



P1.266: Adebrelimab Plus Bevacizumab and Nab-Paclitaxel in Non-Squamous NSCLC After 1st-Line ICI Failure: A Phase II Rechallenge Study

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INTRODUCTION

- Immune checkpoint inhibitors (ICIs) have become standard first-line therapy for patients with advanced, driver alteration-negative non-squamous non-small cell lung cancer (NSCLC) [1]. However, most patients eventually develop resistance to ICI-based therapy, and effective treatment strategies after progression remain limited [2].
- This study evaluated the efficacy, safety, and exploratory biomarkers of adebrelimab rechallenge in combination with bevacizumab and albumin-bound paclitaxel (nab-paclitaxel) in patients with advanced non-squamous NSCLC after progression on first-line ICI-based therapy.

METHODS

- This prospective, single-arm, phase II study (NCT05738317) enrolled patients with advanced non-squamous NSCLC who had progressed after first-line ICI-based therapy.
- Patients received adebrelimab plus bevacizumab and nab-paclitaxel every 3 weeks for 4 cycles, followed by maintenance therapy with adebrelimab and bevacizumab until disease progression or unacceptable toxicity (**Figure 1**).
- DNA sequencing was performed based on plasma cell-free DNA using a 1021-gene panel, with genomic DNA from peripheral blood mononuclear cells was sequenced as germline control.

Key eligibility criteria

- ≥18 years old;
- histologically or cytologically confirmed metastatic or recurrent non-squamous NSCLC;
- have experienced objective radiographic progression (per RECIST version 1.1) after receiving first-line therapy which included ICIs, with PFS ≥3 months;
- at least one measurable lesion per RECIST v1.1;
- ECOG PS of 0–1;
- a life expectancy of ≥3 months.

N=45

Adebrelimab (20 mg/kg, intravenously) + **bevacizumab** (7.5 mg/kg, intravenously) + **nab-paclitaxel** (260 mg/m², intravenously) every 3 weeks for 4 cycles.

Maintenance therapy with adebrelimab and bevacizumab until disease progression or unacceptable toxicity.

Figure 1. Study design

- Primary endpoint: 6-month PFS rate;
- Secondary endpoints: PFS, OS, ORR, DCR, DoR, safety;
- Exploratory endpoint: the association between biomarkers and efficacy outcomes.

RESULTS

Table 1. Baseline demographics and characteristics

Characteristic	Patients (N=46)
Age, years	
Median (range)	62.0 (38.0, 74.0)
Sex, n (%)	
Male	37 (80.4)
Female	9 (19.6)
ECOG performance status, n (%)	
0	23 (50.0)
1	23 (50.0)
Disease stage, n (%)	
IIA	0
IIIA	1 (2.2)
IIIB	3 (6.5)
IIIC	1 (2.2)
IVA	16 (34.8)
IVB	25 (54.3)
Other genomic alterations, n (%)	
Yes	20 (43.5)
No	26 (56.5)
Smoking status, n (%)	
Never	20 (43.5)
Former	24 (52.2)
Current	2 (4.3)
Brain metastases, n (%)	
Yes	16 (34.8)
No	30 (65.2)
Liver metastases, n (%)	
Yes	5 (10.9)
No	41 (89.1)
Bone metastases, n (%)	
Yes	12 (26.1)
No	34 (73.9)
Prior antitumor treatment, n (%)	
Immunotherapy plus chemotherapy	44 (95.7)
Immunotherapy monotherapy	2 (4.3)
PFS on prior first-line ICI-based therapy, n (%)	
<10 months	26 (56.5)
≥10 months	20 (43.5)
Best response to prior first-line ICI-based therapy, n (%)	
CR	1 (2.2)
PR	12 (26.1)
SD	33 (71.7)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; PFS, progression-free survival; CR, complete response; PR, partial response; SD, stable disease.

- From February 2023 to May 2025, a total of 51 patients were screened, of whom 46 were enrolled in the study (**Table 1**). The median age was 62.0 years (range, 38.0-74.0), with the majority of patients being male (80.4%). In terms of prior first-line treatment outcomes, 56.5% of patients had a PFS of less than 10 months, and most patients (71.7%) achieved SD as their best response.
- As of December 1, 2025, 6-month PFS rate was 56.2%, and median PFS was 7.3 months (95% CI, 4.8-10.4); the median OS was 15.4 months (95% CI, 9.6, 21.2). Confirmed ORR and DCR were 37.0% (17/46) and 89.1% (41/46), respectively (**Table 2**). Median DoR was 8.8 months.

Table 2. Tumor response in FAS

	Patients (N=46)
Best overall response,	
n (%)	
CR	0 (0)
PR	17 (37.0)
SD	24 (52.2)
PD	2 (4.3)
NE	3 (6.5)
ORR (95% CI)	37.0 (23.2, 52.5)
DCR (95% CI)	89.1 (76.4, 96.4)

- Somatic circulating tumor DNA (ctDNA) on day 1 of cycle 3 (C3D1) showed significant difference between responders (patients with CR or PR) and non-responders (patients with SD or PD) ($P=0.021$). ctDNA-negative disease or ctDNA <22.5 hGE/mL on C3D1 was independently associated with better PFS compared to ctDNA >22.5 hGE/mL in multivariate analysis.
- Eleven (23.9%) patients had grade ≥3 treatment-related adverse events, mainly including decreased white blood cell (8.7%) and decreased neutrophil count (6.5%). No treatment-related deaths occurred.

CONCLUSION

Rechallenge with adebrelimab combined with bevacizumab and nab-paclitaxel demonstrated promising antitumor activity and a manageable safety profile in patients with advanced non-squamous NSCLC after progression on prior ICI-based therapy. Dynamic monitoring of ctDNA may provide complementary biomarkers for patient stratification and warrants further validation in prospective studies.

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