Dear Reviewers:

Thank you for your review of the manuscript “Localized Management of Soft Tissue Sarcoma Metastasis: A Review of a Multidisciplinary Approach.” We appreciate your comments and have done our best to address each question to your satisfaction. Responses to you assessment are listed below as well as incorporated into the manuscript.

Please let us know if you have any other questions or concerns upon re-review of this article. Thank you for your time and consideration of this paper.

Sincerely,

Meena Bedi

Reviewer 1:

General:
The manuscript provides an overview of the multiple potential local therapeutic options in the management of soft tissue sarcomas. The authors provided background and data within the limits of review. However, the review does not sufficiently describe the search for a rigorous systematic review. Nonetheless, it provides certain useful information.

Specific:

1. Under the methods, malignant fibrous histiocytoma is now largely replaced by UPS, undifferentiated pleomorphic sarcoma, search terms can be updated. Thank you for this comment. The terms “malignant fibrous histiocytoma” has been replaced by “undifferentiated pleomorphic sarcoma.”

2. Under metastectomy, the authors can perhaps make suggestions (based on the studies) on the population of patients who may successfully be considered for metastectomy (as pointed out by Abdalla et al. Curr Treat Options Oncol, 3 (2002), pp. 497 and Cardona et al. Curr Prob Cancer 2013; such as presence of controllable primary tumor, no multivisceral metastases, having completely resectable metastatic disease, etc) We appreciate this comment. As you have requested, recommendations as to which patients would be appropriate candidates for resection are elaborated on and located on page 5.
Reviewer 2:

The authors review local treatment options for metastatic disease in patients with soft tissue sarcoma. Unfortunately, the review feels very superficial, beginning with simple mistakes - the authors state that the rate of distant metastasis ranges from 25-50% in their abstract and 25-30% in their introduction, without taking grading or the different biological behaviour of different histological subtypes into consideration. Further along in the introduction, the authors name lungs, soft tissue, bones and visceral organs as possible sites for metastases, ignoring regional lymph nodes. The authors also state that the mainstay of therapy for metastatic soft tissue sarcoma is chemotherapy. This statement does not reflect the current guidelines, which recommend chemotherapy as standard treatment for patients with synchronous lung metastases or extrapulmonary metastatic disease, whereas surgery is considered standard treatment for metachronous lung metastases (ESMO guidelines - http://annonc.oxfordjournals.org/content/25/suppl_3/iii102.full.pdf).

Thank you for your comments. We have attempted to remove all errors in this paper. Moreover, a discussion on nodal disease and resection was included, taking into consideration NCCN and ESMO guidelines. ESMO guidelines were also referred to and the scope of their recommendations was referred to in this manuscript.

Far more limiting than the above mentioned errors, which can easily be amended, is, however, the fact, that the results of the presented studies on local treatment options are presented with no attempt to synthesize them into a greater whole or indeed any discussion whatsoever. The reader of the review cannot help but feel that the authors identified a number of studies on local treatment of metastatic disease and went on to simply list the results of each study.

The authors appreciate this comment and agree a synthesis of the information provided is necessary to formulate a complete manuscript and provide a summary of the localized treatment options available to patients. This synopsis is located in the “Summary” section on page 9 and 10.

Reviewer 3:

The topic is highly interesting and the method using a Pubmed and medline search to provide a good review is fine. However, a paragraph on the results of this literature search is clearly missing.

How many papers did the authors identify? How many metastatic patients were included? The authors should also score the quality of these papers? Which time period did these publications cover? Monocenter studies? Prospective trials, .....Did the authors see a difference concerning the subentities of STS? E.g. myxoid liposarcoma + trabectidin?

Thank you for this comment. An expansion of the search methods has been added and located on page 2 and 3 in the “Methods” section.
In the end I would like to read some clear recommendations – at the moment it is more a collection of possibilities. What can the authors, based on the literature, clearly recommend in the treatment of metastatic STS?

This point is well taken. The information in the manuscript has been synopsized at the end of the article and recommendations have been conveyed depending on the patient and his or her disease characteristics.