Study registration

Tips and tricks

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Selective reporting

Table 3. Median Proportion of Incompletely Reported Efficacy and Harm Outcomes per Trial, by Study Design

<table>
<thead>
<tr>
<th>Trial Design</th>
<th>No. of Trials</th>
<th>Efficacy Outcomes</th>
<th>No. of Trials</th>
<th>Harm Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>99</td>
<td>50 (4-100)</td>
<td>72</td>
<td>65 (0-100)</td>
</tr>
<tr>
<td>Parallel-group</td>
<td>68</td>
<td>38 (4-78)</td>
<td>57</td>
<td>50 (0-100)</td>
</tr>
<tr>
<td>Crossover</td>
<td>29</td>
<td>98 (0-100)</td>
<td>14</td>
<td>100 (0-100)</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>91 (82-100)</td>
<td>1</td>
<td>71 (NA)</td>
</tr>
</tbody>
</table>
Falsification and intransparent post-hoc changes (CLASS)
Falsification and intransparent post-hoc changes (CLASS)

Annual rates extrapolated from 6 months follow-up

- Ulcer complications
- Ulcer complications plus symptomatic ulcers

Celecoxib vs. NSAIDs

- Celecoxib: P=0.09
- NSAIDs: P=0.02
CLASS: Reality

8059 patients

Celecoxib

1996 Diclofenac

Celecoxib

1985 Ibuprofen

12-16 months duration
CLASS: primary outcome

Cumulative incidence (%) over 0 to 6 months for Celecoxib, Diclofenac, and Ibuprofen.
CLASS: primary outcome

Cumulative incidence (%)

- Celecoxib
- Diclofenac
- Ibuprofen

Months
Art. 56 Registrierung

1 Bewilligte klinische Versuche müssen in einem öffentlichen Register erfasst werden. Der Bundesrat kann Ausnahmen von der Registrierungspflicht bezeichnen; er orientiert sich dabei an den anerkannten internationalen Regelungen.

2 Er bezeichnet das Register, informiert über den Zugang zu diesem und legt dessen Inhalt sowie die Meldepflicht und das Meldeverfahren fest. Erachtet dabei anerkannte internationale Regelungen und berücksichtigt nach Möglichkeit bereits bestehende Register.

3 Er kann:

   a. Organisationen des öffentlichen oder des privaten Rechts mit der Einrichtung und Führung des Registers betrauen;

   b. die Veröffentlichung von Ergebnissen registrierter Forschungsprojekte in solchen Registern vorsehen.
Definition klinischer Versuch

Forschungsprojekt mit Personen, die prospektiv einer gesundheitsbezogenen Intervention zugeordnet werden, um deren Wirkungen auf die Gesundheit oder auf den Aufbau und die Funktion des menschlichen Körpers zu untersuchen.

→ Gesundheitsbezogene Intervention

... präventive, diagnostische, therapeutische, palliative oder rehabilitative Handlung ...
ClinicalTrials.gov

Log-in request
• studyregistration@ctu.unibe.ch

Data entry
• Protocol Registration and Results System at ClinicalTrials.gov
• Complete: e-mail to CTU Bern

Release
• By CTU Bern
• Draft receipt as pdf for final checks

Approve
• E-mail by ClinicalTrials.gov

Publication
Basics

> Sponsor is responsible for registration

> Responsible party registers
  — Select «Sponsor» (you as representative of Inselspital)
  — Do not select «Sponsor-Investigator/PI»

> CTU Bern does not regularly check registrations anymore → send us an e-mail if you want us to check something

> Timeframe
  — Release → Publication: 2-5 working days
  — Changes
Errors

- Restricted character set (special characters often do not work)
- Most entry fields have real-time validations
  - NOTE (blue): can be ignored
  - ERRORS (red): cannot be ignored because it will prevent release
Consistency

> Make sure that all dates and study status are consistent
  — Start date
  — Completion
  — Recruiting/Completed …
> Status == Recruiting $\rightarrow$ at least 1 recruiting site
> «Groups/Arms» == «Interventions»
Completeness (and consistency)

- Responsibility of the Sponsor(-Investigator)
- Be aware that others might check consistency between later publications and register entries (audit trail!)
  — Peer reviewers, readers, ...

<table>
<thead>
<tr>
<th>Table 3 Overall consistency and discrepancy between protocols and corresponding published reports of academic drug trials by protocol-derived type of study, N = 95 protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All trials</strong></td>
</tr>
<tr>
<td><strong>n</strong></td>
</tr>
<tr>
<td>Number of trials</td>
</tr>
<tr>
<td>Overall consistency</td>
</tr>
<tr>
<td>Individual discrepancies</td>
</tr>
<tr>
<td>Type of study</td>
</tr>
<tr>
<td>Primary objective</td>
</tr>
<tr>
<td>Primary endpoint</td>
</tr>
<tr>
<td>Hypothesis</td>
</tr>
<tr>
<td>Sample size calculation</td>
</tr>
</tbody>
</table>

*Prevalence in each subgroup; for example, 21 of 42 exploratory trials (50 %) showed overall consistency
⁹Based on the subgroup of 37 trials with a confirmatory protocol and more than one confirmatory published report

Berendt, Trials 2016
Outcomes (general)

> Usually from a patient perspective
  — Death from any cause
  — NOT: Difference in the proportion of deaths
> Use description (freetext)!
> «Safety Issue» == Safety outcomes
Outcomes: be specific!

- Measurement method, instruments
- Timepoints
  - Fix timepoints (e.g. 3 months) not event-dependent
  - If inevitable, with estimate e.g. «at hospital discharge, expected at 3-7 days»
- Change (repeated measures)

- NOT: Safety; BUT (example): Experiencing at least one serious adverse event

- NOT: Morbidity and mortality; BUT:
  - Either: separate in two outcomes
  - Or: «number of events with events defined as …»
Last but not least

- Acronym
  - No blanks
- Study officials (Chair, …)
  - All three are synonymous
Outlook (general)

> Results reporting

> Sharing trial datasets

Annals of Internal Medicine

Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes that there is an ethical obligation to responsibly share data generated by interventional clinical trials because participants have put themselves at risk. In a growing consensus, many added an element to its registration platform to collect data-sharing plans. We encourage other trial registries to similarly incorporate mechanisms for the registration of data-sharing plans. Trialists who want to publish in ICMJE member journals (or nonmember journals that
Outlook (SNCTP)

- Automatic data transfer from BASEC to kofam.ch
  - Currently, semi-automatic within 30 days
  - Swissethics and FOPH (BAG) are working on an interface
- Timepoint
  - Immediate transfer or
  - Delayed (Phase I trials)
- Conditions for automatic transfer
  1. Name of Primary Registry in BASEC screen #4
  2. External identification number (ID) in BASEC screen #4
  3. Timepoint for transfer specified (see point above)
  4. Ethics committee has (conditional) approval documented in BASEC
     - Automatic reminders will be issued if any of #1-3 is missing
- Transfer will probably require additional authorization
- Final responsibility remains with the Sponsor
BASEC (layout might change)

Primary Registry
Note: At the time of your initial submission you may not yet have the information to fill in the next two fields. You can add the information later, after receiving the approval from the Ethics Committee (see this FAQ-entry on how to submit updates).

Name of Primary Registry
For information about Primary Registries in the WHO Registry Network, please visit http://www.who.int/ictr/network/primary/en/.

External identification number (ID), if available
External identification number (ID) of the trial in the WHO primary registry or clinicaltrials.gov: You received the identification number after registration of your clinical trial in a WHO primary registry or at clinicaltrials.gov.

Registration in SNCTP
Was this project already registered in the SNCTP before the release of this submission portal? *
(Note: for technical reasons you have to fill out the sections above even if you already registered your project through kofam.ch in the past.)
○ yes
○ no

Agreement on automatic data transfer *
Clinical trials must be registered in the Swiss Clinical Trials Portal SNCTP before the trials are conducted. The relevant data will be automatically transferred into SNCTP, once the trial is approved by the Ethics Committee and, if applicable, by Swissmedic and/or the FOPH.

☐ I agree on the automatic transfer of the relevant data into the SNCTP
☐ Please wait with the automatic transfer, I will agree on the transfer later *

* Note: Clinical trials in which the medicinal product under investigation is being administered to adult persons for the first time (Phase I clinical trials) must be registered no later than one year after the completion of the clinical trial.
Questions?

> Lucia Kacina
> studyregistration@ctu.unibe.ch
Next CTU lecture

> 12. April
> Matthias Briel (Basel)
> «Abgebrochene klinische Studien – vermeidbar oder dumm gelaufen?»