Cancer Research Consortium of West Michigan
P: 616.391.1230 | 800.336.6299 | www.crcwm.org

FAST FACTS

SWOG S1400: Lung Map

A BIOMARKER-DRIVEN MASTER PROTOCOL FOR PREVIOUSLY TREATED SQUAMOUS CELL LUNG CANCER (LUNG-MAP)

Commercial Agents: Erlotinib
Drug Company Supplied:
Sub Study S1400I: *Ipilimumab (Cytotoxic T-lymphocyte antigen-4 CTLA-4 is a negative regulator of T-cell activity)*
Nivolumab (Nivolumab is human monoclonal antibody which targets the programmed death–1 (PD-1, cluster of differentiation 279 [CD279]) cell surface membrane receptor)
Sub study S1400G: HRRD – *TALAZOPARIB (BMN 673)*
Sub Study S1400F: MEDI4736 (Durvalumab) and tremelimumab
Sub Study S1400K: *ABBV-399*

ELIGIBILITY CRITERIA

Screening/Pre-Screening Registration

a. Patients must have pathologically proven squamous cell carcinoma (SCCA) cancer of the lung confirmed by tumor biopsy and/or fine-needle aspiration. Disease must be Stage IV SCCA as defined in Section 4.0, or recurrent. The primary diagnosis of SCCA should be established using the current WHO/IASLC-classification of Thoracic Malignancies. *(9)* The diagnosis is based on H&E stained slides with or without specific defined IHC characteristic (p40/p63 positive, TTF1 negative) if required for diagnosis. Mixed histologies are not allowed.

b. Patients must either be eligible to be screened at progression on prior treatment or to be pre-screened prior to progression on current treatment. Patients will either consent to the Screening consent or the Pre-Screening consent, not both. These criteria are:
   1. Screening at progression on prior treatment:
      To be eligible for screening at progression, patients must have received at least one line of systemic therapy for any stage of disease (Stages I-IV) and must have progressed during or following their most recent line of therapy. For patients whose prior systemic therapy was for Stage I-III disease only (i.e. patient has not received any treatment for Stage IV or recurrent disease), the prior systemic therapy must have been a platinum-based chemotherapy regimen and disease progression on the platinum-based chemotherapy must have occurred within one year from the last date that patient received that therapy. For patients whose prior therapy was for Stage IV or recurrent disease, the patient must have received at least one line of a platinum-based chemotherapy regimen or checkpoint inhibitor therapy (e.g. Nivolumab or Pembrolizumab).
   2. Pre-Screening prior to progression on current treatment:
      To be eligible for pre-screening, current treatment must be for Stage IV or recurrent disease and patient must have received at least one dose of the current regimen. Patients must have previously received or currently be receiving a platinum-based chemotherapy regimen or checkpoint inhibitor therapy (e.g. Nivolumab or Pembrolizumab). Patients on first-line treatment are eligible upon receiving Cycle 1, Day 1 infusion. Note: Patients will not receive their sub-study assignment until they progress and the S1400 Notice of Progression is submitted.

c. Patients must have adequate tumor tissue available, defined as ≥ 20% tumor cells and ≥ 0.2 mm3 tumor volume.
   • The local interpreting pathologist must review the specimen.
   • The pathologist must sign the S1400 Local Pathology Review Form confirming tissue adequacy prior to screening/pre-screening registration.
   Patients must agree to have this tissue submitted to Foundation Medicine for common broad platform CLIA biomarker profiling and c-Met IHC (see Section 15.1). If archival tumor material is exhausted, then a new fresh tumor biopsy that is formalin-fixed and paraffin-embedded (FFPE) must be obtained. A tumor block or FFPE slides 4-5 microns thick must be submitted. Bone biopsies are not allowed. If FFPE slides are to be submitted, at least 12 unstained slides plus an H&E stained slide, or 13 unstained slides must be submitted. However, it is strongly recommended that 20 FFPE slides be submitted. Note: Previous next-generation DNA sequencing (NGS) will be repeated if done outside this study for sub-study assignment.

Patients must agree to have any tissue that remains after NGS testing retained for the use of the Translational Medicine (TM) studies (if such TM studies are defined) within any sub-study the patient is enrolled in.

d. Patients must not have a known EGFR mutation or ALK fusion. EGFR/ALK testing is not required prior to registration and is included in the FMI testing for screening/prescreening.
e. Patients must have Zubrod performance status 0-1 (see Section 10.4) documented within 28 days prior to screening/pre-screening registration.
f. Patients must be ≥ 18 years of age.
g. Patients must also be offered participation in banking for future use of specimens as described in Section 15.0.

h. Patients must be willing to provide prior smoking history as required on the S1400 Onstudy Form.
i. As a part of the OPEN registration process (see Section 13.4 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.
j. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
k. U.S. patients who can complete the survey and the interview by telephone or email in English must be offered participation in the **S1400GEN** Survey Ancillary Study (see Sections 15.5 and 18.1f). NOTE: Patients enrolled to **S1400** prior to Revision #12 are not eligible for the **S1400GEN** Survey Ancillary Study. Study physicians will provide participants with a hard copy of the survey (at the time of informed consent) to improve tracking and comprehension during the interview.

Sub-study Registration (Common Eligibility Criteria for all Sub-Studies)

Gene	Alteration type	Ineligible Alteration
EGFR	Substitution	L858R, T790M, A289V, G719A, S768I, G719C, R108K, G598V, R222C, L62R, L861Q, P596L, V774M
	Indel	non-frame shifting insertions or deletions between amino acids 740 and 780, in exons 19 and 20, transcript NM_005228
	Fusion	None
	Amplification	None
ALK	Substitution	None
	Indel	None
	Fusion	EML4-ALK, CLIP4-ALK, CLTC-ALK, KIF5B-ALK, NPM1-ALK, RANB2-ALK, STRN-ALK, TFG-ALK
	Amplification	None

- For patients screened at progression on prior treatment, a sub-study assignment from the SWOG Statistical Center should be received within 16 days of tissue submission.
- For patients pre-screened prior to progression on current therapy, submission of the S1400 Notice of Progression Form is required to receive a sub-study assignment. The sub-study assignment should be received from the SWOG Statistical Center within 1 day of submission of the S1400 Notice of Progression (provided at least 16 days have passed since tissue submission). Patients must then register to the assigned sub-study in order to receive their treatment assignment.
- Patient must meet the eligibility criteria listed in Section 5.0 of the assigned sub-study. The common eligibility criteria are included here. For ease of reference, these common eligibility criteria have also been incorporated into Section 5.0 of each of the sub-studies. If patient does not meet the additional criteria listed in Section 5.0 of the assigned substudy, submit the S1400 Request for Sub-Study Reassignment Form. (See Section 18.1a for biomarker reporting.) Any potential eligibility issues should be addressed to the Data Operations Center in Seattle at S1400question@crab.org prior to registration.

a. Patients whose biomarker profiling results indicate the presence of an EGFR mutation or EML4/ALK fusion are not eligible. Due to existence of approved therapies the biomarker exclusion rules are as follows:

b. Patients must have progressed (in the opinion of the treating investigator) following the most recent line of therapy.

c. Patients must not have received any prior systemic therapy (systemic chemotherapy, immunotherapy or investigational drug) within 21 days prior to sub-study registration. Patients must have recovered (≤ Grade 1) from any side effects of prior therapy. Patients must not have received any radiation therapy within 14 days prior to sub-study registration. (See 5.2e for criteria regarding therapy for CNS metastases).
d. Patients 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 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. All disease must be assessed and documented on the Baseline Tumor Assessment Form. Patients 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 18.1c for guidelines and submission instructions for required central radiology review.
e. Patients must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to sub-study registration. Patient 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 registration, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least 24 hours prior to sub-study registration.
f. Patient must have fully recovered from the effects of surgery at least 14 days prior to sub-study randomization.
g. Patients must not be planning to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for cancer treatment. Concurrent use of hormones for non-cancer-related conditions (e.g., insulin for diabetes and hormone replacement therapy) is acceptable.
h. Patients must have an ANC ≥ 1,500/mcl, platelet count ≥ 100,000 mcl, and hemoglobin ≥ 9 g/dL obtained within 28 days prior to sub-study randomization.
i. Patients 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 registration (if both ALT and AST are done, both must be < 2 IULN). For patients with liver metastases, bilirubin and either ALT or AST must be ≤ 5 x IULN (if both ALT and AST are done, both must be ≤ IULN).

j. Patients must have a serum creatinine ≤ the IULN OR measured or calculated creatinine clearance ≥ 50 mL/min using the following Cockroft-Gault Formula:

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

Multiply this number by 0.85 if the patient is a female. These tests must have been performed within 28 days prior to sub-study randomization. *The Kilogram weight with an upper limit of 140% of the IBW. * Actual lab serum creatinine value with a minimum of 0.8 mg/dL.
k. Patients must have Zubrod performance status 0-1 (see Section 10.4) documented within 28 days prior to sub-study randomization.
l. Patients must not have any Grade III/IV cardiac disease as defined by the New York Heart Association Criteria (i.e., patients 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 Appendix 18.1b.)
m. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection.
n. Patients with a known history of HIV seropositivity:
    1. Must have undetectable viral load using standard HIV assays in clinical practice.
    2. Must have CD4 count ≥ 400/mcL,
    3. Must not require prophylaxis for any opportunistic infections (i.e., fungal, mAC, or PCP prophylaxis)
    4. Must not be newly diagnosed within 12 months prior to sub-study registration.
o. Prestudy history and physical exam must be obtained within 28 days prior to sub-study registration.
p. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, *in situ* cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for five years.
q. Patients must not be pregnant or nursing. Women/men of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" 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. However, if at any point a previously celibate patient 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.

r. As a part of the OPEN registration process (see Section 13.4 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.

s. Patients with impaired decision-making capacity are eligible as long as their neurological or psychological condition does not preclude their safe participation in the study (e.g., tracking pill consumption and reporting adverse events to the investigator).

t. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

PRE-STUDY PARAMETERS (refer to Tables in Section 9 for details)

All Sub-Studies

- History, physical examination weight, ECOG Performance Status (PS)
- Adverse event assessment
- Smoking status assessment
- CBC, CMP, creatinine clearance, LDH
- CT or MRI for disease assessment
- Brain CT/MRI
- Electrocardiogram
- Tissue for biomarker profiling and banking
- Serum for banking
- Image submission

Sub Study S1400B – as listed above

- HBA1c, fasting glucose, lipase and amylase

Sub Study S1400C – as listed above

- HBA1c, serum magnesium

Sub Study S1400D – as listed above

- Ophthalmologic Exam:
    - Visual Acuity
    - Amsler Grid
    - Schirmer's Test
    - Corneal Examination
    - Slit Lamp Examiination
    - Fundoscopy
    - OCT
- Serum Phosphate
- Urinalysis
- LDH
- Troponin I
- MUGA/Echocardiogram