

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY	CORRELATIVE SCIENCE PROCEDURE MANUAL A Randomized Phase 2/3 Study of Olaparib Plus Temozolomide versus Investigator’s Choice for the Treatment of Patients with Advanced Uterine Leiomyosarcoma after Progression on Prior Chemotherapy Short Title- A092104	Version No: 1.1	Effective Date: 07/10/2023
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CORRELATIVE SCIENCE PROCEDURE MANUAL

1. Purpose

This document describes the procedures required for the collection, shipping, and processing of biospecimens from patients enrolled or registered who have consented to participate in A092104. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the Alliance Biorepository (i.e. Siteman Cancer Center Tissue Procurement Core at Washington University), prior to their use for protocol-specified and future, unspecified correlative science research studies. This document should be used by staff involved with any aspect of the A092104 biospecimen collection, processing, and submission, including staff at satellite institutions.

2. Scope

This document applies to all biospecimens collected specifically for A092104 only. Please refer to the trial protocol-specific language for additional details regarding eligibility, participant enrollment, data submission, and specific procurement procedures. **Please ensure that you are reading the most updated version of this document. This document may experience minor updates, revisions, and clarifications independent of a formal protocol amendment. The most recent version of this document may be found on the Alliance website and CTSU.**

3. Definitions

Term	Definition
ABWUSTL	Alliance Biorepository at Washington University in St. Louis
FFPE	Formalin Fixed, Paraffin Embedded
IHC	Immunohistochemistry

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4. Contact Information

Protocol-related questions may be directed as follows:	
Questions	Contact (via email)
Questions regarding patient eligibility, treatment, and dose modification:	Study Chair: Brian Van Tine, MD bvantine@wustl.edu Nursing Contact: Lisa Kottschade, APRN, MSN, CNP kottschade.lisa@mayo.edu Protocol Coordinator: Beth Smith beth10@bsd.uchicago.edu (where applicable) Data Manager: Brandon Bright bright.brandon@mayo.edu
Questions related to data submission, RAVE or patient follow-up:	Data Manager: Brandon Bright bright.brandon@mayo.edu
Questions regarding the protocol document and model informed consent:	Protocol Coordinator: Beth Smith beth10@bsd.uchicago.edu
Questions related to IRB review	Alliance Regulatory Inbox regulatory@allianceNCTN.org
Questions regarding CTEP-AERS reporting:	Alliance Pharmacovigilance Inbox pharmacovigilance@alliancencn.org
Questions regarding specimens/specimen submissions:	Alliance Biorepository at Washington University (WUSTL) alliance@email.wustl.edu
Questions regarding drug supply	PMB: PMBAfterHours@mail.nih.gov
Questions regarding drug administration	Pharmacy Contact: Barbara Todaro, Pharm.D. barbara.todaro@roswellpark.org

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4.1 For information on using the BiOMS system, please refer to the ‘Help’ links on the BiOMS webpage to access the online user manual, FAQs, and training videos. To report technical problems, such as login issues or application errors, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org. For assistance in using the application or questions or problems related to specific specimen logging, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org.

4.2 For all other questions regarding biospecimen procurement and shipping procedures, please contact the Alliance Biorepository Program Manager: 1-314-747-4402 or alliance@email.wustl.edu.

5. Site Preparation

5.1 Please refer to A092104 protocol document for any specific requirements related to patient enrollment, registration, and regulatory compliance.

5.2 Please ensure that you have appropriate log on credentials and can successfully access the BiOMS application. The BiOMS application is used for logging the collection and shipment of biospecimens to the Alliance Biorepository at Washington University. For training and assistance in using the application or questions or problems related to specific specimen logging, please contact: 1-855-55-BIOMS or bioms@alliancenctn.org.

6. Collection Schema

The following biospecimens are to be collected at each of the time points. Please refer to individual biospecimen collection and processing methods and specific shipping procedures below.

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Time Point	Kit (Y/N)	Biospecimen	Quantity	Collection / Processing Method	Shipping	Notes
For patients who are registered to biobanking for A092104						
Within 60 days of registration	N	Fixed tumor tissue block	1 block	Fixed tissue block (9.2)	Ambient	1, 2
Within 60 days of registration	N	H&E stained slide AND Tumor tissue scrolls	1 H&E stained slide AND 10 x 10 micron scrolls	H&E stained slide and fixed tissue scrolls (9.3)	Ambient	1, 2
For patients who are not registered to biobanking for A092104						
Prior to C1D1	N	Whole blood for plasma	6 x 1 ml aliquots	Frozen plasma (10.1)	Dry Ice	1, 3
Prior to C1D1	N	Whole blood for “buffy coat”	4 aliquots	“Buffy Coat” (10.2)	Dry Ice	1, 3, 4
For patients who are registered to biobanking for A092104						
C2D1 (Prior to treatment)	N	Whole blood for plasma	6 x 1 ml aliquots	Frozen plasma (10.1)	Dry Ice	1, 3
For patients who are not registered to biobanking for A092104						
C5D1 (Prior to treatment)	N	Whole blood for plasma	6 x 1 ml aliquots	Frozen plasma (10.1)	Dry Ice	1, 3
For patients who are registered to biobanking for A092104						
Progression/ End of Treatment	N	Whole blood for plasma	6 x 1 ml aliquots	Frozen plasma (10.1)	Dry Ice	1, 3

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Notes:

1. Collection is optional for patients but requires all sites offer patients to consent. Please see protocol-specific consent documents.
2. A representative, archived diagnostic tumor tissue block from biopsy or surgery should be submitted, if available. If entire tissue block cannot be submitted, one H&E stained slide **AND** ten (10 um) serial tissue scrolls will be accepted as an alternative. If tissue is limited, please submit H&E and as many tissue scrolls as possible. **BLOCK SUBMISSION IS STRONGLY PREFERRED.**
3. Peripheral blood (EDTA) 2 x 10 ml to be processed for plasma (6 x 1 ml aliquots) and “buffy coat,” frozen on site and shipped on dry ice.
4. Buffy coat only needs to be collected from a single timepoint. Collection of buffy coat from the prior to C1D1 timepoint is preferred, but collection at other timepoints is also acceptable.

7. Biospecimen Collection Kits

7.1 Blood Specimens

7.1.1 There are no “kits” provided for submission of blood specimens for this study. Sites are responsible for acquiring materials for collection and shipping of biospecimens to the Biorepository.

7.2 Tissue Specimens

7.2.1 There are no “kits” provided for submission of paraffin blocks, H&E slides, or tissue scrolls for this study.

7.2.2 Paraffin blocks, H&E slides, and tissue scrolls should be packaged to avoid breakage using a padded envelope or, preferably, a small Styrofoam cooler.

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7.2.3 During warm weather months, paraffin blocks, H&E slides, and tissue scrolls should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77 degrees F) that may melt paraffin and damage the tissue specimens.

7.3 Please see section 11- Biospecimen Shipping for specific instructions on shipping to ABWUSTL.

8. Biospecimen Labeling and Tracking

8.1 All research biospecimens (cryovials, microcentrifuge tubes, tissue bags) **MUST** be labeled with the Alliance patient ID number, patient initials (Last, First, Middle), the date and time (if applicable) of collection and specimen type (i.e. plasma, buffy coat).

8.2 Surgical pathology tissue blocks should not be labeled in any manner. The institutional surgical pathology number (e.g. “S16-1234”) and the individual block identifier (e.g. “A3”) should be readable on the block. If tissue scrolls are being submitted instead of the block, each H&E stained slide and microcentrifuge tube should be labeled with the Alliance patient ID number, institutional surgical pathology number, and the block identifier.. Provide **a de-identified copy of the surgical pathology report**, labeled with the Alliance patient ID number, corresponding to the block, H&E stained slide, or curls. Please ensure the institutional surgical pathology number and block ID are maintained on the surgical pathology report. See **section 9** for additional details.

8.3 Label all containers and vials with an indelible, solvent-resistant marker when they are at ambient temperature.

8.4 Do not affix any labels to vials, slides or tubes. Label the collection containers directly with the marking pen.

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8.5 All biospecimens that are collected and sent to the Alliance Biorepository must be **logged and tracked in BioMS**. The BioMS system is a web-based application that tracks the collection and shipping of biospecimens. Once individual biospecimens are logged and ‘shipped’ in the BioMS system, a packing manifest will be created by the system. This manifest must be printed out and must accompany all biospecimen shipments. To become familiar with the BioMS system and for further information about training, access, and use, please contact the BioMS Help desk at: 1-855-55-BIOMS or bioms@alliancencn.org.

8.6 In the event that BioMS cannot be accessed, please complete a BioMS Specimen Log and Shipping Manifest form which can be found here- <http://tinyurl.com/alliance-bioms-contingency>.

9. Tissue Collection

9.1 Overview.

9.1.1 Please refer to protocol-specific instructions for procedures related to actual tissue procurement from individual participants. The method for research tissue procurement (needle core biopsy, sampling of surgically resected tumor) is dependent upon the disease site and the individual patient.

9.1.2 When procuring tissue biospecimens by any method, when possible, avoid tissue that is grossly necrotic, hemorrhagic, fatty, or fibrous. If in doubt, briefly (1 min or less) place the tissue segment in a sterile specimen cup containing physiologic (normal) saline to rinse the tissue. Necrotic, hemorrhagic, and fatty tissue will generally dissolve or float on the surface while tumor and parenchymal tissue will remain intact and sink to the bottom of the cup.

9.1.3 Include a copy of the **de-identified pathology report with all tissue submission**.

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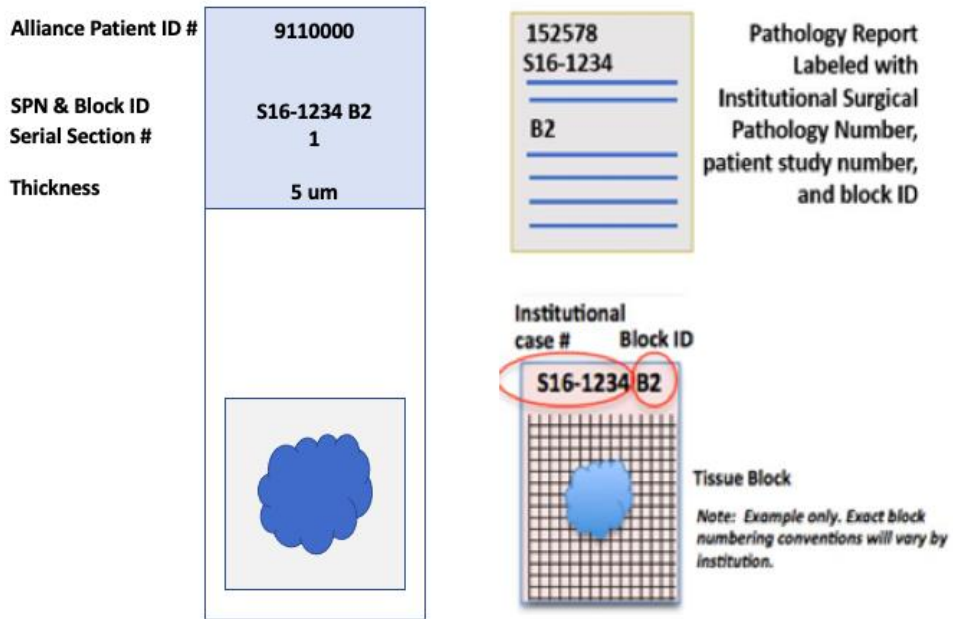
9.2 Fixed Tissue Block

- 9.2.1** For patients who consented to biobanking for A092104, a representative diagnostic block with adequate tumor should be submitted, if applicable.
- 9.2.2** Any clinical surgical pathology block that is submitted for research studies will not be exhausted or rendered unsuitable for future diagnostic use. Any clinical surgical pathology block that is submitted will be returned within ten working days of written request, when needed for clinical management or clinical trial enrollment for a specific patient. Otherwise, all blocks will be returned to the submitting institution when the trial and correlative science study end points have been met.
- 9.2.3** **Include a copy of a de-identified pathology report with block submission.**
- 9.2.4** **During warm weather months, paraffin blocks and slides should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77degrees F) that may melt paraffin and damage the tissue specimens.**

9.3 H&E Stained Slide and Fixed Tissue Scrolls

- 9.3.1** In cases where an institution is unwilling or unable to submit a tissue block for biobanking, a single H&E stained slide for references and serial tissue sections (scrolls, ribbons, curls) from the same block may be submitted.
- 9.3.2** Cut and perform routine H&E stain on a single section from the tumor tissue block. See figure below for proper mounting and labeling.

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- 9.3.3** Cut a “ribbon” (scroll) of 10 paraffin sections at 10 microns. Place the ribbon of tissue directly into a single microcentrifuge tube or any other suitable container. Do not float the tissue ribbon or sections in a water bath. Label the tube of tissue following the guidelines outlined above.
- 9.3.4** Include a copy of a **de-identified** pathology report with all tissue submissions.
- 9.3.5** During warm weather months, paraffin blocks and slides should be shipped in an insulated container that contains a refrigerant pack, to avoid heat > 25 degrees C (77degrees F) that may melt paraffin and damage the tissue specimens.

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10. Blood Collection Methods

10.1 Plasma Processing

- 10.1.1** Collect 20 ml whole blood by standard venous phlebotomy technique into the purple top (EDTA) tubes. Invert tubes 10 times.
- 10.1.2** Within 30 (preferred) to 120 minutes of collection, spin the vacutainer tubes at room temperature in a clinical centrifuge at 2500 xG for 15 minutes. Make sure that the caps are secured tightly on the tubes.
- 10.1.3** Carefully remove the plasma layer from each tube (~3 ml), without touching the white, buffy coat layer, and transfer to new 15 ml conical centrifuge tubes. Keep the vacutainer tubes containing the white, buffy coat layer for white blood cell isolation (**section 10.2**).
- 10.1.4** Spin the centrifuge tubes containing plasma at room temperature in a clinical centrifuge at 2500 xG for 15 minutes.
- 10.1.5** Label 6 cryovials as instructed in **section 8**. Make certain each vial is labeled completely and identically.
- 10.1.6** Carefully remove 6 ml of plasma (without touching the pellet) and divide into 6, 1 ml labeled cryovials. Leave a small amount of plasma to avoid obtaining red blood cells.
- 10.1.7** Freeze plasma containing cryovials on dry ice or a -70 to -90 degree Celsius ultralow freezer. Store at -70 to -90 degrees C until ready for shipment on dry ice.

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10.2 “Buffy Coat” (White Blood Cell) Processing

10.2.1 Follow procedures in **section 10.1** for collecting and processing plasma from EDTA tubes.

10.2.2 Label 4 cryovials as instructed in **section 8**.

10.2.3 After removing the plasma, carefully remove the white, “buffy coat” white blood cell layer, avoiding the red blood cell mass as much as possible.

10.2.4 Transfer the buffy coat layer (approximately 0.2 – 0.5 ml) from each EDTA tube into the labeled cryovials. Immediately freeze the cryovials of buffy coat on dry ice or in liquid nitrogen vapor. Do NOT freeze buffy coat cells by placing a warm tube in a -70 to -90 degree Celsius ultralow freezer. Once completely frozen, the cryovials containing the buffy coat cells may be stored at -70 to -90 degrees C until ready for shipment on dry ice.

11. Biospecimen Shipping

11.1 Overview

11.1.1 Place the original, completed copy of the BioMS packing manifest in the shipment. If sending tissue, include a copy of the de-identified surgical pathology report. Do not send specimens without a completed BioMS Packing Manifest or substitute “BioMS Downtime Form.” Biospecimens cannot be accepted without this completed form.

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11.1.2 Unless otherwise specified, all biospecimens should be shipped on the same day that they are collected (Monday – Thursday) so they are received by the Biorepository within 24 hours of collection. If collected biospecimens cannot be shipped on the same day that they are collected (e.g. Friday – Saturday or Holiday collections), please contact the Alliance Biorepository Program Manager: 1-314-747-4402 or alliance@email.wustl.edu for further instructions, at least 24 hours prior to anticipated collection.

11.1.3 **Do not ship on Friday, Saturday, Sunday or the day before a nationally recognized holiday.**

11.1.4 **Ship container for PRIORITY OVERNIGHT DELIVERY according to IATA guidelines and standard institutional policies and using the preferred vendor.**

Ship to:

Alliance Biorepository

c/o Siteman Cancer Center Tissue Procurement Core

Washington University School of Medicine

425 S. Euclid Ave

Room 5120

St. Louis, MO 63110-1005

Phone: (314) 454-7615

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12. Biospecimen Receipt and Quality Assurance Measures

- 12.1** Upon receipt, all biospecimens will be accessioned into the TPC informatics system, OpenSpecimen.
- 12.2** All biospecimens will be logged, associated, and tracked by the unique patient biopsy control number.
- 12.3** Each individual biospecimen will receive and be physically labeled with a unique biospecimen identifier, associated with the biopsy control number in the TPC informatics system.
- 12.4** Upon receipt, all physical biospecimens received will be reconciled with what is recorded on the BioMS packing manifest. Any discrepancies noted will be communicated to the Program Manager who will contact the submitting site for reconciliation.
- 12.5** Upon receipt, any biospecimen received that is not in appropriate physical condition (broken vials, frozen samples that are thawed, ambient samples that are frozen) will be reported to the Program Manager, who will contact the submitting site for reconciliation.
- 12.6** Frozen aliquoted biofluids will be stored under liquid nitrogen vapor.
- 12.7** All biospecimens will remain in storage until additional processing or review is requested in writing by the appropriate protocol PI.

13. Document History

Version	Description and Justification of Change	Author	Effective Date
1.1	Changed within 30 days of registration timepoint to 60 days, added contact table, changed	KL	7/10/2023

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	wording of tissue sections to scrolls for clarity		
1.0	New	AAW	10/17/2022