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Clinical Pharmacology and Pharmacometrics Online Self-Paced Course

The following lessons provide a structured overview of clinical pharmacology and pharmacometrics, and is part of a set of training activities offered by Pharmacometrics Africa to support the development of pharmacometric competency and expertise in Africa and low and middle income countries.

Pharmacometrics is the science of developing and applying mathematical and statistical models to characterize, understand and predict a drug's pharmacokinetics, pharmacodynamics and biomarker-outcome behavior. By using pharmacometrics, researchers can model the characteristics of new drugs to simulate and predict their behavior when administered, which can then enable more efficient development of new drugs and to improve use of existing drugs.

The Clinical Pharmacology and Pharmacometrics course comprises 12 lessons which cover key aspects of clinical pharmacology and mathematical modelling that underpin the principles of pharmacometrics. This is a companion course to a directed learning program.

Please Note: This course is available free-of-charge. Our only request is that you register before you start so that we can track usage and make improvements.

See something wrong?

Click this button to share your feedback directly with us and improve the course!

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Lesson 12: Model-independent Analysis and Bioequivalence Assessment

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Overview:

- This lesson will address study design, regulatory, statistical and clinical pharmacology principles when analyzing concentration-time data from pharmacokinetic studies e.g. during assessment of alternate drug formulations (bioequivalence or BE), dose linearity or drug interactions. Delegates will work with real clinical trial data to gain insights into how to assess formulations for bioequivalence (BE) so that formulations might be interchanged to achieve the same therapeutic effect.
- The first step of any pharmacokinetic data analysis is to graphically explore the data, in order to understand any inconsistencies. The data analyst will compute Noncompartmental Analysis (NCA) parameters and metrics to generate an initial understanding of the clinical pharmacology properties of the drug.
- The backbone of most regulatory submissions is often clinical pharmacology summaries modules based on NCA results. These are sometimes (and increasingly) supported with model-based analyses. The use of NCA methods are often overlooked as many analysts tend to jump into more complex analysis routines – this lesson will highlight that this is not a good idea.

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Mark as done

Learning objectives:

- Explore selected topics on study design and analysis in clinical pharmacokinetic (PK) studies.
- Graphically display and calculate PK parameters/metrics using non-compartmental (model-independent) analysis methods.
- Compare PK parameters/metrics using appropriate statistical tests.
- Become familiar with relevant regulatory guidance as it relates to bioequivalence assessment.

Mark as done

Objective 1: Evaluate implications of study design for pharmacokinetic (PK) studies:

Presentation

- Lesson 12 - NCA and BE.mp4

The above video will lay the basis for NCA and BE assessment and will provide an overview of the following topics:

- Questions that may be answered with NCA and the stages of drug development where NCA methods are applied
- Importance of Generics in Global Health
- Study Design Considerations for Bioequivalence Assessment
- Review of PK parameters and PK Metrics
- Biowaiver
- Regulatory Guidance Documents

Mark as done

Objective 2: Graphically display and calculate PK parameters/metrics using non-compartmental (model-independent) analysis methods

- **Presentations**

The videos below are in PowerPoint presentation format. You will need to download the presentations and start slide show to play the audio.

Non-compartmental (model-independent) analysis
NCA-hands-on session on PK
Data-PK hands-on. xlsx

Study the above two(2) video presentations that explain how to graphically display and calculate NCA parameters and metrics including

- Maximum concentration (Cmax)
- Time to Cmax (Tmax)
- Area under concentration-time curve (AUC)
- Clearance (CL)
- Elimination rate constant (k)
- Half-life (t1/2)
- Volume of distribution (V)

- **Task**
  - Prepare a plot of concentration vs time for Subject 1 during occasion 1 in dataset "PK Hands-on.xlsx"
  - Obtain the Cmax and Tmax for all individuals in the dataset
  - Compute the elimination half-life, AUC from time 0 to 12, AUC from time 0 to infinity, CL/F, and V/F for Subject 1, during occasion 1

Mark as done

Objective 3: Compare PK parameters/metrics using appropriate statistical

Presentations

Watch the following video presentation that explains how to perform a comparison of pharmacokinetic parameters/metrics using statistical tests

- Statistical Analysis - MP4 File
- Statistical Analysis - Powerpoint presentation

Task

- Using the dataset "NCA_Results", compute the difference in Cmax and AUC with and without Rifampicin
- Graphically explore the PK metrics
- Conduct a statistical comparison of the PK metrics

Mark as done

Objective 4: Become familiar with relevant regulatory guidance as it relates to bioequivalence assessment

Follow the links below and review the following guidance documents

- WHO Technical Report Series, No. 1003, Annex 6, 2017. Guidelines on registration requirements to establish interchangeability (revision) (2017)
- WHO Technical Report Series, No. 1003, Annex 5, 2017. General background notes on the list of international comparator pharmaceutical products (2017)

Week 12 Quiz

Mark as done

Answer the questions by clicking on Week 12 Quiz above. After attempting the quiz, remember to click on "SUBMIT ALL AND FINISH". You will receive feedback immediately.

Mark as done

Tutor-led activity (pre-recorded):

Please find the live tutorial recording here.

Mark as done

OPTIONAL Additional resources and Tasks

This resource is optional and intended for those students who wish to explore this topic further.

- Webinar hosted by Pharmacometrics African entitled Exploratory and Non-Compartmental Analyses of PK PD Data [CP1] and conducted by Dr. Samer Mouksassi, Senior Director, Integrated Drug Development at Certara Strategic Consulting

Exploratory and Non-Compartmental Analyses of PK/PD Data

Thank you for participating in this lesson

Mark as done

We'd welcome any feedback e.g. let us know what worked well, what could be improved, how you used these materials, if there are any other open source resources that might be of value for this lesson. This forum is not actively monitored - we review the posts from time-to-time. We therefore apologize in advance for delays in responding to any questions that you might pose

Feedback on Lesson 12

Mark as done