ESMO-MCBS

ESMO-Magnitude of Clinical Benefit Scale

ESMO-Magnitude of Clinical Benefit Grading Scale (ESMO-MCBS)

Instructions

1. There are 4 forms:

   Evaluation form 1: for new approaches to adjuvant therapy or new potentially curative therapies

   Hyper mature data from studies that were un-blinded after compelling early results with subsequent access to the superior arm are contaminated, subsequently late intention to treat (ITT) follow-up data are not evaluable.

   Evaluation form 2a: for therapies that are not likely to be curative with primary endpoint of OS with separate sheets for:

   - IF median OS with the standard treatment is ≤1 year
   - IF median OS with the standard treatment >1 year

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

   - IF median PFS with standard treatment ≤6 months
   - IF median PFS with standard treatment >6 months

   Evaluation form 2c: for therapies that are not likely to be curative with primary endpoint other than OS or PFS or equivalent studies.

2. The highest grade of the ESMO-MCBS is A in the curative setting and this is restricted to new curative treatments; for non-curative indications 5 is the highest possible grade, yet sufficient to trigger rapid consideration for reimbursement is B and 4.

3. Analysis of phase III trials

   a) Priority: well powered studies showing statistically significant improvement.
   b) Careful analyses "control arm" and identification of endpoints.
   c) Check subgroup analysis. In negative phase III trials often based on emerging candidate biomarkers. They can reveal apparent benefits in the primary endpoint via a subgroup.

   Un-planned not in ESMO-MCBS

   - considered «hypothesis-generating», requires confirmation in an independent data-set

   Pre-planned in ESMO-MCBS

   - when ≤3 subgroups defined «a priori»: benefit in a subgroup for the primary endpoint can be «scaled», provided adjusted for multiple comparisons

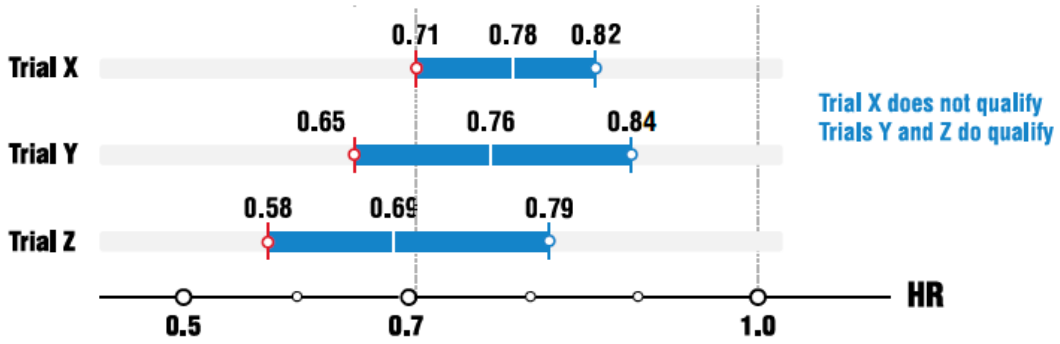
4. More than one outcome may be applicable

   For a required HR, not the point estimate but the lower limit of 95% CI estimated based on the observed HR in the trial should encompass the required HR.

Figure 1

Understanding the meaning of a threshold HR in the ESMO-Magnitude of Clinical Benefit Scale

Example: threshold set at HR ≤0.70



Example: for threshold set at HR ≤0.70 it is the lower limit of the 95% CI which has to be ≤0.70

5. In the case of OS in the non-curative setting check for:
   - Reduced toxicity
   - Improvement in quality of life
   - Report final adjusted grade taken into account toxicity, and QoL when relevant
6. In case of PFS in the non-curative setting check for:
   - Indicators of toxicity
   - Survival data also available
   - Global QoL advantage using validated scale if applicable
   - Report final adjusted grade taken into account toxicity, survival advantage and QoL when applicable