STANDARD OPERATION PROCEDURE OF STUDY NURSE
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Study nurse

Study nurse works as a trial coordinator to support and implement a fully developed protocol in CCTU. Tasks involve protocol review, CRF design, Study implementation, and data management.

Protocol Review

- Designated study nurse to obtain the CCTU approved protocol from Head Nurse
- Review logistics of medication supply, patient recruitment, treatment administration, clinic visits, patient follow-up visit.
- Discuss issues that may affect clinics routine with Head Nurse
- Unresolved issues will be discussed with Principal investigator, which is to be brought to Monday Business Meeting afterward.
- Designated study nurse to remind Principal investigator to call for a meeting with the site-specific investigators
- Notes will be taken for the preparation of both industrial initiation meeting and departmental initiation meeting.

CRF design

Case Report Forms (For in-house study)

- A generic Case Report Forms are available in CCTU.
- Designated study nurse to develop a set of Case Report Form with the generic CRF format for individual study variables.
- A study nurse together with the senior nurse will review the developed Case Report Forms.
- The developed Case Report Form will be discussed with the programmer and statistician.
- The Senior Statistician and Principal Investigator will finalize the reviewed Case Report Forms.
Study implementation

Color Sticker

- Designated study nurse to choose a color sticker for each study for identification of CCTU study patient.

- This sticker is to be put on the front cover of the Source Document (RT folder).

- Study name/number, patient number and enrolled date and off treatment date are written on the Sticker to indicate which study patient is participated in.

- With the identification, RT folders are returned to designated study nurse after used.

Chart and Forms

- Designated study nurse to develop charts and forms to ensure all the procedures and data are well documented.

1. Study flow chart

   - This chart indicates the scheduled procedures that are required during the study period. It includes schedules for physical exams, the required lab. Tests and the radiological tests of the study. This chart will be put in the front page of RT folder to remind other medical officer of the study schedule.

2. Study Tracking chart

   - This chart indicates the date and the radiological tests, which serves as a reminder of assessment tests done for investigators and research nurses during study period.

3. Data collection forms (RT folders)

   - These forms serve as part of source documents that are to be completed, signed and dated by Principal investigators and co-investigators.

   1. Inclusion and exclusion criteria checklists
   2. Physical examination form
   3. Medical History form
   4. Adverse Event form (can be completed by study nurse)
   5. Tumor evaluation form
*Generic data collection forms are available in CCTU, which can be modified according to individual protocol.

- Chemotherapy infusion forms (outpatient clinic)

  - This form is equivalent chemotherapy prescription, which states the instruction of the chemotherapy infusion. It includes pre-medication drugs’ name, infusion time length, and vital signs monitoring.

*Generic Chemotherapy infusion forms are available in Clinic/CCTU, which can be modified according to individual protocol

**Trial Medication Supply/Delivery**

- Designated study nurse to follow CCTU standard operation procedure of medication supply, which is available in CCTU.

**Trial Medication Storage**

- Designated study nurse to ensure a secured place for drug storage according to individual protocol requirement.

- Trial Medication Storage spaces can be discussed with Head Nurse

- Temperature for drug storage is to confirm with sponsors.

- For room temperature storage, individual medication cabinets are located on 1/F and 4/F of Cancer Center

- For 4 to 8 °C storage, a trial medication refrigerator is available with alarm system and electronic temperature recorder, which is located on 3/F of Cancer Center.

  - Refrigerator alert system is activated by temperature discrepancy and electricity problem.

  - Activated alert system is to contact the HA management office.

  - HA management office is to contact the designated research nurses for further action.

  - Designated research nurses go back to hospital to remove all the study medication to the back-up refrigerator, which is located on 1/F of Cancer Center.

  - Documentation of incident is to make on the incident file.
Temperature record sheet is to be changed and checked by CCTU clerk.

For –20 °C storage, a trial medication refrigerator is available which is located on 1/F of Cancer Center

- CCTU clerk to check the temperature daily and document the max. and min. temperature.
- If temperature is deviated from protocol requirement, CCTU clerk to inform the designated nurse for double-checking.
- If double-checked temperature is deviated >0.5°C of upper or lower limit, the designated nurse informs Head Nurse.
- Documentation of incident is to make on the page of Temperature Log.
- Head Nurse is to inform Principal Investigator for further actions.

Medication other than trial drugs would not be allowed to store in CCTU trial medication storage spaces.

**Special Blood Processing Arrangement**

- Special Blood Process is a protocol-specific laboratory storage procedure for further study specific lab. tests.
- Designated study nurse to discuss the responsible personnel for blood processing with Individual Study Principal Investigator
- After special arrangement with laboratory in-charge, designated study nurse to contact the laboratory staff to collect blood sample in the clinic.
- Laboratory staff to sign a sample collection book in the clinic.
- If shipment is required, designated study nurse to contact the courier to pick up the processed blood sample from the designated laboratory.
- Two laboratories are currently processing blood samples for CCTU clinical trials. which are located on the 3/F and 4/F of Cancer Center.

**Special Blood Tests Requested Arrangement**

- Special Blood Test is any test which is other than routine tests and need special arrangement with Hospital Authority laboratories (Biochemistry, Hematology or Virology Department)
Study nurse is to provide a list of special blood tests of the study to Principal investigator for special arrangement with individual labs.

Study Principal Investigator, Director of CCTU and the project co-ordinator are to discuss payment of special tests according to the individual study financial support.

The project co-ordinator is to contact the lab in-charge for the special test request and payment issues.

Initiation Meeting Preparation/Organization

Study initiation meeting is a meeting with all investigators (Departments i.e. Surgical, Medical, Anatomy and Chemical Pathology, Biochemistry, Hematology etc.) medical oncologists and RT medical officers, HA nursing staff and CU nursing staff. All studies would not be implemented prior to the meeting.

For pharmaceutical company studies, designated study nurse to collect all the essential documents and put them in the investigator file prior to initiation meeting. The essential documents are listed in the Appendix A.

For in-house studies, basic essential documents and study-related materials are required which are included:

- Fully developed protocol
- Consent forms in both English and Chinese version
- Case Report Forms
- Ethic Approval from local IRB
- Certificate of Clinical Trial from the Department of Health.
- Trial Drug
- Study-related accessories (Drug filters, Infusion bags, IV tubing etc.)

Copy of following documents is to be kept in CCTU central office:

- Fully developed protocol
- Protocol Amendment
- Final Version of CRF
- Laboratory Normal Ranges
Contract Agreement Form
Correspondences
Ethic Approval from local IRB
Certificate of Clinical Trial from Department of Health

Project co-ordinator is to send a copy of Certificate of Clinical Trial to the Chair of Dept. of Pharmacy.

Designated study nurse together with study principal investigator to organize an initiation meeting.

**Study Involved Parties Communication**

Designated study nurse to establish a communication network of all the study involved parties.

Contact numbers, pager number, e-mail address and/or involved department location should be recorded in order to enhance the communication network.

Trial-related messages can be sent to involved parties via e-mails. If electronic mail device is not available for all parties, memos will be sent to inform involved parties.

**Clinic Visits and Preparation**

To support process of trial recruitment and ensure all required data is documented in the patient charts, designated study nurse to assist study investigators with all trial-related procedures prior to, during and after clinic visits, which are included:

1. Patient screening

   Designated study nurse is to screen the cases for inclusion and exclusion criteria of individual study in site-specific clinics according to Site-Specific Clinic Schedule.

   For studies that recruit new diagnosis cases would be screened in the section of “New cases Clinic”.

   For studies that recruit recurrent and metastatics cases could be screened in the section of Head and Neck clinic, General Clinic and Follow-up Clinic.

   Information that need to be screened before referring to Study investigators are:

      o Disease site
Potential trial cases are referred to Study investigators for patient recruitment procedure

2. Patient recruitment:

- Designated study nurse to assist all proper recruitment procedures have been performed:
  - Information of the clinical trial is being proposed by investigators to patient
  - Patient right is being explained
  - Written informed consent form is signed and dated by investigators, patients and/or witness.
  - With signed consent form, patient particulars such as name, ID no., RT folder number, consent date, sex and age are recorded in the screening log.

3. Study screening period

- Designated study nurse to ensure all the investigational procedures is completed prior to start of treatment such as data collection forms for screening period, blood tests, cellular pathological tests and radiological tests.

- Designated study nurse to ensure all the required forms are put in the folder prior to clinic visit.

- Data collection forms

  - Forms that need to be completed included:
    1. Inclusion and exclusion criteria checklists
    2. Physical examination form
    3. Medical History form

- Blood tests

  - Tests need to be done according to individual protocol for trial screening period. Routine tests may include:
• CBP with Differential counts
• Renal and Liver Function tests (R/LFT)

  o Special tests such as SGOT, EBV-DNA, and HBV-DNA need to have special arrangements with Biochemistry and Virology departments. Special forms will be prepared and sent with the blood sample.

➢ Cellular pathological materials/tests

  o Designated study nurse is to ensure the diagnostic test results are obtained prior to treatment.
  o If cellular materials are required, designated study nurse to make arrangement to collect the tissue materials.

▪ Diagnostic tests done in PWH:

  o If the tests are done in this hospital, reported can be retrieved from the Clinical Master System.
  o Tissue slides/block may be stored in the Anatomy and Cellular department in PWH
  o Retrieval of tissues materials may be required for study-related tests
  o Written informed consent forms need to be done prior to tissue retrieval for individual study.
  o The tissue material can be retrieve by informing the pathologists with lab. Reference number.
  o Principal investigators will arrange study-related tests with pathologists

▪ Diagnostic tests done in HA hospitals:

  o If the diagnostic tests are done in the HA hospital, reports can be retrieved from the Clinical Master System.
  o Tissue slides/blocks may be stored in the Anatomy and Cellular pathology department in the hospital or one of cancer center laboratory of tissue bank.
  o A letter will be sent to the hospital for tissue collection, which is signed and dated by investigators.
  o The designated study nurse will arrange Collection/Delivery of tissues.

▪ Diagnostic tests done in private hospitals:

  o If the diagnostic tests are done in a private hospital, reports can be collected from the patients or patients referred lab.
  o Tissue slides/blocks may be stored in the referred lab.
A letter is sent to the lab with patient consent statement for tissue collection, which signed and dated by investigators.

- The designated study nurse to arrange Collection/Delivery of tissues.

Radiological tests

Tests done in PWH

- Investigators order radiological tests using the PWH ordered form.
- Time interval from ordering date and appointment date for:
  - X-ray is 1 day
  - CT scans is 6 to 8 weeks
  - Bone scans is 3 to 4 weeks
- Urgent CT scan appointment is defined tests need to be done within 2 weeks
  - Designated study nurse need to contact Senior Medical Officer in-person with the patient’s appointment request form for an appointment arrangement.
- Change of CT appointment
  - Appointment may be changed with the previous appointment slip.
  - Designated study nurse needs to contact the clerk of CT department in person for arrangement
- Urgent Bone scan appointment is defined as tests need to be done within 2 weeks
  - Designated study nurse need to contact radiographer or Senior Medical Officer of NM department with a completed Bone scan request form.

Tests done in Private Hospital

- Investigators order radiological tests using private hospital form
- Time interval from ordering date and appointment date for CT and Bone scans is within 2 working days.
- Designated study nurse to fax the scans requested form to hospital with the requested date written on the form.
- Consent of radiological scans can be obtained in the private hospital.

If the inclusion and exclusion criteria are fulfilled after the investigation procedures, patient particulars are recorded in the enrollment log which include patient’s:

- Name
- ID number
- RT folder number
4. Treatment period

Designated study nurse together with HA nursing staff and HA clerical staff to assist investigators during all treatment clinic visits:

- Preparation of Treatment Clinic Visit
  - Designated study nurse to prepare all the necessary documents in the patient chart (RT Folders) such as:
    - Nursing care front sheet (Homework sheet which is attached to the cover of RT folder)
    - Blood test Form
    - Radiological test requested Form
    - Chemotherapy record Form
    - Chemotherapy infusion Form
    - Physical Event Form
    - Adverse Event Form
    - Previous radiological test reports and films
  - Designated study nurse to decide the next follow-up date according to individual protocol and to prepare the booking slip to patients.

- Medication dosage calculation
  - Designated study nurse to calculate trial drug dosage for triple checking during clinic visit.
  - With the pre-calculating dosage, investigator is to double-check the dosage with another co-investigator.

- Clinic Visit Completion
  - Designated study nurse to ensure all the necessary documents have been filed in the RT folders such as:
    - Signed and dated Clinical Master System note
    - Signed and dated Chemotherapy record form
    - Signed and dated Chemotherapy infusion form
    - All the required clinical data form for the visit
- With all the obtained documents, RT folders are to pass to HA nursing staff for the preparation of treatment.
- Chemotherapy infusion Form is sent to Pharmacy for medication preparation.
- Appointment booking slip is given to patients with a written appointment date or time interval.
- When trial medication is arrived at clinic, designated HA nursing staff /Medical officer to administer the trial medication to patients.
  - For trial medication requiring close observations such as vital signs < Q1hr, designated research nurse to be responsible for the monitoring procedure according to protocol
  - For trial medication requiring observation which is >Q1hr, HA nursing staff to be responsible for the monitoring procedure according to the instruction on the Chemotherapy infusion chart.
- Once the visit treatment completed, the patient charts is returned to research nurse by the HA clerks for next visit preparation and CRF completion.

5. End of study Period

Designated research nurse together with HA nursing staff and HA clerical staff to prepare all required materials for the end of study visit.

- Preparation of Treatment Clinic Visit

- Designated research nurse together with HA nursing staff and HA clerical staff to prepare all the necessary documents in the patient chart (RT Folders) such as:
  - Nursing care front sheet (Homework sheet which is attached to the cover of RT folder)
  - Blood test results
  - Radiological test results
  - Physical Event Form
  - Adverse Event Form
  - Tumor assessment Form
  - Previous radiological test reports and films

- Clinic Visit Completion

- Designated study nurse together with HA nursing staff and HA clerical staff to ensure all the necessary documents have been filed in the RT folders such as:
  - Signed Clinical Master System note
All the required clinical data form for the visit
  • Once investigator has seen the patients, appointment for follow-up assessments.

**On-leave Back-up**

- On-leave Nurse will prepare the following documents 2 days before leave:
  - Patient log
  - Patient Visit Date within leave period
  - Protocol - with the highlight of
    - Treatment regime
    - Study drug calculation
    - Dose Modification
    - Flow Chart
    - Randomization
  - Clinic visit instruction for each patient (for leave < 2 weeks)
  - Consent form
  - Study forms for:
    - Recruitment
    - Treatment period assessment
    - Tumor assessment
  - Study Prescription forms

- Back-up nurse will cover all the following tasks for the on-leave nurse:
  - Patient screening
  - Patient recruitment
  - Preparation of Clinic visit
  - Clinic visit
  - Severe Adverse Event Reporting
  - CRF completion (if the leave is > 2 weeks)

**Monitoring Visit**

Designated study nurse to ensure all the study documents is ready during the monitoring visit, which include the followings:

- Completed Case Report Forms
- Source documents:
  - RT folders
  - HN folders (if patients have been admitted to wards)
  - Radiology films
  - Investigator file

Designated study nurse to take minutes of each monitoring visit for specific concerns or issues.
Reply of specific concerns or issues is to be documented and filed in the investigator file.

* Time interval for monitoring visits may vary depending on individual study arrangement. Issues that may concern monitoring visits can discuss with either Head Nurse/CCTU director/Principal Investigator.

**Data Management**

**Data Collection and Handling**

Designated study nurse is responsible for collecting all trial related data, which is filed in the patient charts (source documents).

**Data Flow**

- After each trial visit, all required data is documented in the patient’s chart.
- Patient’s chart is returned to designate nurse within a week for Case Report Form Completion.
- Designated study nurse/ research assistant is to transfer the data from patient chart (source document) to Case Report Forms.
- Prior to data entry, designated study nurse to verify the data in the Case Report Forms with the source documents within 2 weeks.
- After the first data entry, designated study nurse to verify the data in the Case Report Forms with database printout within 2 weeks.
- Notes are made for query documentation for correction.
- Correction is made with signature and date next to it.
- For pharmaceutical company study:
  - Clinical research associate (CRA) is contacted for monitoring visits after verification is completed.
  - CRA to collect the copies of CRF and send to sponsor for analysis
  - Data query forms (DQF)/Data clarification forms (DCF) may send to CCTU after data analysis
  - Designated study nurse is to clarify the queries with source documents and Correspondence Case Report Forms copies.
  - Completed DQF/DCF will send to sponsor for data re-entry according to individual protocol time frame.
  - This on-going process is to continue until study completion.

- For in-house study, the designated nurse to follow the standard operation procedures (SOP) of Data Entry:
  - Designated study nurse to verify the data with source documents and correspondence CRF, and, CRF and printout of data computer system.
  - Corrections are made if discrepancies found after data verification
  - Corrected data is to re-enter to the CCTU computer system
  - Designated study nurse to verify of corrected data
If no discrepancies found, signing “Date Completed” Column indicates data completion.

**Storage of Source Documents**

Research nurses/research associates to have access to the study-related sources documents.

During study period:

- Sources documents that kept and locked by CCTU:
  - Trial Patients charts (RT folders and Hospital notes)
  - Radiological films (both sponsored private and HA radiological films)

- Upon requests, source documents may be transferred to other departments as references for reports and treatments

- Record on In and Out of the source documents is available in the HA computer system.

- Source documents are returned after used.

After study period:

- Sources documents are kept and locked in different places of PWH for the access of other departments:
  - Trial Patients charts
    - RT folders are kept and locked in the Folder storage rooms of Department of Clinical Oncology
    - HA Hospital Notes are kept and locked in the Folder storage rooms of the Central Record Office in PWH
    - No limited time for the storage of Patient charts.
  - Radiological films
    - Sponsored private films are kept and locked by CCTU. No limited time for the storage of these films.
    - HA films are kept and locked for seven years in the Department of radiology. After seven years, films are collected and locked by CCTU.

**Storage of Case Report Forms**

Designated study nurse to ensure all the Case Report Forms is stored in a secured place at all time.

- All Case Report Forms is stored by CCTU during protocol period.
Only the designated personnel to have access to CRF

Upon study completion, all Case Report Forms is locked in the cabinets, which are located in CCTU storage room and 4/F Cancer Center.

Multi-Center Study Co-ordination (Modification of In-house study)

Designated research nurse to ensure all the modification is completed prior to trial activation in another site center.

- Documents need to be obtained prior to the start of study:
  - Amended Protocol
  - Ethical Approval of Amended Protocol
  - Amended Case Report Form

- Designated research nurse together with the Principal Investigator are to organize an investigator meeting with other study sites.

- Designated research nurse is responsible for the following tasks:
  - Prior to the start of study:
    - To discuss the study logistics with other site study nurses.
    - To design/modify the case report forms with multi-center format.
    - To call for a meeting with data entry clerk, programmer and CCTU director to finalize the amended case report forms.
    - To send out a set of amended case report forms to other study site.
    - To document study-related comments or issues and put in the investigator file.
  - During the study:
    - To ensure all the CRF is received within scheduled time frame.
    - To make contact with other sites in a monthly basis and document in the investigator file.
    - To answer study-related questions and document in the investigator file.
    - To send out data queries form
    - To receive completed data queries form
    - To receive other sites’ SAE reports and put it in CCTU SAE file
  - Study Completion
    - To send out a letter to notify other sites that the study is completed
- To put the letter in the investigator file
- To clear up the data for study analysis
Appendix A

Investigator Site File Documents

1. Investigator Brochure + update(s)
2. Final version of the protocol
3. Any Amendments
4. Final Version of the CRF
5. Informed Consent
6. Clinical trial certificate issued by DoH
7. Written approval from the Ethical Committee
8. Delegation of duties & Authorized Signatures Form
9. Laboratory Normal Ranges
10. Investigator’ CV
11. Protocol Agreement Form
12. Confidentiality agreement
13. Insurance
14. Drug Inventory Forms & Accountability Log
15. Serious Adverse Event Reporting