ESMO-MCBS:H

ESMO-Magnitude of Clinical Benefit Scale
for Haematological Malignancies

EVALUATION FORM 2B

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

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

If median PFS with standard treatment ≥12 months

GRADE 3	HR ≤0.65 AND gain ≥5 months	☐
	HR ≤0.65 AND interim PFS gain ≥20% (if PFS is not mature)	☐
GRADE 2	HR ≤0.65 BUT gain <5 months	☐
	HR ≤0.65 AND interim PFS gain ≥10-<20% (if PFS is not mature)	☐
GRADE 1	HR >0.65	☐
	HR ≤0.65 AND interim PFS gain <10% (if PFS is not mature)	☐

Mark with √ if relevant

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

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 "3b" below

Mark with √ if 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 √ if relevant

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

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Reduced grade 3-4 toxicity

Are there statistically significantly fewer grade 3-4 toxicities impacting on daily well-being* ☐

Note: If the answer is "yes" see adjustment "3a" below

Mark with √ if relevant

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

Quality of Life

Was QoL evaluated as secondary outcome? ☐

Does QoL assessment show improvement or delayed deterioration? ☐

Note: If the answer to both is "yes" see adjustment "3a" below

Mark with √ if relevant

Adjustments

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

2. 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

3. Upgrade 1 level if
   a. Improved quality of life or if less 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 ≥10% improvement in PFS at 3-year

Note: No more than 1 upgrade is possible

Final, toxicity and QoL adjusted, magnitude clinical benefit score	**4** ☐	**3** ☐	**2** ☐	**1** ☐

Note: Highest magnitude clinical benefit grade that can be achieved in form 2b is grade 4

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

OS, overall survival; PSF, progression-free survival; QoL, Quality of Life.