Pancreatic cancer represents a leading cause of cancer-associated mortality. Very few patients are eligible for standard chemotherapy, and overall survival remains poor. Previous trials have shown a benefit of adding bevacizumab to gemcitabine, with greater response rates and improved survival in patients with advanced pancreatic adenocarcinoma. However, the mechanism of action of bevacizumab remains poorly understood and the ideal anti-angiogenic strategy is yet to be determined.

Methods

Study design

The AViTA study was a phase II, open-label, randomized study comparing gemcitabine plus erlotinib plus placebo (GE-P) to gemcitabine plus erlotinib plus bevacizumab (GE-B) in patients with advanced pancreatic adenocarcinoma. Patients were stratified by KPS, albumin level, and region before randomization to treatment arms. Eligible patients were those with Eastern Cooperative Oncology Group (ECOG) performance status 0 to 1, no prior chemotherapy or targeted tyrosine kinase inhibitors for metastatic pancreatic cancer, and no prior treatment with gemcitabine or bevacizumab. The primary endpoint was median overall survival (OS), and secondary endpoints included progression-free survival (PFS), response rate, and safety. The study was powered to detect a 3-month improvement in OS from 4 to 7 months, with a 0.80 statistical power.

Results

A total of 607 patients were enrolled. Patient characteristics were well balanced between treatment groups, with no significant differences in age, sex, ECOG performance status, or prior treatment history. The addition of bevacizumab produced a significant benefit in OS and a trend towards improved PFS. Median OS was 5.91 months with gemcitabine monotherapy (hazard ratio [HR] = 0.82; 95% confidence interval [CI]: 0.70–0.96; p = 0.007), 6.11 months with gemcitabine plus erlotinib (HR = 0.80; 95% CI: 0.67–0.95; p = 0.009), and 6.72 months with gemcitabine plus erlotinib plus bevacizumab (HR = 0.73; 95% CI: 0.61–0.86; p < 0.0001). A trend to improved OS in the GE-B arm was observed. There was no difference in OS between treatment groups for patients with or without prior chemotherapy. The observed relationship between higher grades of rash and longer median OS was apparent in both arms of the study. There was no difference in OS between treatment groups in patients with or without prior gemcitabine or anti-vascular endothelial growth factor (VEGF) therapy; the addition of B to GE produced a significant benefit in PFS and a trend towards improved OS in patients with or without prior gemcitabine or anti-VEGF therapy.

Conclusions

The addition of bevacizumab to gemcitabine plus erlotinib improves OS and PFS in patients with advanced pancreatic adenocarcinoma. This study provides further evidence for the potential role of anti-angiogenic therapy in the treatment of pancreatic cancer.