

Ifinatamab deruxtecan (I-DXd) in extensive-stage small cell lung cancer: Extended safety analysis of IDeate-Lung01

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OBJECTIVES

- To perform a comprehensive analysis of select TRAEs reported in patients with previously treated ES-SCLC who received I-DXd 12 mg/kg in the Phase 2 IDeate-Lung01 study (NCT05280470), with an additional 6 months of follow-up from the primary analysis

CONCLUSIONS

- Among the investigated TRAEs, the majority were reported at Grade 1 or 2, had resolved at data cutoff, and did not lead to treatment discontinuation
- Median duration of the first resolved event was short for IRRs, vomiting, and nausea, with longer median durations observed for neutropenia, adjudicated treatment-related ILD/pneumonitis, and anemia
- Across Cycles 1–8, nausea and vomiting were most prevalent in Cycle 1, with consistently lower prevalence thereafter; anemia and neutropenia remained prevalent throughout, with peaks in Cycles 4 and 3, respectively, while most IRRs occurred in Cycle 1; and adjudicated treatment-related ILD prevalence remained low throughout
- Rates of nausea/vomiting and IRRs in this study were lower than in the Phase 1/2 IDeate-PanTumor01 study, where premedication was only introduced partway through the study, whereas the IDeate-Lung01 protocol mandated premedication for nausea/vomiting and strongly recommended it for IRRs from the first protocol amendment
- ILD/pneumonitis is an important identified risk with I-DXd 12 mg/kg that requires prompt evaluation and careful management
- The TRAEs investigated in this analysis were clinically manageable via appropriate treatments through routine clinical practice, dose modifications, and protocol-specified guidelines for management



Plain language summary

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Poster

INTRODUCTION

- Currently available 2L+ chemotherapeutic options for patients with ES-SCLC are commonly associated with hematologic and gastrointestinal AEs^{1–4}
- Although tarlatamab has improved clinical outcomes in 2L+ SCLC, it carries a risk of CRS and neurologic toxicity (including ICANS) and can be associated with infections, hematologic toxicity, and hepatotoxicity^{5,6}
- In the primary analysis of the Phase 2 IDeate-Lung01 study (data cutoff: March 3, 2025), I-DXd 12 mg/kg demonstrated a confirmed ORR of 48.2%, mPFS of 4.9 months, and mOS of 10.3 months, alongside a manageable safety profile, among 137 patients with previously treated ES-SCLC⁷
- We present a comprehensive analysis of select TRAEs reported in these patients, with an additional 6 months of follow-up from the primary analysis (data cutoff: September 3, 2025)

METHODS

- IDeate-Lung01 (NCT05280470) is a Phase 2, multicenter, randomized, open-label, 2-part study that enrolled patients with ES-SCLC who had received ≥1 prior line of PBC and ≤3 prior lines of systemic therapy, and had an ECOG PS of 0–1; patients with asymptomatic brain metastases (either untreated or previously treated) were eligible
- In Part 1 (dose optimization), patients were randomized 1:1 to receive I-DXd 8 or 12 mg/kg IV Q3W, and in Part 2 (extension), all patients received I-DXd 12 mg/kg IV Q3W
- The primary endpoint was ORR by BICR per RECIST 1.1
- Secondary endpoints included DOR, PFS, DCR, and TTR (all by BICR per RECIST 1.1), OS, and safety
- This analysis included patients who received I-DXd 12 mg/kg IV Q3W in either Part 1 or 2 of the study
- TRAEs investigated in this analysis were those that were previously identified from nonclinical studies and the ongoing Phase 1/2 IDeate-PanTumor01 study (NCT04145622) as risks or AEs associated with I-DXd (nausea, vomiting, and the grouped preferred terms anemia* and neutropenia*), and select AESIs for I-DXd (adjudicated treatment-related ILD/pneumonitis and IRRs)
- Before each dose of I-DXd, premedication with a 2- or 3-drug combination regimen (eg, corticosteroids with either a 5-HT₂ receptor antagonist or an NK-1 receptor antagonist, as well as other drugs as indicated) to prevent nausea and vomiting was mandatory; premedication with antihistamines, acetaminophen, and/or corticosteroids to prevent IRRs was strongly recommended
- Patients were permitted to receive supportive treatment with G-CSF or transfusion of blood for hematologic AEs

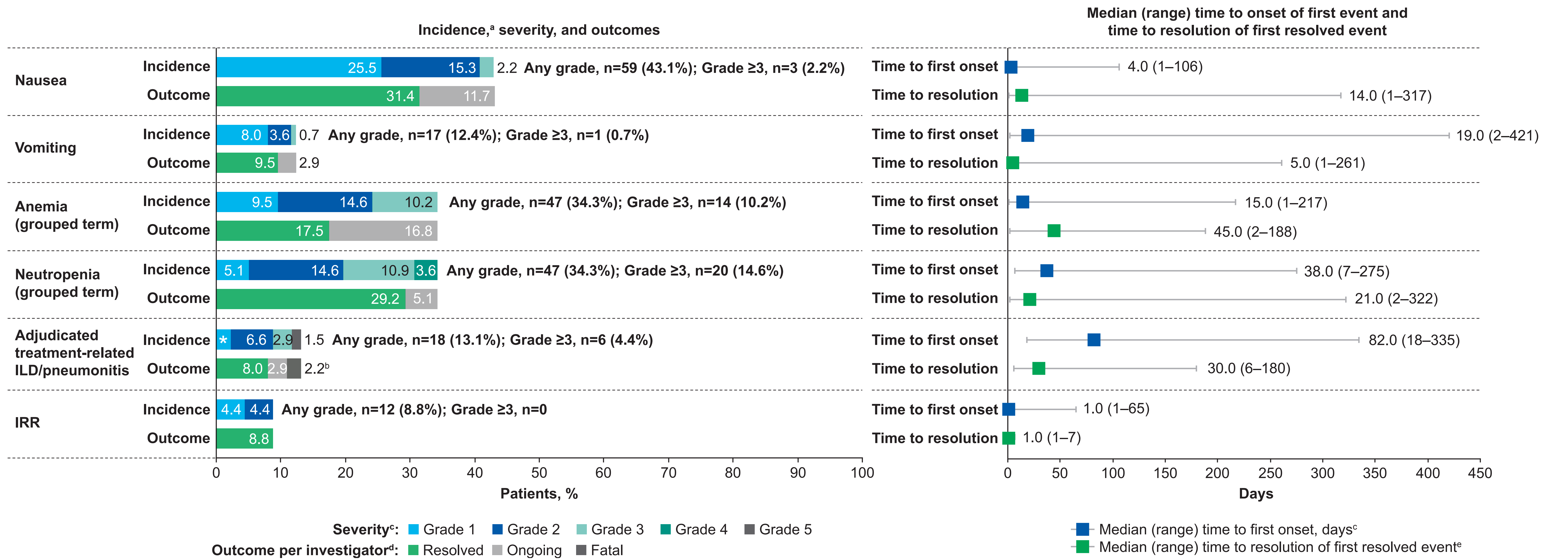
- All suspected ILD or pneumonitis cases were reviewed by an independent ILDAC
 - For adjudicated treatment-related ILD/pneumonitis, event severity and time to onset were determined by the ILDAC; time to resolution (from the date of onset per ILDAC) and outcomes were determined by investigators
 - Management of ILD/pneumonitis was based on protocol-specified guidelines and according to investigator assessment of event severity

*Includes the preferred terms "hemoglobin decreased," "RBC count decreased," "anemia," and "hematocrit decreased." †Includes the preferred terms "neutrophil count decreased" and "neutropenia," with "febrile neutropenia" additionally included when reporting the management of all-cause neutropenia.

RESULTS

- At the September 3, 2025 data cutoff, a total of 137 patients had received I-DXd 12 mg/kg (median age, 63 years; male, 65.7%; ECOG PS 1, 77.4%; median number of prior LOTS, 2 [range, 1–3])

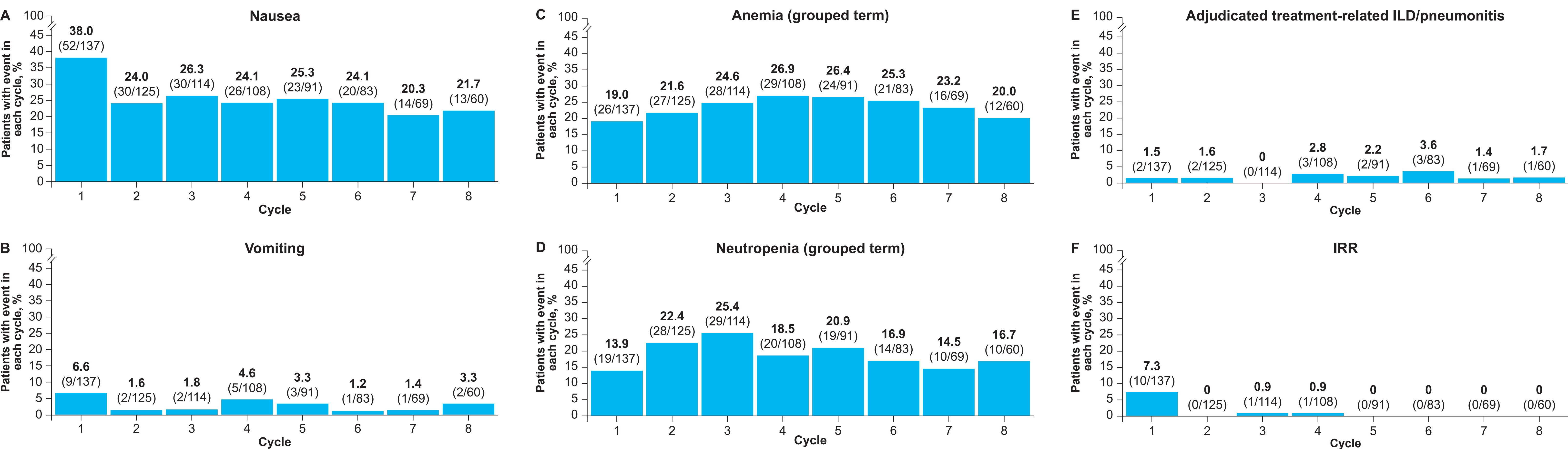
Figure 1. Clinical profile of TRAEs



*≥2.2%.

†Patients with event. ††Of the 3 patients with treatment-related ILD/pneumonitis associated with death per investigator assessment, only 1 had an event subsequently adjudicated as Grade 5 by the ILDAC. Among the remaining 2 patients, 1 had an event that was adjudicated as Grade 1 by the ILDAC (cause of death per ILDAC: respiratory failure due to disease progression), and 1 had an event that was not adjudicated due to insufficient information. A fourth patient had a Grade 3 event per investigator that was subsequently adjudicated as Grade 5 by the ILDAC. ‡Per investigator (nausea, vomiting, anemia, neutropenia, and IRRs) or per ILDAC (adjudicated treatment-related ILD/pneumonitis). §Outcome per investigator of the event with the worst CTCAE grade. ¶From date of onset per investigator until date of resolution per investigator (nausea, vomiting, anemia, neutropenia, and IRRs) or from date of onset per ILDAC until date of resolution per investigator (adjudicated treatment-related ILD/pneumonitis).

Figure 2. Prevalence*



*Defined as new-onset (first or recurring event) or ongoing events reported in each treatment cycle. Data are reported as the percentage of patients with an event in each treatment cycle, using the number of patients treated in each cycle as the denominator.

Table 1. TRAEs associated with dose modifications

Patients, n (%)	Nausea	Vomiting	Anemia (grouped term)	Neutropenia (grouped term)	Adjudicated treatment-related ILD/pneumonitis*	IRR
TRAE associated with treatment discontinuation	1 (0.7)	0	0	0	9 (6.6)	0
TRAE associated with dose delay/interruption	1 (0.7)	0	7 (5.1)	21 (15.3)	4 (2.9)	2 (1.5)
TRAE associated with dose reduction	2 (1.5)	0	3 (2.2)	4 (2.9)	1 (0.7)	0

*Dose modifications for adjudicated treatment-related ILD/pneumonitis were based on the initial assessment of event severity per investigator. Per ILD/pneumonitis management guidelines, I-DXd treatment should have been permanently discontinued for any investigator-determined Grade ≥2 event.

Prevalence

- The prevalence across Cycles 1–8 of each TRAE (defined as onset of first or recurring events or ongoing events, reported as a percentage of patients treated in each cycle) is presented in **Figure 2**
- Nausea, vomiting, and IRRs were most prevalent in Cycle 1, with 10 of 12 IRRs occurring in this cycle; anemia and neutropenia were most prevalent in Cycles 4 and 3, respectively, and the prevalence of adjudicated treatment-related ILD/pneumonitis remained low and consistent throughout

Dose modifications

- Dose modifications due to TRAEs are presented in **Table 1**
- Adjudicated treatment-related ILD/pneumonitis was associated with treatment discontinuation, dose delay or interruption, and dose reduction in 9 (6.6%), 4 (2.9%), and 1 (0.7%) patients, respectively
- Among the 18 patients with adjudicated treatment-related ILD/pneumonitis, 9 had events that were determined by investigators to be Grade 1 treatment-related events (severity per ILDAC: Grade 1, n=2; Grade 2, n=7)
 - Of these 9 patients, 1 did not receive steroids and discontinued treatment due to disease progression, 4 (3 of whom received steroids) were able to continue treatment after a dose delay, 1 received steroids and continued treatment at a reduced dose, and 3 (all of whom received steroids) had treatment withdrawn

Prophylaxis

- Among 125 patients who received ≥2 cycles of I-DXd, 124 received premedication for nausea/vomiting at Cycle 1, and 124 received premedication for IRRs at Cycle 1
 - 75 (60.5%) of the 124 patients who received premedication for nausea/vomiting did not have treatment-related nausea/vomiting events at Cycle 1, and 49 (39.5%) did
 - All 49 (100%) patients continued to receive premedication at Cycle 2, of whom 42 (85.7%) experienced no treatment-related nausea/vomiting during that cycle
 - 115 (92.7%) of the 124 patients who received premedication for IRRs did not have treatment-related IRRs at Cycle 1, and 9 (7.3%) did
 - All 9 (100%) patients continued to receive premedication at Cycle 2 and experienced no treatment-related IRRs during that cycle
- Rates of treatment-related nausea/vomiting and IRRs with I-DXd 12 mg/kg in IDeate-Lung01 were lower than among 136 patients who received the same dose across all tumor types in the Phase 1/2 IDeate-PanTumor01 study (IDeate-PanTumor01 data cutoff: September 15, 2024; median treatment duration, 3.0 months [range, 0.7–31.3])
 - Nausea/vomiting: IDeate-Lung01, n=60 (43.8%); IDeate-PanTumor01, n=86 (63.2%)
 - IRRs: IDeate-Lung01, n=12 (8.8%); IDeate-PanTumor01, n=39 (28.7%)

Management of all-cause anemia and neutropenia

- All-cause anemia (grouped term) was reported in 62 (45.3%) patients, 16 of whom (25.8% [11.7% of the total population]) received a transfusion within 28 days after event onset
- All-cause neutropenia (grouped term) was reported in 52 (38.0%) patients, 28 of whom (53.8% [20.4% of the total population]) received G-CSF within 28 days after event onset

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ABBREVIATIONS

2L+, second-line and beyond; **5-HT₂**, 5-hydroxytryptamine; **AE**, adverse event; **AESi**, adverse event of special interest; **BICR**, blinded independent central review; **CRS**, cytokine release syndrome; **CTCAE**, Common Terminology Criteria for Adverse Events; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **(ES-)SCLC**, (extensive-stage) small cell lung cancer; **G-CSF**, granulocyte colony-stimulating factor; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **I-DXd**, ifinatamab deruxtecan; **ILD(AC)**, interstitial lung disease (adjudication committee); **IRR**, infusion-related reaction; **IV**, intravenous; **LOT**, line of therapy; **(m)OS**, (median) overall survival; **(m)PFS**, (median) progression-free survival; **NK-1**, neurokinin-1; **ORR**, objective response rate; **PBC**, platinum-based chemotherapy; **Q3W**, every 3 weeks; **RBC**, red blood cell; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumours, version 1.1; **TRAE**, treatment-related adverse event; **TTR**, time to response.

REFERENCES

- Trigo J, et al. *Lancet Oncol*. 2020;21:645–654.
- von Pawel J, et al. *J Clin Oncol*. 2014;32:4012–4019.
- Eckardt JR, et al. *J Clin Oncol*. 2007;25:2086–2092.
- O'Brien MER, et al. *J Clin Oncol*. 2006;24:5441–5447.
- Mountzios G, et al. *N Engl J Med*. 2025;393:349–361.
- IMDELLTRA® (tarlatamab-dlle) [prescribing information]. Thousand Oaks, CA: Amgen Inc.; 2025.
- Rudin CM, et al. *J Clin Oncol*. 2026;44:261–273.

DISCLOSURES

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