Improved Resection Rates in Locally Advanced Pancreatic Cancer (LAPC) Following EUS-FNI of Large Surface Area Microparticle Paclitaxel (LSAM Pac)

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ACG 2021
October 22-27
Las Vegas, NV

Overview

- **Overview of Pancreatic Cancer**
- **Background on** Large Surface Area Microparticle Paclitaxel (LSAM Pac) **Nanopac**
- **Research Results**
- Q/A

Background on Pancreatic Cancer

Pancreatic Cancer - Epidemiology

- Approximately 57,600 people (30,400 men and 27,200 women) will be diagnosed with pancreatic cancer.
- About 47,050 people (24,640 men and 22,410 women) will die of pancreatic cancer.
- Pancreatic cancer accounts for about 3% of all cancers in the US and about 7% of all cancer deaths.

Pancreatic Cancer - Epidemiology

- Most Pancreatic cancer cases are adenocarcinomas
- 7-9 % 5 year survival for pancreatic cancer
- High percentage of cases detected in late stage disease

Pancreatic Cancer

- **Staging in Pancreatic Cancer is paramount to optimal treatment**
  - Only R-0 resection has survival value for surgery
  - Often there are large vessels preventing complete resection
  - 50-80% will reoccur in the first 2 years after resection

- **CT scans + EUS for staging**

Pancreatic Cancer - Treatment

- Surgery:
  - Whipple
  - Distal pancreatectomy
- Chemotherapy:
  - Gemcitabine + Abraxane
  - Folfirinox
- Radiation:
  - IMRT
  - Cyberknife (SBRT)

Background On Nanopac

Most Patients are not resectable

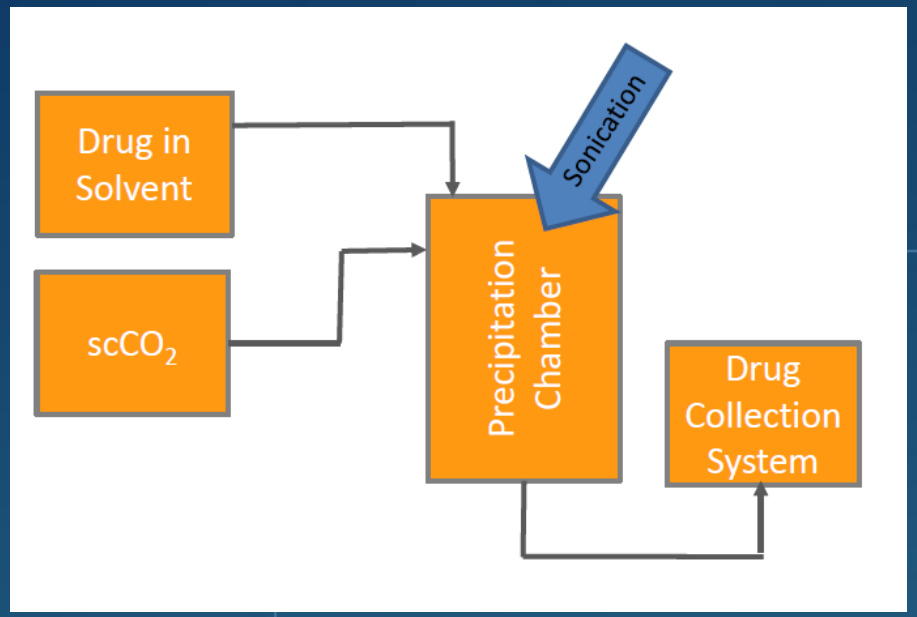
Of the 55-60k new Panc Ca and Cca Patients/Yr, The Vast Majority Are Not Surgical Candidates

80- 85% Pancreatic Ca non-surgical candidates[1]

Opportunity

1. Cidon, E. Una. "Resectable Cholangiocarcinoma: Reviewing the Role of Adjuvant Strategies." Clinical Medicine Insights. Oncology. Libertas Academica, 12 May 2016. Web. 08 May 2017.
2. "Pancreatic Cancer Surgical Treatment and Whipple Procedure." Pancreatica. Cancer Patients Alliance, n.d. Web. 08 May 2017.

Microparticulate Production Technology



Carbon Dioxide (CO_2) above the critical point (> 72.8 bar, >31°C) is supercritical

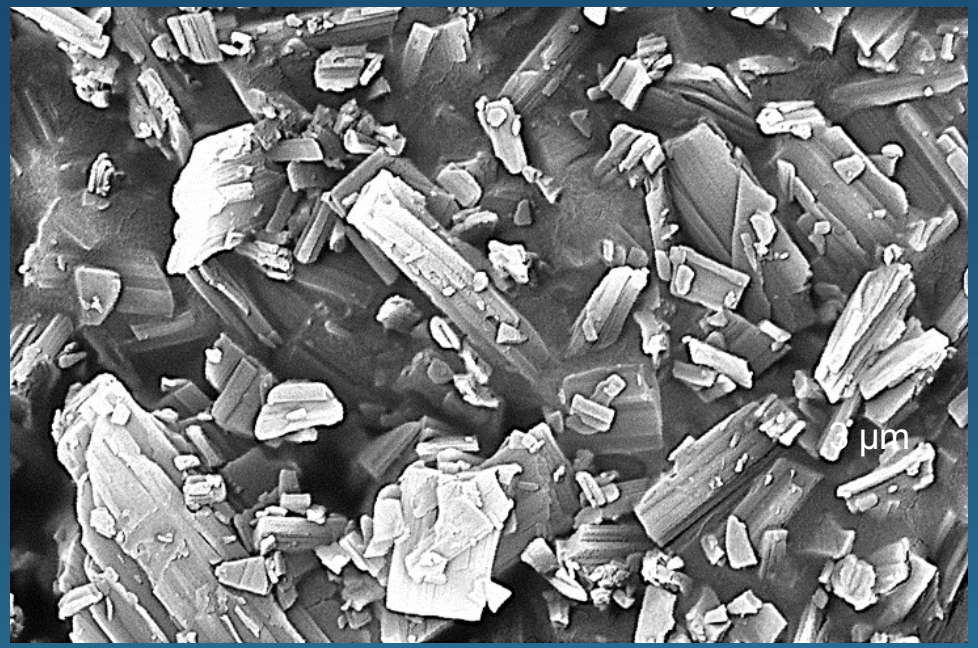
- *sc*CO_2 is miscible with organic solvents
- *sc*CO_2 is a poor solvent for paclitaxel
- Mixing paclitaxel in organic solvent with *sc*CO_2 causes NanoPac to precipitate

- **Technology**
  - **Unique non-mechanical process using supercritical CO_2 and sonication to precipitate nanoparticles in a GMP production environment**
- **Benefits**
  - **Increased microparticle stability without need for additives or coatings**
  - **Small particles with large surface area and narrow particle size distribution (majority in 0.8 micron range)**
  -)

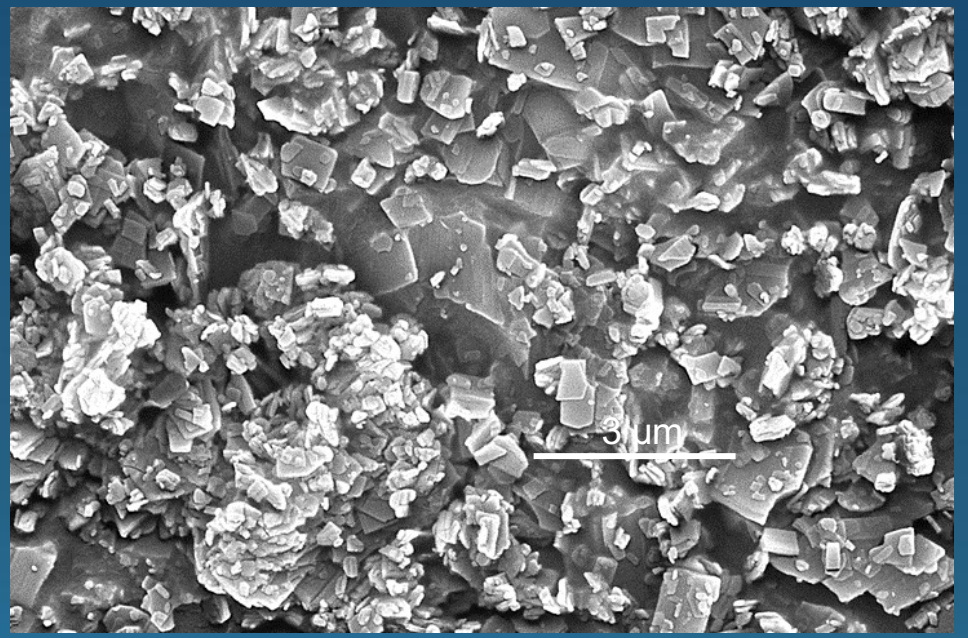
NanoPac Overview

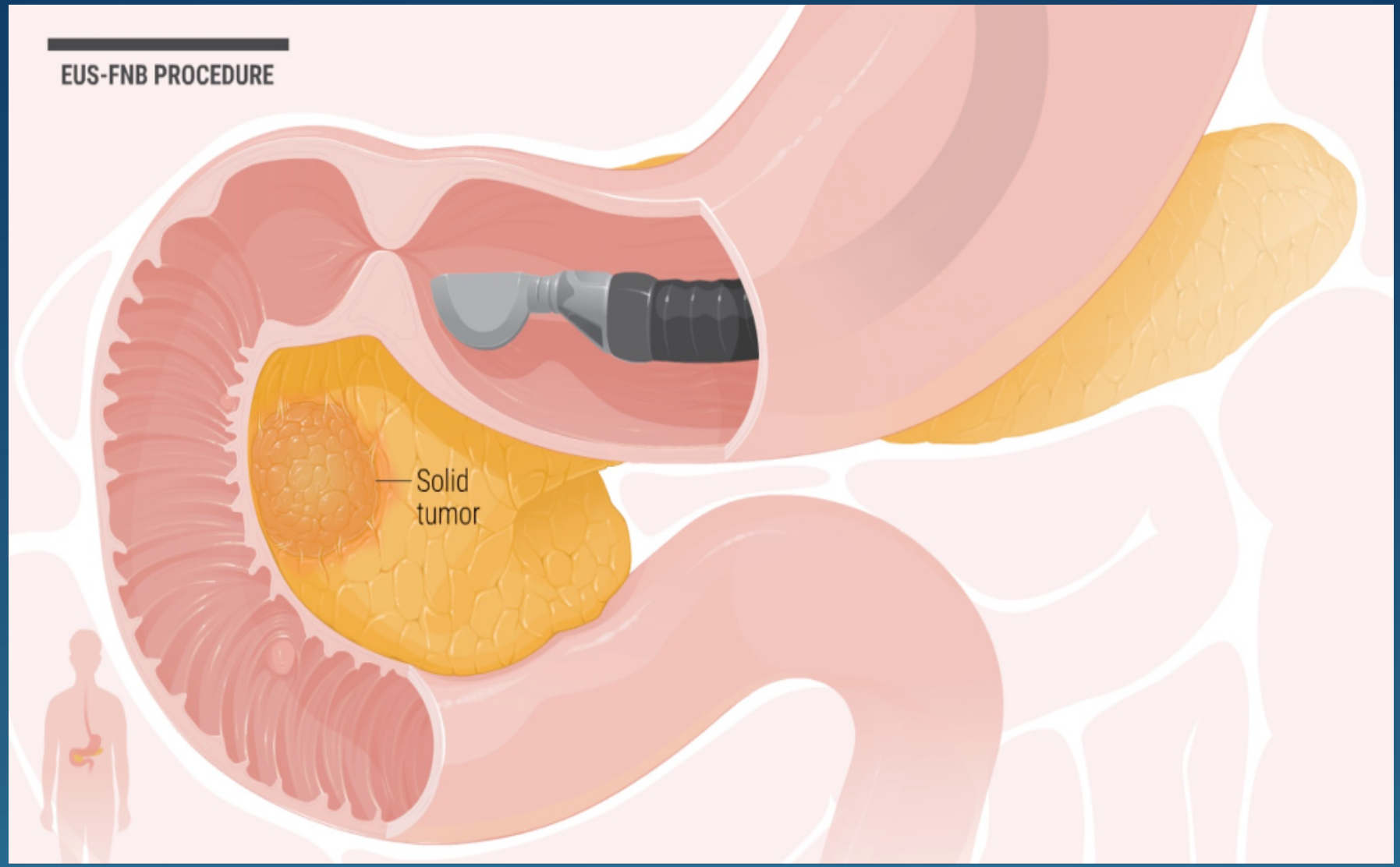
- Paclitaxel vs LSAM Pac

Unprocessed paclitaxel



LSAM Pac




EUS-FNB PROCEDURE
Solid tumor

Background on Large Surface Area Microparticle Paclitaxel (LSAM Pac) **Nanopac**

- **Nanopac**
  - **Phase Ib**
  - **Now completed Phase IIb**
  - **The injection of particle coated with Paclitaxel directly into a pancreatic via an endoscopic procedure**
  - **Goal: To decrease the tumor size so that the patient can get to surgery for tumor resection or possibly avoid the development of cancer in precancerous lesions**

Study Results

Results on Phase II - Single Site Surgical analysis

The aim of the study was to determine safety and tolerability of NanoPac when injected directly to the lesion, and to assess the impact on the lesion by means of imaging assessments at three and six months following the first injection. [NCT#03077685]

In the second phase subjects received two injections of LSAM Pac directly into their pancreatic lesion via endoscopic ultrasound-guided fine needle injection (EUS-FNI) 4 weeks apart, at 15 mg/mL concentration, in a volume equivalent to 20% of the tumor volume.

Results on Phase II Single Site analysis

- Of the 13 subjects considered non-surgical at study entry at this site, seven (54%) were restaged becoming eligible for surgery following LSAM paclitaxel injections.

- Of the 7, six proceeded to surgery and one opted to receive alternate chemotherapy treatment.

- Five of the six subjects underwent surgery with the same surgeon [Schmidt], and the procedure resulted in successful Ro resections; the sixth subject had surgery resulting in an R1 resection.

Results on Phase II -Single Site analysis

Subject Number	Stage at Diagnosis	OR Date	Margins	Regional Lymph	Perineural Invasion	Lymph-vascular Invasion	Treatment Effect	Path Stage	INJ Dates	ChemoRT	Chemo RT	Chemo RT
001	T2N0M0 SMA involvement	7-Jun-2019	All Negative	0/14	Present	None Identified	Moderate Response; Fibrosis and necrosis consistent with	pT2N0	8-Jan-2019 4-Feb-2019	Sep-2018 FOLFIRINOX	Nov- 2018 SBRT	22-Jan-2019 Gem-Abraxane (dose reduced for toxicities)
005	T2N1M0 Portal Vein and SMV abutment	18-Jun-2020	All Negative	0/10	None Identified	None Identified	Minimal Response	pY1cN0	12-Jun-2019 11-Jul-2019	Apr-2019 Gem-Abraxane (progression)	Jun-2019 FOLFIRINOX	Mar-2020 IMRT
006	T4N0M0 encases the GDA, 180° involvement SV as it enters the portal confluence. 5-8mm length of abutment/encasement of SMA <180°	30-Jan-2020	All negative	1/15	None Identified	None Identified	Excellent Response	pT1aN1	24-Jun-2019 24-Jul-2019	18-Mar-2019 FOLFIRINOX (dose reduced for nephrotoxicity)	Oct-2019 SBRT	
007	T2N0M0 Encasement of GDA; abuts portal vein for 1.9 cm	13-Mar-2020	No evidence of residual tumor	0/41	None Identified	None Identified	Complete Response	pT0N0	7-Oct-2019 4-Nov-2019	28-Feb-2019 Gemcitabine (dose reduced for neuropathy)	Jul-2019 SBRT	19-Nov-2019 Chemo on hold-poor performance status and toxicities
012	T2N1M0 There is less than 180° of involvement of the hepatic artery & involvement of SMA	6-Apr-2020	SMV and SMA margins positive, Uncinate margin 0.5mm, Pancreatic neck margin extranodal extension identified	8/13	Multiple Foci	Multiple Foci	Focal Necrosis	pT4N2	16-Dec-2019 13-Jan-2020	Sep-2019 FOLFIRINOX		
013	T4N1M0 encases entire celiac axis, splenic artery, left gastric artery; involvement of hepatic artery	24-Sep-2020	All Negative	0/32	None Identified	None Identified	Moderate Response (minimal residual cancer)	pT4N0	02-Jan-2020 29-Jan-2020	24-Jun-2019 FOLFIRINOX	4-Sep-2019 Gem-Abraxane	Jul-2020 IMRT (Xolada)

Results on Phase II - Single Site analysis

Subject	CA19-9 u/mL Baseline (week 24)	Largest Diameter of Lesion (cm)			% change at week 24	Time from initiating LSAM paclitaxel treatment to surgery
		Baseline	Week 12	Week 24		
001	43 (28)	2.5	1.7	1.9	-24%	6 months
005	342 (65.3)	2.8	3.0	2.7	-4%	12 months
006	132 (36)	2.3	2.1	1.6	-30%	6 months
007	25 (44)	2.2	1.1	n/a*	n/a*	5 months
012	619 (668)	2.6	4.2	n/a*	n/a*	4 months
013	3 (2)	3.1	3.3	2.3	-26%	8.5 months

Questions

&

Answers