Reviewer’s report

Title: Are Rare Cancer Survivors at Elevated Risk of Subsequent New Cancers?

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Reviewer: Laura Mercatali

Reviewer's report:

The authors Finkelstein et al studied a large cohort of patients with personal and/or family history of cancer focusing their attention on rare cancers. The main conclusion is that patients affected by rare tumors, have an increased risk of a second cancer. These interesting results could represent a relevant information in the field of rare diseases, in which we had not previous studies about a possible multiple tumors. The statistical analyses is adequate. However, there are some important points that need to be improved.

1. The authors collected a larger population affected by prior rare cancers. Considering the field of rare diseases with different cancers, the study should report the specific rare tumors. Please, in order to clarify the possible impact on the common follow-up, the Authors could report these data. otherwise the data are not of clinical importance.

2. More than one rare cancer, could be associated with familiarity syndrome like MEN or VHL. The only anamnestic data are not sufficient to consider it.

3. The data were collected from 1998 (CGN creation). In the conclusion section the Authors confirm the importance of cancer pathogenesis to study in high risk cohort. Oncology had undergone many evolution so if the Authors suggest the future study, they should test mutational panels.

4. Furthermore rare tumors classification have further improved in 20 years. This should be considered and samples should be revised according to new classification.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

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.

I am able to assess the statistics

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