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)

Frequently Asked Questions:

Pre-screening prior to progression

I'm interested in registering my patient with EGFR-mutant NSCLC to LUNGMAP. Should I register him as "Pre-screening prior to progression"?
No. Patients with EGFR-mutant lung cancer who are being considered for **S1900G** must only be registered to **LUNGMAP** at the time of progression on osimertinib. The reason for this (and what makes it unique compared to other Lung-MAP sub-studies) is that MET amplification must be assessed after the patient has disease progression on osimertinib.

Prior therapy

I have a patient who progressed on osimertinib and then received chemotherapy with continuation of osimertinib. She is now progressing. Is she eligible since she received chemotherapy?
Yes! Patients can have any number of prior lines of therapy, as long as osimertinib (either on its own or in combination with another therapy) was the most recent prior therapy.

My patient required a dose-reduction of osimertinib to 40mg daily because of side effects. Is she allowed to go on S1900G?
Maybe. Patients must be able to tolerate osimertinib 80mg for at least 14 days prior to sub-study randomization. For a patient who was on 40mg, consideration could be given to increasing the dose back to 80mg at the discretion of the treating physician, and if tolerable this patient may be able to continue onto **S1900G**.

A patient at our site experienced disease progression on osimertinib and then received amivantamab plus chemotherapy. Is that allowed?
Prior amivantamab is allowed under Revision #2 (although please note that prior MET tyrosine kinase inhibitors are not allowed). However, patients must have received osimertinib as the most recent prior therapy.

What about a patient who was on osimertinib plus a VEGF-pathway inhibitor, such as bevacizumab or ramucirumab?
Under Revision #2, prior VEGF inhibitors including bevacizumab or ramucirumab are allowed so this patient could be considered.

Testing for MET amplification

My patient has tissue available from diagnosis prior to starting osimertinib. Can I use that tissue to screen for S1900G?
Unfortunately not. Tumors with EGFR mutations often acquire additional alterations, with MET amplification being one of the most common. MET amplification will not be present in the pre-treatment sample because it is an acquired alteration that only develops after treatment with an EGFR inhibitor such as osimertinib. Therefore, repeat molecular testing must be performed at the time of disease progression on osimertinib.

What if a patient with EGFR-mutant lung cancer who has progressed on osimertinib already underwent a biopsy that was found to have MET amplification using our in-house assay which is performed in a CLIA lab?
This patient can be assigned to **S1900G** using this result. Any tissue-based assay that is performed in a CLIA (or similar) laboratory (in-house or commercial) that shows MET amplification at the time of progression on osimertinib can be used for assignment to **S1900G**. See **LUNGMAP** protocol Section 18.7 for details on how to submit the outside test result for sub-study assignment.

Are liquid biopsies (ctDNA assays) acceptable if they show MET amplification?
Possibly. At this time only Guardant and Foundation Medicine liquid biopsies are acceptable for **S1900G** sub-study assignment.

Do I have to submit tissue if I already have a tissue or liquid biopsy that shows MET amplification?
If tissue is available from the time of progression on osimertinib, it should be submitted for central testing on **LUNGMAP**. However, you do not need to wait for these results to move ahead with screening the patient for **S1900G** as local testing is sufficient for **S1900G** sub-study assignment and enrollment.

My patient with EGFR-mutant lung cancer was found to have disease progression on osimertinib and I'm considering enrollment onto Lung-MAP but I haven't yet tested her for MET amplification. What are my options for testing?
There are 3 options:

1. Obtain a tumor biopsy and submit the tissue for testing by Foundation Medicine through the **LUNGMAP** screening protocol, or
2. Obtain a tumor biopsy and perform tissue testing using any CLIA assay. If MET amplification is detected, the patient can be registered to **LUNGMAP** and the outside test result submitted for assignment to **S1900G**, or
3. Obtain a blood sample and send it for circulating tumor DNA (ctDNA) testing, also known as a liquid biopsy. The only liquid biopsy assays currently allowed for assignment to **S1900G** are Guardant and Foundation Medicine. If the liquid biopsy shows MET amplification, the patient can be registered to **LUNGMAP** and the outside test result submitted for assignment to **S1900G**.

What if the biopsy or blood test at the time of progression on osimertinib shows MET amplification but not an EGFR mutation?
This is very unlikely to occur, as the EGFR mutation prior to treatment with osimertinib is nearly always retained at the time of progression. If this situation does occur, it is acceptable as long as the baseline sample showed an EGFR mutation.