Reviewer's report

Title: KIT exon 10 variant (c.1621 A>C) single nucleotide polymorphism as predictor of GIST patient outcome.

Version: 3 Date: 8 July 2015

Reviewer: Carmine Carbone

Reviewer's report:

I read with interest the manuscript from Brahmi and colleagues entitled: “KIT exon 10 variant (c.1621 A>C) single nucleotide polymorphism as predictor of GIST patient outcome”. The authors analyze the significance of the presence of KIT variant protein on the biology of GIST by transfecting KITL541 in NIH3t3 cell line and by exploring the prevalence and prognostic value of KITL541 in 2 distinct series of GIST patients. The authors candidate KITL541 as a prognostic factor for relapse but not as a predictive factor for response to imatinib.

I found the topic of the manuscript very interesting, the results are clear and the interpretation is well taken and balanced. Moreover the discussion addresses all limitations resulting from the data analysis. However few, but important, points need to be addressed to fully appreciate the manuscript.

Major revision:

In figure 1 A and B., the authors compare KITL541 expression and the resulting activation signaling pathways (p-AKT, p-RAF, p-ERK). However, to determine the expression levels of the different mutated KIT proteins and the relative activation pathways, the authors should run all samples on the same SDS-PAGE. In general it is not recommended to compare samples from different gels, nevertheless a positive control on both gel was suitable. In this case the control sample should be not overexposed and an accurate densitometric analysis was due.

Moreover the WB shown in Figure 1A is of very poor quality; can the authors provide better pictures that distinguish from 145kDa and 125 kDa KIT forms??

Minor revisions:

Please check the text for punctuation error (for example page 12 line 261 “..”).

Page 15 line 338, please change “brut” with “but”

In legend of figure 2. The authors should change “KIT541” in “KITL541” according to figure 2.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests