

## C-6

# A Pilot Study of the Cyclin Dependent Kinases 4, 6 Inhibitor Ribociclib in Patients with Foregut Neuroendocrine Tumors

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**BACKGROUND:** Increased cyclin dependent kinases 4, 6 (cdk 4/6) activity is noted in the majority of well differentiated foregut neuroendocrine tumors (fNETs) due to mutations in MENIN and other aberrations. These tumors also have preserved Rb function making cdk 4/6 inhibitors attractive agents for therapy.

**METHODS:** In this single institution study (NCT02420691), 20 patients (pts) with advanced, progressive fNETs were treated with ribociclib 600 mg by mouth daily for 3 weeks (w) and off for 1 week in 4w cycles (c). All patients were required to have progressive disease in the past 12 months; patients with pancreatic NETs (pNETs) were required to have progression on prior therapy in addition. Paired biopsies were obtained at baseline and c2d1. Re-staging scans were obtained every 3 c.

**RESULTS:** 10 pNET; 7 lung NET and 3 other fNET with median age 56 (range 29 – 76; 65% male) and median prior therapies 2 (range 0-3) were enrolled. Although there were no radiographic responses, an encouraging improvement in progression free survival was noted (median: 10.4 months, m; 95% CI 7.4 m – 13.5 m). 7 patients had PFS > 12 m. No related grade (g) ≥ 4 adverse events (AE) were noted and the most common related g 3 AEs were neutropenia (6 pts), febrile neutropenia, anemia, thrombocytopenia and fatigue (1 pt each). Paired biopsies were obtained in 18 pts and in contrast to clinical benefit, did not show significant reduction in Ki-67 or phospho-Rb levels.

**CONCLUSION:** Ribociclib was well tolerated in this cohort of fNETs without any unanticipated AEs. Although pharmacodynamics studies did not show robust target inhibition perhaps related to intermittent dosing, clinical benefit was noted with prolonged stable disease in patients with prior progression.