Reviewer's report

Title: Bifractionated CPT-11 with LV5FU2 infusion (FOLFIRI-3) in combination with bevacizumab: clinical outcomes in first-line metastatic colorectal cancers according to plasma angiopoietin-2 levels.

Version: 1 Date: 20 May 2013

Reviewer: Eva Segelov

Reviewer's report:

Major Compulsory Revisions
- Cannot conclude from your study whether Ang-2 is a prognostic or predictive factor- should make that clear. Reference any data in the literature that addresses this.
- Comment on impact of bifractionated irinotecan on resources and QOL (extended time in chemo centre)
- Inappropriately long discussion of maintenance therapy in the discussion- should be culled as not aim of study and conclusions are overdrawn, particularly with no quality of life measures.

Only one short paragraph in the discussion addresses Ang-2 results, which was a main aim of study. Particularly need to discuss whether this is prognostic or predictive.

Minor Essential Revisions
- Abstract results section should make clear that surgery was a positive prognostic factor but high AP2 levels were a negative factor (whether prognostic or predictive)
- Include comment on timing of metastatectomy (as enrolled patients with resectable disease)- was it stipulated in the protocol or at discretion of individuals?
- Figure 1 and 2 – only 1 of them should be shown as again not a feature of the study to analyse by surgery or not.
- Intro end of line 2: “with a metastatic disease”- remove ‘a’
- Perfusion is used instead of infusion in the intro.

Discretionary Revisions

Level of interest: An article whose findings are important to those with closely related research interests

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'