

# **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 $\geq$ 12 months

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

Mark with  $\sqrt{}$  if relevant





## Early stopping or crossover

Did the study have an early stopping rule based on interim analysis of survival?	$\bigcirc$
Was the randomisation terminated early based on the detection of overall survival advantage at interim analysis?	$\bigcirc$
Note: If the answer to both is "yes" see adjustment "3b" below	Mark with $$ if relevant

# **Incremental toxicity**

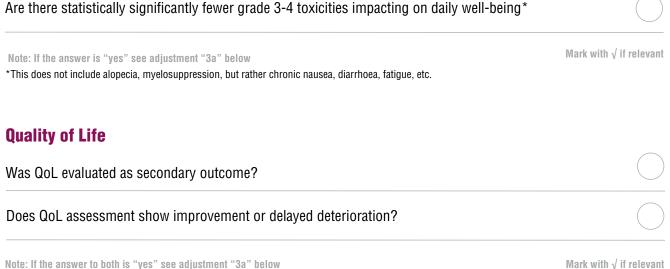
#### Is the new treatment associated with an incremental rate of:

Fatal adverse events in $\ge 2\%$ of patients	$\bigcirc$
Premature discontinuation of therapy in $\geq 10\%$ of patients	$\bigcirc$
Hospitalisation for adverse events in $\geq 10\%$ of patients	$\bigcirc$
Grade ≥3 mucositis in ≥10% of patients	
Grade $\geq$ 3 diarrhoea in $\geq$ 10% of patients	
Grade $\geq$ 3 fatigue in $\geq$ 10% of patients	
Grade $\geq$ 3 neurotoxicity in $\geq$ 10% of patients	$\bigcirc$
Other distressing toxicity grade $\ge$ 3 in $\ge$ 10% of patients	
Overall grade 3-4 toxicity impacting on daily well-being <sup>*</sup> or serious adverse events in $\ge$ 20% of patients	$\bigcirc$

Note: Incremental rate refers to the comparison versus standard therapy in the control arm \*This does not include alopecia, myelosuppression, but rather chronic nausea, diarrhoea, fatigue, etc. Mark with  $\sqrt{}$  if relevant



**Reduced grade 3-4 toxicity** 



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

### **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
  - The treatment ONLY leads to improved PFS (mature data shows no OS advantage) and QoL а 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  $\geq 10\%$  improvement in PFS at 3-year

Note: No more than 1 upgrade is possible



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