PHASE II STUDY OF SUNITINIB (SU) IN JAPANESE PATIENTS WITH WELL-DIFFERENTIATED PANCREATIC NEUROENDOCRINE TUMOR (NET)

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Background: SU is an oral, multitargeted, antiangiogenic, tyrosine kinase inhibitor effective in patients (pts) with unresectable, well-differentiated pancreatic NET. This open-label, phase II study examined whether SU is also effective in Japanese pts with this disease.

Methods: Japanese pts received SU 37.5 mg/day on a continuous daily dosing (CDD) schedule (28-day cycle). The primary endpoint was clinical benefit rate (CBR; complete response [CR] + partial response [PR] + stable disease [SD] more than 24 weeks). Secondary endpoints included: objective response rate (ORR; CR + PR), progression-free survival (PFS), overall survival (OS), safety and pharmacokinetics. Tumor assessments were performed at baseline and 8-wk intervals by CT or MRI (RECIST).

Results: Between July and December 2010, 12 patients were enrolled (median age 54 yrs, range 34-79) and, all received treatment. At cut-off (Jan 17, 2013), all completed treatment. Median treatment duration was 14.0 mos. CBR was 75% (95% CI 42.8, 94.5), comprising 6 PRs and 3 pts with SD more than 24 weeks. ORR was 50% (95% CI 21.1, 78.9). median PFS was 16.8 mos (95% CI 9.3, 26.2). Median OS had not yet been reached. One pt discontinued treatment due to AE. Treatment-related, any-grade (G) AEs included diarrhea (n = 10, 83%), HFS and hypertension (both n = 8, 67%). Neutropenia was the most common G3 AE (n = 6, 50%). Four pts (33.3%) experienced G4 AEs (herpes encephalitis, convulsion, loss of consciousness, enterocolitis [n = 1] and lipase increased [n = 2]). Mean dose-corrected (reference dose: 37.5 mg) trough plasma concentrations for SU, its metabolite, and SU + metabolite were 41.7 ∼ 53.9, 19.6 ∼ 25.7 and 62.9 ∼ 77.5 ng/mL, respectively. SU on a CDD schedule resulted in sustained drug concentrations without accumulation across cycles (cycle 1 to 4).

Conclusions: SU 37.5 mg/day on a CDD schedule demonstrated antitumor activity in Japanese pts with well-differentiated pancreatic NET. Common AEs were consistent with the known safety profile of SU.

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