Reviewer’s report

Title: Analysis of the EGFR, HER2, and TOP2A gene status and chromosomal aneusomy in gastric adenocarcinoma from Chinese patients

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Reviewer: Khawla Al-Kuraya

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Liang et al investigated status of EGFR, HER2, TOP2A and aneusomy of chromosome7, 17 in Chinese gastric carcinoma patients. They used One hundred cases of formalin fixed and paraffin embedded tumor tissues from Chinese gastric carcinoma patients and performed immunohistochemistry and fluorescence in situ hybridization (FISH) methods to analyze the expression and amplification respectively.

Results

Forty-two percent of the cases showed EGFR overexpression; 16% showed EGFR FISH positive; 6% showed HER2 overexpression; and 11% showed HER2 gene amplification, including all six HER2 overexpression cases. TOP2A nuclear staining (nuclear index, NI) was determined in all 100 tumors: NI values ranged from 0.5 - 90%. Three percent of the tumors showed TOP2A gene amplification, which were all accompanied by HER2 gene amplification. Nineteen percent of the tumors showed chromosome 7 polysomy, and 16% showed chromosome 17 polysomy. EGFR overexpression correlated significantly with EGFR aneusomy. Chromosome 7 polysomy correlated significantly with EGFR FISH-positivity, but was not associated with EGFR overexpression. HER2 overexpression associated significantly with HER2 gene amplification. TOP2A gene amplification was significantly associated with HER2 gene amplification. No relationship was found between alterations in the EGFR, HER2, and TOP2A genes and clinicopathologic variables of gastric carcinoma.

Conclusion: chromosome 7 polysomy may be responsible for increased EGFR gene copy number in gastric carcinomas, and that HER2 gene amplification may be the major reason for HER2 protein overexpression.

Comments: This is a well designed paper to identify gastric carcinoma patients for targeted therapies, however the number of samples is small. The FISH figures are very well represented.

The following major corrections have to be made.

1. In figure1,2 and 3 negative/underexpressed controls for immunohistochemistry need to be included.
2. The numbers in text on the results section of page 10 section 3.2 do not match with table2.
3. The manuscript has lot of syntax and spelling errors
The following minor corrections need to be included
1. Abstract Section
   On Page 2 Line 4 The sentence
   “No detailed report about the above three genes in Chinese patients, so we try to
determine the gene status of EGFR, Her2, Top2A genes and aneusomy of
chromosome 7, 17 in Chinese gastric carcinoma patient”. Should be rephrased
   On Page 2 Line 8 the sentence can be written as
   Gastric carcinoma patients were investigated by using immunohistochemistry
   Gastric carcinoma patient tissue samples were investigated by
immunohistochemistry
   On Page 2 Line 21
   Conclusion,
   Remove comma after conclusion
2. In Introduction section
   On Page 3 Line 7
   Recently target therapy has been applied -should be changed to
   -Recently targeted therapy has been applied
   On Page 3 Line 8
   Current target -should be changed to
   -Current targeted
   On Page 28 Legend to figures section
   Figure 2 B: Immunohistochemistry showed Top2A NI(nuclear index)
   Immunohistochemistry showed Top2A NI(nuclear index)
   In figure 4 the heading
   TOP2A Expression Nuclear Index(NI) has to be changed to
   TOP2A Expression Nuclear Index(NI)

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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’