

Materials/Methods: Patients with locally advanced, non-metastatic, unresectable pancreatic cancer without endoscopic or radiographic evidence of duodenal invasion were treated with 50.4 Gy in 28 fractions of radiotherapy with concurrent capecitabine (825 mg/m² orally twice daily on days of radiation) and bevacizumab at 5 mg/kg on days 1, 15, and 29. Patients with stable or responding disease 4 wks after CXRT were continued on maintenance gemcitabine (1 gm IV qwk ×3) and bevacizumab (5 mg/kg q2wks) in 4 week cycles until progression. Radiation treatment volumes included the primary tumor and grossly enlarged lymph nodes only. The study was powered 90% probability to detect a 15% improvement in 1-yr survival over RTOG 98-12 (43%) at a 0.10 significance level.

Results: Of the 94 patients accrued between January 2005 and the date of full accrual was reached (February 2006), 82 were eligible for analysis. Median and 1 yr OS were 11.9 months (CI 10.1,14.2) and 47% (CI 35-57). Median progression-free survival was 9.4 months (CI 7.8, 10.6). A median of 3 cycles of maintenance chemotherapy was given, (range 0–10.3). Overall, 35.4% of patients had CTCv3 G3 or greater treatment related GI toxicity (16.0% during chemoradiation, 17.0% during maintenance chemotherapy, and 2.4% during both phases) and 52% patients had G3 or greater treatment related hematologic toxicity, mostly during maintenance chemotherapy (43%). There were three deaths that were reported as being at least possibly related to treatment (colonic perforation, peritonitis, and sudden death).

Conclusions: The addition of bevacizumab to chemoradiation followed by bevacizumab and gemcitabine resulted in similar median and 1 year survival and acute toxicity rates to similar studies conducted by the RTOG in the past.

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137 Post-resectional CA 19-9 Values >90 are Associated With Significantly Worse Survival in Patients With Pancreatic Carcinoma Treated With Adjuvant Therapy on RTOG 9704 - Implications for Current and Future Trials

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Purpose/Objective(s): Results of the recently reported CONKO-001 trial¹ indicating improved disease free survival but not improved overall survival (OS) with the use of adjuvant Gemcitabine (without RT) have been used to refute/challenge the role of RT in the adjuvant treatment of pancreatic adenocarcinoma. While the results of the US Intergroup/RTOG 9704 adjuvant trial² cannot be directly compared to CONKO-001, fundamental differences in patient characteristics should be pointed out for discussion and/or appropriate debate, including the CONKO-001 requirement of CA 19-9 < 2.5 the upper limit of normal (~ 90), while no such exclusion criteria existed in RTOG 9704. A secondary endpoint of RTOG 9704 was to prospectively evaluate the ability of post-resectional CA 19-9 to predict OS. This analysis evaluates the impact on survival of CA 19-9 values ≤ 90 vs. >90.

Materials/Methods: CA 19-9 expression was analyzed as a dichotomized variable (≤ 90 vs. >90). Cox proportional hazard models were utilized to identify the impact of CA 19-9 value on OS. The following variables were included in the multivariate analyses: treatment, tumor stage, nodal involvement, tumor diameter, margin status, and RT quality assurance (QA) score (per protocol vs < per protocol). Actuarial estimates for OS were calculated using Kaplan-Meier methods.

Results: A total of 538 patients were accrued to this trial, with 385 having analyzable CA 19-9. 132 patients were Lewis Antigen negative and therefore were without CA 19-9 expression. Among the remaining 253 patients, 200 (79%) had CA 19-9 values ≤ 90 vs. 53 (21%) with CA 19-9 > 90. Baseline characteristics were statistically balanced across groups. Both univariate (HR = 3.4 (95% CI = 2.45–4.72) *p* = <0.0001) and multivariate (HR = 3.34 (95% CI = 2.40–4.64) *p* = <0.0001) analyses demonstrated a highly statistically significant decrease in OS for CA 19-9 > 90. This finding was true for all patients as well as for patients with pancreatic head and non-head tumors when analyzed separately. For all patients, the same results for CA 19-9 hold after adjusting for RTQA score which also predicted for a decrease in OS when < per protocol (*p* = 0.02). The median and 3-yr OS for patients with CA 19-9 <90 was 22.8 mos and 33% vs 9.6 mos and 2% for patients with CA 19-9 > 90 (*p* < 0.0001). The median and 3-yr OS for patients in the gemcitabine arm of the CONKO-001 trial were 22.1 months and 34%. The median and 3-yr OS in the gemcitabine arm for patients with pancreatic head tumors, CA 19-9 ≤90, and RTQA score per protocol in RTOG 97-04 were 25.2 months and 46%.

Conclusions: This analysis demonstrates post-resectional CA 19-9 values of >90 are associated with significantly worse survival in patients treated with adjuvant therapy. It also supports the continued inclusion of RT in future adjuvant trials, particularly among patients with elevated post-resectional CA19-9 values.

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