NHS
Greater Glasgow and Clyde

CAVA

CAVA
(Cancer And Venous Access)

A randomised controlled trial with associated qualitative research of venous access devices for the delivery of long-term chemotherapy

(Version 4, 8th April 2016)

CANCER RESEARCH UK

Study Organisation

- Sponsor(Research Governance) - Greater Glasgow and Clyde Health Board (GGCHB)
- Coordinated by CRUK Clinical Trials Unit, Glasgow
- CRUK CTU Glasgow are responsible for setting up, the day-to-day running and statistical analyses of study data
- Chief Investigator is Professor Jon Moss

Study Team

- **CR-UK CTU Team**
  - Chief Investigator: Professor Jon Moss
  - Trial Statisticians: Jim Paul/Elaine McCartney
  - Project Management: Judith Dixon-Hughes
  - Clinical Trial Co-ordinator: Susan Dillon
  - Computer Programmer: Geraldine McBride
  - Clinical Trial Monitor: Calum Innes

Study Summary

- A randomised controlled trial incorporating pre and post trial qualitative research.
- Study recruitment: 1300 patients over 4 years.
- Study population: Patients receiving long term chemotherapy who require a venous access device
- Timelines:
  - Start date for randomised study - November 2013
  - Planned accrual completion - November 2017

Study Objective

- To determine which venous access device – subcutaneously tunnelled central catheters (Hickman type device), peripherally inserted central catheters (PICC) or implantable chest wall ports (Port), offers the best outcome from safety, clinical effectiveness and cost effectiveness perspectives.

Study Endpoints

Primary endpoint

- The primary outcome for the randomised trial is complication rate, a composite of infection (suspected or confirmed) and/or mechanical failure.

Secondary endpoints

- complication event rate. This analysis will estimate the effect of the access devices on the individual component complications (infections and mechanical failure) and will allow an assessment of the similarity of these effects via a likelihood ratio test. The incidence of venous thrombosis will be compared using logistic regression and also as an event rate. The frequency of the various complications will be assessed. The total duration of treatment interruptions will be summarised and compared using a Mann Whitney U-test.

- Scores for the five dimensions of the EQ-5D and the visual analogue score for health will be summarised and the EQ-5D curves will be compared between treatment groups using an area under curve (AUC) approach standardised for the period on study and using the baseline value as a covariate.

- Scores for the 5 functional scales and 9 symptom scales of the EORTC QLQ-C30 will be calculated according to standard EORTC conventions, as will global health status score. These scores will be summarised and analysed as EQ-5D.

- The results from the device-specific questionnaire will be summarised only.

Inclusion Criteria

- Aged ≥ 18 years
- Receiving or to receive chemotherapy
- Duration of chemotherapy ≥ 12 weeks
- Clinical team uncertain as to which device is optimal for this indication
- Solid or haematological malignancy
- Suitable upper extremity vein for all the access devices to which the patient may be randomised
- Able to provide written informed consent

Exclusion Criteria

- Life or treatment expectancy <3 months
- Previous venous access device removed due to complication within last two weeks
- Evidence of active infection
- Requirement for high volume (apheresis) line
- Need for catheter to be placed in a non upper extremity vein
- Patient previously randomised into the CAVA trial

Randomisation Options

- Randomisation Option 1- Hickman v PICC v Port
- Randomisation Option 2 – PICC v Port
- Randomisation Option 3 – PICC v Hickman
- Randomisation Option 4 – Port v Hickman (This option closed 30/11/2015)

We encourage investigators to enter all patients who are eligible for all three devices into the three way randomisation (Option 1)

Informed Consent Process-1

- One or two original Consent Forms to be completed by a clinician (or deputy listed on Staff Contacts & Responsibilities Sheet)
- One or two originals signed and completed by the patient
- Date must be on or prior to registration
- Make one or two photocopy

  - Original to be filed in Investigator File
  - Original or copy to be given to patient
  - Photocopy to be filed in hospital notes

- Consent Form must not be sent to the CRUK Trials Unit, Glasgow

Informed Consent Process-2

- Errors noticed after consent
  - Add explanatory note/file note

- New version of Patient Information Sheet must be provided to patients consented with previous version
  - Give to all patients regardless of trial stage either by post or during clinic visit

- Patients who are still on study may be required to repeat the consent process using the updated form

- If not appropriate to re-consent patient (i.e. patient terminally ill) make a note on the re-consenting log

Patient Registration

Procedure for <u>all</u> sites

- Check that patient has given written informed consent
- Check that patient fulfils eligibility criteria
- Complete Registration Form
- PHONE or FAX registration details to the CRUK CTU Registration Service
- Each patient registered will be allocated a unique trial number

Registration Service

CR-UK CTU Glasgow registration service:

Tel: 0141 301 7952
Fax: 0141 301 7228*
08:30 –17:00 Mon–Thurs,
08.30-16.30 Friday (except public holidays)

***Faxes received outside of office hours will be processed the next working day**

Site Set-up

CR-UK CTU Glasgow is responsible for:

- REC Approval
- Overall Sponsor Approval
- Site initiation calls
- Transfer of SSI to site
- Providing all essential documentation to site for local submission
- Investigator Site File

Site Responsibilities (a *pre-activation checklist* is provided to sites):

- Staff Contacts & Responsibilities Sheets
- SSI submission/R&D Approval
- Investigator/site staff CVs and GCP certificates
- Participating Site Agreement
- PIS/Consent/GP letter on local headed paper
- Qualitative research PIS/Consents on local headed paper

Role of CAVA Champion

Recruitment and randomisation

- Point of contact for referrals to study

Coordination

- Device insertion appointments within treatment schedules/clinic dates

Liaison

- Clinical staff - referrals
- Vascular Access services
- Nursing staff
- Booking clerks
- Primary care staff

Education and dissemination of information

- Raise profile of study/update staff as required
- Advice to ward staff on care and maintenance of Port
- Advise DN of Port insertion/Access to training for DN if required

Presenting equipoise and randomisation*

Recruiters can confirm to potential participants;

- **Patients are eligible for each of the chosen treatment arms**
- **The most effective device is unknown**
- **A trial of the three devices is urgently needed**
- **Randomisation is a plausible way of allocating devices**

*** Donovan 2002**

Case Report Forms (CRFs)

- Consent Notification Form
- Randomisation Form
- Quality of Life Forms – EQ-5D, EORTC- CQ30 and venous access specific questionnaire
- Insertion Form
- Pre-Treatment Form
- Complications Form
- Consent Withdrawal Form

CRF Completion guidelines will be available and will be the first port of call if there are questions regarding CRF completion. Please contact Anna if you have any specific questions.

CRF Completion

- Black ball-point pen
- Correction fluid etc. must not be used
- Errors crossed out with a single stroke, correction inserted and change initialled and dated
- An explanation can be written next to amendment if necessary
- Date format: DD / MON / YYYY
- Information on CRFs must be verifiable in source documents
- Take photocopy of all completed CRFs
- Original to CRUK CTU Glasgow
- CRF completion guidelines will be supplied – please refer to these

Consent Withdrawal

- This is when the patient specifically asks to withdraw their consent at any point in the study

- Ensure that the level of consent withdrawal is clearly documented in the source data

- If this occurs:
  - Document clearly in the patient notes that the patient has withdrawn consent, the level of consent withdrawal and the reason (if the patient has given any)
  - Complete the consent withdrawal notification form
  - Send the consent withdrawal notification form to the CR-UK CTU
  - No further follow-up should be collected on the patient from that point onwards

MONITORING

Central Monitoring

Study sites will be monitored centrally by checking incoming forms for compliance with the protocol, data consistency, missing data and timing. Study staff will be in regular contact with site personnel (by phone/fax/email/letter) to check on progress and deal with any queries that they may have.

Remote Telephone Monitoring

Monitoring for this study will take the form of a remote telephone monitoring visit. Each site will be monitored annually by telephone during the course of the study

- The time & date will be agreed with a member of the Site Study Team
- A pro forma covering the questions which will be covered during the telephone monitoring visit will be sent with confirmation of the confirmation of the agreed date
- Please set aside 50 to 70 minutes for this call.

Quality Assurance

- Trial Investigators and Site Staff must ensure that the trial is conducted in compliance with the protocol, Research Governance Framework 2006 (as amended) and the principles of Good Clinical Practice (GCP) and the applicable regulatory requirements.

- Telephone monitoring will be performed by the Sponsor. Central monitoring of trial data will also be performed by the Study Statistician and the Clinical Trial Co-ordinator. The Sponsor reserves the right to conduct for-cause monitoring visits or audits in the event of non-compliance with the trial protocol.

- The CTU will control data consistency and data quality by entering trial data onto the CTU trial database. Computerised and manual consistency checks will be performed and queries issued in cases of inconsistency or missing information. A full audit trail of any changes to the database will be maintained.

- The Trial Management Group will ensure the study is being managed according to protocol, Research Governance Framework 2006 (as amended) and the principles of Good Clinical Practice (GCP) and the applicable regulatory requirements.

Ethical and Regulatory Standards

- This study conducted in adherence to Research Governance Framework 2006 (as amended) and the principles of GCP
- This study is carried out in accordance with the World Medical Association Declaration of Helsinki 2008

Contact Details

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