

# Neoadjuvant Therapy for Borderline Resectable and Locally Advanced Pancreatic Cancer

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## Abstract

**Objectives:** To evaluate patient outcomes in borderline resectable and locally advanced pancreatic cancer treated with one of three approaches: 1) Total neoadjuvant therapy (TNT) comprised of chemotherapy followed by neoadjuvant stereotactic body radiation (SBRT) followed by pancreaticoduodenectomy. 2) Neoadjuvant Chemotherapy and Surgery (NeoC-S) comprised of chemotherapy followed by immediate pancreaticoduodenectomy. 3) Chemo-SBRT (NeoC-SBRT) comprised of neoadjuvant therapy followed by SBRT without surgery.

**Methods:** Between October 2011 and June 2015, 80 patients with borderline resectable non-metastatic pancreatic adenocarcinoma underwent one of the above treatment approaches including 25 with TNT, 6 with NeoC-S and 49 with NeoC-SBRT. Clinical characteristics at diagnosis including performance status, CA 19-9, clinical stage, degree of vascular involvement and pathologic staging along with margin status were obtained. For patients who received SBRT, the majority of patients received 30 Gy in 3 fractions over 5 days via CyberKnife with fiducial guidance. Kaplan-Meier method with Log-Rank testing for significance was used to compare overall survival (OS), metastasis free survival and local recurrence.

**Results:** After a median follow-up of 13.3 months, median OS for the study group was 22.2 months. Patients in the NeoC-S group were younger (median age 57 yrs), had better performance status (83% ECOG 0) and were less likely to have major vessel involvement (50%). Conversely, NeoC-SBRT patients were older (median age 69.5 years), had worse performance status (37% ECOG 0), had a higher CA 19-9 (median 190) and were less likely to get FOLFIRINOX chemotherapy (53%). Patients who received TNT had a statistically significant longer median OS compared to NeoC-SBRT patients (36.5 mo. vs. 19.3 mo.;  $p=0.02$ ) and a near significant improvement in survival compared to NeoC-S patients (median OS 36.5 mo vs. 22.2 months;  $p$ -value TNT vs. NeoC 0.17). There was no significant difference in OS between patients in the NeoC-S and NeoC-SBRT groups ( $p=0.98$ ). Similarly, metastasis free survival (MFS) was improved with TNT (23.4 mo.) as compared to NeoC-SBRT (15.1 mo.;  $p=0.001$ ) but not significantly different as compared to NeoC (21 mo.;  $p=0.42$ ). There was no significant difference between MFS in the NeoC-S and NeoC-SBRT groups ( $p=0.37$ ). 1-year rates of freedom from local failure were not statistically significant between treatment groups (95% TNT, 83%

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NeoC-S, 78% NeoC-SBRT).

Conclusions: Total neoadjuvant therapy using chemotherapy and SBRT with surgery offers significant improvement in survival compared to patients who do not received all three treatments. Despite worse baseline disease and patient characteristics, patients who received chemotherapy followed by SBRT had similar outcomes compared to patients who received chemotherapy followed by surgery without SBRT. These findings suggest that the use of neoadjuvant chemotherapy and pancreatic SBRT may provide a significant survival benefit and warrants further study.