

Pancreatic Cancer

abstr 0810

Quality of Life in Patients with Advanced Pancreatic Cancer Receiving Gemcitabine, Capecitabine, and Bevacizumab: Results from a Prospective Multicenter Phase II Trial

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Background: The majority of patients with pancreatic cancer have advanced disease at diagnosis that is rapidly fatal, with median survival of only 6 months. Palliative gemcitabine-based chemotherapy has a modest impact on survival but has been used for clinically meaningful improvement in disease-related symptoms and quality of life (QOL), even in patients who do not show objective radiographic tumor response. As newer chemotherapy combinations that are intended to be palliative are developed, measurement of effects on QOL is relevant and important, as these therapies can also be toxic. We performed a multicenter phase II trial of the combination of gemcitabine (G), capecitabine (C), and bevacizumab (B) in patients with advanced pancreatic cancer (APC) and prospectively analyzed QOL to determine the impact of this combination on QOL. In this analysis, we also present the value of using QOL response to predict patient outcomes.

Methods: Fifty patients with APC received G 1,000 mg/m² (day 1, day 8), C 650 mg/m² orally BID (days 1-14), and B 15 mg/kg (day 1) q3 weeks. End points were progression-free survival (PFS), overall survival (OS), and QOL. QOL assessment was done prior to each cycle, utilizing the EORTC PAN-26 QOL questionnaire. An exact 95% confidence interval (Clopper-Pearson method) was used to assess rate of improved QOL that was defined as >5 % decrease in two consecutive scores compared with baseline.

Results: Patient characteristics: 5 stage III, 45 stage IV pancreatic cancer; 28 male, 22 female; median age was 64 years (range, 38-83 years). Median PFS was 5.8 months and OS was 9.8 months. QOL improvement was seen in 28 patients (56%), there was no improvement in 12 patients (24%), and 10 patients (20%) were not evaluable as they had less than three questionnaires surveyed. QOL improvement rate was $28/40 = 70\%$ (95% CI: 0.53-0.83) in evaluable patients (QOL improvement with gemcitabine alone is 0.2). Using rate of QOL improvement, no significant difference was seen in patients with OS >6 months compared with OS <6 months. (Fisher exact P value = .1680). PFS and OS in those with improvement in QOL versus those with no QOL improvement were as follows: PFS in 'QOL improved' 6.6 months vs. 7.1 months in 'QOL unimproved,' log rank P value = .64; OS in 'QOL improved' 11.3 months vs. 7.9 months in 'QOL unimproved', log rank P value = .55. However, post-treatment QOL scores at visits 2 and 3 correlated strongly with 6-month survival (two sample t-test visit 2: $P = .0092$; visit 3: $P = .0081$). Responses per RECIST were as follows: 1 complete response (2%), 10 partial responses (20%), 30 stable disease (60%), 5 progressive disease (10%), and 4 (8%) symptomatic progression; the response rate (CR+PR) in evaluable patients (11/46) was 24% (95% CI: 0.13-0.40). One-year survival rate was 28%.

Conclusion: G, C, and B combination chemotherapy is associated with improvement in PFS, OS, and QOL as compared with data obtained in historic controls treated with gemcitabine alone. Baseline score and change in QOL scores were not predictive of survival greater than 6 months. Use of QOL score after one or two cycles of therapy, however, was predictive of survival greater than 6 months, suggesting that as early as 3 and 6 weeks from start of therapy, the QOL tool alone can potentially predict survival. These intriguing results require evaluation and validation in future prospective studies.