

# C-16

## Clinical Efficacy and Toxicity Data on Phase 1 Study of Fosbretabulin in Combination with Everolimus in Neuroendocrine Tumors

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**BACKGROUND:** Fosbretabulin, a synthetic, phosphorylated prodrug of the natural product combretastatin A4 (CA4P), is the lead compound in a class of agents termed vascular disrupting agents (VDAs) and has shown activity as a single agent in ovarian cancer and GEPNETs. Everolimus, an mTOR inhibitor, is FDA approved for the management of NETs. A Phase I trial combining fosbretabulin and everolimus to determine the recommended Phase II trial dose (RP2D) in metastatic GEPNET patients was conducted.

**METHODS:** Single center, phase I study involving GEPNETs incorporated a partial order continual reassessment method (PO-CRM) to define the dose escalation. Primary objective was to establish the maximum tolerated dose (MTD) in NETs that have progressed after at least one prior regimen for metastatic disease. The secondary objective included identifying the safety profile of the combination using NCI CTCAE4 reporting criteria. Patients received daily oral everolimus (2.5 mg, 5 mg, 7.5 mg, and 10 mg). Fosbretabulin was administered IV 60 mg/m<sup>2</sup> either q3 weekly or q weekly based on PO-CRM. Patients were treated for 12 weeks with all combinations. RECIST 1.1 was used to evaluate radiological responses at 3 months.

**RESULTS:** Of the 17 patients enrolled, 16 were evaluable. No DLTs were observed at day 21. The highest dose of 10 mg daily oral everolimus in combination

with weekly 60mg/m<sup>2</sup> IV fosbretabulin is the RP2D. No grade 4 or 5 toxicities were noted. Grade 3 toxicities were seen in 5 patients that include increased abdominal pain and hyperglycemia (not related to study drug), fatigue (possibly related), decreased lymphocyte count and anemia (related). All evaluable patients except one had stable disease at 3 months. A detailed table with all grade toxicities and waterfall plot of RR will be presented at the meeting.

**CONCLUSION:** Ten mg PO daily everolimus plus 60 mg/m<sup>2</sup> fosbretabulin IV weekly is the RP2D. ClinicalTrials.gov Identifier: NCT0301429