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ORIGINAL ARTICLE

Low prevalence of the *BCR–ABL1* fusion gene in a normal population in southern Sarawak

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Abstract

The *BCR–ABL1* fusion gene is the driver mutation of Philadelphia chromosome-positive chronic myeloid leukemia (CML). Its expression level in CML patients is monitored by a real-time quantitative polymerase chain reaction defined by the International Scale (qPCR^{IS}). *BCR–ABL1* has also been found in asymptomatic normal individuals using a non-qPCR^{IS} method. In the present study, we examined the prevalence of *BCR–ABL1* in a normal population in southern Sarawak by performing qPCR^{IS} for *BCR–ABL1* with *ABL1* as an internal control on total white blood cells, using an unbiased sampling method. While 146 of 190 (76.8%) or 102 of 190 (53.7%) samples showed sufficient amplification of the *ABL1* gene at > 20,000 or > 100,000 copy numbers, respectively, in qPCR^{IS}, one of the 190 samples showed amplification of *BCR–ABL1* with positive qPCR^{IS} of 0.0023% and 0.0032% in two independent experiments, the sequence of which was the *BCR–ABL1* e13a2 transcript. Thus, we herein demonstrated that the *BCR–ABL1* fusion gene is expected to be present in approximately 0.5–1% of normal individuals in southern Sarawak.

Keywords Chronic myeloid leukemia · Asymptomatic people · Clonal hematopoiesis

Introduction

Chronic myeloid leukemia (CML) is a clonal hematological malignancy originating from hematopoietic stem cells harboring the Philadelphia chromosome (Ph) due to translocation (9;22). Ph generating the *BCR–ABL1* fusion gene was the first identified chromosomal anomaly associated with a specific malignant disease in humans [1–3]. BCR–ABL1 tyrosine kinase inhibitors (TKI) are the most successful targeted therapy for preventing the progression of CML in patients [4, 5]. To evaluate the sensitivity of CML cells to TKI, it is important for patients being treated to be quantified based on the residual amount of the *BCR–ABL1* gene in blood cells using a real-time quantitative polymerase chain reaction (qPCR) with standardization on the International Scale (IS) of *BCR–ABL1* (*BCR–ABL1*–qPCR^{IS}) [6, 7].

CML is clinically classified into different disease stages such as the chronic phase (CP), acceleration phase (AP), and blast crisis (BC), according to phenotypic and laboratory data [8]. Pre-clinical CML (pre-CP) was recently proposed to be segregated from CP because pre-CP patients do not exhibit the clinical features of CP or leukocytosis [9]. While pre-CP patients have mildly increased basophil counts and

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