

Bioequivalence studies of highly variable drugs: Case studies

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Bioequivalence studies are performed to demonstrate *in vivo* that two pharmaceutically products are comparable in their rate and extent of absorption. Concerns have been expressed increasingly regarding the difficulty for highly variable drugs and drug products (%CV greater than 30) to meet the standard bioequivalence (BE) criteria using a reasonable number of study subjects. The most important feature of SABE is that a fixed sample size is adequate to demonstrate bioequivalence regardless of within-subject variability.

One of the approach is scaling an average BE criterion to the within-subject variability of the reference product in a crossover BE study, together with a point-estimate constraint imposed on the geometric mean ratio between the test and reference products. This involves determination of variability of the reference product, which requires replication of the reference treatment in each individual.

Case Study: Atazanavir Sulfate Capsules- The BE recommendation by US FDA for Atazanavir Sulfate Capsules is two way, cross over, *in vivo* study with 300 mg strength in both fasting and fed condition. The dosage and administration states that Reyataz must be taken with food. Further the recommended dosages are 400 mg Atazanavir daily once or 300 mg Atazanavir with 100 mg Ritonavir. So based on the information, the BE study recommendation should be revised as

- Only Fed study with 300 mg Atazanavir
- Bioequivalence study with 400 mg Atazanavir (Two 200 mg capsules) with food
- Bioequivalence study with 300 mg Atazanavir + 100 mg Ritonavir (Norvir)

Biography

Shamkant L Shimpi has completed his Ph.D. from Bharati Vidyapeeth Poona College of Pharmacy in Pharmaceutics. Presently, he is working as Associate Director in Formulation Group- Sai Life Sciences Ltd., Pune, India. He has more than 12 years of experience in formulation. He has published more than 15 papers in reputed journals and serving as reviewer and an editorial board member.

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