# Abstract #TPS8126: A Phase 1/2 Clinical Trial of Quaratusugene Ozeplasmid Gene Therapy and Atezolizumab Maintenance Therapy in Patients with Extensive Stage Small Cell Lung Cancer (ES-SCLC)

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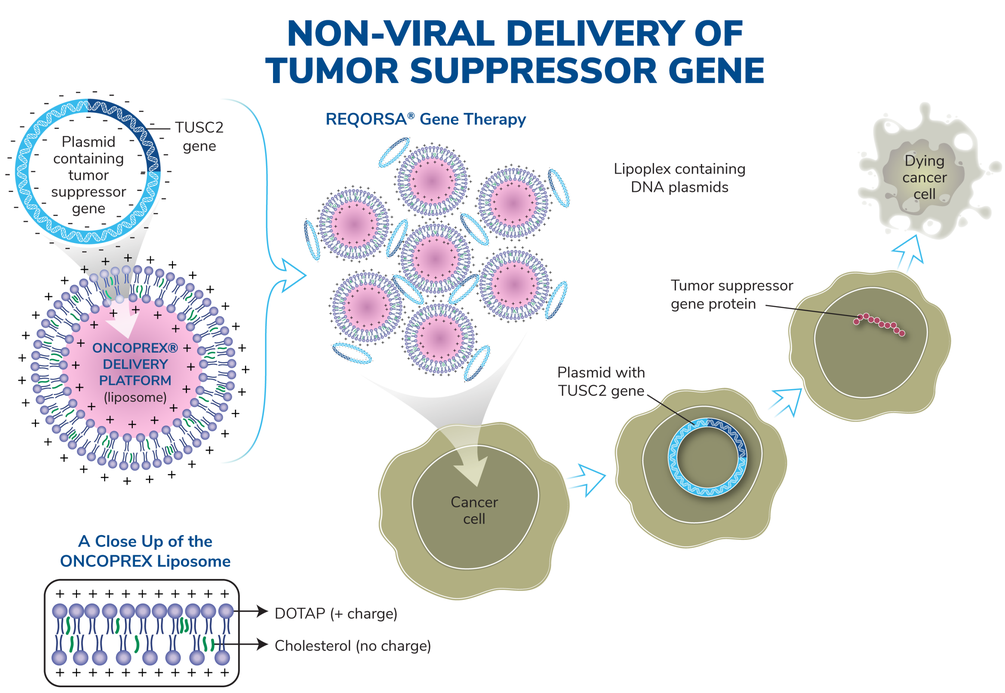
## BACKGROUND

- Tumor Suppressor Candidate 2 (*TUSC2*) is a tumor suppressor gene that encodes a multifunctional protein with effects on various cellular processes, including metabolism, tyrosine kinase inhibition, apoptosis, and immune response to cancer.
- The TUSC2 protein is reduced or absent in 100% of SCLCs.
- Standard treatment for ES-SCLC consists of either atezolizumab or durvalumab added to four cycles of carboplatin and etoposide, and then atezolizumab or durvalumab are continued as maintenance therapy until disease progression.
- In patients receiving atezolizumab and chemotherapy, the PFS after starting maintenance atezolizumab is only 2.6 months. Further improvements in the treatment of ES-SCLC are needed.

## QUARATUSUGENE OZEPLASMID

- Quaratusugene ozeplasmid gene therapy consists of the *TUSC2* gene expressing plasmid encapsulated in non-viral nanoparticles made from lipid-based molecules in a lipoplex form with a positive electrical charge.

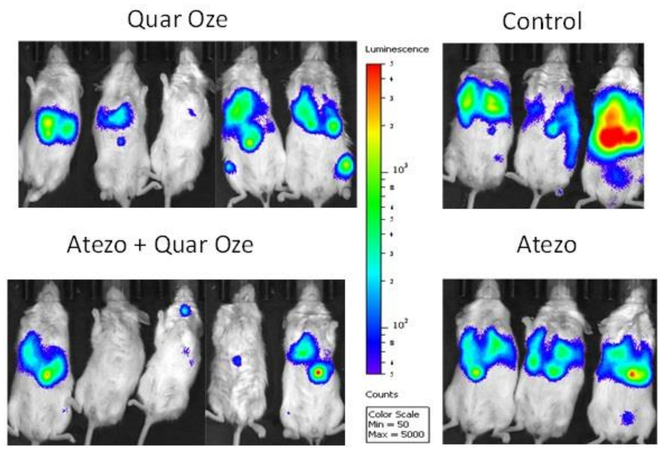
**Figure 1: Quaratusugene Ozeplasmid Utilizes Lipid-Based Nanoparticles in a Lipoplex Form to Encapsulate the TUSC2 Gene**




## PRECLINICAL RATIONALE

- Data from studies in humanized mouse models of SCLC that use human H841 cells have shown that the combination of quaratusugene ozeplasmid and atezolizumab provides significantly better control of tumor burden than either agent alone (Figure 2).
- Data with the combination also showed increases in infiltrating CD8 T-cells, NK cells and dendritic cells, and lower numbers of myeloid derived suppressor cells.

**Figure 2: Bioluminescence Flux after Quaratusugene Ozeplasmid and Atezolizumab as Single Agents and in Combination in H841 SCLC Model in Humanized Mice**




*Atezo = atezolizumab; max = maximum; min = minimum; Quar Oze = quaratusugene ozeplasmid*

## STUDY METHODS

- Quaratusugene ozeplasmid is administered IV every 21 days in escalating dose cohorts and atezolizumab 1200 mg is also administered IV every 21 days. Treatment continues until disease progression or unacceptable toxicity is experienced.
- Dexamethasone, acetaminophen, and diphenhydramine are given prior to each treatment to prevent delayed infusion-related reactions.
- Efficacy is evaluated after every even numbered cycle of treatment using RECIST 1.1 criteria.
- Safety is evaluated using CTCAE v5, with dose limiting toxicities generally defined as ≥Gr 3 AEs.
- TUSC2 protein expression is measured by a validated immunohistochemistry assay in paraffin sections to determine if PFS is related to pretreatment TUSC2 levels.
- A validated assay measures pharmacokinetics in all patients.

## CLINICAL STUDY DESIGN

**Figure 3: Primary Endpoint of Phase 2 is to Determine 18-week PFS Rate of Quaratusugene Ozeplasmid (Quar Oze) + Atezolizumab (Atezo) Maintenance Therapy**


- In Phase 1, two planned dose levels (0.09, and 0.12 mg/kg) of quaratusugene ozeplasmid were administered, and a standard dose escalation with 3-6 patients/dose level was used to determine the Maximum Tolerated Dose (MTD) or Recommended Phase 2 Dose (RP2D).
- The Phase 2 portion will enroll approximately 50 patients at approximately 10 to 15 U.S. sites.
- The primary endpoint of the Phase 2 portion is to determine the 18-week PFS rate from the time of the start of maintenance therapy with quaratusugene ozeplasmid and atezolizumab in patients with ES-SCLC. Patients will also be followed for survival.
- A Phase 2 futility analysis will be performed after the 25th patient enrolled and treated reaches 18 weeks of follow up.

## PATIENT ELIGIBILITY CRITERIA

- Male or female ≥18 years of age with ES-SCLC.
- Complete Response, Partial Response, or Stable Disease after receiving at least three cycles, and no more than four cycles, of atezolizumab, carboplatin, and etoposide.
- Patients must have ECOG Performance Status of 0 to 1.
- Asymptomatic brain metastases must meet ALL criteria of the following (a-d):
  a. No history of seizures in the preceding six months.
  b. Definitive treatment must be completed ≥21 days prior to enrollment.
  c. Must be off steroids administered because of brain metastases or related symptoms for ≥7 days.
  d. If had previous brain irradiation, post-treatment imaging must demonstrate stability or regression of the brain metastases.
- Neither prophylactic cranial irradiation nor consolidation thoracic radiation are allowed. This applies both prior to and during the study.
- Prior cranial irradiation for brain metastases is allowed.

## FURTHER INFORMATION

1. Oncology Associates of Oregon, Eugene, OR
2. Texas Oncology, Dallas, TX
3. Rocky Mountain Cancer Centers, Denver, CO
4. Texas Oncology, Tyler, TX
5. Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR
6. Virginia Cancer Specialists, Fairfax, VA
7. Northwest Cancer Specialists, Vancouver, WA
8. Oncology-Hematology Care, Cincinnati, OH
9. Genprex, Inc., Austin, TX
10. Washington University School of Medicine, St. Louis, MO

For more information, please visit www.genprex.com.

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