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156TiP: Evaluating the Efficacy and Safety of Niraparib Combined with Radiotherapy and Toripalimab in Patients with Recurrent Small Cell Lung Cancer: an Open Label, Single Arm, Phase II Study

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Introduction

- Small cell lung cancer (SCLC) accounts for 15 % of all lung cancer, rapid growth, early metastasize to distant sites of the body.[1]
- SCLC responds well to chemotherapy/ radiotherapy initially, relapses develop resistance.
- SCLC has neuroendocrine (NE) features, is deadly, has a high mortality, recalcitrant cancer.[2]

SCLC Pathogenesis

- Replication stress due to several intrinsic factors causes genotoxicity, cytotoxicity.[3]
- Initiates DNA damage repair pathway, replication stress response pathway.
- Leading to the high burden of mutation in SCLC weakening genome integrity.
- Activation of oncogenes and blocking tumor suppressors.

Toripalimab

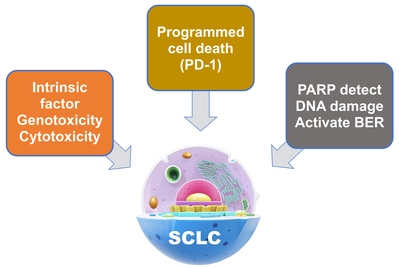
- Toripalimab is an IgG4 monoclonal antibody, specifically binds to PD-1 molecules on the surface of lymphocytes, block the PD-1/ PD-L1 pathway leading to tumor immune tolerance, and reactivate the antitumor activity of lymphocytes.

Niraparib

- Poly(ADP ribose) polymerases (PARP)-detect DNA damage and promote repair, activate the base excision repair (BER) pathway.
- Niraparib is an oral, selective inhibitor of PARP-1 and PARP-2.

Objective

- Although chemo-radiotherapy is effective initially, SCLC relapse.
- Immunotherapy - known to enhance the effects of radiotherapy.
- PARP inhibitors can selectively kill cancer cells with homologous recombination defects and other DNA repair mechanisms.
- Our objective is to take the advantage of these 3 mechanisms to treat SCLC.
- To evaluate the efficacy and safety of niraparib combined with radiotherapy and toripalimab in the treatment of recurrent small-cell lung cancer.



Methods

Study design

Study start date - Enrollment:	April 2022
End of Enrollment:	June 2024
Study end date:	December 2024
Report date:	March 2025

Treatment Plan

- Treat with 200 mg of Niraparib orally QD from the 1st day + Select non-target lesion suitable for SBRT for radiotherapy (8Gy x 3F) from the 4th day + Toripalimab 240 mg iv.drip Q3W from the 7th day.
- The second cycle: Continue to receive the combined treatment of Toripalimab (240 mg D1 Q3W) + Niraparib (200 mg QD) 21 days/ one cycle, until disease progression, up to 2 years.

Statistical analysis

- Descriptive statistics will be used to summarize the demography, clinical, treatment data, primary endpoint, secondary endpoint before and during the trial.
- SAS statical software will be used for statistical analysis.

Study Overview

Screening period

Key inclusion criteria

- Tissue proven ES-SCLC.
- 18-70 years old.
- Previously received 1-2 lines of treatment (including 1 systemic platinum containing treatment).
- Response to first platinum containing treatment.*
- ECOG PS 0-2 points.
- There is ≥ 1 measurable target lesion (RECIST1.1).
- Allow patients to receive PD-L1 inhibitor treatment in advance (≤ 30% of total enrollment).
- Patients with brain metastases will be excluded.

*CR, PR, SD
Radiotherapy focus
A non target lesion suitable for SBRT will be selected for radiotherapy, and the previous radiotherapy site will not receive radiotherapy again.
The selection of lesions will be made by radiotherapy experts based on extracranial location, risk of progression and safety of SBRT implementation.

First stage (N1 = 17)

Induction stage (Cycle 1, D1-D28)

Niraparib 200 mg, QD, D1-28
Radiotherapy 8Gy*3, D4-D6
Toripalimab 240 mg, IV, D7.

Maintenance stage (Cycle 2+, 21 days per cycle)

Niraparib 200 mg, QD, D1-D21
Toripalimab 240 mg, IV, D1, Q3W

Treatment until disease progression, intolerable toxicity, death, or patient withdrawal of informed consent.

CR + PR cases ≤ 2

Early termination

CR + PR cases > 2

Second stage (N2 = 36)

Induction stage (Cycle 1, D1-D28)

Niraparib 200 mg, QD, D1-28
Radiotherapy 8Gy*3, D4-D6
Toripalimab 240 mg, IV, D7.

Maintenance stage (Cycle 2+, 21 days per cycle)

Niraparib 200 mg, QD, D1-D21
Toripalimab 240 mg, IV, D1, Q3W

Treatment until disease progression, intolerable toxicity, death, or patient withdrawal of informed consent.

Efficacy and safety evaluation
N = 53 (N1 + N2)

Follow up period

- During the trial period, each treatment cycle will be followed up once.
- The patients will be followed up every 3 months.
- Follow up indicators include: survival indicators, efficacy indicators, safety indicators, etc.

Primary endpoint

- Objective response rate (ORR)

Secondary endpoints

- Duration of response (DOR)
- Disease control rate (DCR)
- Progression free survival (PFS)
- Overall survival (OS)
- 6-month PFS rate
- 1-year OS rate
- Intrathoracic and extrathoracic recurrence rate
- Safety

Outcomes

Primary Endpoints

- Objective response rate **(ORR)**
- Complete response **(CR)**
- Partial response **(PR)**

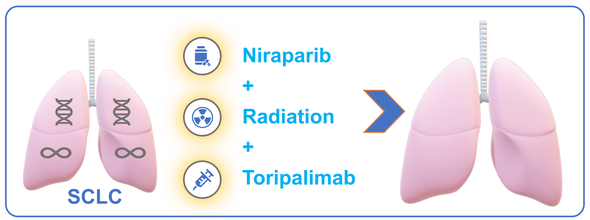
Secondary Endpoints

- Duration of Response (DOR)
- Disease control rate (DCR)
- Progression free survival (PFS)
- Overall survival (OS)
- TRAEs - Treatment-related adverse effects

Summary

This trial is under progress.

Combination therapy may improve overall outcome.



Disclosure

Authors have no conflicts of interest to declare.

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