An Industry Perspective on Successful Prediction of Food Effect and Fed BE Studies

Amitava Mitra, PhD

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Disclaimer

This presentation and the information herein are the opinions of the presenter, and not of the presenter’s current and past employers.
Effect of Food on Pharmacokinetics

Fleisher et al., Clinical Pharmacokinetics, 36, 233-254 (1999)
Primary Mechanism of Food Effect

Fleisher et al., Clinical Pharmacokinetics, 36, 233-254 (1999)
Where/How Can We Predict Effect of Food Reliably?

- BCS 1 & 2 compounds with known food effect mechanism(s)
  - Impact on gastric emptying
  - Impact of fat & bile salts on solubility and dissolution

- Linear PK or non-linearity due to saturation of absorption because of solubility limitation
  - No known/obvious interaction of food with intestinal enzymes &/or transporters

- Moderate to high bioavailability

- Reliable solubility and/or dissolution data

- Reliable estimates of human PK parameters (either from single dose oral or IV data or pop-PK)

- Clinical data are available in at least 1 prandial state for model verification

- Estimates of intrasubject CVs on PK parameters from prior studies
Typical Workflow for Prediction of Effect of Food

**Single Ascending Dose**

Population simulations by incorporating variability in PK parameters from previous clinical studies.

Crossover Population Simulations show BE

**Fasted**

**Fed**

Sandoz Clinical Development

**Virtual fed BE**

Reference

Test
Cross Industry Case Studies

5 case studies from 4 Pharmaceutical companies demonstrating the successful prediction of food effect, using appropriately established and verified models
Summary

• Advances in PBPK modeling allow for waiver of food effect & fed BE studies, on a case-by-case basis
• Within constraints discussed here, there is good success in prediction of food effect & fed BE studies
• Regulatory research should focus on use of these models in waiver of food effect & fed BE studies
  – Fasted state is the most sensitive to assess formulation differences
  – Ethical considerations
  – Reduction in time & cost of development
• ANDA
  – BCS 1 IR product: if sponsor opts for in-vivo BE then only fasting BE should suffice
  – BCS 2 IR product: fed BE studies could be waived if molecules follow constraints discussed here
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