**EVALUATION FORM 2B**

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

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<th>Name of study:</th>
<th>Study medicine:</th>
<th>Indication:</th>
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<th>First author:</th>
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<th>Name of evaluator:</th>
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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)

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**Preliminary magnitude of clinical benefit grade (highest grade scored)**

- 3
- 2
- 1

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HR, hazard ratio; PFS, progression-free survival.
**Reduced grade 3-4 toxicity**

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.

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

**Quality of Life**

Was quality of life evaluated as secondary outcome?  

Does quality of life assessment show improvement or delayed deterioration?  

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

**Adjustments**

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

**B**  
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

**C**  
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 years

Note: no more than 1 upgrade is possible

**Final, toxicity and QoL adjusted, magnitude clinical benefit grade**

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

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

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

**Incremental toxicity**

Is the new treatment associated with an incremental rate of:

- «Toxic» death >2% of patients  
- premature discontinuation of therapy >10% of patients  
- hospitalisation for «toxicity» >10% of patients  
- grade 3+ mucositis >10% of patients  
- grade 3+ diarrhoea >10% of patients  
- grade 3+ fatigue >10% of patients  
- grade 3+ neurotoxicity >10% of patients  
- other distressing toxicity grade 3+ >10% of patients  
- overall grade 3-4 toxicity impacting on daily well-being* or serious adverse events >20% of patients

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