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Intracranial activity of ifinatamab deruxtecan (I-DXd) in patients (pts) with extensive-stage (ES) small cell lung cancer (SCLC) and baseline (BL) brain metastases (BM): Primary analysis of IDEate-Lung01

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Background

Up to ~80% of pts with SCLC develop BM over the course of their disease. In an interim analysis of the dose-optimization part of the Phase II IDEate-Lung01 study (NCT05280470), I-DXd, a B7-H3-directed antibody–drug conjugate, showed encouraging CNS efficacy signals in pts with ES-SCLC and BL BM. We report the primary analysis of pts with BL BM treated with I-DXd 12 mg/kg in the dose-optimization and extension parts of IDEate-Lung01.

Methods

Pts with ES-SCLC with 1–3 prior lines of therapy, including platinum-based chemotherapy, were enrolled. Pts with asymptomatic BM (treated or untreated) were eligible. In the dose-optimization part, pts were randomized 1:1 to I-DXd 8 or 12 mg/kg IV Q3W; in the extension part, pts received I-DXd 12 mg/kg IV Q3W. Brain imaging was performed at BL and at investigators' discretion, and for pts with BL BM (≥1 target and/or non-target CNS lesion), Q6W for 36 weeks then Q12W. CNS ORR was assessed by BICR using RECIST 1.1 modified for CNS tumor assessment.

Results

At data cutoff (March 3, 2025), 65/137 pts (47%) who received I-DXd 12 mg/kg had BL BM; of these, 29/65 (45%) had BL brain target lesions (TL) and 26/65 (40%) had no prior radiotherapy (RT) for BL BM. CNS confirmed ORR was 46.2% (95% CI, 33.7–59.0) in all pts with BL BM, 65.5% (95% CI, 45.7–82.1) in pts with BL TL, and 57.7% (95% CI, 36.9–76.6) in pts with no prior RT for BL BM (Table). The incidence of any-grade treatment-related adverse events (TRAEs) was 88% in pts with BL BM vs 92% in pts without BL BM; of Grade ≥3 TRAEs was 31% vs 42%; of Grade 5 TRAEs was 2% (n=1) vs 7% (n=5); of any-grade interstitial lung disease was 11% vs 17%; and of TRAEs leading to I-DXd discontinuation was 8% vs 11%.Table: 2760MO

	All pts with BL BM (N=65)	No prior brain RT for BL BM (n=26)	With prior brain RT for BL BM (n=39)	BL brain TL (n=29)
CNS ORR, n (%)	30 (46)	15 (58)	15 (38)	19 (66)
95% CI	34–59	37–77	23–55	46–82
CNS best overall response, n (%)				
Complete response	20 (31)	12 (46)	8 (21)	9 (31)
Partial response	10 (15)	3 (12)	7 (18)	10 (34)
Stable disease	29 (45)	9 (35)	20 (51)	9 (31)
Progressive disease	1 (2)	0	1 (3)	0
Not evaluable	5 (8)	2 (8)	3 (8)	1 (3)

	All pts with BL BM (N=65)	No prior brain RT for BL BM (n=26)	With prior brain RT for BL BM (n=39)	BL brain TL (n=29)
CNS disease control rate, n (%)	59 (91)	24 (92)	35 (90)	28 (97)
CNS duration of response, median (95% CI), months	6.2 (4.0–7.9)	6.7 (3.1–not estimable)	5.1 (3.0–7.9)	5.7 (3.1–7.1)
CNS time to response, median (range), months	1.4 (0.9–8.5)	1.3 (1.1–2.8)	1.4 (0.9–8.5)	1.3 (0.9–3.0)

Conclusions

I-DXd demonstrated encouraging CNS activity in pts with ES-SCLC and BL BM regardless of prior RT for BL BM. The safety profile was manageable, similar between pts with and without BL BM, and consistent with the overall 12 mg/kg population.

Clinical trial identification

NCT05280470.

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Legal entity responsible for the study

Daiichi Sankyo, Inc.

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Disclosure

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