Hur du effektivt genomför dina studier med hjälp av elektroniska CRF

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Current problems in clinical trials

Recruitment and performance metrics*
- 70% of clinical trials don’t reach recruitment goal
- Up to 30% of the sites do not recruit any patients
- Up to 95% of all delays are caused by slow recruitment
- Only 8% of all physicians participate in more than one trial
  - 87% of all physicians are not involved in clinical trials
  - 38% of investigators only conduct one trial

More metrics**, between 2005-2010
- Protocol length increased with 18 pages
- Number of eligibility criteria rose 23%
- Number of protocol procedures (lab/heart/imaging/questionnaires/…) rose by 48% (especially in oncology/pain)
- Median enterable fields in the CRFs rose by 103%

*Eglmeir, W, Head Clinical Operations at Grünenthal, presented at DIA Clinical Forum 2010
**Joseph, D, Pfizer US, presented at DIA Clinical Forum 2010
Immediate and clean data

- Data Management
- Drug logistics
- Project Management
- Site Management
- Randomisation
- Metric Analysis

Adaption from Rosenberg, M, President & CEO Health Decisions, presented at DIA Clinical Forum 2010
Hur man effektivt genomför sin studie med hjälp av elektroniska CRF
Seminarium – Lyckad läkemedelsutveckling 9 Juni 2011

Maria Öhlander
Director Clinical Operations
Background information

Phase II study
- Dose-finding study
- Patients:
  - 1000 screened
  - 200 randomized
- 15 clinics in Sweden and Finland
- To be fully outsourced

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Problems!

- No delivery by CRO despite repeatedly discussions

  September…
  - No eCRF available
  - Project team at CRO not communicating

  October…
  - New team in place at CRO
  - Still no eCRF
  - Site complaints – no binders, no information given at Site Initiation Visits

Decision: Change CRO!
Study organisation

- Karo Bio PM
- Viedoc utilized as eCRF
- 2 CROs for monitoring (PCG and Crown)
- I3 safety for pharmacovigilance
- eRT as ECG vendor
- Karolinska as Central lab vendor
- Quintiles as bioanalytical vendor
- NMCT as recruitment agency
- SMF in-house
What to be in control of…

**Start-up**
- Recruitment
- Monitoring
- Site payments
- Safety
- Extra visits
- Data cleaning
- Vendor management

**Study conduct**
- Patient retention
- Reconsiliation
- Database lock

**Reporting**
- Report
What happened?

- eCRF up and running in 2 weeks
  - Training of sites through web and telephone conferences
- Repeat of site initiation visits
- First Patient In according to plan!
- How is this possible?
  - Recruitment agency (NMCT) in charge from beginning of site contracts and recruitment
  - Flexibility and a sense of urgency from all vendors selected
  - Experienced PM at KB
Recruitment and retention

When is information accessible

- eCRF
  - *Site contract – enter in eCRF within 48h of visit*
- NMCT database
- Lab transfers every day

Run report to see…

- Screened
- Enrolled
- Randomized
- Completed
- Early terminations
Site contracting and payments

Managed by NMCT
  • ...and they go bankrupt!

How to handle payments from now on?

KB to manage
  • Payments based on visits entered in Viedoc
  • New contracts by KB with sites
Monitoring

- Very quick recruitment
  - 1000 pts screened in 4 weeks
  - 200 randomized 4 weeks later
  - A couple of very high recruiting sites

- Monitoring reports available in Viedoc
  - Crown
  - PCG

- Challenge
  - Monitoring in time
    - First visit after 2 patients entered at a site
    - Some sites in need of more support
  - Timely entry of reports
    - Completed x days after a visit
    - Management review
    - After that entered in Viedoc
During study conduct

- Swedish hospital strike – includes hospital labs!
  - KS closed during some periods
  - Lab samples analysed at Danderyd

- Any problem?
  - Slightly different LDL cholesterol normal range (x.xx instead of x.x mmol/l)
    - = site problem!
      - *From KS: 3.1 then >3 = inclusion*
      - *From Danderyd: 3.01 then >3 = inclusion*
    - = data problem!
      - 3.01 = 3.0 if one decimal ≠ >3 = not correctly included!
Safety

- Viedoc gave possibility to remote access to individual CRF data by Medical Monitor
  - Vitals
  - AEs
  - Lab
  - ECG
- DSMB same access to individual data
- Reports available to run including
  - Lab listings per patient or per analysis
  - Premature discontinuations
  - AE listings
- ECG data from eRT not daily
  - Only available through eRT web portal
Collaboration partners

- NMCT
  - Screening numbers and dates from NMCT into Viedoc
- KS Lab
  - Daily transfers of lab data
- ECG - eRT
  - Regular transfers to Viedoc
  - Direct access eRT web
- I3 safety
  - Reconsiliation SAE/AE
- Quintiles
  - Bioanalytical data transfer at end of study
- PCG/Crown
  - Monitoring reports
Lessons learnt

🎯 Everything can happen – be prepared 😊

🎯 What to think of:
  ● Be clear on which SOPs which processes to use
  ● Define roles and responsibilities clearly between parties
  ● Fast recruitment requires resources!
  ● Make sure the different systems are compatible and able to "talk"

🎯 Karo Bio learnings:
  ● Keep Project Management in-house
    - Recruit senior personnel to oversee study conduct
  ● Keep study master file in-house
Eprotirome, when added to statin, reduces key markers of CV risk at safe and tolerable doses

Eprotirome could be an attractive add-on to current lipid lowering therapy

*Denotes subjects with pre-treatment levels above treatment goals