# Clinical Trials Data EGFR - Document 37

# Selumetinib in Combination With Gefitinib in NSCLC Patients

## Clinical Trial: https://clinicaltrials.gov/study/NCT02025114

"eligibilityCriteria": "Inclusion Criteria:\n\n1. Written informed consent obtained prior to any screening procedures.\n2. \u226520 years of age.\n3. Must have discontinued any previous anti-cancer and investigational therapy (excluding EGFR TKI) for at least 28 days or radiotherapy \u226514 days before study treatment administration, and must have recovered to Grade 1 from the adverse effects of such treatment before starting study treatment.\n4. Life expectancy \u22653months.\n5. ECOG performance status: 0-1.\n6. Female patients of child-bearing potential should have a negative pregnancy test.\n7. Required baseline laboratory status:\n\n(1) Hemoglobin\\>9g/dL. (2) Platelet count\u2265100x109/L. (3) Absolute neutrophil count (ANC)\u22651.5x109/L without growth factor support. (4) Total bilirubin 1.5x upper limit of normal (ULN). (5) AST/SGOT and/or ALT/SGPT 2.5x ULN. (6) Serum creatinine clearance \\>50 ml/min, by either Cockcroft-Gault formula or by 24-hour urine collection analysis.\n\n8. Willing and able to comply with scheduled visits, treatment plan and laboratory tests.\n\n9. In phase Ib part, lung cancer patients with disease progression after EGFR TKI and at least one line of chemotherapy. If less than 70 years of age, a platinum-based regimen must be included.\n\n10. In phase II part, patients must be willing to perform a re-biopsy of the tumor at the time of study entrance and meet definition of acquired resistance criteria of Jackman's as follows:\n\n(1) Previous treatment with EGFR TKI (gefitinib, erlotinib, afatinib, dacomitinib, AZD9291, or any EGFR TKI under investigation).\n\n(2) Either or both of the followings:\n\n1. A tumor harboring an EGFR mutation known to be associated with drug sensitivity (ie, exon 19 deletion , L858R, L861Q, G719X etc.).\n2. Objectively clinical benefit from treatment with EGFR TKI as defined by either: Documented partial or complete response (RECIST or WHO) or Significant and durable(\u2265 6months) clinical benefit (stable disease as defined by RECIST or WHO) after initiation of EGFR TKI.\n\n (3) Systemic progression of disease (RECIST or WHO) while on continuous treatment with EGFR TKI within the last 30 days.\n\n (4) No intervening systemic therapy between cessation of EGFR TKI and initiation the study treatment.\n\n Exclusion Criteria:\n 1. Unable or unwilling to swallow capsules once or twice daily.\n 2. Patients who had discontinued previous gefitinib treatment due to intolerance of side effects (such as diarrhea \u2265CTCAE Grade 2, intolerable skin rash, ILD or AST/ALT elevation \u2265 CTCAE Grade 3).\n 3. Previous treatment of MEK, Ras, or Raf inhibitors or history of hypersensitivity to selumetinib, or any excipient agents.\n 4. Symptomatic CNS metastases which are neurologically unstable or requiring increasing doses of steroids to control the CNS condition.\n 5. Radiation therapy within 4 weeks prior to the first dose of study drug or limited field radiotherapy within 2 weeks prior to the start of study treatment. Any persistent side effect of prior radiotherapy must be resolved to Grade 1 prior to the first dose of study treatment.\n 6. Any unresolved toxicity from previous anticancer therapy \\> Grade 1.\n 7. Currently receiving any prohibited medications including vitamins supplements, and herbal supplements. Refer to Table 6.5 for a list of excluded medication.\n 8. Unable to undergo an MRI or contrast CT procedures.\n 9. Active HBV or HCV infection, HBV carrier can be enrolled if HBV DNA titer is low under antiviral treatment.\n 10. Known history of HIV seropositivity. HIV testing is not required as part of this study.\n 11. Undergone a bone marrow or solid organ transplant.\n 12. Another malignancy diagnosed or treated within 5 years, except carcinoma in situ or skin cancer.\n 13. Major surgery within 4 weeks prior to initiating study treatment, excluding the placement of vascular access.\n 14. Cardiac conditions as follows:\n\n <!-- -->\n\n 1. Uncontrolled hypertension (BP \u2265150/95 mmHg despite medical therapy).\n 2. Left ventricular ejection fraction \\<55% measured by echocardiography.\n 3. Atrial fibrillation with a ventricular rate \\>100 bpm on ECG at rest.\n 4. Symptomatic heart failure (NYHA grade II-IV), see Appendix A.\n 5. Prior or current cardiomyopathy.\n 6. Severe valvular heart disease.\n 7. Uncontrolled angina (Canadian Cardiovascular Society grade II-IV despite medical therapy), see Appendix A.\n 8. Acute coronary syndrome within 6 months prior to starting treatment\". 15. Ophthalmological conditions as follows:\n\n <!-- -->\n\n 1. Intra-ocular pressure \\>21 mmHg, or uncontrolled glaucoma (irrespective of intra-ocular pressure).\n 2. Current or past history of central serous retinopathy or retinal vein occlusion.\n\n 16. Past medical history of interstitial lung disease, drug-induced interstitial disease, radiation pneumonitis which required steroid treatment, pre-existing idiopathic pulmonary fibrosis or any evidence of clinically active interstitial lung disease.\n\n 17. Pregnant or lactating women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test (\\>5mIU/mL).\n\n 18. Women of child-bearing potential, defined as all women physically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 30 more days after stopping study drug.\n\n 19. Women are considered post-menopausal and not of child baring potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.\n\n 20. Sexually active males must use a condom during intercourse while taking the drug and for 30 more days after stopping study drug and should not father a child in this period. A condom is required to be used also by a vasectomized men in order to prevent delivery of the drug via seminal fluid.\n\n 21. Any other condition that would, in the Investigator's judgment, contraindicate patient's participation in the clinical study due to safety concerns or compliance with clinical study procedures, e.g. infection/inflammation, intestinal obstruction, unable to swallow medication, social/psychological issues, etc.",  
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Question:  
Based on the following clinical trial information, would a patient with a EGFR gene mutation be eligible for the clinical trial?

Answer:  
Yes, a patient with an EGFR gene mutation \*could\* be eligible for this trial, specifically the Phase II portion. The inclusion criteria for Phase II explicitly state:  
  
\* \*\*Requirement for EGFR Mutation & Prior TKI Benefit:\*\* The patient must have a tumor harboring an EGFR mutation known to be associated with drug sensitivity (exon 19 deletion, L858R, L861Q, G719X etc.) AND have experienced clinical benefit from prior EGFR TKI treatment.  
\* \*\*Progression on TKI:\*\* The patient must have experienced disease progression while on continuous treatment with an EGFR TKI within the last 30 days.  
\* \*\*No Intervening Therapy:\*\* There should be no other systemic therapy between stopping the EGFR TKI and starting the study treatment.  
  
\*\*Important Considerations:\*\*  
  
\* \*\*Meeting all other criteria:\*\* Even with an EGFR mutation and prior TKI therapy, the patient must \*also\* meet all other inclusion criteria (age, performance status, lab values, etc.) and \*not\* meet any of the exclusion criteria. The exclusion criteria are extensive and could disqualify a patient even if they have the required mutation.  
\* \*\*Re-biopsy:\*\* The patient must be willing to undergo a tumor re-biopsy upon entering the study.  
\* \*\*Phase Ib Ineligibility:\*\* The Phase Ib portion of the trial requires progression \*after\* EGFR TKI therapy \*and\* at least one line of chemotherapy. A patient solely progressing on a TKI would not be eligible for this phase.  
  
In summary, the presence of an EGFR mutation is a necessary but not sufficient condition for eligibility. A thorough review of all inclusion and exclusion criteria by a qualified medical professional is essential to determine a patient's suitability for this trial.