FAST FACTS

S1929, Phase II Randomized Study of Maintenance Atezolizumab Versus Atezolizumab in Combination with Talazoparib in Patients with SLFN11 Positive Extensive Stage Small Cell Lung Cancer (ES-SCLC)

ELIGIBILITY CRITERIA

STEP 1: SCREENING REGISTRATION

a. Disease Related Criteria

a. Participants must have histologically or pathologically confirmed diagnosis of extensive stage small cell lung cancer (ES-SCLC) at the time of protocol entry as defined in Section 4.0.

b. Prior/Concurrent Therapy Criteria

1. Participants must have completed at least one cycle of frontline induction treatment with platinum plus etoposide plus atezolizumab prior to Step 1 Screening Registration. Cycle 1 of frontline induction treatment may or may not contain atezolizumab.
   NOTE: Participants may be screened while receiving consolidation thoracic radiation or during prophylactic cranial irradiation (PCI) at the time of Step 1 Screening Registration. Participants may or may not receive consolidation thoracic radiation and/or PCI per the discretion of their treating investigator.
2. Participants must not have received any immunotherapy for SCLC prior to starting the frontline induction treatment for ES-SCLC.
3. Participants must not have received any investigational agent for the treatment of ES-SCLC.

c. Clinical/Laboratory Criteria

1. Participants must be ≥ 18 years of age at the time of Step 1 Screening Registration.

d. Specimen Submission Criteria

1. Participants must have adequate tumor tissue available from a core biopsy defined as:
   • at least two (3-5 microns) unstained slides, or;
   • one (3-5 microns) unstained slide plus one H&E stained slide
   Participants must agree to have this tissue submitted to M.D. Anderson Cancer Center (MDACC) for SLFN11 immunohistochemistry (IHC) testing (See Section 15.2).
   Note: A histologic review will be performed at MDACC to confirm adequate cellularity for the testing. If inadequate cellularity, additional unstained slides from the same participant may be submitted if it doesn't exceed the window of starting maintenance therapy.

e. Regulatory Criteria

1. Participants must be informed of the investigational nature of this study and must sign and give informed consent in accordance with institutional and federal guidelines.
2. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

3. Participants with impaired decision-making capacity are eligible as long as their neurological or psychological condition does not preclude their safe participation in the study (e.g., tracking pill consumption and reporting adverse events to the investigator).

STEP 2: RANDOMIZATION

a. Disease Related Criteria
   i. Site must have received notification from the SWOG Statistics and Data Management Center (SDMC) that the participant's tumor sample is SLFN11 positive.
   ii. Participants must have their disease (see Section 10.1) documented by CT or PET/CT of chest, abdomen, and pelvis (with contrast, unless contraindicated). Measurable disease must be assessed within 28 days prior to Step 2 Randomization. Non-measurable disease must be assessed within 42 days prior to Step 2 Randomization. The CT from a combined PET/CT may be used only if it is of diagnostic quality as defined in Section 10.1a. All known sites of disease must be assessed and documented on the Baseline Tumor Assessment Form (RECIST 1.1).
   iii. Patients must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to Step 2 randomization. Patient must not have leptomeningeal disease, spinal cord compression or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, and prior to Step 2 randomization, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least 24 hours prior to Step 2 randomization.
   iv. Participants must not have had disease progression based on post induction imaging in the opinion of treating investigator.

b. Prior/Concurrent Therapy Criteria
   i. Participants must be registered to Step 2 Randomization prior to the start of maintenance atezolizumab.
   ii. Participants must have received no fewer than 2 cycles and no more than 4 cycles of induction treatment with platinum/etoposide/atezolizumab.
   iii. Participant must not have received radiation treatment (RT) or prophylactic cranial irradiation (PCI) within 14 days prior to Step 2 Randomization.
   iv. Participants must not be taking strong P-gp inhibitors (e.g., dronedarone, quinidine, ranolazine), P-gp inducers (e.g., rifampin), or breast cancer resistance protein (BCRP) inhibitors (e.g., elacridar) within 7 days prior to randomization. Participants must not plan to receive the therapies listed above while on protocol treatment (See Section 3.2c3 for the full list of agent names).
   v. Participants must not have experienced the following during induction treatment:
   • Any Grade 3 or worse immune-related adverse event (irAE) in the opinion of the treating investigator. Exception: asymptomatic nonbullous/nonexfoliative rash.
   • Any unresolved Grade 2 irAE.
   • Any toxicity that led to permanent discontinuation of prior anti-PD-1/PD-L1 immunotherapy. Exception to the above: Toxicities of any grade that require replacement therapy and have stabilized on therapy (e.g., thyroxine, insulin, or

physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) are allowed.

c. Clinical/Laboratory Criteria
   i. History and physical exam must be obtained within 28 days prior to Step 2 randomization.
   ii. Participants must have adequate cardiac function. Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function and be considered class 2B or better on the New York Heart Association Functional Classification (see Section 18.2).
   iii. Participants must have Zubrod performance status 0-2 (see Section 10.5) documented within 28 days prior to Step 2 Randomization
   iv. Participants must have normal organ and marrow function within 28 days prior to Step 2 Randomization as defined below:
   • Leukocytes≥ 3,000/mcL
   • Absolute neutrophil count ≥ 1,500/mcL
   • Platelets ≥ 100,000/mcL
   • Total bilirubin ≤ institutional upper limit of normal (ULN)
   • AST/ALT ≤3 × institutional ULN
   • Creatinine ≤ institutional ULN OR estimated creatinine clearance > 30 mL/min
   Calculated Creatinine Clearance = (140 - age) X (weight in kg) †
   72 x serum creatinine *
   Multiply this number by 0.85 if the participant is a female.
   † The kilogram weight is the participant weight with an upper limit of 140% of the IBW.
   * Actual lab serum creatinine value with a minimum of 0.8 mg/dL.
   v. Participants with evidence of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load on suppressive therapy within in 6 months prior to Step 2 Randomization.
   vi. Participants with a history of hepatitis C virus (HCV) infection must have been treated and cured. For participants with HCV infection who are currently on treatment must have an undetectable HCV viral load within in 6 months prior to Step 2 Randomization.
   vii. Participants with known human immunodeficiency virus (HIV) infection must be on effective anti-retroviral therapy and must have undetectable viral load at their most recent viral load test and within 6 months prior to Step 2 Randomization.
   viii. Participants with known diabetes must not have uncontrolled diabetes. (Uncontrolled diabetes is defined as HgA1C > 7%)
   ix. Participants must be able to swallow capsule whole.
   x. Participants must not have any known clinically significant liver disease, including cirrhosis, fatty liver, or inherited liver disease.
   xi. Participants must not have end stage renal or other serious medical illness that may limit survival or the ability to participate in this study.
   xii. Participants must not have a history of idiopathic pulmonary fibrosis, pneumonitis (including drug induced), organizing pneumonia (i.e., bronchiolitis obliterans, cryptogenic organizing pneumonia, etc.), or evidence of active

pneumonitis on screening chest computed tomography (CT) scan. History of radiation pneumonitis in the radiation field (fibrosis) is permitted.

xiii. Participants must not have known active tuberculosis (TB).

xiv. Participants must not have undergone prior allogeneic bone marrow transplantation or prior solid organ transplantation.

xv. Participants must not have history of allergic reaction attributed to compounds of similar chemical or biological composition to atezolizumab and/or talazoparib.

xvi. Participants must not have a prior or concurrent malignancy whose natural history or treatment (in the opinion of the treating physician) has the potential to interfere with the safety or efficacy assessment of the investigational regimen.

xvii. Participants must not be on corticosteroids at doses greater than prednisone 10 mg daily or equivalent within 7 days prior to Step 2 Randomization.

xviii. Participants must not receive any live attenuated vaccines within 28 days prior to Step 2 Randomization or at any time during the study and until 5 months after the last dose of protocol treatment.

xix. Participants must not have severe infections in the form of severe sepsis or septic shock including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia within 14 days prior to Step 2 Randomization.

xx. Participants must not be pregnant due to the potential teratogenic side effects of the protocol treatment. Women of reproductive potential and men must have agreed to use an effective contraception method for the duration of protocol treatment, and for 7 months after the last dose of protocol treatment. A woman is considered to be of “reproductive potential” if she has had a menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate participant chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.
Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with atezolizumab, breastfeeding must be discontinued prior to Step 2 Randomization.

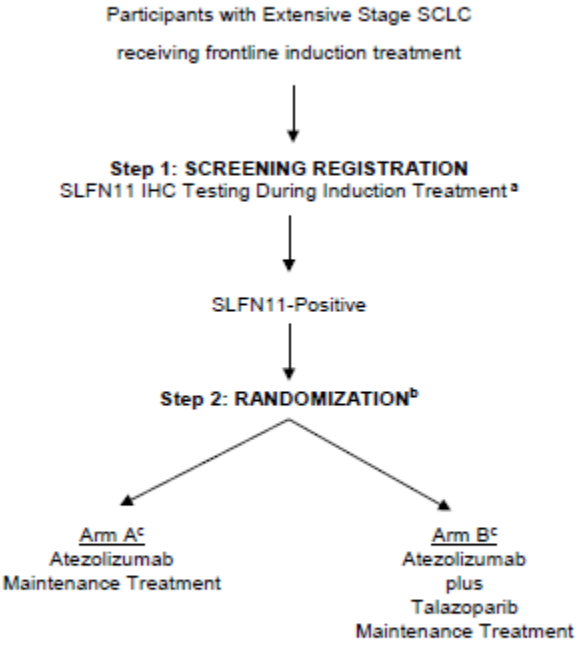
d. Specimen Submission Criteria
   i. Participants must be offered the opportunity to participate in specimen banking as outlined in Section 15.3. With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in Section 15.1.

e. Regulatory Criteria
   i. Participants must be informed of the investigational nature of this study and must sign and give informed consent in accordance with institutional and federal guidelines.
   ii. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to

ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

iii. Participants with impaired decision-making capacity are eligible as long as their neurological or psychological condition does not preclude their safe participation in the study (e.g., tracking pill consumption and reporting adverse events to the investigator).

SCHEMA



a. Induction treatment and timeframe are defined in Section 5.1b
b. After completion of frontline induction treatment
c. One cycle length = 21 days

Note: See Section 15.3e for the specimen timeline