CGFL CENTRE GEORGES FRANÇOIS LECLERC Ensemble, dépassons le cancer	**CRITERES DE SELECTION** **ETUDE ROSALIE**	Identité patient (coller étiquette patient)
Version 1.0 du 14-08-2021	Investigateur en charge du patient : …….. PI : Dr **GHIRINGHELLI** *A contacter pour adresser/inclure patient externe au CGFL*	Arc : Serife Dermirel Poste : *3740*

ROSALIE

Etude de phase 1b-2a, évaluant la sécurité d'emploi, la tolérance, l'immunogénicité et l'efficacité préliminaire de l'EO2401, chez des patients ayant une preuve sans équivoque de glioblastome progressif ou de première récidive.

Arm	Intervention/treatment
Experimental: Cohort 1 Multiple dose of EO2041 monotherapy followed by continued EO2401 in combination with nivolumab	Biological: Multiple dose of EO2401 Multiple dose administration of EO2401 coadministered with or without nivolumab (and bevacizumab, US only) during the priming phase
Experimental: Cohort 2 Multiple dose of EO2041 in combination with nivolumab	Biological: Multiple dose of EO2401 Multiple dose administration of EO2401 coadministered with or without nivolumab (and bevacizumab, US only) during the priming phase
Experimental: Cohort 3 Multiple dose of EO2041 in combination with nivolumab and bevacizumab (US only)	Biological: Multiple dose of EO2401 Multiple dose administration of EO2401 coadministered with or without nivolumab (and bevacizumab, US only) during the priming phase

VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion :

1. Patients with unequivocal documented (including histological confirmation of Glioblastoma-GB- at the primary diagnosis) evidence of first progression/recurrence of GB on MRI, as defined by RANO criteria	□ oui □ non
2. Patients with : A. for Cohorts 1, 2a, and 3: at least 1 measurable lesion B. for Cohort 2b: no measurable enhancing disease	□ oui □ non

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3. Patients with an age ≥ 18 years old	□ oui □ non
4. Patients who are human leukocyte antigen (HLA)-A2 positive	□ oui □ non
5. Patients with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 or Karnofsky performance status ≥ 70	□ oui □ non
6. Patients should have received standard primary therapy, including surgery (biopsy, incomplete or complete resection), radiation, temozolomide, if applicable 1. Radiation therapy must have been finished 28 days before first study treatment administration 2. Patients who received temozolomide as adjuvant therapy must have stopped the treatment and have a wash-out period of 28 days before first study treatment administration (6 weeks for nitrosoureas and 5 half lives for experimental therapies) 3. Patients with unmethylated methylguanine-DNA-methyltransferase (MGMT) promoter can be included even if they have not received temozolomide prior to the inclusion in this clinical study)	□ oui □ non
7. Female patients of childbearing potential must have a negative serum pregnancy test within 72 hours prior to dosing	□ oui □ non

8. Considering the embryofetal toxicity of the nivolumab shown on animals' models, the following recommendations for contraception must be followed: a. If not surgically sterile, female patients of childbearing potential age must use highly effective contraception from signing the Informed Consent Form (ICF) through 6 months after the last treatment dose administered. Highly effective contraception included: i. Combined (estrogen and progesterone containing) hormonal contraception associated with inhibition of ovulation: Oral Intravaginal Transdermal ii. Progestogen-only hormonal contraception associated with inhibition of ovulation: Oral Injectable Implantable iii. Intrauterine device iv. Intrauterine hormone-releasing system v. Bilateral tubal occlusion vi. Sexual abstinence. In each case of delayed menstrual period (over 1 month between menstruations), confirmation of absence of pregnancy is strongly recommended. This recommendation also applies to women of childbearing potential with infrequent or irregular menstrual cycles. b. If not surgically sterile, male with female partner of childbearing potential must use condom from signing the ICF through 8 months after the last treatment dose administered. Males must ensure that their partners of childbearing potential use highly effective contraception also.	□ oui □ non
9. Patients having received the information sheet and who have provided written informed consent prior to any study-related procedures	□ oui □ non
10. Patients willing and able to comply with the scheduled visits, treatment plan, laboratory tests, and other study procedures indicated in the protocol.	□ oui □ non

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Critères de non inclusion

1. Patients treated with dexamethasone > 2 mg/day or equivalent (i.e., 13 mg/day of prednisone) within 14 days before the first EO2401 administration, unless required to treat an adverse event (AE) Note: The criterion implios the patient should not receive treatment with dexamethasone > 2 mg/day or equivalent at the actual time of a screening visit (single time point assessment), and within 14 days before the first EO2401 administration (unless required to treat AE); the latter part of the criterion should be checked at the time of treatment start.	□ oui □ non
2. Patients treated with radiotherapy, and cytoreductive therapy within 28 days (6 weeks for nitrosoureas) before the first EO2401 administration. In addition, patients should not have received any prior treatment with compounds targeting PD-1, PD-L1, CTLA-4, or similar compounds where general resistance against therapeutic vaccination approaches might have developed; also, patients should not have received systemic anti-tumor treatment or radiotherapy for their progressive or first recurrent GB	□ oui □ non
3. Patients with tumors primarily located in the infra-tentorial segment	□ oui □ non
4. Patients with known radiological evidence of extracranial metastases	□ oui □ non
5. Patients with presence of new hemorrhage (excluding, stable Grade 1) or uncontrolled seizure	□ oui □ non
6. Patients with significant leptomeningeal disease	□ oui □ non
7. Patients with abnormal (≥ Grade 2 National Cancer Institute-Common Terminology Criteria for AEs [NCI-CTCAE] version 5.0) laboratory values for hematology, liver, and renal function (serum creatinine). In detail, the following values apply as exclusion criteria: 1. Hemoglobin < 10 g/dL (6.2 mmol/L) 2. White blood cell count decrease (< 3.0 × 109/L) or increase (> 10.0 × 109/L) 3. Absolute neutrophil count decrease (< 1.5 × 109/L) 4. Platelet count decrease (< 75 × 109/L)	□ oui □ non

5. Bilirubin > 1.5 × upper limit of normal (ULN; according to the performing laboratory's reference ranges)); Note, benign hereditary hyperbilirubinemia, e.g. Gilbert's syndrome is permitted. 6. Alanine aminotransferase > 3 × ULN 7. Aspartate aminotransferase > 3 × ULN 8. Gamma-glutamyltransferase > 2.5 × ULN 9. Serum creatinine increase (> 1.5 × ULN) 10. Abnormal thyroid function: 0.3 > thyroid-stimulating hormone > 5 µU(µunit)/mL and 8.6 > free T4 > 25 pmol/L.	
8. For patients who are planned to receive bevacizumab: 1. Patients with nephrotic syndrome 2. Patients with proteinuria ≥ 2g/24 hours 3. Patients with history or active gastrointestinal perforation and fistula 4. Significant surgical procedure in the 4 weeks preceding the start of treatment or planned surgery 5. Unhealed wound 6. Patient with recent (4 weeks) history of hemoptysis of ½ teaspoon or more of red blood 7. Thrombotic episode within 6 months 8. Uncontrolled diabetes mellitus or hypertension 9. Posterior reversible encephalopathy syndrome	□ oui □ non
9. Patients with persistent Grade 3 or 4 toxicities (according to NCI-CTCAE v5.0). Toxicities must be resolved since at least 2 weeks to Grade 1 or less. However, alopecia or other persisting toxicities Grade ≤ 2 not constituting a safety risk based on Investigator's judgment is acceptable	□ oui □ non
10. Patients with contraindication to contrast-enhanced MRI	□ oui □ non
11. Other malignancy or prior malignancy with a disease-free interval of less than 3 years except those treated with surgical intervention and an expected low likelihood of recurrence	□ oui □ non

such as basal cell or squamous cell skin cancer, or carcinoma in situ. Patients with adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ are eligible	
12. Patients with clinically significant active infection, cardiac disease, significant medical or psychiatric disease/condition that, in the opinion of the Investigator, would interfere with the evaluation of EO2401 or interpretation of patient safety or study results or that would prohibit the understanding or rendering of informed consent (i.e. only consent able patients can be enrolled in the study) and compliance with the requirements of the protocol - including (but not limited to): a. Bacterial sepsis or other similarly severe infections b. New York Heart Association > Grade 2 congestive heart failure within 6 months prior to study entry c. Uncontrolled or significant cardiovascular disease, including: i. Myocardial infarction within 6 months prior to obtaining informed consent ii. Uncontrolled/unstable angina within 6 months prior to obtaining informed consent iii. Diagnosed or suspected congenital long QT syndrome iv. Any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or Torsades de pointes) d. Stroke within 6 months prior obtaining informed consent e. Concurrent neurodegenerative disease f. Dementia or significantly altered mental status.	□ oui □ non
13. Patients with suspected autoimmune or active autoimmune disorder or known history of an autoimmune neurologic condition (e.g., Guillain-Barré syndrome) Note, patients with vitiligo, type I diabetes mellitus, hypothyroidism due to autoimmune condition only requiring hormone replacement therapy, psoriasis not requiring systemic therapy, or conditions not expected to recur in the absence of an external trigger are permitted to enroll	□ oui □ non
14. Patients with history of solid organ transplantation or hematopoietic stem cell transplantation	□ oui □ non
15. Patients with history or known presence of tuberculosis	□ oui □ non
16. Pregnant and breastfeeding patients	□ oui □ non

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.	□ oui □ non
17. Patients with history or presence of human immunodeficiency virus and/or potentially active hepatitis B virus/hepatitis C virus	
18. Patients who have received live or attenuated vaccine therapy used for prevention of infectious diseases including seasonal (influenza) vaccinations within 4 weeks of the first dose of study drug	□ oui □ non
19. Patients with a history of hypersensitivity to any excipient present in the pharmaceutical form of investigational medicinal product	□ oui □ non
20. Patients under treatment with immunostimulatory or immunosuppressive medications, including herbal remedies, or herbal remedies known to potentially interfere with major organ function	□ oui □ non
21. Patients with known drug and alcohol abuse	□ oui □ non
22. Patients with known or underlying medical or psychiatric condition that, in the Investigator's opinion, would make the administration of study drug hazardous to the patient or obscure the interpretation of toxicity determination or AEs	□ oui □ non
23. Patients who have received treatment with any other investigational agent, or participation in another clinical trial (clinical trial including active interventions are prohibited; participation in clinical trials for data collection purposes only are permitted) within 28 days prior to first study treatment administration and during the treatment period. Note, for investigational agents there should be a wash-out period of at least 28 days, or 5 half-lives if longer, before first study treatment administration	□ oui □ non
24. Patients deprived of their liberty or under protective custody or guardianship..	□ oui □ non

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Date : _____

Signature de l'investigateur : _____