ESMO Standard Operating Procedure (SOP) for electronic updates (eUpdates) to ESMO Clinical Practice Guidelines (CPGs)

ESMO Guidelines Committee (GLC)

<table>
<thead>
<tr>
<th>Version</th>
<th>Version 1.0; March 2021</th>
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| Changes in this version | Clarified definition and usage of eUpdates  
Clarified authorship criteria  
Added Disclosure of Interests (DOI) collection process  
Added details on submission to an ESMO journal as a Letter to the Editor  
Added pre-submission review procedure  
Submission template updated |
| Approved | Giuseppe Curigliano, GLC Chair |
| Next review planned | After the next GLC meeting (in 2021, date to be confirmed); revisions can be made sooner as required |

1 Definition and usage of eUpdates

An eUpdate is an online update of a specific section of an existing CPG.

eUpdates are suitable when a clinically important breakthrough needs to be rapidly communicated but a time-consuming update of the full CPG is not necessary. This includes new study data, new European Medicines Agency (EMA) or United States Food and Drug Administration (FDA) indication or changes to approved indications and related ESMO Magnitude of Clinical Benefit (ESMO-MCBS) scores and when new data are available to support ESMO Scale for Clinical Actionability of molecular Targets (ESCAT) scores.

To reduce the chance that readers miss important updates, it is preferable to issue fewer eUpdates covering multiple recommendations rather than many individual eUpdates. If updates are extensive, a full CPG update should be considered instead.


2 Initiating an ESMO CPG eUpdate

Production of an eUpdate should be proposed by the lead author of the published CPG, the GLC Subject Editor (SE) or GLC Steering Committee (GLC-SC) member and approved by the GLC Chair.

An eUpdate should be published when:

- Important breakthroughs need to be rapidly communicated
  - i.e., new findings are available that impact clinical decision-making but are not currently included in the published version of the CPG.
  - The content of eUpdates should be supported by peer-reviewed publications. Non-peer-reviewed abstracts from large meetings may be considered as support for new breakthrough data. If an eUpdate is based on data from non-peer-reviewed abstracts, a replacement eUpdate should be issued when new peer-reviewed data are available.
- And only minor updates of a CPG are needed
o e.g., fewer than five sections of the CPG are affected, or fewer than five separate eUpdates have been published.

o For more extensive changes, or if the previously published CPG is over five years old, a full CPG update should be considered.

3 Producing the eUpdate

3.1 Declaration of interests

Up-to-date DOIs must be provided from all authors before any contribution to the eUpdate is made. These DOIs must be provided using the online ESMO DOI platform, available here: https://www.esmo.org/about-esmo/how-we-work/declaration-of-interest.

In addition, each author must provide a disclosure of interest statement included in the Disclosures section of the eUpdate, even if there is nothing to declare. Details on disclosures should be extracted by author from their profile in the ESMO DOI platform. Each individual author is responsible for ensuring that their DOI statement is accurate.

3.2 Writing the eUpdate

Writing of the eUpdate should be done by the SE and/or lead author of the previously published CPG. Other authors of the previously published CPG may also be involved in the writing. Authorship should reflect the individuals who have made substantial contribution to the writing of the eUpdate, as per ICMJE authorship criteria. Other individuals who have provided input but have not substantially contributed to the writing of the eUpdate should be included in the acknowledgements. Authors are considered to be acting on behalf of the ESMO Guidelines Committee, and this will be stated in the eUpdate.

The content must follow the structure outlined in the template provided below. Draft eUpdates that do not follow the template structure will require re-formulation and delays in publication may be expected. It is important that eUpdates are clinically actionable; therefore, clear recommendations with a Level of Evidence and Grade of Recommendation must be provided, as well as updated treatment algorithms.

eUpdates should be as practical as possible for clinicians to follow, including for non-specialist clinicians. Therefore, text should be concise to justify the updated recommendation(s).

ESMO-MCBS scores should be included for therapy/indications approved by the EMA since 1 January 2016 or the FDA since 1 January 2020. Identification of new approvals, and calculations of ESMO-MCBS scores is done by the ESMO-MCBS Working Group. Scores are reviewed and approved by the GLC. eUpdates should include an ESMO-MCBS table if applicable. For full guidance on including ESMO-MCBS scores in ESMO guidelines, please see the ESMO CPG SOP available here: http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology.

3.3 Review of the eUpdate

ESMO Office staff will review the submitted eUpdate to ensure it aligns with this SOP. Two peer reviewers with relevant tumour/tissue expertise will review the eUpdate before publication, preferably a relevant GLC-SC member and/or members of the ESMO Faculty. The review process is not anonymous and the reviewers will be acknowledged in the final publication. Reviewers will be provided with the previously published full CPG and published eUpdates if relevant to provide context to their review.

4 Publication of the eUpdate

The eUpdate is published online on the relevant Guideline page on ESMO.org. To increase awareness, the eUpdate will be submitted as a Letter to the Editor to an ESMO journal. In the event of journal acceptance, publication on ESMO.org and in the ESMO journal must be simultaneous.

5 Further guidance

Guidance on treatment algorithms, Level of Evidence/Grade of Recommendation (LoE/GoR) methodology and ESMO-MCBS scores are given in the ESMO CPG SOP or contact the ESMO Clinical Guidelines Office.
5.1 Treatment algorithm

Treatment algorithms should be provided whenever possible and should include LoEs/GoRs and ESMO-MCBS scores where applicable.

Colour code:
Purple: general/heading boxes related to stratification e.g., type of cancer, or patient sub-group; Red: surgery; Green: radiotherapy; Blue: systemic anticancer therapy; Turquoise: combination of treatments (e.g. CRT) or other systemic treatments (allo-SCT, RBC transfusions, antibiotics, steroids, etc.); White: other aspects of management not covered by the categories above e.g., observation and monitoring.

An example of an algorithm for Management/Therapeutic strategy by stage/risk factors (taken from the 2021 ESMO CPG eUpdate on hepatocellular carcinoma; published 5 March 2021) is shown below.

Figure 1. HCC treatment options depending on BCLC stage.

Purple: general categories or stratification; red: surgery; green: radiotherapy; blue: systemic anticancer therapy; turquoise: combination of treatments or other systemic treatments; white: other aspects of management e.g. monitoring, supportive care.

a Non-standard, alternative treatment.
b ESMO-MCBS v1.1 score for new therapy/indication approved by the EMA since 1 January 2016. The score has been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee.
c Non-inferiority to sorafenib established; no evaluable benefit.
d Regorafenib is not recommended in TKI-naive patients.
e Ramucirumab is only recommended in patients with an AFP level ≥ 400 ng/ml.

AFP, α-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; EMA, European Medicines Agency; HCC, hepatocellular carcinoma; LTX, liver transplantation; MCBS, ESMO-Magnitude of Clinical Benefit Scale; SBRT, stereotactic body radiotherapy; SIRT, selective internal radiotherapy; TACE, transarterial chemoembolisation; TKI, tyrosine kinase inhibitor.

5.2 EMA or FDA approvals and related ESMO-MCBS scores

ESMO-MCBS scores are produced by the ESMO-MCBS Working Group for new EMA or FDA approvals and for changes to approved indications. Scores and supporting information are presented in an ESMO-MCBS table provided
by the ESMO-MCBS Working Group for author review. Final scores are validated by the authors of the CPG/eUpdate and the GLC Chair on behalf of the ESMO Guidelines Committee.

5.3 Level of Evidence and Grade of Recommendation
Levels of Evidence and Grades of Recommendation should be provided for all recommendations, based on the criteria below (adapted from the Infectious Diseases Society of America-United States Public Health Service Grading System).

Levels of evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>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</td>
</tr>
<tr>
<td>II</td>
<td>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</td>
</tr>
<tr>
<td>III</td>
<td>Prospective cohort studies</td>
</tr>
<tr>
<td>IV</td>
<td>Retrospective cohort studies or case–control studies</td>
</tr>
<tr>
<td>V</td>
<td>Studies without control group, case reports, expert opinions</td>
</tr>
</tbody>
</table>

Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strong evidence for efficacy with a substantial clinical benefit, strongly recommended</td>
</tr>
<tr>
<td>B</td>
<td>Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended</td>
</tr>
<tr>
<td>C</td>
<td>Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional</td>
</tr>
<tr>
<td>D</td>
<td>Moderate evidence against efficacy or for adverse outcome, generally not recommended</td>
</tr>
<tr>
<td>E</td>
<td>Strong evidence against efficacy or for adverse outcome, never recommended</td>
</tr>
</tbody>
</table>

References:
ESMO Clinical Practice Guideline (CPG) eUpdate submission template

Please provide your eUpdate to the ESMO Clinical Guidelines Office. Content that does not follow the structure below will require re-formulation and delays in publication may be expected. Guidance on how to use this template is highlighted in grey. For more guidance, please refer to this SOP and also the ESMO CPG SOP, available here: http://www.esmo.org/Guidelines/ESMO-Guidelines-Methodology.

1. **Title of CPG:**
Click or tap here to enter text.

2. **Authors:**
Individuals listed as authors should have made a substantial contribution to the writing of the eUpdate, as per ICMJE authorship criteria. This should include the Subject Editor, Lead Author of the CPG and/or the CPG co-authors who have contributed to the eUpdate. Other individuals who have provided input but have not substantially contributed to the writing of the eUpdate should be included in the acknowledgements.

Click or tap here to enter text.

on behalf of the ESMO Guidelines Committee

Please copy and repeat sections 3 to 6 below if multiple sections require an update.

3. **Section title:**
Title of the section in the published CPG to which the update applies.

Click or tap here to enter text.

4. **New/amended recommendation:**
Include new/amended treatment and management recommendations for this section of the CPG, including Level of Evidence and Grade of Recommendation. ESMO-MCBS scores should also be included where relevant.

Click or tap here to enter text.

5. **Amendment to treatment algorithm:**
Treatment algorithms should be provided whenever possible and should include LoEs/GoRs and ESMO-MCBS scores where applicable.
Figure number in the previously published CPG: Click or tap here to enter text.

Description of amendment to the algorithm:

If a written description is complicated, please provide an annotated diagram of the algorithm to explain the changes needed (e.g., using PowerPoint, or photo of hand-drawn annotations). Please include ESMO-MCBS scores where appropriate.

Click or tap here to enter text.

6. Supporting explanation

Text describing the eUpdate with supporting rationale, data and references where relevant. Tables and figures can be included to support the update if useful.

Click or tap here to enter text.

7. ESMO-MCBS scores

If relevant, ESMO-MCBS scores, produced by the ESMO-MCBS Working Group, will be provided to CPG/eUpdate authors by the ESMO Clinical Guidelines Office. Authors should then validate the scores and include any necessary supporting text in the explanation above.

Click or tap here to enter text.

8. References

Please list the full citation for all references used.

Click or tap here to enter text.

9. Acknowledgements

ESMO reviewers will be acknowledged here (to be included by ESMO Staff). Please provide any details of other experts who should be acknowledged i.e., individuals who have provided input but have not contributed substantially to the written content of the eUpdate.

Click or tap here to enter text.

10. Disclosures

Up-to-date DOIs must be provided from all authors. These DOIs must be provided using the online ESMO DOI platform, available here: https://www.esmo.org/about-esmo/how-we-work/declaration-of-interest. In addition, each author must
provide a disclosure of interest statement, even if there is nothing to declare. This statement may be generated by the author from the ESMO DOI platform. Each individual author is responsible for ensuring that their DOI statement is accurate.

Template disclosure statement:

“XX has received honoraria from Company-A, has a financially compensated leadership role in Company-B, has stocks or other forms of ownership in Company-C, receives licensing fees or royalties from intellectual property from Company-D, received or currently receives direct research funding as a Project Lead from Company-E, performs work in clinical trials or contracted research for which his/her institution received financial support from Company-F, has performed non-remunerated activities for Company-G, non-remunerated leadership roles for Society-H and has non-remunerated membership or affiliation with Group-I.”

Irrelevant parts of the statement, for which the author has no disclosures, should be deleted. Small deviations can be made for grammatical reasons or to avoid repetition. If an author has no disclosures, the statement should read “XX has no disclosures to declare”.

Click or tap here to enter text.