

Inclusion Criteria:

Pathologically documented, advanced/metastatic solid tumor with KRAS p.G12C mutation identified through local or central screening.

For NSCLC: subjects must have progressed after receiving anti-programmed cell death protein 1 (PD-1) or anti-programmed death-ligand 1 (PD-L1) immunotherapy (unless contraindicated) and/or platinum-based combination therapy and targeted therapy (if actionable oncogenic driver mutations were identified [ie, EGFR, ALK, and ROS1]).

For CRC: subjects must have progressed after receiving fluoropyrimidine and oxaliplatin and irinotecan. For those CRC subjects with tumors that are microsatellite instability-high (MSI-H), at least 1 of the prior systemic regimens must have included an anti-PD-1 therapy if they were clinically able to receive inhibitors and 1 of these agents is approved for that indication in the region or country.

For advanced/metastatic solid tumor types other than NSCLC or CRC: subjects must have received at least 1 prior systemic therapy or be intolerant or ineligible for available therapies known to provide clinical benefit.

If KRAS p.G12C status is not available in the subject's medical record, an archived formalin-fixed paraffin-embedded (FFPE) tissue (collected within 5 years) may be used for KRAS p.G12C screening by local or central testing (as applicable). If archived tissue is not available, a tumor biopsy may be performed.

Men and women age ≥ 18 years old.

Subject is of Chinese ancestry (ie, both parents and 4 grandparents are/were of Chinese descent; it is not a necessity for the subject, the subject's parents, or grandparents to be born and raised in Hong Kong/Taiwan to participate in this study).

Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 criteria.

Eastern Cooperative Oncology Group (ECOG) Performance Status of ≤ 2 .

Life expectancy of > 3 months, in the opinion of the investigator.

Ability to take oral medications and willing to record daily adherence to investigational product.

Adequate hematological laboratory assessments, as follows:

Absolute neutrophil count (ANC)³ $1.5 \times 10^9/L$ Platelet count³ $75 \times 10^9/L$ Hemoglobin ≥ 9 g/dL

Adequate renal laboratory assessments, as follows:

Estimated glomerular filtration rate based on Modification of Diet in Renal Disease (MDRD) calculation ³ 60 ml/min/1.73 m².

Adequate hepatic laboratory assessments, as follows:

Aspartate aminotransferase (AST) $< 2.5 \times$ upper limit of normal (ULN) (if liver metastases are present, $\leq 5 \times$ ULN).

Alanine aminotransferase (ALT) < 2.5 x ULN (if liver metastases are present, ≤ 5 x ULN).

Total bilirubin < 1.5 x ULN (< 2.0 x ULN for subjects with documented Gilbert's syndrome or < 3.0 x ULN for subjects for whom the indirect bilirubin level suggests an extrahepatic source of elevation).

Adequate coagulation laboratory assessments, as follows:

Prothrombin time (PT) or partial thromboplastin time (PTT) < 1.5 x ULN, OR International normalized ratio (INR) < 1.5 or within target range if on prophylactic anticoagulation therapy.

Exclusion Criteria:

Active brain metastases from non-brain tumors. Subjects who have had brain metastases resected or have received radiation therapy ending at least 4 weeks prior to study day 1 are eligible if they meet all of the following criteria: a) residual neurological symptoms grade ≤ 2; b) on stable doses of dexamethasone, if applicable; and c) follow-up MRI performed within 30 days shows no new or enlarging lesions appearing.

Other Medical Conditions

History or presence of hematological malignancies unless curatively treated with no evidence of disease > 2 years.

Myocardial infarction within 6 months of study day 1, symptomatic congestive heart failure (New York Heart Association > class II), unstable angina, or cardiac arrhythmia requiring medication.

Gastrointestinal (GI) tract disease causing the inability to take oral medication, malabsorption syndrome, requirement for intravenous (IV) alimentation, uncontrolled inflammatory GI disease (e.g., Crohn's disease, ulcerative colitis).

Exclusion of hepatitis infection based on the following results and/or criteria:

Positive Hepatitis B Surface Antigen (HepBsAg) (indicative of chronic Hepatitis B/ recent acute hepatitis B).

Negative HepBsAg with a positive for hepatitis B core antibody (Hepatitis B core antibody testing is not required for screening, however if this is done and is positive, then hepatitis B surface antibody [Anti-HBs] testing is necessary. Undetectable anti-HBs in this setting would suggest unclear and possible infection, and needs exclusion).

Positive Hepatitis C virus antibody: Hepatitis C virus RNA by polymerase chain reaction (PCR) is necessary. Detectable Hepatitis C virus RNA suggests chronic hepatitis C.

Known positive test for human immunodeficiency virus (HIV).

Unresolved toxicities from prior anti-tumor therapy, defined as not having resolved to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 grade 0 or 1, or to levels dictated in the eligibility criteria with the exception of alopecia (grade 2 or 3 toxicities from prior anti-tumor therapy that are considered irreversible [defined as having been present and stable for > 6 months], such as ifosfamide related proteinuria, may be allowed if they are not otherwise described in the exclusion criteria and there is agreement to allow by both the investigator and sponsor).

Anti-tumor therapy (chemotherapy, antibody therapy, molecular targeted therapy, retinoid therapy, hormonal therapy [except for subjects with breast cancer], or investigational agent) within 28 days of study day 1; concurrent use of hormone deprivation therapy for hormone-refractory prostate cancer or breast cancer is permitted.

Therapeutic or palliative radiation therapy within 2 weeks of study day 1. Subjects must have recovered from all radiotherapy related toxicity.

Currently enrolled in another investigational device or drug study, or less than 28 days since ending treatment on another investigational device or drug study(ies), or receiving other investigational agent(s).

Other investigational procedures are excluded. Major surgery within 28 days of study day 1.

Female subjects of childbearing potential who are unwilling to use 1 highly effective method of contraception during treatment of AMG 510 and for an additional 7 days after receiving the last dose of AMG 510. Refer to Section 11.5 for additional contraceptive information.

Female subjects who are lactating/breast feeding or who plan to breastfeed while on study and for an additional 7 days after receiving the last dose of study drug.

Female subjects with a positive pregnancy test assessed at screening by a highly sensitive serum pregnancy test.

Female subjects planning to become pregnant while on study and for an additional 7 days after receiving the last dose of AMG 510.

Male subjects with a female partner of childbearing potential who are unwilling to practice sexual abstinence (refrain from heterosexual intercourse) or use contraception during treatment and for an additional 7 days after the last dose of AMG 510. Refer to Section 11.5 for additional contraceptive information.

Male subjects with a pregnant partner who are unwilling to practice abstinence or use a condom during treatment and for an additional 7 days after the last dose of AMG 510.

Male subjects unwilling to abstain from donating sperm during treatment and for an additional 7 days after the last dose of AMG 510.

Subject has known sensitivity to any of the products or components to be administered during dosing.

Subject likely to not be available to complete all protocol-required study visits or procedures, and/or to comply with all required study procedures (e.g., Clinical Outcome Assessments) to the best of the subject and investigator's knowledge.

Subject has any kind of disorder that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent and/or to comply with all required study procedures.

History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the opinion of the investigator or Amgen physician, if consulted, would pose a risk to subject safety or interfere with the study evaluation, procedures or completion.

Use of known CYP3A4 and MATE1-sensitive substrates (with a narrow therapeutic window), within 14 days or 5 half-lives of the drug or its major active metabolite, whichever is longer, prior to study day 1 that was not reviewed and approved by the Principal Investigator and the Amgen Medical Monitor.

Use of strong inhibitors of CYP3A4 or P-glycoprotein (P-gp) (including herbal supplements such as Goldenseal) within 14 days or 5 half-lives (whichever is longer) or grapefruit juice or grapefruit containing products within 7 days prior to study day 1 that was not reviewed and approved by the principal investigator and the Amgen medical monitor.

Use of strong inducers of CYP3A4 (including herbal supplements such as St. John's wort) within 14 days or 5 half-lives (whichever is longer) prior to study day 1 that was not reviewed and approved by the principal investigator and the Amgen medical monitor.

History of other malignancy within the past 2 years, with the following exceptions:

Malignancy treated with curative intent and with no known active disease present for „d 2 years before enrollment and felt to be at low risk for recurrence by the treating physician. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.

Adequately treated cervical carcinoma in situ without evidence of disease.

Adequately treated breast ductal carcinoma in situ without evidence of disease.

Prostatic intraepithelial neoplasia without evidence of prostate cancer.

Adequately treated urothelial papillary non-invasive carcinoma or carcinoma in situ.

Previous treatment with a KRASG12C inhibitor