ESMO-MCBS

ESMO-Magnitude of Clinical Benefit Scale

EVALUATION FORM 2B - ESMO-MCBS v2.0

For therapies that are not likely to be curative with primary endpoint PFS

Name of study:					
Study medicine:		**Indication:**			
First author:		**Year:**		**Journal:**	
Name of evaluator:					

If median PFS with standard treatment <6 months

GRADE 3	HR ≤0.65 AND gain ≥1.5 months	☐
GRADE 2	HR ≤0.65 BUT gain <1.5 months	☐
GRADE 1	HR >0.65	☐

Mark with √ if relevant

Preliminary magnitude of clinical benefit score	**3** ☐	**2** ☐	**1** ☐

ESMO-MCBS, European Society For Medical Oncology-Magnitude of Clinical Benefit Scale; HR, hazard ratio; PFS, progression-free survival.

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Early stopping or crossover

Did the study have an early stopping rule based on interim analysis of survival? ☐

Was the randomisation terminated early based on the detection of overall survival advantage at interim analysis? ☐

Note: If the answer to both is "yes" see adjustment 03.b on the following page.

Mark with √ i f relevant

Incremental toxicity

Is the new treatment associated with an incremental rate of:

Fatal adverse events in ≥2% of patients ☐

Premature discontinuation of therapy in ≥10% of patients ☐

Hospitalisation for adverse events in ≥10% of patients ☐

Grade ≥3 mucositis in ≥10% of patients ☐

Grade ≥3 diarrhoea in ≥10% of patients ☐

Grade ≥3 fatigue in ≥10% of patients ☐

Grade ≥3 neurotoxicity in ≥10% of patients ☐

Other distressing toxicity grade ≥3 in ≥10% of patients ☐

Overall grade 3-4 toxicity impacting on daily well-being* or serious adverse events in ≥20% of patients ☐

Note: Incremental rate refers to the comparison versus standard therapy in the control arm.

Mark with √ i f relevant

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

Reduced grade 3-4 toxicity

Are there fewer grade 3-4 toxicities impacting daily well-being*? ☐

Note: If the answer is "yes" see adjustment 03.a on the following page.

Mark with √ if relevant

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

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Quality of life

Was QoL evaluated as secondary outcome?	☐
Is QoL improved according to the ESMO-MCBS QoL checklist?	☐

Note: If the answer to both is "yes" see adjustment 03.a below.

Mark with √ if relevant

Adjustments

01. When OS as secondary endpoint shows improvement, it will prevail and scoring should be done according to form 2a

02. Downgrade 1 level if:

a. The treatment ONLY leads to improved PFS (mature data shows no OS advantage) and QoL assessment does not demonstrate improved QoL

b. The treatment has incremental toxicity

If both criteria are met a two-point downgrade is applied.

03. Upgrade 1 level if:

a. Improved QoL or if fewer grade 3-4 toxicities that bother patients are demonstrated

b. Study had early crossover because of early stopping or crossover based on detection of survival advantage at interim analysis

c. There is a long-term plateau in the PFS curve, and there is either:

- An improvement of ≥25% in PFS at 1 year, OR
- An improvement of ≥10 - <25% in PFS, with ≥20% of patients on experimental arm have reached 1 year.

Note: No more than 1 upgrade is possible.

Toxicity and QoL adjusted, magnitude of clinical benefit score	**4** ☐	**3** ☐	**2** ☐	**1** ☐

Note: Highest magnitude clinical benefit grade that can be achieved in form 2b is grade 4 and the lowest is 1.

Non-curative setting grading 5 and 4 indicate a substantial magnitude of clinical benefit.

OS, overall survival; PFS, progression-free survival; QoL, quality of life.