Meet The Professor

Optimizing the Management of Colorectal Cancer

Thursday, May 18, 2023
5:00 PM – 6:00 PM ET

Faculty

Michael J Overman, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from Lilly, Natera Inc, Seagen Inc, and Taiho Oncology Inc.

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 companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

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

Dr Overman — Disclosures

Consulting Agreements	Bayer HealthCare Pharmaceuticals, Gritstone bio, GSK, Merck, Nouscom, Pfizer Inc, Phanes Therapeutics Inc, Roche Laboratories Inc, Takeda Pharmaceuticals USA Inc, Tempus

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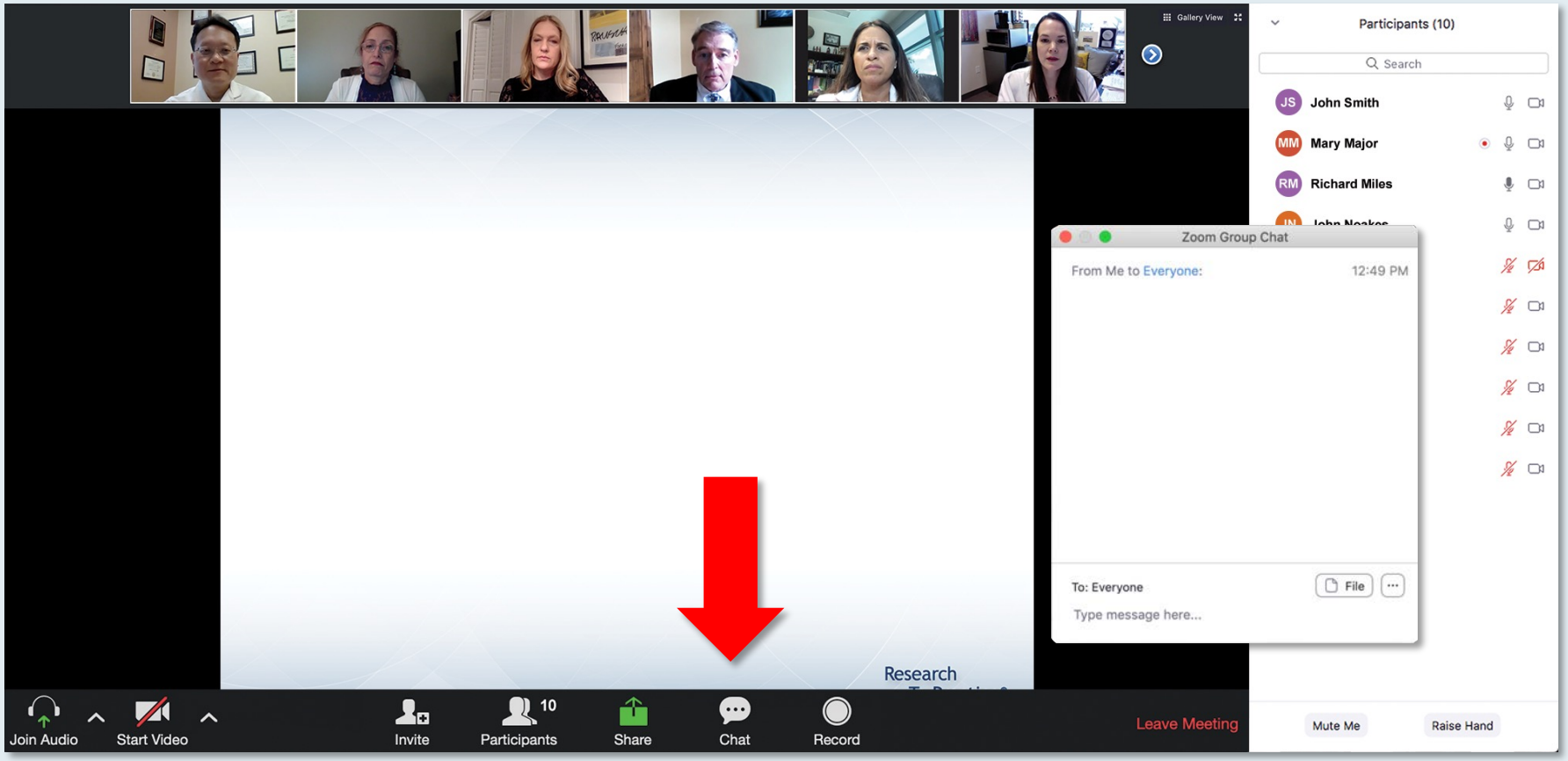

Feel free to submit questions now before the program begins and throughout the program.

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Familiarizing Yourself with the Zoom Interface

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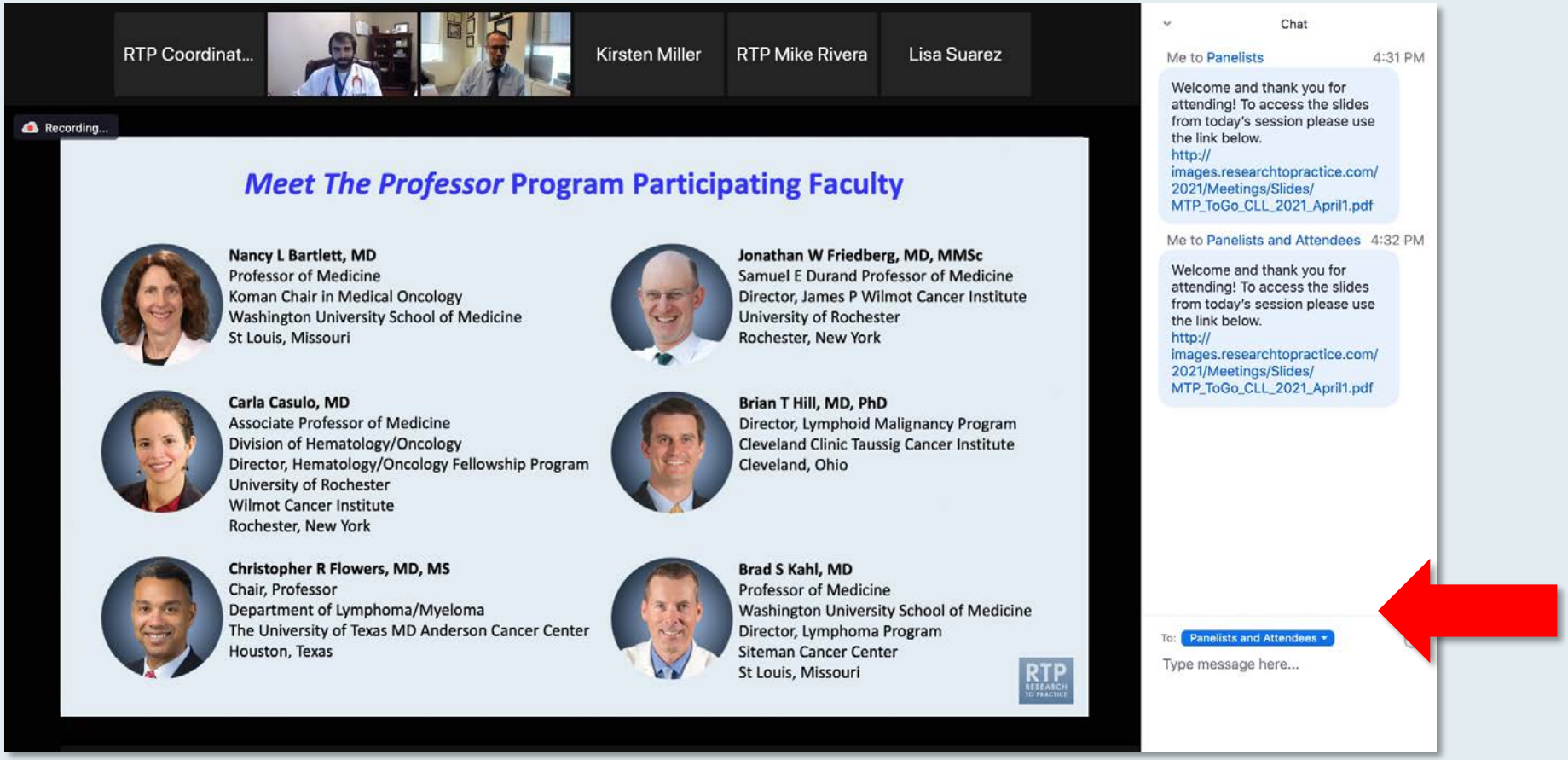

Drag the white line above the submission box up to create more space for your message.

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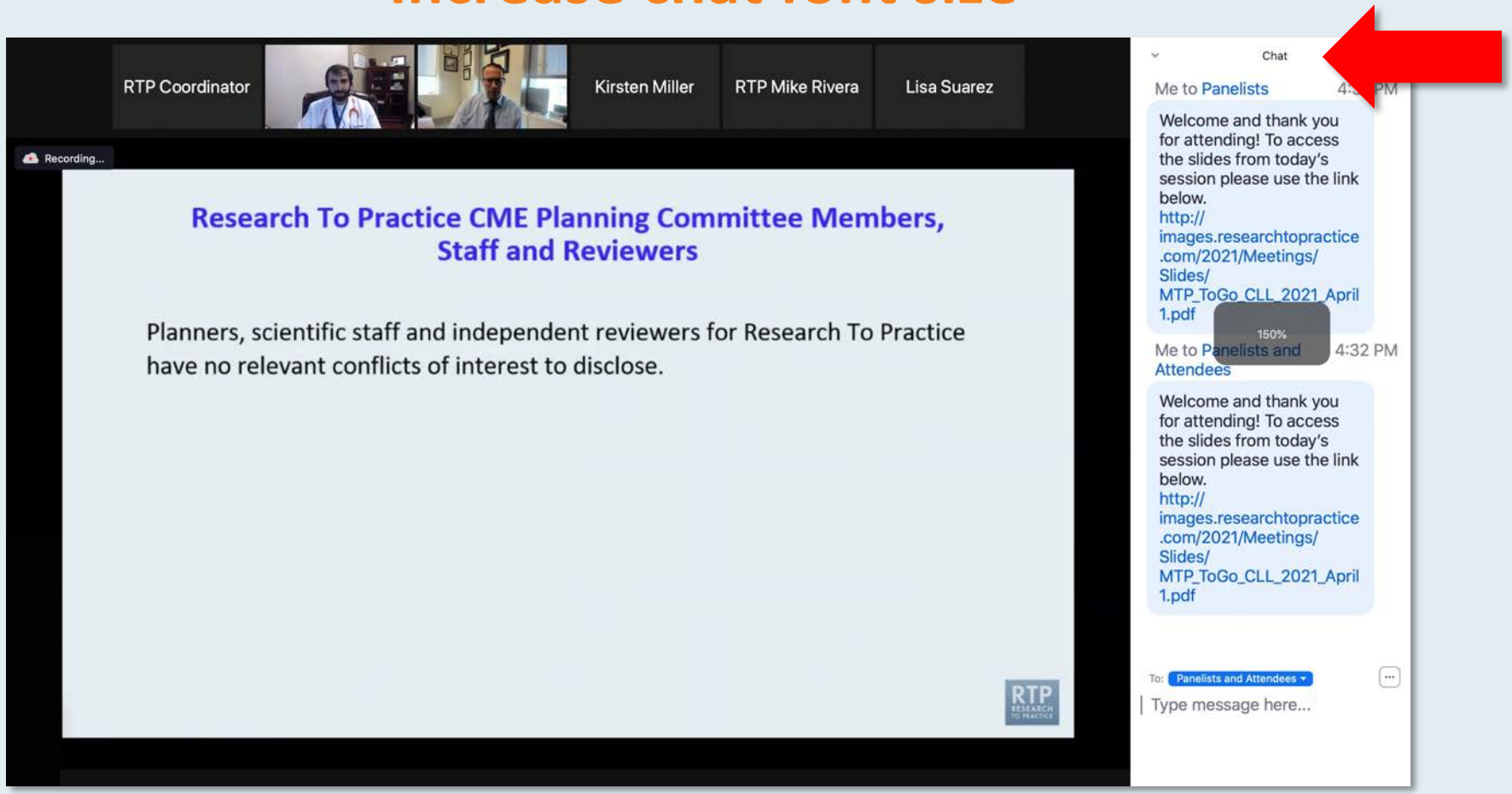
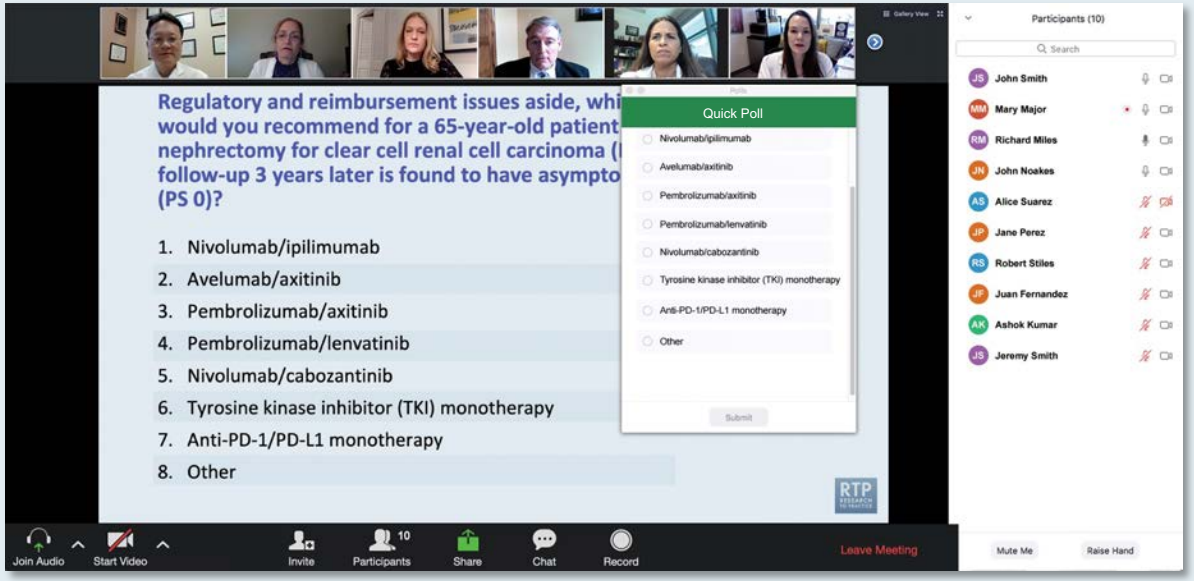
Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



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ONCOLOGY TODAY

WITH DR NEIL LOVE

Management of Gastroesophageal Cancers

DR MANISH SHAH

WEILL CORNELL MEDICINE

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Spotify

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Lunch with the Investigators: Gastroesophageal Cancers

A CME Symposium Held in Conjunction with the 2023 ASCO® Annual Meeting

Friday, June 2, 2023

11:45 AM – 12:45 PM CT (12:45 PM – 1:45 PM ET)

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Manish A Shah, MD

Harry H Yoon, MD, MHS

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Professor Karim Fizazi, MD, PhD
Rana R McKay, MD
Alicia K Morgans, MD, MPH
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David F McDermott, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Michael J Overman, MD
Professor of Gastrointestinal Medical Oncology
Chair, Executive Committee of the Medical Staff
Associate Vice President, Cancer Network Research
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Meet The Professor Program Participating Faculty

Stacey A Cohen, MD
Associate Professor
Fred Hutchinson Cancer Center
University of Washington
Seattle, Washington

Arvind Dasari, MD, MS
Associate Professor
Department of Gastrointestinal Medical Oncology
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Dustin Deming, MD
ACI/Schwenn Family Associate Professor
University of Wisconsin Carbone Cancer Center
Madison, Wisconsin

Christopher Lieu, MD
Associate Professor of Medicine
Associate Director for Clinical Research
Co-Director, GI Medical Oncology
University of Colorado Cancer Center
Aurora, Colorado

Michael J Overman, MD
Professor of Gastrointestinal Medical Oncology
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Houston, Texas

John Strickler, MD
Associate Professor
Duke University
Durham, North Carolina

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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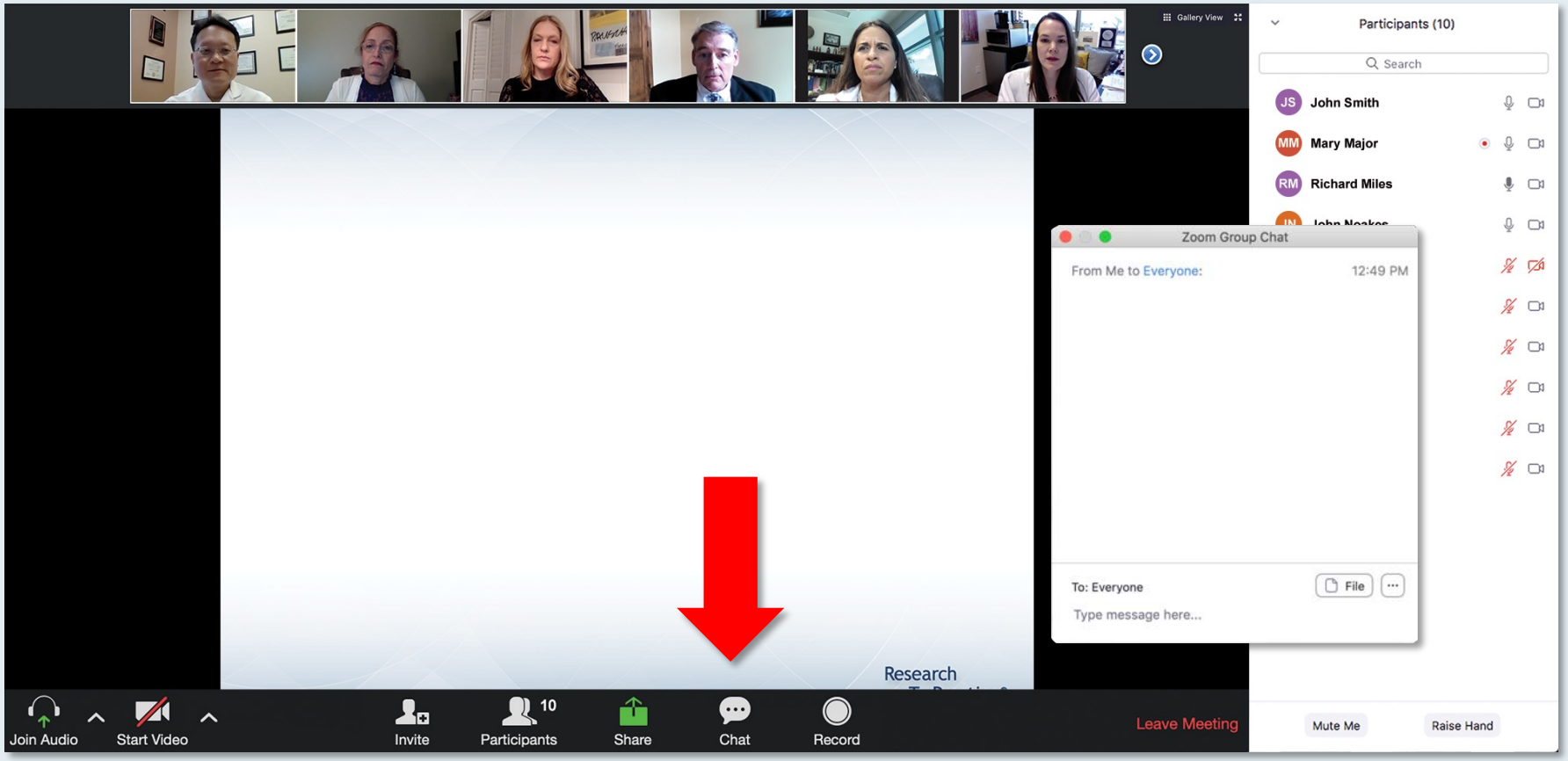

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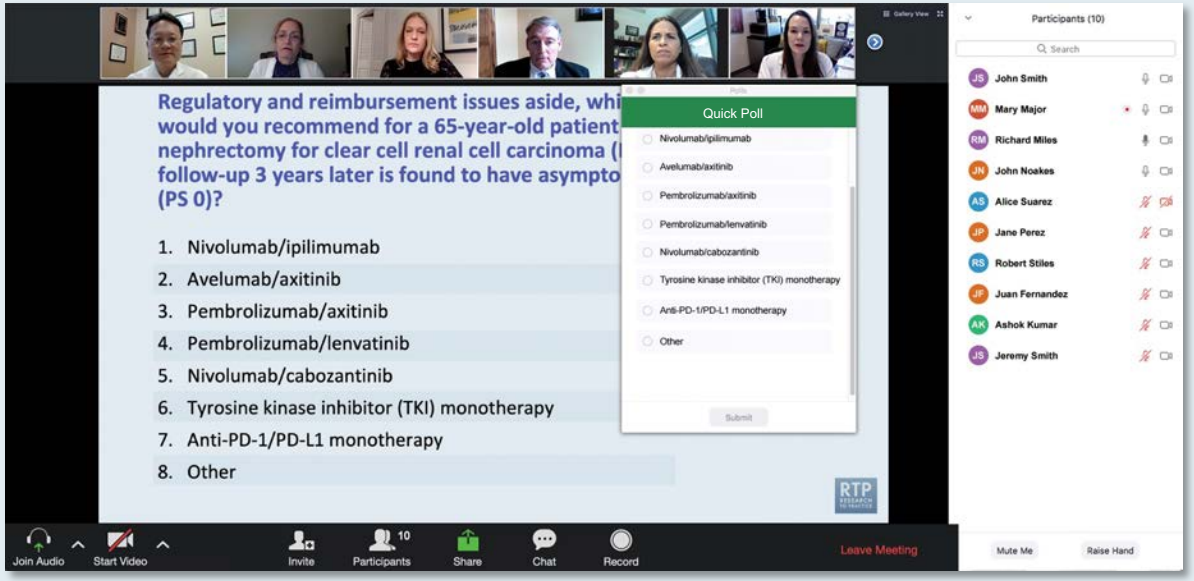

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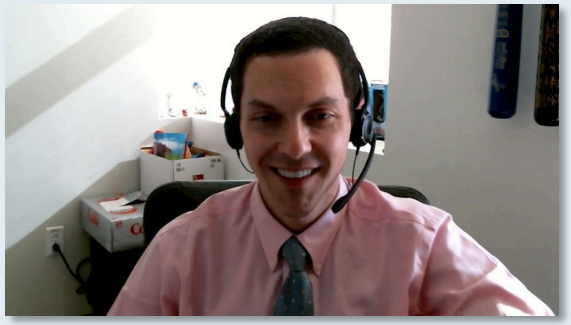
Georges Azzi, MD
Holy Cross Health
Fort Lauderdale, Florida

Eric H Lee, MD, PhD
Compassionate Cancer Care Medical Group
Fountain Valley, California

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida



Jeremy Lorber, MD
Cedars-Sinai Medical Center
Beverly Hills, California

Farshid Dayyani, MD, PhD
Stern Center for Cancer Clinical Trials and Research
Orange, California

Swati Vishwanathan, MD
WVU Medicine
Bridgeport, West Virginia

Sunil Gandhi, MD
Florida Cancer Specialists
Lecanto, Florida

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Meet The Professor with Dr Overman

Introduction

MODULE 1: Case Presentations

MODULE 2: Journal Club

MODULE 3: Appendix

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ARTICLE OPEN

Survival improvement for patients with metastatic colorectal cancer over twenty years

Fadl A. Zeineddine[1], Mohammad A. Zeineddine[1], Abdelrahman Yousef[1], Yue Gu[1], Saikat Chowdhury[1], Arvind Dasari[1], Ryan W. Huey[1], Benny Johnson[1], Bryan Kee[1], Michael S. Lee[1], Maria Pia Morelli[1], Van K. Morris[1], Michael J. Overman[1], Christine Parseghian[1], Kanwal Raghav[1], Jason Willis[1], Robert A. Wolff[1], Yoshikuni Kawaguchi[2], Jean-Nicolas Vauthey[2], Ryan Sun[3], Scott Kopetz[1] and John Paul Shen[1]✉

NPJ Precis Oncol 2023;7(1):16.

JAMA Network Open

Original Investigation | Oncology

Overall Survival in Phase 3 Clinical Trials and the Surveillance, Epidemiology, and End Results Database in Patients With Metastatic Colorectal Cancer, 1986-2016
A Systematic Review

Chan Shen, PhD; Daniel Tannenbaum, MD; Robert Horn, MD; Jane Rogers, PharmD; Cathy Eng, MD; Shouhao Zhou, PhD; Benny Johnson, DO; Scott Kopetz, MD, PhD; Van Morris, MD; Michael Overman, MD; Christine Parseghian, MD; George J. Chang, MD, MS; Maria A. Lopez-Olivo, MD, PhD; Raghav Kanwal, MD; Lee M. Ellis, MD; Arvind Dasari, MD, MS

JAMA Netw Open 2022;5(5):e2213588.

Open access Original research

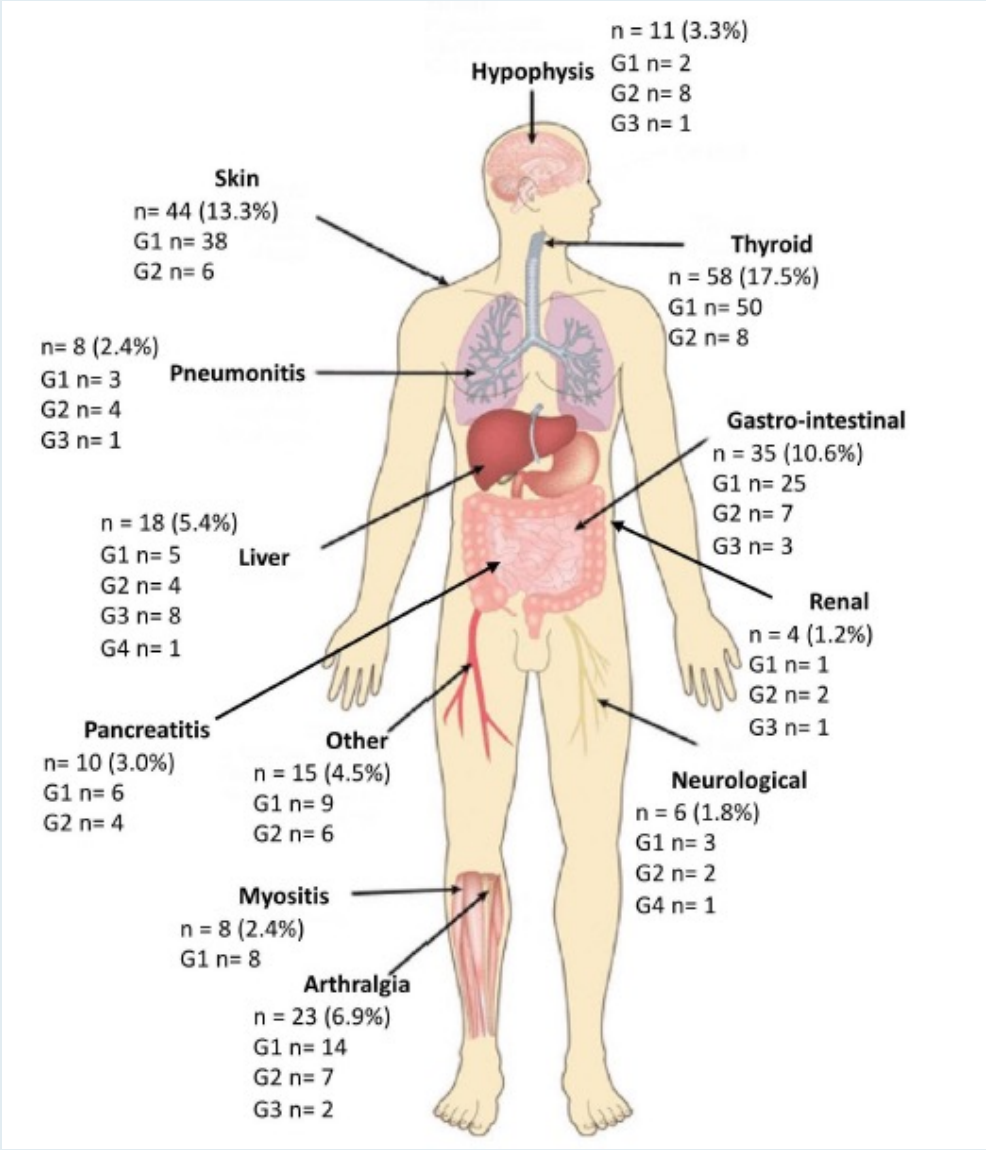
Journal for ImmunoTherapy of Cancer

Association of immune-related adverse events with the outcomes of immune checkpoint inhibitors in patients with dMMR/MSI-H metastatic colorectal cancer

Vincenzo Nasca [1], Francesco Barretta,[2] Francesca Corti,[1] Sara Lonardi [3], Monica Niger,[1] Maria Elena Elez,[4] Marwan Fakih,[5] Priya Jayachandran,[6] Aakash Tushar Shah,[7] Massimiliano Salati,[8] Elisabetta Fenocchio,[9] Lisa Salvatore,[10,11] Chiara Cremolini,[12] Javier Ros,[13,14] Margherita Ambrosini,[1] Giacomo Mazzoli,[1] Rossana Intini,[15] Michael J Overman,[16] Rosalba Miceli [2], Filippo Pietrantonio [1]

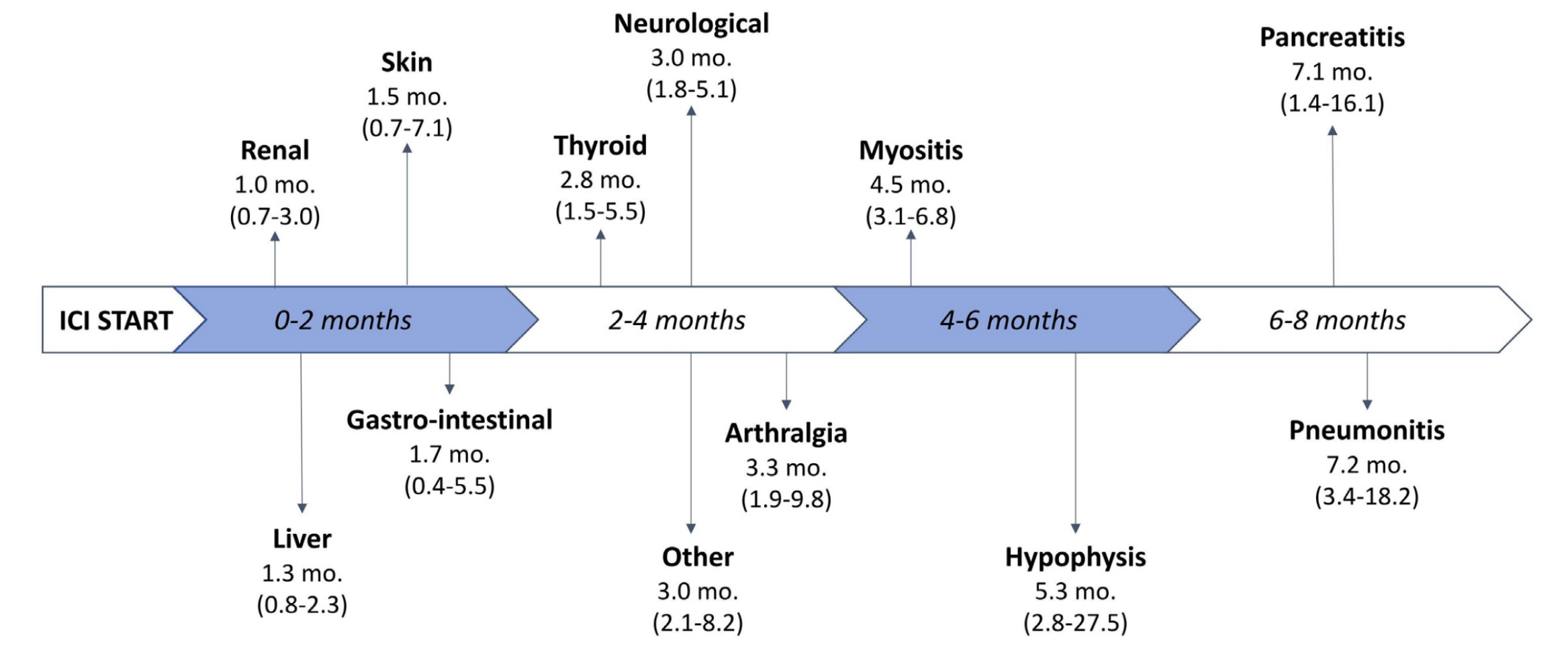
J Immunother Cancer 2023;11(1):e005493.

Summary of Incidence and Severity of Immune-Related Adverse Events Recorded in the Study Population



Nasca V et al. *J Immunother Cancer* 2023;11(1):e005493.

Median Onset Timing (IQR) of Organ-Specific Immune-Related Adverse Events



IQR = interquartile range; ICI = immune checkpoint inhibitor

Nasca V et al. *J Immunother Cancer* 2023;11(1):e005493.

The Oncologist, 2022, **27**, 952–957
https://doi.org/10.1093/oncolo/oyac162
Advance access publication 10 August 2022
Original Article

OXFORD

Antibiotic Exposure Does Not Impact Immune Checkpoint Blockade Response in MSI-H/dMMR Metastatic Colorectal Cancer: A Single-Center Experience

Victoria Serpas Higbie[1], Jane Rogers[2], Hyunsoo Hwang[3], Wei Qiao[3], Lianchun Xiao[3], Arvind Dasari[4], Kerri Mola-Rudd[4], Van K. Morris II[4], Robert A. Wolff[4], Kanwal Raghav[4], Ryan Huey[4], Christine Parseghian[4], Jason Willis[4], Scott Kopetz[4], Michael J. Overman[4], Benny Johnson[*,4]

Open access Original research

Journal for ImmunoTherapy of Cancer

Ascites and resistance to immune checkpoint inhibition in dMMR/MSI-H metastatic colorectal and gastric cancers

Giovanni Fucà ,[1] Romain Cohen ,[2] Sara Lonardi ,[3] Kohei Shitara,[4] Maria Elena Elez,[5] Marwan Fakih,[6] Joseph Chao ,[6] Samuel J Klempner,[7,8] Matthew Emmett,[7,8] Priya Jayachandran,[9] Francesca Bergamo,[10] Marc Díez García,[5] Giacomo Mazzoli,[1] Leonardo Provenzano,[1] Raphael Colle,[2] Magali Svrcek,[11] Margherita Ambrosini,[1] Giovanni Randon,[1] Aakash Tushar Shah,[12] Massimiliano Salati,[13] Elisabetta Fenocchio,[14] Lisa Salvatore,[15] Keigo Chida,[4] Akihito Kawazoe,[4] Veronica Conca,[16,17] Giuseppe Curigliano,[18,19] Francesca Corti,[1] Chiara Cremolini,[16,17] Michael Overman,[20] Thierry Andre ,[2] Filippo Pietrantonio [1]

J Immunother Cancer 2022;10(2):e004001.

RESEARCH ARTICLE

ADVANCED BIOLOGY
www.advanced-bio.com

Understanding Suboptimal Response to Immune Checkpoint Inhibitors

Mojun Zhu, Henan Zhang, Katrina S. Pedersen, Nathan R. Foster, Brandy L. Jaszewski, Xin Liu, Jacob B. Hirdler, Zesheng An, Tanios S. Bekaii-Saab, Thorvardur R. Halfdanarson, Patrick M. Boland, Yiyi Yan, Joleen H. Hubbard, Wen Wee Ma, Harry H. Yoon, Alexander Revzin, Martin E. Fernandez-Zapico, Michael J. Overman, Robert R. McWilliams, and Haidong Dong**

***Adv Biol (Weinh)* 2023;7(4):e2101319.**

Meet The Professor with Dr Overman

MODULE 1: Case Presentations

- Dr Brenner: 44-year-old woman with MSI-H colorectal adenocarcinoma metastatic to the brain receives pembrolizumab – KRAS G13D and somatic BRCA exon 11 mutations
- Dr Lee: 59-year-old woman with MSI-H Stage IIIB adenocarcinoma of the colon, BRAF V600E mutation
- Dr Dayyani: 72-year-old woman with PMH of diverticulitis and partial colectomy diagnosed with T1, MSS cecal colon adenocarcinoma, s/p resection and MRD-negative
- Dr Vishwanathan: 68-year-old woman with PMH of hypothyroidism has mass in right lung consistent with colorectal adenocarcinoma but no evidence of primary or other distant disease
- Dr Gandhi: 66-year-old woman with multiregimen-relapsed RAS WT, HER2-positive metastatic rectal cancer, now receiving trastuzumab/tucatinib
- Dr Brenner: 66-year-old man with MSS metastatic cecal adenocarcinoma and PD on FOLFIRNOX/bevacizumab and capecitabine/bevacizumab maintenance
- Dr Lorber: 66-year-old woman with metastatic BRAF V600E-mutant colon adenocarcinoma, with ctDNA positivity after FOLFOX, HIPEC and colectomy/debulking surgery
- Dr Azzi: 78-year-old man with metastatic rectal adenocarcinoma, s/p first- and second-line chemotherapy with bevacizumab, now with KRAS G12C mutation identified

Case Presentation: 44-year-old woman with MSI-H colorectal adenocarcinoma metastatic to the brain receives pembrolizumab – KRAS G13D and somatic BRCA exon 11 mutations

Dr Warren Brenner (Boca Raton, Florida)

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What is your usual first-line treatment for microsatellite instability (MSI)-high mCRC?

 Dr Cohen	Pembrolizumab	 Dr Lieu	Pembrolizumab
 Dr Dasari	Pembrolizumab	 Dr Overman	Nivolumab/ipilimumab
 Dr Deming	Nivolumab/ipilimumab if fit, otherwise pembrolizumab	 Dr Strickler	Pembrolizumab

How would you generally sequence BRAF-targeted therapy and immunotherapy (IO) for a patient with MSI-high mCRC with a BRAF mutation?

 Dr Cohen	IO → BRAF-targeted tx	 Dr Lieu	IO → BRAF-targeted tx
 Dr Dasari	IO → BRAF-targeted tx	 Dr Overman	IO → BRAF-targeted tx
 Dr Deming	IO → BRAF-targeted tx	 Dr Strickler	IO → BRAF-targeted tx

RTP RESEARCH TO PRACTICE

How would you generally sequence HER2-targeted therapy and immunotherapy (IO) for a patient with HER2-positive, MSI-high mCRC?

 Dr Cohen	IO → HER2-targeted tx	 Dr Lieu	IO → HER2-targeted tx
 Dr Dasari	IO → HER2-targeted tx	 Dr Overman	IO → HER2-targeted tx
 Dr Deming	IO → HER2-targeted tx	 Dr Strickler	IO → HER2-targeted tx

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 Cohen	Yes	 Dr Lieu	Yes
 Dr Dasari	Yes	 Dr Overman	Yes
 Dr Deming	Yes	 Dr Strickler	Yes

Case Presentation: 59-year-old woman with MSI-H Stage IIIB adenocarcinoma of the colon, BRAF V600E mutation

Dr Eric Lee (Fountain Valley, California)

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, for a patient with pan-RAS wild-type metastatic CRC (mCRC) with a BRAF V600E mutation, in which line of therapy would you generally administer BRAF-targeted therapy?

 Dr Cohen	Second line	 Dr Lieu	Second line
 Dr Dasari	Second line	 Dr Overman	Second line
 Dr Deming	Second line	 Dr Strickler	Second line

Regulatory and reimbursement issues aside, 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 Cohen	Encorafenib + cetuximab	 Dr Lieu	Encorafenib + cetuximab
 Dr Dasari	Encorafenib + cetuximab	 Dr Overman	Encorafenib + cetuximab
 Dr Deming	Encorafenib + panitumumab	 Dr Strickler	Encorafenib + panitumumab

RTP RESEARCH TO PRACTICE

Case Presentation: 72-year-old woman with PMH of diverticulitis and partial colectomy diagnosed with T1, MSS cecal colon adenocarcinoma, s/p resection and MRD-negative

Dr Farshid Dayyani (Orange, California)

RTP
RESEARCH
TO PRACTICE

In general, in which settings, if any, do you order a circulating tumor DNA (ctDNA) assay for your patients with colorectal cancer (CRC) outside of a clinical trial?

 Dr Cohen	Stage II-IV after definitive management	 Dr Lieu	Stage II after surgery
 Dr Dasari	Stage II after surgery, Stage III after adjuvant tx, metastatic during tx	 Dr Overman	Stage II after surgery, Stage III after adjuvant tx
 Dr Deming	Across any stage, but only in specific circumstances	 Dr Strickler	Stage II after surgery, all other stages in select circumstances

A patient presents with Stage II CRC with no high-risk features and undergoes R0 resection. What would be your approach to adjuvant therapy?

 Dr Cohen	Order ctDNA assay, then decide	 Dr Lieu	Order ctDNA assay, then decide
 Dr Dasari	Order ctDNA assay, then decide	 Dr Overman	Observation
 Dr Deming	Observation	 Dr Strickler	Order ctDNA assay, then decide

RTP RESEARCH TO PRACTICE

If a ctDNA assay was ordered for a patient with Stage II CRC with no high-risk features who underwent an R0 resection, what would be your approach to treatment if the results were …?

	Negative	Positive
 Dr Cohen	Observation	FOLFOX/CAPOX
 Dr Dasari	Observation	FOLFOX/CAPOX
 Dr Deming	Observation	FOLFOX/CAPOX
 Dr Lieu	Observation	FOLFOX/CAPOX
 Dr Overman	Observation	FOLFOX/CAPOX
 Dr Strickler	Observation	FOLFOX/CAPOX

For a patient with CRC and a solitary hepatic metastasis who receives neoadjuvant FOLFOX and undergoes hepatic resection, would you assess ctDNA as part of the postoperative workup?

 Dr Cohen	Yes	 Dr Lieu	No
 Dr Dasari	Yes	 Dr Overman	Yes
 Dr Deming	No	 Dr Strickler	Yes, if patient agreeable to additional "adjuvant" tx

RTP RESEARCH TO PRACTICE

Case Presentation: 68-year-old woman with PMH of hypothyroidism has mass in right lung consistent with colorectal adenocarcinoma but no evidence of primary or other distant disease

Dr Swati Vishwanathan (Bridgeport, West Virginia)

RTP
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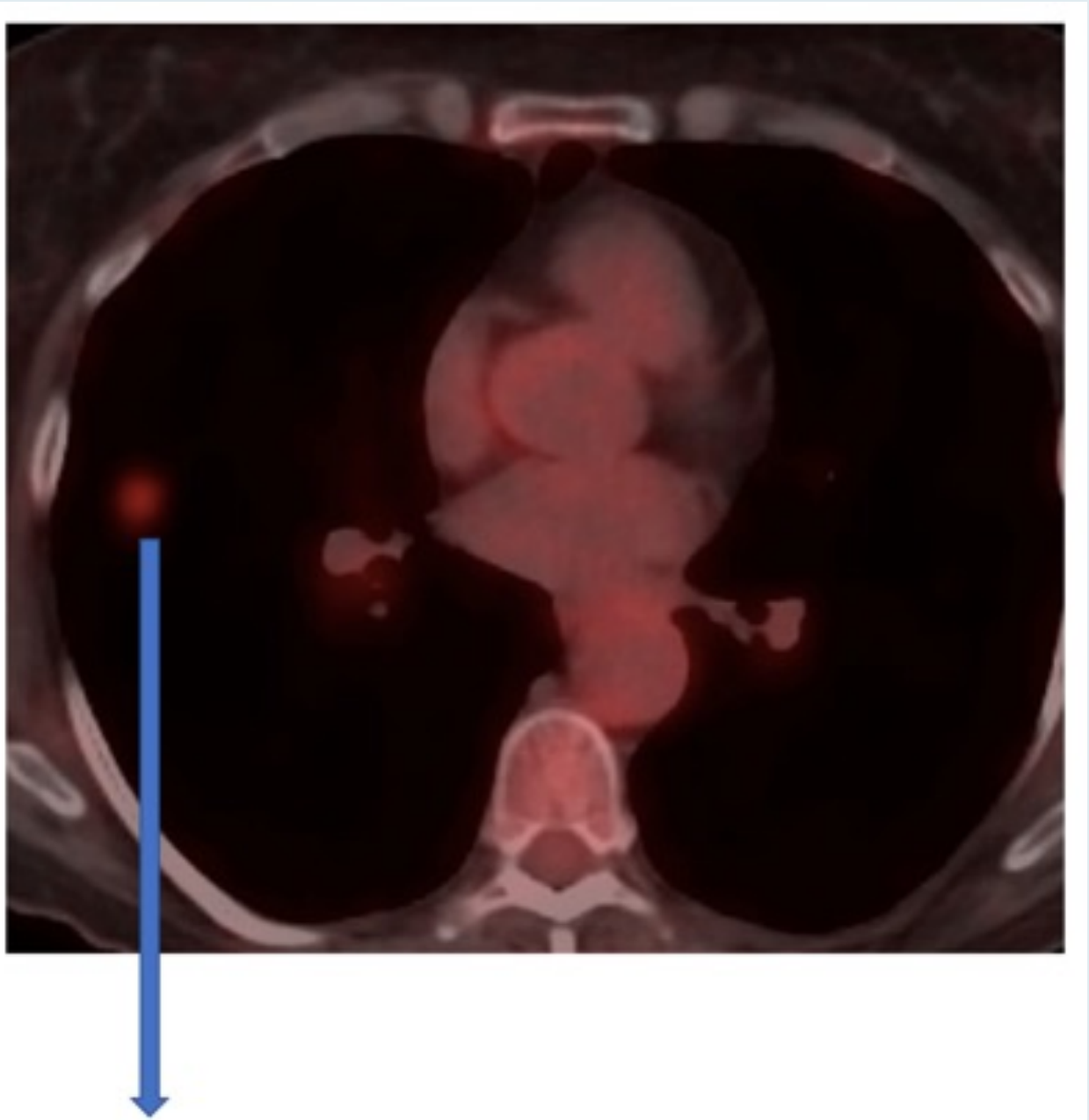
TO PRACTICE



Right lung nodule on PET

Case Presentation: 66-year-old woman with multiregimen-relapsed RAS WT, HER2-positive metastatic rectal cancer, now receiving trastuzumab/tucatinib

Dr Sunil Gandhi (Lecanto, Florida)

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, for a patient with HER2-overexpressing or amplified mCRC, in which line of therapy would you generally administer anti-HER2 therapy?

 Dr Cohen	Second line	 Dr Lieu	Second line
 Dr Dasari	Third line or beyond	 Dr Overman	Second line
 Dr Deming	Second line	 Dr Strickler	Second line

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, what would be your most likely anti-HER2 treatment for a patient with HER2-positive mCRC in the scenarios below?

	Initial therapy	Second line of anti-HER2 therapy
 Dr Cohen	Tucatinib + trastuzumab	Trastuzumab deruxtecan
 Dr Dasari	Tucatinib + trastuzumab	Trastuzumab deruxtecan
 Dr Deming	Trastuzumab/pertuzumab	Tucatinib + trastuzumab
 Dr Lieu	Tucatinib + trastuzumab	Trastuzumab deruxtecan
 Dr Overman	Trastuzumab/pertuzumab	Trastuzumab deruxtecan
 Dr Strickler	Tucatinib + trastuzumab	Trastuzumab deruxtecan

A Randomized Phase 2 Study of Trastuzumab and Pertuzumab (TP) Compared to Cetuximab and Irinotecan (CETIRI) in Advanced/Metastatic Colorectal Cancer (mCRC) with HER2 Amplification: SWOG S1613

Raghav KP et al.

Gastrointestinal Cancers Symposium 2023;Abstract 140.

Case Presentation: 66-year-old man with MSS metastatic cecal adenocarcinoma and PD on FOLFIRNOX/bevacizumab and capecitabine/bevacizumab maintenance

Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH
TO PRACTICE

What is your preferred sequence for administering regorafenib and TAS-102 with or without bevacizumab for your patients with multiregimen-relapsed mCRC?

 Dr Cohen	TAS-102 +/- bev → regorafenib	 Dr Lieu	TAS-102 +/- bev → regorafenib
 Dr Dasari	TAS-102 +/- bev → regorafenib	 Dr Overman	TAS-102 +/- bev → regorafenib
 Dr Deming	TAS-102 +/- bev → regorafenib	 Dr Strickler	TAS-102 + bev → regorafenib

RTP RESEARCH TO PRACTICE

In general, when you administer TAS-102 for mCRC, do you add bevacizumab?

 Dr Cohen	Yes	 Dr Lieu	Yes
 Dr Dasari	Yes	 Dr Overman	Yes
 Dr Deming	Yes	 Dr Strickler	Yes

RTP RESEARCH TO PRACTICE

What is your preferred starting dose of regorafenib for mCRC?

 Dr Cohen	80 mg	 Dr Lieu	80 mg
 Dr Dasari	80 mg	 Dr Overman	80 mg
 Dr Deming	80 mg	 Dr Strickler	80 mg

RTP
RESEARCH
TO PRACTICE

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

 Dr Cohen	TAS-102 + bev	 Dr Lieu	TAS-102 + bev
 Dr Dasari	TAS-102 + bev	 Dr Overman	TAS-102 + bev
 Dr Deming	TAS-102 + bev	 Dr Strickler	TAS-102 + bev

RTP RESEARCH TO PRACTICE

For a patient with mCRC who has received EGFR antibody-containing therapy and experienced disease progression, are there any circumstances in which you will rechallenge with the same or a different EGFR antibody later in the treatment course?

Dr Cohen

Yes, if prior response and new chemo partner available

Dr Dasari

Yes, after tx holiday if liquid biopsy does not show alterations

Dr Deming

Yes, if prior response or durable SD and ≥4 mo since last given

Dr Lieu

Yes, if no other tx options and ctDNA is negative for resistance mutations

Dr Overman

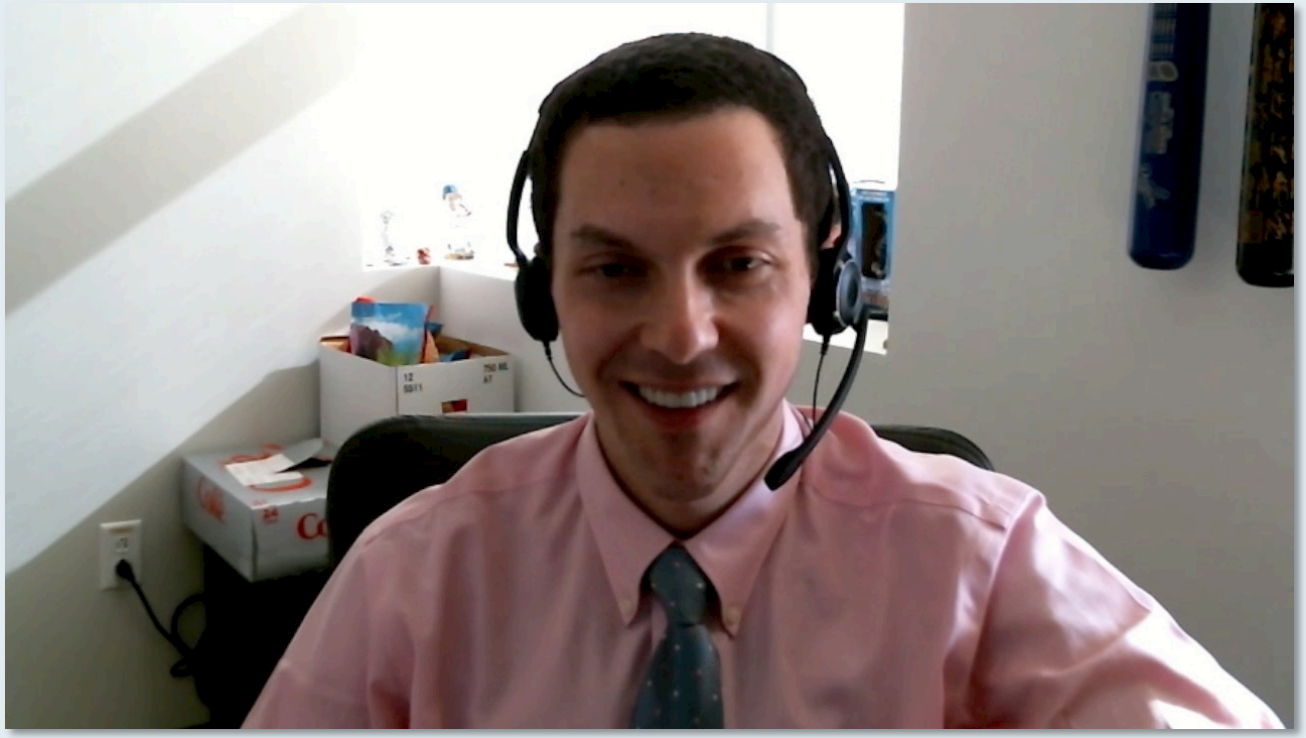
Yes, if initial response, time interval between tx, ctDNA for resistance mutations

Dr Strickler

Yes, if ctDNA is negative for resistance mutations

RTP RESEARCH TO PRACTICE

Case Presentation: 66-year-old woman with metastatic BRAF V600E-mutant colorectal adenocarcinoma, with ctDNA positivity after FOLFOX, HIPEC and colectomy/debulking surgery



Dr Jeremy Lorber (Beverly Hills, California)

RTP
RESEARCH
TO PRACTICE

ORIGINAL ARTICLE

Prospective Study of Perioperative Circulating Tumor DNA Dynamics in Patients Undergoing Hepatectomy for Colorectal Liver Metastases

Timothy E. Newhook, MD,∗ Michael J. Overman, MD,† Yun Shin Chun, MD,∗ Arvind Dasari, MBBS, MD,† Ching-Wei D. Tzeng, MD,∗ Hop S. Tran Cao, MD,∗ Victoria Raymond, MS,‡ Christine Parseghian, MD,† Benny Johnson, DO,† Yujiro Nishioka, MD, PhD,∗ Yoshikuni Kawaguchi, MD, PhD,∗ Abhineet Uppal, MD,§ Timothy J. Vreeland, MD,¶ Ariel Jaimovich, PhD,‡ Elsa M. Arvide, PA-C,∗ Jenilette V. Cristo, PA-C,∗ Steven H. Wei, BA, MPH, MS,∗ Kanwal P. Raghav, MD,† Van K. Morris, MD,† Jeffrey E. Lee, MD,∗ Scott Kopetz, MD, PhD,† and Jean-Nicolas Vauthey, MD∗✉

***Ann Surg* 2022:[Online ahead of print].**

Case Presentation: 78-year-old man with metastatic rectal adenocarcinoma, s/p first- and second-line chemotherapy with bevacizumab, now with KRAS G12C mutation identified

Dr Georges Azzi (Fort Lauderdale, Florida)

RTP
RESEARCH
TO PRACTICE

In general, which KRAS G12C inhibitor would you most likely use if you were going to administer such an agent to a patient with mCRC?

 Dr Cohen	Adagrasib	 Dr Lieu	Adagrasib
 Dr Dasari	Adagrasib	 Dr Overman	Adagrasib
 Dr Deming	Adagrasib	 Dr Strickler	Sotorasib

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, for a patient with mCRC with a KRAS p.G12C mutation, in which line of therapy would you generally administer KRAS-targeted therapy (eg, sotorasib, adagrasib)?

 Dr Cohen	Second line	 Dr Lieu	Second line
 Dr Dasari	Third line or beyond	 Dr Overman	Second line
 Dr Deming	Third line or beyond	 Dr Strickler	Third line or beyond

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Overman

Introduction

MODULE 1: Case Presentations

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TO PRACTICE

Clinical Outcomes Following Termination of Immunotherapy Due to Long-Term Benefit in MSI-H Colorectal Cancer

Simmons K et al.

ASCO 2022;Abstract 3585.

ASCO special articles

Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy: ASCO Endorsement of College of American Pathologists Guideline

Praveen Vikas, MD[1]; Hans Messersmith, MPH[2]; Carolyn Compton, MD, PhD[3]; Lynette Sholl, MD[4]; Russell R. Broaddus, MD[5]; Anjee Davis, MPPA[6]; Maria Estevez-Diz, MD, PhD[7]; Rohan Garje, MD[8]; Panagiotis A. Konstantinopoulos, MD[9]; Aliza Leiser, MD[10]; Anne M. Mills, MD[11]; Barbara Norquist, MD[12]; Michael J. Overman, MD[13]; Davendra Sohal, MD[14]; Richard C. Turkington, MD, PhD[15]; and Tyler Johnson, MD[16]

J Clin Oncol 2023;41(10):1943-8.

Cancer Cell

Article

Genetic and pharmacological modulation of DNA mismatch repair heterogeneous tumors promotes immune surveillance

Amodio V et al. *Cancer Cell* 2023;4(7):100908.

Cell Reports Medicine

CellPress
OPEN ACCESS

Spotlight

Harnessing the therapeutic vulnerability of MMR heterogeneity in colorectal cancer

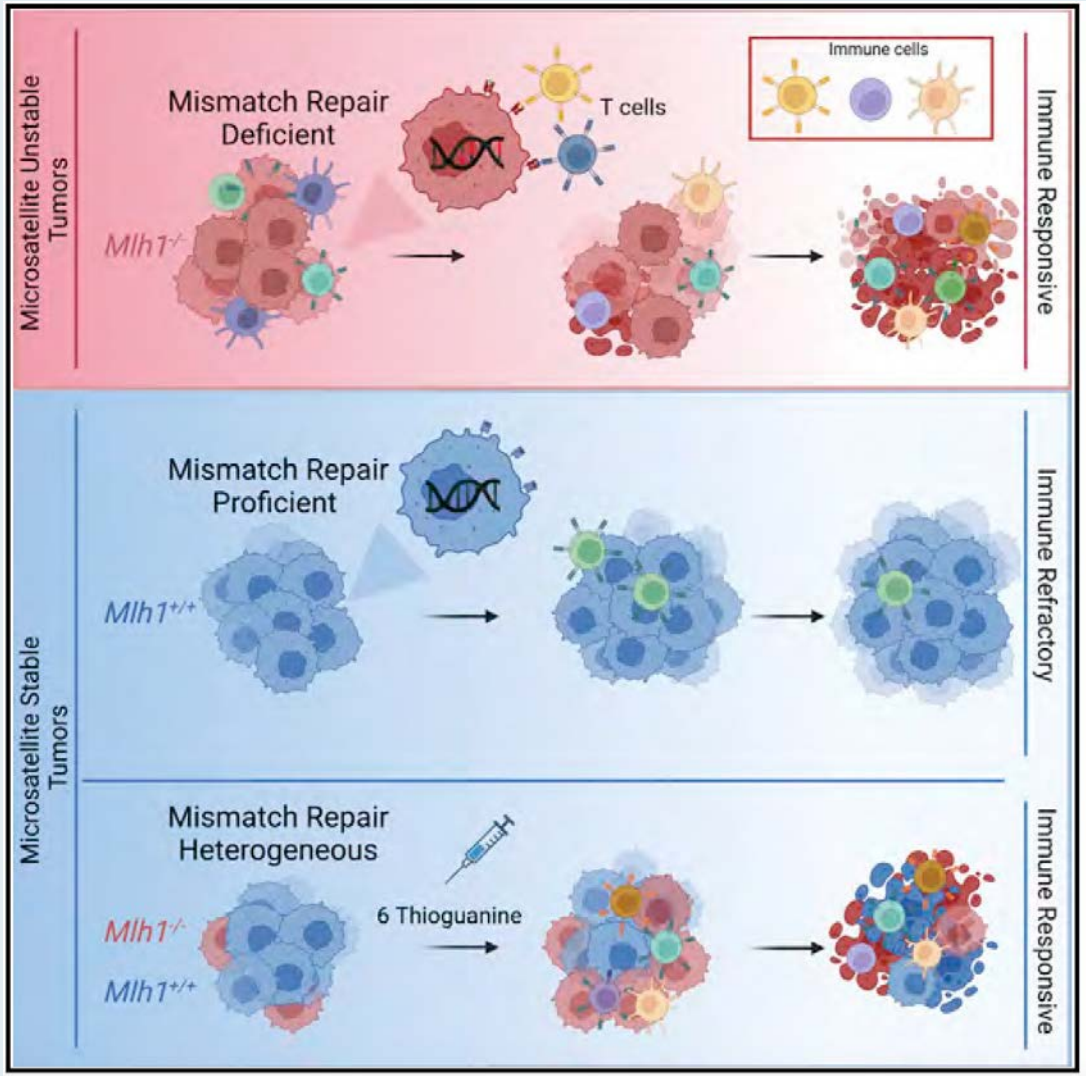
Gayathri Anandappa[1] and Michael J. Overman[1,*]
[1]Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
*Correspondence: moverman@mdanderson.org
https://doi.org/10.1016/j.xcrm.2022.100908

Cell Rep Med 2023;4(1):100908.

JC JOURNAL CLUB

RTP RESEARCH TO PRACTICE

Genetic and Pharmacological Modulation of DNA Mismatch Repair Heterogeneous Tumors Promotes Immune Surveillance



Amodio V et al. *Cancer Cell* 2023;4(7):100908.

Arch Pathol Lab Med 2022;146(10):1194-210.

Mismatch Repair and Microsatellite Instability Testing for Immune Checkpoint Inhibitor Therapy

Guideline From the College of American Pathologists in Collaboration With the Association for Molecular Pathology and Fight Colorectal Cancer

Angela N. Bartley, MD; Anne M. Mills, MD; Eric Konnick, MD, MS; Michael Overman, MD; Christina B. Ventura, MPH, MT(ASCP); Lesley Souter, PhD; Carol Colasacco, MLIS, SCT(ASCP); Zsofia K. Stadler, MD; Sarah Kerr, MD; Brooke E. Howitt, MD; Heather Hampel, MS, LGC; Sarah F. Adams, MD; Wenora Johnson, BS; Cristina Magi-Galluzzi, MD, PhD; Antonia R. Sepulveda, MD, PhD; Russell R. Broaddus, MD, PhD

The Oncologist, 2023, **XX**, 1–9
https://doi.org/10.1093/oncolo/oyad082
Advance access publication 6 April 2023
Original Article

OXFORD

BRAF^{V600E}/*RAS* Mutations and Lynch Syndrome in Patients With MSI-H/dMMR Metastatic Colorectal Cancer Treated With Immune Checkpoint Inhibitors

Raphael Colle[1,2,3], Sara Lonardi[4], Marine Cachanado[3], Michael J. Overman[5], Elena Elez[6], Marwan Fakih[7], Francesca Corti[8], Priya Jayachandran[9], Magali Svrcek[2,10], Antoine Dardenne[1], Baptiste Cervantes[1], Alex Duval[2,3], Romain Cohen[1,2,3], Filippo Pietrantonio[8], Thierry André[*,1,2,3]

Clinical Outcomes Following Termination of Immunotherapy Due to Long-Term Benefit in MSI-H Colorectal Cancer

Fox D et al.

ASCO 2023;Abstract 3610.

OXFORD

BJS, 2022, 109, 489–492
https://doi.org/10.1093/bjs/znac050
Advance Access Publication Date: 4 April 2022
Short Report

Pathological response following neoadjuvant immunotherapy in mismatch repair-deficient/ microsatellite instability-high locally advanced, non-metastatic colorectal cancer

Anai Kothari[1], Michael G. White[2], Oliver Peacock[2], Harmeet Kaur[3], Sarah M. Palmquist[3], Nancy You[2], Melissa Taggart[4], Usama Salem[3], Michael Overman[5], Scott Kopetz[5] and George J. Chang[2,*]

First-Line (1L) Nivolumab (NIVO) + Ipilimumab (IPI) in Patients (pts) with Microsatellite Instability-High/Mismatch Repair Deficient (MSI-H/dMMR) Metastatic Colorectal Cancer (mCRC): 64-Month (mo) Follow-Up from CheckMate 142

Lenz HJ et al.

ASCO 2023;Abstract 3550.

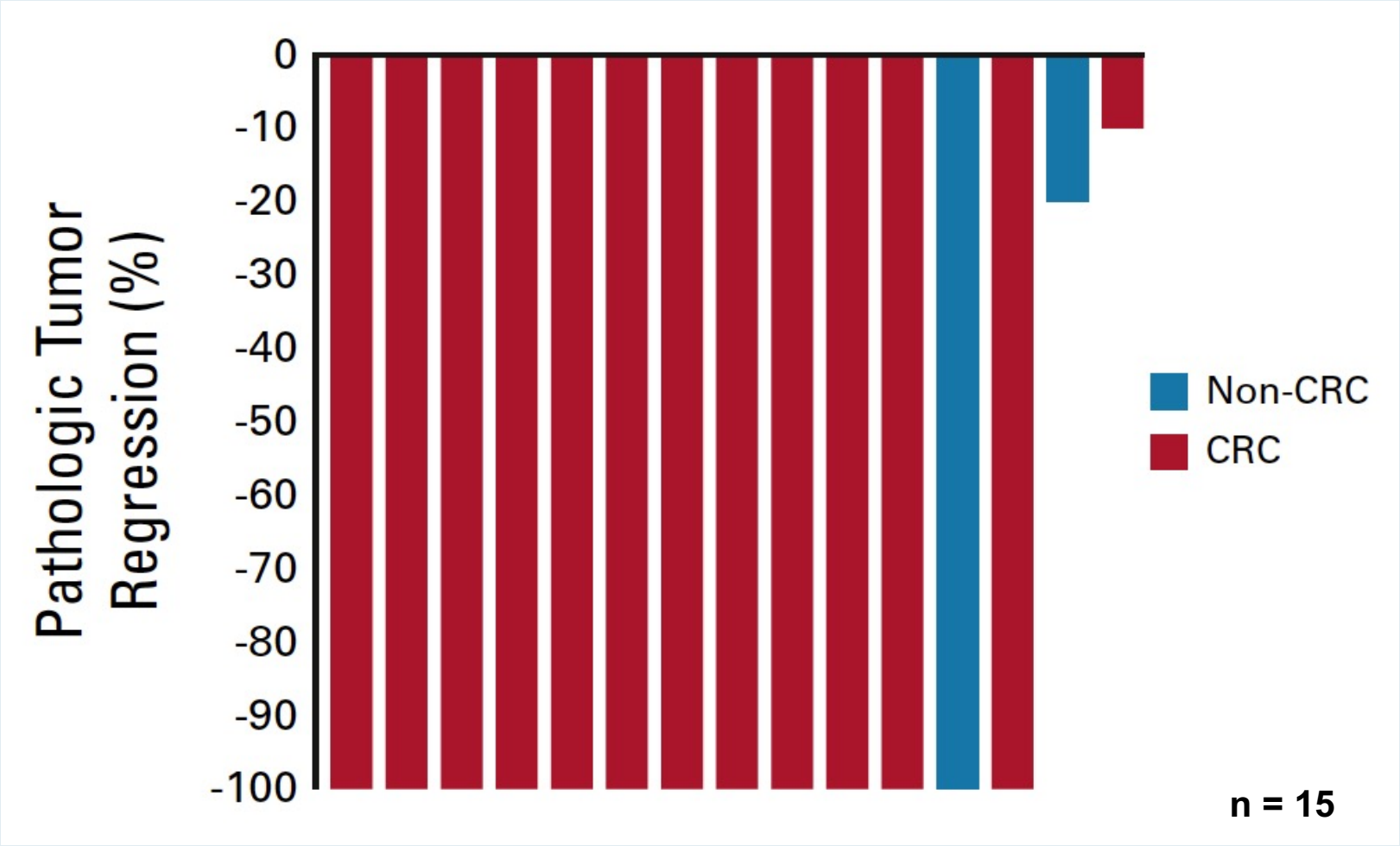
original reports

Neoadjuvant Pembrolizumab in Localized Microsatellite Instability High/Deficient Mismatch Repair Solid Tumors

Kaysia Ludford, MD[1,2]; Won Jin Ho, MD[3]; Jane V. Thomas, MD[2]; Kanwal P.S. Raghav, MBBS[2]; Mariela Blum Murphy, MD[2]; Nicole D. Fleming, MD[4]; Michael S. Lee, MD[2]; Brandon G. Smaglo, MD[2]; Y. Nancy You, MD[5]; Matthew M. Tillman, MD[5]; Carlos Kamiya-Matsuoka, MD[6]; Selvi Thirumurthi, MD[7]; Craig Messick, MD[5]; Benny Johnson, DO[2]; Eduardo Vilar, MD, PhD[8]; Arvind Dasari, MBBS[2]; Sarah Shin, BS[3]; Alexei Hernandez, BS[3]; Xuan Yuan, MD[3]; Hongqui Yang[3]; Wai Chin Foo, MD[9]; Wei Qiao, MS, PhD[10]; Dipen Maru, MD[9]; Scott Kopetz, MD, PhD[2]; and Michael J. Overman, MD[2]

J Clin Oncol 2023;41(12):2181-90.

Pathologic Tumor Regression in the Primary Tumor of Resected Specimens After Neoadjuvant Pembrolizumab



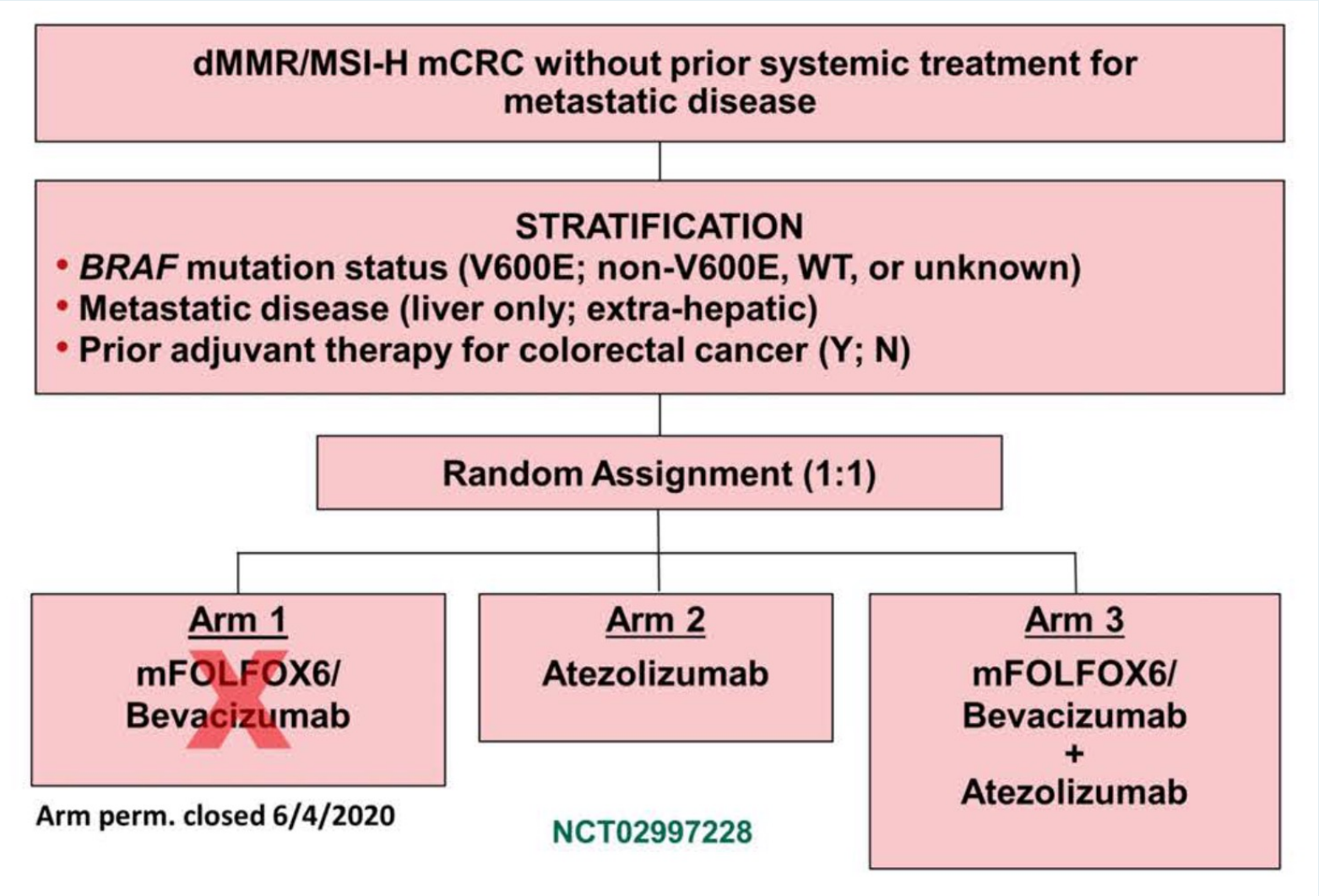
Ludford K et al. *J Clin Oncol* 2023;41(12):2181-90.

Colorectal Cancer Metastatic dMMR Immunotherapy (COMMIT) Study: A Randomized Phase III Study of Atezolizumab (atezo) Monotherapy versus mFOLFOX6/Bevacizumab/Atezo in the First-Line Treatment of Patients (pts) with Deficient DNA Mismatch Repair (dMMR) or Microsatellite Instability High (MSI-H) Metastatic Colorectal Cancer (mCRC)—NRG-GI004/SWOG-S1610 142

Lima CMSPR et al.

ASCO 2022;Abstract TPS3647.

COMMIT Phase III Trial Schema



Lima CMSPR et al. ASCO 2022;Abstract TPS3647.

Meet The Professor with Dr Overman

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RTP
RESEARCH
TO PRACTICE

Current and Future Role of Therapies Targeting BRAF and HER2 in Metastatic Colorectal Cancer (mCRC)

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RESEARCH
TO PRACTICE

PARIS 2022 ESMO congress

BREAKWATER Safety Lead-In (SLI): Encorafenib (E) + Cetuximab (C) + Chemotherapy (Chemo) For *BRAF*^{V600E} Metastatic Colorectal Cancer (mCRC)

Josep Tabernero,[1] Takayuki Yoshino,[2] Tae Won Kim,[3] Rona Yaeger,[4] Jayesh Desai,[5] Harpreet Singh Wasan,[6] Eric Van Cutsem,[7] Fortunato Ciardiello,[8] Tim Maughan,[9] Cathy Eng,[10] Jeanne Tie,[5] Elena Elez,[1] Sara Lonardi,[11] Xiaosong Zhang,[12] Renae Chavira,[12] Tiziana Usari,[13] Erik Hahn,[14] Scott Kopetz[15]

[1]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, UVic-UCC, Barcelona, Spain; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [4]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [5]Peter MacCallum Cancer Centre, Melbourne, Australia; [6]Hammersmith Hospital, Division of Cancer, Imperial College London, UK; [7]University Hospital Gasthuisberg and University of Leuven, Leuven, Belgium; [8]University of Campania Luigi Vanvitelli, Naples, Italy; [9]MRC Oxford Institute for Radiation Oncology, University of Oxford, Oxford, UK; [10]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [11]Veneto Institute of Oncology-IRCCS, Padova, Italy; [12]Pfizer, Inc, New York, NY, USA; [13]Pfizer, Inc, Milan, Italy; [14]Pfizer, Inc, Boulder, CO, USA; [15]MD Anderson Cancer Center, Houston, TX, USA

NCT04607421

Abstract LBA26

RTP RESEARCH TO PRACTICE

BREAKWATER Safety Lead-In: Frequency of Dose-Limiting Toxicities (DLTs) and Safety Summary

Primary endpoint: Frequency of DLTs

- One patient in the EC + FOLFIRI cohort had a DLT of grade 4 neutropenia lasting >7 days; no other DLTs were reported

Secondary endpoint: Safety

	EC + mFOLFOX6		EC + FOLFIRI	
	n=27		n=30	
All causality, n (%)				
TEAEs	27 (100.0)		30 (100.0)	
SAEs	13 (48.1)		10 (33.3)	
Grade ≥3 TEAEs	21 (77.8)		13 (43.3)	
TEAEs leading to dose reduction (any drug)	18 (66.7)		10 (33.3)	
TEAEs leading to permanent discontinuation (any drug)	5 (18.5)		5 (16.7)	
Treatment-related, n (%)				
TEAEs related to any drug	27 (100.0)		27 (90.0)	
SAEs related to any drug	7 (25.9)		4 (13.3)	
Deaths related to TEAEs	0		0	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Most frequent (≥30%) all causality TEAEs[a]	**27 (100.0)**	**21 (77.8)**	**30 (100.0)**	**13 (43.3)**
Nausea	20 (74.1)	0	13 (43.3)	0
Pyrexia	13 (48.1)	1 (3.7)	7 (23.3)	0
Vomiting	11 (40.7)	1 (3.7)	4 (13.3)	0
Diarrhea	10 (37.0)	2 (7.4)	13 (43.3)	1 (3.3)
Peripheral sensory neuropathy	9 (33.3)	1 (3.7)	2 (6.7)	0
Fatigue	8 (29.6)	0	13 (43.3)	1 (3.3)
Constipation	7 (25.9)	0	13 (43.3)	1 (3.3)
Dermatitis acneiform	7 (25.9)	0	12 (40.0)	1 (3.3)

Data cutoff: 16 May 2022

[a]All grade in ≥30% of participants in either the EC + mFOFLOX6 arm or the EC + FOLFIRI arm.

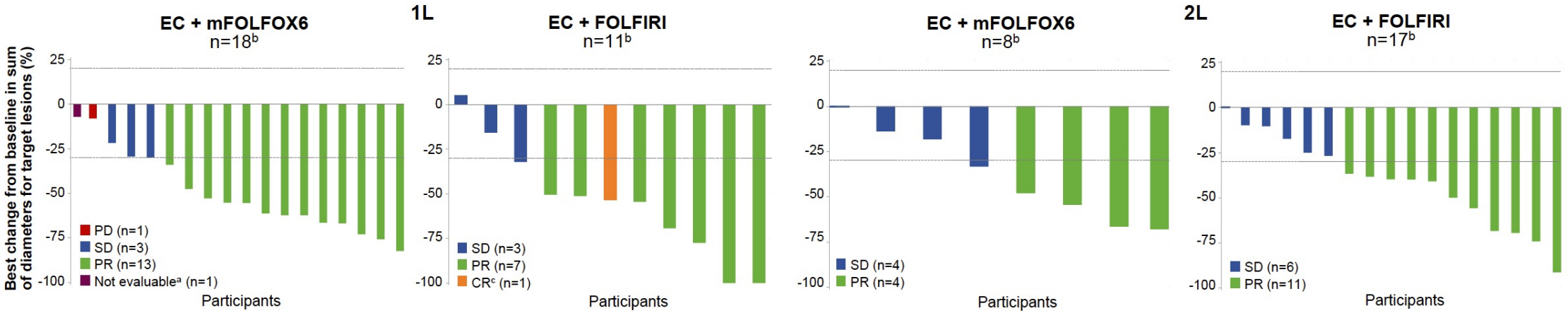
EC = encorafenib and cetuximab; TEAEs = treatment-emergent adverse events; SAEs = serious adverse events

Tabernero J et al. ESMO 2022;Abstract BBA26.

RTP RESEARCH TO PRACTICE

BREAKWATER Safety Lead-In: Overview of Response

	1L		2L	
	EC + mFOLFOX6	EC + FOLFIRI	EC + mFOLFOX6	EC + FOLFIRI
Confirmed best overall response by investigator, n (%)	**n=19**	**n=12**	**n=8**	**n=18**
ORR, % (95% CI)	68.4 (46.0–84.6)	66.7 (39.1–86.2)	50.0 (21.5–78.5)	61.1 (38.6–79.7)
CR	0	1 (8.3)	0	0
PR	13 (68.4)	7 (58.3)	4 (50.0)	11 (61.1)
SD	3 (15.8)	3 (25.0)	4 (50.0)	6 (33.3)
PD	1 (5.3)	0	0	0
Non-CR/non-PD	1 (5.3)	1 (8.3)	0	0
Not evaluable[a]	1 (5.3)	0	0	1 (5.6)
Responders	**n=13**	**n=8**	**n=4**	**n=11**
mTTR, weeks (range)	6.9 (5.9–25.9)	6.6 (6.1–7.0)	9.4 (6.4–18.9)	12.9 (6.1–37.0)
mDOR, months (95% CI)	7.6 (4.1–not estimable)	Not estimable (10.6–not estimable)	Not estimable (2.7–not estimable)	Not estimable (3.4–not estimable)
≥6 months, n (%)	6 (46.2)	7 (87.5)	2 (50.0)	6 (54.5)



Data cutoff: 16 May 2022

[a]Reasons included SD <6 weeks after treatment start date (1 patient in the EC + mFOLFOX6 arm in the 1L setting) and early death (1 patient in the EC + FOLFIRI arm in the 2L setting). [b]Only includes participants with target lesions at baseline and ≥1 non-missing post-baseline % change from baseline assessment up to time of PD or new anti-cancer therapy. [c]This participant had a nodal target lesion that did not completely disappear but became non-pathological by size (<10 mm).

Tabernero J et al. ESMO 2022;Abstract BBA26.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

WORLD CONGRESS ON Gastrointestinal Cancer

Abstract LBA2

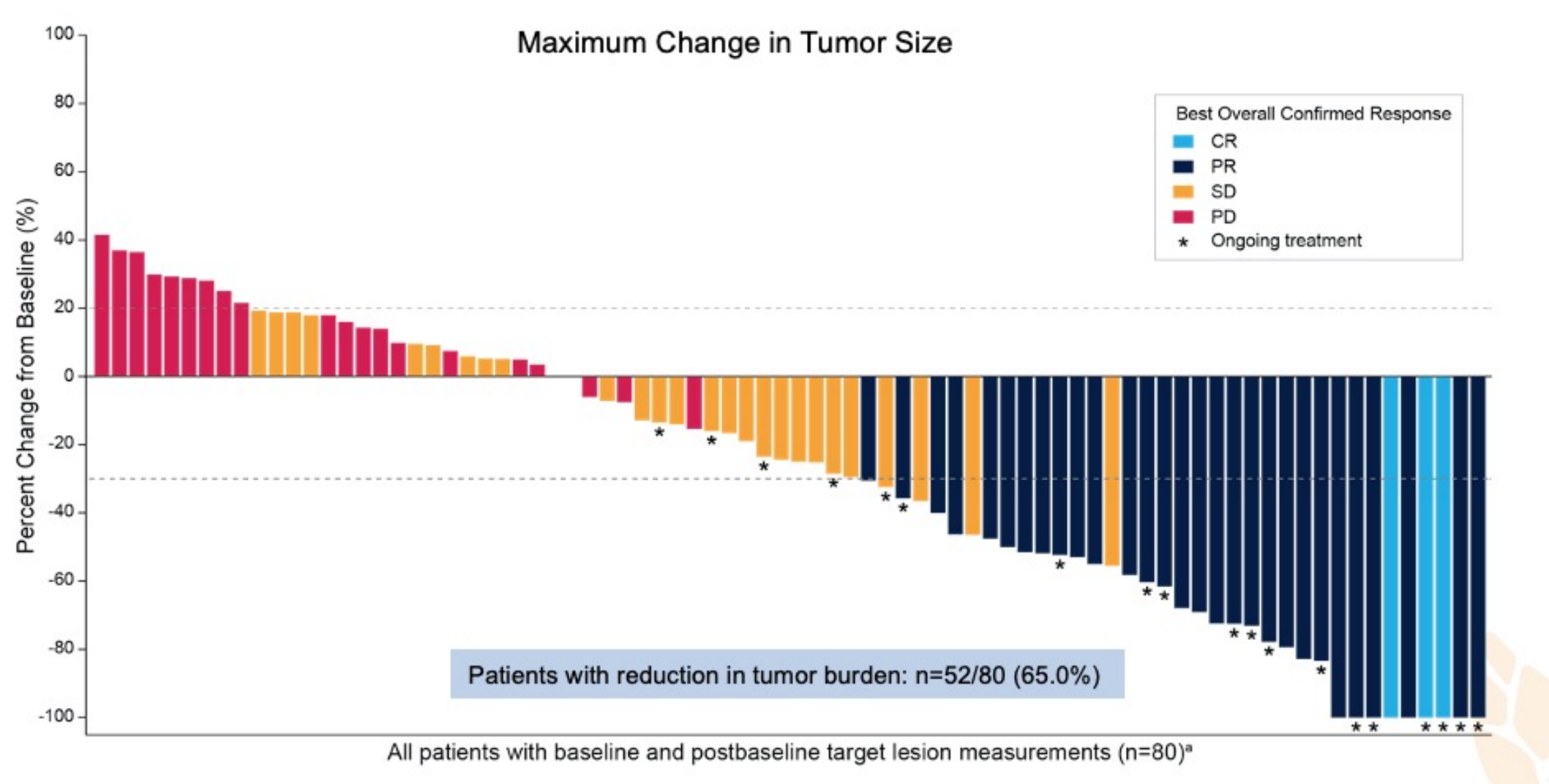
Primary analysis of MOUNTAINEER: A phase 2 study of tucatinib and trastuzumab for HER2-positive mCRC

John H. Strickler, Andrea Cercek, Salvatore Siena, Thierry Andre, Kimmie Ng, Eric Van Cutsem, Christina Wu, Andrew Scott Paulson, Joleen M. Hubbard, Andrew L. Coveler, Christos Fountzilas, Adel Kardosh, Pashtoon Murtaza Kasi, Heinz-Josef Lenz, Kristen Ciombor, Elena Elez, David L. Bajor, Michael Stecher, Wentao Feng, Tanios S. Bekaii-Saab

European Society of Medical Oncology World Congress on Gastrointestinal Cancer. Jun 29-Jul 2, 2022. Abstract LBA-2

RTP RESEARCH TO PRACTICE

MOUNTAINEER: Tucatinib with Trastuzumab Change in Tumor Size



Strickler JH et al. ESMO GI 2022;Abstract LBA-2.

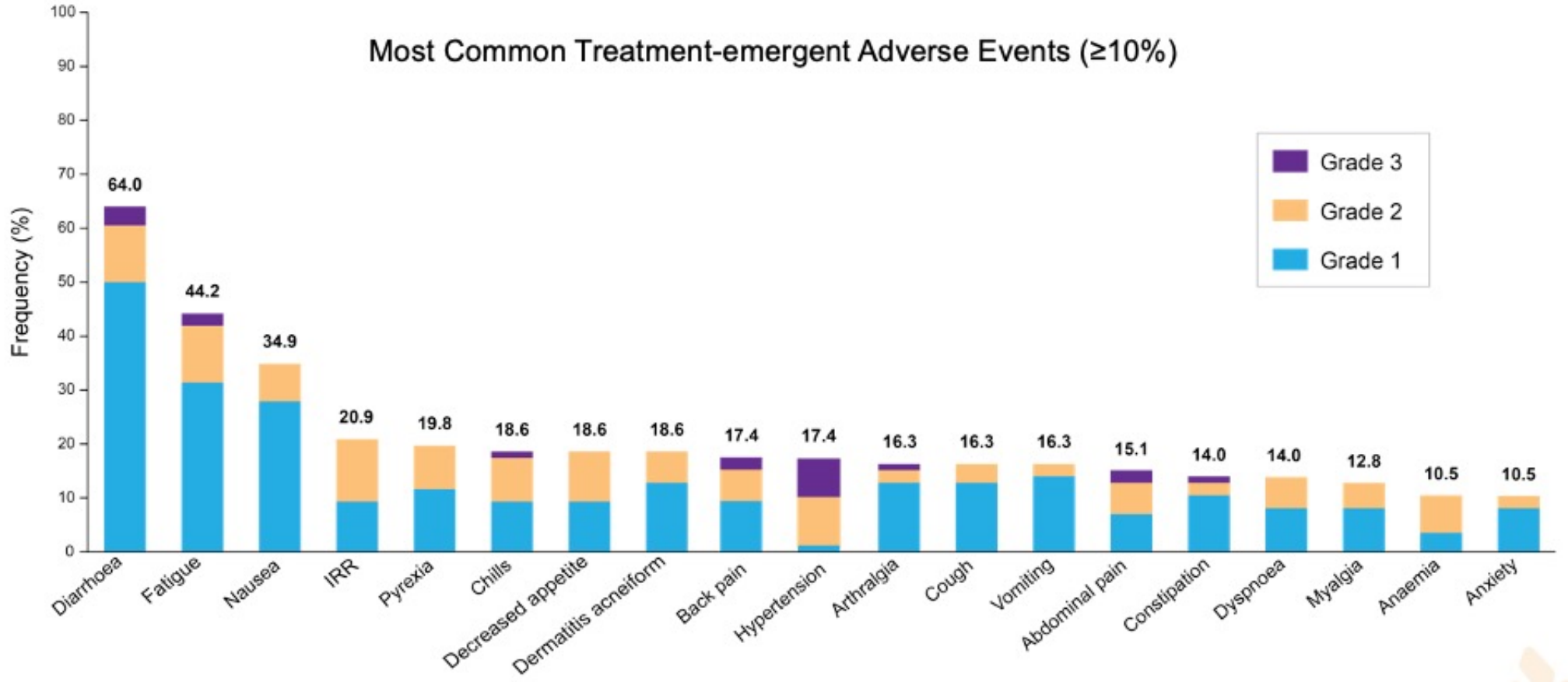
MOUNTAINEER: Tucatinib with Trastuzumab Safety Summary

TEAEs, n (%)	Tucatinib + Trastuzumab Cohorts A+B (n=86)
Any grade AEs	82 (95.3)
Tucatinib-related	63 (73.3)
Trastuzumab-related	58 (67.4)
Grade ≥3 AEs	33 (38.4)
Tucatinib-related	8 (9.3)
Trastuzumab-related	6 (7.0)
SAEs	19 (22.1)
Tucatinib-related	3 (3.5)
Trastuzumab-related	2 (2.3)
AEs leading to study treatment discontinuation[a,b]	5 (5.8)
AEs leading to tucatinib dose modification	22 (25.6)
Deaths due to AEs	0

a TEAEs leading to discontinuation of tucatinib included alanine aminotransferase increase (2.3%), COVID-19 pneumonia (1.2%), cholangitis (1.2%), and fatigue (1.2%); b TEAEs leading to discontinuation of trastuzumab included alanine aminotransferase increase (2.3%) and COVID-19 pneumonia (1.2%)

Strickler JH et al. ESMO GI 2022;Abstract LBA-2.

MOUNTAINEER: Most Common TEAEs (≥10%) with Tucatinib and Trastuzumab



- Most common tucatinib-related AEs (≥10%): diarrhoea (52.3%), fatigue (29.1%), nausea (18.6%), and dermatitis acneiform (17.4%)
  - Grade ≥3 tucatinib-related AEs (≥2%): alanine aminotransferase increase (2.3%) and diarrhoea (2.3%)

Strickler JH et al. ESMO GI 2022;Abstract LBA-2.

Integration of Immune Checkpoint Inhibitors into the Management of mCRC

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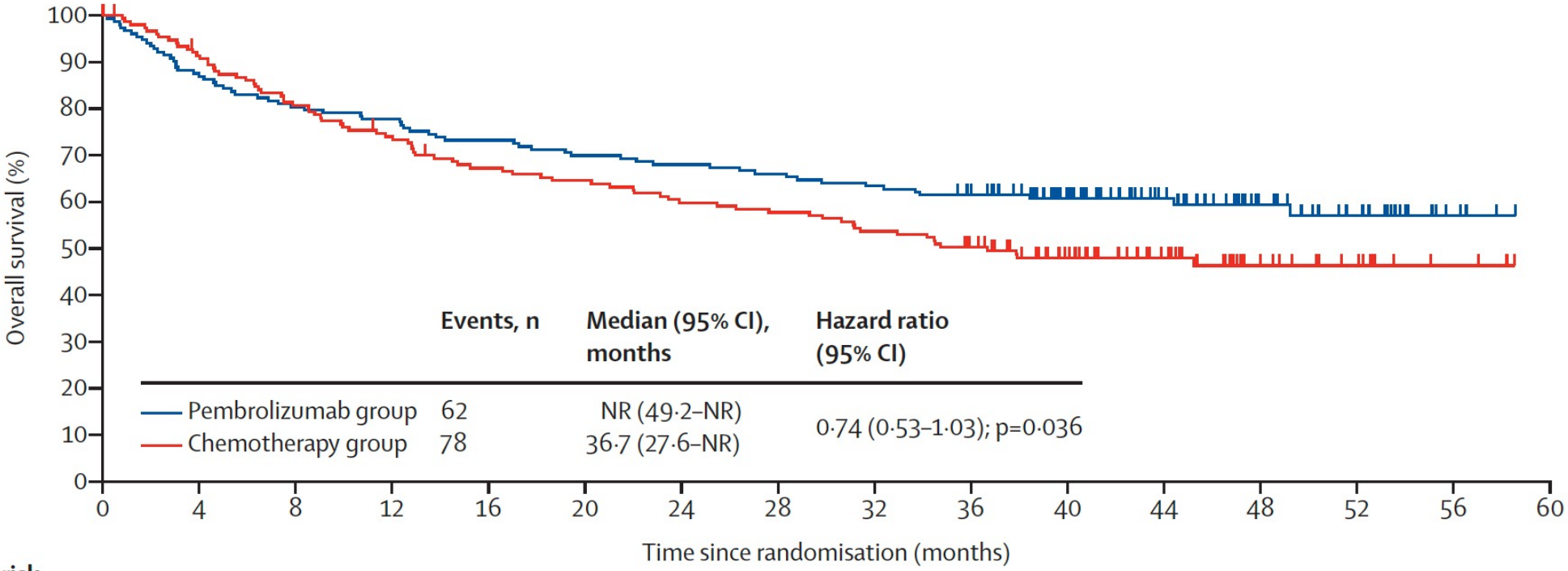
Lancet Oncol 2022 April 12;23(5):659-70.

Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study

*Luis A Diaz Jr, Kai-Keen Shiu, Tae-Won Kim, Benny Vittrup Jensen, Lars Henrik Jensen, Cornelis Punt, Denis Smith, Rocio Garcia-Carbonero, Manuel Benavides, Peter Gibbs, Christelle de la Fourchardiere, Fernando Rivera, Elena Elez, Dung T Le, Takayuki Yoshino, Wen Yan Zhong, David Fogelman, Patricia Marinello, Thierry Andre, on behalf of the KEYNOTE-177 Investigators**

KEYNOTE-177 Coprimary Endpoint: Final Analysis of Overall Survival (Intent-to-Treat Population)



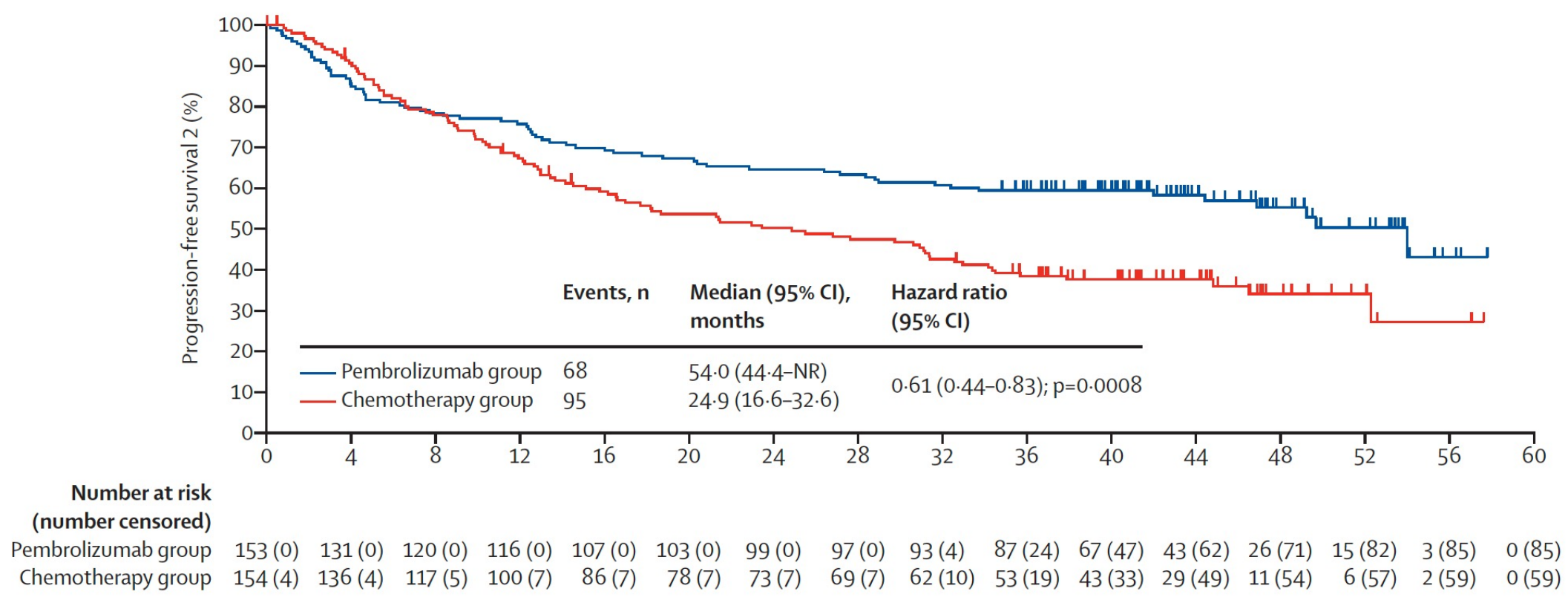
Number at risk (number censored)																
Pembrolizumab group	153 (0)	134 (0)	123 (0)	119 (0)	112 (0)	107 (0)	104 (0)	101 (0)	97 (2)	92 (23)	70 (45)	48 (64)	28 (75)	16 (78)	4 (91)	0 (91)
Chemotherapy group	154 (4)	137 (4)	121 (5)	110 (6)	99 (6)	95 (6)	88 (6)	85 (6)	79 (9)	71 (24)	53 (41)	36 (58)	18 (65)	11 (73)	3 (76)	0 (76)

At final analysis, OS with pembrolizumab versus chemotherapy did not meet the one-sided α boundary of 0.025 required for superiority.

Diaz LA Jr et al. *Lancet Oncol* 2022 April 12;23(5):659-70.

RTP RESEARCH TO PRACTICE

KEYNOTE-177: Time to Progression (PFS2)



At the final analysis, median progression-free survival (PFS) was longer with pembrolizumab (16.5 mo) than with chemotherapy (8.2 mo); however, because superiority was met at the second interim analysis, superiority was not formally tested at the final analysis (HR 0.59).

PFS2 = disease progression on next line of therapy after first progression

Diaz LA Jr et al. *Lancet Oncol* 2022 April 12;23(5):659-70.

RTP RESEARCH TO PRACTICE

Selection and Sequencing of Therapy for Patients with Multiregimen-Relapsed mCRC

Key Studies of Anti-EGFR Rechallenge for Metastatic CRC

Study	Patients enrolled	Anti-EGFR mAb-free interval	Outcomes
PURSUIT	• 50 RAS, BRAF WT	• ≥4 mo interval	ORR: 14% mPFS: 3.6 mo
CRICKET	• 13 RAS WT ctDNA • 12 RAS mut ctDNA	• ctDNA RAS/BRAF status before rechallenge • ≥4 mo interval	RAS ctDNA WT vs ctDNA mut ORR: 31% vs 0% mPFS: 4 vs 1.9 mo mOS: 12.5 vs 5.2 mo
CAVE	• 48 ctDNA WT: RAS, BRAF, EGFR S492R • 19 ctDNA mut	• >4 mo interval	ctDNA WT: • mPFS: 4.1 mo • mOS: 17.3 mo ctDNA mut: • mPFS: 3 mo • mOS: 10.4 mo
CHRONOS	• 27 ctDNA WT: RAS, BRAF, EGFR-ECD	• Median 11.5 mo interval	ORR: 30% mPFS: 16 wk mOS: 55 wk

mAb = monoclonal antibody; WT = wild type; mut = mutant

Doleschal B et al. *Front Oncol* 2022;[Online ahead of print].

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

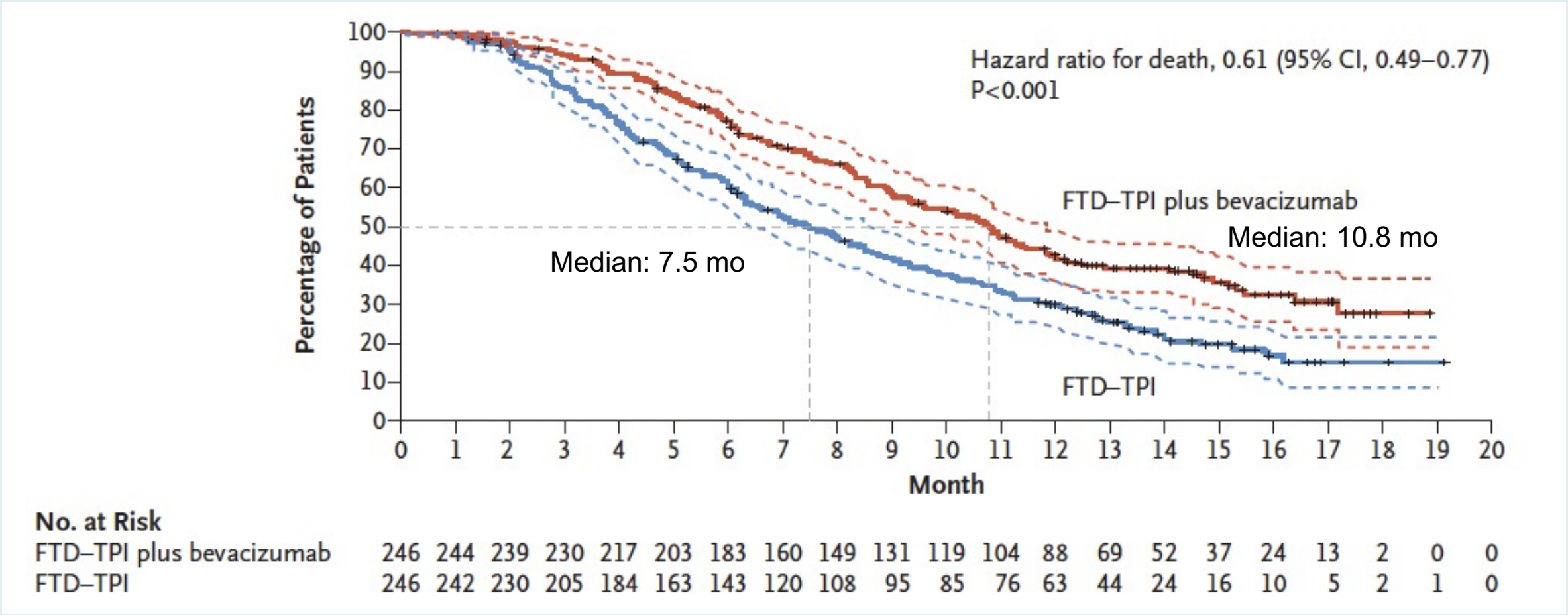
ORIGINAL ARTICLE

Trifluridine–Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer

Gerald W. Prager, M.D., Julien Taieb, M.D., Ph.D., Marwan Fakih, M.D., Fortunato Ciardiello, M.D., Ph.D., Eric Van Cutsem, M.D., Ph.D., Elena Elez, M.D., Ph.D., Felipe M. Cruz, M.D., Ph.D., Lucjan Wyrwicz, M.D., Ph.D., Daniil Stroyakovskiy, M.D., Ph.D., Zsuzsanna Pápai, M.D., Pierre-Guillaume Poureau, M.D., Gabor Liposits, M.D., Chiara Cremolini, M.D., Ph.D., Igor Bondarenko, M.D., Ph.D., Dominik P. Modest, M.D., Karim A. Benhadji, M.D., Nadia Amellal, M.D., Catherine Leger, M.Sc., Loïck Vidot, M.Sc., and Josep Tabernero, M.D., Ph.D., for the SUNLIGHT Investigators*

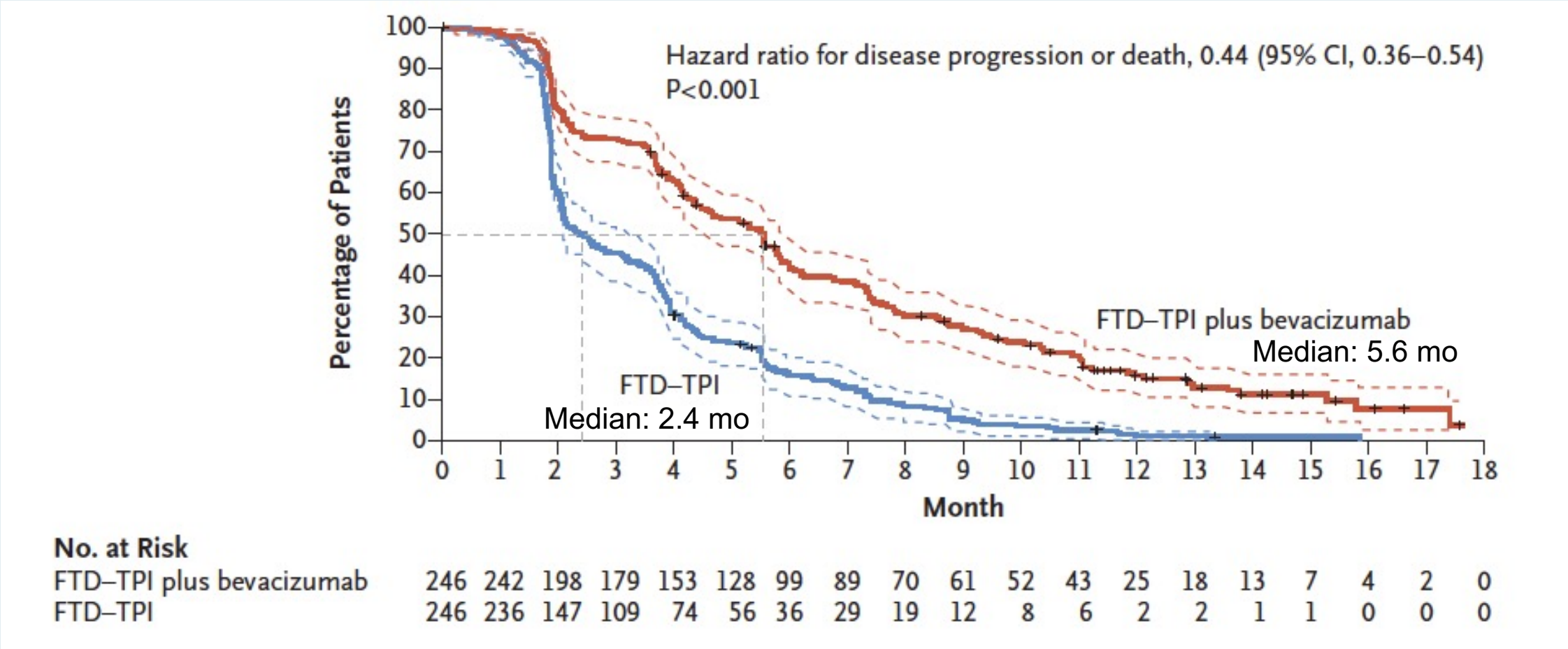
N Engl J Med 2023;388(18):1657-67.

SUNLIGHT Primary Endpoint: Overall Survival



Prager GW et al. *N Engl J Med* 2023;388(18):1657-67.

SUNLIGHT: Progression-Free Survival



Prager GW et al. *N Engl J Med* 2023;388(18):1657-67.

Other Considerations in the Management of CRC; Promising Investigational Strategies

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Circulating Tumor DNA Dynamics as an Early Predictor of Recurrence in Patients with Radically Resected Colorectal Cancer: Updated Results from GALAXY Study in the CIRCULATE-Japan

Oki E et al.

ASCO 2023;Abstract 3521. (Poster Discussion)

Hall D2

June 5, 2023

nature medicine 2023 January 16;[Online ahead of print].

Article https://doi.org/10.1038/s41591-022-02115-4

Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer

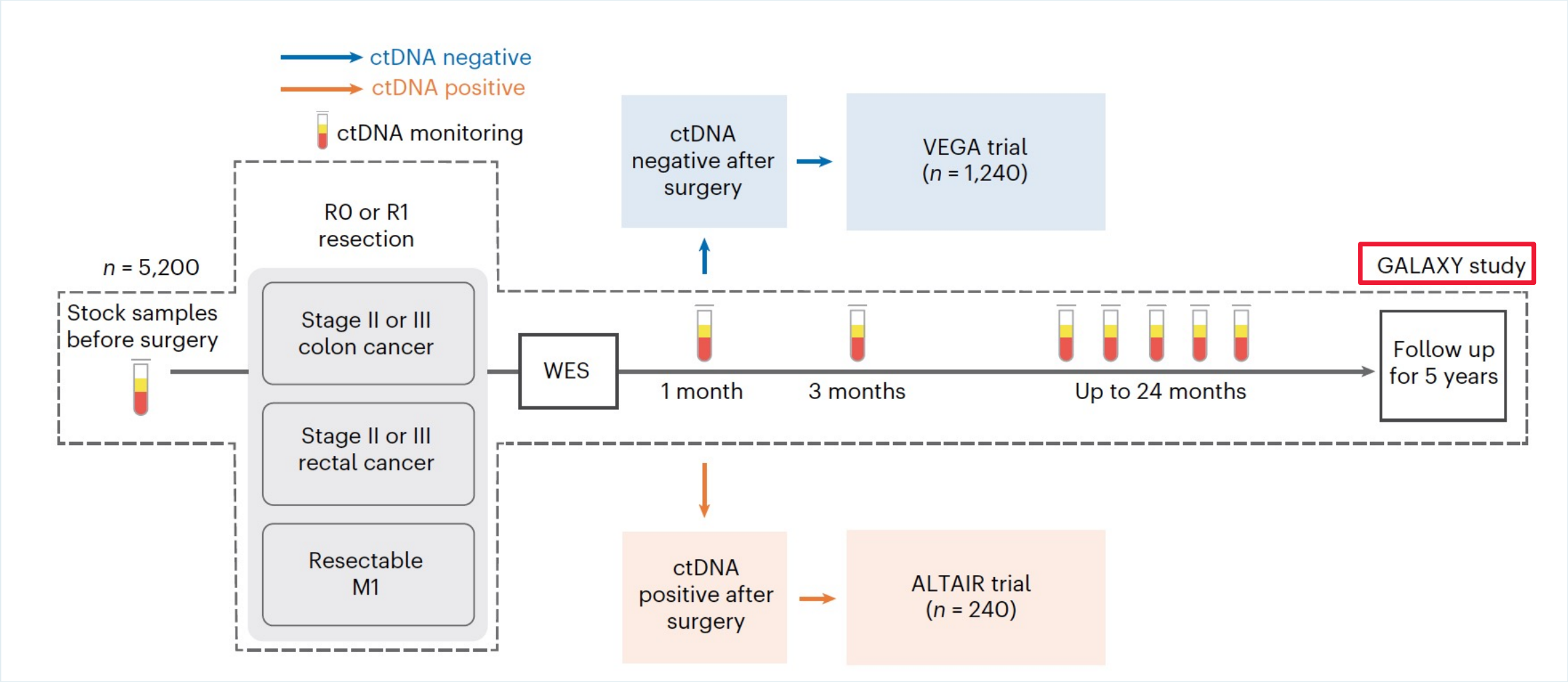
Received: 28 July 2022

Accepted: 1 November 2022

Published online: 16 January 2023

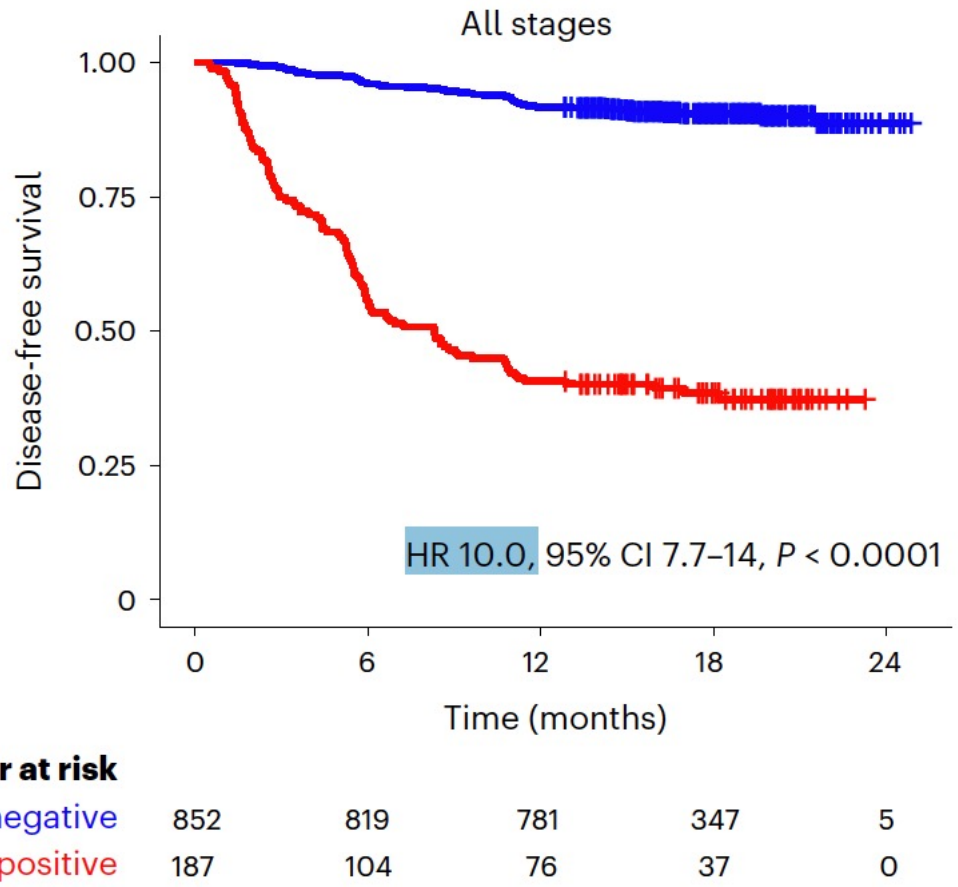
Daisuke Kotani[1,17], Eiji Oki[2,17] ✉, Yoshiaki Nakamura[1,3,17], Hiroki Yukami[1,4], Saori Mishima[1], Hideaki Bando[1,3], Hiromichi Shirasu[5], Kentaro Yamazaki[5], Jun Watanabe[6], Masahito Kotaka[7], Keiji Hirata[8], Naoya Akazawa[9], Kozo Kataoka[10], Shruti Sharma[11], Vasily N. Aushev[11], Alexey Aleshin[11], Toshihiro Misumi[12], Hiroya Taniguchi[13], Ichiro Takemasa[14], Takeshi Kato[15], Masaki Mori[16] & Takayuki Yoshino[1]

Overview of CIRCULATE-JAPAN Study



Kotani D et al. *Nat Med* 2023 January 16;[Online ahead of print].

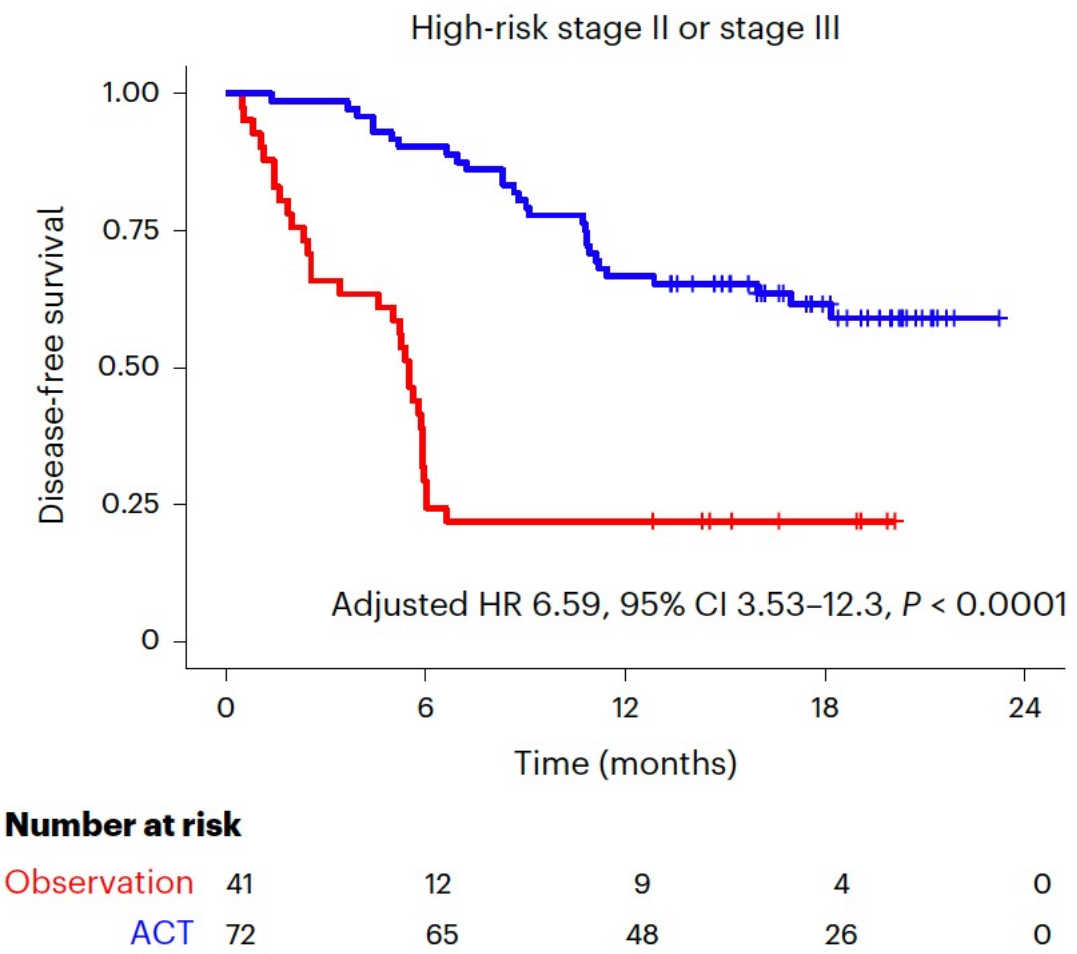
GALAXY: ctDNA-Based Minimal Residual Disease Is Predictive of Survival Outcomes Among Postsurgical Patients with CRC



ctDNA	Number of events	6M-DFS (95% CI)	12M-DFS (95% CI)	18M-DFS (95% CI)
ctDNA negative	81 out of 852	96.1% (94.6–97.2)	91.7% (89.6–93.3)	90.5% (88.3–92.3)
ctDNA positive	115 out of 187	55.6% (48.2–62.64)	40.6% (33.6–47.6)	38.4% (31.4–45.5)

Kotani D et al. *Nat Med* 2023 January 16;[Online ahead of print].

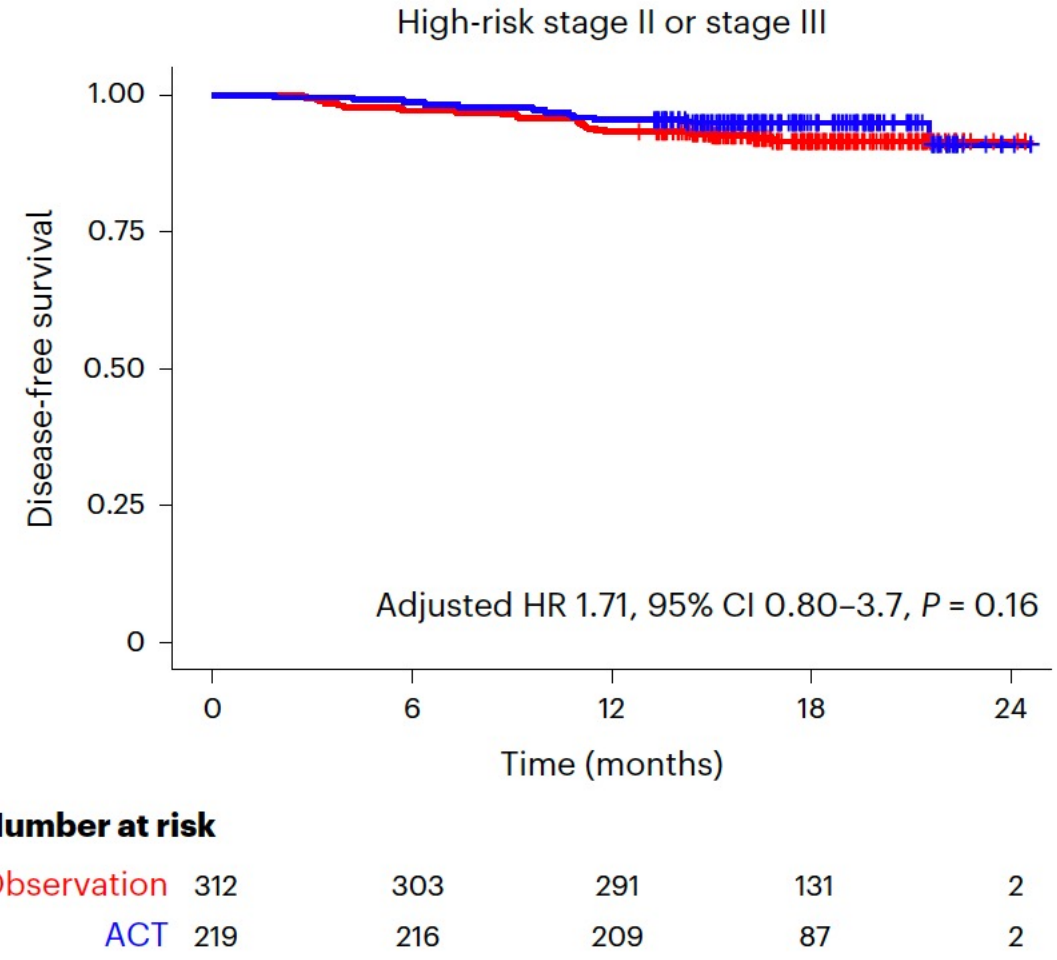
GALAXY: Disease-Free Survival — ctDNA-Positive 4 Weeks After Surgery



Treatment	Number of events	6M-DFS (95% CI)	12M-DFS (95% CI)	18M-DFS (95% CI)
Observation	32 out of 41	29.3% (16.4–43.4)	22.0% (10.9–35.5)	22.0% (10.9–35.5)
ACT	28 out of 72	90.3% (80.7–95.2)	66.7% (54.5–76.3)	61.6% (49.0–71.9)

Kotani D et al. *Nat Med* 2023 January 16;[Online ahead of print].

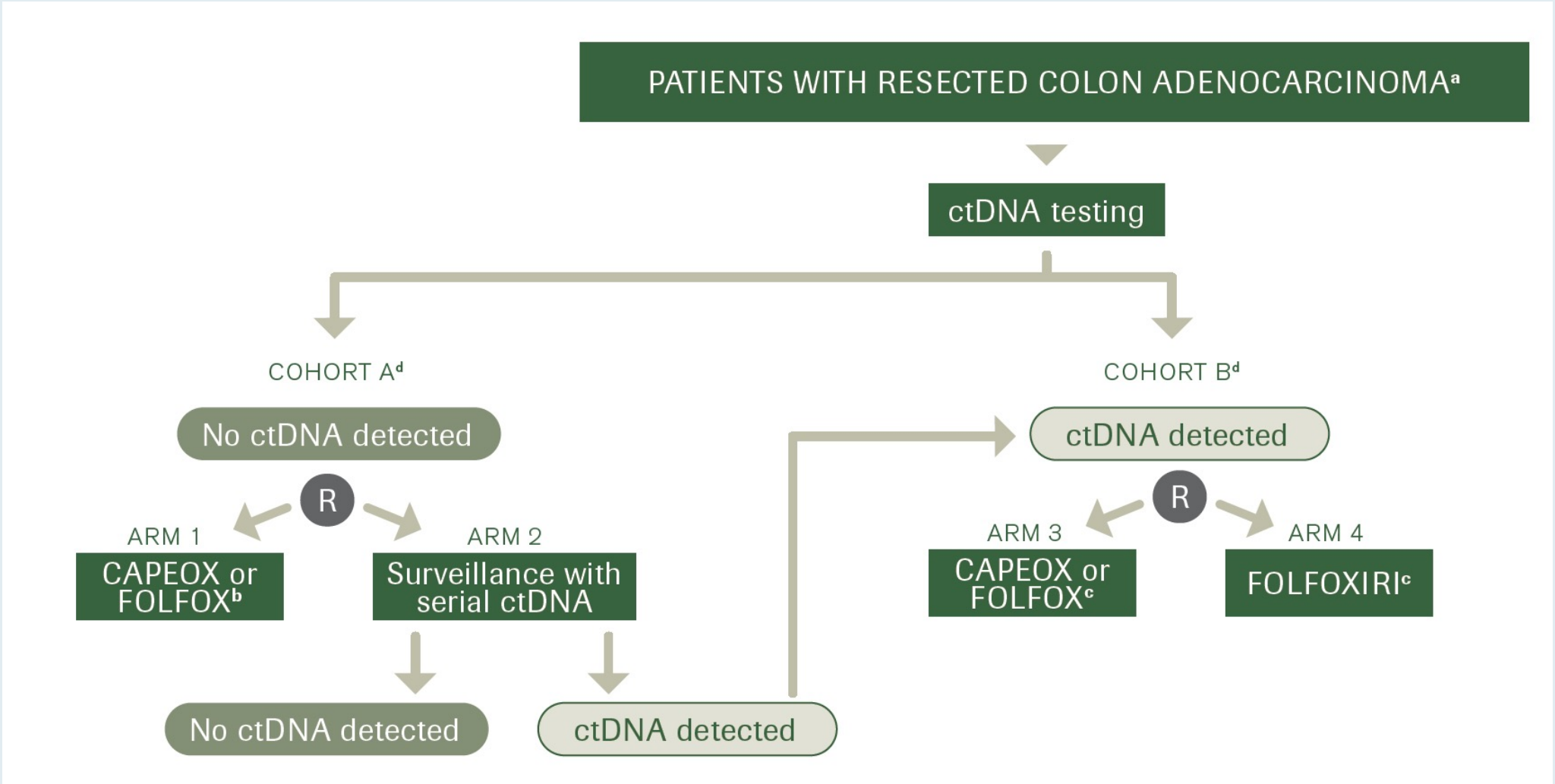
GALAXY: Disease-Free Survival — ctDNA-Negative 4 Weeks After Surgery



Treatment	Number of events	6M-DFS (95% CI)	12M-DFS (95% CI)	18M-DFS (95% CI)
Observation	25 out of 312	97.1% (94.5–98.5)	93.3% (89.9–95.6)	91.5% (87.6–94.2)
ACT	12 out of 219	98.6% (95.8–99.6)	95.4% (91.7–97.5)	94.9% (91.0–97.2)

Kotani D et al. *Nat Med* 2023 January 16;[Online ahead of print].

CIRCULATE-US



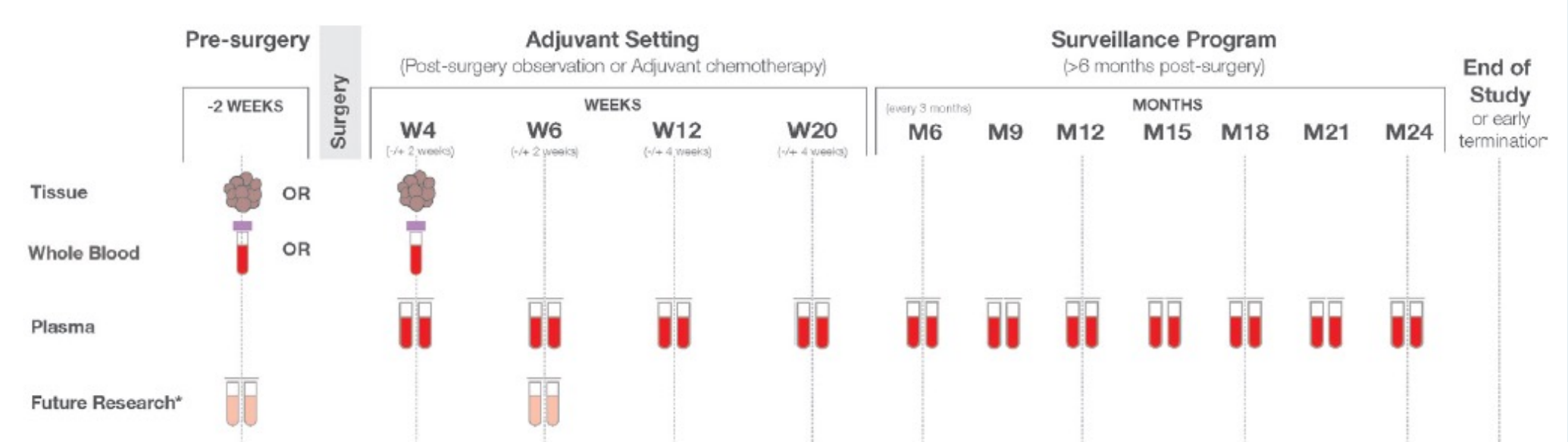
Sahin IH et al. *Oncology* 2022;36(10):604-9.

RTP RESEARCH TO PRACTICE

BESPOKE CRC Prospective, Case-Controlled Observational Study

Estimated enrollment (N = 2,000)

- Stage I-IV CRC or Stage IV CRC with oligometastatic disease eligible for post-operative systemic therapy



www.clinicaltrials.gov. NCT04264702. Accessed February 2023.
Kasi PM et al. *BMJ Open* 2021;11:e047831.

RTP RESEARCH TO PRACTICE

Efficacy of Panitumumab in Patients with Left-Sided Disease, MSS/MSI-L, and RAS/BRAF WT: A Biomarker Study of the Phase III PARADIGM Trial

Yamazaki K et al.

ASCO 2023;Abstract 3508. (Oral)

Hall D2

June 4, 2023, 11:12 AM ET

2022 ASCO® ANNUAL MEETING

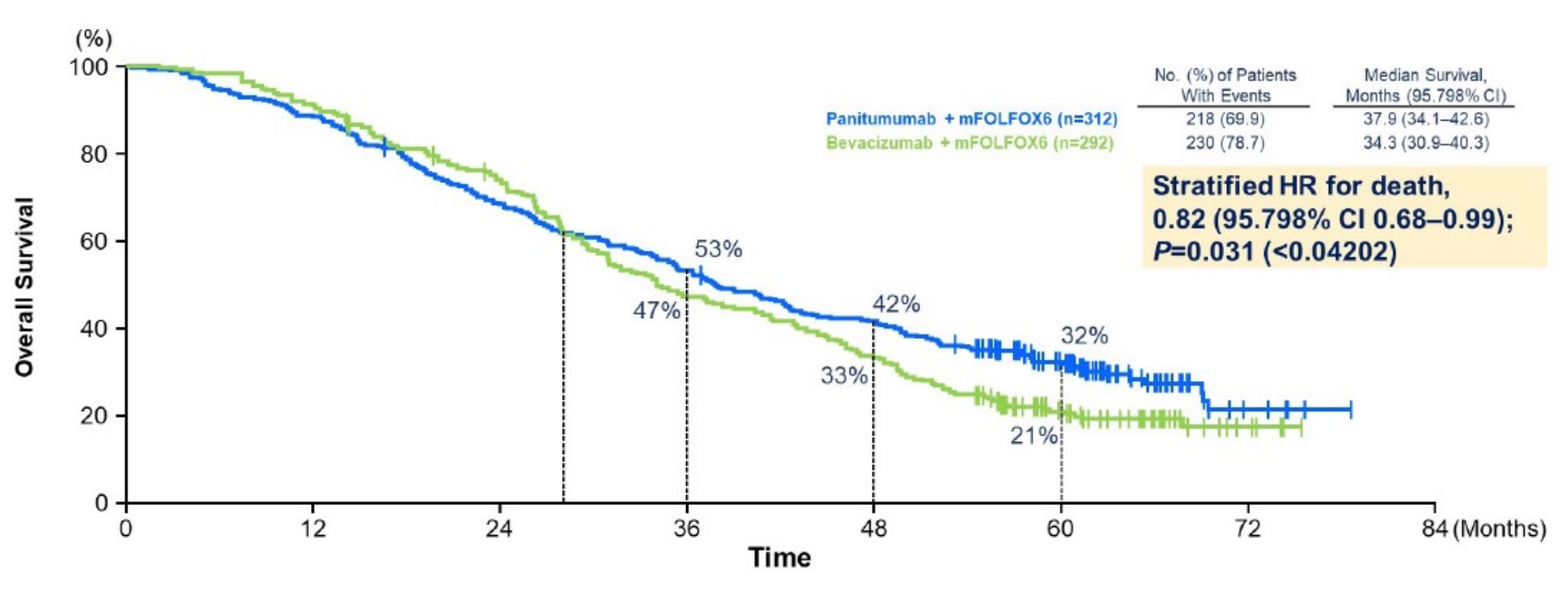
Abstract LBA1

Panitumumab plus mFOLFOX6 versus Bevacizumab plus mFOLFOX6 as first-line treatment in patients with *RAS* wild-type metastatic colorectal cancer: results from the phase 3 PARADIGM trial

Takayuki Yoshino[1], Jun Watanabe[2], Kohei Shitara[1], Kentaro Yamazaki[3], Hisatsugu Ohori[4], Manabu Shiozawa[5], Hirofumi Yasui[4], Eiji Oki[6], Takeo Sato[7], Takeshi Naitoh[8], Yoshito Komatsu[9], Takeshi Kato[10], Masamitsu Hihara[11], Junpei Soeda[11], Kouji Yamamoto[12], Kiwamu Akagi[13], Atsushi Ochiai[14], Hiroyuki Uetake[15], Katsuya Tsuchihara[16], Kei Muro[17]

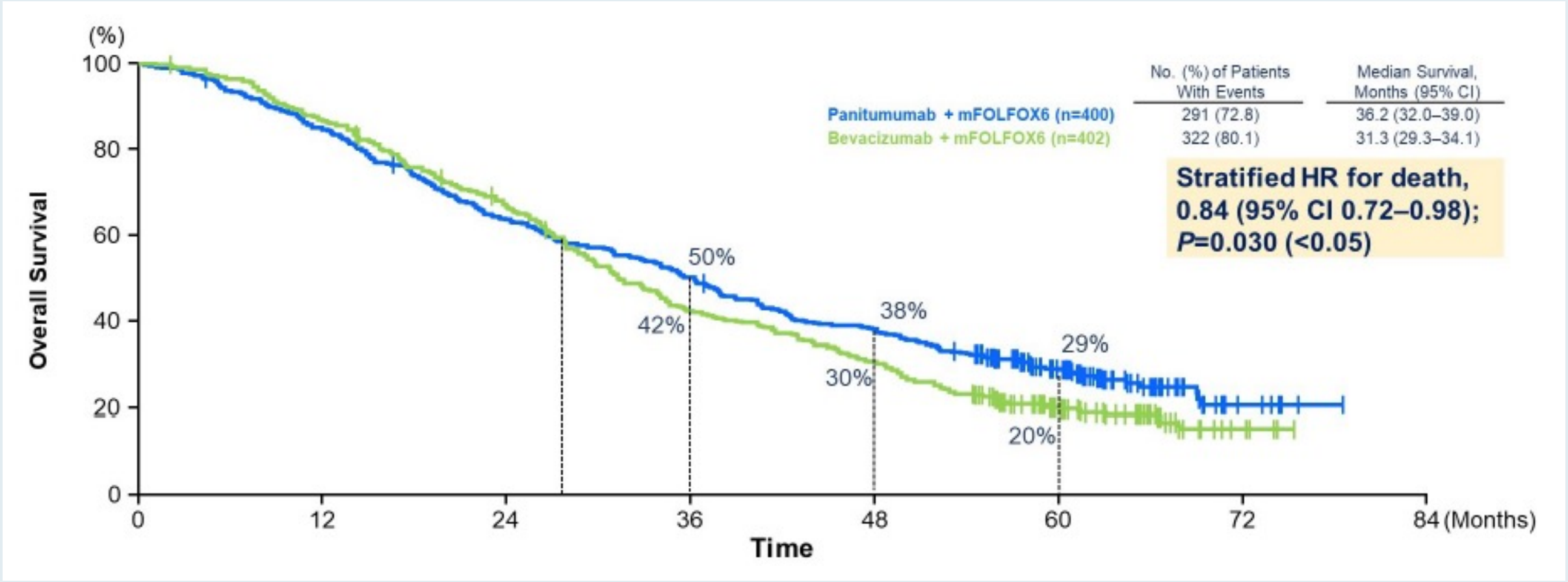
RTP RESEARCH TO PRACTICE

PARADIGM: Overall Survival in Left-Sided Population (Primary Endpoint 1)



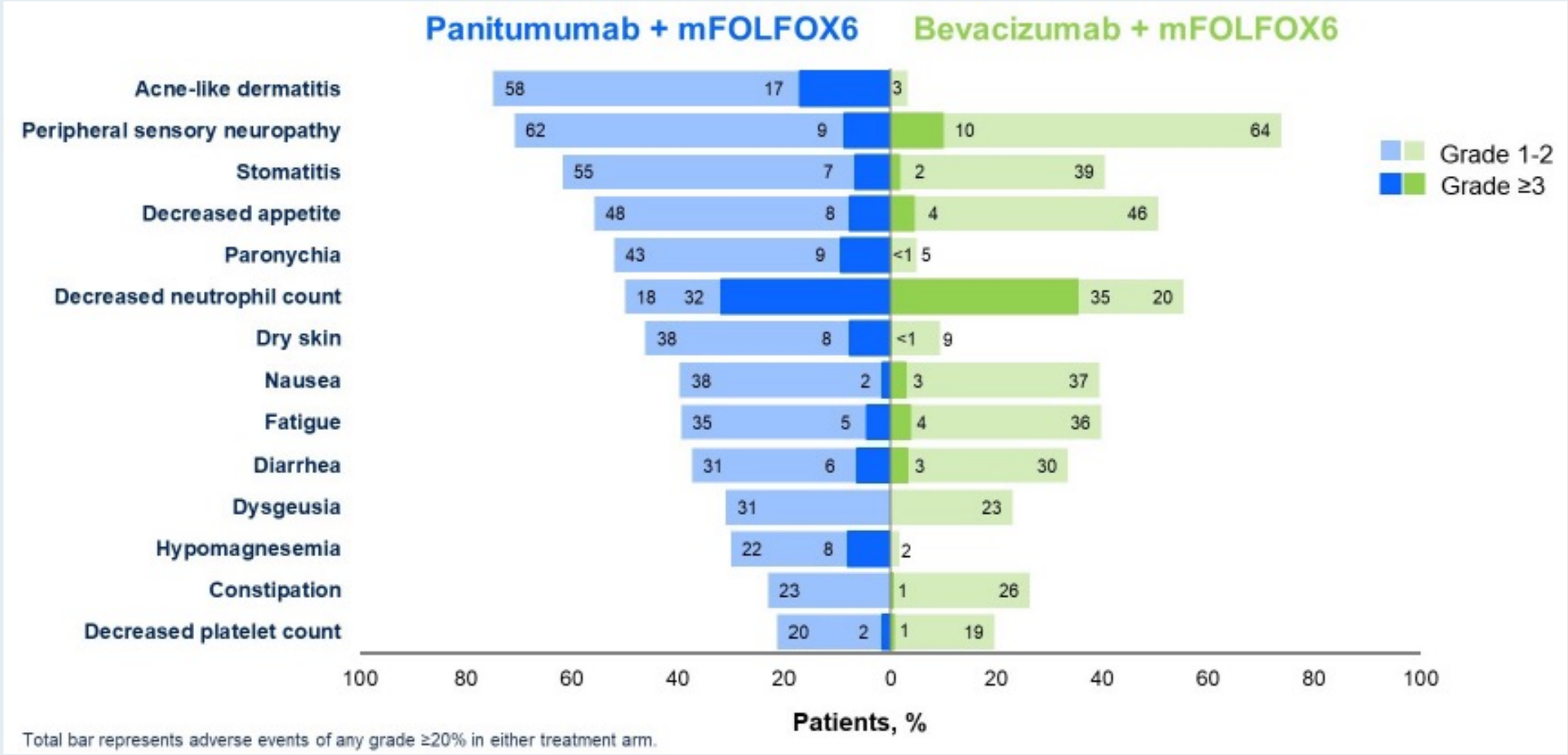
Yoshino T et al. ASCO 2022;Abstract LBA1.

PARADIGM: Overall Survival in Overall Population (Primary Endpoint 2)



Yoshino T et al. ASCO 2022;Abstract LBA1.

PARADIGM: Adverse Events Reported in ≥20% of Patients



Yoshino T et al. ASCO 2022;Abstract LBA1.

Fruquintinib Global Phase III FRESCO-2 Study Has Met Its Primary Endpoint in Metastatic Colorectal Cancer

Press Release: August 8, 2022

"[Manufacturer] today announces that the pivotal global Phase 3 FRESCO-2 trial evaluating the investigational use of fruquintinib met its primary endpoint of overall survival ('OS') in patients with advanced, refractory metastatic colorectal cancer ('CRC').

The FRESCO-2 study was a multi-regional clinical trial conducted in the U.S., Europe, Japan and Australia that investigated fruquintinib plus best supportive care ('BSC') vs placebo plus BSC in patients with metastatic CRC who had progressed on standard chemotherapy and relevant biologic agents and who had progressed on, or were intolerant to, TAS-102 and/or regorafenib. In addition to OS, a statistically-significant improvement in progression-free survival ('PFS'), a key secondary endpoint, was observed. The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported studies."

https://www.hutch-med.com/fresco-2-met-primary-endpoint/

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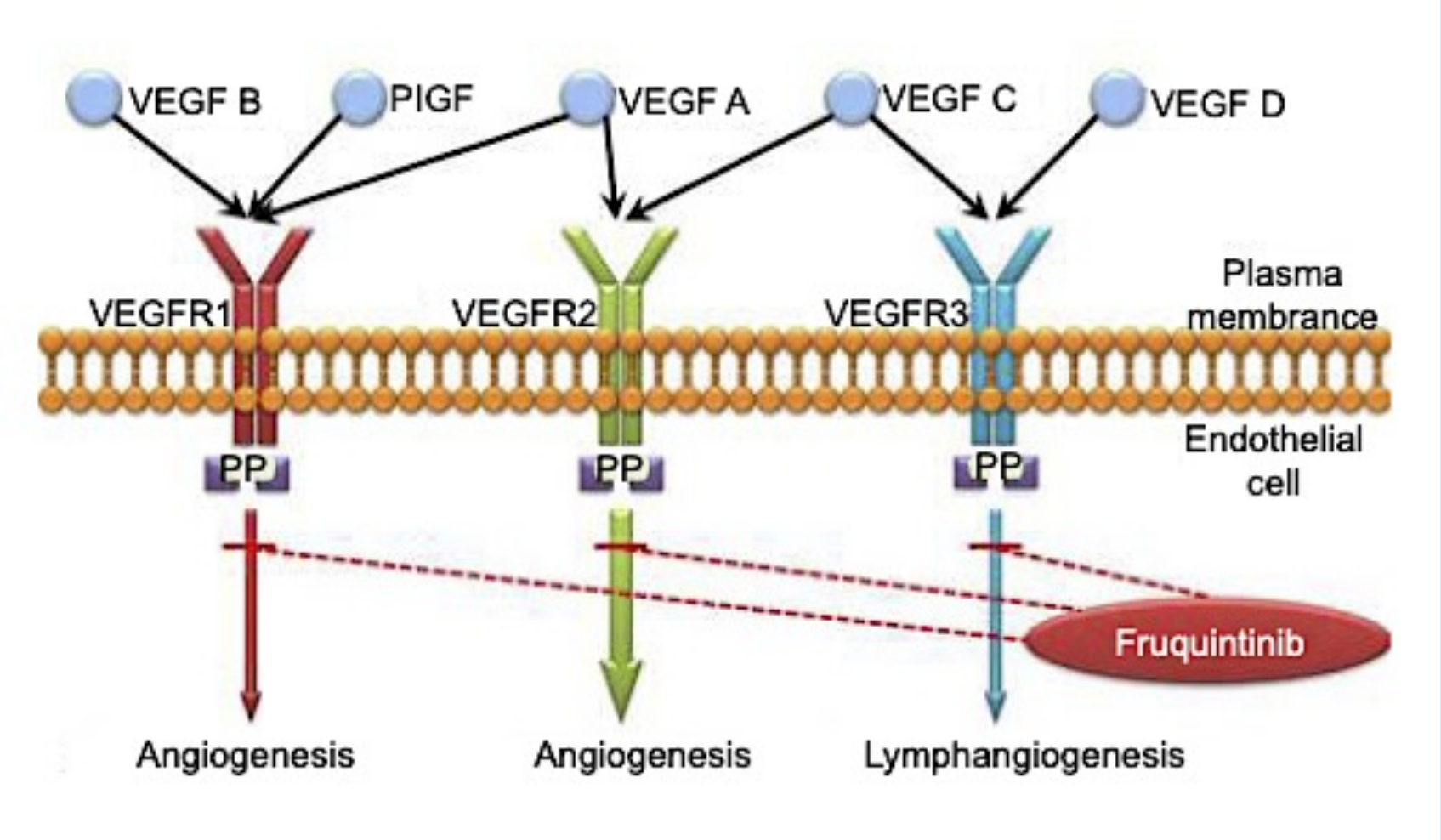
Molecular Targets of Fruquintinib



Zhang Y et al. *Cancer Manag Res* 2019;11:7787-803.

Georges Azzi, MD
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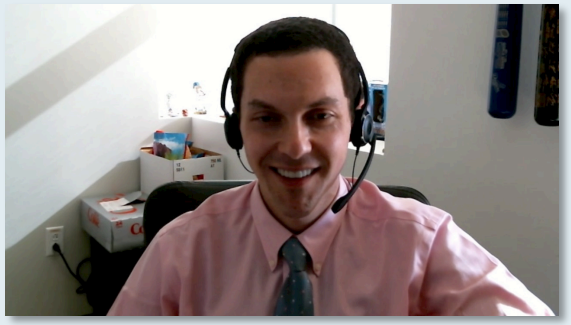
Fountain Valley, California

Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida



Jeremy Lorber, MD
Cedars-Sinai Medical Center
Beverly Hills, California

Farshid Dayyani, MD, PhD
Stern Center for Cancer Clinical Trials and Research
Orange, California

Swati Vishwanathan, MD
WVU Medicine
Bridgeport, West Virginia

Sunil Gandhi, MD
Florida Cancer Specialists
Lecanto, Florida

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RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Management of Soft Tissue Sarcoma and Related Connective Tissue Disorders

Tuesday, May 23, 2023
5:00 PM – 6:00 PM ET

Faculty

Brian Van Tine, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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

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