Reviewer's report

Title: Prognostic factors for outcomes after whole-brain irradiation of brain metastases from relatively radioresistant tumors: a retrospective analysis

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Reviewer: Emmanouil Fokas

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With interest I read the manuscript “Prognostic factors for outcomes after whole-brain irradiation of brain metastases from relatively radioresistant tumors: a retrospective analysis” by Meyners et al. In this retrospective study, the authors analyzed data from 220 patients treated with whole brain irradiation (WBI), using different fractionation schedules, and provide information on the outcome and prognostic factors of brain metastases derived from radioresistant tumors, such as malignant melanoma, renal cell carcinoma, and colorectal cancer. The authors identified important prognostic factors which can be used to stratify patients for more selected aggressive therapy. Notably, the authors report that WBI doses>30 Gy can improve survival of patients. This is an interesting finding and raises a concern regarding the current approach for the treatment of patients with radioresistant cerebral lesions.

The manuscript is well-presented and the question posed by the authors is well-defined. The methods and data analysis are described in a clear manner. However, some points still need attention and should be addressed.

1) There is class I evidence that altered dose/fractionation schedules of WBI do not result in significant differences in median survival and local control (Ref: Gaspar et al., “The role of whole brain radiation therapy in the management of newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline”, Journal of Neuro-Oncology, Volume 96, Number 1, 2010). This is different to what Meyners et al. observed in the current study. The latter is probably because the data from the recent metaanalyses derived from different tumor entities than those reported in the recent studies. The latter should be mentioned and discussed in the manuscript.

2) Did the authors observe any difference in acute and/or late toxicity with WBI doses>30 Gy?

3) In the abstract (section: “Methods”) and elsewhere in the manuscript the authors refer to local control by writing “local (intracerebral) control”. Local and intracerebral control are different end-points. Therefore, the word “intracerebral” should be omitted to avoid any misunderstanding.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests