Reviewer's report

Title: Multimodal therapy in treatment of rectal cancer is associated with improved survival and reduced local recurrence - a retrospective analysis over two decades

Version: 3 Date: 19 August 2014

Reviewer: Francesco Cellini

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MAJOR COMPULSORY REVISIONS

1) INTRODUCTION:

- The recent reports of EURECCA should be mentioned about the general consensus

- References on the mentioned Guidelines should be added

- The definition on a “First Phase” generally including in “preoperative” section both diagnostic evaluation and neoadjuvant treatments seem forced: maybe author could split it into 2 parts, being the latter closer to other phases based on treatment approaches

2) Data Source:

- Has the pathological data on the response (like pCR) been evaluated?

3) Therapeutic Management:

- Maybe Authors should specify also in Results if “neoadjuvant radiotherapy” (line 164) is referred to planned short course treatments. Not only the overall data on neoadjuvant treatments (up to 58%) should be mentioned here, but also the detail for treatment stages: it is probably low due to the 0 and I stages

- If present, also the data on adjuvant Radiotherapy could be mentioned, being interesting to overview treatment changes over time

- The part from line 176 to 181 should be more clearly detailed and explained to avoid confusion between radiotherapy alone as long course, short course radiotherapy (planed at the beginning) and long course radiochemotherapy

- Details on Radiotherapy treatment approaches seem lacking. Being that a crucial part of the integrated multimodal approach, having presented a huge modification over decades, that is at the basis of the improvement of clinical results (as authors conclude): it is strongly important to describe total doses, fractionations and volumes (If possible) to depict the relative role in this Institutional experience
4) Recurrence Rate:
- The last issue, at lines 195-197 seems particularly interesting. Authors says that the improvement is significant in last decades, where the major improvement belongs to stages that include integrated treatments (like Radiochemotherapy, adjuvant chemo, ect) rather than in Stage I: that suggest a role played also in distant metastases control by Radiotherapy or adjuvant chemotherapy. This data should be deepened in stage-by-stage analysis, and stratifications by treatment modalities should be performed.

5) DISCUSSION:
- The paper published by Valentini et al on JCO, analyzing on a pooled analysis results from major randomized trials should be mentioned as overview on recent ameliorations by combined treatments: it could be also interesting the data correlations on the finding about metastases-free survival. Also for the issue at lines 320-321
- Data on pCR (lines 269-272) should be reported in results, analyzed by stages (it could be higher for III and IV), and described in discussion mainly for its clinical implications
- Data reported in lines 288-291, could also be mentioned in Results
- The issue on line 298-301 could ; See also the comment on be analyzed evaluating and reporting data for subgroups of different Stages, and stratifying per Long course RT vs short course RT vs not specified RT, to avoid the bias. Also the data facing the 2 timeframes are really important and interesting. See also the comment in “Recurrence Rate”
- The role of surgery in itself, as cited at line 307-308, in the point of view of the paper, could be generally tested evaluating data from the rate of patient stage III and over, refusing or not candidates to RT (in any form) to at least address a trend

MINOR ESSENTIAL REVISIONS
It is a very interesting paper on a hot topic in literature, analyzed by a particular point of view. It includes a large and adequate number of patients.
General conclusion driven by the study are also interesting and supporting data from general literature with issue on modern research
Few typing errors should be checked through the paper (see line 122 “for 10 years, with.” ; line 144 “+/11.7à”) 
The considerations on WID and its potentials could be empathized through the manuscript (particularly into the Discussion) being part of the general interest of the paper
Discussion should be a little shorter, highlighting the main data that Authors want to be the strongest “take-home messages”
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

No specific competing interest