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STELLAR-311: A randomized phase 2/3 study of zanzalintinib versus everolimus in patients with previously treated advanced neuroendocrine tumors

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BACKGROUND

Targeted therapy options for patients with previously treated neuroendocrine tumors (NETs) include the mammalian target of rapamycin (mTOR) inhibitor everolimus and the vascular endothelial growth factor receptor tyrosine kinase inhibitors (VEGFR-TKIs) sunitinib and cabozantinib. Zanzalintinib, a novel, oral, multi-targeted inhibitor of VEGFR, MET, and the TAM (TYRO3, AXL, and MER) kinases, has a similar kinase inhibition profile to cabozantinib but has a shorter half-life and has shown preferential in vivo tumor distribution. In early-stage clinical studies, zanzalintinib has demonstrated promising antitumor activity and a consistent safety profile across multiple solid tumors. Based on these attributes, STELLAR-311 was designed to evaluate the efficacy and safety of zanzalintinib versus everolimus in patients with locally advanced or metastatic NETs.

METHODS

STELLAR-311 (NCT06943755) is a multicenter, randomized, open-label, phase 2/3 study. Key eligibility criteria include age ≥18 years; locally advanced/unresectable or metastatic, well-differentiated, grade 1–3 NET originating from the gastrointestinal tract, lung, pancreas, thymus, or other primary sites; measurable disease per Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1); and documented radiographic disease progression per RECIST v1.1 within 12 months before randomization. Patients must have received prior systemic treatment based on the site of the NET and functional status (pancreatic NET and nonfunctional extra-pancreatic NET, up to one prior line; functional extra-pancreatic NET, one prior line). Somatostatin analogs do not count toward the requirement of a prior line of systemic therapy. Previous treatment with an mTOR inhibitor or VEGFR-TKI is not permitted.

Patients will be randomized to either once-daily oral zanzalintinib or everolimus. Planned enrollment is 440 patients. The primary endpoint is progression-free survival (PFS) by blinded independent central review (BICR). Secondary endpoints include investigator-assessed PFS; overall survival; BICR- and investigator-assessed objective response rate, duration of response, and disease control rate; quality of life; and safety.

RESULTS

STELLAR-311 is open and enrolling patients.

CONCLUSIONS

N/A

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