Bioequivalence study of nevirapine 200 mg tablet

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Abstract

The bioequivalence study of two oral formulations of nevirapine were evaluated; Neravir® [(Government Pharmaceutical Organization (GPO), Thailand] as the test formulation and Viramune® (Boehringer Ingelheim LTD), as the reference formulation. The two products were orally administered as a single dose of one 200 mg nevirapine tablet according to a randomized two-way crossover design to 24 healthy fasted Thai male volunteers. The washout period between treatment was 4 week. After drug administration, serial blood samples were drawn at a 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 12, 24, 48, 72, 96, 120, 144 and 168 hours. The plasma nevirapine concentration were determined via HPLC technique. Individual plasma nevirapine concentration-time profile was analyzed for relevant pharmacokinetic parameters; the comparative bioavailability of the two products were determined by the analysis of variance (ANOVA) for two way crossover design, using logarithmic transformed data.

The results found that the mean peak ($X \pm SD$) plasma concentration (C_{max}) of Neravir® and Viramune® were 3.36 ± 0.06 and 3.36 ± 0.06 ng/mL, respectively. The 90% confidence interval for the difference of C_{max} mean was 91.83 - 106.41 %. The time to peak plasma concentration (T_{max}) of Neravir® and Viramune® were 4.4 ± 5.11 and 3.1 ± 1.55 hours, respectively. The difference time of peak plasma nevirapine concentration was 41.94%. The mean area under the curve ($AUC_{0 \to t}$) of Neravir® and Viramune® were 5.17 ± 0.07 and 5.16 ± 0.07 ng.hr/mL, respectively. The 90% confidence interval for the difference of $AUC_{0 \to t}$ mean was 99.31 - 105.44 %. The mean area under the curve ($AUC_{0 \to \infty}$) of Neravir® and Viramune® were 5.21 ± 0.09 and 5.20 ± 0.08 ng.hr/mL, respectively. The 90% confidence interval for the difference of $AUC_{0 \to \infty}$ mean was 93.45 - 107.00 %.

The present study revealed that the 90% confidence interval for the difference of C_{max} (91.83 – 106.41%), $AUC_{0\rightarrow t}$ (99.31 - 105.44 %) and $AUC_{0\rightarrow \infty}$ (93.45-107.00%) means were in the criteria of acceptance, which should be within 80-125%. Thus, this study demonstrated the bioequivalence of the test drug (Neravir®) and the reference drug (Virumune®).

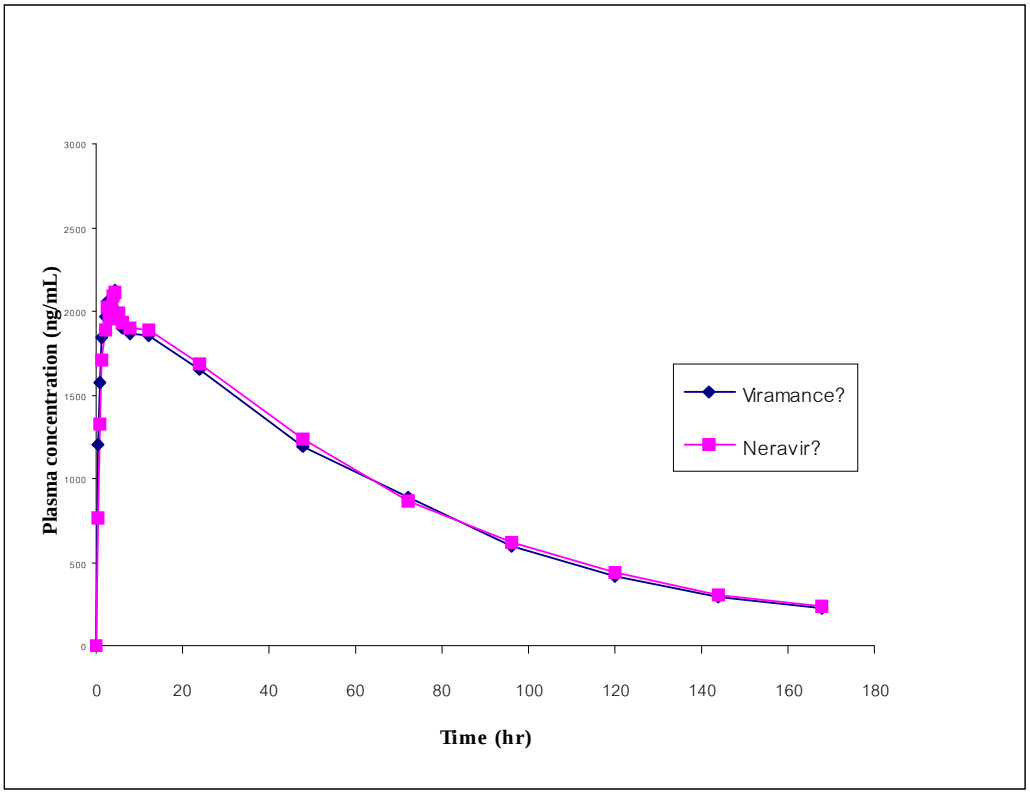

Figure 1 : Mean plasma nevirapine concentration-time profiles from 24 subjects following a single oral dose of one 200 mg tablet of Neravir® and Viramune®.