



SOPs/Instructions for Authors and templates for standard ESMO Clinical Practice Guidelines (CPGs) and ESMO-MCBS Scores

ESMO Guidelines Committee, revision January 2019

Introduction

- ✓ The CPGs should be updated when there is need for such as judged by the Guidelines Committee (GLC). Each updated CPG will be published online once finalised and subsequently submitted for evaluation for publication in regular issues of Annals of Oncology (or in an Annals of Oncology Supplement exceptionally).
- ✓ 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 Clinical Practice Guidelines 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, Flow Charts and 'bullet point' recommendations for daily use: Pocket Guidelines. The corresponding author and Subject Editor (SE) of each CPG will be asked to review and comment on the relevant chapter of the Pocket Guidelines.
- ✓ ESMO will produce slide sets containing key recommendations and flow charts. The corresponding author and Subject Editor of the relevant CPG will be asked to review and comment on the slide set.

Structure of the text 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

Tables/algorithms

The CPG text should be supplemented by Tables and Figures. Preferred tables are shown below and should appear in the following order:

1. Table with diagnostic work-up
2. Table with staging system (preferably TNM) and stage groups
3. ESMO-standardised algorithm with management or therapeutic strategy according to risk factors or stage
4. Optional tables on therapeutic regimens or prognosis
5. Personalised medicine synopsis table
6. Table with bullet point summary of all recommendations
7. MCBS table with ESMO-MCBS score for new therapies/indications approved by EMA
8. Table of Levels of Evidence and Grades of Recommendation

Some ESMO CPGs (specifically those focused on cancer genetics and palliative/supportive care) 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:

Cancers of unknown primary site: 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 15 authors, including the Subject Editor. The coordinating author appears as first author, followed by the other contributors and the SE as last. The coordinating author is responsible for coordination of authorship and submission of the CPG draft. Please include full affiliation details for each author.

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 European and global guideline.

Extent

The manuscript should have no more than **12 000 words** and **particularly focus on the therapeutic recommendations**.

References not to exceed 150 maximum. Authors will be asked to remove references if this number is not respected.

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	LOE, GOR
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 relevance, d) used for medical treatment decisions, e) currently actionable/targetable	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

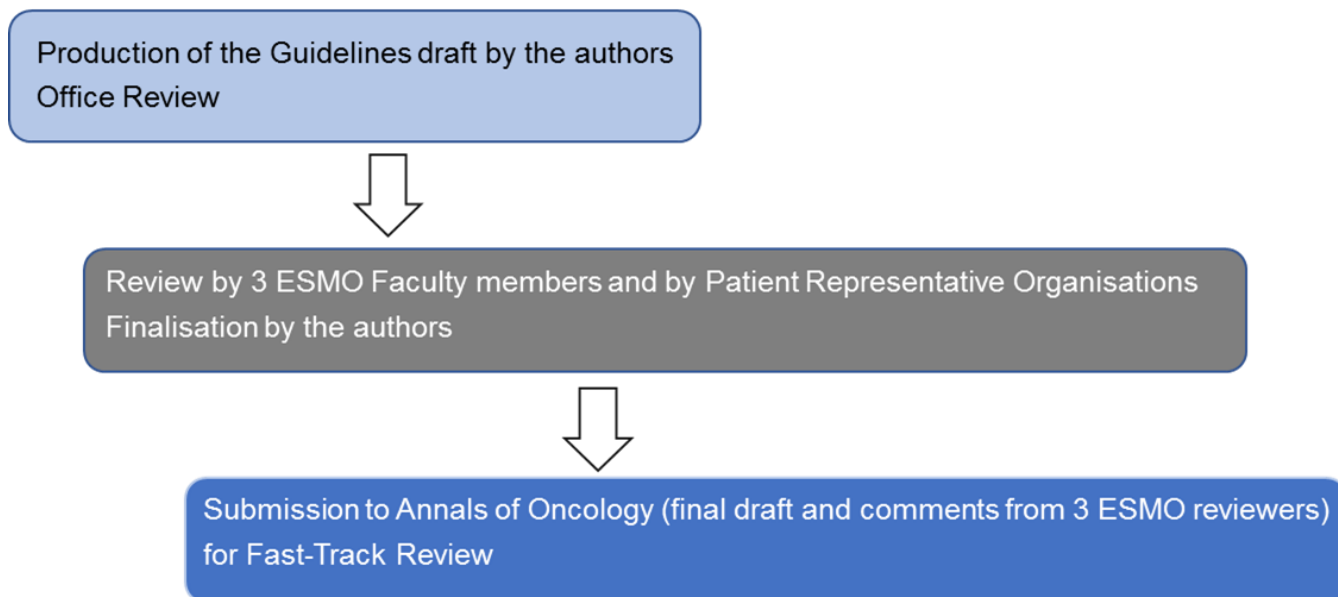
This section will focus on recommendations for patient follow-up and will also include information on long-term toxicities of treatment, second tumours, psychosocial implications, rehabilitation and any other issues related to survivorship.

Methodology

The following paragraph should be included:

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. A summary of recommendations is shown in Table X. Levels of evidence and grades of recommendation have been applied using the system shown in Table X. Statements without grading were considered justified standard clinical practice by the experts and the ESMO Faculty. This manuscript has been subjected to an anonymous peer review process.

Each ESMO Clinical Practice Guideline is reviewed by 3 independent experts, members of the ESMO Faculty, as well as patient representatives. After finalisation, the draft along with ESMO Faculty reviewer feedback is submitted for evaluation of publication to Annals of Oncology.



Disclosure

Each author must provide a disclosure of interest statement. 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.

The disclosure of interest should be general and not limited to interests closely related to the current manuscript.

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 150 maximum.

ESMO-standardised algorithm

It is very important that authors produce an ESMO-standardised algorithm on therapeutic strategy or management according to stage, risk factors and disease/molecular characteristics. This is a priority issue for ESMO. ESMO will prepare the final algorithms using standard formatting/colours for publication.

The following colour-code should 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 below.

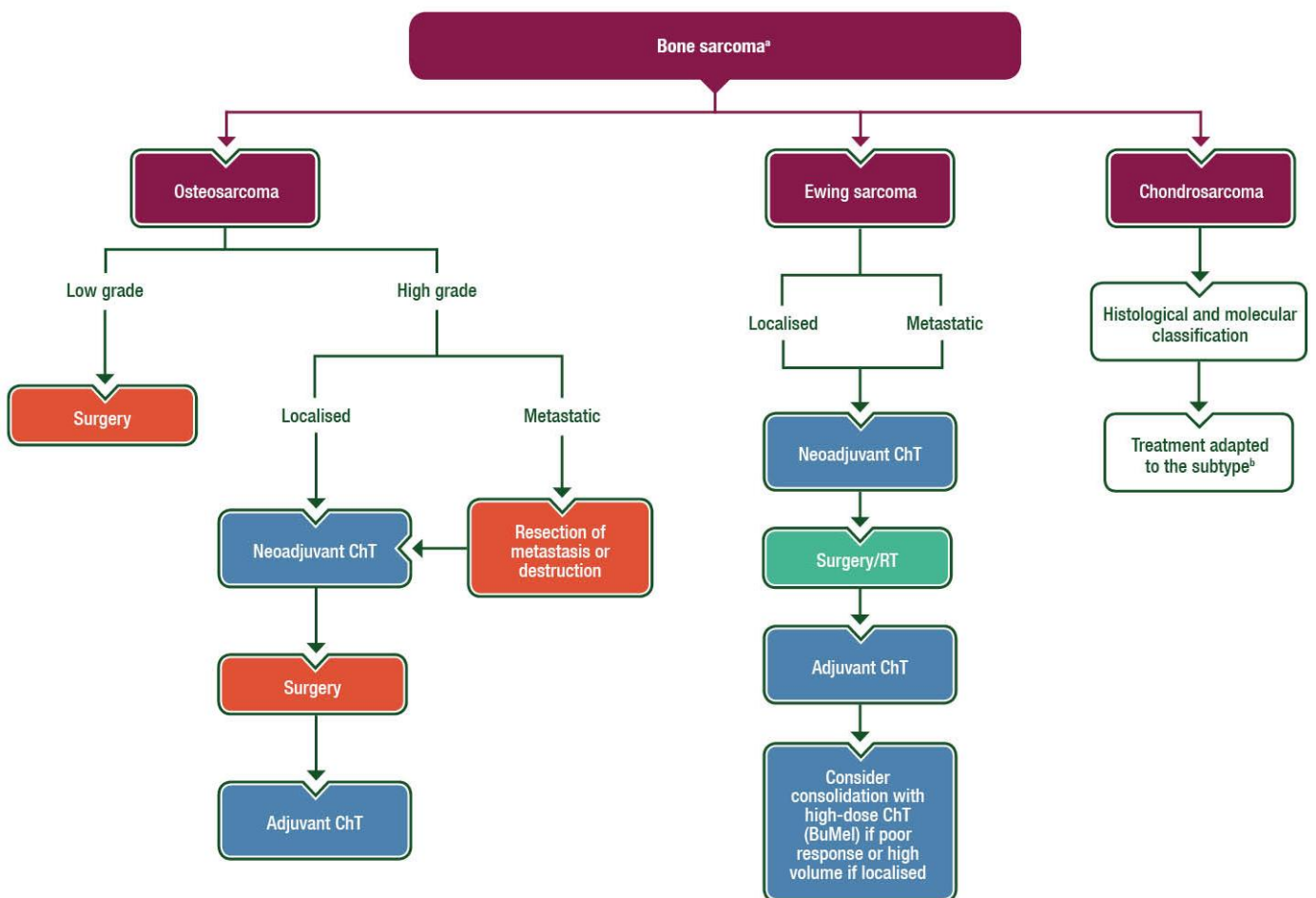


Figure 2. General therapeutic strategy for the three most frequent bone sarcomas

^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.

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

Summary of recommendations

Please include a complete summary of recommendations from each thematic section of the manuscript, including levels of evidence and grades of recommendation where applicable:

Table X. Summary of recommendations

Incidence and epidemiology

- Recommendation 1 [LoE, GoR]

Diagnosis and pathology

- Recommendation 2 [LoE, GoR]

Staging and risk assessment

- Recommendation 3 [LoE, GoR]

Treatment

- Recommendation 4 [LoE, GoR]
- Recommendation 5 [LoE, GoR]

Magnitude of Clinical Benefit Scale (ESMO-MCBS) score

MCBS calculations will be performed by the MCBS Working Group. The scores will be reviewed and approved by the GLC and the MCBS Working Group.

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 whenever a recommendation on the therapy is formulated (e.g. [I, A; ESMO-MCBS v1.1 score: 4]).

Moreover, all ESMO-MCBS scores should be summarised in a Table at the end of the CPG, after the Table Summary of all recommendations.

This table is to be used as a tool providing easily communicable, basic information on the new therapy rather than the formal tool producing the ESMO-MCBS score

Table X. Magnitude of Clinical Benefit Scale (MCBS) table for new therapies/indications in X cancer^a.

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/Toxicity	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)

^aEMA approvals since January 2016.

^bESMO-MCBS version 1.1 [2].

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.

Levels of Evidence (LoE) and Grades of Recommendation (GoR), ESMO-MCBS score:

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 Level of Evidence (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 Grade of Recommendation (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).

Table X. 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, ...), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

^aBy permission 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.

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 Subject Editor will coordinate with the guideline authors and produce an eUpdate. This will be posted in the ESMO Guidelines Website and published at Annals of Oncology every 4-6 months, grouped together with all eUpdates produced.

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