Cancer Research Consortium of West Michigan
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FAST FACTS

S1900E, A PHASE II STUDY OF AMG 510 IN PARTICIPANTS WITH PREVIOUSLY TREATED STAGE IV OR RECURRENT *KRAS G12C* MUTATED NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (ECOG-ACRIN LUNG-MAP SUB-STUDY)

ELIGIBILITY CRITERIA

1. ***Disease Related Criteria***
   a. Participants must be assigned to **S1900E**. Assignment to **S1900E** is determined by the **LUNGMAP** protocol genomic profiling using the FoundationOne assay. Biomarker eligibility for **S1900E** is based on the identification of a $KRAS_{G12C}$ mutation.
   b. Participants must have confirmed Stage IV or recurrent non-squamous non-small cell lung cancer (NSCLC). Mixed histology adeno-squamous NSCLC is allowed.
   c. Participants must have measurable disease (Section 10.1) documented by CT or MRI. The CT from a combined PET/CT may be used to document only non-measurable disease unless it is of diagnostic quality as defined in Section 10.1c. Measurable disease must be assessed within **28 days** prior to sub-study registration. Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease. Non-measurable disease must be assessed within **42 days** prior to sub-study registration. Participants whose only measurable disease is within a previous radiation therapy port must demonstrate clearly progressive disease (in the opinion of the treating investigator) prior to registration. See Sections 15.0 and Section 18.2 for guidelines and submission instructions for required central radiology review. CT and MRI scans must be submitted for central review via TRIAD.
   d. Participants must have a CT or MRI scan of the brain to evaluate for CNS disease within **42 days** prior to sub-study registration.
   e. Participants with known human immunodeficiency virus (HIV) infection must be receiving anti-retroviral therapy and have an undetectable viral load at their most recent viral load test within **6 months** prior to sub-study registration.
   f. Participants with EGFR sensitizing mutations, EGFR T790M mutation, ALK gene fusion, ROS1 gene rearrangement, or BRAF V600E mutation must have progressed following all standard of care targeted therapy.
   g. Participants with spinal cord compression or symptomatic brain metastases must have received local treatment to these metastases and remained clinically controlled and asymptomatic for at least **3 days following stereotactic/local radiation and/or 14 days following whole brain radiation,** and prior to sub-study registration. Participants with untreated asymptomatic brain metastases are eligible.
   h. Participants with spinal cord compression or brain metastases must not have residual neurological dysfunction, unless no further recovery is expected, and the participant has been stable on weaning doses of corticosteroids prior to sub-study registration.
   i. Participants must not have leptomeningeal disease unless: (1) asymptomatic and (2) only detected on radiographic imaging (i.e., not present in cytology from cerebral spinal fluid [CSF] if CSF sampled).
   j. Participants must not have active pneumonitis requiring treatment with sterioids and/or other immunosuppressive therapies. Radiographic evidence of pneumonitis in a radiation field, as long as asymptomatic, is permitted.
2. ***Prior/Concurrent Therapy Criteria***
   a. Participants must have received at least one line of systemic treatment for Stage IV or recurrent NSCLC.

b. Participants must have progressed (in the opinion of the treating physician) following the most recent line of systemic therapy for NSCLC.
c. Participants must have recovered (≤ Grade 1) from side effects of prior therapy. Exceptions are i) alopecia and ii) if a side effect from a prior treatment is known to be permanent without expected further recovery or resolution (i.e., endocrinopathy from immunotherapy or cisplatin neurotoxicity).
d. Participants must not have received any prior systemic therapy within the following windows.
    i. Chemotherapy administered in an every 3-week schedule, anti-cancer monoclonal antibody (mAb) therapy, or investigational agent must not have been received within **21 days** prior to sub-study registration.
    ii. Chemotherapy administered in a daily or weekly schedule must not have been received within 7 days prior to sub-study registration.
    iii. Chemotherapy administered in an every 2-weekschedule must not have been received within 14 days prior to sub-study registration
    iv. Targeted small molecule therapy must not have been received within 7 days prior to sub-study registration.
e. Participants must not have received any radiation therapy within **7 days** prior to sub-study registration, with the exceptions of
    i. stereotactic radiation to CNS metastases (See Section 5.1g for criteria regarding therapy for CNS metastases). And
    ii. palliative radiotherapy to bone metastases which must have been completed at least 1 day prior to sub-study registration.
f. Participants must not have received prior sotorasib (AMG 510), adagrasib, or other *KRAS$_{G12C}$* specific inhibitor.
g. Participants must not be planning to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for cancer treatment while receiving treatment on this study. Exceptions including leuprolide for prostate cancer, octeotide for well-differentiated neuroendocrine tumors, tamoxifen or aromatase inhibitors for breast cancer, as long as per investigator assessment, the other cancer is not expected to interfere with administration or assessment of the study.
h. Participants must not have had a major surgery within **14 days** prior to sub-study registration. Participant must have fully recovered from the effects of prior surgery in the opinion of the treating investigator. Procedures such as PORT placement or biopsies obtained by bronchoscopic, endoscopic, or percutaneous routes are not considered major surgeries.

3. Clinical/Laboratory Criteria

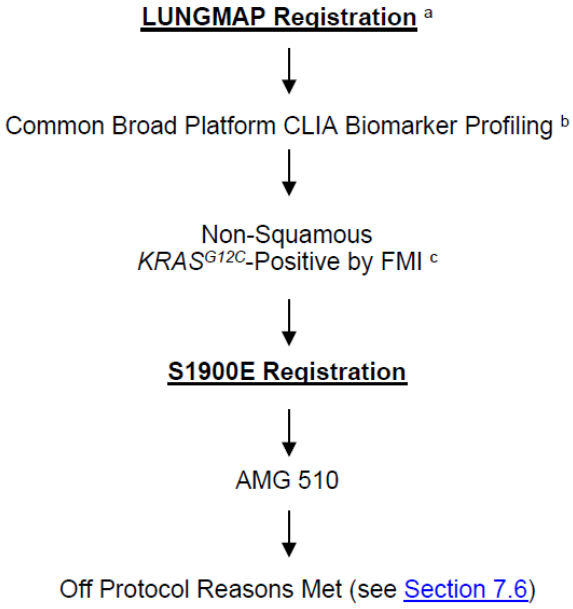
a. Participants must be able to swallow tablets whole.
b. Pre-study history and physical exam must be obtained within **28 days** prior to sub-study registration.
c. Participants must have an ANC ≥ 1.0 x 10^3/uL, platelet count ≥ 75x 10^3/uL, and hemoglobin ≥ 9 g/dL obtained within **28 days** prior to sub-study registration.
d. Participants must have adequate hepatic function as defined by serum bilirubin ≤ 1.5X Institutional Upper Limit of Normal (IULN) and ALT and AST ≤ 2.5 x IULN within **28 days** prior to sub-study registration. For participants with liver metastases, ALT and AST must be ≤ 5 x IULN.
e. Participants must have a serum creatinine ≤ 1.5 x IULN or if creatinine ≥ 1.5x IULN, calculated creatinine clearance ≥ 45 mL/min using the following Cockcroft-Gault Formula. This specimen must have been drawn and processed within 28 days prior to sub-study registration:
    Calculated Creatinine Clearance = (140 - age) X (weight in kg) †
    72 x serum creatinine *
    Multiply this number by 0.85 if the participant is a female.
    † The kilogram weight is the participant weight with an upper limit of 140% of the IBW.
    * Actual lab serum creatinine value with a minimum of 0.7 mg/ dL.
    Creatinine Calculator:
    https://crawb.crab.org/TXWB/CreatinineClearanceCalculator.aspx

f. Participants' most recent Zubrod performance status must be 0-1 (Section 10.4) and be documented within **28 days** prior to sub-study registration.
g. Participants must not have any Grade III/IV cardiac disease as defined by the New York Heart Association Criteria (i.e., participants with cardiac disease resulting in marked limitation of physical activity or resulting in inability to carry on any physical activity without discomfort), unstable angina pectoris, and myocardial infarction within **3 months**, or serious uncontrolled cardiac arrhythmia (see Appendix 18.1).
h. Participants must not have a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the investigational regimen.
i. Participants must not have gastrointestinal disorders that may impact drug absorption.
j. Participants must not have received strong inducers of CYP3A4 (including herbal supplements such as St. John's Wort) within **1 day** prior to sub-study registration and must not be planning to use strong inducers of CYP3A4 throughout protocol treatment. (See Appendix 18.6 for examples).
k. Participants must not be pregnant or nursing. Participants must have agreed to use a highly effective contraceptive method for at least **7 days** after the last dose of sotorasib (AMG 510). Participants are considered to be of "reproductive potential" if they have had menses at any time in the preceding 12 consecutive months and no prior oophorectomy and/or hysterectomy. In addition to routine contraceptive methods, "highly effective contraception" for participants with uteri also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation/occlusion. Acceptable methods of birth control for participants with sperm include sexual abstinence (refraining from heterosexual intercourse); vasectomy; bilateral tubal ligation or occlusion in the partner; or a condom (the female partner should also consider a form of birth control). However, if at any point a previously celibate participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.
l. Participants of reproductive potential must have a negative serum pregnancy test within **28 days** prior to sub-study registration.

4. Specimen Submission Criteria

a. Participants must agree to have blood specimens submitted for circulating tumor DNA (ctDNA) as outlined in Section 15.0.
b. Participants must be offered the opportunity to participate in specimen banking and in correlative studies for collection and future use of specimens as outlined in Section 15.4 With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in Section 15.2.

SCHEMA


LUNGMAP Registration [a]
Common Broad Platform CLIA Biomarker Profiling [b]
Non-Squamous
KRAS G12C-Positive by FMI [c]
S1900E Registration
AMG 510
Off Protocol Reasons Met (see Section 7.6)