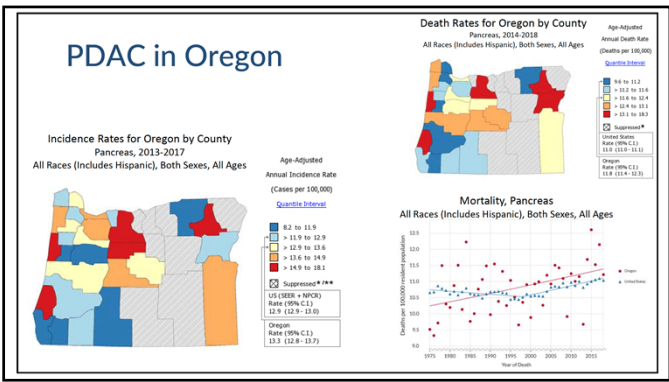


**Pancreatic Adenocarcinoma
Trial Portfolio**

**BRENDEN-COLSON CENTER FOR PANCREATIC
CARE**

DATE: March 12, 2021 PRESENTED BY: Adel Kardosh, MD PhD



Multidisciplinary Palliative Management in Pancreatic Cancer

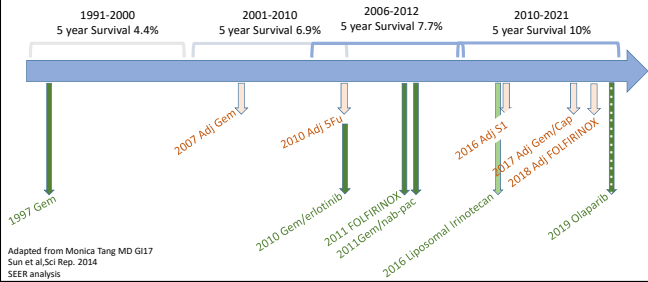
Symptom	Potential Management
Pain	<ul style="list-style-type: none"> Analgesics (opioid) Radiation therapy Chemotherapy Celiac plexus neurolysis
Gastric Outlet Syndrome	<ul style="list-style-type: none"> Prophylactic gastrojejunostomy in unresectable patients during exploratory surgery
Jaundice	<p>Biliary decompression can be achieved through</p> <ul style="list-style-type: none"> Choledochojejunostomy Cholecystojejunostomy Endoscopic stent placement

Adapted from: Friesove and Walting. Am Fam Physician 2000; 73:485. Fernandez-del Castillo. Up to Date Web site. Available at: http://www.upToDate.com/spotcontent/topic.do?topicKey=panc019367&open=selectedT99en=7-48. Accessed March 16, 2007.

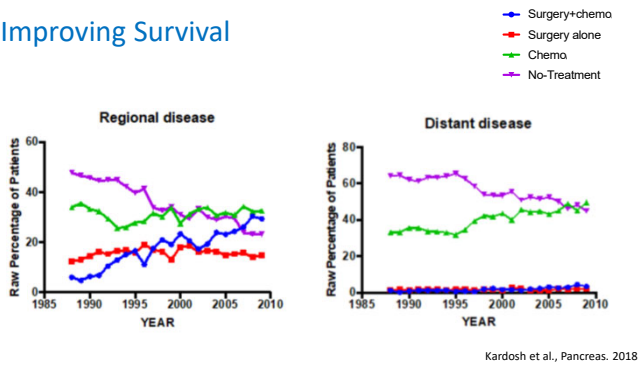
Advances in the Treatment of Pancreatic Cancer

- Better endoscopy (diagnostic and therapeutic)
- Improved pre-operative imaging
- Surgical resections safer
- Pre-operative therapy has allowed resections in patients that would have previously been deemed unresectable
- Median survival has improved with more active systemic chemotherapy
- Earlier and better palliative and supportive care
- **But we still have not made major breakthroughs that have a significant survival impact in most patients**

Pancreatic Cancer Positive Trials.



Improving Survival

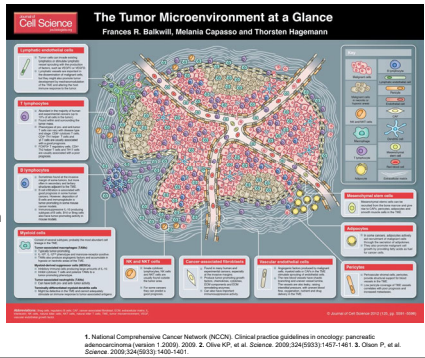


Pathophysiology

~90% is ductal adenocarcinoma, which is characterized by¹:

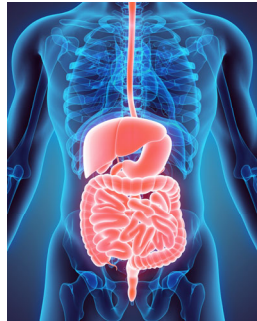
Poor vascularization, which creates a barrier for effective cytotoxic delivery^{2,3}

An enveloping fibrotic stroma of excessive connective tissue and cells that forms hard tumors³



Disease Site

- Pancreatic
 - Resectable
 - Locally Advance
 - Metastatic



Google images OHSU

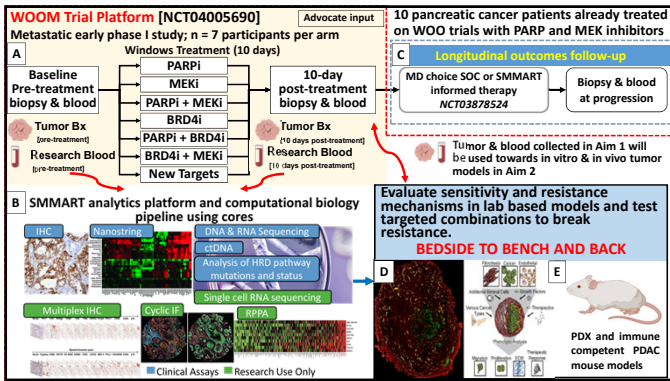
Resectable Pancreatic Adenocarcinoma

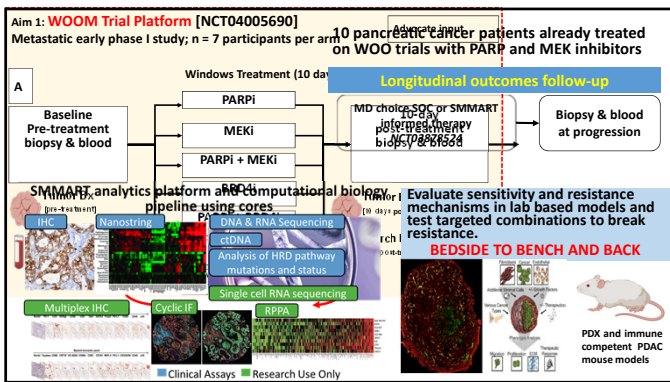


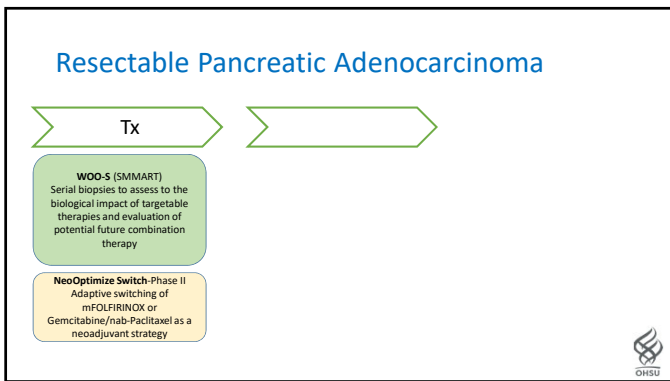
WOO-S (SMART)
Serial biopsies to assess to the biological impact of targetable therapies and evaluation of potential future combination therapy

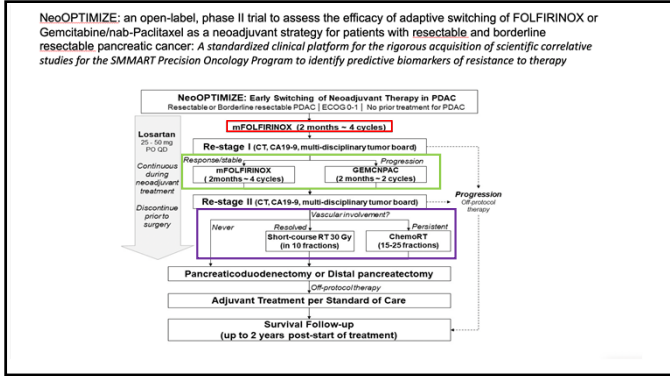
NeoOptimize Switch-Phase II
Adaptive switching of mFOLFIRINOX or Gemcitabine/nab-Paclitaxel as a neoadjuvant strategy

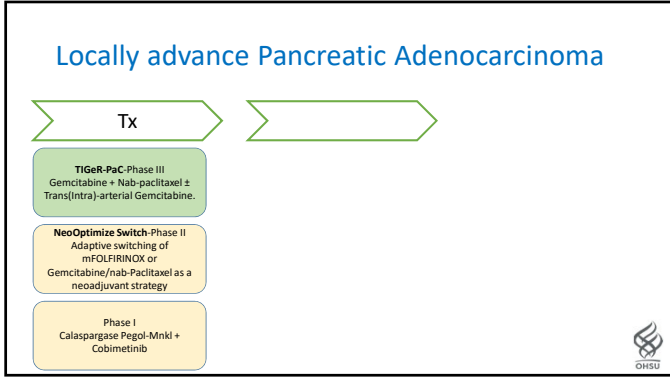
OHSU











Manipulation of cancer metabolism

- Dependence of tumor cells on exogenous asparagine.
- L-asparaginase can be exploited to deplete extracellular asparagine
- But, oncogenic KRAS mediates metabolic reprogramming shifts dependence from asparagine via RAS signaling
- Preclinical mouse models MEK inhibitor plus L-asparaginase treatment reduced tumor growth!!!



Thank You
