Transparency of Phase 1 Trials

Breakout session
May 16th, 2019

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Outline

• Introduction
  • Inventory of backgrounds and upfront questions of the audience

• How transparent are phase 1 trials?
  • Presentation of recent research

• Perspectives on transparency

• Overview of current and upcoming registration requirements

• Plenary conversation/discussion
How transparent are phase 1 trials?
Medical Research Ethics Committee review registration in the Netherlands

Welcome to ToetsingOnline

ToetsingOnline is an internet portal for the submission, review, registration and publication of medical research involving human subjects.
Cohort study

Nationwide database ToetsingOnline containing ALL clinical drug trials

- 2000 – 2006
- 2007
- 2008 – now

622 clinical drug trials follow-up
Cohort study

• Selection
  • All clinical drug trials in the Netherlands
  • Approved in 2007
  • Started recruitment of participants

• Outcomes
  • Before January 2016:
    • Publication in peer-reviewed journal
    • Upload of summary of results in register
Outcome: publication in peer-reviewed journal

Included: 574 clinical drug trials
Outcome: publication in peer-reviewed journal

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Findings:

- All phases: 58% published
  - Phase 3: 73% published
  - Phase 1: 35% published
Outcome: publication in peer-reviewed journal

Findings:

- Phase 1: 35% published
  - Oncology: 68% published
  - Other: 28% published
Outcome: upload of summary of results in register

Findings:

- Upload in registry, all journal-published trials: 34%
  - Upload in registry, journal-published phase 1 trials: < 1%

- Upload in registry, all unpublished trials: 10%
  - Upload in registry, unpublished phase 1 trials: 0
Conclusions

• Transparency is still not optimal
  • In particular among phase 1 trials;

• No difference in publication rates between academia and industry;

• Good reasons exist for improving transparency

• Better registration policies and practices could fix this

• Peer-reviewed paper of these and more findings are available (open access):
  • C.A. van den Bogert et al., Plos One 2016
  • Thesis also open access available through Utrecht University Repository; ISBN 978-90-393-6844-2
Perspectives on transparency in phase 1 trials

• Shareholders

• Trial Volunteers

• Society

• Pharmaceutical industry / sponsors

• Science
The CRO perspective

• Role of CROs

• Costs
Public registration of phase 1 trials

- Registration of summaries of protocols
- Delayed registration
- Exceptions for registration
Publication

• Registration by CRO

• Pharmaceutical industry

• Universities

• Timelines
Requirements

• By law; regulatory authorities

• Pharmaceutical industry

• Universities, journals, NIH

• WHO

• Society
What can/must be published?

Study specific documents
- Summary of the protocol
- Full protocol
- Summary of results
- Scientific publication
- Subject information sheet

Product specific documents
- IB
- IMPD
  - IMPD S and E
  - IMPD-Q

- Marketing authorisation related documents
  - Clinical study report
  - Assessment reports, lists of questions and responses
Upcoming changes in requirements

• European Clinical Trial Regulation (ECTR) 536/2014
  • Postponed implementation: “during 2020” on EC website
  • Launch of EU-databank
    • Article 81, further explained in appendix EMA/42176/2014
    • Managed by the EMA
    • Applicable to all phase 1 trials
    • Penalties can be given in case of non-compliance (article 94)
Commercially confidential information (CCI)

• Article 80: commercially confidential information should be protected

• Appendix explains:
  
  • CCI can lead to postponement, but after all documents must be made public
    • Exception: IMPD-Q

  • Postponement deadlines vary from 12 months (early terminated trials) – 7 years after the end date of the trial
Phase 1 transparency; perspectives

• Nice to have or necessity?
Arguments pro phase 1 transparency

• Protect safety of participants
• Reduce likelihood that participants undergo harmful/ineffective trials
• Reduce overall costs: minimize number of redundant trials
• Assist participants/patients in informed decision making
• Honour the risks taken by participants
• Learn from failed trials
• Data from phase 1 trials are used to inform clinical practice (drug-drug/-food interactions, dosages, contra-indications)
Arguments contra phase 1 transparency

• Curtail incentives to invest in innovation
• Useless to disclose data on products the public cannot use
• Violation of laws protecting CCI/trade secrets
• Results of early development trials can be more misleading than helpful
• Safety is the only objective of phase 1, hence of little interest
• Submission of phase 1 data could divert attention from phase 3
Learning points / take home messages

• Transparency of phase 1 trials can be improved

• Transparency is a major priority in the new ECTR

• Governments provide the platforms; CROs and industry should take the lead