ESMO Magnitude of Clinical Benefit Scale v1.1

Evaluation form 2b: for therapies that are not likely to be curative with primary endpoint PFS

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

IF with median PFS with standard treatment ≤6 months

Grade 3	Mark with X if relevant
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

Early stopping or crossover

Did the study have an early stopping rule based on interim analysis of survival?	
Was the randomization terminated early based on the detection of overall survival advantage at interim analysis?	

(If the answer to both is "yes", then see adjustment "a" below)

Toxicity assessment

Is the new treatment associated with a statistically significant incremental rate of:	**Mark with X if relevant**
«toxic» death >2%	
Cardiovascular ischemia >2%	
Hospitalization for «toxicity» >10%	
Excess rate of severe CHF >4%	
Grade 3 neurotoxicity >10%	
Severe other irreversible or long lasting toxicity >2% please specify:	

(Incremental rate refers to the comparison versus standard therapy in the control arm)

Quality of life/ grade3-4 toxicities assessment

Was quality of life (QoL) evaluated as secondary outcome?	
Does secondary endpoint quality of life show improvement	
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.**

Adjustments

a) **When OS as secondary endpoint shows improvement, it will prevail and the new scoring will be done according to form 2a**
b) **Downgrade 1 level if there is one or more of the above incremental toxicities associated with the new drug**
c) **Downgrade 1 level if the drug ONLY leads to improved PFS (mature data shows no OS advantage) and QOL assessment does not demonstrate improved QoL**
d) **Upgrade 1 level if improved quality of life or if less grade 3-4 toxicities that bother patients are demonstrated**
e) **Upgrade 1 level if study had early crossover because of early stopping or crossover based on detection of survival advantage at interim analysis**
f) **Upgrade 1 level if there is a long term plateau in the PFS curve, and there is ≥10% improvement in PFS at 1 year**

Final, toxicity and QoL adjusted, magnitude clinical benefit grade

4	3	2	1

Highest magnitude clinic benefit grade that can be achieved grade 4.