Symposium 18: Partial Area Under the Curve Analysis in Generic & New Drug Development

ACCP Annual Meeting

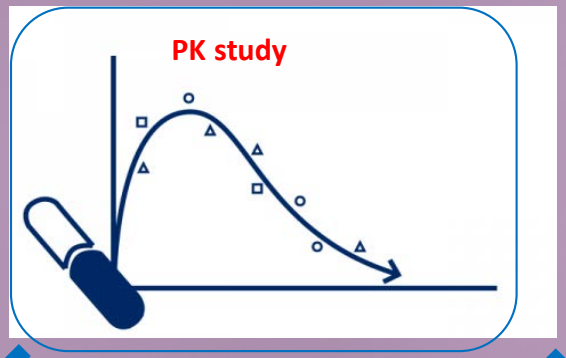
September 21, 2020

Liang Zhao, Ph.D.
Director
Division of Quantitative Methods and Modeling, Office of Research and Standards
Office of Generic Drugs |CDER | U.S. FDA

Keith Gallicano, Ph.D.
Chief Scientific Officer (CSO)
Novum Pharmaceutical Research Service

Application of Pharmacokinetic Studies in NDA and ANDA Drug Development Process

Pharmacokinetic (PK) studies assess bioavailability (BA) and bioequivalence (BE) in New Drug Applications (NDA) and Abbreviated New Drug Applications (ANDA)



NDAs

- *Establish **safety and efficacy** of the investigational new drug by phase-I, phase-II and Phase-III clinical trials.*
  - *Phase-I : Safety, tolerability, PK, biomarkers, proof of principle*
  - *Phase-II: Efficacy, guidance of dose and dosing regimen*
  - *Phase-III : confirmation of efficacious dose, benefit/risk ratio, sub-group selection*

ANDAs

- *Establish **BE** of the generic drug product to that of the reference listed drug (RLD) by pharmacokinetic measure of*
  - *Rate of absorption (peak exposure)*
  - *Extend of absorption (total exposure)*
  - *Partial exposure*

Partial Area Under the Curve (pAUC)

- For two products to be considered bioequivalent, there should be no significant difference in the rate and extent of absorption of the active moiety, which are usually measured by C_{max} (the maximum drug concentration) and AUC (the area under the concentration-time curve), respectively

- For some products with complicated PK profiles, the traditional metrics of AUC and C_{max} may not be sufficient to ensure therapeutic equivalence

- An additional PK metric, such as a pAUC to assess exposure during particular time interval(s), may be necessary to assess differences in BA or BE that may have a clinical impact

Learning Objectives

- Understand the approach in deciding when and how to use an appropriate partial area under the curve (pAUC) metric for the assessment of bioequivalence and comparative bioavailability
- Understand the applicability of pAUC metrics in both generic and new drug development
- Understand the regulatory point of view on pAUC and its impact on different therapeutic areas such as hyperactivity disorder, insomnia and pain
- Understand an industry perspective on the challenges in study design involving pAUC for bioequivalence purposes

Speakers

- **Appropriateness of pAUCs to Evaluate Shape Difference in Pharmacokinetic Profiles** (Keith Gallicano, PhD, CSO, Novum)
- **Partial Area Under the Curve (pAUC): Product-Specific Guidance Development** (Lanyan Lucy Fang, PhD, Associate Director, Division of Quantitative Methods and Modeling, Office of Research and Standards, OGD, CDER, FDA)
- **Partial AUC Improved Metrics for Assessing Bioequivalence: An Industry Perspective** (Charles DiLiberti, MS, Président, Montclair Bioequivalence Service)
- **Usage of pAUC for Evaluation of New Drug Applications for the Treatment of Migraine** (Sabarinath Nair Sreedharan, Ph.D., Team Leader, Division of Neurology Products, Office of Clinical Pharmacology, OTS, CDER, FDA)