일반연제

# The Effect of BCRP Polymorphisms on the Disposition of Lamivudine

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**Objectives:** The disposition of lamivudine, a substrate of BCRP, was evaluated in relation to three BCRP genetic variations' Gln141Lys, Val12Met and Gln126Stop, that cause the altered transport activity *in vitro*.

**Method:** A single oral dose of 100 mg lamivudine was given to 22 Korean healthy male subjects whose BCRP genotypes were predetermined: 7 subjects with wild-type, 6 with Lys141/Lys141, 4 with Gln126/Stop126 and 5 with Met12/Met12, respectively. The plasma and urine of lamivudine were collected up to 24hours and pharmacokinetic parameters were estimated using WinNonlin®.

**Result:**

| | Wild type (n=7) | Lys141/Lys141 (n=6) | Gln126/Stop126 (n=4) | Met12/Met12 (n=5) |
|---|---|---|---|---|
| $T_{1/2}$ (hr) | 5.5±2.4 | 7.7±4.9 | 5.5±2.1 | 7.1±2.0 |
| $T_{max}$ (hr) | 0.8±0.4 | 0.8±0.4 | 0.7±0.3 | 1.0±0.3 |
| $C_{max}$ (ng/ml) | 742±297 | 655±309 | 840±151 | 808±193 |
| $AUC_{inf}$ (hr*ng/ml) | 2,480±502 | 2,207±1019 | 2,422±239 | 2,552±698 |
| $Cl_{total}$ (L/kg/hr) | 0.60±0.12 | 0.66±0.25 | 0.54±0.07 | 0.59±0.12 |
| $Cl_{renal}$ (L/kg/hr) | 0.29±0.05 | 0.28±0.09 | 0.26±0.05 | 0.26±0.05 |

**Conclusion:** In subjects with BCRP variant of Lys141/Lys141, pharmacokinetic parameter such as AUC and Cl varies up to 4 folds. In the other subjects, the variability was relatively small. There was no significant association between genotype and phenotype of BCRP in the disposition of lamivudine. It would be worth contribution of other several transporters (OCTs, MRP4) for lamivudine. Further studies are remained to evaluate the clinical relevance of these genetic variants of BCRP.