C-2

Cabozantinib in high grade neuroendocrine neoplasms.

Nikolaos Trikalinos[1], Rama Suresh[1], Katrina Sophia Pedersen[2], Belal Firwana[3], Melissa A Reimers[1], Paul Tracy Mehan[1], Patrick Grierson[1], Anjali Rohatgi[1], Esther Lu[4], Olive Pressey[1], Nicholas Waldron[1], Amberly Brown[1], Shuang Wu[4], Benjamin R. Tan[1]

[1]Washington University School of Medicine, Division of Medical Oncology, St. Louis, MO, USA; [2]Mayo Clinic Comprehensive Cancer Center, Rochester MN, USA; [3]Heartland Cancer Research NCORP, St Louis, MO, USA; [4]Washington University School of Medicine, Department of Surgery, Division of Biostatistics, St. Louis, MO, USA

BACKGROUND

High grade neuroendocrine neoplasms (HG-NENs) are commonly treated with chemotherapy but progression is common and salvage options are limited in efficacy. Cabozantinib (CABO), a multikinase inhibitor (VEGFR, MET, TYRO3, AXL, and MER) was approved by the FDA for treatment of well differentiated (WD) NENs of both pancreatic and extrapancreatic origins. However, its efficacy in the whole spectrum of HG-NEN patients has not been prospectively explored.

METHODS

This was a single institution, Phase II study. Key inclusion/exclusion criteria were NENs of any origin except SCLC, high grade by Ki-67 of > 20%, ECOG of < = 1, appropriate CBC, no history of bleeding or active cardiac disease. CABO was given orally starting at 60 mg po daily in 3-week cycles. The primary endpoint of this study was overall response rate (ORR). Secondary endpoints included progression free survival (PFS) and overall survival (OS). A Simon optimal 2-stage design tested the null hypothesis that the true ORR is < = 1% at the type I error rate of 5%, resulting in projected enrollment of up to 32 total patients. Toxicities were graded according to CTCAE v5.0 and response was evaluated according to RECIST v1.

RESULTS

All patients have been accrued, with 4/32 patients still on treatment. Median age was 62 years, male:female ratio was 1.46. Origin of tumor was GI (68.8%), thoracic (6.3%), prostate (6.3%) cervical (6.3%) head/neck (3.1%) and unknown (9.4%). Median Ki-67 was 55%, 11 patients had Ki-67 > 70%. Histology was WD-HG (40%) and PDD (60%). Two patients had mixed PDD/other components (MiNEN). Median PFS in evaluable patients was 4.01 months [95% CI 2.66 to 9.30] and mOS was 9.97 mo [95% CI 6.73 to 20.96]. Three patients so far (9.3%) have had partial response as best response (PDD-colon, WD-pancreas and PDD-cervical) while 19/32 (59.4%) patients have had stable disease as best response so far

(disease control rate 68.8%). Five (15.6%) patients have received more than 10 treatment cycles. The three longest treated patients had WD-pancreas (23 and 17 cycles) and PDD-unknown (12 cycles). One patient post resection of a metastatic site is currently without evidence of disease. Three patients withdrew because of toxicities (shortness of breath, GI bleeding, thromboembolism). Twenty-six patients have expired.

CONCLUSIONS

CABO monotherapy showed efficacy in some HG-NEN patients including PDD with no unexpected side effects. Supported by Exelixis and a Siteman investment program grant. Clinical trial information NCT04412629.

ABSTRACT ID #36628