Reviewer’s report

Title: Desmoid tumors complicating Familial Adenomatous Polyposis: a meta-analysis of the mutation spectrum of at-risk individuals

Version: 2
Date: 30 December 2014

Reviewer: Peter P Stanich

Reviewer’s report:

The authors have the aim to compile the genotype phenotype data on FAP and desmoids tumors. They also have an interesting methodology to answer it, as the comparison to the database provides a “general population” so to speak. However, the methods are not adequately described – especially how and why the mutations were grouped - and the results are not clearly presented which take away from the study. With revision and clarification, this would be a useful adjunct to the current literature.

- Major Compulsory Revisions

1. Abstract, lines 28-30: Sentences need clarified. Would consider specifying APC gene mutations and eliminating mention of surveillance as this is not a focus of the paper.

2. Abstract, lines 44-47: Bulk of conclusion does not fit the results. Would be very careful about suggesting surveillance regimens in a paper that is focused on genotype-phenotype correlation without any investigation into clinical management.

3. Intro, lines 94 – 97: This study - A systematic review/meta analysis with focus on genotype correlation with desmoids – does not and should not have the aim of improving surveillance or pathophysiology. The stated aims are misleading and far exceed the scope of paper.

4. Methods: The reasoning behind the groupings on the APC gene used (basically, what is erroneously included in results 134 – 136) needs to be in methods with a full description of how this was determined, what the groups were and relevant citations of previous work that is mentioned in deciding this. Would also benefit from discussing if this was decided a priori and if not why/when.

5. Results: Demographics should be presented of the 222 patients included in analysis, not the larger 274 group that is not mentioned further in the paper/study.

6. Conclusion 199-201: Major reservations about including a proposed surveillance regimen without clear evidence basis and that does not directly relate to the findings of study in the conclusion paragraph of paper.

7. In table 1, it says adjusted p-value. This is usually associated with a multivariate analysis, but I do not see this described in methods.
- Minor Essential Revisions

The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

1. Intro, lines 65-85: Intro is bulky and contains far more information on clinical management of desmoids than is needed for a paper with these aims. Would be better for discussion or to be significantly condensed.

2. Methods/results: I am unclear on why Fishers tests and odds ratios are needed. At least on table would focus on one to simplify and avoid confusion.

3. In results, would use the standard presentation of odds ratios and CI. Ex 1.2 (0.8 – 1.4)

4. Title: Would be more accurate to use affected individuals and not at risk individuals.

5. Discussion, lines 169 – 184: Authors mention “our observations” when discussing desmoids management which implied the findings of this study, although there are no clinically actionable findings from this study. This paragraph needs to be clarified.

- Discretionary Revisions

These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

1. Methods – Consider specifying which authors performed searches and data abstractions.

2. Results, line 124: I believe the word desmoids is missing from first sentence.

3. Discussion: Provide citation for your thyroid cancer paper when first mentioned

4. Figure 1: Extremities is misspelled

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

'I declare that I have no competing interests'