Statistical Concepts in Bioequivalence Studies

Sehyun Kim

College of Medicine, Pochon CHA University

In most bioequivalence trials, a test medicinal product is compared with the standard/reference medicinal product in a group of normal healthy subjects. A crossover design with the two phases of treatment separated by a "washout period" is preferred over a parallel-group design. The various pharmacokinetic parameters are subjected to ANOVA in which the variance is partitioned into components due to subjects, periods and treatments. Testing null hypotheses of non-equivalence at a significance level of 0.05, and the importance of estimating a 90% confidence interval of the ratio (test/reference) of mean AUC and C_{max} values, and of the difference between mean T_{max} values, are now form the current standards for testing bioequivalence. The number of subjects required for a bioequivalence trial with the desired power (at least 80%) and significance level (0.05), depends on the expected difference of the test product from the reference product and the error variance associated with the bioavailability parameters (AUC, C_{max}, T_{max}, *etc.*) of the drug substance. Many bioequivalence trials reports, however, were submitted to the Korea Food and Drug Administration (KFDA) without understanding of the statistical concepts used in bioequivalence trials. As a result, some parts of results were presented incorrect manner and their interpretations may somewhat misleading. In this symposium, the statistical basis for the design, analysis and interpretation in studies to test bioequivalence will be discussed.