Consensus or Controversy? Documenting and Discussing Investigators' Approaches to the Management of Colorectal Cancer

Friday, May 29, 2026

6:30 PM – 8:00 PM CT (7:30 PM – 9:00 PM ET)

Faculty

Stacey A Cohen, MD

Arvind Dasari, MD, MS

Moderator

Tanios Bekaii-Saab, MD

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Faculty

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Moderator
Tanios Bekaii-Saab, MD
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Andrea Cercek, MD — Disclosures PowerPoint Slides

Advisory Boards	3T Biosciences, AbbVie Inc, Agents, Amgen Inc, Daiichi Sankyo Inc, GSK, Janssen Biotech Inc, Merck, Pfizer Inc, Regeneron Pharmaceuticals Inc, Roche Laboratories Inc, Summit Therapeutics, UroGen Pharma
Contracted Research	GSK, Pfizer Inc

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Contributing Clinical Investigators

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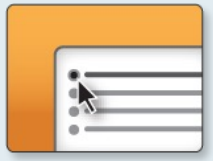
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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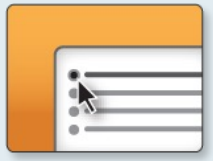
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



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Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Friday May 29	**Gastroesophageal Cancers** 11:30 AM – 1:00 PM CT (12:30 PM – 2:00 PM ET)
	Non-Small Cell Lung Cancer 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
	Chronic Lymphocytic Leukemia 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
	Colorectal Cancer 6:30 PM – 8:00 PM CT (7:30 PM – 9:00 PM ET)
Saturday May 30	**Ovarian Cancer** 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Prostate Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Small Cell Lung Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday May 31	**Oral SERDs and Agents Targeting the PI3K/AKT/mTOR Pathway for Breast Cancer** 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Endometrial Cancer 7:00 PM – 8:30 PM CT (8:00 PM – 9:30 PM ET)
	CAR T-Cell Therapy and Bispecific Antibodies for Non-Hodgkin Lymphoma 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Monday June 1	**ADCs for Breast Cancer** 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Novel Therapies for Non-Hodgkin Lymphoma 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Relapsed/Refractory Multiple Myeloma 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Tuesday June 2	**Myelofibrosis (Webinar)**

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Moderator

Tanios Bekaii-Saab, MD

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Agenda

Module 1: Current and Future Role of Immune Checkpoint Inhibition in the Management of Microsatellite Instability-High (MSI-H)/Mismatch Repair Deficient (dMMR) Localized and Locally Advanced Colorectal Cancer (CRC) — Dr Cohen

Module 2: Clinical Relevance and Practical Utilization of Molecular Residual Disease (MRD) Analysis in CRC — Dr Dasari

Module 3: Recent Advances in Metastatic CRC (mCRC): Optimizing Immunotherapy and Other Approaches — Dr Bekaii-Saab

Agenda

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Module 3: Recent Advances in Metastatic CRC (mCRC): Optimizing Immunotherapy and Other Approaches — Dr Bekaii-Saab

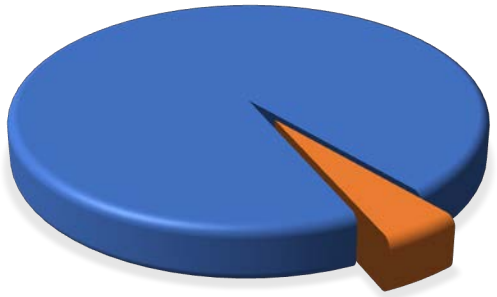
Current and Future Role of Immune Checkpoint Inhibition in the Management of Microsatellite Instability-High (MSI-H)/Mismatch Repair Deficient (dMMR) Localized and Locally Advanced Colorectal Cancer (CRC)

May 29, 2026

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

Presentation slides courtesy of Andrea Cercek, MD

Biomarker selected neoadjuvant therapy: MMRd/MSI



MMRd…

About 5-10% of all rectal cancers

Less sensitive to chemotherapy

Rectal cancer treated with TNT

Outcome	No. of patients (%)	
	dMMR	pMMR
FOLFOX as initial treatment	*n = 21*	*n = 63*
Progression of disease	6 (29)	0
Response or stable disease	15 (71)	63 (100)
Chemoradiation as initial treatment	*n = 16*	*n = 48*
Progression of disease	0	0
Complete pathologic response	2 (13)	8 (17)

Slides courtesy of Andrea Cercek, MD

Cercek, Smith, Stadler Clin Cancer Research 2020

Neoadjuvant PD1 blockade in MMRd locally advanced rectal cancer

Hypothesis

In mismatch repair deficient rectal cancer, PD-1 blockade may be able to <u>either:</u>

a) replace chemotherapy

b) replace chemo *and* radiation therapy

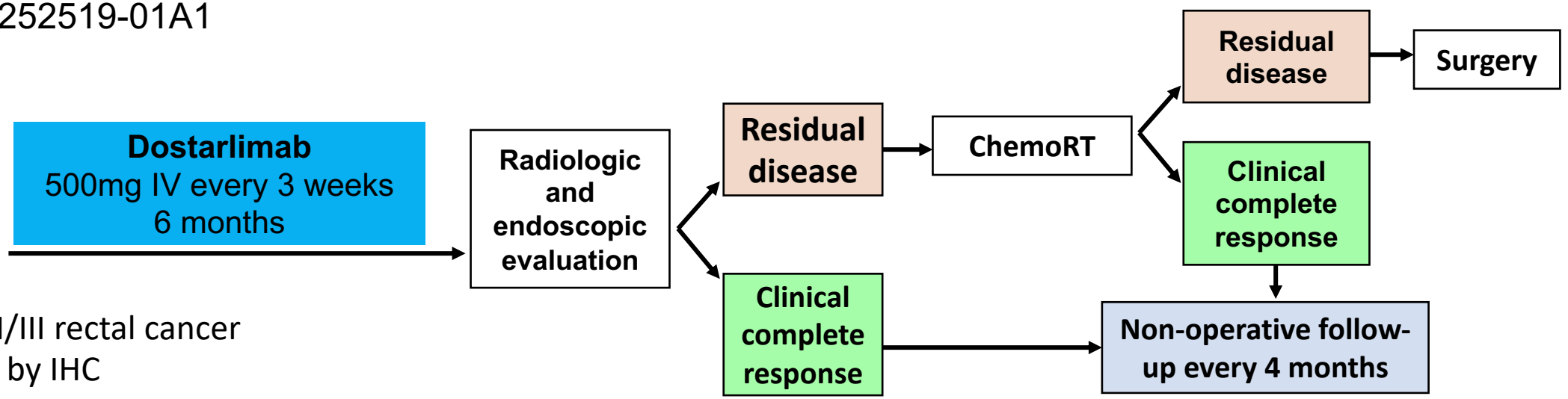
c) replace chemo *and* radiation, *and* surgery

Slides courtesy of Andrea Cercek, MD

Neoadjuvant PD1 blockade in MMRd locally advanced rectal cancer

NCT04165772

R21CA252519-01A1



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 PD1 alone or in combination with chemoRT

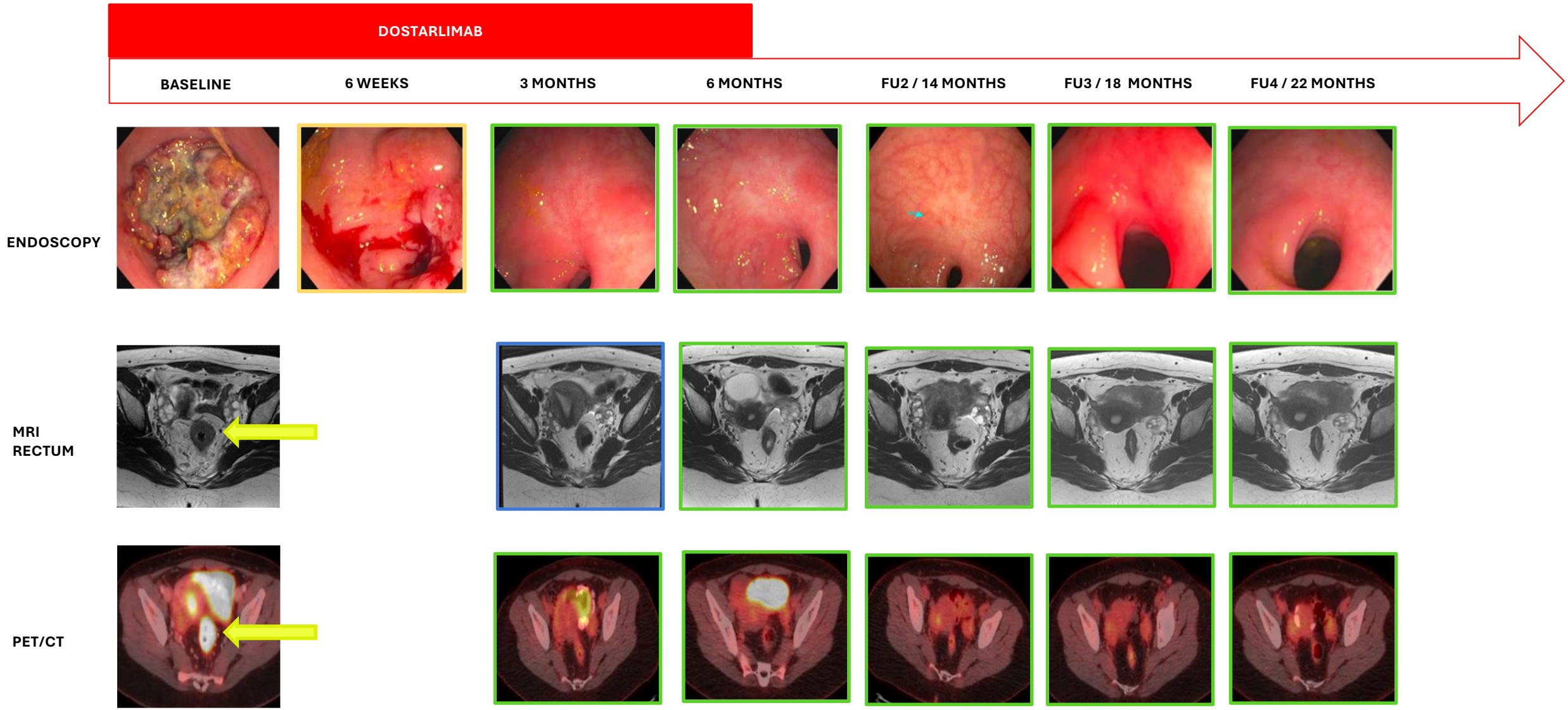
Sample Collection: ctDNA, biopsy, imaging

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

Slides courtesy of Andrea Cercek, MD

Patient with MMRd rectal cancer

- SD / STABLE DISEASE
- PR / PARTIAL RESPONSE
- NCR / NEAR COMPLETE RESPONSE
- CR / COMPLETE RESPONSE



Slides courtesy of Andrea Cercek, MD

Cercek, et al NEJM 2022

Individual responses to PD-1 blockade with dostarlimab

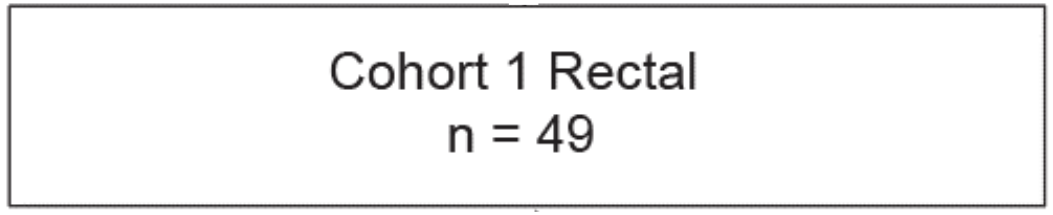
Patients who completed 6-months of dostarlimab

ID	Age	Stage T	Stage N	DFS (months)	Digital rectal exam response	Endoscopic best response	Rectal MRI best response	Overall response
1	38	T4	N+	60.3	CR	CR	CR	**cCR**
2	30	T3	N+	60.3	CR	CR	CR	**cCR**
3	61	T1/2	N+	60.8	CR	CR	CR	**cCR**
4	28	T4	N+	59.1	CR	CR	CR	**cCR**
5	53	T1/2	N+	48.8	CR	CR	CR	**cCR**
6	77	T1/2	N+	50.9	CR	CR	CR	**cCR**
7	77	T1/2	N+	48.6	CR	CR	CR	**cCR**
8	55	T3	N+	42.4	CR	CR	CR	**cCR**
9	68	T3	N+	42.4	CR	CR	CR	**cCR**
10	78	T3	N-	44.5	CR	CR	CR	**cCR**
11	55	T3	N+	44.0	CR	CR	CR	**cCR**
12	27	T3	N+	42.1	CR	CR	CR	**cCR**
13	26	T3	N+	38.9	CR	CR	CR	**cCR**
14	43	T3	N+	36.4	CR	CR	CR	**cCR**

Slides courtesy of Andrea Cercek, MD

Cercek, et al NEJM 2022

Cohort 1 – Rectal Cancers – Response and Surgical Management



Cercek, Diaz NEJM 2025

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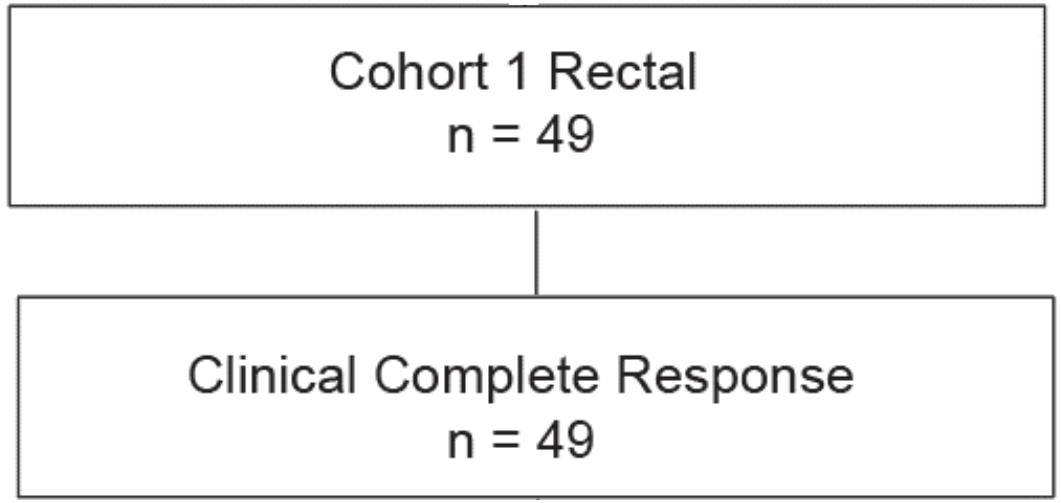
Cohort 1 – Rectal Cancers – Response and Surgical Management



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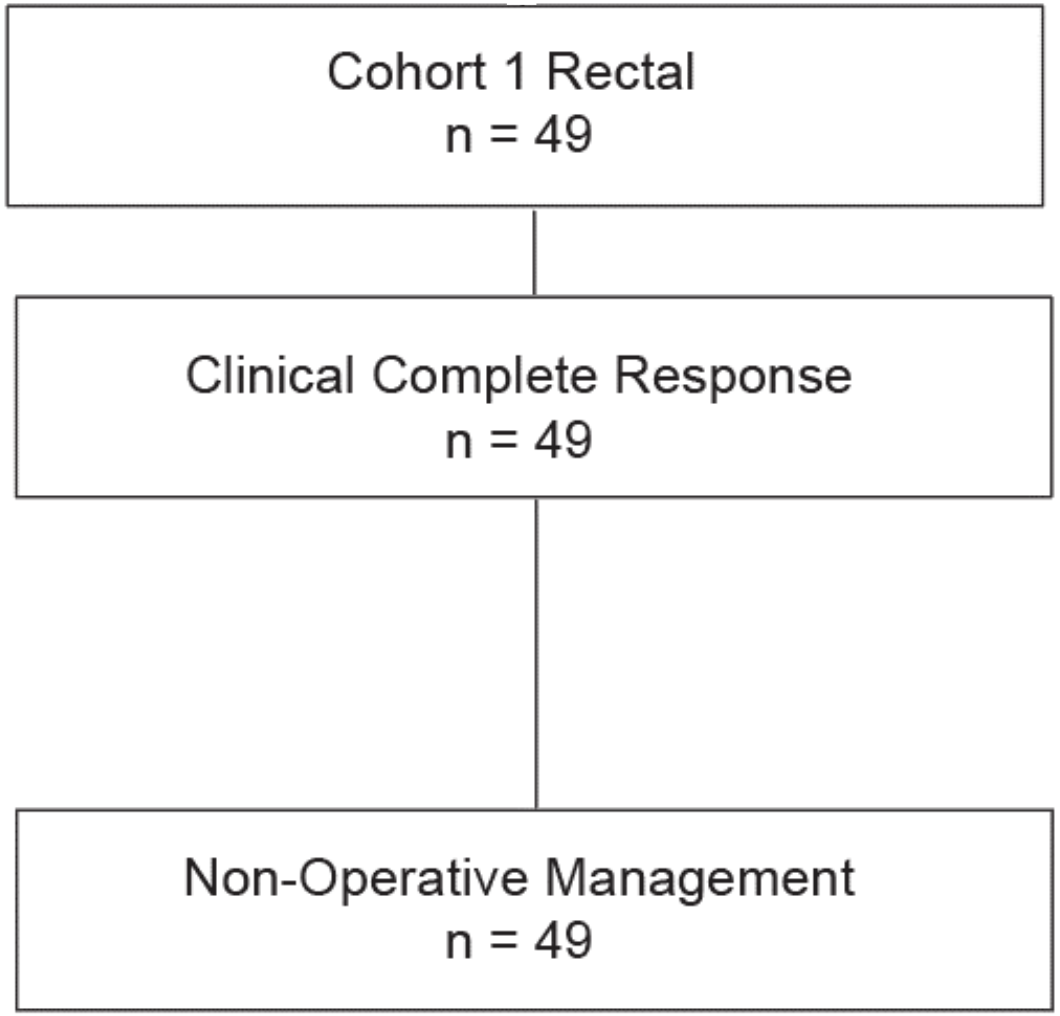
Cohort 1 – Rectal Cancers – Response and Surgical Management



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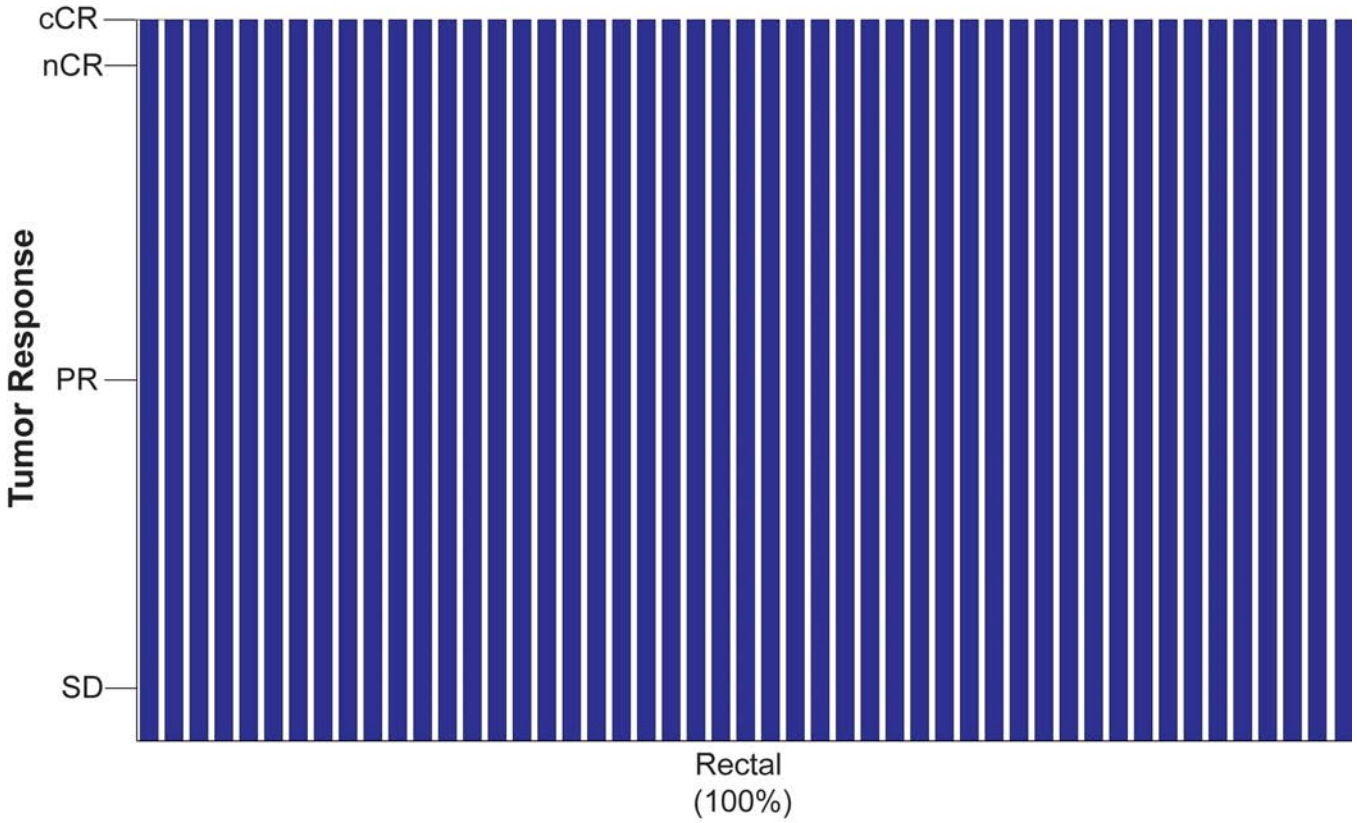
Cohort 1 – Rectal Cancers – Response and Surgical Management

Cohort 1 Rectal
n = 49

Clinical Complete Response
n = 49

Non-Operative Management
n = 49



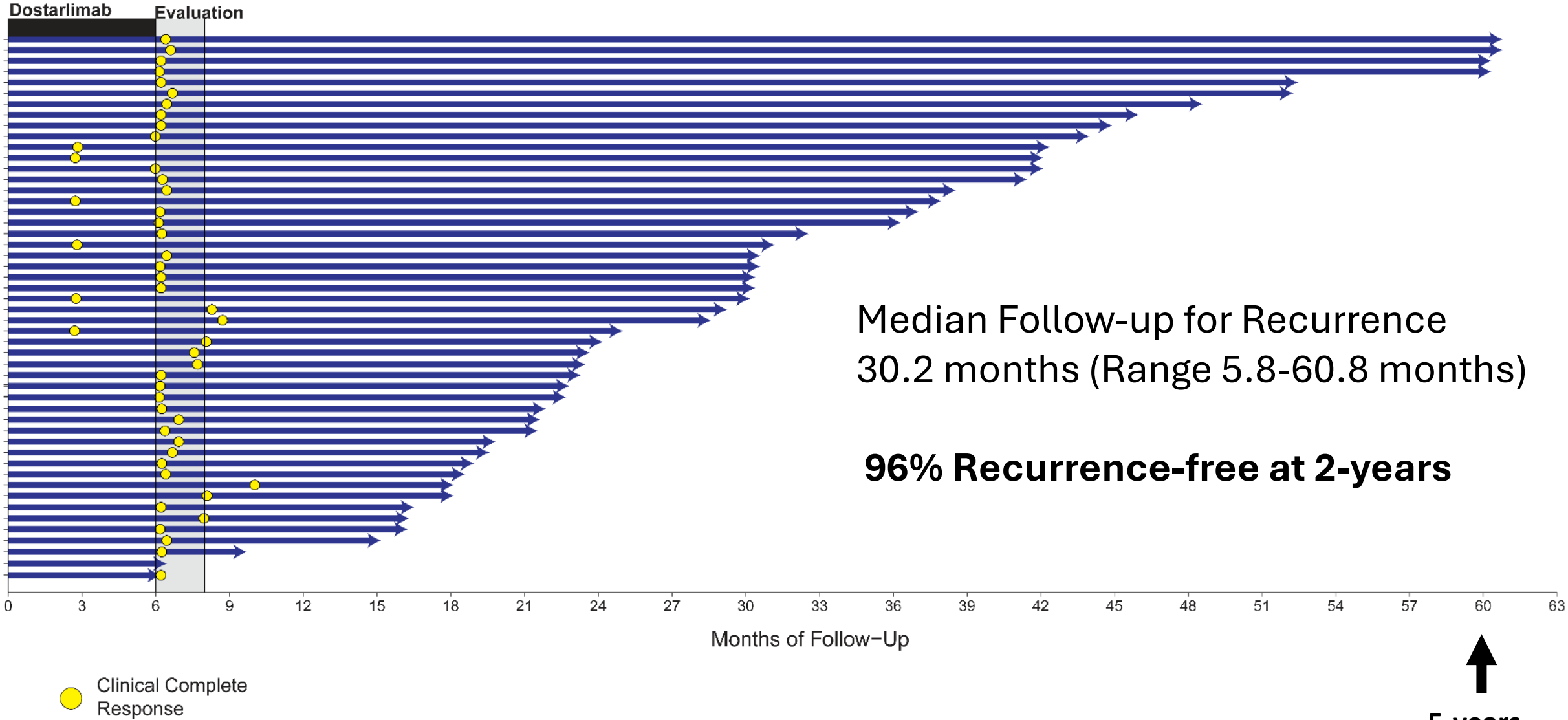
Rectal cancers achieved 100% clinical complete responses

Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

Cohort 1 – Rectal Cancers – Durability of Response

n=50



Median Follow-up for Recurrence
30.2 months (Range 5.8-60.8 months)

96% Recurrence-free at 2-years

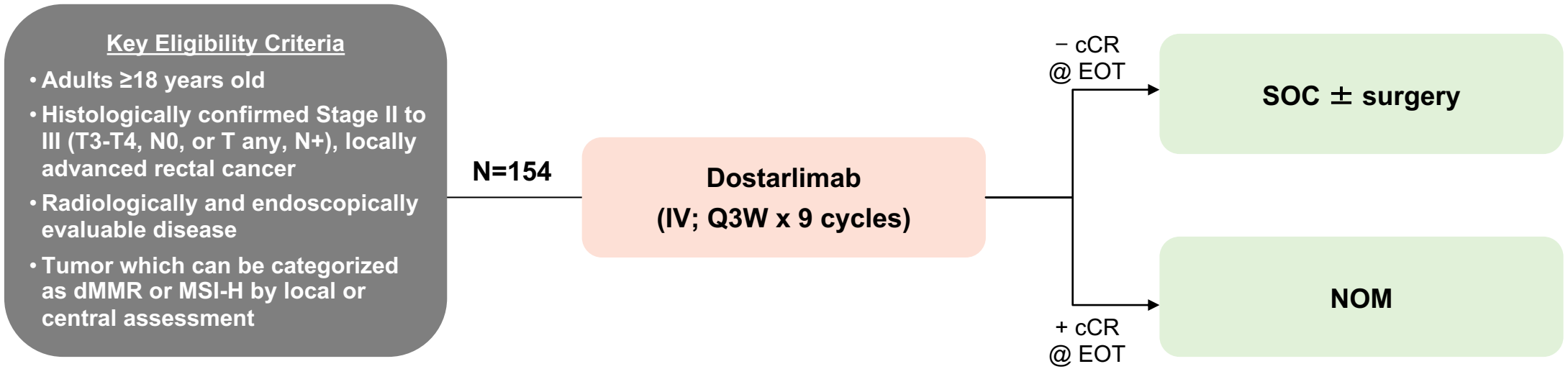
5-years

Slides courtesy of Andrea Cercek, MD

Cercek, Diaz NEJM 2025

AZUR-1: A Phase 2 Study of Dostarlimab in Patients With Untreated dMMR/MSI-H Locally Advanced Rectal Cancer

Study design[1,2]



1 Primary endpoint:
- Proportion who sustain cCR for 12 months (cCR12) by ICR

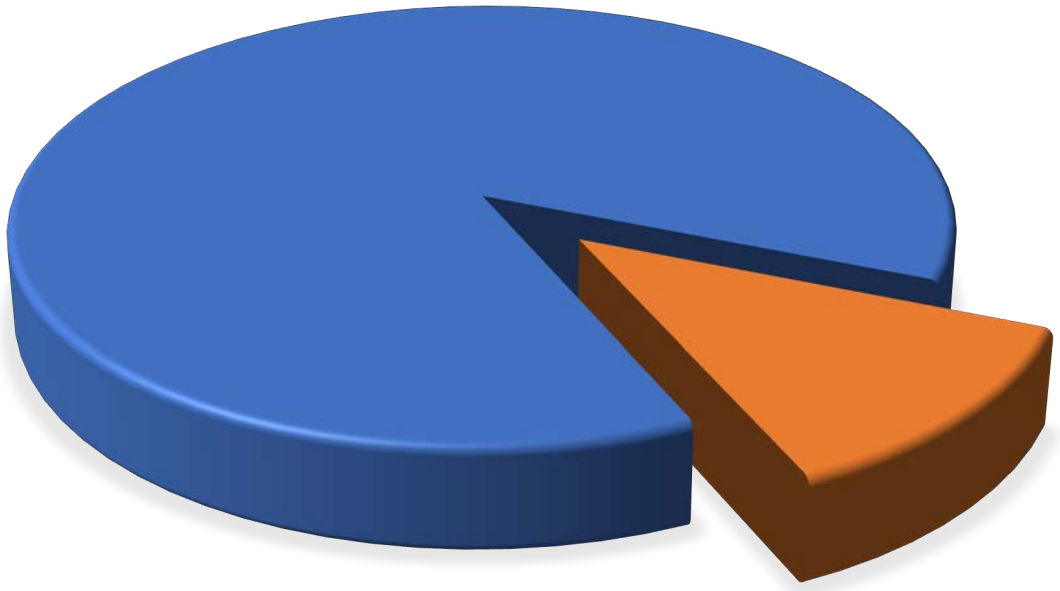
2 Secondary endpoints:
- cCR24 and cCR36 by ICR
- cCR12 by INV
- 3-year EFS by INV
- DSS (overall and 5-year)
- Organ preservation rate
- OS (overall and 5-year)
- ORR by ICR and INV
- Safety (AE, AELD, SAE, irAE)
- PK parameters

AE, adverse event; AELD, adverse event leading to discontinuation; cCR, clinical complete response; DFS, disease-free survival; dMMR, deficient mismatch repair; EFS, event-free survival; EOT, end of treatment; ICR, independent central review; INV, investigator assessment; irAE, immune-related adverse event; IV, intravenous; MSI-H, microsatellite instability-high; NOM, non-operative management; ORR, objective response rate; OS, overall survival; Q3W, every 3 weeks; SAE, serious adverse event; SOC, standard of care.

1. ClinicalTrials.gov (NCT05723562). Accessed May 27, 2025. Available at: https://clinicaltrials.gov/ct2/show/ NCT05723562. 2. Cercek A, et al. *J Clin Oncol*. 2023;41(suppl_16):TPS3639.

Slides courtesy of Andrea Cercek, MD

Colon Cancer: Mismatch repair deficient (dMMR/MSI)



About 10-15% of all early stage colon tumors

Standard treatment includes resection + adjuvant chemotherapy

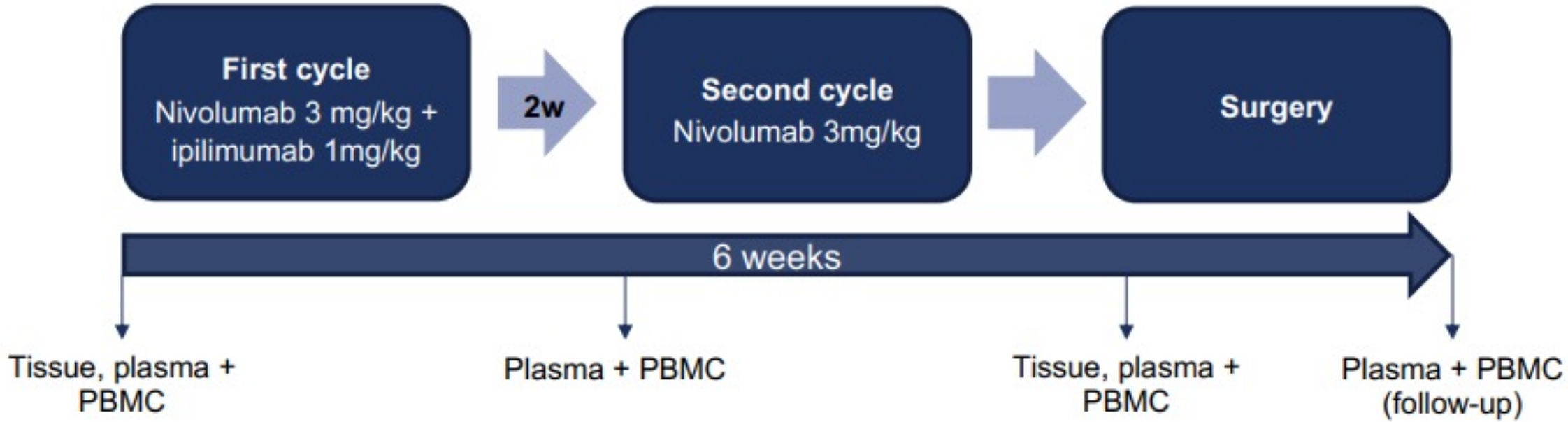
Tumor agnostic approval for ICB MMRd solid tumors in advanced disease

Slides courtesy of Andrea Cercek, MD

Le, et al NEJM 2015

NICHE-2 study design

- Investigator-initiated, non-randomized multicenter* study

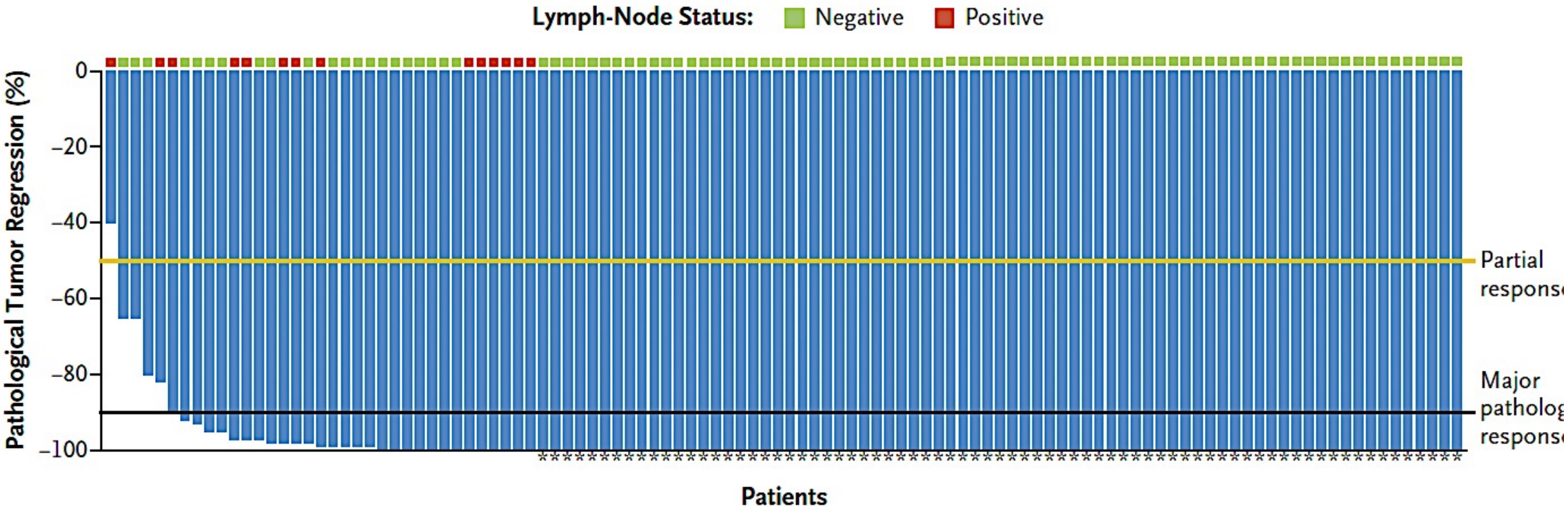


*6 participating hospitals in the Netherlands
PBMC = peripheral blood mononuclear cells

Chalabi M, et al. ESMO 2022

Slides courtesy of Andrea Cercek, MD

NICHE 2: Results

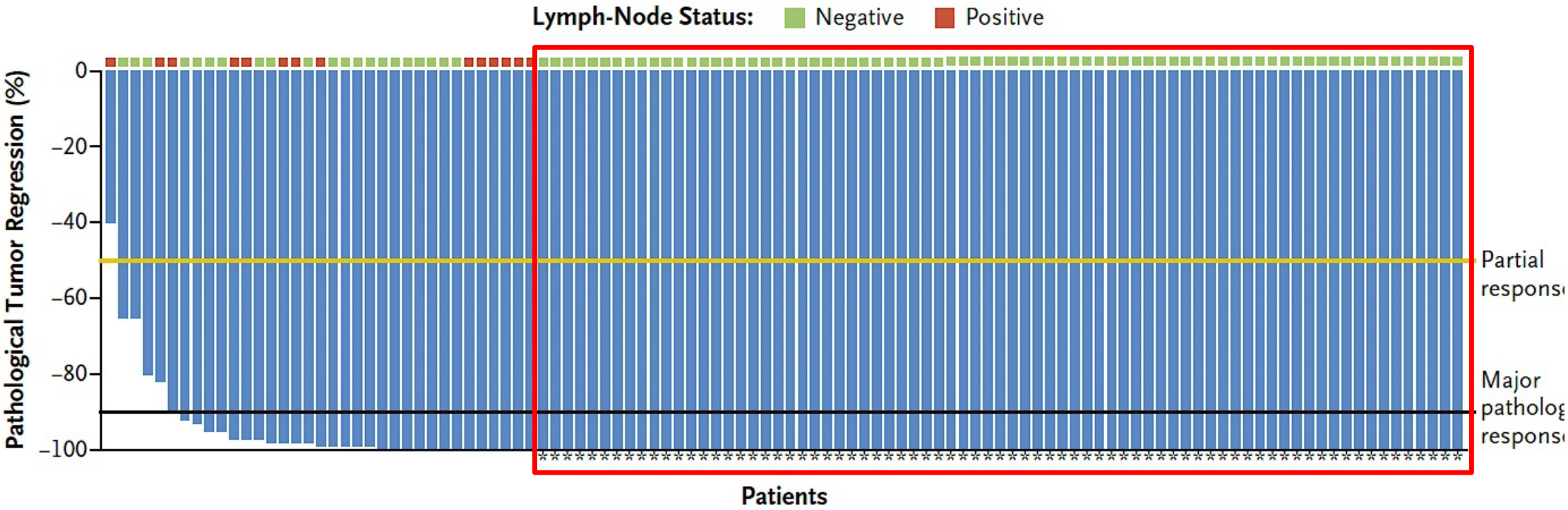


68% pCR

Slides courtesy of Andrea Cercek, MD

Chalabi NEJM 2024

NICHE 2: Results



68% pCR

AEs: Grade 3 or 4 events in 5 patients

Slides courtesy of Andrea Cercek, MD

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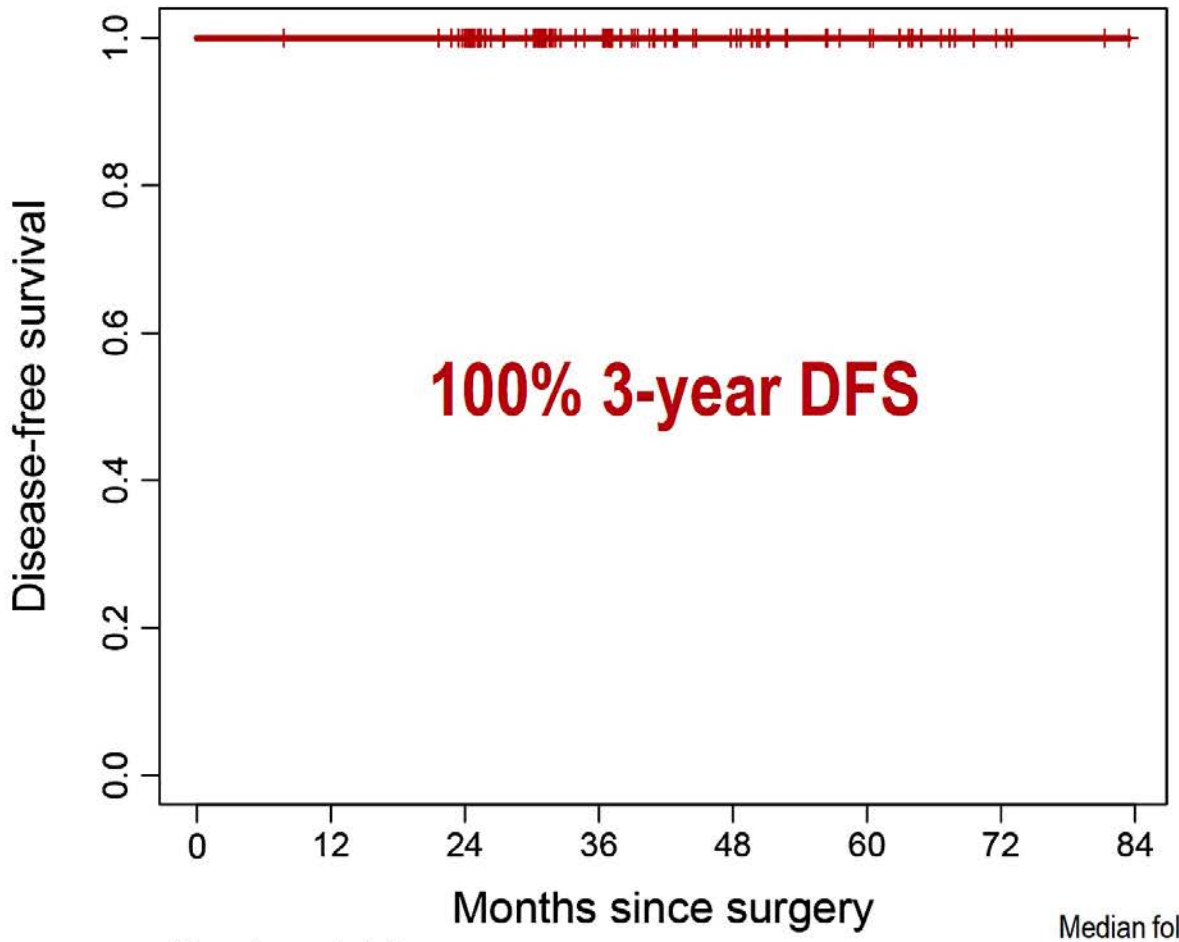
NICHE-2: Results



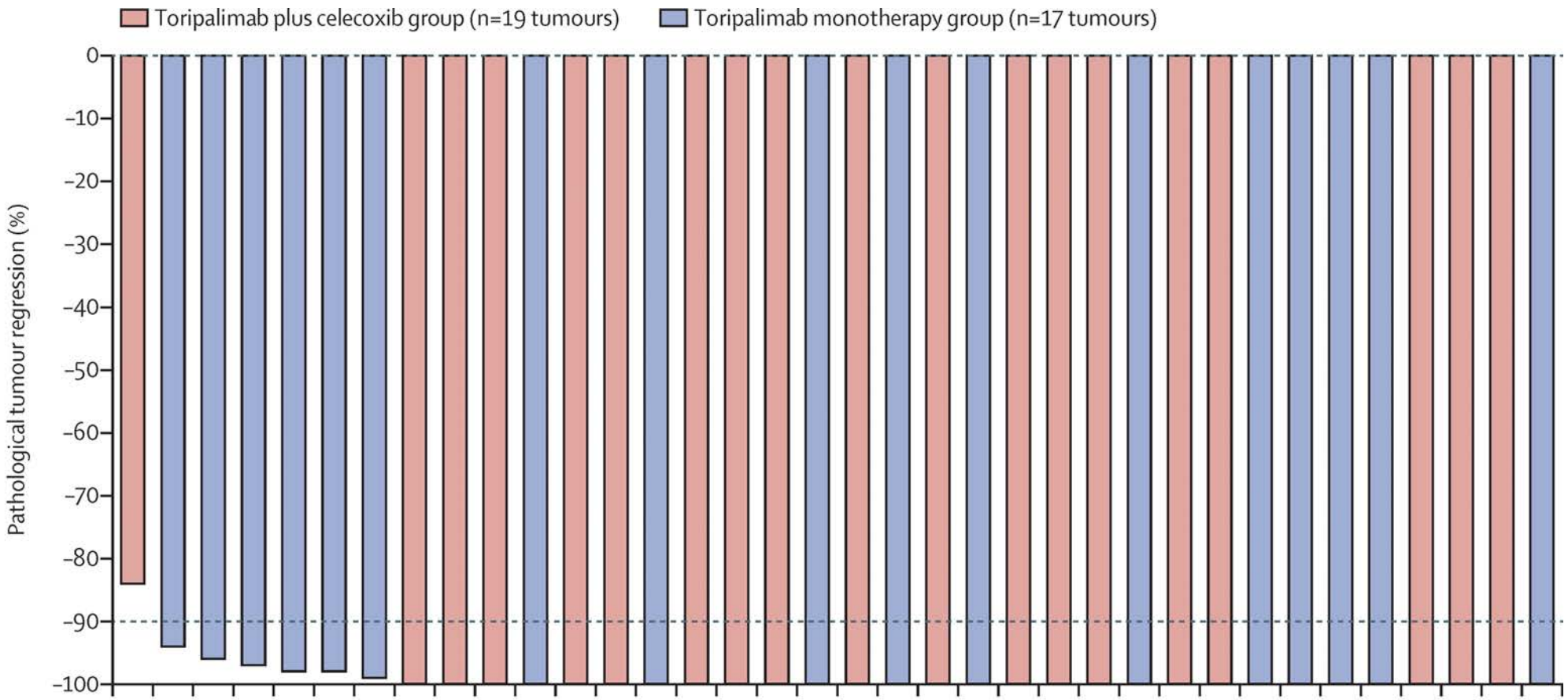
Median follow-up after surgery: 36.6 months (7.8 - 83.4)

BARCELONA 2024 ESMO congress

Data cut-off: 11 September 2024

Slides courtesy of Andrea Cercek, MD

Neoadjuvant PD-1 blockade with toripalimab, with or without celecoxib, in mismatch repair-deficient or microsatellite instability-high, locally advanced, colorectal cancer (PICC): a single-centre, parallel-group, non-comparative, randomised, phase 2 trial



Treatment: Toripalimab (anti PD1) for 3 months with or without celecoxib

Hu et al, The Lancet Gastroenterology and Hepatology 2021

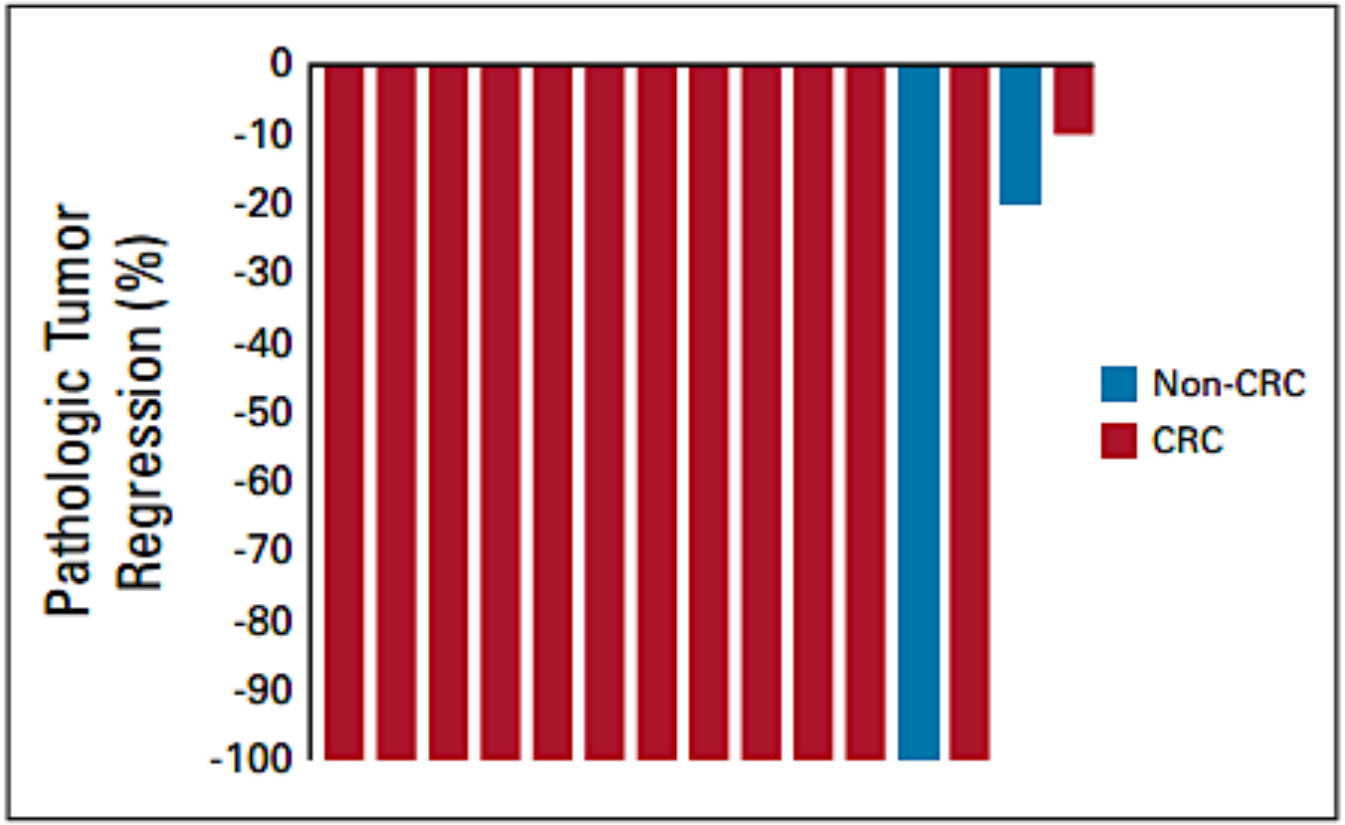
Slides courtesy of Andrea Cercek, MD

Phase II study of neoadjuvant pembrolizumab in localized unresectable MSI solid tumors

Included 19 MSI colon cancer patients

17 underwent surgery

pCR 65%

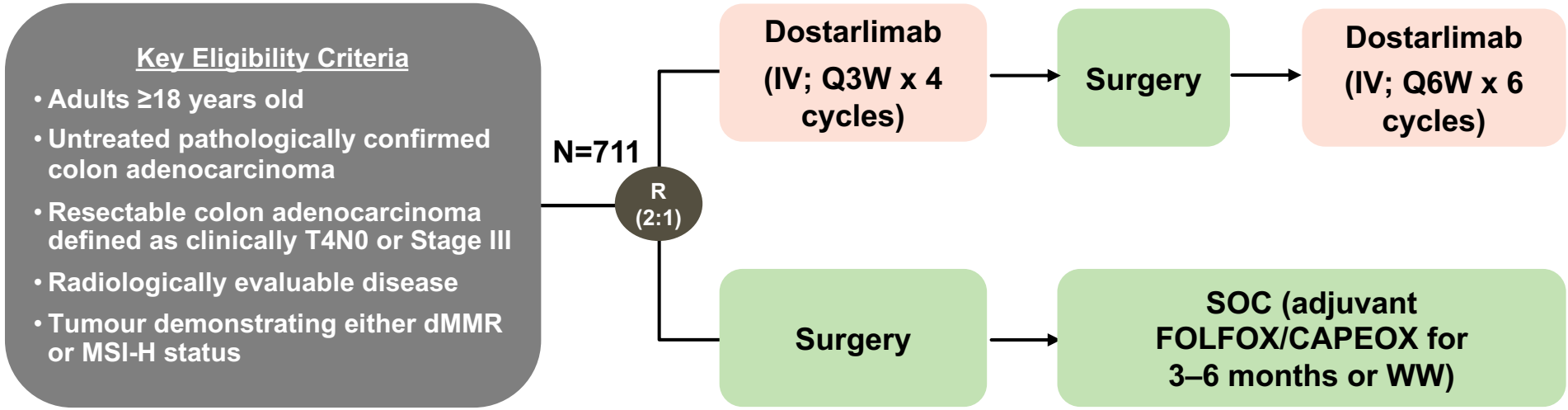


Ludford et al JCO 2023

Slides courtesy of Andrea Cercek, MD

AZUR-2: A Phase 3 Study of Perioperative Dostarlimab in Patients With Untreated T4N0 or Stage III dMMR/MSI-H Resectable Colon Cancer

Study design[1,2]



1 Primary endpoint:
- EFS up to 5 years (BICR)

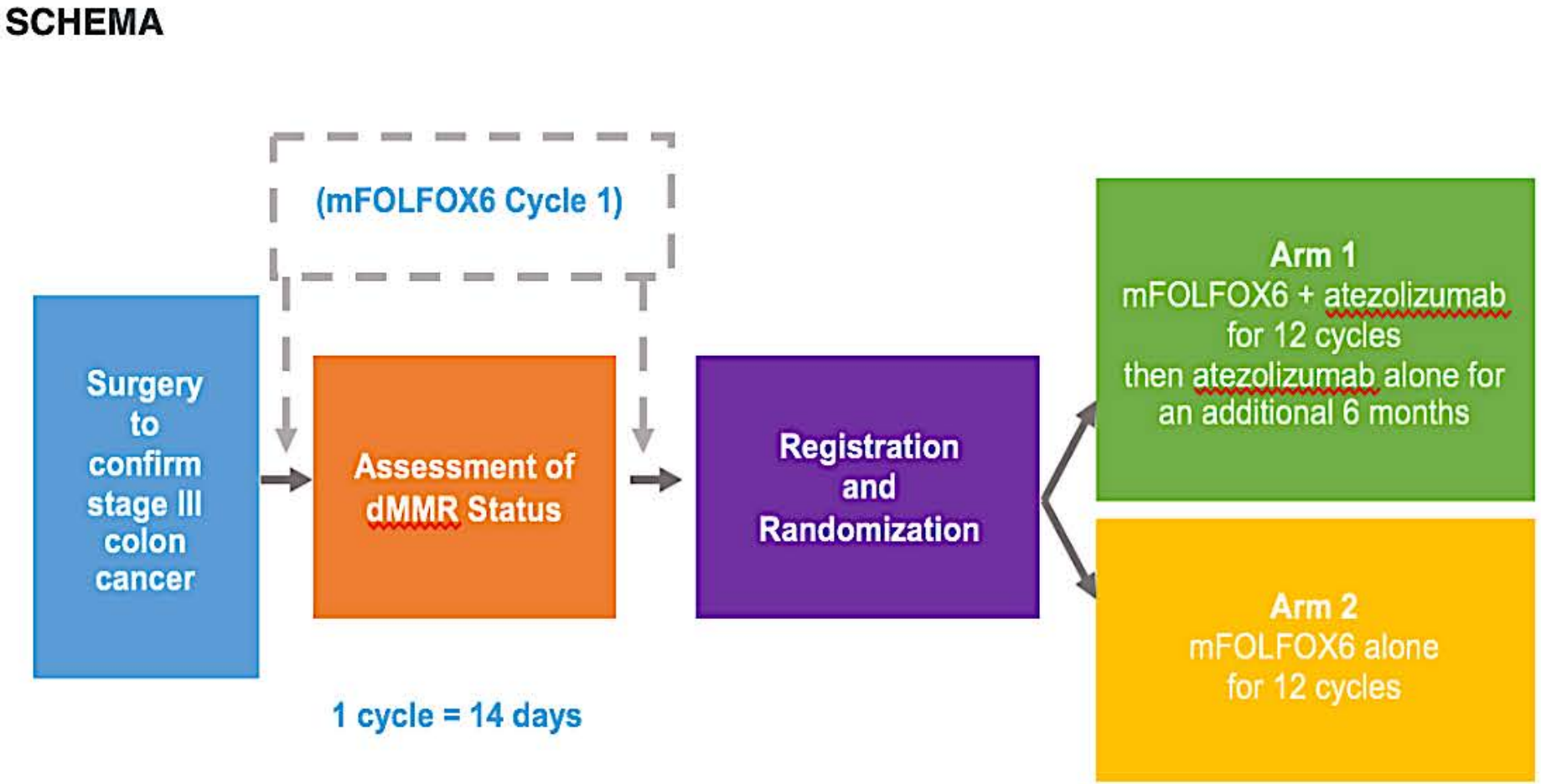
2 Secondary endpoints:
- OS
- Participants with pathological response
- EFS (by LA)
- Participants with treatment-emergent AEs, SAEs, imAEs, AEs leading to death or discontinuation
- PK parameters
- Participants with anti-drug antibodies

AE,adverse event; BICR, blinded independent central review; dMMR, deficient mismatch repair; EFS, event free survival; imAE, immune-mediated adverse event; IV, intravenous; LA, local assessment; MSI-H, microsatellite instability-high; OS, overall survival; QxW, every x weeks; SAE, serious adverse event; SOC, standard of care; WW, watch and wait.

1. ClinicalTrials.gov (NCT05855200). Accessed May 27, 2025. Available at: https://clinicaltrials.gov/ct2/show/NCT05855200. 2. Starling N, et al. *J Clin Oncol* 2024;42 (suppl_3):TPS240

Slides courtesy of Andrea Cercek, MD

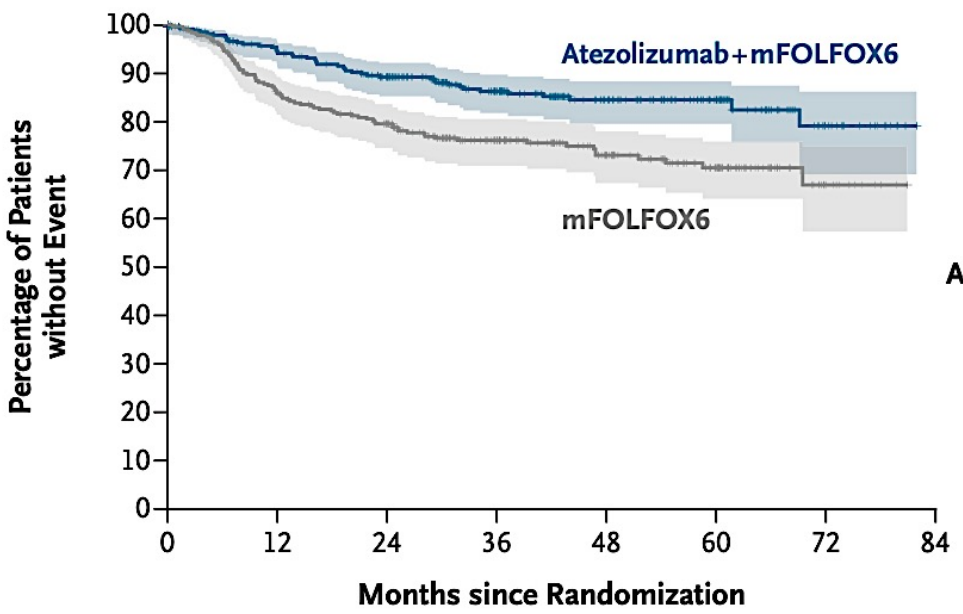
ATOMIC: Randomized study of adjuvant FOLFOX +/- Atezolizumab for MMRd Stage III colon cancer



Sinicrope et al, *NEJM* 2026

Slides courtesy of Andrea Cercek, MD

ATOMIC: Randomized study of adjuvant FOLFOX +/- Atezolizumab for MMRd Stage III colon cancer



	No. of Events/ Total No. of Patients	3-Yr Disease-free Survival (95% CI)
		percent
Atezolizumab+mFOLFOX6	46/355	86.3 (81.8–89.8)
mFOLFOX6	81/357	76.2 (70.9–80.6)

Hazard ratio for disease recurrence or death, 0.50 (95% CI, 0.35–0.73)
Stratified P<0.001 by log-rank test

No. at Risk								
Atezolizumab+mFOLFOX6	355	296	259	181	112	59	17	0
mFOLFOX6	357	264	229	160	109	63	11	0

Figure 2. Disease-free Survival among Patients with Stage III Colon Cancer.

Shown are the results of the primary end-point analysis of disease-free survival. Tick marks indicate censored data, and shaded areas confidence intervals.

Sinicrope et al, *NEJM* 2026

Slides courtesy of Andrea Cercek, MD

MMRd Colon: Possibility of Nonoperative Management

Could non-operative management of MMRd tumors extend beyond rectal cancer?

1. Clinical complete response → Non operative management

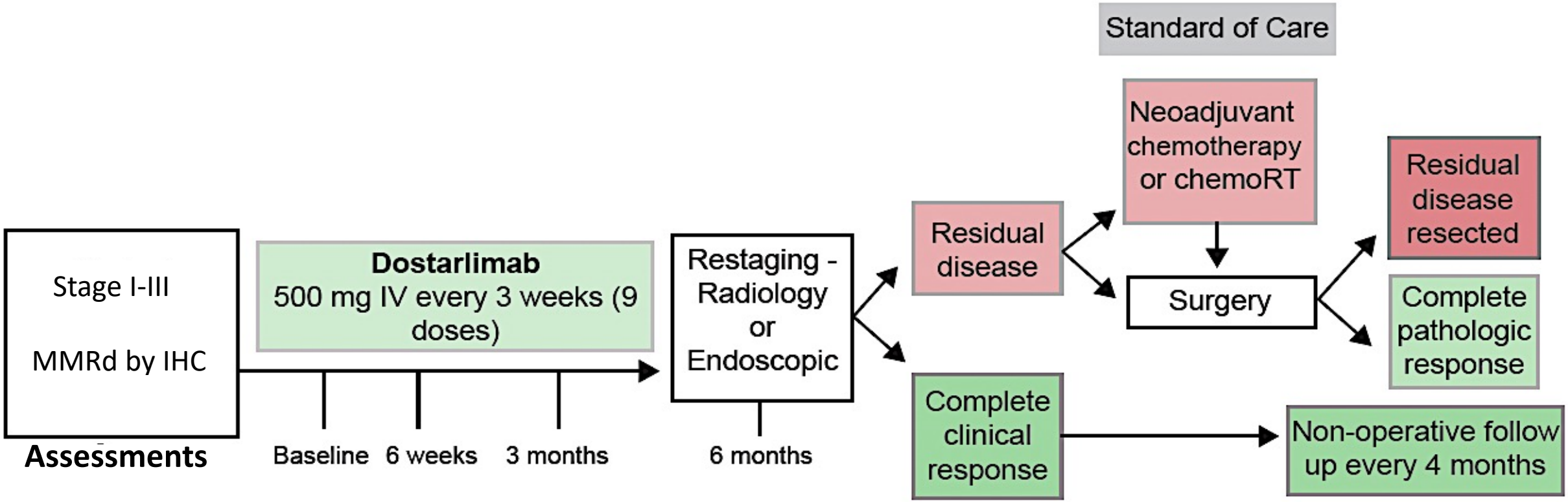
2. Durability of clinical complete response

3. Understand incomplete responses and recurrences

Slides courtesy of Andrea Cercek, MD

Neoadjuvant PD-1 blockade in locally advanced MMRd solid tumors

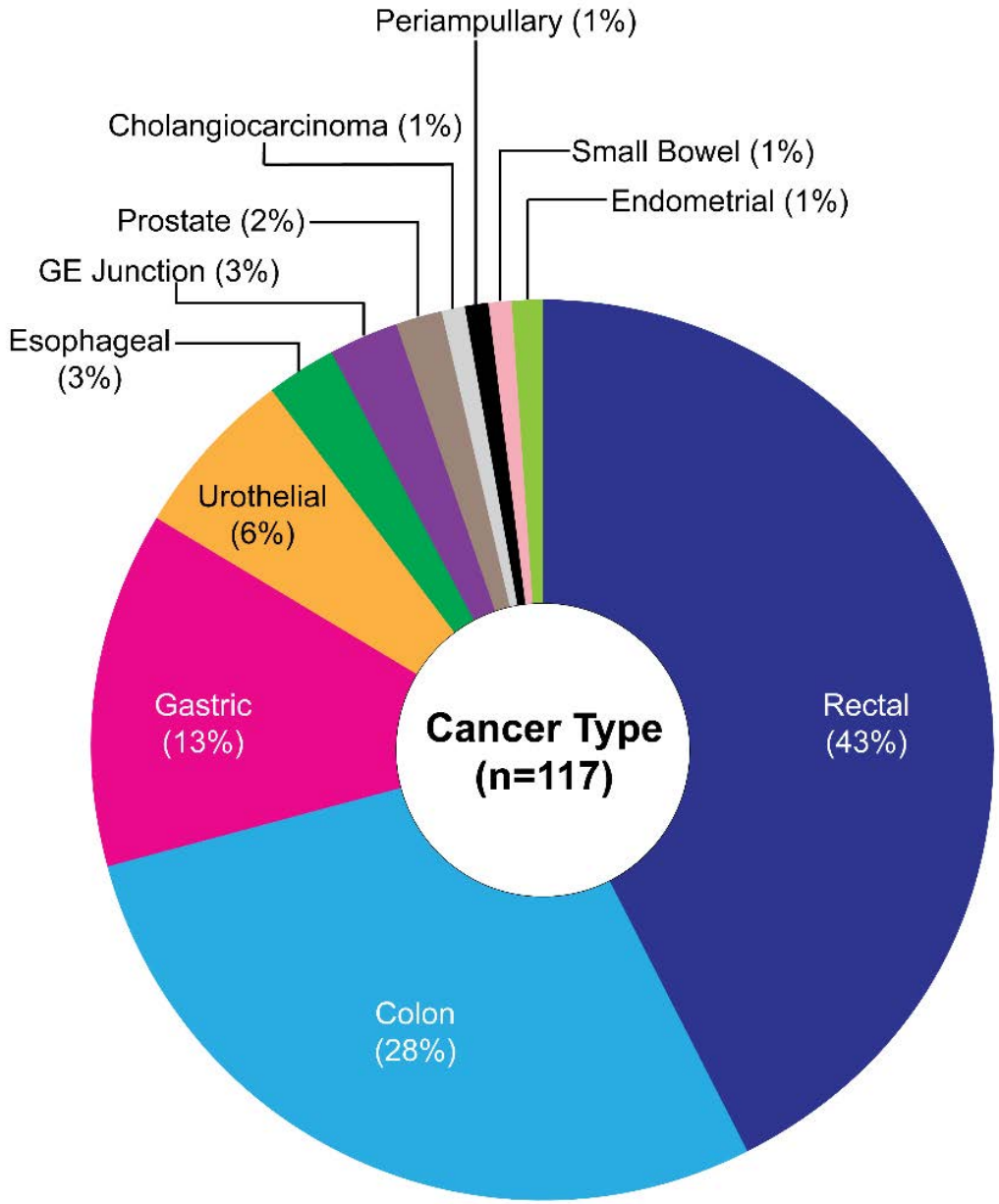
NCT 04165772

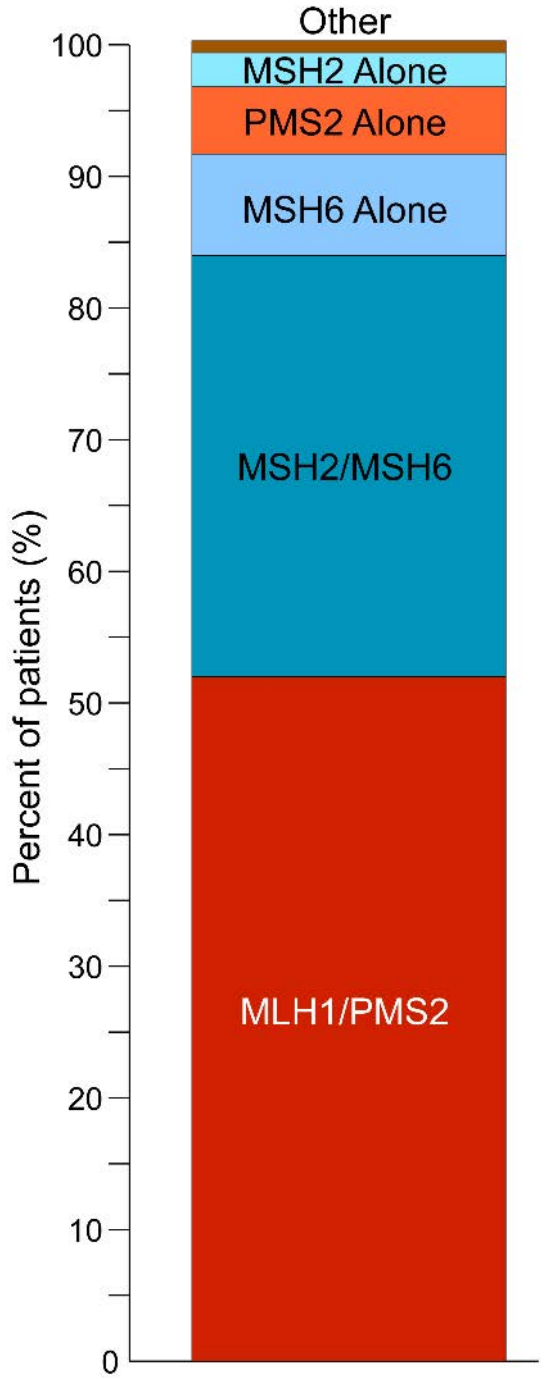


Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

Patient Characteristics

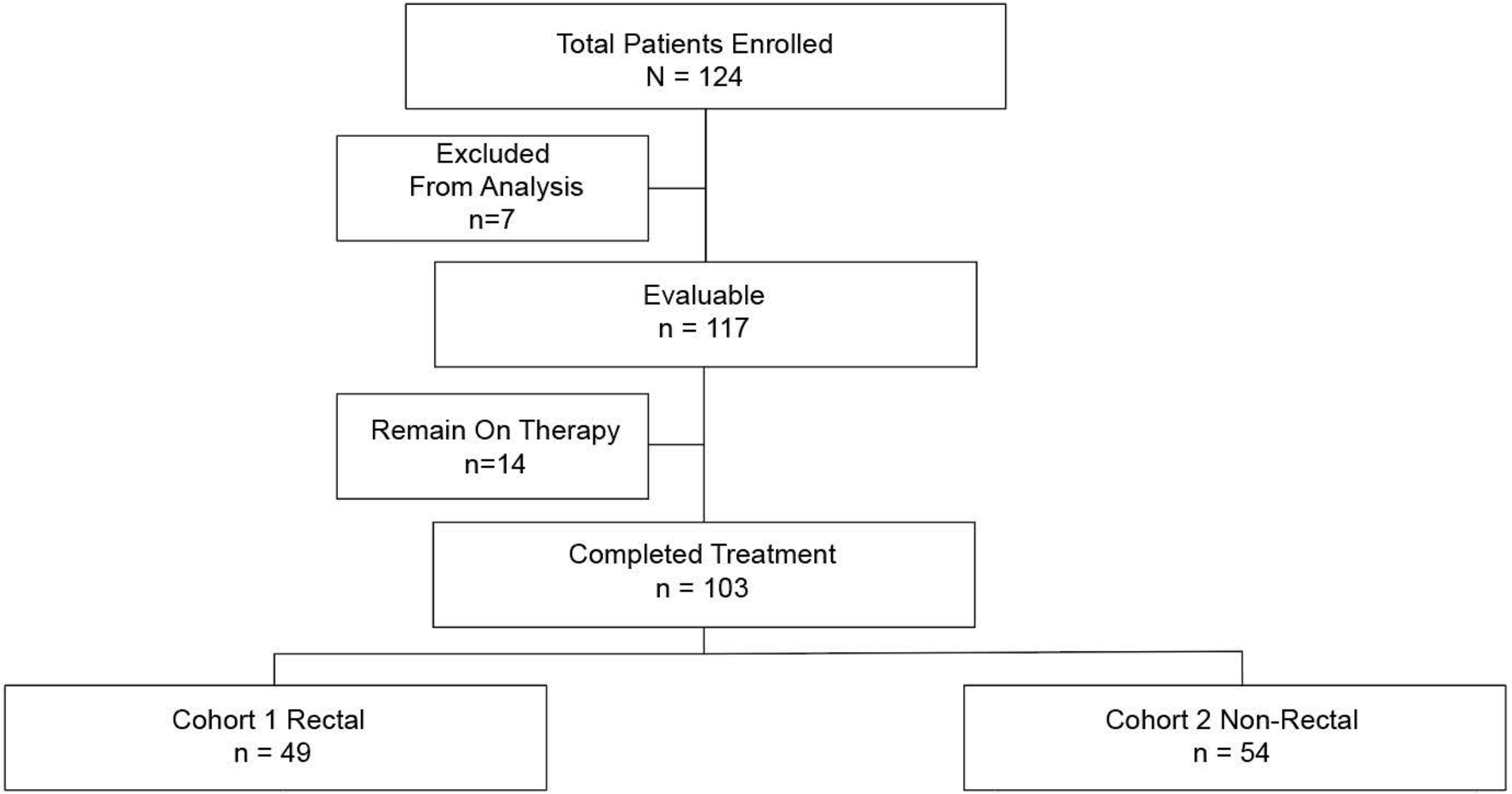




Slides courtesy of Andrea Cercek, MD

Cercek, Diaz NEJM 2025

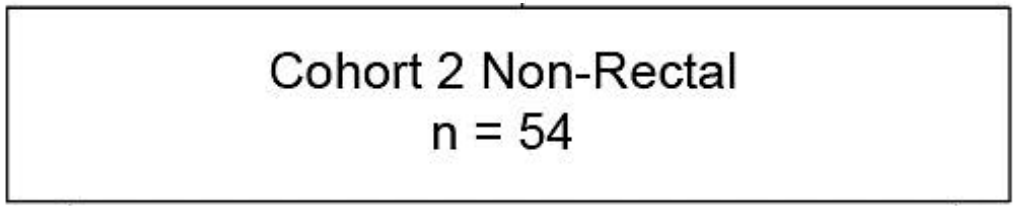
Study Flow Diagram



Slides courtesy of Andrea Cercek, MD

Cercek, Diaz NEJM 2025

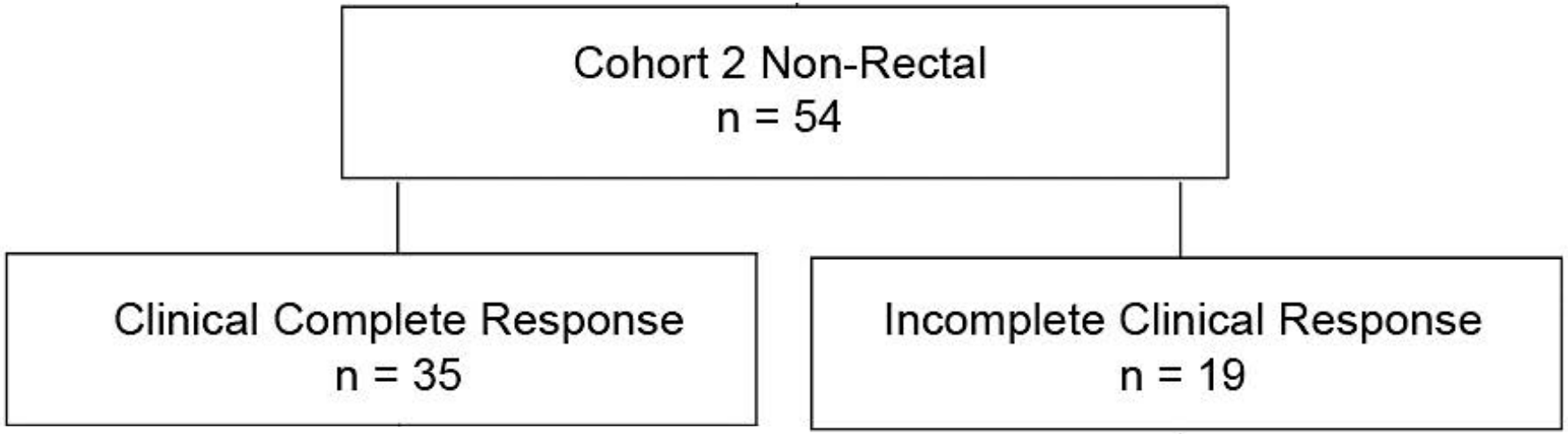
Cohort 2 – Non-rectal cancer – Responses and Surgical Management



Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

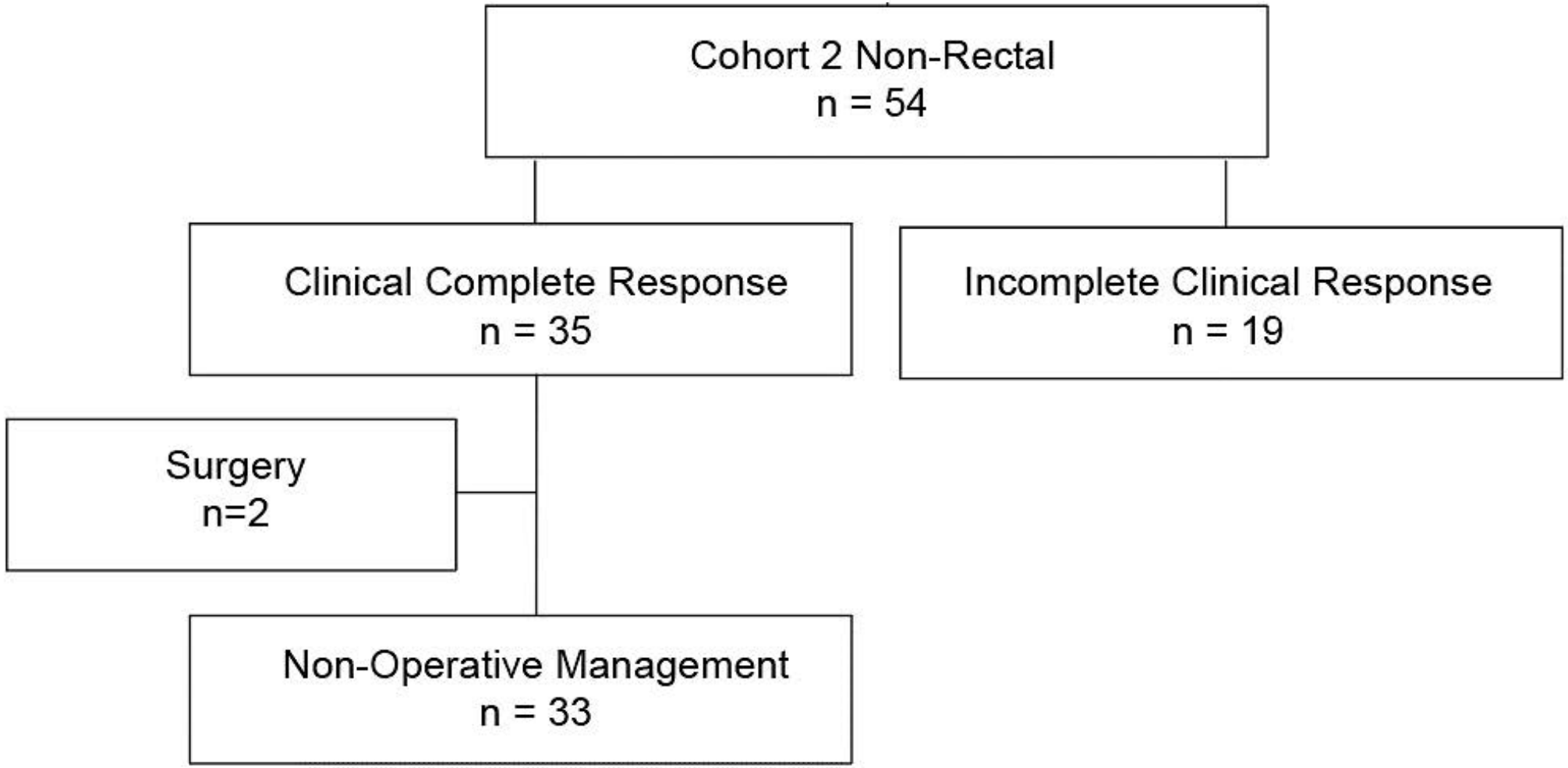
Cohort 2 – Non-rectal cancer – Responses and Surgical Management



Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

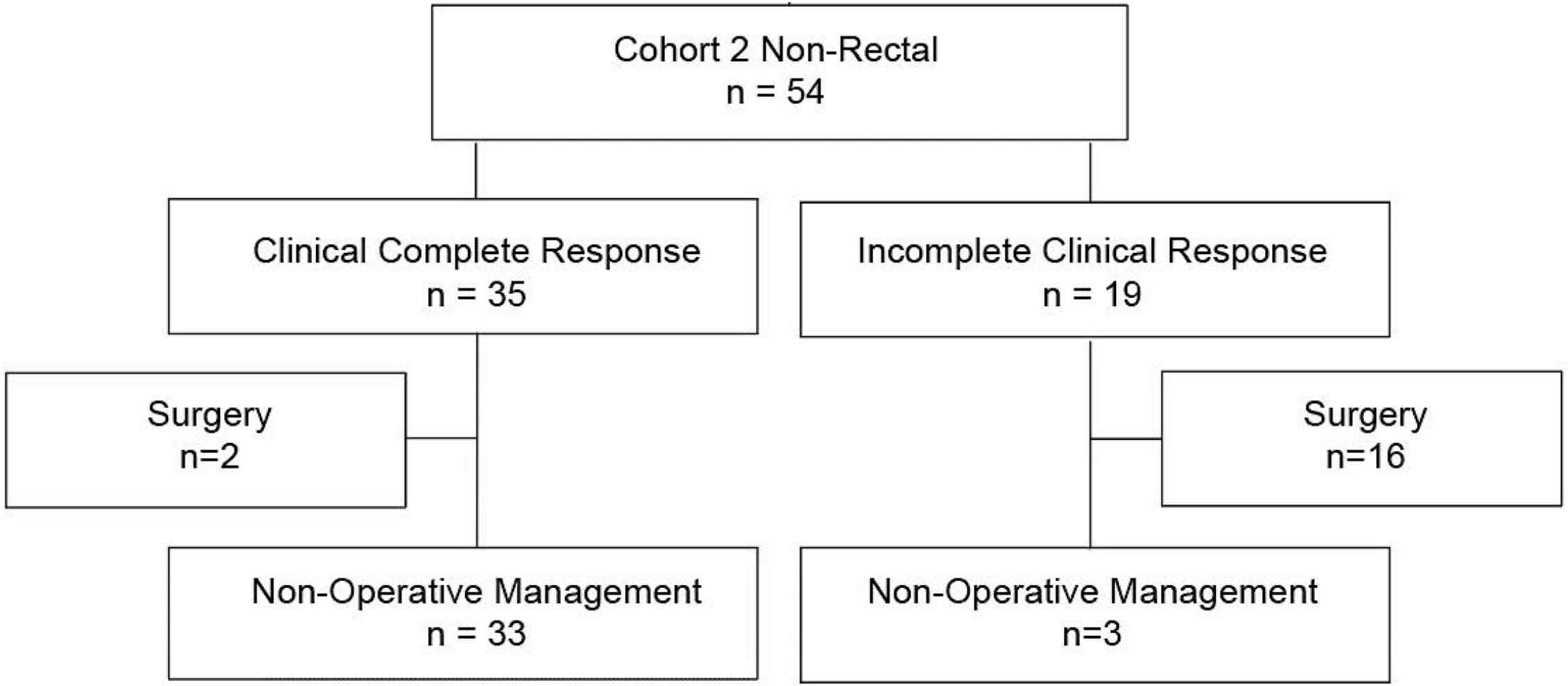
Cohort 2 – Non-rectal cancer – Responses and Surgical Management



Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

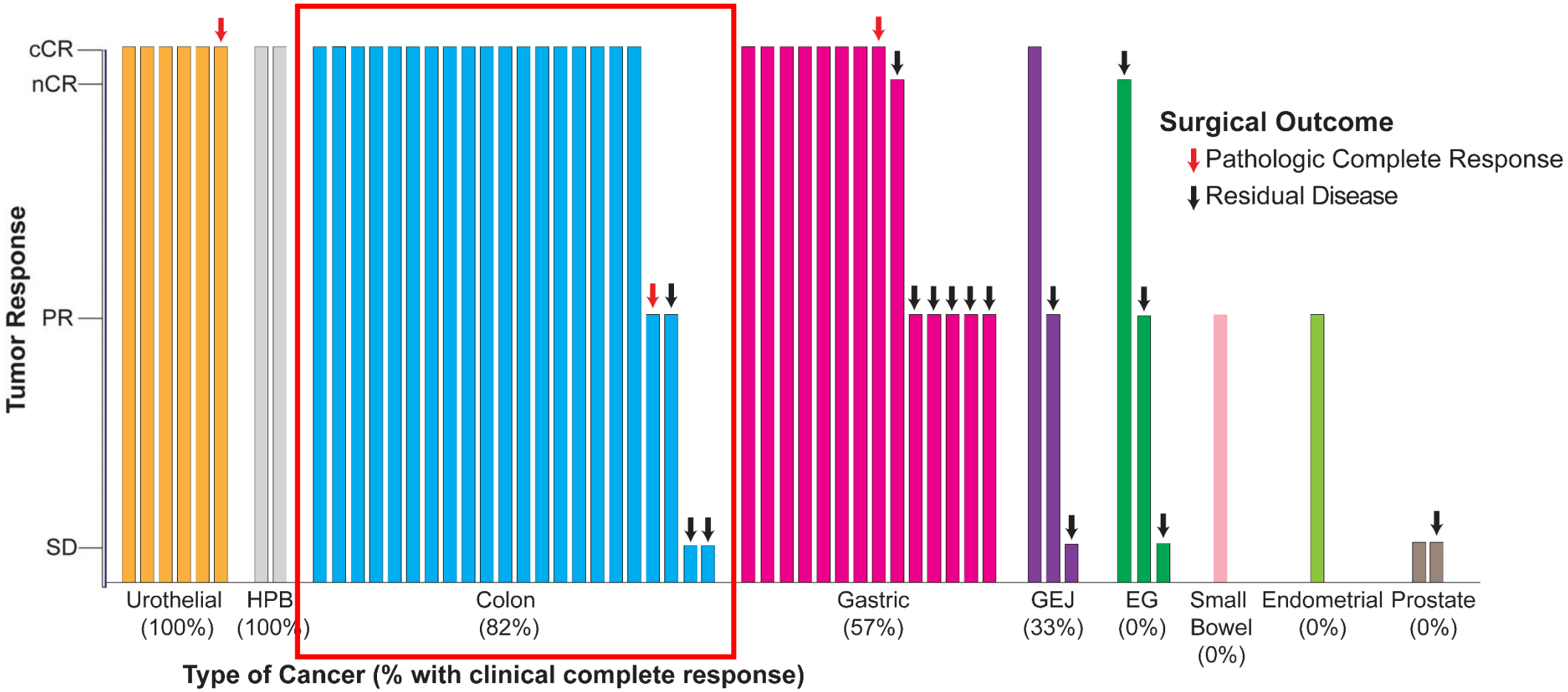
Cohort 2 – Non-rectal cancer – Responses and Surgical Management



Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

Cohort 2 – Non-rectal cancer – Responses and Surgical Management

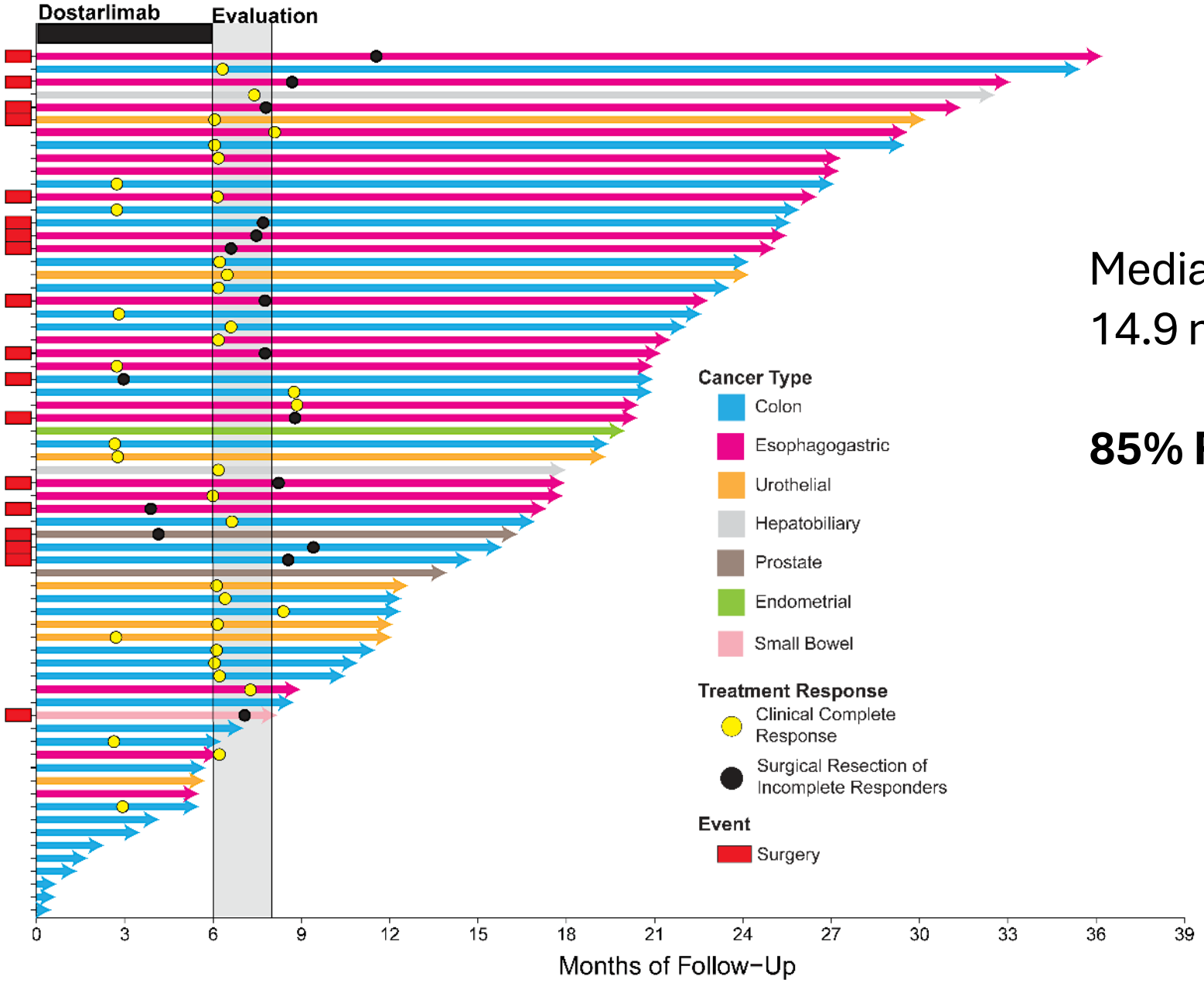


Colon: 82% achieved a clinical complete response

Cercek, Diaz NEJM 2025

Slides courtesy of Andrea Cercek, MD

Cohort 2 – Non-rectal cancer – Durability of response



Median Follow-up for Recurrence
14.9 months (range 0-32.7 months)

85% Recurrence-free at 2-years

Slides courtesy of Andrea Cercek, MD

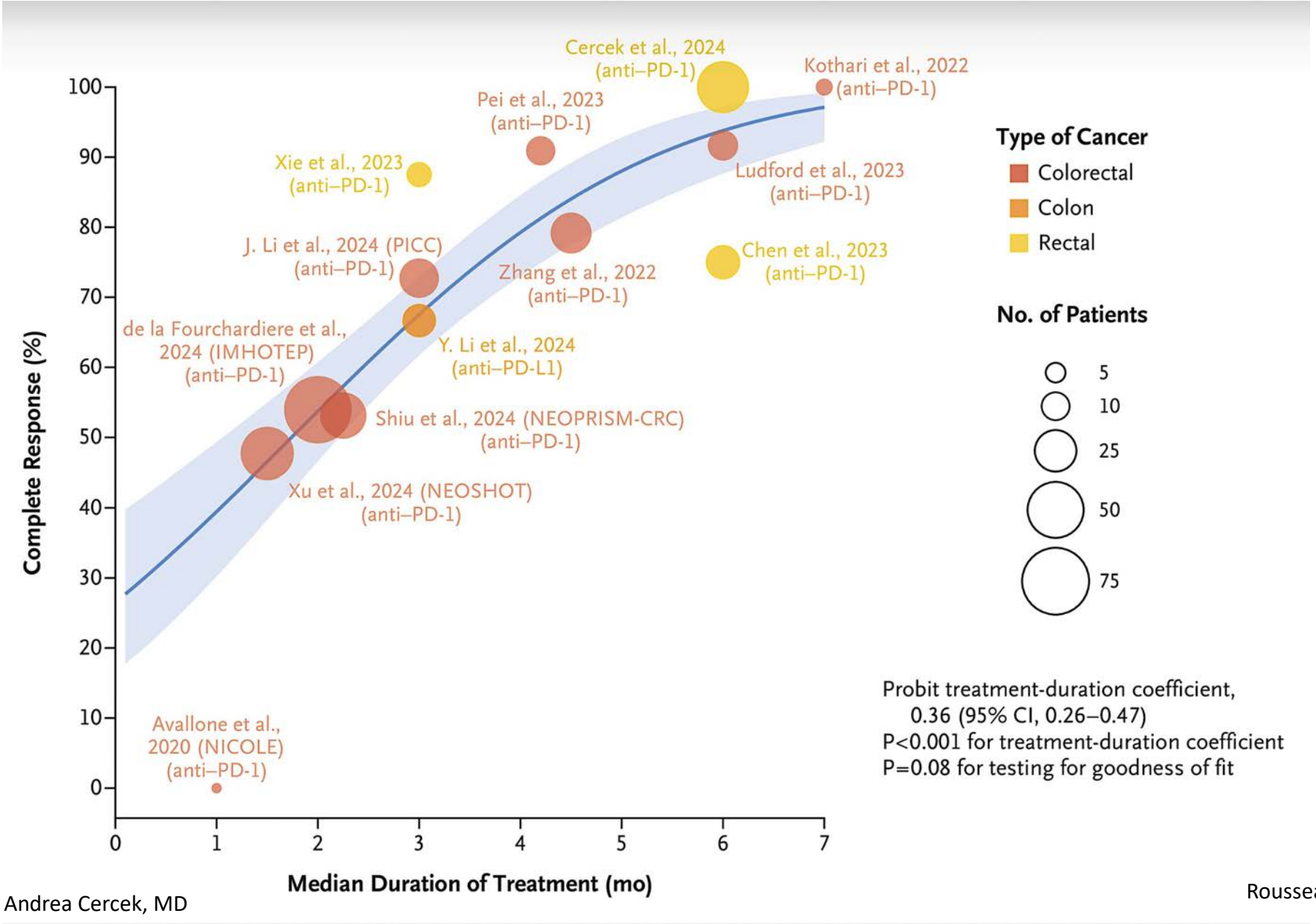
Cercek, Diaz NEJM 2025

Neoadjuvant Immunotherapy in MSI-H Colon Cancer

- Significant tumor regression, 67-75% complete pathologic response
- Duration of immunotherapy was variable 1-6 mo

Slides courtesy of Andrea Cercek, MD

Duration of Neoadjuvant Immunotherapy and Incidence of Complete Response among Patients with MMRd Colorectal Cancer



Slides courtesy of Andrea Cercek, MD

Rousseau, White, Cercek, Diaz NEJM 2025

Assessment of clinical complete response

The large majority of early stage locally advanced solid MMRd tumors are very sensitive to ICB and response is rapid

Although protocol is 6 months…

- IF the tumor is responding, patience and close follow up is key
- Unknown if it is just *time* or if *ICB should be continued*

Endoscopic exams and biopsies to ensure tumor is MMRd, residual disease can be MMRp

Assessment of cCR outside the rectum is challenging

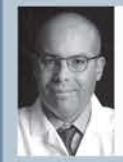
Slides courtesy of Andrea Cercek, MD

Conclusions and future directions

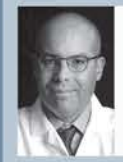
- Further work in markers of cCR is warranted
- Neoadjuvant PD-1 blockade in MMRd tumors could obliviate the need for standard of care chemotherapy, radiation and surgery in 2-3% of all early -stage cancer cases
- ctDNA appears to be a promising marker of complete response
- Some MMRd solid tumors may require longer duration or combination ICB to achieve a clinical complete response
- Evaluation of response and resistance

Slides courtesy of Andrea Cercek, MD

Which testing method do you generally use to assess MSI/MMR status in localized colorectal cancer (CRC)?

 Dr Bekaii-Saab	Tissue testing
 Dr Cohen	Tissue testing
 Dr Dasari	Tissue testing
 Dr Fakih	Tissue testing
 Dr Lieu	Tissue testing
 Dr Saeed	Tissue testing

In general, which assay(s) do you employ to assess MSI/MMR status in localized CRC?

 Dr Bekaii-Saab	Both IHC and NGS
 Dr Cohen	Mainly NGS, ideally would like to do both IHC and NGS
 Dr Dasari	IHC
 Dr Fakih	Both IHC and NGS
 Dr Lieu	IHC
 Dr Saeed	Both IHC and NGS

IHC = immunohistochemistry; NGS = next-generation sequencing

Faculty Discussion

- **Which testing method do you generally use to assess MSI/MMR status in localized colorectal cancer (CRC)?**
- **In general, which assay(s) do you employ to assess MSI/MMR status in localized CRC?**

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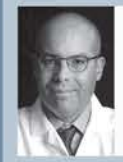
TO PRACTICE

Regulatory and reimbursement issues aside, what would you most likely recommend as neoadjuvant therapy for a 65-year-old patient with MSI-high (MSI-H)/MMR-deficient (dMMR) locally advanced rectal cancer?

 Dr Bekaii-Saab	Dostarlimab or pembrolizumab
 Dr Cohen	Dostarlimab
 Dr Dasari	Dostarlimab
 Dr Fakih	Dostarlimab
 Dr Lieu	Pembrolizumab
 Dr Saeed	Dostarlimab

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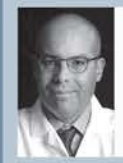
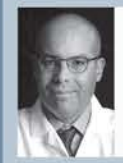
In which clinical situations are you currently administering an immune checkpoint inhibitor as a component of neoadjuvant therapy for a patient with MSI-H/dMMR early-stage rectal cancer?

 Dr Bekaii-Saab	Pretty much everyone and more as a NOM strategy
 Dr Cohen	Preferably for any patient with localized rectal cancer who does not have a contraindication to immunotherapy
 Dr Dasari	Any patient being considered for neoadjuvant therapy
 Dr Fakih	All cases unless the patient has an autoimmune disease that is prohibitive of IO therapy
 Dr Lieu	For any patient eligible for neoadjuvant therapy without contraindications to immune-checkpoint therapy
 Dr Saeed	Stage II and III

NOM = nonoperative management

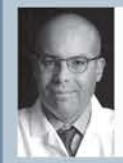
Regulatory and reimbursement issues aside, what would you most likely recommend as neoadjuvant therapy for a 65-year-old patient with MSI-H/dMMR locally advanced colon cancer?

 Dr Bekaii-Saab	None
 Dr Cohen	Nivolumab/ipilimumab
 Dr Dasari	None
 Dr Fakih	Nivolumab/ipilimumab
 Dr Lieu	Pembrolizumab
 Dr Saeed	Nivolumab/ipilimumab

Faculty Discussion

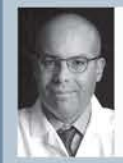
- **Regulatory and reimbursement issues aside, what would you most likely recommend as neoadjuvant therapy for a 65-year-old patient with MSI-H/dMMR locally advanced rectal cancer?**
- **In which clinical situations are you currently administering an immune checkpoint inhibitor as a component of neoadjuvant therapy for a patient with MSI-H/dMMR early-stage rectal cancer?**
- **Regulatory and reimbursement issues aside, what would you most likely recommend as neoadjuvant therapy for a 65-year-old patient with MSI-H/dMMR locally advanced colon cancer?**

Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with MSI-H/dMMR Stage III rectal cancer who receives 6 months of neoadjuvant dostarlimab and achieves a complete clinical response?

 Dr Bekaii-Saab	Observation
 Dr Cohen	Surgical resection followed by observation
 Dr Dasari	Observation
 Dr Fakih	Observation
 Dr Lieu	Observation
 Dr Saeed	Surgical resection followed by observation

RTP RESEARCH TO PRACTICE

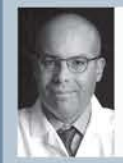
Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with MSI-H/dMMR Stage III rectal cancer who receives 6 months of neoadjuvant dostarlimab and does not achieve a complete clinical response?

 Dr Bekaii-Saab	Surgical resection followed by adjuvant chemotherapy
 Dr Cohen	Continue immunotherapy as long as there is some response even if not a full cCR; If no response or progression, then surgery
 Dr Dasari	Discussion on chemoradiation followed by surgery
 Dr Fakih	Surgical resection followed by observation
 Dr Lieu	Surgical resection followed by observation
 Dr Saeed	Surgical resection followed by observation

cCR = complete clinical response

RTP RESEARCH TO PRACTICE

A 65-year-old patient presents with high-risk Stage II MSI-H/dMMR colon cancer and undergoes R0 resection. Regulatory and reimbursement issues aside, what would be your preferred approach to adjuvant therapy?

 Dr Bekaii-Saab	Atezolizumab +/- CAPOX (3 months)
 Dr Cohen	For many, would observe; for those with T4, would discuss option FOLFOX/CAPOX + atezolizumab
 Dr Dasari	Observation unless MRD+ and/or T4b tumor
 Dr Fakih	Observation
 Dr Lieu	FOLFOX/CAPOX + atezolizumab
 Dr Saeed	FOLFOX/CAPOX + atezolizumab

MRD = molecular residual disease

RTP RESEARCH TO PRACTICE

A 65-year-old patient presents with Stage III MSI-H/dMMR colon cancer and undergoes R0 resection. Regulatory and reimbursement issues aside, what would be your preferred approach to adjuvant therapy?

 Dr Bekaii-Saab	Atezolizumab +/- CAPOX (3 months)
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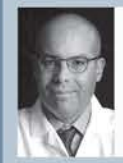
 Dr Dasari	FOLFOX/CAPOX + atezolizumab
 Dr Fakih	FOLFOX/CAPOX + atezolizumab or pembrolizumab monotherapy
 Dr Lieu	FOLFOX/CAPOX + atezolizumab
 Dr Saeed	FOLFOX/CAPOX + atezolizumab

RTP RESEARCH TO PRACTICE

Faculty Discussion

- **Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with MSI-H/dMMR Stage III rectal cancer who receives 6 months of neoadjuvant dostarlimab and achieves a complete clinical response?**
- **Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with MSI-H/dMMR Stage III rectal cancer who receives 6 months of neoadjuvant dostarlimab and does not achieve a complete clinical response?**
- **A 65-year-old patient presents with high-risk Stage II MSI-H/dMMR colon cancer and undergoes R0 resection. Regulatory and reimbursement issues aside, what would be your preferred approach to adjuvant therapy?**
- **A 65-year-old patient presents with Stage III MSI-H/dMMR colon cancer and undergoes R0 resection. Regulatory and reimbursement issues aside, what would be your preferred approach to adjuvant therapy?**

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Agenda

Module 1: Current and Future Role of Immune Checkpoint Inhibition in the Management of Microsatellite Instability-High (MSI-H)/Mismatch Repair Deficient (dMMR) Localized and Locally Advanced Colorectal Cancer (CRC) — Dr Cohen

Module 2: Clinical Relevance and Practical Utilization of Molecular Residual Disease (MRD) Analysis in CRC — Dr Dasari

Module 3: Recent Advances in Metastatic CRC (mCRC): Optimizing Immunotherapy and Other Approaches — Dr Bekaii-Saab

Clinical Relevance and Practical Utilization of Molecular Residual Disease (MRD) Analysis in CRC

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

Key Takeaway Points

1. *MRD assays available for clinical use in the United States and approved by CMS*

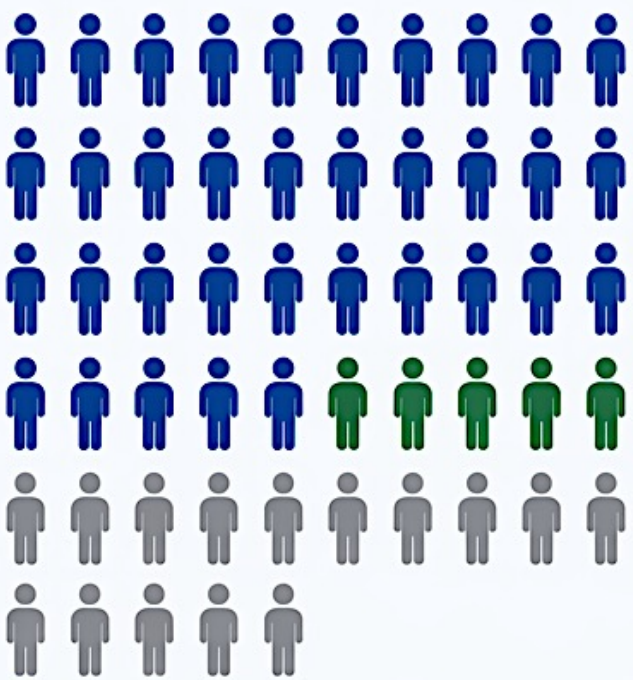
2. *Clinical validity established by observational studies; prospective clinical utility studies are ongoing*

3. *Unique opportunity to integrate research & clinical practice for efficient and rapid generation of missing data*

Adjuvant Therapy for Colon Cancer

What Happens After Surgery for Stage III Colon Cancer?

Right now, we treat many patients with adjuvant chemotherapy, but only some truly benefit.



40%
Cured with surgery (didn't need chemotherapy)

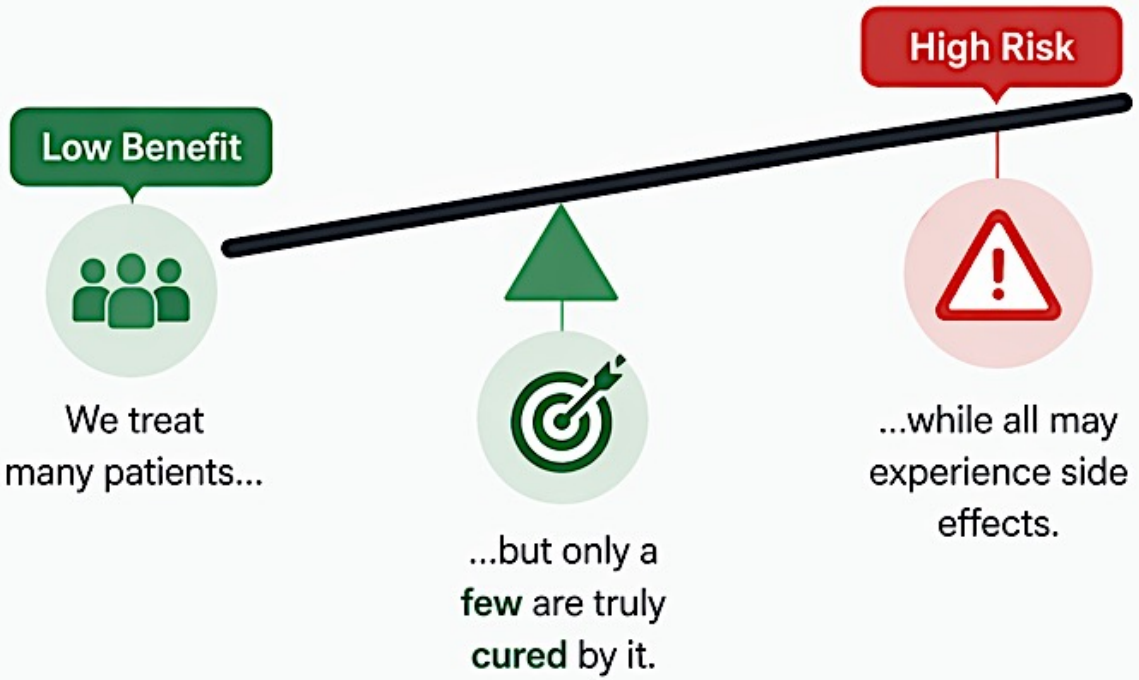
25%
Cured (benefited) from chemotherapy

35%
Cancer comes back (recurrence – no benefit)

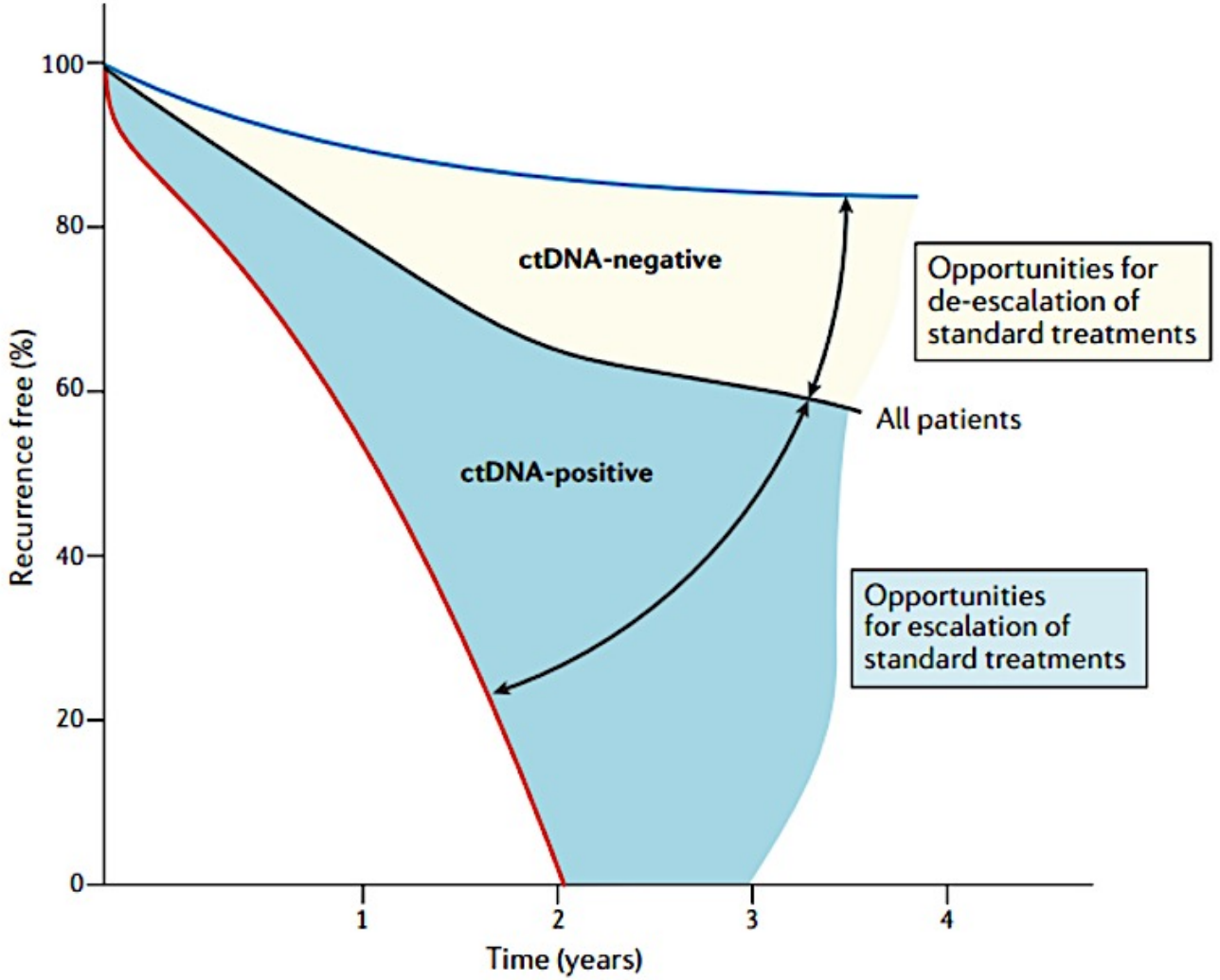
Patients treated with adjuvant chemotherapy

The Current Challenge of Adjuvant Chemotherapy

Finding the right balance between helping patients and avoiding unnecessary side effects.



MRD For Adjuvant Therapy Decisions



Dasari et al, Nat Rev Clin Oncol. 2020

Observational Studies & What We Know

1. MRD is VERY strongly prognostic for recurrence

	BESPOKE	GALAXY	INTERCEPT
n	627	2860	1140
Stage	II-IV	II-III	II-IV
HR for DFS	12.1	10.5	22.6

Kasi et al, J Clin Oncol 42, 2024 (suppl 3; abstr 9)
Kotani et al, Nat Med. 2023 Jan;29(1):127-134
Nakamura et al, Nat Med. 2024 Nov;30(11):3272-3283
Maddalena et al, J Clin Oncol 42, 2024 (suppl 3; abstr 27)
Maddalena et al, unpublished data

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2. MRD-ve: Recurrence low irrespective of adjuvant therapy

	BESPOKE	GALAXY	INTERCEPT
n	530	2860	532
2-year DFS (%)			
With ACT	93.7	89.1	85.6
Without ACT	90.4	90	83.8

Kasi et al, J Clin Oncol 42, 2024 (suppl 3; abstr 9)
Kotani et al, Nat Med. 2023 Jan;29(1):127-134
Nakamura et al, Nat Med. 2024 Nov;30(11):3272-3283
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Dasari A et al. ASCO GI 2025

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Stage	II-IV	II-III	II-IV
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2. MRD-ve: Recurrence low irrespective of adjuvant therapy

	BESPOKE	GALAXY
n	530	2860
2-year DFS (%)		
With ACT	93.7	89.1
Without ACT	90.4	90

3. MRD+ve: Recurrence high even with adjuvant therapy

	BESPOKE	GALAXY	INTERCEPT
n	96	192	532
2-year DFS (%)			
With ACT	42.4	35.8	12.8
Without ACT	12.5	2.8	2.6

Kasi et al, J Clin Oncol 42, 2024 (suppl 3; abstr 9)
Kotani et al, Nat Med. 2023 Jan;29(1):127-134
Nakamura et al, Nat Med. 2024 Nov;30(11):3272-3283
Maddalena et al, J Clin Oncol 42, 2024 (suppl 3; abstr 27)
Maddalena et al, unpublished data

Dasari A et al. ASCO GI 2025

Where Are We Today ?

Acceptable performance & reproducibility

Correlation with clinical endpoint

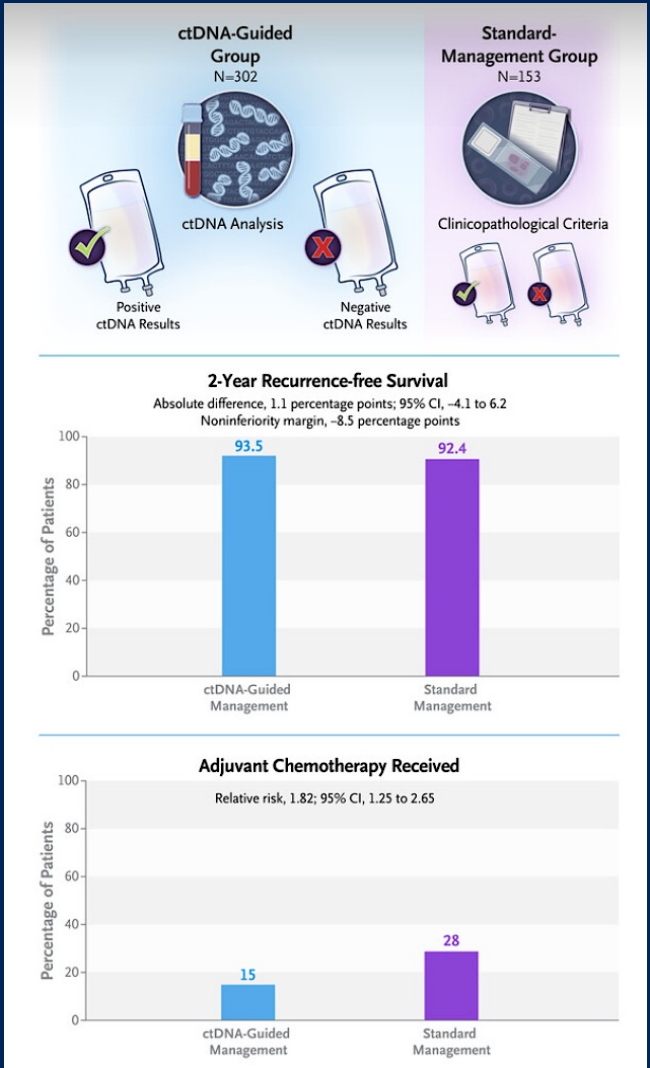
i.e. defining subgroups with different outcomes

MRD in CRC

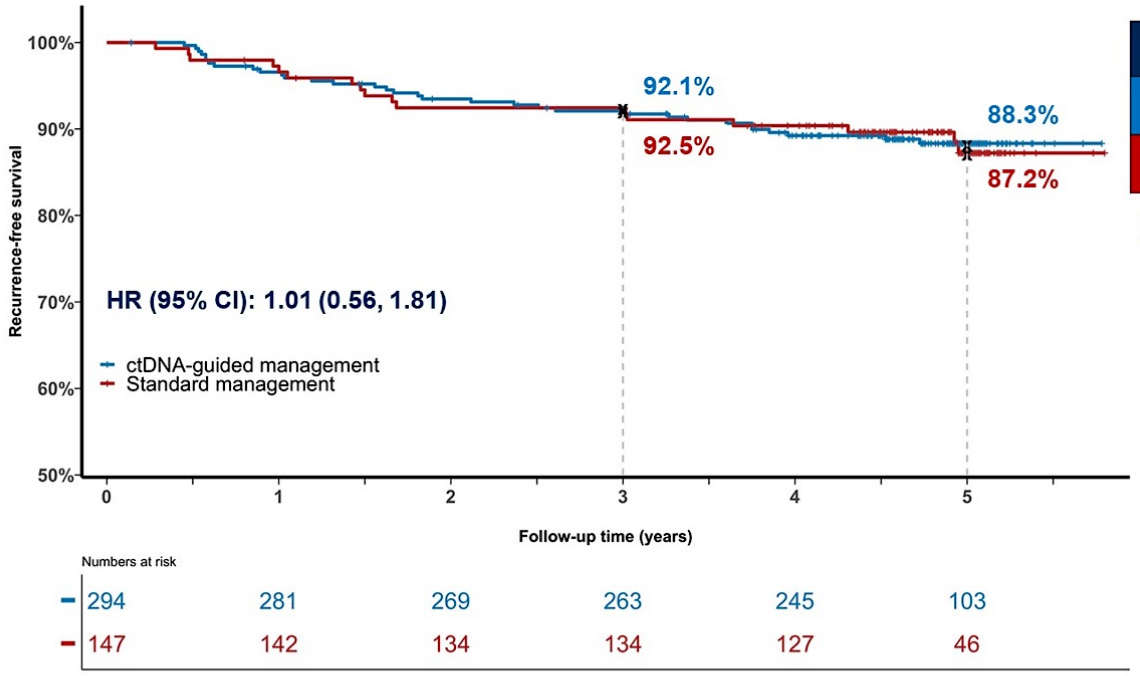
Improving clinical outcomes

Reference. Hayes et al, J Clin Oncol. 2021 Jan 20;39(3):238-248

Completed Randomized Trials: DYNAMIC II



Updated 5-Year RFS Analysis



5-Year RFS Rate, %	
ctDNA	88.3
SoC	87.2

Difference in 5-year RFS rate +1.1%
(95% CI for difference, -5.8 to 8.0%)

Median Follow-Up
ctDNA-Guided 59.7 months
SoC 59.7 months
(IQR 55.0 – 61.5)

Data cut-off: 17 Jan 2024

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Jeanne Tie, MBChB FRACP MD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Tie et al, N Engl J Med. 2022 Jun 16;386(24):2261-2272

DYNAMIC-III Study Design Randomized Phase II/III (ACTRN12617001566325)

Stage III Colon Cancer

- R0 resection
- ECOG 0 – 2
- Fit for at least a fluoropyrimidine (FP)
- Staging CT within 12 weeks
- Provision of adequate tumor tissue < 6 weeks post-operation
- No synchronous colorectal cancer

Tumor-Informed ctDNA Analysis
(SaferSeqS[1] targeted CRC panel)

W5-6

R 1:1

Clinicians nominate SoC Chemo

ctDNA-Informed Management

- **ctDNA-Negative → De-escalate**
- **ctDNA-Positive → Escalate**

1 cycle of pre-planned chemotherapy allowed prior to ctDNA-informed regimen

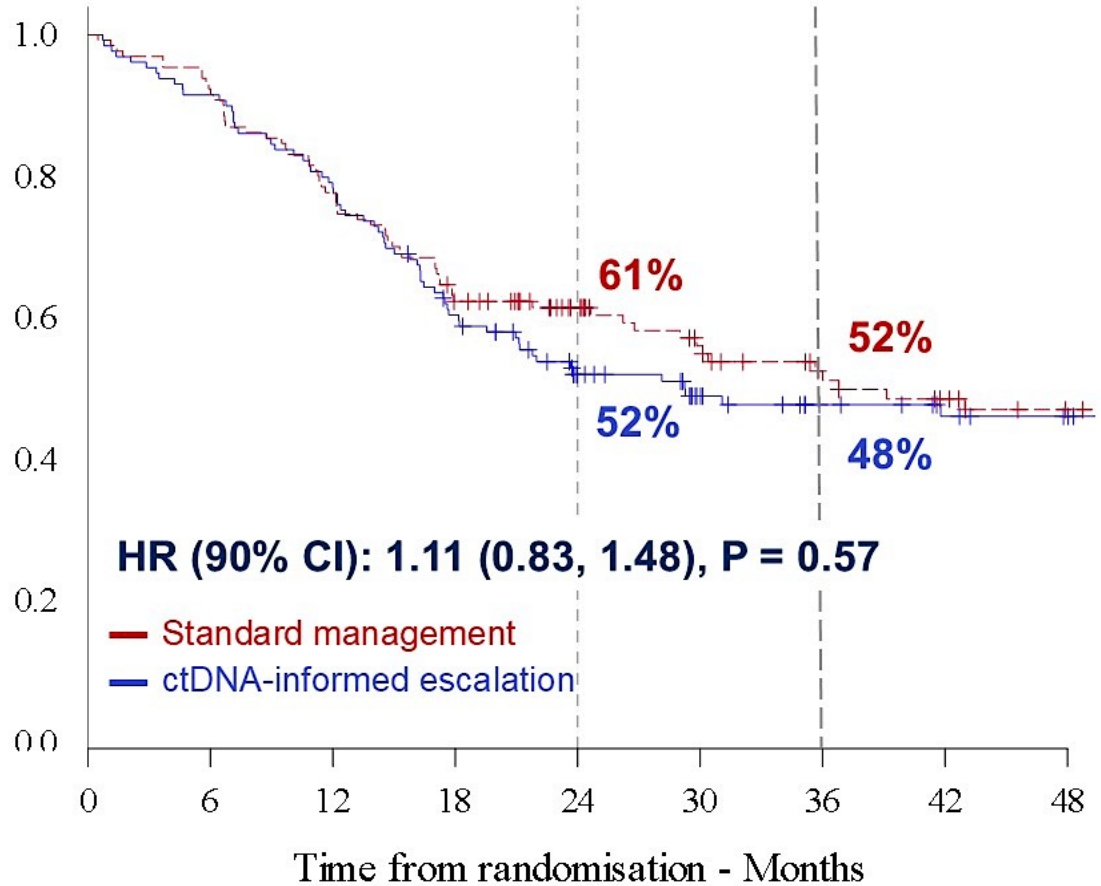
Pre-Planned SoC → Escalation
No chemotherapy → 5FU/Cape
5FU/Cape → 6M Oxaliplatin doublet
3M Oxaliplatin doublet → 6M Doublet or ≥ 3M FOLFOXIRI
6M Oxaliplatin doublet → ≥ 3M FOLFOXIRI

Standard Management

Treatment per clinician's choice (blinded to ctDNA result)

Stratified by clinical risk (low vs high) and sites

Recurrence-Free Survival



	Total	Events	Median RFS (mths)	2-year RFS (90% CI)	3-year RFS (90% CI)
ctDNA	129	66	29.24	52% (44, 59)	48% (40, 55)
SoC	130	62	36.80	61% (54, 68)	52% (44, 60)

Median follow-up 42.2 months (0.78 - 63.0)

Data cut-off: 14 Nov 2024

DYNAMIC-III Study Design Randomised Phase II/III (ACTRN12617001566325)

Stage III Colon Cancer

- R0 resection
- ECOG 0 – 2
- Fit for at least a fluoropyrimidine (FP)
- Staging CT within 12 weeks
- Provision of adequate tumor tissue < 6 weeks post-operation
- No synchronous colorectal cancer

Tumour-Informed ctDNA Analysis
(SaferSeqS[1] targeted CRC panel)

W5-6

R 1:1

Clinicians nominate SoC Chemo

ctDNA-Informed Management

- ctDNA-Negative → De-escalate
- ctDNA-Positive → Escalate

1 cycle of pre-planned chemotherapy allowed prior to ctDNA-informed regimen

Pre-Planned SoC → De-escalation

6M FP → No chemo or 3M FP
3M Oxaliplatin + FP → 3-6M FP
6M Oxaliplatin + FP → 3M Oxaliplatin + FP or 6M FP

FP = fluoropyrimidine

Standard Management

Treatment per clinician's choice (blinded to ctDNA result)

Stratified by clinical risk (low vs high) and sites

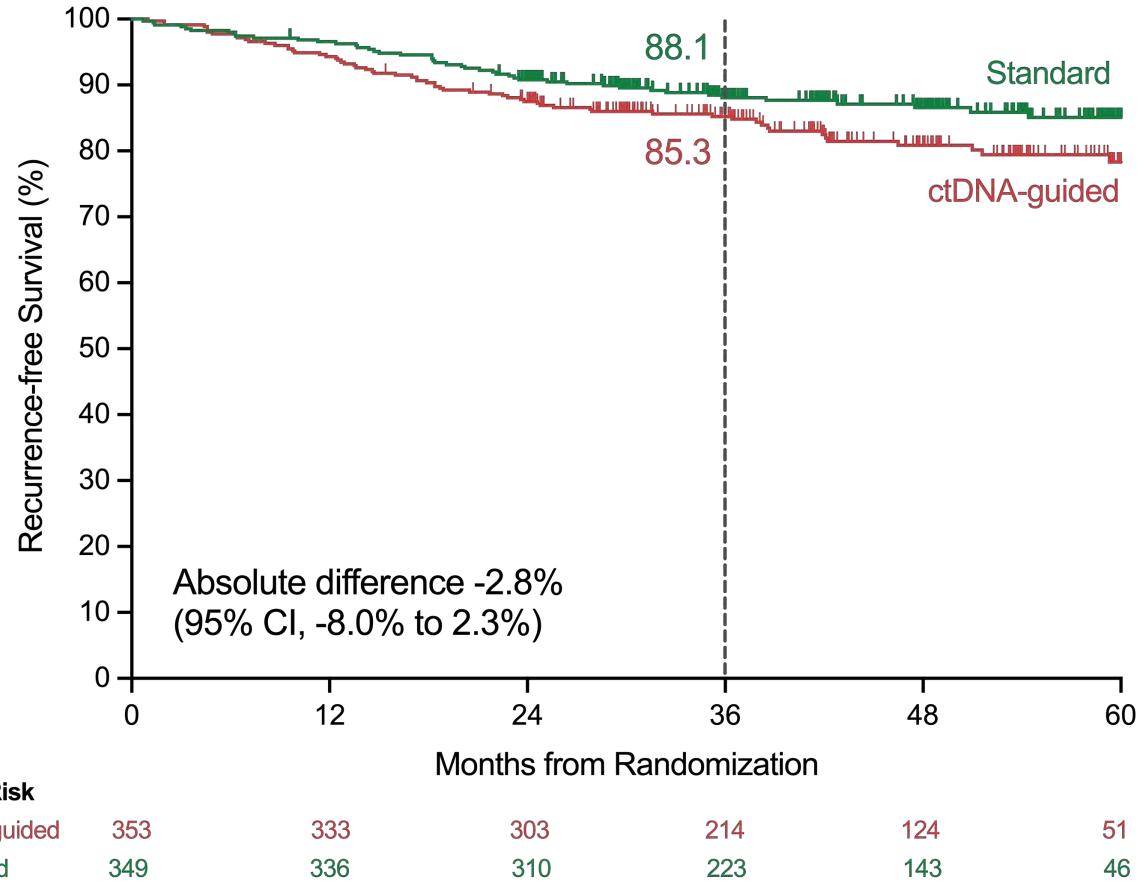
Primary Analysis of ctDNA-Negative Cohort: Endpoints to be Presented Here

Primary	Secondary
Primary: 3-year recurrence-free survival (RFS)	Secondary: treatment adherence, safety

Jeanne Tie

1. Cohen, J.D. et al. Nat Biotechnol 39, 1220–1227 (2021)

Recurrence-Free Survival



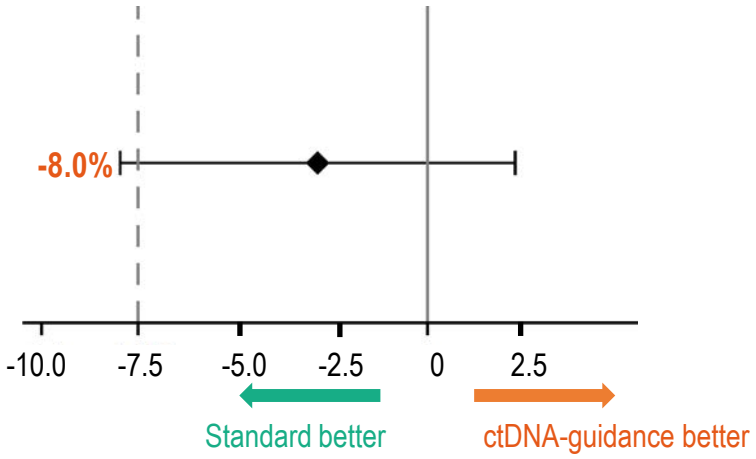
No. at Risk

ctDNA-guided	353	333	303	214	124	51
Standard	349	336	310	223	143	46

Median follow-up 47 months (0.68 - 67.0)

Arm	Total	Events	3-year RFS (95% CI)
ctDNA	353	63	85.3% (81, 89)
Standard	349	45	88.1% (84, 91)

Absolute Difference in 3-year RFS (95% CI)

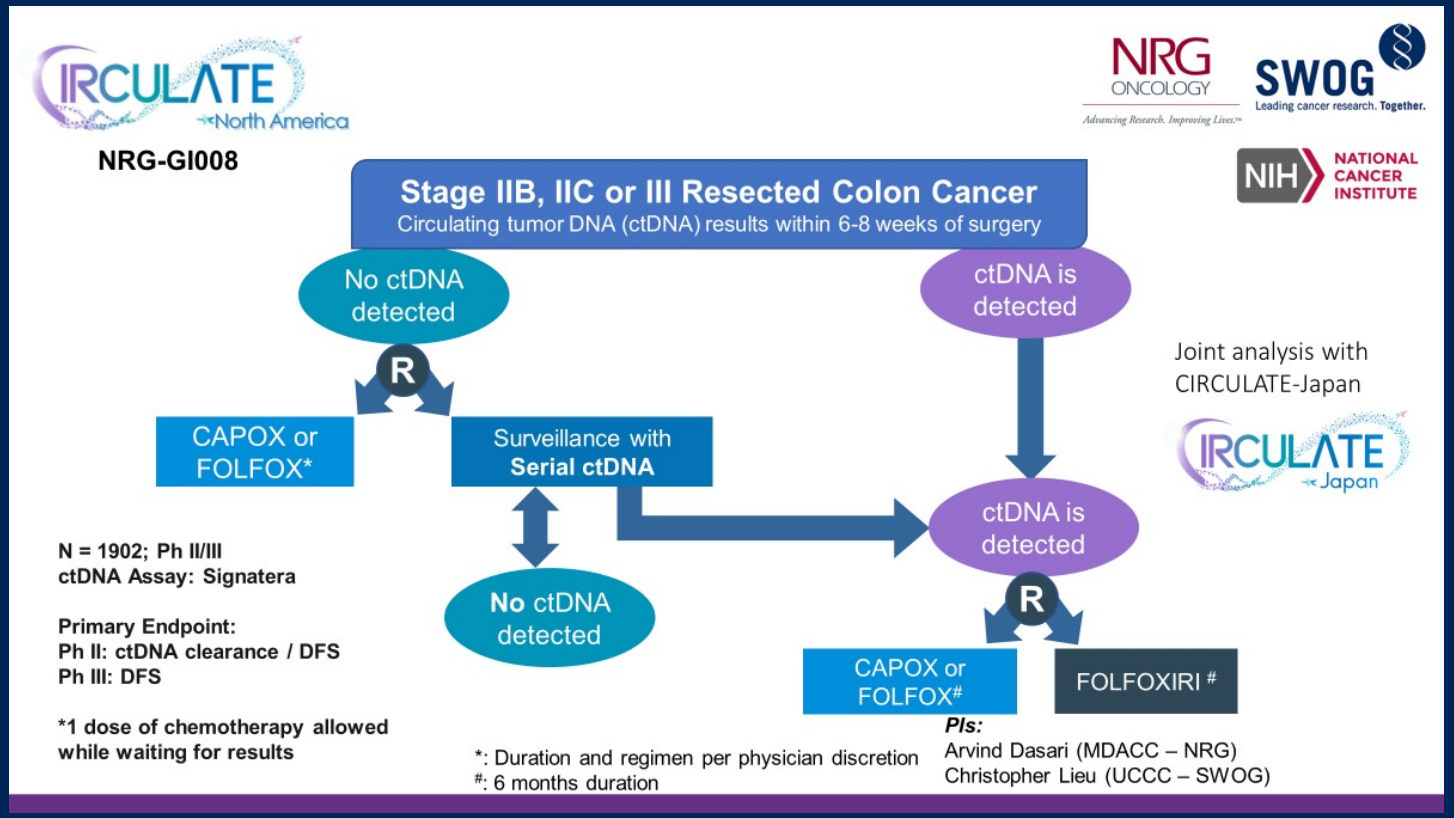


Jeanne Tie

Database lock July 29, 2025

Tie J et al. Nat Med 2025

CIRCULATE – North America (NRG-GI008): Case Study in Research to Practice

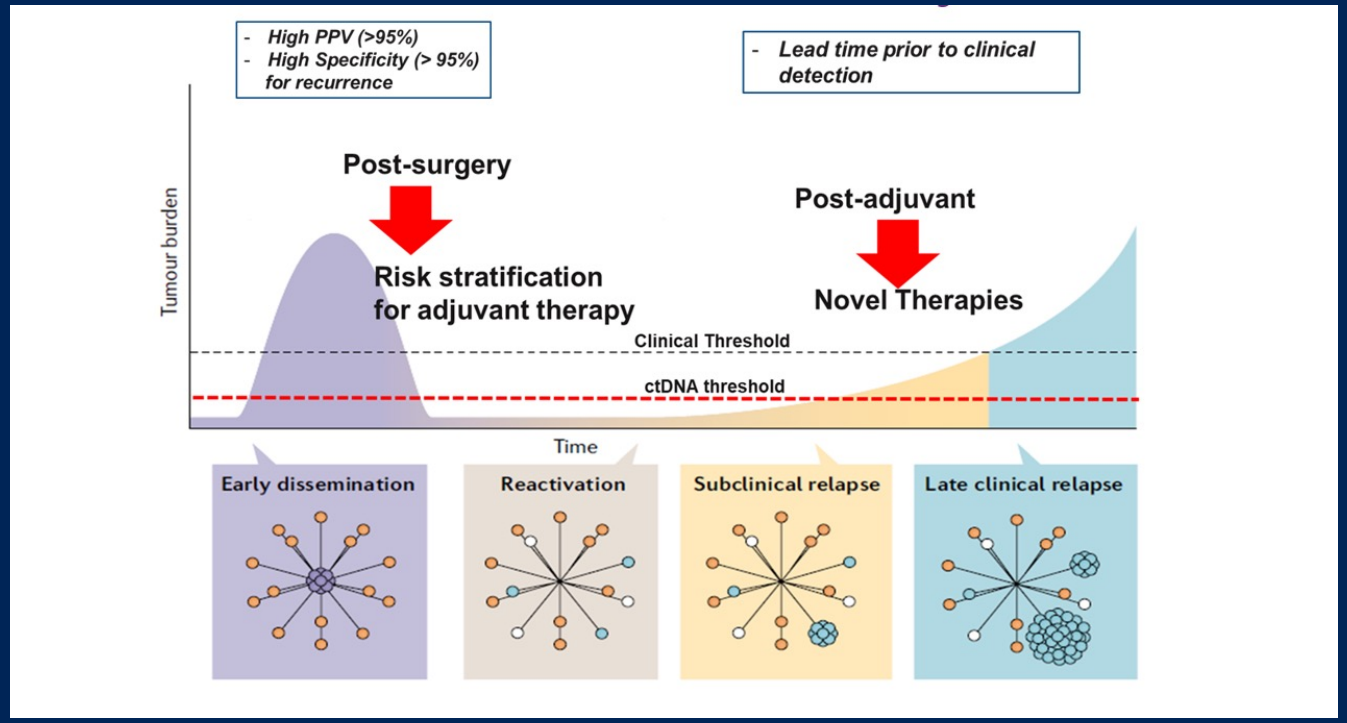


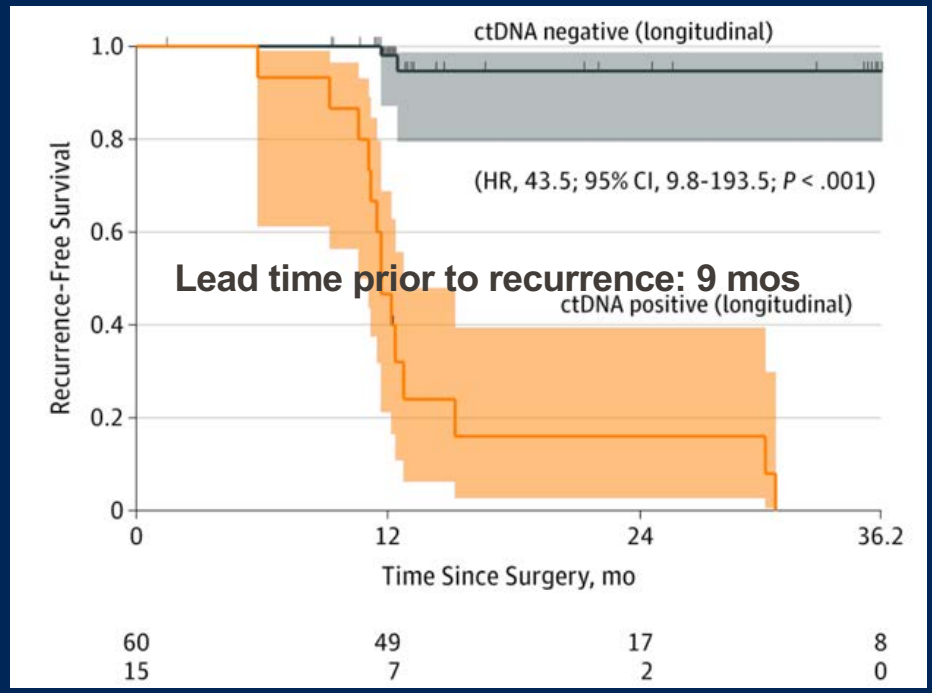
Since initiation, eligibility criteria expanded

Ongoing discussions to:
- **Link on & off study testing**

NCT05174169

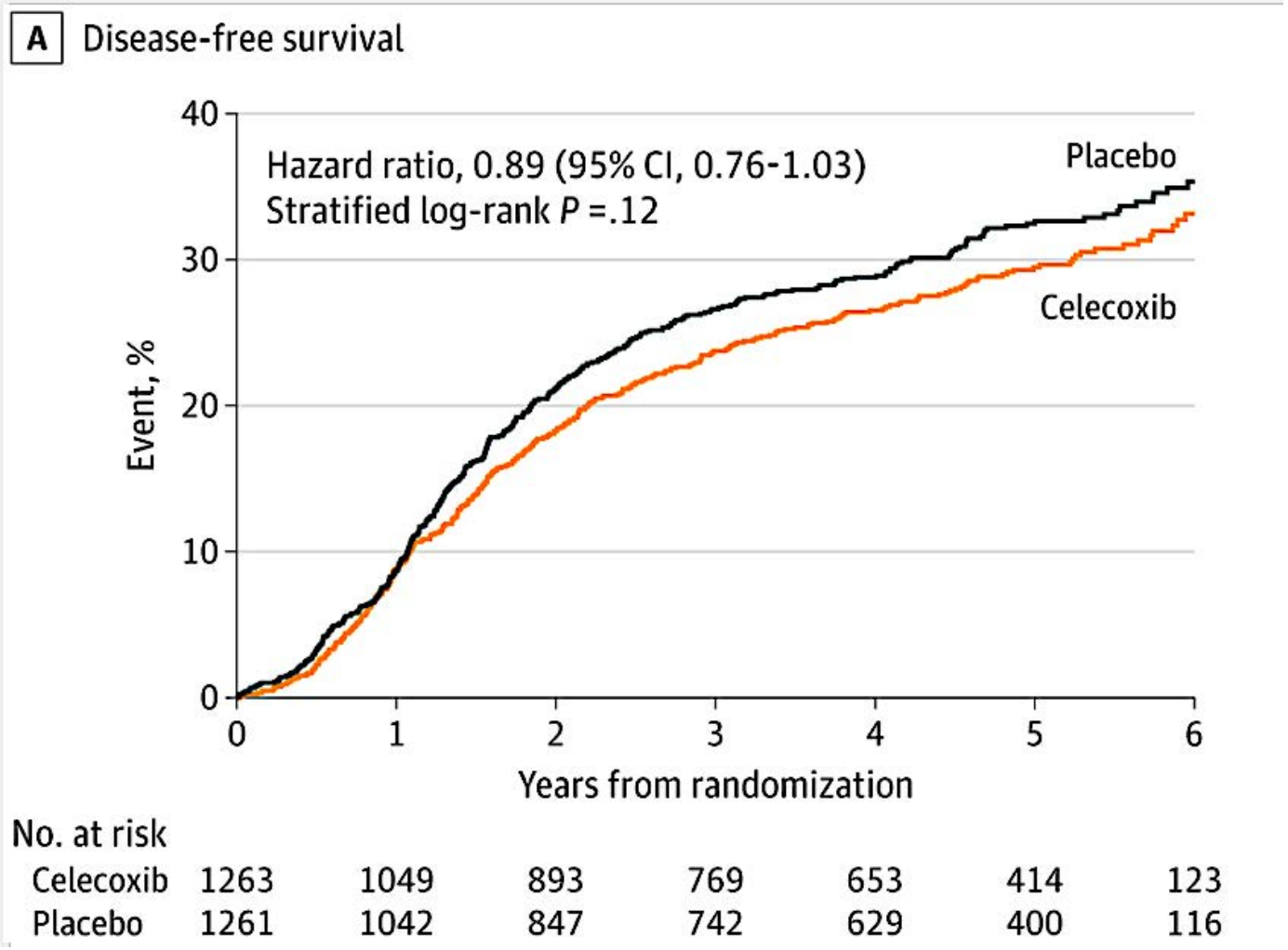
Clinical Validity : Timepoints & Applications





Phan et al, Nat Rev Cancer. 2020 Jul;20(7):398-411
Reinert et al, JAMA Oncology. JAMA Oncol. 2019 Aug 1;5(8):1124-1131

CALGB 80702 Trial: Effect of Celecoxib Added to Adjuvant Therapy : Initial Analysis (All Patients)



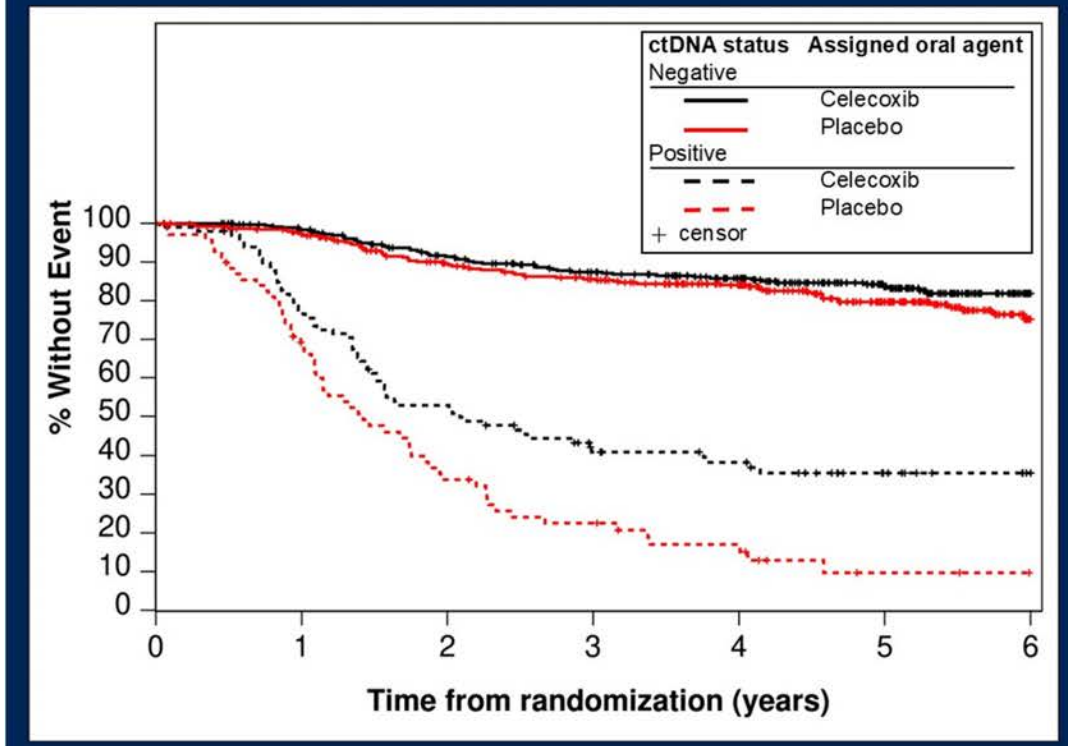
HR = 0.89 (95% CI, 0.76 – 1.03)

Meyerhardt et al, JAMA 2021

CALGB 80702 Study Re-Analysis According to ctDNA Status

13

Disease-free survival by ctDNA status and celecoxib use

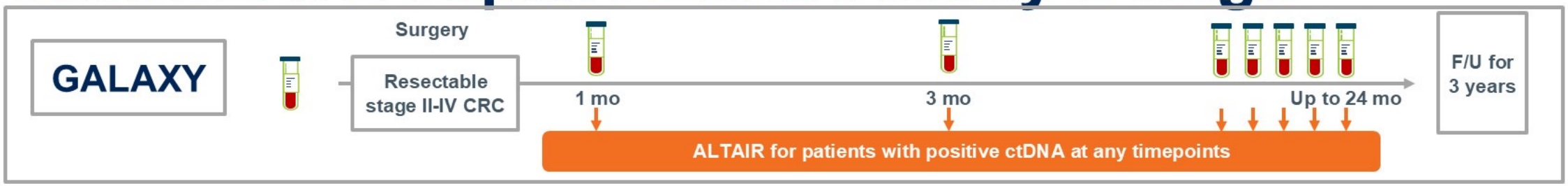


Assigned Oral Agent by ctDNA status	Events / Total	Hazard Ratio (95% CI)[1]	3 Year Survival Estimate (95% CI)[2]	P-value
Negative				0.1293[4]
Celecoxib	58/375	0.76 (0.54-1.08)	87.4 (84.0-91.0%)	
Placebo	73/392	Reference	85.6 (82.0-89.4%)	
Positive				0.0013[4]
Celecoxib	61/99	0.55 (0.39-0.80)	41.0 (32.2-52.2%)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

Zhang GQ et al. JAMA Oncol. 2025

CIRCULATE-Japan ALTAIR Study Design



ALTAIR

Patients with
- Colorectal adenocarcinoma
- Radical resection of the primary and metastatic tumors
- History of standard postoperative chemotherapy
- Positive for ctDNA using Signatera™ within 3 months prior to enrollment
- No evidence of clinical relapse by CT scans
- Aged ≥20 years
- ECOG performance status (PS) of 0 or 1
- Adequate organ function

Stratification factors:
- Stage
- ctDNA status one month after curative resection

R
1:1

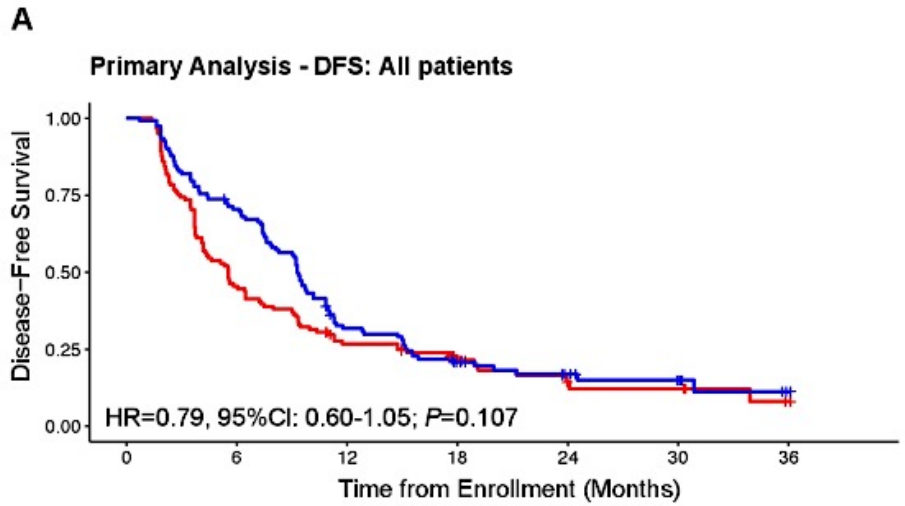
N=243

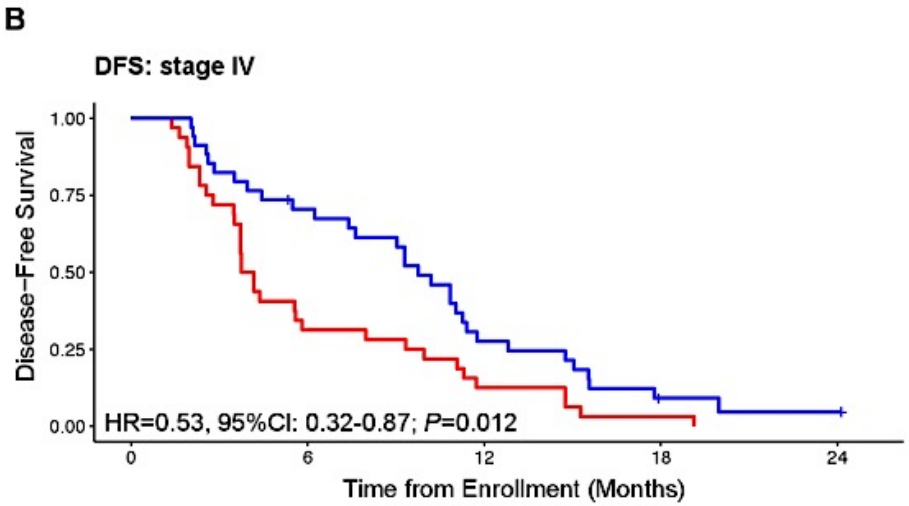
Experimental Arm
Trifluridine/tipiracil
35mg/m2 BSA, BID orally
day 1-5 and day 8-12; Q28D
6 cycles

Control Arm
Placebo
BID orally
day 1-5 and day 8-12; Q28D
6 cycles

Primary endpoint: Disease-free survival (DFS)
Secondary endpoints: ctDNA clearance rate, overall survival, AEs, treatment completion rate, and QOL

ALTAIR Study Results





Treatment status	FTD/TPI	Placebo
Events %	81.15 (99/122)	81.82 (99/121)
6M-DFS %	70.5 (61.5-77.7)	45.5 (36.42–54)
12M-DFS %	31.8 (23.6–40.2)	26.8 (19.16–35)
18M-DFS %	20.8 (13.9–28.7)	21.5 (14.43–29.6)
24M-DFS %	16.9 (10.4–24.8)	14.5 (7.85–23.1)
mDFS (mo)	9.30 (7.92–10.84)	5.55 (4.17–7.33)

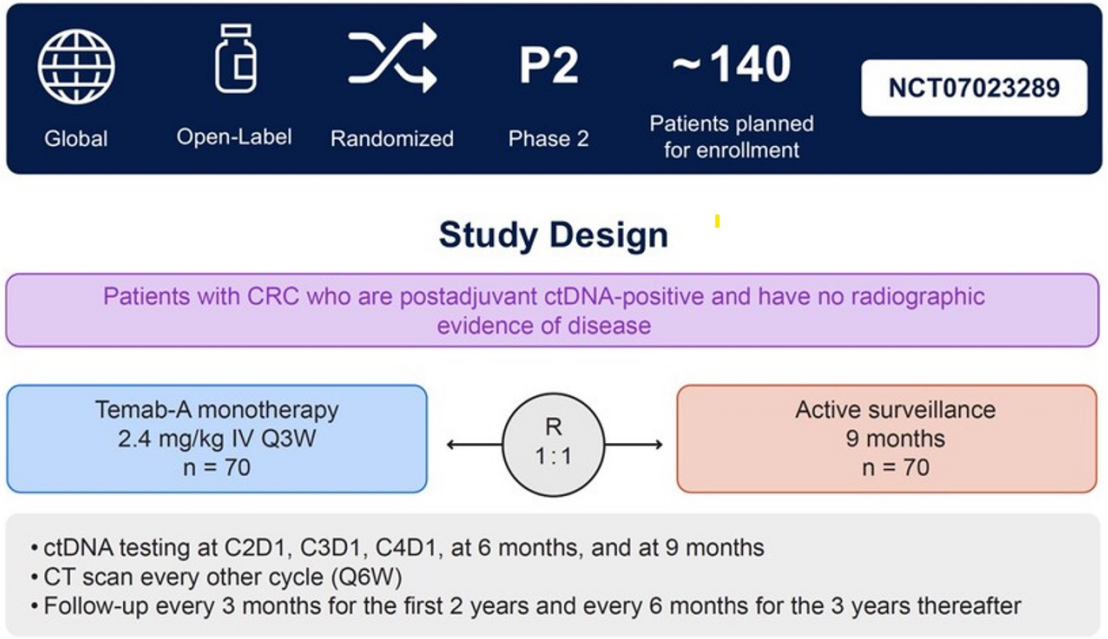
DFS analysis stratified by Stage (Stage II or Lower, Stage III or M1) and ctDNA status 1mo post-surgery (Positive vs Negative/Unmeasured)

Treatment status	FTD/TPI	Placebo
Events %	94.12 (31/34)	100 (32/32)
6M-DFS %	70.47 (52.05–82.9)	31.25 (16.38–47.3)
12M-DFS %	27.57 (13.79–43.3)	12.5 (3.95–26.2)
18M-DFS %	9.19 (.236–21.9)	3.12 (0.24–13.7)
24M-DFS %	4.60 (0.43–17.5)	NR
mDFS (mo)	9.76 (7.62–11.76)	3.96 (3.71–7.98)

Enrollment ctDNA timepoint MTM/mL
Stage IV patients vs non-Stage IV: 0.68 vs 0.32, *P* = 0.024

Bando et al GI ASCO 2025

Ongoing ctDNA Trials



A phase 2 randomized study comparing telisotuzumab adizutecan monotherapy with standard of care in patients with post-adjuvant circulating tumor DNA-positive colorectal cancer (NCT07023289)

Phase 3 STELLAR-316 Pivotal Trial Planned for Patients with Colorectal Cancer

Press Release: May 19, 2026

Zanzalintinib with and without pembrolizumab sc in patients with resected stage II/IIICRC who, following definitive therapy, have tested positive for molecular residual disease (MRD+). The primary endpoint of the trial will be disease-free survival, with key secondary endpoints including circulating tumor DNA clearance.

Raghav et al, GI ASCO 2026; Exelixis Press Release, 5/19/26

Benefit of Adjuvant Chemotherapy in Resected Stage I-IV CRC Patients Based on ctDNA Dynamics Across Two Timepoints: Results from GALAXY Study

Yokota M et al.

ASCO 2026; Abstract 102.

ctDNA in Clinical Practice: From Early Detection to Clinical Decision-Making

Clinical Science Symposium

SATURDAY, MAY 30, 2026

8:00 – 9:30 AM CDT

RTP RESEARCH TO PRACTICE

Disease-Free Survival (DFS) and Time to Recurrence (TTR) with Circulating Tumor (ct) DNA–Based Decision for Adjuvant Treatment in Colon Cancer Stage II (CIRCULATE): An AIO (KRK-0217)/ABCSG Trial

Folprecht G et al.

ASCO 2026; Abstract LBA3500.

Gastrointestinal Cancer—Colorectal and Anal

SUNDAY, MAY 31, 2026

8:00 – 8:12 AM CDT

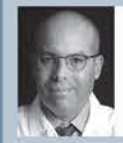
Key Takeaway Points

1. *MRD assays available for clinical use in the United States and approved by CMS*

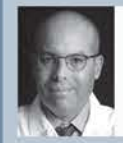
2. *Clinical validity established by observational studies; prospective clinical utility studies are ongoing*

3. *Unique opportunity to integrate research & clinical practice for efficient and rapid generation of missing data*

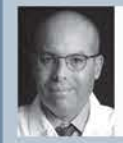
Outside of a clinical trial setting, to what extent do you use ctDNA-based MRD testing in the following scenarios?

	Resected Stage II colon cancer with no high-risk features	Resected Stage II colon cancer with high-risk features
 Dr Bekaii-Saab	Occasionally	Commonly
 Dr Cohen	Usually or always	Usually or always
 Dr Dasari	Usually or always	Usually or always
 Dr Fakih	Usually or always	Usually or always
 Dr Lieu	Commonly	Commonly
 Dr Saeed	Occasionally	Commonly

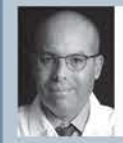
Outside of a clinical trial setting, to what extent do you use ctDNA-based MRD testing in the following scenarios?

	Resected Stage III colon cancer with low-risk features	Resected Stage III colon cancer with high-risk features
 Dr Bekaii-Saab	Commonly	Commonly
 Dr Cohen	Usually or always	Usually or always
 Dr Dasari	Usually or always	Usually or always
 Dr Fakih	Usually or always	Usually or always
 Dr Lieu	Commonly	Commonly
 Dr Saeed	Commonly	Commonly

Outside of a clinical trial setting, to what extent do you use ctDNA-based MRD testing in the following scenarios?

	Resected oligometastatic disease	Localized rectal cancer
 Dr Bekaii-Saab	Usually or always	Commonly
 Dr Cohen	Usually or always	Commonly
 Dr Dasari	Usually or always	Usually or always
 Dr Fakih	Usually or always	Usually or always
 Dr Lieu	Usually or always	Occasionally
 Dr Saeed	Commonly	Commonly

Outside of a clinical trial, would you be comfortable omitting or de-escalating adjuvant systemic therapy on the basis of negative ctDNA results alone for a _____ with Stage II CRC and high-risk features?

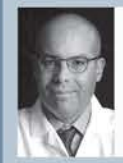
	Younger patient (eg, 65 years old)	Older patient (eg, 85 years old and somewhat frail)
 Dr Bekaii-Saab	No	Yes
 Dr Cohen	No	Yes
 Dr Dasari	No	Yes
 Dr Fakih	Yes	Yes
 Dr Lieu	No	Yes
 Dr Saeed	No	Yes

Faculty Discussion

- **Outside of a clinical trial setting, to what extent do you use ctDNA-based MRD testing in the following scenarios?**
  - **Stage II colon cancer with no high-risk features**
  - **Stage II colon cancer with high-risk features**
  - **Stage III colon cancer with low-risk features**
  - **Stage III colon cancer with high-risk features**
  - **Colorectal cancer and fully resected oligometastatic disease**
  - **Localized rectal cancer**

- **Outside of a clinical trial, would you be comfortable omitting or de-escalating adjuvant systemic therapy on the basis of negative ctDNA results alone for a younger patient (eg, age 65) with Stage II CRC and high-risk features? Older patient (eg, 85 years old and somewhat frail)?**

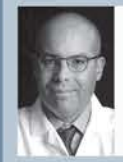
If you were to use serial ctDNA testing for a patient with localized CRC who had undergone surgical resection with or without adjuvant systemic therapy, at what intervals would you do so?

 Dr Bekaii-Saab	Every 3 months for 2-3 years
 Dr Cohen	Post-surgery/pre-chemo, after 3 months of chemo, q3m x 2 years total
 Dr Dasari	Every 3-6 months along with CEA
 Dr Fakih	Every 3 months for 2 years, then every 6 months for 3 years
 Dr Lieu	Every 3 months for 2 years
 Dr Saeed	Every 3 months

CEA = carcinoembryonic antigen

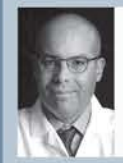
RTP RESEARCH TO PRACTICE

Have you employed or would you employ ctDNA testing to monitor for response to adjuvant therapy in patients with localized CRC?

 Dr Bekaii-Saab	I have not and would not
 Dr Cohen	I have
 Dr Dasari	I have
 Dr Fakih	I have not but would for the right patient
 Dr Lieu	I have
 Dr Saeed	I have

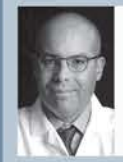
RTP RESEARCH TO PRACTICE

A 65-year-old patient presents with microsatellite-stable (MSS) Stage II CRC with no high-risk features and undergoes R0 resection. What would be your approach to adjuvant therapy?

 Dr Bekaii-Saab	Observation
 Dr Cohen	Observation
 Dr Dasari	Check MRD and offer FOLFOX/CAPOX if positive. Offer 3 mo of capecitabine or 5-FU if the patient wants to do adjuvant tx
 Dr Fakih	Observation
 Dr Lieu	Observation
 Dr Saeed	Observation

RTP RESEARCH TO PRACTICE

A 65-year-old patient presents with MSS Stage II CRC with no high-risk features and undergoes R0 resection. If a ctDNA assay were ordered, what would be your approach to treatment if the results were positive?

 Dr Bekaii-Saab	Close observation (shortened intervals)
 Dr Cohen	Observation
 Dr Dasari	FOLFOX/CAPOX
 Dr Fakih	FOLFOX/CAPOX
 Dr Lieu	FOLFOX/CAPOX
 Dr Saeed	FOLFOX/CAPOX

Faculty Discussion

- **If you were to use serial ctDNA testing for a patient with localized CRC who had undergone surgical resection with or without adjuvant systemic therapy, at what intervals would you do so?**
- **Have you employed or would you employ ctDNA testing to monitor for response to adjuvant therapy in patients with localized CRC?**
- **A 65-year-old patient presents with MSS Stage II CRC with no high-risk features and undergoes R0 resection. What would be your approach to adjuvant therapy?**
- **A 65-year-old patient presents with MSS Stage II CRC with no high-risk features and undergoes R0 resection. If a ctDNA assay were ordered, what would be your approach to treatment if the results were positive?**

Agenda

Module 1: Current and Future Role of Immune Checkpoint Inhibition in the Management of Microsatellite Instability-High (MSI-H)/Mismatch Repair Deficient (dMMR) Localized and Locally Advanced Colorectal Cancer (CRC) — Dr Cohen

Module 2: Clinical Relevance and Practical Utilization of Molecular Residual Disease (MRD) Analysis in CRC — Dr Dasari

Module 3: Recent Advances in Metastatic CRC (mCRC): Optimizing Immunotherapy and Other Approaches — Dr Bekaii-Saab

MAYO CLINIC

Recent Advances in Metastatic CRC (mCRC): Optimizing Immunotherapy and Other Approaches

Tanios Bekaii-Saab, MD , FACP, FASCO

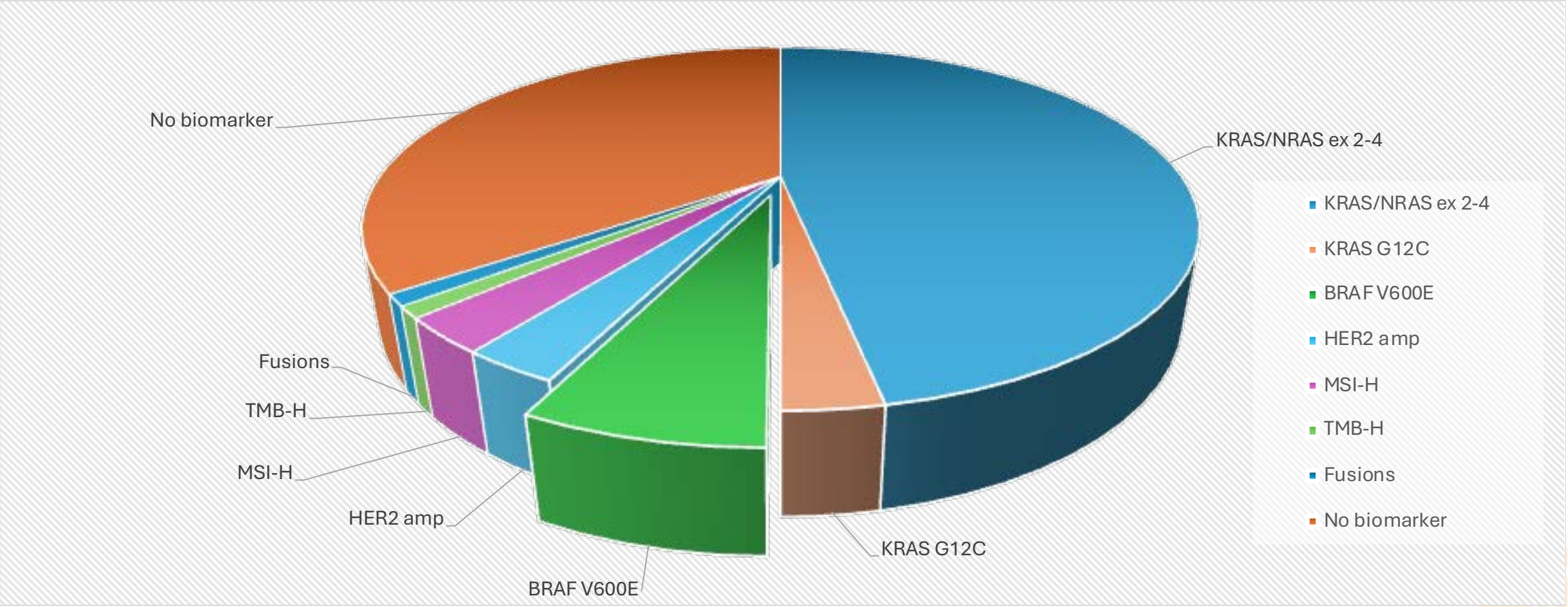
David F. and Margaret T. Grohne Professor of Novel Therapeutics for Cancer Research I

Chair and Consultant, Division of Hematology and Medical Oncology

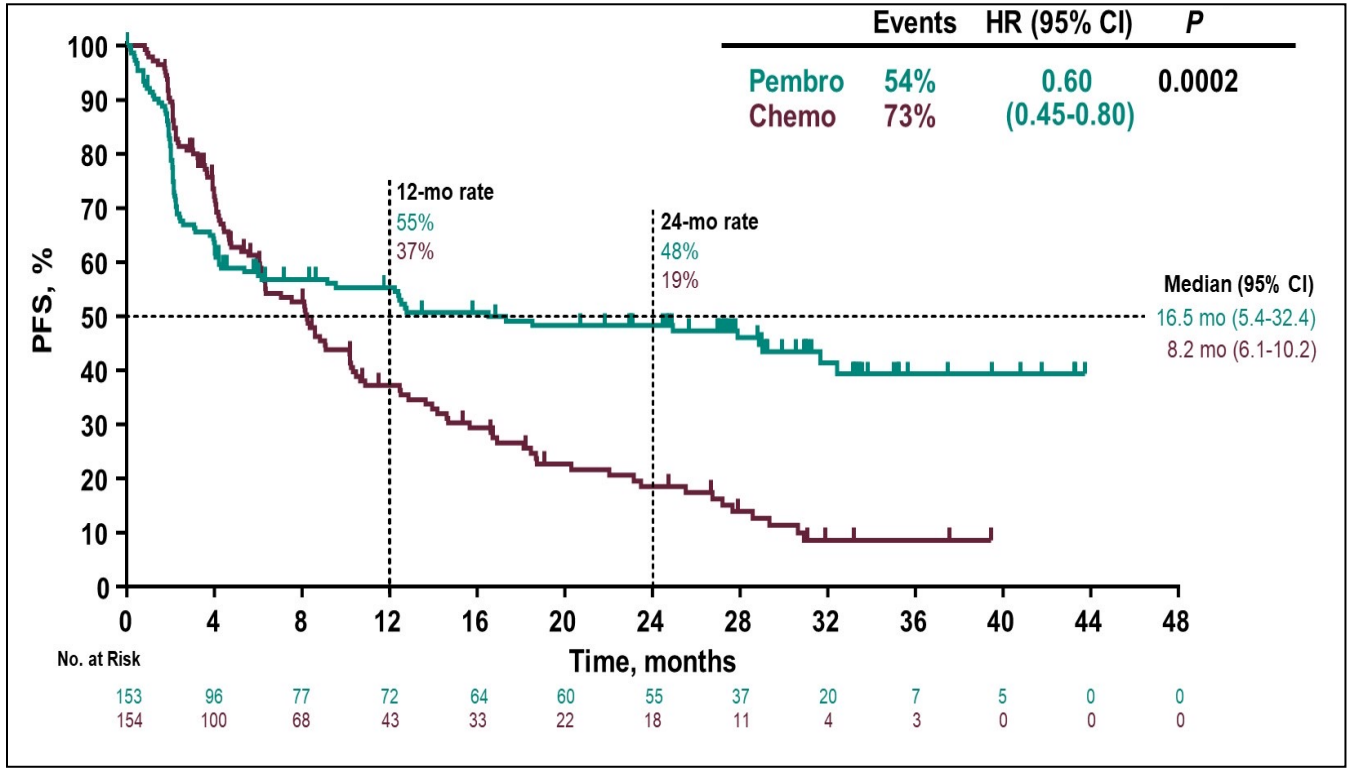
Professor, Mayo Clinic College of Medicine and Science

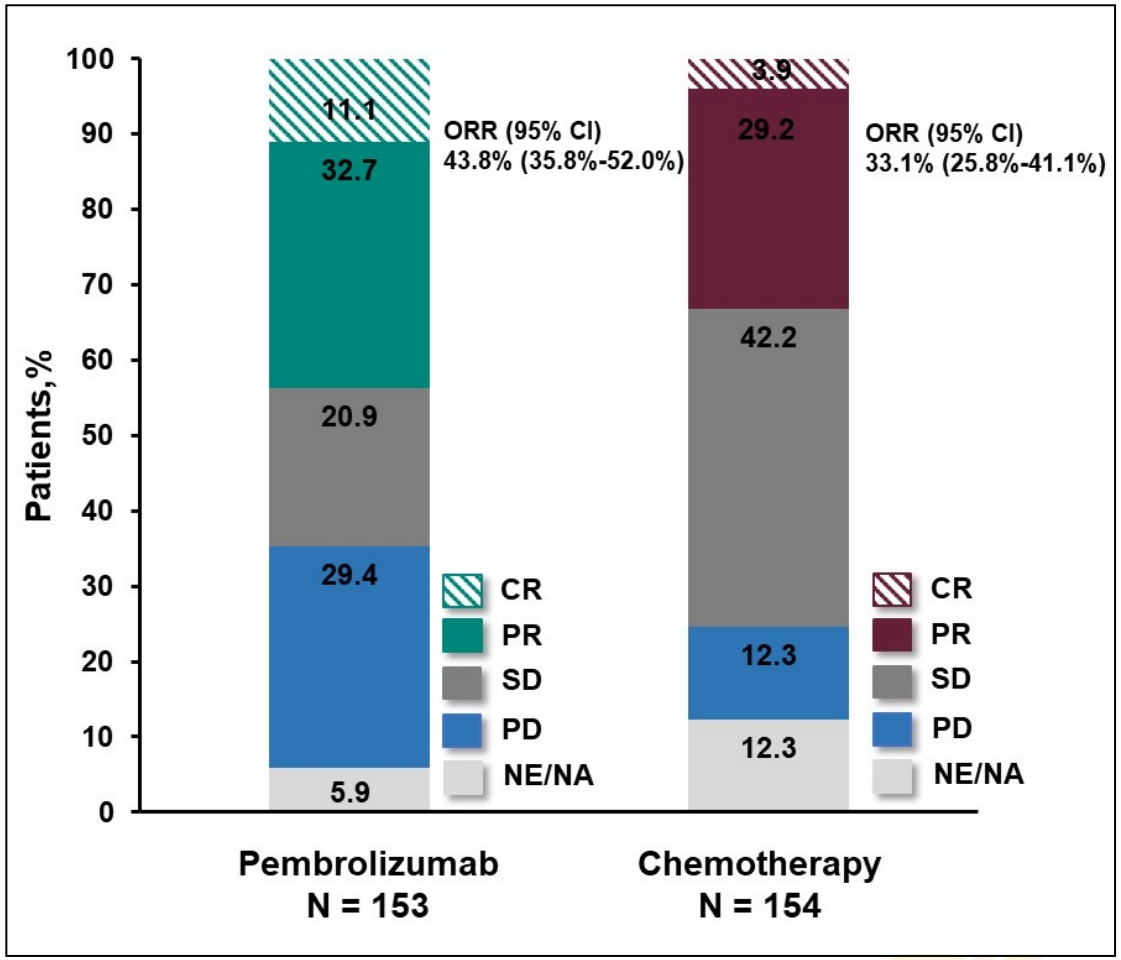
Mayo Clinic in Arizona

Actionable colorectal cancer targets in 2026



KEYNOTE-177: 1L Pembrolizumab vs. Chemo in MSI-H mCRC

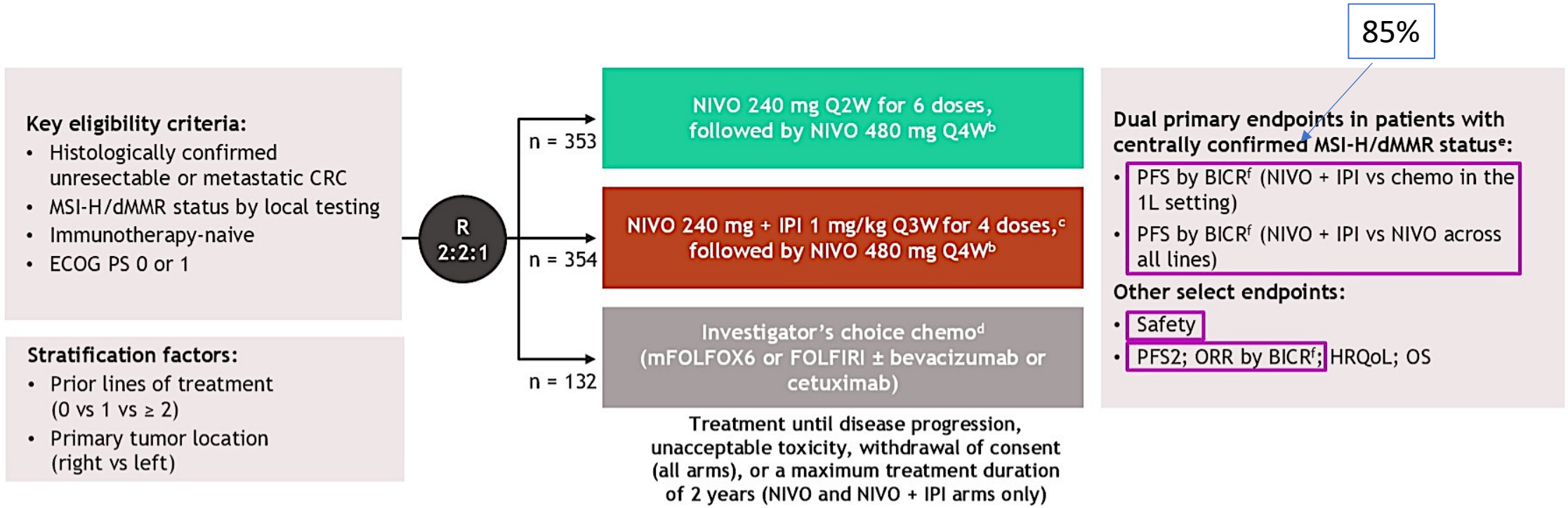




Presented by KK Shiu, ASCO GI 2021

CheckMate 8HW study design

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



- At data cutoff (August 28, 2024), the median follow-up[g] was 47.0 months (range, 16.7-60.5)

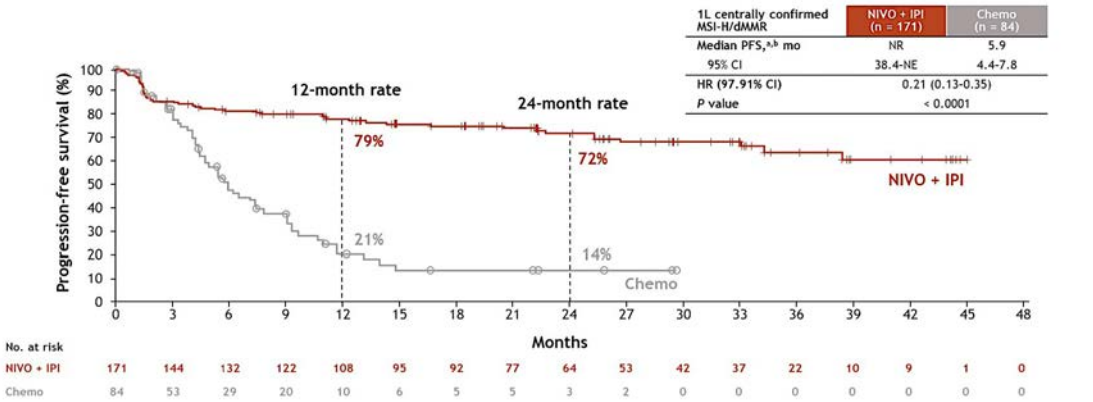
[a]ClinicalTrials.gov. NCT04008030. [b]Patients with ≥ 2 prior lines are randomized only to the NIVO or NIVO + IPI arms. [c]Patients can continue NIVO treatment upon early IPI discontinuation. [d]Patients receiving investigator's choice of chemo are eligible to receive NIVO + IPI upon progression (crossover treatment). [e]Confirmed using either immunohistochemistry and/or polymerase chain reaction-based tests. [f]Evaluated using RECIST v1.1. [g]Time between randomization and data cutoff among all randomized patients across all 3 treatment arms.

Lenz H et al. ASCO 2025; Andre T et al. ASCO GI 2025; Lonardi S et al. ESMO 2025

mPFS: Nivo + Ipi vs. Chemo all Lines

CheckMate 8HW: first results of 1L NIVO + IPI vs chemo

Progression-free survival



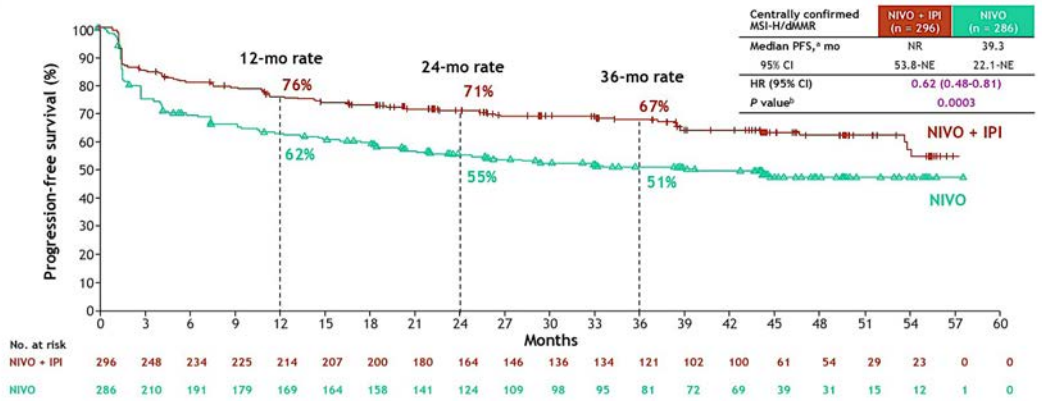
- PFS benefit with NIVO + IPI vs chemo was robust and consistent across the sensitivity analyses, including PFS by BICR in 1L all randomized patients (HR, 0.32; 95% CI, 0.23-0.46)

[a]Per BICR. [b]Median follow-up, 24.3 months.

mPFS: Nivo + Ipi vs. Nivo all Lines

Checkmate 8HW

Progression-free survival: NIVO + IPI vs NIVO (all lines)



- 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 (mPFS: 54.1 vs 18.4 months; HR, 0.64 [95% CI, 0.52-0.79])

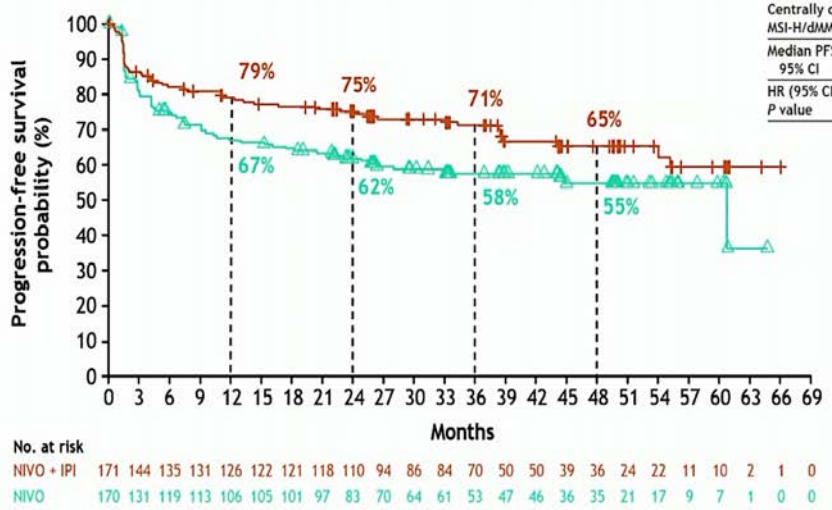
[a]Per BICR. [b]Boundary for statistical significance, $P < 0.0095$.

Lenz H et al. ASCO 2025; Andre T et al. ASCO GI 2025

mPFS: Nivo + Ipi vs. Nivo 1L MSI-H mCRC

CheckMate 8HW

PFS: 1L NIVO + IPI vs NIVO in centrally confirmed patients



Centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 171)	NIVO (n = 170)
Median PFS,[a] mo	NR	60.8
95% CI	55.2-NE	32.8-NE
HR (95% CI)	0.69 (0.48-0.99)	
P value	0.0413	

- In patients with centrally confirmed MSI-H/dMMR mCRC, 1L NIVO + IPI demonstrated clinically meaningful improvement in PFS vs NIVO (HR 0.69, [95% CI 0.48-0.99])
  - The prespecified threshold for statistical significance was not met ($P < 0.0383$)
  - These data are consistent with those observed in the 1L all randomized population by local testing (HR 0.75, [95% CI 0.56-1.01])

Median follow-up for all randomized 1L patients was 50.1 (range 24.7-67.3) months. [a]As assessed by BICR.

CheckMate 8HW

ORR: 1L NIVO + IPI vs NIVO in centrally confirmed patients

	NIVO + IPI (n = 171)	NIVO (n = 170)
ORR,[a,b] %	73	61
95% CI	65-79	53-79
Best overall response,[b,c] %		
CR	35	31
PR	37	31
SD	12	19
PD	11	16
Median time to response (range),[d] months	2.8 (1.2-38.6)	2.7 (1.2-29.5)
Median duration of response (95% CI),[d,e] months	NR (NE)	NR (59.4-NE)

- In patients with centrally confirmed MSI-H/dMMR mCRC, a clinically meaningful improvement in ORR, higher CR rate, and lower PD rate was observed with 1L NIVO + IPI vs NIVO
  - These data are consistent with those observed in the 1L all randomized population by local testing (ORR [95% CI], 66% [59-72] vs 54% [47-61])

Median follow-up for all randomized 1L patients was 50.1 (range 24.7-67.3) months. [a]The proportion of patients with a CR or PR, with confirmation of response ≥ 4 weeks later (due to rounding, the ORR may not equal the sum of the CR and PR rates). [b]As assessed by BICR using RECIST v1.1. [c]Not evaluable/not reported: NIVO + IPI, n = 8 NIVO, n = 6. [d]Calculated only for patients with a confirmed objective response (NIVO + IPI, n = 124; NIVO, n = 104). [e]Median estimated using the Kaplan-Meier method.

Lonardi S et al ESMO 2025

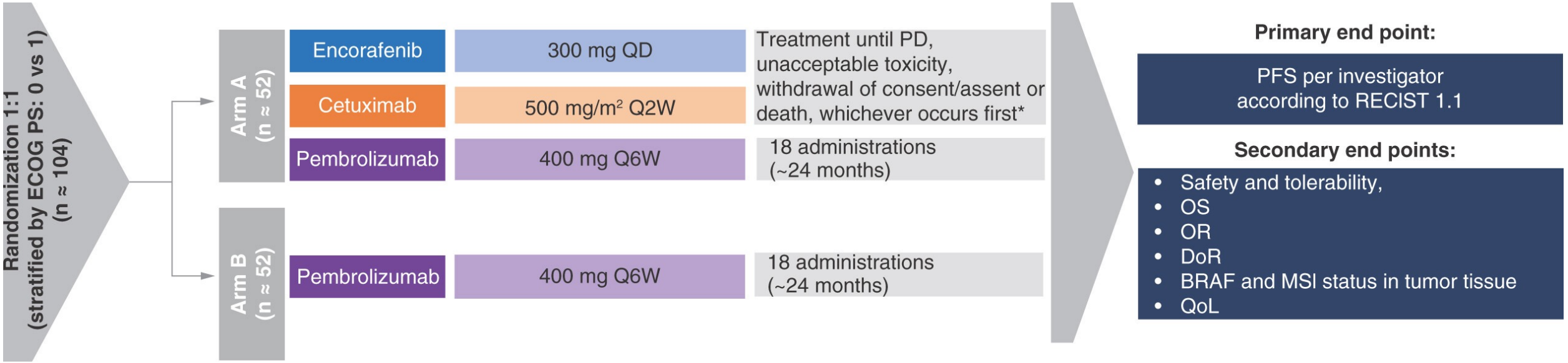
Treatment-related adverse events

All treated patients, n (%)	NIVO + IPI (n = 352)		NIVO (n = 351)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
TRAEs[a]				
Any TRAEs	285 (81)	78 (22)	249 (71)	50 (14)
Serious TRAEs	65 (18)	55 (16)	29 (8)	24 (7)
TRAEs leading to discontinuation[b]	48 (14)	33 (9)	21 (6)	14 (4)
Treatment-related deaths[c]	2 (< 1)[d]		1 (< 1)[e]	
TRAEs[a] reported in ≥ 10% of patients				
Pruritus	91 (26)	0	63 (18)	0
Diarrhea	71 (20)	3 (< 1)	59 (17)	2 (< 1)
Hypothyroidism	61 (17)	2 (< 1)	31 (9)	0
Asthenia	58 (16)	2 (< 1)	44 (13)	2 (< 1)
Fatigue	42 (12)	1 (< 1)	35 (10)	1 (< 1)
Hyperthyroidism	40 (11)	0	16 (5)	0
Arthralgia	38 (11)	1 (< 1)	23 (7)	0
Rash	34 (10)	3 (< 1)	29 (8)	1 (< 1)
Adrenal insufficiency	34 (10)	8 (2)	12 (3)	3 (< 1)

[a]Includes events reported between first dose and 30 days after last dose of study therapy. [b]Discontinuation of any component of the combination regimen was counted as a drug discontinuation event. [c]Treatment-related deaths were reported regardless of timeframe. [d]Includes 1 event each of myocarditis and pneumonitis. No new treatment-related deaths were reported since the previous interim analysis. [e]One event of pneumonitis.

Lenz H et al. ASCO 2025

SEAMARK Phase 2 Study: Immunotherapy +/- Encorafenib/Cetuximab in *BRAF*^{V600E}, MSI-H



Elez, E., Kopetz, S., Tabernero, J., Bekaii-Saab, T., Taieb, J., Yoshino, T., … Morris, V. K. *Future Oncology* (2024).

Conclusions

Test for mismatch repair deficiency/microsatellite instability at diagnosis for every stage of CRC

- Ensure adequate diagnostic testing methods

ICIs are a very helpful therapeutic strategy in most MSI-H/dMMR CRC

- Toxicity profile relatively favorable for majority of patients on single agent PD1i (> with + CTLA4i)

Need biomarkers to help predict response, non-response to ICIs

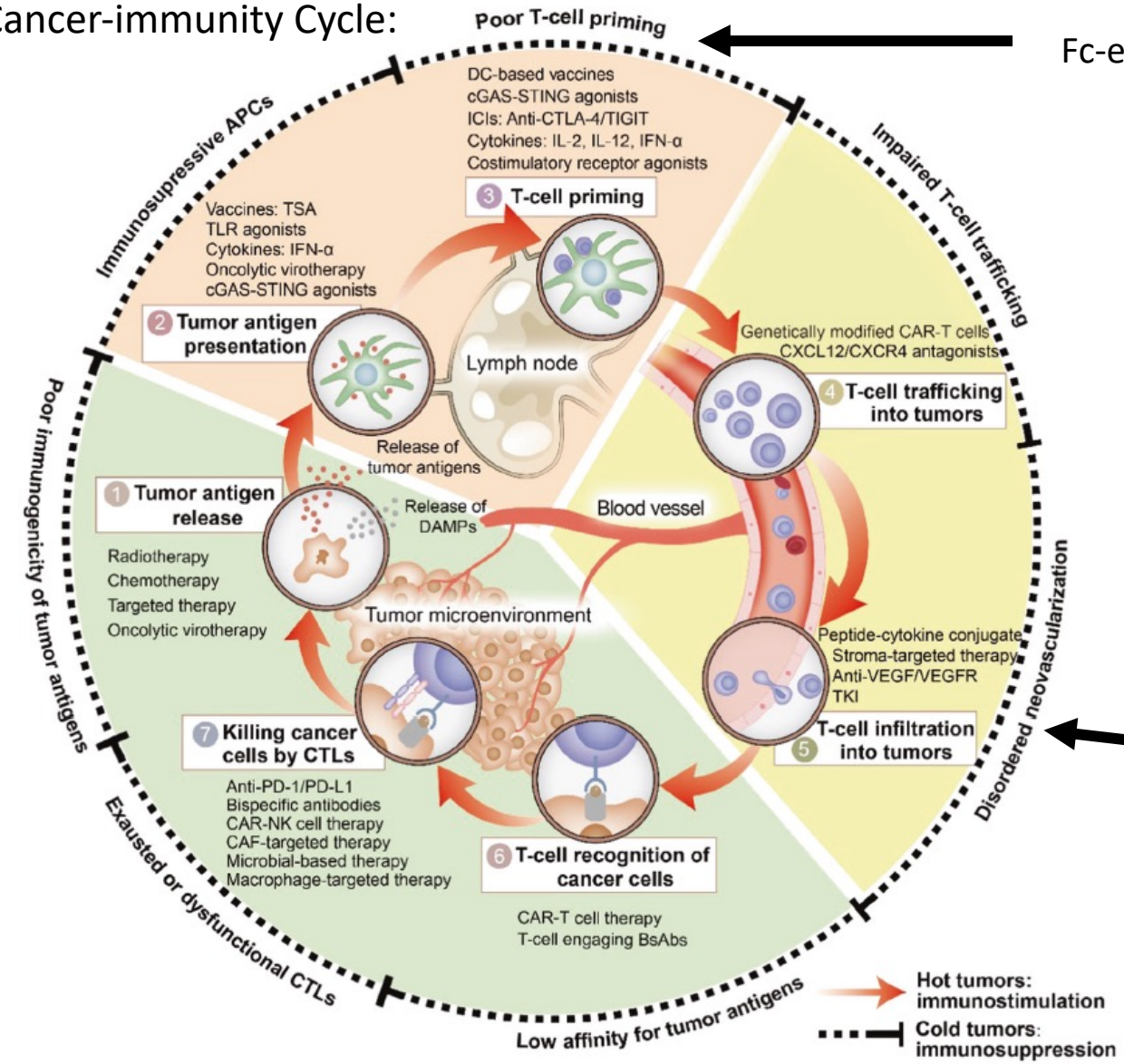
- Molecular markers, Lynch vs. non-Lynch, tumor microenvironment, others

Optimal duration of therapy and role of singlet vs. doublet ICIs remains relatively unclear

- Single agent ICI for Lynch patients and doublet for select in need of Response (especially + BRAF V600E MT) …
- Cross over from singlet to doublet ?
- Circulating tumor DNA may be helpful for assessing/quantifying response

The Path Forward For pMMR (MSS) mCRC

Cancer-immunity Cycle:



Fc-engineered CTLA-4

Anti-VEGF

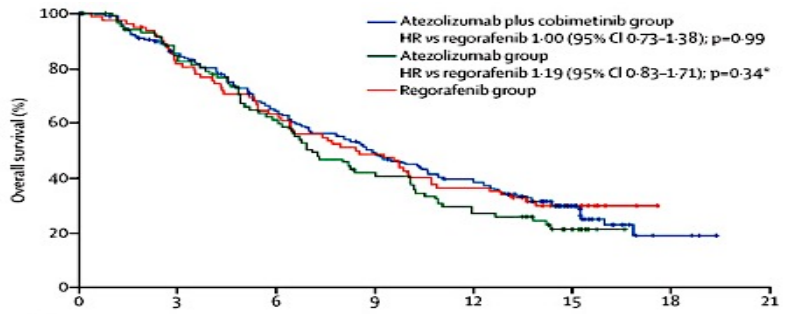
Are there subsets with immune responsiveness?

dMMR
Non-liver metastases
Primary
CMS1+ CMS3 pMMR
POLE
TMB high
ctDNA

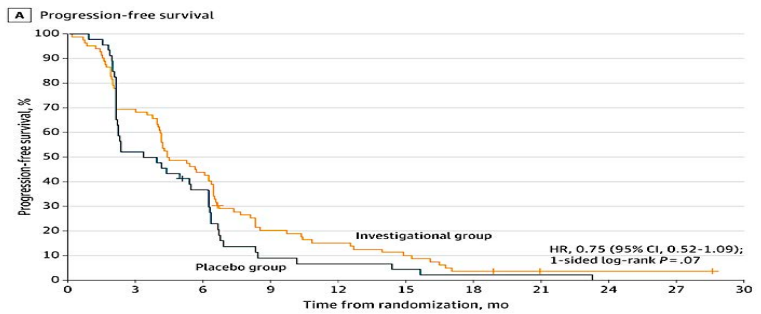
Ni JJ et al. *Acta Pharmacol Sin*. 2023;44(2):288-307.
Mellman I et al. *Immunity*. 2023;56(10):2188-2205.
Chen DS et al. *Immunity*. 2013;39(1):1-10.

Randomized PII/III studies with IO+ for **MSS** mCRC: From Negative to Borderline Positive

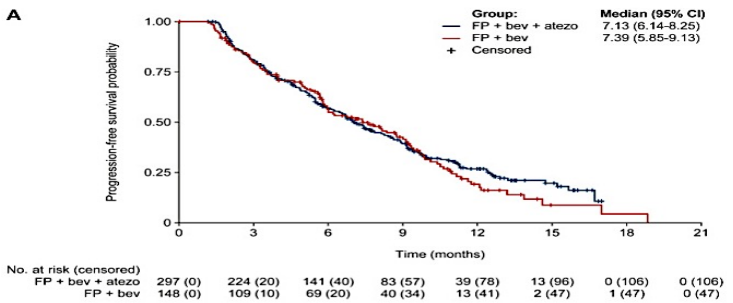
Imblaze 370 : Ref L Atezo +/- cobi vs. Rego



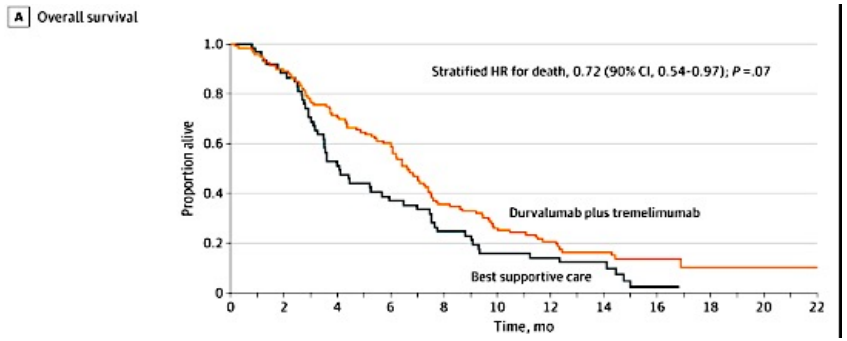
BACCI : Ref L Cape/Bev +/- Atezo/PBO



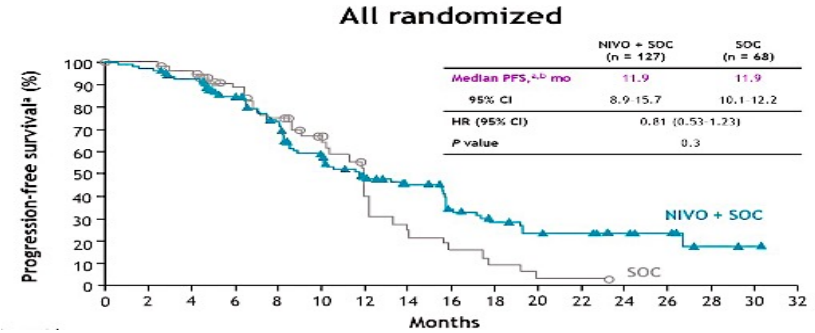
MODUL : Maint FP/Bev +/- Atezo



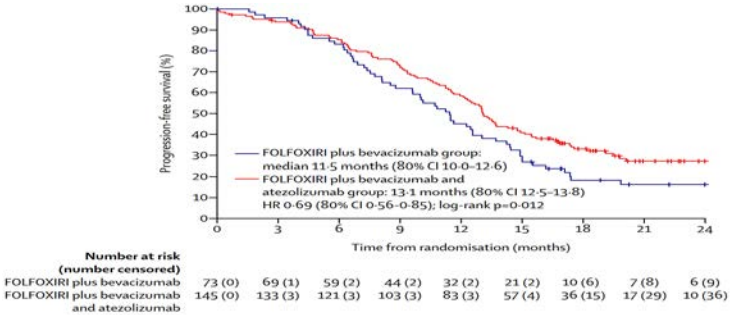
CO.26 : Ref L Tremi/Durva vs. BSC



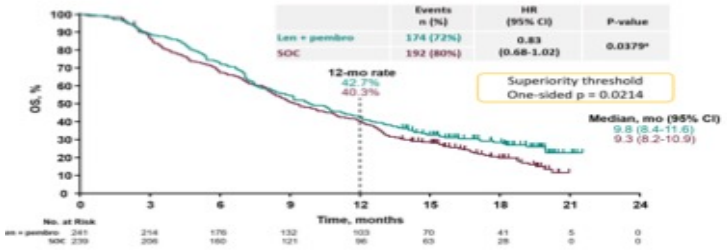
CM 9X8: 1L mFOLFOX6 + Bev +/- Nivo



AtezoTRIBE: 1L FOLFOXIRI/Bev +/- Atezo

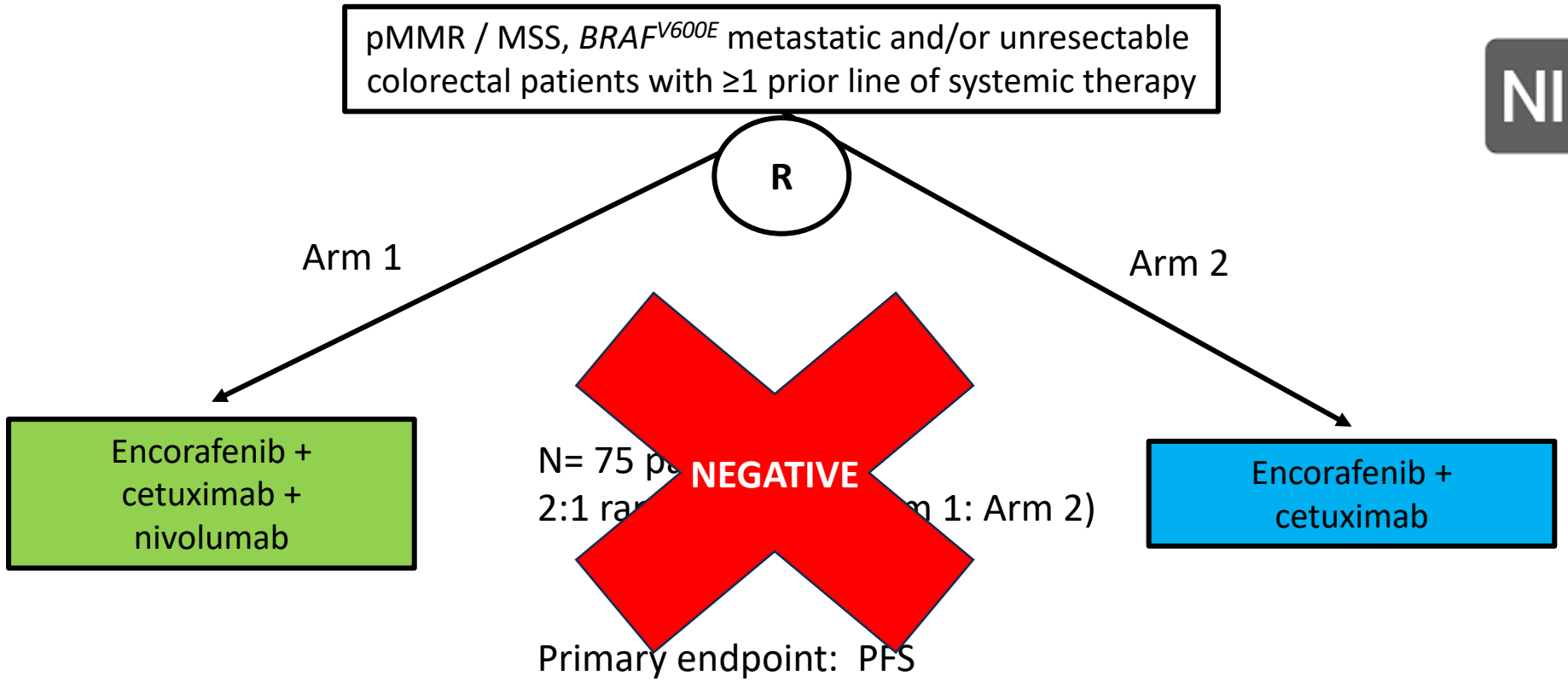


LEAP 017: Lenva + Pembro vs. SOC



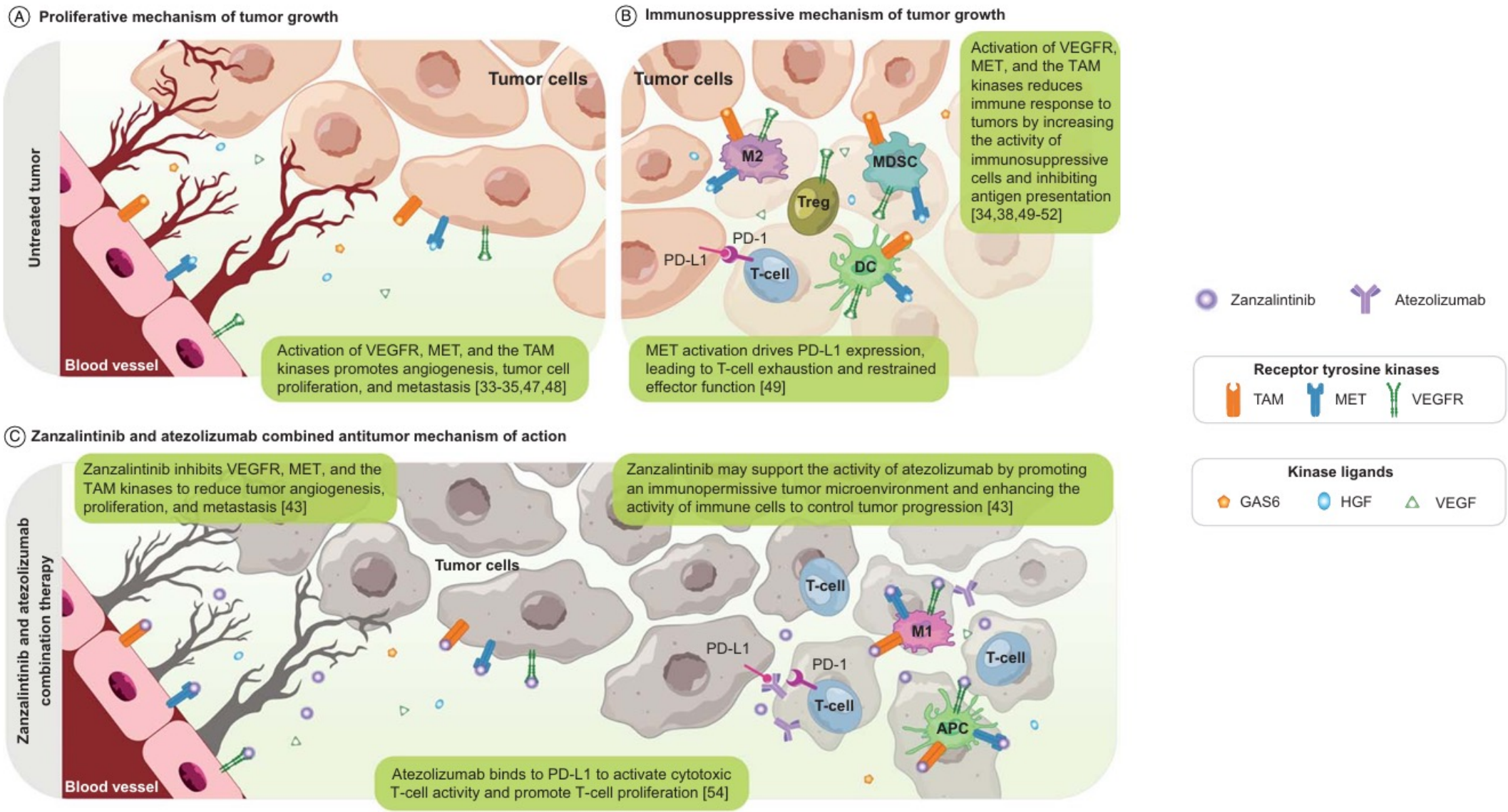
Primary Endpoint OS: NEGATIVE

S2107 Study Schema: Encorafenib/Cetuximab +/- Nivolumab



PI: Van Morris

Zanzalintinib + atezolizumab: MOA

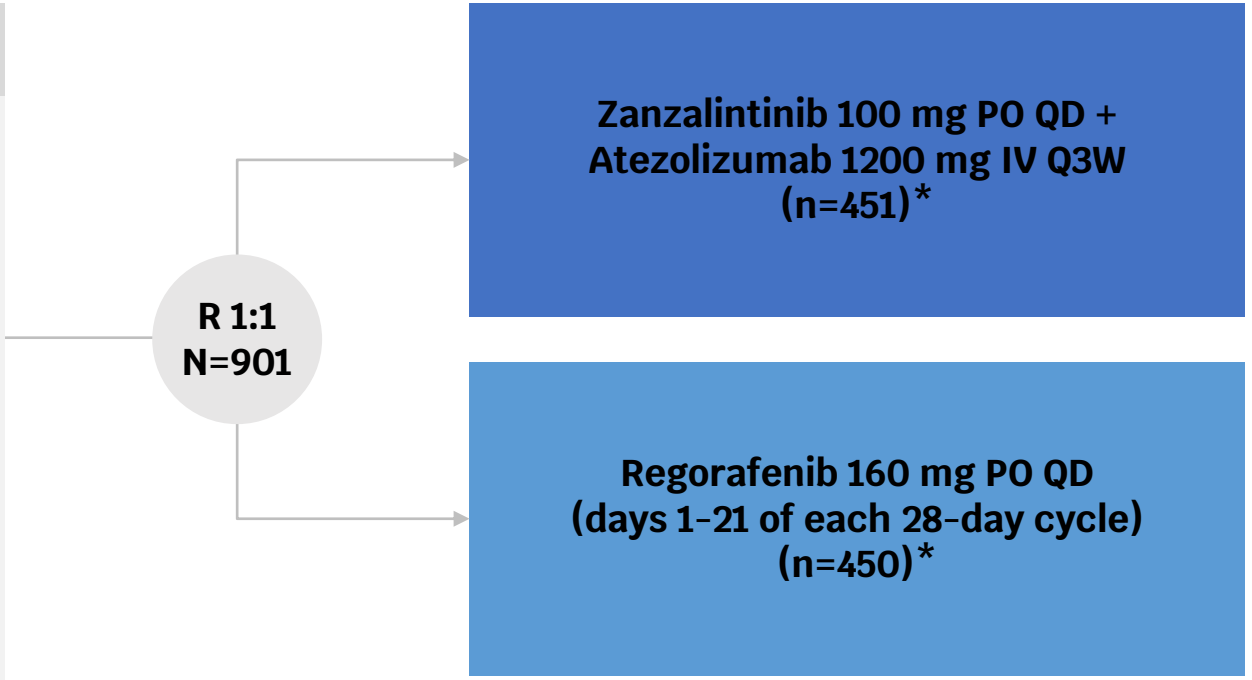


Saeed A, et al. *Future Oncol*. 2024;20:1733-1743.

STELLAR-303 (NCT05425940) Study Design

Patient Population

- Aged ≥18 years
- Documented to not have MSI-H or dMMR status
- mCRC that radiographically progressed on or was refractory or intolerant to prior standard-of-care therapy, which had to include all the following (if approved and available in the country where the patient is randomized):
  - Fluoropyrimidine, irinotecan and oxaliplatin ± anti-VEGF antibody
  - Anti-EGFR antibody (if *RAS* wild type)
  - BRAF inhibitor (if known *BRAF* V600E mutation)



Stratification Factors

- Geographic region (Asia/rest of the world)
- *RAS* status (wild type/mutant)
- Presence of liver metastases (yes/no)

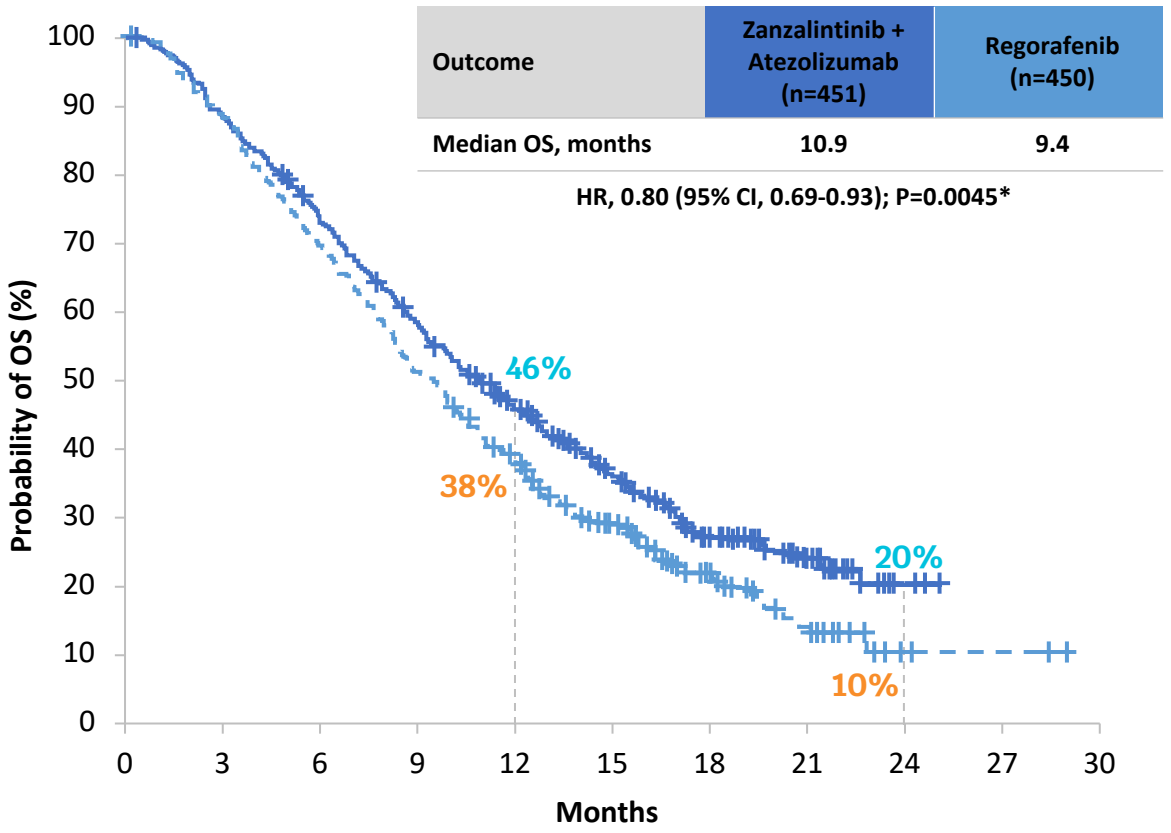
Endpoints

Dual primary	OS in the ITT population OS in patients without liver metastases (nlmITT)
Key secondary	PFS,† ORR,† Safety‡

Saeed, A et al. ESMO 2025

STELLAR-303: Efficacy

OS Analysis (ITT Population)

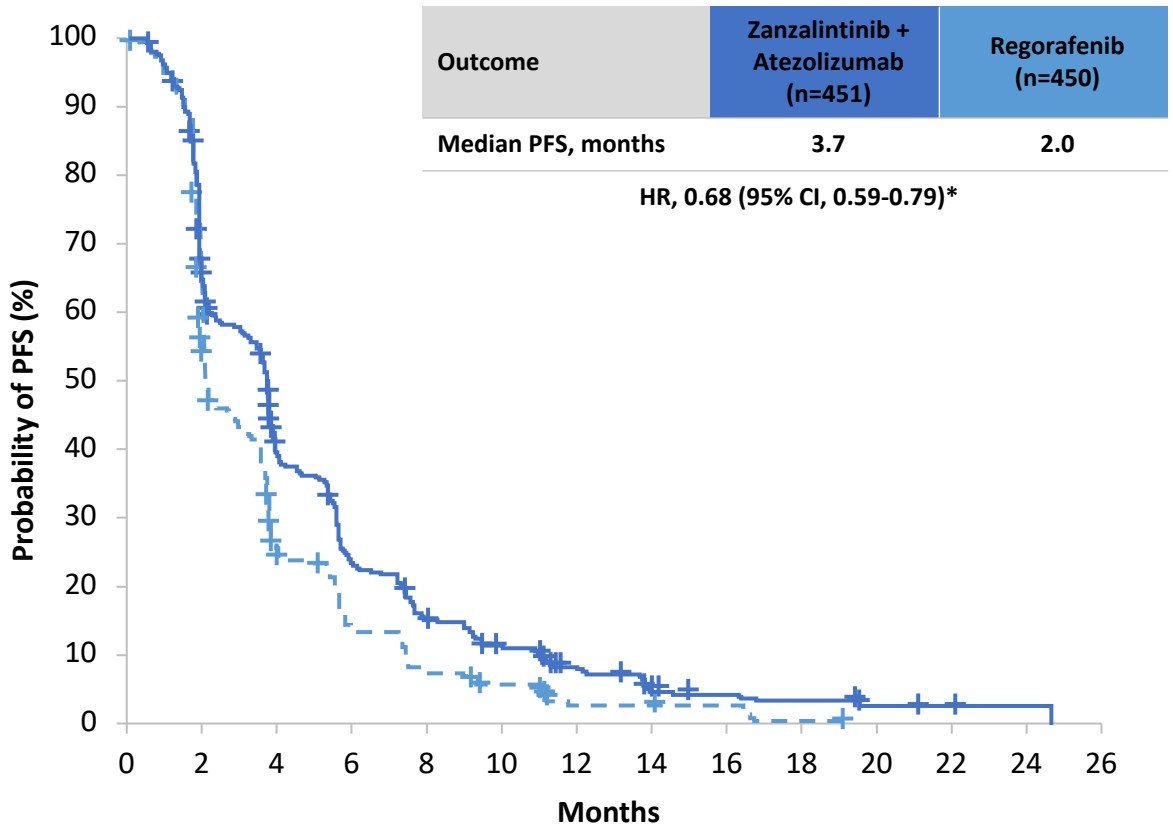


Outcome	Zanzalintinib + Atezolizumab (n=451)	Regorafenib (n=450)
Median OS, months	10.9	9.4

HR, 0.80 (95% CI, 0.69-0.93); P=0.0045*

- The interim analysis in the nlmITT population (dual primary endpoint) showed a trend in OS favoring the combination (stratified HR, 0.79 [95% CI, 0.61–1.03; P=0.087]; median, 15.9 versus 12.7 months with regorafenib)

PFS (ITT Population)



Outcome	Zanzalintinib + Atezolizumab (n=451)	Regorafenib (n=450)
Median PFS, months	3.7	2.0

HR, 0.68 (95% CI, 0.59-0.79)*

- PFS for zanzalintinib + atezolizumab versus regorafenib was generally consistent across subgroups

*Statistical significance for PFS cannot be claimed at this analysis per the prespecified hierarchical testing strategy. ITT, intention to treat; PFS, progression-free survival.

Hecht, R et al. Lancet Nov. 2025

STELLAR-303: Efficacy

OS Subgroup Analyses (ITT Population)-Key Subgroups

An OS benefit with zanzalintinib + atezolizumab vs regorafenib was consistently observed across key subgroups

Subgroup	HR (95% CI)	Zanzalintinib + Atezolizumab median OS, months	Regorafenib median OS, months
Geographic region			
Asia	0.77 (0.59-1.00)	11.5	8.8
Rest of the world	0.82 (0.68-0.99)	10.9	9.8
***RAS* status**			
Wild type	0.79 (0.61-1.01)	12.0	10.4
Mutant	0.80 (0.66-0.98)	10.3	8.7
Liver metastases			
Yes	0.78 (0.65-0.94)	8.9	7.7
No	0.77 (0.59-1.01)	15.9	12.7
Prior anti-VEGF antibody treatment			
Yes	0.80 (0.68-0.95)	10.5	8.8
No	0.80 (0.56-1.15)	11.5	11.1

Best Overall Response (ITT Population)

Response Outcome	Zanzalintinib + Atezolizumab (n=451)	Regorafenib (n=450)
Best overall response, n (%)*		
Complete response	0	0
Partial response	16 (4)	5 (1)
Stable disease	226 (50)	178 (40)
Progressive disease	156 (35)	216 (48)
Not evaluable	53 (12)	51 (11)
Objective response rate, n (%)	16 (4)	5 (1)
95% CI	(2-6)	(0-3)
Disease control rate, n (%)	242 (54)	183 (41)
95% CI	(49-58)	(36-45)

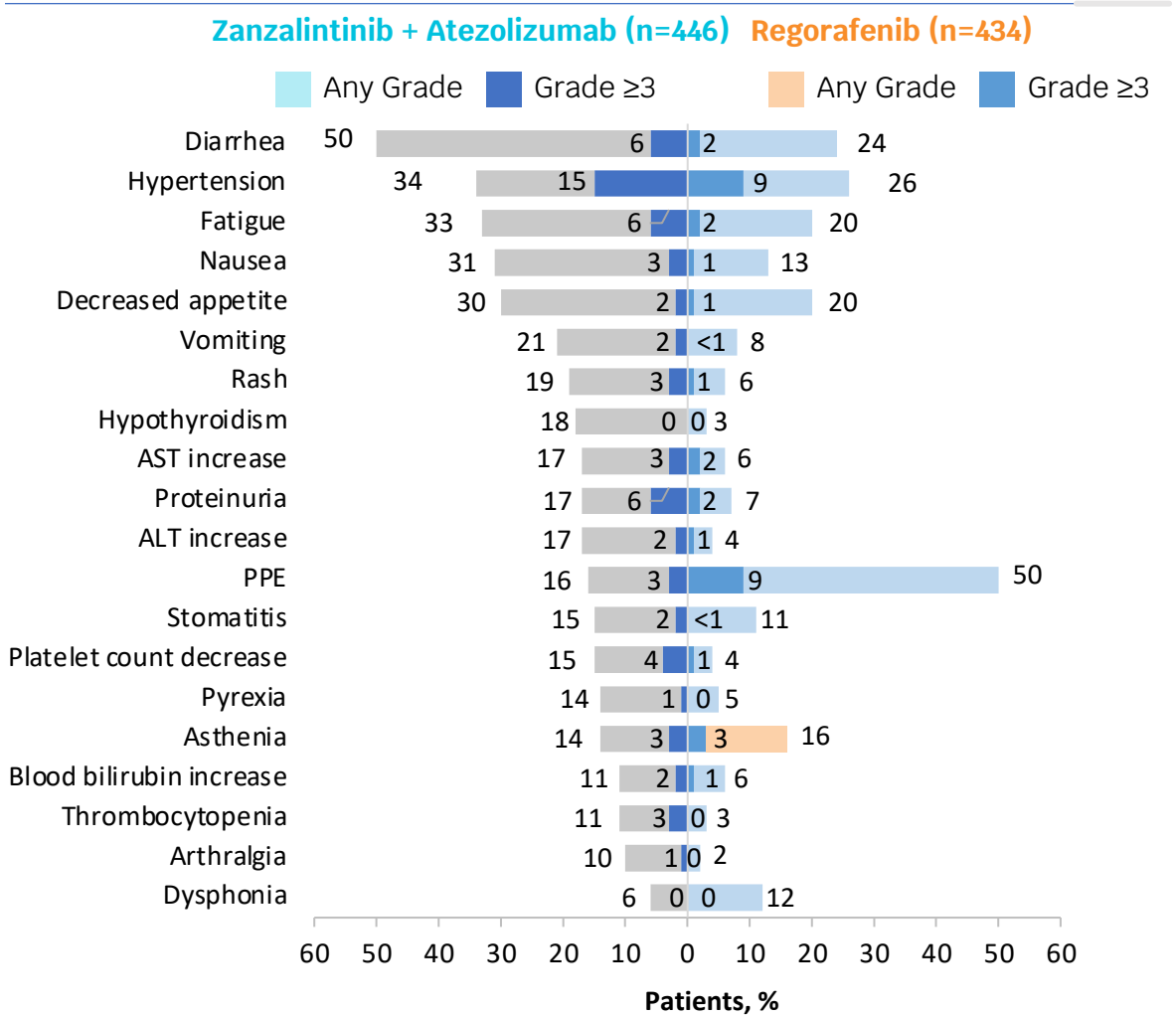
Hecht, R et al. Lancet Nov. 2025

STELLAR-303: Safety

Event, n (%)	Zanzalintinib + Atezolizumab (n=446)	Regorafenib (n=434)
Treatment-related adverse events		
Any-grade	423 (95)	399 (92)
Grade 3	248 (56)	143 (33)
Grade 4	15 (3)	17 (4)
Serious adverse events	255 (57)	184 (42)
Serious treatment-related adverse events	118 (26)	45 (10)
Adverse events leading to discontinuation of all treatment	82 (18)	64 (15)
Dose modification due to an adverse event*		
Dose reduction of zanzalintinib/regorafenib	270 (61)	174 (40)
Dose delay of atezolizumab	193 (43)	NA

- Most frequent AEs leading to discontinuation of zanzalintinib + atezolizumab: abdominal pain, asthenia, and general physical health deterioration (4 [1%] patients each)
- Deaths considered related to treatment by investigators: intestinal perforation (n=2) for zanzalintinib, pneumonitis and renal failure (n=1 each) for atezolizumab, altered state of consciousness (n=1) for zanzalintinib + atezolizumab, and jejunal perforation (n=1) for regorafenib

Summary of TRAEs* (Safety Population)



Hecht, R et al. Lancet Nov. 2025

FDA Accepts the New Drug Application for Zanzalintinib in Combination with Atezolizumab for mCRC

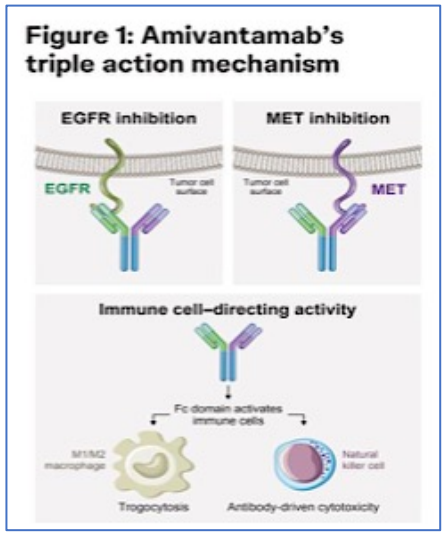
The manufacturer announced that a New Drug Application (NDA) for zanzalintinib, in combination with atezolizumab, has been accepted for review in the U.S. for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, and, if RAS wild-type, an anti-epidermal growth factor receptor (EGFR) therapy.

The Food and Drug Administration (FDA) assigned a standard review with a Prescription Drug User Fee Act target action date of December 3, 2026.

The NDA is based on the results of the phase 3 STELLAR-303 pivotal trial, in which zanzalintinib in combination with atezolizumab demonstrated a statistically significant improvement in overall survival (OS) versus regorafenib in the intention-to-treat (ITT) population of patients with previously treated CRC.

https://ir.exelixis.com/news-releases/news-release-details/exelixis-announces-us-fda-accepted-new-drug-application

Target : EGFR/MET (Bispecific)



OrigAMI-1

(Doublet chemo + amivantamab in RAS/BRAF WT mCRC

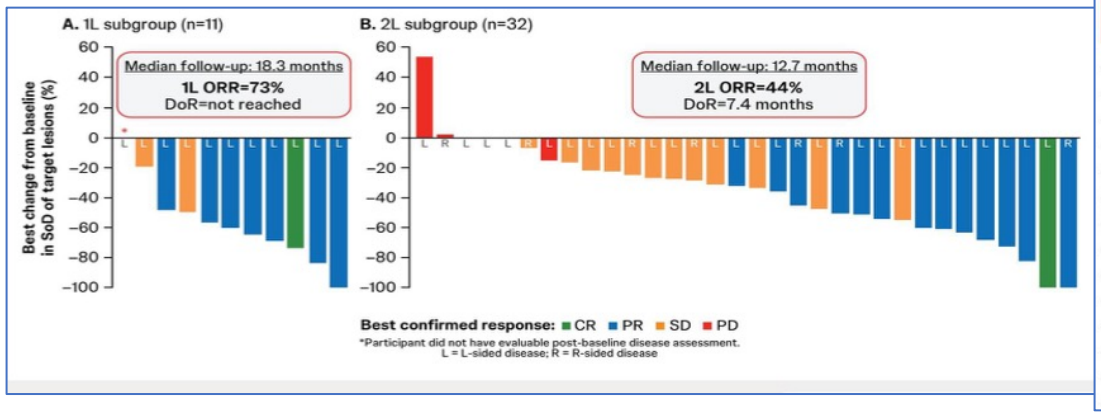


Table 2: Safety profile

Treatment-emergent AEs (≥30%) by preferred term, n (%)	Ami-FOLFOX (n=20)		Ami-FOLFIRI (n=23)	
	All grades	Grade ≥3	All grades	Grade ≥3
Related to EGFR inhibition				
Diarrhea[a]	13 (65)	1 (5)	15 (65)	2 (9)
Stomatitis	11 (55)	1 (5)	11 (48)	0
Rash	10 (50)	3 (15)	11 (48)	1 (4)
Paronychia	10 (50)	0	11 (48)	0
Dermatitis acneiform	5 (25)	0	8 (35)	2 (9)
Related to MET inhibition				
Hypoalbuminemia	9 (45)	0	14 (61)	2 (9)
Peripheral edema	6 (30)	0	8 (35)	0
Related to chemotherapy				
Neutropenia	10 (50)	7 (35)	16 (70)	12 (52)
Anemia	4 (20)	0	11 (48)	2 (9)
Leukopenia	4 (20)	1 (5)	7 (30)	1 (4)
Thrombocytopenia	6 (30)	3 (15)	3 (13)	0

OrigAMI-2

(Doublet chemo + amivantamab vs cetuximab in **1L, left-sided mCRC**)

Key eligibility criteria
- Histologically or cytologically confirmed unresectable or metastatic L-sided CRC
- Treatment naïve for unresectable or metastatic CRC
- *KRAS*, *NRAS*, and *BRAF* WT tumor as determined by local testing
- ECOG PS score of 0 or 1

Stratification factors
- Chemotherapy (FOLFOX/FOLFIRI)
- Limited disease[a] (yes/no)
- Prior adjuvant therapy (yes/no)

1:1 randomization (N≈1000) (R)
- Amivantamab SC[b] + FOLFOX or FOLFIRI (n≈500)
- Cetuximab IV + FOLFOX or FOLFIRI (n≈500)

Dosing (in 28-day cycles)
Amivantamab: 1600 mg SC (2240 mg if body weight ≥80 kg)
Cycle 1: Weekly administration (Days 1, 8, 15, and 22)
Cycle 2+: Biweekly administration (Days 1 and 15)
Cetuximab: Biweekly IV regimen (500 mg/m² on Days 1 and 15) or weekly IV regimen (400 mg/m² on C1D1, then 250 mg/m² weekly)

Primary endpoint:
- PFS per RECIST v1.1 by BICR

Key secondary endpoint:
- OS

Additional secondary endpoints:
- PFS by investigator
- ORR, DoR, DCR (by BICR and investigator)
- PFS after first subsequent therapy (by investigator)
- TTF
- Curative resection rate[c]
- AEs assessed via NCI-CTCAE v5.0 and laboratory abnormalities
- PROs assessed via EORTC QLQ-C30 and EORTC QLQ-CR29

OrigAMI-3

(FOLFIRI + amivantamab vs bev/cetux in **2L mCRC**)

Key eligibility criteria
- Recurrent, unresectable, or metastatic CRC
- Received 1 line of systemic therapy for metastatic CRC
- Anti-EGFR therapy and irinotecan naïve
- *KRAS*, *NRAS*, and *BRAF* WT tumor as determined by local testing
- ECOG PS score of 0 or 1

Stratification factors
- Investigator's choice of control prior to randomization (cetuximab/bevacizumab)
- Primary tumor location (left/right)[a]
- Prior anti-VEGF therapy (yes/no)
- Duration of 1L therapy[b] (<6 mo/≥6 mo)

1:1 randomization (N≈700) (R)
- Amivantamab SC[c] + FOLFIRI (n≈350)
- Cetuximab IV or Bevacizumab IV + FOLFIRI (n≈350)

Dosing (in 28-day cycles)
Amivantamab: 1600 mg SC (2240 mg if body weight ≥80 kg)
Cycle 1: Weekly administration (Days 1, 8, 15, and 22)
Cycle 2+: Biweekly administration (Days 1 and 15)
Cetuximab: Biweekly IV regimen (500 mg/m² on Days and 15) or weekly IV regimen (400 mg/m² on C1D1, th 250 mg/m² weekly)
Bevacizumab: 5 mg/kg IV on Days 1 and 15

Dual primary endpoints:
- PFS per RECIST v1.1 by BICR
- OS

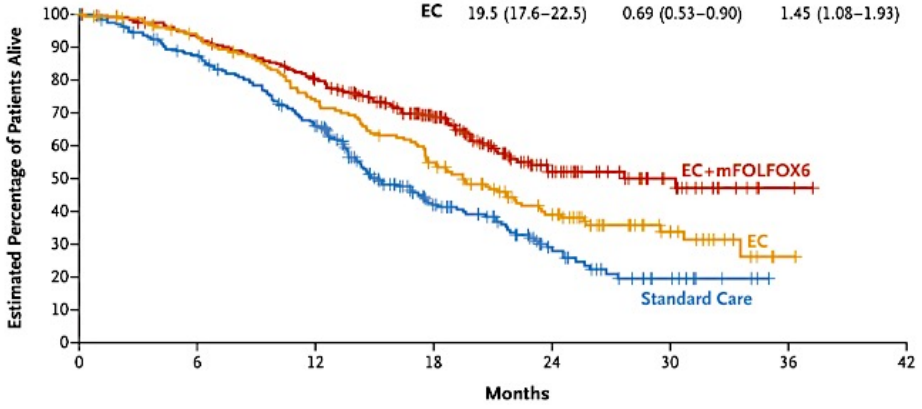
Secondary endpoints:
- PFS by investigator
- ORR, DoR, DCR (by BICR and investigator)
- PFS after first subsequent therapy (by investigator)
- TTF
- Curative resection rate[d]
- AEs assessed via NCI-CTCAE v5.0 and laboratory abnormalities
- PROs assessed via EORTC QLQ-C30, EORTC QLQ-CR29, EQ-5D-5L, and EORTC Q168

Arnold D et al. ASCO 2025. Abstract TPS3636; Chen EX et al. ASCO GI 2026; Harrington KJ et al. ESMO 2025; Hecht JR et al. ASCO 2025. Abstract TPS3638

BREAKWATER: First-line Encorafenib + Cetuximab ± Chemotherapy Versus SOC in Patients With *BRAF* V600E–Mutant mCRC

Overall Survival

	Median Overall Survival (95% CI)	Hazard Ratio for Death vs. Standard Care (95% CI)	Hazard Ratio for Death vs. EC+mFOLFOX6 (95% CI)
	mo		
EC+mFOLFOX6	30.3 (21.7–NE)	0.49 (0.38–0.63) P<0.001	—
Standard Care	15.1 (13.7–17.7)	—	—
EC	19.5 (17.6–22.5)	0.69 (0.53–0.90)	1.45 (1.08–1.93)

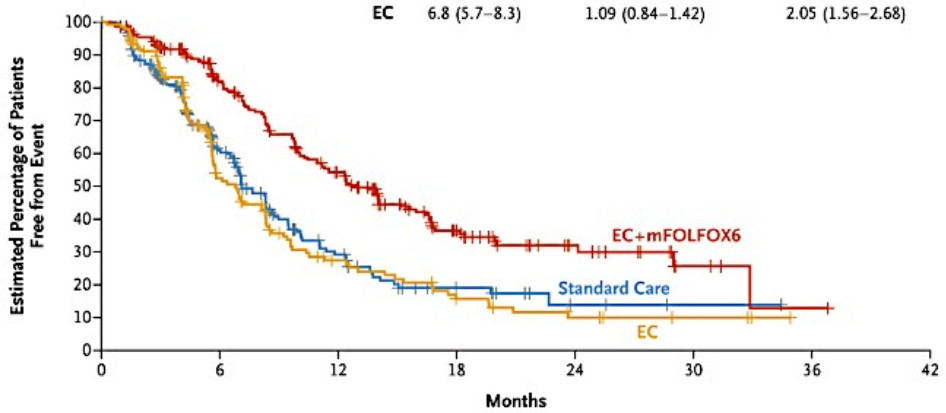


No. at Risk							
EC+mFOLFOX6	236	216	182	121	48	17	2	0
Standard care	243	202	147	64	27	9	0	0
EC	158	137	107	78	44	16	1	0

Elez E et al. ASCO 2025. Abstract LBA3500.

Progression Free Survival

	Median Progression-free Survival (95% CI)	Hazard Ratio for Disease Progression or Death vs. Standard Care (95% CI)	Hazard Ratio for Disease Progression or Death vs. EC+mFOLFOX6 (95% CI)
	mo		
EC+mFOLFOX6	12.8 (11.2–15.9)	0.53 (0.41–0.68) P<0.001	—
Standard Care	7.1 (6.8–8.5)	—	—
EC	6.8 (5.7–8.3)	1.09 (0.84–1.42)	2.05 (1.56–2.68)



No. at Risk							
EC+mFOLFOX6	236	156	96	39	16	4	1
Standard care	243	100	34	11	3	1	0
EC	158	60	24	12	6	3	0

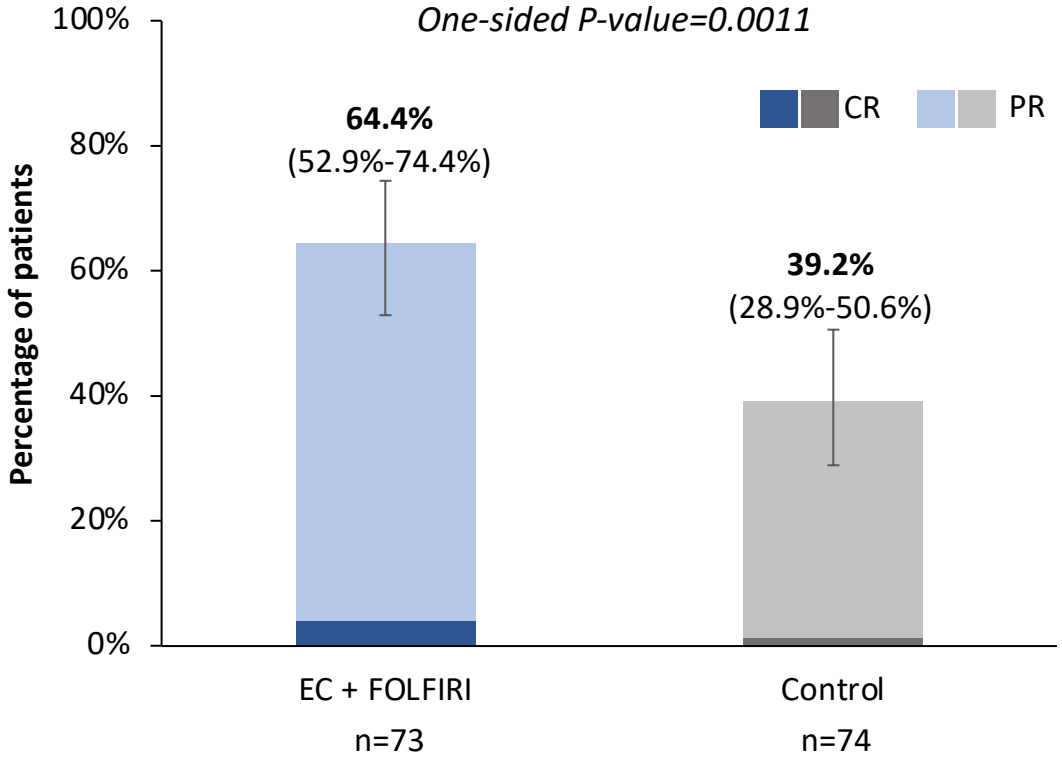
Elez E et al. *NEJM*. 2025

Overview of Response by BICR

EC + FOLFIRI demonstrated statistically significant and clinically meaningful benefit in ORR by BICR, meeting the primary endpoint

Confirmed ORR by BICR

Odds ratio (95% CI): 2.756 (1.420-5.348)
One-sided P-value=0.0011



Confirmed Best Overall Response, TTR, and DOR by BICR

	EC + FOLFIRI n=73	Control[a] n=74
Confirmed best overall response, n (%)		
CR	3 (4.1)	1 (1.4)
PR	44 (60.3)	28 (37.8)
SD	15 (20.5)	25 (33.8)
Non-CR/non-PD[b]	1 (1.4)	0
PD	1 (1.4)	8 (10.8)
Not evaluable	9 (12.3)	12 (16.2)
TTR, median (range), weeks	6.9 (5.4-36.1)	7.1 (5.9-25.3)
Estimated DOR, median (range), months	NE (NE-NE)	NE (7.0-NE)
Patients with a DOR of ≥6 months, n (%)	27 (57.4)	10 (34.5)
Patients with a DOR of ≥12 months, n (%)	2 (4.3)	0

[a]FOLFIRI ± bevacizumab. [b]Patients with only non-target lesions at baseline by BICR.

BICR, blinded independent central review; CR, complete response; DOR, duration of response; EC, encorafenib plus cetuximab; FOLFIRI, fluorouracil/leucovorin/irinotecan; NE, not estimable; PD, progressive disease; PR, partial response; SD, stable disease; TTR, time to response.

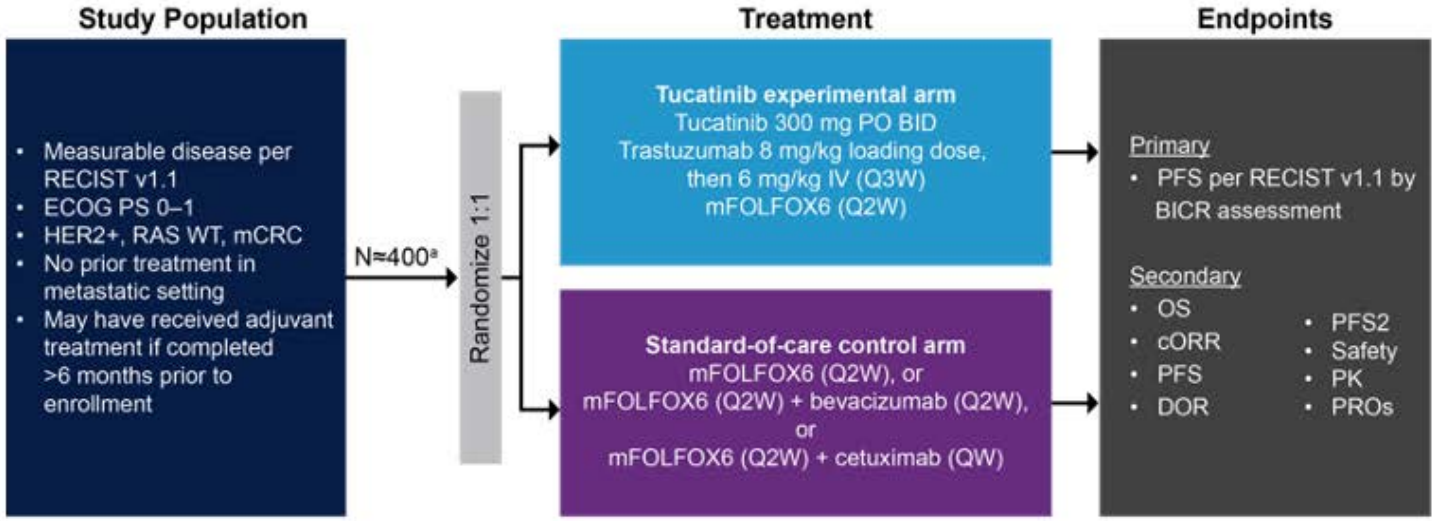
Data of HER2-targeted therapies in patients with mCRC

Regimen	Trial (n) – year	ORR	DOR	PFS	OS	Most common Grade 3+ AEs
Trastuzumab deruxtecan (5.4 mg/Kg)	**DESTINY-CRC02 (N=82) – 2023**	**37.8%**	**5.5m**	**5.8m**	**13.4m**	**Neutropenia 17% Fatigue 10% Nausea 8%**
Tucatinib + trastuzumab	**MOUNTAINEER (n=117) - 2023**	**38.1%**	**12.4m**	**8.2m**	**24.1m**	**Hypertension 7% Diarrhea 3.5%**

Tosi F, Sartore-Bianchi A, et al. Clin Colorectal Cancer. 2020 Dec;19(4):256-262.e2. doi: 10.1016/j.clcc.2020.06.009. Epub 2020 Jun 27.
Meric-Bernstam F, et al. Lancet Oncol. 2019 Apr;20(4):518-530. doi: 10.1016/S1470-2045(18)30904-5. Epub 2019 Mar 8.
Raghav KPS, et al. ASCO 2023.
Sartore-Bianchi A, et al. ESMO Open. 2020 Sep;5(5):e000911.
Siena S, et al; Lancet Oncol. 2021 Jun;22(6):779-789. doi: 10.1016/S1470-2045(21)00086-3. Epub 2021 May 4.
Strickler J et al; *Lancet Oncology* , 2023.

Target : HER2+ in mCRC

- MOUNTAINEER-03 (NCT05253651) is a global, open-label, randomized, phase 3 study of tucatinib with trastuzumab and mFOLFOX6 versus standard of care for the first-line treatment of HER2+ and *RAS* wild-type mCRC

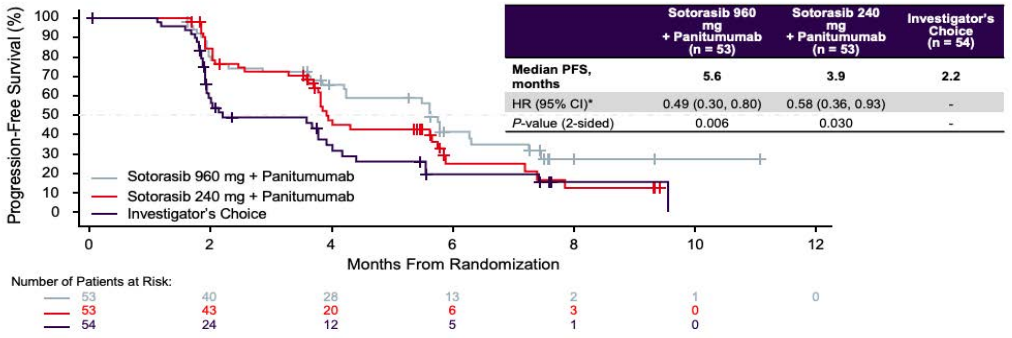


a Stratification by both primary tumor location (left-sided versus all other) and liver metastases (presence or absence)

CR, blinded independent central review; BID, twice a day; cORR, confirmed objective response rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HER2, human epidermal growth factor receptor 2; IV, intravenously; mCRC, etastatic colorectal cancer; mFOLFOX6, modified 5-fluorouracil, leucovorin, and oxaliplatin; OS, overall survival; PFS, progression-free survival; PFS2, time from randomization to disease progression on next-line treatment or death from any cause; PK, pharmacokinetics; PO, by outh; PROs, patient-reported outcomes; Q, each; RAS, rat sarcoma virus; RECIST, Response Evaluation Criteria in Solid Tumors; W, week; WT, wild-type.

KRAS G12C MT and mCRC

CodeBreaK 300(Phase 3) : PFS



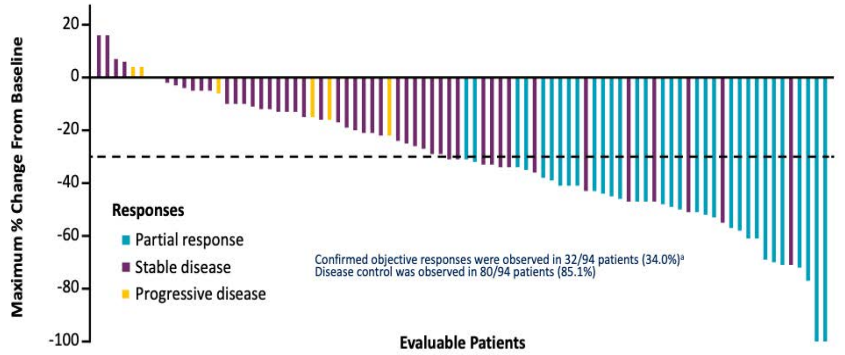
	Sotorasib 960 mg + Panitumumab (n = 53)	Sotorasib 240 mg + Panitumumab (n = 53)	Investigator's Choice (n = 54)
Median PFS, months	5.6	3.9	2.2
HR (95% CI)*	0.49 (0.30, 0.80)	0.58 (0.36, 0.93)	-
P-value (2-sided)	0.006	0.030	-

After a median follow-up of 7.8 months, sotorasib (960 mg and 240 mg) in combination with panitumumab significantly improved PFS by BICR versus investigator's choice

PFS was tested using stratified log-rank test.
*HR is sotorasib 960 mg + panitumumab / investigator's choice therapy, or sotorasib 240 mg + panitumumab / investigator's choice therapy.
BICR, blinded independent central review; HR, hazard ratio; PFS, progression-free survival.

Fakih MG, et al. N Engl J Med. 2023.

Adagrasib and Cetuximab

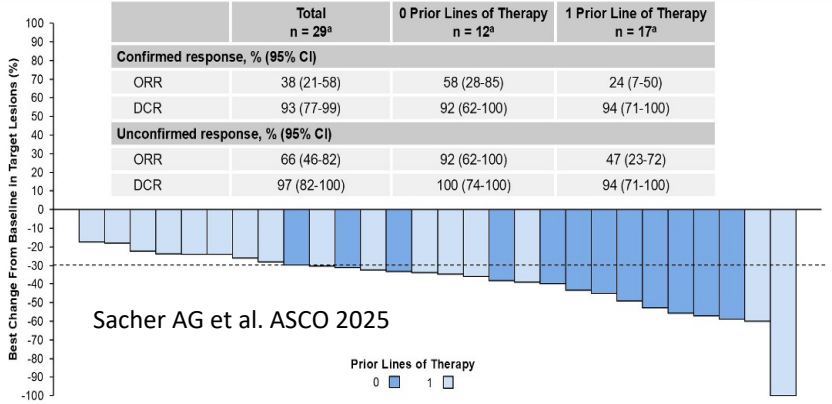


[a]ORR for the Phase 1 portion (n=32) was 43.8%; ORR for the Phase 2 portion (n=62) was 29.0%
All results are based on BICR. Waterfall plot excludes eight patients without any post-baseline scans
Data as of June 30, 2023 (median follow-up 11.9 months)

Yaeger R et al. Cancer Discov 2024

Antitumor Activity, Arm 6: MK-1084 + Cetuximab + mFOLFOX6, CRC (0-1 Lines of Prior Systemic Therapy)

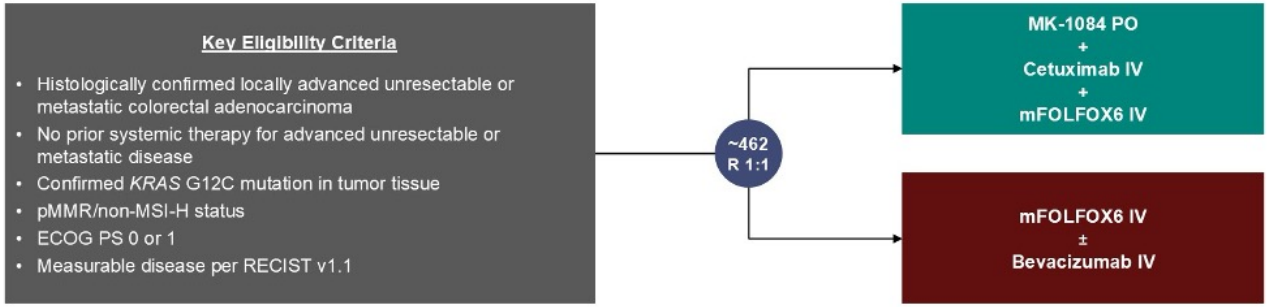
	Total n = 29[a]	0 Prior Lines of Therapy n = 12[a]	1 Prior Line of Therapy n = 17[a]
Confirmed response, % (95% CI)			
ORR	38 (21-58)	58 (28-85)	24 (7-50)
DCR	93 (77-99)	92 (62-100)	94 (71-100)
Unconfirmed response, % (95% CI)			
ORR	66 (46-82)	92 (62-100)	47 (23-72)
DCR	97 (82-100)	100 (74-100)	94 (71-100)



Sacher AG et al. ASCO 2025

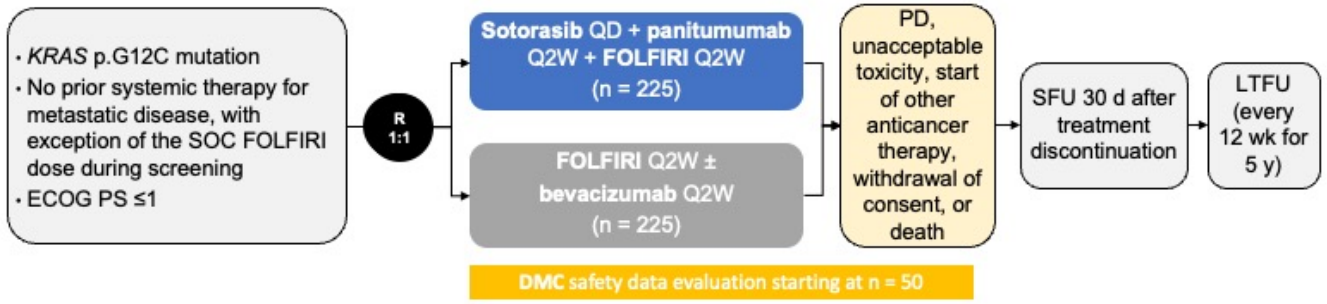
[a]Response was evaluated in the efficacy population, which includes all participants with measurable disease per RECIST v1.1 at baseline who received ≥1 MK-1084 dose ≥5 wk before the data cutoff date. The waterfall plot includes all participants who had ≥1 evaluable post-baseline imaging assessment (n = 28).
Data cutoff date: March 12, 2025 (median follow-up, 4.6 mo [range, 0.1-9.5]).

KANDLELIT-012 Study
Randomized, Open-Label, Phase 3 Trial[a]



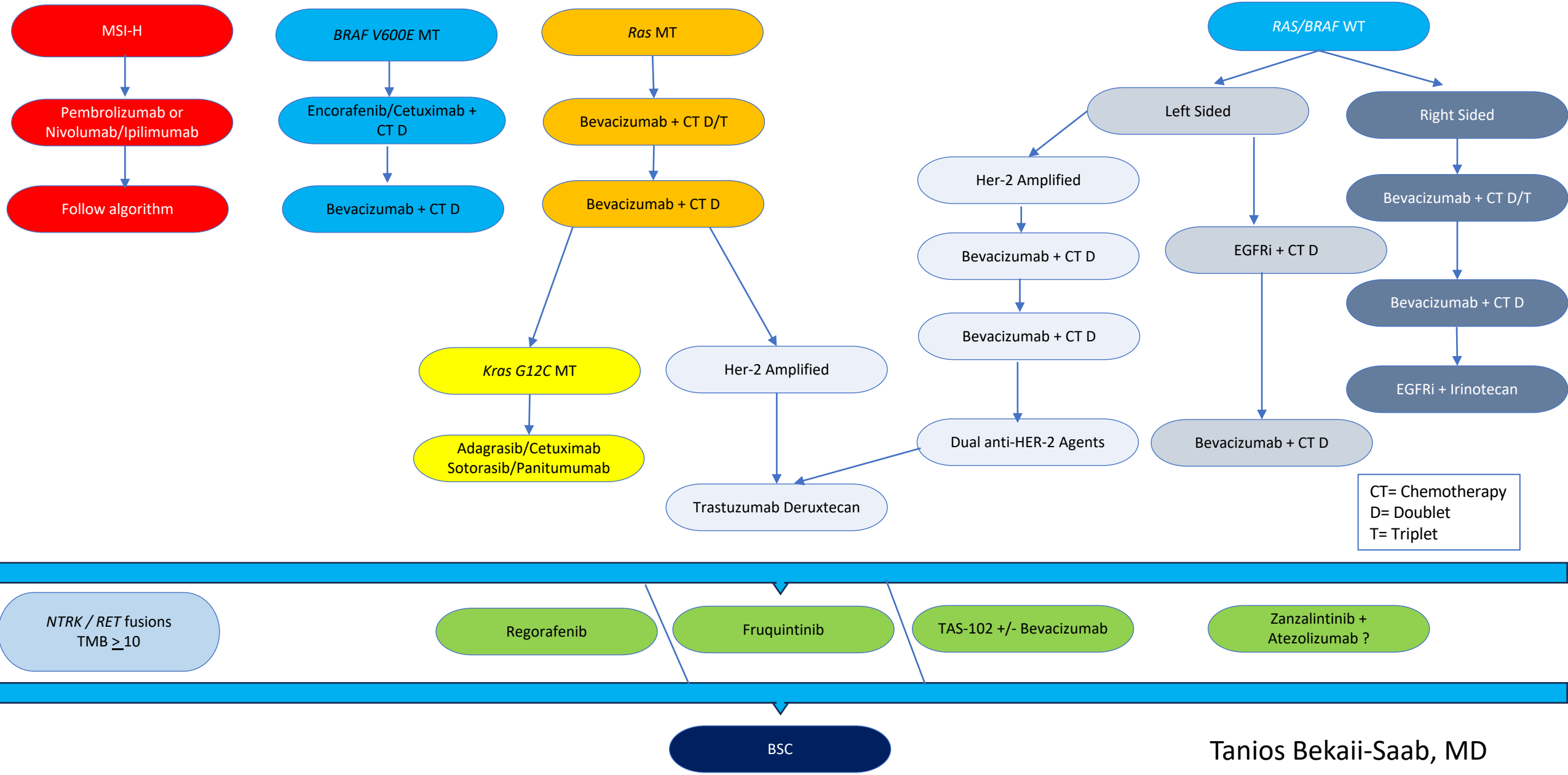
Kawazoe A, et al. ASCO GI 2026

Phase 3 CodeBreaK 301: FOLFIRI + Sotorasib + Panitumumab in mCRC[1]



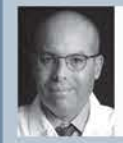
Kim TW, et al. ASCO GI 2025

Metastatic CRC with Unresectable Metastases

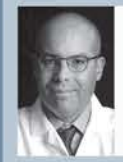


Tanios Bekaii-Saab, MD

What first-line treatment would you most likely recommend for a 60-year-old patient who presents with left-sided, pan-RAS wild-type, BRAF wild-type, HER2-negative, MSI-H mCRC?

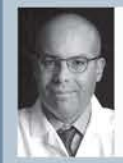
	Clinically stable	Highly symptomatic
 Dr Bekaii-Saab	Nivolumab/ipilimumab	Nivolumab/ipilimumab
 Dr Cohen	Nivolumab/ipilimumab	Nivolumab/ipilimumab
 Dr Dasari	Nivolumab/ipilimumab	Nivolumab/ipilimumab
 Dr Fakih	Nivolumab/ipilimumab	Nivolumab/ipilimumab
 Dr Lieu	Nivolumab/ipilimumab	Nivolumab/ipilimumab
 Dr Saeed	Nivolumab/ipilimumab	Nivolumab/ipilimumab

What first-line treatment would you most likely recommend for a clinically stable 60-year-old patient who presents with left-sided, pan-RAS wild-type, BRAF-mutant, HER2-negative, MSI-H mCRC?

 Dr Bekaii-Saab	Nivolumab/ipilimumab
 Dr Cohen	Nivolumab/ipilimumab
 Dr Dasari	Nivolumab/ipilimumab
 Dr Fakih	Nivolumab/ipilimumab
 Dr Lieu	Nivolumab/ipilimumab
 Dr Saeed	Nivolumab/ipilimumab

RTP RESEARCH TO PRACTICE

Have you used or would you use a ctDNA assay to determine whether to discontinue immunotherapy for a patient with mCRC who is faring well?

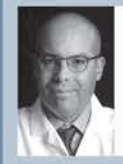
 Dr Bekaii-Saab	I have not but would for the right patient
 Dr Cohen	I have
 Dr Dasari	I have
 Dr Fakih	I have
 Dr Lieu	I have not but would for the right patient
 Dr Saeed	I have

RTP RESEARCH TO PRACTICE

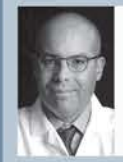
Faculty Discussion

- **What first-line treatment would you most likely recommend for a 60-year-old patient who presents with left-sided, pan-RAS wild-type, BRAF wild-type, HER2-negative, clinically stable MSI-H mCRC? What if the patient were highly symptomatic?**
- **What first-line treatment would you most likely recommend for a clinically stable 60-year-old patient who presents with left-sided, pan-RAS wild-type, BRAF-mutant, HER2-negative, MSI-H mCRC?**
- **Have you used or would you use a ctDNA assay to determine whether to discontinue immunotherapy for a patient with mCRC who is faring well?**

Do you believe there is therapeutic synergy between immune checkpoint inhibitors and multikinase inhibitors?

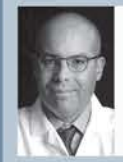
 Dr Bekaii-Saab	There are not enough available data at this time
 Dr Cohen	Yes
 Dr Dasari	Yes
 Dr Fakih	Yes
 Dr Lieu	There are not enough available data at this time
 Dr Saeed	Yes

Do you believe that zanzalintinib/atezolizumab will be endorsed by the FDA for previously treated mCRC?

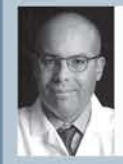
 Dr Bekaii-Saab	Yes
 Dr Cohen	Yes
 Dr Dasari	Yes
 Dr Fakih	No
 Dr Lieu	Yes
 Dr Saeed	Yes

RTP RESEARCH TO PRACTICE

Would you like to be able to access zanzalintinib/atezolizumab today for your patients with previously treated mCRC?

 Dr Bekaii-Saab	Yes
 Dr Cohen	No
 Dr Dasari	Yes
 Dr Fakih	No
 Dr Lieu	Yes
 Dr Saeed	Yes

In what line of therapy do you envision zanzalintinib/atezolizumab will be employed for patients with mCRC?

 Dr Bekaii-Saab	Third line or fourth line
 Dr Cohen	Third or fourth line and later
 Dr Dasari	Fourth line
 Dr Fakih	Fourth line
 Dr Lieu	Third line or fourth line
 Dr Saeed	Third-line setting

RTP RESEARCH TO PRACTICE

Faculty Discussion

- **Do you believe there is therapeutic synergy between immune checkpoint inhibitors and multikinase inhibitors?**
- **Do you believe that zanzalintinib/atezolizumab will be endorsed by the FDA for previously treated mCRC?**
- **Would you like to be able to access zanzalintinib/atezolizumab today for your patients with previously treated mCRC?**
- **In what line of therapy do you envision zanzalintinib/atezolizumab will be employed for patients with mCRC?**

Consensus or Controversy? Documenting and Discussing Investigators' Approaches to the Management of Ovarian Cancer

Saturday, May 30, 2026
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Ramez N Eskander, MD
Ursula Matulonis, MD
Alexander B Olawaiye, MD
David M O'Malley, MD

Moderator

Kathleen N Moore, MD, MS

RTP
RESEARCH
TO PRACTICE

What Clinicians Want to Know: Addressing Community Oncologists' Questions About the Care of Patients with Prostate Cancer

Saturday, May 30, 2026

7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Wassim Abida, MD, PhD

Rahul Aggarwal, MD

Emmanuel S Antonarakis, MD

Karim Fizazi, MD, PhD

Moderator

Rana R McKay, MD, FASCO

RTP RESEARCH TO PRACTICE

Second Opinion: Investigators Provide Perspectives on the Current and Future Management of Small Cell Lung Cancer

Saturday, May 30, 2026
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Anne Chiang, MD, PhD
Apar Kishor Ganti, MD, MS
Luis Paz-Ares, MD, PhD

Moderator

Misty Dawn Shields, MD, PhD

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