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LETTER TO THE EDITOR

Efficacy of ruxolitinib in myeloid neoplasms with *PCM1-JAK2* fusion gene

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Dear Editor,

We read with interest the paper by Schwaab et al. published in September 2014 regarding two cases of myeloid neoplasms associated with *PCM1-JAK2* and *BCR-JAK2* fusion genes treated with ruxolitinib [1]. While they reported a very good initial response for both cases, relapse occurred after 18 and 24 months, respectively. The authors concluded that the response of myeloid disorders with *JAK2* fusion genes to ruxolitinib is short lived, but that ruxolitinib may be an important bridging therapy prior to allogeneic bone marrow transplantation (ASCT).

Our groups previously reported two cases of myeloid neoplasms/chronic eosinophilic leukemia (CEL) with a *PCM1-JAK2* fusion gene who were treated with ruxolitinib after obtainment of their informed consent, and of whom we here report the further follow-up.

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Both cases achieved cytogenetic response, and we provide quantitative PCR data to support this (Fig. 1a, b, respectively).

The first case (patient 1) was a 72-year-old male with a *PCM1-JAK2*-positive CEL who gradually obtained a complete cytogenetic remission over a period of 15 months of therapy with ruxolitinib at a dose of 10–20 mg bid [2]. The hematological course of this patient beyond 15 months, under continued treatment with ruxolitinib (10 mg bid) was uneventful, with moderate anemia (Hb>120 g/L) not requiring blood transfusions, with normal leukocytes and platelet counts and normal eosinophil counts. Consecutive cytogenetic and FISH studies on bone marrow showed complete cytogenetic remission (no aberrant metaphases at 33 months, 20 metaphases analyzed; normal interphase FISH, 200 nuclei analyzed). In addition, the measurement of disease burden by real-time quantitative RT-PCR showed a 2 log decrease at 34 months as compared with the disease burden at the start of ruxolitinib. The last re-evaluation was done 3 months before his death due to unrelated cardiac problems (septic endocarditis) 36 months after the start of ruxolitinib, without evidence of relapse.

The second case (patient 2) was a 31-year-old female affected with CEL [3]. She started ruxolitinib in 2011 at 15 mg bid and obtained a complete clinical remission. She obtained a complete cytogenetic remission at 46 months: at last evaluation, we did not observe aberrant metaphases (20 metaphases analyzed) and aberrant nuclei with *t*(8;9) (300 nuclei analyzed). A marked reduction of the *PCM1-JAK2* fusion transcript was detected. She is still alive in complete hematological remission after 46 months of treatment with Ruxolitinib.

Both patients therefore achieved complete hematologic remission, complete cytogenetic response, and a marked

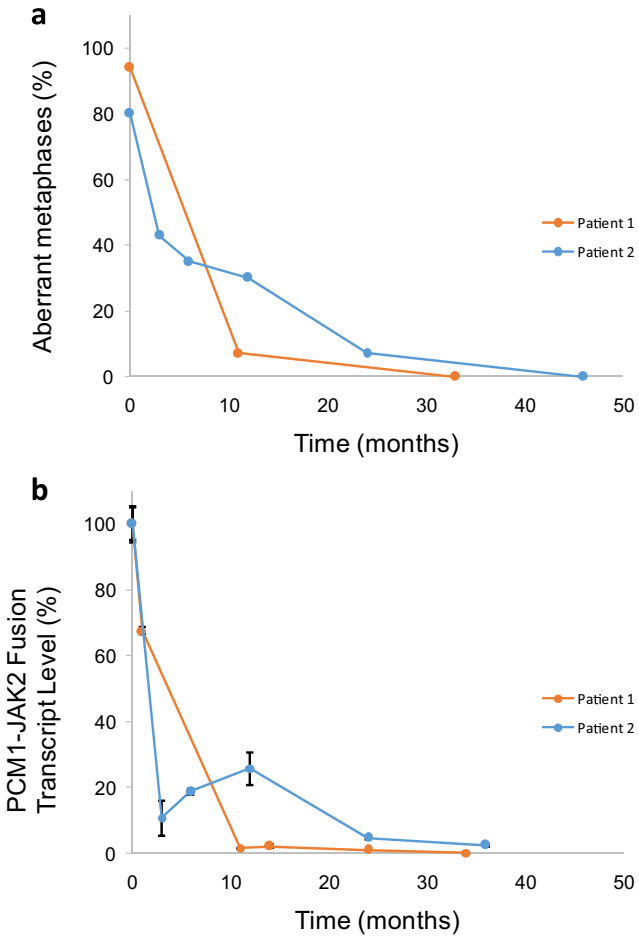

Fig. 1 Reduction of the percentage of metaphases with *t*(8,9) (*1a*) and *PCM1-JAK2* fusion transcript (*1b*) during follow-up. We looked for relative expression of the PCM1-JAK2 to the control gene. The house keeping gene was ABL1 for patient 1 and HPRT1 for patient 2. The fold difference in transcript levels normalized to the baseline sample considered as 100 % is plotted (the maximal burden observed in a particular patient was set to 100 %)

reduction of the *PCM1-JAK2* fusion transcript. In contrast with the patient described by Schwaab et al., these cases demonstrate that the response of myeloproliferative neoplasms with *PCM1-JAK2* fusion genes can be long-lived, without use of ASCT. More clinical data are urgently needed to establish the response rates of hematological neoplasms with *PCM1-JAK2* and other *JAK2*-fusion genes to ruxolitinib, and the durability of responses.

Ethical approval

In both cases, the treatment with ruxolitinib was approved by the local ethics committee and was started after patients provided written informed consent. All procedures were in accordance with the 1964 Helsinki declaration.

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Conflict of interest The authors do not have potential conflicts of interest related to this paper.

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