# Clinical Trials Data BRAF - Document 26

# Selumetinib in Treating Young Patients With Recurrent or Refractory Low Grade Glioma

## Clinical Trial: https://clinicaltrials.gov/study/NCT01089101

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Imaging evaluations necessary to establish eligibility for study entry must be done within three (3) weeks prior to registration\n\* All other evaluations necessary to establish eligibility for study entry must be done within two (2) weeks prior to registration\n\* Patients must start therapy within 7 calendar days of registration\n\* Laboratory values must be no older than seven (7) days prior to the start of therapy; if a test that is repeated after registration and prior to therapy is outside the limits for eligibility, it must be rechecked within 48 hours prior to the start of therapy; if laboratory values still fail to meet eligibility criteria, the patient may not receive protocol therapy\n\* All patients must meet the following inclusion and exclusion criteria; NO EXCEPTIONS WILL BE GIVEN\n\* Participant is willing to sign a screening consent and provide adequate pre-trial tumor material for BRAF testing (both for BRAF V\\^600E mutation and BRAF KIAA1549 fusion assessments)\n\n \* All patients who are candidates for enrollment in stratum 5 based on their tumor histology must be pre-screened\n \* Screening may be applied to potential stratum 1 and 2 patients\n\* Patients whose prior BRAF testing was performed at another lab (Clinical Laboratory Improvement Amendments \\[CLIA\\]/College of American Pathologist \\[CAP\\] certified or otherwise) must send additional tumor material to Brigham and Women's Hospital (BWH) for confirmation; however, to preserve available tumor material, patients whose tumor material has previously undergone BRAF analysis at the Lindeman and Ligon Labs at Brigham and Women's Hospital using the same procedures as described in this protocol, will not be required to submit additional tumor material for analysis; these patients must have both the BRAFV600E mutation and BRAF KIAA1549 fusion assessments done and if only one test was previously conducted; additional tissue will be required for the second test\n\* Patient must be \\>= 3 but =\\< 21 years of age at registration\n\* Patient must have one of the following:\n\n \* For stratum 5: non NF-1 associated low grade glioma (LGG) (other than pilocytic astrocytoma or optic pathway glioma)\n \* For stratum 1 or 2: non NF-1, non-optic pathway pilocytic astrocytoma; note: all patients with non NF-1 associated optic pathway glioma with or without tissue must be enrolled on stratum 4\n\* Patients with sporadic (non NF-1 associated), histologically diagnosed progressive, recurrent or refractory non-optic pathway pilocytic astrocytoma who have pre- treatment tumor tissue available for BRAF analysis\n\* NF-1 patients with radiographic evidence of a progressive, recurrent or refractory low grade glioma, with or without pre-treatment tumor tissue\n\* Patients with progressive, recurrent or refractory optic pathway glioma, with or without pre-treatment tumor tissue\n\* Patients with histologically diagnosed progressive, recurrent or refractory non NF-1 associated LGG (other than pilocytic astrocytoma or optic pathway glioma); these patients must have BRAF aberrations as documented by the Lindeman and Ligon Labs at Brigham and Women's Hospital using the same procedures\n\* Patients will be assigned to one of 6 strata prior to enrollment; all BRAF assessments used for stratification below must be done at the Lindeman and Ligon Labs at Brigham and Women's Hospital using the same procedures as described in this protocol; assessments for both BRAF V\\^600E mutation and BRAF KIAA1549 fusion are required for patients who will enroll on strata 1, 2 and 5\n\n \* Stratum 1: patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and with a BRAF aberration i.e. BRAFV\\^600E mutation and/or BRAF KIAA1549 fusion as determined by IHC and FISH, respectively; patients with optic pathway glioma are excluded\n \* Stratum 2: patients with non NF-1 associated progressive, recurrent or refractory pilocytic astrocytoma with pre-trial tumor material available and without a BRAF aberration i.e. BRAF\\^V600E mutation and/or BRAF KIAA1549 fusion as determined by IHC and FISH, respectively; patients with optic pathway glioma are excluded\n \* Stratum 3: patients with neuro-fibromatosis 1 (NF-1) associated progressive, recurrent or refractory low grade glioma (World Health Organization \\[WHO\\] grade I \\& II), with or without tissue\n \* Stratum 4\\\*: patients with non-NF1 associated progressive, recurrent or refractory optic pathway glioma with or without tissue available for BRAF evaluation\n \* Stratum 5: patients with non NF-1 associated progressive, recurrent or refractory low grade glioma other than pilocytic astrocytoma or optic pathway glioma with a documented BRAF aberration identified in pre-trial tumor material\n \* Stratum 6: patients with non-NF-1 associated progressive, recurrent or refractory low grade glioma (other than optic pathway glioma \\[OPG\\]) with tissue available for BRAF analyses who cannot be classified into stratum 1, 2 or 5 due to inadequate tissue quality, assay failure, etc\n\n \* Clarification: Stratum 4 was specifically designed for patients with hypothalamic/optic pathway gliomas; the intent is that if there is any optic chiasm invasion regardless of where the tumor is originating from (chiasm vs. hypothalamus vs. other location), the patient should be enrolled on Stratum 4, regardless of whether the tumor has been biopsied or not; obviously, there are some tumors that include part of the hypothalamus and clearly do NOT include the chiasm at all; in these situations, and if the tumor is a biopsy proven pilocytic astrocytoma, these patients should be enrolled on Stratum 1 or 2 (depending upon BRAF status)\n\* Patients must have bi-dimensionally measurable disease defined as at least one lesion that can be accurately measured in at least two planes in order to be eligible for this study\n\* Patients must have received prior therapy other than surgery and must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, biologic therapy or radiotherapy prior to study entry\n\* Patients must have received their last dose of known myelosuppressive anticancer chemotherapy at least three weeks prior to study registration or at least six weeks if nitrosourea\n\* Patient must have received their last dose of the biologic agent \\>= 7 days prior to study registration\n\n \* For biologic agents that have a prolonged half-life, at least three half-lives must have elapsed prior to registration\n\* Monoclonal antibody treatment: at least three half-lives must have elapsed prior to registration\n\* Radiation: patients must have:\n\n \* Had their last fraction of local irradiation to primary tumor \\>= 12 months prior to registration; investigators are reminded to review potentially eligible cases to avoid confusion with pseudo-progression\n \* Had their last fraction of craniospinal irradiation (\\> 24 Gy) \\> 3 months prior to registration\n\* Corticosteroids: patients who are receiving dexamethasone must be on a stable or decreasing dose for at least 1 week prior to registration\n\* Patients must be off all colony-forming growth factor(s) for at least 1 week prior to registration (filgrastim, sargramostim, erythropoietin) and at least 2 weeks for long-acting formulations\n\* Patients must have a body surface area (BSA) \\>= 0.55 m\\^2\n\* Patients with neurological deficits should have deficits that are stable for a minimum of 1 week prior to registration\n\* Patients must be able to swallow capsules\n\* Karnofsky performance scale (KPS for \\> 16 years \\[yrs.\\] of age) or Lansky performance score (LPS for =\\< 16 years of age) \\>= 60 assessed within two weeks prior to registration\n\* Absolute neutrophil count \\>= 1,000/uL (unsupported) (within 14 days of registration and within 7 days of the start of treatment)\n\* Platelets \\>= 100,000/L (unsupported) (within 14 days of registration and within 7 days of the start of treatment)\n\* Hemoglobin \\>= 8 g/dL (may be supported) (within 14 days of registration and within 7 days of the start of treatment)\n\* Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \\[SGOT\\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \\[SGPT\\]) =\\< 2.5 X institutional upper limit of normal for age (within 14 days of registration and within 7 days of the start of treatment)\n\* Total bilirubin \\< 1.5 times upper limit of normal for age (within 14 days of registration and within 7 days of the start of treatment)\n\* Albumin \\>= 3 g/dL (within 14 days of registration and within 7 days of the start of treatment)\n\* Serum sodium and potassium within the institutional limits of normal (within 14 days of registration and within 7 days of the start of treatment)\n\* Serum calcium and magnesium above the institutional lower limit of normal (within 14 days of registration and within 7 days of the start of treatment)\n\* Creatinine clearance or radioisotope glomerular filtration rate (GFR) \\>= 70 ml/min/1.73m\\^2 or a serum creatinine based on age as follows (within 14 days of registration and within 7 days of the start of treatment):\n\n \* =\\< 5 years: 0.8 mg/dL\n \* \\> 5 years but =\\< 10 years: 1 mg/dL\n \* \\> 10 years but =\\< 15 years: 1.2 mg/dL\n \* \\> 15 years: 1.5 mg/dL\n\* Left ventricular ejection fraction (LVEF) \\>= 55%\n\* Corrected QT (QTc) interval =\\< 450 msecs\n\* Hypertension:\n\n \* Patients, 3-17 years of age must have a blood pressure that is =\\< 95th percentile for age, height and gender at the time of registration\n\n \* The normal blood pressure by height, age and gender tables can be accessed in the Generic Forms section of the Pediatric Brain Tumor Consortium (PBTC) members' webpage\n \* Patients who are \\>= 18 years of age must have a blood pressure that is \\< 140/90 mm of Hg at the time of registration\n \* Note: if a blood pressure (BP) reading prior to registration is above the 95th percentile for age, height and gender it must be rechecked and documented to be =\\< the 95th percentile for age, height and gender prior to patient registration\n\* Female patients of childbearing potential must not be pregnant or breast-feeding; female patients of childbearing potential must have a negative serum or urine pregnancy test\n\* The effects of AZD6244 on the developing human fetus are unknown; for this reason, women of child-bearing potential and men 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 four weeks after dosing with AZD6244 ceases; women of child-bearing potential must have a negative pregnancy test prior to entry; should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately; please note that the AZD6244 manufacturer recommends that adequate contraception for male patients should be used for 16 weeks post-last dose due to sperm life cycle\n\* Ability to understand and the willingness to sign a written informed consent document according to institutional guidelines\n\* ELIGIBILITY CRITERIA FOR ENROLLMENT ON THE RE-TREATMENT STUDY\n\* Patients must have recurrence or progression of their low-grade glioma after coming off treatment with AZD6244 on PBTC-029 or PBTC-029B, with or without having received additional anti-tumor therapy following discontinuation of AZD6244; the progression must be unequivocal and sufficient to warrant re-treatment in the opinion of the investigator; progression will be defined as either progressive disease (PD) that meets the study definitions of progressive disease by MRI or vision deterioration thought to be related to tumor in patients with optic pathway tumors\n\* Patients must have received treatment on PBTC-029 or PBTC-029B for a minimum of 12 courses with at least stable disease, or had a sustained response (partial response \\[PR\\]/ complete response \\[CR\\]) but remained on treatment \\< 12 courses\n\* Patients must have bi-dimensionally measurable disease defined as at least one lesion that can be accurately measured in at least two planes\n\* Patients must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, biologic therapy or radiotherapy prior to study entry\n\n \* Myelosuppressive chemotherapy: Patients must have received their last dose of known myelosuppressive anticancer chemotherapy at least three weeks prior to registration on the Re-treatment Study or at least six weeks if a nitrosourea\n \* Biologic agent: Patient must have received their last dose of the biologic agent \\>= 7 days prior to study registration; for biologic agents and monoclonal antibody treatment, at least three half-lives must have elapsed prior to registration\n \* Other investigational agents (not fitting into one of the above specified categories): patients must have received their last dose of any other investigational agent greater than 28 days prior to enrollment\n \* Radiation: Patients must have:\n\n \* Had their last fraction of local irradiation to the primary tumor \\>= 12 months prior to registration; investigators are reminded to review potentially eligible cases to avoid confusion with pseudo-progression;\n \* Had their last fraction of craniospinal irradiation (\\> 24Gy) \\> 3 months prior to registration\n \* Corticosteroids: Patients who are receiving dexamethasone must be on a stable or decreasing dose for at least 1 week prior to registration\n \* Growth factors: Patients must be off all colony-forming growth factor(s) for at least 1 week prior to registration (filgrastim, sargramostim, erythropoietin) and at least 2 weeks for long-acting formulations\n\nExclusion Criteria:\n\n\* Patients with any clinically significant unrelated systemic illness (serious infections or significant cardiac, pulmonary, hepatic or other organ dysfunction), likely interfere with the study procedures or results\n\* Patients taken off treatment for progressive disease on PBTC-029 or PBTC-029B\n\* Patients who are receiving any other anticancer or investigational agents\n\* Patients with uncontrolled seizures\n\* Previous mitogen-activated protein kinase (MEK) inhibitor use such as PD-0325901; CI1040; AS73026; GDC 0973; ARRY43182; GSK110212\n\* Prior treatment with a BRAF inhibitor such as vemurafenib or dabrafenib (previous treatment with sorafenib is allowed)\n\* Patients with other factors that increase the risk of QT prolongation or arrhythmic events (e.g., heart failure, hypokalemia, family history of long QT interval syndrome) that meets New York Heart Association (NYHA) class II or above\n\* Required use of a concomitant medication that can prolong the QT interval\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to AZD6244\n\* Patients previously treated with a MEK inhibitor other than AZD6244",  
 "healthyVolunteers": false,  
 "sex": "ALL",  
 "minimumAge": "3 Years",  
"stdAges": [  
"CHILD",  
"ADULT"  
]

Question:  
Based on the following clinical trial information, would a patient with a BRAF gene mutation be eligible for the clinical trial?

Answer:  
This clinical trial has multiple strata, and eligibility regarding BRAF mutation status depends on the stratum.  
  
\* \*\*Stratum 1:\*\* Requires a BRAF aberration (V600E mutation or KIAA1549 fusion). So, a patient with a BRAF mutation \*would\* be eligible for this stratum.  
\* \*\*Stratum 2:\*\* Specifically for patients \*without\* a BRAF aberration. A patient with a BRAF mutation would \*not\* be eligible for this stratum.  
\* \*\*Stratum 3:\*\* NF-1 associated low-grade glioma. BRAF status is not explicitly mentioned as an inclusion or exclusion criterion.  
\* \*\*Stratum 4:\*\* Optic pathway glioma. BRAF status is not explicitly mentioned as an inclusion or exclusion criterion.  
\* \*\*Stratum 5:\*\* Requires a documented BRAF aberration. A patient with a BRAF mutation \*would\* be eligible for this stratum, provided the specific BRAF aberration is documented by the designated labs and procedures.  
\* \*\*Stratum 6:\*\* For patients whose tumors cannot be assessed for BRAF status due to inadequate tissue or assay failure. BRAF status is irrelevant for this stratum.  
  
\*\*In summary:\*\* A patient with a BRAF mutation \*could\* be eligible for this trial, but only under Stratum 1 or 5, depending on the specific type of BRAF mutation, the type of tumor, and confirmation of the mutation by the specified labs using their procedures.