DOI: 10.7860/JCDR/2016/20228.8176

Letter to Editor

Pathology Section

No Benefit of BCR-ABL1 Screening in Polycythemia

STEPHEN E. LANGABEER

Keywords: Chronic myeloid leukemia, Erythrocytosis, Molecular diagnostics

Dear Sir,

Chronic Myeloid Leukaemia (CML) has become the paradigm for the rational development of a molecularly targeted therapy in oncology and is characterised morphologically by leukocytosis due to neutrophils in different stages of maturation, no significant dysplasia, low blast cell numbers, a variable monocytosis, commonly basophilia and/or eosinophilia, and a variable platelet count. The genetic hallmark of CML is (9;22)(q34;q11.2) resulting in the BCR-ABL1 fusion gene [1]. Erythrocytosis is an increase in the number of red blood cells and is a frequent reason for haematological investigation. Common causes include hypoxia (smoking, lung or cardiac disease, sleep apnoea), drugs (diuretics, testosterone, or anabolic steroids, erythropoietin) or the myeloproliferative neoplasm polycythemia vera (PV) [2]. PV is characterised at the molecular level by the presence of JAK2 exon 14 V617F and exon 12 insertion or deletion mutations [3]. The term polycythemia is often used synonymously with erythrocytosis however this is incorrect as polycythemia implies a leukocytosis and thrombocytosis in addition to the increase in red cells. As both CML and PV can present with leukocytosis and thrombocytosis, testing for BCR-ABL1 can often be erroneously triggered in such cases regardless of the presence of an erythrocytosis.

In order to determine whether any continued value exists in screening for the BCR-ABL1 fusion gene as part of the investigation in patients with polycythemia and erythrocytosis, a retrospective audit was performed. In a ten year period from January 2006 to December 2015 inclusive, 6578 diagnostic requests were received for BCR-ABL1 transcript identification at a national testing centre for haematological malignancies. Detection of BCR-ABL1 transcripts was performed according to standardized protocols and guidelines. Of these 6578 requests, 36 (0.5%) had clinical details stated as raised haemoglobin and haematocrit (n=17), polycythemia (n=16) and erythrocytosis (n=3). BCR-ABL1 transcripts were not detected in any of these 36 patients.

The absence of BCR-ABL1 transcripts in patients with polycythemia or erythrocytosis suggests that routine exclusion of CML by BCR-ABL1 fusion transcript identification is not warranted in such cases. However, extremely rare confounding scenarios should always be considered and include the co-existence of CML and PV and singular cases of CML presenting with polycythemia [4,5]. While JAK2 mutation analysis for PV remains high in the diagnostic algorithm for investigation of polycythemia and erythrocytosis [2], more common reasons should be excluded before subsequent investigation of rare underlying causes.

REFERENCES

[1] Vardiman JW, Melo JV, Baccarani M, Thiele J. Chronic myelogenous leukaemia, BCR-ABL1 positive. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 4th ed. Lyon: *International Agency for Research on Cancer*. 2008:32-37.

[2] Keohane C, McMullin MF, Harrison C. The diagnosis and management of erythrocytosis. *BMJ*. 2013;347:f6667.

[3] Barbui T, Thiele J, Vannucchi AM, Tefferi A. Rationale for revision and proposed changes of the WHO diagnostic criteria for polycythemia vera, essential thrombocythemia and primary myelofibrosis. *Blood Cancer J*. 2015;5:e337.

[4] Zhou A, Knoche E, Engle EK, Fisher DA, Oh ST. Concomitant JAK2 V617F-positive polycythemia vera and BCR-ABL-positive chronic myelogenous leukaemia treated with ruxolitinib and dasatinib. *Blood Cancer J*. 2015;5:e351.

[5] Fozza C, Bonfigli S, Longu F, Pardini S, Dore F. Isolated polyglobulia as an uncommon presentation of chronic myeloid leukaemia. *Blood Cells Mol Dis*. 2016;56(1):37.

PARTICULARS OF CONTRIBUTORS:
1. Clinical Scientist, Cancer Molecular Diagnostics, St. James's Hospital, Dublin, Ireland.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Stephen E. Langabeer,
Cancer Molecular Diagnostics, Central Pathology Laboratory
St. James's Hospital, Dublin 8, Ireland.
E-mail: slangabeer@stjames.ie

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Mar 18, 2016**
Date of Peer Review: **Jun 01, 2016**
Date of Acceptance: **Jun 11, 2016**
Date of Publishing: **Jul 01, 2016**