Controverse

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ou bithérapie-TC selon le RAS ?

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Léa Clavel, HPJM, Lyon.

ORIGINAL ARTICLE

Initial Therapy with FOLFOXIR[I] [plus] Bevacizumab for Metastatic Colorec[tal...]

Fotios Loupakis, M.D., Ph.D., Chiara Cremolini, M.D., Gianl[uca...]
Sara Lonardi, M.D., Vittorina Zagonel, M.D., Lisa Salvat[...]
Enrico Cortesi, M.D., Gianluca Tomasello, M.D., Monica Ronzoni, M.D.,
Rosella Spadi, M.D., Alberto Zaniboni, M.D., Giuseppe Tonini, M.D.,
Angela Buonadonna, M.D., Domenico Amoroso, M.D., Silvana Chiara, M.D.,
Chiara Carlomagno, M.D., Ph.D., Corrado Boni, M.D., Giacomo Allegrini, M.D.,
Luca Boni, M.D., and Alfredo Falcone, M.D.

Upfront FOLFOXIRI plus bevacizumab and reintroduction after progression versus mFOLFOX6 plus bevacizumab followed by FOLFIRI plus bevacizumab in the treatment of patients with metastatic colorectal cancer (TRIBE2): a multicentre, open-label, phase 3, randomised, controlled trial

Chiara Cremolini, Carlotta Antoniotti, Daniele Rossini, Sara Lonardi, Fotios Loupakis, Filippo Pietrantonio, Roberto Bordonaro, Tiziana Pia Latiano, Emiliano Tamburini, Daniele Santini, Alessandro Passardi, Federica Marmorino, Roberta Grande, Giuseppe Aprile, Alberto Zaniboni, Sabina Murgioni, Cristina Granetto, Angela Buonadonna, Roberto Moretto, Salvatore Corallo, Stefano Cordio, Lorenzo Antonuzzo, Gianluca Tomasello, Gianluca Masi, Monica Ronzoni, Samantha Di Donato, Chiara Carlomagno, Matteo Clavarezza, Giuliana Ritorto, Andrea Mambrini, Mario Roselli, Samanta Cupini, Serafina Mammoliti, Elisabetta Fenocchio, Enrichetta Corgna, Vittorina Zagonel, Gabriella Fontanini, Clara Ugolini, Luca Boni, Alfredo Falcone, on behalf of the GONO Foundation Investigators*

609-18.

FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study

Chiara Cremolini*, Fotios Loupakis*, Carlotta Antoniotti, Cristiana Lupi, Elisa Sensi, Sara Lonardi, Silvia Mezi, Gianluca Tomasello, Monica Ronzoni, Alberto Zaniboni, Giuseppe Tonini, Chiara Carlomagno, Giacomo Allegrini, Silvana Chiara, Mauro D'Amico, Cristina Granetto, Marina Cazzaniga, Luca Boni, Gabriella Fontanini, Alfredo Falcone

Un gain en PFS

A Progression-free Survival

FOLFOXIRI plus bevacizumab

FOLFIRI plus bevacizumab
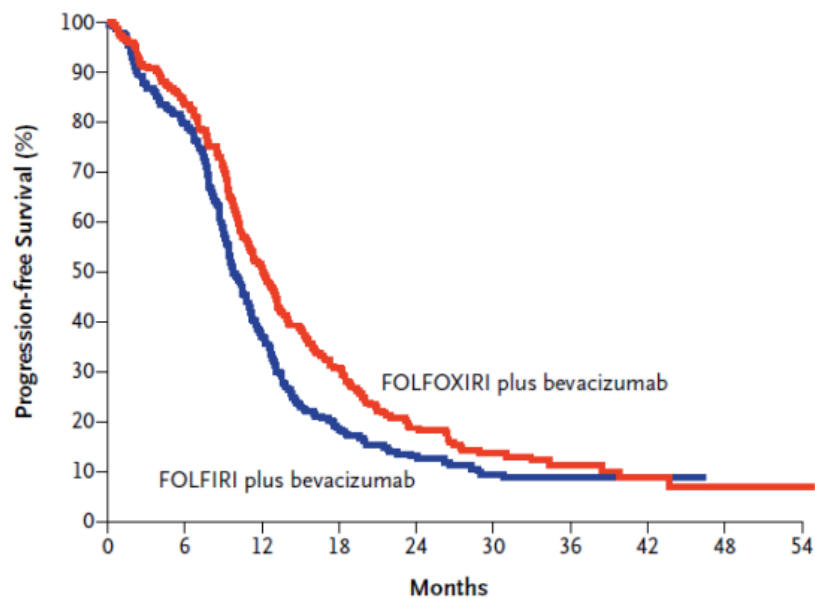
No. at Risk

FOLFIRI plus bevacizumab	256	203	94	46	26	14	7	3	0	0
FOLFOXIRI plus bevacizumab	252	208	125	74	35	21	11	5	2	1

A

HR 0·74 (95% CI 0·63–0·88), log-rank p=0·0005

Control group
Experimental group
+ Censored
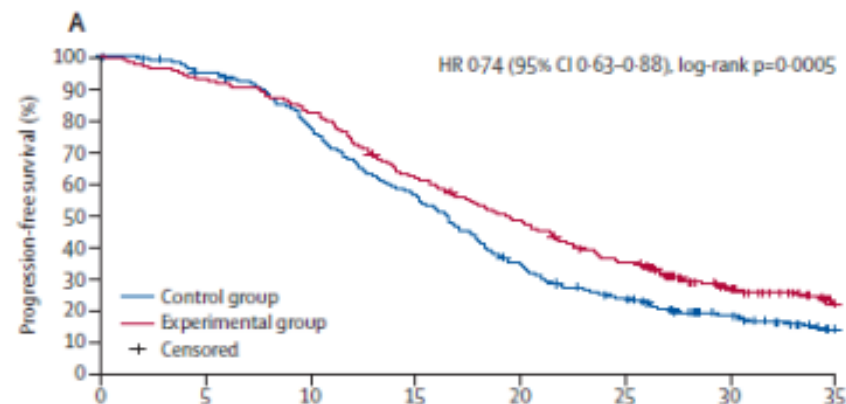
Number at risk (number censored)

Control group	340 (0)	319 (5)	259 (6)	188 (6)	114 (7)	76 (10)	45 (25)	23 (38)
Experimental group	339 (0)	314 (0)	280 (0)	209 (1)	162 (2)	117 (4)	66 (30)	39 (47)

B

HR 0·74 (95% CI 0·63–0·86), log-rank p=0·0002
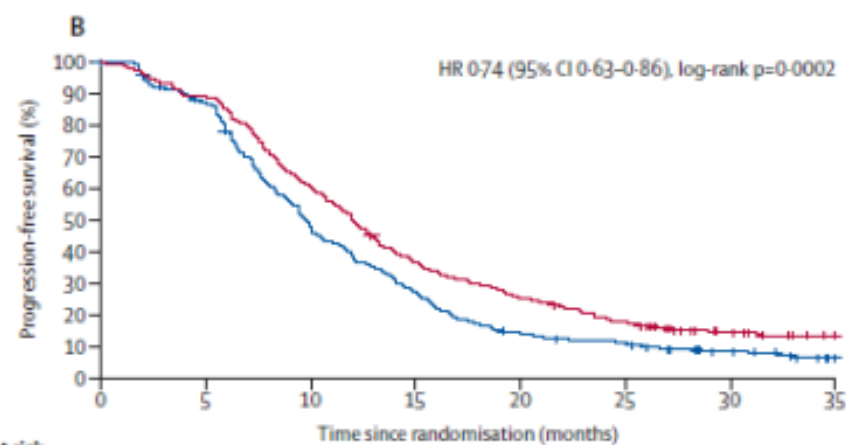
Number at risk (number censored)

Control group	340 (0)	292 (5)	160 (6)	91 (6)	47 (7)	35 (8)	19 (16)	7 (24)
Experimental group	339 (0)	301 (0)	206 (0)	123 (1)	85 (1)	58 (2)	36 (14)	25 (23)

Figure 2: Kaplan-Meier estimates of progression-free survival 2 (A) and progression-free survival 1 (B) in the intention-to-treat population

HR=hazard ratio.

Un gain en SG

B Overall Survival

FOLFOXIRI plus bevacizumab
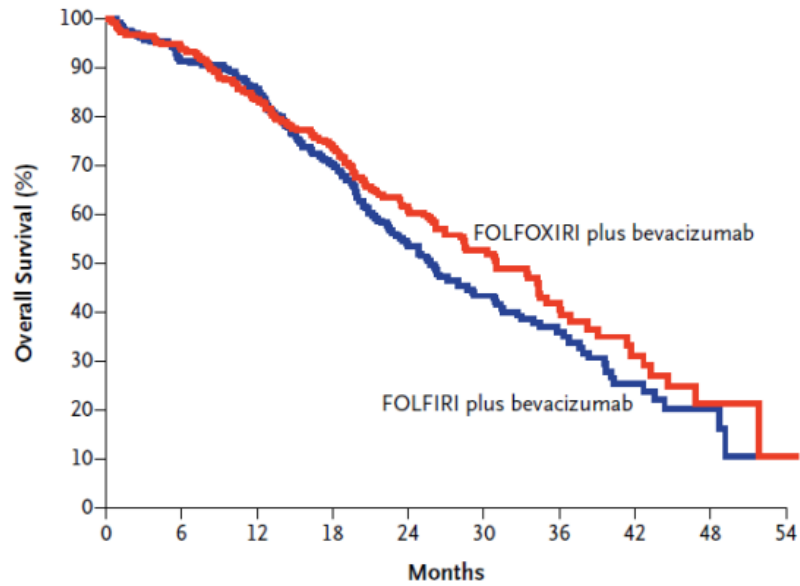
FOLFIRI plus bevacizumab

No. at Risk

FOLFIRI plus bevacizumab	256	233	216	172	109	69	36	15	5	0
FOLFOXIRI plus bevacizumab	252	234	205	175	119	70	35	15	4	0

Control group
Experimental group
Censored

Number at risk
(number censored)

Control group	340 (0)	326 (5)	295 (6)	244 (6)	192 (9)	142 (13)	87 (36)	53 (56)
Experimental group	339 (0)	318 (0)	293 (0)	258 (1)	210 (2)	176 (5)	114 (44)	64 (69)
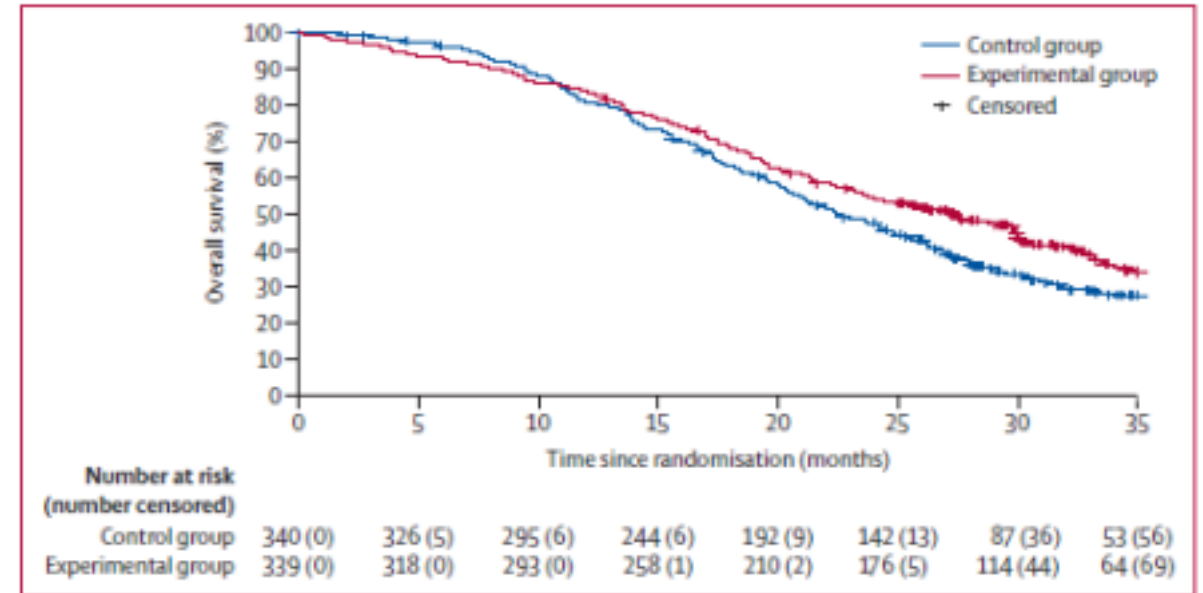
Dans tous les sous groupes

	FOLFIRI plus bevacizumab (n=256)	FOLFOXIRI plus bevacizumab (n=252)	HR (95% CI)	P interaction
Previous adjuvant treatment				
No	224 (88%)	220 (87%)	0·80 (0·65–0·99)	0·46
Yes	32 (13%)	32 (13%)	1·04 (0·55–1·96)	
ECOG performance status				
0	229 (89%)	227 (90%)	0·87 (0·70–1·08)	0·06
1–2	27 (11%)	25 (10%)	0·48 (0·27–0·85)	
Primary tumour site				
Left or rectum	179 (70%)	152 (60%)	0·88 (0·68–1·14)	0·28
Right	61 (24%)	88 (35%)	0·68 (0·47–0·99)	
Liver-only disease				
No	210 (82%)	193 (77%)	0·79 (0·63–0·99)	0·20
Yes	46 (18%)	59 (23%)	1·12 (0·70–1·80)	
Type of metastases				
Metachronous	49 (19%)	55 (22%)	0·79 (0·48–1·32)	0·82
Synchronous	207 (81%)	197 (78%)	0·85 (0·68–1·06)	
Resection of primary tumour				
No	89 (35%)	77 (31%)	0·76 (0·54–1·06)	0·45
Yes	167 (65%)	175 (69%)	0·89 (0·69–1·15)	
Köhne score				
High	29 (11%)	18 (7%)	0·73 (0·39–1·36)	0·81
Intermediate	113 (44%)	111 (44%)	0·90 (0·66–1·21)	
Low	105 (41%)	108 (43%)	0·81 (0·58–1·12)	

0·5 1·0 1·5 2·0

← Favours FOLFOXIRI plus bevacizumab → Favours FOLFIRI plus bevacizumab
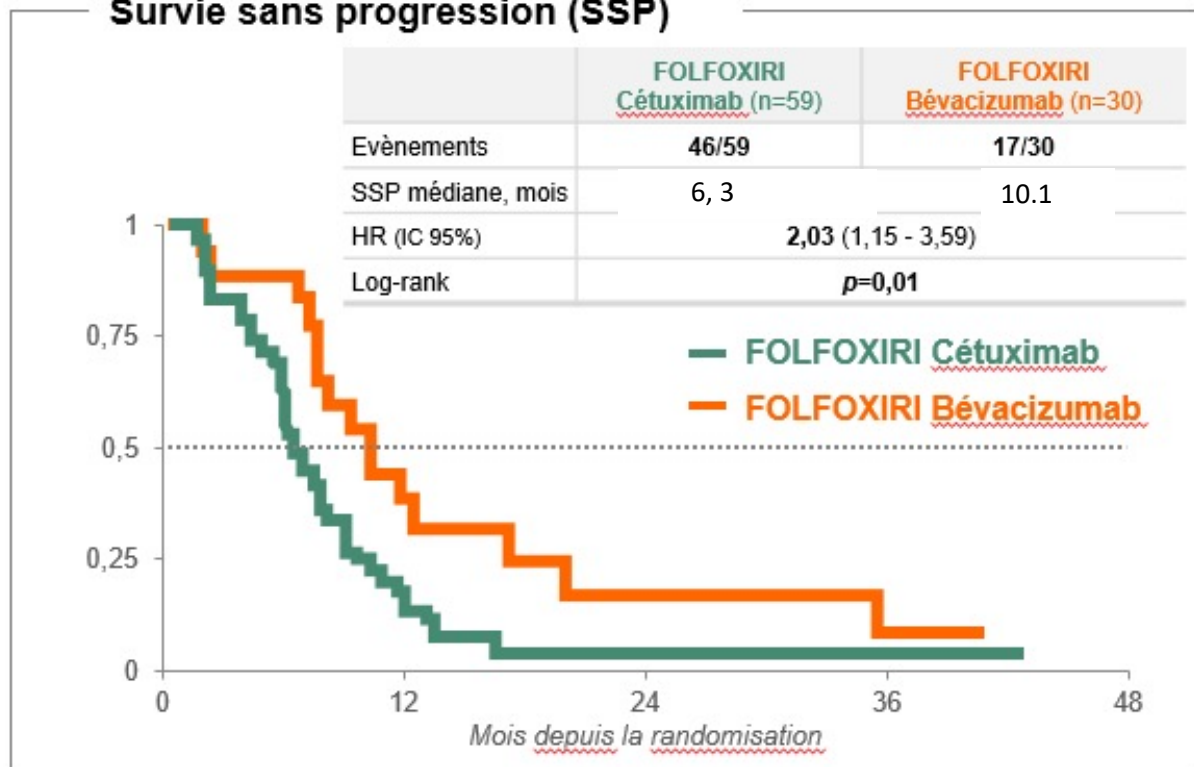
Une concurrence envolée?

Randomized study to investigate FOLFOXIRI plus either bevacizumab or cetuximab as first-line treatment of BRAF V600E-mutant mCRC the phase-II FIRE-4.5 study (AIO KRK-0116)

S. Stintzing et al., ASCO2021, Abs #3502

RECIST, % (n)	FOLFOXIRI Cétuximab (n=59)	FOLFOXIRI Bévacizumab (n=30)
Taux de réponse objective#	49,2% (29)	60,0% (18)
	p= 0,33 OR = 1,55 (IC 80% : 0.87-2.78)	
Taux de contrôle de la maladie	81,4% (48)	90,0% (27)
	p=0,29 OR = 2,06 (IC 95% : 0,53 – 8,04)	

Survie sans progression (SSP)

	FOLFOXIRI Cétuximab (n=59)	FOLFOXIRI Bévacizumab (n=30)
Evènements	46/59	17/30
SSP médiane, mois	6, 3	10.1
HR (IC 95%)	2,03 (1,15 - 3,59)	
Log-rank	p=0,01	

— FOLFOXIRI Cétuximab
— FOLFOXIRI Bévacizumab

Mois depuis la randomisation

Survie globale (SG)

	FOLFOXIRI Cétuximab (n=59)	FOLFOXIRI Bévacizumab (n=30)
Evènements	19/59	9/30
SG médiane, mois	15,2	17,1
HR (IC 95%)	1,35 (0,61 - 3,00)	
Log-rank	p=0,46	

— FOLFOXIRI Cétuximab
— FOLFOXIRI Bévacizumab

Mois depuis la randomisation