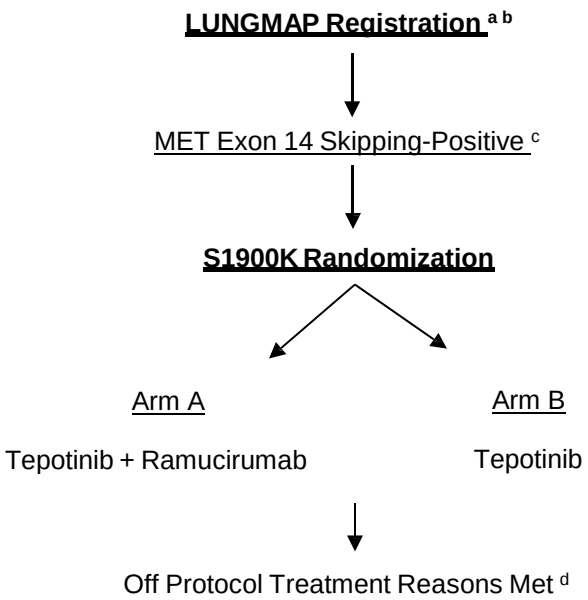
SWOG S1900K SCHEMA



[a] See **LUNGMAP** Section 5.1 for information. On-study biomarker testing or submission of required documentation for previously completed biomarker testing is required.

[b] See **S1900K** 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 MET exon 14 skipping positive results detected outside the Lung-MAP study will be required to submit documentation as outlined in **LUNGMAP** Section 14.4.

[c] See **S1900K** Section 5.0 for the criteria of MET exon 14 skipping positive.

[d] Section 7 provides details for criteria for removal from treatment.

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a participant to be considered eligible for registration in OPEN. Section 5.0 may be printed and used to by the site but is not to be uploaded in RAVE (unless specially stated). For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or LUNGMAPQuestion@crab.org prior to registration. NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient participant scheduling without exceeding the guidelines. If Day 7, 14, 16, 28, or 42 falls on a weekend or holiday, the limit may be extended to the next working day.

5.1 Disease Related Criteria

a. Participants must have been assigned to **S1900K** by the SWOG Statistics and Data Management Center (SDMC). Assignment to **S1900K** is determined by the **LUNGMAP** protocol.

b. Participants must have documentation of NSCLC with a MET exon 14 skipping mutation determined by tissue-based or blood-based (circulating tumor DNA [ctDNA]) NGS assay done within a laboratory with CLIA, ISO/IEC, CAP, or similar certification. Documentation must either be 1) NGS test results from tissue submitted for **LUNGMAP** screening, or 2) submitted documentation in the **LUNGMAP** Rave Electronic Data Capture System of a MET exon 14 skipping mutation from a previously completed tissue or blood-based NGS test (see Section 5.1c and 18.8 of **LUNGMAP**).

NOTE: Participants previously tested for and determined to have a MET exon 14 skipping mutation, outside of **LUNGMAP**, must also submit tissue for central FMI testing on the **LUNGMAP** screening protocol, if available. See **LUNGMAP** Section 18.8.

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 measurable disease ONLY if it is of diagnostic quality as defined in Section 10.1c: otherwise, it may be used to document non-measurable disease only. 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 known sites of 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 sub-study randomization to be considered measurable.

d. Participants must have a CT or MRI scan of the brain to evaluate for CNS disease within **42 days** prior to sub-study randomization.

e. 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 3 days following the stereotactic radiation and/or **14 days** following whole brain radiation, 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.

f. Participants must not have other known actionable oncogenic alterations, such as (but not limited to) EGFR sensitizing mutations, EGFR T790M mutation, ALK gene fusion, ROS1 gene rearrangement, RET gene rearrangement, NTRK rearrangement, HER2 mutation, KRAS activating mutations, and BRAF V600E mutation.

5.2 Prior/Concurrent Therapy Criteria

a. Participants must have progressed (in the opinion of the treating physician) following the most recent line of therapy.

b. Participants must have received at least one line of systemic treatment for Stage IV or recurrent NSCLC.

c. Participants must have recovered (≤ Grade 1) from any side effects of prior therapy except alopecia and vitiligo.

d. Participants must not have received any prior systemic therapy (systemic chemotherapy, immunotherapy or investigational drug) within **21 days** prior to sub-study randomization.

e. Participants must not have received treatment with prior MET inhibitor therapies (e.g., crizotinib, tivantinib, savolitinib, tepotinib, cabozantinib, and foretinib).

f. Participants must not have received treatment with prior angiogenesis inhibitor therapies (including but not limited to bevacizumab and ramucirumab).

g. Participants must not have a history of interstitial lung disease that required steroid treatment.

h. Participants must not have received any radiation therapy within **7 days** prior to sub-study randomization with the exceptions of (i) stereotactic radiation to CNS metastases which must have been completed at least **3 days** prior to sub-study randomization. (See Section 5.1e 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 randomization.

i. Participants must not be planning to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for cancer treatment while receiving treatment on this study.

j. 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.

k. 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.

5.3 Clinical/Laboratory Criteria

a. Participants must have adequate organ and marrow function as defined below within **28 days** prior to sub-study randomization:

- absolute neutrophil count	≥1.5 x 10^3/uL
- hemoglobin	≥ 9.0 g/dL
- platelets	≥100 x 10^3/uL
- total bilirubin	≤ 1.5 x institutional upper limit of normal (ULN) unless history of Gilbert's disease. Participants with history of Gilbert's disease must have total bilirubin ≤ 5 x institutional ULN.
- AST and ALT	≤ 2.5 × institutional ULN. Participants with history of liver metastasis must have AST and ALT ≤ 5 x ULN

b. Participants must have a serum creatinine ≤ the IULN or calculated creatinine clearance ≥ 30 mL/min using the following Cockcroft-Gault Formula. This specimen must have been drawn and processed within **28 days** prior to sub-study randomization:

$$\text{Calculated Creatinine Clearance} = \frac{(140 - \text{age}) \times (\text{weight in kg}\dagger)}{72 \times \text{serum creatinine}^*}$$

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.

* If the participant's serum creatinine value is less than 0.7 mg/ dL, substitute 0.7 mg/dL in place of the actual serum creatinine value in the formula.

c. Participants must have a cystatin C test performed to obtain baseline value within **28 days** prior to sub-study randomization (see Section 7.4).

d. Participants' most recent Zubrod performance status must be 0-1 (see Section 10.4) and be documented within **28 days** prior to sub-study randomization.

e. Participants must have a completed medical history and physical exam within **28 days** prior to sub-study randomization.

f. Participants must have adequate cardiac function. Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification (see Section 18.1). To be eligible for this trial, participants must be class 2B or better.

g. Participants with known human immunodeficiency virus (HIV)-infection must be on effective anti-retroviral therapy and have undetectable viral load test on the most recent test results obtained within **6 months** prior to sub-study randomization.

h. Participants with evidence of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load while on suppressive therapy on the most recent test results obtained within **6 months** prior to sub-study randomization, if indicated by the treating investigator.

i. Participants with a history of hepatitis C virus (HCV) infection must have been treated and cured. Participants currently being treated for HCV infection must have undetectable HCV viral load test on the most recent test results obtained within **6 months** prior to sub-study randomization, if indicated by the treating investigator.

j. Participants must not have cirrhosis at a level of Child-Pugh B (or worse) OR any degree of cirrhosis AND a history of hepatic encephalopathy or clinically meaningful ascites resulting from cirrhosis.

k. Participants must not have grade > 0 of peripheral edema within **28 days** prior to sub-study randomization.

l. Participants must not have experienced any arterial thromboembolic events, including but not limited to transient ischemic attack or cerebrovascular accident within **6 months** prior to sub-study randomization.

m. Participants must not have uncontrolled blood pressure and hypertension within **28 days** prior to sub-study randomization.

n. Participants must not be pregnant or breastfeeding (nursing includes breast milk fed to an infant by any means, including from the breast, milk expressed by hand, or pumped). 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.

o. Participants must have a Lymphoscintigraphy scan performed within **28 days** prior to sub-study randomization. See Section 7.3 for details.

5.4 Specimen Submission Criteria

a. Participants must also be offered participation in specimen banking as outlined in Section 15.2. With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in Section 15.4.

5.5 Regulatory Criteria

NOTE: As a part of the OPEN registration process (see Section 13 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

a. Participants ***must*** be informed of the investigational nature of this study and must sign and give informed consent in accordance with institutional and federal guidelines.

NOTE: Participants with impaired decision-making capabilities, legally authorized representatives may sign and give informed consent on behalf of study participants in accordance with applicable federal, local, and CIRB regulations.