IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

wclc.iaslc.org #WCLC25

Efficacy and Safety of Cadonilimab Plus Pulocimab in NSCLC Patients who Progressed Following Prior Immunotherapy: A Phase 1b/2 Study (AK109-102)

Yulong Zheng[1], Nong Xu[1], Fang Yang[2], Xiang Song[3], Weibo Wang[4], Guojun Zhang[5], Liu Yang[6], Zhiye Zhang[7], Mingxi Wang[8], Suying Qian[9], Ya Wang[10], Xiaoguang Xu[10], Ting Liu[10], Zhongmin Maxwell Wang[10], Baiyong Li[10], Yu Xia[10].

1. The First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, CHINA, 2. Harbin Medical University Cancer Hospital, Harbin, CHINA, 3. Second Hospital of Shanxi Medical University, Taiyuan, CHINA, 4. Shandong Provincial Hospital, Jinan, CHINA, 5. The First Affiliated Hospital of Zhengzhou University, 6. Zhengzhou, CHINA, 6Zhejiang Provincial People's Hospital, Hangzhou, CHINA, 7. The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, CHINA, 8. The First Affiliated Hospital of Bengbu Medical College, Bengbu, CHINA, 9. Ningbo No.2 Hospital, Ningbo, CHINA, 10. Akeso Biopharma, Inc., Zhongshan, CHINA

Background

- PD-(L)1 inhibitors, alone or combined with chemotherapy, are the standard first-line treatment for advanced NSCLC. However, treatment options for patients who progress after first-line immunotherapy-based regimens remain limited, with no established global standard in the second-line setting
- Cadonilimab (AK104) is a PD-1/CTLA-4 bispecific antibody approved by the NMPA for multiple indications, including first- and later-line treatment of cervical cancer and first-line treatment of gastric/gastroesophageal junction (G/GEJ) adenocarcinoma
- Pulocimab (AK109) is a fully human monoclonal antibody targeting VEGFR2
- The combination of cadonilimab and pulocimab has shown promising efficacy in patients with G/GEJ adenocarcinoma who progressed after immunochemotherapy, a phase III trial is ongoing (NCT06341335)
- This presentation highlights the safety and efficacy of cadonilimab plus pulocimab in NSCLC patients who have progressed following first-line immunotherapy-based SOC (phase Ib/II, NCT05142423)

Study Design

Safety Run-in Stage

Cohort A: Solid tumors
Cadonilimab 10mg/kg + Pulocimab 10mg/kg, Q3W

↓

Cohort B: Solid tumors
Cadonilimab 10mg/kg + Pulocimab 15mg/kg, Q3W

Expansion Stage

Advanced NSCLC progressed following immunotherapy based treatment (n=47)
Cadonilimab 10mg/kg + Pulocimab 15mg/kg Q3W

Treatment until:
- Intolerable toxicity
- No clinical benefit
- Up to 24 months

Key inclusion criteria of NSCLC in expansion stage
- Histologically or cytologically confirmed NSCLC
- ECOG PS 0-1
- Progression after anti-PD-(L)1-containg therapy
- No sensitizing EGFR or ALK alterations

Primary endpoints
- Safety
- ORR per RECIST 1.1

Secondary endpoints
- PFS per RECIST 1.1
- DCR per RECIST 1.1
- DoR
- OS

As of January13, 2025, 47 NSCLC patients who had progressed on first-line immunotherapy-based SOC treatment were enrolled，with a median follow-up of 16.7 months (range: 8.1-19.0)

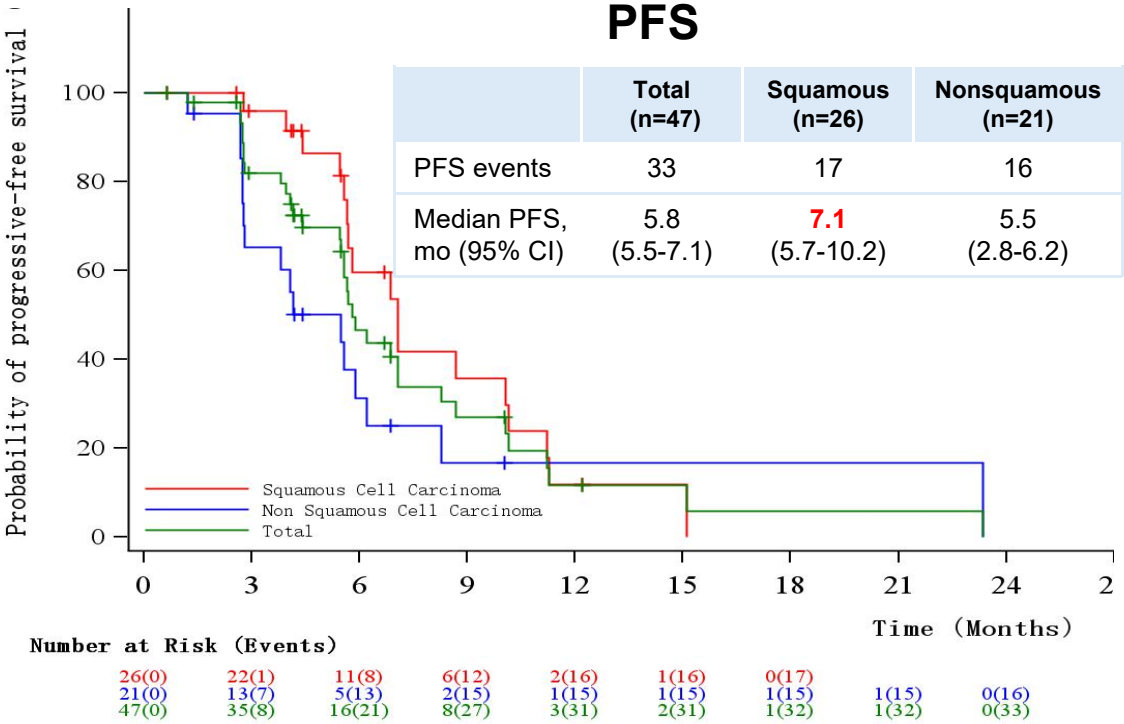
Baseline Characteristics

Baseline Characteristics (n%)	Total (n=47)	Squamous NSCLC (n=26)	Nonsquamous NSCLC (n=21)
Age，year			
Median age (min, max)	60.0 (48, 75)	60.0 (48, 70)	65.0 (49, 75)
≥65	32 (40.4)	8 (30.8)	11 (52.4)
Gender			
Male	38 (80.9)	23 (88.5)	15 (71.4)
Female	9 (19.1)	3 (11.5)	6 (28.6)
ECOG PS			
0	12 (25.5)	5 (19.2)	7 (33.3)
1	35 (74.5)	**21 (80.8)**	14 (66.7)
Resistance Type			
Primary resistance	19 (40.4)	9 (34.6)	10 (47.6)
Secondary resistance	28 (59.6)	17 (65.4)	11 (52.4)
Prior anti-PD-1/PD-L1 efficacy			
Responder	15 (31.9)	13 (50.0)	2 (9.5)
Non-responder	21 (44.7)	11 (42.3)	10 (47.6)
unknown	10 (21.3)	2 (7.7)	8 (38.1)
PD-L1 TPS			
< 1%	20 (42.6)	9 (34.6)	11 (52.4)
≥1%	14 (29.8)	9 (34.6)	5 (23.8)

Efficacy

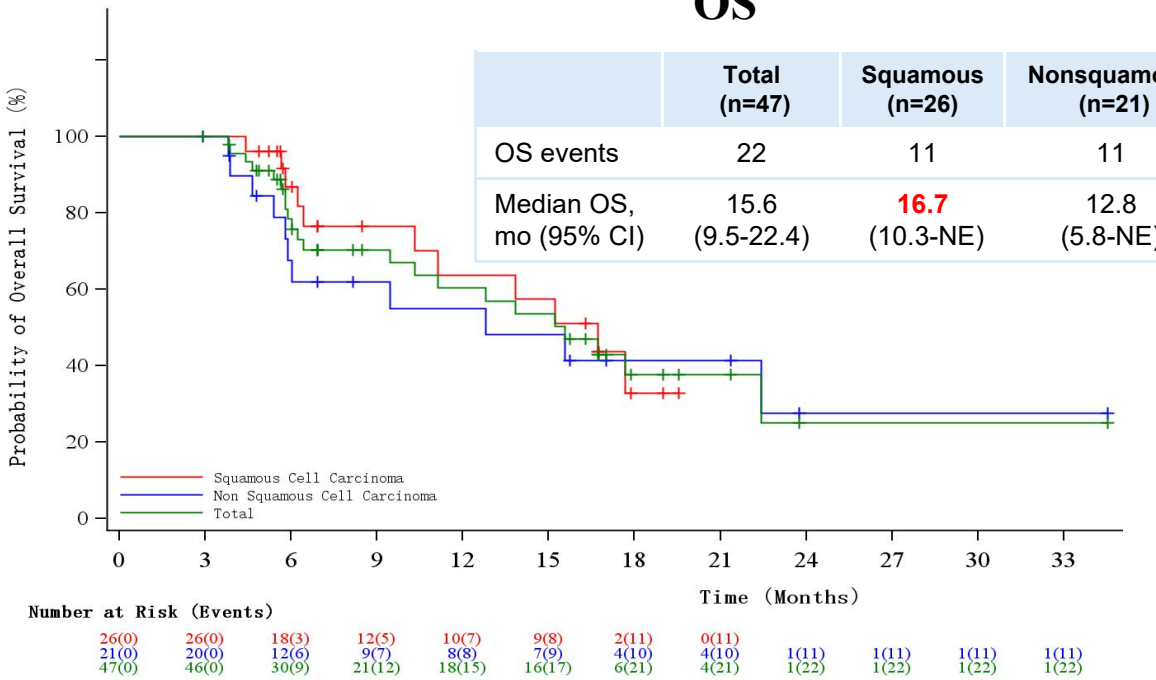
	Squamous NSCLC (n=26)	Nonsquamous NSCLC (n=21)
ORR, %	11.5	14.3
DCR, %	**96.2**	**95.2**

PFS



	Total (n=47)	Squamous (n=26)	Nonsquamous (n=21)
PFS events	33	17	16
Median PFS, mo (95% CI)	5.8 (5.5-7.1)	7.1 (5.7-10.2)	5.5 (2.8-6.2)

OS



	Total (n=47)	Squamous (n=26)	Nonsquamous (n=21)
OS events	22	11	11
Median OS, mo (95% CI)	15.6 (9.5-22.4)	16.7 (10.3-NE)	12.8 (5.8-NE)

Safety Summary

- Cadonilimab in combination with Pulocimab demonstrated a favorable safety profile

AE, n (%)	Total (n=47)	Squamous NSCLC (n=26)	Nonsquamous NSCLC (n=21)
TRAE	44 (93.6)	25 (96.2)	19 (90.5)
≥G3 TRAE	10 (21.3)	7 (26.9)	3 (14.3)
Serious TRAE	11 (23.4)	7 (26.9)	4 (19.0)
TRAE leading to discontinuation of study drug	2 (4.3)	1 (3.8)	1 (4.8)
irAE	9 (19.1)	6 (23.1)	3 (14.3)
≥G3 irAE	3 (6.4)	2 (7.7)	1 (4.8)

- No dose-limiting toxicities (DLTs) observed in the safety run-in phase
- NSCLC cohort in expansion stage
  - The most common TRAEs (any grade): aspartate aminotransferase increased (25.5%), hypothyroidism (25.5%), proteinuria (25.5%)，platelet count decreased (21.3%) and anaemia (21.3%)
  - Grade ≥3 TRAEs: hypertension (4.3%) was the only event occurring in ≥2 patients
- No new safety signals were identified

Conclusions

- Cadonilimab in combination with Pulocimab demonstrated a promising efficacy in advanced or metastatic NSCLC patients who progressed following first-line immunotherapy-based standard of care
- This chemotherapy-free combination offers a compelling and novel approach to address resistance to anti-PD-(L)1 therapy, with notable efficacy and a favorable safety profile
- These findings support further clinical development of the Cadonilimab and Pulocimab combination in this setting, and a phase III study is planned

Thank You