



**ESMO Standard Operating Procedures (SOPs)
for Clinical Practice Guidelines (CPGs) and
ESMO Magnitude of Clinical Benefit (ESMO-MCBS) and ESMO Scale for
Clinical Actionability of molecular Targets (ESCAT) scores**

ESMO Guidelines Committee (GLC)

Version	ESMO CPG SOP Version 2.2; September 2022
Changes in this version	Modified ESMO Declaration of Interest (DOI) collection requirements
Approved	Giuseppe Curigliano, GLC Chair
Next review planned	After the next GLC meeting (in 2022, date to be confirmed); revisions can be made sooner as required

Note: this SOP only applies to ESMO CPG publications and full updates. For additional guidance on updates of original CPG publications, please see the separate electronic update (eUpdate) and Clinical Practice Living Guidelines (Living GLs) SOPs. All three SOP documents are available publicly on the ESMO website [esmo.org](http://www.esmo.org): <http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology>.

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1 Introduction

- The target audience for ESMO CPGs is health professionals working in the field of oncology across Europe and other parts of the world.
- ESMO CPGs should consider the content of any published ESMO Consensus Conference Recommendations manuscripts when available. ESMO CPGs and Consensus Conference Recommendations manuscripts are two separate but complementary products.
- CPGs will be submitted to an ESMO journal for evaluation for publication—*Annals of Oncology* (annalsofoncology.org) or *ESMO Open* (esmoopen.com). ESMO staff will format all ESMO CPGs to align with ESMO journal style prior to submission.
- 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 lead author may also be asked for comment.
- ESMO will produce slide sets containing key recommendations and algorithms. The lead author and SE of the relevant CPG will be asked to review and comment on the slide set.
- ESMO will produce webinars following publication of CPGs, involving case-based discussion around the practical implementation of recommendations.

2 Commissioning of a CPG

CPGs should be proposed for update when there is need for such as judged by the ESMO GLC Chair, a Guidelines Steering Committee (GL-SC) member or the SE. This judgement is based on the availability of new, clinically-significant evidence that requires substantial changes or additions to clinical recommendations. New CPGs may also be considered for topics not currently covered by current ESMO CPG titles.

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 this SOP and methodology, with some adjustments if needed, to generate consent. If applicable, ESMO will provide the necessary Memorandum of Understanding (MOU) with the society(ies), as well as a specific Guideline Development Agreement (GDA) for each CPG title (except for CPGs involving EURACAN).

3 Role of ESMO Guidelines staff

Each guideline will have an ESMO Guidelines staff member responsible for communications, planning and oversight throughout the guideline development process. The ESMO Guidelines staff review and edit all guidelines to ensure they adhere to this SOP and ESMO journal requirements but do not serve as authors. Editing support will be provided and medical writing support can also be provided as agreed with the authors. These roles are considered to be ‘non-author contribution’ and do not replace intellectual contribution from the authors. The exact role of each staff member involved in the guideline will be detailed in the Acknowledgements section of the CPG as editing support and/or medical writing support.

4 Authorship

4.1 Author selection process

For each CPG, the SE should propose the lead author to the GLC Chair for approval. Once approved, the SE and lead author should propose the co-authors. The ESMO GL-SC member and the ESMO Faculty coordinator for the subject area should also be involved during co-author proposals to select the best contributors.

The ESMO Guidelines staff will assist the SE and lead author with coordinating the author selection process, obtaining the GLC Chair’s approval of the proposed authors and sending formal invitations (see below). Invitations are sent on behalf of the lead author, SE and the GLC Chair.

4.2 Authorship criteria

The author group should consist of experts who fulfil the following criteria:

- The author group should consist of a minimum of 8 authors, including the SE (last author) and, if relevant, any GL-SC member(s).
- Each proposed author should have an internationally recognised profile in the field and good reputation.
- The author group should be diverse, gender-balanced and multidisciplinary, and therefore should include medical oncologists, a surgical oncologist, a radiation oncology specialist and/or other disciplines if appropriate.
- The group should also be multinational with authors representing various countries in Europe and elsewhere to ensure validity as both a European and global guideline.
- The group should be multi-institutional, ideally with all authors representing different institutions (i.e. ideally a maximum of one representative from each institution, but exceptions can be granted for rare tumours). This criterion may be easier to achieve for common cancers than for rare cancers.
- At least one early-career, talented expert in the field should be included. There is no specific age requirement; however, these individuals should be relatively junior and their involvement in the ESMO CPG should present a valuable opportunity for their career (members of the ESMO Young Oncologists Committee or the ESMO Leaders Generation Programme may be recommended for consideration pending approval of the SE and the GLC Chair). The ESMO Guidelines staff can provide details of these individuals to SEs and lead authors.
- Inclusion of representative(s) of patient organisations or patient advocacy groups can be considered where appropriate, either as authors, if they meet the authorship criteria, or as reviewers.

All authors should fulfil all four of the following authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE):¹

- Substantial contribution to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

For CPGs involving a large multi-author group, all members of the group named as authors should still meet all four of the above ICMJE authorship criteria, including approval of the final manuscript.

Individuals who do not meet all four criteria should be acknowledged as non-author contributors, either individually or as a group under the Acknowledgements section, with details of the specific contribution, and their written permission obtained in order to include their acknowledgement.

4.3 Contributor roles

Description of individual contributor roles provides transparency over the differing roles of each author and may help to avoid authorship disputes, as well as enable authors to have confidence in the accuracy and integrity of all their co-authors.^{2,3}

As well as the authorship criteria outlined above, certain key authors have the specific responsibilities described below. Other responsibilities for the authors below and other co-authors may also be decided upon on a guideline-specific basis, e.g. allocation of specific sections of the manuscript. Contributions will be described in the contributor statement in the Acknowledgements.

4.3.1 Lead author

The lead author acts as the coordinating author and appears as first author, followed by the other co-authors and the SE as last author.

The Lead Author is responsible for:

- Proposing suitable co-authors, in collaboration with the SE.
- Acting as the coordinating author to drive input and contributions from co-authors and to provide progress updates to the ESMO Guidelines Committee and ESMO Guidelines staff.
- Ensuring that the guideline follows the ESMO methodology as closely as possible.
- Certifying that all authors fulfil the ICMJE criteria and describing their contributions using the ESMO Author Responsibility and Acknowledgement Agreement form (see the ESMO website here: <https://www.esmo.org/guidelines/esmo-guidelines-methodology>).

- Along with the last author (SE), providing review/commentary on related ESMO guideline derivative products, e.g. slide sets and Pocket Guidelines.

4.3.2 Last author and SE

As the Last Author, the SE is responsible for:

- Proposing a suitable first author and co-authors, in collaboration with the GL-SC and relevant ESMO Faculty coordinator.
- Ensuring that the guideline follows the ESMO methodology as closely as possible and providing extensive support to the lead author regarding queries on methodology.
- Providing the cover letter for journal submission, including recommended reviewers (ESMO Faculty where possible).
- Providing commentary on related ESMO guideline derivative products, e.g. slide sets and Pocket Guidelines.

4.3.3 GLC Chair and Deputy Chair

In select cases, the GLC Chair or Deputy Chair will be invited to be a co-author.

4.3.4 GL-SC member

A relevant GL-SC member will be invited to be a co-author on each CPG within his/her tumour area (excluding ex-Officio members, who are members related to their role on another ESMO committee). The GL-SC member can be listed as a joint co-last author (penultimate). Even when the GL-SC member is regarded to be more 'senior' than the SE in the field, the current SE will be the last author of the guideline.

4.3.5 ESMO Faculty coordinator

The lead author, the GL-SC member and SE will work with the ESMO Faculty coordinator for the subject area to select the best contributors for the specific guideline.

4.3.6 Representatives of other societies

For joint guidelines with other societies, specific experts will play a central role as a representative of that society, either as co-first author or co-senior author in 'equal contribution' mode. These authors will work closely with the ESMO lead author and SE to evaluate the author committee and nominate additional multidisciplinary experts (e.g. non-medical oncologists) if needed. The GLC Chair is responsible for approving the entire author panel including representatives of any other societies. Authorship and publication details will be detailed in a specific GDA for each joint CPG title except for EURACAN (see next paragraph). All authors will be expected to comply with the ESMO methodology detailed in this SOP.

In the field of rare adult solid cancers, ESMO may collaborate with EURACAN, the European Reference Network, on CPGs covering single families of rare adult solid cancer (e.g. sarcomas) or tumours/groups of tumours within such families (e.g. thymomas, within rare thoracic tumours). The decision to proceed with any new ESMO-EURACAN CPGs will be made jointly by the GLC Chair and the respective EURACAN coordinator for that disease area on a case-by-case basis. All authors of ESMO-EURACAN CPGs will be expected to comply with the ESMO methodology detailed in this SOP.

4.4 Order of authorship

Unless otherwise specified and approved by the GLC Chair, the CPG author order is as follows:

First author.

Other co-authors: In alphabetical order of surname.

GLC Chair, Deputy Chair or GL-SC member as co-author: In alphabetical order of surname or as a joint co-last author (penultimate).

Last author: SE.

4.5 Author invitations

Once the author group is approved by the GLC Chair, the ESMO Guidelines staff will formally invite all potential authors to participate.

4.6 ESMO Declaration of Interest

As part of the author confirmation process, ESMO will verify and/or request that each potential author has an ESMO account and has provided a valid Declaration of Interest (DOI) in the ESMO DOI Platform. The DOI collection process is centrally managed within ESMO, and the financial value of each disclosure will be treated as confidential. For more information, refer to the ESMO DOI policy available here: <https://www.esmo.org/about-esmo/how-we-work/declaration-of-interest>.

Each author must provide DOI information including financial values, even if there is nothing to declare, before the individual's participation in the guideline can begin including kick-off meetings. After all DOIs are received/confirmed and are reviewed, the CPG kick-off meeting (online) can proceed.

Each author is responsible for ensuring that their DOI statement in the ESMO DOI Platform is true, up to date and complete.

5 CPG kick-off meeting

After submission of all authors' DOIs, the ESMO Guidelines staff will organise an online kick-off meeting with all authors to discuss author roles, timelines and manuscript formatting requirements as detailed in this SOP. The ESMO Guidelines staff will provide the lead author with draft presentation slides for the lead author/SE to review and to include author allocations (if possible before the meeting). Proposed timelines can then be discussed in the meeting.

CPG kick-off meetings will cover:

- Author introductions and roles of first author, last author/SE and other co-authors, including GL-SC member (if relevant)
- Key SOP details
 - Overview of thematic structure/sections
 - Use of levels of evidence (LoEs) and grades of recommendation (GoRs)
 - ESMO-standardised treatment/management algorithms
 - ESMO-MCBS
 - ESCAT
 - Supplementary material
- Author allocations, manuscript development and proposed timelines
 - Author agreement form detailing each author's contribution (to be completed before final manuscript submission)
- ESMO Guidelines staff review and journal submission
 - ESMO provides an author collaboration site for each author group using Microsoft SharePoint Team collaboration software tools. Guidelines staff are not able to support the use of Google docs or other external collaboration sites
 - If the ESMO Guidelines staff members are to provide medical writing support to the author group, the key roles should be outlined, discussed and agreed upon during the kick-off meeting.
- Overview of the plan/concept for Living GLs and CPG derivative products (e.g. planned ESMO slide sets, pocket guidelines, webinars and Pan-Asian adaptations)
- Any other questions

Following the kick-off meeting, ESMO Guidelines staff will provide a CPG manuscript template (Word document), supplementary material template (Word document) and CPG algorithm template (PowerPoint document). The main manuscript template can only be completed once the author allocations to the writing sections are made.

Similarly, the author agreement form can be drafted for the initial kick-off meeting, but the final version can only be completed by the lead author prior to manuscript submission.

6 Development of the CPG: Main manuscript

Note: a main manuscript template will be provided.

6.1 Extent

ESMO journals follow a strict word count policy. 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, disclosures and funding are excluded from the word count). Additional information can be included in the supplementary material.

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.

6.2 Guidance on writing

6.2.1 General guidance

Long discussions about drugs that are controversial or not readily available should be avoided.

When required due to word limit, authors may move some text to the supplementary material. However, clinical recommendations should be kept in the main text.

When relevant, authors are encouraged to consider the relevance of their clinical recommendations to underrepresented demographics/ethnicities and to comment on related gaps in the literature and research when needed.

Drugs that are not yet approved by the European Medicines Agency (EMA) should be identified with the statement 'at the time of publication, [drug/treatment] is not EMA-approved [for X indication]'. This phrasing must be used even if a drug is very likely to receive approval soon [i.e. if a Committee for Medicinal Products for Human Use (CHMP) recommendation for approval has been published]. Statements about expected approvals of drugs should be supported with a reference to the Summary of Product Characteristics/Prescribing Information or a pharmaceutical company's press release if formal EMA approval is not yet publicly available.

6.2.2 Tools available for best practice

The development and writing of ESMO CPGs should follow best practices. To aid this, the following tools may be useful:

The Appraisal of Guidelines, Research and Evaluation (AGREE) Reporting Checklist.^{6,7}

Available here: <http://www.agreetrust.org/resource-centre/agree-reporting-checklist>.

The Template for Intervention Description and Replication (TIDieR) Checklist.

Available here: <https://www.equator-network.org/wp-content/uploads/2014/03/TIDieR-Checklist-PDF.pdf>.

6.2.3 Wording of recommendations

Recommendations should be easy for clinicians to understand and interpret. Therefore, clear details should be provided on the patient population, interventions, comparators and if relevant, the clinical setting. Although passive voice is used in scientific writing to distance researchers from their work, using an active voice rather than passive voice in ESMO CPGs may also enhance clarity, e.g. "Three trials have addressed the question..." as opposed to "The treatment strategies most effective were demonstrated to be...".

The following phrasing is recommended to aid communication of the strength of recommendation, based on advice from the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group:⁸

- Strong positive recommendations (grade A): 'the authors recommend...' or 'clinicians should' or 'Do...'
- Strong negative recommendations (grade E): 'clinicians should not...', or 'Do not...'
- Weak recommendations (grade B and D): 'it is suggested...' or 'clinicians might...' or 'the authors conditionally recommend...'

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 System⁵.

Therefore, it is mandatory for all recommendations to be supported with an LoE and GoR, and where relevant ESMO-MCBS scores should also be included.

The LoE describes the quality of existing evidence (trials, cohort studies, case-control studies, expert opinion) that addresses a specific clinical question. The quality of evidence is assessed in terms of number of trials, sample size, methodology, bias and 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 can be positive (recommended) or negative (not recommended). To avoid confusing negative logic, please construct a logically positive wording for the recommendation, and then assign the appropriate GoR to indicate if the recommendation is positive or negative.

Example:

- 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).

A bullet-point list of all recommendations in each thematic section should be included at the end of the relevant section, 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 can 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 [II, B].¹⁵

6.2.4 Precision medicine

Information relating to biomarkers for precision medicine should be included throughout the CPG text in the various sections where relevant and appropriate (e.g. for disease classification, prognosis, prediction and treatment decisions). Information should be given on whether the biomarkers are validated and actionable or targetable (e.g. ESCAT scores).

6.2.5 Quality control

Authors are responsible for performing a data check of any numerical data (i.e. survival rates, p-values, hazard ratios, etc.) reported in the manuscript against the source publications and verifying the accuracy of data and other content included in the guideline.

6.3 Thematic sections

The thematic section structure described below should be used. Some ESMO CPGs (specifically those focused on cancer genetics and palliative/supportive) may not be compatible with these headings and may therefore follow 'individualised' structure.

6.3.1 Heading

6.3.1.1 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

6.3.1.2 Authors and affiliations

Provide first initial(s) and last names exactly as they should appear in the final manuscripts. Affiliations must be provided separately for each institution and should include a department where possible.

6.3.1.3 Running header

Please include a short running header, according to the following example, 80 character maximum:

ESMO Clinical Practice Guidelines for prostate cancer

6.3.1.4 Word count

The following details should be included:

Word count: XXX (excluding title page, acknowledgements, funding and disclosure sections); References: X; Tables: X; Figures: X; Supplementary material: 1.

6.3.1.5 Key words

Please include up to five key phrases for *ESMO Open* and six key phrases for *Annals of Oncology* can be included. Please review and adapt as needed. Those suggested below are standardised across ESMO CPGs but can be adapted as needed.

X, XX, ESMO Clinical Practice Guideline, diagnosis, treatment, follow-up

6.3.1.6 Highlights (online only)

Highlights are required by ESMO journals for the submission and online promotion of the final manuscript. Please provide three to five bullet points summarising the main points of the article. Each bullet point must not exceed 125 characters per bullet, including spaces.

Those suggested below are standardised across ESMO CPGs but can be adapted if they are not relevant to this title.

- This ESMO Clinical Practice Guideline provides key recommendations for managing [tumour/tissue].
- The guideline covers clinical and pathological diagnosis, staging and risk assessment, treatment and follow-up.
- Treatment and management algorithms for locoregional, advanced/metastatic and recurrent disease are provided.
- ESCAT scores are given to describe the evidence level for genomic alterations as biomarkers for using targeted therapies.
- The author group encompasses a multidisciplinary group of experts from different institutions and countries in Europe and [insert other regions if relevant].
- Recommendations are based on available scientific data and the authors' collective expert opinion.

Example:

- This ESMO Clinical Practice Guideline provides key recommendations on the management of prostate cancer.
- Authorship includes a multidisciplinary group of experts from different institutions and countries in Europe.
- Key treatment recommendations are provided.
- Recommendations have been updated in the light of new evidence.

6.3.2 Incidence and epidemiology

The ESMO guidelines are Europe-centric but also provide guidance worldwide. Therefore, include details of global incidence and epidemiology when relevant, in addition to European data.

6.3.3 Diagnosis, pathology and molecular biology

A table and/or algorithm detailing diagnostic work up-should be included.

6.3.4 Staging and risk assessment

Where possible, refer to the Union for International Cancer Control (UICC) Tumour-Node-Metastasis (TMN) staging system⁴ throughout the manuscript. Staging tables should be included in the supplementary material. These tables can be provided by ESMO.

6.3.5 Management of local and locoregional disease

An ESMO-standardised treatment algorithm must be included on therapeutic strategy or management according to stage, risk factors and disease/molecular characteristics.

6.3.6 Management of advanced and metastatic disease

An ESMO-standardised treatment algorithm must be included on therapeutic strategy or management according to stage, risk factors and disease/molecular characteristics.

6.3.7 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. A subsection of supportive and palliative care should be included when appropriate.

6.3.8 Methodology

Methodology is required in the main text of the manuscript.

The following paragraph will be included in all CPGs:

This Clinical Practice Guideline was developed in accordance with the ESMO standard operating procedures for Clinical Practice Guideline development (<https://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology>). The relevant literature has been selected by the expert authors. A table of ESCAT scores is included in Supplementary Table SX. ESCAT scores have been defined by the authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[ref #] A table of ESMO-MCBS scores is included in Supplementary Table SXX. ESMO-MCBS v1.1[ref ##] was used to calculate scores for new therapies/indications approved by the EMA or FDA (<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. The FDA/EMA or other regulatory body approval status of new therapies/indications is reported at the time of writing this CPG. Levels of evidence and grades of recommendation have been applied using the system shown in Supplementary Table SXXX.[ref ###, ref #####] Statements without grading were considered justified standard clinical practice by the authors. For future updates to this CPG, including eUpdates and Living Guidelines, please see the ESMO Guidelines website: [insert original CPG web link on esmo.org].

ref # = include reference to ESCAT manuscript (framework) in the References section (also include this reference in the supplementary material): Mateo J, Chakravarty D, Dienstmann R, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT). *Ann Oncol.* 2018;29(9):1895-1902.

ref ## = include reference to ESMO-MCBS manuscript (v1.1) in the References section (also include this reference in the supplementary material): Cherny NI, Dafni U, Bogaerts J, et al. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol.* 2017;28(10):2340-2366.

ref ###, ref ##### = include references for LoE/GoR table (also include this reference in the 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.
- Gross PA, Barrett TL, Dellinger EP et al. Purpose of quality standards for infectious diseases. *Clin Infect Dis.* 1994;18:421.

6.3.9 Acknowledgments

Please include any additional acknowledgements as appropriate, following the format of the example below. Individuals who do not meet all four ICMJE authorship criteria should be acknowledged as non-author contributors,¹ either individually or as a group, and their written permission obtained in order to include their acknowledgement. Editing and writing support will be acknowledged, e.g. from ESMO Guidelines staff or freelancers working on behalf of ESMO.

For manuscripts including ESMO-MCBS scores and/or ESCAT scores, the members of the respective working group as well as the ESMO staff and freelancers working on behalf of ESMO will be acknowledged.

e.g. Manuscript editing support was provided by Louise Green and Richard Lutz (ESMO Guidelines staff) and Angela Corstorphine of Kstorfin Medical Communications Ltd (KMC); this support was funded by ESMO. Nathan Cherny, Chair of the ESMO-MCBS Working Group, Urani Dafni ESMO-MCBS Working Group Member/Frontier Science Foundation Hellas and Giota Zygoura of Frontier Science Foundation Hellas provided review and validation of the ESMO-MCBS scores. Nicola Latino (ESMO Scientific Affairs staff) provided coordination and support of the ESMO-MCBS scores and Angela Corstorphine and Sian-Marie Lucas of KMC provided medical writing and editing support in the preparation of the ESMO-MCBS table; this support was funded by ESMO. Dr Joaquin Mateo (Chair of the ESMO Translational Research and Precision Medicine Working Group) and Dr Svetlana Jezdic (ESMO Medical Affairs Advisor) provided validation support for ESCAT scores.

6.3.10 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.

6.3.11 Disclosure

See Section 4.6: ESMO Declaration of Interest.

6.3.12 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 should not exceed 100 maximum.

Reference managing software should be used with a travelling library available to the ESMO Guidelines office to facilitate formatting for journal submission. Endnote is ESMO's recommended choice of software and a free version is available online. The Guidelines office will use Endnote 20 for reference formatting and can assist authors as needed with managing the references.

6.3.13 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 but all content should be provided in an editable format).

The references cited in the tables should also be listed after all references that appear in the main manuscript.

Suggested tables include:

- Table with diagnostic work-up
- Tables on therapeutic regimens or prognosis

6.3.14 Treatment algorithms (mandatory) and other figures

Note: an algorithm template will be provided. All figures should be provided in an editable PowerPoint format.

Algorithms on therapeutic strategy or management according to stage, risk factors and disease/molecular characteristics are required and must be cited within the document. This is a priority issue for ESMO.

Please include LoEs and GoRs where applicable. Please include all acronyms in alphabetical order by acronym and footnotes in the order shown below.

ESMO-MCBS and/or ESCAT scores should 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** (rgb: 133, 25, 74): general/heading boxes related to stratification, e.g. type of cancer or patient sub-group
- **Red** (rgb: 224, 81, 54): surgery
- **Dark green** (rgb: 20, 83, 40): radiotherapy

- **Blue** (rgb: 76, 128, 175): systemic anticancer therapy

- **Turquoise** (rgb: 66, 180, 146): combination of treatments (e.g. CRT) or other systemic treatments (allo-SCT, RBC transfusions, antibiotics, steroids, etc.)

- **White** (rgb: 225, 225, 225): other aspects of management not covered by the categories above, e.g. observation and monitoring.

An example of a treatment algorithm is shown below.

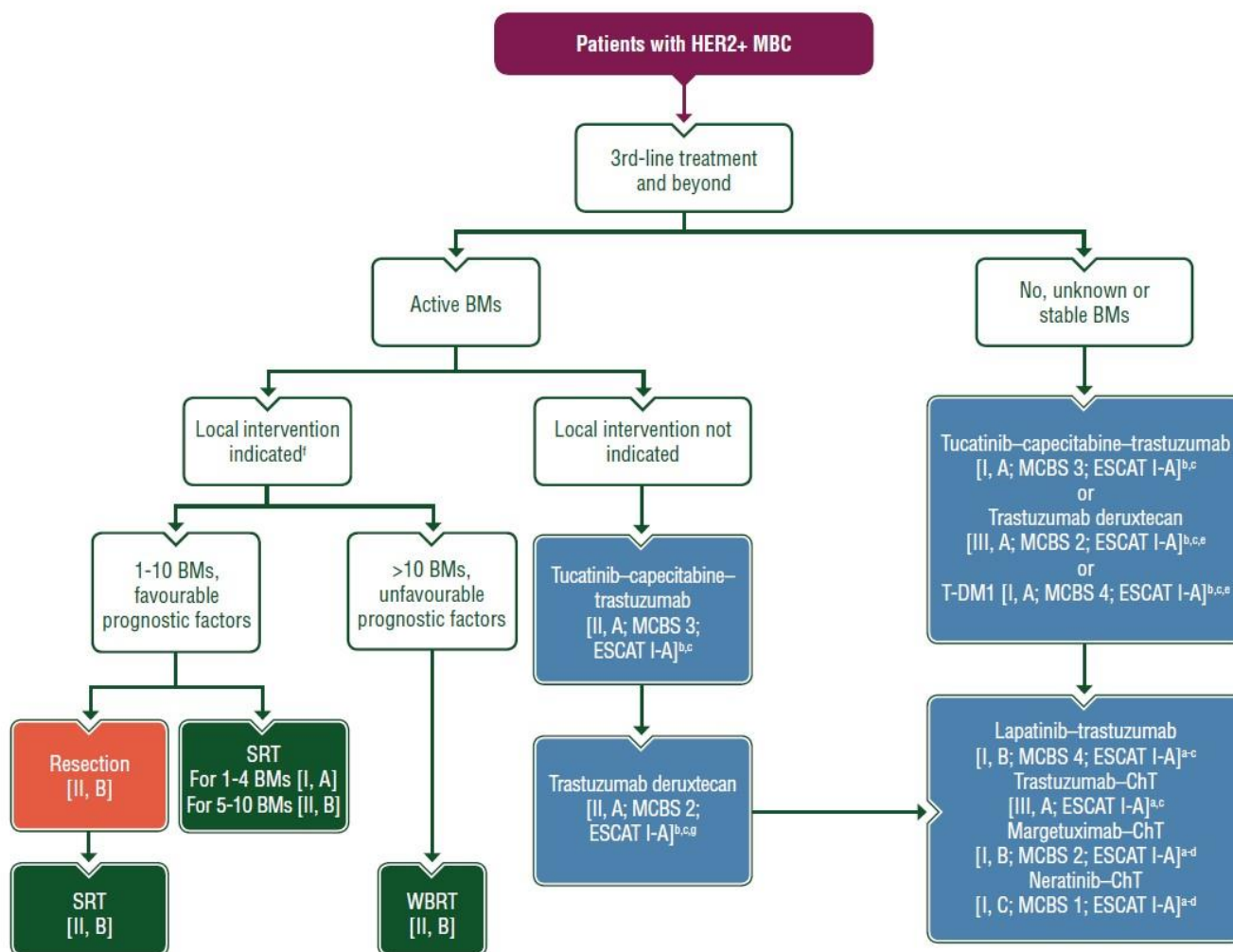


Figure 4. Third-line and beyond treatment of HER2-positive MBC.

Purple: general categories or stratification; red: surgery; turquoise: combination of treatments or other systemic treatments; green: RT; white: other aspects of management; blue: systemic anticancer therapy.

BM, brain metastasis; ChT, chemotherapy; CNS, central nervous system; EMA, European Medicines Agency; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PD, progressive disease; RT, radiotherapy; SRT, stereotactic radiotherapy; T-DM1, ado-trastuzumab emtansine; WBRT, whole brain radiotherapy.

^a There are no data for any of these combinations after tucatinib- and/or trastuzumab deruxtecan-based therapy.

^b ESMO-MCBS v1.1[ref #] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms>).

^c ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[ref ##] See Table SX for more information on ESCAT scores.

^d FDA approved, not EMA approved.

^e If not received as second-line therapy.

^f Keep on current systemic therapy unless PD outside CNS.

^g If not previously used, including all other drugs that are also a second-line treatment option.

ref # = include reference to ESMO-MCBS manuscript (v1.1) in the References section (also include this reference in the supplementary material): Cherny NI, Dafni U, Bogaerts J, et al. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol.* 2017;28(10):2340-2366.

For figures including ESCAT scores:

ref ## = include reference to ESCAT manuscript (framework) in the References section (also include this reference in the supplementary material): Mateo J, Chakravarty D, Dienstmann R, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT). *Ann Oncol.* 2018;29(9):1895-1902.

Table SX = supplementary table of ESCAT scores.

7 Development of the CPG: Supplementary file

Note: a supplementary file template will be provided.

7.1 Extent

Some required elements will be included as supplementary material, which is excluded from the overall word count limit. The supplementary material should follow the same formatting and style requirements as the main manuscript, including for headings and referencing.

All supplementary text sections and tables must be cited within the main manuscript and should be included in the supplementary file (all content should be provided in an editable format).

Supplementary tables should include:

- Supplementary biomarkers and molecular targets for precision medicines and corresponding ESCAT table with ESCAT scores (if applicable)
- Supplementary table(s) with staging system [preferably the European tumour–node–metastasis (TNM)]⁴ and stage groups
- Supplementary ESMO-MCBS table with ESMO-MCBS scores for new therapies/indications approved by the EMA or FDA (if applicable)
- Supplementary LoE/GoR table (required for all ESMO guidelines)

7.2 Precision medicine and ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) scores

Information relating to actionability, clinical utility and clinical validity of biomarkers and molecular targets for precision medicine should be included throughout the CPG text in the various sections where relevant and appropriate, e.g. regarding diagnosis, staging and classification, prognosis, use in medical treatment decisions and follow-up and monitoring.

Where relevant, the guideline authors should calculate and include ESCAT scores for any genomic alteration–drug matches included in the guideline, evaluating previously published ESCAT scores if available or interacting with the ESMO Translational Research and Precision Medicine Working Group (TRPM WG) if no ESCAT scores are available. A member of the TRPM WG who is not an author will review and validate ESCAT scores proposed by the authors. The ESMO Guidelines office will organise this process.

ESCAT scores should be included in the main manuscript with the recommendations and in algorithms, alongside the LoE/GoR and ESMO-MCBS scores, along with a reference in the main manuscript to the

supplementary file, e.g. 'For personalised therapy approaches, ESCAT classifications [ref #] need to be considered (Supplementary Table S1).'

An ESCAT table 'Biomarkers and molecular targets for precision medicines and corresponding ESCAT scores is recommended in the supplementary file. A template table is given below.

7.2.1 ESCAT criteria

The ESCAT score defines clinical evidence-based criteria for prioritising genomic alterations for use as markers to select patients for targeted therapies. The scale is comprised of six tiers based on implications for patient management (Tier I-X; see Table below). These tiers are sub-divided by level of clinical evidence. For pragmatic clinical guidance, the most relevant ESCAT tiers for guidelines may be Tier I and II (targets ready for implementation in routine clinical decisions; and investigational targets that likely define a patient population that benefits from a targeted drug but additional data are needed, respectively).

Criteria for defining the ESCAT score for genomic alteration–drug matches

	ESCAT Tier	Clinical value class	Clinical implication	Level of evidence	Overall ESCAT score (include the in guideline)
Ready for routine use	I: Alteration–drug match is associated with improved outcome in clinical trials.	Drug administered to patients with the specific molecular alteration has led to improved clinical outcome in prospective clinical trial(s).	Access to the treatment should be considered standard of care.	A: prospective, randomised clinical trials show the alteration–drug match in a specific tumour type results in a clinically meaningful improvement of a survival endpoint.	I-A
				B: prospective, non-randomised clinical trials show that the alteration–drug match in a specific tumour type, results in clinically meaningful benefit as defined by ESMO-MCBS v1.1.	I-B
				C: clinical trials across tumour types or basket clinical trials show clinical benefit associated with the alteration-drug match, with similar benefit observed across tumour types.	I-C
Investigational	II: alteration–drug match is associated with antitumour activity, but magnitude	Drug administered to a molecularly defined patient population is likely to result in clinical benefit in a given tumour type, but	Treatment to be considered 'preferable'. in the context of evidence collection either as a prospective	A: retrospective studies show patients with the specific alteration in a specific tumour type experience clinically meaningful benefit with matched drug compared with	II-A

	of benefit is unknown.	additional data are needed.	registry or as a prospective clinical trial.	alteration-negative patients. B: prospective clinical trial(s) show the alteration-drug match in a specific tumour type results in increased responsiveness when treated with a matched drug, however, no data currently available on survival end points	II-B
Hypothetical target	III: alteration–drug match suspected to improve outcome based on clinical trial data in other tumour type(s) or with similar molecular alteration.	Drug previously shown to benefit the molecularly defined subset in another tumour type (or with a different mutation in the same gene), efficacy therefore is anticipated for but not proved.	Clinical trials to be discussed with patients.	A: clinical benefit demonstrated in patients with the specific alteration (as tiers I and II above) but in a different tumour type. Limited/absence of clinical evidence available for the patient-specific cancer type or broadly across cancer types.	III-A
				B: an alteration that has a similar predicted functional impact as an already studied tier I abnormality in the same gene or pathway but does not have associated supportive clinical data.	III-B
	IV: pre-clinical evidence of actionability.	Actionability is predicted based on preclinical studies, no conclusive clinical data available.	Treatment should ‘only be considered’ in the context of early clinical trials. Lack of clinical data should be stressed to patients.	A: evidence that the alteration or a functionally similar alteration influences drug sensitivity in preclinical in vitro or in vivo models. B: actionability predicted in silico.	IV-A IV-B
Combination development	V: alteration–drug match is associated with objective response, but without	Drug is active but does not prolong PFS or OS, probably in part due to mechanisms of adaptation.	Clinical trials assessing drug combination strategies could be considered.	Prospective studies show that targeted therapy is associated with objective responses, but this does not lead to improved outcome.	V

	clinically meaningful benefit.				
	X : lack of evidence for actionability.	There is no evidence, clinical or preclinical, that a genomic alteration is a potential therapeutic target.	The finding should not be taken into account for clinical decision.	No evidence that the genomic alteration is therapeutically actionable.	X

Table adapted from Mateo J, Chakravarty D, Dienstmann R, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT). *Ann Oncol.* 2018;29(9):1895-1902.

7.2.2 ESCAT template

Supplementary Table SX. Biomarkers and molecular targets for precision medicines and corresponding ESCAT scores

Biomarker or genomic alteration	Method of detection	Drug match	ESCAT score^{a,b}
List the biomarker or genomic alteration[ref #]	Describe the methodology or assay used to measure the biomarker/genomic alteration	List the actionable treatment regimen related to the biomarker or genomic alteration	Scores should be calculated by CPG authors and validated by the ESMO Translational Research and Precision Medicine Working Group. References should be included State 'N/A' if an ESCAT score is not relevant for the biomarker (e.g. the biomarker is not a genomic alteration)
EXAMPLE: <i>NTRK</i> mutations[ref #]	Sanger sequencing or NGS	<i>NTRK</i> inhibitors (e.g. larotrectinib, entrectinib)	I-C

The following acronyms, footnotes and references should be added:

ESCAT, ESMO Scale for Clinical Actionability of molecular Targets.

^a ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.

^b I-A, alteration–drug match is associated with improved outcome with evidence from randomised clinical trials showing the alteration–drug match in a specific tumour type results in a clinically meaningful improvement of a survival endpoint; I-B, alteration–drug match is associated with improved outcome with evidence from prospective, nonrandomised clinical

trials showing that the alteration–drug match in a specific tumour type results in clinically meaningful benefit as defined by ESMO-MCBS v1.1; I-C, alteration–drug match is associated with improved outcome with evidence from clinical trials across tumour types or basket clinical trials showing clinical benefit associated with the alteration–drug match, with similar benefit observed across tumour types; III-A, alteration–drug match is suspected to improve outcome based on patients with the specific alteration but in a different tumour type, with limited/absence of clinical evidence available for the patient-specific cancer type or broadly across cancer types.[ref ##]

ref # = include pivotal trial reference(s).

ref ## = include reference to ESCAT manuscript (framework) in the References section (also include this reference in the supplementary material): Mateo J, Chakravarty D, Dienstmann R, et al. A framework to rank genomic alterations as targets for cancer precision medicine: the ESMO Scale for Clinical Actionability of Molecular Targets (ESCAT). *Ann Oncol.* 2018;29(9):1895-1902.

7.3 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.⁴ These tables can be provided by ESMO.

7.4 Supplementary ESMO-MCBS table

Where applicable, ESMO-MCBS calculations will be performed by the ESMO-MCBS Working Group and validated by the GLC.

Relevant ESMO-MCBS scores will be summarised in the CPG in a separate ESMO-MCBS table provided by ESMO-MCBS staff. The table will be included as a supplementary file: 'Supplementary Table SXX. ESMO-MCBS table for new therapies/indications in [tumour type].' 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. Scores and table will be calculated by the ESMO-MCBS Working Group after the first draft of the CPG is received by the Guidelines staff. Authors of the CPG should evaluate the scores and any queries should be addressed to the Guidelines staff for consideration and response from the ESMO-MCBS WG. In case of disagreement, arbitration is performed by the ESMO-MCBS WG Chair with the GLC Chair and, when necessary, by the ESMO Board.

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

The ESMO-MCBS score must be included for any drug that is included in the manuscript where relevant. However, if scores are available for drugs not mentioned in the guidelines (e.g. outdated treatments), the authors are not obliged to include this information. Authors may choose to add specific commentary to scores if they feel additional explanation will be needed by the readership.

Scientific progress can be captured in the CPG text. CPGs can include scores for drugs that are not yet EMA or FDA approved, providing the lack of approval is clearly stated and there is support for the score from a peer-reviewed publication. Only include non-approved therapies that fulfil four criteria:

1. Recommendations and algorithms – scientific breakthrough noted in recommendations and algorithms if substantial, clinical benefit and imminent regulatory approval;
2. LoE and GoR must be included;
3. Studies/drug efficacy should be evaluated and published in a peer-reviewed medical journal (Note: ESMO does not apply ESMO-MCBS scores based on findings reported in abstracts); and
4. The text must clearly highlight that the recommendation is not approved by a regulatory authority (e.g. 'not EMA approved' or similar text is included after the ESMO-MCBS score).

The following acronym, footnote and references should be added:

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.

^a ESMO-MCBS v1.1[ref ##] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms>).

ref # = include pivotal trial reference(s).

ref ## = include reference to ESMO-MCBS manuscript (v1.1 framework) in the main manuscript References section (also include this reference in the supplementary material): Cherny NI, Dafni U, Bogaerts J, et al. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol.* 2017;28(10):2340-2366.

Supplementary Table SXX. ESMO-MCBS table for new therapies/indications in XXX

Therapy	Disease setting	Trial	Control	Absolute survival gain	HR (95% CI)	QoL/Toxicity	ESMO-MCBS Score ^a
Describe the new therapy	Describe the disease setting. Specify (Neo)adjuvant or advanced	Trial acronym (trial name if acronym is not available)[ref #] 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.

^a ESMO-MCBS v1.1.[ref ##] was used to calculate scores for new therapies/indications approved by the EMA or the FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms>).

ref # = include pivotal trial reference(s).

ref ## = Cherny NI, Dafni U, Bogaerts J et al. ESMO-Magnitude of Clinical Benefit Scale Version 1.1. *Ann Oncol* 2017; 28: 2340-2366.

7.5 Supplementary LoE/GoR table

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

Supplementary Table SXXX. 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#, 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.

ref## = Gross PA, Barrett TL, Dellinger EP et al. Purpose of quality standards for infectious diseases. *Clin Infect Dis*. 1994;18:421).

8 Final review and submission

ESMO Guidelines staff carry out the final review and submission and ensure that the final version adheres to the SOP and journal requirements prior to submission.

8.1 Author Responsibility and Acknowledgement Agreement form

Authors should be able to take public responsibility for the CPG and have confidence in the accuracy and integrity of all their co-authors. To aid this, before manuscript submission, the lead author is responsible for confirming that all co-authors fulfil these criteria using the ESMO Author Responsibility and Acknowledgement Agreement form provided on the ESMO website here: <https://www.esmo.org/guidelines/esmo-guidelines-methodology>. The lead author should provide specific details of each author's role in developing the CPG^{2,3}. The completed form must be returned to the ESMO Guidelines office for manuscript submission to proceed.

8.2 ESMO journal requirements

The SE will provide a cover letter for the manuscript submission summarising important details of the CPG, a list of proposed reviewers and professional social media profiles of authors; authors can recommend 3-5 reviewers to propose to the journal, and where possible these should be ESMO Faculty: <https://www.esmo.org/about-esmo/organisational-structure/educational-committee/esmo-faculty>

Three individuals who are not recommended as reviewers can also be proposed.

ESMO journals request the social media profiles of authors that will be tagged by ESMO/Annals of Oncology or ESMO Open when the publication is made available online, e.g. <https://twitter.com/yourname>. Providing this information is voluntary.

In addition, @myESMO is included as standard, as well as other organisational accounts for joint guidelines and @rarecancer where relevant.

8.3 Final DOIs

Each author must provide a written statement extracted from the ESMO DOI Platform to be included in the Disclosure section of the final CPG.

Each author is responsible for ensuring that their DOI statement in the final manuscript is true, up to date and complete (and updated in the ESMO DOI Platform if needed).

If an author has no disclosures, the author DOI statement should read 'XX has declared no conflicts of interest'. Disclosures are not included in the manuscript word count.

8.4 Review and approval of final manuscript

Before manuscript submission to an ESMO journal, ESMO Guidelines staff will circulate the finalised manuscript to all co-authors and gather approvals. All authors must review and approve the manuscript before submission.

ESMO Guidelines staff will submit the manuscript and keep authors informed of progress.

9 CPG eUpdates and Living GLs

In the case of a significant breakthrough that requires rapid communication as updated CPG content or in the case of a new EMA or FDA indication bearing an ESMO-MCBS score, the GL-SC member or the SE will coordinate with the guideline authors to produce an update to the ESMO CPG, preferentially a Living GL update (only for selected titles during 2022) or as an eUpdate. This update will be published on the ESMO website linked to the corresponding original CPG. eUpdates are also submitted to an ESMO journal for simultaneous publication.

Please see the eUpdate and Living GL SOPs for additional guidance about these publications, available here: <http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology>.

10 Presenting ESMO guidelines

Before submission, authors can present an overview of topics that will be addressed in the upcoming guideline, without giving detailed recommendations and without displaying algorithms provided they have received approval from the ESMO Guidelines Committee.

After manuscript acceptance in an ESMO Journal, authors can present the detail of recommendations including algorithms.

11 References used in this SOP

1. Defining the Role of Authors and Contributors. International Committee of Medical Journal Editors. Available at: <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>.
2. CRediT - Contributor Roles Taxonomy. Available at: <https://casrai.org/credit/>. Accessed: 16 December 2020.
3. Elsevier expands CRediT approach to authorship. Elsevier. Published 10 December 2019, Amsterdam. Available at: <https://www.elsevier.com/about/press-releases/corporate/elsevier-expands-credit-approach-to-authorship>. Accessed: 16 December 2020.
4. Brierley J, Gospodarowicz MK, Wittekind C, eds., Union for International Cancer Control. TNM Classification of Malignant Tumours 8th ed. Oxford, UK: John Wiley & Sons, Inc., 2016.
5. 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).
6. Brouwers MC, Kerkvliet K, Spithoff K, AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ*.2016;352:i1152.
7. AGREE Reporting Checklist. Published 2016. Available at: <http://www.agreetrust.org/resource-centre/agree-reporting-checklist/>.

GRADE Handbook. Schönemann H et al. Updated October 2013. Available at: <https://gdt.gradepro.org/app/handbook/handbook.html#h.sc6xi7bnhsg>. Accessed 16 December 2020.

12 Appendix

12.1 Definitions and function of the different types of ESMO Guidelines

A brief overview of the definitions and suitability of the different types of ESMO guidelines is given in the table below.

Type of ESMO Guideline	Definition	Suitability
CPG	A full set of recommendations for the diagnosis, management, treatment and follow-up of a specific cancer type, patient group or clinical setting, supported by peer-reviewed data and clinical rationale	New titles can be proposed for topics not covered by existing ESMO CPGs. A full update to a CPG for an existing title may be appropriate when many clinical recommendations throughout the CPG have become outdated. If updates are minor and limited to a specific section, an eUpdate may be more appropriate than full CPG update
eUpdate	Online update of a specific section of an existing CPG. Published simultaneously on esmo.org as well as in an ESMO journal as Letters to the Editor or Special Articles to allow for greater awareness	Intended to be quick and flexible. Suitable when a more time-consuming update of the full CPG is not necessary, and when a clinically important breakthrough from a peer-reviewed publication needs to be rapidly communicated, or a new MCBS score is issued. To reduce the chance that readers miss important updates, it is preferable to issue fewer eUpdates covering multiple recommendations rather than many individual eUpdates
Living GL (expected from July 2022; to replace the use of eUpdates over time)	Online update of new CPGs or CPG updates. Simultaneous version published on esmo.org when the CPG is published online that includes key recommendations, treatment algorithms and other details. Updated on a regular basis (every 3-12 months), with updates integrated into the online version. The Living GL updates are available on esmo.org and are linked to the original CPG on which the updates are based is published in an ESMO journal	Intended for all future CPG titles from July 2022 to address clinically important breakthroughs and updates to recommendations. To reduce the chance that readers miss important updates, and due to the intensity of work needed for each Living GL, updates to existing Living GLs should currently be combined, when possible, for a maximum of four updates per year. This process will be reviewed and improved as the operation of Living GLs develops further