AN INTERNATIONAL PHASE III STUDY TO ASSESS THE EFFICACY AND SAFETY OF VANDETANIB 300 MG IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC DIFFERENTIATED THYROID CANCER (DTC)

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Background/Purpose: Vandetanib is an oral selective inhibitor of RET, VEGFR and EGFR signaling indicated for the treatment of symptomatic and/or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. A Phase II randomized, placebo-controlled trial has also demonstrated improved progression-free survival (PFS) in patients with vandetanib in RAI-refractory locally advanced or metastatic DTC (HR=0.63, 60% CI 0.54–0.74; *P*=0.008; NCT00537095) (Leboulleux *Lancet Oncol* 2012).

Methods: D4203C00011 is a Phase III double-blind placebo-controlled study to assess the efficacy and safety of vandetanib in RAI-refractory DTC patients. Approximately 227 patients (aged ≥18 years), with histologically confirmed locally advanced (surgically unresectable), metastatic papillary or poorly differentiated (excluding follicular-minimally invasive) thyroid cancer that has progressed within the previous 14 months and is unsuitable for RAI, will be recruited from ~70 international sites and randomized 1:1 to receive once-daily vandetanib 300 mg or matched placebo. The primary objective will be to evaluate PFS (RECIST v1.1). Primary analysis will be at ~155 PFS events based on >80% power to demonstrate superiority of vandetanib versus placebo (two-sided 5% significance level; HR=0.63). Secondary endpoints include objective response rate, duration of response, change in tumor size, overall survival, safety, time to worsening of pain and pharmacokinetics. Biomarker analyses (from archival tumor material) and health-related quality of life will also be assessed (exploratory analyses).

Results:

Discussion & Conclusion: These results will add to the understanding of the efficacy and safety of vandetanib in patients with locally advanced or metastatic DTC.