



STRESS-L Trial, sponsored by: University Hospitals Birmingham NHS Foundation Trust

Substantial and Non-substantial Amendment Log

Study Title:	STRESS-L: Study into the reversal of septic shock with Landiolol (Beta Blockade).
Chief Investigator:	Dr Tony Whitehouse
Sponsor Internal Reference:	RRK5911
Other reference numbers (e.g. EudraCT Number):	EudraCT Number: 2017-001785-14; ISRCTN Number: 12600919

Amendment Number	Date Submitted	Where Submitted			Classification		Purpose of Amendment	Version/ Date of Amended Documents	Date Approved (Substantial Amendments Only)		
		REC	MHRA	HRA	Substantial	Non Substantial		New	REC	MHRA	HRA
SA_01	22/12/17	✓		✓	✓		Addition of new NHS site: Guy's and St Thomas' NHS Foundation Trust (PI: Dr Manu Shankar-Hari) Change of PI at existing site: Heart of England NHS Foundation Trust (New PI: Dr Joyce Yeung)	N/A	04/01/18	N/A	04/01/218
SA_02	30/01/18	✓		✓	✓		Addition of new NHS site: Nottingham University Hospitals NHS	N/A	16/02/18	N/A	16/02/18



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						Trust (PI: Dr Dan Harvey) Change of PI at existing sites: University College London Hospitals NHS Foundation Trust (New PI: Dr Niall MacCallum) Royal Victoria Hospital, Belfast Health & Social Care Trust (New PI: Dr Christopher Nutt)				
SA_03	19/04/18	✓		✓	✓	Addition of new sites: Bristol Royal Infirmary, University Hospitals Bristol NHS Foundation Trust King's Mill Hospital Mansfield, Sherwood Forest Hospitals NHS Foundation Trust Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust Royal Liverpool University Hospital Poole Hospital NHS Foundation Trust Royal Devon & Exeter NHS Foundation Trust Derby Teaching Hospitals NHS Foundation Trust Southmead Hospital, North Bristol NHS Trust Sunderland Royal Hospital, City Hospitals Sunderland NHS Foundation Trust University Hospital Southampton NHS Foundation Trust	N/A	20/04/18	N/A	20/04/18
SA_04	20/06/18	✓		✓	✓	Addition of new sites: King's College Hospitals NHS	N/A	22/06/18	N/A	22/06/18

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							Foundation Trust Royal Cornwall Hospitals NHS Trust University Hospitals Plymouth NHS Trust Dorset Country Hospital NHS Foundation Trust The Dudley Group NHS Foundation Trust Royal Free London NHS Foundation Trust University Hospitals Coventry and Warwickshire NHS Trust				
SA_05	02/08/18	✓	✓	✓	✓		CSM Germany performing labelling and packaging of IMP instead of Reig Jofre. Future batches to comply with SmPC (in reference to ambient stock) Update to team contact details in protocol.	Protocol v 2.0 31 July 2018	14/08/2018	15/08/2018	16/08/2018
NSA01	13/08/18			✓		✓	Addition of text to participant information sheets to clarify data processes in accordance with GDPR transparency requirements.	Patient PIS v2.1 7 June 2018 Legal Rep PIS v2.1 7 June 2018	N/A	N/A	14/08/2018
SA_06	18/09/18	✓		✓	✓		Addition of new sites: Bradford Teaching Hospitals NHS Foundation Trust The Royal Wolverhampton NHS Trust South Warwickshire NHS Foundation Trust North West Anglia NHS Foundation Trust Southern Health and Social Care Trust Leeds Teaching Hospitals NHS Trust	N/A	21/09/2018	N/A	21/09/2018

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NSA02	28/09/18			✓		✓	Correction to version number and date stated on consent forms in reference to the information sheets which were updated previously to comply with GDPR Transparency requirements.	Patient ICFv2.1 28 Sept 2018 Legal Rep ICF v2.1 28 Sept 2018	N/A	N/A	03/10/2018
SA_07	30/11/2018	✓	✓	✓	✓		<p>Protocol amendment includes following key changes (see protocol version log for further details):</p> <ul style="list-style-type: none"> • Update to the exclusion and inclusion criteria to clarify and update existing criteria. Includes extension of vasopressor eligibility timeframe from >48 hours to >72 hours. • Addition of biobank blood sample at EONT. • Minor additional and clarification wording changes regarding staff changes, new data protection act, data collection, consent, safety reporting and DMC meetings. <p>Update to PIS and ICF to include addition of biobank blood sample and samples to be sent to University of Birmingham.</p> <p>New relatives posters to place in ICU relatives waiting rooms.</p>	<p>Protocol v3.0 18 Oct 2018</p> <p>PIS v3.0 18 Oct 2018 Short PIS v3.0 18 Oct 2018 Legal Rep PIS v3.0 18 Oct 2018 Patient ICF v3.0 18 Oct 2018 Legal Rep ICS v3.0 18 Oct 2018</p> <p>Relatives poster v1.0 29 Oct 2018</p>	18/12/2018	20/12/2018	21/12/2018
SA_08	06/12/2018	✓		✓	✓		<p>Addition of new sites: The Newcastle upon Tyne Hospitals NHS Foundation Trust York Teaching Hospital NHS Foundation Trust Buckinghamshire Healthcare NHS</p>	N/A	07/12/2018	N/A	07/12/2018

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							Trust Rotherham NHS Foundation Trust Cambridge University Hospitals NHS Foundation Trust				
SA_09	18/04/2019	✓		✓	✓		Addition of new sites: Northampton General Hospital NHS Trust Brighton and Sussex University Hospitals NHS Trust East and North Hertfordshire NHS Trust	N/A	30/04/2019	N/A	30/04/2019
SA_10	03/07/2019	✓	✓	✓	✓		See protocol version log. Changes include updates to eligibility criteria and removal of secondary outcome.	Protocol v4.0 2 nd April 2019	29/07/2019	25/07/2019	05/08/2019
SA_11	08/07/2019	✓		✓	✓		Addition of new sites: Lancashire Teaching Hospitals NHS Foundation Trust East Lancashire Hospitals NHS Trust Mid Essex Hospital Services NHS Trust NHS Greater Glasgow and Clyde NHS Grampian Hull University Teaching Hospitals NHS Trust	N/A	12/07/2019	N/A	12/07/2019
SA_12	18/09/2019	✓		✓	✓		Addition of new sites: St George's University Hospital NHS Foundation Trust Cwm Taf University Health Board Removal of an existing site: North West Anglia NS Foundation Trust Change of Principal Investigator: Southern Health and Social Care Trust	N/A	30/09/2019	N/A	30/09/2019

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SA_13	20/12/2019	✓		✓	✓		Update to website wording and addition of Twitter account	Twitter Guidance v1.021Oct2019	17/01/2020	N/A	03/02/2020
SA_14	04/02/2020	✓	✓	✓	✓		See protocol version log. Changes included updates to eligibility criteria. Addition of new site: Walsall Healthcare NHS Trust Updates to patient and legal representative information sheets	Protocol v5.0 17 th December 2019 Patient Information Sheet v4.0 24 th January 2020 Legal Representative Information Sheet v4.0 24 th January 2020	15/04/2020	26/02/2020	10/06/2020
NSA_03	08/04/2020	✓		✓		✓	Correction to version number and date stated on consent forms in reference to the information sheets which were updated previously in SA_14	Consent Form V4.0 07 th April 2020 Legal Rep Consent Form V4.0 07 th April 2020	N/A	N/A	13/05/2020
SA_15	Not submitted. Initially thought required to initiate restart and implement COVID-19 related protocol changes but HRA confirmed this was not required.										
SA_16	20/10/2020	✓		✓		✓	<u>Addition of new sites:</u> University Hospitals of Leicester NHS Trust Bolton NHS Foundation Trust Royal United Hospitals Bath NHS Foundation Trust Pennine Acute Hospitals NHS Trust <u>Change of PI at existing site:</u> Northampton General Hospital NHS Trust <u>Information of site closures:</u> Buckinghamshire Healthcare NHS Trust South Warwickshire NHS Foundation Trust University Hospitals Dorset NHS Foundation Trust	N/A	18/11/2020	N/A	18/11/2020

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NSA04	13/01/2021	✓		✓		✓	The purpose of this amendment is to amend the Patient Information Sheet and Legal Representative Sheet to state add two additional personal data special category variables (ethnicity and postcode) will be collected from trial participants. This information is relevant and key for the data analysis for the trial in this patient population. A further change has also been added to clarify the research blood samples will be analysed at Higher Education Institutes other than the University of Birmingham as well.	Patient Information Sheet v6.0 21 st December 2020 Legal Representative Information Sheet v6.0 21 st December 2020	03/02/2021	N/A	03/02/2021
NSA05	23/09/2021			✓		✓	The purpose of this amendment is to extend the project contract to August 2022 to continue with recruitment due to ongoing COVID-19 related delays. Further to this, the amendment is to inform of 4 new recruitment sites and the early closure of 3 recruitment sites.	N/A	N/A	N/A	N/A