

Abstract 249P: A Phase 1/2 Study of RC148 (PD-1/VEGF bispecific antibody) monotherapy or in combination with docetaxel for the treatment of first- or second-line locally advanced or metastatic non-small-cell lung cancer (la/mNSCLC) without actionable genomic alterations (AGA)

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BACKGROUND

- RC148 is an innovative bispecific antibody targeting both PD-1 and vascular endothelial growth factor (VEGF).¹ Dual targeting of PD-1 and VEGF combines two complementary modalities, aiming to improve anti-tumor effects by inhibiting PD-1-mediated immunosuppression and blocking tumor angiogenesis in the tumor microenvironment.²⁻⁴
- RC148-C001 is a phase 1/2 study to evaluate the efficacy and safety of RC148 as monotherapy and combination therapy in patients advanced malignant solid tumors (NCT06016062).
- We report the results from: 1) the RC148 monotherapy expansion cohort of patients with PD-L1-positive, treatment-naïve la/mNSCLC in phase 1; 2) the RC148+Docetaxel cohort of patients with actionable genomic alterations (AGA)-negative la/mNSCLC who were previously treated with PD-(L)1 inhibitor and platinum-based chemotherapy in phase 2.

METHODS

RC148 monotherapy for first-line la/mNSCLC

Key eligibility criteria

- Histologically or cytologically confirmed la/mNSCLC
- PD-L1-positive (TPS $\geq 1\%$)
- Measurable target lesion per RECIST v1.1
- ECOG PS 0-1

N=22

RC148 20 mg/kg
IV Q3W

- Tumors were assessed as per RECIST v1.1 at baseline and then every 6 weeks until disease progression, consent withdrawal, or initiation of new anti-cancer treatment.
- Primary endpoint: objective response rate (ORR) assessed by investigators as per RECIST v1.1. The data cutoff date (DCO) was 17 October, 2025.

Abbreviations: TPS=tumor proportion score, RECIST=Response Evaluation Criteria in Solid Tumors, ECOG PS=Eastern Cooperative Oncology Group performance score, Q3W=once every three weeks

RC148+docetaxel for previously treated la/mNSCLC

Key eligibility criteria

- AGA-negative la/mNSCLC
- Prior treatment with PD-(L)1 inhibitor and (concurrent or sequential) platinum-based chemotherapy
- Measurable target lesion per RECIST v1.1
- ECOG PS 0-1

N=21

R
1:1

RC148 10 mg/kg +
Docetaxel 75 mg/m²
IV Q3W

RC148 20 mg/kg +
Docetaxel 75 mg/m²
IV Q3W

RESULTS

RC148 Monotherapy – Patients

- 22 patients were enrolled. The median follow-up was 7.01 (IQR: 5.52-8.57) months.

Table 1. RC148 monotherapy - baseline characteristics

		RC148 20 mg/kg Monotherapy (N = 22)
Age (years), median (IQR)		65.0 (57.0-69.0)
Gender, n (%)		Male 18 (81.8)
Tumor histology, n (%)		Squamous / non-squamous / unknown 12 (54.5) / 9 (40.9) / 1 (4.5)
Clinical staging, n (%)		IV 14 (63.6)
PD-L1 TPS, n (%)		1%-49% / $\geq 50\%$ 13 (59.1) / 9 (40.9)

IQR=interquartile range, TPS=tumor proportion score.

RC148 Monotherapy - Efficacy

- 21 patients underwent post-baseline tumor assessment. Among them, the ORR was 61.9% (95% CI: 38.4-81.9), with 2 responses pending confirmation; the confirmed ORR (cORR) was 52.4% (95% CI: 29.8-74.3).
- Promising ORR was reported across subgroups of squamous NSCLC (63.6%), non-squamous (55.6%), PD-L1 TPS 1%-49% (50.0%), and TPS $\geq 50\%$ (77.8%).
- The median duration of response (DoR) was not reached.
- The estimated 6-month PFS rate was 85.0%; the median PFS was not reached.

Figure 1. RC148 monotherapy - best tumor change from baseline

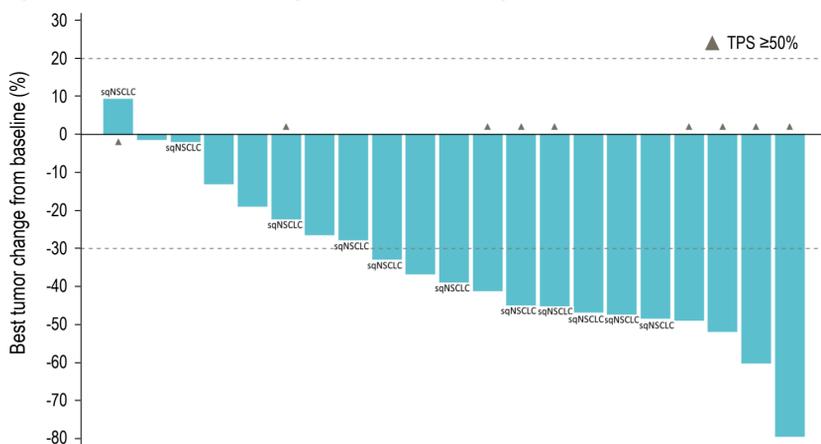
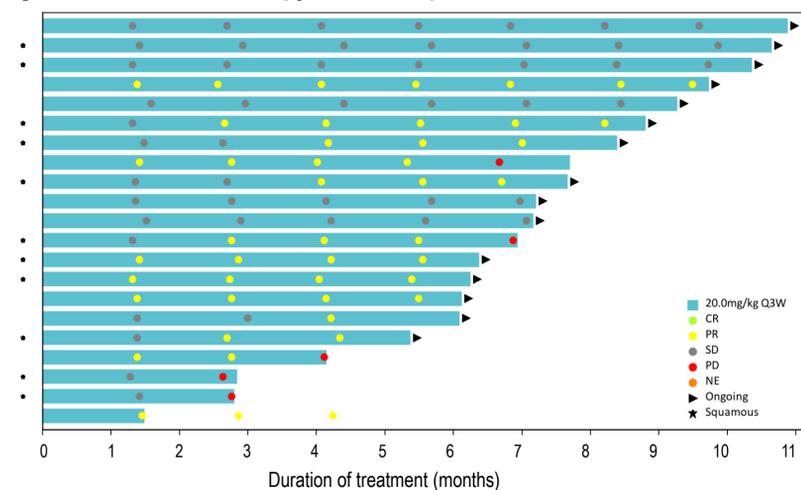


Figure 2. RC148 monotherapy - swimmer plot



Safety Summary – RC148 Monotherapy and RC148+Docetaxel

- The overall safety profiles are summarized in Table 3. RC148 in combination with docetaxel did not increase the overall safety risk as compared with docetaxel monotherapy.
- The most common treatment-related adverse events (TRAEs) occurring in $\geq 30.0\%$ of patients for monotherapy were proteinuria, hypercholesterolaemia, hypertriglyceridaemia, hypertension, and hypothyroidism; for combination therapy were neutrophil count decreased, white blood cell decrease, platelet count decrease, anemia, asthenia, decreased appetite, and weight decreased.

RC148+Docetaxel – Patients

- 42 patients were enrolled. The median follow-up was 6.90 (IQR: 6.31-7.95) months.

Table 2. RC148+docetaxel - baseline characteristics

		RC148 10 mg/kg + Docetaxel (N = 21)	RC148 20 mg/kg + Docetaxel (N = 21)
Age (years), median (IQR)		61.0 (59.0-69.0)	66.0 (62.0-70.0)
Gender, n (%)		Male 18 (85.7)	15 (71.4)
Tumor histology, n (%)		Squamous / non-squamous 11 (52.4) / 10 (47.6)	14 (66.7) / 7 (33.3)
Clinical staging, n (%)		IV 20 (95.2)	18 (85.7)
PD-L1 TPS, n (%)		<1% / $\geq 1\%$ 17 (81.0) / 4 (19.0)	11 (52.4) / 10 (47.6)
Prior treatment line, n (%)		1 / 2 18 (85.7) / 3 (14.3)	17 (81.0) / 4 (19.0)

RC148+Docetaxel - Efficacy

- All patients underwent post-baseline tumor assessment. The 20 mg/kg group showed a higher cORR versus the 10 mg/kg group (66.7% [95% CI: 43.0-85.4] vs 28.6% [11.3-52.2]).
- In the 20 mg/kg group, promising cORR was observed in subgroups of squamous NSCLC (64.3%), non-squamous (71.4%), PD-L1 TPS <1% (54.5%), and TPS $\geq 1\%$ (80.0%).
- The median DoR was not reached in either group.
- The 20 mg/kg group showed a longer median PFS (median: 8.28 [95% CI: 5.98-NE] vs 5.82 [4.14-NE] months; hazard ratio: 0.445) compared with the 10 mg/kg group.

Figure 3. RC148+Docetaxel - best tumor change from baseline

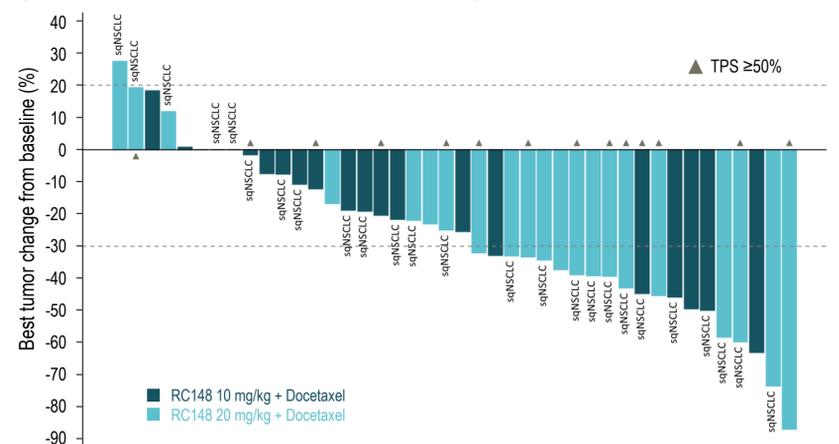


Figure 4. RC148+Docetaxel – progression-free survival (PFS)

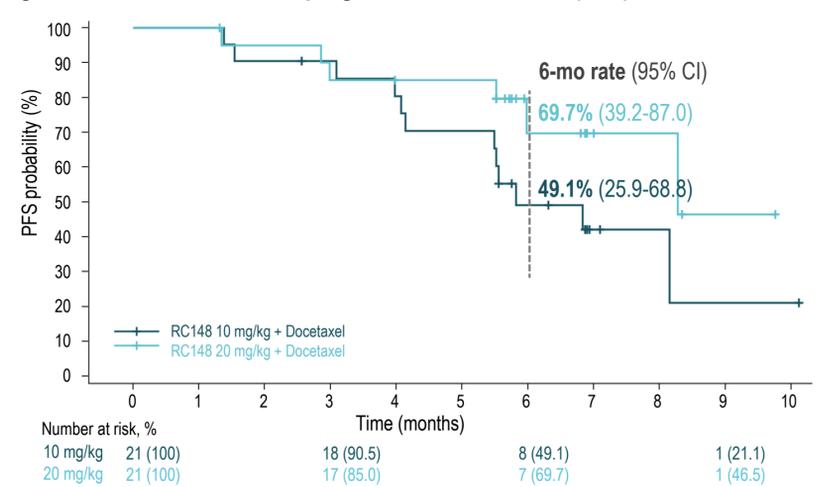


Table 3. Safety summary

n (%)	RC148 20 mg/kg Monotherapy (N = 22)	RC148 10 mg/kg + Docetaxel (N = 21)	RC148 20 mg/kg + Docetaxel (N = 21)
Any TRAE*	22 (100)	21 (100)	21 (100)
\geq Grade 3	9 (40.9)	18 (85.7)	16 (76.2)
Serious	5 (22.7)	10 (47.6)	5 (23.8)
Leading to treatment discontinuation	1 (4.5)	2 (9.5)	4 (19.0)
Leading to death	0	0	0

*Related to any study drug.

CONCLUSIONS

- RC148 monotherapy showed encouraging anti-tumor activity and an acceptable safety profile in patients with first-line PD-L1-positive la/mNSCLC.
- RC148+Docetaxel also showed promising efficacy in patients with AGA-negative la/mNSCLC who were previously treated with PD-(L)1 inhibitor and platinum-based chemotherapy.
- These findings supported phase 3 studies. Currently, confirmatory phase 3 studies in the first- and second-line NSCLC are planned.