ABSTRACT #8568

Penpulimab plus anlotinib as second-line treatment for the small cell lung cancer after failure of platinum-based systemic chemotherapy

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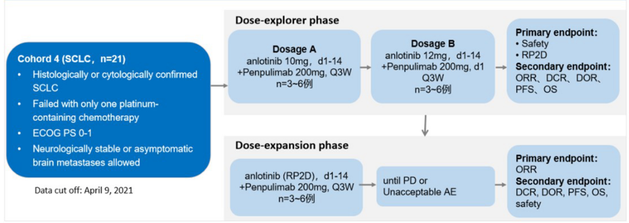
BACKGROUD

- Combined therapy of an immune checkpoint inhibitor with a targeted anti-angiogenic agent had been proved to be effective for the treatment of lung cancer.
- Penpulimab (AK105) was engineered to eliminate FcγR binding and antibody-dependent cell-mediated cytotoxicity (ADCC)/ antibody-dependent celluar phagocytosis (ADCP) completely, where ADCC/ADCP effects could induce T-cell apoptosis and clearance and therefore compromise anti-tumor activity. Penpulimab demonstrated a slower programmed cell death-1(PD-1) antigen binding off-rate, which resulted in better cellular activity and higher receptor occupancy. Penpulimab also showed numerous contacts with N58 glycosylation on the BC loop of PD-1. These structural differentiations enhance the anti-tumor activity of penpulimab and improves its safety profile.
- Anlotinib is a multi-targeted tyrosine kinase inhibitor selective for VEGF receptors 1/2/3, FGF receptors 1-4, PDGF receptors α and β, and c-kit.
- Anlotinib has been conditionally approved by National Medical Products Administration as the treatment for the small cell lung cancer (SCLC) patients, who had progressed/relapsed on or after at least two regimens of chemotherapy.
- Here we report the results of one cohort which received penpulimab plus anlotinib in a Phase II study.

MATHODS

Figure 1. Study Design



The study design is shown in Figure 1.
ClinicalTrials.gov Identifier: NCT04203719

Key Eligibility Criteria for Cohort 4 (SCLC)
Histologically confirmed small cell lung cancer;
Failed with only one platinum-containing chemotherapy;
Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1;
At least one measurable lesion;
have not used anti-angiogenic;
Brain metastases with symptoms or symptoms control for less than 2 month Excluded;

Treatment and Assessments
Patients received penpulimab 200 mg IV Q3W and anlotinib 12mg/10 mg PO 2 weeks on/1 week off.
Anlotinib can be dose-reduced from 12mg to 10mg, and from 10mg to 8mg to manage AEs.
Tumour assessments were done at baseline, then every 6 weeks.
Progression-free survival and objective response were investigator-assessed according to RECIST, version 1.1.
AEs are reported according to NCI CTC AE v5.0.

RESULTS

The data cutoff date was April 9, 2021, with a median duration of follow-up of 5.81 months.

Table 1. Baseline Characteristics of Patients Treated with Second-Line Penpulimab plus Anlotinib

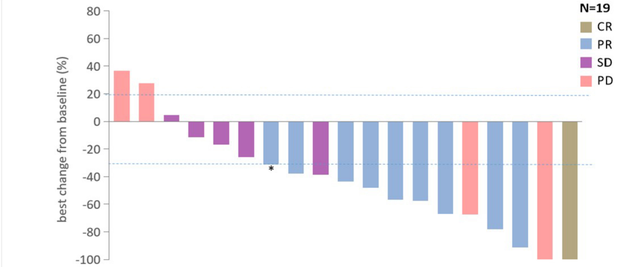
characteristic	SCLC Cohort (N=21)
Median age, y (range)	62 (37-75)
Male, n(%)	14 (66.67)
ECOG PS, n(%)	
0	1 (4.76)
1	20 (95.24)
Smoking status,	
Current/former smoker	12 (57.14)
Never smoker	9 (42.86)
Brain metastasis at enrollment, n(%)	5 (23.81)
anlotinib dosage, n(%)	
10mg/day	3 (14.29)
12mg/day	18 (85.71)

Table 2. Tumor Response per Investigator by RECIST 1.1

	SCLC Cohort (N=21)
Best overall response, n(%)	
CR	1 (4.76)
PR	8 (38.10)
PR (unconfirmed)	1 (4.76)
SD	5 (23.18)
PD	4 (19.05)
Not evaluable	2 (9.52)
Objective response rate, n(%)	9 (42.86)
Objective response rate, n(%) (including unconfirmed PR*)	10 (47.62)
Disease control rate, n(%)	15 (71.43)
Time to response, median(range), mo	1.41(1.28, 4.13)

* unconfirmed PR: tumer assessed PR in the last visit, and the patient is still in the study.

Figure 2. Best Change from Baseline iper Investigator by RECIST v1.1



19 out of 21 patients had at least one post-baseline tumor assessment
* unconfirmed PR

Figure 3.Duration of Response and Duration of Progression-free Survival

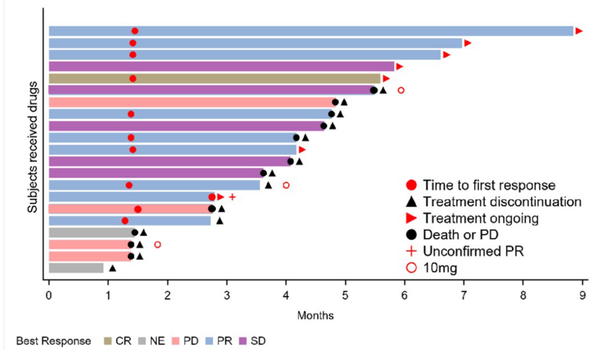
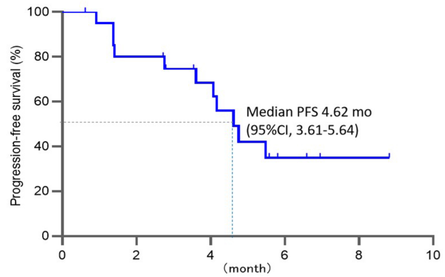


Figure 4. Progresson-free Survival of Patients Treated with Second-Line Penpulimab plus Anlotinib



No. at Risk

Penpulimab+Anlotinib	21	16	11	3	1

Table 3. Safety Summary of Patients Treated with Second-Line Penpulimab plus Anlotinib

	SCLC Cohort N=21
Treatmet-related AE, n (%)	19 (90.48)
Treatmet-related grade 3 AE, n (%)	8 (38.10)
Immune-related grade 3 AE, n (%)	4 (19.05)
Any event leading to discontinuation, n (%)	6 (28.57)
discontinuation of penpulimab, n (%)	1 (4.76)
discontinuation of anlotinib, n (%)	5 (23.81)
Any event leading to anlotinib dose reductions, n (%)	6 (28.57)
No grade 4/5 TRAE occured	

Table 4. Treatment-Related Advers Events Occuring in ≥10% of Patients

	SCLC Cohort N=21	
	Any Grade	Grade 3
hypertension	11 (52.38)	6 (28.57)
Hypothyroidism	8 (38.1)	1 (4.76)
proteinuria	6 (28.57)	0 (0)
Hypertriglyceridemia	6 (28.57)	1 (4.76)
AST increased	6 (28.57)	0 (0)
hand-foot syndrome	6 (28.57)	1 (4.76)
fatigue	5 (23.81)	3 (14.29)
GGT increased	4 (19.05)	2 (9.52)
WBC count decreased	4 (19.05)	0 (0)
ALT increased	4 (19.05)	0 (0)
Hyperthyroidism	4 (19.05)	0 (0)
Loss of appetite	4 (19.05)	0 (0)
Weight loss	4 (19.05)	2 (9.52)
Hypoalbuminemia	3 (14.29)	0 (0)
hyponatremia	3 (14.29)	2 (9.52)
diarrhea	3 (14.29)	0 (0)
hypercholesterolemia	3 (14.29)	0 (0)
hyperlipidemia	3 (14.29)	0 (0)
vomiting	3 (14.29)	0 (0)
anemia	3 (14.29)	0 (0)
fecal occult blood	3 (14.29)	0 (0)
dizzy	3 (14.29)	0 (0)
neutrophils count decreased	3 (14.29)	0 (0)
No grade 4/5 TRAE occured		

CONCLUTION

Penpulimab plus anlotinib showed favorable antitumor activity and an acceptable safety profile in patients with SCLC who failed to platinum-based systemic chemotherapy.

This new combination therapy warrants further evaluation for the treatment of SCLC.

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