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DAREON®-8: A phase I trial of first-line obrixtamig plus chemotherapy and atezolizumab in extensive-stage small cell lung carcinoma (ES-SCLC)

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Background

Obrixtamig (BI 764532) is a DLL3/CD3 IgG-like T-cell engager. We report the first safety and efficacy data for the dose escalation part of the Phase I DAREON®-8 (NCT06077500) trial investigating obrixtamig + first-line (1L) SoC (carboplatin + etoposide + atezolizumab) in patients (pts) with ES-SCLC.

Methods

Pts received IV obrixtamig as step-up dosing followed by target dose (3 dose levels) plus SoC. Dose escalation was guided by a BLRM with overdose control. Obrixtamig treatment (Tx) was continued until progression, unacceptable toxicity, or withdrawal. The primary endpoint was occurrence of dose-limiting toxicities (DLTs) during the maximum tolerated dose (MTD) evaluation period. Secondary endpoints included objective response (OR; investigator-assessed) according to RECIST v1.1.

Results

Pts (n = 22) received ≥1 dose of obrixtamig plus SoC. Median number of cycles for obrixtamig plus SoC was 5 (range: 1–12). Median age was 68 yrs (range: 44–75); ECOG PS was 0/1 in 23/77% of pts. There was one obrixtamig-related DLT during the MTD evaluation period (grade [G]3 tumor-related pain); the MTD was not reached. There were no G5 AEs. Tx-related adverse events (TRAEs) and obrixtamig-related AEs are shown in the table. The rate of cytopenias was as expected for a chemotherapy-based combination; only one case of G2 neutropenia related to obrixtamig but not SoC. Cytokine release syndrome was observed in 46% of patients, with no G≥3 events. No pts discontinued Tx due to TRAEs. The dose expansion part has been initiated based on the safety observation in dose escalation.Table: 2759MO

N (%)	All grade AEs	Grade ≥3 AEs
Any treatment-related AEs*	22 (100)	17 (77)
Neutropenia	15 (68)	12 (55)
Anemia	14 (64)	5 (23)
Obrixtamig-related AEs*	21 (96)	6 (27)
Neutropenia	6 (27)	4 (18)
Only related to obrixtamig	1 (5)	0 (0)
Patients with ≥1 obrixtamig-related potential neurological toxicity	3 (14)	0 (0)
Immune effector cell-associated neurotoxicity syndrome	1 (5)	0 (0)
Dizziness	1 (5)	0 (0)
Muscle spasm	1 (5)	0 (0)
Patients with ≥1 episode of cytokine release syndrome	10 (46)	0 (0)

*In >10% of patients (Grade >3 AEs)

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Conclusions

Obrixtamig + SoC was tolerable with no unexpected toxicities; MTD was not reached. The frequency and severity of AEs reported for the combination were consistent with the expected safety findings of the individual treatments. The combinability of obrixtamig with chemotherapy and an anti-PDL1 antibody observed in this trial warrant further development of this combination in 1L ES-SCLC.

Clinical trial identification

NCT06077500.

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Legal entity responsible for the study

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Disclosure

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