C23

Randomized Phase II Study of Everolimus (E) versus Everolimus plus Bevacizumab (E+B) in Patients (Pts) with Locally Advanced or Metastatic Pancreatic Neuroendocrine Tumors (pNET), CALGB 80701 (Alliance)

Matthew H. Kulke[1]; Donna Niedzwiecki[2]; Nathan R. Foster N[3]; Briant Fruth[3]; Pamela L. Kunz[4]; Hagen Kennecke[5]; Edward M. Wolin[6]; Alan P. Venook[7]

[1]Dana-Farber Cancer Institute, Boston, MA
[2]Alliance Statistics and Data Center and Department of Biostatistics and Bioinformatics, Duke University, Durham, NC
[3]Alliance Statistics and Data Center, Mayo Clinic, Rochester, MN
[4]Stanford Cancer Institute, Palo Alto, CA
[5]Vancouver Center: BC Cancer Agency, Vancouver, CA
[6]University of Kentucky, Lexington, KY
[7]University of California San Francisco, San Francisco, CA

Support: U10CA180821, U10CA180882, CA31946, CA025224

Background: It is not known if the addition of a VEGF pathway inhibitor to an mTOR inhibitor enhances antitumor activity in pNET. This randomized phase II study evaluated E or E+B in pts with advanced pNET.

Methods: Pts were randomized 1:1 to E (10 mg po qd) or E (10 mg po qd) with B (10 mg/kg IV q 2 wks). All pts received octreotide. The primary endpoint was PFS. Potential superiority of E+B vs. E was assessed using a stratified log-rank test with 90% power (1-sided α=0.15) to detect a HR of 0.64. Secondary endpoints included overall survival (OS), response rate (RR), and safety.

Results: 150 pts were randomized: median age was 59 years (21-86), 56% male, ECOG PS 0 (57%)/1 (43%), prior chemotherapy 24%. Median number of 28-day treatment cycles were 13 (E+B) and 12 (E); range 1-44. Median follow up was 25.9 months. Pts on E+B experienced more grade 3 AEs, including diarrhea (14% vs. 3%; p = 0.01), hyponatremia (12% vs. 3%; p = 0.02), hypophosphatemia (11% vs. 3%; p=0.04), proteinuria (16% vs. 1%; p = 0.001), and hypertension (41% vs. 12%; p < 0.0001). The frequency of grade 4 AEs was 11% in both arms. Median PFS was 16.7 mos (E+B) vs. 14 mos (E); HR=0.80 (95% CI: 0.55, 1.17; 116 PFS events), 1-sided p= 0.12. Median OS was 36.7 mos (E+B) vs. 35.0 mos (E), HR =0.75 (95% CI: 0.42-1.33; 49 OS events), 1-sided p=0.16. E+B was associated with a significantly higher RR (31%) compared to E alone (12%), p=0.005).

Conclusions: Treatment with E+B led to superior PFS compared to E but with more adverse events in this randomized phase II study. The RR was significantly higher in pts treated with E+B. The combination of E+B warrants further investigation in pts with advanced pNET.