6090 General Poster Session (Board #16F), Sat, 8:00 AM-11:45 AM

Long-term disease control of ≥2 years achieved with cabozantinib in subjects with metastatic medullary thyroid carcinoma on a phase I study.

Ezra E.W. Cohen, David S. Hong, David G. Pfister, Ravi Salgia, Barbara Burtness, Roger B. Cohen, Douglas Wilmot Ball, Ranee Mehra, Milan Mangeshkar, Yifah Yaron, Frauke Bentzien, Razelle Kurzrock; The University of Chicago Medicine and Biological Sciences, Chicago, IL; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan-Kettering Cancer Center, New York, NY; The University of Chicago, Chicago, IL; Fox Chase Cancer Center, Philadelphia, PA; The Johns Hopkins University, School of Medicine, Baltimore, MD; Exelixis, Inc, South San Francisco, CA; University of California, San Diego, San Diego, CA

Background: Metastatic medullary thyroid cancer (MTC) carries a median survival of about two years (Modigliani et al. 1998; Roman et al. 2006). Cabozantinib inhibits three primary pathways implicated in MTC pathogenesis and progression: MET, vascular endothelial growth factor receptor-2 (VEGFR2), and RET. A phase I study was initiated in September 2005 in patients (pts) with advanced solid tumors. **Methods:** 85 pts, including 37 with MTC were enrolled to evaluate safety, pharmacokinetics, and to determine maximum-tolerated dose (MTD). Once the MTD of 140 mg freebase (equivalent to 175 mg malate salt) was determined, 20 metastatic or locally advanced MTC pts were enrolled in an MTD expansion cohort. 10/37 MTC pts achieved a confirmed partial response (cPR) (Kurzock et al. 2011). We report here on long-term disease control (DC), defined as cPR or progression-free at ≥ 24 months (m), in the MTC cohort. **Results:** After a minimum follow-up period of 52 m, 11 of 37 pts (30%) experienced DC, and have remained progression-free for > 24 m. Time from diagnosis and time since development of metastatic disease was similar in patients with (11) or without (26) long term DC. As of 04 Dec 2012, 5 of these 11 pts remain on treatment for a median time of 55 m (53-73m). A best response of cPR was associated with long-term benefit: 4/5 pts continuing on treatment achieved cPR, one achieved SD. The adverse event profile of cabozantinib was generally predictable and adverse events were managed with symptomatic treatment and dose modifications. The median final dose for pts with long-term DC was 60 mg (range 20-140), with a median number of dose reductions of 2 (range 0E4). Reasons for dose reductions in two or more pts experiencing long-term DC included diarrhea (7), palmar-plantar erythrodysaesthesia syndrome/ rash (6), mucositis/stomatitis (3), anorexia (3), nausea (2), and vomiting (2). **Conclusions:** Treatment with cabozantinib demonstrates long-term DC in a cohort of pts with metastatic MTC. Cabozantinib offers an important new treatment option for patients with progressive, metastatic MTC. Clinical trial information: NCT00215605.