
Background: Sorafenib (BAY 43-9006) is a novel orally active multi-kinase inhibitor with anti-angiogenic and anti-proliferative activity by blocking both the Raf/MEK/ERK pathway at the level of Raf kinase and the receptor tyrosine kinases VEGFR-2 and PDGFR. Previous single-agent phase I studies showed that sorafenib is well tolerated, with manageable and reversible side effects, most commonly hand-foot skin (HFS) reaction, rash, fatigue, and diarrhea. This phase II study was conducted to investigate the activity of sorafenib in previously untreated patients (pts) with locally advanced and/or metastatic pancreatic cancer (PC). Methods: Pts received sorafenib 400 mg bid by continuous oral dosing. Pts with no prior systemic therapy for advanced disease and at least one uni-dimensional measurable lesion according to the RECIST-criteria were eligible for study entry. The primary objective was the proportion of evaluable patients with time to progression (PP-TTP) of ≥ 12 weeks. A minimum of 37 evaluable pts (those completing at least 4 weeks [one cycle] of sorafenib therapy) were required to detect an increase in PP-TTP from 10 to 30% in a one stage design. Secondary endpoints were overall response, overall survival, toxicity according to Common Toxicity Criteria (CTC v2.0) and drug safety. Results: A total of 47 pts with PC were enrolled between August 2004 and January 2005. The majority of pts (n=30, 63.8%) were treated for at least 6 weeks, and 4 pts were treated for > 33 weeks (33-39 wks). Among the 36 pts evaluable for TTP, 9 pts (25%) showed stable disease ≥ 12 weeks and 27 pts (75%) showed disease progression: 15 pts with confirmed progressive disease and 12 pts due to study withdrawal before 12 weeks among those 4 due to tumor-related death. In the 36 pts (76.6%) evaluable for response, a partial response lasting < 4 wks was observed in one patient. A total of 11 pts were not evaluable due to missing information (n=2) or study withdrawal before completing the first cycle (n=9). There were 3 disease-related deaths in patients withdrawn from study. All 47 pts are evaluable for toxicity and adverse events. Serious adverse events were seen in 21 pts (44.7%) but only one (2.1%) was determined to be drug-related. Conclusion: Preliminary results of this study indicate that sorafenib is active in PC. Further investigation in future trials is necessary. Final results will be presented.