

Protocol Version History

Name of Trial: 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 metabolic remission after first or second line salvage therapy

Name of Chief Investigator: Dr Graham Collins

Version Number	Date	Main changes	Amend No.	REC Approval Date	MHRA Approval Date	HRA Approval Date	Date of distribution to:				
							Sites	BMS	Lab - HMDS	Lab - Oxford	PET Core lab
1.0	04.01.2018	N/A Initial version	N/A	01.03.2018	27.02.2018	13.04.2018	N/A	N/A	N/A	N/A	N/A
1.1	21.02.2018	Clarification of rationale for treatment dose/schedule at request of MHRA	1	10.04.2018	N/A	17.04.2018	N/A	N/A	N/A	N/A	N/A
2.0	10.04.2018	References to UCL Cancer Institute replaced by The Weatherall Institute of Molecular Medicine, Oxford who will now be undertaking analysis on peripheral blood samples. Minor changes to eligibility criteria and investigations to bring the protocol more into line with current standard practice. Minor changes to pharmacovigilance reporting requirements.	2	30.04.2018	20.04.2018	08.05.2018	N/A	N/A	N/A	N/A	N/A
2.1	12.06.2018	Minor updates to requirements for hepatitis serology testing to reflect standard of care within the NHS. MRC-University of Glasgow Centre for Virus Research who will now be performing TARC analysis on peripheral blood samples added to Exploratory Biological Studies section	3	13.08.2018	09.07.2018	30.08.2018	N/A	N/A	N/A	N/A	N/A

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		<p>5ml peripheral blood in serum gel tube collection added to peripheral blood samples section for TARC analysis</p> <p>Timelines for data return updated with additional CRFs</p> <p>NHS Wales Informatics Service (Wales) and the Information Services Division (Scotland) added as examples of registries to provide further data if patients are lost to follow-up, Health & Social Care Information Centre amended to NHS Digital in line with recent name change</p> <p>References to the Data Protection Act 1998 replaced by the Data Protection Act 2018</p> <p>Abbreviations updated with CCL-17 (Chemokine (C-C motif) ligand 17) and MRC (Medical Research Council) added</p>									
3.0	10.12.2019	<p>Timings of patient registration/ inclusion criteria amended and clarified:</p> <ul style="list-style-type: none"> ○ Wording amended to make it clearer when the patient can be registered ○ patients receiving brentuximab vedotin can now be registered after 3 or 4 cycles of salvage therapy, previously this had to be 4 cycles ○ Change in PET0 scanning time 14 days (± 3 days) (i.e. day 11-17 inclusive) after last treatment administration in cycle 2 of first or second line salvage chemotherapy (cycle 3 or 4 if being treated with brentuximab vedotin) ○ Guidance on immune related diarrhoea and hepatitis updated in the light of October 2019 MHRA safety advice regarding CMV infection & reactivation reported in patients treated with nivolumab and ipilimumab 	5	15.01.2020	10.01.2020	07.02.2020	NK	NK	NK	NK	NK

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		<ul style="list-style-type: none"> ○ Lipase testing removed from the trial ○ Amylase and ACTH testing changed from being required prior to every cycle to only prior to cycle 5 during trial treatment ○ Thyroid Function Tests changed from being required prior to cycles 4 and 7 to cycles 3, 5 and 7 ○ Timings for pregnancy tests amended to 3 days prior to registration, confirmation of eligibility and trial treatment ○ References to the Sample Tracking Website Manual added to prompt sites to track all samples and scans online, previously omitted in error ○ Clarification added that repeat biopsies should be performed as per standard local procedures ○ Adverse Event form added to list of CRFs, previously omitted in error ○ Minor changes made to Pharmacovigilance section to make it consistent with new UCL CTC template ○ References to Central monitoring changed to centralised monitoring in Trial monitoring and oversight section to make it consistent with new UCL CTC template ○ Dosage unit amended to g/l for haemoglobin, previously given incorrectly as g/dl ○ Reference to MRC-University of Glasgow Centre for Virus Research added to Funding section ○ ceCT, cycle 3 or 4 for BV and more detailed follow up schedule added to Trial Schema ○ ceCT added to reference guide to patient visits ○ Change of Trial Coordinator- Tesha Suddason 									

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		<ul style="list-style-type: none"> ○ Position and site updated for Dr Beth Phillips ○ BMS logo removed 									
4.0	28.05.2020	See protocol table of changes: S:\BNLI\Trials\Open\ANIMATE\03 PROTOCOL\d Protocol Drafts and Reviews\Protocol v4.0\Table of protocol changes v4.0.docx Or refer to appendix 5 (Protocol version history) of the current protocol.	6	02.07.2020	10.06.2020	10.07.2020	10.07.2020	13.07.2020	13.07.2020	13.07.2020	13.07.2020