Thank you for joining us.
The program will commence momentarily.

Recent Advances in Medical Oncology: Hepatocellular Carcinoma and Pancreatic Cancer

Wednesday, August 12, 2020

5:00 PM – 6:30 PM ET

Faculty

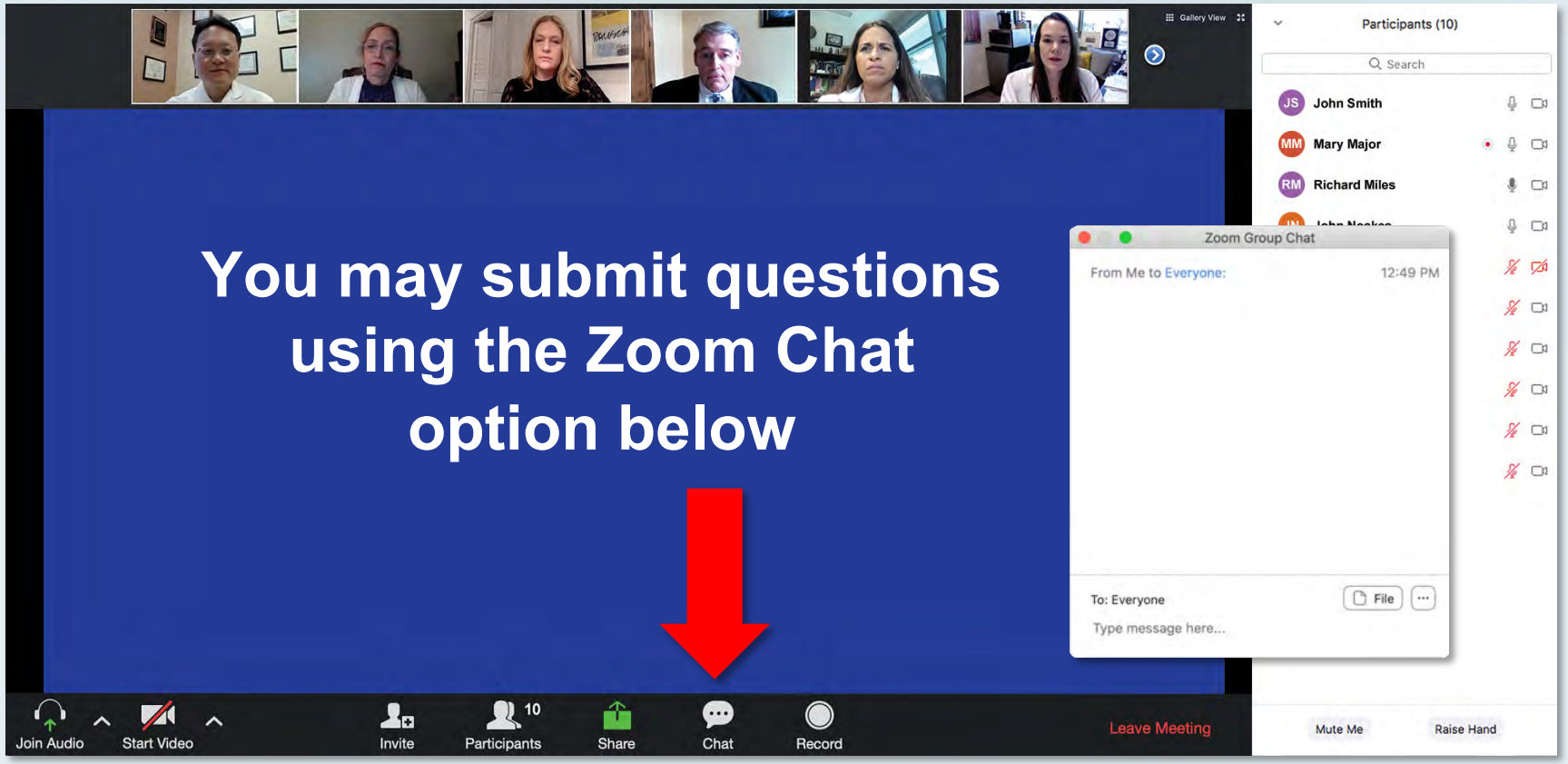
Tanios Bekaii-Saab, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP
Alan P Venook, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Dr Love and Faculty Encourage You to Ask Questions



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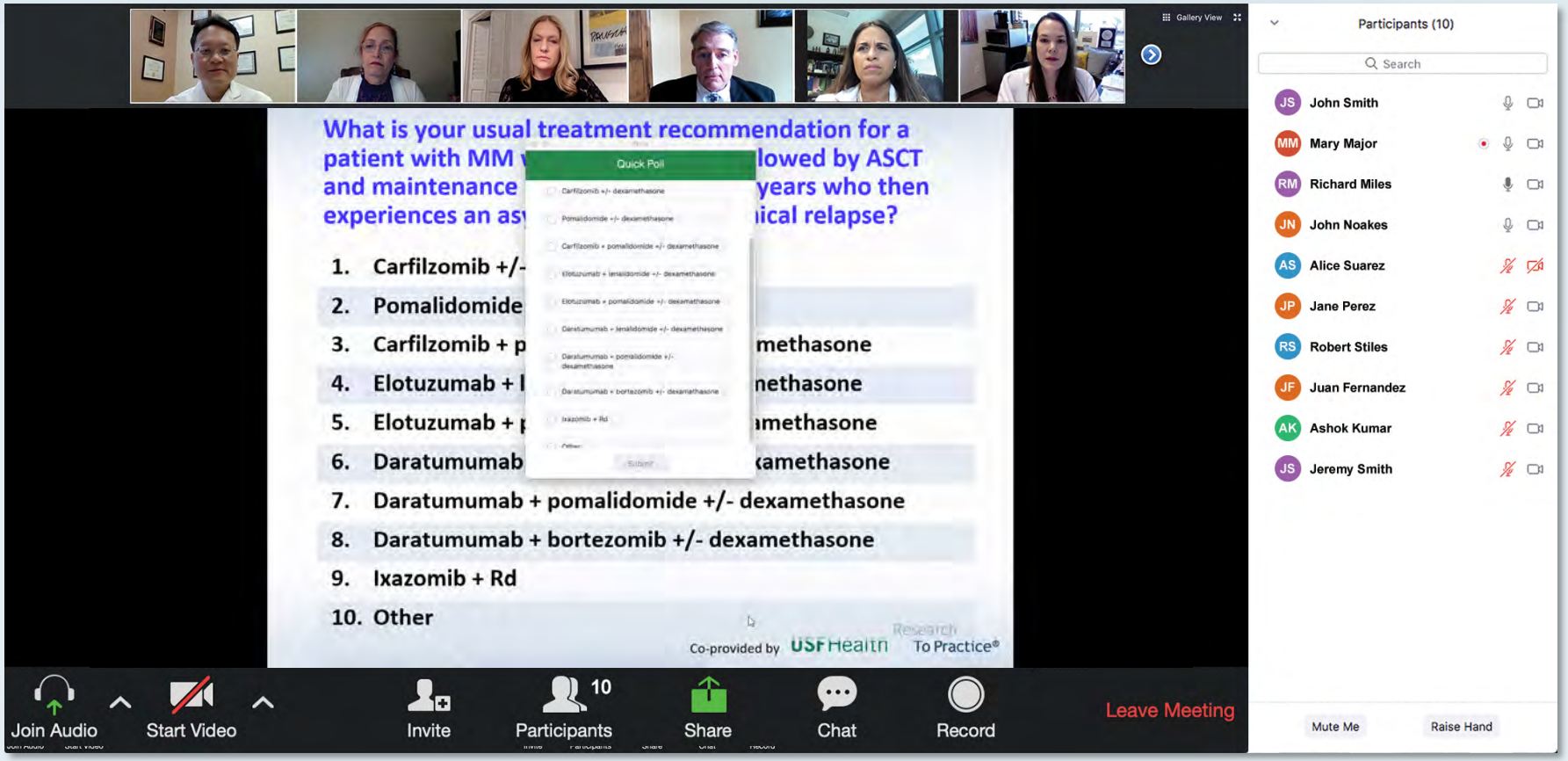
Familiarizing yourself with the Zoom interface
How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc, Tolero Pharmaceuticals and Verastem Inc.

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Upcoming Live Webinars

Friday, August 14, 2020
9:00 AM – 10:00 AM ET

Virtual Molecular Tumor Board: Recognition and Management of Targetable Tumor Mutations in Less Common Cancer Types

Faculty
Marcia S Brose, MD, PhD
Andrew McKenzie, PhD
Milan Radovich, PhD

Moderator
Neil Love, MD

Monday, August 17, 2020
5:00 PM – 6:00 PM ET

Recent Advances in Medical Oncology: ER-Positive Breast Cancer

Faculty
Virginia Kaklamani, MD, DSc
Sara M Tolaney, MD, MPH

Moderator
Neil Love, MD

Upcoming Live Webinars

Tuesday, August 18, 2020
5:00 PM – 6:00 PM ET

Current Questions and Controversies in the Management of Lung Cancer

Faculty
Leora Horn, MD, MSc

Moderator
Neil Love, MD

Wednesday, August 19, 2020
12:00 PM – 1:00 PM ET

Clinical Investigator Perspectives on the Current and Future Management of Multiple Myeloma

Faculty
Noopur Raje, MD

Moderator
Neil Love, MD

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Thursday, August 20, 2020
5:00 PM – 6:00 PM ET

Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

Faculty
Don S Dizon, MD

Moderator
Neil Love, MD

Friday, August 21, 2020
12:00 PM – 1:00 PM ET

Optimizing the Selection and Sequencing of Therapy for Patients with Chronic Lymphocytic Leukemia

Faculty
Brad S Kahl, MD

Moderator
Neil Love, MD

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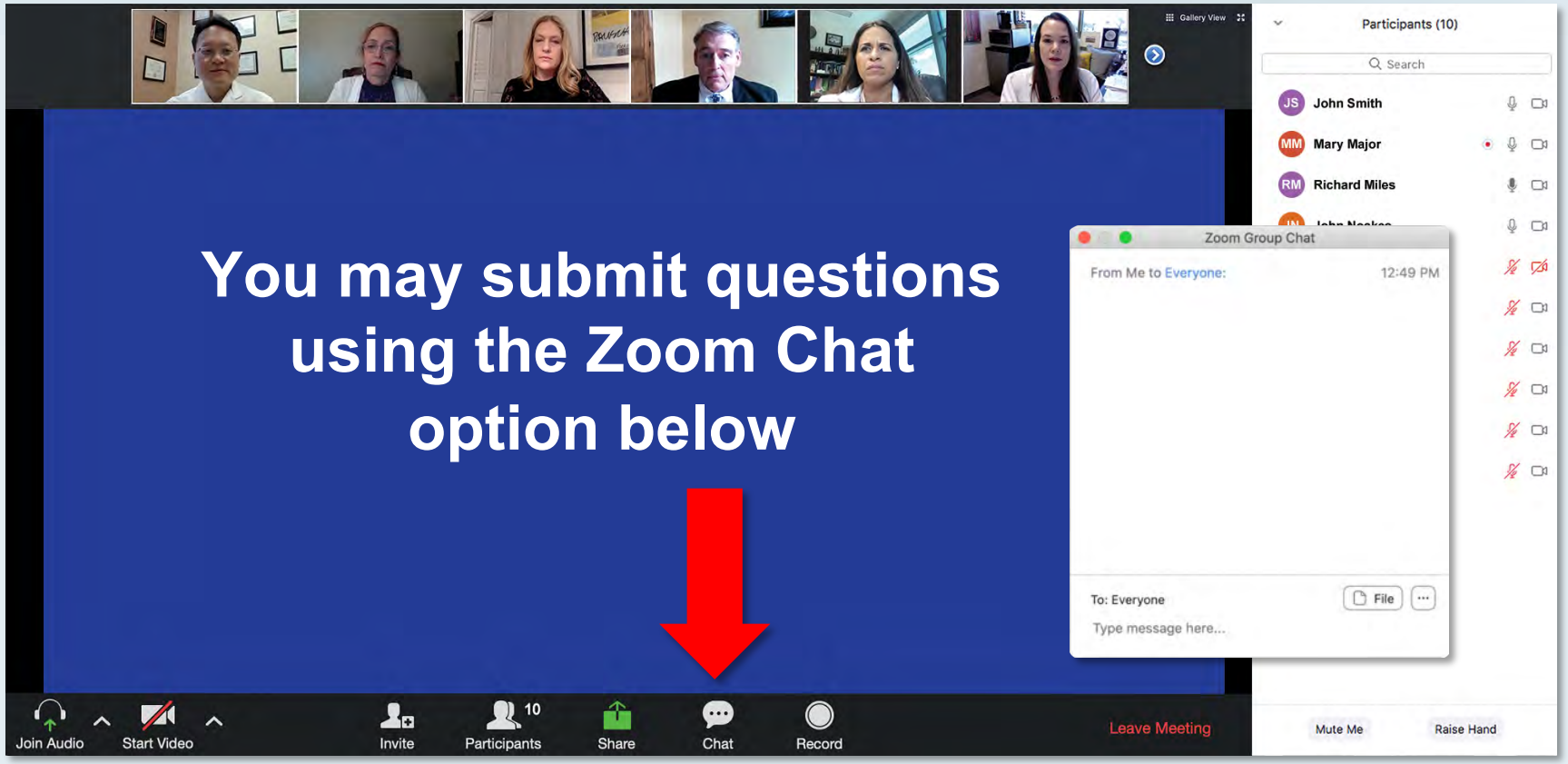
Dr Love and Faculty Encourage You to Ask Questions



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Clinical Investigator Perspectives on the Current and Future Role of PARP Inhibition in the Management of Ovarian Cancer

A Virtual Meet The Professor Series

Starting August 2020

Participating Faculty

Deborah K Armstrong, MD
Don S Dizon, MD
Pofessor Jonathan A Ledermann
Ursula Matulonis, MD
Mansoor Raza Mirza, MD
Kathleen Moore, MD
Professor Ignace Vergote
Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Exploring the Role of Immune Checkpoint Inhibitor Therapy and Other Novel Strategies in Gynecologic Cancers

A Virtual Meet The Professor Series

Starting August 2020

Participating Faculty

Michael J Birrer, MD, PhD
Robert L Coleman, MD
David M O'Malley, MD
Richard T Penson, MD, MRCP
Matthew A Powell, MD
Brian M Slomovitz, MD
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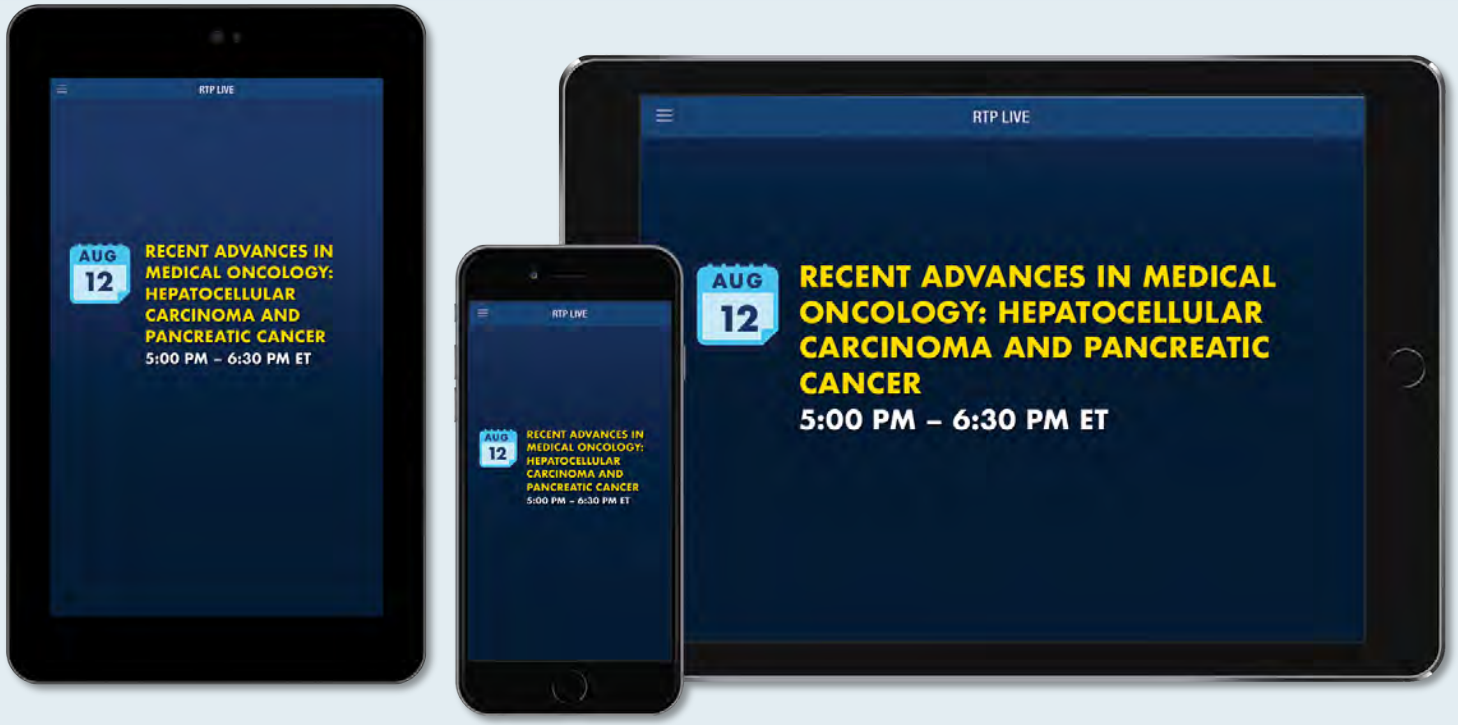

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Oncology Lecture Series

Current Utility of Validated and Emerging Biomarkers to Guide Treatment Decision-Making for Patients with Metastatic Colorectal Cancer

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Crystal Denlinger, MD

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Selection and Sequence of Therapy for Patients with Multiply Relapsed mCRC

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Oncology Lecture Series

Contemporary Treatment Approaches for Patients with Localized Pancreatic Cancer (PDAC)

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Selection and Sequencing of Therapies for Patients with Hepatocellular Cancer

Philip A Philip, MD, PhD, FRCP

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Hepatocellular Carcinoma: First-Line Therapy

Alan P Venook, MD

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Tennessee Oncology, a Partner of
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Murfreesboro, Tennessee

Agenda

MODULE 1: First-Line Treatment of Hepatocellular Carcinoma (HCC)

MODULE 2: Second- and Third-Line Treatment of HCC

MODULE 3: Localized Pancreatic Cancer

MODULE 4: Metastatic Pancreatic Cancer

MODULE 5: Management of Gastrointestinal Cancers in the Era of COVID-19

MODULE 1: First-Line Treatment of HCC

- **Key Relevant Data Sets**
  - IMbrave150: Atezolizumab + bevacizumab vs sorafenib in unresectable HCC
  - KEYNOTE-524: Lenvatinib + pembrolizumab in unresectable HCC
  - Study 22: Durvalumab +/- tremelimumab
- **Faculty Cases – Dr Venook**
  - A 64-year-old patient with sorafenib-intolerant HCC
  - A 25-year-old man with progressive HCC

Dr Favaro: A woman in her 60s with HCC who is on dialysis

Justin Peter Favaro, MD, PhD

- Polyclonal cryoglobulinemia associated with her HCC
- Renal failure; on dialysis
- TACE, RFA, with continued disease progression
- Atezolizumab/bevacizumab, with stable disease at first re-staging
  - Tolerating well, with no hypertensive issues

Questions

- After patients progress on atezolizumab/bevacizumab, what would be a good second-line option for them? Lenvatinib, or another TKI that maybe has a different mechanism of action compared to bevacizumab? Or maybe a TKI that doesn't really depend on the VEGF pathway that might be a way to treat those patients?

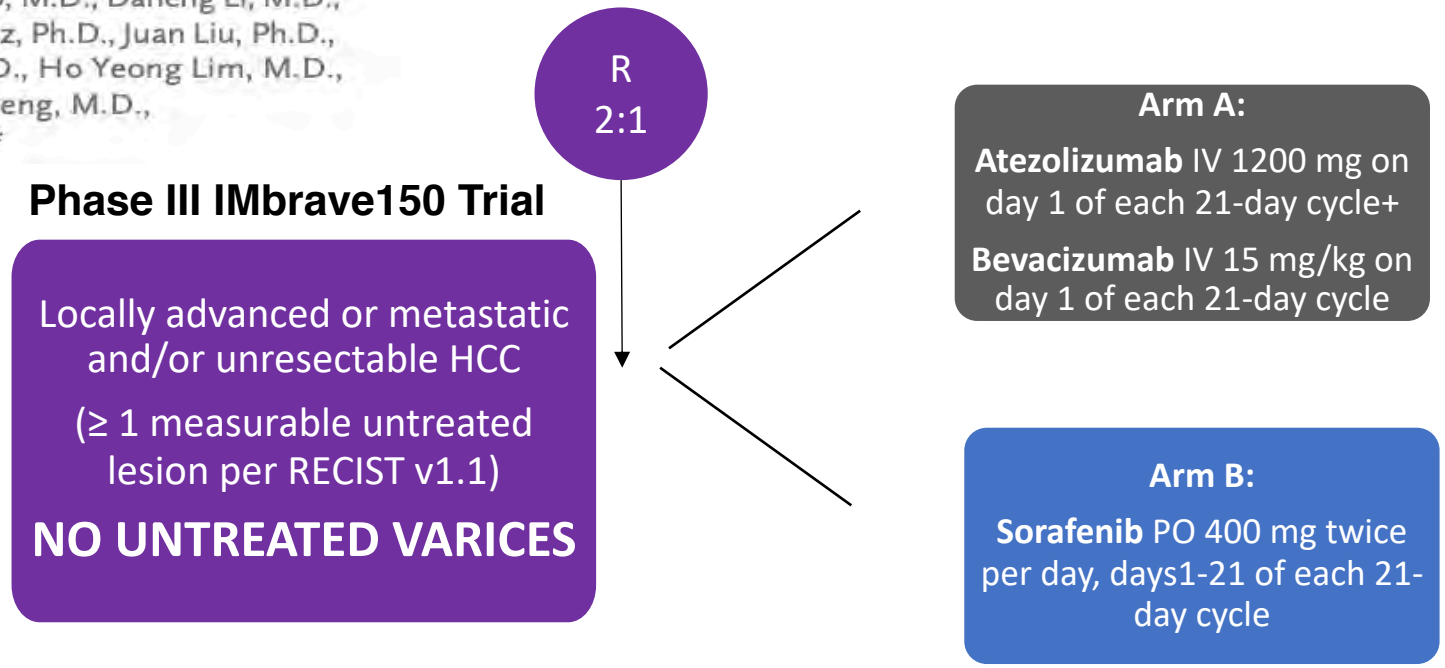
RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma

Richard S. Finn, M.D., Shukui Qin, M.D., Masafumi Ikeda, M.D., Peter R. Galle, M.D., Michel Ducreux, M.D., Tae-You Kim, M.D., Masatoshi Kudo, M.D., Valeriy Breder, M.D., Philippe Merle, M.D., Ahmed O. Kaseb, M.D., Daneng Li, M.D., Wendy Verret, Ph.D., Derek-Zhen Xu, M.D., Sairy Hernandez, Ph.D., Juan Liu, Ph.D., Chen Huang, M.D., Sohail Mulla, Ph.D., Yulei Wang, Ph.D., Ho Yeong Lim, M.D., Andrew X. Zhu, M.D., Ph.D., and Ann-Lii Cheng, M.D., for the IMbrave150 Investigators*



Stratification factors:

- Region (Asia [excluding Japan] vs rest of world)
- Macrovascular invasion and/or extrahepatic spread (presence vs absence)
- Baseline α-fetoprotein level (< 400 vs ≥ 400 ng/mL)
- ECOG PS (0 vs 1)

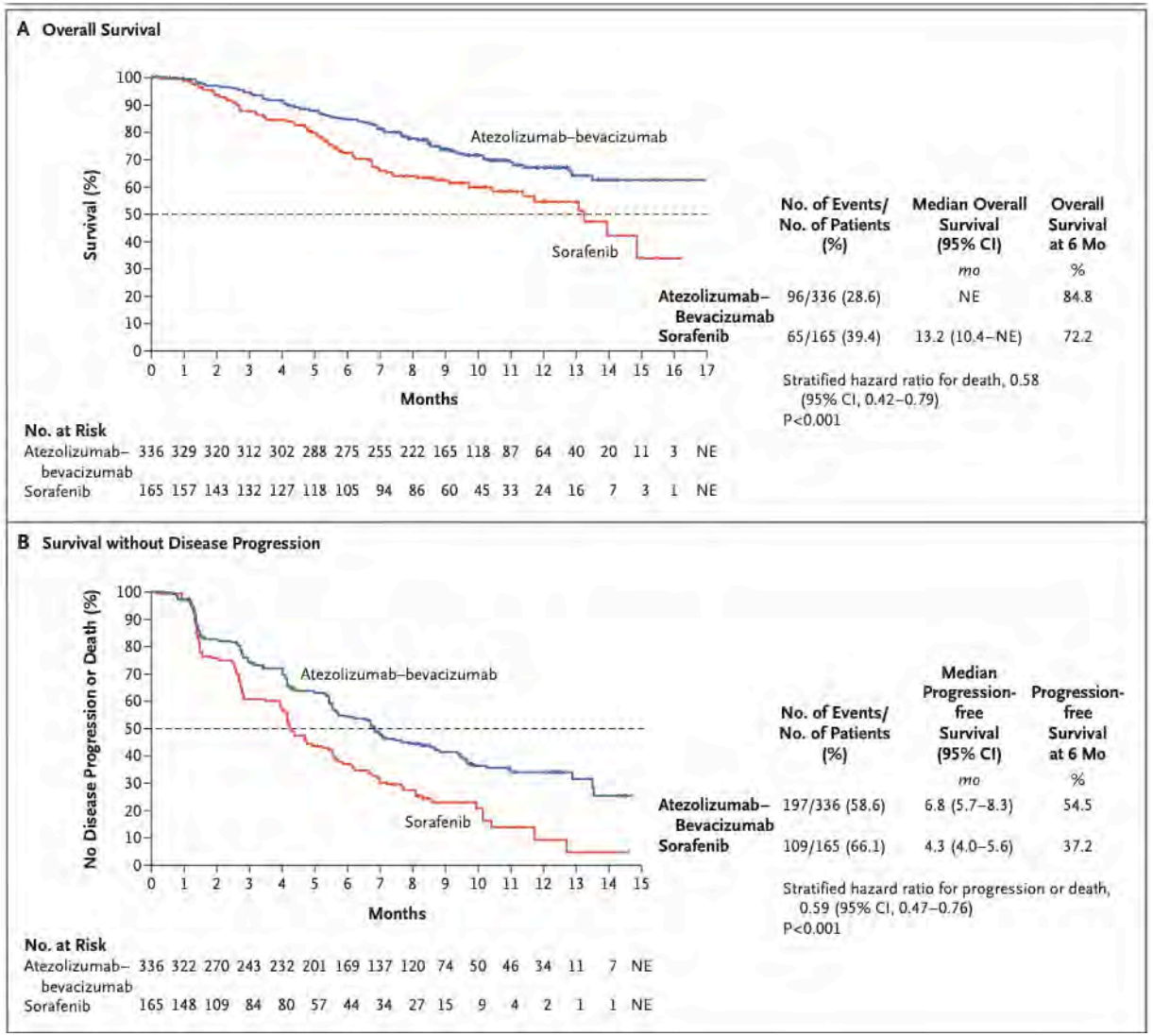
Courtesy of Alan P. Venook, M.D., FASCO

IMbrave150: Atezolizumab / Bevacizumab v. Sorafenib

Table 1. Patient Characteristics at Baseline.*

Variable	Atezolizumab–Bevacizumab (N=336)	Sorafenib (N=165)
Median age (IQR) — yr	64 (56–71)	66 (59–71)
Male sex — no. (%)	277 (82)	137 (83)
Geographic region — no. (%)		
Asia, excluding Japan	133 (40)	68 (41)
Rest of the world†	203 (60)	97 (59)
ECOG performance status score — no. (%)‡		
0	209 (62)	103 (62)
1	127 (38)	62 (38)
Child–Pugh classification — no./total no. (%)§		
A5	239/333 (72)	121/165 (73)
A6	94/333 (28)	44/165 (27)
Barcelona Clinic liver cancer stage — no. (%)¶		
A	8 (2)	6 (4)
B	52 (15)	26 (16)
C	276 (82)	133 (81)
Alpha-fetoprotein ≥400 ng per milliliter — no. (%)	126 (38)	61 (37)
Presence of macrovascular invasion, extrahepatic spread, or both — no. (%)	258 (77)	120 (73)
Macrovascular invasion	129 (38)	71 (43)
Extrahepatic spread	212 (63)	93 (56)
Varices — no. (%)		
Present at baseline	88 (26)	43 (26)
Treated at baseline	36 (11)	23 (14)
Cause of hepatocellular carcinoma — no. (%)		
Hepatitis B	164 (49)	76 (46)
Hepatitis C	72 (21)	36 (22)
Nonviral‖	100 (30)	53 (32)
Prior local therapy for hepatocellular carcinoma — no. (%)	161 (48)	85 (52)

N Engl J Med 2020; 382: 1894-1905



Courtesy of Alan P. Venook, M.D., FASCO

IMbrave150: Atezolizumab / Bevacizumab v. Sorafenib

Table 3. Adverse Events from Any Cause.

Variable	Atezolizumab–Bevacizumab (N=329)	Sorafenib (N=156)
	number (percent)	
Patients with an adverse event from any cause	323 (98.2)	154 (98.7)
Grade 3 or 4 event*	186 (56.5)	86 (55.1)
Grade 5 event†	15 (4.6)	9 (5.8)
Serious adverse event	125 (38.0)	48 (30.8)
Adverse event leading to withdrawal from any trial drug	51 (15.5)	16 (10.3)
Withdrawal from atezolizumab–bevacizumab	23 (7.0)	—
Adverse event leading to dose modification or interruption of any trial drug	163 (49.5)	95 (60.9)
Dose interruption of any trial treatment	163 (49.5)	64 (41.0)
Dose modification of sorafenib	—	58 (37.2)

N Engl J Med 2020; 382: 1894-1905

Courtesy of Alan P. Venook, M.D., FASCO

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2020
Hepatocellular Carcinoma

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF SYSTEMIC THERAPY

First-line systemic therapy

Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
• Sorafenib (Child-Pugh Class A [category 1] or B7)[a,b,1,2] • Lenvatinib (Child-Pugh Class A only)[3,4] (category 1) • Atezolizumab + bevacizumab (Child-Pugh Class A only) (category 1)[c,d,5]	• None	• Nivolumab[c,6] (if ineligible for tyrosine kinase inhibitors [TKIs] or other anti-angiogenic agents) (category 2B) • FOLFOX (category 2B)[e]

Subsequent-line therapy[f] if disease progression[g]

Options

- Regorafenib (Child-Pugh Class A only) (category 1)[h,7]
- Cabozantinib (Child-Pugh Class A only) (category 1)[h,8]
- Ramucirumab (AFP ≥400 ng/mL only) (category 1)[h,9]
- Lenvatinib (Child-Pugh Class A only)
- Nivolumab (Child-Pugh Class A or B)[c,i,10–12]
- Nivolumab + ipilimumab (Child-Pugh Class A only)[c,h,i,14]
- Sorafenib (Child-Pugh Class A or B7)[a,b]
- Pembrolizumab (Child-Pugh Class A only)[c,i,13] (category 2B)

Courtesy of Alan P. Venook, M.D., FASCO

KEYNOTE-524: Phase 1b Study of Lenvatinib + Pembrolizumab in Patients With Unresectable Hepatocellular Carcinoma

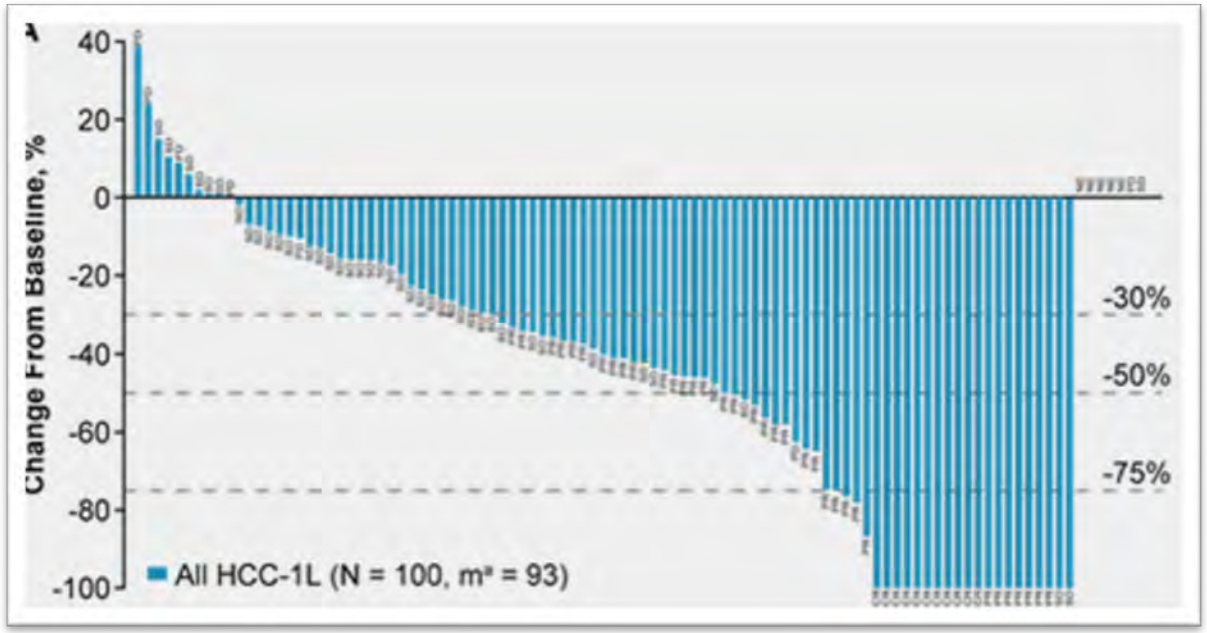
Lenvatinib 12 or 8 mg daily orally (based on body weight) + **pembrolizumab** 200 mg IV on Day 1 (21-day cycle)

DLT Evaluation (Part 1)
- n = 6
- Patients ineligible for other therapies
- Tolerability evaluated by DLTs during cycle 1

Expansion (Part 2)
- n = 98
- No prior systemic therapy for uHCC

Key Eligibility Criteria
- uHCC
- BCLC Stage B (not applicable for TACE) or C
- Child–Pugh class A
- ECOG performance status 0–1
- At least 1 measurable target lesion according to mRECIST

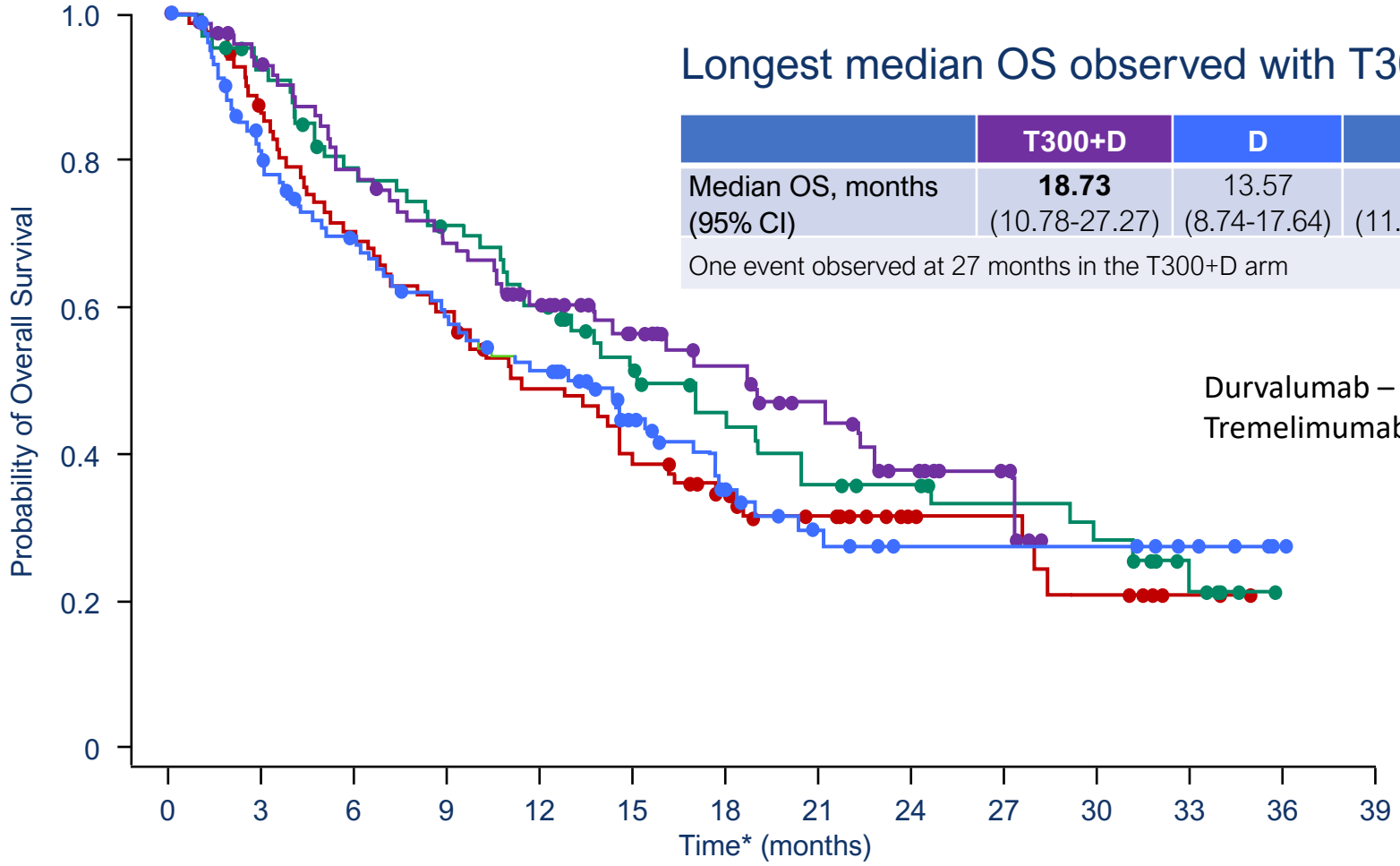
Response Rate: mRECIST



Zhu et al, ASCO, 2020

Courtesy of Alan P. Venook, M.D., FASCO

Study 22: Durvalumab +/- Tremelimumab



Longest median OS observed with T300+D

	T300+D	D	T	T75+D
Median OS, months (95% CI)	**18.73** (10.78-27.27)	13.57 (8.74-17.64)	15.11 (11.33-20.50)	11.30 (8.38-14.95)

One event observed at 27 months in the T300+D arm

Durvalumab – anti-PD1
Tremelimumab - anti-CTL4

Number of patients at risk														
T300+D	75	67	56	48	39	30	22	16	10	5	0	0	0	0
D	104	78	65	54	46	31	20	14	8	8	8	5	1	0
T	69	62	51	45	38	29	23	18	16	13	11	5	0	0
T75+D	84	69	56	48	38	30	23	17	10	9	6	2	0	0

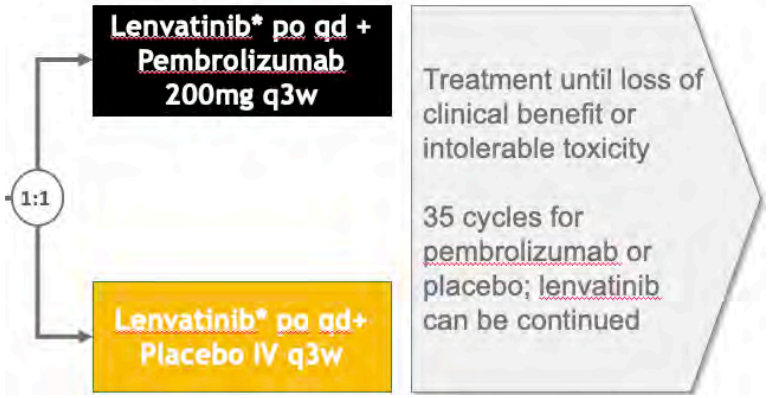
*Time from randomization (Part 2A, 3) or first dose (Part 2B)
CI, confidence interval; D, durvalumab; OS, overall survival; T, tremelimumab

Kelley et al, ASCO, 2020

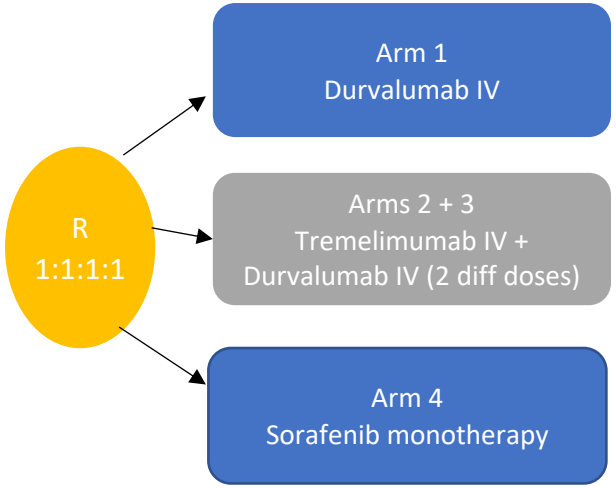
Courtesy of Alan P. Venook, M.D., FASCO

HCC: What's Next?

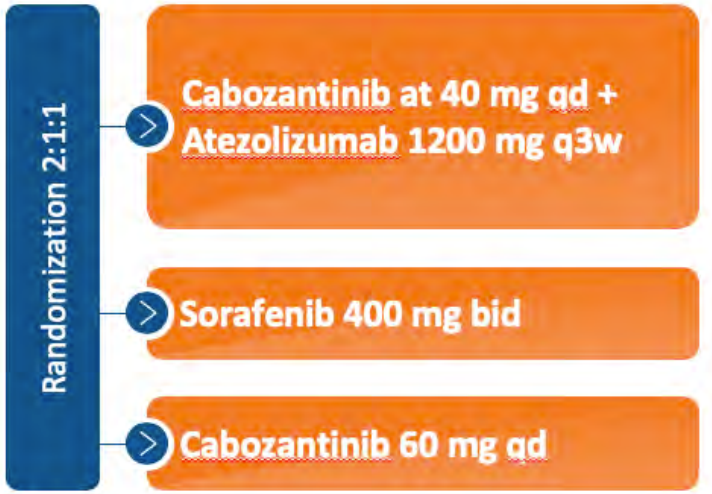
Phase III LEAP-002 Trial



Phase III HIMALAYA Trial

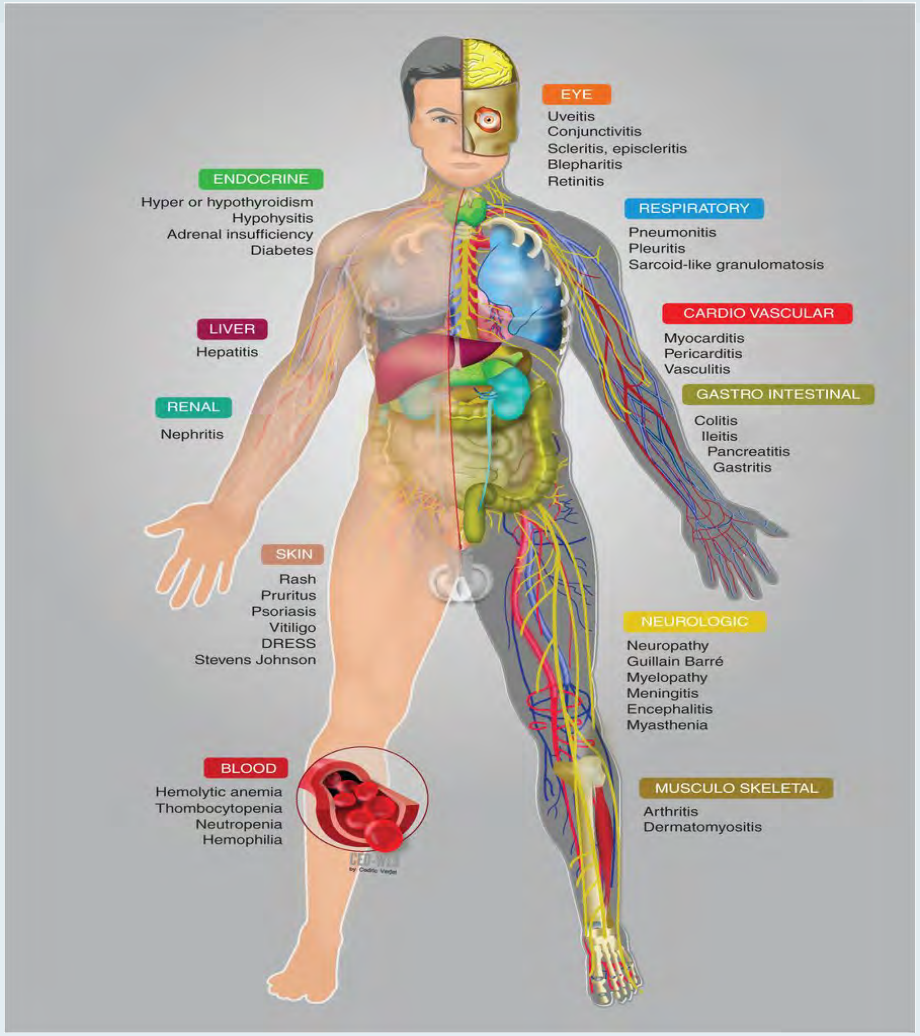


Phase III COSMIC-312 Trial



Courtesy of Alan P. Venook, M.D., FASCO

Spectrum of Immune Toxicity



Champiat et al. Ann Oncol 2016;27:559-574

Courtesy of Nikhil Khushalani, MD

MODULE 1: First-Line Treatment of HCC

- **Key Relevant Data Sets**
  - IMbrave150: Atezolizumab + bevacizumab vs sorafenib in unresectable HCC
  - KEYNOTE-524: Lenvatinib + pembrolizumab in unresectable HCC
  - Study 22: Durvalumab +/- tremelimumab
- **Faculty Cases – Dr Venook**
  - A 64-year-old patient with sorafenib-intolerant HCC
  - A 25-year-old man with progressive HCC

Case Presentation - Dr Venook: A 64-Year-Old Patient with Sorafenib-Intolerant HCC

64 y.o. long-standing history HCV, non-compliant with antiviral therapy.

Presented with pruritus, right shoulder pain and bloating. 10 pound weight loss.

On exam, enlarged liver, 1 + edema, numerous telangiectasia.

Alb = 2.9 g/dL. Bilirubin = 1.9 mg/dL. INR =1.8

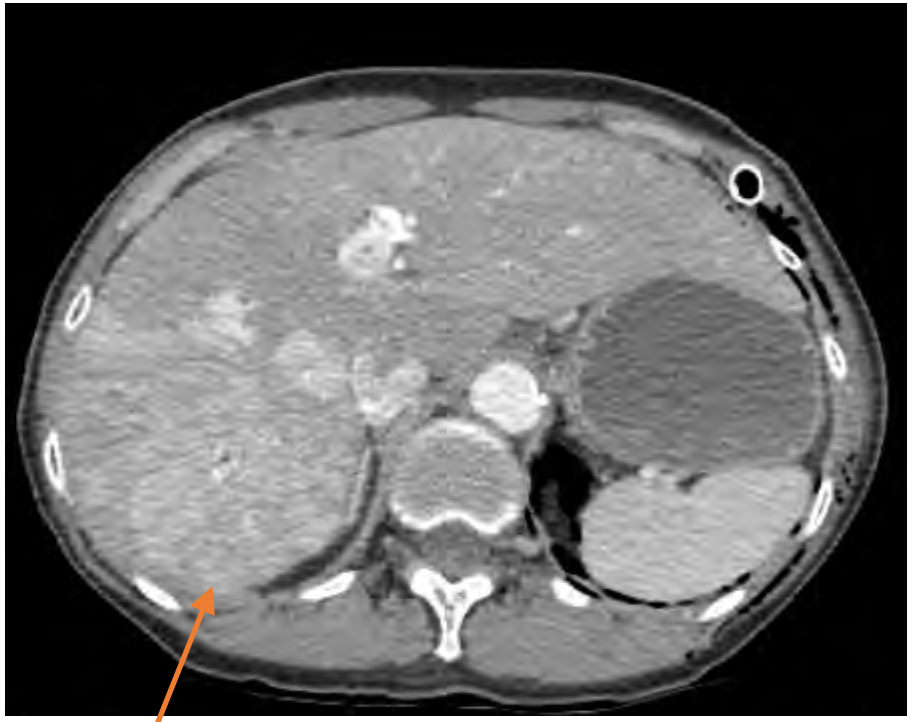
AFP = 3000

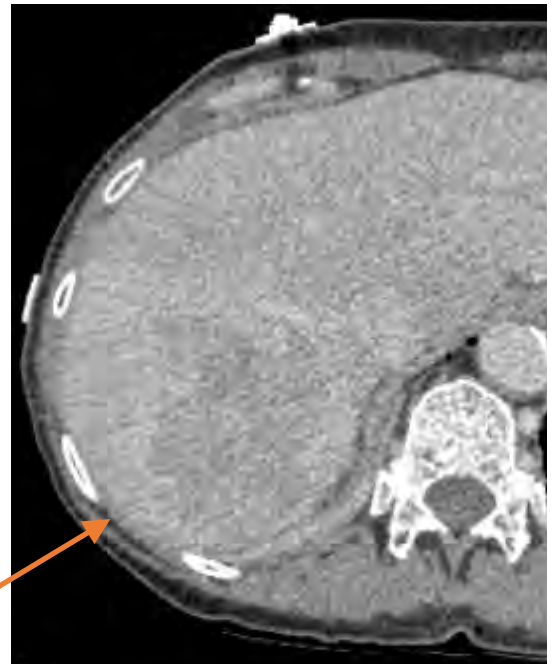
See scans

Started on Sorafenib 400 mg q day, diarrhea and skin rash within first week, Sorafenib discontinued. Initiated Nivolumab 240 mg q 2 weeks.

Case Presentation - Dr Venook: A 64-Year-Old Patient with Sorafenib-Intolerant HCC (continued)

Multifocal HCC in setting of HCV





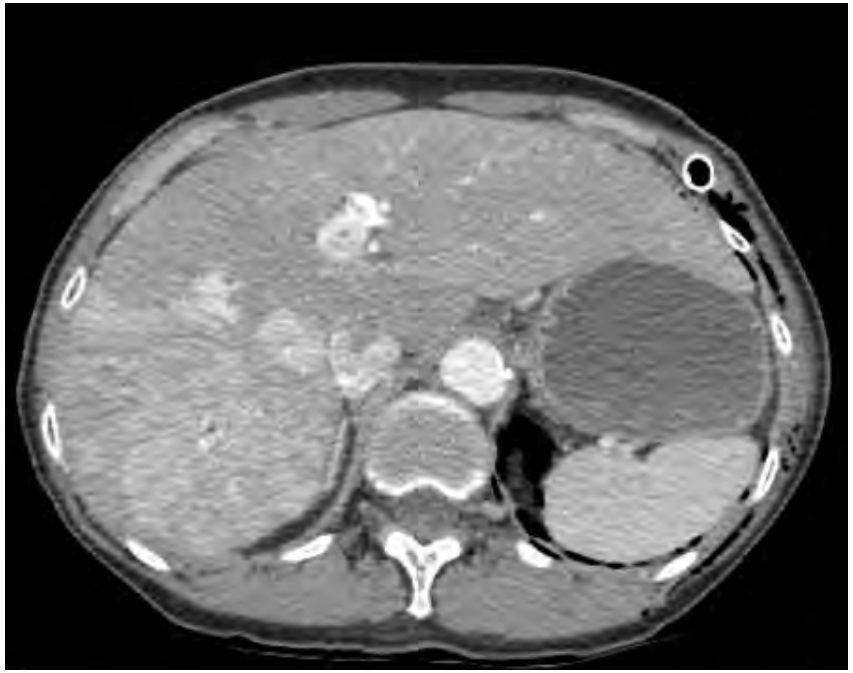
Arterial phase enhancement

Portal venous phase washout

2/2018: R lobe multifocal tumors up to 7.8 cm with tumor thrombus main, Right, and Left Portal Vein

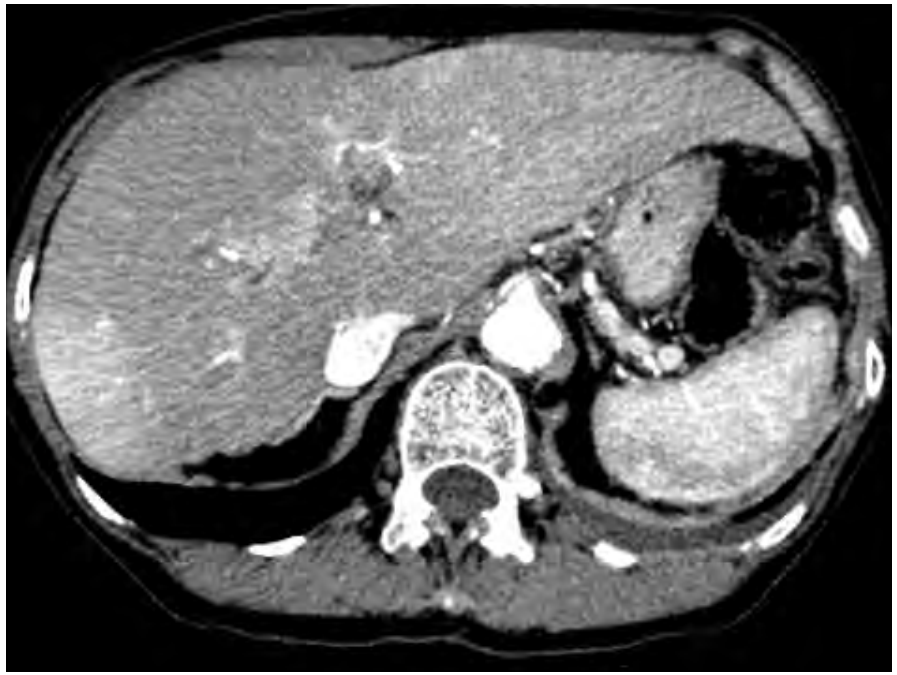
Case Presentation - Dr Venook: A 64-Year-Old Patient with Sorafenib-Intolerant HCC (continued)

Multifocal HCC w/ HCV



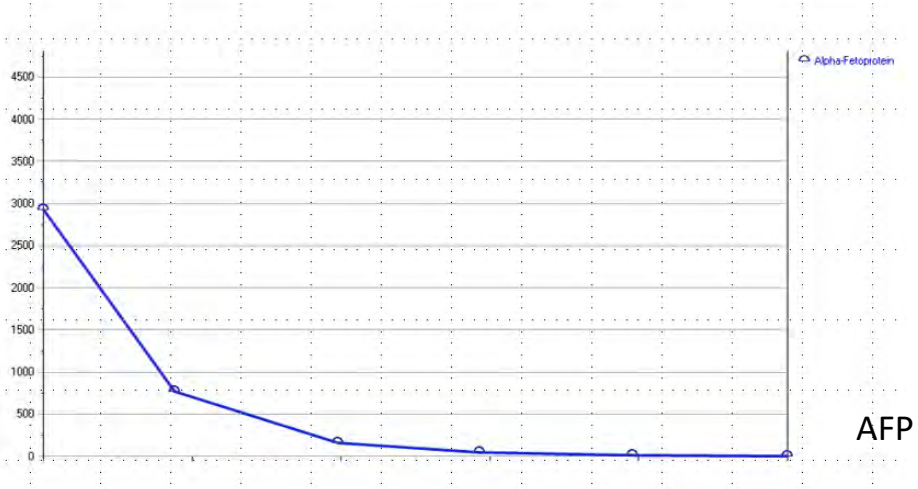
2/2018

NIVOLUMAB



5/2018

AFP = 3000



AFP = 6

Case Presentation – Dr Venook: A 25-Year-Old Man with Progressive HCC

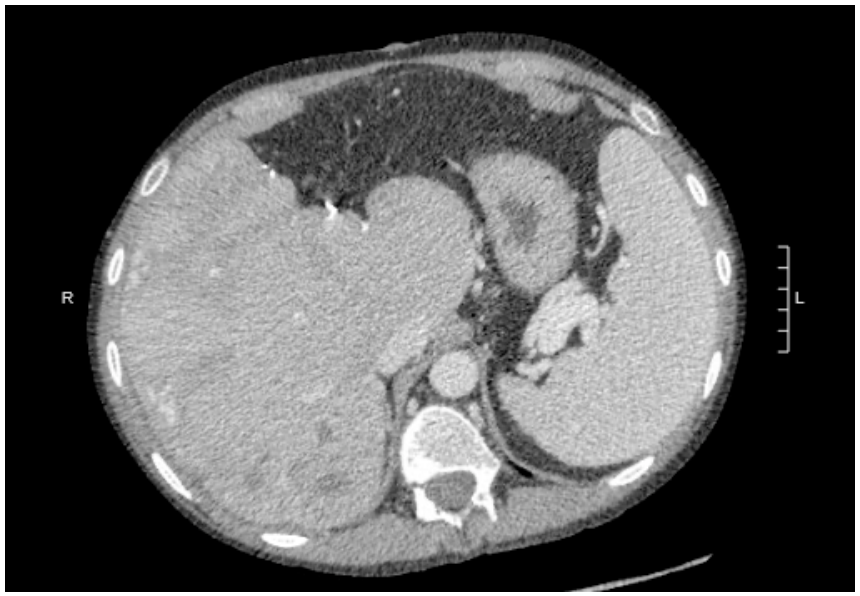
25 y.o. (in 2013) Crohn's colitis since age 10, on immunosuppression for most of 15 years. Develops two liver lesions in left lobe liver, left hepatic lobectomy reveals four lesions, HCC on biopsy. Within 2 months has multifocal recurrence in liver. Undergoes TACE x 2, then sorafenib, then phase I study. Has transient response, then changed to FOLFOX x 3 cycles, progressive disease including bone metastases. See scan June. 2014.

Between June, 2014, and July, 2015, on different phase I study. Immediate progression then receives two cycles of sorafenib + doxorubicin. Poorly tolerated, changed to ramucirumab x 1 cycle, complicated by upper GI bleed. Endoscopy with sclerosis of esophageal varices.

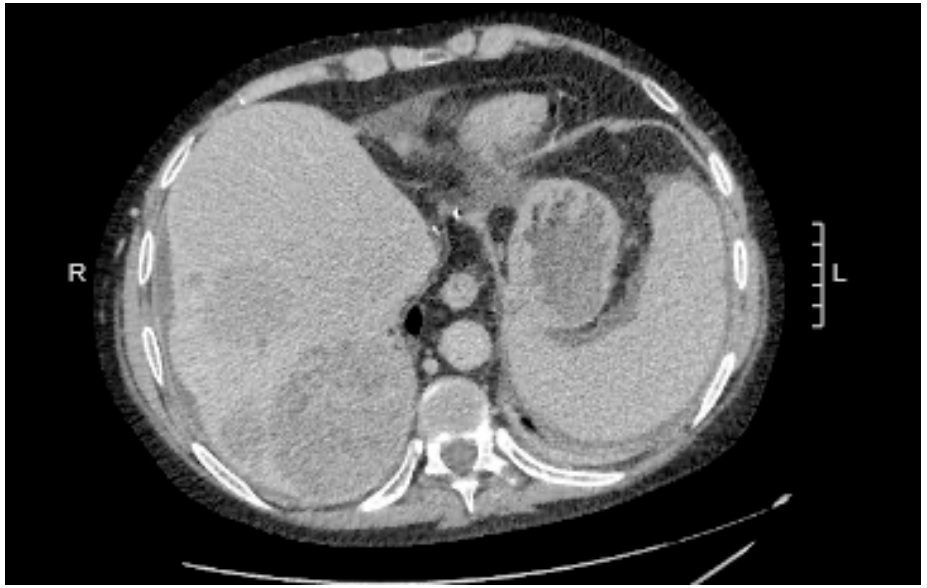
In July 2015, develops painful subcutaneous scalp metastases, now declining liver function. Undergoes XRT to scalp, then begins Nivolumab 240 mg.

Case Presentation – Dr Venook: A 25-Year-Old Man with Progressive HCC (continued)

Multifocal HCC

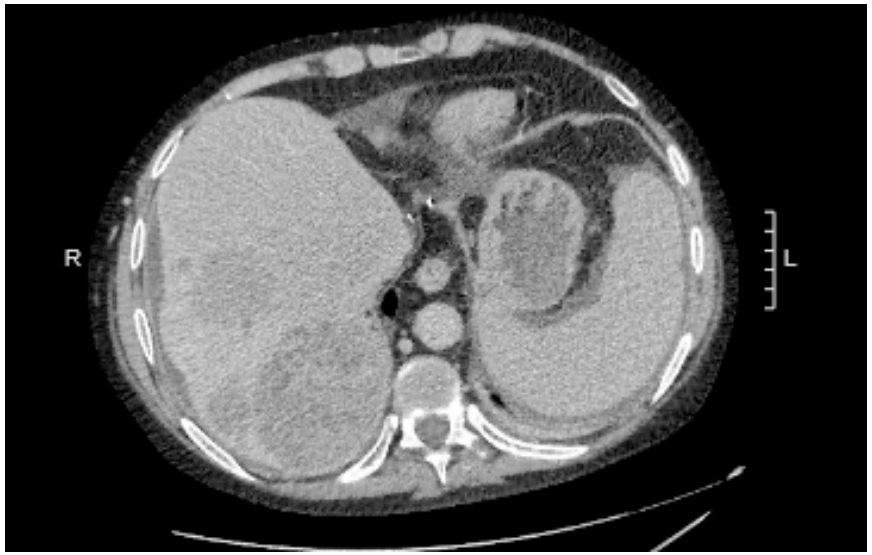


June, 2014

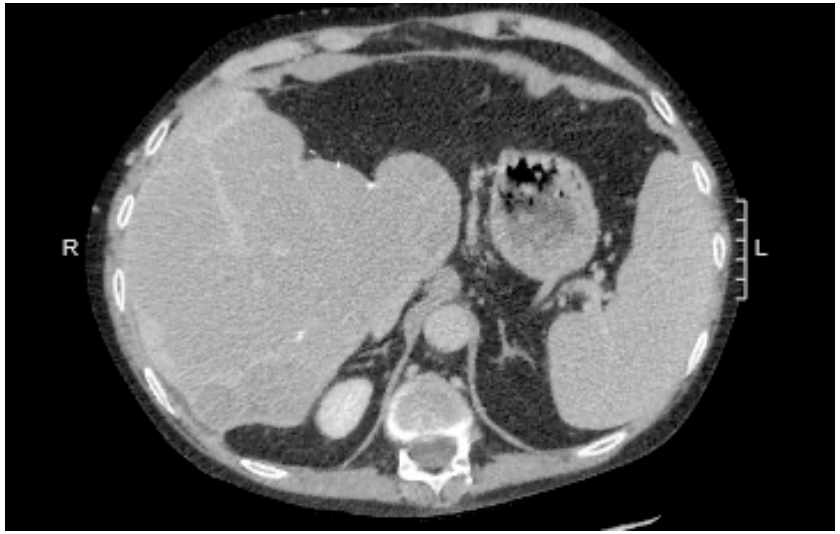


July, 2015

Case Presentation – Dr Venook: A 25-Year-Old Man with Progressive HCC (continued)

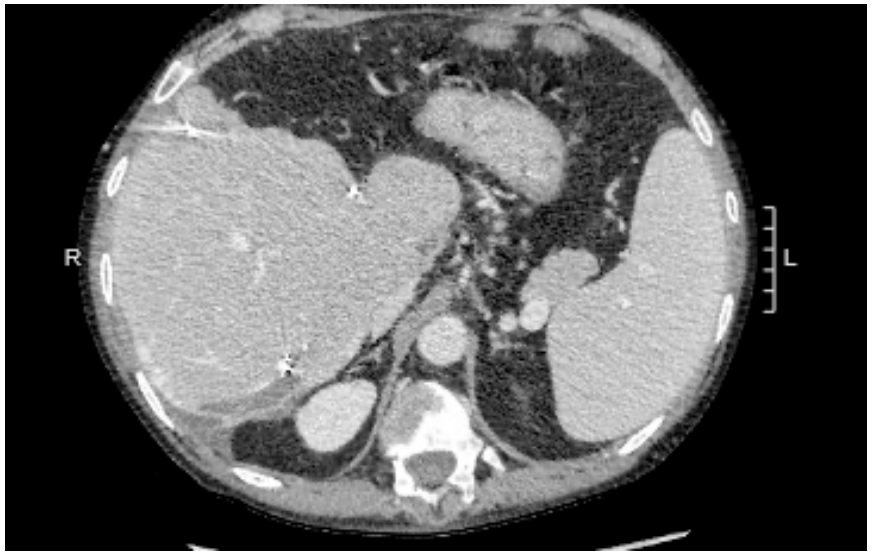


July, 2015



December, 2015

s/p Nivolumab x 67 doses
Last dose April, 2018



April, 2020

AR	*R761R*‡	19.3	There is no change in the amino acid at this position and it is not likely to be a therapeutic target. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
TP53	*Y205C*	10.4	None	None	Trials Available
PDGFRA	*D444H*	10.3	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
MAP2K2	*E77G*	8.7	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
NF1	*D1158Y*	8.6	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
	K2224T	8.0	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
CDK6	*I122V*	8.5	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
KIT	*T544N*	0.4	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		

APC	*H768L*	0.3	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
ROS1	*L1912Q*	0.3	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		
MET	*N379H*	0.1	The functional consequences and clinical significance of this gene variant are not established. The relevance of therapies targeting this alteration is uncertain. Similar to other alterations in circulating cfDNA, the monitoring of this variant may be reflective of disease progression or treatment; clinical correlation is advised.		

MODULE 2: Second- and Third-Line Treatment of HCC

- **Key Relevant Data Sets**
  - CheckMate 040: Nivolumab with ipilimumab in advanced HCC after sorafenib
- **Faculty Cases – Dr Philip**
  - A 61-year-old man with HCC and disease progression on sorafenib
  - A 61-year-old man with newly diagnosed HCC treated with lenvatinib

Dr Maen Hussein: A man with metastatic HCC

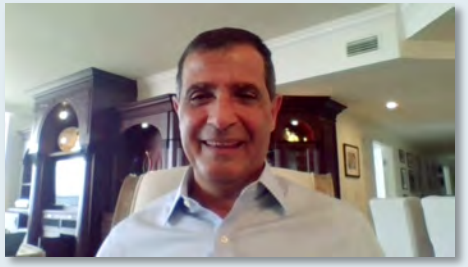
Maen Hussein, MD

- Presents with de novo metastatic HCC
- Atezolizumab/bevacizumab, with good clinical but no objective response → PD
- Plan to initiate lenvatinib

Questions

- In patients progressing on atezolizumab/bevacizumab, what treatments should be considered next? Is lenvatinib really the best second-line option? Cabozantinib is also another good agent. Which treatment would the faculty go to?

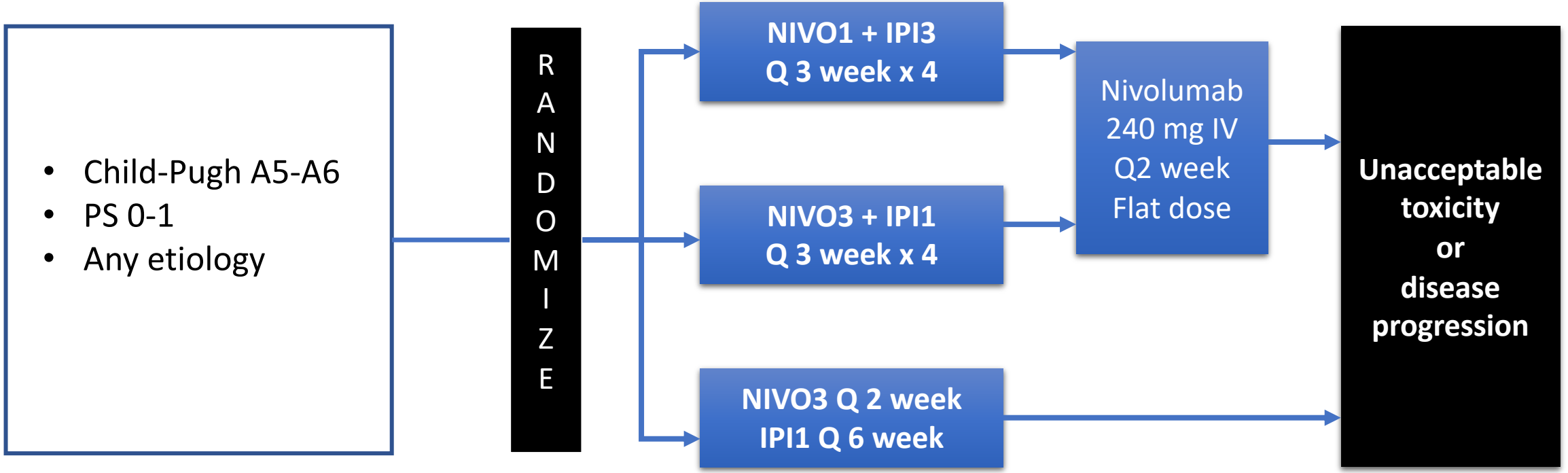
Dr Atif Hussein: A 66-year-old woman with HCC, alcoholic cirrhosis and portal vein thrombosis



Atif Hussein, MD, MMM

- Sorafenib
  - Dose reduction due to toxicity
- Nivolumab x 9+ months and continuing
  - Decrease in alpha fetoprotein, no objective response yet
  - Tolerating well, with grade 1 diarrhea

CheckMate 040: Nivolumab plus ipilimumab in advanced HCC after sorafenib



El-Khoueiry et al ILCA 2019; Yau et al, ASCO, 2019

Courtesy of Philip A Philip, MD, PhD, FRCP

CheckMate 040: efficacy

	NIVO1+IPI3 Q3 wk N = 50	NIVO3+IPI1 Q3 wk N = 49	NIVO3 Q 2 wk/ IPI1 Q 6 wk N = 49
Objective response rate (%)	32	31	31
Median duration of response (months)	17.5	22.2	16.6
Median OS (months)	23.0	12.0	13.0

El-Khoueiry et al ILCA 2019; Yau et al, ASCO, 2019

Courtesy of Philip A Philip, MD, PhD, FRCP

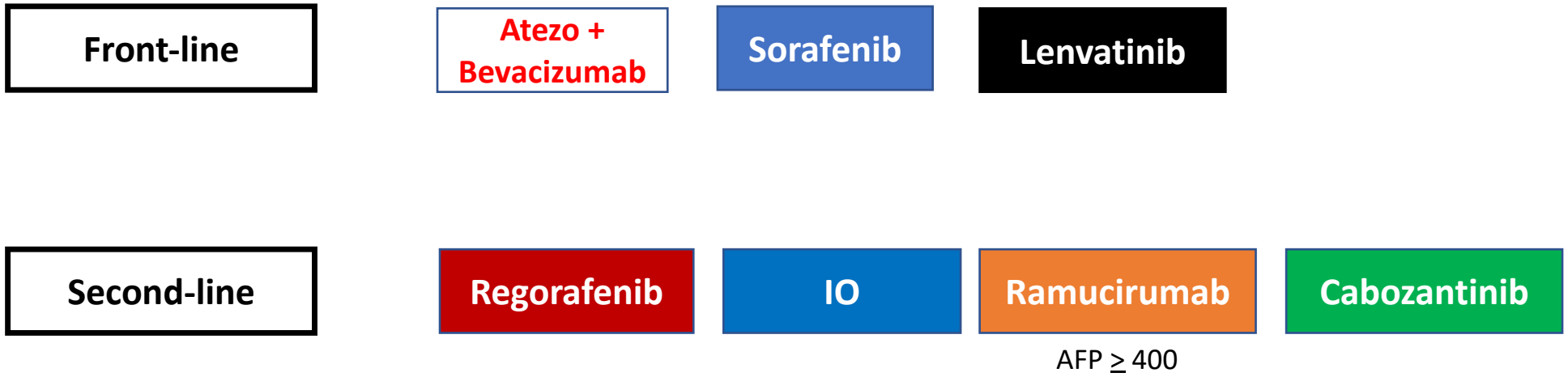
Non-head to head comparison of toxicity from dual checkpoint inhibition

	Tremelimumab 300 + durvalumab (%)	NIVO1/IPI3 Q3 week (%)
Treatment related adverse events grade 3 or 4	35.1	53
TRAEs requiring steroids	24.3	51
TRAEs leading to discontinuation	10.8	22
Rash all grades	32.4	35
Pruritis all grades	32	45
Diarrhea all grades	9.5	10
AST increase all grades	16.2	27

Adapted from Dr Meyer presentation, ASCO 2020

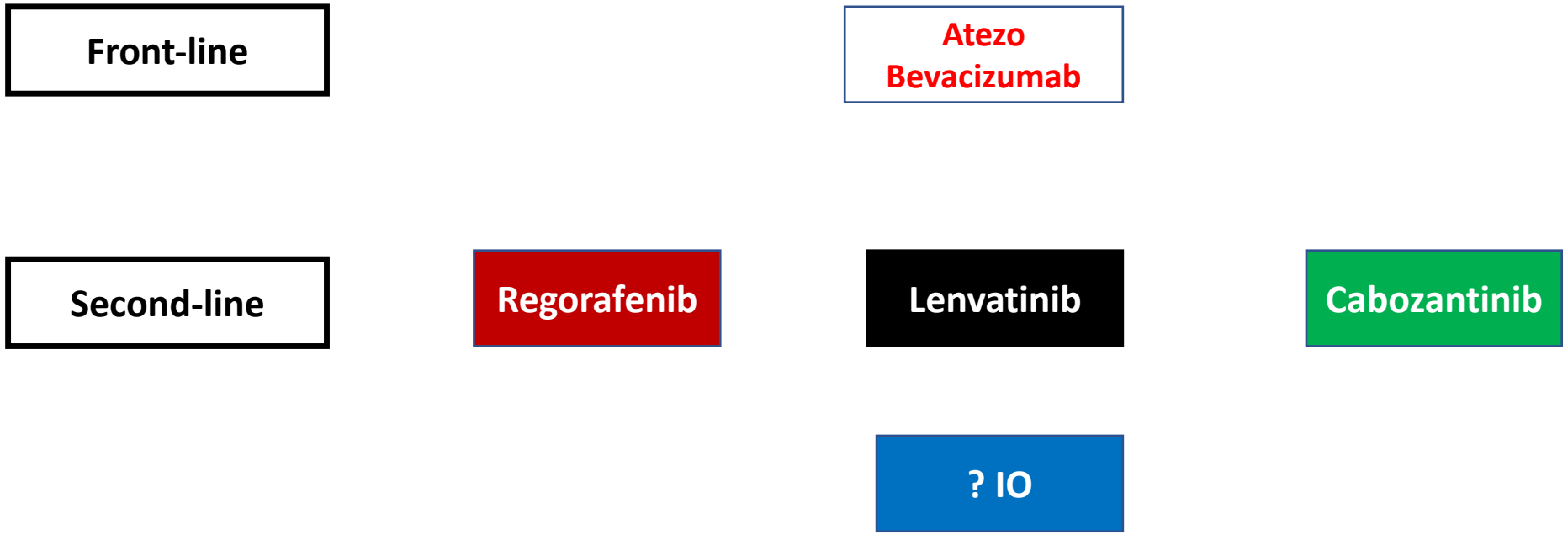
Courtesy of Philip A Philip, MD, PhD, FRCP

Systemic therapy of HCC is getting crowded



Courtesy of Philip A Philip, MD, PhD, FRCP

May be simpler if started with Atezo and Bev



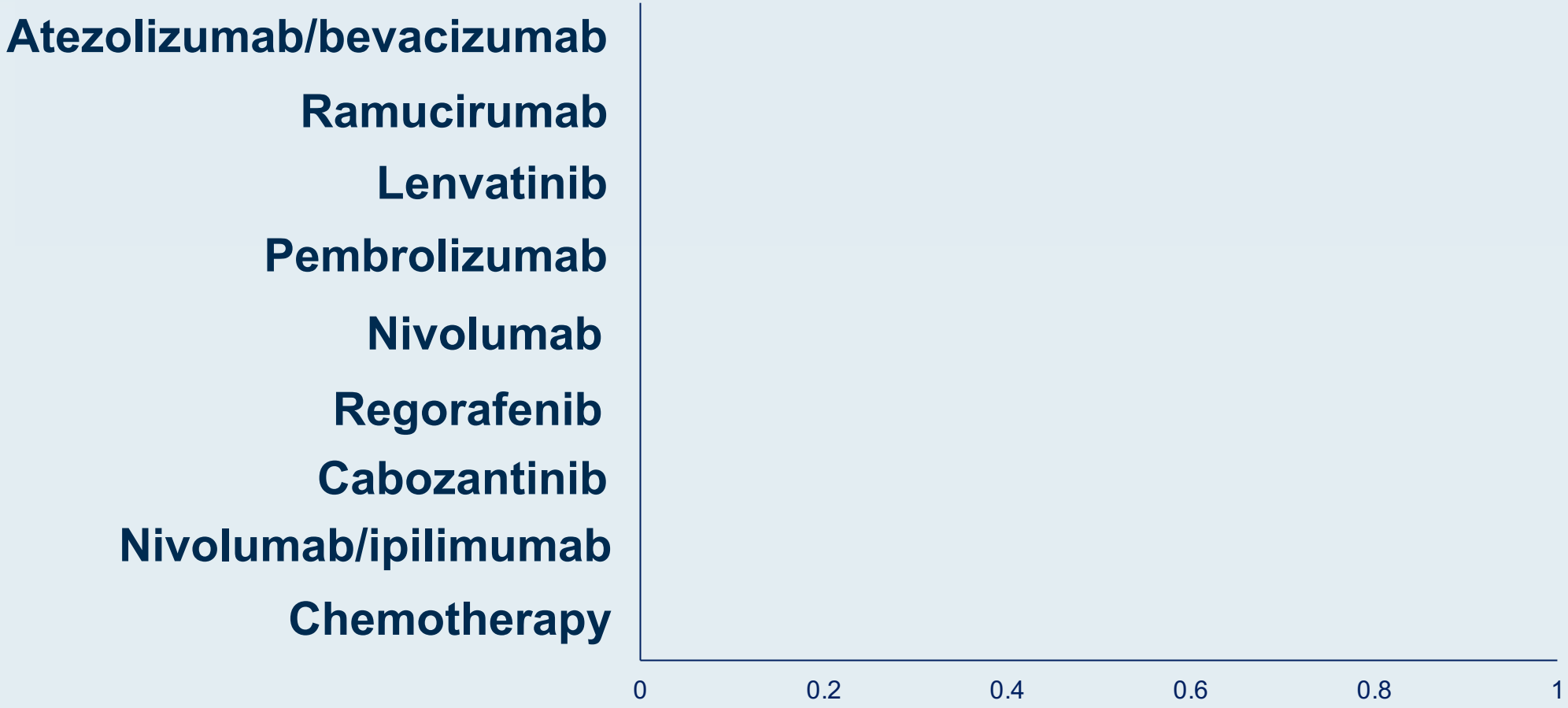
Courtesy of Philip A Philip, MD, PhD, FRCP

How to personalize or sequence drugs in HCC? Mechanism based?

		VEGF/ VEGFR	PDGFR/ C-kit	RAF	FGFR	RET	MET	AXL FLT3 TRKB	TIE-2	Immune
	Bevacizumab	✓								?
	Ramucirumab	✓								?
TKI	Sorafenib	✓	✓	✓						?
TKI	Regorafenib	✓	✓	✓	✓	✓			✓	?
TKI	Cabozantinib	✓				✓	✓	✓	✓	?
TKI	Lenvatinib	✓	✓		✓	✓				?
	Immune checkpoint I									✓

Courtesy of Philip A Philip, MD, PhD, FRCP

Regulatory and reimbursement issues aside, what would be your most likely second-line systemic therapy for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0 who received first-line standard-dose sorafenib with minimal toxicity, had stable disease for 14 months and then experienced disease progression (AFP = 2,500)?



Survey of 50 US-based medical oncologists

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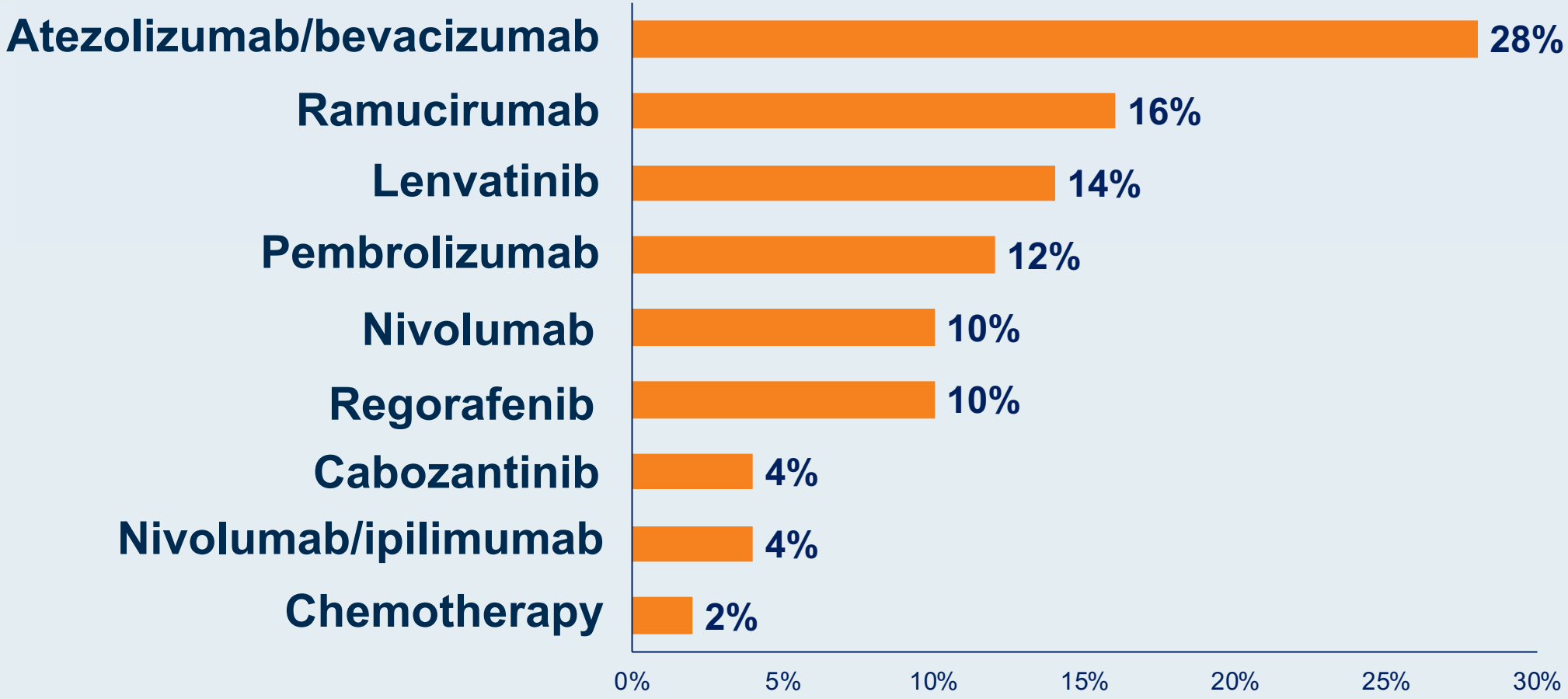

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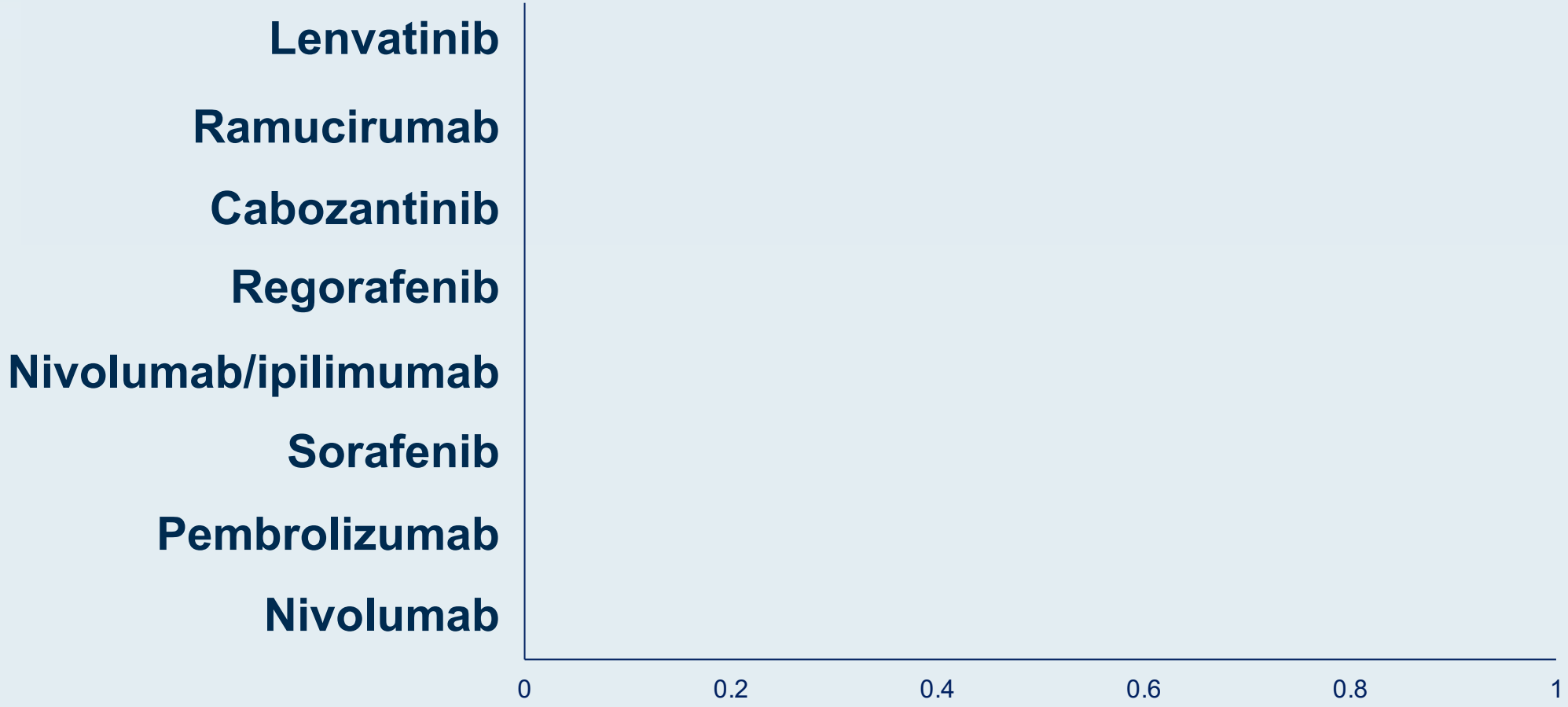
Regulatory and reimbursement issues aside, what would be your most likely second-line systemic therapy for a 65-year-old patient with HCC, a Child-Pugh A score and a PS of 0 who received first-line atezolizumab/bevacizumab with minimal toxicity and then experienced disease progression after 18 months (AFP = 2,500)?



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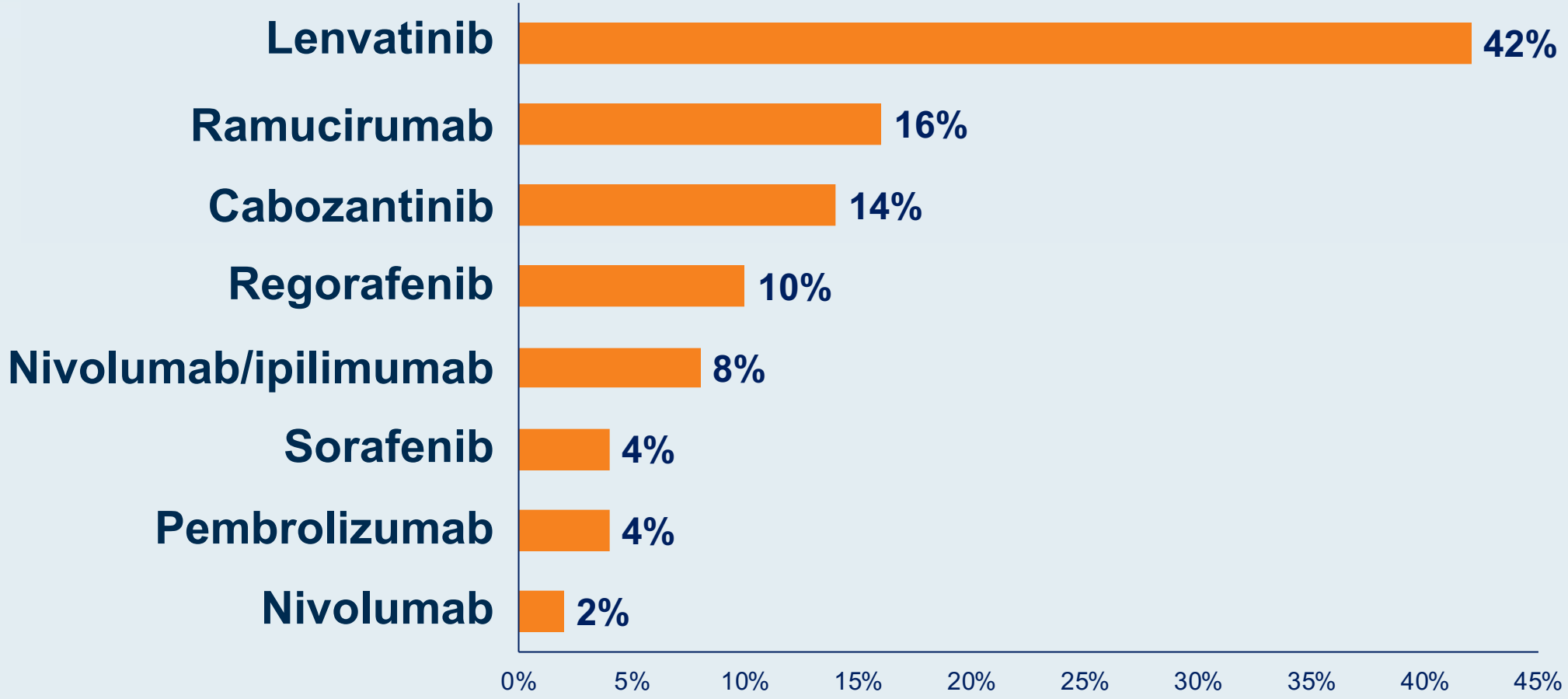
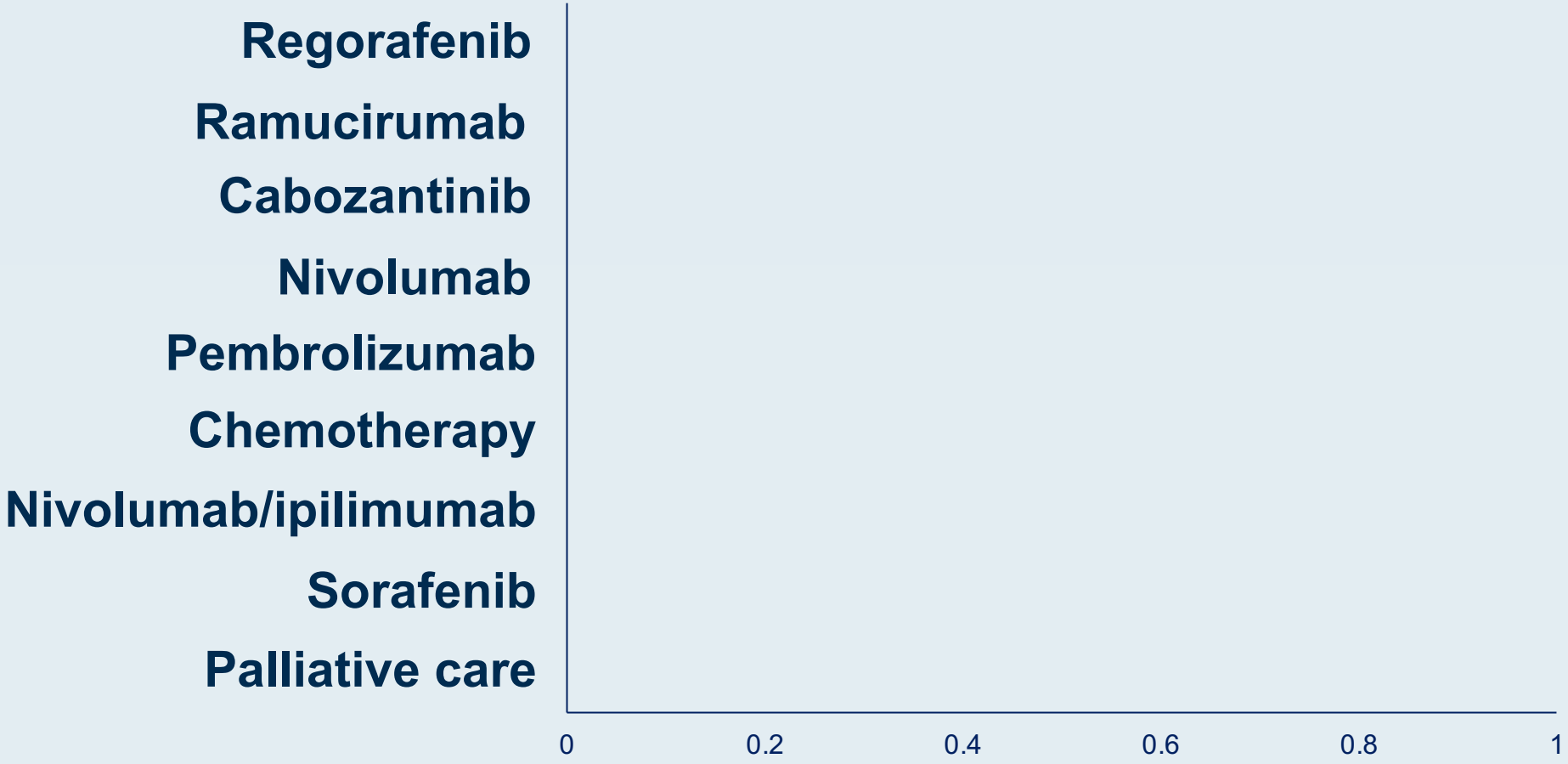


Survey of 50 US-based medical oncologists

What would be your most likely third-line systemic therapy recommendation for an otherwise healthy 65-year-old patient with HCC who experienced disease progression on first-line atezolizumab/bevacizumab and second-line lenvatinib (AFP = 2,500)?



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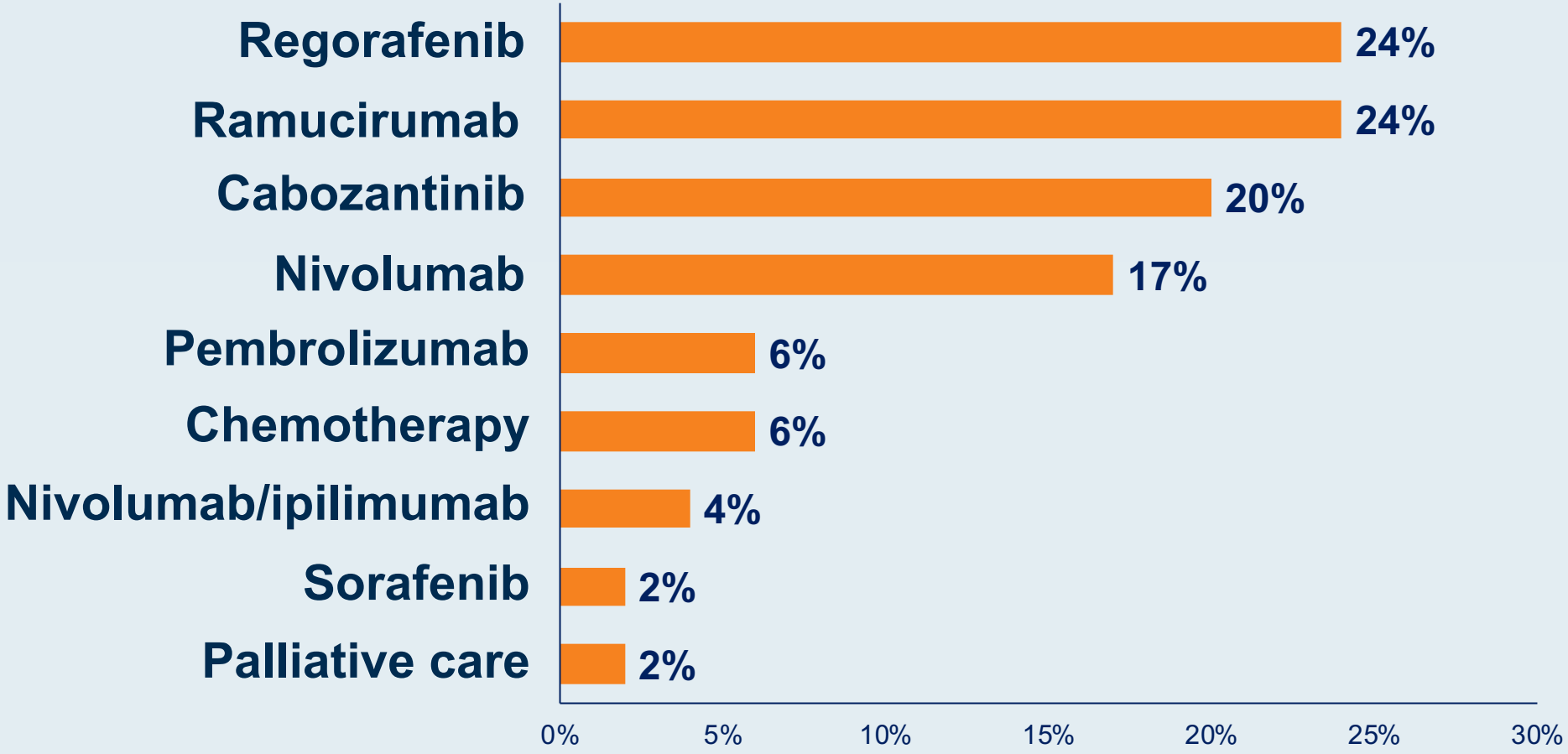

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MODULE 2: Second- and Third-Line Treatment of HCC

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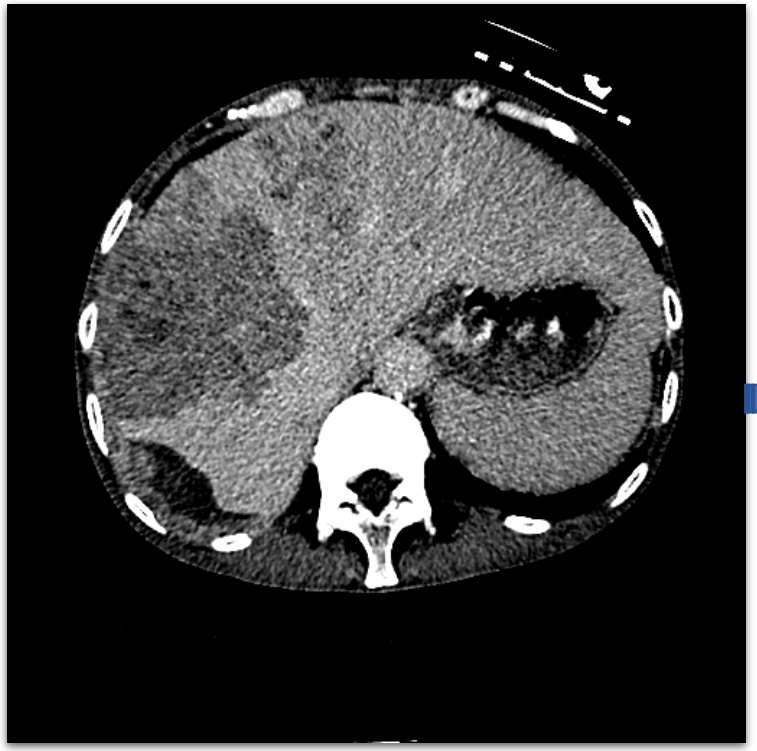
  - A 61-year-old man with HCC and disease progression on sorafenib
  - A 61-year-old man with newly diagnosed HCC treated with lenvatinib

Case Presentation – Dr Philip: A 61-Year-Old Man with HCC and Disease Progression on Sorafenib

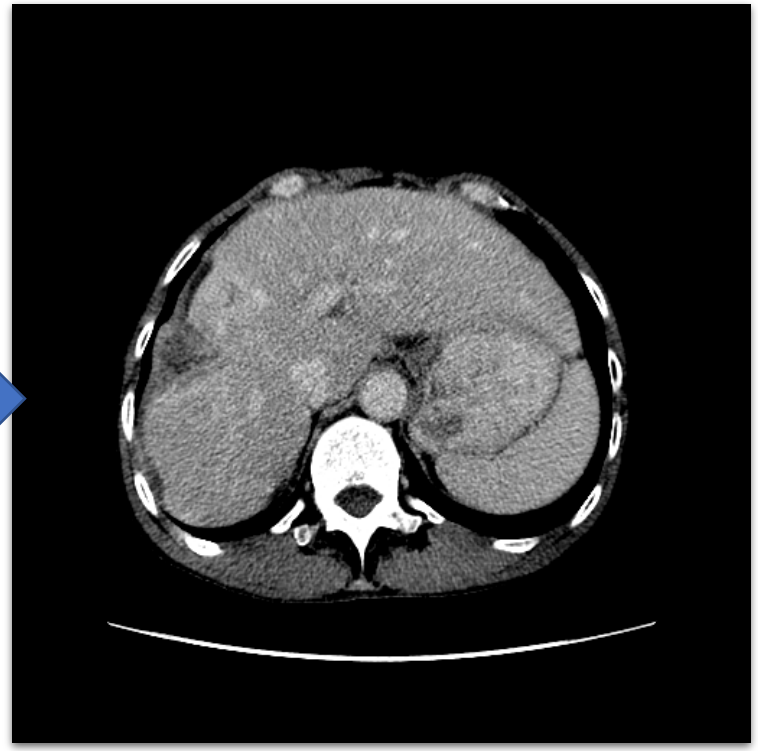
- 61 year old African American male
- 2009 – Hepatitis C
- 2012 – CT scan showed multiple liver masses with serum AFP > 200,000, Child Pugh-A6
- ECOG PS = 2, chronically malnourished
- 6/2012 – Started on sorafenib 400 mg BID
- Marked subjective improvements
- Well tolerated except for palmar hyperkeratosis and G1 transaminitis

Case Presentation – Dr Philip: A 61-Year-Old Man with HCC and Disease Progression on Sorafenib (continued)

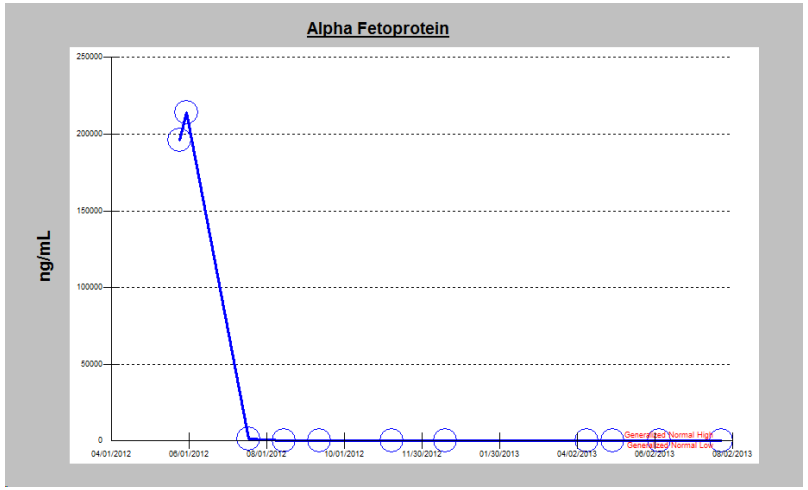
Very marked response to sorafenib!



Pre-Sorafenib



On Sorafenib

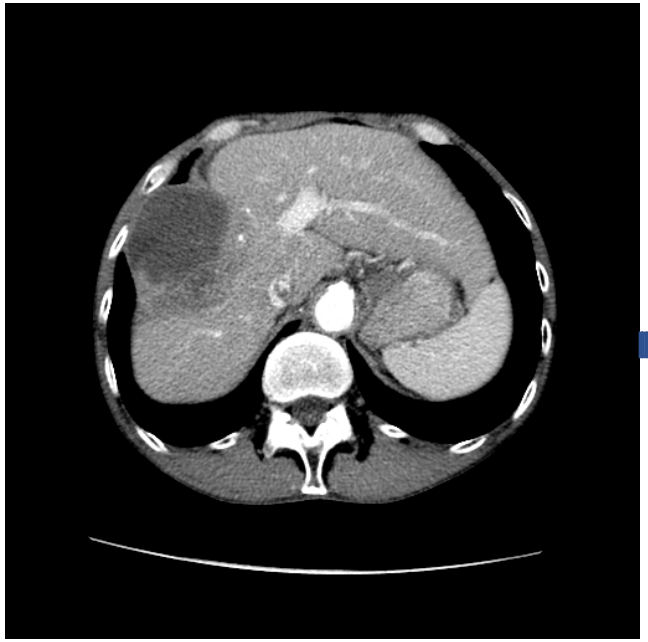


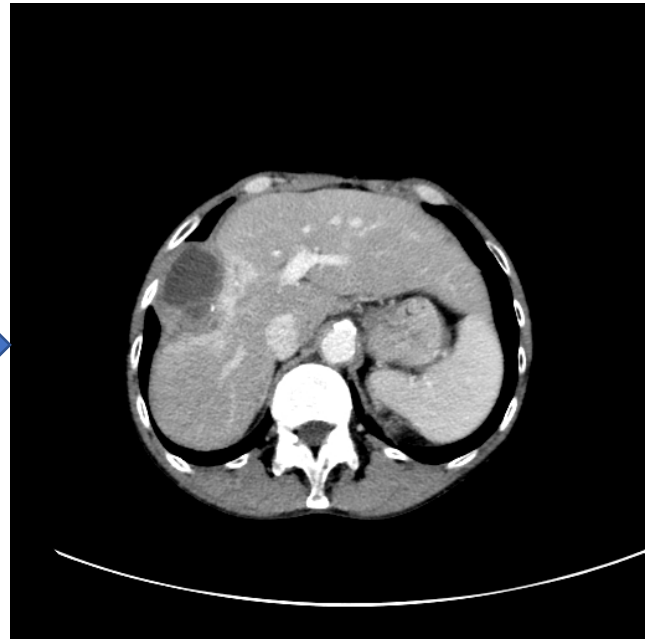
Case Presentation – Dr Philip: A 61-Year-Old Man with HCC and Disease Progression on Sorafenib (continued)

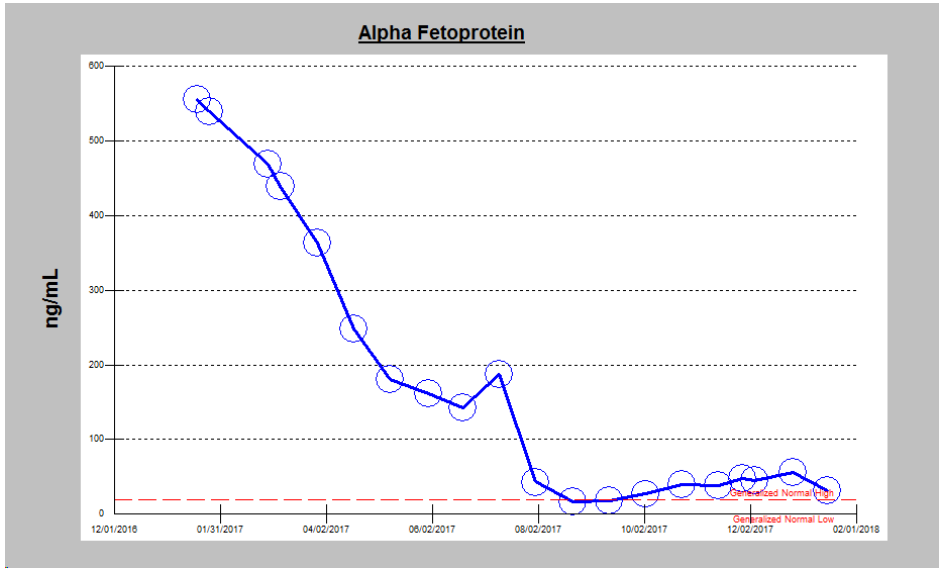
- Liver biopsy = HCC, PD-L1 2+
- After 4.5 years of sorafenib had evidence of disease progression based on radiology and serum AFP
- PS = 1
- Enrolled on phase III randomized trial of pembrolizumab
- 2/2017 – Started treatment (pembrolizumab or placebo)
- Complications
  - Grade 3 skin rash
  - Hypothyroidism

Case Presentation – Dr Philip: A 61-Year-Old Man with HCC and Disease Progression on Sorafenib (continued)

Significant response to pembrolizumab/ placebo







Case Presentation – Dr Philip: A 61-Year-Old Man with HCC and Disease Progression on Sorafenib (continued)

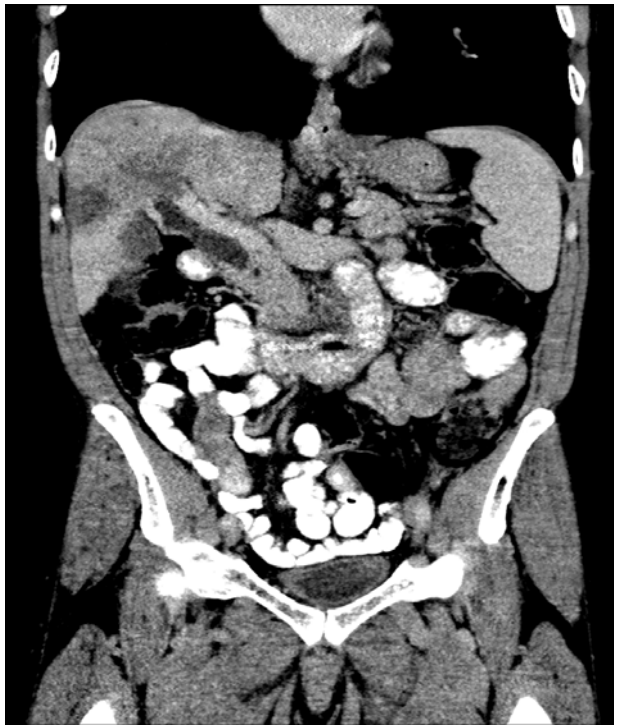
- After completion of 31 cycles of 3-weekly treatments disease progression on imaging and serum AFP
- 1/2019 – Started on Lenvatinib
- Worsening PS after initial drop in AFP
- 4/2019 – CT shows PD
- Hospice

Case Presentation – Dr Philip: A 61-Year-Old Man with Newly Diagnosed HCC Treated with Lenvatinib

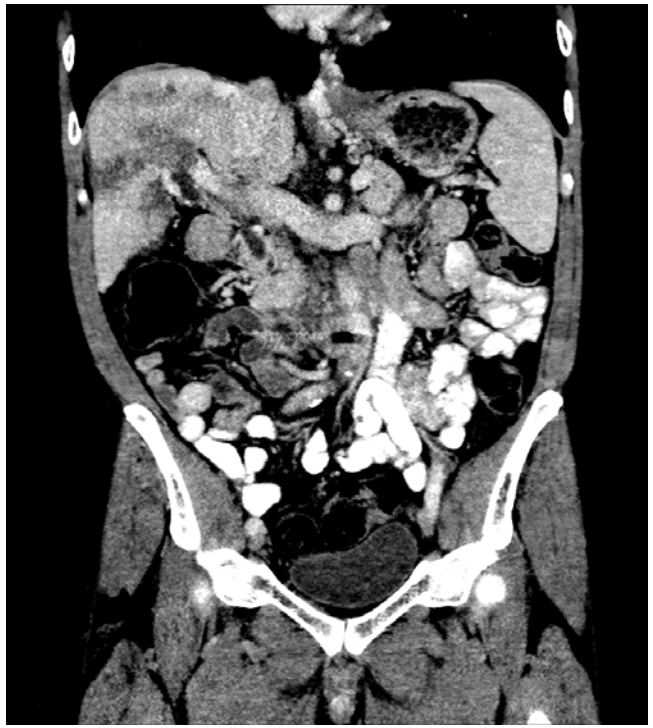
- 61 year old male
- PS 1-2
- Known history of hepatitis C, hypertension
- Child Pugh A6
- Right upper quadrant pain
- CT shows large mass in the liver
- Biopsy – HCC
- Had banding of esophageal varices 5 years earlier

Case Presentation – Dr Philip: A 61-Year-Old Man with Newly Diagnosed HCC Treated with Lenvatinib (continued)

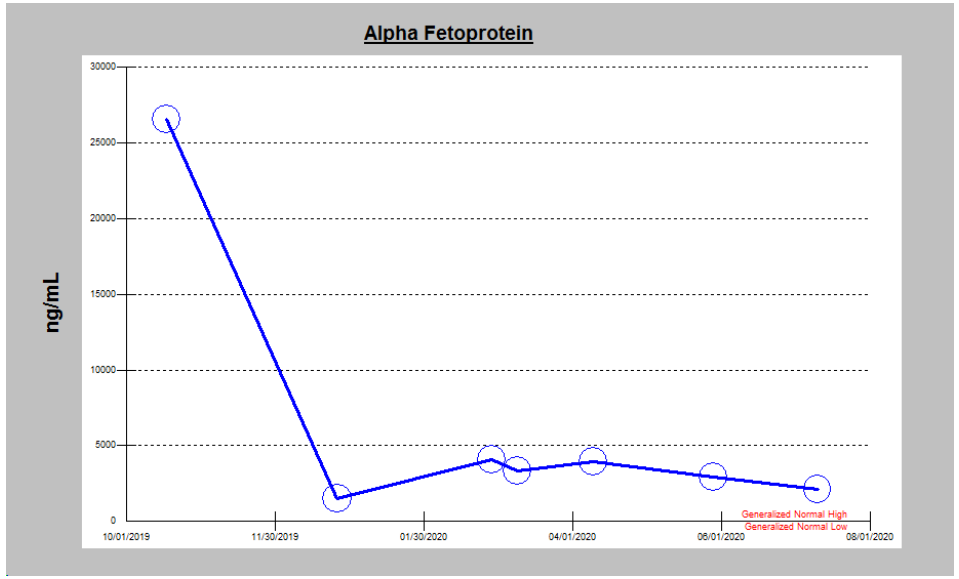
Started on Lenvatinib 9/2019



Pre-Lenvatinib



On-Lenvatinib



Case Presentation – Dr Philip: A 61-Year-Old Man with Newly Diagnosed HCC Treated with Lenvatinib (continued)

- After 10 months of Lenvatinib
- New CT scan shows disease early disease progression
- Will return to clinic for discussion of further management

MODULE 3: Localized Pancreatic Cancer

- **Key Relevant Data Sets**
  - PREOPANC-1: Pre- vs postoperative treatment for localized pancreatic cancer
- **Faculty Cases – Dr Bekaii-Saab**
  - A 57-year-old woman with Stage IIA adenocarcinoma of the pancreas and a BRCA1 mutation
  - A 63-year-old man with Stage IIB adenocarcinoma of the pancreas

Dr Favaro: A man in his 70s with locally advanced unresectable pancreatic cancer

Justin Peter Favaro, MD, PhD

- Locally advanced, unresectable pancreatic cancer
- FOLFIRINOX x 4 months
  - Tumor shrinkage, but still involving the celiac artery

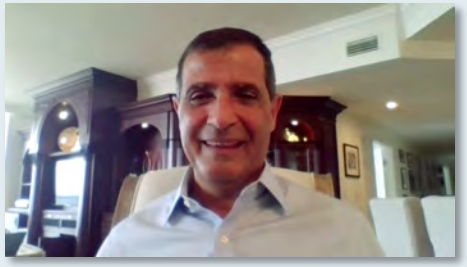
Questions:

- When you have a small primary pancreatic cancer, clear margins, no vessel involvement, and no lymph node involvement, do you take them to surgery up front? Or do you give everybody neoadjuvant chemotherapy and then go to surgery?

RTP RESEARCH TO PRACTICE

Challenging Questions and Cases

Dr Atif Hussein: A 52-year-old man with pancreatic cancer – BRCA2 mutation



Atif Hussein, MD, MMM

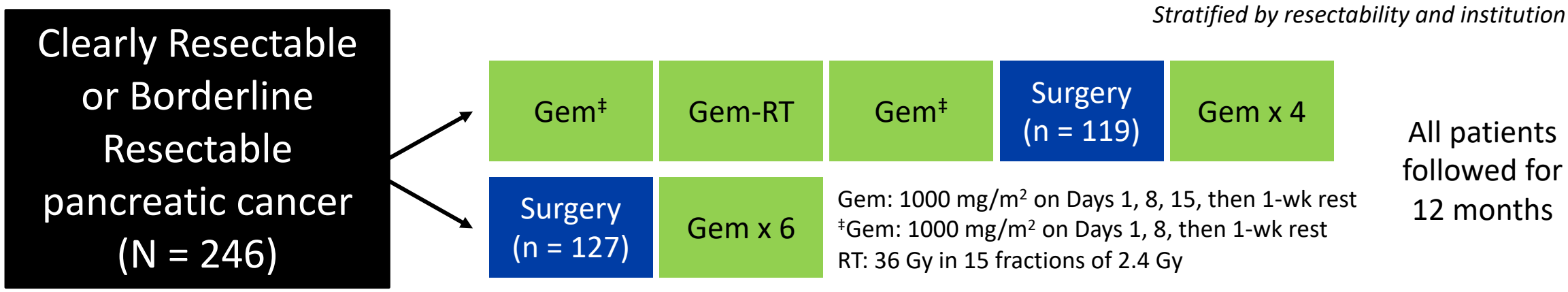
- Presents with right upper quadrant pain, a 10-pound weight loss over 3 months
- Imaging: Mass in the head of the pancreas; No distant metastases
- Upper GI endoscopy and US guided biopsy: Poorly differentiated adenocarcinoma T3 with one 2-cm node positive for adenocarcinoma
- FOLFIRINOX x 6, with excellent PR
- Whipple procedure
  - 9 mm residual adenocarcinoma, 1/9 lymph nodes, negative margins
- Family history positive for breast and ovarian cancer
- Genetic counselling: Deleterious BRCA2 mutation

Questions:

- What therapy would you recommend adjuvantly? Radiation therapy with or without chemotherapy?
- What about maintenance PARP inhibitor?

RTP RESEARCH TO PRACTICE

PREOPANC-1: Phase III Trial Comparing Pre- vs Postoperative Treatment for Localized Pancreatic Cancer



Primary endpoint: OS

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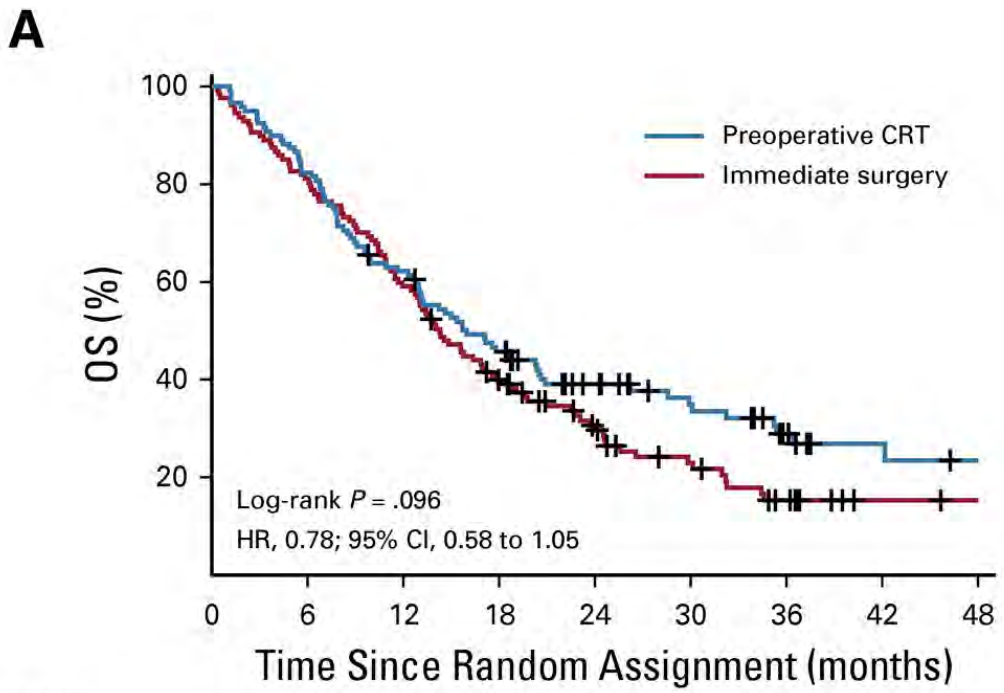
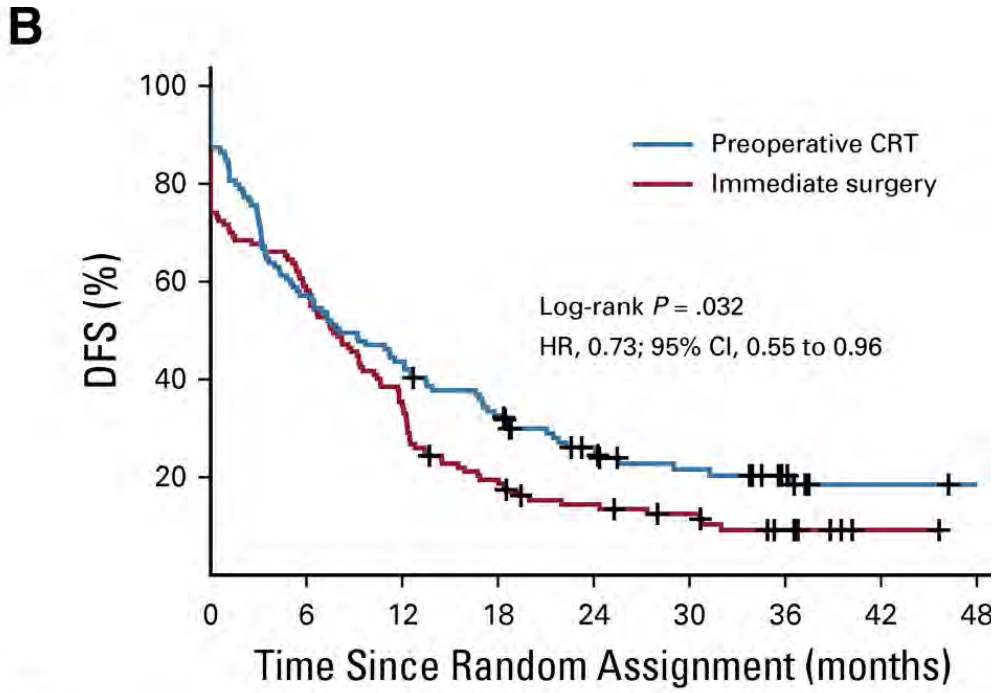
Versteijne E et al. *J Clin Oncol.* 2020;38(16);1763-1773.

Courtesy of Tanios Bekaii-Saab, MD, FACP

PREOPANC-1: Efficacy Results





Median OS 16.0 vs 14.3 months

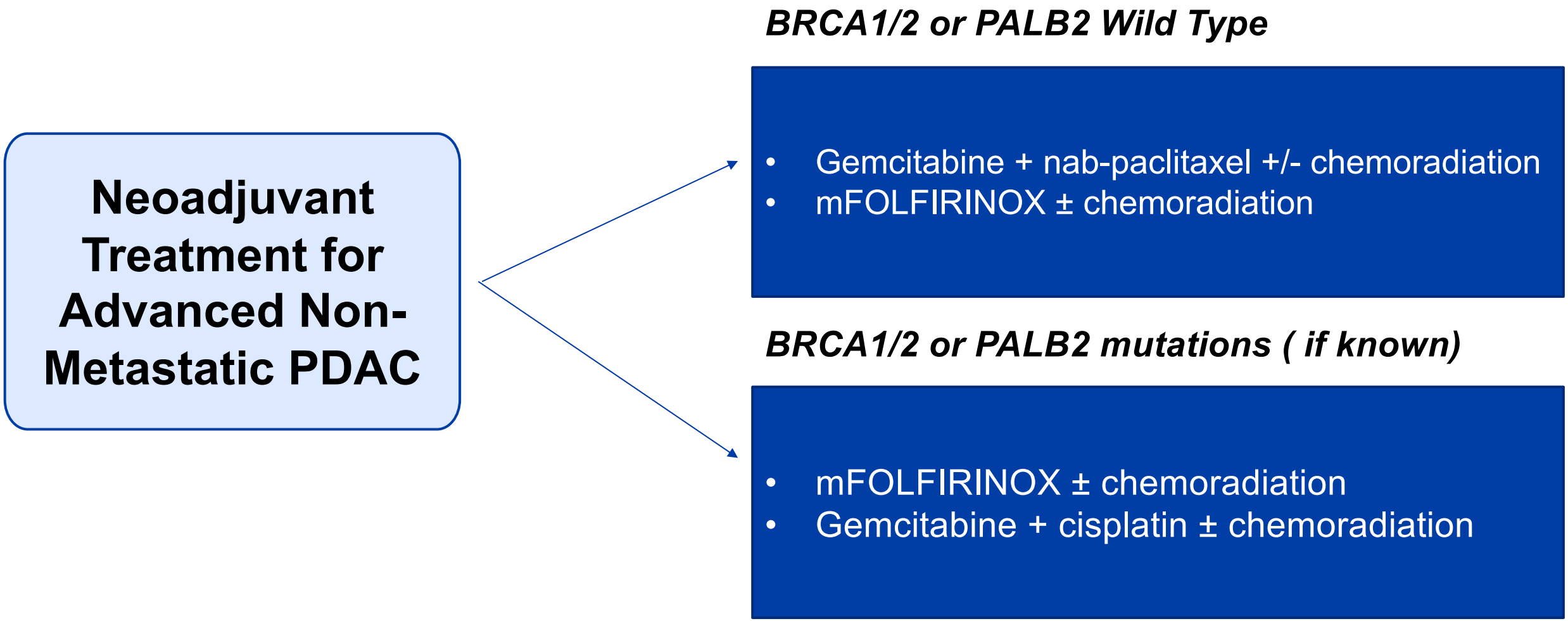
Median DFS 8.1 vs 7.7 months

- ✓ *Both OS and DFS statistically significant in favor of preop tx in borderline resectable, but not resectable, subgroup*
- ✓ *R0 resection rate higher in preop tx group (71% vs 40%, P < 0.001)*

Versteijne E et al. *J Clin Oncol.* 2020;38(16);1763-73.

Courtesy of Tanios Bekaii-Saab, MD, FACP

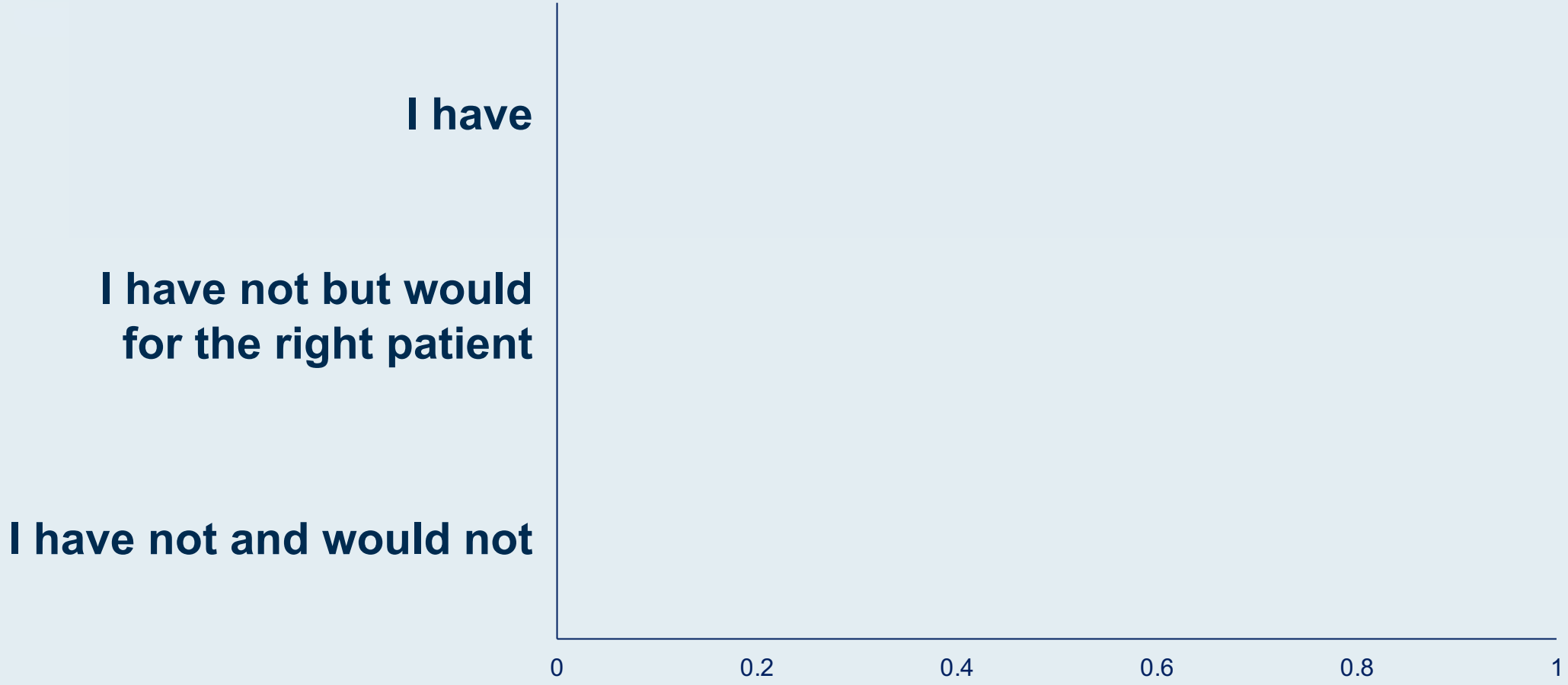
Neoadjuvant Treatment for Advanced Non-Metastatic PDAC



1. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. v1.2020. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed January 8, 2020.

Courtesy of Tanios Bekaii-Saab, MD, FACP

Have you or would you administer neoadjuvant therapy to a patient with pancreatic adenocarcinoma that appears to be resectable?



Survey of 50 US-based medical oncologists

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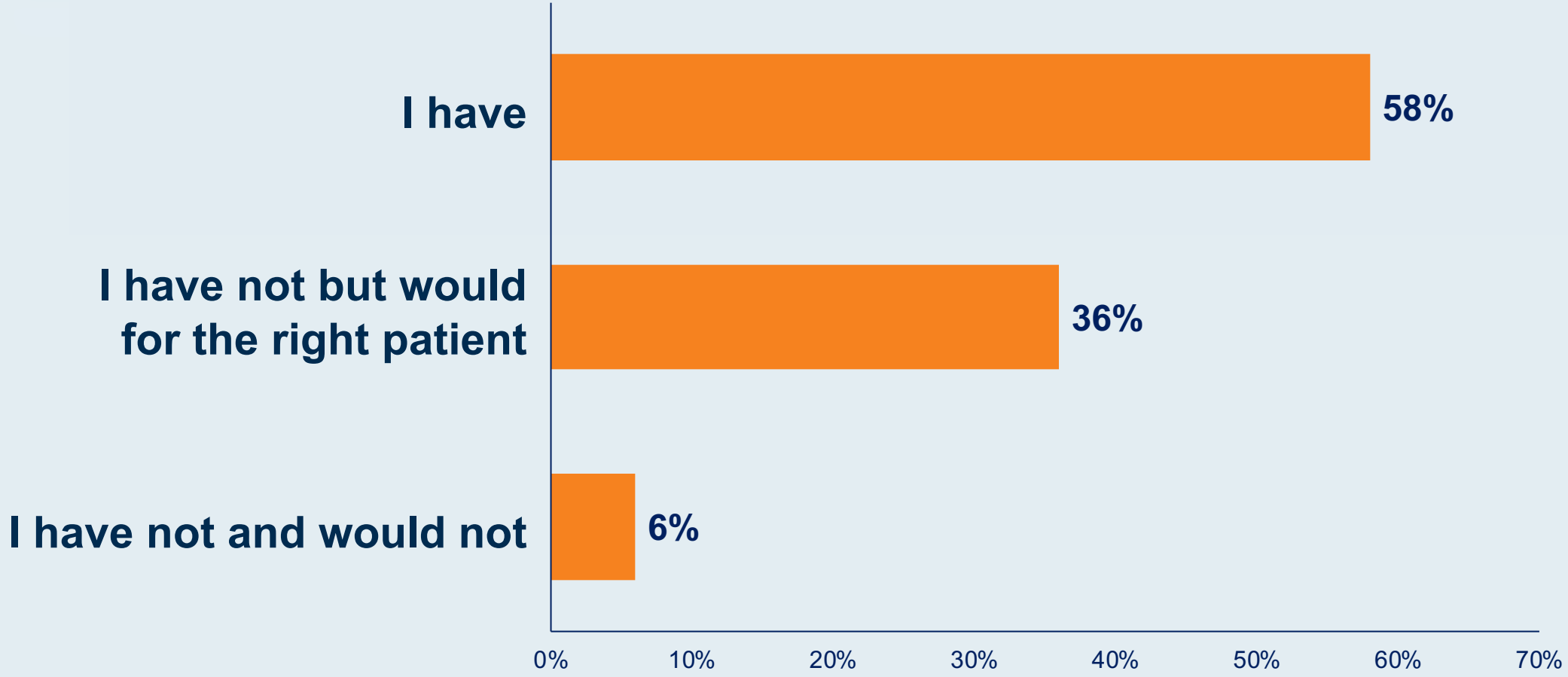
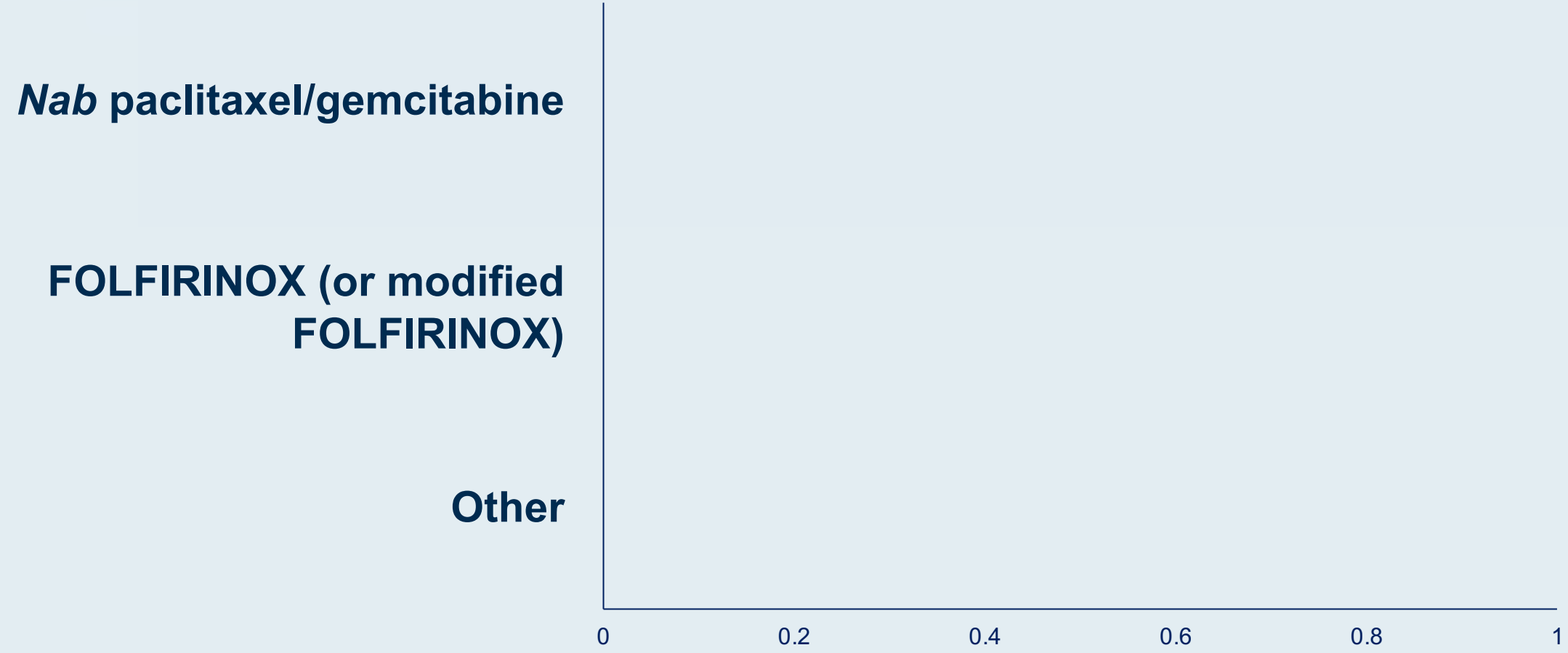


Survey of 50 US-based medical oncologists

What is your usual neoadjuvant systemic therapy recommendation for a 78-year-old patient with borderline resectable pancreatic cancer?



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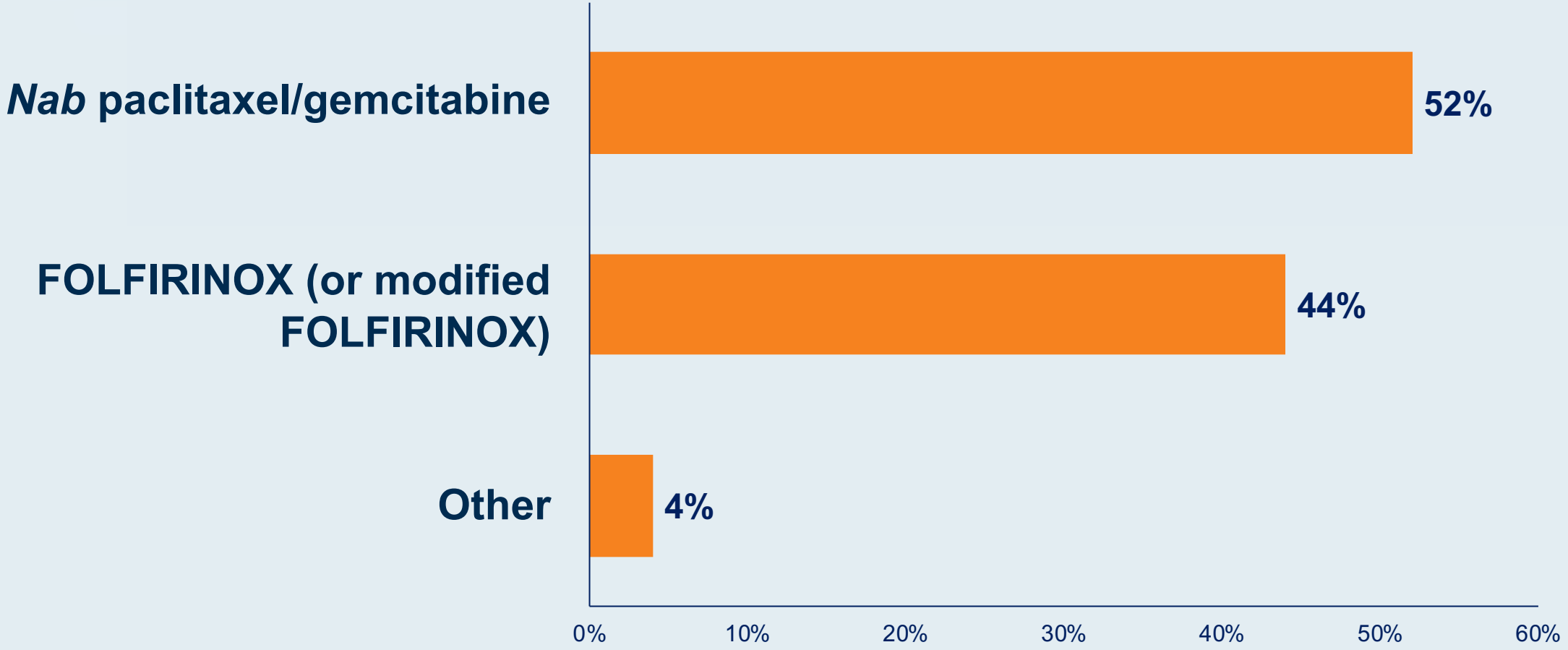
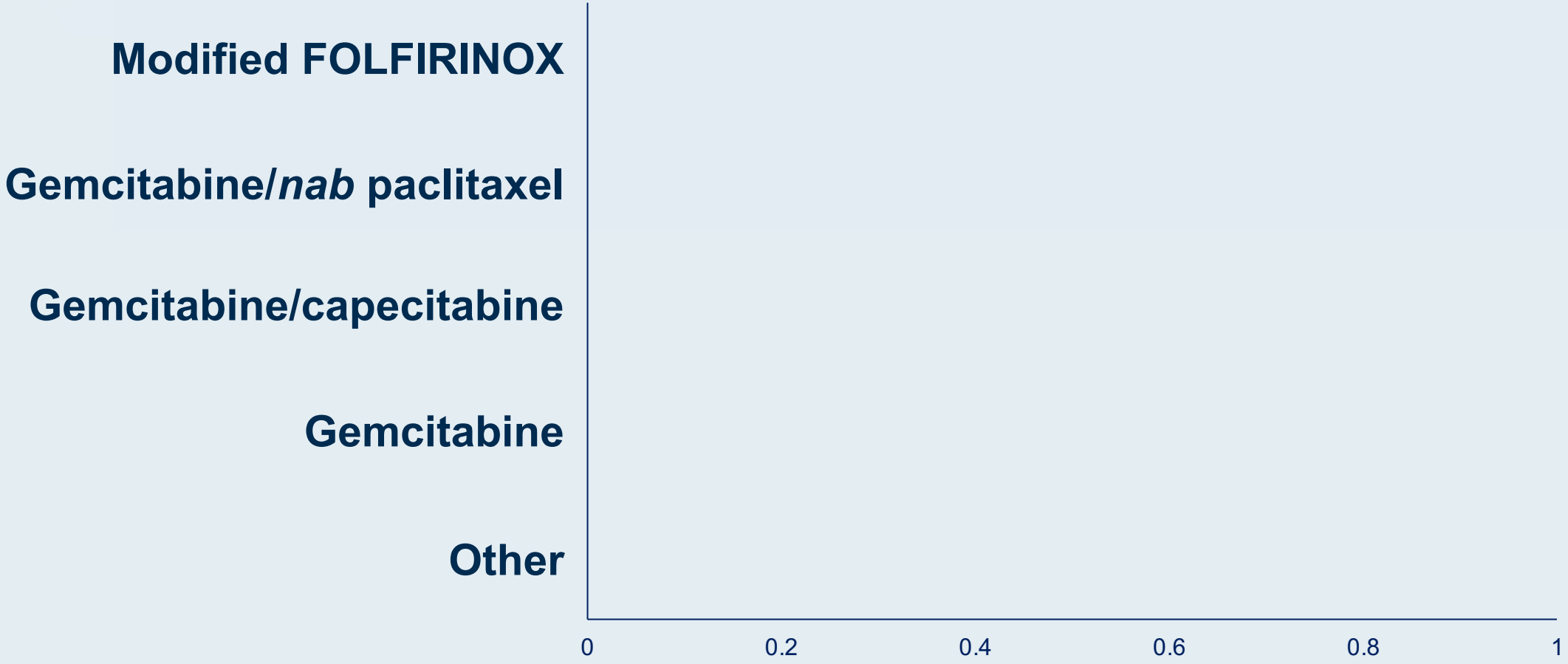


Survey of 50 US-based medical oncologists

What is your likely adjuvant systemic therapy recommendation for an otherwise healthy 65-year-old patient who is s/p surgical resection of pancreatic adenocarcinoma?



Survey of 50 US-based medical oncologists

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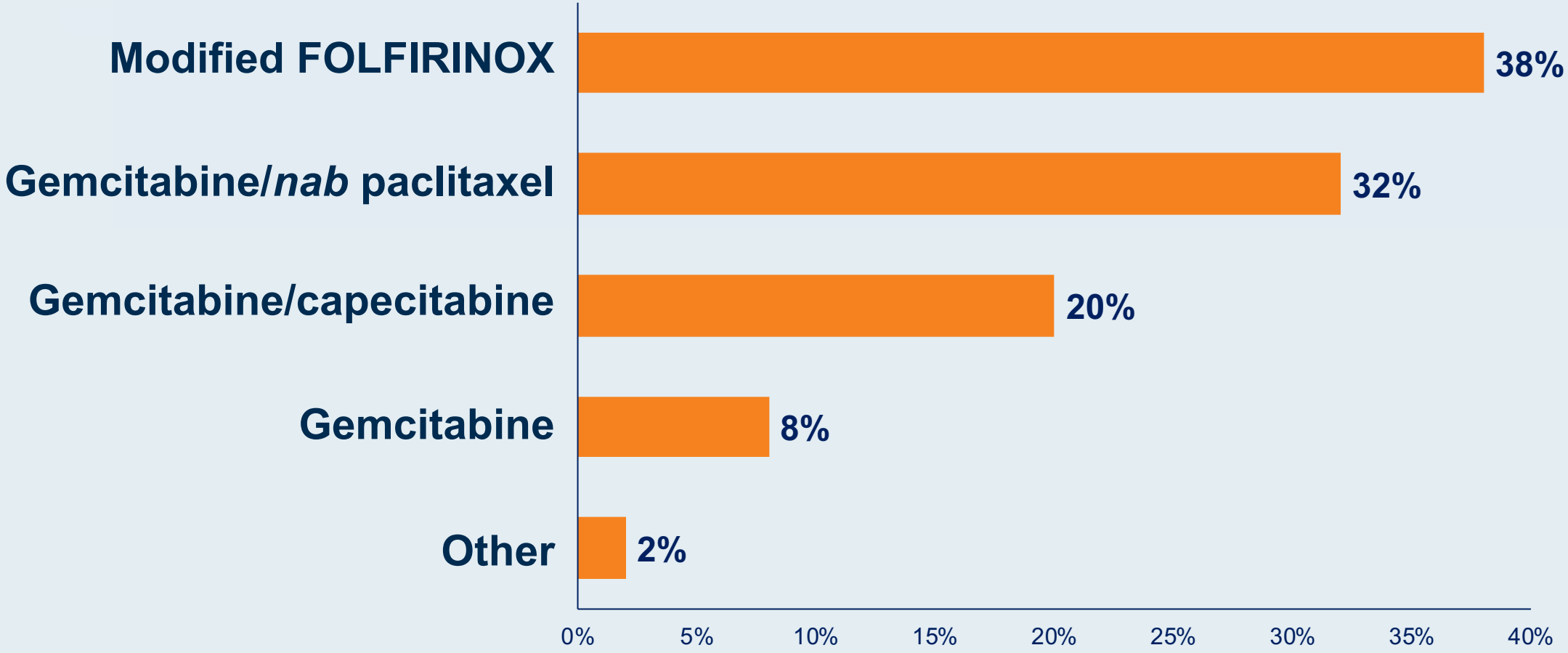

Survey of 50 US-based medical oncologists

MODULE 3: Localized Pancreatic Cancer

- **Key Relevant Data Sets**
  - PREOPANC-1: Pre- vs postoperative treatment for localized pancreatic cancer
- **Faculty Cases – Dr Bekaii-Saab**
  - A 57-year-old woman with Stage IIA adenocarcinoma of the pancreas and a BRCA1 mutation
  - A 63-year-old man with Stage IIB adenocarcinoma of the pancreas

Case Presentation – Dr Bekaii-Saab: A 57-Year-Old Woman with Stage IIA Adenocarcinoma of the Pancreas and a BRCA1 Mutation

- 57-year-old woman presenting with epigastric pain worse with food intake, weight loss of 15 lbs over 2 months and fatigue . She reports recent change in her urine to tea colored and her stools appearing like clay. On physical exam she is mildly cachectic and obviously jaundiced.
  - PMHx significant for well controlled HTN; active overall, with ECOG PS = 0.
  - Fam Hx significant for Breast Cancer , Ovarian Cancer and Pancreas Cancer
- Diagnostic w/u includes as follows:
  - Blood tests showing elevated LFTs, including total bilirubin of 6.7 mg/dL.
  - CT scans C/A/P notable for a 4.3 cm pancreatic head mass with no involvement of the celiac artery, superior mesenteric artery and vein, or portal vein.
  - PET/MRI confirms the pancreas mass and shows no evidence of distant metastases.
  - Endoscopic ultrasound (EUS) with FNA confirms a moderately differentiated adenocarcinoma c/w pancreas
    - Stage 2a
  - ERCP shows a bile duct stricture with placement of a metallic biliary stent
  - Germline testing reveal a mutation in BRCA1
  - Fourteen days later her total bili = 1.4 mg/dL and CA19-9 elevated at 95 U/mL (normal < 33).
  - The patient was initiated on gemcitabine and cisplatin with a plan to proceed with 4 cycles prior to restaging

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Case Presentation – Dr Bekaii-Saab: A 63-Year-Old Man with Stage IIB Adenocarcinoma of the Pancreas

- 63-year-old man presenting with severe pain worse with food intake, appetite loss and weight loss of 25 lbs over 3 months. On physical exam he is cachectic with no jaundice .
  - PMHx non significant. His ECOG PS = 0.
- Diagnostic w/u includes as follows:
  - Blood tests are WNL.
  - CT scans C/A/P notable for a 2.5 cm pancreatic tail mass with abutment of celiac artery of < 180^0.
  - PET/MRI confirms the pancreas mass and shows no evidence of distant metastases.
  - Endoscopic ultrasound (EUS) with FNA confirms a moderately differentiated adenocarcinoma c/w pancreas
    - Stage 2b
  - CA19-9 elevated at 295 U/mL (normal < 33).
  - Germline testing did not reveal any pathologic mutations
  - The patient was initiated on mFOLFIRINOX with a plan to proceed with 4 cycles prior to restaging

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MODULE 4: Metastatic Pancreatic Cancer

- **Key Relevant Data Sets**
  - POLO trial: Maintenance olaparib
  - Phase II study of cisplatin/gemcitabine +/- veliparib in gBRCA/PALB2+ PDAC
- **Faculty Cases – Dr O'Reilly**
  - A 52-year-old man with newly diagnosed pancreatic cancer and a germline BRCA2 mutation
  - A 93-year-old woman with metastatic pancreatic cancer

Dr Leasure: A woman in her early 60s with metastatic pancreatic cancer – BRCA2 mutation

Nick C Leasure, MD

- **PMH: Treated for TNBC many years ago**
- Presents with de novo metastatic pancreatic cancer
- **BRCA2 mutation**
- FOLFIRINOX, with complete remission in pancreas and lung, near complete disappearance in liver
- Plan to enroll on clinical trial **of maintenance PARP inhibitor + either ipilimumab or nivolumab**

Question

- **In a patient like this, who is BRCA2-positive, would you just treat her, stop and put her on a PARP inhibitor just like we would a patient with ovarian cancer?**

Dr Ma: A man in his early 60s with metastatic pancreatic cancer – Significant comorbidities

Yanjun Ma, MD, PhD

- PMH: T2DM, significant cardiovascular (ejection fraction: 15%), peripheral vascular disease
- Metastatic pancreatic cancer
- NGS: MSS, no actionable mutations
- Dose-reduced gemcitabine/nab paclitaxel x 8 months, with good response
  - Treatment discontinued due to leg amputation
  - Patient prefers no more chemotherapy
- Pembrolizumab
  - CA19-9 declined, CR
  - Treatment discontinued due to development of significant arthritic pain

Dr Favaro: A 79-year-old man with metastatic pancreatic cancer – EGFR exon 19 deletion

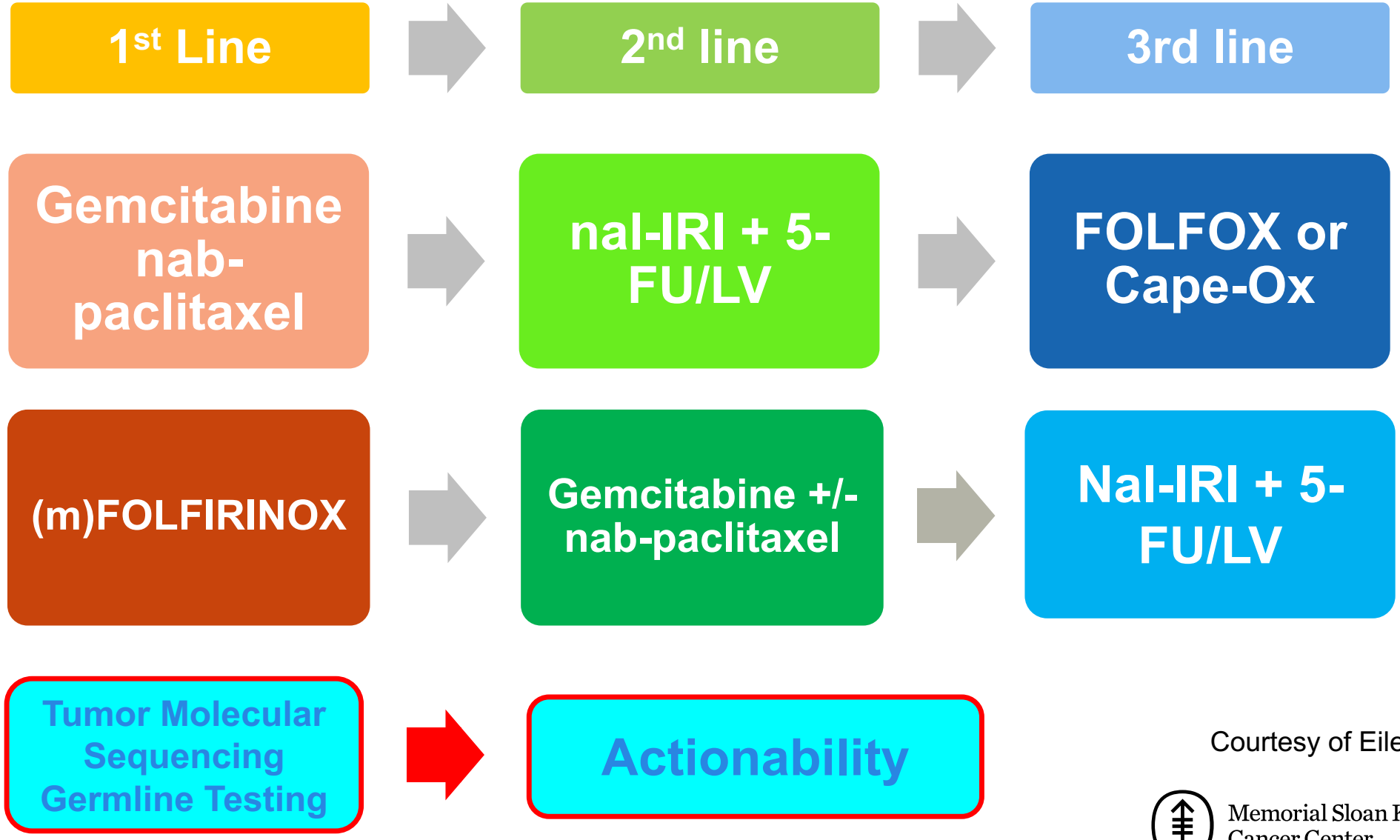
Justin Peter Favaro, MD, PhD

- 12/2018: Diagnosed with Stage IV pancreatic cancer
  - Pancreatic mass, lymphadenopathy, a few lung mets, a supraclavicular node; Minimally symptomatic
- NGS: EGFR exon 19 deletion
- Modified FOLFIRINOX, with CR
- Currently, receiving 5-FU, low-dose irinotecan

Questions:

- What is the role of EGFR exon 19 deletion in the biology of this disease?
- What is the role of EGFR TKIs in these patients?
- What treatments should be considered next?

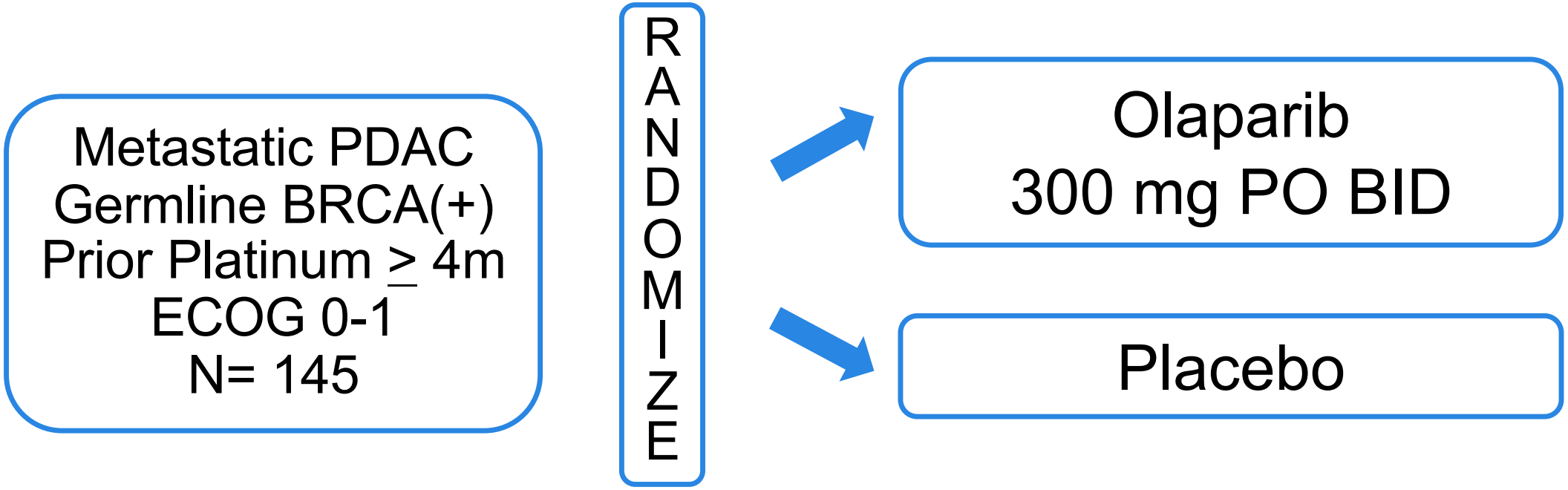
Therapeutic Approach: Advanced PDAC 2020



Courtesy of Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

Phase III Maintenance (POLO)
Platinum Therapy → Olaparib/Placebo



Randomization 3: 2

Primary Endpoint: PFS (blinded independent central review mRECIST 1.1)

N ~ 3,500 screened

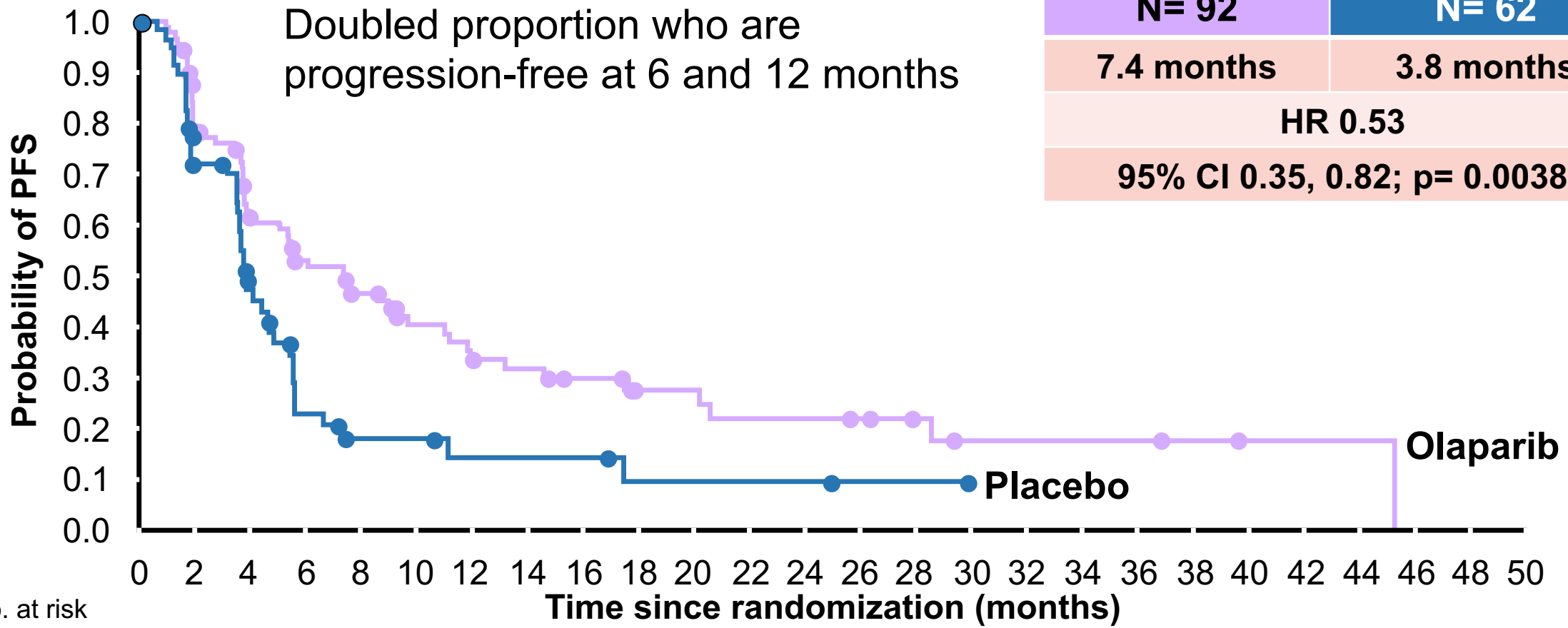
Golan, T. New Engl J Med, 2019

Courtesy of Eileen M. O'Reilly, MD

POLO: Primary Endpoint PFS (BICR)

>3.5 month difference
Doubled proportion who are progression-free at 6 and 12 months

Olaparib N= 92	Placebo N= 62
7.4 months	3.8 months
HR 0.53	
95% CI 0.35, 0.82; p= 0.0038	



No. at risk

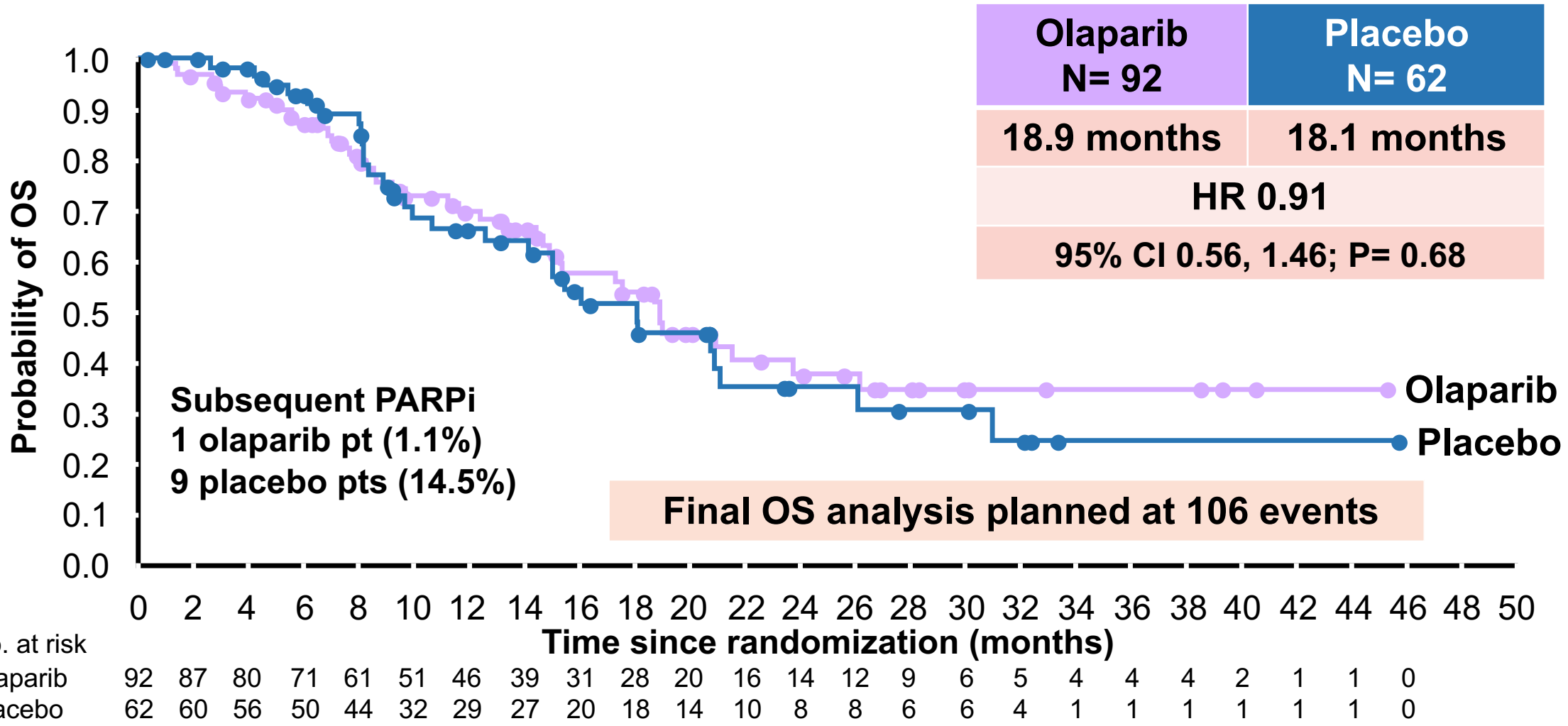
Olaparib	92	69	50	41	34	24	18	17	14	10	10	8	8	7	5	3	3	3	3	2	1	1	1	0
Placebo	62	39	23	10	6	6	4	4	4	2	2	2	2	1	1	0								

Golan, T. New Engl J Med, 2019

Courtesy of Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

POLO Maintenance: Overall Survival (46% Mature)



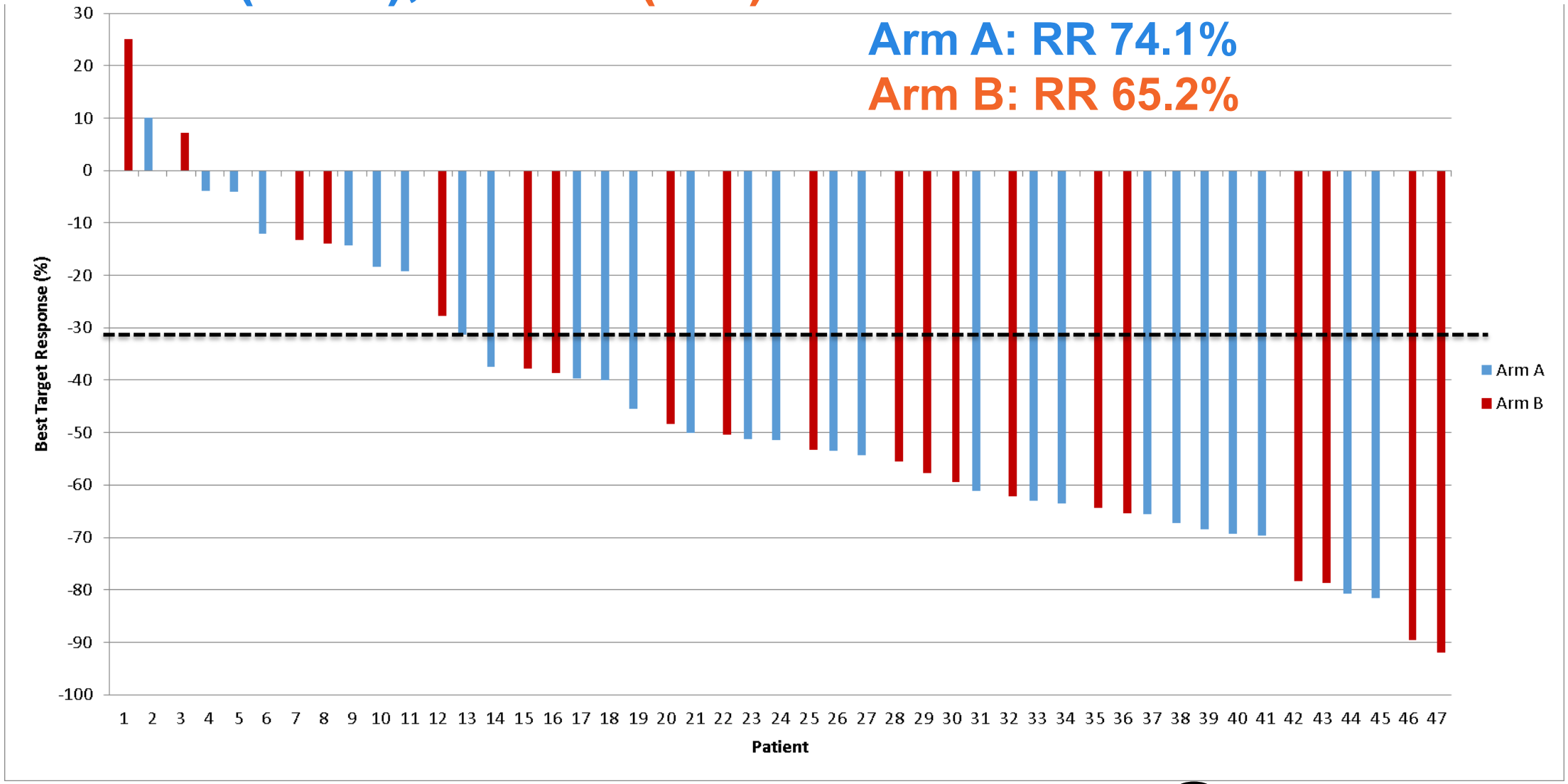
Golan, T. New Engl J Med, 2019

Courtesy of Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

Cisplatin/Gemcitabine +/- Veliparib g*BRCA1/2, PALB2*

Arm A (CGV), Arm B (CG)

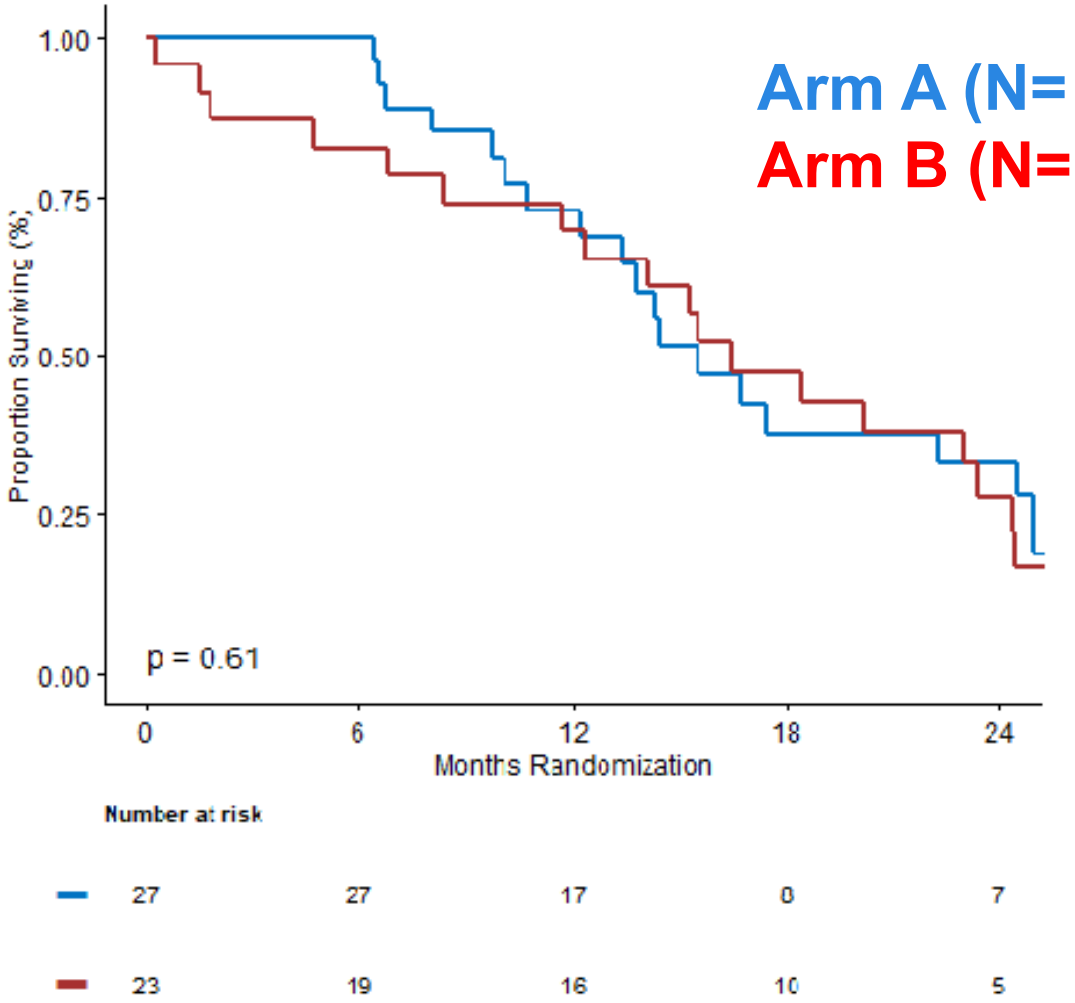


O'Reilly, EM. J Clin Oncol, 2020

Courtesy of Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

Cisplatin/Gemcitabine +/- PARPi g*BRCA/PALB2*: Overall Survival



Arm A (N= 27): 15.5 months (95% CI 12.2- 24.3)
Arm B (N= 23): 16.4 months (95% CI 11.7- 23.4)

Two-year survival
31% (95% CI 17.8%- 44.4%)

Three-year survival
18% (95% CI: 8.1%- 30.7%)

O'Reilly, EM. J Clin Oncol, 2020

Courtesy of Eileen M. O'Reilly, MD

Memorial Sloan Kettering Cancer Center

MSK Phase II Trial: Olaparib + Pembrolizumab Maintenance Q3 2020

Metastatic PDAC

Platinum Response 1st/2nd Line

ECOG 0-1

A. Core DNA-Damage Repair Gene Mutation (N= 32)

Germline/Somatic *BRCA1/2, PALB2*

B. Non-Core Mutation (N= 15)

14 genes: *ATM, BAP1, BARD1, BLM, BRIP1, CHEK2, FAM175A, FANCA, FANCC, NBN, RAD50, RAD51, RAD51C, RTEL1*

C. CR/PR to Platinum Based Therapy (N= 15)

No mutation identified

Pembrolizumab 200mg q 3 weeks + Olaparib 300mg BID

Primary: ORR Simon-2 stage/arm A; Single arm B, C

Park, WP, O'Reilly, EM

Courtesy of Eileen M. O'Reilly, MD

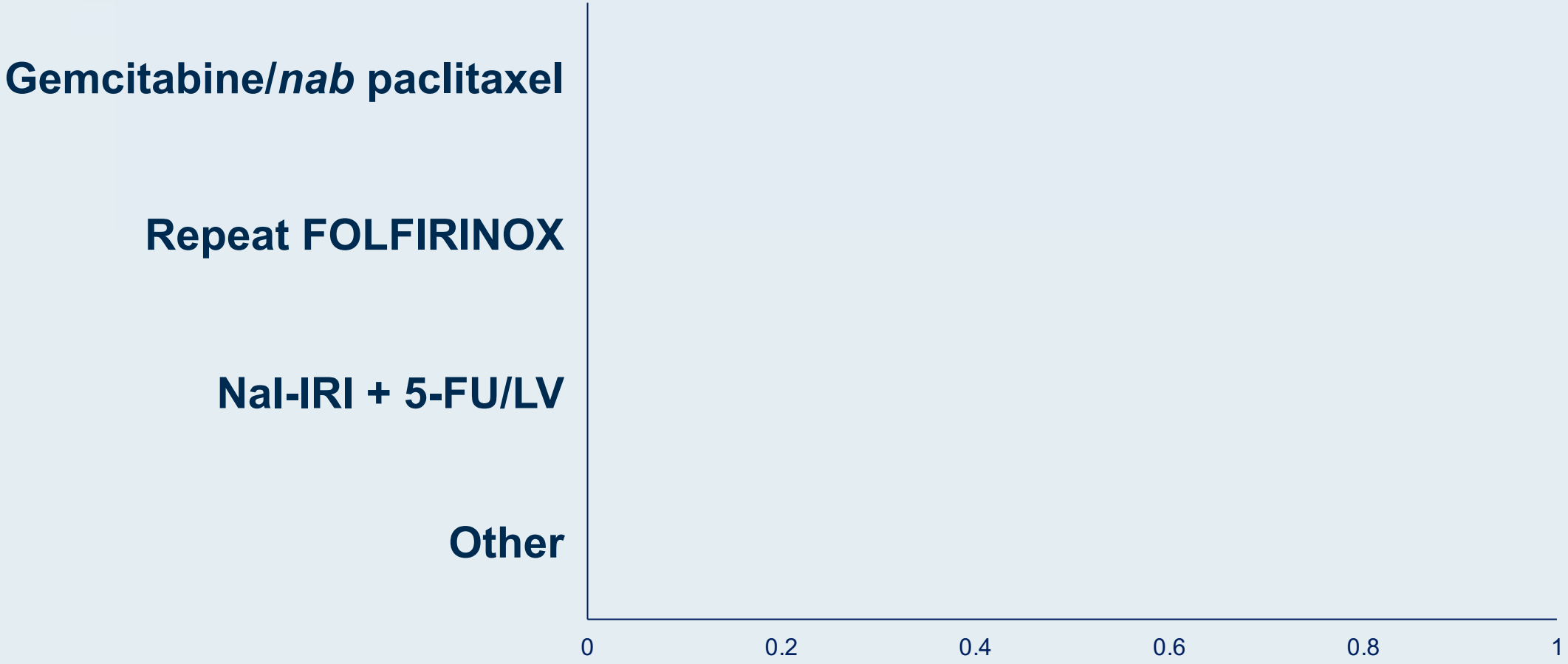
Memorial Sloan Kettering Cancer Center

Major Areas of Novel Therapy Development

- **Cytotoxic therapy**
  - First line: Phase III nal-IRIFOX vs gem/nab-P (N= 750)
- **Metabolism**
  - Phase III AVENGER 500: mFOLFIRINOX + devimistat vs FOLFIRINOX (N= 500)
  - Phase III TRYbeCA-1: Chemo +/- eryaspase (N= 500)
- **Immune therapy**
  - PARKER consortium: Rand phase II Gem/nab-P + APX005M (CD40-targeting antibody) +/- nivolumab (pending)
  - Rand phase II PA.7: Gem/nab-P +/- tremelimumab, durvalumab (Pending)
  - MORPHEUS: Gem/nab-P, atezolizumab + anti-TIGIT, or + bevacizumab
- **DNA-damage repair**
  - Building on platinum (1st line), olaparib (maintenance)

Courtesy of Eileen M. O'Reilly, MD

In general, what treatment would you recommend for a patient with pancreatic cancer who develops metastatic disease 12 months after neoadjuvant FOLFIRINOX followed by surgical resection?



Survey of 50 US-based medical oncologists

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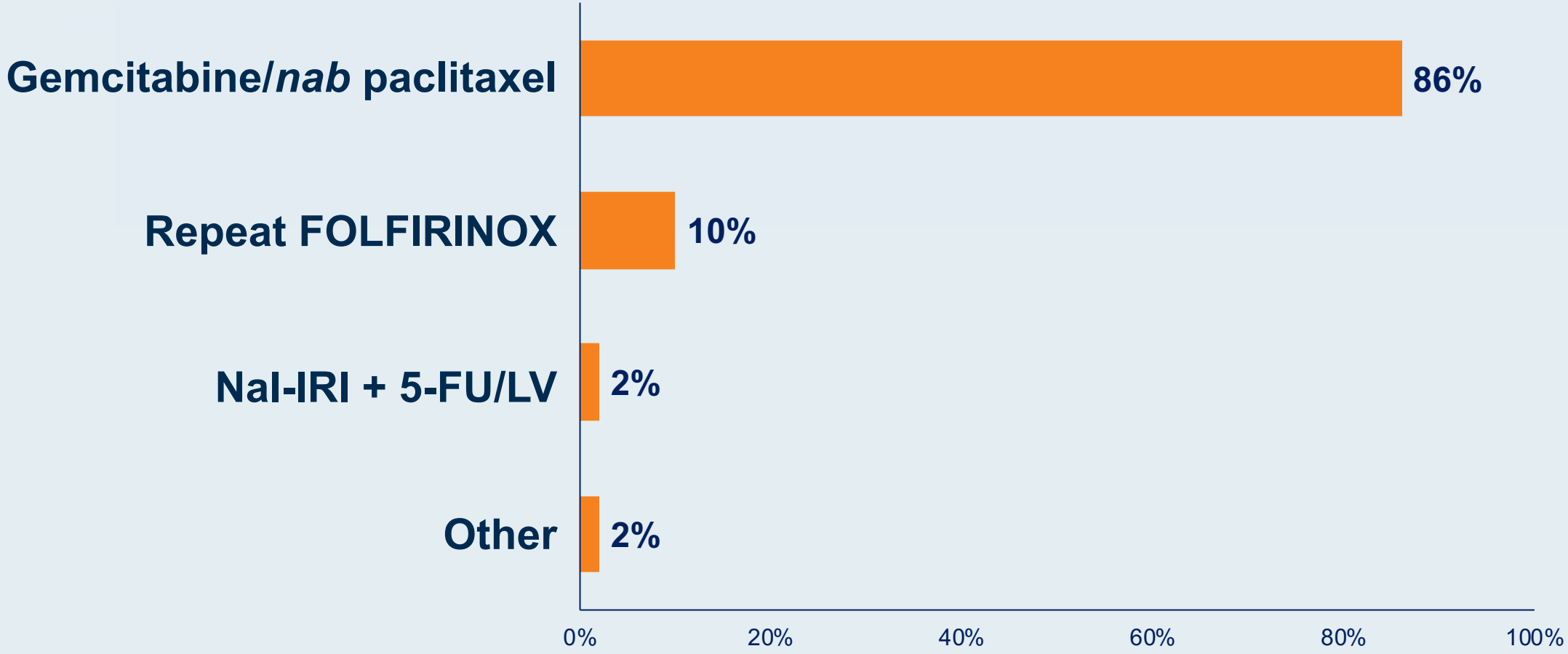
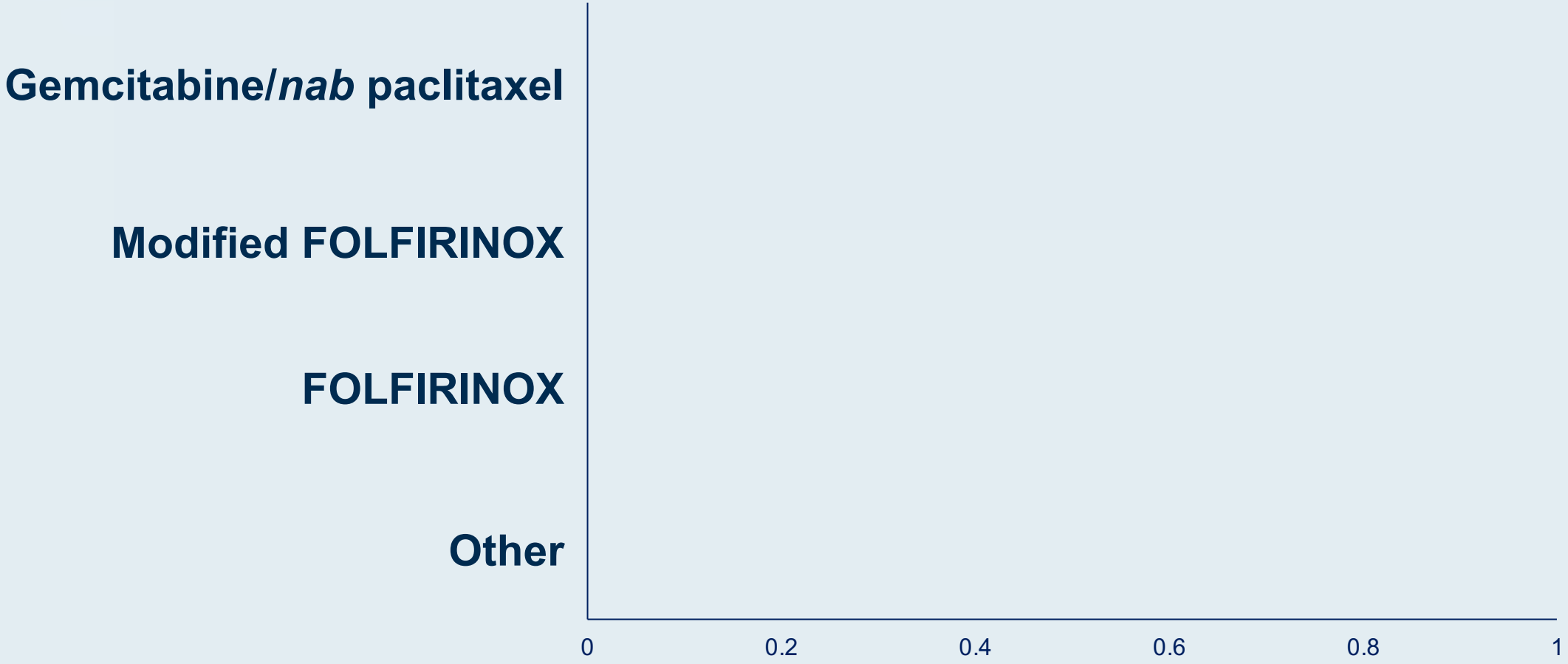


Survey of 50 US-based medical oncologists

What is your usual first-line therapy recommendation for a 75-year-old patient with newly diagnosed metastatic pancreatic cancer and a PS of 0?



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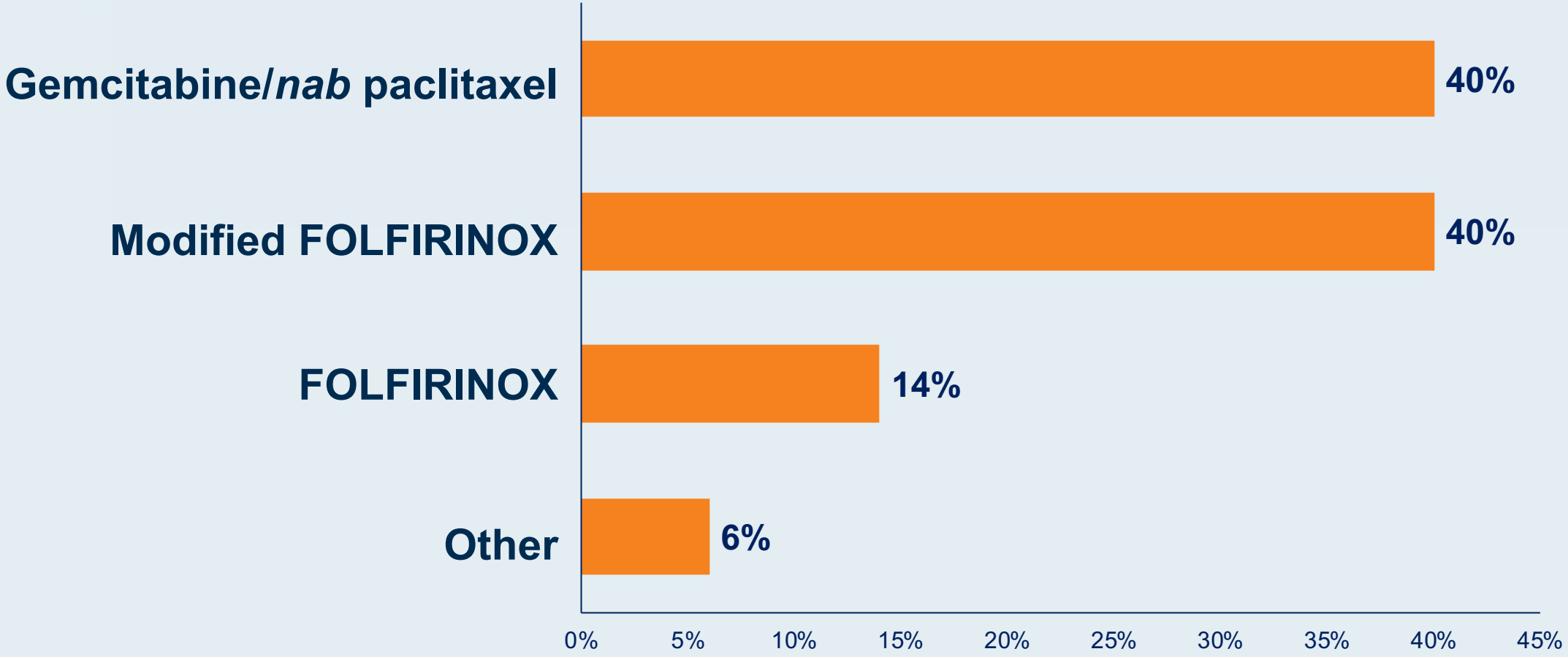
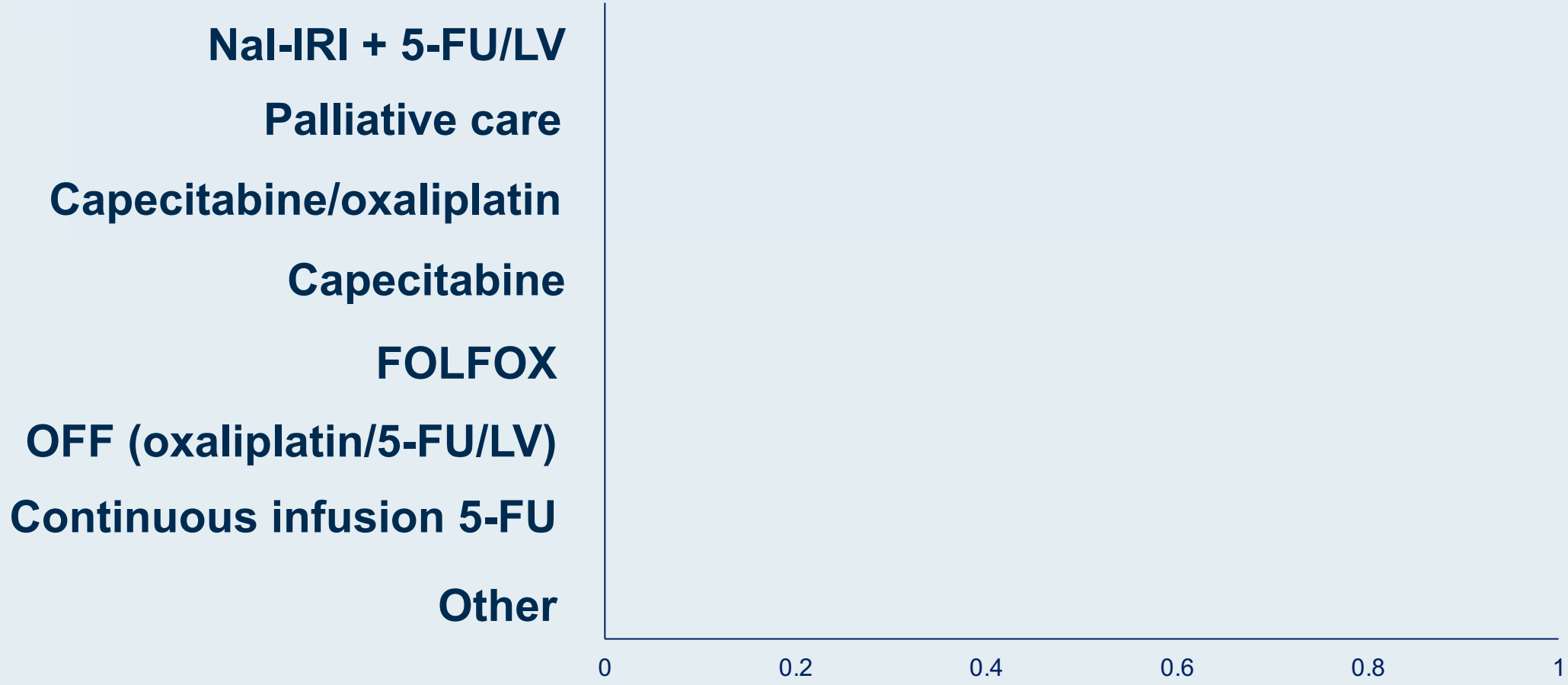


Survey of 50 US-based medical oncologists

In general, which treatment would you recommend for a 65-year-old patient (PS 0) who receives first-line FOLFIRINOX followed by second-line gemcitabine/*nab* paclitaxel for metastatic pancreatic cancer and experiences disease progression?



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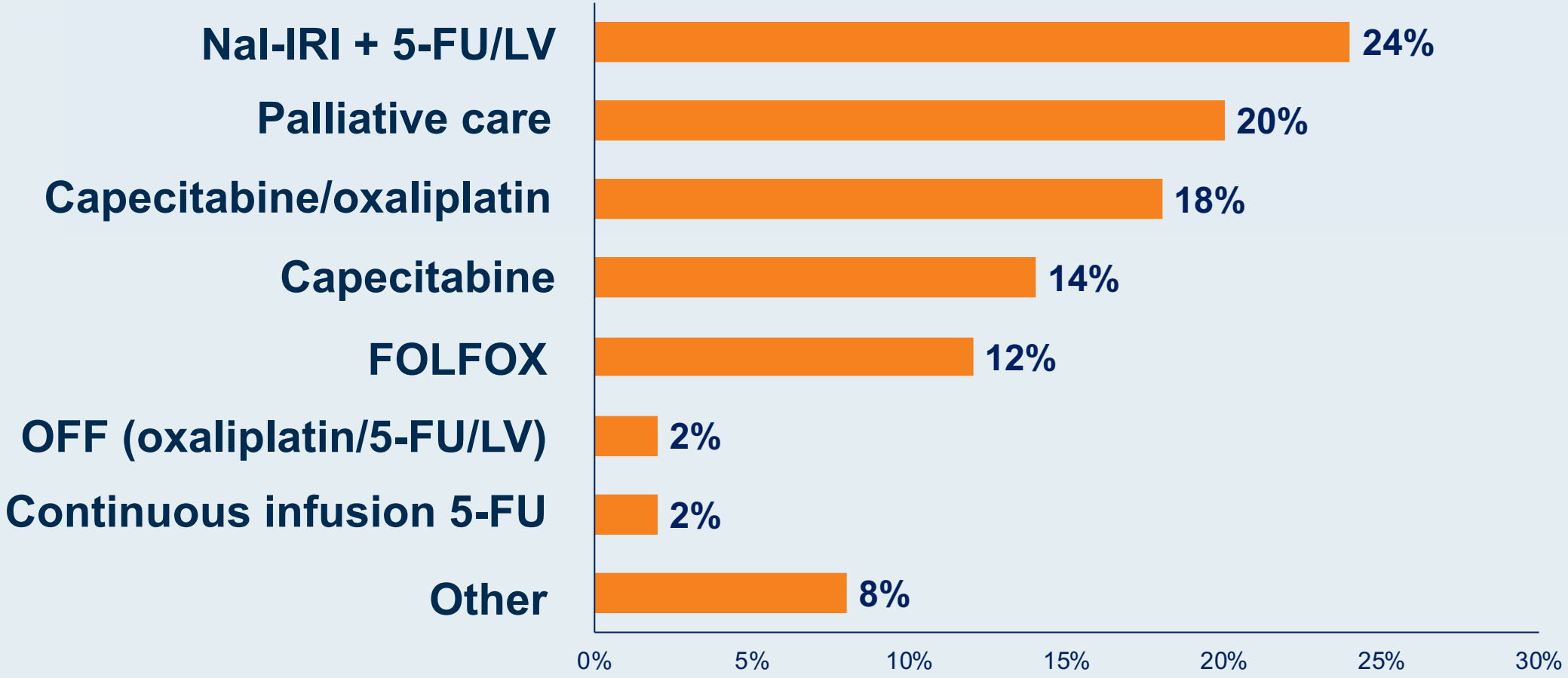
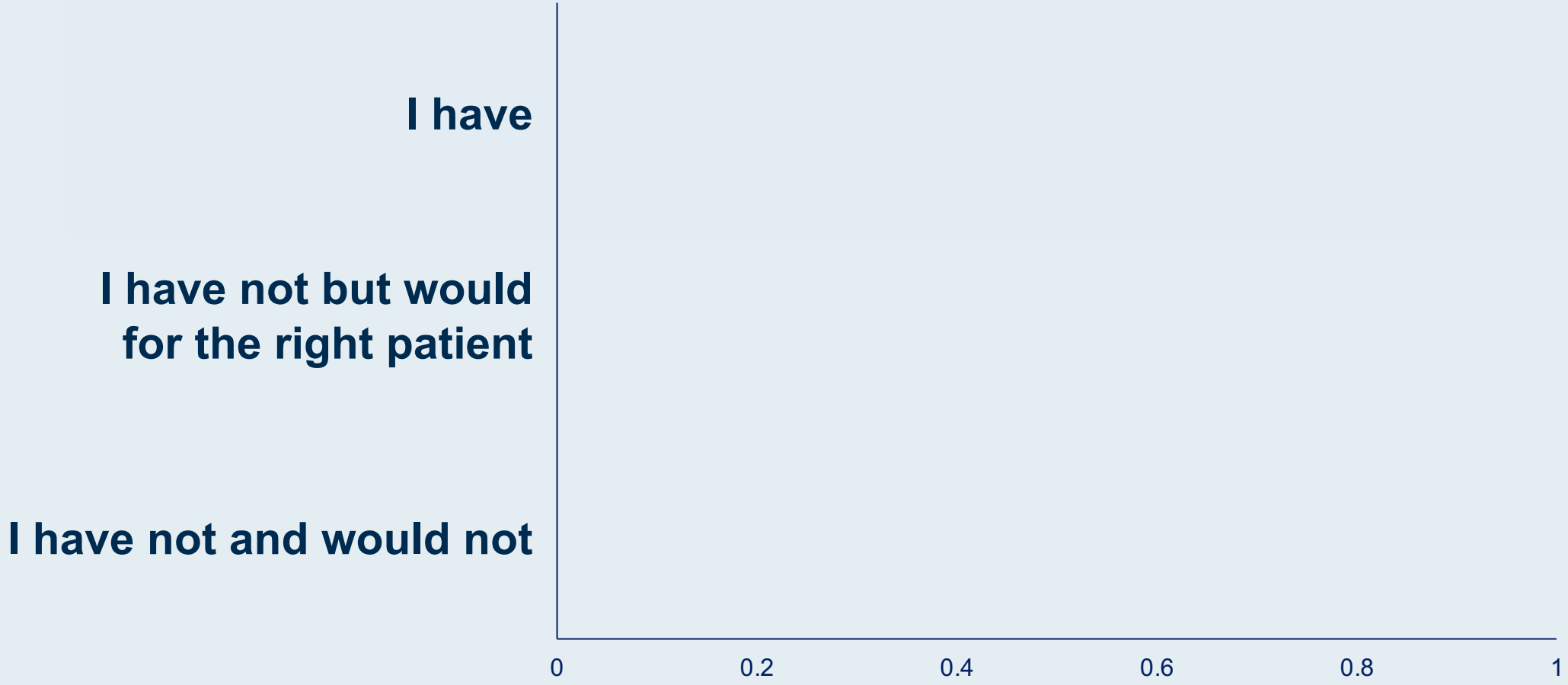


Survey of 50 US-based medical oncologists

Regulatory and reimbursement issues aside, have you or would you attempt to access a PARP inhibitor for a patient with metastatic pancreatic cancer and a germline PALB2 mutation?



Survey of 50 US-based medical oncologists

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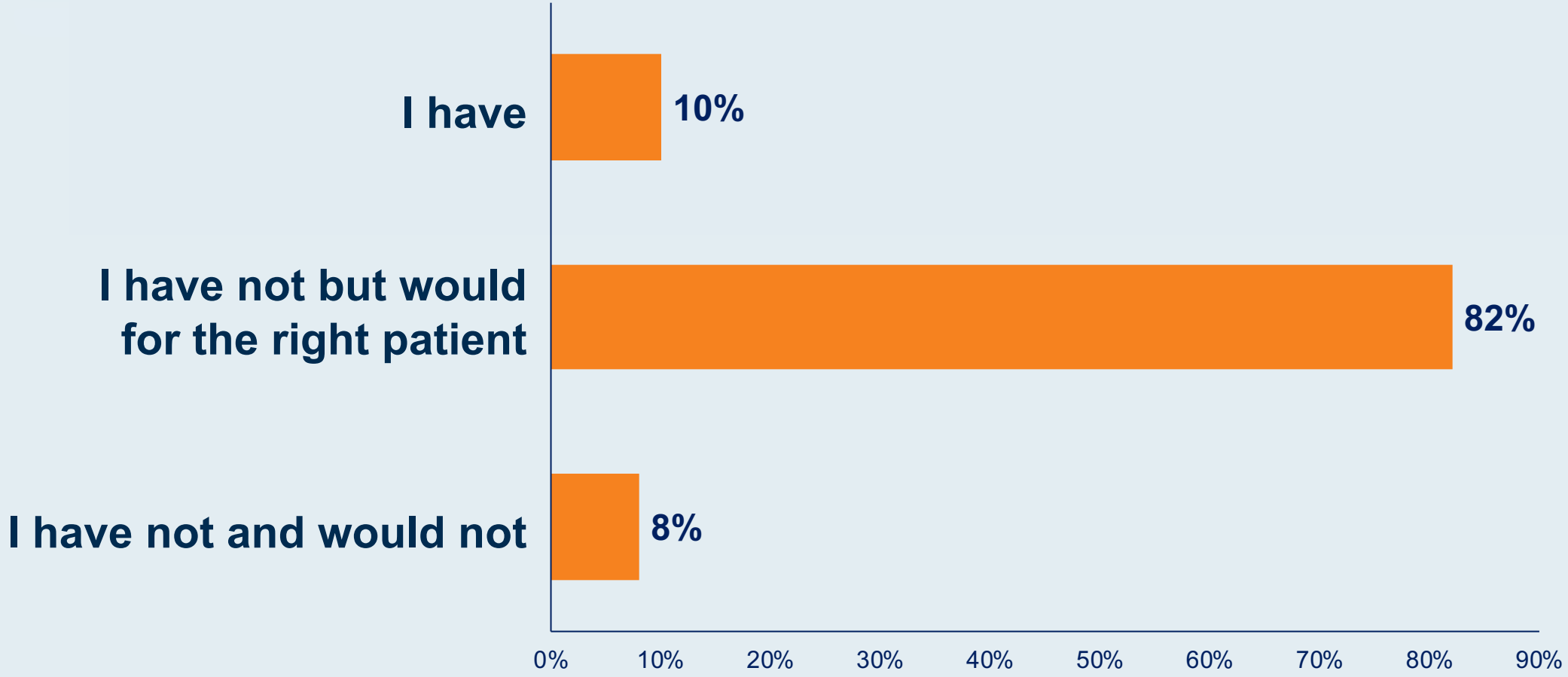

Survey of 50 US-based medical oncologists

MODULE 4: Metastatic Pancreatic Cancer

- **Key Relevant Data Sets**
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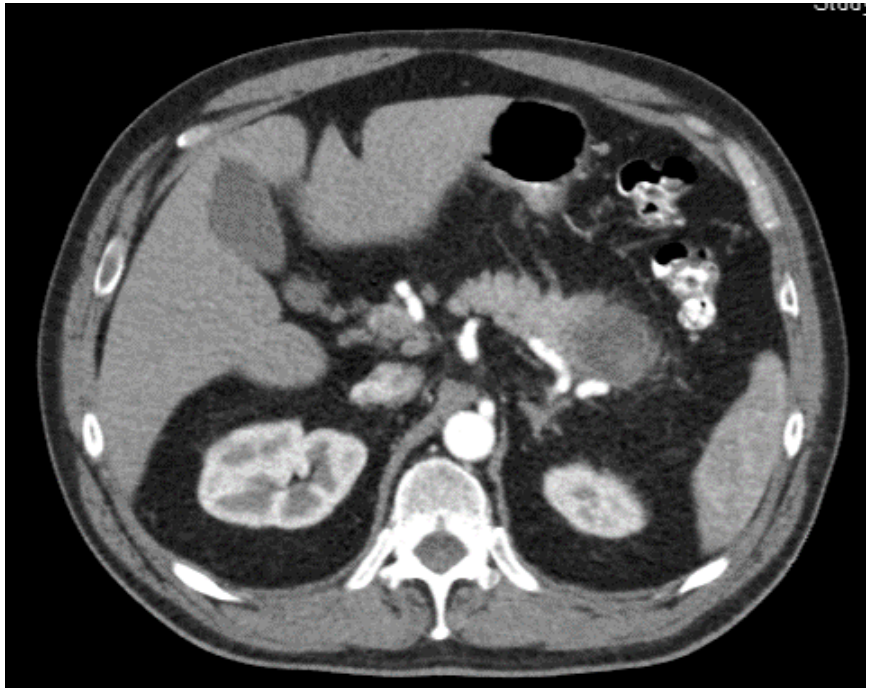
  - Phase II study of cisplatin/gemcitabine +/- veliparib in gBRCA/PALB2+ PDAC
- **Faculty Cases – Dr O'Reilly**
  - A 52-year-old man with newly diagnosed pancreatic cancer and a germline BRCA2 mutation
  - A 93-year-old woman with metastatic pancreatic cancer

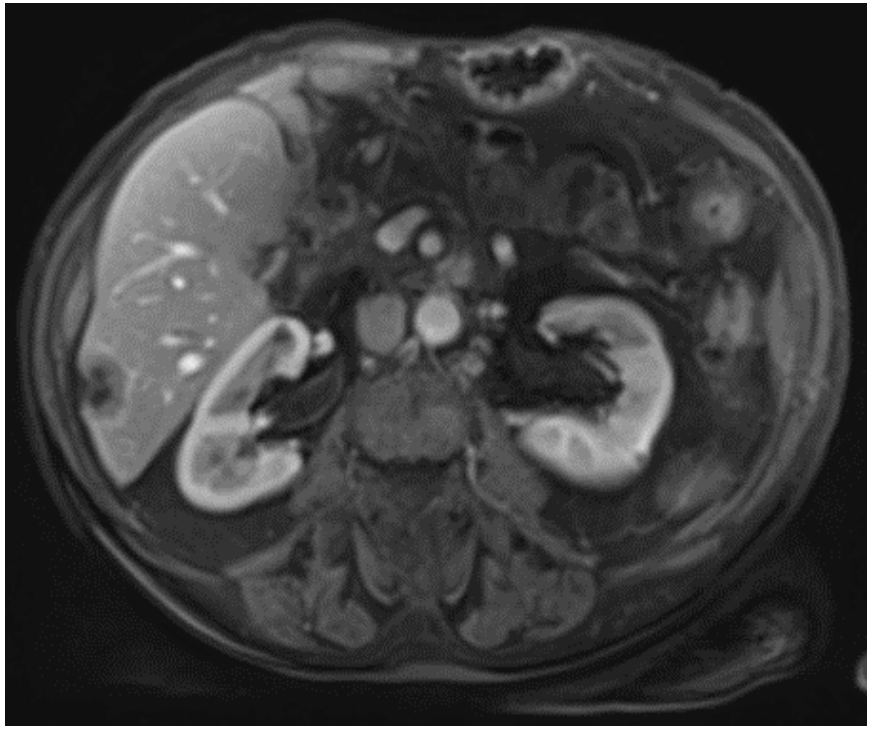
Case Presentation – Dr O'Reilly: A 52-Year-Old Man with Newly Diagnosed Pancreatic Cancer and a Germline BRCA2 Mutation

- 52 year old male
  - 1 year hx of back pain (severe)
  - Family Hx g*BRCA2,* prostate ca
  - Diagnosed March 2020
  - Tail primary, liver, nodes
  - CA 19-9 8 = 613, CEA = 14.1
  - mFOLFIRINOX
  - Confirmed g*BRCA2*
  - At point of maintenance therapy decision



Case Presentation – Dr O'Reilly: A 93-Year-Old Woman with Metastatic Pancreatic Cancer

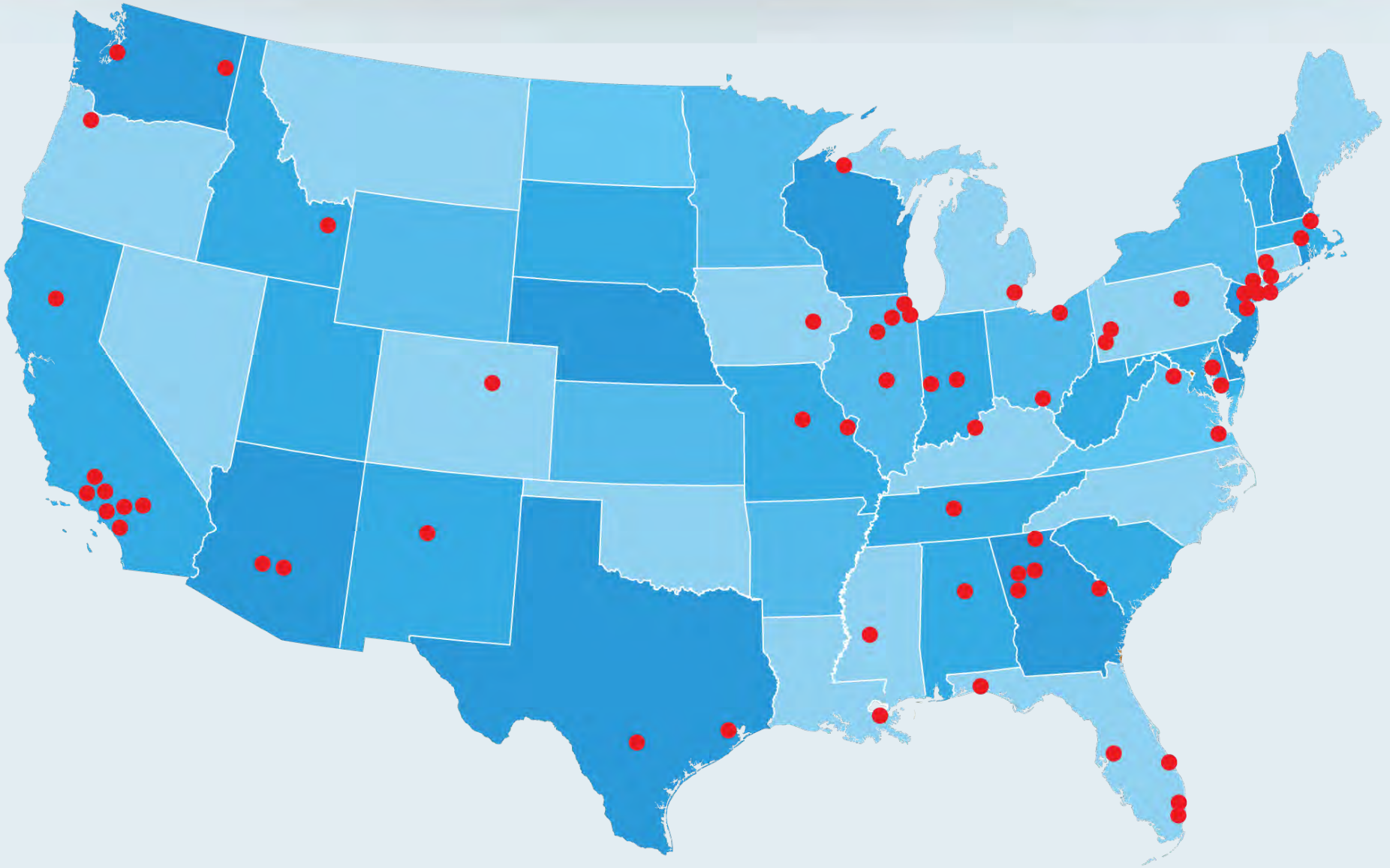
- 93 year old female
  - Whipple 2018, pT2, N1
  - No adjuvant therapy
  - 2020 Liver, peritoneum, bone mets
  - CA 19-9 = 254, CEA = 9
  - To treat or not?
  - Gemcitabine, capecitabine q 2 weeks
  - RT to left hip



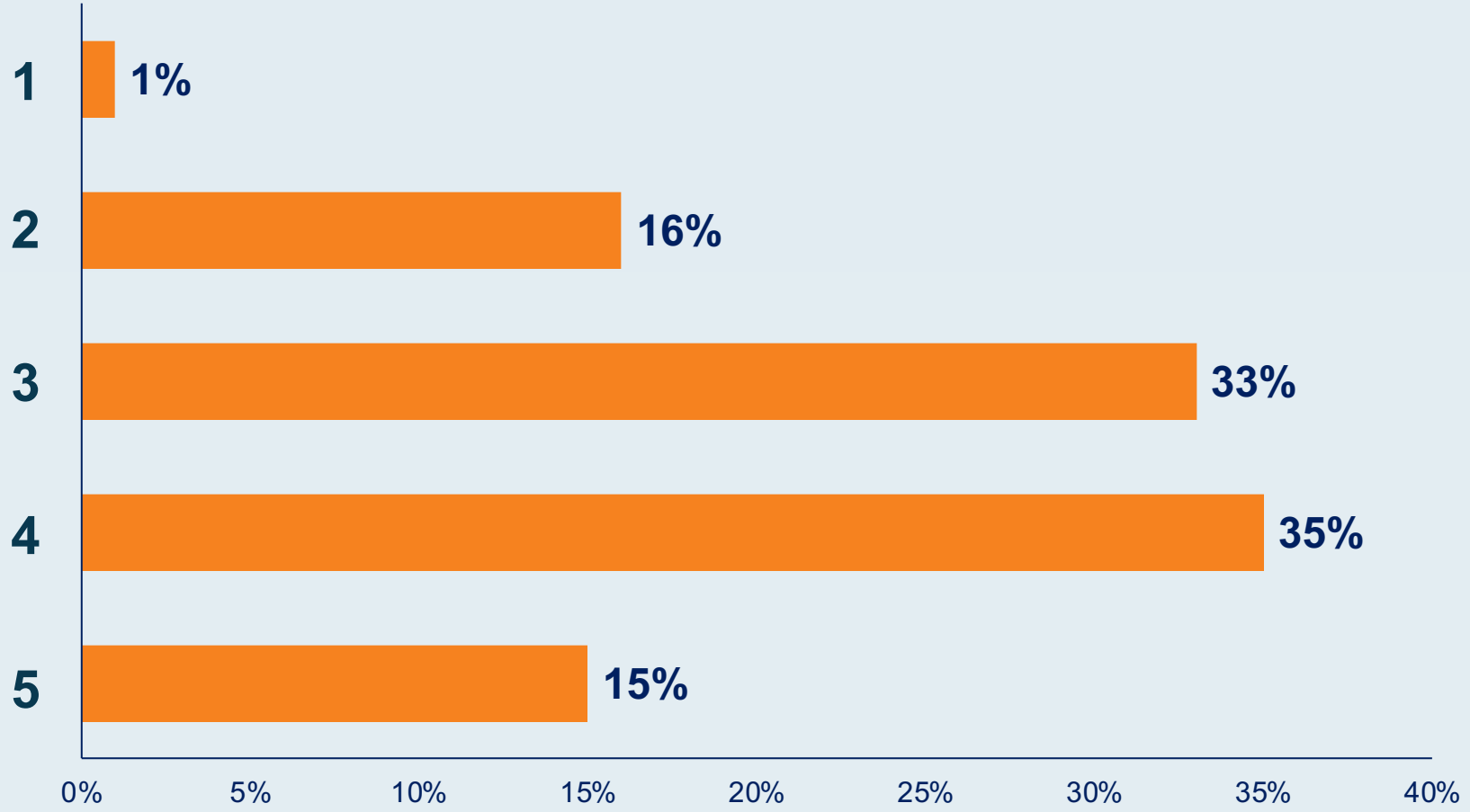
MODULE 5: Management of GI Cancers in the Era of COVID-19

Challenging Questions and Cases

Locations of 75 Participating Community Oncologists



On a scale of 1 to 5, how would you rate the severity of the COVID-19 pandemic in your area? (1 = not affected at all, similar to 2019; 5 = severely affected [eg, New York at its peak])



Survey of 75 US-based community oncologists

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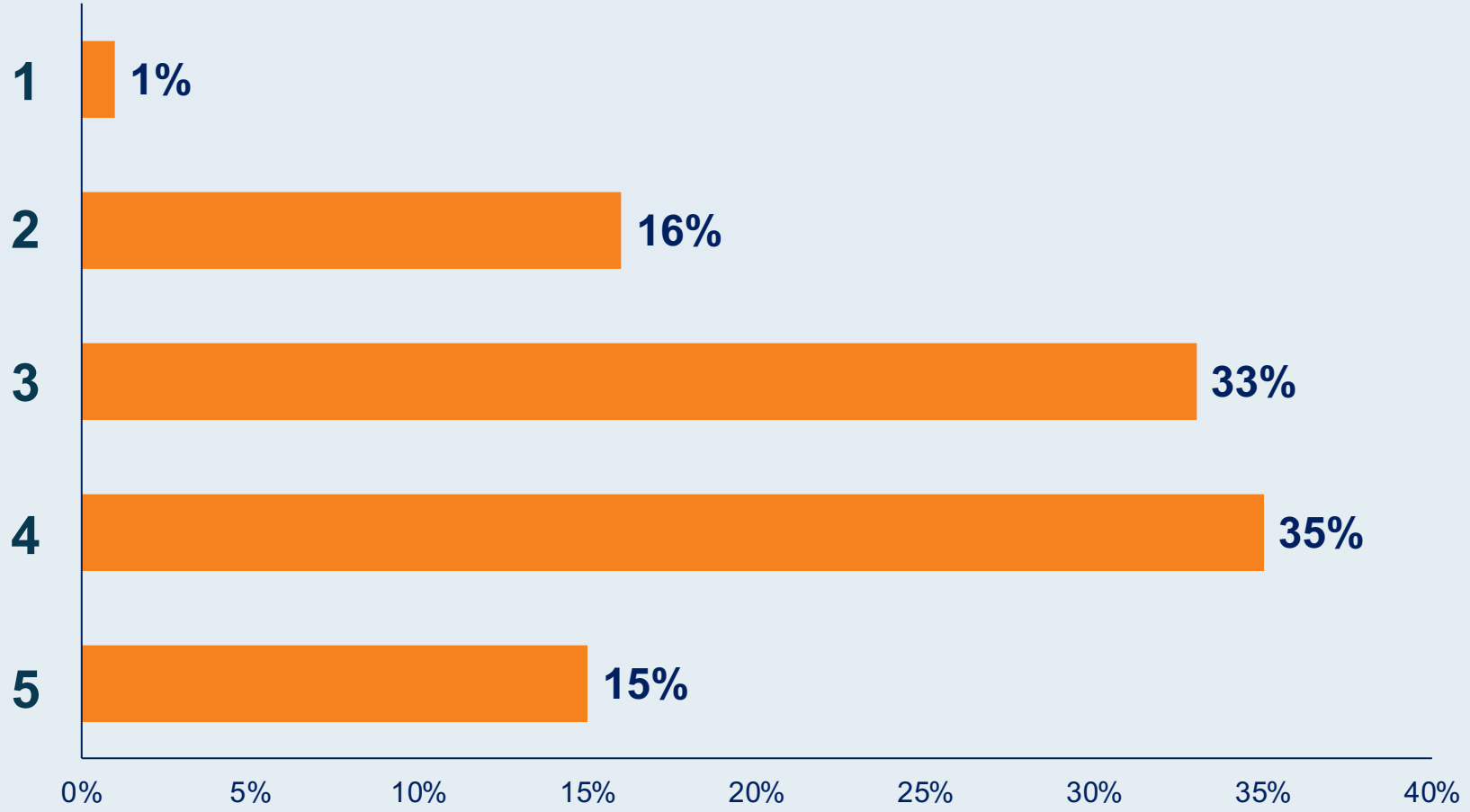
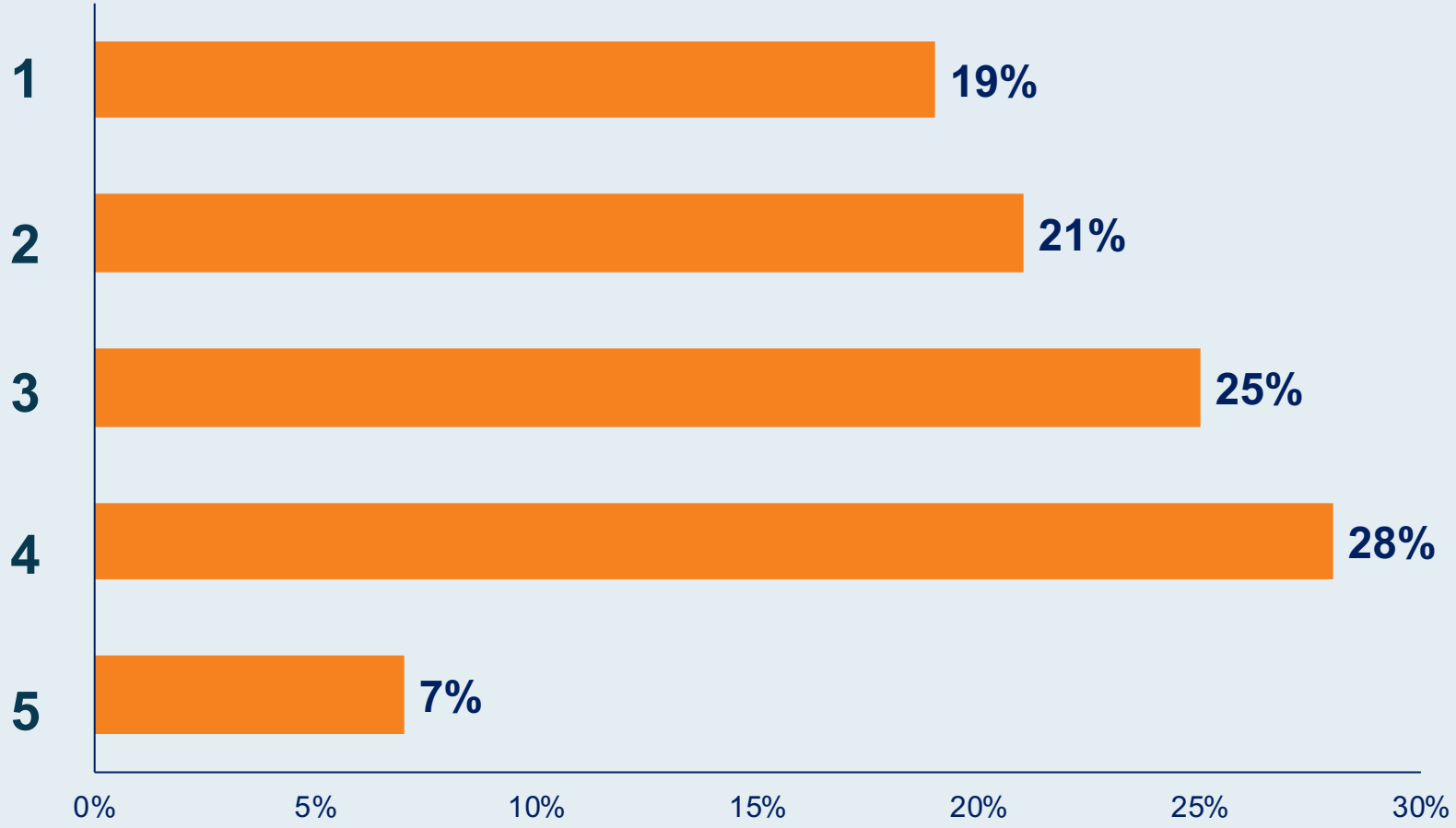


Survey of 75 US-based community oncologists

On a scale of 1 to 5, with 1 being not very disruptive and 5 being very disruptive, to what extent has COVID-19 impacted your ability to keep up with new cancer advances?



Survey of 75 US-based community oncologists

Virtual Molecular Tumor Board: Recognition and Management of Targetable Tumor Mutations in Less Common Cancer Types

Friday, August 14, 2020

9:00 AM – 10:00 AM ET

Faculty

Marcia S Brose, MD, PhD
Andrew McKenzie, PhD
Milan Radovich, PhD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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