Hubungan mutasi C1236T gen ABCB1 dengan pencapaian major molecular response (MMR) pada pasien leukemia granulositik kronik fase kronik yang mendapat imatinib = Association between C1236T mutation in ABCB1 gene to the achievement of major molecular response (MMR) in patient with chronic phase chronic myeloid leukemia treated with imatinib.

Riki Nova, author

Abstrak

Leukemia granulositik kronik (LGK) merupakan salah satu penyakit keganasan hematologi yang prevalensinya dapatterus meningkat di masa depan. Terapi LGK saat ini adalah imatinib yang merupakan tirosin kinase inhibitor. Meskipun imatinib memiliki kemampuan klinis superior, diperkirakan sekitar 20-30% pasien LGK resisten terhadap terapi imatinib,yang salah satu penyebabnya terkait ekspresi P-gp berlebih, sehingga memompakan imatinib intraseluler ke domain ekstraseluler. P-gp disandi oleh gen ABCB1 yang bersifat sangat polimorfik, tiga single nucleotide polymorphism (SNP) telah diteliti pada pasien LGK, yaitu C1236T, C3435T dan G2677T/A. Mutasi yang paling umum terjadi untuk memprediksi respons klinis terapi imatinib pada pasien LGK Asia adalah mutasi C1236T. Penelitian ini bertujuan untuk mengetahui hubungan mutasi C1236T gen ABCB1 dengan pencapaian MMR pada pasien LGK fase kronik yang mendapat imatinib.
Metode: Penelitian ini merupakan penelitian potong lintang (cross-sectional) menggunakan 120 sampel darah pada pasien LGK fase kronik yang mendapat imatinib mesilat selama 12 bulan yang memenuhi kriteria seleksi. Dilakukan amplifikasi dengan metode PCR dilanjutkan dengan sekuensing metode Sanger untuk penentuan mutasi C1236T gen ABCB1.
Hasil: Dari 120 sampel darah yang memenuhi kriteria seleksi dan dianalisis. Terdapat 28,3% pasien LGK fase kronik yang mencapai MMR. Mutasi C1236T adalah 72 pasien (60%). Tidak terdapat hubungan mutasi dengan pencapaian MMR (risiko prevalensi 0,717 [0,275-1,461], p = 0,282).
Kesimpulan: Tidak terdapat hubungan antara mutasi C1236T gen ABCB1 pada pasien LGK fase kronik yang mendapat imatinib 12 bulan dengan pencapaian MMR.
.....Chronic myeloid leukemia (CML) is one of the hematological malignancy disease which prevalence may continue to increase in the future. The treatment option of CML recently is imatinib, the tyrosine kinase inhibitor. Despite its superior clinical performance, imatinib drug resistance is developed in 20-30% patient, one of the causes is related to over expression of P-gp that transfer intracelluler imatinib to the extracelluler domain. P-gp is encoded by ABCB1 gene which is highly polymorphic. Three ABCB1 gene single nucleotide polymorphism (SNP), has been studied in CML patient; C1236T, C3435T, and G2677T/A. The most common mutation that can predict the clinical respond of imatinib therapy in Asian CML patient is C1236T mutation. This study purpose is to find the association between C1236T mutation in ABCB1 gene to the achievement of MMR in chronic phase.
Methods: This is a cross-sectional study using 120 blood samples of chronic phase CML patient who received imatinib mesylate for up to 12 months and met the selection criteria. The amplification process with PCR methods was performed, followed by Sanger methods of sequencing to determine the C1236T

gene ABCB1 mutation.
Results: A total of 120 blood samples that met the selection criteria was obtained and analyzed. About 28,3% of chronic phase CML patient achieved the MMR. C1236T mutation was found in 72 patients (60%). There was no association between mutation and MMR achievement (prevalence risk 0,717 [0,275-1,461] p = 0,282]).
Conclusion: There was no association between C1236T gene ABCB1 mutation of chronic phase CML patient who received imatinib 12 months with the MMR achievement.