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Outcomes with first-line obrixtamig plus standard of care in epNEC by DLL3 expression status: Phase Ib DAREON®-7 study

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BACKGROUND

Obrixtamig (BI 764532) is a DLL3/CD3 IgG-like T-cell engager. This subgroup analysis of the ongoing Phase Ib dose-escalation/expansion DAREON®-7 trial (NCT06132113) examined safety and efficacy of first-line obrixtamig + standard of care (SoC; platinum/etoposide) in patients with extrapulmonary neuroendocrine carcinoma (epNEC) by DLL3 expression status.

METHODS

Patients had advanced epNEC, large cell NEC of the lung (LCNEC-L), or NEC of unknown primary site (CUP-NEC), with confirmed DLL3-expressing tumors (>0% tumor cells [TCs] with moderate-to-strong staining). Patients received 6 cycles of SoC + obrixtamig followed by obrixtamig maintenance (Q3W). Obrixtamig was given as step-up dosing followed by target dose (Part A: 10, 30, or 60 mg; Part B: 60 mg). SoC was given per label. Study endpoints include DLTs, ORR, PFS, DoR (RECIST v1.1, investigator-assessed), and

safety. Subgroup analyses: DLL3^{high} (≥50% of TCs with moderate-to-strong staining) vs DLL3^{low} (<50%) expression status. DLL3 was centrally assessed using an investigational antibody for DLL3 (SP347; Roche Diagnostics).

RESULTS

As of February 3, 2026, 44 patients received ≥1 dose of obrixtamig: epNEC, n=40 (DLL3^{high}/DLL3^{low}: n=21/19); LCNEC-L, n=2 (DLL3^{high}: n=2); CUP-NEC, n=2 (DLL3^{high}/DLL3^{low}: n=1/1). Baseline characteristics were well-balanced across DLL3 subgroups. Efficacy data are in the table. TEAEs (any/Grade ≥3): 100/93%. Obrixtamig-related CRS Grade 1/2: 59/14%; ICANS and potential ICANS-like neurotoxicity: Grade 1/2: 5/0% (all preferred-term ICANS). No Grade ≥3 CRS or Grade ≥2 ICANS were reported.

A notable case was observed in a 63-year-old patient with DLL3^{high} vaginal NEC and liver metastases. Following resection of the primary tumor (August 2024) and initiation of treatment (November 2024), PR was achieved after 6 cycles of SoC + obrixtamig (February 2025). Continued tumor shrinkage in all lesions on obrixtamig maintenance resulted in confirmed CR (April 2026). The patient remains on treatment with ongoing response and resolved early-onset low-grade AEs.

CONCLUSIONS

Encouraging efficacy was observed across both DLL3 subgroups, with a trend towards improved outcomes in patients with DLL3^{high} tumors, pending longer follow-up. These results support further development of obrixtamig + SoC in patients with DLL3-expressing epNEC in the ongoing Phase III DAREON®-NEC-1 trial (NCT07544654).

		Efficacy	
	Total (N=44)	**DLL3^{high} (n=24)**	**DLL3^{low} (n=20)**
Confirmed ORR, % (95% CI)	77 (63-87)	88 (69-96)	65 (43-82)
Median PFS, months (95% CI)*	7.7 (6.0-14.5)	9.5 (6.0-NC)	7.6 (4.6-9.0)
9-month PFS rate, % (95% CI)	44 (26-63)	58 (34-83)	34 (10-57)
Median DoR, months (95% CI)*	12.5 (5.5-NC)	NC (5.1-NC)	7.0 (5.5-NC)
*Immature data.			

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