

CORRELATIVE SCIENCE PROCEDURE MANUAL

AFT-15: A PHASE I STUDY OF IBRUTINIB (PCI-32765) IN COMBINATION WITH REVLIMID/DEXMETHASONE (RD) IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Prepared by:




Patsy Alldredge, MS 11-July-2018
Program Manager, Alliance Foundation Biorepository Date

Approved by:



Jessica Lamp 18-JUL-18
Sr. Project Manager, AFT Date

Flavia Picchiori Date
Correlative Study PI, City of Hope



Shira Dinner, MD 7/17/18
Executive Officer, AFT Date



Mark Watson, MD, PhD 8-14-2018
Director, Alliance Foundation Biorepository Date

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Prepared by:

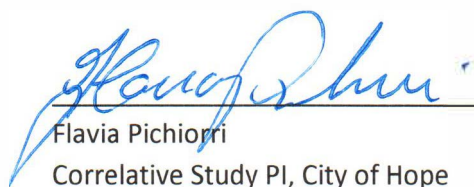
Patsy Alldredge, MS
Program Manager, Alliance Foundation Biorepository

Date

Approved by:

Jessica Lamp
Sr. Project Manager, AFT

Date


Flavia Pichiorri
Correlative Study PI, City of Hope

8/16/2018

Date

Shira Dinner, MD
Executive Officer, AFT

Date

Mark Watson, MD, PhD
Director, Alliance Foundation Biorepository

Date

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1. PURPOSE

This document describes the procedures required for the collection, shipping, and processing of biospecimens from all patients enrolled or registered to AFT-15. This document also describes the procedures that will be followed subsequent to the receipt of biospecimens by the AFT Biorepository (AFB) (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 AFT-15 study biospecimen collection, processing, and submission, including staff at satellite institutions.

2. SCOPE

This document applies to all biospecimens collected specifically for the AFT-15 study only. Please refer to the study 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 can be found on the AFT BioMS web site which is accessible via the AFT portal: (<https://alliancefoundationtrials.org>)

3. CONTACT INFORMATION

- 3.1.** Please send any questions and problems related to protocol administration, eligibility, patient registration, and data submission, to AFT15@alliancefoundationtrials.org.
- 3.2.** For specific questions about kits or shipments, please contact the Siteman Cancer Center Tissue Procurement Core at: 1-314-454-7615 or tbank@wudosis.wustl.edu.
- 3.3.** For questions about using the AFT BioMS web application for ordering kits, or registering and shipping biospecimens, please contact: 1-855-642-4667 or aftbiomshelp@email.wustl.edu
- 3.4.** For any other questions about biospecimen procurement and shipping procedures, please contact the AFB Program Manager at: 1-314-747-4402 or afbhelp@email.wustl.edu

4. SITE PREPARATION

- 4.1.** Please refer to the AFT-15 protocol for any specific requirements related to patient enrollment, registration, and regulatory compliance.
- 4.2.** The AFT BioMS application is used for both requesting biospecimen collection kits and for logging the collection and shipment of biospecimens to the AFT Biorepository. For training and assistance in using the AFT BioMS application, please see the AFT BioMS web site which is accessible via the AFT portal: <https://alliancefoundationtrials.org> or contact the AFT BioMS Help desk at: aftbiomshelp@email.wustl.edu or 1-855-642-4667.
- 4.3.** Prior to collection of biospecimens, a biospecimen collection kit must be at the collection site. Please see section 6 for requesting biospecimen collection kits. Please allow at least 10 working days to receive the collection kit.

5. COLLECTION SCHEMA

The following biospecimens are to be collected at each of the time points specified below, **for patients enrolled during the expansion phase of the study ONLY**. These should not be collected during the dose escalation phase of the study. Please refer to individual collection kit instructions, biospecimen collection and processing methods, and specific shipping procedures below.

Time Point	Biospecimen	Quantity	Collection / Processing Method	Shipping
Pre-treatment	Bone marrow (EDTA tube)	2 x 5 ml	Bone marrow (8.1)	Ambient
Pre-treatment	Whole blood (EDTA tube)	3 x 5 ml	Whole blood (8.2)	Ambient
Cycle 1 Completion	Bone marrow (EDTA tube)	2 x 5 ml	Bone marrow (8.1)	Ambient
Cycle 1 Completion	Whole blood (EDTA tube)	3 x 5 ml	Whole blood (8.2)	Ambient
Cycle 3 Completion	Whole blood (EDTA tube)	3 x 5 ml	Whole blood (8.2)	Ambient
Cycle 6 Completion	Whole blood (EDTA tube)	3 x 5 ml	Whole blood (8.2)	Ambient
Cycle 12 Completion	Whole blood (EDTA tube)	3 x 5 ml	Whole blood (8.2)	Ambient

6. BIOSPECIMEN COLLECTION KITS

- 6.1. To facilitate the proper collection and shipping of all biospecimens, biospecimen collection kits and materials will be provided. The cost of the kit and shipping the kit to the site will be paid for. A pre-paid FedEx waybill is provided for shipping the kit with the biospecimens back to the AFB at Washington University in St. Louis via priority overnight shipping.
- 6.2. Kits should be requested at least 10 working days in advance of the anticipated collection date. As many as 2 kits can be requested at one time. Since many of the collection materials (vacutainer tubes) have expiration dates, do not request kits more than 90 days prior to their anticipated use. **All kits must be requested using the AFT BioMS system.**
- 6.3. Kit contents and specific instructions for use of the kit are provided in the kit box. **Please return any used collection materials with the kit.**
- 6.4. Once a kit is received, **do not discard the outer cardboard overwrap**. The kit, containing biospecimens, is to be shipped back in the same box.
- 6.5. Please return all components of the kit, regardless of whether they have been used or not. Kits and kit components are recycled when possible, minimizing the kit cost.
- 6.6. Well in advance of collecting biospecimens, inspect the biospecimen collection kit to ensure that all components are present and not expired, particularly if the kit has been onsite for longer than 30 days.
- 6.7. Note that individual kit components that are expired, damaged, or missing cannot be replaced. The remedy is to order a complete, new kit. (Please note in your request that you are replacing an expired or damaged kit).

- 6.8. Please return all kits that have expired or missing components. Return the ENTIRE kit using the pre-paid FedEx waybill provided within the kit. DO NOT DISCARD kits that have missing or expired components. Recycling kits keeps the cost of kit materials to a minimum. Please note that all out-going and in coming kits are tracked, and sites that have requested many more kits than they have returned will be charged for non-returned kits.
- 6.9. If a biospecimen collection component (e.g. vacutainer collection tube) is missing, damaged, or expired, the institution may substitute a like-kind collection tube from their own supply.
 - 6.9.1. Note that protocol requirements are based on blood volumes, not tube sizes. If the protocol requires the collection of 8 cc of whole blood, generally a 10 cc tube is provided in the kit for convenience. If desirable or necessary to collect 8 cc in 3 x 3 cc tubes (for example), that is permissible.
- 6.10. Please see **Section 10 – Biospecimen Shipping** for specific instructions on packaging biospecimens into the shipping kit for shipment to the biorepository.

7. BIOSPECIMEN LABELING AND TRACKING

- 7.1. All research biospecimens (vacutainer tubes) MUST be labeled with the participant study number and patient initials (Last, First, Middle). Blood tubes should additionally be labeled with the date and time of collection.
- 7.2. Label all tubes with an indelible, solvent-resistant marker when they are at ambient temperature.
- 7.3. Do not affix any labels to tubes. Label the collection containers directly with a marking pen.
- 7.4. All biospecimens that are collected and sent to the AFT biorepository (AFB) **must be logged and tracked in AFT BioMS**. The AFT BioMS system is a web-based application that tracks the collection and shipping of biospecimens to the AFB. Once individual biospecimens are logged and 'shipped' in the AFT 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 AFT BioMS system and for further information about training, access, and use, please contact the AFT BioMS Help desk at: 1-855-642-4667 or aftbiomshelp@email.wustl.edu. Note that the AFT BioMS system is similar to but independent of the NCI BioMS application, which is used to manage biospecimens collected on NCI NCTN Alliance trials.
- 7.5. In the event that AFT BioMS cannot be accessed, please complete an AFT BioMS specimen manifest form, which can found here-
<https://cbmiapps.wustl.edu/confluence/display/AB/Forms>

8. BLOOD AND BONE MARROW COLLECTION METHODS

8.1. Bone Marrow for Total RNA Sequencing (EDTA Tubes - no processing)

- 8.1.1. Collect 5 ml of bone marrow into each of the EDTA tubes following standard institutional protocol. Invert tubes 10 times.
- 8.1.2. Store EDTA tubes with bone marrow at 4 degrees Celsius (i.e. refrigerated) until shipping. Do not freeze the tubes. **Bone marrow should be collected Monday—Thursday only. The**

tubes must be shipped on the same day they are collected and must be received by the AFB within 24 hours of collection (e.g. Friday—Saturday collections or Holiday collections are not allowed). Ensure that the EDTA tubes are shipped at ambient temperature to avoid freezing.

8.2. Whole blood for immunome studies (EDTA Tubes - no processing)

8.2.1. Collect 5 ml of blood into each of the EDTA tubes using standard venous phlebotomy. Invert tubes 10 times.

8.2.2. Store EDTA tubes with blood at 4 degrees Celsius (i.e. refrigerated) until shipping. Do not freeze the tubes. **Blood should be collected Monday—Thursday only. The tubes must be shipped on the same day they are collected and must be received by the AFB within 24 hours of collection (e.g. Friday—Saturday collections or Holiday collections are not allowed).** Ensure that the EDTA tubes are shipped at ambient temperature to avoid freezing.

9. BIOSPECIMEN SHIPPING

9.1. All biospecimens should be shipped on the same day that they are collected (Monday – Thursday). Biospecimens must be received by the AFB 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 AFB Program Manager at 1-314- 747-4402 for further instructions, at least 24 hours prior to anticipated collection.

9.2. Please see the Directions for Use (DFU) document that is included in each kit, for specific directions on how to package and ship biospecimens. The DFU document is also available for download on the AFT BioMS webpage which is accessible via the AFT portal: (<https://alliancefoundationtrials.org>).

9.3. Place the original, completed copy of the AFT BioMS packing manifest in the kit. **Do not send specimens without a completed AFT BioMS packing manifest or substitute “AFT BioMS Downtime Form.” Biospecimens cannot be accepted without this completed form.**

9.4. Close the cardboard carton overwrap and secure lid with packaging tape; one piece on each side and two pieces over the front flap.

9.5. Ship container for **PRIORITY OVERNIGHT DELIVERY** using the pre-paid FedEx waybill provided within the specimen collection kit. Ship to:

AFT 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

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

10. BIOSPECIMEN RECEIPT AND QUALITY ASSURANCE MEASURES

- 10.1. All biospecimens will be shipped to and received by the AFB at the Siteman Cancer Center Tissue Procurement Core, Washington University in St. Louis, a CAP- accredited biorepository.
- 10.2. All biospecimens will be accessioned into the TPC informatics system, OpenSpecimen.
- 10.3. All biospecimens will be logged, associated, and tracked by the unique patient biopsy control number.
- 10.4. 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.
- 10.5. Upon receipt, all physical biospecimens received will be reconciled with what is recorded on the AFT BioMS packing manifest. Any discrepancies noted will be communicated to the Program Manager who will contact the submitting site for reconciliation.
- 10.6. Upon receipt, any biospecimen received that is not in appropriate physical condition (broken vials, ambient samples that are frozen) will be reported to the Program Manager, who will contact the submitting site for reconciliation.
- 10.7. All biospecimens will remain in storage until additional processing or review is requested in writing by the appropriate protocol principal investigator.

11. DOCUMENT HISTORY

VERSION	DESCRIPTION AND JUSTIFICATION OF CHANGE	AUTHOR	EFFECTIVE DATE
1.0	New	PAA	11-July-2018