Experiences of using routinely collected medical data in a cardiovascular safety trial?

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Issues in clinical trials

- Study feasibility
- Recruitment
- Data capture
- QA/ monitoring
- Pharmacovigilance
- Long-term follow-up within and after trial
- Desire to do large simple trials
  - Comparative safety
  - Comparative efficacy
Data cleaning
This web portal provides an interactive demonstration of some of the e-solutions provided by the Robertson Centre to aid in Clinical Trial data management. Please select an option from the menu on the left to view that application.

**Site 1**
- Western Infirmary
- Total Randomised: 6
- First Subject Randomised: 05/04/2005
- Last Subject Randomised: 14/04/2005

**Site 2**
- Glasgow Royal Infirmary University NHS Trust
- Total Randomised: 0
- First Subject Randomised: N/A
- Last Subject Randomised: N/A

**Site 3**
- The Royal Hospital for Sick Children
- Total Randomised: 1
- First Subject Randomised: 14/04/2005
- Last Subject Randomised: 14/04/2005
From conception to death...

- Mothers ante-natal records
- Maternity
- Neonatal record
- Register birth - NHS number
- Register with GP - CHI
- GP Appointments
- Dental Appointments
- Outpatients
- A&E attendance
- General hospital admission
- Prescribing
- Cancer registration
- Cancer treatment
- Community care
- Death
Inclusion / Exclusion

- **Inclusion**
  - Patients with OA or RA taking NSAIDS (>90 days in previous year)
  - Aged 60 years or over

- **Exclusion**
  - History of vascular disease
Design

Electronic Screen → Eligibility and Consent → Randomised

- Prescribed Celecoxib
- Prescribed Standard NSAID
- Follow-up
Endpoints

- **Primary**
  - CV death, MI, stroke
- **Secondary**
  - GI hospitalisation
Design

• Non-inferiority trial
  – Non-inferiority limit set at HR = 1.3

• Pragmatic trial
  • PROBE design
Design

• Sponsor: University of Dundee
• CI: Prof Tom MacDonald
• Target recruits: 13,682 (611 primary endpoints)
• Recruitment from primary care
• Initial Countries: Scotland, Denmark
Committees

- Executive
- Steering
- IDMC
- CV endpoints
- GI endpoints
Processes (Scotland)

- Pre-screen GP electronic records
- Invite potentially eligible patients for screening
- Consent
- Check inclusion/exclusion
- Record baseline characteristics on eCRF
- Randomise
- Prescribe
- Follow up off-line
Data Collections systems

- Primary Care
  - Electronic search tool
  - Data extract to upload prescription data
- Lab data
- Randomisation
  - IVRS
- E-CRF
  - Screening
- Follow-up data
  - Record linkage (deaths, hospital admissions, cancer registry)
- Pharmacovigilance
Why e-Searching

Pros

• Reduces the amount of manual review
• Tracks each stage in the screening process
• Metrics available earlier in the trial

Cons

• Many varieties of GP system that the software has to work in!
• **Streamlined Trial Adaptable Recruitment Toolset**
  – Identify potential participants
  – Facilitates letter of invitation generation
  – Track screening process
  – Generate files for upload
Lab data in Scotland

- Lab data in Scotland
  - Via hospital labs
  - SCI store(s)

- Issues:
  - Lots of negotiation!
e-CRF – Randomisation

Randomisation

Site: 001   Participant Number: 003
Visit Date: 21 January 2008
Randomisation Visit

1. Is the participant willing to be randomised to celecoxib or their previous NSAID?
   Please contact the study randomisation system on 0800 055 6053 and enter the following details:
   Site 1   Participant ID 3

2. Has randomisation been completed?
   Yes  No

3. Has prescription been written and given to the patient?
   Yes  No

Save
Using SCOT IVRS

- Dial freephone number
- Enter study site and participant ID (screening number)
- Stratification by indication (RA or OA) and screening NSAID
Event follow-up

- Information Services Division

- Electronic linkage to Scottish national linked datasets of hospital admissions, incident cancers and deaths

- Historical approach
  - Link on DOB, name, place of residence
  - Probabilistic matching

- Current/Future
  - Unique identifier matching (CHI)
Follow up datasets

• Datasets transferred routinely to the Data Centre from ISD:

  – SMR 01  General acute inpatient and day case discharges
  – SMR 04  Psychiatric and mental handicap hospitals and units: Admissions, residents and discharges
  – SMR 06  Scottish cancer registrations
  – GRO(S)  death registrations
Dear Sylvia Merino,

This is an automatic email reminder for the Scot Study.

You have patients that are due a follow-up at your site. Please log into the Scot Study web portal https://www.scottrial.com, and complete their follow-up information.

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<th>Follow-up due</th>
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<tr>
<td>56</td>
<td>28 Dec 2008</td>
<td></td>
</tr>
</tbody>
</table>

You will receive another email reminder in 2 weeks time if you have any patients that are due a follow-up.

Kind Regards,
Scot Study Team
Robertson Centre for Biostatistics
University of Glasgow

The University of Glasgow, charity number SC054401
GP: Upload Prescribing Data
GP Follow up- Via web portal

• Every 2 months
  – Adverse Events leading to discontinuation of randomised study treatment
  – Serious Adverse Events
    • Regulatory requirement
Web Portal - GP Follow-up

Current Subject Status

Site: 001  Subject: 001  Subject Initials: TST

Follow-up Visit 18
Follow-up Date: 25/04/2008

A Yes answer to any of the following questions, indicates a change to the subject status

1. Has subject experienced a new treatment related Adverse Event, that has come to your attention?
   - Yes
   - No

2. Has subject experienced a new SAE, that has come to your attention?
   - Yes
   - No

3. Has the subject discontinued the study treatment or permanently discontinued from the trial?
   - Yes
   - No

4. Has there been a change to the subject’s contact details?
   - Yes
   - No
Pharmacovigilance

Investigator records SAE and assesses causality

Linkage data

Further information requested

AE Committee (Pharmacovigilance)

Confirmed SAEs faxed to Pfizer and sponsor notified

Confirmed SUSARs sent in CIOMS or XML format

Funder

SPONSOR

EMEA

MHRA
SAE Reporting

• Report to Sponsor and Pfizer
  – Pfizer insist on communicating by fax!!
• Report to Ethics and Regulatory authorities
WEB portal

- eCRF/ applications/ training
- Views data
- Scan
- Randomisation
- Data transfer

- Monitoring
- Audit

NHS
- Research Nurse
- Study co-ordinator
- Event Supporting Docs
- GP confirms eligibility - prescribes
- Record Linkage

Trial management and regulatory reporting

Sponsor

Committees

SUSARS

Admin

Endpoints Committee

IDMC

Database

Data Management

Statistics
Web portal

- Secure controlled-access
- Demonstration version for training
- Components:
  - Electronic data capture (e-CRF)
  - Source document scan/upload
  - Endpoint Committee Review and Adjudication
  - Reports
  - Documentation library
  - Data upload interface for primary care datasets
  - Automated e-mail reminders to GPs
  - Live study metrics
Challenges...

- Heterogeneity of primary care and lab systems
- Requirements for SAE reporting
  - primary care investigator reporting
  - duplicate reporting resolution
  - reporting of relatedness etc
    >> Do we need this in Phase IV??
- Potential need for adjudication of events
  - non-inferiority studies subject to greater event quality scrutiny
  - uncertainty about quality of event coding in routinely collected health records