Reviewer’s report

Title: A non-randomised, single-centre comparison of induction chemotherapy followed by radiochemotherapy versus concomitant chemotherapy with hyperfractionated radio-therapy in inoperable head and neck carcinomas

Version: 1 Date: 24 August 2005

Reviewer: Gianmauro Numico

Reviewer’s report:

Is the question posed by the authors new and well defined?
The authors report on two series of head and neck cancer patients treated with two schedules of integrated chemo-radiation used during a time frame of 8 years. The first, from 1987 to 1992 included patients treated with a sequential scheme in which a cisplatin-based chemotherapy regimen was used. The second, from 1992 to 1995 included patients treated with a concomitant scheme in which a FU-Mitomycin chemotherapy regimen was used. The general conclusions are that the concomitant scheme improved response rates and loco-regional control in comparison with the sequential scheme.

Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
The patient series described in this report is numerically sound and reflects a rigorous historical experience.

Are the data sound and well controlled?
Although it is well known that current literature supports the superiority of concomitant regimens over sequential ones the presentation of results as a comparison between the two series is misleading and not informative for many reasons:
1. as in several historical comparisons, the time period in which patients were treated is too long to prevent from historical biases. Improvement in disease staging, support measures, treatment planning and radiation therapy technology (factors not always recorded nor accounted for in an historical series) can justify the improvement of results.
2. the two regimens differed not simply in terms of sequencing of chemotherapy and radiation. One of other relevant differences is the chemotherapy regimen (cisplatin based versus non-cisplatin based) This, together with the dose of drugs administered, is a variable that could have had an influence on results
3. the sequential treatment was inadequate for several reasons:
a. low chemotherapy dose (38% of the patients receiving 2 courses or less)
b. low radiotherapy dose (65.3 versus 71.6 Gy)
c. more pauses (more than one week in 36% of the patients versus 14%) and longer treatment time (79.9 versus 43.4 days).
For these reasons I think that results of the two treatment series should be presented separately. Hypothesis-generating features should be prudently suggested. The analysis of results in the context of the current literature should be the basis for further study.

Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes
Are the discussion and conclusions well balanced and adequately supported by the data? See comments on point 3

Do the title and abstract accurately convey what has been found? Yes

Is the writing acceptable? Grammar needs improvement in several points of the report.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

Patients and methods section, page 4: time of response assessment (4-6 weeks) may be too short for a chemoradiotherapy program

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Patients and methods section, page 5: Was the radiotherapy energy used in the CON protocol the same as in the SEQ protocol? Probably not, due to the telecobalt use in the first part of the study. Please specify.

Results section:
§ The “response” and “local control and survival” sessions need a review in order to afford understanding of numbers. Sentences like “5 years after complete remission 55% and 48% in the SEQ group had recurrences on primary nodes” are not the right way of describing results. Instead “5-year disease-free survival was …” would be more linear.  
§ In the “local control and survival” session crude numbers of relapsing patients must be reported, not only percentages. Calculations should be performed on the total number of eligible patients (not only on those evaluable) and this should be evident from the text.

Discussion: The sentence on page 10 line 4 and following needs improvement. The same is trough for the sentence on page 12 line 20 and following.

Conclusion: the sentence should be modified accordin to previous comments.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests