Reviewer's report

Title: A case-control study on the combined effects of p53 and p73 polymorphisms on head and neck cancer risk and progression in an Italian population

Version: 1 Date: 13 November 2008

Reviewer: Sujata Patil

Reviewer's report:

Major Compulsory Revisions

1) It would be useful to see disease and patient characteristics for cases by mutation status.

2) Even after reading the original publication, I was unable to find information on how the sample size was justified. Were all patients who had SCCHN included as potential participants? Was the study prospective (so that samples are collected at the diagnosis?) Was the power analysis (so that samples are collected at the diagnosis?) Was the power analysis on page 10 done apriori? Or was it done after all the data had been collected?

3) In table 2, it looks like several logistic regressions were done—one for each type of SCCHN compared to the controls. Should there be an adjustment for multiple comparisons? Why not do a multinomial logistic regression? How well did the model fit the data (goodness of fit statistic)?

Minor Essential Revisions

1) From the original publication, controls were frequency matched to cases for age and gender. I think this is an important fact to mention in this manuscript. Also, should all matched variables be included in all models?

2) In the figure, there are no tickmarks for censored patients. Also what is time 0? It would be helpful to provide the number at risk at each of the x-axis tickmarks. The labels are should be clarified—for instance, what is the unit of time? It would useful to provide point estimates of survival at say 25 and 50 with confidence intervals. How confident are the authors in this finding?

3) Though not significant, I think it would be good to provide the Kaplan-Meier curve for recurrence. The title of the manuscript has progression in it but there is very little written on progression in the manuscript. Since Kaplan-Meier curves were done, why not include actuarial estimates of mortality and recurrence in the results section rather than rates per person months?

4) Page 6, is the average followup time for survivors only or for the whole group? The median followup time should be reported for survivors only and also a range.

5) Was there any lag of time between diagnosis and blood collection and entry
into the study?
6) Is there any treatment information available? How would treatment affect the survival curve?
7) The statistics section could be better organized as it left me with some questions. Why were results stratified (page 6)? Why were the logistic regression analyses stratified by age, gender, alcohol, smoking status and familiarity for cancer and not adjusted? Why was age categorized at age 45 and how many patients were each of these categories?
8) Did DFS include deaths due to disease as an endpoint or were these deaths treated as censored?

Discretionary Revisions
1) In Table 1, the estimate for familiarity for SCCHN seems highly unstable, with a CI that goes up to 372.82. I would have left that variable out of the table, and rather described the raw numbers in the text noting the small number of controls with familiarity.

What next
Accept after major and minor essential revisions.

Level of Interest
An article whose findings are important to those with closely related research interests.

Quality of written English
Acceptable

Statistical Review
Yes, and I have assessed the statistics in my report.

Declaration of competing interests
I declare that I have no competing interests.