SWOG CANCER RESEARCH NETWORK

NCI National Clinical Trials Network | NCI Community Oncology Research Program

S1900G A RANDOMIZED PHASE II STUDY OF INC280 (CAPMATINIB) PLUS OSIMERTINIB WITH OR WITHOUT RAMUCIRUMAB IN PARTICIPANTS WITH EGFR-MUTANT, MET-AMPLIFIED STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER (Lung-MAP Sub-Study)

WHAT IS THE PRIMARY OBJECTIVE OF THIS STUDY?

The aim of this study is to compare investigator-assessed progression-free survival (IA-PFS) between participants with EGFR mutated, MET amplified NSCLC randomized to INC280 (capmatinib) and osimertinib with or without ramucirumab.

I HAVE A PROSPECTIVE PATIENT I WANT TO ENROLL.

The first step is to confirm that your patient has EGFR-mutant NSCLC and has experienced disease progression on osimertinib as the most recent line of therapy.
(NOTE: any component of SCLC will exclude your patient from the study).

A tissue-based or blood-based (ctDNA) NGS assay must be done to confirm acquired MET amplification.
This assay must have been performed with samples obtained AFTER the patient has progressed on osimertinib (either alone or in combination with other agents). This assay can be done outside of the study or as part of the LUNGMAP screening protocol.

THERE ARE THREE APPROACHES AVAILABLE TO PROVIDE CONFIRMATION OF MET AMPLIFICATION:

OUTSIDE TISSUE-BASED NGS TESTING REPORT

TISSUE-BASED ASSAY RESULTS PERFORMED BY A 3RD PARTY LABORATORY

THE LABORATORY MUST HAVE CLIA, ISO/IEC, CAP, OR SIMILAR CERTIFICATION

OUTSIDE BLOOD-BASED NGS TESTING REPORT

FOR BLOOD-BASED (ctDNA) ASSAY RESULTS

BLOOD-BASED ASSAY RESULTS MUST BE REPORTED BY EITHER A GUARDANT OR FOUNDATION MEDICINE REPORT

LUNGMAP TISSUE-BASED NGS TESTING REPORT

TISSUE-BASED BIOMARKER RESULTS PERFORMED BY FOUNDATION MEDICINE

GENERATED UPON SUCCESSFUL BIOMARKER PROFILING WHEN A PATIENT IS ENROLLED ONTO LUNGMAP, OR SUCCESSFUL RE-ANALYSIS* OF A PRIOR FMI COMMERCIAL CDx REPORT

* CDx REPORTS USING HEME TESTING ARE NOT ALLOWED. ONLY REPORTS GENERATED FROM SOLID TUMOR TISSUE AFTER 9/1/2019 ARE ACCEPTED.

WHAT IF MY PATIENT WAS TESTED FOR MET-AMPLIFICATION OUTSIDE OF LUNGMAP?

If your patient was found to have MET amplification after progression on osimertinib, and has not yet enrolled onto the LUNGMAP screening protocol, they will first need to register to LUNGMAP and submit the EGFR Mutation and MET Amplification Testing Form in the LUNGMAP Rave EDC. If available, also submit tumor tissue for central FMI testing.
Please see the last page of this handout for tissue submission specifications as well as S1900G protocol section 18.6b.

FOR QUESTIONS REGARDING ELIGIBILITY, DATA SUBMISSION, SPECIMEN ISSUES, & S1900G GENERAL INQUIRIES, CONTACT:
LUNGMAPQUESTION@CRAB.ORG

FOR MEDICAL OR TREATMENT-RELATED S1900G QUESTIONS, CONTACT:
S1900GMEDICALQUERY@SWOG.ORG

MORE →

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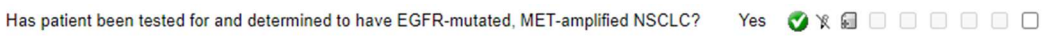
THINGS TO KEEP IN MIND WHEN ENROLLING YOUR PATIENT ONTO LUNGMAP

If enrolling the patient onto LUNGMAP for eventual sub-study assignment to S1900G:

- Has the patient been enrolled using the 'Screening at Progression' approach (see LUNGMAP protocol section 5.1.b.1)?
- Have you made sure that the tissue specimen to be submitted was collected AFTER progression following osimertinib, and is compliant with the specifications detailed on the LUNGMAP Tissue Submission Handout (attached)?
- Ensured that along with tissue submission, that your local pathologist has signed and dated the Pathology Review form prior to LUNGMAP enrollment, and that it has been completed FULLY?
- Confirmed that your OPEN Enrollment Worksheet has this question answered correctly?



- Confirmed that when filling out the LUNGMAP EGFR Mutation and MET Amplification Testing Form eCRF in Rave, that each of the loglines for "EGFR Mutation" and "MET Amplification" contain fully redacted reports, containing the patient's SWOG ID—even if it's the same report?

#	Report Label	Report date	Report upload
1	EGFR Mutation	06 Apr 2023	WA999_PT70000_redactedFMIreport.pdf
2	MET Amplification	06 Apr 2023	WA999_PT70000_redactedFMIreport.pdf

MY PATIENT IS ASSIGNED S1900G! WHAT ABOUT RESEARCH ARMS AND TREATMENTS?

Participants are randomized and balanced between two research arms, depending on a couple things:

Presence of Brain Mets AND 1 vs. 2+ lines of prior therapy for their disease

ARM A TREATMENT: INC280 (capmatinib)/Osimertinib/Ramucirumab

ARM B TREATMENT: INC280 (capmatinib)/Osimertinib

PLEASE PLAN TO INITIATE TREATMENT NO MORE THAN **10 DAYS** AFTER SUB-STUDY RANDOMIZATION

WAIT, I STILL HAVE SOME S1900G-RELATED QUESTIONS!

No problem! Depending on your question, you can contact the LUNGMAP/S1900G Study Team using the contact information below, or try the contact information on the following page of this handout in case it's something a little more specific.

Please also ensure that your institutional copies of both the LUNGMAP screening protocol and the S1900G protocol are kept up to date. Important memorandums concerning these studies, as well as copies of the protocols, printable copies of the forms used in Rave as well as other pertinent information related to both LUNGMAP and S1900G can be viewed on their respective protocol pages at ctsu.org.

FOR QUESTIONS REGARDING ELIGIBILITY, DATA SUBMISSION, SPECIMEN ISSUES, & S1900G GENERAL INQUIRIES, CONTACT:
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CONSIDERATIONS FOR ON-STUDY ASSESSMENTS AND FOLLOW-UPS

Any Disease Assessments should be scheduled based on the date of randomization, and not based off cycle dates or drug administration.

This study utilizes the SWOG Best Practices (https://www.swog.org/%22BestPractice%22) which allows for additional scheduling flexibility to perform any tests or procedures while still remaining compliant with the protocol schedule.

Scheduled procedures and assessments (treatment administration, toxicity assessment for continuous treatment, disease assessment, specimen collection and follow-up activities) are due on Day 1 of the cycle/interval noted on the study calendar using the following established windows unless otherwise indicated in the protocol.

Treatment/Visit/Assessment Interval	7 - 14 Days	21 Days – 2 Months	3 – 9 Months	Annual
Allowed Window	± 1 Day	± 3 Days	± 7 Days	± 14 Days

Note: The window is calculated from the scheduled date of the requirement. For example, if a weekly treatment was given one day early, the next treatment date is calculated from the last scheduled treatment date not the actual treatment date that was one day early.

OVERDUE EXPECTATIONS AND THE IPR REPORT

Your monthly IPR report may not always reflect data recently submitted, so it is important to check the most up-to-date version.
You will need your CTEP-IAM or ID.me credentials. Open your browser, navigate to swog.org and log in.
The landing page will display the following screen:

1. Click on the 'CRA Workbench' icon under Member Resources.
2. Expand the 'Patient Reports / Data Quality' menu on the left-hand side, and then click on 'Institution Performance Review (IPR)'.
3. Scroll down to the bottom, under 'Current Expectation Reports' the most up-to-date IPR for your site should be displayed with a blue hyperlink.

ADDITIONAL S1900G CONTACT INFORMATION (MORE ON PG.5 OF PROTOCOL)

Regulatory, Protocol & Informed Consent Questions:	protocols@swog.org, phone: (210) 614-8808
Patient Advocate:	judyjohnson.519@gmail.com, phone: (314) 477-6139
Specimen Tracking System (STS) Questions or Issues:	technicalquestion@crab.org
Foundation Medicine Inc., (for ordering ctDNA kits):	lung.map@foundationmedicine.com
Access to iMedidata Rave and Delegation Task Log (DTL) Issues:	ctsucontact@westat.com, phone: (888) 823-5923
Serious Adverse Event (SAE) Reporting Questions:	adr@swog.org

FOR QUESTIONS REGARDING ELIGIBILITY, DATA SUBMISSION, SPECIMEN ISSUES, & S1900G GENERAL INQUIRIES, CONTACT: LUNGMAPQUESTION@CRAB.ORG

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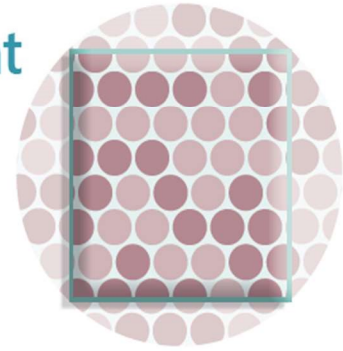
LUNG-MAP TISSUE SPECIFICATIONS FOR LUNGMAP

Study requirement



TUMOR CONTENT ≥ 20%

including tumor volume ≥ 0.2 mm³

It is important that the specimen contains as much tumor content as possible to ensure that there's enough DNA needed for sequencing.

LUNGMAP requires adequate tissue for biomarker profiling.
For details, please refer to the LUNGMAP protocol Section 5 for eligibility requirements and Section 15 for a complete description of tissue requirements. Specimens must be submitted using the SWOG Specimen Tracking System, a process outlined in the LUNGMAP protocol Section 15.

NOTE FOR LIVER SPECIMENS:

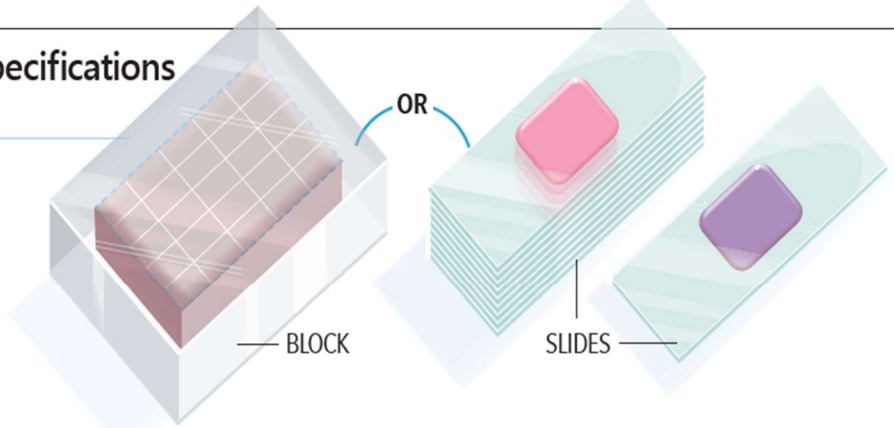
It is recommended that at least 40% of the specimen contain malignant cells to ensure sufficient tumor DNA.

For Best Results, Use These Specifications

SPECIMEN TYPE

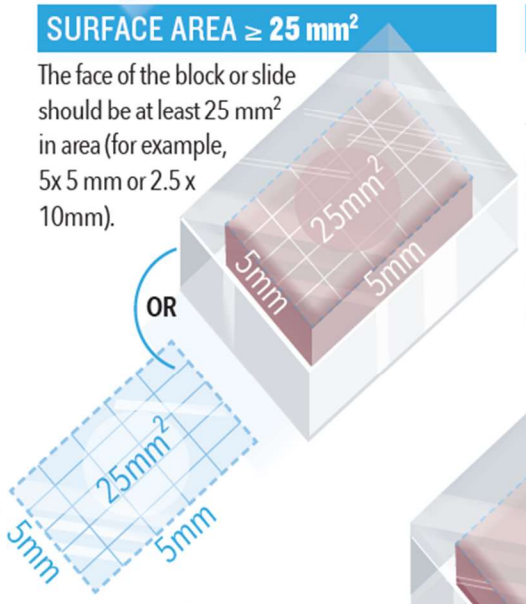
FFPE BLOCK or 12-20 SLIDES (+H&E SLIDE)
Tissue must be formalin-fixed and paraffin embedded. Tissue blocks are preferred in LUNGMAP.

- **If sending slides:**
  - A minimum of 12 unstained, charged, and unbaked 4-5 micron slides are required.
  - 20 slides are highly recommended.
  - Slides should include an additional H&E or Aperio stained slide (If unavailable, submit an extra unstained slide).
- **For core biopsy tissue,** use 3-5 cores embedded in a single block, aligned so that when cut, the blade is running parallel to the long axis of the cores.
- **Fine needle aspirates** with good cellularity are acceptable as long as cell blocks are established.
- **Biopsy tissue** can be from primary or metastatic sites. Bone biopsies are not allowed.



SURFACE AREA ≥ 25 mm²

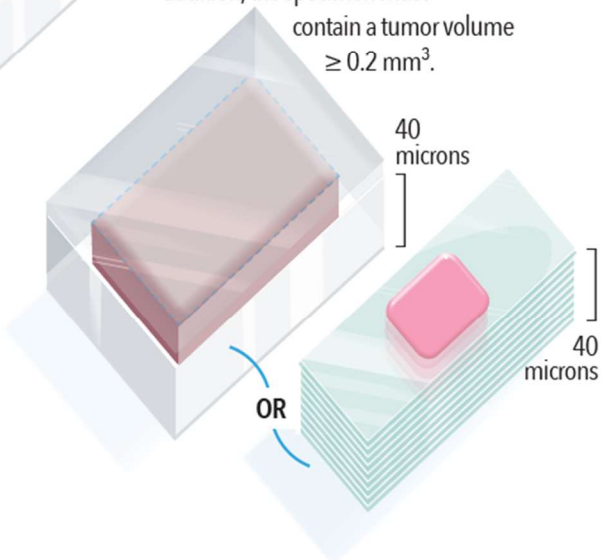
The face of the block or slide should be at least 25 mm² in area (for example, 5x 5 mm or 2.5 x 10mm).



SPECIMEN VOLUME ≥ 1 mm³

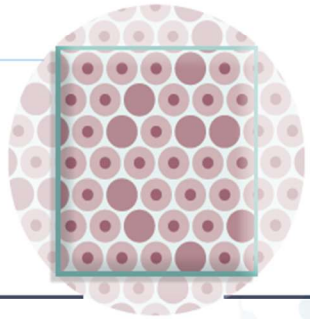
(including tumor volume ≥ 0.2 mm³)

The total volume (surface area x depth) of the block or stacked slides should be at least 1 mm³. If the surface area is 25 mm² as recommended, the depth should be at least 40 microns. For this reason, a minimum of 12 slides is required. In addition, the specimen must contain a tumor volume ≥ 0.2 mm³.



NUCLEATED CELLULARITY ≥ 80 %

Specimens containing less than 80% nucleated cells require greater total volume and may not be suitable to assay. A total of 75,000 to 150,000 nucleated cells are recommended.



PRIOR TO ENROLLMENT, YOUR LOCAL PATHOLOGIST MUST SIGN OFF ON THE LUNGMAP LOCAL PATHOLOGY REVIEW FORM CERTIFYING THAT TISSUE REQUIREMENTS HAVE BEEN MET.

Questions? Email: LungMAPquestion@crab.org

f. Detailed Schema for Patients with known EGFR mutation and MET amplification