**Reviewer's report**

**Title:** Cytoplasmic BRMS1 expression in malignant melanoma is associated with increased disease-free survival

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**Reviewer:** Clelia Miracco

**Reviewer's report:**

**General comments:**

In this paper, the authors evaluated the expression of BRMS1 protein in a series of benign nevi, primary melanomas, and metastases. They suggest its subcellular localization as a novel biomarker of tumor progression, useful for prognostic purposes. The study is of potential interest, since BRMS1 expression at the tissue level in cutaneous melanoma is largely unexplored, however, there are some points to be clarified, and some thinks to be added. Cases of melanoma should be better defined. Correlations with further clinicopathological factors should be provided to support the power of BRMS1 expression as a marker of tumor progression and prognosis.

**Major Compulsory Revisions**

1-In order to assess BRMS1 usefulness as a biomarker in human melanoma, additional clinicopathological prognostic parameters should be taken into account.
   a- Melanoma cases should be grouped based on their clinicopathological stage.
   b-Radial vs vertical growth phase cases should be compared
   c-The mitotic count is more informative than any other marker of proliferation, and mitoses are today considered the second histopathological prognostic factor in primary melanoma. The authors should analyze the correlation between mitotic count and the expression of BRMS1 in primary melanoma cases.

2-Results, page 7: “heterogeneous cytoplasmic and/or nuclear expression was observed”: the authors should specify whether the cytoplasmic and/or nuclear positivity were distributed randomly or not. For instance, in primary melanomas, was the BRMS1 positivity mainly observed in the central tumor areas or at the advancing border of the neoplasms, i.e., at their peripheral and/or deep areas? There was any association between BRMS1 positivity and angiogenesis, tumor cell necrosis, TILs, etc.?

3-The authors claim that BRMS1 positivity was detected in most benign nevi (87%), as well as in many primary melanomas (20%) and metastases (48%), however nuclear positivity is not observable in Fig. 1, which depicts only cytoplasmic staining in a benign nevus, a primary, and a metastatic melanoma. Pictures showing the most representative cases should be included
4-Discussion on contrasting results obtained in other studies (references no 5; 12, 14, 15) should be expanded.

Minor Essential Revisions:
1-Mean + SD thickness should be given for primary melanoma group in Results
2-There are some typewriting mistakes

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests