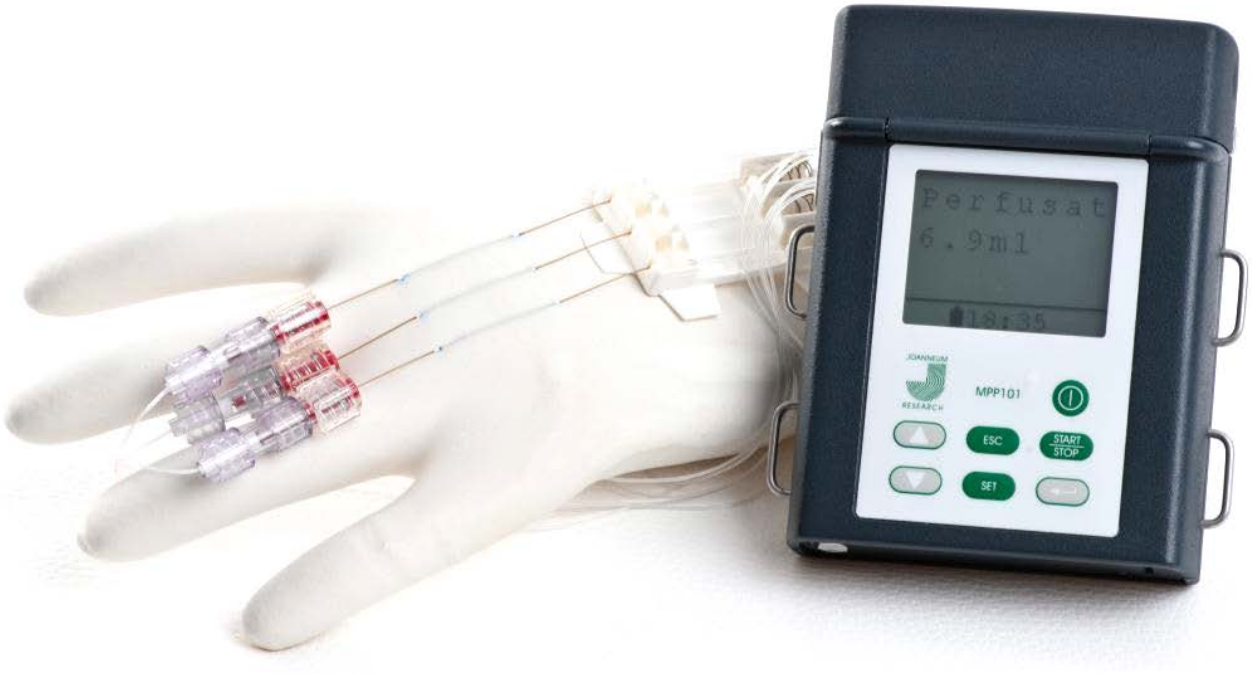
Tissue specific PK and PD enabled by Open Flow Microperfusion:

From bioequivalence to mechanism of drug action PoC studies

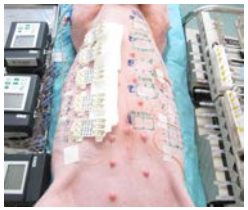


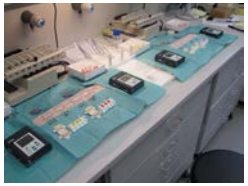
Content

I. Introduction
   a. Why should I bother about dermal compartment
   b. Microdialysis and Open Flow Microperfuion
II. How dOFM may speed up your drug development process
   a. Stability of API
   b. In vivo Proof of Mechanism of API
   c. In vivo dose response of API
   d. PK studies in human skin flaps
   e. In vivo PK and PD ➔ Case Study: Secukinumab©
   f. Bioequivalence ➔ Case Study: FDA Grant
III. Summary

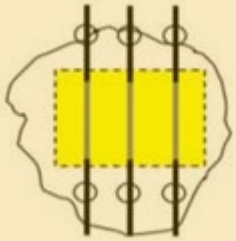
dOFM
Bioequivalence

Apply reference and test product on skin and Analyse for PK of API in dOFM samples

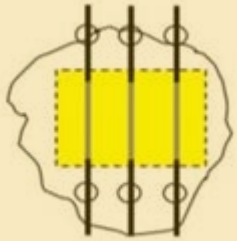




Reference 1



Test 2



One method from ex-vivo to clinical studies

Bioequivalence
Ongoing FDA Project

NOVEL METHODOLOGIES AND IVIVC APPROACHES TO ASSESS BIOEQUIVALENCE OF TOPICAL DRUGS

FDA grant: 1U01 FD004946-01

Institute for Biomedicine and Health Sciences
JOANNEUM RESEARCH

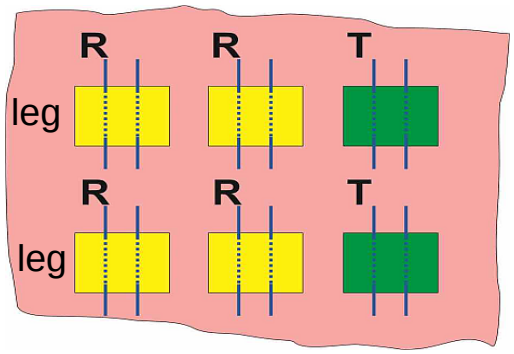
Principal Investigator: **Frank Sinner**
Project leader: **Manfred Bodenlenz** and **Katrin Tiffner**

Bioequivalence
Clinical Study

Overall AIM: Investigate the possibility of dOFM to address BE and non-BE of topical formulations in vivo and ex-vivo

Overview Clinical Studies:

- Optimization Study (6 subjects)
- Formulation Study (6 subjects)
- Pilot BE Study (4 subjects)
- Main BE Study (20 subjects)



Bioequivalence
Clinical Study

- Aims of the Optimization Study
  - **AIM:** Optimization of entire OFM set-up for BE
  - **AIM**: Exclude lateral drug carry-over between adjacent application sites
  - **AIM**: Exclude systemic drug carry-over into application site
- Aims of the Formulation Study:
  - **AIM**: PK evaluation of commercial 5% acyclovir products
  - **AIM**: Choose Reference(R) and Test (T) for subsequent studies

Aims of the Pilot BE Study:

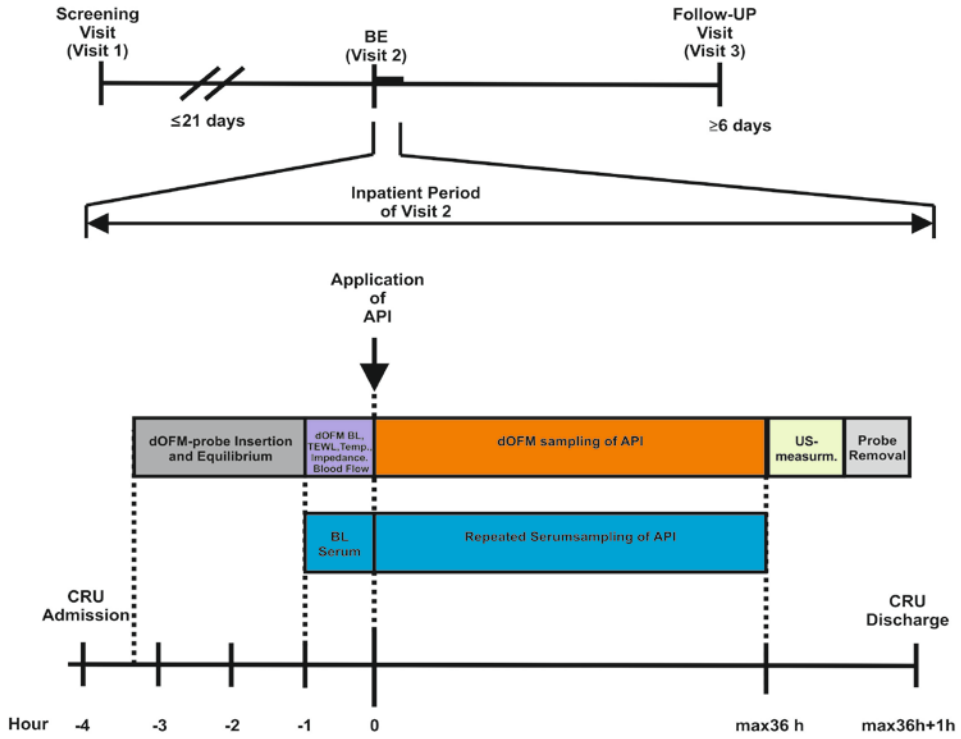
- **AIM**: Study to show non-BE of R and T having strong different PK profiles

Aims of the Main BE Study:

- **AIM**: Study to show BE for R versus R and non-BE for R versus T whereas T having AUC ~ 50% of R

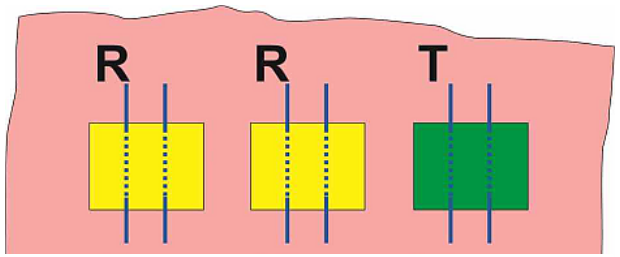
Bioequivalence
Clinical Study

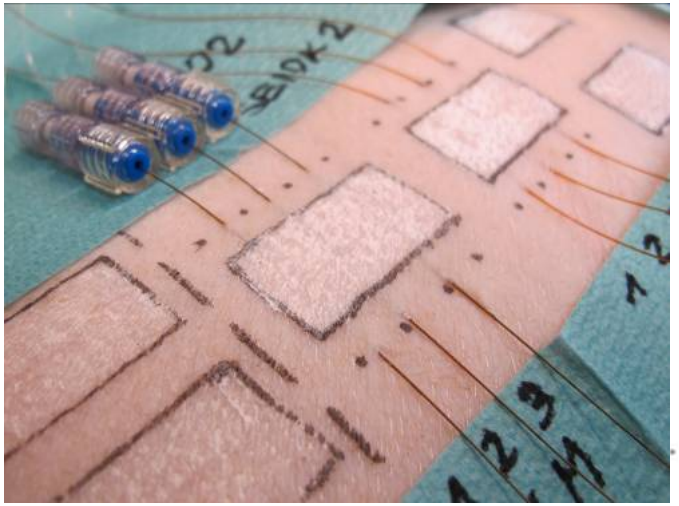
Overall AIM: Investigate the possibility to adress BE and non-BE of topical formulations in vivo



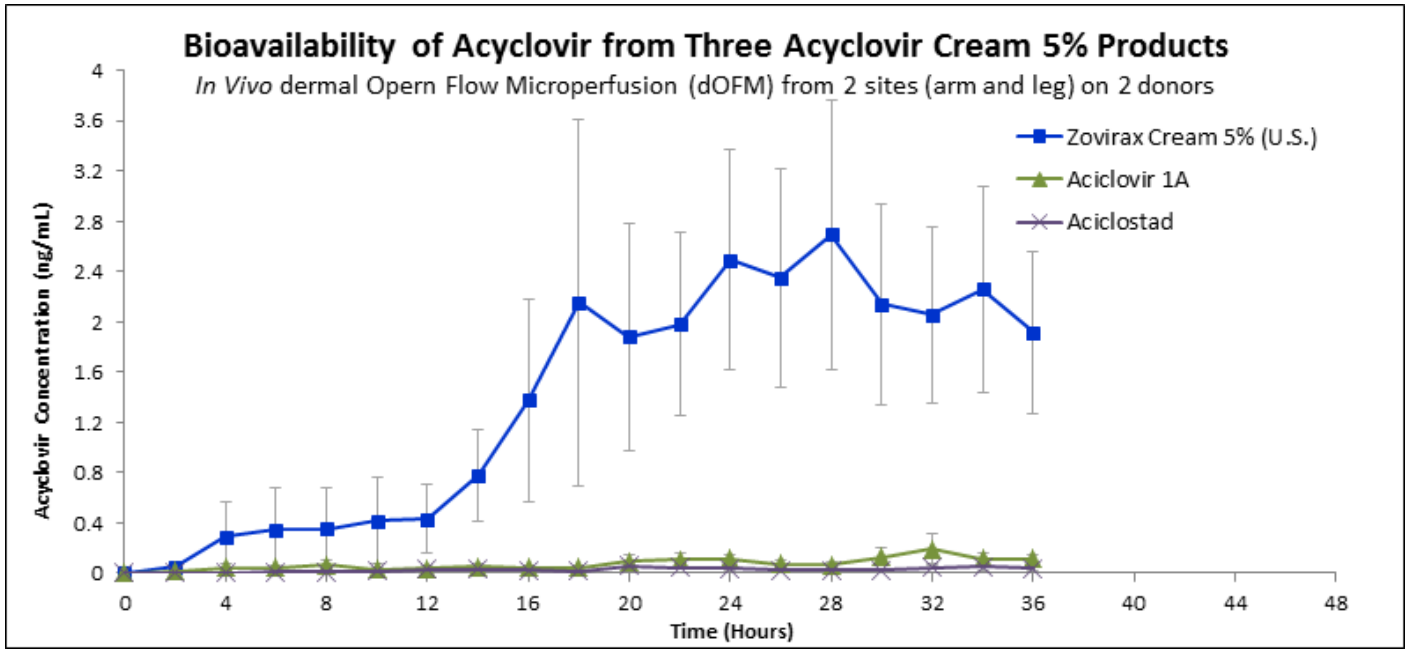
Bioequivalence
Ex-vivo Human Skin Flaps

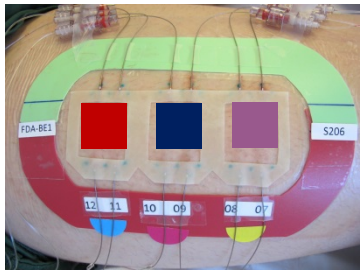
- 40 skin flaps from different donors
- Two application sites for RLD and one for test substance
- 2 OFM probes for each site = 6 OFM probes per skin flap





Bioequivalence
First Results





US Zovirax
Aciclostad cream
Aciclovir cream 1A Pharma

Aciclostad cream and Aciclovir cream 1A Pharma show different PK profile compared to US Zovirax

Thank you for your attention

Dr. Frank Sinner

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