BIOEQUIVALENCE: PREREQUISITE FOR GENERIC DRUGS

Mireia Muriel Masanes[1]

[1]Universitat Autònoma de Barcelona, Bellaterra (Spain)

Introduction

Generic drugs:

- same qualitative and quantitative composition in active substances
- same pharmaceutical form
- bioequivalence → bioavailability studies

Spain:

- First generic drug: Zidovudina (treatment of HIV)
- 5105 approved by Spanish Agency of Medicines and Sanitary Products
- represented of the total pharmaceutical market:
  - 10% in value
  - 23% in volume

OBJECTIVE: Developing stages of a bioequivalence study

Bioequivalence studies

Aim: demonstrate that two formulations of the same active ingredient present similar pharmacokinetic behaviour

Study design

Participants received the two formulations, but in different sequence:

- **1st period:**
  - **50% of volunteers receive reference (R)**
  - **50% of volunteers receive test (T)**
- **2nd period the order is reversed**

Subjects

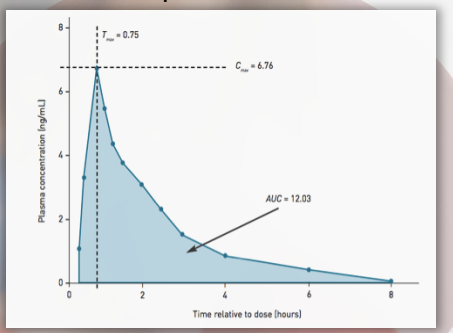
- **Number: never less than 12**
- **Age: between 18-55**
- **Sex: both (risk to pregnant women should be considered)**
- **Non-smokers and without a history of alcohol or drug abuse**
- **Screening: clinical laboratory tests, medical history and physical examination**

**Declaration of Helsinki: all research involving human subjects should be conducted in accordance with the ethical principles*

Drug administration

- **Fluid intake and diet: same every day**
- **Exercise: reduced to the essential minimum**
- **Washout period: between each drug administration (allow all drug and its metabolites be removed from the body)**

Pharmacokinetic profile:



http://www.richmondpharmacology.com/downloads/Publications/Chapter13.pdf

- ***AUC*: area under the 'plasma concentration over time' curve**
- ***Cmax*: peak concentration of the drug in the body**
- ***Tmax*: time, from dosing, to reach *Cmax***

Evaluation parameters

Bioequivalent → no more than a 20% difference between *Cmax* and *AUC*

Ratios of both *Cmax* and *AUC* should be contained within the limits 0.80–1.25

Statistical analysis

CONCLUSIONS

- **Authorization of generic drug is based on the demonstration of bioequivalence.**
- **Generic drugs are easy to identify because the name on the package always includes the initials EFG (Pharmaceutical Generic Equivalent).**
- **Used worldwide in order to optimize spending on medicines (equivalence trial is much less expensive than a clinical trial).**
- **The demonstration of pharmacokinetic bioequivalence is the condition "sine qua non" that confirms:**
  - **two drugs with the same amount of the same active ingredient produce the same therapeutic effect (therapeutic equivalence)**
  - **may be responsible for the occurrence of the same adverse effects (safety)**
  - **can be considered interchangeable in clinical practice**
- **Ratios Test/Reference of *AUC* and *Cmax* meet in the bioequivalence range of 0.8 and 1.25.**

References

1. Di Maio R, Moreale J. Entendiendo los estudios de bioequivalencia. Biomedicina. 2012; 7(2): 6-14.
2. Asociación Española de Medicamentos Genéricos (AESEG) [Internet]. Madrid: Omnimedia. Available at: http://www.aeseg.es/en/generic-medicines-in-the-european-union.
3. Note For Guidance on the Investigation of Bioavailability and Bioequivalence. EMEA, Ref: CPMP/EWP/QWP/1401/98
4. Medsafe. Generic Medicines and Bioequivalence. Media Releases. 2002; 34(1):8-9

[1]**Corresponding Author:** Mireia Muriel Masanes, Autonomous University of Barcelona, Faculty of Biosciencies, Degree in Microbiology. E-mail: mireia.muriel@gmail.com