Author’s response to reviews

Title: FIP1L1-PDGFRA molecular analysis in the differential diagnosis of eosinophilia

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Author’s response to reviews: see over
To the Editor of the journal “BMC Blood Disorders”

Dear Sir,

We are pleased to submit a revised version of our manuscript “FIP1L1-PDGFRA molecular analysis in the differential diagnosis of eosinophilia” for publication in *BMC Blood Disorders*. Below we include a point-by-point response in which all the recommendations have been taken into account.

In particular, considering the recommendations of Dr Walz we have dealt as follows:

**Major compulsory revisions:**

1. The prevalence of FIP1L1-PDGFRA rearrangement in hypereosinophilic syndrome has been corrected according to the reviewer’s recommendation in page 3, lines 19-20.

2. The typographical error of the mutation D816V has been corrected throughout the text.

3. The correct number of the analyzed patients is 15 (as it has been reported in the sections of “Material and Methods” and “Results”), and the abstract has been corrected appropriately (page 2, line 6).

4. The duration of eosinophilia in patients with secondary eosinophilia was longer than 6 months only in one patient, and this point has been indicated in the text (page 6, lines 27-28). Concerning patients with hypereosinophilic syndrome without FIP1L1-PDGFRA rearrangement, the duration of eosinophilia was longer than 6 months and this point has also been indicated in page 7, lines 3-5. For the patients with chronic eosinophilic leukemia (carrying the FIP1L1-PDGFRA rearrangement), the duration of eosinophilia was 18 months for the first one and 2 weeks for the second (already described in the previous version of the manuscript).

5. We consider that our work, describing the early detection of FIP1L1-PDGFRA rearrangement in patients with eosinophilia, emphasizes that molecular analyses can modify established standpoints for the diagnosis of neoplastic diseases. Thus, an early diagnosis of FIP1L1-PDGFRA-positive leukemias, as in our second case, adds more evidence that the diagnostic criteria of hypereosinophilic syndrome have to be modified in the light of the new molecular approaches, with significant impact in undesirable morbidity and mortality. This point has been highlighted in the new version of the manuscript (second paragraph of “Discussion” section).
6. It has been described that in cases of systemic mastocytosis the mutation is detected in microdissected mast cells from lesional areas of bone marrow biopsy tissues (Ref#16, in the new version of the manuscript). However, in our cases, the mutational analysis of C-KIT-D816V has been carried out in bone marrow samples using a PCR-RFLP protocol (and not PCR-sequencing), as it has been described in “Material and Methods”, and the aim of this analysis was the detection of C-KIT-D816V mutation in eosinophils.

7. The second paragraph of “Material and Methods” has been deleted according to reviewer’s recommendations.

Minor Essential Revisions:

1. The reference of Chusid et al. has been cited, according to reviewer’s recommendation (Ref#1).

2. Exon numbering in FIP1L1 is based on a complementary DNA (cDNA) clone (GenBank accession number NM_030917), and this point is indicated in the Figure Legend.

3. The references have been checked and corrected for errors (e.g., ref #5, now ref#6)

4. “Fifteen” has been replaced by “15” in page 6, line 16.

5. The gene names have been typed according to reviewer’s recommendation (upper case and italics).

6. The median time of response was 28.2 months (range: 11-54, considering that the numbering has been updated), and this point has been indicated in the “Abstract”, page 2, lines 19-20.

6b. The phrase “...FIP1L1-PDGFRA fusion tyrosine kinase signal” has been changed, as indicated in page 8, line 12-13.

7. The study of Stover et al, has been cited according to reviewer’s recommendation (Ref#19)

8. Vitamin B12 serum levels were not estimated in our patients, and this is indicated in page 4, line 14-15.

The recommendations of the other reviewers, were included in the response to Dr’ Walz comments.

Finally, a native English speaker proofread the manuscript.

We sincerely hope that you will find the revised version of our manuscript appropriate for publication in BMC Blood Disorders.
Sincerely yours,

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