

ESMO-MCBS: setting the record straight

We applaud Yolande Lievens and colleagues¹ for promoting the development of value scales for surgical and radiotherapy interventions. However, regarding the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS), their evaluation of the current scale has two flaws: multiple mischaracterisations of the ESMO-MCBS, and misappraisal of their own experience. These factors have contributed to an underappreciation of the utility of the ESMO-MCBS in the grading of benefit demonstrated in studies evaluating radiotherapeutic and surgical interventions.

There are six inaccuracies in tables 1–3 describing the characteristics of the ESMO-MCBS. First, regarding treatment modalities that can be evaluated, the ESMO-MCBS is not necessarily restricted to systemic anticancer therapies; it grades benefits reported in studies when usual validated endpoints are part of the study design.² Field testing the scale extensively in studies incorporating surgical or radiotherapeutic interventions will be of interest. Second, regarding the intended users, ESMO encourages use of the scale by patients, advocacy groups, providers, and the public (particularly through medical journalism).² Third, regarding treatment-related mortality, the ESMO-MCBS includes treatment-related mortality in the toxicity assessments incorporated in Form 2b.^{2,3} Fourth, regarding symptom assessment, all quality-of-life scales and their disease-specific subscales validated in cancer incorporate symptom assessment.⁴ The ESMO-MCBS credits symptom improvement that contributes to improved quality of life or delayed deterioration in quality of life. Additionally, when single symptoms or symptom clusters are the primary outcome of a study, they are credited

independent of quality of life (using Form 2c).^{2,3} Fifth, regarding the outcomes of regional control, organ preservation, and reintervention rate, these are all factors that can influence quality of life. Studies evaluating these outcomes that incorporate quality of life as a primary outcome can be graded.^{2,3} Lastly, regarding the grading of meta-analyses and cohort studies, the directions for use of the ESMO-MCBS explicitly state that the scale can be applied to data derived from meta-analyses or case-cohort series.²

When applying the ESMO-MCBS (version 1.1) to seven illustrative studies, Lievens and colleagues write that they were “difficult to appraise” and, importantly, that the generated scores were low, undervaluing the important benefits observed.¹ These conclusions are inaccurate. Four of the seven studies showed benefits in a curative setting and were accurately graded B which, according to the ESMO-MCBS, represents a substantial benefit.² That the ESMO-MCBS does not grade benefits that have not been demonstrated—as was done in the other three studies—STAMPEDE,⁵ ROLARR,⁶ and Badwe and colleagues⁷—shows the desired quality of discernment,⁸ which should not be conflated with difficulty.

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- 1 Lievens Y, Audisio R, Banks I, et al. Towards an evidence-informed value scale for surgical and radiation oncology: a multi-stakeholder perspective. *Lancet Oncol* 2019; **20**: e112–23.
- 2 Cherny NI, Sullivan R, Dafni U, et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol* 2015; **26**: 1547–73.
- 3 Cherny N, Dafni U, Bogaerts J, et al. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol* 2017; **28**: 2340–66.
- 4 Au HJ, Ringash J, Brundage M, Palmer M, Richardson H, Meyer RM. Added value of health-related quality of life measurement in cancer clinical trials: the experience of the NCI CTG. *Expert Rev Pharmacoecon Outcomes Res* 2010; **10**: 119–28.
- 5 Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet Oncol* 2018; **39**: 2353–66.
- 6 Jayne D, Pigazzi A, Marshall H, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer. The ROLARR randomized clinical trial. *JAMA* 2017; **318**: 1569–80.
- 7 Badwe R, Hawaldar R, Nair N, et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet Oncol* 2015; **16**: 1380–88.
- 8 Dafni U, Karlis D, Pedeli X, et al. Detailed statistical assessment of the characteristics of the ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS) threshold rules. *ESMO Open* 2017; **2**: e000216.