Phase I and Randomized Phase II Double-Blind Clinical Trial of Cisplatin and Etoposide in Combination With Veliparib (ABT-888) or Placebo as Frontline Therapy for Extensive Stage Small Cell Lung Cancer

Overall E2511 Study Objective
To first determine the optimal dose of veliparib to be used safely in combination with standard doses of cisplatin and etoposide (CE) in a phase I dose escalation study. Once established, a randomized double-blind phase II study will determine whether the combination of veliparib plus CE improves survival in patients with untreated small cell lung cancer (SCLC)

Study Objectives
Phase I Primary Objective
• Determine the recommended phase II dose of veliparib to be used in combination with CE

Study Schema: Phase I Registration (Arms A, B, and C)

Total accrual goal = maximum of 18 patients.
Phase I study accrual is closed.
1 cycle = 21 days. A maximum of 4 cycles will be given.
Arm B was the established RP2D.
*Pre-registration is required for slot reservation prior to beginning eligibility verification. Only after a slot has been reserved, should the patient be worked up for the study. Slots will automatically expire after 7 days.
†On chemotherapy days, morning veliparib dose is administered after premedications for etoposide, prior to etoposide IV.
‡IV doses are based on patient weight.
§Toxicity will be evaluated during each cycle; trial will follow a traditional 3 + 3 design.
RP2D = recommended phase II dose.
**Phase II Primary Objective**
- Evaluate whether the combination of veliparib plus CE, compared with placebo plus CE, improves progression-free survival as a frontline therapy

**Phase II Secondary Objectives**
- Examine overall survival
- Assess overall response rate and complete response rate
- Determine the toxicity profile
- Examine the impact of veliparib plus CE on select biomarkers
- Compare the overall toxicity profile, specifically the incidence and severity of chemotherapy-induced peripheral neuropathy, of CE versus veliparib plus CE

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**Study Schema: Phase II Randomization (Arms D and E)**

**Arm D**
- Veliparib*† 100 mg PO bid, d 1-7
- Etoposide‡ 100 mg/m² IV, d 1-3
- Cisplatin‡ 75 mg/m² IV, d 1
  - 21 d × 4 cycles‡

**Arm E**
- Placebo* 100 mg PO bid, d 1-7
- Etoposide‡ 100 mg/m² IV, d 1-3
- Cisplatin‡ 75 mg/m² IV, d 1
  - 21 d × 4 cycles‡

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**Stratify**
- Gender (M vs F)
- LDH ≤ ULN or > ULN

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**Total accrual goal = 150 patients.**
- 1 cycle = 21 days. A maximum of 4 cycles will be given.
- Patients participating in the phase I portion are not eligible to enroll in the phase II study.
- *On chemotherapy days, morning veliparib/placebo dose is administered after premedications for etoposide, prior to etoposide IV.
- †Recommended phase II dose—dose for phase II was determined in phase I portion of study.
- ‡IV doses are based on patient weight.
- LDH = lactate dehydrogenase; ULN = upper limit of normal.
Eligibility Criteria*

**Main Inclusion Criteria**
- ≥ 18 years of age with histologically or cytologically confirmed
  - Phase I: extensive stage SCLC, stage IV (M1a or M1b) large cell neuroendocrine non–small cell lung cancer (NSCLC), or small cell carcinoma of unknown primary or extrapulmonary origin
  - Phase II: extensive stage SCLC
- Measurable or nonmeasurable disease based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) (phase I)
- Measurable disease based on RECIST v1.1 (phase II)
- ECOG performance status of 0 or 1
- Adequate organ and marrow function
- Ability to swallow pills

**Main Exclusion Criteria**
- Pregnancy or breast-feeding
- Central nervous system (CNS) metastases or history of CNS metastases
- Prior chemotherapy or biologic therapy for SCLC, large cell neuroendocrine NSCLC, or small cell carcinoma of unknown primary or extrapulmonary origin
- Completion of radiation less than 7 days before study registration
- Receiving investigational agents while on study
- Active seizures or history of seizures
- History of allergic reactions to compounds similar to veliparib or to the other agents used in this study
- Uncontrolled intercurrent illness, such as an ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled cardiac arrhythmia, or psychiatric illness
- HIV-positive status and on combination antiretroviral therapy

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.