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TÍTULO

Frequency of *bcr-abl1* transcript types in peruvian chronic myeloid leukemia patients and its impact on imatinib response

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RESUMEN (ABSTRACT):

Introduction: *BCR-ABL1* gene is a genetic hallmark of chronic myeloid leukemia (CML). In Peru, CML patients are treated mainly with imatinib, a tyrosine kinase inhibitor that blocks the kinase activity of BCR-ABL1 which is essential for carcinogenesis. Despite of high rate of response to imatinib some patients show persistence or relapse of disease. Two important resistance mechanisms to imatinib are acquisition of mutations in tyrosine kinase domain of *BCR-ABL1* and clonal chromosomal alterations in Philadelphia chromosome-positive cells, but others like the type of *BCR-ABL* transcripts, mainly b2a2 and b3a2, have been proposed as an important predictor marker. **Aims:** Determine the frequency of different *BCR-ABL* transcripts in peruvian CML patients and highlight their significance on imatinib treatment. **Methods:** Forty-four CML patients positive for *BCR-ABL* transcripts by RT-PCR were enrolled. Transcript types were established by RT-PCR as proposed by BIOMED program. We divided the patients in three groups: newly diagnosed group (n = 17), imatinib responder group (n=8) and imatinib resistance group (n = 19); the last two groups were identifying according to European LeukemiaNet recommendations, using EAC program methodology to measure *BCR-ABL1* transcripts levels. The presence of mutations was established using a Sanger sequencing in house method. **Results:** The most common transcript variant in the total of patients was b3a2 (45.5%), followed by b2a2 (29.5%), and a group of patients showed co-expression of both variants b2a2/b3a2 (25%). About the patients on treatment, we found a significant correlation between the transcripts variants distribution and imatinib response ($P = 0.039$), highlighting the high proportion of b3a2 variant in imatinib responder group respect to imatinib resistance group (87.5% vs. 31.6%), and the co-expression of both variants only in imatinib resistance group (0% vs. 31.6%). Finally, we didn't found any correlation between *BCR-ABL1* mutations and the type of variants. **Conclusion:** b2a2 and b3a2 are the main variants presents in peruvian CML patients and b3a2 variant may be the most representative. Also, *BCR-ABL1* transcript variants seem to have an impact on imatinib response.

PALABRAS CLAVE (KEYWORDS):

Leukemia, Sanger sequencing, kinase activity, imatinib.