

Hematologic and Gastrointestinal Toxicity of ABBV-706 in Advanced Solid Tumors: Safety Profile From the First-in-Human Study

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OBJECTIVES

To assess the overall, hematologic, and gastrointestinal (GI) safety profile of ABBV-706 monotherapy in advanced solid tumors

CONCLUSIONS

ABBV-706 monotherapy demonstrated an acceptable safety profile in a heavily pretreated population across multiple advanced tumor types, supporting continued clinical evaluation

Patients with R/R SCLC receiving 1.8 mg/kg ABBV-706, which was determined to be the recommended phase 3 dose, had an overall slightly more favorable safety profile compared to the total population

Cytopenias were the most common class of treatment-related adverse event (TRAE) and were effectively managed through dose interruption, reduction, blood transfusions, and growth factor support

GI TRAEs were predominantly grade 1-2; grade ≥3 GI events occurred in 3% of the total patient population (N=240)

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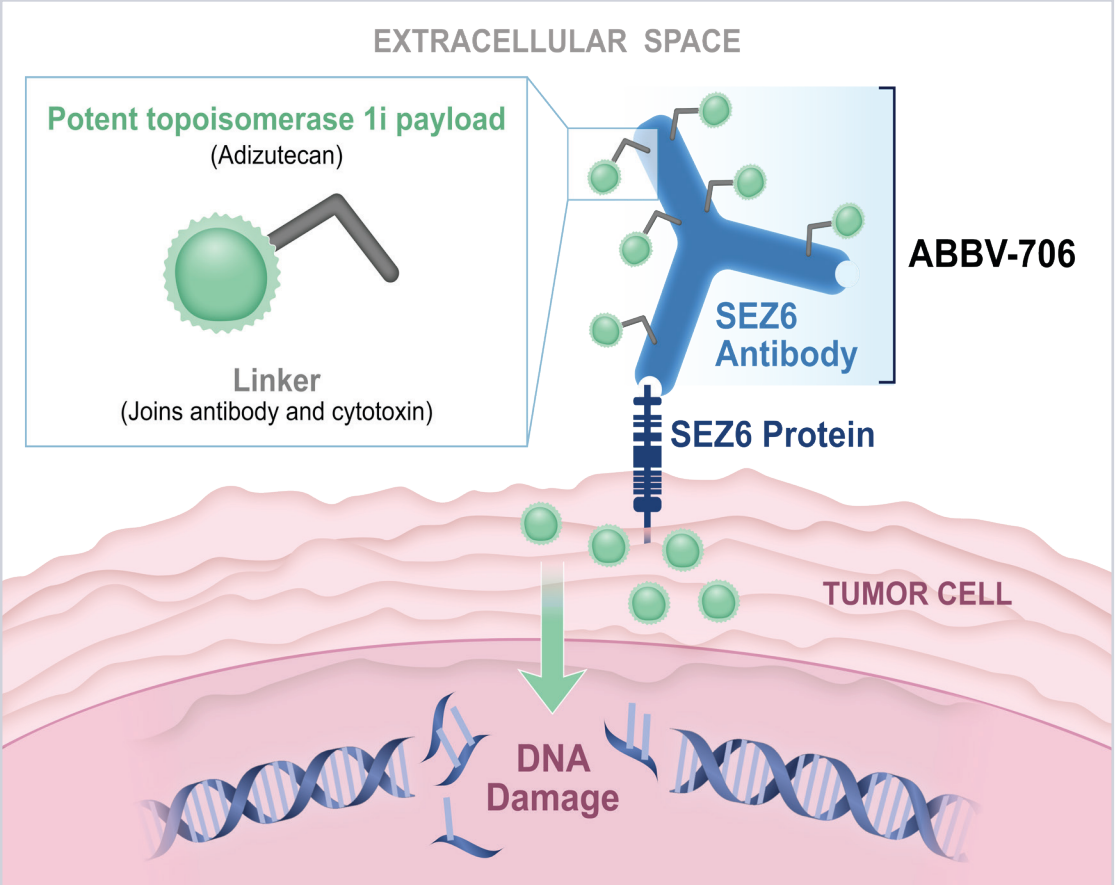
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INTRODUCTION

- ABBV-706 is a first-in-class antibody-drug conjugate (ADC) consisting of a SEZ6-targeting monoclonal antibody conjugated via a stable linker to a potent topoisomerase 1 inhibitor (Top1i) payload¹
- In a first-in-human trial (NCT05599984), ABBV-706 showed promising antitumor activity in heavily pretreated patients with relapsed or refractory (R/R) small cell lung cancer (SCLC)²
 - The objective response rate in patients with SCLC receiving 1.8 mg/kg ABBV-706 (N=41) was 56%, with a median overall survival of 12.4 months²
- The safety profile of ADCs with Top1-inhibitor payload most commonly includes treatment-related cytopenias, gastrointestinal (GI) toxicities, fatigue, and interstitial lung disease (ILD)³⁻⁵
- Preliminary data from the phase 1 study of ABBV-706 monotherapy showed a manageable safety profile, with grade ≥3 treatment-related adverse events (TRAEs) occurring in 54% of patients with SCLC receiving 1.8 mg/kg ABBV-706 (N=41)²
 - The most frequent grade ≥3 TRAE was anemia (42%)²
- We present a detailed safety analysis of this first-in-human study of ABBV-706 in monotherapy-treated patients

ABBV-706 Mechanism of Action



1. Inhibitor, SEZ6, seizure-related homolog protein 6.

RESULTS

- As of September 2025, 240 patients received ABBV-706 monotherapy (R/R SCLC, n=124; NETs/NECs, n=66; CNS tumors, n=48; missing indication, n=2) across all doses (1.8 mg/kg-3.5 mg/kg)
- Among patients with SCLC, 41 received 1.8 mg/kg ABBV-706

Baseline Demographics and Disease Characteristics

Characteristic	Total (N=240)	SCLC 1.8 mg/kg (N=41)
Median age, years (range)	62 (18–86)	64 (48–85)
Sex, n (%)		
Male	144 (60)	25 (61)
Female	96 (40)	16 (39)
Race, n (%)		
White	154 (64)	24 (59)
Asian	68 (28)	16 (39)
Black or African American	9 (4)	0
Not reported	9 (4)	1 (2)
Baseline ECOG performance status, n (%)		
0	57 (24)	9 (22)
1	183 (76)	32 (78)
Median follow-up, months	16.2	16.4
Median treatment duration, months (range)	4.8 (0.4–25.3)	6.2 (0.7–18.1)

ECOG, Eastern Cooperative Oncology Group; SCLC, small cell lung cancer.

Overall Summary of TRAEs

	Total (N=240)	SCLC 1.8 mg/kg (N=41)
Any TRAEs, n (%)	222 (93)	36 (88)
TRAEs grade ≥3, n (%)	147 (61)	22 (54)
Serious TRAEs, n (%)	30 (13)	7 (17)
TRAEs leading to, n (%)		
Discontinuation	16 (7)	5 (12)
Interruption	102 (43)	13 (32)
Reduction	73 (30)	8 (20)
TRAEs leading to death, n (%)	3 (1)	3 (7)

SCLC, small cell lung cancer; TRAE, treatment-related adverse event.

TRAEs of Interest Among Patients Receiving ABBV-706 Monotherapy

		Hematologic Toxicities			GI Toxicities	Others	
		Anemia	Neutropenia	Thrombocytopenia	Nausea/Vomiting	Fatigue/Asthenia	Pneumonitis/ILD ^a
Any grade TRAE, n (%)	Total (N=240)	147 (61)	111 (46)	86 (36)	96 (40)	108 (45)	8 (3)
	SCLC 1.8 mg/kg (N=41)	22 (54)	14 (34)	10 (24)	16 (39)	15 (37)	4 (10)
TRAE grade ≥3, n (%)	Total (N=240)	108 (45)	82 (34)	49 (20)	2 (1)	10 (4)	3 (1)
	SCLC 1.8 mg/kg (N=41)	17 (42)	8 (20)	6 (15)	0	1 (2)	2 (5)
Median time to onset of grade ≥3 TRAE, days (range)	Total (N=240)	64 (3–369)	43 (9–513)	56 (7–297)	18 (4–31)	90 (29–179)	110 (59–291)
	SCLC 1.8 mg/kg (N=41)	93 (29–345)	77 (29–513)	123 (16–248)	NA	126 (126–126)	NA
Median duration of grade ≥3 TRAE, days (range)	Total (N=240)	8 (1–810)	9 (1–559)	13 (1–471)	21 (9–80)	12 (2–401)	NA
	SCLC 1.8 mg/kg (N=41)	8 (1–586)	9 (1–340)	14 (1–471)	NA	389 (389–389)	NA

^aAccording to the Adjudication Committee.

GI, gastrointestinal; ILD, interstitial lung disease; NA, not available; SCLC, small cell lung cancer; TRAE, treatment-related adverse event.

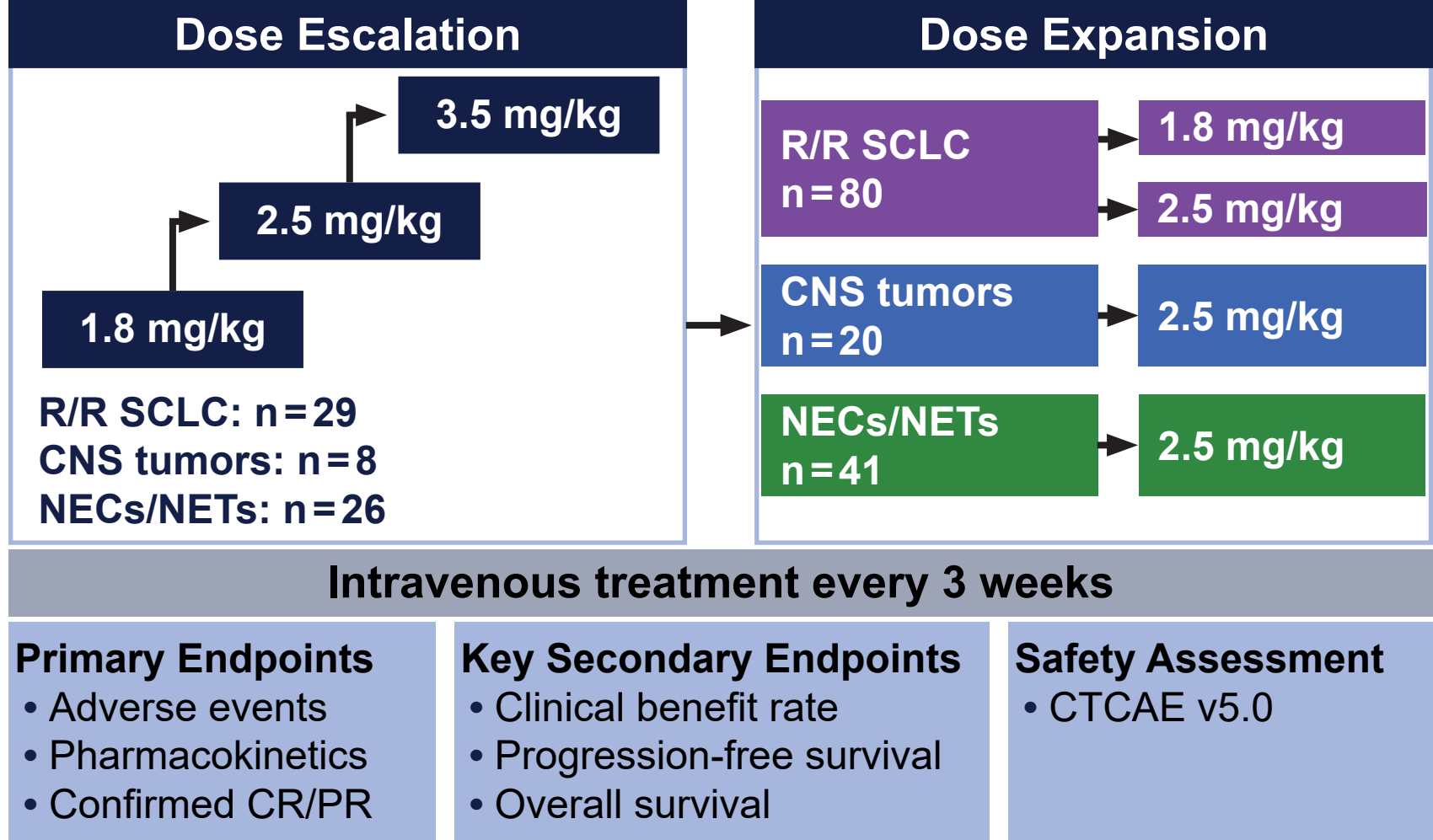
- Among patients with anemia, 3 required hospitalizations. Blood transfusions were given to 105/240 patients (44%) (median per patient: 2), and 20/240 patients (8%) received growth factors
- Treatment-related grade ≥3 febrile neutropenia occurred in 4 patients (2%). After management with dose interruption/reduction (n=1 each) and growth factors (n=1), all events resolved
- Most common GI TRAEs included nausea (36%), vomiting (18%), and diarrhea (11%)
- Grade ≥3 GI events occurred in 3% of patients, with a median time to onset of 31 (range: 4–288) days
- Most GI toxicities required no dose adjustments (93%) and were recovering/resolved (68%) at data cut (09/2025)
- Other common TRAEs were fatigue (38%) and decreased appetite (21%), with fatigue being the most common nonhematologic, non-GI grade ≥3 TRAE (4%)

METHODS

Eligibility criteria:

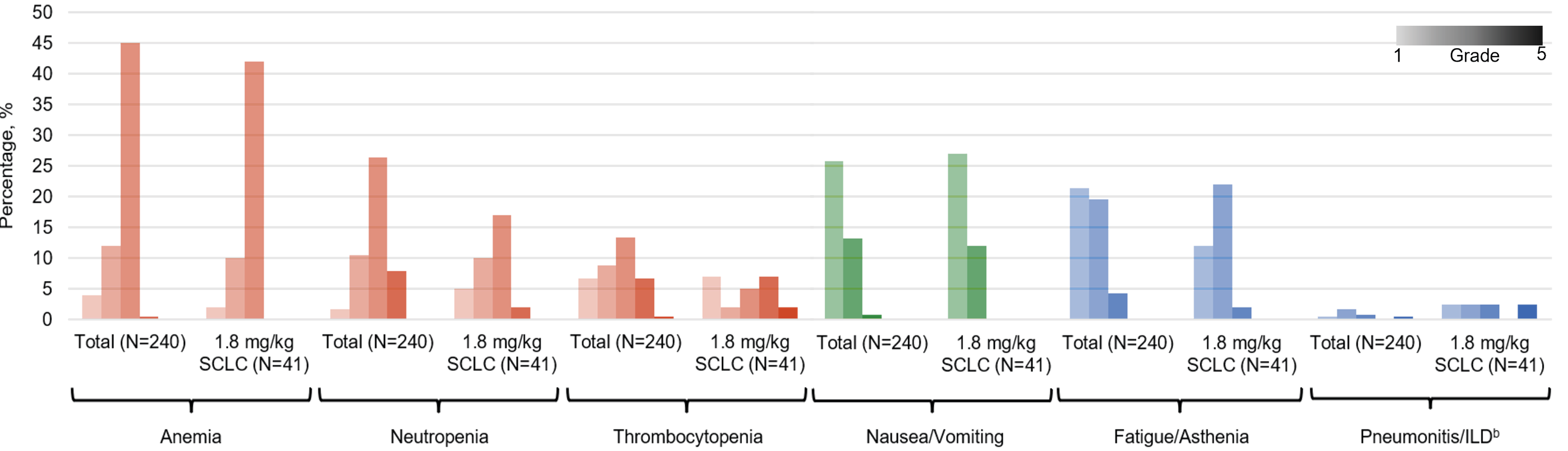
- ≥18 years old
- ECOG PS 0 or 1
- Patients with R/R SCLC:
 - ≥1 prior line of platinum-based chemotherapy
 - ≥1 measurable lesion per RECIST v1.1
- Patients with high-grade CNS tumors:
 - GBM, IDH-wildtype grade 4; astrocytoma, IDH-mutant grade 3/4
 - Prior surgical resection, radiation, temozolomide or procarbazine, lomustine, and vincristine (PCV)
 - ≥1 measurable lesion per RANO
- Patients with high-grade NECs/NETs
 - ≥1 prior line of standard of care chemotherapy

Study Design



CNS, central nervous system; CR, complete response; CTCAE v5.0, Common Terminology Criteria for Adverse Events version 5.0; ECOG PS, Eastern Cooperative Oncology Group performance score; GBM, glioblastoma; IDH, isocitrate dehydrogenase; NEC, neuroendocrine carcinoma; NET, neuroendocrine tumor; PR, partial response; R/R, relapsed or refractory; RANO, Response Assessment in Neuro-Oncology; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SCLC, small cell lung cancer.

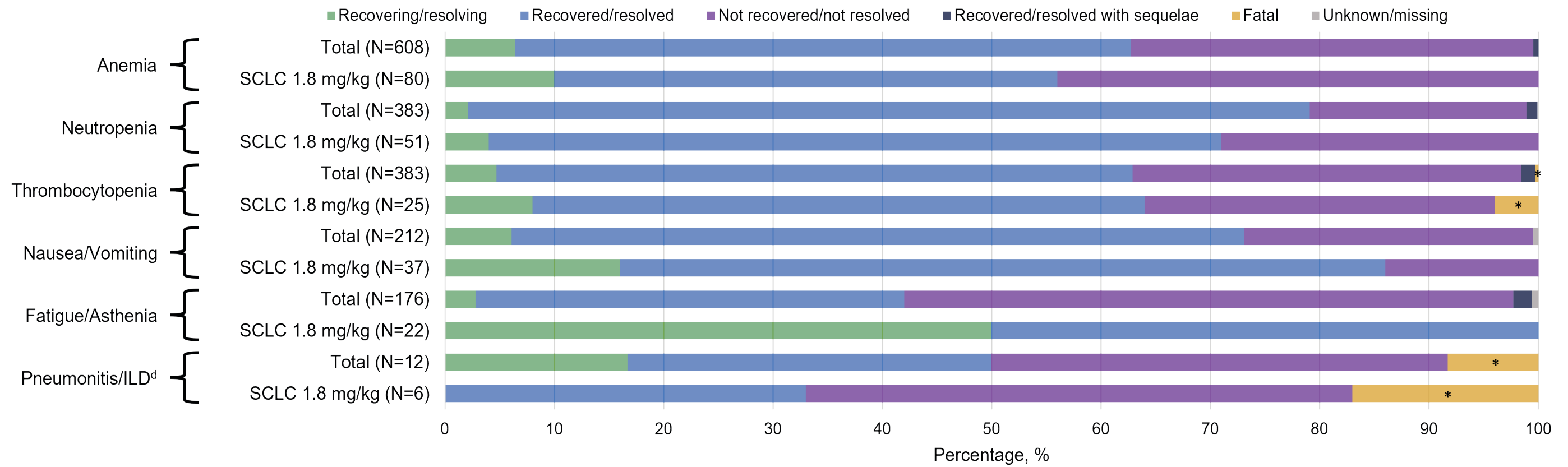
Maximum Grade of TRAE by Patient^a



^aPercentages based on patients receiving ABBV-706 monotherapy (Total: N=240; SCLC 1.8 mg/kg: N=41). ^aAccording to Adjudication Committee.

ILD, interstitial lung disease; SCLC, small cell lung cancer.

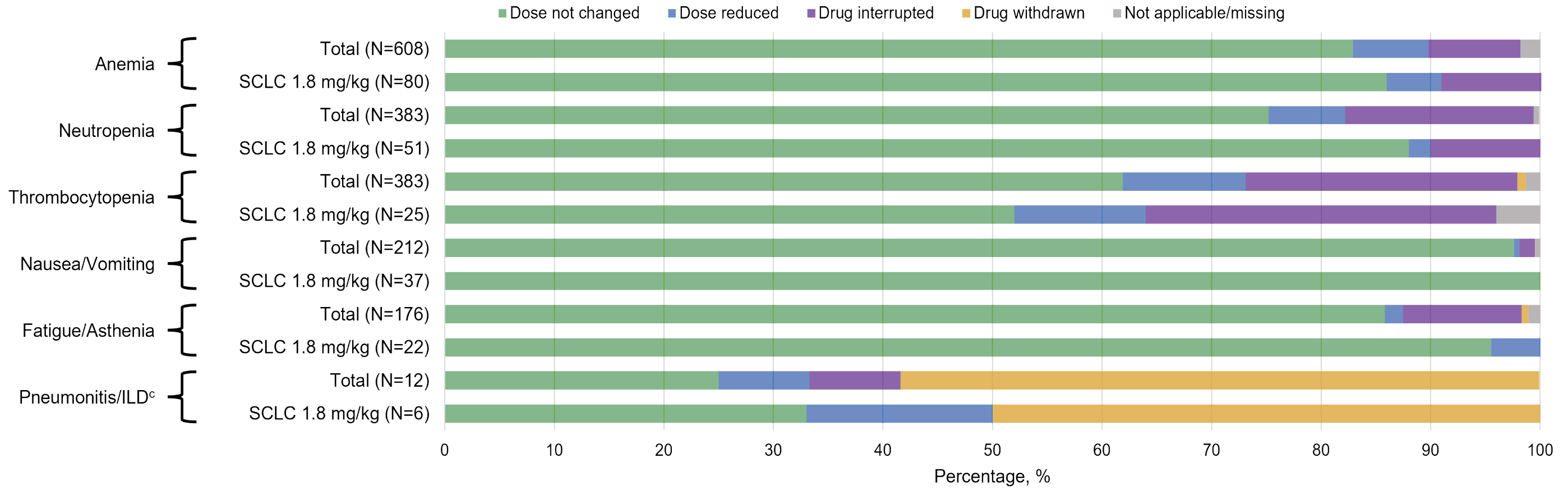
Events by Outcome^{a,b,c}



^aPercentages based on total events. ^bDue to rounding, percentages may not total 100%. ^cData entered at time of data cut (September 2025). ^aAccording to the Adjudication Committee. ^bn=1 fatality.

ILD, interstitial lung disease; SCLC, small cell lung cancer.

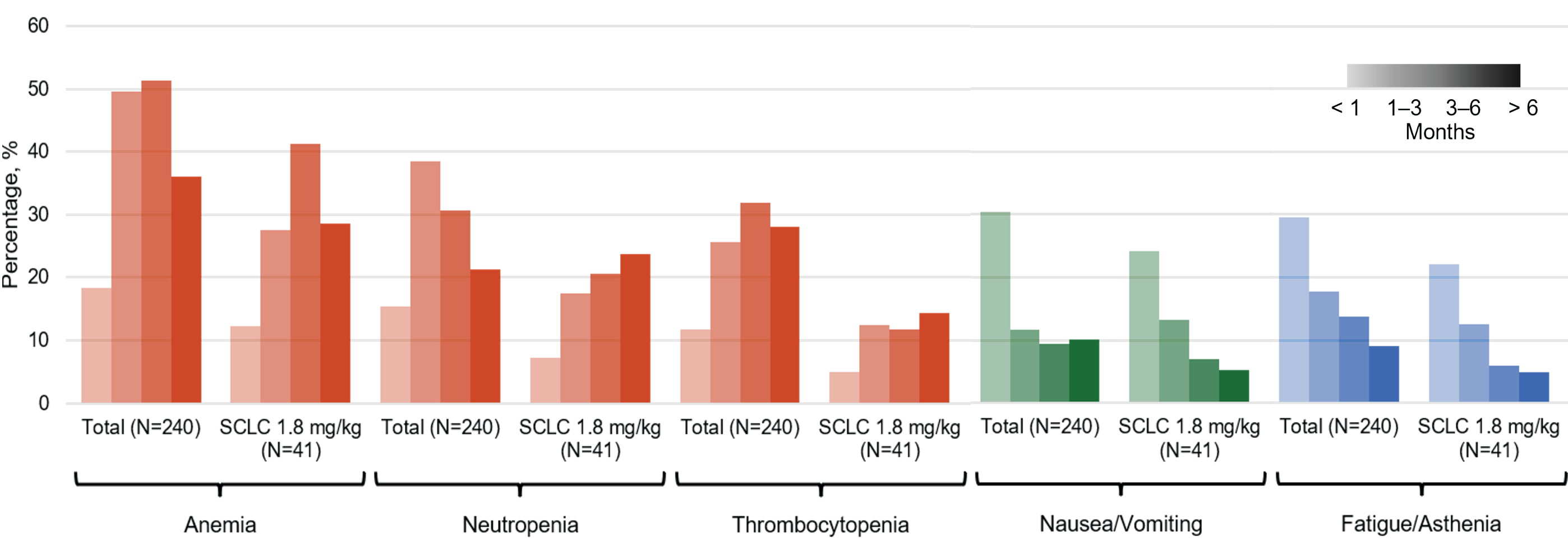
Events by Action Taken With Study Drug^{a,b}



^aPercentages based on total events. ^bDue to rounding, percentages may not total 100%. ^aAccording to the Adjudication Committee.

ILD, interstitial lung disease; SCLC, small cell lung cancer.

TRAEs by Time on Treatment



SCLC, small cell lung cancer; TRAE, treatment-related adverse event.

- Cytopenias generally increased over time with peak incidences between 1 and 6 months on treatment
- GI toxicities and fatigue/asthenia were most common in the beginning of treatment and decreased over time
- Patients with SCLC receiving 1.8 mg/kg ABBV-706 consistently showed lower incidences of TRAEs compared with the overall cohort