

RC148 (ABBV-1480, PD-1/VEGF Bispecific Antibody) plus Chemotherapy in First-line Locally Advanced or Metastatic Non-Small-Cell Lung Cancer

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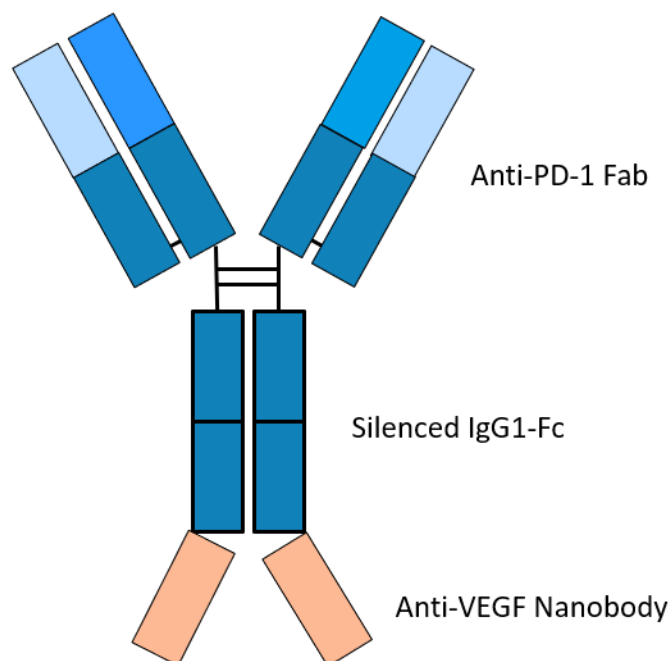
Disclosure

- Dr. Zhao has no conflicts of interest to declare.
- This study was sponsored by RemeGen Co., Ltd., Yantai, China. RemeGen participated in the study design, research, analysis, and data collection. RemeGen and AbbVie participated in the interpretation of data, reviewing and approving of the publication. No honoraria or payments were made for authorship.
- Artificial intelligence (AI) was not used in the development of the slides.

RC148 differentiated molecular design for dual targeting of PD-1 and VEGF

RC148 (ABBV-1480)

(tetraivalent PD-1 x VEGF BsAb, ~170 KD)¹



- **RC148 Enhances Therapeutic Efficacy via:**
 - **Potent PD-1 Backbone**
Demonstrates a robust ability to relieve immunosuppression
 - **Unique VEGF Epitope**
Distinct from bevacizumab, delivers stronger signal-blocking capabilities
 - **Silenced Fc Effector Function**
Eliminates ADCC/ADCP to mitigate potential immune-related side effects
 - **Favorable Clinical Pharmacokinetics**
Linear and dose proportional PK across the evaluated dose range
- **RC148 effective half life: ~23 days**

- **RC148 monotherapy and combination with docetaxel have shown encouraging anti-tumor activity with manageable safety in NSCLC.²**

Study design

- This was a randomized, open-label, dose-optimization phase 1b study evaluating first-line RC148 in combination with platinum-based chemotherapy in patients with advanced NSCLC.
- This report focuses mainly on the recommended phase 3 dose of 10 mg/kg Q3W.

All Q3W

Key Eligibility Criteria

- Pathologically confirmed NSCLC
- Stage IIIB/C or IV
- Systemic treatment-naïve
- Without actionable genomic alterations (AGA)
- ECOG PS 0 or 1

Squamous

N=60

R
1:1

**RC148 (10 mg/kg) +
Carboplatin + Paclitaxel
4 cycles**

**RC148 (10 mg/kg)
maintenance**

RC148 (20 mg/kg) +
Carboplatin + Paclitaxel
4 cycles

RC148 (20 mg/kg)
maintenance

Non-squamous

N=60

R
1:1

**RC148 (10 mg/kg) +
Carboplatin + Pemetrexed
4 cycles**

**RC148 (10 mg/kg) + Pemetrexed
maintenance**

RC148 (20 mg/kg) +
Carboplatin + Pemetrexed
4 cycles

RC148 (20 mg/kg) + Pemetrexed
maintenance

Treatment continued until:

- Disease progression
- Intolerable toxicity
- Consent withdrawal

Primary endpoint: ORR assessed as per RECIST v1.1; **Secondary endpoints:** DCR, DoR, PFS, OS, PK, and safety

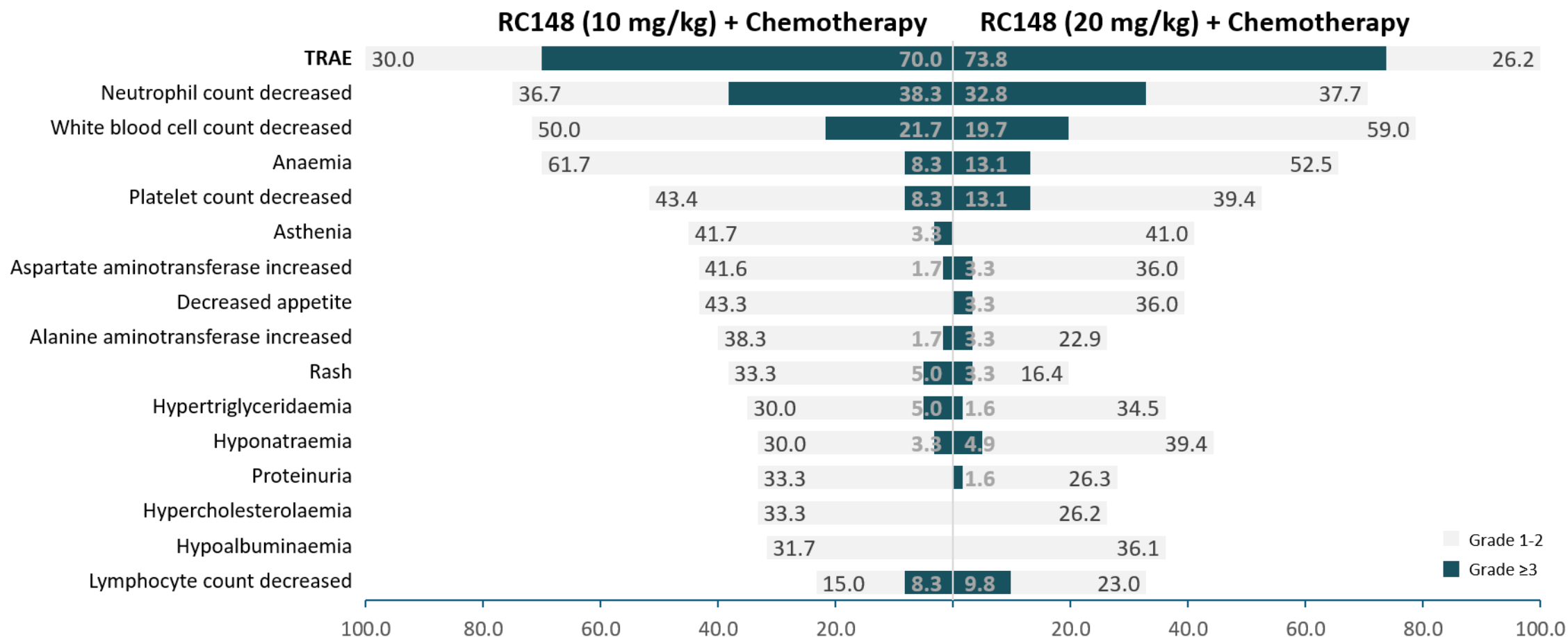
Baseline characteristics were typical of locally advanced/ metastatic NSCLC populations

		Squamous NSCLC		Non-squamous NSCLC	
		RC148 (10 mg/kg) + Carboplatin + Paclitaxel (N=30)	RC148 (20 mg/kg) + Carboplatin + Paclitaxel (N=31)	RC148 (10 mg/kg) + Carboplatin + Pemetrexed (N=30)	RC148 (20 mg/kg) + Carboplatin + Pemetrexed (N=30)
Age (years)	Median (IQR)	67.0 (60.0-71.0)	65.0 (59.0-70.0)	63.0 (57.0-69.0)	63.0 (58.0-69.0)
	<65	10 (33.3)	15 (48.4)	15 (50.0)	18 (60.0)
	≥65	20 (66.7)	16 (51.6)	15 (50.0)	12 (40.0)
Sex, n (%)	Male	28 (93.3)	24 (77.4)	19 (63.3)	19 (63.3)
	Female	2 (6.7)	7 (22.6)	11 (36.7)	11 (36.7)
ECOG PS score, n (%)	0	5 (16.7)	6 (19.4)	5 (16.7)	8 (26.7)
	1	25 (83.3)	25 (80.6)	25 (83.3)	22 (73.3)
PD-L1 TPS, n (%)	<1%	15 (50.0)	10 (32.3)	15 (50.0)	18 (60.0)
	≥1%	14 (46.7)	16 (51.6)	13 (43.3)	11 (36.7)
	Unknown	1 (3.3)	5 (16.1)	2 (6.7)	1 (3.3)
Site of metastatic lesion, n (%)	≥3 Metastatic lesions	10 (33.3)	12 (38.7)	17 (56.7)	12 (40.0)
	Liver metastases	0	8 (25.8)	8 (26.7)	6 (20.0)
	Brain metastases	0	0	3 (10.0)	1 (3.3)

IQR, interquartile range; ECOG PS, Eastern Cooperative Oncology Group performance status; TPS, tumor proportion score.

Treatment-related adverse events were mostly grade 1-2

Combined SQ and NSQ NSCLC



TRAEs were defined as adverse events “related”, “likely related”, or “possibly related” to any study drug and graded as per CTCAE Version 5.0. TRAEs of any grade occurring in ≥30.0% of SQ and NSQ patients receiving RC148 10 mg/kg (left) and 20 mg/kg (right) combined with chemotherapy are listed. SQ, squamous; NSQ, non-squamous.

VEGF- and immune-related TRAEs were mainly grade 1-2

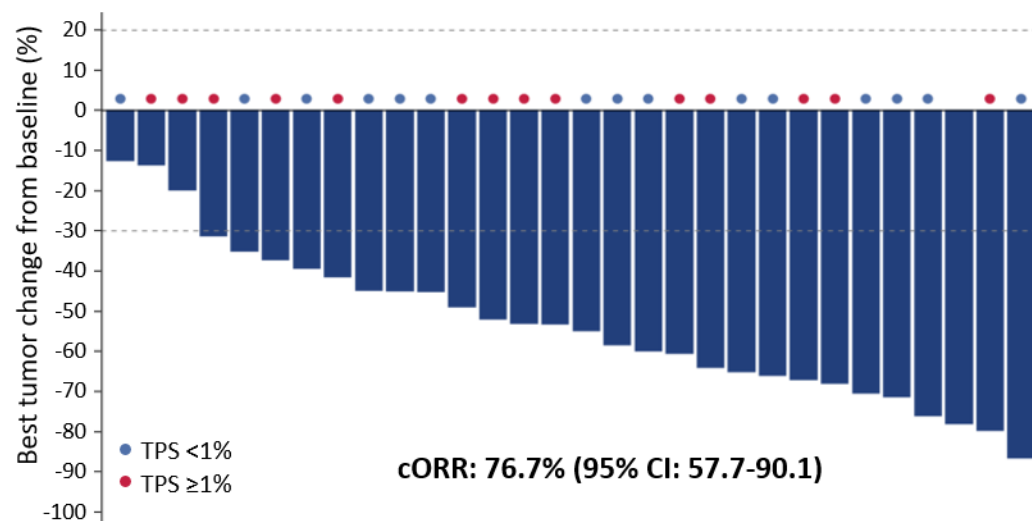
TRAEs, n (%) (Related to any study drug)	Squamous NSCLC				Non-squamous NSCLC			
	RC148 (10 mg/kg) + Carboplatin + Paclitaxel (N=30)		RC148 (20 mg/kg) + Carboplatin + Paclitaxel (N=31)		RC148 (10 mg/kg) + Carboplatin + Pemetrexed (N=30)		RC148 (20 mg/kg) + Carboplatin + Pemetrexed (N=30)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
VEGF-related TRAEs	17 (56.7)	1 (3.3)	21 (67.7)	8 (25.8)	19 (63.3)	3 (10.0)	11 (36.7)	2 (6.7)
Most common VEGF-related TRAEs (any grade in ≥5% patients in either group)								
Proteinuria	11 (36.7)	0	10 (32.3)	0	9 (30.0)	0	7 (23.3)	1 (3.3)
Haemoptysis	3 (10.0)	0	5 (16.1)	4 (12.9)	2 (6.7)	0	0	0
Epistaxis	2 (6.7)	0	3 (9.7)	0	1 (3.3)	0	0	0
Urinary occult blood positive	0	0	2 (6.5)	0	0	0	2 (6.7)	0
Hypertension	3 (10.0)	1 (3.3)	8 (25.8)	3 (9.7)	8 (26.7)	2 (6.7)	2 (6.7)	0
Blood pressure increased	2 (6.7)	0	1 (3.2)	1 (3.2)	0	0	1 (3.3)	0
Deep vein thrombosis	0	0	1 (3.2)	0	0	0	2 (6.7)	1 (3.3)
Immune-related TRAEs	11 (36.7)	2 (6.7)	12 (38.7)	3 (9.7)	10 (33.3)	4 (13.3)	9 (30.0)	0
Most common immune-related TRAEs (any grade in ≥5% patients in either group)								
Hypothyroidism	3 (10.0)	0	2 (6.5)	0	1 (3.3)	0	1 (3.3)	0
Rash	2 (6.7)	1 (3.3)	2 (6.5)	1 (3.2)	2 (6.7)	2 (6.7)	2 (6.7)	0
Pruritus	0	0	3 (9.7)	0	0	0	0	0

TRAEs are preferred terms and were graded according to CTCAE Version 5.0. VEGF-related AEs were coded and grouped according to Standardised MedDRA Queries (SMQs) based on MedDRA Version 29.0. VEGF, vascular endothelial growth factor.

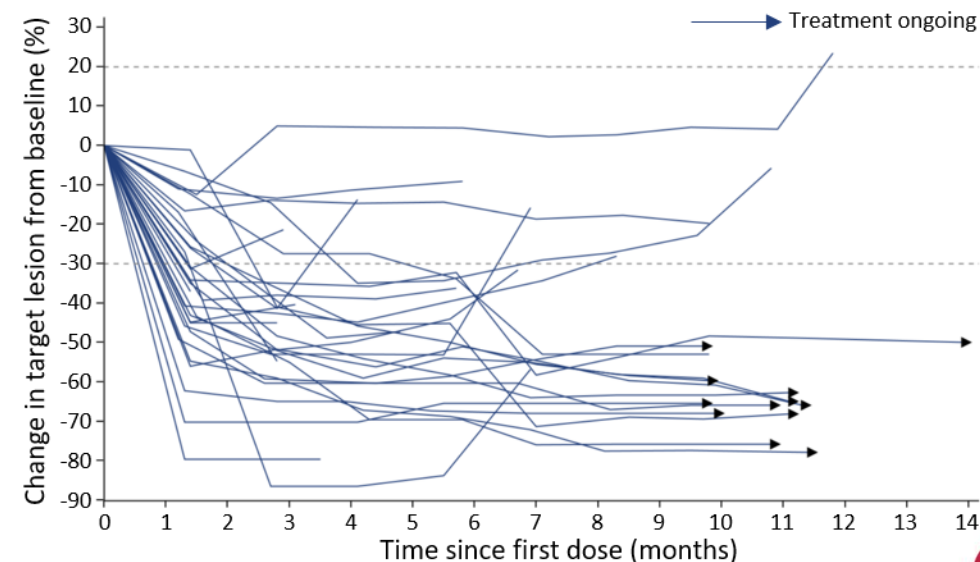
Robust and durable anti-tumor activity in squamous NSCLC

- As of the data cutoff date, the median follow-up was 11.7 months (95% CI: 11.0-12.3); 12 (52.2%) of 23 responders remained on treatment.

RC148 (10 mg/kg) + Carboplatin + Paclitaxel						
		TPS <1% (N=15)	TPS ≥1% (N=14)	Age <65 years (N=10)	Age ≥65 years (N=20)	Overall (N=30)
Unconfirmed ORR, % (95% CI)		93.3 (68.1-99.8)	85.7 (57.2-98.2)	90.0 (55.5-99.7)	90.0 (68.3-98.8)	90.0 (73.5-97.9)
Confirmed ORR, % (95% CI)		86.7 (59.5-98.3)	64.3 (35.1-87.2)	60.0 (26.2-87.8)	85.0 (62.1-96.8)	76.7 (57.7-90.1)
Confirmed best overall response, n (%)	Partial response	13 (86.7)	9 (64.3)	6 (60.0)	17 (85.0)	23 (76.7)
	Stable disease	2 (13.3)	5 (35.7)	4 (40.0)	3 (15.0)	7 (23.3)
	Progressive disease	0	0	0	0	0
DoR	Median (95% CI), month	NR	NR	NR	NR	NR



PD-L1 TPS status was unknown in one patient. NR, not reached; cORR, confirmed ORR



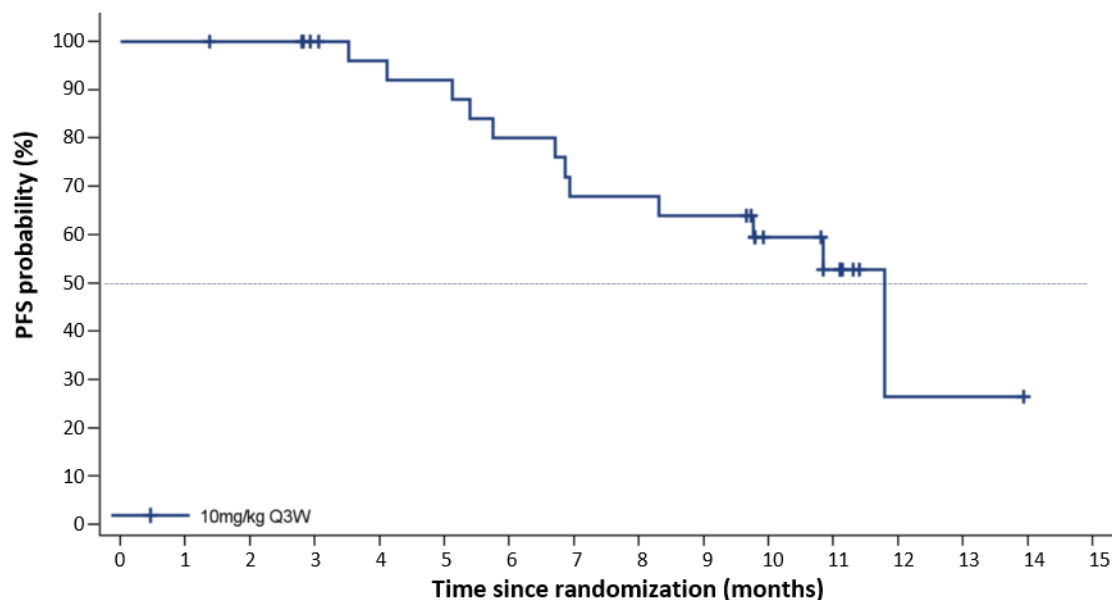
Encouraging trends in PFS and OS were observed in squamous NSCLC, although outcomes remain immature

Progression-free Survival

RC148 (10 mg/kg) + Carboplatin + Paclitaxel
(N=30)

Events, n (%) 12 (40.0)

Median PFS (95% CI), mo 11.8 (6.9-NR)

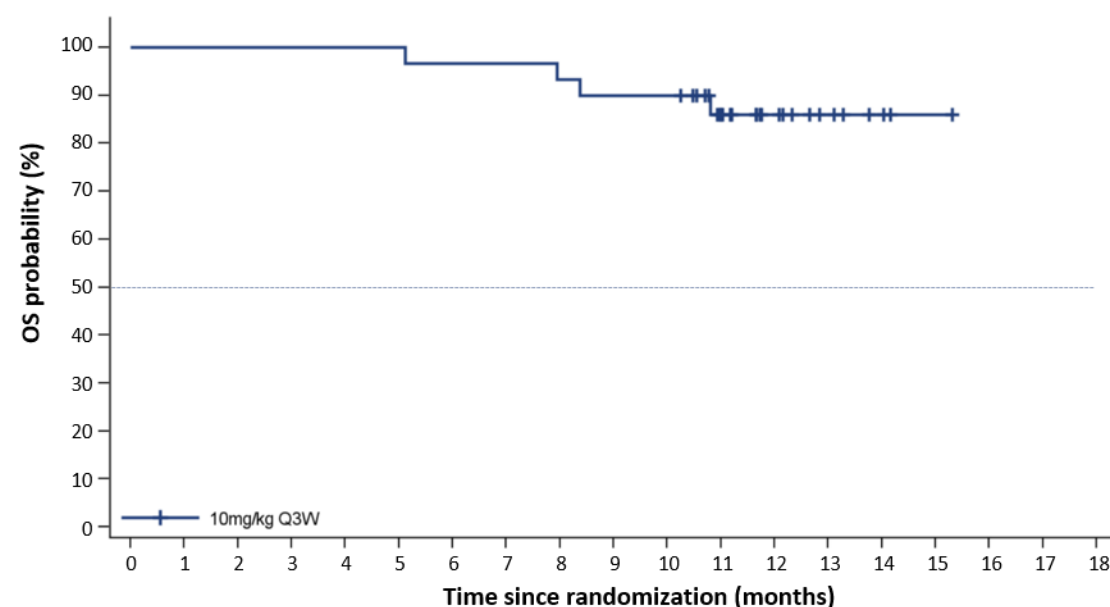


Overall Survival

RC148 (10 mg/kg) + Carboplatin + Paclitaxel
(N=30)

Events, n (%) 4 (13.3)

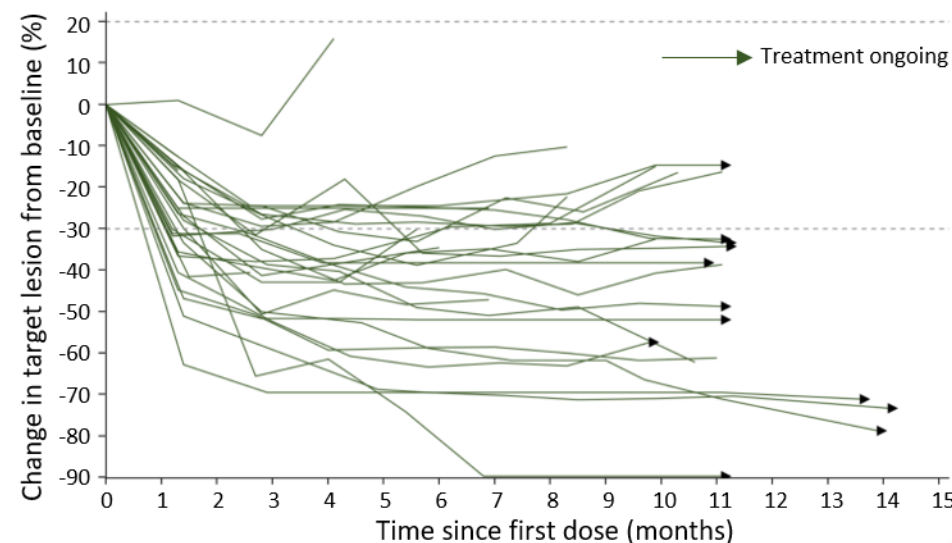
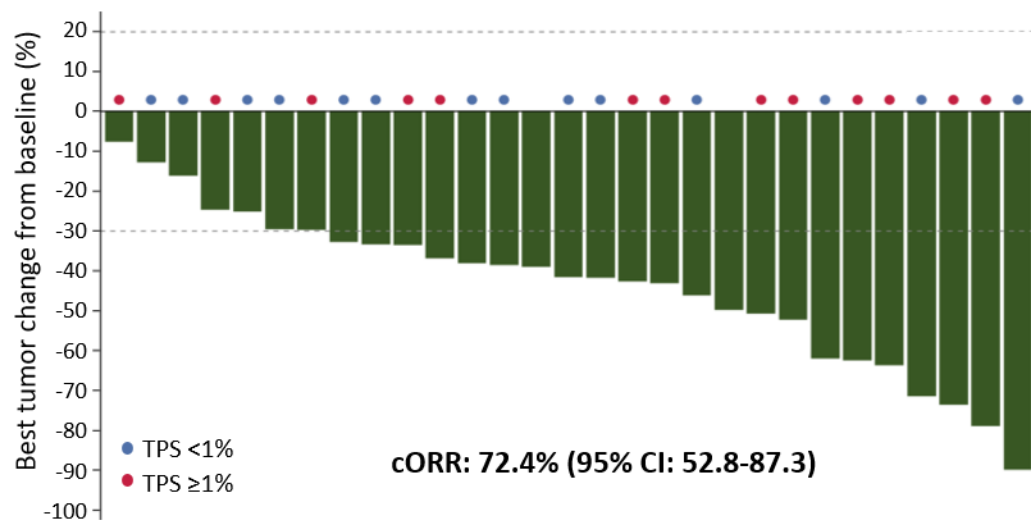
Median OS (95% CI), mo NR



Robust and durable anti-tumor activity in non-squamous NSCLC

- As of the data cutoff, the median follow-up was 12.3 months (95% CI: 11.5-12.8); 11 (52.4%) of 21 responders remained on treatment.

RC148 (10 mg/kg) + Carboplatin + Pemetrexed					
	TPS <1% (N=14)	TPS ≥1% (N=13)	Age <65 years (N=15)	Age ≥65 years (N=14)	Overall (N=29)*
Unconfirmed ORR, % (95% CI)	71.4 (41.9-91.6)	76.9 (46.2-95.0)	53.3 (26.6-78.7)	100 (76.8-100)	75.9 (56.5-89.7)
Confirmed ORR, % (95% CI)	64.3 (35.1-87.2)	76.9 (46.2-95.0)	53.3 (26.6-78.7)	92.9 (66.1-99.8)	72.4 (52.8-87.3)
Confirmed best overall response, n (%)	Partial response	9 (64.3)	10 (76.9)	8 (53.3)	13 (92.9)
	Stable disease	4 (28.6)	3 (23.1)	6 (40.0)	1 (7.1)
	Progressive disease	1 (7.1)	0	1 (6.7)	0
DoR	Median (95% CI), month	8.6 (3.3-NR)	NR	7.2 (4.1-9.7)	9.7 (5.7-NR)



*Tumor response was assessed in patients with at least one post-baseline assessment. PD-L1 TPS status was unknown in two patients.

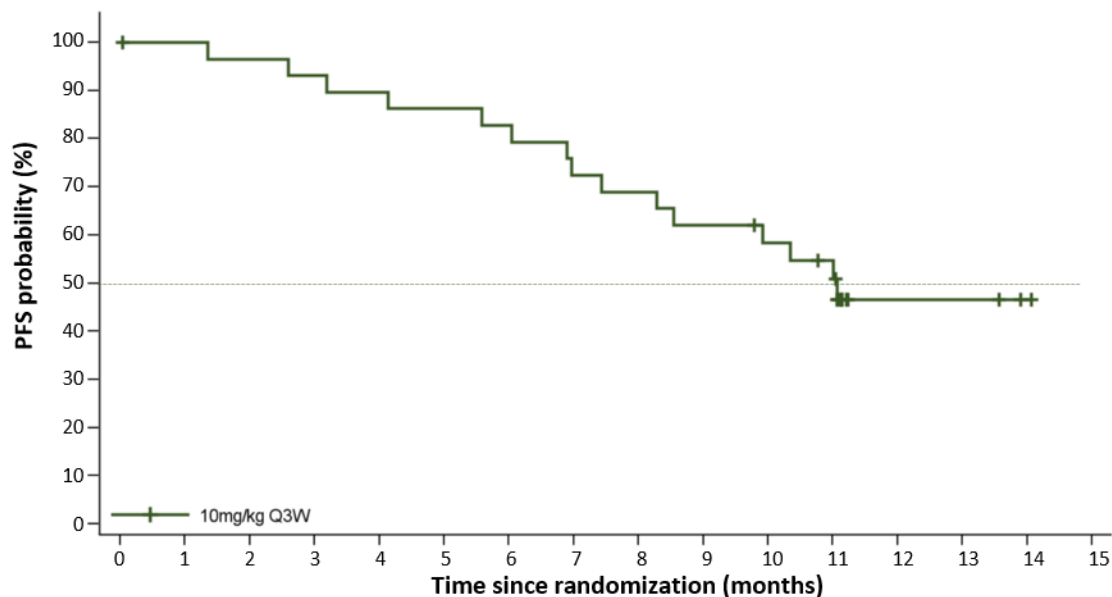
Encouraging trends in PFS and OS were observed in non-squamous NSCLC, although outcomes were immature

Progression-free Survival

RC148 (10 mg/kg) + Carboplatin + Pemetrexed
(N=30)

Events, n (%) 15 (50.0)

Median PFS (95% CI), mo 11.1 (7.4-NR)

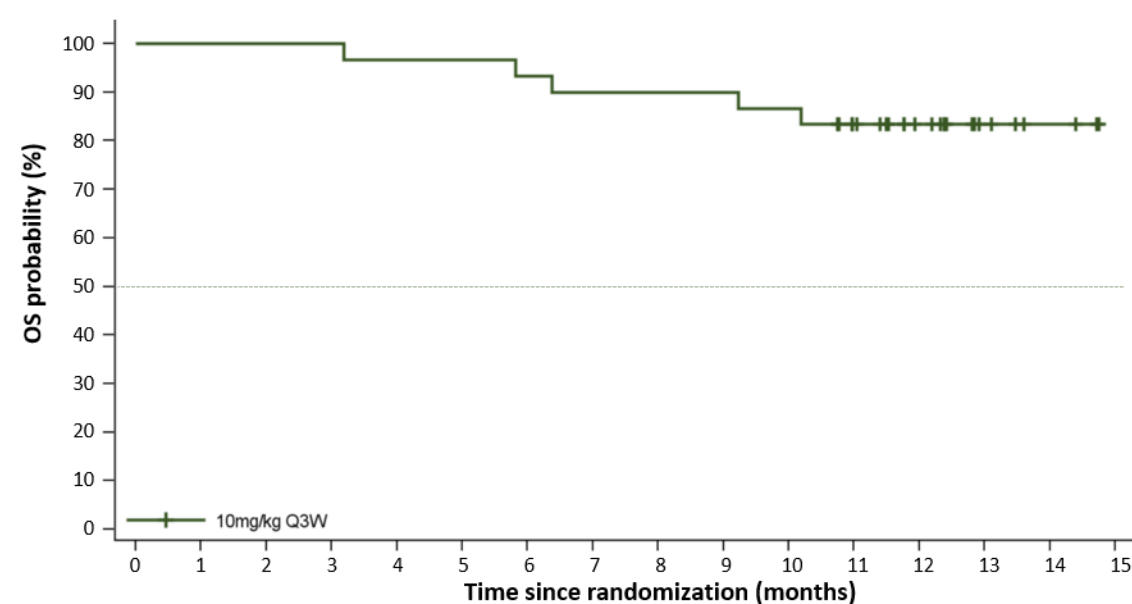


Overall Survival

RC148 (10 mg/kg) + Carboplatin + Pemetrexed
(N=30)

Events, n (%) 5 (16.7)

Median OS (95% CI), mo NR



Conclusions

1

RC148 (ABBV-1480) is a unique PD1/VEGF bsAb and the phase 1b data supported selection of 10 mg/kg as the RP3D in 1L NSCLC.

2

The safety profile of RC148 + chemo was manageable with infrequent and mainly low grade VEGF- and immune-related toxicities.

3

RC148 + chemo demonstrated robust and durable efficacy in both SQ and NSQ 1L NSCLC irrespective of PD-L1 status or age.

Pivotal phase 3 studies have been initiated in China and globally.

- Phase 3 trial of RC148 plus chemotherapy in 1L squamous NSCLC (RC148-C301, NCT07416474) is actively recruiting in China. (TiP Abstract #795 at WCLC)
- Phase 3 trial of RC148 plus chemotherapy in 1L non-squamous NSCLC is being initiated in China.
- A global phase 3 trial of ABBV-1480 plus chemotherapy in 1L NSCLC is actively recruiting (NCT07756645).

Acknowledgement

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