T-4

Multicenter Phase 2 Study of Nintedanib in Patients (pts) with Advanced Progressing Carcinoid Tumors

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BACKGROUND: Serotonin is the cause of carcinoid symptoms and can signal the formation of fibroblasts via fibroblast growth receptors (FGFR). Nintedanib is an oral inhibitor of the FGFR pathway and several angiogenic signaling pathways thought to drive carcinoid tumor progression. We hypothesized that nintedanib may slow tumor progression in pts with progressing carcinoids.

METHODS: This phase 2 study will include 30 pts with unresectable/metastatic carcinoids on a stable dose of somatostatin analogue for ≥ 3 months from two sites. (NCT02399215). Primary Endpoint: To assess progression free survival (PFS). A true PFS rate at 16 weeks of less than p0 =0.40 is considered unacceptable in carcinoid, and evidence of such will deem the treatment not worthy of further study. The null and alternative hypotheses to be tested are H0: $p \leq p0$ versus HA: $p > p0$. If 16 or more pts are alive and progression free at 16 weeks, the agent would be promising. Secondary Endpoints: To assess the objective response (complete response + partial response) using standard RECISTv1.1 criteria; overall survival (OS); change in QOL throughout treatment using the EORTC QLQ–GI.NET21 questionnaire for carcinoid pts, in all pts who have filled out at least two QOL questionnaires will be reported by response groups. Toxicity (graded using the NCI CTCAE version 4.0) will be closely monitored and all toxicities will be tabulated.

RESULTS: Accrual is complete as of June 2017 and analysis is ongoing. Steady-state PK of nintedanib, Treg and cytokine expression and growth factors will be reported in groups based on response. Gene mutations and copy number alterations in the mTOR pathway, protein expression of activation of Akt (as well as other downstream targets) will be analyzed in a subset.

CONCLUSION: Evaluation of a much needed novel agent for treatment of advanced progressing carcinoids is ongoing and will be reported in 2017/2018.