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Obrixtamig (BI 764532) in relapsed/refractory delta-like ligand 3 (DLL3)-high extrapulmonary neuroendocrine carcinoma: Phase II DAREON®-5 dose-expansion trial in progress

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BACKGROUND

Patients with relapsed/refractory extrapulmonary neuroendocrine carcinoma (epNEC) have poor outcomes with currently available therapies. DLL3 is expressed on the surface of many epNEC cells, offering a promising therapeutic target. Obrixtamig (BI 764532) is a DLL3/CD3 IgG-like T-cell engager that binds simultaneously to CD3 on T-cells and to DLL3 on tumor cells, resulting in immune-mediated tumor cell lysis. In an ongoing first-in-human Phase I trial (NCT04429087), obrixtamig monotherapy had promising efficacy in patients with DLL3+ small-cell lung cancer (SCLC), epNEC or large-cell NEC of the lung (LCNEC-L) and a manageable toxicity profile, justifying further clinical investigation. The Phase II DAREON®-5 trial (NCT05882058) is a dose selection and expansion trial of obrixtamig monotherapy in patients with histologically confirmed relapsed/refractory SCLC, epNEC or LCNEC-L after prior standard of care. The completed dose selection part evaluated the safety and efficacy of two obrixtamig doses in patients with relapsed/refractory SCLC, epNEC or LCNEC-L. We describe the expansion part of the study that is currently enrolling.

METHODS

The expansion part of DAREON®-5 is assessing obrixtamig antitumor activity at the selected dose for expansion in patients with centrally assessed DLL3-high expressing epNEC. DLL3-high is defined as ≥50% of evaluable tumor cells with moderate to strong membrane and/or cytoplasmic DLL3 staining using the VENTANA DLL3 (SP347) assay. Eligible patients have relapsed/refractory, advanced/metastatic, histologically confirmed DLL3-high epNEC after prior platinum-based chemotherapy (≥1 lines of therapy). Patients will receive intravenous obrixtamig infusions as step-up doses followed by the target dose, which was defined in the dose selection part of the trial. The primary endpoint is objective response per RECIST v1.1, assessed by blinded independent central review. Secondary endpoints include duration of objective response, progression-free survival, disease control rate,

overall survival, treatment-emergent adverse events, and patient-reported outcomes. The planned enrollment for the expansion cohort is ~50 patients recruited from the following countries: Belgium, China, Germany, Japan, South Korea, Spain, UK, and USA.

RESULTS

N/A

CONCLUSIONS

N/A

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