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 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** ☐

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.

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.

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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

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

3. Upgrade 1 level if:
- a. Improved QoL 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 1 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 gr ade 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.