Peer Review File

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Comment 1: While the authors claim they present epidemiological data, the majority of the data presented are demographical data (age, gender) and histology (squamous vs non-squamous), which are quite general. Is there enough information in literature to make any comments about mutation status? Initial stage at diagnosis (for OPD and ORD)? Primary lesion-controlled vs. uncontrolled (for OPD and ORD)?

Reply 1: Thank you for your suggestions. Information about T and N status have been collected and added to Tables 1-4. This include TNM classification for of primary disease for OPD/ORD cases. Few and not exhaustive data are available about the mutational status of patients included in the selected trials, so this information cannot be reported.

Changes in the text 1: TN-status details have been integrated in Table 1-4 and in the text for the whole cohort description and in each session dedicated to a specific oligometastatic status. Oligometastatic patients was found to have a TN-status lower than expected and this was stated in the abstract, in the part dedicated to the description of the whole cohort and in the discussion.

Comment 2: If this paper is not a pure literature review and the authors are presenting their results of pooled analysis (i.e., results displayed in Figure 1), the methods used for the analysis should be described.

Reply 2: Thank you for your comment. We completely agree.

Changes in the text 2: A dedicated paragraph (Material and Method for the systematic review and the pooled analyses) was added in the text, a figure describing the consort diagram according to the PRISMA guidelines was created (Figure 1) and Narrative Review Checklist was fulfilled. A dedicate paragraph was created talking about results of the pooled analysis in

the whole cohort and more details were reported in each session dedicated to a specific oligometastatic status.

Comment 3: The authors mention that clinical features of OPD and ORD lung cancer patients in "selected" published case series are included. Unless they were systematically selected using specific criteria, is the pooled analysis in Figure 1 valid?

Reply 3: We agree with your comment.

Changes in the text 3: In the Material and Method, we specified all inclusion criteria used for the study selection.

Comment 4: Section 2: Is there a reason why the cohort from IASLC study and Hendriks et al. study was not included in Table 1 (and presumably the pooled analysis done to generate Figure 1)?

Reply 4: Thank you for your comment. We did not include Hendriks et al in the pooled analysis because in this study, the number of metastatic sites in the group of patients with a single-metastatic organ is not described. Moreover, the IASLC cohort was not included because it did not provide clinical characteristics of patients. As per inclusion criteria, only articles proving a clear definition of oligometastatic disease with at least the number of metastasis stated and only those reporting clinical data of patients were included. However, we discussed about your suggestion and we decided to provide a supplementary Figure 1 in which we compare data from the pooled analysis, those form the IASLC cohort and those from Hendriks et al. just concerning the organs involved.

Changes in the text 4: Figure 1.

Comment 5: IASLC study does not provide specific demographic data, however there is adequate data from the single organ met subpopulation to include in the pooled analysis.

Reply 5: Thank you for your suggestion. As said in the replay to comment 4, we decided to

create a new figure (Figure 1) putting together data from the pooled analysis, those form the IASLC cohort and those from Hendriks et al. However, these studies did not respect the inclusion criteria for the pooled analysis.

Changes in the text 5: Figure 1.

Comment 6: Hendriks et al. study also presented data (demographics and organ) on the subgroup of patients with metastases in a single organ, which could be presented in Table 1 and included in the pooled analysis.

Reply 6: We did not include Hendriks et al in the pooled analysis because in this study, the number of metastatic sites in the group of patients with a single-metastatic organ is not described (not respecting the inclusion criteria for the pooled analysis). However, we decided to provide a Figure 1 in which we compare data from the pooled analysis, those form the IASLC cohort and those from Hendriks et al. just concerning the organs involved.

Changes in the text 6: Figure 1.

Comment 7: Section 2.2, lines 143-154: Surgery is not always a part of definitive treatment of SOM (e.g., medically inoperable patients, preference for SBRT, etc.), and the profile based on this search would be biased.

Reply 7: Adapted accordingly.

Changes in the text 7: Page 8 line 24 a sentence has been added.

Comment 8: Section 3, lines 197-198: Per ESTRO/EORTC consensus paper (which this manuscript cites), OPD specifically refers to a state of limited metastatic progression during systemic therapy, not after.

Reply 8: Thank you for your comment. All studies selected for the pooled analysis as OPD were ongoing with systemic treatment except for Iyengar et al. 2014. In this trial we do not have information enough to understand if the progression occurred during or after the end of

systemic treatment. Thus, we decided to put off this trial from the pooled analysis (Table 2 and Figure 2 adapted).

Changes in the text 8: Iyengar et al. 2014 was sorted out from the pooled analysis. Consequently, Table 2, Figure 2 and description of OPD clinical characteristics in the text have been adapted.

Comment 9: Section 3, lines 199-201: While there is no high-level evidence, this is an active area of research and whatever evidence available to date could be discussed. For example, Ashworth et al (2014, Clinical Lung Cancer) found favourable OS in oligometastatic NSCLC where the metastatic sites received local treatment (metastectomy or radical dose RT), especially in the metachronous oligomet group (although "metachronous" is defined as ≥2 months in this paper, not ≥6 months).

Reply 9: The article has been mentioned in the introduction as a positive example.

Changes in the text 9: Sentence added in the introduction.

Comment 10: Section 3.1: All of the 5 studies listed in Table 3 were limited to EGFR+ population. The demographic data reported from these studies are likely to be biased toward EGFR+ population. This is unlikely to be representative of the demographic data of NSCLC patients who present with OPD. This should be clearly stated.

Reply 10: Thank you, a statement has been added.

Changes in the text 10: Sentence added on page 12 line 6-7.

Comment 11: Section 3.1: Even when examining the subset of EGFR+ patients, the vast majority of the patients included in these studies were receiving first generation TKIs which have poor CNS penetrance. Can we expect the metastatic site distribution to be changing given more widespread use of osimertinib now?

Reply 11: Thank you for the valuable comment. A sentence has been implemented.

Changes in the text 11: Sentence added on page 12 line 6-7.

Comment 12: The paper would benefit from a more organized and consistent structure. Perhaps each of the 4 oligometastatic state should be under its own section (i.e., why is oligoprogressive disease and oligorecurrent disease combined into one section)?

Reply 12: This structure reflects clinical approach; oligoprogressive and oligorecurrent disease reflects secondary resistance and therefore we put them together. However, we dedicated two different paragraphs for each one, in order to show that they are two different states.

Changes in the text 12: No changes done.

Comment 13: Lines 119-124 are not related to incidence of SOM. For the purposes of this paper, outcomes should be discussed in a separate section. As well, if outcomes are within the scope of this paper, outcomes related to the other 3 oligometastatic states should also be addressed.

Reply 13: Thank you for this comment. We were invited to write this article for a special issue focused on the oligometastatic disease that will include dedicated paper on outcomes and all other aspects of the oligometastatic disease. For this reason, we think that including a session on outcomes could be redundant.

Changes in the text 13: We eliminated the sentence cited.

Comment 14: Authors should clearly state in the Introduction which epidemiological data they will report or comment on (i.e., incidence, demographics, distribution of mets).

Reply 14: It has been better explained in the introduction.

Changes in the text 14: Please see modification in line 5 page 4 of the introduction.

Comment 15: Figures need title for at least y-axis.

Reply 15: A title has been added.

Changes in the text 15: The title incidence has been added in all figures.

Comment 16: There are multiple duplicate citations. Please check for errors: Citation #11 and #38 are the same. #38 is included in both Table 1 (SOM) and Table 3 (OPD), written with different years and demographic data.

Reply 16: Thank you for checking. We verified all the references.

Changes in the text 16: References updated and corrected.