

Progression-Free Survival (PFS) by Blinded Independent Central Review (BICR) and Updated Overall Survival (OS) of Sunitinib versus Placebo for Patients with Progressive, Unresectable, Well-Differentiated Pancreatic Neuroendocrine Tumor (NET)

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Background: In a double-blind phase III trial, sunitinib improved PFS vs. placebo (11.4 vs. 5.5 months; HR: 0.418, 95% CI: 0.263–0.662; P=0.0001) and was well

tolerated in patients with progressive, unresectable, well-differentiated pancreatic NET that had progressed ≤ 12 months before baseline (Raymond et al, NEJM 2011). Initial OS revealed a benefit for sunitinib over placebo, but median OS was not reached (NR). We now report PFS assessed by BICR and updated median OS.

Methods: Patients were randomized 1:1 to sunitinib 37.5 mg on a continuous-daily-dosing schedule or placebo, each with best supportive care. The primary endpoint was PFS; OS was a secondary endpoint. Baseline and on-study CT/MRI scans were evaluated by a 2-reader, 2-time point lock, followed by a sequential locked-read, batch-mode paradigm by blinded, third-party radiologists. Patients in the placebo arm with disease progression were eligible to receive sunitinib in an extension study.

Results: 171 patients were randomized (sunitinib, n=86; placebo, n=85) from 6/2007 to 4/2009. The trial ended when an independent data monitoring committee noted efficacy favoring sunitinib and more serious AEs and deaths with placebo. The study was unblinded at closure; patients were offered open-label sunitinib and followed for survival. Median PFS by BICR was 12.6 vs. 5.8 months, sunitinib vs. placebo, respectively (HR: 0.315, 95% CI: 0.181–0.546; P=0.000015). At study end, there were 9 and 21 deaths in the sunitinib and placebo arms (HR: 0.409, 95% CI: 0.187–0.894; P=0.0204). By 6/2010, there were 34 and 39 deaths; median OS was 30.5 (95% CI: 20.6–NR) and 24.4 (95% CI: 16.3–NR) months, respectively (HR: 0.737; 95% CI: 0.465–1.168; P=0.1926). 69% of patients crossed over to sunitinib on progression.

Conclusion: BICR of PFS demonstrated a 6.8-month improvement in median PFS with sunitinib, confirming the treatment effect reported with investigator assessment.