

Efficacy and Safety of ABBV-706 Versus Standard of Care in Relapsed/Refractory Small Cell Lung Cancer: A Phase 3 Study

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OBJECTIVE

This Phase 3 study will demonstrate the superiority of ABBV-706 monotherapy and assess the safety and tolerability compared to standard of care chemotherapy in patients with ES-SCLC following prior treatment with platinum-based chemoimmunotherapy and tarlatamab

TRIAL DESIGN

Phase 3 (NCT07365241)

Randomized, open-label

Global, multicenter

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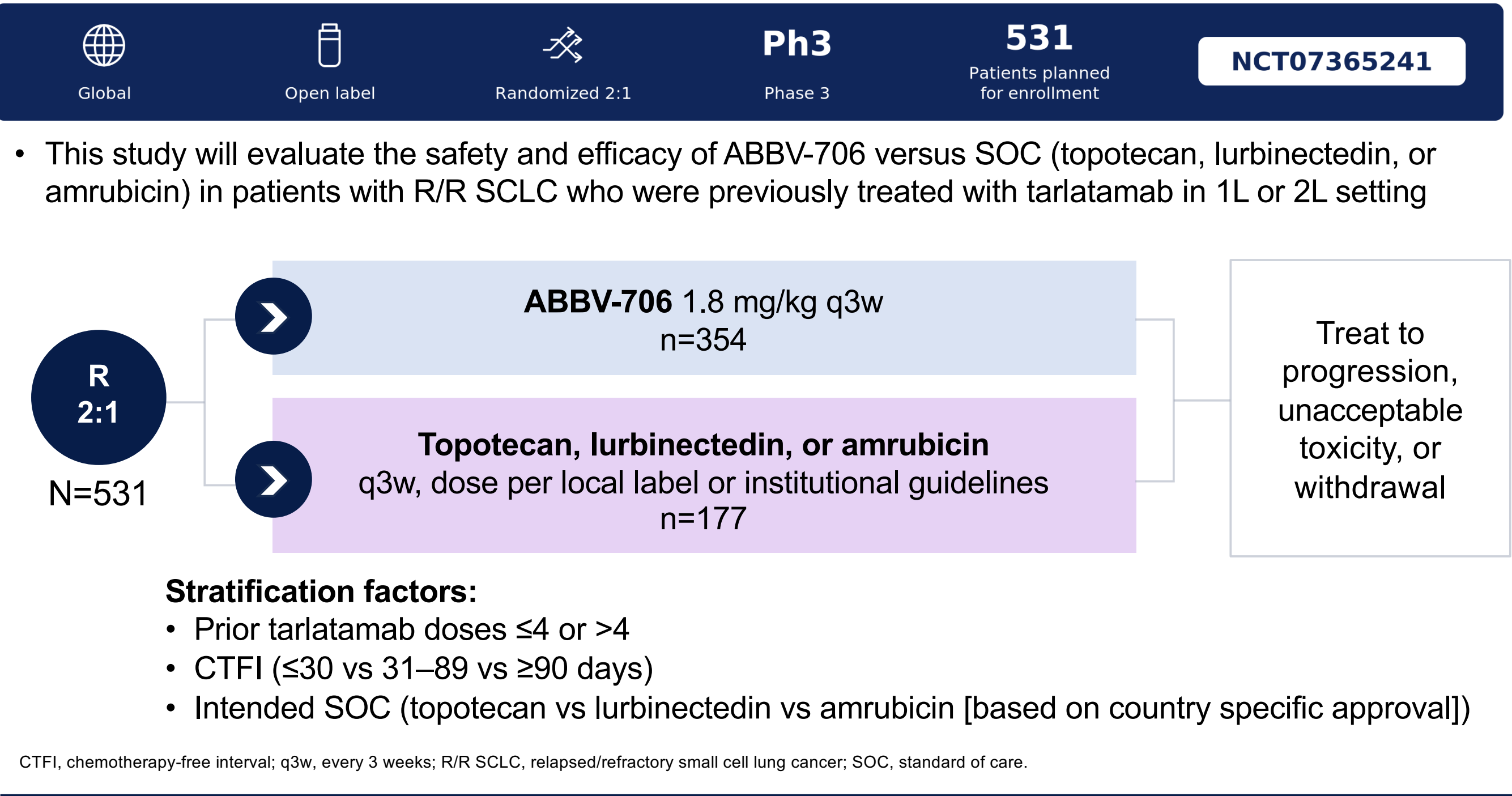
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BACKGROUND

- In patients with newly diagnosed extensive-stage SCLC (ES-SCLC), platinum-based chemotherapy significantly extends overall survival (OS) and improves patient quality of life, but the disease relapses in most patients^{1,2}
- Relapsed ES-SCLC is an aggressive malignancy with a poor prognosis; Tarlatamab, a delta-like ligand 3 (DLL3)-directed bispecific T-cell engager immunotherapy in the second-line setting offers improved mOS, 13.6 months vs chemotherapy, mOS 8.3 months, and a lower incidence of Grade 3 or higher events with tarlatamab than chemotherapy (54% vs. 80%)
- Tarlatamab plus a PD-L1 inhibitor in the first-line maintenance therapy setting in patients with ES-SCLC has demonstrated a manageable safety profile and a median OS of 25.3 months in a Phase 1b study (DeLLphi-303). A randomized Ph3 study is ongoing.
- Improved treatment options following tarlatamab remains an area of high unmet need.
- Seizure-related protein 6 homolog (SEZ6) is a transmembrane protein that is overexpressed in SCLC⁵
- 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) payload (adizutecan)⁶
- Findings from the first-in-human Phase 1 open-label study (NCT05599984) of ABBV-706 demonstrated strong antitumor activity and a manageable safety profile for monotherapy (IV, 1.8 mg/kg q3w) in patients previously treated for SCLC (**Table**)⁶

STUDY SCHEMA



KEY ELIGIBILITY CRITERIA

Patient
✓ Age ≥ 18 years ✓ ECOG PS 0–1 ✓ Archival or recently obtained tumor specimen or consents to a fresh tumor specimen collection
Disease
✓ Histologically/cytologically confirmed R/R SCLC ✓ Measurable disease per RECIST v1.1 ✓ Subjects with brain metastasis are eligible - Previously treated or untreated and symptomatic; not requiring anticonvulsants or steroids for at least 7 days prior to first dose of study treatment

Prior Systemic Therapy
✓ Progression on prior systemic therapy: - Platinum-based chemotherapy ± PD-(L)1 and tarlatamab in the <u>1L setting</u> or - Platinum-based chemotherapy ± PD-(L)1 in the <u>1L setting</u> and tarlatamab in the <u>2L setting</u> ✓ Eligible to receive the SOC comparator ✗ No prior therapy with a SEZ6-targeted ADC or a TOP1i

Comorbidities
✗ No prior history of ILD/pneumonitis that required systemic steroids or no evidence of active ILD/pneumonitis ✗ No history of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis, or radiation pneumonitis ✗ No history of other clinically significant intercurrent lung-specific illnesses or underlying pulmonary disorders ✗ No active tuberculosis

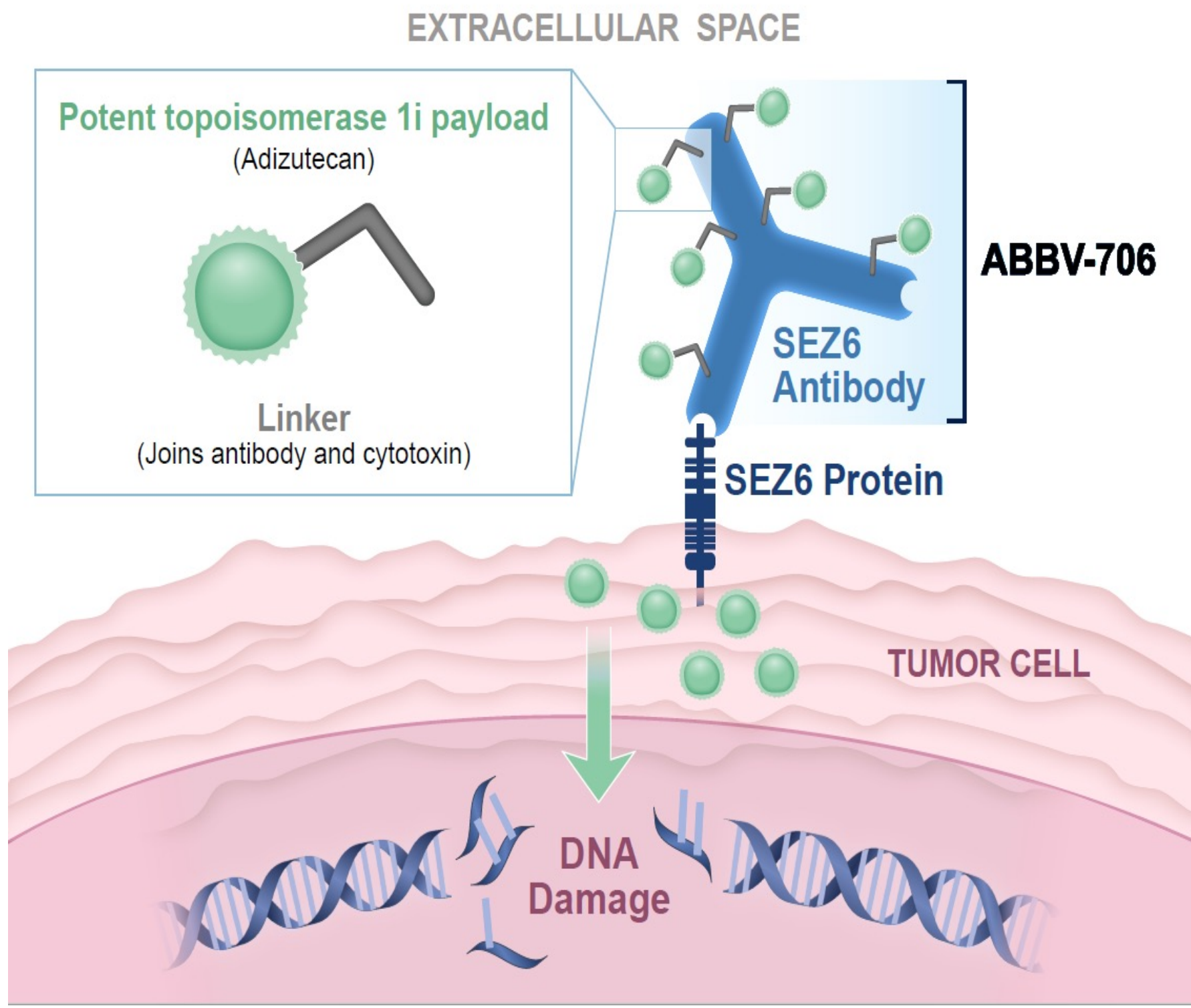
1L, first-line; 2L, second-line; ADC, antibody-drug conjugate; CNS, central nervous system; GPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; ILD, interstitial lung disease; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; R/R SCLC, Relapsed/refractory small cell lung cancer; SEZ6, seizure-related protein 6 homolog; SOC, standard of care; TOP1i, topoisomerase-1 inhibitor.

FIH Study Results

FIH Study (NCT05599984)	
Efficacy	1.8 mg/kg N = 41
ORR, n (%)	23 (56)
Median PFS, months (95% CI)	6.4 (4.0–8.1)
Median DoR, months (95% CI)	5.9 (3.6–11.1)
Median OS, months (95% CI) 18-month OS, (95% CI)	12.4 (8.2–17.3) 0.2 (0.1–0.4)
Safety	
Grade ≥3 TRAEs, n (%)	22 (53.7)
Anemia	17 (42)
Decreased neutrophil count	8 (20)
Decreased platelet count	6 (15)
Median follow-up time, months	16.4

DOR, duration of response; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; q3w, every 3 weeks; TRAE, treatment-related adverse event.

Mechanism of Action



STUDY ENDPOINTS

Primary objective	Demonstrate superior efficacy vs SOC
Primary endpoints	- Dual primary endpoints: - OR (confirmed CR or confirmed PR) based on BICR per RECIST v1.1 - OS
Key secondary endpoints	- PFS and DOR based on BICR per RECIST v1.1 - PROs - Change from baseline at Week 12 in physical functioning as measured by the physical functioning domain of the EORTC QLQ-C30 - Change from baseline at Week 12 in GHS/QoL as measured by the EORTC QLQ-C30 GHS/QoL scale
Secondary endpoints	- Investigator-assessed ORR, PFS, DOR per RECIST v1.1 - DCR by investigator and BICR per RECIST v1.1
Exploratory endpoints	- PROs: - Change from baseline and time to deterioration in remaining domains of the EORTC QLQC30 - Change from baseline and time to deterioration in scales/items of the EORTC QLQ-LC13 - Tolerability - Patient perspectives on symptomatic AEs as measured by selected items from the PRO-CTCAE - GP5 item of FACT-G to assess overall bother due to side effects from patient's perspectives - PGIS - PGIC - Change from baseline in EQ-5D-5L, including VAS - Retrospective tumor SEZ6 expression and potential predictive biomarkers
PK and immunogenicity	PK and immunogenicity of ABBV-706
Safety/tolerability endpoints	Safety evaluations include AE monitoring, physical examinations, vital sign measurements, ECG variables, and clinical laboratory testing as measures of safety and tolerability

AE, adverse event; BICR, blinded independent central review; CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; DCR, duration of complete response; DOR, duration of response; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ-5D-5L, EuroQol 5-Dimension 5-Level; FACT-G, Functional Assessment of Cancer Therapy–General; GHS, Global Health Status; OR, objective response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity; PK, pharmacokinetics; PR, partial response; PRO, patient-reported outcome; QLQ-LC13, Quality of Life Questionnaire–Lung Cancer 13; QoL, quality of life; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SOC, standard of care; VAS, Visual Analog Scale.

ENROLLMENT IS ONGOING

