Reviewer's report

Title: Addition of platinum derivatives to neoadjuvant single-agent fluoropyrimidine chemoradiotherapy in patients with stage II/III rectal cancer - protocol for a systematic review and meta-analysis (PROSPERO CRD4201707306) (PROSPERO CRD4201707306)

Version: 0 Date: 20 Nov 2017
Reviewer: Larysa Rydzewska

Reviewer's report:

This interesting and relevant protocol plans to assess whether adding oxaliplatin to fluoropyrimidine-based neoadjuvant chemoradiotherapy can improve survival in patients with stage II-III rectal cancer. A previous review on this topic only assessed short-term outcomes, whereas this review plans to address more meaningful, long-term outcomes such as disease-free and overall survival, which have far greater potential to influence clinical policy/practice decisions. Assessment of toxicity and quality of life, may also play a key role in the making of decisions around treatment options. It is commendable that the authors have obtained patients' perspectives as to which outcomes are most important to them.

The protocol is generally clear and methodologically sound. Just a few minor comments:

Page 2; Para 1: The second sentence could benefit from additional context to explain why oxaliplatin may hold the potential for positively affecting survival e.g. positive results of in palliative/adjunctive setting (see general comments at end)

Page 4; Para 1: …it is the third most common cause…. (remove the word "under")

Page 7; Systematic literature search: Is there a reason only MEDLINE was searched? Generally good practice to search at least two electronic databases e.g. MEDLINE and EMBASE. Will study authors be contacted to ascertain if they know of any other studies (unpublished/ongoing) that should be included in the systematic review? How will retrieved references (and duplicates) be managed e.g. with reference management software? Add detail. Also provide time parameters for searches e.g. MEDLINE 1966-2017.

Page 7/8; Last para: I am not sure I understand what the last sentence means ("Eligibility will be assessed for the results?") - consider revising/re-wording.
Page 9: Data extraction: Will authors of the individual studies be contacted to obtain any additional/missing data (or to check data if anything is unclear from the study report?) or to obtain summary data from any unpublished studies identified?

Page 10: Para 2: Should this be extirpation?

Page 10: Endpoints: Would be useful to define outcomes e.g. time from randomisation to death (OS) etc. Are there likely to be differing definitions of disease-free survival across trials? If so, how will authors deal with this?

Page 11: Qualitative analysis: Perhaps a better heading would be "Qualitative assessment of included trials"? Also, how many assessors will there be and how will judgments be made / disagreements be resolved? If there is not enough information to make an assessment, will the study authors be contacted? Also, the last para on page 11 seems a bit disjointed - perhaps better to include this information as part of the previous paragraph about using the risk of bias tool.

Page 12: Line 23: "…mean difference((S)MD) with its 95% confidence interval will be used"

Page 12: Line 38: Consider changing sentence to state that meta-analysis will be performed if identified trials are sufficiently similar in design/comparison and if heterogeneity in the results is observed, this will be further explored via subgroup/sensitivity analyses.

Page 14: Line 30: Better to use the words "allow for better" rather than "guarantee" generalisability of results?

Page 16: Author contributions: Who is the guarantor for this work?

General comments:

Authors switch between using (chemo-)radiation, chemoradiotherapy and radiochemotherapy throughout. It would be better to keep this descriptor consistent.

There is quite a bit of overlap between the Background section and the first paragraph of the Discussion section. Consider amalgamating these two sections into the Background section and then leading the discussion from the second paragraph.

I wish the authors the best of luck with their review.
Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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