ALLELIC AND GENOTYPIC DISTRIBUTION OF CYP2C9 (rs179985) IN RELATION TO DIFFERENCES IN HEMATOPOIETIC STEM CELL MOBILIZATION EFFICACY

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Background. Multiple myeloma (MM) is a malignant plasma cell disorder for which high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation (HSCT) is an important treatment strategy in eligible patients. A key step in preparation for transplantation is the pharmacological mobilization of hematopoietic stem cells (HSCs) from the bone marrow into the peripheral blood. The efficacy of this process varies considerably between individuals and may be influenced by clinical, biological, and genetic factors. In particular, the CYP2C9 (rs179985) polymorphism may potentially contribute to interindividual variability in drug response. However, its association with HSC mobilization efficacy in patients with MM requires further investigation.

Objective. To investigate the distribution of CYP2C9 (rs179985) alleles and genotypes and assess their association with the efficacy of pharmacological HSC mobilization in patients with MM.

Materials and Methods. The study included 38 patients with MM and 45 controls. Based on the efficacy of pharmacological HSC mobilization, patients were divided into two groups: those with a satisfactory response (n=20) and those with an inadequate response (n=18). Genomic DNA was extracted from whole blood using the DNA-Sorb-B reagent kit (Russia). CYP2C9 (rs179985) genotyping was performed by polymerase chain reaction (PCR) using a universal amplification reagent kit (Litech, Russia) on a Rotor-Gene 6000 instrument (Corbett Research, Australia). Statistical

analyses were conducted using OpenEpi software, version 9.2. The frequencies of the C and T alleles and the CC, CT, and TT genotypes were assessed. Genotype distributions were evaluated for conformity with Hardy–Weinberg equilibrium (HWE). Between-group differences were analyzed using the chi-square (χ^2) test, odds ratios (ORs), and 95% confidence intervals (CIs). Differences were considered statistically significant at $p \leq 0.05$.

Results. In the control group, the CYP2C9 (rs179985) genotype distribution was consistent with Hardy–Weinberg equilibrium ($\chi^2=0.005$; $p=0.896$; $df=1$). The frequencies of the C and T alleles were 85.6% and 14.4%, respectively, while the frequencies of the CC, CT, and TT genotypes were 73.3%, 24.4%, and 2.2%, respectively.

In the overall MM group, the frequencies of the C and T alleles were 85.5% and 14.5%, respectively. The CC, CT, and TT genotypes were observed in 73.7%, 23.7%, and 2.6% of patients, respectively. No statistically significant differences in allele or genotype distributions were found between patients with MM and controls ($p>0.05$).

Among patients with a satisfactory HSC mobilization response (n=20), the frequency of the T allele was 17.5%, compared with 14.4% in controls ($\chi^2=0.2$; $p=0.76$; OR=1.3; 95% CI: 0.46–3.43). The frequency of the C allele was 82.5%, compared with 85.6% in controls ($\chi^2=0.2$; $p=0.76$; OR=0.8; 95% CI: 0.29–2.17). The frequencies of the CC, CT, and TT genotypes were 70.0%, 25.0%, and 5.0%, respectively. Differences in genotype distribution were also not statistically significant ($p>0.05$).

Among patients with an inadequate mobilization response (n=18), the frequencies of the C and T alleles were 88.9% and 11.1%, respectively. Compared with controls, no statistically significant difference was observed for the C allele ($\chi^2=0.2$; $p=0.79$; OR=1.4; 95% CI: 0.41–4.44) or the T allele ($\chi^2=0.2$; $p=0.79$; OR=0.7; 95% CI: 0.23–2.44). The CC and CT genotypes were observed in 77.8% and 22.2% of

patients, respectively, whereas the TT genotype was not detected. Differences in genotype distribution between this group and the control group were also not statistically significant ($p>0.05$).

Thus, despite a trend toward higher frequencies of the T allele and the CT and TT genotypes among patients with a satisfactory mobilization response, no statistically significant association between CYP2C9 (rs179985) polymorphism and HSC mobilization efficacy was established ($p>0.05$). The wide confidence intervals and low frequency of the TT genotype highlight the need for further studies involving larger cohorts.

Conclusion. The C allele and CC genotype of CYP2C9 (rs179985) predominated in both patients with MM and controls. Patients with a satisfactory response to pharmacological HSC mobilization showed a trend toward higher frequencies of the T allele and the CT and TT genotypes than patients with an inadequate response. However, these differences were not statistically significant, and the findings do not establish an independent role for the studied polymorphism in determining HSC mobilization efficacy.