PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Standard Maintenance Therapy versus Local Consolidative Radiation Therapy and Standard Maintenance Therapy in 1-5 sites of Oligometastatic Non-Small Cell Lung Cancer: A Study Protocol of Phase III Randomized Controlled Trial
AUTHORS	Tibdewal, Anil; Agarwal, JaiPrakash; Srinivasan, Shashank; Mummudi, Naveen; Noronha, Vanita; Prabhash, Kumar; Patil, Vijay; Purandare, Nilendu; Janu, Amit; Kannan, Sadhna

VERSION 1 – REVIEW

REVIEWER	Wen-Zhong Zhao Guangdong Lung Cancer Institute, China
REVIEW RETURNED	03-Oct-2020

GENERAL COMMENTS	Thank you so much for inviting me to review the article titled "Standard Maintenance Therapy versus Local Consolidative Radiation Therapy and Standard Maintenance Therapy in 1-5 sites of Oligometastatic Non-Small Cell Lung Cancer: A Study Protocol of Phase III Randomized Controlled Trial". In this paper, Tibdewal et al described a detailed protocol of a phase III trial which explored the value of local consolidative radiation therapy for oligometastatic NSCLC patients. Overall, I am impressed and enjoyed the read. Though this work is interesting, but it lacks the novelty and innovativeness to warrant publication in BMI Open. My major comments are as follow: 1) As mentioned in Table 5, there are six ongoing randomized trials in oligometastatic NSCLC. I did not notice the main differences between this protocol and the others. 2) The structure of this paper is very confusing. 3) Brian enhanced MR should be added to pre-randomization assessment. 4) In the sample size calculation, "we expected an absolute increase in median OS of 10 months ie. to 27 months with a hazard ratio (HR) of death of 0.63 in the SMT plus LCRT (experimental arm)." What is the basis for this 10 months?

REVIEWER	Fang Wenfeng Sun Yat-sen university; China
REVIEW RETURNED	09-Oct-2020

GENERAL COMMENTS	The protocol written by Dr. Anil Tibdewal and colleagues is about a phase III RCT which will evaluate the efficacy of local consolidation radiation therapy in OM NSCLC after completion of initial systemic therapy. Overall, it is a well-organized and clinically meaningful study protocol. There are my comment for the author:

	the clinical plan must clarify the statistical methods of the main indicators and secondary indicators, how to deal with missing data and the analysis of the subject population, etc.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 comments:
1) As mentioned in Table 5, there are six ongoing randomized trials in oligometastatic NSCLC. I did not notice the main differences between this protocol and the others.
Response: As mentioned in table 5, our study includes
a) ≤ 5 sites of oligometastases as also suggested by the Pan-European Consensus guidelines for oligometastases
b) Includes only synchronous oligometastases as compared to others which includes both synchronous and metachronous, which have different outcomes.
c) Includes only NSCLC with negative oncogene mutation compared to OMEGA, CORE and PROMISE – 005
d) Primary endpoint is OS
2) The structure of this paper is very confusing.
Response: Apologies, we didn't understand whether the reviewer is trying to comment about the study or manuscript content and flow. We will try to improve if provided with more specific inputs. Figure 1 is modified.

3) Brian enhanced MR should be added to pre-randomization assessment.
Response: Brain enhanced MRI is already there in pre-randomization assessment "if not done earlier", which will be the case in majority of patients as MRI is not done in a metastatic patient unless symptomatic. Same is added in Table 3.

4) In the sample size calculation, "we expected an absolute increase in median OS of 10 months ie. to 27 months with a hazard ratio (HR) of death of 0.63 in the SMT plus LCRT (experimental arm)." What is the basis for this 10 months?
Response: Correction done in Statistical Analysis section. However, it is based on previous single arm phase II studies of Sutera et al. and Petty et al. (references in text)

Reviewer: 2
Comments to the Author
The protocol written by Dr. Anil Tibdewal and colleagues is about a phase III RCT which will evaluate the efficacy of local consolidation radiation therapy in OM NSCLC after completion of initial systemic therapy. Overall, it is a well-organized and clinically meaningful study protocol. These are my comment for the author:
1) The clinical plan must clarify the statistical methods of the main indicators and secondary indicators, how to deal with missing data and the analysis of the subject population, etc.

Response: Statistical plan is modified and highlighted in the revised manuscript, Missing data plan is all added.

VERSION 2 – REVIEW

REVIEWER	Wenzhao Zhong

	Guangdong Lung Cancer Institute
REVIEW RETURNED	26-Dec-2020

GENERAL COMMENTS	Thanks for inviting me to review the article titled “Standard Maintenance Therapy versus Local Consolidative Radiation Therapy and Standard Maintenance Therapy in 1-5 sites of Oligometastatic Non-Small Cell Lung Cancer: A Study Protocol of Phase III Randomized Controlled Trial” again. In this paper, Tibdewal et al described a detailed protocol of a phase III trial that explored the value of local consolidative radiation therapy for oligometastatic NSCLC patients. Overall, I am impressed and enjoyed the read. Thank the authors for answering the questions. This work is interesting and forward-looking. The revised protocol of this study is well-organized.