AB030. PS01.12. A phase II study of regorafenib in patients with thymoma and thymic carcinoma previously treated with chemotherapy

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Background: Available evidence suggests that angiogenesis has an important role in thymic epithelial tumours; VEGF is overexpressed in these cancers, and VEGF expression and microvessel density are associated with invasiveness and stage. Higher serum concentrations of VEGF and b-FGF have been noted in patients with thymic carcinoma. Overexpression of KIT has been reported in about 80% of thymic carcinomas, and mutations in the gene encoding this receptor are noted in about 10% of these cancers. PDGF and PDGFRα are also overexpressed in thymic epithelial cells. Recently, in a phase II trial, Sunitinib showed to be active in patients with thymic carcinoma achieving PR and SD in 26% and 65% of patients, respectively. Regorafenib potently inhibits the angiogenic and stromal RTKs VEGFR1, 2, and 3, TIE2 and PDGFR-β that promote tumor neo-vascularization, vessel stabilization and lymphatic vessel formation and play an important role in the tumor microenvironment, which all contribute to tumor development and metastasis formation. Regorafenib demonstrated nanomolar inhibition (3–200 nM) of the RTKs VEGFR2, PDGFR-β and FGFR in biochemical and cellular assays. The aim of this study is to determine the activity of Regorafenib as monotherapy in patients with advanced or recurrent thymoma (type B2–B3) and thymic carcinoma previously treated with cisplatin-containing chemotherapy.

Methods: This is a Fleming single arm, single-stage, phase II trial to evaluate the activity of Regorafenib administered at the dosage of 160 mg once a day oral 3 weeks on/1 week off. Patients with advanced or recurrent thymoma (type B2–B3) and thymic carcinoma previously treated with cisplatin-containing chemotherapy are enrolled. Subjects continue on treatment until at least one of the following occurs (main criteria): progressive disease by radiological assessments or clinical progression (measurements are made at intervals and with methods that comply with the institution's best standard of care); death; unacceptable toxicity; subject withdraws consent; treating physician determines discontinuation of treatment is in the subject's best interest. The primary objective of the study is to evaluate activity of Regorafenib. Two months progression free survival rate will be considered as primary endpoint considering the number of patients progression free at 2 months. The secondary objectives are to explore the prognosis in terms of progression-free survival (PFS) and overall survival (OS) and to assess the safety. This design would effectively reject the null hypothesis of a progression free survival rate ≤25% with a type I error of 0.10 and a statistical power of 80% at the alternative hypothesis of a progression free survival rate of ≥50%. The drug will be recommended for further study if 8 or more of the 19 total evaluable patients will be progression free at 2 months. Clinical trial information: NCT02307500.

Keywords: Regorafenib; thymoma; thymic carcinoma

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