

Practical Perspectives: Investigators Discuss Current Management and Actual Cases of Relapsed/Refractory Metastatic Colorectal Cancer

A CME/MOC-Accredited Virtual Event

Wednesday, September 20, 2023

5:00 PM – 6:00 PM ET

Faculty

Kristen K Ciombor, MD, MSCI

J Randolph Hecht, MD

Moderator

Neil Love, MD

Faculty



Kristen K Ciombor, MD, MSCI
Associate Professor of Medicine
Division of Hematology/Oncology
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee



Moderator
Neil Love, MD
Research To Practice



J Randolph Hecht, MD
Professor of Clinical Medicine
Director, UCLA GI Oncology Program
Carol and Saul Rosenzweig Chair
in Cancer Therapies Development
UCLA David Geffen School of Medicine
Santa Monica, California

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Seagen Inc, Taiho Oncology Inc, and Takeda Pharmaceuticals USA 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, 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, Legend Biotech, 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, R-Pharm US, 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.

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

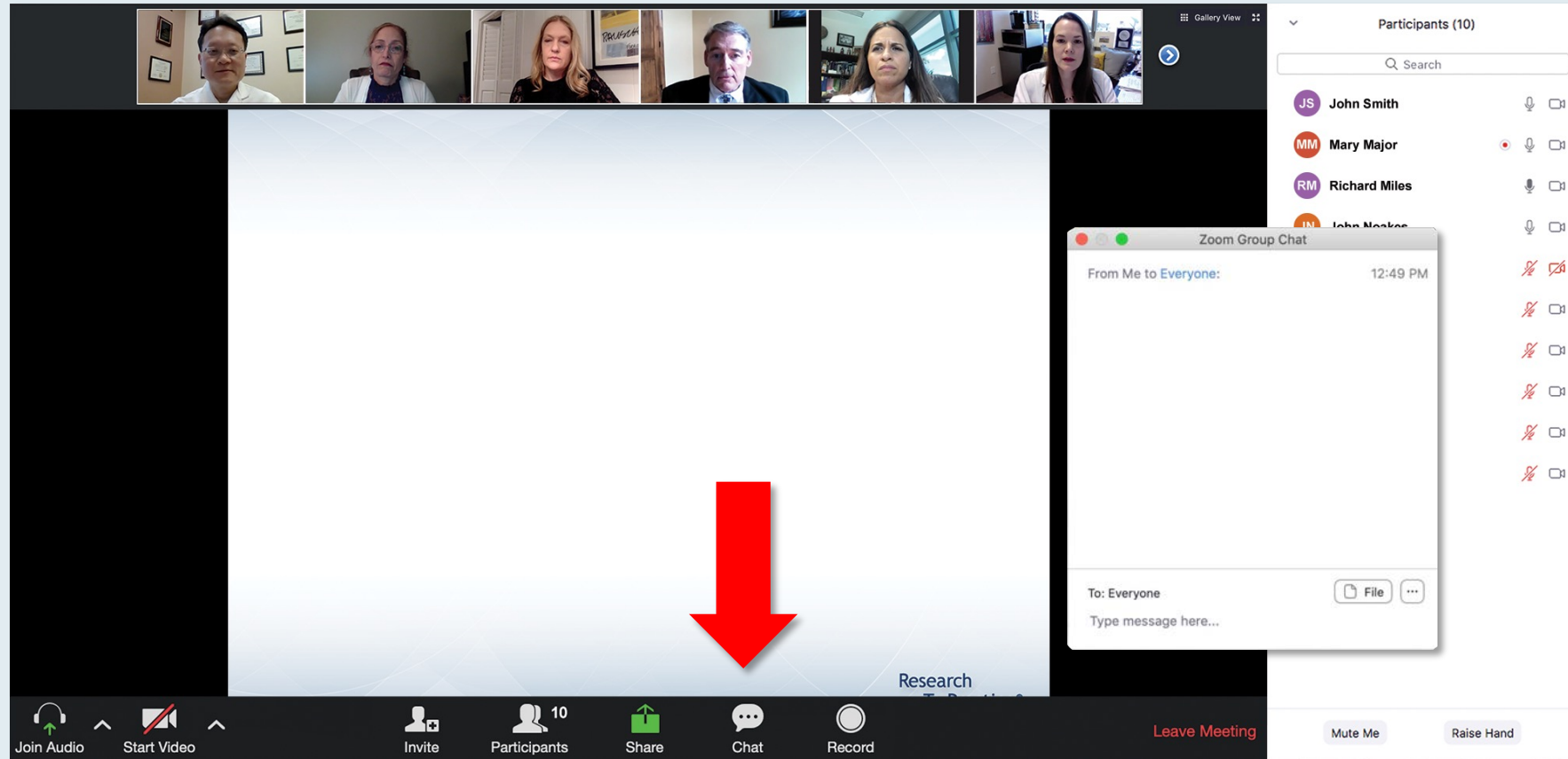
Dr Ciombor — Disclosures

Advisory Committee	Bayer HealthCare Pharmaceuticals, Exelixis Inc, Incyte Corporation, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Personalis, Pfizer Inc, Replimune, Seagen Inc
Consulting Agreements	Merck, Pfizer Inc
Contracted Research	Array BioPharma Inc, a subsidiary of Pfizer Inc, Bristol Myers Squibb, Calithera Biosciences, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Incyte Corporation, Merck, NuCana, Pfizer Inc, Seagen Inc

Dr Hecht — Disclosures

Advisory Committee	Actym Therapeutics, Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc, Mirati Therapeutics Inc, Rafael Pharmaceuticals Inc
Contracted Research	AbbVie Inc, Amgen Inc, Astellas, Merck, Mirati Therapeutics Inc, Tesaro, A GSK Company

We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot displays a Zoom meeting interface. At the top, there's a header bar with participant names: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below this, a slide titled "Meet The Professor Program Participating Faculty" is shown. The slide lists six faculty members with their photos and titles:

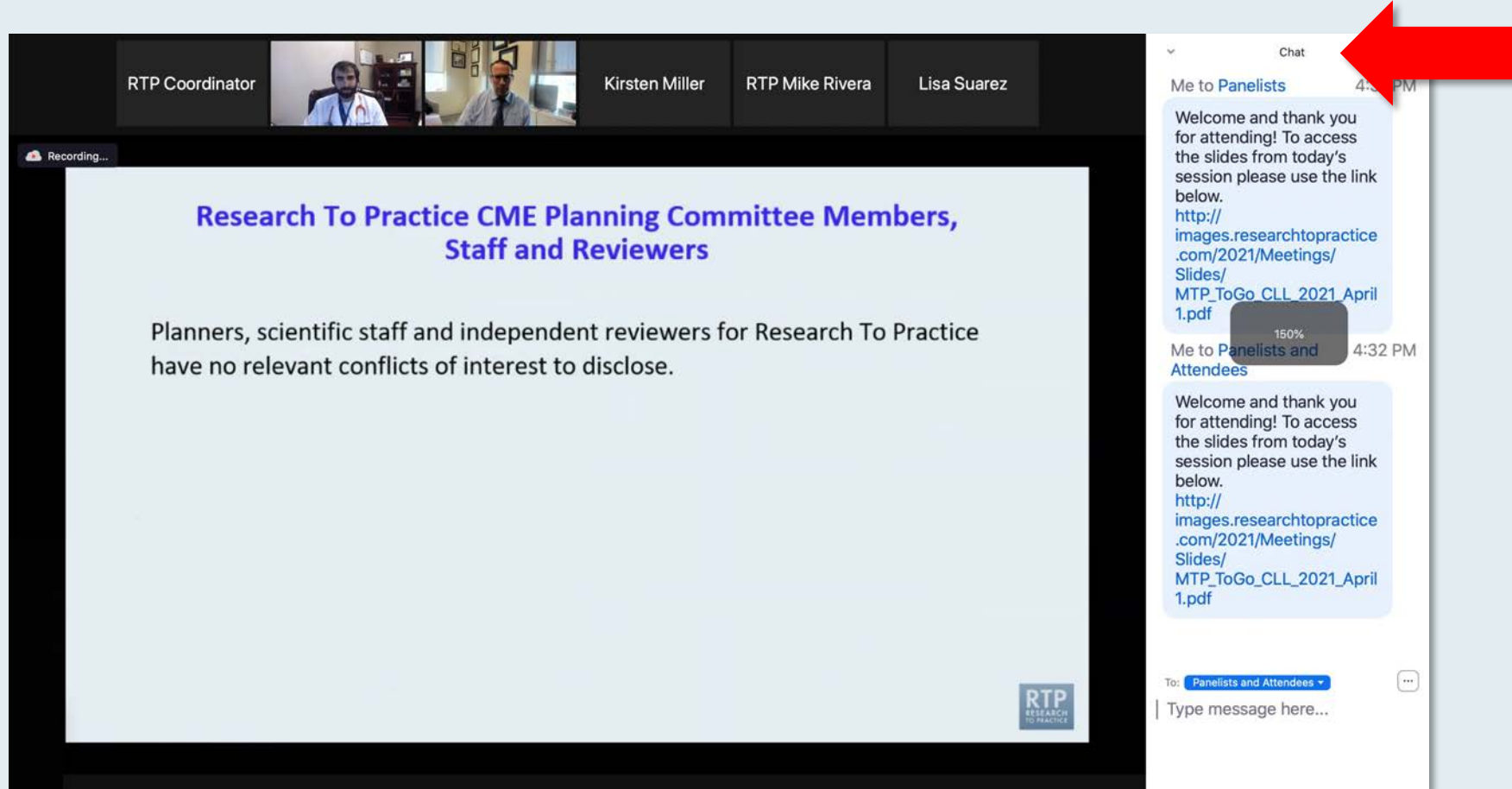
- Nancy L Bartlett, MD**
Professor of Medicine
Koman Chair in Medical Oncology
Washington University School of Medicine
St Louis, Missouri
- Jonathan W Friedberg, MD, MMSc**
Samuel E Durand Professor of Medicine
Director, James P Wilmot Cancer Institute
University of Rochester
Rochester, New York
- Carla Casulo, MD**
Associate Professor of Medicine
Division of Hematology/Oncology
Director, Hematology/Oncology Fellowship Program
University of Rochester
Wilmot Cancer Institute
Rochester, New York
- Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
- Christopher R Flowers, MD, MS**
Chair, Professor
Department of Lymphoma/Myeloma
The University of Texas MD Anderson Cancer Center
Houston, Texas
- Brad S Kahl, MD**
Professor of Medicine
Washington University School of Medicine
Director, Lymphoma Program
Siteman Cancer Center
St Louis, Missouri

On the right side, a chat window is open. It shows two messages from "Me to Panelists" and "Me to Panelists and Attendees". At the bottom of the chat window, there's a white line above the submission box, which is highlighted by a red arrow. The submission box is labeled "To: Panelists and Attendees" and "Type message here..."

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

Familiarizing Yourself with the Zoom Interface

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

The screenshot shows a Zoom meeting window. At the top, a row of seven participant video thumbnails is visible. The main content area displays a presentation slide with the following text:

Meet The Professionals
Optimizing the Selection and Timing of Therapy for Patients with Gastrointestinal Cancer
Wednesday, August 25, 2022
5:00 PM – 6:00 PM EST
Faculty
Wells A Messersmith, MD
Moderator
Neil Love, MD

A "Quick Survey" pop-up window is overlaid on the slide, listing various treatment combinations with radio button options:

- ☐ Ceritinib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Ceritinib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Isaxozim + Rd

The "Participants (10)" list on the right side of the window includes:

- John Smith
- Mary Major
- Richard Miles
- John Noakes
- Alice Suarez
- Jane Perez
- Robert Stiles
- Juan Fernandez
- Ashok Kumar
- Jeremy Smith

The bottom toolbar contains icons for Join Audio, Start Video, Invite, Participants, Share, Chat, Record, and a red "Leave Meeting" button.

The screenshot shows the same Zoom meeting window. The presentation slide now displays a poll question:

Regulatory and reimbursement issues aside, which treatment would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) if follow-up 3 years later is found to have asymptomatic (PS 0)?

A "Quick Poll" pop-up window is overlaid, showing the following options:

- ☐ Nivolumab/ipilimumab
- ☐ Avelumab/axitinib
- ☐ Pembrolizumab/axitinib
- ☐ Pembrolizumab/lenvatinib
- ☐ Nivolumab/cabozantinib
- ☐ Tyrosine kinase inhibitor (TKI) monotherapy
- ☐ Anti-PD-1/PD-L1 monotherapy
- ☐ Other

The "Participants (10)" list on the right remains the same as in the previous screenshot.

The bottom toolbar is identical to the previous screenshot, featuring icons for Join Audio, Start Video, Invite, Participants, Share, Chat, Record, and a red "Leave Meeting" button.

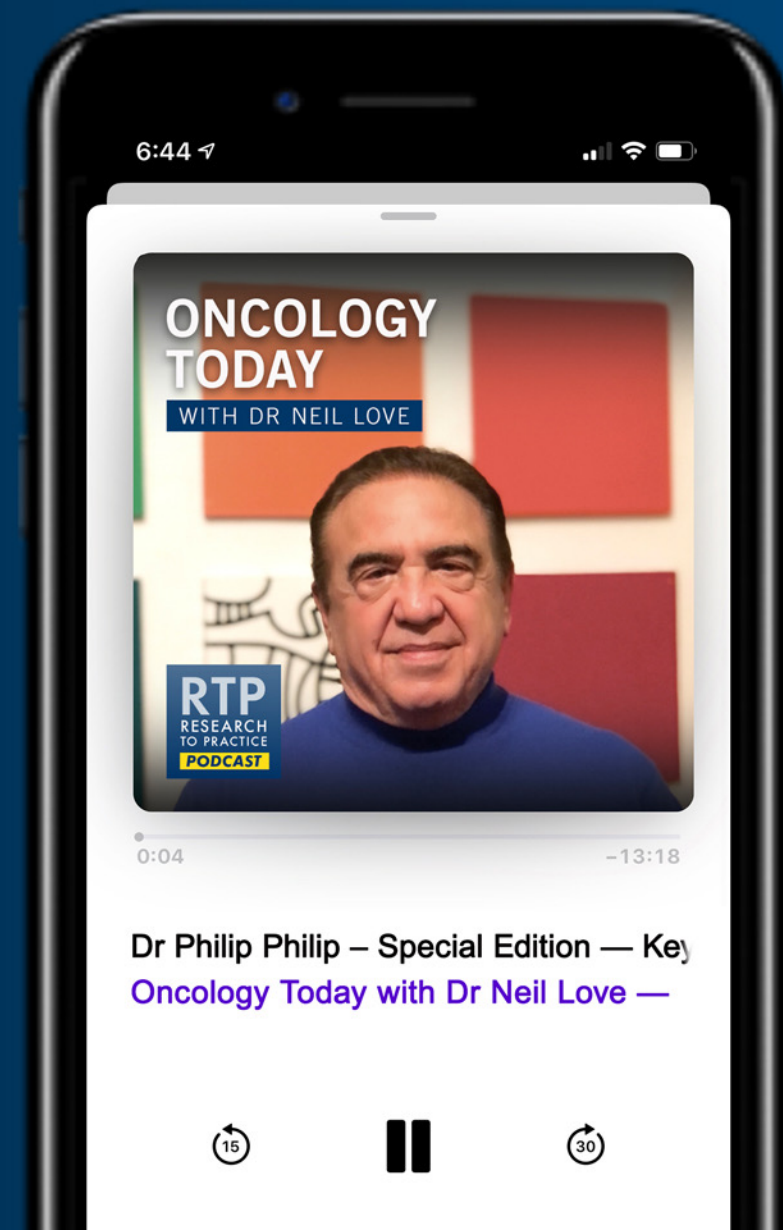
ONCOLOGY TODAY

WITH DR NEIL LOVE

**Special Edition — Key Presentations from
the 2023 American Society of Clinical
Oncology (ASCO) Annual Meeting,
Gastrointestinal Cancers Issue**



DR PHILIP PHILIP
WAYNE STATE UNIVERSITY



Inside the Issue: Integrating Targeted and Immunotherapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, September 21, 2023

5:00 PM – 6:00 PM ET

Faculty

Jamie E Chافت, MD

John V Heymach, MD, PhD

Moderator

Neil Love, MD

What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Tuesday, September 26, 2023

5:00 PM – 6:00 PM ET

Faculty

Toby A Eyre, MBChB, DipMedEd, MRCP, MD

Brad S Kahl, MD

Moderator

Neil Love, MD

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

**Thursday, September 28, 2023
5:00 PM – 6:00 PM ET**

Faculty

Peter C Enzinger, MD

Moderator

Neil Love, MD

Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, October 3, 2023

5:00 PM – 6:00 PM ET

Faculty

Nikhil I Khushalani, MD

Anna C Pavlick, DO, MBA

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

ER-Positive Breast Cancer

7:15 AM – 8:15 AM ET

Faculty

Harold J Burstein, MD, PhD

Komal Jhaveri, MD

Prostate Cancer

8:15 AM – 9:15 AM ET

Faculty

Alicia K Morgans, MD, MPH

Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

Non-Small Cell Lung Cancer

9:30 AM – 10:30 AM ET

Faculty

Gregory J Riely, MD, PhD

Heather Wakelee, MD, FASCO

Colorectal and Gastroesophageal Cancers

10:30 AM – 11:30 AM ET

Faculty

Tanios Bekaii-Saab, MD

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

Chronic Lymphocytic Leukemia

11:30 AM – 12:30 PM ET

Faculty

Asher Chanan-Khan, MD

Brad S Kahl, MD

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Lymphoma

**9:30 AM – 10:30 AM PT
(12:30 PM – 1:30 PM ET)**

Faculty

**Christopher R Flowers, MD, MS
Ann S LaCasce, MD, MMSc**

Urothelial Bladder Cancer and Renal Cell Carcinoma

**10:30 AM – 11:30 AM PT
(1:30 PM – 2:30 PM ET)**

Faculty

**Thomas E Hutson, DO, PharmD
Guru P Sonpavde, MD**

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Hepatobiliary and Pancreatic Cancers

**11:50 AM – 12:50 PM PT
(2:50 PM – 3:50 PM ET)**

Faculty

**Mitesh J Borad, MD
Anthony El-Khoueiry, MD**

Gynecologic Cancers

**1:30 PM – 2:30 PM PT
(4:30 PM – 5:30 PM ET)**

Faculty

**Bradley J Monk, MD
Kathleen N Moore, MD, MS**

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Multiple Myeloma

**2:30 PM – 3:30 PM PT
(5:30 PM – 6:30 PM ET)**

Faculty

**Amrita Krishnan, MD
Robert Z Orlowski, MD, PhD**

HER2-Positive and Triple-Negative Breast Cancer

**3:50 PM – 4:50 PM PT
(6:50 PM – 7:50 PM ET)**

Faculty

**Sara A Hurvitz, MD, FACP
Heather McArthur, MD, MPH**

**Moderator
Neil Love, MD**

Thank you for joining us!

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

Practical Perspectives: Investigators Discuss Current Management and Actual Cases of Relapsed/Refractory Metastatic Colorectal Cancer

A CME/MOC-Accredited Virtual Event

Wednesday, September 20, 2023

5:00 PM – 6:00 PM ET

Faculty

Kristen K Ciombor, MD, MSCI

J Randolph Hecht, MD

Moderator

Neil Love, MD

Faculty



Kristen K Ciombor, MD, MSCI
Associate Professor of Medicine
Division of Hematology/Oncology
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee

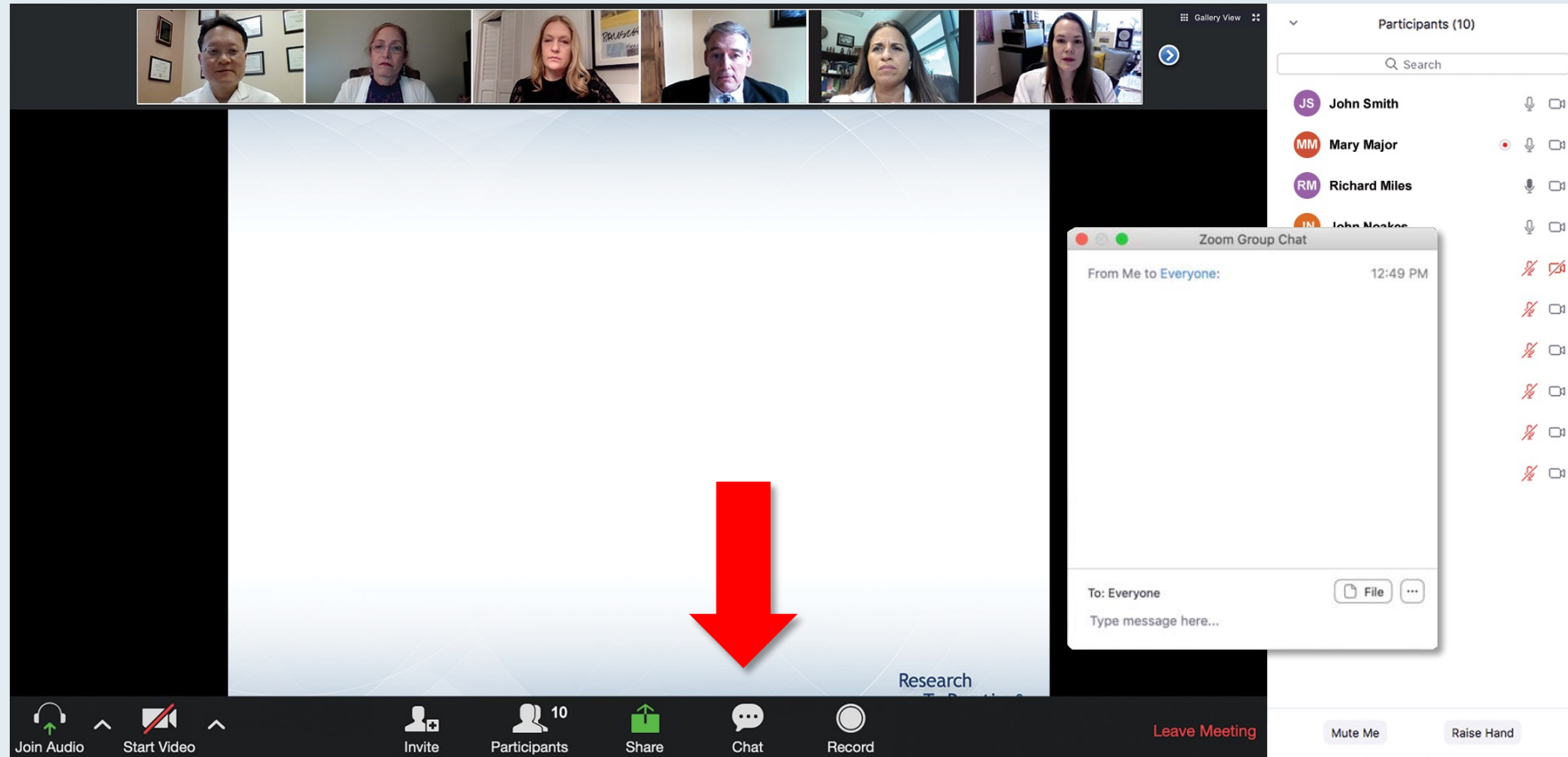


Moderator
Neil Love, MD
Research To Practice



J Randolph Hecht, MD
Professor of Clinical Medicine
Director, UCLA GI Oncology Program
Carol and Saul Rosenzweig Chair
in Cancer Therapies Development
UCLA David Geffen School of Medicine
Santa Monica, California

We Encourage Clinicians in Practice to Submit Questions



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

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

The screenshot shows a Zoom meeting window. At the top, a row of seven participant video thumbnails is visible. The main content area on the left displays a presentation slide with the title "Meet The Professionals" and the subtitle "Optimizing the Selection and Timing of Therapy for Patients with Gastrointestinal Cancer". Below the title, it says "Wednesday, August 25, 5:00 PM – 6:00 PM EST" and lists "Faculty: Wells A Messersmith, MD" and "Moderator: Neil Love, MD". A "Quick Survey" pop-up window is centered over the slide, listing various treatment combinations with radio button options. To the right of the main content is a "Participants (10)" list showing names and icons for audio, video, and chat. At the bottom is a Zoom toolbar with icons for Join Audio, Start Video, Invite, Participants, Share, Chat, Record, and a red "Leave Meeting" button.

Meet The Professionals
Optimizing the Selection and Timing of Therapy for Patients with Gastrointestinal Cancer

Wednesday, August 25, 5:00 PM – 6:00 PM EST

Faculty
Wells A Messersmith, MD

Moderator
Neil Love, MD

Quick Survey

- ☐ Ceritinib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Ceritinib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Isosorbide + Rd
- ☐ Other

Participants (10)

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

Join Audio Start Video Invite Participants Share Chat Record Leave Meeting

The screenshot shows a Zoom meeting window. At the top, a row of seven participant video thumbnails is visible. The main content area on the left displays a presentation slide with the title "Regulatory and reimbursement issues aside, which would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) if follow-up 3 years later is found to have asymptomatic (PS 0)?" Below the title is a numbered list of eight treatment options. A "Quick Poll" pop-up window is centered over the slide, listing the same eight treatment options with radio button options. To the right of the main content is a "Participants (10)" list showing names and icons for audio, video, and chat. At the bottom is a Zoom toolbar with icons for Join Audio, Start Video, Invite, Participants, Share, Chat, Record, and a red "Leave Meeting" button.

Regulatory and reimbursement issues aside, which would you recommend for a 65-year-old patient with clear cell renal cell carcinoma (ccRCC) if follow-up 3 years later is found to have asymptomatic (PS 0)?

1. Nivolumab/ipilimumab
2. Avelumab/axitinib
3. Pembrolizumab/axitinib
4. Pembrolizumab/lenvatinib
5. Nivolumab/cabozantinib
6. Tyrosine kinase inhibitor (TKI) monotherapy
7. Anti-PD-1/PD-L1 monotherapy
8. Other

Quick Poll

- ☐ Nivolumab/ipilimumab
- ☐ Avelumab/axitinib
- ☐ Pembrolizumab/axitinib
- ☐ Pembrolizumab/lenvatinib
- ☐ Nivolumab/cabozantinib
- ☐ Tyrosine kinase inhibitor (TKI) monotherapy
- ☐ Anti-PD-1/PD-L1 monotherapy
- ☐ Other

Participants (10)

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

Join Audio Start Video Invite Participants Share Chat Record Leave Meeting

Inside the Issue: Integrating Targeted and Immunotherapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, September 21, 2023

5:00 PM – 6:00 PM ET

Faculty

Jamie E Chافت, MD

John V Heymach, MD, PhD

Moderator

Neil Love, MD

What Clinicians Want to Know About the Management of Relapsed/Refractory Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Tuesday, September 26, 2023

5:00 PM – 6:00 PM ET

Faculty

Toby A Eyre, MBChB, DipMedEd, MRCP, MD

Brad S Kahl, MD

Moderator

Neil Love, MD

Meet The Professor

Optimizing the Management of Gastroesophageal Cancers

**Thursday, September 28, 2023
5:00 PM – 6:00 PM ET**

Faculty

Peter C Enzinger, MD

Moderator

Neil Love, MD

Inside the Issue: Optimizing the Management of Nonmelanoma Skin Cancer

A CME/MOC-Accredited Live Webinar

Tuesday, October 3, 2023

5:00 PM – 6:00 PM ET

Faculty

Nikhil I Khushalani, MD

Anna C Pavlick, DO, MBA

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

ER-Positive Breast Cancer

7:15 AM – 8:15 AM ET

Faculty

Harold J Burstein, MD, PhD

Komal Jhaveri, MD

Prostate Cancer

8:15 AM – 9:15 AM ET

Faculty

Alicia K Morgans, MD, MPH

Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

Non-Small Cell Lung Cancer

9:30 AM – 10:30 AM ET

Faculty

Gregory J Riely, MD, PhD

Heather Wakelee, MD, FASCO

Colorectal and Gastroesophageal Cancers

10:30 AM – 11:30 AM ET

Faculty

Tanios Bekaii-Saab, MD

Philip A Philip, MD, PhD, FRCP

Moderator

Neil Love, MD

Join Us In Person or Virtually

Current Approaches and Future Strategies in Oncology

*A Multitumor Educational Symposium in Partnership
with Florida Cancer Specialists & Research Institute*

Saturday, October 7, 2023

Chronic Lymphocytic Leukemia

11:30 AM – 12:30 PM ET

Faculty

Asher Chanan-Khan, MD

Brad S Kahl, MD

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Lymphoma

**9:30 AM – 10:30 AM PT
(12:30 PM – 1:30 PM ET)**

Faculty

**Christopher R Flowers, MD, MS
Ann S LaCasce, MD, MMSc**

Urothelial Bladder Cancer and Renal Cell Carcinoma

**10:30 AM – 11:30 AM PT
(1:30 PM – 2:30 PM ET)**

Faculty

**Thomas E Hutson, DO, PharmD
Guru P Sonpavde, MD**

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Hepatobiliary and Pancreatic Cancers

**11:50 AM – 12:50 PM PT
(2:50 PM – 3:50 PM ET)**

Faculty

**Mitesh J Borad, MD
Anthony El-Khoueiry, MD**

Gynecologic Cancers

**1:30 PM – 2:30 PM PT
(4:30 PM – 5:30 PM ET)**

Faculty

**Bradley J Monk, MD
Kathleen N Moore, MD, MS**

Moderator

Neil Love, MD

Join Us In Person or Virtually

Oncology in the Real World

*A Daylong Multitumor Educational Symposium
in Partnership with the American Oncology Network*

Saturday, October 14, 2023

Multiple Myeloma

**2:30 PM – 3:30 PM PT
(5:30 PM – 6:30 PM ET)**

Faculty

**Amrita Krishnan, MD
Robert Z Orlowski, MD, PhD**

HER2-Positive and Triple-Negative Breast Cancer

**3:50 PM – 4:50 PM PT
(6:50 PM – 7:50 PM ET)**

Faculty

**Sara A Hurvitz, MD, FACP
Heather McArthur, MD, MPH**

**Moderator
Neil Love, MD**

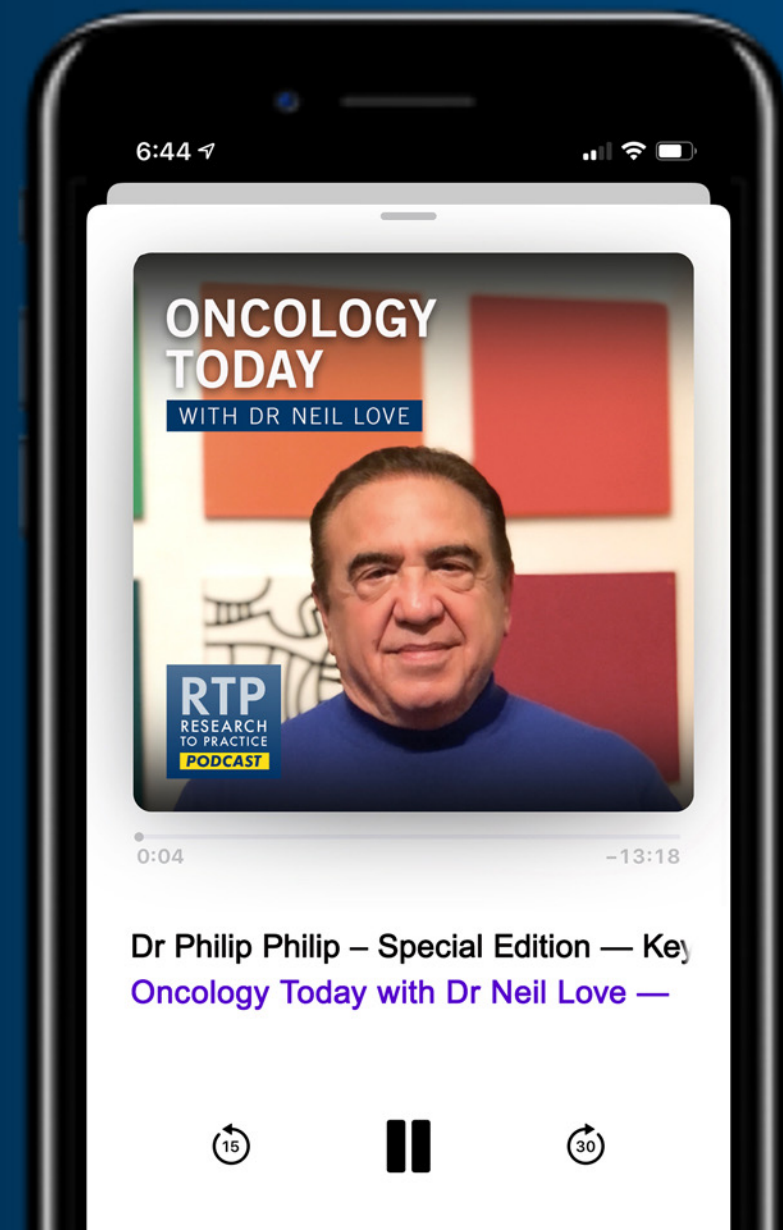
ONCOLOGY TODAY

WITH DR NEIL LOVE

**Special Edition — Key Presentations from
the 2023 American Society of Clinical
Oncology (ASCO) Annual Meeting,
Gastrointestinal Cancers Issue**



DR PHILIP PHILIP
WAYNE STATE UNIVERSITY



Practical Perspectives: Investigators Discuss Current Management and Actual Cases of Relapsed/Refractory Metastatic Colorectal Cancer

A CME/MOC-Accredited Virtual Event

Wednesday, September 20, 2023

5:00 PM – 6:00 PM ET

Faculty

Kristen K Ciombor, MD, MSCI

J Randolph Hecht, MD

Moderator

Neil Love, MD

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Seagen Inc, Taiho Oncology Inc, and Takeda Pharmaceuticals USA Inc.

Research To Practice CME Planning Committee Members, Staff and Reviewers

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

Dr Ciombor — Disclosures

Advisory Committee	Bayer HealthCare Pharmaceuticals, Exelixis Inc, Incyte Corporation, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Personalis, Pfizer Inc, Replimune, Seagen Inc
Consulting Agreements	Merck, Pfizer Inc
Contracted Research	Array BioPharma Inc, a subsidiary of Pfizer Inc, Bristol Myers Squibb, Calithera Biosciences, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Incyte Corporation, Merck, NuCana, Pfizer Inc, Seagen Inc

Dr Hecht — Disclosures

Advisory Committee	Actym Therapeutics, Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Gilead Sciences Inc, Mirati Therapeutics Inc, Rafael Pharmaceuticals Inc
Contracted Research	AbbVie Inc, Amgen Inc, Astellas, Merck, Mirati Therapeutics Inc, Tesaro, A GSK Company



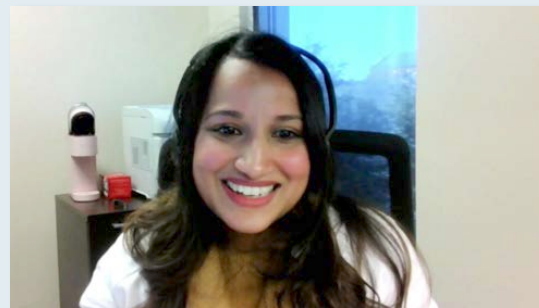
Georges Azzi, MD
Holy Cross Health
Fort Lauderdale, Florida



Zanetta S Lamar, MD
Florida Cancer
Specialists and Research Institute
Naples, Florida



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



Ina J Patel, DO
Hematologist Oncologist
Fort Worth, Texas



Farshid Dayyani, MD, PhD
UCI Chao Family Comprehensive
Cancer Center
Orange, California



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



Nikesh Jasani, MD
Texas Oncology
Houston, Texas



Nontargeted Treatment Approaches for Relapsed/Refractory Metastatic Colorectal Cancer (mCRC)

Kristen K. Ciombor, MD, MSCI
Associate Professor of Medicine
Vanderbilt-Ingram Cancer Center

VANDERBILT UNIVERSITY
MEDICAL CENTER



Targeted Treatment for R/R mCRC

J. Randolph Hecht, MD
Professor of Clinical Medicine
Director, UCA GI Oncology Program

Key Data Sets

Kristen Ciombor, MD, MSCI

- Bekaii-Saab TS et al. Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate dosing strategies for regorafenib in refractory metastatic colorectal cancer (mCRC) – An ACCRU Network study. *Gastrointestinal Cancers Symposium 2018*;Abstract 611.
- Cremolini C et al. Rechallenge for patients with RAS and BRAF wild-type metastatic colorectal cancer with acquired resistance to first-line cetuximab and irinotecan: A phase 2 single-arm clinical trial. *JAMA Oncol* 2019;5(3):343-50.
- Dasari A et al. Fruquintinib versus placebo in patients with refractory metastatic colorectal cancer (FRESCO-2): An international, multicentre, randomised, double-blind, phase 3 study. *Lancet* 2023;402(10395):41-53.
- Grothey A et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): An international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet* 2013;381(9863):303-12.
- Martinelli E et al. Cetuximab rechallenge plus avelumab in pretreated patients with RAS wild-type metastatic colorectal cancer: The phase 2 single-arm clinical CAVE trial. *JAMA Oncol* 2021;7(10):1529-35.

Key Data Sets

Kristen Ciombor, MD, MSCI (continued)

- Mayer RJ et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. *N Engl J Med* 2015;372(20):1909-19.
- Pfeiffer P et al. TAS-102 with or without bevacizumab in patients with chemorefractory metastatic colorectal cancer: An investigator-initiated, open-label, randomised, phase 2 trial. *Lancet Oncol* 2020;21(3):412-20.
- Prager GW et al. Trifluridine-tipiracil and bevacizumab in refractory metastatic colorectal cancer. *N Engl J Med* 2023;388(18):1657-67.
- Sartore-Bianchi et al. Circulating tumor DNA to guide rechallenge with panitumumab in metastatic colorectal cancer: The phase 2 CHRONOS trial. *Nat Med* 2022;28(8):1612-8.
- Tabernero J et al. Trifluridine/tipiracil plus bevacizumab for third-line treatment of refractory metastatic colorectal cancer: The phase 3 randomized SUNLIGHT study. *Gastrointestinal Cancers Symposium* 2023;Abstract 4.

Key Data Sets

J Randolph Hecht, MD

- Grothey A et al. Management of BRAF-mutant metastatic colorectal cancer: A review of treatment options and evidence-based guidelines. *Ann Oncol* 2021;32(8):959-67.
- Kopetz S et al. BREAKWATER: An open-label, multicenter, randomized, phase 3 study, with a safety lead-in (SLI), of first-line (1L) encorafenib (E) + cetuximab (C) \pm chemotherapy (CT) vs standard-of-care (SOC) CT for BRAF V600E-mutant metastatic colorectal cancer (mCRC). ASCO 2023;Abstract TPS3627.
- MOUNTAINEER-03: A study of tucatinib with trastuzumab and mFOLFOX6 versus standard of care treatment in first-line HER2+ metastatic colorectal cancer. NCT05253651
- Ogitani Y et al. Bystander killing effect of DS-8201a, a novel anti-human epidermal growth factor receptor 2 antibody-drug conjugate, in tumors with human epidermal growth factor receptor 2 heterogeneity. *Cancer Sci* 2016;107(7):1039-46.
- Raghav K et al. Trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-overexpressing/amplified (HER2+) metastatic colorectal cancer (mCRC): Primary results from the multicenter, randomized, phase 2 DESTINY-CRC02 study. ASCO 2023;Abstract 3501.

Key Data Sets

J Randolph Hecht, MD (continued)

- Strickler JH et al. Tucatinib plus trastuzumab for chemotherapy-refractory, HER2-positive, RAS wild-type unresectable or metastatic colorectal cancer (MOUNTAINEER): A multicentre, open-label, phase 2 study. *Lancet Oncol* 2023;24(5):496-508.
- Yoshino T et al. Final results of DESTINY-CRC01 investigating trastuzumab deruxtecan in patients with HER2-expressing metastatic colorectal cancer. *Nat Commun* 2023;14(1):3332.
- Tabernero J et al. 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. *J Clin Oncol* 2021;39(4):273-84.
- Wu C. Molecular targets in colorectal cancer: Moving beyond EGFR, BRAF, and dMMR. Education Session. ASCO 2023.
- Yaeger R et al. Adagrasib with or without cetuximab in colorectal cancer with mutated KRAS G12C. *N Engl J Med* 2023;388(1):44-54.

Agenda

Introduction

Case Presentations

- Dr Lamar: 81-year-old woman with KRAS-mutated, HER2-positive metastatic colorectal adenocarcinoma
- Dr Azzi: 78-year-old man with metastatic KRAS G12C-mutated rectal adenocarcinoma treated with third-line sotorasib/panitumumab
- Dr Rudolf: 58-year-old man with KRAS-mutated metastatic colon cancer and very slow disease progression on second-line FOLFIRI/bevacizumab
- Dr Patel: 46-year-old man with KRAS WT metastatic colon cancer and disease progression on third-line treatment
- Dr Brenner: 82-year-old man with right-sided MSS (TMB 10), KRAS G12D-mutated mCRC currently receiving third-line TAS-102
- Dr Jasani: 79-year-old man with MSI-high, BRAF V600E-mutated recurrent cecal adenocarcinoma
- Dr Dayyani: 58-year-old woman with MSS BRAF V600E-mutated mCRC with brain and bone mets who has good response to dose-reduced FOLFOX after progression on first-line encorafenib/cetuximab
- Dr Azzi: 66-year-old woman with RAS WT, BRAF V600E-mutated, MSS mCRC, now on encorafenib/cetuximab after progression on FOLFOX/bevacizumab

Agenda

Introduction

Case Presentations

- Dr Lamar: 81-year-old woman with KRAS-mutated, HER2-positive metastatic colorectal adenocarcinoma
- Dr Azzi: 78-year-old man with metastatic KRAS G12C-mutated rectal adenocarcinoma treated with third-line sotorasib/panitumumab
- Dr Rudolf: 58-year-old man with KRAS-mutated metastatic colon cancer and very slow disease progression on second-line FOLFIRI/bevacizumab
- Dr Patel: 46-year-old man with KRAS WT metastatic colon cancer and disease progression on third-line treatment
- Dr Brenner: 82-year-old man with right-sided MSS (TMB 10), KRAS G12D-mutated mCRC currently receiving third-line TAS-102
- Dr Jasani: 79-year-old man with MSI-high, BRAF V600E-mutated recurrent cecal adenocarcinoma
- Dr Dayyani: 58-year-old woman with MSS BRAF V600E-mutated mCRC with brain and bone mets who has good response to dose-reduced FOLFOX after progression on first-line encorafenib/cetuximab
- Dr Azzi: 66-year-old woman with RAS WT, BRAF V600E-mutated, MSS mCRC, now on encorafenib/cetuximab after progression on FOLFOX/bevacizumab

Targetable Alterations and Testing

- Targetable Molecular Alterations
 - FDA Approved
 - MSI ~3%
 - BRAF V600E 5-10%
 - HER-2 amplification 5%
 - NTRK 0.35%
 - RET fusion <1%
 - Likely soon
 - KRAS G12C 3%
 - Aspirational
 - Other RAS mutations ~50%

Agenda

Introduction

Case Presentations

- Dr Lamar: 81-year-old woman with KRAS-mutated, HER2-positive metastatic colorectal adenocarcinoma
- Dr Azzi: 78-year-old man with metastatic KRAS G12C-mutated rectal adenocarcinoma treated with third-line sotorasib/panitumumab
- Dr Rudolf: 58-year-old man with KRAS-mutated metastatic colon cancer and very slow disease progression on second-line FOLFIRI/bevacizumab
- Dr Patel: 46-year-old man with KRAS WT metastatic colon cancer and disease progression on third-line treatment
- Dr Brenner: 82-year-old man with right-sided MSS (TMB 10), KRAS G12D-mutated mCRC currently receiving third-line TAS-102
- Dr Jasani: 79-year-old man with MSI-high, BRAF V600E-mutated recurrent cecal adenocarcinoma
- Dr Dayyani: 58-year-old woman with MSS BRAF V600E-mutated mCRC with brain and bone mets who has good response to dose-reduced FOLFOX after progression on first-line encorafenib/cetuximab
- Dr Azzi: 66-year-old woman with RAS WT, BRAF V600E-mutated, MSS mCRC, now on encorafenib/cetuximab after progression on FOLFOX/bevacizumab

Dear Dr Love,

I am a general oncologist in Germany and I need help with the following case:

40-year-old female from Russia, two young kids, colon cancer with liver and lung metastasis. Primary and samples from liver and lung show KRAS G13D and HER2 overexpression (3+).

She progressed quickly on TAS 102 and is now receiving FOLFIRI + ramucirumab. Would the experts recommend T-DXd despite the KRAS mutation?

So far, I have not been able to get her on a clinical trial and the insurance declined payment of T-DXd. The patient is very informed and wants to receive T-DXd. She would be willing to cover the costs herself.

Kind Regards,
Dr Mithun Scheytt

Case Presentation: 81-year-old woman with KRAS-mutated, HER2-positive metastatic colorectal adenocarcinoma



Dr Zanetta Lamar (Naples, Florida)

HER-2 in Colorectal Cancer

- HER-2 amplification is found in 3-5% of CRCs
- Decreased sensitivity to anti-EGFR
- Early studies showed activity with older agents

Regimen	Trial (n) – year	ORR	PFS	OS	Most common Grade 3+ AEs
Trastuzumab + lapatinib	HERACLES-A (n=32) – 2016	28%	4.7m	10m	Fatigue 16% Decreased LVEF 6%
Trastuzumab + pertuzumab	MyPathway (n=84; 57 evaluable) – 2019	32%	2.9m	11.5m	Hypokalemia 5% Abdominal pain 5%

FDA Grants Accelerated Approval to Tucatinib with Trastuzumab for Colorectal Cancer

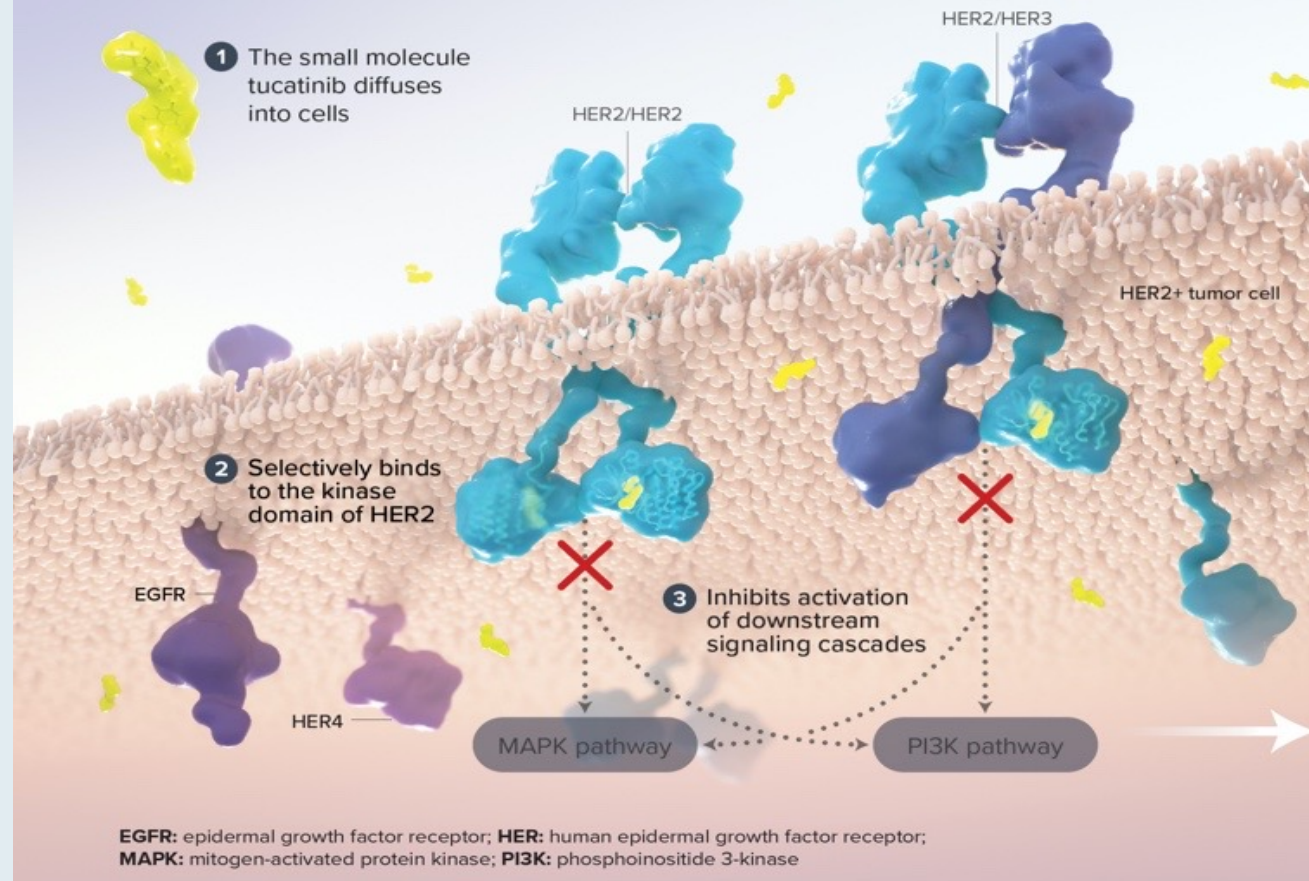
Press Release – January 19, 2023

“On January 19, 2023, the Food and Drug Administration (FDA) granted accelerated approval to tucatinib in combination with trastuzumab for RAS wild-type HER2-positive unresectable or metastatic colorectal cancer that has progressed following fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

Efficacy was evaluated in 84 patients in MOUNTAINEER (NCT03043313), an open-label, multicenter trial. Patients were required to have HER2-positive, RAS wild-type, unresectable or metastatic colorectal cancer and prior treatment with fluoropyrimidine, oxaliplatin, irinotecan, and an anti-vascular endothelial growth factor (VEGF) monoclonal antibody (mAb). Patients whose tumors were deficient in mismatch repair (dMMR) proteins or were microsatellite instability-high (MSI-H) must also have received an anti-programmed cell death protein-1 mAb. Patients who received prior anti-HER2 targeting therapy were excluded.”

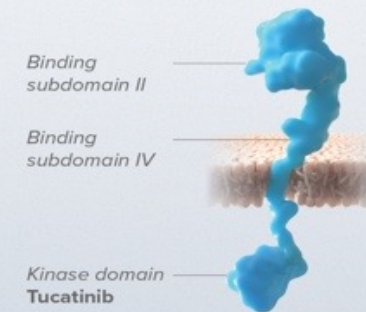
Tucatinib Mechanism of Action

Tucatinib: A tyrosine kinase inhibitor selective for HER2

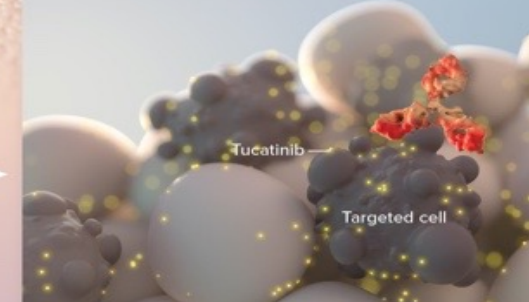


Dual inhibition of HER2

Tucatinib has been combined with other agents that target the extracellular domain of HER2 in clinical trials.



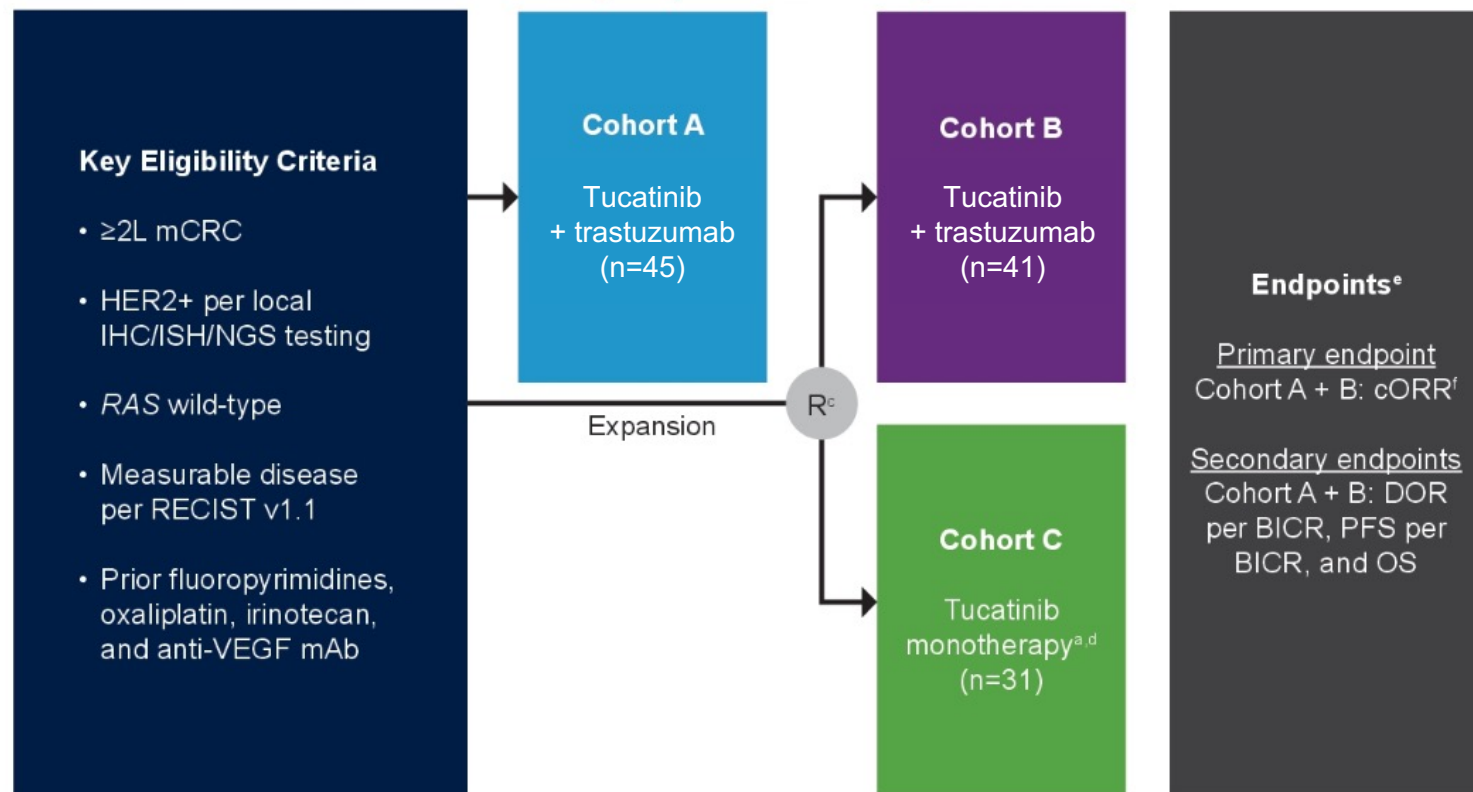
4 Decreased HER2 signaling reduces tumor cell proliferation, survival, and metastasis



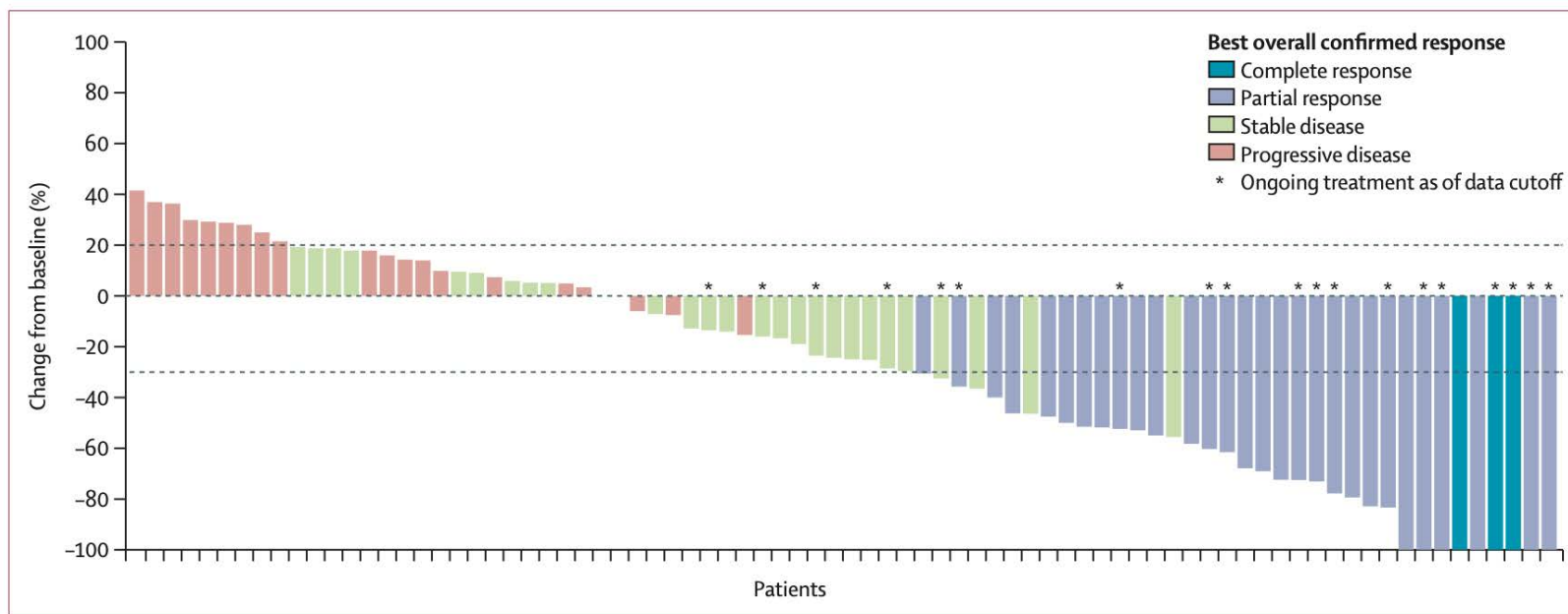
Tucatinib

- Small molecule HER-2 selective TKI
- Approved in breast cancer
- MOUNTAINEER trial (Strickler 2023)
 - Originally an investigator initiated trial
 - Expanded to global trial

MOUNTAINEER: Global, Open-Label, Phase 2 Trial

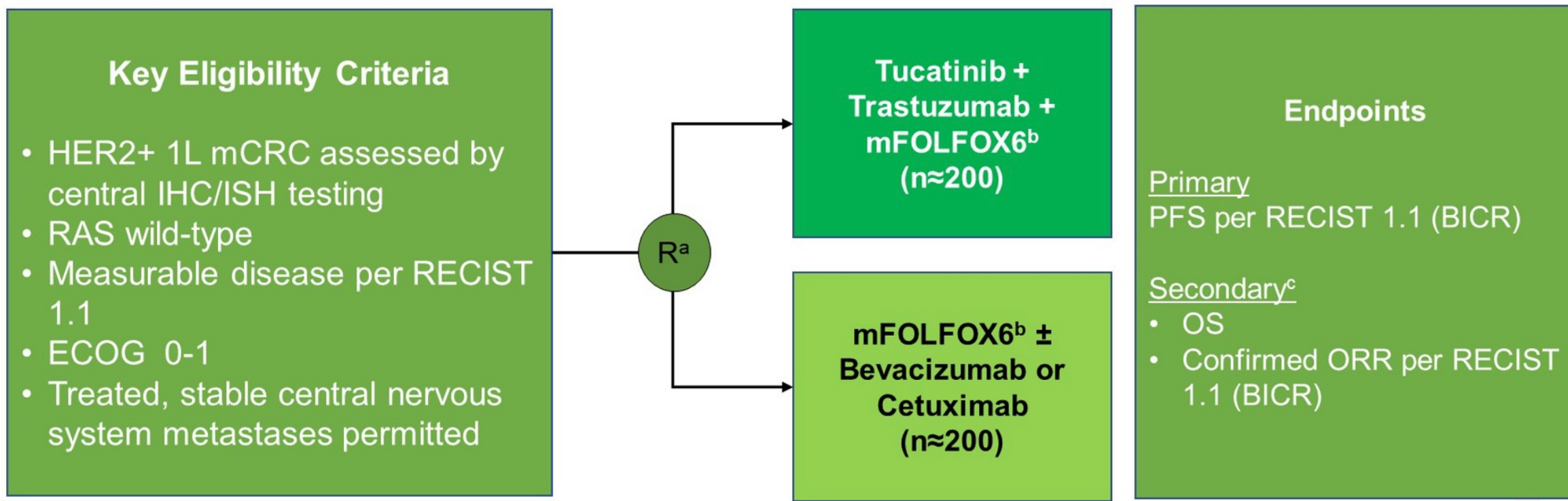


MOUNTAINEER Results

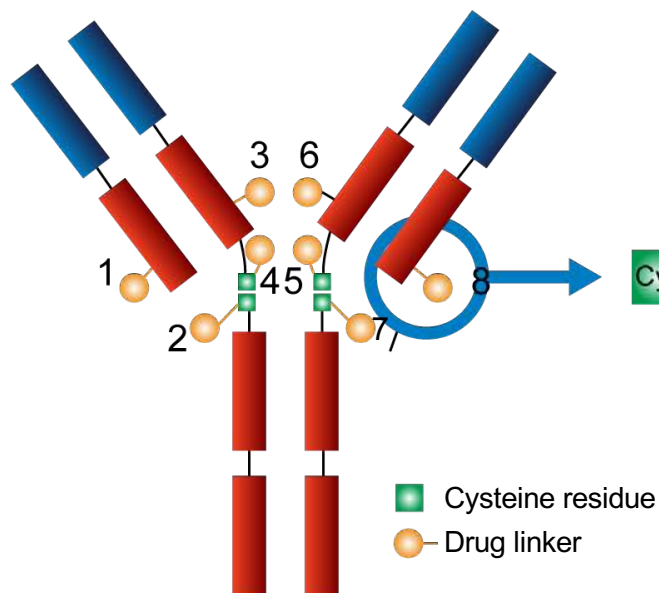


- Tucatinib+trastuzumab
 - 38% RR PFS 7.0m OS 24.1m
- Tucatinib monotherapy
 - 3% RR PFS not done due to crossover
- G3 AE diarrhea 3.5%
- Approved 1/2023

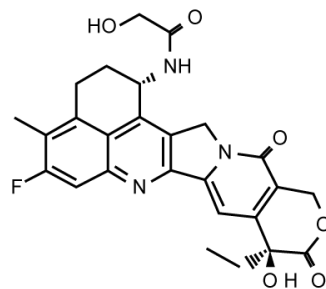
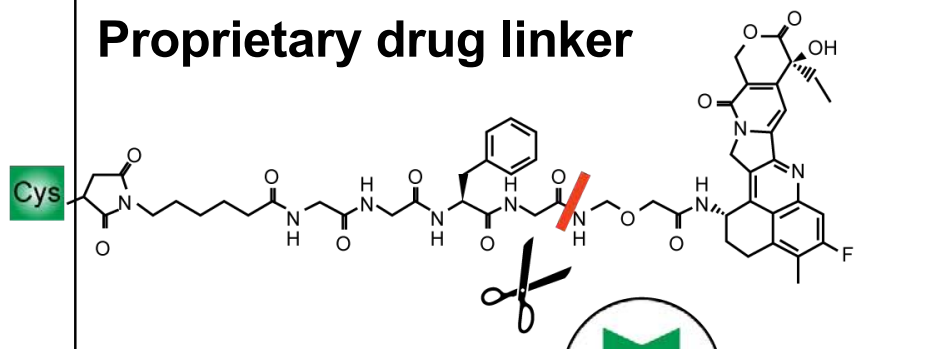
MOUNTAINEER-03: Global, Randomised, Open-Label, Phase 3 Trial



Trastuzumab Deruxtecan (T-DXd; DS8201a)



Proprietary drug linker



Payload (DXd)

Exatecan derivative

	T-DXd	T-DM1
Antibody	Anti-HER2 mAb	Trastuzumab
Payload	Topoisomerase I inhibitor	Tubulin inhibitor
DAR	7-8	3.5
Membrane Permeability	Yes (bystander effect)	No

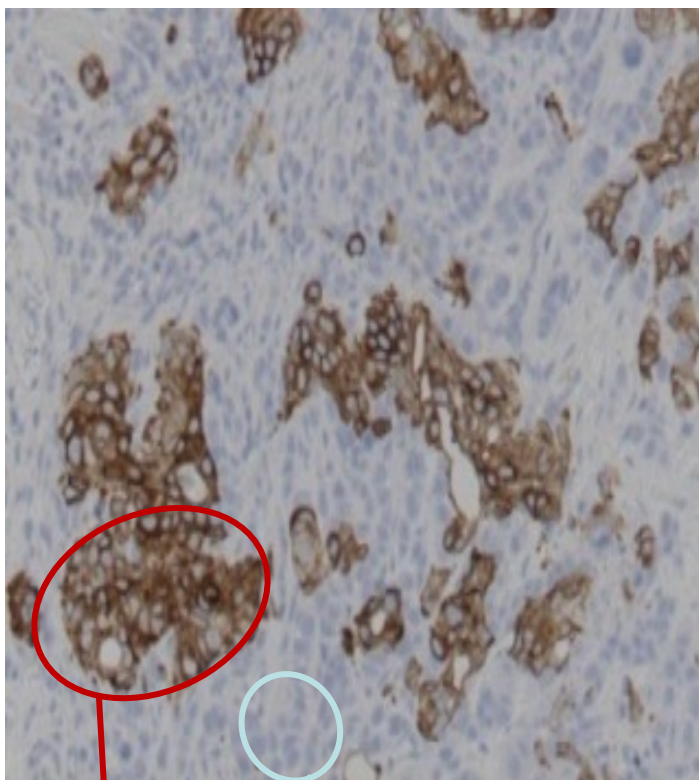
Conjugation chemistry

The linker is connected to cysteine residue of the antibody

Bystander Effect of T-DXd Versus T-DM1¹

Control

Co-inoculation of HER2+ and HER2- tumors in vivo

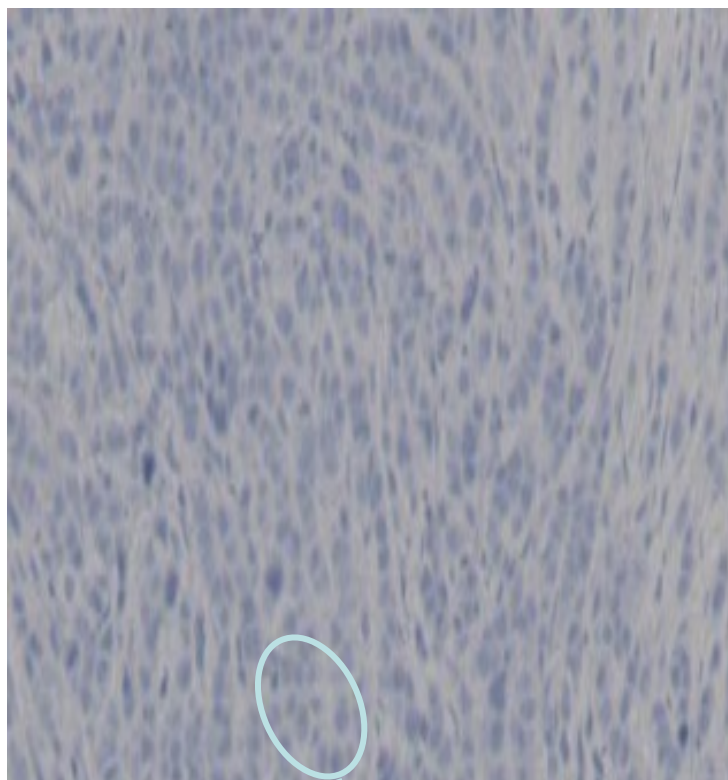


HER2+
cells
NCI-N87

HER2-
cells
MDA-MB-468

T-DM1, 10 mg/kg

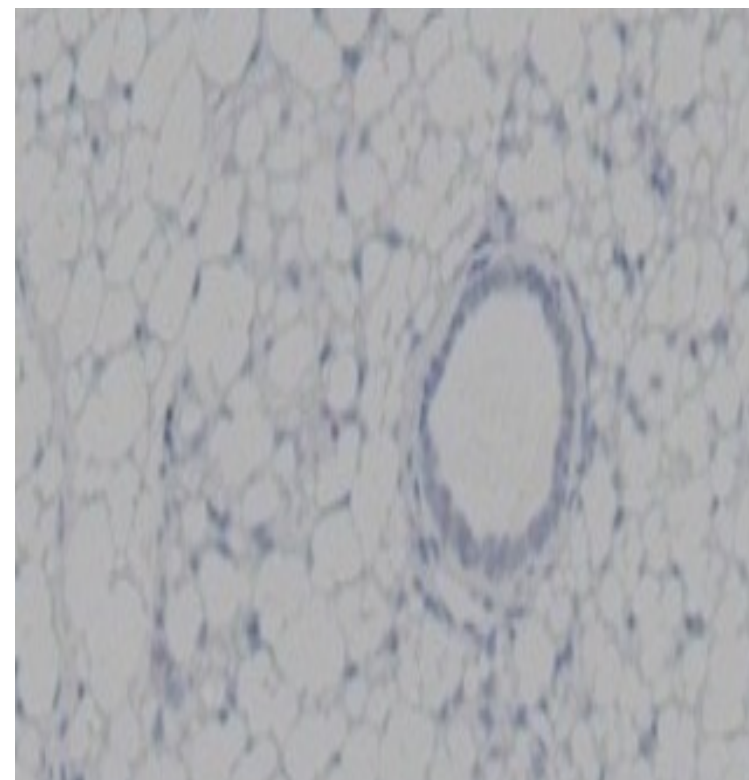
HER2- cells still persist



HER2-
cells
MDA-MB-468

T-DXd, 3.0 mg/kg

Both HER2+ and HER2- are impacted



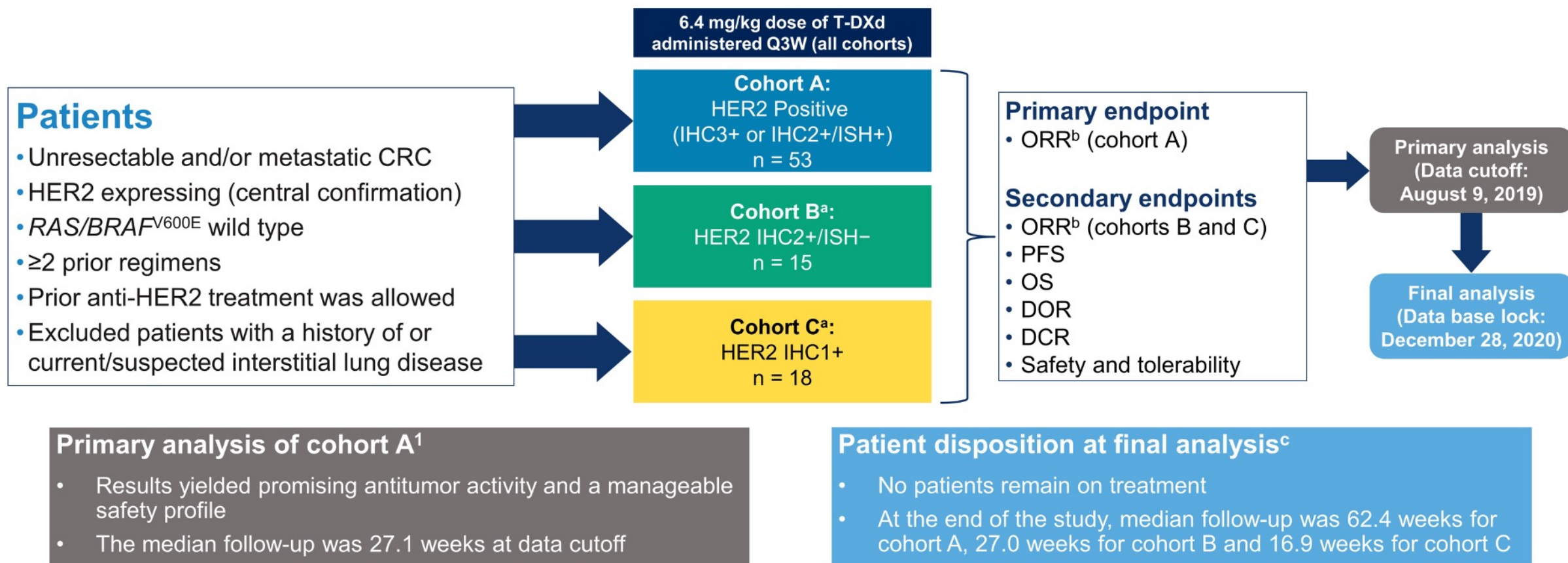
Tumor regression

Ogitani Cancer Sci 2016

Courtesy of J Randolph Hecht, MD

DESTINY-CRC01 Study Design

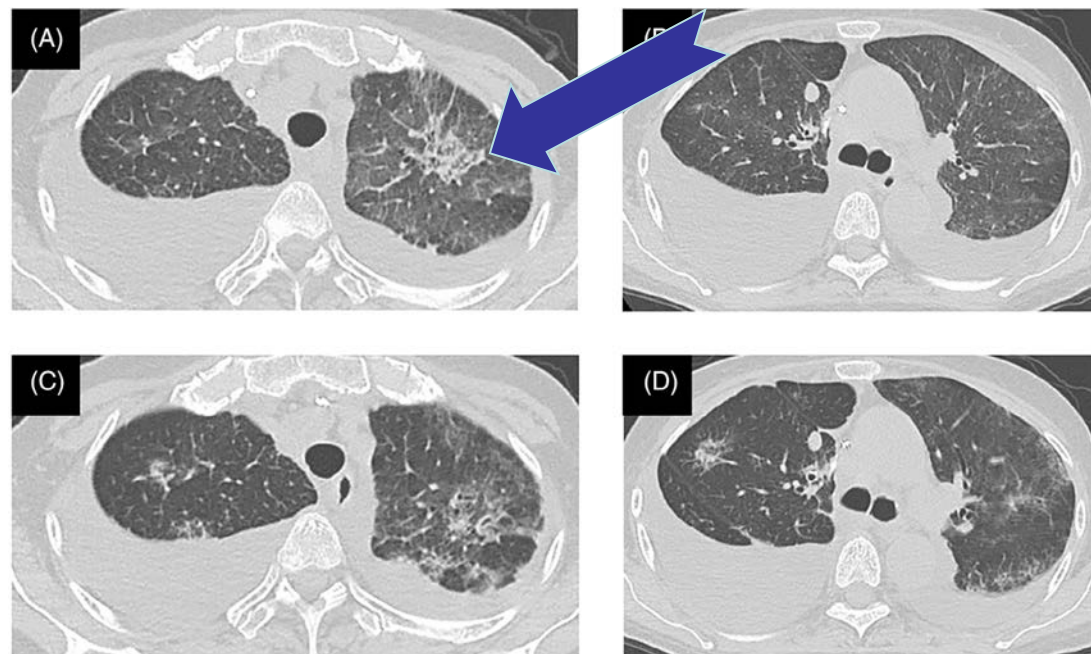
An open-label, multicenter, phase 2 study (NCT03384940)



DESTINY-CRC01 Outcomes

- Cohort A 3+ or 2+/ISH+: 45% RR 6.9m PFS 15.5m OS
- Cohort B 2+/ISH-: 0% RR (60%SD) 2.1m PFS 7.3m OS
- Cohort C 1+: 0% RR (22% SD) 1.4m PFS 7.7m OS

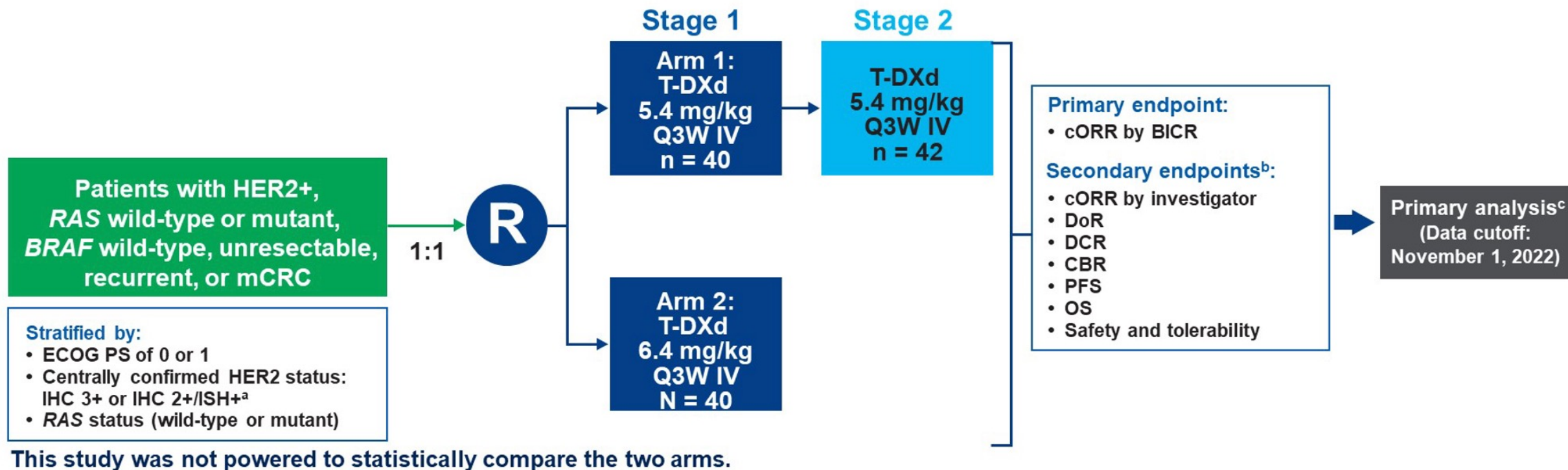
- Toxicity
 - Cytopenias
 - 9.3% pneumonitis
 - 3.5% G5 pneumonitis



DESTINY-CRC02 Study Design

A randomized, blinded, 2-stage, 2-arm, multicenter, global, phase 2 study (NCT04744831)

- Stage 1 (randomized) was followed by Stage 2 (nonrandomized), which enrolled an additional 42 patients



DESTINY-CRC02 Results

Efficacy Results

	T-DXd 5.4 mg/kg Q3W			T-DXd 6.4 mg/kg Q3W
	Stage 1 n = 40	Stage 2 n = 42	Total N = 82	Stage 1 N = 40
cORR, n (%) [95% CI]	18 (45.0) [29.3-61.5]	13 (31.0) [17.6-47.1]	31 (37.8) [27.3-49.2]	11 (27.5) [14.6-43.9]
CR	0	0	0	0
PR	18 (45.0)	13 (31.0)	31 (37.8)	11 (27.5)
SD	20 (50.0)	20 (47.6)	40 (48.8)	23 (57.5)
PD	2 (5.0)	6 (14.3)	8 (9.8)	4 (10.0)
NE	0	3 (7.1)	3 (3.7)	2 (5.0)

- PFS: 5.4 mg/kg 5.8m; 6.4 mg/kg 5.5m
- OS: 5.4 mg/kg 13.4m; 6.4 mg/kg 9.9m
- 1 G5 pneumonitis 6.4; none 5.4



DESTINY-CRC02 Takeaways

- Clear benefits 3+, again ? 2+
- Low dose is as good if not better than higher dose (Project OPTIMUS)
- No G5 pneumonitis 5.4 mg/kg
 - Lower dose
 - Also, better awareness now

Case Presentation: 78-year-old man with metastatic KRAS G12C-mutated rectal adenocarcinoma treated with third-line sotorasib/panitumumab



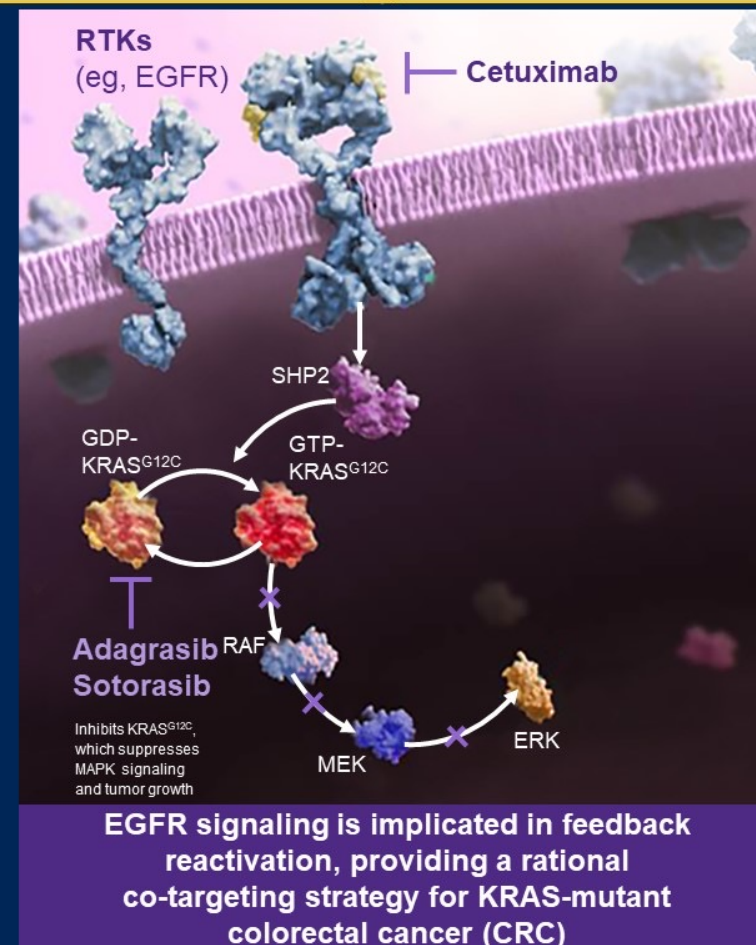
Dr Georges Azzi (Fort Lauderdale, Florida)

KRAS in Colorectal Cancer

- Resistance to inhibitors: Other RAS mutations, other MAPK pathways
- Other RAS mutations
 - Direct inhibitors: Multi, G12C, G12D, Q61H, G13C
 - Inhibitors of adapter molecules: SOS1, SHP2
- Target of immunotherapy
 - Vaccines
 - G12D TCR (Leidner NEJM 2022)

KRAS G12C Mutations in CRC : Background

- KRAS^{G12C} mutations occur in 3–4% of CRC, act as oncogenic drivers, and are a negative predictor of cetuximab efficacy^{1–4}
- The KRAS protein cycles between guanosine triphosphate (GTP)-on and guanosine diphosphate (GDP)-off states and has a protein resynthesis half-life of ~24 hours^{5,6}
- **Adagrasib**, a covalent inhibitor of KRAS^{G12C}, irreversibly and selectively binds KRAS^{G12C} in its inactive, GDP-bound state and was optimized for desired properties⁷
- **Sotorasib** is another first-in-class, irreversible inhibitor of the KRAS^{G12C} protein⁸
- Combining KRAS G12C inhibitors with an epidermal growth factor receptor (EGFR) inhibitor, may enhance inhibition of KRAS-dependent signaling or overcome adaptive feedback to improve outcomes⁹



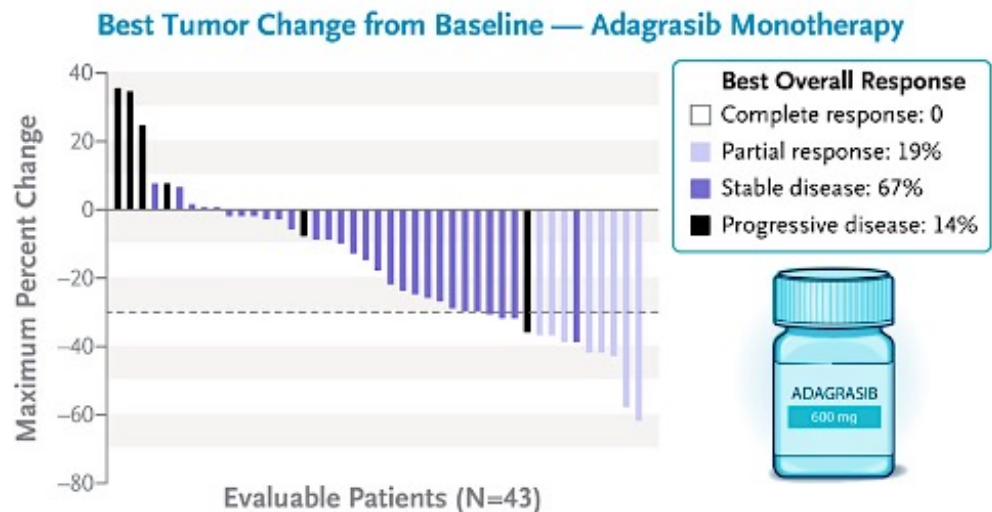
1. Zehir A, et al. *Nat Med*. 2017;23(6):703-713; 2. Schirripa M, et al. *Clin Colorectal Cancer*. 2020;S1533-0028(20)30067-0; 3. NIH TCGA: *The Cancer Genome Atlas*. February 11, 2021; <https://www.cbioportal.org>; 4. Modest DP, et al. *Oncology*. 2012;83:241-247; 5. Bos JL, et al. *Cell*. 2007;129:865-877; 6. Shukla S, et al. *Neoplasia*. 2014;16(2):115-128; 7. Hallin J, et al. *Cancer Discov*. 2020;10(1):54-71; 8. Lanman BA, et al. *J Med Chem*. 2020;63:52-65; 9. Tabernero J, et al. Presented at ESMO 23rd World Congress on Gastrointestinal Cancer; June 30-July 3, 2021; virtual.



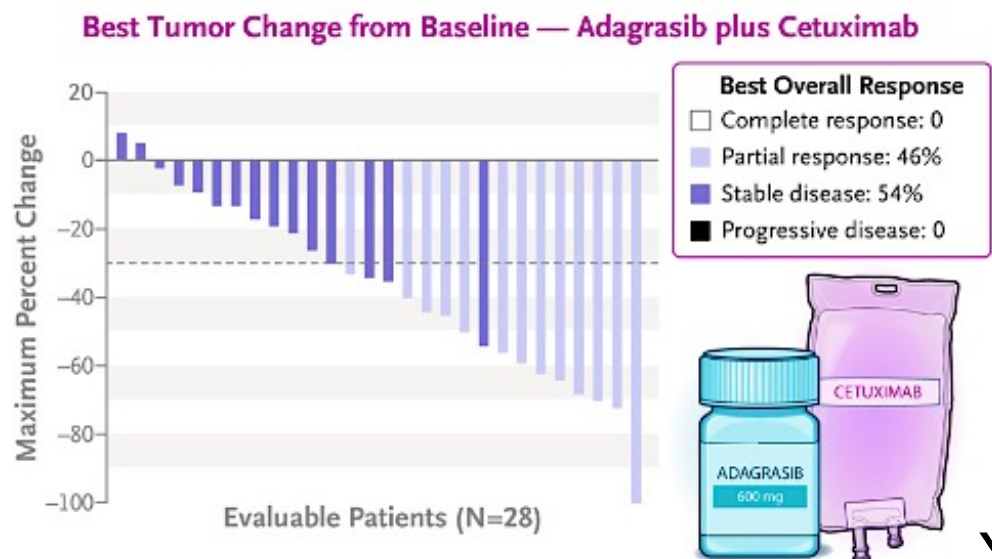
Sotorasib (AMG 510)

- CODEBREAK 100 (Fakih Lancet Oncol 2022)
 - Multitumor trial; CRCs 10% RR PFS 4.0m
 - Once again blocking leads to increased signaling through EGFR
- CODEBREAK 101 (Hong ASCO 2023)
 - Phase 1b Pmab+ sotorasib+FOLFIRI
 - RR 55% DCR 93% G3 diarrhea 10-15%
- CODEBREAK 300
 - Phase III sotorasib/Pmab vs TAS-102 or regorafenib

Colorectal Cancer KRYSTAL-1



- KRYSTAL-1
 - Adagrasib with and without cetuximab
- KRYSTAL 10
 - Phase III adagrasib/cetuximab vs FOLFIRI optional VEGFRi



Yaeger NEJM 2023



**Dr Priya Rudolph
(Athens, Georgia)**

Case Presentation: 58-year-old man with KRAS-mutant metastatic colon cancer and very slow disease progression on second-line FOLFIRI/bevacizumab



**Dr Ina Patel
(Fort Worth, Texas)**

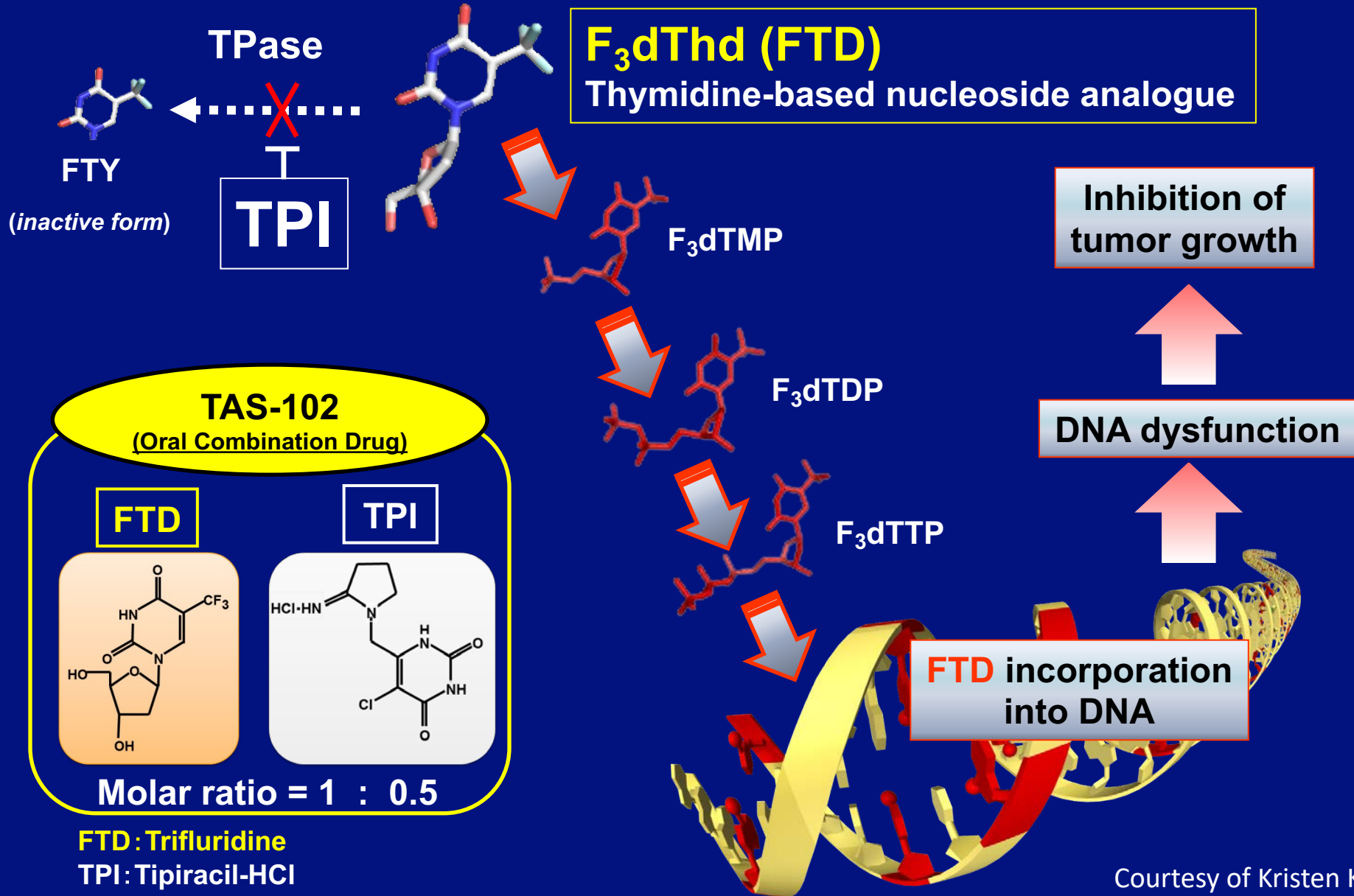
Case Presentation: 46-year-old man with KRAS WT metastatic colon cancer and disease progression on third-line treatment

Case Presentation: 82-year-old man with right-sided MSS (TMB 10), KRAS G12D-mutated mCRC currently receiving third-line TAS-102



Dr Warren Brenner (Boca Raton, Florida)

TAS-102: Mechanism of Action



Phase II: TAS-102 +/- Bev in Refractory mCRC

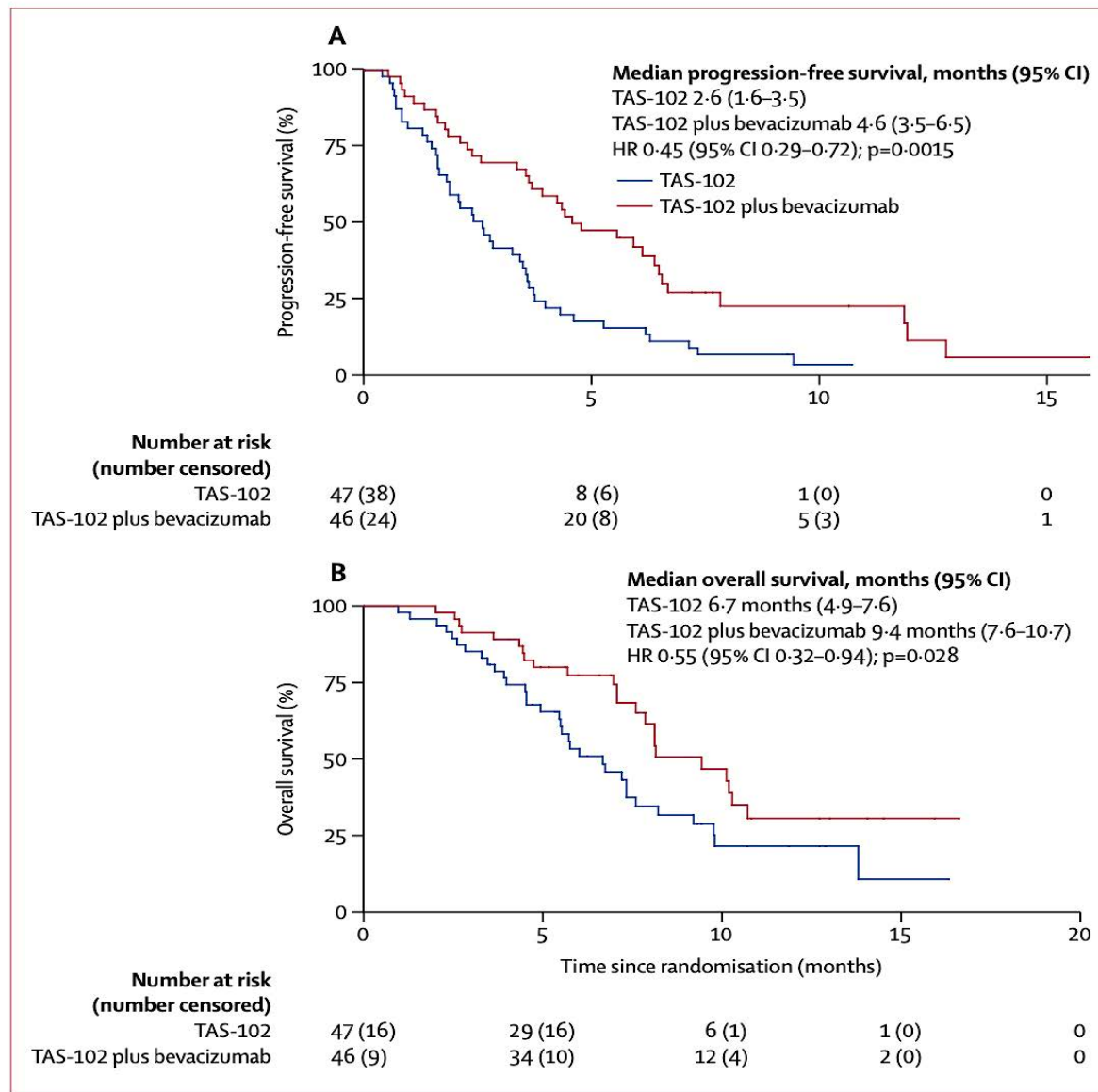
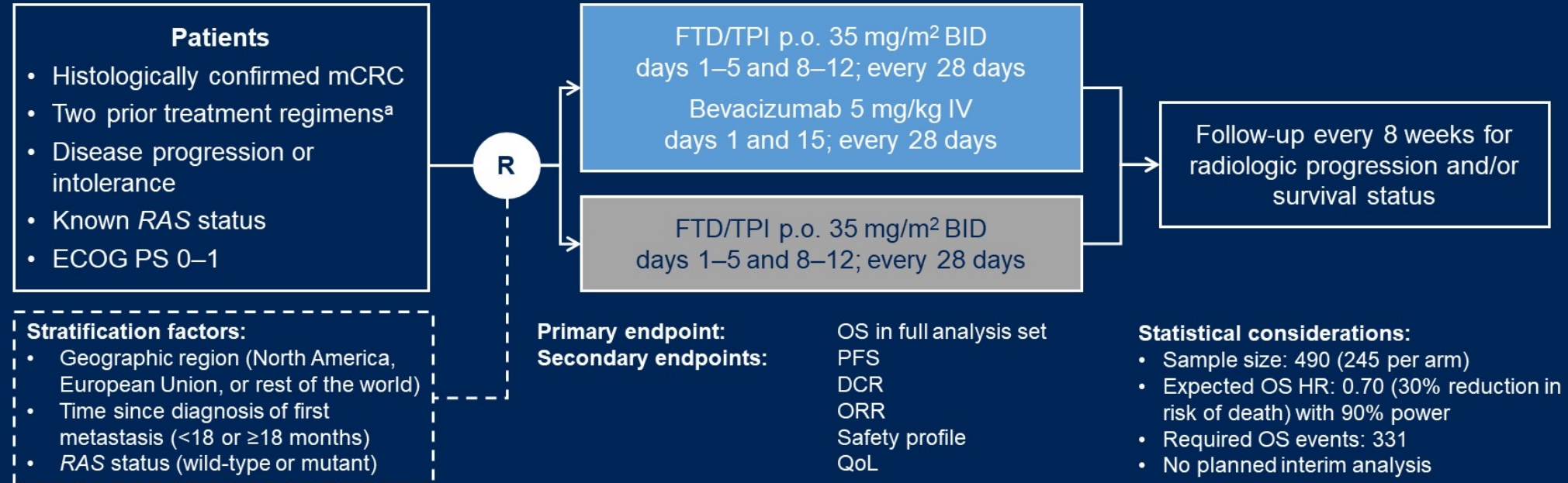


Figure 2: The efficacy of TAS-102 monotherapy versus TAS-102 plus bevacizumab combination therapy
 (A) Progression-free survival. (B) Overall survival. HR=hazard ratio.

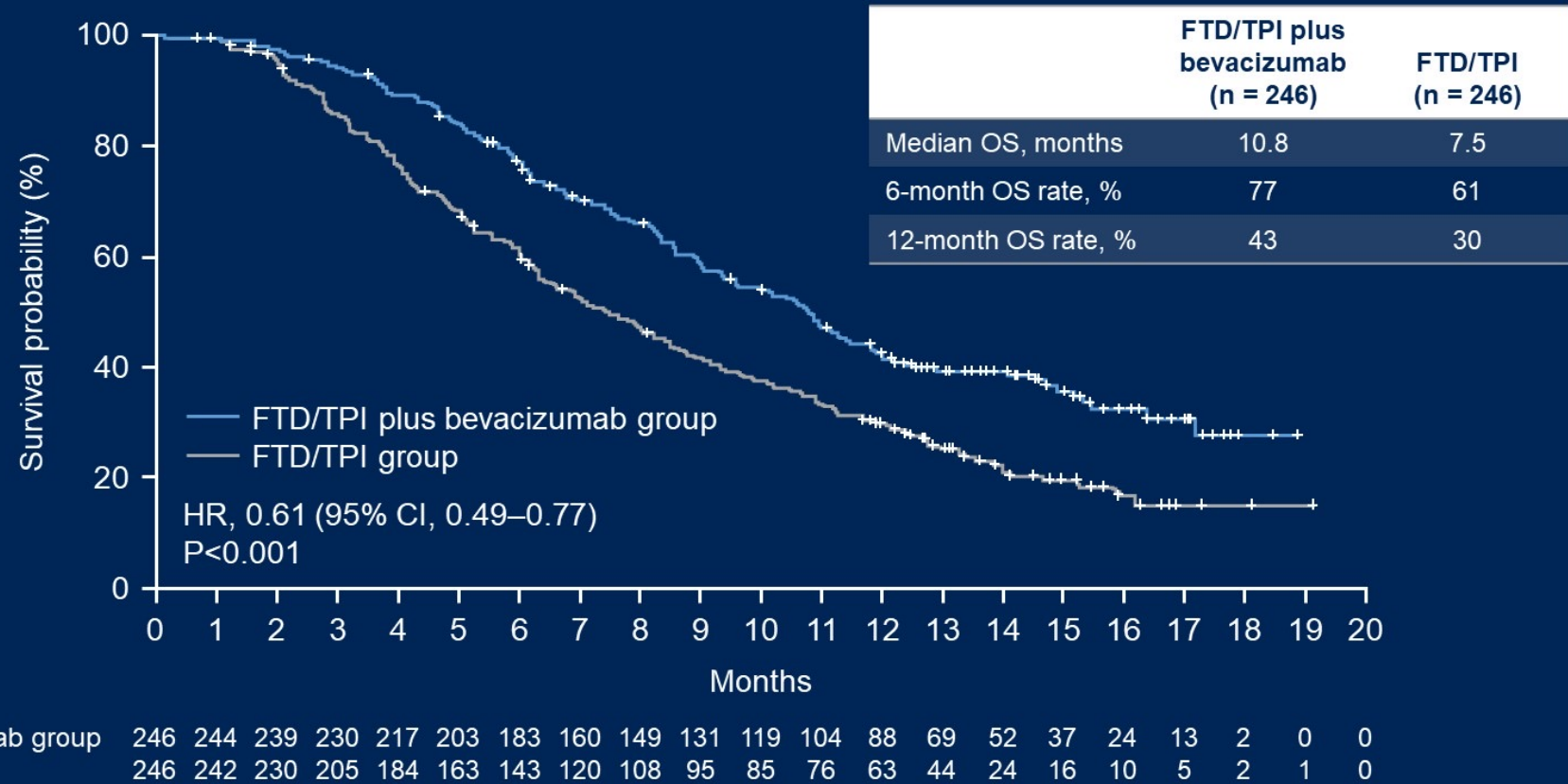
SUNLIGHT study design

- An open-label, randomized, phase 3 study in patients with refractory mCRC (NCT04737187)



^a Prior treatment must have included a fluoropyrimidine, irinotecan, oxaliplatin, an anti-VEGF monoclonal antibody (not necessarily bevacizumab), and/or an anti-EGFR monoclonal antibody for patients with *RAS* wild-type and could have included (neo)adjuvant chemotherapy if disease had recurred during treatment or within 6 months of the last administration of (neo)adjuvant therapy. BID, twice daily; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; IV, intravenous; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; p.o., orally; QoL, quality of life; R, randomization; VEGF, vascular endothelial growth factor.

OS in full analysis set (primary endpoint)



CI, confidence interval; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; OS, overall survival.

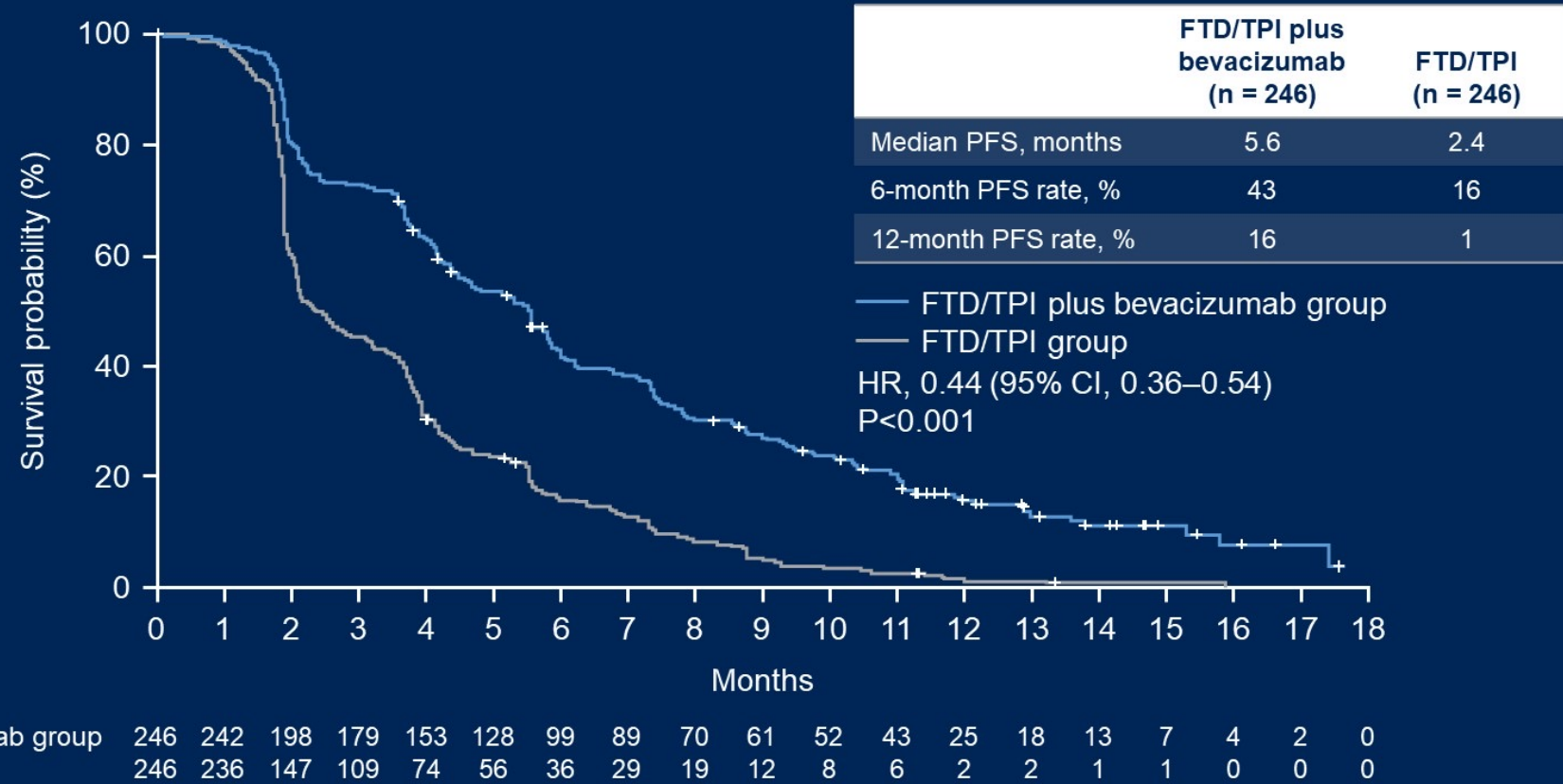
ASCO[®] Gastrointestinal
Cancers Symposium

#GI23

PRESENTED BY: Josep Tabernero, MD PhD

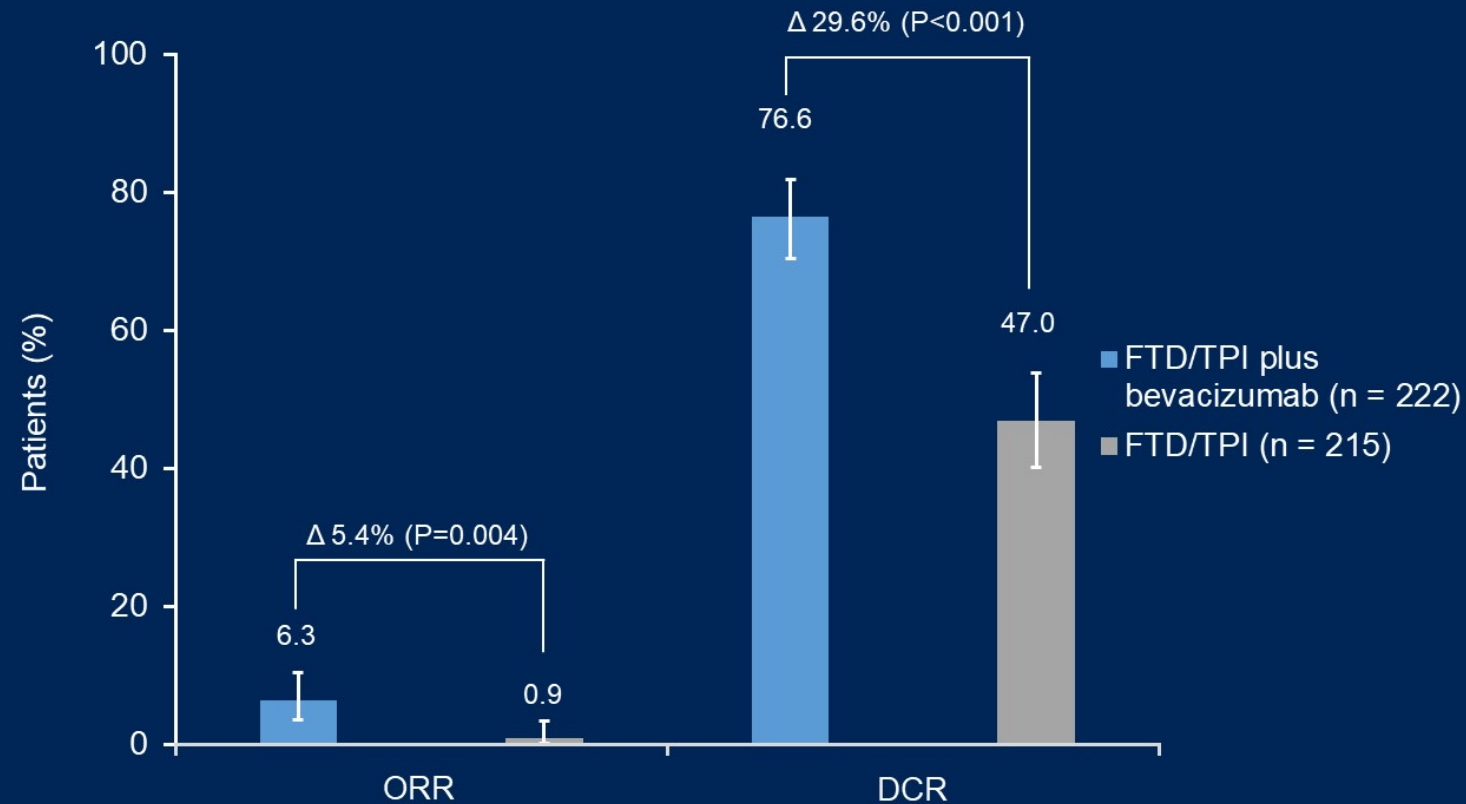
ASCO[®] AMERICAN SOCIETY OF
CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PFS in full analysis set



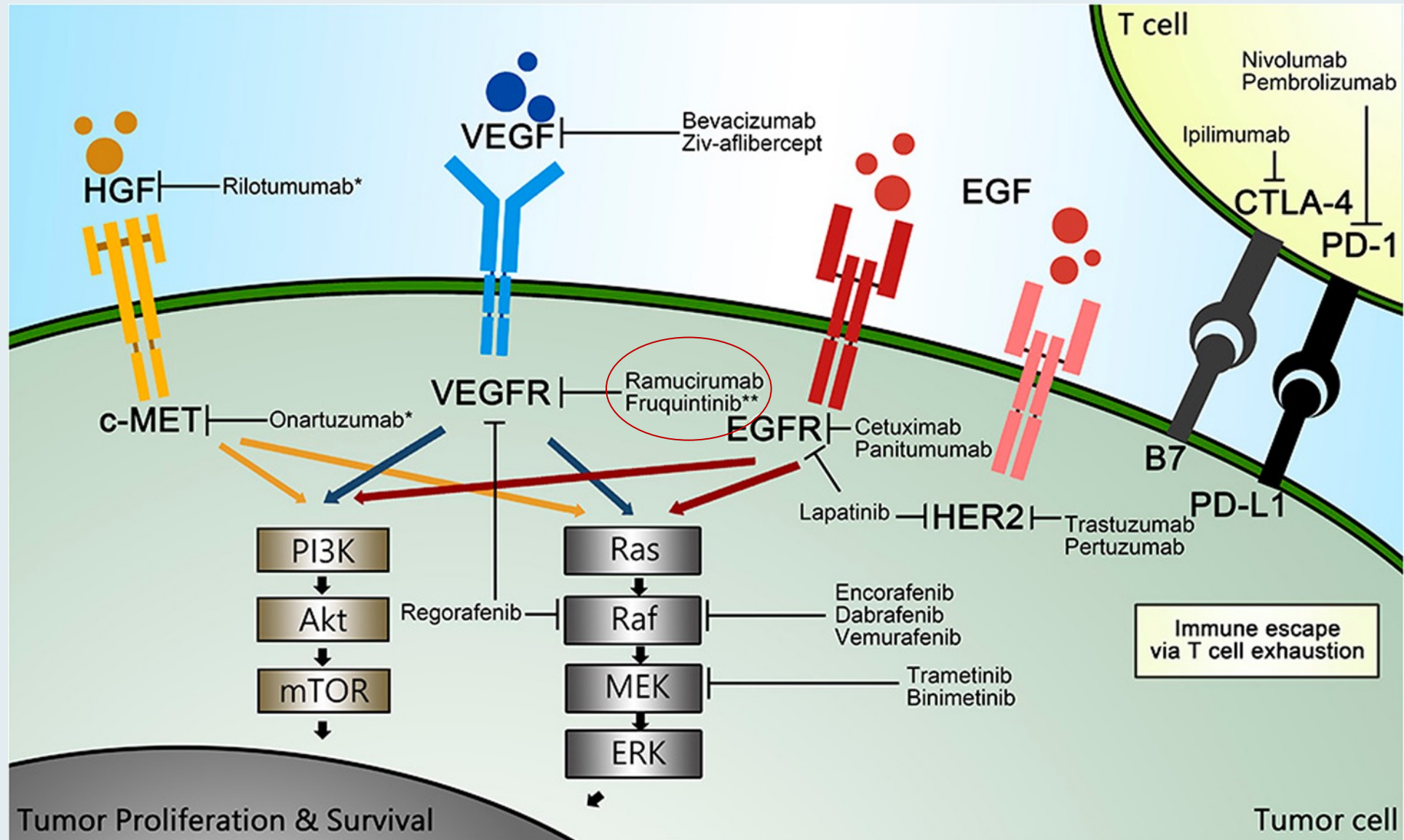
CI, confidence interval; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; PFS, progression-free survival.

ORR and DCR in patients evaluable for tumor response



DCR, disease control rate; FTD/TPI, trifluridine/tipiracil; ORR, objective response rate.

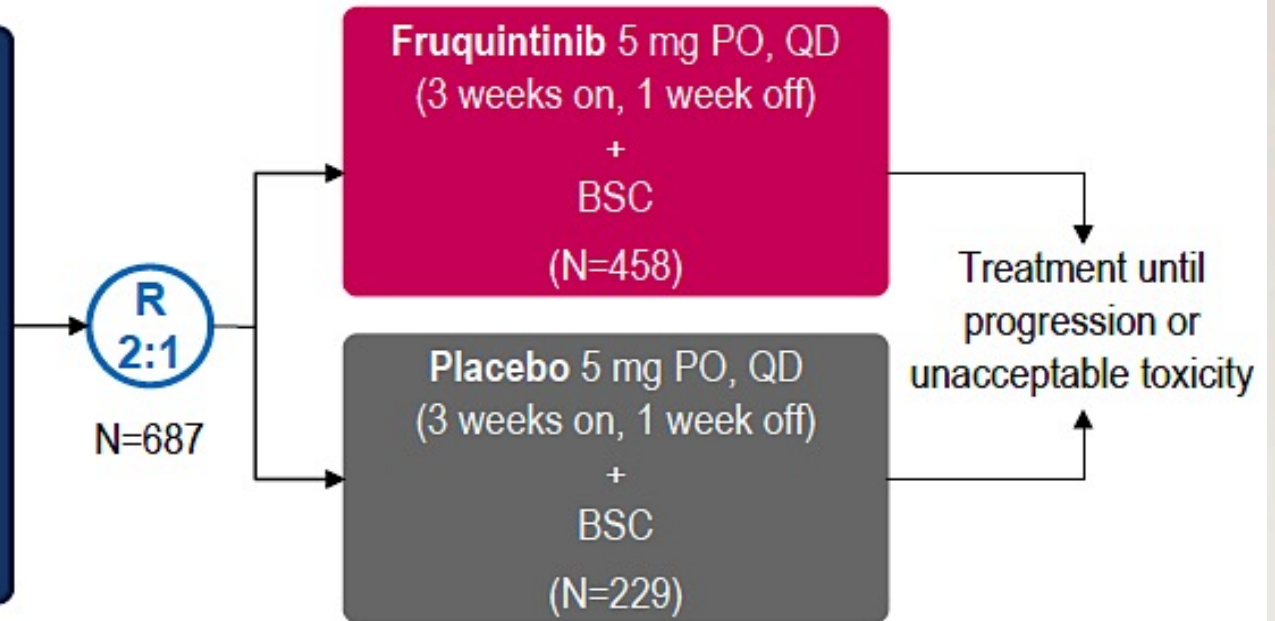
NCCN-Recommended Targeted Agents for CRC



FRESCO-2 Study Design

Patient Eligibility

- Prior treatment with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if *RAS* wild type, an anti-EGFR therapy
- Progression on, or intolerance to, TAS-102 and/or regorafenib
- Prior treatment with an immune checkpoint inhibitor or BRAF inhibitor if indicated



Stratification Factors

- Prior therapy (TAS-102 vs regorafenib vs TAS-102 and regorafenib)
- *RAS* mutational status (wild-type vs mutant)
- Duration of metastatic disease (≤ 18 months vs > 18 months)

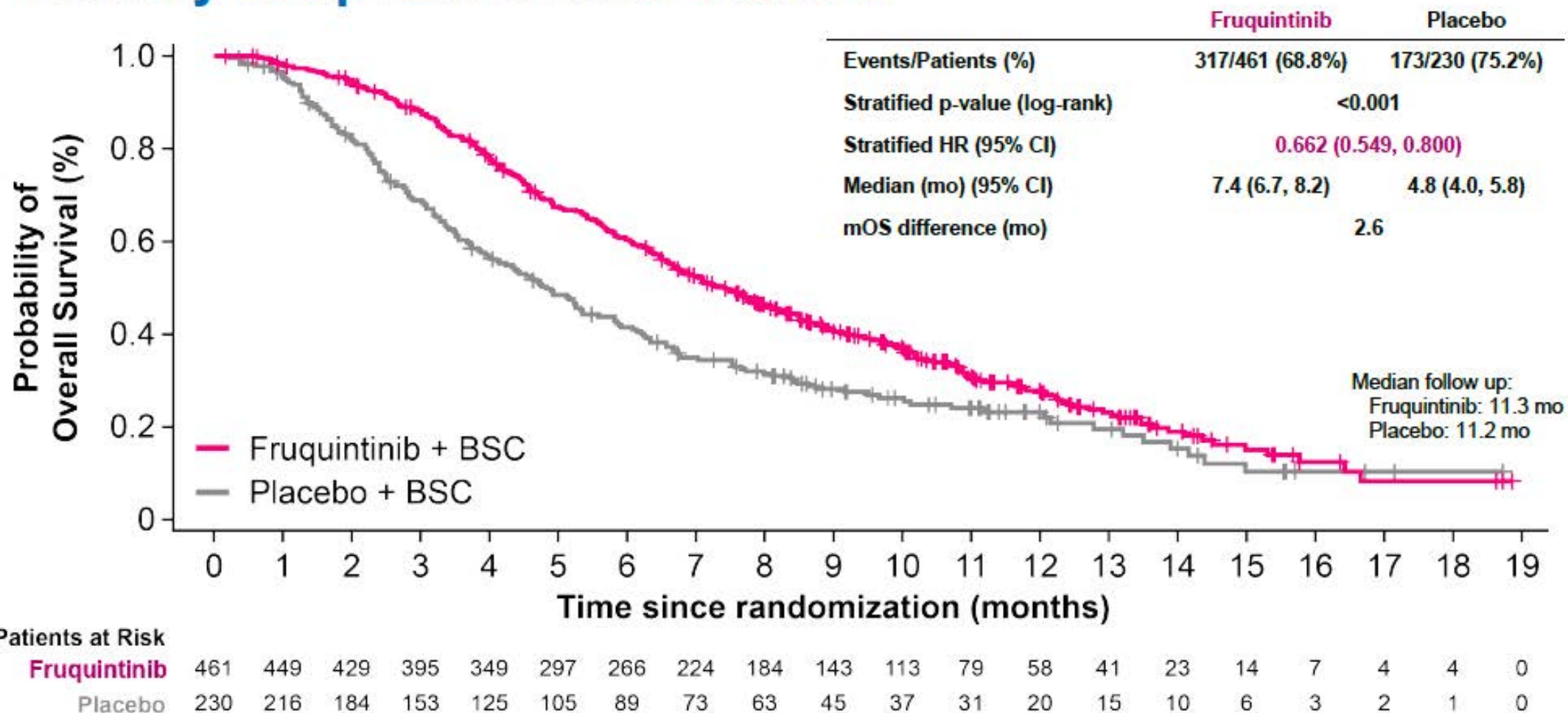
Note: To ensure the patient population is reflective of clinical practice, the number of patients treated with prior regorafenib was limited to 344 patients (50%)

BSC, best supportive care.
NCT04322539.

Dasari A et al. ESMO 2022, Presentation LBA25

Primary Endpoint: Overall Survival

ITT Population

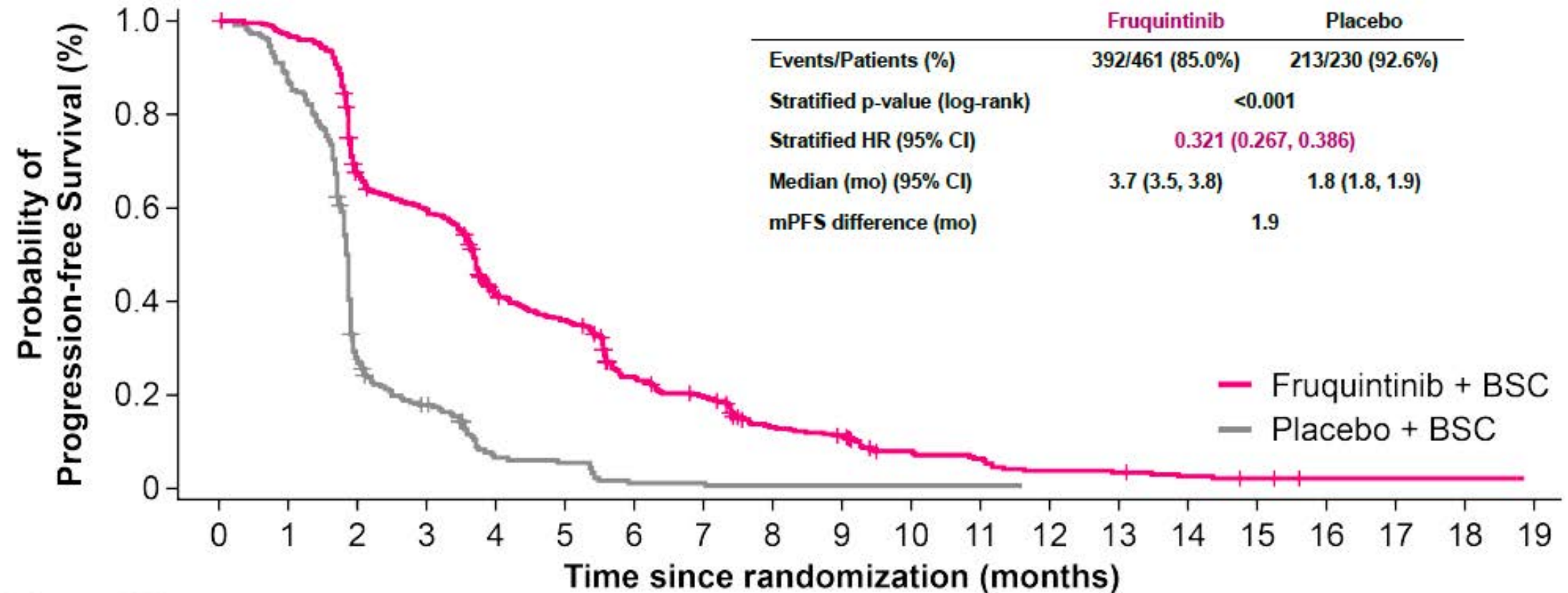


Subsequent anti-cancer medication balanced between the two arms: 29.4% fruquintinib arm vs. 34.3% placebo arm

Dasari A et al. ESMO 2022, Presentation LBA25

7

Progression-Free Survival



Patients at Risk

Fruquintinib

Placebo

461	430	291	256	170	146	89	71	43	36	21	17	10	9	6	4	2	2	2
230	194	60	36	12	10	2	2	1	1	1	1	0						

Dasari A et al. ESMO 2022, Presentation LBA25

9

Most Common TEAEs

(Any Grade \geq 15% in Either Arm)

TEAE, n (%)	Fruquintinib (N=456)		Placebo (N=230)	
	Any Grade	Grade \geq 3	Any Grade	Grade \geq 3
Patients with \geq 1 TEAE	451 (98.9)	286 (62.7)	213 (92.6)	116 (50.4)
Hypertension	168 (36.8)	62 (13.6)	20 (8.7)	2 (0.9)
Asthenia	155 (34.0)	35 (7.7)	52 (22.6)	9 (3.9)
Decreased appetite	124 (27.2)	11 (2.4)	40 (17.4)	3 (1.3)
Diarrhea	110 (24.1)	16 (3.5)	24 (10.4)	0
Hypothyroidism	94 (20.6)	2 (0.4)	1 (0.4)	0
Fatigue	91 (20.0)	18 (3.9)	37 (16.1)	2 (0.9)
Hand-foot syndrome	88 (19.3)	29 (6.4)	6 (2.6)	0
Abdominal pain	83 (18.2)	14 (3.1)	37 (16.1)	7 (3.0)
Nausea	79 (17.3)	3 (0.7)	42 (18.3)	2 (0.9)
Proteinuria	79 (17.3)	8 (1.8)	12 (5.2)	2 (0.9)
Constipation	78 (17.1)	2 (0.4)	22 (9.6)	0
Dysphonia	74 (16.2)	0	12 (5.2)	0

Dasari A et al. ESMO 2022, Presentation LBA25

14

Case Presentation: 79-year-old man with MSI-high, BRAF V600E-mutated recurrent cecal adenocarcinoma



Dr Nikesh Jasani (Houston, Texas)



Dr Farshid Dayyani
(Orange, California)

Case Presentation: 58-year-old woman with MSS BRAF V600E-mutated mCRC with brain and bone mets who has good response to dose-reduced FOLFOX after progression on first-line encorafenib/cetuximab



Dr Georges Azzi
(Fort Lauderdale, Florida)

Case Presentation: 66-year-old woman with RAS WT, BRAF V600E-mutated, MSS mCRC, now on encorafenib/cetuximab after progression on FOLFOX/bevacizumab



BRAF in Colorectal Cancer

- 5-10% of colorectal cancer
- More likely to be right sided, MSI, CMS1
- Poor outcome median OS ~ 11m
- Resistant to anti-EGFR antibodies
- Most are V600E (class I)
- Class III may result in sensitivity to anti-EGFR (Yaeger Clin Cancer Res 2019) and long survival (60m) (Jones JCO 2017)



BEACON Updated Results

- FDA Approved 4/2020
- Updated results Tabernero JCO 2021

Confirmed Best Overall Response	ENCO/BINI/CETUX (n = 224)	ENCO/CETUX (n = 220)	Control (n = 221)
Central assessment ^a			
ORR, n (%)	60 (27)	43 (20)	4 (2)
95% CI	21 to 33	15 to 25	< 1 to 5
<i>P</i> value v control	< 0.0001	< 0.0001	

- Triplet 9.3m OS HR 0.60
- Doublet 9.3m OS HR 0.61
- Control 5.9m OS
- Toxicity G3 diarrhea triplet 11%, doublet 3%, control 10%

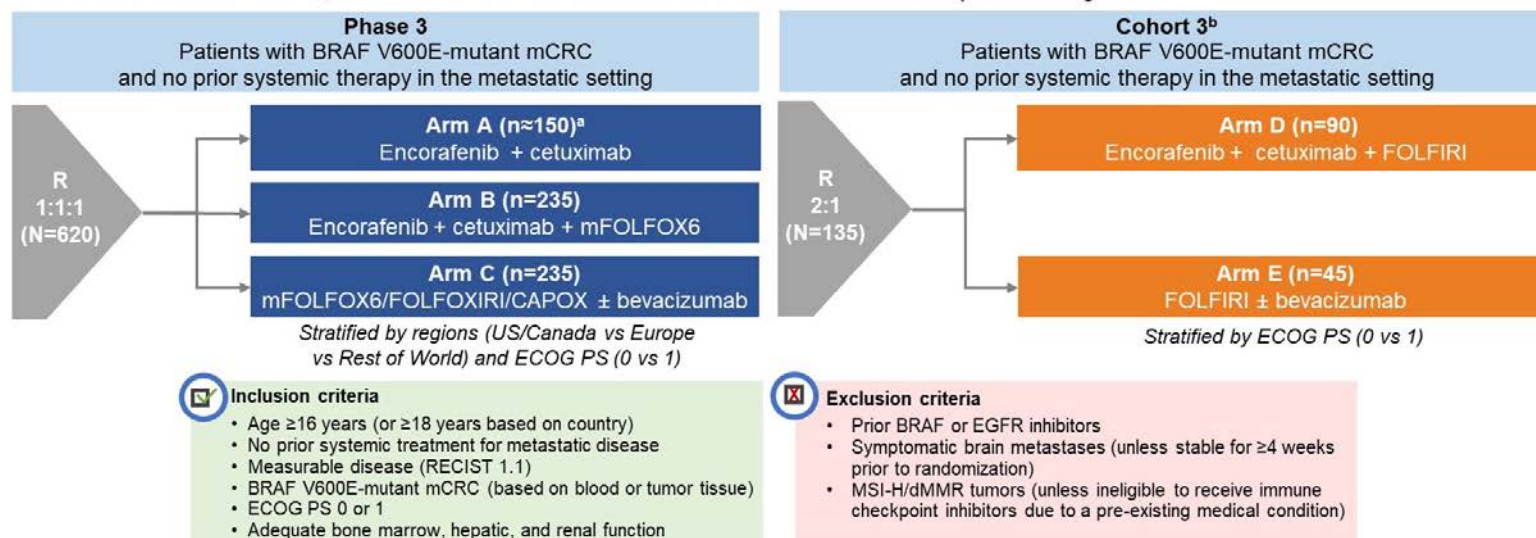
Other BRAF Trials

BREAKWATER

- ANCHOR
 - Van Cutsem
 - JCO 2023
 - Single arm
 - triplet 1st line
 - 47.4% RR, PFS 5.5m, OS 18.3m
 - G3 diarrhea 9.3%

Phase 3 and Cohort 3 Study Design

- BREAKWATER (NCT04607421) is an ongoing, open-label, multicenter, randomized, phase 3 study evaluating 1L EC ± CT vs SOC CT alone in patients with BRAF V600E-mutant mCRC
 - In the BREAKWATER SLI, which evaluated 57 patients with mCRC who had received ≤1 prior treatment, EC + CT showed encouraging antitumor activity
 - Based on these SLI results, EC + mFOLFOX6 was selected as the recommended phase 3 regimen



Appendix

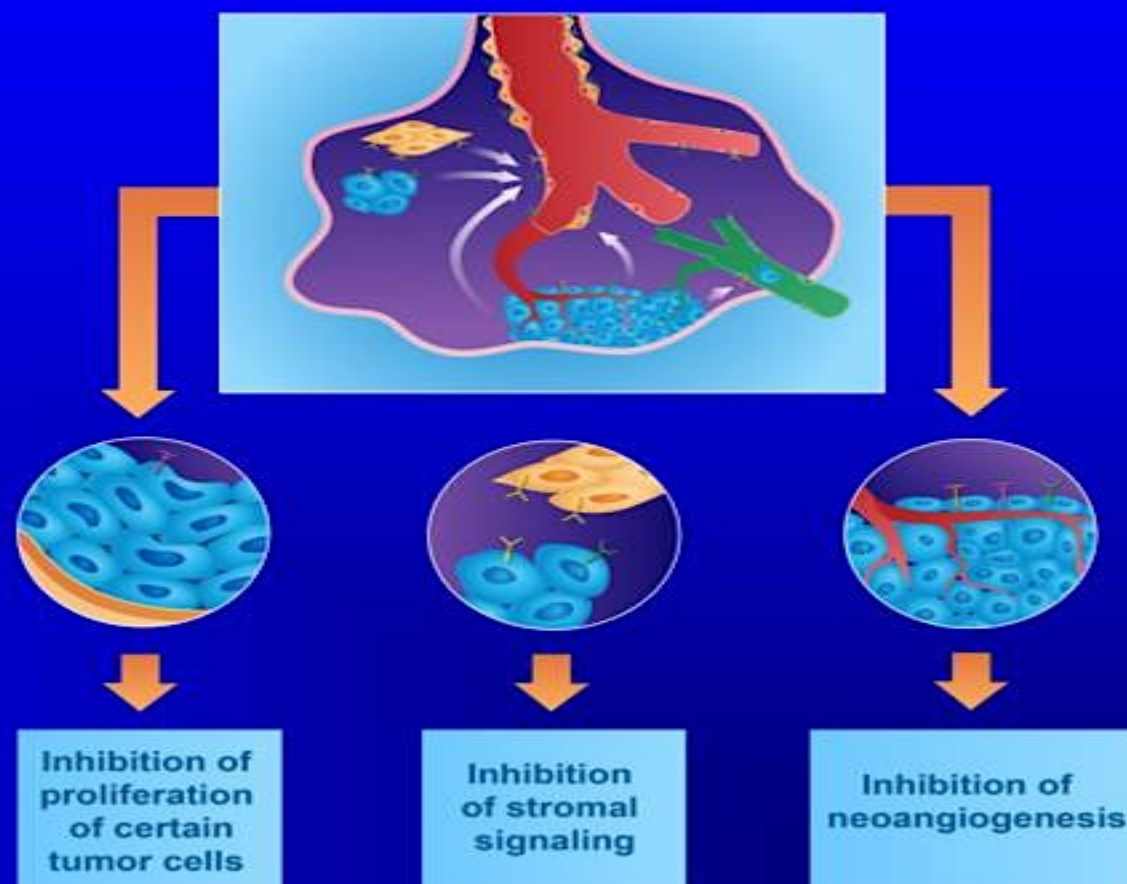
Mode of action of regorafenib (BAY 73-4506)

- **Regorafenib inhibits multiple cell-signaling kinases:**

- Angiogenic
 - VEGFR1–3, TIE2
- Stromal
 - PDGFR- β , FGFR
- Oncogenic
 - KIT, PDGFR, RET

- **$T_{1/2}$ in man: approx. 26-28 hrs**

- **Two major metabolites (M2, M5) are pharmacologically active**

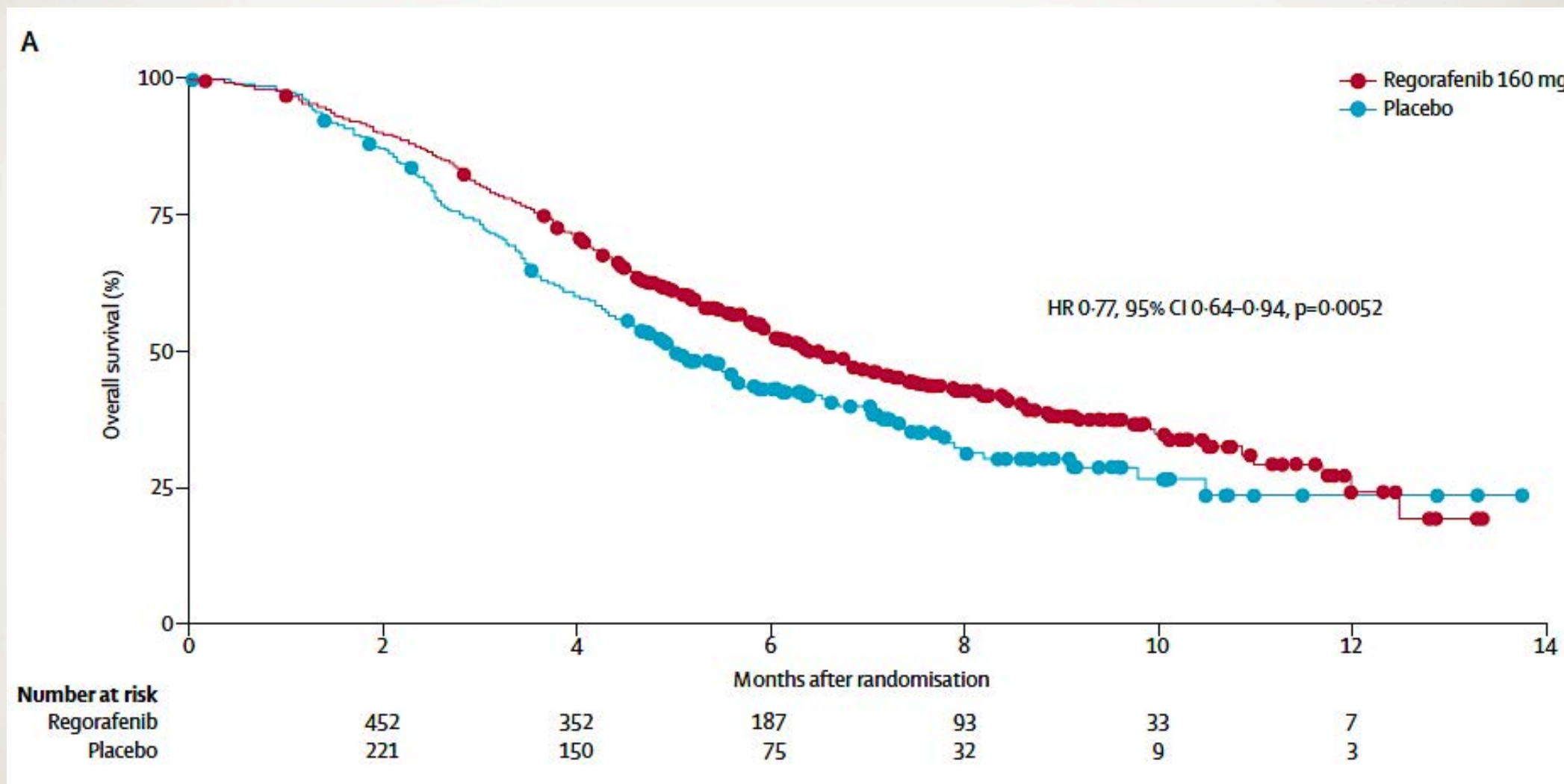


CORRECT study design



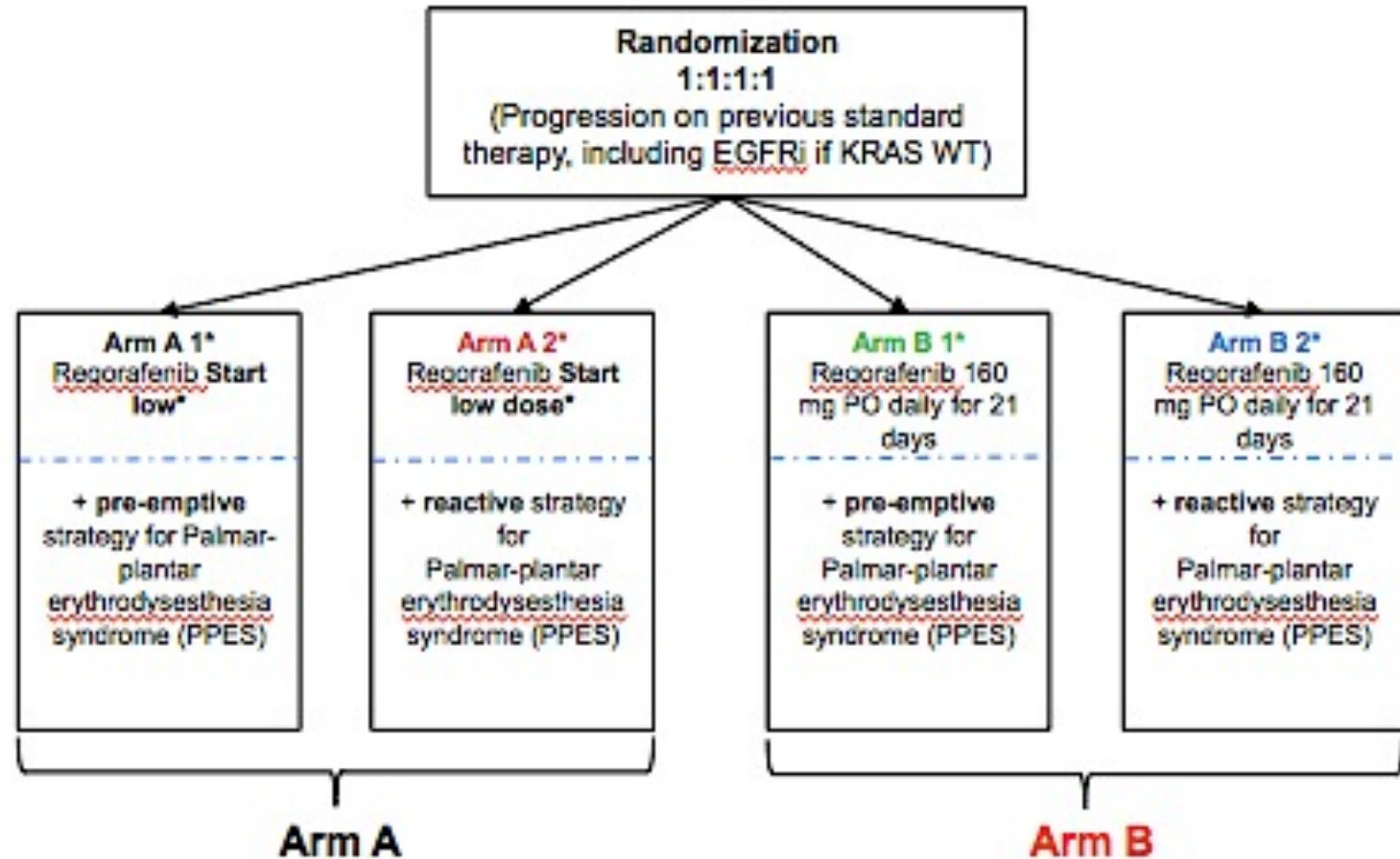
- Multicenter, randomized, double-blind, placebo-controlled, phase III
 - **2:1 randomization**
 - Strat. factors: prior anti-VEGF therapy, time from diagnosis of mCRC, geographical region
- Global trial: 16 countries, 114 active centers
 - 1,052 patients screened, **760 patients randomized within 10 months**
- Secondary endpoints: PFS, ORR, DCR
- Tertiary endpoints: duration of response / stable disease, QOL, pharmacokinetics, biomarkers

CORRECT (Regorafenib)



Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate dosing strategies for regorafenib in refractory mCRC

WEEK of C1		DOSE
1	Starting dose C1	80 mg
2	↓	120 mg
3	End dose C1	160 mg
4		off
WEEK of C2+		DOSE
1		160 mg
2		160 mg
3		160 mg
4		off

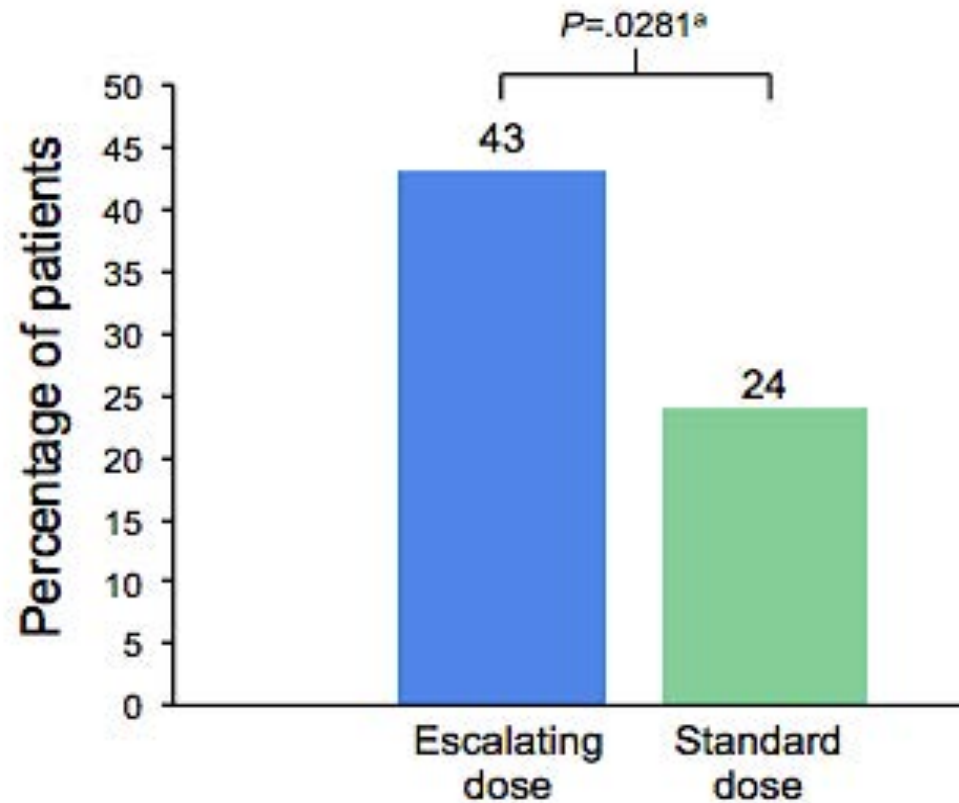


1ary endpoint: proportion of patients who complete 2 cycles of protocol treatment and initiate cycle 3 in arm A and arm B

2ary endpoints: OS, PFS, TTP

ReDOS: Regorafenib Dose-Optimization Study

% of Patients Starting Cycle 3 (Primary Endpoint)

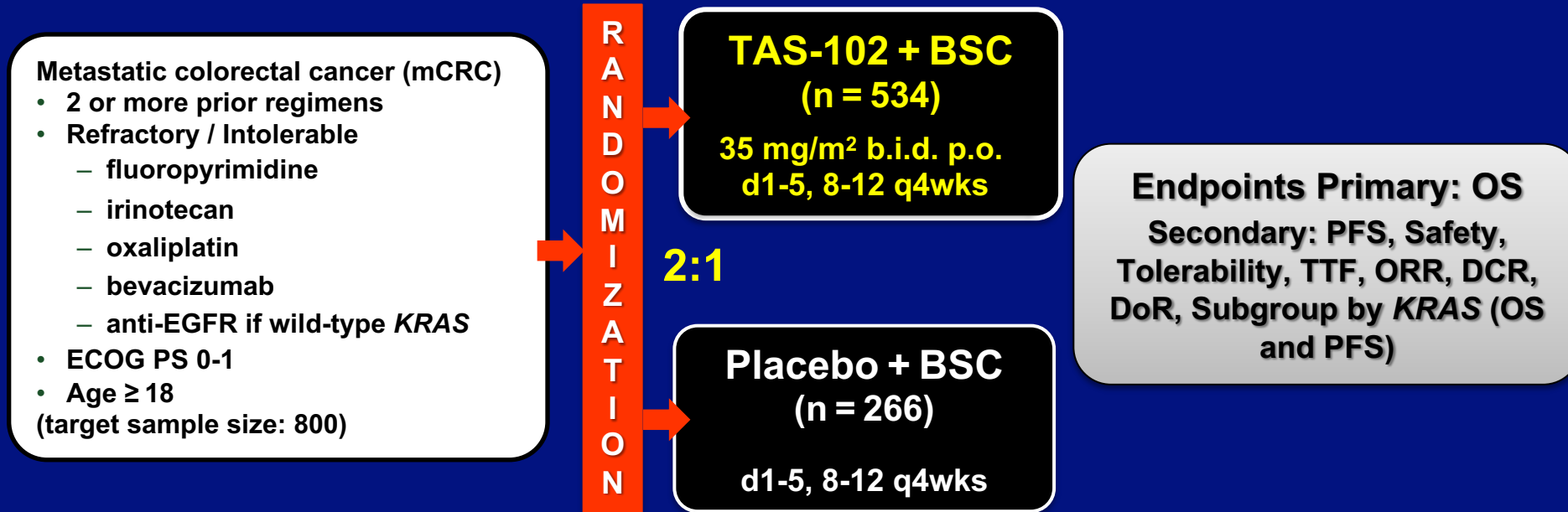


^aFisher's exact test (1-sided)

	Arm A n=54	Arm B n=62	P-Value
Primary Endpoint (patients initiating 3rd cycle)	43%	25%	0.028
mOS (mos)	9	5.9	0.094
mPFS (mos)	2.5	2.0	0.553
% HFSR	15%	16%	n/a
% HTN	7%	15%	n/a
% Fatigue	13%	18%	n/a

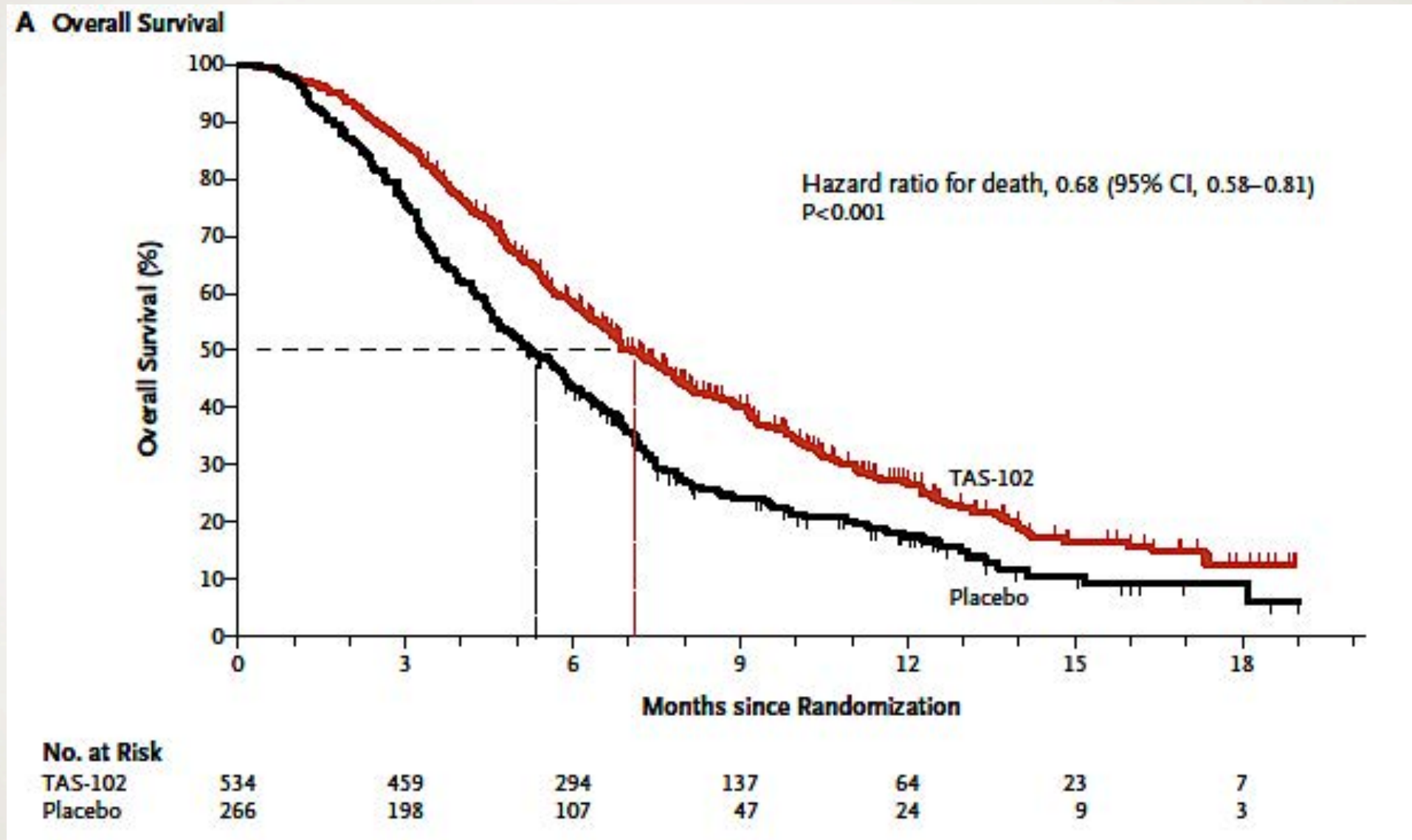
Global Randomized Phase III study

RECOURSE: Refractory Colorectal Cancer Study (NCT01607957)



- Treatment continuation until progression, intolerant toxicity or patient refusal
- Multicenter, randomized, double-blind, placebo-controlled, phase III
 - Stratification: *KRAS* status, time from diagnosis of metastatic disease, geographical region
- Sites: 13 countries, 114 sites
- Enrollment: June 2012 to October 2013

RECOURSE (TAS-102)



Key baseline characteristics

Characteristic		FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Age	Median (range), years	62 (20–84)	64 (24–90)
	<65 years, n (%)	146 (59)	129 (52)
	≥65 years, n (%)	100 (41)	117 (48)
Sex, n (%)	Male	122 (50)	134 (55)
Region	European Union	158 (64)	157 (64)
	North America	8 (3)	8 (3)
	Rest of the world	80 (33)	81 (33)
Primary tumor localization, n (%)	Right	62 (25)	77 (31)
	Left	184 (75)	169 (69)
Time from diagnosis of first metastasis to randomization, ^a n (%)	<18 months	104 (42)	105 (43)
	≥18 months	142 (58)	141 (57)
RAS status, ^a n (%)	Mutant	171 (70)	170 (69)
	Wild-type	75 (31)	76 (31)
Prior treatment with anti-VEGF, n (%)	Yes	188 (76)	188 (76)
Prior treatment with bevacizumab, n (%)	No	68 (28)	69 (28)
	Yes	178 (72)	177 (72)
ECOG PS, n (%)	0	119 (48)	106 (43)
	1	127 (52)	139 (57)
	2	0	1 (0.4) ^b

^a As documented in the Interactive Web Response System set for randomization. ^b Patient had an ECOG PS of 1 at randomization but was assessed as having an ECOG PS of 2 on day 1, cycle 1. ECOG PS, Eastern Cooperative Oncology Group performance status; FTD/TPI, trifluridine/tipiracil; VEGF, vascular endothelial growth factor.



Georges Azzi, MD
Holy Cross Health
Fort Lauderdale, Florida



Zanetta S Lamar, MD
Florida Cancer
Specialists and Research Institute
Naples, Florida



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



Ina J Patel, DO
Hematologist Oncologist
Fort Worth, Texas



Farshid Dayyani, MD, PhD
UCI Chao Family Comprehensive
Cancer Center
Orange, California



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



Nikesh Jasani, MD
Texas Oncology
Houston, Texas

Inside the Issue: Integrating Targeted and Immunotherapy into the Management of Localized Non-Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Thursday, September 21, 2023

5:00 PM – 6:00 PM ET

Faculty

Jamie E Chافت, MD

John V Heymach, MD, PhD

Moderator

Neil Love, MD

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 for 5 minutes after the meeting ends.

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