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PURPOSE

- IDeate-Lung02 (NCT06203210) is a Phase 3 trial of I-DXd in adult patients with relapsed SCLC and only 1 prior line of platinum-based therapy¹
- The study will compare I-DXd with TPC chemotherapy (topotecan, amrubicin, or lurbinectedin) to evaluate the efficacy and safety profile of I-DXd

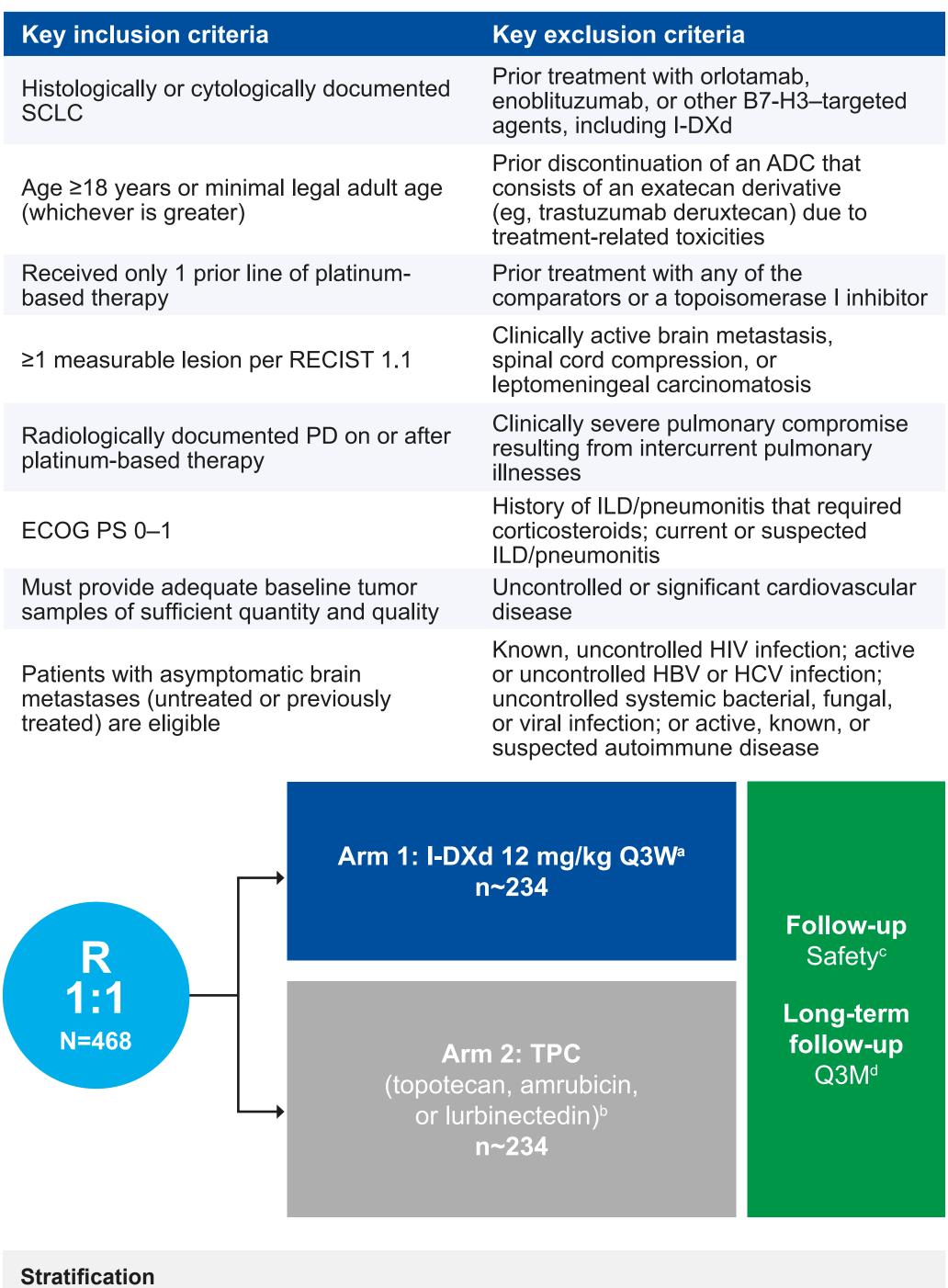
INTRODUCTION

- Patients with ES-SCLC have few effective treatment options beyond 1L therapy, and there is a substantial unmet need for therapies that provide durable clinical benefit
- Despite high initial response rates to combination platinumbased chemotherapy plus immunotherapy in 1L ES-SCLC, median OS is 12.3-13.0 months^{2,3}
- Patients with brain metastases have worse survival outcomes (median OS of 8.5 months)² and remain difficult to treat⁴
- Treatment options beyond 1L have limited efficacy (median OS of 6.0–8.1 months with topotecan, 7.5 months with amrubicin, and 9.3 months with lurbinectedin in 2L) and are associated with high rates of hematologic toxicity,^{5–8} highlighting the need for novel therapies
- B7-H3 (CD276), a type 1 transmembrane protein belonging to the B7 family, is expressed in many solid tumors but has low or no expression in normal tissue^{9–11}
- B7-H3 exhibits moderate-to-high expression in 65% of patients with SCLC, which is associated with a shorter OS (7.4 months vs 23.8 months in patients with low or absent B7-H3)¹²
- I-DXd is a B7-H3—directed ADC comprising a B7-H3 mAb linked to a topoisomerase I inhibitor payload (DXd) via a stable cleavable linker, designed to enhance selective tumor-cell death and reduce systemic exposure¹³ (**Figure 1**)
- In the Phase 1/2 IDeate-Pantumor01 study (NCT04145622), I-DXd demonstrated durable efficacy (ORR, 52.4%; median DOR, 5.9 months; median OS, 12.2 months) irrespective of B7-H3 status in 21 patients with pretreated SCLC¹⁴
- I-DXd is being investigated in a dose-optimization Phase 2 study in patients with pretreated ES-SCLC (IDeate-Lung01 [NCT05280470])¹⁵
- Here, we describe IDeate-Lung02 (NCT06203210), a Phase 3 trial comparing I-DXd with TPC (topotecan, amrubicin, or lurbinectedin) in patients with relapsed SCLC who have received only 1 prior line of platinum-based therapy¹

METHODS

- IDeate-Lung02 (NCT06203210) is a global, multicenter, randomized, open-label, Phase 3 trial comparing I-DXd with TPC in adult patients with relapsed SCLC who had received only 1 prior line of platinum-based therapy
- A total of 468 patients (~234 in each arm) will be randomized 1:1 to receive either I-DXd 12 mg/kg IV Q3W or TPC (topotecan, amrubicin, or lurbinectedin; Figure 2)
- The dual primary endpoints are ORR assessed by BICR per RECIST 1.1 and OS; study endpoints are presented in **Table 1**
- Patients are being enrolled across sites in Asia, Australia, Europe, North America, and South America (Figure 3)

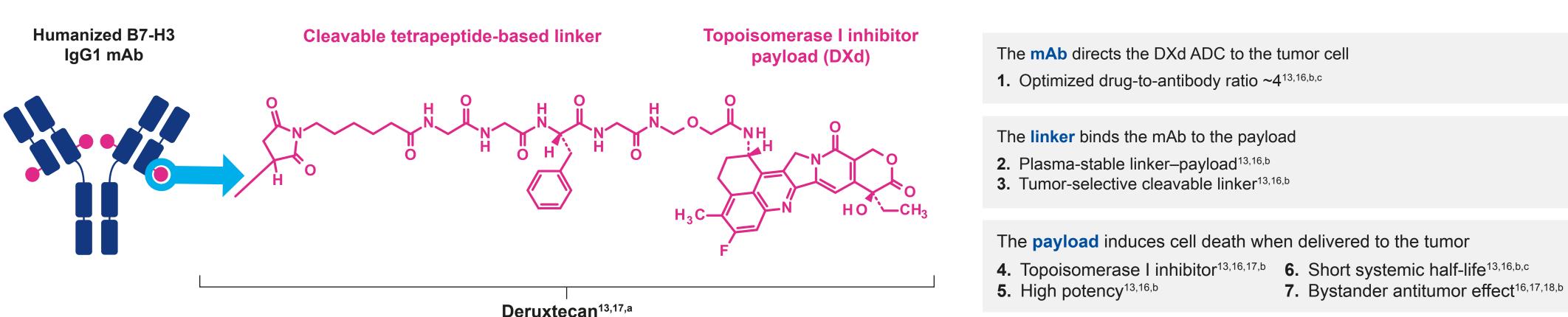
Figure 2. Study design



Chemotherapy-free interval following 1L therapy (<90 vs ≥90 days) TPC (topotecan vs amrubicin vs lurbinectedin) Treatment with prior PD-(L)1 inhibitors (yes vs no) Presence or history of asymptomatic brain metastases (yes vs no)

^aUntil PD, unacceptable toxicity, loss to follow-up, consent withdrawal, death, or other reason. ^bComparator treatments will only be utilized in countries where they are approved in second and subsequent LoTs for patients with SCLC who progressed on or after platinum-based therapy; ≥50% of patients in the comparator group will receive topotecan. Safety follow-up visit will occur 40 days (+7 days) after the last dose. dLong-term follow-up will occur to assess survival; assess tumor progression until PD for patients discontinuing for reasons other than PD; and to collect information on further anticancer treatments, Q3M (90 ±14 days) from study-drug discontinuation (end of treatment), withdrawal of consent, or from when a study-termination criterion is met.

Figure 1. I-DXd was designed with 7 key attributes



^aRefers to the linker and payload. ^bThe clinical relevance of these features is under investigation. ^cBased on animal data.

Key statistical considerations:

- BICR-assessed ORR will be analyzed using a Cochran–Mantel– Haenszel test at a 2-sided 1% alpha level
- OS will be analyzed using a log-rank test at a 2-sided 4% significance level, under a 2-look group sequential design
- An estimated 356 OS events will be needed to detect a hazard ratio of 0.70 with 90% power

Table 1. Study endpoints

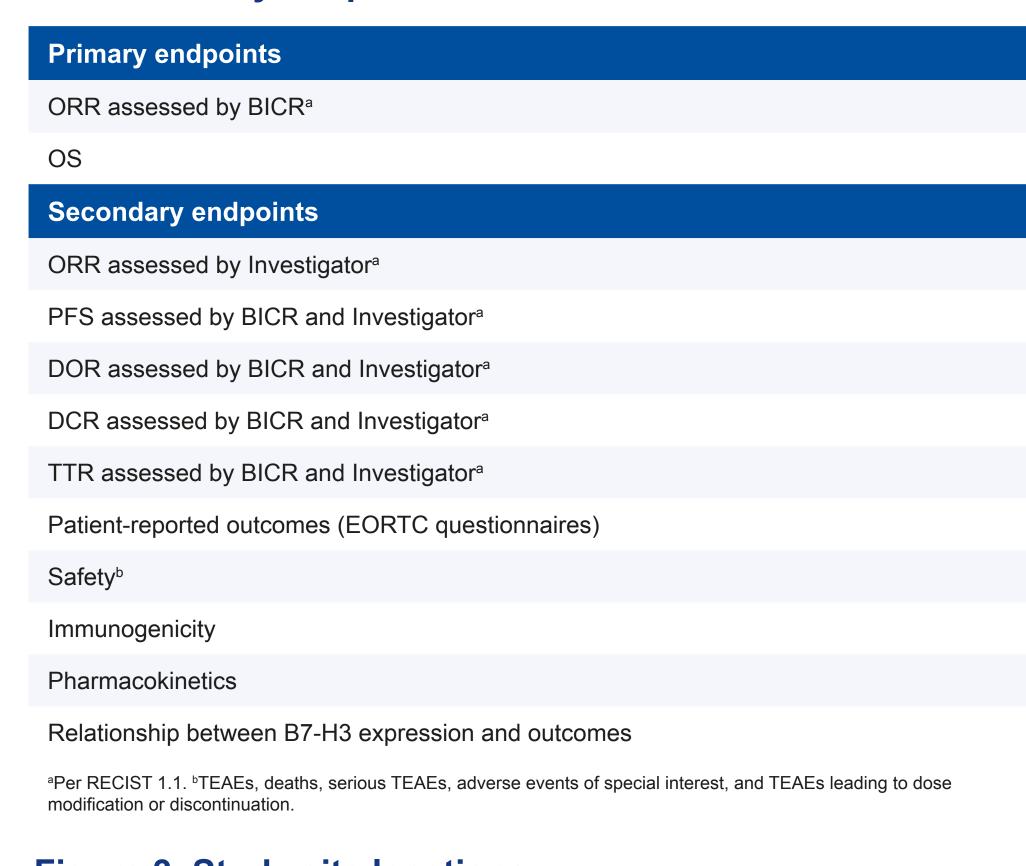
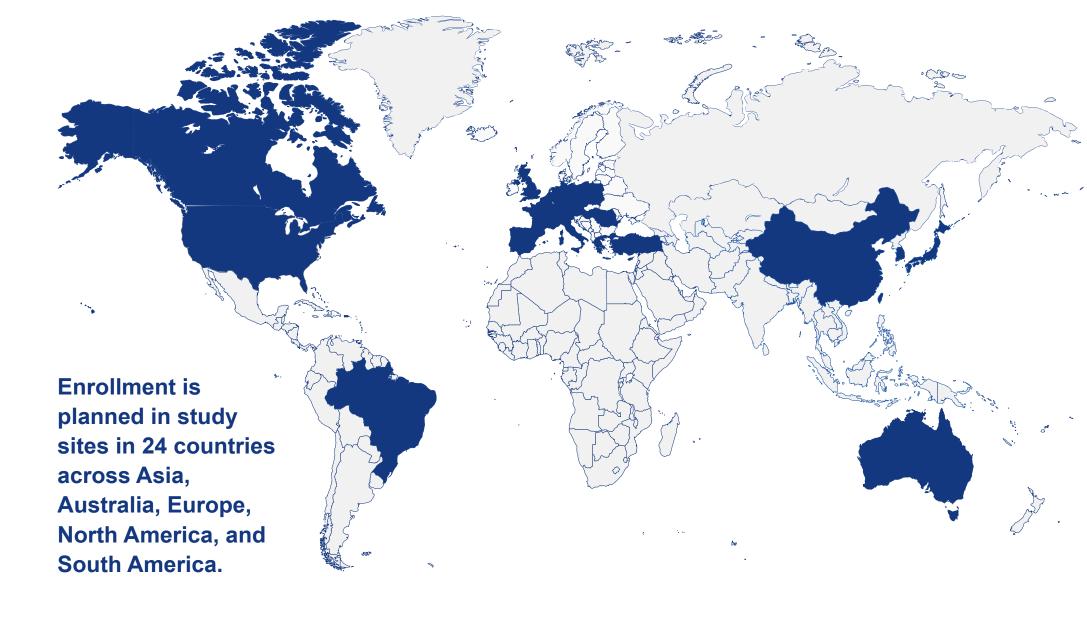


Figure 3. Study site locations



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ABBREVIATIONS

1L, first-line; 2L, second-line; ADC, antibody–drug conjugate; B7-H3, B7 homolog 3; BICR, blinded independent central review; CD276, cluster of differentiation 276; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; **EORTC**, European Organisation for Research and Treatment of Cancer; ES, extensive-stage; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; I-DXd, ifinatamab deruxtecan; IgG1, immunoglobulin G1; ILD, interstitial lung disease; IV, intravenously; LoT, line of therapy; mAb, monoclonal antibody; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q3M, every 3 months; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SCLC, small cell lung cancer; TEAE, treatment-emergent adverse event; TPC, treatment of Physician's choice; TTR, time to response.

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