S1800A Phase II

Coordinating Group: SWOG

A Phase II Randomized Study of Ramucirumab plus MK3475 (Pembrolizumab) versus Standard of Care for Patients Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Non-Matched Sub-Study)

Participants:
SWOG, CTSU (Supported by Alliance, CCTG, ECOG-ACRIN, and NRG)

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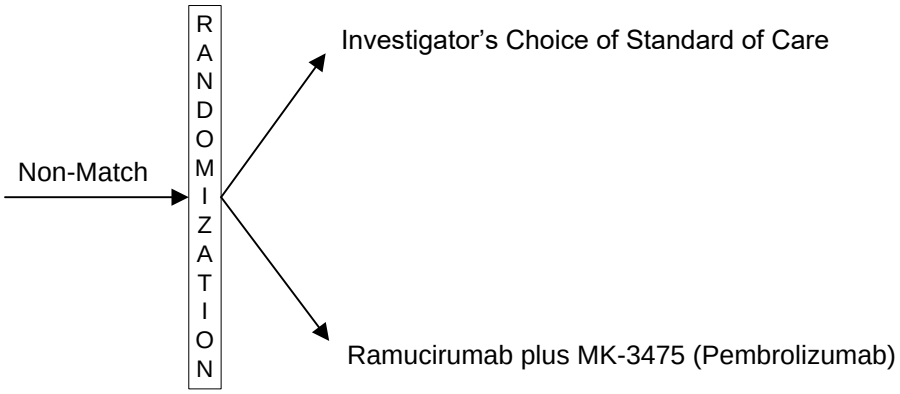
SCHEMA



Objectives

To compare overall survival (OS) between patients previously treated with platinum-based chemotherapy and immunotherapy for Stage IV or recurrent non-small cell lung cancer randomized to ramucirumab plus MK-3475 (pembrolizumab) versus standard of care.

To compare response rates between the arms, including complete response (CR) and partial response (PR) (confirmed and unconfirmed).

To compare the disease control rate (CR, PR, confirmed and unconfirmed, and stable disease).

To evaluate the duration of response among responders within each arm.

To evaluate the frequency and severity of toxicities within each arm.

To compare investigator-assessed progression-free survival (IA-PFS) between the arms.

To evaluate the clinical outcomes (OS, IA-PFS, response) by randomization stratification factors by comparing outcomes within the ramucirumab and MK-3475 (pembrolizumab) arm, performing a sub-group analysis of the arms, and by evaluating an interaction between the factors and treatment arm.

Patient Population

Patients must have been eligible for the screening study and must have been assigned to the S1800A sub-study based on biomarker profiling results. Patients must have received exactly one line of anti-PD-1 or anti-PD-L1 therapy for at least 84 days as their most recent line of therapy, either alone or in combination with platinum-based chemotherapy and must have experienced disease progression during or after this regimen. Patients whose most recent line of therapy was anti-PD-1 or anti-PD-L1 monotherapy must have also experienced disease progression during or after prior platinum-based chemotherapy. Patients must have measurable disease documented by CT or MRI. Patients must not have leptomeningeal disease, spinal cord compression or brain metastases unless they meet the criteria in the protocol. Patients must not have EGFR sensitizing mutations, EGFR T790M mutations, ALK gene fusions, ROS1 gene rearrangements, or BRAF V600E mutations unless they have progressed following all standard of care targeted therapy.

Patients must not have received nitrosoureas or mitomycin-c within 42 days prior to sub-study randomization. Patients must not have received any prior systemic therapy within 21 days prior to sub-study randomization. Patients must have recovered (≤ Grade 1) from any side effects of prior therapy. Patients must not have received systemic treatment with corticosteroids or other immunosuppressive medications within seven days prior to sub-study randomization. Patients must not have received any radiation therapy within 14 days prior to sub-study randomization or lung radiation therapy of > 30 Gy within six months prior to first planned dose. Patients must not have undergone major surgery within 28 days prior to sub-study randomization, or subcutaneous venous access device placement within seven days prior to randomization. Patients must not be planning to receive any concurrent therapy for cancer while receiving treatment on this study.

Patients must have Zubrod performance status of 0-1 and adequate hepatic, cardiac, coagulation, hematologic, renal, and gastrointestinal function. Patients must not have experienced a Grade 3 or worse immune-related adverse event (irAE) or any unresolved Grade 2 irAE, nor have experienced a toxicity that led to permanent discontinuation of prior anti-PD-1/PD-L1 immunotherapy. Patients must not have any history of organ transplant that requires use of immunosuppressives. Patients must not have clinical signs or symptoms of active tuberculosis infection or received a live attenuated vaccination within 28 days prior to sub-study randomization. Patients must not have history of non-infectious pneumonitis that required steroids or current pneumonitis/interstitial lung disease. Patients must not have had a serious or nonhealing wound, ulcer, or bone fracture within 28 days prior to sub-study randomization. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection. Patients with a known history of HIV seropositivity must have undetectable viral load, an adequate CD4 count, must not require prophylaxis for any opportunistic infections, and must not be newly diagnosed within the last 12 months. Patients must not have gross hemoptysis within two months of sub-study randomization. Patients must not have an active autoimmune disease that has required systemic treatment in the past two years or have any history of primary immunodeficiency.

Patients must agree to have blood specimens submitted for circulating tumor DNA. Patients must be offered participation in banking and in the correlative studies for collection and future use of specimens.

Stratification/Descriptive Factors

Randomization will be stratified by the following factors: (1) PD-L1 status: negative (<1%) vs positive (≥1%) or unknown; and (2) histology: squamous (including mixed histology with any squamous component) vs non-squamous; and (3) if patient is randomized to standard of care arm, does the planned treatment include ramucirumab?: yes vs no.

Accrual Goals

The accrual goal is 144 patients to achieve 130 eligible patients. The first interim analysis will be performed when at least 24 weeks have elapsed since the 18th eligible patient was randomized to the investigational arm. The second interim analysis will be performed when at least 45 (50%) of the expected deaths have occurred.