Reviewer's report

Title: Randomized clinical trial of efficacy and safety of colchicine 0.5% cream versus photodynamic therapy with methyl aminolevulinate in treatment of skin field cancerization: study protocol

Version: 2 Date: 09 Oct 2017

Reviewer: Jared Jagdeo

Reviewer's report:

1. Major grammatical revisions required as the manuscript is difficult to read due to improper grammar, including spelling errors (e.g. "aminolevulinate", singular form of AKs is "actinic keratosis").

2. Discussion of abstract: Consider stating the potential impact of the study.

3. The flow of the Background section may be improved by changing order of introduction to first discuss AKs, then discuss field cancerization. Currently, you first discuss how skin field cancerization involves AKs next to normal skin. In the next section, you explain what an AK is and then you discuss different types of field therapy for AKs. It can be difficult for the reader to understand.

4. Recommend removing regular sunscreen discussion from the section regarding treatments for AKs. As stated, sunscreen use is a protective measure against formation of AKs rather than a treatment modality.

5. Include AK as one of the pre-malignant skin cancers that PDT targets (page 6, line 41) since AKs are the main focus of this study.

6. Recommend mentioning the adverse effects of topical colchicine (page 7, line 46). Systemic colchicine side effects are listed, but these side effects may not be applicable to topical colchicine use.

7. Why was MAL-PDT used as a comparison instead of the other treatments mentioned (e.g. 5FU, imiquimod, etc.)? (page 8, line 24)

8. Will only curetting the AK lesions treated with MAL-PDT be a confounding factor? (page 11, line 38)
9. Distal and proximal limits on the forearm are mentioned. Will you be treating both anterior and posterior surfaces of the forearm with MAL-PDT or colchicine cream? (page 12, line 1)

10. State if the biopsy of center of the middle third of the forearm will be on the anterior or posterior side of the forearm. (page 12, line 1)

11. State if biopsy will be a shave biopsy or punch biopsy. If punch biopsy, state size. (page 12, line 1)

12. How will you monitor subject's adherence to colchicine cream twice daily for 10 days? (page 12, line 10)

13. Is assessment of adverse effects and tolerability at T15 too long of a time period for MAL-PDT? (page 12, line 10)

14. What objective questionnaires or scales will be used to assess incidence, impact, and severity of adverse events? (page 12, line 10)

15. In the "Interventions" section, T60 should also include assessment of adverse events and tolerability (page 12, line 11).

16. If the impact of the study is reducing the cost of AK treatment, consider comparing benefits and costs of MAL-PDT vs colchicine cream. What other benefits does colchicine cream have over MAL-PDT? (page 14, line 42)

17. T15 should be included on consent form. (page 22)

18. T15 should also be included on Figure 1.

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**

If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**

If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:
Not suitable for publication unless extensively edited

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