

## C-8

# DAREON®-7: Phase I open-label dose-escalation/-expansion study of first-line obixtamig (BI 764532) plus chemotherapy in patients with DLL3-positive neuroendocrine carcinomas

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## BACKGROUND

Delta-like ligand 3 (DLL3) is widely expressed in neuroendocrine carcinomas (NECs). Obixtamig is a DLL3/CD3 IgG-like T-cell engager that binds simultaneously to DLL3 on tumor cells and CD3 on T-cells. We report initial safety and efficacy data from the dose escalation part of the Phase I DAREON®-7 (NCT06132113) trial assessing obixtamig plus simultaneous chemotherapy (carboplatin plus etoposide) in patients with DLL3-positive NECs.

## METHODS

Patients had locally advanced/metastatic DLL3-positive extrapulmonary NEC (epNEC), large cell NEC of the lung (LCNEC-L), or NEC of unknown primary site. Obixtamig was given as step-up dosing followed by target dose (3 dose levels), guided by a Bayesian Logistic Regression Model with overdose control. Carboplatin plus etoposide was given per label. Antitumor activity was assessed using RECIST v1.1 (investigator-assessed). The ongoing dose expansion part will assess obixtamig plus chemotherapy at the dose selected during dose escalation.

## RESULTS

As of May 16, 2025, 27 patients were enrolled (epNEC: 78%, LCNEC-L: 7%, unknown primary site: 15%; median age: 67 years (range: 42–79); ECOG PS: 0/1, 70%/30%). Overall, 26 patients received  $\geq 1$  dose of obixtamig plus carboplatin and etoposide; in these patients, median number of obixtamig cycles: 7 (range: 1–14); median treatment exposure: 4.4 months (range: 0.1–8.9). There were no dose-limiting toxicities; maximum tolerated dose was not reached. Most frequent adverse events (AEs) are shown in Table 1. No patients discontinued obixtamig due to AEs. One patient (4%) experienced a potential obixtamig-related neurotoxicity (grade [G]1 immune effector cell-associated neurotoxicity syndrome). One patient (4%) experienced G3 febrile neutropenia. Among 16 patients with cytokine release syndrome (CRS; 59%), most cases (n=13, 48%) were G1, with no cases  $G \geq 3$ . Confirmed objective response rate in evaluable patients (n=21): 76% (95% CI: 55–89; partial response 76%, stable disease 10%, progressive disease 10%); disease control rate: 86% (95% CI: 65–95). Confirmed median duration of response was not reached.

Most common AEs		
n (%)		
<b>AEs (in n<math>\geq</math>10)</b>	25 (93)	21 (78)
Neutropenia and/or neutrophil count decreased	17 (63)	16 (59)
CRS	16 (59)	0
Constipation	13 (48)	0
Anemia	12 (44)	9 (33)
Decreased appetite	10 (37)	1 (4)
Dysgeusia	10 (37)	0
<b>Obixtamig-related AEs</b>	23 (85)	1 (4)

## CONCLUSIONS

Obixtamig plus chemotherapy was tolerable with no unexpected toxicities. The reported frequency/severity of AEs was consistent with the expected safety profile of the individual treatments, with no additional toxicities. Preliminary efficacy results were encouraging, warranting further development of the combination in this setting.

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