Author’s response to reviews

Title: Testicular cancer in Geneva, Switzerland, 1970-2012: incidence trends, survival and risk of second cancer

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Author’s response to reviews:

We thank the Reviewers for their very helpful comments which have all been considered in the revised manuscript. Please refer to the highlighted version of the manuscript.

Reviewer 1 Hooman Djaladat, MD, MS (Reviewer 1):

I reviewed this manuscript. Herein are my comments:

1) Line 110-113 (based on figure 1 and 2): p-values for the trends should be included

We included the p values both in the text and in the figures.

2) All the p-values of 0.000 (in both tables and the text) should be changed to <0.001

We changed the p-values in the text and in the figures according to the reviewer suggestion

3) It is better to classify the morphology subtypes into two groups (Seminoma and non-seminoma) rather than three groups (seminoma, NSGCT and mixed)
We agree with the reviewer. We regrouped the morphology in two groups including the mixed morphology with NSGCT. All the figures concerning the morphology of the tumor have been changed accordingly in the text and in the tables (lines 81-84; lines 120-124; table 1; table 2).

4) Line 122-124 (based on Table 1): The authors reported the mode of treatment (i.e. radiotherapy and chemotherapy) in all patients. While the treatment of seminoma and NSGCT is totally different in different stages, it is better to report the type of treatment in these two morphological groups, separately.

We reported the treatments separately for the two morphological types as suggested from both reviewer 1 and 2. (lines 120-124, table 1)

5) Limitations of the study should be added at the end of discussion

We added the following paragraph at the end of the discussion (lines 214 - 223):

“One limitation of our study is the relatively small number of cancer cases due to the rarity of testicular cancer and the small size of the population under study. Nevertheless, we included all of the 590 testicular cancer cases that occurred in the Geneva population over a 40-year period.

Another potential limitation is the possible lack of completeness of case ascertainment or lack of completeness of follow-up and treatment data. However, the accuracy of the Geneva cancer registry is rather high in general and again as demonstrated in this study by the fact that only 1 case was discovered after death. Furthermore, the median time of follow-up was 11 years, cumulating in 7733 person-years of observation. Another marker of accuracy of the data is that all included cases were morphologically defined. Given the above the findings are definitively generalizable to the overall patient population of Geneva, while caution should be used when trying to generalize them to other settings.”

6) Conclusion part should be added after discussion

We added the paragraph Conclusions at the end of the discussion (line 224).

Shomik Sengupta, FRACS (Reviewer 2): This registry based study shows time trends in Testicular cancer in Geneva, treatment patterns, survival outcomes and second malignancy risk
Some issues with the study:

1. Very small numbers, restricted to a small population - how reliable and generalisable are the findings?

We agree with the reviewer that our study population is small and so is the power of the study. We added this point as a limitation of the study (line 214). We believe, however, that the accuracy of the registration is very high as we covered the entire Canton of Geneva and followed up the patients for more than 40 years (median time 11 years, 7733 person-years at risk). Furthermore, only 1 case was discovered after death and all cases were morphologically classified. For all these reasons we believe our data are very reliable and definitively generalizable to the overall patient population of Geneva. On the other hand, these data may not accurately represent the profile observed in other settings. (we added this point to the limitations of the study (line 222-223).

2. Grouping treatment details between seminoma and non-seminoma is not appropriate

We reported the treatments separately for the two morphological types as suggested from both reviewer 1 and 2 (lines 81-84; lines 120-124; table 1; table 2).

Geoffrey Gotto (Reviewer 3): The authors should be commended on this excellent study which includes a huge patient population with data from a central registry over a 40 year period. The documentation of the impact of SES on testicular cancer outcomes and of rates of secondary cancers will be of interest to the reader.

We thank the reviewer for his positive comments.