patients with any 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;	□ oui □ non
18. Patients with history of non compliance to medical regimens or unwilling or unable to comply with the protocol	□ oui □ non
19. Interstitial lung disease with ongoing signs and symptoms at the time of informed consent	□ oui □ non
20. Non-healing wound, non-healing ulcer, or non-healing bone fracture	□ oui □ non
21. Patients with evidence or history of any bleeding diathesis, irrespective of severity	□ oui □ non
22. Any hemorrhage or bleeding event ≥ CTCAE Grade 3 within 4 weeks prior to the start of study medication	□ oui □ non
23. Use of biological response modifiers, such as granulocyte colony stimulating factor (G-CSF), within 3 weeks of study entry.	□ oui □ non

Date : _____

Signature de l'investigateur : _____