Year in Review: Management of Colorectal Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 19, 2025
5:00 PM – 6:00 PM ET

Faculty

Scott Kopetz, MD, PhD
Jeffrey Meyerhardt, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2025

Faculty

Scott Kopetz, MD, PhD
Professor
Deputy Chair for Translational Research
Department of Gastrointestinal Medical Oncology
Associate Vice President
for Translational Integration
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Jeffrey Meyerhardt, MD, MPH
Douglas Gray Woodruff Chair in Colorectal Cancer Research
Chief Clinical Research Officer
Dana-Farber Cancer Institute
Boston, Massachusetts

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from GSK and Natera 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, ADC Therapeutics, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Hologic Inc, 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, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

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 Kopetz — Disclosures

Consulting Agreements	Agenus Inc, Amgen Inc, AmMax Bio, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Carina Biotech, Clasp Therapeutics, Cytovation ASA, Dewpoint Therapeutics, Frontier Medicines, Genentech, a member of the Roche Group, Harbinger Health, Ikena Oncology, Kestrel Therapeutics, Leap Therapeutics Inc, Marengo Therapeutics, Merck, Mirati Therapeutics Inc, Pfizer Inc, Replimune, Revolution Medicines, Roche Laboratories Inc, SageMedic Corporation, Servier Pharmaceuticals LLC, Sibylla Biotech, T-Cypher Bio, Tachyon Therapeutics, Tempus, Xaira Therapeutics, Zentalis Pharmaceuticals
Contracted Research	Amgen Inc, BioMed Valley Discoveries, Boehringer Ingelheim Pharmaceuticals Inc, BridgeBio, Bristol Myers Squibb, Cardiff Oncology, Daiichi Sankyo Inc, EMD Serono Inc, Frontier Medicines, Genentech, a member of the Roche Group, Guardant Health, Jazz Pharmaceuticals Inc, Johnson & Johnson Pharmaceuticals, Lilly, Pfizer Inc, Zentalis Pharmaceuticals

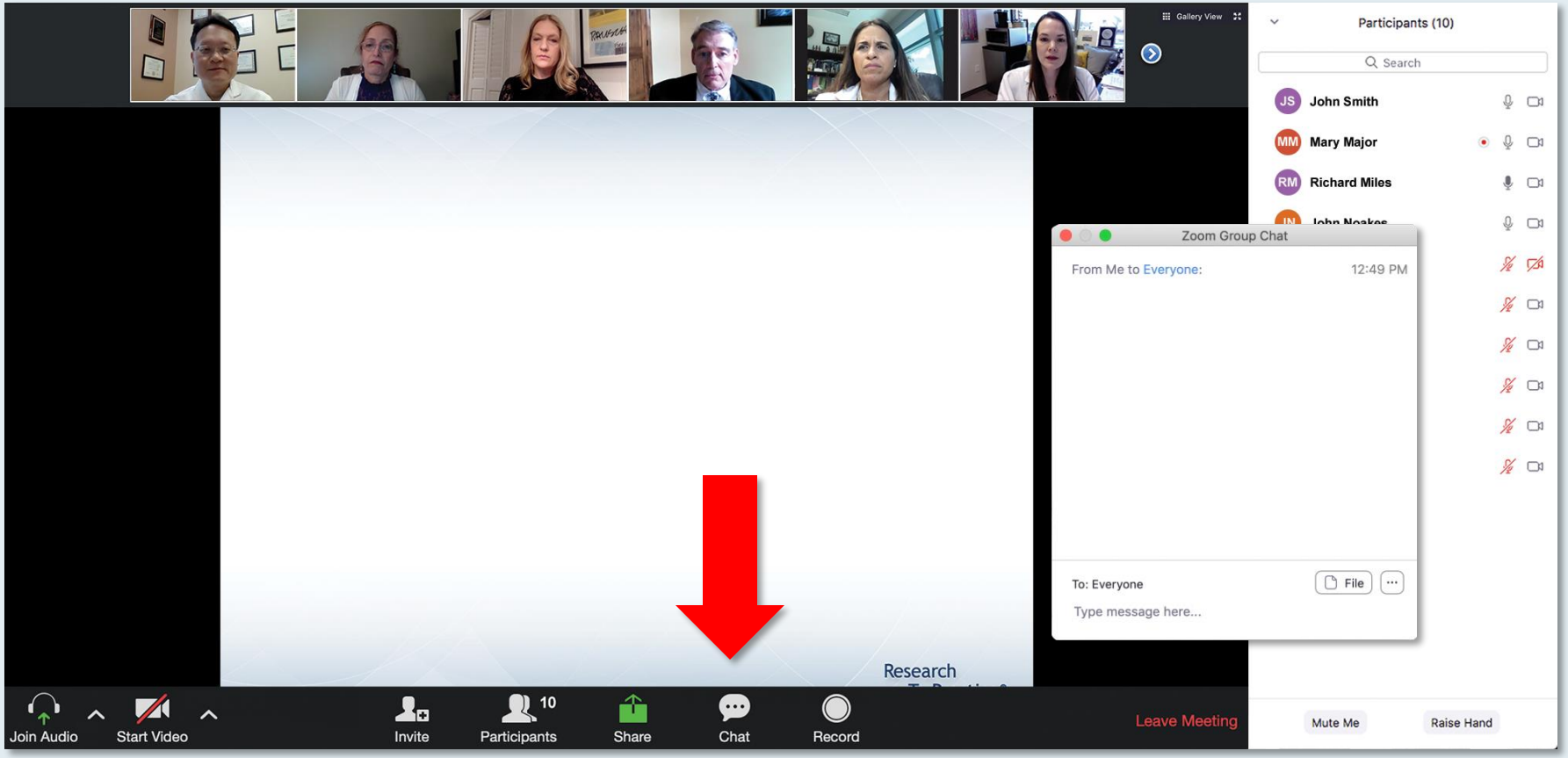
Dr Meyerhardt — Disclosures

No relevant conflicts of interest to disclose

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

RTP
RESEARCH TO PRACTICE

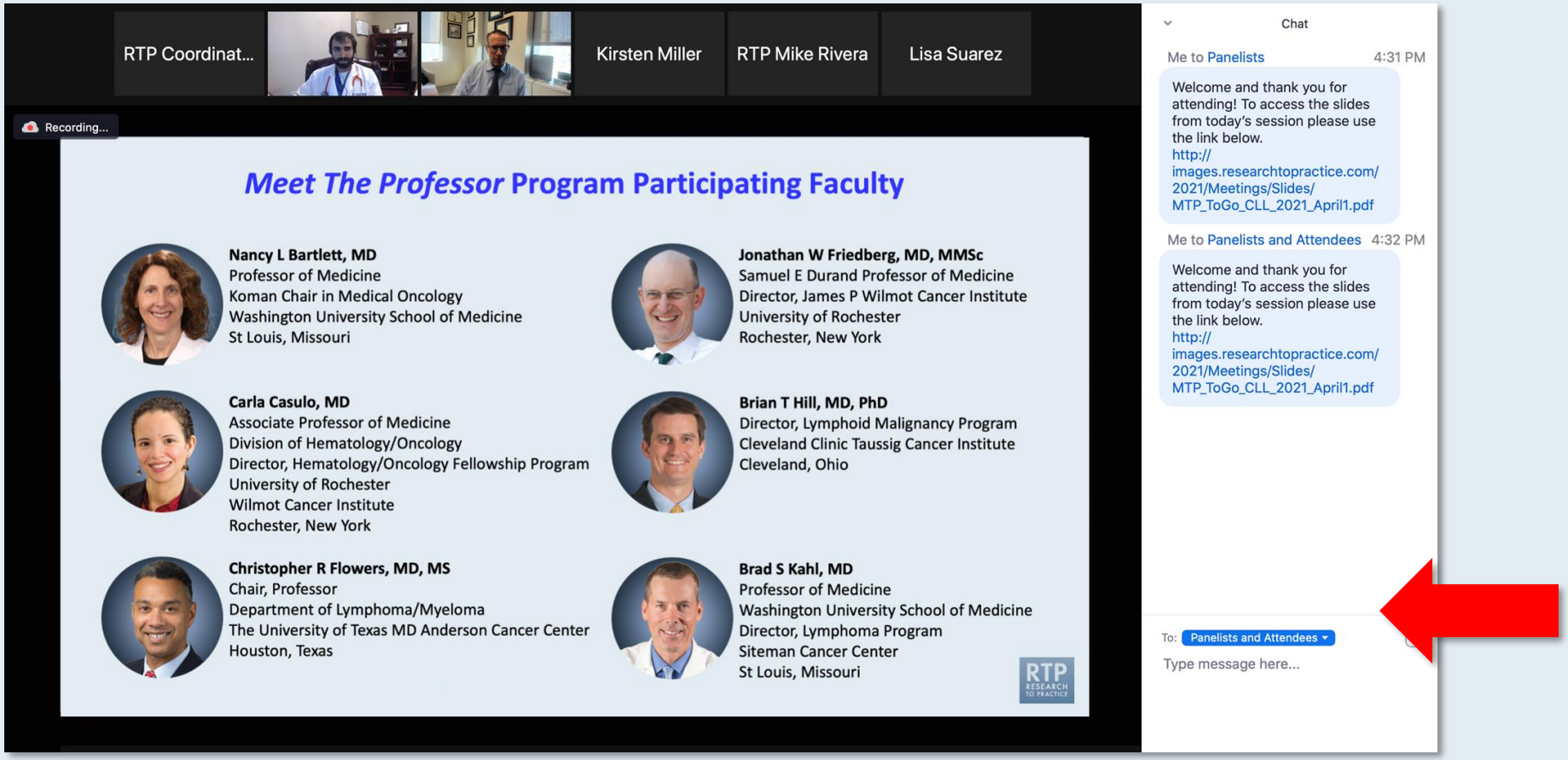
We Encourage Clinicians in Practice to Submit Questions



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

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

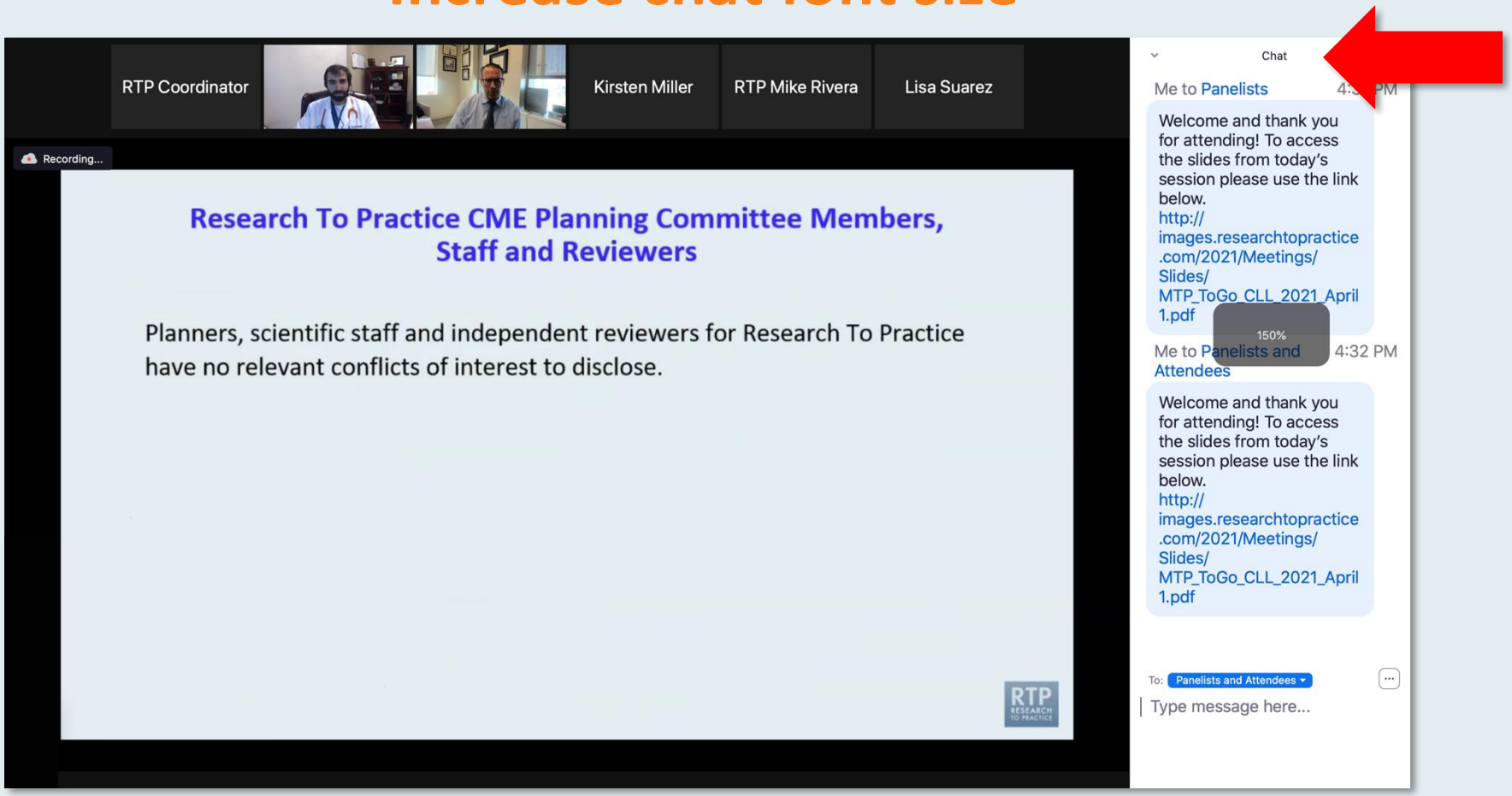


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

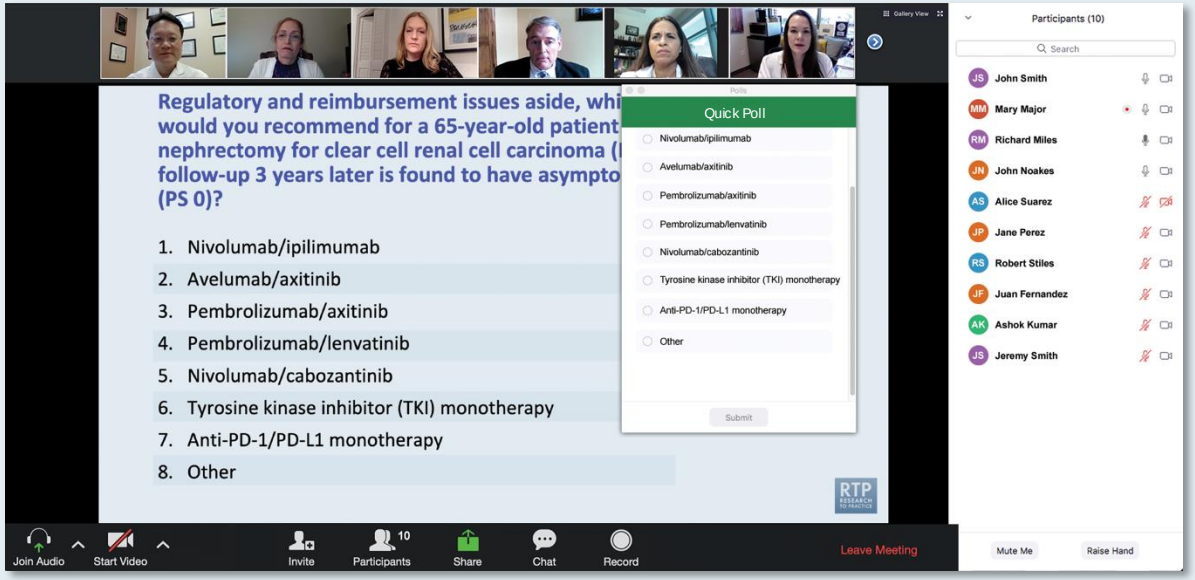
Familiarizing Yourself with the Zoom Interface

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



What Clinicians Want to Know: Biomarker Assessment and Related Treatment Decision-Making for Patients with Colorectal Cancer

DR ARVIND DASARI
THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

DR JENNY SELIGMANN
UNIVERSITY OF LEEDS

DR VAN K MORRIS
THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

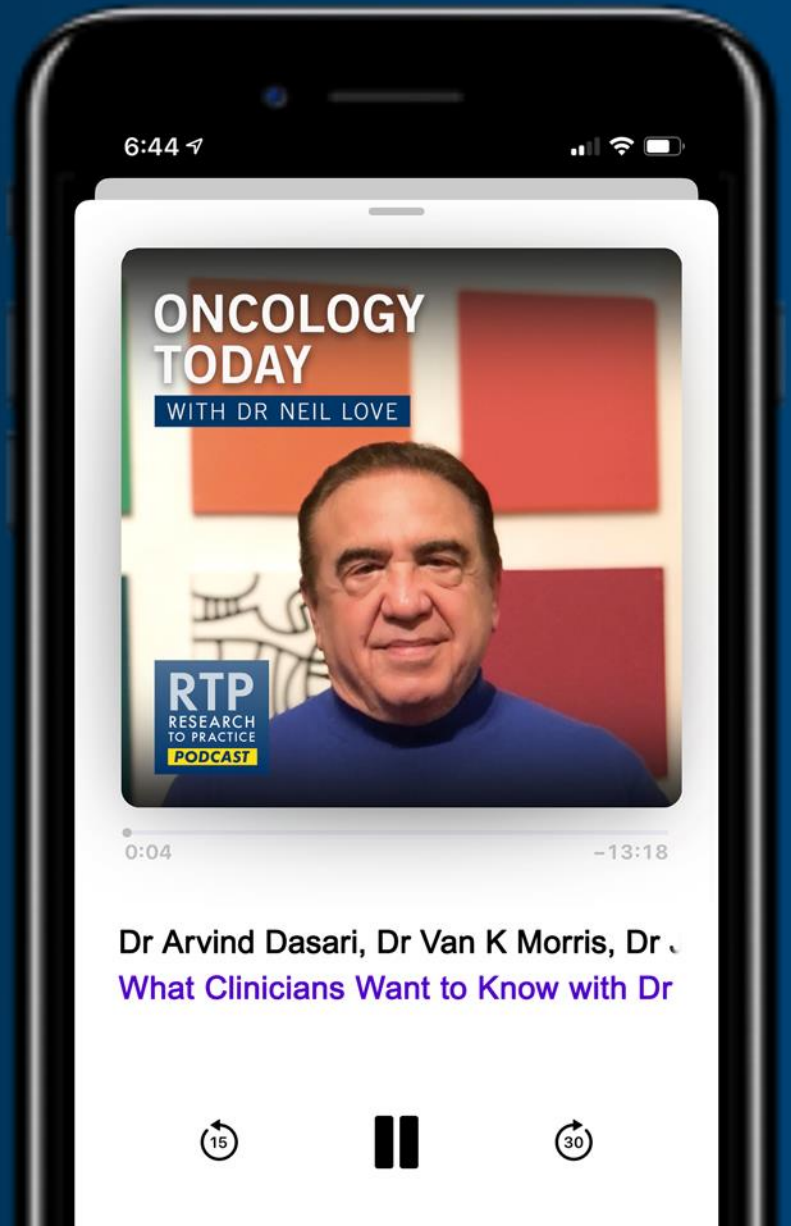
PROF ERIC VAN CUTSEM
UNIVERSITY HOSPITALS LEUVEN

MODERATOR
CHRISTOPHER LIEU
UNIVERSITY OF COLORADO CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Patterns of Care: Examining the Current Use of Genetic Testing and Related Clinical Management for Patients with Localized Breast Cancer

A CME/MOC-Accredited Webinar in Partnership with the American Society of Breast Surgeons

Thursday, February 20, 2025

5:00 PM – 6:00 PM ET

Faculty

Kevin S Hughes, MD

Mark Robson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Fourth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, February 28 to March 2, 2025

Fontainebleau Hotel, Miami Beach, Florida

Moderated by Neil Love, MD

Cases from the Community: Investigators Discuss the Optimal Clinical Care of Patients with HER2-Positive Gynecologic Cancers

An Independent CME Symposium During the 2025 SGO Annual Meeting on Women's Cancer®

Saturday, March 15, 2025

12:30 PM – 2:00 PM PT (3:30 PM – 5:00 PM ET)

Faculty

Kathleen N Moore, MD, MS

Alessandro D Santin, MD

Moderator

David M O'Malley, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Care of Patients with Ovarian Cancer

An Independent CME Symposium During
the 2025 SGO Annual Meeting on Women's Cancer®

Sunday, March 16, 2025
12:30 PM – 2:00 PM PT (3:30 PM – 5:00 PM ET)

Faculty

Kathleen N Moore, MD, MS
Ritu Salani, MD, MBA
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Angeles Alvarez Secord, MD, MHSc

RTP RESEARCH TO PRACTICE

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

RTP Year in Review 2025

Thank you for joining us!

Information on how to obtain CME, ABIM MOC and ABS credit will be provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2025

Year in Review: Management of Colorectal Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 19, 2025
5:00 PM – 6:00 PM ET

Faculty

Scott Kopetz, MD, PhD
Jeffrey Meyerhardt, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2025

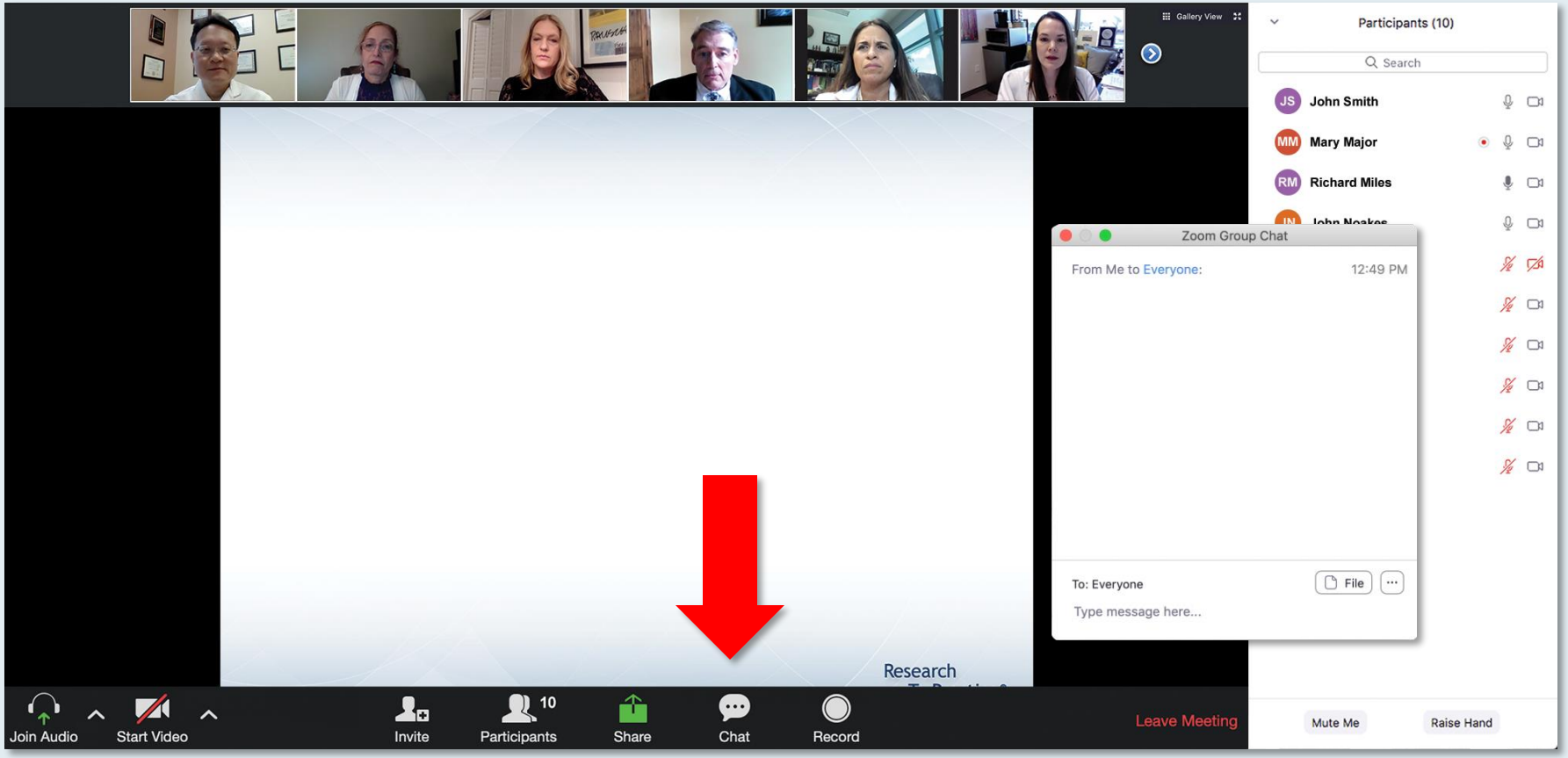
Faculty

Scott Kopetz, MD, PhD
Professor
Deputy Chair for Translational Research
Department of Gastrointestinal Medical Oncology
Associate Vice President
for Translational Integration
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Jeffrey Meyerhardt, MD, MPH
Douglas Gray Woodruff Chair in Colorectal Cancer Research
Chief Clinical Research Officer
Dana-Farber Cancer Institute
Boston, Massachusetts

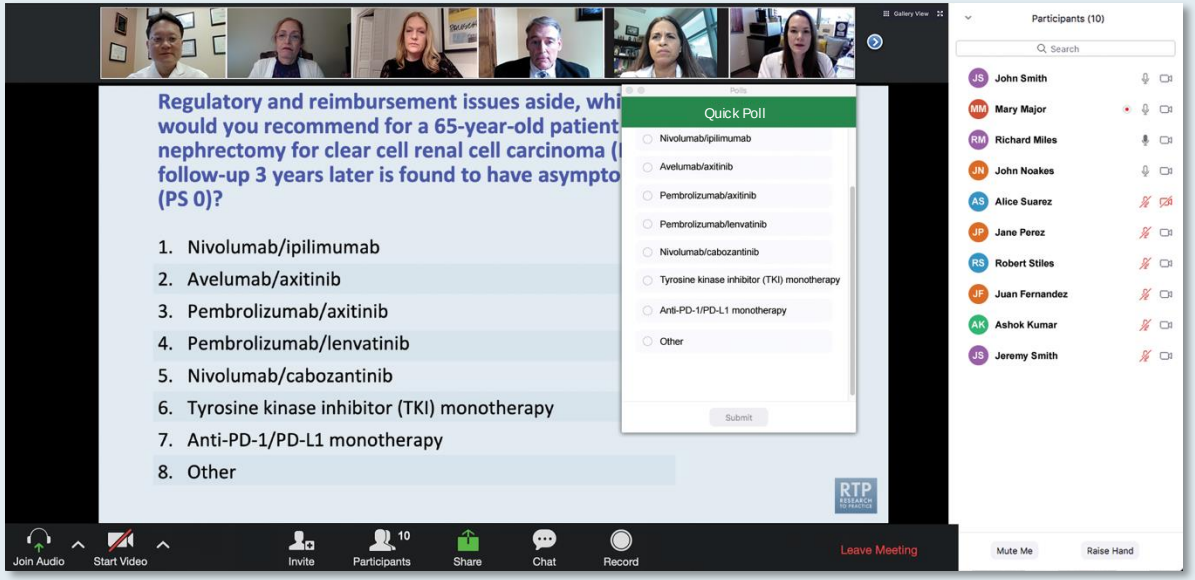
MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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



What Clinicians Want to Know: Biomarker Assessment and Related Treatment Decision-Making for Patients with Colorectal Cancer

DR ARVIND DASARI
THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

DR JENNY SELIGMANN
UNIVERSITY OF LEEDS

DR VAN K MORRIS
THE UNIVERSITY OF TEXAS
MD ANDERSON CANCER CENTER

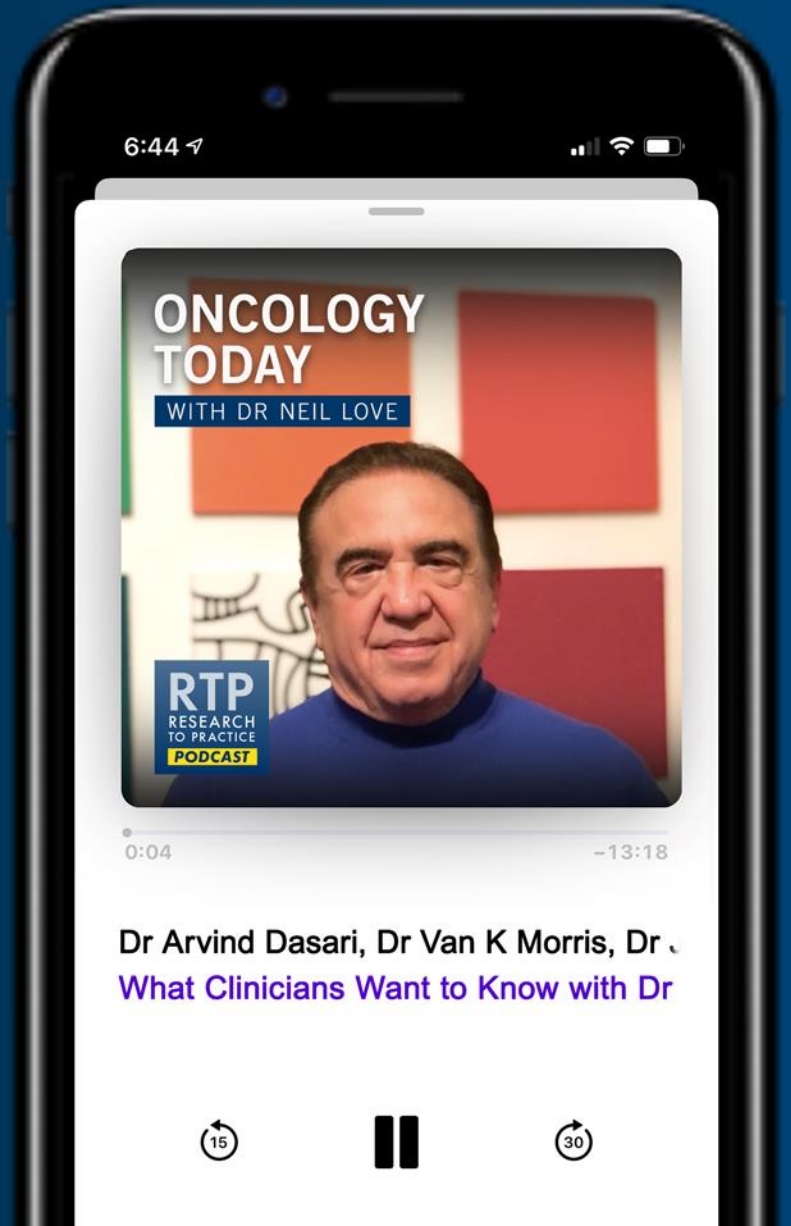
PROF ERIC VAN CUTSEM
UNIVERSITY HOSPITALS LEUVEN

MODERATOR
CHRISTOPHER LIEU
UNIVERSITY OF COLORADO CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



Patterns of Care: Examining the Current Use of Genetic Testing and Related Clinical Management for Patients with Localized Breast Cancer

A CME/MOC-Accredited Webinar in Partnership with the American Society of Breast Surgeons

Thursday, February 20, 2025

5:00 PM – 6:00 PM ET

Faculty

Kevin S Hughes, MD

Mark Robson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Fourth Annual
National General Medical Oncology Summit

A Multitumor CME/MOC-, NCPD- and ACPE-Accredited Educational Conference Developed in Partnership with Florida Cancer Specialists & Research Institute

Friday to Sunday, February 28 to March 2, 2025

Fontainebleau Hotel, Miami Beach, Florida

Moderated by Neil Love, MD


Columbia

Cases from the Community: Investigators Discuss the Optimal Clinical Care of Patients with HER2-Positive Gynecologic Cancers

An Independent CME Symposium During the 2025 SGO Annual Meeting on Women's Cancer®

Saturday, March 15, 2025

12:30 PM – 2:00 PM PT (3:30 PM – 5:00 PM ET)

Faculty

Kathleen N Moore, MD, MS

Alessandro D Santin, MD

Moderator

David M O'Malley, MD

RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Care of Patients with Ovarian Cancer

An Independent CME Symposium During
the 2025 SGO Annual Meeting on Women's Cancer®

Sunday, March 16, 2025
12:30 PM – 2:00 PM PT (3:30 PM – 5:00 PM ET)

Faculty

Kathleen N Moore, MD, MS
Ritu Salani, MD, MBA
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Angeles Alvarez Secord, MD, MHSc

RTP RESEARCH TO PRACTICE

Year in Review: Management of Colorectal Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 19, 2025
5:00 PM – 6:00 PM ET

Faculty

Scott Kopetz, MD, PhD
Jeffrey Meyerhardt, MD, MPH

Moderator

Neil Love, MD

RTP Year in Review 2025

Commercial Support

This activity is supported by educational grants from GSK and Natera 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.

RTP Year in Review 2025

Dr Kopetz — Disclosures

Consulting Agreements	Agenus Inc, Amgen Inc, AmMax Bio, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Carina Biotech, Clasp Therapeutics, Cytovation ASA, Dewpoint Therapeutics, Frontier Medicines, Genentech, a member of the Roche Group, Harbinger Health, Ikena Oncology, Kestrel Therapeutics, Leap Therapeutics Inc, Marengo Therapeutics, Merck, Mirati Therapeutics Inc, Pfizer Inc, Replimune, Revolution Medicines, Roche Laboratories Inc, SageMedic Corporation, Servier Pharmaceuticals LLC, Sibylla Biotech, T-Cypher Bio, Tachyon Therapeutics, Tempus, Xaira Therapeutics, Zentalis Pharmaceuticals
Contracted Research	Amgen Inc, BioMed Valley Discoveries, Boehringer Ingelheim Pharmaceuticals Inc, BridgeBio, Bristol Myers Squibb, Cardiff Oncology, Daiichi Sankyo Inc, EMD Serono Inc, Frontier Medicines, Genentech, a member of the Roche Group, Guardant Health, Jazz Pharmaceuticals Inc, Johnson & Johnson Pharmaceuticals, Lilly, Pfizer Inc, Zentalis Pharmaceuticals

Dr Meyerhardt — Disclosures

No relevant conflicts of interest to disclose

This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

Year in Review:
Treatment of Localized Colorectal Cancer

Jeffrey Meyerhardt, MD, MPH
Douglas Gray Woodruff Chair in Colorectal Cancer Research
Chief Clinical Research Officer
Dana-Farber Cancer Institute
Boston, Massachusetts

Year in Review – Advances in the Management of Metastatic CRC (mCRC)

S. Kopetz

RTP Year in Review 2025

Key Datasets

Jeffrey Meyerhardt, MD, MPH

- Shah PK et al. **Circulating tumor DNA** for detection of molecular residual disease **(MRD)** in patients (pts) with **stage II/III** colorectal cancer (CRC): **Final analysis** of the **BESPOKE CRC sub-cohort**. Gastrointestinal Cancers Symposium 2025;Abstract 15.
- Nakamura Y et al. **ctDNA-based molecular residual disease** and survival in resectable colorectal cancer. *Nat Med* 2024;30(11):3272-83.
- Kataoka K et al. Survival benefit of adjuvant chemotherapy based on **molecular residual disease detection** in resected colorectal liver metastases: **Subgroup analysis** from **CIRCULATE-Japan GALAXY**. *Ann Oncol* 2024;35(11):1015-25.
- Nowak JA et al. Prognostic and predictive role of circulating tumor DNA **(ctDNA)** in **stage III** colon cancer treated with **celecoxib**: Findings from **CALGB (Alliance)/SWOG 80702**. Gastrointestinal Cancers Symposium 2025;Abstract LBA14.
- Tie J et al. **Circulating tumor DNA** analysis guiding adjuvant therapy in **stage II** colon cancer: **Overall survival** and **updated 5-year results** from the randomized **DYNAMIC** trial. ASCO 2024;Abstract 108.

Key Datasets

Jeffrey Meyerhardt, MD, MPH (Continued)

- Lieu CH et al. **NRG-GI008:** Colon adjuvant chemotherapy based on evaluation of **residual disease (CIRCULATE-NORTH AMERICA)**. ASCO 2024;Abstract TPS243.
- Cercek A et al. Durable complete responses to **PD-1 blockade** alone in **mismatch repair deficient** locally advanced rectal cancer. ASCO 2024;Abstract LBA3512.
- Chalabi M et al. **Neoadjuvant immunotherapy** in locally advanced **mismatch repair-deficient** colon cancer. *N Engl J Med* 2024;390(21):1949-58.
- Chalabi M et al. **Neoadjuvant immunotherapy** in locally advanced **MMR-deficient** colon cancer: **3-year disease-free survival** from **NICHE-2**. ESMO 2024;Abstract LBA24.
- de Gooyer PG et al. **Neoadjuvant nivolumab** and **relatlimab** in locally advanced **MMR-deficient** colon cancer: A phase 2 trial. *Nat Med* 2024;30(11):3284-90.
- Martling A et al. **Low-dose aspirin** reduces recurrence rate in colorectal cancer patients with **PI3K pathway** alterations: **3-year results** from the **ALASCCA** trial. Gastrointestinal Cancers Symposium 2025;Abstract LBA125.

Key Datasets

Scott Kopetz, MD, PhD

- Adam R et al. **Liver transplantation** plus **chemotherapy** versus **chemotherapy** alone in patients with **permanently unresectable** colorectal liver metastases **(TransMet)**: Results from a multicentre, open-label, prospective, randomised controlled trial. *Lancet* 2024;404(10458):1107-18.
- Lenz HJ et al**. Nivolumab (NIVO)** plus **ipilimumab (IPI)** vs chemotherapy (chemo) as **first-line (1L)** treatment for microsatellite instability-high/mismatch repair-deficient **(MSI-H/dMMR)** metastatic colorectal cancer (mCRC): Expanded efficacy analysis **from CheckMate 8HW**. ASCO 2024;Abstract 3503.
- Andre T et al. **Nivolumab** plus **ipilimumab** versus **nivolumab** in **microsatellite instability-high** metastatic colorectal cancer **(CheckMate 8HW)**: A randomised, open-label, **phase 3** trial. *Lancet* 2025;405(10476):383-95.
- Kopetz S et al. Molecular profiling of **BRAF-V600E-mutant** metastatic colorectal cancer in the **phase 3 BEACON CRC** trial. *Nat Med* 2024;30(11):3261-71.
- Kopetz S et al. **Encorafenib, cetuximab** and **chemotherapy** in **BRAF-mutant** colorectal cancer: A randomized **phase 3** trial. *Nat Med* 2025;[Online ahead of print].

Key Datasets

Scott Kopetz, MD, PhD (Continued)

- Strickler JH et al. **Final results** of a phase 2 study of **tucatinib** and **trastuzumab** for **HER2-positive** mCRC **(MOUNTAINEER)**. ASCO 2024;Abstract 3509.
- Siena S et al. **HER2-related biomarkers** predict clinical outcomes with **trastuzumab deruxtecan** treatment in patients with **HER2-expressing** metastatic colorectal cancer: **Biomarker analyses** of **DESTINY-CRC01**. *Nat Commun* 2024;15(1):10213.
- Raghav K et al. **Trastuzumab deruxtecan** in patients with **HER2-positive** advanced colorectal cancer **(DESTINY-CRC02)**: **Primary results** from a multicentre, randomised, phase 2 trial. *Lancet Oncol* 2024;25(9):1147-62.
- Fakih M et al. Overall survival (OS) of **phase 3 CodeBreaK 300** study of **sotorasib** plus **panitumumab** (soto+pani) versus investigator's choice of therapy for **KRAS G12C-mutated** metastatic colorectal cancer (mCRC). ASCO 2024;Abstract LBA3510.
- Yaeger R et al. **Adagrasib (ada)** + **cetuximab (cetux)** for **KRASG12C-mutated** metastatic colorectal cancer (mCRC): **Longer follow-up** analysis from **KRYSTAL-1**. Gastrointestinal Cancers Symposium 2025;Abstract 131.

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

RTP Year in Review 2025

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

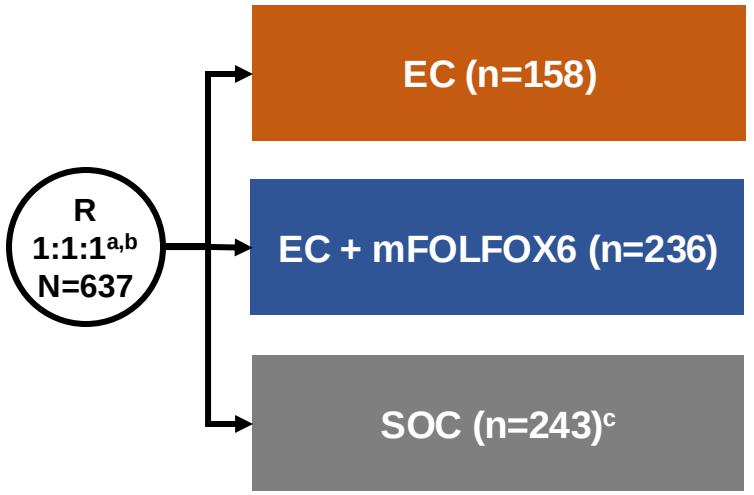
Discussion Question:
First-Line Treatment of BRAF V600E-Mutant mCRC

- **Regulatory and reimbursement issues aside, what would be your most likely first-line treatment recommendation for a clinically stable 60-year-old patient with left-sided, pan-RAS wild-type, microsatellite stable (MSS), HER2-negative mCRC with a BRAF V600E mutation?**

BREAKWATER: Study Design

- BREAKWATER (NCT04607421) is an open-label, multicenter, phase 3 study in first line BRAF V600E-mutant mCRC

Inclusion criteria
• Age ≥16 years (or ≥18 years based on country) • No prior systemic treatment for metastatic disease • Measurable disease (RECIST 1.1) • BRAF V600E-mutant mCRC by local or central laboratory testing • ECOG PS 0 or 1 • Adequate bone marrow, hepatic, and renal function
Exclusion criteria
• Prior BRAF or EGFR inhibitors • Symptomatic brain metastases • MSI-H/dMMR tumors (unless patients were ineligible to receive immune checkpoint inhibitors due to a pre-existing medical condition) • Presence of a *RAS* mutation



Stratified by regions (US/Canada vs Europe vs Rest of World) and ECOG PS (0 vs 1)

Dual primary endpoints:
PFS and ORR[d] by BICR
(EC + mFOLFOX6 vs SOC)

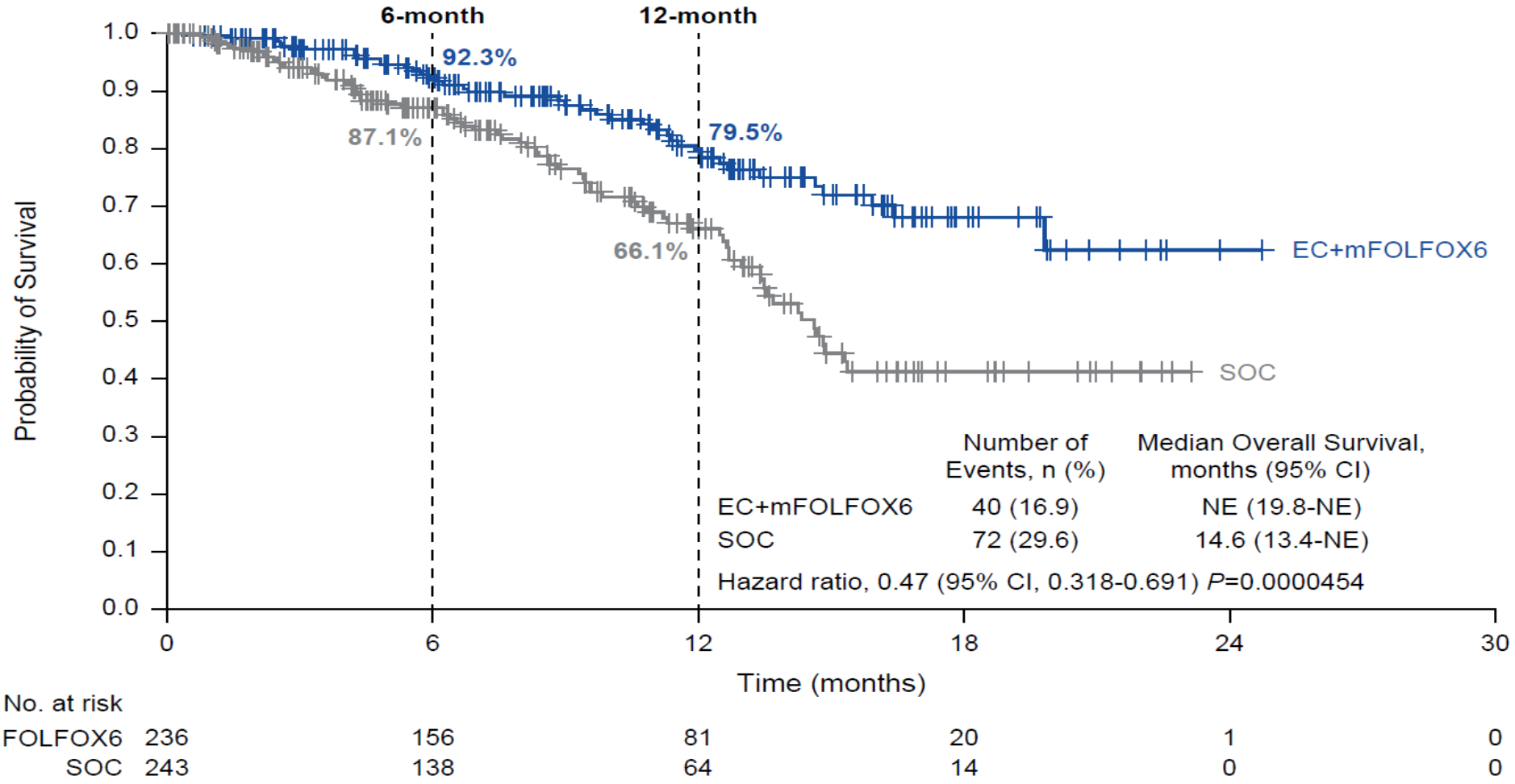
Key secondary endpoint:
OS (EC + mFOLFOX6 vs SOC)

Here we present the primary analysis of ORR by BICR (one of the dual primary endpoints), an interim analysis of OS, and safety in the EC + mFOLFOX6 and SOC arms

[a]Following a protocol amendment, enrollment to the EC arm was stopped and patients were randomized 1:1 to the EC+mFOLFOX6 or SOC arms; data in the EC arm will be reported at a later date. [b]Patients were enrolled between November 16, 2021, and December 22, 2023. [c]mFOLFOX6/FOLFOXIRI/CAPOX ± bevacizumab. [d]In the first 110 patients in each of the EC+mFOLFOX6 and SOC arms.

CAPOX, capecitabine/oxaliplatin; BICR, blinded independent central review; dMMR, deficient mismatch repair; EC, encorafenib plus cetuximab; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; mFOLFOX6, modified fluorouracil/leucovorin/oxaliplatin; FOLFOXIRI, fluorouracil/leucovorin/oxaliplatin/irinotecan; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instability-high cancer; RECIST, Response Evaluation Criteria in Solid Tumors.

Interim Overall Survival[a]



Data cutoff: December 22, 2023.

[a]OS was tested following the prespecified plan with one-sided alpha of 0.000000083, calculated as a portion of the nominal one-sided alpha of 0.001. Statistical significance was not achieved at this time.

EC, encorafenib plus cetuximab; mFOLFOX6, modified fluorouracil/leucovorin/oxaliplatin; NE, not estimable; SOC, standard of care.

Positive Topline Results Announced from Pivotal Phase III BREAKWATER Study

Press Release: February 3, 2025

"Positive topline results [were announced] from the progression-free survival (PFS) analysis of the Phase 3 BREAKWATER study of encorafenib in combination with cetuximab and mFOLFOX6 (fluorouracil, leucovorin and oxaliplatin) in patients with metastatic colorectal cancer (mCRC) harboring a *BRAF V600E* mutation. The trial showed a statistically significant and clinically meaningful improvement in PFS, one of its dual primary endpoints, as assessed by blinded independent central review (BICR) compared to patients receiving chemotherapy with or without bevacizumab. Further, the encorafenib combination regimen demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS), a key secondary endpoint in the trial.

'We are extremely pleased with the clinically meaningful progression-free survival and overall survival results from the BREAKWATER study, which have the potential to be practice-changing for this patient population that has historically had limited treatment options and poor outcomes,' said [the company's chief oncology officer]. 'The encorafenib regimen is emerging as a new standard of care as the first targeted therapy approved for use as early as first-line for patients with mCRC with a *BRAF V600E* mutation. We look forward to discussing these data with global health authorities to bring this treatment to more patients around the world, as soon as possible.'"

https://www.pfizer.com/news/press-release/press-release-detail/pfizers-braftovir-combination-regimen-significantly

EC+FOLFOX is the new standard of care for first-line $BRAF^{V600E}$ CRC

Results appear synergistic and may follow improved understanding of tumor plasticity

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

RTP Year in Review 2025

Discussion Questions:
Cell-Free DNA MRD Assays in Clinical Practice

- **How would you capsulize the current available data with cell-free DNA in the adjuvant setting? If cell-free DNA is evaluated, when should the assay be ordered? What is your global conclusion on the clinical relevance? (Other issues: CALGB/SWOG-80702 trial – celecoxib and ctDNA)**

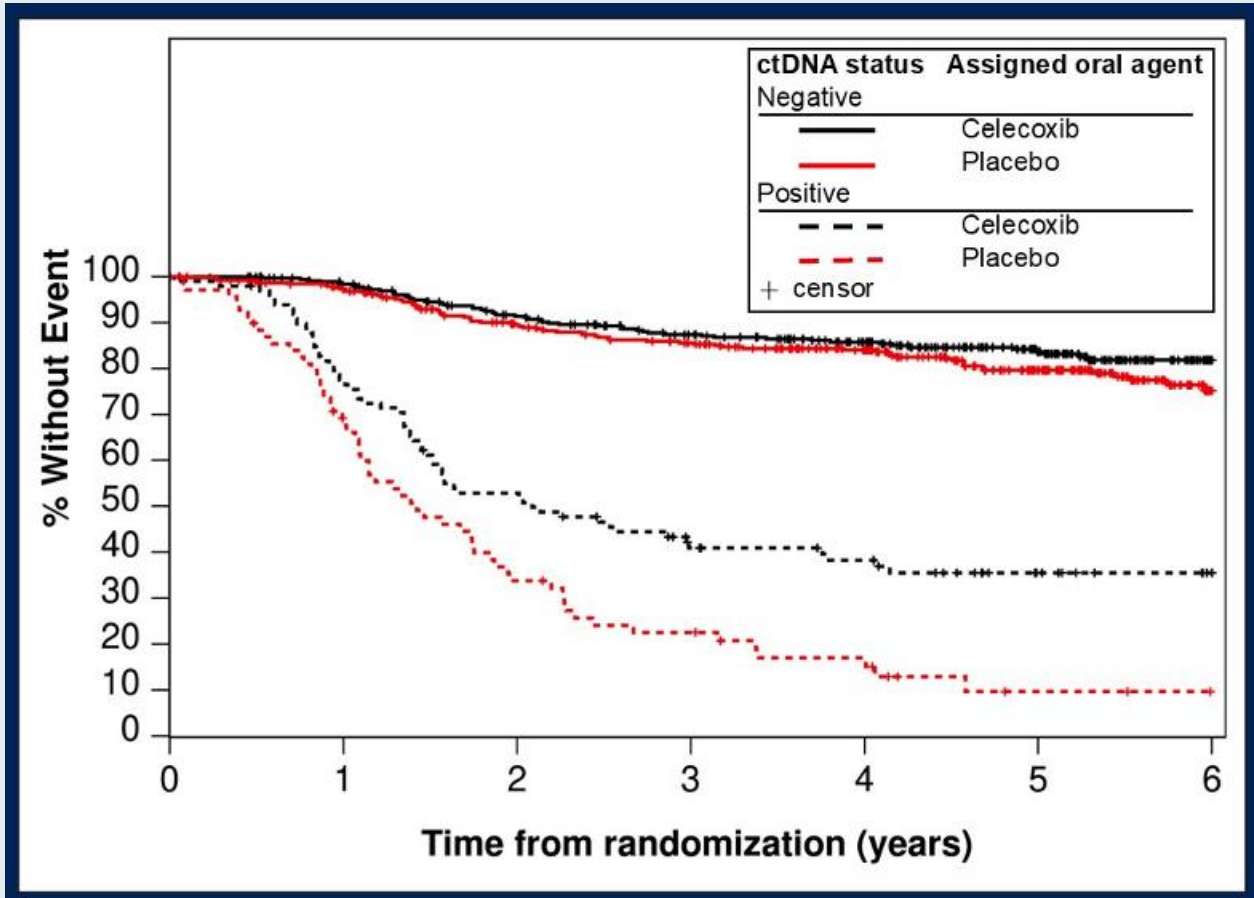
ASCO Gastrointestinal Cancers Symposium 2025

Prognostic and predictive role of circulating tumor DNA (ctDNA) in stage III colon cancer treated with celecoxib: Findings from CALGB (Alliance)/SWOG 80702

Jonathan A. Nowak, Qian Shi, Tyler Twombly, Levi Pederson, Chao Ma, Juha P. Väyrynen, Melissa Zhao, Yasutoshi Takashima, Ardaman Shergill, Pankaj Kumar, Felix Couture, Philip Kuebler, Smitha Krishnamurthi, Benjamin Tan, Eileen M. O'Reilly, Anthony F. Shields, Shuji Ogino, Alexey Aleshin, and Jeffrey A. Meyerhardt

Abstract LBA14

CALGB/SWOG-80702 Trial: Disease-Free Survival by ctDNA Status and Celecoxib Use

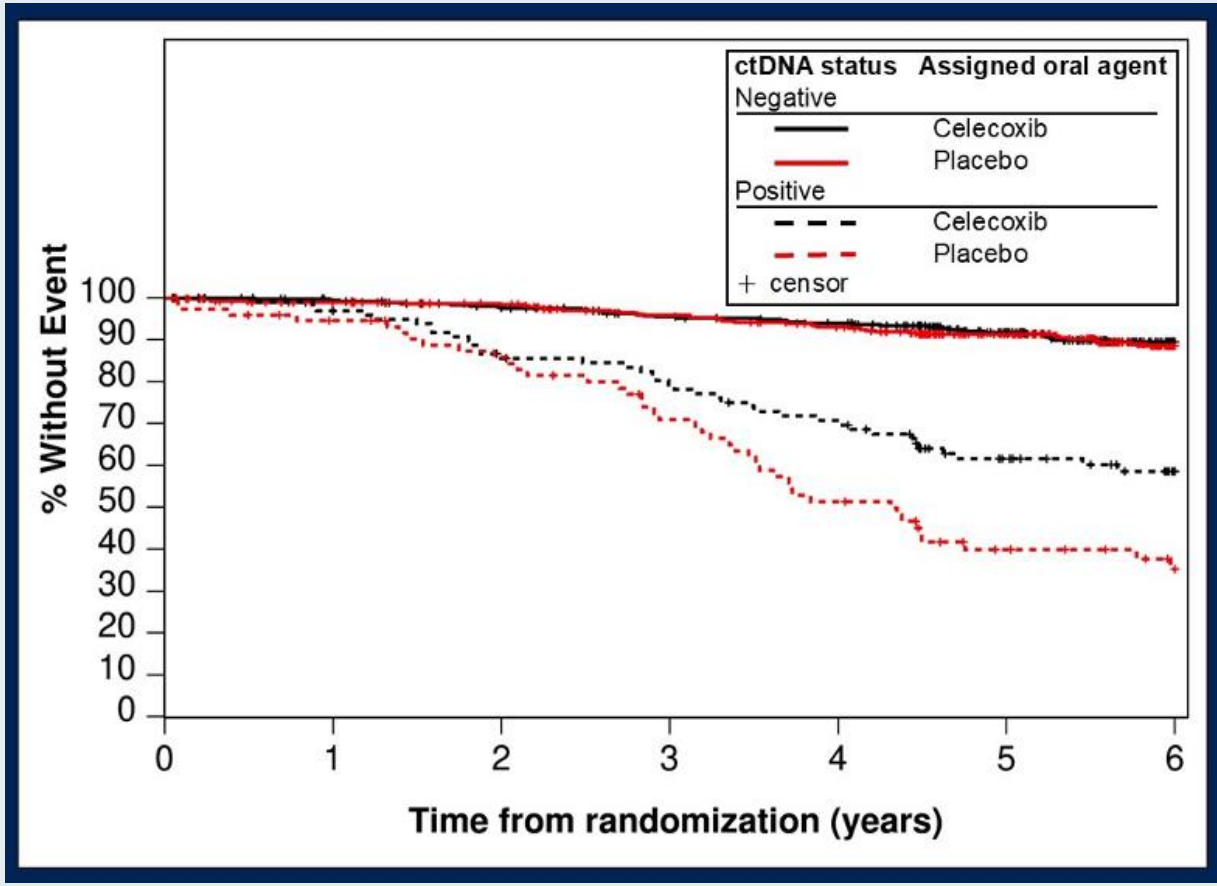


Assigned Oral Agent by ctDNA status	Events / Total	Hazard Ratio (95% CI)[1]	3 Year Survival Estimate (95% CI)[2]	P-value
Negative				0.1293[4]
Celecoxib	58/375	0.76 (0.54-1.08)	87.4 (84.0-91.0%)	
Placebo	73/392	Reference	85.6 (82.0-89.4%)	
Positive				0.0013[4]
Celecoxib	61/99	0.55 (0.39-0.80)	41.0 (32.2-52.2%)	
Placebo	57/74	Reference	22.6 (14.3-35.5%)	
Interaction P-value: 0.1359[3]				

[1] Unadjusted Cox model, [2] Kaplan-Meier method, [3] Likelihood-ratio test, [4] Log-rank test

Nowak JA et al. Gastrointesinal Cancers Symposium 2025;Abstract LBA14.

CALGB/SWOG-80702: Overall Survival by ctDNA Status and Celecoxib Use



Assigned Oral Agent by ctDNA status	Events / Total	Hazard Ratio (95% CI)[1]	5 Year Survival Estimate (95% CI)[2]	P-value
Negative				0.5098[4]
Celecoxib	36/375	0.86 (0.55-1.35)	91.8 (88.9-94.7%)	
Placebo	41/392	Reference	91.3 (88.4-94.3%)	
Positive				0.0135[4]
Celecoxib	41/99	0.58 (0.38-0.90)	61.6 (52.4-72.4%)	
Placebo	44/74	Reference	39.9 (29.6-53.8%)	
Interaction P-value: 0.2061[3]				

[1] Unadjusted Cox model, [2] Kaplan-Meier method, [3] Likelihood-ratio test, [4] Log-rank test

Nowak JA et al. Gastrointesinal Cancers Symposium 2025;Abstract LBA14.

CALGB/SWOG-80702: Celecoxib and ctDNA

- ctDNA is highly prognostic
- Celecoxib seemed to benefit patients with ctDNA-positive status, but the interaction *p*-value was not significant
- Benefit was observed for patients with PIK3CA wild-type and mutated tumors
- Data are suggestive but not definitive for using celecoxib when ctDNA-positive

Discussion Questions:
Cell-Free DNA MRD Assays in Clinical Practice

- **Should all patients with localized CRC undergo cell-free DNA testing?**
- **How, if at all, do you currently use this strategy in the adjuvant setting outside of a clinical trial protocol? Treatment escalation and/or de-escalation? If you opt to not order a cell-free DNA assay but another clinician does, do you consider the results when deciding on treatment?**

Stage II/III BESPOKE CRC Study

- ctDNA positivity is highly predictive of outcome – both immediately after surgery (MRD) and during surveillance
- ctDNA MRD influences 16.3% of decisions on adjuvant therapy – 60% de-escalated and 36% escalated
- ctDNA clearance is associated with improved outcomes (HR 0.43)
- ctDNA MRD (+) had superior DFS (HR 0.48) with adjuvant therapy compared to observation; ctDNA MRD (-) did not have significant benefit (HR 0.93) for adjuvant therapy compared to observation
- This is an observational study – not randomized and decision for therapy not controlled and likely confounded

DYNAMIC Trial: Stage II Colon Cancer

- Noninferiority of standard (non-ctDNA approach) to ctDNA-guided management can be interpreted either as checking MRD does not change outcome or as checking MRD reduces the use of chemotherapy among patients with Stage II disease
- Fewer patients on ctDNA-guided management received chemotherapy (15% vs 28%), but more received oxaliplatin (9.5% vs 2.7%)
- Median time from surgery to start of therapy increased by 30 days with ctDNA-guided management (53 vs 83 days)

Discussion Questions:
Cell-Free DNA MRD Assays in Clinical Practice

- **Beyond localized disease, in what clinical settings do you currently order a cell-free DNA assay? Surgically resectable liver metastases? Other sites of metastatic disease? Determining duration of immunotherapy for MSI-high CRC?**
- **Which ongoing trials will be most helpful in further delineating the clinical application of cell-free DNA assays (eg, NRG-GI008/CIRCULATE-North America)?**

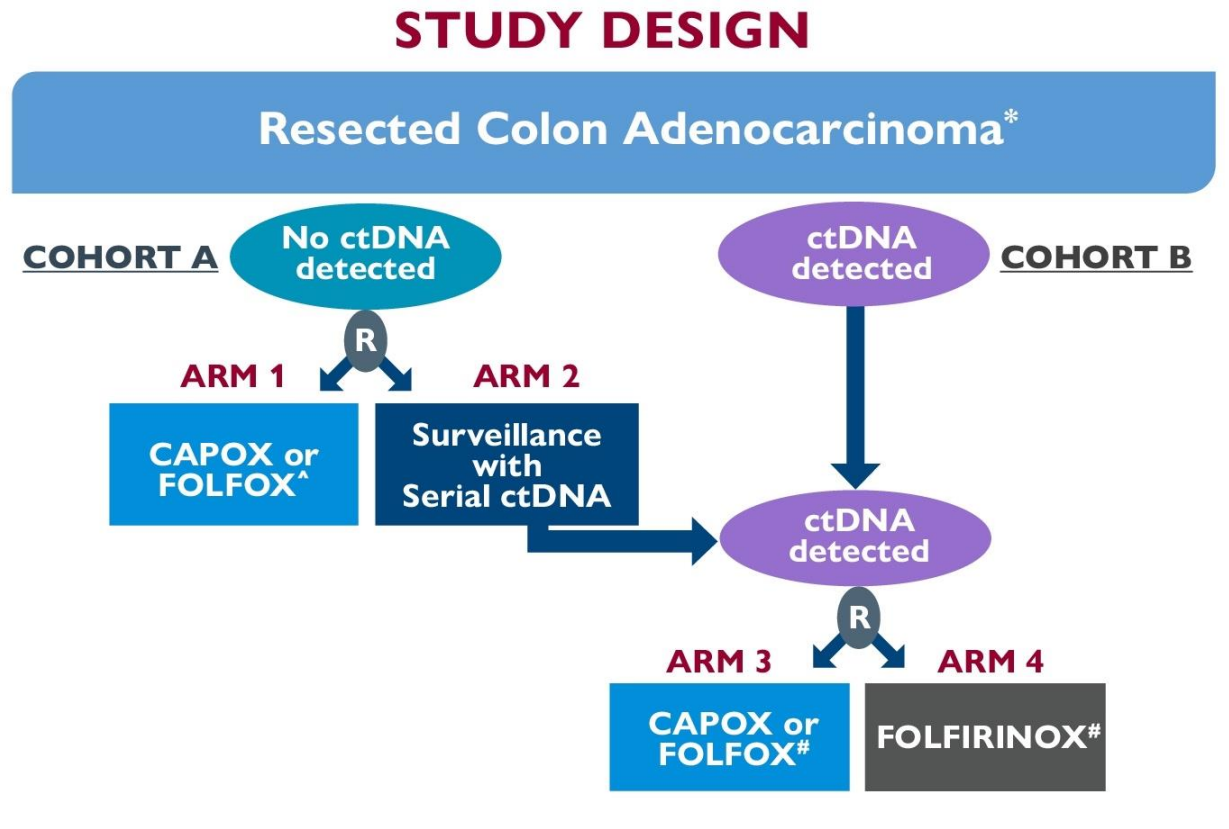
NRG-GI008: Colon adjuvant chemotherapy based on evaluation of residual disease (CIRCULATE-NORTH AMERICA).

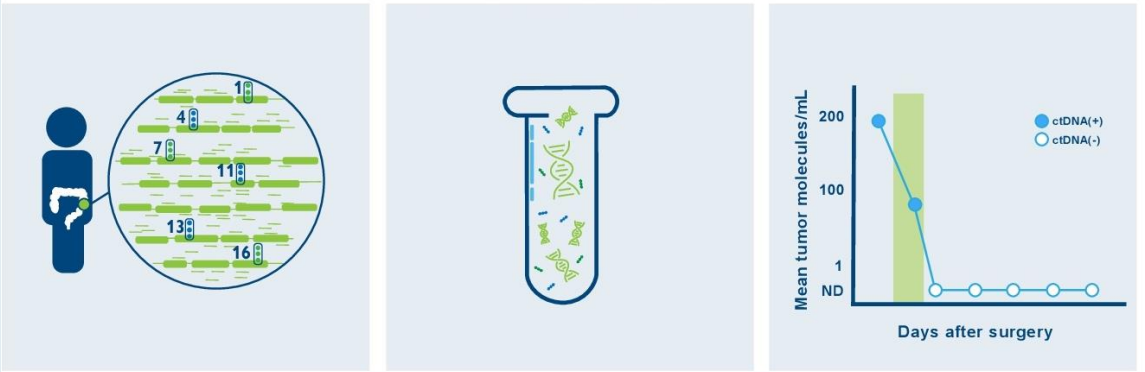
Christopher Hanyoung Lieu
University of Colorado Cancer Center, Aurora, CO

Christopher Hanyoung Lieu , Guan Yu , Scott Kopetz , Shannon L. Puhalla , Peter C. Lucas , Ibrahim Halil Sahin , Dustin A. Deming , Philip A. Philip , Theodore S. Hong , Yesenia Rojas-Khalil , Jonathan M. Loree , Norman Wolmark , Greg Yothers , Thomas J. George , Arvind Dasari

Gastrointestinal Cancers Symposium 2024;Abstract TPS243.

Phase II/III NRG-GI008 Study Design and ctDNA Testing





- Whole exome sequencing of matched tumor and normal blood samples to identify clonal tumor-specific single nucleotide variants (SNV) while excluding clonal hematopoiesis of indeterminate potential.
- Personalized PCR primers targeting SNVs used for testing for ctDNA in plasma samples via barcoded sequencing methods at baseline and serially during surveillance.
- Test positive if ≥2 SNVs above threshold and reported as positive / negative plus mean tumor molecules / mL plasma.

Primary endpoints **(cohort A, ctDNA-)**:

- Time to ctDNA-positive status (Phase II)
- Disease-free survival (Phase III)

Primary endpoint **(cohort B, ctDNA+)**:

- Disease-free survival (Phase II/III)

Lieu CH et al. Gastrointestinal Cancers Symposium 2024;Abstract TPS243.

Phase II/III NRG-GI008 — CIRCULATE-North America

- As of February 2025, ~1/3 accrued
- Stage IIB, IIC and III, microsatellite stable, colon only
- Several questions are addressed in this trial:
  - To compare disease-free survival (DFS) in the ctDNA(-) cohort after resection of colon cancer treated with immediate versus delayed chemotherapy (based on serial ctDNA surveillance)
  - To compare DFS in the ctDNA(+) cohort after resection of colon cancer treated with FOLFOX versus FOLFIRINOX

CIRCULATE-Japan GALAXY CRC Study

- In this expanded cohort of 2,240 patients with Stage I to IV colorectal cancer, a majority of the cohort did not receive chemotherapy
- ctDNA MRD highly prognostic of outcome
- Clearance also prognostic – 181 ctDNA(+) received adjuvant therapy – 38% sustained clearance, 31% transient clearance, 31% no clearance
- Observational study – decision on who received chemotherapy and who did not likely confounded by other factors

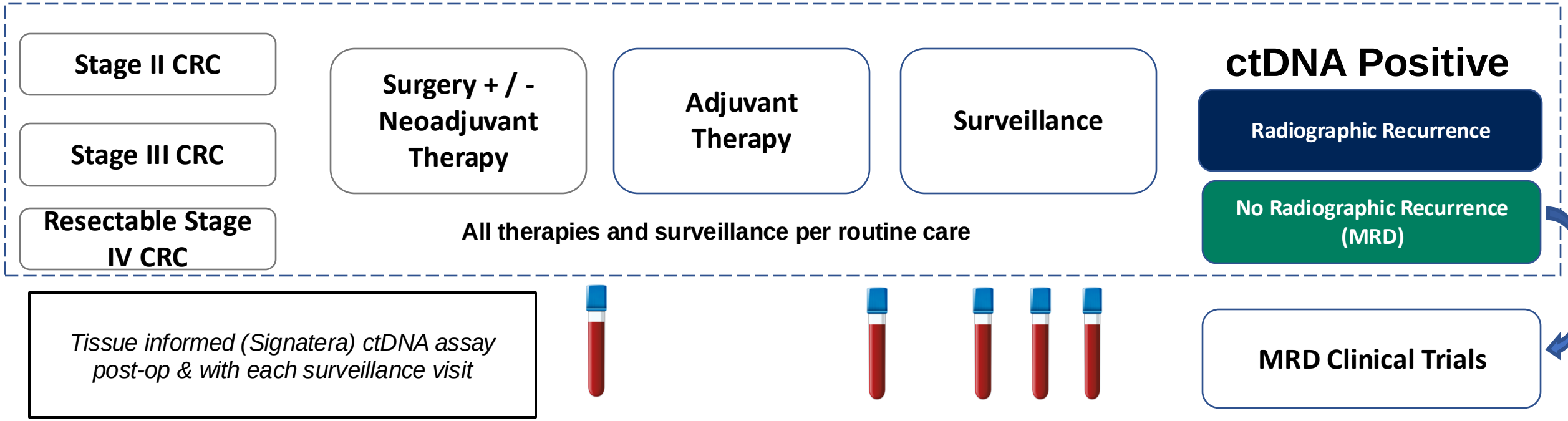
CIRCULATE-Japan GALAXY Resected Liver Met Subset

- 190 patients with surgically resected colorectal liver metastases without any preoperative chemotherapy were included
- 32% MRD-positive; only 25% received adjuvant chemotherapy
- MRD-negative not statistically different between chemotherapy and observation but absolute 10% difference at 2 years
- Observational and small numbers

Discussion Question:
Cell-Free DNA MRD Assays in Clinical Practice

- **What is the future clinical relevance of the INTERCEPT basket trial evaluating cell-free DNA-positive CRC (personalized mRNA vaccines, immunotherapy, BRAF V600E mutation-positive disease, etc)?**

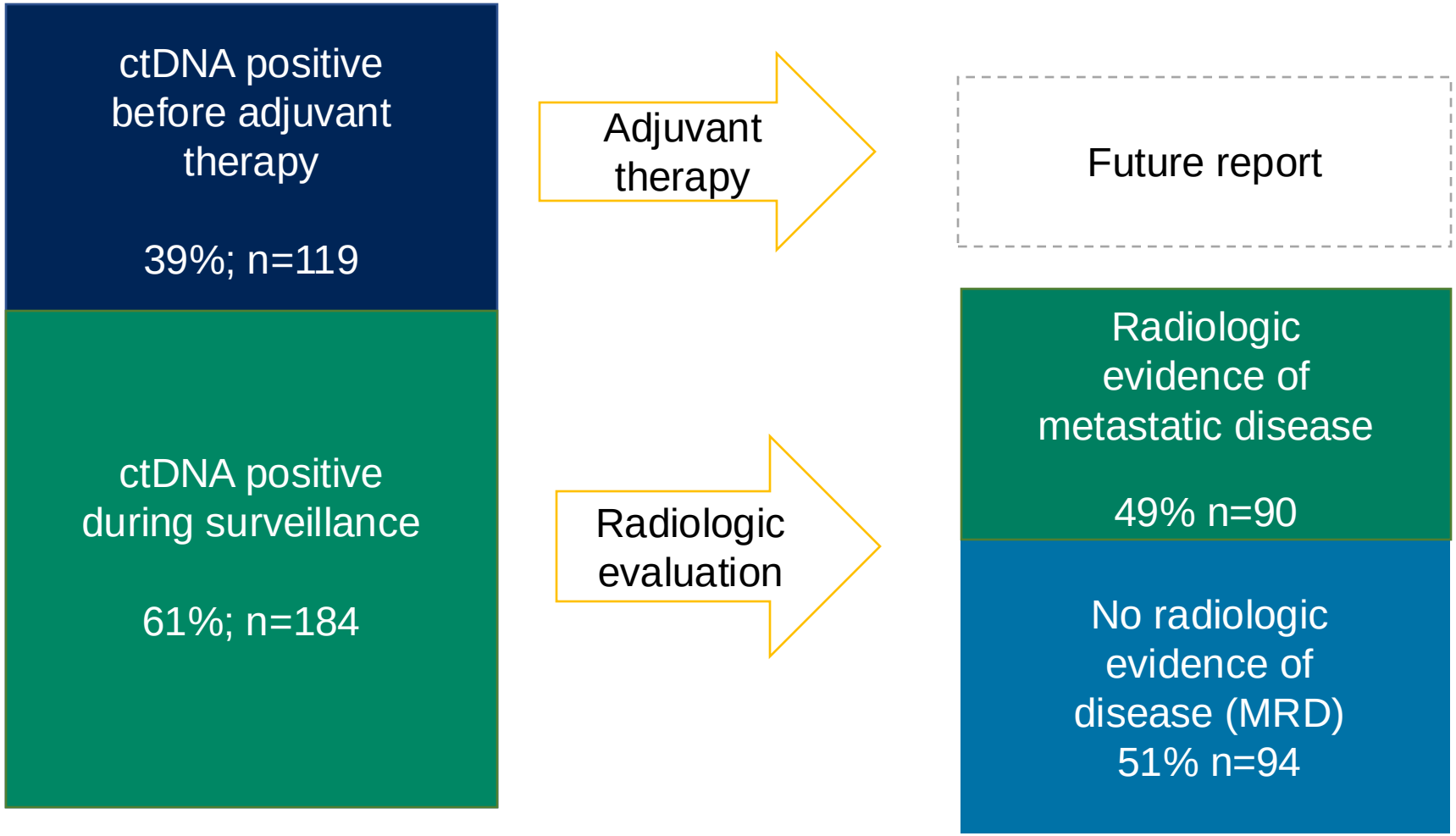
INTERCEPT Study: Positive ctDNA-based Minimal Residual Disease Assays During Surveillance Are Associated with High Rates of Undiagnosed Concomitant Radiographic Recurrences in Colorectal Cancer (CRC)



1,115 patients stages II-IV
Signatera, Natera, Inc (tumor informed) assay used

Dasari et al, ASCO 2023

Clinical Utility: Radiographic Findings of Patients ctDNA+ During Surveillance, n = 184



Dasari et al, ASCO 2023

Clinical Utility: Enrollment onto MRD Trials

Future report on recurrence patterns & outcomes

ctDNA positive during surveillance

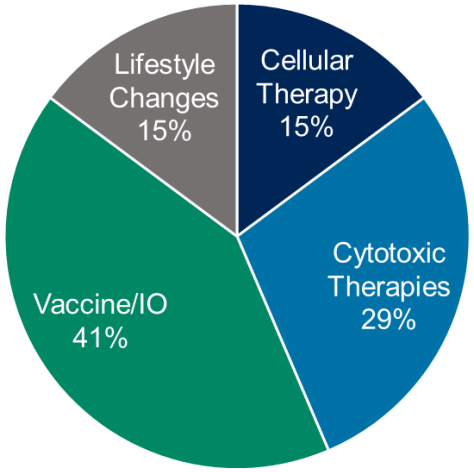
61%; n=184

Radiologic evidence of metastatic disease 49% n=90

No radiologic evidence of disease (MRD) 51% n=94

Enrolled into clinical trials of MRD

59% N=55



Dasari et al, ASCO 2023

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

Discussion Questions: Immunotherapy for Localized and Metastatic MSI-High CRC

- What are the pitfalls, if any, in MSI testing? How frequently do false-positive results occur and what is the cause of these results?
- In what clinical situations should immunotherapy be administered as initial treatment for patients with localized MSI-high CRC? Which immunotherapy should be used and for how long in this setting? When should patients undergo surgery and/or other local therapy relative to receiving immunotherapy?

Discussion Question: Immunotherapy for Localized and Metastatic MSI-High CRC

- **Based on the data from the NICHE-1 and NICHE-2 studies in addition to the results with dostarlimab as neoadjuvant treatment for rectal cancer, should MSI testing be conducted for all patients with localized CRC prior to initiating treatment?**

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2024 VOL. 390 NO. 21

Neoadjuvant Immunotherapy in Locally Advanced Mismatch Repair–Deficient Colon Cancer

Myriam Chalabi, M.D., Ph.D., Yara L. Verschoor, M.D., Pedro Batista Tan, M.Sc., Sara Balduzzi, Ph.D., Anja U. Van Lent, M.D., Ph.D., Cecile Grootscholten, M.D., Ph.D., Simone Dokter, M.Sc., Nikè V. Büller, M.D., Ph.D., Brechtje A. Grotenhuis, M.D., Ph.D., Koert Kuhlmann, M.D., Ph.D., Jacobus W. Burger, M.D., Ph.D., Inge L. Huibregtse, M.D., Ph.D., Tjeerd S. Aukema, M.D., Ph.D., Eduard R. Hendriks, M.D., Steven J. Oosterling, M.D., Ph.D., Petur Snaebjornsson, M.D., Ph.D., Emile E. Voest, M.D., Ph.D., Lodewyk F. Wessels, Ph.D., Regina G. Beets-Tan, M.D., Ph.D., Monique E. Van Leerdam, M.D., Ph.D., Ton N. Schumacher, Ph.D., José G. van den Berg, M.D., Ph.D., Geerard L. Beets, M.D., Ph.D., and John B. Haanen, M.D., Ph.D.

BARCELONA 2024 ESMO congress

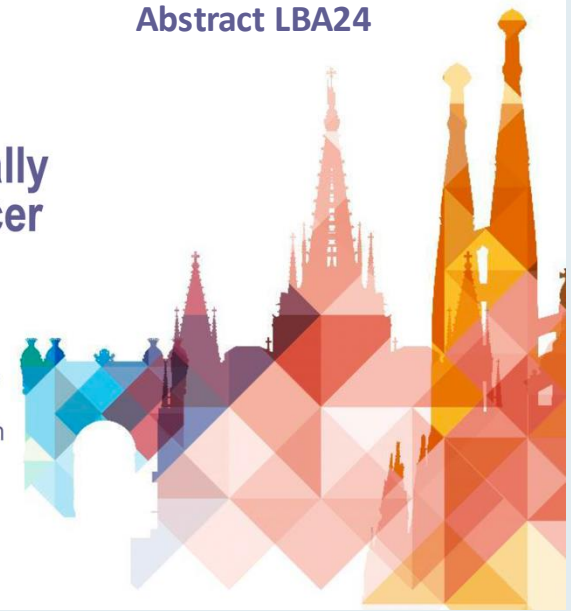
Abstract LBA24

Neoadjuvant immunotherapy in locally advanced MMR-deficient colon cancer

3-year disease-free survival from NICHE-2

M. Chalabi[1], L. van den Dungen, Y. Verschoor, S. Balduzzi, P. de Gooyer, N. Kok, E. Kerver, C. Grootscholten, E. Voest, J. Burger, E. Hendriks, T. de Wijkerslooth, A. Tin, T. Aukema, S. Oosterling, A. Aalbers, J. van den Berg, M. Van Leerdam, T. Schumacher, J. Haanen

[1]Netherlands Cancer Institute, Amsterdam

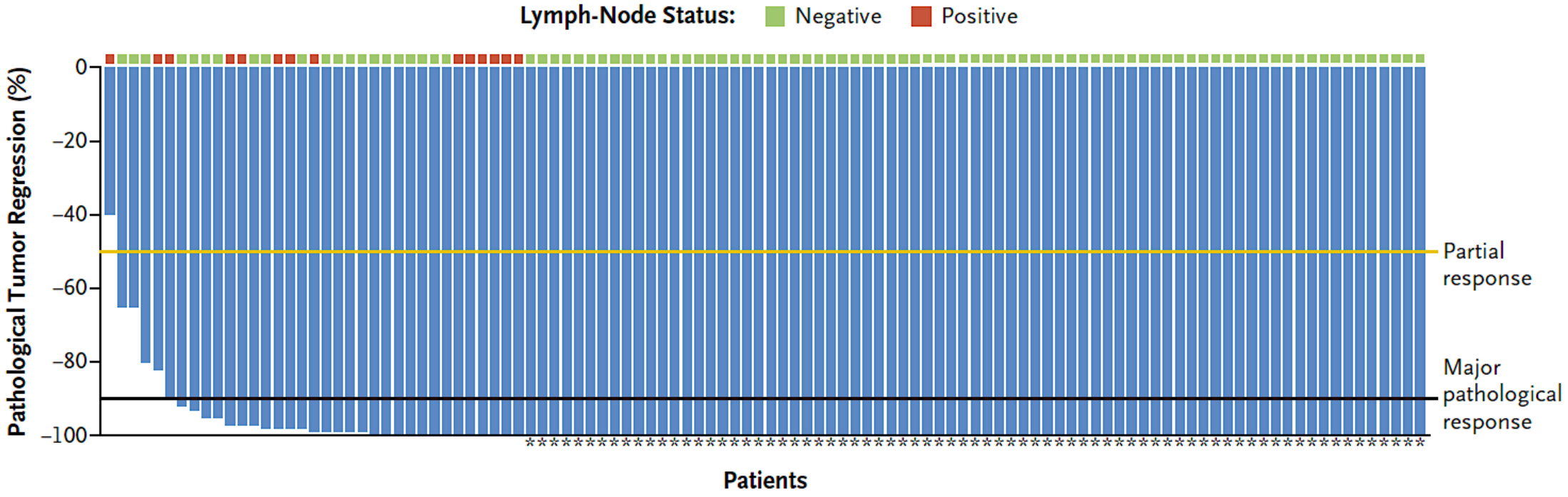


RTP Year in Review 2025

NICHE-2 Trial: Pathologic Response

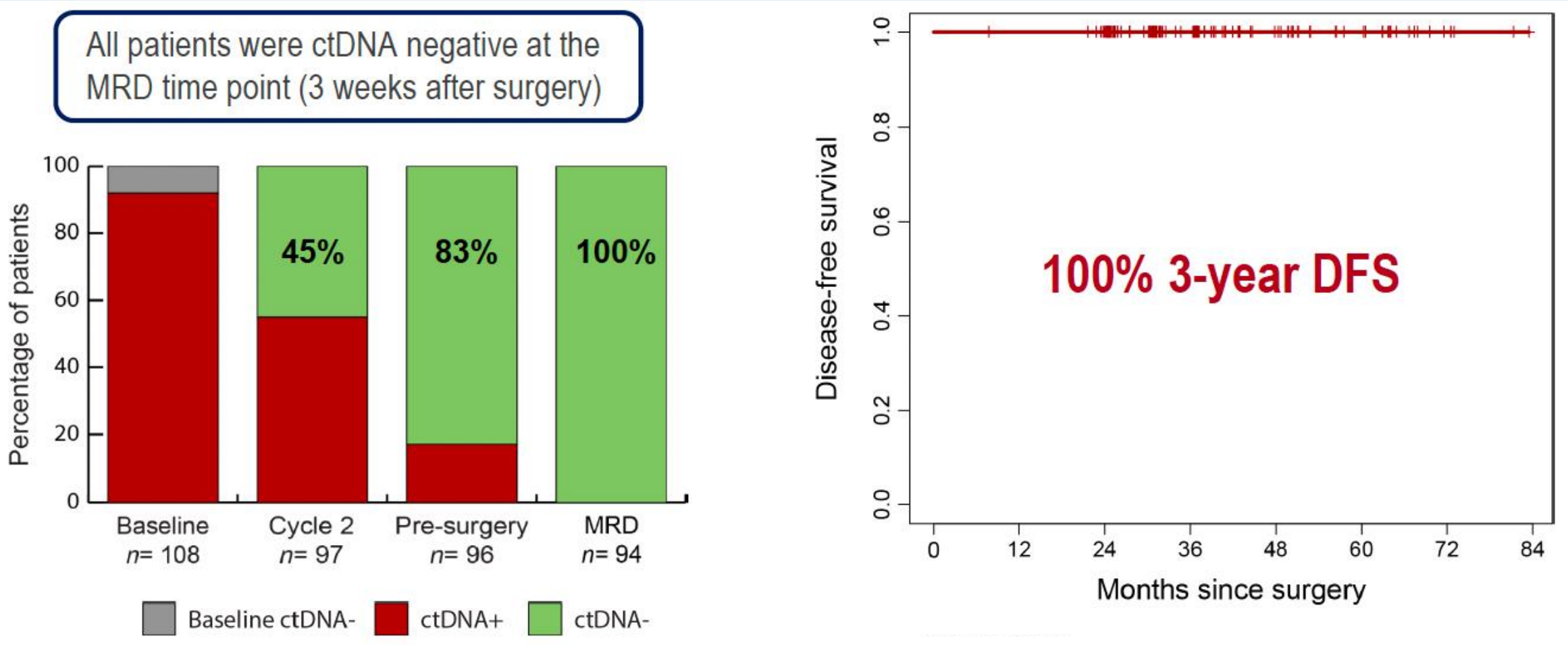
Pathologic response in **98%** of 111 patients in efficacy analysis

- Major pathologic response (≤10% residual viable tumor): **95%**
- Pathologic complete response: **68%**



Chalabi M et al. *N Engl J Med* 2024 June 6;390(21):1949-58; ESMO 2024;Abstract LBA24.

NICHE-2: Minimal Residual Disease (MRD)



Chalabi M et al. ESMO 2024;Abstract LBA24.

NICHE-2: Author Conclusions and Future Perspectives

Unprecedented 3-year DFS of 100% in patients with high-risk, locally advanced dMMR colon cancer with only two cycles of neoadjuvant immunotherapy

All patients were ctDNA negative at MRD time point, in line with 0% recurrences

Association of (early) clearance with pCR: ctDNA may aid in organ preservation

Collaboration between regulatory authorities, pharmaceutical companies and academic researchers is essential to bring this highly effective treatment to patients

dMMR = mismatch repair deficient; pCR = pathologic complete response

Chalabi M et al. ESMO 2024;Abstract LBA24.

NICHE-1 and NICHE-2 Studies in Colon Cancer

- Patients received 2 doses of nivolumab and 1 dose of ipilimumab
- Only 2.7% received chemotherapy after surgery (3/14 with positive nodes – 1 had 60% residual tumor in specimen)
- Very few patients had delay of surgery beyond 6 weeks from study enrollment
- Radiographic response only seen in 2 of 75 with pCR
- Identifying the patients (both stages – NICHE-2 was limited to clinical Stage II and III) and MMR status is the challenge to implementation
- Difference in response and duration of response for localized disease compared to metastatic disease (71% PFS at 2 years with combination in mCRC)

Abstract LBA3512

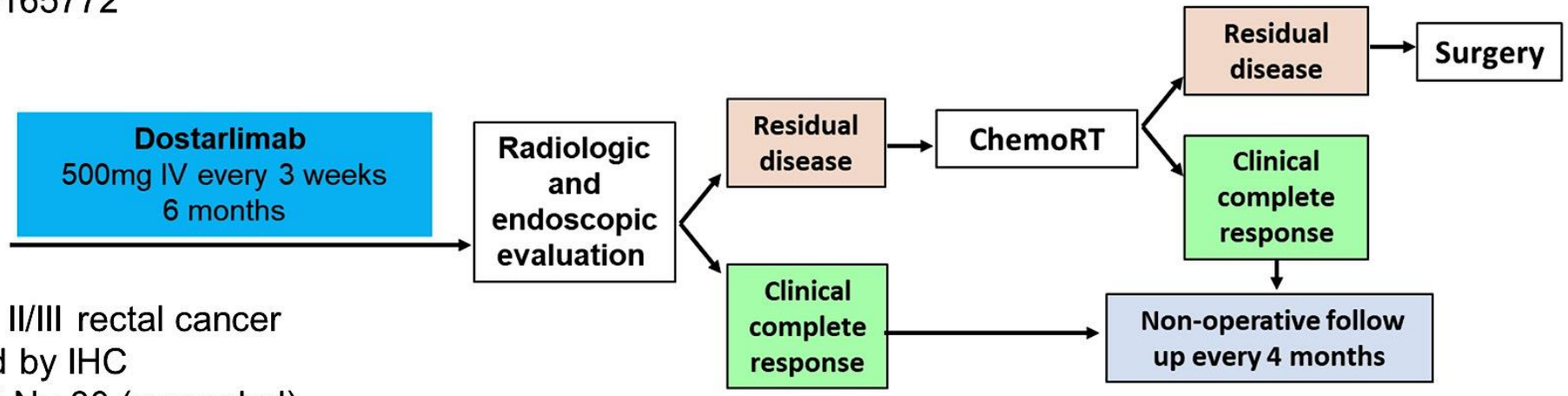
2024 ASCO ANNUAL MEETING

Durable complete responses to PD-1 blockade alone in dMMR locally advanced rectal cancer

Andrea Cercek, M.D. , J. Joshua Smith, M.D., Ph.D. , Jinru Shia, M.D., Michael B. Foote, M.D., Jenna Sinoploi, N.P. Jill Weiss, B.A., Lindsay Temple, B.A., Henry Walch, M.S. , Miteshkumar Patel, M.S., Callahan Wilde, B.S., Leonard B. Saltz, M.D., Melissa Lumish, M.D., Benoit Rousseau, M.D., Ph.D., Guillem Argiles, M.D. , Zsofia Stadler, M.D. , Rona Yaeger, M.D. , Neil Segal, M.D., Philip Paty M.D., Marina Shcherba, M.D., Ryan Sugarman, M.D., Christopher Crane, M.D., Paul B. Romesser, M.D., Avni Desai, M.D., Imane El Dika, M.D., Maria Widmar, M.D., Iris Wei, M.D., Emmanouil Pappou, M.D., Ph.D., Gerard Fumo, M.D., Santiago Aparo, M.D., Mithat Gonen, M.D., Marc Gollub, M.D., Vetri S. Jayaprakasham, M.B.B.S., F.R.C.R., Tae-Hyung Kim, M.D., Julio Garcia Aguilar, M.D., Ph.D., Martin Weiser, M.D., and Luis A. Diaz, Jr., M.D.

Neoadjuvant PD-1 blockade in dMMR locally advanced rectal cancer

NCT04165772



Stage II/III rectal cancer
MMRd by IHC
Target N= 30 (expanded)

Primary Endpoints:

- ORR after completion of PD-1 alone or in combination with chemoRT
- pCR or sustained cCR for 12 mo after completion of PD-1 alone or in combination with chemoRT

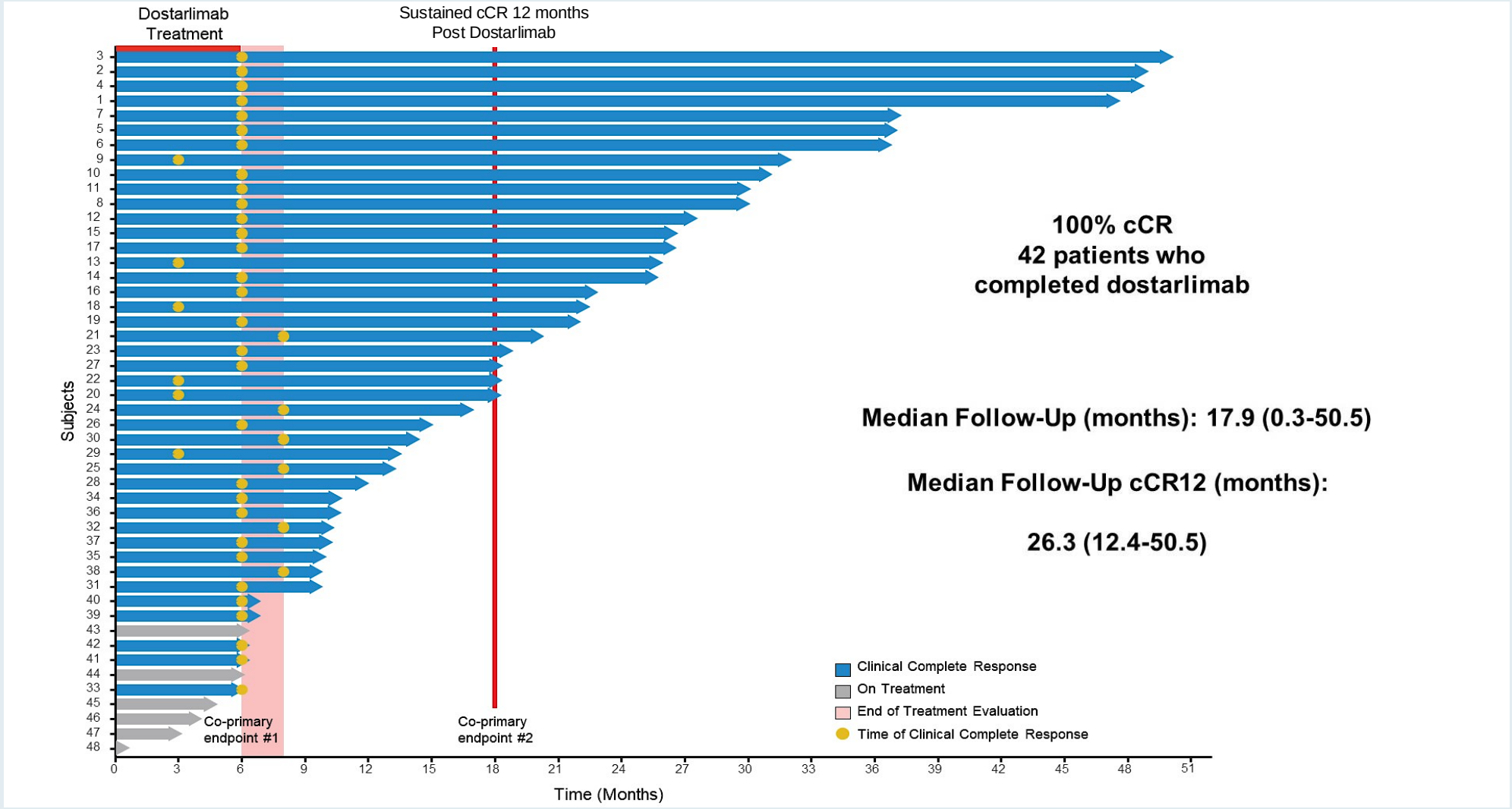
Sample Collection: ctDNA, biopsy, imaging

Baseline, 6 weeks, 3 mo, 6 mo and q4 mo during NOM

Cercek, et al. NEJM 2022

Cercek A et al. ASCO 2024;Abstract LBA3512.

Dostarlimab: Clinical Complete Response (cCR) Rates After PD-1 Blockade



Cercek A et al. ASCO 2024;Abstract LBA3512.

Neoadjuvant Therapy for MSI-H Rectal Cancer

- 5% to 10% of rectal cancers are microsatellite instability high (MSI-H)
- To date, no patient has received standard chemotherapy, radiation or surgery
- Sample size is still modest, but it is continuing to hold up
- Is this applicable to all checkpoint inhibitors? How many doses are needed? Will there be late recurrences?

Key Ongoing Studies of (Neo)Adjuvant Dostarlimab for Patients with Resectable MSI-H/dMMR CRC

Study	N	Phase	Eligibility	Randomization	Estimated primary completion
China AZUR-1 (NCT06640049)	23	II	Stage II-III dMMR rectal adenocarcinoma	• Dostarlimab	December 2028
AZUR-2 (NCT05855200)	711	III	T4N0 or Stage III dMMR colon adenocarcinoma	• Dostarlimab • Standard of care – CAPOX or FOLFOX	December 2028
AZUR-4 (NCT06567782)	120	II	T4N0 or Stage III dMMR colon adenocarcinoma	• Dostarlimab • CAPOX	September 2028
NAIO (NCT05239546)	25	II	Stage II-III dMMR CRC	• Dostarlimab	April 2026

www.clinicaltrials.gov. Accessed February 2025.15

Discussion Questions: Immunotherapy for Localized and Metastatic MSI-High CRC

- **What is the optimal first-line treatment for metastatic MSI-high CRC? What is the ideal duration of immunotherapy in this setting? For which patients should dual immunotherapy be considered (eg, as in the CheckMate 8HW trial)?**

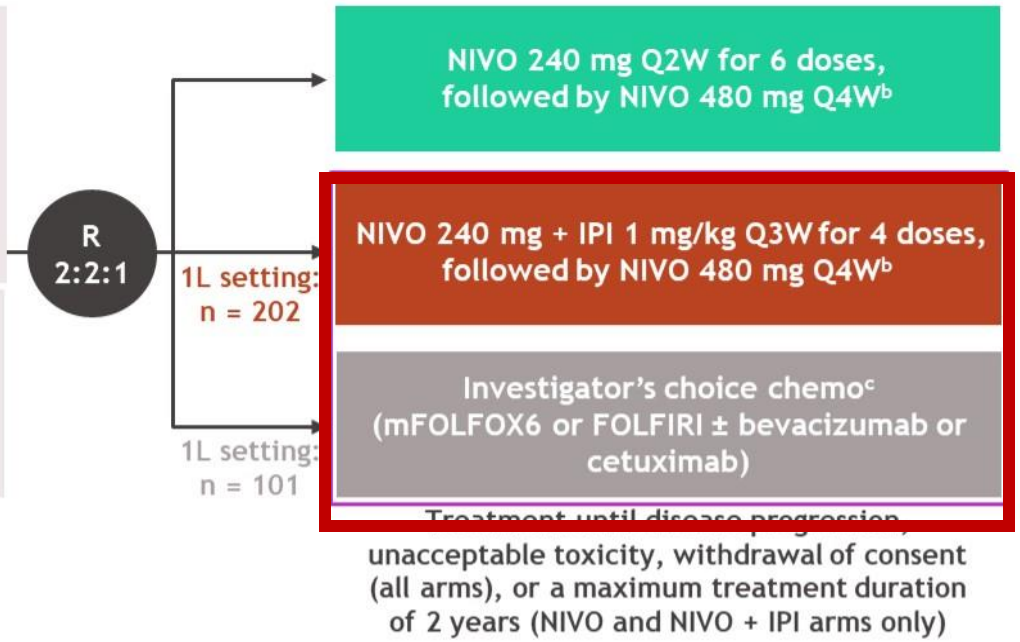
CheckMate 8HW study design

- CheckMate 8HW is a randomized, multicenter, open-label phase 3 study[a]

16% of pts not MSI-H confirmed

Key eligibility criteria:
- Histologically confirmed unresectable or metastatic CRC
- MSI-H/dMMR status by local testing
- ECOG PS 0 or 1

Stratification factors:
- Prior lines of treatment (0 vs 1 vs ≥ 2)
- Primary tumor location (right vs left)



Dual primary endpoints in patients with centrally confirmed MSI-H/dMMR status[d]:
- PFS by BICR[e] (NIVO + IPI vs chemo in the 1L setting)
- PFS by BICR[e] (NIVO + IPI vs NIVO across all lines)

Other select endpoints:
- Safety
- OS; ORR by BICR[e]; PROs

- At data cutoff (October 12, 2023), the median follow-up[f] was 24.3 months

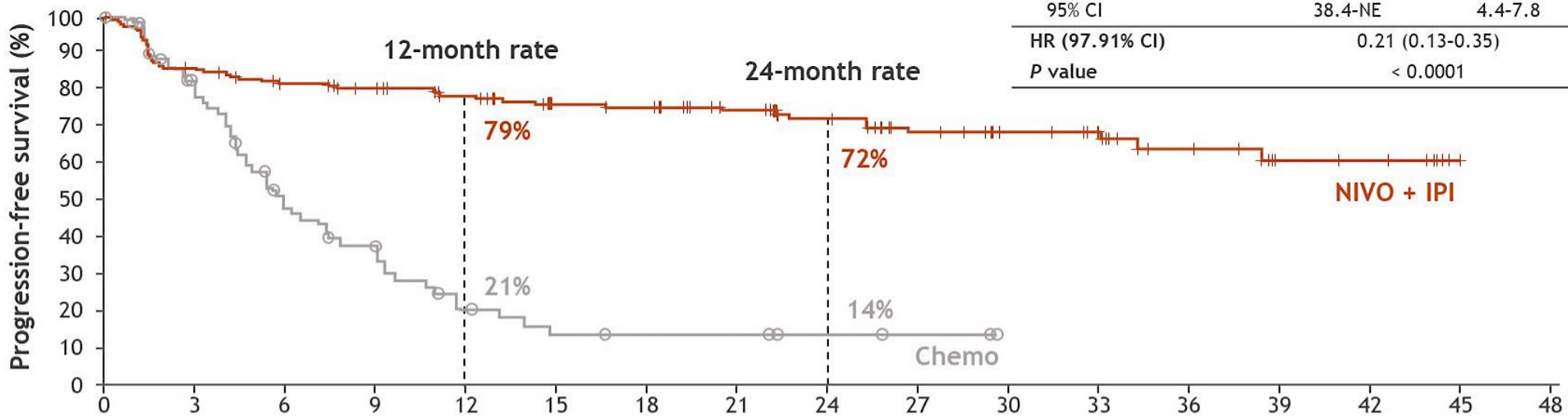
[a]ClinicalTrials.gov. NCT04008030. [b]Patients with ≥ 2 prior lines are randomized only to the NIVO or NIVO + IPI arms. [c]Patients receiving investigator's choice of chemotherapy are eligible to receive NIVO + IPI upon progression (crossover treatment). [d]Confirmed using either immunohistochemistry and/or polymerase chain reaction-based tests. [e]Evaluated using RECIST v1.1. [f]Time between randomization and last known date alive or death.

Courtesy of Scott Kopetz, MD, PhD

Lenz et al. ASCO 2024; Andre et al. GI ASCO 2024

CheckMate 8HW: Progression-Free Survival with Nivo/Ipi versus Chemotherapy

1L centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 171)	Chemo (n = 84)
Median PFS,[a,b] mo	NR	5.9
95% CI	38.4-NE	4.4-7.8
HR (97.91% CI)	0.21 (0.13-0.35)	
P value	< 0.0001	



No. at risk

NIVO + IPI	171	144	132	122	108	95	92	77	64	53	42	37	22	10	9	1	0
Chemo	84	53	29	20	10	6	5	5	3	2	0	0	0	0	0	0	0

Safety (1L; All Treated), n (%)	NIVO + IPI (n = 200)	Chemo (n = 88)
Any grade/grade 3–4 TRAEs	160 (80)/46 (23)	83 (94)/42 (48)
Any grade/grade 3–4 serious TRAEs	38 (19)/32 (16)	17 (19)/14 (16)
Any grade/grade 3–4 TRAEs leading to discontinuation	33 (17)/23 (12)	28 (32)/9 (10)
Treatment-related deaths	2 (1)	0 (0)[a]

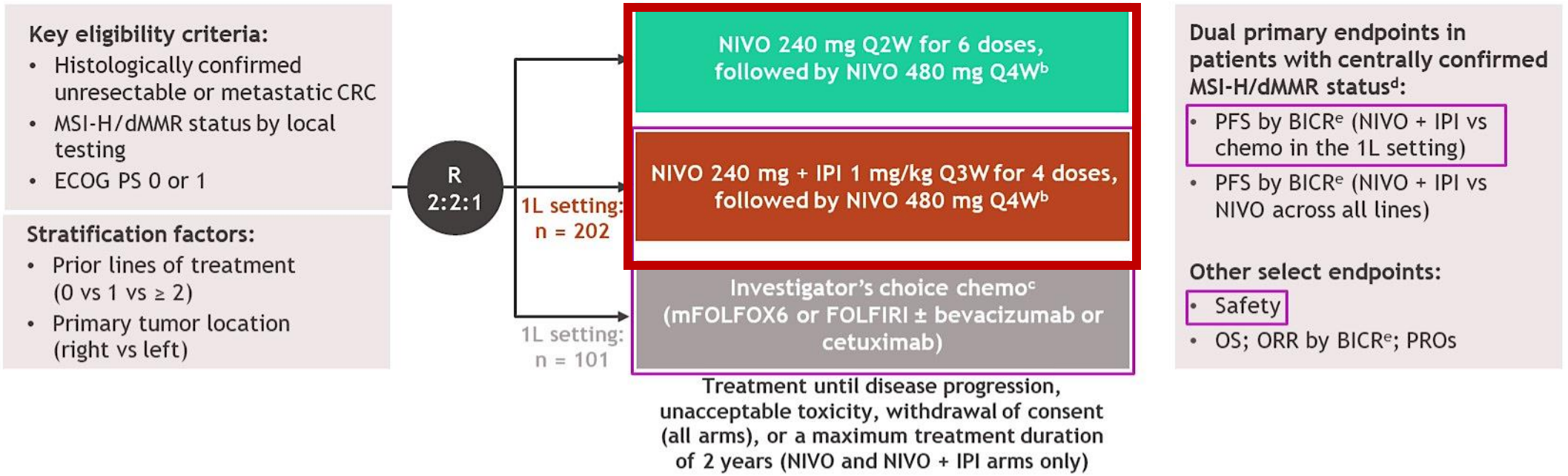
Myocarditis and pneumonitis

Andre T et al. *N Engl J Med* 2024 Nov 28;391(21):2014-2026; Lenz et al. ASCO 2024.

Courtesy of Scott Kopetz, MD, PhD

CheckMate 8HW study design

- CheckMate 8HW is a randomized, multicenter, open-label phase 3 study[a]

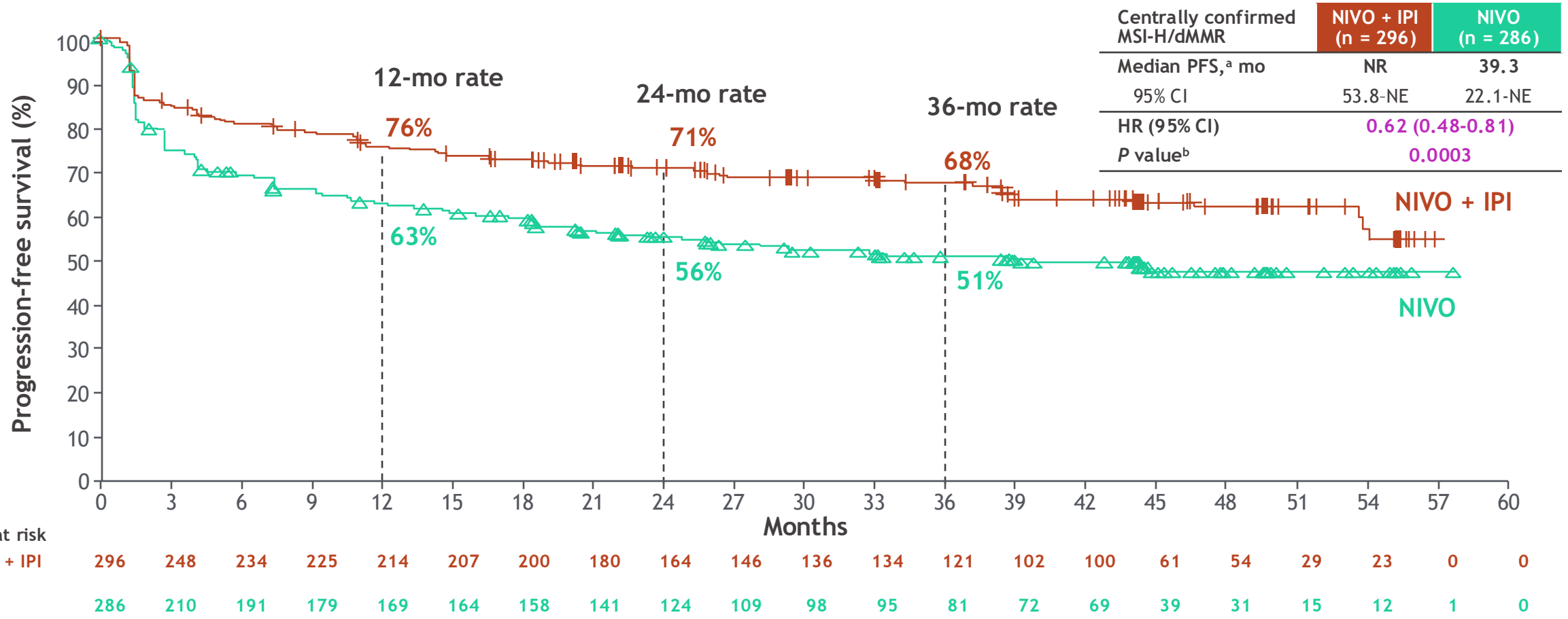


- At data cutoff (October 12, 2023), the median follow-up[f] was 24.3 months

[a]ClinicalTrials.gov. NCT04008030. [b]Patients with ≥ 2 prior lines are randomized only to the NIVO or NIVO + IPI arms. [c]Patients receiving investigator's choice of chemotherapy are eligible to receive NIVO + IPI upon progression (crossover treatment). [d]Confirmed using either immunohistochemistry and/or polymerase chain reaction-based tests. [e]Evaluated using RECIST v1.1. [f]Time between randomization and last known date alive or death.

Courtesy of Scott Kopetz, MD, PhD

CheckMate 8HW: Progression-Free Survival with Nivo/Ipi versus Nivo



Centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 296)	NIVO (n = 286)
Median PFS,[a] mo	NR	39.3
95% CI	53.8-NE	22.1-NE
HR (95% CI)	0.62 (0.48-0.81)	
P value[b]	0.0003	

- NIVO + IPI demonstrated statistically significant and clinically meaningful PFS benefit vs NIVO in patients with centrally confirmed MSI-H/dMMR mCRC across all lines of therapy
  - PFS benefit with NIVO + IPI vs NIVO was consistent in all randomized patients (median PFS: 54.1 vs 18.4 months; HR, 0.64 [95% CI, 0.52-0.79])

[a]Per BICR. [b]Boundary for statistical significance, p < 0.0095.

Courtesy of Scott Kopetz, MD, PhD

Andre T et al. *Lancet* 2025;405:383–95.

PD-1 + CTLA-4 is the new standard of care
for first-line MSI-H CRC

This is likely improving *CURE* rates for this population

AGENDA

Year in Review: Management of Colorectal Cancer (CRC)

MODULE 1: First-Line Treatment of BRAF V600E-Mutant Metastatic CRC (mCRC)

MODULE 2: Cell-Free DNA Molecular Residual Disease (MRD) Assays in Clinical Practice

MODULE 3: Immunotherapy for Localized and Metastatic MSI-High CRC

MODULE 4: Other Important Datasets

- Hepatic transplant for liver-limited mCRC
- HER2-positive CRC: Tucatinib, trastuzumab deruxtecan
- KRAS G12C-mutant CRC: Adagrasib, sotorasib, EGFR inhibitors

RTP Year in Review 2025

Discussion Question:
Hepatic Transplant for Liver-Limited mCRC

- **What, if any, is the current clinical role of hepatic transplant for liver-limited mCRC?**

Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial

*René Adam, Céline Piedvache, Laurence Chiche, Jean Philippe Adam, Ephrem Salamé, Petru Bucur, Daniel Cherqui, Olivier Scatton, Victoire Granger, Michel Ducreux, Umberto Cillo, François Cauchy, Jean-Yves Mabrut, Chris Verslype, Laurent Coubeau, Jean Hardwigsen, Emmanuel Boleslawski, Fabrice Muscari, Heithem Jeddou, Denis Pezet, Bruno Heyd, Valerio Lucidi, Karen Geboes, Jan Lerut, Pietro Majno, Lamiae Grimaldi, Francis Levi, Maïté Lewin, Maximiliano Gelli on behalf of the Collaborative TransMet group**

Lancet 2024 Sep 21;404(10458):1107-18

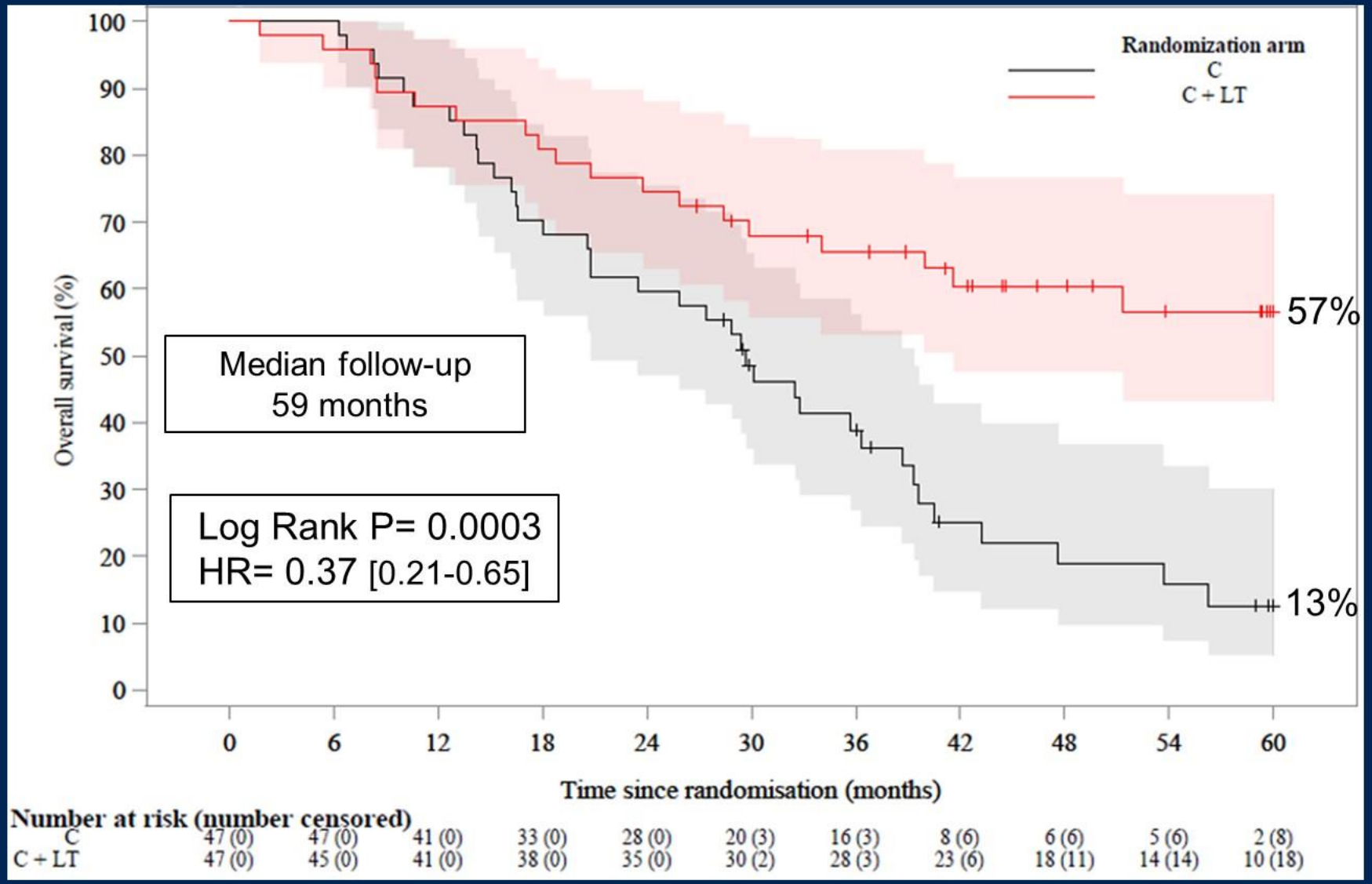
2024 ASCO ANNUAL MEETING

Abstract 3500

Liver Transplantation and Chemotherapy versus Chemotherapy alone in patients with definitively unresectable colorectal liver metastases : results from a prospective, multicentre, randomised trial (TransMet)

R Adam, C Piedvache, L Chiche, E Salamé, O Scatton, V Granger, M Ducreux, U Cillo, F Cauchy, JY Mabrut, C Verslype, L Coubeau, J Hardwigsen, E Boleslawski, F Muscari, J Lerut, L Grimaldi, F Levi, M Lewin, M Gelli

TransMet Trial : Primary Endpoint 5-Yr OS (ITT)



Impressive results for liver transplant in selected patients

But required high priority for livers on the donor list, which is currently not feasible in the US

Access to living related donor may improve feasibility in US in the future

Discussion Question: HER2-Positive mCRC

- **What is your current approach to sequencing tucatinib/trastuzumab and trastuzumab deruxtecan for patients with HER2-positive mCRC?**

Trastuzumab and Tucatinib remains a standard of care for 2L+ RAS/BRAF^{wt} HER2^{amp}

Trastuzumab deruxtecan remains a standard of care for 2L+ $HER2^{amp}$ without regard for RAS/BRAF

Resistance is *NOT* through loss of $HER2^{amp}$ or acquired RAS mutations, so no concerns about sequencing T+T vs T-DXd

Discussion Question:
KRAS G12C-Mutant mCRC

- **What is the practical application of the data evaluating the combinations of adagrasib/cetuximab and sotorasib/panitumumab for patients with KRAS G12C-mutant CRC?**

Both Adagrasib + Cetuximab and Sotorasib + Panitumumab are standard of care options for $KRAS^{G12C}$ tumors

But efficacy may differ between $KRAS^{G12C}$ inhibitors

Patterns of Care: Examining the Current Use of Genetic Testing and Related Clinical Management for Patients with Localized Breast Cancer

A CME/MOC-Accredited Webinar in Partnership with the American Society of Breast Surgeons

Thursday, February 20, 2025

5:00 PM – 6:00 PM ET

Faculty

Kevin S Hughes, MD

Mark Robson, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

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.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2025