Stereoselective Disposition of Lansoprazole in Extensive and Poor Metabolizers of CYP2C19

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The effect of CYP2C19 genetic polymorphism on the disposition of lansoprazole enantiomers was assessed in order to evaluate the contribution of CYP2C19 in the stereoselective metabolism of lansoprazole.

After single oral dose of 30mg lansoprazole racemate in 6 CYP2C19 PMs and 6 EM, the plasma concentrations of R-enantiomers were consistently higher than those of S-enantiomer, in both EM and PM subjects.

The AUC of R-enantiomer was significantly greater than that of S-enantiomer and AUCs of both enantiomers were significantly greater in PM than EM subjects (11.4±2.7 vs 2.5±0.4 mg/ml/h for R-enantiomer and 2.1±0.5 vs 0.36±0.2 mg/ml/h for S-form in PM and EM subjects, respectively). Both oral clearance (Cl/F) and volume of distribution (Vd/F) of R-enantiomer were significantly lower than those of S-enantiomer in both genotypes. The mean R/S ratios for Cmax, AUC, Cl/F and Vd/F were 12.1, 8.6, 0.15, and 0.10 in EM subjects and were compared to those of PM subjects 2.8, 5.7, 0.19 and 0.29, respectively. From the plasma protein binding studies in vitro, mean unbound fraction of S-enantiomer was over 2-fold greater than that of R-form (5.6±1.1 vs 2.5±0.4, respectively).

These results suggest that CYP2C19 genetic polymorphism influence on the enantioselective disposition of lansoprazole. Both stereoselective metabolism and protein binding of lansoprazole seems to involve in the enantioselective disposition of lansoprazole.