Ethnic Differences in Pharmacokinetics and Dermatopharmacokinetics

Eunhee Chung¹, Hiroko Kumashiro², Izumi Noritomo², Kaori Inoue², Hinako Uchimaru², Kayo Tahira², Masanari Shiramoto², Shin Irie³

¹SOUSEIKAI Global Clinical Research Center, Japan, ²SOUSEIKAI Hakata Clinic, Japan, ³SOUSEIKAI, Japan

Background

As a large- scale clinical research center where over 4,300 studies have been conducted, we have witnessed ethnicity differences in plasma drug pharmacokinetics between Japanese and Caucasian populations.

In addition to the fact that the influence of ethnic factors on a drug's efficacy and safety are recommended to be evaluated in accordance with International Conference on Harmonization (ICH) guidance, the growing importance of ethnic differences continue to attract attention in global clinical development.

In this study, we have reviewed ethnicity comparison PK studies conducted for Japanese and Caucasians to understand the characteristics of these differences.

Also, to investigate the dermatopharmacokinetic (DPK) differences between Japanese and Caucasian populations, we developed a DPK methodology and conducted DPK clinical research in both ethnicity subject groups.

Methods

To evaluate the PK differences between Japanese and Caucasians, we reviewed the published PK data for these populations and compared with our data.

To establish the methodology to perform DPK studies, we developed clinical research to perform a bioequivalent study using Tacrolimus Ointment 0.1% and Protopic Ointment 0.1% in 8 Japanese subjects and 8 Caucasian subjects. Tape stripping was done at 2, 4, 6 and 12 hours after the application of each ointment, and the drug concentration in Stratum Corneum (SC) were measured. At the 4 and 12 hr before and after the application of the study drugs, trans-epidermal water loss (TEWL) was also measured to assess skin barrier function.

Results

Due to specific genetic differences between Japanese and Caucasian populations for cytochrome p-450 (CYP 450), many drugs demonstrated PK differences in the metabolism of investigational drugs.

In this DPK study, we confirmed that our method passed the Tacrolimus and Protopic bioavailability evaluation criteria. Furthermore, we found that the drug concentration in SC was higher in Japanese subjects when compared with Caucasian subjects at several time points for both ointments, and the TEWL was higher in Japanese 4 and 12 hours after the tape stripping.

Conclusion

In global drug development, safety and efficacy of new drugs can be more accurately ensured by the careful assessment and evaluation of ethnic PK/DPK differences.