ESMO-MCBS

ESMO-Magnitude of Clinical Benefit Scale

EVALUATION FORM 1A - ESMO-MCBS v2.0

For RCTs evaluating new approaches to adjuvant therapy or new potentially curative therapies

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

GRADE A	≥5% improvement of survival gain	☐
	Improvements in DFS alone (primary endpoint) HR ≤0.65 AND absolute gain ≥3% in studies without mature* survival data	☐
GRADE B	≥3 - <5% improvement of survival gain	☐
	Improvements in DFS (primary endpoint) HR ≤0.65 AND absolute gain ≥1% - <3% in studies without mature* survival data	☐
	Improvement in DFS (primary endpoint) HR >0.65 - 0.75 AND absolute gain ≥3% without mature* survival data	☐
	Non-inferior DFS or OS with reduced treatment toxicity or improved QoL (assessed with the ESMO-MCBS QoL checklist)	☐
	Non-inferior OS or DFS with reduced treatment cost as reported study outcome (with equivalent outcomes and risks)	☐
GRADE C	<3% improvement of survival gain	☐
	Improvement in DFS (primary endpoint) HR ≤0.65 AND absolute gain <1% in studies without mature* survival data	☐
	Improvement in DFS (primary endpoint) HR >0.65 - 0.75 AND absolute gain <3% in studies without mature* survival data	☐
	Improvement in DFS (primary endpoint) HR >0.75 in studies without mature* survival data	☐
	Improvements in pCR alone (primary endpoint) by ≥30% relative AND ≥15% absolute gain in studies without mature* survival data	☐

Mark with √ if relevant

Preliminary magnitude of clinical benefit score	**A** ☐	**B** ☐	**C** ☐

*For guidelines regarding maturity of survival data see instructions point 7 or adjustments on the following page.

DFS, disease-free survival; ESMO-MCBS, European Society For Medical Oncology-Magnitude of Clinical Benefit Scale; HR, hazard ratio; OS, overall survival; pCR, pathologic complete response/remission; QoL, quality of life; RCTs, randomised-controlled trials.

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TOXICITY ANNOTATION

Acute Transient Toxicity (AT)

Is the new treatment associated with:

Grade ≥3 adverse events impacting well-being in >30% of patients	☐
Premature discontinuation of therapy due to adverse events in >10% of patients	☐
Hospitalisation for adverse events in >10% of patients	☐

Mark with √ if relevant

Persistent Toxicity (PT)

Is the new treatment associated with:

Chronic neuropathy in >20% of the patients*	☐
Other grade ≥3 chronic toxicity adversely impacting well-being in >20% of patients	☐

*All adjuvant and curative therapies incorporating taxanes and/or >3 months oxaliplatin will be annotated PT on the basis of accumulated evidence of persistent neuropathy.

Mark with √ if relevant

Adjustments

Downgrade 1 level if mature* OS does not demonstrate significant benefit

*Maturity of survival data may be protocol defined or, if not defined, determined by the specific clinical entity. Example:

Disease	Median follow up for OS data maturity
Pancreatic cancer, gastric cancer, oesophageal cancer	3 years
Colorectal cancer, bladder cancer, triple negative breast cancer, hormone receptor negative breast cancer, NSCLC, melanoma, sarcoma	5 years
Hormone receptor-positive breast cancer, GIST	8-10 years

Magnitude of clinical benefit score with toxicity annotation	**A**	**B**	**C**
	☐	☐	☐
	(AT) ☐ (PT) ☐	(AT) ☐ (PT) ☐	(AT) ☐ (PT) ☐

Note: Highest magnitude clinical benefit grade that can be achieved in form 1a is grade A and the lowest is C.

Curative setting grading - A and B indicate a substantial magnitude of clinical benefit.

AT, acute toxicity; GIST, gastrointestinal stromal tumours; NSCLC, non-small cell lung cancer; OS, overall survival; PT, persistent toxicity.