Reviewer's report

Title: In vitro study on the schedule-dependency of the interaction between pemetrexed, gemcitabine and irradiation in non-small cell lung cancer and head and neck cancer cells.

Version: 2 Date: 17 March 2010

Reviewer: Wainer Zoli

Reviewer's report:

2nd Revision

Although the article has been revised sufficiently to render it acceptable for publication, the fact that some of the previously requested molecular elucidations (i.e. additional experiments) were not performed lessens it overall interest value.

Major Compulsory Revisions

2nd Revision

In response to reviewer’s 3 first comment, the authors clearly state their point of view, but it appears only to be a personal one. Moreover, they declare that “…previous studies […] often included no more than two cell lines (see table below) …”, but those studies often included cell lines from the same histotype.

Although the authors’ rebuttal is somewhat questionable, it is nevertheless acceptable because they stress in the text that they only wanted “to explore the interaction between pemetrexed and gemcitabine alone or combined with radiation using various treatment schedules …” at a preclinical level and that “extrapolation of in vitro data to the clinic should be considered with caution”.

In response to reviewer 3’s sixth comment, the authors asserted that further investigation of induction of apoptotic cell death would be beyond the scope of their paper. However, it is not completely clear from their results whether the proposed therapeutic option would really kill cancer cells or only block their proliferation, leaving the possibility of “late” cell regrowth. The authors should thus underline that their results are undoubtedly preliminary and will be followed by more in depth molecular/functional studies.

In relation to the above, the authors have wisely added in the Discussion that in vitro data should be considered with caution before being translated into a clinical setting.

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

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.