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Research Paper

Bio-statistical Analysis in Bioequivalence studies

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Abbreviations:

BE	Bioequivalence
BA	Bioavailability
ANOVA	Analysis of Variance
C_{max}	Maximum Plasma Concentration
AUC	Area Under the Curve
AUC_{0-t}	Area Under the Curve from time zero to time of last measurable concentration.
SAS	Statistical Analysis Software
R	R Software
PK	Pharmacokinetic Parameters

I. Introduction:

In order to compare the rate and extent of absorption of two or more formulations, bioequivalence studies are recommended.
The study objective of bioequivalence studies is -
Primary Objective: To assess bioequivalence of the Test product in Comparison with Reference Product.
Secondary Objective: To assess safety and tolerability of the test product in Comparison with the Reference product.
The goal of these studies is to present evidences of similar bioavailability [1].
In many countries, these studies are necessary for the commercialization of generic drugs.
The Pharmacokinetic parameters are calculated using a non -compartmental model using SAS / R / Phoenix Winnonlin / Other Software.
PK parameters are leads to a comparison of relative bioavailability [2].
Generally, the pharmacokinetic parameters considered in a bioequivalence study are the Maximum Concentration (C_{max}) and the Area under the plasma concentration curve (AUC_{0-t}) at a previously defined time. These parameters are obtained directly from the plasma concentration curve of each individual, for each study formulation [3].
Statistical analysis of PK Parameters is performed using SAS / R / Phoenix Winnonlin / Other Software.
The Statistical analysis are including: a) Descriptive Statistics; b) ANOVA; c) Power analysis; d) Ratio analysis e) Acceptance criteria for bioequivalence [4].
a) Descriptive Statistics:
The Calculated PK parameters are tabulated for each subject –product combination wise. Descriptive statistics for untransformed data of all PK Parameters and geometric least square mean and intra CV % for log natural transformed data (primary PK parameters) for test and reference products.
b) ANOVA:
In bioequivalence study used Schuirmann's two one-sided ANOVA tests procedure. ANOVA are performed on natural log transformed for Primary PK parameters.
c) Power analysis:
The power of the test to detect at least a 20% mean difference between test and reference formulations are reported.

d) Ratio analysis:
Ratio calculations using the least squares mean of the Ln-transformed primary PK Parameters are performed for bioequivalence assessment. The comparison of interest is Test product vs Reference product.
e) Acceptance criteria for bioequivalence:
The test product is considered bioequivalent to reference product, if 90% confidence intervals for ratio (test/reference) of geometric least square means based on log transformed primary PK parameters fall within acceptance BE limits of 80.00% to 125.00%.

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