A PHASE I/II TRIAL OF INTRACEREBROVENTRICULAR 177LU DTPA OMBURTAMAB RADIOIMMUNOTHERAPY FOR LEPTOMENINGEAL METASTASIS FROM SOLID TUMORS

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Background Leptomeningeal metastasis (LM) from solid tumors may be diagnosed in approximately 10% of patients with metastatic cancer and can occur with virtually all malignant tumors. Median overall survival (OS) is poor and limited to a few months with LM-directed treatment, including available targeted therapy, immunotherapy and radiation therapy. Omburtamab specifically binds to B7-H3 (CD276), a transmembrane glycoprotein of the immunoglobulin superfamily. The limited expression of B7-H3 on normal cells, including normal brain, combined with the broad expression in various types of solid tumors, makes B7-H3 a target for radioimmunotherapy of LM from solid tumors. In this first-in-human trial the safety and efficacy of intracerebroventricular administration of radiolabeled omburtamab, 177Lu-DTPA-omburtamab, will be evaluated in patients with LM from ductal or lobular breast cancer, non-small cell lung cancer, or melanoma.

Methods This is an open-label phase I/II study. Part 1 is a dose-escalation phase to be conducted at ~4 sites (US/Europe) with a primary objective of identifying the maximum tolerated dose and/or recommended phase II dose for Part 2 (RP2D). It will follow a 3+3 design with pts receiving up to five 5-week cycles of 177Lu-DTPA-omburtamab. Part 2 is a cohort-expansion phase at ~9 sites (US/Europe) in which a maximum of 48 patients in 3 cohorts (ductal or lobular breast cancer [cohort A], non-small cell lung cancer [cohort B], and melanoma [cohort C]) with up to 16 patients in each will receive up to five 5 week cycles of treatment with intracerebroventricular 177Lu DTPA omburtamab at the RP2D determined in Part 1. The primary objective of Part 2 is to establish the safety of repeat doses of 177Lu-omburtamab. Additional objectives of Parts 1/2 include the evaluation of absorbed radiation doses, PK profile, investigator-assessed response, duration of response, progression-free survival, and OS. Key inclusion criteria include diagnosis of either ductal or lobular breast cancer, non-small cell lung cancer, or malignant melanoma and diagnosis of recurrent or refractory LM; prior standard of care treatment of leptomeningeal disease; acceptable hematological, liver and kidney status; and a life expectancy of >2 months. The study has been approved by each institution’s ethics board, and patients provided informed consent before taking part.

Trial Registration NCT04315246

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