Meet The Professor
Optimizing the Management of Colorectal Cancer

Wednesday, March 22, 2023
5:00 PM – 6:00 PM ET

Faculty

John Strickler, 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, 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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Dr Strickler — Disclosures

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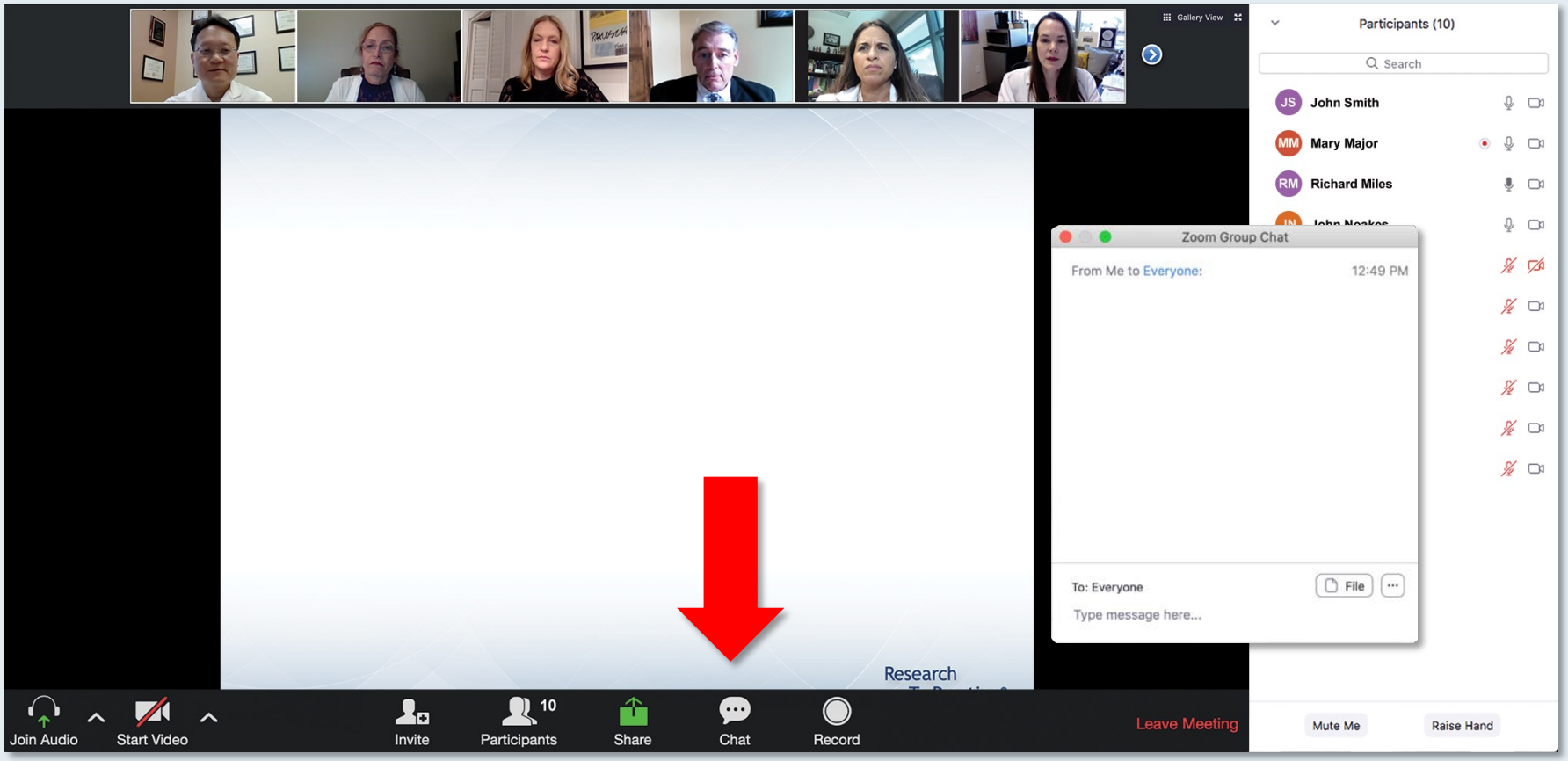

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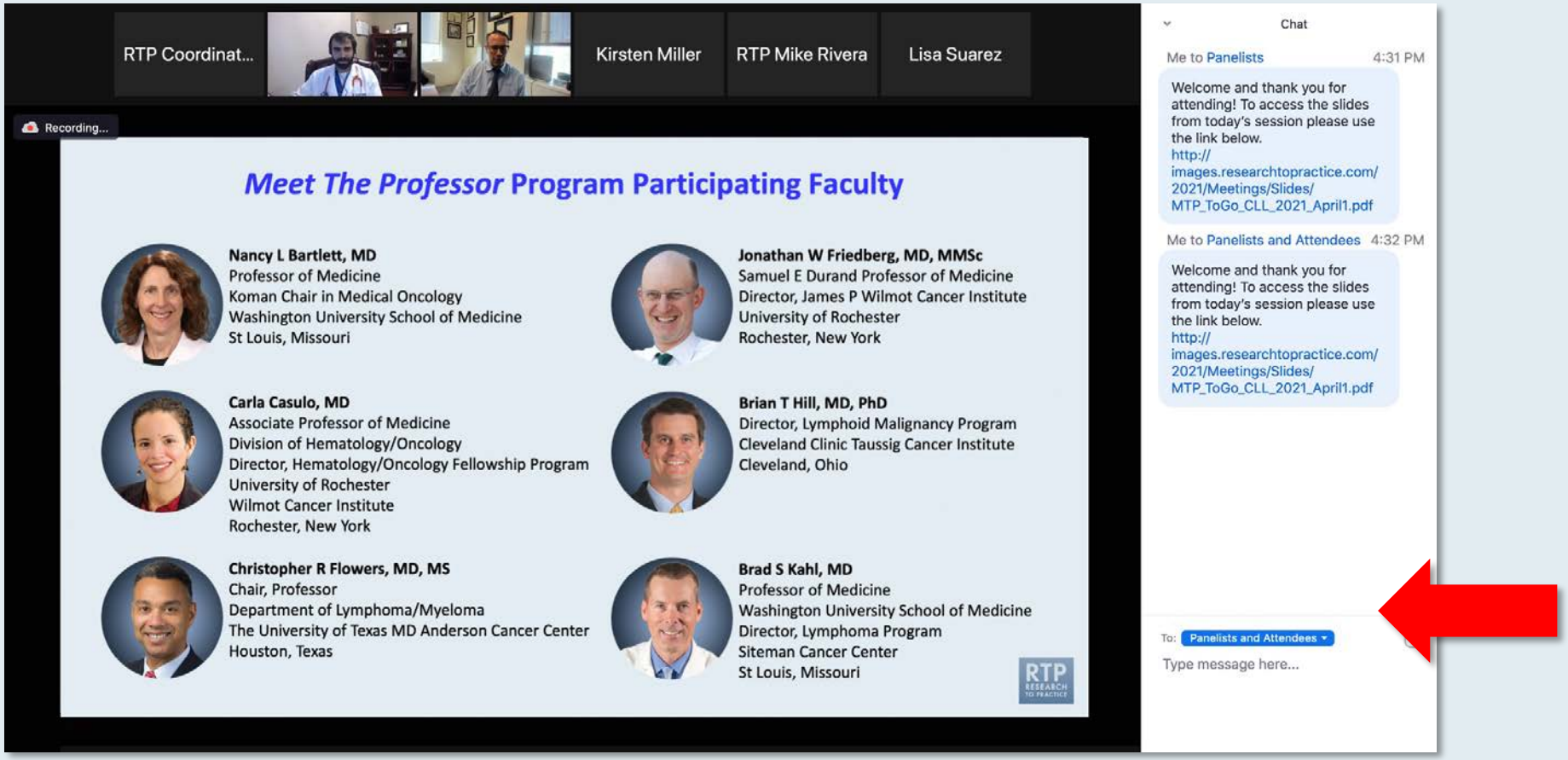

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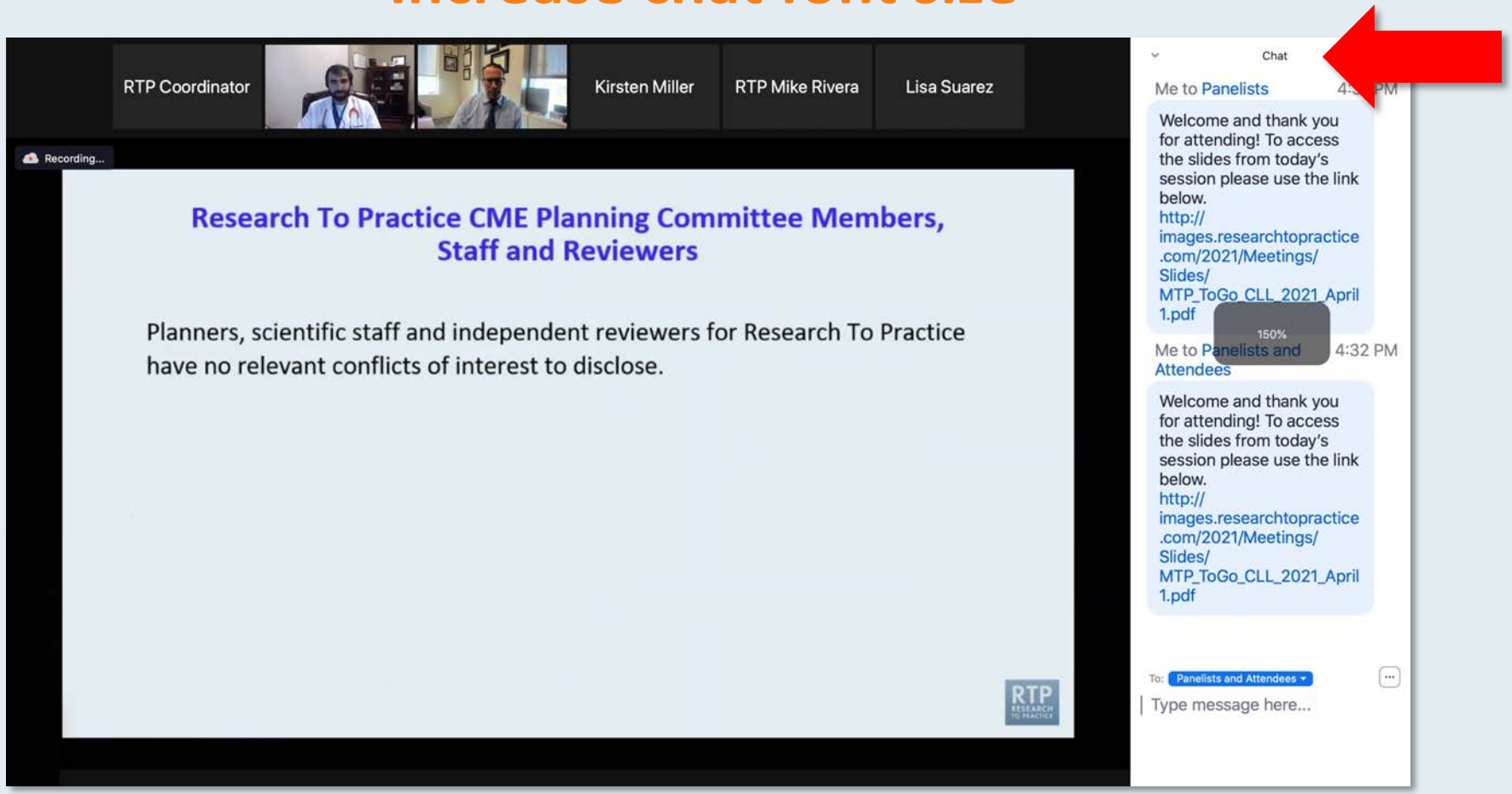

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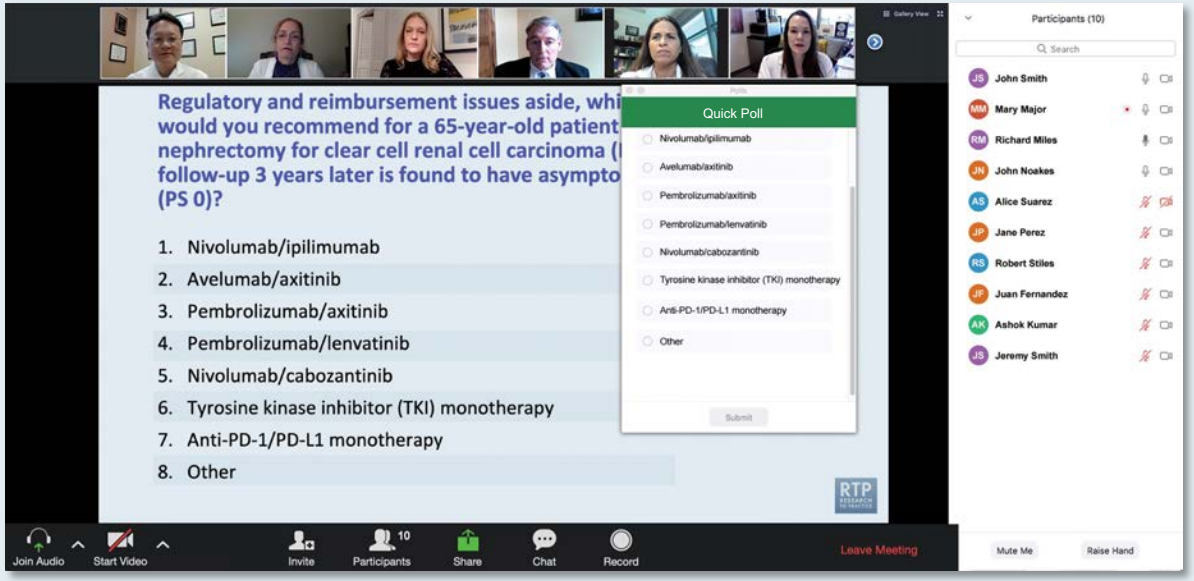

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Key Presentations Related to Gastrointestinal Cancers from Recent Major Oncology Conferences

DR RACHNA SHROFF

UNIVERSITY OF ARIZONA CANCER CENTER

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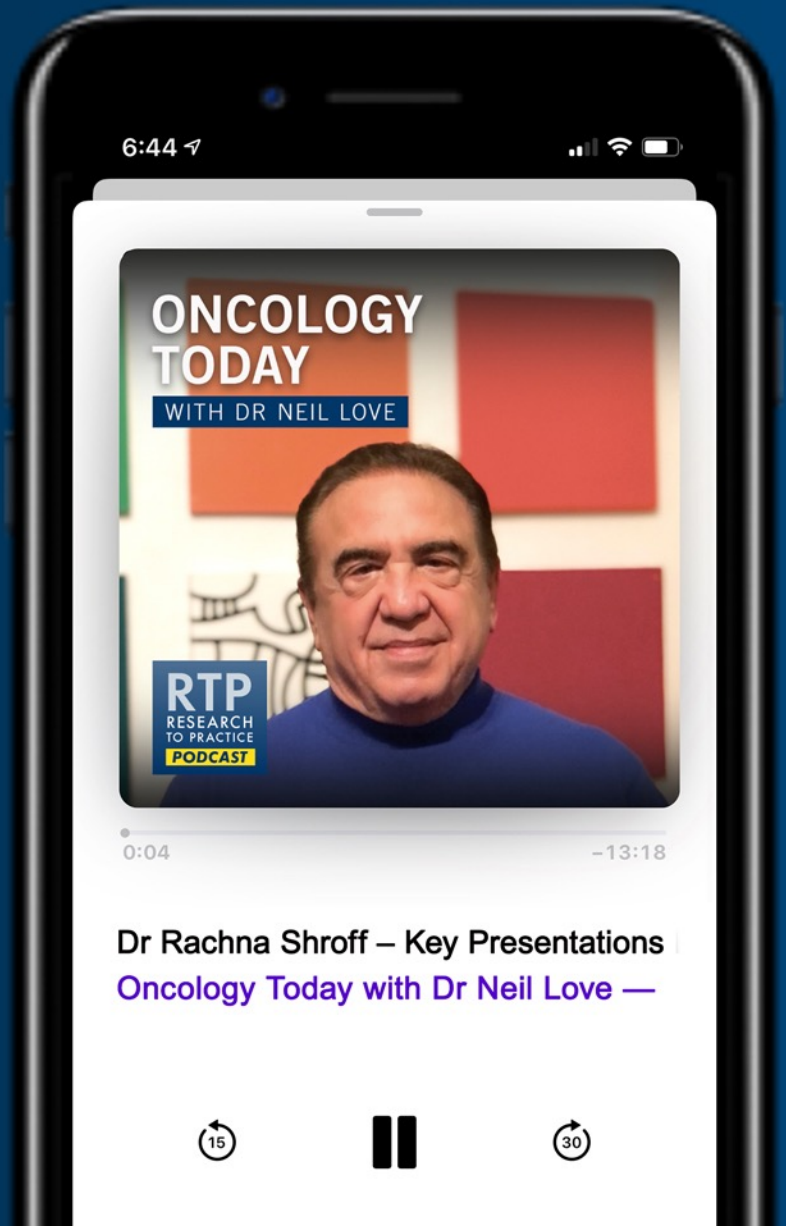

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Ovarian Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2023 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Sunday, March 26, 2023

11:45 AM – 1:15 PM ET

Faculty

Mansoor Raza Mirza, MD

Amit M Oza, MD

Richard T Penson, MD, MRCP

Moderator

Joyce F Liu, MD, MPH

RTP RESEARCH TO PRACTICE

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Endometrial Cancer

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2023 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Monday, March 27, 2023

11:45 AM – 1:15 PM ET

Faculty

Robert L Coleman, MD

Matthew A Powell, MD

Brian M Slomovitz, MD

Moderator

Shannon N Westin, MD, MPH

RTP RESEARCH TO PRACTICE

Oncology Today: Recent Research Advances in Prostate Cancer and the Clinical Implications – A 2023 Post-ASCO GU Activity

A CME/MOC-Accredited Virtual Event

Wednesday, March 29, 2023
5:00 PM – 6:00 PM ET

Consulting Clinical Investigator

Daniel P Petrylak, MD

Faculty Panel

Andrew J Armstrong, MD, ScM
Rana R McKay, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Tuesday, April 4, 2023
5:00 PM – 6:00 PM ET

Faculty

Uma Borate, MD, MS

Andrew H Wei, MBBS, PhD

Moderator

Neil Love, MD

RTP Year in Review 2023

Meet The Professor

Optimizing the Management of ER-Positive and Triple-Negative Breast Cancer

Wednesday, April 12, 2023
5:00 PM – 6:00 PM ET

Faculty

Sara A Hurvitz, MD

Moderator

Neil Love, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

A Multitumor CME/MOC-Accredited Live Webinar Series

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, April 13, 2023
5:00 PM – 6:00 PM ET

Faculty

Luis Paz-Ares, MD, PhD

Heather Wakelee, MD

Moderator

Neil Love, MD

RTP Year in Review 2023

Thank you for joining us!

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

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Meet The Professor

Optimizing the Management of Colorectal Cancer

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

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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
Chair, Executive Committee of the Medical Staff
Associate Vice President, Cancer Network Research
The University of Texas
MD Anderson Cancer Center
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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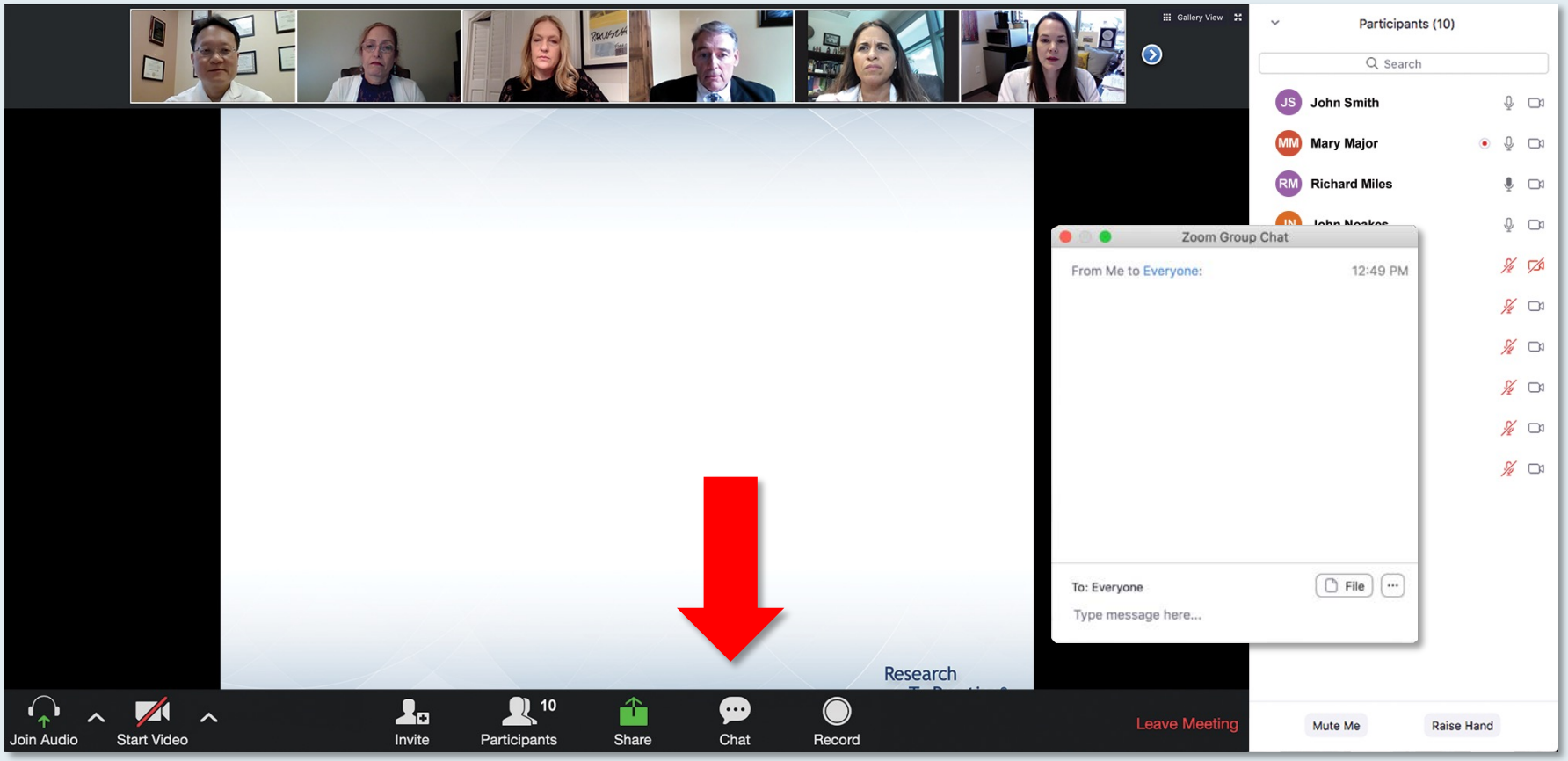

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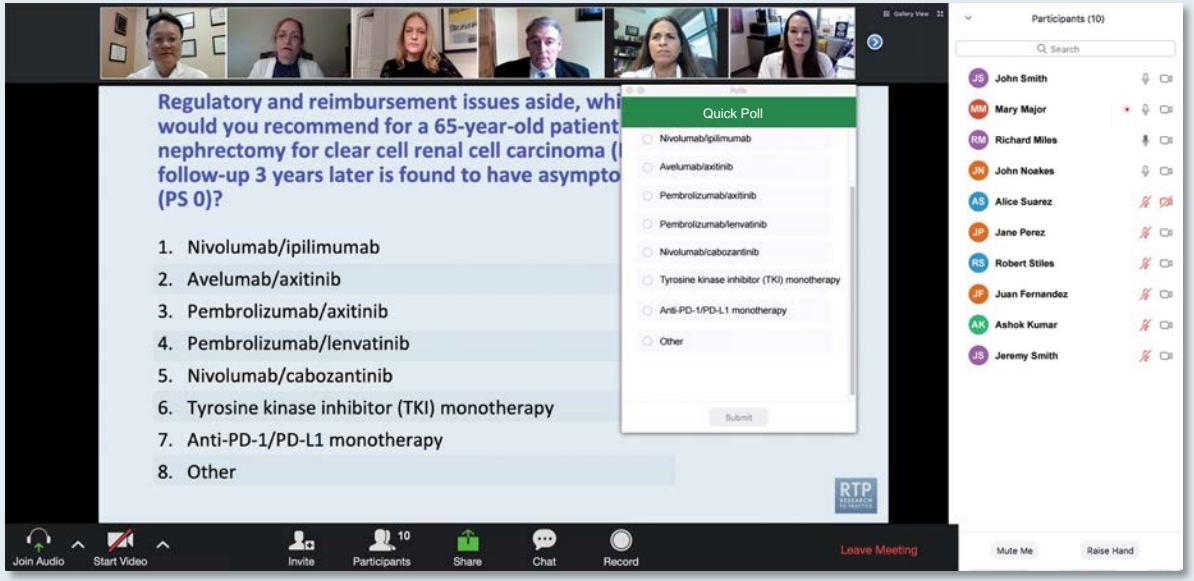

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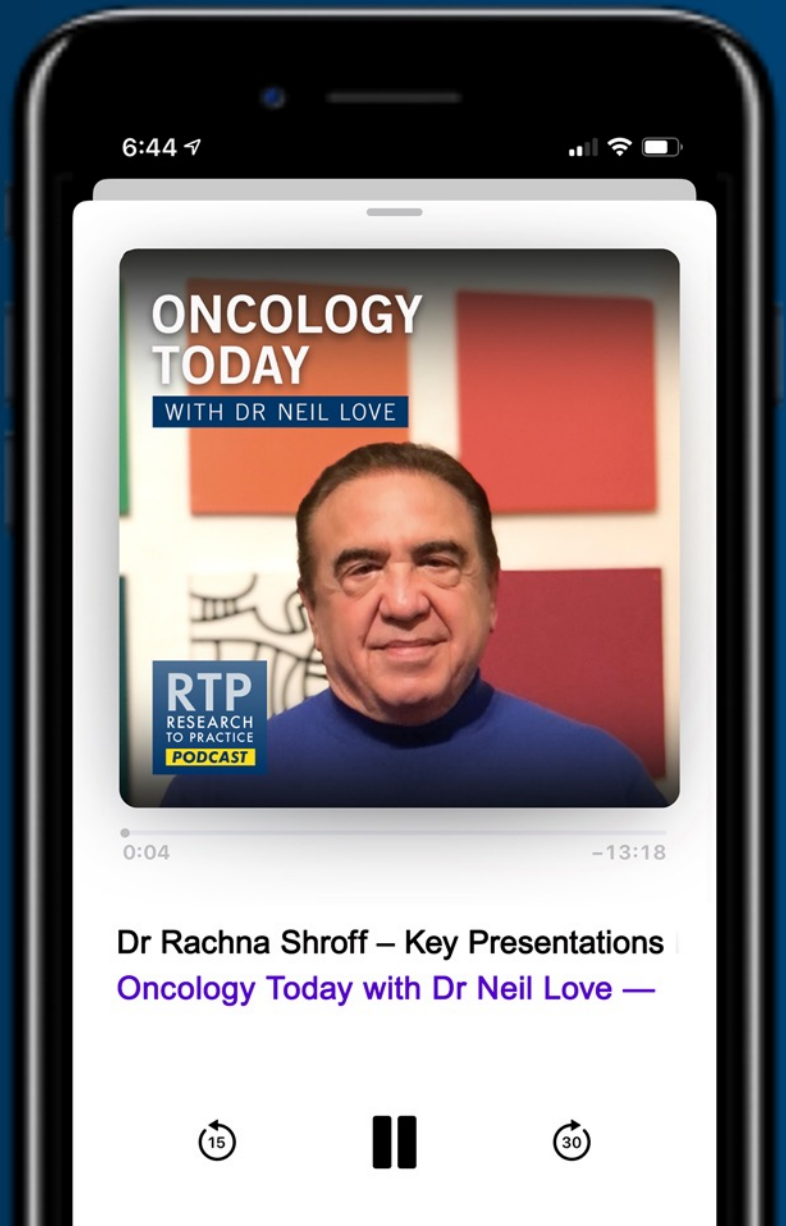

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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Dr Strickler — Disclosures

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Consulting Agreement	Zentalis Pharmaceuticals
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Data and Safety Monitoring Board/Committee	AbbVie Inc, BeiGene Ltd, Pionyr Immunotherapeutics

Georges Azzi, MD
Holy Cross Health
Fort Lauderdale, Florida

Sunil Gandhi, MD
Florida Cancer Specialists
Lecanto, Florida

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

Ranju Gupta, MD
Lehigh Valley Topper
Cancer Institute
Bethlehem, Pennsylvania

Gigi Chen, MD
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Pleasant Hill, California

Shaachi Gupta, MD, MPH
Florida Cancer Specialists
Lake Worth, Florida

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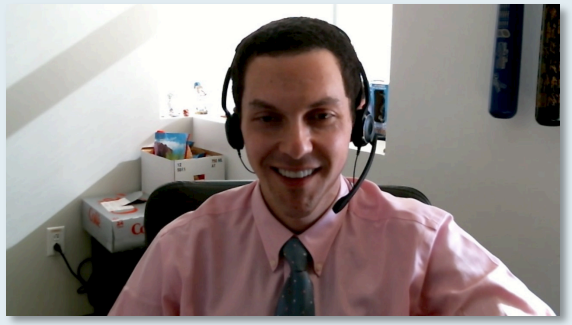

Jeremy Lorber, MD
Cedars-Sinai Medical Center
Beverly Hills, California

Priya Rudolph, MD, PhD
Georgia Cancer Specialists
Athens, Georgia

Swati Vishwanathan, MD
WVU Medicine
Bridgeport, West Virginia

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Meet The Professor with Dr Strickler

Introduction: ASCO Guidelines for the Treatment of Metastatic Colorectal Cancer

MODULE 1: Case Presentations and Faculty Survey

MODULE 2: Journal Club

MODULE 3: Appendix

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Meet The Professor with Dr Strickler

Introduction: ASCO Guidelines for the Treatment of Metastatic Colorectal Cancer

MODULE 1: Case Presentations and Faculty Survey

MODULE 2: Journal Club

MODULE 3: Appendix

ASCO special articles

Treatment of Metastatic Colorectal Cancer: ASCO Guideline

Van K. Morris, MD[1]; Erin B. Kennedy, MHSc[2]; Nancy N. Baxter, MD, PhD[3]; Al B. Benson III, MD[4]; Andrea Cercek, MD[5]; May Cho, MD[6]; Kristen K. Ciombor, MD, MSCI[7]; Chiara Cremolini, MD, PhD[8]; Anjee Davis, MPPA[9]; Dustin A. Deming, MD[10]; Marwan G. Fakih, MD[11]; Sepideh Gholami, MD[12]; Theodore S. Hong, MD[13]; Ishmael Jaiyesimi, DO[14]; Kelsey Klute, MD[15]; Christopher Lieu, MD[16]; Hanna Sanoff, MD, MPH[17]; John H. Strickler, MD[18]; Sarah White, MD[19]; Jason A. Willis MD, PhD[1]; and Cathy Eng, MD[7]

J Clin Oncol 2022 October 17;[Online ahead of print].

Clinical Review & Education

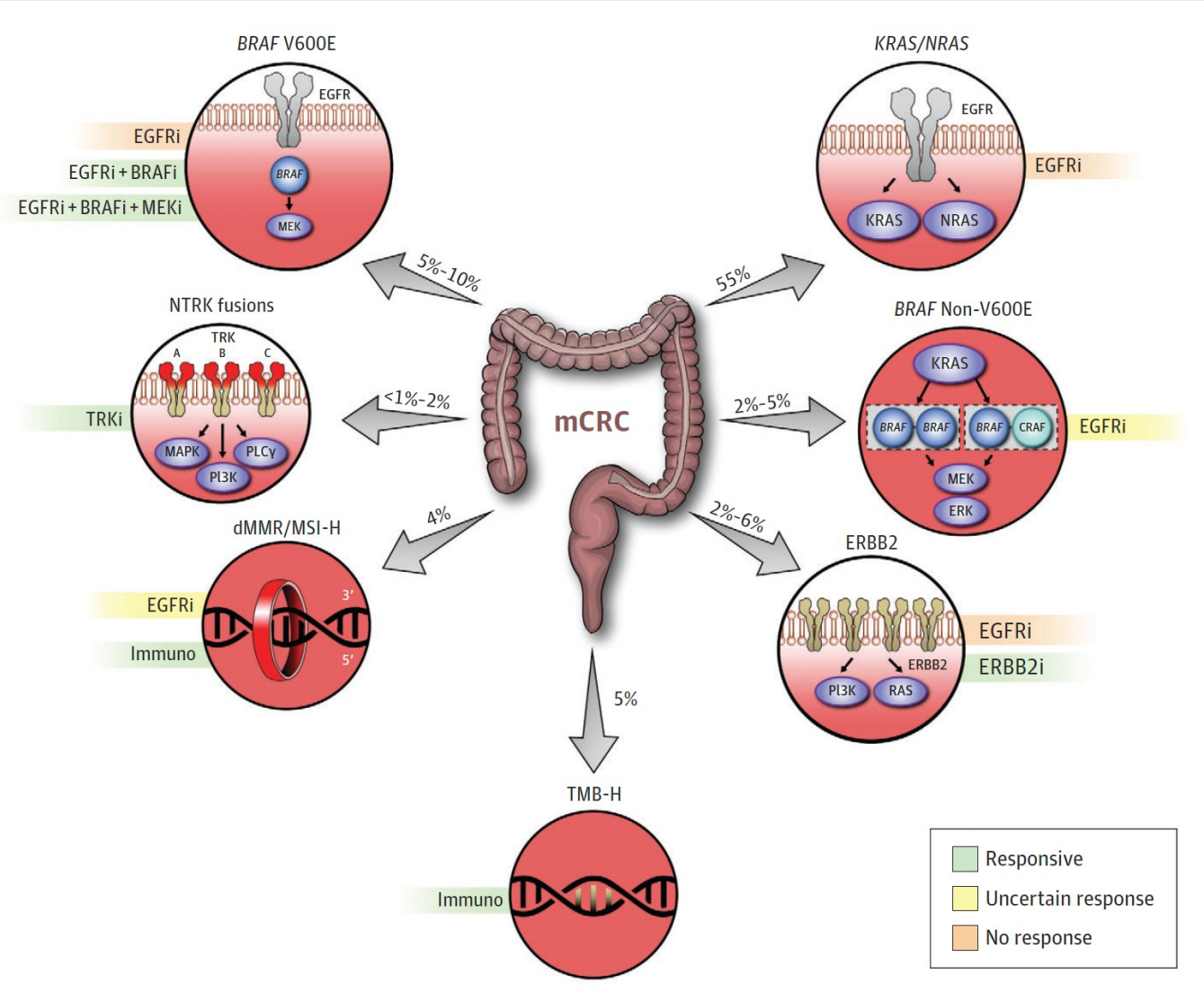
2022 May 1;8(5):760-9.

JAMA Oncology | Review

Diagnosis and Treatment of ERBB2-Positive Metastatic Colorectal Cancer
A Review

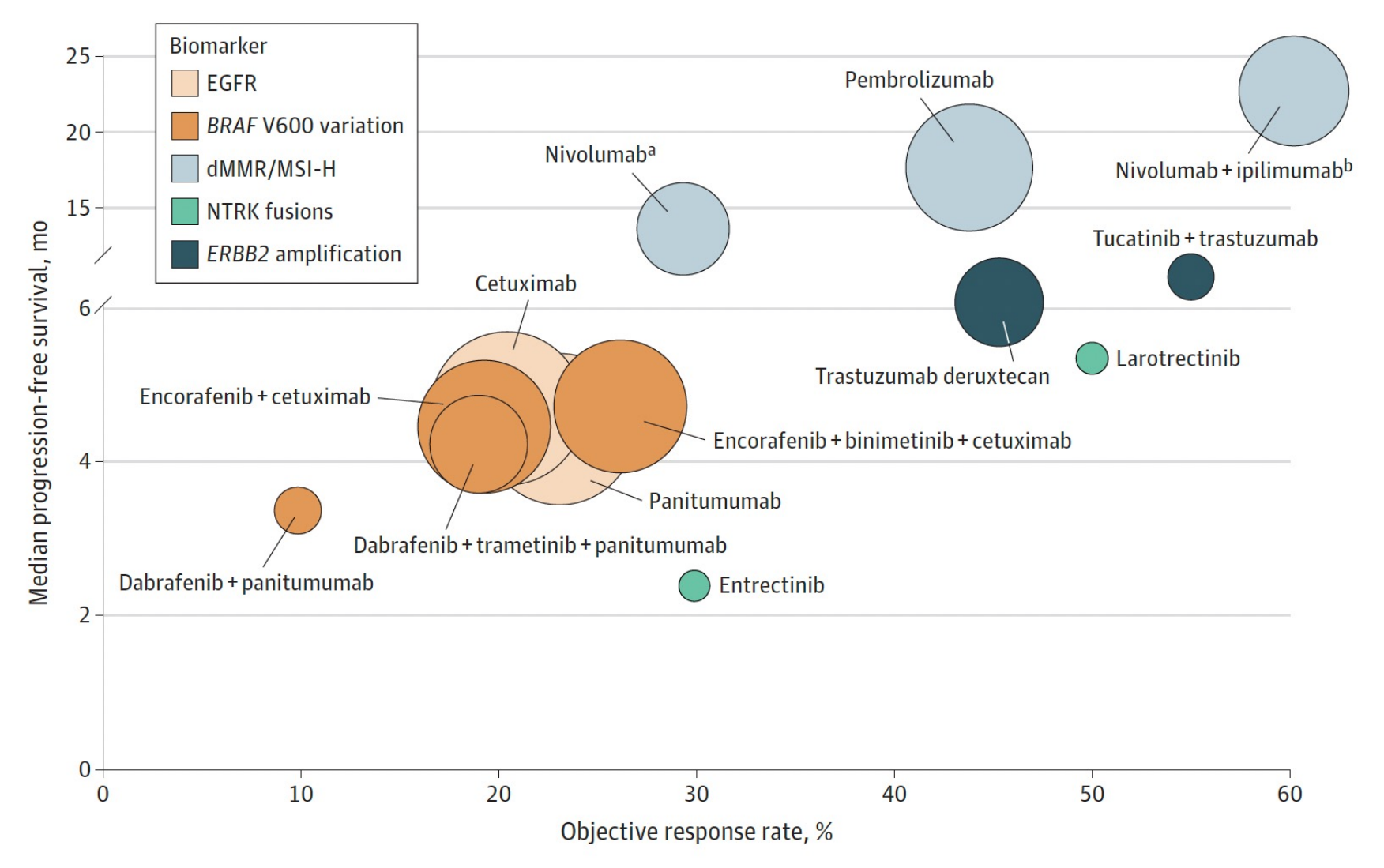
John H. Strickler, MD; Takayuki Yoshino, MD, PhD; Rondell P. Graham, MBBS; Salvatore Siena, MD; Tanios Bekaii-Saab, MD

Established or Investigational Biomarkers for Treating mCRC



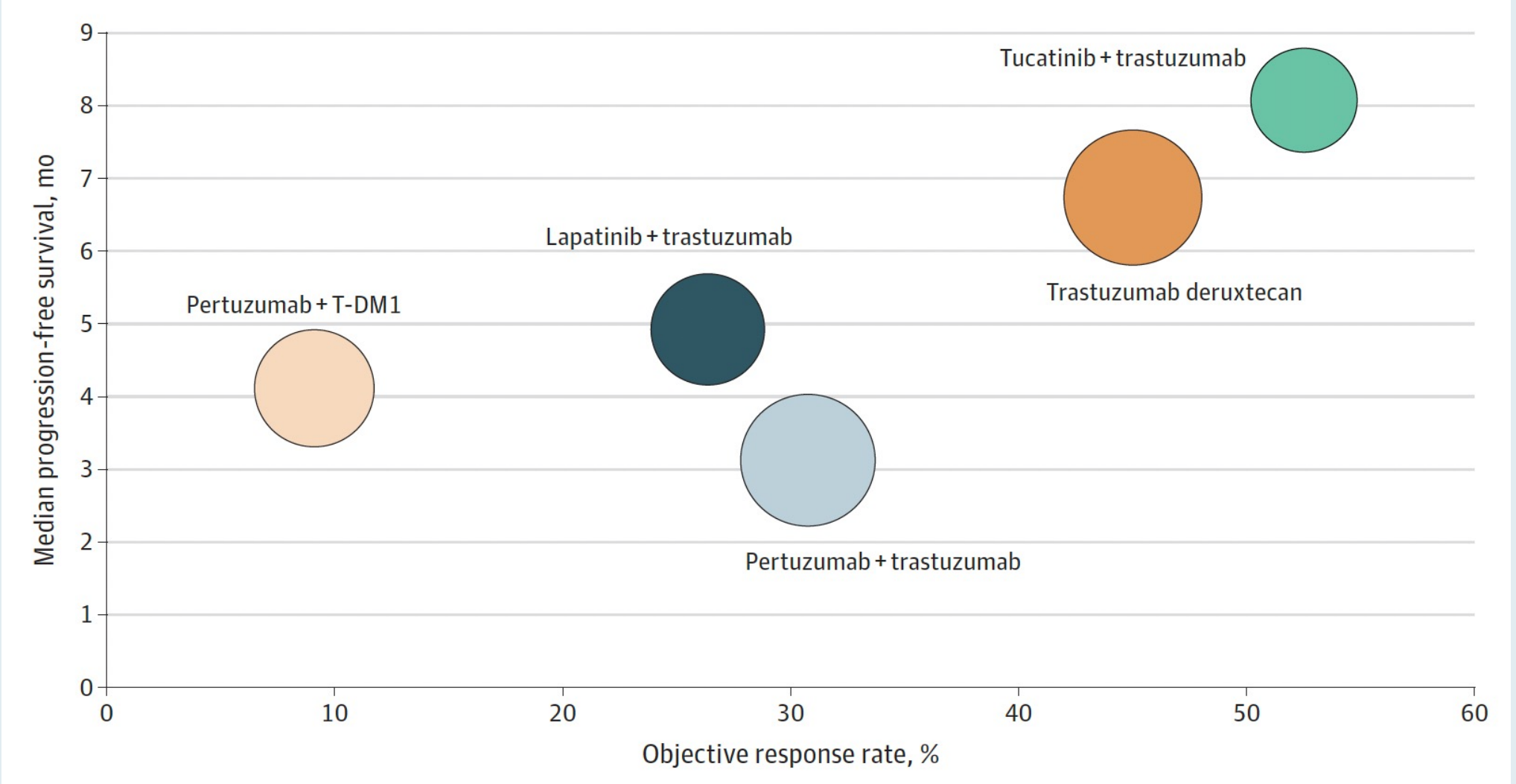
Strickler JH et al. *JAMA Oncol* 2022 May 1;8(5):760-9 .

Studies of Biomarker-Driven Therapies for mCRC



Strickler JH et al. *JAMA Oncol* 2022 May 1;8(5):760-9 .

Studies of Anti-ERBB2 Agents for ERBB2-Positive mCRC



Strickler JH et al. *JAMA Oncol* 2022 May 1;8(5):760-9 .

Meet The Professor with Dr Strickler

MODULE 1: Case Presentations and Faculty Survey

- Dr Gandhi: 74-year-old woman with metastatic colon cancer
- Dr Azzi: 77-year-old man with T3N0 MSS adenocarcinoma of the colon who is ctDNA-negative s/p colectomy and would like to avoid chemotherapy
- Dr Chen: 80-year-old woman with pMMR Stage IIIC high-risk adenocarcinoma of the colon with neuroendocrine features, s/p adjuvant FOLFOX
- Dr Vishwanathan: 49-year-old man with a HER2-amplified ascending colon adenocarcinoma and liver metastases who undergoes perioperative FOLFOXIRI and liver resection
- Dr Rudolph: 58-year-old man with metastatic adenocarcinoma of the colon and disease progression s/p multiple lines of chemotherapy
- Dr S Gupta: 78-year-old man with metastatic rectal adenocarcinoma, high TMB and multiple genetic alterations by liquid biopsy, including KRAS G12C
- Dr R Gupta: 61-year-old man with rectal cancer and synchronous liver metastases, s/p perioperative FOLFOX and resection of the primary and liver metastases, now with lung oligometastases
- Dr Brenner: 76-year-old woman with ctDNA-identified metastatic recurrence of BRAF V600E mutation-positive, MSI-H adenocarcinoma of the colon s/p pembrolizumab
- Dr Lorber: 66-year-old woman with metastatic BRAF V600E-mutant colon adenocarcinoma, with ctDNA positivity after FOLFOX, HIPEC and colectomy/debulking surgery

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Case Presentation: 74-year-old woman with metastatic colon cancer

Dr Sunil Gandhi (Lecanto, 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

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

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Case Presentation: 77-year-old man with T3N0 MSS adenocarcinoma of the colon who is ctDNA-negative s/p colectomy and would like to avoid chemotherapy

Dr Georges Azzi (Fort Lauderdale, Florida)

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Case Presentation: 80-year-old woman with pMMR Stage IIIC high-risk adenocarcinoma of the colon with neuroendocrine features, s/p adjuvant FOLFOX

Dr Gigi Chen (Pleasant Hill, California)

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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

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Case Presentation: 49-year-old man with a HER2-amplified ascending colon adenocarcinoma and liver metastases who undergoes perioperative FOLFOXIRI and liver resection

Dr Swati Vishwanathan (Bridgeport, West Virginia)

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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

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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 targeted therapy	Second line targeted 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

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

Case Presentation: 58-year-old man with metastatic adenocarcinoma of the colon and disease progression s/p multiple lines of chemotherapy

Dr Priya Rudolph (Athens, Georgia)

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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

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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

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

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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

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Case Presentation: 78-year-old man with metastatic rectal adenocarcinoma, high TMB and multiple genetic alterations by liquid biopsy, including KRAS G12C

Dr Shaachi Gupta (Lake Worth, Florida)

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Approved in indication Approved in other indication Lack of Response

DETECTED ALTERATION(S) / BIOMARKER(S)	% CFDNA OR AMPLIFICATION	ASSOCIATED FDA-APPROVED THERAPIES	CLINICAL TRIAL AVAILABILITY
KRAS Q61H	1.6%	Cetuximab, Panitumumab	Yes
KRAS G12C	0.3%	Sotorasib Cetuximab, Panitumumab	Yes
KRAS G12V	0.1%	Cetuximab, Panitumumab	Yes
CHEK2 Copy Number Loss	DETECTED	Olaparib	Yes

ADDITIONAL BIOMARKERS

BIOMARKER	ADDITIONAL DETAILS
Tumor Mutational Burden (TMB)	31.58 mut/Mb
MSI-High	NOT DETECTED

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

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 Lieu	Yes, if no other tx options and ctDNA is negative for resistance mutations
 Dr Dasari	Yes, after tx holiday if liquid biopsy does not show alterations	 Dr Overman	Yes, if initial response, time interval between tx, ctDNA for resistance mutations
 Dr Deming	Yes, if prior response or durable SD and ≥4 mo since last given	 Dr Strickler	Yes, if ctDNA is negative for resistance mutations

RTP RESEARCH TO PRACTICE

Case Presentation: 61-year-old man with rectal cancer and synchronous liver metastases, s/p perioperative FOLFOX and resection of the primary and liver metastases, now with lung oligometastases

Dr Ranju Gupta (Bethlehem, Pennsylvania)

RTP
RESEARCH
TO PRACTICE

Case Presentation: 76-year-old woman with ctDNA-identified metastatic recurrence of BRAF V600E mutation-positive, MSI-H adenocarcinoma of the colon s/p pembrolizumab

Dr Warren Brenner (Boca Raton, Florida)

RTP
RESEARCH
TO PRACTICE

FINAL RESULTS SUMMARY

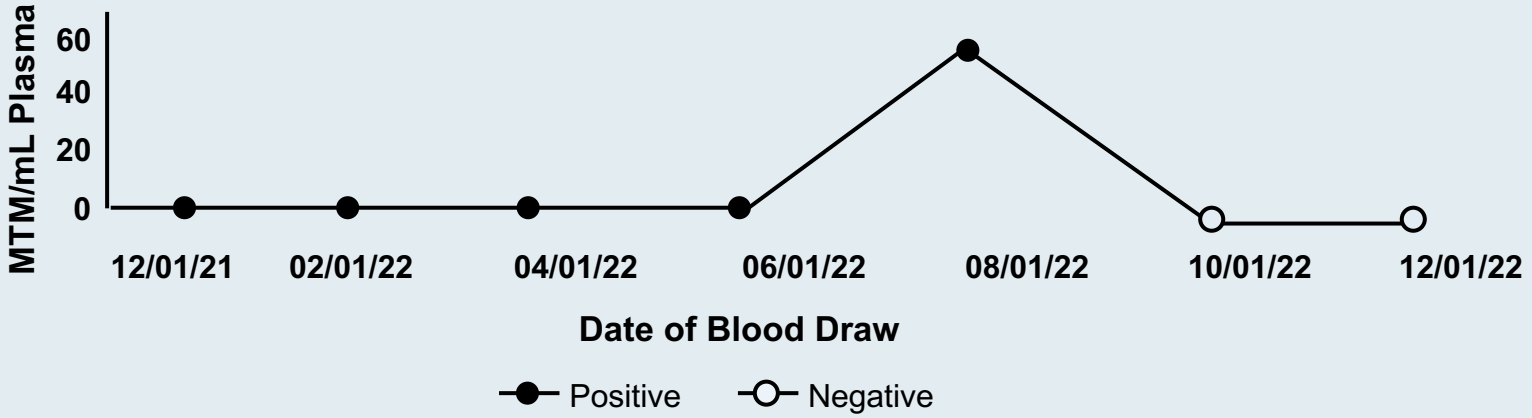
Signatera Negative

⊖

MTM/mL:
Not Detected

Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma. ***See limitations section below***

Historical Results



Date	Reported MTM/mL
Nov 14, 2022	0.00
Jul 14, 2022	59.77
Mar 15, 2022	0.33
Dec 09, 2021	0.05

RTP RESEARCH TO PRACTICE

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

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

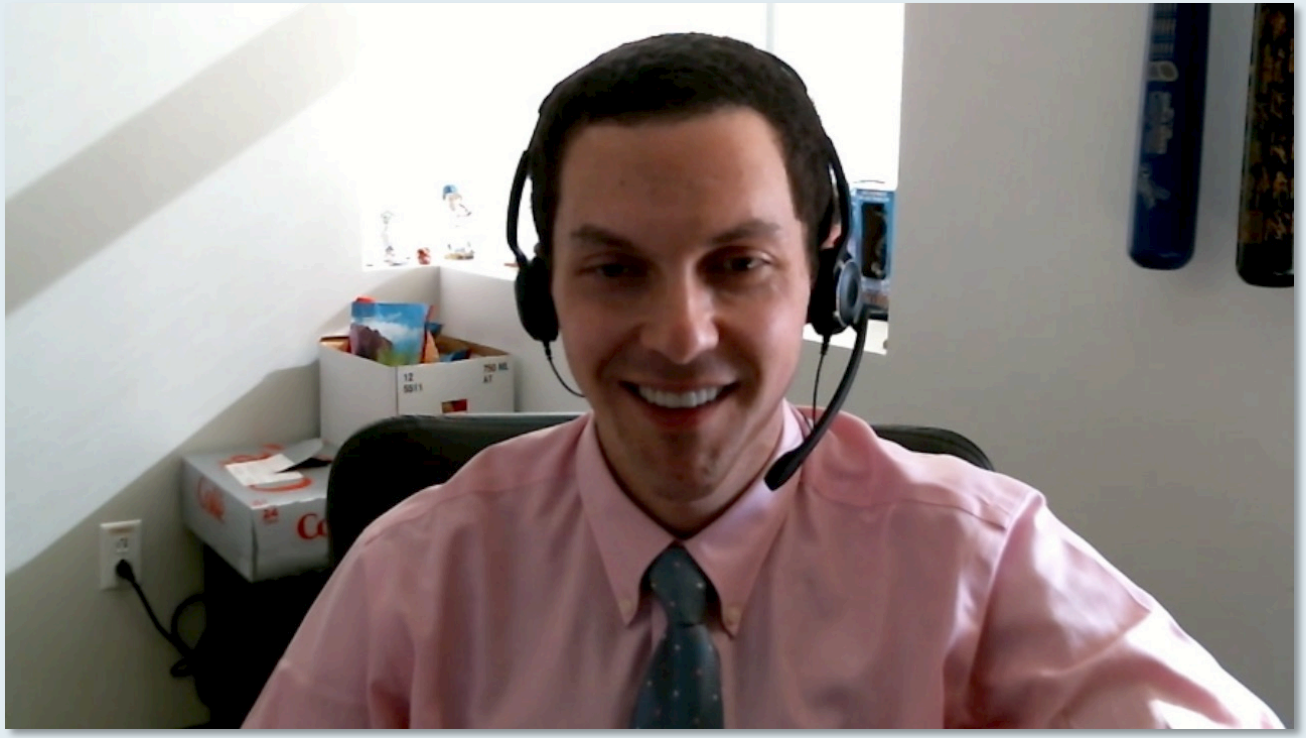
RTP RESEARCH TO PRACTICE

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



Dr Jeremy Lorber (Beverly Hills, California)

RTP
RESEARCH
TO PRACTICE

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

Meet The Professor with Dr Strickler

Introduction: ASCO Guidelines for the Treatment of Metastatic Colorectal Cancer

MODULE 1: Case Presentations and Faculty Survey

MODULE 2: Journal Club

MODULE 3: Appendix

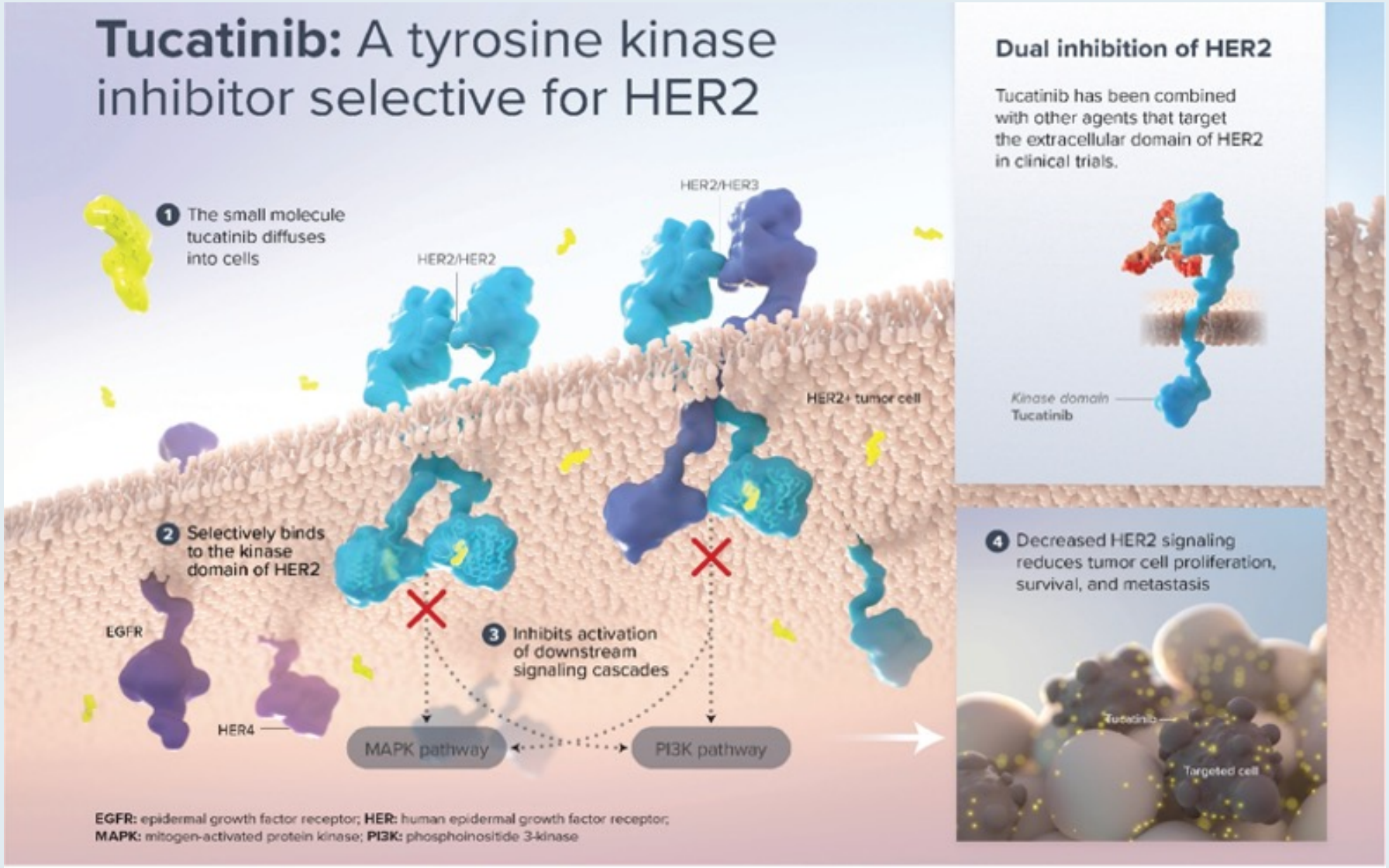
RTP
RESEARCH
TO PRACTICE

Phase 1b/2, Open-Label, Dose-Escalation and Expansion Trial of Tucatinib in Combination with Trastuzumab with and without Oxaliplatin-Based Chemotherapy or Pembrolizumab in Patients with Unresectable or Metastatic HER2+ Gastrointestinal Cancers (Trial in Progress)

Park H et al.

Gastrointestinal Cancers Symposium 2022;Abstract TPS376.

Tucatinib Proposed Mechanism of Action



Park H et al. Gastrointestinal Cancers Symposium 2022;Abstract TPS376.

Assessment of HER2 (ERBB2) Amplification (HER2amp) Using Blood-Based Circulating Tumor DNA (ctDNA) Next Generation Sequencing (NGS) and Correlation with Tissue-Based Testing in Metastatic Colorectal Cancer (mCRC)

Raghav KPS et al.

ASCO 2021;Abstract 3589.

Tucatinib plus Trastuzumab in Patients (Pts) with HER2-Positive Metastatic Colorectal Cancer (mCRC): Patient-Reported Outcomes (PROs) From Ph 2 Study MOUNTAINEER

Wu C et al.

ESMO 2022;Abstract 361P.

MOUNTAINEER-03: Phase 3 Study of Tucatinib, Trastuzumab, and mFOLFOX6 as First-Line Treatment in HER2+ Metastatic Colorectal Cancer—Trial in Progress

Bekaii-Saab TS et al.

Gastrointestinal Cancers Symposium 2023;Abstract TPS261.

MOUNTAINEER-02: Phase II/III Study of Tucatinib, Trastuzumab, Ramucirumab, and Paclitaxel in Previously Treated HER2+ Gastric or Gastroesophageal Junction Adenocarcinoma (GEC): Trial in Progress

Catenacci DV et al.

ESMO 2021;Abstract 1434TiP.

HER2 Testing in Colorectal Cancer: Concordance Analysis Between Breast and Gastric Scoring Algorithms from the MOUNTAINEER Trial

Cercek A et al.

Gastrointestinal Cancers Symposium 2023;Abstract 198.

Impact of Anti-EGFR Therapies on HER2-Positive Metastatic Colorectal Cancer (HER2+ mCRC): A Systematic Literature Review and Meta-Analysis of Clinical Outcomes

Bekaii-Saab TS et al.

ESMO 2022;Abstract 376P.

review articles

SPECIAL SERIES: PRECISION MEDICINE AND IMMUNOTHERAPY IN GI MALIGNANCIES

BRAF-Mutated Advanced Colorectal Cancer: A Rapidly Changing Therapeutic Landscape

Kristen K. Ciombor, MD, MSCI[1]; John H. Strickler, MD[2]; Tanios S. Bekaii-Saab, MD[3]; Rona Yaeger, MD[4]

J Clin Oncol 2022 August 20;40(24):2706-15.

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

CodeBreaK 101

PARIS 2022 ESMO congress

Abstract 315O

Sotorasib in combination with panitumumab in refractory *KRAS G12C*-mutated colorectal cancer: safety and efficacy for phase 1b full expansion cohort

Yasutoshi Kuboki[1], Rona Yaeger[2], Marwan Fakih[3], John Strickler[4], Toshiki Masuishi[5], Edward J. Kim[6], Christine Bestvina[7], Corey Langer[8], John Krauss[9], Sonam Puri[10], Panli Cardona[11], Emily Chan[11], Qui Tran[11], David S. Hong[12]

[1]National Cancer Center Hospital East, Kashiwa-shi-Chiba, Japan; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [4]Duke University Medical Center, Durham, NC, USA; [5]Aichi Cancer Center Hospital, Nagoya-shi, Aichi, Japan; [6]UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [7]University of Chicago, Chicago, IL, USA; [8]University of Pennsylvania, Philadelphia, PA, USA; [9]University of Michigan, Ann Arbor, MI, USA; [10]Huntsman Cancer Institute, Salt Lake City, UT, USA; [11]Amgen Inc., Thousand Oaks, CA, USA; [12]University of Texas MD Anderson Cancer Center, Houston, TX, USA

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

ASCO Gastrointestinal Cancers Symposium

Trifluridine/tipiracil plus bevacizumab for third-line treatment of refractory metastatic colorectal cancer

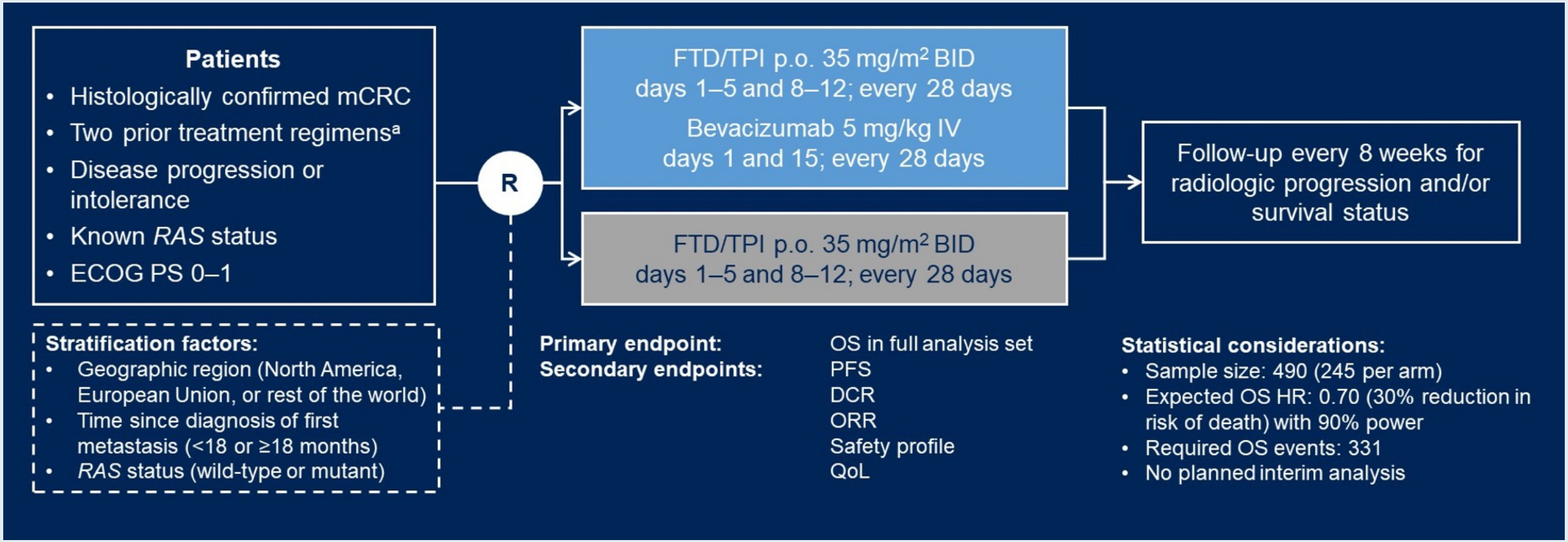
The phase 3 randomized SUNLIGHT study

Josep Tabernero[1], Gerald W. Prager[2], Marwan Fakih[3], Fortunato Ciardiello[4], Eric Van Cutsem[5], Elena Elez[1], Felipe Melo Cruz[6], Lucjan Wyrwicz[7], Daniil Stroyakovskiy[8], Zsuzsanna Pápai[9], Pierre-Guillaume Poureau[10], Gabor Liposits[11], Chiara Cremolini[12], Igor Bondarenko[13], Dominik Paul Modest[14], Karim A. Benhadji[15], Ronan Fougeray[16], Catherine Leger[16], Nadia Amellal[16], and Julien Taieb[17]

[1]Vall d'Hebron University Hospital and Institute of Oncology (VHIO), Barcelona, Spain; [2]Medical University Vienna, Vienna, Austria; [3]City of Hope Comprehensive Cancer Center, Duarte, USA; [4]Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy; [5]University Hospitals Leuven and KU Leuven, Herent, Belgium; [6]Núcleo de Pesquisa e Ensino da Rede São Camilo, Sao Paulo, Brazil; [7]Maria Sklodowska-Curie National Cancer Research Institute, Warsaw, Poland; [8]Moscow City Oncological Hospital #62, Moscow, Russian Federation; [9]Duna Medical Centre, Budapest, Hungary; [10]Institut de Cancérologie, Brest, France; [11]University of Southern Denmark, Odense, Denmark; [12]University of Pisa, Pisa, Italy; [13]Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [14]Charité Universitätsmedizin, Berlin, Germany; [15]Taiho Oncology, Inc., Princeton, USA; [16]Servier International Research Institute, Suresnes, France; [17]Université Paris-Cité, (Paris Descartes), Georges Pompidou European Hospital, SIRIC CARPEM, Paris, France.

PRESENTED BY: Josep Tabernero, MD PhD

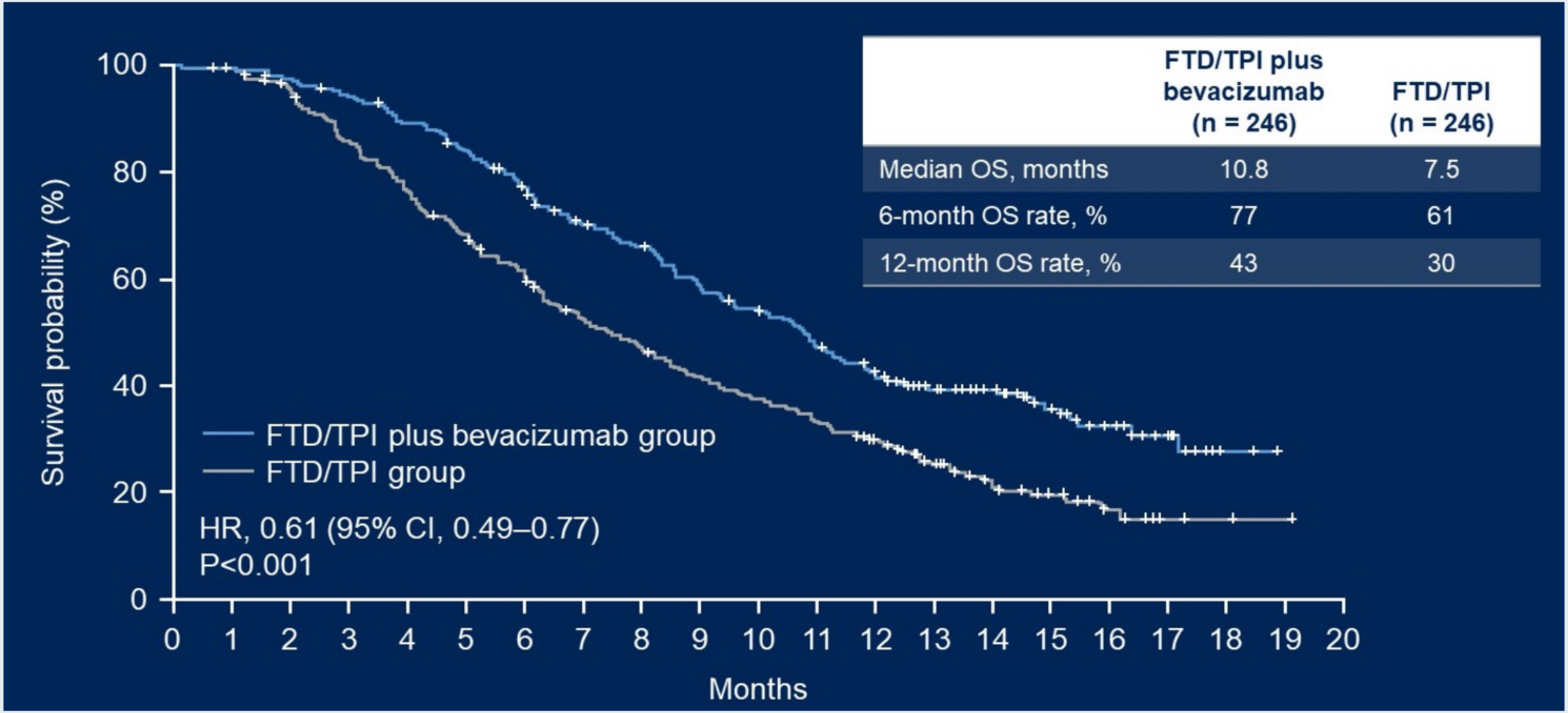
SUNLIGHT Phase III Study Design



FTD/TPI = trifluridine/tipiracil

Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

SUNLIGHT: Overall Survival in Full Analysis Set (Primary Endpoint)

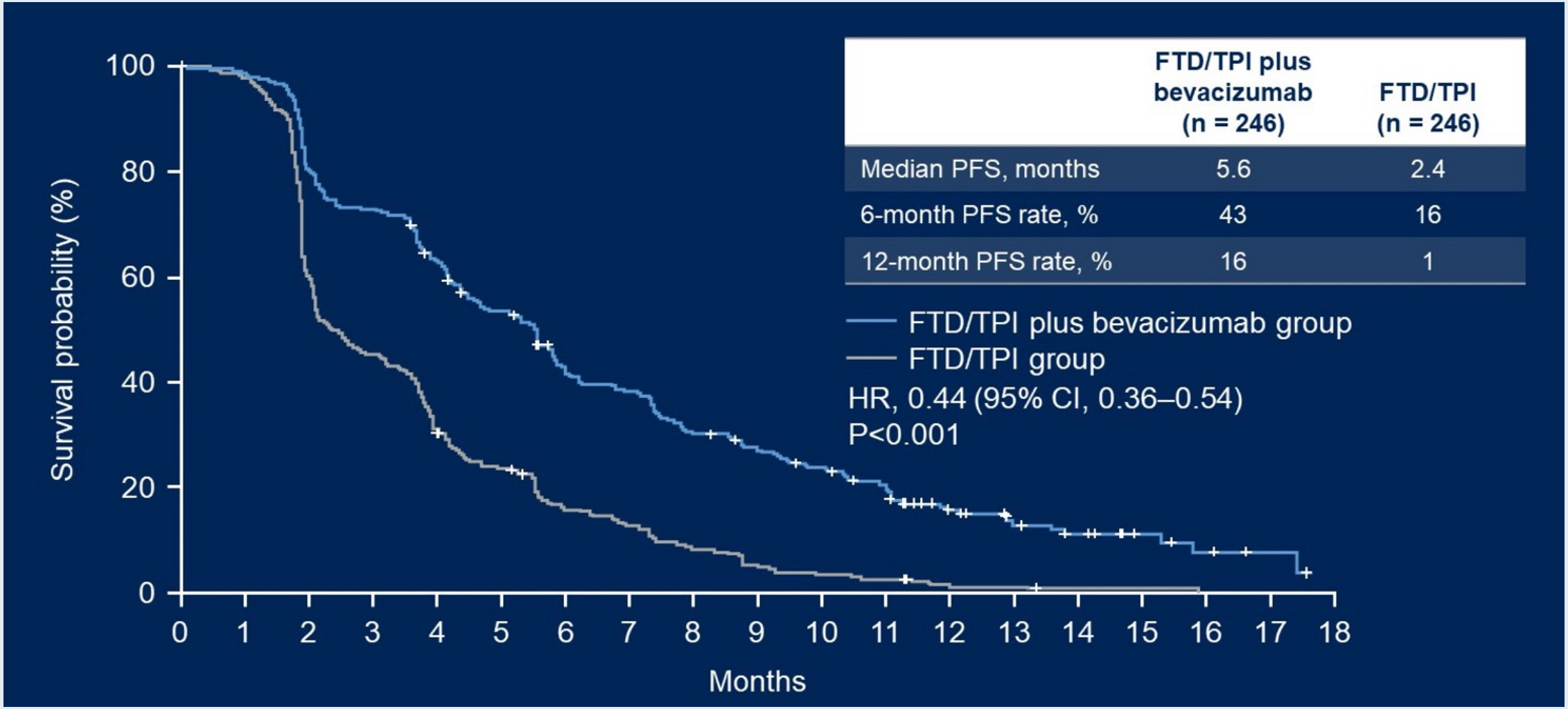


	FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Median OS, months	10.8	7.5
6-month OS rate, %	77	61
12-month OS rate, %	43	30

Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

RTP RESEARCH TO PRACTICE

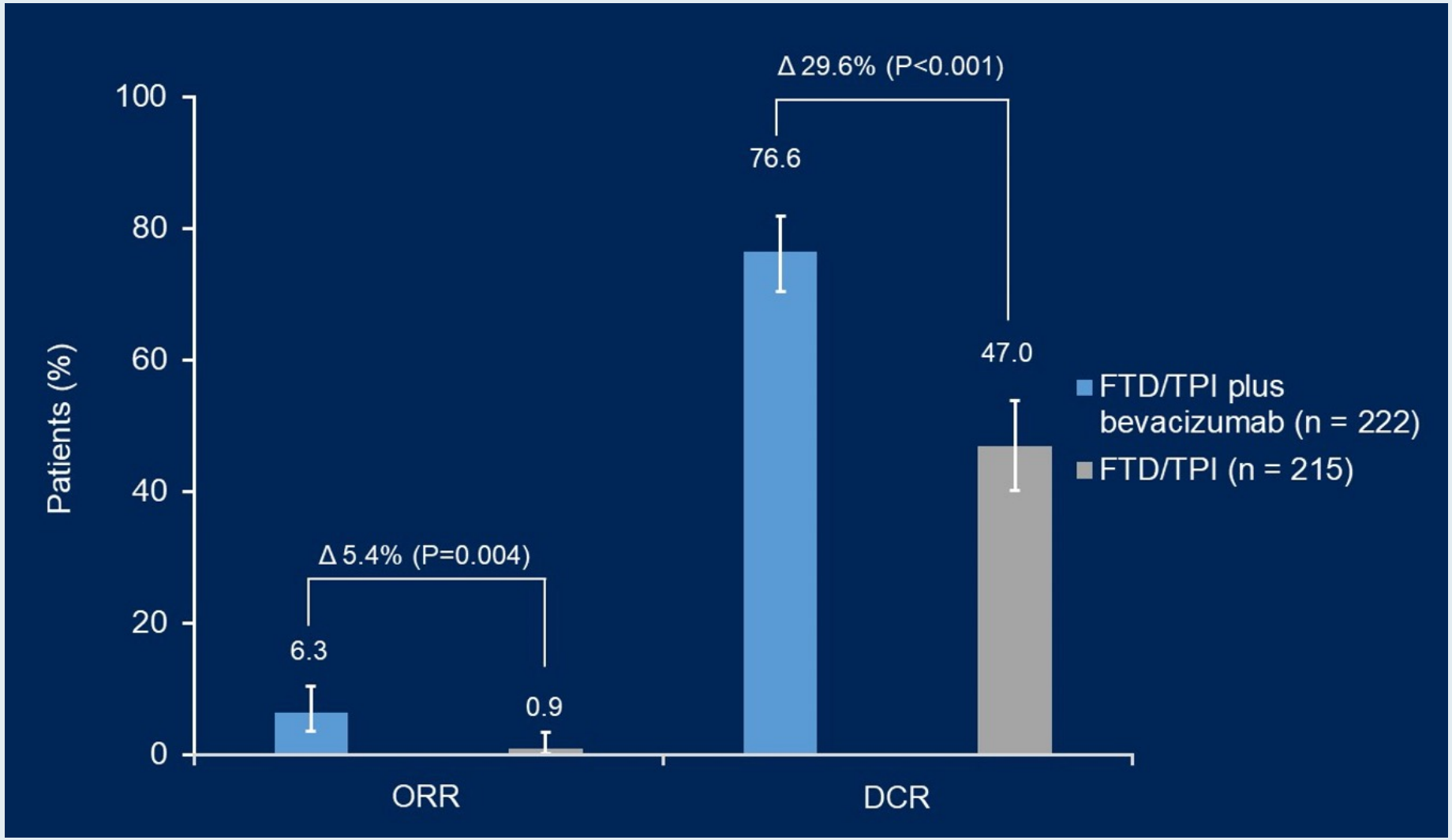
SUNLIGHT: Progression-Free Survival in Full Analysis Set



	FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Median PFS, months	5.6	2.4
6-month PFS rate, %	43	16
12-month PFS rate, %	16	1

Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

SUNLIGHT: ORR and DCR for Patients Evaluable for Tumor Response



ORR = overall response rate; DCR = disease control rate

Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

SUNLIGHT: Overall Safety Summary

Event (any cause), n (%)	FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Overall AEs	241 (98)	241 (98)
FTD/TPI-related AEs	221 (90)	200 (81)
Bevacizumab-related AEs	119 (48)	NA
Severe (grade ≥3) AEs	178 (72)	171 (70)
Serious AEs	61 (25)	77 (31)
Treatment-related deaths	0	0
AEs leading to withdrawal from the study	31 (13)	31 (13)

Dose modification, n (%)	FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Dose reductions	40 (16)	30 (12)
Dose delays	171 (70)	131 (53)

Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

SUNLIGHT: Treatment-Emergent Adverse Events (TEAEs) in ≥20% of Patients

	FTD/TPI plus bevacizumab (n = 246)		FTD/TPI (n = 246)	
TEAE, n (%)	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Neutropenia	153 (62)	106 (43)	126 (51)	79 (32)
Nausea	91 (37)	4 (2)	67 (27)	4 (2)
Anemia	71 (29)	15 (6)	78 (32)	27 (11)
Asthenia	60 (24)	10 (4)	55 (22)	10 (4)
Fatigue	53 (22)	3 (1)	40 (16)	9 (4)
Diarrhea	51 (21)	2 (1)	46 (19)	6 (2)
Decreased appetite	50 (20)	2 (1)	38 (15)	3 (1)

Hypertension (10% vs 2%), nausea, and neutropenia were more common in the combination group; there was one case of febrile neutropenia with FTD/TPI plus bevacizumab versus six with FTD/TPI

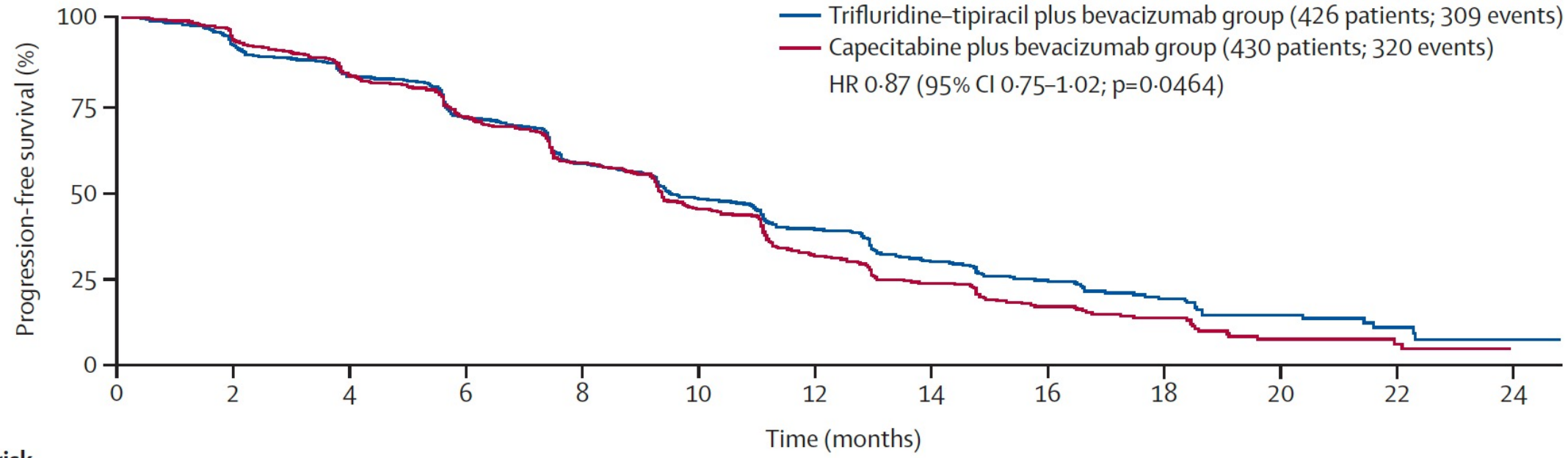
Tabernero J et al. Gastrointestinal Cancers Symposium 2023;Abstract 4.

Lancet Gastroenterol Hepatol 2023;8(2):133-44.

Trifluridine–tipiracil plus bevacizumab versus capecitabine plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer ineligible for intensive therapy (SOLSTICE): a randomised, open-label phase 3 study

Thierry André, Alfredo Falcone, Yaroslav Shparyk, Fedor Moiseenko, Eduardo Polo-Marques, Tibor Csöszi, Arinilda Campos-Bragagnoli, Gabor Liposits, Ewa Chmielowska, Paul Aubel, Lourdes Martín, Ronan Fougeray, Nadia Amellal, Mark P Saunders

SOLSTICE Primary Endpoint: Investigator-Assessed PFS (Intent-to-Treat Population)



Number at risk (number censored)													
Trifluridine–tipiracil plus bevacizumab group	426 (0)	382 (8)	345 (10)	294 (11)	237 (14)	178 (32)	126 (53)	93 (56)	58 (75)	33 (90)	18 (98)	8 (105)	1 (110)
Capecitabine plus bevacizumab group	430 (0)	385 (16)	339 (21)	286 (25)	232 (27)	158 (50)	96 (67)	69 (70)	41 (80)	23 (91)	9 (98)	4 (100)	0 (103)

André T et al. *Lancet Gastroenterol Hepatol* 2023;8(2):133-44.

RTP RESEARCH TO PRACTICE

SOLSTICE: Treatment-Emergent Adverse Events

	Trifluridine–tipiracil plus bevacizumab group (n=423)			Capecitabine plus bevacizumab group (n=427)		
	Grade 3	Grade 4	Any grade*	Grade 3	Grade 4	Any grade*
Any treatment-emergent adverse event	234 (55%)	102 (24%)	418 (99%)	218 (51%)	24 (6%)	412 (96%)
Any treatment-emergent adverse-event leading to death	..	..	30 (7%)	..	..	39 (9%)
Any treatment-related adverse event	230 (54%)	94 (22%)	396 (94%)	171 (40%)	17 (4%)	375 (88%)
Treatment-emergent haematological events						
Neutropenia†	151 (36%)	69 (16%)	278 (66%)	3 (1%)	2 (<1%)	37 (9%)
Anaemia	58 (14%)	2 (<1%)	188 (44%)	16 (4%)	0	58 (14%)
Neutrophil count decreased	59 (14%)	19 (4%)	91 (22%)	2 (<1%)	2 (<1%)	11 (3%)
Thrombocytopenia	14 (3%)	2 (<1%)	81 (19%)	0	0	26 (6%)
Leukopenia	21 (5%)	2 (<1%)	71 (17%)	1 (<1%)	0	13 (3%)

	Trifluridine–tipiracil plus bevacizumab group (n=423)			Capecitabine plus bevacizumab group (n=427)		
	Grade 3	Grade 4	Any grade*	Grade 3	Grade 4	Any grade*
Treatment-emergent non-haematological events						
Diarrhoea	30 (7%)	0	154 (36%)	20 (5%)	0	145 (34%)
Nausea	7 (2%)	0	148 (35%)	4 (1%)	0	102 (24%)
Fatigue	25 (6%)	0	101 (24%)	17 (4%)	0	107 (25%)
Decreased appetite	6 (1%)	1 (<1%)	95 (22%)	7 (2%)	0	77 (18%)
Asthenia	25 (6%)	1 (<1%)	95 (22%)	20 (5%)	0	76 (18%)
Vomiting	7 (2%)	0	68 (16%)	5 (1%)	0	44 (10%)
Hypertension	36 (9%)	0	56 (13%)	48 (11%)	0	74 (17%)
Stomatitis	6 (1%)	0	55 (13%)	3 (1%)	0	51 (12%)
Constipation	2 (<1%)	0	51 (12%)	2 (<1%)	0	46 (11%)
Abdominal pain	7 (2%)	0	50 (12%)	8 (2%)	0	63 (15%)
Weight loss	2 (<1%)	0	47 (11%)	1 (<1%)	0	40 (9%)
Blood bilirubin increased	4 (1%)	0	22 (5%)	7 (2%)	0	47 (11%)
Hand–foot syndrome	0	0	5 (1%)	62 (15%)	0	225 (53%)

André T et al. *Lancet Gastroenterol Hepatol* 2023;8(2):133-44.

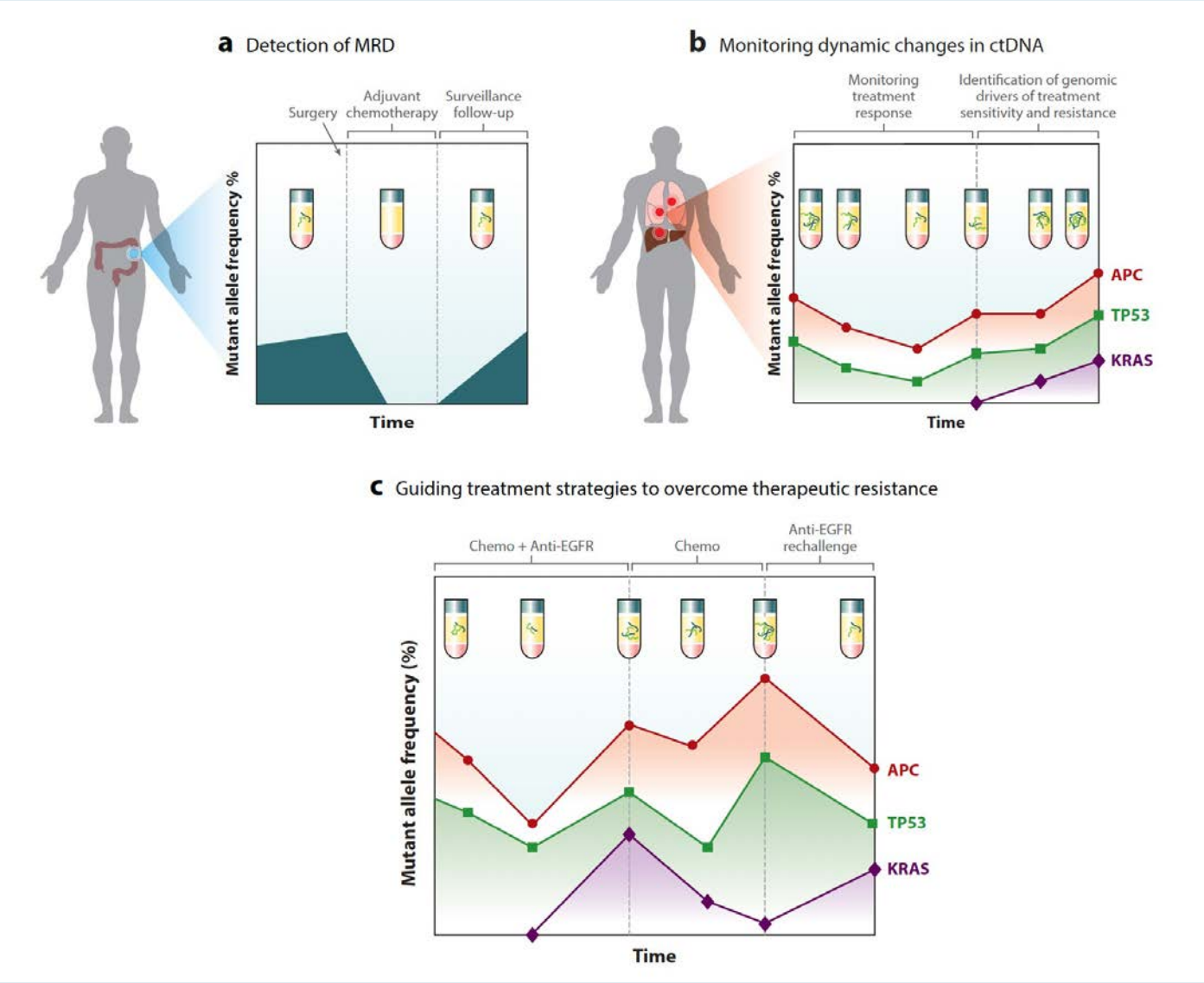
2021;72:399-413.

Annual Review of Medicine

Use of Circulating Cell-Free DNA to Guide Precision Medicine in Patients with Colorectal Cancer

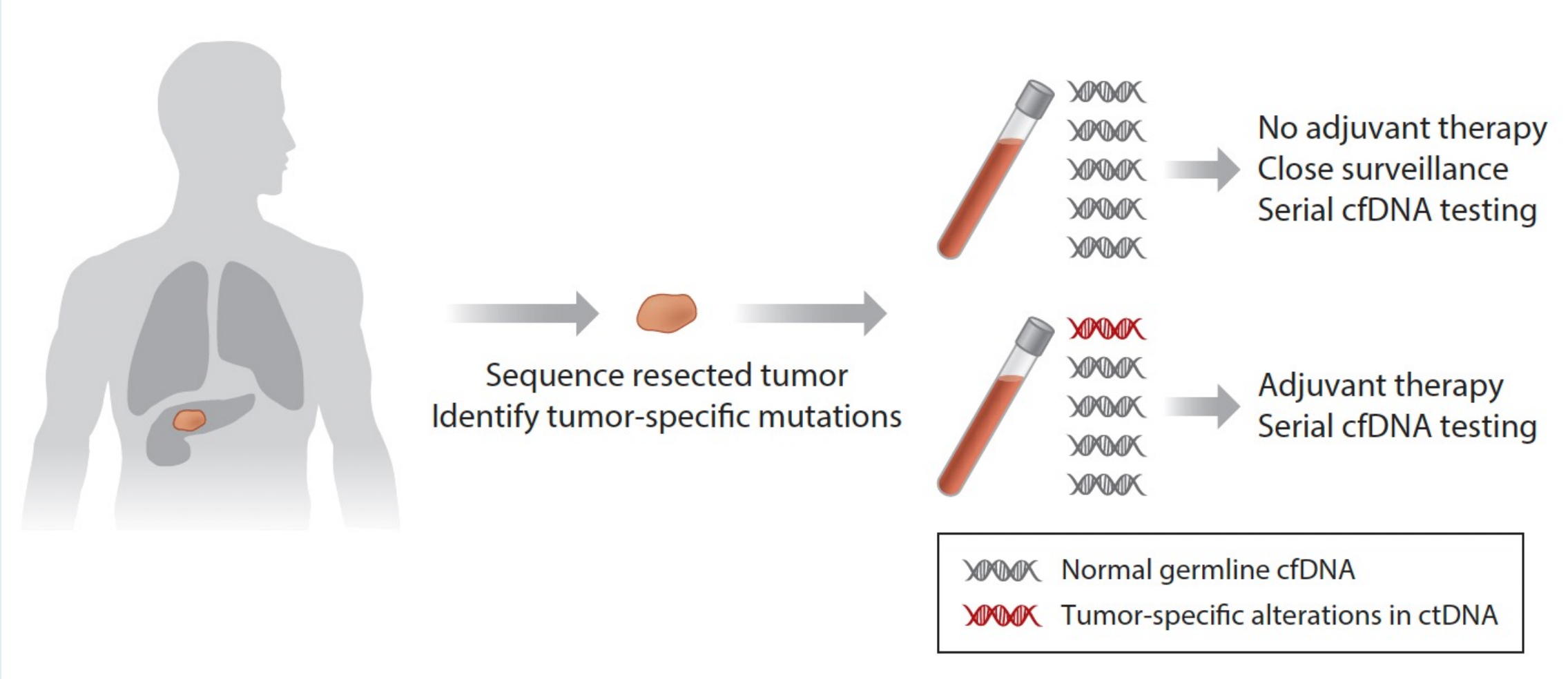
Van K. Morris[1] and John H. Strickler[2]

Clinical Applications of Cell-Free DNA (cfDNA) in Patients with Colorectal Cancer



Morris VK, Strickler JH. *Annu Rev Med* 2021;72:399-413.

Tumor-Informed cfDNA Profiling to Guide Adjuvant Chemotherapy Decision-Making



Morris VK, Strickler JH. *Annu Rev Med* 2021;72:399-413.

Real-World Monitoring of Circulating Tumor DNA Reliably Predicts Cancer Recurrence in Patients with Resected Stages I-III Colorectal Cancer

Cohen SA et al.

ESMO 2022;Abstract 319MO.

Background

Colorectal Cancer (CRC)

- For patients with operable colon and rectal cancers, adjuvant chemotherapy (ACT) is recommended based on TNM stage and other clinical features [1]
- Even with use of ACT, relapse rates remain high (20-30%) [2,3]
- Current risk factors for prognostication fall short from accurately predicting relapse rates.
- Identification of post-surgical molecular residual disease (MRD) could improve treatment selection and enable timely treatment of patients who are identified to be at high risk of recurrence
- Several studies have established the presence of post-surgical circulating tumor DNA (ctDNA) to be an early prognostic marker of relapse [3,4]

Objectives:

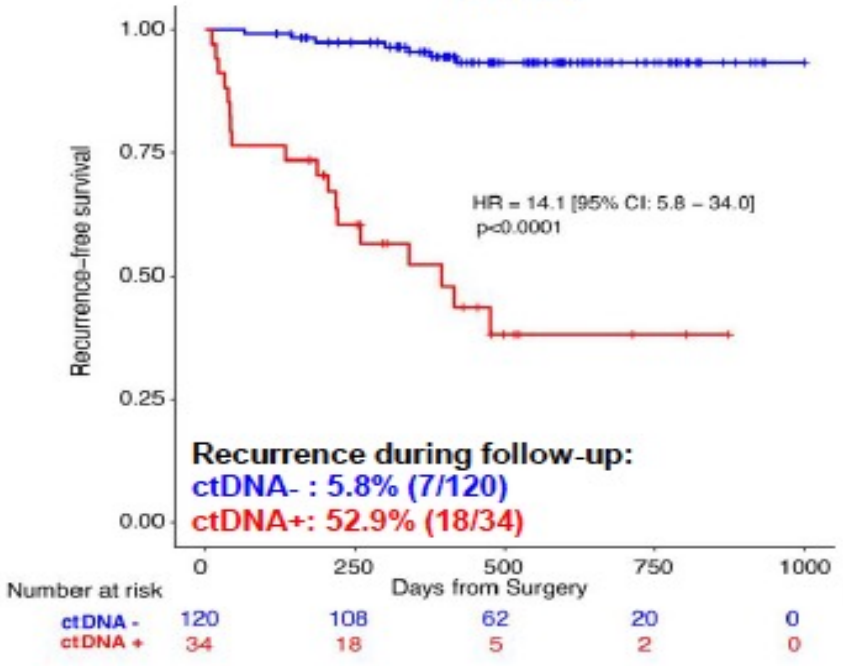
- ***Assess ctDNA-based MRD detection rates in a "real world" cohort of patients with stage I-III CRC who underwent curative intent treatment***
- ***Determine recurrence rates and recurrence-free survival in patients stratified by MRD status***
- ***Determine the benefit of ACT in ctDNA-negative group***

1. NCCN Clinical practice guidelines in oncology. Colon cancer version 2.2021. *J Natl Compr Canc Network*. 2;19(3):329-359. doi: 10.6004/jnccn.2021.0012.
2. Chen, G., et al., Postoperative circulating tumor DNA as markers of recurrence risk in stages II to III colorectal cancer. *J Hematol Oncol*, 2021. **14**(1): p. 80.
3. Reinert, T., et al., Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. *JAMA Oncol*, 2019. **5**(8): p. 1124-1131.
4. Taniguchi H, Nakamura Y, Kotani D, et al. CIRCULATE-Japan: Circulating tumor DNA-guided adaptive platform trials to refine adjuvant therapy for colorectal cancer. *Cancer Science*. 2021;112:2915–2920

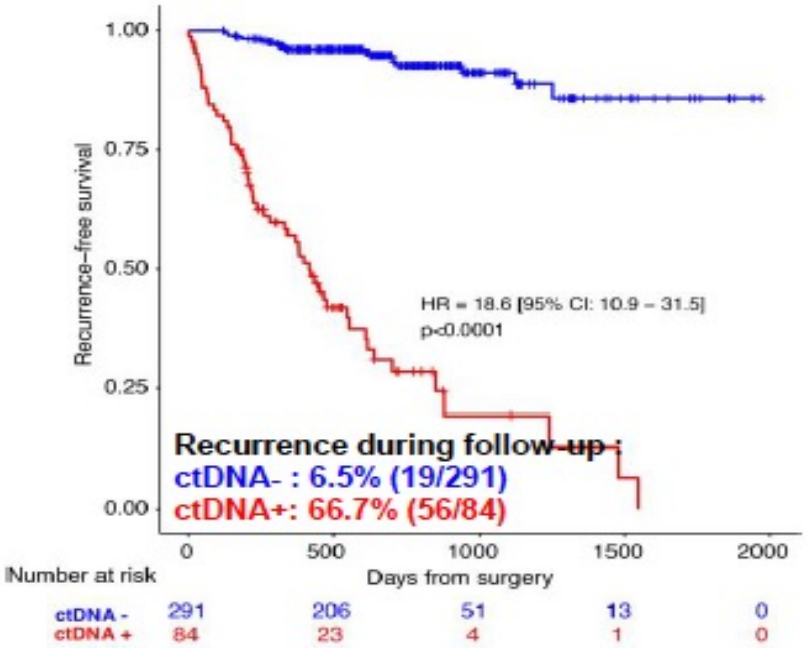
Results

Postoperative ctDNA-positivity is significantly associated with shorter recurrence-free survival

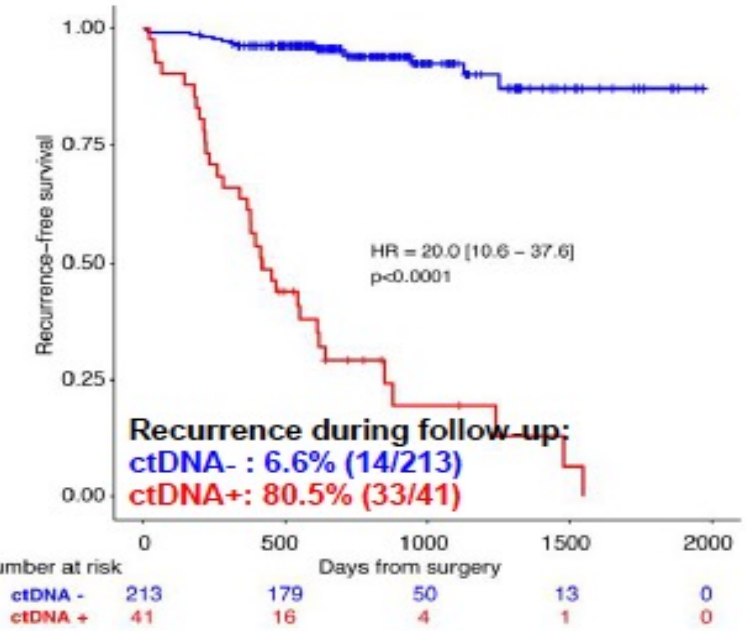
MRD window (2-8 weeks after surgery), N = 154



Anytime Positivity (any time post-surgery), N = 376



Surveillance window (6 months post-surgery & post any ACT), N = 254



PARIS 2022 ESMO congress

Stacey A. Cohen, M.D.

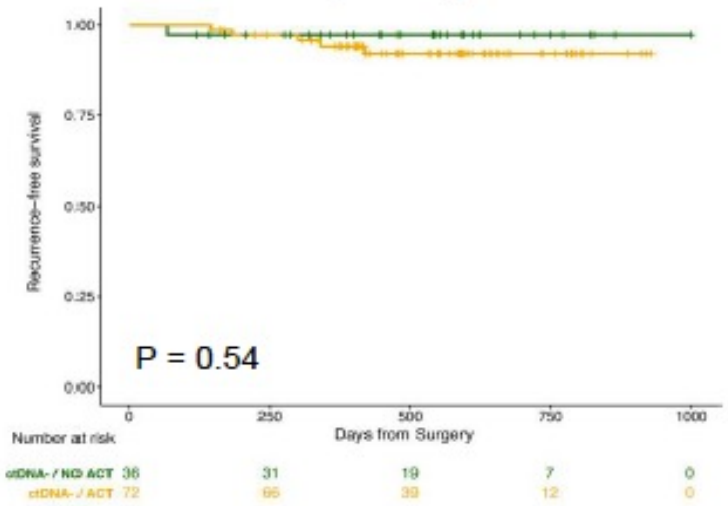
RTP RESEARCH TO PRACTICE

Results

Patients identified as ctDNA-negative during the MRD window showed no trend in benefit from ACT.

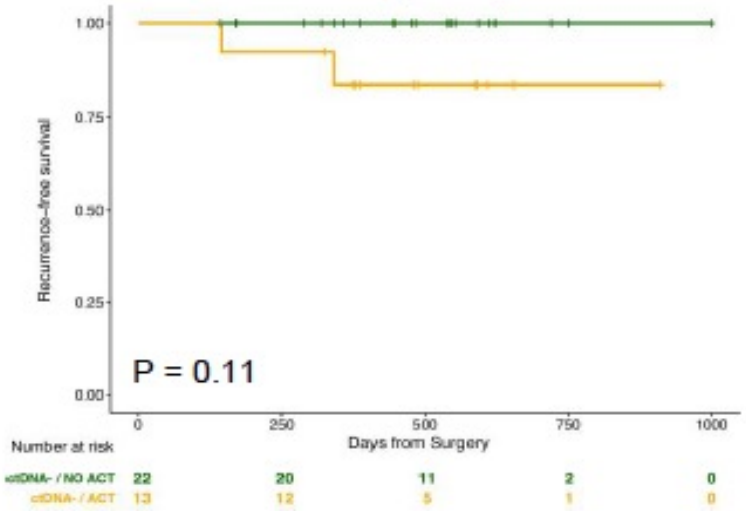
All stages ctDNA-negative Patients

(N = 120)



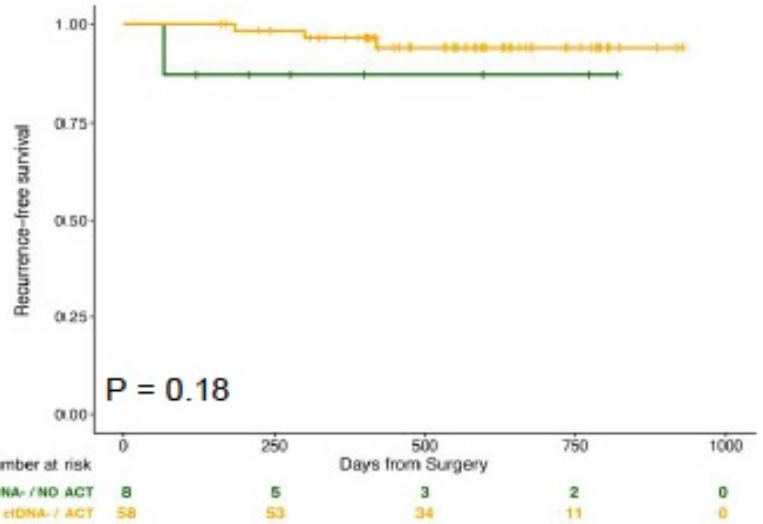
Stage II ctDNA-negative Patients

(N = 35)



Stage III ctDNA-negative Patients

(N = 66)



PARIS 2022 ESMO congress

Stacey A. Cohen, M.D.

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 16, 2022 VOL. 386 NO. 24

Circulating Tumor DNA Analysis Guiding Adjuvant Therapy in Stage II Colon Cancer

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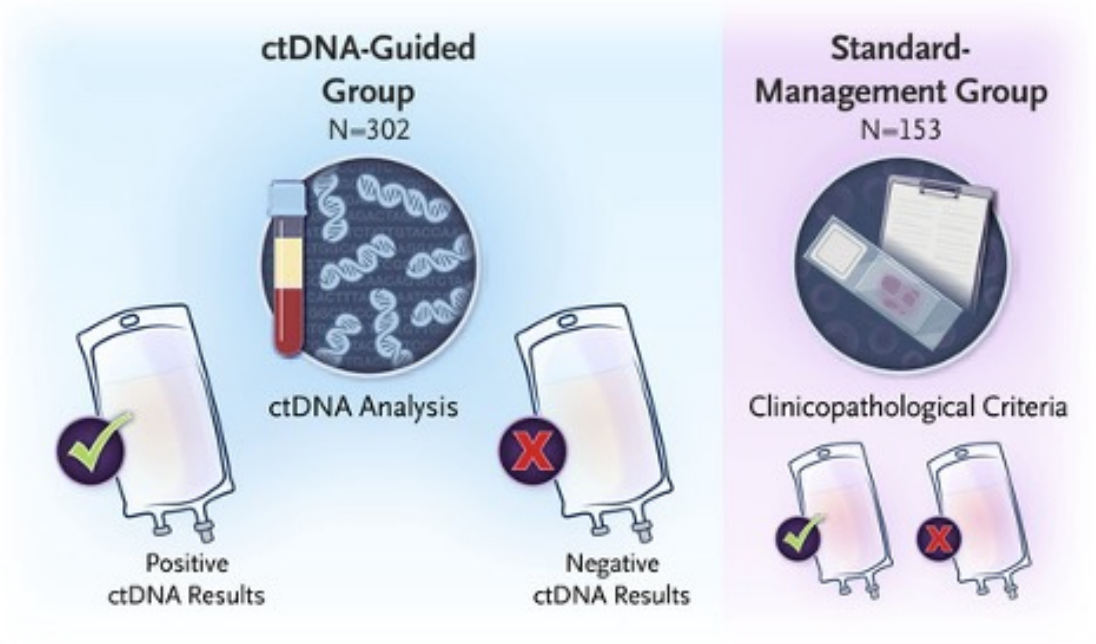
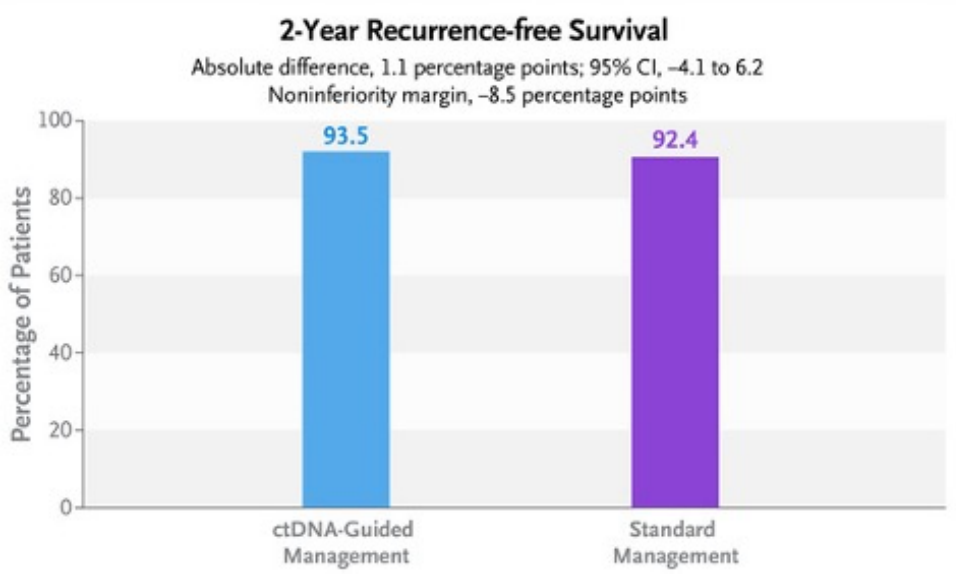
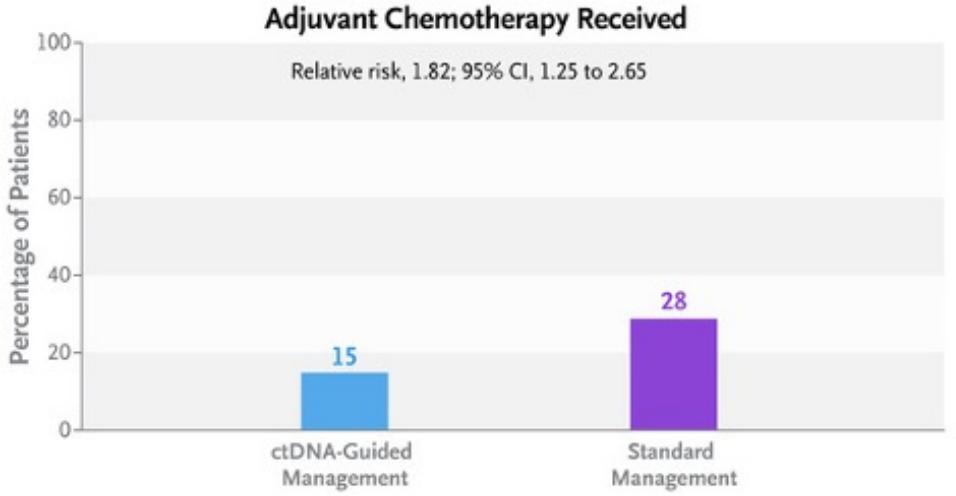
DYNAMIC: Results Summary



CONCLUSIONS

Among patients with stage II colon cancer, ctDNA-guided management was noninferior to standard management with respect to 2-year recurrence-free survival and resulted in reduced use of adjuvant chemotherapy.





Tie J et al. *N Engl J Med* 2022;386(24):2261-72.

RTP RESEARCH TO PRACTICE

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

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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]

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

Meet The Professor with Dr Strickler

Introduction: ASCO Guidelines for the Treatment of Metastatic Colorectal Cancer

MODULE 1: Case Presentations and Faculty Survey

MODULE 2: Journal Club

MODULE 3: Appendix

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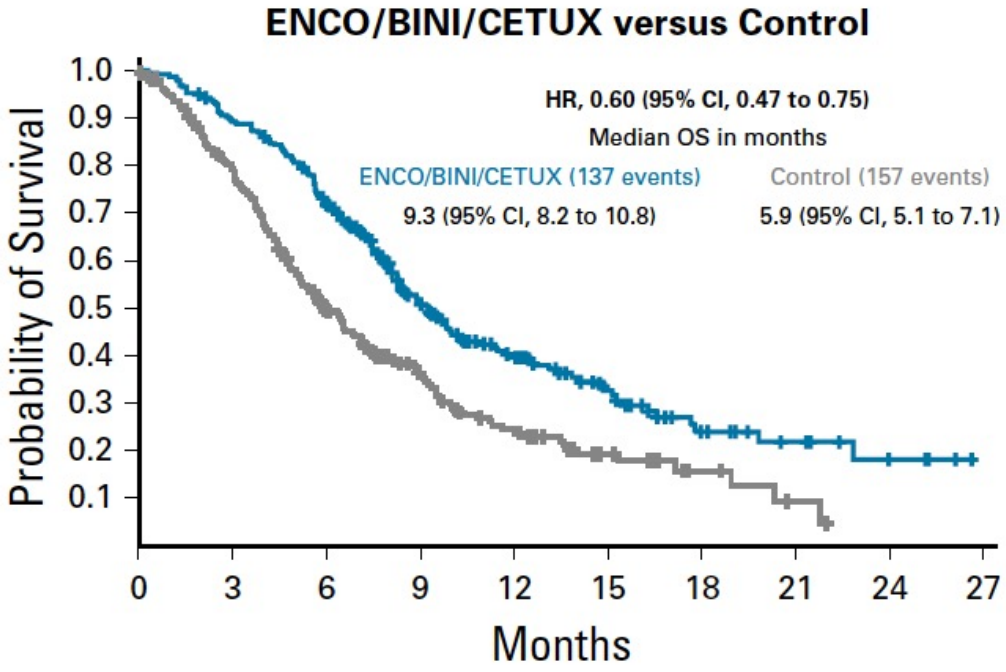
rapid communications

Encorafenib Plus Cetuximab as a New Standard of Care for Previously Treated *BRAF* V600E–Mutant Metastatic Colorectal Cancer: Updated Survival Results and Subgroup Analyses from the BEACON Study

Josep Tabernero, MD, PhD[1]; Axel Grothey, MD[2]; Eric Van Cutsem, MD, PhD[3]; Rona Yaeger, MD[4]; Harpreet Wasan, MD[5]; Takayuki Yoshino, MD, PhD[6]; Jayesh Desai, MBBS[7]; Fortunato Ciardiello, MD, PhD[8]; Fotios Loupakis, MD, PhD[9]; Yong Sang Hong, MD, PhD[10]; Neeltje Steeghs, MD, PhD[11]; Tormod Kyrre Guren, MD, PhD[12]; Hendrik-Tobias Arkenau, MD, PhD[13]; Pilar Garcia-Alfonso, MD[14]; Elena Elez, MD, PhD[1]; Ashwin Gollerkeri, MD[15]; Kati Maharry, PhD[15]; Janna Christy-Bittel, MSN[15]; and Scott Kopetz, MD, PhD[16]

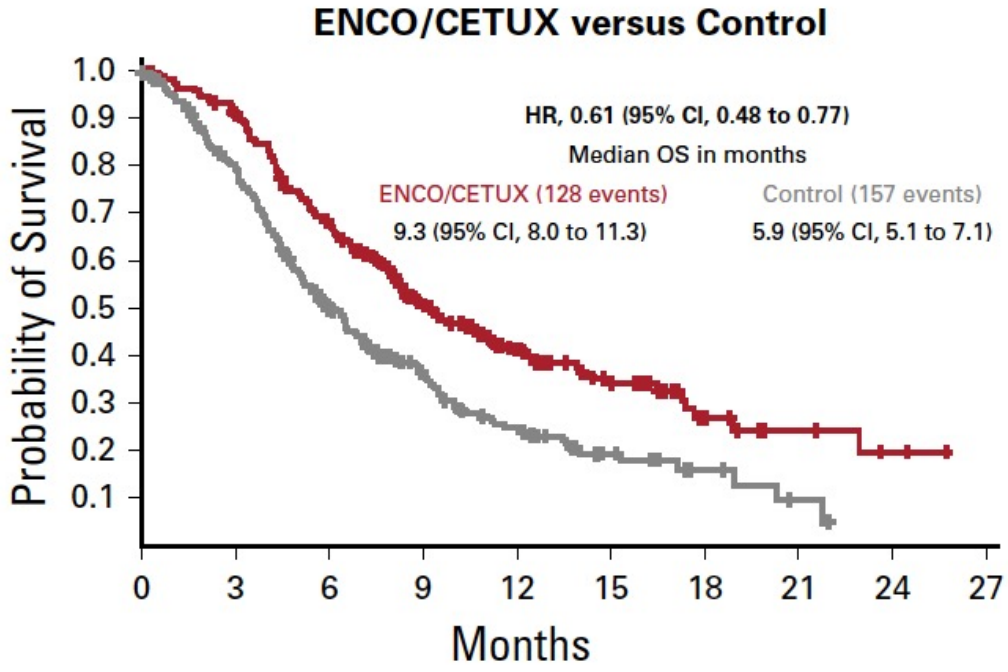
J Clin Oncol 2021;39(4):273-84.

BEACON: Overall Survival Results



Number of patients at risk

ENCO/BINI/CETUX	224	198	157	89	56	33	15	9	4	0
Control	221	166	98	54	33	15	6	2	0	0



Number of patients at risk

ENCO/CETUX	220	197	143	83	47	28	13	7	2	0
Control	221	166	98	54	33	15	6	2	0	0

Tabanero J et al. *J Clin Oncol* 2021;39(4):273-84.

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ESMO WORLD CONGRESS ON Gastrointestinal Cancer

ANCHOR CRC: a single-arm, phase 2 study of encorafenib, binimetinib plus cetuximab in previously untreated *BRAF*^{V600E}–mutant metastatic colorectal cancer

Eric Van Cutsem, Julien Taieb, Rona Yaeger, Takayuki Yoshino, Evaristo Maiello, Elena Elez Fernandez, Jeroen Dekervel, Paul Ross, Ana Ruiz Casado, Janet Graham, Takeshi Kato, Jose Carlos Ruffinelli, Thierry André, Edith Carrière Roussel, Isabelle Klauck, Mélanie Groc, Axel Grothey, Jean-Claude Vedovato, Josep Tabernero*

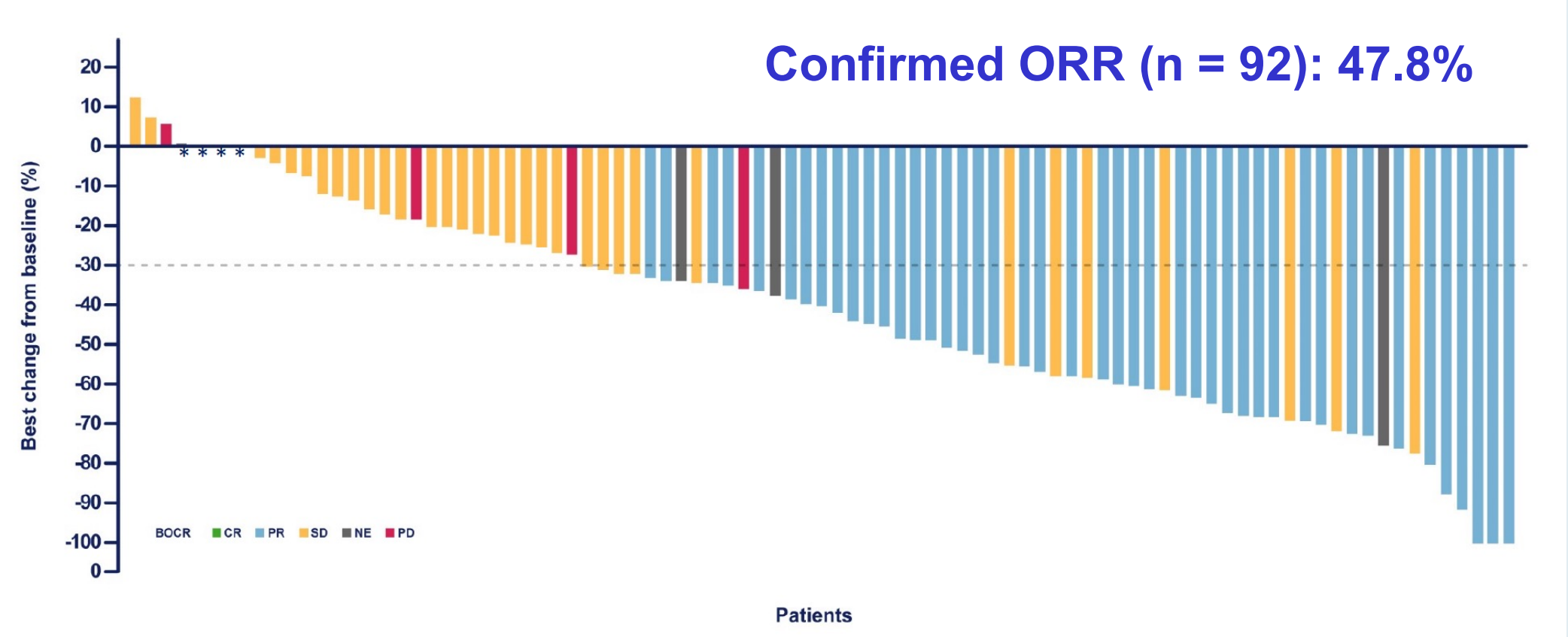
** University Hospitals Leuven, Belgium*

ANCHOR CRC: encorAfenib, biNimetinib and Cetuximab in subjects witH previOusly untreated BRAF-mutant ColoRectal Cancer

ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

RTP RESEARCH TO PRACTICE

ANCHOR CRC: Results Summary



ORR, objective response rate.

- Overall survival was 17.2 mo (with a median follow-up of 14.4 mo)
- The triplet combination was well tolerated and there were no unexpected toxicities

Van Cutsem E et al. ESMO World Congress on Gastrointestinal Cancer 2021;Abstract O-10.

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

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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.

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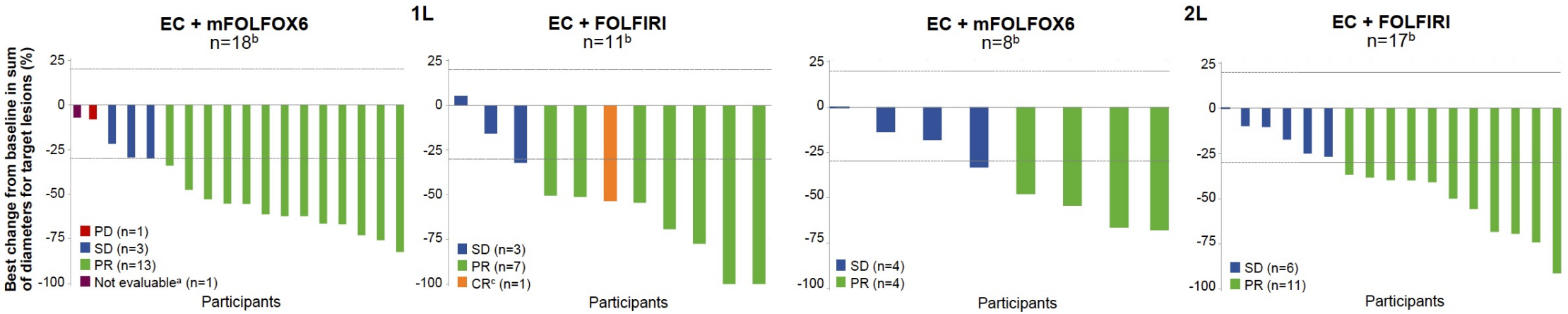
BREAKWATER Safety Lead-In: Overview of Response

	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

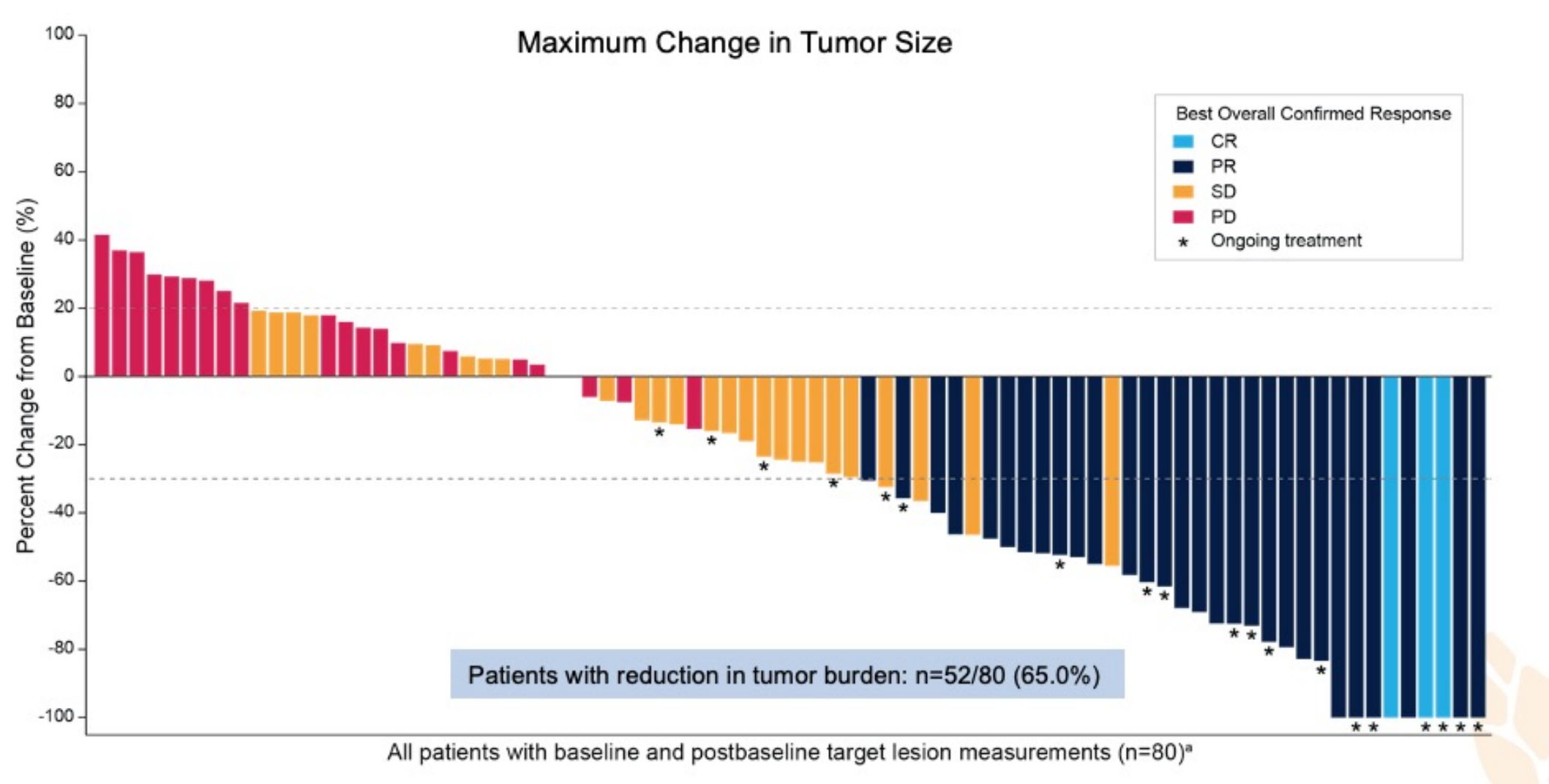
Primary analysis of MOUNTAINEER: A phase 2 study of tucatinib and trastuzumab for HER2-positive mCRC

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



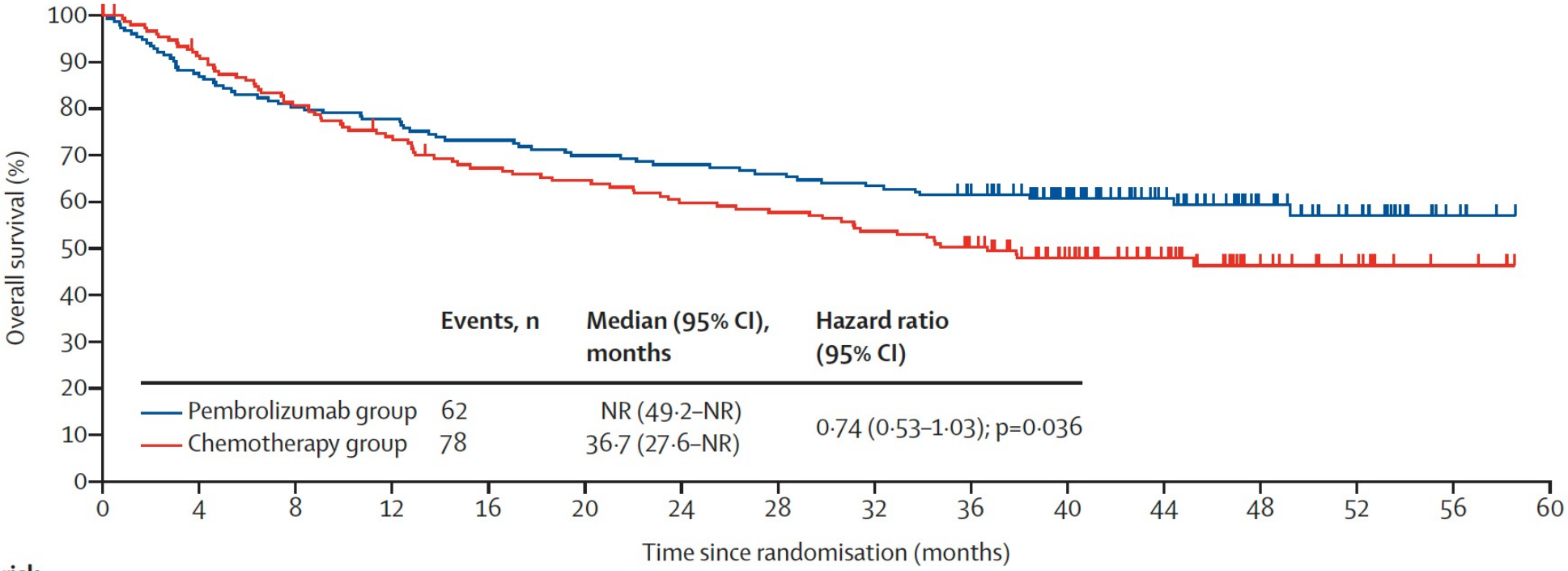
Strickler JH et al. ESMO GI 2022;Abstract LBA-2.

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)



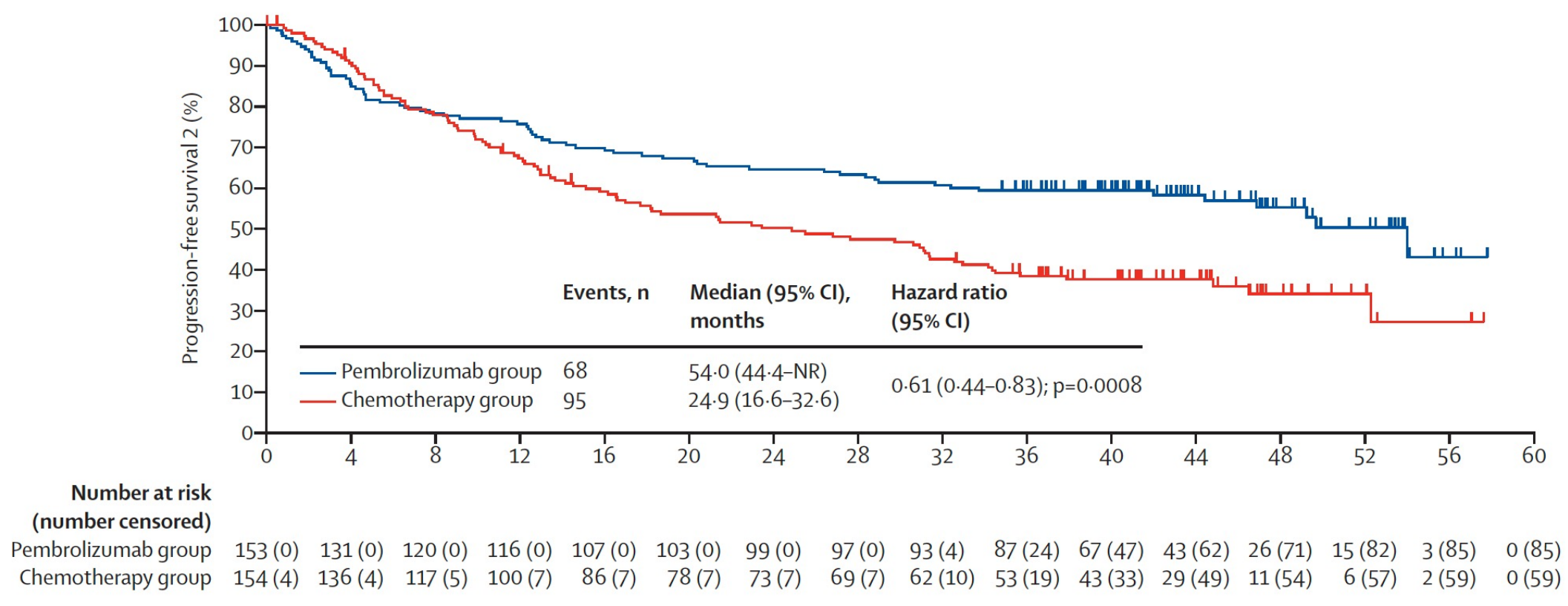
Number at risk (number censored)																
Pembrolizumab group	153 (0)	134 (0)	123 (0)	119 (0)	112 (0)	107 (0)	104 (0)	101 (0)	97 (2)	92 (23)	70 (45)	48 (64)	28 (75)	16 (78)	4 (91)	0 (91)
Chemotherapy group	154 (4)	137 (4)	121 (5)	110 (6)	99 (6)	95 (6)	88 (6)	85 (6)	79 (9)	71 (24)	53 (41)	36 (58)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



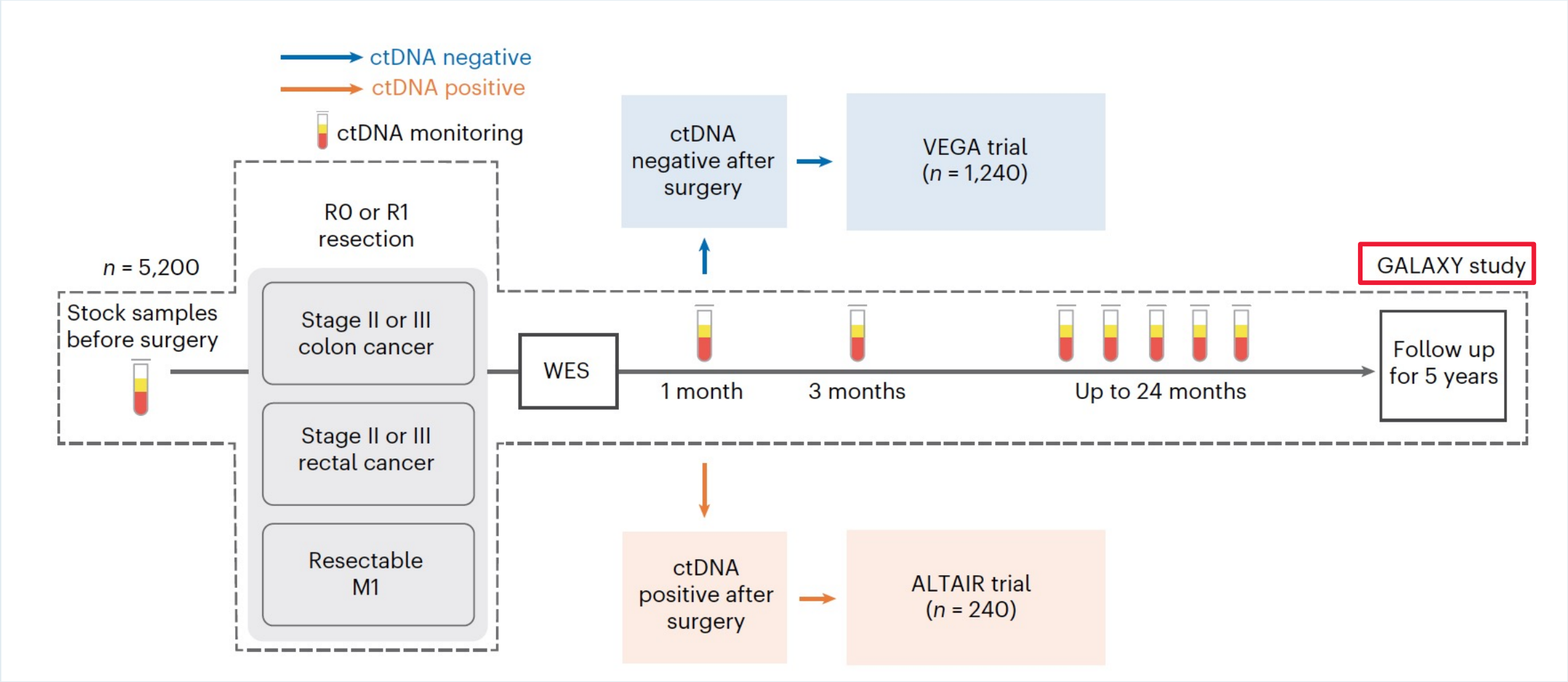
At the final analysis, median progression-free survival (PFS) was longer with pembrolizumab (16.5 mo) than with chemotherapy (8.2 mo); however, because superiority was met at the second interim analysis, superiority was not formally tested at the final analysis (HR 0.59).

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.

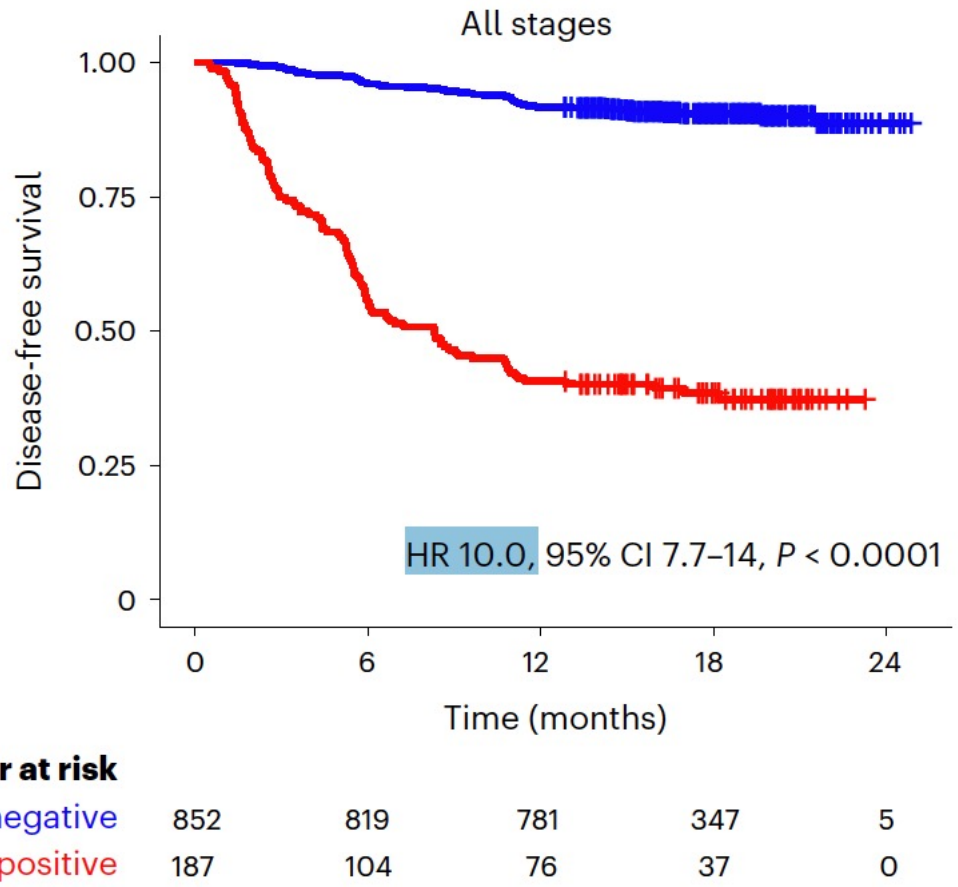
RTP RESEARCH TO PRACTICE

Overview of CIRCULATE-JAPAN Study



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

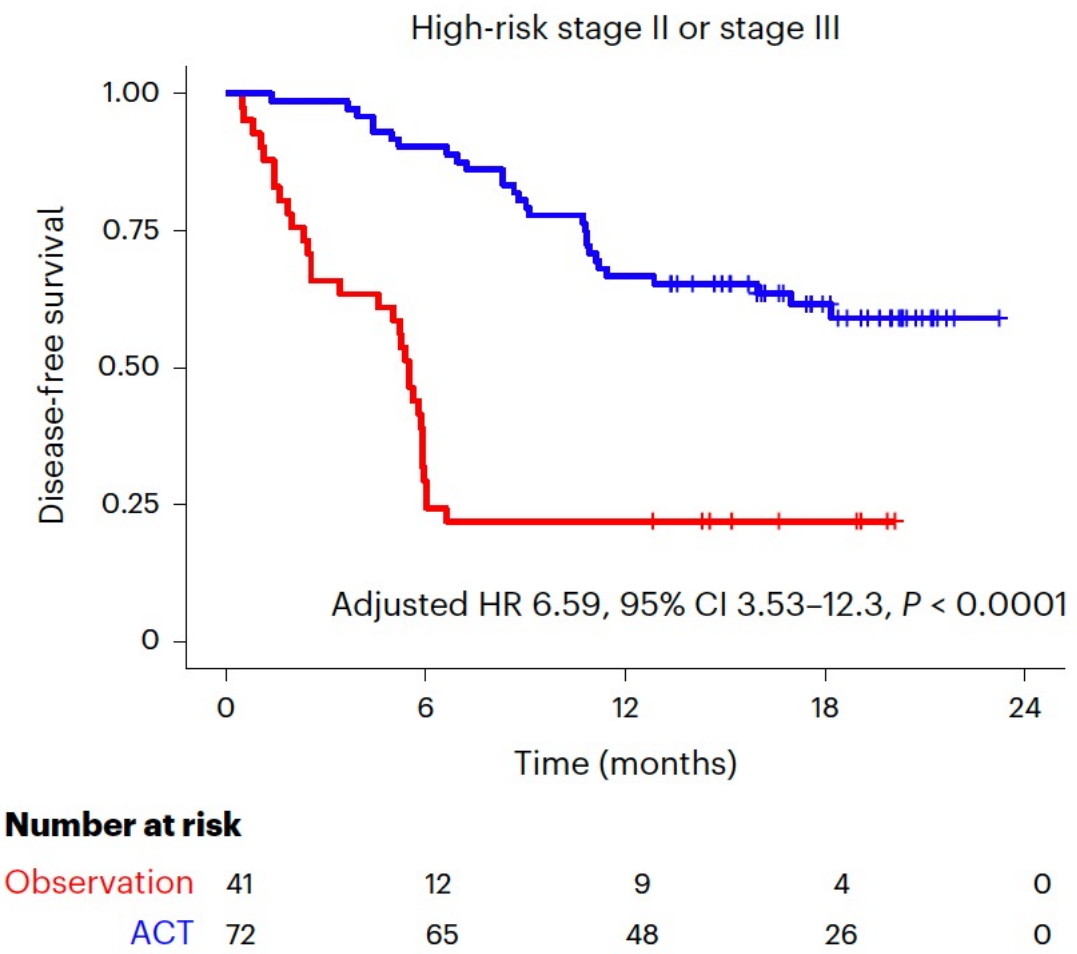
GALAXY: ctDNA-Based Minimal Residual Disease Is Predictive of Survival Outcomes Among Postsurgical Patients with CRC



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].

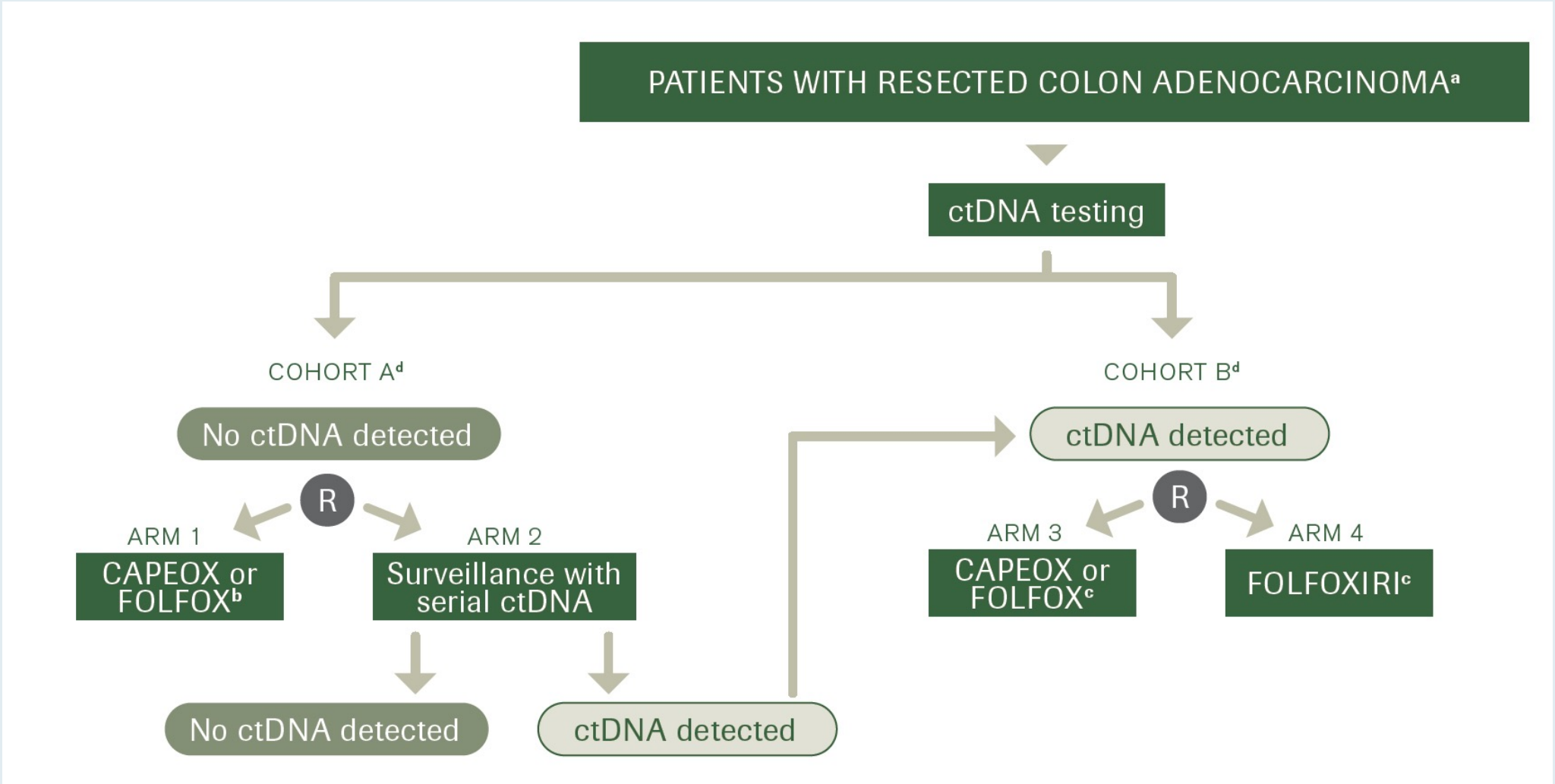
GALAXY: Disease-Free Survival — ctDNA-Positive 4 Weeks After Surgery



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].

CIRCULATE-US



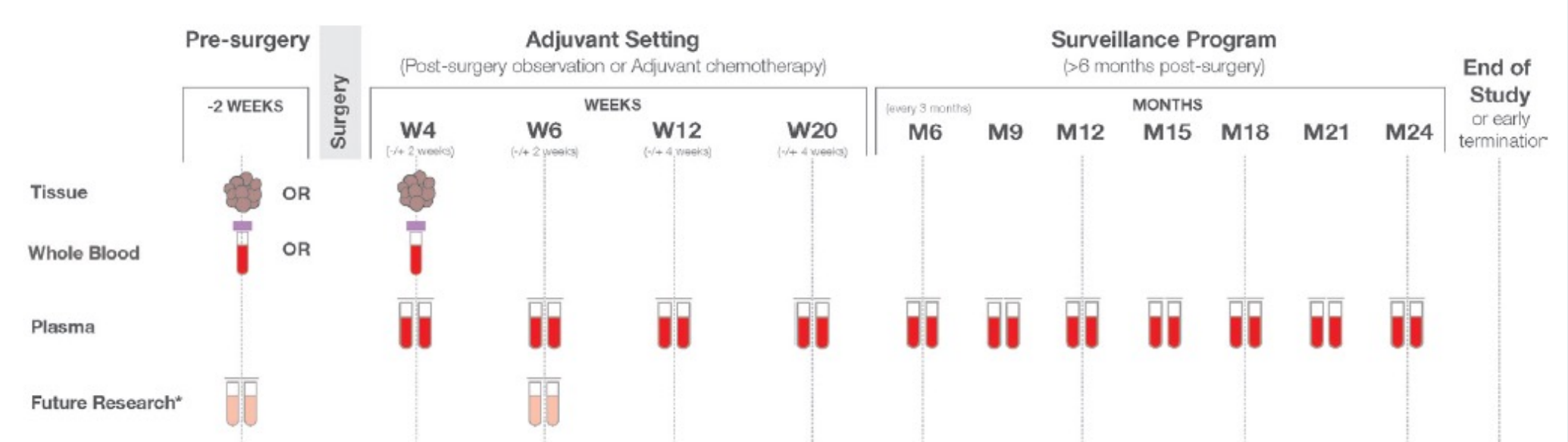
Sahin IH et al. *Oncology* 2022;36(10):604-9.

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.

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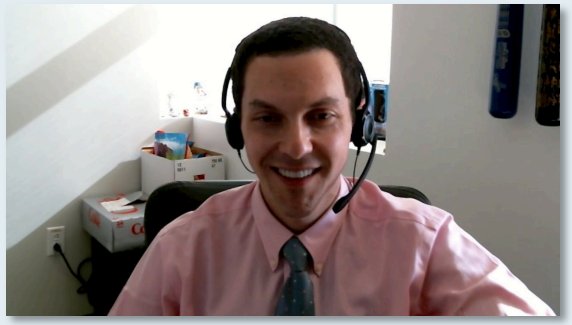

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Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Ovarian Cancer

Part 1 of a 2-Part CME Symposium Series Held in Conjunction with the 2023 Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer®

Sunday, March 26, 2023

11:45 AM – 1:15 PM ET

Faculty

Mansoor Raza Mirza, MD

Amit M Oza, MD

Richard T Penson, MD, MRCP

Moderator

Joyce F Liu, MD, MPH

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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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