Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Pancreatic Cancer

Friday, April 11, 2025

6:00 PM – 7:30 PM

Faculty

Farshid Dayyani, MD, PhD
Caroline Kuhlman, MSN, APRN-BC
Philip A Philip, MD, PhD
Amanda K Wagner, APRN-CNP, AOCNP

Moderator

Neil Love, MD

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Faculty

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Dr Dayyani — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Eisai Inc, Jazz Pharmaceuticals Inc, Sirtex Medical Ltd, Taiho Oncology Inc
Contracted Research	AbbVie Inc, Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Exelixis Inc, Genentech, a member of the Roche Group, Natera Inc, Pfizer Inc, Taiho Oncology Inc
Speakers Bureaus	Astellas, Ipsen Biopharmaceuticals Inc, Sirtex Medical Ltd, Takeda Pharmaceuticals USA Inc

Ms Kuhlman — Disclosures

No relevant conflicts of interest to disclose.

Dr Philip — Disclosures

Advisory Committees	Agenus Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Daiichi Sankyo Inc, Gilead Sciences Inc, HUYA Bioscience International, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Novocure Inc, Pfizer Inc, Processa Pharmaceuticals Inc, Seagen Inc, Takeda Pharmaceuticals USA Inc
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Speakers Bureaus	Astellas, Incyte Corporation

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Ms Wagner — Disclosures

No relevant conflicts of interest to disclose.

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Commercial Support

This activity is supported by an educational grant from Ipsen Biopharmaceuticals Inc.

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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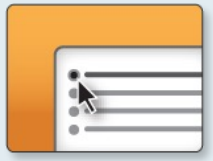
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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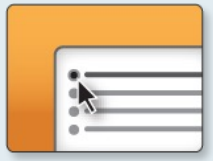
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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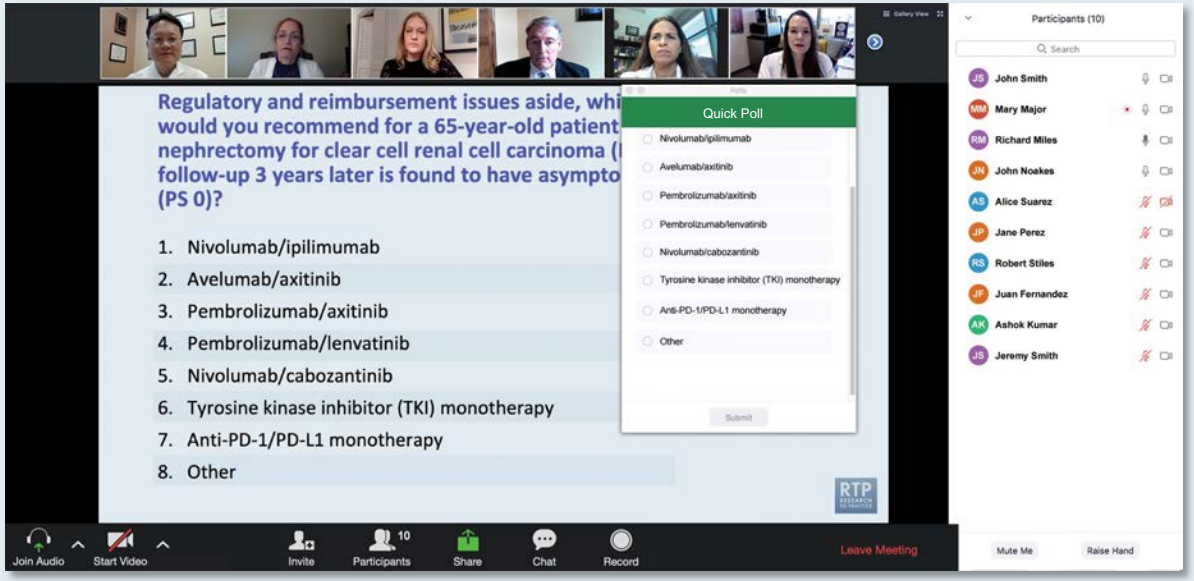
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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ONCOLOGY NURSING UPDATE WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 1 — An Interview with Ms Robin Klebig for Oncology Nurses

MS ROBIN KLEBIG
MAYO CLINIC

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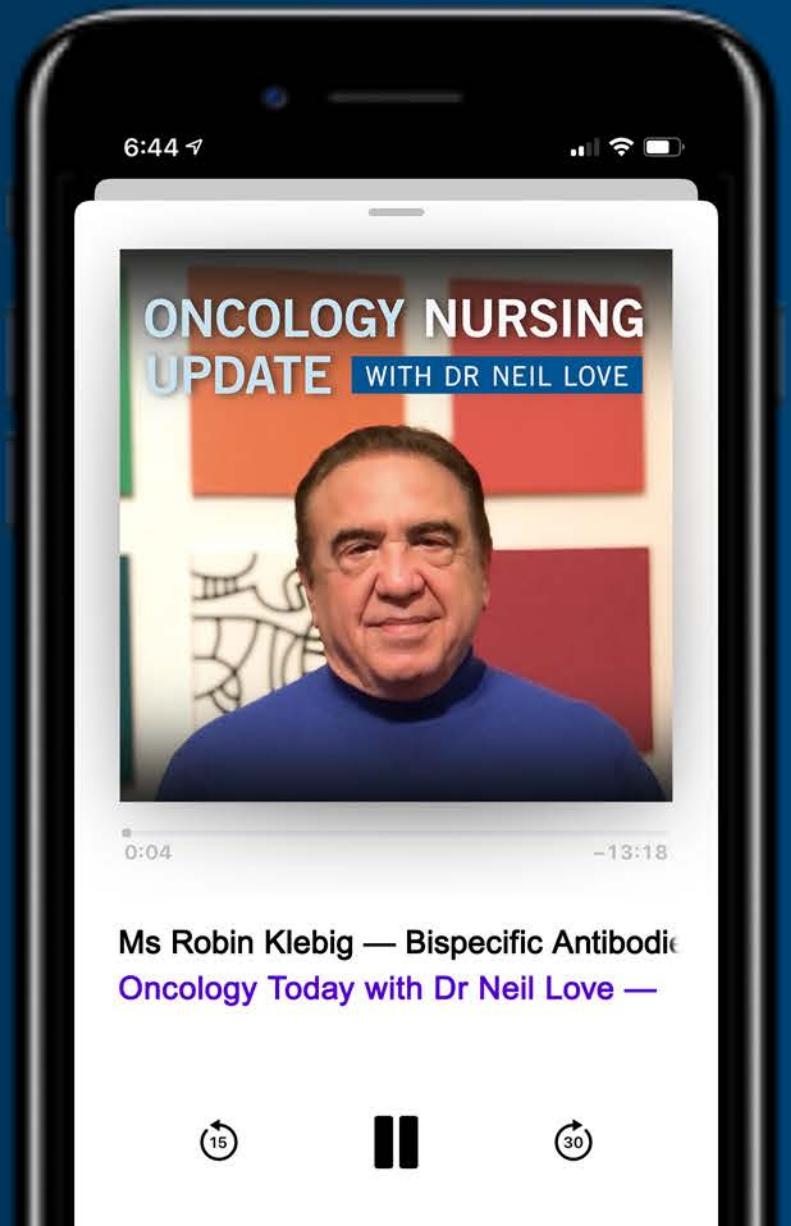
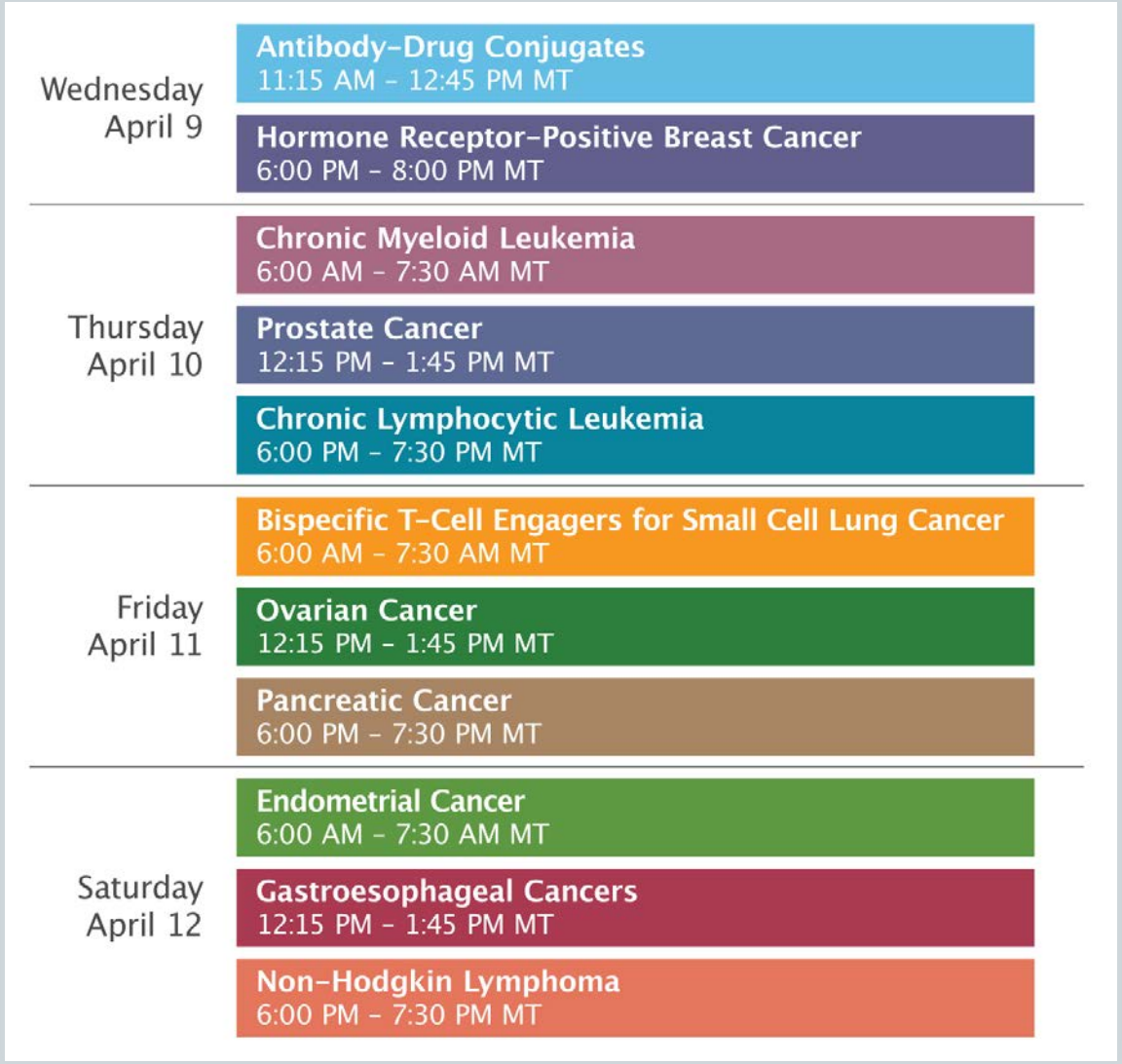
Spotify

Listen on Google Podcasts



“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Agenda

Introduction: Initial Management of Pancreatic Adenocarcinoma (PAD)

Module 1: Clinical Presentation and Prognosis of PAD; Recent Advances in Up-Front Treatment for Metastatic PAD

Module 2: Selection and Sequencing of Therapy for Relapsed/Refractory Metastatic PAD

Module 3: Importance of Palliative Care for Advanced PAD

Module 4: Role of PARP Inhibitor Maintenance Therapy for Newly Diagnosed Metastatic PAD

Module 5: Promising Investigational Strategies for PAD

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Module 5: Promising Investigational Strategies for PAD

Ms Wagner: Case Presentation

- 42 yo male with no significant PMH presented to local ED after a syncopal episode while at church with his family
- Prior to this episode, had been experiencing generalized fatigue, weakness, anorexia, and dark urine
- Labs showed acute anemia (hemoglobin of 7) and hyperbilirubinemia (t. bili 7)
- Imaging showed a pancreatic head mass with associated biliary ductal dilation as well as several liver lesions concerning for metastatic spread
- EGD showed an oozing pancreas mass invading into the duodenum, +adenocarcinoma (pMMR)
- Liver biopsy confirmed metastatic disease
- Underwent ERCP, biliary stent placement
- Also diagnosed with diabetes, started on insulin
- NGS: KRAS G12D, TP53, low TMB, microsatellite stable
- Germline genetic testing—negative

Ms Wagner: Case Presentation (continued)

EVALUATION AT 1ST APPOINTMENT

- Physical symptoms-weight loss, poor appetite (30 lb weight loss). Fatigued, but still trying to work. Abdominal pain resolved with biliary stent placement. Dizziness resolved with PRBC transfusion.
- Performance status 1
- Psychological symptoms-anxiety re: diagnosis and prognosis
- Social support-married with 2 young children. Parents also supportive but mother recently diagnosed with uterine cancer
- Discussed first line treatment with NALIRIFOX

Ms Wagner: Case Presentation (continued)

- Overall tolerated treatment well-had grade 1 diarrhea and nausea which were controlled
- Clinical symptoms improved, gained weight and had improved energy
- Restaging scans after 4 months of therapy with interval decrease in size of liver lesions and pancreas mass
- Oxaliplatin eventually discontinued d/t neuropathy

Agenda

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Clinical Scenario

A patient with newly diagnosed metastatic PAD who is about to start treatment with first-line NALIRIFOX

Clinical Presentation and Prognosis of PAD

Amanda K Wagner, APRN-CNP, AOCNP
The James
The Ohio State University Comprehensive Cancer Center
Columbus, Ohio

Pancreatic Cancer Statistics

- Pancreatic cancer is the 10th most common cancer in the USA
- 3rd leading cause of cancer death
- SEER database estimated 66,440 new cases of pancreatic cancer in 2024
  - 3.3% of all new cancer cases
- 51,750 estimated deaths in 2024
- 12.8% 5 Year Relative Survival
- Overall lifetime risk of developing pancreatic cancer is 1.7% by age 75

https://seer.cancer.gov/statfacts/html/pancreas.html

Clinical Risk Factors

- Acute and Chronic Pancreatitis
- Smoking and Alcohol Use
- Obesity
- Diabetes
- Intraductal papillary mucinous neoplasms (IPMNs)
- Mucinous cystic neoplasms (MCNs)

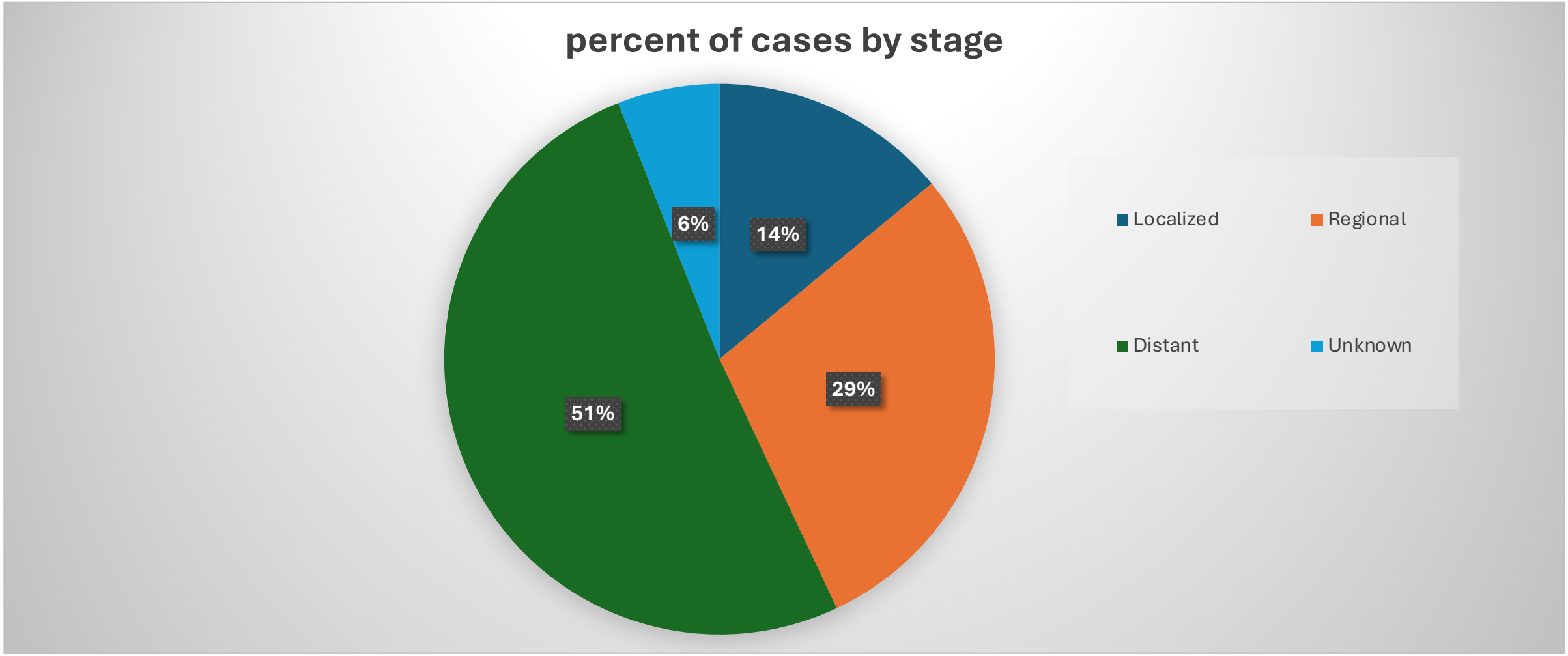
Stoffel EM, Brand RE, Goggins M. Pancreatic Cancer: Changing Epidemiology and New Approaches to Risk Assessment, Early Detection, and Prevention. Gastroenterology. 2023 Apr;164(5):752-765. doi: 10.1053/j.gastro.2023.02.012. Epub 2023 Feb 18. PMID: 36804602; PMCID: PMC10243302.

Inherited Risk Factors

Gene	Genetic Syndrome	Average lifetime risk for PDAC
ATM	Ataxia telangiectasia	5-10%
BRCA1/2, PALB2	Hereditary breast ovarian cancer syndrome	5-8%
CDKN2A	Familial atypical multiple mole melanoma	16-20%
MLH1, MLH2, MSH6	Lynch Syndrome	0.5-7%
PRSS1	Hereditary Pancreatitis	10%
STK11	Peutz-Jeghers syndrome	11-32%
TP53	Li-Fraumeni syndrome	Unknown

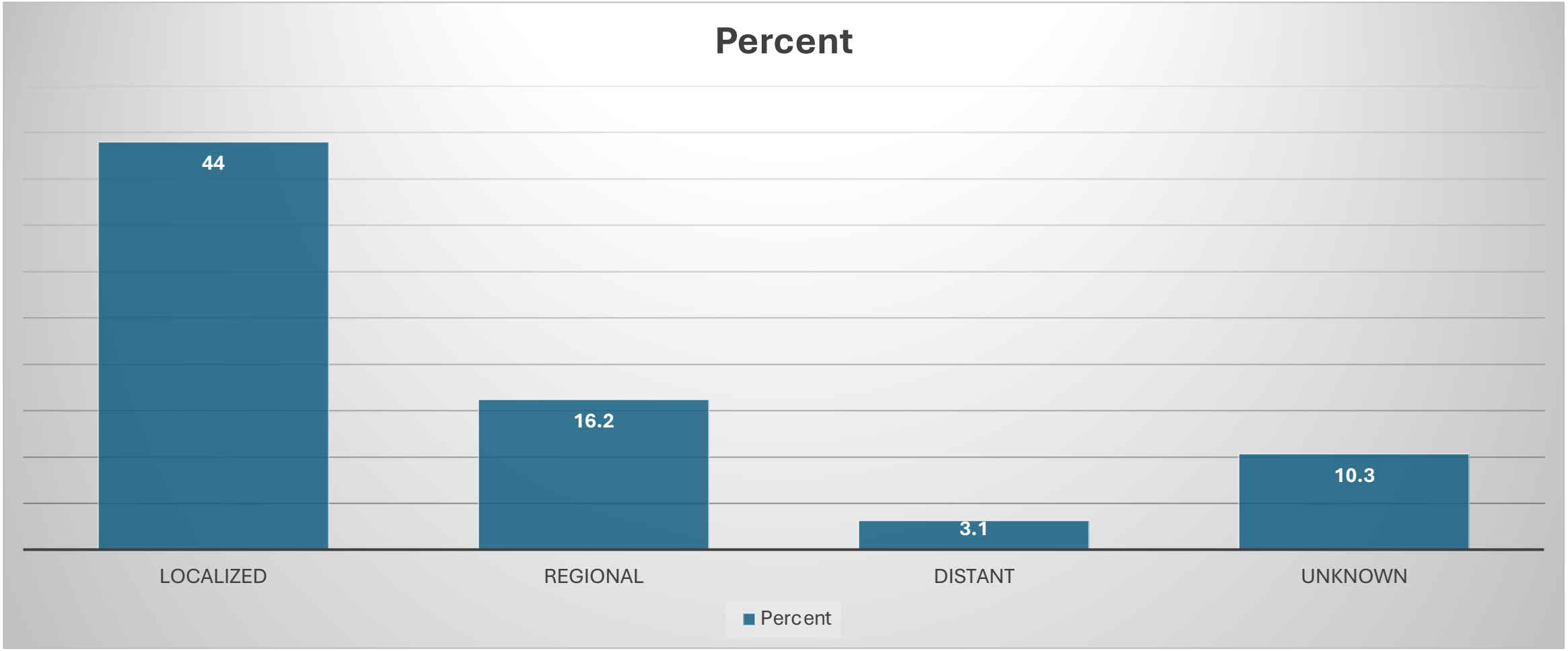
Stoffel EM, Brand RE, Goggins M. Pancreatic Cancer: Changing Epidemiology and New Approaches to Risk Assessment, Early Detection, and Prevention. Gastroenterology. 2023 Apr;164(5):752-765. doi: 10.1053/j.gastro.2023.02.012. Epub 2023 Feb 18. PMID: 36804602; PMCID: PMC10243302.

Pancreatic Stage Distribution at Diagnosis (%)



https://seer.cancer.gov/statfacts/html/pancreas.html

5 year Relative Survival Percentage by Stage



https://seer.cancer.gov/statfacts/html/pancreas.html

Presenting Symptoms

Disease is most often diagnosed at advanced stage once patient develops symptoms

- Anorexia/weight loss
- Fatigue
- Abdominal pain
- Back pain
- Muscle weakness/wasting
- Jaundice
- Change in bowel habits
- Indigestion
- New onset or worsening diabetes

Park W, Chawla A, O'Reilly EM. Pancreatic Cancer: A Review. JAMA. 2021;326(9):851–862. doi:10.1001/jama.2021.13027

Roundtable Discussion

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Case Presentation

- 54 yo male with hx of substance use disorder who developed epigastric pain. Diagnosed with pancreatitis and treated conservatively
- Had recurrent admissions for similar symptoms over the next several months. Underwent EUS with FNA of pancreas, no evidence of malignancy, imaging with new indeterminate hepatic lesions.
- 2 months later, presented to the ED with worsening pain. Liver lesions grew as well as pancreas mass, biopsy of liver lesion +adenocarcinoma consistent with pancreatic primary
- NGS: KRAS G12D, TP53. indeterminate variant in DPYD
- Germline genetic testing: negative

Case Presentation (continued)

EVALUATION AT 1ST APPOINTMENT

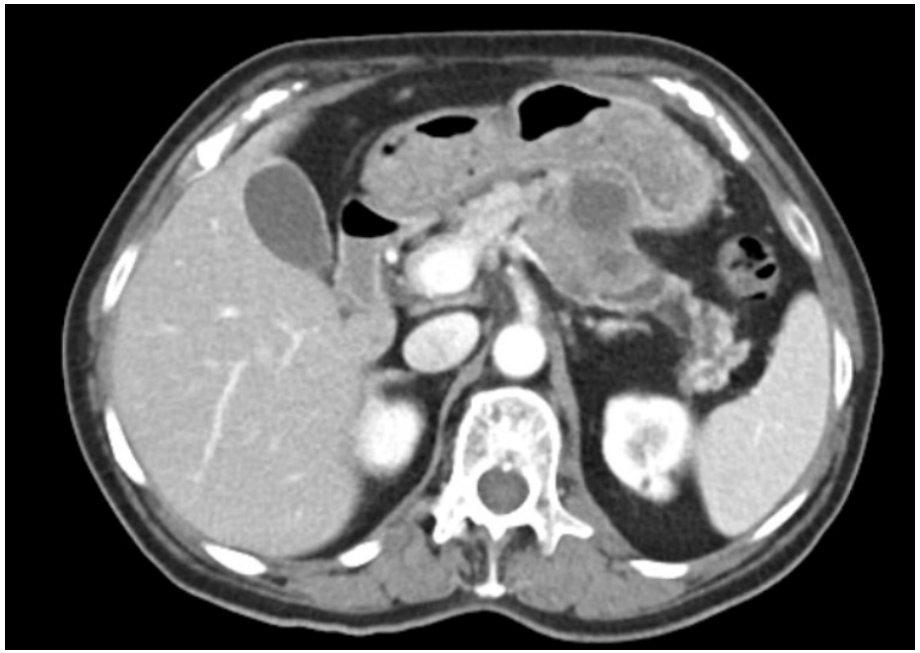
- Physical symptoms-weight loss, poor appetite, uncontrolled abdominal pain, constipation
- Established with harm reduction clinic d/t history of substance abuse—started on SL buprenorphine and morphine for pain
- Performance status 1
- Psychological symptoms-depression regarding diagnosis
- Social support-married. Works as a barber. Has been sober >20 years
- Discussed first line treatment with NALIRIFOX

Case Presentation (continued)

- Developed mucositis, neutropenia, and diarrhea after the first 2 treatments. DPD gene mutation noted to be + with activity score of 1-2. 5FU dose reduced by 20% with resolution in his symptoms
- Clinically improved dramatically after 3 months of therapy with improvement in abdominal pain, improvement in fatigue and weight gain
- CT scans after 3 months of therapy with interval improvement in pancreatic mass and hepatic mets.

Recent Advances in Up-Front Treatment for Metastatic PAD

Farshid Dayyani, MD, PhD



- 72 year old female with family history of pancreatic cancer in her mother presented with 20 LB weight loss over six months, weakness and fatigue
- CT scan of abdomen and pelvis showed a 4.4cm pancreatic tail then systemic mass and multiple smaller lesions in the liver suspicious for metastases
- Endoscopic ultrasound and fine needle biopsy confirmed moderately differentiated adenocarcinoma of the pancreas
- CA19 9 at baseline was 19,000
- ECOG performance status is 1
- Past medical history includes hypertension, hyperlipidemia and type 2 diabetes mellitus, all very well controlled with medication
- The patient is interested in a treatment option which will maximize survival

PRODIGE 4 / ACCORD 11
FOLFIRINOX vs Gemcitabine in mPDAC

Phase III PRODIGE 4/ACCORD 11 Study Design

Eligibility (n = 342)
Metastatic pancreatic cancer
ECOG PS 0-1
No prior chemotherapy or abdominal RT

R

FOLFIRINOX n = 171

O, 85 mg/m² d1
I, 180 mg/m² d1
LV, 400 mg/m² d1
5-FU, 400 mg/m² bolus d1 and 2,400 mg/m² 46h continuous infusion biweekly

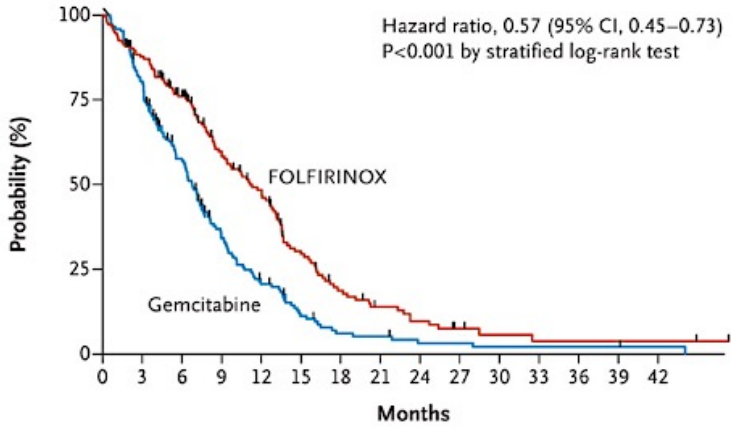
Gemcitabine n = 171

1,000 mg/m² IV weekly x 7, 1 week rest, then weekly x 3 q4w

6 months of chemotherapy recommended and CT scans performed every 2 months for both arms

Conroy T et al. *Proc ASCO* 2010;Abstract 4010.

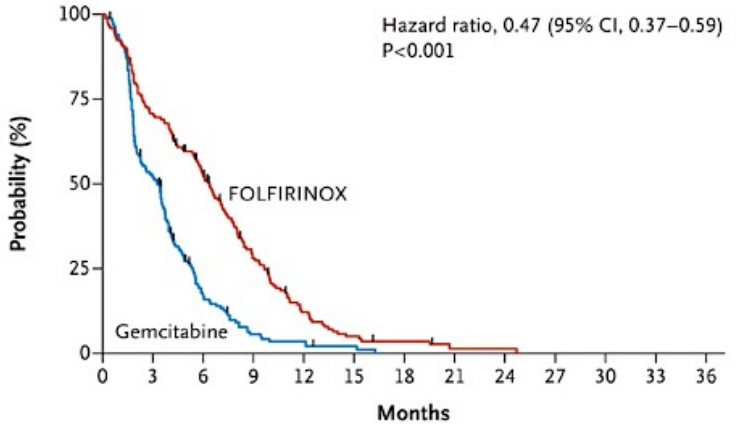
Overall Survival



No. at Risk

Gemcitabine	171	134	89	48	28	14	7	6	3	3	2	2	2	2	1
FOLFIRINOX	171	146	116	81	62	34	20	13	9	5	3	2	2	2	2

Progression-free Survival



No. at Risk

Gemcitabine	171	88	26	8	5	2	0	0	0	0	0	0	0
FOLFIRINOX	171	121	85	42	17	7	4	1	1	0	0	0	0

- ECOG 0 or 1
- Age 75 or less
- Adequate organ function
- No prior chemotherapy

Young, fit patients with excellent performance status

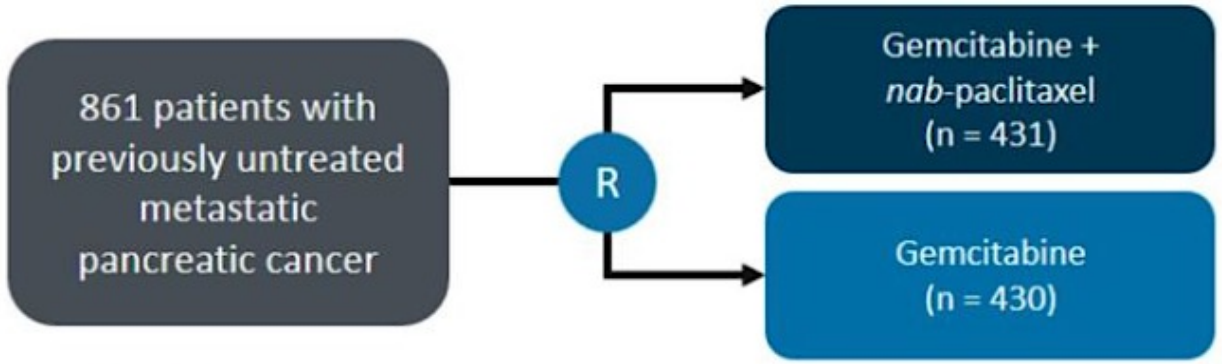
N Engl J Med. 2011;364(19):1817-1825

Real World Use Is with *Modified* FOLFIRINOX

oxaliplatin	85 mg /m²	IV over 2 hours	Day 1
THEN,			
leucovorin	400 mg /m²	IV over 2 hours	Day 1
30 minutes after starting leucovorin, give:			
irinotecan	150 mg /m²	IV over 90 minutes, concurrently with leucovorin	Day 1
THEN,			
fluorouracil	2400 mg /m²	IV continuous infusion over 46 hours (single dose)	Start on Day 1

No available randomized phase 3 data to show non-inferiority to the original FOLFIRINOX regimen

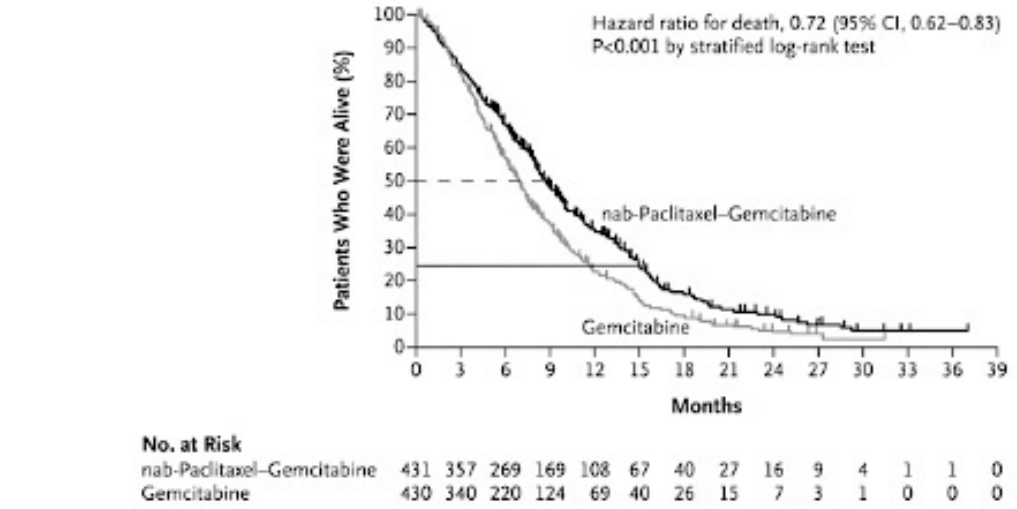
MPACT Trial
nab-Paclitaxel plus Gemcitabine vs Gemcitabine in mPDAC



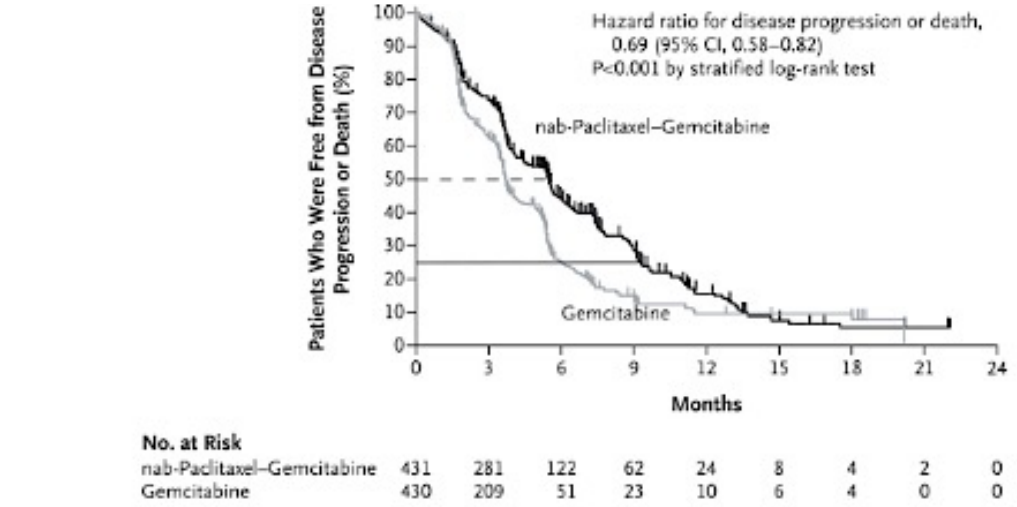
- KPS 70 or more
- No age limit; 41% ≥65 years
- Adequate organ function
- Prior Chemo-XRT allowed if > 6 months

Older patients, reduced performance status

Overall Survival

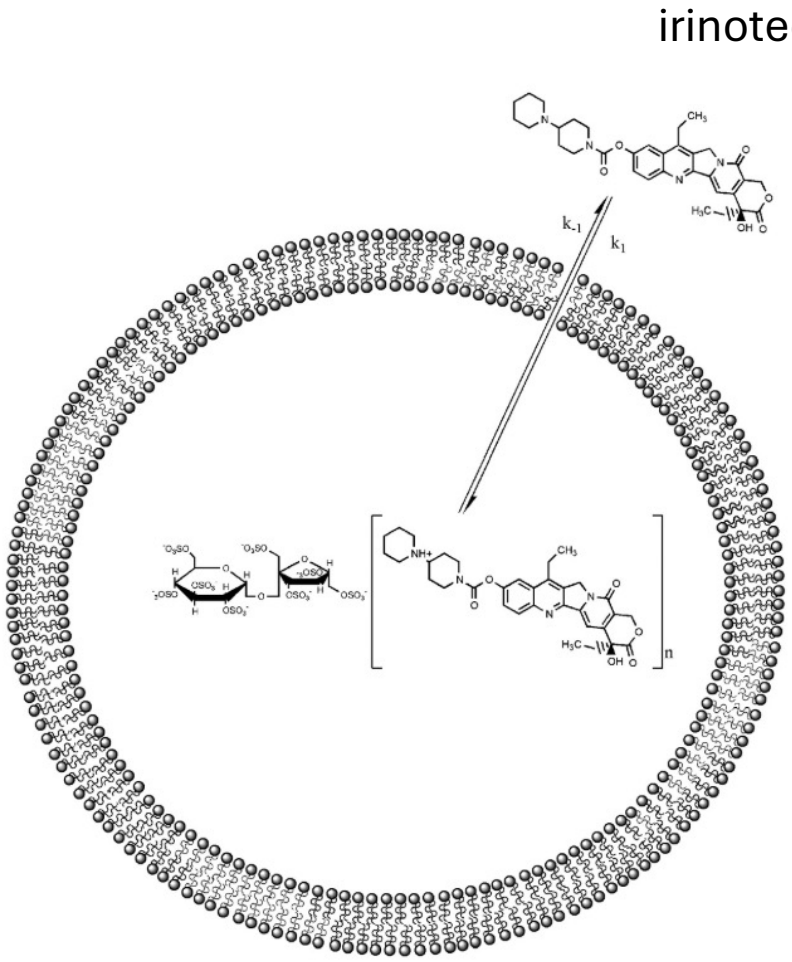


Progression-free Survival, According to Independent Review



N Engl J Med. 2013 Oct 31;369(18):1691-703.

Nanoliposomal Irinotecan (Nal-IRI) ≠ Irinotecan



- Enhanced stability
- 95% encapsulated in circulation
- Longer half-life (~ 2 days)
- Able to penetrate the leaky tumor vasculature

Nal-IRI's enhanced stability, penetration, and retention could enhance intratumoral accumulation and subsequent cytotoxicity

Cancer Res. 2006 Mar 15;66(6):3271-7.

NAPOLI-3 Trial
NALIRIFOX vs nab-Paclitaxel plus Gemcitabine in mPDAC

Global (18 countries)

Multicenter
- 187 community/academic sites

Large study
- N=770

Randomized, open-label

- **ECOG 0 or 1**
- **Adequate organ function**
- **Adjuvant Chemotherapy allowed if > 12 months**
- **Patients were aged 20-85 years**
  - **50% of patients were aged 65 or older**
  - **6.9% of patients were aged 75 or older**

NALIRIFOX
(N=383)

liposomal irinotecan (50 mg/m^2 IV),
oxaliplatin (60 mg/m^2 IV),
leucovorin (400 mg/m^2 IV),
fluorouracil (2400 mg/m^2 IV)

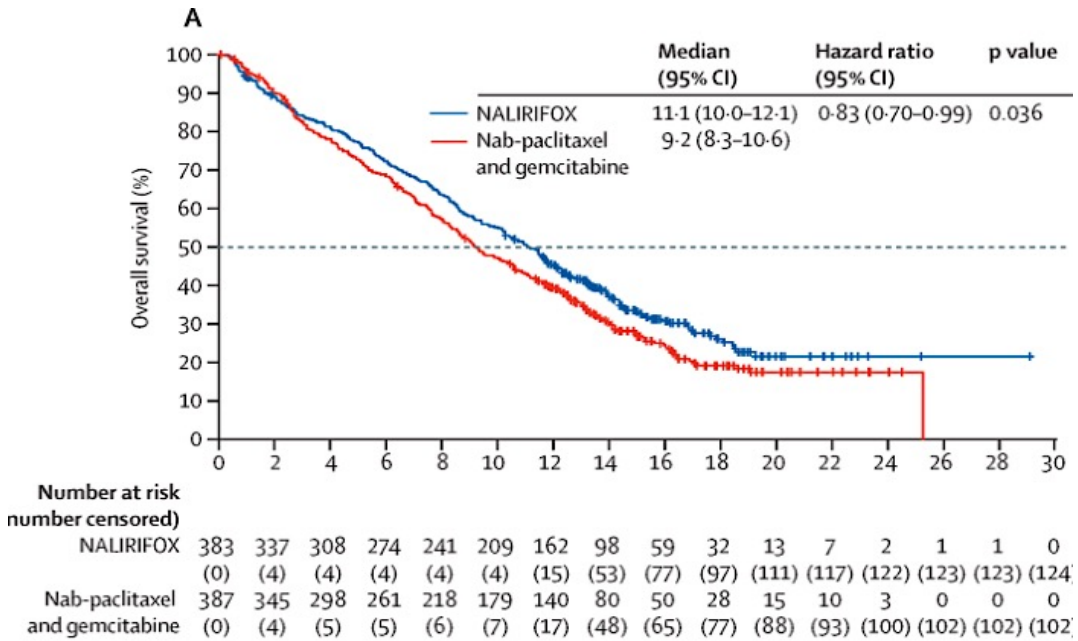
Administered every 2 weeks

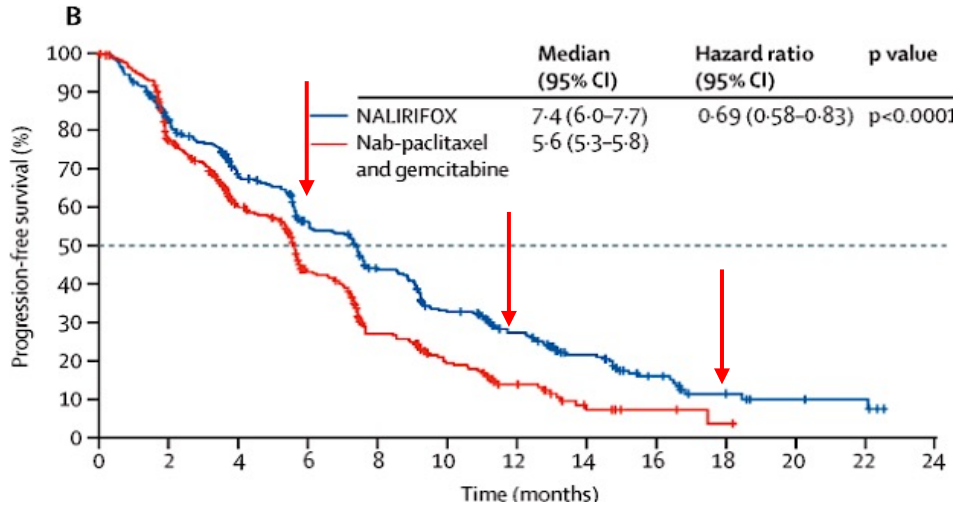
Gem+NabP
(N=387)

Nab-paclitaxel (125 mg/m^2 IV),
gemcitabine (1000 mg/m^2 IV)

Administered on days 1, 8, and 15 of
a 28-day cycle

NAPOLI-3 Trial
NALIRIFOX vs nab-Paclitaxel plus Gemcitabine in mPDAC





	NALIRIFOX (n=383)	Nab-paclitaxel and gemcitabine (n=387)
Overall survival		
Median overall survival, months (95% CI)	11·1 (10·0–12·1)*	9·2 (8·3–10·6)*
Survival rate, % (95% CI)		
6 months	72·4 (67·6–76·6)	68·4 (63·5–72·8)
12 months	45·6 (40·5–50·5)	39·5 (34·6–44·4)
18 months	26·2 (20·9–31·7)	19·3 (14·8–24·2)
Progression-free survival		
Median progression-free survival, months (95% CI)	7·4 (6·0–7·7)*	5·6 (5·3–5·8)*
Progression-free survival rate, % (95% CI)		
6 months	56·4 (50·7–61·6)	43·2 (37·6–48·6)
12 months	27·4 (22·3–32·7)	13·9 (9·7–18·9)
18 months	11·4 (7·1–16·9)	3·6 (0·5–12·3)

Lancet 2023; 402: 1272–81

European Journal of Cancer 181 (2023) 135–144

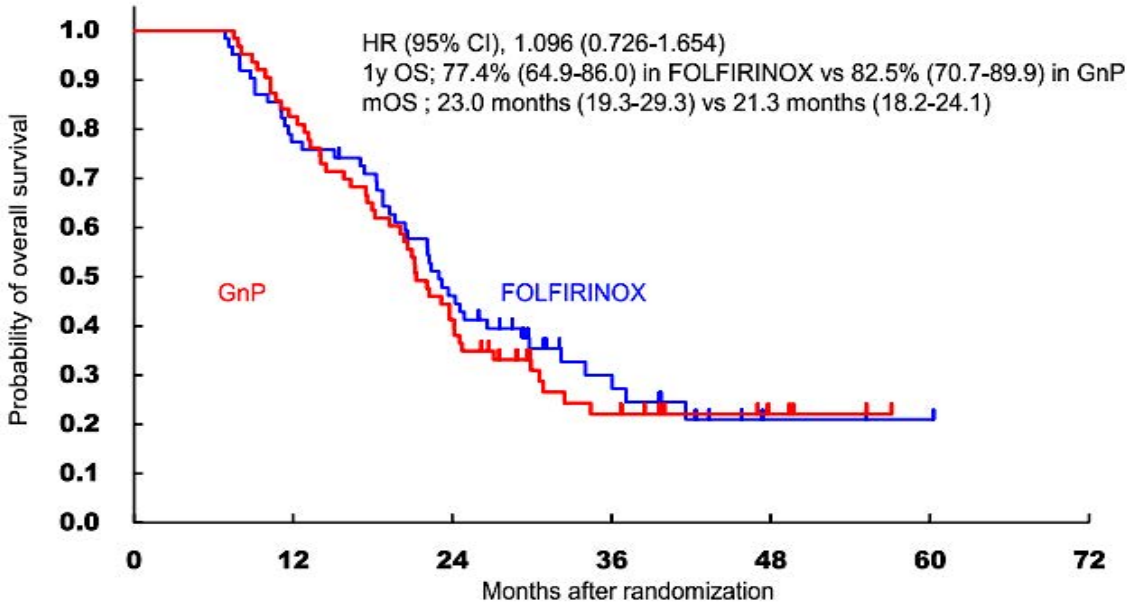
Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

A randomised phase II study of modified FOLFIRINOX versus gemcitabine plus nab-paclitaxel for locally advanced pancreatic cancer (JCOG1407)☆



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

PANCREATIC CANCER

16160 **Nab-paclitaxel plus gemcitabine versus modified FOLFIRINOX or S-IROX in metastatic or recurrent pancreatic cancer (JCOG1611, GENERATE): A multicentred, randomized, open-label, three-arm, phase II/III trial**

A. Ohba[1], M. Ozaka[2], G. Ogawa[3], T. Okusaka[1], S. Kobayashi[4], T. Yamashita[5], M. Ikeda[6], I. Yasuda[7], K. Sugimori[8], N. Sasahira[2], K. Ikezawa[9], I. Miki[10], N. Okano[11], N. Mizuno[12], M. Furukawa[13], H. Shirakawa[14], Y. Sano[3], H. Katayama[3], J. Furuse[4], M. Ueno[4]

Overall Survival:

- nab-paclitaxel plus gemcitabine — 17.1 months
- mFOLFIRINOX — 14.0 months
- S-IROX — 13.6 months

Summary of available prospective randomized data in unresectable PDAC:

FOLFIRINOX > gemcitabine (Accord 11)

nab-paclitaxel plus gemcitabine (GA) > gemcitabine (MPACT)

mFOLFIRINOX ≈ nab-paclitaxel plus gemcitabine (GA) (JCOG 1407 / 1611)

NALIRIFOX > nab-paclitaxel plus gemcitabine (GA) (Napoli-3)

If mFFX = GA and NalFx > GA, then NalFx 👉 mFFx ?????

Roundtable Discussion

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Mass General Brigham
Mass General Cancer Center

Management of the Patient with Metastatic Pancreatic Cancer

Caroline Kuhlman, MSN, APRN-BC
Tucker Gosnell Center for Gastrointestinal Cancers
Massachusetts General Hospital Cancer Center

04/2025

Case Presentation

- 81 yo woman, presented in 10/2024 with new diagnosis of diabetes, diarrhea, attributed to metformin and unintentional weight loss of approx 30 LBs.
- Developed mid epigastric abdominal pain and underwent CTAP which demonstrated pancreatic mass in head of pancreas and multiple liver lesions. CA19-9 3600, CEA 50, ALK phos 960 Tbili 2.3
- EUS demonstrated 3.5cmx 2.9 cm ill defined pancreatic head mass, involving portal vein and dilatation of CBD. Biliary stent placement and bx of lesion demonstrates adenocarcinoma
- DPD normal, UGT1A intermediate metabolizer
- 11/2024 FOLFIRINOX @ DR with Oxali 85, Irinotecan 150mg/m2, 5-FU 1200mg/m2/day x 46 hours. Adjustment to oxalis 65mg irinotecan 120mg/m2 initial response with ca199 1606 CEA 35
- February scans with POD started gemcitabine *nab* paclitaxel
- March elevated LFT alphas 1200, Tbili 2.9 ERCP- diffuse liver disease without stentable obstruction. Elevated alkphos likely from intrahepatic mets. Underwent intrahepatic drain placement. Subsequent admission for confusion, fever- c/f biliary infection.

Case Presentation (continued)

- PMH significant for anxiety, depression, diabetes, osteoarthritis (hip), GERD
- Treatment course complicated by fatigue, diarrhea, pancreatic insufficiency, weight loss, anorexia
- Co-managed with medical oncology, social work, palliative care and interventional radiology GI.
- Retired music teacher. Married, husband has Parkinson's disease, chronically ill and intermittently hospitalized after falls at home. Three children and several grandchildren who all live close by

Options:

FOLFIRINOX: 5-Fluorouracil, Leucovorin, Irinotecan, Oxaliplatin

NALIRIFOX: Substitute nal-IRI- liposomal formulation of Irinotecan, meant to reduce systemic toxicity compared to conventional Irinotecan

Nal-IRI: NAPOLI-1 trial focused on pts who had not received prior irinotecan, some studies suggest nal-IRI might still be considered in patient with previous exposure to irinotecan.

Where to start?

FOLFIRINOX / NALIRIFOX vs. Gemcitabine +nab-paclitaxel

- What's the data : NAPOLI 3 trial retrospective review, meta analysis of 7 trials with data on 2581 pts compared NALIRIFOX to gem/*nab* paclitaxel as first line tx of met panc
- RESULTS 383 pt NALIRIFOX, 433 FOLFIRINOX, 1756 GEM/*nab* paclitaxel
- Median PFS longer in pts tx with NALIRIFOX , no difference with FOLFIRINOX

Nichetti F et al. *JAMA Netw Open* 2024;7(1):e2350756.

NALIRIFOX/ FOLFIRINOX Side Effects

Common

- Lowered blood counts, nausea, vomiting, diarrhea neuropathy (acute, cold-induced and chronic numbness) Fatigue or tiredness; Decreased appetite; hair loss

Less common

- Arterial vasospasm, severe diarrhea, allergic rx, changes in LFTs

Rare

- Severe side effects that can lead to death (<1%)

Metastatic disease – 1st line

PRODIGE 4-ACCORD 11 trial

Table 3. Most Common Grade 3 or 4 Adverse Events Occurring in More Than 5% of Patients in the Safety Population.*

Event	FOLFIRINOX (N=171)	Gemcitabine (N=171)	P Value
	no. of patients/total no. (%)		
Hematologic			
Neutropenia	75/164 (45.7)	35/167 (21.0)	<0.001
Febrile neutropenia	9/166 (5.4)	2/169 (1.2)	0.03
Thrombocytopenia	15/165 (9.1)	6/168 (3.6)	0.04
Anemia	13/166 (7.8)	10/168 (6.0)	NS
Nonhematologic			
Fatigue	39/165 (23.6)	30/169 (17.8)	NS
Vomiting	24/166 (14.5)	14/169 (8.3)	NS
Diarrhea	21/165 (12.7)	3/169 (1.8)	<0.001
Sensory neuropathy	15/166 (9.0)	0/169	<0.001
Elevated level of alanine aminotransferase	12/165 (7.3)	35/168 (20.8)	<0.001
Thromboembolism	11/166 (6.6)	7/169 (4.1)	NS

* Events listed are those that occurred in more than 5% of patients in either group. NS denotes not significant.

Conroy et al, NEJM 2011

How do these regimens compare?

Toxicity

	FOLFIRINOX	Gem/*nab* paclitaxel
Neutropenia	46%	38%
Febrile neutropenia	5%	3%
Growth factor usage	43%	26%
Thrombocytopenia	9%	13%
Diarrhea	13%	6%
Fatigue	24%	17%
Neuropathy	9%	17%

Metastatic disease – 1st line
NAPOLI-3

TEAEs of grade 3–4 occurring in ≥5% of patients in either treatment arm

Diarrhoea	75 (20%)	17 (5%)
Nausea	44 (12%)	10 (3%)
Vomiting	26 (7%)	8 (2%)
Decreased appetite	32 (9%)	10 (3%)
Hypokalaemia	56 (15%)	15 (4%)
Fatigue	23 (6%)	20 (5%)
Asthenia	33 (9%)	19 (5%)
Neutropenia	52 (14%)	93 (25%)
Neutrophil count decreased	36 (10%)	51 (14%)
Anaemia	39 (11%)	66 (17%)
Peripheral neuropathy	12 (3%)	22 (6%)
Increased γ-glutamyltransferase	23 (6%)	21 (6%)

HARVARD MEDICAL SCHOOL

Wainberg et al, Lancet 2023

Managing Side Effects:

- Patient education about management of common side effects crucial
- Also important to educate patients about when to call

Notify your team or get medical help right away if you have any signs or symptoms, including:

- Fever of 100.4 degrees or higher
- Low blood pressure or dizziness
- Diarrhea
- Shortness of breath or trouble breathing
- Nausea and vomiting
- Problems with walking, or loss of balance or coordination
- Unusual bleeding
- Weakness or shaking (tremors)

Metastatic Disease: 1st line summary

FOLFIRINOX/NALIRIFOX most effective, use in fit patients.
Gem/*nab* paclitaxel for less fit patients

Utilize dose adjustments- Palliative intent

Side effect management

- **As needed antiemetics and bowel medications**
- **Encourage fluids and small, frequent meals/snacks with emphasis on protein**
- **Nutrition consultation**
- **Pain management**
- **Speak to provider before beginning any new medications, herbs or supplements**

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Initial Management of Pancreatic Adenocarcinoma (PAD)

Module 1: Clinical Presentation and Prognosis of PAD; Recent Advances in Up-Front Treatment for Metastatic PAD

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Module 4: Role of PARP Inhibitor Maintenance Therapy for Newly Diagnosed Metastatic PAD

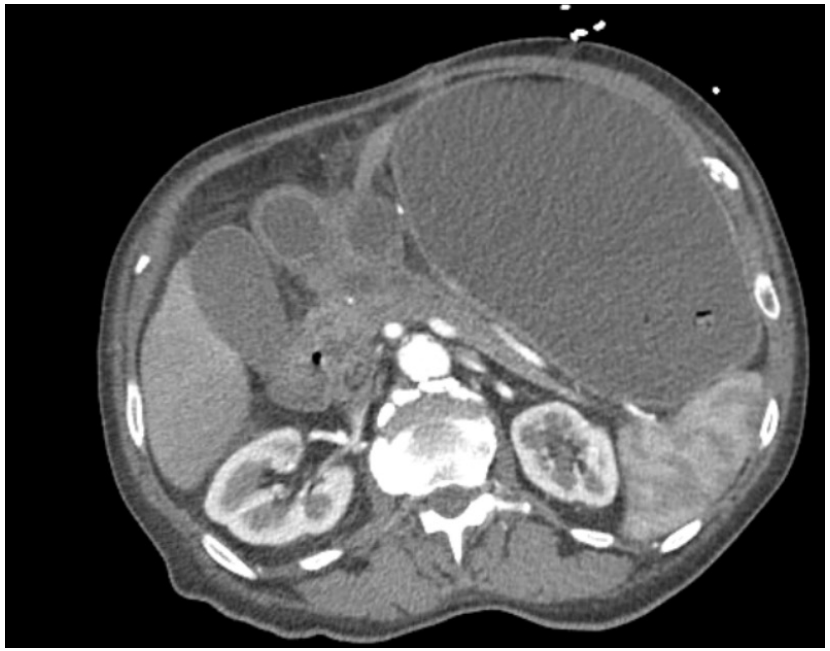
Module 5: Promising Investigational Strategies for PAD

Clinical Scenario

A patient with metastatic PAD who has experienced disease progression on first-line gemcitabine/nab paclitaxel and is about to start treatment with nal-IRI + 5-FU/LV

Selection and Sequencing of Therapy for Relapsed/Refractory (R/R) Metastatic PAD

Farshid Dayyani, MD, PhD

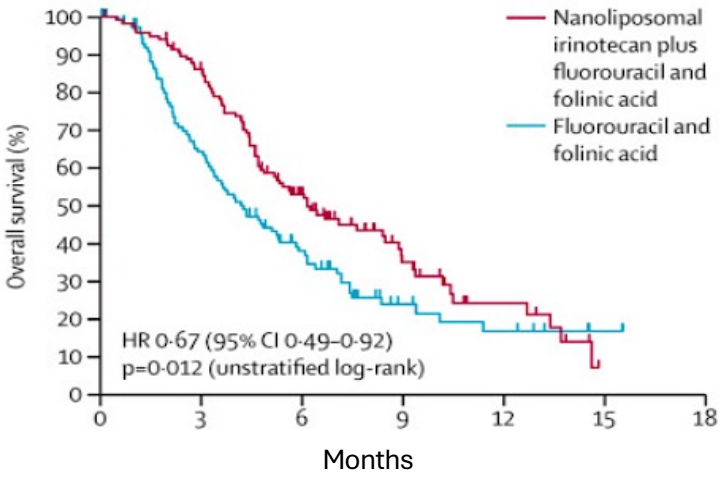


- 74 year old male with history of testicular cancer as a teenager, in complete remission, who was diagnosed with pancreatic body adenocarcinoma when he presented to outside with gastric outlet obstruction from the tumor, status post stent placement and aborted Whipple procedure since he was found to be locally advanced unresectable.
- Started treatment with gemcitabine and nab-paclitaxel based on the LAPACT trial for locally advanced PDAC
- Pretreatment CA 19/9 was elevated at 1200 units per ML, and after five months of treatment it normalized to 18. Imaging showed mild decrease in the primary tumor
- He had more peripheral neuropathy which was bothering him and therefore the schedule was adjusted and albumin bound paclitaxel was dose reduced
- After another three months his CA 19-9 started to slowly rise and repeat imaging unfortunately showed new hypodense lesions in the liver consistent with early metastatic disease
- Options were discussed with him based on available data, performance status, toxicities from prior treatment, and the treatment was initiated with nano liposomal irinotecan, 5-FU and Leucovorin (NALIRI)

Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial

Andrea Wang-Gillam*, Chung-Pin Li, György Bodoky, Andrew Dean, Yan-Shen Shan, Gayle Jameson, Teresa Macarulla, Kyung-Hun Lee, David Cunningham, Jean F Blanc, Richard A Hubner, Chang-Fang Chiu, Gilberto Schwartsmann, Jens T Siveke, Fadi Braiteh, Victor Moyo, Bruce Belanger, Navreet Dhindsa, Eliel Bayever, Daniel D Von Hoff*, Li-Tzong Chen*, for the NAPOLI-1 Study Group†

Lancet 2016; 387: 545–57



Open-label clinical trial of 417 patients randomized across 3 arms[1,15*]

KEY PATIENT ELIGIBILITY CRITERIA (N=417)

- Confirmed mPDAC
- Progression of locally advanced or metastatic disease
- Prior gemcitabine-based therapy†
- Normal bilirubin
- Albumin ≥3.0 g/dL
- KPS ≥70

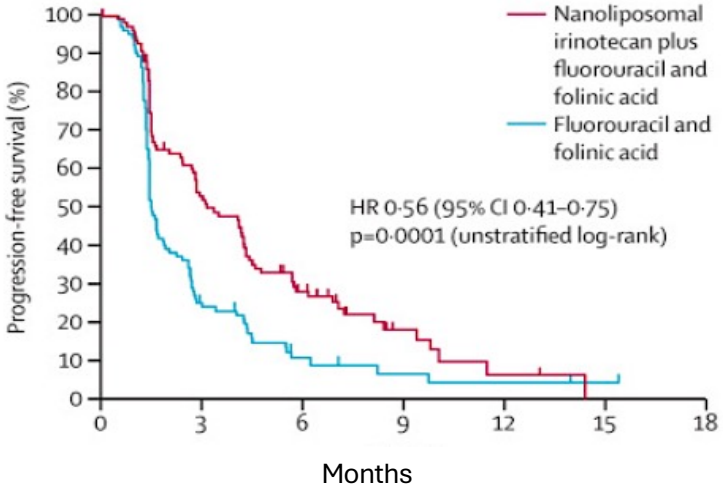
RANDOMIZATION PATIENT STRATIFICATION FACTORS

- KPS 70-80 vs 90-100
- Albumin level ≥4.0 g/dL vs 3.0-3.9 g/dL
- Ethnicity (Caucasian, Asian, other)

Nanoliposomal irinotecan + FU/LV (every 2 weeks)
nanoliposomal irinotecan (70 mg/m² IV), leucovorin (400 mg/m² IV), fluorouracil (2400 mg/m² IV) (N=117)

FU/LV (weekly 4x over 6 weeks)
leucovorin (200 mg/m² IV), fluorouracil (2000 mg/m² IV) (N=149)

Nanoliposomal irinotecan alone (every 3 weeks)
nanoliposomal irinotecan (100 mg/m² IV), (N=151)



	Nanoliposomal irinotecan plus fluorouracil and folinic acid combination therapy (n=117)		Fluorouracil and folinic acid control (n=134)	
	Any grade	Grades 3–4	Any grade	Grades 3–4
Diarrhoea	69 (59%)	15 (13%)	35 (26%)	6 (4%)
Vomiting	61 (52%)	13 (11%)	35 (26%)	4 (3%)
Nausea	60 (51%)	9 (8%)	46 (34%)	4 (3%)
Decreased appetite	52 (44%)	5 (4%)	43 (32%)	3 (2%)
Fatigue	47 (40%)	16 (14%)	37 (28%)	5 (4%)
Neutropenia*	46 (39%)	32 (27%)	7 (5%)	2 (1%)
Anaemia	44 (38%)	11 (9%)	31 (23%)	9 (7%)
Hypokalaemia	14 (12%)	4 (3%)	12 (9%)	3 (2%)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025
Pancreatic Adenocarcinoma

PRINCIPLES OF SYSTEMIC THERAPY

Subsequent Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease

	Preferred Regimens	Other Recommended Regimens
Good PS 0–1	• Entrectinib (if *NTRK* gene fusion-positive) • Larotrectinib (if *NTRK* gene fusion-positive) • Repotrectinib (if *NTRK* gene fusion-positive)[p,21] If no prior immunotherapy: • Pembrolizumab[j] (if MSI-H, dMMR, or TMB-H [≥10 mut/Mb])	• Dabrafenib + trametinib (if *BRAF* V600E mutation-positive)[19,20] • Selpercatinib (if *RET* gene fusion-positive)[30] If no prior immunotherapy: • Dostarlimab-gxly[j] (if MSI-H or dMMR) • Nivolumab + ipilimumab[j] (if TMB-H [≥10 mut/Mb]) (category 2B) If prior gemcitabine-based therapy: • 5-FU + leucovorin + liposomal irinotecan[31] (category 1 for metastatic disease) • Bolus 5-FU + leucovorin • Capecitabine • CapeOx • Continuous infusion 5-FU • FOLFIRI[32-34] • FOLFIRINOX or modified FOLFIRINOX[e,35] • FOLFOX • OFF
Intermediate PS 2	If prior fluoropyrimidine-based therapy: • 5-FU + leucovorin + liposomal irinotecan[31] (if no prior irinotecan) • Gemcitabine + albumin-bound paclitaxel If prior gemcitabine-based therapy: • 5-FU + leucovorin + liposomal irinotecan[31] (category 1 for metastatic disease)	Preferred Regimens

If Prior Gemcitabine → Fluoropyrimidine-Based Therapy

BRIEF ARTICLE

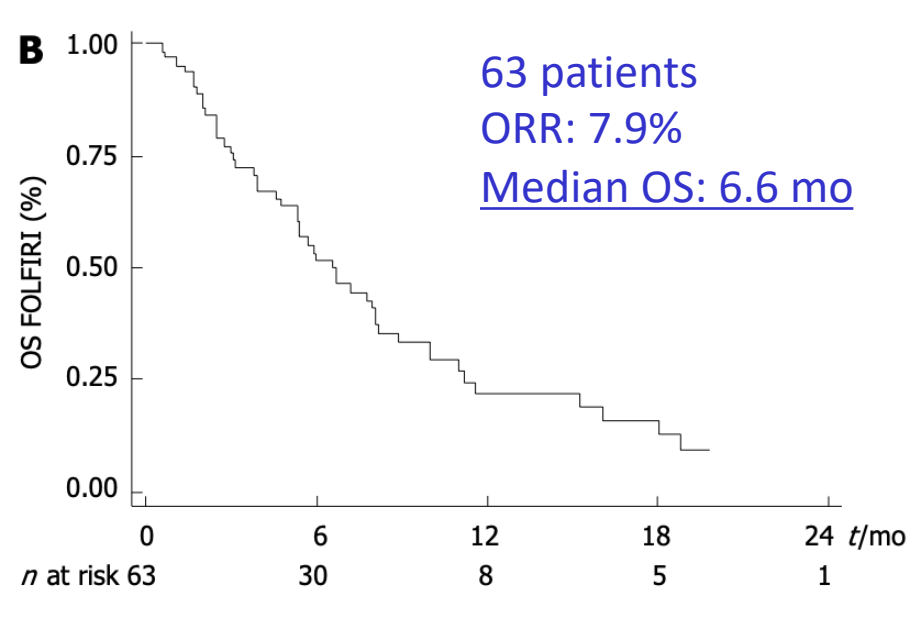
FOLFIRI regimen in metastatic pancreatic adenocarcinoma resistant to gemcitabine and platinum-salts

Cindy Neuzillet, Olivia Hentic, Benoît Rousseau, Vinciane Rebours, Léïla Bengrine-Lefèvre, Franck Bonnetain, Philippe Lévy, Eric Raymond, Philippe Ruszniewski, Christophe Louvet, Pascal Hammel

ORIGINAL ARTICLE

FOLFIRI as second-line chemotherapy for advanced pancreatic cancer: a GISCAD multicenter phase II study

Alberto Zaniboni · Enrico Aitini · Sandro Barni · Daris Ferrari · Stefano Cascinu · Vincenzo Catalano · Giuseppe Valmadre · Domenica Ferrara · Enzo Veltri · Claudio Codignola · Roberto Labianca



63 patients
ORR: 7.9%
Median OS: 6.6 mo

Table 1 Overall response rate and survival data

	N = 50	%	95 % Confidence interval
Partial response	4	8	0.5–15.5
Stable disease	14	28	
Disease control rate (PR+SD)	18	36	22.7–49.3
Progressive disease	26	52	
Not evaluable*	6	12	
PFS (months) median, 3.27; range, 1–11			
OS (months) median, 5.0; range, 1–17			

Neuzillet C et al. *World J Gastroenterol* 2012;18(33):4533-4541. Zaniboni A et al. *Cancer Chemother Pharmacol* 2012;69(6):1641-1645.

RTP RESEARCH TO PRACTICE

FOLFIRINOX as Second-Line Therapy?

- May be too toxic for many patients following 1L treatment with gemcitabine/nab-paclitaxel
- Efficacy/safety data limited mostly to small retrospective series – subject to patient selection bias
- Randomized phase 3 trial in Korea (MPACA-3) comparing mFOLFIRINOX vs S-1 in this second-line setting (n = 80)

	mFOLFIRINOX	S-1	Significant?
ORR	15%	2%	*P* = .04
DCR	67%	37%	*P* = .007
PFS, median (and at 6 months)	5.2 months (40.7%)	2.2 months (10.6%)	Multivar HR 0.4, *P* = .002
OS, median (and at 6 and 12 months)	9.2 months (75% and 24%)	4.9 months (46% and 20%)	Multivar HR 0.4, *P* = .002

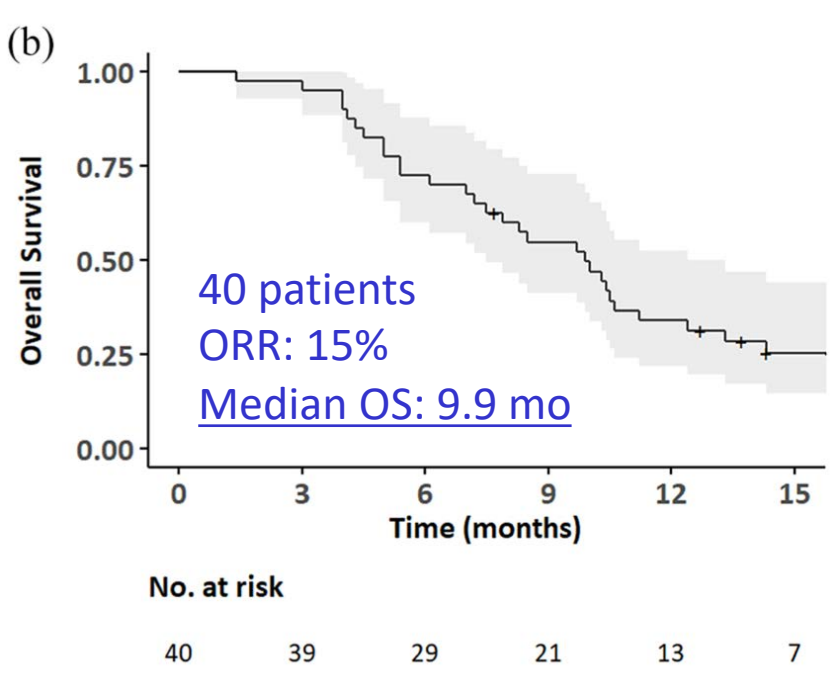
Go S, et al, Eur J Cancer 2021;157:21-30.

Courtesy of Zev Wainberg, MD, MSc

If Prior Fluoropyrimidine → Gemcitabine-Based Therapy

Gemcitabine plus Nab-paclitaxel as a second-line treatment following FOLFIRINOX failure in advanced pancreatic cancer: a multicenter, single-arm, open-label, phase 2 trial

Gunn Huh, Hee Seung Lee, Jin Ho Choi, Sang Hyub Lee, Woo Hyun Paik, Ji Kon Ryu, Yong-Tae Kim, Seungmin Bang and Eaum Seok Lee



Huh G et al. *Ther Adv Med Oncol* 2021;13:17588359211056179.

Efficacy of gemcitabine plus nab-paclitaxel in second-line treatment of metastatic pancreatic cancer

Yasin Sezgin[1], Oğur Karhan[2], Mehmet Naci Aldemir[1], Muslih Ürün[1], Berrak Mermit Erçek[1], Zuhat Urakcı[3], Hayati Arvas[3], Sezai Tunç[4], Mehmet Erdem[5], Halis Yerlikaya[6], Serdar İleri[7], İbrahim Aydın[8], Abdurrahman Bicer[8], Ahmet Ufuk Kömüroğlu[9], Nargiz Majidova[10], Savaş Gökçek[11], Hacer Demir[12], Sedat Yıldız[12], Sinem Akbaş[13], Esra Özen[14], Burcu Ulaş Kahya[15], Mürsel sali[16], Hicran Anık[17], Talat Aykut[18], Murat Araz[18], Ali Alkan[19], Melike Özçelik[20], Abudllah Sakin[21], Musa Barış Aykan[22], Mirmehdi Mehtıyev[23], Bilgin Demir[24], Mehmet Nuri Başer[24], Müge Sönmez[25], İlkay Gültürk[1], Nilüver Avcı[1], Semiha Urvay[1], Mustafa Özgür Arıcı[1], Mehmet Emin Kalender[1], Mustafa Yıldırım[1], Ali Alper Solmaz[26], Mustafa Gürbüz[26] & Yakup Ergün[27]

*retrospective review published April 5, 2025

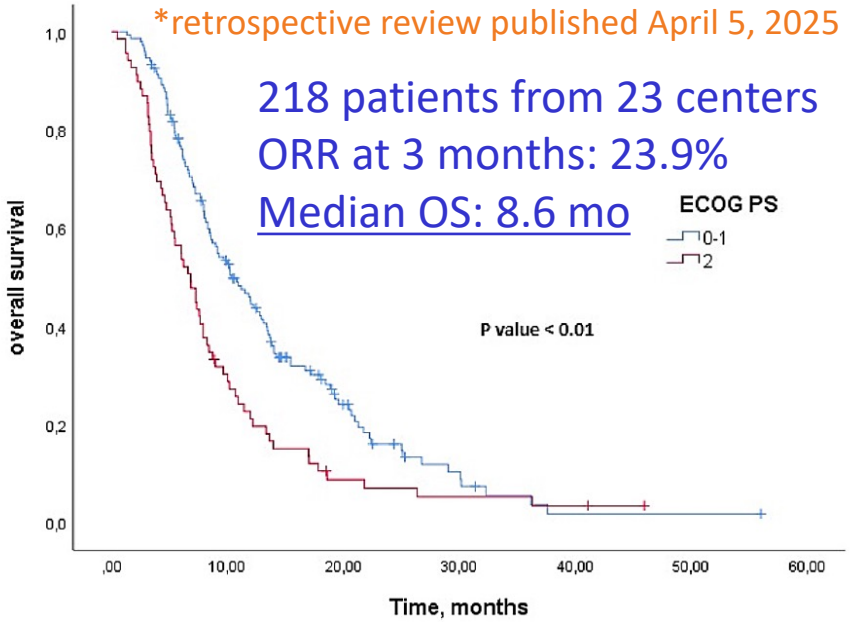


Fig. 6. Overall survival in patients with ECOG PS 0–1 and 2.

Sezgin Y et al. *Sci Rep* 2025;15:11675.

RTP RESEARCH TO PRACTICE

What Are the Data for Second-Line Treatment With Gemcitabine and Nab-Paclitaxel Post-FOLFIRINOX?

Type of Study	ORR, %	PFS, mos
Prospective cohort (N = 57)[a]	17.5	5.1
Retrospective (N = 28)[b]	18	3
Retrospective (N = 59)[c]	10	3
Prospective (N = 30)[d]	13.3	3.8
Retrospective (N = 100)[e]	Not reported	5.9

a. Portal A, et al. Br J Cancer. 2015;113:989-995; b. Zhang Y, et al. Exp Hematol Oncol 2015;4:29. c. Palacio S, et al. J Gastrointest Oncol. 2019;10:1133-1139. d. Mita N, et al. J Clin Med 2019; 8:761.e.Tsang et al. Am J Clin Oncol. 2019;42:196-201..

Courtesy of Zev Wainberg, MD, MSc

Factors to consider when choosing 2nd line treatment

Roundtable Discussion

RTP
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TO PRACTICE

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Module 5: Promising Investigational Strategies for PAD

Clinical Scenario

A patient with metastatic PAD who has experienced disease progression on first-line gemcitabine/nab paclitaxel and second-line nal-IRI + 5-FU/LV

Mass General Brigham

Importance of Palliative Care in Advanced PDAC

Caroline Kuhlman, MSN, APRN-BC

Case Presentation

69 yo man presented with abdominal pain, weight loss. CT demonstrates pancreatic head mass, left adrenal mass, multiple liver lesions and bilateral pulmonary nodules. Biopsy c/w invasive ductal adenocarcinoma. Ca199 1024

He is married with 2 adult children. Retired as a high school English teacher. Lives in New Hampshire. Enjoys working on the land, being outdoors, gardening, tending to chickens and dogs. Loves to cook and entertain.

9/2024 started FOLFIRINOX. Abdominal pain, makes moving around, eating and sleeping difficult. Expressed feelings of depression, lost interest in activities, avoids seeing family and friends. Moody and angry at home. Tearful during initial visits.

Supportive interventions: a team approach

Referral to social work

Referral nutrition

Referral to Palliative care team- pain management, goal setting symptom management

Interventional Radiology for para/thoracentesis

GI- stent changes

Early involvement with palliative care

2010 NEJM paper from MGH supportive oncology group.

Randomized study- randomized patients with newly diagnosed met lung cancer to standard management vs. early intervention with palliative care.

QOL and mood assessed at baseline and at 12 weeks

151 patients randomized.

RESULTS of early palliative care

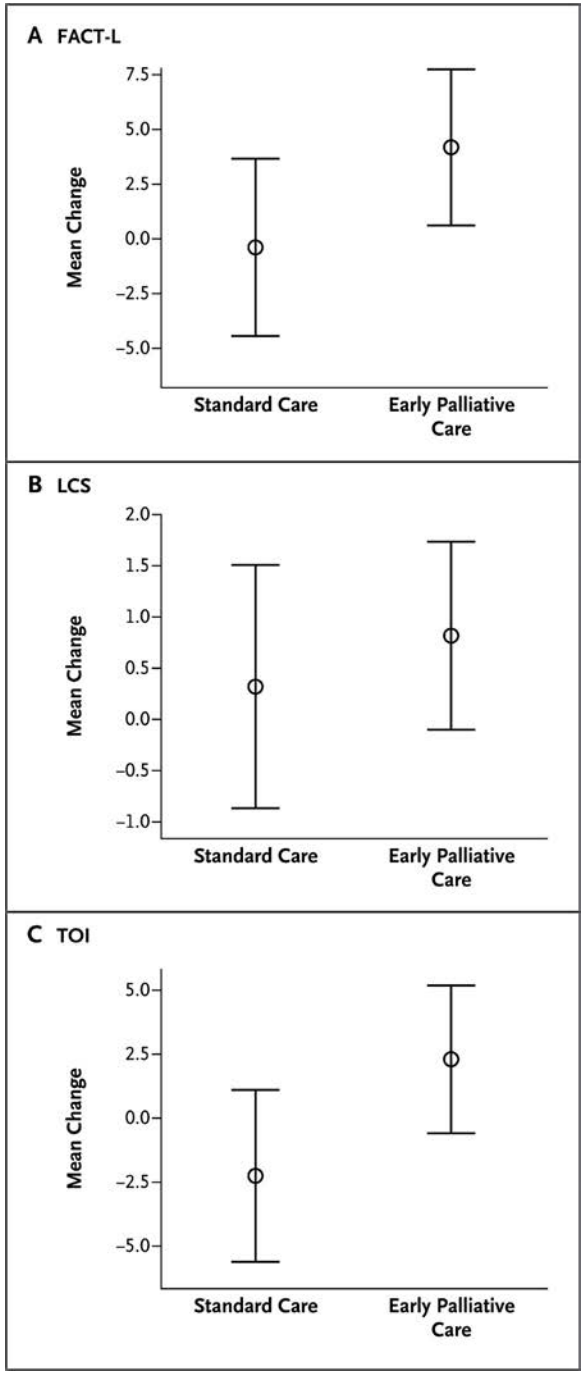
Palliative care group reported better QOL and less depressive symptoms

Fewer patients in the pall care group received aggressive end of life care, despite this the median survival in this group was longer (11.6 months vs. 8.9 months p=0.02)

Subsequent studies have validated this outcome

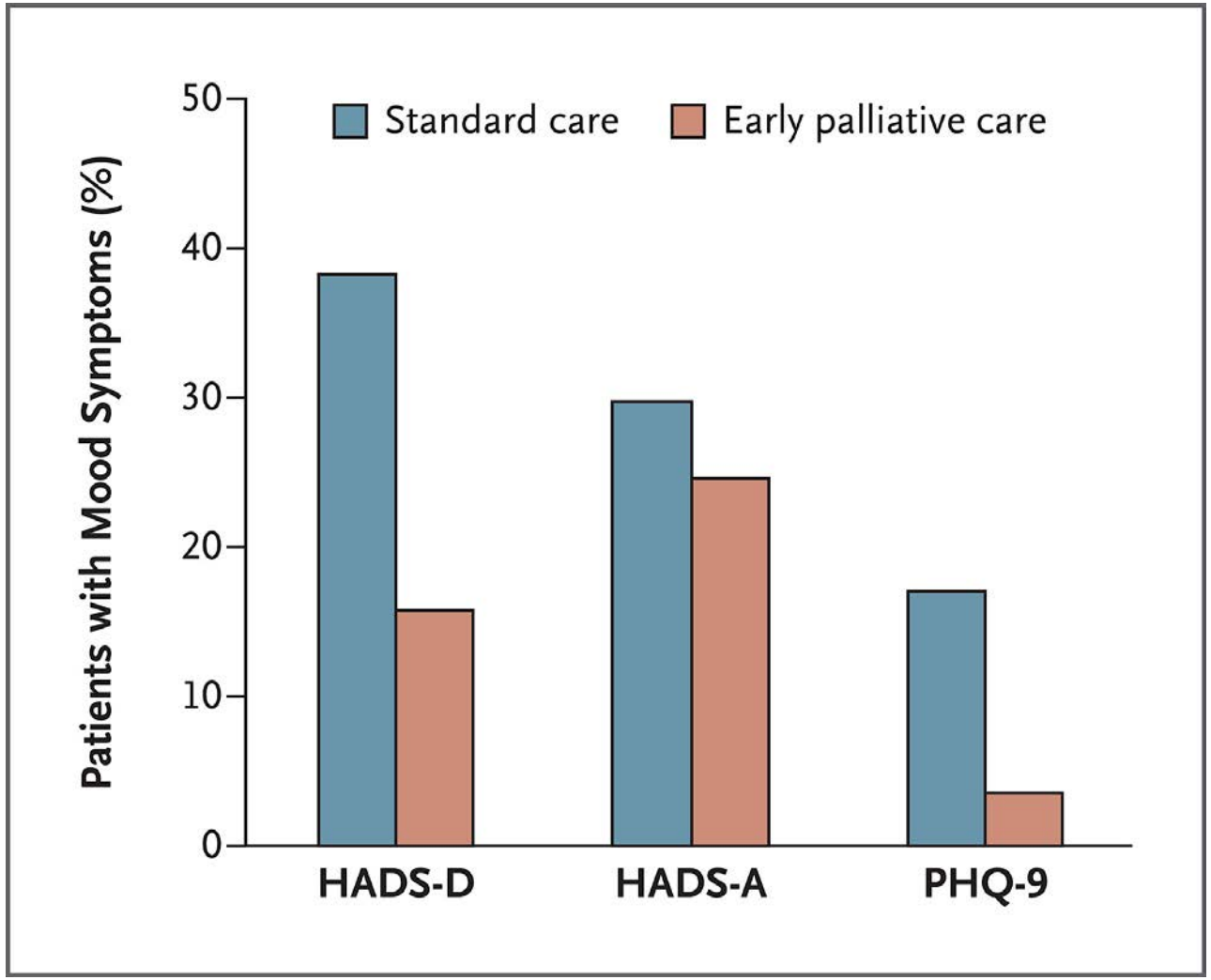
JS Temel, et al NEJM 2010; 363: 733-742

QOL Scores



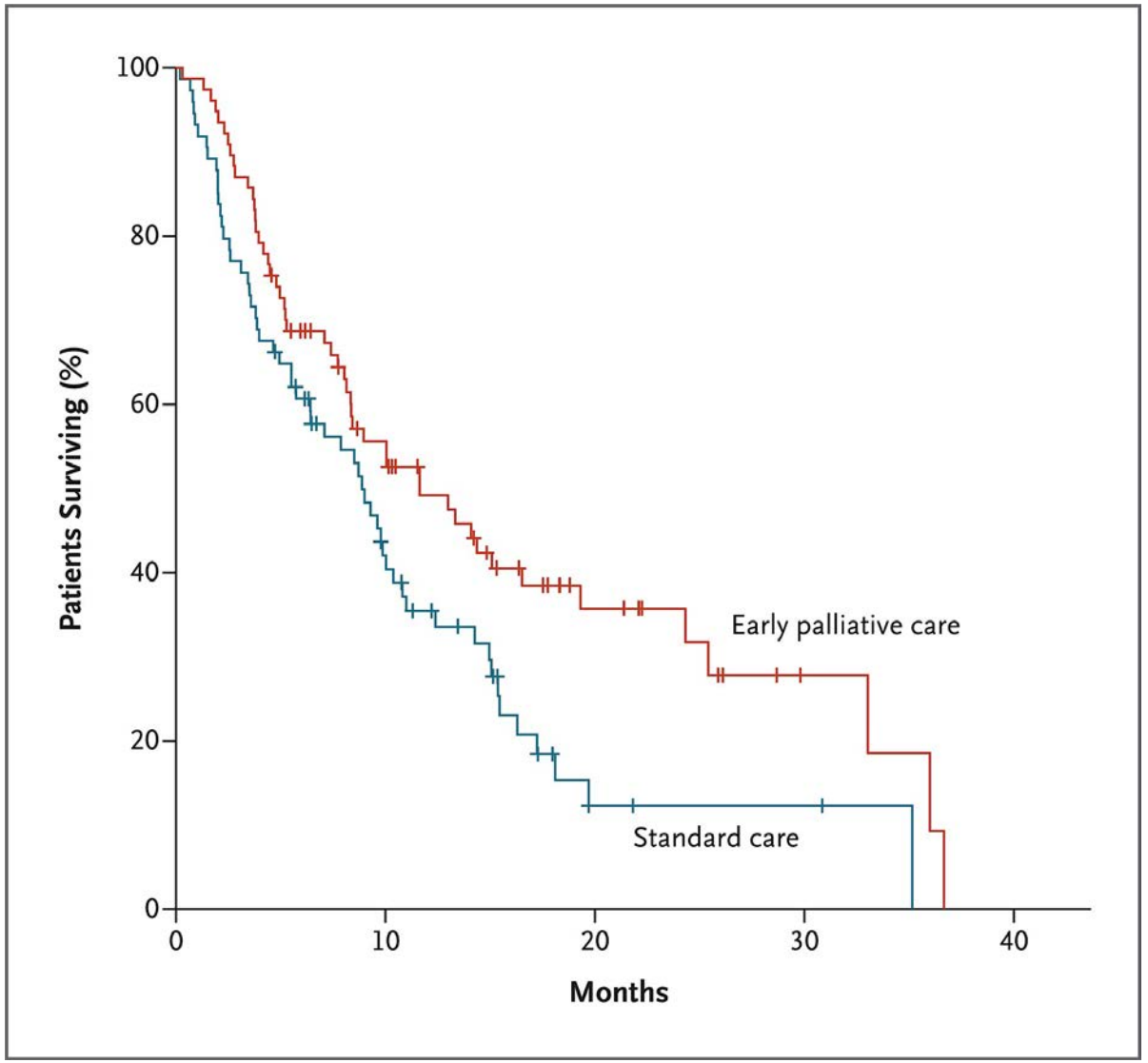
JS Temel, et al NEJM 2010; 363: 733-742

Depression Scores



JS Temel, et al NEJM 2010; 363: 733-742

Survival Data



JS Temel, et al NEJM 2010; 363: 733-742

Serious Illness Conversation

Assess what are their goals

Sharing our hopes and worries

"Tell me what is important to you"

"If you know your time is limited - how do you want to spend this time?"

Supportive care: the hardest work we do

Aggressive pain management with LA opioids, breakthrough, thoughtful about delivery mode

Coordination with GI/IR for management of biliary stents and drains, paracentesis, thoracentesis

Delayed gastric emptying: metoclopramide, erythromycin,

Weight loss- small, frequent, calorie dense meals and snacks. Supplements - ensure, boost

Manage pancreatic insufficiency with pancreatic enzymes to address chronic diarrhea, gas and bloating with meals

Case Presentation (continued)

Initial patient had excellent response to FOLFIRINOX, with decreased tumor burden and dropping CA19-9
Initiated social work visits at time of treatment
Referral to palliative care. Together we started LA opioid with breakthrough. This allowed the patient to be more active, improved appetite.
Added pancreatic enzymes- now able to eat and maintain weight. Resolved diarrhea
Started citalopram for depression. This was well tolerated and patient and his wife report benefit with more engagement. Less tearful moments.

Conclusions

Supportive care, with chemotherapy or without, is the hardest work we do.

In met panc, supportive care is as important as any treatment we give patients.

Early involvement of supportive care in patients with met panc can not only alleviate suffering and help patients live better, but it can also help people live longer.

Roundtable Discussion

RTP
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Clinical Scenario

A patient with newly diagnosed metastatic PAD who has a germline BRCA2 mutation

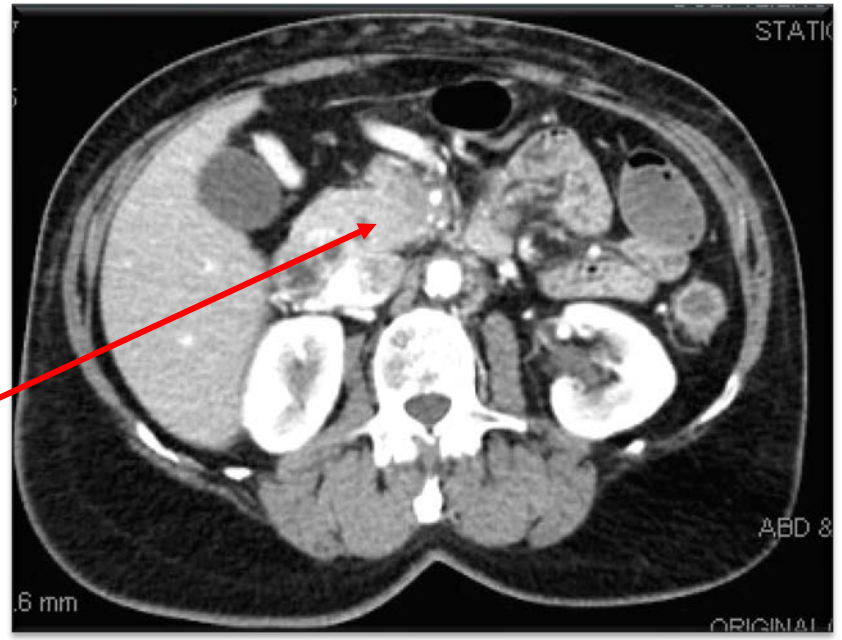
Pancreatic Cancer

Philip Agop Philip, MD, PhD, FRCP

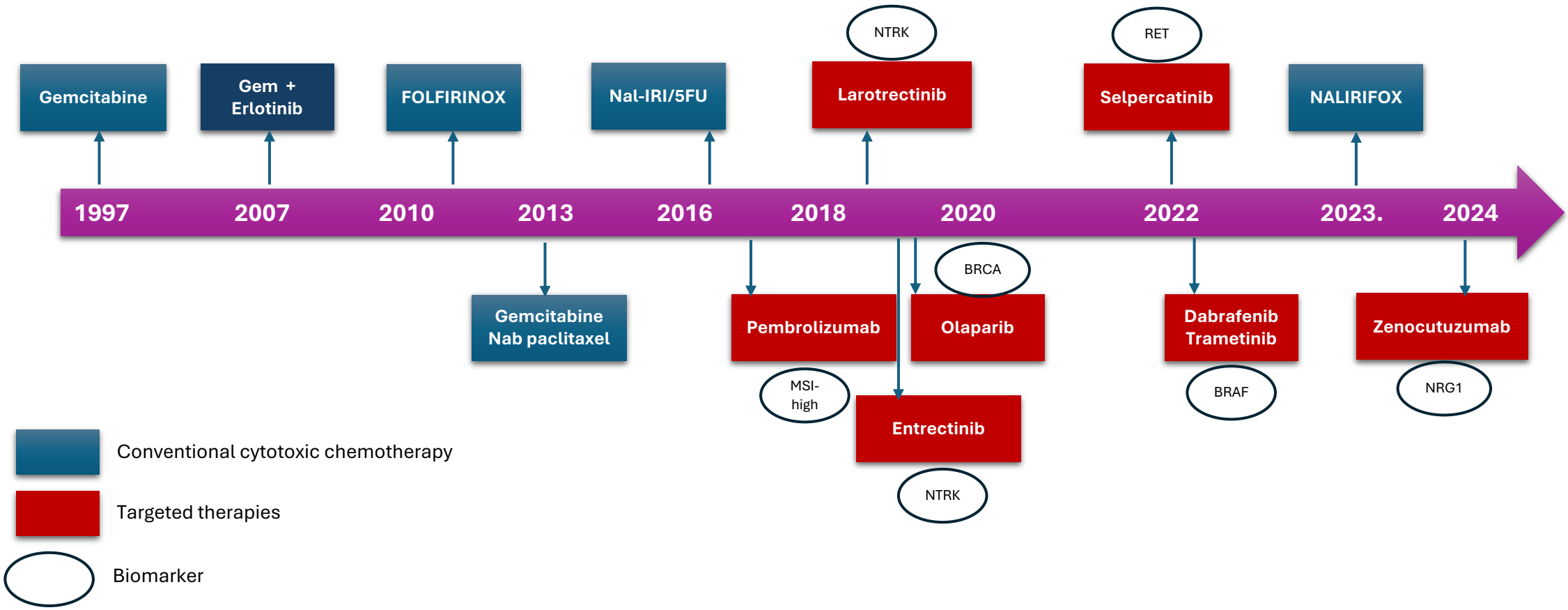
Henry Ford Health
Wayne State University School of Medicine
Detroit, Michigan
USA

Case

- 66-year-old female, Italian ancestry, residency program coordinator
  - Pre-diabetic, anxiety, performance status 1
- 1999 and 2018 had DCIS left breast
  - *BRCA2* mutation (2 sisters breast ca, father prostate ca)
  - Underwent bilateral mastectomy and oophorectomy
- 2025
  - Abdominal pain and weight loss
  - CT = pancreatic mass and liver metastasis
  - Biopsy showed adenocarcinoma
- Goals of management: pain control & prolonging life

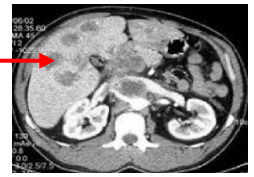


Evolution to include targeted drugs in pancreatic ca

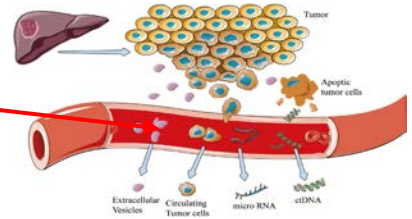


Molecular profiling of the tumor and germline testing of the patient must be part of an initial workup in pancreatic cancer

- Tumor profiling
  - Tumor tissue
    - Whole panel NGS
    - Limited gene study



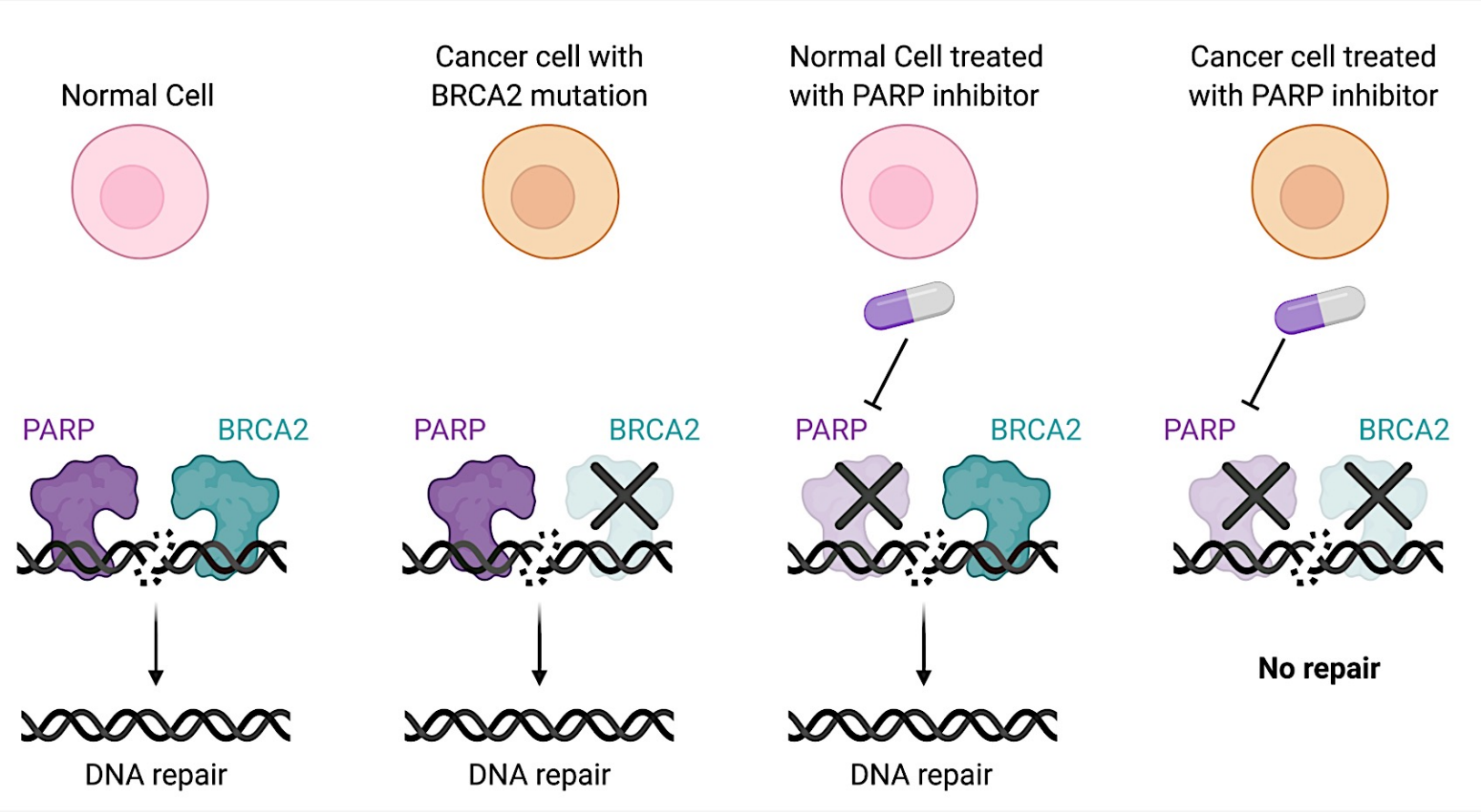
  - Plasma ctDNA



- Germline testing
  - Blood
  - Saliva

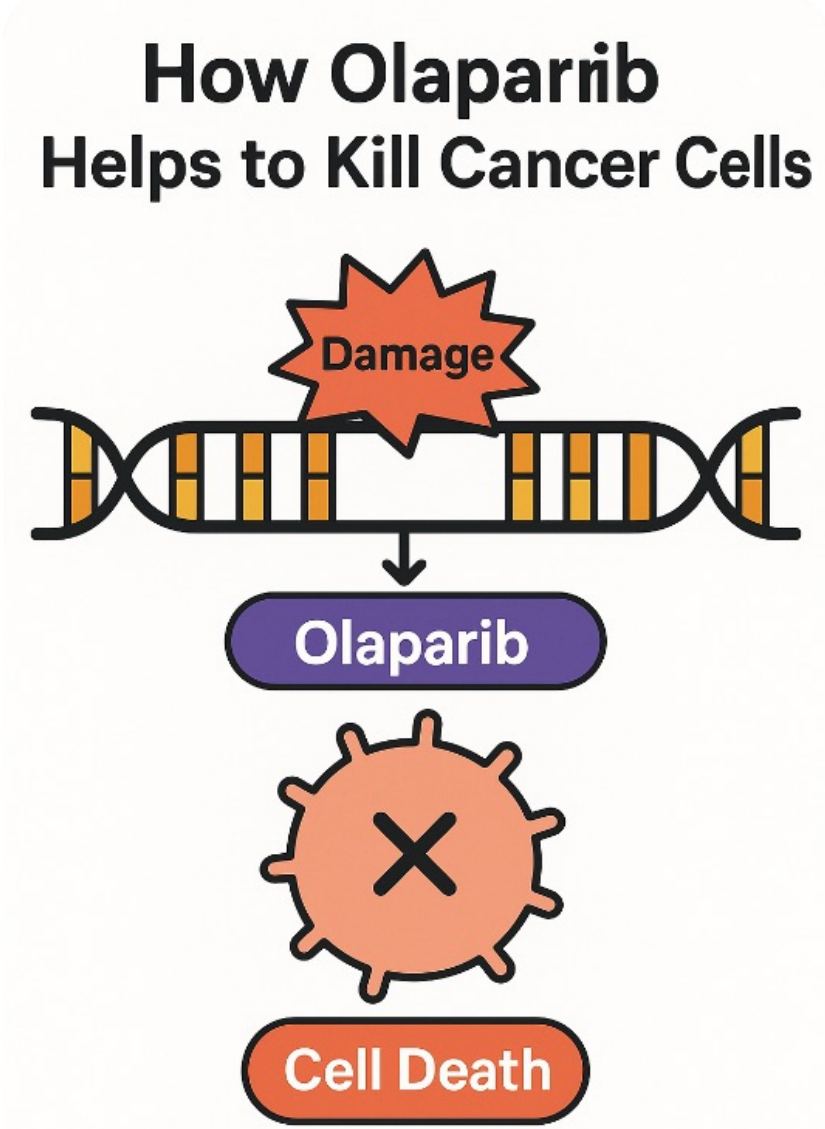
- Benefits of the molecular data
  - Choice of initial and subsequent therapies
  - Eligibility on clinical trials
  - Prognosis
  - Cancer risk in family members

A PARP inhibitor takes away the ability of the cancer cell to repair its damaged DNA leading to its death



https://thisisepigenetics.ca/about-epigenetics/epigenetics-and-highly-mutating-cancer-story-evolution

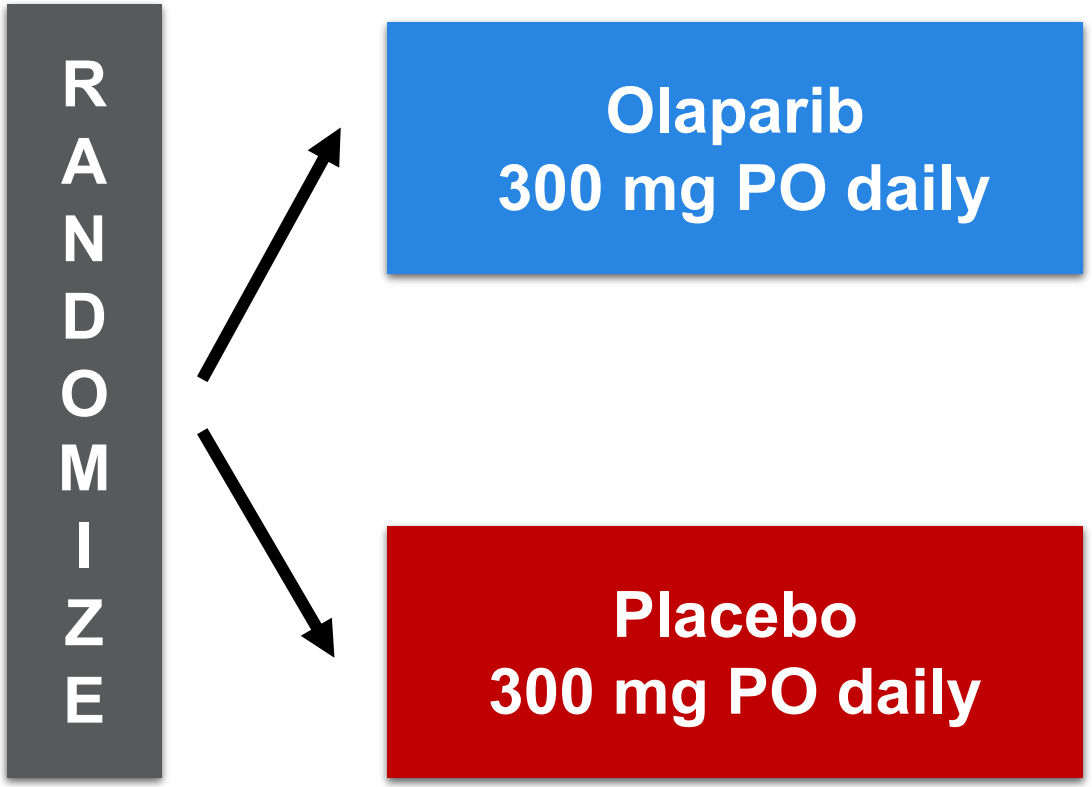
Oral olaparib a PARP inhibitor is targeted therapy in BRCA mutated pancreatic cancer



POLO was a phase 3 study of olaparib maintenance in patients with metastatic pancreatic cancer with *germline BRCA* mutation

- Metastatic disease
- Stable or better on prior platinum therapy (≥ 4 months)
- ECOG 0-1

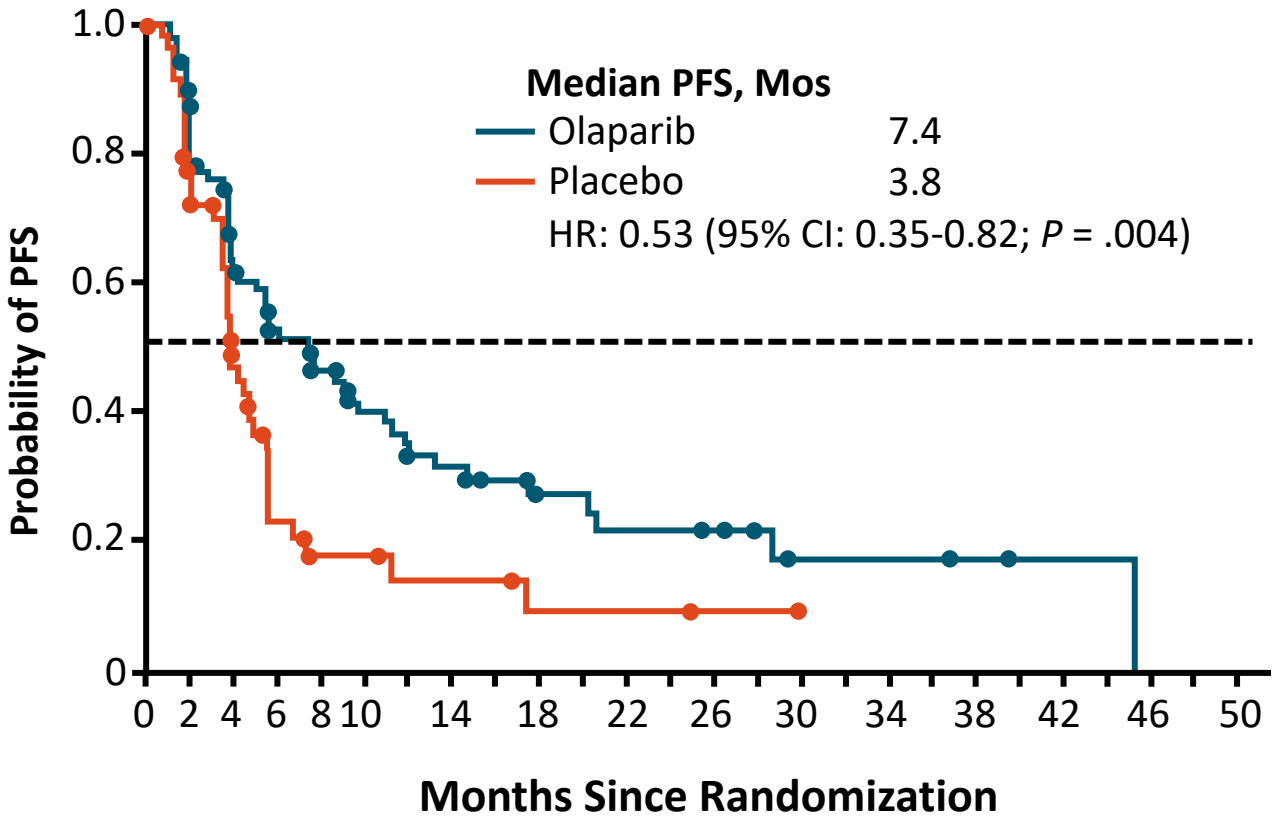
N = 154
Primary endpoint = PFS



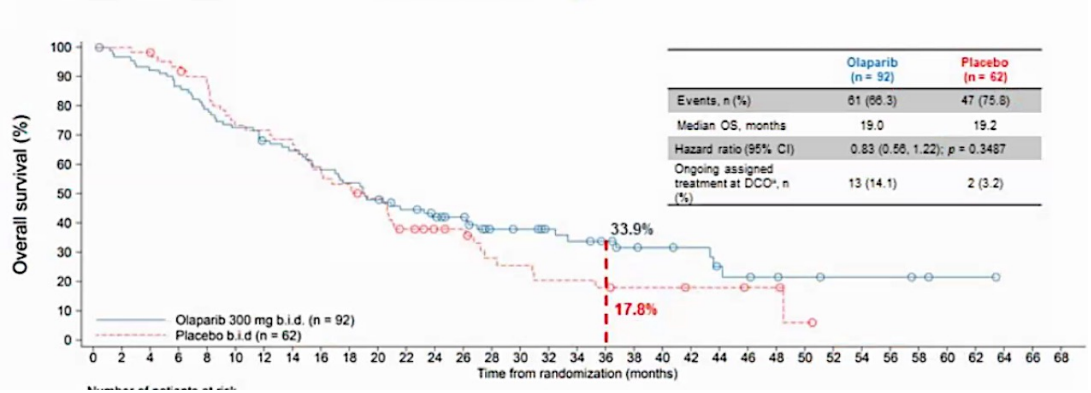
mPCA = metastatic pancreatic cancer; PARPi = PARP inhibitor; PFS = progression-free survival.

Kindler HL, et al. ASCO 2019. Abstract LBA4; Golan T, et al. *N Engl J Med.* 2019 Jun 2. [Epub ahead of print]; ClinicalTrials.gov. NCT02184195.

POLO met the primary study endpoint leading to FDA approval of olaparib in metastatic pancreatic cancer with BRCA germline mutation



Patients With Measurable Disease at Baseline	Olaparib (n = 78)	Placebo (n = 52)
Objective response n (%)	18 (23.1)	6 (11.5)
Median time to response, mos	5.4	3.6
Median duration of response, mos	24.9	3.7



Golan et al. NEJM. 2019;381:317;Kindler et al. JCO 2022;40:3929-39.

Grade 3/4 adverse events in the POLO study

Side effect	Olaparib (%)	Placebo (%)
Fatigue	5.6	0
Anemia	12.2	3.3
Treatment related	24.4	3.3
Discontinuation because of AE	8.9*	1.6*

*Only Grade1-2

Kindler et al, JCO, 2022

Germline Testing in Pancreatic Cancer: Guidelines & Recommendation

Germline testing is recommended for *any* patient with confirmed pancreatic cancer

Roundtable Discussion

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Nursing Considerations for Patients Receiving a PARP Inhibitor

Amanda K Wagner, APRN-CNP, AOCNP

The James

The Ohio State University Comprehensive Cancer Center

Columbus, Ohio

Genetic Counseling

- For patients with newly discovered germline alteration, we refer to cancer genetics for counseling to discuss:
  - The medical implications of positive, negative, and uncertain results
  - The psychological risks and benefits of learning the results
  - The risk of passing a variant to children
  - The impact of testing for the family
  - Risk reduction strategies and necessary screenings
  - Referral to support groups

https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet#what-are-the-benefits-and-downsides-of-genetic-testing-for-cancer-risk

Maintenance Olaparib. How does it work?

For patients with BRCA mutations, who have received at least 16 weeks of platinum-based chemotherapy, they are then eligible to switch to maintenance Olaparib

- Olaparib is a PARP inhibitor, which blocks the activity of the PARP enzyme-this enzyme plays a crucial role in helping the cancer cell repair damaged DNA.
- Cancer cells with BRCA mutations have known defective DNA repair mechanisms which make them sensitive to PARP inhibitors
- Switching to a maintenance therapy, offers an opportunity for a break from IV chemotherapy in the hopes of improved QoL

https://www.nejm.org/doi/full/10.1056/nejmoa1903387

Olaparib Side Effects

- Fatigue
- Anemia, Thrombocytopenia, Neutropenia
- Nausea, vomiting, diarrhea
- Headache
- Stomatitis
- Indigestion
- Decreased appetite
- URI symptoms

Administration/Dosing-

- 300 mg PO twice daily (until disease progression or unacceptable toxicity)
- Can be taken with or without food, but a small snack may help prevent nausea/vomiting

lexicomp.com

Monitoring Parameters

- CBC d/p at baseline and every month, or as clinically indicated as needed for monitoring of prolonged hematologic toxicity
- Verify pregnancy status
- Monitor for signs/symptoms of VTE, PE, pneumonitis
- Ensure patient has anti-emetics, antidiarrheals prescribed
- Instruct patient when to call-any uncontrolled GI side effect, new or worsening cough/sob, swelling, chest pain

Patient case

- 60 yo female with a history of triple negative left breast cancer in 2006 s/p neoadjuvant chemo, surgery, and radiation and ovarian cancer in 2012 s/p surgery and adjuvant chemo.
- BRCA1 mutation found after ovarian cancer diagnosis
- Social history-married with 3 grown children, 4 grandchildren. Still working full time in insurance (worked from home). Social alcohol, no smoking
- Presented in late 2022 with worsening abdominal pain, was found to have a pancreatic tail mass with evidence of metastatic disease to the liver and peritoneum.
- Liver biopsy +adenocarcinoma, consistent with a pancreatic primary
- At initial diagnosis of pancreatic cancer, was extremely tearful and anxious regarding a third cancer diagnosis. Goal was to be able to watch her grandchildren part time and still wanted to work

Patient case (continued)

- She received 5 months of therapy with FOLFIRINOX with scans showing evidence of response
- She overall did well with chemo, aside from one admission with uncontrolled diarrhea/AKI. Irinotecan was dose reduced with resolution in her symptoms.
- She did develop mild non painful neuropathy
- Was then started on maintenance Olaparib
- Tolerated well, had mild anemia and nausea, was able to continue x 7 months and then had disease progression

Roundtable Discussion

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Agenda

Introduction: Initial Management of Pancreatic Adenocarcinoma (PAD)

Module 1: Clinical Presentation and Prognosis of PAD; Recent Advances in Up-Front Treatment for Metastatic PAD

Module 2: Selection and Sequencing of Therapy for Relapsed/Refractory Metastatic PAD

Module 3: Importance of Palliative Care for Advanced PAD

Module 4: Role of PARP Inhibitor Maintenance Therapy for Newly Diagnosed Metastatic PAD

Module 5: Promising Investigational Strategies for PAD

Clinical Scenario

A patient with unresectable, locally advanced PAD who is interested in learning about promising novel investigational strategies

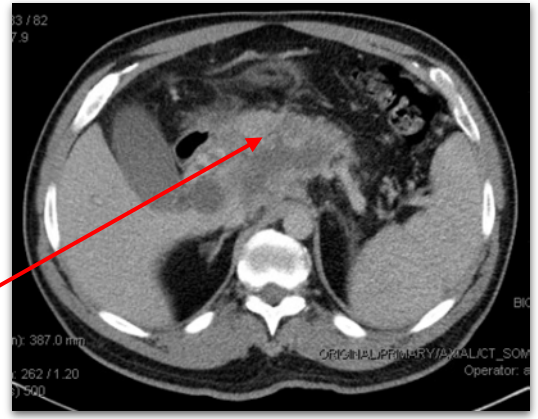
Pancreatic Cancer

Philip Agop Philip, MD, PhD, FRCP

Henry Ford Health
Wayne State University School of Medicine
Detroit, Michigan
USA

Case

- 49, male, automotive engineer
  - Performance status is 0
  - No comorbidities
  - No cancer in immediate family
- Abdominal pain x 2 weeks
- CT abdomen/chest
  - 7 x 9 cm pancreatic mass –
  - Unresectable –
- EUS = adenocarcinoma
- CA199 > 4,000
- Germline testing = negative
- Goals of management; pain control, prolonging life, possible resection



Tissue NGS

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
Mismatch Repair Status	IHC	Protein	Deficient (Loss)	BENEFIT	dostarlimab	Level 1
MSI	Seq	DNA-Tumor	High		pembrolizumab	Level 2
TMB	Seq	DNA-Tumor	High, 19 mut/Mb			

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
KRAS	Seq	DNA-Tumor	Pathogenic Variant Exon 2 | p.G12D

Liquid NGS

Biomarker	Additional Details
MSI-High	NOT DETECTED

KRAS G12C targeting in advanced pancreatic cancer

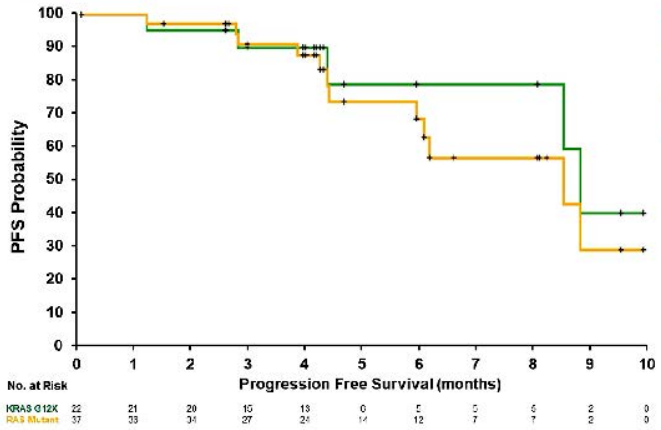
Drug	Number of Patients	Overall Response	Disease Control
Sotorasib	38	21.1%	84.2%
Adagrasib	10	50.0%	100%

Strickler et al, N Engl J Med 2023;388:33-43; Bekaii-Saab, et al, J Clin Oncol 41:4097-4106
.

Early encouraging results in pretreated pancreas cancer using Pan-KRAS inhibitor Daraxonrasib (RMC-6236)

Daraxonrasib Progression-Free Survival in Patients with 2L PDAC

Efficacy plotted for 300 mg, data for 160-300 mg shown in table for comparison

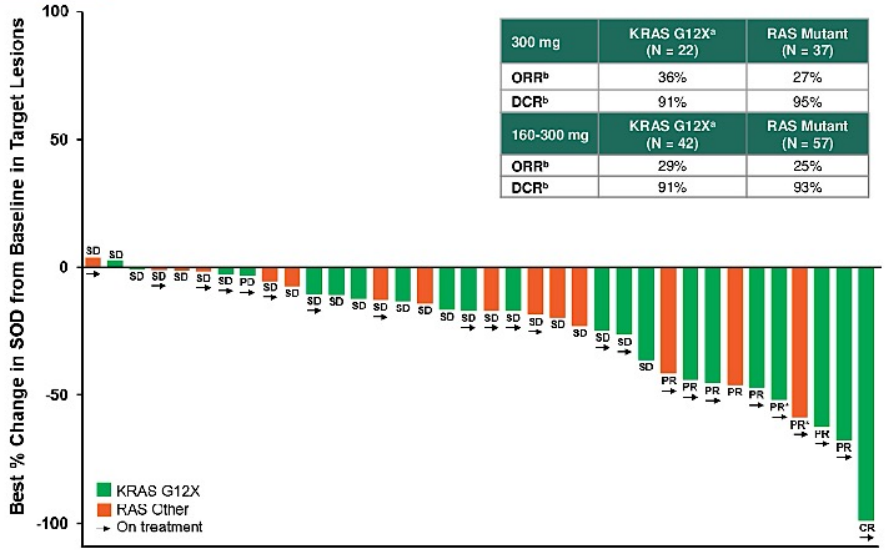


300 mg	KRAS G12X[a] (N = 22)	RAS Mutant[b] (N = 37)
Median PFS, Months (95% CI)	**8.8** (8.5, NE)	**8.5** (5.9, NE)
160-300 mg	**KRAS G12X[a] (N = 42)**	**RAS Mutant[b] (N = 57)**
Median PFS, Months (95% CI)	**8.5** (5.3, 11.7)	**7.6** (5.9, 11.1)

Data cutoff 23 Jul 2024. 2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose. Median follow-up was 6.1 months for KRAS G12X and 6.6 months for RAS mutant for 300 mg. Median follow-up was 6.2 months for KRAS G12X and 6.6 months for RAS mutant for 160-300 mg.
[a]KRAS G12X mutations are defined as nonsynonymous mutations in KRAS codon 12 (G12) mutant metastatic PDAC.
[b]RAS mutant is defined as patients with G12, G13, or Q61 mutant metastatic PDAC.

Daraxonrasib Best Response in Patients with 2L PDAC

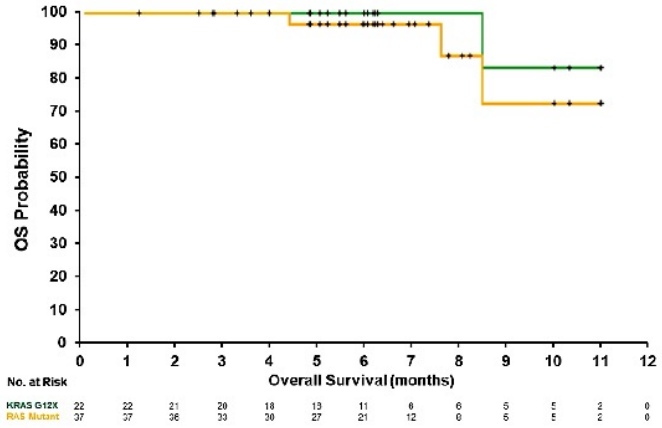
Efficacy plotted for 300 mg, data for 160-300 mg shown in table for comparison



300 mg	KRAS G12X[a] (N = 22)	RAS Mutant (N = 37)
ORR[b]	36%	27%
DCR[b]	91%	95%
160-300 mg	**KRAS G12X[a] (N = 42)**	**RAS Mutant (N = 57)**
ORR[b]	29%	25%
DCR[b]	91%	93%

Daraxonrasib Overall Survival in Patients with 2L PDAC

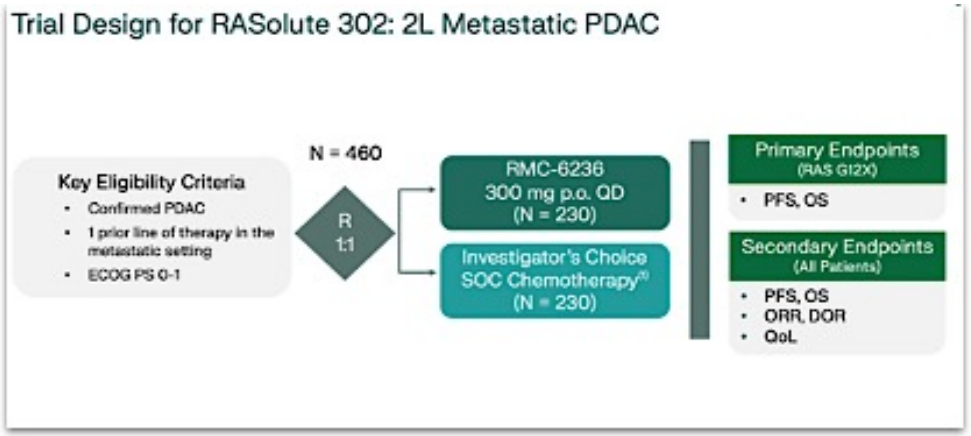
Efficacy plotted for 300 mg, data for 160-300 mg shown in table for comparison



300 mg	KRAS G12X[a] (N = 22)	RAS Mutant[b] (N = 37)
Median OS, Months (95% CI)	**NE** (NE, NE)	**NE** (8.5, NE)
OS Rate at 6 months, % (95% CI)[c]	**100** (100, 100)	**97** (79, 100)
160-300 mg	**KRAS G12X[a] (N = 42)**	**RAS Mutant[b] (N = 57)**
Median OS, Months (95% CI)	**14.5** (8.8, NE)	**14.5** (8.8, NE)
OS Rate at 6 months, % (95% CI)[c]	**89** (70, 97)	**91** (77, 96)

Data cutoff 23 Jul 2024.
Median follow-up was 6.1 months for KRAS G12X and 6.6 months for RAS mutant for 300 mg. Median follow-up was 6.2 months for KRAS G12X and 6.6 months for RAS mutant for 160-300 mg.
[a]KRAS G12X mutations are defined as nonsynonymous mutations in KRAS codon 12 (G12).
[b]RAS mutant is defined as patients with G12, G13, or Q61 mutant metastatic PDAC.
[c]OS rate at 6 months and 95% CI are from Kaplan-Meier analysis.

Trial Design for RASolute 302: 2L Metastatic PDAC

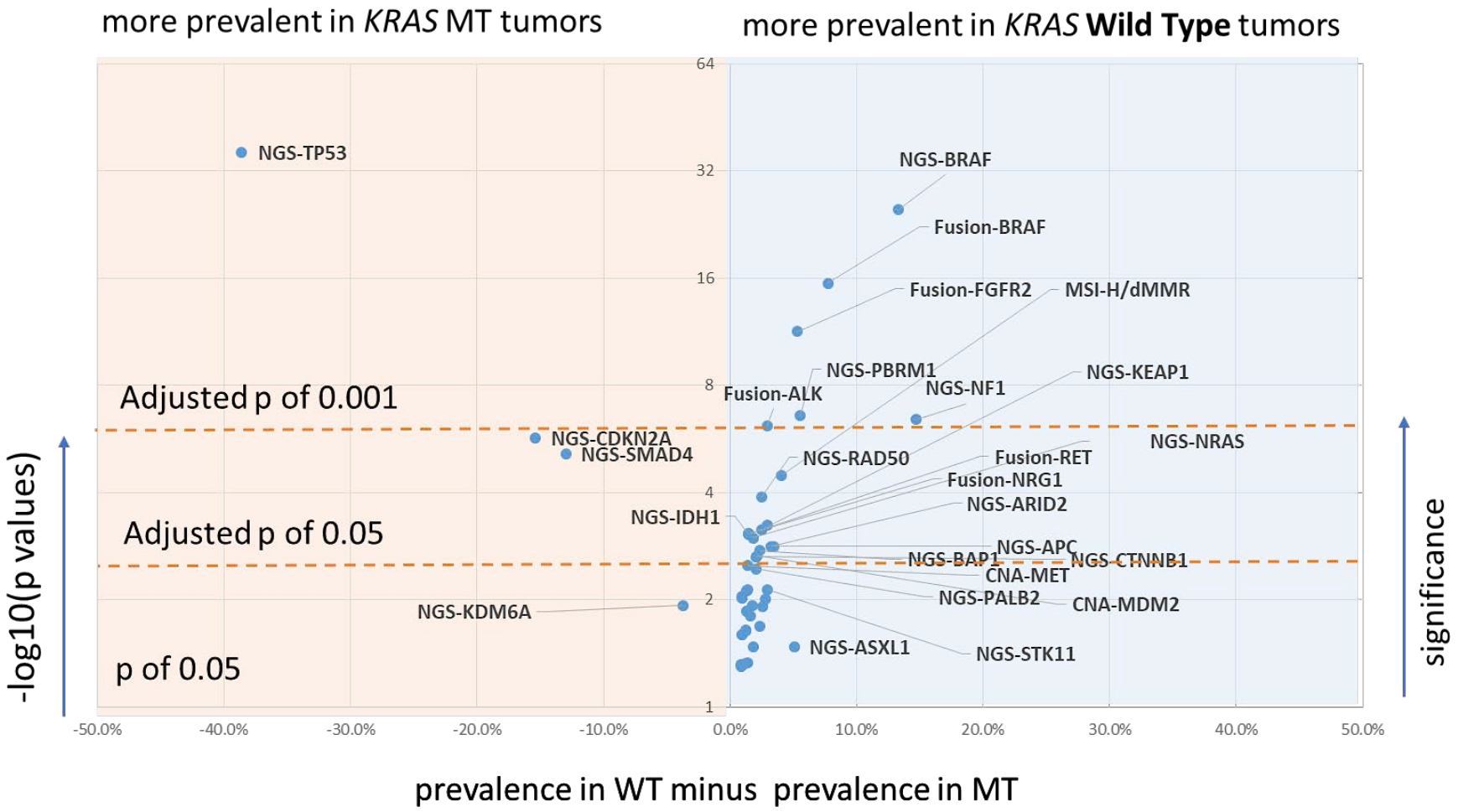


Garrido-Laguna I et al. Gastrointestinal Cancers Symposium 2025;Abstract 722.

Select KRAS inhibitor studies in pancreatic cancer- a fast expanding field!

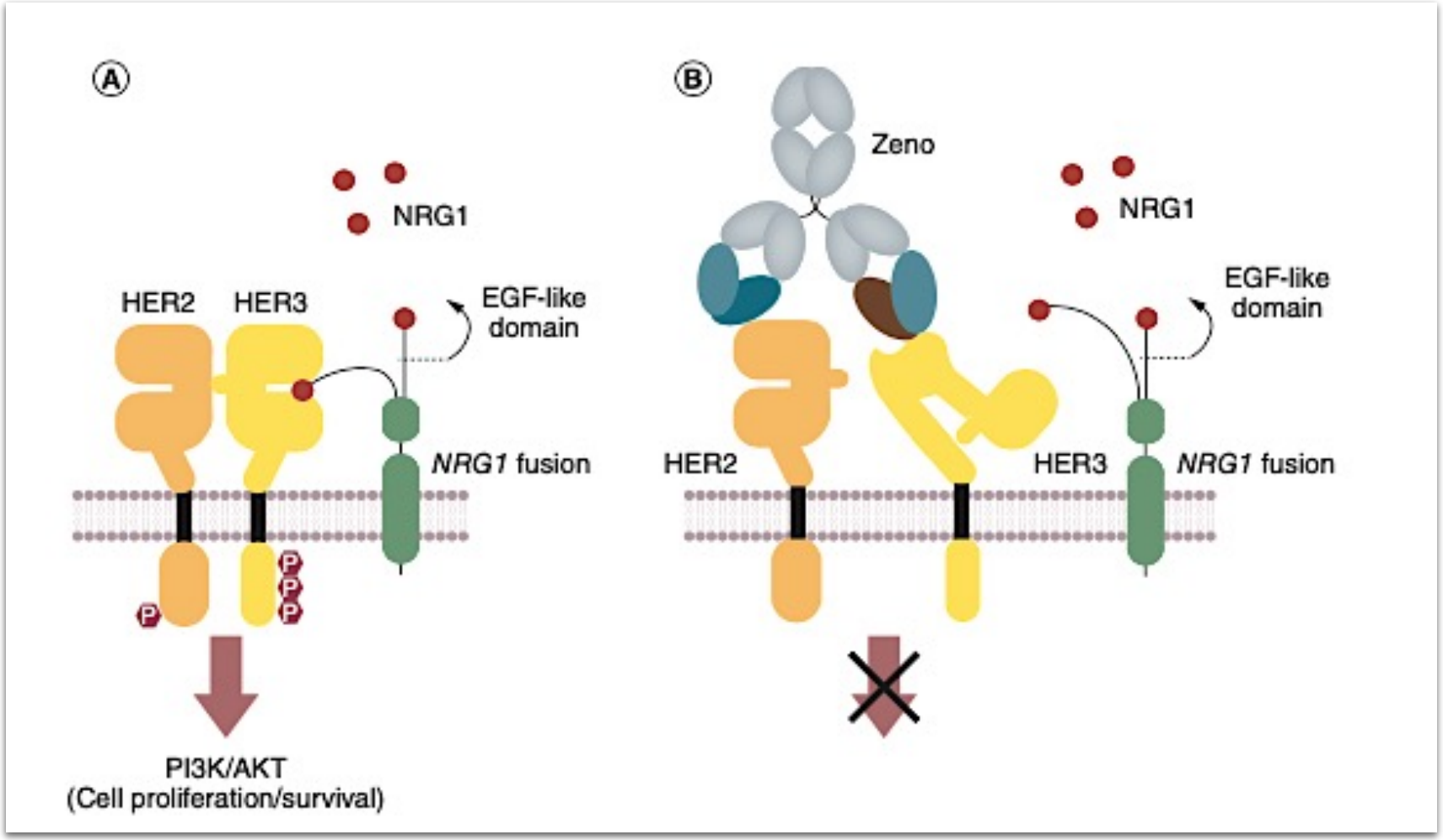
KRAS inhibitor	Trial/phase	Target	Mechanism	Reported data
KRAS G12D inhibitors				
MRTX1133 Mirati Therapeutics	NCT05737706 Phase 1/2	KRAS G12D	OFF state inhibitor	No data
RMC-9805 Revolution Medicines	NCT06040541 Phase 1	KRAS G12D	ON state, tri-complex inhibitor	No data
HRS-4642 Jiangsu HengRui Medicine	NCT05533463 Phase 1[66]	KRAS G12D	Unknown	NSCLC (n=10) ORR: 10%, DCR: 90% Other solid tumors (n=8) ORR: 0%, DCR: 62%
ASP3082 Astellas	NCT05382559 Phase 1	KRAS G12D	PROTAC	No data
Pan/multi-RAS inhibitors				
RMC-6236 Revolution Medicines	NCT05379985 Phase 1 (ref. 76)	Pan-RAS RAS wild type	RAS-multi, ON state, tri-complex inhibitor	NSCLC (n=40) ORR: 38%, DCR: 85% PDAC (n=46) ORR: 20%. DCR: 87%
BI-3706674	NCT06056024 Phase 1	Pan-KRAS KRAS wild type	Pan-KRAS, OFF state inhibitor	No data

Patients with *RAS* wild type (not mutated) can have other druggable targets including *NRG-1* fusions



Philip et al Clinical Cancer Research, 2022

Zenocutuzumab: a novel bispecific antibody targeting both HER2 and HER3

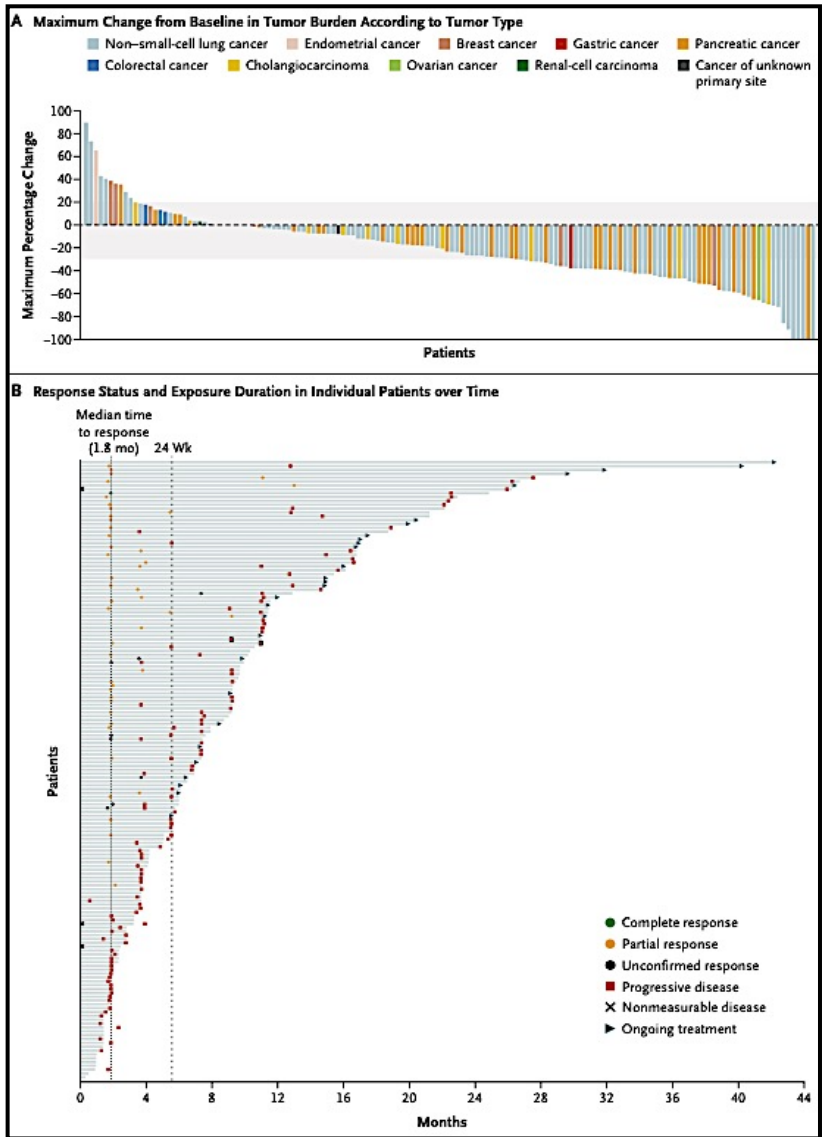


Kim et al, Future Oncology, 2024

Efficacy of zenocutuzumab in 32 patients with previously treated pancreatic cancers

- Total 204 patients/Pancreatic cancer = 32 (22%)

	Investigator Assessed		Central review	
	ORR, %	Med Duration of Response, mon	ORR, %	Med Duration of Response, mon
All *NRG-1* fusion tumors	30	11.1	31	11.5
Pancreatic ca	42 (25-59)	7.4 (2.1 – 20.7)	44 (28 -62)	9.1 (1.9+ – 16.6)



Schram et al, NEJM, 2025

Why enrollment on clinical trials should be encouraged?

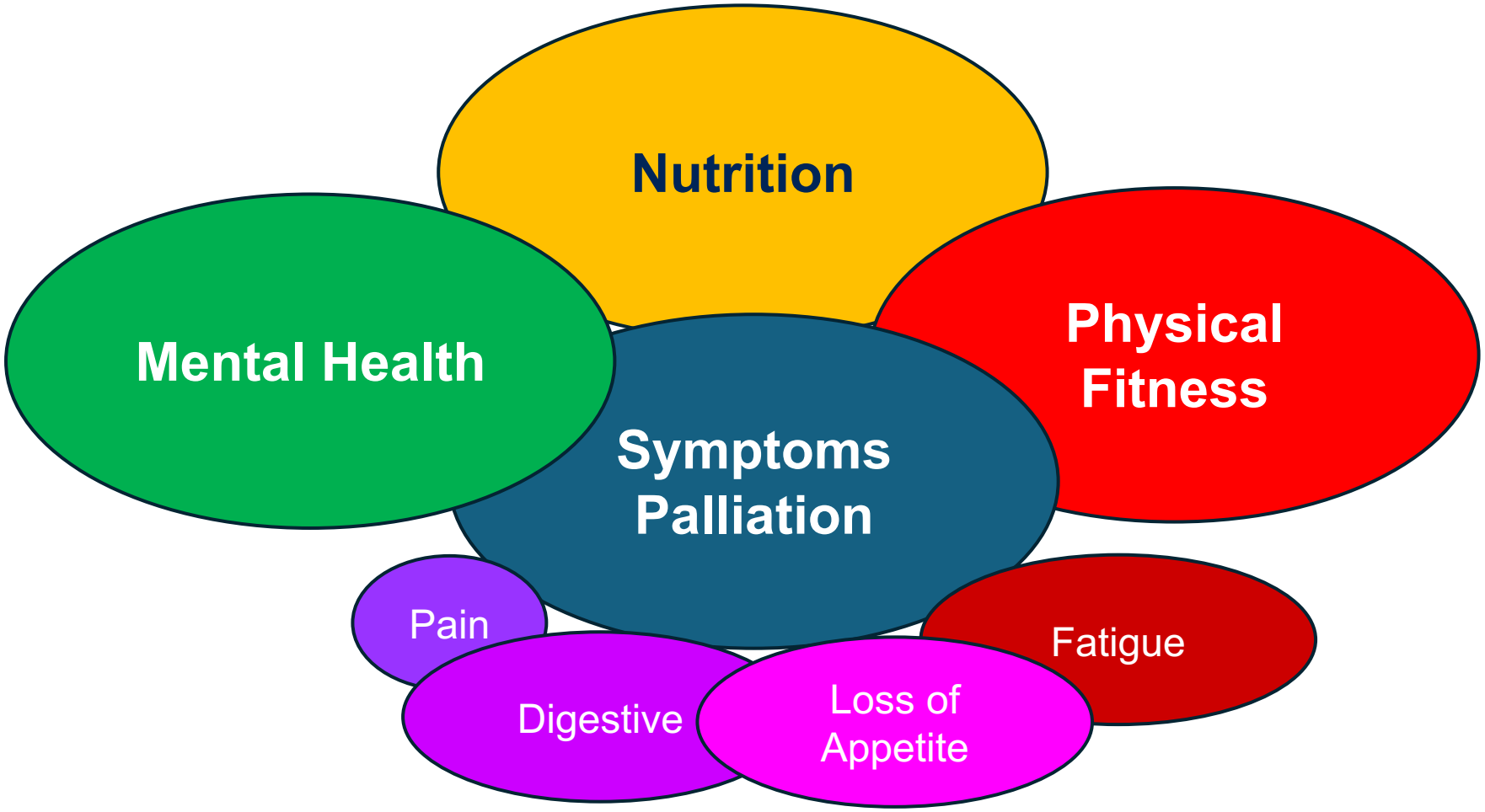
- The modest short lived and non-curative benefits of current therapies in advanced disease
- 5% of USA pancreatic cancer patients go on trials
- Access to new, unique and novel therapies
- Examples of very promising therapies
  - Targeting KRAS
  - Immunotherapy, vaccines and cell therapies
  - TTF
  - MTAP deletions and other targeted treatments

Challenges of enrolling patients in clinical trials

- Patient factors
  - Awareness of the nature and value of clinical trials
  - Concerns about “experimental” therapies (delaying treatment, side effects, placebo, cost, etc.)
- Provider factors
  - Starting “standard of care” prior to discussing trials with patients
  - Informing and educating patients on clinical trials
- Logistical challenges
  - Not having molecular profiling information upfront
  - Access to trials (e.g., availability, distance)

Oncology nurses can play a critical role as educators & patient advocates

Multidisciplinary Supportive Care



Courtesy of E. Gabriela Chiorean, MD, FASCO

Roundtable Discussion

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Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Endometrial Cancer

Saturday, April 12, 2025

6:00 AM – 7:30 AM

Faculty

Kathryn M Lyle, MSN, WHNP-BC, AGNP-C
Ritu Salani, MD, MBA
Jaclyn Shaver, MS, APRN, CNP, WHNP
Brian M Slomovitz, MD

Moderator

Neil Love, MD

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Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

To Claim NCPD Credit

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Virtual attendees: The NCPD credit link is posted in the chat room.

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