# Advances in Pancreatic Cancer: Trans-arterial Therapy on the Horizon

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# Disclosures

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

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# OBJECTIVES

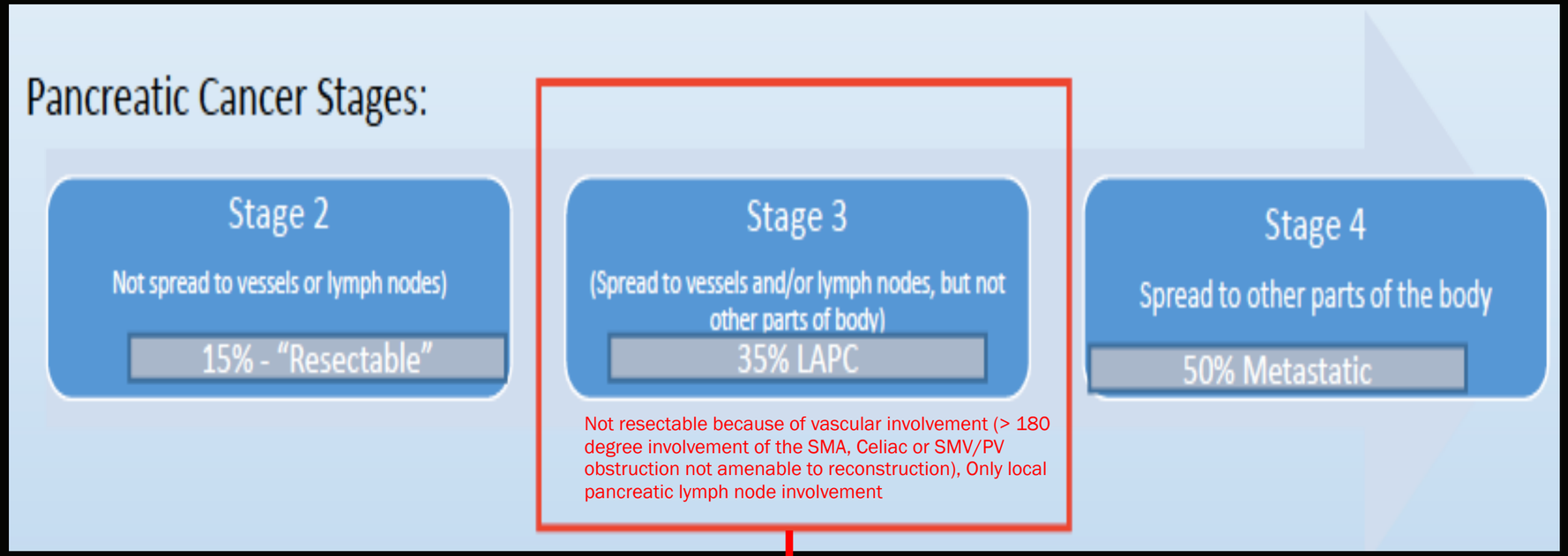
- Overview of Pancreatic Cancer
- Locally Advanced Pancreatic Cancer (LAPC)
- Treatment of LAPC with Intra-Arterial Gemcitabine – TAMP Mechanism of Action
- Clinical Data
- TIGeR PaC Phase III Clinical Trial

# PANCREATIC CANCER

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

| 5-Year Relative Survival |
| --- |
| 10.8% |
| 2011–2017 |

## PANCREATIC CANCER STAGING

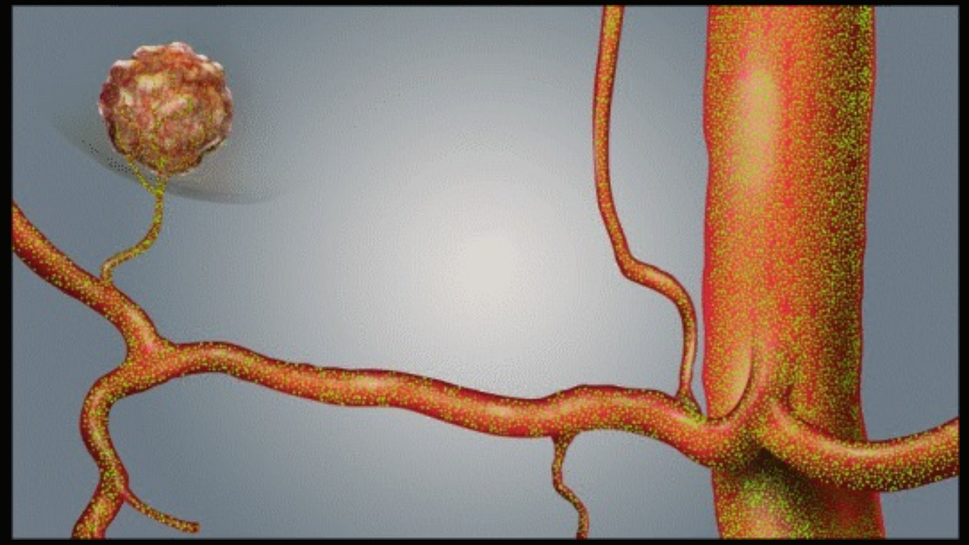



Current best standard of care chemo: 15-16 months median survival

Rahib L, et al, Cancer Res. 2014 Jun 1;74(11):2913-2; Park W, Chawla A, O'Reilly EM, JAMA. 2021 Sep 7;326(9):851-862

# CHEMOTHERAPY IS NOT EFFECTIVELY DELIVERED TO PRIMARY PANCREATIC TUMORS

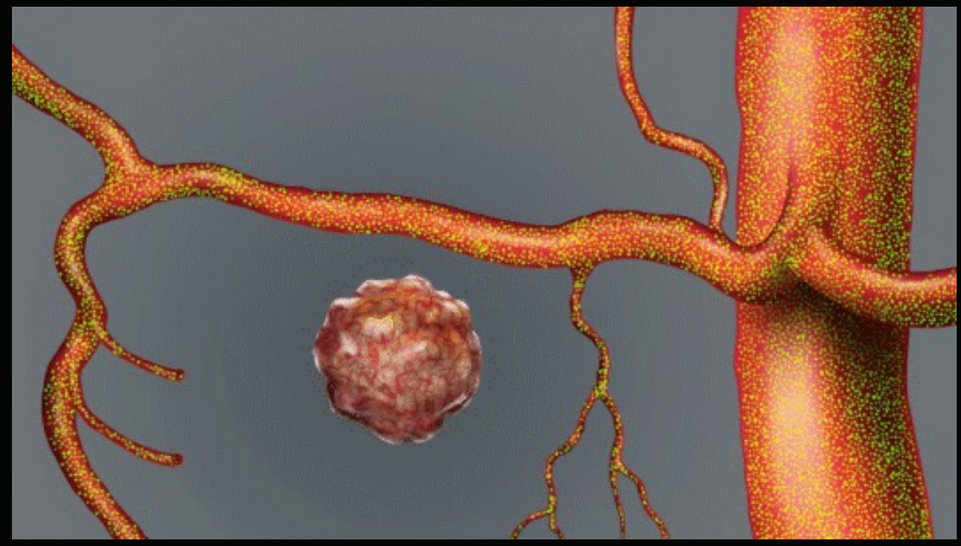
## HYPOVASCULAR TUMORS, DENSE FIBROTIC STROMA, AND SPARSE TUMOR CELLULARITY



### Hypervascular Tumor Treatment with Current Therapies

**Liver tumors are highly vascularized**

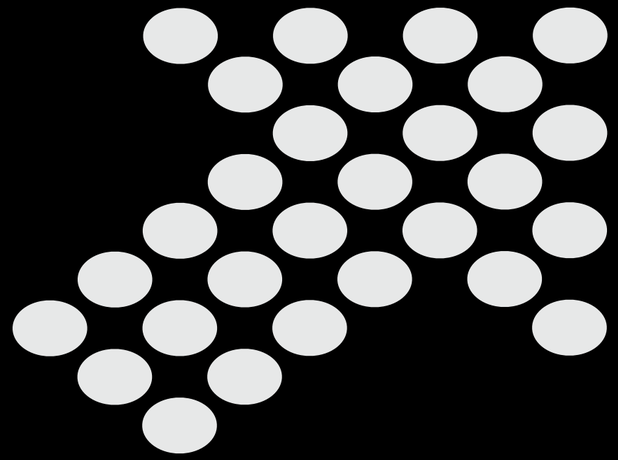
- Large tumor feeders – excellent targets for systemic therapy
- Can be accessed and treated with current local therapy techniques



### Hypovascular Tumors Post Major Barrier to Chemotherapy Treatment Success

**Pancreatic tumors have poor blood supply**

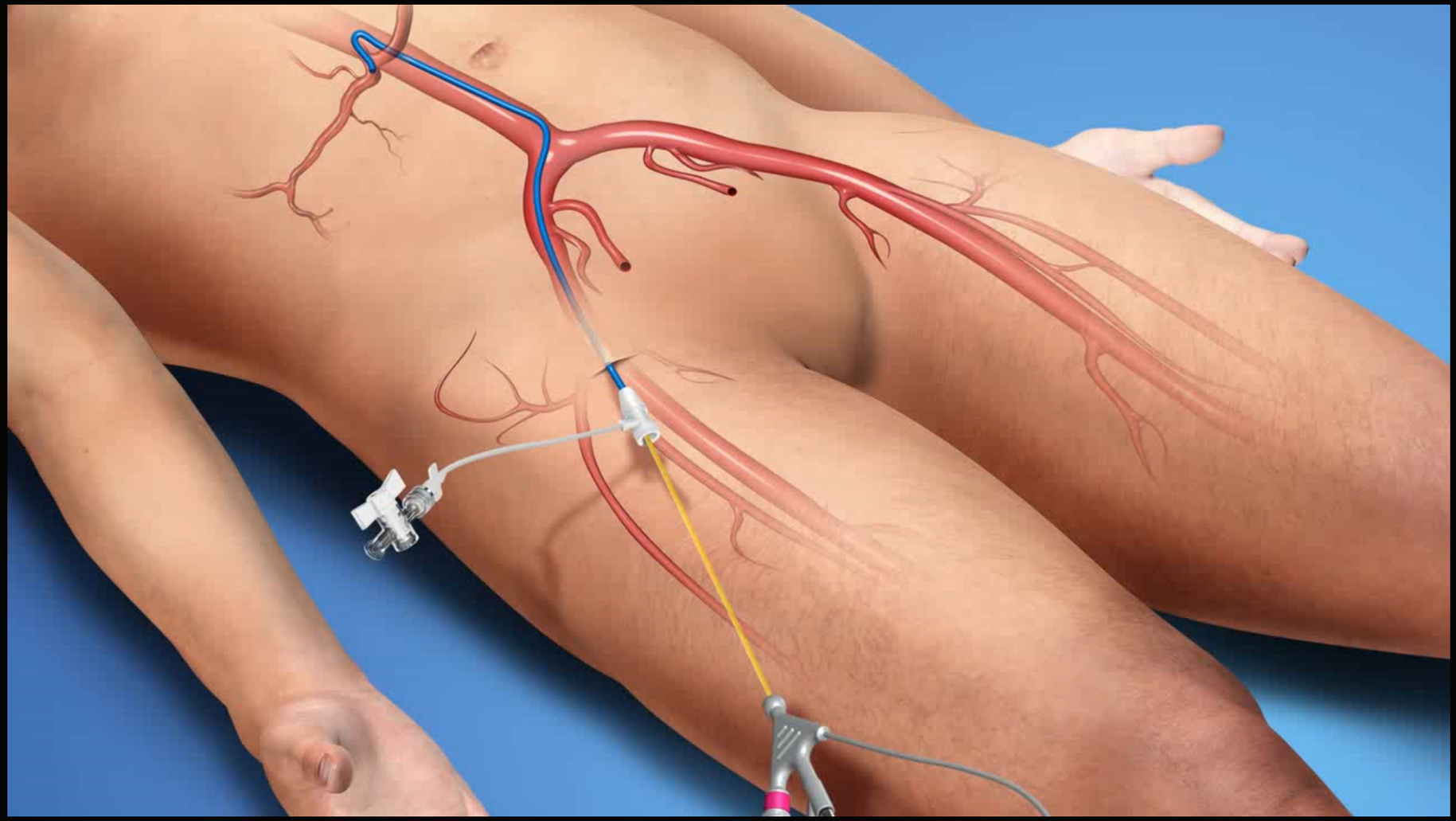
- No visible tumor feeder vessels
- Systemic chemotherapy has limited penetration into pancreatic cancer
- Systemic toxicity



# One Possible Solution:

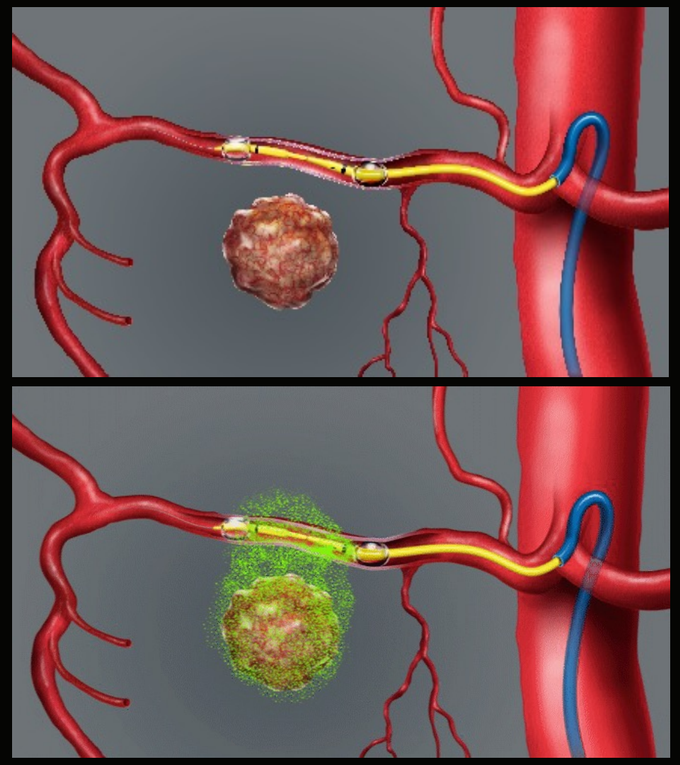
# Trans-Arterial Micro-Perfusion (RenovoTAMP)

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

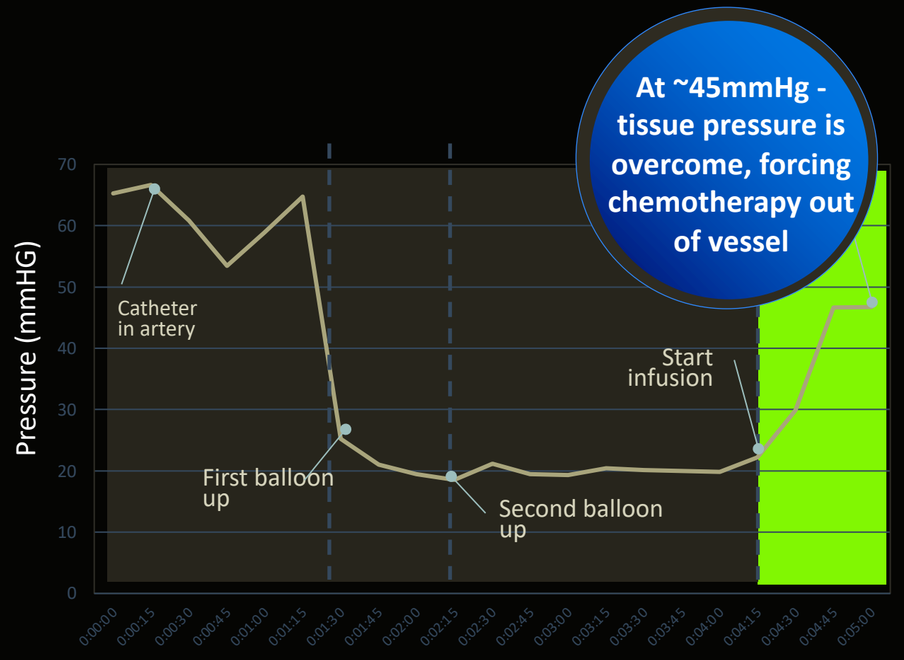


# Trans-Arterial Micro-Perfusion(RenovoTAMP)

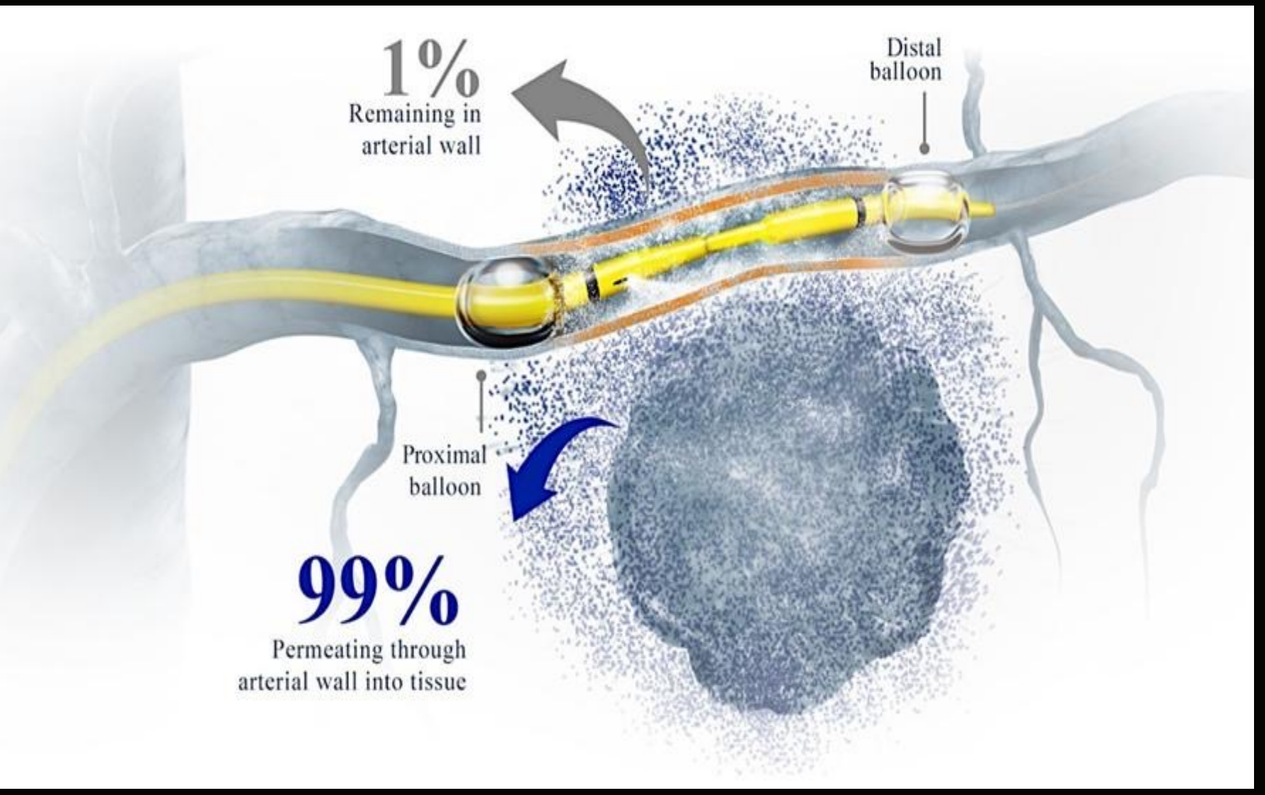
**Blood vessel segment is isolated to deliver drug across blood vessel wall into tissue**

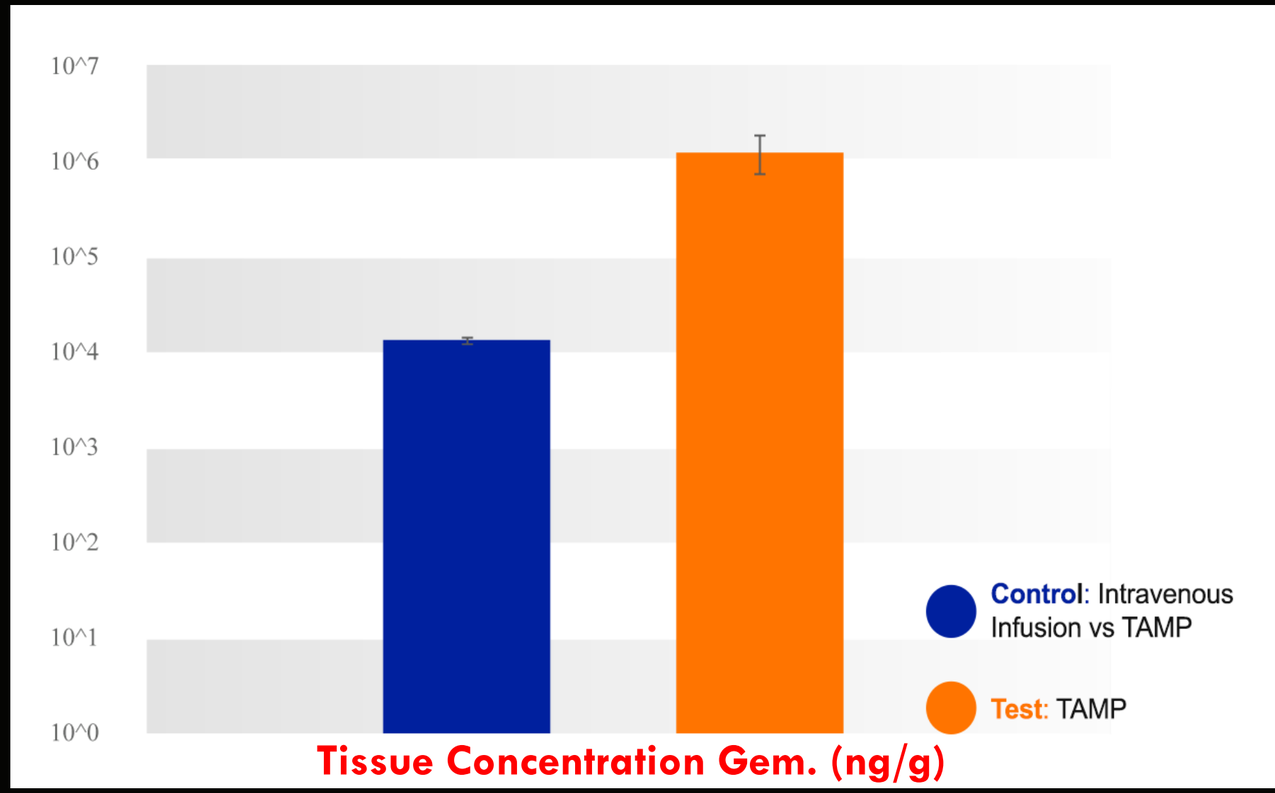


**Mechanism: after vessel isolation, increase in pressure forces drug into tissue**



# 99% of Chemotherapy Crosses Arterial Wall with RenovoTAMP Delivery with Increased Target Drug Concentration




Increases Drug Concentration to Target Pathological Site by ~100X* Compared to IV Administration*

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* K. Farsad, et al. Trans-pulmonary artery selective chemotherapy delivery to lung using a double balloon-occlusion catheter. JVIR. March 2019; 30 (3).

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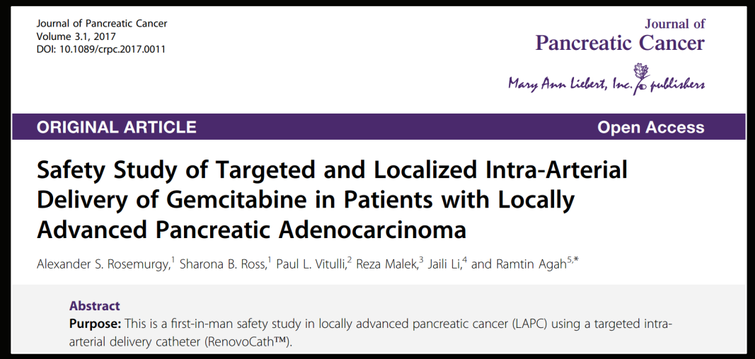
# Clinical Trials and Results

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



Journal of Pancreatic Cancer
Volume 3.1, 2017
DOI: 10.1089/crpc.2017.0011

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ORIGINAL ARTICLE Open Access

**Safety Study of Targeted and Localized Intra-Arterial Delivery of Gemcitabine in Patients with Locally Advanced Pancreatic Adenocarcinoma**

Alexander S. Rosemurgy,[1] Sharona B. Ross,[1] Paul L. Vitulli,[2] Reza Malek,[3] Jaili Li,[4] and Ramtin Agah[5,*]

**Abstract**

**Purpose:** This is a first-in-man safety study in locally advanced pancreatic cancer (LAPC) using a targeted intra-arterial delivery catheter (RenovoCath™).

## 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

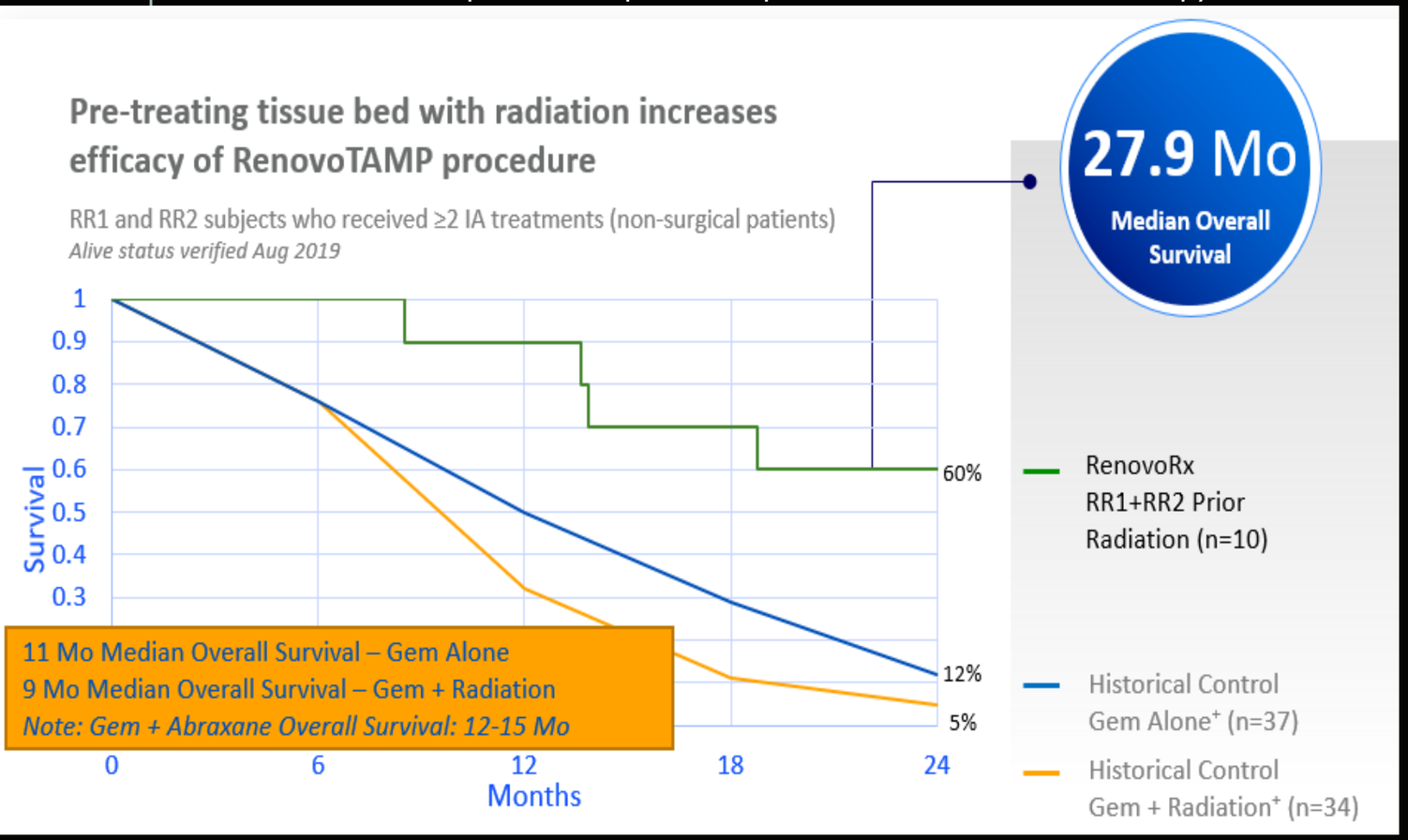
- Primary endpoints: Survival, tumor response
- 6 centers Initiated Jan. 2016
- Limited to patient with Prior Radiation: March 2017
- Limited to one active site w/ Initiation of Phase 3 TIGeR-PaC: May 2018

**25 Patients**

- 96 Treatments

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

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

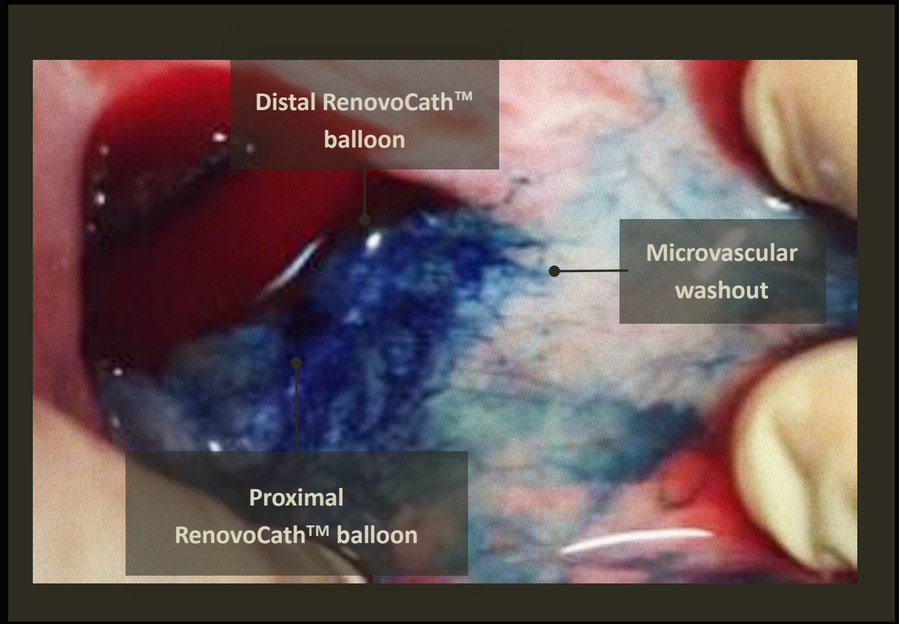



| Group | Median Overall Survival |
|---|---|
| All Comers | 12.4 months |
| Prior Radiation | 27.8 months |

*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).

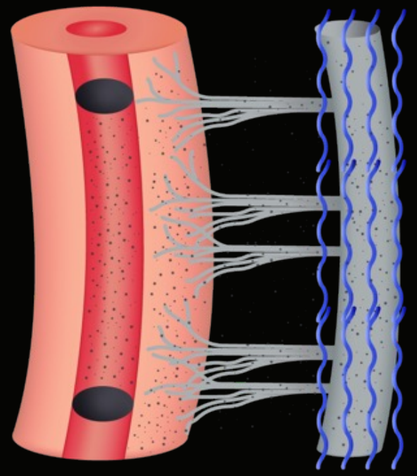
^ Loehrer, P. J. et al. Alone Versus Gemcitabine Plus Radiotherapy in Patients With Locally Advanced Pancreatic Cancer: An Eastern Cooperative Oncology Group Trial. Journal of Clinical Oncology 29, 4105–4112 (2011).

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

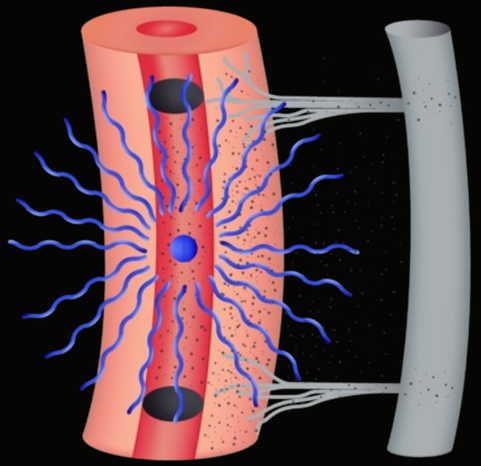



# Radiation reduces venous outflow by decreasing the microvasculature

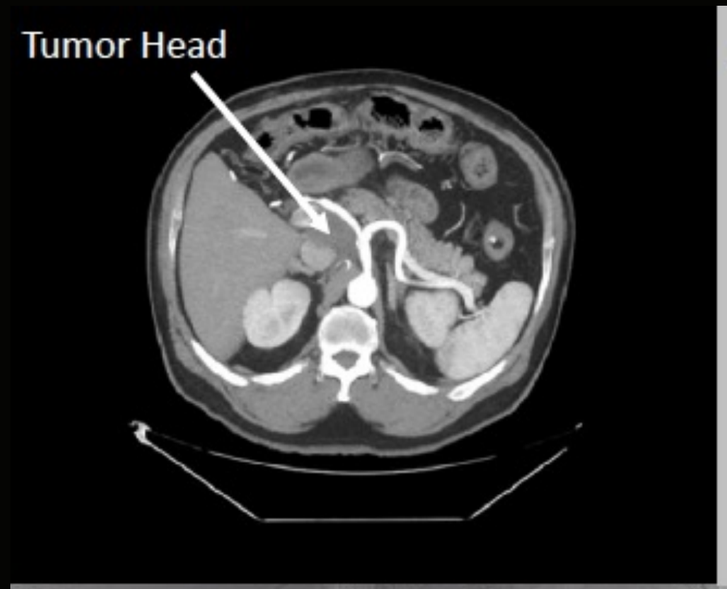
Native vasculature and IA chemo lead to **Micro-vascular washout**

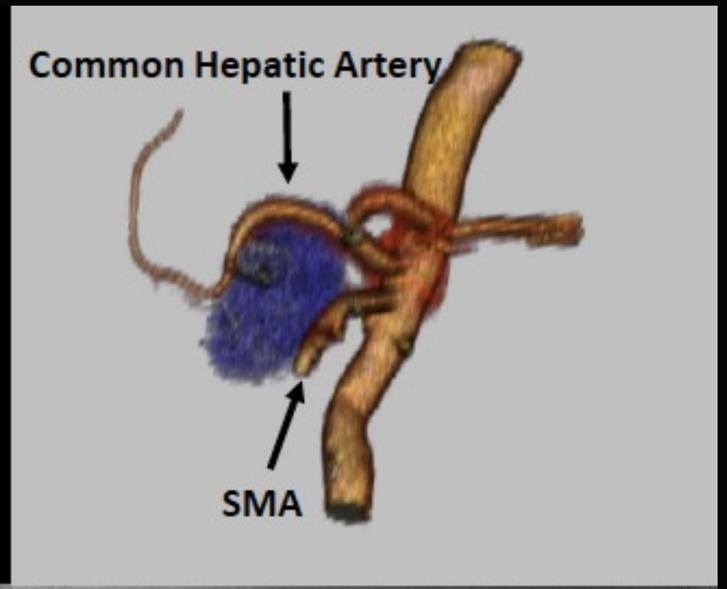


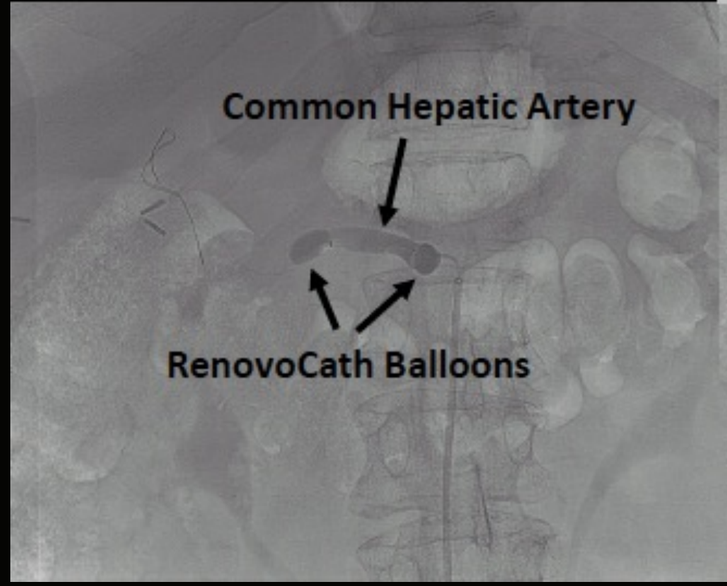
Irradiated vasculature and IA chemo lead to **Diffusion**

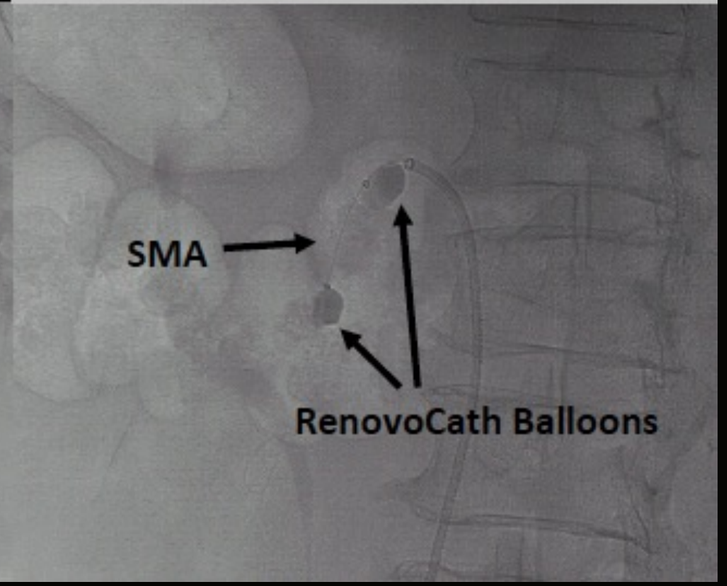


# CT IMAGING PROVIDES A SIMPLE APPROACH TO THE VASCULATURE

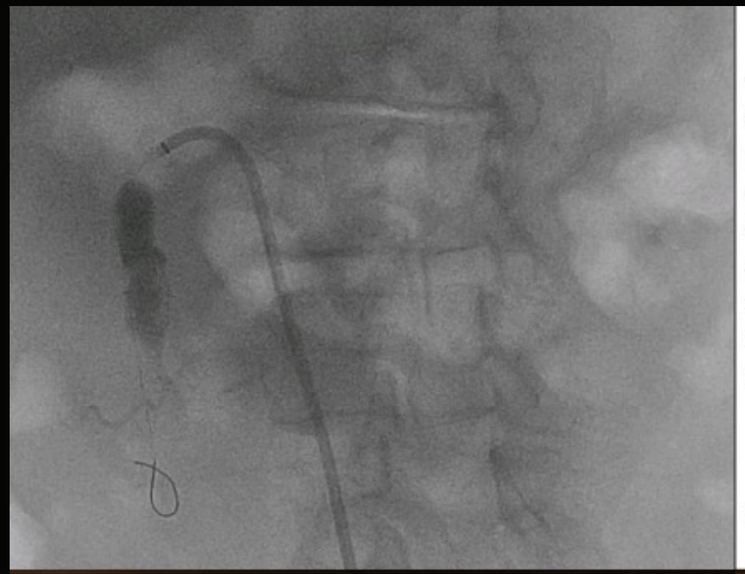


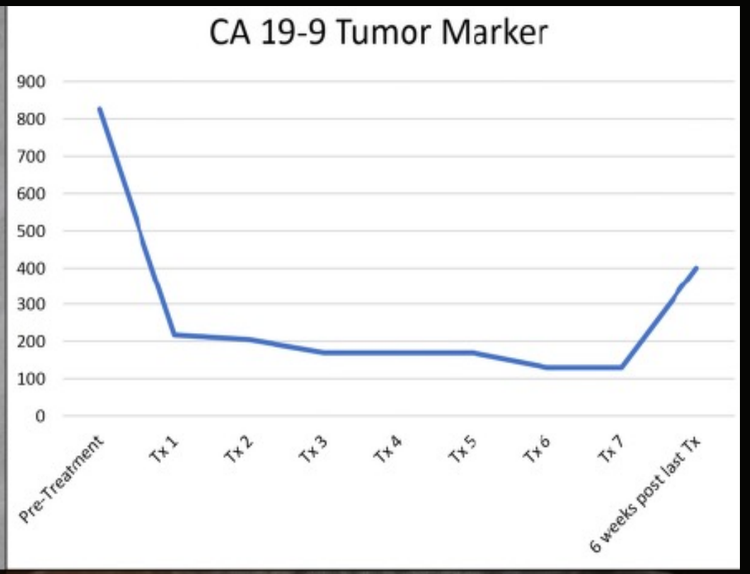



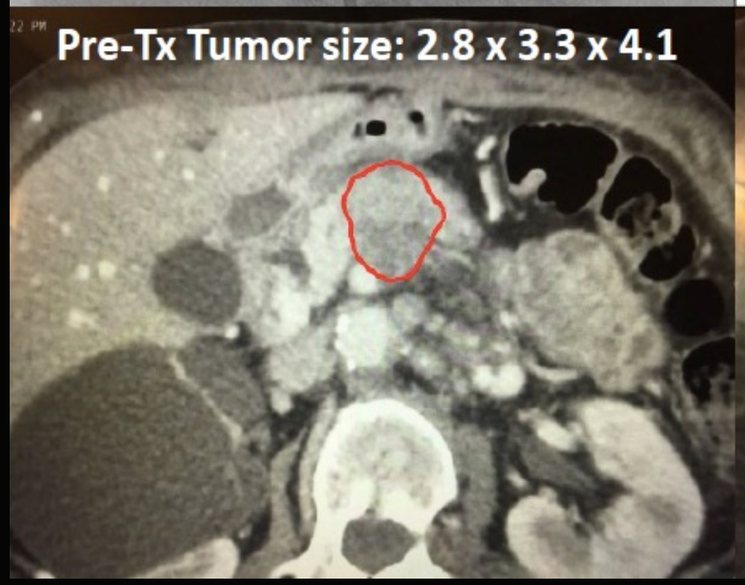



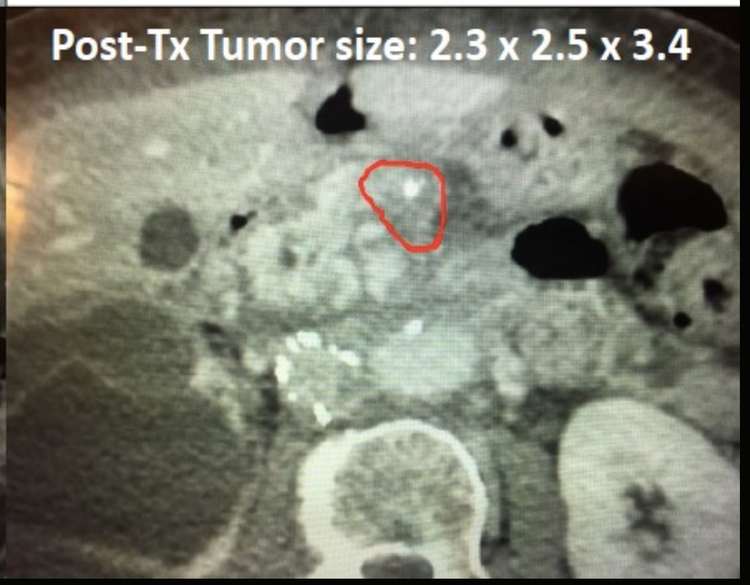



# CASE EXAMPLE





# TIGeR-PaC Randomized Phase 3 Clinical Trial

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

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# 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)**

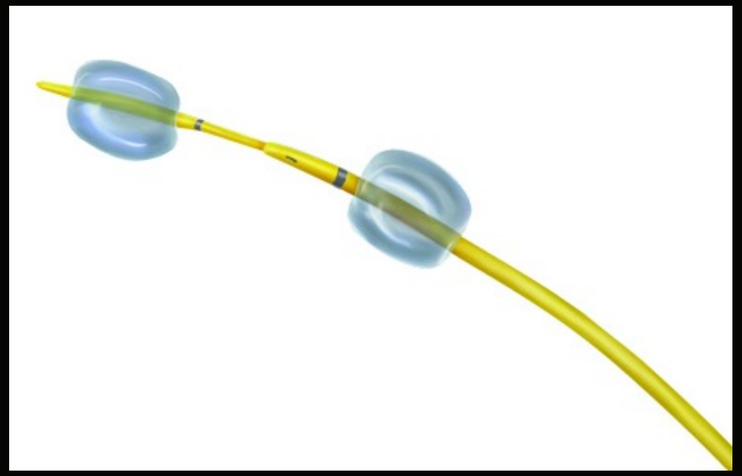
## Objectives:

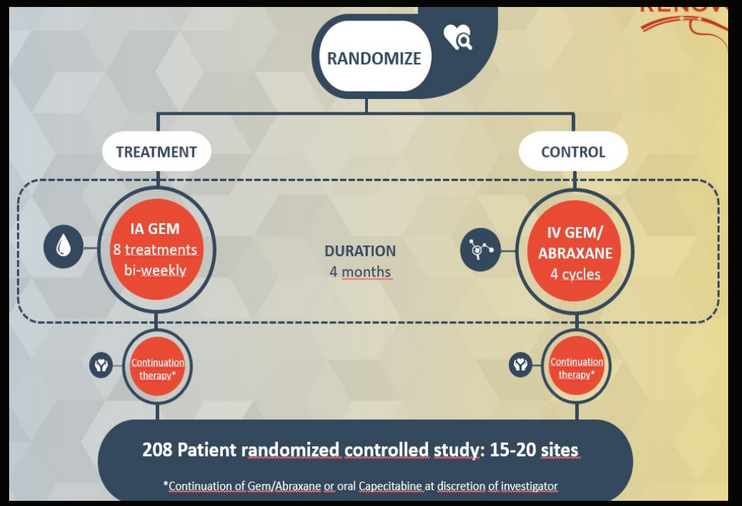
- Primary Objective: Overall Survival from time of randomization
- Secondary Objectives: PFS, objective response rate, duration of response, HR-QOL, degree of peripheral neuropathy, incidence of neutropenia, tolerability, and safety

## Inclusion Criteria:

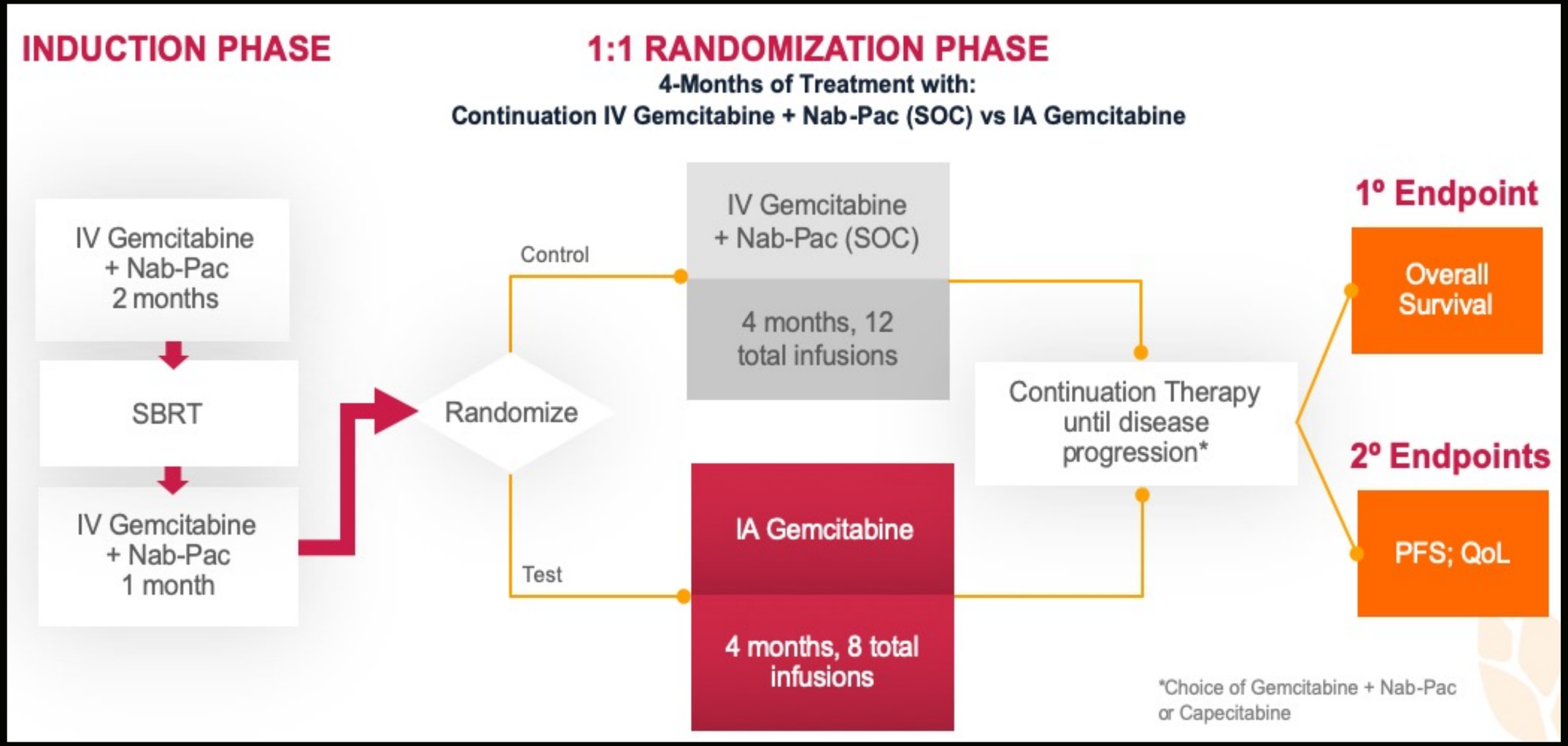
1. Histologically confirmed pancreatic adenocarcinoma with initial diagnosis within 6 weeks of consent
2. Locally advanced, unresectable disease, as defined by **NCCN Guidelines**
3. ECOG 0-1

(Exclusion criteria include any prior treatment except one cycle of gem/abraxane, other malignancy or metastatic disease)





# PHASE 3 TIGER-PAC RCT STUDY SCHEMA



# TIGERPAC – 1ST INTERIM ANALYSIS FEB 2023

## AFTER 30% (26) OF ALL EVENTS (DEATHS) OCCURRED

At the first interim analysis,

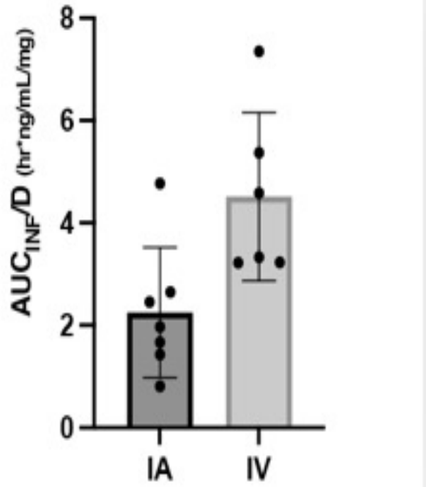
- 45 patients randomized:
  - 23 intra-arterial gemcitabine
  - 22 IV gemcitabine + abraxane
- 13 events in each arm
- 19 patients alive and in the study (data censored as of date data lock)

| Baseline Characteristics+ | IA Gemcitabine (n = 23) | IV Gemcitabine + Nab-Pac (n = 22) |
|---|---|---|
| Gender (Male/Female) | 10/13 | 10/12 |
| Mean Age | 65 (43-85) | 70 (47-83) |
| Tumor size (sum diameters-cm) | 6.5 (2.5,12.9) | 6.95 (2.8, 15.0) |
| Race: Caucasian/Black/Other | 75%/10%/15% | 95%/5%/0% |

Patients were stratified for ECOG Performance Status and Tumor Response (restaged) at time of randomization per protocol design.

# TOLERABILITY AND SAFETY OF TREATMENT

**Drug Exposure IA vs. IV Route**

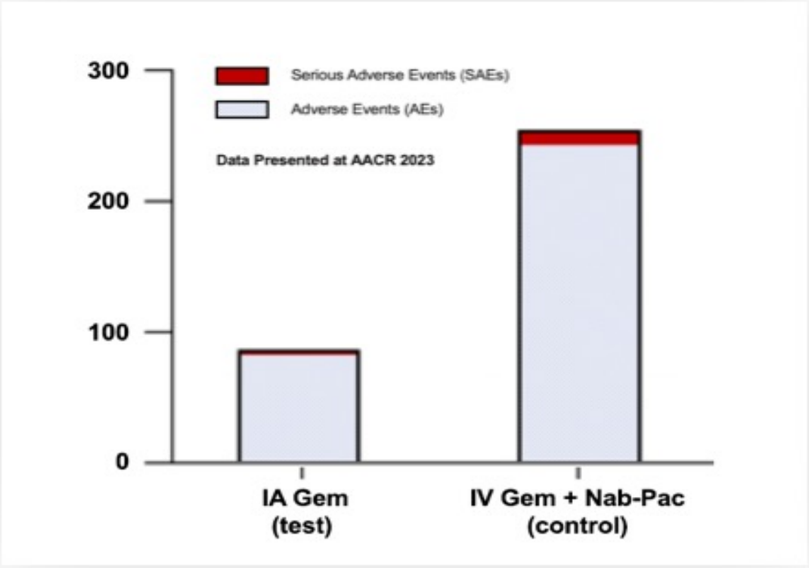



Impact of route of administration on drug exposure Area Under Curve-Normalized for Total Dose (hr*ng/mL/mg, p<0.015)

**Tolerability during active treatment:**

- 61% of IA patients received all planned treatments at the pre-specified dose vs. 18% of IV (primarily due to AEs or SAEs)
- Patients receiving IA therapy had more nausea and abdominal pain events
- Patients receiving IV therapy had more myelosuppression, fatigue, dehydration, neuropathy, and metabolic derangements

**65% fewer total AEs and SAEs in IA vs. IV arm**




**AEs with greater than 10% frequency in each arm (All Grades)**

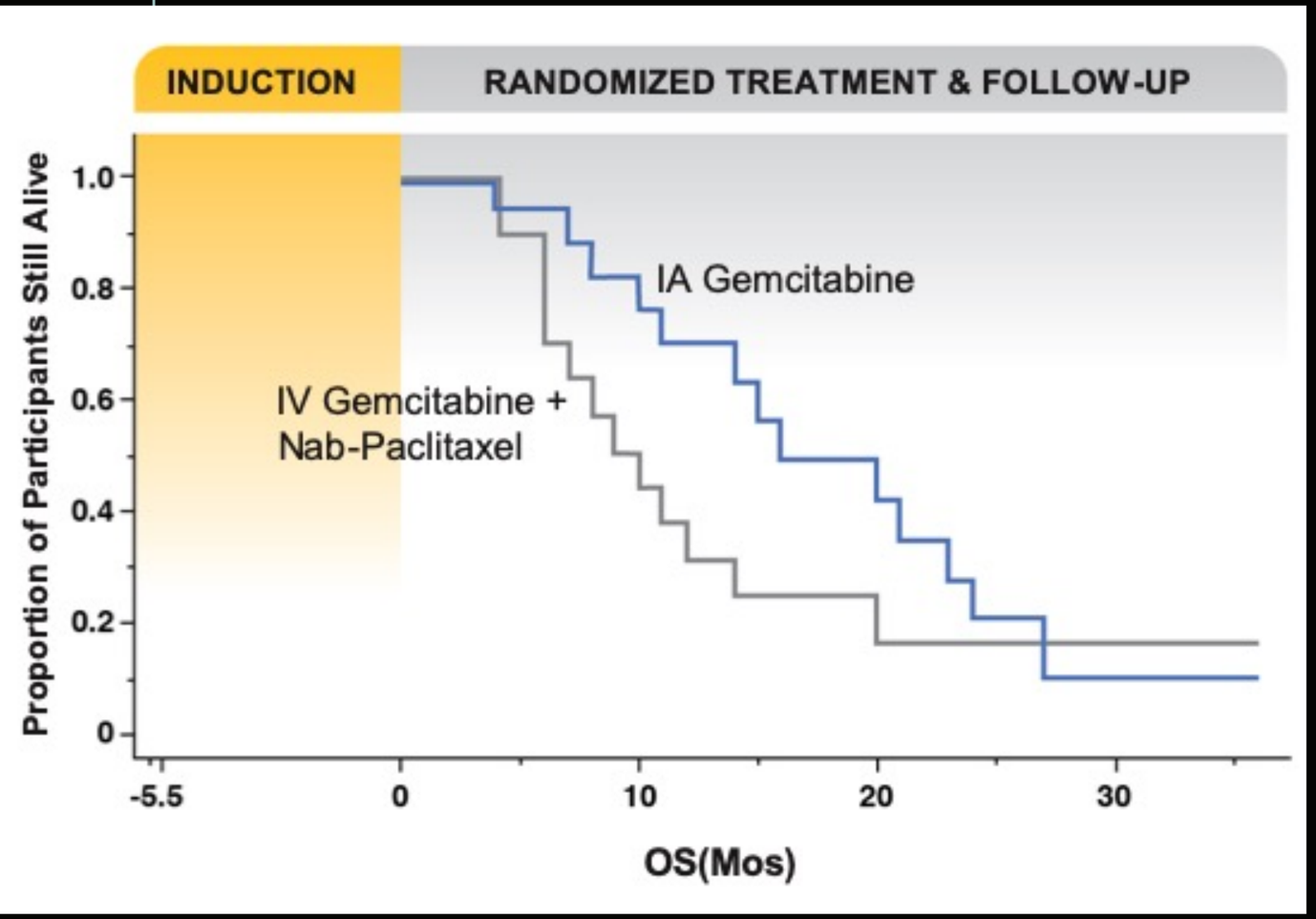
| Adverse Events | IV Gem + Nab-Pac | IA Gemcitabine |
|---|---|---|
| Neutropenia | 81% | 21% |
| Anemia | 48% | 8% |
| Thrombocytopenia | 38% | 4% |
| Elevated AST | 33% | 4% |
| Elevated ALT | 29% | 13% |
| Fatigue | 19% | 8% |
| Neuropathy | 19% | 0% |
| Dehydration | 19% | 8% |
| Hypertension | 14% | 4% |
| Hypokalemia | 14% | 4% |
| Hypoalbunemia | 14% | 4% |
| Abdominal Pain | 0% | 21% |
| Nausea | 10% | 17% |

Adverse event prevalence: IA IV

PK Analysis

65% fewer AE and SAE in the Intra-Arterial Arm of the Study

# OVERALL SURVIVAL




**Data on 45 patients randomized**

- 23 randomized to IA gemcitabine
- 22 randomized to IV gem + nab-pac

**Median Overall Survival (OS) Difference: 6-months**

**IV Gem + Nab-Pac (control arm)**

Avg 5.5 mo dx to randomization | 10 mo from randomization

**10** Months from randomization

**~15.5 months from diagnosis**

**IA Gemcitabine (test arm)**

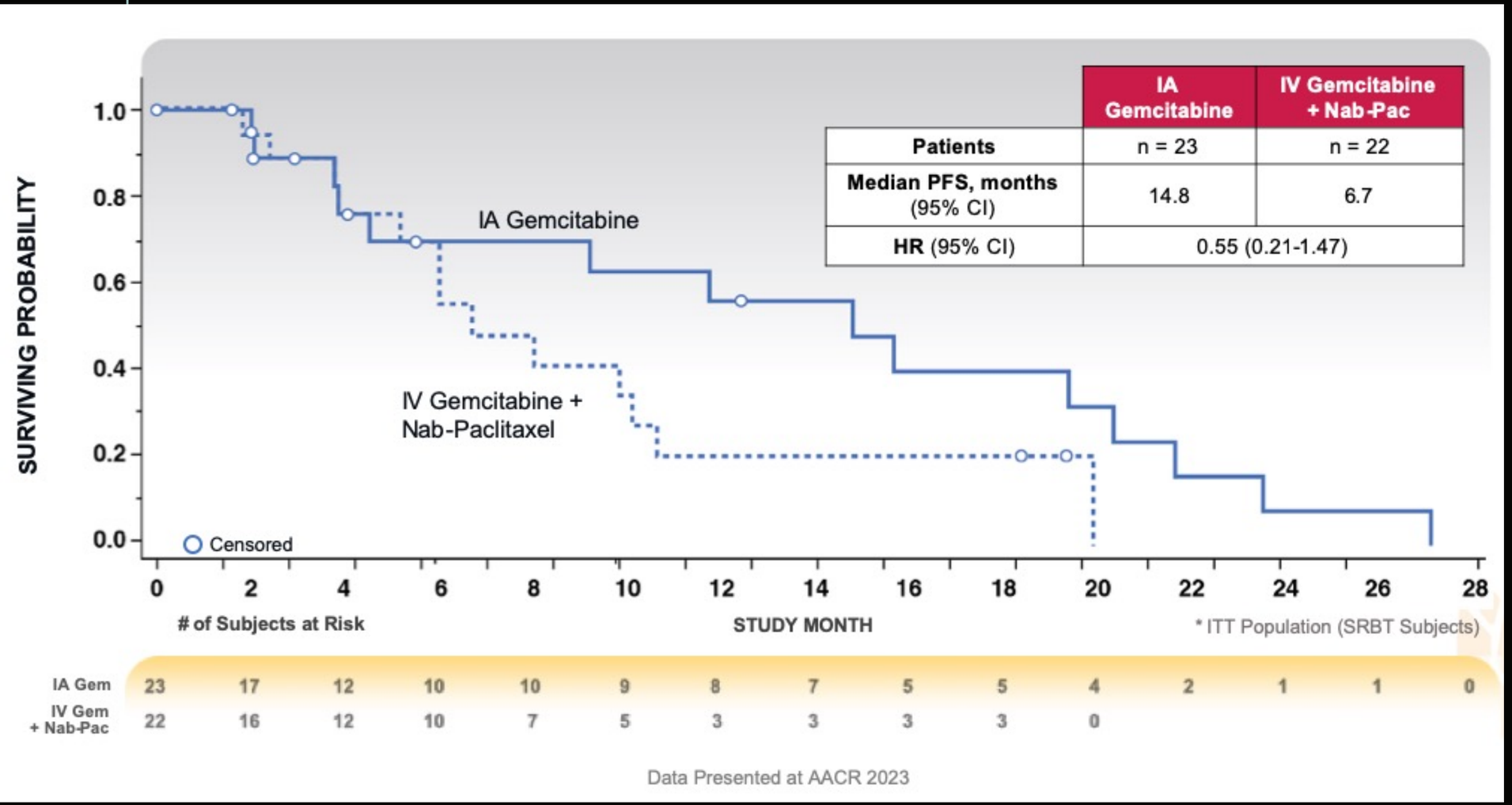
Avg 5.5 mo dx to randomization | 16 mo from randomization

**16** Months from randomization

**~21.5 months from diagnosis**

A positive trend in median overall survival by 24-weeks (6 months); in this interim analysis, the statistical significance was not reached to stop the study early (p=0.051)

# SECONDARY ENDPOINT: PFS




| | IA Gemcitabine | IV Gemcitabine + Nab-Pac |
|---|---|---|
| **Patients** | n = 23 | n = 22 |
| **Median PFS, months** (95% CI) | 14.8 | 6.7 |
| **HR** (95% CI) | 0.55 (0.21-1.47) | |

Data Presented at AACR 2023

PFS improved by 8.1 months in the intra-arterial arm

# CONCLUSIONS

Localized intra-arterial delivery of gemcitabine using RenovoCath treatment is associated with 65% reduced SAEs and AEs

Trend towards improved overall survival by 6 months in the intra-arterial arm of study vs IV chemotherapy arm (p=0.084); PFS improved by 8.1 months in the intra-arterial arm

Study accrual is ongoing with the results of the second-interim analysis anticipated in 2024

# THANK YOU