Guck, Jonathan

From: STRESS-L, resource
Sent: 06 September 2019 13:25
To: STRESS-L, resource
Subject: FW: [Test] STRESS-L September 2019 Newsletter

STRESS-L September Newsletter, Issue 11

@StressLTrial Trial Website

Welcome to the STRESS-L Newsletter!
Please let us know if you have any suggestions for improvements or information you would like to see included on a monthly basis.

Please click on the headers below which will take you to the different sections.

Trial Update

The summer may be over and it is getting colder already but STRESS-L recruitment has hit a high of **60** patients! Thank you for your hard work during this busy period.

Guy's & St Thomas', King's College and Rotherham

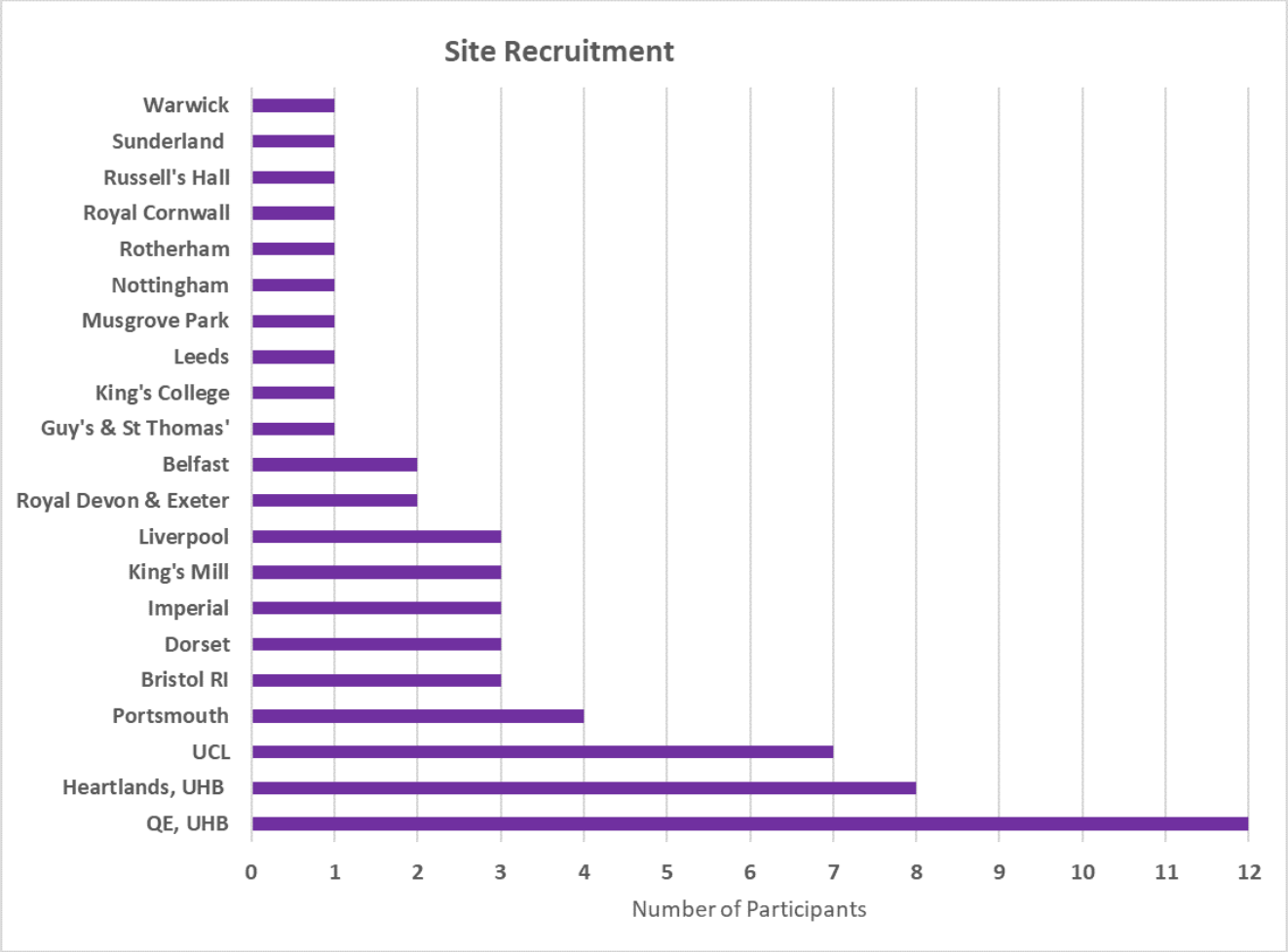
Well done to the above sites for recruiting your first participants in August and September!

Milestones

60 patients recruited so far

29 sites open to recruitment

32 sites initiated to date



Eligibility Clarifications

Time lines:

Please note that for eligibility, noradrenaline dose should be ≥ 0.1 mcg/kg/min at the time of randomisation **not** at the start of the 24 hour window.

If a patient's noradrenaline dose is below this threshold 24 hours after the start of vasopressor therapy, the patient should be reviewed throughout the 24-72 hour window to assess whether noradrenaline dose reaches this threshold.

Likewise, heart rate should be ≥ 95bpm at the time of randomisation but does not necessarily need to be ≥ 95 at the start of the 24 hour window.

Advanced liver disease:
The trial excludes patients who have advanced liver disease and a Child Pugh score of ≥ B is used to guide this, however, it is important to distinguish between patients who genuinely exhibit pre-existing advanced liver disease and those who exhibit liver dysfunction as a result of septic shock.

A previous diagnosis of advanced liver disease is clearly a good indicator but it is important to consider that not all patients will have received a formal diagnosis.

If a patient presents at hospital with no diagnosis of advanced liver disease, no history of alcoholism, lacks jaundice and displays good bilirubin counts, it is likely that any subsequent liver dysfunction is caused by septic shock and these patients should be considered for the trial.

Clinical assessment here is vital and should you have any queries, please don't hesitate to get in touch with the coordinating team.

Protocol Amendment v4.0 02/Apr/2019

As we have now passed the implementation deadline for substantial amendmnet 10, please ensure the protocol V4.0 02/Apr/2019 is followed.

The main changes to the protocol are outlined below. Please refer to Protocol Version log V4.0 for a comprehensive list.

Changes to the Exclusion Criteria

Addition of:

- Any form of compensatory tachycardia
- Any form of vasodilatory shock that is not caused by sepsis
- Decision of withdrawal of care is in place or imminently anticipated

Removal of:

- Having been treated with any beta blocker during in the seventy two hours prior to randomisation

Amendment and clarification of Efficacy Secondary Outcomes

Removal of:

- Individual organ failure days in 28 day survivors through measures of oxygenation, renal, hepatic and coagulation function
- Changes in ECG between Randomisation and End of ICU

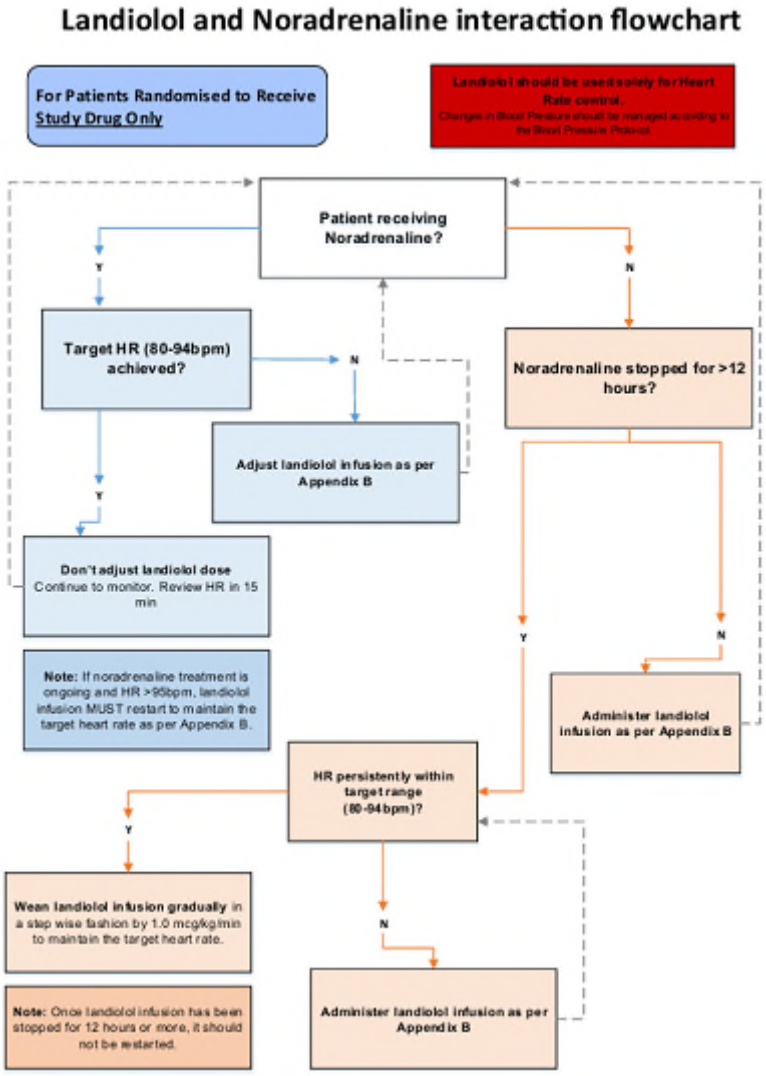
Clarification of landiolol infusion and stopping infusion

Please see updated landiolol dosing laminate (v3.0) for guidance.

Changes to Documentation following the Protocol Amendment v4.0

Following the protocol amendment, the following documents will be updated and circulated form implementation;

- Temporary Beta Blocker CRF - to collect any beta blocker the participants may be on prior to and after randomisation up to 14 days
- Updated Eligibility CRF - to amend the inclusion/exclusion criteria. **Please note** that whilst the paper CRF has been updated, the eCRF on the database is still the previous version, so please leave the Eligibility Form on the database blank until this has been resolved
- Updated Day 28 Follow Up CRF - to remove the collection of SOFA Score data. **Please note** that whilst the paper CRF has been updated, the eCRF on the database is still the previous version, so please leave the SOFA Score section of the eCRF blank until this has been resolved
- Updated Patient CRF Record - in line with the changes to the CRFs listed above
- Updated SAE Form - it will no longer be possible to fax SAE forms to the coordinating team. The coordinating team will also now be responsible for the expectedness assessment and the event classification, so these sections will no longer be completed by site staff.
- Updated Document and Protocol Version Logs
- Updated Screening Log - in line with the changes to to the inclusion/exclusion eligibility criteria
- Updated eligibility cards - these will be circulated to all sites following approval of the amendment



Important Update on IMP Management

After review of landiolol protocol compliance we have identified a number of instances where landiolol administration is not inline with the infusion protocol for a prolonged period. These instances have all occurred overnight and highlight the difficulty of handing over IMP management and maintaining compliance with the trial protocol.

We appreciate that each centre has a large pool of bedside nurses who assist with the administration of IMP

out of hours and that it can prove difficult to maintain training in a trial with low target recruitment rates.

Discussions with several sites has identified a number of ideas to help reduce deviations from the trial infusion protocol which are summarised below. Please let us know if you have any further tips to suggest!

- Conduct 1:1 handovers with ICU staff to ensure Landiolol infusion protocol is understood
- Ring overnight staff once handover complete to ensure they understand the protocol
- Ideally, research nurse team stay until overnight staff arrive to conduct the handover themselves as all non-compliances so far have happened overnight, often involving a secondary handover
- Ring ICU staff daily over the weekend if possible
- Distribution of trial landiolol infusion laminates to bedside nursing team or storage at the bedside to guide administration
- Detailed handover to flag up participation in the study and how to oversee IMP infusion
- Hosting research coffee mornings where principles of the study can be reinforced
- Reminders of study in internal newsletter
- Circulation of trial training slides for ICU clinical staff
- Display of posters in staff facing areas - the current Poster for clinical areas can aid recruitment

WCTU Action Points

- WCTU will prepare an additional poster displaying tips for landiolol infusion
- WCTU will prepare certificates of recognition which can be distributed to colleagues who support trial activity
- WCTU will further explore the development of an instructional video guiding landiolol infusion. We would appreciate your input to help assess whether this would be a useful venture

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Buddy Scheme

As mentioned recently we have implemented a site buddy scheme to help sites share experiences and learn from each other. We are really pleased to hear that this will be a useful tool for some sites and we will continue to organise the trial monthly teleconferences and catch up calls to maintain our own contact with centres. If you would like to be included in the buddy scheme, please let us know.

One of our trial sites has recently asked for guidance on the use of electronic systems for patient screening. If your site uses the EPR Philips system for identifying potential patients we would appreciate any tips you may have!

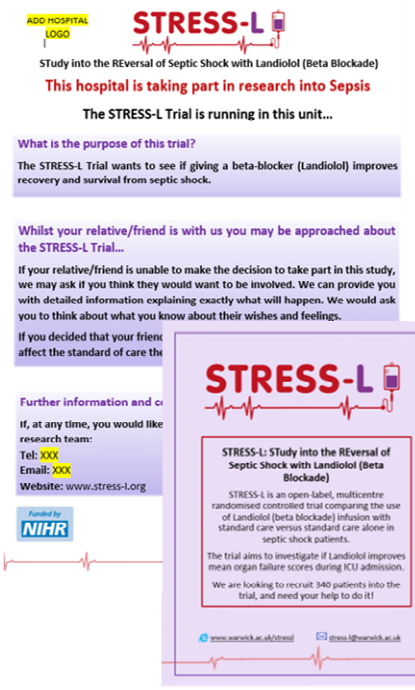
World Sepsis Day - 13th September

We will be marking World Sepsis Day by hosting an event here at the Warwick Clinical Trials Unit. Talks will be provided by STRESS-L CI Dr Tony Whitehouse, ADAPT-Sepsis CI Prof Paul Dark and by one of our valued PPI members. We will be discussing the background to sepsis including a personal account of the condition, the current vital research which you are all facilitating and the promising new horizons.

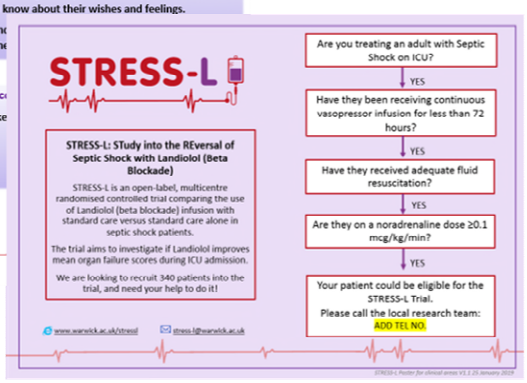
If you are marking the occasion in any way, we would love to hear about it. The World Sepsis Day website provides further information on how you can be involved and engage via social media:
https://www.worldsepsisday.org/wsd2019

Trial Materials

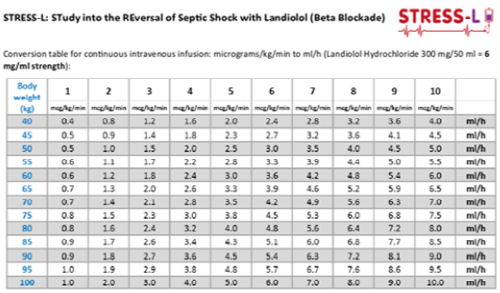
Please let us know if you would like to receive any of our trial materials below!



ICU Staff and Relative posters



Landiolol dosage chart laminates

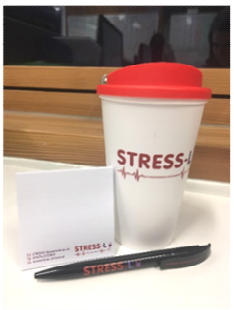


STRESS-L: STudy into the REversal of Septic Shock with Landiolol (Beta Blockade) STRESS-L

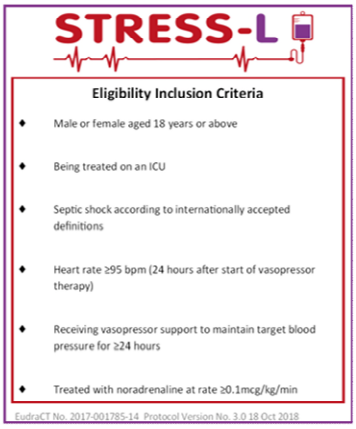
Conversion table for continuous intravenous infusion: micrograms/kg/min to ml/h (Landiolol Hydrochloride 300 mg/50 ml = 6 mg/ml strength):

Body weight (kg)	1 mcg/kg/min	2 mcg/kg/min	3 mcg/kg/min	4 mcg/kg/min	5 mcg/kg/min	6 mcg/kg/min	7 mcg/kg/min	8 mcg/kg/min	9 mcg/kg/min	10 mcg/kg/min	
40	0.4	0.8	1.2	1.6	2.0	2.4	2.8	3.2	3.6	4.0	ml/h
45	0.5	0.9	1.4	1.8	2.3	2.7	3.2	3.6	4.1	4.5	ml/h
50	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0	ml/h
55	0.6	1.1	1.7	2.2	2.8	3.3	3.9	4.4	5.0	5.5	ml/h
60	0.6	1.2	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0	ml/h
65	0.7	1.3	2.0	2.6	3.3	3.9	4.6	5.2	5.9	6.5	ml/h
70	0.7	1.4	2.1	2.8	3.5	4.2	4.9	5.6	6.3	7.0	ml/h
75	0.8	1.5	2.3	3.0	3.8	4.5	5.3	6.0	6.8	7.5	ml/h
80	0.8	1.6	2.4	3.2	4.0	4.8	5.6	6.4	7.2	8.0	ml/h
85	0.9	1.7	2.6	3.4	4.3	5.1	6.0	6.8	7.7	8.5	ml/h
90	0.9	1.8	2.7	3.6	4.5	5.4	6.3	7.2	8.1	9.0	ml/h
95	1.0	1.9	2.9	3.8	4.8	5.7	6.7	7.6	8.6	9.5	ml/h
100	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0	ml/h

Travel mugs, post it notes & pens!



Eligibility card laminates



Please let us know if you have any further suggestions

Co-enrolment update

Please see below for our list of currently approved co-enrolling trials. Discussions are in progress with further studies but please let us know if there are any at your site which are a priority!

- A-STOP
- ADAPT-Sepsis
- BLING III
- CRYOSTAT-2
- FLO-ELA
- REST
- STARRT-AKI
- TAME

- VACIRiSS