

BACKGROUND

Limited-stage (LS) SCLC is an aggressive disease with a high-risk of relapse. Although concurrent chemoradiotherapy is the standard of care, many patients are not eligible due to age, comorbidities, or tumour-related factors and instead receive sequential chemotherapy.

Despite high initial response rates, relapse after first-line treatment is extremely frequent, and no standard maintenance therapy has demonstrated a survival benefit in this setting. In this context, DLL3-targeting drugs such as tarlatamab have shown promising antitumor activity and a manageable safety profile.

The MERLIN trial aims to evaluate the efficacy of tarlatamab as maintenance therapy after sequential chemoradiotherapy in patients with LS-SCLC who are not eligible for concurrent treatment.

OBJECTIVES

Primary endpoint: To evaluate the efficacy of tarlatamab as maintenance therapy after sequential chemoradiotherapy in LS-SCLC, as assessed by progression-free survival (PFS).

Secondary endpoints: Evaluate objective response rate (ORR), overall survival (OS) at 6, 12, and 24 months, PFS rates at 6, 12, and 24 months, and assess the safety and tolerability profile of tarlatamab, including the frequency and severity of adverse events.

Exploratory endpoints: Characterization of the tumor microenvironment at baseline and peripheral antitumor immune responses during treatment, and the association of these biomarkers with clinical outcomes.

KEY ELIGIBILITY CRITERIA

Inclusion criteria:

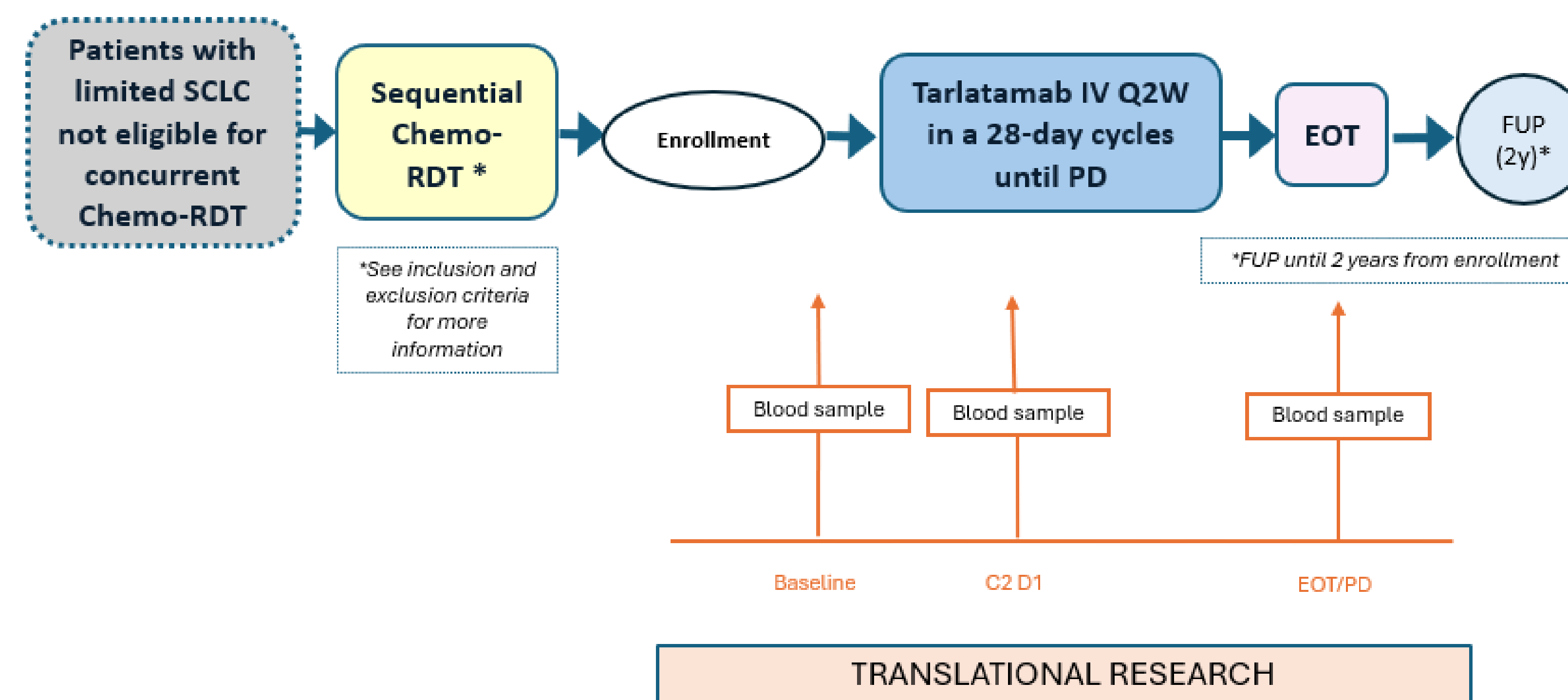
- Adults with histologically or cytologically confirmed LS-SCLC.
- Patients who are not eligible for concurrent chemoradiotherapy, previously treated with sequential chemoradiotherapy or with chemotherapy alone.
- No disease progression after completion of prior treatment according to RECIST v1.1.
- ECOG performance status 0-2 and at least one measurable lesion according to RECIST v1.1.

Exclusion criteria:

- Extensive-stage SCLC or mixed SCLC-NSCLC histology.
- Requirement for concurrent thoracic radiotherapy.
- Active neurologic paraneoplastic syndrome of autoimmune origin.
- Uncontrolled infections, interstitial lung disease, or active pneumonitis.
- Significant comorbidities compromising study participation or safety.

TRIAL DESIGN AND PROCEDURES

MERLIN is an ongoing, open-label, exploratory, multicentre, phase II clinical trial (EuCT Number: 2024-515201-26-00).



A total of **37 patients** with LS-SCLC who are not eligible for concurrent chemoradiotherapy and/or who have completed sequential chemoradiotherapy or chemotherapy alone without disease progression **will be enrolled**.

At enrollment, patients will undergo radiological assessment according to RECIST v1.1 and collection of tumor tissue and peripheral blood samples for translational research.

Patients will then receive **tarlatamab maintenance therapy with a step-up dosing regimen** consisting of 1 mg on cycle 1 day 1, followed by 10 mg on days 8 and 15, and then 10 mg every 2 weeks in 28-day cycles. Tumor assessments* will be performed according to protocol-defined schedules throughout treatment.

Peripheral blood samples will be collected at baseline, at cycle 2 day 1, and at end of treatment or disease progression to evaluate immune biomarkers, tumor microenvironment characteristics, and their association with clinical outcomes.

Treatment will continue until disease progression, unacceptable toxicity, withdrawal of consent, investigator's decision, or study discontinuation. After treatment completion, patients will enter a follow-up period until 2 years after enrollment.

Safety evaluations will be conducted throughout treatment, including monitoring of adverse events and treatment tolerability.

**All patients will undergo contrast-enhanced chest and upper abdomen CT (unless contraindicated), full body PET-CT, CT of the pelvis or neck when indicated, brain MRI or CT, and bone scans if clinically indicated.*

STATISTICAL CONSIDERATIONS

The sample size was calculated using a one-arm survival design based on the log-rank test.

As an exploratory proof-of-concept phase II study, **the sample size was estimated assuming an improvement in median PFS from 8 months** under the null hypothesis **to 18 months** under the alternative hypothesis, using a one-sided α of 0.025 and 80% power. Accrual and follow-up will each be 24 months, and allowing for a 10% dropout rate, **37 patients will be enrolled**.

Efficacy analyses will be performed in the intention-to-treat (ITT) population, while safety analyses will include all patients receiving at least one dose of tarlatamab.

Time-to-event endpoints, including PFS and OS, will be estimated using the Kaplan-Meier method with corresponding confidence intervals. Objective response rate (ORR), safety, and other categorical variables will be summarized using descriptive statistics.

RECRUITMENT

- Approval by health authorities received on 2 October 2025.
- Participating sites: 20
- Total patients requested: 37
- Total patients included: 3

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