Antitumor Activity and Safety Profile of Trilaciclib in Chinese Patients with Extensive-Stage Small Cell Lung Cancer (ES-SCLC) receiving Chemotherapy (TRACES): Updated results from TRACES

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Y. Liu[1], L. Wu[2], D. Huang[3], Q. Wang[4], Y. Fan[5], Z. Liu[6], H. Fan[7], W. Yao[8], B. Liu[9], G. Yu[10], Y. Pan[11], F. Xu[12], Z. He[13], X. Dong[14], R. Ma[15], X. Min[16], X. Ge[17], H. Chen[18], Q. Liu[19], Y. Cheng[1]

[1]Thoracic Oncology Department, Jilin Cancer Hospital, Changchun, China, [2]Department of Thoracic Medical Oncology, Hunan Cancer Hospital, Changsha, China, [3]Department of Pulmonary Oncology, TMUCIH - Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, [4]Ward 3, Respiratory Department, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China, [5]Department of Thoracic Medical Oncology, Zhejiang Cancer Hospital - Cancer Research Institute, Hangzhou, China, [6]Ward 3, Respiratory Department, Shandong Cancer Hospital and Institute, Jinan, China, [7]Department of Thoracic Medical Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [8]Department of Thoracic Medical Oncology, Sichuan Cancer Hospital and Institute/The Affiliated Cancer Hospital School of Medicine, UESTC, Chengdu, China, [9]Ward 1,Respiratory Department, Cancer Hospital Affiliated to Harbin Medical University, Harbin, China, [10]Department of Oncology, Weifang People Hospital, Weifang, China, [11]Department of Oncology, Anhui Provincial Hospital, Hefei, China, [12]Department of respiratory and critical care medicine, The First Affiliated Hospital of Nanchang University, Nanchang, China, [13]Division 25, Department of Thoracic Oncology, Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China, [14]Department of thoracic Oncology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology/ Cancer Center Union Hospital, Wuhan, China, [15]Medical Oncology, Liaoning Cancer Hospital & Institute, Shenyang, China, [16]Tumor radiotherapy department, Anhui Chest Hospital, Hefei, China, [17]Department of Oncology, Affiliated Hospital of Jiangnan University, Wuxi, China, [18]Oncology Center (District 1), Affiliated Hospital of Guangdong Medical College, Zhanjiang, China, [19]Department of respiratory and critical care medicine, The First Affiliated Hospital of Xiamen University, Xiamen, China

BACKGROUND

- Trilaciclib, a potent and reversible intravenous CDK4/6 inhibitor, has been approved by US FDA and China NMPA to prevent multilineage chemotherapy-induced myelosuppression in ES-SCLC patients.
- The TRACES study is a phase III trial assessing the efficacy and safety of trilaciclib in Chinese ES-SCLC patients.
- The bone marrow protection effect was significant which was reported in WCLC 2022【1】.

METHODS

- This study included an open-label safety run-in part (Part 1) and a randomized, double-blinded, placebo-controlled part (Part 2).
- Treatment-naïve or previously treated ES-SCLC patients received trilaciclib (240 mg/m^2) or placebo before etoposide/cisplatin (E/P) or topotecan (TPT) respectively.
- The primary endpoint was the duration of severe neutropenia in Cycle 1.
- The exploratory endpoints for anti-tumor effect were OS and ORR, PFS and DOR assessed by RECIST v1.1. The anti-tumor results are presented here.

RESULTS

Patient disposition and PK analysis

- As of 30 December 2022, a total of 83 patients were enrolled in Part 2, with 41 receiving trilaciclib (E/P: 23; TPT:18) and 42 receiving placebo (E/P: 23; TPT:19).
- Among all the patients receiving trilaciclib in Part 1 and Part 2, the infusion time was between 30-35 minute for most (94.5%). In addition, the shortest and longest infusion duration were 20 and 76 minutes respectively.
- Simulation using a PopPK model indicated that infusion time had a minor effect on AUC but significant effect on Cmax.
- Results from exposure-response analyses showed that efficacy is more correlated with AUC and therefore the fluctuations of Cmax do not affect myeloprotective and anti-tumour efficacy.
- Although shortened infusion time will increase Cmax, which may lead to an increased incidence of AE, the incidence of AE was manageable within the actual infusion time range of 20-76mins.

Table 1 :Infusion time of trilaciclib in Part 1 and Part 2

Infusion time (M)	Part 1		Part 2		Total	
	INF#	Pct (%)	INF#	Pct (%)	INF#	Pct (%)
20-29	5	2.7	16	2	21	2.1
30-35	175	94.6	772	94.4	947	94.4
36-59	3	1.6	22	2.6	25	2.5
60-80	2	1.1	8	1.0	10	1.0
Total	185	100	818	100	1003	100

Minutes: M; Number of infusion: INF#; Percentage: Pct

Safety

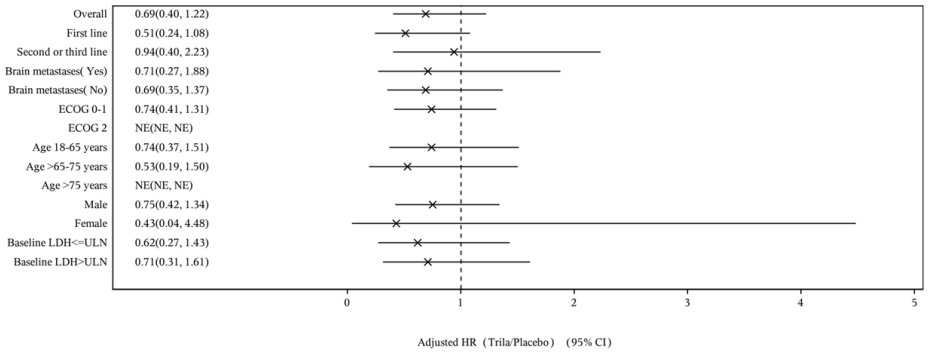
- Trilaciclib was well tolerated, with lower incidence of ≥Grade 4 TEAEs, SAEs, TEAEs leading to treatment discontinuation.
- No TEAEs leading to death were reported related to trilaciclib.

RESULTS

Antitumor efficacy

- The confirmed ORR in trilaciclib group and placebo group were 44.7% and 39.5% (p=0.4996) respectively.
- The median progression-free survival in trilaciclib group and placebo group was 4.8 months and 4.3 months, respectively (HR, 0.86; 95% CI, 0.53 to 1.39).
- After a median follow-up of 14.1 months, the median overall survival was 12.0 months in the trilaciclib group and 8.8 months in the placebo group (hazard ratio [HR], 0.69; 95% confidence interval [CI], 0.40 to 1.22).
- Although the subgroup analysis of OS didn't suggest any statistically significant differences; the HR in all subgroups favored the trilaciclib group.

Figure 1 :Hazard ratio forest plot for overall survival in Part 2



CONCLUSIONS

Trilaciclib was well tolerated in Chinese patients. Administering trilaciclib prior to chemotherapy in ES-SCLC patients improved patients' tolerability to chemotherapy, and suggested potential survival benefit.

Reference:1:Myeloprotection with Trilaciclib in Chinese Patients with Extensive-Stage Small Cell Lung Cancer Receiving Standard Chemotherapy (TRACES). 2022 WCLC: EP08.02-078.