Transparency of Phase 1 Trials

Breakout session

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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

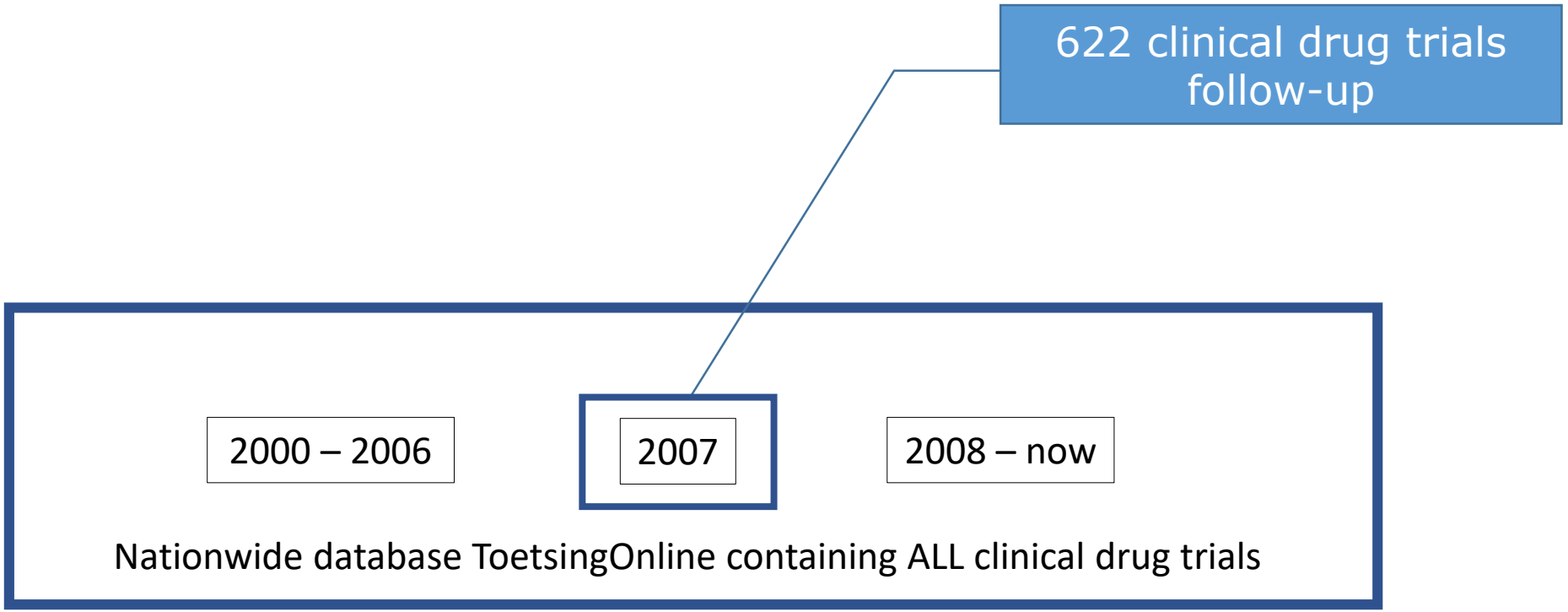
ccmo *Centrale Commissie Mensgebonden Onderzoek*

About CCMO | User manual | FAQ | Nederlands | Login ToetsingOnline

Welcome to ToetsingOnline

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

Cohort study



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

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119 phase 1
130 phase 2
172 phase 3
57 phase 4
96 other than phase 1-4

Outcome: publication in peer-reviewed journal

Included: 574 clinical drug trials	% published
119 phase 1	34.5%
130 phase 2	60.0%
172 phase 3	72.7%
57 phase 4	56.1%
96 other than phase 1-4	60.4%

Outcome: publication in peer-reviewed journal

Included: 574 clinical drug trials	% published
119 phase 1	34.5%
130 phase 2	60.0%
172 phase 3	72.7%
57 phase 4	56.1%
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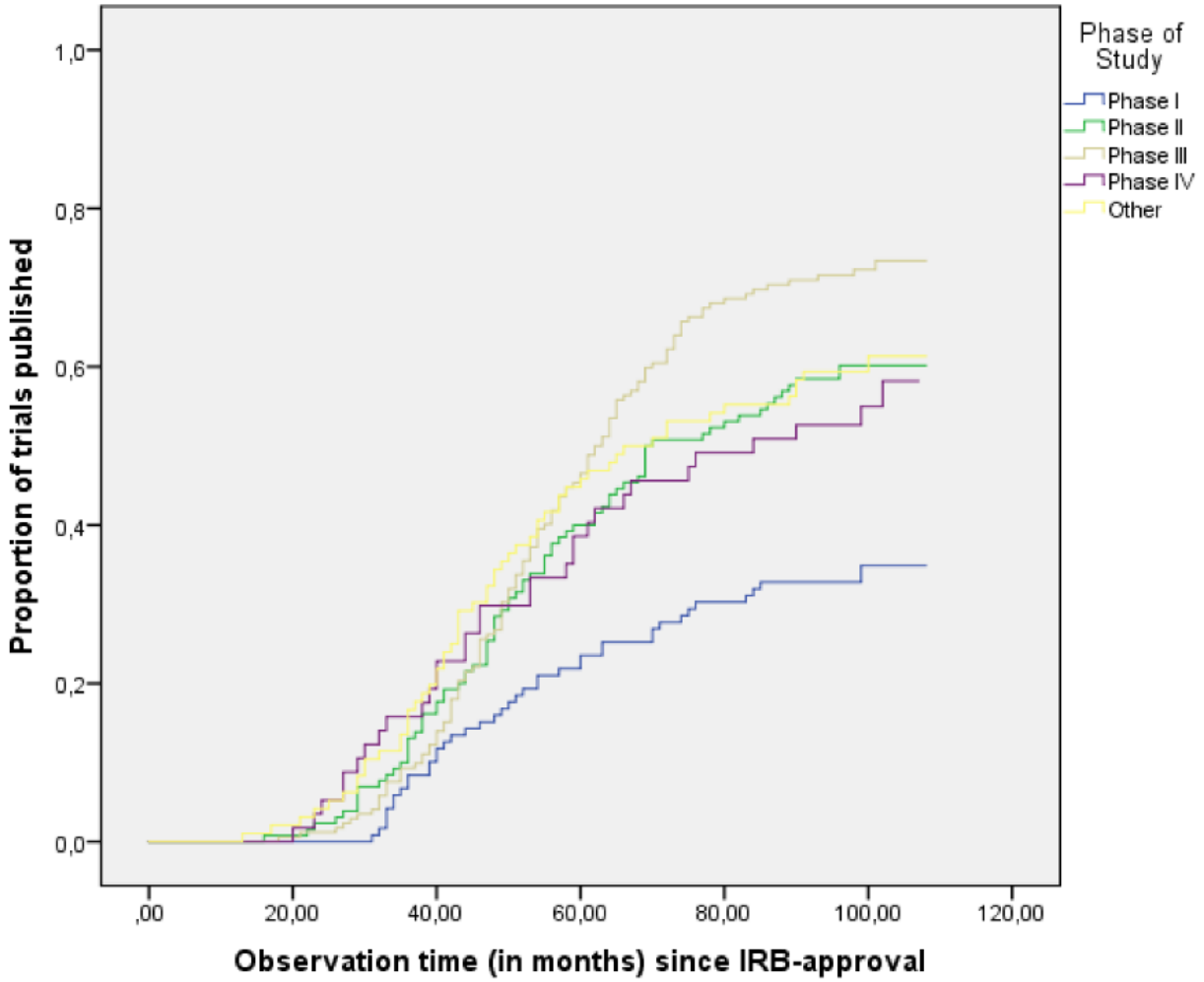
Outcome: publication in peer-reviewed journal

Findings:

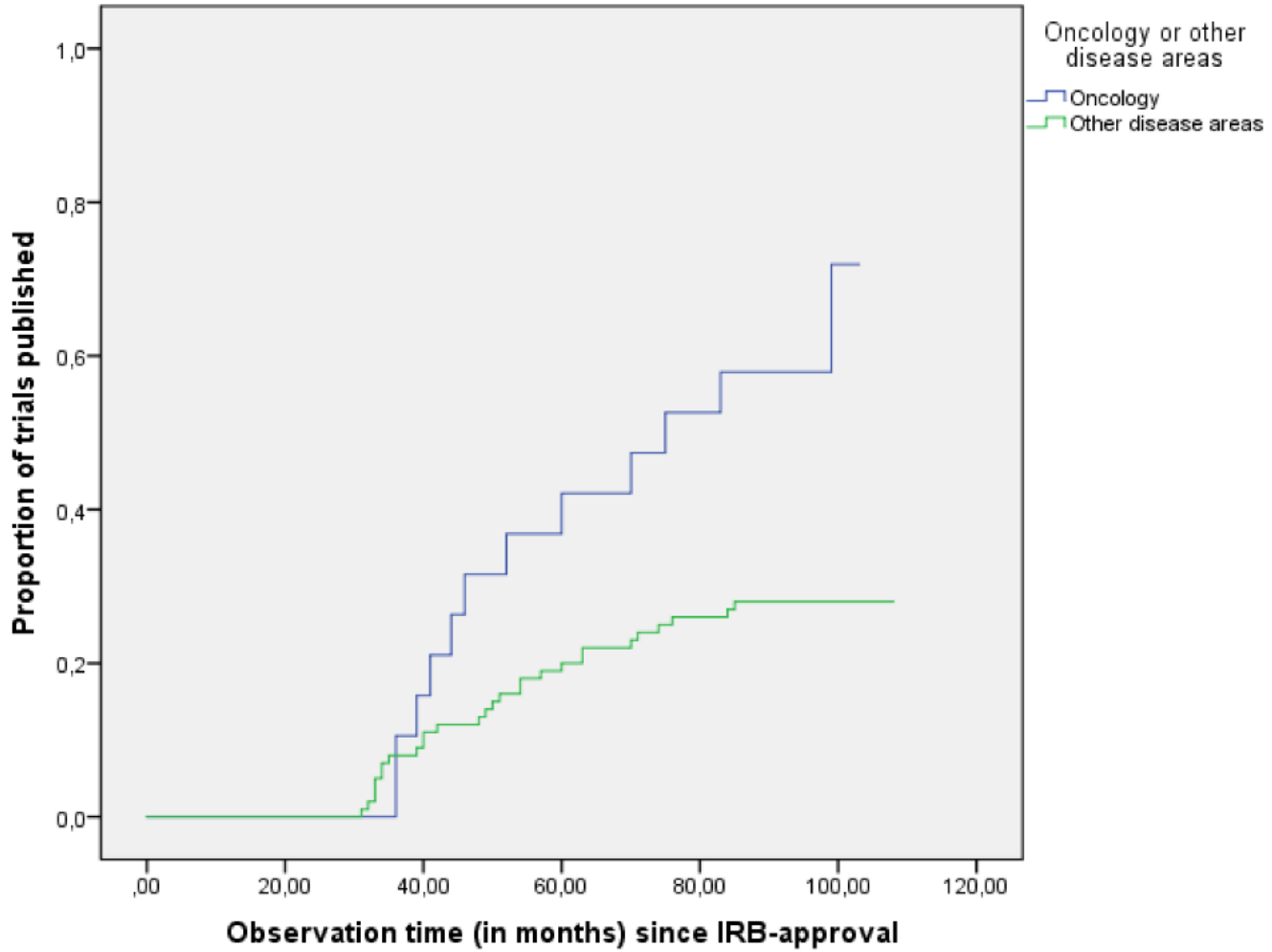
- All phases: 58 % published
  - Phase 3: 73% published
  - Phase 1: 35% published



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