Author's response to reviews

Title: TACE performed in patients with single nodule of hepatocellular carcinoma

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Author's response to reviews: see over
Bologna, 28 March 2014

To the Editors of
BMC Cancer

Dear Editors,

we would like to thank you for your comment. We thoughtfully considered it, but no change was field necessary for our manuscript. The explanation for our decision, answering your request is reported here below. We are therefore proceeding to submit our manuscript entitled “TACE performed in patients with single nodule of hepatocellular carcinoma” for consideration for publication in BMC Cancer.

Editorial comment to the Author(s):
I am concerned about the statistics of this article. Very small upticks in some labs post TACE, and the error bars encompass that, but they show marked statistical significance in only 148 patients. I would like to ask the submitters to send the exact statistic calculations used.

Re: We agree with you that the changes on laboratory tests after TACE are quite small, but this was not unexpected. Our goal was to evaluate whether there was a negative impact of TACE on laboratory tests the day after the procedure, analyzing whether a significant number of patients showed a worsening of some labs post TACE.
To this end we used the Wilcoxon signed-rank test, as stated in the article whose significance is primarily related to the number of patients who met a decrease/increase of post-TACE laboratory tests (Tab 1) rather than the relative magnitude of laboratory changes (even if also the magnitude of changes certainly influences the result of the test). The use of the Wilcoxon signed-rank test was chosen on purpose because the extent of changes was not expected to (and indeed it did not) follow a Gaussian distribution, thus a non parametric test for paired data, namely the Wilcoxon signed-rank test, was needed. Additionally, it was well expected that the uptick on lab data post TACE would have been quite small, since otherwise a large uptick of data would mean a very bad impact of therapy (namely TACE),
thus TACE would not be anymore a recommended treatment. What makes the statistics
significant is the fact that changes, despite small and with a large variability (making the
error bars wide), went into the same direction in the very large majority of patients,
indicating that indeed there is some impact of TACE treatment on liver function, regardless
of the low median effect. Thus the findings and the statistical significance should not be held
as surprising, but quite logical.

<table>
<thead>
<tr>
<th></th>
<th>Decrease post-TACE labs</th>
<th>Increase post-TACE labs</th>
<th>No changes in post-TACE labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin, n (%)</td>
<td>116 (78)</td>
<td>16 (11)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Bilirubin, n (%)</td>
<td>23 (16)</td>
<td>122 (82)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>INR, n (%)</td>
<td>45 (31)</td>
<td>79 (53)</td>
<td>24 (16)</td>
</tr>
<tr>
<td>Creatinine, n (%)</td>
<td>75 (51)</td>
<td>67 (45)</td>
<td>6 (4)</td>
</tr>
<tr>
<td>MELD score, n (%)</td>
<td>21 (14)</td>
<td>93 (63)</td>
<td>34 (23)</td>
</tr>
</tbody>
</table>

**Tab 1.** Number of patients who met an increase/decrease of post-TACE laboratory tests.

We hope we were able to fully explain the logic and strategy behind our findings. Looking forward
to hear from you. We also hope that the submission date remains November 2013 as originally
done.

Yours sincerely

Fabio Piscaglia