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Cabozantinib in High Grade Neuroendocrine Neoplasm

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BACKGROUND: High grade neuroendocrine neoplasms (HG-NENs) are treated with platinum doublets mimicking the current guidelines for small cell lung cancer (SCLC). Unfortunately, recurrences are common and most patients with metastatic disease succumb to it within a year. Salvage options are usually limited in efficacy and there is urgent need for more regimens.

METHODS: This study aims to recruit patients with histologically confirmed HG-NENs (excluding SCLC) that have progressed on first line therapy. These includes any tumor with a Ki-67 of >=20% / mitotic count of > 20 mitoses / high power field, poorly differentiated NEN and any other NEN deemed high grade by pathology consensus. This trial will also enroll transformed NENs, NENs of unknown origin and MiNENs, assuming there is a high grade component.

Cabozantinib will be given at 60 mg po daily on days 1-21 of a 21 day cycle.

The primary objective is to evaluate the response rate (RR) of cabozantinib. The secondary objective is to evaluate drug safety and if cabozantinib prolongs the overall survival (OS) and progression-free survival (PFS) of patients with HG-NENs compared to historical values.

Sample size: A Simon optimal 2-stage design will test the null hypothesis that the true response rate is less than or equal to 1% at the type I error rate of

5%. In the first stage, 14 patients will be accrued. If the study continues, 18 additional patients will be accrued.

Correlative studies include blood and tissue aquisition including a mandatory pretreatment and pre C2 biopsy for genetic and proteomic analysis.

RESULTS: This is a signal finding study aiming to expand the indications of cabozantinib in the HG-NEN population.

CONCLUSION: The proposed study has the potential to expand the use of cabozantinib in high grade NENs and potentially offer another therapeutic option in this grossly understudied population. ClinicalTrials.gov Identifier: NCT04412629

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