From late phase to early phase: experiences of establishing a disease-specific early phase trials unit

Sarah Brown, Louise Flanagan

On behalf of the Myeloma UK Trial Team

Society for Clinical Trials
May 20th-22nd 2013
Leeds Institute of Clinical Trials Research

- A National Cancer Research Institute (NCRI) accredited and UKCRC registered clinical trials unit based at the University of Leeds
- One of 37 fully registered trials units in the UK
- International track record in late phase trials, across many disease areas
- Portfolios:
  - Cancer (incl. myeloma, breast and colorectal)
  - Health Sciences (incl. stroke, obesity and mental health)
  - Comprehensive Health Research (incl. cardiovascular, musculoskeletal and dental)
  - Methodology (incl. survival, phase II trials and adaptive design)
- Over 100 staff (trial and data management, statistics, IT department)
Development of a new portfolio

- Myeloma UK Early Phase Clinical Trial Co-ordinating Office (CTCO)
- Dedicated team of clinicians, trialists and statisticians
- Aiming to develop studies that allow patients faster access to novel therapies and inform UK clinical practice

Ultimately, the CTN is about Delivering Better Treatments for Patients
1. Key areas to develop

Early phase trials are quite different to late phase trials.

- Arranged visits to other early phase (phase I and II) units to learn from experience.
- Everything happens so much faster – you need to be able to respond QUICKLY
- SAFETY, SAFETY, SAFETY – higher-risk studies (phase I) compared to late phase; lots of discussion with Sponsor
- Dealing with attrition – need to be flexible to deal with changing workload

**ACTION:** establish a core team of researchers
Knowledge retention; specialisation
2. Standard operating procedures and guidelines

- Key differences in protocol development between phase I & III
- Recruitment and registration
- Dose escalation – who, what, when?
- Pharmacovigilance – requirements for reporting dose limiting toxicities in phase I
- Data monitoring – more data, more intense
- Network implementation manual – working with a number of collaborators; essential to document differing roles and remit

ACTION: initiate a training program
- All staff on early phase portfolio
3. Standard case report forms (CRFs)

- Disease-specific, same centres, same investigators, same endpoints – *should* be possible
- Differences in detail between phase I and II
- Lots of data to collect – not always clear how best to collect
- Learning curve – still not fully standardised

**Phase I/II vs. III:**
- Wouldn’t ordinarily do this for phase III trials but due to number of small trials it can improve efficiency
- Need faster turn-around of data at sites;
- More data monitoring in house and at site
4. Understand different methodologies

- Methodological experience in phase II
- Challenges to educate clinical collaborators
- Various approaches to phase I
  - Which are most appropriate?
  - What are the risks?
  - Clinical understanding of statistical designs
- Important to understand the true aim of the studies

**IMPACT:** Need to take time to understand and consider alternative approaches, and to explore these with the clinical investigators
5. Build relationships with pharmaceutical companies

- Work with same companies on multiple trials
- Opportunities to access novel therapies early in development – not always possible at phase III
- As the network has developed our relationships with industry have become stronger
- Build reputation
Challenges and Achievements

Challenges

• Investment of time and resources were required initially to set up the CTCO and establish the Clinical Trials Network
• Working practices had to become more flexible and adapt to the requirements of early phase studies
• CTN worked hard to get support from pharmaceutical companies to gain access to new drugs, since at that stage had no performance to demonstrate
• Initial protocols took up to 6 months to develop

Achievements

• Last protocol developed within 2 months
• Consistent workload now for trial management
• Workload is managed closely by a CTN Working Group
• Strategic direction is developed by a CTN Steering Group
Lessons learned

• Developing studies through a network is very different to developing individual studies – need to ensure consistency and focus of network remains
• There are many differences between early and later phase trials, it initially took longer to develop protocols
• Core staff essential for knowledge retention
• Communication is key

NB. Later presentations on collaborative partnerships and document standardisation
Acknowledgements

The Myeloma UK CTCO Trial team:

• Louise Flanagan
• Fiona Collinson
• Sarah Flynn
• Debbie Sherratt
• Avie-Lee Coney
• Sam Hinsley
• Rachel Naylor
• Paul McGarry
• Sarah Brown
• Walter Gregory
• Gill Booth
• Julia Brown
• Lorraine Bate

Myeloma UK