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COLORECTAL CANCER

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# GI ASCO 2023 Recap with Dr. Eng

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# Colorectal Cancer Updates From ASCO GI 2023

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February 6, 2023

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# Discussion Points

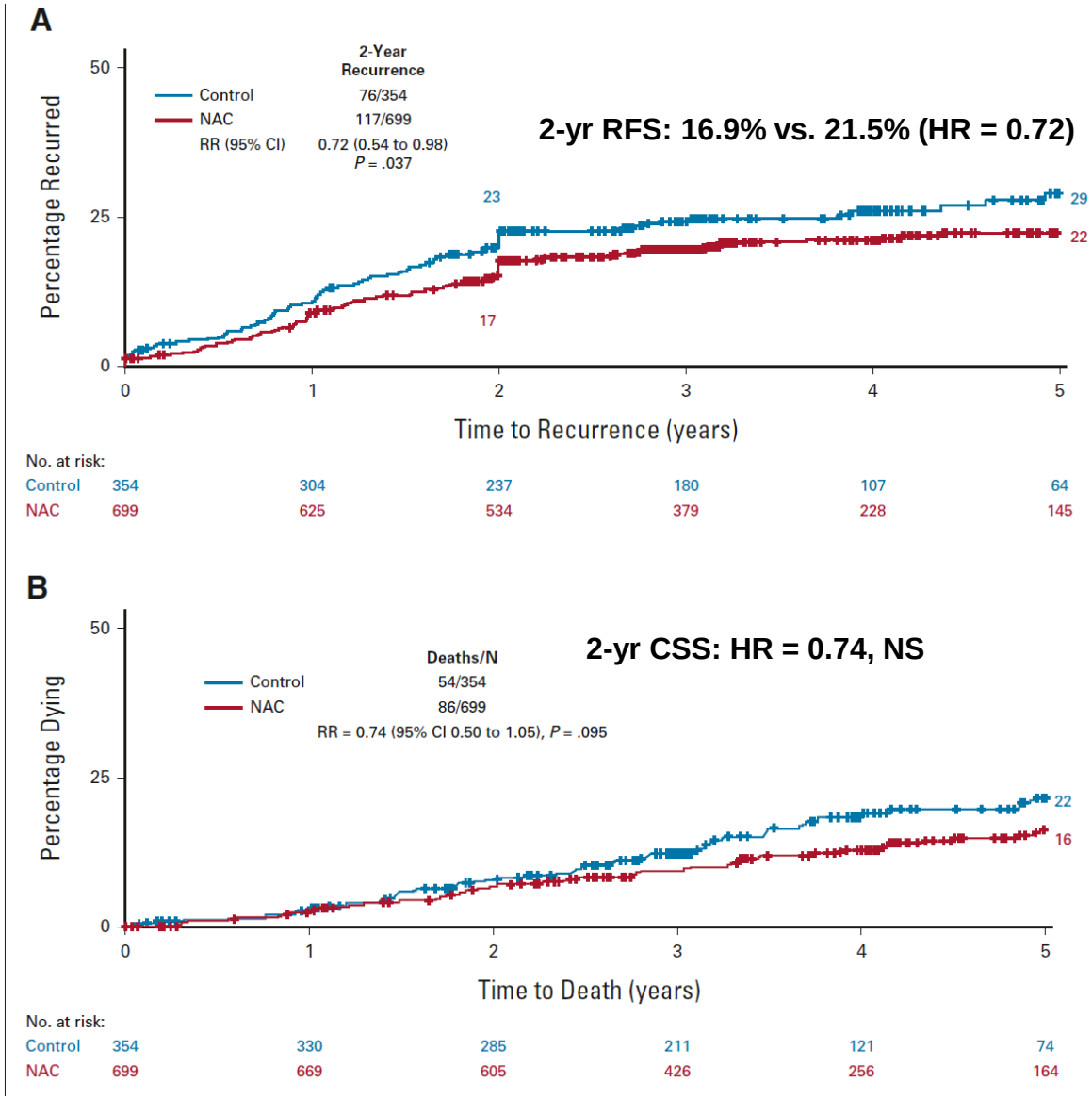
- Neoadjuvant MSI-S Colon CA
- Rectal Cancer
- Metastatic CRC
  - Rare subsets
    - BRAF MT
    - HER-2 Amplification
    - KRAS G12C
- The role of ctDNA

# Neoadjuvant Chemotherapy in Stage III MSI-S Colon Ca

# Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial

Dion Morton, MD[1]; Matthew Seymour, MD[2]; Laura Magill, PhD[3]; Kelly Handley, PhD[3]; James Glasbey, MD[1]; Bengt Glimelius, MD[4]; Andy Palmer[3]; Jenny Seligmann, MD[2]; Søren Laurberg, MD[5]; Keigo Murakami, MD[6]; Nick West, MD[6]; Philip Quirke, FMedSci[6]; and Richard Gray, MSc[7]; on behalf of the FOxTROT Collaborative Group

- N=1038 pts
- Majority were MSI-S
- Patients with radiologically staged T3-4, N0-2, M0 colon cancer
- Randomized to 6 weeks oxaliplatin-fluoropyrimidine preoperatively plus 18 postoperatively (NAC group) or SOC 6M (control group).
- Primary end point was residual disease or recurrence within 2 years

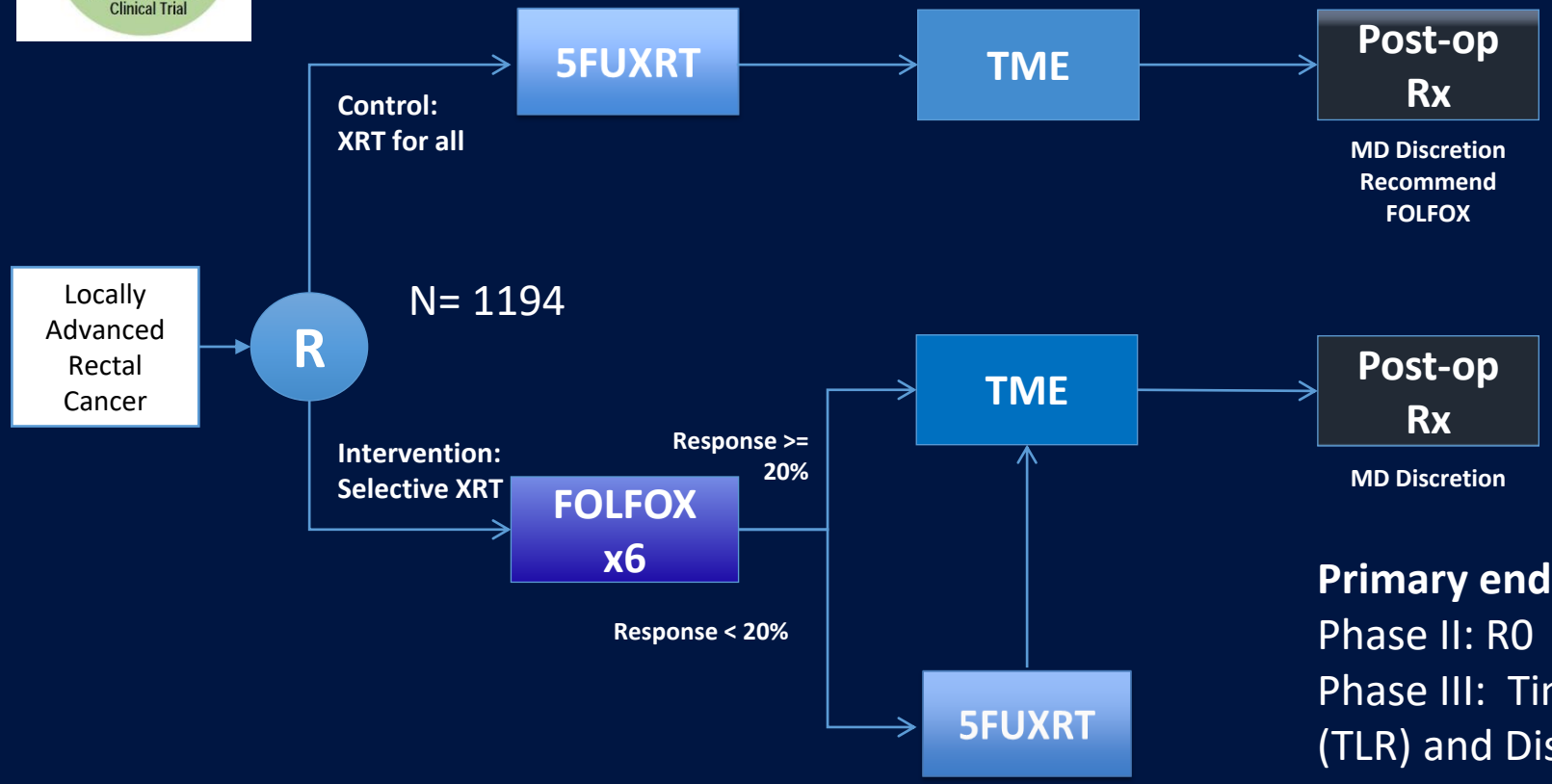



Morton et al: JCO, 2023

# Locally Advanced Rectal Cancer

# Protocol Schema for PROSPECT Trial: Omission of Radiation Therapy

PROSPECT
N1048: Rectal Cancer Clinical Trial




**Primary endpoints**:
Phase II: R0
Phase III: Time to Local Recurrence (TLR) and Disease-Free Survival (DFS)

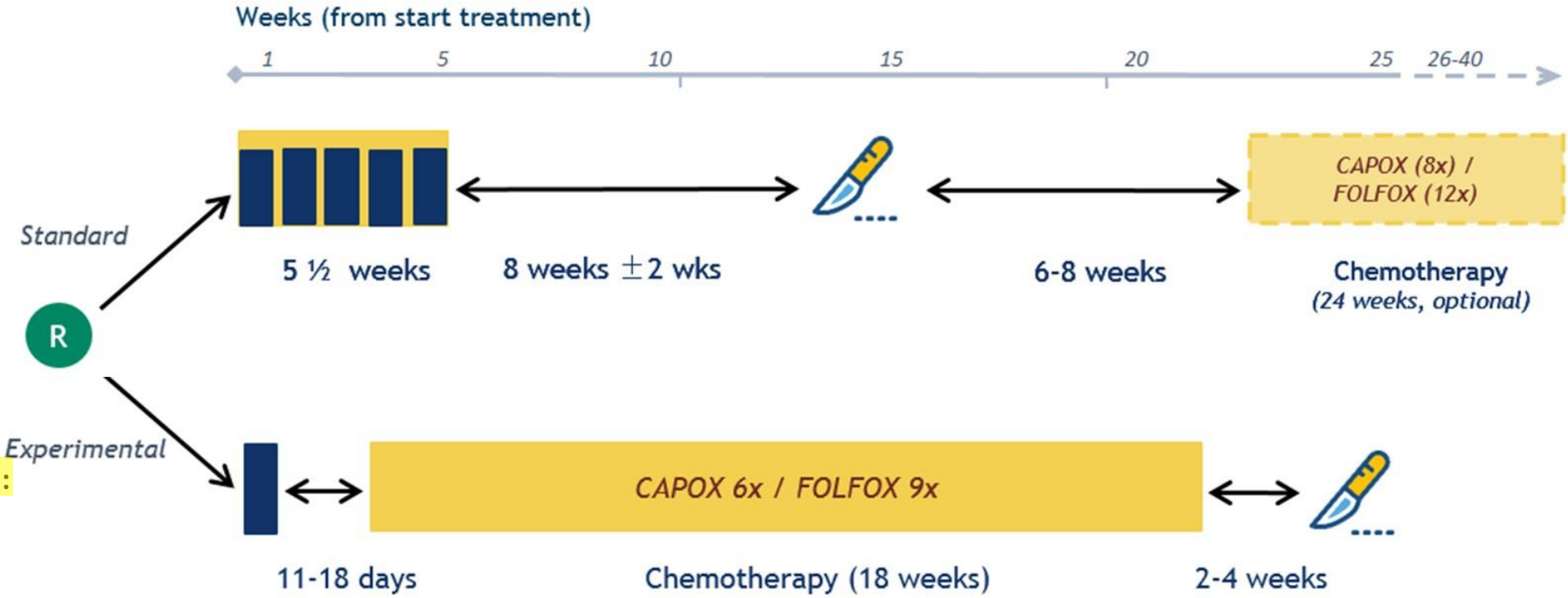
*Accepting proposals for correlatives

Final data: 2023-2024?

**PI: D. Schrag**

NCT01515787

# Study design Rapido Study Design




**Inclusion criteria:**

- T4a/b
- EMVI
- N2
- Mesorectal fascia (+)
- Enlarged lateral LN's

**Standard:** week 1-6: 28x1.8 Gy or 25x2 Gy at working days combined with capecitabine b.i.d. 825 mg/m$^2$ (twice daily) day 1-33-38.
**Experimental:** week 1: 5x5 Gy, week 3-20: 6x CAPOX (capecitabine b.i.d.1000 mg/m$^2$ (twice daily) day 1-14 every 3 weeks orally, oxaliplatin 130 mg/m$^2$ day 1 every 3 weeks iv or alternatively 9x FOLFOX4 (folinic acid, fluorouracil and oxaliplatin all iv every 2 weeks)

# High-risk criteria

| | Standard (n=450) | | Experimental (n=462) | |
|---|---|---|---|---|
| **High-risk criteria on MRI** | | | | |
| T4 | 137 | (30.4) | 147 | (31.8) |
| N2 | 295 | (65.6) | 302 | (65.4) |
| Enlarged lateral nodes | 69 | (15.3) | 66 | (14.3) |
| Extramural vascular invasion + | 125 | (27.8) | 148 | (32.0) |
| Mesorectal fascia + | 271 | (60.2) | 285 | (61.7) |
| **Number of high-risk factors per patient** | | | | |
| 1 | 168 | (37.3) | 158 | (34.2) |
| 2 | 146 | (32.4) | 160 | (34.6) |
| 3 | 96 | (21.3) | 98 | (21.2) |
| 4 | 29 | (6.4) | 39 | (8.4) |
| 5 | 11 | (2.4) | 7 | (1.5) |

Data is presented as n (%)

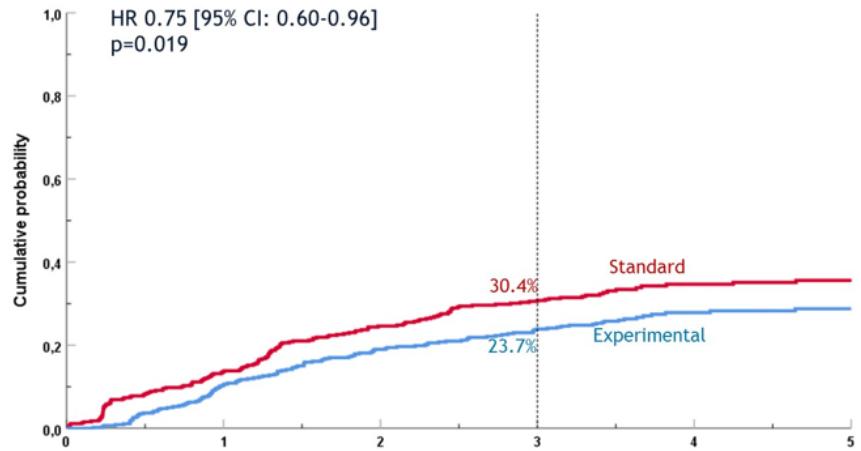
# Pathology of resected rectal tumor

| | Standard (n=398) | | Experimental (n=423) | | p-value |
|---|---|---|---|---|---|
| **Residual tumor** | | | | | 0.62 |
| R0 > 1 mm | 360 | (90.5) | 383 | (90.5) | |
| R1 ≤ 1 mm | 37 | (9.3) | 37 | (8.7) | |
| R2 | 1 | (0.3) | 3 | (0.7) | |
| **Pathological complete response** | | | | | <0.001 |
| Yes | 57 | (14.3) | 120 | (28.4) | |
| No | 341 | (85.7) | 303 | (71.6) | |

Data is presented as n (%)

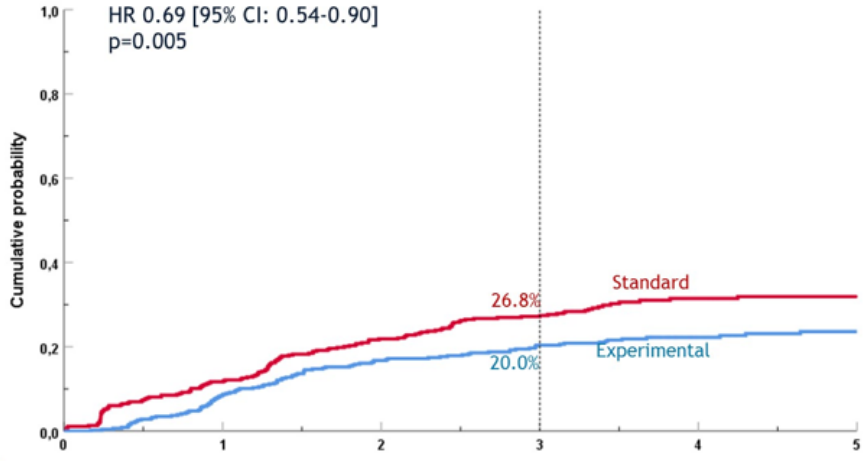
# Results from the RAPIDO Trial

## Disease-related Treatment Failure




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Standard | 450 | 385 | 334 | 300 | 152 | 127 |
| Experimental | 462 | 410 | 367 | 338 | 168 | 135 |

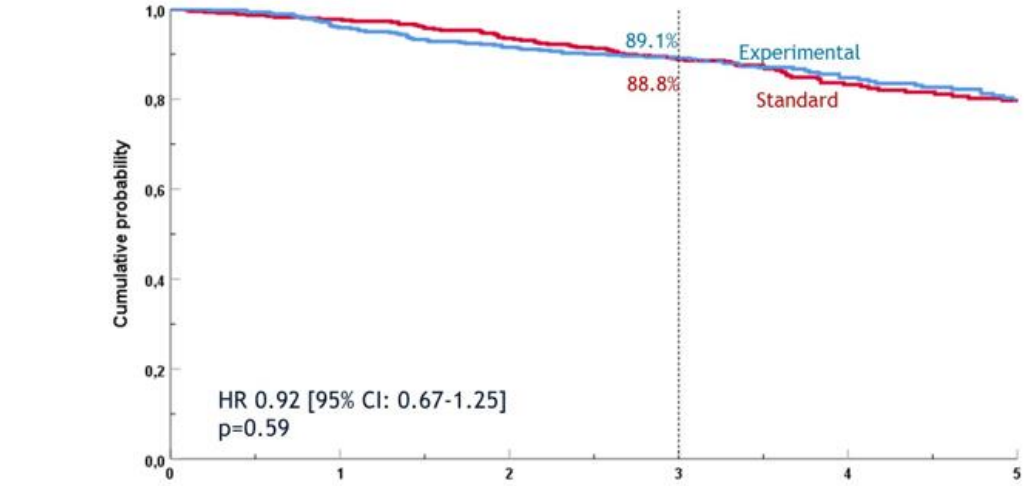
## Distant metastases




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Standard | 450 | 390 | 343 | 311 | 156 | 130 |
| Experimental | 462 | 414 | 372 | 348 | 178 | 144 |

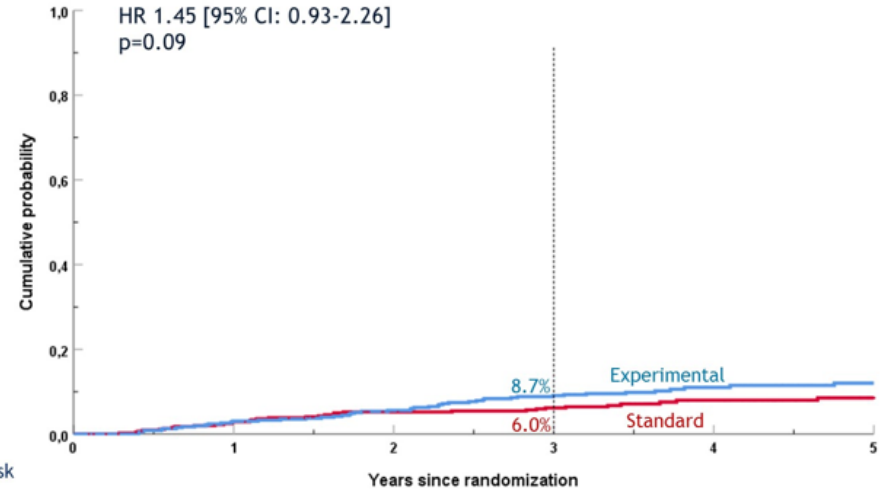
# Results from the RAPIDO Trial

## Overall Survival




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Standard | 450 | 438 | 418 | 391 | 204 | 163 |
| Experimental | 462 | 442 | 421 | 402 | 205 | 159 |

## Locoregional Failure




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Standard | 450 | 428 | 405 | 379 | 200 | 162 |
| Experimental | 462 | 434 | 410 | 382 | 192 | 149 |

**Median follow-up of 4.5 years**

# RAPIDO (Short Course) – 5-YR FOLLOW-UP

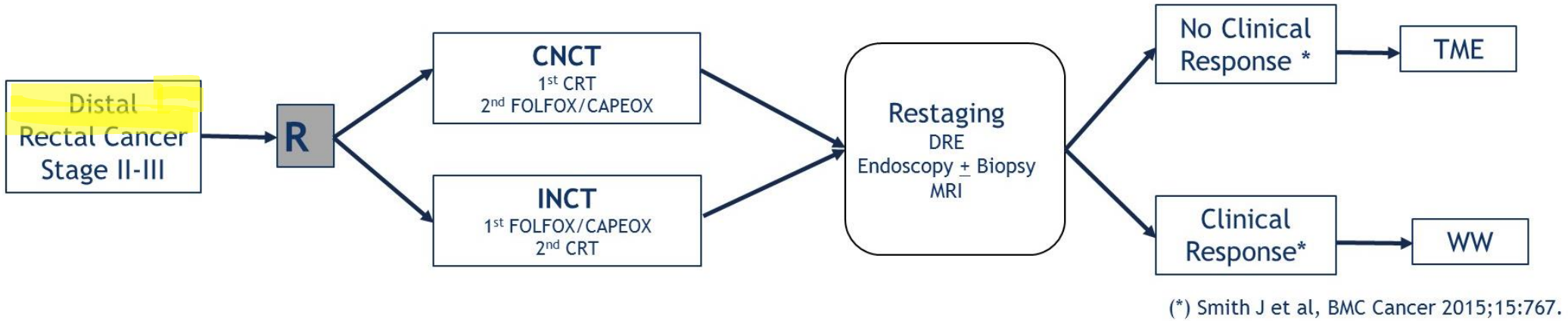
ANNALS OF SURGERY

| | RAPIDO | Standard of Care | P-value |
|---|---|---|---|
| Local regional failure (LRF) | 12% | 8% | 0.07 |
| Local regional recurrence (LRR) | 10% | 6% | **0.027** |
| Disease-related treatment failure (DrTF) | 28% | 34% | 0.048 |
| Distant Mets | 23% | 30% | **0.011** |
| Overall survival (OS) | 82% | 80% | 0.50 |

Dikjstra, et al: Annals of Surg, 2023

# Organ Preservation in Rectal Cancer Trial (OPRA)

## Investigational Arm




(*) Smith J et al, BMC Cancer 2015;15:767.

## Sample Size Calculation

- Each group (CNCT and INCT) was designed as a single-stage study
- Primary Endpoint: DFS
  - Not powered for a formal comparison between groups
  - 3-year DFS rates of ***75% (historical)*** *vs* alternative of ***85% (investigational)***
  - Assume 85% power and two-sided type 1 error of 5%
  - Initial target accrual: 202 patients (101 in each groups)
  - 10% attrition/ 222 total accrual

Garcia-Aguilar et al: JCO 2022

# Methods

Rectal Adenocarcinoma stage II-III

Randomized to total neoadjuvant therapy (TNT):

- **Consolidation (CNCT)**

**OR**

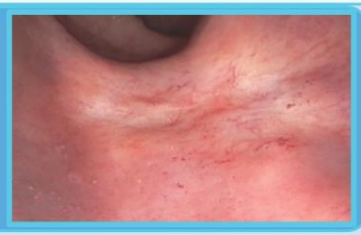
- **Induction (INCT)**

8 +/- 4 weeks

## Three-Tier Clinical Response Assessment Schema

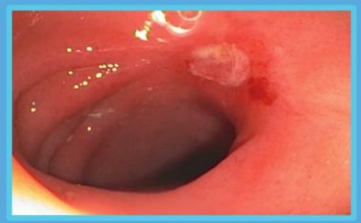
### Clinical Complete Response (cCR)

- Flat, white scar
- Telangiectasia
- No ulceration or nodularity
- Digital rectal exam (DRE): normal



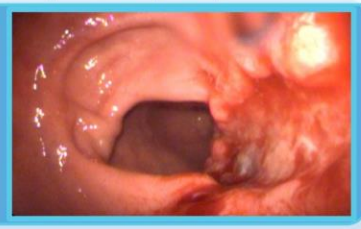
### Near Complete Clinical Response (nCR)

- Irregular mucosa
- Small nodules/minor mucosal abnormality
- Superficial ulceration
- Mild persisting erythema
- DRE: smooth induration/minor mucosal abnormality on DRE



### Incomplete Clinical Response (iCR)

- Visible Tumor
- DRE: palpable tumor nodules



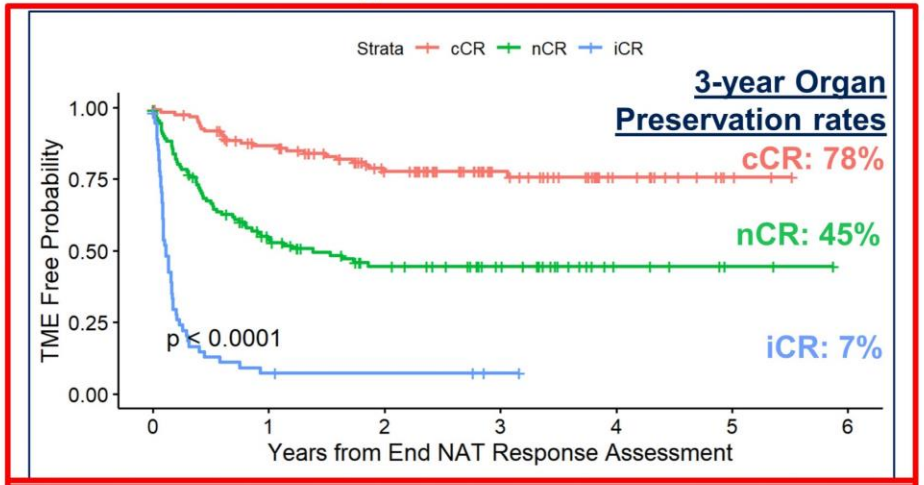
Recommend WW

or

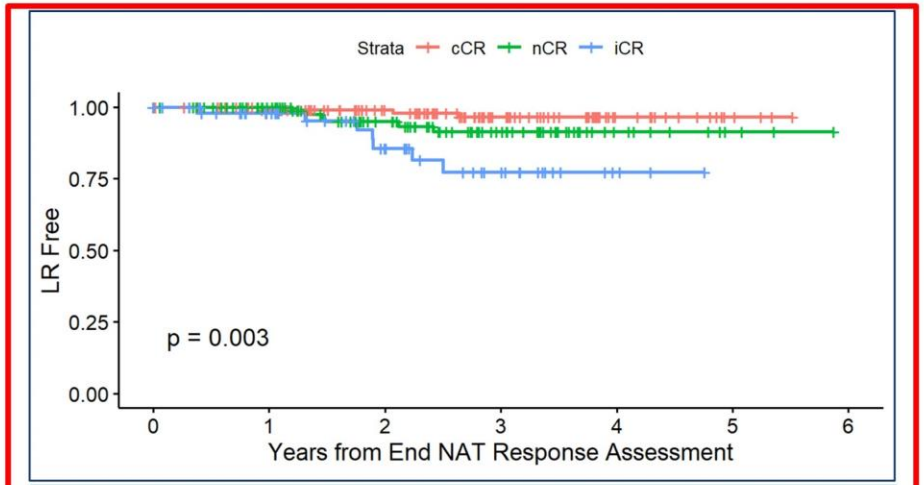
Recommend TME

# Organ Preservation and Survival Outcomes by Clinical Response

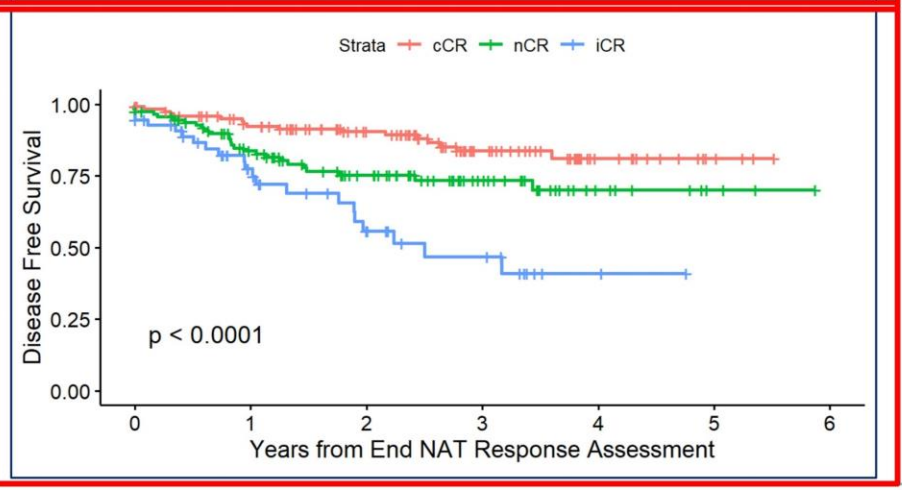
**Organ Preservation**



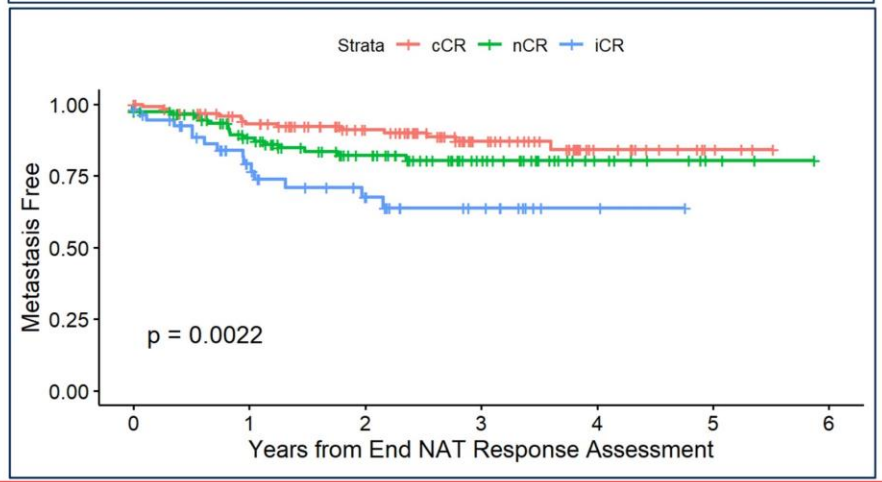

**Local Recurrence-Free Survival**



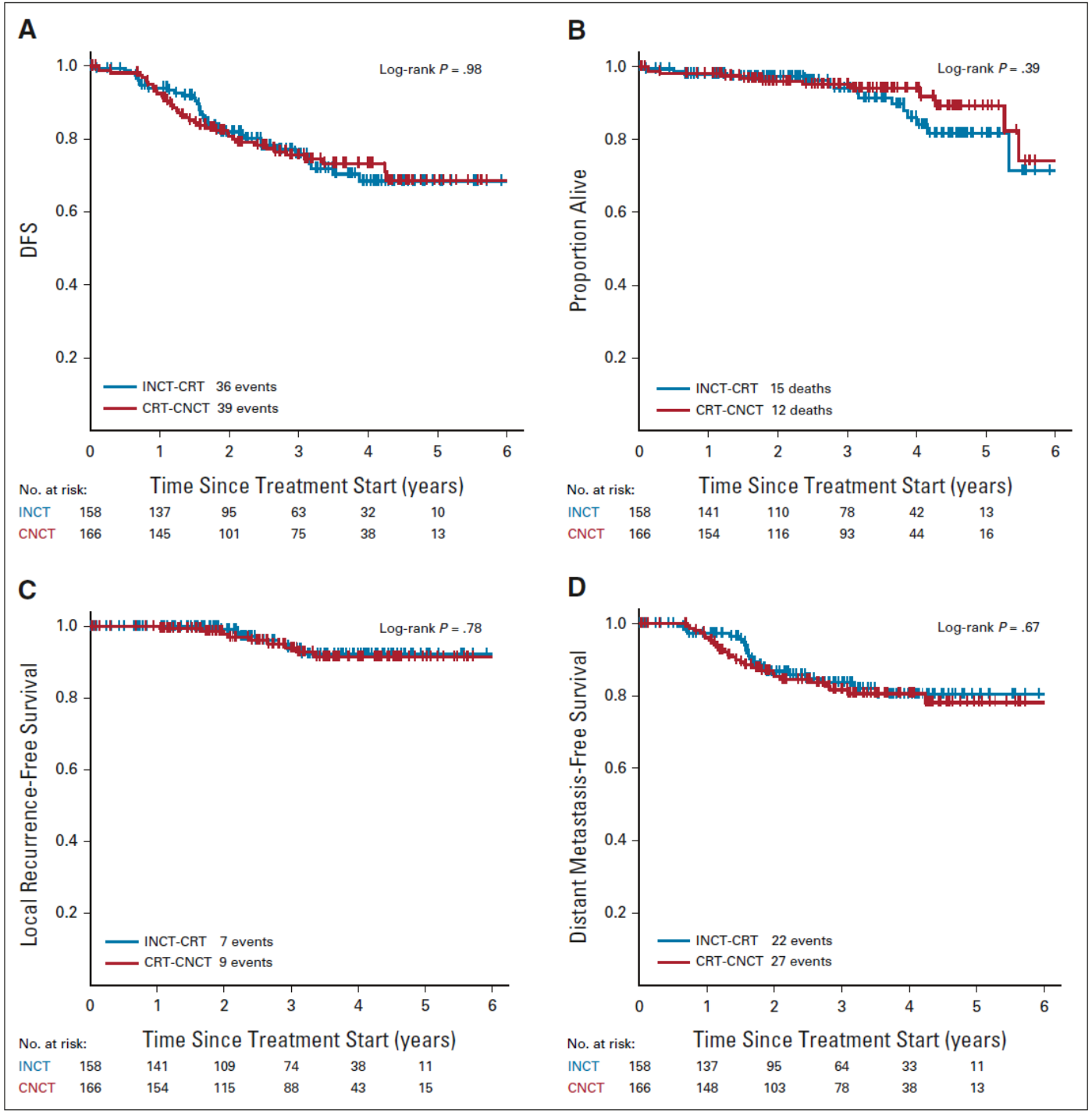

**Disease-Free Survival**




**Metastasis-Free Survival**

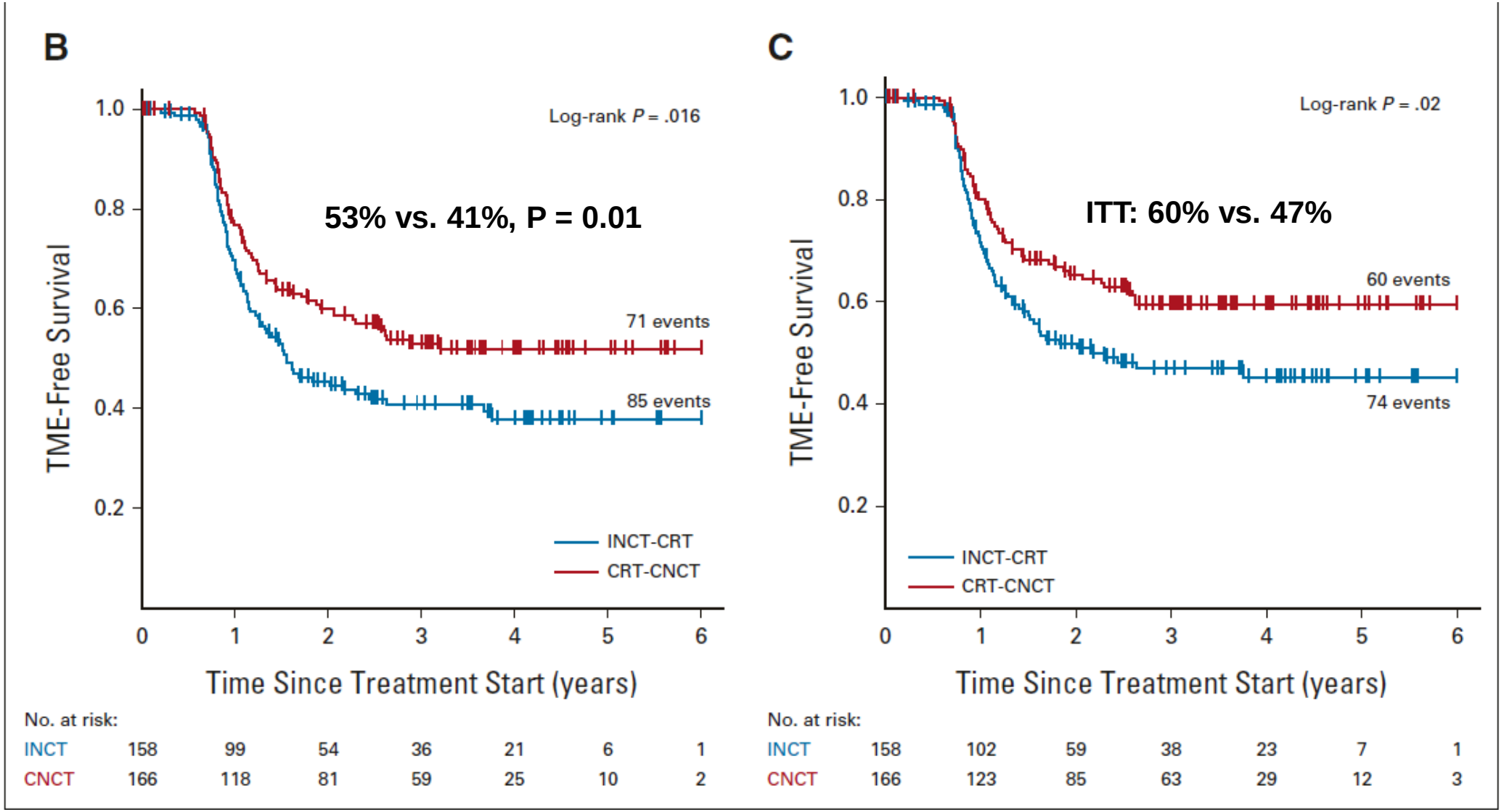


# Results of OPRA (Median follow-up = 3 yrs)




Garcia-Aguilar et al: JCO 2022

# OPRA: 3-yr TME-Free Survival and ITT




Garcia-Aguilar et al: JCO 2022

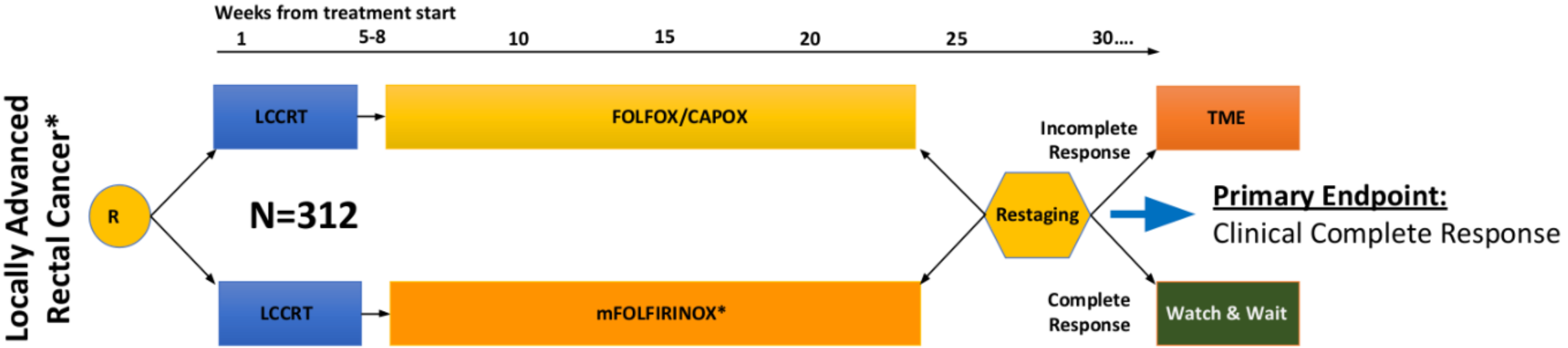
# The Janus Rectal Cancer Study: A Randomized Phase II Trial

NCT05610163

## A022104 – An Alliance, NRG & SWOG Study



**Opened: 9 Nov 2022!**




**PI's: J. Smith, A. Dasari, W. Hall**

**Schema Legend**: Randomization = R; LCCRT = long-course chemoradiation; Restaging determination = endoscopy, MRI and clinical exam 8-12 weeks post-completion of assigned TNT regimen

* <=12cm, cT4N0, anyT, N+; T3N0 that would require APR or coloanal anastomosis

# Short vs. Long-Course RT w/Organ Preservation for High-Risk Rectal Cancer Patients (ACO/ARO/AIO-18.1)

- Any cT3 < 6 cm
- cT3c/d in the middle third of the rectum (≥ 6-12 cm) with EMVI > 5 mm (>cT3b)
- cT3 with clear cN+
- cT4 tumors
- N+
- mrCRM+ (< 1mm)
- Extramural venous invasion (EMVI+)

**N=712**

**Short Course 5x5** → **FOLFOX x 9 or CapeOx x 6**

**ChemoXRT Long Course** → **FOLFOX x 6 or CapeOx x 4**

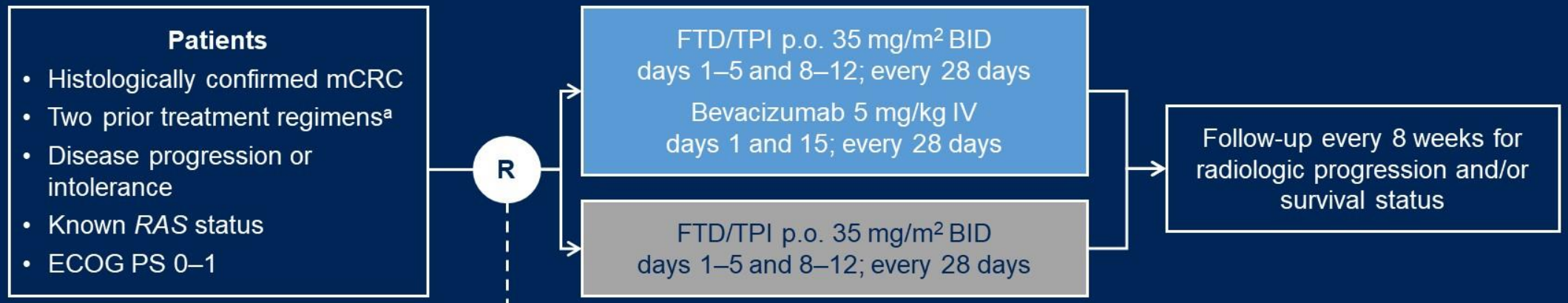
**Primary endpoint: Organ Preservation**
**PI: C. Roedel**

NCT04246684

# Updates on MCRC

# SUNLIGHT study design

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



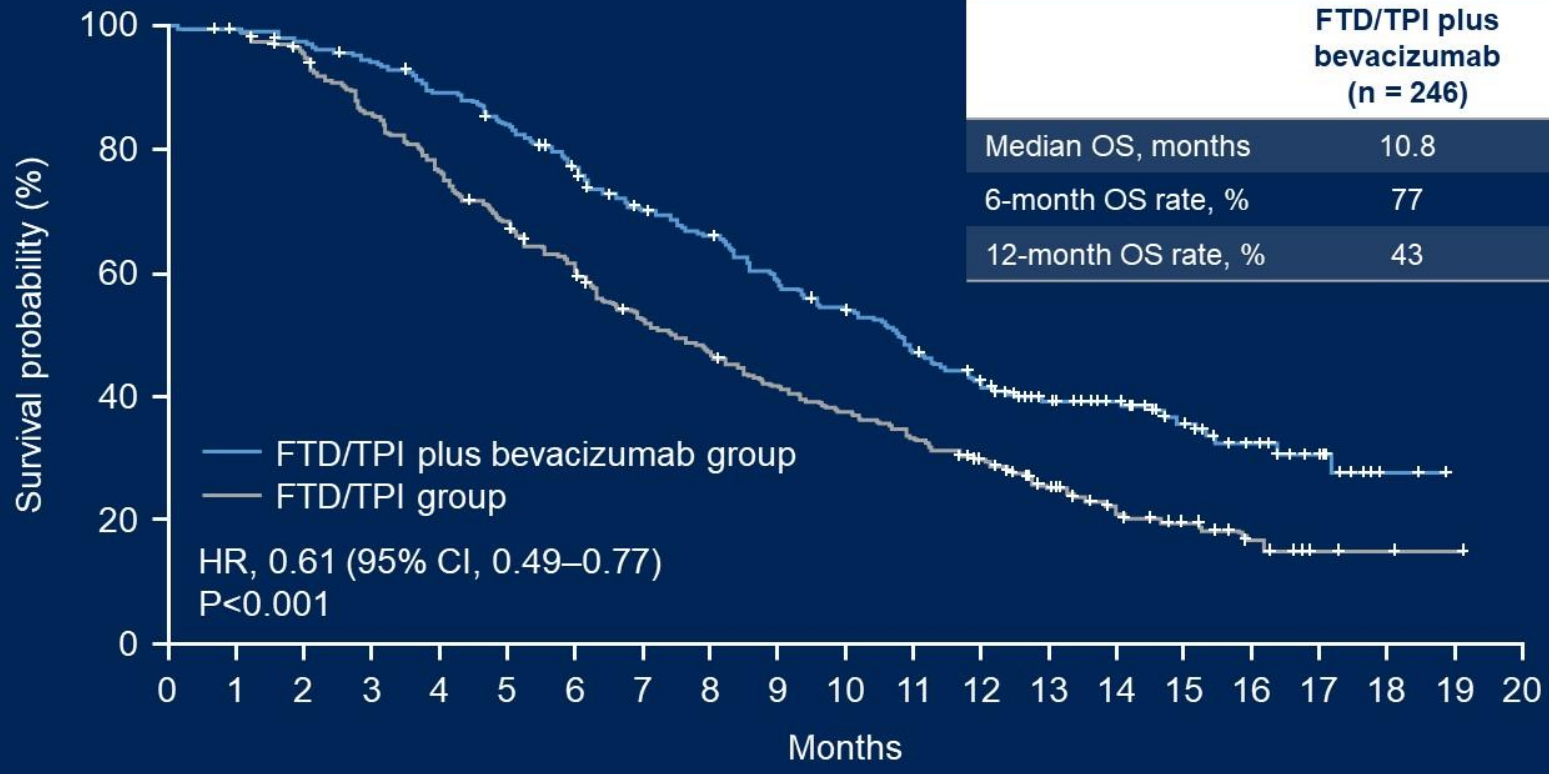

[a] Prior treatment must have included a fluoropyrimidine, irinotecan, oxaliplatin, an anti-VEGF monoclonal antibody (not necessarily bevacizumab), and/or an anti-EGFR monoclonal antibody for patients with *RAS* wild-type and could have included (neo)adjuvant chemotherapy if disease had recurred during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

# Key baseline characteristics

| Characteristic | | FTD/TPI plus bevacizumab (n = 246) | FTD/TPI (n = 246) |
|---|---|---|---|
| **Age** | Median (range), years | 62 (20–84) | 64 (24–90) |
| | <65 years, n (%) | 146 (59) | 129 (52) |
| | ≥65 years, n (%) | 100 (41) | 117 (48) |
| **Sex, n (%)** | Male | 122 (50) | 134 (55) |
| **Region** | European Union | 158 (64) | 157 (64) |
| | North America | 8 (3) | 8 (3) |
| | Rest of the world | 80 (33) | 81 (33) |
| **Primary tumor localization, n (%)** | Right | 62 (25) | 77 (31) |
| | Left | 184 (75) | 169 (69) |
| **Time from diagnosis of first metastasis to randomization,[a] n (%)** | <18 months | 104 (42) | 105 (43) |
| | ≥18 months | 142 (58) | 141 (57) |
| ***RAS* status,[a] n (%)** | Mutant | 171 (70) | 170 (69) |
| | Wild-type | 75 (31) | 76 (31) |
| **Prior treatment with bevacizumab, n (%)** | No | 68 (28) | 70 (29) |
| | Yes | 178 (72) | 177 (72) |
| **ECOG PS, n (%)** | 0 | 119 (48) | 106 (43) |
| | 1 | 127 (52) | 139 (57) |
| | 2 | 0 | 1 (0.4)[b] |

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

# OS in full analysis set (primary endpoint)



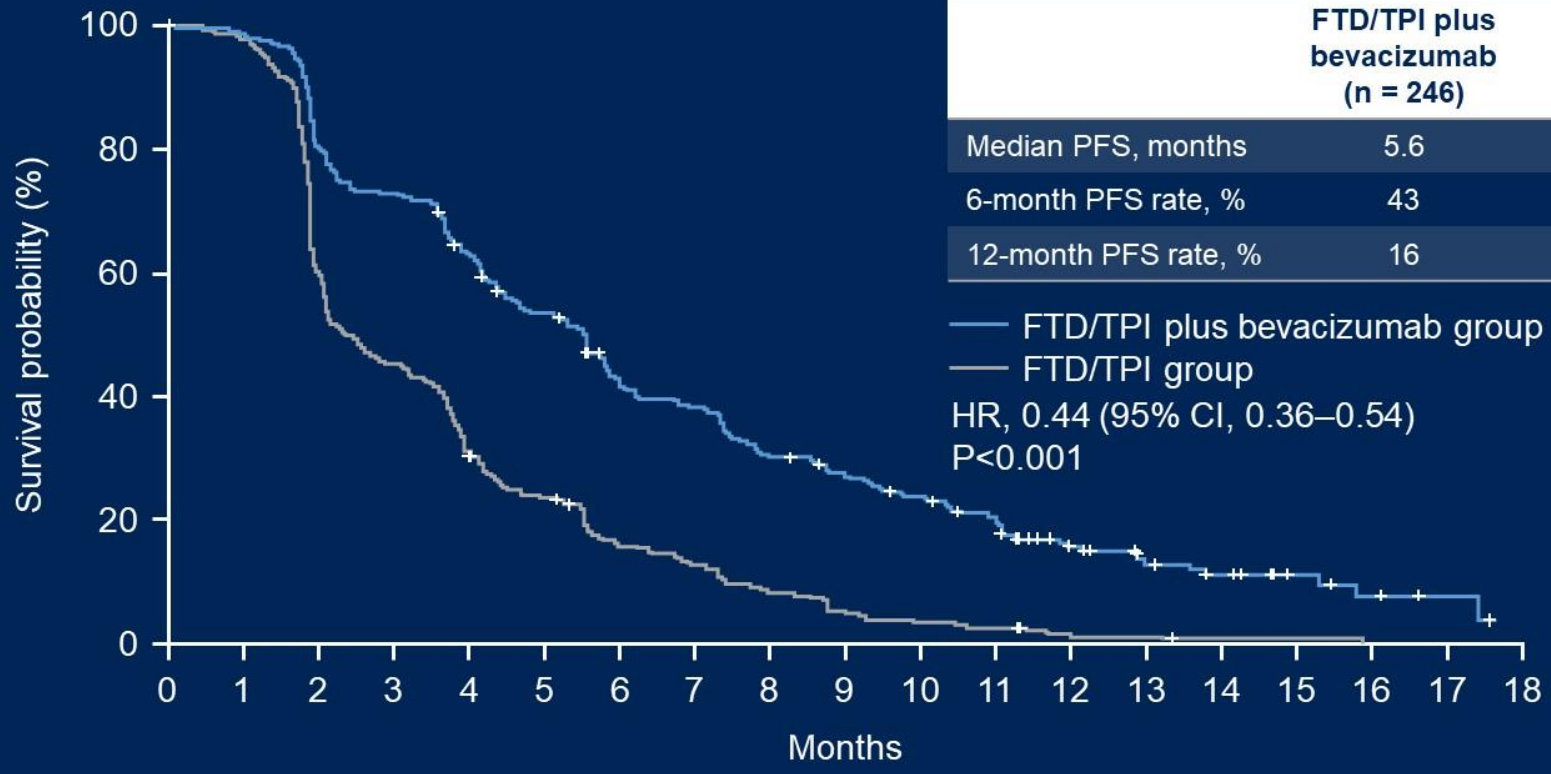

| | FTD/TPI plus bevacizumab (n = 246) | FTD/TPI (n = 246) |
|---|---|---|
| Median OS, months | 10.8 | 7.5 |
| 6-month OS rate, % | 77 | 61 |
| 12-month OS rate, % | 43 | 30 |

**No. at risk**

| | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FTD/TPI plus bevacizumab group | 246 | 244 | 239 | 230 | 217 | 203 | 183 | 160 | 149 | 131 | 119 | 104 | 88 | 69 | 52 | 37 | 24 | 13 | 2 | 0 | 0 |
| FTD/TPI group | 246 | 242 | 230 | 205 | 184 | 163 | 143 | 120 | 108 | 95 | 85 | 76 | 63 | 44 | 24 | 16 | 10 | 5 | 2 | 1 | 0 |

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

# PFS in full analysis set



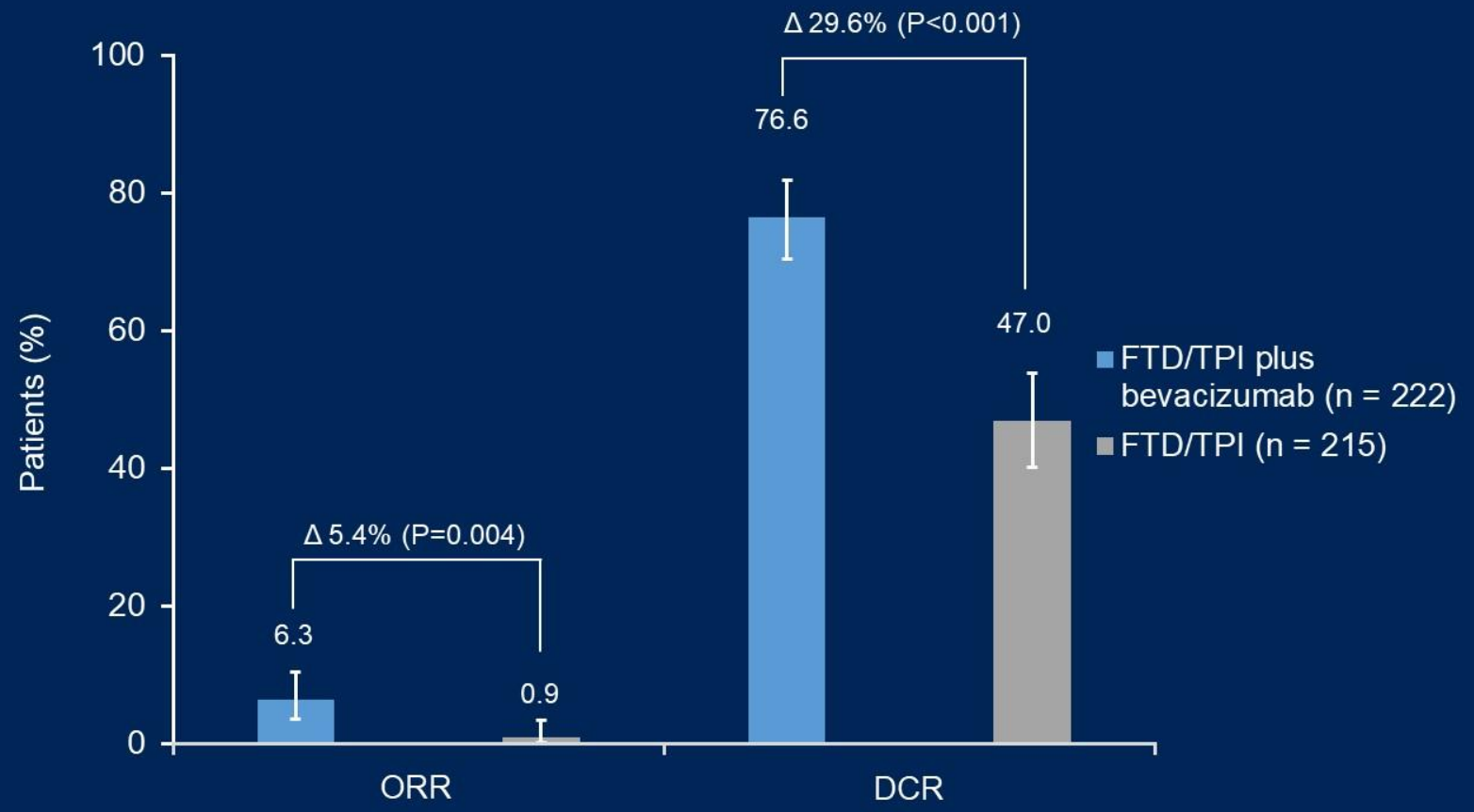

| | FTD/TPI plus bevacizumab (n = 246) | FTD/TPI (n = 246) |
|---|---|---|
| Median PFS, months | 5.6 | 2.4 |
| 6-month PFS rate, % | 43 | 16 |
| 12-month PFS rate, % | 16 | 1 |

**No. at risk**

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| FTD/TPI plus bevacizumab group | 246 | 242 | 198 | 179 | 153 | 128 | 99 | 89 | 70 | 61 | 52 | 43 | 25 | 18 | 13 | 7 | 4 | 2 | 0 |
| FTD/TPI group | 246 | 236 | 147 | 109 | 74 | 56 | 36 | 29 | 19 | 12 | 8 | 6 | 2 | 2 | 1 | 1 | 0 | 0 | 0 |

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

# ORR and DCR in patients evaluable for tumor response




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

# TEAEs in ≥20% of patients

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

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

FTD/TPI, trifluridine/tipiracil; TEAE, treatment-emergent adverse event.

# FRESCO-2 Study Design

## Patient Eligibility

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

R 2:1

N=687

**Fruquintinib** 5 mg PO, QD
(3 weeks on, 1 week off)
+
BSC
(N=458)

**Placebo** 5 mg PO, QD
(3 weeks on, 1 week off)
+
BSC
(N=229)

Treatment until progression or unacceptable toxicity

**Stratification Factors**

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

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

BSC, best supportive care.
NCT04322539.

# Patient and Disease Characteristics

**ITT Population**

**Enrollment:** Sep 2020 to Dec 2021

**Data Cutoff:** 24 June 2022

| Characteristic, n (%) | | Fruquintinib (N=461) | Placebo (N=230) |
|---|---|---|---|
| **Age, y** | Median (range) | 64 (25, 82) | 64 (30, 86) |
| | ≥ 65 | 214 (46.4) | 111 (48.3) |
| **Sex** | Female | 216 (46.9) | 90 (39.1) |
| | Male | 245 (53.1) | 140 (60.9) |
| **Region** | North America | 82 (17.8) | 42 (18.3) |
| | Europe | 329 (71.4) | 166 (72.2) |
| | Asia Pacific | 50 (10.8) | 22 (9.6) |
| **ECOG PS** | 0 | 196 (42.5) | 102 (44.3) |
| | 1 | 265 (57.5) | 128 (55.7) |
| **Primary site at 1st diagnosis** | Colon left | 192 (41.6) | 92 (40.0) |
| | Colon right | 97 (21.0) | 53 (23.0) |
| | Colon left and right | 4 (0.9) | 2 (0.9) |
| | Colon unknown | 25 (5.4) | 13 (5.7) |
| | Rectum only | 143 (31.0) | 70 (30.4) |
| **Liver metastases** | Yes | 339 (73.5) | 156 (67.8) |

| Characteristic, n (%) | | Fruquintinib (N=461) | Placebo (N=230) |
|---|---|---|---|
| **Duration of metastatic disease** | ≤ 18 mo | 37 (8.0) | 13 (5.7) |
| | > 18 mo | 424 (92.0) | 217 (94.3) |
| **RAS status** | WT | 170 (36.9) | 85 (37.0) |
| | Mutant | 291 (63.1) | 145 (63.0) |
| **BRAF V600E mutation** | No | 401 (87.0) | 198 (86.1) |
| | Yes | 7 (1.5) | 10 (4.3) |
| | Other/Unknown | 5 (11.5) | 22 (9.6) |
| **Number of prior treatment lines in metastatic disease** | Median (range) | 5 (2, 16) | 5 (2, 12) |
| | ≤ 3 | 125 (27.1) | 64 (27.8) |
| | > 3 | 336 (72.9) | 166 (72.2) |
| **Prior therapies** | VEGF inhibitor | 445 (96.5) | 221 (96.1) |
| | EGFR inhibitor | 180 (39.0) | 88 (38.3) |
| **Prior TAS-102 and/or regorafenib** | TAS-102 | 240 (52.1) | 121 (52.6) |
| | Regorafenib | 40 (8.7) | 18 (7.8) |
| | Both | 181 (39.3) | 91 (39.6) |

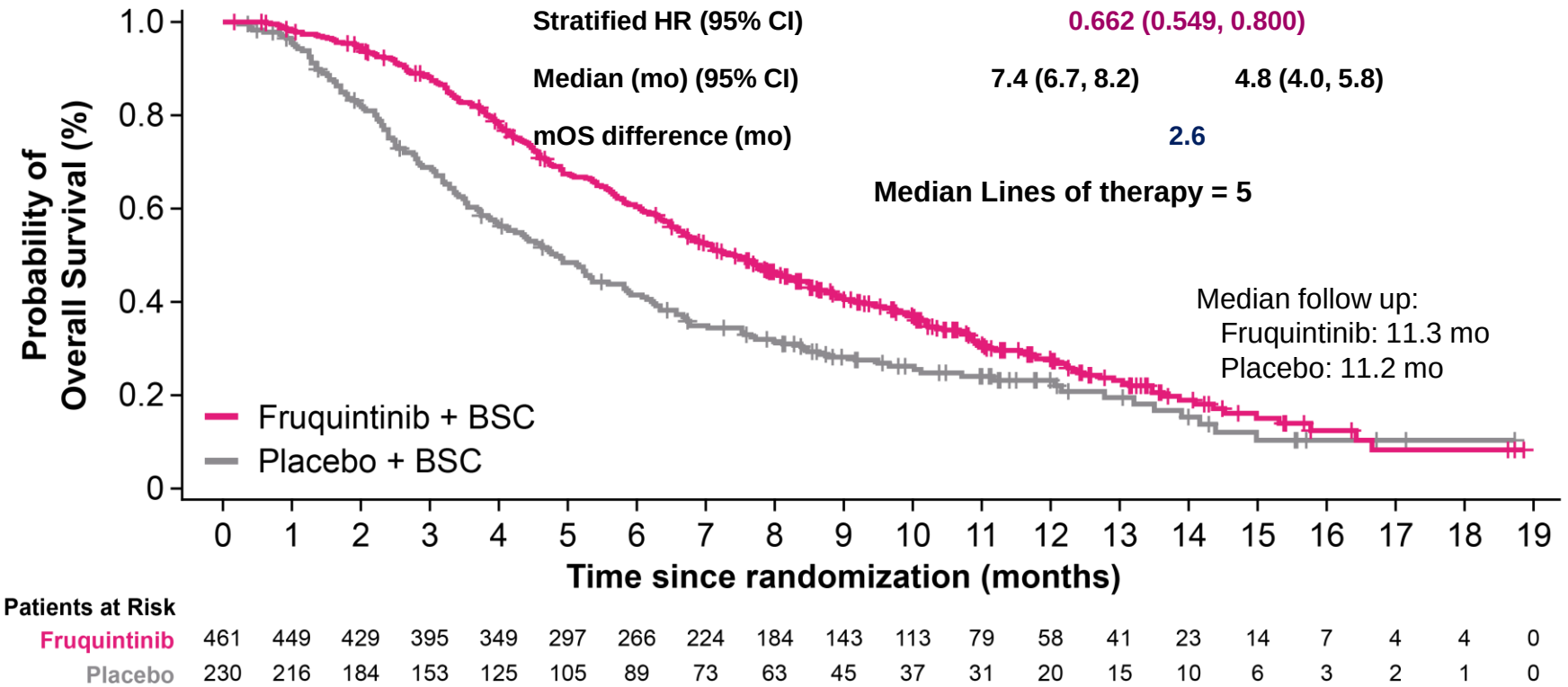
Dasari A et al. ESMO 2022, Presentation LBA25

# Practice-Changing Options in mCRC

## FRESCO-2: A global phase 3 multiregional clinical trial evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer (*Pending FDA review*)

| | Fruquintinib | Placebo |
|---|---|---|
| Events/Patients (%) | 317/461 (68.8%) | 173/230 (75.2%) |
| Stratified p-value (log-rank) | <0.001 | |
| Stratified HR (95% CI) | 0.662 (0.549, 0.800) | |
| Median (mo) (95% CI) | 7.4 (6.7, 8.2) | 4.8 (4.0, 5.8) |
| mOS difference (mo) | 2.6 | |

**Median Lines of therapy = 5**




Median follow up:
Fruquintinib: 11.3 mo
Placebo: 11.2 mo

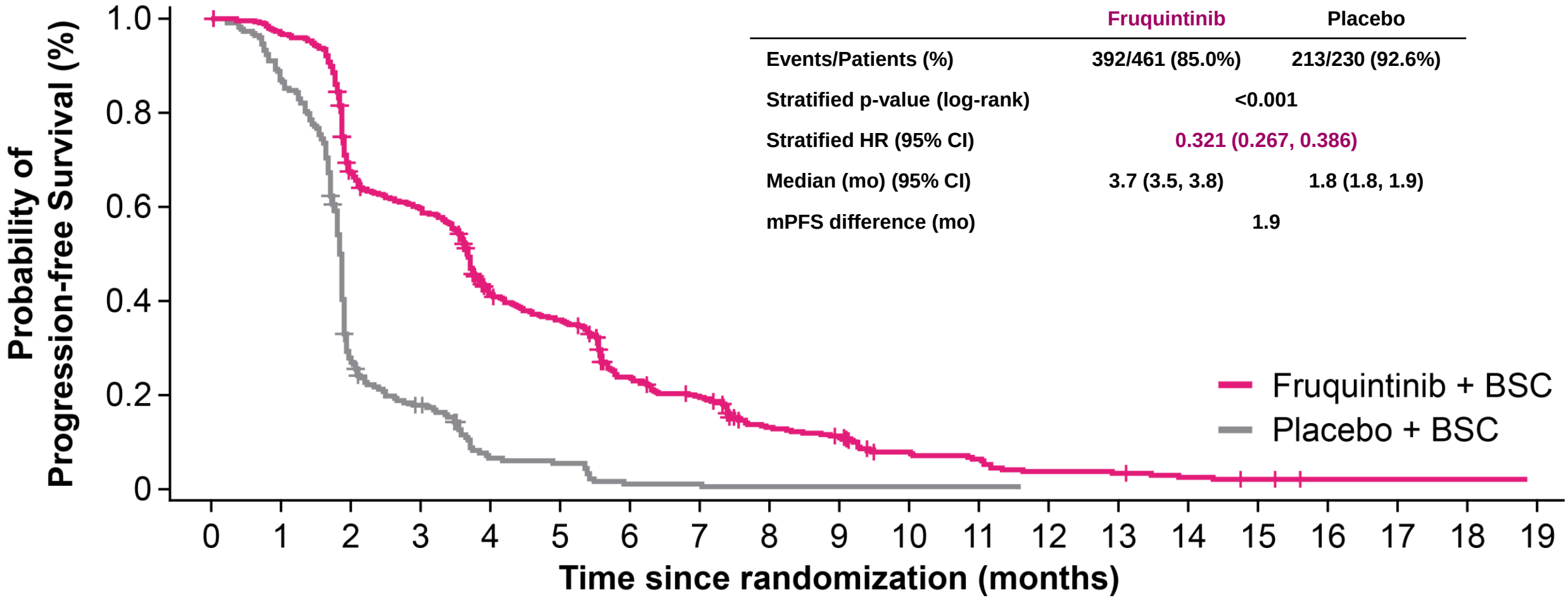
| Patients at Risk | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Fruquintinib | 461 | 449 | 429 | 395 | 349 | 297 | 266 | 224 | 184 | 143 | 113 | 79 | 58 | 41 | 23 | 14 | 7 | 4 | 4 | 0 |
| Placebo | 230 | 216 | 184 | 153 | 125 | 105 | 89 | 73 | 63 | 45 | 37 | 31 | 20 | 15 | 10 | 6 | 3 | 2 | 1 | 0 |

PARIS 2022 ESMO congress

VANDERBILT-INGRAM CANCER CENTER

# Progression-Free Survival

ITT Population




| | Fruquintinib | Placebo |
|---|---|---|
| Events/Patients (%) | 392/461 (85.0%) | 213/230 (92.6%) |
| Stratified p-value (log-rank) | <0.001 | |
| Stratified HR (95% CI) | 0.321 (0.267, 0.386) | |
| Median (mo) (95% CI) | 3.7 (3.5, 3.8) | 1.8 (1.8, 1.9) |
| mPFS difference (mo) | 1.9 | |

**Patients at Risk**

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

Dasari A et al. ESMO 2022, Presentation LBA25

# My Perspective

## SUNLIGHT

- TAS-102, is a chemotherapeutic agent tested in the **3rd** line setting
- Largely completed in the EU
- **24%** of pts did not receive prior bevacizumab
- Could not be conducted in the US since most patients were already using continuation of bevacizumab
- Myelosuppression is the main side effect which was expected in both arms
- Likely will NOT change practice patterns in the US

## FRESCO-2

- Fruquintinib is an oral targeted agent not a “me too” since it selectively blocks VEGFR 1,2,and 3
- No chemotherapy involved
- International trial involving Asia, EU, Australia and the US
- Heavily pretreated setting (**UP to** median 5 lines) allowing patients to receive lonsurf and/or rego
  - >50% had received prior lonsurf
  - ~40% had received both lonsurf and rego
- More flexible agent use?
- **96%** of patients had received bevacizumab
- Main side effects: Hypertension (class effect); 6-7% of hand-foot syndrome and asthenia

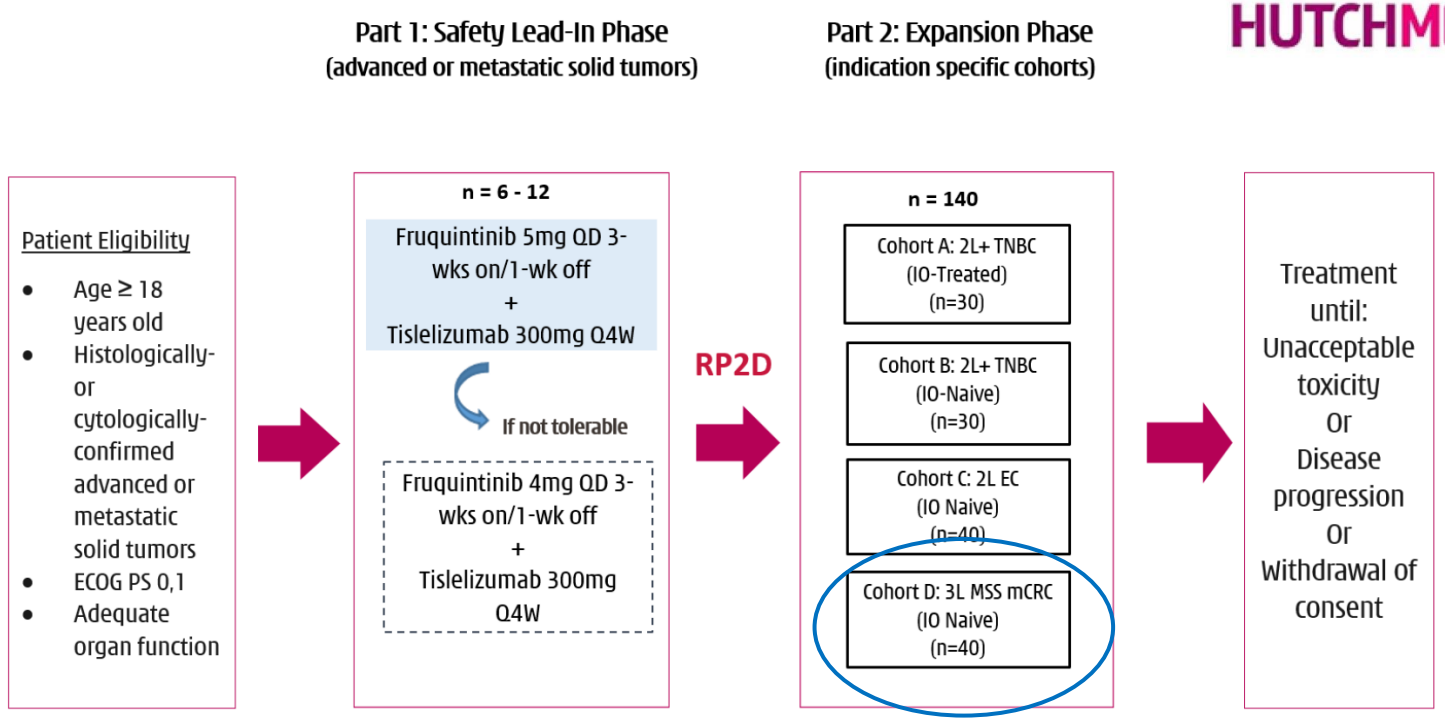
***Take home message: They both have utility in our mCRC patients**

# Phase II Fruquintinib + Tislelizumab in MSI-S mCRC

## Clinical Study Protocol

**AN OPEN-LABEL, PHASE 1b/2 STUDY TO EVALUATE THE SAFETY AND EFFICACY OF FRUQUINTINIB IN COMBINATION WITH TISLELIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS**

**Figure 1 Study Schematic**




4 sites: Vanderbilt-Ingram Cancer Center, MD Anderson Cancer Center, Mayo Clinic, and other (completed enrollment in < 3 months)

NCT04577963

# NCT04776148: Phase III Lenvatinib (MK-7902/E7080) + Pembrolizumab (MK-3475) Versus Standard of Care in Participants With Metastatic Colorectal Cancer (MK-7902-017/E7080-G000-325/LEAP-017)

## Final Results Pending

**Eligibility:**
Unresectable and metastatic colorectal adenocarcinoma

Previously treated with disease progression ***or*** could not tolerate standard treatment

Must **NOT** be microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) by local testing

**No** presence of malabsorption or other gastrointestinal conditions

**Accrual Goal**
**N = 434**

**RANDOMIZATION**

**Arm A: Lenvatinib + pembrolizumab**

Pembrolizumab (400 mg) IV on Day 1 of each 6-week cylce
*Repeat cycle for up to 18 cycles ( approximately 2 years)*
+
Lenvatinib (20 mg) oral capsule once daily until progressive disease

**Arm B: Standard of care treatment**

Regorafenib (160 mg) oral tablet once daily on Days 1 -21 of each 4-week cycle

***or***

TAS-102 (trifluridine and tipiracil hydrochloride) (35 mg/m$^2$) oral tablet twice daily on Day 1-5 + Day 8-12 of each 4-week cycle

**Enrollment completed!**

**FOLLOW-UP**

**Primary Endpoint:**
Overall Survival (OS)

**Secondary Endpoints:**
Progression Free Survival (PFS), Objective Response Rate (ORR), and Serious Adverse Events (SAE)

# NCT05425940: Study of XL092 + Atezolizumab vs Regorafenib in Subjects With Metastatic Colorectal Cancer (STELLAR-303)

**Eligibility:**
Unresectable and metastatic colorectal adenocarcinoma

Previously treated with disease progression ***or*** could not tolerate standard treatment

Must **NOT** be microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR) by local testing

**No** presence of malabsorption or other gastrointestinal conditions

**Accrual Goal**
**N = 600**

**RANDOMIZATION**

**Arm A: Investigational Arm**

**XL092 + atezolizumab**

**Arm B: Standard of care treatment**

**Regorafenib (160 mg) oral tablet once daily on Days 1 -21 of each 4-week cycle**

**FOLLOW-UP**

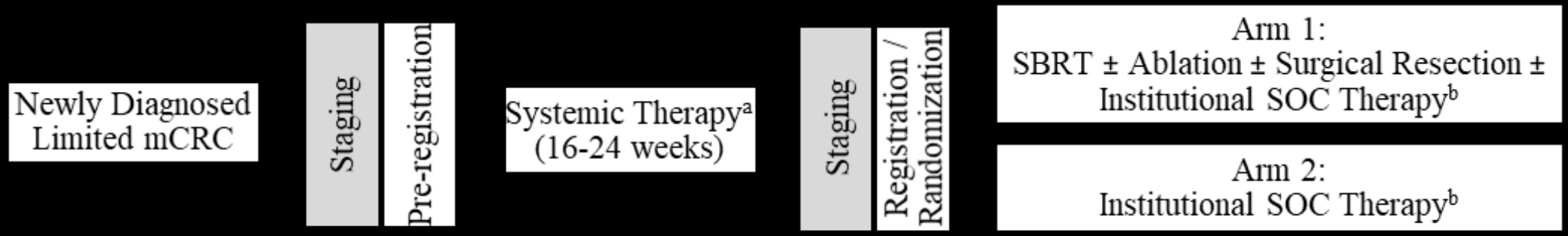
**Primary Endpoint:**
**Overall Survival (OS)**

**Secondary Endpoints:**
**Progression Free Survival (PFS), Objective Response Rate (ORR), and Serious Adverse Events (SAE)**

**PI's: R. Hecht and A. Saeed**

# A Pragmatic Randomized Phase III Trial Evaluating Total Ablative Therapy for Patients with Limited Metastatic Colorectal Cancer: Evaluating Radiation, Ablation, and Surgery (ERASur)

AO2011101

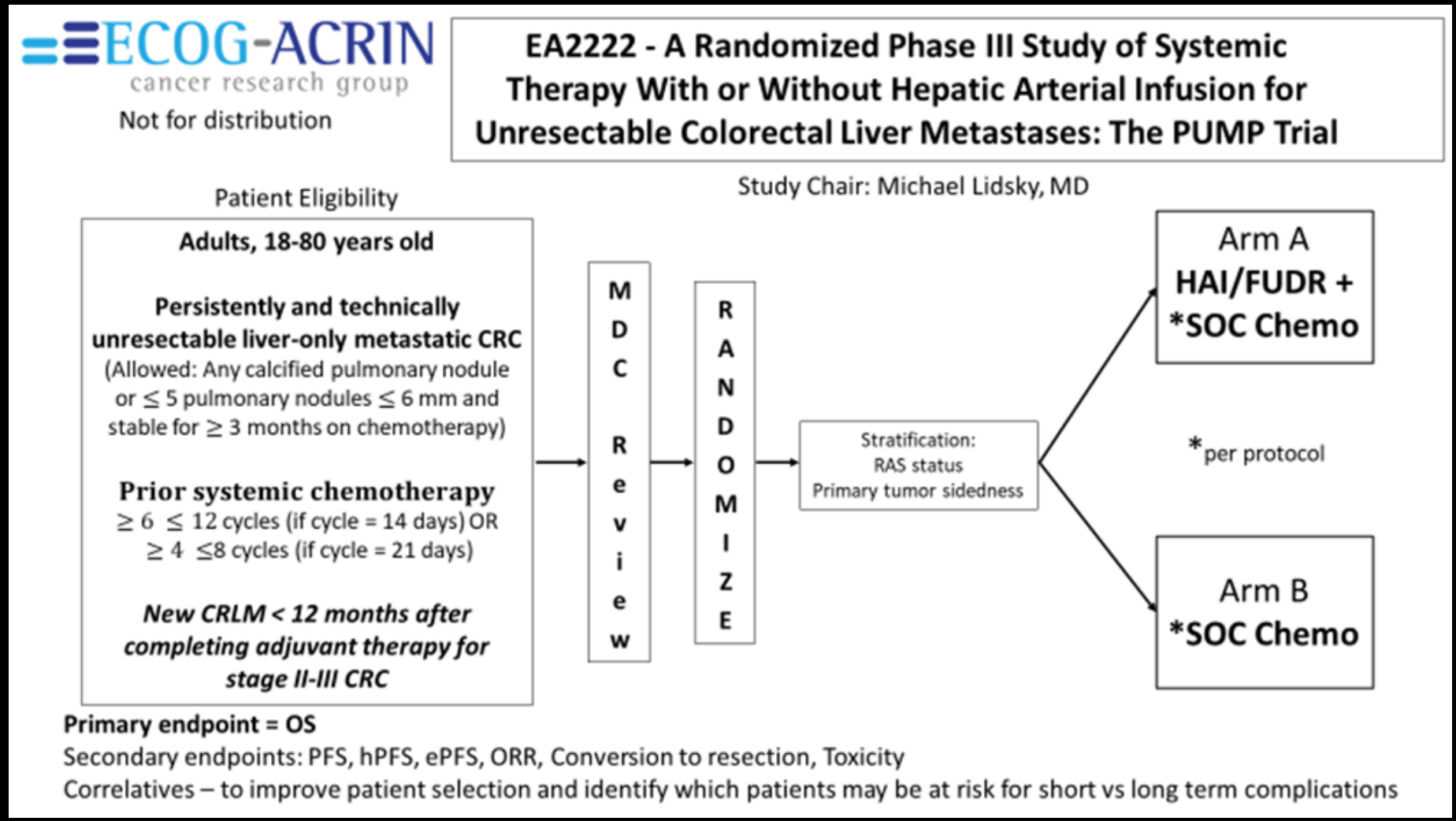



**PI's: Miller, Romesser, and Hitchcock**

N= 364

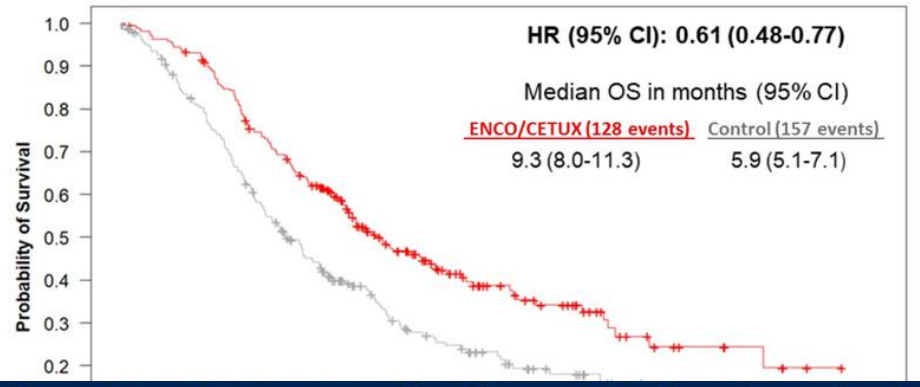
- OS is primary endpoint
- There must be at least one other site of metastasis in addition to the liver
- Adjuvant must have been completed 12 months prior

# NCI Approved/Pending Trials



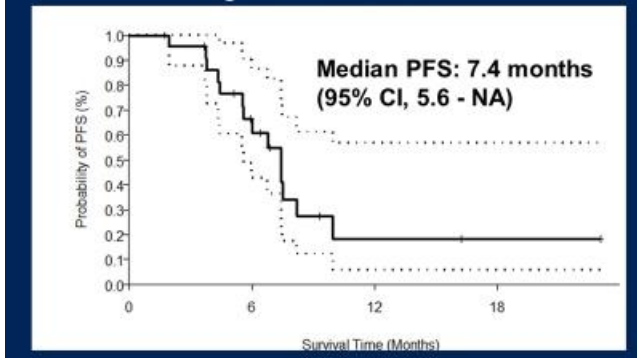
# BRAF MT V600E MCRC

# BRAF V600E MT Previously Treated MCRC

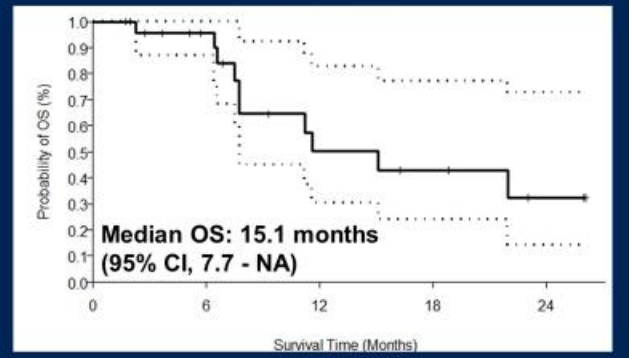



## Survival outcomes: encorafenib + cetuximab + nivolumab

**Progression-free survival**




**Overall survival**




Median follow-up time: 16.3 months (95% CI, 6.9 –NA)
Median duration of response: 7.7 months (95% CI, 3.8 – NA)

Encorafenib + cetuximab: median PFS 4.2 months (95% CI, 3.7-5.4), median OS 8.4 months (95% CI, 7.5-11.0) [1]

[1]Kopetz S et al, NEJM 2019

ASCO Gastrointestinal Cancers Symposium #GI22 PRESENTED BY: Van Morris, MD



ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

## SWOG 2107

Pts with MSS, *BRAF*$^{V600E}$ metastatic CRC, AND
- 1-2 prior lines of systemic therapy
- ECOG PS 0-1
- No prior (1) BRAF, MEK, ERK; (2) anti-EGFR; or (3) immune checkpoint therapy

R

2:1

N=75

Encorafenib + cetuximab + nivolumab

Encorafenib + cetuximab

PI: V. Morris

SWOG
Leading cancer research. Together.

# Study Design

BREAKWATER (NCT04607421) is an ongoing, open-label, global, multicenter, randomized phase 3 study evaluating 1L EC ± chemotherapy vs SOC chemotherapy alone in participants with BRAF V600E-mutant mCRC

## Safety Lead-In

Participants who have received ≤1 prior treatment for mCRC

**Cohort 1 (n=30)**
Encorafenib 300 mg QD
+ cetuximab 500 mg/m$^2$ Q2W
+ FOLFIRI Q2W in 28-day cycles

**Cohort 2 (n=27)**
Encorafenib 300 mg QD
+ cetuximab 500 mg/m$^2$ Q2W
+ mFOLFOX6 Q2W in 28-day cycles

**Primary Endpoint**

- Safety (frequency of DLTs)

**Secondary Endpoints**

- Safety (AEs, dose interruptions/ modifications/discontinuations)
- PKs
- Antitumor activity by investigator (ORR, DOR, TTR, PFS, OS)

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| • BRAF V600E-mutant mCRC (blood or tumor tissue)<br>• ≤1 prior systemic treatment for mCRC<br>• Evaluable disease (RECIST 1.1)<br>• ECOG PS 0 or 1<br>• Adequate BM, hepatic, and renal function | • Prior treatment with BRAF or EGFR inhibitors or both oxaliplatin and irinotecan<br>• Symptomatic brain metastases<br>• MSI-H or dMMR tumors[a] |

## Phase 3

Participants who have not received prior systemic treatment for mCRC

R

**Arm A (n≈235)**
Encorafenib + cetuximab

**Arm B (n≈235)**
Encorafenib + cetuximab
+ mFOLFOX6

**Control (n≈235)**
mFOLFOX6/FOLFOXIRI/
CAPOX ± bevacizumab

**Primary Endpoint**

- PFS by BICR

**Secondary Endpoints**

- OS
- ORR, DOR, and TTR by BICR and by investigator
- PFS by investigator
- Safety
- PROs
- Biomarkers

Here we present an updated analysis from the BREAKWATER SLI, including updated safety and antitumor activity data by BICR, as well as preliminary biomarker data

**Data cutoff: September 5, 2022.**

[a]Unless patient ineligible to receive immune checkpoint inhibitors due to pre-existing medical condition.

BICR, blinded independent central review; BM, bone marrow; DLT, dose-limiting toxicity; dMMR, deficient mismatch repair; EC, encorafenib + cetuximab; MSI-H, microsatellite instability-high; PK, pharmacokinetic; Q2W, every 2 weeks; QD, once daily; SLI, safety lead-in; SOC, standard of care.



PRESENTED BY: Scott Kopetz, MD, PhD

# Overview of Response by BICR

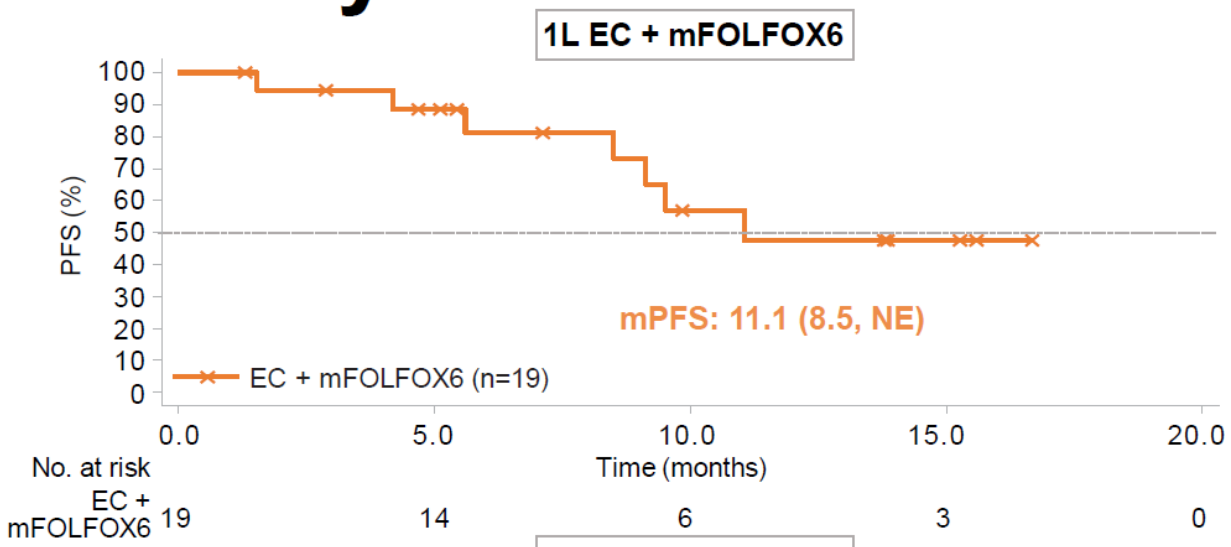
| | 1L | | 2L | |
|---|---|---|---|---|
| | EC + mFOLFOX6 | EC + FOLFIRI | EC + mFOLFOX6 | EC + FOLFIRI |
| **Confirmed best overall response, n (%)** | **n=19** | **n=12** | **n=8** | **n=18** |
| ORR, % (95% CI) | 68.4 (46.0, 84.6) | 75.0 (46.8, 91.1) | 37.5 (13.7, 69.4) | 44.4 (24.6, 66.3) |
| CR | 1 (5.3) | 2 (16.7) | 0 | 1 (5.6)[a] |
| PR | 12 (63.2) | 7 (58.3) | 3 (37.5) | 7 (38.9) |
| SD | 4 (21.1) | 2 (16.7) | 5 (62.5) | 7 (38.9) |
| PD | 1 (5.3) | 0 | 0 | 0 |
| Non-CR/non-PD[b] | 0 | 1 (8.3) | 0 | 2 (11.1) |
| Not evaluable[c] | 1 (5.3) | 0 | 0 | 1 (5.6) |
| **Responders** | **n=13** | **n=9** | **n=3** | **n=8** |
| mTTR, weeks (range) | 6.9 (5.9–30.0) | 7.0 (6.1–42.7) | 6.9 (6.4–23.1) | 13.0 (6.1–47.3) |
| mDOR, months (95% CI) | 9.8 (6.9, NE) | 12.4 (6.9, NE) | NE (5.6, NE) | 9.9 (5.5, NE) |
| ≥6 months, n (%) | 7 (53.8) | 6 (66.7) | 1 (33.3) | 4 (50.0) |

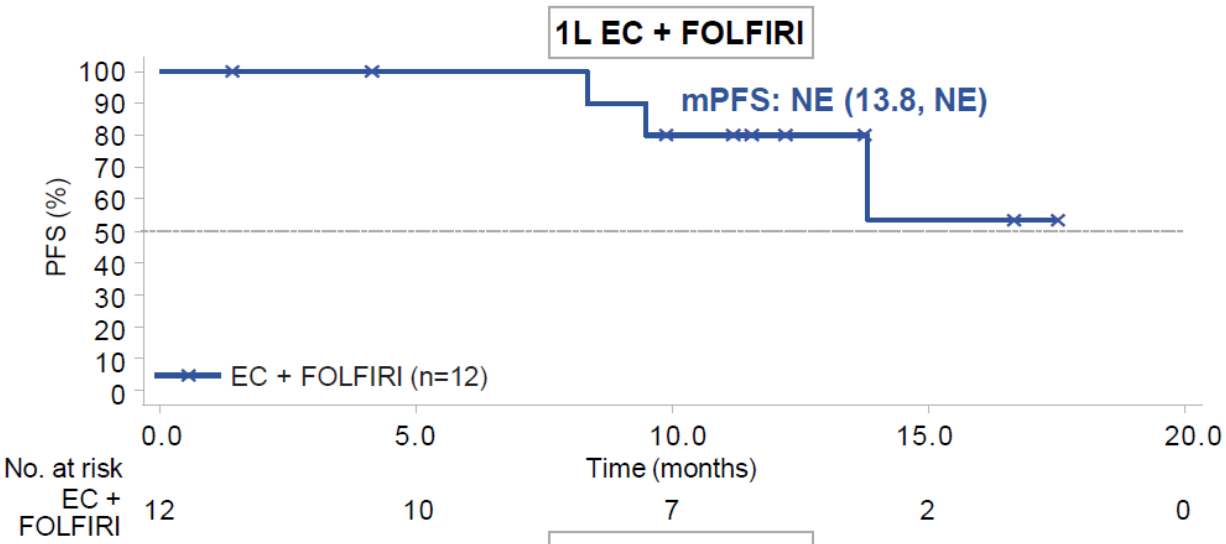
**Data cutoff: September 5, 2022.**

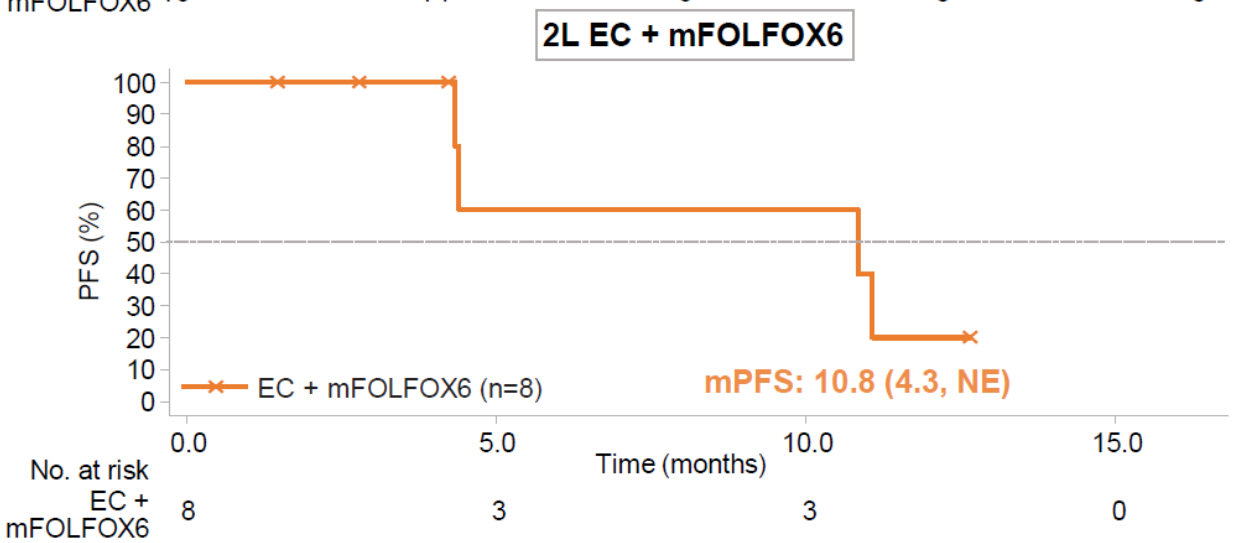
[a]This participant with CR only had nontarget lesions at baseline. [b]Participants with only nontarget lesions at baseline. [c]Reasons included SD <6 weeks after treatment start date (1 patient in the EC + mFOLFOX6 cohort in the 1L setting) and early death (1 patient in the EC + FOLFIRI cohort in the 2L setting).

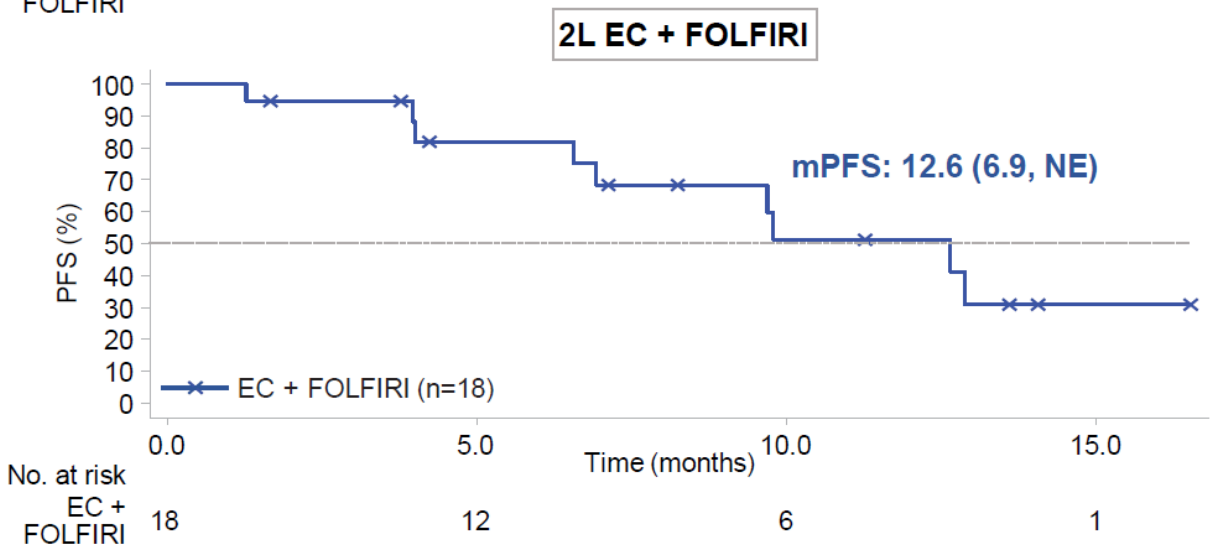
BICR, blinded independent central review; EC, encorafenib and cetuximab; NE, not estimable.

# PFS by BICR



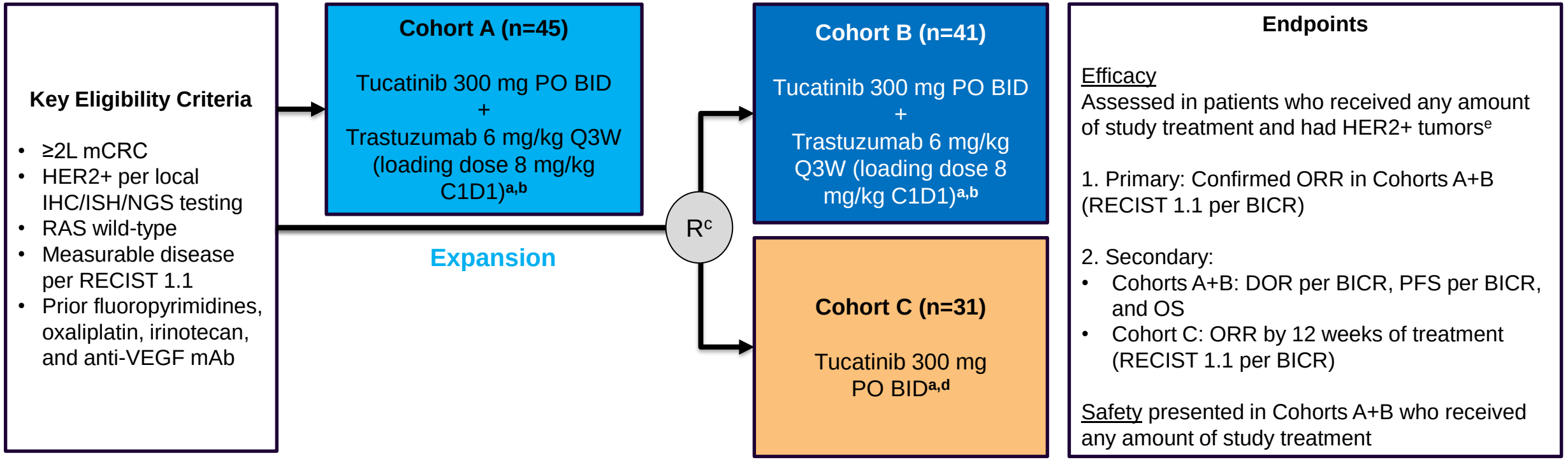




**Data cutoff: September 5, 2022.**

BICR, blinded independent central review; EC, encorafenib and cetuximab; NE, not estimable.

# HER-2 Amplified MCRC

# MOUNTAINEER: Global, Open-Label, Phase 2 Trial




MOUNTAINEER began as a US Investigator-Sponsored Trial and initially consisted of a single cohort (Cohort A) and was expanded globally to include patients randomised to receive tucatinib + trastuzumab (Cohort B) or tucatinib monotherapy (Cohort C)

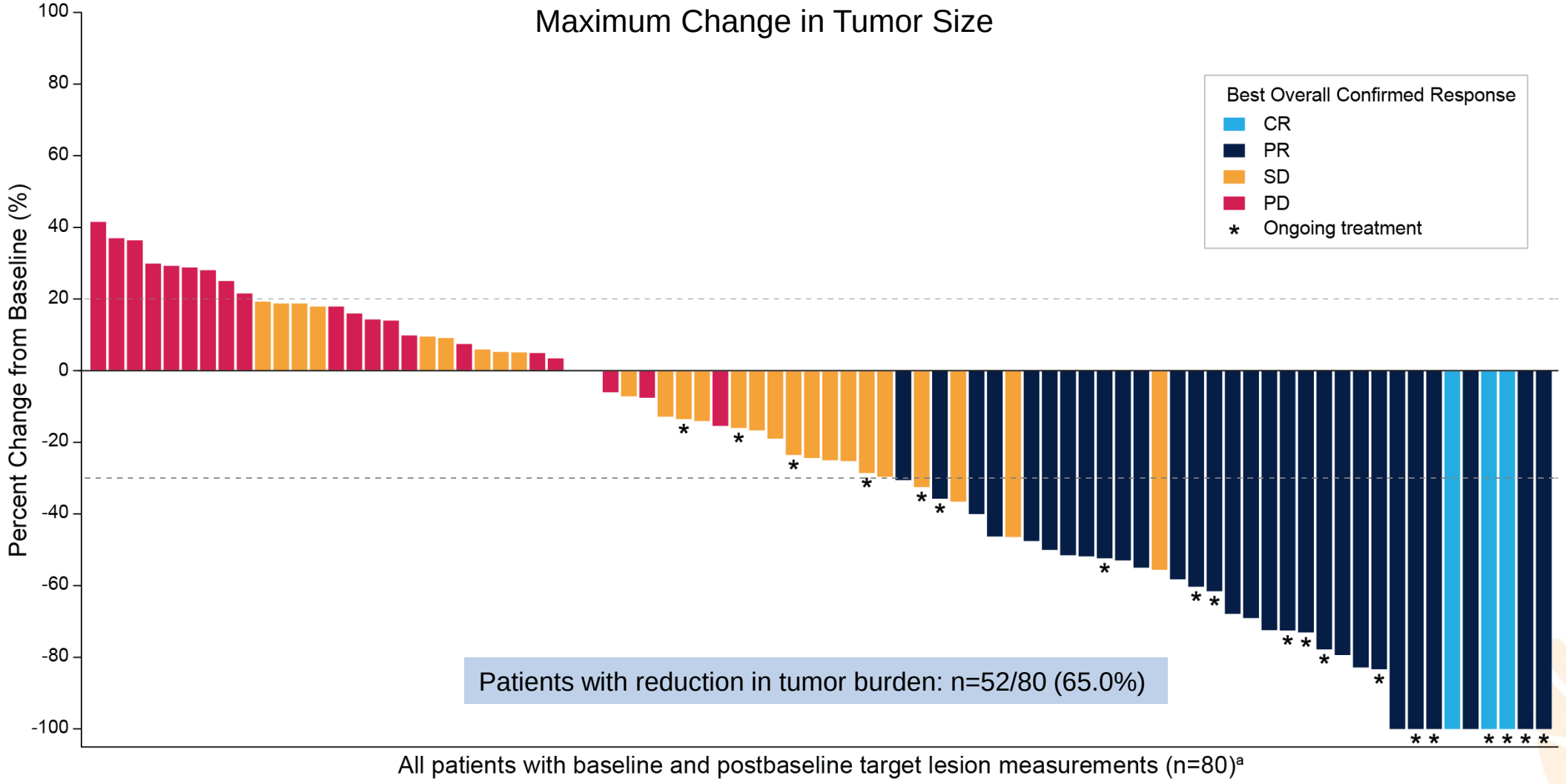
Data cut-off for current analysis, March 28, 2022

a Each treatment cycle is 21 days; b Patients remained on therapy until evidence of radiographic or clinical progression, unacceptable toxicity, withdrawal of consent, or study closure; c Stratification: Left sided tumor primary vs other; d Patients were allowed to cross over and receive tucatinib and trastuzumab if they experienced radiographic progression at any time point or if they had not achieved a PR or CR by week 12; e Patients had HER2+ tumors as defined by one or more protocol required local tests: IHC 3+ (n=46), amplification by ISH (n=36), or amplification by NGS (n=69)

2L+, second line and later; BICR, blinded independent central review; BID, twice a day; C1D1, cycle 1 day 1; CR, complete response; DOR, duration of response; HER2, human epidermal growth receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mAb, monoclonal antibody; mCRC, metastatic colorectal cancer; NGS, next-generation sequencing; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; PR, partial response; R, randomisation; RAS, rat sarcoma virus; RECIST, Response Evaluation Criteria in Solid Tumors; US, United States; VEGF, vascular endothelial growth factor.

https://clinicaltrials.gov/ct2/show/NCT03043313

# Tucatinib + Trastuzumab: Change in Tumor Size




a Four patients who did not have baseline and/or post-baseline target lesion measurements are excluded

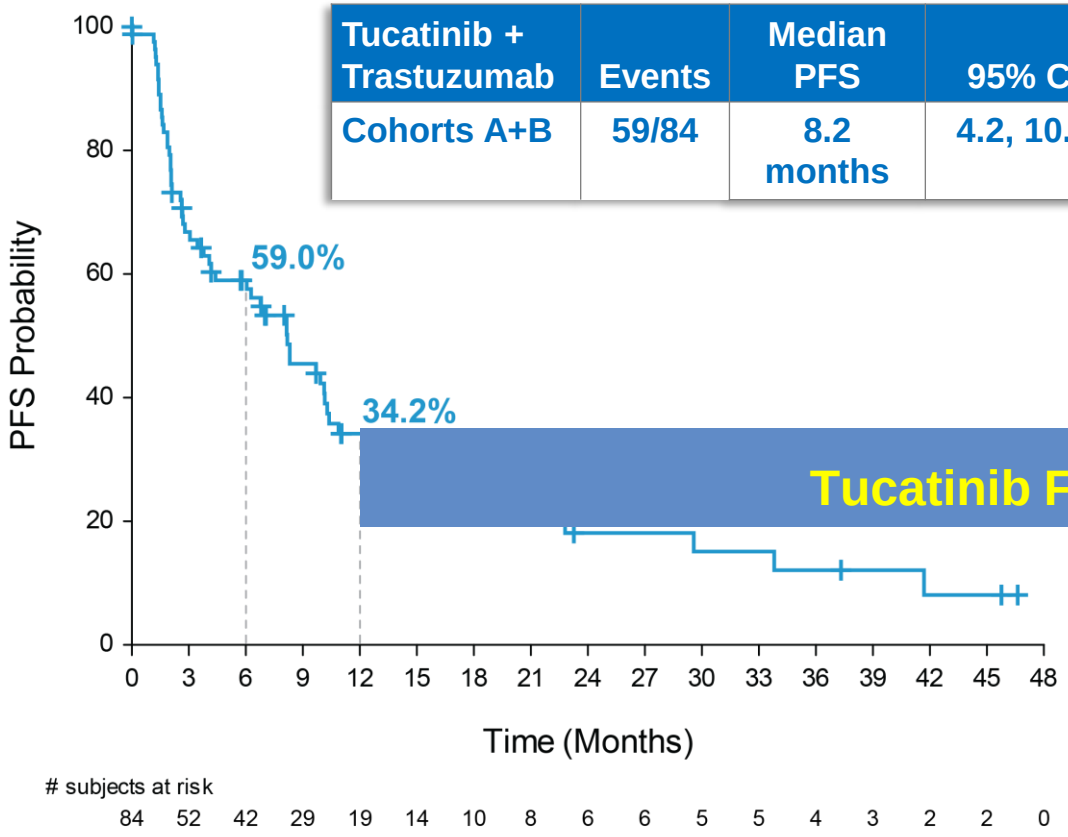
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Data cutoff: 28 Mar 2022

# Tucatinib + Trastuzumab: PFS and OS

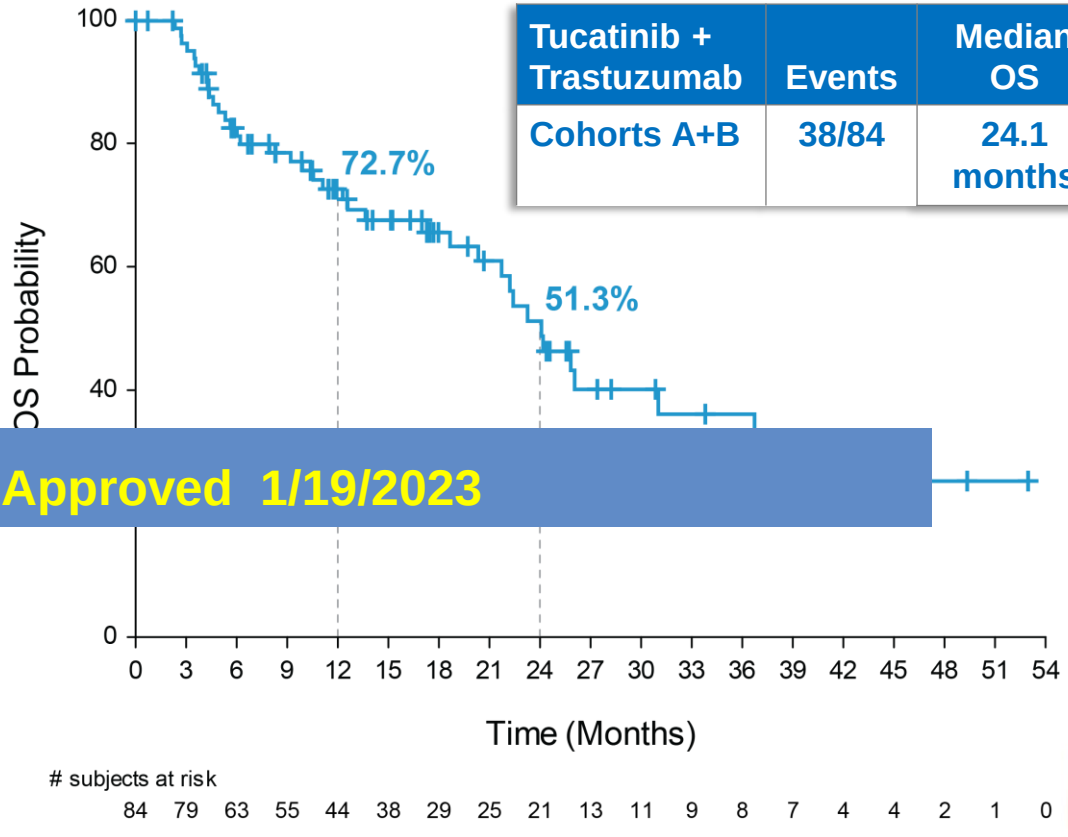
## Progression-free Survival per BICR

| Tucatinib + Trastuzumab | Events | Median PFS | 95% CI |
|---|---|---|---|
| Cohorts A+B | 59/84 | 8.2 months | 4.2, 10.3 |




## Overall Survival

| Tucatinib + Trastuzumab | Events | Median OS | 95% CI |
|---|---|---|---|
| Cohorts A+B | 38/84 | 24.1 months | 20.3, 36.7 |



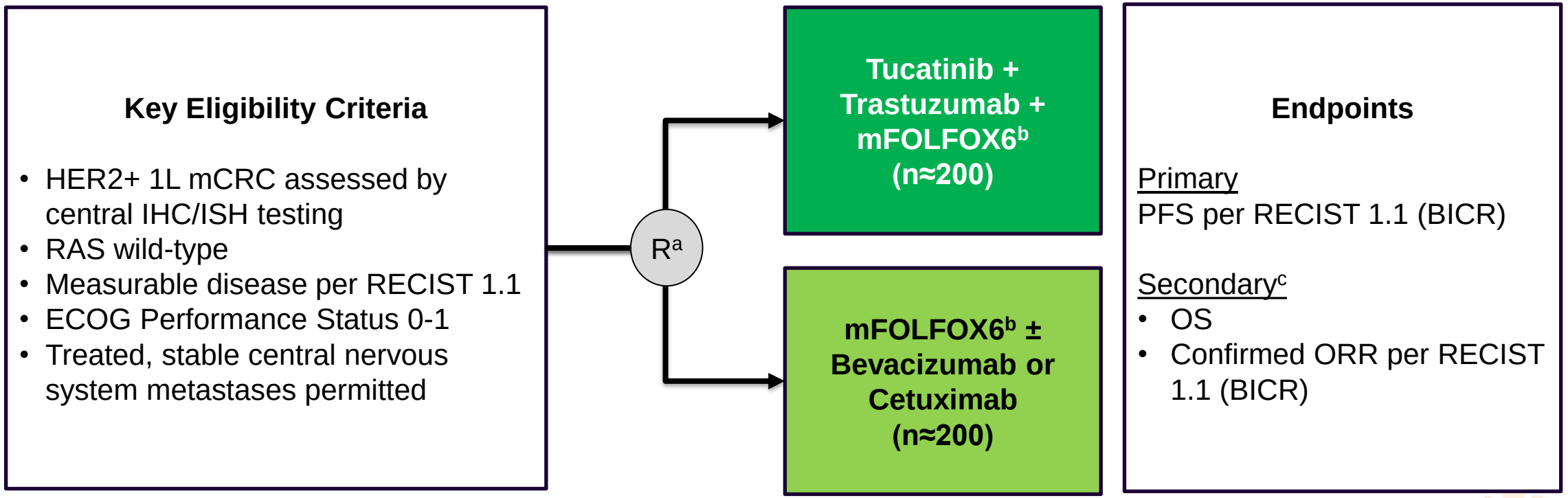

**Tucatinib FDA Approved 1/19/2023**

Median follow-up for Cohorts A+B was 20.7 months (IQR, 11.7, 39.0)

BICR, blinded independent central review; IQR, interquartile range; OS, overall survival; PFS, progressive-free survival.

Data cutoff: 28 Mar 2022

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




a Stratification: Primary tumor sidedness, liver metastases; b Levoleucovorin may be given in place of leucovorin; c Alpha-controlled

1L, first line; BICR, blinded independent central review; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mCRC, metastatic colorectal cancer; mFOLFOX6, 5-fluorouracil, leucovorin, and oxaliplatin; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomisation; RAS, rat sarcoma virus; RECIST, Response Evaluation Criteria in Solid Tumors.

https://clinicaltrials.gov/ct2/show/NCT05253651

# KRAS G12C MCRC

# CodeBreaK 101 Subprotocol H Study Design

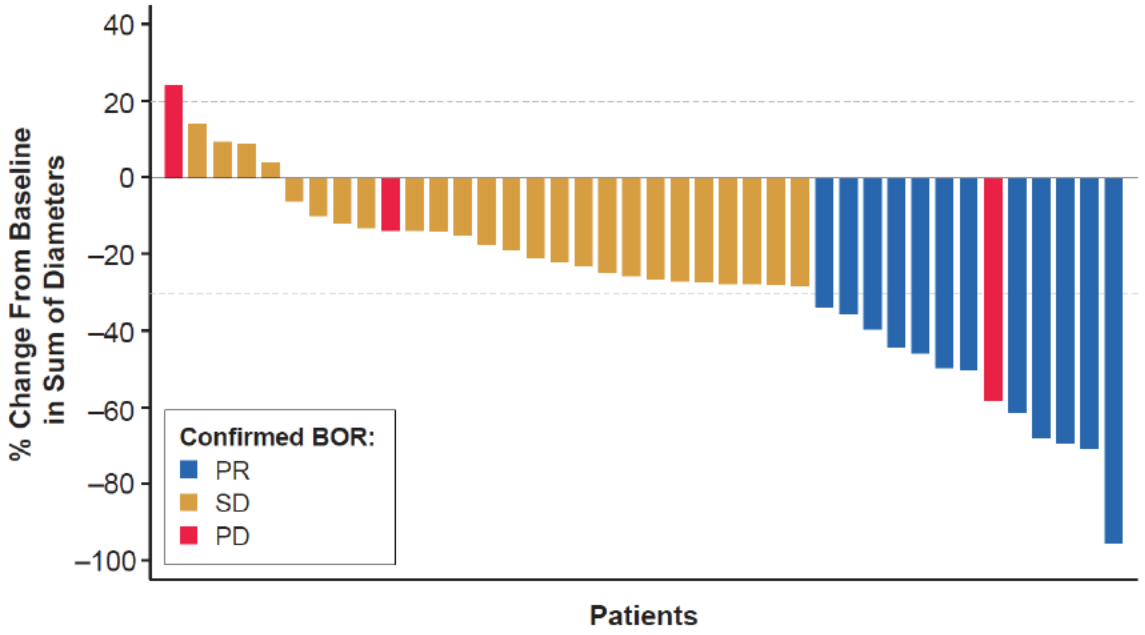
**Phase 1b, multicentre study*:**
**Sotorasib + panitumumab in chemorefractory *KRAS G12C*-mutated mCRC**

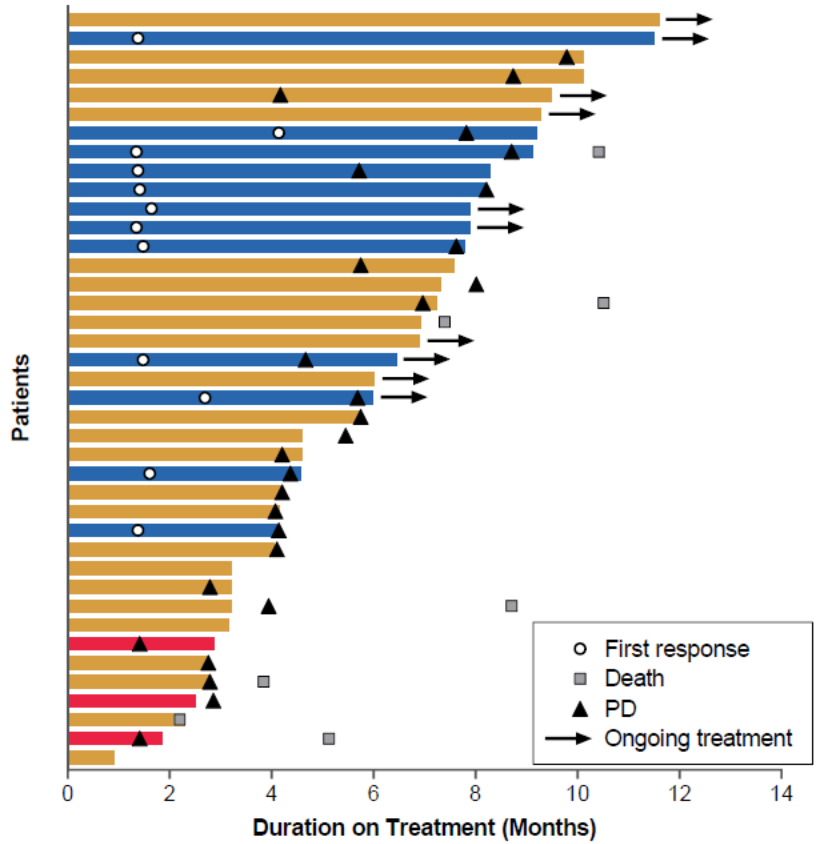
| Screening/enrolment | Part 1: Cohort A dose exploration‡ | Part 2: Cohort A dose expansion (N=40) |
|---|---|---|
| **Key eligibility criteria (Part 2 Cohort A)**<br>• *KRAS G12C*-mutated mCRC, identified through molecular testing<br>• $KRAS^{G12C}$ inhibitor-naive<br>• ≥1 prior treatment for advanced disease†<br>• Progressed on or after fluoropyrimidine, oxaliplatin, irinotecan, and an anti-angiogenic agent | Sotorasib PO daily<br>+<br>Panitumumab 6 mg/kg IV Q2W | **Sotorasib: 960 mg PO daily**<br>**+**<br>**Panitumumab: 6 mg/kg IV Q2W**<br>Treatment until disease progression, withdrawal of consent, or end of study |

**Primary endpoint: Safety/tolerability**
**Secondary endpoints: Anti-tumour efficacy** (ORR, DCR, DOR, TTR, PFS per RECIST v1.1, and OS) **and PK**

*NCT04185883; EudraCT 2020-004721-23.
†For patients with tumours known to be microsatellite instability high, prior checkpoint inhibitor therapy is required if clinically appropriate and locally available for that indication.
‡Dose exploration is completed.
DCR, disease control rate; DOR, duration of response; IV, intravenous; *KRAS*, Kirsten rat sarcoma; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; Q2W, every 2 weeks; PFS, progression-free survival; PK, pharmacokinetics; PO, orally; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

# CodeBreak 101
# Tumour Response




- **Reduction in RECIST target lesions observed in 88% of patients**
- **Median (range) duration of treatment was 5.9 (0.5, 11.3) months, with 25% of patients remaining on treatment**

Data cutoff: June 24, 2022.
BOR, best overall response; PD, progressive disease, PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

# KRYSTAL-1 (849-001) Phase 1b/2 CRC Cohorts Study Design

**Key Eligibility Criteria**

- CRC with a KRAS$^{G12C}$ mutation[a]
- Unresectable or metastatic disease
- Prior systemic treatment for metastatic disease
- No available treatment with curative intent or available standard of care

**Phase 1b**
CRC Combination

**Adagrasib 600 mg BID[b] + cetuximab[c] (n=32)**

**Phase 2**
CRC Monotherapy

**Adagrasib 600 mg BID[b] (n=44)**

**Study Objectives**

**Phase 1b**

- Primary endpoints: safety, RP2D, PK
- Secondary endpoints: ORR (RECIST 1.1), DOR, PFS, OS

**Phase 2**

- Primary endpoint: ORR (RECIST 1.1)[d]
- Secondary endpoints: safety, DOR, PFS, OS

- Previously reported data demonstrated clinical activity of adagrasib monotherapy and adagrasib + cetuximab in patients with previously treated KRAS$^{G12C}$-mutated CRC[10,e]
- Here we report updated data for adagrasib 600 mg BID as monotherapy (Phase 2; median follow-up: 20.1 months) and in combination with cetuximab (Phase 1b; median follow-up: 17.5 months) in patients with previously treated KRAS$^{G12C}$-mutated CRC

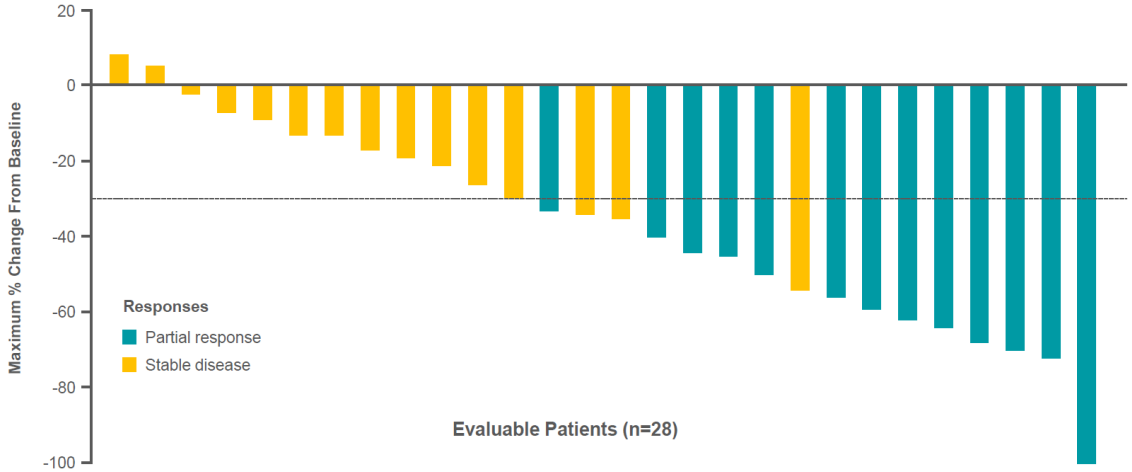
[a]KRAS$^{G12C}$ mutation detected in tumor tissue and/or ctDNA per protocol. [b]Capsule, fasted. [c]Cetuximab dosing, 400 mg/m$^2$ followed by 250 mg/m$^2$ QW, or 500 mg/m$^2$ Q2W. [d]Response was analysed in the clinically evaluable population with local radiology review. [e]Previous data were reported for 46 patients (n=2 in Phase 1/1b and n=44 in Phase 2) receiving adagrasib monotherapy (median follow-up: 8.9 months) and 32 patients receiving adagrasib + cetuximab (median follow-up: 7 months)[10]

ClinicalTrials.gov, NCT03785249

# KRYSTAL-1: Updated Efficacy and Safety of Adagrasib (MRTX849) With or Without Cetuximab in Patients With mCRC with a KRASG12C MT

KRYSTAL-1: Adagrasib (MRTX849) KRAS$^{G12C}$ Inhibitor ± Cetuximab in CRC

## Adagrasib + Cetuximab in Previously Treated Patients with KRAS$^{G12C}$-Mutated CRC: Best Tumor Change From Baseline

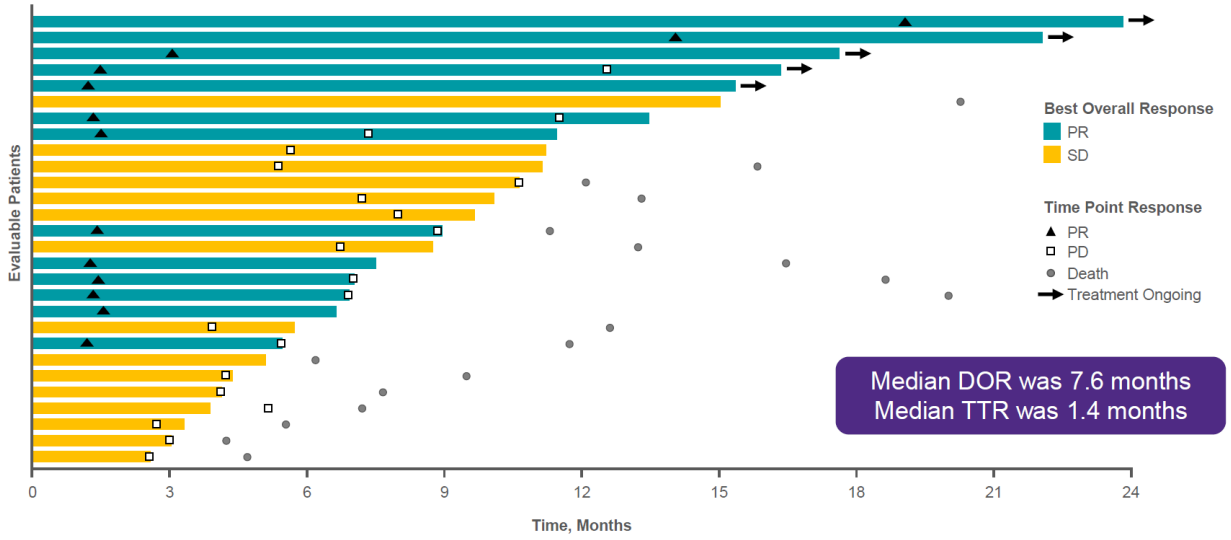



- Confirmed objective responses were observed in 46% (13/28[a]); DCR was 100% (28/28)
- Tumor shrinkage of any magnitude occurred in 93% of patients

[a]Response per investigator assessment (n=28; four patients are not included due to no post-baseline assessment of target lesions)

KRYSTAL-1: Adagrasib (MRTX849) KRAS$^{G12C}$ Inhibitor ± Cetuximab in CRC

## Adagrasib + Cetuximab in Previously Treated Patients with KRAS$^{G12C}$-Mutated CRC: Duration of Treatment




Median DOR was 7.6 months
Median TTR was 1.4 months

Response outcomes per investigator assessment (n=28; four patients are not included due to no post-baseline assessment of target lesions)

Yaeger et al: NEJM, 2022

# Ongoing Phase I and III Trials: Amgen, Mirati and Eli-Lilly

## Phase 3: Sotorasib + Panitumumab

**Patients**

- > 1 prior line of treatment for mCRC
- KRAS G12C MT
- ECOG PS 0-2
- **N=193**
- ***Not yet recruiting**

**NCT05198934**

**Arms A: Sotorasib 960 mg + Panitumumab or Arm B: Sotorasib (240 mg) + PMab**

**1:1 Randomization**

**Physician's Choice: Regorafenib or TAS-102**

**Primary Endpoint: PFS**

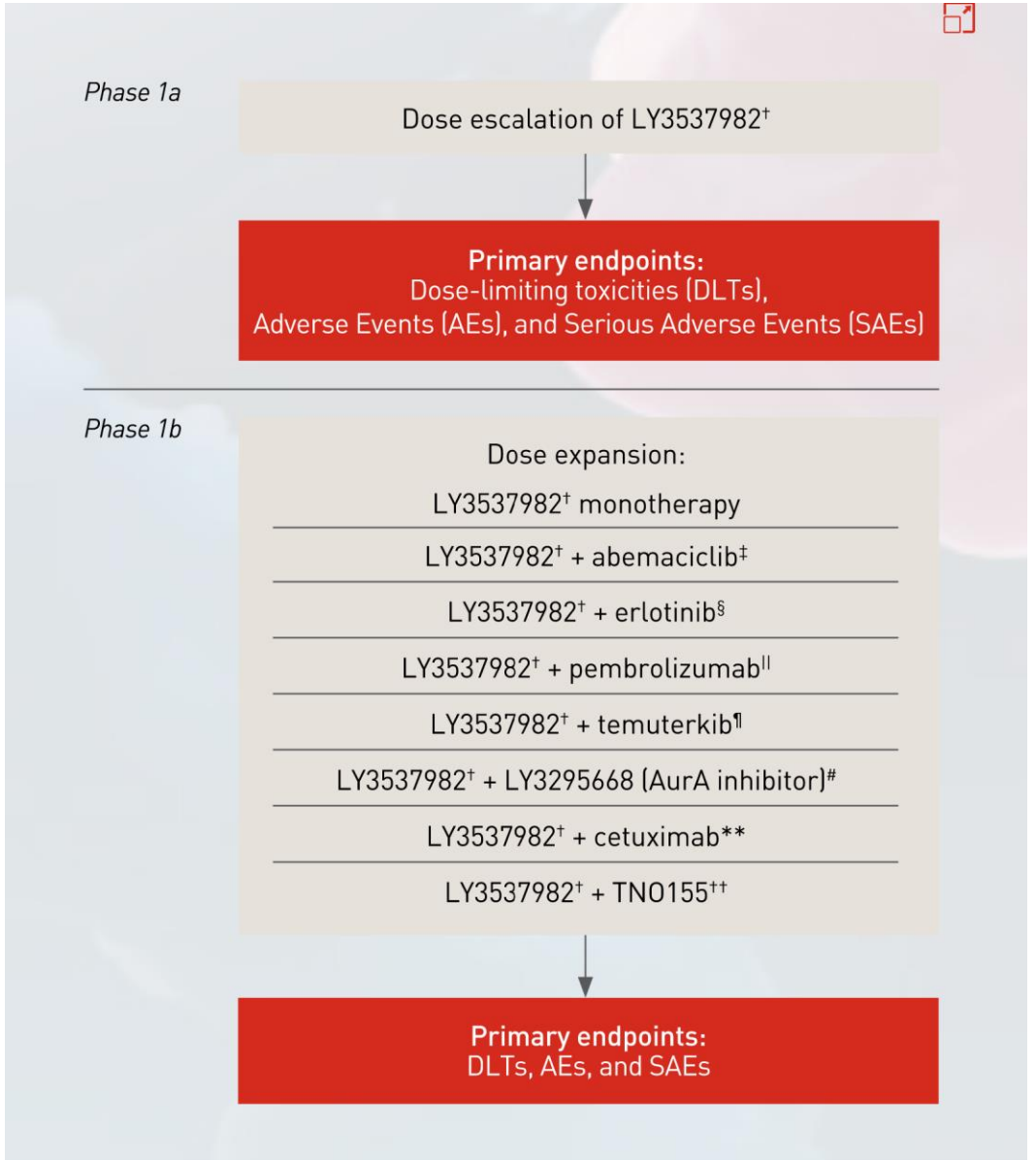
- **Metastatic CRC**
- ***KRAS* G12C in tumor**
  - Local test acceptable for enrollment; central confirmation req'd w/in 30d
- **PD on 1L fluoropyrimidine + oxaliplatin or irinotecan**
- **No prior anti-EGFR or direct KRAS G12Ci**

**1:1**
**N~420**

**Adagrasib 600 mg BID + Cetuximab 500 mg/m² Q2W**

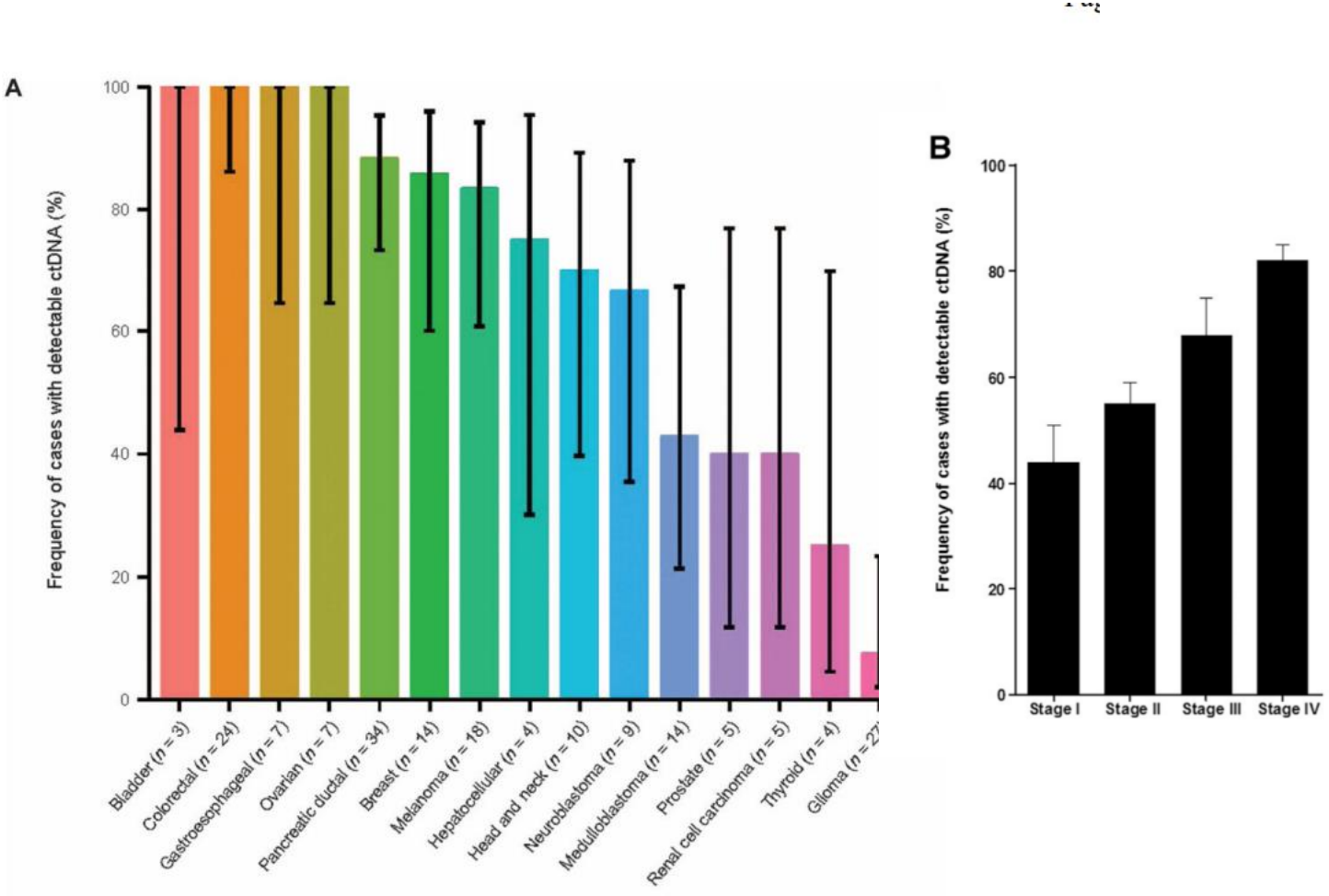
**FOLFIRI or mFOLFOX6§**

**§Anti-VEGF/VEGFR allowed per Investigator discretion**



# The role of ctDNA

# Variability in ctDNA by Primary Tumor and Stage



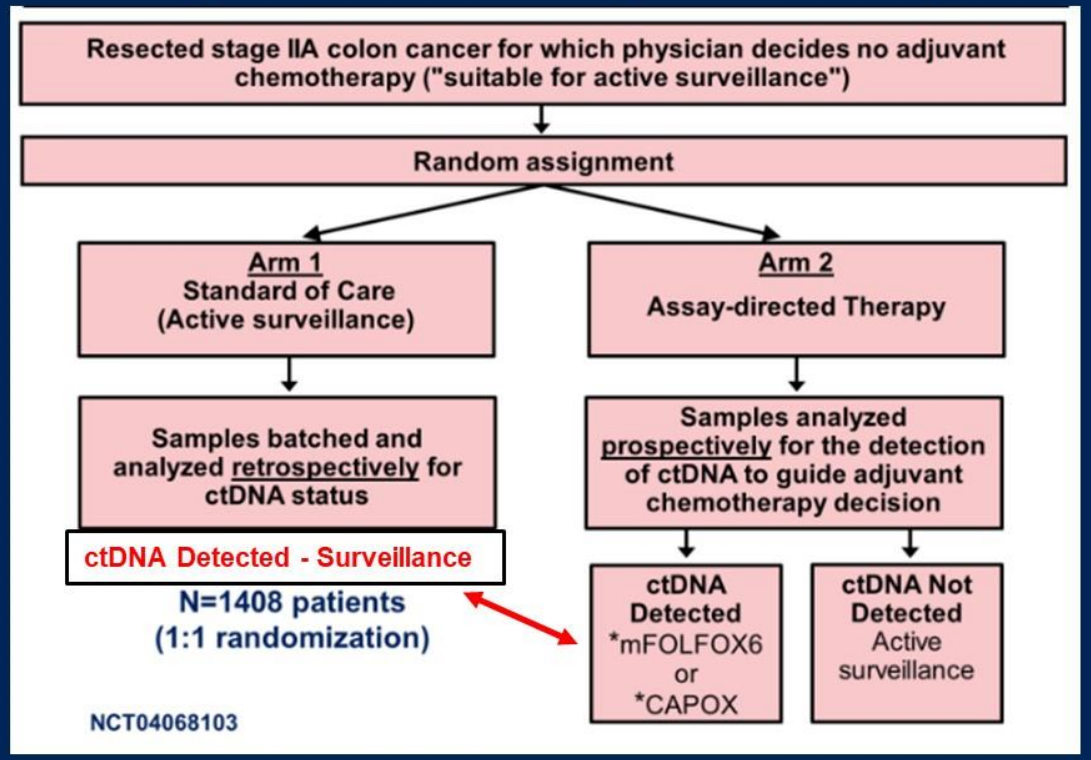

- Additional factors:
  - Disease site: Liver > lymph node > peritoneum > lung> brain
  - Size of mets ≥ 2 cm
  - Number of mets
  - Histology: SCCA > adenoCA > mucinous
  - Method and timing of collection: -80°C
    - EDTA or STRECK tubes
    - Environment:
      - Recent surgery, inflammation, chemotherapy

Bettogowda et al: Sci Transl Med. 2014; Bando et al: JCO Precision Onc, 2022; Pascual et al: Ann of Onc, 2022

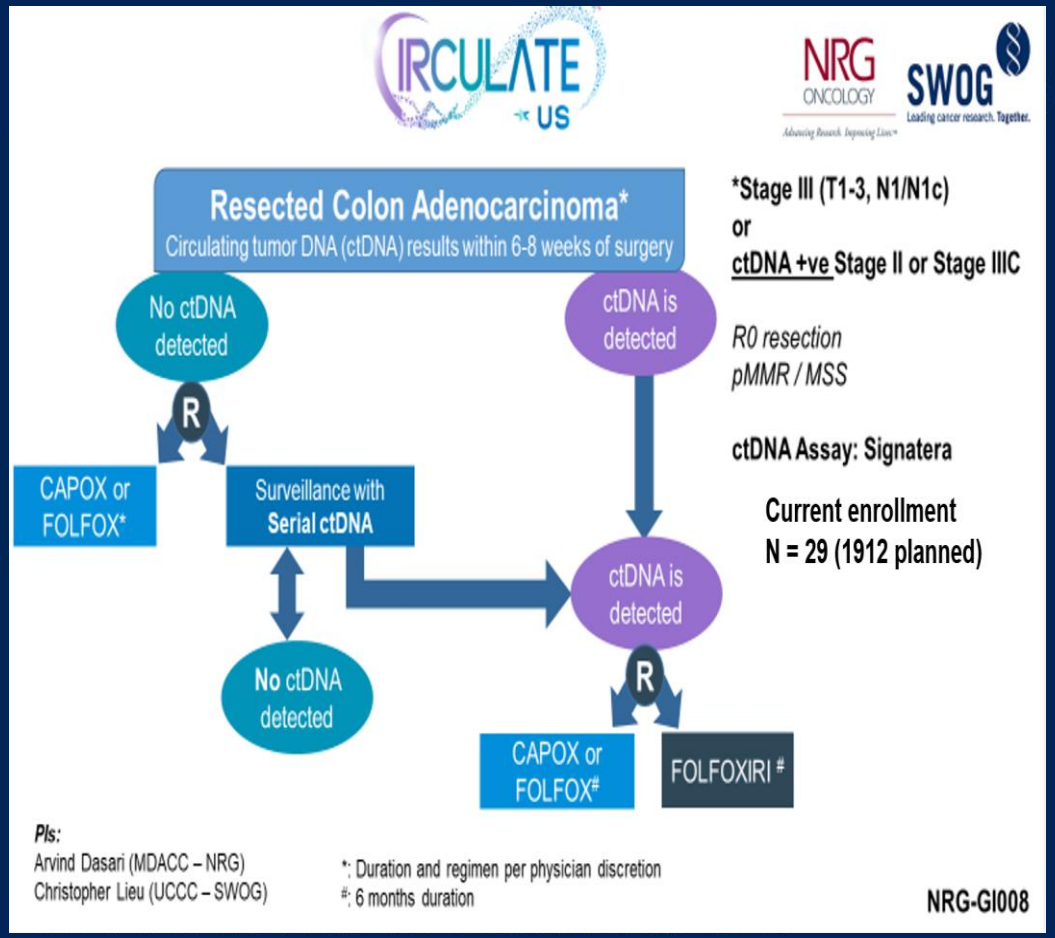
# Can ctDNA-Positive Patients Benefit from Adjuvant Chemo?

## NRG-GI005 (COBRA)

Stage IIA Colon Cancer (LUNAR-1 assay)




Morris V et al. GI ASCO 2022, TPS233



# Recommended ctDNA Perioperative Collection Timepoints

| Timepoint | Timeframe | Potential correlative outcomes |
|---|---|---|
| Treatment naive | Prior to treatment, concurrent with initial clinical staging | Pathological response to neoadjuvant therapy, long-term survival and disease status |
| Post-neoadjuvant therapy and/or restaging | ≥4 weeks after completing neoadjuvant therapy; ≤2 weeks of concurrent clinical assessment or restaging and/or resection | Pathological response to neoadjuvant therapy, neoadjuvant rectal score |
| Post-resection | 4–8 weeks after surgical resection with a curative intent | Long-term survival and disease status, including overall survival, disease-free survival and recurrence-free survival |
| After adjuvant therapy or completion of all potentially curative therapy; minimal residual disease | 2–8 weeks after completion of all curative-intent therapy | |
| Disease relapse or recurrence | ≤2 weeks, concurrent with clinical assessment and/or restaging showing evidence of disease relapse and/or recurrence | |

Dasari et al: Nat Rev, 2020

# One of the First Young Adult Cancers Program Nationally

VANDERBILT-INGRAM CANCER CENTER

## YOUNG ADULT CANCER PROGRAM

FOR THOSE 45 AND UNDER

We're here to help you get the support you need on topics you're concerned about:

- Reproductive health, fertility, and sexuality
- Financial/ insurance guidance
- Access to age-specific support groups and individual counseling
- Nutritional and exercise consults
- Educational and vocational resources
- Navigating relationships
- Parenting with cancer
- Music, art, and pet therapy
- Pain management
- And more....

For updates on events, services, and more please join our mailing list by scanning the QR Code and signing up today.

We look forward to helping you navigate your cancer journey!

**Never Miss a Monday: YA Wellness Series**

In collaboration with Survivor Fitness Foundation and Gilda's Club Middle Tennessee, we invite you to join us for **Never Miss A Monday: Young Adult Wellness Series.**

Start off your week on the right track with an all levels/survivor friendly movement class. Come on out and connect with other young adults impacted by cancer, the 2nd Monday of every month.

**Co-Directors:**

**Elizabeth Davis, MD and Bhagi Dholaria MBBS**

**Director: Cathy Eng, MD, FACP, FASCO**

FIGHT™ COLORECTAL CANCER

Colorectal Cancer Awareness


Courtesy of Anjee Davis

# ASCO GI highlights as a patient advocate

Allison Rosen
Fight CRC Research Advocate
2-6-2023

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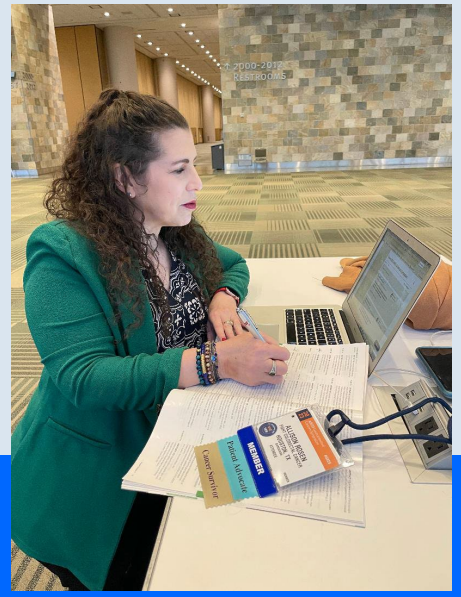
# Overall Takeaways



- BIOMARKER testing is important in colorectal cancer patients
- New drugs and drug combinations are coming out: 2 were FDA approved at the mtg
- Healthcare professionals are considering treatment side effects and long term effects when deciding options
- Early onset is on the rise we need to do more
- Less is more when it comes to treatment in some cases

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# MOUNTAINEER

**FDA approval of tucatinib combined with trastuzumab for HER2-positive metastatic colorectal cancer**

- Approved 1/19/2023
- Already being used in breast so some **trust** in this drug
- **Chemo-free** approach to HER2+ RAS wild-type
- Proves that **biomarker test is important**

# PARADIGM

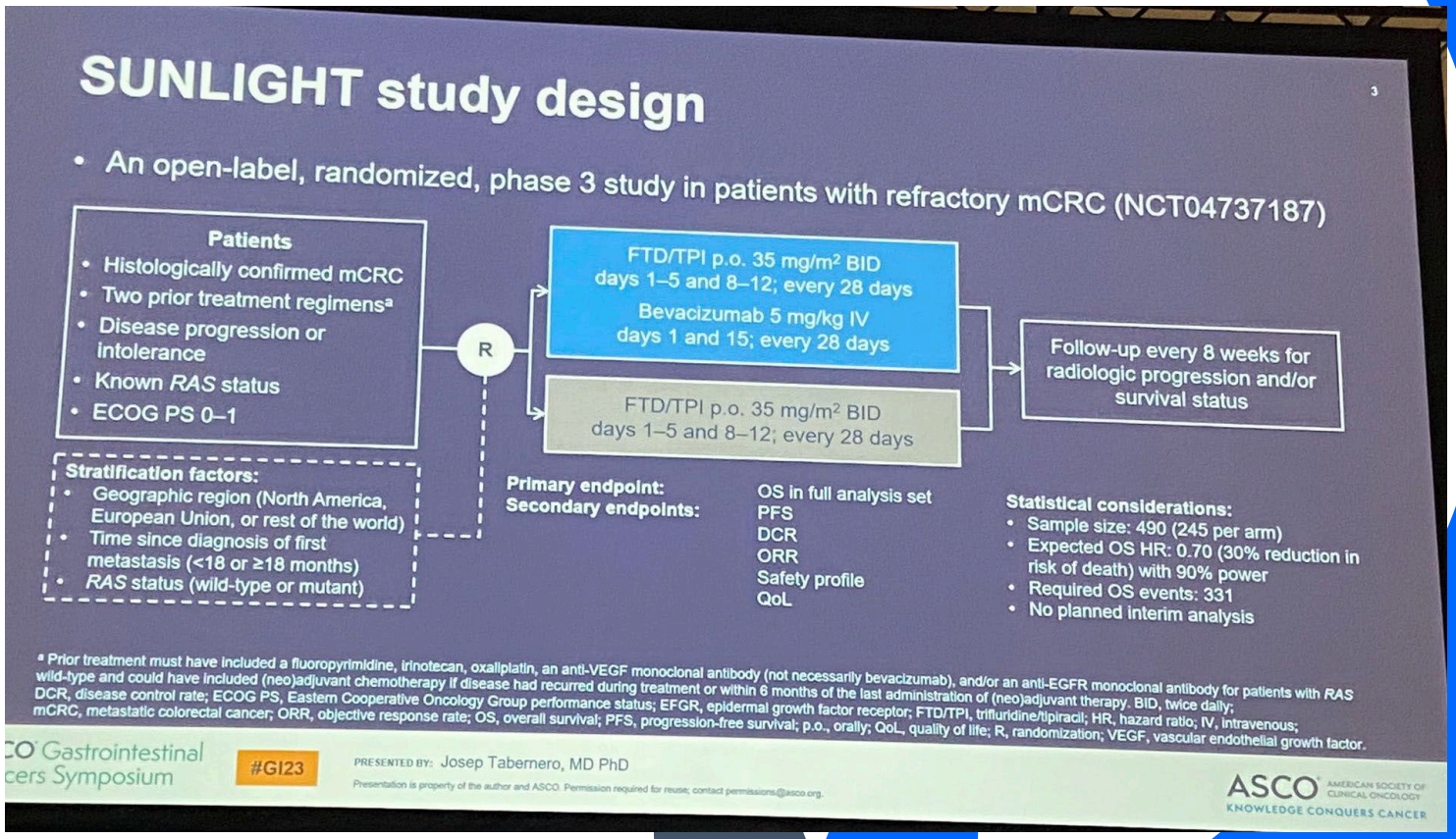
**RAS wild-type mCRC FOLFOX with panitumumab vs bevacizumab in patients with RAS wild-type left-sided mCRC**

- Of the 802 patients 91% had ctDNA and 28% had at least one gene alteration
- Proved that you can use **ctDNA** to define negative hyperselection rather than look at left sided and right sided to help select patient with **frontline therapy** in terms of PAN versus BEV

# SUNLIGHT

**Trifluridine/Tipiracil plus Bevacizumab provides benefit in refractory metastatic colorectal cancer**

- **Improved overall survival and progression-free survival**
- This can be used for **microsatellite stable colon cancer population if not candidates for immunotherapy**
- ¼ of patients did not see bevacizumab in this study: appealing doublet in these patients
- Could be considered a **standard of care**

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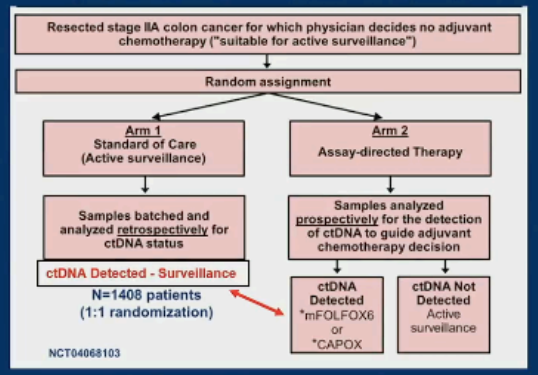
# ctDNA: Prime Time or Jumping too Soon?

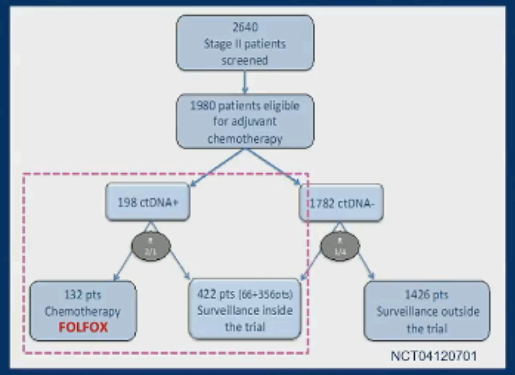
## Can ctDNA-Positive Patients Benefit from Adjuvant Chemo?

### NRG-GI005 (COBRA)
Stage IIA Colon Cancer (LUNAR-1 assay)




Morris V et al. GI ASCO 2022, TPS233

### CIRCULATE-PRODIGE 70
Stage IIA and IIB Colon Cancer (Methylation assay)

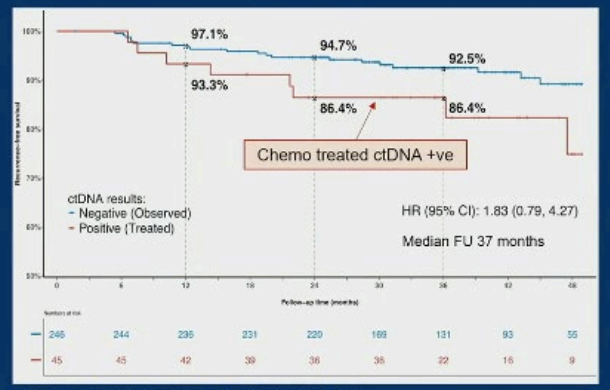



Taieb J, et al. Digestive and Liver Disease 2020;52(7):730–733.



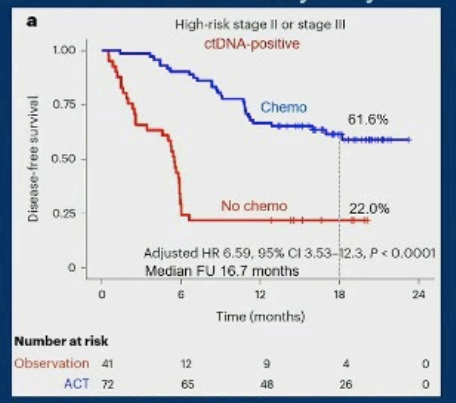
## Post-op ctDNA-Positive: Impact of Adjuvant Chemo

### DYNAMIC (Stage II) Randomized Trial
ctDNA-Guided Cohort




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

### CIRCULATE-Japan
Observational Galaxy Study




Kotani D et al. *Nat Med* (2023). Online 16 Jan.



## Conclusion/Takeaway

- Detection of ctDNA after curative intent surgery predicts for high risk of recurrence (prognostic)
  - Post-op ctDNA testing can be helpful to guide adjuvant therapy in scenarios where treatment benefit is uncertain/modest, e.g., low/intermediate risk or dMMR/MSI stage II
- Favorable RFS in treated ctDNA-positive patients and the high ctDNA clearance rate suggest potential benefit from adjuvant chemo
  - Ongoing randomized trials will provide more definitive evidence
- ctDNA detection post-chemotherapy or during surveillance is prognostic but its clinical utility remains the subject of ongoing trials
  - Caution: over-investigation, anxiety provoking without survival gain

# Despite remarkable advances in cancer care, we demonstrate an alarming recent trend where mortality rate has remained stable & recently increased in younger individuals with GI cancers

## DEMOGRAPHIC AND REGIONAL TRENDS OF GI CANCER MORTALITY IN ADOLESCENTS AND YOUNG ADULTS (AYA) IN THE US, 1999-2019

**S. M. Qasim Hussaini[1], Amanda Blackford[1], Ramy Sedhom[2], Arjun Gupta[3]**

[1]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Hospital, Baltimore, Maryland, [2]University of Pennsylvania, Philadelphia, Pennsylvania, [3]Masonic Cancer Center, University of Minnesota, Minneapolis, Minnesota

### OVER A 20-YEAR PERIOD (1999-2019)

**74** THOUSAND AYAs (AGES 15-44) DIED FROM GI CANCER

39% Female
16% Hispanic
20% NH Black

16% Rural
42% Southern-located

52% Colorectal
17% Pancreas
17% Hepatobiliary
17% Gastric

### MORTALITY RATES

**HIGHEST MORTALITY RATES OBSERVED IN:**
NON-HISPANIC BLACKS
HISPANIC INDIVIDUALS
RURAL REGIONS

NO IMPROVEMENT IN MORTALITY RATE OVER 20-YEAR PERIOD

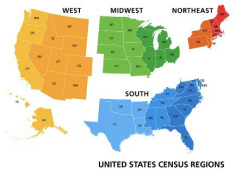
| | AAMR, 1999 | AAMR, 2019 | APC trends (year range) |
|---|---|---|---|
| **Overall** | 3.3 | 3.3 | +0.49 (2009-19) |
| **Women** | 2.6 | 2.7 | +0.80 (2011-19) |
| **Men** | 3.9 | 3.9 | +0.40 (2007-19) |
| **Hispanic** | 2.8 | 3.3 | +1.99 (2011-19) |
| **White** | 2.9 | 3.1 | -1.43 (2017-19) |
| **Black** | 5.4 | 4.0 | -1.53 (1999-2012) |
| **Large Metro** | 3.1 | 3.3 | +1.04 (2013-19) |
| **Medium/Small** | 3.2 | 3.2 | -1.27 (2016-19) |
| **Rural** | 3.8 | 3.7 | +0.67 (2004-19) |
| **Age 45+** | 131.7 | 109.7 | -0.69 (2007-19) |

*AAMR = Age-Adjusted Mortality Rate*
*APC = Annual Percentage Change, using Joinpoint*

### TEMPORAL TRENDS IN MORTALITY RATES

**1999-2009**
OVERALL STABILITY TO SLIGHT DECREASE

**2009-2019**
SLIGHT INCREASE




HIGHEST AAMRs IN **SOUTHERN** STATES

### #TLDR

Mortality rates for AYAs with GI cancers remained relatively stable from 1999 to 2009, but have since risen, with significant sociodemographic and regional variation. These data highlight the need to better understand risk factors (diet, environmental, and other), screening trends, and variation in receipt of guideline-concordant care to ensure appropriate and equitable risk reduction and cancer management in AYAs

### PROVIDER & POLICY IMPLICATIONS

PREVENTION | TARGETED SURVEILLANCE | ACCESS | SURVIVORSHIP CARE | ADVOCACY & AWARENESS | REGIONAL INFRASTRUCTURE

ASCO Gastrointestinal Cancers Symposium #GI23
@QasimHussainiMD

- EOCRC mortality rates were stable 1999-2009 but have risen significantly with significant sociodemographic and regional variation
- 74,000 AYAs (15-44) have passed from GI cancers the highest being 52% from colorectal
- Highest mortality rate was in rural areas, Non-Hispanic Blacks and Hispanic individuals
- Mortality highest in Southern states at 42%

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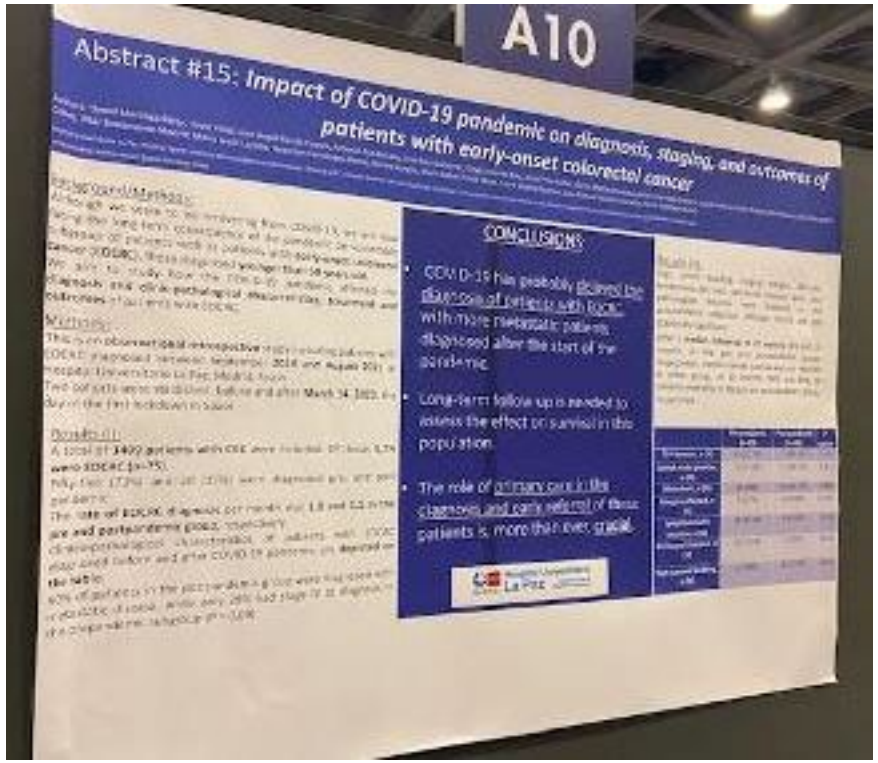
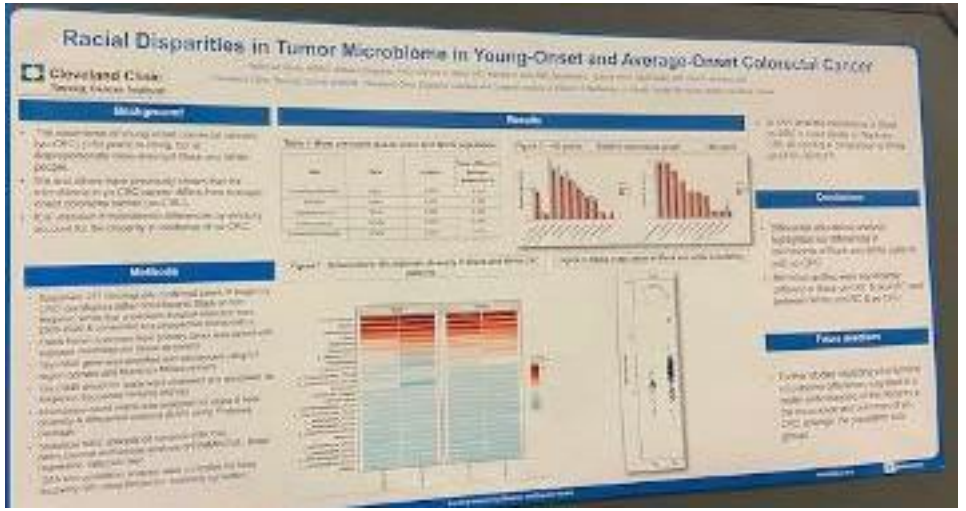
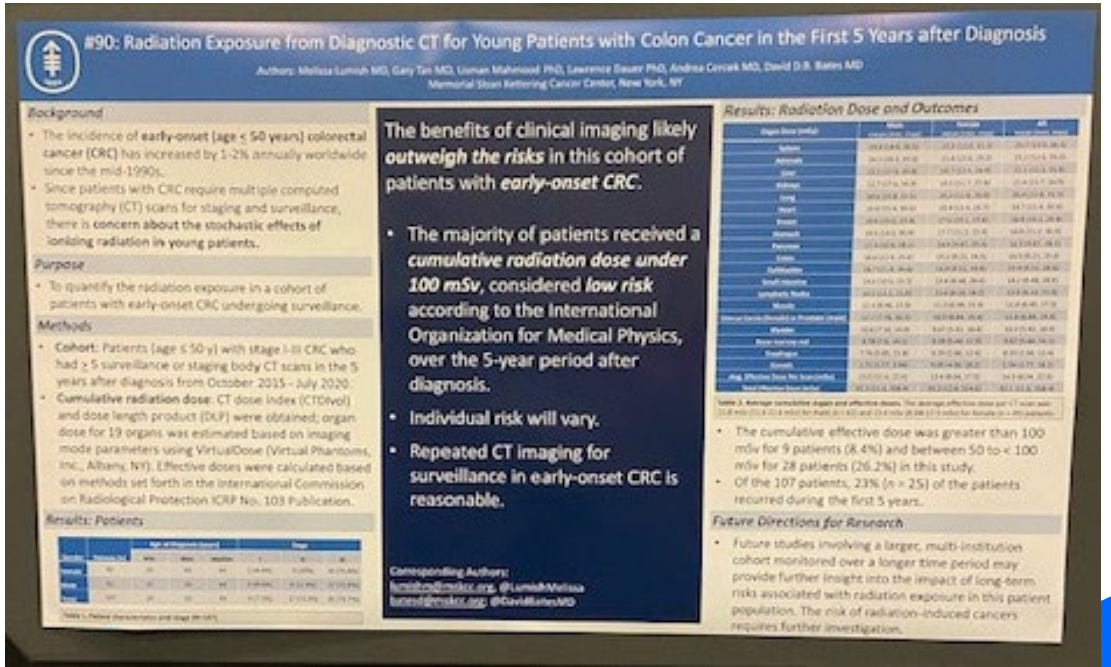
## Other poster topics: patient navigation vital, COVID effects on screening, treatment evolutions (harmful or not), and health disparities




COVID-19 delayed the diagnosis of patients with EOCRC

There were key differences in microbiome in black vs White EOCRC




Benefits of imaging outweigh the risk of patients with EOCRC

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# THANK YOU

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FIGHT™ COLORECTAL CANCER

# QUESTION AND ANSWER

Type in your questions on the panel on the right side of your screen

# Fight Colorectal Cancer Mission

We FIGHT to cure colorectal cancer and serve as relentless champions of hope for all affected by this disease through informed patient support, impactful policy change, and breakthrough research endeavors.

FIGHT COLORECTAL CANCER

# THANK YOU