

First-in-Human Study of BG-C477, a Novel CEA-Targeting ADC, in Advanced Solid Tumors: Initial Results in NSCLC

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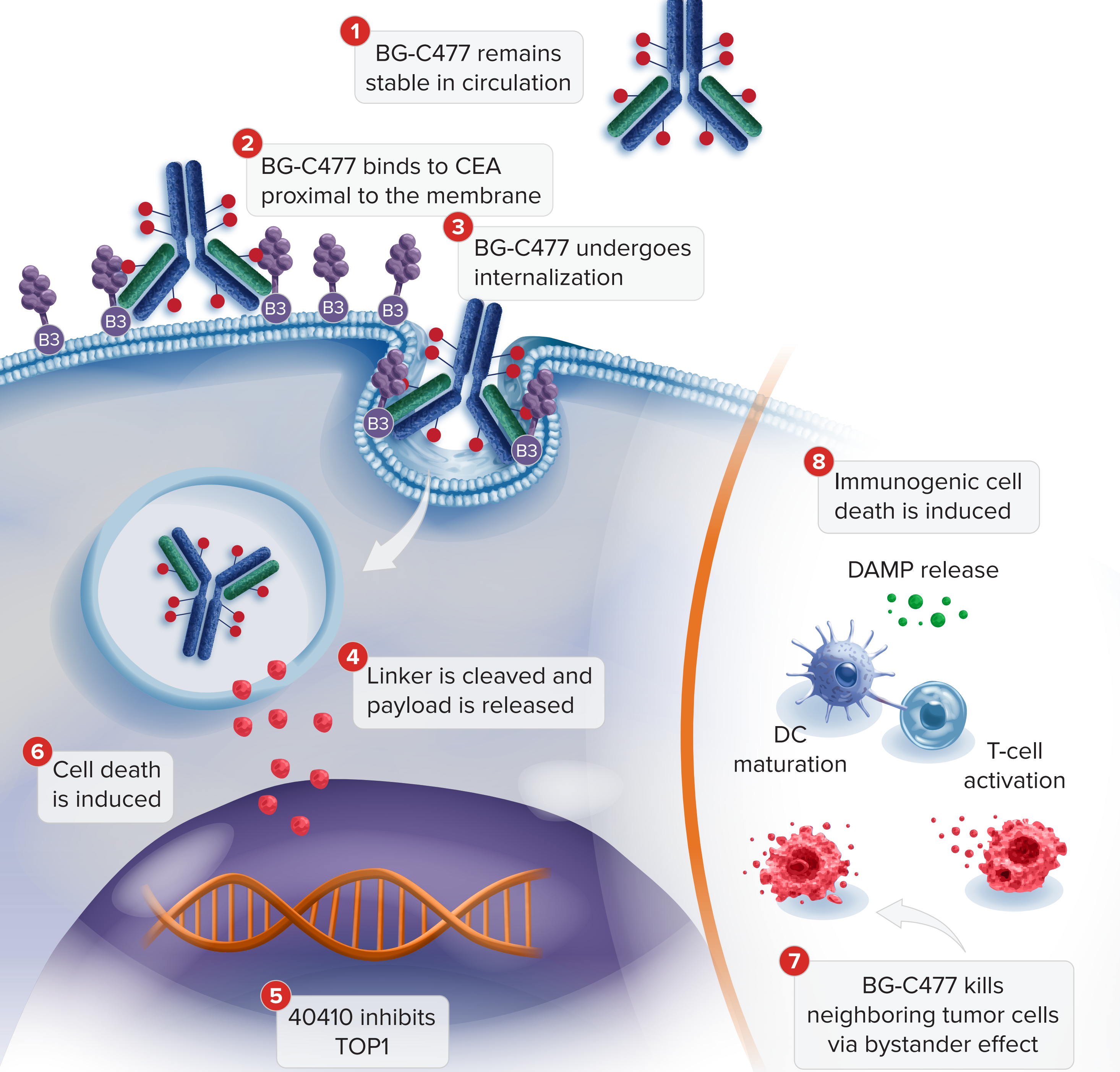
CONCLUSIONS

- BG-C477, a differentiated CEA-targeting ADC with a TOP1 inhibitor payload, had a favorable safety profile, including no grade ≥3 ILD or ocular events, in heavily pretreated patients with NSCLC
- BG-C477 demonstrated encouraging clinical activity with sustained responses in patients with metastatic, previously treated CEA^{high} NSCLC, with a 60% confirmed ORR and tumor shrinkage observed in nearly all evaluable patients
- These findings support the clinical relevance of CEA^{high} expression as a biomarker and the advancement of BG-C477 into pivotal development in NSCLC

INTRODUCTION

- Carcinoembryonic antigen (CEA) is frequently overexpressed in multiple tumor types, including in roughly one-third of all non-small cell lung cancer (NSCLC)¹⁻³
- BG-C477 is a novel antibody-drug conjugate (ADC) designed to overcome the historical limitations and limited efficacy of prior CEACAM5 ADCs⁴ (Figure 1). BG-C477 is constructed with a differentiated design via²:
 - Proprietary antibody with high affinity and specificity for the membrane-proximal CEA B3 domain
 - Highly stable conjugation chemistry
 - Hydrophilic protease-cleavable linker
 - Topoisomerase I (TOP1) inhibitor payload 40410 with a drug-to-antibody ratio of 8
- In pre-clinical studies, BG-C477 exhibited strong internalization, potent antitumor activity, and tolerable safety^{2,3}
- This phase 1 global trial evaluates BG-C477 as monotherapy and in combination with anticancer agents for advanced solid tumors (NCT06596473)
- Here we present preliminary results from phase 1a monotherapy in patients with NSCLC

Figure 1. Proposed Mechanism of Action of BG-C477



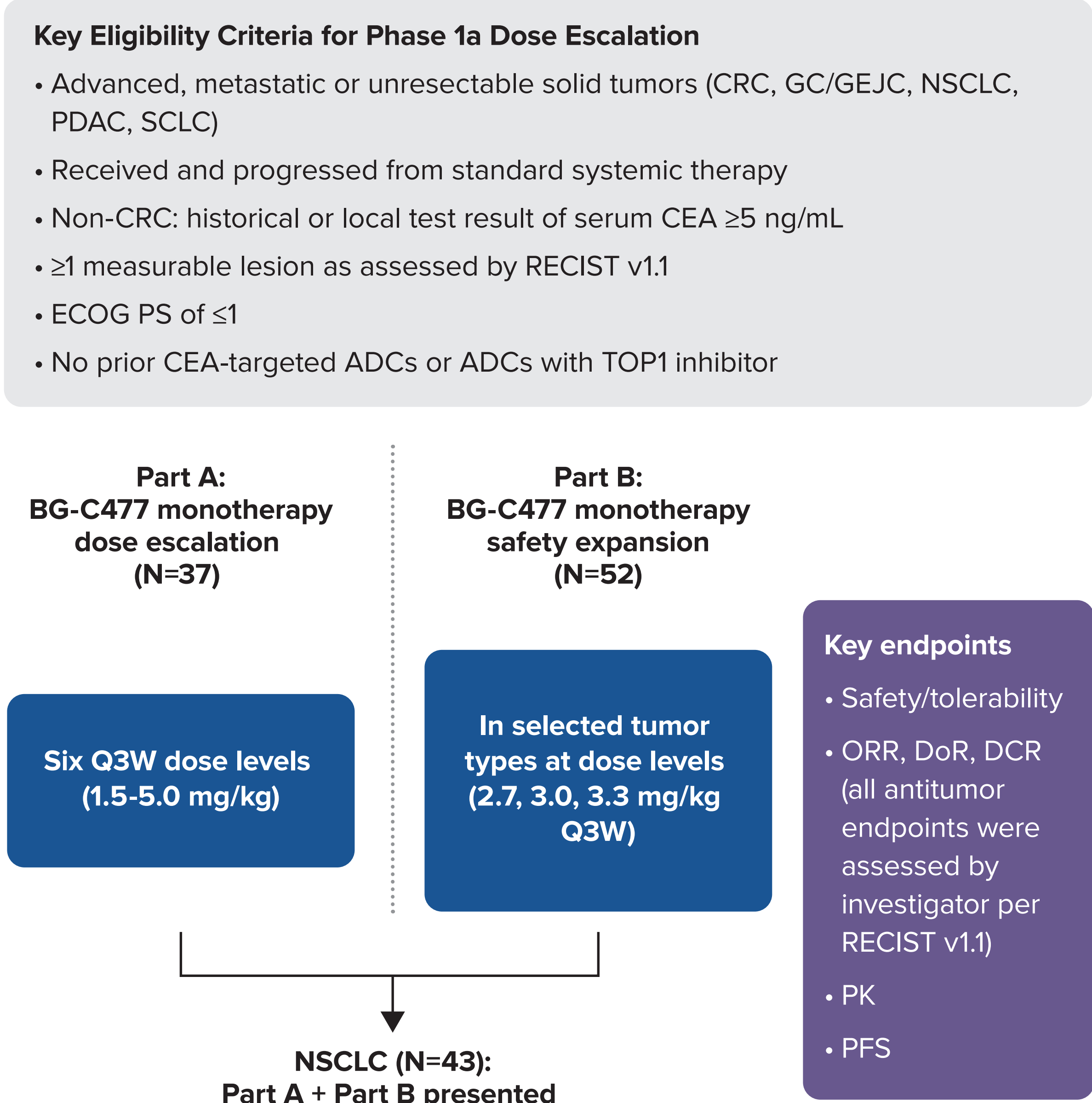
Follow the numbers in sequence.
Abbreviations: CEA, carcinoembryonic antigen; DAMP, damage-associated molecular pattern; DC, dendritic cell; TOP1, topoisomerase I.

METHODS

Trial Design

- This first-in-human, phase 1, dose-escalation/expansion, open-label, multicenter trial was conducted in multiple countries, including Australia, the United States, and China, and consists of two parts (Figure 2)
- Tumor CEA expression was assessed retrospectively by central lab immunohistochemistry (IHC) using the CEA T84.66 assay

Figure 2. Study Design



The dose escalation/de-escalation decision was by the modified toxicity probability interval design.
Abbreviations: ADC, antibody-drug conjugate; CEA, carcinoembryonic antigen; CRC, colorectal cancer; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GC/GEJC, gastric cancer/gastroesophageal junction cancer; NSCLC, non-small cell lung cancer; PDAC, pancreatic ductal adenocarcinoma; PK, pharmacokinetic; Q3W, once every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SCLC, small-cell lung cancer; TOP1, topoisomerase I.

Analysis and Statistical Methods

- Safety was assessed by the type, frequency, and severity (as graded by the National Cancer Institute Common Terminology Criteria for Adverse Events v5.0) of adverse events, timing, seriousness, and relationship to study treatment
- An independent adjudication committee evaluated all cases of possible interstitial lung disease (ILD)/pneumonitis

RESULTS

Baseline Characteristics and Patient Disposition

- From April 2025 to January 2026, 43 patients with NSCLC were enrolled and treated with ≥1 dose of BG-C477 at dose levels of 2.7, 3.0, 3.3 or 3.6 mg/kg Q3W in Phase 1a; of these, 25 (58.1%) patients had CEA^{high} expression (IHC 2/3+ in ≥50% of tumor cells)
- Data cut-off date was September 10, 2026, with a median follow-up of 7.6 months for all patients; 14/43 (32.6%) patients, including 12/25 (48.0%) CEA^{high} patients, remain on treatment
- Baseline characteristics are shown in Table 1
 - The majority of patients had non-squamous/epidermal growth factor receptor (EGFR) wild-type NSCLC
 - Patients were heavily pre-treated; approximately half the patients received ≥3 prior lines of systemic therapy

Table 1. Baseline Characteristics for Phase 1a Monotherapy (Safety Analysis Set)

	CEA ^{high} NSCLC (n=25)	All NSCLC (N=43)
Median (range) age, years	63 (36-81)	62 (36-81)
Sex, n (%)		
Male	12 (48.0)	23 (53.5)
Female	13 (52.0)	20 (46.5)
Geographic region, n (%)		
Australia	3 (12.0)	5 (11.6)
China	15 (60.0)	28 (65.1)
United States	7 (28.0)	10 (23.3)
ECOG PS, n (%)		
0	5 (20.0)	9 (20.9)
1	19 (76.0)	33 (76.7)
2	1 (4.0)	1 (2.3)
Brain metastases, n (%)	7 (28.0)	11 (25.6)
Number of prior lines of systemic therapies, n (%)		
1	4 (16.0)	5 (11.6)
2	10 (40.0)	15 (34.9)
≥3	11 (44.0)	23 (53.5)
Prior anticancer therapy, n (%)		
Anti-PD(L)-1 antibody	20 (80.0)	35 (81.4)
Platinum-based chemotherapy	23 (92.0)	40 (93.0)
EGFR tyrosine kinase inhibitor	9 (36.0)	15 (34.9)
Docetaxel	10 (40.0)	15 (34.9)
Disease histology/EGFR status, n (%)		
Squamous	1 (4.0)	8 (18.6)
Non-squamous/EGFR mutant	9 (36.0)	12 (27.9)
Non-squamous/EGFR wild-type	15 (60.0)	23 (53.5)
Diameter of target lesions at baseline, n (%)		
0-≤5 cm	8 (32.0)	13 (30.2)
5-10 cm	13 (52.0)	20 (46.5)
≥10 cm	4 (16.0)	10 (23.3)

Abbreviations: CEA, carcinoembryonic antigen; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PD(L)-1, programmed death (ligand)-1.

Safety and Tolerability

- Median treatment duration was 5.95 months (range, 0.1-16.7); 48.8% of patients had ≥6 months of treatment exposure
- The overall safety summary is presented in Table 2

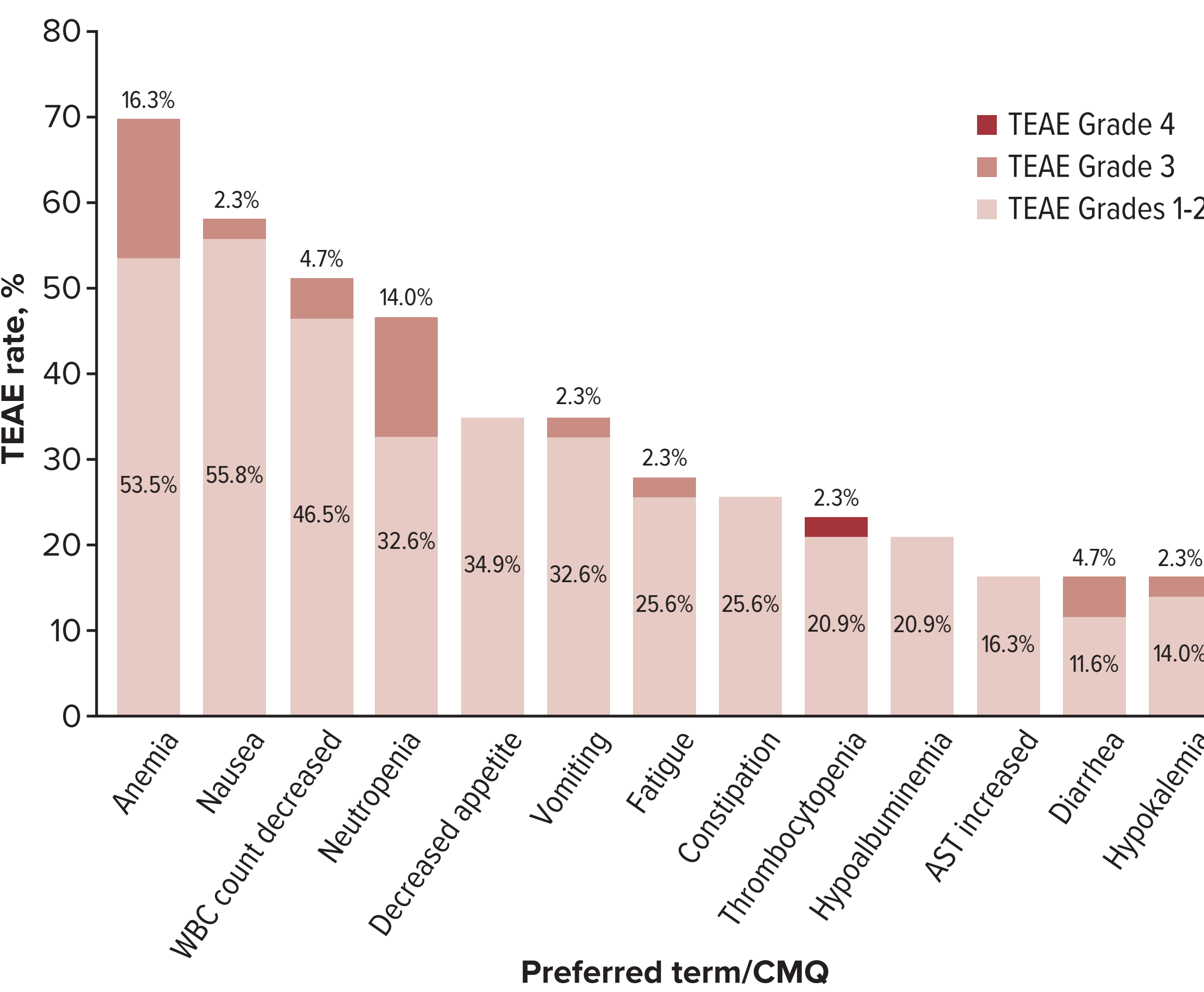
Table 2. Overall Safety Summary for Phase 1a Monotherapy Dose Escalation (Safety Analysis Set)

	All NSCLC (N=43)
Any TEAE, n (%)	43 (100.0)
Grade ≥3	19 (44.2)
Serious	15 (34.9)
Leading to death	1 (2.3) ^a
Leading to treatment discontinuation	2 (4.7)
Leading to dose reduction	5 (11.6)

^aMultifocal pneumonia with concurrent acute kidney injury in a patient with advanced disease and a pre-existing renal malignancy.
Abbreviation: NSCLC, non-small cell lung cancer.

- Most common TEAEs and treatment-related TEAEs were grades 1-2 gastrointestinal and hematologic events (Figure 3)
- No febrile neutropenia was reported
- Two patients (4.7%) experienced TEAEs leading to permanent treatment discontinuation
- No treatment-related deaths were reported
- There were no reports of keratitis or infusion-related reactions
- One case was adjudicated as grade 2 treatment-related ILD; the event was asymptomatic, with grade 2 classification driven by protocol-required steroid treatment

Figure 3. TEAEs Occurring in ≥15% of Patients by Preferred Term (Safety Analysis Set; N=43)



Anemia, neutropenia, and thrombocytopenia are defined by CMQ.
Abbreviations: AST, aspartate aminotransferase; CMQ, Customised MedDRA Query; WBC, white blood cell.

Antitumor Activity

- Confirmed ORR in the overall NSCLC population (N=43) was 37.2% (95% CI, 23.0-53.3), with 16 partial responses (PRs) (Table 3)
- Antitumor activity was primarily observed in the 25 patients with CEA^{high} expression by central lab assessment (Table 3; Figures 4 and 5)
 - Confirmed ORR was 60.0% (95% CI, 38.7-78.9), with 15 PRs across different histological subtypes and regardless of EGFR status (Table 4)
- Ten out of 15 responders are still on treatment at time of data cutoff
- Median PFS was not reached (6.7 months-not estimable) (Figure 6)

Table 3. Antitumor Activity Data for Phase 1a Monotherapy Dose Escalation (Safety Analysis Set)

	CEA ^{high} NSCLC (n=25)	All NSCLC (N=43)
Confirmed ORR, n (%) [95% CI]	15 (60.0) [38.7-78.9]	16 (37.2) [23.0-53.3]
Confirmed BOR, n (%)		
CR	0	0
PR	15 (60.0)	16 (37.2)
SD	8 (32.0)	20 (46.5)
PD	1 (4.0)	4 (9.3)
Not evaluable	1 (4.0)	3 (7.0)
DCR, n (%) [95% CI]	23 (92.0) [74.0-99.0]	36 (83.7) [69.3-93.2]
Median time to response, months (range)	1.38 (1.2-2.9)	1.36 (1.2-2.9)
Median DoR, months (range)	NR (4.0-NE)	NR (4.1-NE)
6-month DoR rate, % (95% CI)	73.3 (43.6-89.1)	75.0 (46.3-89.8)

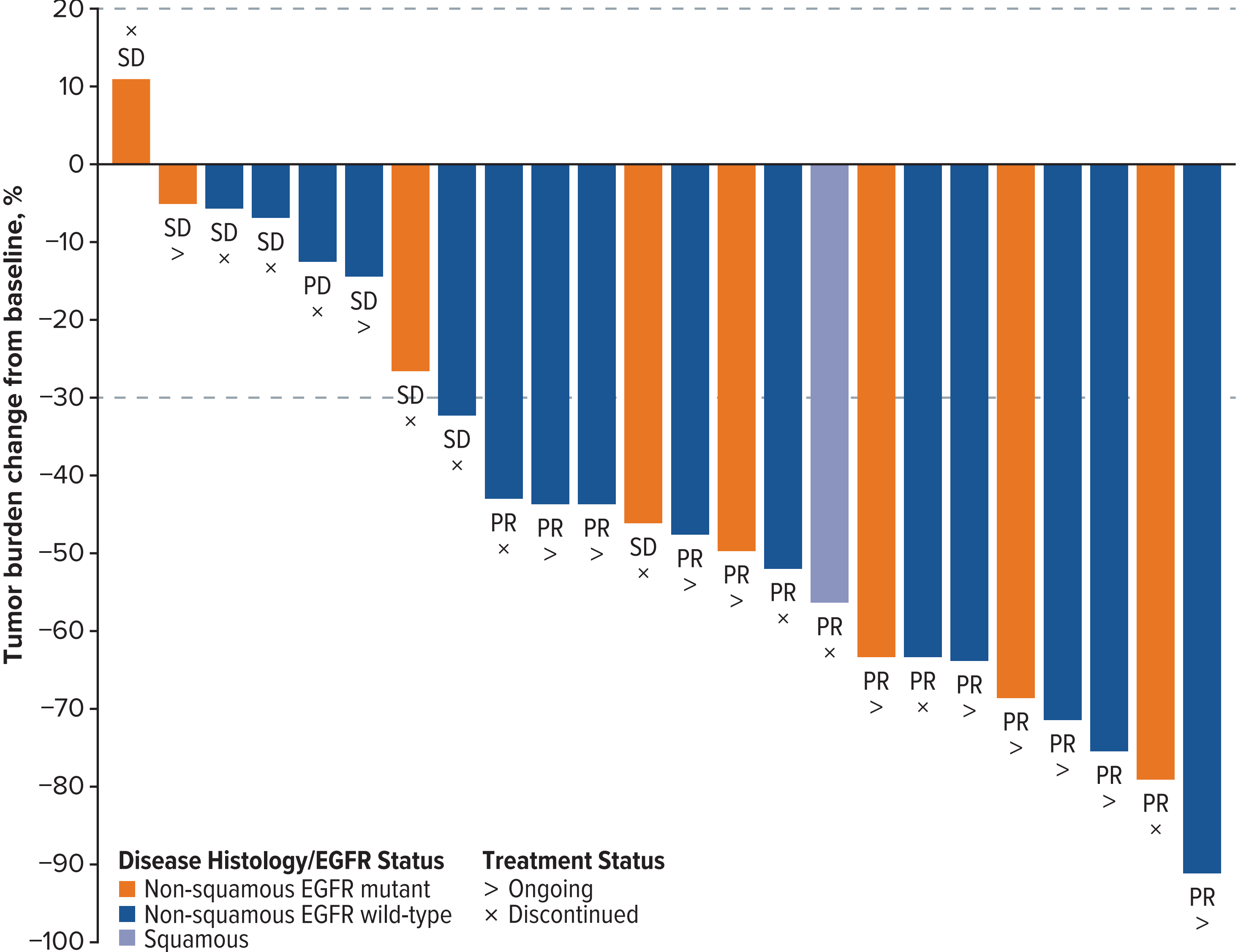
ORR was assessed per investigator by RECIST v1.1.
Abbreviations: BOR, best overall response; CEA, carcinoembryonic antigen; CR, complete response; DCR, disease control rate; NE, not evaluable; NR, not reached; NSCLC, non-small cell lung cancer; PD, progressive disease; RECIST v1.1, Response Evaluation Criteria in Solid Tumors v1.1; SD, stable disease.

Table 4. Antitumor Activity Data for Phase 1a Monotherapy Dose Escalation by Histology/EGFR Status in CEA^{high} NSCLC (Safety Analysis Set; n=25)

	Squamous NSCLC (n=1)	Non-squamous NSCLC (EGFR mutant) (n=9)	Non-squamous NSCLC (EGFR wild-type) (n=15)
Confirmed ORR n (%) [95% CI]	1 (100.0) [2.5-100.0]	4 (44.4) [13.7-78.8]	10 (66.7) [38.4-88.2]
DCR, n (%) [95% CI]	1 (100.0) [2.5-100.0]	8 (88.9) [51.8-99.7]	14 (93.3) [68.1-99.8]
Median DoR, months (range)	4.1 (NE-NE)	NR (7.2-NE)	NR (3.0-NE)

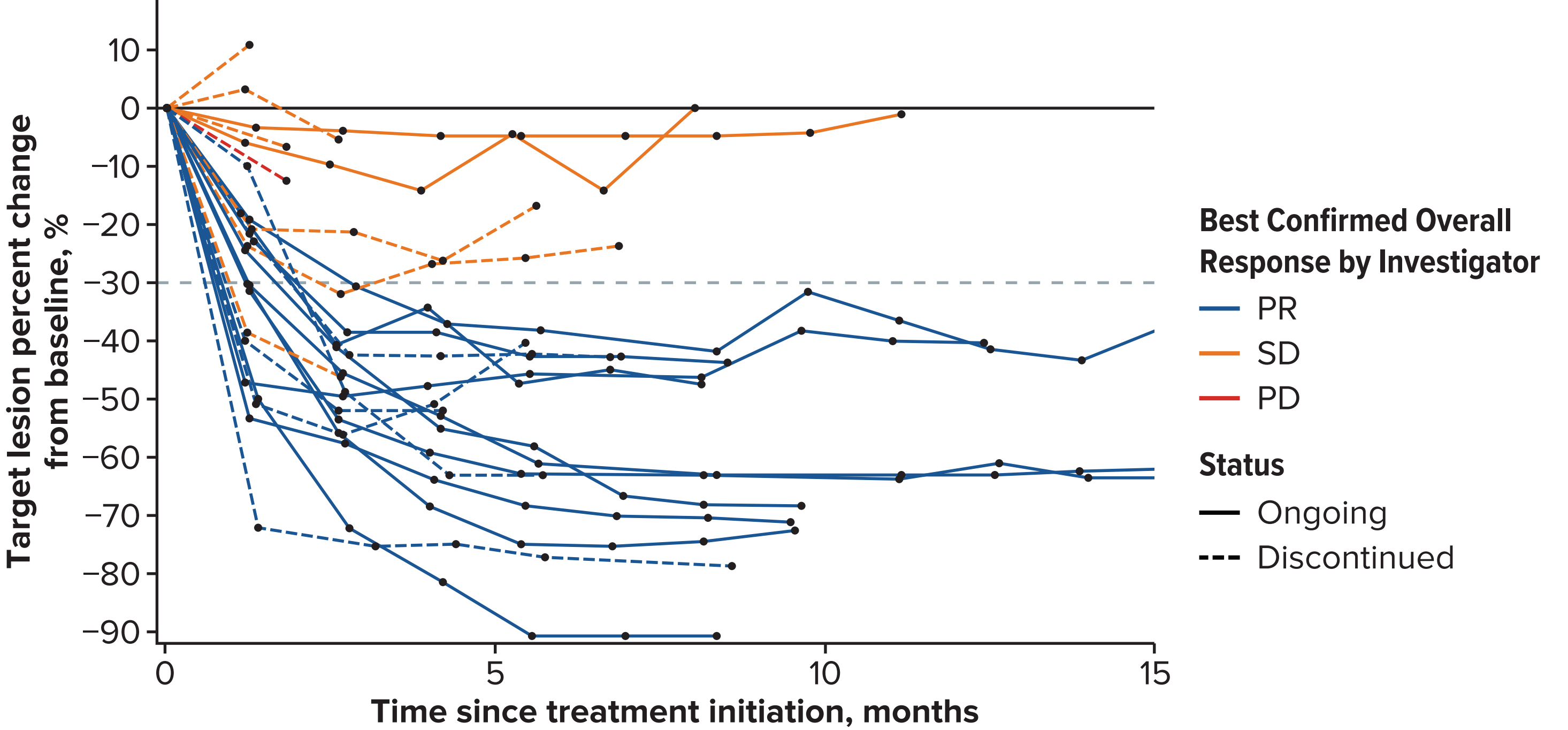
Abbreviations: CEA, carcinoembryonic antigen; DCR, disease control rate; EGFR, epidermal growth factor receptor; NE, not estimable; NR, not reached; NSCLC, non-small cell lung cancer.

Figure 4. Best Confirmed Overall Response in CEA^{high} NSCLC Patients (Efficacy Evaluable Analysis Set; n=24)



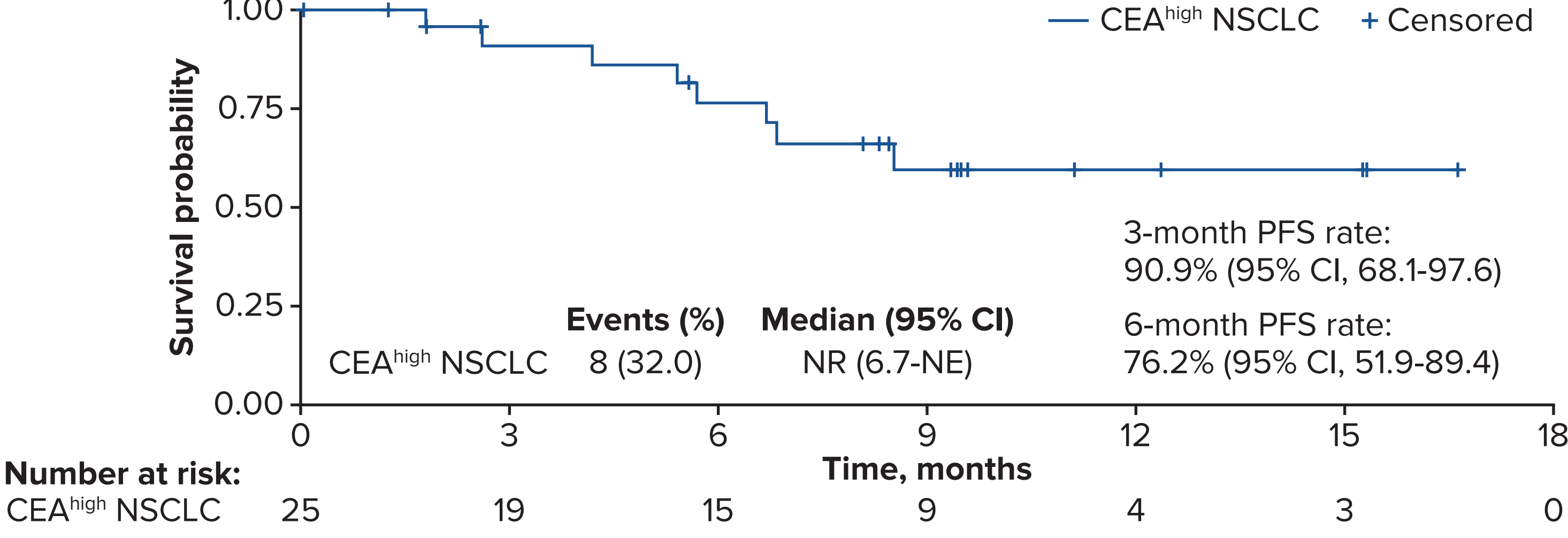
One patient withdrew from study before the first tumor assessment and is not included.
Abbreviations: CEA, carcinoembryonic antigen; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

Figure 5. Percent Change From Baseline in Target Lesion Sum of Diameters in CEA^{high} NSCLC patients (Efficacy Evaluable Analysis Set; n=24)



One patient withdrew from study before the first tumor assessment and is not included.
Abbreviations: CEA, carcinoembryonic antigen; NSCLC, non-small cell lung cancer.

Figure 6. KM Plot for PFS in CEA^{high} NSCLC Patients (Safety Analysis Set; n=25)



Abbreviations: CEA, carcinoembryonic antigen; KM, Kaplan-Meier; NE, not estimable; NR, not reached; NSCLC, non-small cell lung cancer.

REFERENCES

1. Hammarström S. *Cancer Biol*. 1999;9:67-8. 2. He D, et al. *Cancer Res*. 2025;85(8_Suppl_1):5461. 3. BeOne Medicines, unpublished data. 4. Besse B, et al. *J Thorac Oncol*. 2024;19:S25-S26.

DISCLOSURES

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