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Exciting Results With Weekly "Metronomic Dosing" of Paclitaxel, Oxaliplatin, Leucovorin, and 5-Fluorouracil (POLF) in the Treatment of Metastatic Pancreatic Cancer

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Background: Patients with metastatic pancreatic cancer have a dismal prognosis and poor quality of life. Weekly "metronomic dosing" of chemotherapy allows for increased dose density, dose intensity, and antiangiogenic effects, yet affords good tolerability, allowing for a better quality of life and perhaps improved survival. We report exciting interim results of 11 patients treated for at least 11 weeks with the POLF (paclitaxel [P], oxaliplatin [O], leucovorin [L], 5-fluorouracil [5-FU]) regimen.

Methods: Eleven patients, ages 35 to 75 years, with metastatic biopsy-proven pancreatic cancer were treated with weekly POLF (P: 60 mg/m^2, O: 50 mg/m^2, L: 20 mg/m^2, 5-FU: 425 mg/m^2) for 12 weeks. One patient (A.B.) also received intermittent cetuximab treatment. Glutathione, calcium, and magnesium were used to prevent oxaliplatin-related neuropathy.

Results: After at least 11 weeks of treatment, 9 of 11 patients had greater than 50% reduction of CA 19-9 levels (see Table), improvement of cancer-related symptoms, and shrinkage of tumor. Bilirubin level in one patient (D.P.) was 27 and in another patient (L.C.) was 9.6, both of which normalized with treatment without need for stent placement. Patient A.B. was severely debilitated (Eastern Cooperative Oncology Group [ECOG] performance status [PS] of 4) following progression of disease after two previous lines of chemotherapy but is alive and well nearly 3 years since diagnosis, with an ECOG PS of 0. G.B. had a small bowel obstruction, with ECOG PS of 4, but now is

unobstructed, with ECOG PS of 2. The regimen was well tolerated with two cases of grade 3 neurotoxicity (L.C., F.T.) and two cases of grade 3 diarrhea (B.P., F.T.). Median survival has not been reached.

Conclusions: The weekly combination of paclitaxel, oxaliplatin, leucovorin, and 5-FU has significant activity against advanced pancreatic cancer with manageable side effects. A phase II study is open to enrollment, and we welcome participation.

Patient	Gender	Age (yr)	Tumor Sites	Prior Chemotherapy	CA 19-9		Survival (mo)		Clinical Response	Sensory Neuropathy
					Before POLF	After 12 Weeks	Since Diagnosis	Since POLF Treatment		
A.B.	Male	35	Body of pancreas, liver	1)Gemcitabine + docetaxel 2)Gemcitabine + capecitabine	489	18	34.6+	29.4+	PR	Grade 2
D.P.	Male	55	Head of pancreas, liver	1)Gemcitabine + cisplatin	9,015	53	12.0	10.6	PR	Grade 1
L.C.	Female	43	Neck of pancreas, lungs, retroperitoneal and supraclavicular LN	None	8,893	326	24.6+	23.3+	MR/PR	Grade 3
I.S.	Female	53	Body & tail of pancreas, liver	1)Gemcitabine 2)Capecitabine	124,692	23,131	22.5	10.4	MR/PR	Grade 1
R.R.	Male	66	Head of pancreas, liver	None	3,658	1,136	7.5	6.7	PR	Grade 1
B.P.	Male	65	Neck of pancreas, liver	1)Mitomycin C + 5-FU+ cisplatin 2)Gemcitabine	3,453	1,445	17.4	11.3	MR	Grade 1
G.L.	Female	75	Head of pancreas, liver, lung	1)Capecitabine	3,594	302	13.4*/7.9**	6.2	MR	Grade 1
W.S.	Male	66	Head of pancreas, liver, periaortic LN	None	112	66	15.0	12.3	Mixed	Grade 1
H.G.	Male	73	Head of pancreas, liver, lung	1)5-FU/ leucovorin 2)Gemcitabine+ erlotinib 3)Capecitabine	5,690	3,978	22.4*/6.6**	6.2	MR	Grade 1
F.T.	Female	44	Head of pancreas, liver	1)Gemcitabine + docetaxel+ erlotinib 2)Gemcitabine + capecitabine	3,378	326	21.2+*/20.0+**	5.2+	PR	Grade 3
G.B.	Male	65	Body of pancreas, liver	1)Gemcitabine + Docetaxel+ capecitabine	6,928	917	5.8+	3.8+	PR	Grade 1

**Time since original diagnosis of pancreatic cancer.*
***Time since diagnosis of metastatic pancreatic cancer.*

Abbreviations: LN = lymph nodes; MR = minor response; POLF = paclitaxel, oxaliplatin, leucovorin, 5-fluorouracil; PR = partial response