157P

Surufatinib plus toripalimab in patients with advanced small cell lung cancer (SCLC) after failure of 1L systemic chemotherapy

Ying Cheng[1], Lin Shen[2], Xianjun Yu[3], Zhendong Chen[4], Lijie Song[5], Yanqiao Zhang[6], Chunjiao Wu[1], Ming Lu[2], Heli Gao[3], Wei Chen[4], Minjie Yang[5], Yue Ma[6], Zhou Jinghong[7], Haiyan Shi[7], Panfeng Tan[7], Songhua Fan[7], Weiguo Su[7]

1 Jilin Cancer Hospital, Changchun; 2 Peking university cancer Hospital & institute, Beijing; 3 Fudan University Shanghai Cancer Center, Shanghai; 4 The Second Hospital of Anhui Medical University, Hefei; 5 The First Affiliated Hospital of Zhengzhou University, Zhengzhou; 6 Harbin Medical University Cancer Hospital; 7 HUTCHMED, Shanghai, China

INTRODUCTION

- Patients with advanced SCLC have a rapid relapse after 1L treatment, and there is only one approved agent for 2L treatment, topotecan. [1,2]
- Surufatinib (S) is a small-molecule inhibitor of VEGFR1-3, FGFR1 and CSF-1R; toripalimab (T) is an anti-PD-1 antibody. Combination of the two drugs has exhibited encouraging efficacy in a neuroendocrine carcinoma cohort in a trial evaluating S + T in patients with selected solid tumors. [3]
- Here we report the safety and efficacy results of the combination therapy (S + T) in the SCLC cohort.

STUDY DESIGN

Phase 2, single-arm, multi-center study (NCT04169672)

Safety run-in
N=6

Primary endpoint
- Safety and tolerability

Secondary endpoint
- PK
- ORR, DoR, DCR, PFS (RECIST v1.1), OS

Surufatinib

250 mg Oral QD

+

Toripalimab

240 mg IV Q3W

Safety analysis

Multi-cohort study
N=220 (n=~20 pts/each cohort)

Primary endpoint
- ORR assessed by investigator (RECIST v1.1)

Secondary endpoints
- DoR, DCR, PFS(RECIST v1.1), OS
- Safety, immunogenicity
- PK, efficacy-related biomarkers

- ✓ SCLC
- ✓ G/GEJ adenocarcinoma
- ✓ ESCC
- ✓ NET
- ✓ NEC
- ✓ BTC
- ✓ TC
- ✓ Sarcoma
- ✓ EMC
- ✓ Prior Immunotherapy Cohort
- ✓ NSCLC

Data analysis

Key Inclusion Criteria

- Histologically or cytologically confirmed unresectable or metastatic advanced solid tumors
- Progression on 1 line (NEC, G/GEJ adenocarcinoma, ESCC, BTC and SCLC Cohorts) or 1-2 lines (NET and Sarcoma Cohorts) or ≥1 lines (TC, EMC and Prior anti-PD-1/-PD-L1 treatment cohorts) of prior anti-tumor therapy. NSCLC cohort only enrolled patients without prior systemic chemotherapy to advanced disease
- ECOG PS 0-1, measurable disease (RECIST v1.1) and adequate organ function
- Baseline tumor tissue for biomarker analysis.

Key Exclusion Criteria

- Previously treated with anti-PD-1 antibody, anti-PD-L1 antibody, anti-PD-L2 antibody, anti-CTLA-4 antibody, any other antibody acting on the T cell stimulation or checkpoint pathway (except for Prior Immunotherapy cohort) or Surufatinib;
- Previously received anti-VEGF/VEGFR targeted drugs and progressed during the treatment or within 4 months after these drugs;
- History or presence of a serious hemorrhage (>30 mL within 2 months, presence of hematemesis, melena, hematochezia), hemoptysis (>5 mL blood within 4 weeks) within 2 months.

Efficacy evaluation

- Every 6 weeks after first dose to 48 weeks; every 12 weeks thereafter.

NEC: neuroendocrine carcinoma; G/GEJ: gastric or gastroesophageal junction; ESCC: esophageal squamous cell carcinoma; BTC: biliary tract cancer; SCLC: small cell lung cancer; NET: neuroendocrine tumours; TC: thyroid cancer; EMC: endometrial carcinoma; NSCLC: non-small cell lung cancer; ECOG PS: Eastern Cooperative Oncology Group performance status; QD: once daily; IV: intravenous injection; ORR: objective response rate; DoR: duration of response; DCR: disease control rate; PFS: progression-free survival; OS: overall survival; PK: pharmacokinetics.

BASELINE CHARACTERISTICS AND TREATMENT

- At cutoff date (Aug 1, 2021), 20 patients were enrolled and received the combination treatment.
- Median follow-up duration for OS was 11.10 months (95%CI 11.01, 13.50).

Baseline Characteristics		ITT, N=20
Age (yrs)	Median (range)	58 (43.5, 72.5)
Gender, n (%)	Male	16 (80.0)
	Female	4 (20.0)
ECOG PS, n (%)	0	3 (15.0)
	1	17 (85.0)
TNM Staging at screening, n (%)	III	5 (25.0)
	IV	14 (70.0)
	Unknown	1 (5.0)

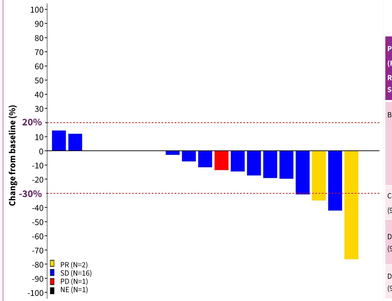
Baseline Characteristics		ITT, N=20
Prior therapies, n (%)	1	20 (100)
PD-L1 CPS, n (%)	<1	16 (80.0)
	≥1-<10	2 (10.0)
	≥10-<50	1 (5.0)
	Missing	1 (5.0)
Time from last treatment to disease progression, n(%)	Platinum-resistant§	12 (60)
	Platinum-sensitive δ	8 (40)

CPS: combined positive score.

§ patients with disease relapse <90 days after platinum-based chemotherapy; δ patients with disease relapse ≥90 days after platinum-based chemotherapy.

TUMOR RESPONSE

Best change in sum of target lesions from baseline (RECIST v1.1) – ITT (SCLC)



Patients (RECIST v1.1) Response Evaluable Set*	Total N=19	Platinum-resistant§ N=11	Platinum-sensitive δ N=8
BOR, n (%)			
CR	0	0	0
PR	2 (10.5)	2 (18.2)	0
SD	16 (84.2)	9 (81.8)	7 (87.5)
PD	1 (5.3)	0	1 (12.5)
Confirmed ORR (95%CI), %	10.5 (1.30, 33.14)	18.2 (2.28, 51.78)	0
DCR (95%CI), %	94.7 (73.97, 99.87)	100 (71.51, 100)	87.5 (47.35, 99.68)
DoR (95% CI), months	NA (9.79, NA)	NA (9.79, NA)	NA

Cutoff date: Aug 1, 2021.

BOR: Best of response; CR: complete response; PR: partial response;

SD: stable disease; PD: progressive disease; NE: not evaluable;

CI: confidence interval; NA: not available.

* patients had at least one post treatment tumor assessment;

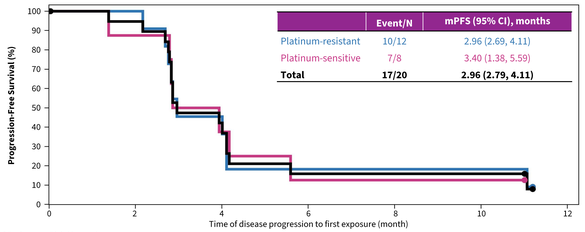
§ patients with disease relapse <90 days after platinum-based chemotherapy;

δ patients with disease relapse ≥90 days after platinum-based chemotherapy.

PROGRESSION-FREE SURVIVAL

- Median PFS (mPFS) was 2.96 months (95%CI 2.79, 4.11).
- In platinum-resistant and –sensitive subgroups, mPFS were 2.96 months (95%CI 2.69, 4.11) and 3.4 months (95%CI 1.38, 5.59), respectively.

KM Curve of Progression-Free Survival (RECIST v1.1) – ITT (SCLC)

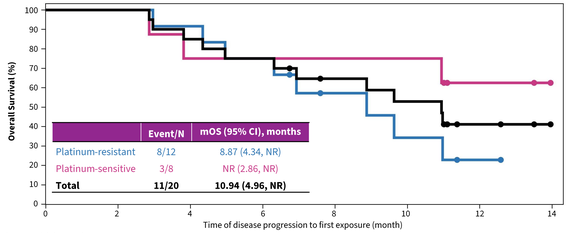


Number of Patients at Risk (Censor)							
Platinum-resistant	12 (0)	11 (1)	5 (1)	2 (1)	2 (1)	2 (1)	0 (2)
Platinum-sensitive	8 (0)	7 (0)	3 (0)	1 (0)	1 (0)	1 (0)	0 (1)
Total	20 (0)	18 (1)	8 (1)	3 (1)	3 (1)	3 (1)	0 (3)

OVERALL SURVIVAL

- Median OS (mOS) was 10.94 months (95%CI 4.96, NR).
- In platinum-resistant and –sensitive subgroups, mOS were 8.87 months (95%CI 4.34, NR), and not reached, respectively.

KM Curve of Overall Survival – ITT (SCLC)



Number of Patients at Risk (Censor)								
Platinum-resistant	12 (0)	12 (0)	11 (0)	9 (0)	5 (2)	3 (2)	1 (3)	0 (4)
Platinum-sensitive	8 (0)	8 (0)	6 (0)	6 (0)	6 (0)	6 (0)	2 (3)	0 (5)
Total	20 (0)	20 (0)	17 (0)	15 (0)	11 (2)	9 (2)	3 (6)	0 (9)

SAFETY

Treatment duration Median treatment duration of S + T was 3 months (range 1, 14); S: 3 months (range 1, 14); T: 3 months (range 1, 11).

Safety Summary

	Surufatinib + Toripalimab (N=20), n (%)		
		Surufatinib-related	Toripalimab-related
Any TEAE	20 (100.0)	-	-
Grade ≥3 TEAEs	12 (60.0)	-	-
Serious TEAEs	10 (50.0)	-	-
TEAEs leading to death	3 (15.0)	-	-
TEAEs leading to discontinuation	1 (5.0)	-	-
TEAEs leading to interruption or dose reduction*	11 (55.0)	-	-
Any TRAE	19 (95.0)	19 (95.0)	17 (85.0)
Grade ≥3 TRAEs	9 (45.0)	8 (40.0)	7 (35.0)
TRAEs leading to death	0	0	0
TRAEs leading to discontinuation	0	0	0
TRAEs leading to interruption or dose reduction*	11 (55.0)	9 (45.0)	7 (35.0)

Common TEAE (≥20%) or Grade ≥3 TEAEs (≥2 patients)

	Surufatinib + Toripalimab (N=20), n (%)	
	Any Grade	Grade ≥3
Any TEAE	20 (100.0)	12 (60.0)
Hypertriglyceridemia	8 (40.0)	4 (20.0)
Asthenia	8 (40.0)	1 (5.0)
Weight decreased	8 (40.0)	0
Diarrhoea	7 (35.0)	1 (5.0)
Proteinuria	7 (35.0)	0
Amylase increased	6 (30.0)	1 (5.0)
Hypoalbuminaemia	6 (30.0)	0
Sinus tachycardia	6 (30.0)	0
Blood bilirubin increased	5 (25.0)	1 (5.0)
Decreased appetite	5 (25.0)	0
Hypercholesteremia	5 (25.0)	0
Hypertension	4 (20.0)	3 (15.0)

	Surufatinib + Toripalimab (N=20), n (%)	
	Any Grade	Grade ≥3
Any TEAE	20 (100.0)	12 (60.0)
Hyponatraemia	4 (20.0)	2 (10.0)
Gamma-glutamyltransferase increased	4 (20.0)	1 (5.0)
Hypochloraemia	4 (20.0)	1 (5.0)
Constipation	4 (20.0)	1 (5.0)
Occult blood positive	4 (20.0)	0
Back pain	4 (20.0)	0
Stethalgia	4 (20.0)	0
Blood thyroid stimulating hormone increased	4 (20.0)	0
Blood thyroid stimulating hormone decreased	4 (20.0)	0
Blood alkaline phosphatase increased	4 (20.0)	0
Blood creatine phosphokinase increased	4 (20.0)	0
Malignant neoplasm progression	3 (15.0)	3 (15.0)

*surufatinib interruption or dose reduction; toripalimab interruption; TEAEs: treatment emergent adverse events; TRAEs: treatment-related TEAEs.

CONCLUSIONS

- Surufatinib plus toripalimab showed a promising anti-tumor activity in patients with advanced SCLC after failure of 1L chemotherapy.
- Surufatinib plus toripalimab demonstrated an acceptable safety profile with no new safety signals.
- The combination of the two agents should be further investigated for the treatment of SCLC.

REFERENCES

1 Luis Paz-Ares, et al. Lancet. 2019;394(10212):1929-1939.
2 Michael T Serzan, et al. J Thorac Dis. 2020;12(10):6298-6307.
3 Yanshuo C, et al. 2020 AACR abstract 9563.

ACKNOWLEDGMENT

- Authors would like to thank all patients and their family members, investigators and their teams, as well as all staff involved in the study
- Authors would like to acknowledge the sponsor for this trial: HUTCHMED.

DISCLOSURES

Jinghong Zhou, Haiyan Shi, Panfeng Tan, Songhua Fan, Weiguo Su are all employees of HUTCHMED.

CONTACT EMAIL

Ying Cheng, jl.cheng@163.com,
Department of Medical Oncology, Jilin Cancer Hospital, Changchun, China.