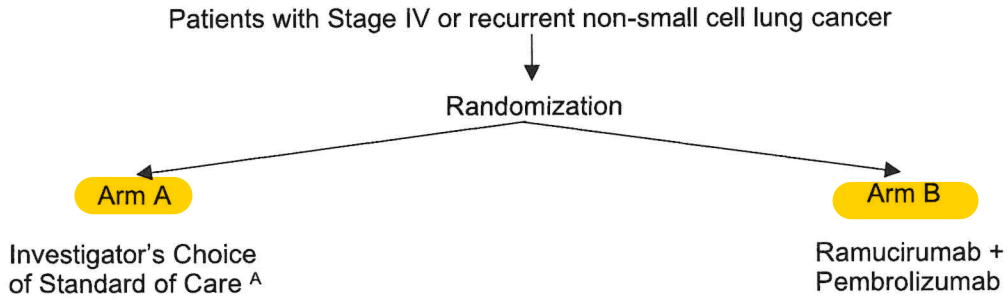
PROTOCOL CONTACT INFORMATION (see Section 18.1)

CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION (see Section 18.2)

SCHEMA



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

1.0 OBJECTIVES

1.1. Primary Objective

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

1.2. Secondary Objective

To summarize reports of serious and unexpected high-grade (≥ Grade 3) treatment-related adverse events determined by the treating physician within each treatment arm.

2.0 BACKGROUND

2.1. Background / Rationale

Cancer clinical trials have become increasingly complex placing barriers on enrollment. Efforts to broaden eligibility to promote diverse and representative populations have been utilized in recent studies. *(1, 2)* In support of the FDA draft guidance, "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Subgroups in Clinical Trials," we propose a pragmatic randomized trial with the aim to validate overall survival (OS) results from a randomized phase II trial. S1800A was a Phase II Randomized Study of Ramucirumab plus Pembrolizumab versus Standard of Care for Patients Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer performed within the Lung-MAP platform that was reported at ASCO 2022 and co-published in JCO at the time of presentation. *(3)* The primary endpoint in this study was overall survival (OS). A non-match sub-study within Lung-MAP, the trial enrolled 136 eligible patients who acquired resistance to prior immunotherapy, defined as disease progression during or after a platinum-based doublet and anti-PD-1 or anti-PD-L1 therapy at least 84 days following initiation of anti-PD-1 or anti-PD-L1 therapy (combination or monotherapy). OS was significantly improved with a hazard ratio (HR) and 80 percent confidence interval (CI) of 0.69 (0.51-0.92), with median OS of 14.5 (13.9-16.1) and 11.6 (9.9-13.0) months, for pembrolizumab and ramucirumab vs. standard of care, respectively. A follow-on randomized study is needed to confirm these results.

This proposed study presents a novel and potentially practice-changing paradigm to conduct a generalizable study with a combination of FDA approved drugs with well-known safety profiles with limited toxicity overlap. Previously, the QUASAR (QUick And Simple And Reliable) collaborative group led studies with a similar paradigm in colorectal cancer