# 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)

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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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **FOLFOX4 +/-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** | | 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 (0.41-0.740 | | | **4** | [104] |
| **FOLFOX4 +/-panitumumab** | PRIME | 1st line metastatic KRAS-WT | 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] |
| **FOLFIRI +/- cetuximab** | CRYSTAL | 1st line metastatic stratified for KRAS-WT | PFS | 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] |
| **ILF +/- bevacizumab** | | 1st line metastatic | OS | | | | 15.6 mth | 4.7 mth | 0.66 (0.54–0.81) | | | **3** | [105] |
| **FOLFIRI +/- panitumumab** | | 2nd line metastatic KRAS-WT | PFS | 3.9 mth | 2 mth | 0.73 (0.59-0.90) | | | | | | **3** | [106] |
| **FOLFOX + /- bevacizumab vs bevacizumab alone** | E3200 | 2nd line metastatic after FOLFIRI | OS | | | | 10.8 mth | 2.1 mth | 0.75 (0.63–0.89) | | | **2** | [107] |
| **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 (.058-0.81) | | | **2** | [110] |
| **Regorafenib vs placebo** | CORRECT | 3rd line metastatic | OS | | | | 5 mth | 1.4 mth | 077 (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 | 2nd 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 ≤ 1 year

| **Grade 4** | *Mark with X if relevant* |
|---|---|
| HR ≤ 0.65 AND Gain ≥ 3 months | |
| Increase in 2 year survival alone ≥ 10% | |

| **Grade 3** | |
|---|---|
| HR ≤ 0.65 AND Gain 2.5-2.9 months | |
| Increase in 2 year survival alone 5 - <10% | |

| **Grade 2** | |
|---|---|
| HR > 0.65-0.70 AND Gain 1.5-2.4 months | |
| Increase in 2 year survival alone 3 - <5% | |

| **Grade 1** | |
|---|---|
| HR > 0.70 OR Gain <1.5 months | |
| Increase in 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

| | *Mark with X if relevant* |
|---|---|
| HR ≤ 0.70 AND Gain ≥ 5 months | |
| Increase in 3 year survival alone ≥ 10% | |

### Grade 3

| | |
|---|---|
| HR ≤ 0.70 AND Gain 3-4.9 months | |
| Increase in 3 year survival alone 5 - <10% | |

### Grade 2

| | |
|---|---|
| HR > 0.70-0.75 AND Gain 1.5-2.9 months | |
| Increase in 3 year survival alone 3 - <5% | |

### Grade 1

| | |
|---|---|
| HR > 0.75 OR Gain <1.5 months | |
| Increase in 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 |
|---|---|---|---|---|
| | | | | |