

## Peer Review File

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### Reviewer A

This is comprehensive work on an important clinical issue. However, one important aspect is missing: oligoprogression under immune checkpoint inhibitors. Frequency of OPD under immunotherapy is about 10-20%, which is lower than the 30-50% for EGFR/ALK+ disease under TKI, but these patients are also eligible for local therapies and the subject of clinical trials (shown in Table 2). There are some published reports on OPD under immunotherapy, which the literature search of the authors failed to detect, for example PMID 32340408 (Rheinheimer et al, 2020). I suggest to add a short paragraph about OPD under immunotherapy and cite the aforementioned PMID 32340408 and possibly also other relevant works on this.

**Reply:** Appreciate the suggestion. Paragraph has been added with appropriate citations.

**Changes in Text:** Paragraph added under the section titled “Oligoprogression Under Immune Checkpoint Inhibitors”.

### Reviewer B

I applaud the authors for the excellent review and managing to cover a very broad topic, succinctly and eloquently. I am sure many practioners will find this review article helpful.

**Reply:** We appreciate the review commentary!

**Changes in Text:** Not applicable

### Reviewer C

The evolving concept in management of oligoprogression (OP) and oligometastatic disease in lung cancer has gained increasing awareness in the past decades. Application of local ablative therapy, mainly SBRT, to OP is getting popular. However, scepticism still exists due to the lack of large-scale randomized studies in this relatively heterogenous population of disease. OP still lacks universally agreed definition. Treatment schemes (like SBRT dosage and organ-at-risk dose constraints) are also highly variable. Therefore, a comprehensive review is helpful for readers to understand this important subject.

However, can the authors explain the selection criteria of selecting the quoted studies in the articles while excluding other published data?

The discussion on the study on Tsai et al. (from line 233-247) are too detailed for a review article and it's a bit disproportionate. Table 1 should probably be removed.

Table 2 seems irrelevant as many of the trials are exploring the combination of SBRT

and immunotherapy rather than studying SBRT on oligoprogressive diseases. Abscopal effect has been showed in some anecdotal reports after the application of SBRT in oligoprogression. However, in the section under Abscopal Effect, there is no explicit discussion of how this effect may be of use in the management of OP. And the quoted studies are not studying treatment of OP as well.

Quite a number of discussions lack proper citations, e.g. line 322-324, 330-341  
More discussion on the Pros and cons of different modalities of treating OP should be discussed. Though the merits of SBRT in treating OP have been discussed, the limitations of these studies and possible biases have not been thoroughly discussed.

**Reply:**

- As per the nature of a narrative review, selection criteria was based on relevant studies that fit the discussion of concepts within oligoprogression. If there are any other notable studies we may have missed, we would be happy to include them
- Regarding Tsai et al discussion, we have appropriately shortened this discussion and removed the table.
- We would like to keep Table 2, as the combination of SBRT with immunotherapy is relevant to OPD. The idea of synergy (or possibly to the next point, abscopal effect), can be better explored by evaluating the patterns of these trials
- Abscopal Effect: Agree that it is still early/mainly case reports. We are not at the point in which would change management of oligoprogression based on this concept that is not already discussed within but have added some discussion
- Reviewed and added citations
- Agree with adding discussion of other modalities of treating OP

**Changes in Text:**

- Removed Table 1
- Shortened discussion regarding Tsai et al
- Table 2 kept with clinical trials (now re-labeled to Table 1)
- Added discussion to Abscopal Effect paragraph
- We have reviewed and added appropriate citations. 330 - 341 is a description of seed and soil with common mechanisms and has already been included in the previous and next citation.
- Discussion held regarding different modalities of LAT added

**Reviewer D**

Overall this is a very comprehensive review of current literature and helpful summary.

However due to the amount of data presented a few comments mainly with regards to nomenclature and structure to make it easier for the reader to follow:

1) Structure:

- OPD disease is defined in a specific paragraph, whereas OMD is introduced in section historical perspective. I suggest to have specific paragraphs named

accordingly for both definitions

- Even though there is a specific section for OMD/OPD in patients with EGFR/ALK I would appreciate if the article could be restructured to have clearly all data in patients with oncogenic drivers versus in patients without presented separately and in specific paragraphs, as these are completely different scenarios.
- intracranial OPD/OMD is listed separately however otherwise no specific mentioning of metastatic site-more structure to first present data exclusively in extra cranial OMD/OPD versus intracranial would be helpful

2) Tables:

- Table 1 not very helpful only illustrating one trial. Separate summary tables for evidence in OMD in patients with and without driver and OPD in these two populations would be much more helpful
- also type of local treatment in these trials should be listed, eg dose of RT/Type of surgery etc as this is crucial for the reader

3) Nomenclature:

- the authors often use targeted therapy when introducing the concept of local treatment to metastatic sites. As targeted treatment is in the literature mainly addressing targeted systemic treatments with TKIs etc I would prefer the term local treatment

**Reply 1 (Structure):**

- Agree with changing organization and Revised structure of OPD and OMD definitions
- Agree that there are different types of scenarios of how OPD can present. Structure-wise, it would be very difficult to have parallel discussions in the way suggested and we would like to keep the layout. In addition, much of the crux of this discussion is in regards to the future of OPD, in which most patients will have some sort of targeted systemic therapy in which they progress (whether it is EGFR/ALK, immune checkpoint inhibitor)
- Focus is more extracranial since SRS is already utilized for metastasis, but have done some restructuring

**Changes in Text:**

- Page 5 and 7 have been re-organized and appropriately titled

**Reply 2:**

– Removed table. As discussion is in text, table not added. Can be added upon request if you feel this is helpful to the text.

**Changes in Text:** Removed Table 1 as suggested (previously on Page 12 and 13)

**Reply 3:** Appreciate the comment

**Changes in Text:** Changed verbiage as suggested.