Decrement of Serum CA 19-9 Concentration after Initial Chemotherapy Predict Favorable Outcome in Patients with Advanced Pancreatic Cancer

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Background & Aims

- **Pancreatic ductal adenocarcinoma (PDAC)**
  - 5th leading cause of cancer-related death in Korea (2012)
  - No effective modalities for early detection
  - Present with locally advanced and/or metastatic disease
  - Unresectable PDAC: Median OS ~ 6 months, 5-YSR ~ 6%

- **Role of CA 19-9 in diagnose and predict prognosis of PDAC**
  - Some role for distinguish PDAC from benign conditions
    : Sensitivity ~ 78.2%, Specificity ~ 82.8%
  - Predict tumor stage & resectability, overall survival, & response to therapy (operative treatment)
  - Correlate with the progression or remission of disease after treatment

- **Dynamic change of CA 19-9?**
  - In 26 patients, 20% decrement of CA19-9 ∝longer survival
  - 36 patients, 20% decrement of CA 19-9, after 8 week of gemcitabine chemotherapy ∝longer survival
  - 75 patients, 50% decrement of CA 19-9, after 6 week of gemcitabine monotherapy or gemcitabine plus capecitabine
    : failed to show significance
  - Pooled analysis of 6 prospective trials - 104 patients: 5% rise of CA19-9 ∝shorter survival

- **Aim**

  Can early decrement in CA 19-9 concentration predict PDAC prognosis during the chemotherapy?

Methods

- **Retrospective review in single center (SNUH)**
- **Between January 2012 and December 2013**
- **Patients with ---**
  - Unresectable or metastatic PDAC
  - Underwent chemotherapy
- **Exclude** CA19-9 data was unavailable (Baseline, f/u)
- **Patients demographic data / Cancer stage / Tumor location / Pretreatment biliary drainage / Chemo regimen**
- **Serum CA 19-9 concentrations:** baseline & 8 weeks after the initial chemotherapy
- **Outcome measurement**
  - Response rate (after 9 week)
  - Progression free survival [PFS]
 - Overall survival [OS]

Results

- **Clinical Characteristics of Patients: total 216 patients**

Sex		Pre-treatment CA 19-9	1364 (86.8 - 7770.5)
Male	128 (59.3%)	**Post treatment CA 19-9**	697.5 (61 - 7748.3)
Female	88 (40.7%)	**CA 19-9 (Post/Pre)**	79.8% (37.8% - 112.1%)
Age (year)	63.2 ± 9.5	**ChemoTx. Regimen**	
Cancer Stage		Gemcitabine + capecitabine	1 (0.4%)
III	78 (36.1%)	Gemcitaine+erlotinib	164 (61.4%)
IV	138 (63.9%)	Gemcitabine + cisplatin	27 (10.1%)
Tumor Location		FOLFIRINOX	29 (10.9%)
HEAD	93 (43.1%)	Gemcitabine monotherapy	46 (17.2%)
BODY	63 (29.2%)	**ChemoTx. Response (after 9 cycle)**	
TAIL	60 (27.8%)	PR	58 (26.9%)
Biliary Drainage		SD	73 (33.8%)
Done	57 (26.4%)	PD	77 (35.6%)
Not done	159 (73.6%)	N/A	8 (3.7%)

Dynamic change of CA 19-9 at 8 weeks & clinical factors

	CA19-9 decrease ≥ 10%	CA19-9 increase or decrease < 10%	P-value
n	118	98	
Sex (male)	64 (54.2%)	64 (65.3%)	0.099
Age (year)	62.9 ± 9.33	63.6 ± 9.79	0.605
Pre-treatment CA 19-9	866.0 (87.8 - 4881.5)	2385.5 (85 - 12000)	0.070
Post-treatment CA 19-9	247.0 (32.5 - 1198.3)	6851.0 (384 - 12000)	< 0.001
Post/Pre CA 19-9	39.9% (19.1% - 65.6%)	123.3% (100% - 228.5%)	< 0.001
Cancer Stage			0.001
Stage III	54 (45.8%)	24 (24.5%)	
Stage IV	64 (54.2%)	74 (75.5%)	
Tumor Location			0.313
Head	55 (46.6%)	38 (38.8%)	
Body	35 (29.7%)	28 (28.6%)	
Tail	28 (23.7%)	32 (32.7%)	
Biliary Drainage	31 (26.3%)	26 (26.5%)	0.966
ChemoTx. Regimen			0.179
Gemcitabine-based	100 (84.7%)	89 (90.8%)	
FOLFIRINOX	18 (15.3%)	9 (9.2%)	
ChemoTx. Response			< 0.001
PR	40 (35.4%)	18 (18.9%)	
SD	51 (45.1%)	22 (23.2%)	
PD	22 (19.5%)	55 (57.9%)	

PFS and OS with dynamic change of CA 19-9 at 8 weeks
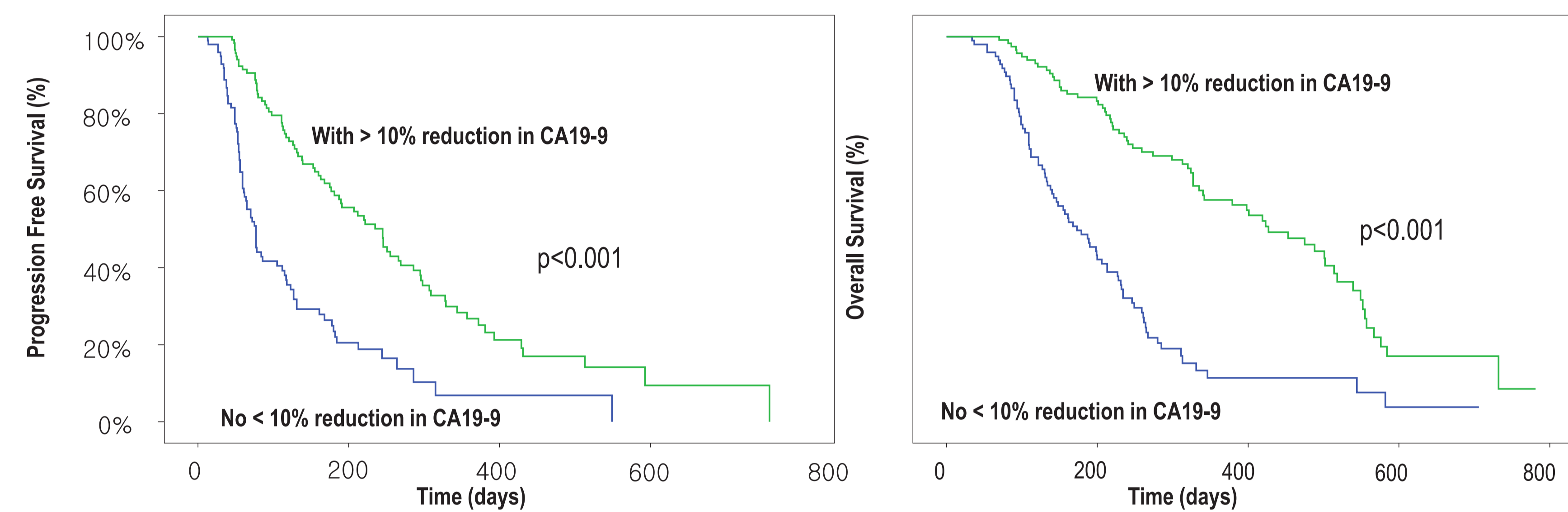
Median PFS

10% reduction in CA19-9: 245 (193.5 - 296.5)

Without 10% reduction in CA19-9 : 77 (65.2 - 88.8)

Median OS

10% reduction in CA19-9: 427 (332.6 - 521.4)

Without 10% reduction in CA19-9 : 262 (213.8 - 310.2)

Factors related with longer OS

	n	Univariate		Multivariate	
		Median OS	P-value	Hazard ratio (95% C.I)	P-value
Sex			0.816		0.180
Male	128	264 (208.8 – 319.2)		1	
Female	88	262 (182.0 – 342.0)		1.268 (0.896 - 1.794)	
Age			0.115		0.423
< 65	119	274 (206.0 – 342.0)		1	
≥ 65	97	246 (194.8 – 297.2)		1.145 (0.822 - 1.596)	
Cancer Stage			< 0.001		< 0.001
Stage III	78	518 (303.8 – 732.2)		1	
Stage IV	138	213 (179.3 – 246.7)		2.202 (1.478 - 3.282)	
Tumor location			0.025		0.416
Head	93	247 (170.6 – 323.4)		1	
Body	63	324 (167.5 – 480.5)		0.725 (0.444 - 1.183)	
Tail	60	227 (173.9 – 280.1)		0.881 (0.531 - 1.461)	
Pretreatment biliary drainage			0.663		0.264
Not done	159	264 (208.1 – 319.9)		1	
Done	57	259 (160.5 – 357.5)		0.753 (0.457 - 1.239)	
Chemoregimen			< 0.001		< 0.001
Gemcitabine based	189	236 (206.1 – 265.9)		1	
FOLFIRINOX	27	-		0.196 (0.079 - 0.485)	
CA19-9 reduction			< 0.001		< 0.001
≥ 10%	118	427 (332.6 - 521.4)		1	
< 10%	98	262 (213.8 - 310.2)		3.317 (2.304 - 4.776)	

Summary

- **For patients whose serum CA 19-9 concentration decreased more than 10% from baseline**
- Median PFS was significantly longer (245 vs. 77 days, p<0.001)
- Median OS also was significantly longer (427 vs. 262 days, p<0.001)

Conclusions

- **Early decrement in CA 19-9 concentration during chemotherapy can predict better outcome of advanced PDAC.**