Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Colorectal and Gastroesophageal Cancers

Tuesday, August 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Chloe E Atreya, MD, PhD
Dustin Deming, MD
Eric Van Cutsem, MD, PhD
Zev Wainberg, MD, MSc

Moderator

Neil Love, MD

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Faculty

Chloe E Atreya, MD, PhD
Associate Professor in Residence
Gastrointestinal Oncology Program
University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center
San Francisco, California

Dustin Deming, MD
ACI/Schwenn Family Associate Professor
University of Wisconsin
School of Medicine and Public Health
Madison, Wisconsin

Eric Van Cutsem, MD, PhD
Professor of Medicine
Digestive Oncology
University Hospitals Leuven
Leuven, Belgium

Zev Wainberg, MD, MSc
Co-Director, GI Oncology Program
Director of Early Phase Clinical Research
Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Commercial Support

This activity is supported by educational grants from Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Daiichi Sankyo Inc, Eisai Inc, Exelixis Inc, Lilly, Merck and Taiho Oncology Inc.

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Dr Love — Disclosures

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Prof Van Cutsem — Disclosures

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Dr Wainberg — Disclosures

Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Five Prime Therapeutics Inc, Gilead Sciences Inc, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Molecular Templates
Contracted Research	Arcus Biosciences, Five Prime Therapeutics Inc, Novartis, Plexxikon Inc
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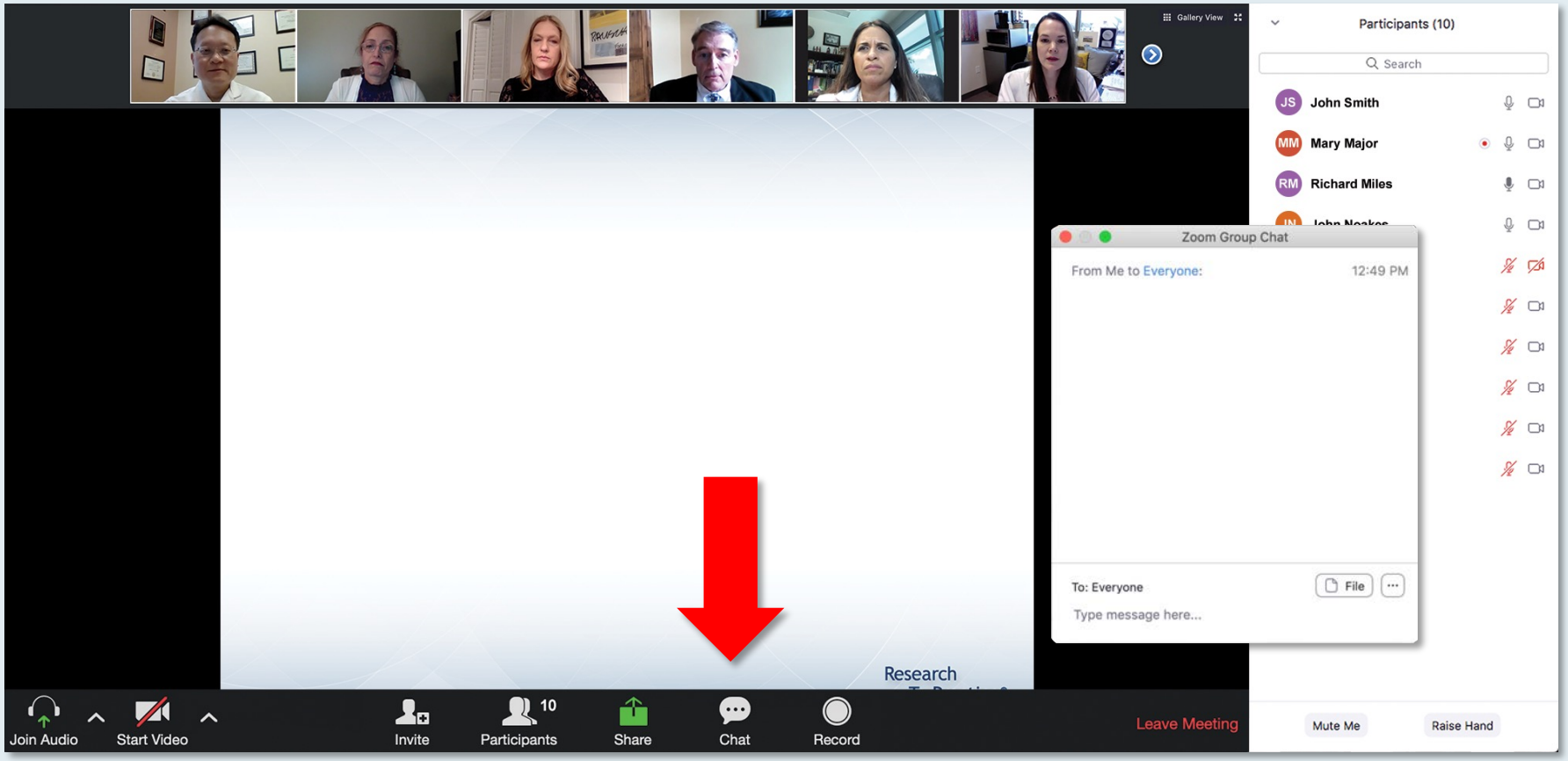
We Encourage Clinicians in Practice to Submit Questions



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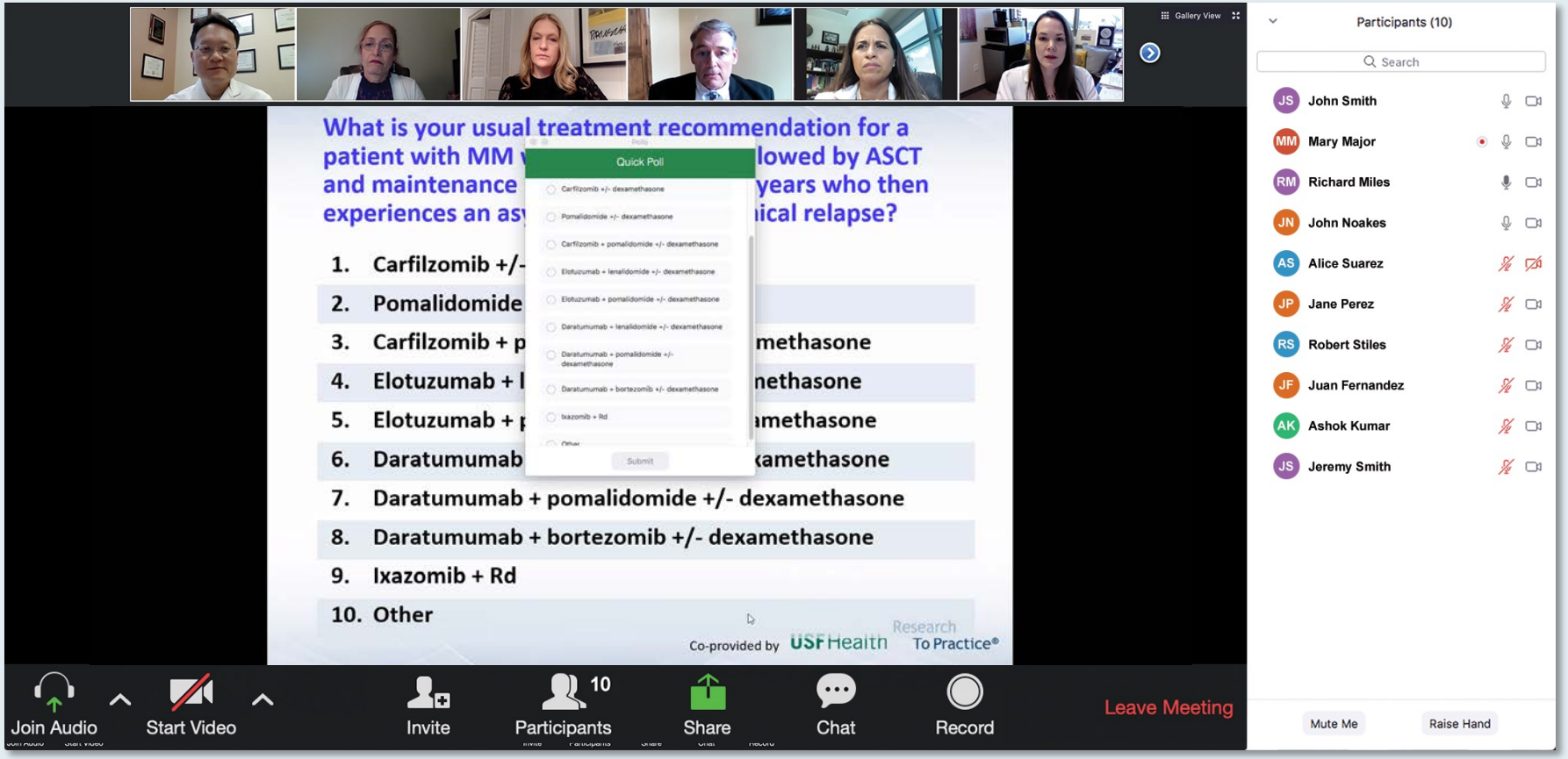

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Familiarizing Yourself with the Zoom Interface

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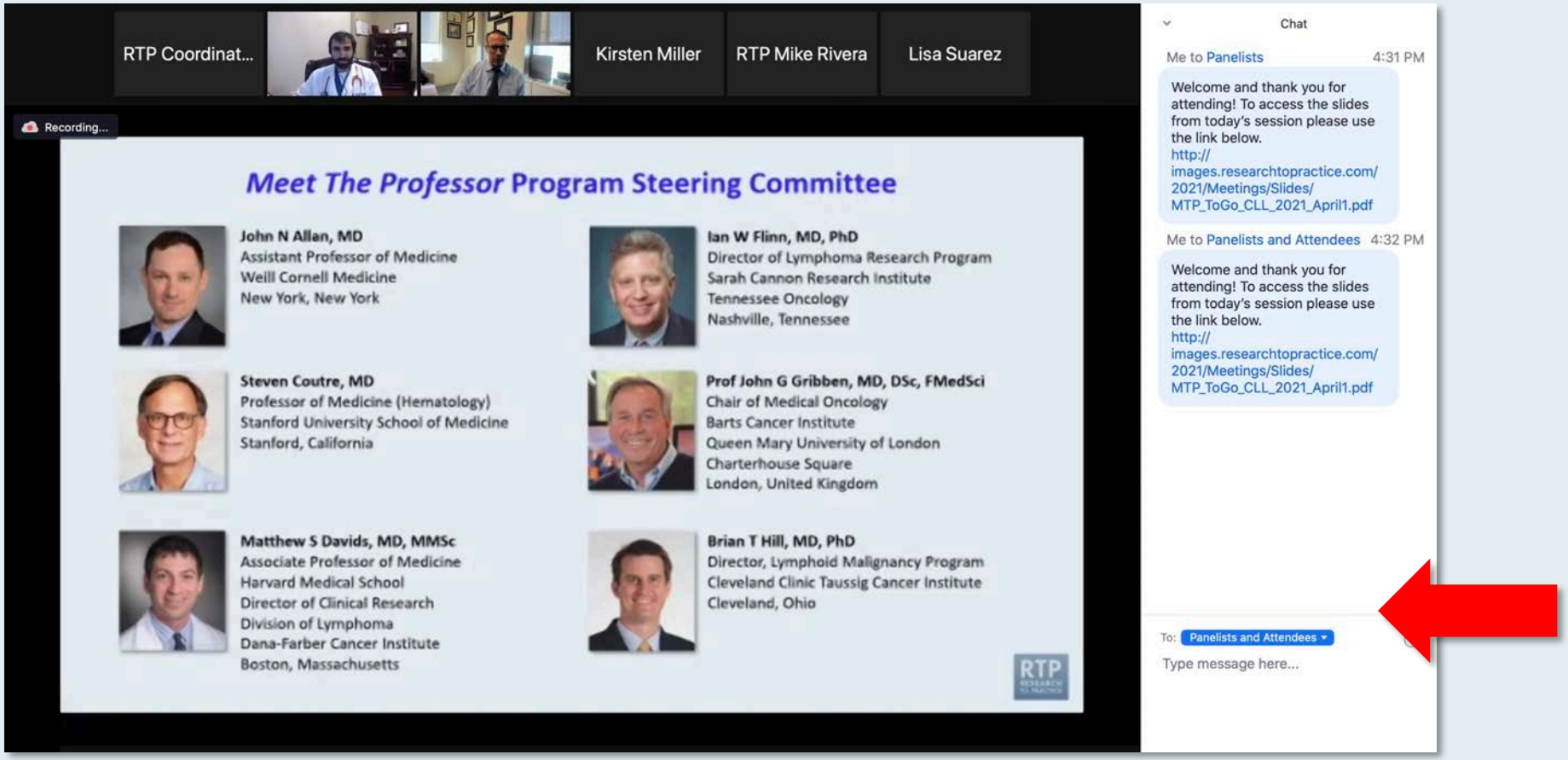

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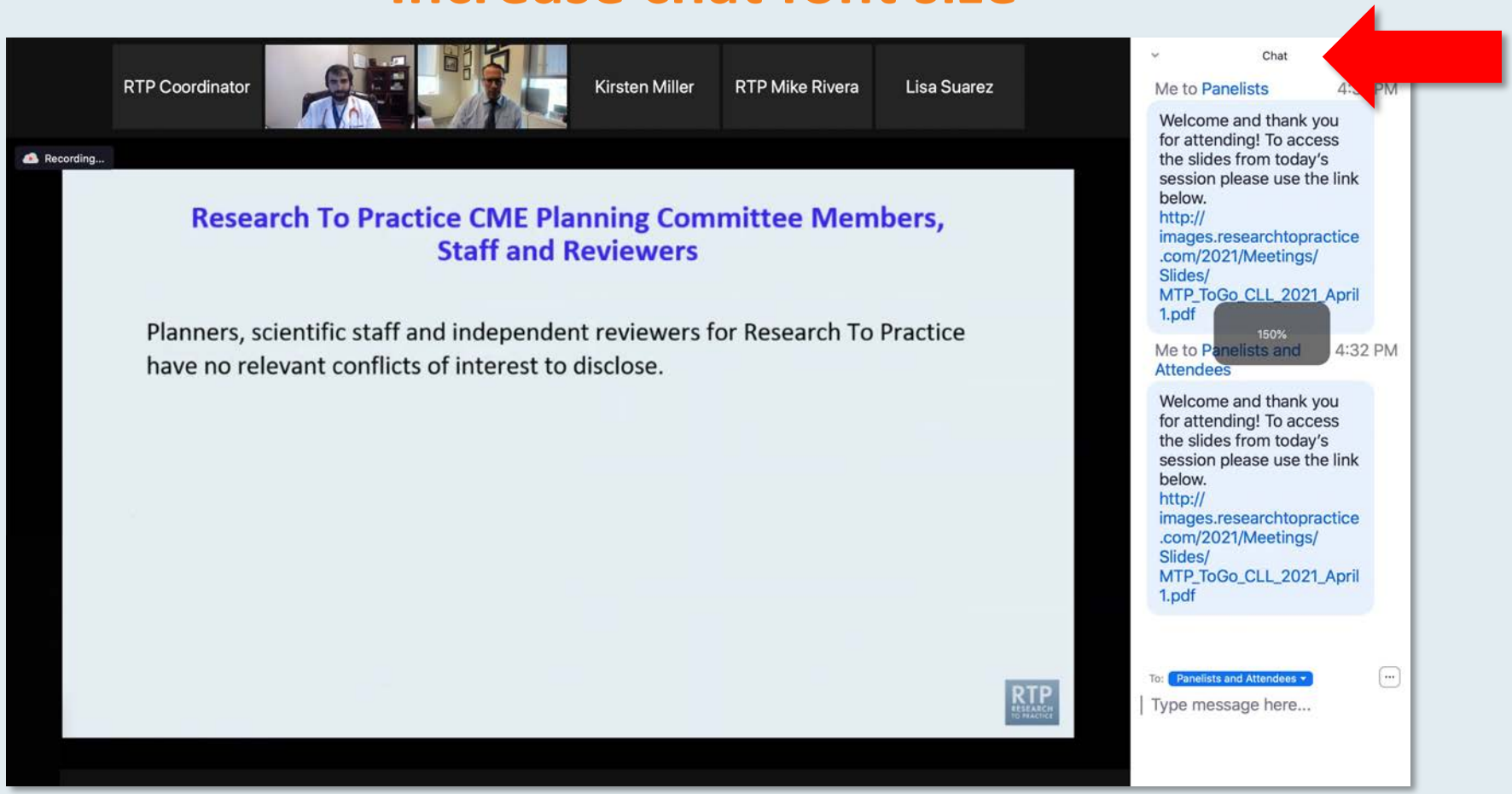

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Gastroesophageal Cancers

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Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Hepatocellular Carcinoma and Pancreatic Cancer

Wednesday, August 4, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanios Bekaii-Saab, MD
Kim A Reiss Binder, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

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Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Chronic Lymphocytic Leukemia

Thursday, August 5, 2021
5:00 PM – 6:00 PM ET

Faculty

John M Pagel, MD, PhD
Lesley Camille Ballance, MSN, FNP-BC

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Friday, August 6, 2021
12:00 PM – 1:00 PM ET

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Thomas Powles, MBBS, MRCP, MD

Moderator

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Three Exciting Educational Events Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

In Partnership with the University of Nebraska Medical Center

Expert Second Opinion — Acute Myeloid Leukemia and Myelodysplastic Syndromes

Monday, August 9, 2021
7:00 PM – 8:30 PM ET

Faculty
Krishna Gundabolu, MD
Richard M Stone, MD
Eunice S Wang, MD

Moderator
Harry Paul Erba, MD, PhD

Beyond the Guidelines — Chronic Lymphocytic Leukemia

Tuesday, August 10, 2021
7:00 PM – 9:00 PM ET

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Susan O'Brien, MD
Sonali M Smith, MD
Julie M Vose, MD, MBA

Moderator
Matthew S Davids, MD, MMSc

Cases from the Community — Multiple Myeloma

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Joseph Mikhael, MD
Nina Shah, MD

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Robert Z Orlowski, MD, PhD

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Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

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A Conversation with the Investigators: Perspectives on the Management of Head and Neck Cancer

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 2-3 business days.

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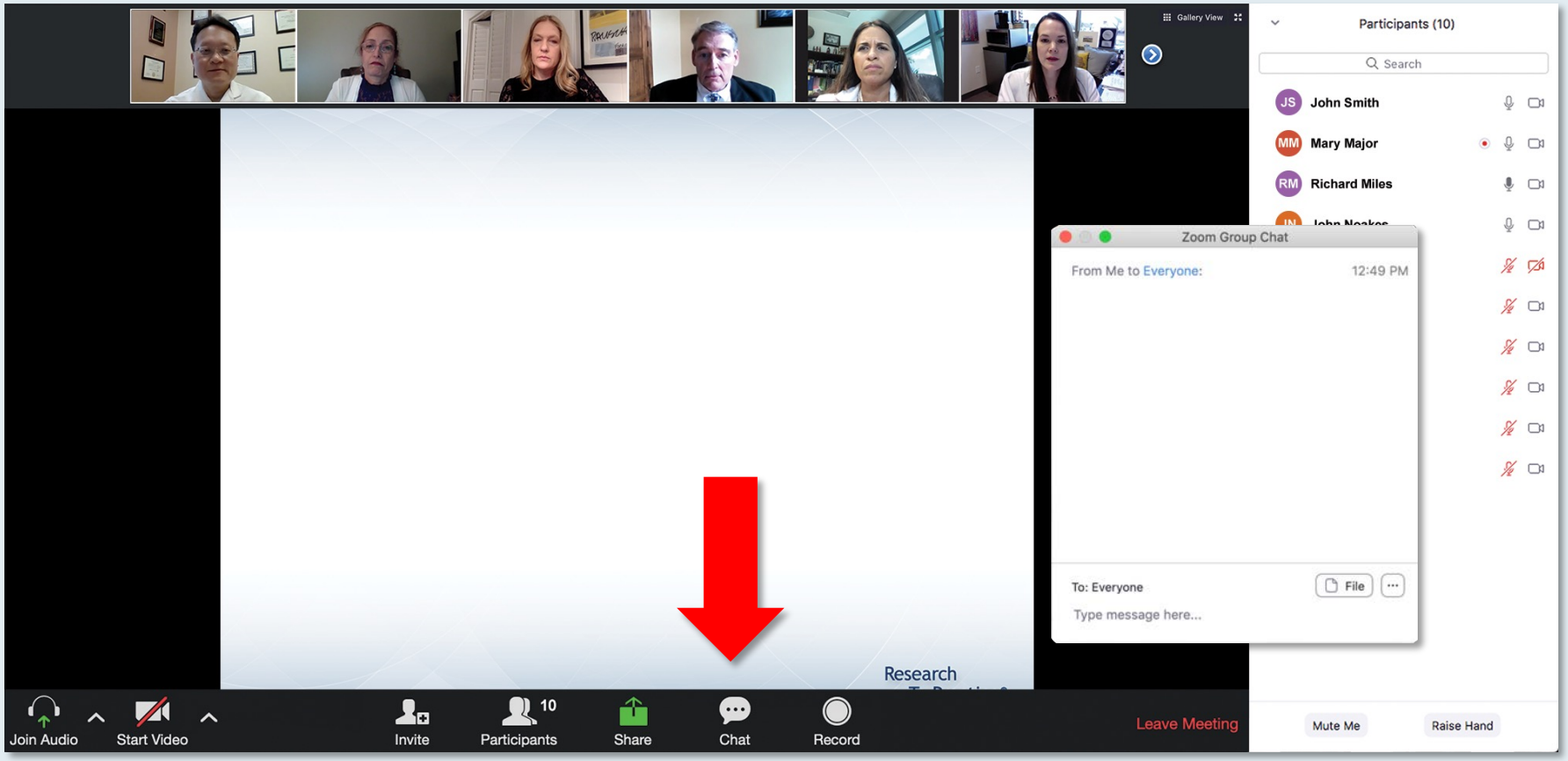

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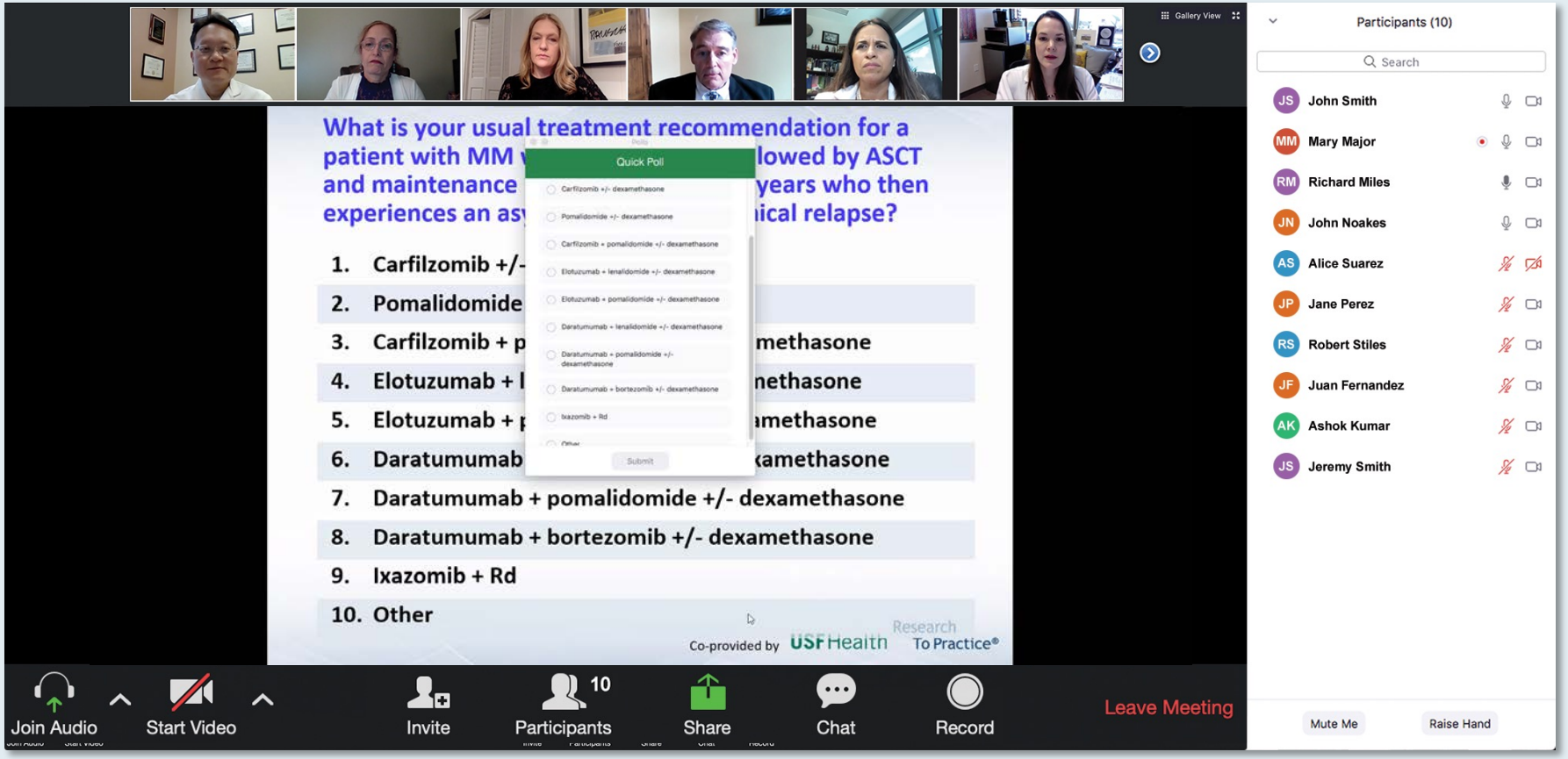

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ASCO 2021 Colorectal and Gastroesophageal Cancers Presentation Library

Selection and Sequencing of Treatment for Advanced Gastroesophageal Cancers
Zev Wainberg, MD, MSc

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Recent Advances in the Management of HER2-Positive Advanced Gastric Cancer; Other Promising Targeted Strategies
Eric Van Cutsem, MD, PhD

Download Slides

Incorporation of Immunotherapy and HER2-Targeted Therapy into the Management of Metastatic Colorectal Cancer (mCRC)
Dustin Deming, MD

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Other Considerations in the Treatment of mCRC: Cytotoxics, Biologics and RAS/RAF-Targeted Therapies
Chloe E Atreya, MD, PhD

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Agenda

Interdisciplinary Management of Gastrointestinal Cancers – Part 1

Module 1: Advanced Gastroesophageal Cancers

- **Should an IO be added to chemotherapy as part of first-line treatment for metastatic upper GI (mUGI) cancers ?**
- **What is the optimal IO to add to chemotherapy as first-line treatment for mUGI cancers?**
- **Should patients receiving neoadjuvant chemoradiation therapy for esophageal cancer be offered adjuvant nivolumab if there is residual disease?**
- **What is the optimal first- and second-line treatment for HER2-positive mUGI cancers, and does this vary based on combined positive score?**

Agenda

Interdisciplinary Management of Gastrointestinal Cancers – Part 2

Module 2: Metastatic Colorectal Cancer (mCRC)

- **What is the optimal first-line systemic treatment for RAS/BRAF wild-type mCRC in a symptomatic and an asymptomatic patient, and does this vary by side of the primary tumor?**
- **What is the optimal first-line treatment for MSI-high mCRC?**
- **What is the optimal targeted treatment for BRAF-mutated mCRC, and in which line of therapy should it be used?**
- **What is your preferred sequencing of EGFR TKIs, TAS-102 (+/- bevacizumab) and regorafenib?**
- **What is your preferred sequencing of therapies for HER2-positive mCRC, including T-DXd?**

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Interdisciplinary Management of Gastrointestinal Cancers – Part 1

Module 1: Advanced Gastroesophageal Cancers

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Should an IO be added to chemotherapy as part of first-line treatment for mUGI cancers?

Dr Tanios Bekaii-Saab

Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

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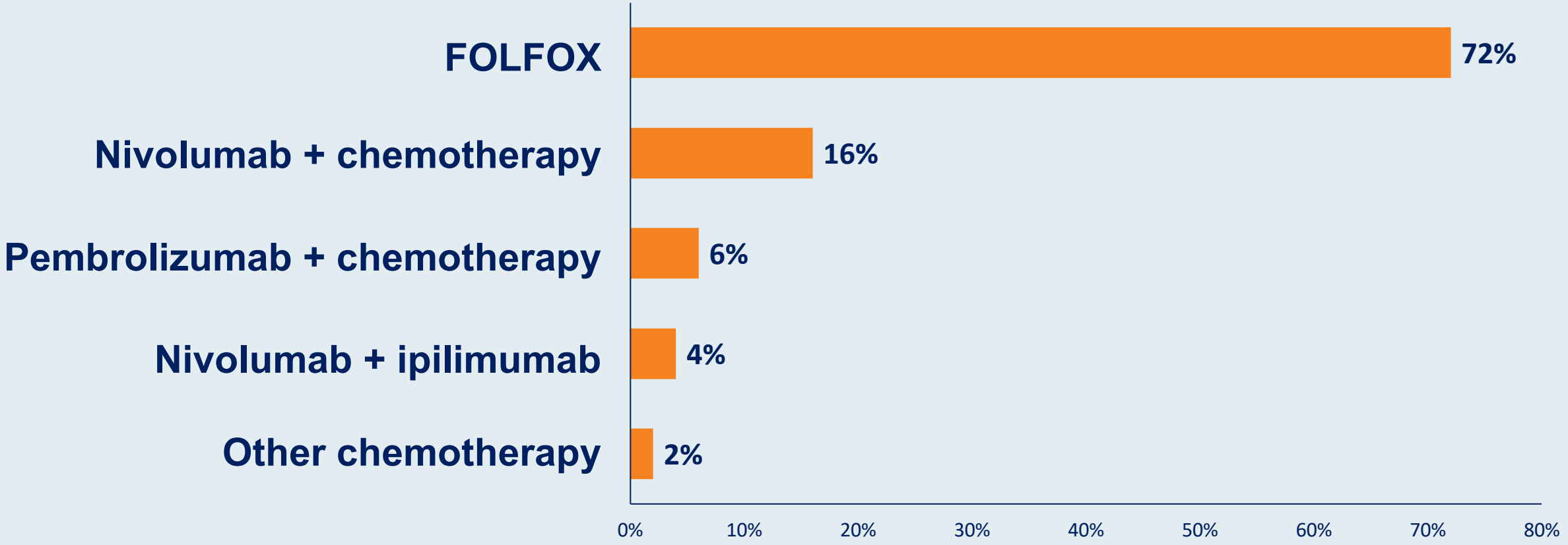
Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-negative, microsatellite-stable (MSS) adenocarcinoma of the gastroesophageal junction (GEJ) with a PD-L1 combined positive score (CPS) of 0?



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 Dr Atreya	Nivolumab + chemotherapy	 Dr Bekaii-Saab	FOLFOX
 Dr Deming	FOLFOX	 Dr O'Reilly	FOLFOX
 Prof Van Cutsem	FOLFOX	 Dr Philip	Nivolumab + chemotherapy
 Dr Wainberg	FOLFOX	 Dr Reiss Binder	FOLFOX

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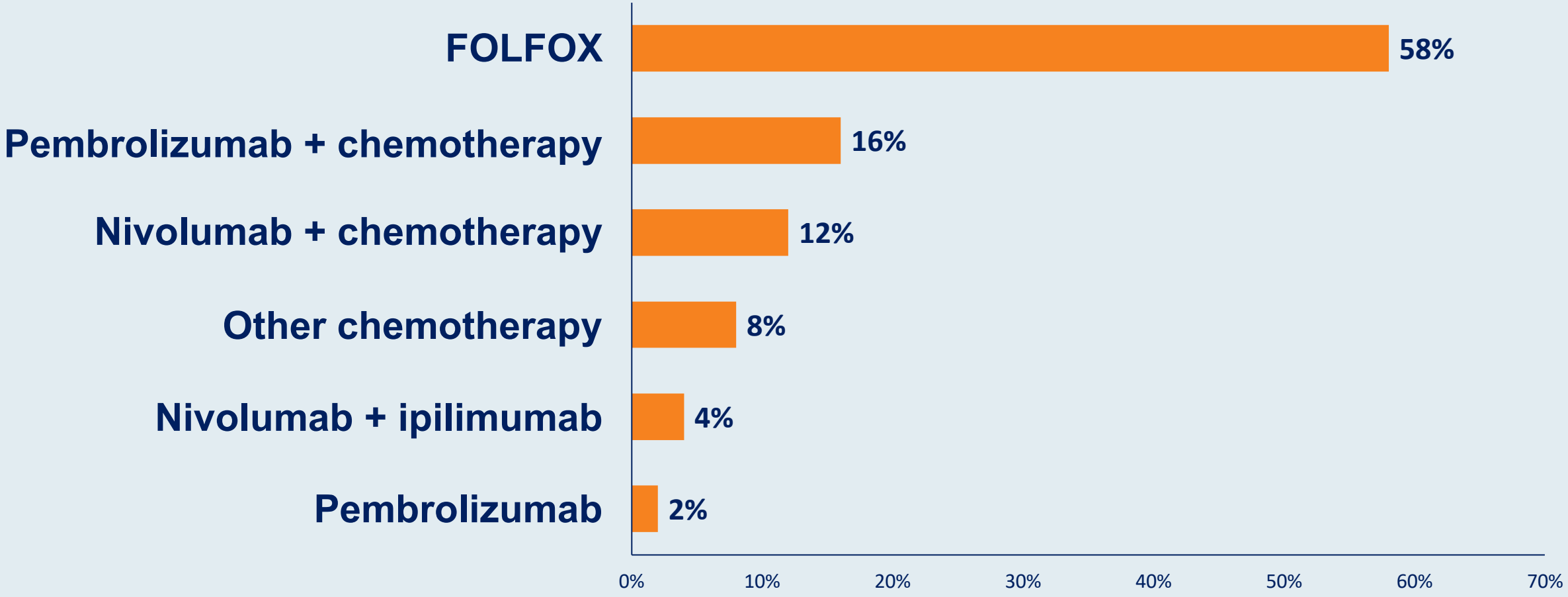
Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 0?



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What is the optimal IO to add to chemotherapy as first-line treatment for mUGI cancers?

Dr Tanios Bekaii-Saab

Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

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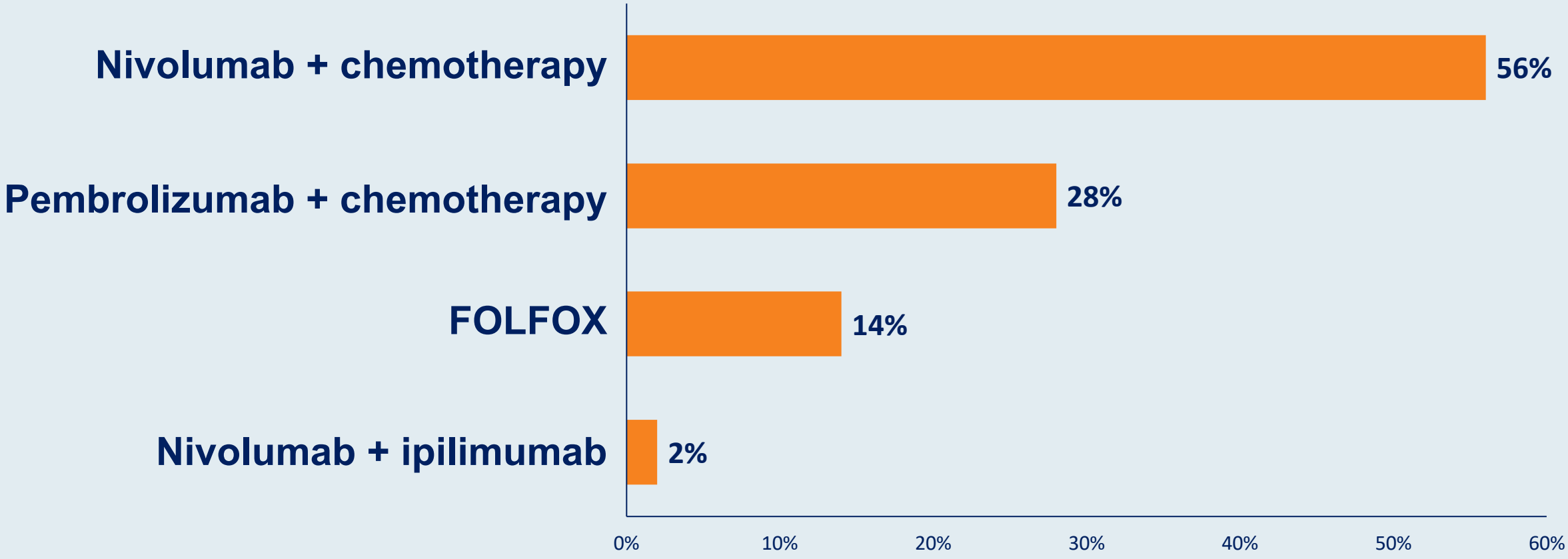
Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ with a PD-L1 CPS of 5?



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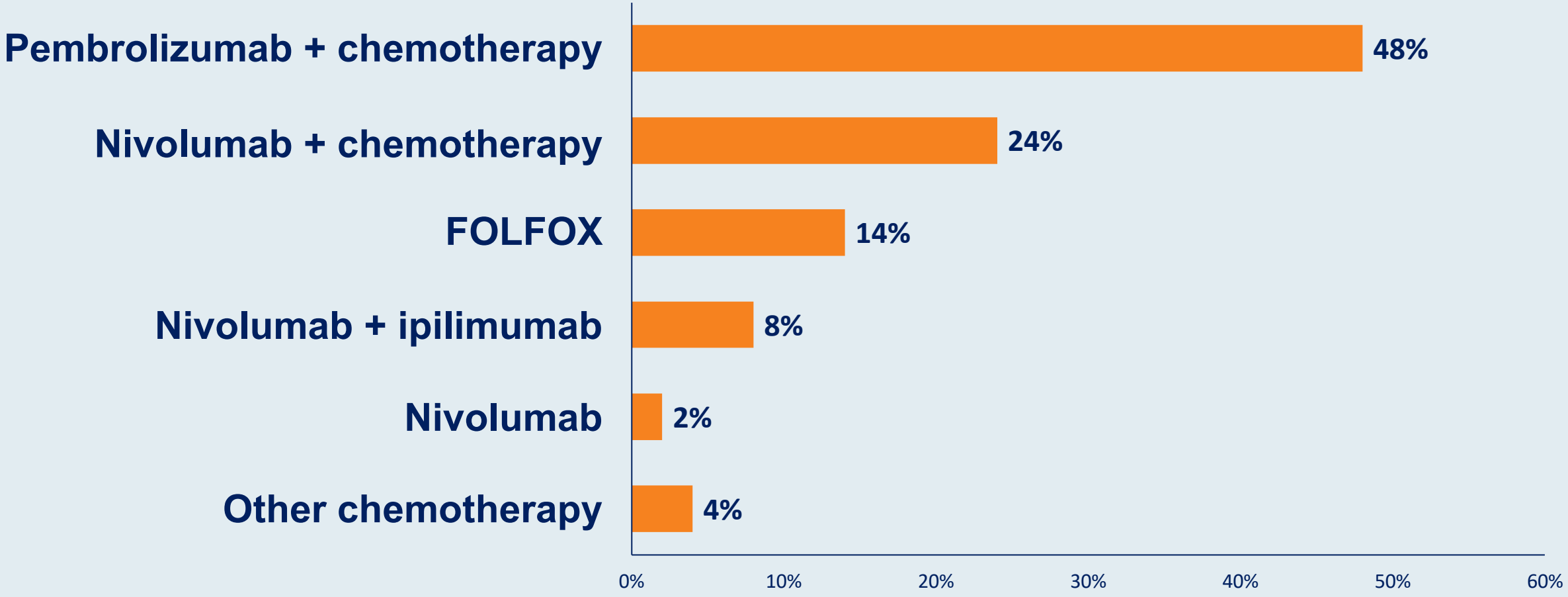
 Dr Deming	Pembrolizumab + chemotherapy or Nivolumab + chemotherapy	 Dr O'Reilly	Nivolumab + chemotherapy
 Prof Van Cutsem	Nivolumab + chemotherapy	 Dr Philip	Nivolumab + chemotherapy
 Dr Wainberg	FOLFOX	 Dr Reiss Binder	Nivolumab + chemotherapy

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-negative, MSS squamous cell carcinoma of the esophagus with a PD-L1 CPS of 5?



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 Dr Wainberg	Pembrolizumab + chemotherapy or Nivolumab + chemotherapy	 Dr Reiss Binder	FOLFOX

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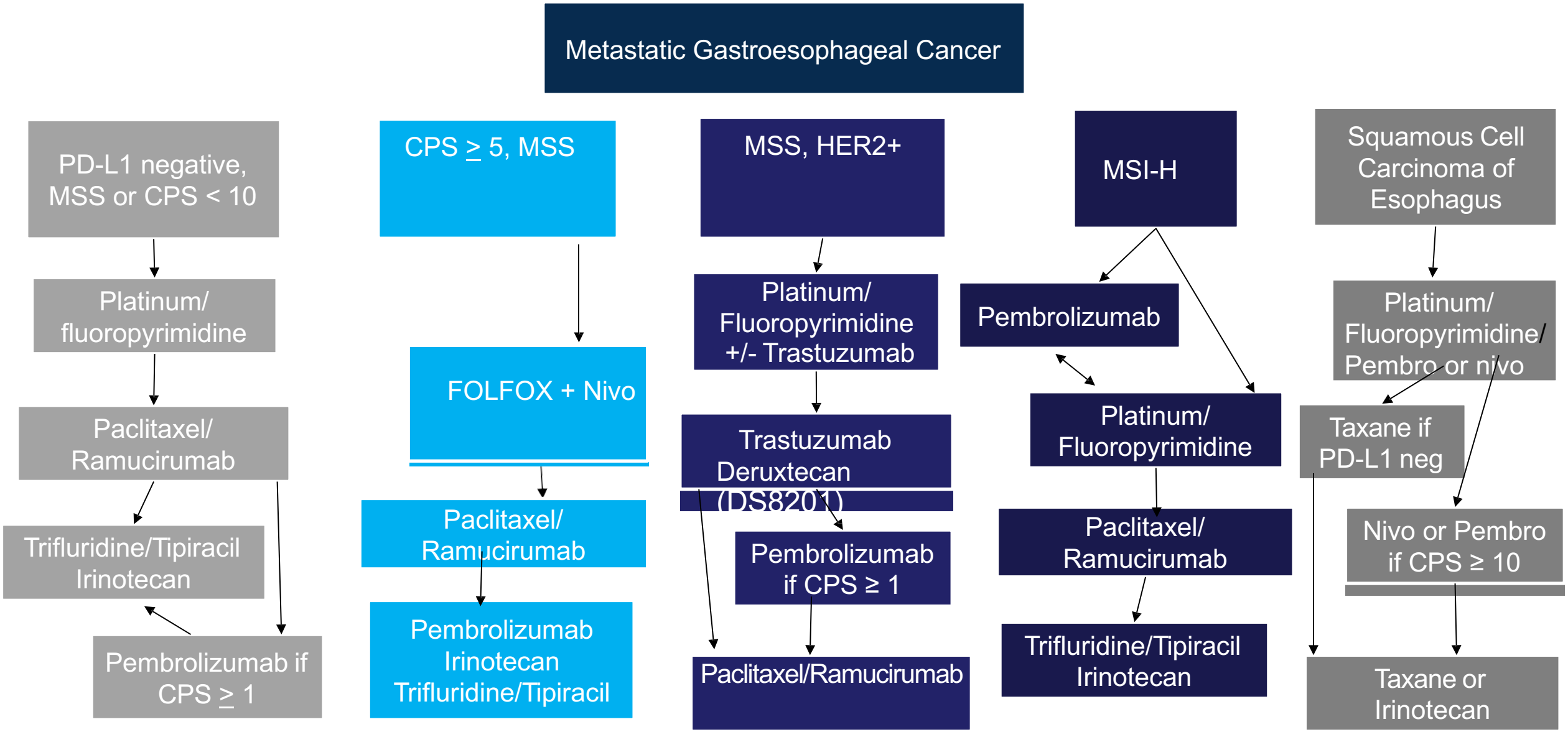
Regulatory and reimbursement issues aside, what is the optimal first-line therapy for a patient with metastatic HER2-negative, microsatellite-stable (MSS) gastric/gastroesophageal junction (GEJ) adenocarcinoma, and how does PD-L1 CPS affect this decision?

- Numerous studies have established fluoropyrimidine/platinum combinations as the optimal chemotherapy backbone for metastatic GEJ adenocarcinoma
- On the basis of recent studies (CheckMate 649, Janjigian et al, Lancet 2021, and KEYNOTE-590- ESMO 2020) demonstrating improvements in overall survival, the FDA has approved both nivolumab in combination with chemo and pembrolizumab for metastatic esophageal adenocarcinoma
- Because the studies primary endpoints were in CPS ≥5 (CheckMate 649) and CPS ≥10 (KEYNOTE-590), the majority of the benefit of both nivolumab and pembrolizumab is in these groups of patients
- The true benefit of PD-1 inhibitors in adenocarcinoma of the GEJ with CPS <5 is questionable and should be considered in select patients

Regulatory and reimbursement issues aside, what is the optimal first-line therapy for a patient with metastatic HER2-negative, microsatellite-stable (MSS) squamous cell carcinoma of the esophagus, and how does PD-L1 CPS affect this decision?

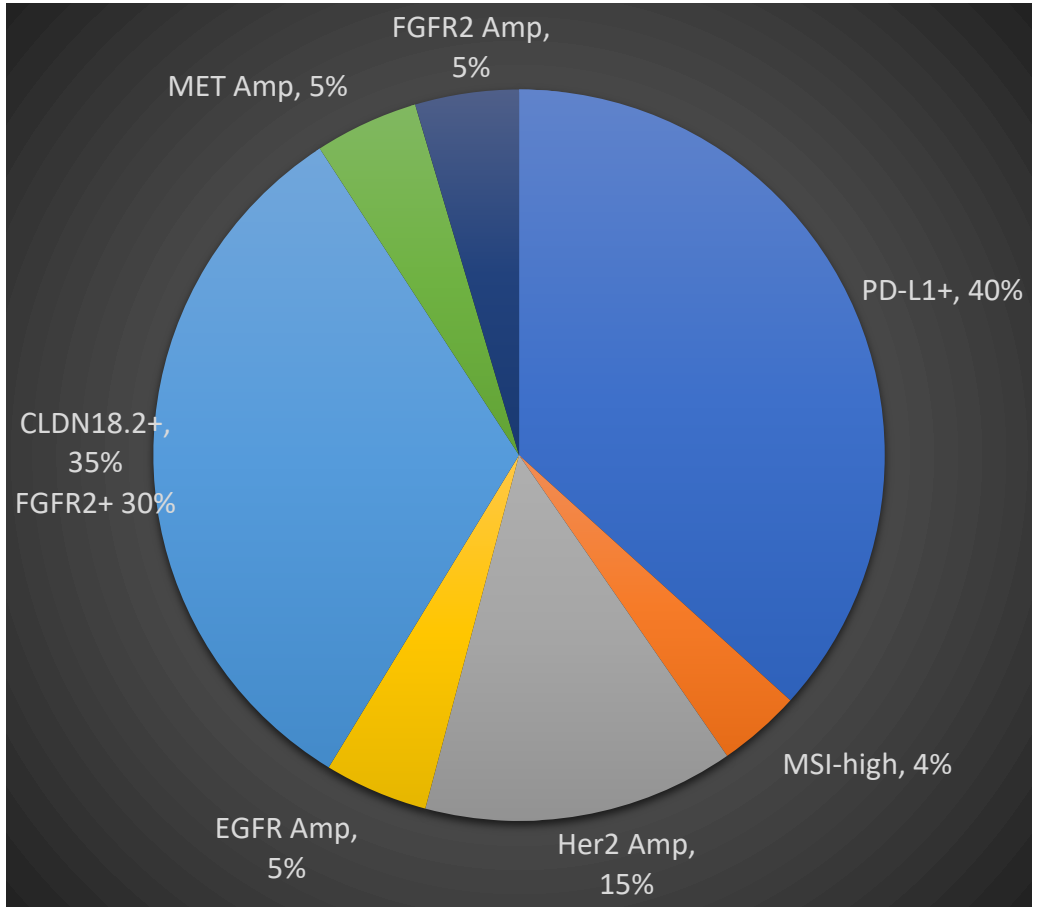
- On the basis of recent studies (CheckMate 648, ASCO 2020, and KEYNOTE-590-ESMO 2020) there is a clear role for both nivolumab and pembrolizumab in combination with chemotherapy for metastatic esophageal adenocarcinoma
- In the majority of studies with PD-1 inhibitors, there is likely greater benefit for PD-1 inhibitors in squamous cell carcinoma of the esophagus rather than adenocarcinoma
- In the CheckMate 648 study, in patients with PD-L1 ≥1%, the benefit of nivo + chemo over chemo was greater than in PD-L1 <1%
- The true benefit of PD-1 inhibitors in squamous cell carcinoma of the esophagus CPS <1 is questionable and combinations with nivo and pembro should be considered in select patients

How to Treat Metastatic Gastroesophageal Cancer in 2021?



Courtesy of Zev Wainberg, MD, MSc

Novel Biomarkers



KEY MARKERS IN ADVANCED DISEASE

- **HER2** positive – 15-20% of patients, improved survival with chemo + trastuzumab and in 2nd line with trastuzumab deruxtecan (DS8201)
- **MSI** high – 3-5% of patients, high response rates and survival with PD-1 inhibitors
- **PD-L1** positive – 30-50% of patients, identifies those more likely to benefit from immune therapies, likely gradation within PD-L1+

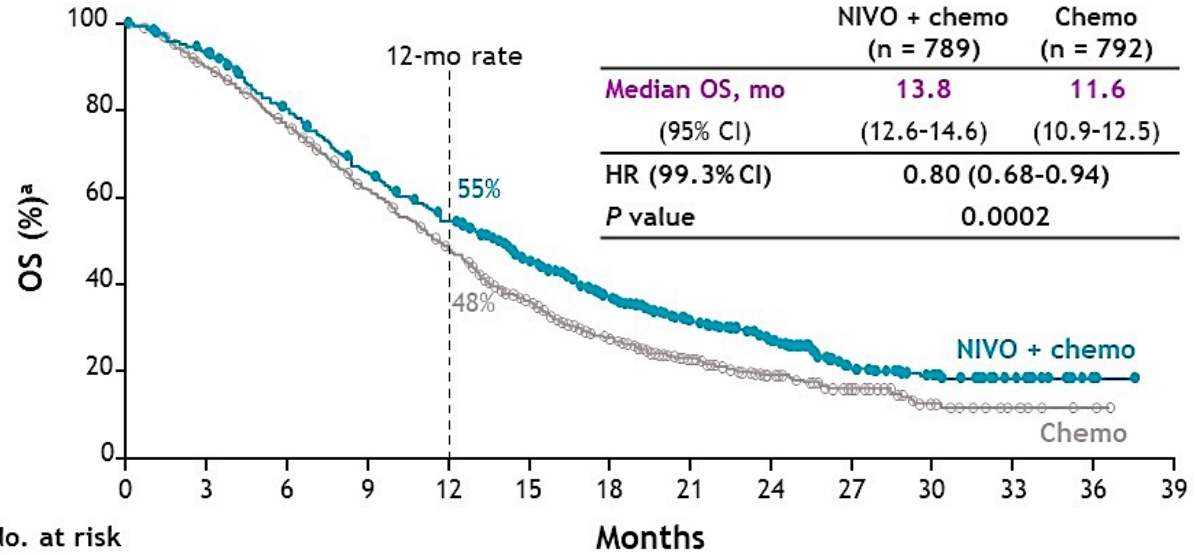
INVESTIGATIONAL BIOMARKERS

- **CLDN18.2** high – 30-35% of patients, response predictor for zolbetuximab (FAST Trial, Sahin et al, Ann of Onc 2021)
- **FGFR2** + (IHC) 30% of patients, response predictor for bemarituzumab (FIGHT Trial, Wainberg et al, GI ASCO 2021)
- **FGFR2** amp – 5-7%, predicts response to bemarituzumab

Courtesy of Zev Wainberg, MD, MSc

CheckMate 649: Overall survival and progression-free survival in all randomized patients

Overall survival

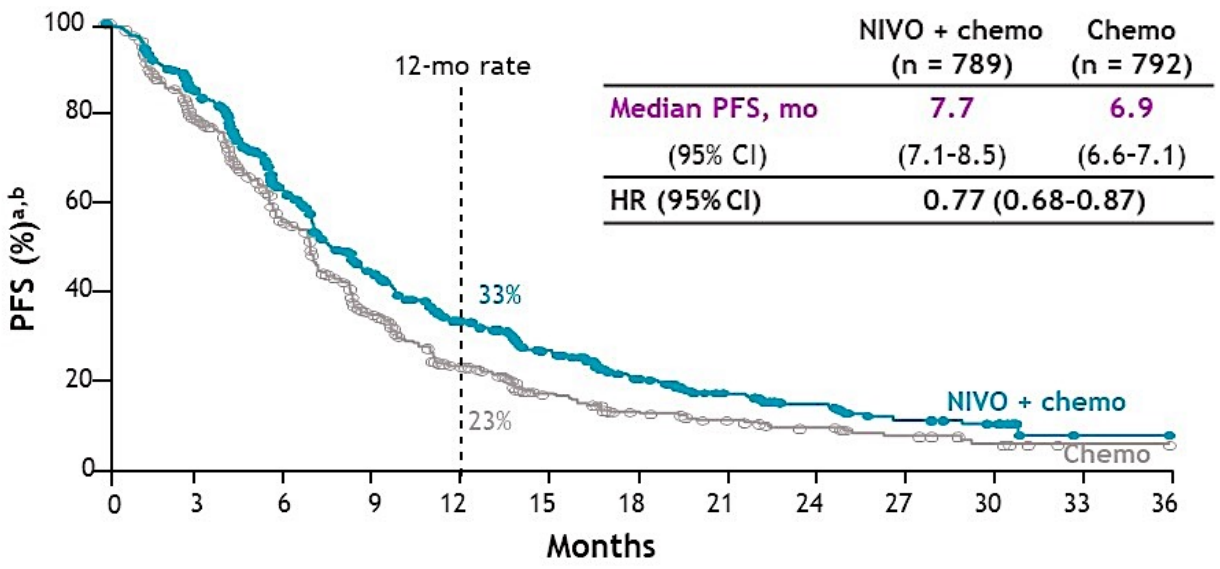


	NIVO + chemo (n = 789)	Chemo (n = 792)
Median OS, mo	13.8	11.6
(95% CI)	(12.6-14.6)	(10.9-12.5)
HR (99.3% CI)	0.80 (0.68-0.94)	
P value	0.0002	

No. at risk

NIVO + chemo	789	731	621	506	420	308	226	147	100	49	34	14	2	0
Chemo	792	697	586	469	359	239	160	94	59	35	15	7	2	0

Progression-free survival



	NIVO + chemo (n = 789)	Chemo (n = 792)
Median PFS, mo	7.7	6.9
(95% CI)	(7.1-8.5)	(6.6-7.1)
HR (95% CI)	0.77 (0.68-0.87)	

NIVO + chemo	789	639	429	287	197	136	83	51	31	15	11	1	0	
Chemo	792	544	351	202	120	65	38	28	18	12	6	1	0	

- Superior OS benefit and clinically meaningful PFS improvement in all randomized patients with NIVO + chemo vs chemo
- Median OS with NIVO + chemo vs chemo in patients with PD-L1 CPS ≥ 5 was 14.4 vs 11.1 months and median PFS was 7.7 vs 6.0 months[1]

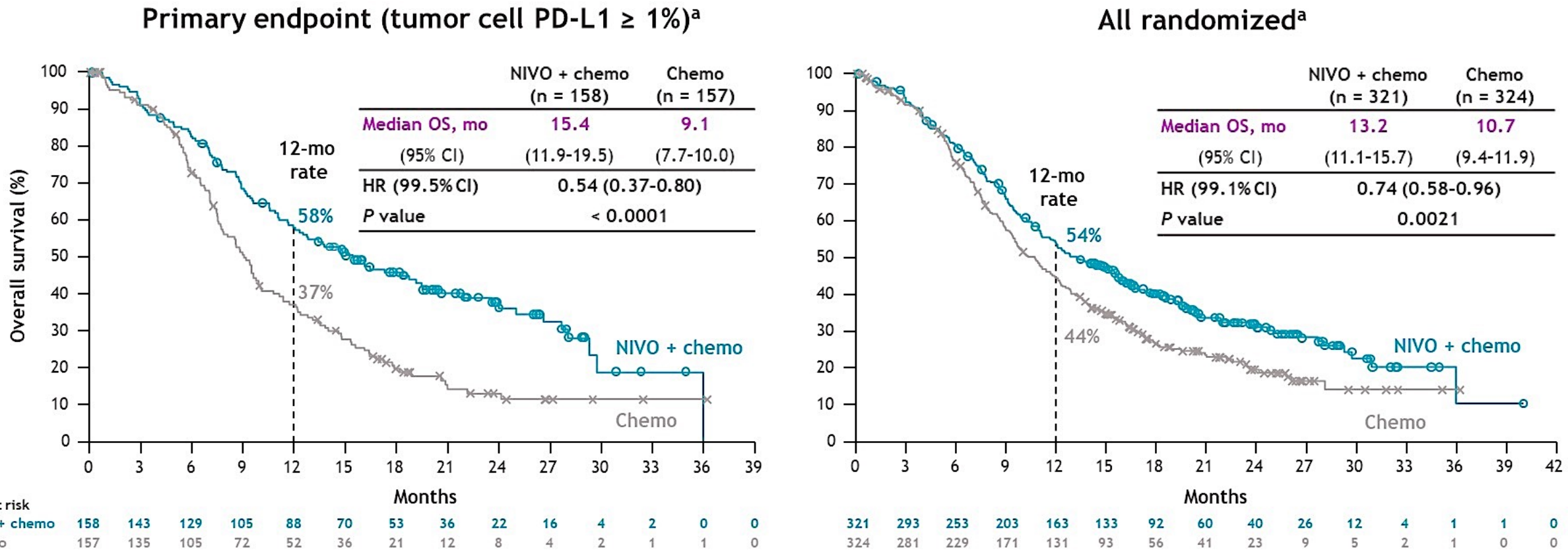
[a]Minimum follow-up, 12.1 months; [b]Per BICR assessment.

1. Moehler M, et al. Oral presentation at the ESMO Virtual Annual Meeting; September 19-21, 2020. Presentation LBA6.

Courtesy of Zev Wainberg, MD, MSc

Moehler et al, ASCO 2021.

CheckMate 648: Overall survival with NIVO + chemo vs chemo

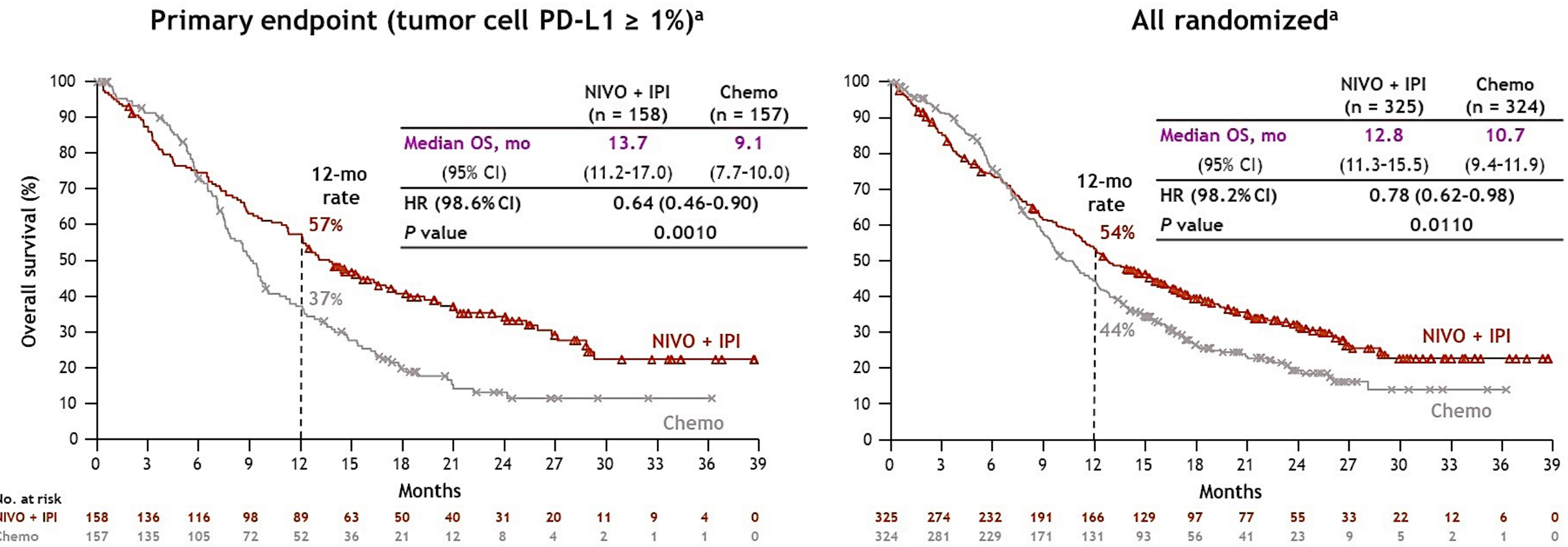


- Superior OS with NIVO + chemo vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 46% reduction in the risk of death and a 6.3-month improvement in median OS
  - All randomized: 26% reduction in the risk of death and a 2.5-month improvement in median OS

[a]Minimum follow-up 12.9 months.

Courtesy of Zev Wainberg, MD, MSc

CheckMate 648: Overall survival with NIVO + IPI vs chemo



- Superior OS with NIVO + IPI vs chemo in tumor cell PD-L1 ≥ 1% and all randomized populations
  - Tumor cell PD-L1 ≥ 1%: 36% reduction in the risk of death and a 4.6-month improvement in median OS
  - All randomized: 22% reduction in the risk of death and a 2.1-month improvement in median OS

[a]Minimum follow-up 12.9 months.

Courtesy of Zev Wainberg, MD, MSc

Should patients receiving neoadjuvant chemoradiation therapy for esophageal cancer be offered adjuvant nivolumab if there is residual disease?

Dr Tanios Bekaii-Saab

Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

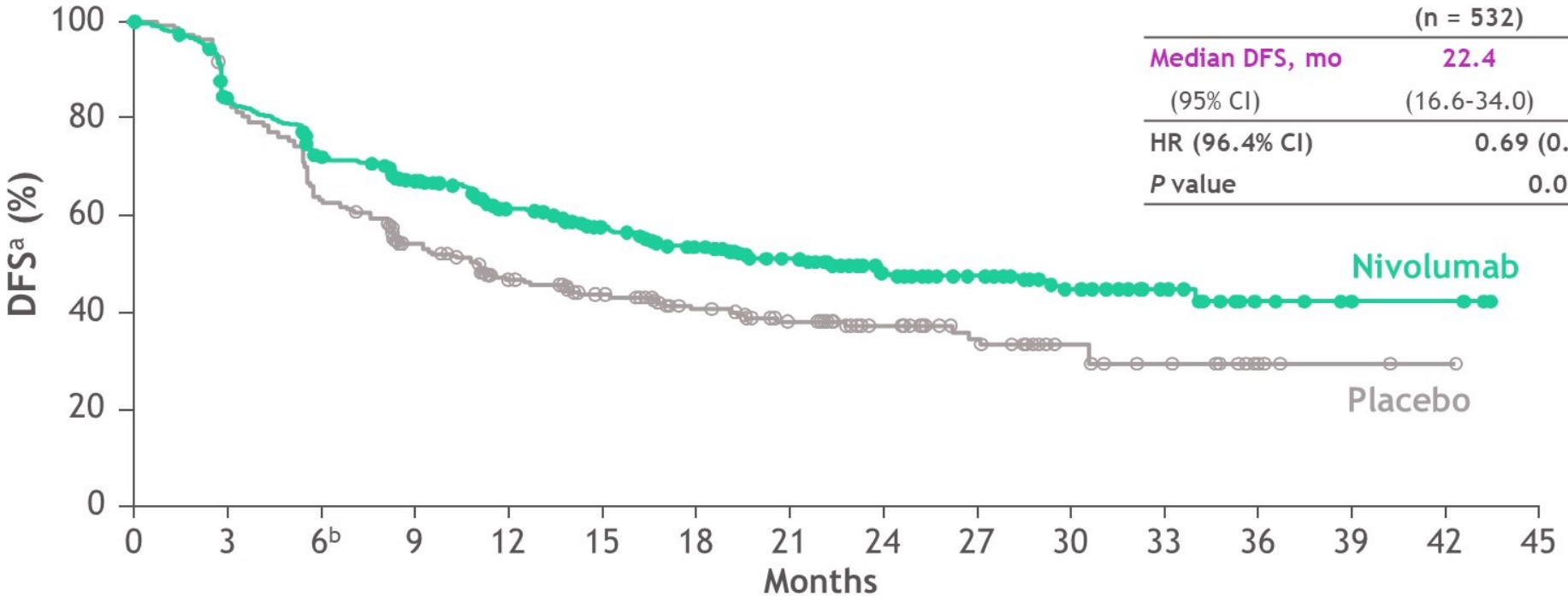
RTP RESEARCH TO PRACTICE

Have you administered or would you administer adjuvant nivolumab outside of a clinical trial setting to a patient with esophageal or GEJ cancer who receives neoadjuvant chemoradiation therapy and is found to have a pathologic complete response at surgery?

 Dr Atreya	I have not but would for the right patient	 Dr Bekaii-Saab	I have not but would for the right patient
 Dr Deming	I have not but would for the right patient	 Dr O'Reilly	I have not but would for the right patient
 Prof Van Cutsem	I have not and would not	 Dr Philip	I have not and would not
 Dr Wainberg	I have not but would for the right patient	 Dr Reiss Binder	I have not and would not

RTP RESEARCH TO PRACTICE

CheckMate 577: Disease-free survival (DFS)



	Nivolumab (n = 532)	Placebo (n = 262)
Median DFS, mo	22.4	11.0
(95% CI)	(16.6-34.0)	(8.3-14.3)
HR (96.4% CI)	0.69 (0.56-0.86)	
P value	0.0003[c]	

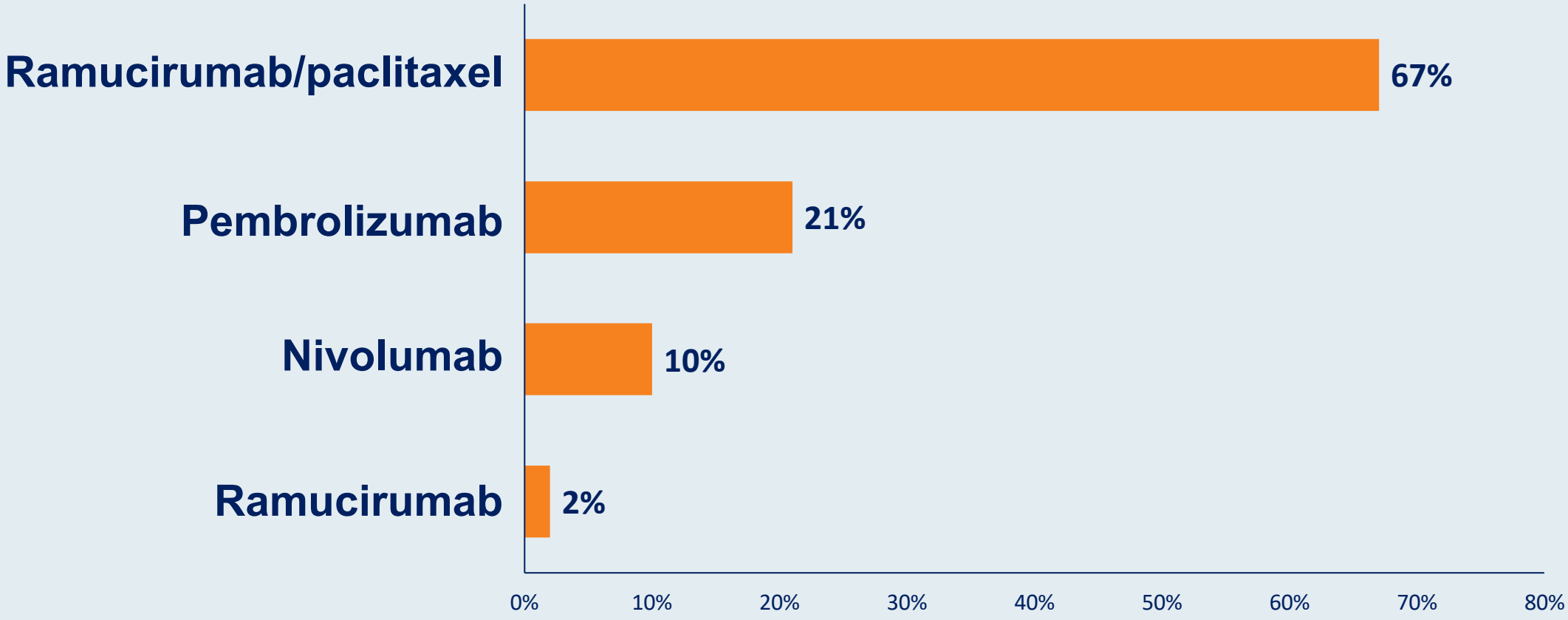
No. at risk																
Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

[a]Per investigator assessment; [b]6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; [c]The boundary for statistical significance at the prespecified interim analysis required the *P* value to be less than 0.036.
Kelly RJ, et al. *N Engl J Med* 2021;384:1191-1203.

Courtesy of Zev Wainberg, MD, MSc

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ (PD-L1 CPS ≥1) who has experienced disease progression on first-line FOLFOX?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-negative, MSS adenocarcinoma of the GEJ (PD-L1 CPS ≥1) who has experienced disease progression on first-line FOLFOX?

 Dr Atreya	Pembrolizumab	 Dr Bekaii-Saab	Ramucirumab/ paclitaxel
 Dr Deming	Ramucirumab/ paclitaxel	 Dr O'Reilly	Ramucirumab/ paclitaxel
 Prof Van Cutsem	Ramucirumab/ paclitaxel	 Dr Philip	Ramucirumab/ paclitaxel
 Dr Wainberg	Pembrolizumab	 Dr Reiss Binder	Ramucirumab/ paclitaxel

RTP RESEARCH TO PRACTICE

Chalk Talk – Zev Wainberg, MD, MSc

Regulatory and reimbursement issues aside, what is the optimal second-line therapy for a patient with metastatic HER2-negative, MSS gastric/GEJ adenocarcinoma who experiences disease progression on first-line FOLFOX? What if the patient has experienced disease progression on first-line FOLFOX/nivolumab? How, if at all, does PD-L1 CPS affect this decision?

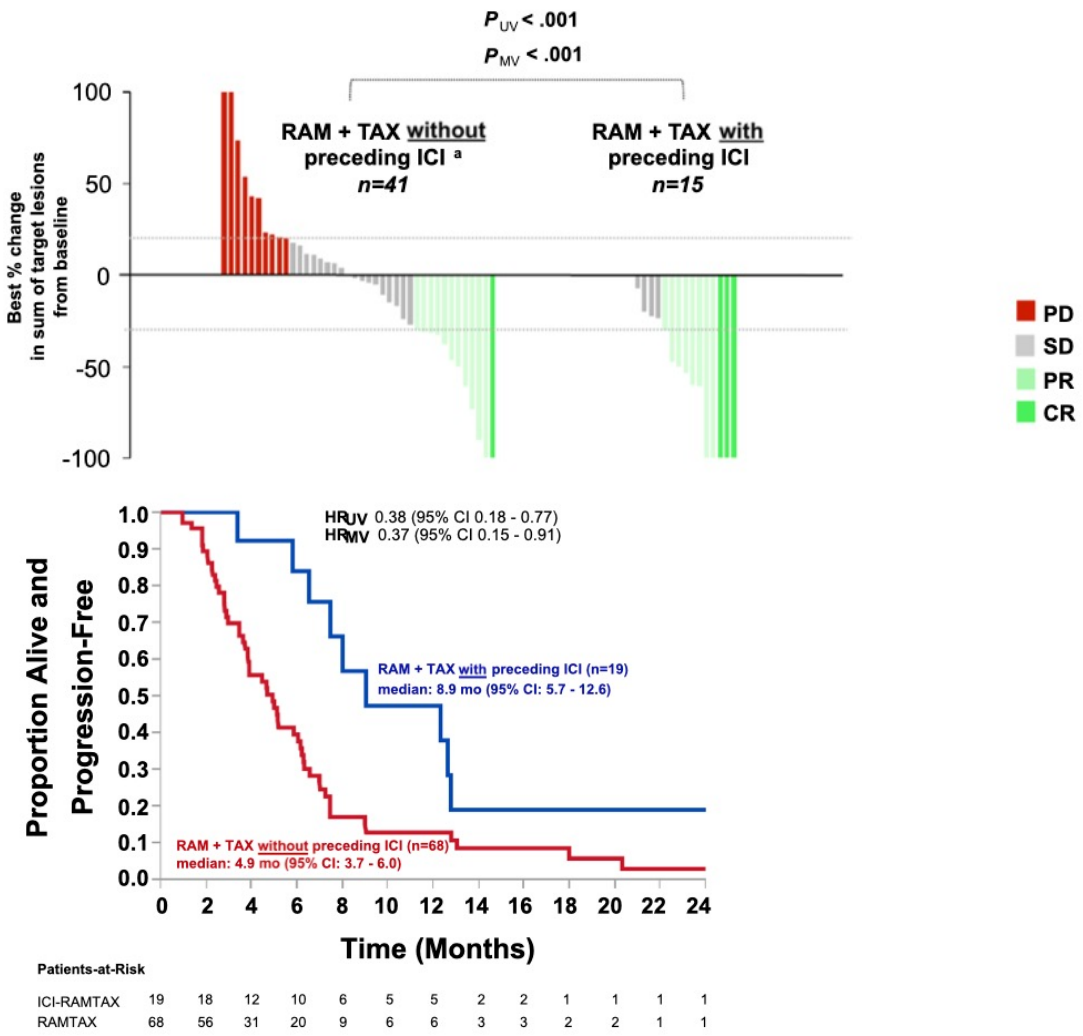
- In patients with 2nd-line MSS gastric/GEJ HER2-negative adenocarcinoma, there is no clear role for PD-1 inhibitors regardless of PD-L1 score
- The RAINBOW trial (Wilke et al, Lancet 2014) established a regimen of paclitaxel/ramucirumab if a patient progresses on front line therapy (FOLFOX among others)
- There have been no large 2nd-line studies in patients who progress on FOLFOX/nivo, so the standard of paclitaxel/ramucirumab is still appropriate
- We have no data to support a role for any PD-1 inhibitor after they have progressed on front line chemo/PD-1 inhibitor combination therapy in gastric/GEJ adenocarcinoma
- The FDA has withdrawn the indication for 3rd-line pembrolizumab in CPS ≥1
- If a patient with metastatic gastric/GEJ adenocarcinomas has a CPS>5 and is anti-PD-1 antibody-naïve, either nivolumab or pembrolizumab should be considered (ATTRACTION 3-Nivo, KEYNOTE-059-pembro)

How are you currently integrating TAS-102 into your clinical algorithms for metastatic gastric/GEJ cancers? In which line of therapy do you generally use this drug? How, if at all, is this impacted by PD-L1 status?

- TAS-102 (trifluridine/tipiracil) is indicated in fit patients with good organ function, regardless of molecular markers, failing cytotoxic therapy (including 5FU, oxaliplatin, docetaxel/paclitaxel, irinotecan combinations).
  - In patients with a HER2-positive tumors, prior treatments should have included trastuzumab and trastuzumab deruxtecan.
  - In patients with a PD-L1 CPS >5 positive tumor, prior treatments (first line) should have included nivolumab in combination FOLFOX in first line
  - Ramucirumab is usually added to cytotoxics in second line, in HER2-negative patients
  - In patients with a MSI-H tumor, prior treatments included pembrolizumab

- So this means in reality: TAS-102 is indicated in third or fourth line (TAGS study)
- The integration of TAS-102 is regardless of molecular markers in third/fourth line

The efficacy of Ramucirumab may be enhanced by the preceding ICI in mGC



Kankeu Fonkoua LA, et al. *Int J Cancer* 2021;[Online ahead of print].

Courtesy of Zev Wainberg, MD, MSc

Phase II Trial of TAS-102 and Ramucirumab

Patients with mGC/GEJ cancer
- ECOG PS 0/1
- Age ≥20 y
- Refractory/intolerant to last prior therapy

Cohort A (n=30) — 2nd line
1 prior regimen including:
- Fluoropyrimidine

Cohort B (n=30) — 3rd or later line
2-4 prior regimens including:
- Fluoropyrimidine
- Platinum
- Either a taxane and/or irinotecan
- Ramucirumab (one regimen)

FTD/TPI + ramucirumab
FTD/TPI 35 mg/m² BID orally on days 1–5 and 8–12 of each 28-day cycle
plus intravenous ramucirumab 8 mg/kg on days 1 and 15

- Treatment until disease progression, intolerable toxicity, physician's decision or patient withdrawal
- Tumor response was evaluated by each investigator according to RECIST version 1.1 every 6 weeks until week 18, and then every 8 weeks

Endpoints

Primary
- DCR

Secondary
- ORR
- PFS
- TTF
- Exposure to FTD/TPI and ramucirumab
- Time to ECOG PS ≥2
- Safety

	Cohort A (n=33)		Cohort B (n=31)	
	Previous use (n=7)	No previous use (n=26)	Previous use (n=15)	No previous use (n=16)
Overall response rate*	2 (29%, 4–71)	1 (4%, 0–20)	5 (33%, 12–62)	0 (0%, 0–21)
Disease control rate†	7 (100%, 59–100)	21 (81%, 61–93)	10 (67%, 38–88)	14 (88%, 62–98)
Progression-free survival, months	6·1 (4·1–NA)	5·3 (3·6–7·9)	5·4 (1·4–NA)	5·0 (2·1–6·1)
Event	3 (43%)	15 (58%)	9 (60%)	12 (75%)
Censored	4 (57%)	11 (42%)	6 (40%)	4 (25%)

Data are n (%, 95% CI), n (95% CI), or n (%). NA=not available. *Complete response plus partial response. †Complete response plus partial response plus stable disease.

Table 3: **Antitumour endpoints according to previous use of an immune checkpoint inhibitor (full analysis set)**

Kawazoe A, et al. *Lancet Gastroenterol Hepatol* 2021;6:209–17.

FOLFIRI and Ramucirumab: A Non-Taxane Option

Phase II RAMIRIS Trial

Inclusion (selection)

- Histologically proven metastatic or locally advanced adenocarcinoma stomach/EGJ
- progression during / within 6 months of the last dose of first-line platinum and fluoropyrimidine doublet with or without anthracycline or docetaxel
- ECOG ≤ 1

STRATIFICATION

Previous docetaxel-containing therapy
yes vs. no
Time of progression during or after end of first-line therapy
≤3 months vs. >3 months

RANDOMISATION

2:1

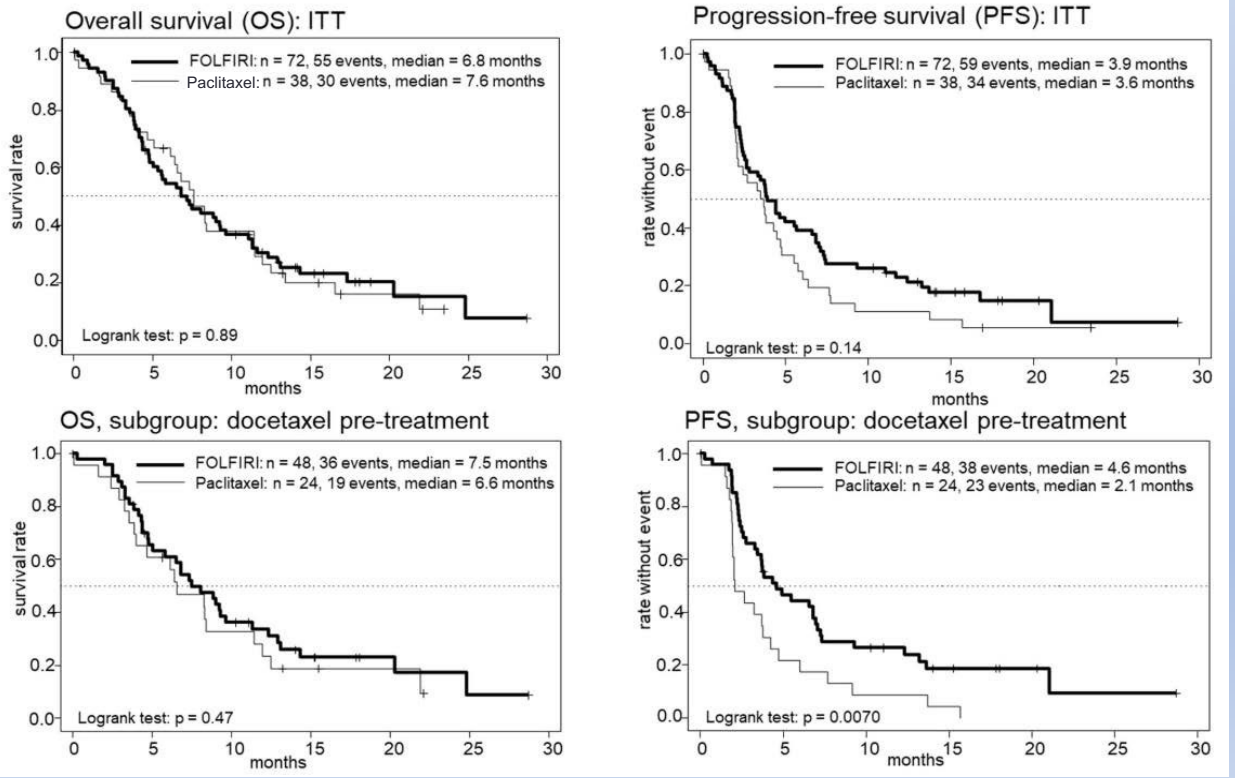
Arm A
Irinotecan 180 mg/m²
5-FU bolus 400 mg/m²
Leucovorin* 400 mg/m²
5-FU 2400 mg/m² 46-hour continuous administration
day 1 and 15, qd28
plus
Ramucirumab 8 mg/kg i.v. infusion
day 1 and 15, qd28
67 patients

Arm B
Paclitaxel 80 mg/m²
day 1, 8, 15
plus
Ramucirumab 8mg/kg
day 1 and 15
qd28
34 patients

Table 3: Objective Response Rate (ORR) and Disease Control Rate (DCR)

Event	FOLFIRI+ Ramucirumab	Paclitaxel+ Ramucirumab
ORR %	22% (16/72)	11% (4/38)
ORR % in Docetaxel pre-treated pts	25% (12/48)	8% (2/24)
DCR %	61% (44/72)	58% (21/38)
DCR % in Docetaxel pre-treated pts	65% (31/48)	37% (9/24)

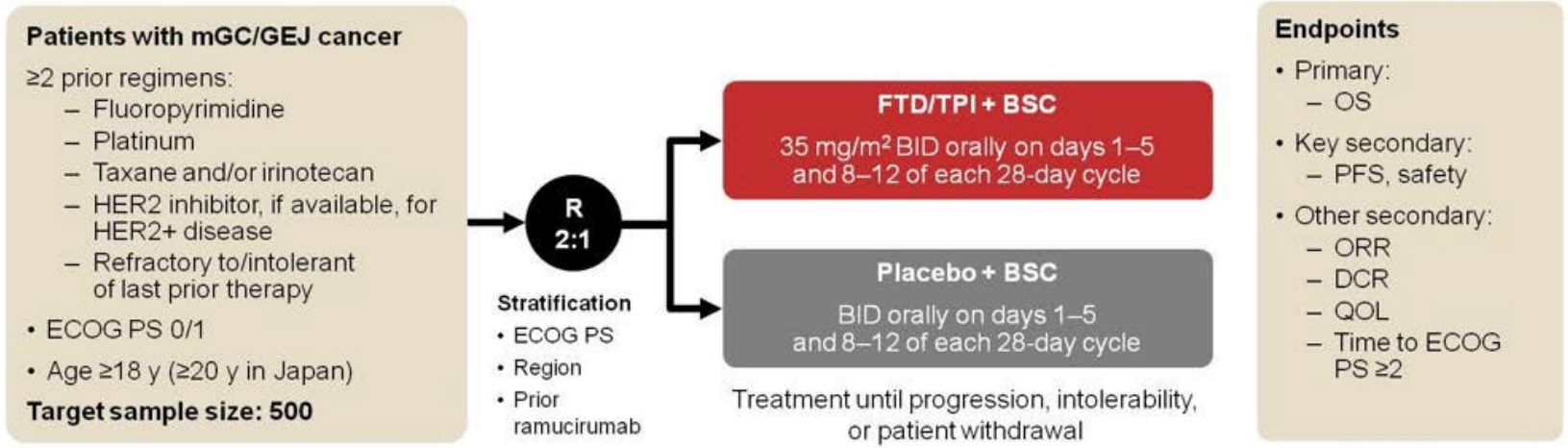
Figure 2: Overall and Progression-free Survival



Lorenzen ASCO 2020 abs 4514

Courtesy of Zev Wainberg, MD, MSc

TAGS – Multicenter, Randomized, Double-blind, Phase 3 Study



	Trifluridine/Tipiracil	Placebo	P value
Overall Survival	5.7 months	3.6 months	P=0.00058
	HR 0.69 (95% CI 0.56-0.85)		
12-month OS	21%	13%	
Progression-Free Survival	2.0 months	1.8 months	P< 0.0001
	HR 0.57 (95% CI 0.47-0.70)		
6-month PFS	15%	6%	
Overall Response Rate	4%	2%	P=0.28
Disease Control Rate	44%	14%	P<0.0001

Shitara et al Lancet Oncology 2018, 19: 1427-1448

Courtesy of Zev Wainberg, MD, MSc

How do we fight against mGC with CPS<5 ?

CLDN18.2-Zolbetuximab

GLOW

Key eligibility criteria:
- Age ≥ 18 years
- Locally advanced unresectable or metastatic disease
- Gastric or gastroesophageal junction cancer
- Histologically confirmed adenocarcinoma
- prior systemic chemotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma,
- CLDN18.2 in ≥ 75% of tumor cells
- ECOG PS of 0 or 1

R 2:1

CAPOX+zolbetuximab

CAPOX+placebo

N = 500

Primary endpoint:
- PFS

2nd endpoints:
- OS
- ORR
- DOR, DCR)
- Safety

Spotlight

Key eligibility criteria:
- Age ≥ 18 years
- Locally advanced unresectable or metastatic disease
- Gastric or gastroesophageal junction cancer
- Histologically confirmed adenocarcinoma
- prior systemic chemotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma,
- CLDN18.2 in ≥ 75% of tumor cells
- ECOG PS of 0 or 1

R 2:1

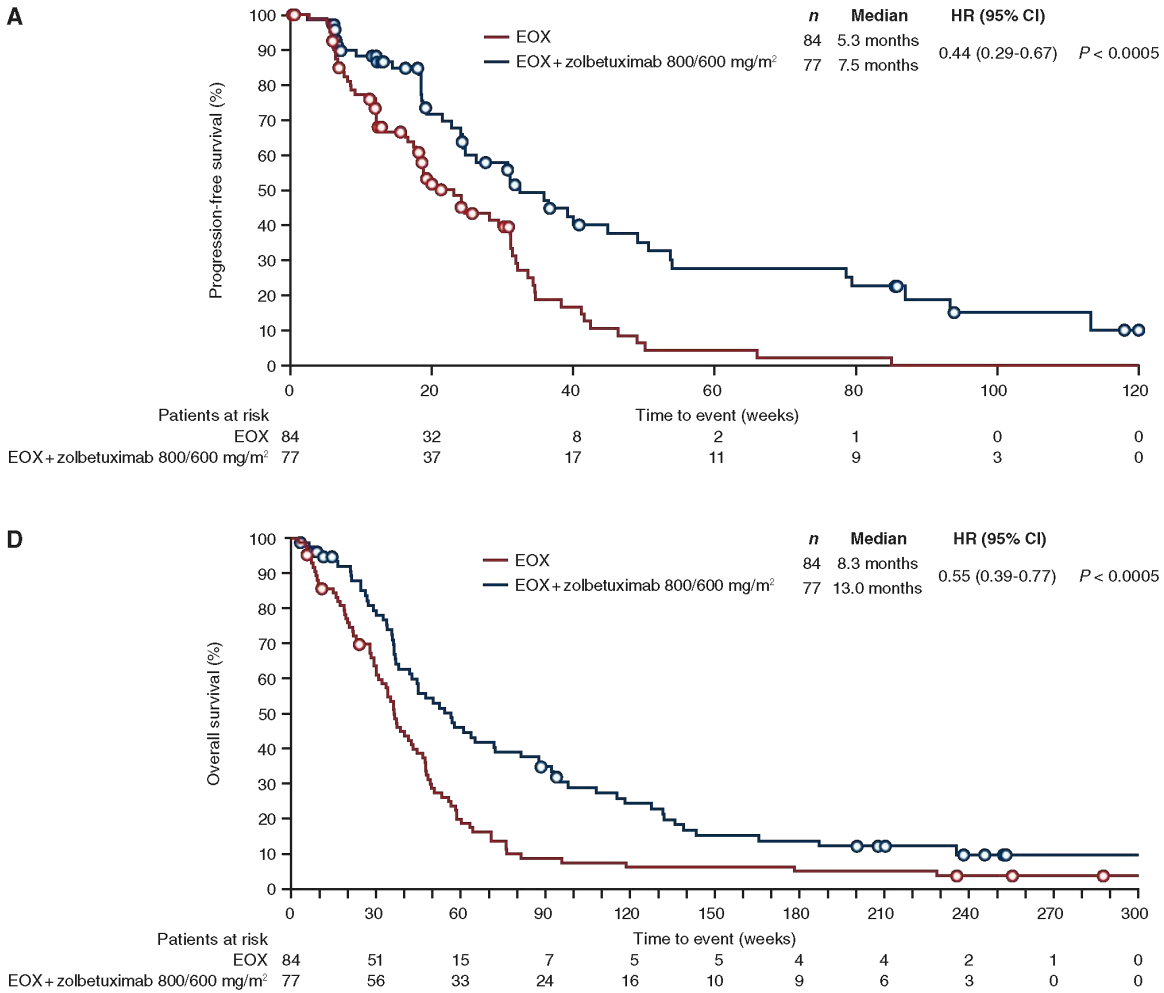
FOLFOX+zolbetuximab

FOLFOX+placebo

N = 550

Primary endpoint:
- PFS

2nd endpoints:
- OS
- ORR
- DOR, DCR)
- Safety



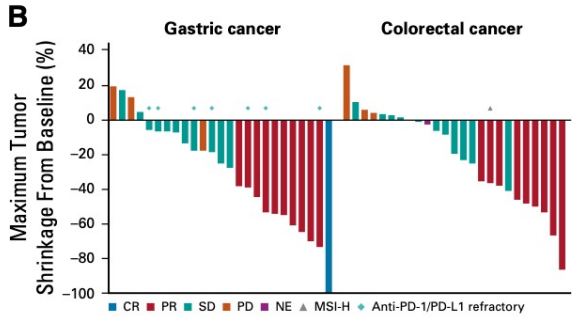
Sahin U, et al. *Ann Oncol* 2021;32:609–19.

Courtesy of Zev Wainberg, MD, MSc

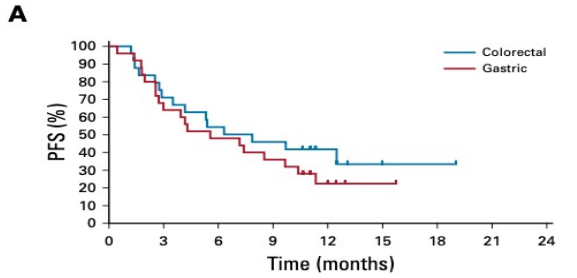
Is chemotherapy the best partner of anti-PD-1 antibody?

Phase Ib | Regorafenib | Nivolumab

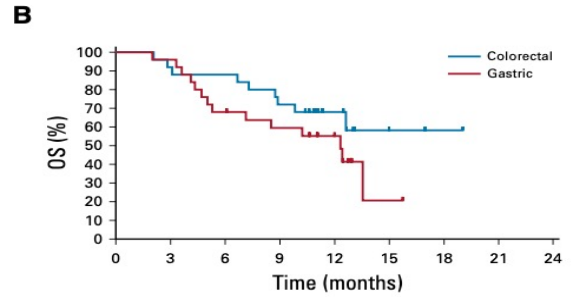
Standard treatment refractory GC/CRC,PS 0-1



ORR
CRC 36%
GC 44%



mPFS
CRC 5.6m
GC 7.9m

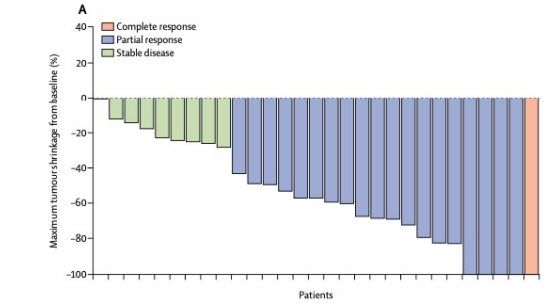


mOS
CRC NR
GC 12.3m

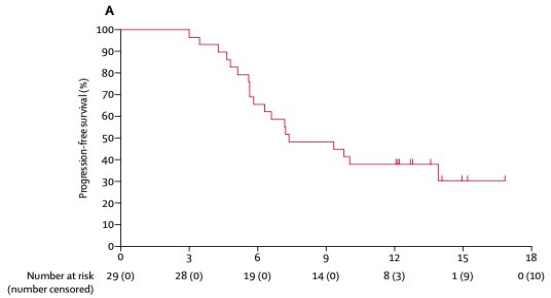
Fukuoka S, et al. *J Clin Oncol* 2020;38:2053–61.

Phase II | Lenvatinib | Pembrolizumab

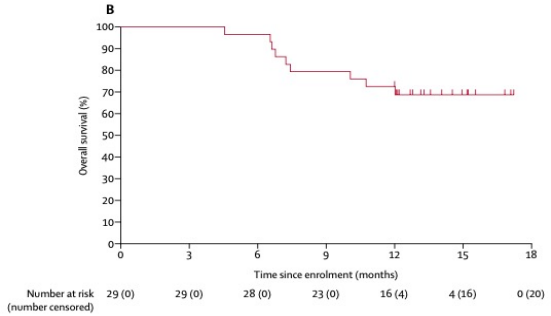
Chemotherapy-naive or 1st line refractory GC, PS 0-1



ORR 69%



mPFS 7.0m



mOS NR

Kawazoe A, et al. *Lancet Oncol* 2020;21:1057–65.

Courtesy of Zev Wainberg, MD, MSc

What is the optimal first- and second-line treatment for HER2-positive mUGI cancers, and does this vary based on CPS?

Dr Tanios Bekaii-Saab

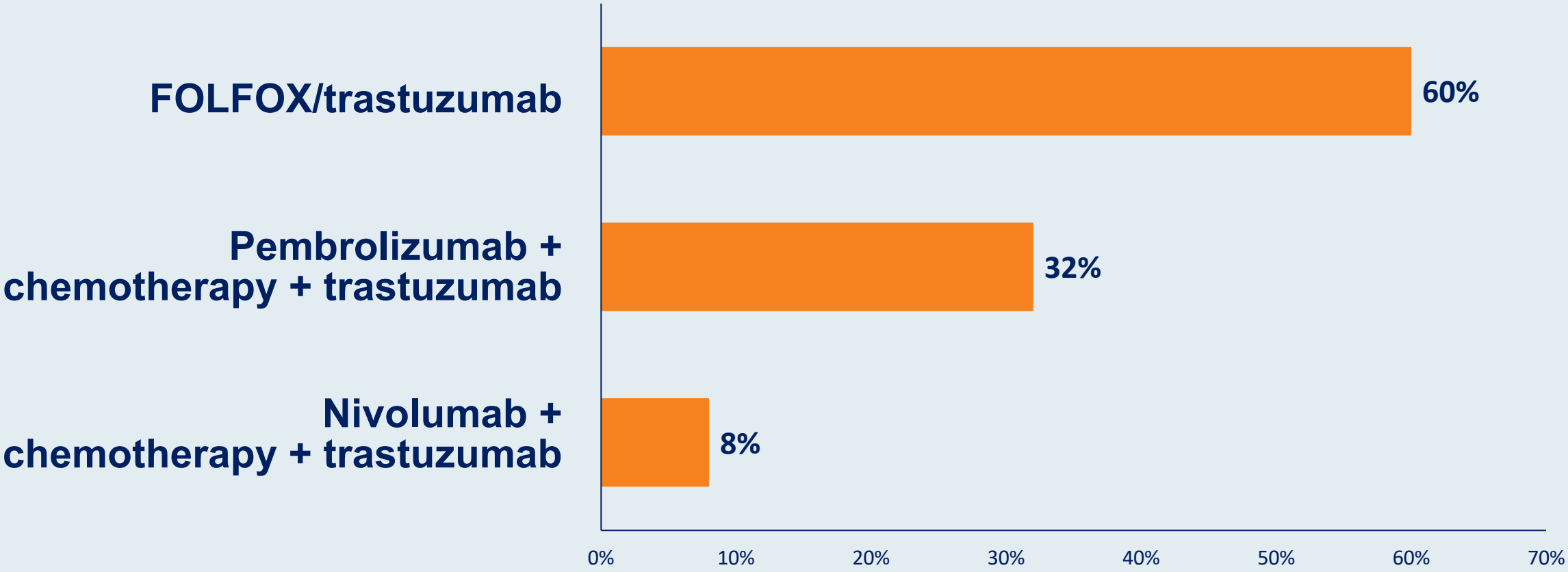
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ (PD-L1 CPS <1)?



Premeeting survey: July 2021

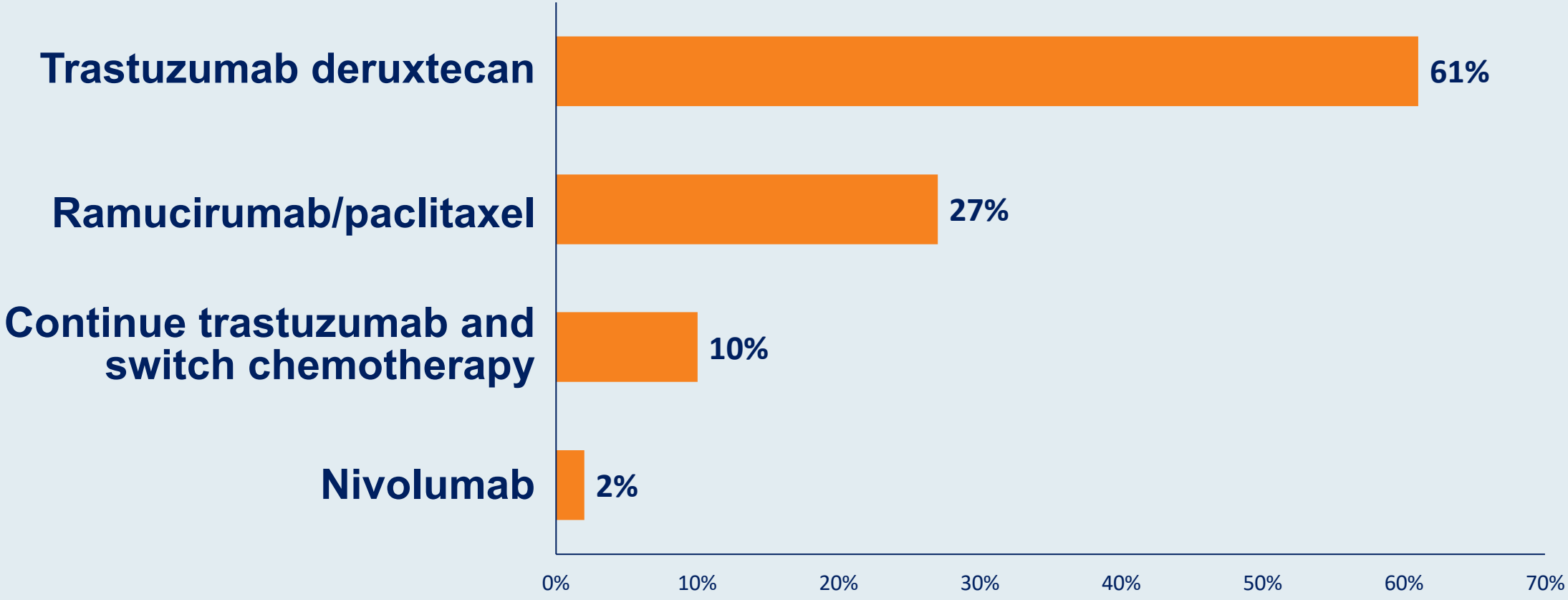
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what first-line therapy would you recommend for a 65-year-old patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ (PD-L1 CPS <1)?

 Dr Atreya	FOLFOX/trastuzumab	 Dr Bekaii-Saab	Pembrolizumab + chemotherapy + trastuzumab
 Dr Deming	FOLFOX/trastuzumab	 Dr O'Reilly	Pembrolizumab + chemotherapy + trastuzumab
 Prof Van Cutsem	Pembrolizumab + chemotherapy + trastuzumab	 Dr Philip	Pembrolizumab + chemotherapy + trastuzumab
 Dr Wainberg	Pembrolizumab + chemotherapy + trastuzumab	 Dr Reiss Binder	FOLFOX/trastuzumab

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ (PD-L1 CPS <1) with disease progression on FOLFOX/trastuzumab?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would you currently recommend as second-line therapy for a patient with metastatic HER2-positive, MSS adenocarcinoma of the GEJ (PD-L1 CPS <1) with disease progression on FOLFOX/trastuzumab?

 Dr Atreya	Trastuzumab deruxtecan	 Dr Bekaii-Saab	Trastuzumab deruxtecan
 Dr Deming	Trastuzumab deruxtecan	 Dr O'Reilly	Trastuzumab deruxtecan
 Prof Van Cutsem	Trastuzumab deruxtecan	 Dr Philip	Trastuzumab deruxtecan
 Dr Wainberg	Trastuzumab deruxtecan	 Dr Reiss Binder	Trastuzumab deruxtecan

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside,what is the optimal first-line therapy for a patient with metastatic HER2-positive, MSS gastric/GEJ adenocarcinoma?

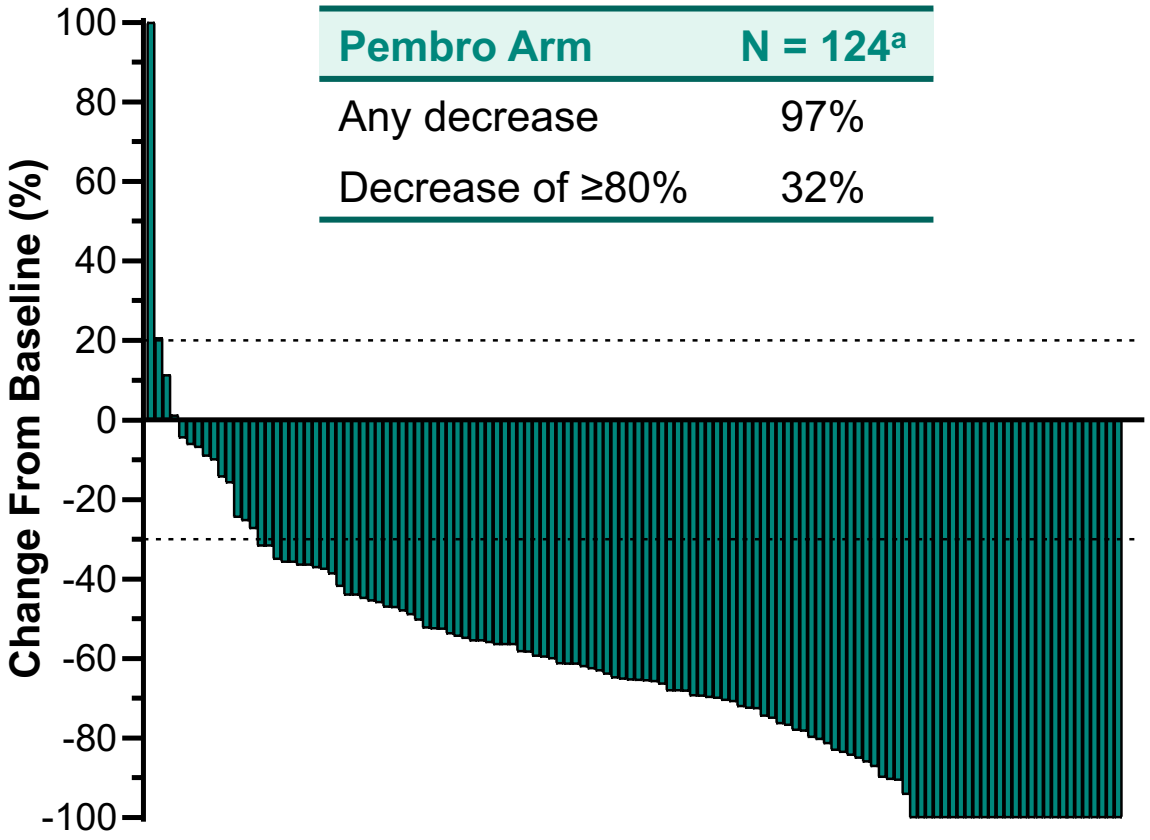
- The recent new standard of care in fit patients with good organ function is chemo doublet + trastuzumab + pembrolizumab
- The data of KEYNOTE-811 are practice-changing, although it is only a preplanned interim analysis on RR, and data on OS and PFS are still awaited
- Preferred chemo doublet in gastric cancer is FOLFOX; data say that CAPOX is also an option, although this is not my favourite combination

Regulatory and reimbursement issues aside, in what line of therapy would you like to offer trastuzumab deruxtecan to your patients with HER2-positive gastric/GEJ cancer?

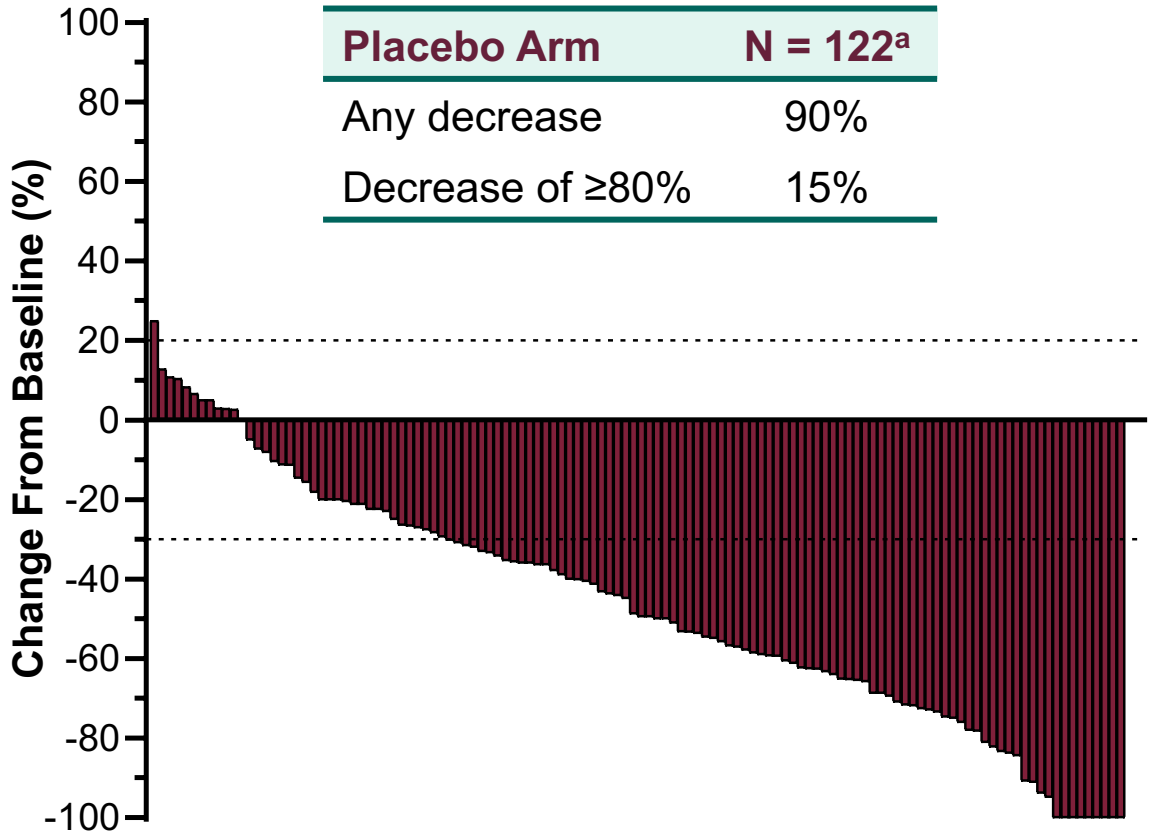
- Trastuzumab deruxtecan is active in trastuzumab-pretreated HER2-positive adenocarcinoma, as was shown in DESTINY-Gastric01 study.
- DESTINY-Gastric01 was carried out in patients who had progressed while they were receiving at least two previous therapies, including trastuzumab
- However, there is no standard HER2-targeted therapy in second line after progression on trastuzumab. The standard treatment was paclitaxel/ramucirumab until the trastuzumab deruxtecan studies were performed. However, trastuzumab deruxtecan seems to be clearly more active and should be proposed in **second line** after progression on trastuzumab and after rechecking for HER2 positivity.
- Confirmation of HER2 positivity on a new biopsy is necessary
- The ongoing DESTINY-Gastric02 study includes US/EU patients in second line.

KEYNOTE-811: Best Percentage Change From Baseline in Size of Target Lesions at IA1, Efficacy Population

ORR	74.4%	51.9%



Pembro Arm	N = 124[a]
Any decrease	97%
Decrease of ≥80%	32%



Placebo Arm	N = 122[a]
Any decrease	90%
Decrease of ≥80%	15%

[a]Participants with RECIST-measurable disease at baseline and ≥1 post-baseline measurement evaluable for change from baseline in target lesions.
The treatment regimen in both arms included trastuzumab and chemotherapy. Data cutoff date: June 17, 2020.

Courtesy of Eric Van Cutsem, MD, PhD

ESMO GI/WCIGC Ann Onc 2021,LBA4

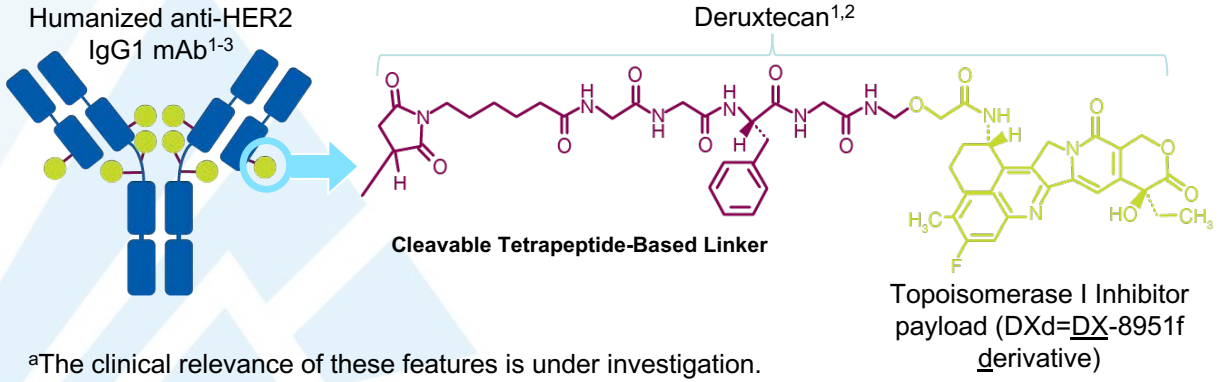
Trastuzumab-deruxtecan (T-DXd), a novel ADC (Antibody-Drug-Conjugate)

An ADC composed of 3 components[1,2]:

A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab, covalently linked to:

A topoisomerase I inhibitor payload, an exatecan derivative, via

A tetrapeptide-based cleavable linker



[a]The clinical relevance of these features is under investigation.

Characteristics

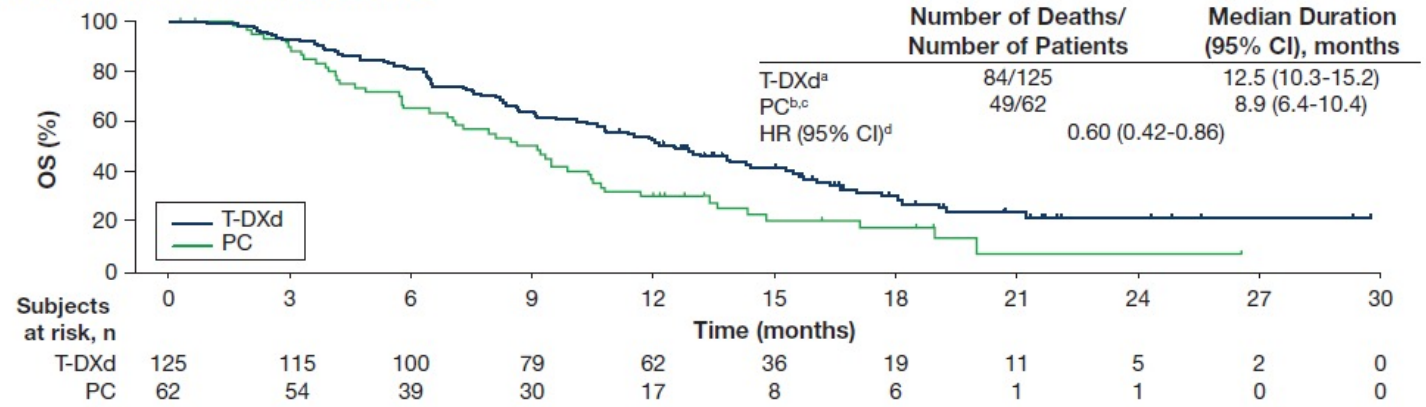
- Payload MOA: topoisomerase I **inhibitor**[1,2,a]
- High potency of payload[1,2,a]
- High DAR ≈8[1,2,a]
- Payload with short systemic half-life[1,2,a]
- Stable linker-payload[1,2,a]
- Tumor-selective cleavable linker[1,2,a]
- Membrane permeable payload[1,4,a]

1. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. Clin Cancer Research. 2016;22(20):5097-5108. 3. Trail PA, et al. Pharmacol Ther. 2018;181:126-142. 4. Ogitani Y, et al. Cancer Sci. 2016;107(7):1039-1046.

Courtesy of Eric Van Cutsem, MD, PhD

DESTINY-Gastric01: Survival

Figure 4. Kaplan-Meier Analysis of OS

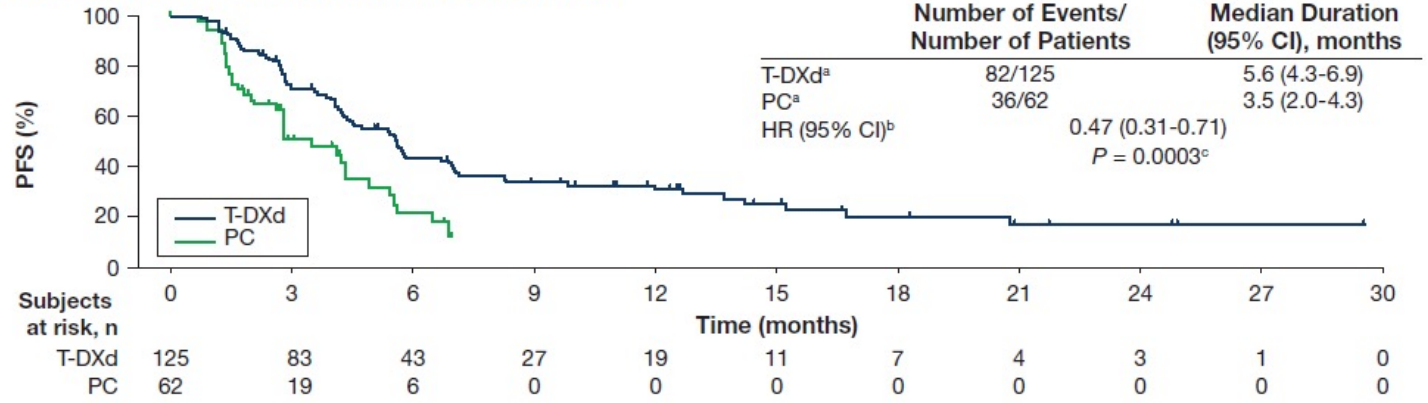


	Number of Deaths/ Number of Patients	Median Duration (95% CI), months
T-DXd[a]	84/125	12.5 (10.3-15.2)
PC[b,c]	49/62	8.9 (6.4-10.4)
HR (95% CI)[d]	0.60 (0.42-0.86)	

HR, hazard ratio; OS, overall survival; PC, physician's choice; T-DXd, trastuzumab deruxtecan.

[a]In the T-DXd arm, 41 patients (32.8%) were censored.
[b]In the PC arm, 13 patients (21.0%) were censored.
[c]One patient in the PC arm received crossover treatment of T-DXd.
[d]HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region.

Figure 5. Kaplan-Meier Analysis of PFS Based on ICR



	Number of Events/ Number of Patients	Median Duration (95% CI), months
T-DXd[a]	82/125	5.6 (4.3-6.9)
PC[a]	36/62	3.5 (2.0-4.3)
HR (95% CI)[b]	0.47 (0.31-0.71)	
	P = 0.0003[c]	

HR, hazard ratio; ICR, independent central review; PC, physician's choice; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

[a]In the T-DXd arm, 71 patients (56.8%) had PD and 11 (8.8%) had death as the first event. In the PC arm, 34 patients (54.8%) had PD and two (3.2%) had death as the first event. 43 (34.4%) and 26 (41.9%) patients were censored in the T-DXd and PC arms, respectively, for no baseline (T-DXd [n = 0]; PC [n = 2]) or postbaseline tumor assessment (n = 1; n = 3), receiving new anticancer therapy (n = 14; n = 14), and missing two consecutive tumor assessments (n = 5; n = 1); the remaining patients were censored without an event.
[b]HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region.
[c]Comparison between T-DXd and PC overall using a stratified log-rank test with region as a stratification factor.

Data cutoff: June 3, 2020

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Courtesy of Eric Van Cutsem, MD, PhD

Yamaguchi K, et al. Presented at ASCO 2021 Virtual Meeting; June 4-8, 2021.

DESTINY-Gastric01
Primary Endpoint: ORR

	Primary Cohort[1,a]		Exploratory Cohorts[2,b]	
	T-DXd (n = 119)	PC Overall (n = 56)	Cohort 1 IHC 2+/ISH− (n = 19)	Cohort 2 IHC 1+ (n = 21)
ORR by ICR (CR + PR)[c]	**51.3% (n = 61) 95% CI, 41.9-60.5;**	**14.3% (n = 8) 95% CI, 6.4-26.2**	**36.8% (n = 7) 95% CI, 16.3%-61.6%**	**19.0% (n = 4) 95% CI, 5.4%-41.9%**
	***P* < .0001[d]**			
Confirmed ORR by ICR (CR + PR)[c]	**42.0% (n = 50) 95% CI, 33.0-51.4**	**12.5% (n = 7) 95% CI, 5.2-24.1**	**26.3% (n = 5) 95% CI, 9.1%-51.2%**	**9.5% (n = 2) 95% CI, 1.2%-30.4%**
CR	8.4% (n = 10)	0	0	0
PR	33.6% (n = 40)[e]	12.5% (n = 7)	26.3% (n = 5)	9.5% (n = 2)
SD	43.7% (n = 52)	50.0% (n = 28)	63.2% (n = 12)	61.9% (n = 13)
PD	11.8% (n = 14)	30.4% (n = 17)	10.5% (n = 2)	28.6% (n = 6)
NE	2.5% (n = 3)	7.1% (n = 4)	0	0
Confirmed DCR (CR + PR + SD)[c]	85.7% (n = 102) 95% CI, 78.1-91.5	62.5% (n = 35) 95% CI, 48.5-75.1	89.5% (n = 17) 95% CI, 66.9%-98.7%	71.4% (n = 15) 95% CI, 47.8%-88.7%
Median Confirmed DOR	12.5 months 95% CI, 5.6 months-NE	3.9 months 95% CI, 3.0-4.9 months	7.6 months 95% CI, 4.1 months-NE	12.5 months 95% CI, NE-NE

[a]Data cutoff: June 3, 2020. [b]Data cutoff: November 8, 2019. [c]Includes data for the response-evaluable set: all randomized patients who received ≥1 dose of study drug and had measurable tumors based on ICR at baseline. [d]Comparison between T-DXd and PC overall using Cochran-Mantel-Haenszel test stratified by region. [e]According to the procedure of the ICR, the adjudicator assessment was changed from PR to SD in 1 patient at data cutoff of the final OS analysis.

Courtesy of Eric Van Cutsem, MD, PhD

1. Yamaguchi K, et al. Presented at ASCO 2021 Virtual Meeting; June 4-8, 2021.
2. Yamaguchi K, et al. Presented at ESMO Virtual Congress 2020; 19-21 September 2020.

DESTINY-Gastric01: Safety

TEAEs in ≥20% of Patients Treated with T-DXd[a]

	T-DXd (n = 125)			PC (n = 62)		
		Grade			Grade	
Preferred Term, %	Any	3	4	Any	3	4
Neutrophil count decreased[b]	64.8	38.4	12.8	35.5	16.1	8.1
Nausea	63.2	5.6	0	46.8	1.6	0
Decreased appetite	60.8	16.8	0	45.2	12.9	0
Anemia[c]	57.6	38.4	0	30.6	21.0	1.6
Platelet count decreased[d]	40.0	9.6	1.6	6.5	1.6	1.6
White blood cell count decreased[e]	38.4	20.8	0	35.5	8.1	3.2
Malaise	34.4	0.8	0	16.1	0	0
Diarrhea	32.8	2.4	0	32.3	1.6	0
Vomiting	26.4	0	0	8.1	0	0
Pyrexia	24.8	0	0	16.1	0	0
Constipation	24.8	0	0	24.2	0	0
Lymphocyte count decreased[f]	23.2	7.2	4.8	3.2	0	1.6
Alopecia	22.4	0	0	14.5	0	0
Fatigue	21.6	7.2	0	24.2	3.2	0

- 16 patients (12.8%) had T-DXd–related ILD (determined by an independent adjudication committee); there were no ILD events in the PC arm

Data cutoff: June 3, 2020. No additional TEAEs were observed in ≥20% of patients receiving PC. [a]There were no grade 5 events. [b]Includes preferred terms "neutrophil count decreased" and "neutropenia." [c]Includes preferred terms "hemoglobin decreased," "red blood cell count decreased," "anemia," and "hematocrit decreased." [d]Includes preferred terms "platelet count decreased" and "thrombocytopenia." [e]Includes preferred terms "leukopenia" and "white blood cell count decreased." [f]Includes preferred terms "lymphocyte count decreased" and "lymphopenia."

Courtesy of Eric Van Cutsem, MD, PhD

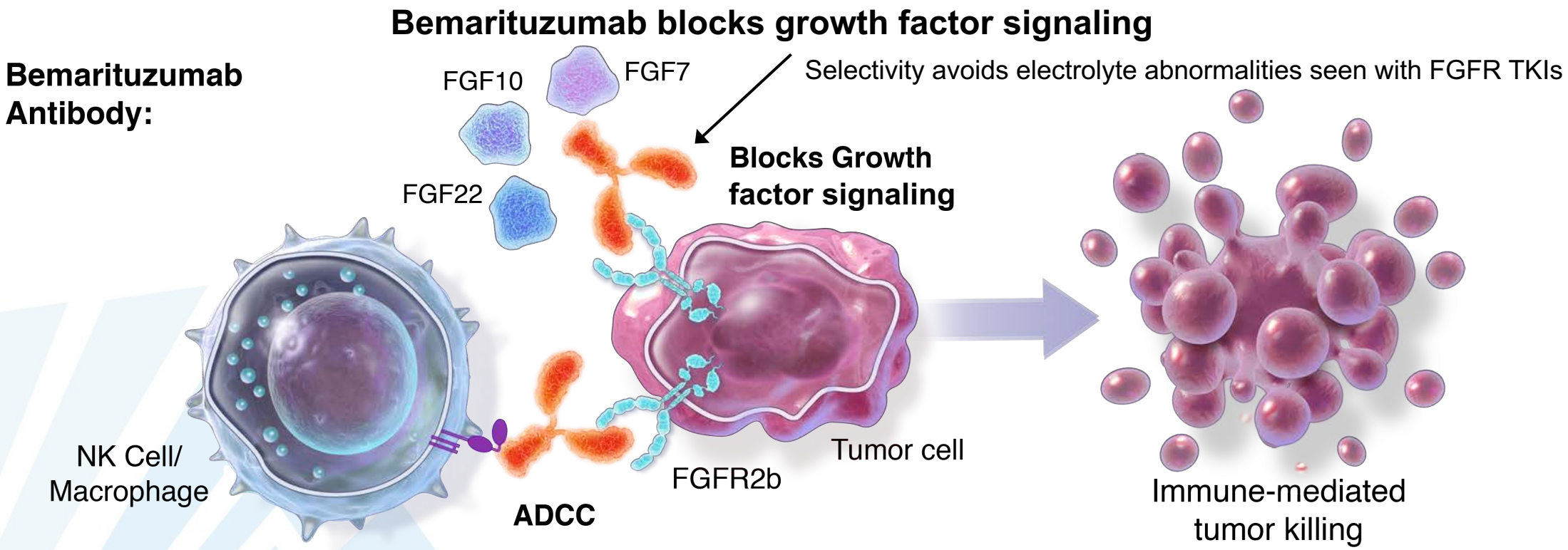
Yamaguchi K, et al. Presented at ASCO 2021 Virtual Meeting; June 4-8, 2021.

Ongoing studies evaluating T-DXd in earlier lines of treatment and/or in combination with other systemic therapies

- DESTINY-Gastric02 study of 2nd-line T-DXd (N=79) US/Europe completed accrual [NCT04014075]
- DESTINY-Gastric03 phase 2 study of novel combinations with T-DXd (chemo, ICI) is now open [NCT04379596]
- DESTINY-Gastric04 phase III (N=490) study of 2nd-line T-DXd is now open. [NCT04704934]

Courtesy of Eric Van Cutsem, MD, PhD

FGFR2 Amplification ~5% GEA



Catenacci DVT. Phase I Escalation & Expansion Study of Bemarituzumab (FPA144) in Pts With Advanced Solid Tumors and FGFR2b-Selected Gastroesophageal Adenocarcinoma JCO 2020

Catenacci DVT. Bemarituzumab with modified FOLFOX6 for advanced FGFR2-positive gastroesophageal cancer: FIGHT Phase III study design. Future Oncol 2019

Courtesy of Eric Van Cutsem, MD, PhD

FGFR2 Amplification: Bemarituzumab

FIGHT Phase 2 Study Design

Key Eligibility Criteria

- No prior therapy for unresectable, locally advanced or metastatic gastric/GEJ adenocarcinoma
- RECIST v1.1 evaluable disease
- FGFR2b overexpression and/or *FGFR2* gene amplification
- Not HER2-positive

Stratification Factors

- Geographic region
- Single dose of FOLFOX while screening
- Prior perioperative chemotherapy

Randomization 1:1

- Bemarituzumab* + mFOLFOX6 (n = 77)
- vs
- Placebo + mFOLFOX6 (n = 78)

Primary endpoint
- PFS

Secondary endpoints
- OS
- Response rate

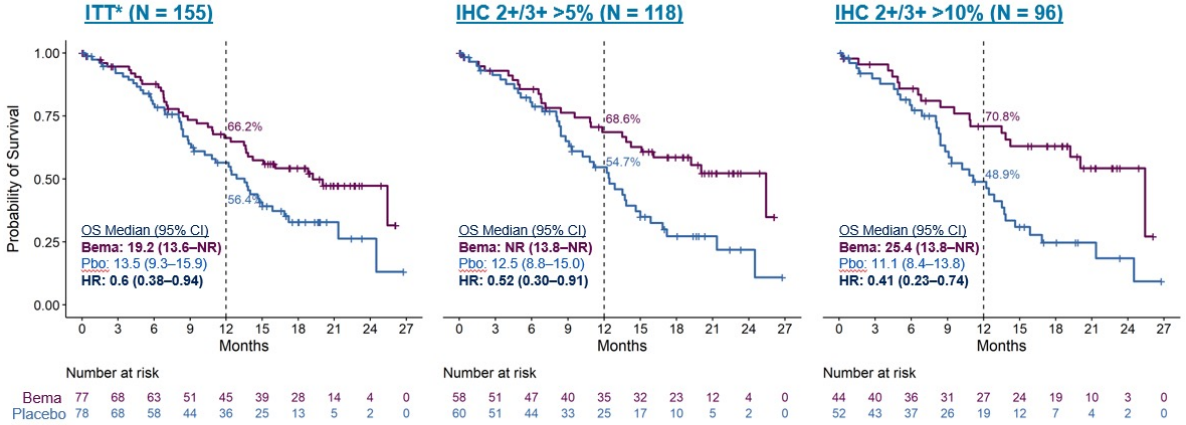
Treatment may continue until progression, unacceptable toxicity, or the patient meets other withdrawal criteria

*Bemarituzumab dosing: 15 mg/kg Q2W beginning cycle 1 day 1 (plus 1 dose of 7.5 mg/kg on day 8 of cycle 1 only). FOLFOX6 dosing: standard fixed doses Q2W.
FGFR2b, fibroblast growth factor receptor 2b.

Median OS Reached With Longer Follow-up

11

Addition of Bemarituzumab Showed a +5.7 Month Improvement in Median OS



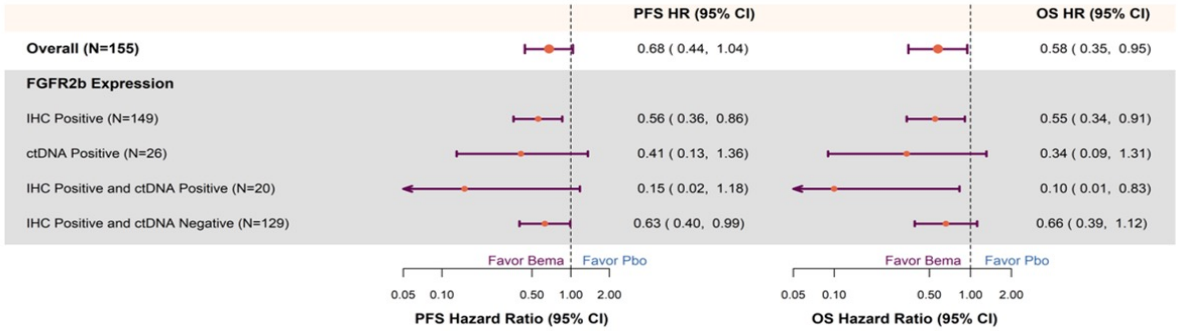
*ITT = includes 149 patients with IHC 2+/3+ and 6 with IHC <2+ or not available who were enrolled based on ctDNA alone.
NR, not reached.
Median Follow-up 12.5 months

*Based on February, 28th 2021 data cut

Evaluation of Efficacy by Biomarker Status

10

Overexpression was Sufficient, ctDNA+ with Most Pronounced Benefit



Catenacci et al. FIGHT: A randomized, double-blind, placebo-controlled, phase 2 study of bemarituzumab (bema) combined with modified FOLFOX6 in 1L FGFR2b+ advanced gastric/gastroesophageal junction adenocarcinoma (GC) (NCT03694522). ASCO abstr 2021

Courtesy of Eric Van Cutsem, MD, PhD

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- With so many approvals and use of immunotherapy with different CPS scores — can you please go through the algorithm of treatment of metastatic squamous cell carcinoma of the esophagus and metastatic adenocarcinoma of esophagus or GE junction or gastric with HER2/neu positive and negative patients?

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- Choosing immunotherapy wisely

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- FOLFOX vs FOLFOX/trastuzumab in metastatic HER2+ GEJ adenocarcinoma CPS < 1. Second line: ramucirumab/paclitaxel vs trastuzumab deruxtecan

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- For the patients that can qualify perioperative FLOT regimen, do you change to CROSS regimen +/- postop nivolumab now?

Premeeting survey: July 2021

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- Is FOLFOX the ideal backbone for squamous cell esophageal cancer or do you prefer something else?

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- Outline treatment algorithm and how it differs by histology, mutation analysis and PD-L1 value

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- Re-check the HER2 status on disease progression?

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- Adjuvant therapy for locally advanced GE or E cancer after Chemo/XRT when patient is not resectable surgically

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Gastroesophageal Cancers

- If someone is positive for H2N and PD-L1 both, how would you target and sequence the treatment?

Premeeting survey: July 2021

Agenda

Interdisciplinary Management of Gastrointestinal Cancers – Part 2

Module 2: Metastatic Colorectal Cancer (mCRC)

- **What is the optimal first-line systemic treatment for RAS/BRAF wild-type mCRC in a symptomatic and an asymptomatic patient, and does this vary by side of the primary tumor?**
- **What is the optimal first-line treatment for MSI-high mCRC?**
- **What is the optimal targeted treatment for BRAF-mutated mCRC, and in which line of therapy should it be used?**
- **What is your preferred sequencing of EGFR TKIs, TAS-102 (+/- bevacizumab) and regorafenib?**
- **What is your preferred sequencing of therapies for HER2-positive mCRC, including T-DXd?**

RTP RESEARCH TO PRACTICE

Agenda

Interdisciplinary Management of Gastrointestinal Cancers – Part 2

Module 2: Metastatic Colorectal Cancer (mCRC)

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RTP RESEARCH TO PRACTICE

What is the optimal first-line systemic treatment for RAS/BRAF wild-type mCRC in a symptomatic and an asymptomatic patient, and does this vary by side of the primary tumor?

Dr Tanios Bekaii-Saab

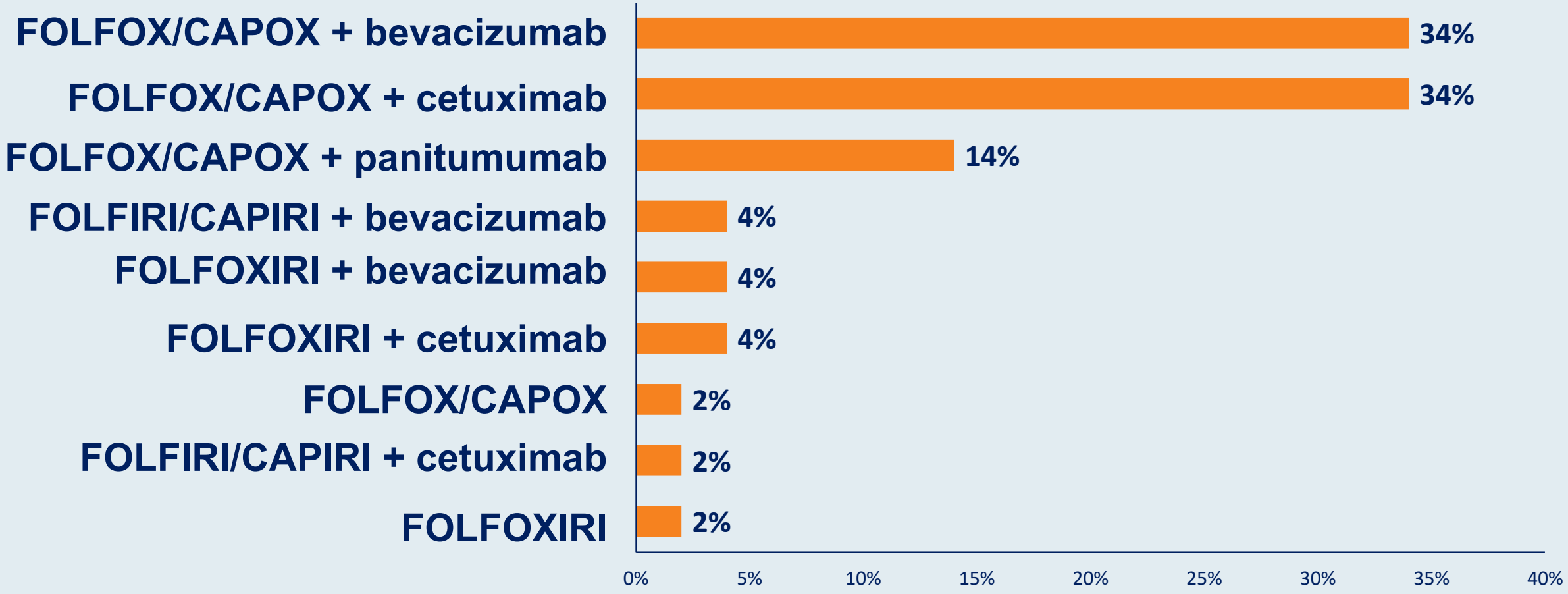
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, MSS, pan-RAS wild-type, BRAF wild-type metastatic colorectal cancer (mCRC)?



Premeeting survey: July 2021

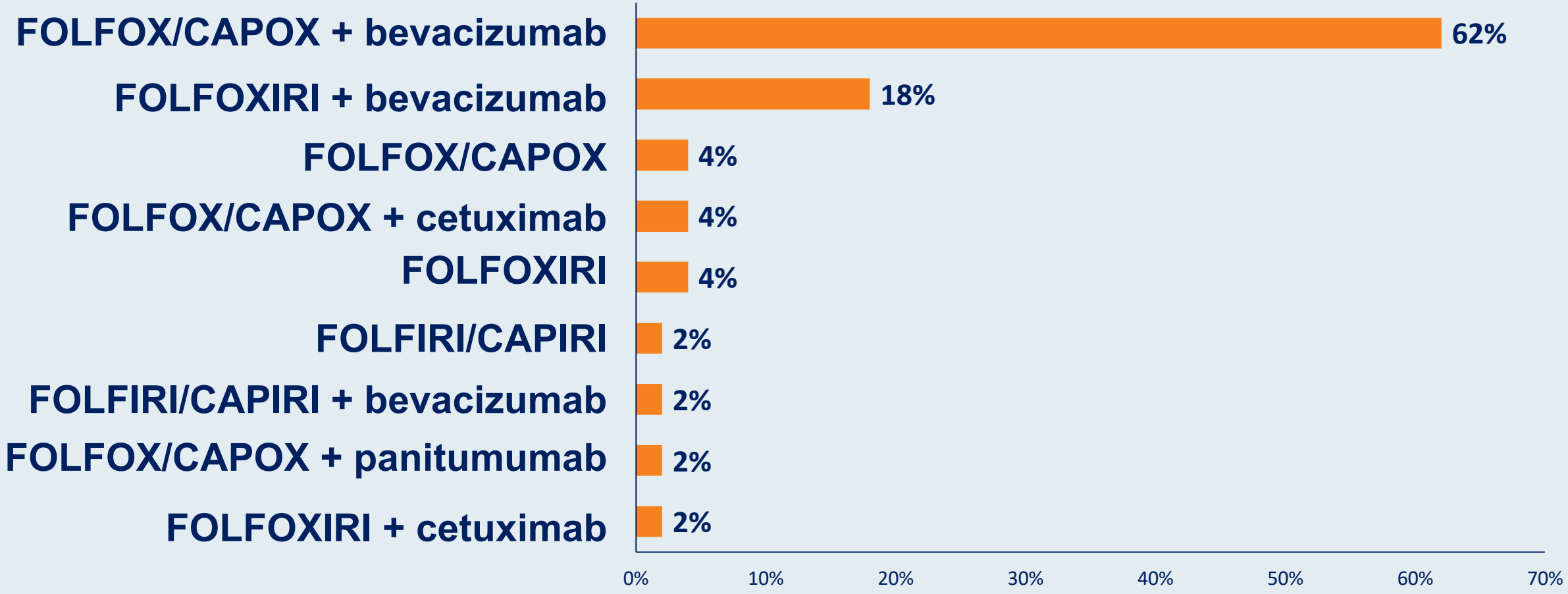
RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, MSS, pan-RAS wild-type, BRAF wild-type metastatic colorectal cancer (mCRC)?

 Dr Atreya	Nuanced decision dependent on several factors	 Dr Bekaii-Saab	FOLFIRI/CAPIRI + bevacizumab
 Dr Deming	FOLFOX/CAPOX + bevacizumab	 Dr O'Reilly	FOLFOX/CAPOX + bevacizumab
 Prof Van Cutsem	FOLFOX + cetuximab	 Dr Philip	FOLFOX/CAPOX + bevacizumab
 Dr Wainberg	FOLFOX/CAPOX + cetuximab	 Dr Reiss Binder	FOLFOX/CAPOX + bevacizumab

RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with right-sided, MSS, pan-RAS wild-type, BRAF wild-type mCRC?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with right-sided, MSS, pan-RAS wild-type, BRAF wild-type mCRC?

 Dr Atreya	Chemotherapy ± bevacizumab	 Dr Bekaii-Saab	FOLFOXIRI + bevacizumab
 Dr Deming	FOLFOX/CAPOX + bevacizumab	 Dr O'Reilly	FOLFOX/CAPOX + bevacizumab
 Prof Van Cutsem	FOLFOX + bevacizumab	 Dr Philip	FOLFOX/CAPOX + bevacizumab
 Dr Wainberg	FOLFOX/CAPOX + bevacizumab	 Dr Reiss Binder	FOLFOX/CAPOX + bevacizumab or FOLFIRI/CAPIRI + cetuximab

RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a 60-year-old patient with left-sided, MSS, pan-RAS wild-type, BRAF wild-type mCRC who is highly symptomatic and requires a response to treatment?

 Dr Atreya	Chemotherapy + panitumumab	 Dr Bekaii-Saab	FOLFOXIRI + bevacizumab
 Dr Deming	FOLFOX/CAPOX + bevacizumab	 Dr O'Reilly	FOLFOXIRI + bevacizumab
 Prof Van Cutsem	FOLFOX + cetuximab	 Dr Philip	FOLFOXIRI + bevacizumab
 Dr Wainberg	FOLFOXIRI + bevacizumab	 Dr Reiss Binder	FOLFOXIRI or FOLFOXIRI + bevacizumab

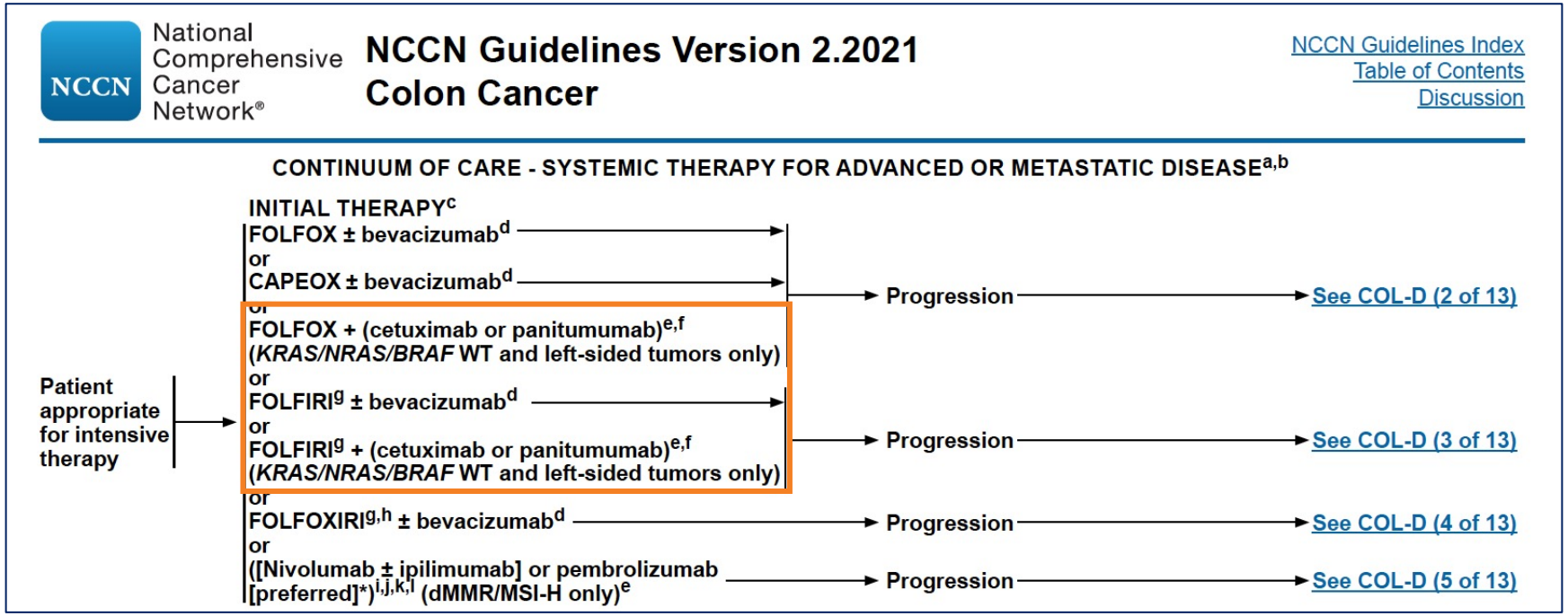
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what is the optimal 1st-line therapy for a patient with MSS, pan-RAS wild-type, BRAF wild-type mCRC, and how do tumor sidedness, patient age and symptomatology affect this decision?

	5FU/ CAP	OX	IRI	+ BEVA	or + EGFR
High volume/aggressive dx				[R]	[L]
Rt Sided tumor					X
~Age >65/ ECOG >0-1		X			
~Age >80/ ECOG 2	[No CAP]	X	X		
Symptoms/Comorbidities					
Obstructive Sx.			X	X	
Liver dysfunction			X		
Recent/future surgery				X	
Bleeding or fistula risk				X	
Clotting risk (CVA, CAD)				X	
Renal dysfunction	No CAP				
Neuropathy (DM)		X			
Preferences					
Quality of life > quantity		X			
Most aggressive tx				[R]	[L]
No 5FU pump	CAP		X (no CAPIRI)		
No neuropathy (eg. artist)		X			
No hair loss			X		
No rash					X

Courtesy of Chloe E Atreya, MD, PhD

Correlation between location of the primary tumor and outcomes with specific systemic therapies



Right-sided mCRC:
-Worse prognosis
-Impaired response to EGFR-targeted therapies (FIRE3, CALGB 80405…)

Courtesy of Chloe E Atreya, MD, PhD

UCSF

What is the optimal first-line treatment for MSI-high mCRC?

Dr Tanios Bekaii-Saab

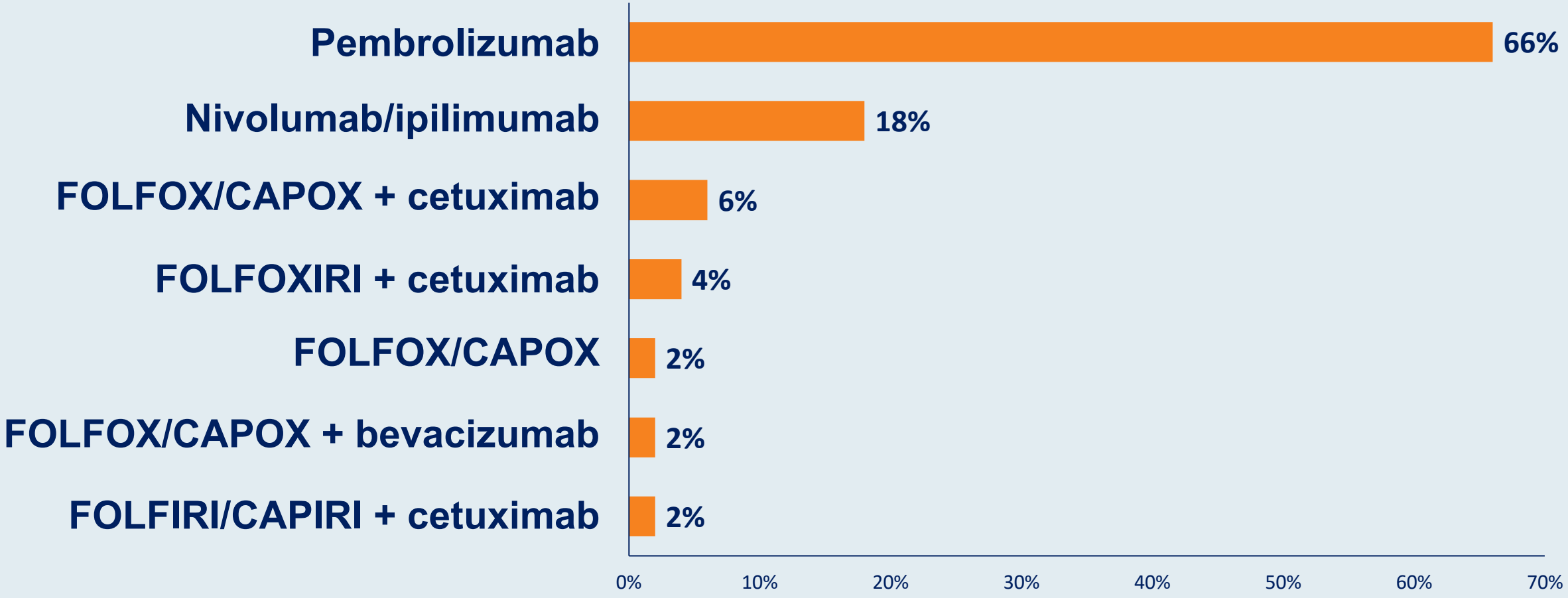
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP
RESEARCH
TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, pan-RAS wild-type, BRAF wild-type, MSI (microsatellite instability)-high mCRC?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

What is your usual first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, pan-RAS wild-type, BRAF wild-type, MSI-high mCRC?

 Dr Atreya	Pembrolizumab	 Dr Bekaii-Saab	Pembrolizumab
 Dr Deming	Nivolumab/ipilimumab	 Dr O'Reilly	Pembrolizumab
 Prof Van Cutsem	Pembrolizumab	 Dr Philip	Pembrolizumab
 Dr Wainberg	Pembrolizumab	 Dr Reiss Binder	Pembrolizumab or Nivolumab/ipilimumab

RTP RESEARCH TO PRACTICE

For an asymptomatic patient with MSI-high mCRC who is experiencing slow disease progression on anti-PD-1 therapy alone, would you consider switching to the combination of nivolumab and ipilimumab?

 Dr Atreya	Yes	 Dr Bekaii-Saab	Yes
 Dr Deming	Yes	 Dr O'Reilly	Yes
 Prof Van Cutsem	Yes	 Dr Philip	Yes
 Dr Wainberg	No	 Dr Reiss Binder	Yes

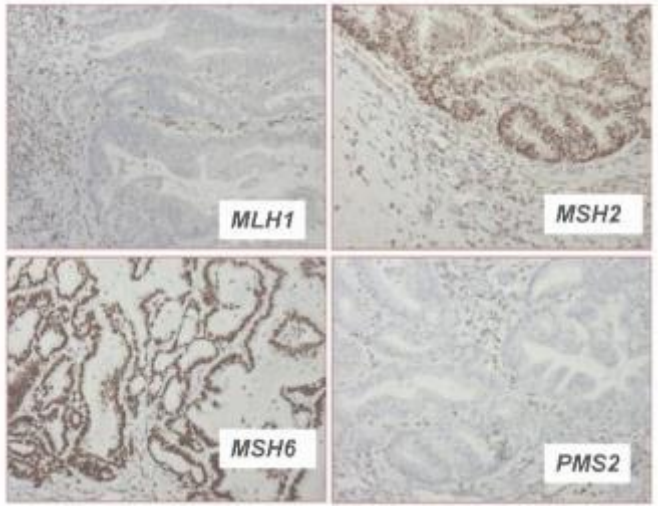
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what is the optimal first-line therapy for a patient with MSI-high mCRC, and how, if at all, do patient age and symptomatology affect this decision?

- Pembrolizumab is the standard of care therapy given KEYNOTE-177 showing an improvement over chemotherapy.
- The combination of nivolumab and ipilimumab has shown the greatest response rate and progression free survival, however, this was not a direct comparison to anti-PD-1 therapy alone (CheckMate 142).
- Benefit has been seen for immunotherapy in all subgroups explored in KEYNOTE-177 and CheckMate 142.
- Prefer nivolumab and ipilimumab except for those that are older or less fit to using pembrolizumab.
- Eagerly await data of chemotherapy in combination with immunotherapy in this setting.

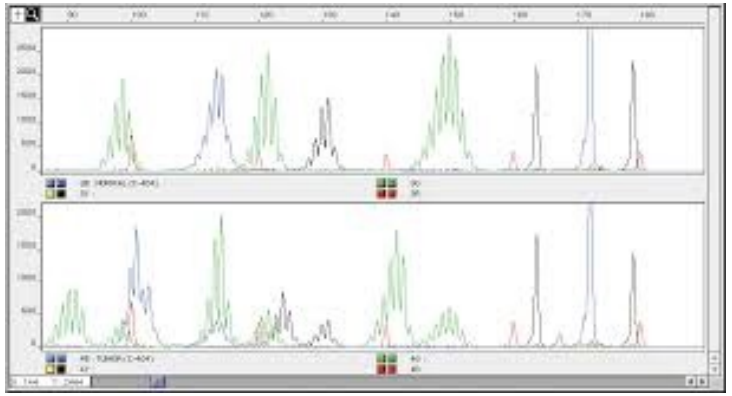
MMR/MSI Testing

MMR IHC



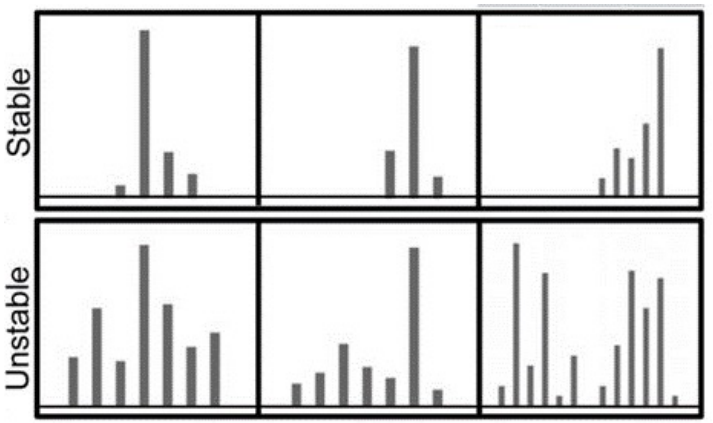
- **Easily done at most centers**
- **Detects most common changes**
- **Altered proteins can still be detected as present**

PCR Microsatellite



- **Functional assay**
- **Very well validated**
- **Does not identify specific alteration**
- **Is a stand alone test**

Next Gen Sequencing



- **Increasingly more common**
- **Detects mutations and MSI status**
- **Validation of assays not as robust**

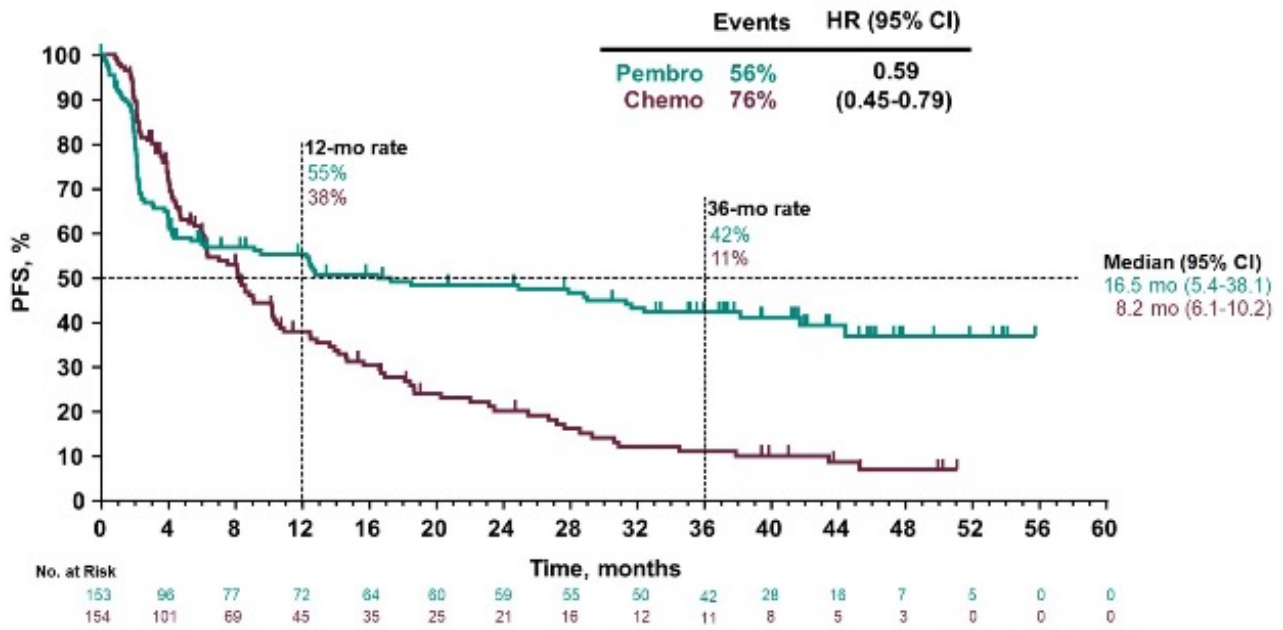
Courtesy of Dustin Deming, MD

Phase 3 KEYNOTE-177

Antitumor Response

	Pembrolizumab N = 153	Chemotherapy N = 154
ORR, n (%)	**69 (45.1)[a]**	**51 (33.1)**
Best Overall Response, n (%)		
Complete response	20 (13.1)[b]	6 (3.9)
Partial response	49 (32.0)[c]	45 (29.2)
Stable disease	30 (19.6)	65 (42.2)
Disease control rate (CR+PR+SD)	99 (64.7)	116 (75.3)
Progressive disease	45 (29.4)	19 (12.3)
Not evaluable	3 (2.0)	2 (1.3)
No assessment	6 (3.9)	17 (11.0)
Median duration or response (range), mo	NR (2.3+ to 53.5+)	10.6 (2.8 to 48.3+)
≥ 24 months response duration, %	83.5	33.6

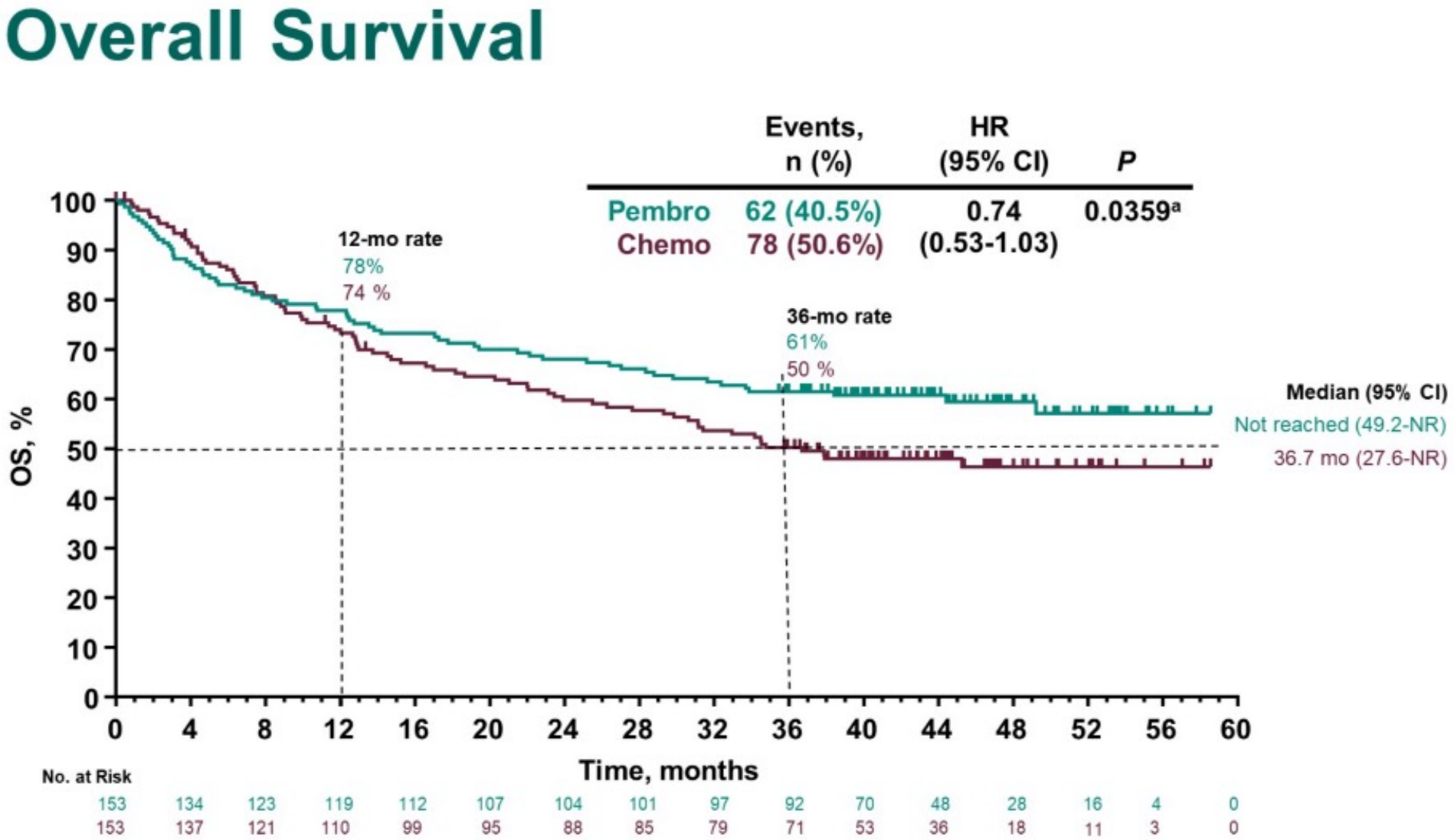
Progression-Free Survival



Courtesy of Dustin Deming, MD

(Andre, et al., ASCO Annual Meeting 2021)

Phase 3 KEYNOTE-177



Courtesy of Dustin Deming, MD

(Andre, et al., ASCO Annual Meeting 2021)

CheckMate 142: First-line treatment with nivolumab and low-dose ipilimumab for MSI-H/dMMR metastatic CRC

- CheckMate 142 is an ongoing, multicohort, nonrandomized phase 2 trial evaluating the efficacy and safety of NIVO-based therapies in patients with mCRC[a]

- Histologically confirmed metastatic or recurrent CRC
- MSI-H/dMMR per local laboratory
- No prior treatment for metastatic disease

→ NIVO3 Q2W + IPI1 Q6W[b]

Primary endpoint:

- ORR per investigator assessment (RECIST v1.1)

Other key endpoints:

- ORR per BICR, DCR,[c] DOR, PFS, OS, and safety

- At data cutoff (October 2019), the median duration of follow-up was 29.0 months (range, 24.2-33.7)[d]

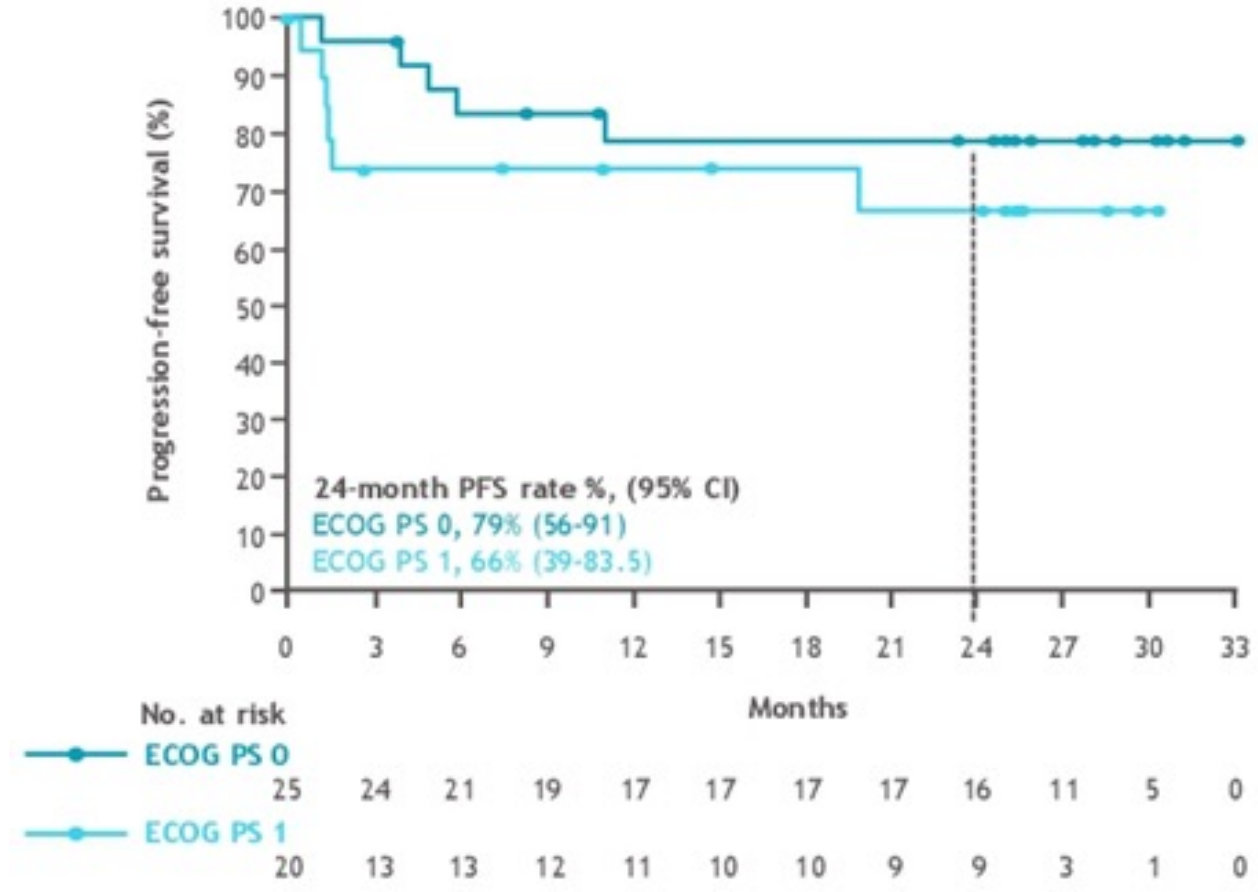
Courtesy of Dustin Deming, MD

(Lenz, et al., Gastrointestinal Cancer Symposium, 2020)

CheckMate 142

N=45	
Overall ORR	69%
Median PFS	Not reached after 29 months median follow-up
24-month PFS rate	74%
24-month Overall Survival rate	79%

Progression Free Survival by ECOG PS



Courtesy of Dustin Deming, MD

(Lenz, et al., Gastrointestinal Cancer Symposium, 2020)

What is the optimal targeted treatment for BRAF-mutated mCRC, and in which line of therapy should it be used?

Dr Tanios Bekaii-Saab

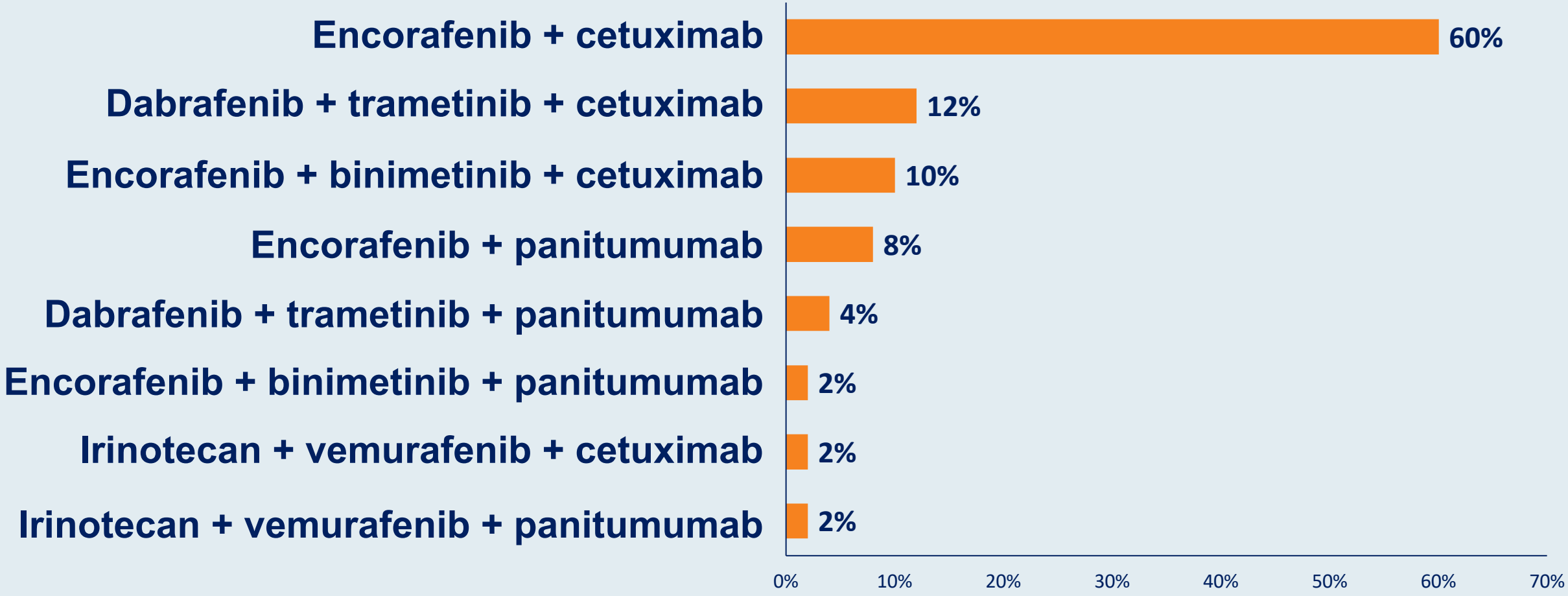
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP
RESEARCH
TO PRACTICE

For a patient with mCRC with a BRAF V600E mutation to whom you would administer BRAF-targeted therapy, what would be your preferred treatment?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

For a patient with mCRC with a BRAF V600E mutation to whom you would administer BRAF-targeted therapy, what would be your preferred treatment?

 Dr Atreya	Encorafenib + panitumumab or cetuximab	 Dr Bekaii-Saab	Encorafenib + panitumumab
 Dr Deming	Encorafenib + panitumumab	 Dr O'Reilly	Encorafenib + cetuximab
 Prof Van Cutsem	Encorafenib + cetuximab	 Dr Philip	Encorafenib + panitumumab
 Dr Wainberg	Encorafenib + cetuximab	 Dr Reiss Binder	Encorafenib + cetuximab

RTP RESEARCH TO PRACTICE

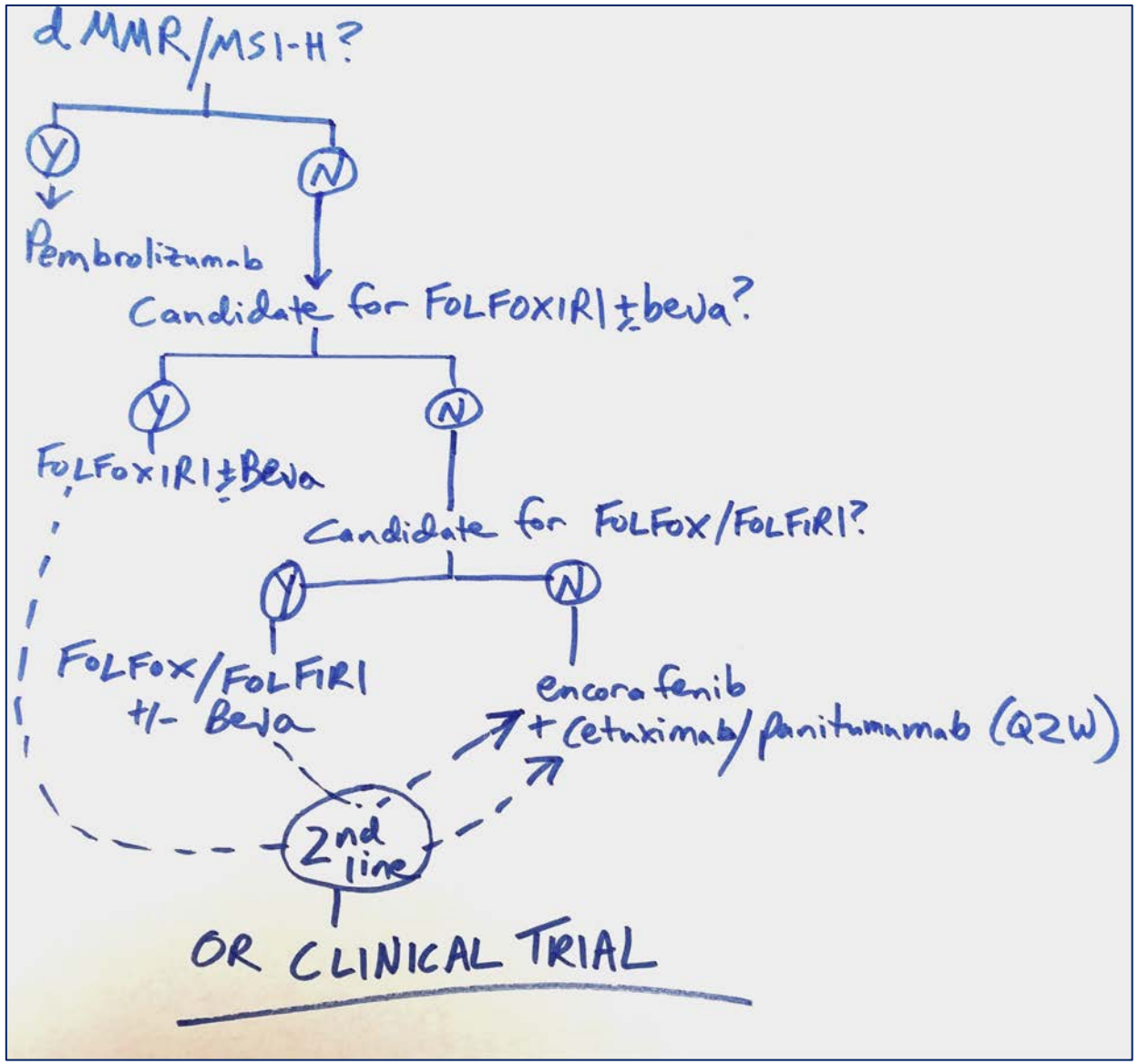
Have you administered or would you administer a BRAF inhibitor in combination with an EGFR antibody as first-line therapy to a patient with mCRC with a BRAF V600E mutation who could not tolerate or did not wish to receive chemotherapy?

 Dr Atreya	I have not but would for the right patient	 Dr Bekaii-Saab	I have not but would for the right patient
 Dr Deming	I have	 Dr O'Reilly	I have not but would for the right patient
 Prof Van Cutsem	I have not but would for the right patient	 Dr Philip	I have not but would for the right patient
 Dr Wainberg	I have not but would for the right patient	 Dr Reiss Binder	I have not but would for the right patient

RTP RESEARCH TO PRACTICE

Chalk Talk - Chloe Atreya, MD, PhD.

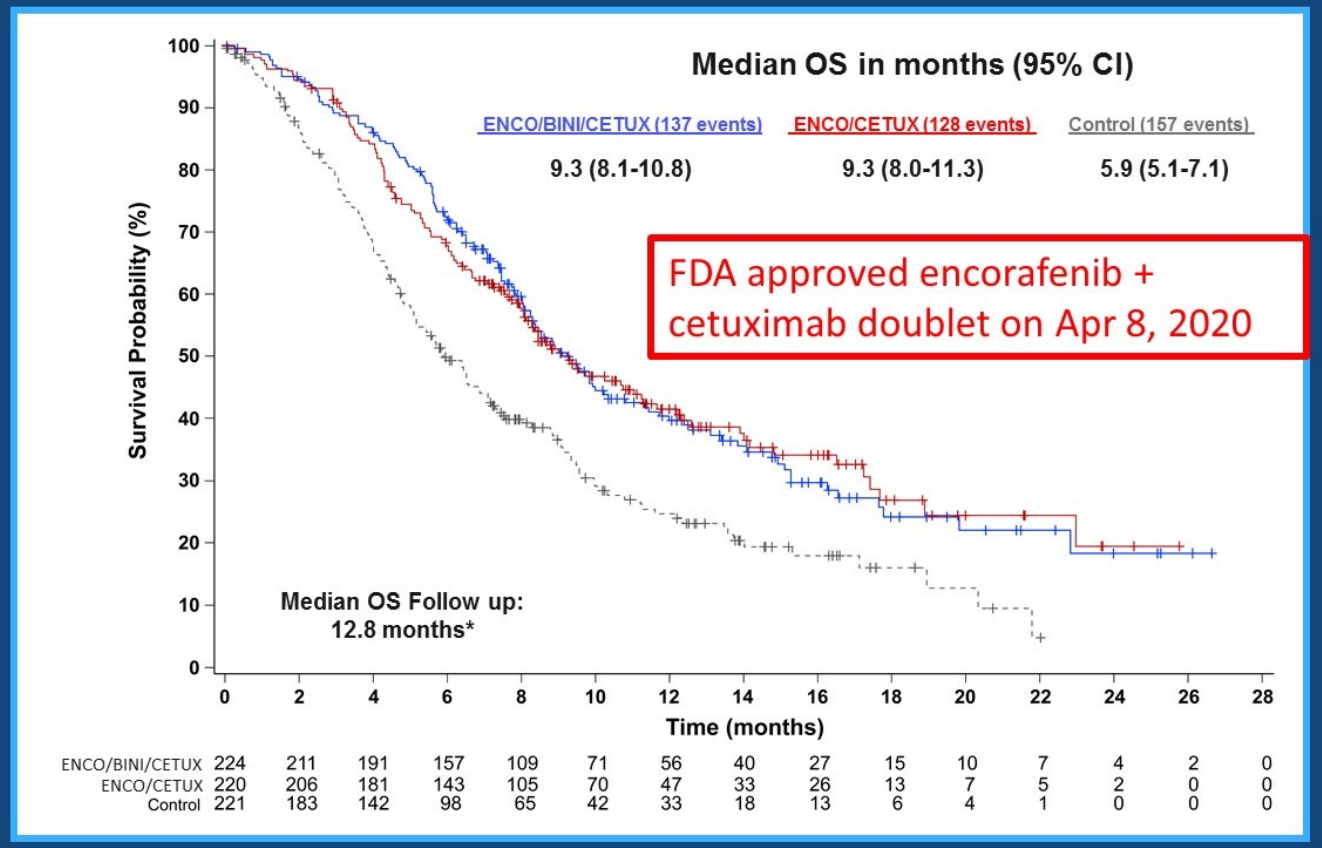
Regulatory and reimbursement issues aside, for a patient with pan-RAS wild-type mCRC with a BRAF V600E mutation, in what line of treatment would you generally administer BRAF-targeted therapy, and which specific regimen would you choose? Would you offer BRAF-targeted therapy as a front-line option to any of your patients with mCRC?



Courtesy of Chloe E Atreya, MD, PhD

BRAF(V600E) mCRC: the BEACON CRC Trial

Updated Overall Survival: ENCO/BINI/CETUX vs ENCO/CETUX vs Control



Courtesy of Chloe E Atreya, MD, PhD

UCSF

BRAF(V600E) mCRC: context

	N	Objective response rate	Median PFS	Median OS
Vemurafenib + Cetuximab + Irinotecan (Ph IB)	17	35% (14-62)	7.7 mo (3.1-NE)	
Vemurafenib + Cetuximab + Irinotecan (Ph II S1406)	49	16%	4.3 mo (3.6-5.7)	9.6 mo (7.5-13.1)
Dabrafenib + Trametinib	43	12%	3.5 mo (3.4-4.0)	
Dabrafenib + Trametinib + Panitumumab	91	21% (13.1-30.7)	4.2 mo (4.0-5.6)	9.1 mo (7.6-20.0)
Dabrafenib + Panitumumab	20	10% (1.2-31.7)	3.5 mo (2.8-5.8)	13.2 mo (6.7-22.0)
Trametinib + Panitumumab	31	0% (0-11.2)	2.6 mo (1.4-2.8)	8.2 mo (6.5-9.4)
Encorafenib + Binimetinib + Cetuximab (BEACON safety lead-in)	30	41% (24-61)	5.5 mo (4.2-9.3)	15.3 mo (9.6-NE)
Encorafenib + Binimetinib + Cetuximab (BEACON update)	**224**	**27% (21-33)**	**4.5 mo (4.2-5.5)**	**9.3 mo (8.2-10.8)**
Encorafenib + Cetuximab (BEACON update)	**220**	**20% (15-25)**	**4.3 mo (4.1-5.5)**	**9.3 mo (8.0-11.3)**

Hong DS, Cancer Discov 2016; Kopetz S, ASCO 2017; Corcoran RB, J Clin Oncol 2015; Corcoran RB, Cancer Discov 2018; Van Cutsem E, J Clin Oncol 2019; Kopetz S, ASCO 2020

Courtesy of Chloe E Atreya, MD, PhD

How do you generally sequence BRAF-targeted therapy and immunotherapy for a patient with BRAF-mutated, MSI-high mCRC?

 Dr Atreya	Immunotherapy → BRAF-targeted therapy
 Dr Bekaii-Saab	Immunotherapy → BRAF-targeted therapy
 Dr Deming	Immunotherapy → BRAF-targeted therapy
 Dr O'Reilly	Immunotherapy → BRAF-targeted therapy
 Prof Van Cutsem	Immunotherapy → BRAF-targeted therapy
 Dr Philip	Immunotherapy → BRAF-targeted therapy
 Dr Wainberg	Immunotherapy → BRAF-targeted therapy
 Dr Reiss Binder	Immunotherapy → BRAF-targeted therapy

RTP RESEARCH TO PRACTICE

How should BRAF-targeted therapy and immunotherapy generally be sequenced for patients with BRAF-mutant, MSI-high mCRC?

- *BRAF V600* mutations significantly predict a worse prognosis for patients with mCRC, though this is improved in the setting of dMMR.
- *BRAF* mutations do not predict for lack of response to immunotherapy across studies.
- Sequencing of therapies for patients with BRAF V600 mutant mCRC has not been well studied.
- Immunotherapy approaches are generally recommended first given the chance of durable benefit.

	Pembrolizumab	Ipi/Nivo	Chemotherapy	Encorafenib/Binimetinib/Cetuximab
ORR (%)	45*	76	33-50	50*
Median PFS (months)	16*	Not reached 24-mo PFS: 76%	5-8	4.9*

What is your preferred sequencing of EGFR TKIs, TAS-102 (+/- bevacizumab) and regorafenib?

Dr Tanios Bekaii-Saab

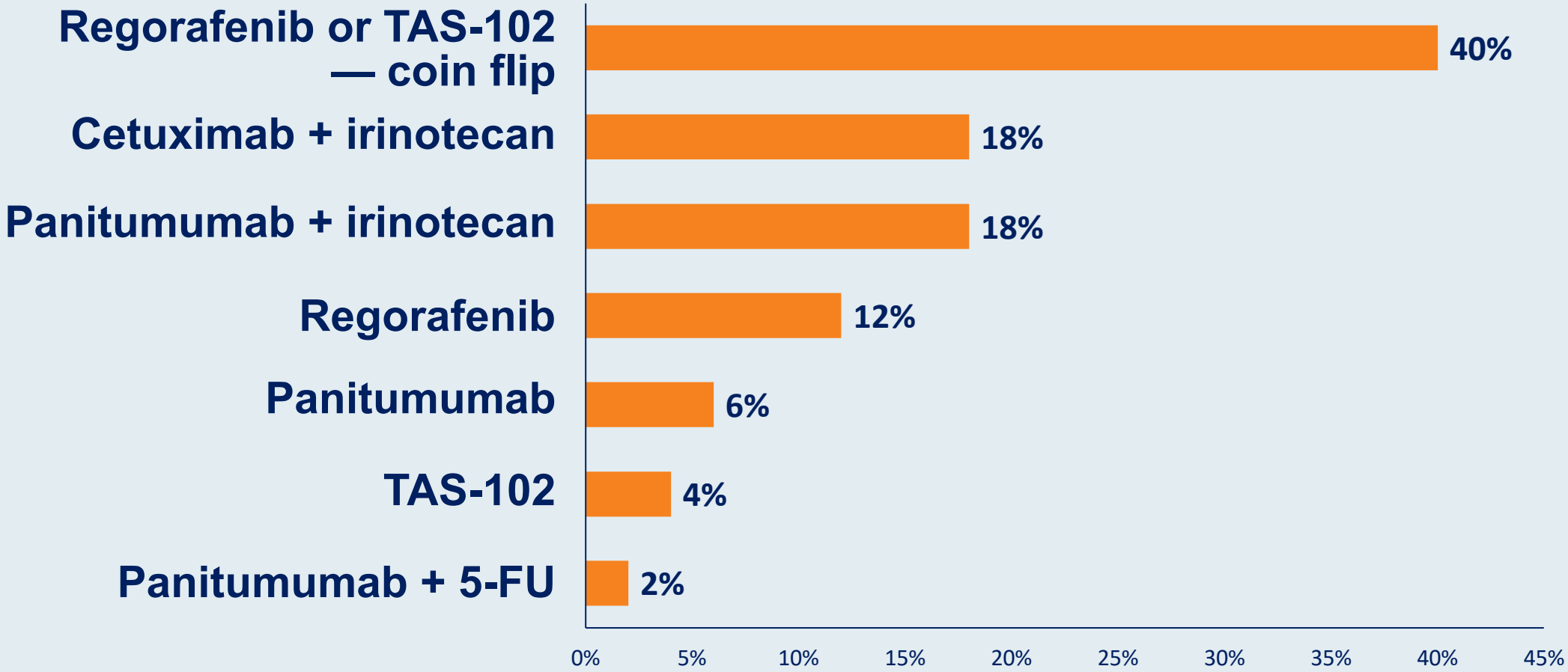
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP RESEARCH TO PRACTICE

A 65-year-old patient with right-sided, MSS, pan-RAS wild-type mCRC receives first-line FOLFOX/bevacizumab and second-line FOLFIRI/bevacizumab and is now experiencing disease progression with a PS of 0. What would be your most likely third-line treatment recommendation?



Premeeting survey: July 2021

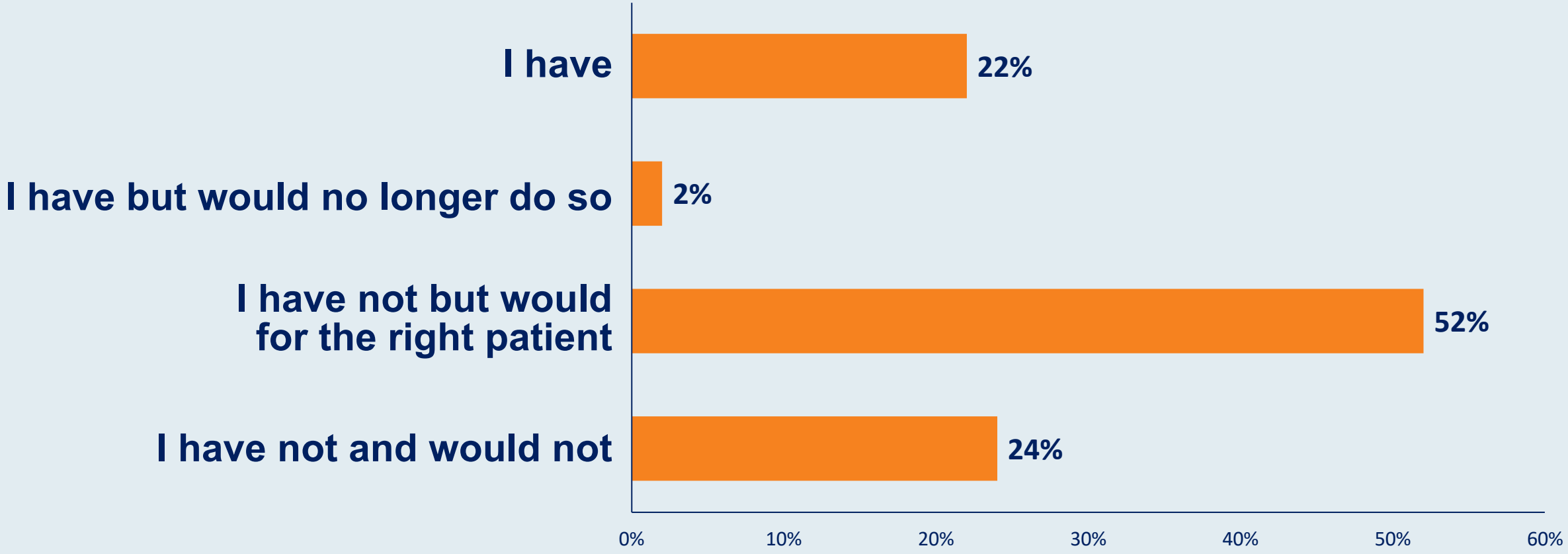
RTP RESEARCH TO PRACTICE

A 65-year-old patient with right-sided, MSS, pan-RAS wild-type mCRC receives first-line FOLFOX/bevacizumab and second-line FOLFIRI/bevacizumab and is now experiencing disease progression with a PS of 0. What would be your most likely third-line treatment recommendation?

 Dr Atreya	TAS-102 + bevacizumab	 Dr Bekaii-Saab	Regorafenib
 Dr Deming	Panitumumab + irinotecan	 Dr O'Reilly	Panitumumab + irinotecan
 Prof Van Cutsem	Cetuximab + irinotecan	 Dr Philip	TAS-102
 Dr Wainberg	Cetuximab or Panitumumab	 Dr Reiss Binder	Cetuximab + irinotecan

RTP RESEARCH TO PRACTICE

Have you used or would you use TAS-102 in combination with bevacizumab outside of a clinical trial setting for a patient with mCRC?



Premeeting survey: July 2021

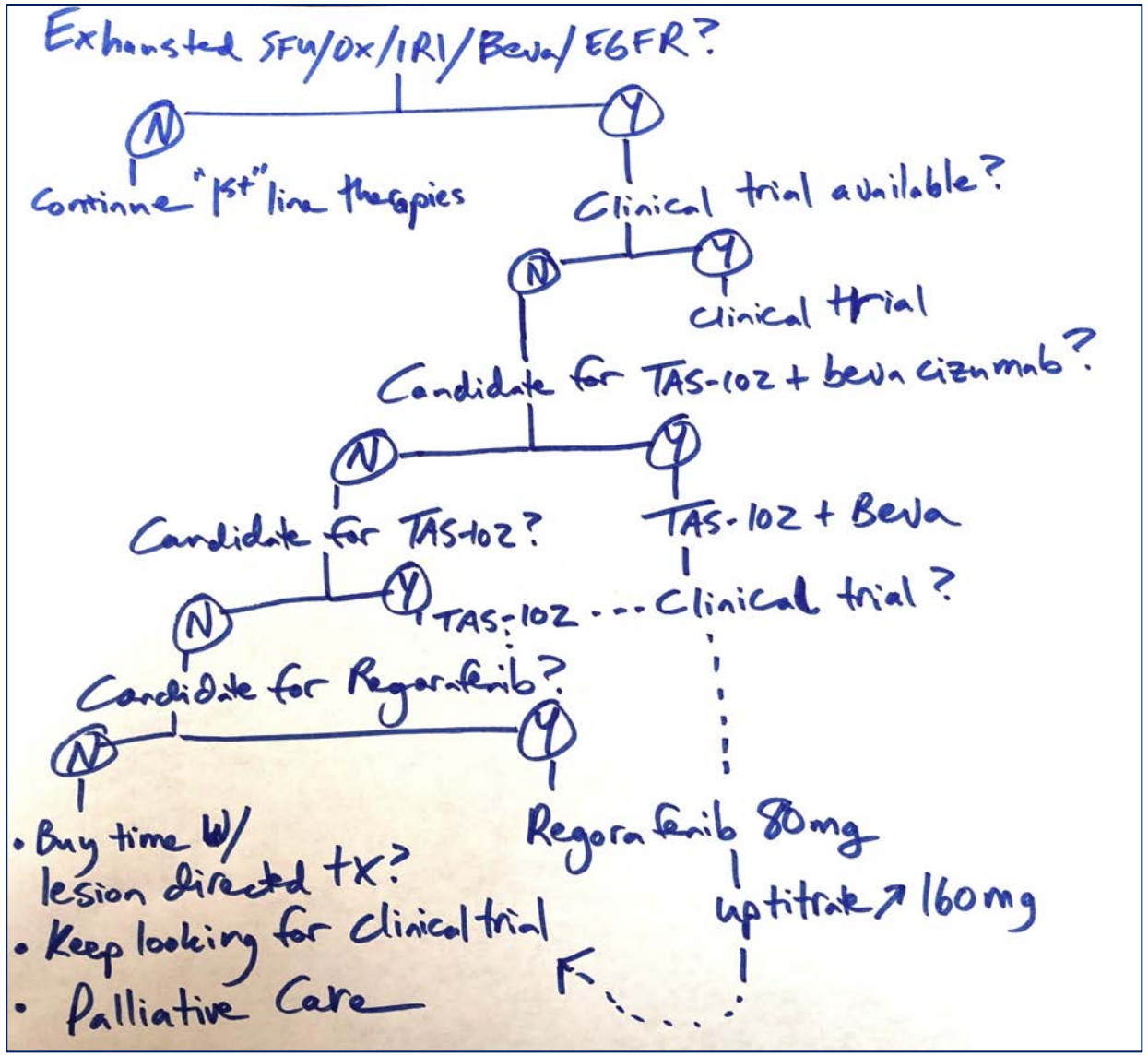
RTP RESEARCH TO PRACTICE

Have you used or would you use TAS-102 in combination with bevacizumab outside of a clinical trial setting for a patient with mCRC?

 Dr Atreya	I have	 Dr Bekaii-Saab	I have but would no longer do so
 Dr Deming	I have	 Dr O'Reilly	I have not but would for the right patient
 Prof Van Cutsem	I have	 Dr Philip	I have
 Dr Wainberg	I have	 Dr Reiss Binder	I have

RTP RESEARCH TO PRACTICE

How do you generally sequence regorafenib and TAS-102 for your patients with relapsed/refractory mCRC? What clinical, biologic and/or practical factors would influence you to offer a patient with mCRC regorafenib before TAS-102 or vice versa?



TOXICITIES

TAS-102: mainly cytopenias

Regorafenib

- all VEGF toxicities
- Black box warning: hepatotoxicity
- Dermatologic: QoL impact

Courtesy of Chloe E Atreya, MD, PhD

Regorafenib and TAS-102

- Efficacy similar: OS improvement ~2 mos, low RR
  Regorafenib – CORRECT & CONCUR
  TAS-102 – RECOURSE & TERRA

- Distinct toxicities:
  - TAS-102: **cytopenias (**neutropenia) [diarrhea, fatigue]
  - Regorafenib: hand-foot **skin toxicity**, rash, loss of appetite, fatigue, risk of bleeding, black box warning for liver failure.

- *Patient preference matters.*

- If regorafenib used, start at 50% dose (ReDOSE).

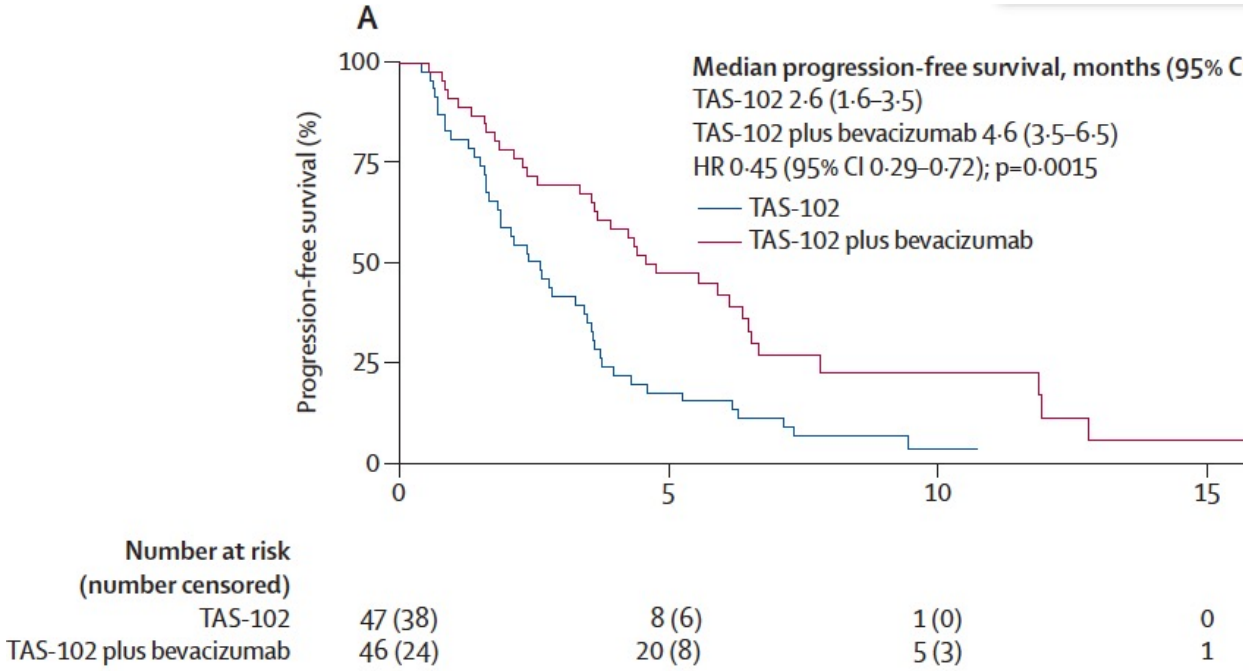
Courtesy of Chloe E Atreya, MD, PhD

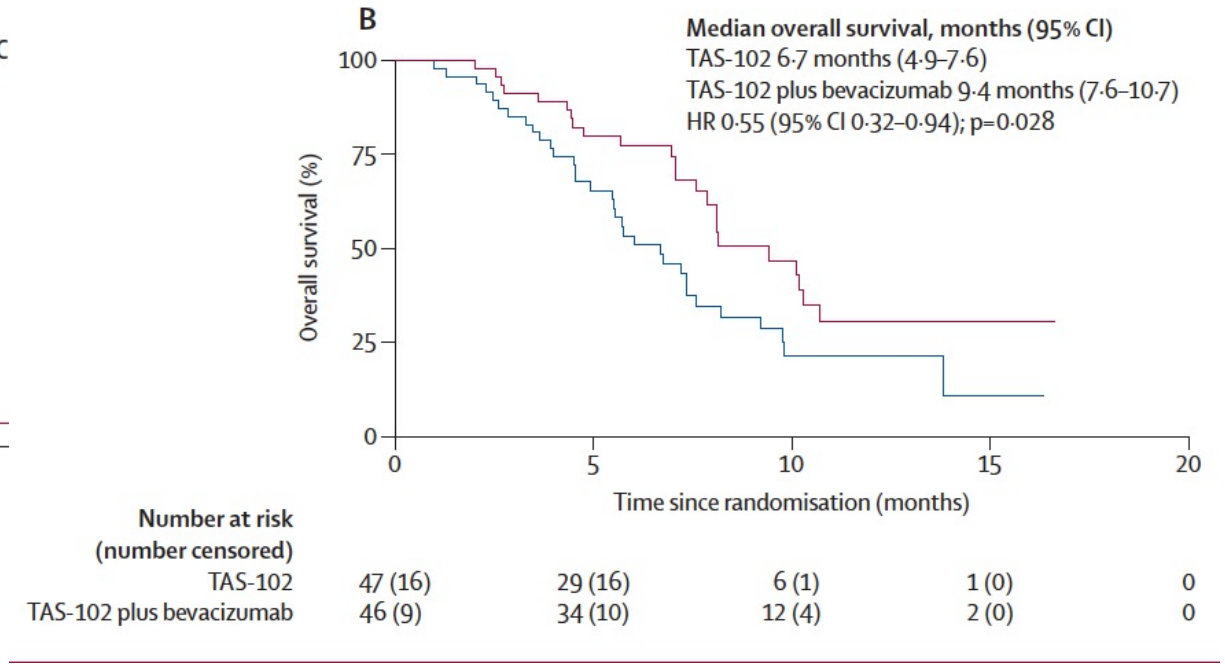
UCSF

More on TAS-102: C-TASK FORCE Trial

In pts with refractory and regorafenib-untreated advanced CRC

- RCT: TAS-102 +/- beva (Pfeiffer et al., *Lancet Oncology 2020*)





TAS-102 + beva in 2.2021 NCCN Guidelines

Courtesy of Chloe E Atreya, MD, PhD

UCSF

More on TAS-102: TRUSTY study

Abstract 3507, Dr. Kuboki
Phase 2/3 TAS-102 +beva vs. FOLFIRI +beva as 2nd Line

Non-inferiority

Prior to randomization, either 5-FU or S-1 was declared by each investigator when allocated FP+IRI+BEV.

mCRC in 2nd-line

- Progression on 1st-line treatment
  - Fluoropyrimidine (5-FU/*l*-LV, Capecitabine, S-1)
  - Oxaliplatin
  - BEV or anti-EGFR antibody
- ECOG PS: 0 or 1
- Age: 20 years or older

R 1:1

n=524

Fluoropyrimidine+Irinotecan+BEV
(FP+IRI+BEV)

FOLFIRI + BEV (*q2w*), **S-1 + irinotecan + BEV** (*q3w, q4w*) selected on an individual patient basis

FTD/TPI+BEV

BEV: 5 mg/kg IV d1, d15
FTD/TPI : 35 mg/m^2 bid orally d1-5 and d8-12 *q4w*

Primary endpoint
- Overall survival (OS)

Secondary endpoints
- Progression-free survival (PFS)
- Time to treatment failure (TTF)*
- Response rate (RR)
- Disease control rate (DCR)
- Subsequent treatment
- Time to post-study treatment failure (TTF2)
- Quality of life (QOL)*
- Adverse events (AE)

*not included in this presentation.

Stratification factors
- *RAS* status (Wild-type vs. Mutant)
- Primary tumor location (Left-sided vs. Right-sided)
- 1st-line treatment with molecularly targeted drug (BEV vs. Anti-EGFR antibody†)

†*RAS* Wild-type only

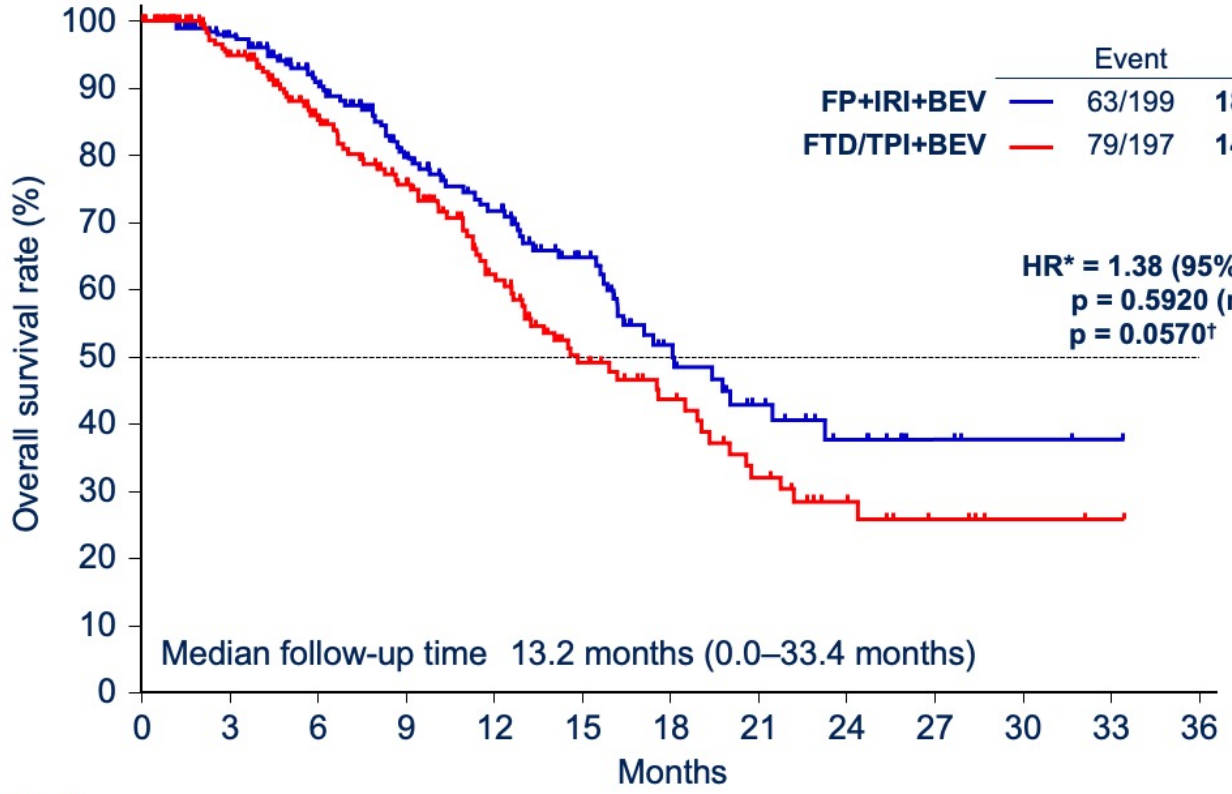
Courtesy of Chloe E Atreya, MD, PhD

UCSF

More on TAS-102: TRUSTY study

Primary endpoint

Overall survival



	Event	Median	95% CI
FP+IRI+BEV	63/199	18.1 months	16.0–23.2
FTD/TPI+BEV	79/197	14.8 months	12.6–19.1

HR* = 1.38 (95% CI: 0.99–1.93)
p = 0.5920 (non-inferiority)
p = 0.0570†

Number at risk

FP+IRI+BEV	199	167	134	98	78	54	32	20	12	4	2	1	-
FTD/TPI+BEV	197	163	122	98	66	44	28	19	12	5	2	1	-

TAS-102 +beva Inferior to FOLFIRI +beva as 2nd line therapy

Courtesy of Chloe E Atreya, MD, PhD

UCSF

What is your preferred sequencing of therapies for HER2-positive mCRC, including T-DXd?

Dr Tanios Bekaii-Saab

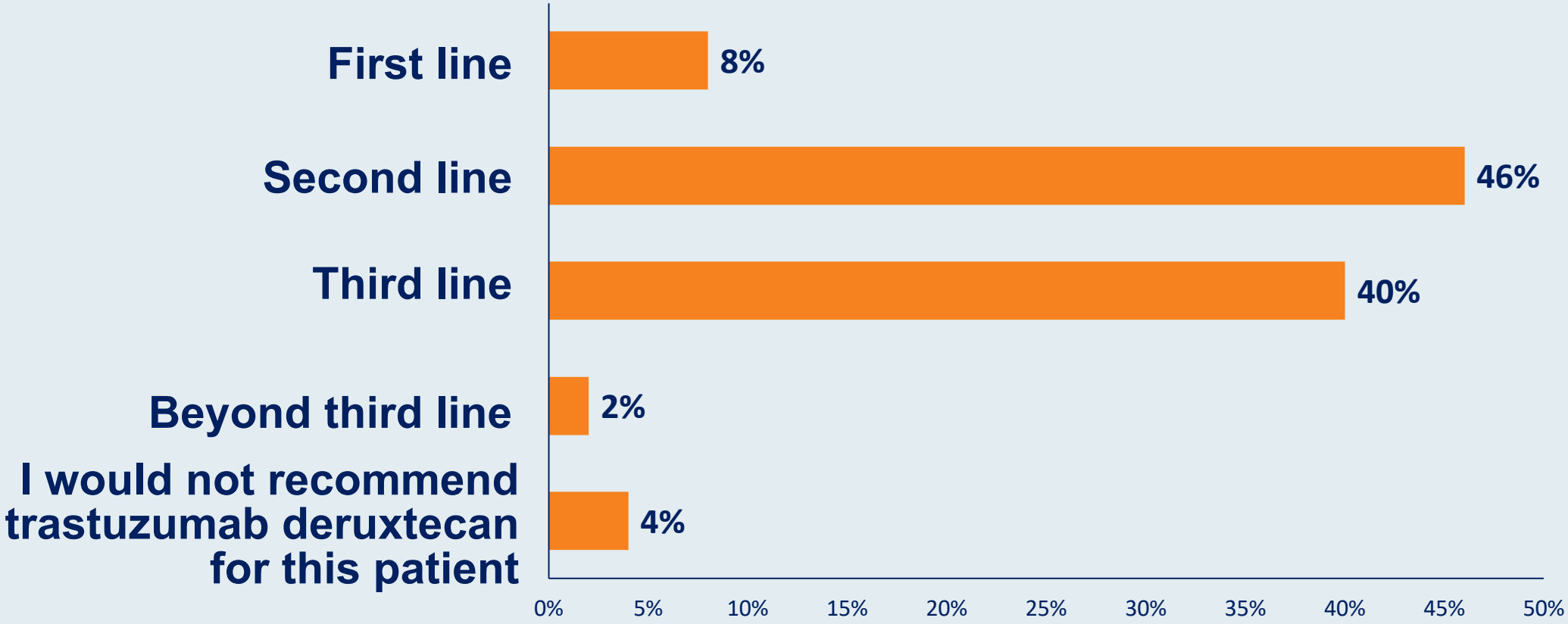
Dr Eileen O'Reilly

Dr Philip Philip

Dr Kim Reiss Binder

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend trastuzumab deruxtecan for a 65-year-old patient with HER2-positive mCRC?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally recommend trastuzumab deruxtecan for a 65-year-old patient with HER2-positive mCRC?

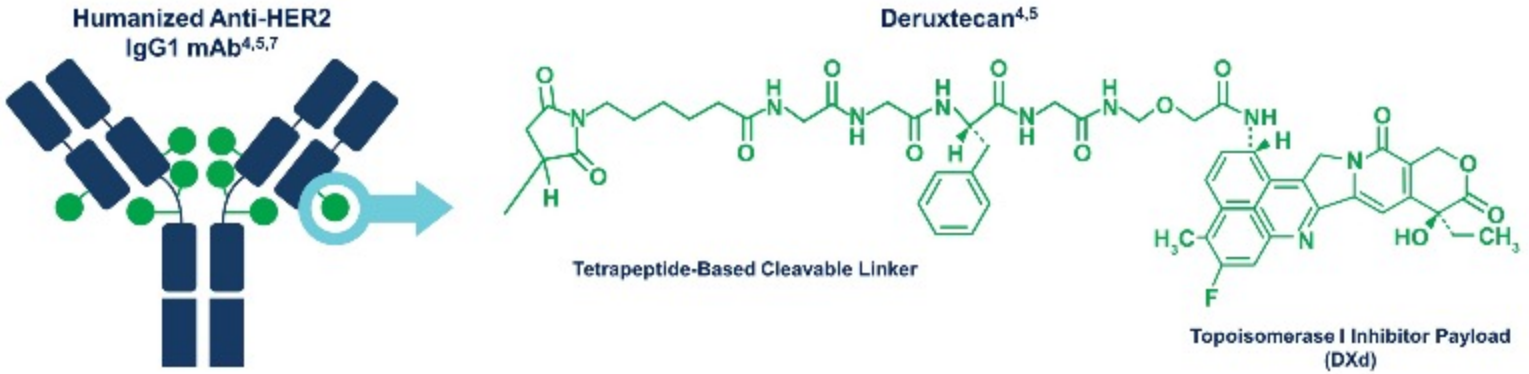
 Dr Atreya	Third line	 Dr Bekaii-Saab	Third line
 Dr Deming	Beyond third line	 Dr O'Reilly	Third line
 Prof Van Cutsem	Third line	 Dr Philip	Third line
 Dr Wainberg	Third line	 Dr Reiss Binder	Third line

RTP RESEARCH TO PRACTICE

At the current time, should patients with HER2-positive mCRC receive trastuzumab deruxtecan at some point in their treatment course? If so, when is the optimal time to do so?

- HER2-positive mCRC is a relatively new important subtype of mCRC that deserves specific considerations.
- This subtype typically does well with standard FOLFOX or FOLFIRI.
- In the refractory setting, the use of trastuzumab/pertuzumab has become a standard of care.
- The DESTINY-CRC01 trial demonstrated exciting activity for trastuzumab deruxtecan, even in the setting of resistance to prior HER2 targeting.
- This therapy should be considered after progression on trastuzumab/pertuzumab.
- Care needs to be taken when monitoring for toxicities, especially ILD.

DESTINY-CRC01: Trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer



Patients
- Unresectable and/or metastatic CRC
- HER2 expressing (central confirmation)
- *RAS/BRAF*^{V600E} wild type
- ≥2 prior regimens
- Prior anti-HER2 treatment was allowed
- Excluded patients with a history of or current/suspected interstitial lung disease

6.4 mg/kg dose of T-DXd administered Q3W (all cohorts)

Cohort A: HER2 Positive (IHC3+ or IHC2+/ISH+) n = 53

Cohort B[a]: HER2 IHC2+/ISH− n = 15

Cohort C[a]: HER2 IHC1+ n = 18

Primary endpoint
- ORR[b] (cohort A)

Secondary endpoints
- ORR[b] (cohorts B and C)
- PFS
- OS
- DOR
- DCR
- Safety and tolerability

Primary analysis (Data cutoff: August 9, 2019)

Final analysis (Data base lock: December 28, 2020)

Courtesy of Dustin Deming, MD

(Yoshino, et al., ASCO, 2021)

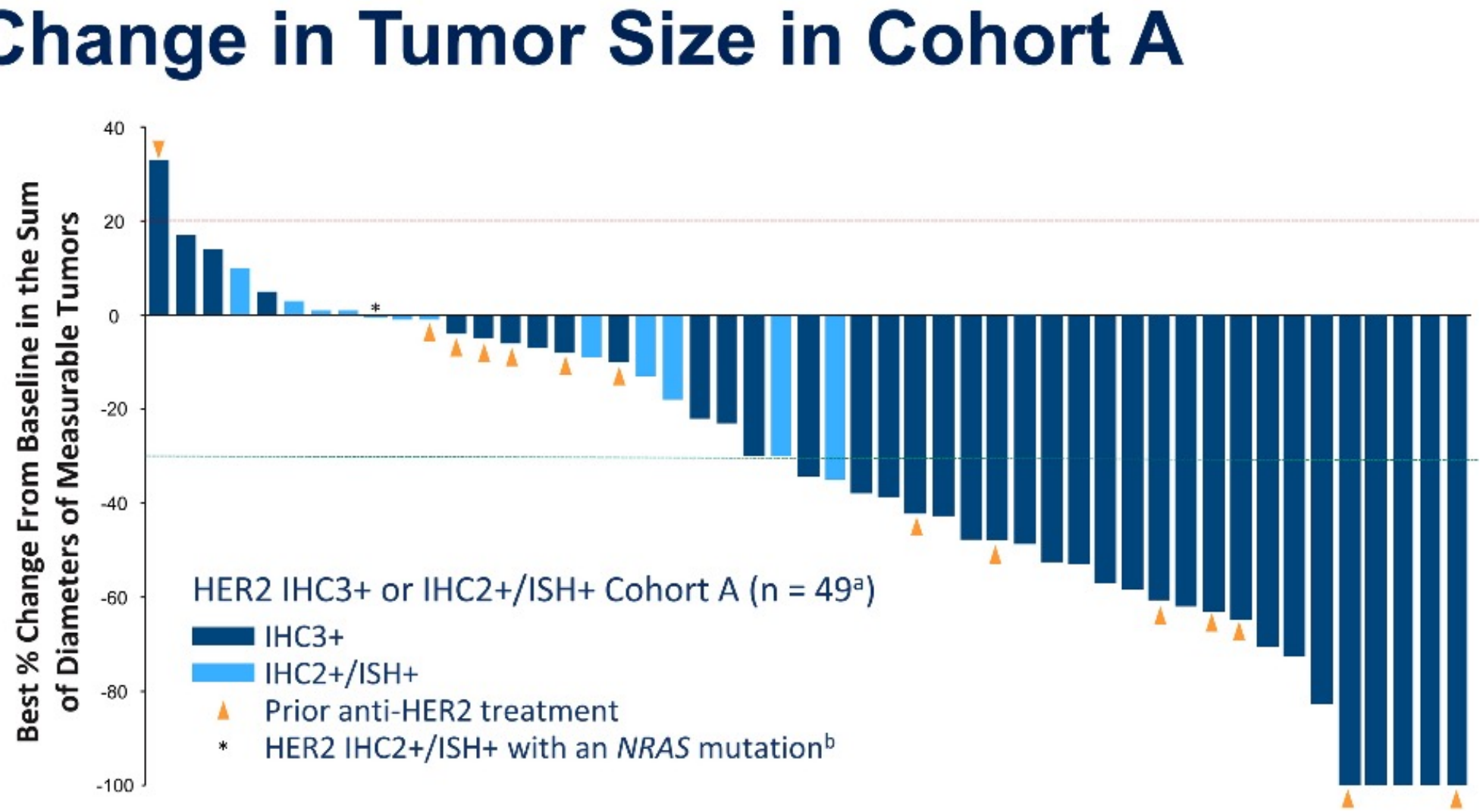
DESTINY-CRC01

	HER2 IHC3+ or IHC2+/ISH+ Cohort A (n = 53)	HER2 IHC2+/ISH– Cohort B (n = 15)	HER2 IHC1+ Cohort C (n = 18)
Confirmed ORR by ICR, n (%) [95% CI]	**24 (45.3)** [31.6-59.6]	0 [0.0-21.8]	0 [0.0-18.5]
CR	0	0	0
PR	24 (45.3)	0	0
SD	20 (37.7)	9 (60.0)	4 (22.2)
PD	5 (9.4)	5 (33.3)	10 (55.6)
Not evaluable[a]	4 (7.5)	1 (6.7)	4 (22.2)
Disease control rate, % (95% CI)	83.0 (70.2-91.9)	60.0 (32.3-83.7)	22.2 (6.4-47.6)
Median duration of response, (95% CI) months	7.0 (5.8-9.5)	NE (NE-NE)	NE (NE-NE)
Median treatment duration, (95% CI) months	5.1 (3.9-7.6)	2.1 (1.4-2.6)	1.4 (1.3-1.5)

Courtesy of Dustin Deming, MD

(Yoshino, et al., ASCO, 2021)

DESTINY-CRC01



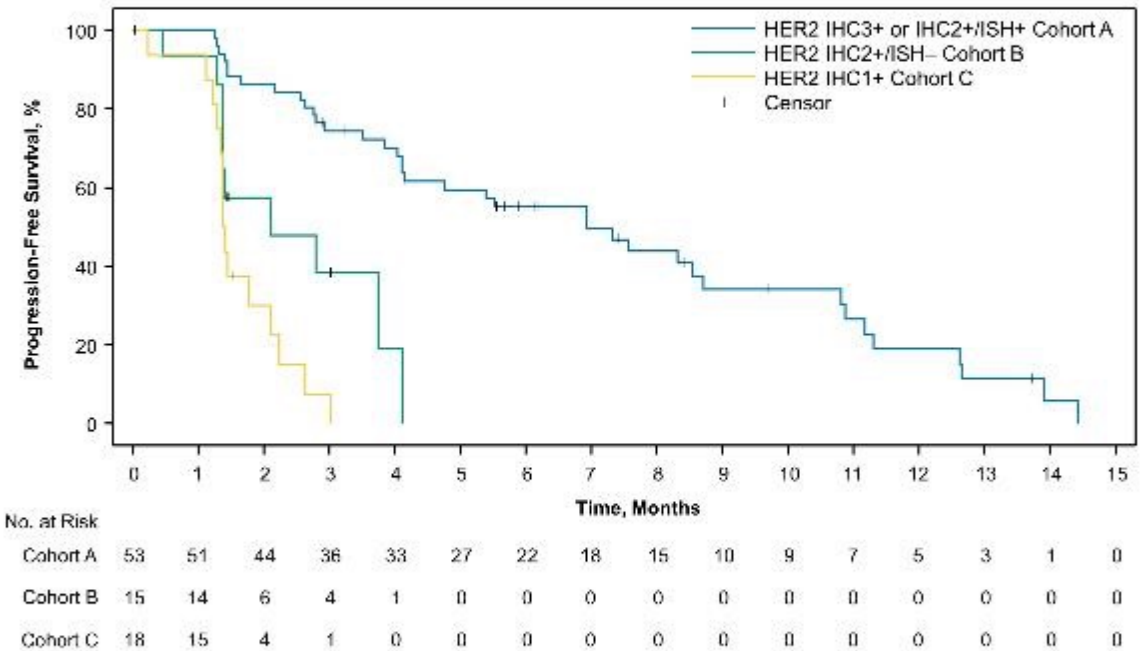
Courtesy of Dustin Deming, MD

(Yoshino, et al., ASCO, 2021)

DESTINY-CRC01

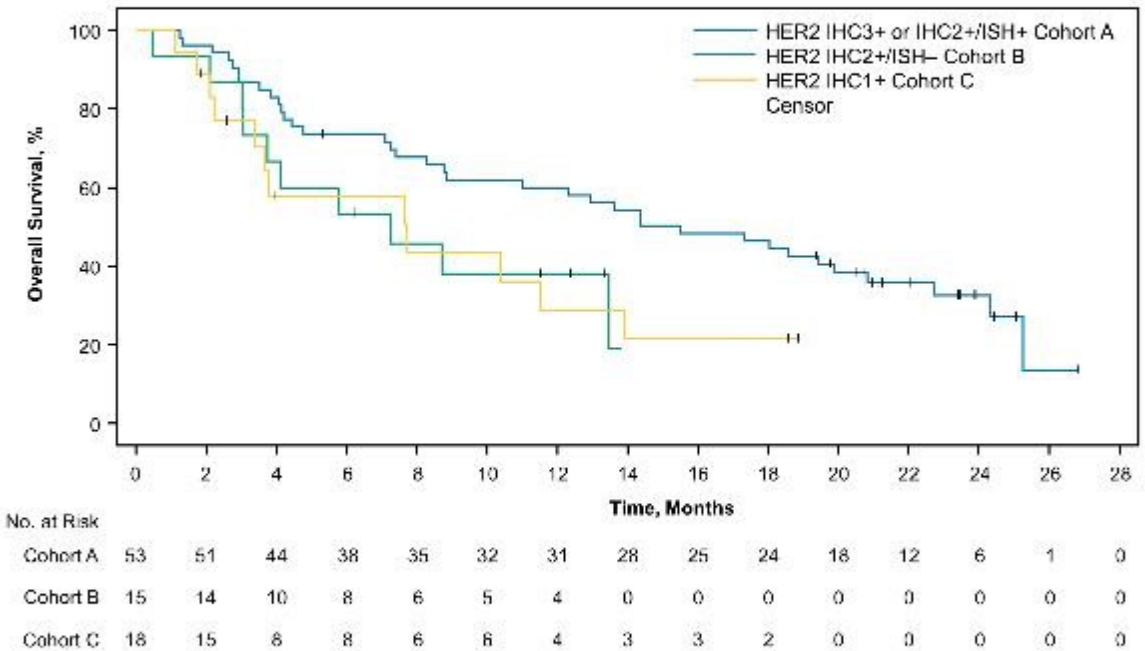
Progression-Free and Overall Survival

Progression-Free Survival



	HER2 IHC3+ or IHC2+/ISH+ Cohort A (n = 53)	HER2 IHC2+/ISH– Cohort B (n = 15)	HER2 IHC1+ Cohort C (n = 18)
mPFS (95% CI), months	6.9 (4.1-8.7)	2.1 (1.4-4.1)	1.4 (1.3-2.1)

Overall Survival



	HER2 IHC3+ or IHC2+/ISH+ Cohort A (n = 53)	HER2 IHC2+/ISH– Cohort B (n = 15)	HER2 IHC1+ Cohort C (n = 18)
mOS (95% CI), months	15.5 (8.8-20.8)	7.3 (3.0-NE)	7.7 (2.2-13.9)

Courtesy of Dustin Deming, MD

(Yoshino, et al., ASCO, 2021)

DESTINY-CRC01 – Interstitial lung disease

All Patients (N=86)	n (%)
Grade 1	0
Grade 2	4 (4.7)
Grade 3	1 (1.2)
Grade 4	0
Grade 5	3 (3.5)[a]
Any Grade/Total	8 (9.3)[b,c]

Adjudicated drug-related ILDs:

- Median time to adjudicated onset was 61.0 days (range, 9-165 days)
- 8 of 8 patients received corticosteroids
- 4 patients with grade 2 recovered and 1 patient with grade 3 did not recover (later died due to disease progression)
- Median time from adjudicated onset date to initiation of steroid treatment in the 8 ILD cases was 3.5 days, (range 0-50)

Grade 5 ILDs:

- In the 3 fatal cases adjudicated as drug-related ILD, onset was from 9 days to 120 days (median: 22 days); and death occurred 6-19 days after diagnosis (median: 6 days)

Updated ILD/pneumonitis guidelines recommend to monitor for symptoms, interrupt or discontinue T-DXd, conduct imaging (as clinically indicated), and start steroids as soon as ILD is suspected.

Courtesy of Dustin Deming, MD

(Yoshino, et al., ASCO, 2021)

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- What is the current role of intrahepatic arterial chemotherapy for patients with predominant liver metastases?

Premeeting survey: July 2021

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Any upcoming trial of KRAS inhibitor that looks promising?

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Does Onco*type* DX® colon have any real value?

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Second line therapy use in left-sided vs right-sided CRC. Any difference in usage of drugs?
  Role of trastuzumab deruxtecan in HER2+ metastatic CRC

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- BRAF treatment in first line?

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Would you use IO therapy in MSS patient with TMB>10?

Premeeting survey: July 2021

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Will CAR T-cell therapy work in mCRC?

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- How often would you retest with liquid biopsy? At every progression?

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- If resectable oligometastatic liver lesion — resect upfront or systemic therapy and then resect?

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- Adjuvant therapy for 85-year-old woman left side colon with MSI high, poor ECOG, how long to give IO? 6 months, 1 year or…?

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Webinar Registrant Questions for the Faculty

Colorectal Cancer

- First line treatment for BRAF V600E mutated mCRC (BEACON combined with chemo vs chemo) while we are waiting for the BREAKWATER study result

Consensus or Controversy? Clinical Investigator Perspectives on the Current and Future Management of Hepatocellular Carcinoma and Pancreatic Cancer

Wednesday, August 4, 2021
5:00 PM – 6:30 PM ET

Faculty

Tanios Bekaii-Saab, MD
Kim A Reiss Binder, MD
Eileen M O'Reilly, MD
Philip A Philip, MD, PhD, FRCP

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 2-3 business days.

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