

Pneumonitis/Interstitial Lung Disease in the First-in-Human ABBV-706 Study: Incidence, Management, and Risk Factors

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OBJECTIVES

To assess the incidence, management, and risk factors of pneumonitis/interstitial lung disease (ILD) in patients with solid tumors receiving ABBV-706 monotherapy

CONCLUSIONS

ABBV-706 demonstrated a manageable pneumonitis/ILD risk, with an adjudicated pneumonitis/ILD rate of 4.2% in patients with solid tumors treated with ABBV-706 monotherapy (N = 240)

Pneumonitis/ILD was managed with appropriate clinical oversight with corticosteroids and/or antimicrobials; 8 of 16 patients had recovered by data cut

Although rare (0.8%), the occurrence of high-grade and fatal treatment-emergent pneumonitis/ILD events emphasizes the need for careful patient monitoring and adherence to management protocols

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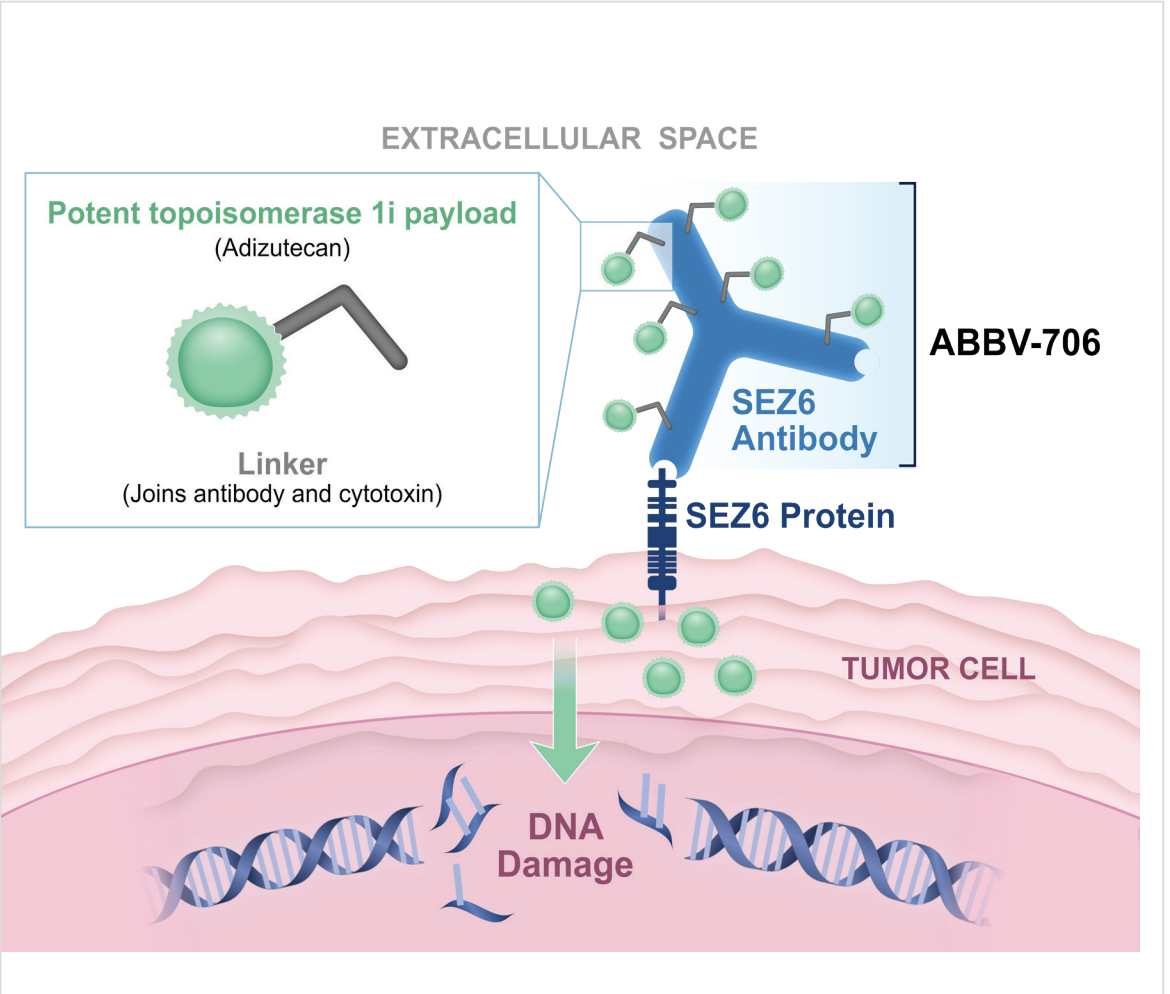
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INTRODUCTION

- 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
- Certain ADCs are associated with a higher risk of developing pneumonitis/interstitial lung disease (ILD)^{3,4}
 - Although further studies are required, some risk factors for the development of pneumonitis/ILD during ADC treatment have been identified, including prior thoracic radiotherapy and treatment with immune checkpoint inhibitors⁵
- 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 61% of patients²
 - The most frequent TRAE grade ≥ 3 was anemia (45%)²
- We present an analysis of pneumonitis/ILD in this first-in-human study of ABBV-706

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)

Baseline Demographics and Disease Characteristics

Characteristic	Total (N = 240)
Median age, years (range)	62 (18–86)
Sex, n (%)	
Male	144 (60)
Female	96 (40)
Race, n (%)	
White	154 (64)
Asian	68 (28)
Black or African American	9 (4)
Not reported	9 (4)
Ethnicity, n (%)	
Hispanic or Latino	13 (5)
Not Hispanic or Latino	216 (90)
Not reported	5 (2)
Unknown	6 (3)
Baseline ECOG performance status, n (%)	
0	57 (24)
1	183 (76)
Median follow-up, months	16.2
Median treatment duration, months (range)	4.8 (0.4–25.3)

ECOG, Eastern Cooperative Oncology Group.

Pneumonitis/ILD Incidence and Severity as Assessed by the Investigator and Adjudication Committee

	Investigator assessment	Adjudicated pneumonitis/ILD ^a
Patients with pneumonitis/ILD, n (%) ^d		
ABBV-706-related	16 (6.7)	10 ^c (4.2)
Not ABBV-706-related	11 (4.6)	8 (3.3)
Patients with serious pneumonitis/ILD events, n (%) ^d		
ABBV-706-related	9 (3.8)	6 (2.5)
Not ABBV-706-related	6 (2.5)	4 (1.7)
Pneumonitis/ILD leading to death, n (%) ^d		
ABBV-706-related	3 (1.3)	2 (0.8)
Not ABBV-706-related	2 (0.8)	1 (0.4)

^aAdjudication Committee decided whether or not an event was indeed pneumonitis/ILD; severity and relation of the event to ABBV-706 was rated by the investigator only. ^bSMQ (Narrow) MedRA "ILD" and SMQ (Broad) "Organizing pneumonia" search terms were used for identifying adjudication cases. ^c4 patients did not have pneumonitis/ILD per Adjudication Committee, and a decision for 2 patients was outstanding at time of data cut (September 2025). Percentages are based on all patients receiving ABBV-706 monotherapy (N = 240). ^dILD, interstitial lung disease.

- The most common chest CT feature among patients with pneumonitis/ILD was ground glass opacities (n = 5)
- Five cases of pneumonitis/ILD required hospitalization
- Patients with pneumonitis/ILD were appropriately managed; patients received corticosteroids (n = 13) and antimicrobials (n = 11)
- Among patients with adjudicated pneumonitis/ILD (n = 10), 3 had pneumonia as a concomitant lung infection
- The patient with ABBV-706-related fatal adjudicated pneumonitis/ILD presented with substantial emphysema at baseline, required hospitalization, received steroids and antibiotics, and progressed from an initial grade 2 event to grade 5

METHODS

Eligibility Criteria:

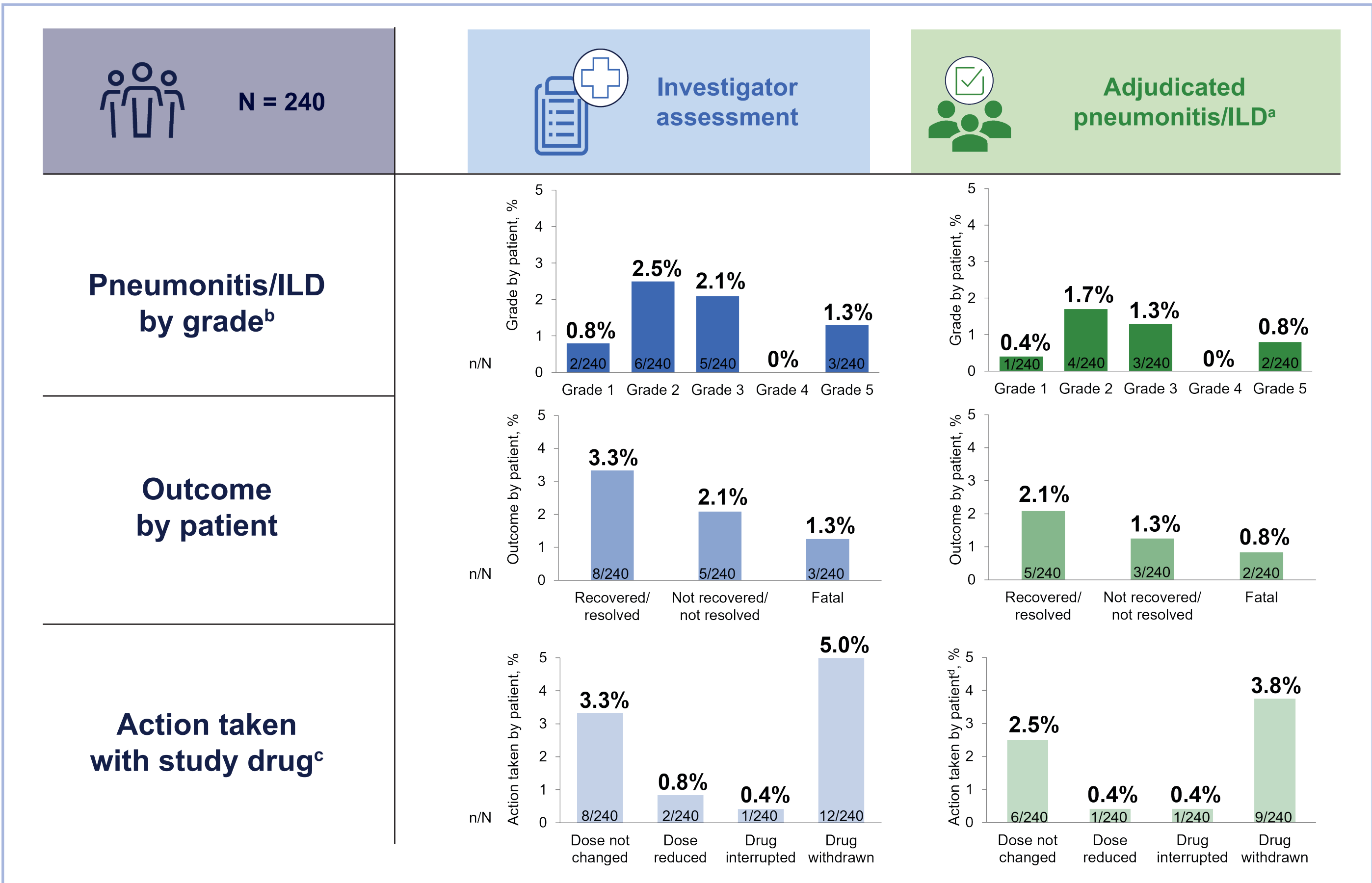
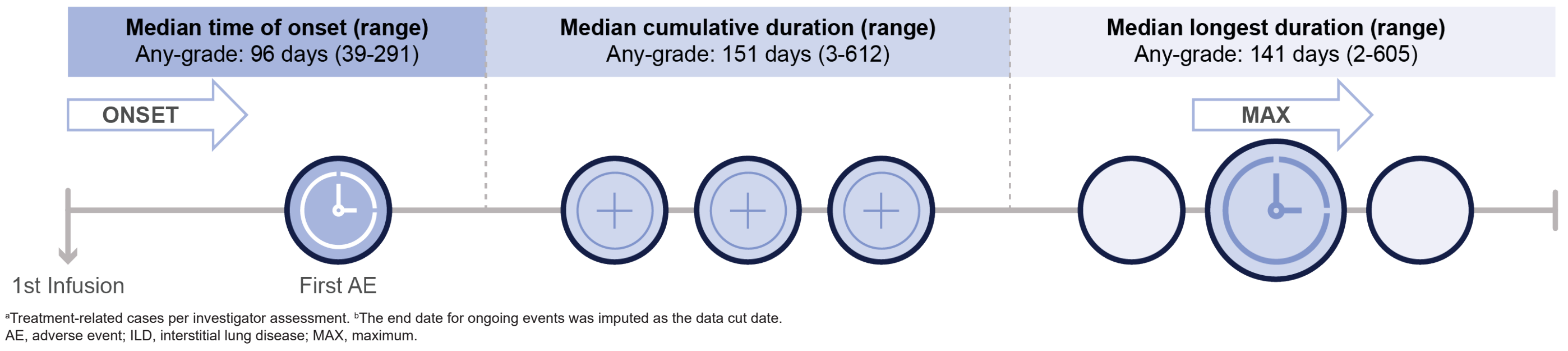
- ≥ 18 years old
- ECOG PS 0 or 1
- Patients with R/R SCLC:
 - ≥ 1 prior line of platinum-based chemotherapy
 - ≥ 1 measurable lesion per RECIST v1.1
 - Patients with LS-SCLC were permitted
- Patients with high-grade CNS tumors:
 - GBM, IDH-wildtype Grade 4;
 - astrocytoma, IDH-mutant Grade 3/4
 - Prior 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

Safety Assessment:

- Diagnosis and management of pneumonitis/ILD events followed the ASCO clinical practice guidelines
- Patients with Grade ≥ 2 pneumonitis/ILD discontinued study treatment
- To ensure adequate case evaluation, a central ILD adjudication was instituted for this study^a

^aSMQ (Narrow) MedRA "ILD" and SMQ (Broad) "Organizing pneumonia" search terms were used for identifying adjudication cases. ASCO, American Society of Clinical Oncology; CNS, central nervous system; CR, complete response; CTCAE v5, Common Terminology Criteria for Adverse Events version 5.0; ECOG PS, Eastern Cooperative Oncology Group performance score; GBM, glioblastoma; IDH, isocitrate dehydrogenase; LS-SCLC, limited-stage small cell lung cancer; MedRA, Medical Dictionary for Regulatory Activities; 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; SMQ, standardized MedDRA queries.

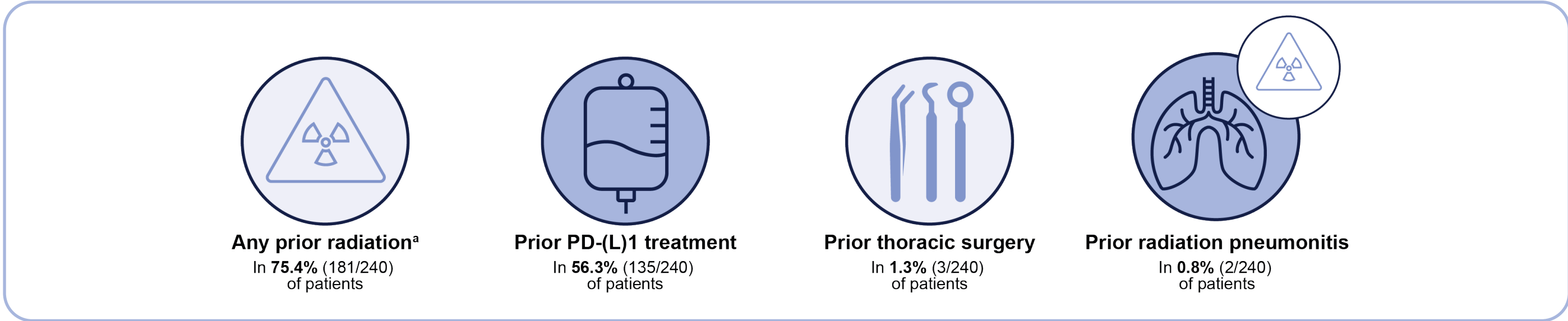
Adjudicated Pneumonitis/ILD^a Onset and Duration^b



^aAdjudication Committee decided whether or not an event was indeed pneumonitis/ILD; severity of the event was rated by the investigator only. ^bHighest grade per patient with at least 1 event. ^cMultiple actions per patient might have been taken. ^dILD, interstitial lung disease.

- Most patients with pneumonitis/ILD experienced grade 2–3 events; some patients experienced progressive worsening of their pneumonitis/ILD
- Eight of 16 patients with pneumonitis/ILD had recovered at data cut (September 27, 2025)
- Study treatment was withdrawn in 9 of 10 patients with adjudicated pneumonitis/ILD

Potential Risk Factors for Pneumonitis/ILD



^aNot limited to thoracic radiation. ^bILD, interstitial lung disease; PD-(L)1, programmed death protein (ligand) 1.

- Prior PD-L1 therapy and prior thoracic radiation were present in 7 and 1 adjudicated pneumonitis/ILD cases, respectively
- Conclusions are limited by sample size