Inside the Issue: Optimizing the Management of Metastatic Pancreatic Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, August 8

5:00 PM – 6:00 PM ET

Faculty

Eileen M O'Reilly, MD

Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Faculty

Eileen M O'Reilly, MD
Winthrop Rockefeller Endowed Chair in Medical Oncology
Section Head, Hepatopancreaticobiliary and Neuroendocrine Cancers
Co-Director, Medical Initiatives
David M Rubenstein Center for Pancreatic Cancer Research
Chair, Human Research Protection Program and IRB
Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
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Los Angeles, California

Moderator
Neil Love, MD
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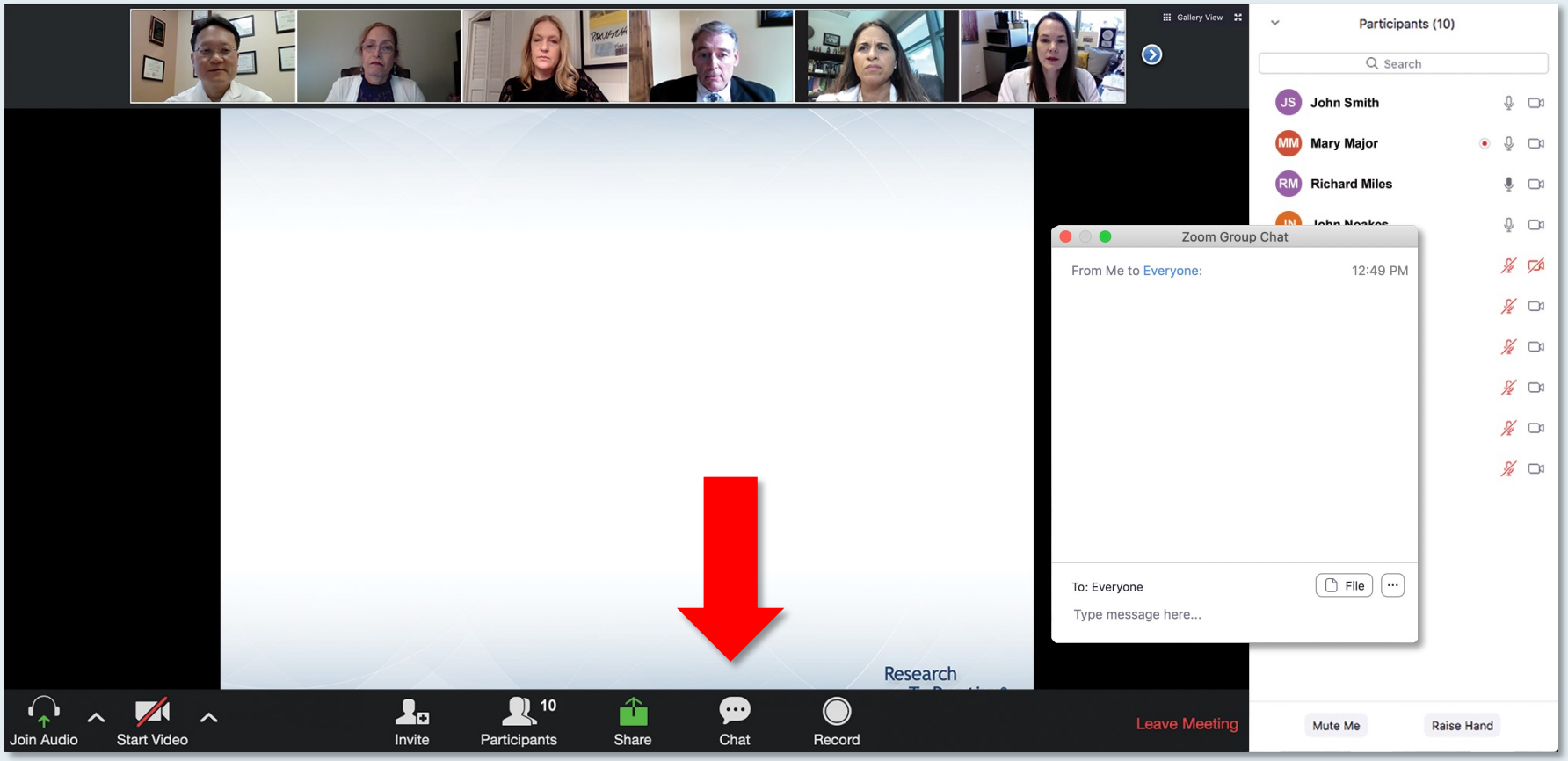

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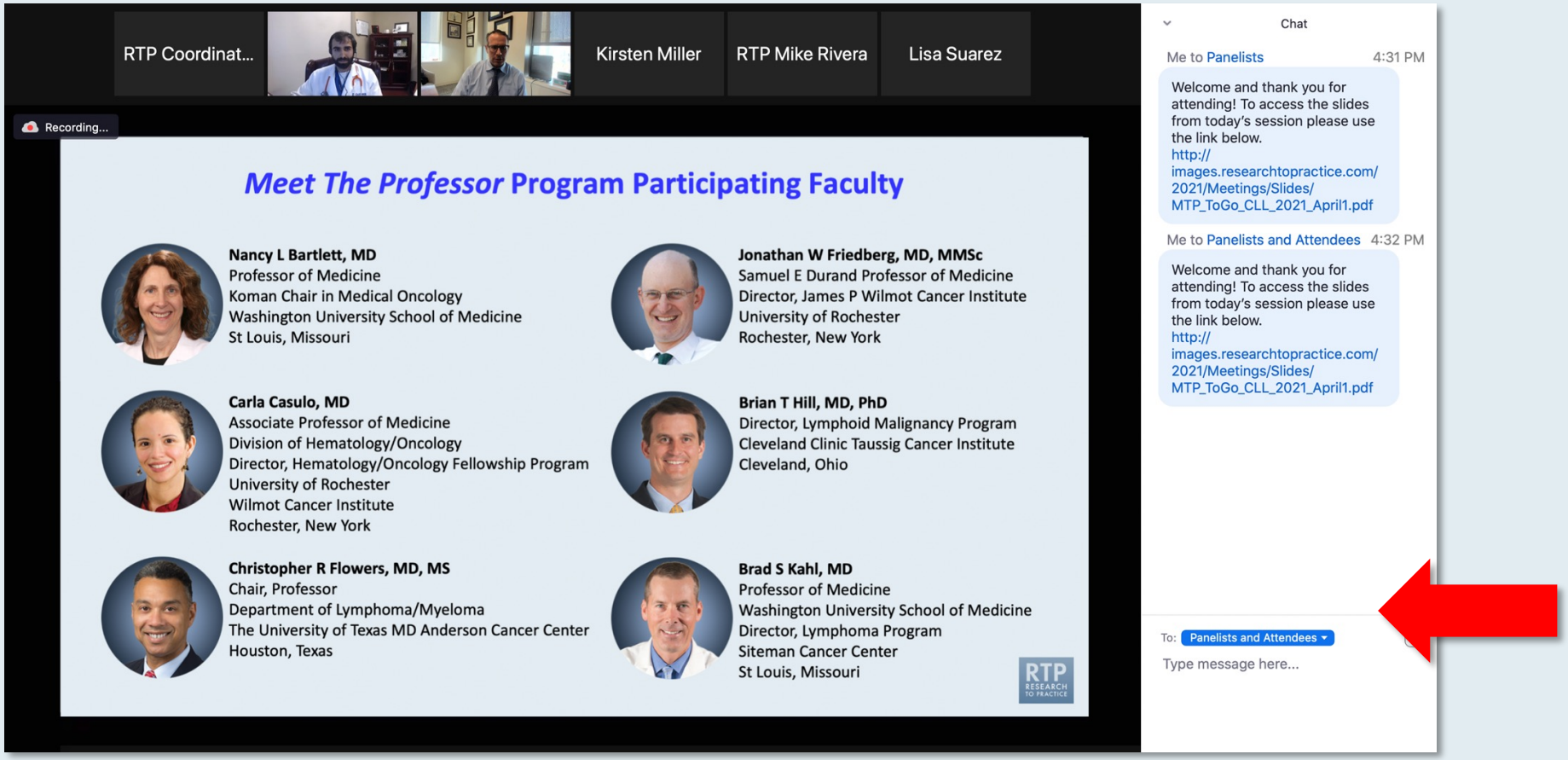

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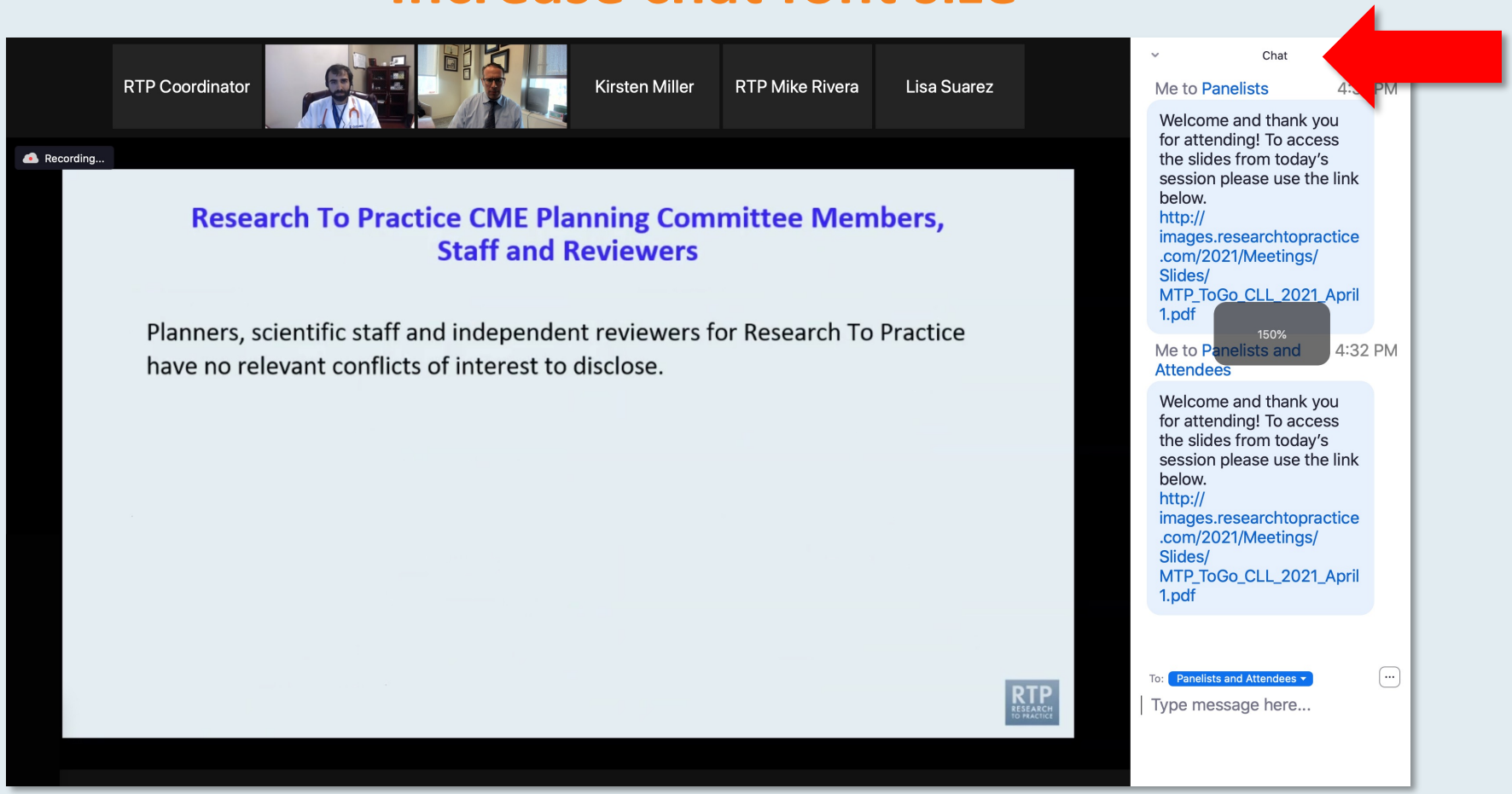

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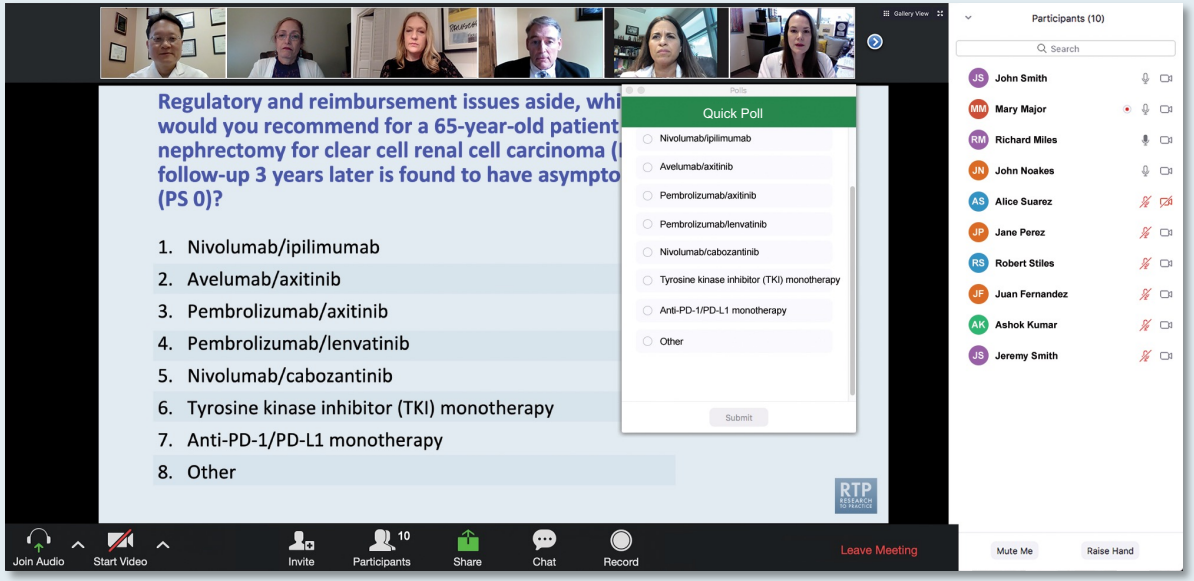

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Key Presentations Related to Gastrointestinal Cancers from Recent Major Oncology Conferences

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UNIVERSITY OF ARIZONA CANCER CENTER

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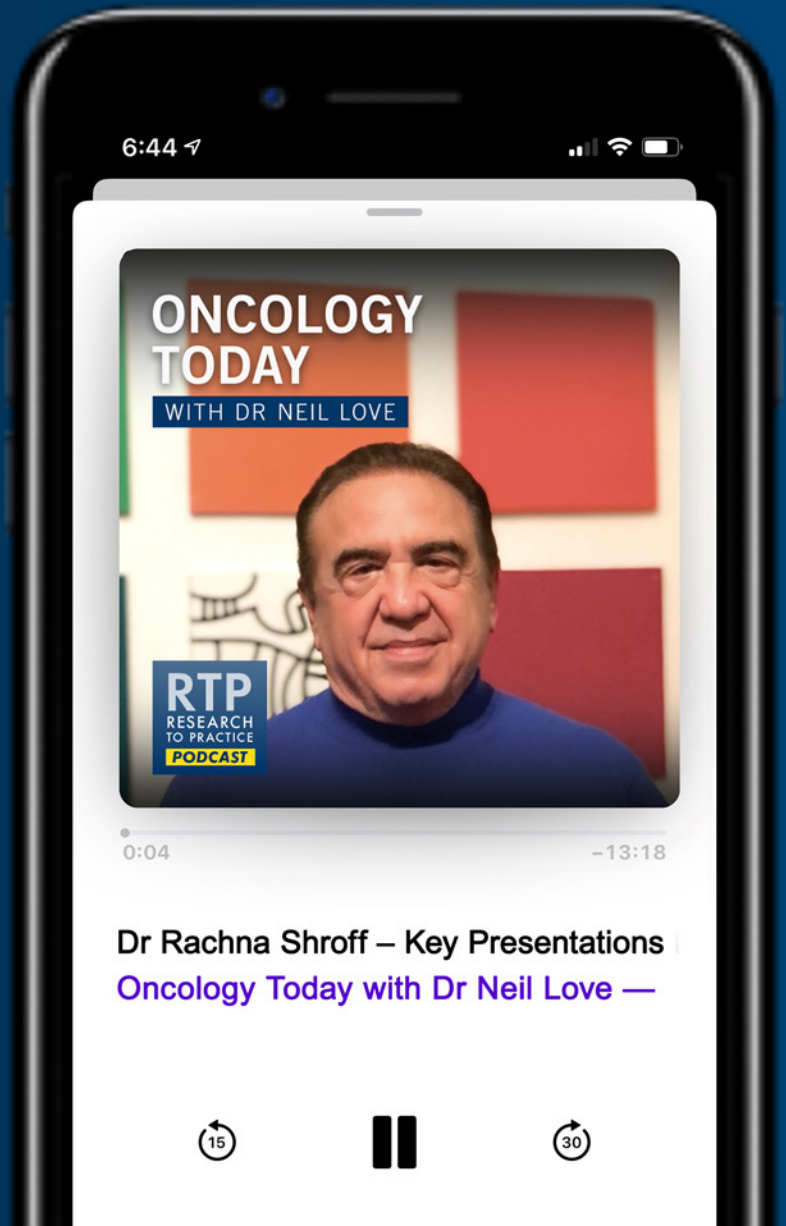

Meet The Professor

Optimizing the Management of Melanoma

Thursday, August 10, 2023
5:00 PM – 6:00 PM ET

Faculty

Prof Georgina Long, AO, BSc, PhD, MBBS

Moderator

Neil Love, MD

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What Clinicians Want to Know About Toxicity Considerations Associated with BTK Inhibitors

A CME/MOC-Accredited Virtual Event

Wednesday, August 30, 2023
5:00 PM – 6:00 PM ET

Faculty

Nicole Lamanna, MD
William G Wierda, MD, PhD

Moderator

Neil Love, MD

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Consensus or Controversy? Documenting and Discussing Clinical Investigators' Practice Patterns in Myelofibrosis

A CME Satellite Symposium During the Society of Hematologic Oncology 2023 Annual Meeting

Thursday, September 7, 2023
6:34 PM – 7:34 PM CT

Faculty

Prithviraj Bose, MD
Andrew T Kuykendall, MD

Moderator

John Mascarenhas, MD

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Cases from the Community: Investigators Discuss the Application of Available Research in the Care of Patients with Diffuse Large B-Cell Lymphoma

A CME Satellite Symposium During the Society of Hematologic Oncology 2023 Annual Meeting

Friday, September 8, 2023
11:37 AM – 12:37 PM CT

Faculty

Matthew Lunning, DO
Laurie H Sehn, MD, MPH

Moderator

Christopher R Flowers, MD, MS

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Inside the Issue: Optimizing the Management of Metastatic BRCA-Negative, Triple-Negative Breast Cancer

A CME/MOC-Accredited Live Webinar

Monday, September 11, 2023
5:00 PM – 6:00 PM ET

Faculty

Hope S Rugo, MD
Tiffany A Traina, MD, FASCO

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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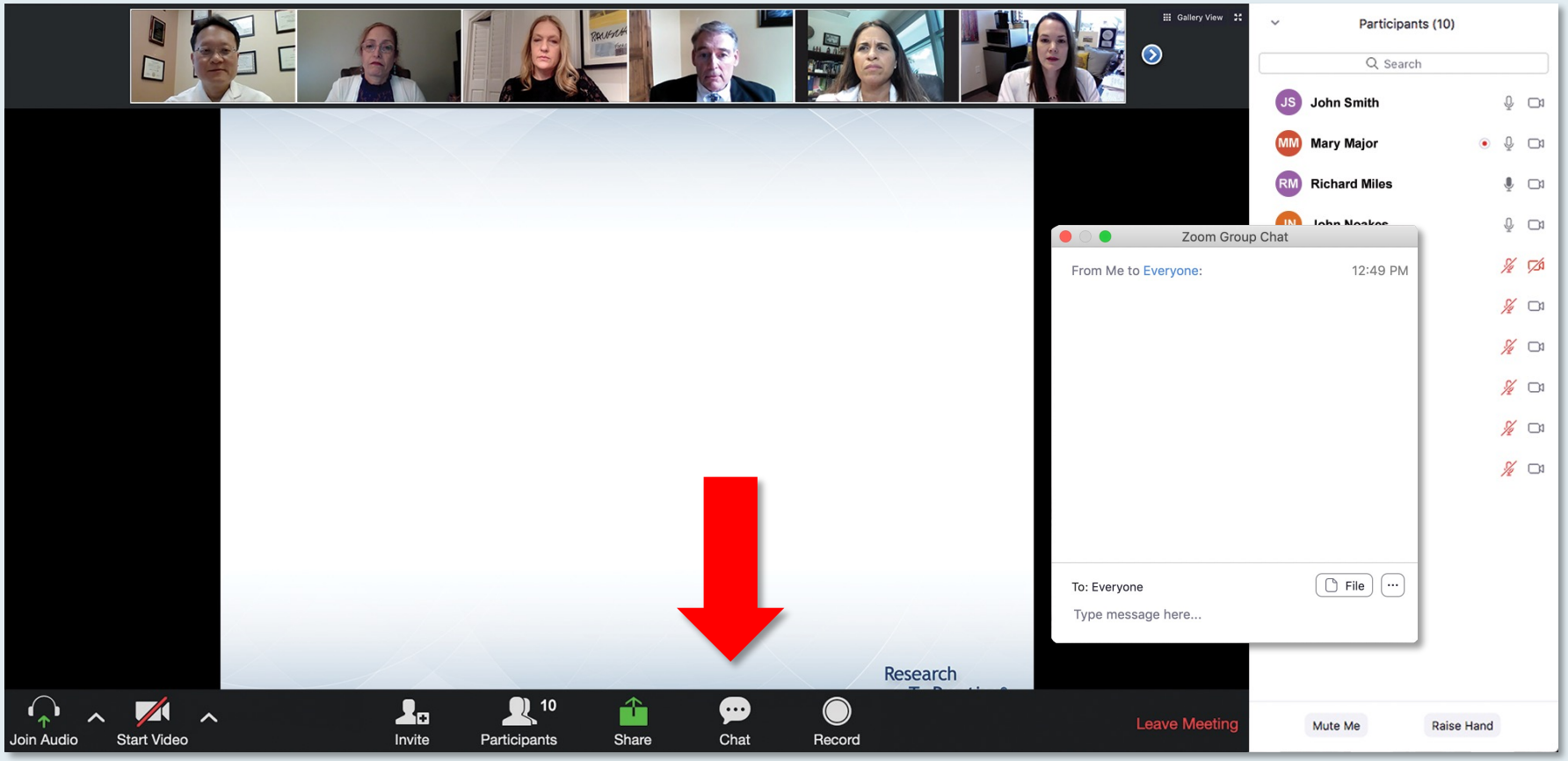

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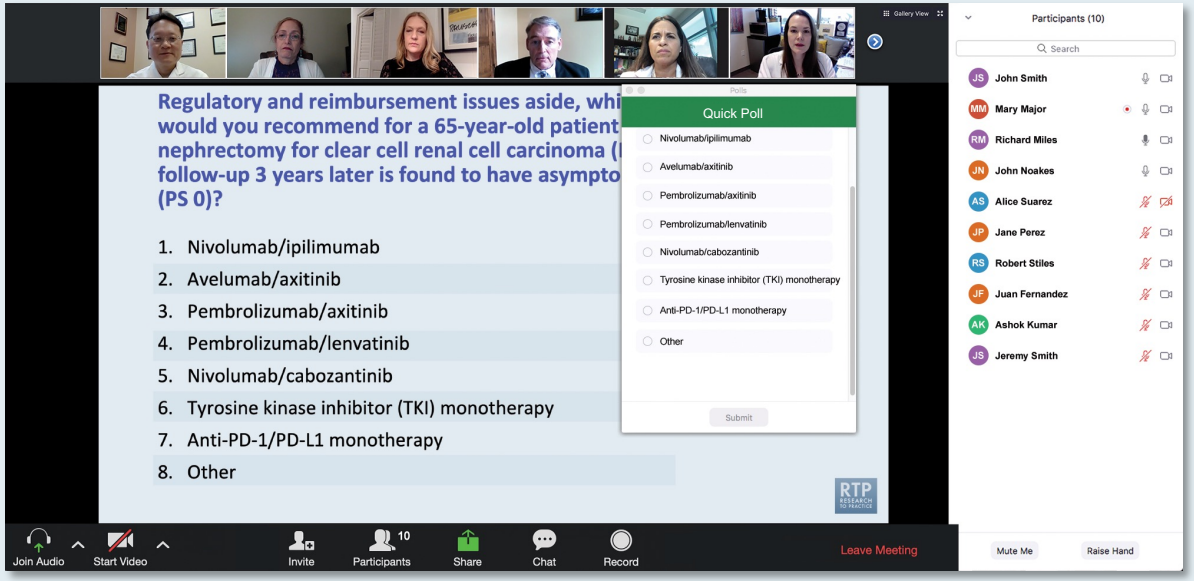

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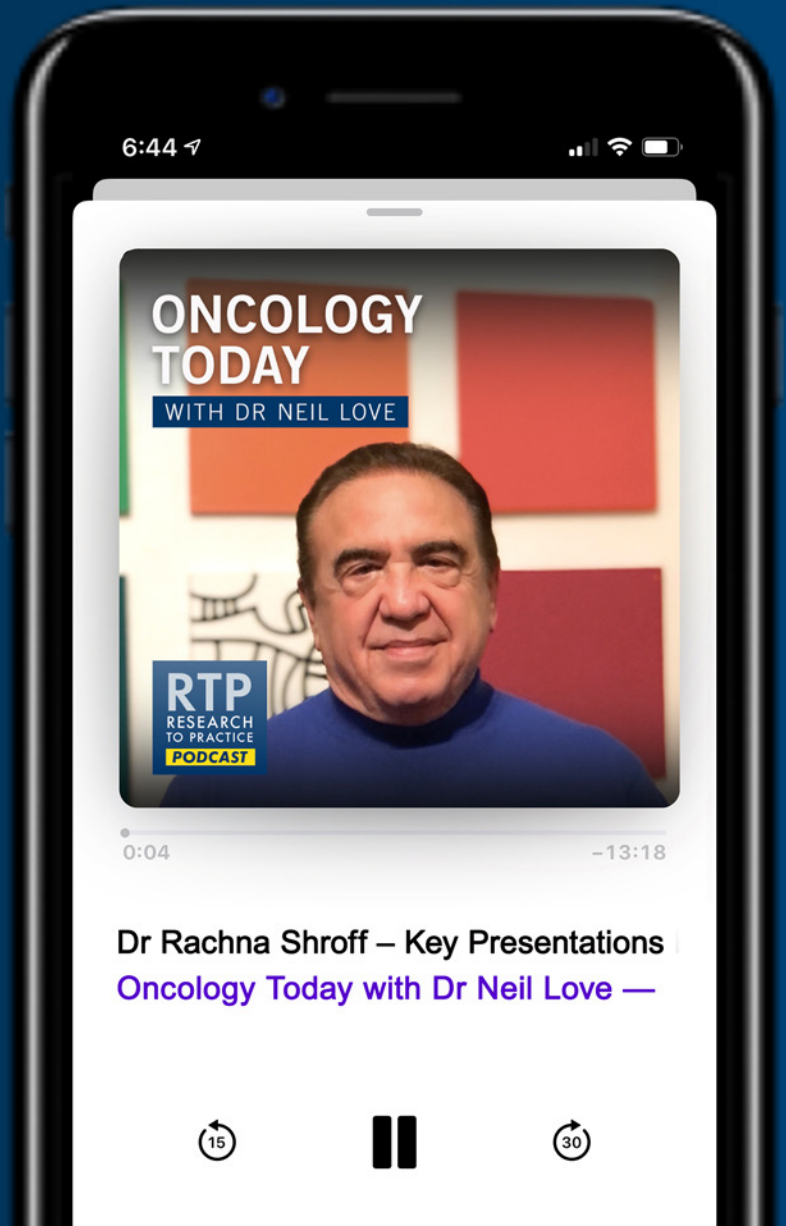

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Selection and Sequencing of Therapy for Patients with Metastatic Pancreatic Cancer

Zev Wainberg, MD, MSc

Research To Practice

Current and Future Role of Biomarker-Based Decision-Making in Metastatic Pancreatic Cancer

Eileen M. O'Reilly, MD
Memorial Sloan Kettering Cancer Center

08-03 2023

Memorial Sloan Kettering Cancer Center

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Key Data Sets

Zev Wainberg, MD, MSc

- Conroy T et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011 May 12;364(19):1817-25.
- Von Hoff DD et al. Increased survival in pancreatic cancer with *nab*-paclitaxel plus gemcitabine. *N Engl J Med* 2013 October 31;369(18):1691-703.
- Wainberg ZA et al. NAPOLI-3: A randomized, open-label phase 3 study of liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin (NALIRIFOX) versus *nab*-paclitaxel + gemcitabine in treatment-naïve patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). Gastrointestinal Cancers Symposium 2023;Abstract LBA 661.
- De Dosso S et al. Treatment landscape of metastatic pancreatic cancer. *Can Treat Rev* 2021;96:102180.
- Wang-Gillam A et al. 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. *Lancet* 2016 February 6;387(10018):545-57.

Key Data Sets

Zev Wainberg, MD, MSc (continued)

- Go S et al. Modified FOLFIRINOX versus S-1 as second-line chemotherapy in gemcitabine-failed metastatic pancreatic cancer patients: A randomised controlled trial (MPACA-3). *Eur J Cancer* 2021;157:21-30.
- Zaibet S et al. Gemcitabine + *nab*-paclitaxel or gemcitabine alone after FOLFIRINOX failure in patients with metastatic pancreatic adenocarcinoma: A real-world AGEO study. *Br J Cancer* 2022;126(10):1394-400.
- De la Fouchardière C et al. Evaluation of gemcitabine and paclitaxel versus gemcitabine alone after FOLFIRINOX failure or intolerance in metastatic pancreatic ductal adenocarcinoma: Results of the randomized phase III PRODIGE 65 – UCGI 36 – GEMPAX UNICANCER study. ESMO 2022;Abstract LBA60.
- Rivera F et al. Tumor treating fields in combination with gemcitabine or gemcitabine plus *nab*-paclitaxel in pancreatic cancer: Results of the PANOVA phase 2 study. *Pancreatology* 2019; 19(1):64-72.
- Picozzi VJ et al. Tumor treating fields (TTFields) concomitant with gemcitabine and *nab*-paclitaxel (GnP) for front-line treatment of locally advanced pancreatic cancer: The phase 3 PANOVA-3 study. Gastrointestinal Cancers Symposium 2023;Abstract TPS770.

Key Data Sets

Eileen M O'Reilly, MD

- Park W et al. Pancreatic cancer: A review. *JAMA* 2021 September 7;326(9):851-62.
- O'Reilly EM et al. Randomized, multicenter, phase II trial of gemcitabine and cisplatin with or without veliparib in patients with pancreas adenocarcinoma and a germline BRCA/PALB2 mutation. *J Clin Oncol* 2020 May 1;38(13):1378-88.
- Kindler HL et al. Overall survival results from the POLO trial: A phase III study of active maintenance olaparib versus placebo for germline BRCA-mutated metastatic pancreatic cancer. *J Clin Oncol* 2022 December 1;40(34):3929-39.
- Asimgil H et al. Targeting the undruggable oncogenic KRAS: The dawn of hope. *JCI Insight* 2022 January 11;7(1):e153688.
- Strickler JH et al. Sotorasib in KRAS p.G12C-mutated advanced pancreatic cancer. *N Engl J Med* 2023 January 5;388(1):33-43.
- Bekaii-Saab TS et al. Adagrasib in advanced solid tumors harboring a KRAS G12C mutation. *J Clin Oncol* 2023 April 26;[Online ahead of print].

Key Data Sets

Eileen M O'Reilly, MD (continued)

- O'Reilly EM et al. AMPLIFY-201, a first-in-human safety and efficacy trial of adjuvant ELI-002 2P immunotherapy for patients with high-relapse risk with KRAS G12D- or G12R-mutated pancreatic and colorectal cancer. ASCO 2023;Abstract 2528.
- Varghese AM et al. Early-onset pancreas cancer: Clinical descriptors, genomics, and outcomes. *J Natl Cancer Inst* 2021 September 4;113(9):1194-202.
- Qin S et al. Nimotuzumab combined with gemcitabine versus gemcitabine in K-RAS wild-type locally advanced or metastatic pancreatic cancer: A prospective, randomized-controlled, double-blinded, multicenter, and phase III clinical trial. ASCO 2022;Abstract LBA4011.
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- Rojas LA et al. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. *Nature* 2023 June;618(7963):144-50.
- O'Kane GM et al. GATA6 expression distinguishes classical and basal-like subtypes in advanced pancreatic cancer. *Clin Cancer Res* 2020 September 15;26(18):4901-10.

Agenda

INTRODUCTION

MODULE 1: Selection and Sequencing of Therapy for Patients with Metastatic Pancreatic Cancer

MODULE 2: Ongoing Clinical Trials

MODULE 3: Current and Future Role of Biomarker-Based Decision-Making in Metastatic Pancreatic Cancer

MODULE 4: Clinical Investigator Survey

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MODULE 4: Clinical Investigator Survey

Increasing Pancreatic Cancer Incidence in Young Women in the United States: A Population-Based Time-Trend Analysis, 2001–2018

Yazan Abboud,[1] Jamil S. Samaan,[2] Janice Oh,[2] Yi Jiang,[1] Navkiran Randhawa,[3] Daniel Lew,[1] Jenan Ghaith,[1] Pranav Pala,[4] ChristineAnn Leyson,[1] Rabindra Watson,[1] Quin Liu,[1] Kenneth Park,[1] Shirley Paski,[1] Arsen Osipov,[5] Brent K. Larson,[6] Andrew Hendifar,[5] Katelyn Atkins,[7] Nicholas N. Nissen,[8] Debiao Li,[9] Stephen J. Pandol,[1] Simon K. Lo,[1] and Srinivas Gaddam[1]

Gastroenterology 2023 May;164(6):978-89.e6.

Editorial

Cause for concern: the rising incidence of early-onset pancreatic cancer

Lancet Gastroenterol Hepatol 2023 April;8(4):287.

Clinical Research Relevance[1]

"Our research reveals a notable increase in the occurrence of pancreatic cancer among younger women, particularly among those of Black race. Furthermore, a significant proportion of these cases involve tumors situated in the head of pancreas, and are localized at the time-of-diagnosis."

Editorial[2]

"Funding for pancreatic cancer research has been historically neglected. In Europe, it receives less than 2% of cancer-related funding, and in the USA it is one of the most underfunded cancers relative to mortality burden."

[1] Abboud Y et al. *Gastroenterology* 2023 May;164(6):978-89.e6; [2] *Lancet Gastroenterol Hepatol* 2023 April;8(4):287.

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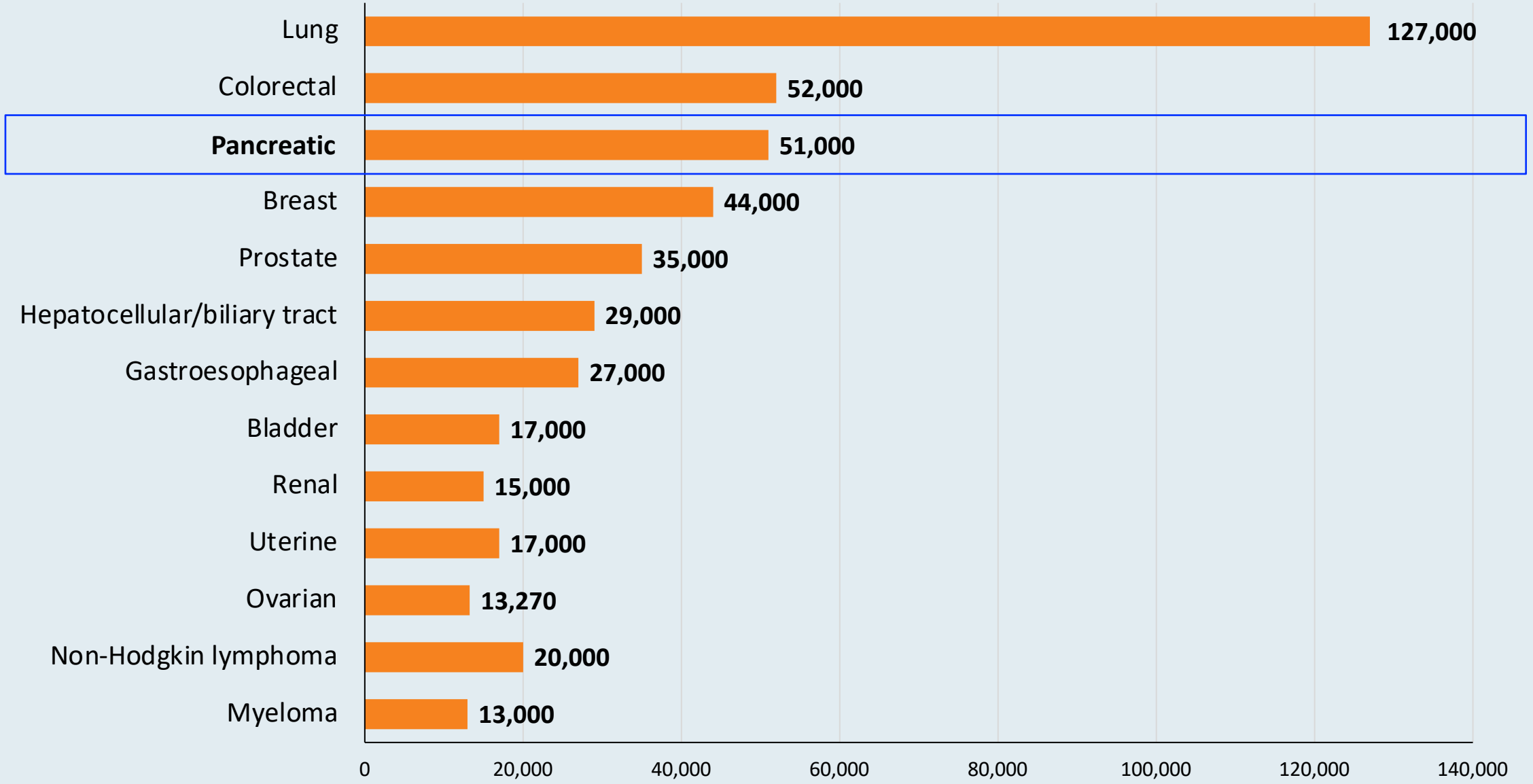
US Mortality Rates of Common Cancers



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Selection and Sequencing of Therapy for Patients with Metastatic Pancreatic Cancer

Zev Wainberg, MD, MSc

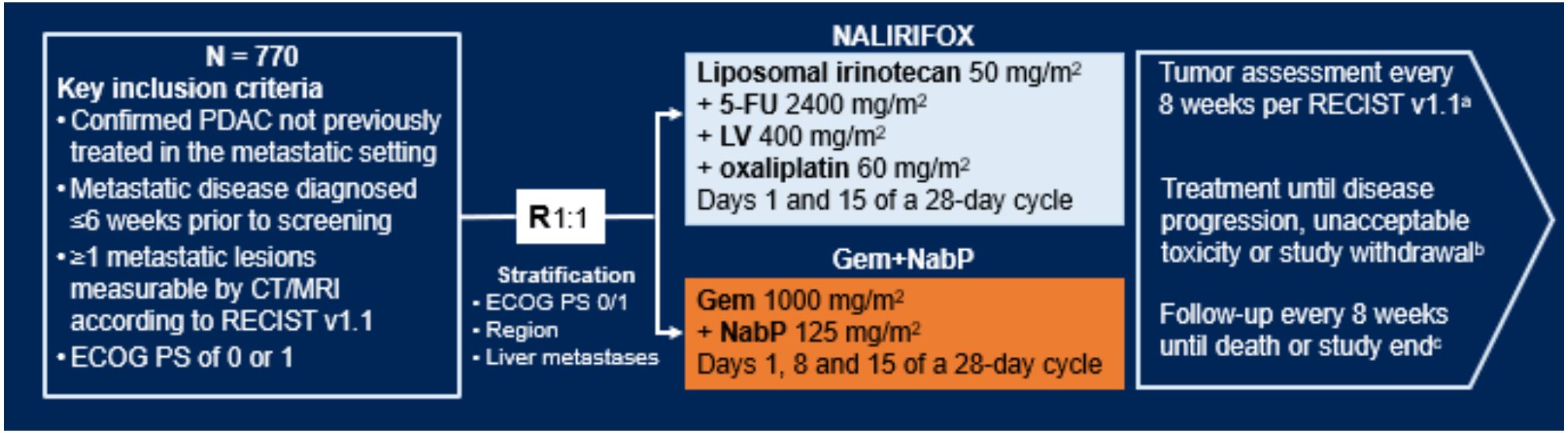
Dr Wainberg – Case Study 1

- 63-year-old with diabetes who presents with epigastric pain radiating to his back and a 10 lb weight loss
- Exam: Scleral icterus, jaundice
- Labs: ALT 37, AST 36, Tbili 4.5, Alk Phos 106, Alb 3.3
- CT A/P shows a 4.5 × 4.1 cm hypoenhancing heterogeneous mass in the pancreatic head with intrahepatic biliary dilatation and multiple hypoattenuating lesions in the liver measuring up to 3 cm in size
- ERCP: common bile duct stent is placed; LFTs normalized
- FNA of the liver lesion confirms adenocarcinoma
- Unable to obtain NGS given FNA and patient declines additional biopsy
- Germline testing reveals no abnormalities

Dr Wainberg – Case Study 1 (con't)

- He enrolls on the NAPOLI-3 trial and is randomized to chemotherapy with NALIRIFOX and responds well on follow-up imaging after cycle 4
- Requires a 20% dose reduction of oxaliplatin for peripheral neuropathy at cycle 8
- By cycle 10, neuropathy is becoming more bothersome, lingering into his off-week from treatment
- Oxaliplatin is discontinued, and he is on "maintenance" FOLFIRI
- By cycle 12, his CA 19-9 is increasing, and CT scans show stable disease
- Discussion with the patient and oxaliplatin re-introduced at a lower dose (45 mg/m^2)

NAPOLI-3 Trial: First-Line Liposomal Irinotecan + 5-FU/Leucovorin + Oxaliplatin vs Nab-Paclitaxel + Gemcitabine



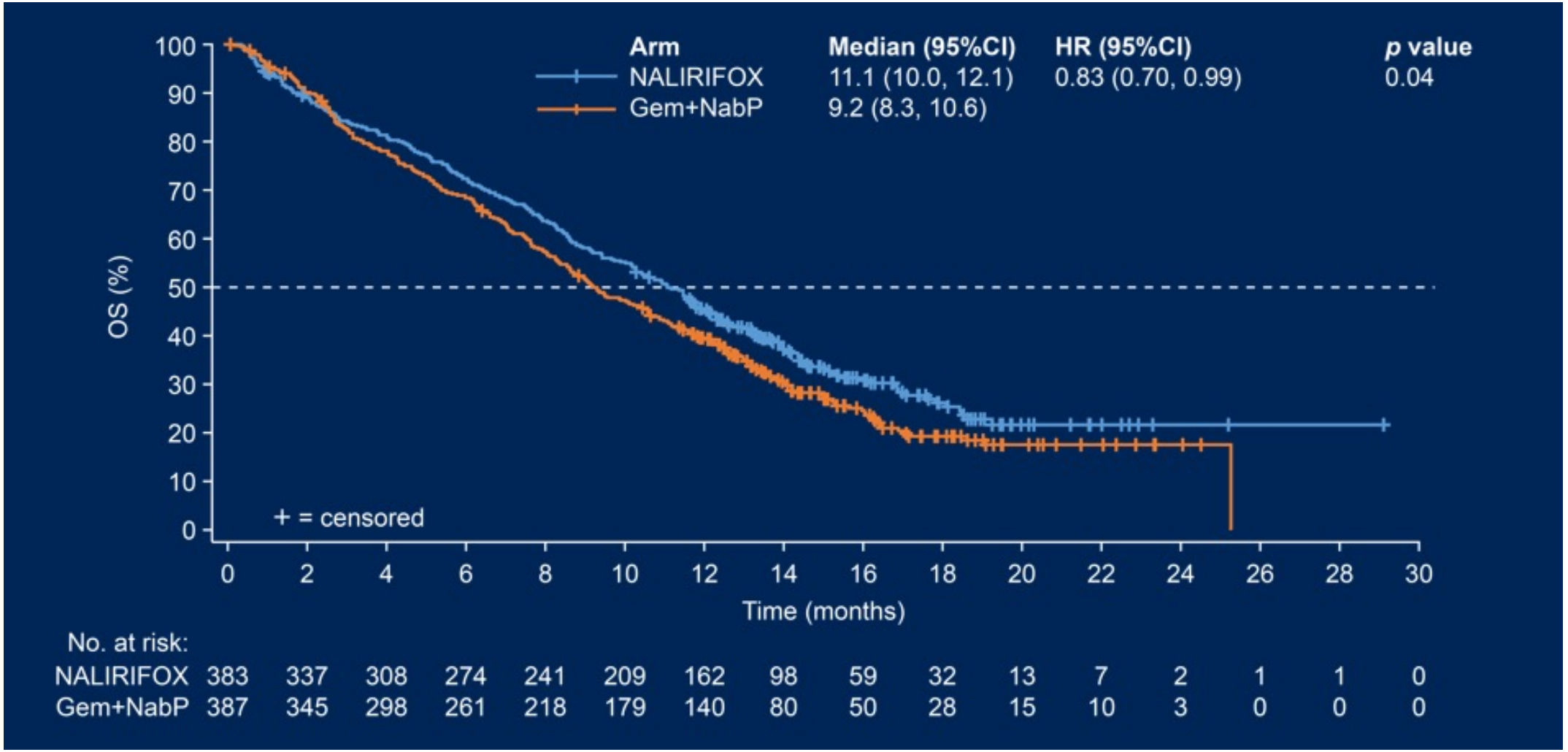
Primary endpoint: OS
Secondary endpoints: PFS and ORR per investigator using RECIST v1.1, safety
Exploratory endpoints: HRQOL, biomarker assessments
Statistical analysis: Stratified log-rank test with 2-sided alpha of 0.05, 90% power
First patient enrolled: February 2020
All data reported are based on a data cut-off of 23 July 2022

Overall median follow-up: 16.1 (95% CI:15.3–16.8) months

Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

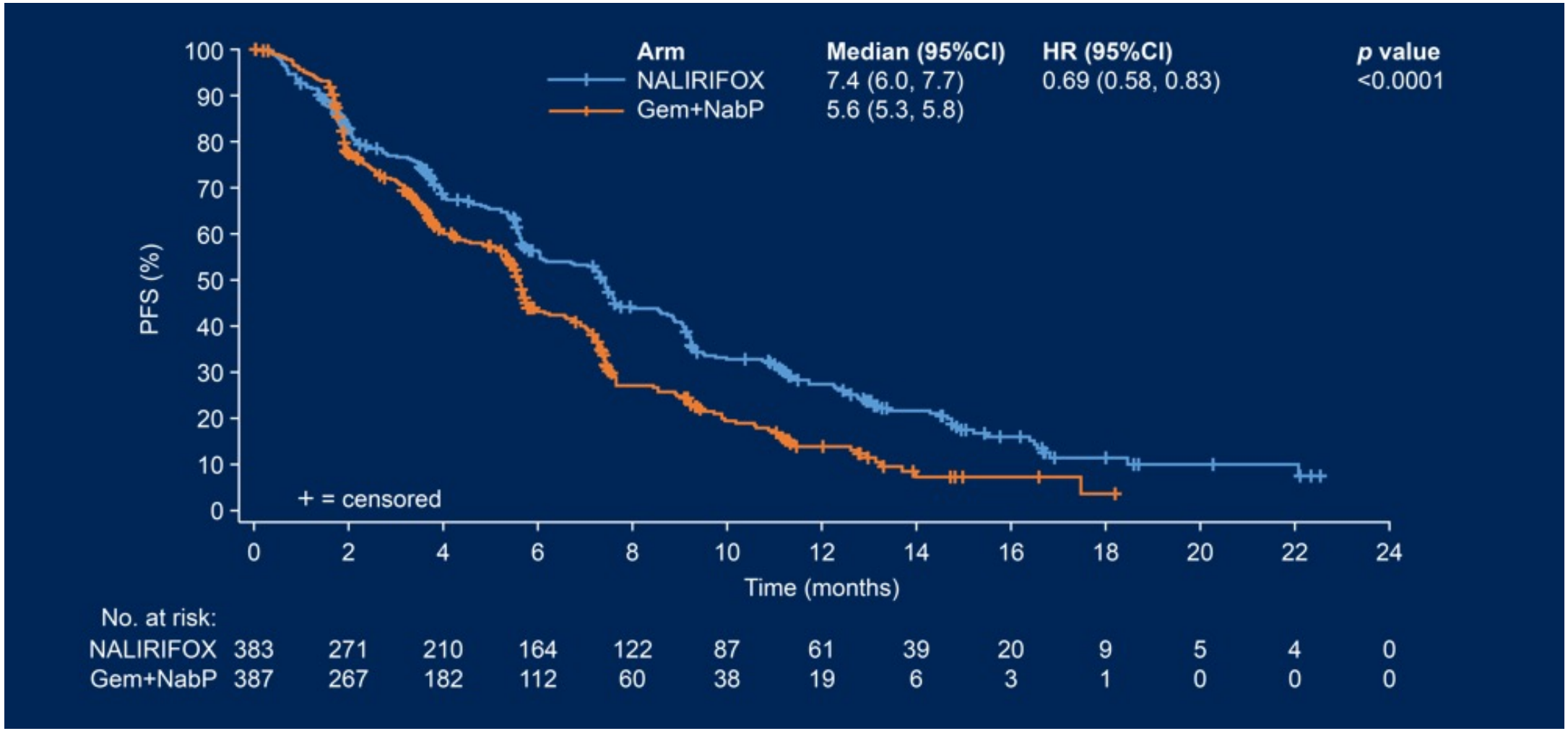
NAPOLI-3 Trial: mOS (ITT Population)



Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-3 Trial: mPFS per investigator (ITT population)



Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-3 Trial: Tumor Response & Subsequent Anti-Cancer Therapy

Tumor Response	NALIRIFOX (N = 383)	Gem+NabP (N = 387)
Objective response rate (95% CI), %	41.8 (36.8–46.9)	36.2 (31.4–41.2)
Best overall response, %		
Complete response	0.3	0.3
Partial response	41.5	35.9
Stable disease	25.8	26.1
Progressive disease	9.9	14.5
Not evaluable[b]	22.5	23.3

Subsequent Anti-Cancer Therapy	NALIRIFOX (N = 383)	Gem+NabP (N = 387)
Any further subsequent anti-cancer therapy, %	50.5	54.4
Systemic anti-neoplastic therapy[a]	50.5	54.1
Surgery	0.3	0.5
Radiotherapy	0.5	1.1

Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-3 Trial: Overall Summary of AEs

	NALIRIFOX (N = 370)	Gem+NabP (N = 379)
Median (range) duration of treatment, weeks	24.29 (0.4–100.9)	17.57 (0.7–81.7)
TEAEs all grade, %	99.7	99.2
Related to treatment regimen	95.1	92.9
TEAE Grade ≥3, %	87.0	86.0
Related to treatment regimen	70.8	68.1
Serious TEAEs, %	54.3	51.5
Related to treatment regimen	26.5	19.0
TEAEs leading to death, %	5.9	6.1
Related to treatment regimen	1.6	2.1

Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-3 Trial: Selected Any-Cause TEAEs in ≥10% of Patients

	NALIRIFOX (N = 370)		Gem+NabP (N = 379)	
Any-cause TEAEs in ≥10% of patients, %[a]	**Any grade**	**Grade 3–4**	**Any Grade**	**Grade 3–4**
Hematologic				
Neutropenia / neutrophil count decreased / febrile neutropenia	29.5 / 20.5 / 2.4	14.1 / 9.7 / 2.4	31.9 / 18.7 / 2.6	24.5 / 13.5 / 2.4
Anemia	26.2	10.5	40.4	17.4
Thrombocytopenia / platelet count decreased	13.5 / 10.5	0.8 / 0.8	22.7 / 17.9	3.7 / 2.4
Non-hematologic				
Diarrhea	70.5	20.3	36.7	4.5
Nausea	59.5	11.9	42.7	2.6
Vomiting	39.7	7.0	26.4	2.1
Hypokalemia	31.6	15.1	12.9	4.0
Peripheral neuropathy	17.8	3.2	17.4	5.8
Peripheral sensory neuropathy	15.1	3.5	13.5	2.9
Paresthesia	11.9	0.3	8.7	0.5
Pyrexia	10.5	0.8	23.0	1.6

Wainberg ZA, et al. Presented at: the 2023 ASCO® GI Cancers Symposium; January 19-21, 2023; San Francisco, CA. Abstract LBA 661,

Courtesy of Zev Wainberg, MD, MSc

Based on your personal clinical experience and knowledge of available data, in general how would you compare the global efficacy and tolerability of gemcitabine/*nab* paclitaxel to those of modified FOLFIRINOX?

	More efficacious	More tolerable
 Dr O'Reilly	Modified FOLFIRINOX	About the same
 Dr Wainberg	Modified FOLFIRINOX	Modified FOLFIRINOX
 Dr Bekaii-Saab	Modified FOLFIRINOX	About the same – gemcitabine/*nab* paclitaxel more tolerable if given q2wk
 Dr Ciombor	Modified FOLFIRINOX	Modified FOLFIRINOX (if giving gemcitabine/*nab* paclitaxel weekly)
 Dr Messersmith	Modified FOLFIRINOX	About the same
 Dr Philip	Modified FOLFIRINOX	Gemcitabine/*nab* paclitaxel (when used every other week)
 Dr Pishvaian	About the same	Gemcitabine/*nab* paclitaxel (when used every other week)

FOLFIRINOX = leucovorin/fluorouracil/irinotecan/oxaliplatin; *nab* paclitaxel = nanoparticle albumin-bound paclitaxel

Based on your personal clinical experience and knowledge of available data, in general how would you compare the global efficacy and tolerability of NALIRIFOX to those of gemcitabine/*nab* paclitaxel?

	More efficacious	More tolerable
 Dr O'Reilly	NALIRIFOX	About the same
 Dr Wainberg	NALIRIFOX	NALIRIFOX
 Dr Bekaii-Saab	NALIRIFOX	About the same – gemcitabine/*nab* paclitaxel more tolerable if given q2wk
 Dr Ciombor	NALIRIFOX	Gemcitabine/*nab* paclitaxel, especially if given q2wk
 Dr Messersmith	I have not used this agent	I have not used this agent
 Dr Philip	NALIRIFOX	About the same
 Dr Pishvaian	I have not used this agent	I have not used this agent

NALIRIFOX = liposomal irinotecan/oxaliplatin/leucovorin/fluorouracil

Based on your personal clinical experience and knowledge of available data, in general how would you compare the global efficacy and tolerability of NALIRIFOX to those of modified FOLFIRINOX?

	More efficacious	More tolerable
 Dr O'Reilly	About the same	About the same
 Dr Wainberg	About the same	NALIRIFOX
 Dr Bekaii-Saab	About the same	About the same
 Dr Ciombor	About the same	About the same
 Dr Messersmith	I have not used NALIRIFOX	I have not used NALIRIFOX
 Dr Philip	About the same	NALIRIFOX
 Dr Pishvaian	About the same	About the same

Dr Wainberg – Case Study 2

- 76-year-old woman presents with 1 month of progressive epigastric pain
- CT scan shows a 4-cm pancreatic body/tail mass, along with multiple hepatic lesions and retroperitoneal lymphadenopathy
- A core biopsy of 1 of the liver lesions confirms adenocarcinoma
  - Serum CA19-9 = 2450 U/mL
- She initiates gemcitabine and nab-paclitaxel and initially demonstrates a partial response on follow-up CT scans, with a 60% decline in CA19-9
- However, repeat imaging after cycle 4 shows progression in the size of her liver lesions and pancreatic head mass, with uptrending CA19-9
- She has Grade 1 neuropathy but otherwise remains highly functional, with an ECOG PS of 1

Dr Wainberg – Case Study 2(con't)

- Based on NAPOLI-1 Trial, she initiates 5-FU/liposomal irinotecan (NALIRI) and demonstrates a 30% decline in CA19-9, with improvement in weight and appetite
- Repeat imaging after cycle 5 shows disease stabilization in liver lesions and pancreatic mass
- She has Grade 1 diarrhea and grade 1 neuropathy but feels well overall

Beyond Front-Line Therapy For Metastatic Pancreatic Cancer

- Historically, 40% to 50% of patients are suitable candidates for post-progression treatment
  - Clinical deterioration often limits patient eligibility for further treatment
  - Limited clinical data (mostly single-arm; mixture of respective and prospective studies)
  - Before 2015, no approved drugs/regimens in this setting
  - Survival rates generally in the 4- to 6-month range for chemotherapy agents, either alone or in combination
  - Minimal to no responses observed from targeted or IO agents alone

- De Dosso S, et al. Can Treat Rev. 2021;96:102180.

Courtesy of Zev Wainberg, MD, MSc

NCCN Guidelines: Second-Line Treatment Decisions

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

(If prior gemcitabine-based therapy)

- 5-FU + leucovorin + liposomal irinotecan[n] (category 1 for metastatic disease)
- 5-FU + leucovorin + irinotecan (FOLFIRI)[24-27]
- FOLFIRINOX or modified FOLFIRINOX[a,e,28]
- Oxaliplatin + 5-FU + leucovorin (OFF)
- FOLFOX
- Capecitabine + oxaliplatin
- Capecitabine
- Continuous infusion 5-FU

(If prior fluoropyrimidine-based therapy)

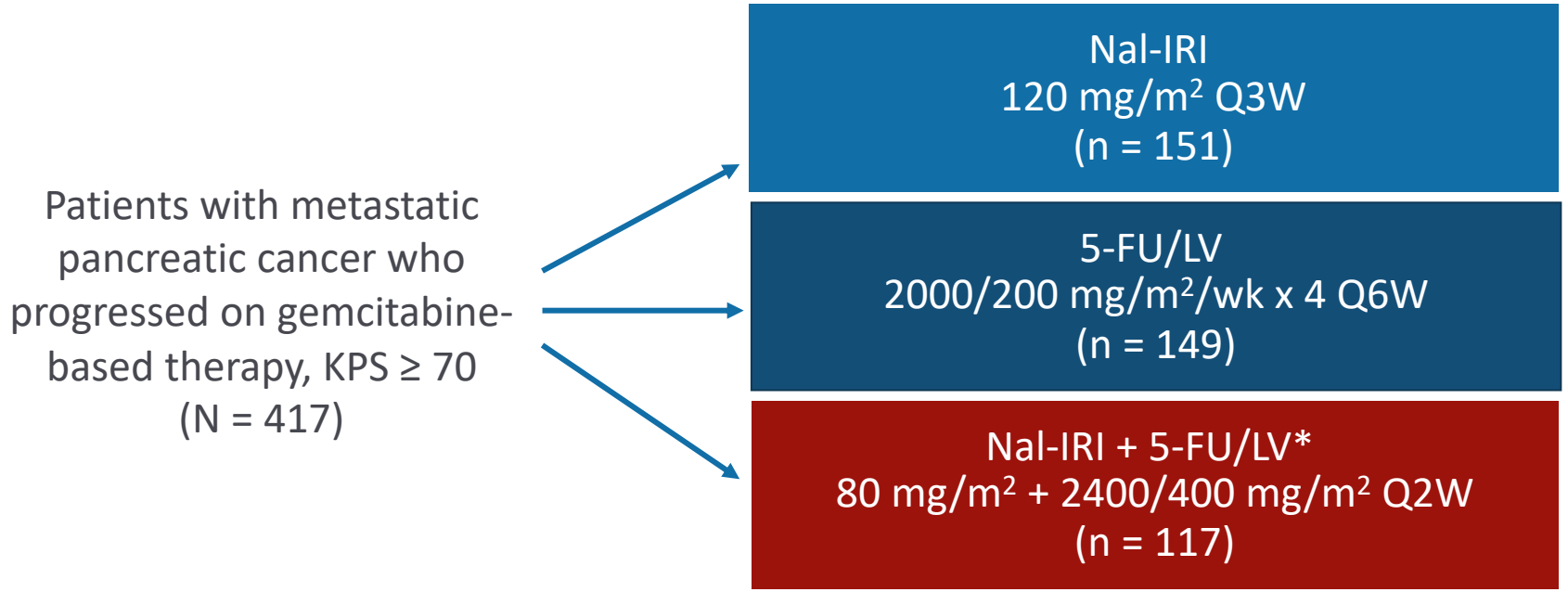
- Gemcitabine
- Gemcitabine + albumin-bound paclitaxel[f]
- Gemcitabine + cisplatin (only for known *BRCA1/2* or *PALB2* mutations)
- Gemcitabine + erlotinib[g,29]
- 5-FU + leucovorin + liposomal irinotecan[n] (if no prior irinotecan)
- Gemcitabine + albumin-bound paclitaxel + cisplatin[14,15] (category 2B)

NCCN Guidelines. Pancreatic Adenocarcinoma. V2.2022.

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-1: Nanoliposomal Irinotecan ± 5-FU/LV vs 5-FU/LV After Progression on Gem-Based Therapy

Multicenter, randomized, open-label phase 3 trial



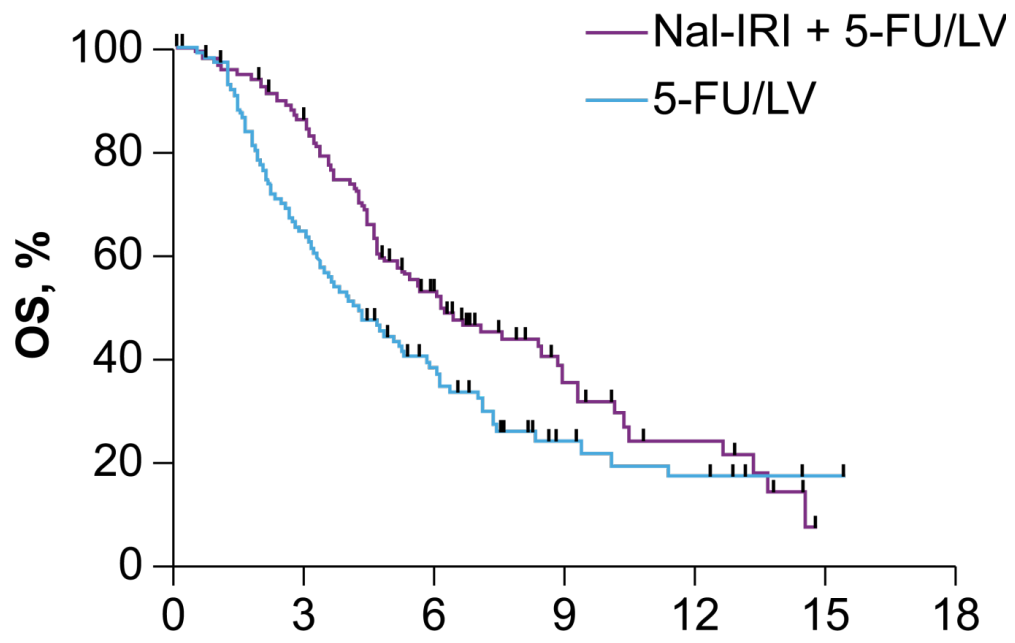
Primary endpoint: OS

*Combination arm added after safety data were available. Patients in 5-FU/LV arm used as controls for combination arm.

Wang-Gillam A, et al. Lancet. 2016;387:545-557.

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-1: Efficacy Results



OS: 6.1 vs 4.2 months
HR = 0.67 (0.49-0.92)
P = .012 (unstratified log-rank)

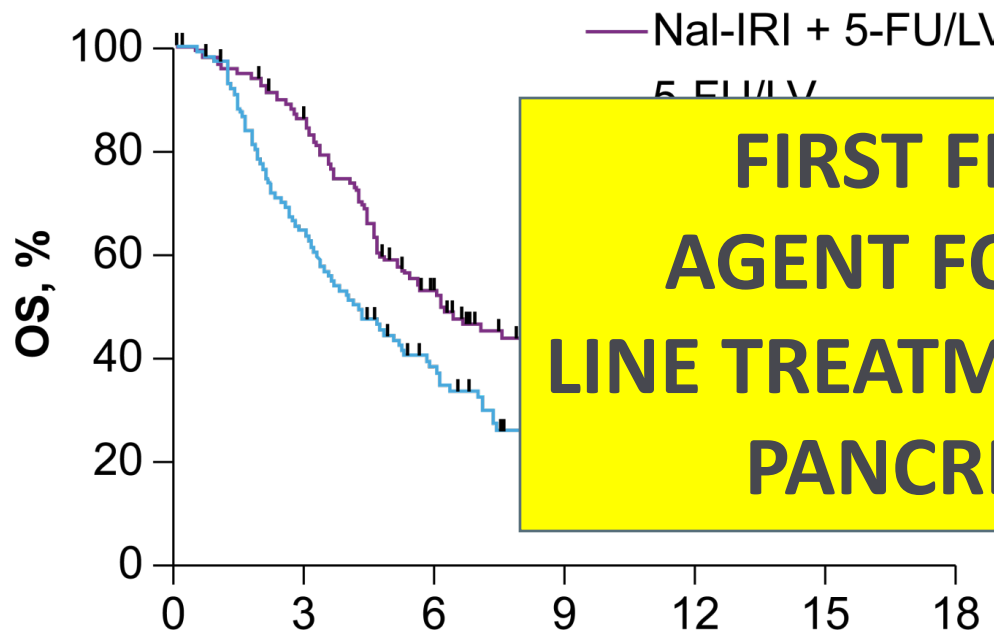
	Nal-IRI + 5-FU/LV (n = 117)	5-FU/LV (n = 119)
Median PFS, mos	3.1	1.5
	P = .0001	
ORR, %	16	1
	P < .001	
CA19-9 reduction, %	36	12
	P = .0009	

Grade ¾ AEs in > 5% of patients:
Nausea, vomiting, diarrhea, anemia

*Combination arm added after safety data were available. Patients in 5-FU/LV arm used as controls for combination arm.
Wang-Gillam A, et al. Lancet. 2016;387:545-557.

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-1: Efficacy Results



OS: 6.1 vs 4.2 months
HR = 0.67 (0.49-0.92)
P = .012 (unstratified log-rank)

FIRST FDA-APPROVED AGENT FOR THE SECOND-LINE TREATMENT OF ADVANCED PANCREATIC CANCER

	Nal-IRI + 5-FU/LV (n = 117)	5-FU/LV (n = 119)
	3.1	1.5
	P = .0001	
	16	1
	P < .001	
CA19-9 reduction, %	36	12
	P = .0009	

Grade ¾ AEs in > 5% of patients:
Nausea, vomiting, diarrhea, anemia

*Combination arm added after safety data were available. Patients in 5-FU/LV arm used as controls for combination arm.
Wang-Gillam A, et al. Lancet. 2016;387:545-557.

Courtesy of Zev Wainberg, MD, MSc

NAPOLI-1: Safety

AEs, %	Nal-IRI + 5-FU/LV (n = 117)		5-FU/LV (n = 134)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Diarrhea	59	13	26	4
Vomiting	52	11	26	3
Nausea	51	8	34	3
Decreased appetite	44	4	32	2
Fatigue	40	14	28	4
Neutropenia	39	27	5	1
Anemia	38	9	23	7
Hypokalemia	12	3	9	2

Wang-Gillam A, et al. Lancet. 2016;387:545-557.

Courtesy of Zev Wainberg, MD, MSc

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

Current Maintenance Approaches

First-Line Chemotherapy[a]	Maintenance Recommendations
FOLFIRINOX	• Capecitabine • 5-FU/LV • FOLFIRI • FOLFOX
Gemcitabine/nab-paclitaxel	• Gemcitabine • Gemcitabine/nab-paclitaxel (modified schedule)
Platinum-based chemotherapy, *BRCA1/2* or *PALB2* mutations	• PARP inhibitor (olaparib, rucaparib)

a. NCCN Guidelines. Pancreatic Adenocarcinoma. V2.2022.

Courtesy of Zev Wainberg, MD, MSc

Dr Wainberg – Case Study 3

- 80-year-old woman presents with 1 month of weight loss and fatigue
- CT scan shows a 6-cm pancreatic body mass, along with 4 liver lesions and retroperitoneal lymphadenopathy
- CT guided biopsy of 1 of the liver lesions confirms adenocarcinoma
  - Serum CA19-9 = 85000 U/mL
- Tumor sent for NGS reveals MSS, point mutations seen in KRAS G12D, p53
- She initiates chemotherapy with low doses of modified FOLFIRINOX (irinotecan at 90 mg/meter squared, no bolus) and initially demonstrates a partial response on follow-up CT scans in all liver lesions, with a 40% decline in CA19-9
- However, repeat imaging after cycle 4 shows progression in the size of her liver lesions and pancreatic mass, with uptrending CA19-9
- She has Grade 1 neuropathy but otherwise remains highly functional, with an ECOG PS of 1

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

Agenda

INTRODUCTION

MODULE 1: Selection and Sequencing of Therapy for Patients with Metastatic Pancreatic Cancer

MODULE 2: Ongoing Clinical Trials

MODULE 3: Current and Future Role of Biomarker-Based Decision-Making in Metastatic Pancreatic Cancer

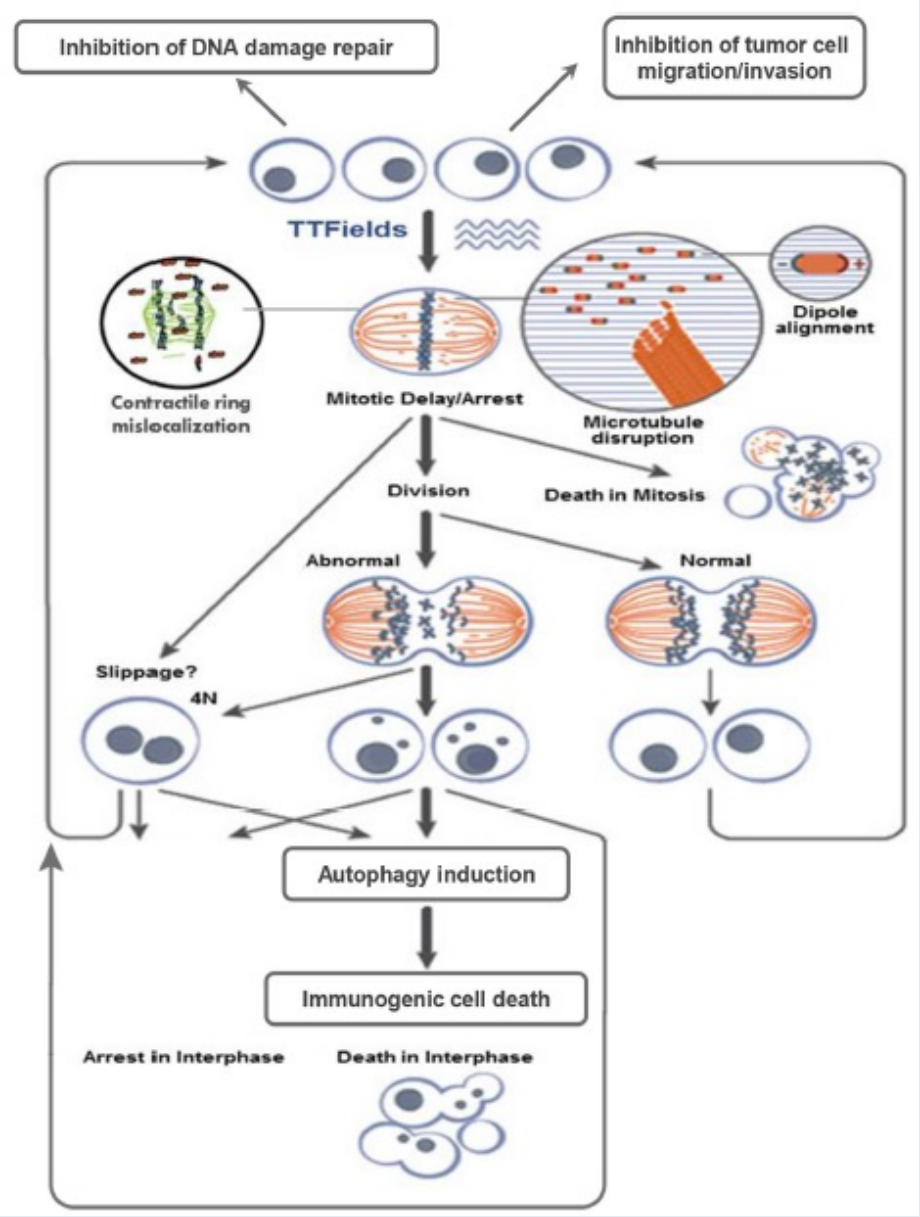
MODULE 4: Clinical Investigator Survey

For which ongoing Phase III clinical trials in pancreatic cancer are you most interested in seeing results?

 Dr O'Reilly	ALLIANCE A021806, APOLLO
 Dr Wainberg	ALLIANCE A021806, adjuvant vs neoadjuvant European trial
 Dr Bekaii-Saab	ALLIANCE A021806
 Dr Ciombor	ALLIANCE A021806, TIGeR PaC
 Dr Messersmith	ALLIANCE A021806, KRAS inhibitor Phase II trials
 Dr Philip	ALLIANCE A021806, APOLLO
 Dr Pishvaian	ALLIANCE A021806, TIGeR PaC, Gemcitabine + *nab* paclitaxel/zolbetuximab in CLDN 18.2+ mPDAC

RTP
RESEARCH
TO PRACTICE

PANOVA Phase II Study: Rationale and Mechanism of Action of TTFields



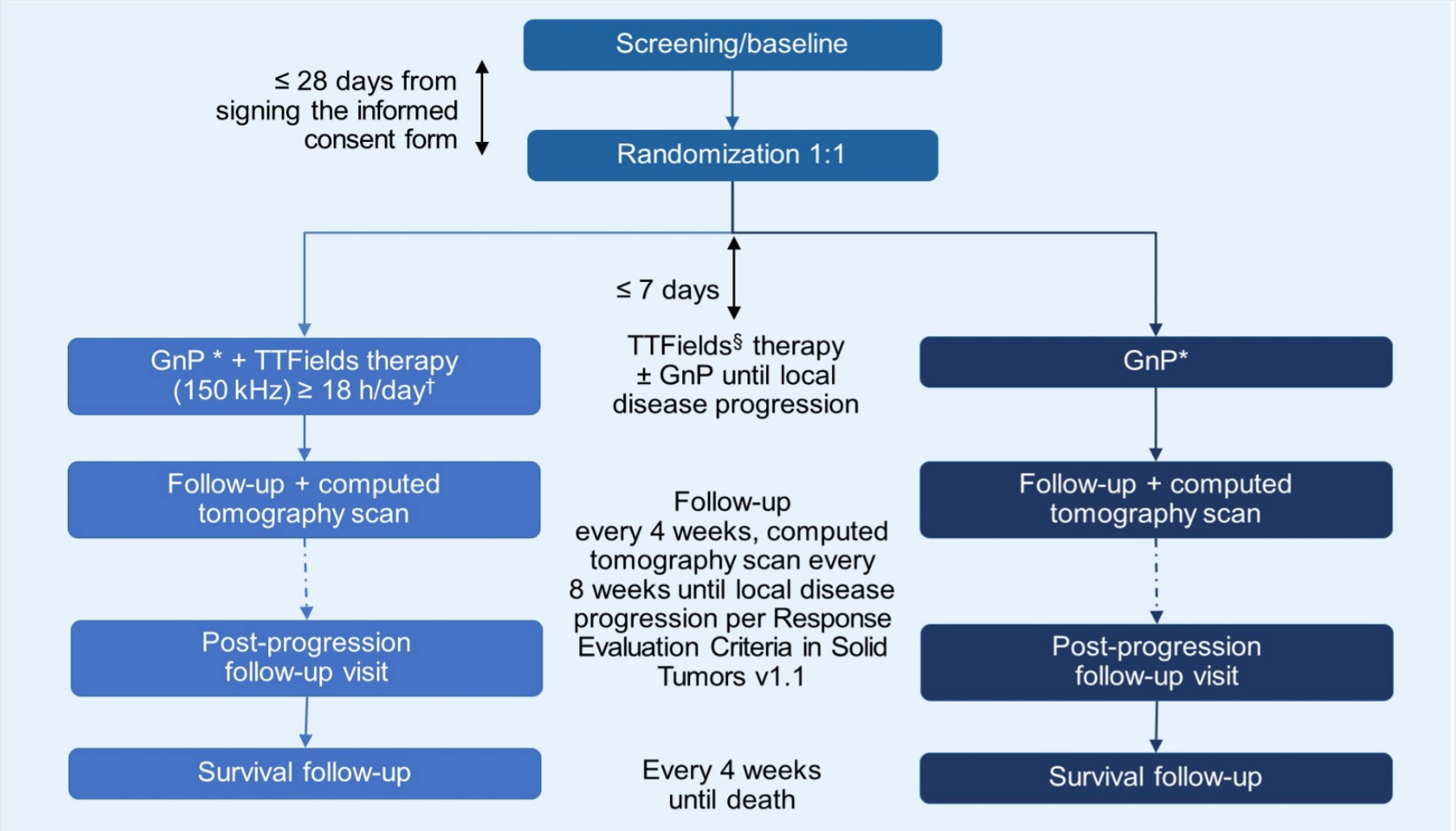
- TTFields have demonstrated survival benefit in glioblastoma.
- The treatment benefit of TTFields in a number of cancer types, including NSCLC, ovarian cancer, mesothelioma and brain metastases, is under investigation.
- This first proof-of-concept clinical study of TTFields in pancreatic cancer was initiated based on preclinical data on TTFields in pancreatic cancer models.

	TTFields + gemcitabine cohort (n = 20)	TTFields + gemcitabine + *nab* paclitaxel cohort (n = 20)
Median PFS	8.3 mo	12.7 mo
Median OS	14.9 mo	Not reached

Rivera F et al. *Pancreatology* 2019;19(1):64-72.

RTP RESEARCH TO PRACTICE

PANOVA-3: An Ongoing Phase III Study of TTFields with Gemcitabine and *Nab* Paclitaxel as Front-Line Therapy for Locally Advanced Pancreatic Adenocarcinoma



Picozzi VJ et al. Gastrointestinal Cancers Symposium 2023;Abstract TPS770.

PANOVA-3: A Phase III study of tumor treating fields with gemcitabine/*nab* paclitaxel as front-line treatment for locally advanced PDAC (LAPC): What are your thoughts on the clinical need being addressed?

 Dr O'Reilly	Interesting strategy, safe, well tolerated, would love to understand mechanism
 Dr Wainberg	LAPC is understudied, so it will provide value of a local therapy here
 Dr Bekaii-Saab	LAPC remains very challenging with very few patients achieving resection and almost none are curable
 Dr Ciombor	Need for better treatments for LAPC is high, but not sure this is the best way
 Dr Messersmith	We need a locoregional intervention in LAPC that adds efficacy over systemic therapy and better control of disease. Radiation therapy has not shown enough survival benefit
 Dr Philip	There is a very high clinical need in LAPC
 Dr Pishvaian	TTFields seem to have very limited efficacy, don't make much scientific sense, and require a lot from the patient

PDAC = pancreatic adenocarcinoma

RTP RESEARCH TO PRACTICE

APOLLO: A randomized Phase II study of olaparib versus placebo after curative-intent therapy for patients with resected pancreatic cancer and a BRCA1, BRCA2 or PALB2 mutation: What are your thoughts on the clinical need being addressed?

 Dr O'Reilly	Very straightforward, practical design and addresses a very practical question for a small patient population. Potential for practice change
 Dr Wainberg	Important
 Dr Bekaii-Saab	Although more patients are achieving cure from early-stage PDAC, most will recur and eventually die from their disease. This study addresses an important question for a subgroup with BRCA or PALB mutations
 Dr Ciombor	Important to utilize and investigate targeted therapies in pancreas cancer when we can
 Dr Messersmith	This is an important study addressing 5%-7% of patients with BRCA mutations. However, overall impact is limited given the very low frequency of BRCA mutations
 Dr Philip	Very high unmet need to improve cure rates (relapse-free survival times) for resected patients
 Dr Pishvaian	Could be effective for a small subset

RTP RESEARCH TO PRACTICE

NEO-Nal-IRI: A Phase II study of NALIRIFOX as preoperative treatment for PDAC: What are your thoughts on the clinical need being addressed?

 Dr O'Reilly	Single-arm Phase II important proof of principle study – under way, adds to other neoadjuvant trials
 Dr Wainberg	If we can prove a role for neoadjuvant, it will eliminate adjuvant
 Dr Bekaii-Saab	Although improved preoperative approaches are needed to continue enhancing outcomes for early-stage PDAC, I am not sure another chemo backbone, at best slightly better than FOLFIRINOX, is the right strategy
 Dr Ciombor	FOLFIRINOX is an adequate neoadjuvant chemo regimen for PDAC – in metastatic setting, though no head-to-head comparisons, NALIRIFOX not significantly better or less toxic than mFFX but much more expensive – would not expect this to be different in the neoadjuvant setting
 Dr Messersmith	Not a major need by any means because at best it may offer a marginal benefit over existing strategies
 Dr Philip	The role of neoadjuvant therapy for resectable PDAC is very important, BUT there are ongoing, definitive Phase III trials
 Dr Pishvaian	We have FOLFIRINOX already, so we don't need this trial

RTP RESEARCH TO PRACTICE

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Research To Practice

Current and Future Role of Biomarker-Based Decision-Making in Metastatic Pancreatic Cancer

Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

08-03 2023

Memorial Sloan Kettering Cancer Center

Research To Practice

PDAC: Standard Therapy & Genomically Defined 2023 →

Untreated mPDAC
ECOG 0-1

DNA Damage Repair Directed Therapy

Courtesy of Eileen M O'Reilly, MD

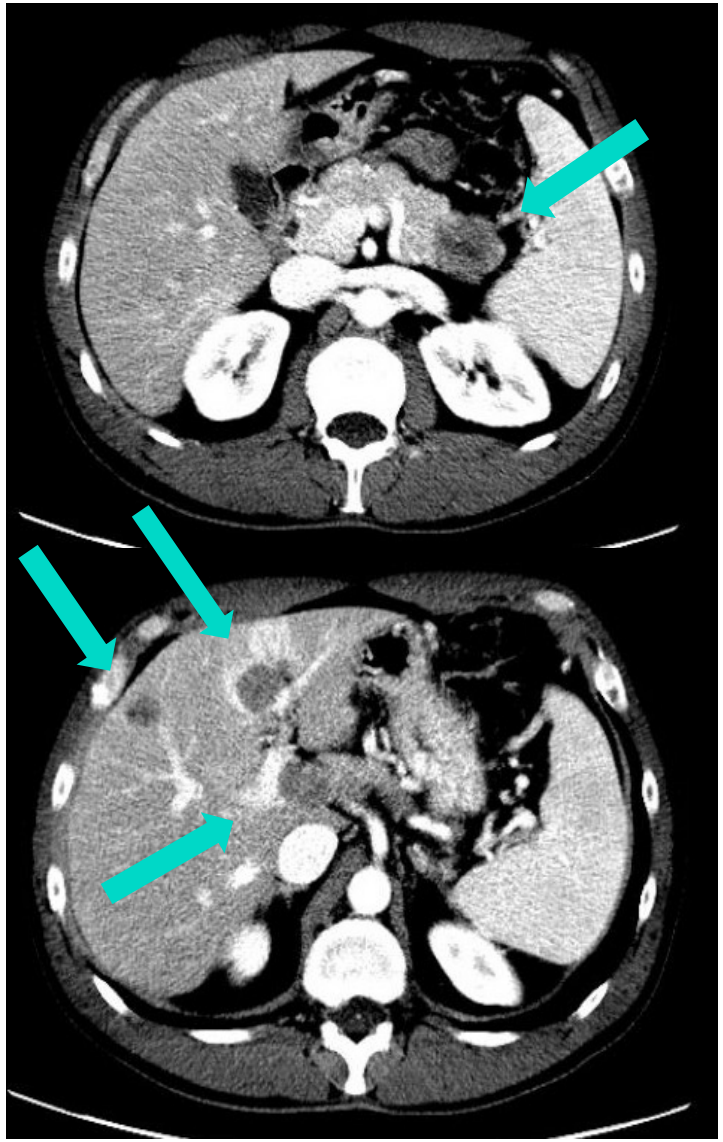
Research To Practice

Case #1A: g*BRCA2*

52-year-old female

- 1 year history of progressive back pain
- Fm Hx g*BRCA2,* prostate ca
- CT: Tail primary, liver, nodes
- Ca 19-9 8,613 IU, CEA 14.1
- Cisplatin/gemcitabine x 8 cycles
- Confirmed g*BRCA2*
- Somatic: *KRAS* G12D*, TP53*, *ARID1A*
  MSS, TMB 2.3 Mut/Mb

- Maintenance therapy decision

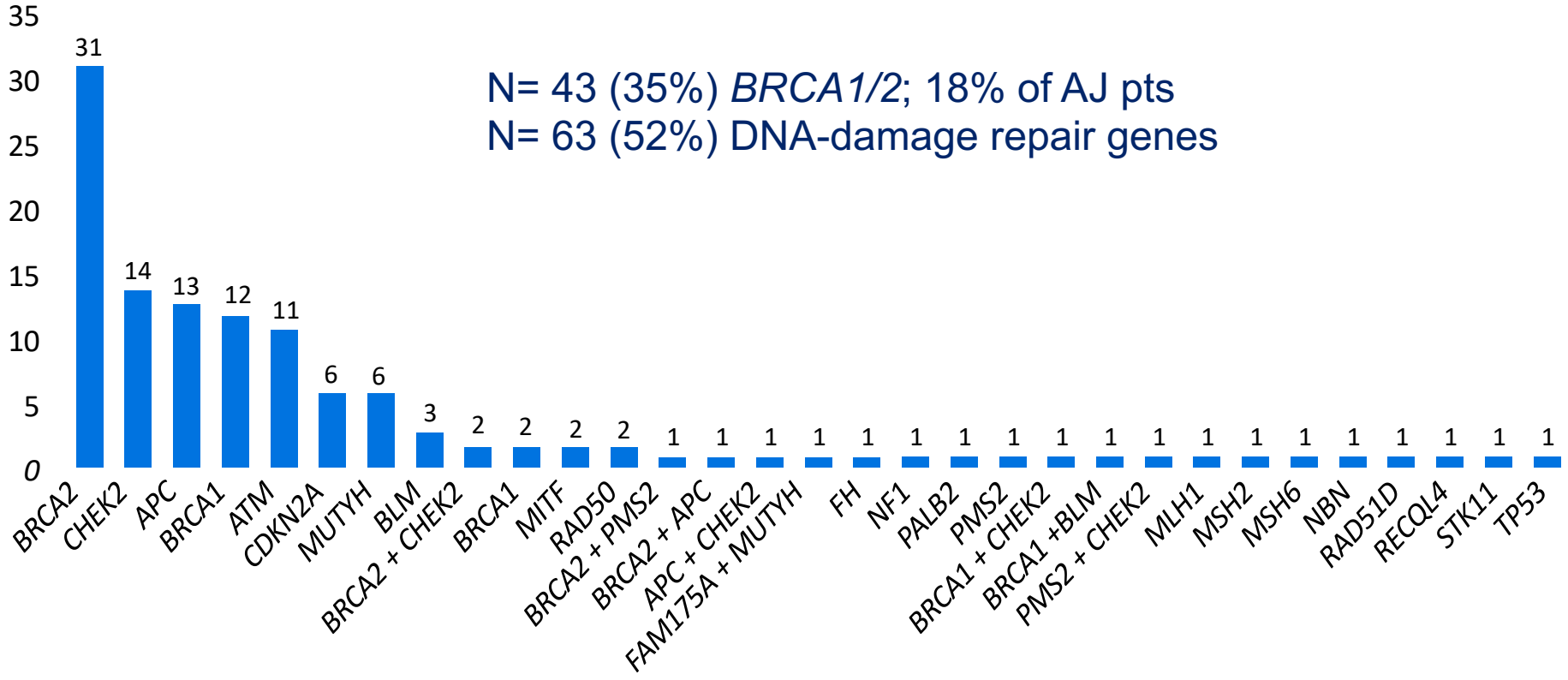


Courtesy of Eileen M O'Reilly, MD

Research To Practice

Pathogenic Germline Alterations in PDAC

N= 122/615 in 24 genes; 19%



N= 43 (35%) *BRCA1/2*; 18% of AJ pts

N= 63 (52%) DNA-damage repair genes

Pancreas cancer: Core HRD: 5-8% (including somatic *BRCA1/2, PALB2)*

Lowery. M.. J Nat Cancer Inst, 2018. Park, W…O'Reilly, EM. JAMA, 2021

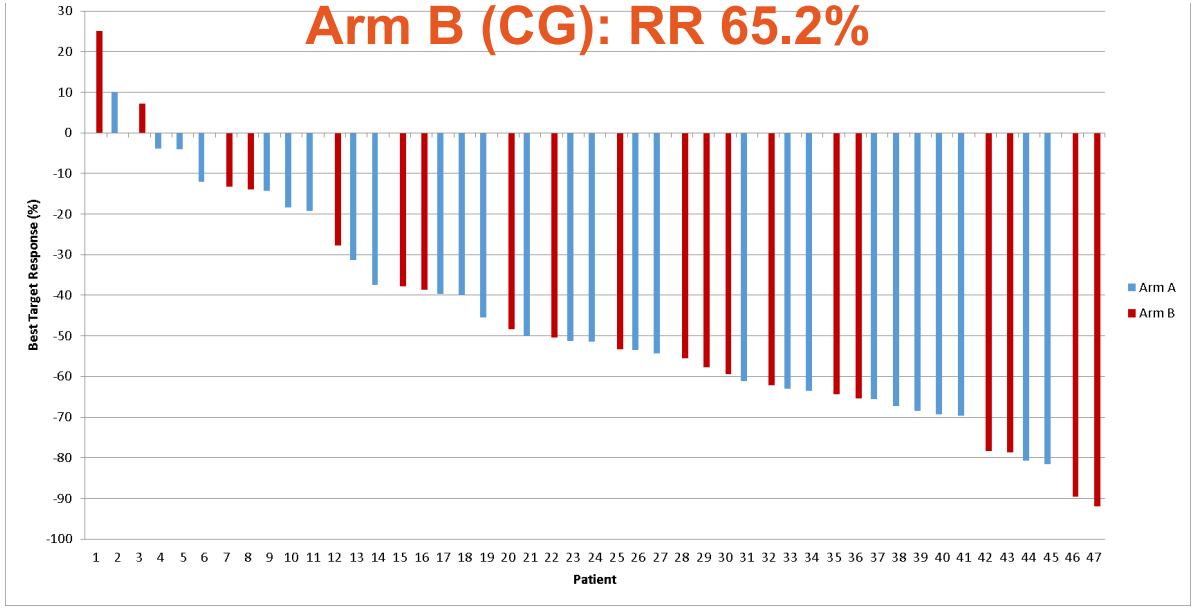
Courtesy of Eileen M O'Reilly, MD

Research To Practice

Cisplatin/Gem +/- Veliparib g*BRCA1/2, PALB2*: Randomized Phase II Advanced PDAC

Arm A (CGV): RR 74.1%

Arm B (CG): RR 65.2%



	Cis, Gem, V N= 27	Cis, Gem N= 23
Response Rate	74%	65%
Overall Survival	15.5 m	16.4 m
Combined Analyses (N= 50)		
2-Year OS	31% (CI 17.8%- 44.4%)	
3-Year OS	18% (CI:8.1%- 30.7%)	
Platinum → PARPi	23 m (CI: 6.5- 53.9)	

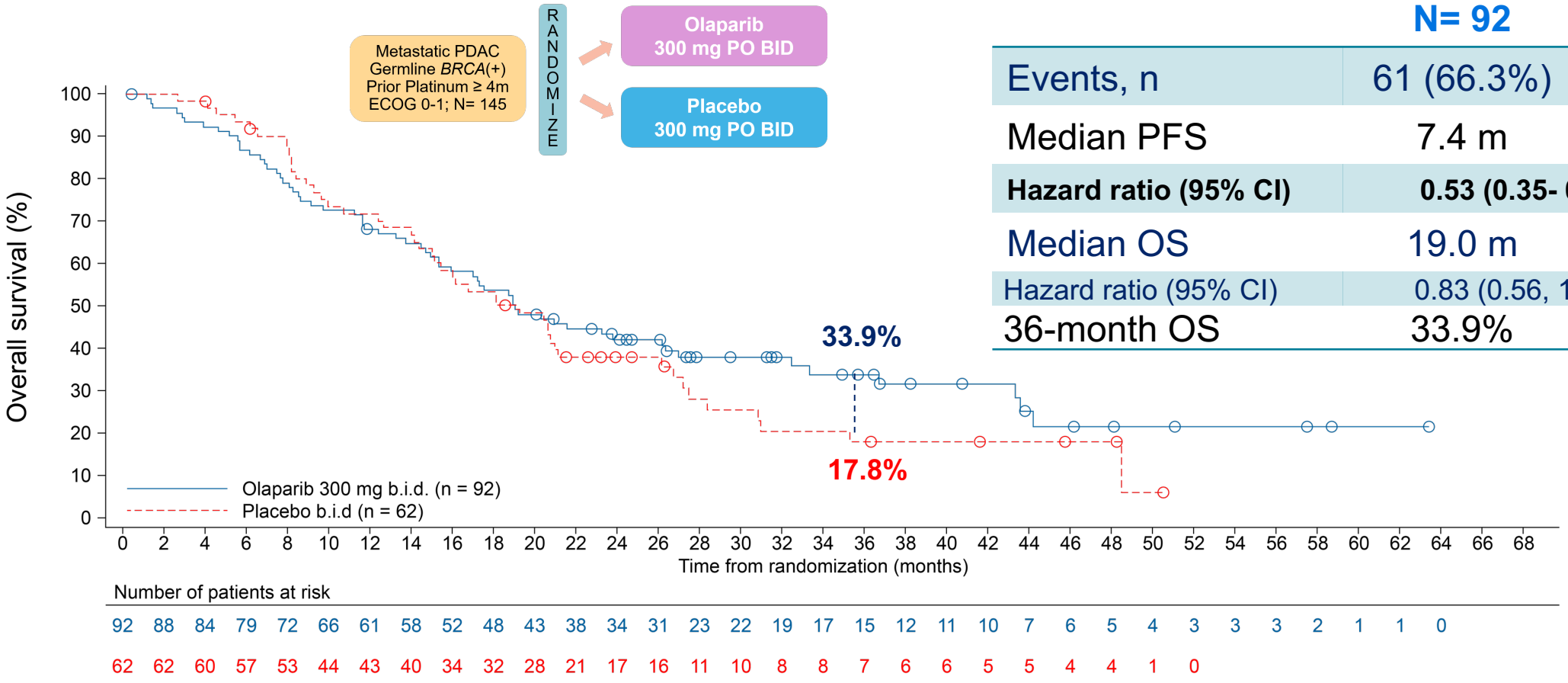
- Defines a standard regimen *BRCA1/2, PALB2*

O'Reilly, EM…Kelsen, DP. J Clin Oncol, 2020

Courtesy of Eileen M O'Reilly, MD

Research To Practice

POLO g*BRCA*: Maintenance Olaparib vs Placebo



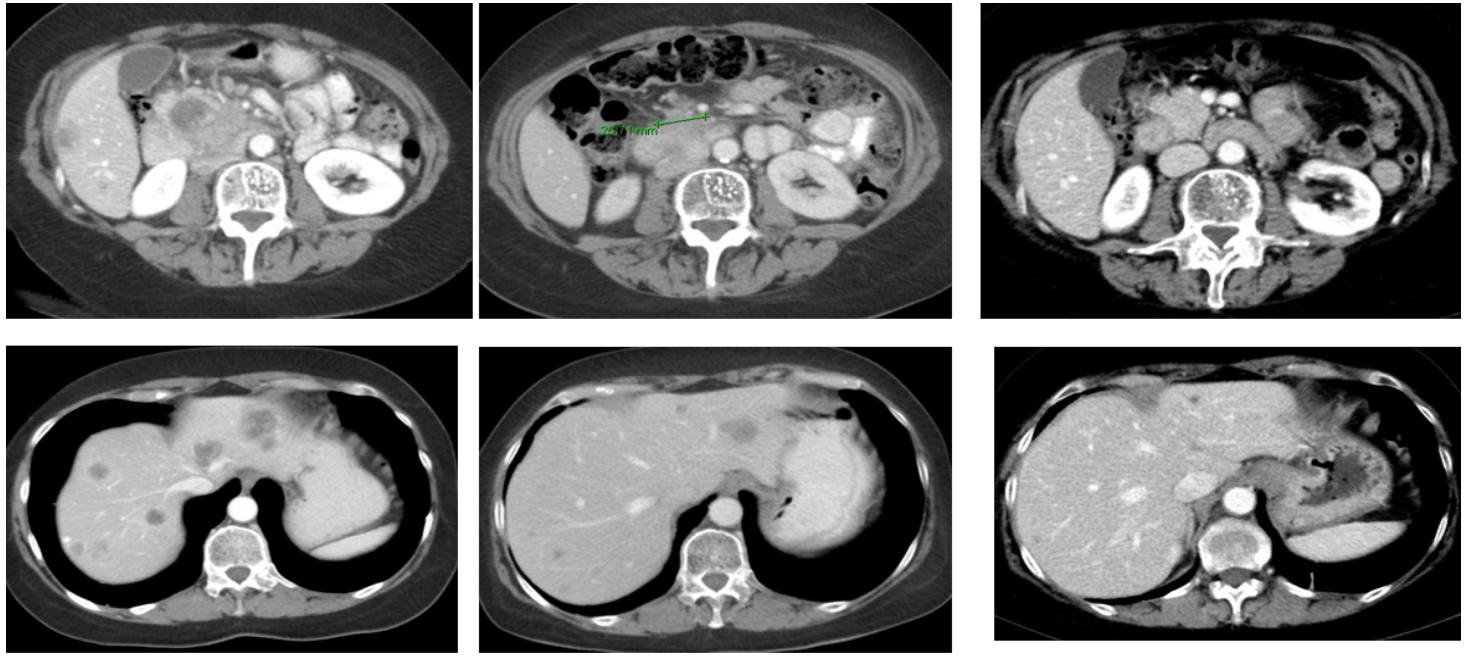
	Olaparib N= 92	Placebo N= 62
Events, n	61 (66.3%)	47 (75.8%)
Median PFS	7.4 m	3.8 m
Hazard ratio (95% CI)	**0.53 (0.35- 0.82); p= 0.004**	
Median OS	19.0 m	19.2 m
Hazard ratio (95% CI)	0.83 (0.56, 1.22); p= 0.3487	
36-month OS	33.9%	17.8%

Golan, T. New Eng J Med, 2019
Kindler, H. J Clin Oncol, 2022

Courtesy of Eileen M O'Reilly, MD

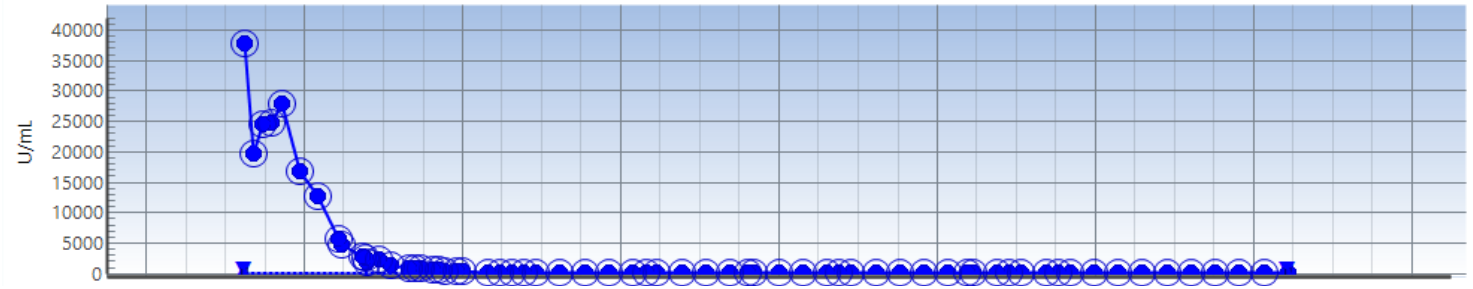
Research To Practice

Case #1B: 66 Years F: Platinum → PARPi g*BRCA* Met PDAC



Platinum → PARP Inhibitor →

Ca 19-9 37,500+

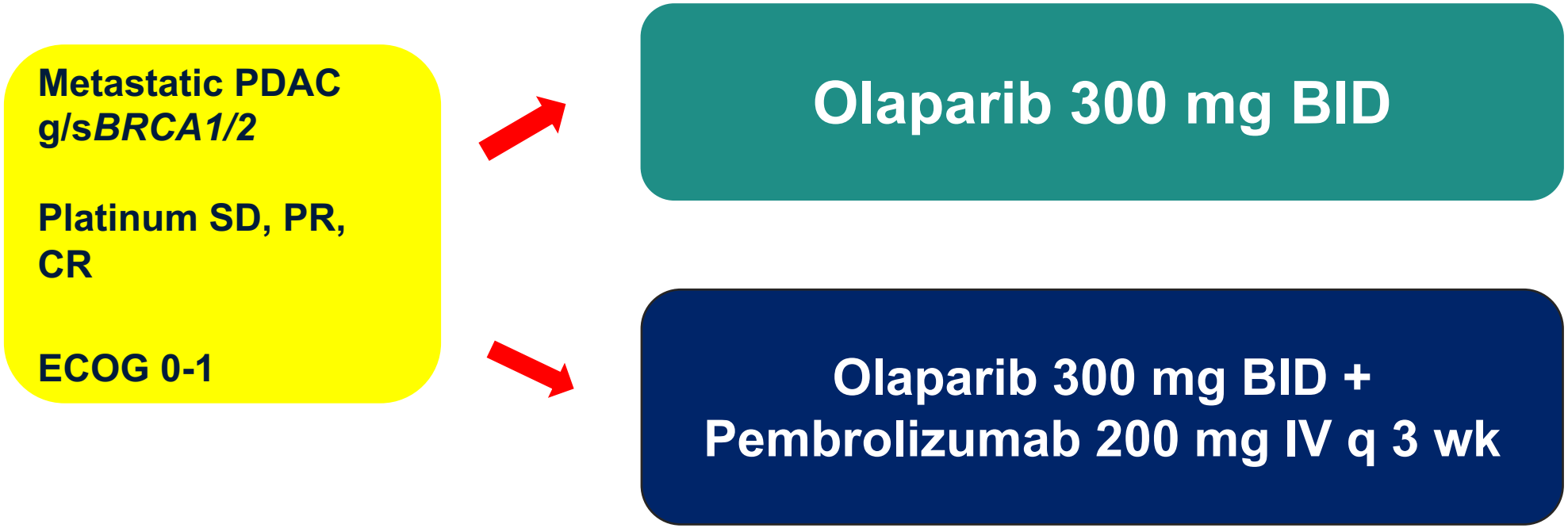


Ca 19-9 <ULN

Courtesy of Eileen M O'Reilly, MD

Research To Practice

SWOG S2001: Olaparib +/- Pembrolizumab Maintenance Trial… Building on POLO



Primary endpoint: PFS (HR 0.6; 7→ 11.7 m)

Chung, V (SWOG), Pishvaian, M (Alliance). NCT04548752

Courtesy of Eileen M O'Reilly, MD

Research To Practice

APOLLO EA2192: Adjuvant Olaparib vs Placebo PDAC

Primary endpoint: Relapse free survival 22 → 44 months (90% power, 1 sided alpha; HR 0.5)
Stratify: R0 vs R1; Platinum vs Non-platinum; Neoadjuvant vs No

Reiss Binder, K (ECOG); Kasi, A (SWOG); Pishvaiain, M, O'Reilly, EM (Alliance) NCT04858334

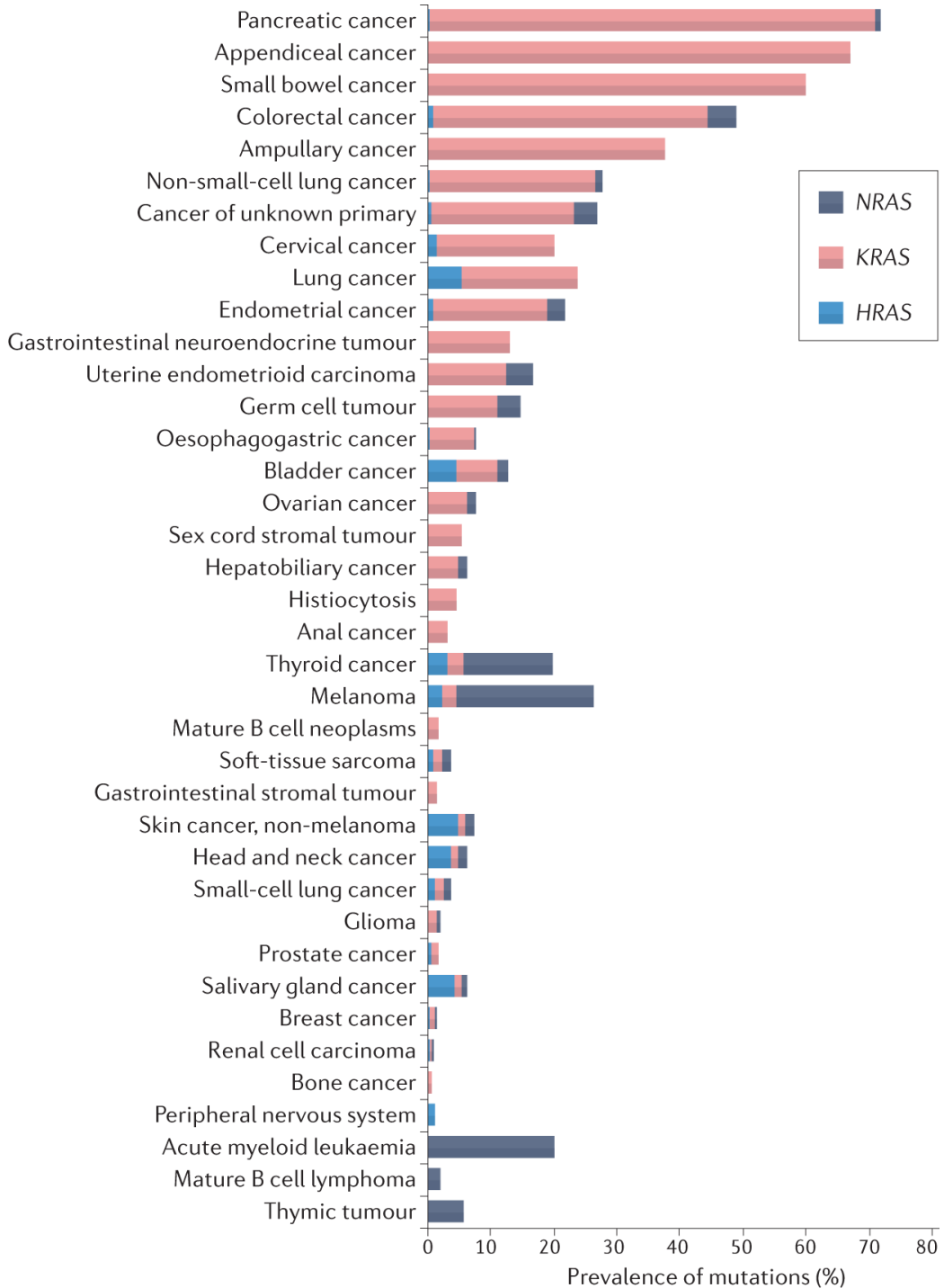
Courtesy of Eileen M O'Reilly, MD

KRAS Directed Therapy

Courtesy of Eileen M O’Reilly, MD

Research To Practice

RAS Mutation Type per Disease



cbioportal TCGA, MSK IMPACT Cohorts, 2022

Courtesy of Eileen M O'Reilly, MD

Research To Practice

Case #2: 67-Year-Old F, *KRAS* G12C

Metastatic PDAC peritoneum, small lung mets

Never smoker

Strong Fm Hx cancer; germline NEG

Somatic genomics:
KRAS G12C, SMAD4, CDKN2A/B, MTAP
MSS, TMB 1.6 Mut/Mb

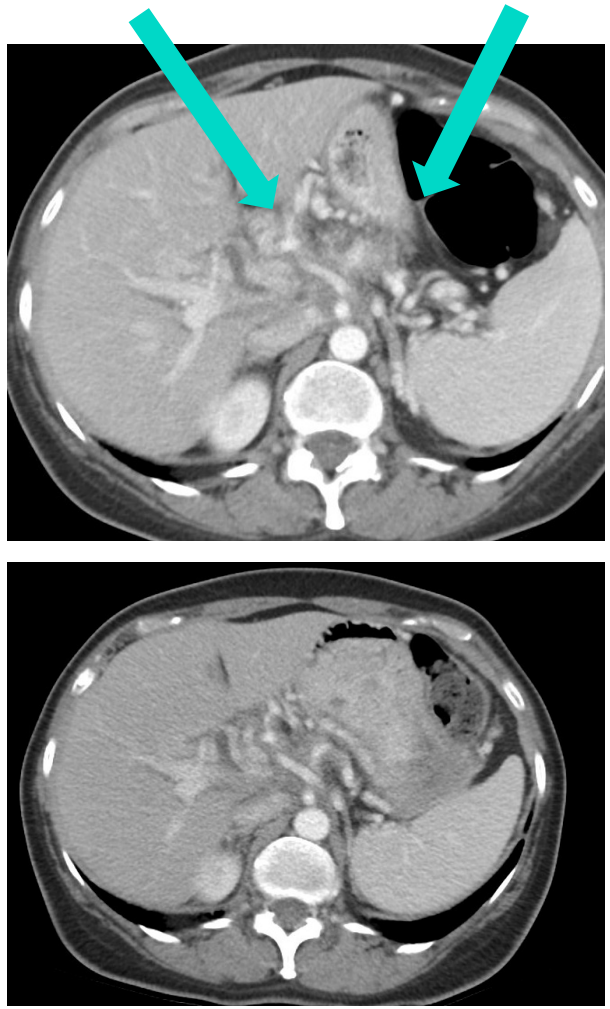
<u>Treatment Course</u>

mFOLFIRINOX (poorly tolerated); POD

Gemcitabine, nab-Paclitaxel; POD

Investigational *KRAS* G12C inhibitor x 1 year: SD

Major clinical improvement: ↓ pain, ↑5 kg+, returned to work



Courtesy of Eileen M O'Reilly, MD

Research To Practice

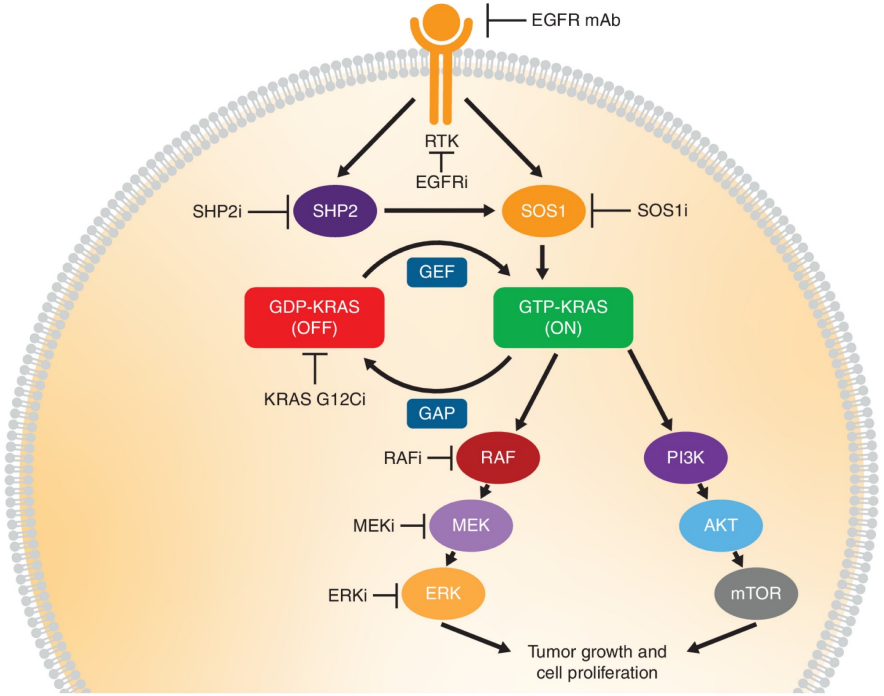
Allele Specific Small Molecule *KRAS* G12C Inhibition

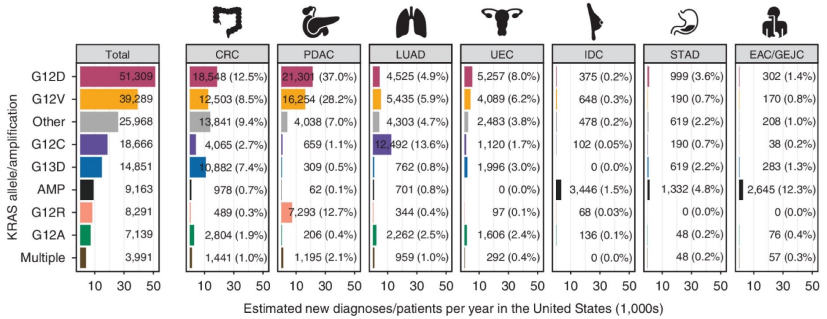
KRAS^{G12C} covalent Inhibitors target approx. 13% of *KRAS* driven cancers

12 Cysteine residue
Allosteric pocket on *KRAS* locks GTP bound G12C form in inactive state

Proof of principle targeting *KRAS* G12C

Most current inhibitors target GDP-bound ‘OFF’ form of *KRAS*
Some drugs targeting cyclophilin A, ‘ON’ state



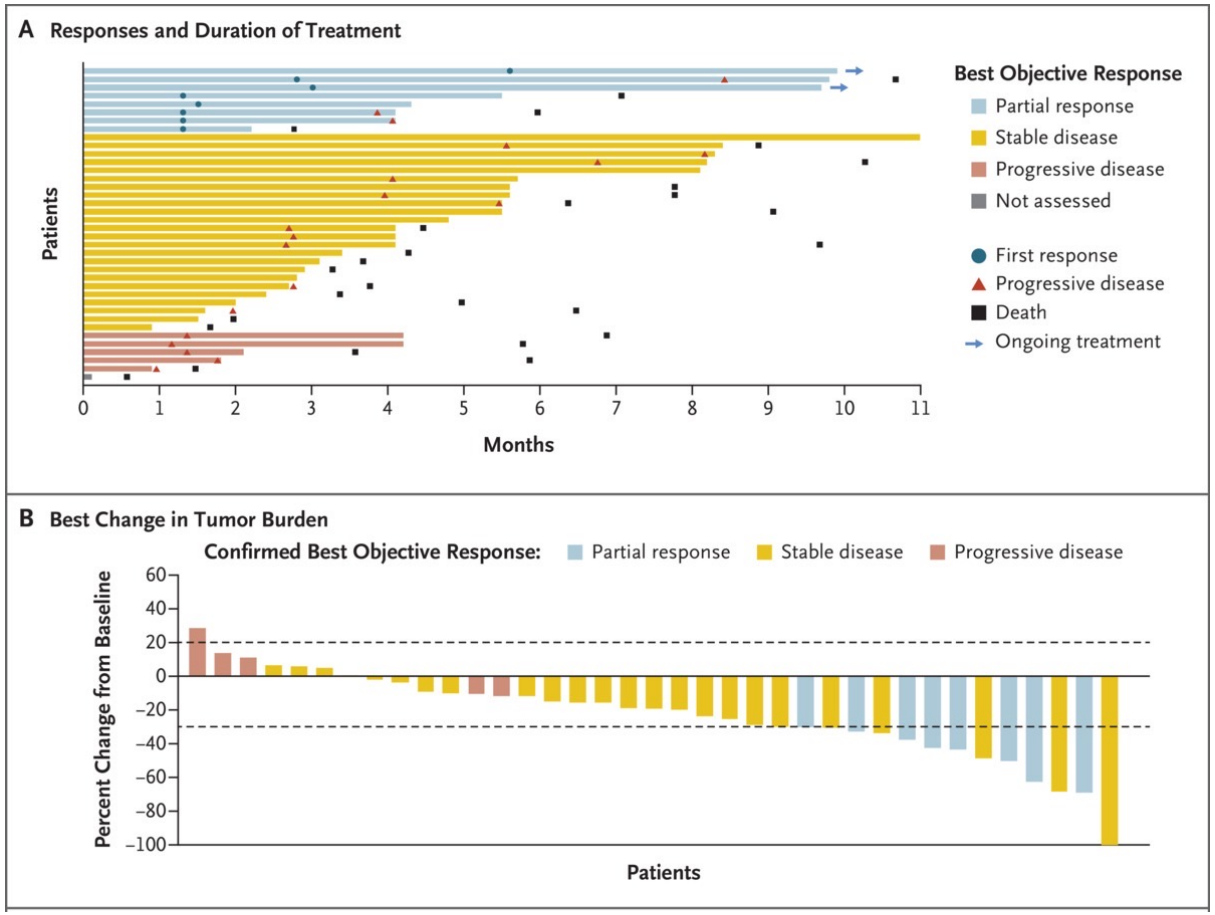


Hoffman, M. Cancer Discovery, 2022
Ostrem, JM.. Shokat, KM. Nature, 2013. Asmigil, H. JCI insight, 2022

Courtesy of Eileen M O’Reilly, MD

Research To Practice

Allele Covalent Specific *KRAS* G12C Sotorasib in PDAC: CodeBreaK 100 Phase I/II Trial



Sotorasib (AMG510) 960 mg PO daily;
KRAS G12C (Glyceine → Cysteine)

Summary

N= 38 PDAC
Median 2 lines (1-8)
RR 21% (N= 8)
mDOR 5.7 m (1.9- NR)
mPFS 4.0 m (2.8- 5.6)
mOS 6.9 m (5.0- 9.1)

Hong, DS….Li, B. NEJM, 2020. NCT03600883, NCT03785249, NCT04006301

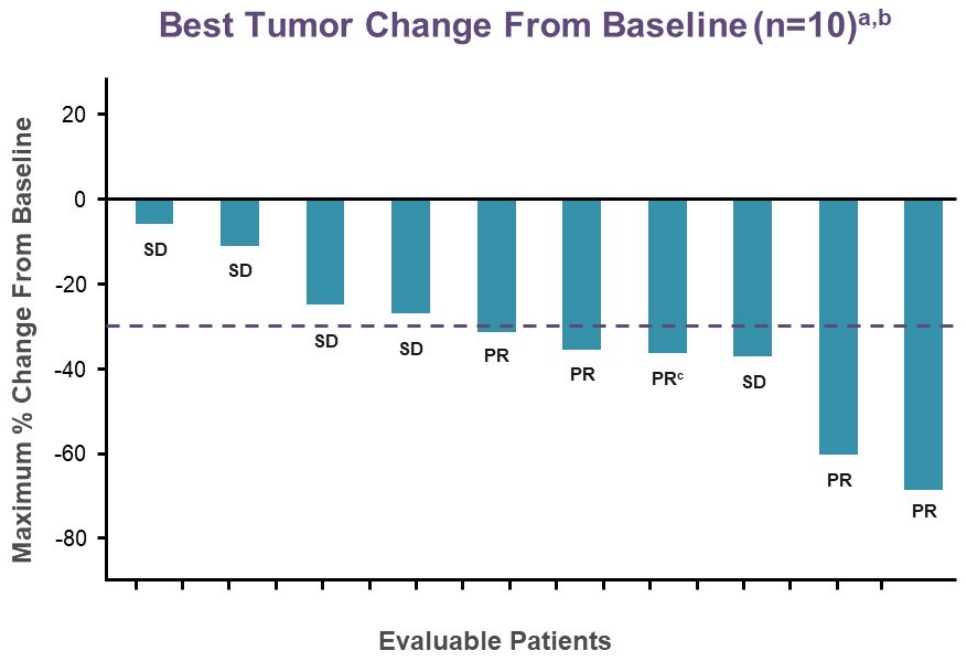
Strickler, JH…Hong, DS, NEJM, 2023

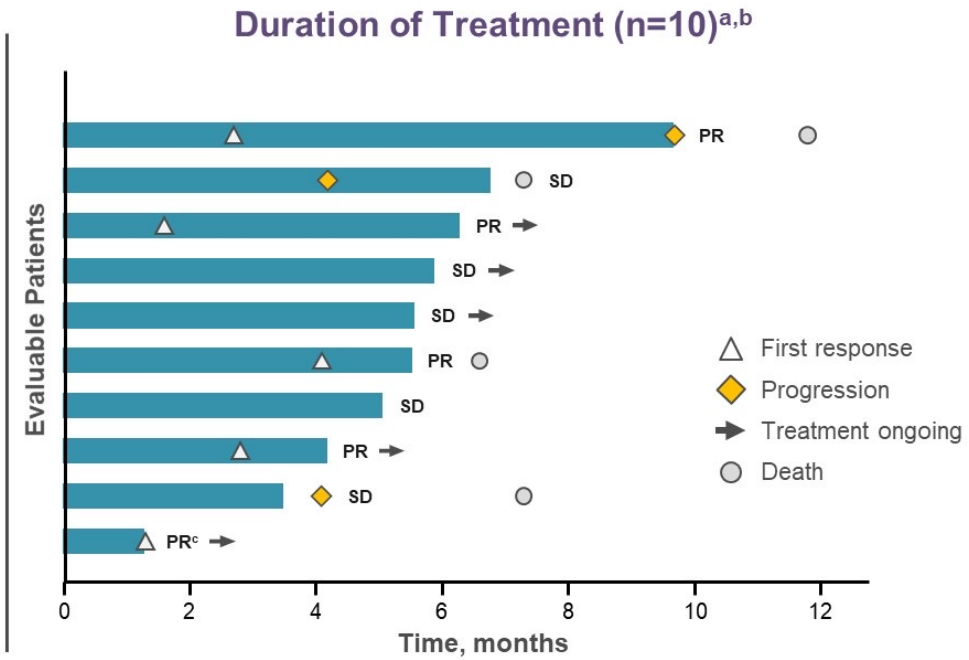
Courtesy of Eileen M O'Reilly, MD

Research To Practice

KRYSTAL-1: Adagrasib *KRAS* G12C in PDAC (N= 12; 21)

Adagrasib 600 mg PO BID; *KRAS* G12C (Glyceine → Cysteine)





Updated Cohort:

Median lines therapy: 2.5

Median RR 33% Median duration of response 6.9 m

Median PFS 5.4 m; Median OS: 8 m

Bekaii-Saab, T….Pant, S. J Clin Oncol, 2023

Pant, S. ASCO Virtual Plenary 2023

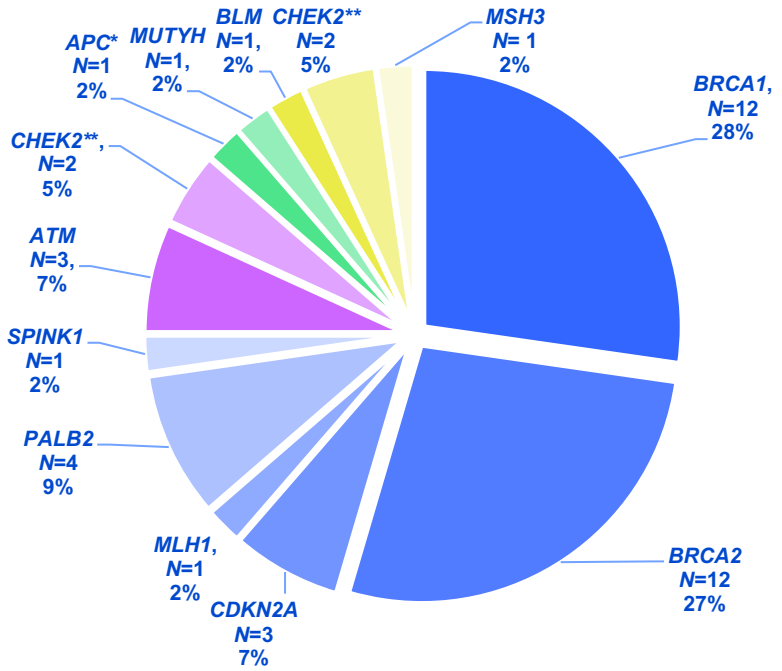
NCT03785249

Courtesy of Eileen M O'Reilly, MD

Research To Practice

Early Onset PDAC (≤ 50 years): Germline & *KRAS* Alterations

N= 450 ≤ 50 years 01/2008- 07/2019



32% (44/138) Pathogenic/LPV

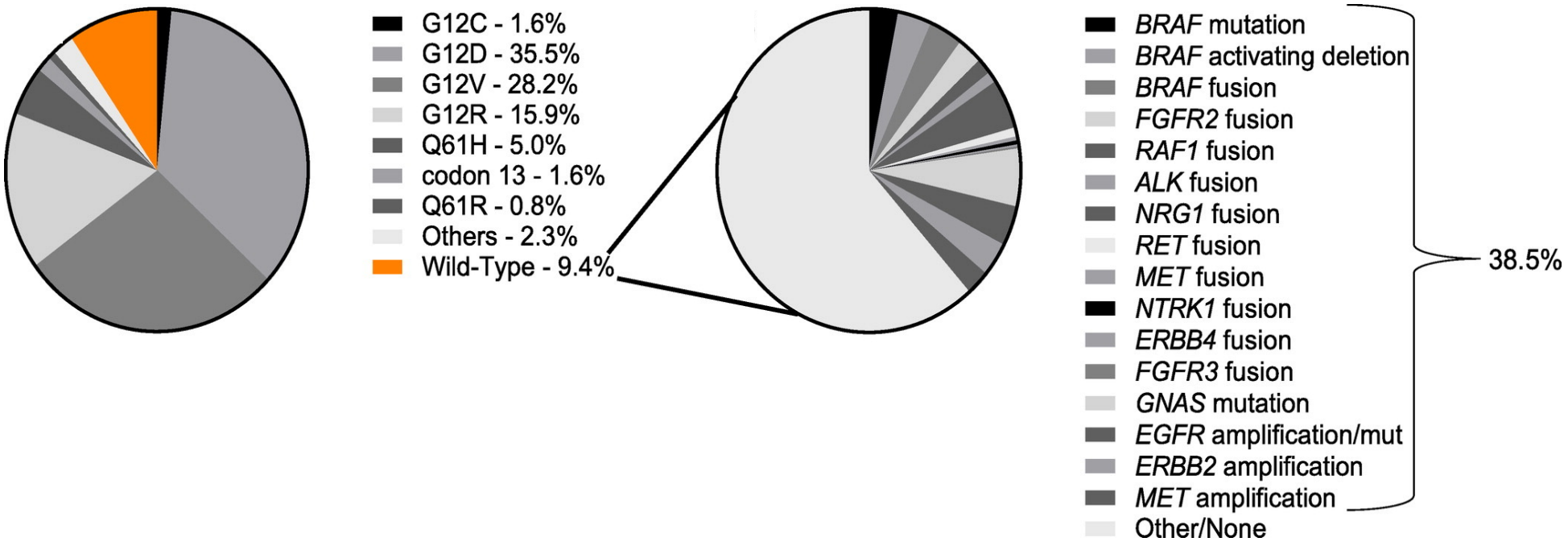
***KRAS* Alteration**	**N**	**Percent**
KRAS Alterations	110	83%
KRAS Amplification	1	1%
KRAS G12D	58	44%
KRAS G12V	25	19%
KRAS G12R	13	9%
KRAS G12C	1	1%
KRAS G12L	1	1%
KRAS Q61X	9	6%
NRAS Q61R	1	1%
***RAS* wild-type**	**21**	**16%**

Varghese, A... O'Reilly, EM. J Nat Can Inst, 2021. Singhi, AD. Gastroenterology, 2019

Courtesy of Eileen M O'Reilly, MD

Research To Practice

KRAS Wild-Type PDAC (~8% All PDAC)

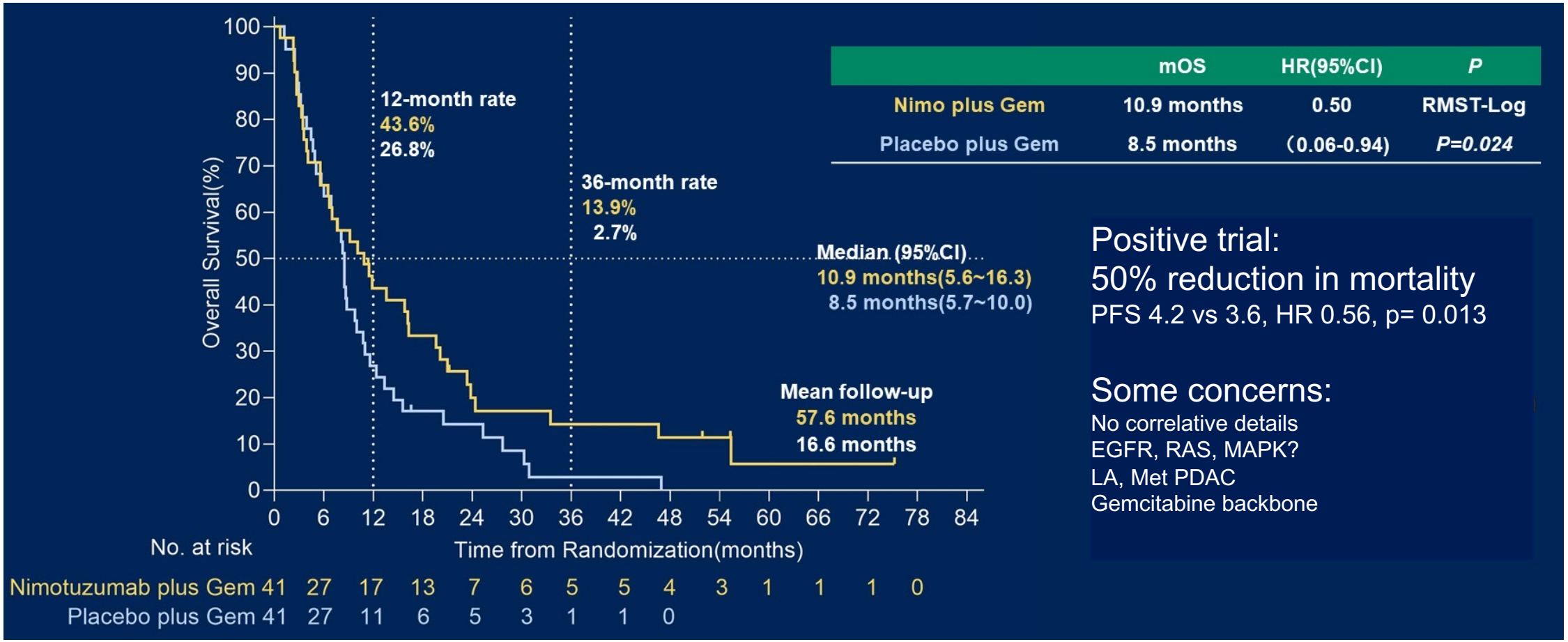


Lee, MS, Pant, S. ASCO Educational Book, 2021

Courtesy of Eileen M O'Reilly, MD

Research To Practice

Phase III NOTABLE Trial
Gemcitabine +/- Nimotuzumab *KRAS* WT PDAC



	mOS	HR(95%CI)	*P*
Nimo plus Gem	10.9 months	0.50	RMST-Log
Placebo plus Gem	8.5 months	(0.06-0.94)	*P=0.024*

Positive trial:
50% reduction in mortality
PFS 4.2 vs 3.6, HR 0.56, p= 0.013

Some concerns:
No correlative details
EGFR, RAS, MAPK?
LA, Met PDAC
Gemcitabine backbone

Qin, S. ASCO, 2022 Abstract LBA 4011 (In review)

Courtesy of Eileen M O'Reilly, MD

Research To Practice

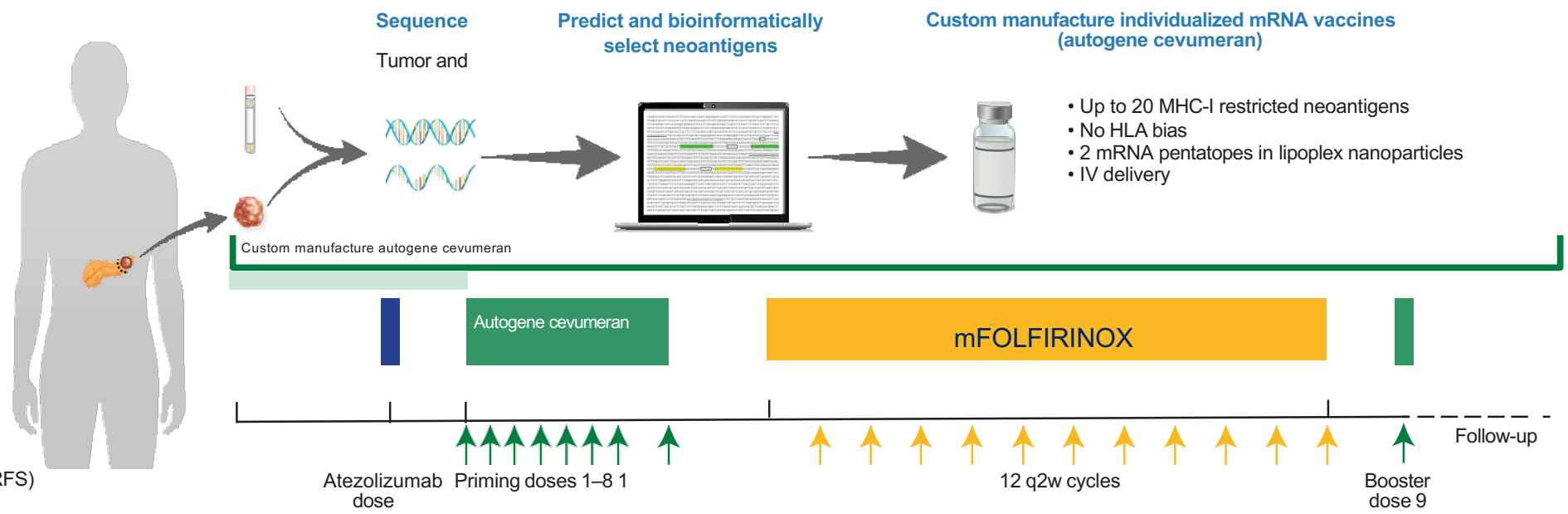
Personalized Neoantigen Vaccines: Phase I Trial Autogene Cevumeran in Resected PDAC

Investigator-initiated single-center phase I Target accrual: 20 patients

Eligible patients with PDAC:
- All surgically resectable
  - No borderline resectable
  - No locally advanced/metastatic
  - No neoadjuvant therapy

Primary endpoint: Safety

Other endpoints:
- Immunogenicity
- Feasibility
- 18-month recurrence-free survival (RFS)



Vaccination: safe, feasible, in clinically relevant timeline
Personalized mRNA vaccine expands neoantigen specific T cells; Highly immunogenic in 50%
Immunity adjudicated: Elispot, T cell expansion; Immune responder required both (+)
mRFS: Not Reached (N= 8) vs 13.7 m (N= 8) in immune responders vs non-responders, HR 0.08, p= 0.03

Rojas, L….O'Reilly, EM, Balachandran, V. Nature, 2023

Courtesy of Eileen M O'Reilly, MD

Agenda

INTRODUCTION

MODULE 1: Selection and Sequencing of Therapy for Patients with Metastatic Pancreatic Cancer

MODULE 2: Ongoing Clinical Trials

MODULE 3: Current and Future Role of Biomarker-Based Decision-Making in Metastatic Pancreatic Cancer

MODULE 4: Clinical Investigator Survey

Regulatory and reimbursement issues aside, what would you generally recommend as neoadjuvant therapy for a 65-year-old patient with BRCA wild-type pancreatic adenocarcinoma (PDAC) and no significant comorbidities if the disease was ...?

	Borderline resectable	Resectable
 Dr O'Reilly	Modified FOLFIRINOX	Pending specific characteristics
 Dr Wainberg	FOLFIRINOX	None
 Dr Bekaii-Saab	FOLFIRINOX +/- CRT	FOLFIRINOX
 Dr Ciombor	FOLFIRINOX +/- CRT	FOLFIRINOX
 Dr Messersmith	FOLFIRINOX	FOLFIRINOX
 Dr Philip	FOLFIRINOX + CRT	FOLFIRINOX
 Dr Pishvaian	FOLFIRINOX	FOLFIRINOX

FOLFIRINOX = leucovorin/fluorouracil/irinotecan/oxaliplatin; CRT = chemoradiation therapy

Regulatory and reimbursement issues aside, what would you generally recommend as adjuvant therapy after primary surgery for a 65-year-old patient with BRCA wild-type PDAC and no significant comorbidities?

 Dr O'Reilly	Modified FOLFIRINOX
 Dr Wainberg	Modified FOLFIRINOX
 Dr Bekaii-Saab	Modified FOLFIRINOX
 Dr Ciombor	Modified FOLFIRINOX
 Dr Messersmith	Modified FOLFIRINOX
 Dr Philip	Modified FOLFIRINOX
 Dr Pishvaian	Modified FOLFIRINOX

Regulatory and reimbursement issues aside, what would you generally recommend as first-line therapy for a 65-year-old patient with no significant comorbidities and moderately symptomatic BRCA wild-type metastatic PDAC (mPDAC) to the liver, bone and lungs?

 Dr O'Reilly	Modified FOLFIRINOX
 Dr Wainberg	NALIRIFOX
 Dr Bekaii-Saab	NALIRIFOX
 Dr Ciombor	Modified FOLFIRINOX
 Dr Messersmith	FOLFIRINOX
 Dr Philip	Modified FOLFIRINOX
 Dr Pishvaian	Modified FOLFIRINOX

FOLFIRINOX = leucovorin/fluorouracil/irinotecan/oxaliplatin; NALIRIFOX = liposomal irinotecan/oxaliplatin/leucovorin/fluorouracil

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you generally recommend as first-line therapy for a 65-year-old patient with no significant comorbidities and asymptomatic BRCA wild-type mPDAC to the lymph nodes and lungs?

 Dr O'Reilly	Modified FOLFIRINOX
 Dr Wainberg	NALIRIFOX
 Dr Bekaii-Saab	NALIRIFOX
 Dr Ciombor	Modified FOLFIRINOX
 Dr Messersmith	FOLFIRINOX
 Dr Philip	Modified FOLFIRINOX
 Dr Pishvaian	Modified FOLFIRINOX

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for a 65-year-old patient with BRCA wild-type mPDAC and no significant comorbidities who received first-line gemcitabine/*nab* paclitaxel?

 Dr O'Reilly	Modified FOLFIRINOX
 Dr Wainberg	Modified FOLFIRINOX
 Dr Bekaii-Saab	Nal-IRI + 5-FU/LV
 Dr Ciombor	Modified FOLFIRINOX
 Dr Messersmith	Modified FOLFIRINOX
 Dr Philip	Nal-IRI + 5-FU/LV
 Dr Pishvaian	Nal-IRI + 5-FU/LV

Nal-IRI = nanoliposomal irinotecan; LV = leucovorin

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for a 65-year-old patient with BRCA wild-type mPDAC and no significant comorbidities who received first-line modified FOLFIRINOX?

 Dr O'Reilly	Gemcitabine/*nab* paclitaxel
 Dr Wainberg	Gemcitabine/*nab* paclitaxel
 Dr Bekaii-Saab	q2wk gemcitabine/*nab* paclitaxel
 Dr Ciombor	q2wk gemcitabine/*nab* paclitaxel
 Dr Messersmith	Gemcitabine/*nab* paclitaxel
 Dr Philip	Gemcitabine/*nab* paclitaxel
 Dr Pishvaian	q2wk gemcitabine/*nab* paclitaxel

Nab paclitaxel = nanoparticle albumin-bound paclitaxel

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for a 65-year-old patient with BRCA wild-type mPDAC and no significant comorbidities who received first-line NALIRIFOX?

 Dr O'Reilly	Gemcitabine/*nab* paclitaxel
 Dr Wainberg	Gemcitabine/*nab* paclitaxel
 Dr Bekaii-Saab	q2wk gemcitabine/*nab* paclitaxel
 Dr Ciombor	q2wk gemcitabine/*nab* paclitaxel
 Dr Messersmith	Gemcitabine/*nab* paclitaxel
 Dr Philip	Gemcitabine/*nab* paclitaxel
 Dr Pishvaian	q2wk gemcitabine/*nab* paclitaxel

Regulatory and reimbursement issues aside, what would you generally recommend as first-line therapy for an 80-year-old patient with mild chronic renal failure (CRF), Type 2 diabetes mellitus (DM) and controlled hypertension with moderately symptomatic BRCA wild-type mPDAC to the liver, bone and lungs?

 Dr O'Reilly	Gemcitabine/*nab* paclitaxel (adjusted dose and schedule)
 Dr Wainberg	Modified FOLFIRINOX or NALIRIFOX
 Dr Bekaii-Saab	q2wk gemcitabine/*nab* paclitaxel
 Dr Ciombor	q2wk gemcitabine/*nab* paclitaxel
 Dr Messersmith	Modified FOLFIRINOX
 Dr Philip	Lower-dose gemcitabine 800 mg/m^2 and *nab* paclitaxel 100 mg/m^2, q2wk
 Dr Pishvaian	q2wk gemcitabine/*nab* paclitaxel

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you generally recommend as first-line therapy for an 80-year-old patient with mild CRF, Type 2 DM and controlled hypertension with asymptomatic BRCA wild-type mPDAC to the lymph nodes and lungs?

 Dr O'Reilly	Gemcitabine/*nab* paclitaxel (adjusted dose and schedule)
 Dr Wainberg	Modified FOLFIRINOX or NALIRIFOX
 Dr Bekaii-Saab	q2wk gemcitabine/*nab* paclitaxel
 Dr Ciombor	q2wk gemcitabine/*nab* paclitaxel
 Dr Messersmith	Modified FOLFIRINOX
 Dr Philip	Lower-dose gemcitabine 800 mg/m^2 and *nab* paclitaxel 100 mg/m^2, q2wk
 Dr Pishvaian	q2wk gemcitabine/*nab* paclitaxel

Regulatory and reimbursement issues aside, what would you generally recommend as second-line therapy for an 80-year-old patient with BRCA wild-type mPDAC, mild CRF, Type 2 DM and controlled hypertension who received first-line gemcitabine/*nab* paclitaxel?

 Dr O'Reilly	Nal-IRI + 5-FU/LV
 Dr Wainberg	Nal-IRI + 5-FU/LV
 Dr Bekaii-Saab	Nal-IRI + 5-FU/LV
 Dr Ciombor	Continuous infusion 5-FU
 Dr Messersmith	Modified FOLFIRINOX
 Dr Philip	Nal-IRI lower-dose (35-50 mg/m^2) + 5-FU/LV
 Dr Pishvaian	Nal-IRI + 5-FU/LV

RTP RESEARCH TO PRACTICE

For a patient with PDAC and a germline BRCA mutation, what is the optimal point at which to introduce a PARP inhibitor?

 Dr O'Reilly	As part of first-line therapy for metastatic disease
 Dr Wainberg	As part of first-line therapy for metastatic disease
 Dr Bekaii-Saab	As part of first-line therapy for metastatic disease
 Dr Ciombor	As part of first-line therapy for metastatic disease (maintenance)
 Dr Messersmith	As part of first-line therapy for metastatic disease
 Dr Philip	As part of first-line therapy for metastatic disease
 Dr Pishvaian	As part of first-line therapy for metastatic disease (maintenance)

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RESEARCH TO PRACTICE

For a patient with PDAC and a germline BRCA mutation to whom you would administer a PARP inhibitor, how would you do so?

 Dr O'Reilly	As maintenance therapy after platinum-based chemotherapy
 Dr Wainberg	As maintenance therapy after platinum-based chemotherapy
 Dr Bekaii-Saab	If used, as maintenance therapy after platinum-based chemotherapy
 Dr Ciombor	As maintenance therapy after platinum-based chemotherapy
 Dr Messersmith	As maintenance therapy after platinum-based chemotherapy
 Dr Philip	As maintenance therapy after platinum-based chemotherapy
 Dr Pishvaian	As monotherapy, maintenance and third-line therapy for appropriately selected patients

RTP RESEARCH TO PRACTICE

In general, when you administer olaparib, do you initiate preemptive medication for nausea and vomiting?

 Dr O'Reilly	No
 Dr Wainberg	No
 Dr Bekaii-Saab	No
 Dr Ciombor	Yes
 Dr Messersmith	No
 Dr Philip	No
 Dr Pishvaian	No

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TO PRACTICE

Do you reduce the dose of olaparib for patients experiencing toxicity?

 Dr O'Reilly	Yes
 Dr Wainberg	Yes, for bone marrow suppression
 Dr Bekaii-Saab	Yes, for bone marrow suppression and/or GI toxicities
 Dr Ciombor	Yes, from 300 mg → 250 mg; further down to 200 mg if needed
 Dr Messersmith	Yes
 Dr Philip	Yes
 Dr Pishvaian	Yes, from 300 mg po BID → 200 mg → 100 mg

RTP RESEARCH TO PRACTICE

In general, when administering olaparib to a patient with PDAC, do you discuss the risk of developing myelodysplastic syndromes/acute myeloid leukemia?

 Dr O'Reilly	Yes
 Dr Wainberg	No
 Dr Bekaii-Saab	Yes
 Dr Ciombor	Yes
 Dr Messersmith	No
 Dr Philip	Yes
 Dr Pishvaian	Yes

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RESEARCH
TO PRACTICE

To approximately how many patients with mPDAC have you administered olaparib? Approximately how many of these patients have required a transfusion due to anemia?

	Number who received olaparib	Number who required transfusion
 Dr O'Reilly	100	5
 Dr Wainberg	12	7
 Dr Bekaii-Saab	30	2-3
 Dr Ciombor	4	2
 Dr Messersmith	2	0
 Dr Philip	10	2
 Dr Pishvaian	20	1

What is the longest time for which you have maintained a patient with mPDAC on a PARP inhibitor?

 Dr O'Reilly	7-8 years
 Dr Wainberg	3 years
 Dr Bekaii-Saab	130 weeks
 Dr Ciombor	16 weeks
 Dr Messersmith	12 weeks
 Dr Philip	36 weeks
 Dr Pishvaian	Over 5 years

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TO PRACTICE

What is the percent chance that a patient will experience toxicity during treatment with modified FOLFIRINOX that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr O'Reilly	50% to 75% over time	Fatigue, nausea, vomiting, diarrhea, neuropathy
 Dr Wainberg	100%	Neuropathy, GI toxicity
 Dr Bekaii-Saab	25%	Bone marrow suppression, neuropathy and GI toxicity
 Dr Ciombor	30%	Neuropathy
 Dr Messersmith	100% by cycle 4-6	Cytopenias, nausea/vomiting, fatigue
 Dr Philip	30%	Myelosuppression, GI toxicity
 Dr Pishvaian	30%	Myelosuppression or fatigue

What is the percent chance that a patient will experience toxicity during treatment with gemcitabine/*nab* paclitaxel that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr O'Reilly	50%	Fatigue, alopecia, edema, neuropathy, rare HUS, pneumonitis
 Dr Wainberg	100%	Cytopenias, neuropathy
 Dr Bekaii-Saab	Weekly, 40%	Neuropathy and bone marrow suppression
 Dr Ciombor	Weekly, 75%; q2wk, 25%	Cytopenias (weekly)
 Dr Messersmith	100% by cycle 4-6	Cytopenias, fatigue
 Dr Philip	40%	Myelosuppression, neuropathy, fatigue
 Dr Pishvaian	90% (3 on/1 off) 10% (every other week)	Myelosuppression

HUS = hemolytic uremic syndrome

What is the percent chance that a patient will experience toxicity during treatment with olaparib that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr O'Reilly	33%	Anemia, fatigue, nausea, vomiting, diarrhea
 Dr Wainberg	100%	Cytopenias
 Dr Bekaii-Saab	30%	GI toxicity, fatigue and cytopenias
 Dr Ciombor	30%	Cytopenias
 Dr Messersmith	Rarely used	Cytopenias, nausea/vomiting, fatigue
 Dr Philip	25%	Myelosuppression, fatigue
 Dr Pishvaian	50%	Myelosuppression

What is the percent chance that a patient will experience toxicity during treatment with nal-IRI + 5-FU/LV that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr O'Reilly	50%	Fatigue, diarrhea
 Dr Wainberg	100%	GI toxicity
 Dr Bekaii-Saab	25%	GI toxicity
 Dr Ciombor	30%	GI toxicity (diarrhea)
 Dr Messersmith	Rarely used	Cytopenias, diarrhea
 Dr Philip	25%	Myelosuppression, GI toxicity
 Dr Pishvaian	25%	Myelosuppression

What is the percent chance that a patient will experience toxicity during treatment with NALIRIFOX that will require withholding dosing or discontinuation? What is the primary toxicity patients experience that leads to withholding dosing?

	Chance of holding or discontinuation	Primary toxicity
 Dr O'Reilly	50%	Fatigue, nausea, vomiting, diarrhea
 Dr Wainberg	100%	GI toxicity, neuropathy
 Dr Bekaii-Saab	30%	Bone marrow suppression and GI toxicity
 Dr Ciombor	30%	GI toxicity (diarrhea, nausea)
 Dr Messersmith	Never used this agent	N/A
 Dr Philip	25%	Myelosuppression, GI toxicity
 Dr Pishvaian	Not enough experience with this agent	Not enough experience with this agent

Meet The Professor

Optimizing the Management of Melanoma

Thursday, August 10, 2023
5:00 PM – 6:00 PM ET

Faculty

Prof Georgina Long, AO, BSc, PhD, MBBS

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.

CME and MOC credit information will be emailed to each participant within 5 business days.

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