The epidemiology of chronic myeloid leukaemia in southern Sarawak, Borneo Island

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ABSTRACT

Objectives: There are very few published chronic myeloid leukaemia (CML) epidemiology studies in South-East Asia and no representative from Malaysia.

Methods: This is a cross-sectional study of adult CML patients (citizen) in a single but representative centre in southern Sarawak.

Results: Total 79 patients (Malay 39%, Chinese 30.4%, Iban 17.7%, Bidayuh 12.7%) were identified from the databases. Median age at diagnosis was younger, 40, compared to developed countries due to population structure. M:F ratio was higher, 2.6:1 compared to other countries 1.3-1.7:1. Majority presented at chronic phase (89.5%), low/intermediate risk score (80%) and started imatinib (96%) as first line tyrosine kinase inhibitor (TKI), which 40% of them switched to other TKI due to intolerance (17%) and failure (including disease progression) not achieving major molecular response (83%). Quantitative polymerase chain reaction (qPCR) assessment after three months of TKI treatment had higher positive predictive value to predict Imatinib failure, 75%, than qPCR assessment after six months of TKI treatment, 58%. Presenting phase, symptoms, signs and laboratory data were like most countries. Estimated prevalence and incidence of CML in southern Sarawak was 69.2/1,000,000 population at the Year 2011 (similar to most developing countries) and 8.0/1,000,000 population per year at the Year 2011-2016 (similar to most countries), respectively. The incidence increased with age and was lowest among Iban, 12.8 and highest among Chinese, 19.5, which was 4x higher than Chinese in China. The prevalence of different BCR-ABL1 transcript type was like other Asia countries.

Conclusion: Significant epidemiological differences on M:F ratio and ethnic groups compared to other countries warrant further study.

KEY WORDS:
CML, BCR-ABL1, tyrosine kinase inhibitor, epidemiology, Malaysia, Asia

INTRODUCTION

Chronic myeloid leukaemia (CML) is a myeloproliferative neoplasm that originated in an abnormal pluripotent bone marrow (BM) stem cell and is consistently associated with the BCR-ABL1 fusion gene located in the Philadelphia (Ph) chromosome. Philadelphia chromosome is the derivative chromosome 22 resulting from the translocation between the long arm of chromosomes 9 and 22, designated as t(9;22)(q34.12;q11.23). On chromosome 9, the v-abl Abelson murine leukaemia viral oncogene homolog 1 (ABL1) gene breaks, usually at the intron between exon 1a and exon a2 or between exon a2 and exon a3. On chromosome 22, the breakpoint cluster region (BCR) gene breaks, usually at a region called major breakpoint cluster region (M-BCR), i.e., the intron between exon e13 and e14 or exon e14 and e15, which after translocation fused with ABL1 gene (at the exon a2 or exon a3) and remaining part from chromosome 9, resulting in a fusion gene, BCR-ABL1 (e13a2, e13a3, e14a2 or e14a3), which produce 210 kilodalton protein, designated as p210BCR-ABL1. Much less found in CML when BCR gene breaks at minor breakpoint cluster region (m-BCR) or micro breakpoint cluster region (µ-BCR), it would result in a fusion gene, BCR-ABL1 (e1a2 or e1a3) or BCR-ABL1 (e19a2 or e19a3), which produce 190 or 230 kilodalton protein, designated as p190BCR-ABL1 or p230BCR-ABL1, respectively. These proteins were an abnormal kinase, Tyrosine Kinase, that apparently was the stimulant for the proliferation of myeloid cells to produce CML.

The first Tyrosine Kinase Inhibitor (TKI), Imatinib (Glivec® or Gleevec®, Novartis Pharmaceuticals Corporation), was approved by the United State Food and Drug Administration at 2001. The invention of TKI has changed the paradigm of CML treatment and revolutionised the direction of oncology. Secondary (Nilotinib, Tasigna®, Novartis Pharmaceuticals Corporation; Dasatinib, Sprycel®, Bristol-Myers Squibb) and third generation TKI (Bosutinib, Bosulif®, Pfizer Inc.; Ponatinib, Iclusig®, ARIAD Pharmaceuticals, Inc.) are now available for clinical use. In Malaysia, Imatinib was available starting around 2000 under trial. Later, majority of patients from hospital in Ministry of Health (MOH), Ministry of Higher Education (MOHE) or private sector received Imatinib free of charge via Glivec International Patient Assistance Program (GIPAP), which officially started in 2003 and managed by Max Foundation (MF), a non-profit cancer organisation (personal communication with Dr Ong Tee Chuan). Very minority self-purchased Imatinib, which the cost per month was around two times of the 2014 median monthly household income. Imatinib supply for patients in MOH hospitals experienced smooth transition on 29th Nov 2007 from GIPAP to Malaysia Patient Assistance Program (MYPAP), which meant Malaysia’s...