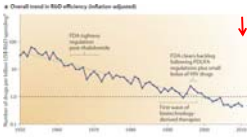
Translation Science – The Impossible Dream?

Katja Remlinger, Statistical Consulting Group, GlaxoSmithKline

Biannual Non Clinical Statistics Conference
September 2012, Potsdam

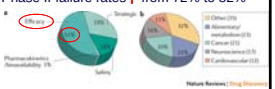
Let's Review….The Pharmaceutical "Ice Age"

- Developing drugs is an ever increasing challenge

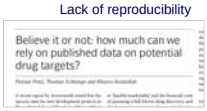


↓ FDA approved drugs/$ billion spent

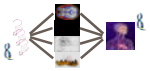
Phase II failure rates ↑ from 72% to 82%



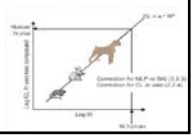
Lack of reproducibility



Lack of translation



Challenges in FTIH dose selection



Causes & Solutions for Drug Discovery Challenges

- Causes
  - Biological limitations of animal models
  - Lack of quality in pre-clinical (e.g. animal) data
  - Drugs don't work for everyone
  - Lack of validated translational biomarkers
  - Lack of reproducibility of literature/academic findings due to insufficient quality of targets, false positive findings, inappropriate statistical design and analysis, ….
  - No "one best method" for translation from animal PK data to FTIH dosing
- Solutions
  - Better animal models and more robust pre-clinical data through more involvement of statisticians
  - Personalized medicine; **BUT:** Need for translational biomarkers
  - Tighter collaborations between academia and industry as well as within industry; change of culture
  - Form partnerships to tackle some of these very challenging questions in collaboration, e.g. IMI, PharmaCog, PhRMA

What Is Our Role As Statisticians?

Specifically as Non-Clinical Statisticians?

- Animal Models
  - Biological validity of animal models is outside our area of expertise
  - **BUT:** Even an excellent biological model will not translate if data quality is insufficient: ***"Garbage in - Garbage out"***
  - Big opportunity for statisticians to improve data quality
    - Use of simple design of experiment principles: randomization, blinding, ….
    - Rigorous review of animal studies, e.g. through mandatory involvement in IACUC/3R protocol review – is this feasible given the size of non-clinical statistics groups?
  - How can we streamline the use of animal PK data for FTIH dose selection? Increase collaborations between non-clinical and clinical statisticians?
- Personalized medicine
  - Biomarker strategy?
  - GSK Example: Dedicated biomarker group for oncology, however no clear strategy for other therapeutic areas.
  - Role of clinical or non-clinical statisticians?

What Is Our Role As Statisticians? (Cont.)

Specifically as Non-Clinical Statisticians?

- Collaborations
  - Be involved in academic collaborations; provide guidance & encourage involvement of statisticians at **early planning stage**
  - Collaborations between statisticians across industry & academia – How can we establish working groups and networks in the current climate of ever shrinking resources?
  - The world is a large, but also a small place, thanks to modern technology. Can/should we bring together non-clinical statisticians around the globe?
- Change of Culture
  - Encourage publication of all findings, not just positive results – how can we leverage our influence?
  - Change of culture also needed within industry
    - At GSK, there is a new generation of biology leaders with very strong academic background.
    - How do we get them on board?

Additional Questions

- Grants4Targets
  - How do you make sure that academic collaborator don't just focus on positive results?
  - Are experiments being run simultaneously in academia and industry?
- IMI
  - Sharing of knowledge across industry – how open can we really be?
  - Next steps for collaboration?
  - Plan to translate findings to other therapeutic areas?
- PK to FTIH
  - How easy will it be to streamline approaches within GSK, across industry?

Questions

- Trends in Translational Science
  - What are factors influencing reproducibility rate?
  - Can it be that we are wrong?
  - What are the reasons for the low reproducibility?
  - What are our conclusions ?
- Difficulties in translation from animal to man
  - Need to standardise and validate protocols.
  - Are the studies sufficiently powered?
  - Can we replicate them between sites?
  - What are the best ways to analyse and compare their results?
- Translation of preclinical PK to FTIH dose selection
  - How much has been adopted in companies and what are the relative implications?