

Hualin. Chen,¹* Dongxiao. Yang,² Guohu. Zhang,¹ Ruqi. Chen,¹ Guanbin Huang,¹ Tongtong. Xia,¹ Jiamin. Li,¹ Junhong Jiang,¹ Yiping. Luo,¹ Xiaolin. Li,¹ Muwen. Lin,¹ Yuying. Chen,¹ Zhixiong. Yang¹

¹Department of Pulmonary Oncology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; ²The First Naval Hospital of the Southern Theater Command of the People's Liberation Army, Zhanjiang, China

BACKGROUND

Treatment options are limited for patients with advanced non-small-cell lung cancer (NSCLC) after progression on immunotherapy. This study evaluated the efficacy and safety of cadonilimab, a programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) bispecific antibody, plus docetaxel versus docetaxel monotherapy in patients with locally advanced or metastatic NSCLC who progressed on first-line PD-(L)1 inhibitors and platinum-based doublet chemotherapy.

METHODS

This single-centre, retrospective cohort study was conducted at the Affiliated Hospital of Guangdong Medical University (China). Eligible patients were adults treated between Jan, 2022, and Jan, 2025, who had advanced NSCLC without driver mutations and progressed on first-line PD-(L)1 inhibitor therapy after achieving clinical benefit. We compared clinical outcomes between patients treated with cadonilimab plus docetaxel (combination group) and those receiving docetaxel alone (monotherapy group). The primary endpoints were progression-free survival (PFS) and objective response rate (ORR). Secondary endpoints included overall survival (OS) and safety.

RESULTS

Patient disposition and baseline

Of 63 patients included, 31 were in the combination group and 32 in the monotherapy group; baseline characteristics were balanced. Median follow-up was 24.6 months (range 7.0–43.5) in the combination group and 18.7 months (range 3.5–45.5) in the monotherapy group.

Table 1 Key baseline characteristics (combination / monotherapy)

Characteristic	Overall (N=63)	Combination group (n=31)	Monotherapy group (n=32)	P
Age, Median (range), years	65 (47–84)	65 (47–84)	64 (49–79)	0.90
Age group				0.25
< 65	30 (48%)	15 (48%)	15 (47%)	
≥ 65	33 (52%)	16 (52%)	17 (53%)	
Sex				0.84
Male	46 (73%)	23 (74%)	23 (72%)	
Female	17 (27%)	8 (26%)	9 (28%)	
ECOG PS				0.25
0-1	29 (46%)	12 (39%)	17 (53%)	
≥ 2	34 (54%)	19 (61%)	15 (47%)	
Smoking history				0.90
Never smoker	31 (49%)	15 (48%)	16 (50%)	
Ever smoker	32 (51%)	16 (52%)	16 (50%)	
Histology				0.88
Squamous	27 (43%)	13 (42%)	14 (44%)	
Non-squamous	36 (57%)	18 (58%)	18 (56%)	
Disease stage				0.72
IIIB/IIIC	19 (30%)	10 (32%)	9 (28%)	
IV	44 (70%)	21 (68%)	23 (72%)	
Metastatic sites				
Brain	19 (30%)	9 (29%)	10 (31%)	0.85
Liver	17 (27%)	8 (26%)	9 (28%)	0.94
Bone	27 (43%)	11 (36%)	16 (50%)	0.24
Prior first-line PFS				0.71
< 9 months	31 (49%)	16 (52%)	15 (47%)	
≥ 9 months	32 (51%)	15 (48%)	17 (53%)	

Efficacy

Table 2 Tumour response

	Combination group (n=31)	Monotherapy group (n=32)
Complete response	0 (0%)	0 (0%)
Partial response	10 (32%)	3 (9%)
Stable disease	16 (52%)	13 (41%)
Progressive disease	5 (16%)	16 (50%)
Objective response rate	10 (32%)	3 (9%)
P		0.029
Disease control rate	26 (84%)	16 (50%)
P		0.004

Data are n (%). Assessed per RECIST 1.1. P values by Pearson's χ^2 test.

Figure 2A PFS — red: Cadonilimab + Docetaxel; teal: Docetaxel

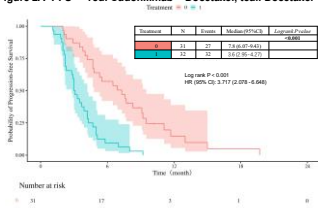
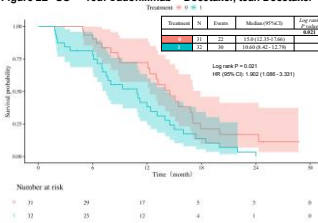


Figure 2B OS — red: Cadonilimab + Docetaxel; teal: Docetaxel



Safety

Grade 3 or worse adverse events were reported in 54.8% of patients in the combination group and 46.9% in the monotherapy group (p=0.572). The most frequent events were myelosuppression and gastrointestinal toxicities. No permanent discontinuations or treatment-related deaths occurred.

Table 3 Incidence of treatment-related adverse events (TRAEs), n (%)

Adverse events	Combination group (n=31)		Monotherapy group (n=32)		P*
	Any grade	≥Grade 3	Any grade	≥Grade 3	
Any TRAE	22 (71.0)	17 (54.8)	19 (59.4)	15 (46.9)	0.335
Leukopenia	15 (48.4)	3 (9.7)	14 (43.8)	3 (9.4)	0.712
Gastrointestinal disorders †	13 (41.9)	2 (6.5)	14 (43.8)	3 (9.4)	0.884
Neutropenia	12 (38.7)	2 (6.5)	12 (37.5)	2 (6.3)	0.921
Hepatic function abnormal ‡	10 (32.3)	2 (6.5)	9 (28.1)	1 (3.1)	0.721
Anaemia	9 (29.0)	2 (6.5)	10 (31.3)	3 (9.4)	0.848
Thyroid disorders §	9 (29.0)	2 (6.5)	7 (21.9)	1 (3.1)	0.514
Thrombocytopenia	6 (19.4)	1 (3.2)	5 (15.6)	1 (3.1)	0.699
Diarrhoea	5 (16.1)	1 (3.2)	4 (12.5)	1 (3.1)	0.683
Pneumonia or pneumonitis ¶	3 (9.7)	0	0	0	0.074
Proteinuria	3 (9.7)	0	3 (9.4)	0	0.968
Skin and subcutaneous tissue disorders **	2 (6.5)	0	2 (6.3)	0	0.974
Cardiac arrhythmias	2 (6.5)	1 (3.2)	1 (3.1)	0	0.539
Gastrointestinal haemorrhage	2 (6.5)	0	2 (6.3)	0	0.974
Infusion-related reaction	2 (6.5)	1 (3.2)	1 (3.1)	0	0.539

*P-values compare the incidence of any-grade TRAEs between the two groups. † Included decreased appetite and vomiting. ‡ Included elevated alanine aminotransferase, aspartate aminotransferase, serum bilirubin, or γ -glutamyl transpeptidase. § Included hyperthyroidism, hypothyroidism, and hypoparathyroidism. ¶ Due to the retrospective design of the study and overlapping clinical and radiological features, infectious pneumonia and immune-related pneumonitis could not be definitively distinguished in these cases, and are therefore reported as a combined composite event. ** Included pruritus, rash, and dermatitis.

CONCLUSION

Cadonilimab plus docetaxel demonstrated superior survival outcomes and antitumour activity compared with docetaxel monotherapy in patients with advanced NSCLC resistant to prior PD-(L)1 inhibitor therapy, with a tolerable safety profile. These findings suggest that this combination shows potential as a therapeutic option for this population and warrants confirmation in randomised controlled trials.

ACKNOWLEDGEMENTS

We thank the patients and their families, health-care professionals and study staff.

*Corresponding author: H. Chen | warren2008@163.com

Declaration of interest: The authors declare no conflicts of interest. Funding: None.