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

Alexander Rosemurgy, M.D., Sharona Ross, M.D., Paul Vitulli, M.D.,
Florida Hospital – Tampa, Tampa, FL

Reza Malek, M.D., Jiali Li, M.D., Ramtin Agah, M.D.,
El Camino Hospital – Mountain View, CA

Disclosures

The study was funded by RenovoRx (Los Altos, CA)

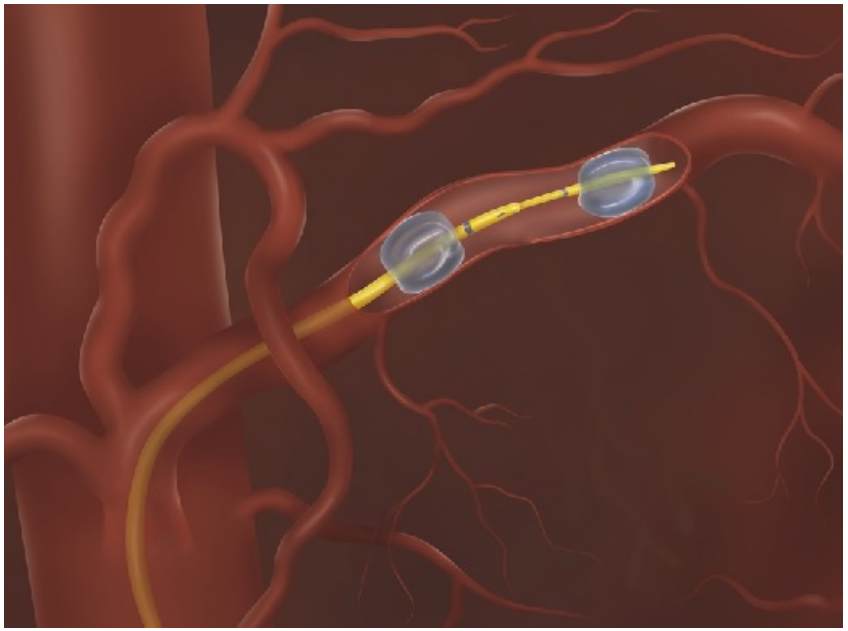
Aim: A dose escalation study of Gemcitabine for treatment of unresectable pancreatic cancer, using a targeted intra-arterial delivery catheter (RenovoCath™).

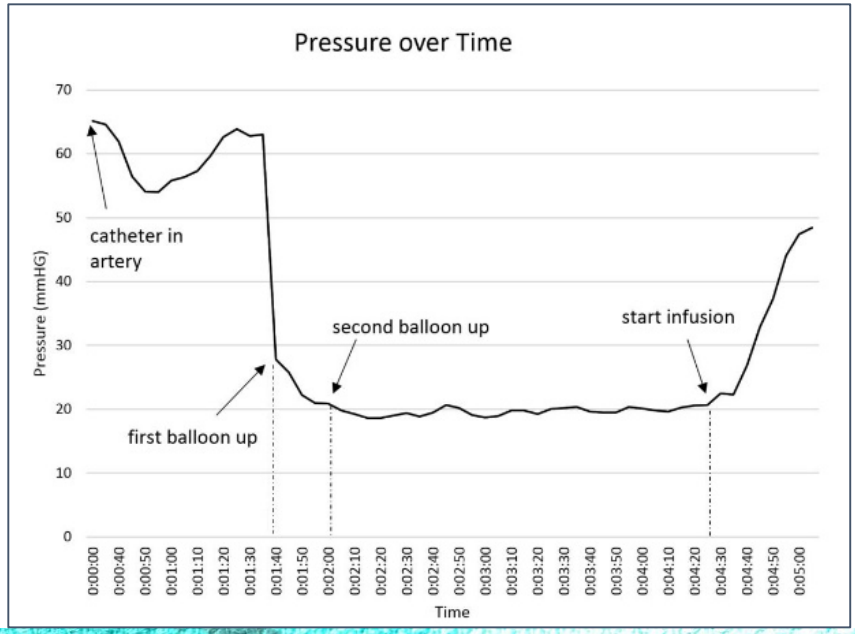
Methods: 20 patients at two centers were enrolled with a four-stage dose escalation of gemcitabine up to 1000 mg/m2. Enzyme markers, blood count, and constitutional endpoints were monitored to assess for dose-limiting toxicities. Feasibility and safety of repeated intra-arterial treatment sessions were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

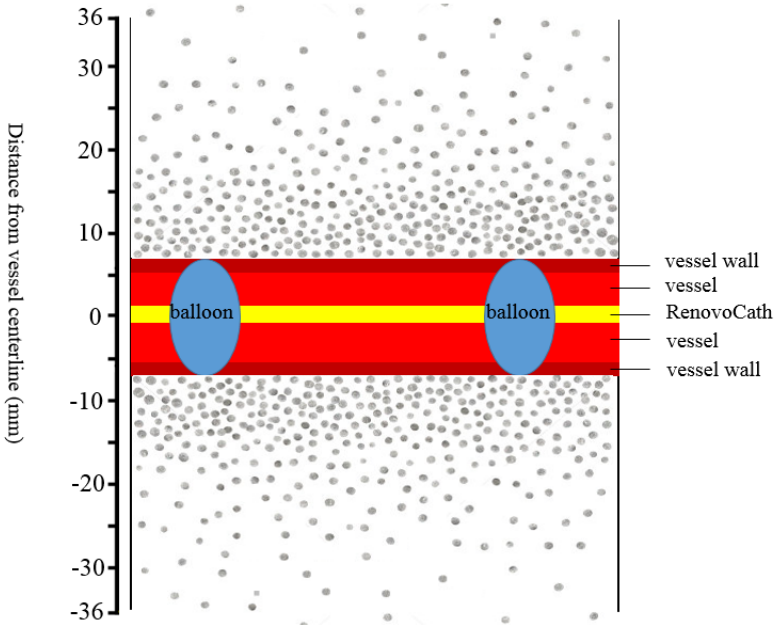
Results: Data for 20 patients enrolled is presented. Efficacy analysis was limited to the 15 patients who received more than two treatments.

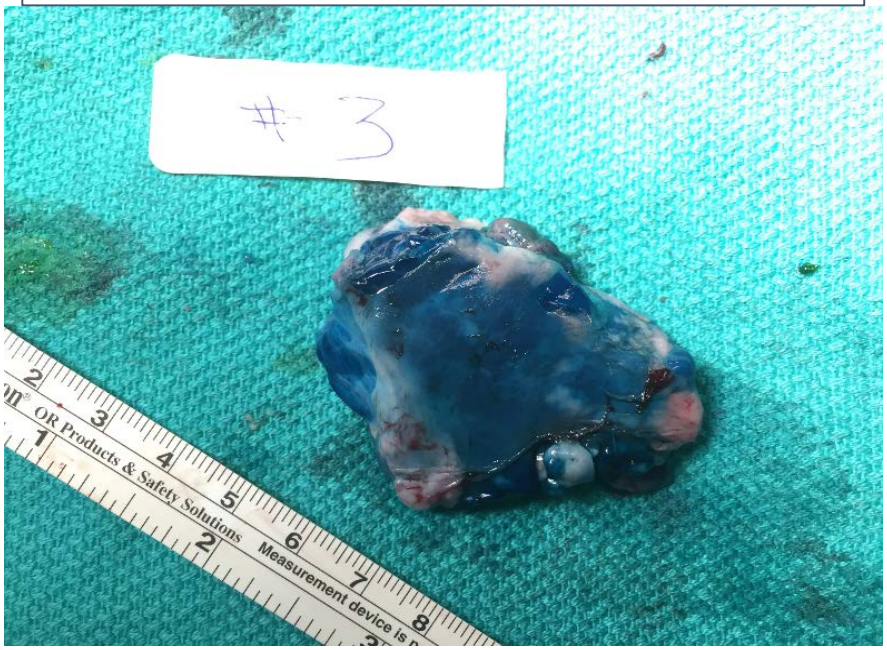
Table 1. Treatment Regimen			
Cycle	Day	Chemotherapy	Dose
1*	1	Gemcitabine	250 mg/m^2
	8		
	15	Gemcitabine	250 mg/m^2
	22		
	29		
2	1	Gemcitabine	500 mg/m^2
	8		
	15	Gemcitabine	500 mg/m^2
	22		
	29		
3	1	Gemcitabine	750 mg/m^2
	8		
	15	Gemcitabine	750 mg/m^2
	22		
	29		
4	1	Gemcitabine	1000 mg/m^2
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

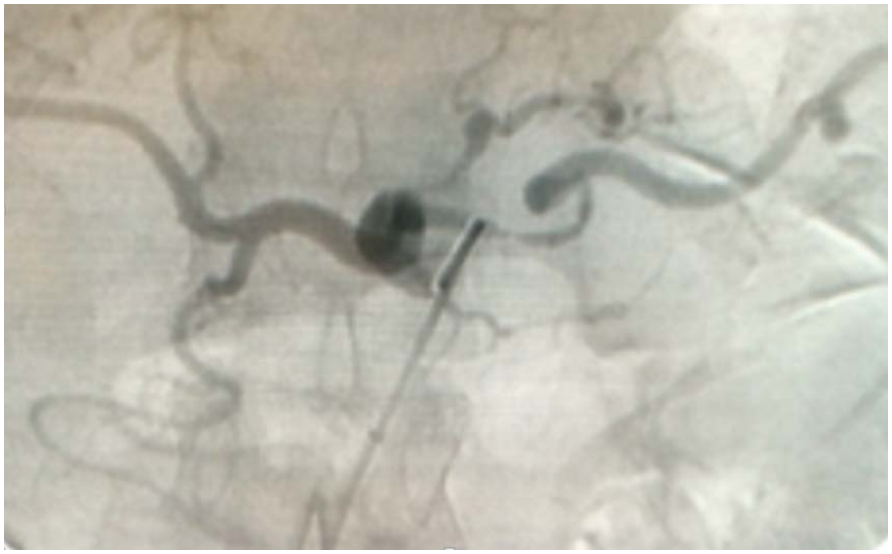
*Starting with patient RR1-109, the dose for the first cycle increased to 500 mg/m^2.



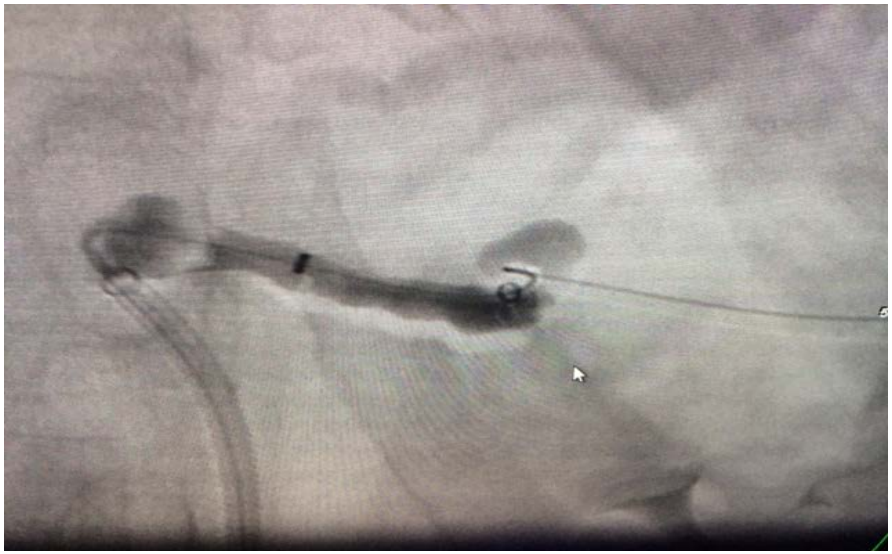

Pressure over Time
Pressure (mmHG)
70
60
50
40
30
20
10
0
catheter in artery
first balloon up
second balloon up
start infusion
0:00:00
0:00:40
0:00:50
0:01:00
0:01:10
0:01:20
0:01:30
0:01:40
0:01:50
0:02:00
0:02:10
0:02:20
0:02:30
0:02:40
0:02:50
0:03:00
0:03:10
0:03:20
0:03:30
0:03:40
0:03:50
0:04:00
0:04:10
0:04:20
0:04:30
0:04:40
0:04:50
0:05:00
Time


Distance from vessel centerline (mm)
36
30
20
10
0
-10
-20
-30
-36
balloon
balloon
vessel wall
vessel
RenovoCath
vessel
vessel wall


#3
OR Products & Safety Solutions
Measurement device is



Splenic artery narrowing with tumor impingement



RenovoCath™ isolation of the tumor region with drug delivery

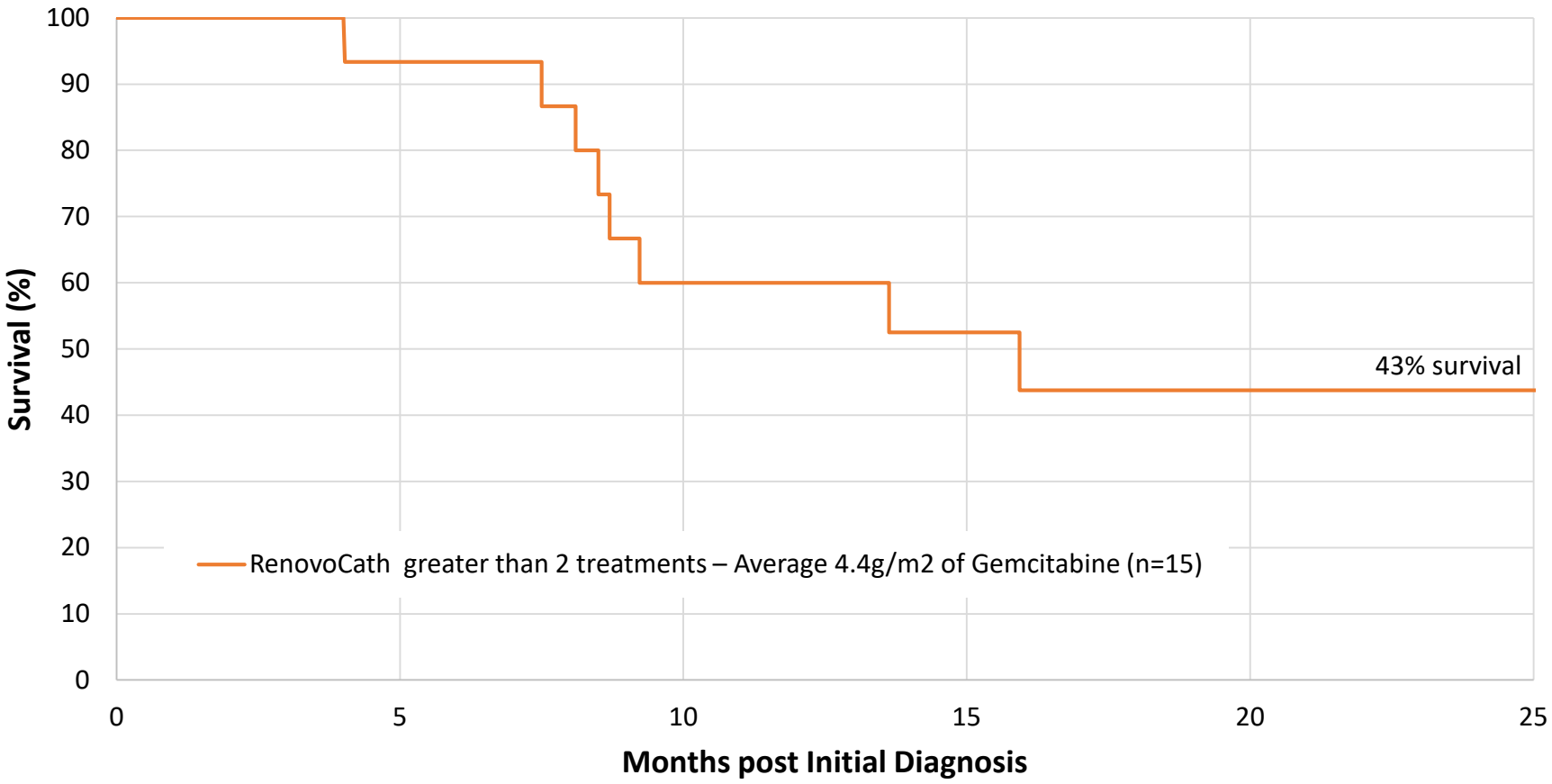
Table 2. Patient Characteristics		
Characteristic	No.	%
Age, years		
Median	70	
Range	51-84	
Sex		
Male	9	45%
Female	11	55%
Stage of Tumor		
I	0	0
II	0	0
III	20	100%
IV	0	0
Prior Treatment		
Yes	11	55%
No	9	45%
Prior Chemotherapy Only		
Yes	5	25%
No	15	75%
Prior Chemoradiation		
Yes	6	30%
No	14	70%
Prior Surgery		
Yes	0	0%
No	20	100%

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	0	0%	0	0
Elevated Liver Function (LFP)	0	0%	0	0
Elevated Pancreatic Enzymes	0	0%	0	0
Gastritis	1	5%	0	0

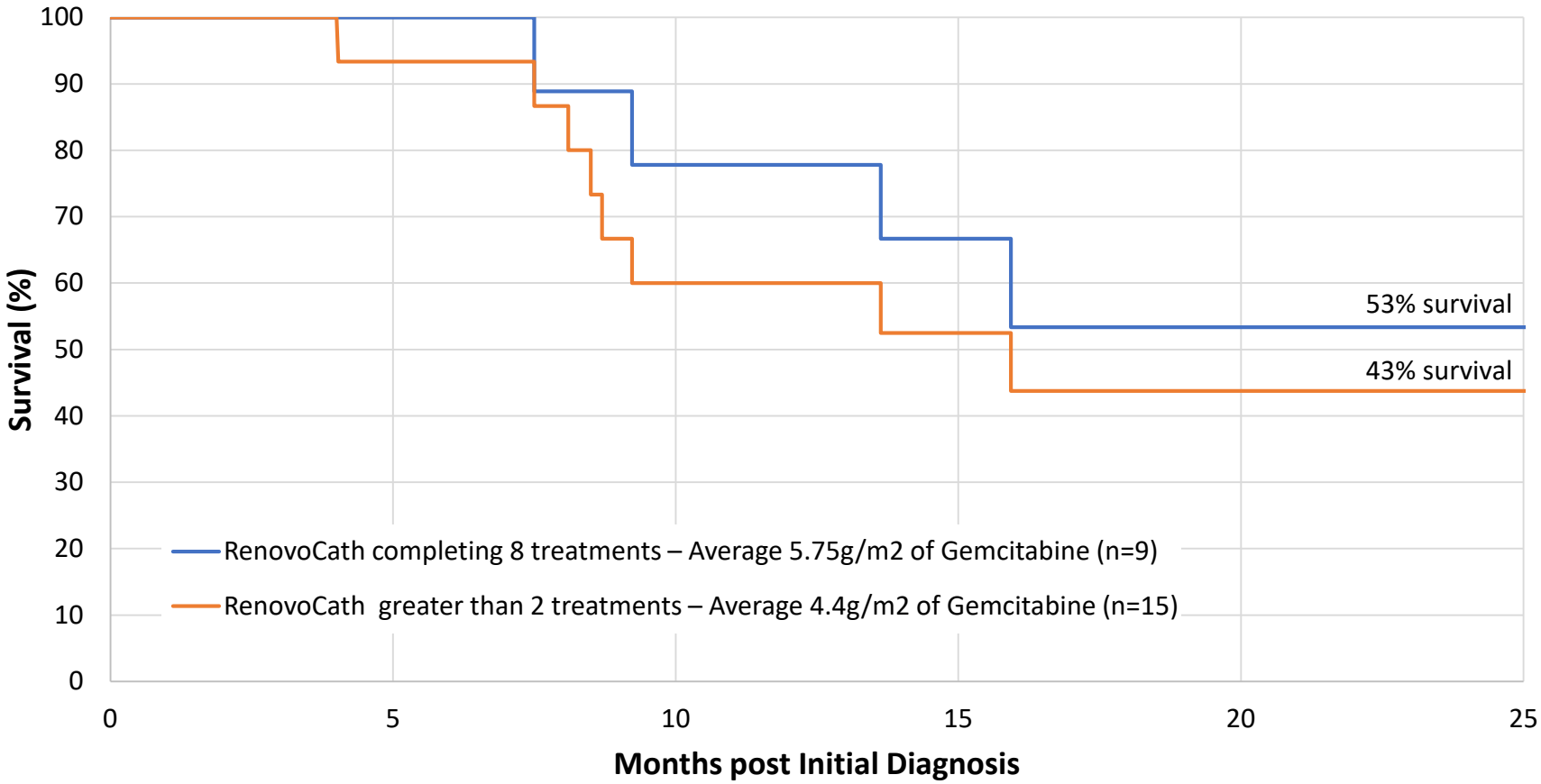
Table 4. Serious Adverse Events	
Parameter	No. of Patients
Vascular	
Visceral Arterial Dissection	
Requiring termination of further treatment	2
Continuing further treatment	1
Vascular access complication	
Hematoma (self-limited, conservative management)	1
Non-Vascular	
Pulmonary Distress	1
Sepsis	3
Gastritis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

Table 5. Efficacy: Tumor Response (clinical and or radiological progression), RECIST Criteria CT response, CA19-9		
Parameter	No. of Patients	%
Stable Disease	10	67%
Progression	3	20%
Partial Response	2	13%
CA 19-9 Reduction	9	60%
> 20% CA 19-9 Reduction	5	33%

RenovoCath treatment (>2 treatments): 43% survival



RenovoCath treatment (8 treatments): 53% survival



RenovoCath treatment (>prior radiation): 75% survival

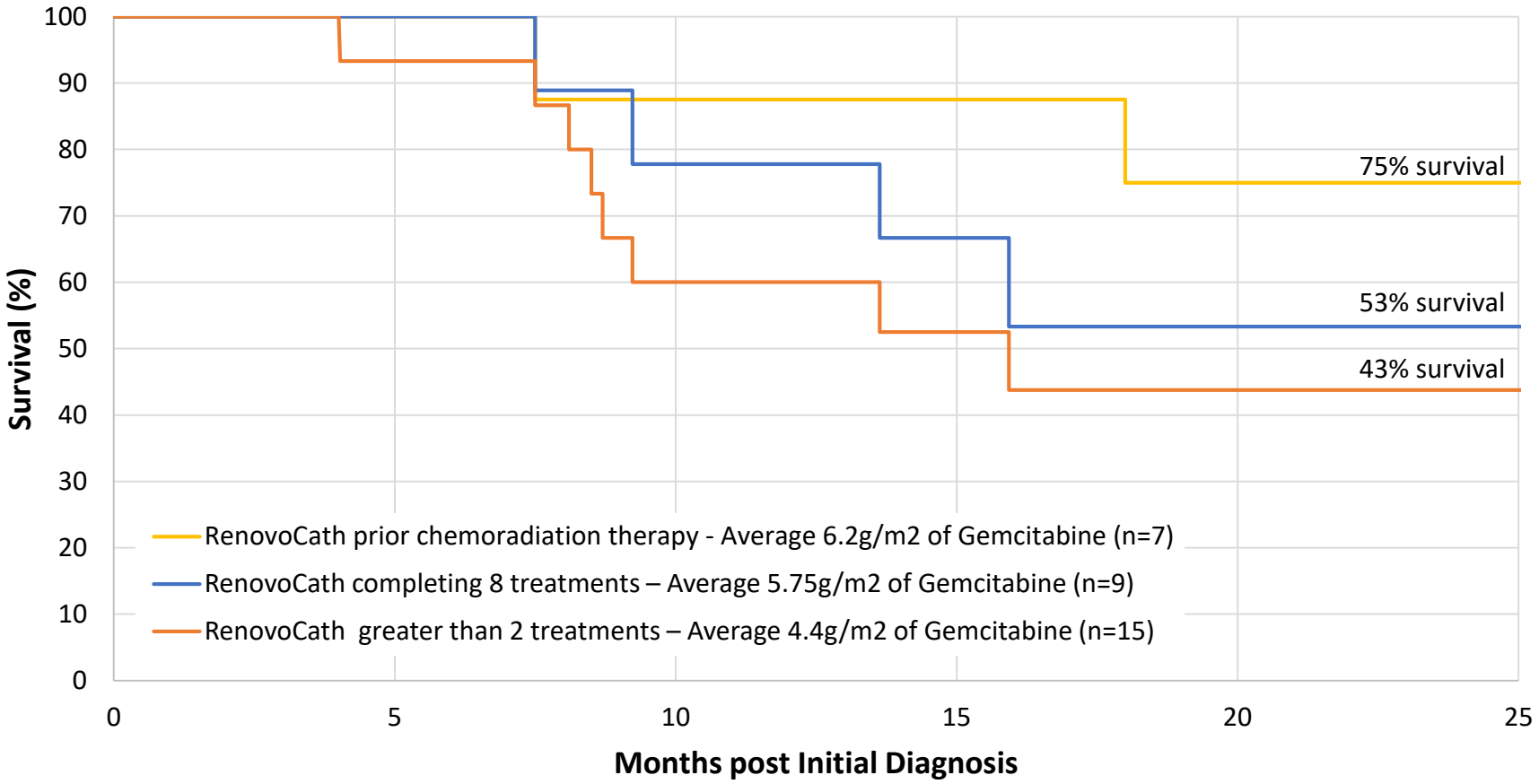
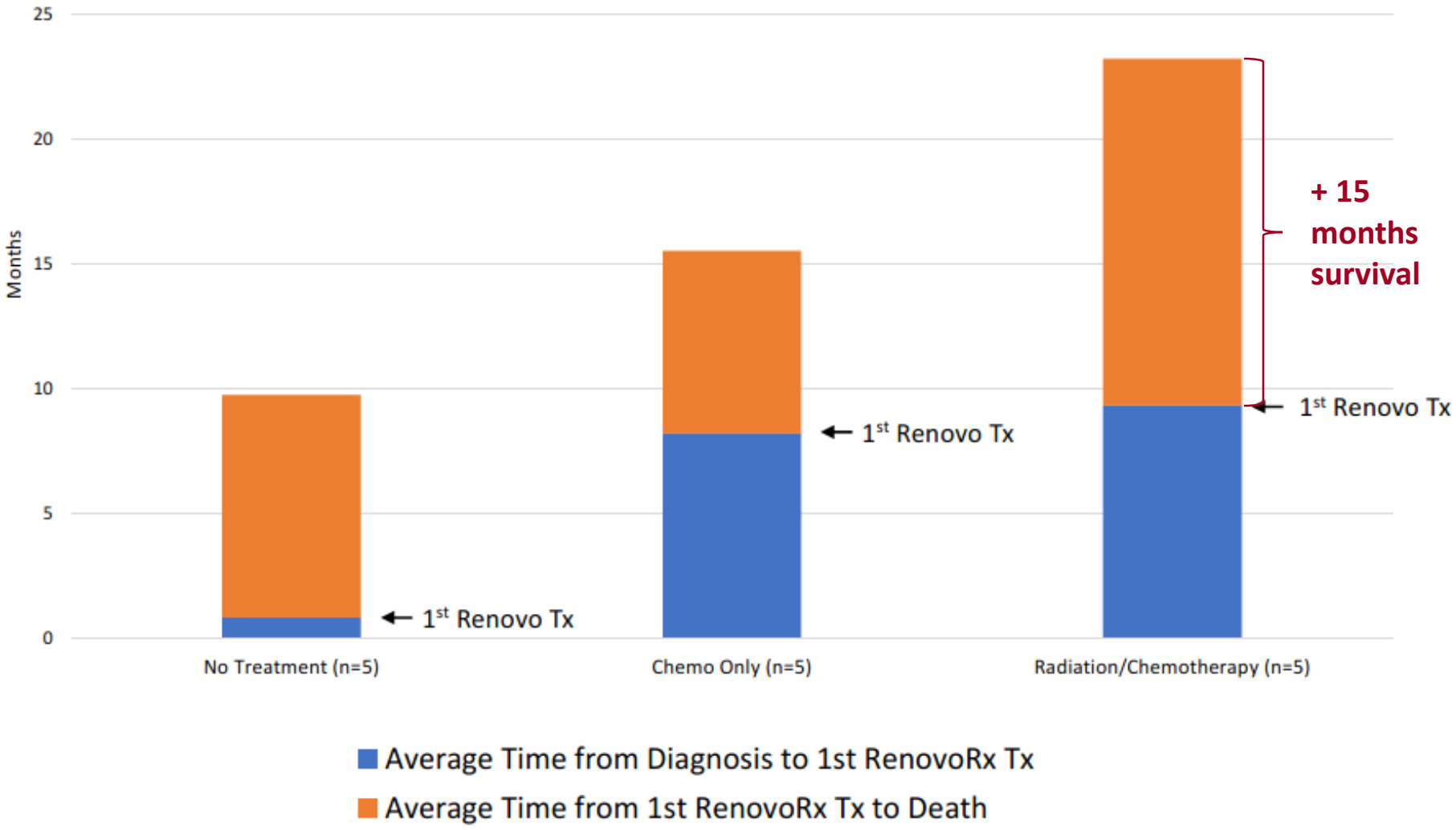
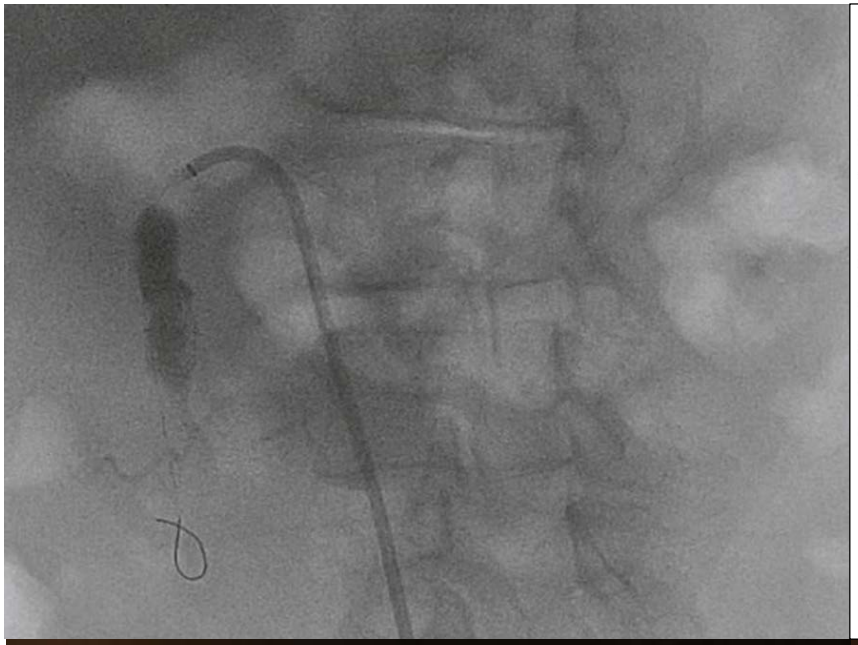
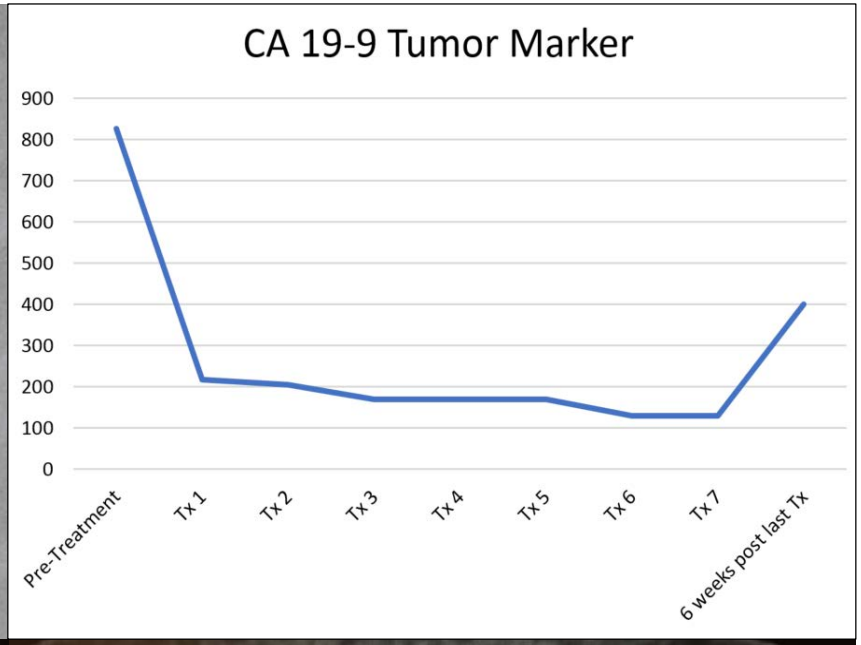


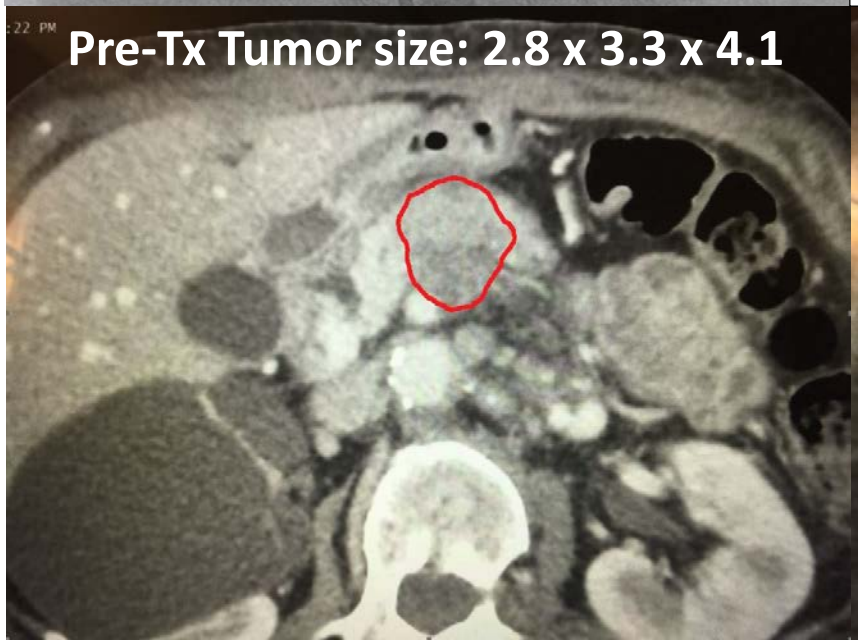
Table 6. Prior chemoradiation vs. others, clinical response: Median Survival, CA19-9 reduction, CT response			
	Prior Chemoradiation (n=5)	All Others (n=10)	P value
Median Survival	846 days	327 days	P < 0.1
Survived more than two years post-diagnosis	4	1	p < 0.005
>20% CA 19-9 Reduction	3	2	P < 0.1
Consecutive CA 19-9 Reduction	4	1	p< 0.05
Tumor Size Reduction	2	0	P < 0.05

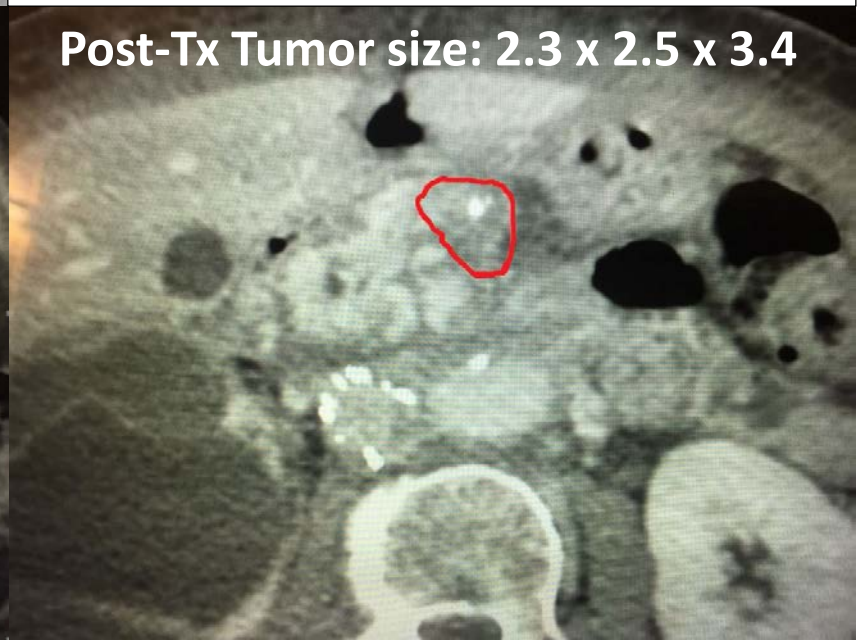
Survival: RenovoCath Effect



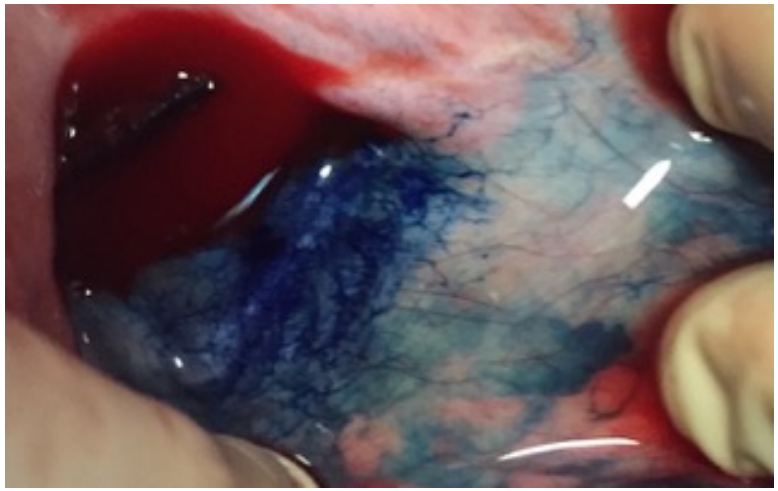



CA 19-9 Tumor Marker
900
800
700
600
500
400
300
200
100
0
Pre-Treatment
Tx 1
Tx 2
Tx 3
Tx 4
Tx 5
Tx 6
Tx 7
6 weeks post last Tx

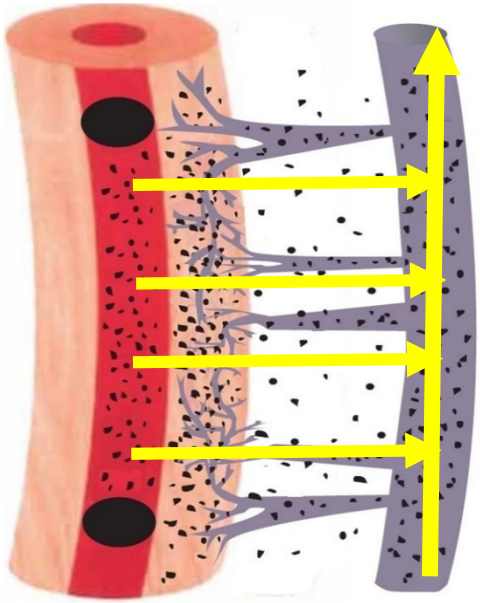

Pre-Tx Tumor size: 2.8 x 3.3 x 4.1


Post-Tx Tumor size: 2.3 x 2.5 x 3.4

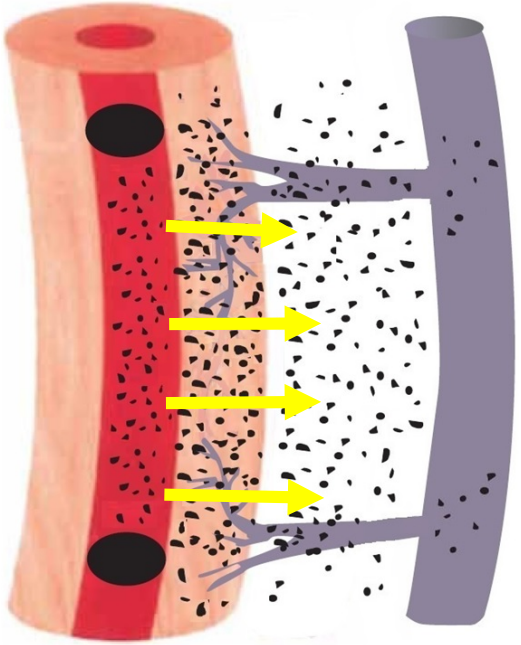
Trans-Arterial Micro-Perfusion



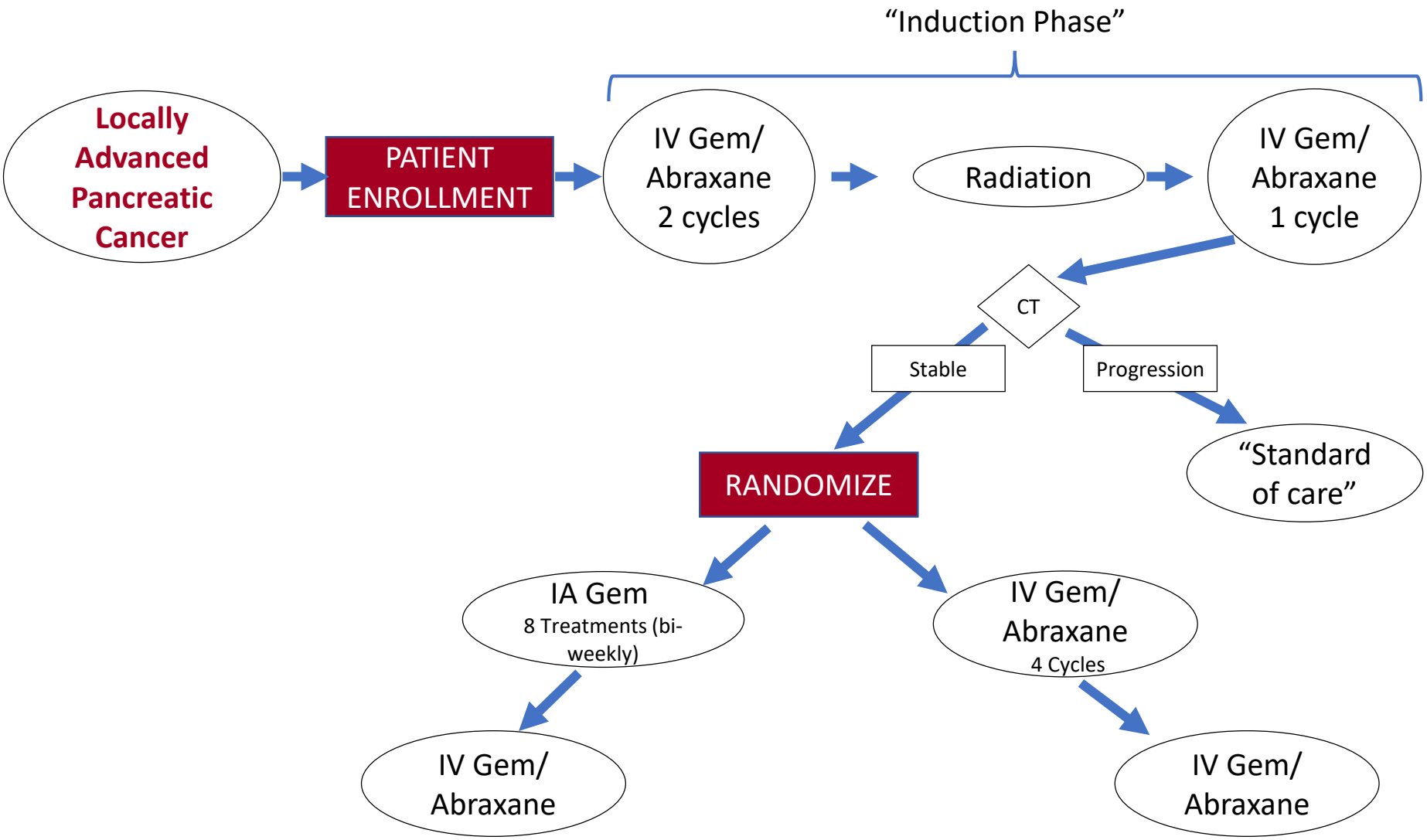
Native tissue/vasculature + IA chemo



Irradiated tissue/vasculature + IA chemo



Next Steps: RR3 Phase 3 Study Design



SUMMARY

Intra-arterial delivery of gemcitabine using localized delivery catheter, RenovoCath, is safe provided:

Patients with prior biliary stent/drain receive peri-op antibiotics

IR training/support is necessary to avoid guide mediated vascular complications

Early efficacy results of survival is encouraging, especially in patients with prior radiation where there may exist a synergistic effect with localized trans-arterial delivery of gemcitabine

END