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Zanzalintinib Maintenance in Patients with High Grade Neuroendocrine Neoplasms (HG-NENs)

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BACKGROUND

Metastatic high-grade neuroendocrine neoplasms (HG-NENs) are aggressive and often fatal, necessitating urgent upfrontchemotherapy, such as platinum and etoposide. However, regimens are harsh and patients will receive a limited number oftreatments before considering a break or observation, as there are no approved maintenance regimens. Unfortunately, theoverwhelming majority will progress within a few weeks to months of treatment break, again with very aggressive disease.There is an unmet need for a maintenance regimen that delays further chemotherapy administration, and that allows for abetter quality of life.

Our prior study NCT04412629 showed efficacy of the multi kinase inhibitor cabozantinib in patients with recurrent orprogressive HG-NENs. Zanzalintinib, a novel, oral, multi-targeted inhibitor of VEGFR, MET, and the TAM (TYRO3, AXL, andMER) kinases, has a similar kinase inhibition profile to cabozantinib but has a shorter half-life and has shown preferentialin vivo tumor distribution. The purpose of this study is to test zanzalintinib as a maintenance therapy in the HG-NEN population.

METHODS

This is a single arm Phase II study.

A total of 32 eligible patients will be offered zanzalintinib starting at 60 mg orally daily in 28-day cycles. Treatment willcontinue until disease progression or unacceptable toxicity. Eligible patients have HG-NENs of any origin except for smallcell lung and Merkel cell cancer, have received their first instance of chemotherapy and have achieved at least stabledisease as of the most recent imaging modality. Other key eligibility criteria include age >=18 years, ECOG 0-1. Keyexclusion criteria are concurrent malignancies, known untreated brain metastases and uncontrolled significantcardiovascular disorders, significant bleeding risk or unhealed wounds.

Primary endpoint is Progression Free Survival (PFS). Secondary endpoints include overall response rate (ORR), overallsurvival (OS) and safety. There are mandatory pre and on-

treatment (pre C2) biopsies. Recruitment is ongoing. Resultsfrom this trial will inform on the use of zanzalintinib as a maintenance therapy in patients with HG-NENs who are eligiblefor a chemotherapy break.

RESULTS

Supported by Exelixis.

Clinical trial identification NCT06926634.

CONCLUSIONS

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