XX JORNADA DE ACTUALIZACIÓN

ASCO GI 2026

24 de febrero de 2026

¿Qué hay de nuevo en los tumores colorrectales?

Dr. Javier Soto Alsar

Hospital General Universitario Gregorio Marañón, Madrid

DISCLOSURE INFORMATION

- Employment: Sanofi (mother), Pfizer (father)
- Consultant or Advisory Role: Takeda
- Research Funding: Pierre Fabre, Amgen
- Speaking: Leo Pharma, Roche, Merck, MSD, Servier, BMS, AstraZeneca, Ipsen, Recordati, Abbott

- **ORALES**
  - BREAKWATER
  - COMMIT
  - DISCO
  - Ejercicio en CCR – astenia y calidad de vida
  - * ALTAIR

- **MINIORALES**
  - FOxTROT
  - CCR MSI: EOCRC vs LOCRC
  - Prevención: agonistas GLP1 vs aspirina
  - Trasplante hepático – RWD
  - PLATO ACT 5

- **POSTERS**
  - TIRANUS
  - INTRINSIC
  - UNION TNT

ORALES

ASCO Gastrointestinal Cancers Symposium

BREAKWATER: Primary analysis of first-line (1L) encorafenib + cetuximab (EC) + FOLFIRI in BRAF V600E-mutant metastatic colorectal cancer (mCRC)

Scott Kopetz,[1] Harpreet S. Wasan,[2] Takayuki Yoshino,[3] Tae Won Kim,[4] Cathy Eng,[5] Eric Van Cutsem,[6] Fortunato Ciardiello,[7] Jayesh Desai,[8] Timothy S. Maughan,[9] Rona Yaeger,[10] Xiaoxi Zhang,[11] Elena Beyzarov,[11] Ave Mori,[12] Xiaosong Zhang,[13] Josep Tabernero[14]

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PRESENTED BY: Scott Kopetz, MD, PhD

BREAKWATER Cohort 3: Study Design

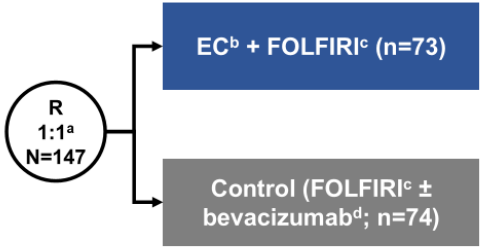
- BREAKWATER (NCT04607421) is an open-label, multicenter, phase 3 study in first line BRAF V600E-mutant mCRC

Inclusion criteria

- Age ≥16 years (or ≥18 years based on country)
- No prior systemic treatment for metastatic disease
- Measurable disease (RECIST 1.1)
- BRAF V600E-mutant mCRC by local or central laboratory testing
- ECOG PS 0 or 1
- Adequate bone marrow, hepatic, and renal function

Exclusion criteria

- Prior BRAF or EGFR inhibitors
- Symptomatic brain metastases
- MSI-H/dMMR tumors (unless patients were ineligible to receive immune checkpoint inhibitors due to a preexisting medical condition)
- Presence of a *RAS* mutation



Primary endpoint:
ORR by BICR[e]

Key secondary endpoint:
PFS by BICR

Other secondary endpoints:
OS, DOR, TTR, safety

Here we present the primary analysis of ORR by BICR (the primary endpoint), an analysis of OS, and safety in the EC + FOLFIRI and control arms

[a]Patients were enrolled between December 28, 2023, and July 1, 2024; enrollment to Cohort 3 started after enrollment to Phase 3 was complete. The planned sample size was approximately 136 patients (68 in each arm). [b]Encorafenib 300 mg orally QD; cetuximab 500 mg/m² IV Q2W. [c]Irinotecan 180 mg/m² IV Q2W; leucovorin 400 mg/m² IV Q2W; and 5-FU 400 mg/m² IV bolus, then 5-FU 2400 mg/m² continuous IV infusion over 46-48 hours Q2W. [d]Per prescribing information. [e]Using a one-sided chi-square test at a significance level of 0.025.
BICR, blinded independent central review; dMMR, deficient mismatch repair; DOR, duration of response; EC, encorafenib plus cetuximab; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FOLFIRI, fluorouracil/leucovorin/irinotecan; IV, intravenously; mCRC, metastatic colorectal cancer; MSI-H, microsatellite instability–high; Q2W, once every 2 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

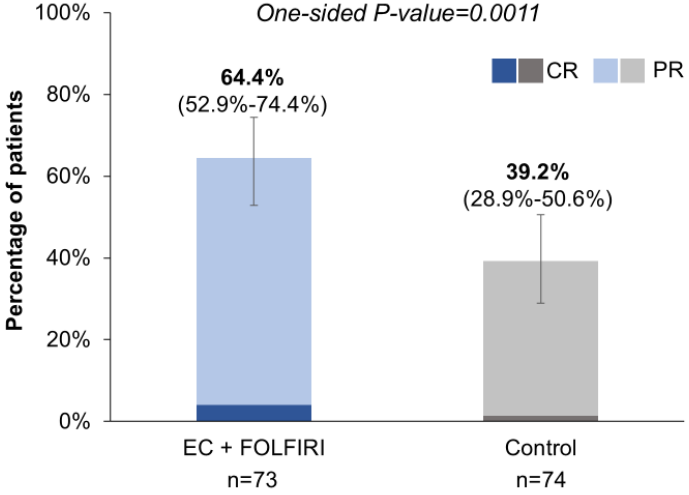
PRESENTED BY: Scott Kopetz, MD, PhD

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 cetuxima; SD, stable disease; TTR, time to response.

Intra-trial comparison of BREAKWATER data: oxaliplatin vs. irinotecan-based

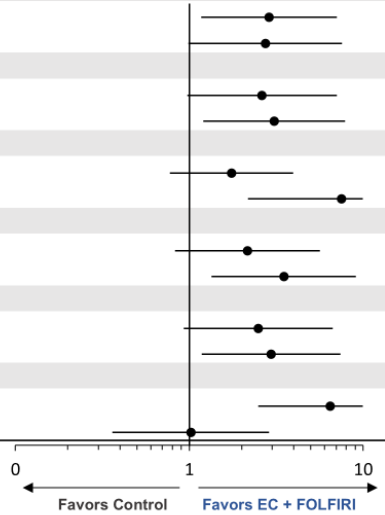
	EC + FOLFIRI	FOLFIRI +/- Bev	EC + FOLFOX	SOC chemo
ORR	64.40%	39.20%	65.70%	37.40%

PRESENTED BY: Scott Kopetz, MD, PhD

Subgroup Analysis of ORR by BICR

The clinical benefit with EC + FOLFIRI was observed across key prespecified subgroups

	Number of responders/ Number of patients		ORR (%)		Odds ratio (95% CI)
	EC + FOLFIRI	Control[a]	EC + FOLFIRI	Control[a]	
Age					
<65 years	24/37	18/46	64.9	39.1	2.87 (1.17-7.05)
≥65 years	23/36	11/28	63.9	39.3	2.73 (0.99-7.57)
Sex					
Male	18/33	11/35	54.5	31.4	2.62 (0.97-7.04)
Female	29/40	18/39	72.5	46.2	3.08 (1.21-7.85)
ECOG PS at baseline					
0	29/47	23/48	61.7	47.9	1.75 (0.77-3.96)
1	18/26	6/26	69.2	23.1	7.50 (2.18-25.80)
Number of organs involved at baseline per BICR					
≤2	26/38	17/34	68.4	50.0	2.17 (0.83-5.65)
≥3	21/35	12/40	60.0	30.0	3.50 (1.35-9.11)
Side of tumor					
Left	19/31	14/36	61.3	38.9	2.49 (0.93-6.67)
Right	27/41	15/38	65.9	39.5	2.96 (1.18-7.39)
Liver metastases at baseline per BICR					
Yes	34/43	17/46	79.1	37.0	6.44 (2.50-16.63)
No	13/30	12/28	43.3	42.9	1.02 (0.36-2.89)



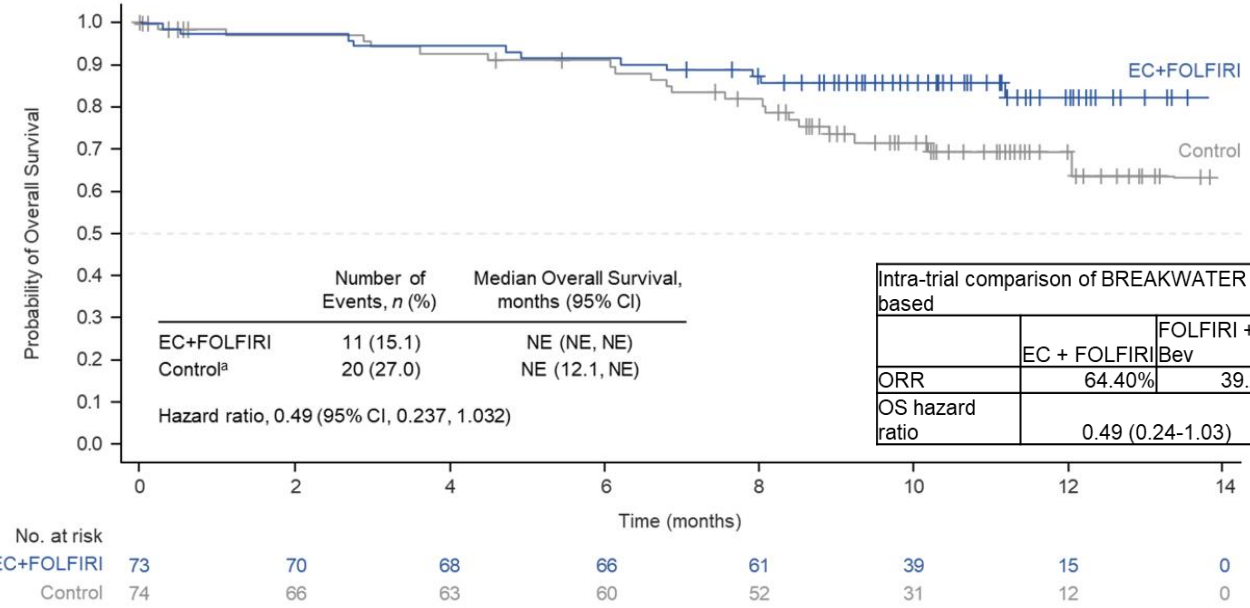
[a]**FOLFIRI ± bevacizumab.**

BICR, blinded independent central review; EC, encorafenib plus cetuximab; ECOG PS, Eastern Cooperative Oncology Group performance status; FOLFIRI, fluorouracil/leucovorin/irinotecan.

PRESENTED BY: Scott Kopetz, MD, PhD

Overall Survival

Data are immature but showed a trend for OS improvement with EC + FOLFIRI vs control



	Number of Events, *n* (%)	Median Overall Survival, months (95% CI)
EC+FOLFIRI	11 (15.1)	NE (NE, NE)
Control[a]	20 (27.0)	NE (12.1, NE)

Hazard ratio, 0.49 (95% CI, 0.237, 1.032)

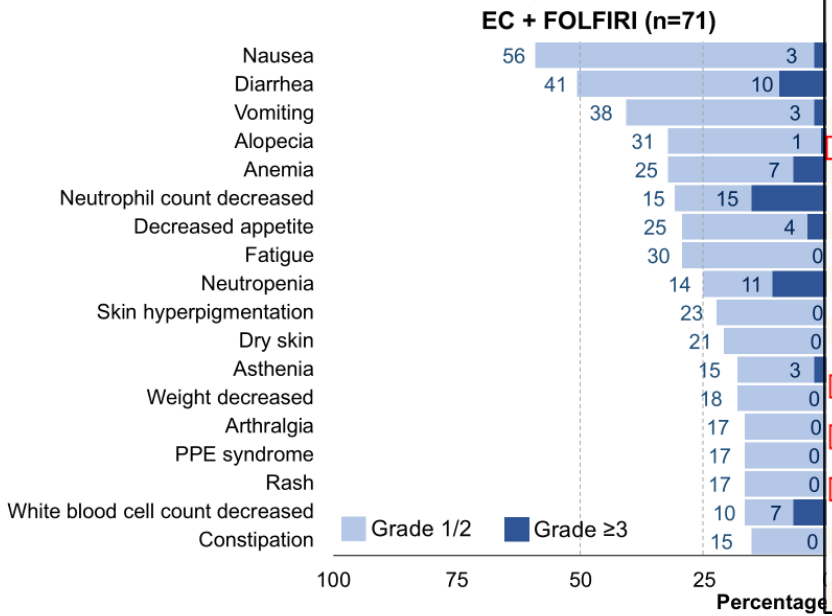
Intra-trial comparison of BREAKWATER data: oxaliplatin vs. irinotecan-based				
	EC + FOLFIRI	FOLFIRI +/- Bev	EC + FOLFOX	SOC chemo
ORR	64.40%	39.20%	65.70%	37.40%
OS hazard ratio	0.49 (0.24-1.03)		0.49 (0.38-0.63)	

[a]**FOLFIRI ± bevacizumab.**
EC, encorafenib plus cetuximab; FOLFIRI, fluorouracil/leucovorin/irinotecan; NE, not estimable.

PRESENTED BY: Scott Kopetz, MD, PhD

Most Frequent (≥15%)[a] Treatment-Related TEAEs

No new safety signals were observed, and AEs were consistent with those that were expected for each of the study drugs



Event	EC (N=153)		EC+mFOLFOX6 (N=232)		Standard Care (N=229)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients with event (percent)					
Nausea	31 (20.3)	2 (1.3)	125 (53.9)	7 (3.0)	114 (49.8)	9 (3.9)
Anemia	32 (20.9)	10 (6.5)	107 (46.1)	35 (15.1)	58 (25.3)	9 (3.9)
Diarrhea	28 (18.3)	2 (1.3)	97 (41.8)	3 (1.3)	115 (50.2)	11 (4.8)
Decreased appetite	25 (16.3)	1 (0.7)	87 (37.5)	5 (2.2)	62 (27.1)	3 (1.3)
Vomiting	22 (14.4)	2 (1.3)	84 (36.2)	9 (3.9)	51 (22.3)	5 (2.2)
Neutrophil count decreased	2 (1.3)	1 (0.7)	79 (34.1)	44 (19.0)	67 (29.3)	39 (17.0)
Arthralgia	53 (34.6)	1 (0.7)	73 (31.5)	6 (2.6)	12 (5.2)	1 (0.4)
Rash	27 (17.6)	1 (0.7)	70 (30.2)	3 (1.3)	9 (3.9)	0
Asthenia	28 (18.3)	1 (0.7)	68 (29.3)	12 (5.2)	34 (14.8)	3 (1.3)
Pyrexia	26 (17.0)	2 (1.3)	67 (28.9)	5 (2.2)	36 (15.7)	1 (0.4)
Peripheral neuropathy	2 (1.3)	0	64 (27.6)	18 (7.8)	54 (23.6)	8 (3.5)
Constipation	22 (14.4)	1 (0.7)	63 (27.2)	1 (0.4)	52 (22.7)	1 (0.4)
Peripheral sensory neuropathy	3 (2.0)	0	62 (26.7)	16 (6.9)	54 (23.6)	8 (3.5)
Fatigue	33 (21.6)	2 (1.3)	61 (26.3)	6 (2.6)	64 (27.9)	8 (3.5)
Neutropenia	3 (2.0)	2 (1.3)	56 (24.1)	35 (15.1)	57 (24.9)	23 (10.0)
Alopecia	13 (8.5)	0	53 (22.8)	0	26 (11.4)	0
Platelet count decreased	3 (2.0)	0	53 (22.8)	3 (1.3)	32 (14.0)	4 (1.7)
Lipase increased	10 (6.5)	5 (3.3)	52 (22.4)	40 (17.2)	27 (11.8)	14 (6.1)
Abdominal pain	25 (16.3)	5 (3.3)	47 (20.3)	11 (4.7)	53 (23.1)	3 (1.3)

[a]**Frequency is based on the EC + FOLFIRI arm.** [b]**FOLFIRI ± bevacizumab.**
EC, encorafenib plus cetuximab; FOLFIRI, fluorouracil/leucovorin/irinotecan; PPE, palmar-plantar erythrodysaesthesia; TEAE, treatment-emergent adverse event.

Élez E et al. N Engl J Med. 2025

PRESENTED BY: Scott Kopetz, MD, PhD

Is EC + FOLFIRI a viable alternative to EC + FOLFOX as front-line treatment for BRAF p.V600E mutant CRC?

- The data looks strikingly similar albeit it is overall less mature and we do not yet have statistical significance for the survival data.
- One downside to combining EC with FOLFOX is that neuropathy can become a dose limiting toxicity particularly with prolonged use
- EC + FOLFIRI deserves immediate consideration in patients with absolute or relative contraindications to oxaliplatin (ex: pre-existing neuropathy)
- FOLFIRI may ultimately prove to be a better first-line partner for EC in most patients but need more mature survival data before full adoption

PRESENTED BY: Eric Christenson, M.D. Assistant Professor of Oncology, Johns Hopkins University

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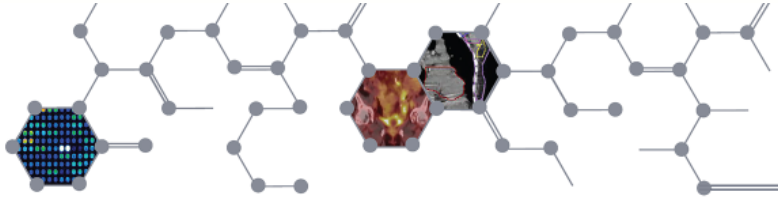

ASCO® Gastrointestinal Cancers Symposium
January 8-10, 2026

NRG-GI004/SWOG-S1610: COlorectal cancer dMMR Immuno-Therapy (COMMIT) study

A randomized phase III study of atezolizumab monotherapy versus mFOLFOX6/bevacizumab/atezo in the first-line treatment of patients with dMMR or MSI-H metastatic colorectal cancer

Caio Max Sao Pedro Rocha Lima,* Greg Yothers, Thomas J. George, Howard S. Hochster, Hanna K. Sanoff, Deirdre J. Cohen, Katherine A. Guthrie, Samuel A. Jacobs, Anwaar Saeed, Scott Kopetz, Linda H. Colangelo, Tanner J. Freeman, Scott W. Cole, Dan S. Zuckerman, Theodore S. Hong, N. Lynn Henry, Patricia A. Ganz, Charles D. Blanke, Norman Wolmark, Michael J. Overman*

**Drs. Rocha Lima and Overman contributed equally.*

SWOG CANCER RESEARCH NETWORK

Study Design

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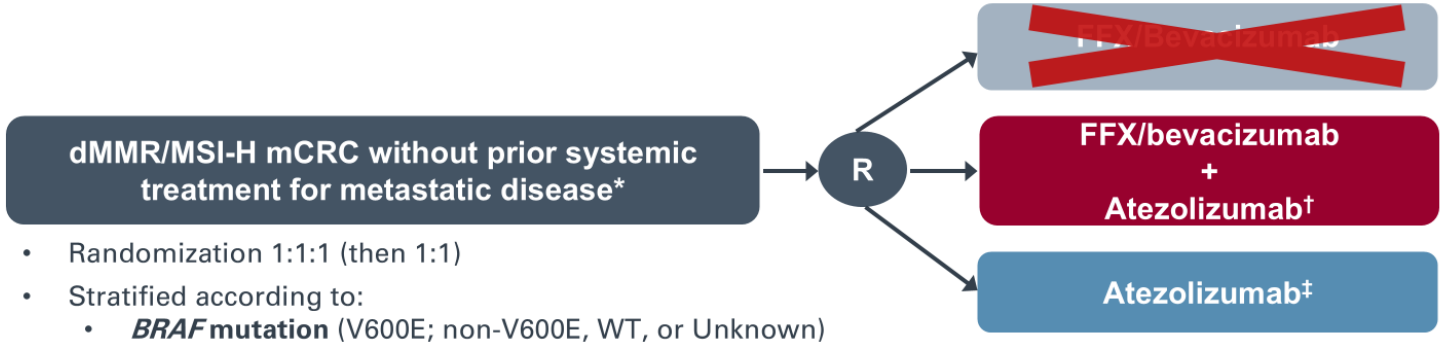


- Randomization 1:1:1 (then 1:1)
- Stratified according to:
  - ***BRAF* mutation** (V600E; non-V600E, WT, or Unknown)
  - **Metastatic disease:** (liver-only; extra-hepatic)
  - **Prior adjuvant therapy for CRC**

Due to KEYNOTE 177 results, COMMIT's FFX/bev arm was closed (trial amended 6/4/20), leaving two arms:
- **FFX/bev/atezo**
- **Atezo monotherapy**

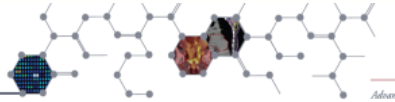
The study was also modified to enroll 120 total patients.
- **80% power to detect a hazard ratio of 0.6 for PFS, one-sided alpha=0.025.**

* One cycle of FOLFOX or CAPOX with or without bev (or biosimilar) allowed prior to enrollment

† **FFX/bev/atezo:** oxaliplatin 85 mg/m2 IV + leucovorin 400 mg/m2 IV + bevacizumab 5 mg/kg IV+ 5-FU 400 mg/m2 IV bolus on Day 1 followed by 5-FU 2400 mg/m2 IV over 46 hours plus atezo (840mg IV q2wks)

‡ **Atezo monotherapy:** 840mg IV q2wks

Study Suspension/Pre-planned Interim Analysis



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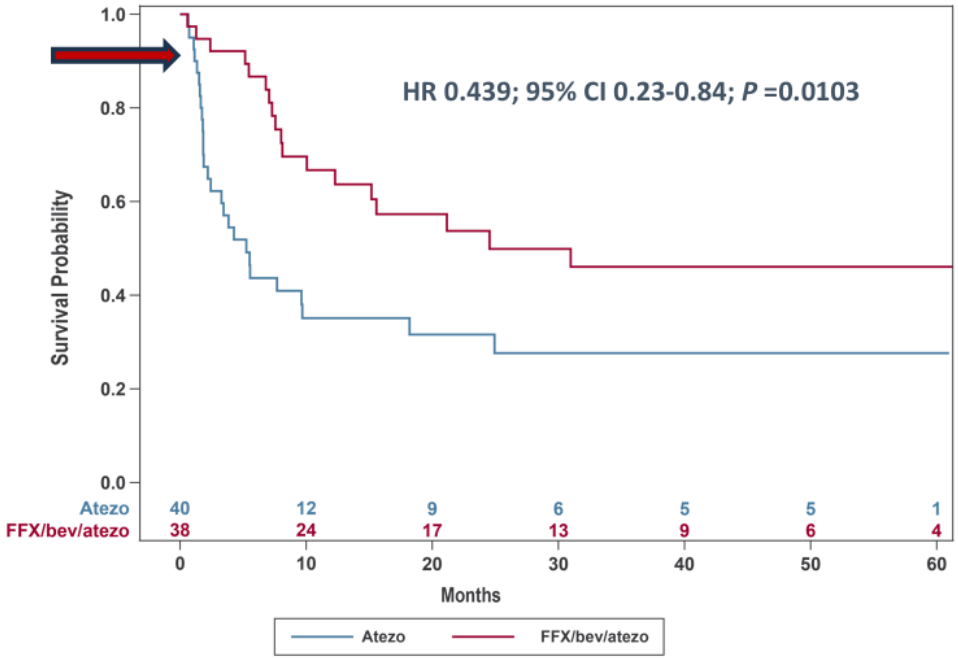
- Accrual suspended March 31, 2025, because of the results from the Checkmate 8HW trial.
- A pre-planned interim analysis occurred near the same time.
- A total of 102 patients enrolled from 11/2017 to 3/2025.

- **FFX/bev: n=20**
- **FFX/bev/atezo: n=41**
- **Atezo: n=41**

} **Statistical Analytic Population**

Progression-free Survival

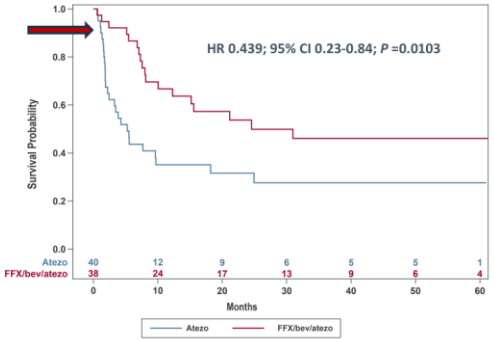


Median PFS (months)

24.5 (95% CI, 10.1–not estimable)

5.3 (95% CI, 2.2–18.2)

Progression-free Survival



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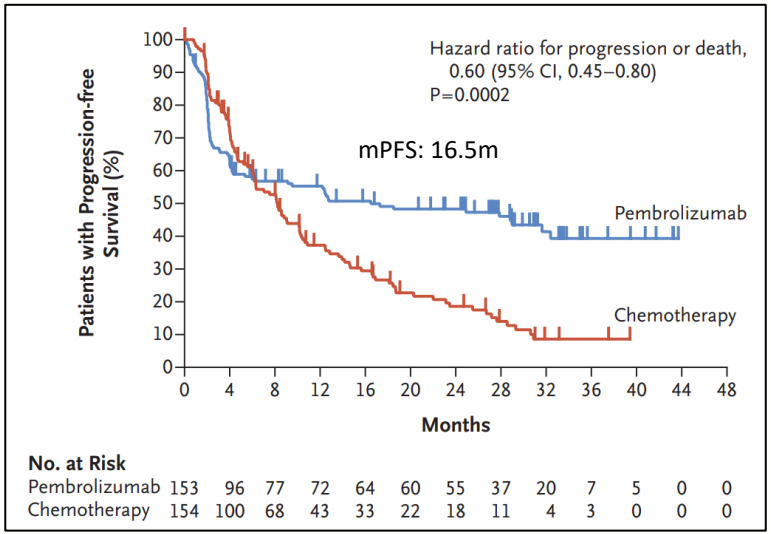
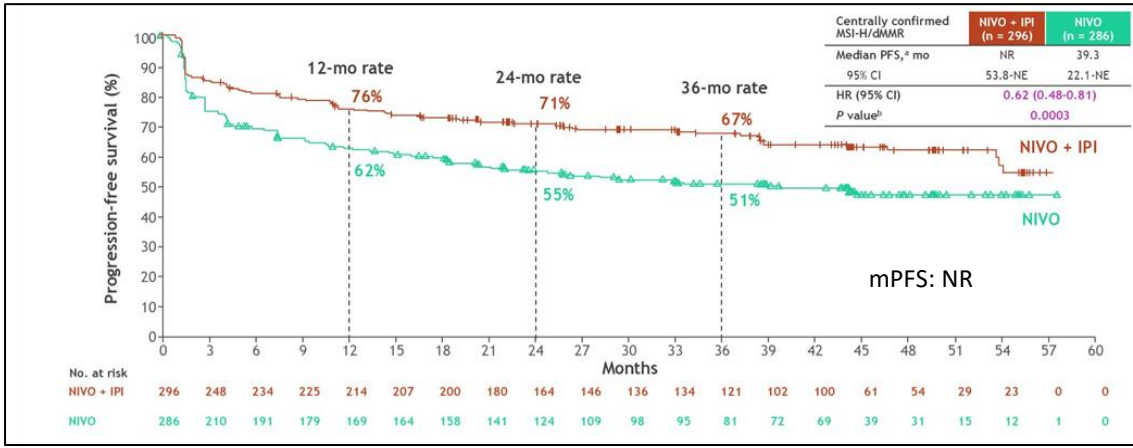
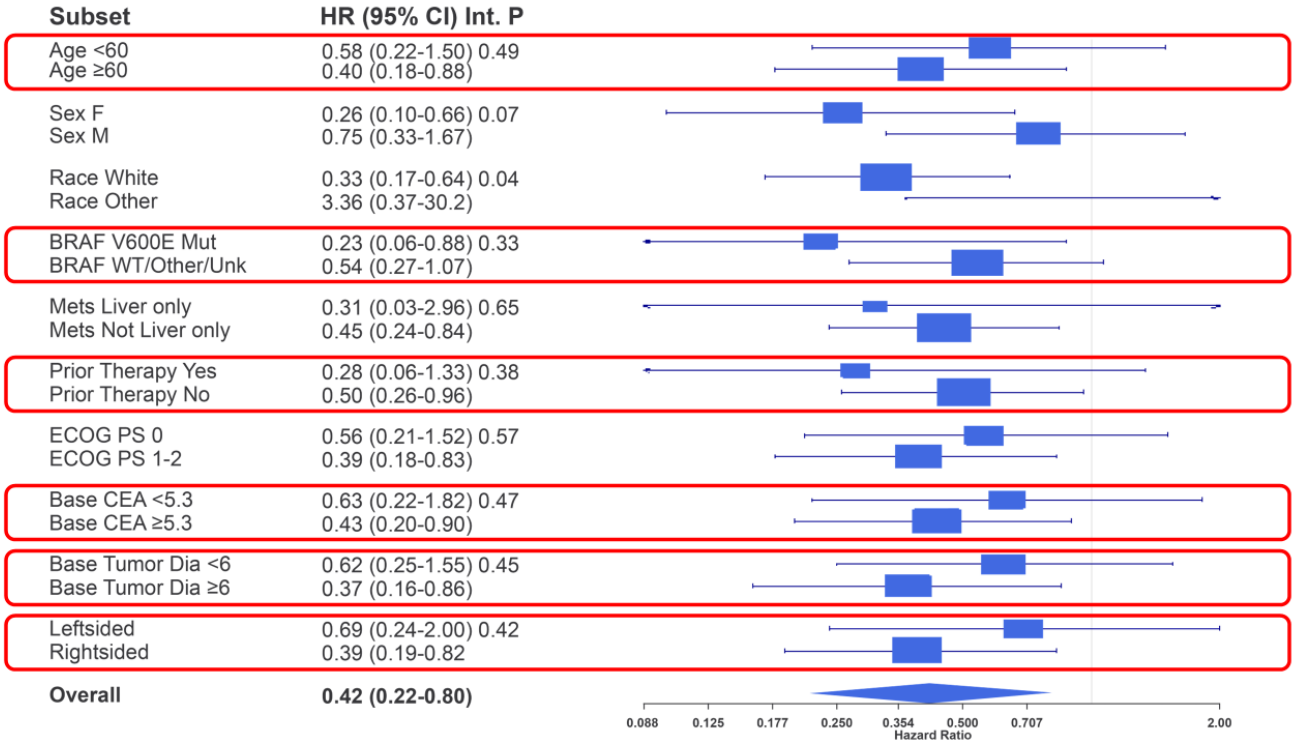
Jan 8-10, 2026 ASCO Gastrointe Cancers Symposi



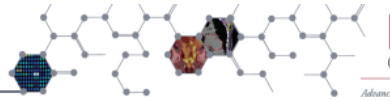


1. Rocha Lima CMS. ASCO GI 2026.
2. André T et al. N Engl J Med. 2020.
3. André T et al. Lancet. 2025.

Forest Plot

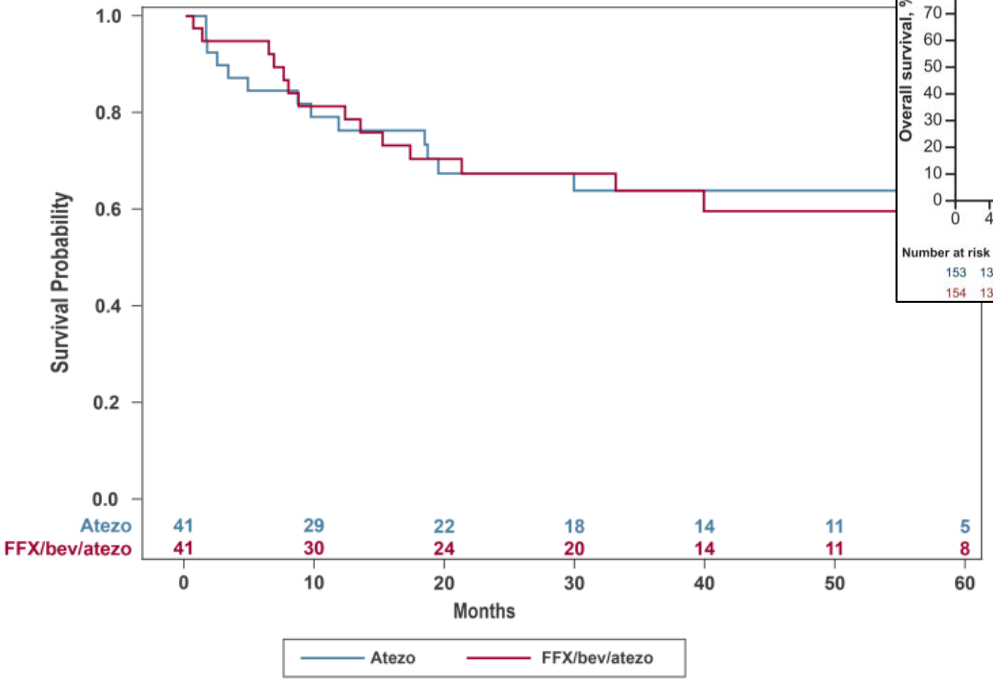


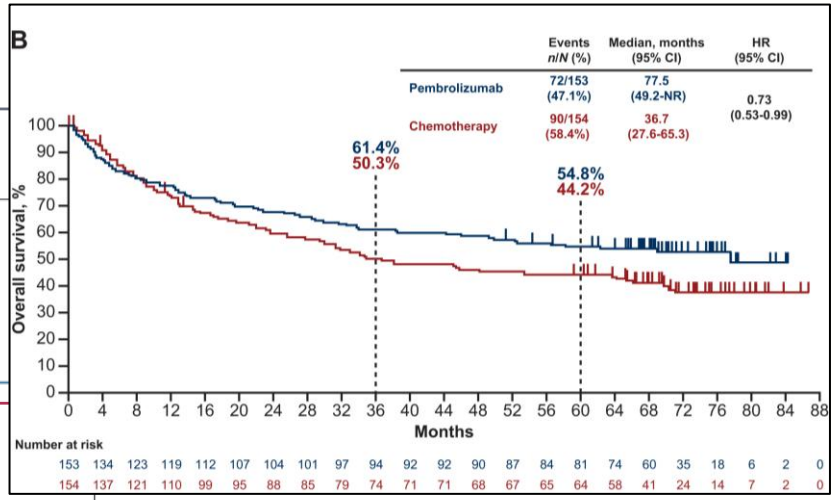
Additional Efficacy Outcomes



Efficacy Outcome	FFX/bev/atezo	Atezo
Progression-free Survival		
12 months	66.7%	35.1%
24 months	53.7%	31.6%
Overall Response Rate	**86.1%**	**46%**
Response Status		
CR	36.1%	18.9%
PR	50%	27%
SD	11.1%	21.6%
PD	2.8%	32.4%
Disease Control Rate		
12 months	64.7%	32.4%

Overall Survival

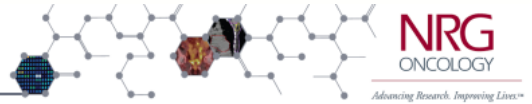




- 24-month OS:
  - **FFX/bev/atezo: 67%**
  - **Atezo: 67%**

André T. Ann Oncol. 2025

All Adverse Events



All Treated Patients, n (%)	FFX/bev/atezo	Atezo
AEs Grade 2–5 (%)	Any grade: **38** (92.7) Grade 3–4: **30** (73.2)	Any grade: **33** (80.5) Grade 3–4: **17** (41.5)
AEs Grade 3–5 (%)	**34** (82.9)	**18** (43.9)
Deaths during treatment (%)	**4** (9.8)	**1** (2.4)
AEs >10% • Diarrhea • Fatigue • Neutropenia • Sensory neuropathy • Hypertension • Infection • Hypoalbuminemia	Any grade / G 3–4 **14** (34.2%) / **5** (12.2%) **14** (34.2%) / **2** (4.9%) **18** (43.9%) / **11** (26.8%) **12** (29.2%) / **1** (2.4%) **16** (39.0%) / **8** (19.5%) **19** (46.4%) / **11**(26.8%) **0/0**	Any grade / G 3–4 (14.6%) / **0** **6** (14.6%) / **1** (2.4%) **1** (2.4%)**/0** **0/0** **7** (17%) / **1** (2.4%) **9** (22.0%) / **5** (12.2%) **5** (12.2%) / **0**

Note: Adverse events reported are regardless of their relationship to the treatment.

ASCO Gastrointestinal Cancers Symposium

Diffusion-weighted magnetic resonance imaging versus surgical staging in patients with colorectal peritoneal metastases; the multicenter, international, randomized controlled DISCO trial

Lizzel van der Snee, MD; Guoxiang Cai, MD, PhD; Joost Nederend, MD, PhD; Ignace H.J.T. de Hingh, MD, PhD; Erik J.R.J. van der Hoeven, MD, PhD; Djamila Boerma, MD, PhD; Charlotte J.V. Rijsemus, MD; Maurits P. Engbersen, MD, PhD; Arend G.J. Aalbers, MD; Brechtje A. Grotenhuis, MD, PhD; Renjie Wang, MD, PhD; Ruiqi Gu, MD; Patrick H.J. Hemmer, MD; Eva V.E. Madsen, MD, PhD; Philip R. de Reuver, MD, PhD; Jurriaan B. Tuynman, MD, PhD; Peter Zhi Qing Choo, MD, PhD; Valesca Retèl, PhD; Doenja M.J. Lambregts, MD, PhD; Marta Lopez-Yurda, PhD; Regina G.H. Beets-Tan, MD, PhD; Niels F.M. Kok, MD, PhD *; and Max J. Lahaye, MD, PhD *

Lizzel van der Snee, MD

DISCO trial design

International, multicenter, open-label RCT

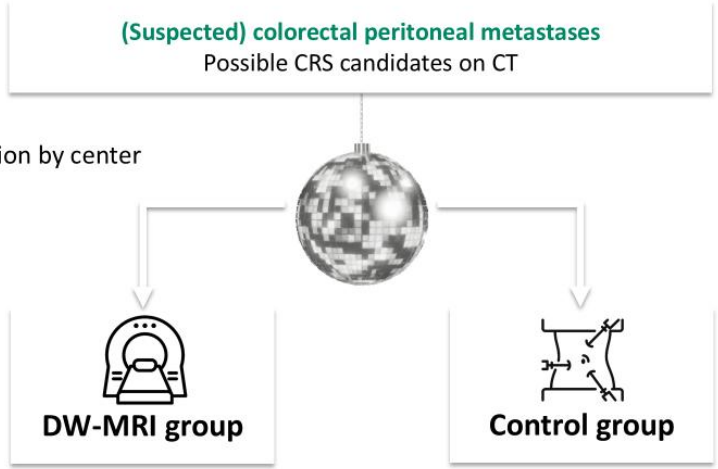
7 CRS-HIPEC centers in the Netherlands and Fudan University Shanghai Cancer Center

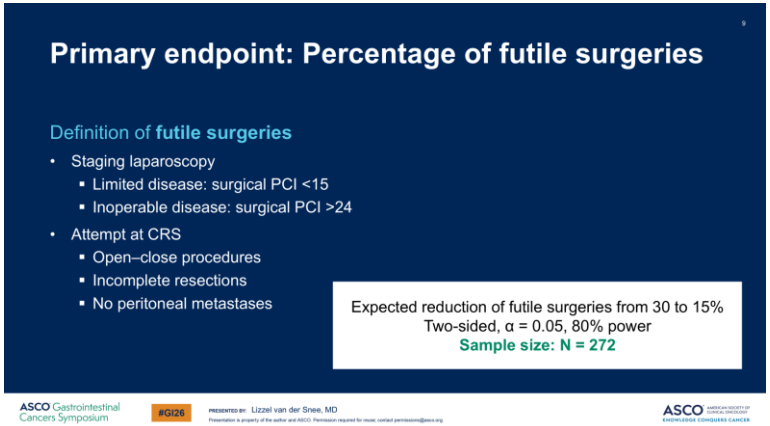
Dutch cohort

FUSCC cohort

Can DW-MRI reduce futile surgeries in patients with colorectal peritoneal metastases?

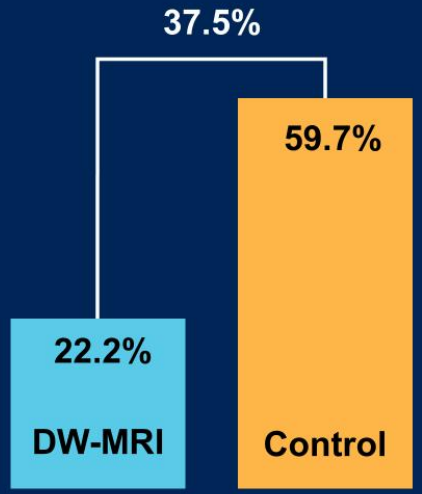
PRESENTED BY: Lizzel van der Snee, MD


(Suspected) colorectal peritoneal metastases
Possible CRS candidates on CT
1:1 ratio, stratification by center
DW-MRI group
Control group


Primary endpoint: Percentage of futile surgeries
Definition of futile surgeries
Staging laparoscopy
Limited disease: surgical PCI <15
Inoperable disease: surgical PCI >24
Attempt at CRS
Open–close procedures
Incomplete resections
No peritoneal metastases
Expected reduction of futile surgeries from 30 to 15%
Two-sided, α = 0.05, 80% power
Sample size: N = 272
ASCO Gastrointestinal Cancers Symposium
#GI26
PRESENTED BY: Lizzel van der Snee, MD
ASCO

Futile surgeries by country

Dutch Cohort
n = 144



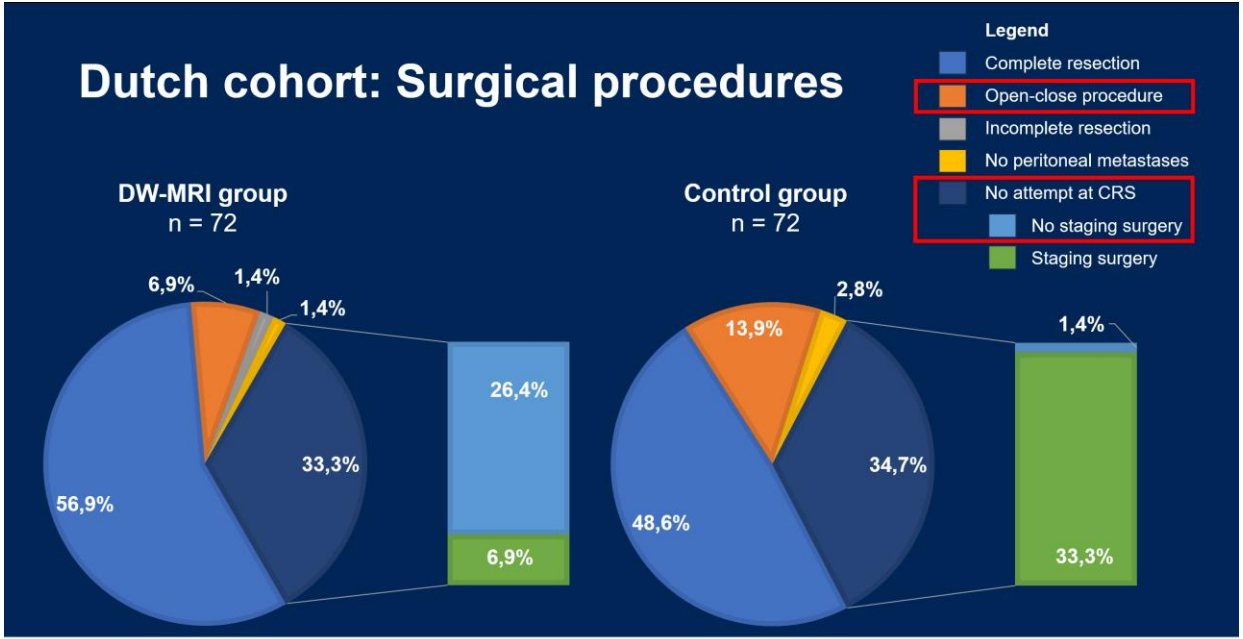
P < .0001

FUSCC Cohort
n = 99

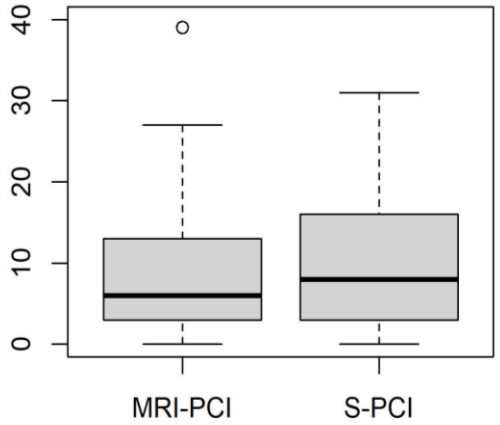
- Central review of MRI after trial
- Laparoscopy usually at initiation of CRS
- Surgical PCI cut-off more liberal

P = .0564

PRESENTED BY: Lizzel van der Snee, MD



Buena correlación entre PCI mediante RM y PCI quirúrgico



ASCO Gastrointestinal Cancers Symposium

Cedars Sinai

Longitudinal Study on the Influence of Physical Activity in Managing Cancer-Related Fatigue in Patients with Colorectal Cancer

Louisa Liu, MD
Samuel Oschin Comprehensive Cancer Institute
Cedars-Sinai Medical Center

Methods

- N = 1718 patients (835 colon, 859 rectal) from the ColoCare Study
- Physical activity assessed using IPAQ questionnaire at baseline, 6, 12, and 24 months
- Physical activity measured by calculated MET-minutes per week
- Fatigue and Quality of Life (QoL): EORTC QLQ-C30
- Stratified by metastatic vs non-metastatic
- Mixed effects + lagged models

Results: Fatigue in Non-Metastatic Patients

		Baseline		6 months		12 months		24 months	
Metastatic Status	Physical Activity	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-Metastatic	Walking	0.96 (0.81 to 1.15)	0.685	0.74 (0.58 to 0.95)	0.018	0.75 (0.58 to 0.98)	0.032	0.71 (0.49 to 1.03)	0.069
	Moderate	0.88 (0.74 to 1.05)	0.171	0.79 (0.61 to 1.01)	0.061	0.85 (0.66 to 1.10)	0.225	0.69 (0.48 to 1.00)	0.049
	Vigorous	1.05 (0.89 to 1.25)	0.54	0.75 (0.58 to 0.96)	0.021	0.76 (0.58 to 0.98)	0.036	0.69 (0.47 to 1.02)	0.061
	Total	1.05 (0.89 to 1.24)	0.552	0.76 (0.60 to 0.97)	0.028	0.77 (0.59 to 1.01)	0.059	0.72 (0.50 to 1.03)	0.072

- Walking and vigorous activity were associated with significantly lower odds of severe fatigue at 6 months and 12 months

Results: Fatigue in Metastatic Patients

		Baseline		6 months		12 months		24 months	
Metastatic Status	Physical Activity	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Metastatic	Walking	0.70 (0.47 to 1.03)	0.067	1.00 (0.56 to 1.80)	0.998	0.65 (0.34 to 1.23)	0.186	1.34 (0.41 to 4.36)	0.626
	Moderate	0.77 (0.52 to 1.14)	0.192	1.15 (0.65 to 2.05)	0.628	1.16 (0.58 to 2.33)	0.671	0.95 (0.30 to 3.04)	0.936
	Vigorous	0.68 (0.46 to 1.01)	0.059	1.19 (0.66 to 2.12)	0.565	1.62 (0.88 to 3.00)	0.123	0.20 (0.02 to 1.75)	0.146
	Total	0.69 (0.48 to 1.00)	0.047	1.57 (0.87 to 2.86)	0.137	0.99 (0.53 to 1.84)	0.976	0.64 (0.15 to 2.66)	0.538

- No consistent association between physical activity and fatigue over time

Results: QoL in Non-Metastatic Patients

		Baseline		6 months		12 months		24 months	
Metastatic Status	Physical Activity	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-Metastatic	Walking	0.87 (0.74 to 1.02)	0.089	1.71 (1.34 to 2.17)	<0.001	1.77 (1.37 to 2.28)	<0.001	1.83 (1.27 to 2.63)	0.001
	Moderate	0.94 (0.79 to 1.11)	0.437	1.45 (1.14 to 1.85)	0.002	1.50 (1.17 to 1.94)	0.002	1.85 (1.26 to 2.69)	0.002
	Vigorous	0.97 (0.82 to 1.14)	0.689	1.33 (1.05 to 1.69)	0.018	1.46 (1.11 to 1.91)	0.006	1.61 (1.08 to 2.41)	0.019
	Total	0.90 (0.76 to 1.05)	0.172	1.44 (1.13 to 1.82)	0.003	1.34 (1.04 to 1.73)	0.024	1.24 (0.88 to 1.76)	0.223

- All PA types were associated with significantly higher odds of improved QoL at all follow-up timepoints

Results: QoL in Metastatic Patients

		Baseline		6 months		12 months		24 months	
Metastatic Status	Physical Activity	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Metastatic	Walking	1.23 (0.87 to 1.75)	0.234	1.22 (0.71 to 2.09)	0.468	1.62 (0.87 to 3.00)	0.129	1.57 (0.51 to 4.78)	0.428
	Moderate	1.06 (0.75 to 1.51)	0.735	1.11 (0.66 to 1.87)	0.683	0.84 (0.47 to 1.48)	0.538	0.59 (0.19 to 1.86)	0.367
	Vigorous	1.47 (0.98 to 2.20)	0.061	0.98 (0.55 to 1.74)	0.934	0.88 (0.47 to 1.66)	0.694	1.83 (0.41 to 8.29)	0.431
	Total	1.29 (0.91 to 1.85)	0.157	0.84 (0.49 to 1.44)	0.524	1.57 (0.84 to 2.94)	0.16	1.04 (0.29 to 3.75)	0.957

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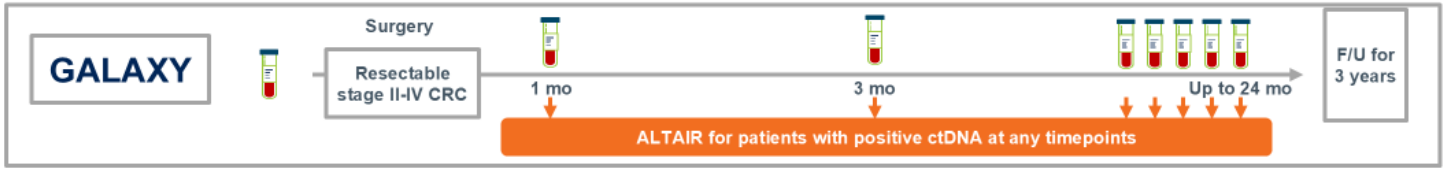
Impact of Postoperative ctDNA Dynamics on Eligibility for ALTAIR Randomized Trial in Patients with Colorectal Cancer: Implications for Clinical Trial Enrollment

Hideaki Bando, on behalf of Yoshiaki Nakamura and the CIRCULATE-Japan investigators

National Cancer Center Hospital East, Kashiwa, Japan

Yoshiaki Nakamura, Vasily N. Aushev, Jun Watanabe, Yusuke Takahashi, Masahito Kotaka, Nobuhisa Matsuhashi, Eiji Oki, Yoshito Komatsu, Manabu Shiozawa, Keiji Hirata, Yuji Miyamoto, Kentaro Yamazaki, Kun-Huei Yeh, Adham Jurdi, Saori Mishima, Daisuke Kotani,
Hiroya Taniguchi, Takayuki Yoshino, and Takeshi Kato

CIRCULATE-Japan ALTAIR Study Design



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

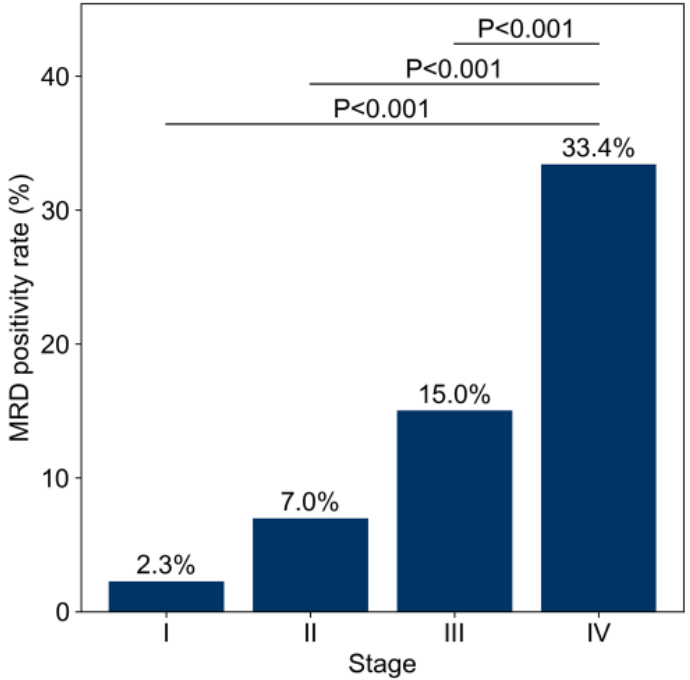
N=243

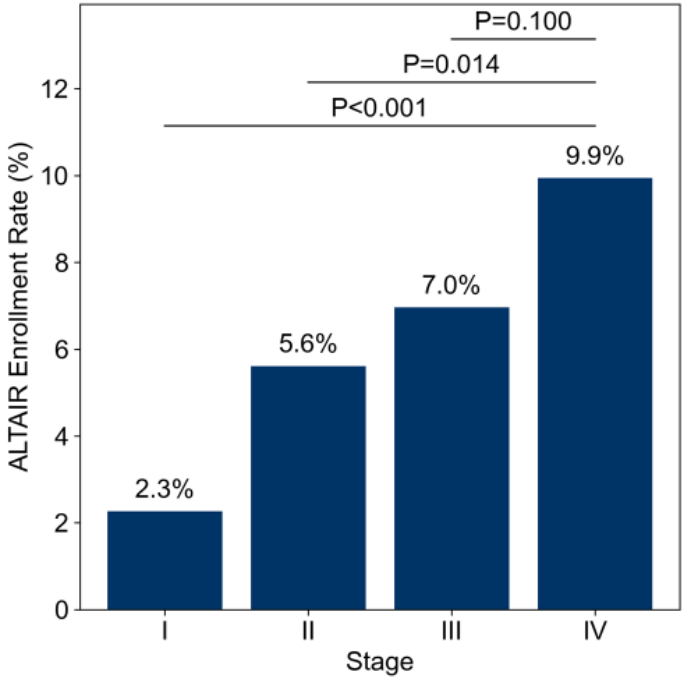
Experimental Arm
Trifluridine/tipiracil
35mg/m2 BSA, BID orally
day 1-5 and day 8-12; Q28D
6 cycles

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

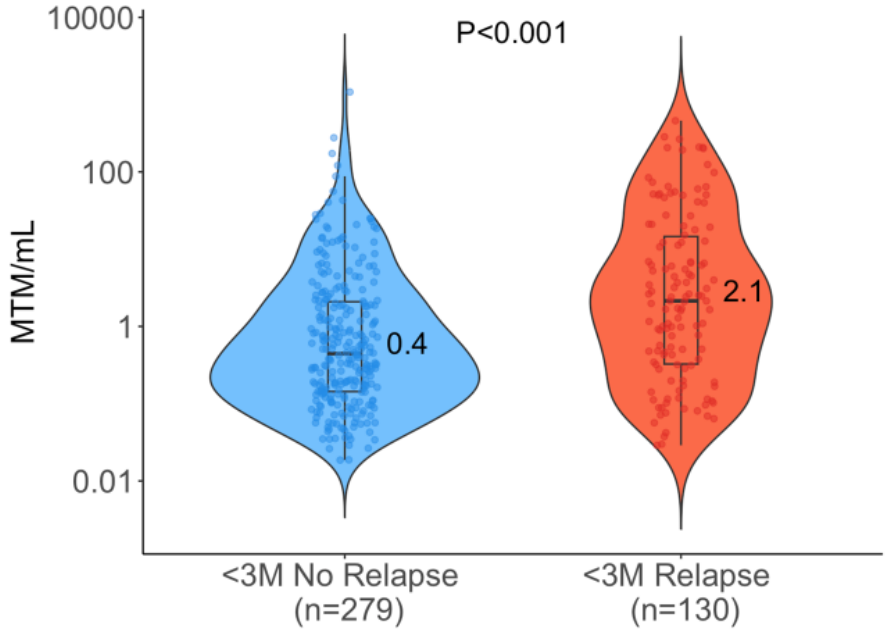
MRD Positivity and ALTAIR Enrollment Rate by Stage





MRD positivity: ctDNA positivity in the MRD window (2-10 weeks post-surgery)

ctDNA Level at the Time of First ctDNA Positivity among Patients Who Relapsed and Didn't Relapse within 3 Months



Poster Session C
1/10/2026, 7:00-7:55 AM; 12:00-1:30 PM

Abstract # 220: **Correlation between the timing of recurrence and circulating tumor DNA (ctDNA) doubling time in patients (pts) with resected colon cancer**

Abstract # 221: **Prognostic value of presurgical circulating tumor DNA (ctDNA) levels and other clinical factors in colon cancer**

Higher ctDNA levels correlated with clinical relapse within 3 months of ctDNA positivity.

MINIORALES

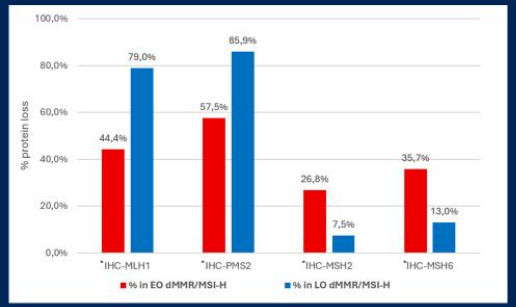
ASCO Gastrointestinal Cancers Symposium

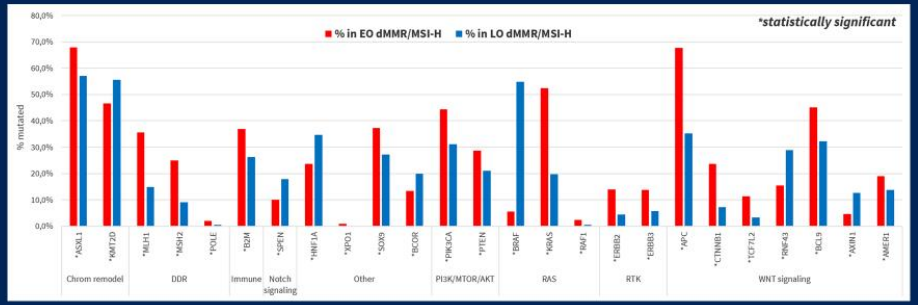
Decoding Molecular, Clinico-Pathological and Outcome Differences between Early-Onset and Late-Onset Mismatch Repair deficient/Microsatellite Instability-High CRC: Insights from Real World data

Michela Bartolini[1,2,3], Yasmine Baca[4], Rituparna Ganguly[4], David de Semir[4], Francesca Battaglin[1], Yan Yang[1,4], Shivani Soni[1], Pooja Mittal[1], Sandra Algaze[1], Unnati Hemant Shah[1], Lesly Torres-Gonzalez[1], Andrew Elliott[1], Rachna T. Shroff[1], Joshua Millstein[5], Wu Zhang[1], Alberto Puccini[2,3], Heinz-Josef Lenz[1]

1. Division of Medical Oncology, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA 90089, USA; 2. Department of Biomedical Sciences, Humanitas University, via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy; 3. IRCCS Humanitas Research Hospital, Medical Oncology and Hematology Unit, via Manzoni 56, 20089 Rozzano, Milan, Italy; 4. Caris Life Sciences, Phoenix, Arizona; 5. Department of Population and Public Health Sciences, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.

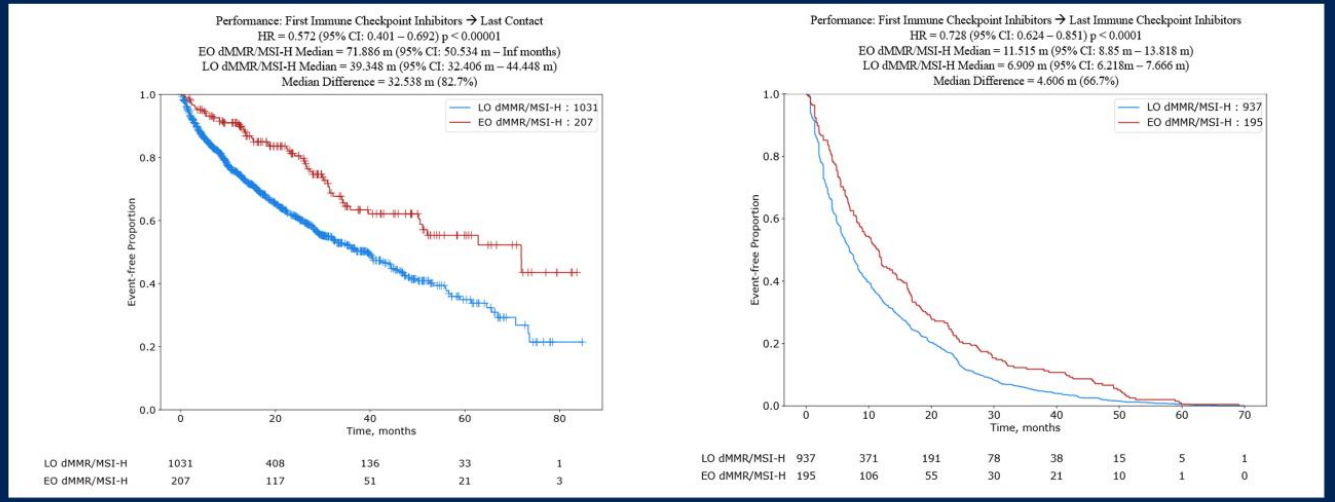
Results – Molecular Features





- dMMR was mostly due to loss of the MSH2/MSH6 complex in EO CRC
- EO CRC had higher mutation rates in *KRAS* (52.4% vs 19.7%, p < 0.001), *APC* (67.8% vs 35.2%, p < 0.001), *MLH1* (35.6% vs 14.9%, p < 0.001) and *MSH2* (25.1% vs 9.1%, p < 0.001%)
- LO CRC more often harbored *BRAF* (54.7% vs 5.6%, p < 0.001) and *KMT2D* mutations (55.6% vs 46.6%, p = 0.0002)

Results – Outcomes



- Patients with EO CRC have better OS and ToT compared to LO when treated with Immune Check-Point Inhibitors

ASCO Gastrointestinal Cancers Symposium

CONQUER CANCER THE ASCO FOUNDATION

FOxTROT

FOxTROT: predictive effects of *ERBB2* (*HER2*) and *ERBB3* (*HER3*) on neoadjuvant panitumumab benefit in *RAS/BRAF* wild-type locally advanced colon cancer (LACC)

J. W. Appleyard [1], J. F. Seligmann [1], D. Morton [2], F. Elliott [1], K. Handley [2], B. Glimelius [3], G. Hemmings [4], D. Bottomley [4], P. Quirke [4], L. Magill [2], N. P. West [4], A. D. Beggs [5], C. J. M. Williams [1]

[1] Division of Oncology, Leeds Institute of Medical Research, University of Leeds, Leeds, United Kingdom; [2] University of Birmingham, Birmingham, United Kingdom; [3] Uppsala University, Uppsala, Sweden; [4] Division of Pathology and Data Analytics, Leeds Institute of Medical Research, University of Leeds, Leeds, United Kingdom; [5] Institute of Cancer & Genomic Sciences, University of Birmingham, Birmingham, United Kingdom

UNIVERSITY OF LEEDS

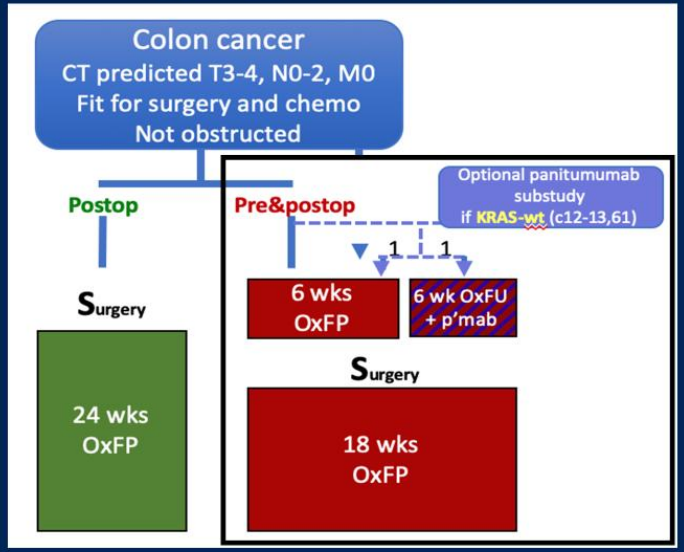
UNIVERSITY OF BIRMINGHAM

CANCER RESEARCH UK

Yorkshire Cancer Research

Methods

FOxTROT 1 trial schema



Research questions:

1. Can *HER2* & *HER3* expression improve patient selection for neoadjuvant FOLFOX + panitumumab?
2. What additional impact does *AREG/EREG* expression have?

Design:

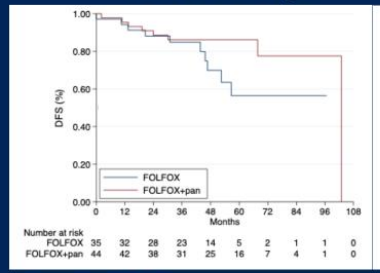
- Endpoints:
  - DFS and OS.
- Molecular testing:
  - Extended *RAS* (*KRAS* codons 12,13,59,61,117,146 & *NRAS* codons 12,13,59,61) and *BRAF* codon 600 status.
  - RNAseq.
- Analyses conducted:
  - *HER2* & *HER3* analyzed as a binary measure,
  - Prognostic effect,
  - Predictive effect on panitumumab,
  - Exploratory joint model of *HER3* with *AREG/EREG*.

FOxTROT

HER2 had no association with panitumumab efficacy

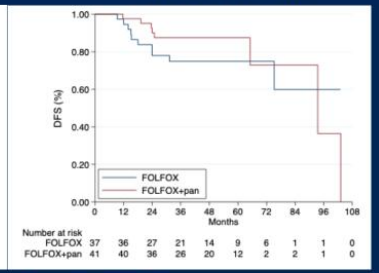
- *HER2* inferiorly prognostic for DFS in FOLFOX arm: HR 1.53 (1.02-2.31), p=0.04

DFS: *HER2* high



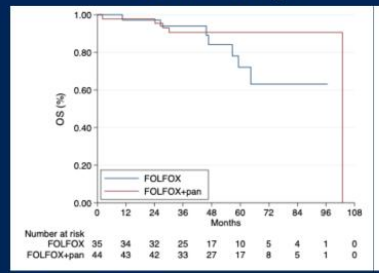
Events 18/79
Median 51.7 vs 40.5 months
HR=0.45 (0.17-1.19), p=0.11

DFS: *HER2* low



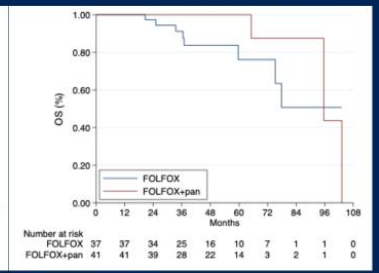
Events 18/78
Median 41.9 vs 37.3 months
HR=0.60 (0.23-1.59), p=0.30

OS: *HER2* high



Events 12/79
Median 55.6 vs 46.7 months
HR=0.40 (0.12-1.38), p=0.15

OS: *HER2* low



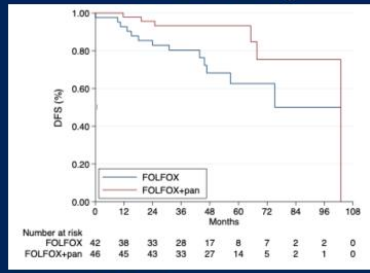
Events 11/78
Median 51.6 vs 38.4 months
HR=0.24 (0.05-1.18), p=0.08

FOxTROT

High *HER3* associated with significant benefit from the addition of panitumumab to neoadjuvant FOLFOX

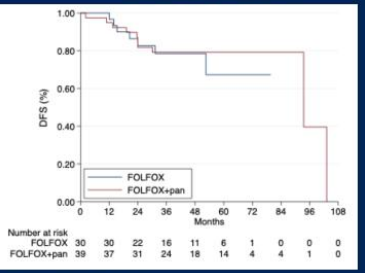
- *HER3* had no prognostic effect on DFS or OS.

DFS: *HER3* high



Events 19/88
Median 51.2 vs 40.3 months
HR=0.37 (0.14-0.97), p=0.04

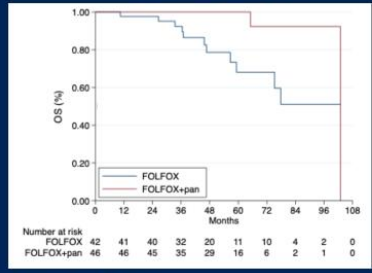
DFS: *HER3* low



Events 17/69
Median 38.5 vs 36.7 months
HR=0.80 (0.29-2.22), p=0.67

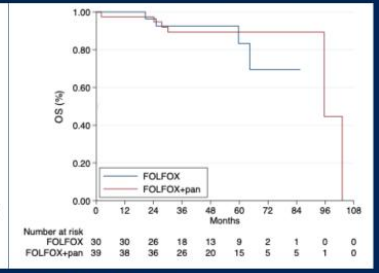
Interaction p=0.28

OS: *HER3* high



Events 13/88
Median 57.6 vs 46.2 months
HR=0.16 (0.04-0.75), p=0.02

OS: *HER3* low



Events 10/69
Median 50.4 vs 39.0 months
HR=0.71 (0.18-2.84), p=0.63

Interaction p=0.14

ASCO Gastrointestinal Cancers Symposium

Glucagon-Like Peptide-1 Receptor Agonist vs Aspirin For Primary Prevention Of Colorectal Cancer: Evidence From A Real-World Head-to-Head Comparison

Colton Frisco Jones, MD; Elvis Obomanu MD, Arianna Neely, MD, Karecia Byfield, MD, Chidiebube Ugwu, MD, Muluken Megiso, MD, Tarfa Verinumbe, MD, Danielle Lewis, MD, Fnu Deepali, MD, Damion Persad, MD, Akil Olliverrie, MD, and Sukeshi Patel Arora, MD.

1University of Texas Health Science Center, San Antonio, San Antonio, Texas; 2Jefferson Einstein Philadelphia Hospital, Department of Internal Medicine, Philadelphia, Pennsylvania; 3 South Brooklyn Health Hospital, Brooklyn, New York; 4 Mays Cancer Center, UT Health San Antonio, MD Anderson Cancer Center, San Antonio, Texas

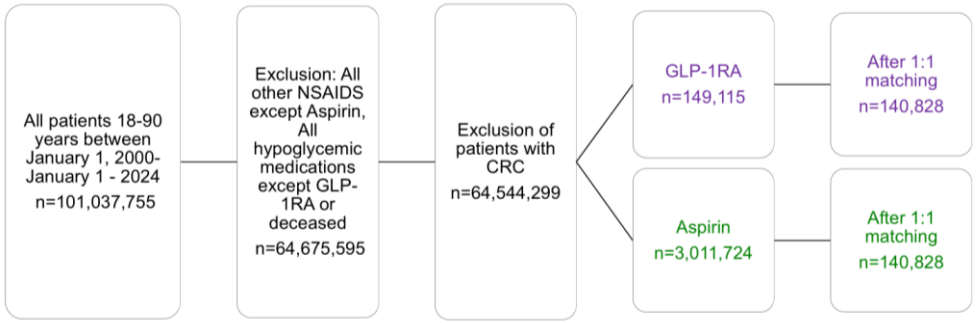
Background

- Aspirin has long been investigated for colorectal cancer (CRC) prevention, yet its modest efficacy and bleeding risks limit broad use.
- Emerging evidence suggests that GLP-1 receptor agonists (GLP-1RAs) possess anti-inflammatory and anti-neoplastic properties (inhibit the **PI3K/AKT/mTOR** pathway); however, the role of GLP-1RAs in cancer prevention remains underexplored.
- This study is the first real-world, head-to-head comparison on the efficacy and safety of GLP-1RA versus aspirin for primary prevention of CRC.

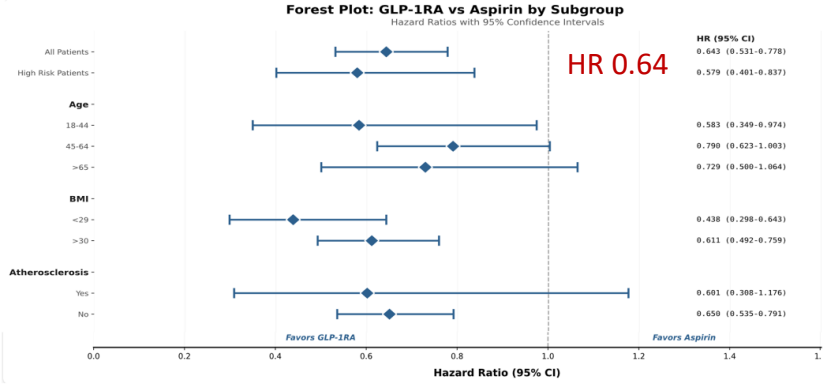
Methodology

- We used de-identified data from the TrinetX database, which encompasses 150 million patients across 106 health organizations.
- GLP-1RA users (Cohort A) were matched to aspirin users (Cohort B) utilizing propensity score matching
- The **primary endpoint** was CRC incidence.
- The **secondary endpoint** was the incidence of adverse events (AEs) related to GLP-1RA and Aspirin.
- Sensitivity and subgroup analysis were performed.
- Patients with outcomes before the study window were excluded.
- Multivariate logistic regression assessed associations, and Cox proportional-hazards models determined time to event outcome.

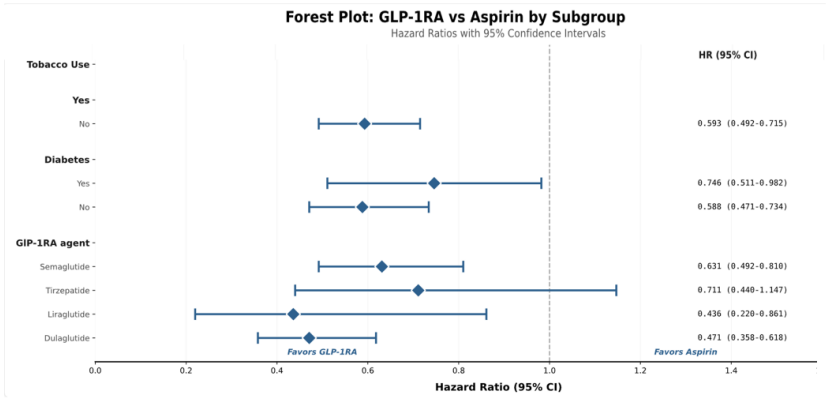
Flow Diagram of Patient Selection



Colorectal Cancer Incidence Among Subgroups



Colorectal Cancer Incidence Among Subgroups



Adverse Events Related To GLP-1RA & Aspirin

AAS

GLP1-RA

Adverse Events	GLP-1RA Cases/patients	Aspirin Cases/patients	HR & 95% CI	P value
Gastrointestinal Bleeding	2,738/136,547 (2%)	2,907/136,219 (2.1%)	0.852 (0.809-0.898)	0.018
Gastric Ulcers	680/136,902 (0.5%)	758/136,831 (0.55%)	0.815 (0.735-0.904)	0.038
Acute Kidney Injury	1,577/136,720 (1.15%)	3,841/135,493 (2.8%)	0.369 (0.348-0.391)	0.0001
Nausea & Vomiting	14,136/134,335 (10.5%)	12,790/132,316 (9.7%)	0.980 (0.957-1.004)	0.0001
Diarrhea	9,154/135,417 (6.8%)	7,336/135,215 (5.4%)	1.131 (1.096-1.166)	0.0001
Abdominal Pain	25,052/131,155 (19%)	21,144/129,419 (16.3%)	1.055 (1.036-1.075)	0.0001

ASCO Gastrointestinal Cancers Symposium

Liver transplantation for unresectable colorectal liver metastases:

Pooled real-world data from all Belgian liver transplant centers

Gertjan Rasschaert, Morgan Vandermeulen, Marc Van den Eynde, Hasan Eker, Timon Vandamme, Catherine Loly, Bart Bracke, Xavier Verhelst, Jef Verbeek, Hans Van Vlierberghe, Virginie Labille, Bart Op de Beeck, Valerio Lucidi, Chris Verslype, Karen Geboes, Thiery Chapelle, Geraldine Dahlqvist, Jacques Pirenne, Olivier Detry, Laurent Coubeau

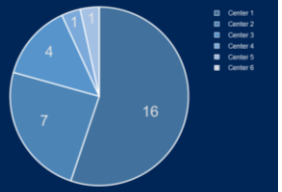
PRESENTED BY: Gertjan Rasschaert, MD | Attending, GI Oncology Department, UZ Leuven | CRC research, Tejpar lab, KU Leuven

Methods

- Retrospective collection of all LTx for uCLM cases between June 2016 and August 2025
- Across all six accredited LTx centers in Belgium
- In the absence of a national protocol, the patient selection for LTx was guided by differing local practices

Patient characteristics

- 29 patients underwent LTx for uCLM
- 69% male, 31% female
- Median age: 56 (IQR 50-61)



Distribution per center

Patient characteristics

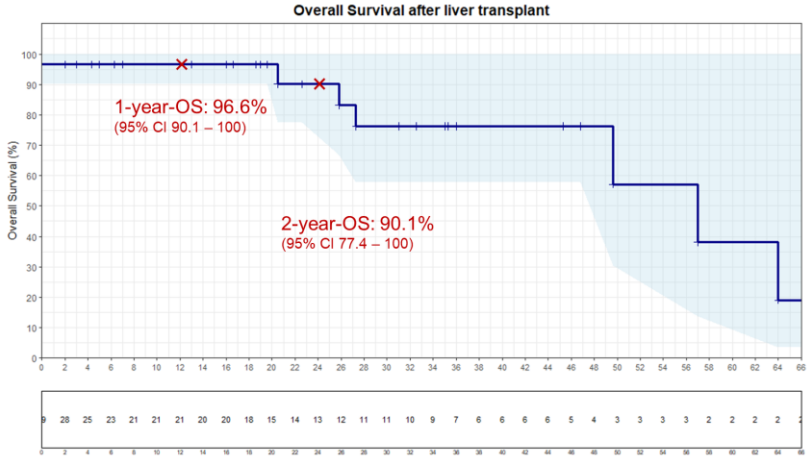
Primary tumor	
Site	Right: 21% (6) Left: 69% (20) Rectum: 10% (3)
Mismatch repair status	Proficient: 100% (29) Deficient: 0% (0)
Mutational status	*KRAS* mt: 7% (2) *BRAF* V600E mt: 7% (2) *RAS/BRAF* wt: 86% (25)
(y)pT	x: 7% (2) 2: 21% (6) 0: 0% (0) 3: 45% (13) 1: 17% (5) 4: 10% (3)
(y)pN	x: 10% (3) 1: 35% (10) 0: 31% (9) 2: 24% (7)
Timing resection in synchronous presentation (n=24)	At diagnosis: 17% (4) After chemotherapy: 83% (20)
Median time from resection to LTx	11 months (IQR 5-26)

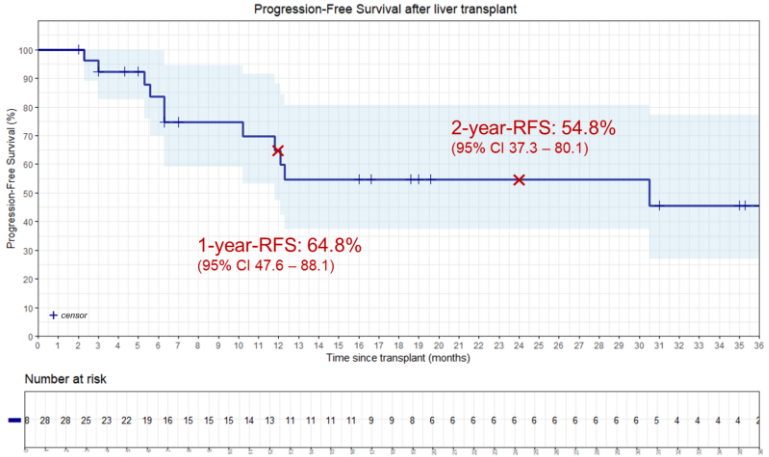
Systemic treatment		
Before primary resection	Yes: 62% (18) No: 38% (11)	
Number of lines before LTx	1: 69% (20) 2: 31% (9) 3: 0% (0)	
First line	Doublet: 62% (18) Triplet: 38% (11)	
Targeted therapy in first line	Anti-VEGF: 28% (8) Anti-EGFR: 65% (19)	Other: 0% (0) None: 7% (2)
Median duration of chemotherapy	13 months (IQR 9-18)	

Colorectal liver metastases	
Presentation	Synchronous: 83% (24) Metachronous: 17% (5)
Prior local therapy (surgery, ablation, radiotherapy, other)	21% (6)
Graft	
Type of donor	DBD: 28% (8) DCD: 38% (11) Living: 34% (10)

Outcome

- Median follow-up: 20.5 months (IQR 7.0-35.3)
- **Recurrence:** 38% (11)
  - Pulmonary: 73% (8)
  - Peritoneal: 27% (3)
  - Hepatic: 0% (0)
  - Multiple sites: 0% (0)
- **Subsequent therapy:** 100% (11)
  - Surgery: 18% (2)
  - Radiotherapy: 9% (1)
  - Systemic treatment: 73% (8)
- Median time to recurrence 6.3 months (IQR 5.3-6.7)
- Median overall survival post recurrence was 26.5 months (IQR 14.5-36.0)





ASCO Gastrointestinal Cancers Symposium

Early outcomes of the PLATO ACT5 randomised trial - Personalizing Anal Cancer Radiotherapy dose

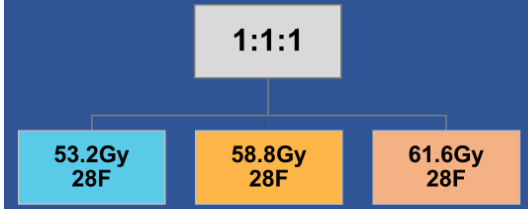
M. Hawkins, A. Gilbert, R. Adams, M. Harrison, L. Berkman, J. Copeland, D. Gilbert , C. Gaul, R.Glynne-Jones, V. Goh, M. Norris, R. Muirhead, A. Renehan, S. Richman, S. Ruddock, A. Smith, J.Webster, S. Brown, D. Sebag-Montefiore

M.A. Hawkins on behalf of PLATO trial management group

ACT5

Leads - Hawkins and Sebag-Montefiore

T3/4 Nany,T2N1-3



Randomised Phase 3 trial n=459

Internal pilot n=60, Phase II n=80

Acute toxicities

No differences at any timepoints

*no grade 4 after RT completion

Maximum CTCAE grade reported across all toxicities	Standard dose 53.2 Gy 28F N (%)	Dose escalation 1 58.8 Gy 28F N (%)	Dose escalation 2 61.6 Gy 28F N (%)	Total N (%)
During treatment				
1+2	71 (44.6%)	71(46.4%)	70 (47.9%)	212 (46.3%)
3+4	88 (55.4%)	76 (53.6%)	74(52.1%)	246 (53.7%)
6 weeks				
No ARs at timepoint	22 (15.9%)	20 (15.2%)	21 (16.5%)	63 (15.9%)
1+2	108(78.2%)	92 (69.7%)	92(72.4%)	292 (73.6%)
3*	4 (2.9%)	17 (12.9%)	12 (9.4%)	33 (8.3%)
3 months				
No ARs at timepoint	46 (33.3%)	43 (32.6%)	38 (29.9%)	127 (32.0%)
1+2	86 (62.3%)	83 (62.9%)	76 (60.7%)	246 (62.0%)
3*	4 (2.9%)	4 (3.0%)	8 (6.3%)	16 (4.0%)
6 months				
No ARs at timepoint	52 (37.7%)	55 (41.7%)	43 (33.9%)	150 (37.8%)
1+2	76 (65.1%)	69 (62.3%)	70 (55.2%)	215 (54.1%)
3*	5 (3.6%)	5 (3.8%)	9 (7.1%)	19 (4.8%)

Clinical and radiological 6 months complete response rates

Response to treatment	SD 53.2 Gy 28F N (%)	DE1 58.8 Gy 28F N (%)	DE2 61.6 Gy 28F N (%)	Total N (%)
Complete response on Clinical exam (DRE)	112 (72.7%)	109 (70.3%)	98 (63.6%)	319 (68.9%)
Complete clinical response MRI: TRG 1&2 with NO visible T2 weighted nodes	100 (64.9%)	103 (66.5%)	101 (65.6%)	304 (65.7%)

POSTERS

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A10
ASCO GI 2026

Atezolizumab plus Tiragolumab in combination with chemoradiotherapy in localized squamous cell carcinoma of the anal canal: TIRANUS (GEMCAD-2103) trial

Jaume Capdevila [1], David Paez [2], Mercedes Martínez Villacampa [3], Alejandro Garcia-Alvarez [1], Jorge Aparicio [4], Montse Pampols [5], Maria del Carmen Riesco-Martínez[6], Eduardo Polo [7], Ana Ruiz-Casado [8], Carmen Castañón [9], Sandra Soriano [10], Jorge Hernando [1], Begoña Navalpotro [11], David Armario [12], Guillermo Villacampa [13], Evelin Horvath[14], Anna C. Virgili [2], Leyre Asiain[15], Alejandra Giménez [4], Mónica Guillot [14]

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BACKGROUND

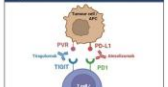
Radical chemoradiotherapy (CRT) is the standard of care for patients with localized squamous cell carcinoma of anal canal (SCAC). However, about 30% of patients fail to achieve a complete clinical response (CCR) and require salvage surgery [1], underscoring the necessity for more efficacious and targeted treatment strategies.

In the realm of molecular markers, the expression of poliovirus receptor (PVR) has been documented in several squamous cell carcinomas [2] and approximately 84% of anal carcinomas are associated with high-risk types of human papillomavirus (HPV) [3].

Furthermore, PD-L1 expression has been correlated with PVR expression and has been observed in up to 74% of patients with squamous cell anal cancer [3,4]. These findings suggest that dual inhibition of PVR and PD-L1 may represent a viable mechanism for overcoming resistance to immune checkpoint monotherapy [5].

In this context, antibodies **atezolizumab** (anti-PD-L1) [6] and **tiragolumab** (anti-TIGIT) [7] have been reported to be effective treatment strategies (**Figure 1**) that target inhibitory receptors, thereby enhancing antitumor activity.

Figure 1. Atezolizumab and tiragolumab mechanism of action.



Adapted from *Rodriguez-Abreu et al ASCO 2020*

Objectives

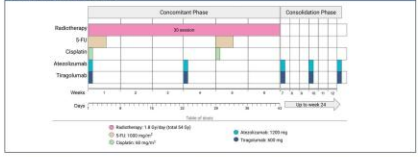
- The primary objective was to determine the efficacy of concomitant administration of **atezolizumab and tiragolumab in concomitancy with chemoradiotherapy (CRT)** as first line in achieving complete clinical response (CCR), defined as radiologic CR by RECIST 1.1 and no presence of residual disease assessed by biopsy, at week 26.
- The secondary endpoints included the **clinical complete response (CCR)** and **colostomy-free survival** (CFS).

PATIENTS AND METHODS

TIRANUS is Phase II, single-arm, open-label, multicentre clinical trial that expected to include 45 SCAC patients with untreated locoregional squamous-cell carcinoma of anal canal (SCAC). Patients were treated with **standard CRT plus atezolizumab (1200mg) and tiragolumab (600 mg)** for 8 cycles (Q3W) (**Figure 2**) to obtain a complete clinical response (CCR) precision estimation of 85% ±10.4% (α=0.05).

Eligible patients were ≥18 years of age with confirmed diagnosis of localised SCAC eligible for CRT, while candidates for curative surgery, patients who obtained prior treatments or who had contraindications to study treatment were excluded.

Figure 2. Treatment scheme



RESULTS

Table 1. Baseline disease characteristics of the full analysis set of patients

N = 46																			
Sex		**Patient Age**			**T Stage**		**N stage**				**ECOG ps**		**HIV status**			**HPV status**		
Female	Male	Median (Range)	≥70 years	<70 years	T1-T2	T3-T4	N0	N1a	N1b	N1c	0	1	Negative	Positive	NA	Positive	Negative
33 (71.7%)	13 (28.3%)	58 (36.0-80.0)	7 (15.2%)	39 (84.8%)	18 (39%)	28 (61%)	12 (26.1%)	27 (58.7%)	3 (6.5%)	4 (8.7%)	18 (39.1%)	27 (58.7%)	43 (93.5%)	2 (4.3%)	12	30 (88.2%)	4 (11.8%)

(*) Percentages take into account missing data from "ECOG" (1 patient) and "HIV status" (1 patient)
Data are presented as n (%) unless otherwise stated. ECOG ps=Eastern Cooperative Oncology Group performance status

Between 23 March and 24 October, 46 patients were enrolled; at week 26, 44 patients were evaluable (2 excluded due to withdrawal/protocol deviation).

The median age was 58 years (range: 36-80). Most patients were female (72%), all had an ECOG performance status (ps) of 0 or 1, 61% had T3-T4 tumours, most with nodal involvement (74%), and the HPV test was positive in 88% of the patients (Table 1).

Efficacy

Figure 3. Cumulative incidence of patients achieving Complete Clinical Response (CCR), with a focus on the results observed at week 26

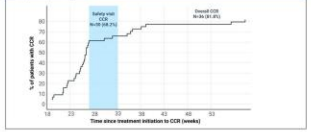


Figure 4. Waterfall plot of best overall radiological response achieved by each patient

At safety visit, the CCR rate was 68.2% (95% CI: 52.4-81.4). Notably, a greater proportion of patients attained CCR at a later stage with a median follow-up of 15 months. The overall CCR rate was 81.8% (95% CI: 67.3–91.8) (**Figure 3**), including 3 patients with radiological partial response, and 1 patient with stable disease without residual tumour cells after salvage surgery. All patients experienced some degree of cytoreduction after concomitant therapy (**Figure 4**), with 72.7% (95% CI: 57.2-85.0) achieving a complete response (CR) and 20.5% (95% CI: 9.8-35.3) achieving a partial response (PR) according to RECIST 1.1.

Secondary endpoints

The combination of CRT and dual A-T immunotherapy resulted in an estimated colostomy-free survival (CFS) rate of 93.2% (CI 95%) (**Figure 5**), with four patients remaining at risk 24 months post-initial treatment and 3 patients requiring colostomy. An extended follow-up period is necessary for a comprehensive comparison. The quality of life did not experience a significant decline during the course of the treatment (**Figure 6**). Outcomes were reported through the EORTC QLQ-C30 questionnaire.

Figure 5. Kaplan-Meier estimate of Colostomy-Free survival (CFS) ratio in the evaluable population per protocol

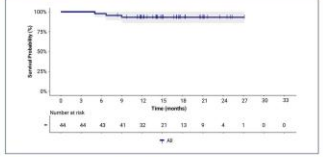
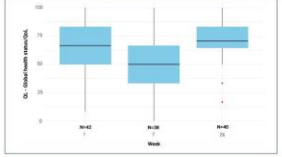


Figure 6. Global health status determined at weeks 1, 7 and 26

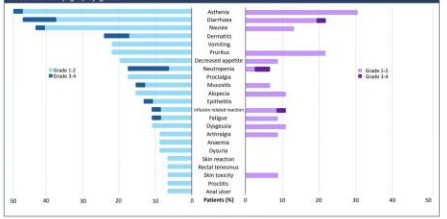


Safety

The study treatment was completed as scheduled in 84% of patients, while **13.2% discontinued due to unacceptable toxicity**.

The most common adverse events (AEs) of any grade were asthenia (50.0%), diarrhoea (47.8%), and nausea (43.5%). G3-G4 common AEs were neutropenia (10.9%) and diarrhoea (8.7%). The most frequent G1-G2 immune-mediated reactions were pruritus (21.7%), infusion-related reaction (8.7%), arthralgia (8.7%), mucositis (6.5%) and skin toxicity (6.5%), while G3-4 was neutropenia (6.5%) (**Figure 7**). Additionally, no death-related toxicity (G5 AEs) was reported.

Figure 7. Treatment-related AEs to any treatment (left) and to immunotherapy with tiragolumab and/or atezolizumab (right) by grade



*Overall threshold of 5%

CONCLUSIONS

- The addition of **atezolizumab** and **tiragolumab** to CRT was **feasible** and generally well **tolerated**.
- CCR rate increased over time and reached a plateau at week 40, which might be a more appropriate time point for its assessment when evaluating neoadjuvant immune checkpoint inhibitors combinations.
- Further follow-up is warranted to confirm efficacy and assess long-term benefit in reducing the need for surgical rescue.

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Conflicts of interest: Consulting or Advisory Role: Bayer, Eisai, Sanofi, Exelixis, Novartis, Ipsen, Pfizer, Merck Serono; Advanced Accelerator Applications, Lilly, Isotopen Technologien, Roche/Genentech, Esteve; Speakers' Bureau: Bayer, Eisai, Sanofi, Novartis, Ipsen, Pfizer, Merck Serono, Lilly, Isotopen Technologien, Esteve, Hutchison MediPharma; Travel, Accommodations, Expenses: Eisai, Ipsen, Pfizer, Gilead Sciences; Research Funding: Eisai, AstraZeneca, Advanced Accelerator Applications, Bayer, Novartis, Ipsen, Roche/Genentech, Gilead Sciences, ITM Solucin

Funding source: GEMCAD with the collaboration of industry partner Roche Farma S.A. // We acknowledge MFAR Clinical Research staff for their assistance in the development of this communication.
EU CT: 2023-509485-38-00 // Clinicaltrials.gov: NCT05661188

Phase I/Ib study of inavolisib (INAVO) + bevacizumab (BEV) or cetuximab (CETUX) for *PIK3CA*-mutated (mut) metastatic colorectal cancer (mCRC).

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Marwan Fakih,[1] Eric Chen,[2] Keun-Wook Lee,[3] Tanios Bekaii-Saab,[4] Sara Lonardi,[5] Jun Gong,[6] Elena Elez,[7] Janet Lau,[8] Vanessa Breton,[9] Omara Khan,[10] Olga Chertkova,[10] Saket Jain,[8] Sae Won Han[11]

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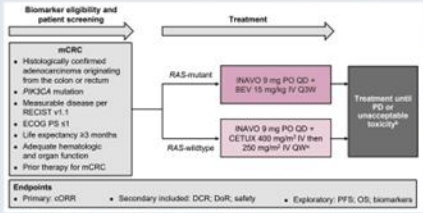
BACKGROUND

- *PIK3CA* mutations are found in 15–20% of patients with CRC and may be a negative prognostic factor[1]
- INAVO is a potent and selective PI3Kα inhibitor that also promotes degradation of mut p110α[2]
- BEV and CETUX are standard treatment components for *RAS*-mutant mCRC and *RAS*-wildtype mCRC, respectively[3]
- The Phase I/Ib INTRINSIC global, multicenter, open-label umbrella study (NCT04929223) aims to evaluate targeted therapies in biomarker-selected mCRC subpopulations
- Here, we report results from the INAVO + BEV and INAVO + CETUX arms

METHODS

- The study design for the INAVO + BEV and INAVO + CETUX arms only, including eligibility criteria and endpoints, is shown in **Figure 1**
- The clinical cutoff date for the INAVO + BEV arm was January 19, 2025, and for the INAVO + CETUX arm was April 21, 2025

Figure 1. INTRINSIC study design for the INAVO + BEV and INAVO + CETUX arms only



[a] CETUX was initiated at 400 mg/m² IV as a single dose, followed by 250 mg/m² weekly. [b] Patients could re-enroll into a different arm if they had ≥1 biomarker; other biomarker eligible arms for the study were *KRAS* G12C mutations, high microsatellite instability, and *BRAF* V600 mutations.
BEV, bevacizumab; CETUX, cetuximab; cORR, confirmed objective response rate; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; INAVO, inavolisib; IV, intravenous; mCRC, metastatic colorectal cancer; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, by mouth; QD, daily; QW, weekly; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

RESULTS

Patients

- At the respective clinical cut-off dates, 16 patients were enrolled in the INAVO + BEV arm and 35 were enrolled in the INAVO + CETUX arm
- Patient demographics and baseline characteristics are shown in **Table 1**
- Most patients had ≥2 metastatic sites at enrollment (n = 16 [100%] in the INAVO + BEV arm and n = 30 [85.8%] in the INAVO + CETUX arm) and ≥2 prior lines of metastatic therapy (n = 16 [100%] and n = 28 [80.0%], respectively)
- In the INAVO + BEV arm, three patients (18.8%) had no prior BEV
- In the INAVO + CETUX arm, 25 patients (71.4%) had no prior CETUX; 17 patients (48.6%) had prior anti-epidermal growth factor receptor (EGFR) therapy, including CETUX or panitumumab
- All patients in the INAVO + BEV arm and 34 patients in the INAVO + CETUX arm were evaluated for efficacy and safety
- Median follow-up was 9.4 months (interquartile range: 5.5–14.4) in the INAVO + BEV arm and 12.6 months (interquartile range 8.9–16.6) in the INAVO + CETUX arm

Table 1. Patient demographics and disease characteristics (intention-to-treat population[a])

	INAVO + BEV (n = 16)	INAVO + CETUX[b] (n = 35)
Median age, years (range)	54.0 (36–75)	59.0 (34–84)
Female, n (%)	9 (56.3)	18 (51.4)
Race, n (%)		
White	8 (50.0)	20 (57.1)
Asian	7 (43.8)	10 (28.6)
Black or African American	0	2 (5.7)
Other/Unknown	1 (6.3)	3 (8.6)
ECOG PS at baseline, n (%)		
0	8 (50.0)	19 (54.3)
1	8 (50.0)	16 (45.7)
Metastatic sites at enrollment, n (%)		
1	0	5 (14.3)
2	7 (43.8)	15 (42.9)
≥3	9 (56.3)	15 (42.9)
Median HbA_{1c}, mmol/mol (IQR)	33.3 (31.2–36.1)	36.6 (34.4–40.0)
Metastatic liver disease, n (%)	12 (75.0)	24 (68.6)
Metastatic lung disease, n (%)	10 (62.5)	25 (71.4)
Prior lines of metastatic therapy, range	2–8	0–8
Prior lines of metastatic therapy, n (%)		
≤2	6 (37.5)	17 (48.6)
≥3	10 (62.5)	18 (51.4)
Prior CETUX, n (%)	–	10 (28.6)
Prior BEV, n (%)	13 (81.3)	–

[a] All patients assigned to either the INAVO + BEV or INAVO + CETUX arms.
[b] Seventeen patients (48.6%) had prior anti-EGFR therapy, including CETUX or panitumumab.
[c] "Other" includes Native Hawaiian or other Pacific Islander, and American Indian or Alaska Native.
BEV, bevacizumab; CETUX, cetuximab; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HbA_{1c}, glycated hemoglobin; INAVO, inavolisib; IQR, interquartile range.

Efficacy

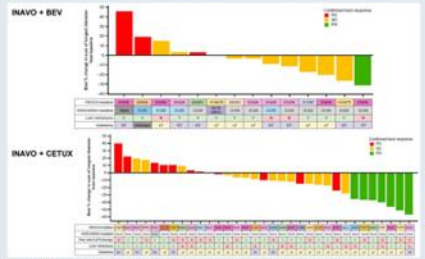
- An efficacy summary, including best confirmed objective response, duration of response, progression-free survival, and overall survival, is shown in **Table 2**
- One partial response occurred in the INAVO + BEV arm and seven occurred in the INAVO + CETUX arm; disease control rates were 68.8% and 44.1%, respectively
- Best change from baseline in the sum of tumor diameters is shown in **Figure 2**

Table 2. Efficacy summary (efficacy-evaluable population[a])

	INAVO + BEV (n = 16)	INAVO + CETUX (n = 34)
Confirmed responders, n (%) [90% CI]	1 (6.3) [0.3–26.4]	7 (20.6) [10.1–35.2]
CR, n (%)	0	0
PR, n (%)	1 (6.3)	7 (20.6)[b]
Non-responders, n (%)	15 (93.8)	27 (79.4)
SD, n (%)	10 (62.5)	17 (50.0)
PD, n (%)	3 (18.8)	9 (26.5)
Missing or NE	2 (12.5)	1 (2.9)
Median DoR, months (90% CI)	7.7 (NE)	4.4 (4.2–5.3)
Disease control rate, n (%)[c]	11 (68.8)	15 (44.1)
Median PFS, months (90% CI)	4.2 (2.8–6.8)	3.5 (2.8–4.4)
Median OS, months (90% CI)	11.0 (8.5–14.5)	12.8 (10.7–13.8)

[a] One patient who was assigned to INAVO + CETUX was enrolled in error, received no study treatment, and was not evaluated for efficacy or safety.
[b] Three patients with PR received prior anti-EGFR therapy: one had a best prior response of SD (last dose 233 days before study treatment) and two had best prior responses of partial responses (last doses 134 and 171 days before study treatment, respectively).
[c] CR, PR, or SD for ≥12 weeks.
BEV, bevacizumab; CETUX, cetuximab; CI, confidence interval; CR, complete response; DoR, duration of response; EGFR, epidermal growth factor receptor; INAVO, inavolisib; NE, not evaluable; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Figure 2. Best change from baseline in the sum of tumor diameters (efficacy-evaluable population[a])

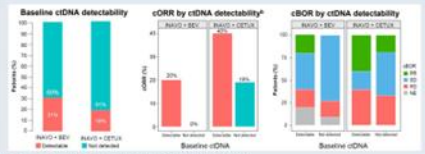


[a] One patient who was assigned to INAVO + CETUX was enrolled in error, received no study treatment, and was not evaluated for efficacy or safety.
BEV, bevacizumab; CETUX, cetuximab; EGFR, epidermal growth factor receptor; INAVO, inavolisib; LF, left; N, no; PD, disease progression; PR, partial response; RT, right; SD, stable disease; Y, yes.

Biomarkers

- All patients in the INAVO + BEV arm and 26 in the INAVO + CETUX arm were evaluated for circulating tumor DNA (ctDNA) detectability at baseline using the FoundationOne®Liquid CDx assay
- **Figure 3** shows baseline ctDNA detectability with stacked bars representing the proportion of patients with detectable vs. non-detectable ctDNA (left panel), confirmed objective response rate stratified by baseline ctDNA detectability within each arm (middle panel), and best confirmed overall response distributions by ctDNA detectability (right panel)

Figure 3. Baseline ctDNA detectability, and cORR and cBOR by ctDNA detectability[a]



[a] Baseline samples for ctDNA detection were only available for 39 patients in the INAVO + CETUX arm.
[b] The denominator for ORR calculation included all patients within each baseline ctDNA group (detectable vs. not detectable).
BEV, bevacizumab; cBOR, confirmed best overall response; CETUX, cetuximab; cORR, confirmed objective response rate; ctDNA, circulating tumor DNA; INAVO, inavolisib; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Safety

- A safety summary is shown in **Table 3**
- The most common adverse events (AEs) were hyperglycemia, weight decreased, diarrhea, and decreased appetite in the INAVO + BEV arm, and hyperglycemia, dermatitis acneiform, and hypomagnesemia in the INAVO + CETUX arm
- Hyperglycemia was also the most common treatment-related AE and AE leading to dose reduction/interruption in both arms
- Hypertension (a known risk of BEV) was observed more frequently with INAVO + BEV, while dermatitis acneiform and dry skin were observed more frequently with INAVO + CETUX (skin reactions are a known risk of CETUX)

Table 3. Safety summary (safety-evaluable population[a])

Patients with ≥1 AE, n (%)	INAVO + BEV (n = 16)	INAVO + CETUX (n = 34)
All grade AE	16 (100)	34 (100)
Related to any treatment	15 (93.8)	34 (100)
Related to INAVO	15 (93.8)	32 (94.1)
Related to BEV	12 (75.0)	–
Related to CETUX	–	34 (100)
Grade 3–4 AE	8 (50.0)	17 (50.0)
Related to any treatment	5 (31.3)	12 (35.3)
Grade 5 AE	0	1 (2.9)
Related to any treatment	0	0
Serious AE	2 (12.5)	11 (32.4)
Related to any treatment	0	6 (17.6)
AE leading to dose modification/interruption	12 (75.0)	27 (79.4)
INAVO	10 (62.5)	24 (70.6)
BEV	8 (50.0)	–
CETUX	–	17 (50.0)
AE leading to treatment withdrawal	0	4 (11.8)
INAVO	0	4 (11.8)
BEV	0	–
CETUX	–	4 (11.8)
Most common AEs occurring in ≥30% of patients in either arm		
Hyperglycemia	10 (62.5)	21 (61.8)
Dermatitis acneiform	0	21 (61.8)
Hypomagnesemia	0	20 (58.8)
Weight decreased	8 (50.0)	17 (50.0)
Diarrhea	6 (37.5)	15 (44.1)
Dry skin	2 (12.5)	17 (50.0)
Fatigue	2 (12.5)	14 (41.2)
Decreased appetite	6 (37.5)	10 (29.4)
Stomatitis	2 (12.5)	12 (35.3)
Hypertension	5 (31.3)	6 (17.6)

[a] One patient who was assigned to INAVO + CETUX was enrolled in error, received no study treatment, and was not evaluated for efficacy or safety.
AE, adverse event; BEV, bevacizumab; CETUX, cetuximab; INAVO, inavolisib.

CONCLUSIONS

- INAVO + BEV and INAVO + CETUX both showed encouraging efficacy in patients with pretreated *PIK3CA*mut mCRC
- The safety profiles of the combination regimens were consistent with the known profiles of the individual treatment components, with no new or unexpected safety signals observed

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Abstract 128: Short-course radiotherapy (SCRT) followed by immunochemotherapy plus fruquintinib as the total neoadjuvant therapy (TNT) for locally advanced rectal cancer (LARC): a multicenter, single-arm, open-label, phase II study (UNION TNT)

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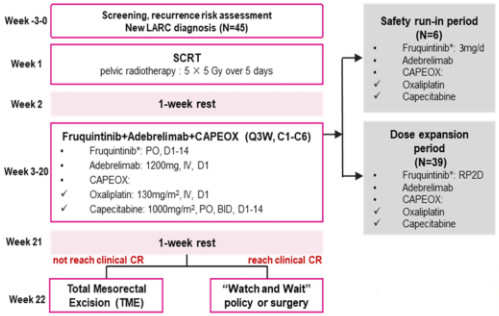
Background

- The phase III trial (UNION) evaluating SCRT followed by immunochemotherapy in patients (pts) with LARC has reported a pathological complete response (pCR) rate of 39.8%.
- The phase II UNION TNT (NCT06234007) study aimed to assess the benefit of adding fruquintinib (VEGFR-1, -2, and -3 inhibitor) to the immunotherapy-based TNT in high risk LARC.

Methods

- This is a prospective, open-label, multi-centers, single-arm phase 2 study (NCT06234007).



- **Primary:** CR rate (including cCR & pCR)
- **Secondary:** 3-year EFS rate, OS, R0 resection rate, AEs
- **Exploratory:** To evaluate the correlation between potential biomarkers and efficacy

Results

Baseline characteristics

- As of 30 Aug 2024, 45 pts were enrolled (Table 1).

Table 1. Baseline characteristics of the pts

Characteristics, n (%)		N=45
Age, Median (range)		59 (24-75)
Gender	Male	26 (57.78)
	Female	19 (42.22)
ECOG PS	0	10 (22.22)
	1	35 (77.78)
Clinical T Stage	T3	22 (48.89)
	T4	23 (51.11)
Clinical N Stage	N0	3 (6.67)
	N1	22 (48.89)
	N2	20 (44.44)
EMVI Status	Positive	37 (82.22)
	Negative	8 (17.78)
MRF Status	Positive	32 (71.11)
	Negative	13 (28.89)
Distance from anal verge, cm	≤5	22 (48.89)
	5-10	23 (51.11)

Table 2. Compliance with treatment in surgical pts

Characteristics		N=41	
Compliance with SCRT		41	100%
Compliance with combined treatment	Completed 2 cycles	40	97.56%
	Completed 4 cycles	34	82.93%
	Completed 6 cycles	26	63.41%
Compliance with Surgery		33	80.49%

Efficacy

- Up to 31 Mar 2025, 41 were included in efficacy analysis. All received the full dose of radiotherapy and 26 pts (63.4%) completed at least 6 cycles of combined regimen. (Table 2).
- 7 pts achieved cCR and were offered watch-and-wait. Of the remaining 34 pts without cCR, 33 pts underwent total mesorectal excision (TME), 57.6% (19/33) pts achieved pCR and R0 resection rate was 100%. The overall CR rate was 63.4% (Table 3).

Table 3. Overall efficacy of treatment

Overall efficacy	N	%
CR rate	26	63.4
cCR	7	17.1
pCR	19	57.6
R0 rate	33	100

Safety

- Out of 33 patients who underwent TME, 33.3% (11 pts) experienced surgical complications.
- The most frequent grade 3 to 4 TEAEs during TNT treatment were lymphocyte count decreased (46.3%), leukopenia (9.8%) and AST elevation (7.3%). 4pts experienced SAEs of intestinal perforation, while all of them achieved pCR. Grade 3 complications according to Clavien-Dindo classification were reported in 4 pts, including one intestinal obstruction, one extremity vein thrombosis, and two anastomotic fistulas.

Conclusions

The new UNION TNT regimen with acceptable toxicity remarkably improved CR rate in high risk LARC compared with historical benchmark.

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MUCHAS GRACIAS POR SU ATENCIÓN