Reviewer’s report

Title: Low rate of mutation and modest effect of SF3B1, U2AF1, and SRSF2 on prognosis in the myelodysplastic syndrome without ring sideroblasts

Version: 2 Date: 16 November 2014

Reviewer: Omar Abdel-Wahab

Reviewer’s report:

This is a study of the effect of spliceosomal gene mutations on clinical outcome in non-RARS MDS. This is a topic which has been heavily studied previously (despite the authors statements otherwise) but these data are worth presenting as the results on this question have not been uniform amongst studies. A number of edits to the manuscript are needed to improve the text as follows:

Minor Essential Revisions:
- The title does not reflect the data in the manuscript. It should be retitled “Prognostic impact of spliceosomal gene mutations in non-RARS MDS” (or something like that) as there is a prognostic impact of U2AF1 and SRSF2 mutations seen here and mutations in SF3B1+U2AF1+SRSF2 represented ~25% of MDS patients here.
- There have actually been quite a few studies of the impact of spliceosomal gene mutations in non-RARS MDS so the parts of the Abstract (last sentence of the Background) and the Introduction which suggest otherwise should be revised (particularly the last sentence of the 2nd to last paragraph in the Introduction).
- The Introduction describes a mechanistic impact of spliceosomal gene mutations which is written far too definitively (Lines 115-118) as the true mechanistic effects of these mutations in the pathophysiology of MDS are not well known now. This section needs to be heavily revised to reflect the uncertain role of these mutations in leukemogenesis. It is also not clear what the authors mean by spliceosomal genes being “tumor suppressors” and this needs to be revised.
- Table 1 is unnecessary in the main manuscript given the >20 publications which have already reported on the location of spliceosomal gene mutations in these genes.
- Section of the 1 of the Results can be greatly abbreviated. The mutual exclusivity of spliceosomal gene mutations and the locations of these mutations have been repeatedly described and don’t need to be stated in the main text yet again here.
- The Discussion section needs to be greatly abbreviated. It is too long here.

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