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A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS).

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CORRIGENDUM

A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)

N. I. Cherny, R. Sullivan, U. Dafni, J. M. Kerst, A. Sobrero, C. Zielinski, E. G. E. de Vries & M. J. Piccart

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In the original manuscript, there were two errors.

In Table 6, the scoring for ramucirumab vs placebo in the RAISE trial should acknowledge the reported 2- year survival advantage of 5–10%. This would result in an upgrade of the ESMO-MCBS score to 3.

In Appendix 1 form 2a of the ESMO-MCBS v1.0 the criteria for grade 2 was incorrectly stated. For studies with control median OS < 12 months the criteria should be HR > 0.65–0.70 AND Gain 1.5–2.4 months. For studies with control median OS >12 months the criteria should be HR > 0.70–0.75 AND Gain 1.5–2.9 months.

The corrected Table and Appendix are as below.

Appendix I

ESMO Magnitude of Clinical Benefit Scale v1.0

Form 2a: for therapies that are not likely to be curative with primary endpoint of OS

Table 6: Field testing ESMO-MCBS v1.0: Colorectal Cancer

COLORECTAL CANCER												
Medication	Trial name	Setting	Primary outcome	PFS control	PFS gain	PFS HR	OS control	OS gain	OS HR	QoL	Toxicity	ESMO-MCBS ref
FOLFOLX4 +/-panitumumab	PRIME	1st line metastatic (Post hoc KRAS, NRAS BRAF WT)	PFS	7.9 mth	2.3 mth	0.72 (0.58-0.90)	20.2 mth	5.8 mth	0.78 (0.62-0.99)			4 [62]
Panitumumab + mFOLFOX6 vs bevacizumab + mFOLFOX6	PEAK	1st line metastatic (KRAS-WT)	PFS			NS	24.3 mth	9.9 mth	0.62 (0.44-0.89)			4* [103]
FOLFIRI +/- cetuximab	CRYSTAL	1st line metastatic stratified for KRAS-WT (Post hoc KRAS, NRAS WT)	PFS	8.4 mth	3.0 mth	0.56 (0.41-0.76)	20.2 mth	8.2 mth	0.69 (0.54-0.88)			4 [65]
Cetuximab vs best supportive care												
FOLFOLX4 +/-panitumumab	PRIME	Refractory metastatic KRAS-WT	OS	1.9 mth	1.8 mth	0.4 (0.30-0.54)	4.8 mth	4.7 mth	0.55 (0.4-0.740)			4 [104]
FOLFIRI +/- cetuximab	CRYSTAL	1st line metastatic	PFS	8 mth	1.6 mth	0.80 (0.66-0.97)	19.4 mth	4.4 mth	0.83 (0.70-0.98)			3 [60, 61]
ILF +/- bevacizumab		1st line metastatic stratified for KRAS-WT	OS	8.4 mth	1.5 mth	0.70 (0.56-0.87)	20 mth	3.5 mth	0.80 (0.67-0.95)			3 [63, 64]
FOLFIRI +/- panitumumab	E3200	2nd line metastatic	PFS	3.9 mth	2 mth	0.73 (0.59-0.90)	15.6 mth	4.7 mth	0.66 (0.54-0.81)			3 [105]
FOLFOX +/- bevacizumab vs bevacizumab alone		2nd line metastatic after FOLFIRI	OS				10.8 mth	2.1 mth	0.75 (0.63-0.89)			3 [106]
Panitumumab, vs best supportive care		3rd line metastatic stratified for KRAS	PFS	7.3 wk	5 wk	0.45 (0.34-0.59)						2 [108]
FOLFIRI bevacizumab vs FOLFOXIRI bevacizumab		1st line metastatic	PFS	9.7 mth	2.4 mth	0.75 (0.62-0.90)			NS			2 [109]
TAS-102 vs placebo	CONCOURSE	3rd line or beyond metastatic	OS				5.3 mth	1.8 mth	0.68 (0.58-0.81)			2 [110]
Regorafenib vs placebo	CORRECT	3rd line metastatic	OS				5 mth	1.4 mth	0.77 (0.64-0.94)			1 [111]
2nd line chemotherapy +/-bevacizumab	ML18147	2nd line beyond progression on bevacizumab	OS				9.6 mth	1.5 mth	0.81 (0.69-0.94)			1 [112]
FOLFIRI +/- aflibercept	VELOUR	2nd line after oxaliplatin based treatment	OS	4.7 mth	2.2 mth	0.76 (0.66-0.87)	12.1 mth	1.5 mth	0.82 (0.71-0.94)			1 [113]
FOLFIRI +/-Ramucirumab	RAISE	2 nd line metastatic after bevacizumab, oxaliplatin, fluoropyrimidine	OS				11.7 mth	1.6 mth, 5-10% gain in 2 year survival	0.84 (0.73-0.97)			3 [114]

*unbalanced crossover

Form 2a: for therapies that are not likely to be curative with primary endpoint of OS

Name of study:		
Study drug:	Indication:	
First author:	Year:	Journal:
Name of evaluator:		

IF median OS with the standard treatment is \leq 1 year

Grade 4	Mark with X if relevant
HR \leq 0.65 AND Gain \geq 3 months	
Increase <u>in</u> 2 year survival alone \geq 10%	

Grade 3	Mark with X if relevant
HR \leq 0.65 AND Gain 2.5-2.9 months	
Increase <u>in</u> 2 year survival alone 5 - <10%	

Grade 2	Mark with X if relevant
HR > 0.65-0.70 AND Gain 1.5-2.4 months	
Increase <u>in</u> 2 year survival alone 3 - <5%	

Grade 1	Mark with X if relevant
HR > 0.70 OR Gain <1.5 months	
Increase <u>in</u> 2 year survival alone <3%	

Preliminary magnitude of clinical benefit grade (highest grade scored)

4	3	2	1

Quality of Life assessment /grade 3-4 toxicities assessment*

Does secondary endpoint quality of life show improvement	
Are there statistically significantly less grade 3-4 toxicities impacting on daily well-being*	

*This does not include alopecia, myelosuppression, but rather chronic nausea, diarrhoea, fatigue, etc.

Adjustments

Upgrade 1 level if improved quality of life and/or less grade 3-4 toxicities impacting daily well-being are shown

Final adjusted magnitude of clinical benefit grade

5	4	3	2	1

IF median OS with the standard treatment > 1 year

Grade 4	<i>Mark with X if relevant</i>
HR ≤ 0.70 AND Gain ≥ 5 months	
Increase <u>in</u> 3 year survival alone ≥ 10%	

Grade 3	
HR ≤ 0.70 AND Gain 3-4.9 months	
Increase <u>in</u> 3 year survival alone 5 - <10%	

Grade 2	
HR > 0.70-0.75 AND Gain 1.5-2.9 months	
Increase <u>in</u> 3 year survival alone 3 - <5%	

Grade 1	
HR > 0.75 OR Gain <1.5 months	
Increase <u>in</u> 3 year survival alone <3%	

Preliminary magnitude of clinical benefit grade (highest grade scored)

4	3	2	1

Quality of Life assessment /grade 3-4 toxicities assessment*

Does secondary endpoint quality of life show improvement	
Are there statistically significantly less grade 3-4 toxicities impacting on daily well-being*	

*This does not include alopecia, myelosuppression, but rather chronic nausea, diarrhoea, fatigue, etc.

Adjustments

Upgrade 1 level if improved quality of life and/or less grade 3-4 toxicities impacting daily well-being are shown

Final adjusted magnitude of clinical benefit grade

5	4	3	2	1