Reviewer's report

Title: Randomized controlled phase I/II study to investigate immune stimulatory effects by low dose radiotherapy in liver metastases of colorectal cancer

Version: 3 Date: 27 April 2011

Reviewer: Andrew Vickers

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Mets liver protocol

There are several major problems with this study that would need to be addressed.

1. Randomization. You need to describe in detail, the exact logistics of randomization to ensure that allocation cannot be guess before a patient is placed on trial nor changed afterwards. The CONSORT statement has more details on this point.

2. The statistical methods, sample size and objectives are inconsistent. The primary objective is given as "the determination of the single fraction radiation dose, which leads to an optimal anti-tumor immune response." However, the sample size is based on a hypothesis test that different radiation doses have different effects and the analysis is based not only on an overall ANOVA but on a comparison of each dose with every other dose. This is surely a modeling problem, where dose (and perhaps a non-linear term such as dose squared) are used to predict response and the optimal dose chosen on the basis of the dose response curve. it might make sense to test whether dose affects response (as in the ANOVA) but the multiple comparisons of groups appear to be entirely irrational.

3. The SDs of the primary endpoint are highly implausible, especially for an immune endpoint for which often very large variation is seen.

4. Analysis of secondary endpoints is barely described. For example, quality of life is assessed but not even mentioned in the statistical analysis section.

Minor comments

1. The language is poor and needs to be edited by a native English speaker.

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

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

'I declare that I have no competing interests'