Reviewer's report

Title: p53 expression is significantly correlated with high risk of malignancy and epithelioid differentiation in gastrointestinal stromal tumors. An immunohistochemical study with 104 GISTs.

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Reviewer: Muna Sabah

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The authors have investigated 104 casts of GISTs using immunohistochemical stains for p53, bcl-2 and Cyclin D1. They concluded that positive staining may be used as a marker for predicting GIST with an aggressive clinical behaviour. The study is not novel and numerous studies have investigated the role of p53 immunostaining in the prognostigation of GISTs. The findings of this study are in concordance with those previously reported.

Major Compulsory Revisions

1- There is a new classification of GISTs by Miettinen which takes into consideration, tumour size, site and mitotic count. It classifies GISTs into 6 groups (1, 2, 3a, 3b, 4, 5, 6a and 6b). This classification is a combination between Fletcher classification and the old Miettinen classification. Therefore the old groups (probably benign, uncertain malignant potential and probably malignant) are not used anymore.

By using an outdated classification, the authors may have drawn inappropriate conclusions. The authors should revise their findings taking into consideration the new classification.

2- The authors have stated that the epithelioid subtype of GISTs is known to be associated with an aggressive behaviour. This cellular pattern is present in one third of gastric tumours, but is usually associated with more aggressive behaviour when found in the small intestine. It would be useful to state how many of the GISTs with positive p53 staining and epithelioid morphology were gastric in origin and how many were non gastric.

3- The authors use the percentage 7% as a cut off point for KI67 immunostaining, but have 0% as a cut off point for all other markers. They have reported that any positive staining is regarded as positive. This is in contrast with other major p53 studies which use a minimum of 5-10% as a cut off point.

4- The poor punctuation and grammatical mistakes, made some paragraphs ambiguous.

Minor Compulsory Revisions

1- The authors have stated that 50% of GISTs are malignant, but fail to cite a reference for this percentage. This is a high percentage and a reference should
be included.

2- The authors have classified GISTs histologically into 2 groups only (epithelioid and spindle). Were there any other subtypes (mixed pattern which is seen in 20% of cases and pleomorphic 5%)? Perhaps the cases in this study with severe cytological atypia should be classified as pleomorphic.

3- The authors have stated that “GISTs with metastasis expressed p53 more often than GISTs without metastasis”. Has this been seen in primary resection specimens or in the recurrence / metastatic sections? Was there a difference between primary tumours and their recurrences?

4- The authors have discussed their findings on CD34 in the “discussion paragraph”, but there is no mentioning of CD34 in the “Material and Method” section nor in the “Result” section.

5- The incubation period of the antibodies used should be added to Table 1.

6- Were appropriate positive and negative controls used in this study?

7- c-kit protein expression should be referred to as KIT ( page 3 line 4 and page 4 line20).

8- KIS5 should be replaced by KI67 (page 6 line 25 and table 1).

9- There are some typing errors (e.g., page 4 line 16 should read as have rather than habe).

10- Reference 12 is inappropriate for this study (Biankin) as it is about p21 which has not been investigated in this study.

The authors should revise the manuscript, taking the above mentioned points into consideration.

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

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