# Clinical Trials Data KRAS - Document 19

# Trametinib With or Without GSK2141795 in Treating Patients With Recurrent or Persistent Endometrial Cancer

## Clinical Trial: https://clinicaltrials.gov/study/NCT01935973

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Patients must have recurrent or persistent endometrial carcinoma, which is refractory to curative therapy or established treatments; histologic confirmation of the original primary tumor is required\n\n \* Patients with the following histologic epithelial cell types are eligible: endometrioid adenocarcinoma, serous adenocarcinoma, undifferentiated carcinoma, mixed epithelial carcinoma, uterine clear cell carcinoma, and adenocarcinoma not otherwise specified (N.O.S.)\n\* Formalin-fixed, paraffin-embedded tumor tissue must be submitted to Baylor College of Medicine (BCM) - Cancer Genetics Laboratory for Clinical Laboratory Improvement Amendments (CLIA)-certified KRAS mutation testing; results must be reported on the eligibility checklist during registration in order to receive treatment assignment\n\n \* Note: if CLIA-certified KRAS mutation tumor testing is available from local or other source (e.g., Foundation Medicine) this report can be submitted to Statistical and Data Center (SDC) to meet this requirement\n\* All patients must have measurable disease; measurable disease is defined by Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1); measurable disease is defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded); each lesion must be \\>= 10 mm when measured by computed tomography (CT), magnetic resonance imaging (MRI) or caliper measurement by clinical exam; or \\>= 20 mm when measured by chest x-ray; lymph nodes must be \\>= 15 mm in short axis when measured by CT or MRI\n\* Patients must have at least one \"target lesion\" to be used to assess response on this protocol as defined by RECIST version 1.1; tumors within a previously irradiated field will be designated as \"non-target\" lesions unless progression is documented or a biopsy is obtained to confirm persistence at least 90 days following completion of radiation therapy\n\* Gynecologic Oncology Group (GOG) performance status of 0 or 1\n\* Recovery from effects of recent surgery, radiotherapy, or chemotherapy\n\* Patients should be free of active infection requiring antibiotics (with the exception of uncomplicated urinary tract infection \\[UTI\\])\n\* Any hormonal therapy directed at the malignant tumor must be discontinued at least one week prior to registration\n\* Any other prior therapy directed at the malignant tumor, including chemotherapy and immunotherapy, must be discontinued at least three weeks prior to registration; any investigational agent must be discontinued at least 30 days prior to registration\n\* Any prior radiation therapy must be discontinued at least four weeks prior to registration\n\* At least 4 weeks must have elapsed since the patient underwent any major surgery (e.g., major: laparotomy, laparoscopy); there is no delay in treatment for minor procedures (e.g., tumor core biopsy)\n\* Patients must have had one prior chemotherapeutic regimen for management of endometrial carcinoma; initial treatment may include chemotherapy, chemotherapy and radiation therapy, or consolidation/maintenance therapy; chemotherapy administered in conjunction with primary radiation as a radio-sensitizer WILL be counted as a systemic chemotherapy regimen\n\* Patients are allowed to receive, but are not required to receive, one additional cytotoxic regimen for management of recurrent or persistent disease\n\* Patients MAY HAVE received non-cytotoxic (biologic or targeted) agent(s) as part of initial treatment and/or for management of recurrent or persistent disease, with the below stated exceptions (see NOTE below); prior hormonal therapy is allowed, but must be discontinued at least one week prior to registration\n\n \* NOTE: Prior therapy with PI3K inhibitors, AKT inhibitors and/or mammalian target of rapamycin (mTor) inhibitors (e.g., everolimus, temsirolimus) is NOT allowed; prior therapy with MEK inhibitors (e.g., AZD6244 or selumetinib) is NOT allowed\n\* Absolute neutrophil count (ANC) \\>= 1,500/mcl\n\* Platelets \\>= 100,000/mcl\n\* Hemoglobin \\>= 9 g/dl\n\* Creatinine =\\< 1.5 x institutional/laboratory upper limit of normal (ULN) OR calculated creatinine clearance (Cockcroft-Gault formula) \\>= 50 ml/min OR 24-hour urine creatinine clearance \\>= 50 ml/min\n\* Bilirubin =\\< 1.5 x ULN\n\* Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) =\\< 2.5 x ULN\n\* Alkaline phosphatase =\\< 2.5 x ULN\n\* Albumin \\>= 2.5 g/dL\n\* Fasting glucose \\< 160 mg/dL\n\* Hemoglobin A1C (HbA1C) =\\< 8 if patient has diabetes\n\* Thyroid-stimulating hormone (TSH) within institutional/laboratory normal limits\n\* Left ventricular ejection fraction (LVEF) greater than or equal to institutional/laboratory lower limit of normal (LLN) by echocardiogram (ECHO) or multi gated acquisition scan (MUGA)\n\* International normalized ratio (INR) and partial thromboplastin time (PTT) =\\< 1.5 x ULN\n\* For patients on Coumadin, INR/prothrombin time (PT)/PTT must be \\> 1.5 ULN\n\* Hemodynamic parameters:\n\n \* Systolic blood pressure \\< 140 mmHg\n \* Diastolic blood pressure \\< 90 mmHg\n\* All prior treatment-related toxicities must be CTCAE v4 grade =\\< 1 (except alopecia) at the time of randomization\n\* Patients with abnormal fasting glucose values at screening will be excluded (fasting glucose \\>= 160); in addition, patients with type 1 diabetes will also be excluded; however, patients with type 2 diabetes will be allowed if diagnosed \\>= 6 months prior to enrollment, and if presenting with hemoglobin A1C (HbA1C) =\\< 8% at screening\n\* Patients must be able to swallow and retain orally-administered medication and must not have any clinically significant gastrointestinal abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels\n\* Women of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation AND for 4 months following discontinuation; women of child-bearing potential must have a negative serum pregnancy test within 14 days prior to randomization; should a woman become pregnant or suspect she is pregnant while she is participating in this study, she should inform her treating physician immediately\n\* Patients must meet pre-entry requirements as specified\n\* Patients must have signed an approved informed consent and authorization permitting release of personal health information\n\nExclusion Criteria:\n\n\* Patients who have had prior therapy with GSK2141795 or any other PI3K/AKT/MTOR pathway inhibitor\n\* Patients who have prior therapy with trametinib or any other MEK inhibitor\n\* Patients who have mucinous, squamous, sarcomas, or carcinosarcomas\n\* Patient with a history of other invasive malignancies, with the exception of non-melanoma skin cancer are excluded if there is any evidence of other malignancy being present within the last three years; patients are also excluded if their previous cancer treatment contraindicates this protocol eligibility\n\* Patients with symptomatic or untreated leptomeningeal or brain metastasis or spinal cord compression\n\* Patients with a history of interstitial lung disease or pneumonitis\n\* Patients with known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the trametinib, GSK2141795 or dimethyl sulfoxide (DMSO)\n\* Current use of a prohibited medication; the following medications or non-drug therapies are prohibited:\n\n \* Other anti-cancer therapy while on study treatment\n \* Concurrent treatment with bisphosphonates is permitted; however, treatment must be initiated prior to the first dose of study therapy; prophylactic use of bisphosphonates in patients without bone disease is not permitted, except for the treatment of osteoporosis\n \* The concurrent use of all herbal supplements is prohibited during the study (including, but not limited to, St. John's Wort, kava, ephedra \\[ma huang\\], gingko biloba, dehydroepiandrosterone \\[DHEA\\], yohimbe, saw palmetto, or ginseng)\n\* Drugs that potently inhibit cytochrome P450 family 3, subfamily A, polypeptide 4 (CYP3A4) should be prohibited or used with caution; drugs which are strong inducers of CYP3A and may result in lower exposures of GSK2141795 should also be prohibited; drugs that are substrates of CYP3A4 or cytochrome P450 family 2, subfamily C, polypeptide 8 (CYP2C8) with a narrow therapeutic index may be prohibited; drugs that are sensitive substrates of CYP3A4 or CYP2C8 should be used with caution\n\n \* Caution should be exercised when dosing trametinib concurrently with medications with narrow therapeutic windows that are substrates of CYP2C8; drugs that potently inhibit or induce CYP3A4 should be administered with caution\n \* Because the lists of these agents are constantly changing, it is important to regularly consult a frequently-updated list such as http://medicine.iupui.edu/clinpharm/ddis/table.aspx; medical reference texts such as the Physicians' Desk Reference may also provide this information; as part of the enrollment/informed consent procedures, the patient will be counseled on the risk of interactions with other agents, and what to do if new medications need to be prescribed or if the patient is considering a new over-the-counter medicine or herbal product\n \* The following medications (including but not limited to) are prohibited during the study:\n\n \* PROHIBITED-highly sensitive and/or low therapeutic index\n\n \* Cisapride\n \* Pimozide\n \* Astemizole\n \* Rosuvastatin, sulfasalazine\n \* PROHIBITED-strong inducers/inhibitors of CYP3A4\n\n \* Clarithromycin, telithromycin, rifamycin class agents (e.g., rifampin, rifabutin, rifapentine), troleandomycin\n \* Itraconazole, ketoconazole\n \* Nefazodone\n \* Atazanavir, delavirdine, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, nevirapine\n \* Carbamazepine, phenobarbital, phenytoin\n \* The following medications (including but not limited to) that may alter the concentrations of trametinib or GSK2141795 or have their elimination altered by trametinib or GSK2141795 should be administered WITH CAUTION:\n\n \* USE WITH CAUTION-Drugs potentially affecting trametinib or GSK2141795 concentrations\n\n \* Quinidine, diltiazem, verapamil\n \* Fluvoxamine, fluoxetine, paroxetine, nefazodone\n \* Aprepitant, cimetidine\n \* Fluconazole, terbinafine, voriconazole\n \* Ciprofloxacin, erythromycin, isoniazid\n \* Mibefradil, diltiazem, verapamil\n \* Aprepitant, oxandrolone, tizanidine, gemfibrozil\n \* USE WITH CAUTION-Drugs that may inhibit permeability (P)-glycoprotein (gp) and breast cancer resistance protein (BCRP)\n\n \* Valspodar\n \* Atorvastatin\n \* Carvedilol\n \* Methadone\n \* Meperidine\n \* Omeprazole\n \* USE WITH CAUTION-Drugs that may have their concentrations altered by trametinib or GSK2141795\n\n \* Repaglinide, rosiglitazone, pioglitazone\n \* Alfentanil, fentanyl\n \* Quinidine\n \* Cilostazol\n \* Astemizole\n \* Diergotamine, ergotamine, eletriptan\n \* Pimozide\n \* Buspirone\n \* Felodipine\n \* Sildenafil, tadalafil, vardenafil\n \* Cerivastatin, lovastatin, simvastatin, atorvastatin\n \* Alprazolam, diazepam, midazolam, triazolam\n \* Cyclosporine, sirolimus, tacrolimus\n \* Cisapride\n \* Cyclosporine, torsemide, chloroquine, zopiclone\n \* Eplerenone\n \* Chloroquine, zopiclone\n \* Use of repaglinide, rosiglitazone and/or pioglitazone is permitted only after consultation with the Cancer Therapy Evaluation Program (CTEP) Medical Monitor\n\* Known hepatitis B virus (HBV) or hepatitis C virus (HCV) infection (unless cleared) will be excluded\n\* Human immunodeficiency virus (HIV)-positive patients on combination antiretroviral therapy are ineligible\n\* History or current evidence/risk of retinal vein occlusion (RVO)\n\* History or evidence of cardiovascular risk including any of the following:\n\n \* LVEF \\< LLN\n \* A QT interval corrected for heart rate using the Bazett's formula (QTcB) \\>= 480 msec\n \* History or evidence of current clinically significant uncontrolled arrhythmias (exception: patients with controlled atrial fibrillation for \\> 30 days prior to registration are eligible)\n \* History of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting within 6 months prior to registration\n \* History or evidence of current \\>= class II congestive heart failure as defined by the New York Heart Association (NYHA) functional classification system\n \* Treatment-refractory hypertension defined as a blood pressure of systolic \\> 140 mmHg or diastolic \\> 90 mmHg which cannot be controlled by anti-hypertensive therapy\n \* Patients with intra-cardiac defibrillators or permanent pacemakers\n \* Known cardiac metastases\n\* Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements\n\* Patients who are pregnant or nursing; women of childbearing potential should be advised to avoid pregnancy and use effective methods of contraception; if a patient becomes pregnant while the patient receives trametinib and/or GSK2141795, the potential hazard to the fetus should be explained to the patient",  
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Question:  
Based on the following clinical trial information, would a patient with a KRAS gene mutation be eligible for the clinical trial?

Answer:  
Based on the eligibility criteria provided for the clinical trial, a patient with a KRAS gene mutation would not be explicitly excluded from participating in the trial. The inclusion criteria specify that formalin-fixed, paraffin-embedded tumor tissue must be submitted for CLIA-certified KRAS mutation testing, but there is no indication that a positive result for a KRAS mutation itself would disqualify a patient from participating. The criteria do not state that the presence or absence of a KRAS mutation affects eligibility; rather, it seems that the testing is required for treatment assignment or further stratification within the trial.  
  
However, other inclusion and exclusion criteria must also be met for a patient to be eligible. It’s important to consider all other health conditions and previous treatments of the patient that might pertain to additional inclusion or exclusion criteria from the clinical trial.