



## Influence of *ABCB1*, *CYP3A4*\*18B and *CYP3A5*\*3 polymorphisms on cyclosporine A pharmacokinetics in bone marrow transplant recipients

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### Abstract:

The aim of this study was to retrospectively evaluate the effect of polymorphisms in the *CYP3A4*, *CYP3A5* and *ABCB1* genes on the dose-adjusted concentration and dose requirement of cyclosporine A (CsA) in Chinese recipients during the early period after bone marrow or hematopoietic stem cell transplantation. Ninety-one bone marrow transplant recipients were genotyped by the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay or by direct sequencing for the C1236T, G2677T/A and C3435T polymorphisms in *CYP3A4*\*18B, *CYP3A5*\*3, and *ABCB1*, respectively. The concentration at zero before administration ( $C_0$ ) and concentration at 2 h after administration ( $C_2$ ) of whole blood CsA were measured by fluorescence polarization immunoassay. Dose-adjusted  $C_0$  and  $C_2$  were determined and compared among groups with different genotypes. Compared with *CYP3A5*\*3/\*3 individuals, *CYP3A5*\*1/\*1 subjects have a significantly lower dose-adjusted  $C_0$  and  $C_2$  at days 1–10 and a higher dose requirement for CsA at days 16–30 ( $p < 0.05$ ). In addition, homozygotes for the *ABCB1* 3435T mutant have a significantly higher dose-adjusted  $C_0$  and  $C_2$  and a lower dose requirement compared with wildtype ( $p < 0.05$ ). Similar results were also derived for carriers of the T-G-C haplotype in *CYP3A5* producers compared with non-carriers ( $p < 0.05$  and  $p < 0.01$ , respectively). In summary, the *ABCB1* 3435T SNP, T-G-C haplotype in *CYP3A5* producers, and *CYP3A5*\*3 SNP are all associated with differences in CsA pharmacokinetics and dose requirements during the first month after bone marrow or hematopoietic stem cell transplantation. Genetic testing can therefore help to determine initial dosage and individualize immunosuppressive therapy.

### Key words:

*ABCB1*, bone marrow transplantation, cyclosporine A, *CYP3A4*\*18B, *CYP3A5*\*3, hematopoietic stem cell transplantation

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