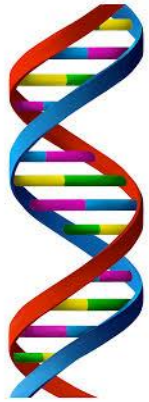


Post-ASCO 2025

Frédéric Lemay, MD

Université de Sherbrooke

Université de Sherbrooke

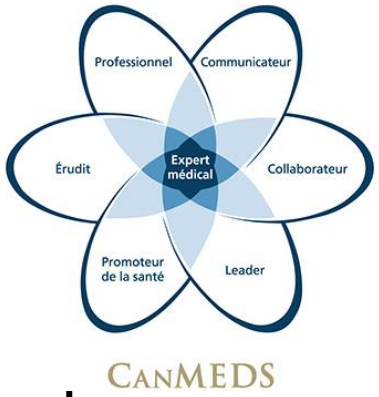
CENTRE DE RECHERCHE | CHUS


222

Conflits d’intérêts potentiels

Nature des relations	Nom de l’organisation à but lucratif ou sans but lucratif
Les paiements directs incluant les honoraires	BMS Canada,Merck Canada,Pfizer Canada,Incyte, Astellas, Amgen, Ipsen
La participation à des comités consultatifs ou des bureaux de conférenciers	BMS Canada Merck Canada Pfizer Canada Incyte Astellas Amgen Ipsen
Le financement de subventions ou d’essais cliniques	
Les brevets sur un médicament, un produit ou un appareil	
Tout autre investissement ou toute autre relation qu’un participant raisonnable et bien informé pourrait considérer comme un facteur d’influence sur le contenu de l’activité éducative	

Compétences CanMEDS

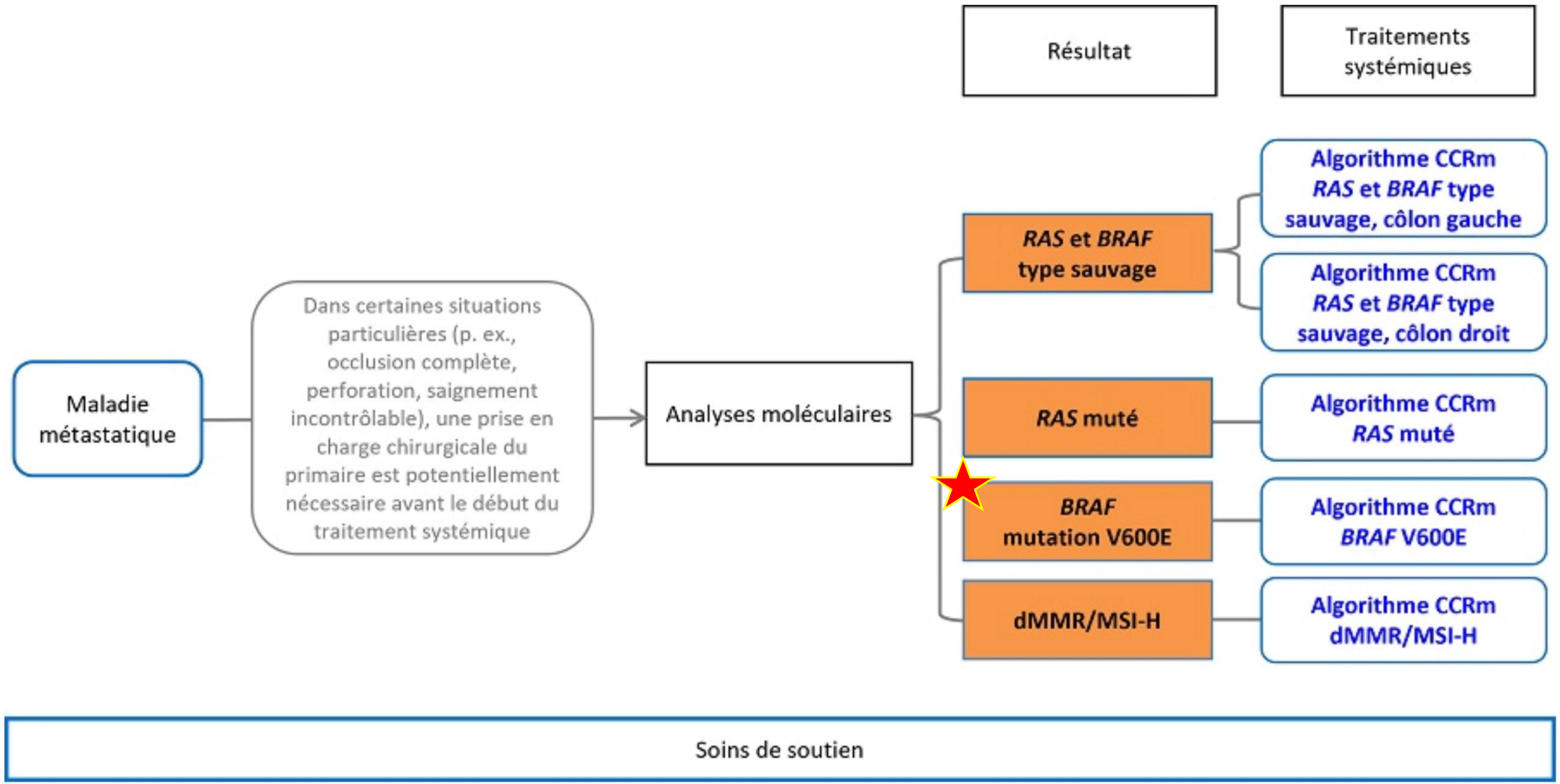


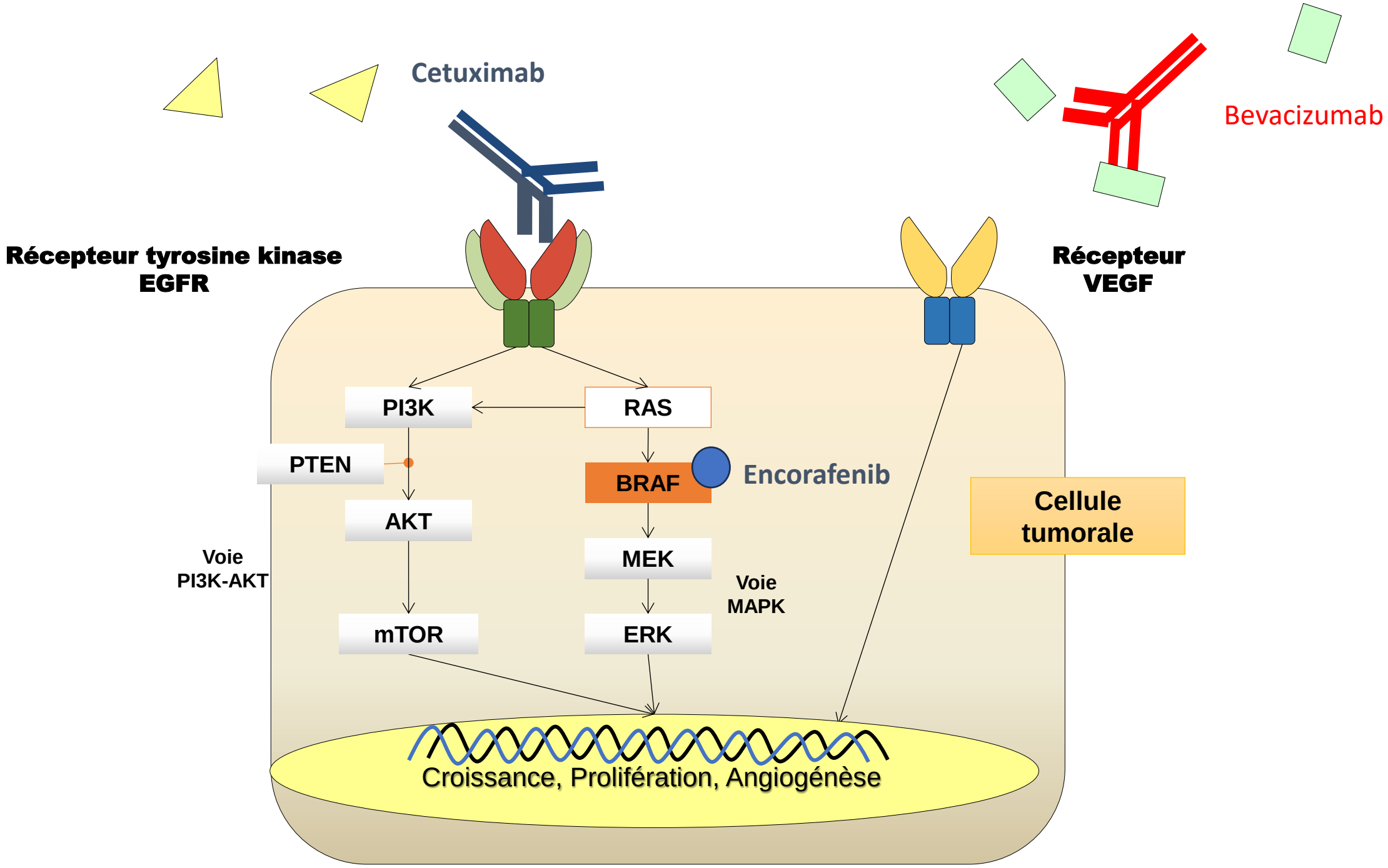
X	**Expert médical** (En tant qu'experts médicaux, les médecins assument tous les rôles CanMEDS et s'appuient sur leur savoir médical, leurs compétences cliniques et leurs attitudes professionnelles pour dispenser des soins de grande qualité et sécuritaires centrés sur les besoins du patient. Pivot du référentiel CanMEDS, le rôle d'expert médical définit le champ de pratique clinique des médecins .)
	Communicateur (En tant que communicateurs, les médecins développent des relations professionnelles ave patient et ses proches ce qui permet l'échange d'informations essentielles à la prestation de soins de qualité.)
	Collaborateur (En tant que collaborateurs, les médecins travaillent efficacement avec d'autres professionnels de la santé pour prodiguer des soins sécuritaires et de grande qualité centrés sur les besoins du patient.)
	Leader (En tant que leaders, les médecins veillent à assurer l'excellence des soins, à titre de cliniciens, d'administrateurs, d'érudits ou d'enseignants et contribuent ainsi, avec d'autres intervenants, à l'évolution d'un système de santé de grande qualité.)
	Promoteur de santé (En tant que promoteurs de la santé, les médecins mettent à profit leur expertise et leur influence en oeuvrant avec des collectivités ou des populations de patients en vue d'améliorer la santé. Ils collaborent avec ceux qu'ils servent afin d'établir et de comprendre leurs besoins, d'être si nécessaire leur porte-parole, et de soutenir l'allocation des ressources permettant de procéder à un changement.)
X	**Érudit** (En tant qu'érudits, les médecins font preuve d'un engagement constant envers l'excellence dans la pratique médicale par un processus de formation continue, en enseignant à des tiers, en évaluant les données probantes et en contribuant à l'avancement de la science.)
	Professionnel (En tant que professionnels, les médecins ont le devoir de promouvoir et de protéger la santé et le bien-être d'autrui, tant sur le plan individuel que collectif. Ils doivent exercer leur profession selon les normes médicales actuelles, en respectant les codes de conduite quant aux comportements qui sont exigés d'eux, tout en étant responsables envers la profession et la société. De plus, les médecins contribuent à l'autoréglementation de la profession et voient au maintien de leur santé.)

Plan

- Colon métastatique 1e ligne
  - Mutation BRAF: BREAKWATER
  - dMMR/MSI-H: CM-8HW
    Sténose post I-O
- Colorectal adjuvant
  - PI3K: ALASCCA
- GI haut
  - ADK oesophage périop: chimio vs RCT

1.7 Cancer colorectal métastatique ou avancé, visée palliative (schéma général)




Cetuximab
Bevacizumab
Récepteur tyrosine kinase
EGFR
Récepteur
VEGF
PI3K
RAS
PTEN
BRAF
Encorafenib
AKT
MEK
Voie
PI3K-AKT
Voie
MAPK
mTOR
ERK
Cellule
tumorale
Croissance, Prolifération, Angiogénèse

BREAKWATER: Study Design

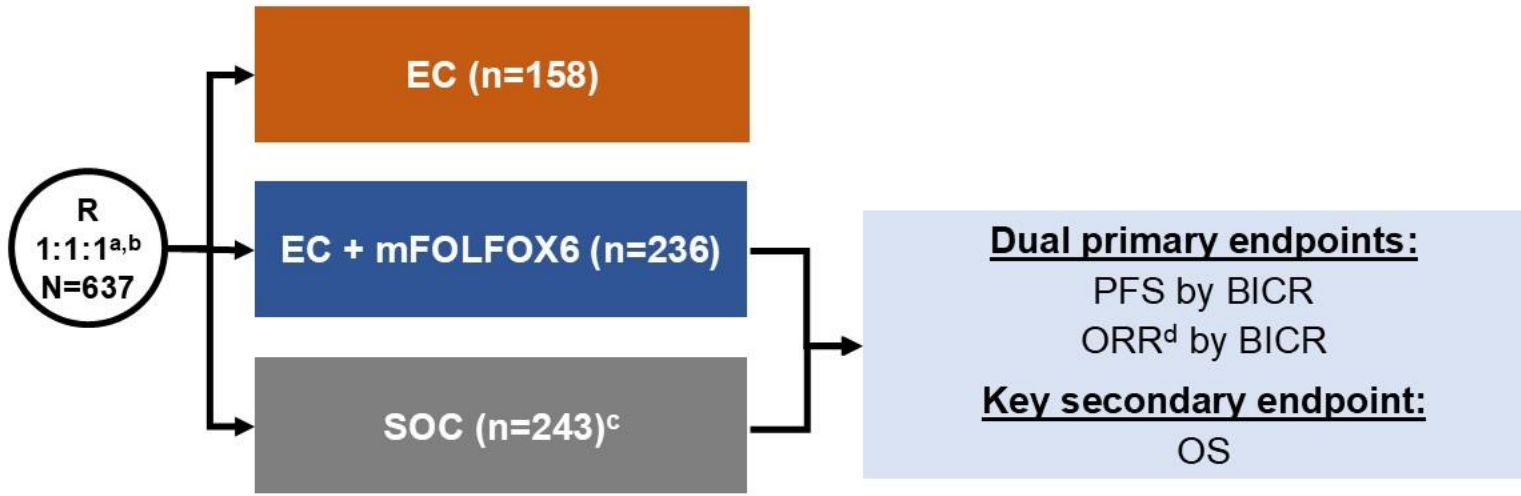
BREAKWATER (NCT04607421) is an open-label, multicenter, phase 3 study in first-line BRAF V600E-mutant mCRC

Inclusion criteria

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

Exclusion criteria

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



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

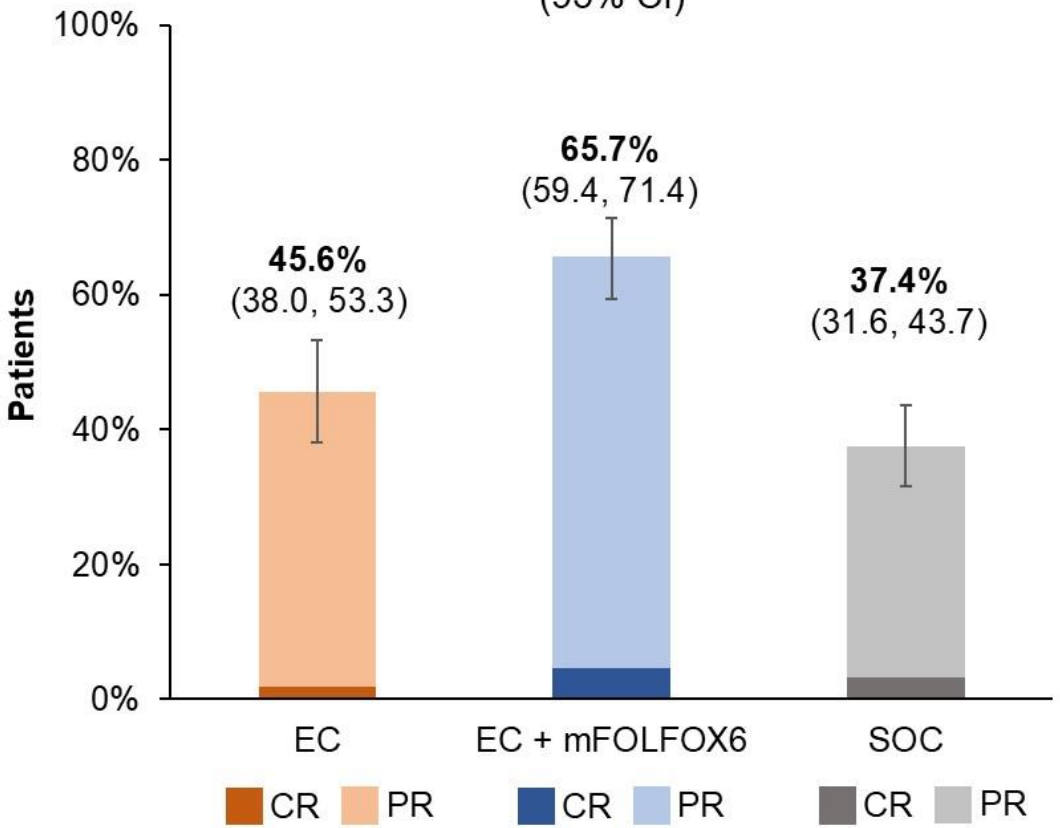
We present the primary analysis of PFS by BICR and a second interim analysis of OS in the EC + mFOLFOX6 and SOC arms, the efficacy data in the EC arm, and safety data in all arms

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

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

Best Overall Response by BICR (All Randomized Patients)

Confirmed ORR by BICR
(95% CI)



Confirmed Best Overall Response, TTR, and DOR by BICR

All randomized patients	EC n=158	EC + mFOLFOX6 n=236	SOC n=243
Confirmed best overall response, n (%)[a]			
CR	3 (1.9)	11 (4.7)	8 (3.3)
PR	69 (43.7)	144 (61.0)	83 (34.2)
SD	57 (36.1)	50 (21.2)	85 (35.0)
PD	12 (7.6)	8 (3.4)	21 (8.6)
Responders	**n=72**	**n=155**	**n=91**
TTR, median (range), weeks	6.6 (4.3 to 86.4)	7.0 (5.1 to 103.6)	7.3 (5.4 to 48.0)
DOR, median (95% CI), months	7.0 (4.2, 11.6)	13.9 (10.9, 18.5)	10.8 (7.6, 13.4)
Patients with a DOR of ≥6 months, n (%)	29 (40.3)	110 (71.0)	38 (41.8)
Patients with a DOR of ≥12 months, n (%)	15 (20.8)	54 (34.8)	16 (17.6)

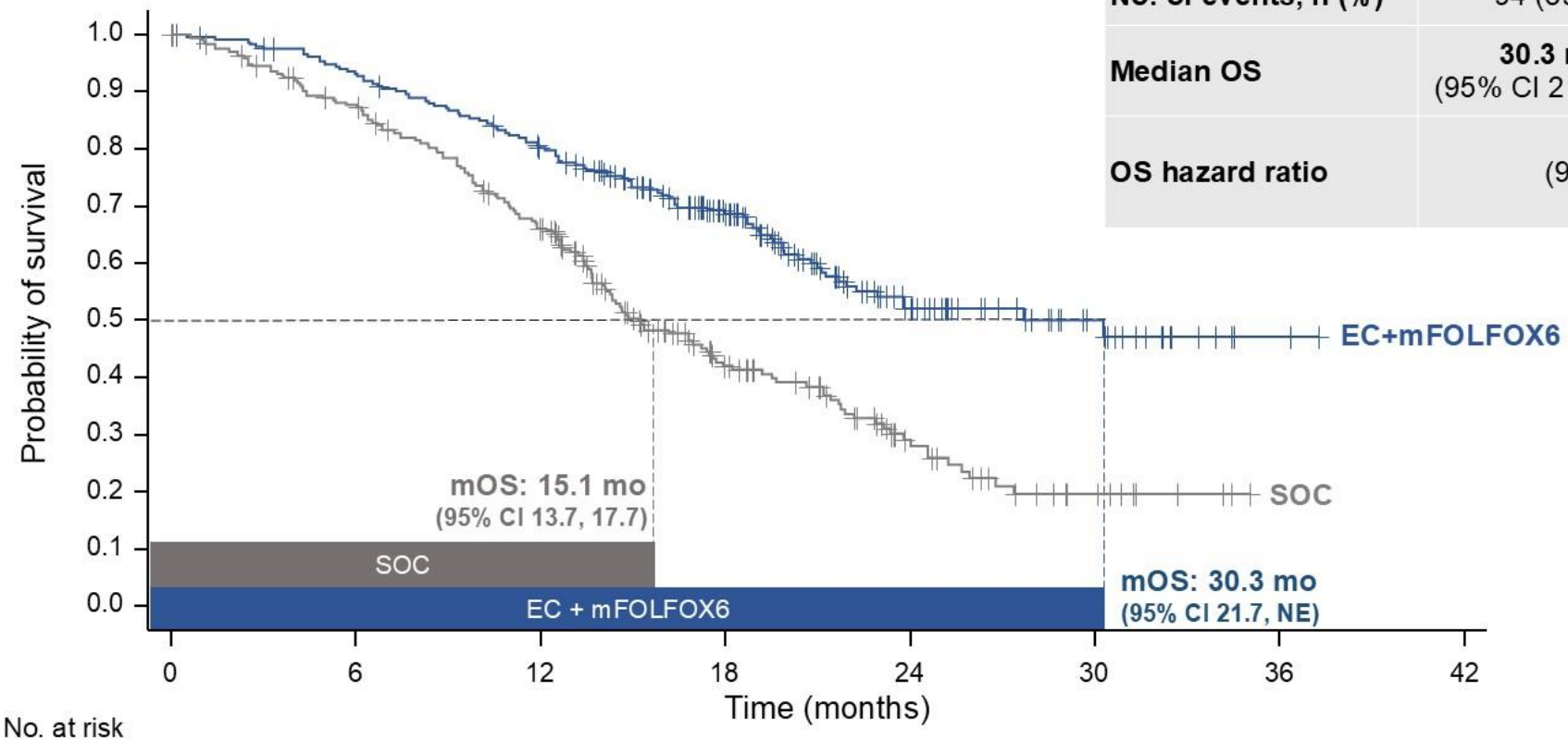
Data cutoff: January 6, 2025.

[a]Non-CR/PD: 7 (4.4%), 5 (2.1%), and 9 (3.7%), respectively; not evaluable: 10 (6.3%), 18 (7.6%), and 37 (15.2%), respectively.

BICR, blinded independent central review; CR, complete response; DOR, duration of response; EC, encorafenib plus cetuximab; mFOLFOX6, modified fluorouracil/leucovorin/oxaliplatin; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care; TTR, time to response.

OS (EC + mFOLFOX6 and SOC)

	EC + mFOLFOX6 n=236	SOC n=243
No. of events, n (%)	94 (39.8)	148 (60.9)
Median OS	**30.3 mo** (95% CI 21.7, NE)	**15.1 mo** (95% CI 13.7, 17.7)
OS hazard ratio	**0.49** (95% CI 0.375, 0.632) ***P*<0.0001[a]**	

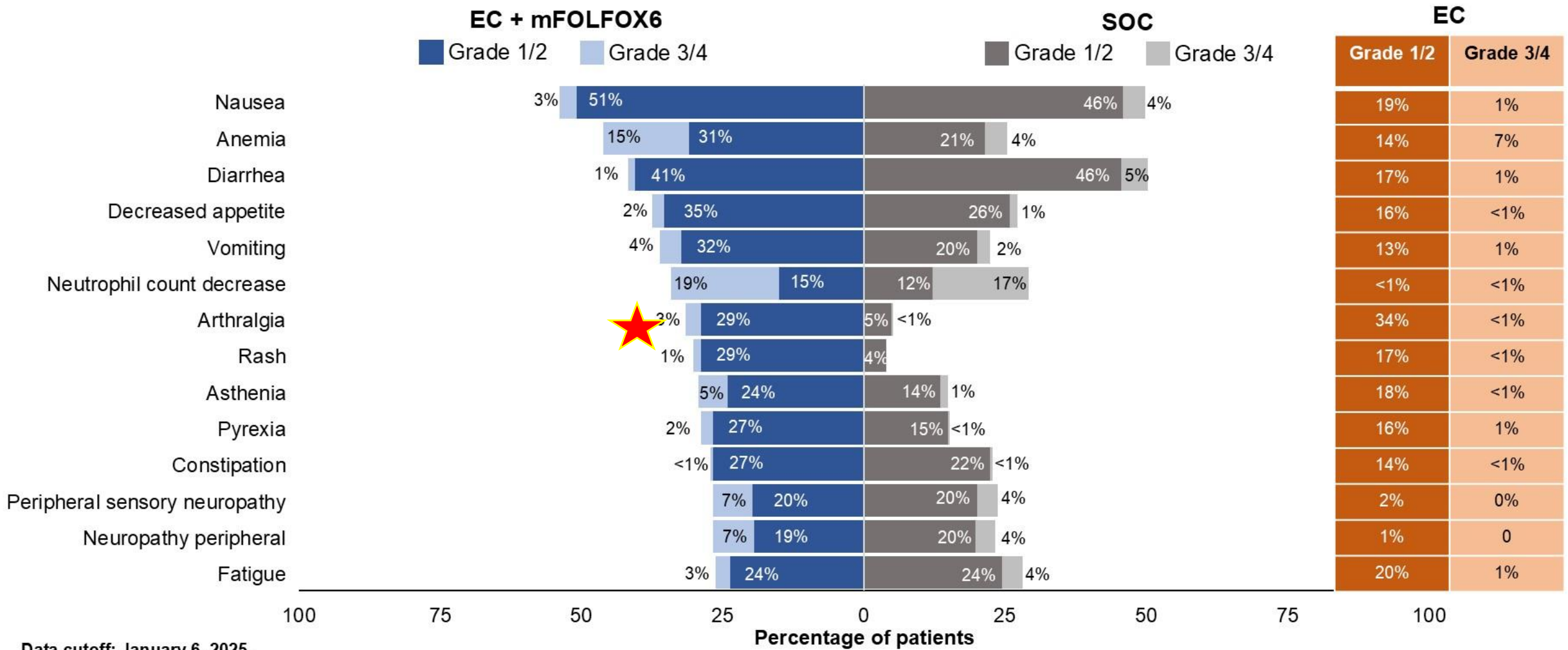


No. at risk								
EC+mFOLFOX6	236	216	182	121	48	17	2	0
SOC	243	202	147	64	27	9	0	0

Data cutoff: January 6, 2025. [a]Exceeding the threshold for statistical significance in this interim analysis.

EC, encorafenib plus cetuximab; mFOLFOX6, modified fluorouracil/leucovorin/oxaliplatin; NE, not estimable; SOC, standard of care; mOS, median overall survival

Most Frequent (≥25%)[a] All-Causality TEAEs



	EC	
	Grade 1/2	Grade 3/4
Nausea	19%	1%
Anemia	14%	7%
Diarrhea	17%	1%
Decreased appetite	16%	<1%
Vomiting	13%	1%
Neutrophil count decrease	<1%	<1%
Arthralgia	34%	<1%
Rash	17%	<1%
Asthenia	18%	<1%
Pyrexia	16%	1%
Constipation	14%	<1%
Peripheral sensory neuropathy	2%	0%
Neuropathy peripheral	1%	0
Fatigue	20%	1%

Data cutoff: January 6, 2025.

[a]Frequency is based on the EC + mFOLFOX6 arm.

EC, encorafenib plus cetuximab; mFOLFOX6, modified fluorouracil/leucovorin/oxaliplatin; SOC, standard of care; TEAE, treatment-emergent adverse event.

CCR avancé + mut v600E (10%)

- Chimiothérapie + anti-BRAF (Encorafenib) + anti-EGFR (Cetuximab) = nouveau standard de traitement pour CCR stade 4 mut V600E
- Double la survie globale (30 vs 15 mois)
- Importance des analyses moléculaires au diagnostic

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

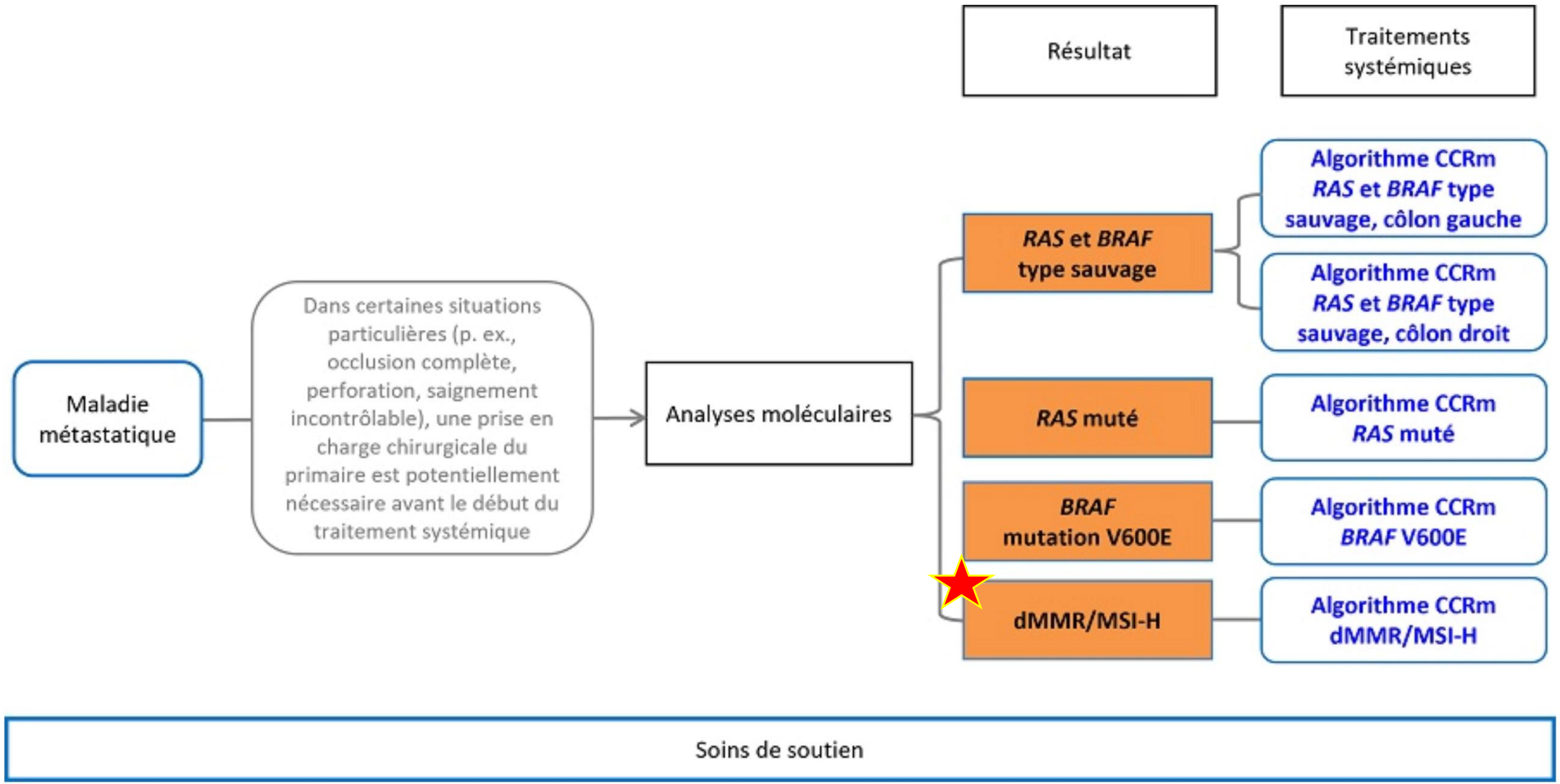
Encorafenib, Cetuximab, and mFOLFOX6 in *BRAF*-Mutated Colorectal Cancer

E. Elez,[1,2] T. Yoshino,[3] L. Shen,[4] S. Lonardi,[5] E. Van Cutsem,[6,7] C. Eng,[8] T.W. Kim,[9] H.S. Wasan,[10] J. Desai,[11,12] F. Ciardiello,[13] R. Yaeger,[14] T.S. Maughan,[15] V.K. Morris,[16] C. Wu,[17] T. Usari,[18] R. Laliberte,[19] S.S. Dychter,[20] X. Zhang,[21] J. Tabernero,[1,2,22] and S. Kopetz,[16] for the BREAKWATER Trial Investigators*

ABSTRACT

This article was published on May 30, 2025, at NEJM.org.

1.7 Cancer colorectal métastatique ou avancé, visée palliative (schéma général)

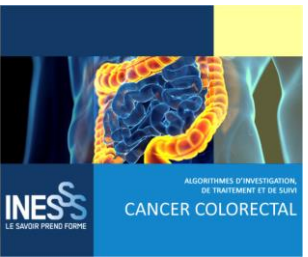


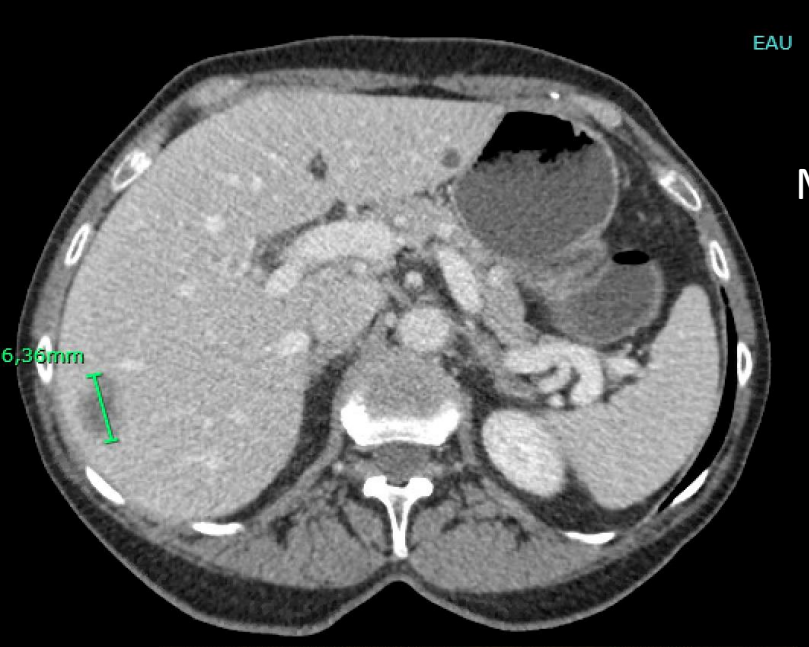
1.7.5 Instabilité microsatellitaire élevée ou déficience du système de réparation des mésappariements (dMMR/MSI-H)

Mise à jour: 4 juillet 2024

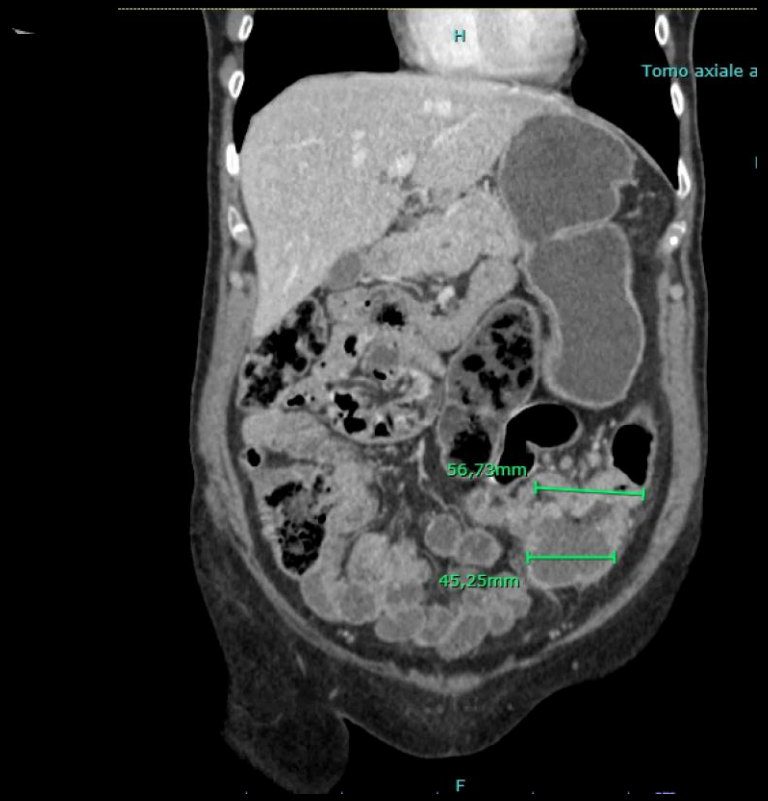
Médicaments systémiques | **Recommandations**

1re intention	2e intention	Ne intention
Séquence de traitement privilégiée		
Pembrolizumab[1]	**Algorithme CCRm *RAS* et *BRAF* type sauvage, côlon gauche**	
	Algorithme CCRm *RAS* et *BRAF* type sauvage, côlon droit	
	Algorithme CCRm *RAS* muté	
	Algorithme CCRm *BRAF* V600E	





Mars 2021 **Pembro 2 ans** avril 2023



Date/heure	CEA
210304 1124	185,0
210316 0840	208,0
210517 0810	26,1
210723 0830	4,6
210902 0800	3,9
211015 0815	3,8
220224 0730	3,7
220411 0815	3,8
220524 0753	3,5
220704 0830	4,0
220816 0800	3,9
220927 0830	3,3
221107 0800	3,9
221220 0800	4,1
230131 0801	3,6
230314 0815	3,8
230612 0815	3,6
230920 0800	3,3
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240215 0845	3,9
240509 0800	3,9
240802 0800	4,0
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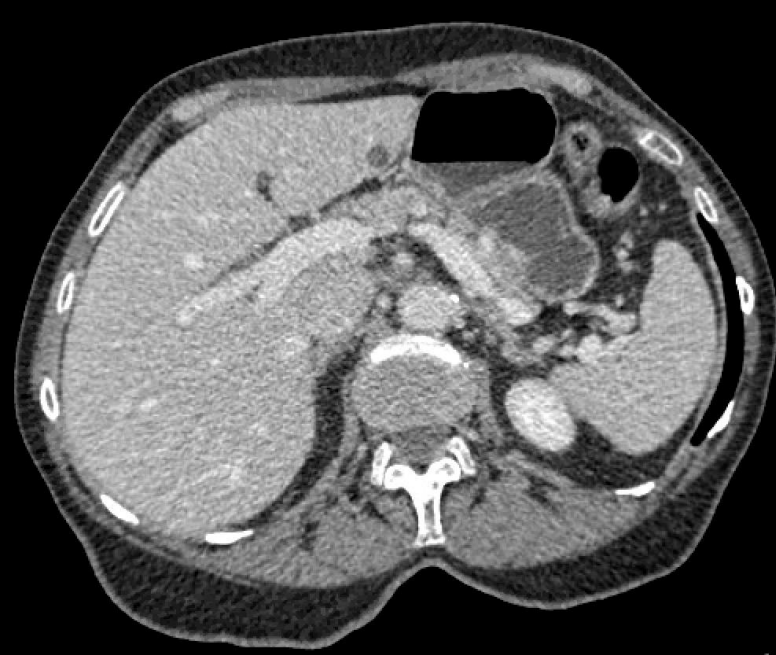
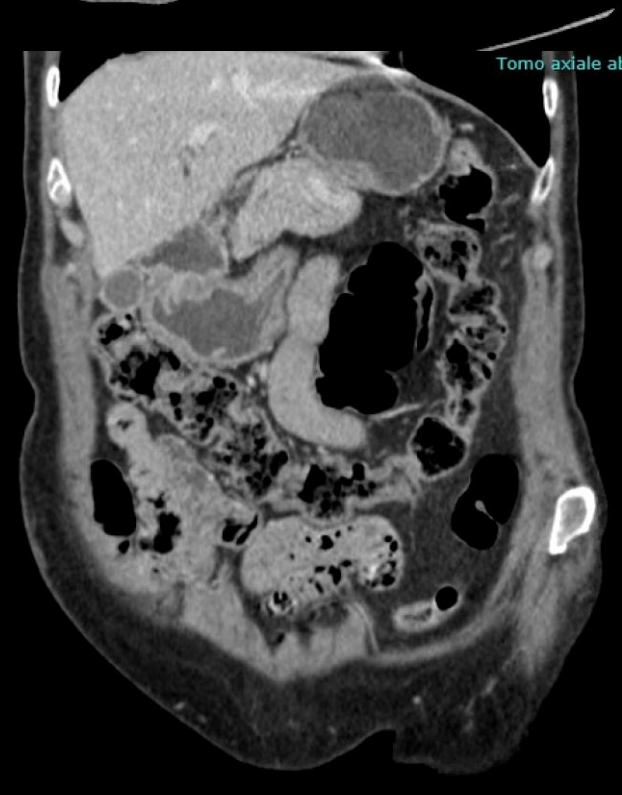
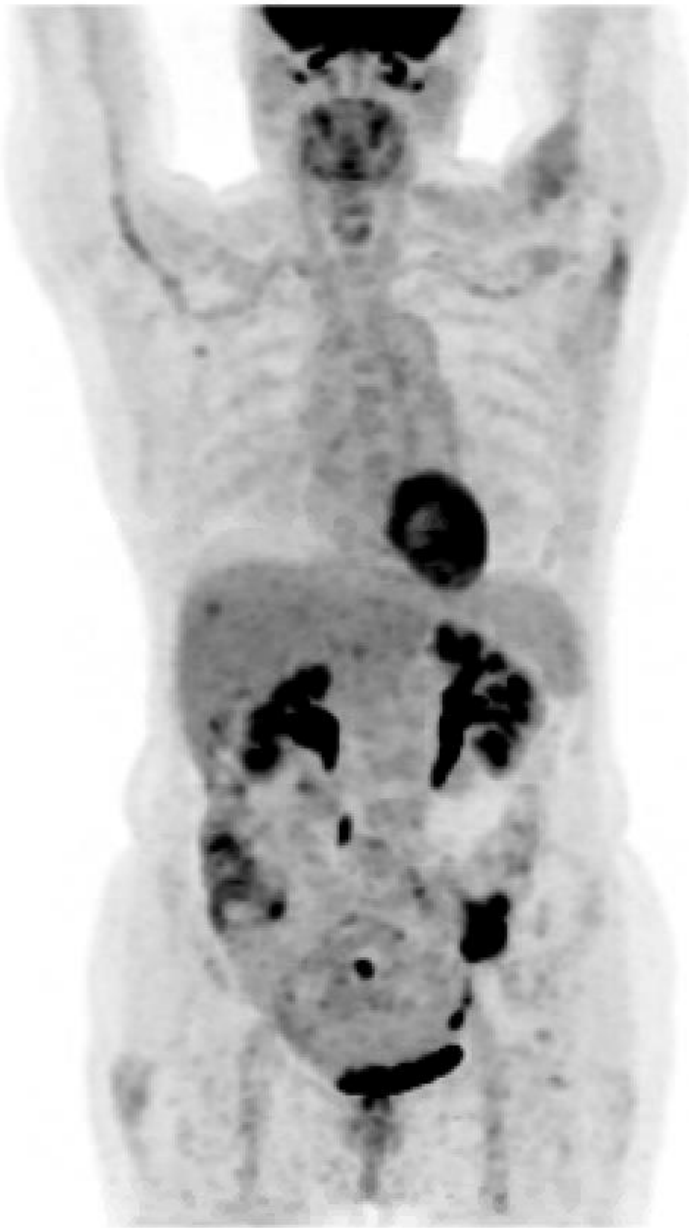
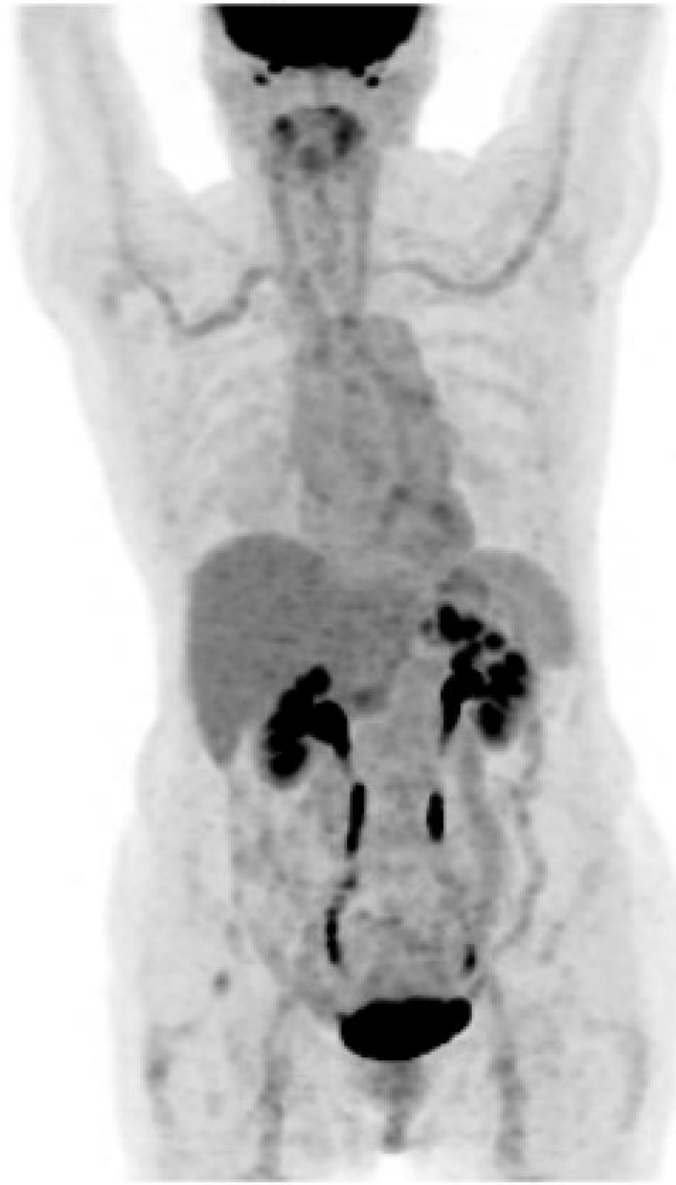






AVR 2021



OCT 2024

CheckMate 8HW study design

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

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

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

R 2:2:1

- n = 353: NIVO 240 mg Q2W for 6 doses, followed by NIVO 480 mg Q4W[b]
- n = 354: NIVO 240 mg + IPI 1 mg/kg Q3W for 4 doses,[c] followed by NIVO 480 mg Q4W[b]
- n = 132: Investigator's choice chemo[d] (mFOLFOX6 or FOLFIRI ± bevacizumab or cetuximab)

Treatment until disease progression, unacceptable toxicity, withdrawal of consent (all arms), or a maximum treatment duration of 2 years (NIVO and NIVO + IPI arms only)

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

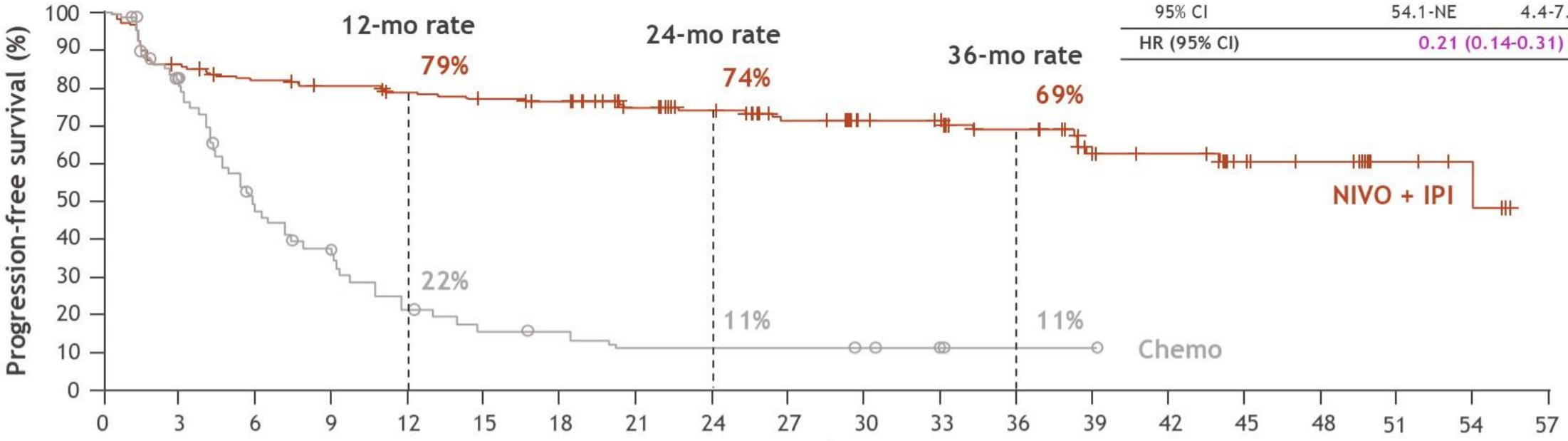
Other select endpoints:
- Safety
- PFS2; ORR by BICR[f]; HRQoL; OS

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

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

Progression-free survival: NIVO + IPI vs chemo (1L)

1L centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 171)	Chemo (n = 84)
Median PFS,[a] mo	54.1	5.9
95% CI	54.1-NE	4.4-7.8
HR (95% CI)	0.21 (0.14-0.31)	



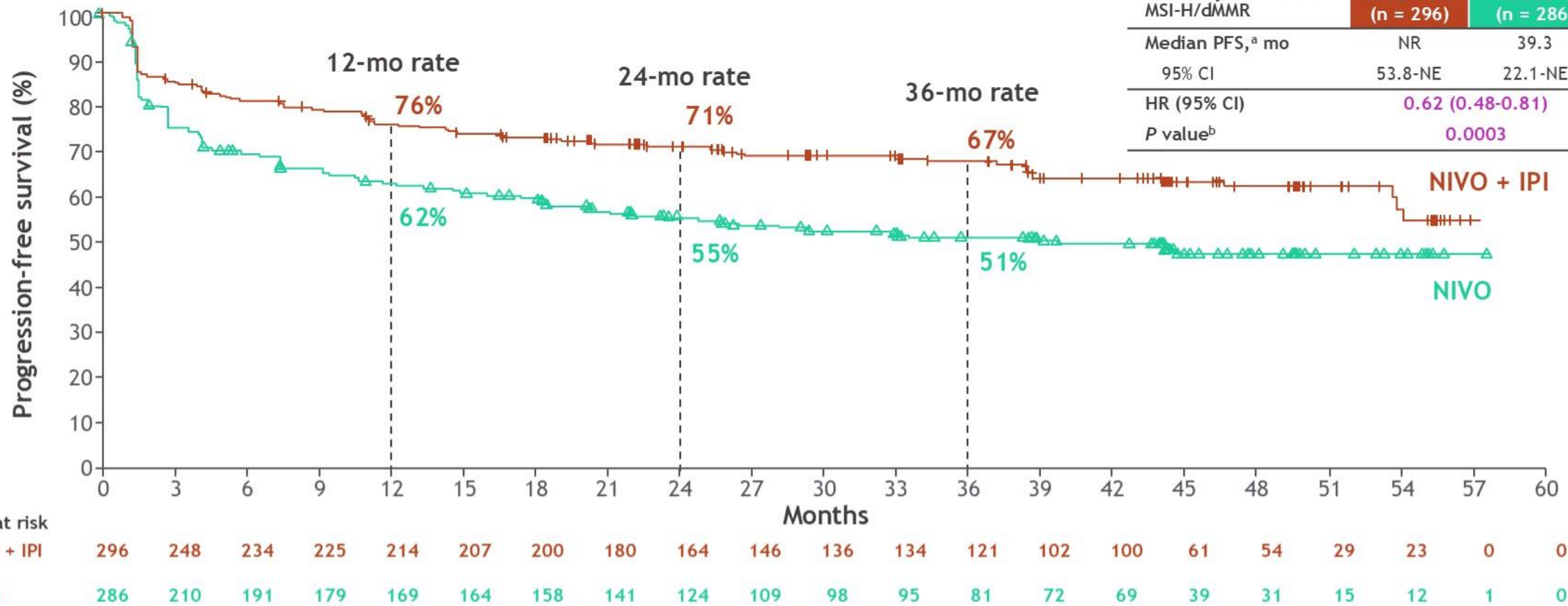
No. at risk

NIVO + IPI	171	144	135	131	126	122	117	102	90	75	66	64	51	34	32	20	17	7	5	0
Chemo	84	52	29	21	12	8	7	5	5	5	4	2	1	1	0	0	0	0	0	0

- NIVO + IPI continued to demonstrate clinically meaningful PFS benefit vs chemo with longer follow-up in patients with centrally confirmed MSI-H/dMMR mCRC in the 1L setting

[a]Per BICR. Median follow-up, 47.0 mo.

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



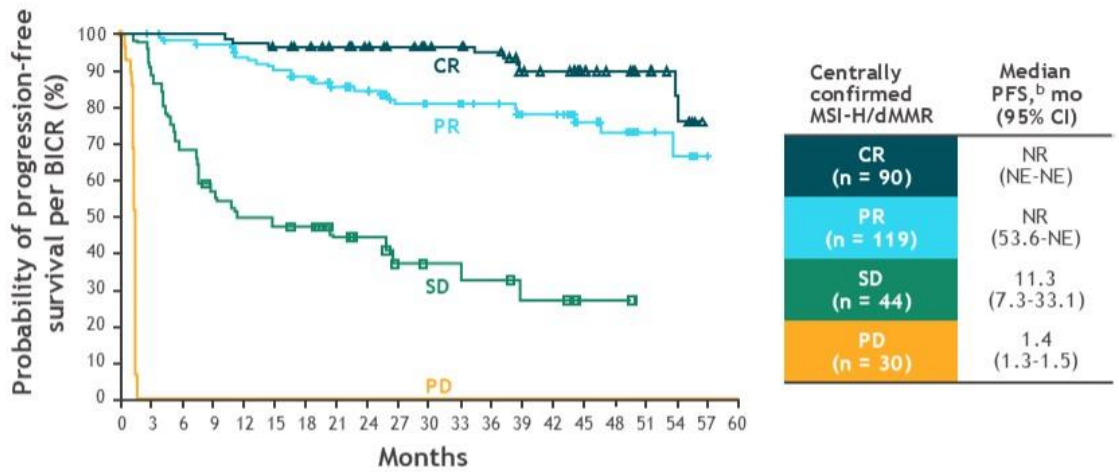
Centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 296)	NIVO (n = 286)
Median PFS,[a] mo	NR	39.3
95% CI	53.8-NE	22.1-NE
HR (95% CI)	0.62 (0.48-0.81)	
P value[b]	0.0003	

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

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

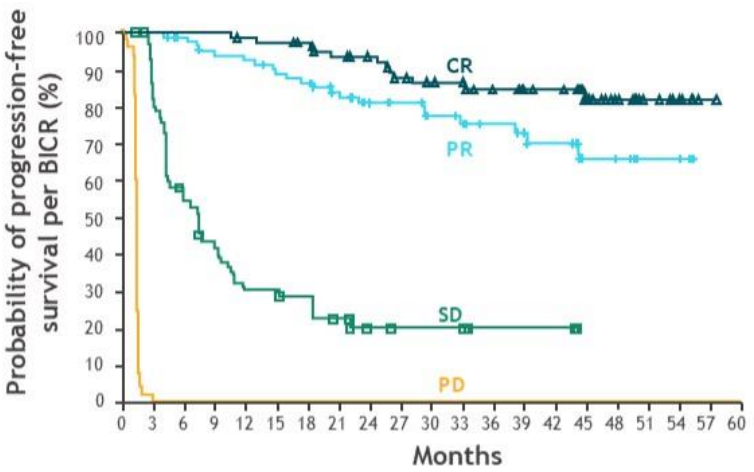
PFS by response: NIVO + IPI vs NIVO (all lines)

NIVO + IPI (n = 296)



Centrally confirmed MSI-H/dMMR	Median PFS,[b] mo (95% CI)
CR (n = 90)	NR (NE-NE)
PR (n = 119)	NR (53.6-NE)
SD (n = 44)	11.3 (7.3-33.1)
PD (n = 30)	1.4 (1.3-1.5)

NIVO (n = 286)

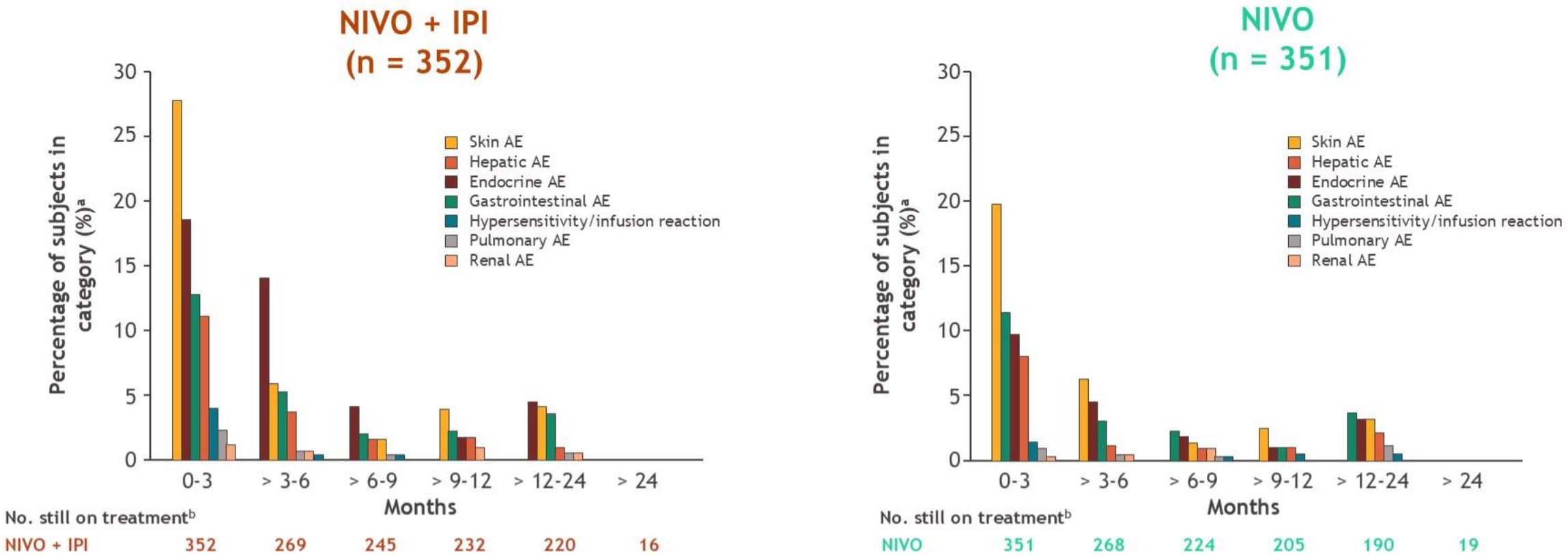


Centrally confirmed MSI-H/dMMR	Median PFS,[b] mo (95% CI)
CR (n = 80)	NR (NE-NE)
PR (n = 85)	NR (NE-NE)
SD (n = 59)	7.3 (4.2-10.2)
PD (n = 54)	1.4 (1.4-1.5)

- Statistically significant and clinically meaningful improvement in ORR was observed with NIVO + IPI vs NIVO (Difference in ORR, 13% [95% CI, 5-21]; *P* = 0.0011)

[a]CR + PR does not add up to ORR due to rounding. [b]Per BICR.

Emergence of TRAEs with potential immunologic etiology over time



- The majority of any-grade TRAEs with potential immunologic etiology[c] in the NIVO + IPI and NIVO groups emerged within the first 6 months of treatment across organ categories
  - Frequencies were generally comparable between the two treatment groups, except skin and endocrine TRAEs were more frequent with NIVO + IPI

[a]Includes events reported between first dose and 30 days after last dose of study treatment. Patients with ≥ 1 any grade event in a given category were counted only once in the time interval corresponding to the first event. Patients with multiple events from different categories within the same time interval were counted once in each category. Proportion of patients in each category is based on the patients still on treatment for the respective time interval. [b]Number of patients still receiving treatment is identified at the beginning of each respective time interval. [c]TRAEs with potential immunologic etiology that require frequent monitoring/intervention.

Nivo + Ipi CM 8HW / CCR stade 4 dMMR

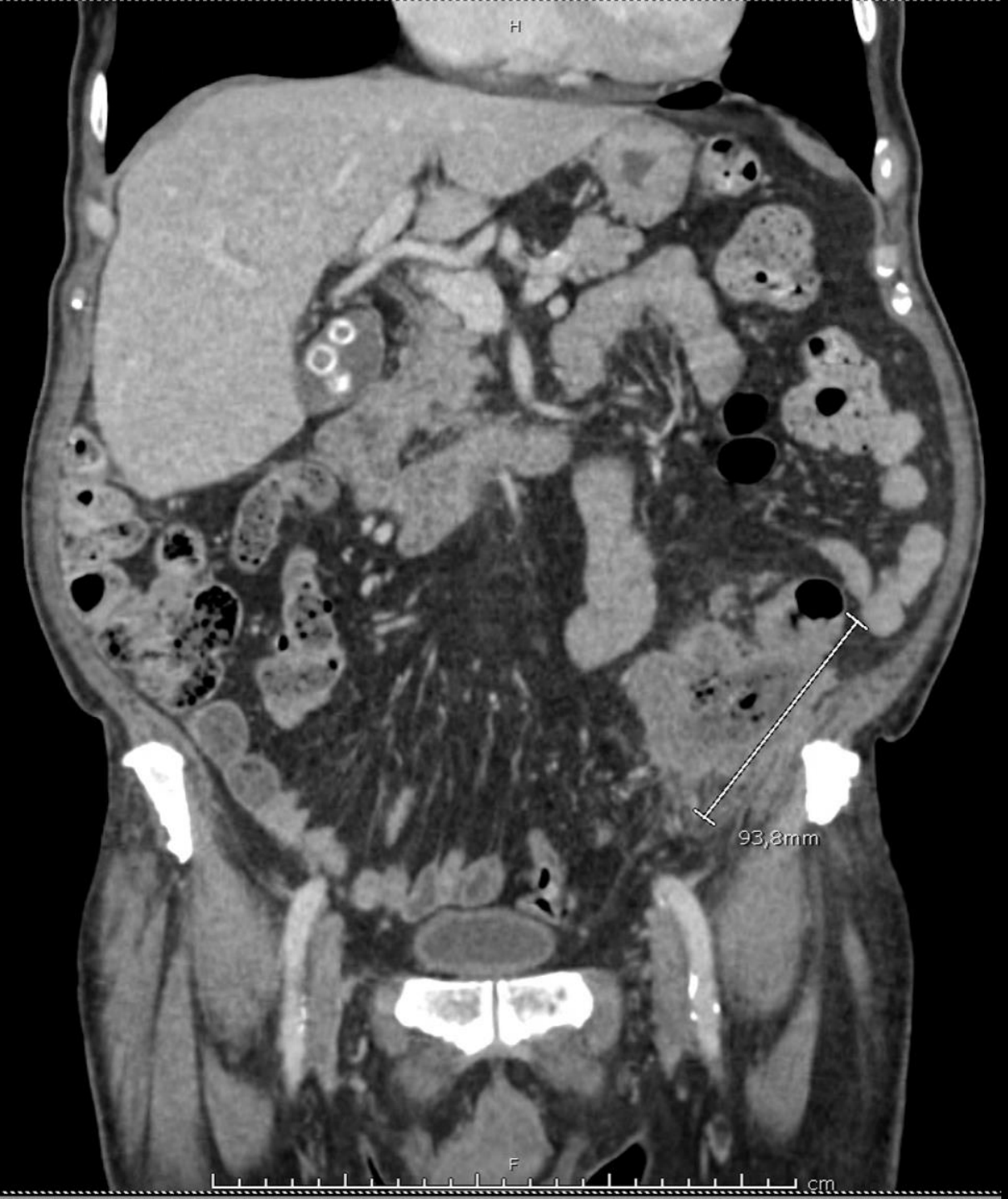
- Avantage Nivo/Ipi
  - vs Nivo seul et vs chimio
  - 10 vs 19% non-réponse primaire (vs 29% Pembro)
  - Tolérance semble raisonnable
- Nivo/Ipi = nouveau standard traitement
  - Monothérapie pour patients frêle, atcd immun, greffés…
- Importance des analyses moléculaires au diagnostic

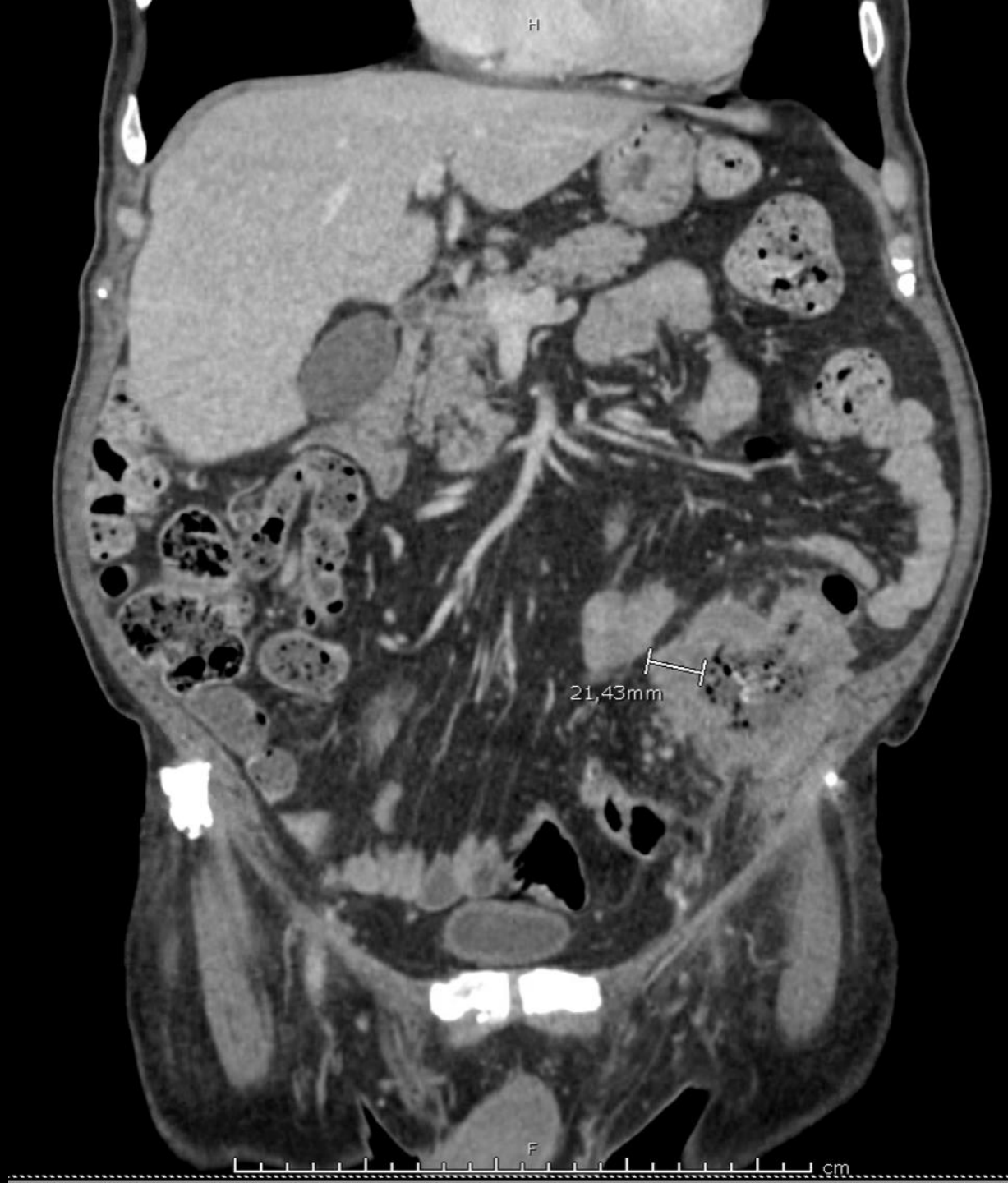
Cas CCR dMMR/MSI-H

- H, 84
- Anémie ferriprive (Hb 67)

- Masse abdominale palpable
- Colonoscopie: ADK sigmoide, large, dMMR (perte MLH1)

- CDTC: Pembrolizumab (neoadjuvant)


H
93,8mm
F
cm


H
21,43mm
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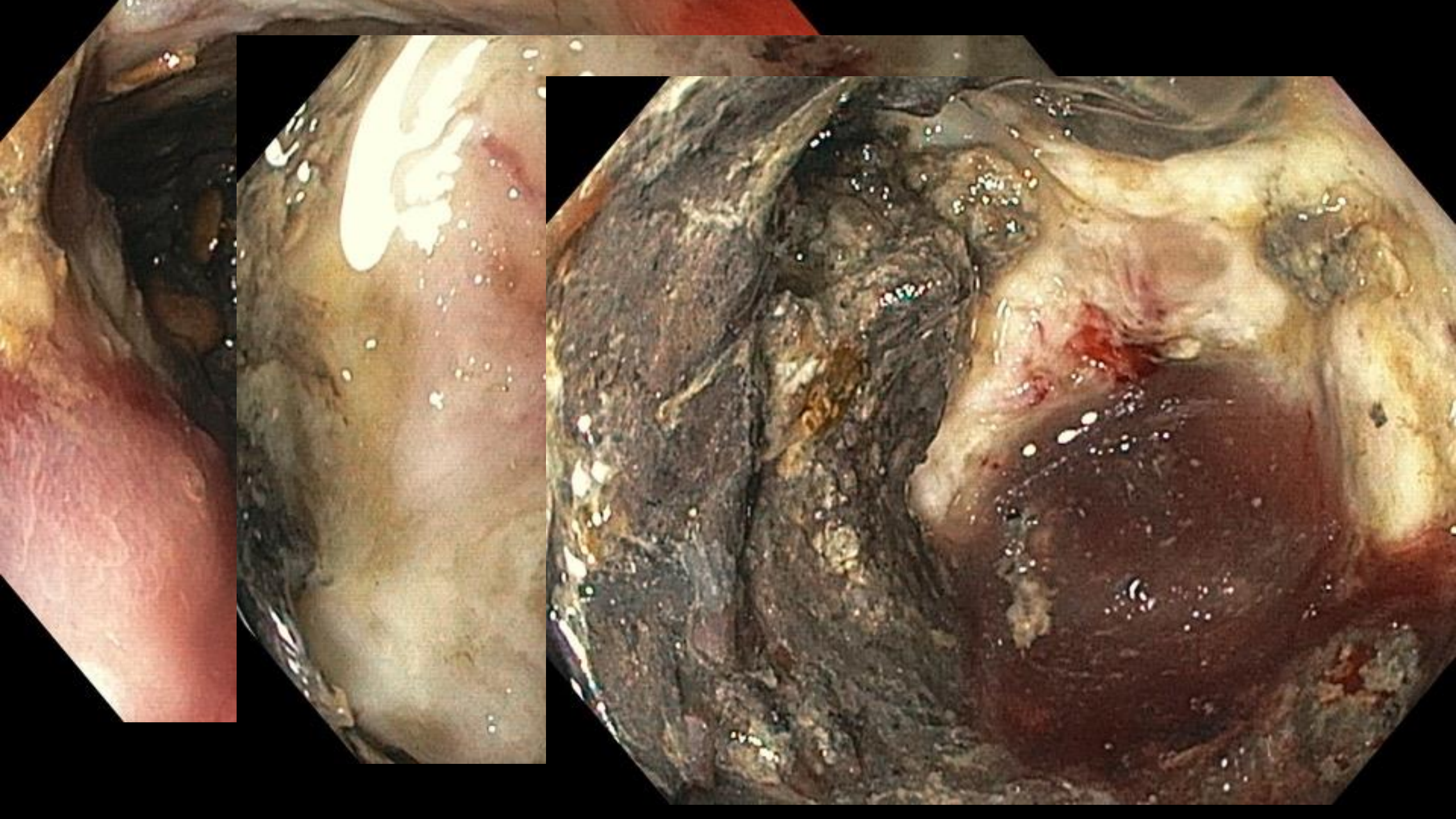
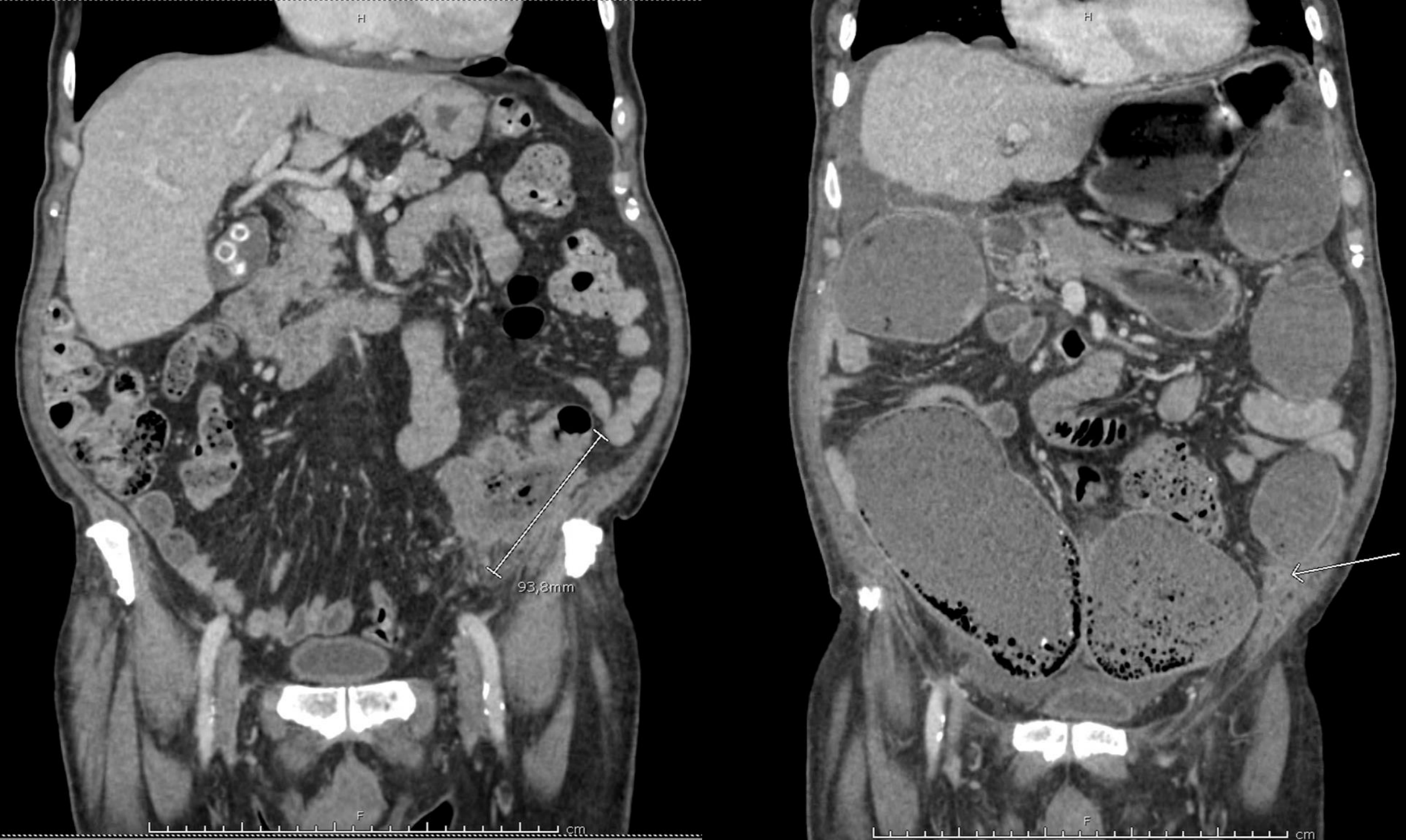
cm



Cas CCR dMMR/MSI-H

- Pembrolizumab x 3

- Constipation


H
93,8mm
F
cm
H
F
cm

Cas CCR dMMR/MSI-H

- Colectomie urgente –ileostomie terminale
- ypT0N0
- Aucune récidive (>3 ans)

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

SHORT COMMUNICATION

Risk of bowel obstruction in patients with colon cancer responding to immunotherapy: an international case series

J. R. Platt[1*], J. Allotey[2], E. Alouani[3], J. Glasbey[4], R. Intini[5], S. Lonardi[6], G. Mazzoli[7], A. M. Militello[8], D. P. Modest[9,10], J. Palle[11,12], F. Pietrantonio[7], K. Riyad[13], L. Samuel[2], A. V. Schulze[9], K. K. Shiu[8], J. Taieb[14], D. J. M. Tolan[15], N. P. West[16], A. C. Westwood[16], C. J. M. Williams[1] & J. F. Seligmann[1]

ESMO Open 2024

Sténose colique/ dMMR CCR / I-O

- 9 patients avec dMMR CCR et occlusion durant immunothérapie

- Angle hépatique (5/9)
- Aspect annulaire/circonférentiel (8/9)
- Obstruction endoscopique (6/9)
- cT4 (6/9)

Platt, ESMO Open 2024

Sténose colique/ dMMR CCR / I-O

- 7/7 avec réponse pathologique (4 cPR)
- Histologie distinctive:
  - Changements fibrotiques prolifératifs + infiltrats cellules immunes
- « Stricturing immunotherapy response » = nouveau phénomène

Platt, ESMO Open 2024
Kasi, Oncogene 2023

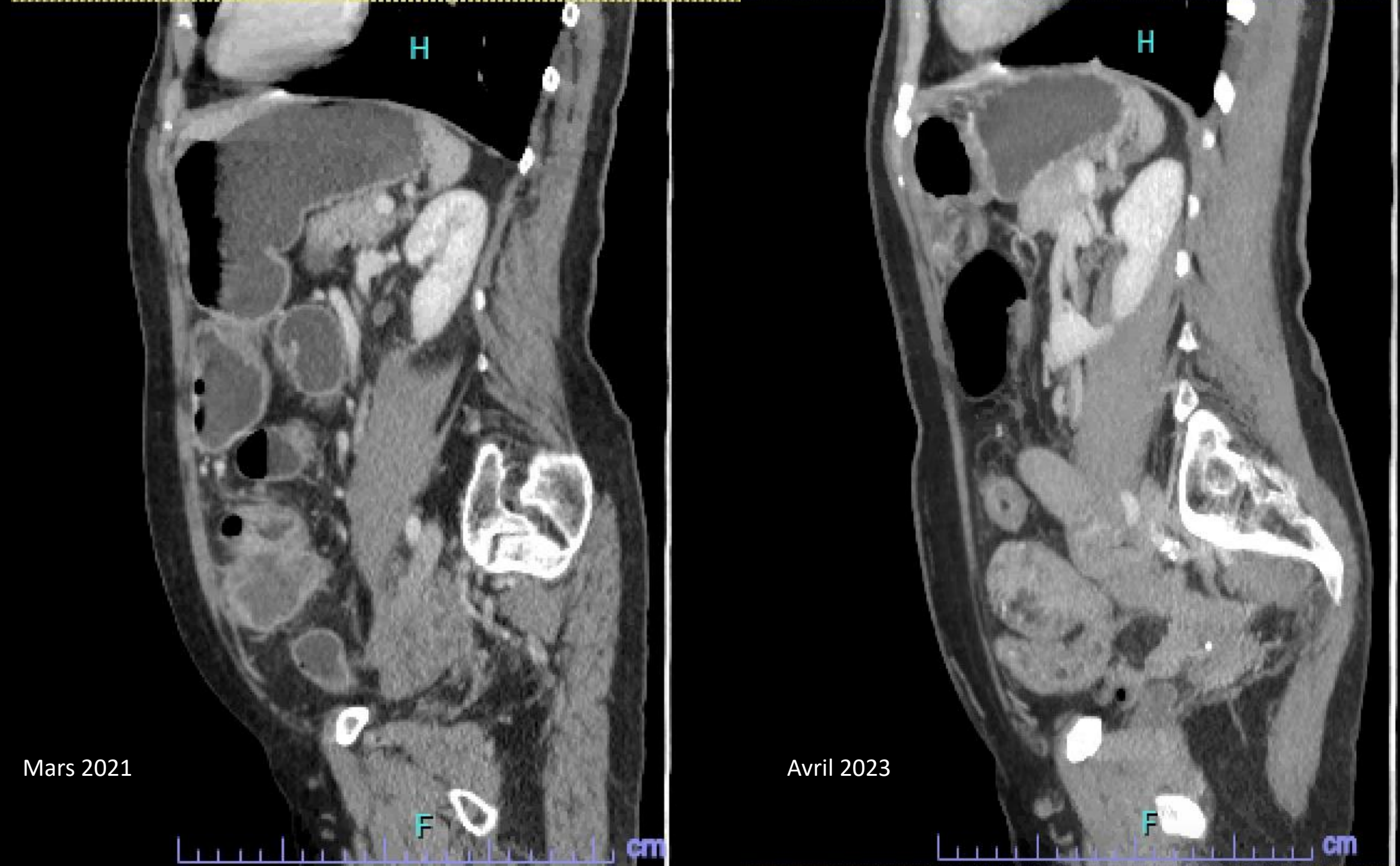
Expérience locale (CHUS + CHUM)

Table 1: Characteristics of cohort

Sex and age	Able to pass endoscope initially	Baseline staging	Location of tumor	ADK / dMMR	MLH1 & PMS2 status	MLH1 Hyper-meth	Mutation NRAS | KRAS | BRAF	Evidence of oncologic response (Patho | Scan | Endoscopy | Recurrence)	Days from 1st IO to stenosis	Symptomatic / Intervention
F61	No	cT4bN2bM1c (IVc)	Transverse colon	Yes	Loss	Yes	WT | WT | V600E	---- | PR | Yes | No	297	No / No
F80	No	cT4bN2bM1c (IVc)	Right colon Hepatic angle	Yes	Loss	NA	NA	---- | PR | ---- | No	78	Yes / derivation ileostomy
M84	No	cT3N1M0 (IIIA)	Sigmoid	Yes	Loss	No	NA	pCR | CR | ---- | No	61	Yes / Subtotal colectomy + ileostomy
F75	No	cT4N1M1 (IV)	Splenic angle	Yes	Loss	Yes	WT | WT | WT	---- | CR | Yes | No	903	No / No
F73	No	cT4aN1M0	Right colon	Yes	Loss	Yes	WT | WT | V600E	---- | PR | Yes | No	245	No / Yes

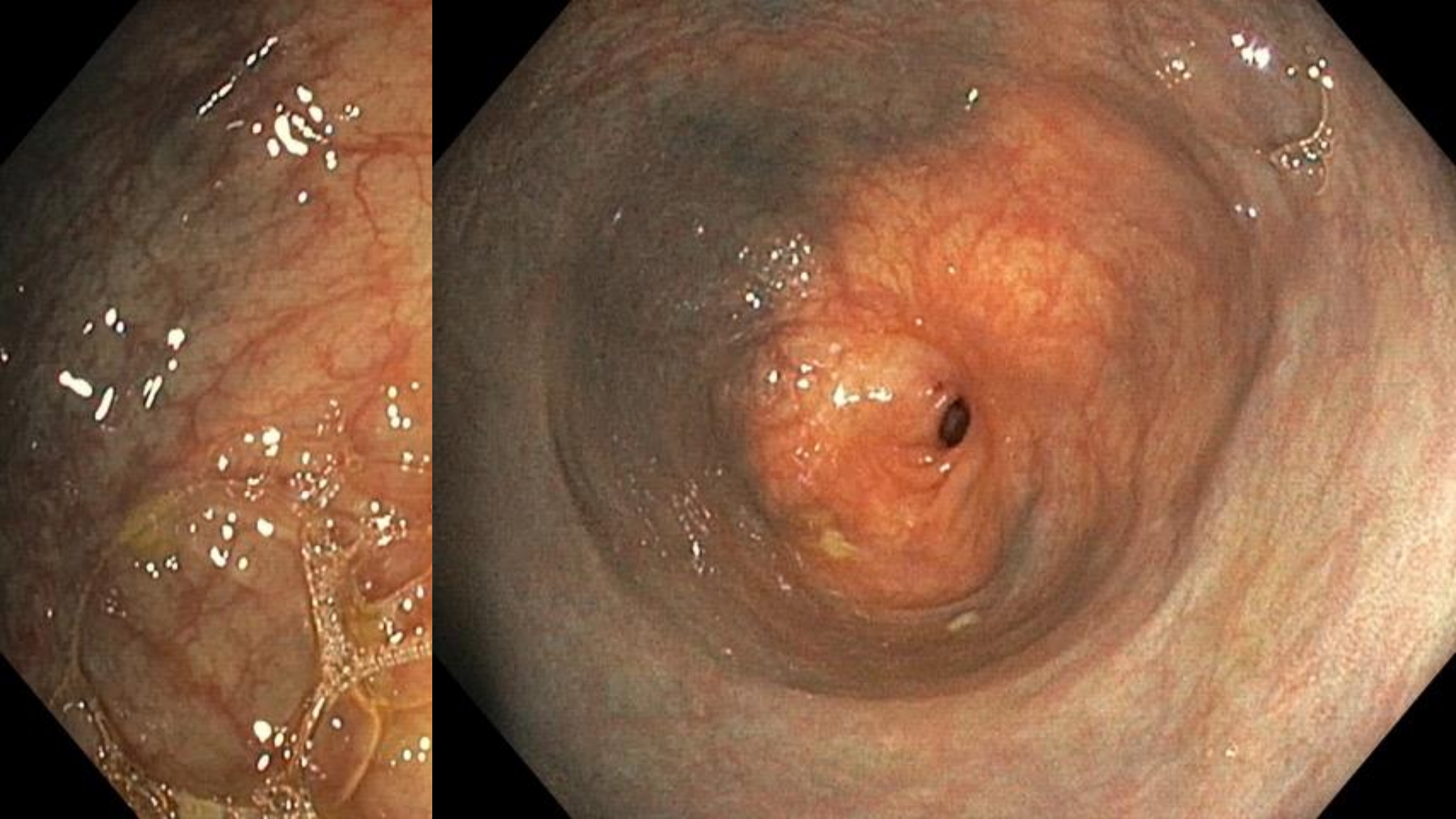
Legend: ADK: Adenocarcinoma, dMMR: Deficient mismatch repair, PR: Partial Response, CR: Complete Response

Unpublished data, 2025



Mars 2021

Avril 2023



Au final: Sténose colique/ dMMR CCR

- Sténose colique / rectale après I-O = nouvel effet secondaire (rare?)
- Sténoses fibrotiques / pas (peu) cellules cancéreuses viables (souvent pCR)

- Facteurs de risque?

  Impossibilité de passer le scope, T4, forme annulaire

- Surveillance rappochée: sx GI, dérivation?

Plan

- Colon métastatique 1e ligne
  - Mutation BRAF: BREAKWATER
  - dMMR/MSI-H: CM-8HW
    Sténose post I-O
- Colon adjuvant
  - PI3K: ALASCCA
- GI haut
  - ADK oesophage périop: chimio vs RCT

ASCO Gastrointestinal Cancers Symposium

ALASCCA
Adjuvant ASA vid kolorektalcancer

Low-Dose Aspirin Reduces Recurrence Rate in Colorectal Cancer Patients with PI3K Pathway Alterations

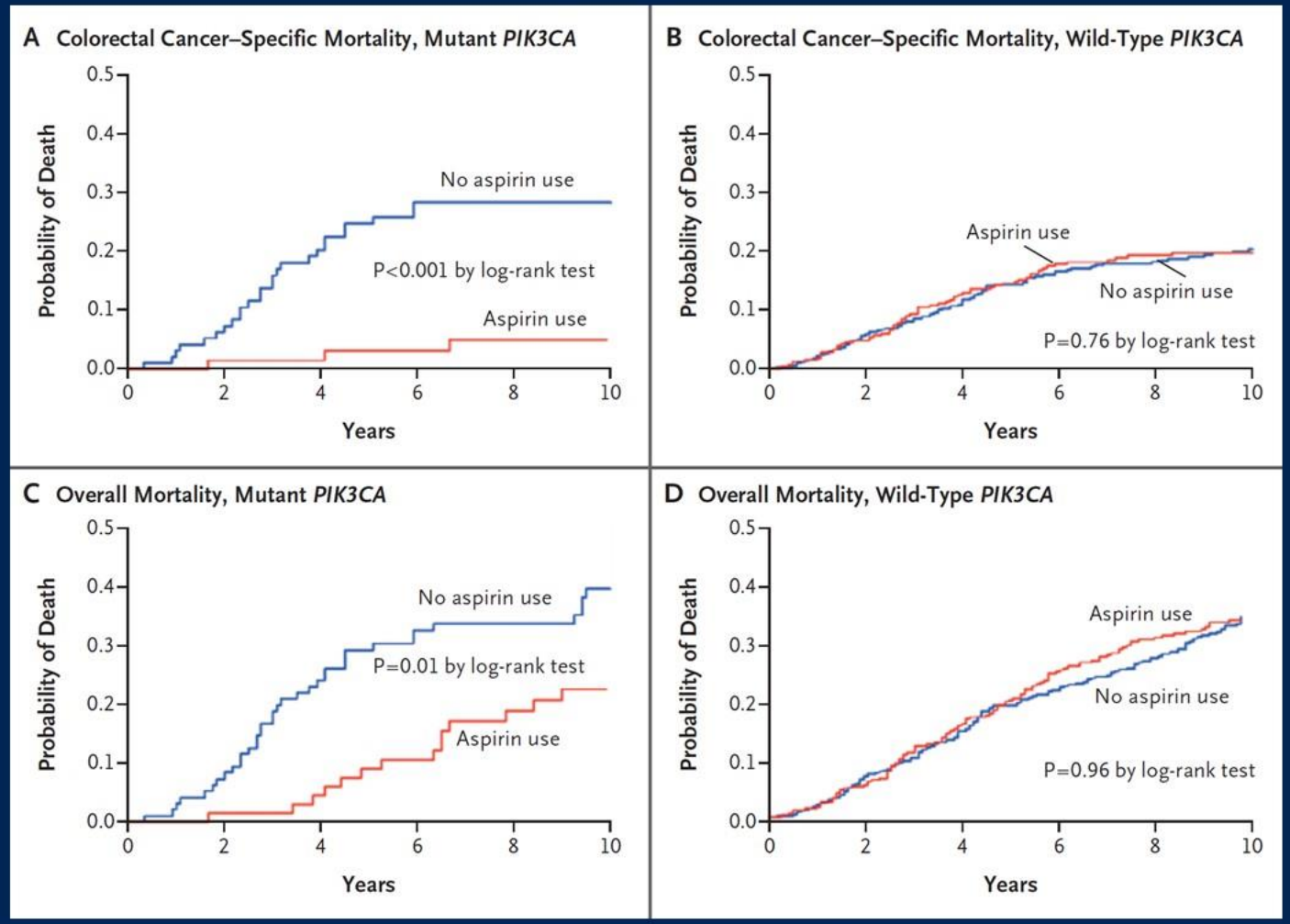
3-Year Results from the ALASCCA Trial

Prof. Anna Martling M.D, PhD, FACS (Hon), FASCRS (Hon)
Karolinska Institutet & Karolinska University Hospital, Stockholm, Sweden

PRESENTED BY: Anna Martling Low-Dose Aspirin Reduces Recurrence Rate in Colorectal Cancer Patients with PI3K Pathway Alterations: 3-Year Results from a Randomized Placebo-Controlled Trial (Abstract Number: LBA125)

Aspirin in CRC

- **Shown in RCTs to reduce incidence of colorectal adenomas**
- **Reduced CRC incidence & slightly reduced mortality in observational studies**
- **PIK3CA mutations possible predictor of treatment effect**



Liao et al. Aspirin use, tumor PIK3CA mutation, and colorectal-cancer survival. N Engl J Med. 2012 Oct 25;367(17):1596-606. doi: 10.1056/NEJMoa1207756.

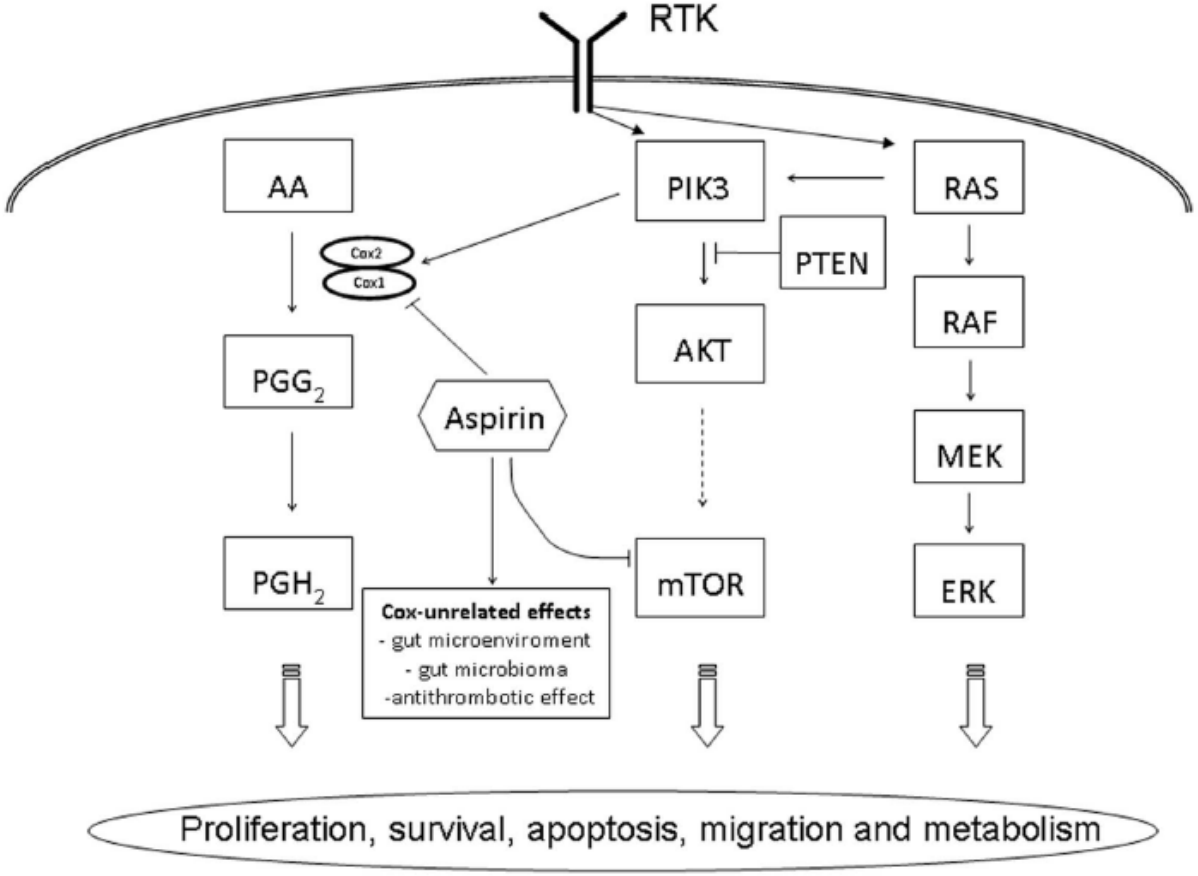
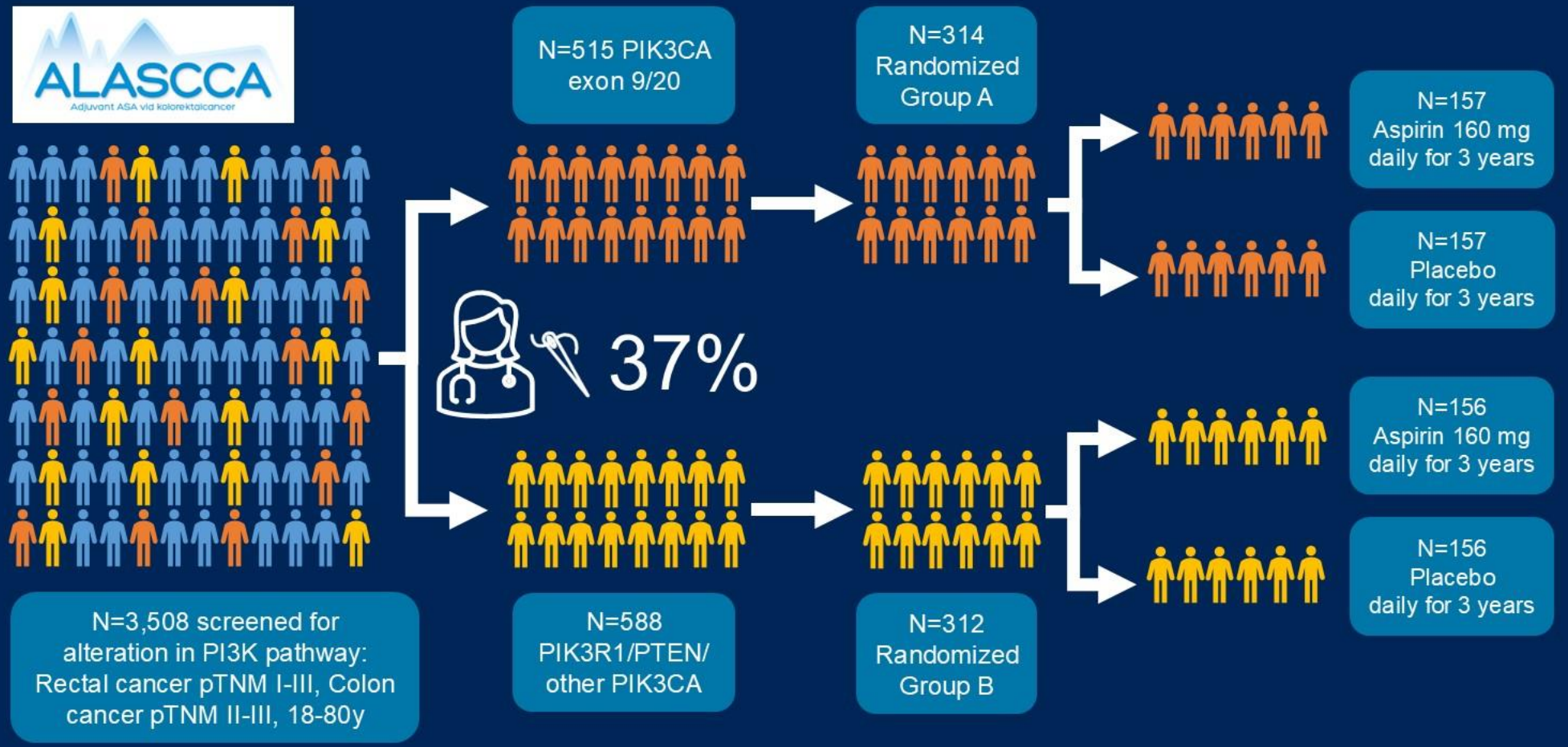


FIGURE 1 | Schematic overview of PIK3CA related cell signaling pathways in colorectal cancer. AA, arachidonic acid; AKT, protein kinase B; ERK, extracellular signal-regulated kinase, MEK, MAP kinase kinase; mTOR, mammalian target of rapamycin; PTEN, phosphatase and tensin homolog deleted on chromosome 10; PGG_2, prostaglandin G2; PGH_2, prostaglandin H2; PI3K, phosphatidylinositol-3-kinase; RAF, rapidly accelerated fibrosarcoma; RAS, rat sarcoma; RTK, receptor tyrosine kinase.

Frontiers in Oncology 2014

The ALASCCA Trial (NCT02647099)



Primary outcome:
Time to CRC recurrence (TTR) in Group A

Secondary outcomes:
- Disease-Free Survival (DFS) in Group A
- TTR in Group B
- DFS in Group B
- Safety

April 2016: Start of screening

July 2016: First patient randomized

July 2021: Last patient randomized

July 2024: Complete 3-year follow-up

PRESENTED BY: Anna Martling: Low-Dose Aspirin Reduces Recurrence Rate in Colorectal Cancer Patients with PI3K Pathway Alterations: 3-Year Results from a Randomized Placebo-Controlled Trial (Abstract Number: LBA125)

Patient Characteristics

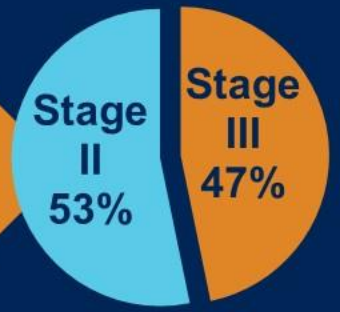
626 patients randomized

Median age 66 years (range 31-80)

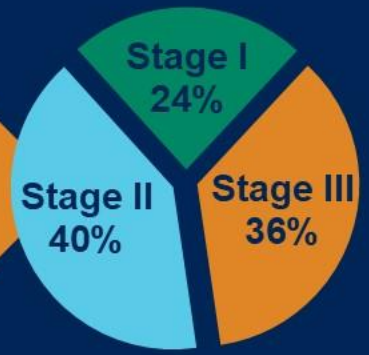
52% Females

67% Colon cancer
33% Rectal cancer

pTNM Stage in colon cancer patients



pTNM Stage in rectal cancer patients



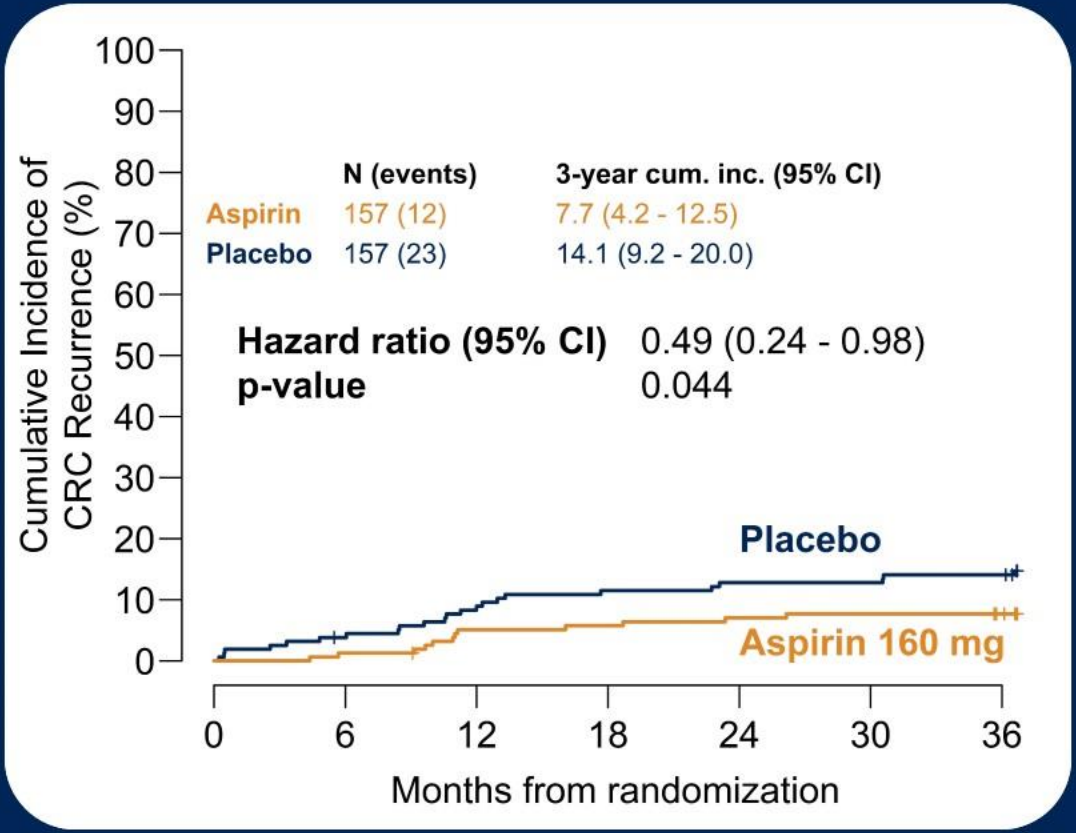
50% of rectal cancer patients given neoadjuvant therapy

50% of colon cancer patients given adjuvant therapy

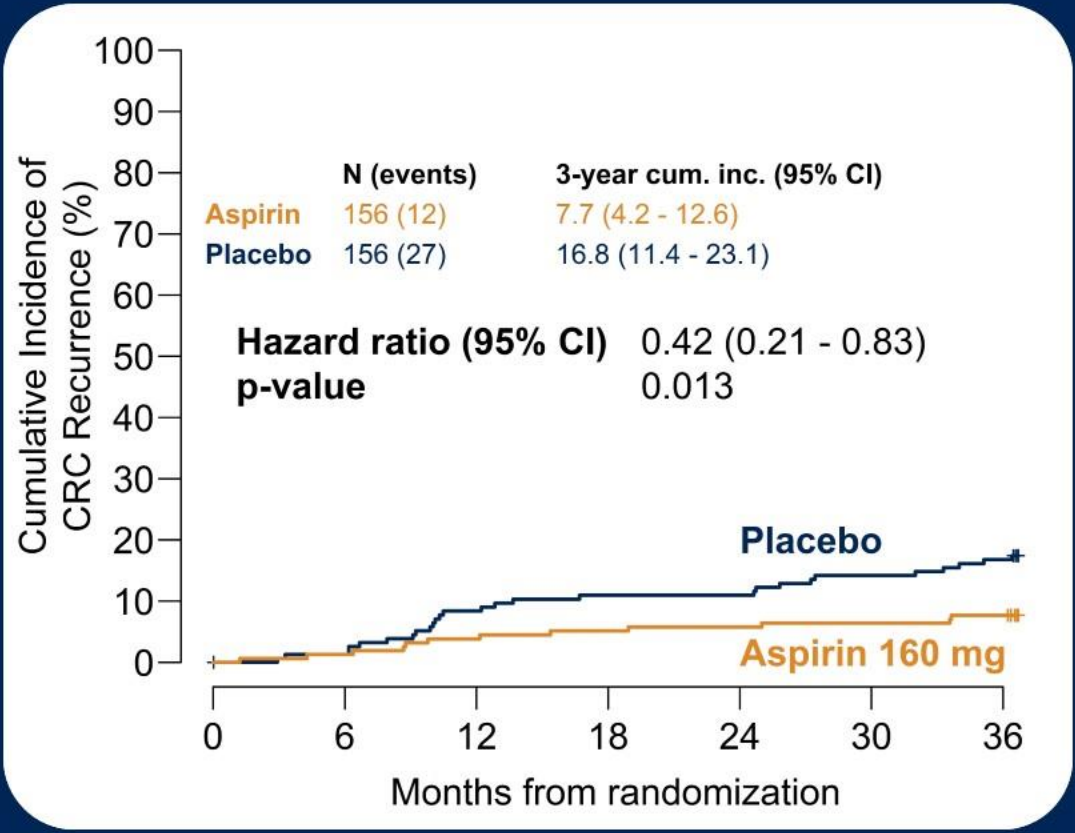
PRESENTED BY: Anna Martling: Low-Dose Aspirin Reduces Recurrence Rate in Colorectal Cancer Patients with PI3K Pathway Alterations: 3-Year Results from a Randomized Placebo-Controlled Trial (Abstract Number: LBA125)

Primary Outcome: CRC Recurrence

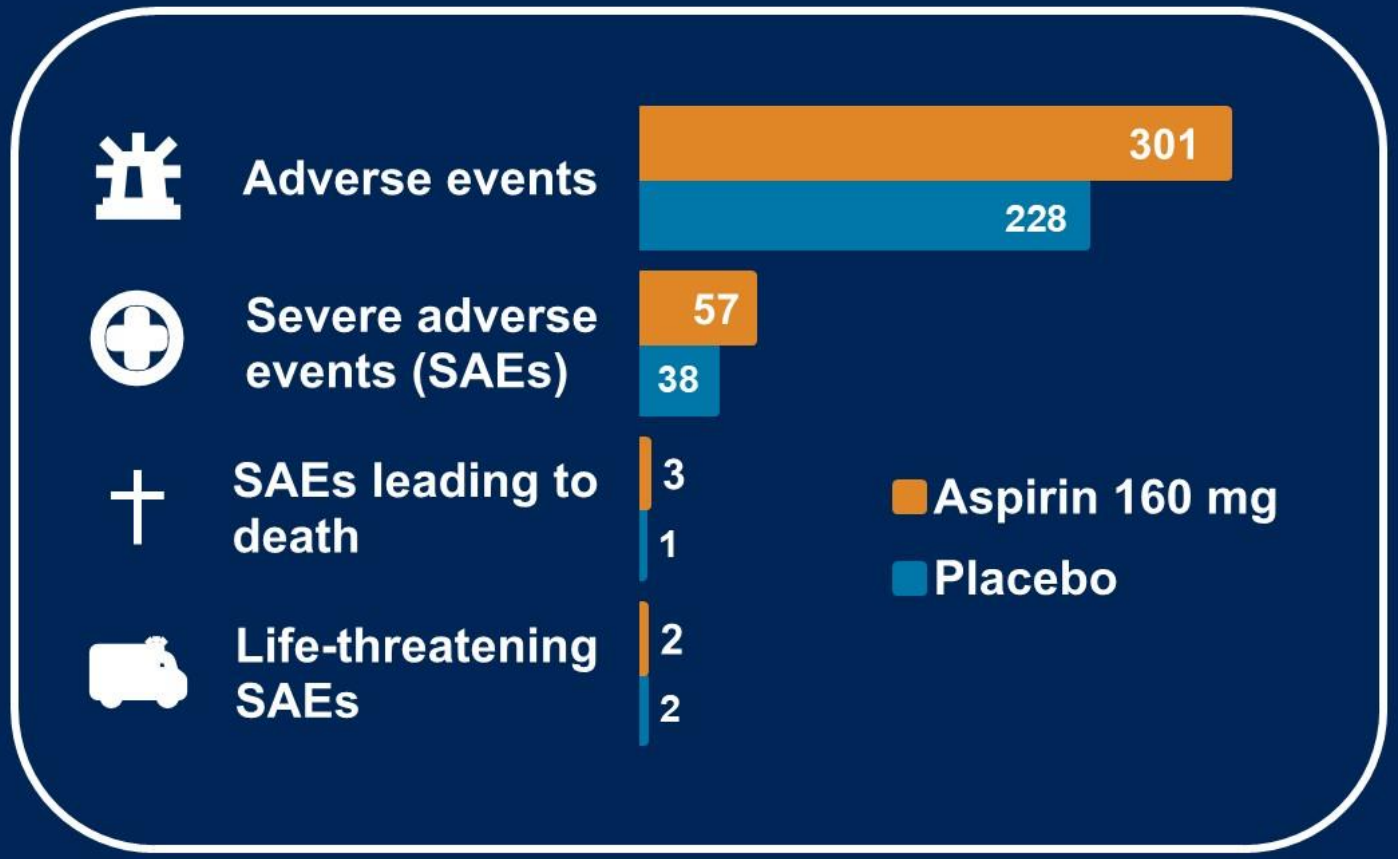
Group A (PIK3CA Exons 9/20)



Group B (PIK3R1/PTEN/Other PIK3CA)



Safety



Most common SAEs (N):	Aspirin 160 mg	Placebo
Late post-operative Complication	15	8
Deep vein Thrombosis	9	7
Embolism	6	4
Infection	4	4
Heart disease	4	3
Inflammatory Disorder	3	4
Hemorrhage	4	0

À retenir

- ASA 160mg diminue 50% taux récidive CCR opéré avec mut PIK3
- Peut aider 1/3 des patients opérés
- Médicament accessible, pas cher
- Importance des analyses moléculaires au diagnostic

Plan

- Colon métastatique 1e ligne
  - Mutation BRAF: BREAKWATER
  - dMMR/MSI-H: CM-8HW
    Sténose post I-O
- Colon adjuvant
  - PI3K: ALASCCA
- GI haut
  - ADK oesophage périop: chimio vs RCT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 23, 2025 VOL. 392 NO. 4

Perioperative Chemotherapy or Preoperative Chemoradiotherapy in Esophageal Cancer

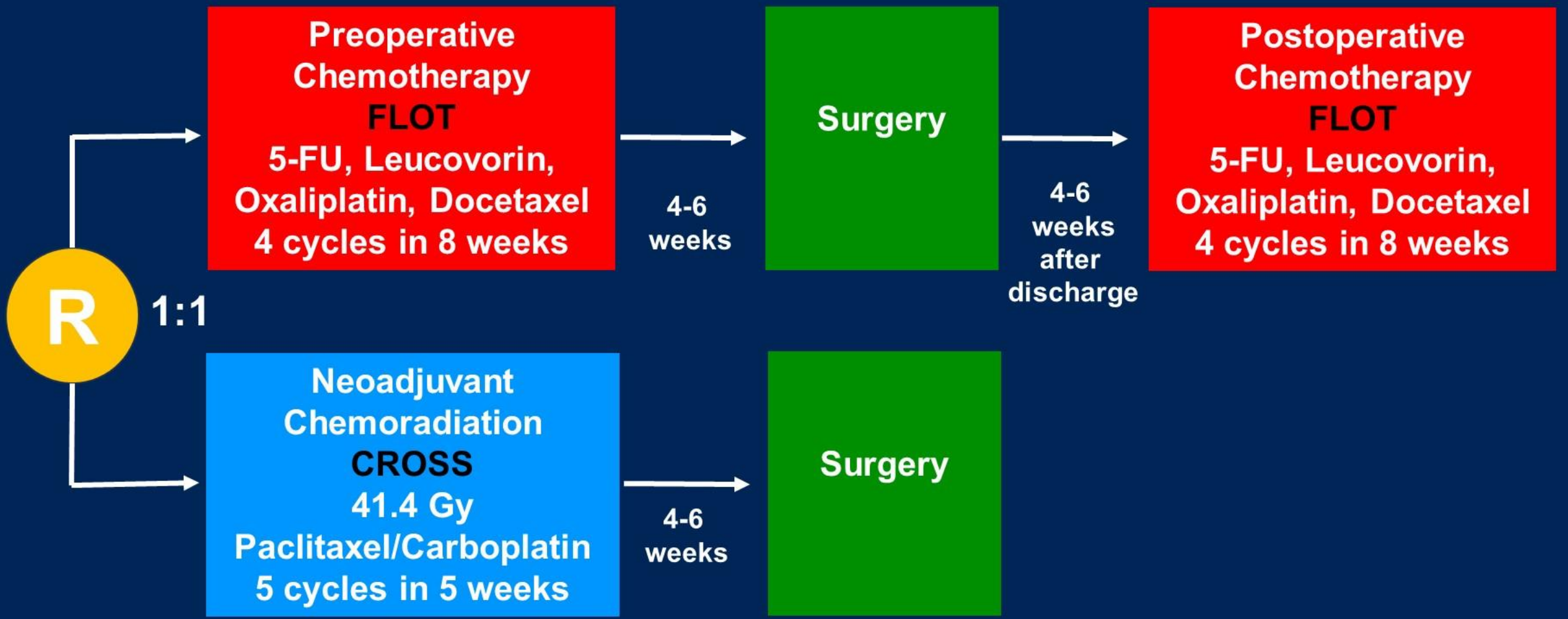
J. Hoeppner, T. Brunner, C. Schmoor, P. Bronsert, B. Kulemann, R. Claus, S. Utzolino, J.R. Izbicki, I. Gockel, B. Gerdes, M. Ghadimi, B. Reichert, J.F. Lock, C. Bruns, E. Reitsamer, M. Schmeding, F. Benedix, T. Keck, G. Folprecht, P. Thuss-Patience, U.P. Neumann, A. Pascher, D. Imhof, S. Daum, T. Strieder, C. Krautz, S. Zimmermann, J. Werner, R. Mahlberg, G. Illerhaus, P. Grimminger, and F. Lordick

Current Treatment of Resectable Esophageal Adenocarcinoma (EAC)

- cT1<sm1, cN0: Endoscopic resection alone
- cT1b/2, cN0: Surgery alone
- cT2-4a,cN+/-: Neoadjuvant chemoradiation plus surgery
- cT2-4a,cN+/-: Perioperative chemotherapy plus surgery

1. Van Hagen NEJM 2012,
2. Cunningham NEJM 2006
3. Al-Batran Lancet 2019

ESOPEC Trial Scheme



Key Trial Endpoints

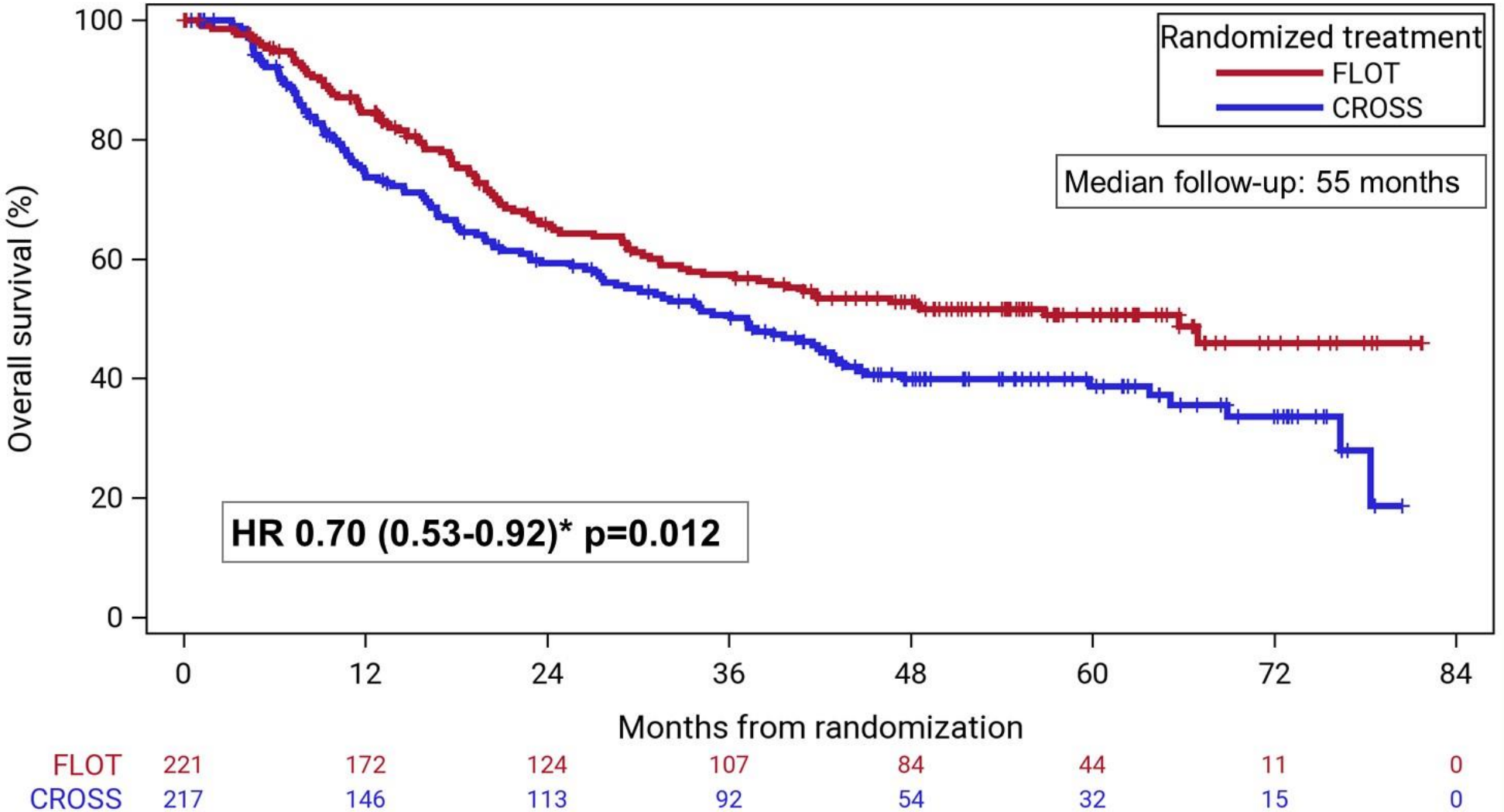
Primary Endpoint

- Overall survival (OS)

Secondary Endpoints

- Progression free survival (PFS)
- Postoperative pathological stage
- Postoperative complications
- Adverse events
- Recurrence free survival
- Site of tumor recurrence
- Quality of life

Overall Survival - ITT Population



	FLOT	CROSS
Events	97	121
Median OS time (months)	66 95% CI 36 – n.e	37 95% CI 28 – 43
3-year OS rate	57.4%	50.7%
5-year OS rate	50.6%	38.7%

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

FLOT vs CROSS

- Fin du débat
- Rôle immunothérapie en péri-opératoire?

Methods

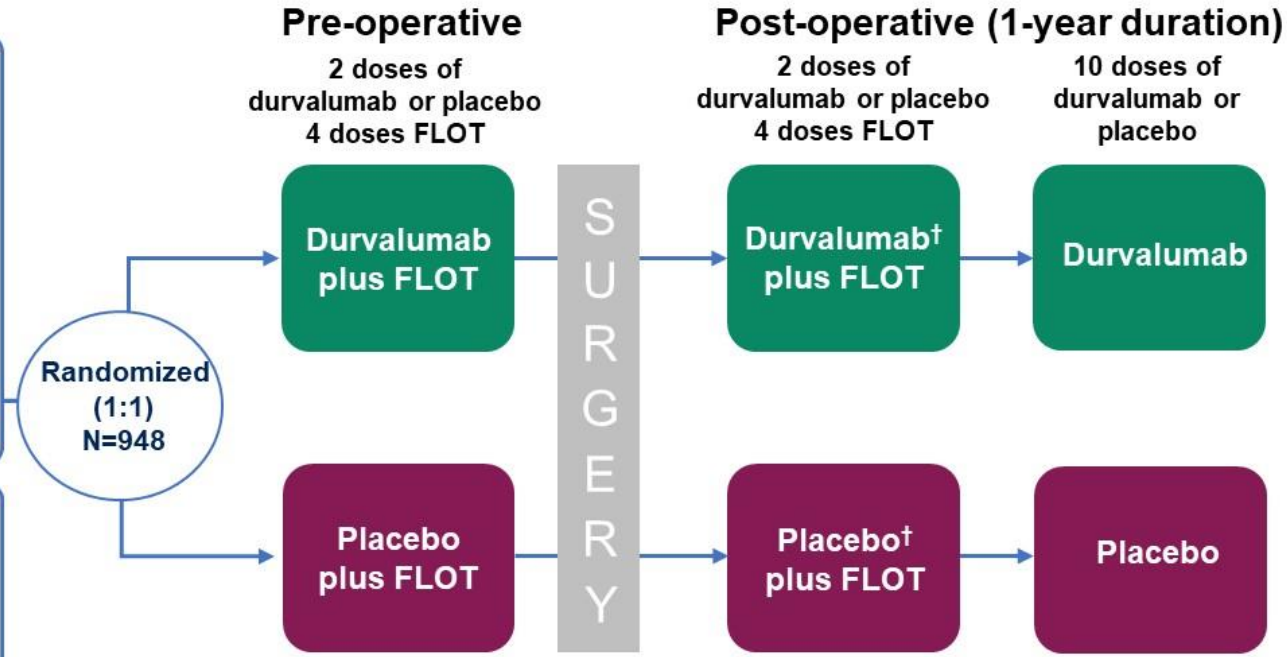
MATTERHORN is a global, Phase 3, randomized, double-blind, placebo-controlled study

Study population

- Gastric and GEJ adenocarcinoma
- Stage II, III and IVA (>T2 N0-3 M0 or T0-4 N1-3 M0)
- No evidence of metastasis
- No prior therapy
- ECOG PS 0 or 1
- Global enrolment from Asia, Europe, North America, and South America

Stratification factors

- Geographic region: Asia versus non-Asia
- Clinical lymph node status: positive versus negative
- PD-L1 status: TAP <1% versus TAP ≥1%*



Primary objective:

- EFS

Key secondary objectives:

- Central review of pathological complete response by modified Ryan criteria
- OS

Durvalumab 1500 mg or placebo Q4W (Day 1) plus FLOT Q2W (Days 1 and 15) for 4 cycles (2 doses of durvalumab or placebo plus 4 doses of FLOT pre- and post-operative), followed by durvalumab or placebo Q4W (Day 1) for 10 further cycles

FLOT: 5-fluorouracil 2600 mg/m², oxaliplatin 85 mg/m², docetaxel 50 mg/m², leucovorin 200 mg/m² on Days 1 and 15 of a 4-week cycle for 2 cycles (4 doses) pre- and post-operative; durvalumab: 1500 mg on Day 1 of a 4-week cycle, 2 cycles (2 doses) of durvalumab or placebo pre- and post-operative, followed by 10 cycles (10 doses) of durvalumab or placebo on Day 1 of a 4-week cycle.
*Measured by VENTANA PD-L1 (SP263) assay. †Durvalumab or placebo monotherapy may be continued if post-operative FLOT is discontinued due to toxicity.
ECOG, Eastern Cooperative Oncology Group; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; GEJ, gastrooesophageal junction; OS, overall survival; PD-L1, programmed cell death ligand-1; PS, performance status; Q2W, every 2 weeks; Q4W, every 4 weeks; TAP, tumor area positivity.

Plenary Session

Add to Agenda

Plenary Session

Primary Track: Special Sessions

1 juin – 13:00 HAC Hall B1 |

Event-free survival (EFS) in MATTERHORN: A randomized, phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel chemotherapy (FLOT) in resectable gastric/gastroesophageal junction cancer (GC/GEJC).

15:13 HAC Yelena Y. Janjigian, MD Abstract LBA5

À retenir

- CCR stade 4
  - mutBRAF (10%): nouveau combo qui double la survie
  - dMMR/MSI (5%): nouveau combo qui (peut) guérit
  - Sténose colique post-immunothérapie = nouveau
- CCR stade 1-3
  - 2 aspirines si mut PIK3, réduit récidive de moitié
- Importance des biomarqueurs pour tous CCR
- ADK œsophage opérable: chimio d'abord +/- IO

Merci!