



VII SIMPOSIO NACIONAL
de **ONCOLOGÍA** de **PRECISIÓN**

Vigo, 20 y 21 de febrero de 2025

Cáncer COLORRECTAL

Novedades 2024 en 20 diapositivas

Paula González Villarroel
Hospital Alvaro Cunqueiro

Conflictos de Interés

- Advisory role or speaking: Amgen, Servier, Merck
- Travel and accommodation: Amgen, Merck

En resumen, los 5 Principales Temas en CCR han sido...

- Enfermedad residual y ctDNA
- Inmunoterapia en Tumores Inestables en diferentes escenarios:
 - Neoadyuvancia
 - Estadios IV
- Mutaciones de BRAF
- Mutación G12C de KRAS
- HER2 positivos

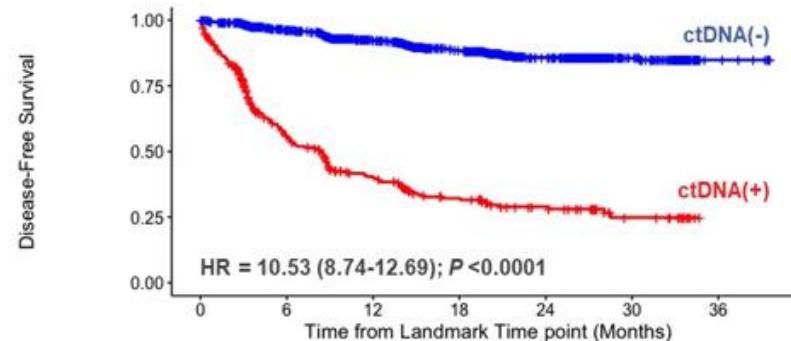
ASCO Gastrointestinal
Cancers Symposium

Circulating tumor DNA (ctDNA) dynamics in colorectal cancer (CRC) patients with molecular residual disease: Updated analysis from GALAXY study in the CIRCULATE-JAPAN

Presenting Author: Hiroki Yukami, MD, PhD

Co-authors: Yoshiaki Nakamura, Saori Mishima, Koji Ando, Hideaki Bando, Jun Watanabe, Keiji Hirata, Naoya Akazawa, Masataka Ikeda, Mitsuaki Yokota, Kentaro Kato, George Lalliotis, Vasily N. Aushayev, Adam A. Jurd, Minetta C. Liu, Daisuke Kotani, Eiji Oki, Ichiro Takemasa, Takeshi Kato, Takayuki Yoshino

- Determinación dinámica de ctDNA en pacientes con cirugía radical estadios II-IV.
- Muestras en meses 1, 3, 6, 9, 12, 18 y 24
- 1000 pacientes con adyuvancia y 1518 en observación
- Objetivo primario Supervivencia Libre de Enfermedad
- 309 positivos (14.8%) y 1784 negativos (85.2%)
- Los negativos tienen una supervivencia libre de enfermedad mayor, a los 24 meses (86 vs 29%)



	Number at risk						
ctDNA Negative	2491	2031	1441	1041	495	135	8
ctDNA Positive	369	165	98	59	35	13	0

ctDNA status	Negative	Positive
Events %	9.4 (235/2491)	58.8 (127/369)
24M-DFS % (95% CI)*	85.9 (83.9-87.7)	28.9 (23.4-34.8)

*DFS % from landmark time point

MRD window: 2-10 weeks post surgery, prior to start of any adjuvant therapy - Landmark 10 weeks post-surgery

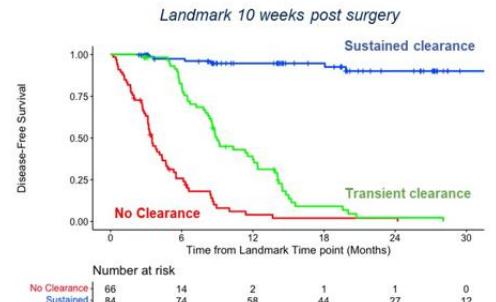
ASCO Gastrointestinal
Cancers Symposium

Circulating tumor DNA (ctDNA) dynamics in colorectal cancer (CRC) patients with molecular residual disease: Updated analysis from GALAXY study in the CIRCULATE-JAPAN

Presenting Author: Hiroki Yukami, MD, PhD

Co-authors: Yoshiaki Nakamura, Saori Mishima, Koji Ando, Hideaki Bando, Jun Watanabe, Keiji Hirata, Naoya Akazawa, Masataka Ikeda, Mitsuhiro Yokota, Kentaro Kato, George Lallotis, Vasily N. Aushayev, Adam A. Jurd, Minetta C. Liu, Daisuke Kotani, Eiji Oki, Ichiro Takemasa, Takeshi Kato, Takayuki Yoshino

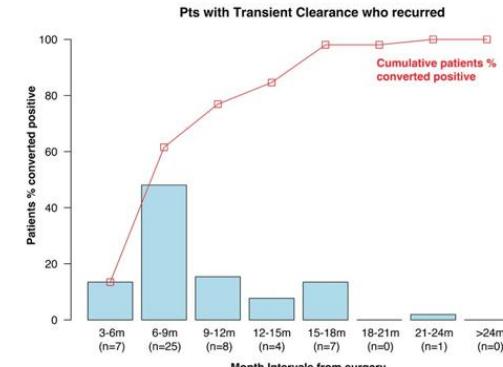
- De los 309 positivos, 181 recibieron adyuvancia
- El 72% (132) negativizaron el ctDNA
- La recurrencia molecular es en los 18 meses

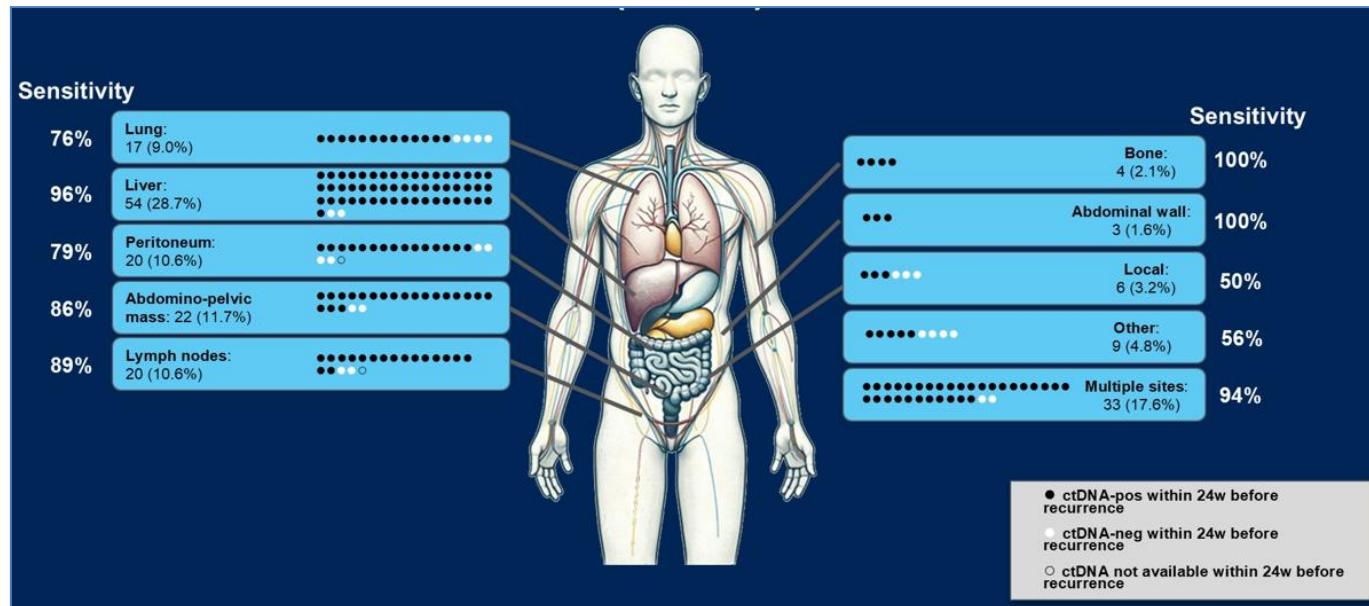


ctDNA Clearance	Sustained Clearance	Transient Clearance	No Clearance
Events %	7.1 (6/84)	85.2 (52/61)	89.4 (59/66)
Median DFS months (95% CI)	NR	9 (8.5–12.4)	3.5 (3.2–4.7)
24M-DFS % (95% CI)*	90.1 (78.6–95.6)	2.3 (0.02–10.3)	2 (0.02–9.2)
HR	Reference	25.13	87.08
95% CI	Not applicable	10.57–59.73	36.14–209.84
P	Not applicable	<0.0001	<0.0001

*DFS % from landmark time point

For recurrent pts with transient clearance, 98% of pts turned back positive by 18 months post-surgery.





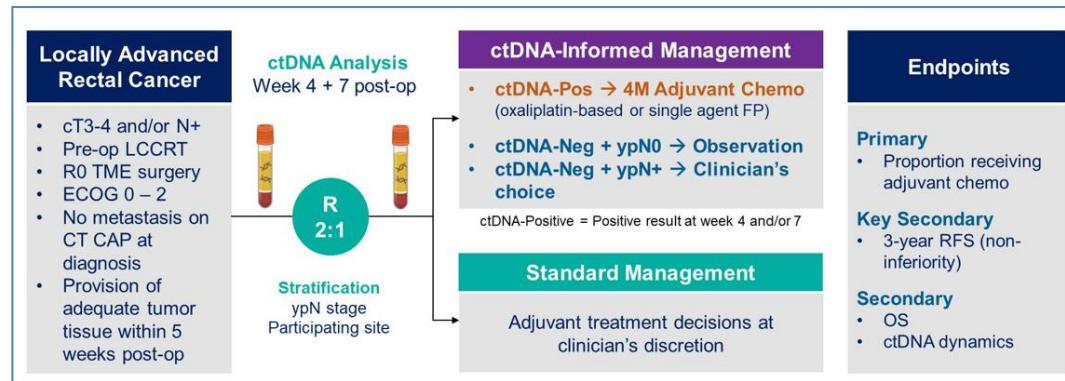
ASCO Gastrointestinal
Cancers Symposium

SAGITG
Society of Australian Gastrointestinal
Therapists

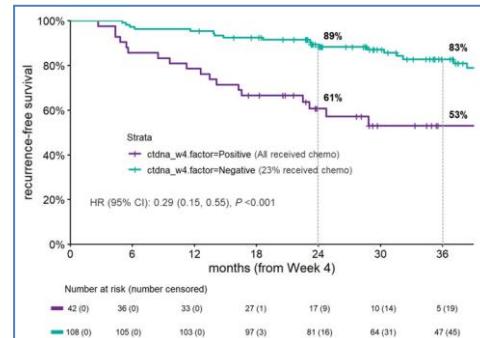
**Circulating Tumor DNA Analysis Informing Adjuvant
Chemotherapy in Locally Advanced Rectal Cancer**

The Randomized AGITG DYNAMIC-Rectal Study

Jeanne Tie
Peter MacCallum Cancer Centre and Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia
On behalf of the DYNAMIC-RECTAL Investigators



- Reciben más quimioterapia los pacientes del grupo estándar (77 vs 46%)
- Menos riesgo de recurrencia en los ctDNA negativos a los 3 años (83 vs 53%)
- Localización de la recaída: ctDNA negativos pulmón y los positivos a nivel hepático



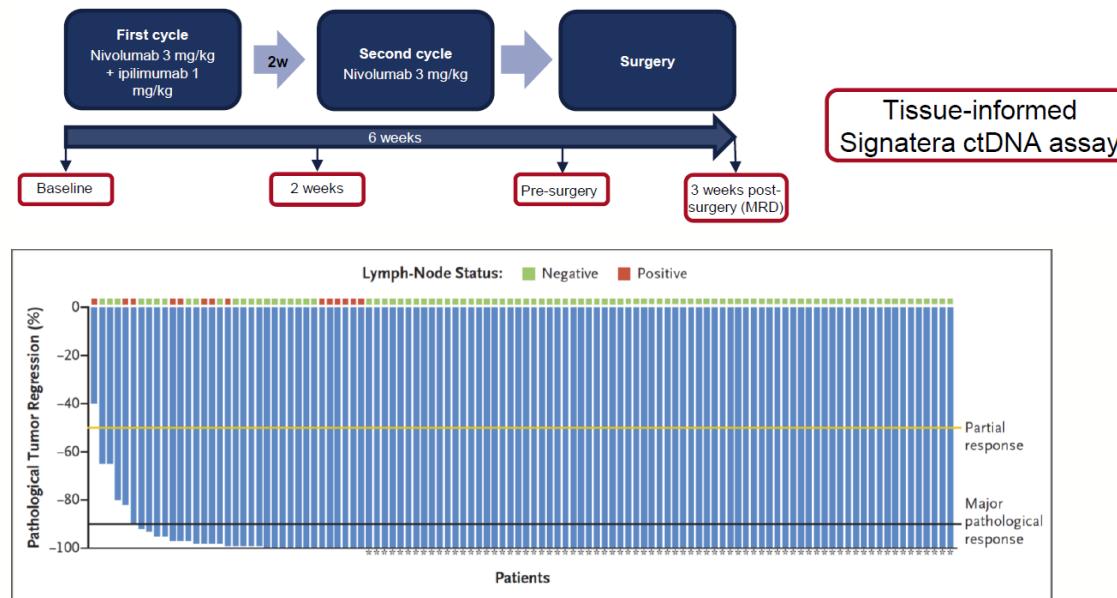
CCR INESTABLES: PEMBROLIZUMAB EN NEOADYUVANCIA

ESTUDIO	PACIENTES	TRATAMIENTO	RESULTADOS
NEOPRISM CCR (ASCO 2024) Fase II	n=32 Estadios II alto riesgo y III	3 ciclos (9 semanas)	ypRC 59% Seguimiento 9 meses sin recaída
IMHOTEP (ESMO 2024) Fase II	n=77 (operados 72) 63 colon 9 recto Estadios II y III	1-2 ciclos (400 mg /6s) Adyuvancia (completar 1 año = 9 ciclos)	Tras 1 ciclo: 46% Tras 2 ciclos: 68%

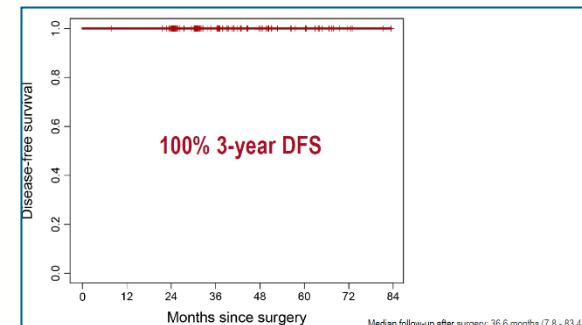
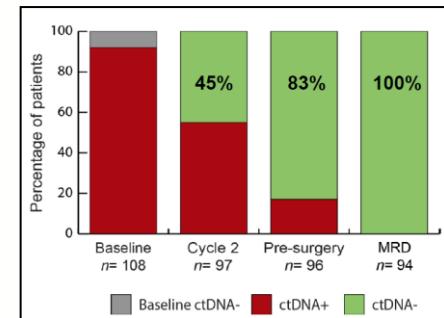


	Colon (N=63)	Rectum (N=9)	All CRC (N=72)
pCR (ypT0N0) rate	35/63 (55.6%)	3/9 (33.3%)	38/72 (52.8%)
↳ After 1 pembrolizumab cycle	21/45 (46.7%)	2/5 (40.0%)	23/50 (46.0%)
↳ After 2 pembrolizumab cycles	14/18 (77.8%)	1/4 (25.0%)	15/22 (68.2%)

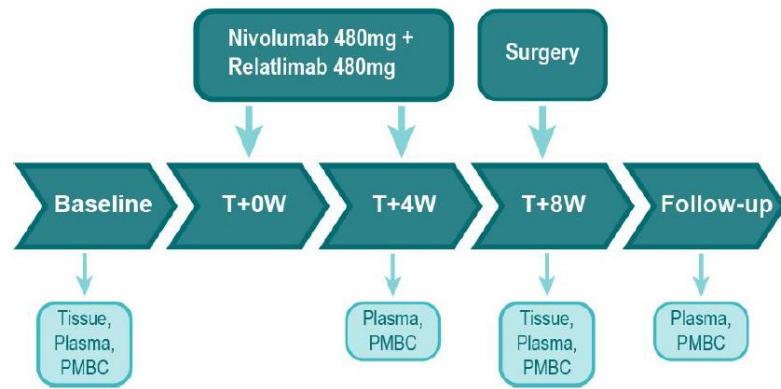
NIVOLUMAB-IPILIMUMAB NEOADYUVANTE: NICHE-2



98% de respuesta
95% respuesta patológica mayor (<10% de células tumorales)
68% ypRC



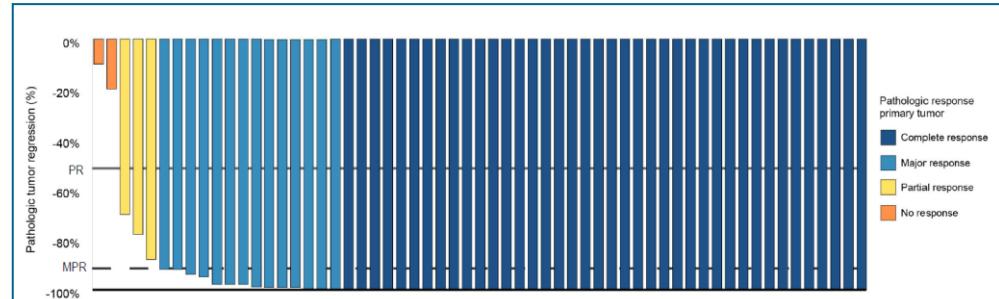
Neoadjuvant nivolumab plus relatlimab in MMR-deficient colon cancer: results of the NICHE-3 study



70% T4 y 60% N +

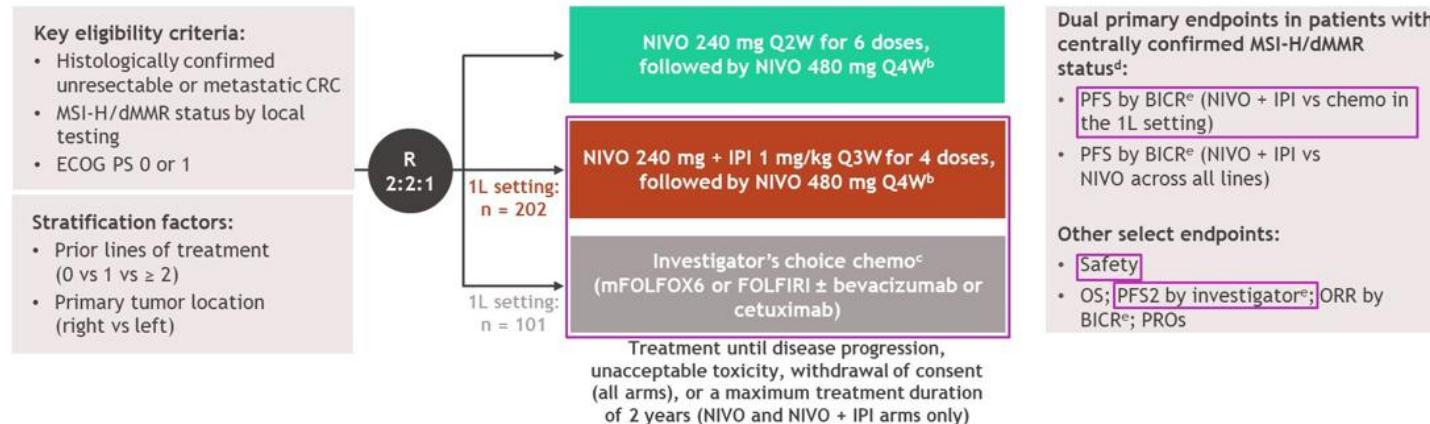
Respuesta patológica 97%
ypRC 68%

Toxicidad grados 3-4: 10%

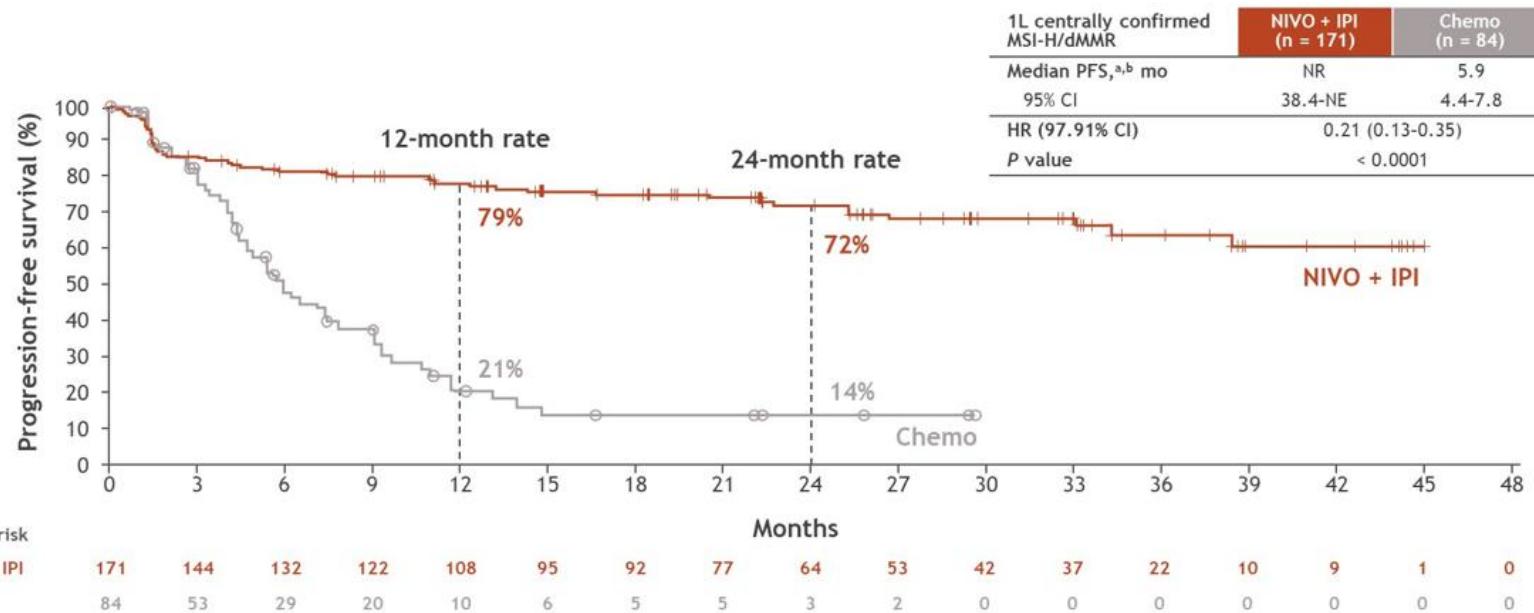


Nivolumab plus ipilimumab vs chemotherapy as first-line treatment for microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: expanded efficacy analysis from CheckMate 8HW

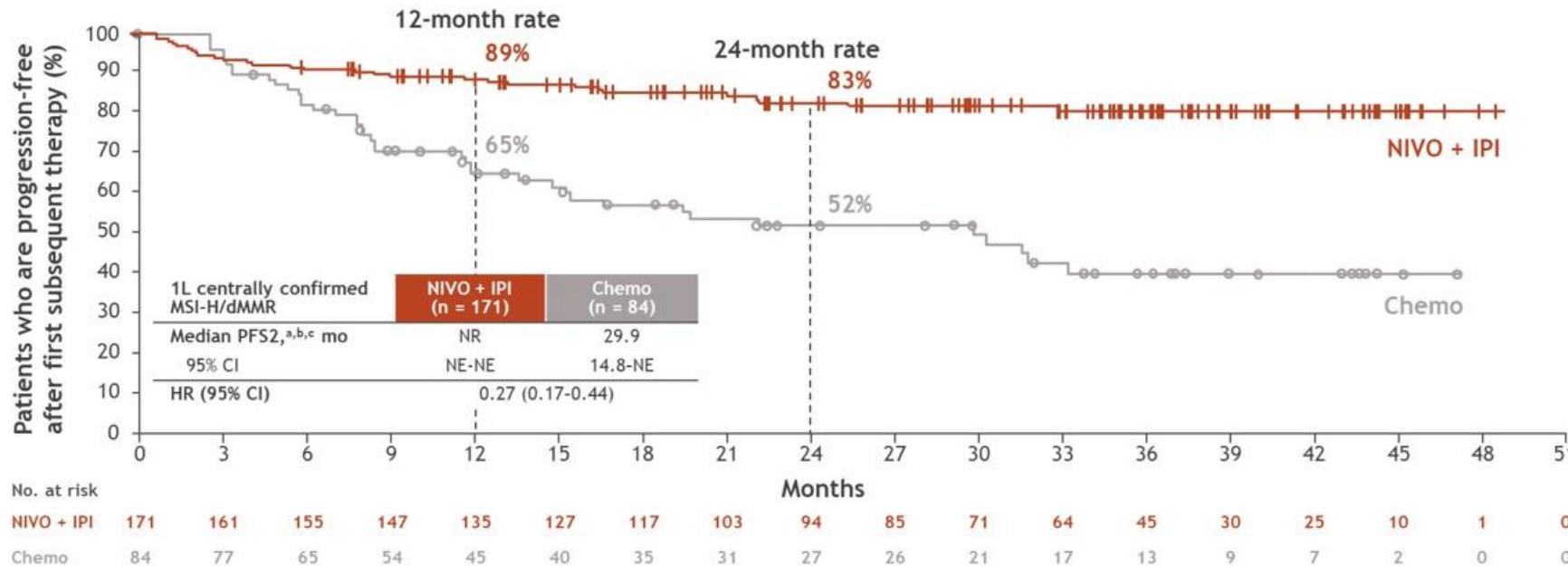
Heinz-Josef Lenz,¹ Sara Lonardi,² Elena Elez Fernandez,³ Eric Van Cutsem,⁴ Lars Henrik Jensen,⁵ Jaafar Bennouna,⁶ Guillermo Ariel Mendez,⁷ Michael Schenker,⁸ Christelle de la Fouchardiere,⁹ Maria Luisa Limon Miron,¹⁰ Takayuki Yoshino,¹¹ Jin Li,¹² Jose Luis Manzano Mozo,¹³ Giampaolo Tortora,¹⁴ Rocio Garcia-Carbonero,¹⁵ Rohit Joshi,¹⁶ Elvis Cela,¹⁷ Tian Chen,¹⁷ Lixian Jin,¹⁷ Thierry Andre¹⁸



Progression-free survival



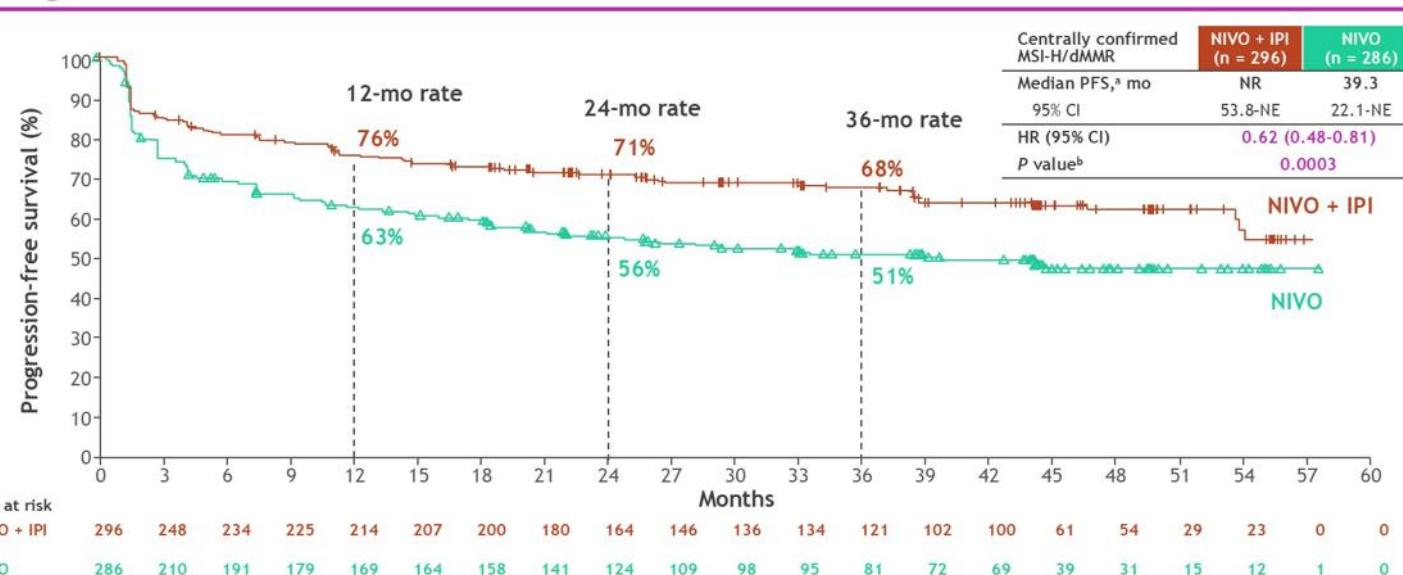
PFS2: progression-free survival after subsequent therapy



First results of nivolumab plus ipilimumab vs nivolumab monotherapy for microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer from CheckMate 8HW

Thierry Andre,¹ Elena Elez,² Heinz-Josef Lenz,³ Lars Henrik Jensen,⁴ Yann Toucheuf,⁵ Eric Van Cutsem,⁶ Rocío García-Carbonero,⁷ David Tougeron,⁸ Guillermo Ariel Mendez,⁹ Michael Schenker,¹⁰ Christelle de la Fouchardiere,¹¹ María Luisa Limón Miron,¹² Takayuki Yoshino,¹³ Jin Li,¹⁴ Francine Aubin,¹⁵ Elvis Cela,¹⁶ Tian Chen,¹⁶ Ming Lei,¹⁶ Lixian Jin,¹⁶ Sara Lonardi¹⁷

Progression-free survival



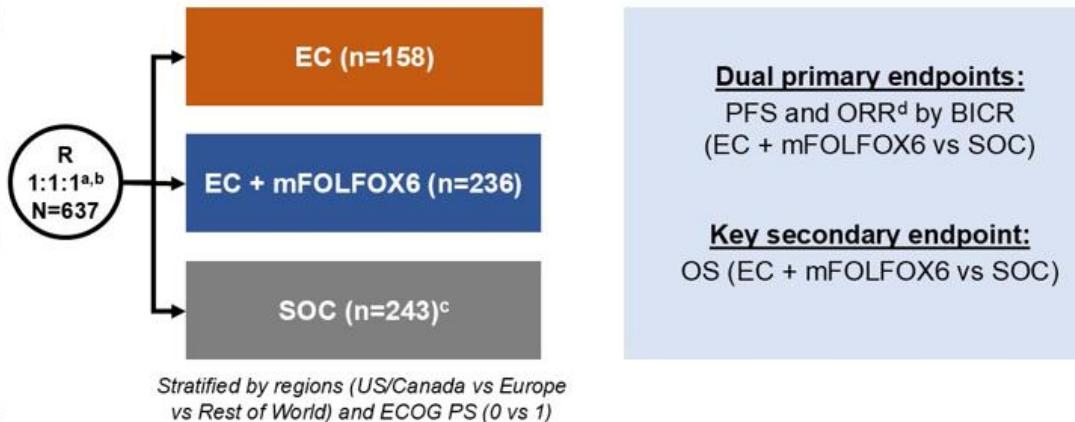
BRAF MUTADOS

BREAKWATER: Analysis of first-line encorafenib + cetuximab + chemotherapy in BRAF V600E-mutant metastatic colorectal cancer

Scott Kopetz, MD, PhD,¹ Takayuki Yoshino, MD, PhD,² Eric Van Cutsem, MD, PhD,³ Cathy Eng, MD, FACP, FASCO,⁴
Tae Won Kim, MD, PhD,⁵ Harpreet Singh Wasan, MD,⁶ Jayesh Desai, FRACP,⁷ Fortunato Ciardiello, MD, PhD,⁸
Rona Yaeger, MD,⁹ Timothy S. Maughan, MD,¹⁰ Elena Beyzarov, PharmD,¹¹ Xiaoxi Zhang, PhD,¹¹ Graham Ferrier, PhD,¹¹
Xiaosong Zhang, MD, PhD,¹¹ Josep Tabernero, MD, PhD¹²

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

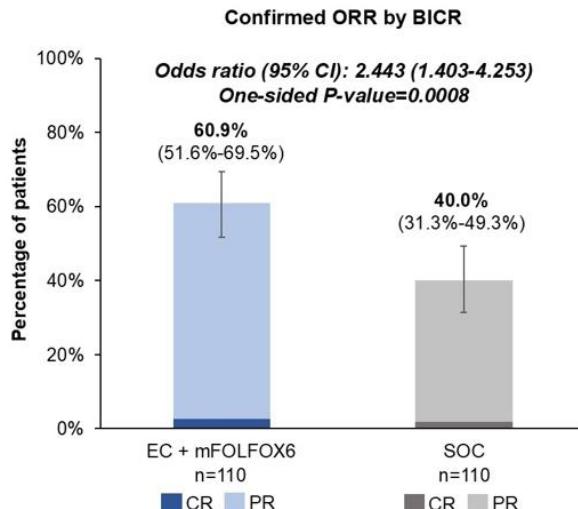
<u>Inclusion criteria</u>	
• Age ≥ 16 years (or ≥ 18 years based on country)	
• No prior systemic treatment for metastatic disease	
• Measurable disease (RECIST 1.1)	
• BRAF V600E-mutant mCRC by local or central laboratory testing	
• ECOG PS 0 or 1	
• Adequate bone marrow, hepatic, and renal function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



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

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

BRAF MUTADOS

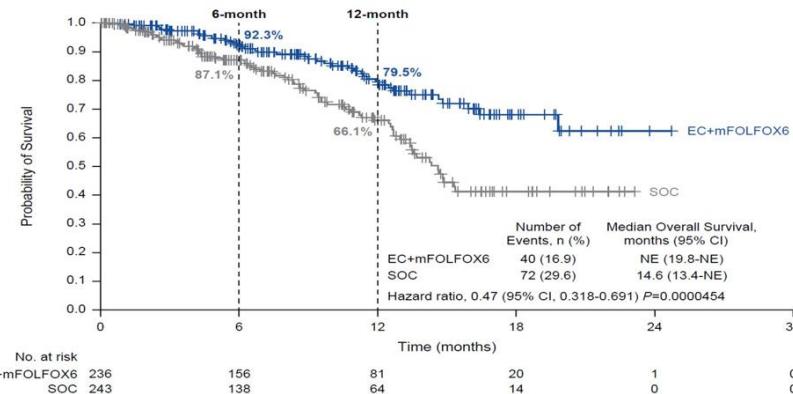


Confirmed Best Overall Response, TTR, and DOR by BICR

	EC + mFOLFOX6 n=110	SOC n=110
Confirmed best overall response, n (%)		
CR	3 (2.7)	2 (1.8)
PR	64 (58.2)	42 (38.2)
SD	31 (28.2)	34 (30.9)
Non-CR/non-PD	3 (2.7)	4 (3.6)
PD	3 (2.7)	9 (8.2)
NE	6 (5.5)	19 (17.3)
	n=67	n=44
TTR, median (range), weeks	7.1 (5.7-53.7)	7.3 (5.4-48.0)
Estimated DOR, median (range), months	13.9 (8.5-NE)	11.1 (6.7-12.7)
Patients with a DOR of ≥6 months, n (%)	46 (68.7)	15 (34.1)
Patients with a DOR of ≥12 months, n (%)	15 (22.4)	5 (11.4)

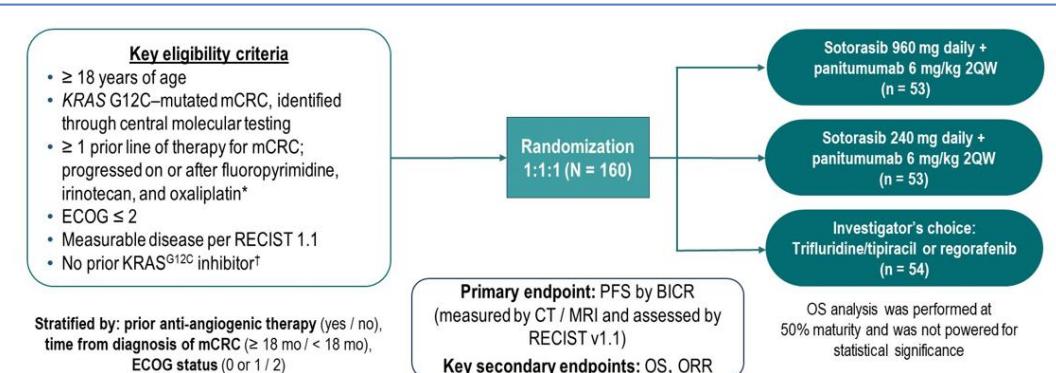
BRAF MUTADOS

Interim Overall Survival^a



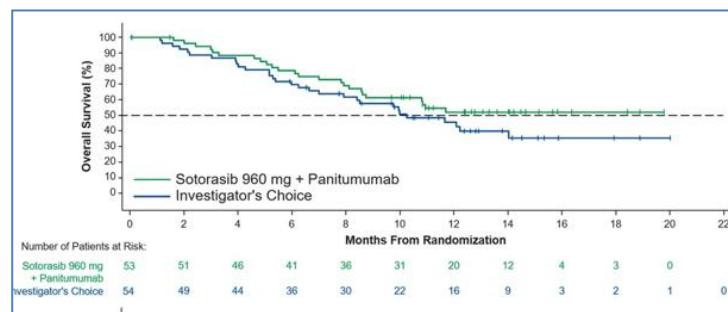
Patients, n (%)	EC + mFOLFOX6 n=231	SOC n=228
All causality		
TEAE	230 (99.6)	223 (97.8)
Grade 3 or 4 TEAE	171 (74.0)	139 (61.0)
Grade 5 TEAE	10 (4.3)	10 (4.4)
Serious TEAE	87 (37.7)	79 (34.6)
TEAE leading to permanent discontinuation of any study treatment	48 (20.8)	34 (14.9)
TEAE leading to dose reduction of any study treatment	141 (61.0)	109 (47.8)
TEAE leading to dose interruption of any study treatment	196 (84.8)	146 (64.0)
Treatment-related		
AE related to any drug	228 (98.7)	212 (93.0)
Grade 3 or 4 TRAE	161 (69.7)	123 (53.9)
Grade 5 TRAE	0	1 (0.4) ^a
Serious AE related to any drug	42 (18.2)	44 (19.3)

MUTACIÓN G12C



Overall survival (OS) of phase 3 CodeBreaK 300 study of sotorasib plus panitumumab (soto+pani) versus investigator's choice of therapy for KRAS G12C-mutated metastatic colorectal cancer (mCRC)

Marwan G. Fakih,¹ Lisa Salvatore,^{2,3} Taito Esaki,⁴ Dominik Paul Modest,⁵ David Paez Lopez-Bravo,⁶ Julien Taieb,⁷ Michalis V. Karamouzis,⁸ Erika Ruiz-Garcia,⁹ Tae Won Kim,¹⁰ Yasutoshi Kuboki,¹¹ Fausto Menghi,¹² David Cunningham,¹³ Kun-Huei Yeh,^{14,15} Emily Chan,¹⁶ Joseph Chao,¹⁸ Qui Tran,¹⁶ Chiara Cremonini,¹⁷ Filippo Pietrantonio¹⁸

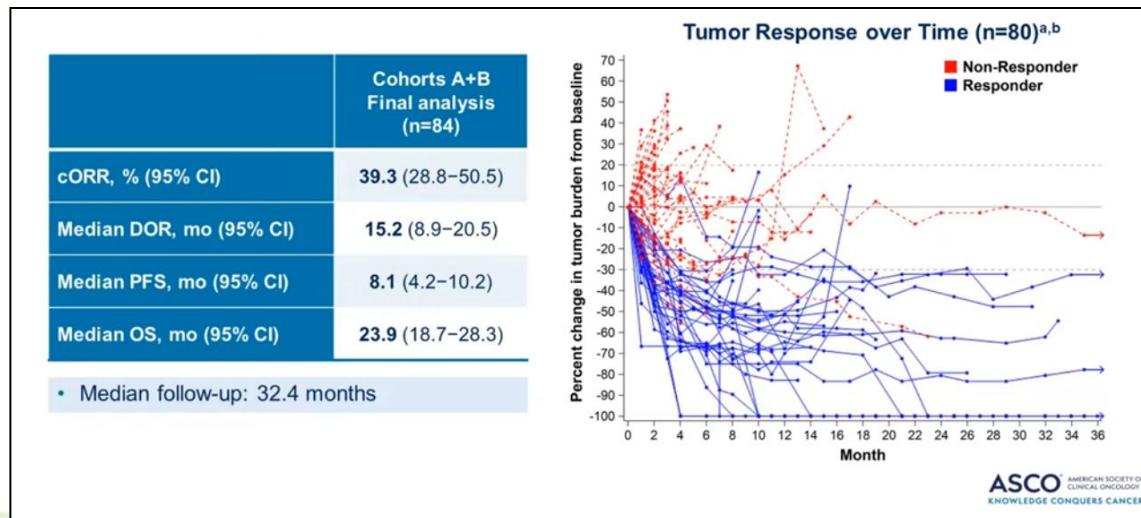


- Seguimiento de 13 meses
- Supervivencia con Sotorasib (dosis 960) + Panitumumab no alcanzada y en el control 10.3 m
- Respuesta 30 vs 2%

HER 2 POSITIVOS

MOUNTAINEER: FINAL RESULTS OF A PHASE 2 STUDY OF TUCATINIB AND TRASTUZUMAB FOR HER2-POSITIVE METASTATIC CRC

John H. Strickler, MD; Andrea Cercek, MD; Salvatore Siena, MD; Thierry Andre, MD; Kimmie Ng, MD, MPH; Eric Van Cutsem, MD, PhD; Christina Wu, MD; Andrew Scott Paulson, MD; Joleen M. Hubbard, MD; Andrew L. Coveler, MD; Christos Fountzilas, MD, FACP; Adel Kardosh, MD, PhD; Pashtoon Murtaza Kasi, MD, MSc; Heinz-Josef Lenz, MD; Kristen Keon Ciombor, MD, MS; Elena Elez, MD; David L. Bajor, MD; Mina Nayeri, PharmD; Wentao Feng, PhD; Tanios S. Bekaii-Saab, MD



¿Qué hemos aprendido?

- El ctDNA positivo tras la cirugía del CCR marca pronóstico. Su determinación puede cambiar el manejo de nuestros pacientes
- El contexto neoadyuvante la IT en pacientes inestables ofrece tasas de ypRC de >60% con diferentes esquemas
- Los tumores inestables estadio IV tienen un nuevo estándar de tratamiento
- Los BRAF mutados podrían tener un nuevo estándar en 1^a línea, con tasas de respuesta del 60%, datos prometedores de beneficio en SG
- Los portadores de mutación G12C tienen un nuevo tratamiento en 3^a línea, con respuestas de un 30%
- Los tumores HER2 en líneas avanzadas tienen esquemas activos con tratamientos dirigidos, respuestas 40%