S1800E, A Randomized Phase II/III Study of Docetaxel and Ramucirumab with or without Cemiplimab (REGN2810) for Participants Previously Treated with Platinum-based Chemotherapy and Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Matched Sub-Study)

Frequently Asked Questions:

Eligibility

1. **Are patients who have received prior docetaxel eligible?**
   No. Patients who have received prior docetaxel are not eligible for this study.

2. **Are patients who have received prior bevacizumab or ramucirumab eligible?**
   Yes. Patients who have received prior bevacizumab or ramucirumab are eligible.

3. **A patient received pembrolizumab, and their cancer progressed during that time. Carboplatin/pemetrexed was added to the treatment with the continuation of pembrolizumab. Will this count as 1 or 2 anti-PD-1/anti-PD-L1 therapies?**
   If a patient is on pembrolizumab and then receives chemotherapy + pembrolizumab it will count as 1 anti-PD-(L)1 therapy, since the patient stayed on the same immunotherapy agent. If they receive 2 different anti-PD-(L)1 drugs, it would count as two therapies.

4. **A patient received carboplatin/paclitaxel/pembrolizumab, progressed, then started carboplatin/pemetrexed/pembrolizumab. Will this count as 1 or 2 anti-PD-(L)1 therapies?**
   This will count as 1 anti-PD-(L)1 therapy, since pembrolizumab was continued without interruption.

5. **A patient received carboplatin/pemetrexed/pembrolizumab, progressed, then received pembrolizumab/ramucirumab. Is the patient eligible? Will this count as 1 or 2 anti-PD-(L)1 therapies?**
   Yes, the patient is eligible. Prior ramucirumab is allowed, and the patient has had only one type of anti-PD1 therapy.

6. **A patient with stage II NSCLC had tumor resection and then received adjuvant chemotherapy followed by immunotherapy. There was no evidence for recurrence at 3 months, but the patient developed disease progression 6 months after starting adjuvant therapy. Is this patient eligible?**
   Yes. If the patient received neoadjuvant, adjuvant or consolidation immunotherapy for non-metastatic NSCLC and has tumor progression more than 84 days but less than 365 days from the start of immunotherapy, this would count as the required anti-PD-(L)1 agent and chemotherapy.

7. **A patient with stage II NSCLC had tumor resection and then received adjuvant platinum-based chemotherapy followed by immunotherapy and progressed 6 months after starting immunotherapy. Is this patient eligible?**
   Yes. If the patient received neoadjuvant, adjuvant or consolidation immunotherapy for non-metastatic NSCLC and has tumor progression more than 84 days but less than 365 days from the start of immunotherapy, this would count as the required anti-PD-(L)1 agent and chemotherapy.

8. **A patient with resectable stage III NSCLC received neoadjuvant chemotherapy with immunotherapy followed by resection and then received adjuvant immunotherapy and progressed 6 months after starting adjuvant therapy. Is this patient eligible?**
   Yes. If the patient received neoadjuvant, adjuvant or consolidation immunotherapy for non-metastatic NSCLC and has tumor progression less than 365 days from the start of immunotherapy, this would count as the required anti-PD-(L)1 agent and chemotherapy.

9. **A patient with unresectable stage III NSCLC received concurrent chemotherapy with radiation followed by consolidation durvalumab and progressed 6 months after starting consolidation therapy. Is this patient eligible?**

Yes. If the patient received neoadjuvant, adjuvant or consolidation immunotherapy for non-metastatic NSCLC and has tumor progression more than 84 days but less than 365 days from the start of immunotherapy, this would count as the required anti-PD-(L)1 agent and chemotherapy.

10. **A patient received ipilimumab and nivolumab with initial partial response followed by progression after 9 months on therapy. Is this patient eligible?**
No, but if the patient receives chemotherapy without a new anti-PD-(L)1 agent, the patient could be eligible after progression on platinum-based chemotherapy.

11. **A patient received carboplatin/pemetrexed/pembrolizumab, progressed, and next received *[paclitaxel, gemcitabine, etc.].* Is this patient eligible?**
Yes. There is no limit on the number of lines of prior therapy that do not include an anti- PD-(L)1 agent, though they must not have had prior docetaxel.

12. **A patient with *[for example: KRAS G12V, BRAF G466A]* mutation has not been treated with a targeted therapy for this mutation. Would this patient be eligible?**
Yes. If the alteration does not have an approved specific targeted therapy available, the criterion about targeted therapy for a known mutation (5.2.e) does not apply. For details regarding which mutations have approved targeted therapies, view the NCCN guidelines for non-small cell lung cancer as a reference: https://www.nccn.org/

13. **A patient with *[for example: EGFR mutation or ALK gene rearrangement]* has received prior targeted therapy, and platinum-based chemotherapy. Would this patient be eligible?**
No. Prior immunotherapy is required for eligibility with disease progression >84 days after initiation.

14. **If a patient is scheduled to initiate palliative radiation and/or radiosurgery, could the patient be eligible for the trial after radiation and/or radiosurgery?**
Yes. Once the radiation washout (14 days, or 7 days for bone radiation) is complete and the treating investigator feels it is safe to start systemic therapy.

15. **If a patient had a physical exam and urinalysis completed 29 days prior to randomization, are they eligible?**
No. The eligibility criteria state that urinary protein test, completed history and physical exam must be completed within 28 days prior to randomization.

16. **If a patient has a skin cancer, can they enroll?**
Participants must not have a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or efficacy assessment of the investigational regimen. If the biopsy shows a separate malignancy, as long as the treating physician feels the natural history would not interfere with safety or efficacy analysis on the study, this would not be exclusionary. If they need to undergo surgery- please note the 28-day washout from a major surgery.

17. **A patient takes prednisone 5 mg orally once daily for appetite stimulation. Is this permitted on study?**
Yes, prednisone doses below 10 mg per day (or equivalent corticosteroid dose) are allowable. Since 5 mg of prednisone daily is less than the physiologic replacement dose, and since it is not taken for autoimmune issues, it is permitted.

18. **A patient is scheduled to have a plate fixed to their clavicle. How long does the patient need to wait before starting study therapy?**
There is a 28-day washout from surgery, though a shorter washout of 7 days is permitted for port-a-cath placement.

19. **A patient with stage IV NSCLC received prior immunotherapy with response and developed a grade 3 immune-related adverse event (irAE) with discontinuation of therapy. The patient**

now has tumor progression one year later and the investigator would like to enroll this patient on trial. Would the prior immune-related adverse event exclude the patient from trial?
Yes. Any Grade 3 or worse immune-mediated adverse event (except asymptomatic nonbullous/nonexfoliative rash) is excluded. Other exceptions include toxicities of any grade that require replacement therapy and has stabilized on therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) are allowed.

20. **A patient is being treated with leflunomide for immune checkpoint inhibitor induced arthritis. Is the patient eligible for S1800E?**
No. The patient is not eligible.

21. **Does metastatic disease or recurrent disease need to be biopsy-confirmed to meet protocol eligibility?**
No. The diagnosis of NSCLC needs to be pathologically or cytologically confirmed. Metastatic or recurrent disease can be shown on imaging only.

22. **An MRI has indicated that the patient has brain metastases. Is this patient eligible?**
Yes. Patients with brain metastases are eligible if the treating investigator determines that protocol treatment is safe for them.

Treatment

23. **A patient on study experiences a weight loss of 11%. Do the treatment doses need to be recalculated?**
Yes. Please follow SWOG Policy #38.

24. **What is the dose rounding policy for the study?**
Please follow dose rounding policy per SWOG Policy #38.

25. **Are growth factors permitted on study?**
Yes. Per section 7.2 a. supportive care (including growth factors) may be given as indicated by the current American Society of Clinical Oncology (ASCO) guidelines.

Study Calendar

26. **My patient got a PET scan at baseline, but the scanner specifications later changed, where CT from PET cannot be used for study. Is it okay to use a CT scan moving forward?**
A CT would be used for assessment, but this would need to be noted as a deviation, since the same type of test needs to be used for assessment.

27. **A patient has a 6.2 cm ground glass opacity in the lung. Is this considered a target lesion?**
No, ground glass is not considered measurable disease

28. **My patient was found to have 2+ proteinuria (grade 2) on urine dipstick. Is the patient required to undergo 24-hour urine protein collection before treating?**
Per protocol, if there is grade 2 proteinuria on urine dipstick, 24-hour urine protein needs to be checked. If urine protein is >2g/24 hours, ramucirumab needs to be held until resolution to <2g/24 hours and restarted at the next lower dose.

29. **A patient consented to optional sample collection. How many EDTA tubes need to be collected?**
Please ship at least 2 tubes of each of the following to SWOG biobank.
Plasma - 0.5 ml aliquots in cryovials
Buffy coat - 2 ml cryovials

Please review the details in section 15.5.

30. **If a target or non-target lesion is biopsied while on study, should they be marked as unevaluable on the RECIST 1.1 report?**
    No. The protocol does not specify that assessment of lesions that are biopsied is in any way different from those that are not. No need to exclude such lesions from assessment or make them unevaluable.

31. **A subject was registered and scheduled to start 5 days after registration. The start date was delayed due to an unexpected family event and the patient will be outside of the 7-day window from the date of registration. The patient is still interested in starting on study. Please advise.**
    The expectation is to have the planned start within 7 days after registration, and we understand that unexpected circumstances may delay the actual start date. Please have the investigator document the reasons for the delay in the patient chart.

For answer to questions not addressed in this FAQ, please use the contact information below:

- Eligibility, RAVE, Data Submission: LUNGMAPquestion@crab.org
- Regulatory, Protocol, Informed Consent: protocols@swog.org
- Medical Queries (treatment or toxicity related questions): S1800Emedical Query@swog.org