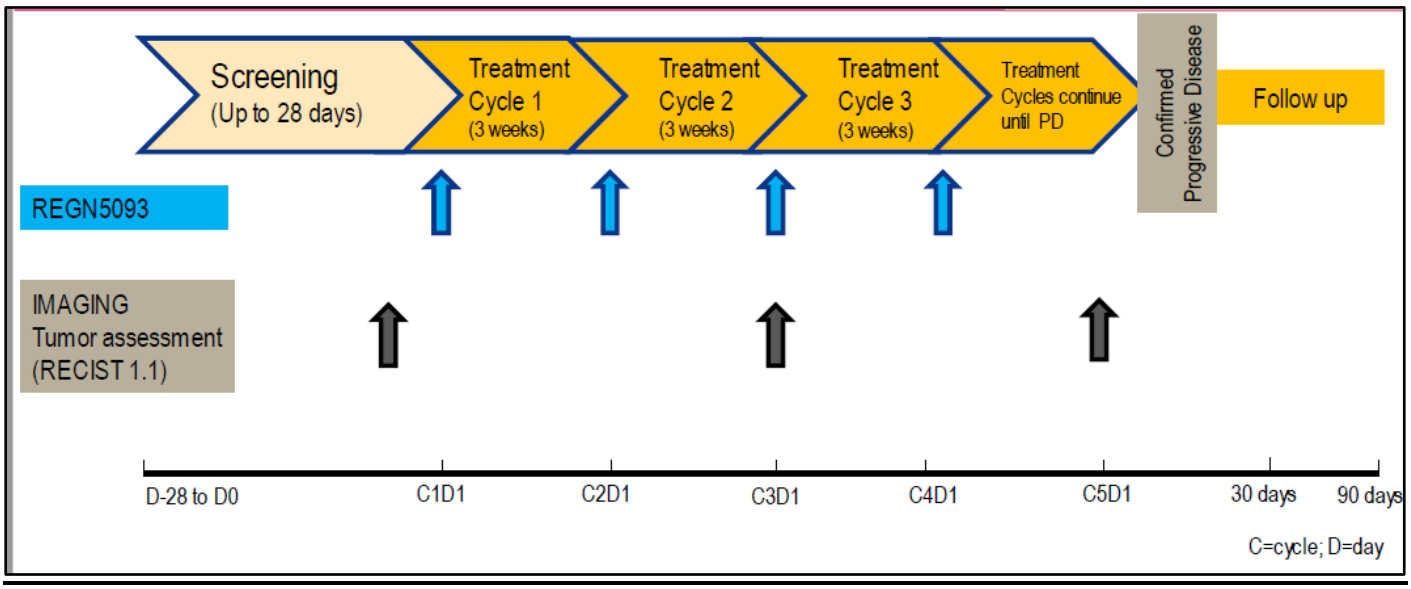
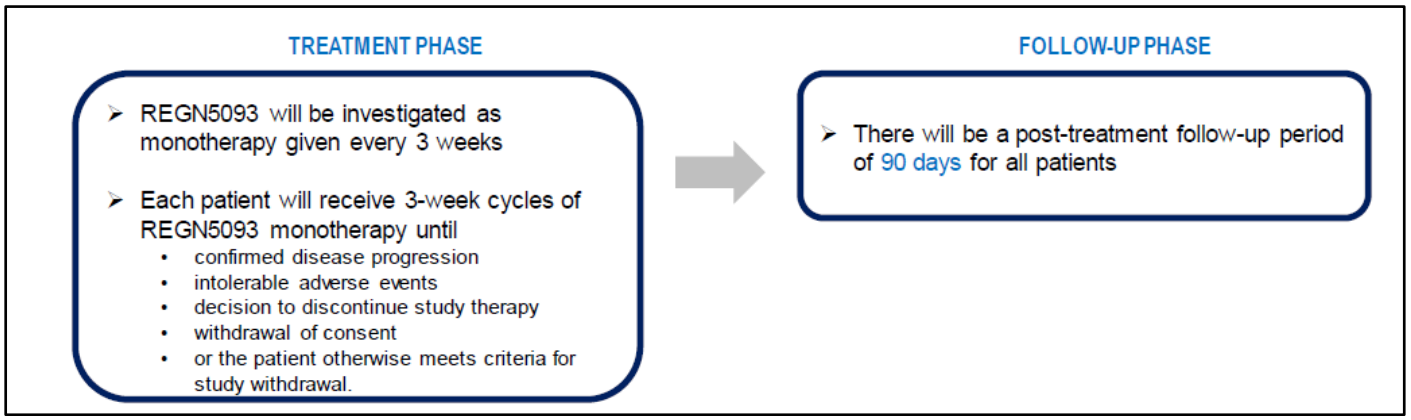
	CRITERES DE SELECTION **ETUDE R5093-ONC-1863 REGENERON**	Identité patient (coller étiquette patient)
Version 1.0 du 26/10/2021	Investigateur en charge du patient : …….. PI : **Dr Jean David FUMET** Mail : jdfumet@cgfl.fr *A contacter pour adresser/inclure patient externe au CGFL*	Arc : **Hélène DUROUX** Poste : 3460

« REGENERON »

Etude de phase I/II portant sur REGN5093 chez des patients atteints d'un cancer du poumon non à petites cellules avancé avec altération de MET





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VALIDATION DES CRITERES DE SELECTION

Critères d'inclusion :

1/ Histologically confirmed NSCLC that is at advanced stage and for which there is no standard therapy option likely to convey clinical benefit. Advanced is defined as unresectable or metastatic disease. Patients must have exhausted all approved available therapies appropriate for the patient	□ oui □ non
2/ Has available archival tumor tissue, unless discussed with the medical monitor	□ oui □ non
3/ Previously documented presence of: a. For dose escalation cohorts: either MET-exon14 gene mutation and/or MET gene amplification (by any local CLIA laboratory MET amplification call), and/or elevated MET protein expression (IHC ≥2+ or H score of >150) b. For dose expansion cohorts 1 A and 1B: MET exon 14-mutation; MET TKI experienced or no prior MET TKI, respectively c. for dose expansion cohort 2A : MET gene highly amplified (MET/CEP7 ratio ≥4 or MET gene fold change of ≥2* or MET fold change ≥2 in ctDNA ; or MET GCN ≥6) ; no prior MET TKI d. For dose expansion cohort 2B: MET protein highly overexpressed (IHC 3+ or H score of ≥200) ; no prior MET TKI e. for dose expansion cohort 2C : MET gene highly amplified (MET/CEP7 ratio ≥4 by MET gene fold change of ≥2* or MET fold change >2 in ctDNA ; or MET GCN ≥6) and MET protein highly overexpressed (IHC 3+ or H score of ≥200) ; no prior MET TKI *if >40% tumor content in biopsy is observed then FISH or ctDNA local results must be in the range specified f. placeholder for deleted inclusion criteria	□ oui □ non
4/Willing to provide tumor tissue from newly obtained biopsy. Newly obtained biopsies at screening are required unless medically contra indicated and discussed with the medical monitor. For patients in expansion cohorts, biopsies should be taken from tumor site which has not been irradiated previously and is not the only measurable target lesion	□ oui □ non
5/For expansion cohorts only: At least 1 lesion that is measurable by RECIST 1.1. Tumor lesions in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions after radiation.	□ oui □ non

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6/Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1	□ oui □ non
7/Adequate organ and bone marrow function documented by: a. Hemoglobin ≥9.0 g/dL b. Absolute neutrophil count ≥1.5 x 109/L c. Platelet count ≥75 x 109/L d. Either serum creatinine ≤1.5 x ULN or estimated glomerula filtration rate (GFR) ≥30mL/min/1.73m2 e. Adequate hepatic function: − Total bilirubin ≤1.5 x ULN (≤3 x ULN if tumor liver involvement) − AST ≤2.5 x ULN (≤5 x ULN if tumor liver involvement) − ALT ≤2.5 x ULN (≤5 x ULN if tumor liver involvement) − Alkaline Phosphatase ≤2.5 x ULN (≤5 x ULN if tumor liver or bone involvement) NOTES: a. Patients with tumor liver involvement if levels of AST ≥3 x ULN or ALT ≥3 x ULN, and bilirubin levels ≥2 x ULN, will be excluded regardless of the above criteria. b. Patients with Gilbert's syndrome do not need to meet total bilirubin requirements provided their total bilirubin is not greater than their historical level. Gilbert's syndrome must be documented appropriately as past medical history.	□ oui □ non
8/Adult patients ≥18 years of age (or the legal age of adults to consent to participate in a clinical study per country-specific regulations).	□ oui □ non
9/Willing and able to comply with clinic visits and study-related procedures and requirements	□ oui □ non
10/Must be willing and able to provide informed consent as specified by health authorities and institutional guidelines	□ oui □ non
11/Provide informed consent signed by study patient or legally acceptable representative	□ oui □ non

Critères de non inclusion :

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1/Has received treatment with an approved systemic therapy or has participated in any study of an investigational agent or investigational device according to the following timeframe: − For small molecule cytotoxins or other agents unlikely to interact with study drug: within 2 weeks or 5 half-lives of the prior treatment whichever is shorter with a minimum of 7 days from the first dose of study therapy. − Exception: Patients who have received or are enrolled in a study involving treatment with an investigational immunoPET reagent are not excluded	□ oui □ non

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2/Has not yet recovered (ie, grade ≤1 or baseline) from any acute toxicities resulting from prior therapy except for laboratory changes as described in inclusion criteria and patients with grade ≤2 neuropathy. NOTE: Endocrine immune-mediated AEs controlled with hormonal or other nonimmunosuppressive therapies (without resolution) or grade 1 irAEs affecting any organ system with resolution prior to enrollment are allowed	□ oui □ non
3/Has received radiation therapy or major surgery within 14 days of first administration of study drug or has not recovered (ie, grade ≤1 or baseline) from AEs, except for laboratory changes as described in inclusion criteria and patients with grade ≤2 neuropathy	□ oui □ non
4/For expansion cohorts only: prior treatment with MET-targeted biologic therapy (functionblocking antibodies or ADCs). In addition, for expansion cohorts 1B, 2A, 2B, and 2C,prior treatment with any MET-targeted agent including small molecule tyrosine kinase inhibitors eg, crizotinib, capmatinib, tepotinib	□ oui □ non
5/For expansion cohorts only: Another malignancy, with the following exceptions: a. Non-melanoma skin cancer that has undergone potentially curative therapy or b. In situ cervical carcinoma or c. Any other tumor that has been treated, and the patient is deemed is be in complete remission for at least 2 years prior to enrollment and no additional therapy is required during the study period	□ oui □ non
6/Untreated or active primary brain tumor, CNS metastases, leptomeningeal disease or spinal cord compression − Exception: Patients with previously treated central nervous system metastases or spinal cord compression may participate provided: − No evidence of progression for at least 2 weeks prior to the first dose of study therapy, and any neurologic symptoms have returned to baseline	□ oui □ non
7/Encephalitis, meningitis, organic brain disease (eg, Parkinson's disease), or uncontrolled seizures in the year prior to first dose of study therapy	□ oui □ non
8/Uncontrolled infection with human immunodeficiency virus, hepatitis B or hepatitis C infection; or diagnosis of immunodeficiency NOTES: • Patients with known HIV infection who have controlled infection (undetectable viral load [HIV RNA PCR] and CD4 count above 350 either spontaneously or on a stable antiviral regimen) are permitted. For patients with controlled HIV infection, monitoring will be performed per local standards. • Patients with known hepatitis B (HepBsAg+) who have controlled infection (serum hepatitis B virus DNA PCR that is below the limit of detection AND receiving anti-viral therapy for hepatitis B) are permitted. Patients with controlled infections must undergo periodic monitoring of HBV DNA.	□ oui □ non

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Patients must remain on anti-viral therapy for at least 6 months beyond the last dose of investigational study drug. • Patients who are known hepatitis C virus antibody-positive (HCV Ab+) who have controlled infection (undetectable HCV RNA by PCR either spontaneously or in response to a successful prior course of anti-HCV therapy) are permitted.	
9/ Any infection requiring hospitalization or treatment with IV anti-infectives within 2 weeks prior to first dose of study therapy.	□ oui □ non
10/Placeholder for deleted exclusion criteria	□ oui □ non
11/Placeholder for deleted exclusion criteria	□ oui □ non
12/Known psychiatric or substance abuse disorders that would interfere with participation with the requirements of the study	□ oui □ non
13/Any medical condition, co-morbidity, physical examination finding, or metabolic dysfunction, or clinical laboratory abnormality that, in the opinion of the investigator, renders the patient unsuitable for participation in a clinical trial due to high safety risks and/or potential to affect interpretation of results of the study	□ oui □ non
14/Women with a positive serum hCG pregnancy test at the screening/baseline visit. Breastfeeding women are also excluded	□ oui □ non
15/Women of childbearing potential* or men who are unwilling to practice highly effective contraception prior to the initial dose/start of the first treatment, during the study, and for at least 6 months after the last dose. Highly effective contraceptive measures include: a. Stable use of combined (estrogen- and progestogen-containing) hormonal contraception (oral, intravaginal, transdermal) or progestogen-only hormonal contraception (oral, injectable, implantable) associated with inhibition of ovulation initiated 2 or more menstrual cycles prior to screening b. Intrauterine device (IUD); intrauterine hormone-releasing system (IUS) c. Bilateral tubal ligation	□ oui □ non

d. Vasectomized partner (provided that the male vasectomized partner is the sole sexual partner of the study participant and that the partner has obtained medical assessment of surgical success for the procedure) e. And/or sexual abstinence *Women of childbearing potential are defined as women who are fertile following menarche until becoming post-menopausal, unless permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. A post-menopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle stimulating hormone (FSH) level in the post-menopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient to determine the occurrence of a post-menopausal state. The above definitions are according to Clinical Trial Facilitation Group (CTFG) guidance. Pregnancy testing and contraception are not required for women with documented hysterectomy or tubal ligation. † Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study drugs. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient. ‡ Periodic abstinence (calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method (LAM) are not acceptable methods of contraception. Female condom and male condom should not be used together	

Date : _____ Signature de l'investigateur : _____