Figure S1. Subgroup analysis of objective response rate in patients treated with cadonilimab 15mg/kg and 10mg/kg every 3 weeks (Q3W)

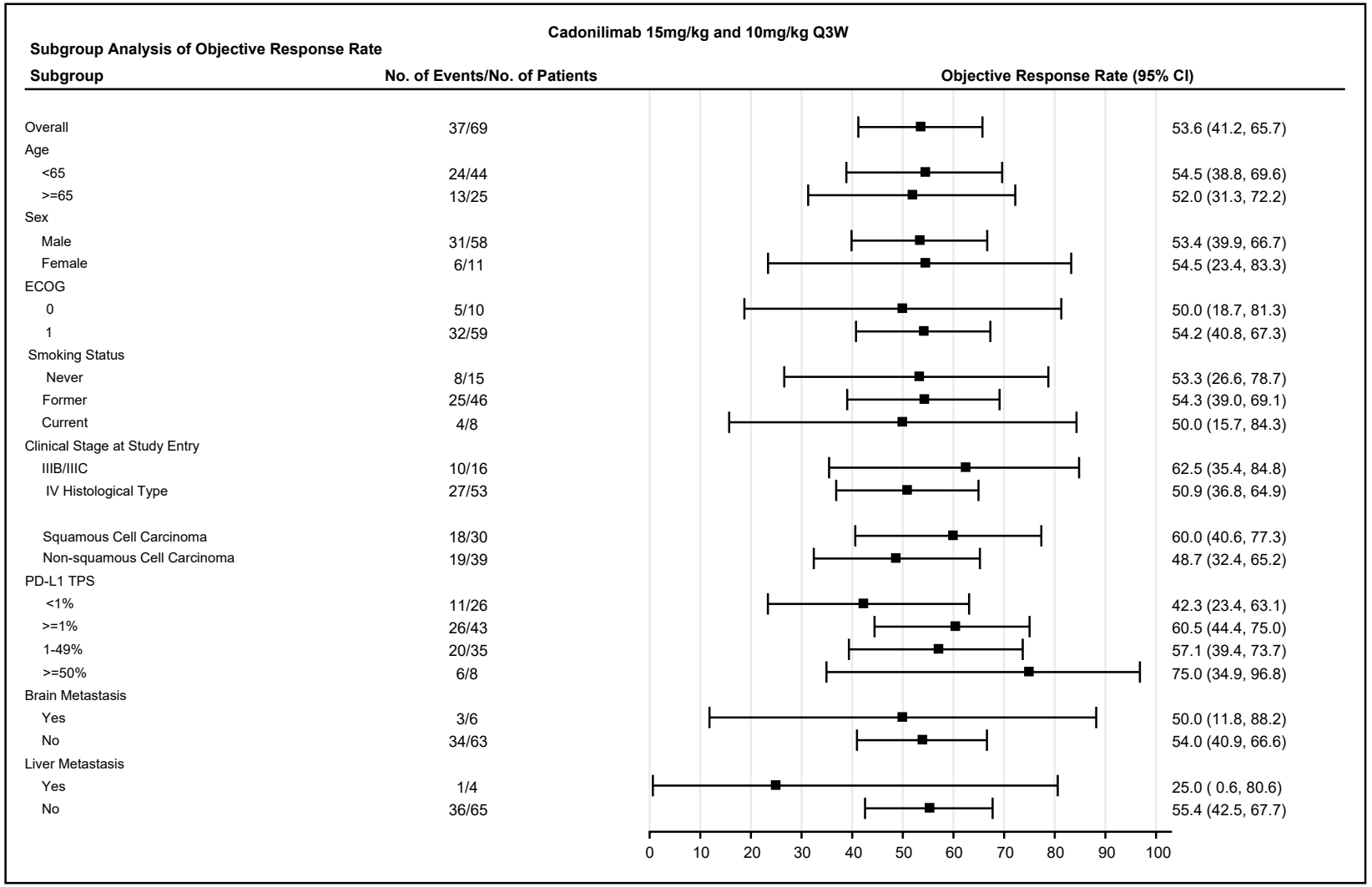
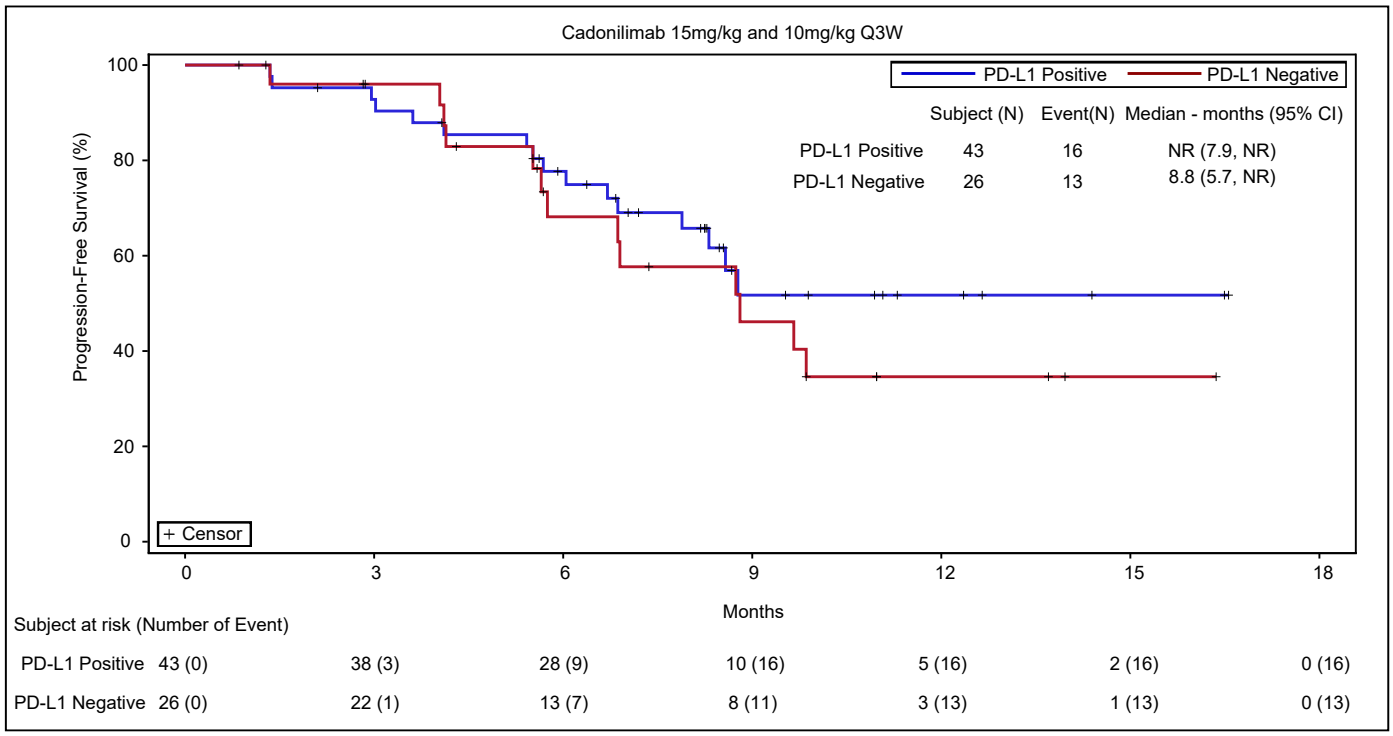


Figure S2. Kaplan-Meier curves of progression-free survival in patients treated with cadonilimab 15mg/kg and 10mg/kg every 3 weeks (Q3W). (A) By programmed cell death ligand-1 status (positive versus negative). (B) By pathology (squamous versus non-squamous carcinoma)

A



B

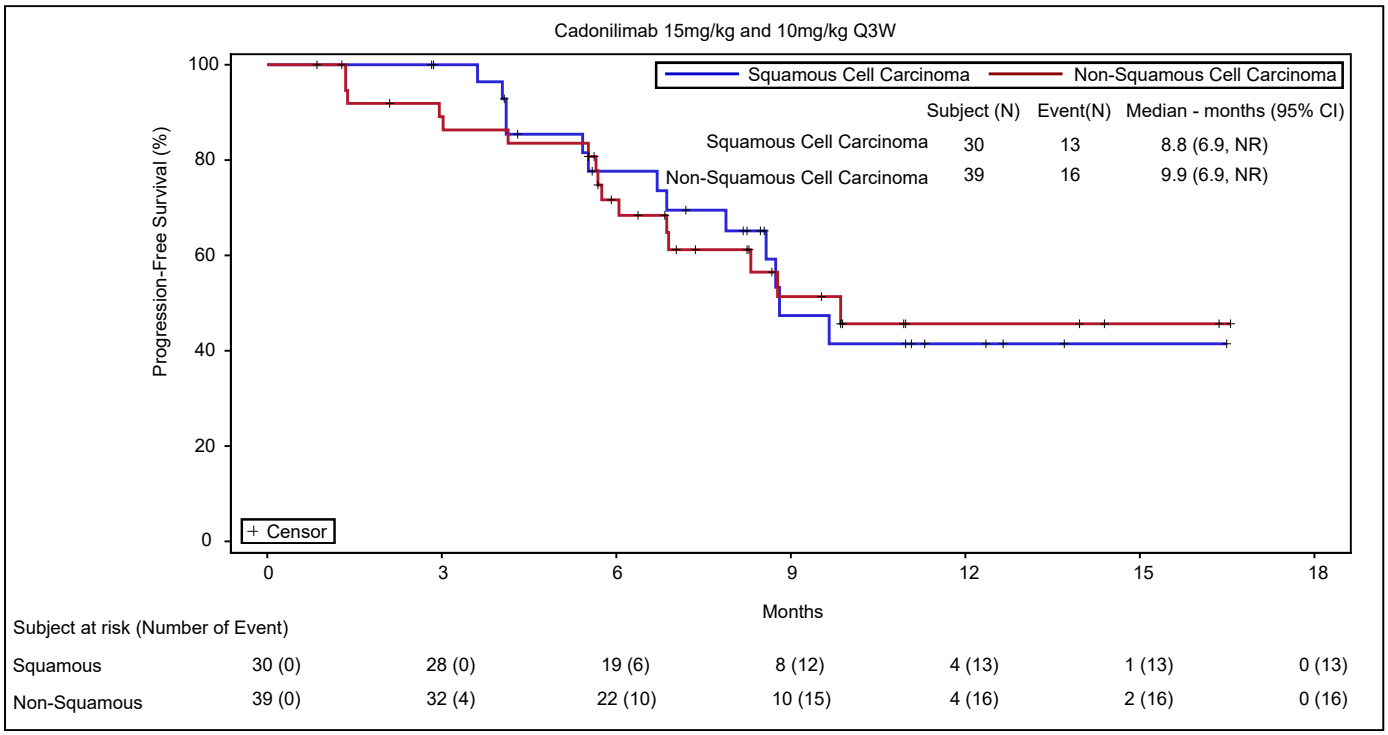


Table S1. Treatment-related adverse events occurring in ⩾ 10% of patients in either dosing group

	Cadonilimab 15mg/kg Q3W (N=49)		Cadonilimab 10mg/kg Q3W (N=20)		Overall (N=69)	
Preferred Term	**All Grade**	**≥ Grade 3**	**All Grade**	**≥ Grade 3**	**All Grade**	**≥ Grade 3**
Subject with any TRAEs, n (%)	48 (98.0)	29 (59.2)	19 (95.0)	5 (25.0)	67 (97.1)	34 (49.3)
Hypothyroidism	22 (44.9)	0	5 (25.0)	0	27 (39.1)	0
Aspartate aminotransferase increased	17 (34.7)	0	6 (30.0)	0	23 (33.3)	0
Decreased appetite	17 (34.7)	2 (4.1)	2 (10.0)	0	19 (27.5)	2 (2.9)
Amylase increased	14 (28.6)	1 (2.0)	4 (20.0)	0	18 (26.1)	1 (1.4)
Blood thyroid stimulating hormone increased	13 (26.5)	0	4 (20.0)	0	17 (24.6)	0
Hypertension	12 (24.5)	5 (10.2)	5 (25.0)	0	17 (24.6)	5 (7.2)
Hypertriglyceridaemia	12 (24.5)	0	5 (25.0)	0	17 (24.6)	0
Proteinuria	12 (24.5)	0	5 (25.0)	0	17 (24.6)	0
Hyperthyroidism	12 (24.5)	0	4 (20.0)	0	16 (23.2)	0
Alanine aminotransferase increased	10 (20.4)	0	5 (25.0)	0	15 (21.7)	0
Fatigue	13 (26.5)	0	2 (10.0)	0	15 (21.7)	0
Myalgia	10 (20.4)	0	5 (25.0)	0	15 (21.7)	0
Palmar-plantar erythrodysaesthesia syndrome	14 (28.6)	0	1 (5.0)	0	15 (21.7)	0
Chest discomfort	11 (22.4)	0	3 (15.0)	0	14 (20.3)	0
Dyspnoea	10 (20.4)	1 (2.0)	4 (20.0)	0	14 (20.3)	1 (1.4)
Haemoptysis	12 (24.5)	1 (2.0)	2 (10.0)	0	14 (20.3)	1 (1.4)
Infusion related reaction	12 (24.5)	1 (2.0)	2 (10.0)	0	14 (20.3)	1 (1.4)
Hyperlipidaemia	11 (22.4)	0	2 (10.0)	0	13 (18.8)	0
Rash	8 (16.3)	0	5 (25.0)	0	13 (18.8)	0
Hepatic function abnormal	11 (22.4)	4 (8.2)	1 (5.0)	1 (5.0)	12 (17.4)	5 (7.2)
Muscular weakness	8 (16.3)	0	3 (15.0)	0	11 (15.9)	0
Weight decreased	8 (16.3)	0	3 (15.0)	0	11 (15.9)	0
Platelet count decreased	7 (14.3)	1 (2.0)	3 (15.0)	1 (5.0)	10 (14.5)	2 (2.9)
Pyrexia	6 (12.2)	1 (2.0)	4 (20.0)	0	10 (14.5)	1 (1.4)
Blood bilirubin increased	8 (16.3)	0	1 (5.0)	0	9 (13.0)	0
Drug-induced liver injury	7 (14.3)	3 (6.1)	1 (5.0)	0	8 (11.6)	3 (4.3)
Hypercholesterolaemia	6 (12.2)	0	2 (10.0)	0	8 (11.6)	0
Anaemia	5 (10.2)	0	2 (10.0)	0	7 (10.1)	0
Blood cholesterol increased	5 (10.2)	0	2 (10.0)	0	7 (10.1)	0
Blood urine present	7 (14.3)	0	0	0	7 (10.1)	0
Diarrhoea	6 (12.2)	0	1 (5.0)	0	7 (10.1)	0
Hyponatraemia	6 (12.2)	2 (4.1)	1 (5.0)	1 (5.0)	7 (10.1)	3 (4.3)
Neutrophil count decreased	6 (12.2)	0	1 (5.0)	0	7 (10.1)	0
Pain in extremity	6 (12.2)	0	1 (5.0)	0	7 (10.1)	0
Pneumonitis	6 (12.2)	2 (4.1)	0	0	6 (8.7)	2 (2.9)
Blood creatinine increased	5 (10.2)	0	0	0	5 (7.2)	0
Hyperuricaemia	3 (6.1)	0	2 (10.0)	0	5 (7.2)	0
Hypochloraemia	5 (10.2)	2 (4.1)	0	0	5 (7.2)	2 (2.9)
White blood cell count decreased	5 (10.2)	0	0	0	5 (7.2)	0
Electrocardiogram abnormal	2 (4.1)	0	2 (10.0)	0	4 (5.8)	0
Haematuria	2 (4.1)	0	2 (10.0)	1 (5.0)	4 (5.8)	1 (1.4)
Bilirubin conjugated increased	1 (2.0)	0	2 (10.0)	0	3 (4.3)	0
Blood glucose increased	1 (2.0)	0	2 (10.0)	0	3 (4.3)	0
Agitation	0	0	2 (10.0)	0	2 (2.9)	0

TRAEs: Treatment-related adverse events; Q3W: every 3 weeks.

Table S2. Overview of immune-related adverse events (irAEs)

	Cadonilimab 15mg/kg Q3W (N=49)	**Cadonilimab 10mg/kg Q3W (N=20)**	**Overall (N=69)**
irAEs, n (%)	10 (20.4)	4 (20.0)	14 (20.3)
Grade ≥3 irAEs, n (%)	2 (4.1)	2 (10.0)	4 (5.8)
Serious irAEs, n (%)	7 (14.3)	3 (15.0)	10 (14.5)
irAEs leading to cadonilimab and anlotinib discontinuation, n (%)	0	1 (5.0)	1 (1.4)
irAEs leading to cadonilimab discontinuation, n (%)	0	1 (5.0)	1 (1.4)
irAEs leading to anlotinib discontinuation, n (%)	0	1 (5.0)	1 (1.4)
irAEs leading to death, n (%)	0	0	0

irAEs: Immune-related adverse events; Q3W: every 3 weeks.

Table S3. irAEs by Preferred Terms in either dosing group

	Cadonilimab 15mg/kg Q3W (N=49)		Cadonilimab 10mg/kg Q3W (N=20)		Overall (N=69)	
Preferred Term	**All Grade**	**≥ Grade 3**	**All Grade**	**≥ Grade 3**	**All Grade**	**≥ Grade 3**
Subjects with Any irAEs	10 (20.4)	2 (4.1)	4 (20.0)	2 (10.0)	14 (20.3)	4 (5.8)
Hypothyroidism	3 (6.1)	0	1 (5.0)	0	4 (5.8)	0
Hypopituitarism	2 (4.1)	1 (2.0)	1 (5.0)	0	3 (4.3)	1 (1.4)
Lymphocytic hypophysitis	2 (4.1)	0	0	0	2 (2.9)	0
Immune-mediated arthritis	1 (2.0)	1 (2.0)	0	0	1 (1.4)	1 (1.4)
Immune-mediated myositis	1 (2.0)	0	0	0	1 (1.4)	0
Osteoarthritis	1 (2.0)	0	0	0	1 (1.4)	0
Autoimmune hepatitis	0	0	1 (5.0)	1 (5.0)	1 (1.4)	1 (1.4)
Cortisol abnormal	1 (2.0)	0	0	0	1 (1.4)	0
Ketoacidosis	0	0	1 (5.0)	1 (5.0)	1 (1.4)	1 (1.4)
Immune-mediated pneumonitis	1 (2.0)	0	0	0	1 (1.4)	0

irAEs: Immune-related adverse events; Q3W: every 3 weeks.

Table S4. Tumor response in patients treated with cadonilimab 15mg/kg and 10mg/kg every 3 weeks (Q3W)

	Cadonilimab 15mg/kg and 10mg/kg Q3W				
	PD-L1 Positive	**PD-L1 Negative**	**Squamous Cell Carcinoma**	**Non-Squamous Cell Carcinoma**	**Overall**
	(N=43)	**(N=26)**	**(N=30)**	**(N=39)**	**(N=69)**
ORR, % (95% CI)	60.5 (44.4, 75.0)	42.3 (23.4, 63.1)	60.0 (40.6, 77.3)	48.7 (32.4, 65.2)	53.6 (41.2, 65.7)
DCR, % (95% CI)	93.0 (80.9, 98.5)	92.3 (74.9, 99.1)	100 (88.4, 100)	87.2 (72.6, 95.7)	92.8 (83.9, 97.6)
Best Overall Response, n (%)					
CR	0	0	0	0	0
PR	26 (60.5)	11 (42.3)	18 (60.0)	19 (48.7)	37 (53.6)
SD	14 (32.6)	13 (50.0)	12 (40.0)	15 (38.5)	27 (39.1)
PD	2 (4.7)	1 (3.8)	0	3 (7.7)	3 (4.3)
NE	0	1 (3.8)	0	1 (2.6)	1 (1.4)
NA	1 (2.3)	0	0	1 (2.6)	1 (1.4)
DOR, Median (months), (95% CI)	NR (5.8, NR)	NR (2.9, NR)	NR (5.6, NR)	NR (4.5, NR)	NR (5.8, NR)

PD-L1, programmed cell death ligand-1; ORR, objective response rate; DCR, disease control rate; CI, confidence interval. NE, not evaluable; NA, no post-baseline tumor assessment; DOR, duration of response; NR, not reached; Q3W, every 3 weeks.