Les 3 papiers qui ont changé notre pratique en 2026 ? En oncologie digestive

22ème journée de gastro-entérologie de l'hôpital Cochin

Samedi 20 juin 2026

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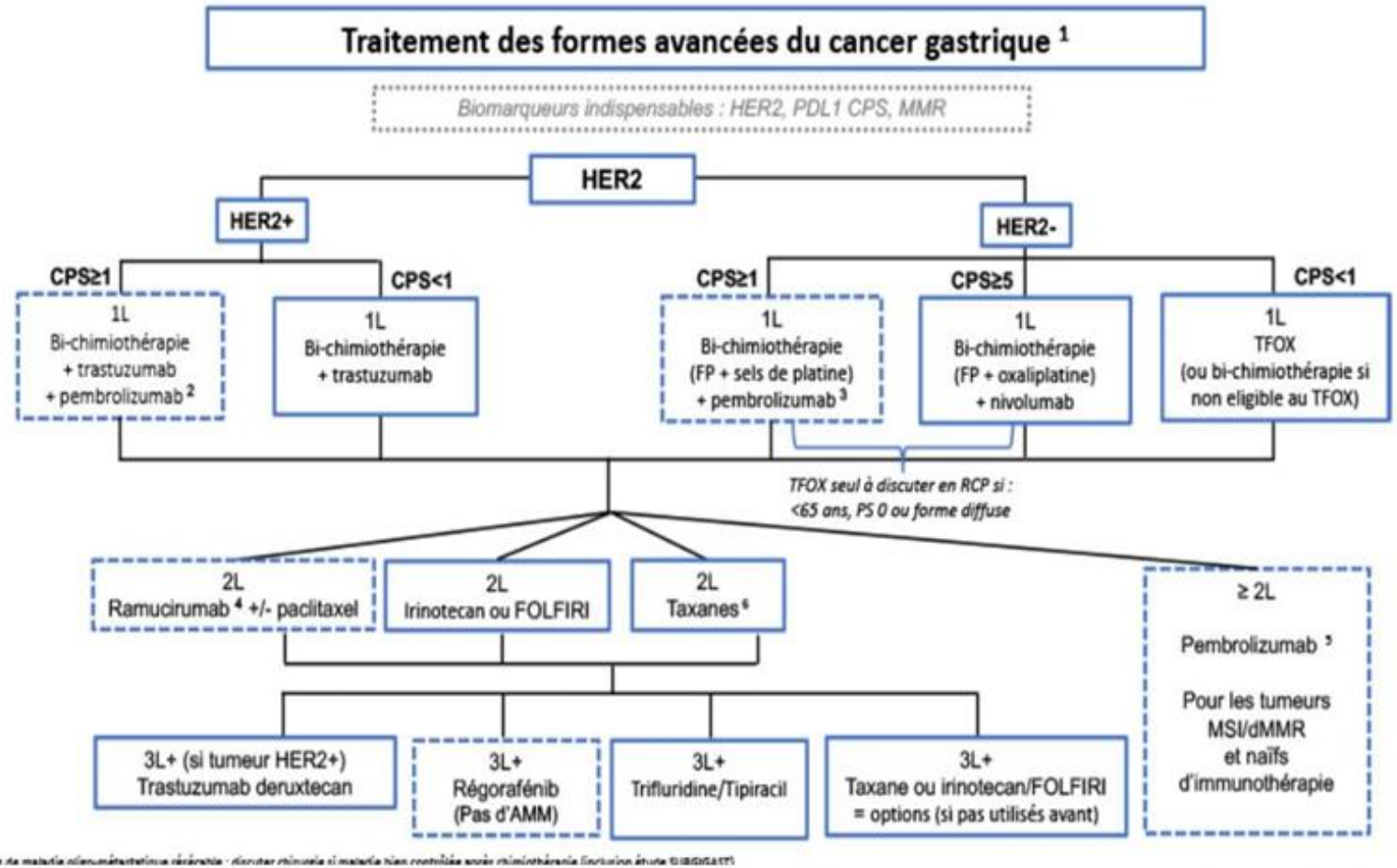
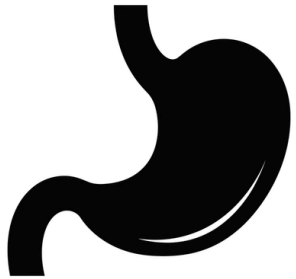
Les 3 papiers qui ont changé notre pratique en 2026 ?
En oncologie digestive


Traitement des formes avancées du cancer gastrique 1
Biomarqueurs indispensables : HER2, PDL1 CPS, MMR
HER2
HER2+
HER2-
CPS≥1
CPS<1
CPS≥1
CPS≥5
CPS<1
1L
Bi-chimiothérapie
+ trastuzumab
+ pembrolizumab 2
1L
Bi-chimiothérapie
+ trastuzumab
1L
Bi-chimiothérapie
(FP + sels de platine)
+ pembrolizumab 3
1L
Bi-chimiothérapie
(FP + oxaliplatine)
+ nivolumab
1L
TFOX
(ou bi-chimiothérapie si
non eligible au TFOX)
TFOX seul à discuter en RCP si :
<65 ans, PS 0 ou forme diffuse
2L
Ramucirumab 4 +/- paclitaxel
2L
Irinotecan ou FOLFIRI
2L
Taxanes 5
≥ 2L
Pembrolizumab 3
Pour les tumeurs
MSI/dMMR
et naïfs
d'immunothérapie
3L+ (si tumeur HER2+)
Trastuzumab deruxtecan
3L+
Régorafénib
(Pas d'AMM)
3L+
Trifluridine/Tipiracil
3L+
Taxane ou irinotecan/FOLFIRI
= options (si pas utilisés avant)

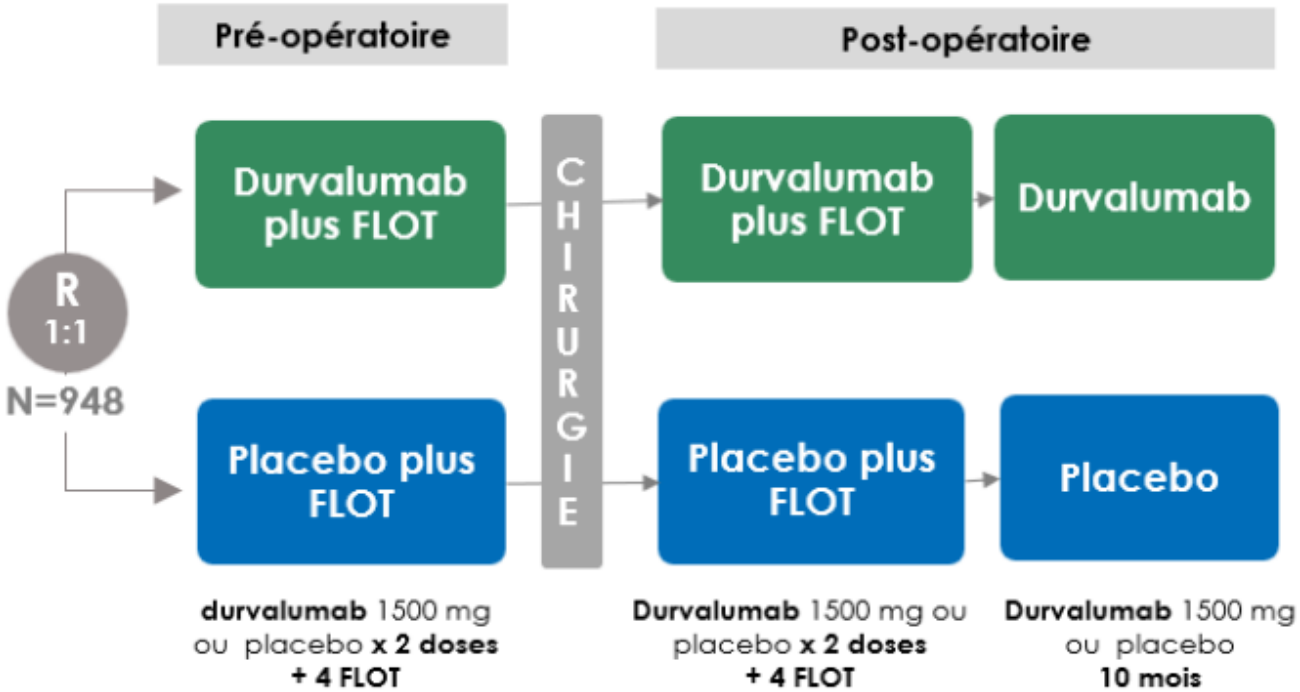


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 17, 2025 VOL. 393 NO. 3

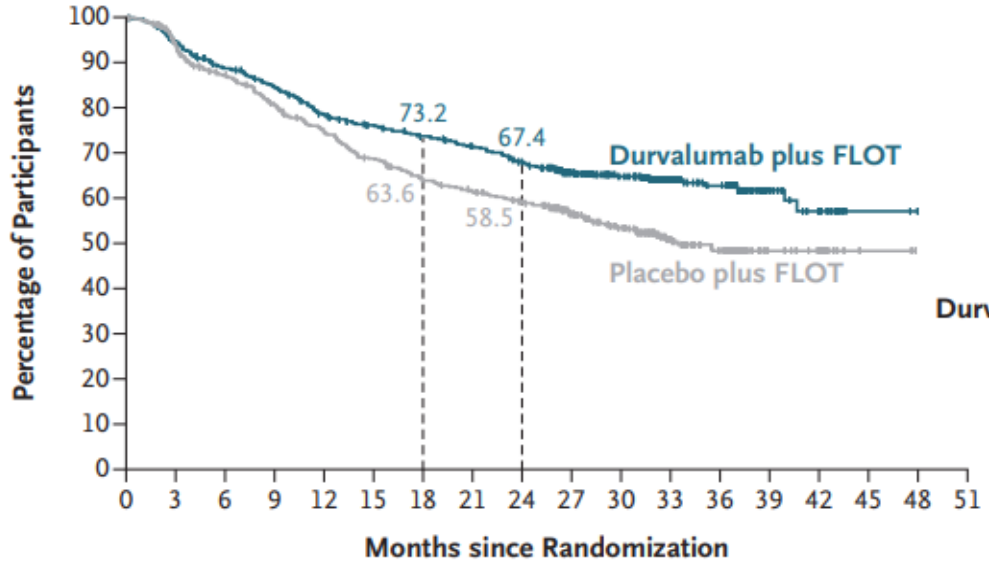
Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer

Y.Y. Janjigian,[1] S.-E. Al-Batran,[2] Z.A. Wainberg,[3] K. Muro,[4] D. Molena,[5] E. Van Cutsem,[6] W.J. Hyung,[7] L. Wyrwicz,[8] D.-Y. Oh,[9] T. Omori,[10] M. Moehler,[11] M. Garrido,[12] S.C.S. Oliveira,[13] M. Liberman,[14] V.C. Oliden,[15] E.C. Smyth,[16] A. Stein,[17] M. Bilici,[18] M.L. Alvarenga,[19] V. Kozlov,[20] F. Rivera,[21] A. Kawazoe,[22] O. Serrano,[23] E. Heilbron,[24] A. Negro,[24] J.F. Kurland,[24] and J. Tabernero,[25] for the MATTERHORN Investigators*



Objectif principal: survie sans récidive

Objectifs secondaires: SG, réponse histologique complète



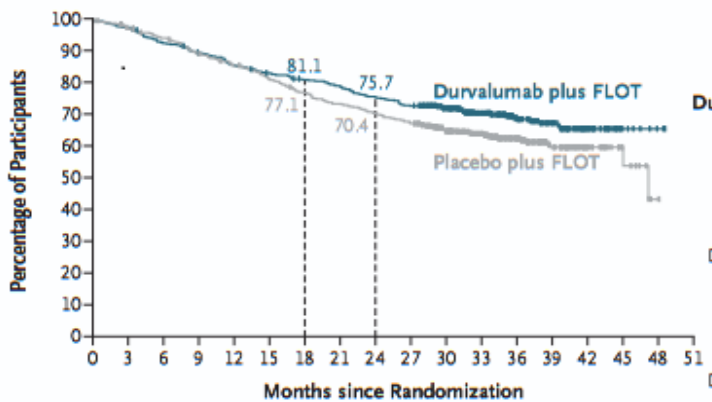
	No. of Participants with Event/ Total No. of Participants (%)	Median Event-free Survival (95% CI)
		mo
Durvalumab plus FLOT	167/474 (35.2)	NR (40.74–NR)
Placebo plus FLOT	218/474 (46.0)	32.8 (27.86–NR)

Stratified hazard ratio for event or death, 0.71 (95% CI, 0.58–0.86)
P<0.001 by stratified log-rank test

No. at Risk

Durvalumab plus FLOT	474	436	404	381	351	334	320	307	288	234	187	107	88	33	20	2	1	0
Placebo plus FLOT	474	429	392	360	329	302	278	264	249	202	160	89	65	26	21	2	1	0

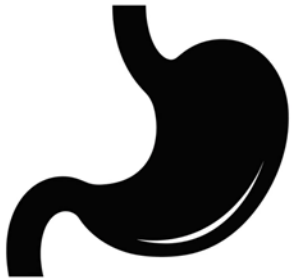
A Overall Survival

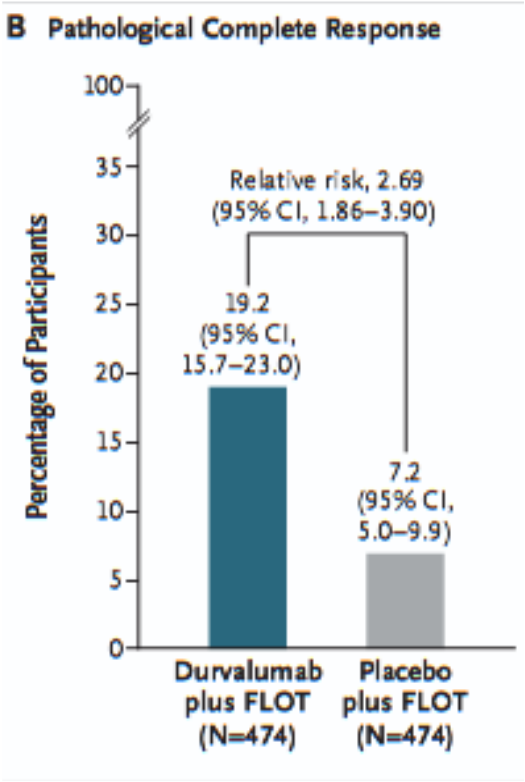


	No. of Deaths/Total No. of Participants (%)	Median Overall Survival (95% CI)
		mo
Durvalumab plus FLOT	145/474 (30.6)	NR (NR–NR)
Placebo plus FLOT	176/474 (37.1)	47.2 (45.1–NR)
	P=0.03 by stratified log-rank test (exceeding significance threshold of P<0.0001)	
0 to 12 Months		
Durvalumab plus FLOT	67/474 (14.1)	NR (NR–NR)
Placebo plus FLOT	67/474 (14.1)	NR (NR–NR)
	Hazard ratio for death, 0.99 (95% CI, 0.70 to 1.39)	
≥12 Months		
Durvalumab plus FLOT	78/403 (19.4)	NR (NR–NR)
Placebo plus FLOT	109/395 (27.6)	NR (45.1–NR)
	Hazard ratio for death, 0.67 (95% CI, 0.50 to 0.90)	

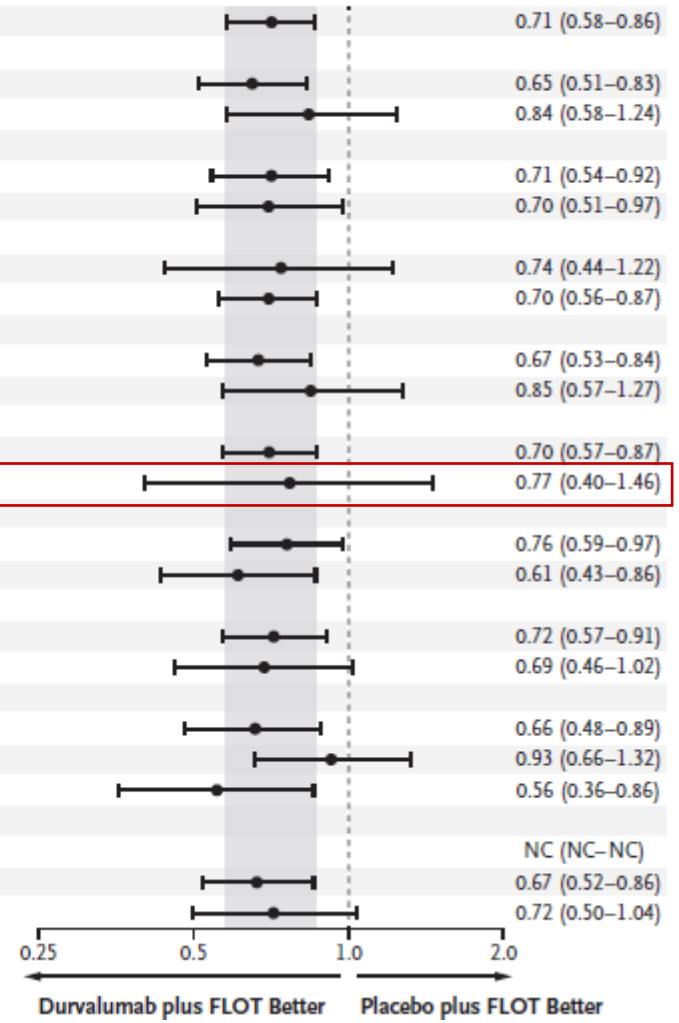
No. at Risk

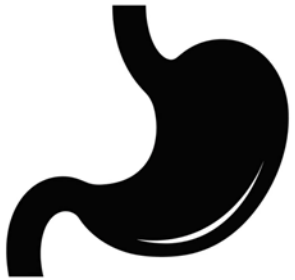
Durvalumab plus FLOT	474	464	438	422	403	389	376	367	351	338	293	205	143	80	38	8	2	0
Placebo plus FLOT	474	457	439	414	395	374	354	337	323	309	262	197	128	72	33	11	2	0





Subgroup	Durvalumab plus FLOT	Placebo plus FLOT	Hazard Ratio for Event (95% CI)
	no. of participants with event/total no. of participants (%)		
All participants	167/474 (35.2)	218/474 (46.0)	0.71 (0.58–0.86)
Sex			
Male	111/326 (34.0)	168/356 (47.2)	0.65 (0.51–0.83)
Female	56/148 (37.8)	50/118 (42.4)	0.84 (0.58–1.24)
Age at randomization			
<65 yr	104/291 (35.7)	123/265 (46.4)	0.71 (0.54–0.92)
≥65 yr	63/183 (34.4)	95/209 (45.5)	0.70 (0.51–0.97)
Geographic region			
Asia	26/90 (28.9)	35/90 (38.9)	0.74 (0.44–1.22)
Rest of the world	141/384 (36.7)	183/384 (47.7)	0.70 (0.56–0.87)
Clinical lymph-node status			
Positive	121/334 (36.2)	165/333 (49.5)	0.67 (0.53–0.84)
Negative	45/137 (32.8)	52/140 (37.1)	0.85 (0.57–1.27)
PD-L1 expression, according to TAP			
≥1%	150/426 (35.2)	197/427 (46.1)	0.70 (0.57–0.87)
<1%	17/48 (35.4)	21/47 (44.7)	0.77 (0.40–1.46)
Primary tumor location			
Gastric	114/324 (35.2)	139/316 (44.0)	0.76 (0.59–0.97)
Gastroesophageal junction	53/150 (35.3)	79/158 (50.0)	0.61 (0.43–0.86)
ECOG performance-status score			
0	118/337 (35.0)	169/366 (46.2)	0.72 (0.57–0.91)
1	49/137 (35.8)	49/108 (45.4)	0.69 (0.46–1.02)
Histologic type			
Intestinal	72/245 (29.4)	97/238 (40.8)	0.66 (0.48–0.89)
Diffuse	63/130 (48.5)	63/119 (52.9)	0.93 (0.66–1.32)
Indeterminate	32/99 (32.3)	58/117 (49.6)	0.56 (0.36–0.86)
Microsatellite instability status			
High	8/25 (32.0)	6/24 (25.0)	NC (NC–NC)
Not high	106/301 (35.2)	148/310 (47.7)	0.67 (0.52–0.86)
Not evaluable or missing	53/148 (35.8)	64/140 (45.7)	0.72 (0.50–1.04)





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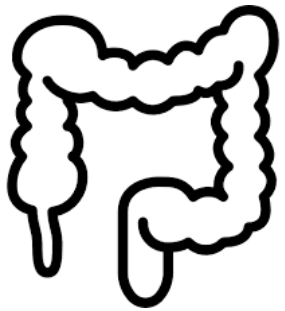
- FLOT +DURVALUMAB péri-opératoire avec DURVALUMAB seul jusqu'à 1 an de traitement = nouveau traitement de référence
- Si patient trop fragile : FOLFOX +/- immunothérapie ou schéma CROSS si jonction oesogastrique



ORIGINAL ARTICLE

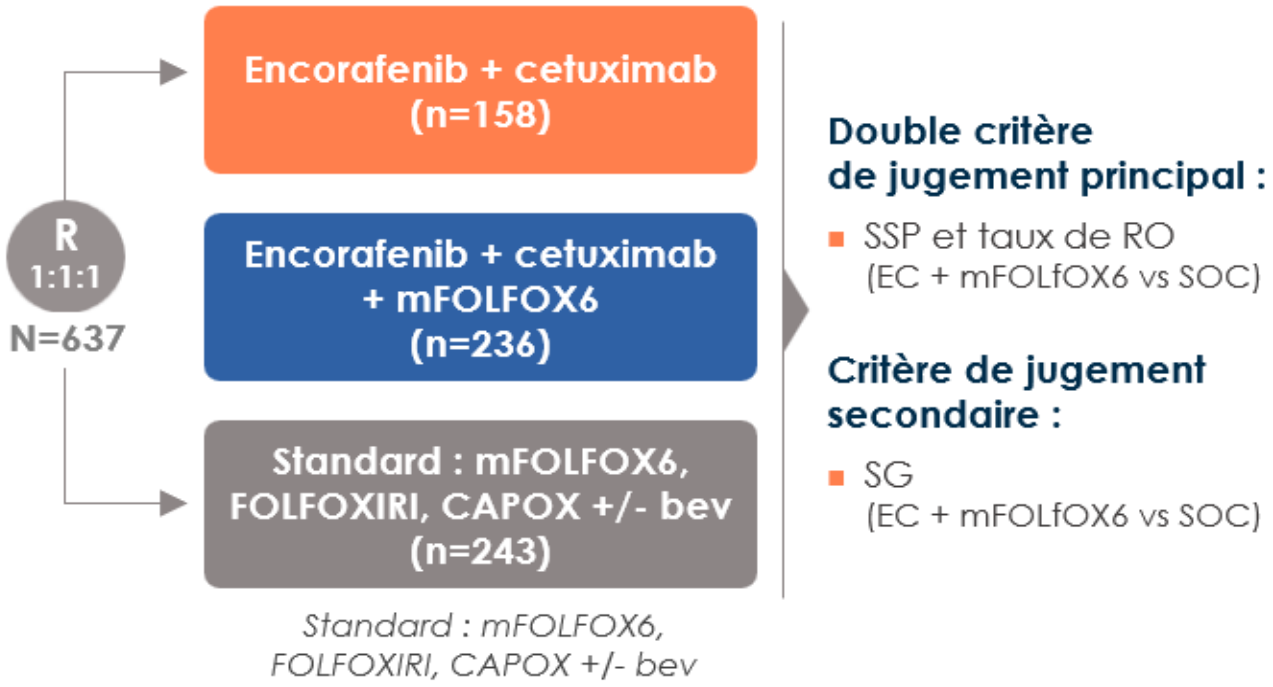
Encorafenib, Cetuximab, and mFOLFOX6 in *BRAF*-Mutated Colorectal Cancer

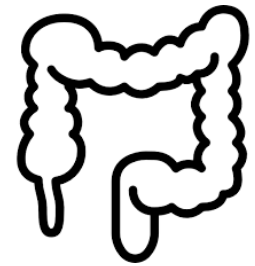
E. Elez,[1,2] T. Yoshino,[3] L. Shen,[4] S. Lonardi,[5] E. Van Cutsem,[6,7] C. Eng,[8] T.W. Kim,[9] H.S. Wasan,[10] J. Desai,[11,12] F. Ciardiello,[13] R. Yaeger,[14] T.S. Maughan,[15] V.K. Morris,[16] C. Wu,[17] T. Usari,[18] R. Laliberte,[19] S.S. Dychter,[20] X. Zhang,[21] J. Tabernero,[1,2,22] and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

Adénocarcinome colique métastatique muté BRAF V600E

8 à 12 % des CCRM

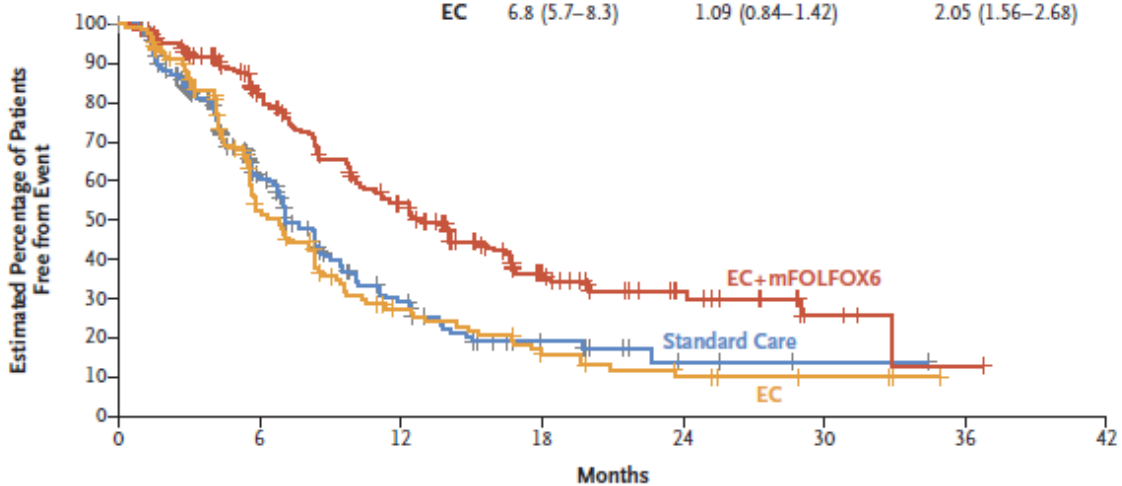
L1 : FOLFOX + Bevacizumab
L2 : encorafenib + cetuximab
(étude Beacon –NEJM 2019)



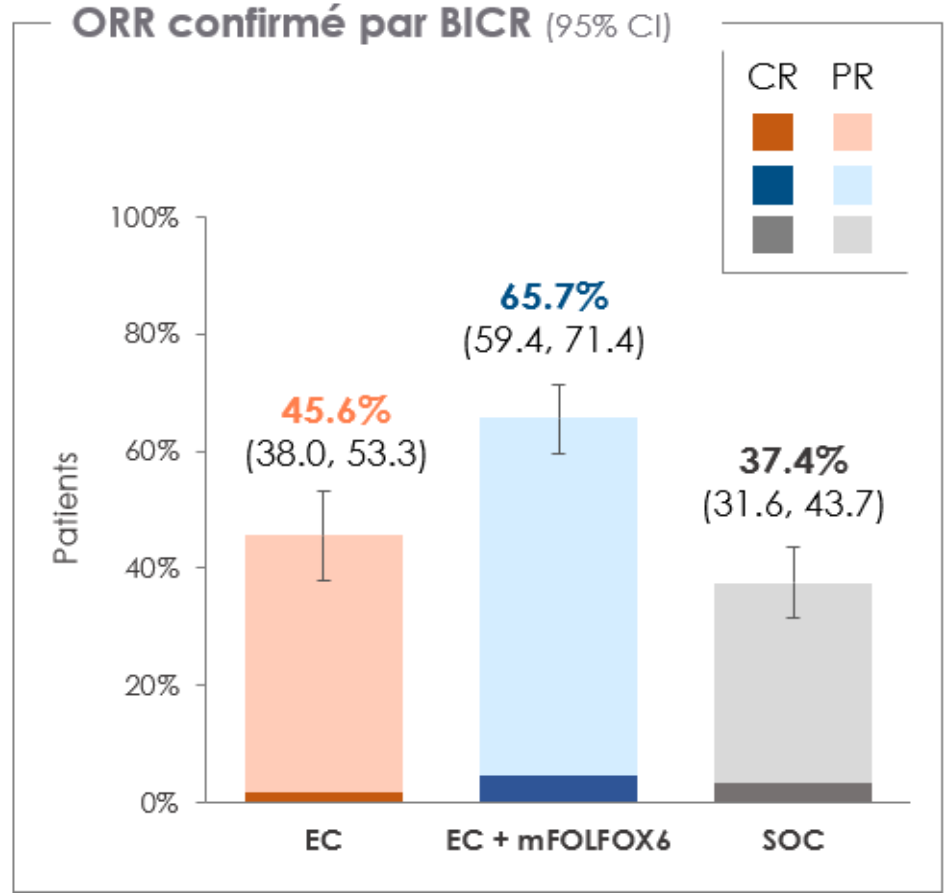


A Progression-free Survival

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



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



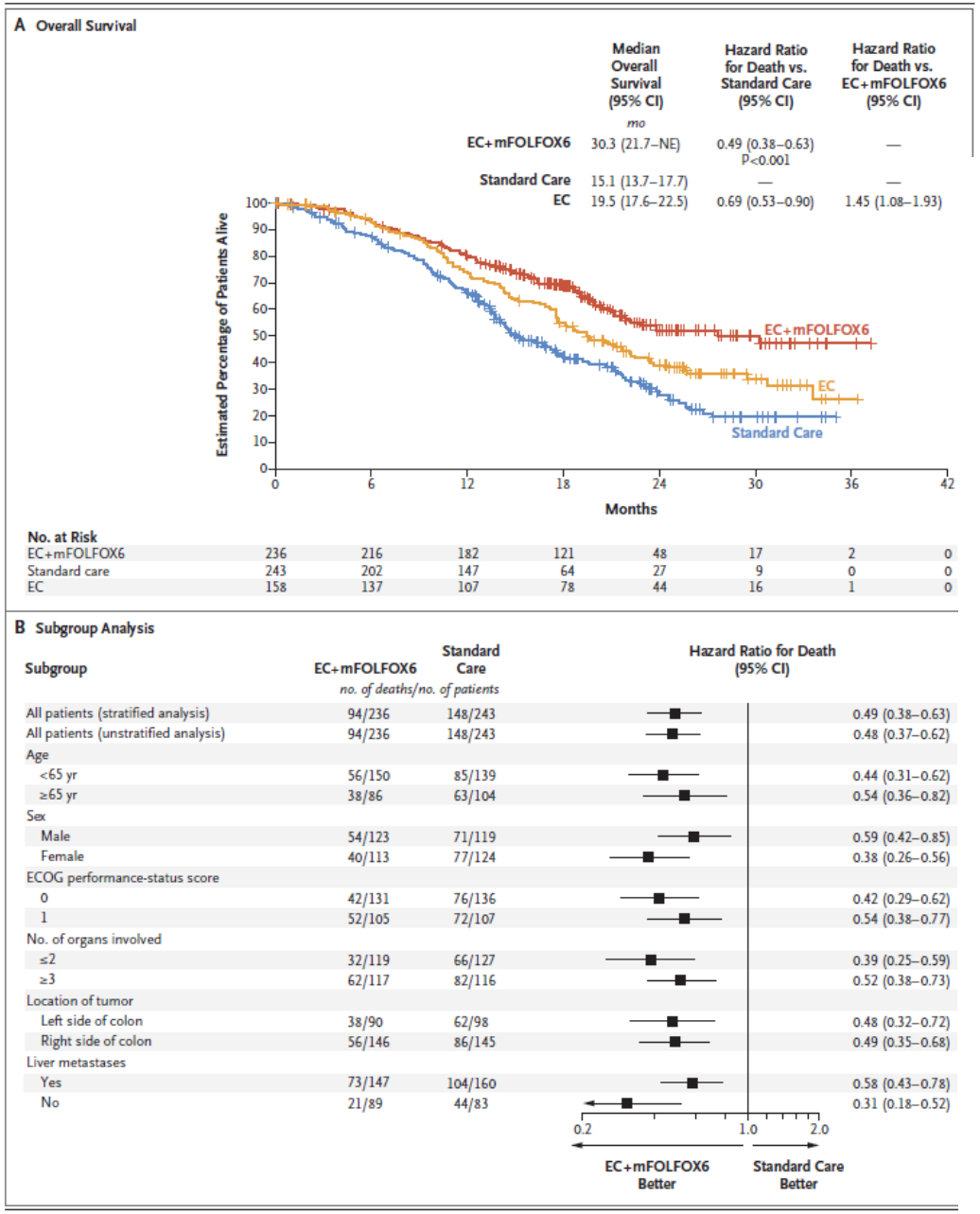


Table 2. Most Frequent Adverse Events during Treatment (Safety Analysis Set).*

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)

* The safety analysis set included all the patients who received at least one dose of trial drug. The most frequent adverse events during treatment shown here are those reported in more than 20% of the patients in the EC+mFOLFOX6 group.

ASCO 26 : avec le FOLFIRI ?

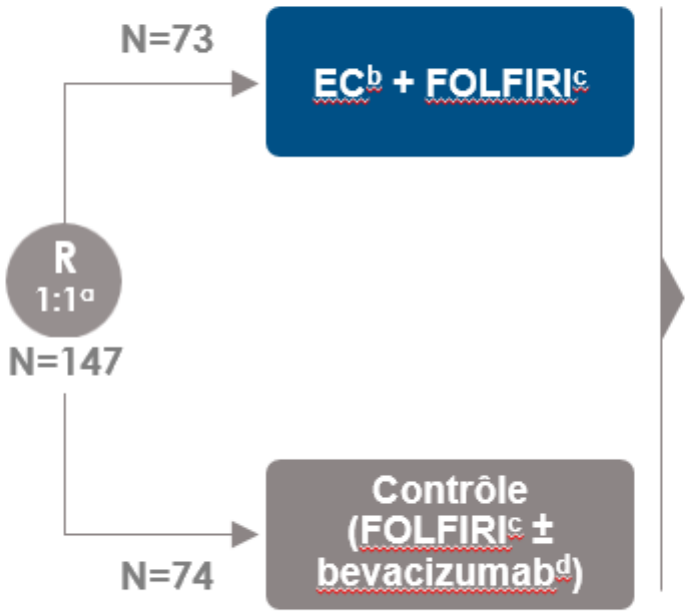
BREAKWATER Cohorte 3

Critères d'inclusion

- Âge ≥16 ans (ou ≥18 ans selon le pays)
- Pas de traitement systémique antérieur pour la maladie métastatique
- Maladie mesurable (RECIST 1.1)
- BRAF V600E-mutant mCRC by local ou test en laboratoire central
- ECOG PS 0 or 1
- Fonction médullaire, hépatique et rénale adéquate

Exclusion

- Inhibiteurs BRAF ou EGFR antérieurs
- Métastases cérébrales symptomatiques
- MSI-H/dMMR tumeurs(sauf si les patients n'étaient pas éligibles aux inhibiteurs de points de contrôle immunitaires en raison d'une condition médicale préexistante)
- Présence d'une mutation RAS



Stratifié selon le PS ECOG

Objectif primaire :

- ORR par BICR:

Objectifs secondaires clés :

- SSP par BICR

Objectifs secondaires :

- SG

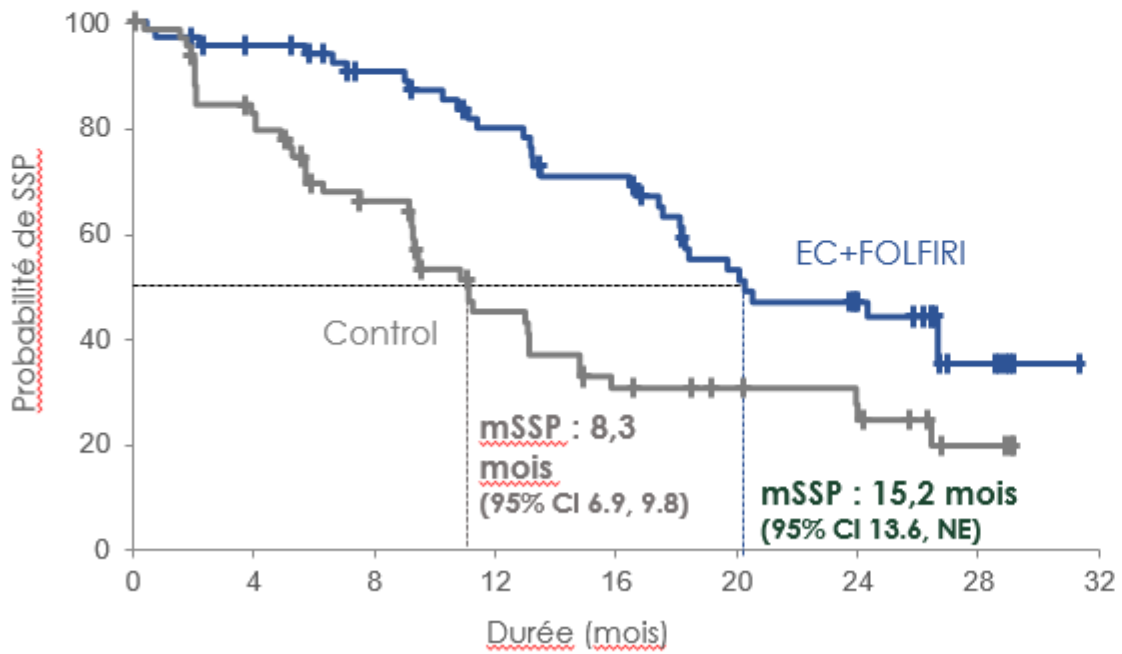
Présentée ici : analyse finale de la SSP (relecture centralisée), de la SG et de la tolérance

ASCO 26 : avec le FOLFIRI ?

Taux de réponse (relecture centralisée): **64.4% vs 39.2%;** OR: 2.756 (95% CI 1.420, 5.348); *p*=0.001

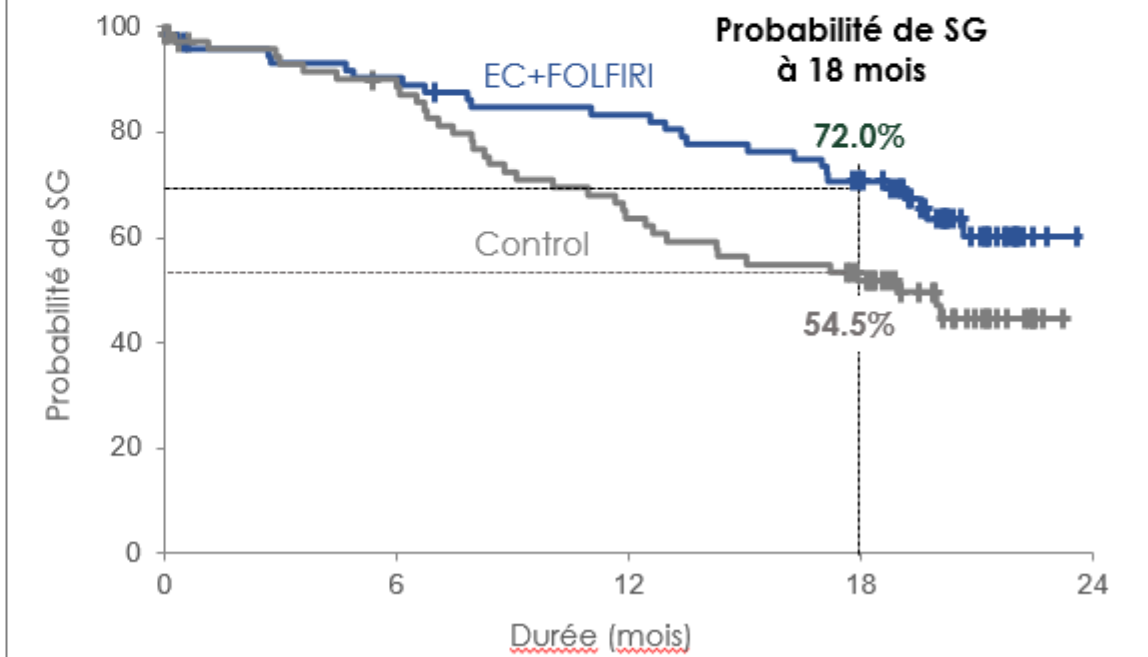
SSP

	Évènements N (%)	HR (95% CI)	*valeur-p*
EC+FOLFIRI (n=73)	32 (43,8)	0,44 (0,27-0,70)	0,0002 unilatéral
Control (n=74)	42 (56,8)		



SG

	Évènements N (%)	HR (95% CI)	HR (95% CI)
EC+FOLFIRI (n=73)	25 (34,2)	NE (0,21-NE)	0,56 (0,34-0,94)
Control (n=74)	35 (47,3)	20,3 (13,2-NE)	



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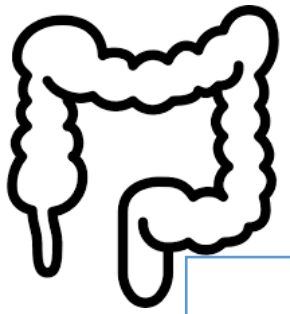
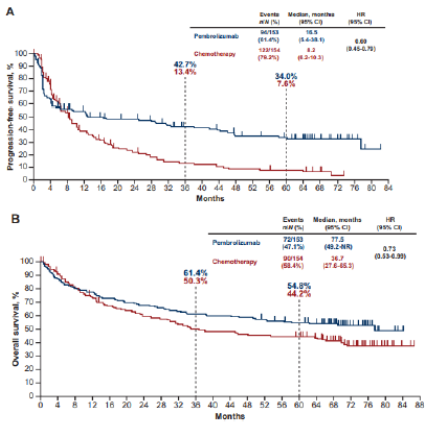
- La double thérapie ciblée encorafenib + cetuximab marche aussi bien avec le FOLFIRI qu'avec le FOLFOX (malgré l'interaction démontrée SN38/encorafénib sur le CytP450)
- La tolérance de ces associations est acceptable
- le risque de rechute après chimiothérapie adjuvante par FOLFOX étant deux fois supérieur chez les patients BRAFmutés : alternative du FOLFIRI +++



Adénocarcinome colique métastatique dMMR/MSI

4 à 7% des CCRm

L1 : Pembrolizumab en monothérapie
(étude Keynote 177, André T et al., NEJM 2020)
30% de « progresseurs rapides »

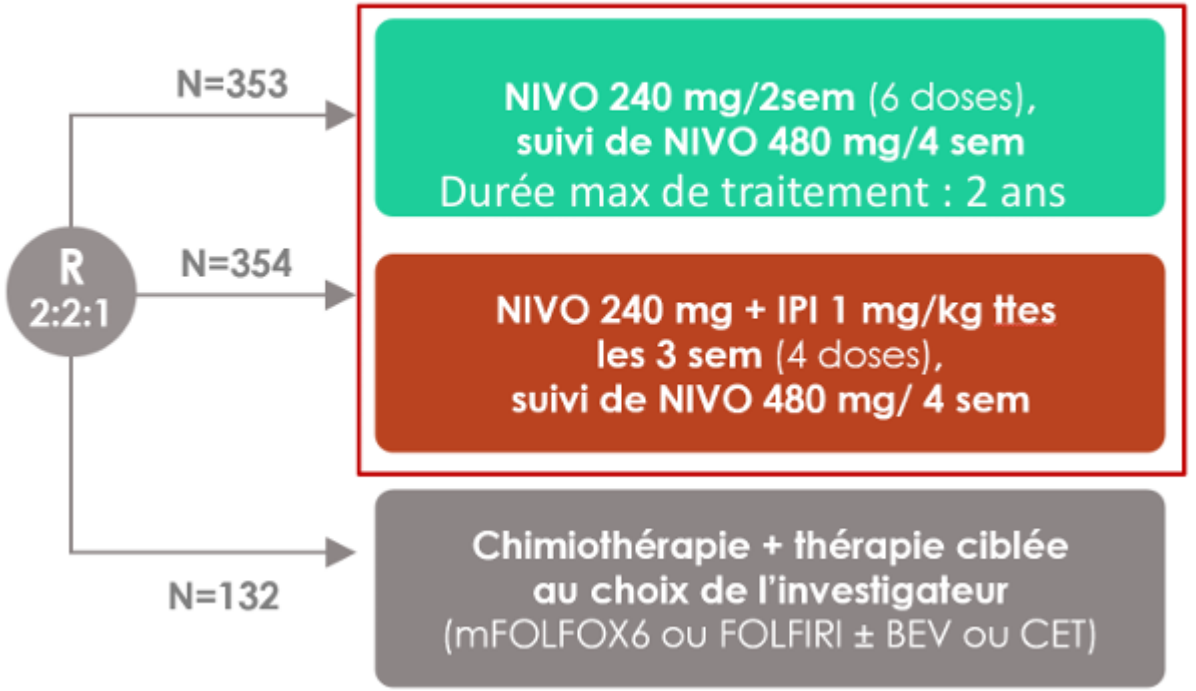


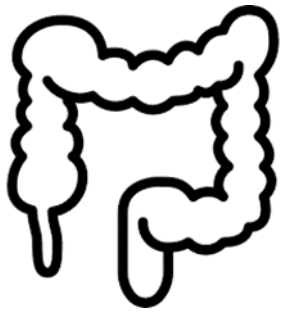
André, Lancet 2025, actualisation à 5 ans de KEYNOTE 177

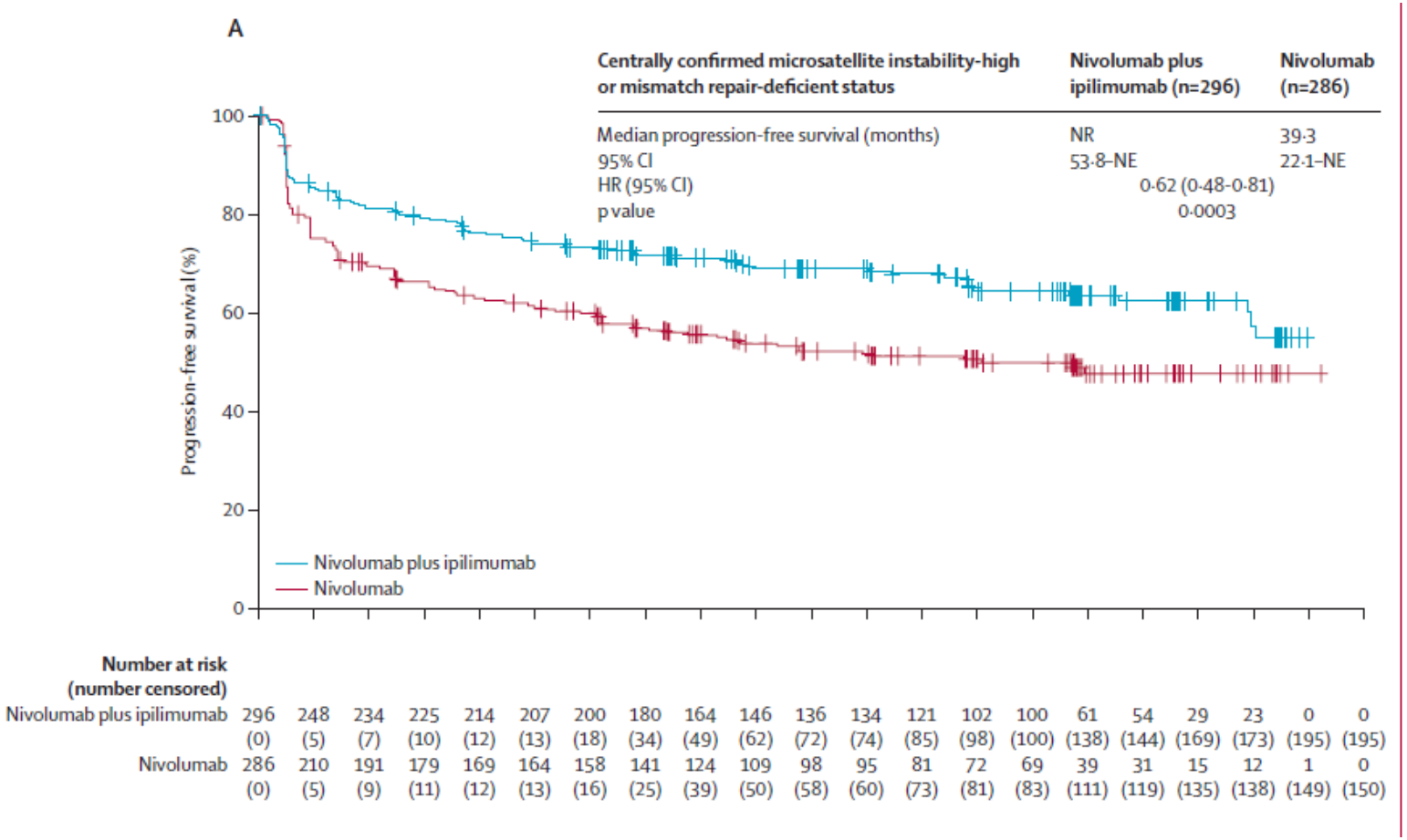
Nivolumab plus ipilimumab versus nivolumab in microsatellite instability-high metastatic colorectal cancer (CheckMate 8HW): a randomised, open-label, phase 3 trial

Thierry André, Elena Elez, Heinz-Josef Lenz, Lars Henrik Jensen, Yann Touchefeu, Eric Van Cutsem, Rocio Garcia-Carbonero, David Tougeron, Guillermo Ariel Mendez, Michael Schenker, Christelle de la Fouchardiere, Maria Luisa Limon, Takayuki Yoshino, Jin Li, Jose Luis Manzano Mozo, Laetitia Dahan, Giampaolo Tortora, Myriam Chalabi, Eray Goekkurt, Maria Ignez Braghiroli, Rohit Joshi, Timucin Cil, Francine Aubin, Elvis Cela, Tian Chen, Ming Lei, Lixian Jin, Steven I Blum, Sara Lonardi

Lancet 2025; 405 : 383-95





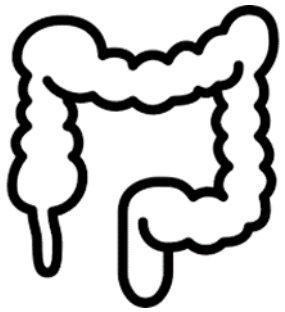


	Nivolumab plus ipilimumab group (n=296)	Nivolumab group (n=286)	p value
Objective response rate (95% CI)	209 (71%) [65–76]	165 (58%) [52–64]	0·0011
Best overall response			..
Complete response	90 (30%)	80 (28%)	..
Partial response	119 (40%)	85 (30%)	..
Stable disease	40 (14%)	53 (19%)	..
Progressive disease	30 (10%)	54 (19%)	..
Unevaluable	17 (6%)	14 (5%)	..
Median time to response, months (IQR)	2·8 (1·4–4·2)	2·8 (1·5–4·2)	..
Median duration of response, months (95% CI)	NR (NE)	NR (NE)	..

Data are n (%), unless otherwise indicated. NE=not estimable. NR=not reached.

Table 2: **Best overall response by blinded review in patients with centrally confirmed microsatellite instability-high or mismatch repair-deficient status**

	Nivolumab plus ipilimumab group (n=352)		Nivolumab group (n=351)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Any treatment-related adverse event	285 (81%)	78 (22%)	249 (71%)	50 (14%)
Treatment-related serious adverse event	65 (18%)	55 (16%)	29 (8%)	24 (7%)
Treatment-related adverse event leading to discontinuation of any drug in the regimen	48 (14%)	33 (9%)	21 (6%)	14 (4%)
Treatment-related deaths*	2 (1%)	..	1 (<1%)	..



Nivolumab plus ipilimumab versus nivolumab in microsatellite instability-high metastatic colorectal cancer (CheckMate 8HW): a randomised, open-label, phase 3 trial

Thierry André, Elena Elez, Heinz-Josef Lenz, Lars Henrik Jensen, Yann Touchefeu, Eric Van Cutsem, Rocio Garcia-Carbonero, David Tougeron, Guillermo Ariel Mendez, Michael Schenker, Christelle de la Fouchardiere, Maria Luisa Limon, Takayuki Yoshino, Jin Li, Jose Luis Manzano Mozo, Laetitia Dahan, Giampaolo Tortora, Myriam Chalabi, Eray Goekkurt, Maria Ignez Braghiroli, Rohit Joshi, Timucin Cil, Francine Aubin, Elvis Cela, Tian Chen, Ming Lei, Lixian Jin, Steven I Blum, Sara Lonardi

Remboursement de l'association Nivolumab + ipilimumab en 1ère ligne de CCRM dMMR /MSI
MAIS toxicité non négligeable à réserver aux patients OMS 0-1
Résultats de survie globale en attente

Merci de votre attention