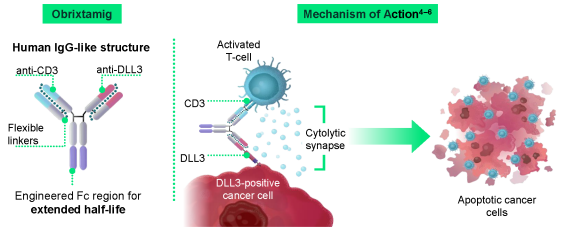
Subgroup analysis of the ongoing Phase Ib DAREON®-7 study: Outcomes with first-line obrixtamig plus standard of care in neuroendocrine carcinomas by DLL3 expression status

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

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

Introduction

- Platinum + etoposide is the current 1L SoC treatment for extrapulmonary NEC,[1] but **median OS remains ≤1 year**[2]
- DLL3 is expressed on tumor cells in up to ~83% of patients with extrapulmonary NEC, with substantial variability in expression levels[3]
- Obrixtamig (BI 764532) is a novel, DLL3/CD3 IgG-like T-cell engager[4–6]
- In the ongoing DAREON®-7 trial, 1L obrixtamig + SoC showed manageable safety and encouraging efficacy in patients with DLL3-positive NEC[7]
- We report a subgroup analysis of the DAREON®-7 trial by DLL3 expression status



1L, first-line; CD3, cluster of differentiation 3; DLL3, delta-like ligand 3; Fc, fragment crystallizable region; IgG, Immunoglobulin G; NEC, neuroendocrine carcinoma; OS, overall survival; SoC, standard of care

Methods

DAREON®-7 (NCT06132113): Phase I dose-escalation/expansion trial of 1L obrixtamig + SoC

Patient population
- Locally advanced/metastatic extrapulmonary NEC, 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: DLTs
Secondary endpoint: Part A: AEs and DLTs; Part B: ORR and DoR†
Further endpoint: PFS†

DLL3 expression status
Categorized by the proportion 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%

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
AE, adverse event; BLRM, Bayesian logistic regression model; DLT, dose-limiting toxicity; DoR, duration of response; LCNEC-L, large cell neuroendocrine carcinoma of the lung; ORR, objective response rate; PFS, progression-free survival; Q3W, every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; RP2D, recommended Phase II dose.

Key Findings and Conclusions

- Overall, 44 patients with DLL3-positive NEC received 1L obrixtamig + SoC
- Of these patients:
  - 54.5% had DLL3^{high} tumors
  - 45.5% had DLL3^{low} tumors
- A favorable safety profile was maintained regardless of DLL3 expression status
- Encouraging efficacy was shown across both DLL3 subgroups, with numerically higher response rates and durable responses in the DLL3^{high} subgroup; longer follow up is needed
- These findings provide a strong rationale for evaluating 1L obrixtamig + SoC in patients with DLL3-positive extrapulmonary NEC in the ongoing Phase III DAREON®-NEC-1 trial (NCT07544654)

Patients

- Baseline characteristics were similar across DLL3 subgroups; 54.5% of patients had DLL3^{high} tumors

n (%)**	All (N=44)	DLL3^{high} (n=24)	DLL3^{low} (n=20)
Median age, years (range)	64.5 (35–79)	65.0 (35–78)	62.0 (39–79)
Female	21 (47.7)	12 (50.0)	9 (45.0)
Male	23 (52.3)	12 (50.0)	11 (55.0)
Race			
White	27 (61.4)	16 (66.7)	11 (55.0)
Asian	9 (20.5)	4 (16.7)	5 (25.0)
Black	2 (4.5)	0	2 (10.0)
Other†† or missing	6 (13.6)	4 (16.7)	2 (10.0)
ECOG PS			
0	26 (59.1)	14 (58.3)	12 (60.0)
1	18 (40.9)	10 (41.7)	8 (40.0)
Metastases			
Brain	1 (2.3)	1 (4.2)	0
Liver	34 (77.3)	18 (75.0)	16 (80.0)
Primary tumor location			
Extrapulmonary NEC	40 (90.9)	21 (87.5)	19 (95.0)
LCNEC-L	2 (4.5)	2 (8.3)	0
CUP-NEC	2 (4.5)	1 (4.2)	1 (5.0)

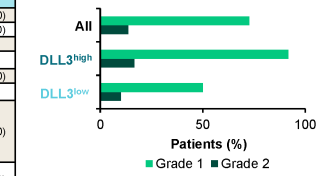
At data cut-off (February 3, 2026), 44 patients had received ≥1 cycle of obrixtamig.
**Unless otherwise specified; ††One patient of American Indian/Alaska Native descent.
CUP-NEC, neuroendocrine carcinoma of unknown primary site; ECOG PS, Eastern Cooperative Oncology Group performance status.

Safety

- The safety profile of obrixtamig + SoC was aligned with known profiles of individual components across both DLL3 subgroups

n (%)	All N=44		DLL3^{high} n=24		DLL3^{low} n=20	
	Any grade	Grade ≥3‡‡	Any grade	Grade ≥3	Any grade	Grade ≥3
TEAEs	44 (100)	41 (93.2)	24 (100)	22 (91.7)	20 (100)	19 (95.0)
Obrixtamig-related AEs	39 (88.6)	8 (18.2)	23 (95.8)	4 (16.7)	16 (80.0)	4 (20.0)
Most common obrixtamig-related AEs¶¶						
CRS	32 (72.7)	0	22 (91.7)	0	10 (50.0)	0
Chemotherapy-related AEs	44 (100)	35 (79.5)	24 (100)	17 (70.8)	20 (100)	18 (90.0)
Most common chemotherapy-related AEs¶¶						
Neutropenia	30 (68.2)	24 (54.5)	14 (58.3)	10 (41.7)	16 (80.0)	14 (70.0)
Anemia	25 (56.8)	19 (43.2)	15 (62.5)	12 (50.0)	10 (50.0)	7 (35.0)
Dysgeusia	23 (52.3)	0	13 (54.2)	0	10 (50.0)	0

All cases of CRS were grade 1 or 2

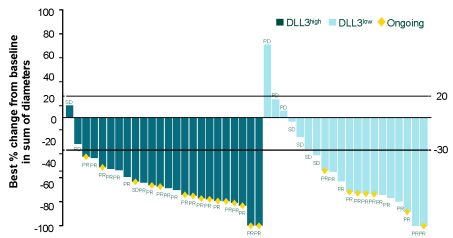


Obrixtamig-related ICANS and potential ICANS-like neurotoxicity were infrequent (n=2; 4.5%) and grade 1[a]

‡‡One grade 5 AE occurred (malignant neoplasm progression), this was not related to obrixtamig; ¶¶Any-grade AEs in ≥50% of patients in the overall population; [a]Both cases were ICANS (DLL3^{high}: n=1; DLL3^{low}: n=1).
CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent AE.

Efficacy

- High antitumor activity was seen across DLL3 subgroups, with a trend toward deeper and more durable benefit in the DLL3^{high} subgroup



	All (N=44)	DLL3^{high} (n=24)	DLL3^{low} (n=20)
ORR, % (95% CI)	77.3 (63.0–87.2)	87.5 (69.0–95.7)	65.0 (43.3–81.9)
PR, n (%)	34 (77.3)	21 (87.5)	13 (65.0)
DCR, % (95% CI)	90.9 (78.8–96.4)	95.8 (79.8–99.3)	85.0 (64.0–94.8)
SD, n (%)	6 (13.6)	2 (8.3)	4 (20.0)
PD, n (%)	4 (9.1)	1 (4.2)	3 (15.0)
Median DoR, months (95% CI)[b]	12.5 (5.5–NC)	NC (5.1–NC)	7.0 (5.5–NC)
12-month DoR rate, % (95% CI)[c]	51 (29–73)	54 (24–85)	46 (13–79)
Median PFS, months (95% CI)[b]	7.7 (6.0–14.5)	9.5 (6.0–NC)	7.6 (4.6–9.0)
12-month PFS rate, % (95% CI)[c]	35 (17–54)	47 (18–75)	27 (5–49)

At data cut-off (February 3, 2026), 22 patients remained on obrixtamig treatment (DLL3^{high}: n=15; DLL3^{low}: n=7).
[b]Median duration of follow-up in the overall population: DoR, 7.1 months (95% CI: 4.9–11.0); PFS, 11.8 months (95% CI: 5.8–14.3); [c]Kaplan–Meier estimates.
CI, confidence interval; DCR, disease control rate; NC, not calculable; PD, progressive disease; PR, partial response; SD, stable disease.

References

1. Eads JR, et al. Endocr Relat Cancer 2023;30:e220206; **2.** Raj N & Byers LA. Cancer Treat Rev 2026;149:103195; **3.** Gambardella V, et al. ASCO 2026; Poster #2642; **4.** Wermke M, et al. Future Oncol 2022;18(24):2639–49; **5.** Hipp S, et al. Clin Cancer Res 2020;26(19):5258–68; 6. Boehringer Ingelheim. Data on File; **7.** Capdevila J, et al. ENETS 2026; Oral presentation #E05.

Jaume Capdevila reports advisory role for Advanced Accelerator Applications, Bayer, Boehringer Ingelheim, Eisai, Eli Lilly, Esteve, Exelixis, Ipsen, Isotopen Technologien, Merck, Novartis, Pfizer, Roche/Genentech, and Sanofi; Travel, accommodations, and expenses for Eisai, Gilead Sciences, Ipsen, Novartis, and Pfizer; Research funding for Advanced Accelerator Applications, Amgen, AstraZeneca, Bayer, Eisai, Gilead Sciences, Ipsen, ITM Solucin, Novartis, Pfizer, and Roche/Genentech; Speaker's bureau for Bayer, Boehringer Ingelheim, Eisai, Eli Lilly, Esteve, Hutchison MediPharma, Ipsen, Isotopen Technologien, Merck, Novartis, Pfizer, and Sanofi.

Presented at the Network for Collaborative Oncology Development & Advancement (NCODA) International Fall Summit, Orlando, FL, USA, October 28–30, 2026

Originally presented at the European Society for Medical Oncology (ESMO) congress, Madrid, Spain, October 23–27, 2026

*Corresponding author email address: jcapdevila@vhio.net

Reused with permission from the European Society for Medical Oncology (ESMO). This abstract was accepted and previously presented by Jaume Capdevila et al. at ESMO 2026, FPN (Final Publication Number): XXX, Annals of Oncology, Volume XX, 2026 Supplement XX. All rights reserved

This study is funded by Boehringer Ingelheim. The authors meet the criteria for authorship as recommended by the International Committee of Medical Journal Editors. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development, and have approved the final version. The authors did not receive payment related to the development of the poster. Editorial support for this encore poster (in the form of poster layout and formatting) was provided by Isabela Laughland, MSc, of Nucleus Global, an Inizio company, and funded by Boehringer Ingelheim Pharmaceuticals, Inc (BIPI). Writing, editorial support, and formatting assistance for the original presentation was provided by Lucinda Sinclair, MSc, of Ashfield MedComms, an Inizio company. BIPI was given the opportunity to review the poster for medical and scientific accuracy as well as intellectual property considerations

Scan this QR code or visit the URL to access the poster presentation

https://qo.boehringer.com/xv2m

Materials obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from the authors of this presentation