2015 Symposium for Research Administrators

INSIDE OUT

Ins and Outs of Reading Study Documents from a Financial Perspective

November 10, 2015

Objectives

- Describe the study documents to review to develop an internal cost assessment (ICA) and budget
- Describe what to look for in study documents that may have associated research-specific cost that need to be covered by the sponsor
- Describe types of costs associated with performing a study

Documents to Review

- Protocol
  - *Subject Selection (Inclusion/Exclusion Criteria)*

    Exclusion Criteria states:
    - Renal or hepatic insufficiency

      Yes, include a renal function panel and hepatic function panel, if not Routine.
    - Known history of renal or hepatic disease/insufficiency

      No, "history" can be determined by reviewing the medical record.

  - *Study Evaluations/Procedures (including Schedule of Events/Study Calendar)*

    NOTE: Don't forget to read the footnotes.

Table 2

Study [redacted] Schedule of Events: Cohort Expansion Phase (Phase 2, Parts A and B): [redacted]

Assessment	Screening/Baseline (within 28 days prior to Dose 1)	Cycle 1 Day (21-day regimen)			Cycle 2 Day (21-day regimen)			Subsequent Cycles Day (21-day regimen)			EOT	Follow-up (~4 wks after last dose)
		1 [a]	8	15	1	8	15	1	8	15		
Informed consent	×											
EphA3 expression (BM biopsy) [b]	×	For study entry, must be EphA3+ by IHC (expression of EphA3+ to be determined by [redacted].										
Demographics	×											
Medical and surgical history	×											
History of hematologic malignancy	×											
Diagnostic classification	×	For [redacted] use NCCN guidelines (v. 2.2014). For [redacted] use 2008 revised WHO criteria. For [redacted] use Durie-Salmon.										
Prior treatment for cancer and response history	×											
Physical examination	×											
ECOG performance status	×											
Chest X-ray	×											
Urinalysis	×											
Pregnancy test (serum or urine)	×											
ECG	×	× [f]	× [f]	× [f]	× [f]	× [f]	× [f]				×	
Weight		×			×			×				
Vital signs	×	× [f]	× [f]	× [f]	× [f]	× [f]	× [f]	× [f]	× [f]	× [f]	×	
Chemistry and hematology	×	×	×	×	×			×			×	
Disease status/tumor response [b]	×				×			×	D1 every 3 cycles [c]		× [d]	
PT/PTT	×	×	×	×	×	×	×	×				
Platelets	×	×	×	×	×	×	×	×				
Fibrinogen, D-dimers, and factors		×		×	×		×	×				
Pharmacodynamics (PD) [b, e, m]	×	× [f]			×			×	D1 every 3 cycles [c]		× [d, f]	
[redacted] serum concentration (PK)		× [g]	×	×	×	×	×	×	D1 only on Cycle 3		×	×
NIA and tissue microarray (PD) [redacted] only [n]	×				×			× [n]			×	
Anti[redacted] serum antibody samples		×	×	×	×			×	D1 every 3 cycles [c]		×	×
Premedication administration [i]		×	×	×	×	×	×	×	×	×		
[redacted] administration		×	×	×	×	×	×	×	×	×		
Adverse events — Pre, during, and post dose	× [j]	×	×	×	×	×	×	×	×	×	×	× [k]
Infusion-related signs and symptoms — During and post dose		×	×	×	×	×	×	×	×	×		
Concomitant medication	×	×	×	×	×	×	×	×	×	×	×	×
Subsequent anticancer therapy												×

Table 1

[redacted]

Footnotes

[a] Cycle 1, Day 1 predosing assessments do not require repeating if the Screening/Baseline assessments were collected within 48 hours prior to dosing. Whenever possible, predosing assessments should occur on the day of dosing.

[b] More than 1 sample may be collected (1 for usual standard care, 1 for the purpose of this protocol). See Laboratory Manual.

[c] Cycle 3, then every third cycle thereafter (cycles 3, 6, 9, 12, 15, 18, 21), and as clinically indicated. Unscheduled samples may be taken as clinically indicated.

[d] If subject is being withdrawn for progressive disease, there is no requirement for a repeat bone marrow biopsy.

[e] PD sample collection to include peripheral blood for collection of NK cells, bone marrow aspirate for RT-PCR and bone marrow biopsy for IHC. See Laboratory Manual.

[f] PD sample collection Cycle 1 Day 1 (pre-dose) is only for collection of NK cells (peripheral blood). At EOT there is no collection of NK cells.

[g] Also on Days 2, 3, and 5. See protocol Section 9.2.2 and Laboratory Manual for time points.

[h] See protocol Section 7.7.2 for premedication requirements.

[i] See protocol Section 11.1.3 for reporting requirements for AEs that occur prior to first dose.

[j] See protocol Section 9.2.3 for AE and SAE reporting requirements.

[k] Pre and post dose.

Documents to Review

- Protocol
  - *Study Procedures*

9. STUDY PROCEDURES

Study drug will be administered as described in Section 7.7.2, and evaluations will be performed as described in Section 9.2.

9.1 Informed Consent

Prior to study-related procedures or screening evaluations, written informed consent and authorization for use of protected health information must be obtained from the subject in accordance with applicable laws and regulations. Prior to use, the format and content of the informed consent form (ICF) must be approved by the appropriate Institutional Review Board (IRB)/Human Research Ethics Committee (HREC).

9.2 Study Visits

9.2.1 Screening/Baseline

Subjects may undergo the following Screening/Baseline procedures anytime during the 28 days prior to Cycle 1, Day 1 to confirm eligibility.

Required for all study subjects unless otherwise noted:

Note: Bone marrow biopsy is obtained for both phases. More than 1 sample may be collected (1 for usual standard care, 1 for the purpose of this protocol).

- Written informed consent
- Demographics
- Medical and surgical history (see Section 11.1.3 for documenting AEs)
- Physical examination including vital signs
- ECOG performance status
- Clinical laboratories including hematology, chemistry, PT/PTT, platelets, urinalysis, serum protein, and serum or urine pregnancy test (for females of childbearing potential)
- Collection of NK cells
- ECG and chest X-ray
- Diagnosis and disease classification, including:
  - For [redacted] National Comprehensive Cancer Network (NCCN) guidelines (version 2.2014)
  - [redacted]
  - For other hematologic malignancies: 2008 revised WHO criteria
- History of the hematologic malignancy
- Prognostic factors relevant to the malignancy and stage of disease

Documents to Review

- Protocol
  - *Study Drug/Device Information*

5.4. Drug Supplies

5.4.1. Dosage Form(s) and Packaging

[redacted], placebo for t[redacted], [redacted]PR and placebo for [redacted]PR will be supplied by the Sponsor or designee.

  - *Record Retention*

    Investigator records must be kept for a minimum of 15 years after completion or discontinuation of the study or for longer if required by applicable local regulations.

Documents to Review

- Protocol
  - *Monitoring and Auditing*

10. QUALITY CONTROL AND QUALITY ASSURANCE

During study conduct, [redacted] or its agent will conduct periodic monitoring visits to ensure that the protocol and Good Clinical Practices (GCPs) are being followed. The monitors may review source documents to confirm that the data recorded on CRFs is accurate. The Investigator and institution will allow [redacted]monitors/auditors or its agents and appropriate regulatory authorities direct access to source documents to perform this verification.

  - *Appendices*

APPENDICES

Documents to Review

- Consent Form
  - *How Many People Will Take Part in This Study?*
  - *What is Involved in the Study?*

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign this consent form. You will have the following tests and procedures to make sure that you are eligible:

- Physical exam and medical history
- Vital signs
- Blood tests
- Electrocardiogram (EKG), a tracing of the electrical activity of the heart

Documents to Review

- Consent Form
  - *What are the Costs?*

WHAT ARE THE COSTS?

(If the subject is responsible for costs and the research involves medical care and the use of a drug)

You or your insurance provider will be responsible for all costs related to your medical care, including the drugs used in this study.

(If the sponsor is responsible for costs)

There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company.

  - *What About Compensation?*

Documents to Review

- Consent Form
  - *What About Research Related Injuries?*

For **Commercial/Industry Sponsored Studies:**

Option 1: When the sponsor provides for payment for research-related injury (not conditioned on first billing third party payers)

Option 2: When the sponsor conditions its obligation to pay for research-related injury on a primary effort to obtain payment from a non-governmental third party payer

Option 3: When the sponsor makes no provision for payment for research-related injury (standard paragraphs with addition of "the study sponsor, Company X")

For **Studies NOT Commercial/Industry Sponsored:**

Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

Documents to Review

- Agreement/Contract
  - Term and Termination
  - Supplies/Return of Materials and/or Equipment
  - Study Budget and Payment Terms
  - Recordkeeping/Record Retention
  - Monitoring and Auditing
  - Costs and Payment/Compensation
  - Appendices/Exhibits

Documents to Review

- Agreement/Contract
  - *Appendices/Exhibits*

SCHEDULE A

A1 STUDY BUDGET

Medpace, as Sponsor's payment agent, shall make payment to the payee specified in the Payee Information Table ("Payee") under this Agreement from funds escrowed by Sponsor for services provided according to the payment schedule below. All fees listed include: overhead, taxes, and patient stipend or travel reimbursement, as applicable. Payments are based on electronic case report forms ("eCRFs"), laboratory data, IVRS data or other specific data source. All amounts shown herein are calculated in USD.

A1.1 Fee for Each Evaluable Subject **$10,100**

An "evaluable subject" is one who has been enrolled (randomized to treatment) and in whom all the applicable terms and conditions of the Protocol and this Agreement have been satisfied. Randomization occurs at Visit 1.

A1.2 Total Subject Budget (Estimated) **$60,600**

The total subject budget is based on 6 subjects expected to be randomized at site.

A2 SETUP FEES & VISIT PAYMENTS

A2.1 Setup Fees

Table 1 - Setup Fees

FEES	COST
Administrative Start-up Fee	$8,448
IDS Pharmacy Start-up Fee	$2,560
Data Mining Fee	$2,000

Payment will be made within forty-five (45) days of:

- Sponsor declaring Institution to be ready for Study Initiation;
- IRB/EC approval; and

Documents to Review

- Case Report Forms (CRFs)
  - time to complete, paper vs electronic, query rate, number
- Investigator's Brochure (IB)
- Sponsor's Budget Proposal
- Study Manuals (radiology, pharmacy, lab, etc.)

Subject Care Costs: Questions to Ask

- Would the procedure/test be done, at the time point specified in the protocol, if the subject was not on the study?
  - If Yes, Routine: Bill to insurance (unless sponsor indicates they will pay). Billable to insurance
  - If No, Research-specific: Bill to study. Billable to grant
- What procedure/test will be ordered? Will a "read" be needed?
- Where will the procedure/test be performed?
- Is the clinic hospital-based (HBC) or PDC?
- Will a local or central lab be used? If central, who will draw the samples?
- Will a "research" machine be used? (e.g., 12-lead ECG)

NOTE: Communication with the study team is **VERY** important in answering these questions.

Subject Care Costs

- Submit a price request for each study.
- Submit a “new” price request at the beginning of each budget year of a grant to verify current prices.
- For “bundled” procedures, request a bill of a known patient who underwent similar procedure (supplies, medicines, etc.) from Revenue Manager.

Fixed Costs

Occur regardless of how many subjects are enrolled:

- Administrative Start-up
- Study Team Meetings/Training
- Site Initiation Visit
- Institutional Review Board (IRB)
- Duke Clinical Research Unit (DCRU), if applicable
- Pharmacy, if applicable
- Radiology, if applicable
- Record Retention (based on number of years)
- Study Close-out

Study Costs: Forms and Templates

https://medschool.duke.edu/research/clinical-and-translational-research/duke-office-clinical-research/irb-and-institutional-6

Negotiating the Contract and Budget
(Industry-Funded Research)

Forms and Templates

Grant Pricing Request Form

Budget Request Form for the Investigational Drug Services (IDS) Pharmacy

Cardiac Diagnostic Unit (CDU) Research Protocol Overview Form

Indirect or Facilities and Administrative (F&A) Costs

Internal Cost Assessment-Budget Template

Radiology Logistics Implementation Review form

Request to Add a Sponsor into SPS - Use this form to add a sponsor in SPS before submitting an application to the Office of Research Administration (ORA).

Hidden Costs

- Pass-through Fees (e.g., items to be invoiced)
- Advertising Fees
- Screen Failure Fees
- Pharmacy Maintenance Fees, if applicable
- Supplies (e.g., shipping, etc.)
- Unscheduled Visits
- Monitoring Visits
- Record Retention Fees
- Study Team Meetings/Training

Variable Costs

Occur for each subject enrolled:

- Personnel Costs
- Subject Care Costs (e.g., procedures/tests, etc.)
- Facility Fees (e.g., DCRU, etc.)
- Supplies, Shipping, etc.
- Pharmacy Dispensing, if applicable
- Subject Compensation – include additional costs for Duke ClinCard
  - $3.50 one-time cost for issuing card (cannot be charged on federal grants)
  - $1.00 load fee per transaction

Variable Costs?

Sponsor will provide device explant kits as well as shipping costs. The site will be responsible for the requirements in the retrieval process but the Sponsor will assist with providing the kits and shipping costs.

Yes, the "requirements" in the retrieval process will involve study team time.

Internal Cost Assessment (ICA)

CRUs are required to complete an ICA for studies funded externally and internally.

- To determine actual cost of conducting the study
- To determine if sponsor's budget proposal covers actual costs of the study
- To assist in determining if the study is financially feasible
- To assist in calculating final study budget

NOTE1: Foundation and federally-funded study budgets should be developed on a cost-basis and; therefore, do not require the separate completion on an ICA

NOTE2: Communication is **VERY** important since each role (study team, financial, etc.) has a different perspective regarding the study documents and costs.

Facilities & Administrative (F&A) rate

The current published Duke University School of Medicine F&A rate is:

- 28% for industry-sponsored **clinical trials** only
- 59% On-campus research (federal/foundation and industry clinical research)
- http://research.som.duke.edu/research-administration/financial-administration/indirect-costs

Service Providers

https://medschool.duke.edu/research/clinical-and-translational-research/duke-office-clinical-research/irb-and-institutional-6

Negotiating the Contract and Budget (Industry-Funded Research)

Partner Resources

Duke service providers can assist with the costs of their services that are associated with your study. This list of Duke service providers provides information about services and who to contact.

Service	Contact	E-mail	Phone	Website
Radiology	Steve Shipes	steven.shipes@duke.edu	919-684-7732	http://radiology.duke.edu/research/research-support/
Institutional Review Board (IRB)			919-668-5111	http://irb.duhs.duke.edu/modules/irb_fees/index.php?id=1

Contacts

Duke Office of Clinical Research (DOCR)

Tracy Kerby
tracy.kerby@duke.edu
684-3714

Lindsey Spangler
lindsey.spangler@duke.edu
681-6650

Additional Resources

http://docr.som.duke.edu/

DOCR Training:

- Financial Basics for Clinical Research
- Budget Development and Negotiation Training