# IDeate-Lung02: Phase 3 study of ifinatamab deruxtecan (I-DXd) in relapsed small cell lung cancer



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## OBJECTIVES

- IDeate-Lung02 (NCT06203210) is a Phase 3 trial of I-DXd in adult patients with relapsed SCLC following only 1 prior line of systemic treatment, which must have included platinum-based chemotherapy[1]
- 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 platinum-based chemotherapy with 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 their treatment remains a clinical challenge[4]
  - 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
  - More recently, tarlatamab has demonstrated a median OS of 15.2 months,[9] and received US FDA accelerated approval for patients with ES-SCLC with disease progression on or after platinum-based chemotherapy[10]
- 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[11–13]
- 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)[14]
- 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 exposure[15] (**Figure 1**)
- In the dose-optimization part of the Phase 2 IDeate-Lung01 study (NCT05280470), I-DXd 12 mg/kg IV Q3W demonstrated promising antitumor activity among 42 patients with pretreated ES-SCLC (ORR, 54.8%; median DOR, 4.2 months; median OS, 11.8 months)[16]
- Here, we describe IDeate-Lung02 (NCT06203210), a Phase 3 trial comparing I-DXd with TPC (topotecan, amrubicin, or lurbinectedin) in patients with relapsed SCLC following only 1 prior line of systemic treatment, which must have included platinum-based chemotherapy[1]

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

The **mAb** directs the DXd ADC to the tumor cell

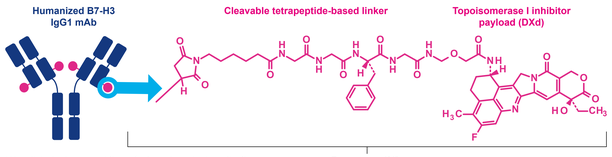
1. Optimized drug-to-antibody ratio of ~4[15,17,a,b]

The **linker** binds the mAb to the payload

2. Plasma-stable linker–payload[15,17,a]
3. Tumor-selective cleavable linker[15,17,a]

The **payload** induces cell death when delivered to the tumor

4. Topoisomerase I inhibitor[15,17,18,a]
5. High potency[15,17,a]
6. Short systemic half-life[15,17,a,b]
7. Bystander antitumor effect[17–19,a]




[a]The clinical relevance of these features is under investigation. [b]Based on animal data. [c]Refers to the linker and payload.

## 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 following only 1 prior line of systemic treatment, which must have included platinum-based chemotherapy
- Key enrollment criteria are presented in **Table 1**
- A total of 540 patients (~270 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 2**
- Patients are being enrolled across sites in Asia, Australia, Europe, North America, and South America (**Figure 3**)

## Table 1. Key enrollment criteria

| Key inclusion criteria |
|---|
| Histologically or cytologically documented ES-SCLC |
| Aged ≥18 years or minimal legal adult age (whichever is greater) |
| Received only 1 prior line of systemic treatment for SCLC, which must have included ≥2 cycles of platinum-based chemotherapy (± anti–PD-[L]1), with a CTFI of ≥30 days |
| ≥1 measurable lesion per RECIST 1.1 |
| Radiologically documented PD on or after platinum-based chemotherapy |
| ECOG PS 0–1 |
| Patients with asymptomatic brain metastases (untreated or previously treated) are eligible |
| **Key exclusion criteria** |
| Prior treatment with orlotamab, enoblituzumab, or other B7-H3–targeted agents, including I-DXd |
| Prior discontinuation of an ADC that consists of an exatecan derivative (eg, trastuzumab deruxtecan) due to treatment-related toxicities |
| Prior treatment with any of the comparators or a topoisomerase I inhibitor |
| Clinically active brain metastasis, spinal cord compression, or leptomeningeal carcinomatosis |
| Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses |
| History of ILD/pneumonitis that required corticosteroids; current or suspected ILD/pneumonitis |
| Uncontrolled or significant cardiovascular disease |
| Known, uncontrolled HIV infection; active or uncontrolled HBV or HCV infection; uncontrolled systemic bacterial, fungal, or viral infection; or active, known, or suspected autoimmune disease |

## Figure 2. Study design

- Relapsed SCLC
- ECOG PS 0–1
- Received only 1 prior line of systemic treatment, which must have included platinum-based chemotherapy ± anti–PD-(L)1 therapy[a]
- N=540

R 1:1

**Arm 1:** I-DXd 12 mg/kg Q3W[b] n≈270

**Arm 2: TPC** (topotecan, amrubicin, or lurbinectedin)[c] n≈270

**Follow-up** Safety[d]

**Long-term follow-up** Q3M[e]

**Stratification**

CTFI 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)

[a]≥80% of patients are expected to have received prior anti–PD-(L)1 therapy. [b]Until PD, unacceptable toxicity, loss to follow-up, consent withdrawal, death, or other reason. [c]Comparator 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; ≥70% of patients in the comparator group will receive topotecan. [d]Safety follow-up visit will occur 40 days (+7 days) after the last dose. [e]Long-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.

## Key statistical considerations

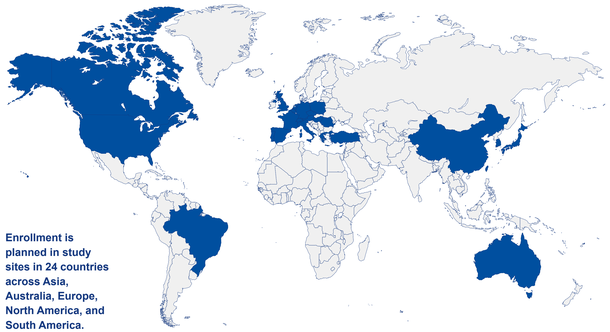
- BICR-assessed ORR will be analyzed using a Cochran–Mantel–Haenszel test at a 2-sided 1% alpha level
- OS will be analyzed using a log-rank test at a 2-sided 4% significance level, under a 2-look group sequential design

## Table 2. Study endpoints

| Primary endpoints |
|---|
| ORR assessed by BICR[a] |
| OS |
| **Secondary endpoints** |
| ORR assessed by investigator[a] |
| PFS assessed by BICR and investigator[a] |
| DOR assessed by BICR and investigator[a] |
| DCR assessed by BICR and investigator[a] |
| TTR assessed by BICR and investigator[a] |
| Patient-reported outcomes (EORTC questionnaires) |
| Safety[b] |
| Immunogenicity |
| Pharmacokinetics |
| Relationship between B7-H3 expression and outcomes |

[a]Per RECIST 1.1. [b]TEAEs, deaths, serious TEAEs, adverse events of special interest, and TEAEs leading to dose modification or discontinuation.

## Figure 3. Study site locations



**Enrollment is planned in study sites in 24 countries across Asia, Australia, Europe, North America, and South America.**

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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; **CTFI**, chemotherapy-free interval; **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-(L)1**, 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 Tumours, version 1.1; **SCLC**, small cell lung cancer; **TEAE**, treatment-emergent adverse event; **TPC**, treatment of Physician's choice; **TTR**, time to response; **US FDA**, United States Food and Drug Administration.

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