Operations Manual

SARC037

A Phase I/II Study to Evaluate the Safety of Trabectedin Administered as a 1-Hour Infusion in Ewing Sarcoma Patients in Combination with Low Dose Irinotecan and 3'-Deoxy-3'-18F Fluorothymidine (18F-FLT) Imaging

Summary of Changes

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<thead>
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<th>Section</th>
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<th>Version 8</th>
</tr>
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</table>
| Contact information| President and CEO  
|                    | Sarcoma Alliance for Research Through Collaboration  
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|                    |                                                    | Ann Arbor, MI 4810  
|                    | Lindsey Overman  
|                    | Leoverman (in all instances in the document)  
|
18F-FLT Administration
The 18F-FLT tracer will be administered according to institutional standards at a dose of 0.07mCi/kg, with a maximum dose of 5 mCi.

The PET imaging will be from head to toe with a scan time of 3 minutes per bed position.

9.1 Travel to the NCI
Melissa Spencer
Melissa.spencer@nih.gov
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1. Contact Information

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Center for Cancer Research
National Cancer Institute
Building 10, Room 13C103
Bethesda, MD 20892

SARC Contact:
Research Project Manager (RPM)
2. Data Collection

2.1. Database Access

This study uses Medidata Rave, a web based data entry system for electronic data capture (EDC). All patient registrations and Case Report Forms (CRFs) will be submitted electronically via the study database.

Prometrika will supply site personnel with a username and password to access the study database. All personnel entering data will be required to take an eLearning course and submit the eLearning completion certificate to SARC (Section 1, Contact Information) prior to use of the study database.

For personnel who are no longer involved in the study, SARC will ensure that the appropriate account has been deactivated.

eCRF Completion Guidelines will be provided to the site personnel.

For questions or assistance in using the study database, please contact the SARC RPM (Section 1, Contact Information).

2.2. Enrolling a Patient

A signed informed consent document must be obtained prior to evaluation for eligibility and entry into the study. Histologic confirmation of EWS-FLI1 fusion and fusion type Ewing sacoma and relapsed Ewing sarcoma is required for eligibility. Patients who consent and are being evaluated for eligibility should be tracked on the Site Screening Log (Appendix A).

For patients enrolling in the study as part of the dose escalation cohort, the site will contact the SARC RPM (Section 1, Contact Information) to confirm dose level assignment and 18F-FLT PET designation. Please note: patients designated to receive the 18F-FLT PET will travel to the NCI for the first Cycle of treatment. SARC will coordinate between the site and NCI for patients needing to travel for Cycle 1. Please note: patient travel support options are available (Section 9: Patient Travel and Accommodation).

Following consent and verification of eligibility, all eligible patients must be enrolled in the study database prior to the start of treatment. Please note that only patients who meet all eligibility criteria will be enrolled in the study. SARC RPM will transfer patients who will travel to the NCI for the first week of treatment in the Medidata/Rave database. If the patient returns to the referring site, SARC RPM will transfer patients from NCI to the referring site for cycle 2 through the end of treatment in the Medidata/Rave database.

Once patient initials and date of birth are entered and saved on the Subject Enrollment eCRF, a patient identification (ID) number is automatically generated and assigned to that patient. Please note that all documents for the patient that are uploaded into the database or submitted to SARC via email or fax must include the patient’s study ID number and initials and must have patient’s PHI redacted (with the exception of patient’s initials and date of birth).
The following documents must be uploaded into the study database at the time of patient enrollment/registration:

1. Signed Informed Consent Form
   Prior to uploading into the database, please ensure the following:
   - The file name does not include patient’s name.
   - Patient identifying information is redacted (with the exception of patient’s initials and date of birth).
   - Patient study ID number and initials are included on every page.
   - PI signature and date signed are included.
   - Date consent was signed is not after enrollment date in database.

2. Eligibility Checklist (Appendix B)
   Prior to uploading into the database, please ensure the following:
   - The file name does not include patient’s name.
   - Patient identifying information is redacted (with the exception of patient’s initials and date of birth).
   - Patient study ID number and initials are included on every page.
   - PI signature and date signed are included.

3. Pathology report
   Prior to uploading into the database, please ensure the following:
   - The file name does not include patient’s name.
   - Patient identifying information is redacted (with the exception of patient’s initials and date of birth).
   - Patient study ID number and initials are included on every page.
   - PI signature and date signed are included on every page.

Patients can be registered in the study database electronically any time of the day, any day of the week.
2.3. Data Entry

Electronic Case Report Forms (eCRFs)

eCRFs should be completed no later than 10 working days after the required visit with the exception of Subject Enrollment, baseline eCRFs and SAEs (see below).

Subject Enrollment and Baseline eCRFs

Subject Enrollment, accessible on the patient home page, and the Eligibility eCRF, found in the Baseline folder, should be completed at the time of patient registration.

Serious Adverse Events (SAEs)

SAEs should be entered into the database as soon as possible, but no later than 3 days after the site Principal Investigator becomes aware of the event.

Expedited time frame

At times, data entry and data query resolution will be requested in a shorter time frame for data reports or for abstract submission deadlines.

Source documents

Throughout the course of the study, source documents will be uploaded into the database. For details, refer to the eCRF Guidelines.

The following source documents will be uploaded into the database throughout the course of the study:

1. RECIST sheets
   a) Include patient study ID number and initials.
   b) Include site PI signature and date signed.
   c) Redact patient’s Personal Health Information (PHI) (with the exception of patient’s initials).
2. Imaging report corresponding to submitted RECIST sheet
   a) Include patient study ID number and initials
   b) Redact patient’s PHI (with the exception of patient’s initials)
3. Sample Collection Requisition forms
   a) Include patient study ID number and initials

Compliance

If sites are unable to comply with the timelines for data entry, please contact SARC. Institutions will be contacted by SARC if data entry is delinquent.

Please refer to the eCRF Completion Guidelines for specific data entry conventions.

2.4. Uploading imaging files to QARC

Tumor assessments/imaging studies, must be obtained at baseline, at the end of cycle 2, 4 and 6, and every other cycle thereafter, and then at the end of study regardless of the reason for stopping protocol therapy. The same method of assessment and the same technique should be used to characterize each identified and reported lesion. Minor unavoidable departures (up to 72 hours) from scheduled disease evaluations for valid clinical,
patient and family logistical, or facility, procedure and/or anesthesia scheduling issues are acceptable. Additional imaging or assessments may be done if clinically indicated.

Imaging studies at baseline and continuing assessments as indicated above will be submitted to the Quality Assurance Review Center (QARC) for retrospective central review and archiving. Diagnostic studies should be submitted as soon as they are available. The results of the central review will not be returned to the institution.

Submission of Diagnostic Imaging data in digital DICOM format is required. These files should be submitted electronically via sFTP. Information for obtaining an sFTP account and submission instructions can be found at www.QARC.org. Follow the link labeled digital data. Submission by CD is discouraged. Only when electronic submission is not possible, the imaging may be burned to a CD and sent to QARC via courier at the address below. Multiple studies for the same patient may be submitted on one CD; however, please submit only one patient per CD.

QARC
Building B, Suite 201
640 George Washington Highway
Lincoln, Rhode Island 02865-4207
Please contact QARC for questions regarding imaging submission:
DataSubmission@QARC.org
Phone: (401) 753-7600

3. Procedures for Collection, Handling, and Shipment of Samples

Correlative studies, as described in the protocol, will be performed on peripheral blood and tumor biopsy samples.

After the completion of studies, any remaining blood and tumor tissue will be stored at the SARC designated specimen bank, Nationwide Children’s Hospital, for patients who provide written consent.
<table>
<thead>
<tr>
<th>Samples</th>
<th>shipped To/Timing</th>
<th>Total Volume</th>
<th>Container</th>
<th>#</th>
<th>Shipping Temp.</th>
<th>Collection timepoints (calculated from the end of Trabectedin infusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pre-treatment</td>
</tr>
<tr>
<td>Pharmacokinetic analysis (PK)</td>
<td>NCI/ Batched by patient</td>
<td>40 ml</td>
<td>NaHep (green top)</td>
<td>8</td>
<td>Dry Ice</td>
<td>Prior to Cycle 1</td>
</tr>
<tr>
<td>Circulating Tumor DNA</td>
<td>DFCI/ Overnight</td>
<td>50 ml (10 ml per collection)</td>
<td>10 ml PAXgene Blood ccfDNA</td>
<td>5</td>
<td>Cold Pack</td>
<td>Prior to Cycle 1</td>
</tr>
<tr>
<td>Circulating Tumor Cell</td>
<td>UC/ Overnight</td>
<td>30 ml (10 ml per collection)</td>
<td>CellSave tube</td>
<td>3</td>
<td>Room Temp</td>
<td>Prior to Cycle 1</td>
</tr>
<tr>
<td>UGT1A1</td>
<td>NCI/ Overnight</td>
<td>4 ml</td>
<td>EDTA (purple top)</td>
<td>1</td>
<td>Cold Pack</td>
<td>Day 1</td>
</tr>
<tr>
<td><strong>Tissue</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pre-treatment</td>
</tr>
<tr>
<td>Formalin Fixed Paraffin-Embedded (FFPE) Tissue</td>
<td>CHOP</td>
<td>1 FFPE cores per time point</td>
<td>Cassettes</td>
<td>2</td>
<td>Room Temp</td>
<td>Prior to first treatment</td>
</tr>
<tr>
<td>Fresh Tissue</td>
<td>OSU/ Roberts</td>
<td>1 x 1 x 1 - cm, up to 2 cm</td>
<td>50 ml conical with 40 mL transport media</td>
<td>1</td>
<td>SAF-T-Temp Pak</td>
<td>Prior to Cycle 1</td>
</tr>
<tr>
<td>Snap Frozen Tissue</td>
<td>CHOP/ Overnight</td>
<td>Up to 3 samples (0.5 x 0.5 x 0.5-cm)</td>
<td>Cryovials</td>
<td>6</td>
<td>Dry Ice</td>
<td>Prior to Cycle 1</td>
</tr>
<tr>
<td>Viable Frozen Tissue</td>
<td>CHOP/ Overnight</td>
<td>Up to 2 samples (0.5 x 0.5 x 0.5-cm)</td>
<td>Cryovials</td>
<td>4</td>
<td>Dry Ice</td>
<td>Prior to Cycle 1</td>
</tr>
</tbody>
</table>
3.1. Sample Collection Kits

Sample collection kits for the CTC blood collection will be ordered from the University of Colorado. Please order 2 kits per patient. One kit will be returned for the Day 8 sample collection.

**CellSave Kit:** includes an insulated shipper, shipping supplies, and 1 Cell Save tube

Prior to enrollment request kits using the following email:
sarcomaresearch@ucdenver.edu
cc: SARC037@sarctrials.org
Phone 919-491-1352 (emergency only)

The remaining sample collection kits will be provided by The Biopathology Center (BPC), at the Abigail Wexner Research Institute at Nationwide Children’s Hospital.

This will include kits for the collection and shipment of frozen tissue (snap frozen and frozen viable), fresh tissue, blood in PAXgene Blood ccfDNA tubes, and plasma for PK. Sample kits will not be provided for FFPE.

**Frozen Tissue Kit:** includes an insulated shipper and shipping supplies

**Viable Tissue Kit:** includes a shipper, shipping supplies and 1 50ml conical tube containing 15ml hypothermosol

**PAXgene ccfDNA Kit:** includes an insulated shipper, shipping supplies, cold pack, and PAXgene Blood ccfDNA tubes

**PK Kit:** includes an insulated shipper, cryovials and shipping supplies

Prior to enrollment request kits using the following email for SARC:
SARC037 SARC037@sarctrials.org
Lindsey Overman: leoverman@sarctrials.org
Phone: (734) 930-7600

Sites can track kits via the BPC Kit Management application at: [https://kits.bpc-apps.nchri.org](https://kits.bpc-apps.nchri.org). Upon first access of application, sites will follow registration instructions.

Please allow up to 5 business days for kits to arrive.

For questions about the Kit Management Application, please contact the Biopathology Center by email (BPCBank@nationwidechildrens.org) or phone (800-347-2486).

**Note:** Kits for other SARC studies may be visible on the application; therefore, it is imperative that sites be sure to only order kits for SARC037.

Samples will be shipped in compliance with current regulatory guidelines for the transport of biological specimens. Sample collection and processing will be conducted per institutional guidelines and in accordance with the details described in this section, as well as in the protocol. For assistance, please contact SARC (see section 1.2 for contact information).
3.2. Blood Samples

Collection of blood samples is mandatory for study participation. Pharmacokinetic (PK) analysis will be done. The presence of circulating tumor DNA and circulating tumor cells will be analyzed in peripheral blood. Please see Table 1 for complete blood sample collection schedule.

3.2.1. Pharmacokinetic (pK) samples

**PK Blood collection schedule (See Table 1 for collection time points)**

Blood will be collected for PK studies of trabectedin serum concentrations via **6 mL sodium heparin** (3-5 mL collection) (NaHep; Green Top tube; BD Biosciences) as follows:

- On cycle 1 day 1, before first dose of trabectedin
- 30 minutes post dose (+/- 5 minutes)
- 1 hour post dose (+/- 5 minutes)
- 2 hours post dose (+/- 5 minutes)
- 3 hours post dose (+/- 5 Minutes)
- 24 hours post dose (+/- 60 minutes)
- 48 hours post dose (+/- 60 minutes)
- 168 hours post dose (+/- 60 minutes)

**PK sample acquisition and preparation**

- Collect 3-5 ml of whole blood into NaHep Green Top tube
  - Samples collected within the NCI: clinic staff should call the clinic staff should call the NCI Blood Processing Core at 240-760-6180 so that a Blood Core staff member can pick up the blood sample immediately to process (centrifuge, aliquot, etc).
- Samples will be immediately centrifuged at 4°C for 10min @4000xg
- Aliquot the supernatant plasma into cryotubes
- Enter the required information onto the sample label provided in the kit and adhere it to the tube.
- Store at -80°C until batch shipment to the NCI

**Shipment of PK plasma samples (Overnight to NCI)**

- Complete the Requisition Form for Blood Samples (Appendix C)
- Prior to shipping, email completed Requisition Form to SARC at SARC037@sarctrials.org and leoverman@sarctrials.org.
- Prepare the shipping container provided in the whole blood collection kit according to the accompanying instructions.
- Include a copy of the Requisition Form in the shipment
- Attach the Exempt Human Specimen label to the side of the box.
- Samples must be shipped overnight on dry ice on Monday, Tuesday, or Wednesday for next day delivery to NCI Blood Processing Center. If samples collected on Thursday or Friday, shipment must wait until the following Monday to avoid weekend delivery.
- Ship via FedEx Priority Overnight using account # 284 417 593
3.2.2. Circulating Tumor DNA (ctDNA) Samples

See Table 1 for collection time points.

**Blood for ctDNA acquisition and preparation**

Draw blood into one **10 mL PAXgene Blood ccfDNA tube**. Invert each tube gently 8 times to mix and prevent clotting. Close the tube firmly. Refrigerate tube until shipment if not shipped within 2 hours of collection. Apply participant identification to tube (label provided in kit—add patient study ID, collection date, collection time).

**Shipment of ctDNA samples**

- Samples will shipped overnight at 4 degrees on with a cold pack
- Complete the Requisition Form for Blood Samples (Appendix D)
- Prior to shipping, email completed Requisition Form to SARC at SARC037@sarctrials.org and leoverman@sarctrials.org
- Prepare the shipping container provided in the whole blood collection kit according to the accompanying instructions
- Include a copy of the Requisition Form in the shipment
- Attach the Exempt Human Specimen label to the side of the box
- Samples must be shipped overnight for next day delivery to Dana Farber Cancer Institute
- Ship via FedEx Priority Overnight using account #284 417 593
  Dana-Farber Cancer Institute
  Attn: Kelly Klega
  450 Brookline Avenue
  Boston, MA 02215
  Phone: 321-514-9821

3.2.3. Notification of Shipment (applies to pK, ctDNA, and CTC samples)

The site will complete the following steps for notification of shipment:

- Enter the appropriate data into the Sample Shipment eCRF
- Complete and email the corresponding Requisition Form to SARC037@sarctrials.org and eantalis@sarctrials.org
- Send a notification of shipment email to the SARC RPM with the following information (see section 1.2 for contact information):
  - Date of shipment
  - Patient ID and initials
  - Type of sample
3.2.4. Circulating Tumor Cell (CTC) Blood Collection

See Table 1 for collection time points. See section 3.1 for kit ordering information.

**CTC sample acquisition and preparation**

- Draw blood into one **10 mL Cell Save tubes**.
- Invert each tube gently 8 times to mix and prevent clotting. Close the tube firmly.
- Apply participant identification to tube (label provided in kit—add patient study ID, collection date, collection time).
- Keep the tube **at room temperature** at all times.

**Shipment of CTC samples (Overnight to UC)**

- Upon blood collection, email sarcomaresearch@ucdenver.edu to obtain a FedEx label
- Complete the Requisition Form for Blood Samples (Appendix E)
- Prior to shipping, email completed Requisition Form to SARC at SARC037@sarctrials.org / leoverman@sarctrials.org
- Include a copy of the Requisition Form in the shipment
- Attach the Exempt Human Specimen label to the side of the box
- Samples must be shipped via FedEx Priority Overnight (with provided label) at room temperature to University of Colorado
- Samples must be shipped overnight on Monday through Thursday for next day delivery to the University of Colorado, Hayashi Lab. If samples must be collected on Friday, please give advance notice to prepare for a Saturday delivery.
- Ship blood samples to:
  
  Masanori Hayashi, MD  
  University of Colorado Anschutz Medical Campus  
  12800 E 19th Ave, Rm 4402K  
  Aurora CO 80045  
  Phone: (303) 724-4634

3.2.5 UGT1A1 Blood Collection

See Table 1 for collection time points. There are no kits for this blood collection

**UGT1A1 sample acquisition and preparation**

- Draw blood into one **4 mL EDTA purple top tube**.
- Invert each tube gently 8 times to mix and prevent clotting.
- Close the tube firmly.
- Refrigerate tube until shipment if not shipped within 2 hours of collection. Apply participant identification to tube (label provided in kit—add patient study ID, collection date, collection time).

**Shipment of UGT1A1 samples (Overnight to NCI)**

- Email NCIBloodcore@mail.nih.gov to notify of shipment
- Samples will shipped overnight at 4 degrees on with a cold pack
3.3. Tumor Biopsy Samples

The pretreatment tumor biopsy should not be completed until after it has been confirmed that the patient meets all other eligibility criteria for this study. Table 2 provides the schedule for biopsies.

<table>
<thead>
<tr>
<th>Time point</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment tumor biopsy</td>
<td>≤ 28 days before Cycle 1, Day 1</td>
</tr>
<tr>
<td>Cycle 1* 18 years old and older with biopsy accessible disease</td>
<td>Day 2, prior to administration of irinotecan</td>
</tr>
<tr>
<td>Cycle 1 (expansion cohort)</td>
<td>Schedule B: Day 2, after irinotecan is administered</td>
</tr>
<tr>
<td></td>
<td>Schedule C: Day 3</td>
</tr>
<tr>
<td></td>
<td>Schedule D: Day 4</td>
</tr>
<tr>
<td></td>
<td>Schedule E: Day 5</td>
</tr>
</tbody>
</table>

*Mandatory for patients 18 years and older with biopsy accessible disease. Optional for patients < 18 years old with or without biopsy accessible disease.

3.3.1. Tumor biopsy sample acquisition and preparation

Biopsy should consist of an excisional or core needle biopsy of at least one piece of tissue equivalent to 1 mm diameter x 5 mm long. 3-6 cores should be taken at each biopsy if possible. Samples should be prepared in order of priority:

B1= Each biopsy will consist of between 3 and 6 cores in the order of priority

1. Core for FFPE
2. Core Snap Frozen
3. Core Fresh Viable
4. Core Viably frozen
5. Core Snap Frozen
6. Core Snap Frozen

B2= Each biopsy will consist of between 3 and 6 cores in the order of priority

1. Core for FFPE
2. Core Snap Frozen
3. Core viably Frozen
4. Core Snap Frozen
5. Core viably Frozen
6. Core snap Frozen

3.3.2. Preparation and shipping of FFPE tumor tissue samples

Specimen Labeling
Label each block with:

- Protocol ID
- Patient ID
- Block Number
- Tissue Type (Primary or Metastatic)
- Date of Procedure

Tissue should be formalin-fixed and paraffin-embedded per standard institutional protocol. General guidelines are below.

- To preserve sample integrity, tissue should be placed in a cassette and into 10% neutral buffered formalin as soon as possible post-biopsy or post-surgery (ideally within 30 minutes) and fixed in formalin for 6 - 72 hours. Samples should then be transferred to 70% ethanol pending paraffin embedding, which will be performed per institutional protocol. Label the tissue as described above.

The total time elapsed between biopsy collection and placement into the formalin is of key importance to biomarker analysis; biopsies should be placed in formalin within 30 min of collection or as soon as possible.

Complete the Paraffin-Embedded Tissue Requisition Form for biopsy tumor sample (Appendix G). Completed requisition form should be uploaded into the database before shipping.

Shipping of FFPE Tumor Samples

- Blocks will be shipped in a padded envelope.
- When shipping slides, place them in a plastic slide holder and stabilize by placing cotton or soft paper under the lid.
- Enter into the database prior to shipment and upload completed Requisition Form (Appendix G). Print to include in shipment
- Complete the Sample Shipment eCRF, enter submit and print the eCRF for your records.
- Each patient sample submitted must be sent with the printed copy of completed Requisition Form (Appendix G); one requisition form per time point) and corresponding pathology report(s) labeled with the patient ID.
- Tape the lid so that it does not pop open during shipment (one piece of tape is enough).
- Wrap the slide holder(s) in bubble wrap or mail in a padded envelope.
- Ship via FedEx Ground (no need for express shipping) using account # 284 417 593.
- Tissue samples will be sent to Dr. Patrick Grohar at the Children’s Hospital of Philadelphia (see address below).
Shipping Address please contact in advance and send tracking number at:

groharp@email.chop.edu
cc: SARC037@sarctrials.org
leoverman@sarctrials.org

Patrick J. Grohar, MD, PhD
Colket Translational Research Building Room 4030
Children’s Hospital of Philadelphia
3501 Civic Center Blvd
Philadelphia, PA 19104

3.3.3. Preparation and shipping of viably frozen tumor tissue samples

**Specimen Labeling**
Label each block with:

- Protocol ID
- Patient ID
- Block Number
- Tissue Type (Primary or Metastatic)
- Date of Procedure

In a sterile environment, carefully dissect the core and separate out obvious necrotic tissue as soon as possible following the procedure.

- Further separate the tissue into sections approximately 2X2X2 mm pieces
- Place each piece into a cryogenic vial in approximately 1 mL of freezing medium (see below).
- Make sure to label the tube.
- Place the cryogenic vial(s) containing the pieces of tissue into a “slow freeze” cryogenic freezing container containing 2-propanol.
- Place in the -80C freezer for 24 hours, removed and freeze in the vapor phase of liquid nitrogen until shipment on dry ice.

Freezing medium is RPMI-1640 supplemented with glutamine, 10% Fetal Bovine Serum and 10% DMSO. To Make Freezing medium: In a sterile environment combine 8 mL of RPMI-1640 containing glutamine with 1 mL of sterile, heat inactivated Fetal Bovine Serum and 1 mL of sterile DMSO.

A completed Viable Frozen Tissue Samples Requisition Form (Appendix H) should be uploaded into the database before shipping (see below instructions for shipping samples).

**Shipping of Viable Frozen Samples:**

All viable frozen samples will be batch shipped with the snap frozen tissue to attn: Dr. Patrick Grohar at CHOP on dry ice in an insulated shipping container using FedEx Priority Overnight delivery service. When shipping frozen samples, leave sufficient room for at least 5 lbs. of dry ice to be included. Specimens from each patient and time point must be properly labeled and placed in separate zip-lock bags prior to packaging for shipment.

1. Pre-fill the chamber of the specimen kit about 1/3 full with dry ice.
2. Place samples for each specimen type and time point in a separate zip-lock bags.
3. Place the samples in the Biohazard envelope containing absorbent material. Put the secondary envelope into a Tyvek envelope. Expel as much air as possible before sealing the envelopes.
4. Place the Tyvek envelope containing frozen specimens into the chamber of the kit and cover the samples with additional dry ice until the chamber is almost completely full. There should be enough dry ice to maintain the samples at -20°C for at least 24 hours).
5. Place the lid on top of the chamber to insulate the samples during shipment.
6. Enter into the database prior to shipment and upload completed Requisition Form (Appendix H).
7. Complete the Sample Shipment eCRF, enter submit and print the eCRF for your records.
8. Each patient sample submitted must be sent with the printed copy of the completed Requisition Forms and corresponding pathology report(s) for the tissue.
9. Close the outer box and tape with filament or other durable sealing tape.
10. Attach a shipping label to the top of the outer box.
11. Complete the dry ice label.
12. Attach the dry ice and Exempt Human Specimen labels to the side of the outer box.
13. Only send samples on Monday through Thursday.
14. Ship via FedEx Priority Overnight using account # 284 417 593
15. Samples will be sent to Dr. Patrick Grohar at the Children’s Hospital of Philadelphia (see address below).

Shipping Address please contact in advance and send tracking number at:

groharp@email.chop.edu
cc: SARC037@sarctrials.org
leoverman@sarctrials.org

Patrick J. Grohar, MD, PhD
Colket Translational Research Building Room 4030
Children’s Hospital of Philadelphia
3501 Civic Center Blvd
Philadelphia, PA 19104

3.3.4. Preparation and shipping of snap frozen tumor tissue samples

Specimen Labeling
Label each block with:

- Protocol ID
- Patient ID
- Block Number
- Tissue Type (Primary or Metastatic)
- Date of Procedure

Tumor should be placed in pre-labeled pre-chilled 2 mL cryovials and snap-frozen in the vapor phase of liquid nitrogen (do not submerge the tissue in liquid nitrogen) or on dry ice. Immediately store
3.3.5. Preparation and shipping of viable tumor tissue samples

1. Fresh tumor tissue (1 x 1 x 1 cm or greater, up to 2 cm) should be aseptically placed into a 50-ml conical centrifuge tube containing at least 25-30 ml of pre-prepared, chilled transport media, hypothermisol. The provided kit will include the 50-ml conical centrifuge tube with transport media.

2. Tighten the cap of the 50-ml tube and refrigerate the sample in transport media until shipment. Ship fresh tissue at the next available FedEx pickup time for delivery to Dr. Ryan Roberts at Nationwide Children’s Hospital within 24 hours of tissue collection.

3. Record the following labeling information on the tube:
   a) Protocol ID
   b) Patient Identification Number
   c) Date of Procedure
   d) Tissue type (Primary or Metastatic)
   e) Sample Collection Date and time

4. Fill out the Fresh Tumor Sample Requisition Form (Appendix F) and send this sheet along with sample.
5. Prior to shipment, confirm that the cap of the 50-ml tube is tightened and cover in parafilm. Place the tube in a small zip lock bag. Manually seal the bag. Place the bagged tube into a Biohazard envelope with absorbent material (provided in the kit), expel the excess air, and seal.

6. Ship the sample (including the completed Fresh Tumor Sample Requisition Form in (Appendix F) overnight via FedEx. Samples can be shipped out Monday through Thursday for arrival at Dr. Ryan Roberts’ Lab Monday through Friday:

If sample must be shipped Friday for Saturday delivery, include to the following delivery instructions to the FedEx courier:

PLEASE DO NOT DELIVER TO THE DOCK
Upon arrival, call 614-746-1623 (backup 614-746-1273)
We will meet you at the research building on Raymond St adjacent to the dock
If you call ahead, we will be waiting when you arrive

7. Sample will be shipped at room temperature

8. Email SARC037@sarctrials.org, leoverman@sarctrials.org and Amy.Gross@nationwidechildrens.org to inform them of the pending shipment. Include in the email the date of the scheduled shipment and expected delivery day and date. Make sure to send a copy of the air bill, with the tracking # clearly visible. Please also include tracking # notifications.

Shipment of viable tumor biopsy samples

- Complete the Requisition Form for Fresh/Viable Tumor Biopsy Sample (Appendix F).
- Prior to shipping, email completed Requisition Form to SARC SARC037@sarctrials.org, leoverman@sarctrials.org;
  cc: Amy.Gross@nationwidechildrens.org
  cc: local study manager/coordinator
- Include a copy of the Requisition Form in the shipment.
- Attach the Exempt Human Specimen label to the side of the box
- Samples must be shipped overnight for next day delivery to Dr. Ryan Roberts at Ohio State University.
- Ship tumor tissue samples to the following address:
  Dr. Ryan Roberts MD
  Attn: Amy Gross
  Nationwide Children’s Hospital

Notification of shipment:

- Send a notification of shipment email to the SARC RPM with the following information (see section 1.2 for contact information):
  - Date of shipment
  - Patient ID and initials
  - Type of sample

- Ship tumor tissue samples to the following address:
  Dr. Ryan Roberts MD
  Attn: Amy Gross
  Nationwide Children’s Hospital
4. **18F-FLT PET**

Along with the pre-treatment biopsy, patients will undergo the 18F-FLT scans. Patients will also receive a second 18F-FLT scan with biopsy 18-24 hours after trabectedin administration and before irinotecan is administered.

Once the recommended RD is established, an expansion cohort will be opened and 18F-FLT scans with biopsy (if necessary) will be performed on the first cycle

- 24 hours after trabectedin, 24 hours after irinotecan (3 patients)
- 48 hours after trabectedin, 24 hours after irinotecan (3 patients)
- 72 hours after trabectedin, 48 hours after first irinotecan, before second irinotecan (3 patients)
- 96 hours after trabectedin, 72 hours after first irinotecan, 24 hours after second irinotecan (3 patients)

For the phase II portion, a total of nine patients, 18 years and older, receiving treatment at a center performing 18F-FLT scans, or for whom it is feasible to travel to a site performing 18F-FLT scans, who meet eligibility criteria with biopsy accessible disease receiving 18F-FLT scans will be biopsied at 2 timepoints. All nine patients will have a biopsy and 18F-FLT scan at no more than 28 days before cycle. The second biopsy and 18F-FLT will be completed according to either Schedule A, B, or C (3 patients enrolled in each Schedule in this order) as noted below:

Schedule A: cycle 1, day 2, 12-24 hours after trabectedin administration and before irinotecan is administered and before or after 18F-FLT scan (3 patients)

OR

Once Schedule A has completed enrollment patients will have the second scan and biopsy per Schedule B on day 3, 48 hours +/- 12 hours after trabectedin and before or after 18F-FLT scan (3 patients)

OR

Once Schedule B has completed enrollment, patients will have the second scan and biopsy per Schedule C on day 8. The biopsy will be performed before or after 18F-FLT scan (3 patients)

4.1. **18 F-FLT Supply**

The 18 F-FLT tracer will be compounded by the University of Pennsylvania Department of Radiology, Nuclear Medicine Division, Cyclotron Facility and delivered by a courier service.

4.2. **18F-FLT Ordering**

Orders for the 18F-FLT dose may only be placed by sites approved to perform the 18F-FLT PET scans.

Orders should not be placed until consent is documented and eligibility is confirmed. Orders must be placed up to 2 business days in advance of delivery, during the hours of 9 AM to 5 PM, Monday through Friday, excluding holidays. For example, if dose delivery is desired for Thursday, the order must be received at Penn by 5 pm on Monday, which is two full business days (Tuesday and Wednesday) prior to the desired delivery date.)
Patients receiving the 18F-FLT PET scan will receive 2 doses. Each dose must be ordered separately in accordance with the 18F-FLT PET schedule as described in the protocol (Section 9.2 18F-FLT PET). Cancellation requests must be received by the facility by 5pm one full business day prior to the desired delivery date (E.g., if dose delivery is desired for Thursday, the cancellation must be received by Penn by 5pm on Tuesday, which is one full business day (Wednesday) prior to the desired delivery date.

Orders may be placed by emailing a completed 18F-FLT Dose order from (Appendix R) to address below:

Penn Cyclotron Facility
Sharon Lee, Penn Cyclotron Facility Manager
RP_ORDERS@lists.upenn.edu
cc: LeeHsi@pennmedicine.upenn.edu
(ph) 215-573-9456

4.3. 18F-FLT Delivery

The 18F-FLT tracer will be compounded on the day of delivery and released no earlier than 10:30 AM. The 18F-FLT tracer will be delivered by a courier designated by the UPenn Cyclotron facility.

4.4. 18F-FLT Administration

The 18F-FLT tracer will be administered according to institutional standards at a dose of 0.07 mCi/kg. with a maximum dose of 5 mCi.

The PET imaging will be from head to toe with a scan time of 3 minutes per bed position.

5. Procedure for Collection and Submission of Images for Central Review

All required study images (CT, MRI, PET scans) will be reviewed by central radiology. All collected images will be uploaded to a secure database when the patient completes treatment and is off study (refer to section 2.4).

6. Drug Administration and Supply

Patients will be administered trabectedin and irinotecan in clinic using the following schedule:

Trabectedin:  Day 1 of each cycle
Irinotecan:  Days 2 and 4 of each cycle

Cycles are 21 days.

6.1. Trabectedin Supply

Trabectedin will be packaged and shipped to the site/institutional pharmacy by RxCrossroads by McKesson.

6.2. Initial Supply

Initial trabectedin supply at each site will be ordered at the time of site activation. SARC will work with the site pharmacist on placing the initial order and on determining site’s initial allotment based on anticipated accrual.
To receive the initial supply of trabectedin, please complete the Drug Supply Form (Appendix J) and email (preferred) or fax it to the SARC RPM (see section 1.2 for contact information).

SARC will authorize the initial supply shipment after the following occur:

- All regulatory documents have been received from the site
- Contract with the site has been fully executed
- Site initiation visit has been completed

Requests for drug supply should be submitted at least 5-7 business days before the desired delivery date.

SARC requires a confirmation of receipt via email for all study drug orders.

6.3. Additional Trabectedin Supply

When needed, site pharmacist (or an authorized designee) may request additional supplies of trabectedin for their participating sites. Additional supply must be ordered within recommended time frame (please see below) to avoid delays in patients' treatment.

The Drug Supply Form (Appendix J) should be submitted to SARC via email (preferred) or fax (see Section 1.2 for contact information).

SARC will review the form and, approve it, and forward to McKesson.

Requests should be submitted to SARC at least 5-7 business days before the desired delivery date. McKesson will ship within 2-3 days of receiving the Drug Supply Form. Delivery can be expected 2 days after request was received by McKesson. Shipping is not available on Fridays or weekends; however, overnight shipping can be requested.

SARC requires a confirmation of receipt via email for all study drug orders.

6.4. Trabectedin Storage

Trabectedin should be stored in a refrigerator at 2°C to 8°C (36°F-46°F), protected from light until use.

6.5. Study Drug Accountability

Refer to Section 8.2 in the protocol for information on agent accountability and details on the drug dispensing log.

Drug dispensing logs must be kept up to date as copies of these logs may be occasionally requested by SARC for remote monitoring purposes. These logs will be requested at the end of the study.

6.6. Destruction of Trabectedin

All unused study drug (not dispensed to patients) must be destroyed at study closure (Appendix K).

6.7. Irinotecan

Irinotecan is commercially available and will be obtained through each site’s typical procedures for this agent. Storage, preparation, and dosage will be according to institutional standards. Irinotecan will be administered intravenously per section 5 of the protocol.
7. Protocol Deviations

Any events inconsistent with the protocol are considered protocol deviations and must be reported as such on the Protocol Deviation Form (Appendix L) as soon as possible. Submit the form to SARC via email (preferred) or fax (see section 1 for contact information).

8. Adverse Event Reporting

All SARC investigators will use the same Adverse Event (AE) definitions as defined in Section 7 of the protocol.

AE reporting applies to all Aes that occur during the study from the date of enrollment until 30 days after the last dose of Trabectedin and Irinotecan. The site PI must assess an AE for attribution/causality to the study drug. Due to multiple study agents (trabectedin, irinotecan, and 18F-FLT) each agent causality will be documented separately and documented within the study database on the Adverse Event Log eCRF in the SARC037 study database.

8.1. Serious Adverse Event Reporting

Any clinical adverse event or abnormal laboratory test value that is serious (SAE) must be reported within 24 hours of the site PI becoming aware of the event. All reporting must be done by the site PI or authorized staff member (i.e. on the signature list) to confirm the accuracy of the report. All SAEs must be reported on Form FDA 3500 A (MedWatch) and, along with the completed SAE Email/Fax Coversheet, must be emailed (preferred) or faxed to SARC. The MedWatch Form and the SAE Email/Fax Coversheet are provided in Appendix M-N. The site PI must assess and record the relationship of each SAE to each study drug. An initial SAE report, with as much information as is currently available, must be submitted.

All SAEs should be reported at the participating sites according to their institutional guidelines. The original SAE Form must be kept on file at the study site.

Please note: All SAEs occurring during the study, from the date patient is enrolled until 30 days after the last study treatment, must be reported to SARC. SAEs that are considered to be likely related to study drug(s) or study participation must be reported even if they occur outside of the SAE detection period (after the 30-days period).

8.2. Follow-up Reports

If only limited information was available at the time of the initial report, follow-up reports are required and should be forwarded to SARC. Complications or progression of the initial SAE must be reported as follow-up to the original event within 24 hours of the investigator receiving the follow-up information.

Follow-up information is reported by its addition to the original SAE report. A new SAE Email/Fax Coversheet must be submitted with the follow-up MedWatch form with the appropriate follow-up number clearly indicated.

8.3. Pregnancy Reporting

Pregnancy occurring during a patient’s participation in this trial must be reported to the investigator within the same timelines as an SAE (within 24 hours). See Section 7.1.4.3 of the protocol.

9. Patient Travel and Accommodation
There are three partners to support patient travel and accommodation to participate in this trial. This support may be sought to travel patients to a participating site and to travel patients from a participating site to the NCI for cycle 1, and back to original participating site. The partner organizations and details to contact are listed below and in the associated appendixes: NCI, Alex’s Lemonade Stand, Lazarex Cancer Foundation.

One patient from each of the dose escalation cohorts will travel to the NCI for the first cycle of treatment. All patients in the expansion cohort will travel to the first cycle of treatment. After cycle 1, patients will return to their home location for the remaining cycles, up to 26 cycles.

Patients enrolling in the as part of the dose escalation cohort, the site will contact the SARC RPM (Section 1, Contact Information) to confirm dose level assignment and 18F-FLT PET designation. Please note: patients designated to receive the 18F-FLT PET will travel to the NCI for the first Cycle of treatment. SARC will coordinate between the site and NCI for patients needing to travel for Cycle 1.

Patients who are identified as eligible will follow the workflow below. Patients or their parent/guardian are encouraged to request a financial assessment. A social worker from the NCI will contact the patient or patient guardian and conduct a financial assessment to determine financial assistance status. There are travel support options for patients who meet the criteria below.

9.1. Travel to the NCI

All patients (plus a guardian for patients <22 years old) traveling to NIH will receive assistance with travel. Additional support is available to patients who qualify for financial assistance. An evaluation will be completed by an NIH social worker when requested.

Please note, travel must be booked directly through the NIH travel agent AFTER the patient has been registered with NIH by the study coordinator.

Please contact Elaine Thomas, research nurse and study coordinator at NIH, for additional information or to request a financial assessment:

Elaine Thomas, RN
Research Nurse Specialist
Elaine.Thomas@nih.gov
240-760-6191
Fax: 301-451-5746

Patients ≤ 21 years old are eligible to apply for travel support through Alex’s Lemonade Stand Travel for Care program (APPENDIX O). Applications must be submitted by a member of the oncology care team via the portal: https://www.alexslemonade.org/childhood-cancer/for-families/travel-for-care

For questions and extenuating circumstances, please reach out to Family Services directly: FamilyServices@AlexsLemonade.org or 610-649-3034.

Patients of all ages are eligible to apply for the Lazarex Cancer Foundation Lazarex Financial Reimbursement Program (FRP) (APPENDIX P). Applications must be submitted in partnership with a member of the oncology care team by contacting the in-take team via fax (925-552-7305) or email (Rnoonan@lazarex.org).
Lazarex FRP may be sought for patients seeking support in traveling to the NCI or traveling to the participating site for care.

9.2. Patient Accommodation at the NCI

Patients traveling to the NCI are eligible for travel and accommodation assistance. To request assistance for patients contact Elaine Thomas (cc:Amanda Carbonell) at Elaine.Thomas@nih.gov; Amanda.Carbonell@nih.gov OR 240-760-6191.
Appendix A: Site Screening Log Form
SARC037 Site Screening Log

SARC037: A Phase I Study to Evaluate the Safety of Trabectedin Administered as a 1-Hour Infusion in Ewing Sarcoma Patients in Combination with Low Dose Irinotecan and 3’-Deoxy-3’-18F Fluorothymidine (18F-FLT) Imaging

Site Name: _________________________________________________

<table>
<thead>
<tr>
<th>Patient Initials</th>
<th>Patient Date of Birth</th>
<th>Was Consent Signed? (Yes/No)</th>
<th>Date of Consent</th>
<th>Is the Patient Eligible (Yes/No)</th>
<th>If No, Specify the Reason</th>
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Only patients who meet all eligibility criteria will be entered into the Medidata Rave database

SARC Contact Information:
SARC037: SARC037@sarctrials.org
(cc) eantalis@sarctrials.org
Phone: (734) 930-7600
Fax: (734) 930-7557
Appendix B: Eligibility Checklist
**SARC037 Eligibility Checklist (Page 1 of 2)**

Patient Study ID: ________________________________ Patient Initials: ___________

**Inclusion Criteria:**

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Yes</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td><strong>Age ≥ 6</strong></td>
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<tr>
<td>Histologically confirmed recurrent or relapsed Ewing sarcoma with measurable disease</td>
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<td>Documented EWS-FLI1 fusion and fusion type</td>
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<tr>
<td>Adequate performance status Lansky or Karnofsky ≥ 50% or ECOG 0-2</td>
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<td><strong>Adequate organ function defined as:</strong></td>
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<td>- ALT/AST ≤ 125 U/L</td>
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<td>- Total bilirubin ≤ 1.5 x ULN (except Gilbert’s syndrome, &lt;3 x ULN)</td>
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<td>- Creatinine ≤ 1.5 x ULN or clearance (Cockcroft-Gault formula for patients ≥ 18 years; Schwartz equation for patients &lt; 18 years) ≤ 50 mL/min/m²</td>
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<tr>
<td>- Adequate bone marrow function (ANC ≥ 1000/µL (independent of growth factor support within two weeks of screening laboratories); PLTs ≥ 75,000/µL (without platelet transfusion within previous 7 days of screening laboratories); Hb ≥ 8 g/dL)</td>
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<td>- LVEF or shortening fraction ≥ LLN</td>
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<td>- CPK ≤ 2.5 x ULN</td>
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<td><strong>Written, voluntary informed consent</strong></td>
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<tr>
<td><strong>Negative HCG at enrollment and uses contraception; if male, partner uses contraception</strong></td>
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<tr>
<td><strong>Both male and female post-pubertal study subjects agree to use birth control methods during treatment and for 90 days after treatment is stopped. These methods include double barrier method, total abstinence (no sex), oral contraceptives (“the pill”), an intrauterine device (IUD), levonorgestrol implants (Norplant), or medroxyprogesterone acetate injections (Depo-provera shots).</strong></td>
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<tr>
<td><strong>For patients ≥ 18 years, disease is accessible to biopsy, or biopsy is contraindicated (requires study PI approval) Patients enrolled in the phase II portion must have at least one site of measurable disease on CT or MRI as defined by RECIST 1.1</strong></td>
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<tr>
<td><strong>Recovered from all hematological effects of past therapy, ≥ 3 weeks for myelosuppressive therapy, ≥ 2 weeks for radiation or surgery</strong></td>
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<tr>
<td><strong>Note:</strong></td>
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</table>

**Note:** Recovered from all hematological effects of past therapy, ≥ 3 weeks for myelosuppressive therapy, ≥ 2 weeks for radiation or surgery.
# SARC037 Eligibility Checklist (Page 2 of 2)

Patient Study ID: ________________________________ Patient Initials: ___________

Exclusion Criteria:

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
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</thead>
<tbody>
<tr>
<td>Prior systemic therapy with trabectedin or lurbinectedin</td>
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<td>CNS metastases to the brain parenchyma, but not bony lesions</td>
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<tr>
<td>bleeding diathesis</td>
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<td>pregnant or breastfeeding</td>
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<td>Currently receiving another investigational drug, anticancer agent, or OTC herbal supplement with potential hepatotoxicity (see protocol for full list)</td>
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<td>Clinically significant uncontrolled infection</td>
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<td>Known active liver disease such as Hepatitis A, B or C</td>
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I have reviewed all inclusion/exclusion criteria and confirm that this patient is eligible for this study.

Site Principal or Co-Principal Investigator:

Print Name: ______________________________

Signature: ______________________________

Date: ______________________________
Appendix C: PK Plasma Sample Requisition Form (Green top tubes)
Appendix C: PK Plasma Sample Requisition Form (Green Top)

Batch ship samples after day 8 collection

SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
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<tbody>
<tr>
<td>PATIENT NUMBER:</td>
</tr>
<tr>
<td>PATIENT INITIALS:</td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
</tr>
<tr>
<td>SITE EMAIL &amp; PHONE NUMBER:</td>
</tr>
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SECTION 2

Ensure that the specimen labels include the following information: protocol ID, patient ID and initials, specimen type (Whole), collection time point (HH:MM) and collection date (MM-DD-YY).

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<thead>
<tr>
<th>(MM/DD/YYYY)</th>
<th>(HH:MM)</th>
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<tbody>
<tr>
<td>☐ Prior to 1st Tx</td>
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<tr>
<td>☐ 30 min. post</td>
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<td>☐ 1 hr post</td>
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<td>☐ 168 hours post</td>
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# of specimens shipped

SECTION 3

<table>
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<th>Ship to: Paula Carter</th>
</tr>
</thead>
<tbody>
<tr>
<td>c/o NCI Blood Processing Core</td>
</tr>
<tr>
<td>10 Center DriveRoom 5A08</td>
</tr>
<tr>
<td>Bethesda, MD 20892</td>
</tr>
<tr>
<td>Telephone: 240-760-6180</td>
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</table>

<table>
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<tr>
<th>Date of Shipment:</th>
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<tr>
<th>FedEx account number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>___________</td>
</tr>
</tbody>
</table>
Appendix D: Circulating Tumor DNA Sample Requisition Form
Appendix D: Circulating Tumor DNA Sample Requisition Form

### SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT NUMBER:</td>
<td></td>
</tr>
<tr>
<td>PATIENT INITIALS:</td>
<td></td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
<td></td>
</tr>
<tr>
<td>SITE CONTACT NAME:</td>
<td></td>
</tr>
<tr>
<td>CONTACT EMAIL &amp; PHONE NUMBER:</td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 2

Ensure that the specimen labels include the following information: protocol ID, patient ID, specimen type, time point, collection time (HH:MM) and collection date (MM-DD-YY).

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Collection Date</th>
<th>Collection Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Prior to 1st Tx</td>
<td>(MM/DD/YYYY)</td>
<td>(HH:MM)</td>
</tr>
<tr>
<td>☐ Day 2/ 24 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Cycle 1, Day 8 (168 hours post)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Cycle 2, Pre-treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Progression</td>
<td></td>
<td></td>
</tr>
<tr>
<td># of specimens shipped</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 3

<table>
<thead>
<tr>
<th>Ship to:</th>
<th>Dana-Farber Cancer Institute</th>
<th>Attn: Kelly Klega</th>
<th>450 Brookline Avenue</th>
<th>Boston, MA 02215</th>
<th>Phone: 321-514-9821</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Shipment:</td>
<td></td>
<td>FedEx tracking number:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FedEx tracking number:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix E: Circulating Tumor Cell (CTC) Sample Requisition Form
Appendix E: Circulating Tumor Cell (CTC) Sample Requisition Form

Please use a separate requisition form for each time point.

<table>
<thead>
<tr>
<th>SECTION 1</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SITE NAME &amp; NUMBER:</strong></td>
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<td><strong>PATIENT NUMBER:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>PATIENT INITIALS:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>INVESTIGATOR:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>SITE CONTACT NAME:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>CONTACT EMAIL &amp; PHONE NUMBER:</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SECTION 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ensure that the specimen labels include the following information: protocol ID, patient ID, specimen type, time point, collection time (HH:MM) and collection date (MM-DD-YY).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(MM/DD/YYYY)</td>
</tr>
<tr>
<td>☐ Prior to 1st Tx</td>
<td></td>
</tr>
<tr>
<td>☐ Day 2/24 hrs</td>
<td></td>
</tr>
<tr>
<td>☐ Cycle 1, Day 8 (168 hours post)</td>
<td></td>
</tr>
<tr>
<td># of specimens shipped</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SECTION 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ship to:</strong></td>
<td><strong>Date of Shipment:</strong></td>
</tr>
<tr>
<td>Masanori Hayashi, MD</td>
<td>_____________</td>
</tr>
<tr>
<td>University of Colorado Anschutz Medical Campus</td>
<td></td>
</tr>
<tr>
<td>12800 E 19th Ave, Rm 4402K</td>
<td></td>
</tr>
<tr>
<td>Aurora CO 80045</td>
<td></td>
</tr>
<tr>
<td>Phone: (303) 724-4634</td>
<td></td>
</tr>
</tbody>
</table>
Appendix F: Fresh Viable Tumor Sample Requisition Form
Appendix F: Fresh (VIABLE) Tumor Sample Requisition Form

SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT NUMBER:</td>
<td></td>
</tr>
<tr>
<td>PATIENT INITIALS:</td>
<td></td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
<td></td>
</tr>
<tr>
<td>SITE CONTACT NAME:</td>
<td></td>
</tr>
<tr>
<td>SITE EMAIL &amp; PHONE NUMBER:</td>
<td></td>
</tr>
</tbody>
</table>

SECTION 2

Must ship priority overnight in 50 ml conical tube containing 15 ml of hypothermosol.

Ensure that the specimen labels include the following information: protocol ID, patient ID, date of procedure, and tissue type (primary or metastatic). Note: Patient identifiers such as name and date of birth must be removed from pathology report and specimen.

☐ Pre-Treatment

# of specimens:_______________________

Date of procedure: _____/_____/_____ (MM/DD/YYYY)

Time of collection:_______________(HH:MM)

Person responsible for obtaining sample:_______________________

SECTION 3

<table>
<thead>
<tr>
<th>Ship To: Ryan Roberts</th>
<th>Date of Shipment:</th>
<th>FedEx tracking number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATTN: Amy Gross</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nationwide Children’s Hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>700 Children’s Drive, WA5108</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Columbus, Ohio 43205</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telephone: 614-355-2985 or 614-722-2996</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix G: Paraffin-Embedded Tissue Requisition Form
Appendix G: Paraffin-Embedded Tissue Requisition Form

Please use a separate Requisition Form for each time point.

SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>PATIENT INITIALS:</td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
</tr>
<tr>
<td>SITE CONTACT NAME:</td>
</tr>
<tr>
<td>SITE CONTACT EMAIL &amp; PHONE NUMBER:</td>
</tr>
</tbody>
</table>

SECTION 2

Samples should be formalin fixed and paraffin embedded as a block.

Ensure that the specimen labels include the following information: protocol ID, patient ID, date of procedure, block number, and tissue type (primary or metastatic). Note: Patient identifiers such as name and date of birth must be removed from pathology report and specimen.

- ☐ Pre-Treatment
- ☐ Cycle 1

# of specimens: _______________________
Date of procedure: ______/_____/______ (MM/DD/YYYY)
Time of collection: ____________________ (HH:MM)
Person responsible for obtaining sample: ________________________

SECTION 3

| Ship To: Patrick J. Grohar, MD, PhD |
| Colket Translational Research Building |
| Room 4030 |
| Children’s Hospital of Philadelphia |
| 3501 Civic Center Blvd |
| Philadelphia, PA 19104 |
| Date of Shipment: | FedEx tracking number: |
| ______________________ | ______________________ |
Appendix H: Viable Frozen Tissue Requisition Form
Appendix H: Viable Frozen Tissue Requisition Form

Please use a separate Requisition Form for each time point.

SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT NUMBER:</td>
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</tr>
<tr>
<td>PATIENT INITIALS:</td>
<td></td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
<td></td>
</tr>
<tr>
<td>CONTACT NAME:</td>
<td></td>
</tr>
<tr>
<td>SITE CONTACT EMAIL &amp; PHONE NUMBER:</td>
<td></td>
</tr>
</tbody>
</table>

SECTION 2

Ensure that the specimen labels include the following information: protocol ID, patient ID, date of procedure, and tissue type (primary or metastatic). Note: Patient identifiers such as name and date of birth must be removed from pathology report and specimen.

- ☐ Pre-Treatment
- ☐ Cycle 1

# of specimens: __________________
Date of procedure: _____ / _____ / _____ (MM/DD/YYYY)
Time of collection: ______ / ______ (HH:MM)
Person responsible for obtaining sample: ___________________

SECTION 3

<table>
<thead>
<tr>
<th>Ship To:</th>
<th>Date of Shipment:</th>
<th>FedEx tracking number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patrick J. Grohar, MD, PhD</td>
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</tr>
<tr>
<td>Colket Translational Research</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building Room 4030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3501 Civic Center Blvd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philadelphia, PA 19104</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix I: Snap Frozen Tissue Requisition Form
Appendix I: Snap Frozen Tissue Requisition Form

Please use a separate Requisition Form for each time point.

SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
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</thead>
<tbody>
<tr>
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<tr>
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<td>INVESTIGATOR:</td>
</tr>
<tr>
<td>CONTACT NAME:</td>
</tr>
<tr>
<td>SITE CONTACT EMAIL &amp; PHONE NUMBER:</td>
</tr>
</tbody>
</table>

SECTION 2

Ensure that the specimen labels include the following information: protocol ID, patient ID, date of procedure, and tissue type (primary or metastatic). Note: Patient identifiers such as name and date of birth must be removed from pathology report and specimen.

<table>
<thead>
<tr>
<th>Pre-Treatment</th>
<th>Cycle 1</th>
</tr>
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<tbody>
<tr>
<td># of specimens: ___________________</td>
<td></td>
</tr>
<tr>
<td>Date of procedure: <em><strong><strong>/</strong></strong></em>/______ (MM/DD/YYY)</td>
<td></td>
</tr>
<tr>
<td>Time of collection: ________________ (HH:MM)</td>
<td></td>
</tr>
<tr>
<td>Person responsible for obtaining sample: ________________</td>
<td></td>
</tr>
</tbody>
</table>

SECTION 3

<table>
<thead>
<tr>
<th>Ship To: Patrick J. Grohar, MD, PhD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colket Translational Research Building</td>
</tr>
<tr>
<td>Room 4030</td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
</tr>
<tr>
<td>3501 Civic Center Blvd</td>
</tr>
<tr>
<td>Philadelphia, PA 19104</td>
</tr>
<tr>
<td>Date of Shipment: ________________</td>
</tr>
<tr>
<td>FedEx tracking number: ________________</td>
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</tbody>
</table>
Appendix J: Trabectedin Drug Supply Form
# Appendix J: Trabectedin Drug Supply Form

Request for Drug Shipment to Site

<table>
<thead>
<tr>
<th>Protocol Number</th>
<th>Site Name (as Institution) and Number: ___________________________</th>
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</thead>
<tbody>
<tr>
<td>SARC037</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigator Name:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigator Address:</th>
<th>Pharmacy Address – Where Supplies Should Be Delivered:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(If Different from Investigator Address and Contact)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pharmacy Contact:</th>
<th>Telephone Number:</th>
<th>E-mail (if available):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DRUG REQUIRED:</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Study Drug:</td>
<td>Trabectedin</td>
</tr>
<tr>
<td>Strength/ Dose Form:</td>
<td>mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quantity Requested :</th>
</tr>
</thead>
<tbody>
<tr>
<td>(number of bottles)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Comments:</th>
</tr>
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<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

Please email or fax this document to the following at SARC office:
Email: SARC037@sarctrials.org; leoverman@sarctrialsorg
Fax: 734-930-7557

For SARC Office use only:

SARC verifies that all required regulatory and contractual documentation for this Site/Study is complete:

<table>
<thead>
<tr>
<th>Signature:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Date:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>
Appendix K: Unused Study Drug Disposition Form
Appendix K: SARC037 Unused Study Drug Disposition Form

**Destruction Confirmation**

<table>
<thead>
<tr>
<th>Study Drug Provided</th>
<th>Study Drug Unused</th>
<th>Study Drug Destroyed</th>
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</thead>
<tbody>
<tr>
<td></td>
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</tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I hereby confirm that the product described above was destroyed on:

---

**Date of product destruction**

Witness (Pharmacist of PI) ______________________________________
(Print name)
Witness Signature: _____________________________________________
Telephone Number: _____________________________________________
Fax Number: _________________________________________________
E-mail: _____________________________________________________

Upon completion, email (preferred) or fax this form to:

SARC037@sarctrials.org
Lindsay Overman: leoverman@sarctrials.org
Fax: 734-930-7557
Appendix L: Protocol Deviation Form
Appendix L: SARC037 Protocol Deviation Form

GENERAL INFORMATION
Protocol No.: SARC037
Protocol Version/Amendment No.: ____________________________
Site/Institution Name: _______________________________________
Site Principal Investigator Name: ______________________________
Date the Deviation Occurred: _________________________________
Date of Deviation Discovery: _________________________________
Date of Deviation Report: ________________________________

PATIENT INFORMATION
Patient Study ID: __________________________ Patient Initials: __________

DEVIAITION INFORMATION

Protocol Deviation: Departure from the defined procedures set forth in the IRB-approved protocol that has not been reviewed or approved in advance of the occurrence. Designation of major or minor violation will be determined based on impact on subject’s rights, safety, or welfare, or the integrity of the data results.

 Briefly describe the protocol deviation [attach relevant page from protocol and any supporting documentation, i.e. medical record, dictation, etc., if applicable]

REPORTING INFORMATION
Was IRB notified?  Yes, date notified: _______________
 No, explain: __________________
CORRECTIVE/PREVENTATIVE MEASURES:
Briefly describe corrective/preventative measures that have been developed/implemented to prevent similar violation from occurring in the future; NA if not applicable.

FORM COMPLETED BY:
Name: ____________________________________  Title: ____________________________________
Signature: ________________________________  Date: __________________

SITE PRINCIPAL INVESTIGATOR’S SIGNATURE
Signature: ________________________________  Date: __________________

Please email a completed copy of this form to SARC at email or fax it to 734-930-7557. Please retain the original with the patient’s source documentation.

STUDY PRINCIPAL INVESTIGATOR’S SIGNATURE
Signature: ________________________________  Date: __________________
Appendix M: SAE Email/Fax Coversheet
SAE Coversheet

Email (preferred) or fax within 24 hours of site PI becoming aware of event:

SARC RPM: Lindsey Overman
email: alerts@sarctrials.org; SARC037@sarctrials.org; leoverman@sarctrials.org
Fax: (734) 930-7557

<table>
<thead>
<tr>
<th>Study Title:</th>
<th>SARC037:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site PI Name:</td>
<td></td>
</tr>
<tr>
<td>Patient Study ID:</td>
<td></td>
</tr>
<tr>
<td>Adverse Event (CTCAE v 4.03)</td>
<td></td>
</tr>
</tbody>
</table>
| Adverse Event Grade: | Trabectedin
☑ Yes
☐ No
| Adverse Event Causality: | Irinotecan
☑ Yes
☐ No |
| Type of Report (Check one) | ☑ Initial ☐ Follow-up #___________ |

All serious adverse events will be reported and documented on Form FDA 3500 A (MedWatch Form). Please email or fax completed MedWatch Form along with this Email/Fax Coversheet.
Appendix N: MedWatch Form FDA 3500A


Please refer to the link to the most up-to-date version of the MedWatch Form for Industry.
Appendix O: Alex’s Lemonade Stand Travel for Care
Travel For Care

Made possible with the support of TD Bank, Rita’s Water Ice, Northwestern Mutual and other private donors.

The mission of ALSF’s Travel For Care program is to ensure children battling childhood cancer have the financial assistance needed to travel to clinical trials, experimental therapeutics, or treatment innovations not currently available at their local institution.

- Child must be diagnosed with cancer or a cancer predisposition (Beckwith-Wiedemann syndrome, Histiocytosis, Li-Fraumeni syndrome, Myelodysplastic syndrome (MDS), Post-Transplant Lymphoproliferative Disorders (PTLD), etc.).
- Child’s original diagnosis must be before age 18, and child must currently be under age 21.
- Patient must be in active oncology treatment and one of the following:
  1. Experiencing a pediatric oncology relapse
  2. Enrolling in or currently enrolled in a clinical trial for active oncology treatment intervention
  3. Receiving a treatment intervention that is not considered standard therapy (e.g.: Proton Beam Therapy, MIBG, etc.)
- Travel for Care is not meant to be the sole source of travel assistance for a family to get to treatment.
- All applications must be submitted by a member of the patient’s oncology treatment team.
- Referrals must be completed entirely and truthfully; false or misleading information will result in an automatic denial.

Things to know before applying:
- Travel For Care provides up to $4,000 annually ($8,000 for patients enrolled in ALSF-funded trials) in assistance as long as all eligibility criteria are met.
- Family’s estimated annual household income at the time of request must be less than $100,000.
- Travel assistance is intended for the patient and 1 caregiver to get to treatment.
- ALSF pays travel vendors directly: we cannot reimburse travel expenses, pay for travel that has already taken place, or cover reservations made through a third party (Expedia, Travelocity, etc.).
- At this time, assistance is only available for travel within the US and Canada.
- Please provide as much lead time on travel dates as possible.
- ALSF requires a referral for each request for travel assistance. Requests must be submitted through our secure online application portal: [http://alstapps.force.com](http://alstapps.force.com)
- We process applications within 1 business day during our office hours: 9AM – 5PM Eastern Standard Time.

The program does not assist with:
- Travel for second opinions (i.e. cancer diagnosis has not been confirmed), integrative therapy, follow up appointments after active treatment is complete, and non-cancer treatments (dentist, PT, etc.).
- Expenses that are not travel related (mortgage, rent, utilities, childcare, etc.).
- Travel for visitations.

For Lodging Requests:
- Charity lodging (such as Ronald McDonald House) must be accessed first, unless there are mitigating circumstances (Please note, ALSF does not cover donations to RMH per their website’s statement: “The RMHC Global Policy is that families are never turned away; if it’s not possible to pay, the fee is waived.”).
- Patient must reside at least 2 hours or 100 miles from treatment facility.
- Please include exact dates for lodging.
- ALSF provides funding directly to hotels for room and tax only: incidentals will need to be covered by the family or hospital.
- Reservations must be made directly with the hotel; most hotels offer a deeply discounted medical rate.
- Lodging credit cards are shipped via FedEx; Please include the best address to receive the FedEx delivery.

For Airfare Requests:
- ALSF books commercial airline for the patient and 1 caregiver.
- Airfare requests MUST include: full legal names and birthdates of both travelers, departure and arrival airports, country and state of residence, and exact dates of travel.
- Please indicate if there are special accommodations needed for the patient upon arrival to the airport (i.e. wheelchair assistance).

For Gas Requests:
- Gas assistance is approved based solely on mileage for driving the patient to/from active cancer treatment.
- Travel must be a minimum of 700 miles
- Assistance amount formula: (# miles per round trip) / (20 - avg mileage per gallon) x (local cost of gas) x (# of trips)
- Fuel-only credit cards are shipped via FedEx; Please include the best address to receive the FedEx delivery

After Submission:
We respond to all requests within 1 business day. For exceptions or emergency requests, please contact Family Services directly.
Follow up requests for approved families should be submitted through the Approved Applicant Request: [http://alstapps.force.com](http://alstapps.force.com)

ALSF reserves the right to change these guidelines at any time without notice and to apply these guidelines at its reasonable discretion. Please contact Family Services with questions at 610-649-3034 or e-mail FamilyServices@AlexsLemonade.org.

Revised 12/17/18
Appendix P: Lazarex Cancer Foundation

Lazarex Financial Reimbursement Program
Appendix Q: Safety Checklists
Safety Checklist

Email (preferred) to SARC RPM upon completion of Safety Follow Ups:

SARC RPM: Lindsey Overman
e-mail: alerts@sarctrials.org; SARC037@sarctrials.org; leoverman@sarctrials.org
Fax: (734) 930-7557

* Please see Section 10 Study Evaluations and Study Calendar of the protocol for a list of both safety procedures to be completed at each time point.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Completed (Yes or No. If no, please explain.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
</tr>
<tr>
<td>C1D1</td>
<td></td>
</tr>
<tr>
<td>C1D2</td>
<td></td>
</tr>
<tr>
<td>C1D3</td>
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<tr>
<td>C1D4</td>
<td></td>
</tr>
<tr>
<td>C1D5</td>
<td></td>
</tr>
<tr>
<td>C1D8</td>
<td></td>
</tr>
<tr>
<td>C1D15</td>
<td></td>
</tr>
<tr>
<td>(additional Cycles n Days 1, 2, 4, 8, and 15 to be captured below)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix R: $^{18}$F-FLT Dose Order Form
## Appendix R: Dose Order Form

For Study Site Use Only

<table>
<thead>
<tr>
<th>Protocol No.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotracer Requested</td>
<td>$^{18}$FFLT</td>
</tr>
<tr>
<td>Institution</td>
<td></td>
</tr>
<tr>
<td>Prescribing Physician (AU, PI)</td>
<td></td>
</tr>
<tr>
<td>Patient ID Number</td>
<td></td>
</tr>
<tr>
<td>Requested Date and Time</td>
<td></td>
</tr>
<tr>
<td>Request by</td>
<td></td>
</tr>
<tr>
<td>Radiotracer Delivery Date and Time</td>
<td></td>
</tr>
</tbody>
</table>

Please send the request email to: RP_ORDER@lists.upenn.edu, with a copy to leehsi@pennmedicine.upenn.edu

For Study Site Use Only

<table>
<thead>
<tr>
<th>Dose Accepted</th>
<th>□ YES □ NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>If Not, Specify Alternate Date and/or Time</td>
<td></td>
</tr>
<tr>
<td>Accepted by (signature)</td>
<td></td>
</tr>
<tr>
<td>Date and Time</td>
<td></td>
</tr>
</tbody>
</table>
Appendix S: 18F-FLT Ordering Guidelines
Appendix S

18F-FLT ordering and delivery communication flow:

<table>
<thead>
<tr>
<th>Institution</th>
<th>Person</th>
<th>Role</th>
<th>Email</th>
<th>Phone</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARC</td>
<td>Lindsey Overman</td>
<td>Research Manager (primary</td>
<td><a href="mailto:leoverman@sarctrials.org">leoverman@sarctrials.org</a></td>
<td>734-930-7600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>contact)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCI</td>
<td>Elaine Thomas</td>
<td>Research NurseCoordinator</td>
<td><a href="mailto:Elaine.Thomas@nih.gov">Elaine.Thomas@nih.gov</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Philip Eclarinal</td>
<td>PET-CT Imaging Technologist</td>
<td><a href="mailto:Philip.Eclarinal@nih.gov">Philip.Eclarinal@nih.gov</a></td>
<td>(240) 858-3061</td>
</tr>
<tr>
<td></td>
<td>Mona Lisa Cedo</td>
<td></td>
<td><a href="mailto:MonaLisa_edo@nih.gov">MonaLisa_edo@nih.gov</a></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chris Leyson</td>
<td></td>
<td><a href="mailto:Christopher.leyson@nih.gov">Christopher.leyson@nih.gov</a></td>
<td></td>
</tr>
<tr>
<td>Cyclotron Facility</td>
<td>Sharon Lee</td>
<td>Penn Cyclotron Manager</td>
<td><a href="mailto:LeeHsi@penmedicine.upenn.edu">LeeHsi@penmedicine.upenn.edu</a></td>
<td></td>
</tr>
<tr>
<td>(Upenn)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Institution</th>
<th>Person</th>
<th>Role</th>
<th>Email</th>
<th>Phone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<p>| Time line from          | Communication from    | Communication to              | Topic                                       |
|-------------------------|-----------------------|-------------------------------|--------------------------------------------|-------------|
| Patient Cycle 1,       | SARC                  | NCI and Penn                  | SARC notifies sites of a potential patient |
| Day 1                   |                       |                               |                                            |             |
| 1-2 weeks               |                       |                               |                                            |             |
| 5-7 days                |                       | NCI                           | SARC confirms patient eligibility.        |
|                         |                       | cc: Penn                      | • NCI assists site in patient travel       |
|                         |                       |                               | arrangement                              |
|                         |                       |                               | • NCI schedules patient procedures        |
| 3-5 days                |                       | Penn                          | NCI places order for 2 doses FLT          |
|                         |                       | cc: SARC                      | compounding. 1st for C1D1 and 2nd for     |
|                         |                       |                               | C1D2 (minimum 2 business days in advance) |
| 1 day                   |                       | NCI                           | Upenn confirms patient schedule           |
|                         |                       | cc: SARC                      |                                            |             |
|                         |                       |                               |                                            |             |</p>
<table>
<thead>
<tr>
<th>Cycle 1 Day 1</th>
<th>Penn</th>
<th>NCI</th>
<th>Upenn notifies NCI of dose release (approximately 10 AM EST) and provides an estimated time of delivery (between 1:30 and 3:30 PM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Tuesday is preferable)</td>
<td></td>
<td>cc: SARC</td>
<td></td>
</tr>
<tr>
<td>Cycle 1 Day 1</td>
<td>Penn</td>
<td>NCI</td>
<td>Driver calls Philip Eclarinal on arrival (240) 858-3061</td>
</tr>
<tr>
<td>Cycle 1 Day 2</td>
<td>Penn</td>
<td>NCI</td>
<td>Upenn notifies NCI of dose release (approximately 10 AM EST) and provides an estimated time of delivery (between 1:30 and 3:30 PM)</td>
</tr>
<tr>
<td>(Wednesday is preferable)</td>
<td></td>
<td>cc: SARC</td>
<td></td>
</tr>
<tr>
<td>Cycle 1 Day 2</td>
<td>Penn</td>
<td>NCI</td>
<td>Driver calls Philip Eclarinal on arrival (240) 858-3061</td>
</tr>
</tbody>
</table>

**Delivery Instructions**

**Delivery Contact:** Philip C. Eclarinal, BS, CNMT, NMTCB(CT)
PET-CT Imaging Technologist
NCI/Molecular Imaging Program
Phone: (240) 858-3061

**Delivery Address:** Department of Radiation Safety, Bldg #21
9000 Rockville Pike
Bethesda, MD 20892
Attn: Molecular Imaging Program

**Commercial Vehicle Inspection Facility (entry)**
The Commercial Vehicle Inspection Facility (CVIF) is located just off Rockville Pike between the North Drive and the Wilson Drive Employee Entrances. (#67 on map)

Final destination will be at Building #21.

NIH will return delivery container to driver
Appendix T: Cycle 1 Day 1-2 Correlative Collection Schema
Cycle 1 Day 1

- **Biopsy**
  - Pre-treatment

- **Trabectedin Infusion**
  - PK – green top tube
  - +30 min, +1 hr, +2 hr, +3 hr (+/- 1 hr)

- **Research Blood Draw**
  - PK – green top tube
  - ctDNA – PAXgene tube
  - CTC – Cellsave tube

- **Research Blood Draw**
  - AM appt

- **Biopsy + observation + irinotecan Infusion**
  - Biopsy-accessible patients must be biopsied prior to irinotecan
  - Local obs. requirement post-biopsy will vary
  - Start irinotecan infusion 18-24 post-Trabectedin

- **Research Blood Draw**
  - PK - green top tube
  - ctDNA- PAXgene tube
  - CTC - Cellsave tube

**Timeline**

- **Baseline**
  - 3 pm
  - 5 pm
  - 7 pm
  - 9 pm
  - 11 pm
  - 3 am
  - 5 am
  - 7 am
  - 9 am
  - 11 am
  - 1 pm
  - 3 pm

- **+12 hrs**
  - 3 PM
  - (12-24 hours prior to biopsy; 18-24 hours prior to irinotecan)

- **+18 hrs**
  - AM appt
  - 9 AM - 3 PM – 18-24 hours after trabectedin

- **+24 hrs**
  - 3 PM
  - +24 hrs after trabectedin infusion
Appendix U: UGT1A1 Sample Requisition Form
Appendix U: UGT1A1 Sample Requisition Form

Please use a separate requisition form for each time point.

### SECTION 1

<table>
<thead>
<tr>
<th>SITE NAME &amp; NUMBER:</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT NUMBER:</td>
</tr>
<tr>
<td>PATIENT INITIALS:</td>
</tr>
<tr>
<td>INVESTIGATOR:</td>
</tr>
<tr>
<td>SITE CONTACT NAME:</td>
</tr>
<tr>
<td>CONTACT EMAIL &amp; PHONE NUMBER:</td>
</tr>
</tbody>
</table>

### SECTION 2

Ensure that the specimen labels include the following information: protocol ID, patient ID, specimen type, time point, collection time (HH:MM) and collection date (MM-DD-YY).

<table>
<thead>
<tr>
<th>(MM/DD/YYYY)</th>
<th>(HH:MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 1, Day 1</td>
<td></td>
</tr>
</tbody>
</table>

# of specimens shipped

### SECTION 3

<table>
<thead>
<tr>
<th>Ship to:</th>
<th>Date of Shipment:</th>
<th>FedEx tracking number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figg Lab</td>
<td>________________</td>
<td>___________</td>
</tr>
<tr>
<td>9000 Rockville Pike</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Building 10 Room 5A08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bethesda, MD 20892</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(240) 760-6810</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FedEx tracking number: