C-14

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

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BACKGROUND: Serotonin drives carcinoid tumorigenesis, symptoms and signals fibroblasts via fibroblast growth receptors (FGFR). We examined whether nintedanib that inhibits the FGFR pathway and several angiogenic signaling pathways thought to drive carcinoid tumor progression could slow tumor progression in carcinoid pts.

METHODS: Thirty pts with unresectable/metastatic carcinoids on stable dose of somatostatin analogue for ≥3 months were included from two sites (NCT02399215). Primary Endpoint: progression free survival (PFS) rate at 16 wks. Secondary Endpoints: Objective response (complete + partial responses) using standard RECISTv1.1 criteria; overall survival (OS); change in QOL throughout treatment using EORTC QLQ–GI.NET21 questionnaire for carcinoid pts; and toxicity (graded using the NCI CTCAE version 4.0).

RESULTS: Baseline characteristics: M/F: 15/15, ECOG PS: 0/1/2: 11/17/2; Median age (years): 64.9 (45.1-77.2); site of origin: small bowel (13), colon (7), lung (4), gastric (1), unknown primary (5); PD on prior everolimus: 23%. PFS rate at 16 wks was 86.7%; 95%CI: 72-95.3% (26 pts). The study was designed to compare to a historic PFS rate of 0.40 with everolimus. Kaplan Meier median PFS and OS estimates were 11 and 27.6 months, respectively, with 6 pts currently on therapy. RECIST response: PR 1(4%), SD 20(83%), PD 2(8%), NE 1(4%). Reasons for coming

off therapy: progression 14 (58%), toxicity 5(21%), other (17%), death due to disease 1(4%). QOL was maintained or improved in at least 50% of subjects while on therapy. Treatment was held in 7 pts (23%) due to AEs. Highest grade AEs: gr2 in 14(47%) and gr3 in 8(27%) pts. The most common gr 2 were GI (9), heme (8) and gr 3 were hypertension (6) and anorexia (2). Nintedanib pop PK model showed correlation between actual and predicted exposures with 61% variability between pts.

CONCLUSION: Nintedanib has encouraging PFS and is well tolerated in advanced carcinoid pts. Biomarker studies may allow optimal pt selection.