Reviewer’s report

Title: CA15-3 is a useful serum tumor marker for diagnostic integration of hybrid Positron Emission Tomography with integrated Computed Tomography during follow-up of breast cancer patients

Version: 1 Date: 24 November 2013

Reviewer: Massimo Gion

Reviewer’s report:

Major Compulsory Revisions

The manuscript by Incoronato et al. reports a retrospective study - performed on a limited case series - aimed at comparing tumor marker results and PETCT findings in women monitored after the treatment of primary breast cancer. The study, as it is presented, seems similar to other investigations previously published on tumor markers in breast cancer follow-up. In addition, the study presents - in my opinion - a selection bias due to the fact that the Authors enrolled only cases in which PETCT was available. The sensitivity and specificity values of cancer markers should be examined in a consecutive patient series in which the outcome is definitely known, irrespectively of the availability of PETCT.

Nevertheless, the paper reports some interesting findings concerning the lead time of CA15-3 with reference to PETCT. Therefore I do suggest to the Authors to rewrite the manuscript in a shorter version (i.e., in short communication stile) focusing only on the findings concerning the value of CA15-3 in anticipating a positive PETCT result.

The assessment of CA125 should be omitted. In fact, CA125 is not recommended in breast cancer and its use is therefore not appropriate. I think that a scientific investigation should not consider a marker that is inappropriately used, even if the study is retrospective.

Statistical analysis (and other points in the manuscript). The Authors say that increased CA15-3 has ‘prognostic’ significance since it predict a shorter time to relapse. This is certainly true from a generic point of view. However, the information that CA15-3 provides, is an earlier detection of the relapse in comparison to PETCT; that is, an anticipation with reference to imaging techniques. The authors should emphasize the predictive role of (and the anticipation provided by) CA15-3. In addition the analysis of serial CA15-3 values – if available - would add interest to the study (see for an example: Mariani L et al. Serial determination of CEA and CA 15.3 in breast cancer follow-up: An assessment of their diagnostic accuracy for the detection of tumour recurrences Biomarkers, 2009; 14: 130–136)

Minor Essential Revisions
Introduction, lines 6-7. The sentence ‘so diagnostic tools for … are needed’ should be omitted or mitigated: why are the tools needed, when the usefulness of the follow-up is itself still under debate?

Discussion, pg 11 lines 2-8. ‘.. are frequently required by clinical oncologists as ….’. It is difficult to believe that the request of cancer biomarker in patients with breast cancer is motivated by the knowledge of the biochemistry of the markers. I suggest to omit the paragraph.

Discussion, pg 11 lines 12-14. ‘clinicians have the tendency to add in lots of extra tumor markers for monitoring BC patients …’. May be that this ordering modality occurs in some institutions or in some Countries, but certainly it cannot be presented as a general behavior of ‘clinicians’, as the authors seem to state. Please, omit or amend this sentence.

Conclusions, lines 1-2. The statement ‘there is a general consensus …. As well as early detection of disease relapse’ is not entirely true. There is no consensus on the usefulness of follow-up in breast cancer. The sentence should be omitted or changed.

Discretionary Revisions
Introduction, lines 1-2. The sentence ‘as stated by …’ is not necessary - the citation of the reference is sufficient.

Results, pg 8 lines 9-10. ‘Interestingly, the highest serum levels of CA15-3 … and hepatic involvement’. I would omit ‘Interestingly’ since this pattern is well know.

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests