A Neoadjuvant Approach to Borderline Resectable Pancreatic Cancer: The Virginia Mason Experience

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ABSTRACT

Background: The optimum neoadjuvant approach to BRPC is unknown. Since 2008, we have used a neoadjuvant approach based on extended course chemotherapy (CT) without routine neoadjuvant chemoradiation (CRT). We present current findings here.

Methods: Patients (pts) were prospectively identified beginning in 2008 from our institutional pancreaticobiliary cancer database. Inclusion criteria were 1) bx-proven PC; 2) radiographic staging per AHPBA/NCCN criteria; 3) no prior therapy (Rx); 4) Negative staging laparoscopy prior to Rx initiation 5) all neoadjuvant therapy at parent institution, 6) pts follow-up ≥ 24 weeks (wks.) from therapy initiation. Pts received gemcitabine/docetaxel (G/D) as neoadjuvant chemotherapy (CT) x 24 weeks unless prevented by systemic disease progression or therapeutic intolerance. At that time, all pts adjudged likely to achieve R0 resection were offered surgery (S); all other pts were offered fluoropyrimidine –based CRT if deemed medically fit.

Results: Using the above, 142 pts were identified who met the above criteria: Pt characteristics include median age 65 yrs (range 44-82 yrs), ECOG PS 0/1/2+ 98/37/7. 97% (138/142) pts had venous involvement; 43% (61/136 pts) arterial involvement. 78% (111/142) pts completed ≥80% of intended CT. 51% (73/142) pts underwent resection (46 R0, 27 R1) 49% (69/142) pts failed to do so; reasons included: 37 pts disease progression, 10 pts medical intolerance (CT toxicity, medical comorbidity), 5 pts, pt withdrawal from therapy, 19 pts surgeon discretion. 48% resected (35/73) pts and 25% (18/73) pts received postoperative CRT/CT respectively.

With median f/u of 31.5 months (mo), 52% (38/73) pts have recurred: For resected pts, median disease free survival is 23.0 (95% CI: 16.0-31.7) mo., median OS is 35.7(95% CI: 25.8-58.5) mo. 5-yr OS is 17.6%. Median OS for non-resected pts is 14.0 mo .Median OS for the entire patient population is 22.3 (95% CI: 19.6-27.3) mo.

Conclusions:

This is one of the largest clinical series in BRPC and includes laparoscopic staging and homogeneous neoadjuvant CT. Median OS for the entire patient population compares favorably with both previous experience in BRPC and cooperative group experience in *de novo* resectable PC.

Information from this experience can aid future clinical research in BRPC.

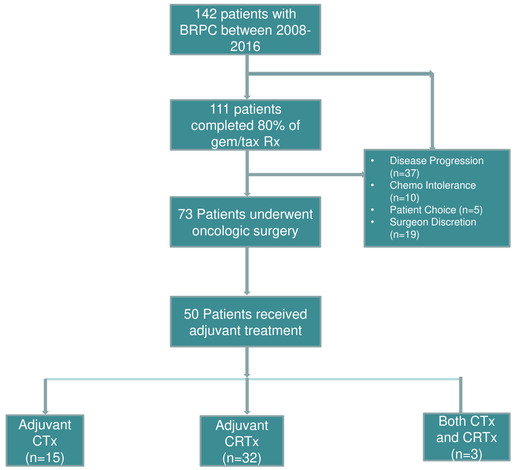
BACKGROUND

- Pancreatic Cancer (PC) is the 3rd leading cause of cancer death in the US/Canada[1]
- Neoadjuvant therapy can assist in facilitating a successful resection in borderline resectable disease[2]
- Up to 25% of post surgical patients do not receive adjuvant treatment
- Combination gemcitabine/taxane chemotherapy has shown a benefit in overall survival in the metastatic setting[4]

OBJECTIVES

- To analyze our institutional experience with combination gemcitabine/docetaxel (gem/tax) in the neoadjuvant setting on patients with borderline resectable pancreatic cancer.

METHODS

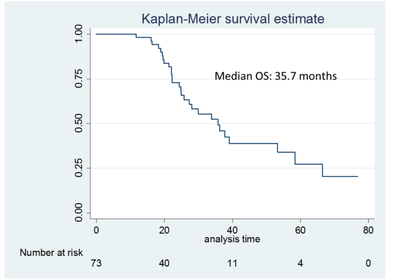


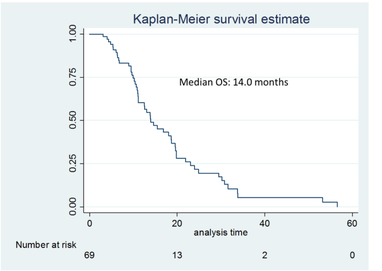
INCLUSION CRITERIA:

- AHPBA Defined Borderline Resectable PC
- Administer gem/tax as first neoadjuvant treatment
- All neoaduvant/surgical treatment performed at VMMC

EXCLUSION CRITERIA:

- Metastatic Disease on Diagnostic Laparoscopy
- Received Previous Treatment





RESULTS

Baseline Characteristics	
Variables	**Patients (n=142)**
Age median years (Range)	64.9 (43.5-81.6)
Distribution (%)	
≥65	64 (45.1)
<65	78 (54.9)
Sex M/F (%)	54.2/45.8
ECOG (%)	
0	69.0
1	26.1
2	4.2
Median Pre-Chemotherapy Charleson Score (Range)	3 (0-14)
Median Pre-Chemotherapy BMI (Range)	26.2 (16.8-59)
Median Pre-Chemotherapy CA 19-9 (U/mL) (Range)	429.3 (3-33876)
AJCC Stage at Presentation (%)	
2	71.1
3	28.9
Diagnostic Laparascopy (%)	100
Positive Washings (%)	98.9
Vessel Involvement	
Venous Only (%)	57.0
Arterial and Venous (%)	40.1
Median Pre-Chemotherapy NLR (Range)	2.7 (0.6-23.7)
NLR<2.7 (%)	47.2
NLR>4.0 (%)	23.9
Median Pre-Chemotherapy Albumin (Range)	3.8 (2.7-5.1)
Tumour Characteristics (Resected Patients)	**Patients (n=73)**
Median tumour size mm (Range)	22.0 (0-53)
Tumour Location (%)	
Head	95.8
Neck	1.4
Body	2.1
Tail	0.7
Differentiation (%)	
Well	2.9
Moderate	45.7
Poor	40.0
No Tumor	11.4
Lymph Node Status (%)	
Positive	55.6
Negative	44.4

Surgical Characteristics	
Variables	**Patients (n=73)**
Type of operation (%)	
Pancreaticoduodenectomy	97.2
Distal Pancreatectomy	2.8
Vascular Resection (%)	
Resection Margins	
R0	63.0
R1	37.0
R2	0.0
Re-operation rate (%)	
Operative blood loss mL, median (Range)	
Number of Lymph Nodes Harvested, median (Range)	17.0 (7-34)
LN Ratio (%)	
≥20%	19.7
<20%	80.3
Treatment Characteristics	
Completed >80% of Neoadjuvant Chemotherapy	
Yes (%)	111 (78.2)
No (%)	31 (21.8)
Completed >100% of Neoadjuvant Chemotherapy	
Yes (%)	100 (70.4)
No (%)	42 (29.6)
Received Neoadjuvant CRTx (%)	22 (15.5)
Patients Resected (%)	73 (51.4)
Reasons for No Surgery (%)	
Disease Progression	53.6
Intolerance without Progression/Medical	14.5
Patient Choice	7.3
Surgeon Discretion	27.5
Received Adjuvant Treatment	50 (68.5)
Adjuvant CTx (%)	30.0
Adjuvant CRTx (%)	64.0
Both (%)	6.0

Variables	Resected Patients (n=73)	Resected Patients if Completed Neodjuvant CTx (n=68)	Unresected Patients (n=69)
Median length of follow-up, months (95% CI)	29.2 (22.0-44.8)	29.2 (22.0-44.8)	NR (31.3-NR)
Overall Survival			
Median overall survival, months (95% CI)	35.7 (25.8-58.5)	36.3 (25.8-58.5)	14.0 (11.1-18.7)
Survival Rate % (95% CI)			
6months	98.4 (89.0-99.8)	98.1 (87.1-99.7)	61.3 (47.9-72.1)
12 months	74.3 (59.8-84.2)	79.2 (63.7-88.6)	23.7 (13.3-35.8)
24 months	50.4 (34.5-64.4)	57.4 (39.7-71.7)	6.2 (1.5-16.2)
36 months	29.4 (14.3-46.3)	33.5 (16.2-51.8)	0.0 (NR)
60 months	17.6 (3.4-41.1)	20.1 (3.7-45.8)	0.0 (NR)
Disease Free Survival			
Median disease free survival, months (95% CI)	23.0 (16.0-31.7)	24.5 (17.2-32.7)	
Disease Free Survival Rate % (95% CI)			
6 months	87.6 (75.8-93.9)	87.8 (74.8-94.3)	
12 months	48.7 (33.9-61.9)	53.6 (37.6-67.2)	
24 months	23.6 (11.9-37.7)	26.1 (13.1-41.1)	
36 months	15.0 (5.2-29.8)	16.6 (5.7-32.5)	
60 months	15.0 (5.2-29.8)	16.6 (5.7-32.5)	

Variables	Hazard Ratio	95% CI	P-Value
Overall Survival			
Tumor Differentiation	2.99	1.24-7.17	0.01
Disease Free Survival			
Margins	4.48	2.0-9.8	0.0000
Completed 100% Neoadjuvant Chemo	0.1	0.02-0.49	0.004
Tumour Size ≥30mm	2.37	1.02-5.49	0.04
Received Adjuvant Treatment	0.23	0.10-0.53	0.001

CONCLUSIONS

- This is the largest series of patients with Borderline Resectable Pancreas Cancer treated with homogenous chemotherapy
- Combination gem/tax treatment is tolerable with the vast majority of patients completing intended course therapy
- Tumor Differentiation affects overall survival on multivariate analysis
- Future studies aiming to predict treatment responders are underway

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