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Compose: Pivotal Phase III Trial of ^{177}Lu-Edotreotide Versus Best Standard of Care in Well-differentiated Aggressive Grade 2 and Grade 3 Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs), which represent approximately 70% of NETs, frequently develop metastatic disease with limited treatment options. Current standard therapies for the subset of well-differentiated high grade 2 and grade 3 GEP-NETs include cytoreductive procedures, somatostatin analogues, molecular targeted therapies (everolimus or sunitinib), chemotherapy and peptide receptor radionuclide therapy (PRRT), with no specified sequence of use. PRRT may stabilize disease and induce objective tumor responses. This treatment uses radiolabeled somatostatin analogues to selectively target tumor cells expressing somatostatin receptor 2. PRRT in the form of ^{177}Lu-edotreotide is an innovative radiolabeled somatostatin analogue with a favorable safety profile and promising efficacy. The currently recruiting Phase III trial COMPETE in grade 1 and grade 2 GEP-NETs is comparing

the efficacy and safety of ^{177}Lu-edotreotide, versus everolimus. Retrospective data in metastatic GEP-NETs treated with two or more ^{177}Lu-edotreotide cycles demonstrated a PFS of at least 30 months.

METHODS: COMPOSE (NCT04919226) is a prospective, randomized, controlled, open-label, multi-center Phase III study to evaluate efficacy, safety and patient-reported outcomes of first- or later-line treatment with ^{177}Lu-edotreotide PRRT compared to best standard of care in patients with well-differentiated high grade 2 and 3 (Ki-67 index 15_55), SSTR+, GEP-NETs. It aims to randomize 202 patients 1:1 to a defined number of cycles of 177Lu-Edotreotide or an active comparator - either chemotherapy (CAPTEM or FOLFOX) or everolimus - according to investigator´s choice. The primary endpoint is progression free survival, assessed every 12 weeks until disease progression (RECIST v1.1), or death, whichever occurs earlier. Secondary outcomes include overall survival, assessed up to 2 years after disease progression.

RESULTS: Study recruitment for COMPOSE commenced in September 2021.

CONCLUSION: It is expected that COMPOSE will increase treatment options for patients with well-differentiated high grade 2 and grade 3 GEP-NETs, including for first-line therapy.

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