Cancer Research Consortium of West Michigan
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FAST FACTS

LUNGMAP, A MASTER PROTOCOL TO EVALUATE BIOMARKER-DRIVEN THERAPIES AND IMMUNOTHERAPIES IN PREVIOUSLY-TREATED NON-SMALL CELL LUNG CANCER (LUNG-MAP SCREENING STUDY)

S1900F - A Randomized Phase II Study of Carboplatin and Pemetrexed with or without Selpercatinib (LY3527723) in Participants with Non-Squamous RET Fusion-Positive Stage IV Non-Small Cell Lung Cancer and Progression of Disease on Prior RET Directed Therapy (Lung-MAP Sub-Study)

ELIGIBILITY CRITERIA

Disease Related Criteria

a. Participants must have been assigned to S1900F based on biomarker analysis of tissue and/or blood and determined to have RET fusion-positive NSCLC as defined here:
b. Participants must have RET fusion-positive non-squamous NSCLC. Mixed histology NSCLC with less than 50% squamous component is allowed.
c. Participants must have RET rusion-positive NSCLC determined by the FMI tissue-assay or other tumor-based assays such as NGS, PCR, or FISH, or by cfDNA blood assay as outlined in Section 7.1 of the LUNGMAP Screening Protocol. Participants previously tested for and determined to have RET-fusion-positive NSCLC outside of LUNGMAP, must also submit tissue for central FMI testing on the LUNGMAP Screening Protocol. Participants with RET fusions detected by IHC alone are not eligible. The testing must be done within a laboratory with CLIA, ISO/IEC, CAP, or similar certification. Presence of RET fusions detected on tests performed outside of LUNGMAP must have been confirmed by the study biomarker review panel (see Section 15.2).
d. Participants must be negative for all additional validated oncogenic drivers that could cause resistance to selpercatinib treatment. This includes EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene fusion, KRAS activating mutations, BRAF V600E mutation and MET exon 14 skipping mutations or high-level amplification and expression.
NOTE: EGFR, ALK, ROS, KRAS, and BRAF testing is performed as part of the LUNGMAP screening/pre-screening FoundationOne test. If prior data is not available, results from the FMI testing must be obtained prior to sub-study randomization.
e. Participants must have measurable disease (see 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 randomization. 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 randomization. All disease must be assessed and documented on the Baseline Tumor Assessment Form. 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 randomization. See Section 15.7 and Section 18.7 for guidelines and submission instructions.
f. Participants must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to sub-study randomization.
g. Participants must not have leptomeningeal disease, spinal cord compression or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, and prior to sub-study randomization, AND (2) participant has no residual neurological dysfunction and has been off corticosteroids for at least 24 hours prior to sub-study randomization.

Prior/Concurrent Therapy Criteria

a. Participants must have received and developed disease progression during or after an anti-RET inhibitors treatment (See Section 18.6). The anti-RET inhibitor therapy must be the most recent therapy.
b. Participants must have progressed (in the opinion of the treating physician) following the most recent line of therapy.
c. Participants must have recovered (≤ Grade 1) from any side effects of prior therapy. Participants must not have received any radiation therapy within 14 days prior to sub-study randomization.
d. For participants with Stage IV or recurrent disease, the participant must not have received a platinum-based chemotherapy regimen. For participants whose prior systemic therapy was for Stage I-III disease only (i.e., participant has not received any treatment for Stage IV or recurrent disease), disease progression on platinum-based chemotherapy must not have occurred within one year (365 days) from the last date that the participant received that therapy. Prior anti-PD-1/PD-L1 therapy, alone or in combination (e.g., Nivolumab, Pembrolizumab, or Durvalumab) is allowed.
e. Participants must not have received any prior systemic therapy (systemic chemotherapy, TKI, immunotherapy or investigational drug) within 14 days prior to sub-study randomization.
f. Participants must not be planning to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for cancer treatment while receiving treatment on this study. Concurrent use of hormones for non-cancer-related conditions (e.g., insulin for diabetes and hormone replacement therapy) is acceptable.
g. Participants must not have a prior or concurrent malignancy whose natural history or treatment (in the opinion of the treating physician) has the potential to interfere with the safety or efficacy assessment of the investigational regimen.
h. Participants must not have had a major surgery within 14 days prior to sub-study randomization. Participants must have fully recovered from the effects of prior surgery in the opinion of the treating investigator.

Clinical/Laboratory Criteria

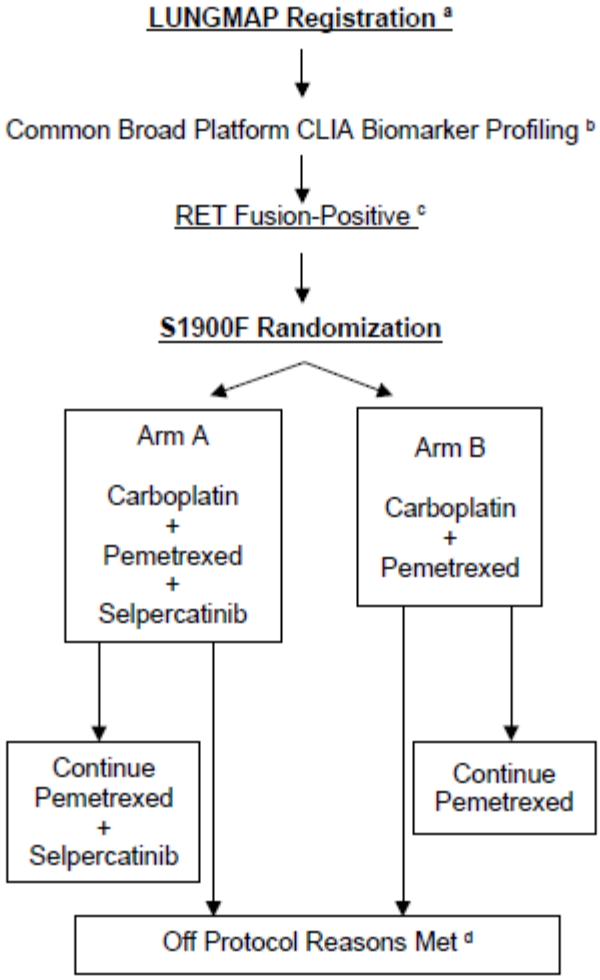
a. Participants must have an ECG performed within 28 days prior to sub-study randomization to obtain a baseline value. It is suggested that a local cardiologist review the QTcF intervals.
b. Participants must have an ANC ≥ 1.5 x 10^3/uL, platelet count ≥ 100 x 10^3/uL, and hemoglobin ≥ 9 g/dL obtained within 28 days prior to sub-study randomization.
c. Participants must have adequate hepatic function as defined by serum bilirubin ≤ Institutional Upper Limit of Normal (IULN) and either ALT or AST ≤ 2 x IULN within 28 days prior to sub-study randomization (if both ALT and AST are done, both must be < 2x IULN). For participants with liver metastases, bilirubin and either ALT or AST must be ≤ 5 x IULN (if both ALT and AST are done, both must be ≤ 5 x IULN).
d. Participants must have a serum creatinine ≤ the IULN OR measured or calculated creatinine clearance ≥ 50 mL/min using the following Cockcroft-Gault Formula. This specimen must have been drawn and processed within 28 days prior to sub-study randomization:
   Calculated Creatinine Clearance = (140 - age) X (actual body 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
e. Participants must have Zubrod performance status 0-1 documented within 28 days prior to sub-study randomization. (See Section 10.4)
f. Participants must provide pre-study history and physical exam within 28 days prior to sub-study randomization.
g. Participants with evidence of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load on suppressive therapy within 28 days prior to sub-study randomization.

h. Participants with a history of hepatitis C virus (HCV) infection must have been treated and cured. Participants with HCV infection who are currently on treatment must have an undetectable HCV viral load within 28 days prior to sub-study randomization.
i. Participants with known human immunodeficiency virus (HIV) infection are eligible, provided they are on effective anti-retroviral therapy and have undetectable viral load at their most recent viral load test and within 6 months prior to sub-study randomization.
j. Participants must be able to swallow capsules.
k. 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 6 months, or serious uncontrolled cardiac arrhythmia (see Section 18.1).
l. Participants must not be pregnant or nursing. Individuals who are of reproductive potential must have agreed to use an effective contraceptive method with details provided as a part of the consent process. A person who has had menses at any time in the preceding 12 consecutive months or who has semen likely to contain sperm is considered to be of "reproductive potential." In addition to routine contraceptive methods, "effective contraception" also includes refraining from sexual activity that might result in pregnancy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) including hysterectomy, bilateral oophorectomy, bilateral tubal ligation/occlusion, and vasectomy with testing showing no sperm in the semen.

Specimen Submission Criteria

a. Participants must agree to have blood specimens submitted for circulating tumor DNA (ctDNA). (See Section 15.5)
b. Participants must also be offered participation in banking and in the correlative studies for collection and future use of specimens. (See Section 15.6)

SCHEMA



[a] See **LUNGMAP** Section 5.1 for registration information.

[b] See **S1900F** Section 5.1. Participants must either submit tissue for biomarker profiling or submit previous commercial FoundationOne CDx test results (see **LUNGMAP** Section 5.1 for details). Participants with RET fusion-positive results detected outside the Lung-MAP study will be required to submit documentation as outlined in **LUNGMAP** Section 14.4. A committee will review the documentation per **S1900F** Section 15.2.

[c] See Section 5.0 for the criteria of RET fusion-positive.

[d] Section 7 of the **S1900F** protocol will list details for criteria for removal from treatment.