CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**CRITERES DE SELECTION** **ETUDE MIRATI 516-005**	Identité patient (coller étiquette patient)
Version 1.0 du 10/03/2015	**Investigateur : Dr KADERBHAI**	**Arc : Anaïs 3466**

VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion

1. Histologically or cytologically confirmed non-squamous NSCLC with metastatic (Stage IV) or unresectable, locally advanced (Stage IIIB/IIIC) disease, not amenable to treatment with curative intent including concurrent chemoradiotherapy	☐ oui ☐ non
2. Receipt of at least one but not more than two prior treatment regimens in the advanced disease setting to include: • Treatment with a CIT (i.e., anti-PD-1/PD-L1) and a platinum-based chemotherapy, which may have been in combination or in sequence (i.e., platinum-based chemotherapy followed by CIT) o Prior treatment may have included maintenance therapy with a chemotherapy agent (e.g., pemetrexed) and/or a CIT • Most recent treatment regimen must have included a CIT with radiographic disease progression on or after treatment, for example: o 1 prior treatment regimen: platinum-based chemotherapy in combination with CIT → radiographic disease progression, or o 2 prior treatment regimens: platinum-based chemotherapy → disease progression → CIT → radiographic disease progression **NOTE:** Platinum-based adjuvant, neoadjuvant, or definitive chemoradiation therapy given for locally advanced disease followed by recurrent or metastatic disease within 6 months of completing chemotherapy may be considered treatment in the advanced disease setting.	☐ oui ☐ non
3. Duration of at least 4 months (120 days) from first dose of most recent CIT to date of radiographic disease progression	☐ oui ☐ non
4. Availability of source documents for historical disease evaluations to allow Investigator certification of disease progression on or after most recent CIT.	☐ oui ☐ non
5. Most recent prior therapy (e.g., chemotherapy, CIT, or radiation therapy) discontinued at minimum of 2 weeks before the date of randomization.; palliative radiation therapy to skeletal metastases and stereotactic radiation for brain metastases allowed if discontinued at least 7 days before the date of randomization.	☐ oui ☐ non
6. Candidacy to receive treatment with docetaxel as the next line of therapy if randomized to the comparator arm.	☐ oui ☐ non

7. Recovery from adverse effects of prior therapy to baseline or Grade 1 (excluding alopecia).	☐ oui ☐ non
8. ≥ 18 years of age.	☐ oui ☐ non
9. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1.	☐ oui ☐ non
10. Life expectancy of at least 3 months.	☐ oui ☐ non
11. Adequate bone marrow and organ function demonstrated by: a. Absolute neutrophil count 1,500/mm3 (1.5 × 109/L). b. Hemoglobin ≥ 9.0 g/dL not dependent on transfusion support. c. Platelet count ≥ 100 × 109/L (≥ 100,000 per mm3). d. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 1.5 × ULN without liver metastases; < 5.0 x ULN if documented liver metastases; if alkaline phosphatase > 2.5 × ULN then ALT and AST must be ≤ 1.5 × ULN with or without liver metastases. e. Serum bilirubin ≤ 1.0 x ULN. f. Calculated creatinine clearance ≥ 40 mL/min, using the Cockcroft-Gault formula.	☐ oui ☐ non
12. Women of child-bearing potential (WOCBP) or men whose partner is a WOCBP agrees to use contraception while participating in this study, and for a period of 6 months following termination of study treatment.	☐ oui ☐ non
13. Completed informed consent process, including signing IRB/EC-approved informed consent form.	☐ oui ☐ non
14. Willing to comply with clinical trial instructions and requirements.	☐ oui ☐ non

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Critères de non inclusion

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1. Discontinuation of prior treatment with CIT more than 90 days prior to the date of randomization.	☐ oui ☐ non
2. Receipt of systemic cancer therapy since discontinuation of CIT, with the exception of maintenance chemotherapy.	☐ oui ☐ non
3. Active brain metastases. Patients are eligible if brain metastases are adequately treated and patients are neurologically stable (except for residual signs or symptoms related to the central nervous system (CNS) treatment) for at least 2 weeks prior to randomization without the use of anticonvulsants and without the use of corticosteroids (or are on a stable or decreasing dose of ≤10 mg daily prednisone or equivalent).	☐ oui ☐ non
4. Carcinomatous meningitis.	☐ oui ☐ non
5. Known history of tumors that test positive for EGFR, ROS1, ALK mutations, or ALK fusions.	☐ oui ☐ non
6. Prior therapies: a. Immunotherapies not previously specified, including anti- OX40 and anti‑CD137; prior anti-CTLA-4 is permitted b. Cancer therapy having the same mechanism of action as sitravatinib (e.g., tyrosine kinase inhibitor with a similar target profile or bevacizumab).	☐ oui ☐ non
7. Known toxicity on prior checkpoint inhibitor treatment: a. ≥ Grade 3 immune-related AE related to checkpoint inhibitor. b. Grade 2 immune-related AE associated with checkpoint inhibitor unless the AE resolved or was well controlled by withholding the checkpoint inhibitor and/or treatment with steroids, with the exception of prior colitis, myocarditis, and pneumonitis, which are exclusionary. c. CNS or ocular AE of any grade related to checkpoint inhibitor. **NOTE: Patients with a prior endocrine AE are permitted to enroll if they are stably maintained on appropriate replacement therapy and are asymptomatic.**	☐ oui ☐ non
8. Active or prior documented autoimmune disease: a. Inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis). b. History of interstitial lung disease (ILD), drug-induced ILD, radiation pneumonitis which required steroid treatment, or any evidence of clinically active ILD. c. Active or prior documented autoimmune disease within the past 2 years. **NOTE: Patients with Type 1 diabetes, vitiligo, Graves' disease, residual hypothyroidism due to an autoimmune condition only requiring hormone**	☐ oui ☐ non

replacement, or psoriasis not requiring systemic treatment (within the past 2 years) are not excluded.	
9. Active or prior immunocompromising conditions: a. Current or prior use of immunosuppressive medication within 28 days before the date of randomization, with the exceptions of topical, ocular, intranasal and inhaled corticosteroids (with minimal systemic absorption) or systemic corticosteroids at physiological doses, which are not to exceed 10 mg/day of prednisone, or an equivalent corticosteroid. A brief course (≤ 3 days) of systemic corticosteroids >10 mg/day of prednisone (or equivalent corticosteroid) for prophylaxis (e.g., contrast dye allergy) or for treatment of non-immune conditions (e.g., delayed-type hypersensitivity reaction caused by a contact allergen) is permitted within the 28 days. b. Known acute or chronic human immunodeficiency virus (HIV); - Sites in Germany and Switzerland only: HIV infection at screening (positive HIV test). c. History of primary immunodeficiency. d. History of allogeneic transplant.	☐ oui ☐ non
10. History of severe hypersensitivity reaction to any monoclonal antibody or polysorbate 80.	☐ oui ☐ non
11. Criterion #11 removed, but numbering maintained.	☐ oui ☐ non
12. Use of live vaccines against infectious disease (e.g. varicella) within 28 days of the date of randomization (note: killed vaccinations (e.g. influenza) are allowed at any appropriate time before and during the study).	☐ oui ☐ non
13. Known acute or chronic hepatitis B or hepatitis C. Patients treated for hepatitis C with no detectable viral load are permitted. • Sites in Germany and Switzerland (testing required during screening): positive hepatitis B surface antigen [HBsAg] or positive hepatitis C virus [HCV] antibody; i. patients with past or resolved hepatitis B virus (HBV) infection (defined as the presence of hepatitis B core antibody [HBcAb] and absence of HBsAg) are eligible only if HBV DNA is negative ii. patients treated for hepatitis C with no detectable viral load (HCV RNA negative) are permitted.	☐ oui ☐ non
14. History of hypersensitivity to study treatment excipient.	☐ oui ☐ non
15. History of stroke or transient ischemic attack within the previous 6 months.	☐ oui ☐ non
16. Any of the following cardiac abnormalities: a. Unstable angina pectoris within the past 6 months. b. Symptomatic or uncontrolled atrial fibrillation within the past 6 months. c. Congestive heart failure ≥ NYHA Class 3 within the past 6 months. d. Prolonged QTc on electrocardiogram >480 milliseconds. e. Left ventricular ejection fraction (LVEF) < 40%.	☐ oui ☐ non
17. Ongoing need for treatment with concomitant medication known to cause prolonged QTc. Such medication may be discontinued or changed to a different medication prior to enrollment.	☐ oui ☐ non
18. Uncontrolled arterial hypertension (> 150 mm Hg systolic or > 100 mm Hg diastolic) on multiple observations despite standard of care treatment.	☐ oui ☐ non
19. Major surgery within 4 weeks of the date of randomization.	☐ oui ☐ non

20. History of significant hemoptysis or hemorrhage within 4 weeks of the date of randomization.	☐ oui ☐ non
21. Known or suspected presence of another malignancy that could be mistaken for the malignancy under study during disease assessments.	☐ oui ☐ non
22. Pregnancy. WOCBP must have a negative serum or urine pregnancy test documented within the screening period prior to the date of randomization.	☐ oui ☐ non
23. Breast-feeding or planning to breast-feed during the study or within 30 days following the last dose of docetaxel or sitravatinib and within 5 months following the last dose of nivolumab.	☐ oui ☐ non
24. Any serious illness, uncontrolled inter-current illness, psychiatric illness, active or uncontrolled infection, or other medical condition or history, including laboratory results, which, in the Investigator's opinion, interferes with the patient's capacity to provide informed consent, or would be likely to interfere with the patient's participation in the study, or with the interpretation of the results	☐ oui ☐ non

Date : _____

Signature de l'investigateur : _____