Intra-arterial Targeted Delivery of Gemcitabine in Treatment of Patients with Loco-regional Pancreatic Tumors

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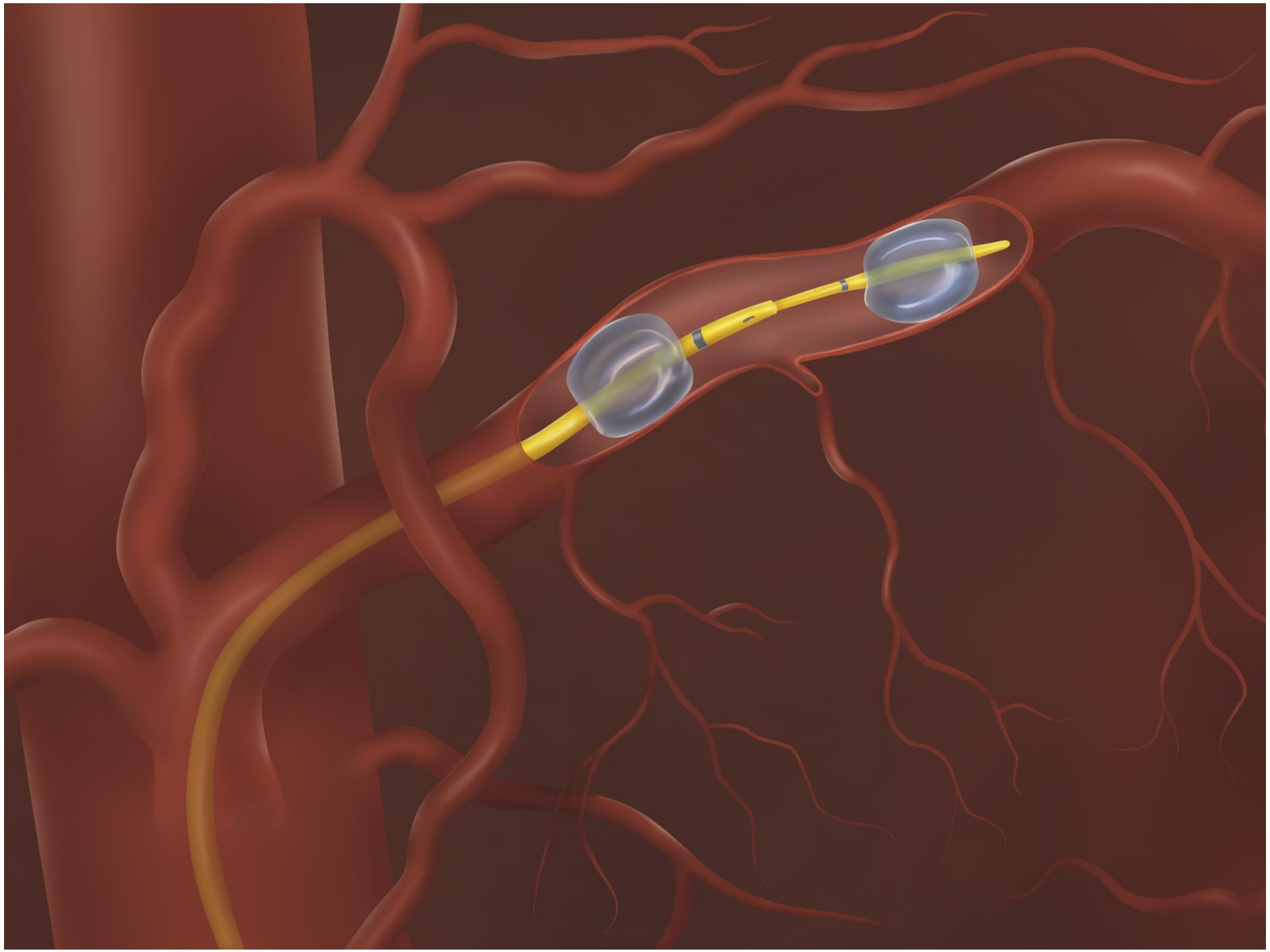


Aim: A dose escalation study of Gemcitabine for treatment of unresectable pancreatic cancer, using a targeted intra-arterial delivery catheter (RenovoCath™).

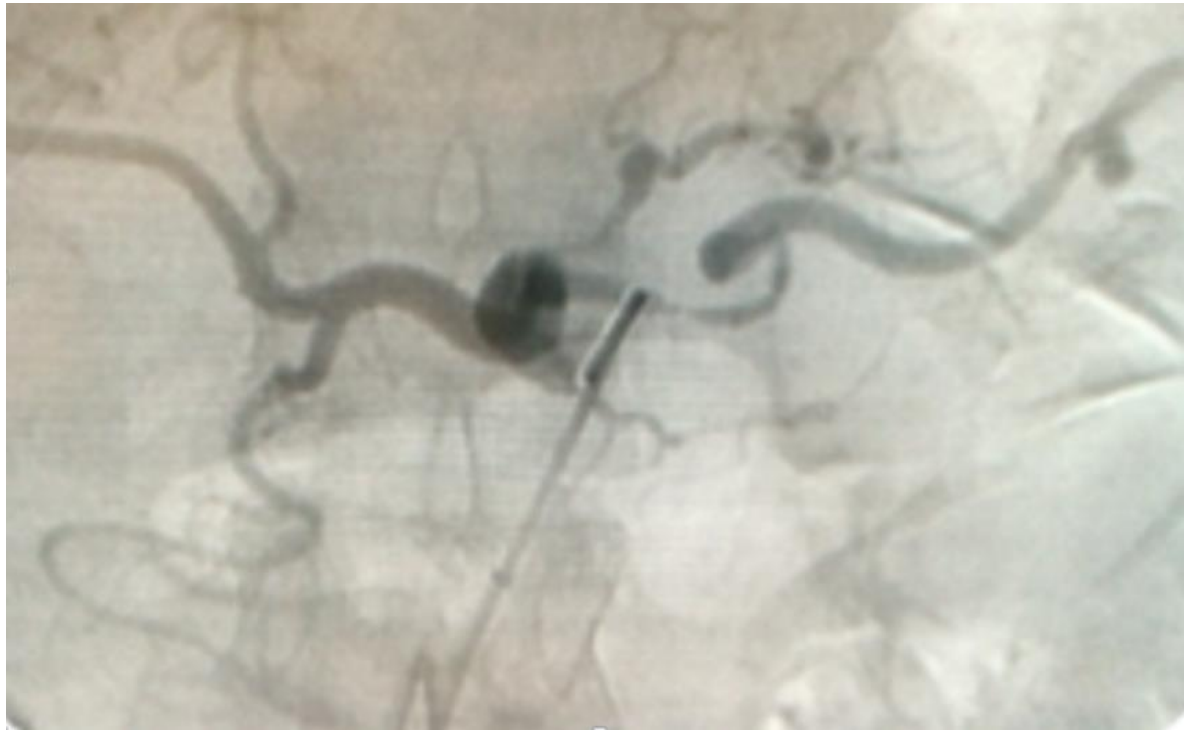
Methods: 20 patients at two centers were enrolled with a four-stage dose escalation of gemcitabine up to 1000 mg/m2. Enzyme markers, blood count, and constitutional endpoint were monitored to assess for dose-limiting toxicities. Feasibility and safety of repeated intra-arterial treatment sessions are assessed. Secondary endpoints includesthe effect on tumor size by imaging, tumor markers, and conversion to resectability.

Results: Data for the 20 patients enrolled is presented (11 of 20 patients are still being followed – data to date is included for these patients).

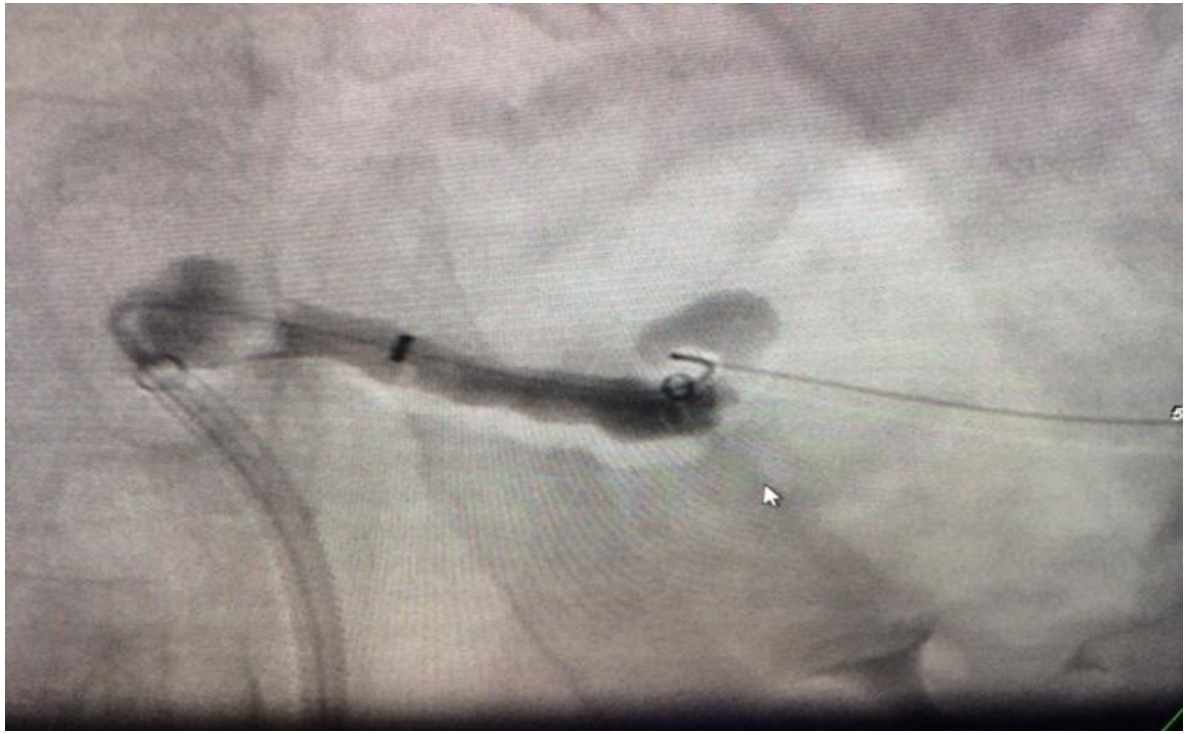
Table 1. Treatment Regimen			
Cycle	Day	Chemotherapy	Dose
1*	1	Gemcitabine	250 mg/m^2
	8		
	15	Gemcitabine	250 mg/m^2
	22		
	29		
2	1	Gemcitabine	500 mg/m^2
	8		
	15	Gemcitabine	500 mg/m^2
	22		
	29		
3	1	Gemcitabine	750 mg/m^2
	8		
	15	Gemcitabine	750 mg/m^2
	22		
	29		
4	1	Gemcitabine	1000 mg/m^2
	8		
	15	Gemcitabine	1000 mg/m^2
	22		
	29		

*Starting with patient RR1-109, the dose for the first cycle increased to 500 mg/m^2.

Table 2. Patient Characteristics		
Characteristic	No.	%
Age, years		
Median	70	
Range	51-84	
Sex		
Male	9	45%
Female	11	55%
Stage of Tumor		
I	0	0
II	0	0
III	20	100%
IV	0	0
Prior Treatment		
Yes	13	65%
No	7	35%
Prior Chemotherapy		
Yes	11	55%
No	9	45%
Prior Radiation		
Yes	5	25%
No	15	75%
Prior Chemotherapy and Radiation		
Yes	5	25%
No	15	75%
Prior Surgery		
Yes	0	0%
No	20	100%
Patient Completed Study/Ongoing		
Yes	10	50%
No	10	50%



Splenic artery narrowing with tumor impingement



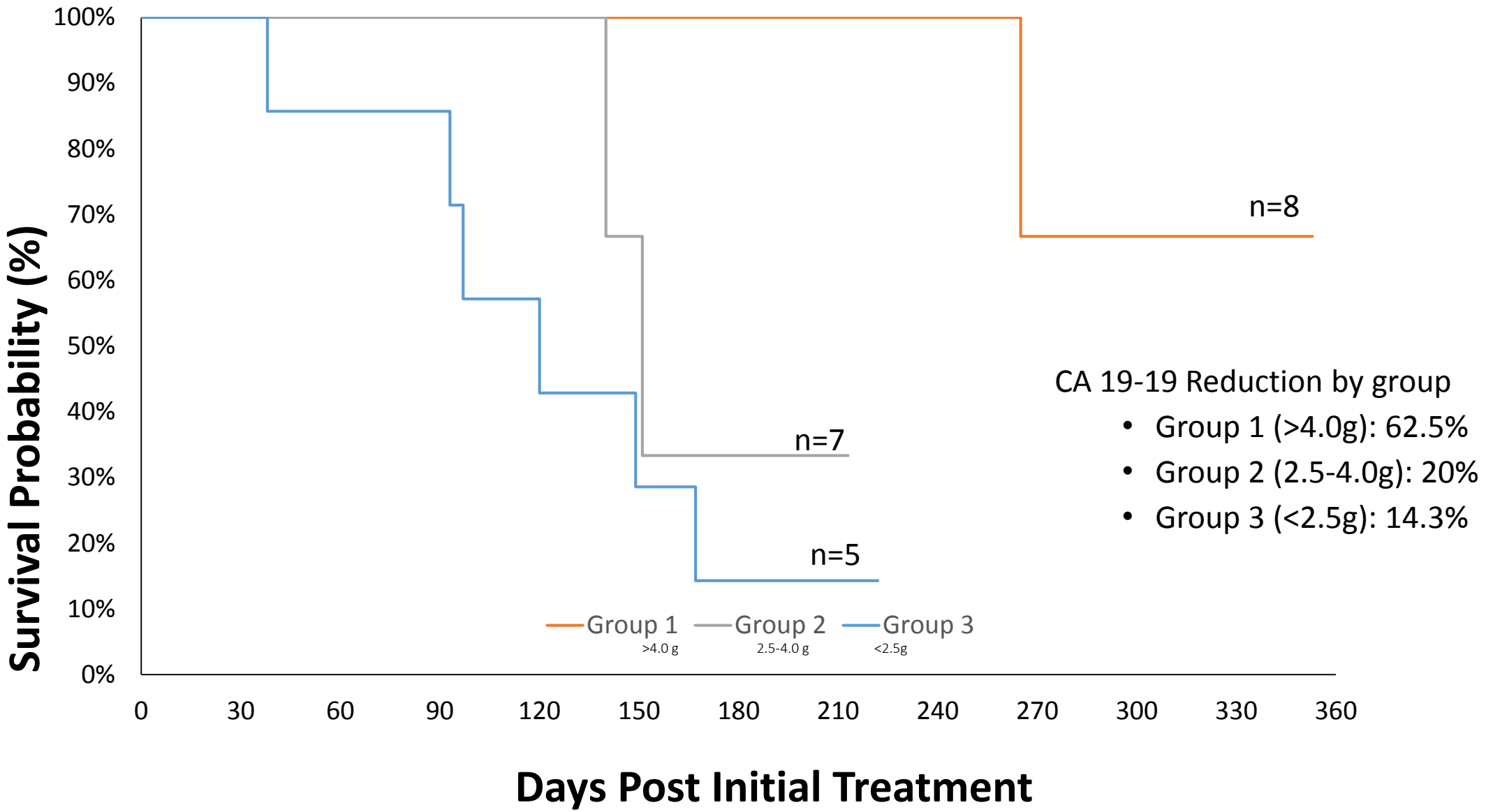
RenovoCath™ isolation of the tumor region with drug delivery

Table 3. Toxicities (grade 3 and grade 4)				
	Grade 3		Grade 4	
Toxicity	No. of Patients	%	No. of Patients	%
Hematologic				
Neutropenia	3	15%	0	0
Thrombocytopenia	0	0%	0	0
Leukopenia	0	0%	0	0
Non-hematologic				
Bilirubin	0	0%	0	0
Hyperglycemia	3	15%	0	0
Elevated Liver Function (LFP)	0	0%	0	0
Elevated Pancreatic Enzymes	0	0%	0	0
Gastritis	1	5%	0	0

Table 4. Serious Adverse Events	
Parameter	No. of Patients
Vascular	
Visceral Arterial Dissection	
Requiring termination further treatment	2
Continuing treatment further treatment	1
Vascular access complication	
Hematoma (self-limited, conservative management)	1
Non-Vascular	
Pulmonary Distress	1
Sepsis	3
Gastritis	1
Duodenal Obstruction	1

Table 5. Tumor Response for Patients Completing Study (RECIST Criteria using CT images and CA-19 Marker)		
Parameter	No. of Patients	%
CR	0	0%
PR	0	0%
SD	5	84%
PD	1	16%
Overall Response Rate (CR+ PR)	0	0%
Disease Control Rate (CR + PR + SD)	5	84%
CA 19-19 Reduction (<20% from Baseline)	5	84%

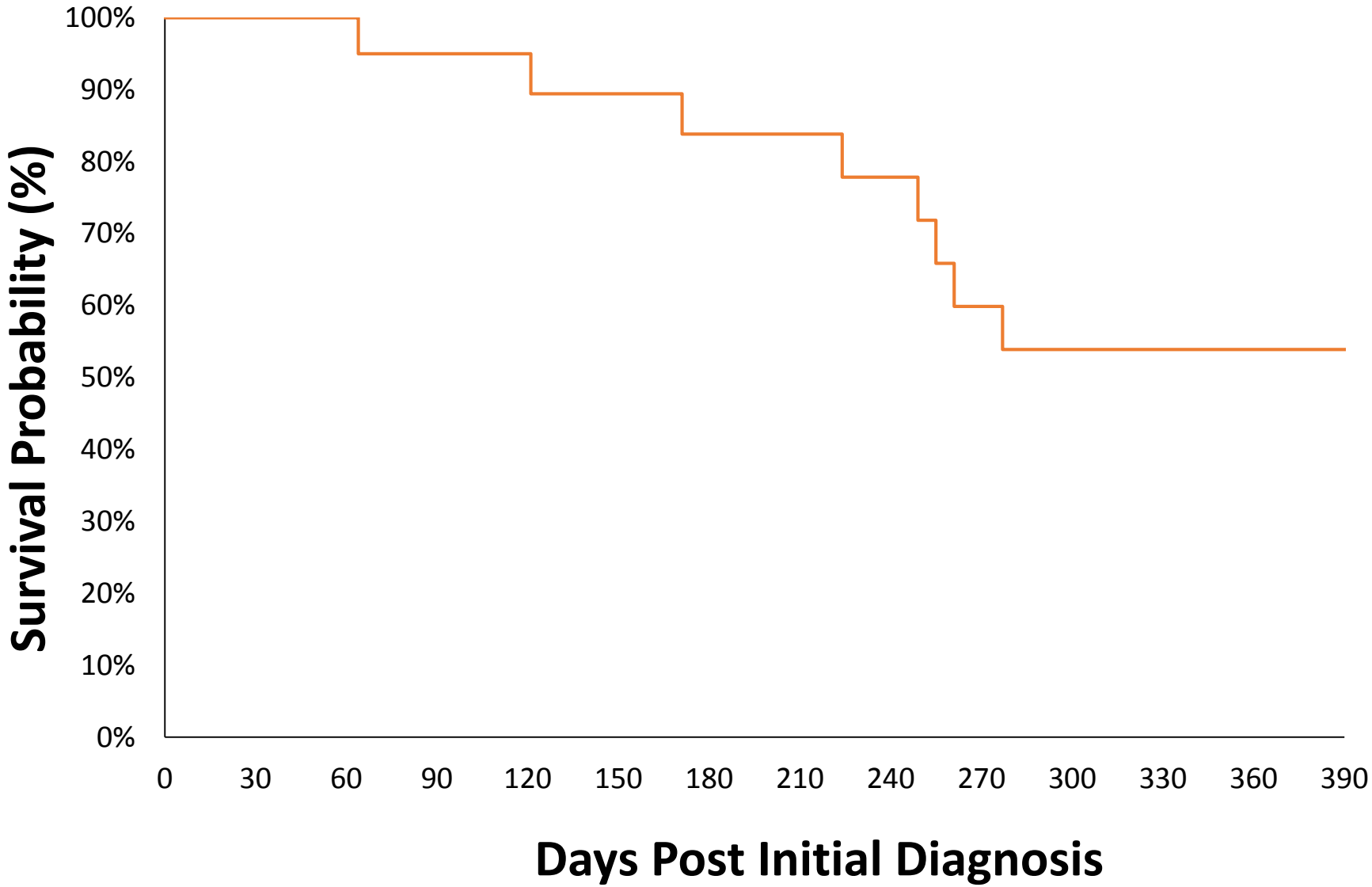
Dose Response by Group



CA 19-19 Reduction by group

- Group 1 (>4.0g): 62.5%
- Group 2 (2.5-4.0g): 20%
- Group 3 (<2.5g): 14.3%

Survival: Intention to Treat



Summary

- Intra-arterial gemcitabine can be given using localized delivery via RC-120 Catheter with acceptable safety profile
- There is less Systemic side effects of gemcitabine as assessed by hematologic markers, using RC-120 localized delivery
- In patients who received more than 4 grams of intra-arterial gemcitabine there is reduction of CA 19-9 tumor markers, disease stability based on CT, and survival benefit (compared to historical control)