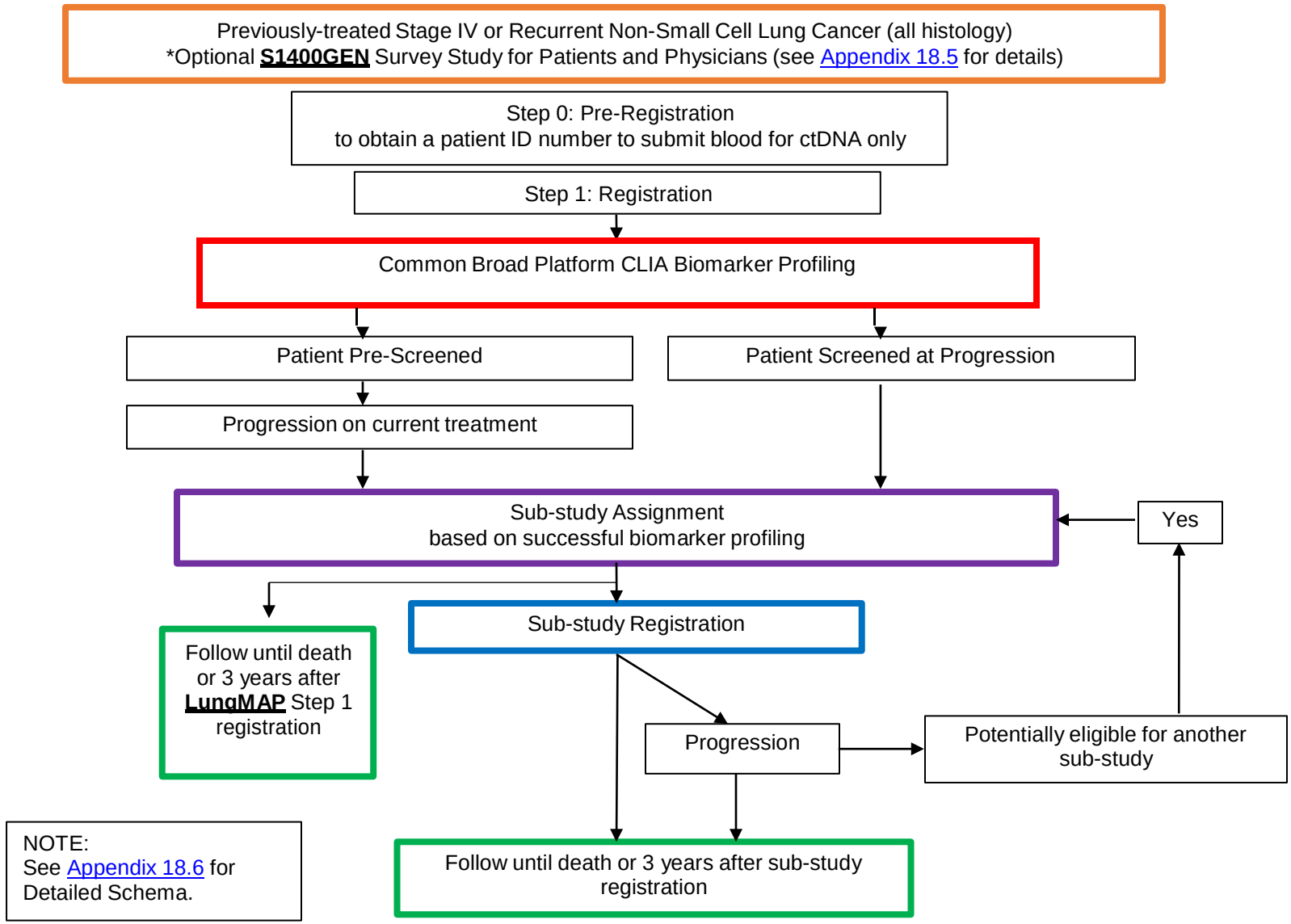
HIGH-LEVEL SCHEMA



5.0 ELIGIBILITY CRITERIA

For each criterion requiring test results and dates, please record this information on the **LungMAP** Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the SWOG Statistics and Data Management Center in Seattle at 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 patient scheduling without exceeding the guidelines. If Day 7, 14, 21, 28 or 42 falls on a weekend or holiday, the limit may be extended to the next working day.

5.1 Registration

Step 0:

a. Patients who need the fresh biopsy must also submit whole blood for ctDNA testing (see Section 15.3). These patients must be registered to Step 0 to obtain a patient ID number for the submission.

Patients registered to Step 0 are not registered to the **LungMAP** protocol. To participate in **LungMAP**, patients must be registered to Step 1 after evaluation of patient eligibility, including tumor tissue adequacy, per protocol Section 5.1, Step 1.

Patients registered at Step 0 must use the same SWOG patient ID for registration at Step 1.

Step 1:

b. Patients must have pathologically proven non-small cell lung cancer (all histologic types) confirmed by tumor biopsy and/or fine-needle aspiration. Disease must be Stage IV as defined in Section 4.0, or recurrent. The primary diagnosis of non-small cell lung cancer should be established using the current WHO/IASLC-classification of Thoracic Malignancies. *(13)* All histologies, including mixed, are allowed.

c. Patients must either be eligible to be screened at progression on prior treatment or to be pre-screened prior to progression on current treatment.

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), disease progression on platinum-based chemotherapy must have occurred within one year from the last date that patient received that therapy. For patients treated with consolidation anti-PD-1 or anti-PD-L1 therapy for Stage III disease, disease progression on consolidation anti-PD-1 or anti-PD-L1 therapy must have occurred within one year from the date or initiation of such 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 anti-PD-1/PD-L1 therapy, alone or in combination (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 anti-PD-1/PD-L1 therapy, alone or in combination (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 LungMAP Notice of Progression is submitted.**

d. Patients must have adequate tumor tissue available, defined as ≥ 20% tumor cells and ≥ 0.2 mm^3 tumor volume.
- The local interpreting pathologist must review the specimen.
- The pathologist must sign the **LungMAP** Local Pathology Review Form confirming tissue adequacy prior to Step 1 registration.

Patients must agree to have this tissue submitted to Foundation Medicine for common broad platform CLIA biomarker profiling, PD-L1, and c-MET IHC (see Section 15.2). If archival tumor material is exhausted, then a new fresh tumor biopsy that is formalin-fixed and paraffin-embedded (FFPE) must be obtained. Patients who need the fresh biopsy must also submit whole peripheral blood for ctDNA testing. 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 testing retained for the use of sub-study Translational Medicine (TM) studies at the time of consent the patient is enrolled in.

e. Patients with known EGFR sensitizing mutations, EGFR T790M mutation, ALK gene fusion, ROS 1 gene rearrangement, or BRAF V600E mutation are not eligible unless they have progressed following all standard of care targeted therapy. EGFR/ALK/ROS/BRAF testing is not required prior to Step 1 registration, as it is included in the Foundation One testing for screening/pre-screening.

f. Patients must have Zubrod performance status 0-1 (see Section 10.2) documented within 28 days prior to Step 1 registration.

g. Patients must be ≥ 18 years of age.

h. Patients must also be offered participation in banking for future use of specimens as described in Section 15.0.

i. Patients must be willing to provide prior smoking history as required on the **LungMAP** Onstudy Form.

j. 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.

k. 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.

l. 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 if local institution's policies allow participants to receive the Amazon gift card (see Sections 15.7 and 18.5). Patients at institutions that cannot offer the survey must still participate in the main study.

6.0 STRATIFICATION FACTORS

Not applicable.