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

Preliminary magnitude of clinical benefit grade (highest grade scored)  3  2  1

HR, hazard ratio; PFS, progression-free survival.
**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

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**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

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**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

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

03. 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. If 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 grade

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<th>Grade</th>
<th>Value</th>
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<tr>
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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.