Reviewer’s report

Title: Ketogenic Diets as an Adjuvant Therapy in Glioblastoma (The KEATING Trial): Study Protocol for a Randomised Pilot Study

Version: 0 Date: 24 May 2017

Reviewer: Christopher Jones

Reviewer's report:

Overall this protocol is well written with clear aims and rationale and the choice of KDs for the interventions are well justified.

This study is described as a pilot study, but I think it would be more appropriately described as a feasibility study for the following reasons:

1. It is on the feasibility of the KD interventions, rather than being a mini version of the full study. An obvious omission from this study is a control group that either does not follow a specified diet, or follows a specified non-KD diet. Some discussion should be included around why no such control group is present in this study, as the obvious comparison for the main study would be to this control group.

2. Possible primary outcomes for the main study are not really discussed - I would expect the primary outcome for the main study to be clear if this was a pilot. Whether labelled as "pilot" or "feasibility", Some indication of what the primary outcome for a full trial will be should be included.

Specific comments

Inclusion/exclusion criteria

- I'm not familiar with the definition of "Performance status" (as in "Performance status ≤2" and "Performance status ≥3"). What this is a measure of should be described briefly.

- Exclusion criterion 1 says "1. Having prior use of a KD, kidney dysfunction," - "kidney dysfunction" should be a separate criterion. Also "Having prior use of a KD" should include a time period - e.g. within the last year?

- Exclusion criterion 5 "Eating disorder" - how is "Eating disorder" defined?
Allocation strategy

- "A permuted block randomisation method will be adopted" - state block size(s). Will the block sizes be randomised?

Statistical considerations

- With small numbers in each group, even if there are no drop-outs, estimates of retention rates, adherence, biochemistry results etc. will be very imprecise, so should be used with caution when planning a larger study. This could only really be addressed by including more patients, which is unlikely to be possible at this stage, but this limitation should be acknowledged.

- Data management - data collection and storage are not described. A section for this should be added.

- Numbers are sometimes written as numbers, sometimes as words - e.g "... 6 weeks from initiation, 12 weeks from initiation (primary completion) and every three months..."

Level of interest

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Please indicate the quality of language in the manuscript:

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