International Investigator Initiated Trials in the ELN

Conducting International Investigator Initiated Studies: Challenges and Possible Strategies

Content:

International Investigator-Initiated-Trials, European LeukemiaNet (ELN) (6th symposium)
Mannheim, February 04, 2009

Zoë Doran, CLINT

February 01, 2009

International Investigator Initiated Trials in the ELN

1. Who can I get to Sponsor my study?

- Cooperative Group
- University
- Lead Institution

Note: The main concern is that the study is adequately resourced for all Sponsorship activities; if this can be demonstrated to the potential Sponsor's satisfaction then any of the groups above may agree to function as Study Sponsor

2. How can you maintain Version control of the protocol when it is conducted in multiple countries?

- Ensure person responsible for overall version control is clearly identified.
- Version number and date all protocol pages in the footer e.g. Version 1 date: 6th Jan 2008
- Consider "test" submission to a single or limited number of countries to identify any problems suggest BfArM +/- MHRA to identify any potential issues
- Check (and translate if applicable) all Competent Authority and Ethic Committees to check for requested changes, maintain a list of all necessary changes divided into administrative and scientific
- Avoid making any amendments, unless serious error effecting protocol treatment and/or safety of subjects until all submissions complete, then make amendment accommodating all requirements, version control e.g. Version 2, incorporating Amendment 1 date: 4th April 2008
- Provide *sample* Patient Information Leaflet/Consent Form as an appendix to the protocol, never make locally required changes to this sample.
- Institution specific PIL/IC should be provide and version controlled with reference to the protocol citing the date of the actual protocol for clarity, e.g. Version 1 Date 6th Jan 2008, Heidelberg PIL/IC date 6th Jan 2008
- If a protocol amendment does not require a change to the PIL/IC submit a new version with an updated version and date to ensure correct PIL/IC easily is easily identifiable.
- Keep a protocol distribution and tacking log

3. Submitting the study – what helps?

- Find out per country requirements
    - Use all potential sources of information – do not re-invent the wheel
    - Put submission packs of common documents together
    - Check if additional review required e.g. Federal Government in Germany
- Test submit – chose a demanding country if it passes there then problems inother countries less likely
- Know your ethics committees – chose well, their requirement differ widely
- Establish electronic copies of documents per site e.g. CVs, lab norms
- Find out what additional information each institution requires, e.g. R&D approval, Convention with Directeur Génerale
- Early review of contracts/agreements – use theirs, it's easier to agree changes!
- Completing the paperwork
    - If possible by Clinical Trials Office staff but consider
        - CROs (especially in countries where language and requirements difficult)
        - Junior staff

4. How can I fulfil the monitoring requirements for my study?

- Basic requirements
    - Initiation – consider teleconference supported by slides
    - During the study
    - Close out
- Frequency not specified and can be tailored to resources
- Potential monitoring solutions
    - Inter or Intra institutional i.e. sites monitor each other
    - Small cost effective CROs

- Use resources from a funded study to support an unfunded study in the same institution
- Remote monitoring i.e. provide checklist for “self monitoring” by site
- Statistical analysis for trends and anomalies in submitted data

- Focus on essential data
- Peer review end point data, more valuable than monitoring
- Monitor a sample for an overall quality check, results guide further monitoring requirements

5. Pharmacovigilance

- Provide clear forms using tick boxes where possible
- Ask each institution to provide a regular list of hospitalisations of patients
  - Easily generated by Hospital Admin, then anonymised
  - Majority of SAEs due to hospitalisation/extended hospitalisation
- Get a timely update on patient survival status – as above
- Store reported SAEs in a manner compatible with the annual report for a “one stop shop” approach
- Ensure initiation includes clear guidance on use of Investigator Brochures (IB) and/or Summary of Medicinal Product Characteristics (SMPC) and consideration of the underlying disease
- If using SMPCs make check licensed dosage; if different to protocol ensure staff know to consider clinical experience/literature of protocol dosage e.g. an SMPC on dexamthasone will not consider common side effects of high-dose.
- Consider expected adverse events and expected reasons for admission, specify in protocol and exclude from reporting requirements
- Remember you can upgrade to a SUSAR but cannot downgrade; be sure, ask questions

6. Case Report Forms

- Keep them simple, the KISS principle – if you don’t crunch it, don’t collect it!
  - Demographics

- Relevant epidemiology
- End points
- Safety data

- Keep a paper trial if using single copy paper versions
  - Photocopy original and keep copy at site
  - If corrected/amended do correction of another photocopy and send in keeping a copy of the amended form at site i.e. paper trial at study management office and each institution should be identical