

ANIMATE

A phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma, fit for autologous stem cell transplant, who fail to reach complete remission after first or second line salvage therapy

LABORATORY MANUAL

For the collection, processing, storage and shipping of samples for central analysis

Version 2 28.03.2019

Cancer Research UK and
UCL Cancer Trials Centre



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1. Introduction

The purpose of this laboratory manual is to describe the collection and shipping of samples for central analysis in the ANIMATE trial.

Formalin-fixed and paraffin-embedded tumour biopsy samples will be collected from all patients at all participating sites and shipped to the Haematological Malignancy Diagnostic Service (HMDS) in Leeds.

Blood samples in EDTA and serum gel will be collected from all patients who undergo treatment with nivolumab at all participating sites and shipped to the Weatherall Institute of Molecular Medicine in Oxford.

In order to preserve the integrity of the patient samples, designated staff at each participating site are responsible for ensuring that research samples are collected, handled, and (where necessary) stored at their site in accordance with the instructions in this manual and the current approved version of the trial protocol. Designated staff should be appropriately trained and listed on the Site Staff Delegation Log as authorised by the Principal Investigator to carry out these tasks before any trial related activities and procedures can be performed by them.

It is important that site staff ensure that all research samples are transported to the specified laboratories within the time frames specified in the trial protocol and as set out in this laboratory manual and that samples are not shipped to arrive at the laboratories either on a weekend or Bank Holiday.

For more information on the analyses that will be performed on biological samples for the ANIMATE trial, please refer to section 10 of the protocol.

2. Site activation requirements

Samples must be tracked online using the sample tracking website. At least one site staff member must be registered to use the tracking website before site activation, although it is highly recommended that as many members of the site research team as possible have access to allow for prompt tracking of samples.

To request access, email the names and email addresses of the staff members requiring access to the ANIMATE trial coordinator (ctc.animate@ucl.ac.uk).

For more information about using the tracking website see the Sample Tracking Website Manual.

3. Consent for sample collection

Some aspects of consent for sample collection and use in ANIMATE are compulsory and others are optional:

Compulsory	Optional
<ol style="list-style-type: none">1. Use of a stored tumour biopsy and (if taken) tumour biopsy taken at relapse for use in research related to the ANIMATE trial2. Up to 6 blood samples to be taken and used in research related to the ANIMATE study	<ol style="list-style-type: none">1. Additional bone marrow biopsy if PET positive after 8 cycles of Nivolumab2. Use of left-over biopsy material in future ethically-approved research3. Use of left-over blood samples in future ethically-approved research.

Site staff will be required to indicate on the Registration CRF which aspects of sample collection the patient has consented to. You will also be asked to confirm this on the Biological Sample Collection Form. Samples must not be taken/submitted for those which the patient has not been consented to or for any patient that has withdrawn consent.

If a patient withdraws consent for any aspects of sample collection during the course of the trial, please notify UCL CTC in writing.

4. Samples required

ANALYSIS	SAMPLE	TIMEPOINTS	DESTINATION
Fluorescence in situ hybridisation (FISH) and Gene expression profiling	Formalin-fixed and paraffin-embedded (FFPE) tissue specimens (blocks) ¹	<ul style="list-style-type: none"> Archival Tumour biopsy at first relapse (if available) or diagnostic biopsy. Send following patient registration Repeat tumour biopsy after 8 cycles if patient is PET positive and has given optional consent Repeat tumour biopsy at relapse if clinically indicated 	HMDS, Leeds
Immunophenotyping	Peripheral blood in EDTA	<ul style="list-style-type: none"> 50ml within 3 days prior to start of cycle 1 20ml within 3 days prior to start of cycle 2 20ml within 3 days prior to start of cycle 4 20ml within 3 days prior to start of cycle 6 20ml within 3 days prior to start of cycle 8 20ml at the 1 month post-treatment follow up visit 	Weatherall Institute of Molecular Medicine, Oxford
TARC (CCL17) analysis	Peripheral blood in serum gel tube	<ul style="list-style-type: none"> 5ml within 3 days prior to start of cycle 1 5ml within 3 days prior to start of cycle 2 5ml within 3 days prior to start of cycle 4 5ml within 3 days prior to start of cycle 6 5ml within 3 days prior to start of cycle 8 5ml at the 1 month post-treatment follow up visit 	Weatherall Institute of Molecular Medicine, Oxford

¹ Preferably lymph node biopsy or biopsy of an extranodal tumour mass. In the absence of this, any other diagnostic material acceptable (e.g. bone marrow trephine biopsy involved with lymphoma).

5. Contact details

5.1 Cancer Research UK and UCL Cancer Trials Centre

All **ANIMATE trial management and general queries** should be directed to the ANIMATE Trial Coordinator (this should be your first point of contact for most queries):

Contact: ANIMATE Trial Coordinator
Address: Cancer Research UK & UCL Cancer Trial Centre
90 Tottenham Court Road
London W1T 4TJ
Email: ctc.animate@ucl.ac.uk
Telephone: 0207 679 9860
Fax: 0207 679 9861

5.2 HMDS

Primary Contact:
Dr Cathy Burton
Email: cathy.burton1@nhs.net

Secondary Contact:
Sharon Barrans
Email: sharonb@hmds.org.uk

HMDS Tel: 0113 206 7851

Address: HMDS
Level 3, Bexley Wing
St. James's Institute of Oncology
Beckett Street
Leeds LS9 7TF

5.3 Weatherall Institute of Molecular Medicine

Primary Contact:
Prof Paresh Vyas
Email: paresh.vyas@imm.ox.ac.uk

Secondary Contact:
Dr Paolo Polzella
Email: paolo.polzella@imm.ox.ac.uk

Weatherall Institute Tel: 01865 222443

Address: Vyas Lab, Room 326
Weatherall Institute of Molecular Medicine
University of Oxford
John Radcliffe Hospital
Hedley Way
Oxford OX3 9DS

5.4 MRC-University of Glasgow Centre for Virus Research

Primary Contact:

Prof Ruth Jarrett

Email: Ruth.Jarrett@glasgow.ac.uk

Secondary Contact:

Annette Lake

Email: Annette.lake@glasgow.ac.uk

Jarrett Group Tel: 0141 3305775

Address: Jarrett Group
Botham Building
MRC-University of Glasgow Centre for Virus Research
Garscube Estate
464 Bearsden Road
Glasgow
G61 1QH

6. Tubes and packaging

UCL CTC will not supply tubes and packaging for samples.

The per-Trial Subject payment to sites includes funds for tubes and postage of samples. Please see the Clinical Trial Site Agreement for more information.

7. Procedure for taking and sending samples

7.1 Formalin-fixed paraffin embedded tumour blocks

- FFPE blocks should be retrieved from the hospital's tissue archive.
(Preferably a lymph node biopsy at first relapse, or an initial diagnostic sample if this is not available. Tissue should be a biopsy from an involved lymph node, or solid tumour mass. If not available any diagnostic material is acceptable (e.g. bone marrow trephine biopsy with involvement by Hodgkin))
- Label the sample clearly with the following information:
 - Trial name
 - Initials
 - Date of birth
 - Trial number
 - Date of sample collection
- Complete the Biological Sample Collection Form (template form can be found in the 'Laboratory' of the Investigator Site File):
 - Complete both pages. Make sure all fields are completed (except for the section labelled 'for laboratory use only')
 - Complete one form for each sample being sent
 - Take a photocopy of the completed form and file in the 'Laboratory' section of the Investigator Site File.
- To ship samples:
 - Wrap the block in tissue and place in a sealed plastic bag
 - Place the sample and Biological Sample Collection Form in a secure container which conforms to current postal regulations (P650) with the outer box labelled as "UN3373 Biological Substances Category B"
 - Send by first class post.

- Samples should be sent to:
ANIMATE Trial c/o Dr Cathy Burton
HMDS
Level 3, Bexley Wing
St. James's Institute of Oncology
Beckett Street
Leeds
LS9 7TF
- Log the date that the sample was taken and sent on the:
 - ANIMATE sample tracking website (see the Sample Tracking Website Manual for full guidance)

The Sample Tracking Website will be reviewed by UCL CTC staff as part of central monitoring activities for the trial.

- Please indicate on the sample form whether blocks should be returned after analysis. If so, provide a return address on the Biological Sample Collection Form.

7.2 Peripheral blood samples (EDTA)

- Peripheral blood samples should be drawn into hospital stock EDTA tubes. Please see section 4 for details of the quantity of blood required at each sampling timepoint. No processing is required before sending to the central laboratory.
- Label the sample clearly with the following information:
 - Trial name
 - Initials
 - Date of birth
 - Trial number
 - Date of sample collection
- Complete the Biological Sample Collection Form (template form can be found in the 'Laboratory' section of the Investigator Site File):
 - Complete both pages. Make sure all fields are completed (except for the section labelled 'for laboratory use only')
 - Complete one form for each sample being sent
 - Take a photocopy of the completed form and file in the Investigator Site File.
- To ship samples:
 - Wrap the tubes in absorbent material and place in a sealed plastic bag
 - Place the sample and Biological Sample Collection Form in a secure container which conforms to current postal regulations (P650) with the outer box labelled as "UN3373 Biological Substances Category B"
 - Send by first class post.

N.B. Samples taken on a Friday should be refrigerated over the weekend and sent on the next working day.

- Samples should be sent to:
ANIMATE Trial c/o Prof Paresh Vyas
Vyas Lab, Room 326 Weatherall Institute of Molecular Medicine
University of Oxford
John Radcliffe Hospital
Hedley Way
Oxford OX3 9DS
- Log the date that the sample was taken and sent on the:
 - ANIMATE sample tracking website (see Sample Tracking Website Manual for full guidance)

The Sample Tracking Website will be reviewed by UCL CTC staff as part of central monitoring activities for the trial.

7.3 Peripheral blood samples (serum)

- 5ml Peripheral blood for should be drawn into hospital stock serum gel tubes. No processing is required before sending to the central laboratory.
- Label the sample clearly with the following information:
 - Trial name
 - Initials
 - Date of birth
 - Trial number
 - Date of sample collection
- Complete the Biological Sample Collection Form (template form can be found in the 'Laboratory' section of the Investigator Site File):
 - Complete both pages. Make sure all fields are completed (except for the section labelled 'for laboratory use only')
 - Complete one form for each sample being sent
 - Take a photocopy of the completed form and file in the Investigator Site File.
- To ship samples:
 - Wrap the tubes in absorbent material and place in a sealed plastic bag
 - Place the sample and Biological Sample Collection Form in a secure container which conforms to current postal regulations (P650) with the outer box labelled as "UN3373 Biological Substances Category B"
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The Sample Tracking Website will be reviewed by UCL CTC staff as part of central monitoring activities for the trial.

ANIMATE Laboratory Manual - Version History Log

Version number	Date	Summary of changes from previous version	Changes made by
1.0	15.08.2018	N/A	Pip Patrick / Oliver Schofield
2.0	28.03.2019	<ul style="list-style-type: none"> • All references to Patient-specific Biological Sample Shipping Log removed as document no longer in use on the trial. • BMS logo removed. • Minor grammatical errors amended and clarifications added. 	Oliver Schofield / Jon Teague