

# Trans-Arterial Microperfusion Therapy for Pancreatic Cancer

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# Disclosures

- ◆ Sirtex
- ◆ Medtronic
- ◆ BD
- ◆ Boston Scientific
- ◆ Cordis
- ◆ Trisalus Life Sciences
- ◆ Genentech









# OBJECTIVES

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Overview of Pancreatic Cancer

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Locally Advanced Pancreatic Cancer (LAPC)

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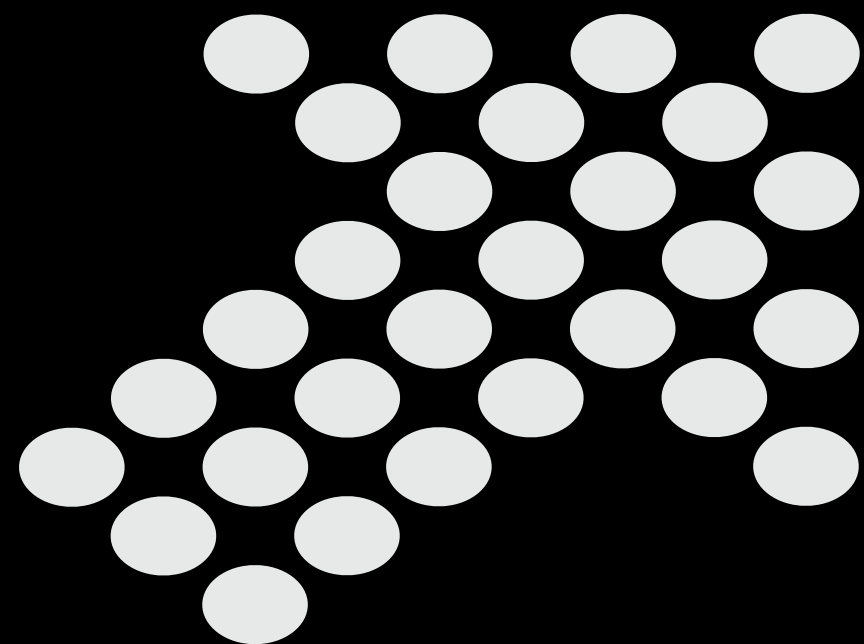
Treatment of LAPC with Intra-Arterial Gemcitabine –  
Mechanism of Action

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Clinical Data

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Future Directions – TIGeR PaC Phase II Clinical Trial



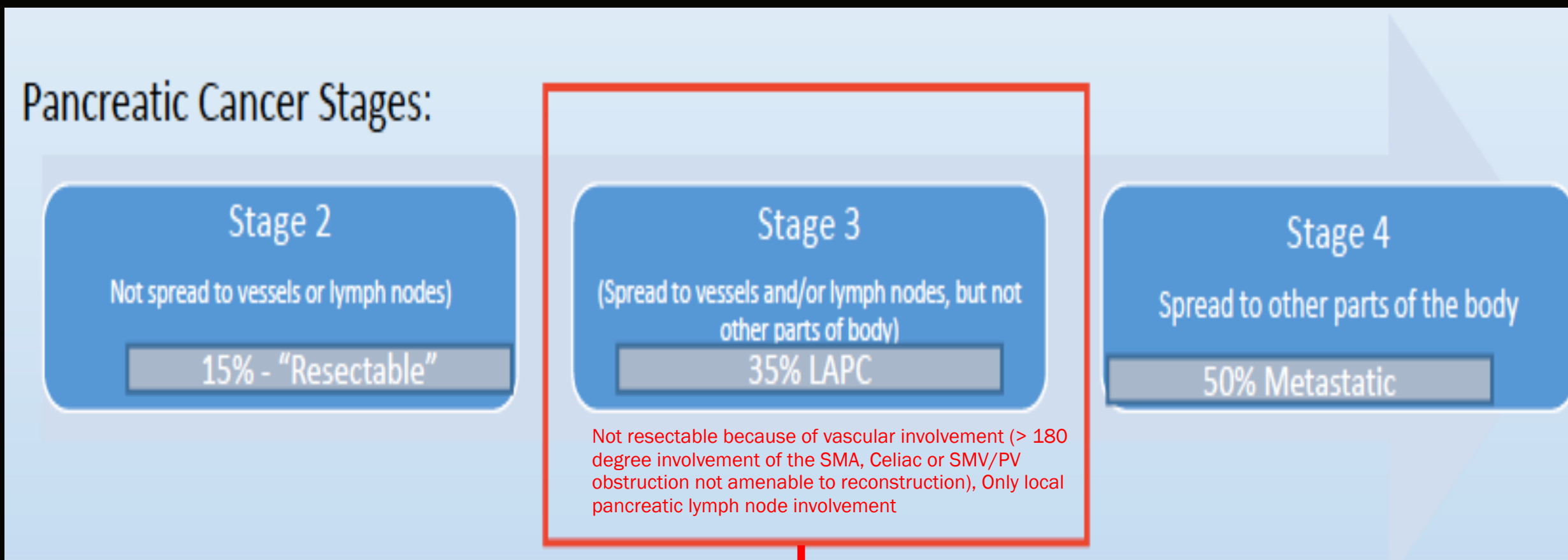
# Pancreatic Cancer

# PANCREATIC CANCER

- Pancreatic cancer is 3<sup>rd</sup> leading cause of cancer death in USA (projected 2<sup>nd</sup> leading cause by 2030)
  - Over 60,000 new cases per year in USA in 2021
  - Worldwide > 300,000 new cases/year



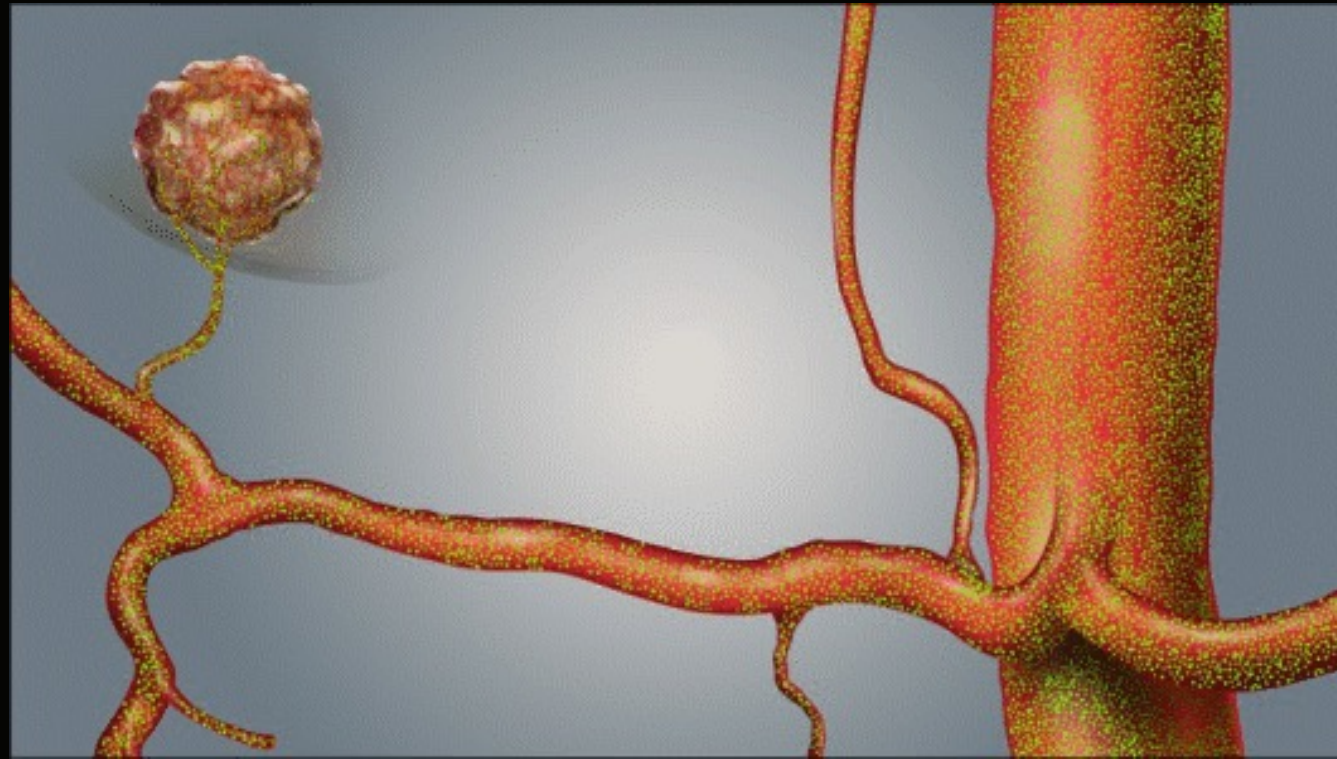
## PANCREATIC CANCER STAGING



Current best standard of care chemo:  
15-16 months median survival



# TECHNICAL PROBLEM: PRESENT CHEMOTHERAPY REGIMENS HAVE LIMITED EFFICACY IN HYPOVASCULAR TUMORS



## Hypervascular Tumor Treatment with Current Therapies

### Liver tumors are highly vascularized

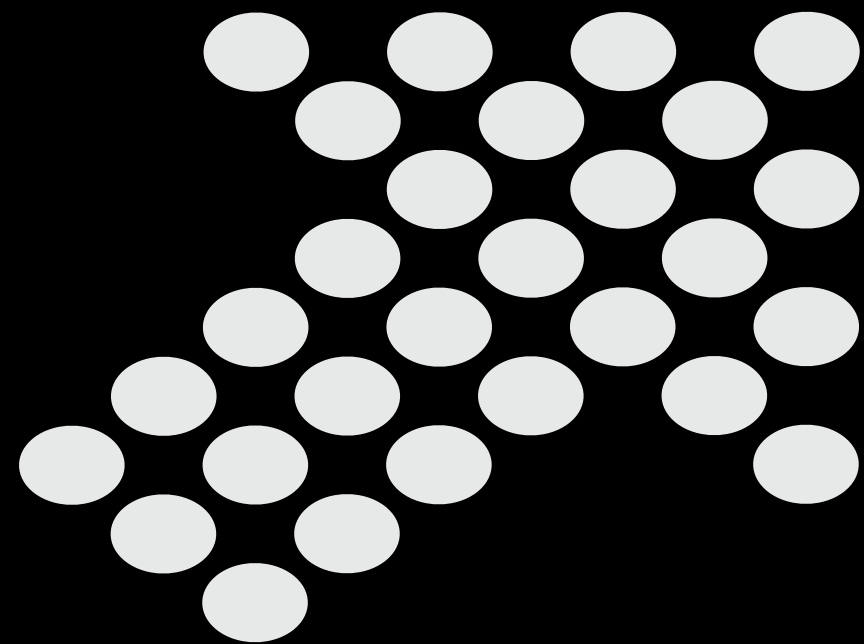
- Large tumor feeders – excellent targets for systemic therapy
- Can be accessed and treated with current local therapy techniques



## Hypovascular Tumors Post Major Barrier to Chemotherapy Treatment Success

### Pancreatic tumors have poor blood supply

- No visible tumor feeder vessels
- Systemic chemotherapy has limited penetration into pancreatic cancer
- Systemic toxicity

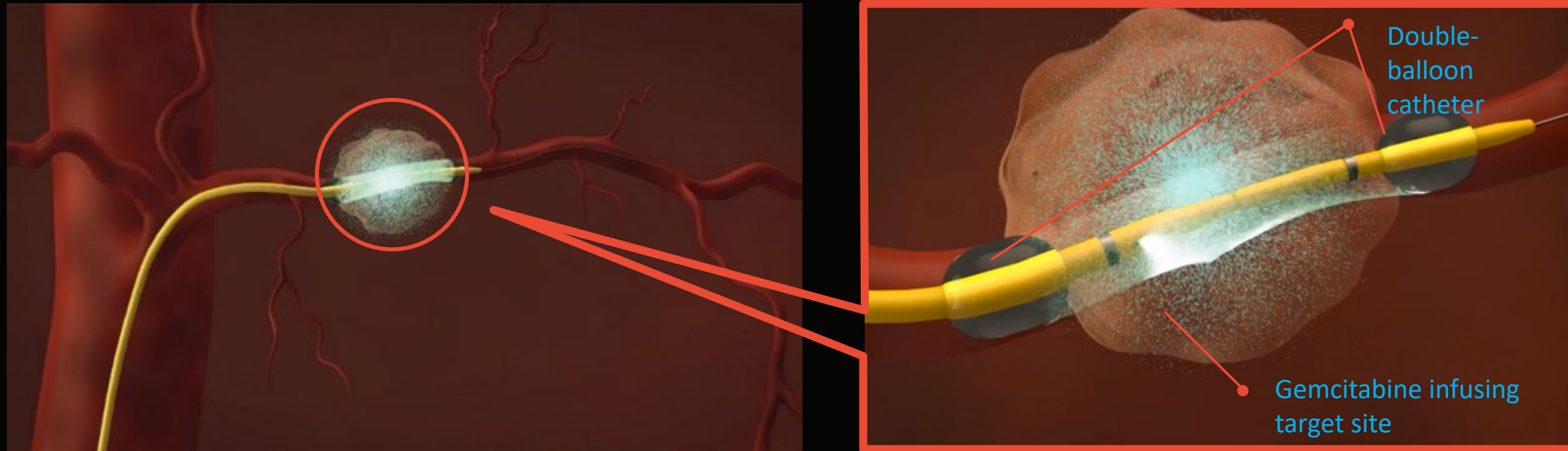


# One Possible Solution: Trans-Arterial Micro- Perfusion (RenovoTAMP)

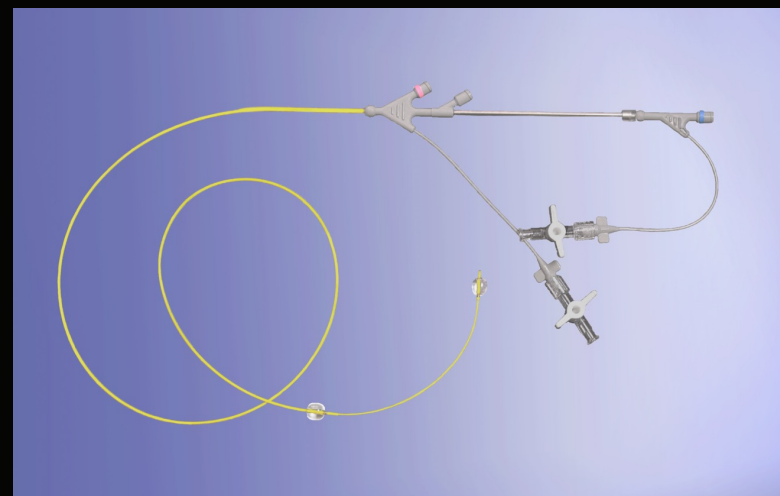




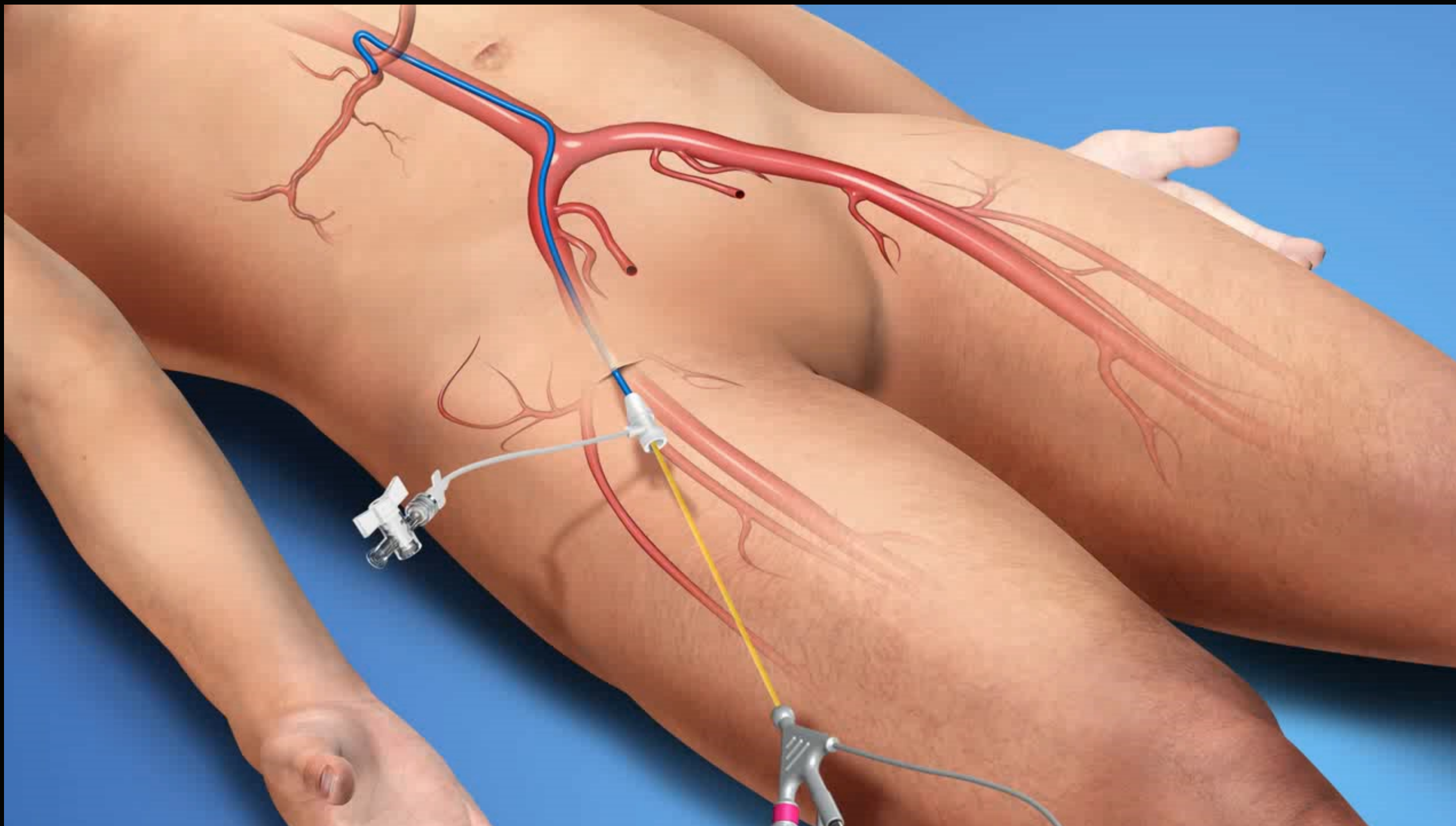
# TRANS-ARTERIAL MICRO-PERFUSION (RENOVOTAMP) ALLOWS FOR TARGETED THERAPY



The **RenovoCath™ System** isolates the anatomy and micro-perfuses targeted tissue with gemcitabine



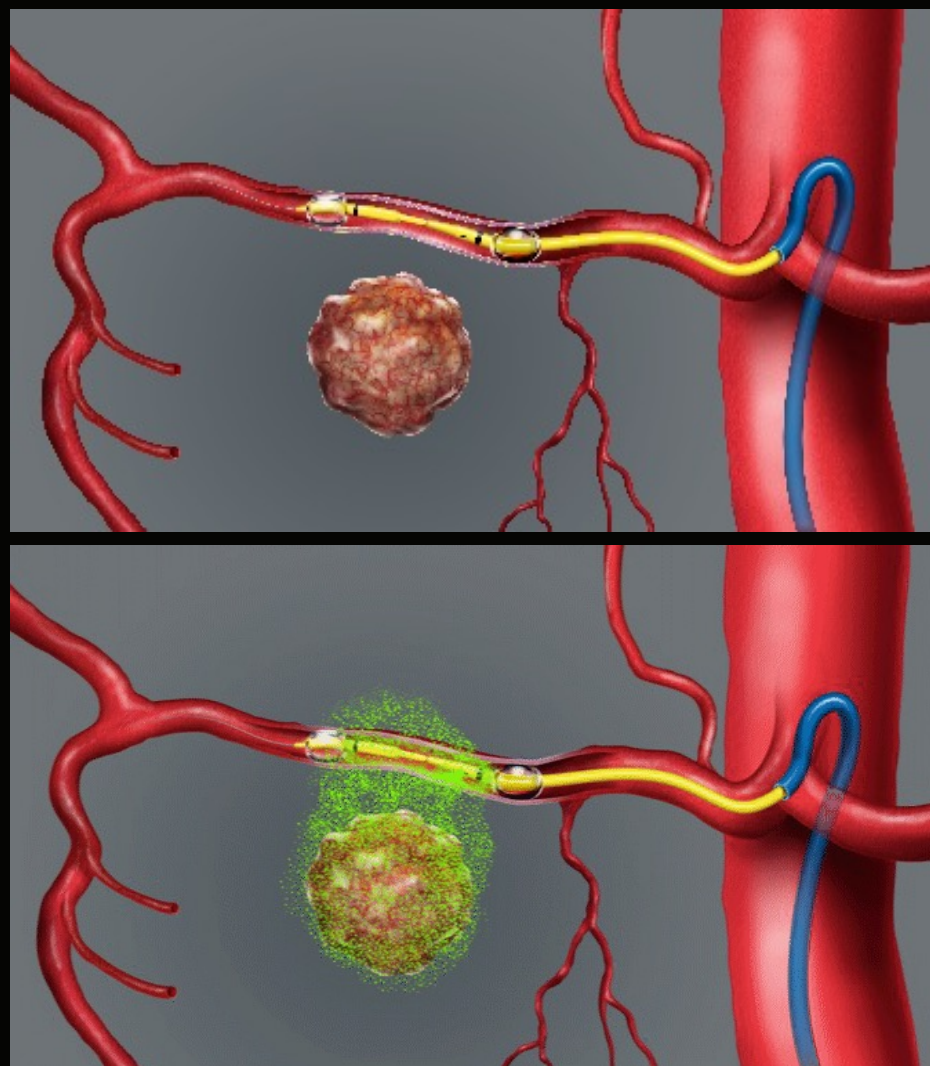
# TARGETED DELIVERY TO PANCREATIC CANCER: TRANS-ARTERIAL MICRO-PERFUSION (RENOVOTAMP)



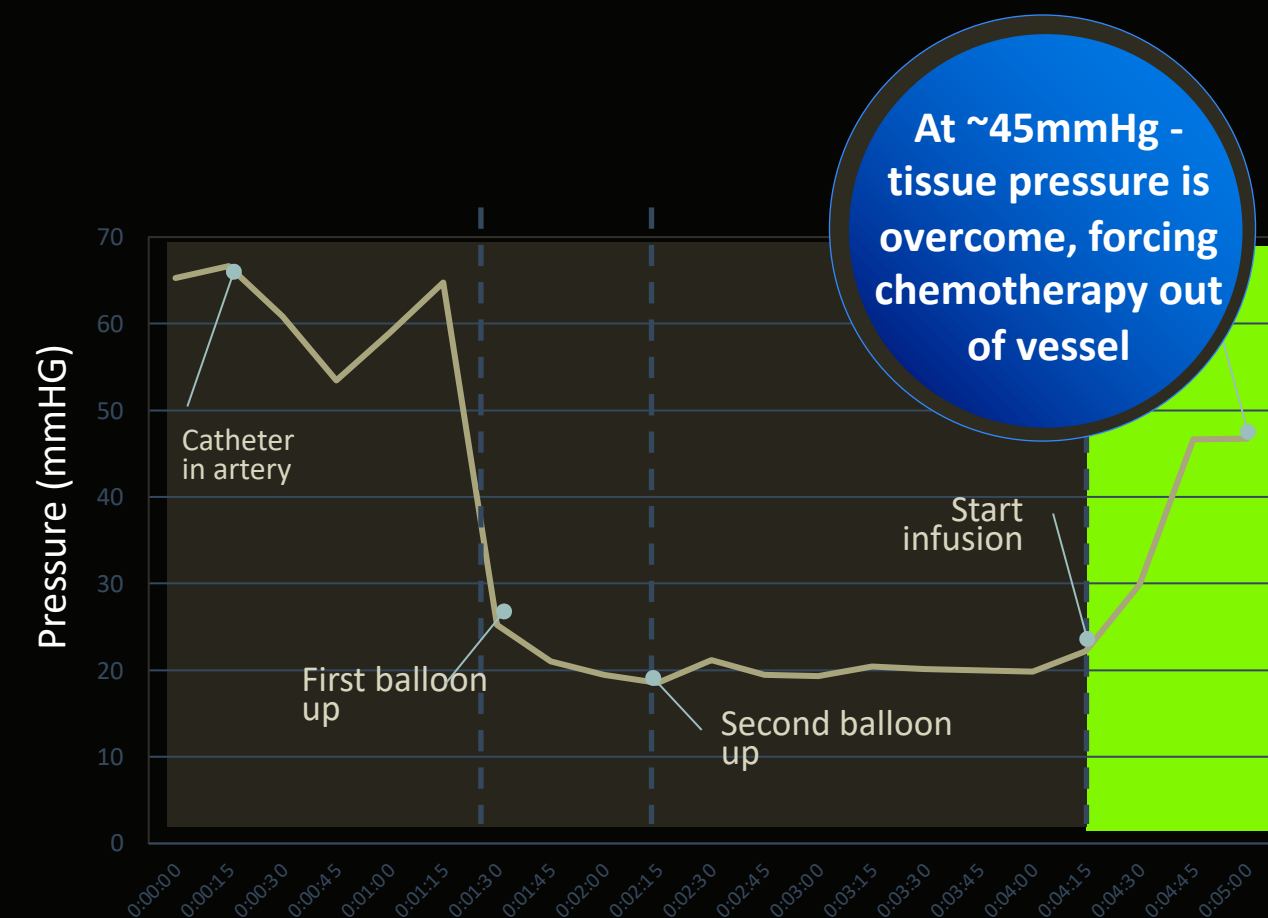


# Trans-Arterial Micro-Perfusion(RenovoTAMP)

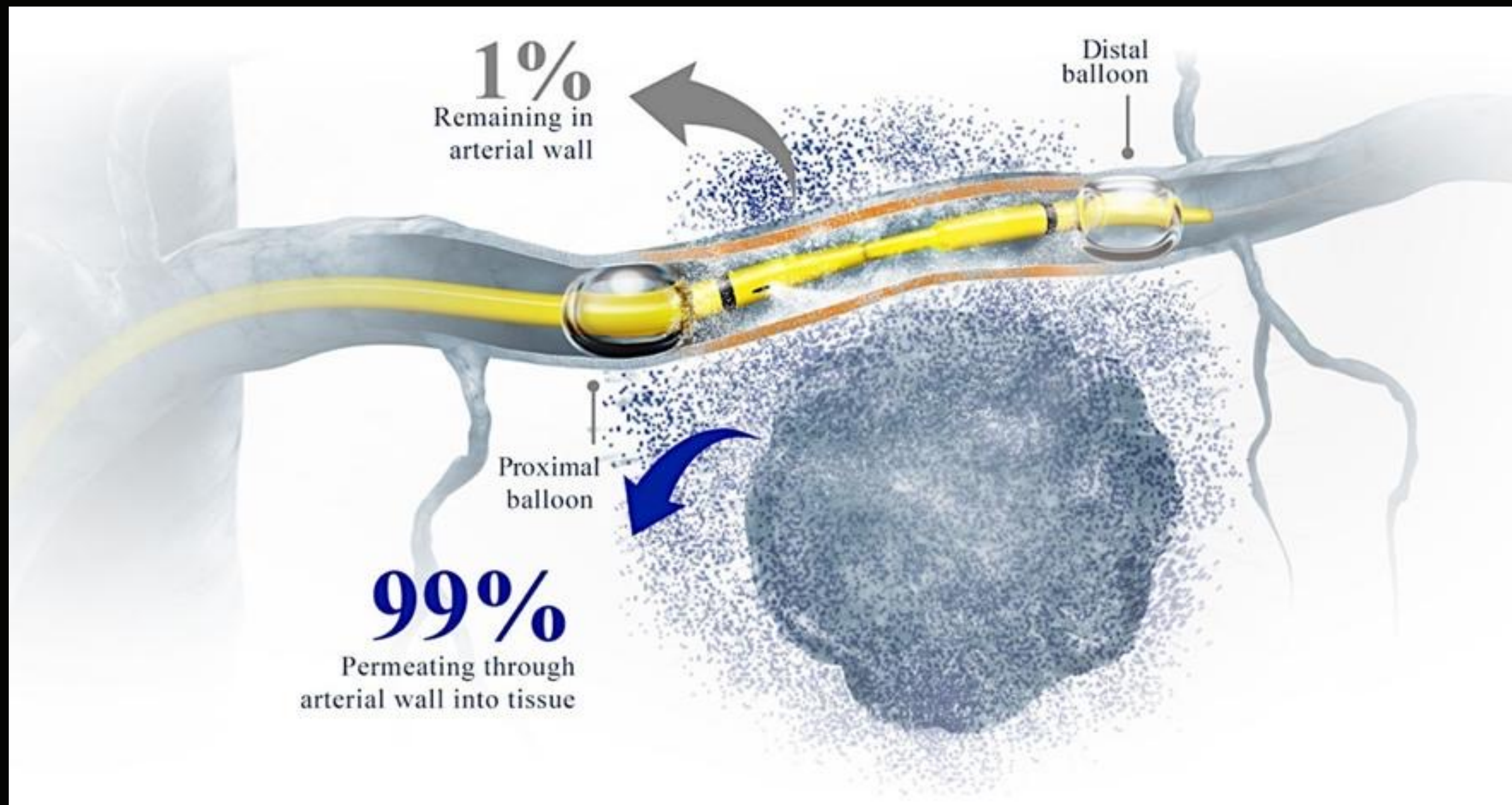
Blood vessel segment is isolated to deliver drug across blood vessel wall into tissue



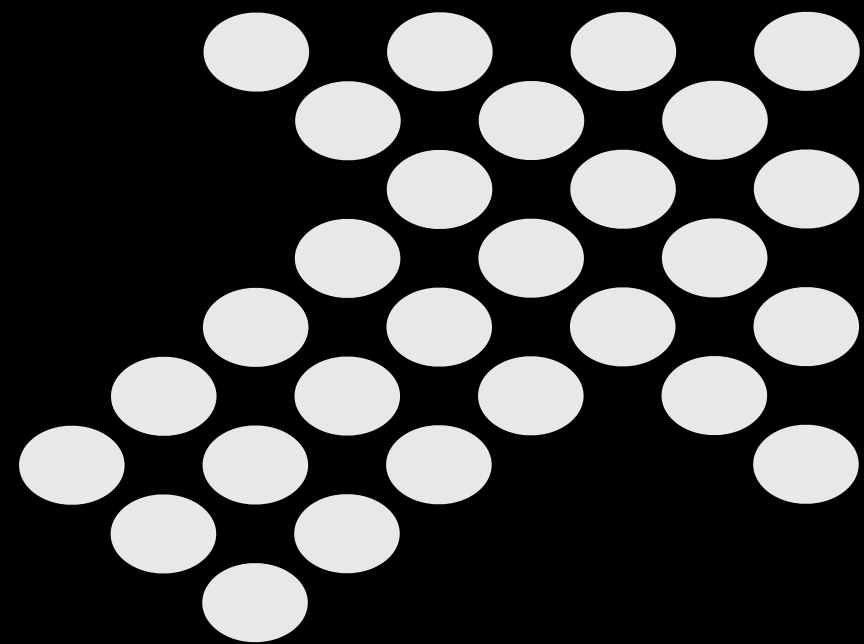
Mechanism: after vessel isolation, increase in pressure forces drug into tissue



# 99% of Chemotherapy Crosses Arterial Wall with RenovoTAMP Delivery







# Clinical Trials and Results



# RENOVOCATH IN PANCREATIC CANCER: PHASE I/II STUDIES TO EXPLORE CLINICAL ENDPOINTS

## RR1 - Dose Escalation Safety Study

- Primary Endpoint: Safety, Max Tolerated Dose, Dose Limiting Toxicity
- Secondary Endpoint: Survival
- Completed July 2016

**20 Patients**

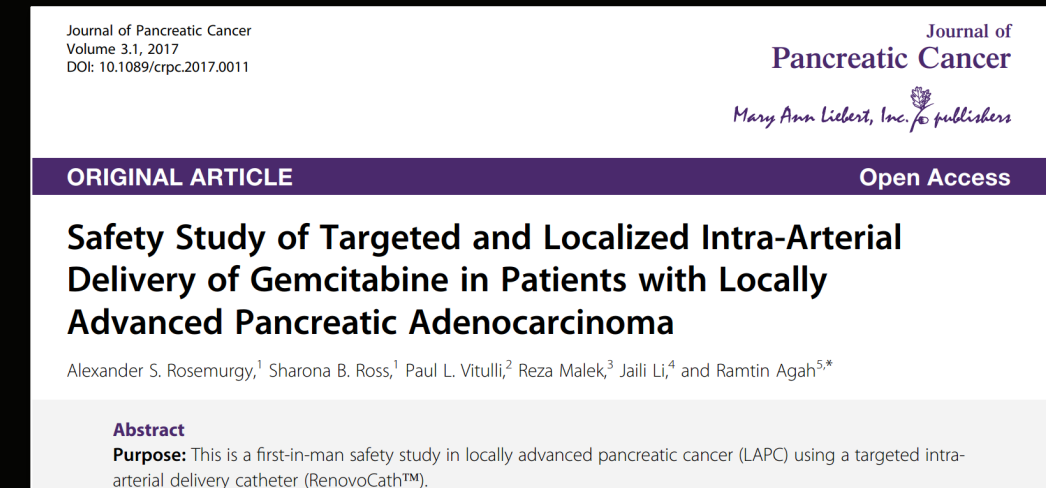
• 101 Treatments

## RR2 – Observational Registry

- Primary endpoints: Survival, tumor response
- 6 centers Initiated Jan. 2016
- Limited to patient with Prior Radiation: March 2017
- Limited to one active site w/ Initiation of Phase 3 TIGeR-PaC: May 2018

**25 Patients**

• 96 Treatments





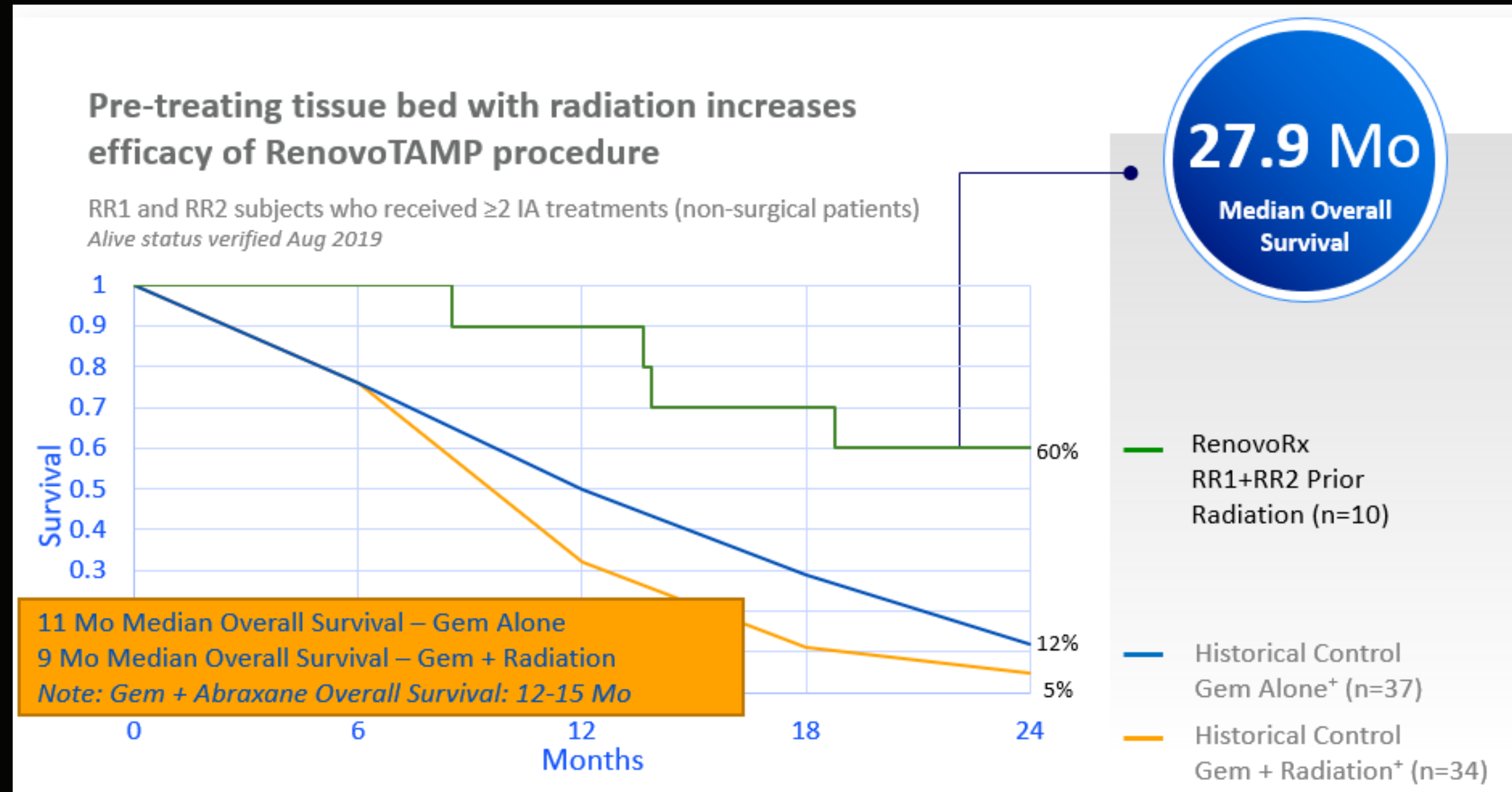
# RESULTS: PHASE I AND II CLINICAL TRIALS

- To date, 43 patients treated with Intra-Arterial Gemcitabine using RenovoCath between the 2 studies from May 2015 to Dec 2018
- Average age of patient enrolled was 69.9 years
- Median gemcitabine dose was 1000mg/m<sup>2</sup>
  - Full 1000mg/m<sup>2</sup> dose administered to 33 of the 43 patient cohort
- On average each pt. received four intra-arterial treatments, ranging from 1-14 treatments
  - 13 of 43 patients completed the planned 8 treatments of IA therapy

## Reasons for early discontinuation of IA therapy:

- Tumor progression (n=12)
- Patient/physician preference (n=8)
- Serious adverse events (n=6)
- Others (n=4)

# PROMISING DATA FROM PHASE 1/2 AND OBSERVATIONAL REGISTRY STUDIES ADVANCED CLINICAL DEVELOPMENT PROGRAM TO PHASE 3



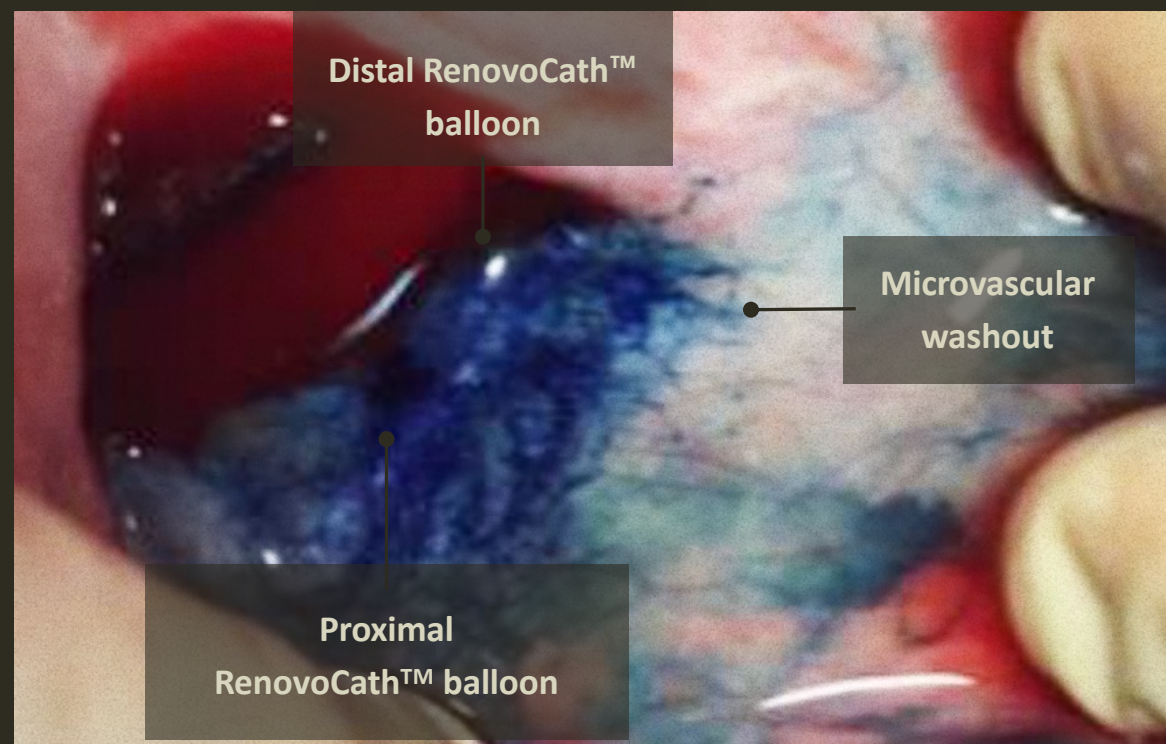
\*Chauffert, B. et al. Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000-01 FFCD/SFRO study. Annals of Oncology 19, 1592–1599 (2008).

<sup>+</sup> Loehrer, P. J. et al. Alone Versus Gemcitabine Plus Radiotherapy in Patients With Locally Advanced Pancreatic Cancer: An Eastern Cooperative Oncology Group Trial. Journal of Clinical Oncology 29, 4105–4112 (2011).

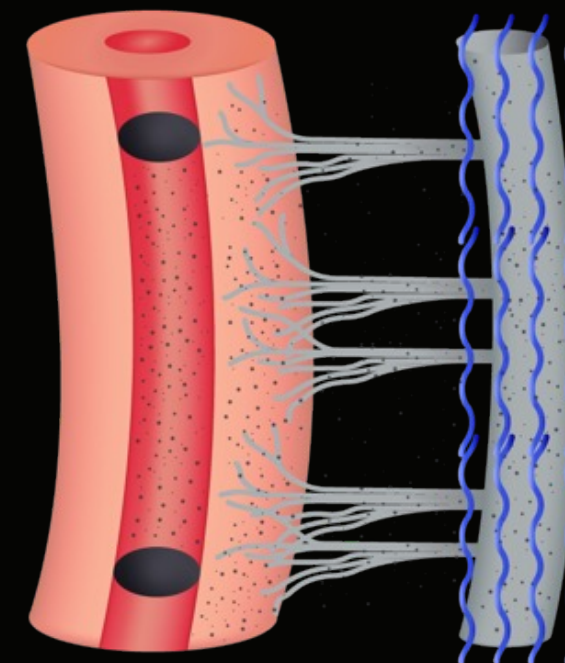


**Mechanism : Trans-Arterial Micro-Perfusion (TAMP) combined with radiation**

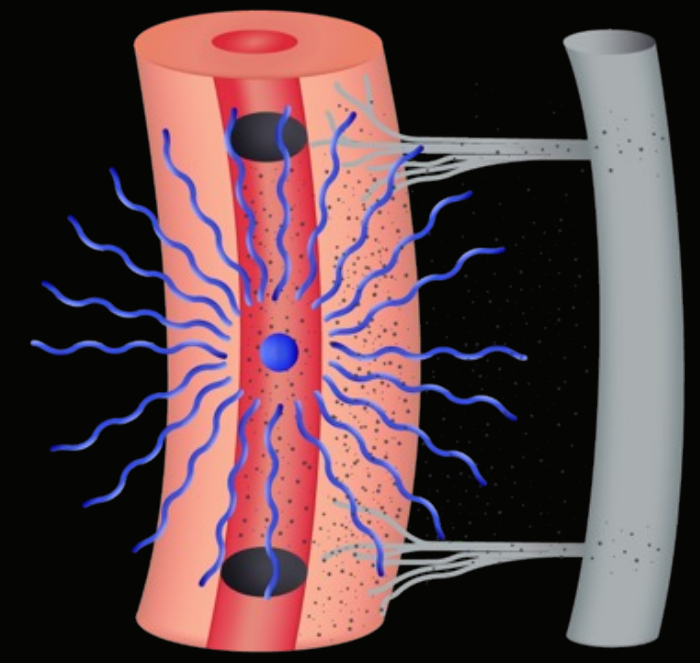
**Radiation reduces venous outflow by decreasing the microvasculature**



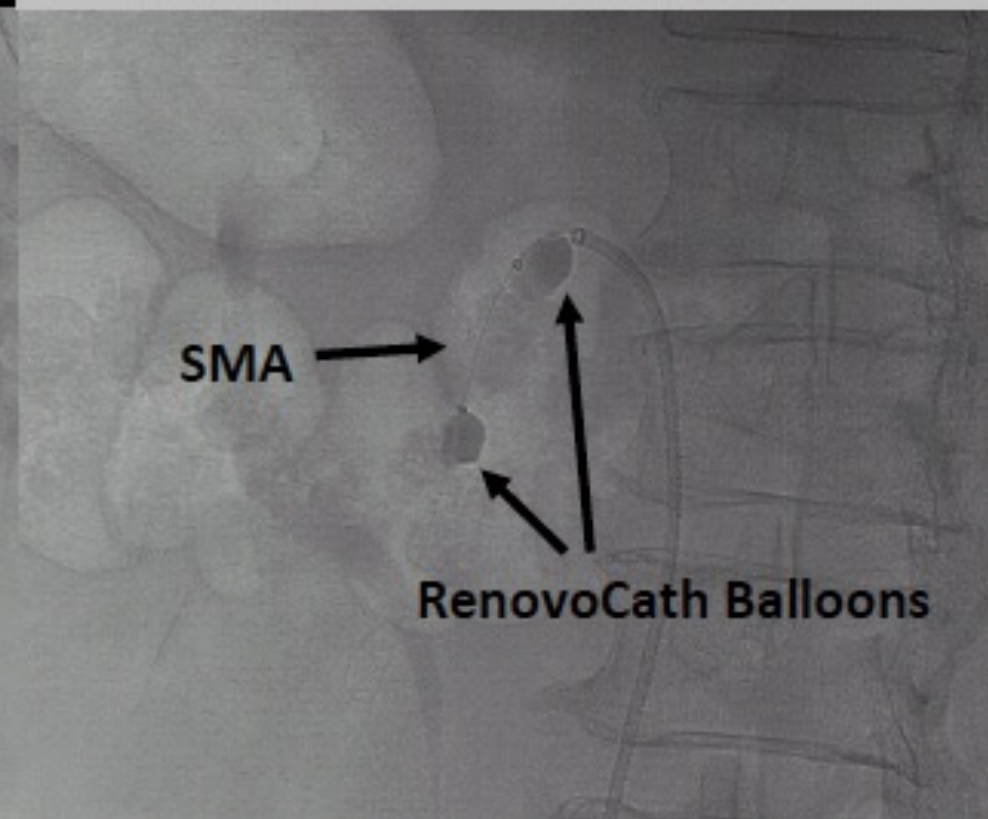
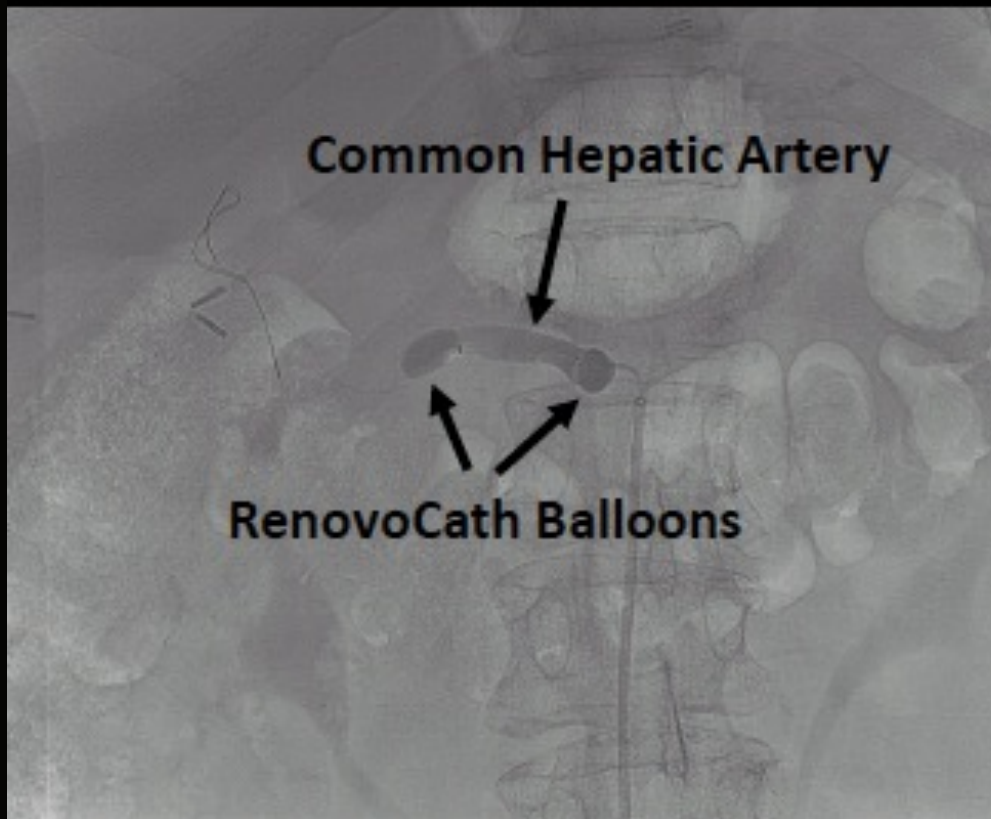
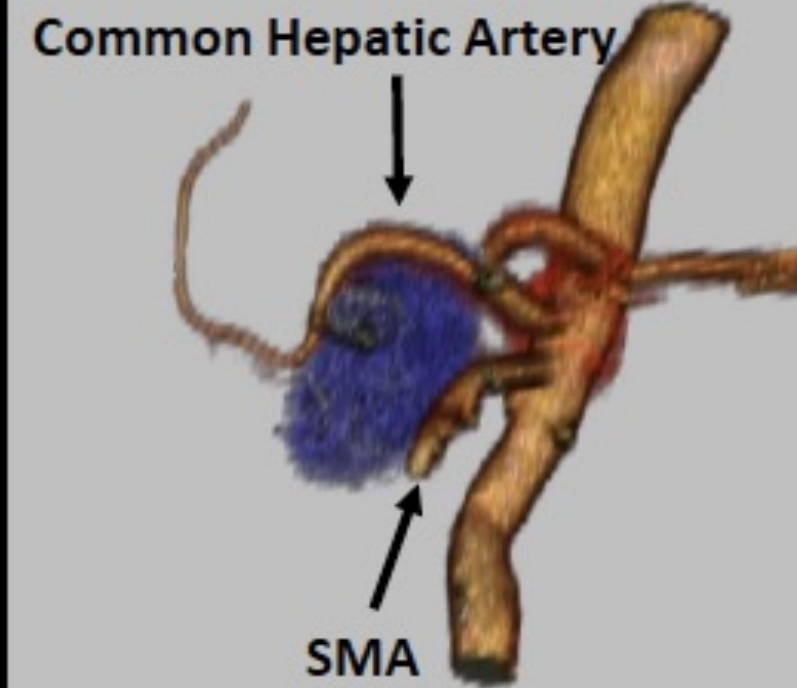
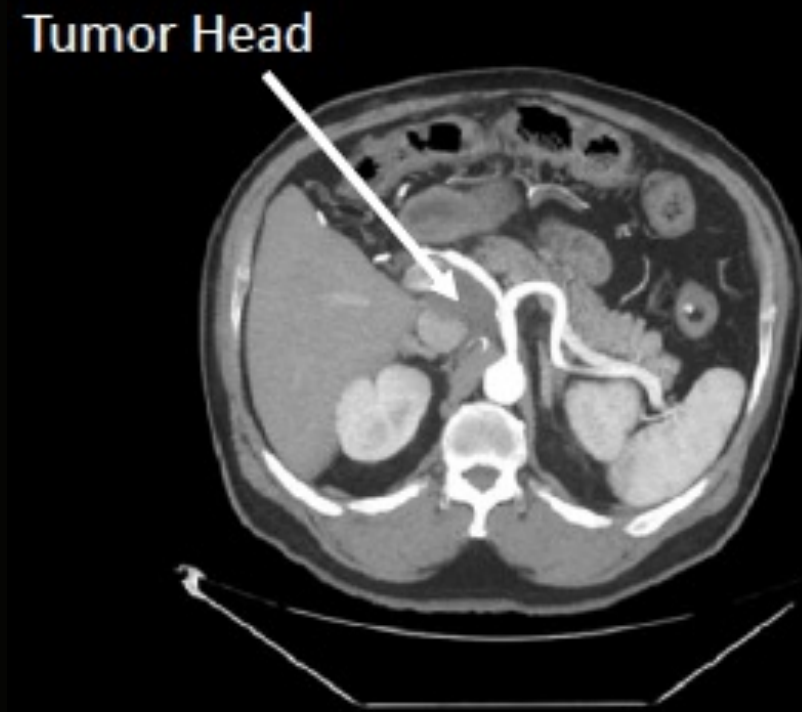
Native vasculature and IA chemo lead to **Micro-vascular washout**



Irradiated vasculature and IA chemo lead to **Diffusion**

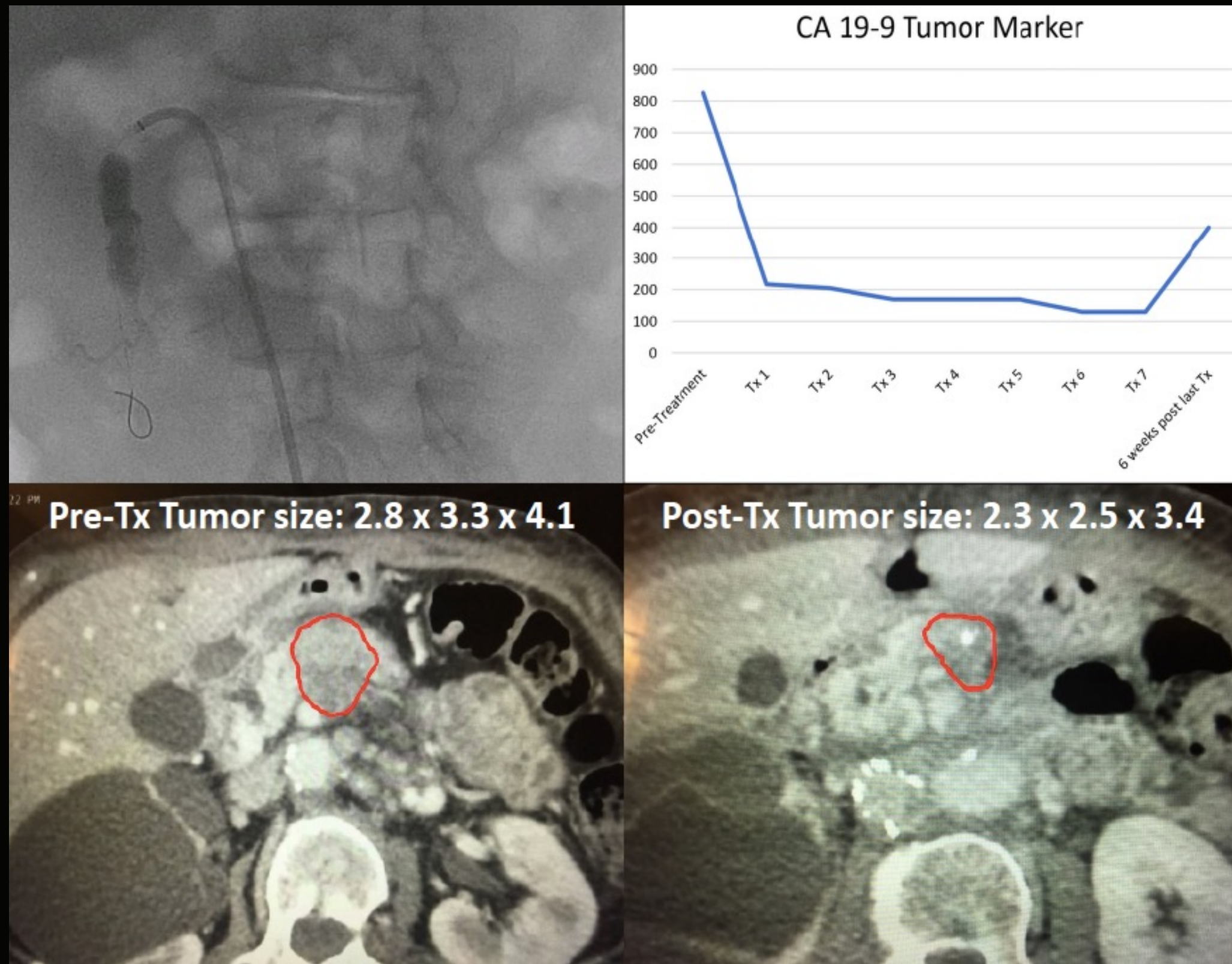


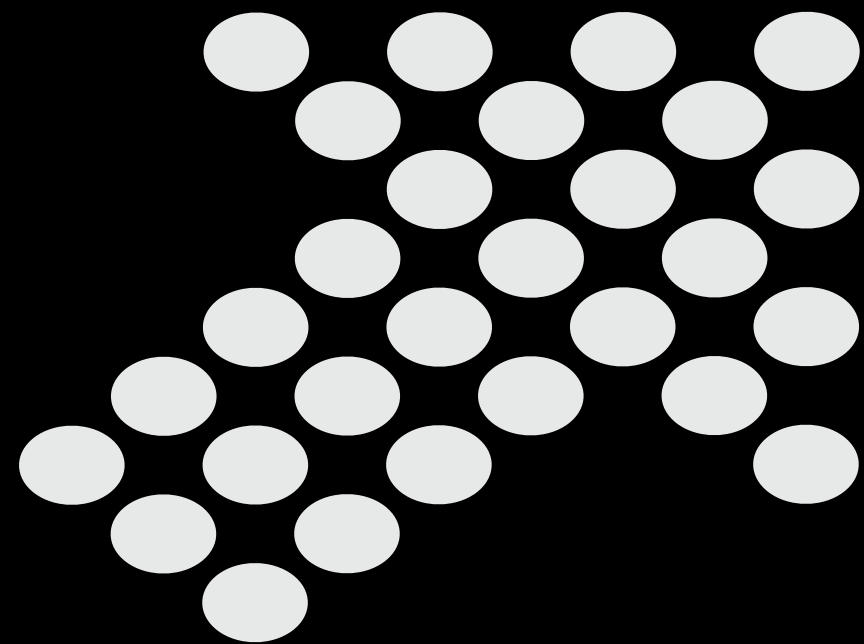
# CT IMAGING PROVIDES A SIMPLE APPROACH TO THE VASCULATURE





# CASE EXAMPLE





# Future Directions:

## TIGeR-PaC Randomized Phase 3 Clinical Trial

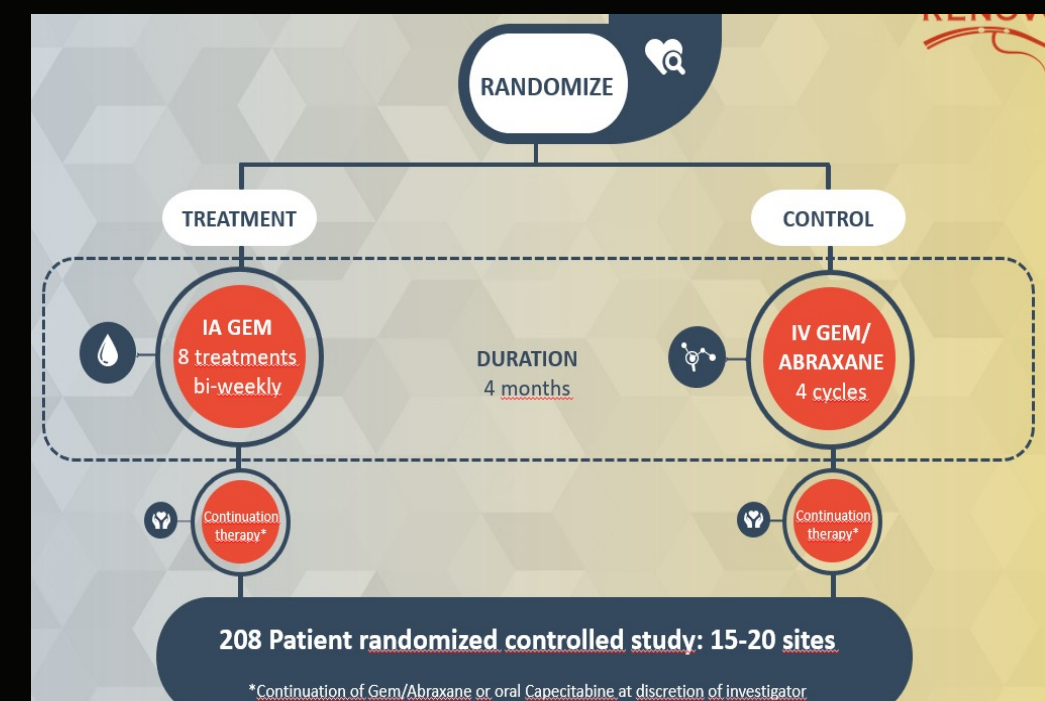
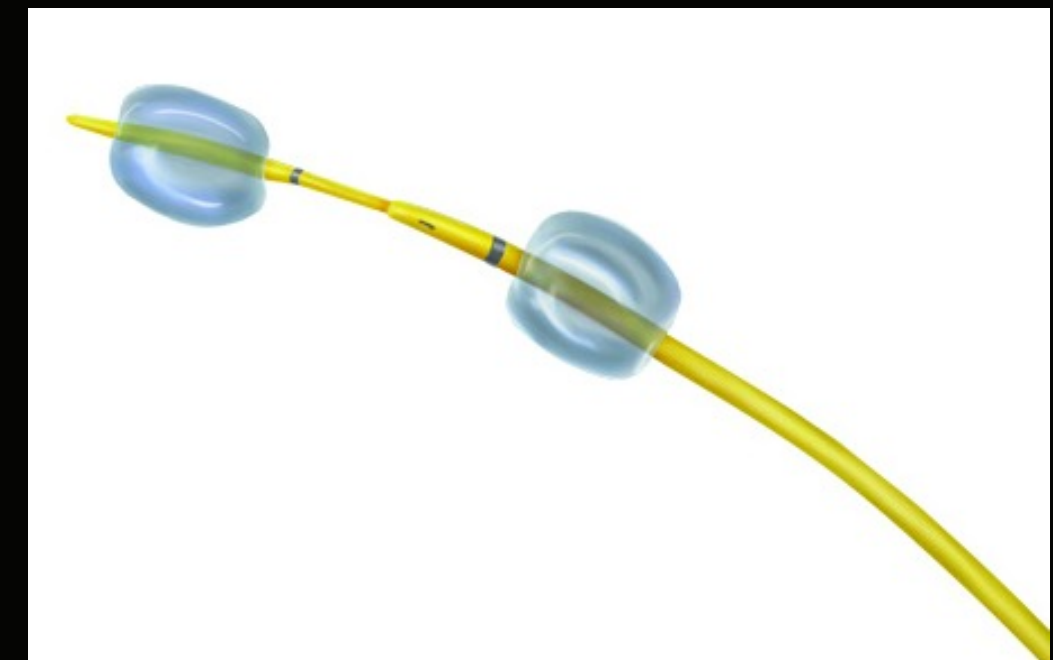
This study is to test the efficacy of approach as part of a phase 3 randomized clinical trial



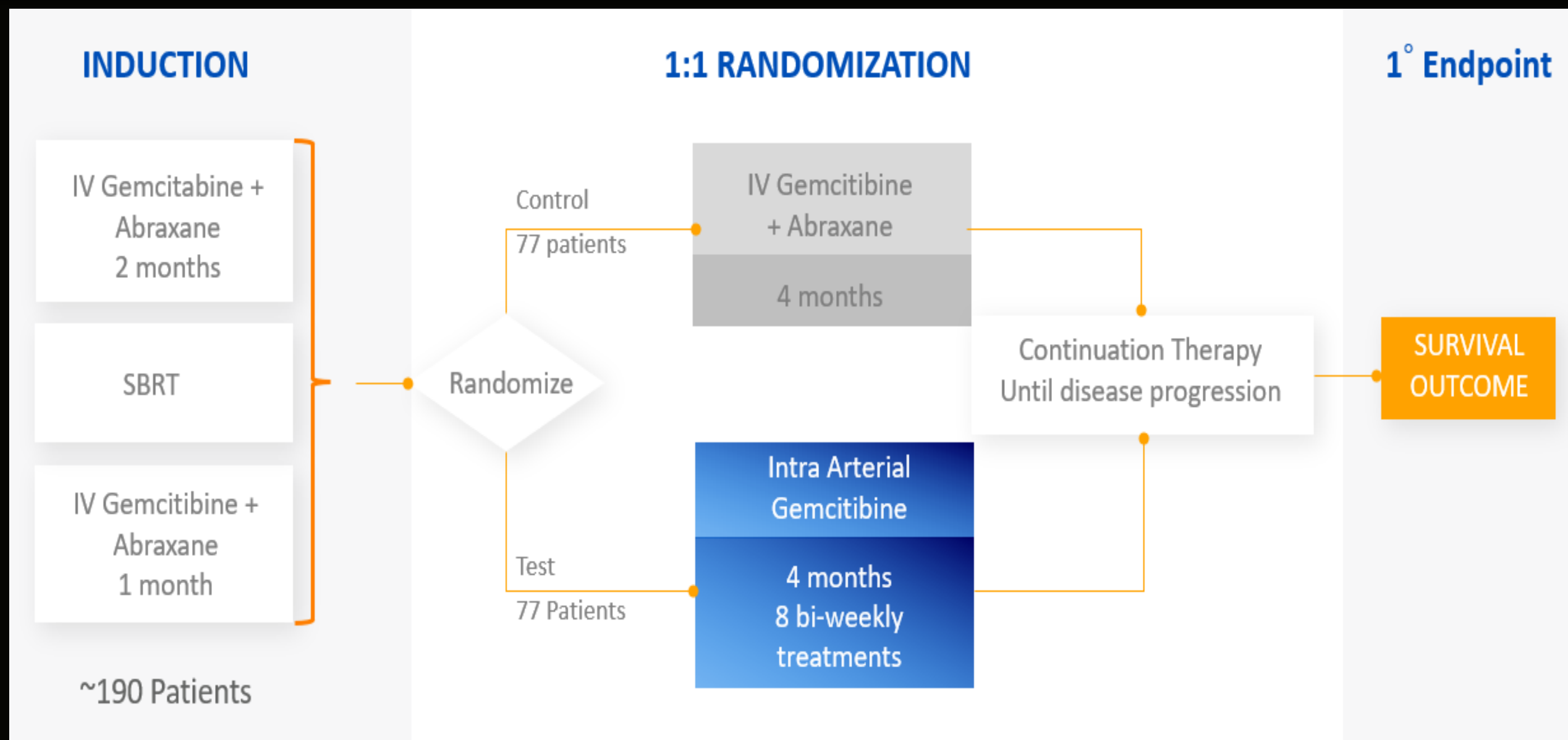
# TIGER-PAC RANDOMIZED CLINICAL TRIAL –PHASE 3 MULTICENTER TRIAL

**Trans (Intra)-arterial Gemcitabine vs. Continuation of IV Gemcitabine and Nab-Paclitaxel following Radiotherapy for Locally Advanced Pancreatic Cancer (TIGeR-PaC Randomized Clinical Trial)**

- Prospective multicenter randomized clinical Trial evaluating systemic therapy versus intraarterial gemcitabine for pancreatic cancer
- Primary Objective: **Overall Survival** from time of randomization
- Secondary Objectives: PFS, objective response rate, duration of response, HR-QOL, degree of peripheral neuropathy, incidence of neutropenia, tolerability, and safety
- Inclusion Criteria:
  - Histologically confirmed pancreatic adenocarcinoma with initial diagnosis within 6 weeks of consent
  - Locally advanced, unresectable disease, as defined by **NCCN Guidelines**
  - ECOG 0-1



# PHASE 3 TIGER-PAC RCT STUDY SCHEMA





# CONCLUSIONS

Localized intra-arterial delivery of gemcitabine using RenovoCath demonstrates encouraging results in stabilizing local disease

This benefit is especially pronounced in patients with prior induction therapy with radiation (**median OS is 27.9 months**)

The phase 3 multicenter, randomized TIGeR-PaC ([clinical trial.gov #NCT03257033](https://clinicaltrials.gov/ct2/show/study/NCT03257033)) will provide definitive evidence whether this therapy provides survival benefit





# THANK YOU



**Miami Cancer  
Institute**  
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