Sunitinib malate (SUTENT®) is an inhibitor of vascular endothelial growth factor receptors, platelet-derived growth factor receptors, c-kit receptor and cellular retinoid x receptors. We conducted a multinational, randomized, double-blind, placebo-controlled, phase III study in patients with advanced, well-differentiated, progressive pancreatic neuroendocrine tumor (NET). The study was closed after the independent data and safety monitoring committee noted a difference in progression-free survival (PFS) in favor of sunitinib and more serious adverse events (AEs) and deaths in the placebo group.

The primary endpoint of the study was PFS. At the time of study closure there was also an advantage for sunitinib over placebo in the secondary endpoint of overall survival (OS). We performed an retrospective analysis of PFS by blinded independent central review (BICR). This analysis, along with updated OS, is presented here.

OBJECTIVE

To determine whether BCR confirms the investigator-assessed PFS advantage for sunitinib, and whether sunitinib increases OS despite patient crossover from placebo to sunitinib.

METHODS

Trial Population

Inclusion criteria:
- Histologically or cytologically diagnosed well-differentiated, progressive pancreatic neuroendocrine tumor (WHO 2000 classification)
- Inadequate or metastatic disease with disease progression in the previous 12 months
- ≤1 measurable target lesion according to RECIST
- Karnofsky performance status ≥70
- No current or previous treatment with tyrosine-kinase inhibitors or anti-vascular endothelial growth factor inhibitors

Exclusion criteria:
- Prior radiation therapy
- Prior somatostatin analog, n (%)
- Pancreatic resection
- Diabetic neuropathy
- Prior chemotherapy
- Prior immunotherapy
- Current cancer treatment other than somatostatin analog
- Other active malignancy

PFS and OS were summarized using Kaplan–Meier methods; PFS advantage for sunitinib, and whether sunitinib increases OS despite patient crossover from placebo to sunitinib.

RESULTS

Baseline Characteristics and Disposition

Between June 2007 and April 2009, 171 patients were randomized to treatment (sunitinib, n=86; placebo, n=85) following investigator assessments (n=170).

Patient demographics and baseline disease characteristics are presented in Table 1. The median age was 65.5 years (range: 22–84). Most patients (82%) had functioning tumors; the most common functional tumors were gastrinomas (33%); 25% of patients had a history of prior radiation therapy.

Safety

The most common treatment-emergent (all causality) grade 3/4 AEs in the sunitinib arm were neutropenia (12%), hypertension (10%), and fatigue (9%). In the placebo arm, the most common AEs were abdominal pain (10%), fatigue (9%), and back pain (5%).

CONCLUSIONS

The BCR analysis of PFS demonstrated a 6.8 month improvement in median PFS in favor of sunitinib, confirming the treatment effect reported with investigator assessment.

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REFERENCES


Figure 1. Kaplan–Meier estimates of OS.

Figure 2. Kaplan–Meier estimates of OS based on investigator assessment vs BCR assessment.

Figure 3. Kaplan–Meier estimates of OS.

Table 1. Objectives, baseline characteristics, PFS and OS.

Table 2. Analysis of investigator-assessed and BCR-assessed PFS.

Table 3. Analysis of investigator-assessed and BCR-assessed OS.

Table 4. PFS and OS events.