

Association of PDGFRA gene polymorphisms at exon 12, 14 and 18 with clinical response to Imatinib mesylate treatment among chronic myeloid leukemia patients

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Abstract

Platelet-derived growth factor receptor alpha (PDGFRA), a type III tyrosine kinase receptor has been implicated in some cancers. Mutation of PDGFRA gene which leads to constitutive activation of the receptor was associated with the development of resistance toward Imatinib mesylate (IM). This study was aimed to detect the PDGFRA gene polymorphisms at exon 12 (c.1701 A>G), exon 14 (c.1664 A>G) and exon 18 (c.2525 A>T) in association with treatment response among chronic myeloid leukaemia (CML) patients who treated with IM. A total of 86 patients (43 CML responses and 43 CML resistances) treated with IM for more than 12 months were recruited. High resolution melt (HRM) analysis was performed to detect PDGFRA gene polymorphism at exon 12, 14 and 18. The HRM curve was able to distinguish the genotypes by three difference clusters (homozygous wild-type, heterozygous and homozygous variant). Homozygous wild-type was used as the reference. HRM curve analysis for exon 12 was successfully differentiating the wild-type with the homozygous variant by a different melting curve, and no heterozygous variant was found. While for exon 14 and 18 the curve showed no difference with the wild-type. Few selected representative samples from different HRM clusters were sent for DNA sequencing for validation. The association of the genotypes with IM treatment response was assessed by means of odds ratio (OR) with 95% CI calculated by logistic regression analysis. The study revealed that CML patients carrying the homozygous variant (GG) genotype of exon 12 PDGFRA gene showed a higher risk of acquiring resistant; however, the association was not statistically significant with OR: 1.597 (95% CI: 0.681-3.745, $P = 0.281$). For exon 14 and 18, all the analyzed samples showed no polymorphism that associated with IM treatment response. Thus, the results were concluded that CML patients with exon 12 (c.1701 A>G) polymorphism are posing higher risk towards developing resistance to IM treatment but not for exon 14 and 18 which showed no significant findings.

Keywords: Chronic myeloid leukaemia; *PDGFRA*; Imatinib mesylate; polymorphisms

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