9094 **General Poster Session (Board #52D), Sat, 8:00 AM-11:45 AM**

Activity of cabozantinib in metastatic uveal melanoma: Updated results from a phase II randomized discontinuation trial (RDT).

Adil Daud, Harriet M. Kluger, Gerald Edelman, Michael S. Gordon, Frauke Schimmoller, Aaron Weitzman, Thomas A. Samuel, Ali H. Moussa, Keith Flaherty, Geoffrey Shapiro; University of California, San Francisco, San Francisco, CA; Yale University, New Haven, CT; Texas Oncology, Irving, TX; Pinnacle Oncology Hematology, Scottsdale, AZ; Exelixis, Inc, South San Francisco, CA; Georgia Regents University, Augusta, GA; Cancer Care Associates, Tulsa, OK; Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; Dana-Farber Cancer Institute, Boston, MA

Background: MET and VEGF signaling are implicated in angiogenesis, invasion, and metastasis, and upregulation of MET as a consequence of GNAQ/GNA11 mutation has been implicated in uveal melanoma. Historical rates of median overall survival (OS) in patients (pts) with metastatic uveal melanoma range from 6-9 months (mos). A RDT evaluated activity and safety of cabozantinib, a MET and VEGFR2 inhibitor, in 9 tumor types including a metastatic melanoma cohort where 55% and 5% of pts experienced objective tumor regression and confirmed partial response, respectively (J. Clin. Oncol. 30, 2012 (suppl; abstr. 8531)). Here we report on the longer term followup of metastatic uveal melanoma pts enrolled to this cohort. **Methods:** Eligible pts were required to have progressive measurable disease per RECIST. Pts received cabozantinib at 100 mg po qd over a 12 wk Lead-in stage. Tumor response (mRECIST) was assessed q6 wks. Treatment $\geq$ wk 12 was based on response: pts with PR continued open-label cabozantinib, pts with SD were randomized to cabozantinib vs placebo, and pts with PD discontinued. Pts were followed for overall survival. **Results:** 23 of 77 pts enrolled in the melanoma cohort had the uveal subtype. Median age was 65 yrs; median prior regimens was 1 (range 0-5). Tumor mutation status was determined for 10/23 pts. 9/10 harbored either a GNAQ or GNA11 mutation, while GNA11 status was unknown for one pt. Pts had substantial tumor burden; median sum of the longest diameter of target lesions was 11.9 cm (range, 2-37.2). Median follow-up was 26.5 mos. (range 21.7-33.8). Median PFS from Study Day 1 was 4.8 mos. The estimate of PFS at month 6 (PFS6) was 41% and median OS was 12.6 mos. Most common Grade 3/4 AEs were HTN (13%), abdominal pain (9%), hypokalaemia (9%), hyperbilirubinaemia (9%) and increased lipase (9%). **Conclusions:** Cabozantinib is active in pts with metastatic uveal melanoma. Treatment with cabozantinib is associated with encouraging progression-free and overall survival. The safety profile of cabozantinib was comparable to that of other VEGFR TKIs. A randomized Phase 2 study is planned comparing cabozantinib to temozolomide plus dacarbazine in pts with uveal melanoma. Clinical trial information: NCT00940225.