Sunitinib versus Placebo for the Treatment of Progressive, Well-Differentiated Pancreatic Islet Cell Tumors: A Phase III, Randomized, Double-Blind Trial

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Background: Sunitinib, an oral, multitargeted tyrosine kinase inhibitor, is approved for treatment of advanced renal cell carcinoma and imatinib-resistant/intolerant gastrointestinal stromal tumors. Non-clinical data and a phase II study showed activity of sunitinib against pancreatic islet cell tumors. This international placebo controlled phase III study assessed the safety and efficacy of sunitinib for the treatment of progressive pancreatic islet cell tumors.

Methods: Patients had local, locally advanced, or metastatic, well-differentiated pancreatic islet cell tumors, with disease progression in the previous 12 months and not amenable to curative therapy. They received either placebo or sunitinib 37.5 mg/day continuous daily dosing, with best supportive care. Progression-free survival (PFS) was the primary endpoint; safety and tolerability were monitored. The study was powered to detect a 50% improvement in PFS (target enrollment: 340 patients).

Results: By February 2009 154 patients had been enrolled; 75 received sunitinib and 79 placebo. Median age was 56 years (range 25–78). The preliminary results demonstrated that median PFS was 11.1 months (95% CI: 7.4–NR) for sunitinib versus 5.5 months (95% CI: 3.5–7.4) for placebo (73 events evaluated, including 63 incidences of disease progression). Patients receiving sunitinib were significantly less likely to have experienced disease progression/death (hazard ratio for PFS, 0.397 (95% CI: 0.243–0.649) in favor of sunitinib (p<0.001). The study was stopped early as recommended by an independent Data Monitoring Committee; patients receiving placebo were permitted to receive sunitinib treatment. Five and 15 deaths occurred in sunitinib and placebo arms, respectively; overall survival analyses are ongoing. The most frequent grade 3–4 adverse events in sunitinib-treated patients were neutropenia (12%), hypertension (9%), abdominal pain, diarrhea, hypoglycemia and hand-foot syndrome (7% each).

Conclusions: Sunitinib demonstrated clinical efficacy and acceptable safety in the treatment of progressive, well-differentiated pancreatic islet cell tumors; further data analyses are ongoing.