



Standard Operating Procedures (SOPs) for Authors and templates for ESMO Clinical Practice Guidelines (CPGs) and ESMO-MCBS Scores

ESMO Guidelines Committee, May 2020

Introduction

- ✓ The CPGs should be updated when there is need for such as judged by the Guidelines Committee (GLC). New CPGs may also be considered by the GLC for topics not currently covered by the current ESMO CPGs.
- ✓ The target audience for the CPGs is health professionals working in the field of oncology across Europe and other parts of the world, with an emphasis on Medical Oncology.
- ✓ The standard CPGs should take into account and be in agreement with the content from the ESMO Consensus Conference Guidelines when available (these are two separate products that are complementary).
- ✓ In selected circumstances, ESMO may opt to produce joint CPGs with other formally recognised scientific societies, after careful consideration by the GLC of the science, characteristics, scope and strategy. In this case, there is a mutual agreement to follow the ESMO SOPs and methodology with some necessary minimal adjustments in order to generate consent.
- ✓ ESMO will produce pocket versions of standard CPGs as ‘hands-on’ booklets with tables, algorithms and ‘bullet point’ recommendations for daily use: Pocket Guidelines. The Subject Editor (SE) of each CPG will be asked to review and comment on the relevant chapter of the Pocket Guidelines. The corresponding author may also be asked for comment.
- ✓ ESMO will produce slide sets containing key recommendations and algorithms. The corresponding author and SE of the relevant CPG will be asked to review and comment on the slide set.

Structure of the manuscript in thematic sections

1. Incidence and epidemiology
2. Diagnosis and pathology/molecular biology
3. Staging and risk assessment
4. Management of local/locoregional disease
5. Management of advanced/metastatic disease
6. Follow-up, long-term implications and survivorship
7. Methodology
8. Disclosure
9. References
10. Tables and Figures
 - Table with diagnostic work-up
 - Tables on therapeutic regimens or prognosis
 - Personalised medicine synopsis table
 - ESMO-standardised algorithms with management or therapeutic strategy according to risk factors or stage
11. Supplementary files (available online only)
 - Table(s) with staging system (preferably TNM) and stage groups
 - MCBS Table with ESMO-MCBS score for new therapies/indications approved by the European Medicines Agency (EMA)
 - Table of Levels of Evidence and Grades of Recommendation

Some ESMO CPGs (specifically those focused on cancer genetics and palliative/supportive) may not be compatible with the thematic section structure above. These may follow a more 'individualised' structure, though it is advised to adhere to the following general format:

1. Incidence
2. Assessment/diagnosis
3. Management and monitoring

4. Follow-up

Title

The title should be formatted according to the following example:

Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

For the titles that do not include diagnosis, treatment and follow-up, the title should be formatted according to the following example:

Central venous access in oncology: ESMO Clinical Practice Guidelines

Authorship

Authorship should consist of a minimum of 5 authors and a maximum of 20 authors, including the SE. The coordinating author appears as first author, followed by the other contributors and the SE as last author. The coordinating author is responsible for coordination of authorship and submission of the CPG draft. Full affiliation details for each author should be included.

The authorship should be multidisciplinary. Thus, authors should include medical oncologists, a surgical oncologist and a radiation oncology specialist as far as possible (and/or other disciplines if appropriate).

The authors should include experts from different institutions and different countries in Europe and abroad to ensure recognition as a European and global guideline.

Extent

The manuscript should **focus on the therapeutic recommendations** and should not exceed **10 000 words including tables, figure legends and references** (only the manuscript heading, acknowledgements and funding are excluded from the word count). Additional information can be included in supplementary files.

References should not exceed **100 maximum**.

Authors will be asked to revise the manuscript and/or remove references if these size limits are not respected.

Recommendations with Levels of Evidence (LoEs) and Grades of Recommendation (GoRs), including ESMO-MCBS scores where indicated

Please include recommendations at the end of each thematic section of the manuscript, including LoEs and GoRs and ESMO-MCBS scores where applicable.

Example:

Recommendations:

- mpMRI should be carried out before prostate biopsy [I, B]
- A prostate cancer risk calculator and/or mpMRI should be used to confirm the indication for biopsy in men with elevated PSA [III, C]
- Transperineal biopsies are recommended, rather than transrectal ultrasound (TRUS)-guided biopsies [III, B]
- Each biopsy should be reported individually and evaluated using the ISUP Consensus recommendations [8] [II, B]

Evidence levels are mandatory. Recommendations should be accompanied by proper evidence level and grade of recommendation according to the adapted Infectious Diseases Society of America-United States Public Health Service Grading System.

The LoE describes the quality of existing evidence (trials, cohort studies, case-control studies, expert opinion) that address a specific clinical question. The quality of evidence is assessed in terms of number of trials, sample size, methodology, bias, heterogeneity.

The GoR is a composite parameter, as it incorporates both the quality of evidence (as in LoE) as well as the clinical significance/magnitude of benefit or harm given by a novel therapy.

Any therapy can be assigned a GoR which varies from positive (recommended) to negative (not recommended). To avoid confusion, please refer to the therapy being evaluated as a logically positive definition and then assign the appropriate GoR (which can be positive or negative).

Accordingly, always use the GoR in the following template manner:

Administration of Therapy A (logically positive definition) > GoR assigned (positive: Recommended or negative: Not Recommended). Please avoid doing the opposite.

EXAMPLES:

Correct:

Administration of anti-EGFR antibodies does not result in survival improvement in patients with RAS-mutated advanced colon cancer and is not recommended (GoR E).

To be avoided:

Non-administration of anti-EGFR antibodies is the correct clinical strategy for patients with RAS-mutated advanced colon cancer and is strongly recommended (GoR A).

Personalised medicine

Information relating to personalised medicine should be included throughout the CPG text in the various sections where relevant and appropriate.

At the end of the CPG, before the Follow-up final section, a Personalised Medicine Synopsis table will provide summary information on **validated** biomarkers used for any of the following:

a) disease classification, b) prognostic relevance, c) predictive relevance, d) used for medical treatment decisions, e) currently actionable/targetable.

Template for a Personalised medicine synopsis table

Biomarker	Method	Use	Level of Evidence, Grade of Recommendation
Describe the biomarker	Describe the methodology or assay used to measure biomarker	Describe the biomarker's use/significance: (a) disease classification, b) prognostic relevance, c) predictive	Provide level of evidence and grade of recommendation

If no such table is feasible, provide a brief statement on research and potential biomarkers.

Follow-up, long-term implications and survivorship

This section will focus on recommendations for patient follow-up and will also include information on long-term toxicities of treatment, second tumours, psychosocial implications, rehabilitation and any other issues related to survivorship.

Methodology

Methodology is required in the main text of the manuscript. The following paragraph will be included in all CPGs:

These Clinical Practice Guidelines were developed in accordance with the ESMO standard operating procedures for Clinical Practice Guidelines development (<http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology>). The relevant literature has been selected by the expert authors. An ESMO-MCBS table with MCBS scores is included in Supplementary Table SX. ESMO-MCBS v1.1 [ref #] was used to calculate scores for new therapies/indications approved by the EMA since 1 January 2016 (<https://www.esmo.org/Guidelines/ESMO-MCBS>). The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee. Levels of evidence and grades of recommendation have been applied using the system shown in Supplementary Table SX [ref ##]. Statements without grading were considered justified standard clinical practice by the authors.

ref # = Include reference to ESMO-MCBS manuscript (version 1.1) in References section (also include in supplementary file):

Cherny NI, Dafni U, Bogaerts J et al. ESMO-Magnitude of Clinical Benefit Scale Version 1.1.

Ann Oncol 2017; 28: 2340–2366.

ref ## = include reference for LoE/GoR table (also include in supplementary file):

Dykewicz CA. Summary of the guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. Clin Infect Dis 2001; 33: 139–144 (Adapted from: Gross PA, Barrett TL, Dellinger EP et al. Purpose of quality standards for infectious diseases. Clin Infect Dis 1994; 18: 421).

Acknowledgments

Please include any acknowledgements as appropriate.

Funding

A general funding statement is required. The following general statement will be included in all CPGs:

No external funding has been received for the preparation of these guidelines.
Production costs have been covered by ESMO from central funds.

Disclosure

A disclosure section is required in the main text of the manuscript. Each author must provide a disclosure of interest statement, even if there is nothing to declare. The disclosure of interest should be general and not limited to interests closely related to the current manuscript.

Examples are noted below:

XX has reported honoraria from Roche. XY has reported research grants from Pfizer, AstraZeneca, GlaxoSmithKline, Celgene and is a member of speaker's bureau for Novartis, Janssen. XZ has declared no potential conflicts of interest.

References

Refer to the most recently published randomised controlled trials (RCTs), meta-analyses and/or systematic reviews. Review articles may be used as citations in order to summarise data; however, it is preferable that pivotal RCTs or meta-analyses are cited in order to support a recommendation. Trials used for ESMO-MCBS score calculation(s) should also appear in the reference list. References not to exceed 100 maximum.

Tables

All tables must be cited within the document and should be included in the manuscript file following the references (separate word files are not needed).

Figures

It is very important that authors produce ESMO-standardised algorithms on therapeutic strategy or management according to stage, risk factors and disease/molecular characteristics. This is a priority issue for ESMO.

All figures must be cited within the document and should be included in the manuscript following the tables (separate word or PowerPoint files are not needed). Please include LoEs and GoRs where applicable. ESMO-MCBS scores will be added in the final version.

ESMO will prepare the final algorithms using standard formatting/colours for publication. The following colour code will be used:

- Purple for general/heading boxes
- Red for surgery
- Green for radiotherapy
- Blue for systemic therapy
- Turquoise for other treatments

An example of an algorithm for Management/Therapeutic strategy by stage/risk factors (from the 2018 ESMO CPGs on bone sarcoma) is shown on the next page.

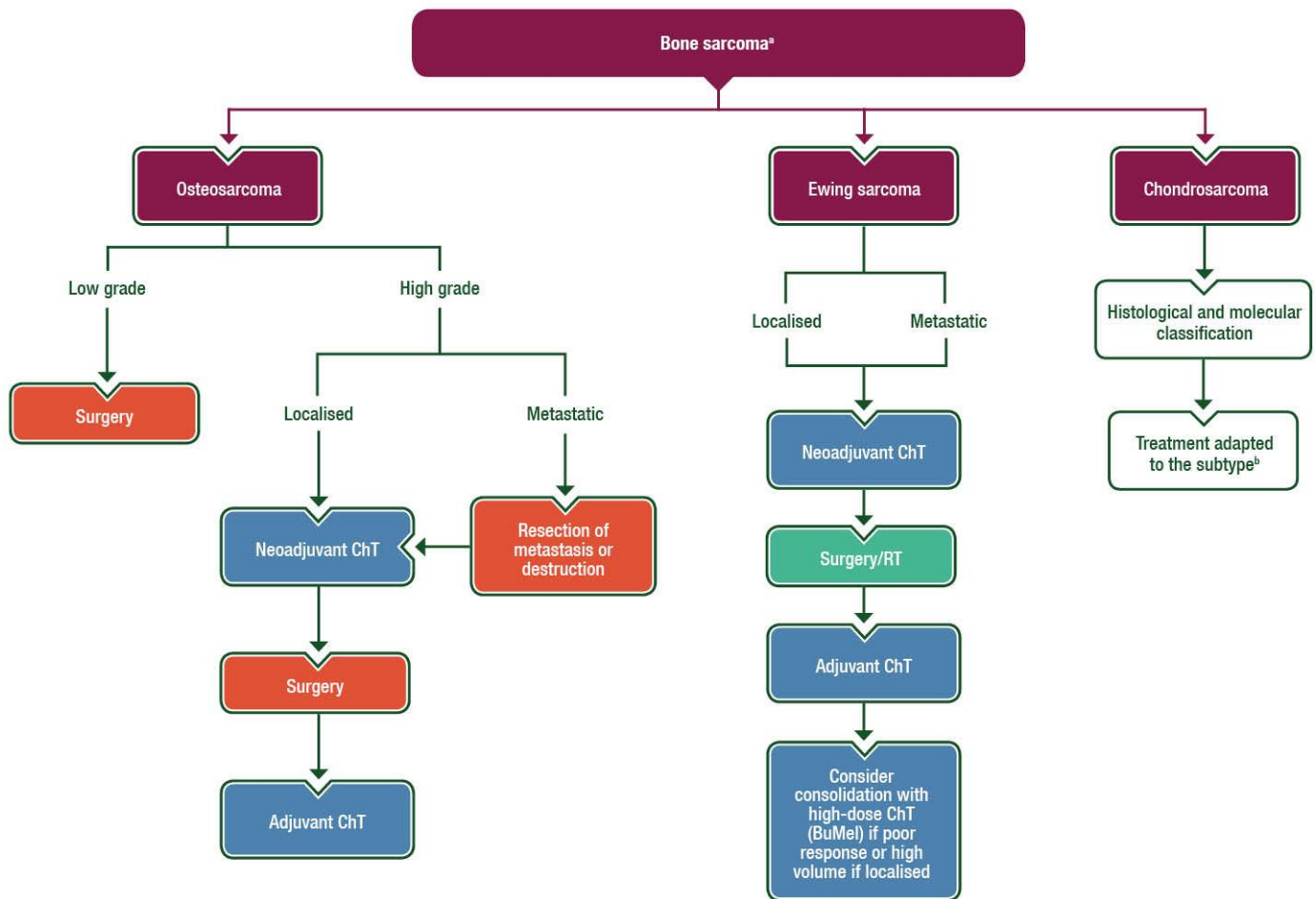


Figure 1. General therapeutic strategy for the three most frequent bone sarcomas

BuMel, busulfan and melphalan; ChT, chemotherapy; RT, radiotherapy.

^aThe treatment of primary bone sarcoma must be carried out in a bone sarcoma reference centre.

^bDepending on the chondrosarcoma subtype, treatment can be surgery, neoadjuvant and adjuvant ChT or RT.

Supplementary Material

Some required elements will be included as supplementary material, which appear online only and are excluded from the overall word count limit. All supplementary data including tables and figures should be prepared as one document (separate word files are not needed).

Supplementary Table(s) with staging system (preferably TNM) and stage groups

Please include any appropriate staging tables as supplementary files. Where possible, refer to the Union for International Cancer Control (UICC) staging system. These tables can be provided by ESMO.

Supplementary Magnitude of Clinical Benefit Scale (ESMO-MCBS) Table

Where applicable, ESMO-MCBS calculations will be performed by the ESMO-MCBS Working Group. The scores will be reviewed and approved by the GLC.

Relevant ESMO-MCBS scores will be summarised in a separate ESMO-MCBS table by ESMO staff. The table will be included as a supplementary file. This table is to be used as a tool to provide basic information on the new therapy rather than the formal tool producing the ESMO-MCBS score.

When an ESMO-MCBS score has been produced for a new therapy or a new indication of existing therapy by the EMA, it should appear next to LoE, GoR in the text and in the algorithms whenever a recommendation on the therapy is formulated (e.g. [I, A; ESMO-MCBS v1.1 score: 4]).

For MCBS scores, in case of disagreement, arbitration is performed by the MCBS WG Chair with the GLC Chair and, when necessary, by the President's Council.

Supplementary Table SX. ESMO-MCBS table for new therapies/indications in XXX^a

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/Toxicity	ESMO-MCBS Score^b
Describe the new therapy	Describe the disease setting. Specify (Neo)adjuvant or Advanced	Name [1], phase of trial, NCT number	Describe the control arm	Median, in months (state OS, PFS or both)	Median and 95% CI	Improved or Deteriorated or Similar or Not Available	Score X (Form X)

CI, confidence interval; EMA, European Medicines Agency; ESMO-MCBS, ESMO-Magnitude of Clinical Benefit Scale; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; QoL, quality of life.

^aEMA approvals since January 2016.

^bESMO-MCBS version 1.1 [2]. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee.

Include in References:

1. Pivotal trial reference.
2. Cherny NI, Dafni U, Bogaerts J et al. ESMO-Magnitude of Clinical Benefit Scale Version 1.1. *Ann Oncol* 2017; 28: 2340–2366.

Supplementary Levels of Evidence and Grades of Recommendation Table

The following table will be included as a supplementary file to explain the methodology regarding the LoEs and GoRs.

Supplementary Table SX. Levels of evidence and grades of recommendation (adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System^a)

Levels of evidence

I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well- conducted randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, expert opinions

Grades of recommendation

A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

^aReprinted by permission of Oxford University Press on behalf of the Infectious Diseases Society of America [Ref#].

Include in References:

Ref#. Dykewicz CA. Summary of the guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. Clin Infect Dis 2001; 33: 139–144 (Adapted from: Gross PA, Barrett TL, Dellinger EP et al. Purpose of quality standards for infectious diseases. Clin Infect Dis 1994; 18: 421).

eUpdates

In the case of a significant breakthrough that necessitates rapid communication as Guideline content or in the case of a new EMA indication bearing an MCBS score, the relevant SE will coordinate with the guideline authors and produce an eUpdate. This will be posted in the ESMO website linked to the appropriate guideline.

Any eUpdate that is contemplated for integration into a Living Guideline will also be reviewed by two ESMO Faculty members or other experts.

Please see the SOPs/instructions for Authors and templates for ESMO eUpdates: <http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology>.