Comment personnaliser la 1re ligne du CCRm ?

Du 1+1 au 3+1, comment adapter la 1re ligne au profil patient ?

David Malka

Gustave Roussy, Villejuif

Liens d'intérêt

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ESMO consensus guidelines for the management of patients with metastatic colorectal cancer

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Table 7. Systemic therapy choices according to the Zurich treatment algorithm for patients with unresectable metastatic disease (excluding those with oligometastatic disease)[a]

Category	Fit patients[b]						Unfit[b]	
							May be unfit	Unfit
Treatment goal	Cytoreduction (tumour shrinkage)			Disease control (control of progression)			Palliation	
Molecular profile	*RAS* wt	*RAS* mt	*BRAF* mt	*RAS* wt	*RAS* mt	*BRAF* mt	Any	Any
First-line								
Preferred choice (s)	CT doublet + EGFR antibody[c,d]	CT doublet + bevacizumab	FOLFOXIRI + bevacizumab	CT doublet + bevacizumab or CT doublet + EGFR antibody[c]	CT doublet + bevacizumab	FOLFOXIRI ± bevacizumab	FP + bevacizumab	BSC
Second choice	FOLFOXIRI ± bevacizumab	FOLFOXIRI + bevacizumab	CT doublet + bevacizumab	FP + bevacizumab		CT doublet + bevacizumab	Reduced-dose CT doublet	—
Third choice	CT doublet + bevacizumab	FOLFOXIRI	FOLFOXIRI				If *RAS* wt may consider EGFR antibody therapy	—
Maintenance								
Preferred choice	FP + bevacizumab[e]	FP + bevacizumab	FP + bevacizumab	FP + bevacizumab[e]	FP + bevacizumab	FP + bevacizumab	FP + bevacizumab	—
Second choice	Pause	Pause	Pause	Pause	Pause	Pause	FP	—
Second line								
Preferred choice(s)	CT doublet + bevacizumab	CT doublet + bevacizumab	CT doublet + bevacizumab	CT doublet + bevacizumab or CT doublet + EGFR antibody	CT doublet + bevacizumab	CT doublet + bevacizumab		—
Second choice	CT doublet + EGFR antibody[c,d] or FOLFIRI + aflibercept/ ramucirumab	FOLFIRI + aflibercept/ ramucirumab	FOLFIRI + aflibercept/ ramucirumab	FOLFIRI + aflibercept/ ramucirumab	FOLFIRI + aflibercept/ ramucirumab	FOLFIRI + aflibercept/ ramucirumab		-
Third line								
Preferred choice (s)	CT doublet + EGFR antibody[c,d] or irinotecan + cetuximab[f]	Regorafenib or trifluridine/ tipiracil	Regorafenib or trifluridine/ tipiracil	CT doublet + EGFR antibody[c] or irinotecan + cetuximab	Regorafenib or trifluridine/tipiracil	Regorafenib or trifluridine/tipiracil		—
Second choice	EGFR antibody monotherapy[f]			EGFR antibody monotherapy[f]				—
Third choice	Regorafenib or trifluridine/ tipiracil			Regorafenib or trifluridine/ tipiracil				—

BSC, best supportive care; CT, chemotherapy; EGFR, epidermal growth factor receptor; FP, fluoropyrmidine; FOLFOXIRI, infusional 5-fluorouracil, leucovorin, irinotecan and oxaliplatin; mt, mutant; wt, wild-type.

[a]Cross references to Figure 4.

[b]Patients assessed as fit or unfit according to medical condition not due to malignant disease.

[c]EGFR antibodies: cetuximab and panitumumab.

[d]In patients in need of a rapid reduction in tumour burden because of impending clinical threat, impending organ dysfunction and severe disease-related symptoms, a similar strategy can be proposed, although the consensus on the preferred treatment of choice was less strong. For those patients who have *RAS* wild-type disease, a cytotoxic doublet plus an EGFR antibody is a preferred option, although a cytotoxic doublet plus bevacizumab is an equally valid alternative. A cytotoxic triplet plus or minus bevacizumab may be an alternative for selected, very fit and motivated patients.

[e]In patients where a bevacizumab-containing regimen was started. In patients where a cetuximab-containing combination was started: pause or less intensive regimen.

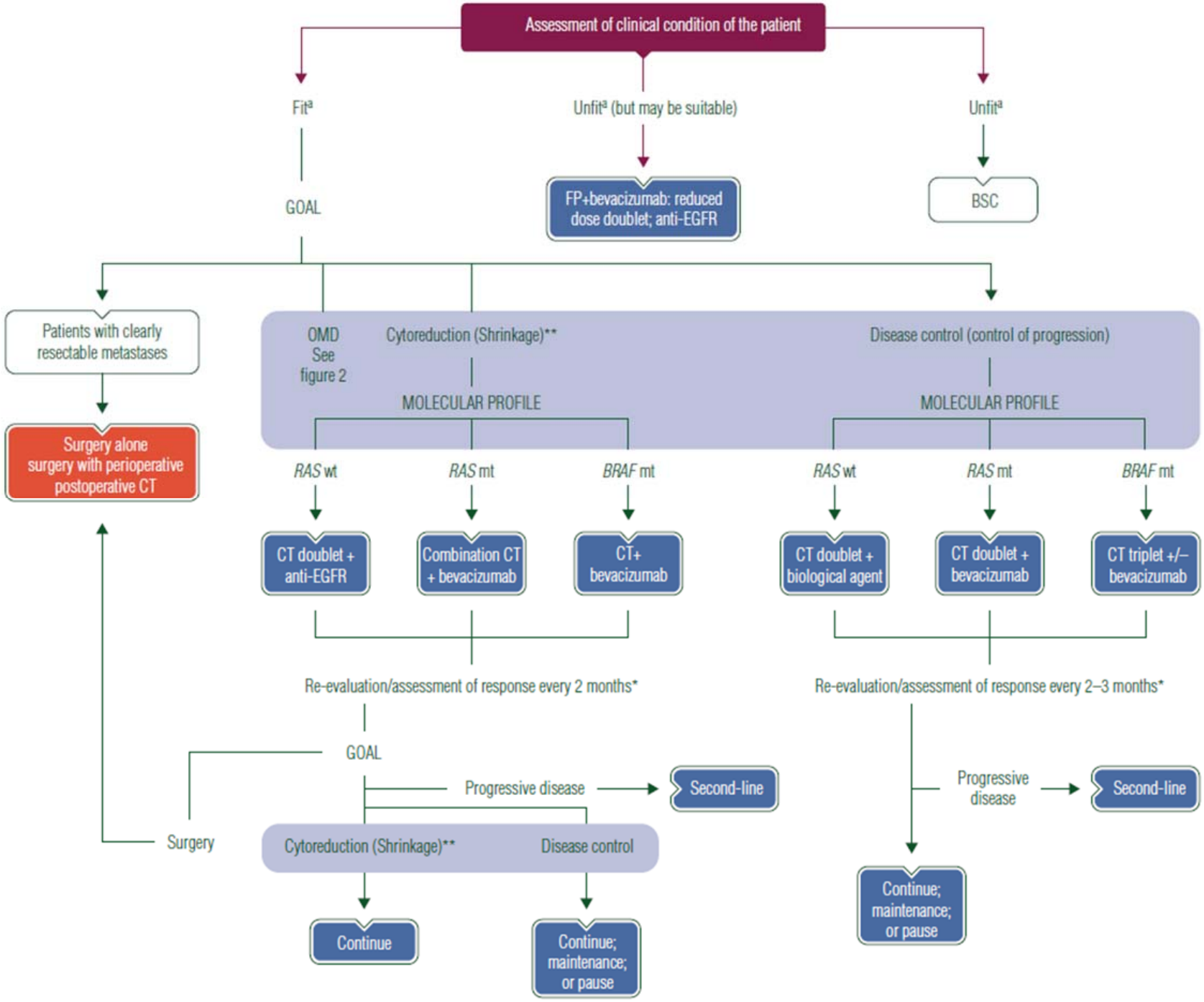
[f]If not yet pretreated with an EGFR antibody.

Guidelines ESMO : profils patients

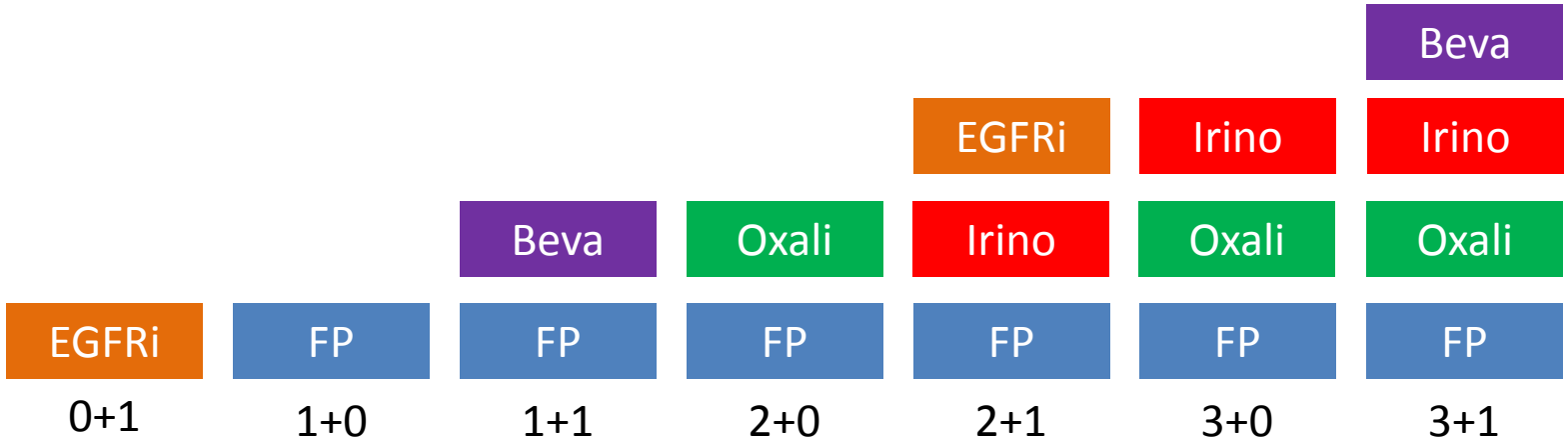
Table 6. Revised ESMO groups for treatment stratification of patients according to whether patients are 'fit' or 'unfit'

Patient's classification	'Fit' patients		'Unfit' patients
	Group 1	Group 2	
Clinical presentation	A) Conversion and achievement of NED B) Impending clinical threat, impending organ dysfunction and severe (disease-related) symptoms Treatment biomarker driven: *RAS* wt, *RAS* mt, *BRAF* mt patient subgroups	Asymptomatic patients No impending clinical threat Resection not an option Treatment biomarker driven: *RAS* wt, *RAS* mt, *BRAF* mt patient subgroups	Best supportive care
Treatment goal	A) Cytoreduction, followed by R0 resection; NED achieved by LAT B) Improvement of symptoms and hence avoidance of rapid evolution and prolonged survival	Disease control and hence prolonged survival	Palliative

LAT, local and ablative therapy; mt, mutant; NED, no evidence of disease; wt, wild-type.


Assessment of clinical condition of the patient
Fit[a]
Unfit[a] (but may be suitable)
Unfit[a]
GOAL
FP+bevacizumab: reduced dose doublet; anti-EGFR
BSC
Patients with clearly resectable metastases
OMD See figure 2
Cytoreduction (Shrinkage)**
Disease control (control of progression)
MOLECULAR PROFILE
MOLECULAR PROFILE
Surgery alone surgery with perioperative postoperative CT
RAS wt
RAS mt
BRAF mt
RAS wt
RAS mt
BRAF mt
CT doublet + anti-EGFR
Combination CT + bevacizumab
CT+ bevacizumab
CT doublet + biological agent
CT doublet + bevacizumab
CT triplet +/– bevacizumab
Re-evaluation/assessment of response every 2 months*
Re-evaluation/assessment of response every 2–3 months*
GOAL
Progressive disease
Second-line
Progressive disease
Second-line
Surgery
Cytoreduction (Shrinkage)**
Disease control
Continue
Continue; maintenance; or pause
Continue; maintenance; or pause

1+1, 2+1, 3+1…


Beva
EGFRi
Irino
Irino
Beva
Oxali
Irino
Oxali
Oxali
EGFRi
FP
FP
FP
FP
FP
FP
0+1
1+0
1+1
2+0
2+1
3+0
3+1

Lignes *vs* molécules

HAS
HAUTE AUTORITÉ DE SANTÉ

COMMISSION DE LA TRANSPARENCE
Avis
14 mai 2014
Le projet d'avis adopté par la Commission de la transparence le 22 janvier 2014 a fait l'objet d'une audition le 14 mai 2014

STIVARGA 40 mg, comprimé pelliculé
B/28 (CIP : 3400927520006)

Laboratoire BAYER SANTE

DCI	régorafénib
Code ATC (2012)	L01XE21 (inhibiteurs de protéine kinases)
Motif de l'examen	**Inscription**
Listes concernées	**Sécurité Sociale** (CSS L.162-17) **Collectivités** (CSP L.5123-2)
Indications concernées	**« Stivarga est indiqué dans le traitement des patients adultes atteints d'un cancer colorectal (CCR) métastatique qui ont été traités antérieurement ou qui ne sont pas éligibles aux traitements disponibles, notamment une chimiothérapie à base de fluoropyrimidine, un traitement par anti-VEGF et un traitement par anti-EGFR. »**

HAS
HAUTE AUTORITÉ DE SANTÉ

COMMISSION DE LA TRANSPARENCE
Avis
9 novembre 2016

Date d'examen par la Commission : 5 octobre 2016

L'avis de la commission de la Transparence adopté le 19 octobre 2016 a fait l'objet d'observations écrites examinées le 9 novembre 2016.

trifluridine / tipiracil

LONSURF 15 mg / 6,14 mg, comprimé pelliculé
B/20 (CIP : 34009 300 577 7 3)
B/60 (CIP 34009 300 577 9 7)

LONSURF 20 mg/8,19 mg, comprimé pelliculé
B/20 (CIP 34009 300 578 0 3)
B/60 (CIP 34009 300 578 2 7)

Laboratoire SERVIER

Code ATC	**L01BC59 (analogue de la pyrimidine)**
Motif de l'examen	**Inscription**
Listes concernées	**Sécurité Sociale** (CSS L.162-17) **Collectivités** (CSP L.5123-2)
Indications concernées	**« Lonsurf est indiqué chez les adultes atteints d'un cancer colorectal métastatique (CCRm) :** **- précédemment traités par les traitements disponibles comprenant les chimiothérapies à base de fluoropyrimidine, d'oxaliplatine et d'irinotecan, les agents anti-VEGF et les agents anti-EGFR,** **- ou qui ne sont pas éligibles à ces traitements. »**

Continuum de soins : un exemple