Outcomes with First-Line Obrixtamig Plus Standard of Care in epNEC by DLL3 Expression Status: Phase Ib DAREON®-7 Study

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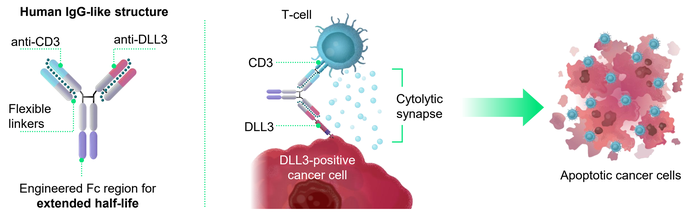
Aman Chauhan,[1]* Saori Mishima,[2] Ana Custodio,[3] Emmanuel Mitry,[4] Rocio Garcia-Carbonero,[5] Janie Zhang,[6] Ken Kato,[7] Julia Koevi,[8] Svenja Maria Palm,[9] Zilu Liu,[10] Valeria Lifke,[11] Timon Vandamme,[12,13] Jaume Capdevila[14]

[1]Department of Internal Medicine, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [2]Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3]Medical Oncology Department, Hospital Universitario La Paz, Instituto de Investigación Biomédica Hospital Universitario La Paz (IdiPAZ), Madrid, Spain; [4]Department of Medical Oncology, Institut Paoli Calmettes, Marseille, France; [5]Medical Oncology Department, Hospital Universitario 12 de Octubre, Medicine Faculty, Universidad Complutense de Madrid, Spain; [6]Department of Internal Medicine, Division of Malignant Hematology and Medical Oncology, University of Pittsburgh School of Medicine and Hillman Cancer Center, Pittsburgh, PA, USA; [7]Department of Head and Neck, Esophageal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; [8]Global Clinical Development ONCO, Boehringer Ingelheim International GmbH, Biberach an der Riss, Germany; [9]Global Clinical Development Operations, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany; [10]Global Biostatistics & Data Sciences, Boehringer Ingelheim (China) Investment Co., Ltd., Shanghai, China; [11]Global Experimental Medicine Oncology, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany; [12]Center for Oncological Research (CORE), University of Antwerp, Belgium; [13]NETwerk & Department of Oncology, Antwerp University Hospital, Antwerp, Belgium; [14]Department of Medical Oncology, Vall d'Hebron University Hospital & Vall d'Hebron Institute of Oncology, Barcelona, Spain

Introduction

- Extrapulmonary NEC (epNEC) is a rare, heterogeneous, and aggressive group of cancers[1]
- Platinum + etoposide is the current 1L SoC treatment for epNEC,[2] but median OS remains ≤1 year[3]
- DLL3 is expressed on tumor cells in up to ~83% of patients with epNEC, with substantial variability in expression levels[4]

Mechanism of action of obrixtamig[5–7]



Trial Design

- DAREON®-7 is a Phase I dose-escalation/expansion trial of obrixtamig + SoC in patients with 1L DLL3-positive NEC

Patient population

- Locally advanced/metastatic 1L epNEC, LCNEC-L, or NEC of unknown primary site
- DLL3-positive (central testing)
- No prior treatment with DLL3-targeted T-cell engagers or cell therapies

Primary endpoint: Occurrence of DLTs

Secondary endpoint: Part A: Occurrence of AEs and DLTs, and ORR† Part B: ORR and DoR†

Further endpoint: Progression-free survival†

Part A: dose escalation (BLRM with overdose control; N=25)
Obrixtamig (target dose levels: 10, 30, 60 mg)‡ + SoC§

RP2D

Part B: dose expansion (N=19)
Obrixtamig 60 mg‡ + SoC§

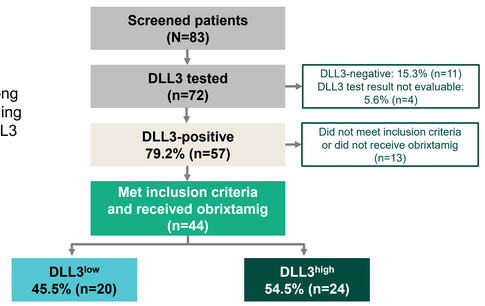
Treatment schedule

Induction		Maintenance
Cycle 1: SoC§	**Cycle 2–6: Obrixtamig** + SoC§	**Cycle 7 onwards:¶ Obrixtamig** Q3W

†RECIST v1.1 (investigator-assessed); ‡patients received obrixtamig as step-up dosing followed by target dose; §Part A: carboplatin + etoposide, Part B: investigator's choice of platinum (carboplatin/cisplatin) + etoposide; ¶treatment continues until disease progression or another reason requiring termination, for up to 36 months

DLL3 Testing

- Overall, 54.5% of patients in the DAREON®-7 trial had DLL3^{high} tumors
- **DLL3 expression status:** % of tumor cells with moderate-to-strong cytoplasmic and/or membranous staining with an investigational antibody for DLL3 (SP347; Roche Diagnostics)
  - DLL3-positive: >0%
    - **DLL3^{low}:** <50%
    - **DLL3^{high}:** ≥50%



Data cut-off: Feb 3, 2026

Plain Language Summary

Extrapulmonary neuroendocrine carcinoma (epNEC) is a rare and aggressive cancer. Current treatment options often have limited effectiveness, highlighting the need for new therapies

Obrixtamig is an investigational compound designed to help the body's immune system recognize and attack cancer cells by targeting a protein called delta-like ligand 3 (DLL3). DAREON®-7 is a clinical trial investigating whether obrixtamig is effective when combined with existing chemotherapy in patients with DLL3-positive NEC

The safety and efficacy results observed are promising and provide rationale for further research in patients with DLL3-positive epNEC

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Key Findings and Conclusions

- In total, 44 patients with 1L DLL3-positive NEC were treated with obrixtamig + SoC; 54.5% had DLL3^{high} tumors
- The observed safety profile was consistent with the known safety profiles of individual treatment components across DLL3 subgroups
- Encouraging response rates were observed regardless of DLL3 expression status, with a trend toward improved duration of response in the DLL3^{high} subgroup; longer follow-up is needed
- These findings provide a strong rationale for evaluating obrixtamig + SoC in patients with 1L DLL3-positive epNEC in the ongoing Phase III DAREON®-NEC-1 trial (NCT07544654)

Patients

n (%)**	All (N=44)	DLL3^{low} (n=20)	DLL3^{high} (n=24)
Median age, years (range)	64.5 (35–79)	62.0 (39–79)	65.0 (35–78)
Female	21 (47.7)	9 (45.0)	12 (50.0)
Male	23 (52.3)	11 (55.0)	12 (50.0)
Race			
White	27 (61.4)	11 (55.0)	16 (66.7)
Asian	9 (20.5)	5 (25.0)	4 (16.7)
Black	2 (4.5)	2 (10.0)	0
Other†† or missing	6 (13.6)	2 (10.0)	4 (16.7)
ECOG PS			
0	26 (59.1)	12 (60.0)	14 (58.3)
1	18 (40.9)	8 (40.0)	10 (41.7)
Metastases			
Brain	1 (2.3)	0	1 (4.2)
Liver	34 (77.3)	16 (80.0)	18 (75.0)

Tumor type, n (%)	All (N=44)	DLL3^{low} (n=20)	DLL3^{high} (n=24)
epNEC	40 (90.9)	19 (95.0)	21 (87.5)
GEP	35 (79.5)	17 (85.0)	18 (75.0)
GU	2 (4.5)	0 (0.0)	2 (8.3)
Other	3 (6.8)	2 (10.0)	1 (4.2)
LCNEC-L	2 (4.5)	0 (0.0)	2 (8.3)
NEC of unknown primary site	2 (4.5)	1 (5.0)	1 (4.2)

**Unless otherwise specified; ††one patient of American Indian/Alaska Native descent

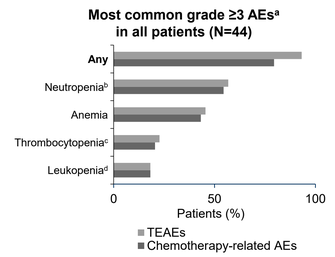
- As of February 3, 2026, 44 patients had received ≥1 cycle of obrixtamig
- Baseline characteristics were similar between DLL3 subgroups

Safety

- Obrixtamig + SoC had a manageable safety profile across DLL3 subgroups
- All cases of obrixtamig-related CRS were grade 1 or 2
- Obrixtamig-related ICANS and potential ICANS-like neurotoxicity events were infrequent (n=2; 4.5%) and grade 1¶¶
- Grade ≥3 TEAEs were predominantly chemotherapy-related

n (%)	All (N=44)		DLL3^{low} (n=20)		DLL3^{high} (n=24)	
	Any grade	Grade ≥3‡‡	Any grade	Grade ≥3	Any grade	Grade ≥3
TEAEs	44 (100)	41 (93.2)	20 (100)	19 (95.0)	24 (100)	22 (91.7)
Obrixtamig-related AEs	39 (88.6)	8 (18.2)	16 (80.0)	4 (20.0)	23 (95.8)	4 (16.7)
Most common obrixtamig-related AEs§§						
CRS	32 (72.7)	0	10 (50.0)	0	22 (91.7)	0

n (%)	All (N=44)		DLL3^{low} (n=20)		DLL3^{high} (n=24)	
	Any grade	Grade ≥3‡‡	Any grade	Grade ≥3	Any grade	Grade ≥3
TEAEs	44 (100)	41 (93.2)	20 (100)	19 (95.0)	24 (100)	22 (91.7)
Chemotherapy-related AEs	44 (100)	35 (79.5)	20 (100)	18 (90.0)	24 (100)	17 (70.8)
Most common chemotherapy-related AEs§§						
Neutropenia	30 (68.2)	24 (54.5)	16 (80.0)	14 (70.0)	14 (58.3)	10 (41.7)
Anemia	25 (56.8)	19 (43.2)	10 (50.0)	7 (35.0)	15 (62.5)	12 (50.0)
Dysgeusia	23 (52.3)	0	10 (50.0)	0	13 (54.2)	0



‡‡One grade 5 AE occurred (malignant neoplasm progression), this was not related to obrixtamig; §§any-grade AEs in ≥50% patients in the overall population; ¶¶both events were ICANS (DLL3^{high}: n=1; DLL3^{low}: n=1); [a]grade ≥3 AEs in ≥10% patients in the overall population; [b]neutropenia includes preferred terms of neutropenia and neutrophil count decreased; [c]thrombocytopenia includes preferred terms of thrombocytopenia and platelet count decreased; [d]leukopenia includes preferred terms of leukopenia and white blood cell decreased

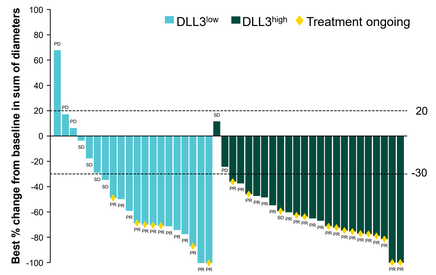
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1. Dasari A, et al. Cancer 2018;124:807–15; **2.** Eads J, et al. Endocr Relat Cancer 2023;30:e220206; **3.** Raj N & Byers LA. Cancer Treat Rev 2026;149:103195; **4.** Gambardella V, et al. ASCO 2026; Poster #2642; **5.** Wermke M, et al. Future Oncol 2022;18:2639–49; **6.** Hipp S, et al. Clin Cancer Res 2020;26:5258–68; **7.** Albayrak G, et al. Br J Cancer 2025;133:1241–49

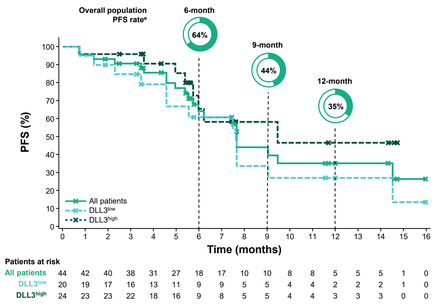
Abbreviations: 1L, first-line; AE, adverse event; BLRM, Bayesian logistic regression model; CD3, cluster of differentiation 3; CI, confidence interval; CRS, cytokine release syndrome; DCR, disease control rate; DLL3, delta-like ligand 3; DLTs, dose-limiting toxicities; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; epNEC, extrapulmonary neuroendocrine carcinoma; Fc, fragment crystallizable region; GEP, gastroenteropancreatic; GU, genitourinary; ICANS, immune effector cell–associated neurotoxicity syndrome; IgG, immunoglobulin G; LCNEC-L, large cell neuroendocrine carcinoma of the lung; NC, not calculable; NEC, neuroendocrine carcinoma; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; Q3W, once every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; RP2D, recommended Phase II dose; SD, stable disease; SoC, standard of care; TEAE, treatment-emergent AE

Efficacy

- Obrixtamig + SoC achieved deep and durable responses across DLL3 subgroups, with a trend toward enhanced efficacy in the DLL3^{high} subgroup
- Promising PFS was observed with obrixtamig + SoC, particularly in the DLL3^{high} subgroup



	All (N=44)	DLL3^{low} (n=20)	DLL3^{high} (n=24)
ORR, % (95% CI)	**77.3** (63.0–87.2)	**65.0** (43.3–81.9)	**87.5** (69.0–95.7)
PR, n (%)	34 (77.3)	13 (65.0)	21 (87.5)
DCR, % (95% CI)	**90.9** (78.8–96.4)	**85.0** (64.0–94.8)	**95.8** (79.8–99.3)
SD, n (%)	6 (13.6)	4 (20.0)	2 (8.3)
PD, n (%)	4 (9.1)	3 (15.0)	1 (4.2)
Median DoR, months (95% CI)	**12.5** (5.5–NC)	**7.0** (5.5–NC)	**NC** (5.1–NC)
12-month DoR rate, % (95% CI)[e]	**51** (29–73)	**46** (13–79)	**54** (24–85)



	All (N=44)	DLL3^{low} (n=20)	DLL3^{high} (n=24)
Median PFS, months (95% CI)	7.7 (6.0–14.5)	7.6 (4.6–9.0)	9.5 (6.0–NC)
PFS rate, % (95% CI)[e]			
6-month	64 (48–80)	61 (38–84)	66 (42–89)
9-month	44 (26–63)	34 (10–57)	58 (34–83)
12-month	35 (17–54)	27 (5–49)	47 (18–75)

[e]Kaplan–Meier estimates

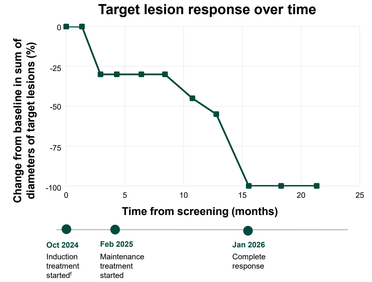
Median duration of follow up for PFS in the overall population: 11.6 months (95% CI: 5.8–14.3)

Case Study: Complete Response in DLL3^{high} epNEC

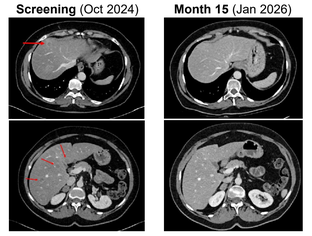
- **July 2024:** 63-year-old female diagnosed with primary tumor of the vagina, classified as epNEC
- **October 2024:** surgical resection
  - DLL3 testing of the primary tumor showed **76% tumor cell staining (DLL3^{high})**
  - Initial staging showed hepatic metastases across several segments, with one target lesion of 20 mm in the liver dome
- **October 2024–January 2025:** 6 cycles of induction (obrixtamig + carboplatin + etoposide)[f]
  - Induction treatment resulted in a **partial response**
- **February 2025:** obrixtamig maintenance initiated
  - During maintenance treatment liver lesions showed consistent tumor shrinkage
- **January 2026:** the patient reached a **complete response**, confirmed in **July 2026**

Sustained shrinkage of liver lesions was observed, leading to durable complete response

Target lesion response over time



Radiologic response



No visible target lesions at Month 15

As of last follow-up, the patient is in complete response and has remained on treatment for nearly 2 years, demonstrating favorable long-term tolerability

We thank Dr Mitry for providing this case study

[f]Obrixtamig treatment initiated as planned on Nov 7, 2024, after one cycle of carboplatin + etoposide (administered per protocol in Oct 2024, during DLL3 testing)

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*Corresponding author email address: Aman.Chauhan@ucsf.edu

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