S2302 PRAGMATICA-LUNG
A PROSPECTIVE RANDOMIZED STUDY OF RAMUCIRUM (LY3009806; NSC 749128) PLUS PEMBROLIZUMAB (MK-3475; NSC 776864) VERSUS STANDARD OF CARE FOR PARTICIPANTS PREVIOUSLY TREATED WITH IMMUNOTHERAPY FOR STAGE IV OR RECURRENT NON-SMALL CELL LUNG CANCER

ACTIVATION DATE: 06-MAR-2023

SCHEMA

Patients with Stage IV or recurrent non-small cell lung cancer

Randomization

Arm A
Investigator’s Choice of Standard of Care

Primary Endpoint: Overall Survival
Accrual Goal: 700 participants

Arm B
Ramucirumab + Pembrolizumab

For guidance on Investigator's Choice of Standard of Care, see Section 7.2.

Treatment assignment will be determined by block randomization with equal probability within block. Stratification factors are:

1. Most recent line of therapy for NSCLC included anti-PD-1 or anti-PD-L1 therapy (yes versus no), and
2. Performance status (0 or 1 versus 2).

ARM A  Investigator’s Choice of Standard of Care

• The specific treatment is to be determined by the treating investigator and participant.
• Recommended that the choice of SoC drug(s) is based on NCCN guidelines for a “systemic therapy for advanced or metastatic disease-subsequent.”
• Dosing administration should be based on participant’s previous therapy and disease.
• Drug(s) should be administered according to the current FDA-approved package insert(s).

ARM B  Ramucirumab + Pembrolizumab

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>DAY</th>
<th>SCHEDULE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramucirumab</td>
<td>10 mg/kg</td>
<td>IV (over 30-60 minutes)</td>
<td>Day 1</td>
<td>Q 21 days</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>200 mg</td>
<td>IV over 30 minutes</td>
<td>Day 1</td>
<td>Q 21 days up to 35 cycles</td>
</tr>
</tbody>
</table>

FOR QUESTIONS REGARDING ELIGIBILITY, DATA SUBMISSION & GENERAL INQUIRIES, CONTACT: LungQuestion@crab.org

FOR MEDICAL OR TREATMENT-RELATED S2302 QUESTIONS, CONTACT: S2302Chairs@swog.org
PRAGMATIC DESIGN CONSIDERATIONS

The goals of **S2302** include:
- Empowerment of investigators to treat patients as would be done in real world practice.
- To decrease barriers to enrollment, and
- To minimize the data collection burden.

This means:
- **No** protocol-required disease assessments (CT, imaging). Instead, imaging should be done per institution standard. Tumor measurements and images are **not** collected in the Rave EDC.
- **No** protocol-required lab tests. Labs should be done per institutional standard and FDA-approved package inserts(s) and are **not** collected in the Rave EDC.
- **No** specimen collection.
- **No** Patient Reported Outcome instruments.
- **Only** report Grade 5 and unexpected treatment-related serious Grade 3 and Grade 4 Adverse Events. In other words, **only** AEs requiring expedited reporting via CTEP-AERS are required to be entered in the Rave EDC.
- **No** cycle-based Treatment Forms. Treatment information will be captured once at initiation and once at discontinuation of protocol treatment.
- **No** detailed Follow-up Form, only Vital Status (alive or not).

RESOURCES AND MATERIALS

All available on protocol page on www.CTSU.org:
- Link to site initiation training in CLASS – recorded presentation and slides available
- Funding Sheet & Coverage Analysis: Note additional $500 per participant payment
- EMR template to assist with EMR implementation
- Coming soon: Patient-friendly plain language trial summary

ADDITIONAL CONTACT INFORMATION (SEE PROTOCOL SECTION 18.1):

<table>
<thead>
<tr>
<th>Regulatory, Protocol &amp; Informed Consent Questions:</th>
<th><a href="mailto:protocols@swog.org">protocols@swog.org</a>, phone: (210) 614-8808</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Advocate:</td>
<td><a href="mailto:judyjohnson.519@gmail.com">judyjohnson.519@gmail.com</a></td>
</tr>
<tr>
<td>Access to iMedidata Rave, Delegation Task Log (DTL) Issues, OPEN:</td>
<td><a href="mailto:ctsucontact@westat.com">ctsucontact@westat.com</a>, phone: (888) 823-5923</td>
</tr>
<tr>
<td>Serious Adverse Event (SAE) Reporting Questions:</td>
<td><a href="mailto:adr@swog.org">adr@swog.org</a></td>
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