Poster# **2798eTiP**

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Trial in progress: A Phase Ib/II study assessing [^{177}Lu]Lu-DOTA-TATE plus standard of care as a first-line treatment for patients with extensive-stage small cell lung cancer

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KEY FINDINGS & CONCLUSIONS

- There is a high unmet need for novel treatments in ES-SCLC.
- Patients with newly diagnosed ES-SCLC have a poor prognosis and often experience disease relapse after initially responding to current SOC.
- Expression of SSTR2 in ~50% of SCLC tumors makes ^{177}Lu-DOTATATE an attractive therapeutic candidate.
- The Phase II part of this study is assessing the efficacy and safety of the RP2D of ^{177}Lu-DOTATATE in combination with carboplatin, etoposide, and atezolizumab (as determined in Phase Ib) in patients with newly diagnosed ES-SCLC.

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INTRODUCTION

- Patients with newly diagnosed extensive-stage small cell lung cancer (ES-SCLC) have a poor prognosis, with a 5-year survival rate of ≤12%. Although patients generally respond to standard of care (SOC; platinum-based chemotherapy + etoposide + checkpoint inhibitor [CPI]), relapse is common. This highlights the need for new and improved therapies.[1–5]
- Approximately 50% of SCLC tumors express somatostatin receptor 2 (SSTR2) and SSTR2 expression has been identified as a poor prognostic biomarker.[6] SSTR imaging has shown high sensitivity for the detection of primary SCLC tumors.[7,8]
- [^{177}Lu]Lu-DOTA-TATE (^{177}Lu-DOTATATE) is a radioligand therapy with high affinity for SSTR2.[9]
- In an SCLC xenograft model, ^{177}Lu-DOTATATE plus carboplatin/etoposide was more effective at tumor regression than either treatment alone.[10]
- A Phase I study in nine patients with ES-SCLC demonstrated that ^{177}Lu-DOTATATE in combination with nivolumab (a CPI) was well tolerated with indications of antitumor activity.[11]
- NCT05142696[12] is the first clinical study to assess ^{177}Lu-DOTATATE in combination with carboplatin/etoposide and a CPI in patients with newly diagnosed ES-SCLC. The Phase Ib part of the study was presented previously;[13] here, we describe Phase II.

PHASE II OBJECTIVES

Primary

- To assess the efficacy of ^{177}Lu-DOTATATE in combination with carboplatin, etoposide, and atezolizumab (SOC) versus SOC alone, measured by overall survival (OS).

Secondary

- To evaluate the antitumor activity of ^{177}Lu-DOTATATE in combination with SOC versus SOC alone.
- To characterize the safety and tolerability of ^{177}Lu-DOTATATE in combination with SOC in induction treatment and with atezolizumab in maintenance treatment.
- To assess the safety and tolerability of [^{68}Ga]Ga-DOTA-TATE (^{68}Ga-DOTATATE).

STUDY DESIGN

- Both phases of the study consist of a screening period, treatment period (induction period and maintenance period), and follow-up period.

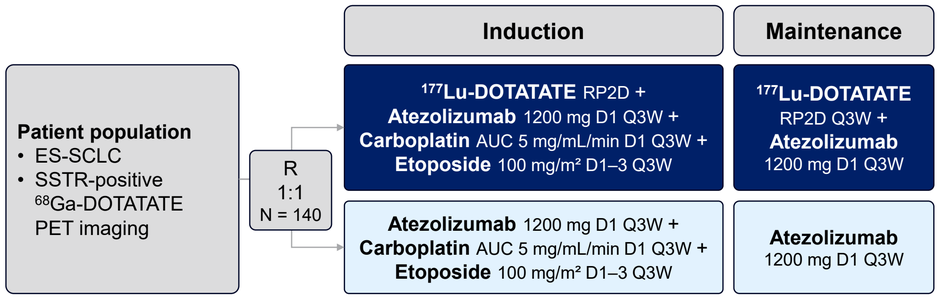
Phase Ib

- Phase Ib was a dosage-escalation study with concurrent backfill to determine the recommended Phase II dosage (RP2D) of ^{177}Lu-DOTATATE in combination with carboplatin, etoposide, and tislelizumab.[13]
- Following a protocol amendment, the CPI for Phase Ib was changed from tislelizumab to atezolizumab to align more closely with current SOC, and a Phase II expansion part was added to the study.
- There were six provisional dosage levels (DLs) of ^{177}Lu-DOTATATE to be assessed, with each DL providing an incremental dosage increase, during either the induction period or the maintenance period.
- Within each DL, 3–6 patients were enrolled to evaluate the dosage-limiting toxicity (DLT) rate within the first 6 weeks of ^{177}Lu-DOTATATE treatment; each DL could be backfilled up to a total of 10 patients.
- Dosage-escalation decisions were guided by the DLT rate at the current DL (per the Bayesian Optimal Interval design) plus all available safety data.

Phase II

- Phase II is a randomized controlled study designed to assess the efficacy and safety of the RP2D of ^{177}Lu-DOTATATE (as determined in Phase Ib) in combination with SOC, i.e., carboplatin, etoposide, and atezolizumab (experimental arm) versus SOC alone (control arm) (**Figure 1**).
- Approximately 140 patients with newly diagnosed ES-SCLC will be randomized in a 1:1 ratio to the experimental arm or the control arm.

Figure 1. Phase II design



AUC, area under the curve; C, cycle; D, day; ES-SCLC, extensive-stage small cell lung cancer; PET, positron emission tomography; Q3W, every 3 weeks; R, randomized; RP2D, recommended Phase II dosage; SSTR, somatostatin receptor.

- Before/during screening, both arms will receive one cycle of carboplatin/cisplatin + etoposide ± atezolizumab.
- In the induction period, both arms will receive SOC (3 cycles); the experimental arm will also receive ^{177}Lu-DOTATATE (2 administrations).
- In the maintenance period, both arms will receive atezolizumab (Q3W); the experimental arm will also receive ^{177}Lu-DOTATATE (Q3W).
- The treatment period continues until confirmed radiological disease progression or discontinuation for another reason, including unacceptable toxicity.
- This study is recruiting and is being conducted in Europe, North America, and Asia.

STUDY POPULATION

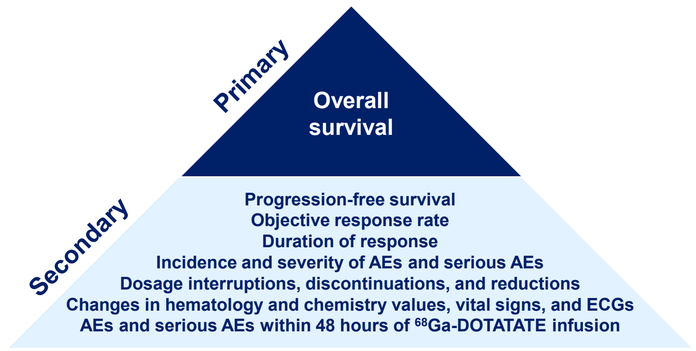
- An overview of the key inclusion and exclusion criteria is provided in **Table 1.**

Table 1. Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
Adults aged ≥18 years	Prior therapy with an antibody or drug against immune checkpoint pathways
Histologically or cytologically confirmed ES-SCLC (per the AJCC Cancer Staging Manual, 8th edition)	Any condition that requires systemic treatment with corticosteroids (>10 mg daily of prednisone or equivalent) or other immunosuppressant medication ≤14 days before commencing study treatment
Measurable disease in ≥1 target lesion per RECIST v1.1 assessed by conventional CT scan	
SSTR-positive ^{68}Ga-DOTATATE imaging PET scan with uptake ≥ liver uptake in ≥1 target or non-target lesion	
No prior systemic treatment for ES-SCLC (except for the one cycle of chemotherapy ± atezolizumab received before/during screening)	

AJCC, American Joint Committee on Cancer; CT, computed tomography; ES-SCLC, extensive-stage small cell lung cancer; PET, positron emission tomography; RECIST, Response Evaluation Criteria in Solid Tumors; SSTR, somatostatin receptor.

PHASE II ENDPOINTS



AE, adverse event; ECG, electrocardiogram.

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Disclosures

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