Author's response to reviews

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

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Version: 4 Date: 15 January 2009

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Larissa 14-1-2009

To the Editor of “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 to 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 editorial requests we have dealt as follows:

1. Another colleague, who is a native English speaker, has proofread the manuscript and corrected the syntactic and typographical errors. The changes have been underlined throughout the manuscript.

2. We have revised the second paragraph of page 4 (regarding the type of informed consent and the statement of the names of the institutions that permitted us to perform our investigation), according to editor's recommendation.

Considering the discretionary revisions of the first reviewer, they have been incorporated in the Abstract (page 2, lines 19 and 22, respectively).

The second reviewer had no recommendations.

Finally, considering the comments of the third reviewer, we speculate that these might be the result of a possible misunderstanding of the general concept of our manuscript. However, we could not exclude the possibility that this could be the result of our own inadequacy, especially considering our first version of the manuscript, to present clearly our objectives.

In our manuscript, as indicated even in the title, we determined the prevalence of FIP1L1-PDGFRA rearrangement in patients with profound eosinophilia, and
among them, only five have primary eosinophilia (2 chronic eosinophilic leukemia, 2 primary hypereosinophilic syndrome and 1 systemic mastocytosis), for whom the diagnosis was based on standard criteria. Thus, the reviewer’s first and principal statement that “The authors study a small series of so-called hypereosinophilic syndrome, of which several turn out to have another diagnosis that is associated with eosinophilia, but that is incompatible with the diagnosis of HES” is, at least, not correct.

The second comment that we did not present the clinicopathological features of our patients with primary eosinophilia (especially “the presence or absence of cardiac disease, neuropathy, fluid retention”) is also not correct. We present all their clinical and laboratory findings in Table 1, and especially for the patients carrying the FIP1L1-PDGFRA rearrangement, in detail, in page 8. Indeed, one of them (patient 1 of Table 1), displayed at diagnosis peripheral neuropathy (Table 1 and page 8, lines 4-6).

Moreover, regarding his statement that he did not see any novelty to our work, since, oddly enough, “the data that are shown essentially confirm the literature on the subject” (despite his doubt for our diagnoses and the presumed absence of clear and distinctive data), we have a completely different view. As highlighted in the first revised version of our manuscript (second paragraph of “Discussion”), 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 new molecular approaches, with significant impact in undesirable morbidity and mortality.

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

Sincerely yours,

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