A Phase II Trial of Cabozantinib for the Treatment of Radioiodine (RAI)-refractory Differentiated Thyroid Carcinoma (DTC) in the First-line Setting (Abstract 8)

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Purpose/Objective(s): Cabozantinib is a multi-tyrosine kinase inhibitor targeting VEGF receptor kinase, RET, MET and AXL. We participated in a Phase I study which suggested activity in the RAI-refractory patients that had previously been treated with one or more VEGF receptor inhibitor or other therapy. In order to further understand the activity of this agent in differentiated thyroid cancer, we conducted a single-arm open-label phase II study of cabozantinib in patients in the first-line setting with metastatic, RAI-refractory thyroid carcinoma (clinicaltrials.gov: NCT02041260).

Materials/Methods: Patients with metastatic, RAI-refractory, unresectable or locally-advanced thyroid cancer were administered cabozantinib 60 mg orally QD. Responses were monitored by PET at 4 weeks and CT every 2 months. The primary outcome was response rate (RR) and secondary outcomes included progression-free survival (PFS), time to progression (TTP), duration of response and clinical benefit rate

Results: Since March 2014, 35 patients were treated on study. Study accrual was completed in August 2017. The median time on study is 19.5 weeks. Median age is 65 years (range 45 to 84); 17 pts (49%) are male. Of these patients 22 (63%) have papillary, 3 (9%) have Hürthle cell and 10 (29%) patients have poorly differentiated histology. Among the 30 patients who are evaluable for response, partial response (PR) was achieved in 16 (53%) patients with a duration of response of 11 to 174+ weeks. Fourteen (47%) had stable disease (SD) with a duration of response of 8 to 119+ weeks. Median PFS has not been reached. Among the four patients who progressed, the median time to disease progression was 35 weeks. Eighteen patients remain on study. Cabozantinib was well-tolerated with dose interruptions and dose adjustments as needed; the most common treatment-related adverse events included fatigue, weight loss, deep vein thrombosis, pulmonary embolism, hypertension, diarrhea, and mucositis.

Conclusion: This is the first study to document the anti-tumor activity of cabozantinib in patients with RAI-refractory differentiated thyroid cancer in the first-line setting with an overall response rate of 53% and warrants further investigation in this patient population.