T-5

Phase 1/2 Open-Label Trial to Assess the Safety and Preliminary Efficacy of ^{177}Lu-OPS201 as Peptide Receptor Radionuclide Therapy in Patients with Somatostatin Receptor-Positive, Progressive Neuroendocrine Tumors

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BACKGROUND: Peptide receptor radionuclide therapy (PRRT) with radiolabeled somatostatin receptor (SSTR) agonists is a highly effective neuroendocrine tumor (NET) treatment. However, tumor uptake and tumor-to-tissue dose ratios may be higher with radiolabeled SSTR antagonists than agonists. OPS201 (DOTA-JR11) is a very promising next-generation SSTR antagonist selective for SSTR2 (expressed by NETs). This phase 1/2, international, single-arm, open-label study will evaluate ^{177}Lu-OPS201 as PRRT in 45 adults with unresectable, SSTR-positive, progressive gastroenteropancreatic (GEP)-NETs, lung NETs, phaeochromocytomas and paragangliomas.

METHODS: Patients are recruited at 15 sites in Australia, Europe, and the USA with experience in PRRT (or other radionuclide therapy). The core trial comprises phases A and B. Phase A: six patients receive three cycles of ^{177}Lu-OPS201 at 4.5 GBq over 24 weeks; another nine patients receive three cycles of ^{177}Lu-OPS201 at 4.5 GBq, or an activity not evoking dose-limiting toxicity, dependent on initial safety/dosimetry data. Phase B: 30 patients receive three cycles of ^{177}Lu-OPS201 at up to 7.4 GBq, dependent on phase-A safety/dosimetry data. In a subsequent long-term follow-up, tumor response (centrally reviewed [RECIST v1.1]) will be assessed every 3 months from the end-of-core-trial visit for 2 years, or until progressive disease/death. This core study and long-term follow-up are together expected to last 42–45 months.

RESULTS: The primary endpoint is safety/tolerability (based on physical examination, vital signs, electrocardiogram, laboratory measurements, adverse events, dose-limiting toxicities, concomitant medication, pituitary markers, and bone marrow aspirate in case of persisting toxicities of grade 3 or more). Secondary endpoints include: biodistribution and pharmacokinetics (maximal uptake, area-under-curve, terminal half-life); radiation dosimetry; preliminary efficacy (tumor response, progression-free survival), and quality-of-life. Treatment in phase A is underway.

CONCLUSION: This study will provide information regarding the safety and efficacy of ^{177}Lu-OPS201 as PRRT in SSTR-positive, progressive GEP-NETs, lung NETs, phaeochromocytomas and paragangliomas (EudraCT 2015-002867-41; NCT02592707).