Universität Ulm | 89069 Ulm | Germany

Medizinische Fakultät
Institut für Epidemiologie und Medizinische Biometrie

Leitung: Prof. Dr. D. Rothenbacher
http://www.uni-ulm.de/med/epidemiologie-biometrie

Gruppe Biometrie
Prof. Dr. R. Muche
Schwabstraße 13
89075 Ulm, Germany

Dr. Arne Ring
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University of Leicester
Clinical Trials Unit

Module: Clinical Trial

01-MAY-2013

Clinical Trials Synopsis

Course schedule (4 blocks) Room: N23/2622

Note: For potential updates on lecture dates, please see the course home page frequently.
http://www.uni-ulm.de/med/epidemiologie-biometrie/med-biometrie/lehre/molekularmedizin.html

25-MAY-2013 Introduction, Course schedule, What is a clinical trial?

09.30 – 11.30 Overview of the lecture
Randomised trials as cornerstone of Evidence based medicine
Phases of clinical trials
Aims, concept, fundamentals, necessity, types of clinical trials

25-MAY-2013 Planning a Study and Recruitment of study participants

12.30 – 14.00 Reporting as basis for planning (ICH E6/E8/E10, CONSORT)
Study protocol, Study documents (Trial Master File)
Recruitment, Informed consent, data protection
Regulatory approval of protocols (AMG)

25-MAY-2013 Randomisation, Statistical Hypotheses and Sample Size

14.30 – 16.00 Randomisation
Superiority vs. Non-Inferiority hypotheses
Sample size estimation and software
Introduction to first student case study

08-JUN-2013 CASE-Study: TGN 1412 and its consequences

09.30 – 11.30 Study performance, Outcomes, Implications for future studies
EMEA Guidelines for first-in-man trials

Discussion as seminar (student presentations)

All presentations need to be uploaded to the course homepage

08-JUN-2013 Data collection and Quality Control

12.30 – 14.00 Types of data and their recording (Case Report Forms)
Data Management, Data Checks and correction (audit trail)
Database: structure and design, database-close and data release
Software for data and project management in clinical trials (e.g. audit trail)
Coding of Adverse events and concomitant medication
Quality assurance: Monitoring, Audits

08-JUN-2013 Regulatory aspects

14.30 – 16.00 Official rules for Clinical Trials (Guidelines):
ICH-GCP, Declaration of Helsinki, AMG
Company policies, guidelines and standard operating procedures (SOPs)
Involved persons and institutions: Principal Investigator, (local) Investigator, Sponsor, Steering Committee, Endpoint Committee, Data Safety Committee

Introduction to second student case study

28-JUN-2013 Analyzing a Study and Issues in Data Analysis

09.30 – 11.30 Statistical considerations (ICH E9)
12.30 – 14.00 Analysis populations (Full Sample Analysis FSA, Per Protocol Analysis PPA),
14.30 – 16.00 Drop-out-definition, Performing of the analysis
Special Issues: - adjustment for confounder
- subgroup analysis
- multiple testing
- graphical presentations

CASE-Studies: Identification of metabolic pathways in Phase IIa

Discussion as seminar (student presentations)

All presentations need to be uploaded to the course homepage

29-JUN-2013 Reporting and Interpreting the Study Results

09.30 – 11.30 ICH-E3: Structure and content of Clinical Study Reports
Description of patients in the study (external validity) and comparability of (treatment) groups (internal validity)
Efficacy, safety (unexpected events, laboratory measures)
Explorative data analysis (EDA), sources of bias
CASE-Studies: Reporting and publication of randomised trials
Discussion as seminar (student presentations)
All presentations need to be uploaded to the course homepage

29-JUN-2013 Scientific appraisal of clinical trial reports

12.30 – 14.00 PICO assessment (Population, Intervention, Control, Outcome)
Clinical trial registries and the ALLTRIALS initiative
Medical science in the public press

29-JUN-2013 Beyond the individual clinical trial

14.30 – 16.00 Planning drug development
Systematic reviews for Evidence Based Medicine
Forest plot and Funnel plot

Examination

The examination of the course is based on the following tests

- The **7 certificates** of the GCP training at the following link https://live.blueskybroadcast.com/bsb/client/CL_DEFAULT.asp?Client=6&title=Home You need to login to the system using your own mail account, and you will receive personalized certificates (select “Quintiles certificate”). The GCP training is divided into 7 modules with 25-50 minutes each. The printed certificates must be provided until the end of the term (19-JUL-2013).
- **Two own presentations** during the course (see next page), and the upload of the group’s presentation

Student presentations

Group	1st round *(all on 08-JUN-2013)*	2nd round *(all on 28/29-JUN-2013)*
1	TGN: Overview on drug & trial • Drug properties and planning of the trial	Background and content of the CONSORT and SPIRIT statement • CONSORT 2010 / SPIRIT 2013 • Improvements of reporting over time?
2	What happened in the FIM trial ? • Interpretations and discussions	Why was the “paper of the year” awarded to the ECASS 3 paper ? • Fulfillment of all CONSORT items ?
3	Regulatory guidance for FIM in 2006 • ICH E6/E8/E10/M3/S6 • Ethical considerations	Linagliptin: Overview on the drug • Drug properties and mechanism of action • Outcome of pre-clinical studies
4	The Duff Report • Evaluation of trial planning and conduct	Linagliptin: Outcome of Phase I – IIb studies • Overview on published studies • Results of patient trials in detail • Role of UKPDS in defining endpoints
5	New regulatory guidance and implications • NOAEL and MABEL • Design considerations for new “high risk trials	Linagliptin: Outcome of Phase III studies • Details of the phase III program • Major clinical claims • Outline of cardiovascular outcome trials
6	How would new studies for “high risk” compounds be planned? • Which steps should be done? • Example for testing a monoclonal antibody (e.g. TAM-163, modelling MABEL)	Background and concepts of clinical trial registries • Examples of issues with unpublished trials – the ALLTRIALS initiative • Examples of Boehringer studies at Clinicaltrials.gov (incl. result reporting) • Comparison with published papers

Each group contains of 5-6 students.
Each student presents 4-5 min on its own as part of the group’s presentation.

All presentations need to be uploaded to the course homepage, the names of all group members shall be given on the title page. For the upload of student presentations, please contact *iris.lichtblau@uni-ulm.de* or *bettina.mack@uni-ulm.de* .

Module: Clinical Trial

Study Programme:	Master Degree in Molecular Medicine
Responsible Lecturer:	Prof. Dr. Rainer Muche
Further Lecturers:	Dr. Arne Ring
Learning Objectives:	Students should - have the ability of summing up the main steps in clinical trials - be able to recapitulate the key steps in planning, conducting, monitoring and reporting a clinical trial - be able to distinguish between different types of studies - be able to get the ideas of planning the sample size - know the important role and problems of randomization - be able to plan a short trial - be able to name the measures for quality assurance - learn the advantages of study software (database, statistics …) - learn how to report a clinical trial - know the most important guidelines
Module Contents:	- Clinical trials as basis for evidence based medicine - Planning a clinical trial - Aspects of performing a clinical trial - Aspects of data management before analyzing a trial - Reporting a trial
Literature:	- Machin D, Campbell MJ. Design of studies for medical research, Wiley, 2005. - Turner JR. New drug development. Design, Methodology, Analysis. Wiley 2007 - Friedman L, Furberg CD, DeMets DL. Fundamentals of Clinical Trials. Springer 3rd ed. 1998. Corr. 3rd printing, 2006, XVIII, 361 p., - Guidelines ICH E3 and E6/GCP from ich.org - Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trial. BMJ 2010; 340: c869. - Goldacre: Bad science. Harper Perennial, 2009.
Classification:	Compulsory Subject
Prerequisites:	Biometrics
Teaching methods:	Lecture (30%), Seminar (20%), Self study (50%)
Examinations:	Presentation of Literature (2 presentations) + online test GCP
ECTS-Points:	5 ECTS
Grade composition:	
Number of Academic Hours:	52 academic hours
Length of the Module:	Full term
Usability:	- Module in BSc Course of studies “Mathematical Biometrics” - Module in MSc Course of studies “Molecular Medicine”
Date and Capacity:	SS, 40 students