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DAREON™-7: Phase 1 trial of BI 764532 (a delta-like ligand 3 [DLL3]-targeting T-cell engager) plus chemotherapy for DLL3+ neuroendocrine carcinomas

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BACKGROUND

Neuroendocrine carcinomas (NECs) have limited treatment options. Delta-like ligand 3 (DLL3) is highly expressed in NECs and is a promising treatment target. In an ongoing phase 1 trial (NCT04429087), BI 764532, a DLL3/CD3 immunoglobulin G (IgG)-like T-cell engager, was tolerable with promising activity in patients with DLL3-positive (+) tumors, including those with NECs. DAREON™-7 (NCT06132113) is a phase 1, open-label, dose-escalation (Part A) and dose-expansion (Part B) trial that aims to determine the maximum-tolerated dose (MTD), the recommended dose for expansion (RDE)/recommended phase 2 dose (RP2D), and the safety and efficacy of BI 764532 in combination with platinum and etoposide in patients with DLL3+ NEC.

METHODS

Part A: ~25 patients will receive intravenous BI 764532 (target dose after step-in dosing) plus carboplatin/etoposide until progression per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, intolerable toxicity, or for a maximum of 36 months. BI 764532 dose escalation will be guided by a Bayesian logistic regression model with overdose control. Part B: 2 cohorts (~15 patients each) will receive BI 764532 at RDE/RP2D + carboplatin/etoposide or cisplatin/etoposide (carboplatin/etoposide or cisplatin/etoposide are the most-used standard of care [SOC] regimens). Key inclusion criteria: Patients must have no prior systemic treatment for DLL3+ locally advanced or metastatic NEC (extrapulmonary or unknown primary) or large-cell NEC of the lung except for 1 cycle of standard platinum/etoposide regimen as first-line treatment prior to entering the treatment period of the trial; patients with localized NEC or resectable disease who received prior adjuvant therapy can participate in the trial if they experienced a treatment-free interval of >6 months prior to the diagnosis of metastatic disease; and patients must have at least 1 measurable lesion as defined per RECIST v1.1. Patients must be adequate candidates to receive platinum/etoposide as the SOC treatment.

Primary endpoints: Occurrence of dose-limiting toxicities (DLTs) in the MTD evaluation (Part A) and on-treatment (Part B) periods. Secondary endpoints: Occurrence of DLTs and adverse events during the on-treatment period (Part B), and efficacy measured by objective response and duration of response (Part B).

RESULTS

DAREON™-7 is currently enrolling.

CONCLUSIONS

Not applicable—the trial is currently in progress.

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