



P2.283: Efficacy and Safety of Sequential HER3-ADC or Trop2-ADC Following Prior ADC Progression in NSCLC

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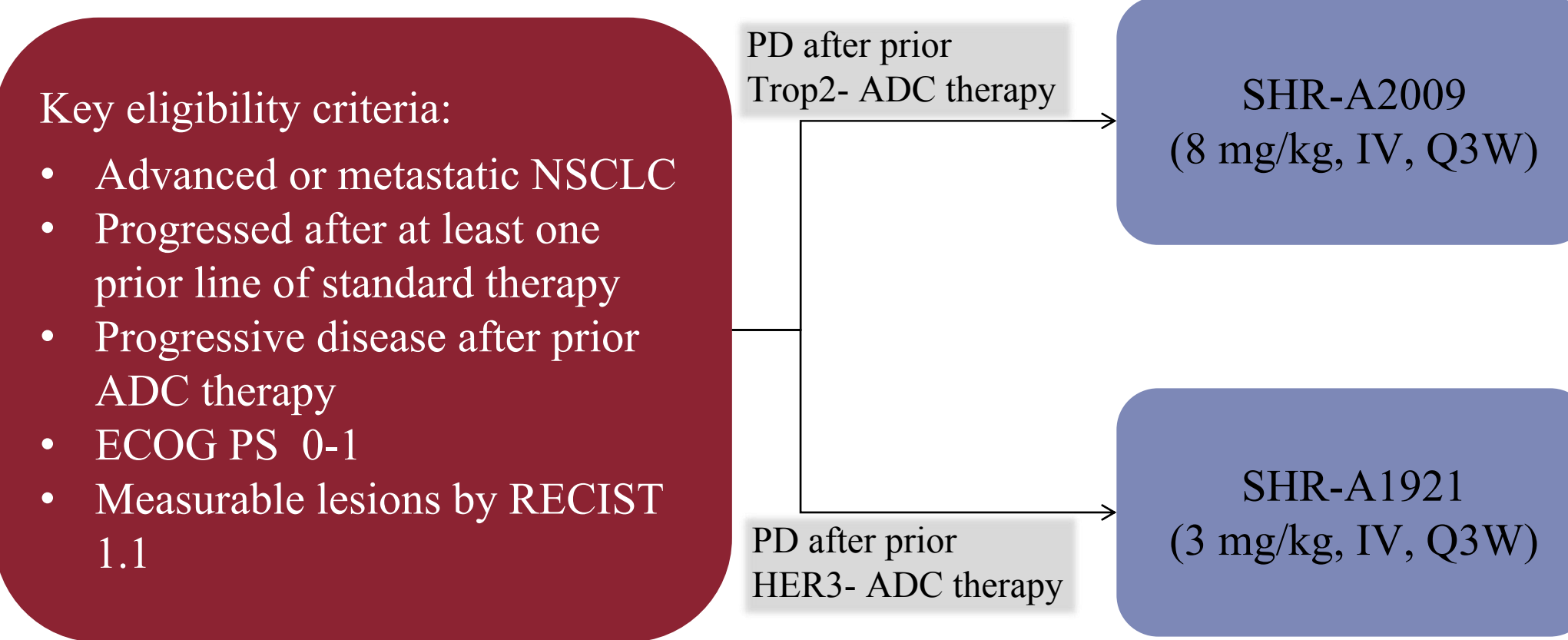
INTRODUCTION

- Antibody-drug conjugates (ADCs) have redefined the treatment landscape of metastatic non-small cell lung cancer (NSCLC), offering durable responses.
- As multiple ADCs with similar payloads become available to the same patient during disease course, determining optimal sequencing has become an urgent need, particularly given concerns about cross-resistance and reduced efficacy.

METHODS

- Patients with advanced NSCLC who failed standard therapy and experienced disease progression after prior ADC treatment were assigned to two cohorts based on their prior ADC exposure. (Clinical trial information: NCT06465238)
- Those with prior Trop2-ADC treatment received SHR-A2009 (HER3-ADC, 8 mg/kg, IV, q3w); those with prior HER3-ADC treatment received SHR-A1921 (Trop2-ADC, 3 mg/kg, IV, q3w).
- Treatment continued until disease progression, intolerable toxicity, or other protocol-specified discontinuation reasons.
- The primary endpoint was objective response rate (ORR) per RECIST v1.1. Secondary endpoints included progression-free survival (PFS), disease control rate (DCR), overall survival (OS), and safety.

Figure 1. study design



RESULTS

Patients

- Between September 2024 and July 2025, a total of 12 patients were enrolled, including 8 who received SHR-A2009 and 4 who received SHR-A1921.
- Baseline characteristics of patients are listed in **Table 1**.
- The median age was 60 years (range, 44–73), and 58.3% were male. The median line of previous treatment was 3.5 (range 1-6). 8 (66.7%) patients had received at least three prior lines of systemic therapy.

Table 1. Baseline characteristics of patients

Characteristics	All patients (N=12)
Age, years, median (range)	60 (44,73)
< 65 years, n(%)	9 (75.0%)
≥ 65 years, n(%)	3 (25.0%)
Sex, n (%)	
Male	7 (58.3%)
Female	5 (41.7%)
ECOG PS, n(%)	
0	0
1	12 (100%)
Lines of previous treatment, median (range)	3.5 (1,6)
1L, n(%)	1 (8.3%)
2L, n(%)	3 (25.0%)
≥3L, n(%)	8 (66.7%)
Histological subtype, n (%)	
Adenocarcinoma	11 (91.7%)
Squamous-cell carcinom	0
Other	1 (8.3%)
EGFR-activating mutations, n (%)	
EGFR exon21 L858R+	3 (25.0%)
EGFR exon19 Del	5 (41.7%)

Efficacy

- As of the data cutoff date of February 1, 2026, the median follow-up was 11.7 months. 11 patients had undergone post-baseline tumor assessments.
- In the SHR-A2009 cohort, 2 of the 8 patients achieved clinical benefit: 1 confirmed partial response and 1 stable disease, both occurring in patients with previously treated EGFR-mutant tumors and exhibiting PFS exceeding 9 months. As shown in **Table2**, the overall confirmed ORR was 12.5% (1/8) and DCR was 25.0% (2/8) .
- In the SHR-A1921 cohort, 2 patients had stable disease, with a DCR of 50.0% (2/4).

Table 3. Grade ≥3 Treatment-related adverse events (TRAEs)

	All (n=12)	SHR-A2009 (n=8)	SHR-A1921 (n=4)
Neutrophil count decreased	2 (16.7%)	2 (25.0%)	0
Vomiting	1 (8.3%)	1 (12.5%)	0
White blood cell count decreased	1 (8.3%)	1 (12.5%)	0
Platelet count decreased	1 (8.3%)	1 (12.5%)	0
Stomatitis	1 (8.3%)	0	1 (25.0%)

Ssfety

- Grade ≥3 treatment-related adverse events (TRAEs) occurred in 4 of 12 patients (33.3%) overall.
- In the SHR-A2009 cohort, Grade ≥3 TRAEs were observed in 3 patients (37.5%), predominantly hematologic toxicities. The most common Grade ≥3 TRAE was neutrophil count decreased (2/8, 25.0%); vomiting, white blood cell count decreased and platelet count decreased each occurred in 1 patient.
- In the SHR-A1921 cohort, only 1 patient (25.0%) reported Grade ≥3 TRAE, which was stomatitis.

Table2. The best overall responses

Response	SHR-A2009 (n=8)	SHR-A1921 (n=4)
PR	1 (12.5)	0
SD	1 (12.5)	2 (50.0)
PD	5 (62.5)	2 (50.0)
NE	1 (12.5)	0
Confirmed ORR, n (%)	1 (12.5)	0
DCR, n (%)	2 (25.0)	2 (50.0)

CONCLUSIONS

- In this heavily pretreated population, sequential Trop2-ADC and HER3-ADC therapy showed limited activity overall.
- However, durable clinical benefit was observed in a subset of patients with EGFR-mutant tumors, with both responders achieving PFS exceeding 9 months.
- These signals warrant further investigation to identify biomarkers that may predict benefit from sequential ADC therapy with similar payloads.

During the preparation of this poster, the authors did not use any artificial intelligence tools.