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

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On behalf of the Myeloma UK Trial Team

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MyelomaUK

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)

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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

Leeds Clinical Trials Coordinating Office
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8 Active Trial Centres
NHS
NHS Foundation Trust

Ultimately, the CTN is about Delivering Better Treatments for Patients

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ICR The Institute of Cancer Research

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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

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