The role of the Clinical Trials Unit

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What is a CTU?

- Specialist academic units – university or hospital based
- Specific remit to design, conduct, analyse & publish clinical trials
- Provide specialist expert statistical, epidemiological and other methodological advice and coordination to undertake successful clinical trials

UK Clinical Research Collaboration Registered CTUs

- Track record of experience in coordinating multi-centre trials, expert staff to develop studies, robust quality assurance systems

http://www.ukcrc-ctu.org.uk/
Cancer / Radiotherapy CTUs

• A number of CTUs are recognised by the NCRI as having a professional specialism in the development and delivery of cancer trials

• CTUs may declare areas of interest – by disease site or mode of intervention

Searching for “Cancer” and “Radiotherapy” identifies 12 CTUs:

Bristol Randomised Trials Collaboration
CACTUS, Glasgow
CR UK CTU Birmingham
CR UK & UCL Cancer Trials Centre, London
ICR-CTSU, London
Leeds CTRU

MAHSC-CTU, Manchester
MRC CTU, London
Northern Ireland CTU, Belfast
OCTRU, Oxford
Tayside CTU, Dundee
WCTU, Cardiff
The trial process

The Clinical Trials Toolkit - Routemap

*Version 1.1 – August 2013. Please visit www.ct-toolkit.ac.uk to ensure you have the latest version of the routemap.
What do CTUs do?

- Trial development
- Trial set-up
- Trial management
- Trial conduct
- Trial oversight
- Statistical analysis
- Reporting
Trial development – “science”

- CTU brings methodological expertise often with some disease site knowledge
- Refine questions & propose appropriate methodology
- Conduct literature reviews
- Liaise with NCRI Clinical Studies Groups / CTRad for peer support & prioritisation/portfolio fit
- Discuss with different disciplines for different trial components/sub-studies e.g. quality of life, health economics, imaging, associated translational research
- Opportunities for trials related methodology research
Trial development – “operations”

- CTU brings regulatory expertise – “Operations lead”
- Consider regulatory, governance & QA issues
- Communicate with Cancer Research Networks regarding feasibility & levels of interest
- Negotiate with international collaborators
- Negotiate with industry
- Cost the trial & plan staffing required to develop & manage the trial
Non-commercial trial costs – NHS AcoRD

**Research costs** – end when research is done (paid by research funder)
- CTU central trial co-ordination (staff, consumables)
- Some costs reimbursed to sites e.g. extra visits, trial specific investigations e.g. scans/biopsies, costs of central review, (Annex A, part A)
- CRF completion, local trial co-ordination (Annex A, Part B
  (Association of Medical Research Charities members exempt)

**NHS Treatment costs** (met through normal commissioning process)
- patient care costs which would continue if the experimental treatment continued to be provided after trial activity had stopped

**NHS support costs** (from NHS R&D budget)
- additional patient care costs associated with the research, which would end once the trial had stopped – incl. consenting patients, RT QA

Trial development – “logistics”

- Consider regulatory, governance & QA issues
- Communicate with Cancer Research Networks regarding feasibility & levels of interest
- Negotiate with international collaborators
- Negotiate with industry
- Cost the trial & plan staffing required to develop & manage the trial
- Coordinate and prepare grant application

Funding application
Trial set-up

- Coordinate **protocol development**
- Liaise with potential centres, to identify & initiate participating centres, and maintain good communication
- Set up trial & obtain relevant permissions (sponsor, ethics approval, MHRA approval, etc.)
- Trial agreements
- Design trial database / (e)CRFs
Who should be involved in developing a protocol?

Key contributors can include:

• Chief Investigator
• Clinical collaborators
• Research Nurse / Clinical Nurse Specialist
• Statistician
• Trial management specialists
• Trials pharmacist or IMP specialist
• Trial physicist and/or radiographer; RTTQA team
• Laboratory/biological collaborators
• Consumers
• Members of any proposed Trial Steering Committee/Data Monitoring Committee
• Pharmaceutical partners
What to include in a protocol?

Many CTUs / Sponsor’s will have a template protocol

Key areas to consider:
• ‘Schedule of assessments’ (should be developed at time of funding application as informs trial costings)
• Radiotherapy Quality Assurance
• Pharmacovigilance (safety) reporting
• Management of toxicities
• Drug handling
• Statistical considerations
• Governance arrangements
• Translational aspects – samples/interventions/logistics

CTRad Radiotherapy protocol checklist
http://ctrad.ncri.org.uk/research-support/trial-development-service-radcas
Trial set-up

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Trial database

• With move to electronic data capture there is need to have the database ready before first patient recruited.

• Build this in to trial set up timelines

• CTUs will have defined SOPS for this which will usually include the following:
  • Draft CRFs
  • Review
  • Final CRFs
  • Annotated CRF
  • Database design & build
  • Database testing
  • Database sign off
Trial management

- Recruit clinical sites in order to identify and recruit eligible trial patients
- Allocate trial entry number & treatment to trial patients
- Centrally coordinate & manage essential trial documents & patient data collected from participating sites
- Liaise with participating sites
Trial conduct

- Data queries – assess completeness & consistency
- Monitor
  - Risk based
  - Central statistical monitoring
  - On site source document verification
- Organise TMG and other meetings
- Prepare progress reports

Data management and data monitoring

Ongoing trial management including reports, to and meetings of, trial oversight committees (TSC, TMG, IDMC); annual reports to trial funders; support to participating sites
Trial oversight

Prepare reports e.g. for:
- Funding bodies
- Main REC
- MHRA
- Independent Data Monitoring Committee
- Trial Steering Committee
- Sponsor
Trial oversight

**Trial Management Group:**
- Chaired by the Chief Investigator
- Multidisciplinary Committee
- Day to day running of the trial
- Represents the investigators

**Independent Data Monitoring Committee:**
- Independent committee
- Clinical and statistical members
- Consider confidential safety and efficacy data
- Recommendations in light of emerging data

**Trial Steering Committee:**
- Independent members
- CI + CTU + 1-2 key TMG members
- “Umbrella” TSC
- Oversight of the trial on behalf of funder and sponsor
Statistical analysis & reporting

- Develop statistical analysis plan
- Conduct interim and final analyses
- Prepare abstracts & posters
- Contribute to manuscript writing
- Co-ordinate journal submissions
- Disseminate results (sites & patients)
What do CTUs do?

**Concept**
- Advise on trial concept and trial design
- Review available literature to inform sample size calculations
- Conduct feasibility assessments
- Manage completion of grant application
- Calculate research costs

**Set-up**
- Develop all trial materials incl. protocol and PIS
- Conduct risk assessment
- Obtain regulatory, ethics and global NHS permissions
- Ensure appropriate sponsorship arrangements
- Oversee contract development
- Ensure appropriate arrangements for treatment allocation, labelling & distribution
- Develop trial materials & guidance notes for investigator & pharmacy files
- Ensure appropriate arrangements for sample collection and tracking
- Develop plans for data management, central and on-site data monitoring and statistical analysis
- Develop CRFs & trial database
- Develop databases to track and monitor data & sample flow

**Conduct**
- Organise launch meetings & conduct initiations of participating sites
- Provide a randomisation service
- Provide on-going oversight & advice to participating sites
- Monitor & administer site payments
- Centrally collate and enter data
- Review data for completeness & accuracy - chasing data & querying where necessary
- Conduct central and on-site monitoring
- Develop newsletters & promotes the trial
- Identify & address barriers to timely recruitment and conduct
- Manage pharmacovigilance activities in accordance with regulations
- Arrange, contribute to and administer TMG and TSC meetings
- Maintain trial approvals
- Prepare reports for funders, regulators, sponsors etc
- Maintain essential documentation
- Facilitate audits & regulatory inspections

**Analysis & Reporting**
- Conduct statistical analyses according to pre-defined analysis plans
- Arrange, contribute to and administer IDMC meetings
- Provide statistical reports for IDMC meetings
- Conduct additional exploratory analyses as agreed by the TMG
- Contribute significantly to drafting of manuscripts, abstracts and presentations
- Administer the submission of manuscripts, abstracts and presentations
- Present at (inter)national symposia as required
Role of the CTU - summary

To collaborate with you as academic investigators in the successful design, development, set-up, conduct, management and analysis of clinical trials.
Any questions?

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