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From: STRESS-L, resource
Sent: 24 June 2019 09:56
To: STRESS-L, resource
Subject: STRESS-L June 2019 Newsletter

STRESS-L June Newsletter, Issue 9

@StressLTrial Trial Website

Welcome to the new email format of the STRESS-L Newsletter which we hope is more accessible! 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 STRESS-L trial has reached a major milestone with **50** patients recruited! Congratulations to Royal Liverpool for recruiting patient 50 and for all site contributions so far.

May in particular was a busy month with 9 patients enrolled and a number of sites recruiting their first patients. Well done to Belfast, Nottingham, Musgrove Park, Royal Liverpool, Russell's Hall, Warwick and Leeds for recruiting their first patients since our last newsletter. Your persistence is greatly appreciated!

Queen Alexandra Hospital, Portsmouth

Well done to **QAH** for hitting your yearly target of 4 participants!

Milestones

50 patients recruited so far

29 sites open to recruitment

31 sites initiated to date

IMPORTANT: Changes to IMP Management

As you will know from recent correspondence, the trial is shortly due to transition to refrigerated IMP stock which must be stored between 2-8 degrees. The new IMP stock is due to be delivered to sites on Wednesday 26 June unless otherwise agreed with the WCTU trial team.

Please be aware no further ambient IMP stock will be supplied.

Once the refrigerated stock is received and QP release is issued, the existing ambient stock must be quarantined immediately in pharmacy and the new refrigerated stock released. The coordinating team should then be contacted to authorise destruction of the ambient stock. Please ensure that you read our IMP transition process document v1.0 13 June 2019 and updated IMP Management Manual v4.0 9 May 2019 where you will find further details regarding the transition from ambient to refrigerated IMP stock. If not already done so please contact WCTU trial team to confirm you have read and filed these documents as soon as possible.

UKCCRG

Emma Skilton (Trial Manager) and Maddy Flawn (Trial Coordinator) attended this year's UK Critical Care Research Group at the Rose Bowl in Leeds on Friday 7 June 2019. Thanks to all who attended our trial update meeting during the Friday session. It was great to see familiar faces as well as new sites who are interested in becoming a recruitment site for the trial.

Care Withdrawal Guidance

Patients should not be recruited if a withdrawal of care decision is in place or imminent. HOWEVER, as the target population under study are very sick (don't forget Morelli's [JAMA, 2013] population had a mortality of 80%!), patients should be considered for a trial where a withdrawal of care decision is not in place.

Landiolol and Noradrenaline Infusion

Landiolol Units

Some sites have entered the Landiolol doses in ml/hr instead of mcg/kg/min on the e-CRF. For the purposes of the trial, this data must be entered in mcg/kg/min. This helps us to monitor the correct dose has been given and that it does not exceed the max dose of 40 mcg/kg/min.

We apologise for our contribution to this confusion as the previous paper CRF stated ml/hr. This has been amended and the updated v5.0 18 April 2019 (see attached) has been circulated to all sites on 23 April 2019.

It has also come to light on some occasions although the Landiolol dose has been entered in mcg/kg/min and stepped up or down by 1 mcg/kg/min this might result in a decimal fraction dose being administered and entered in to the database. This is because the providing dosing chart provides dosing for weights in 5kg blocks and NHS Trust clinical systems can convert the dose between ml/hr to mcg/kg/min based on the exact weight of the patient which might fall between these blocks resulting in a decimal dose. If this is the case this is absolutely fine but the trial team will get in touch to confirm this to ensure the dosing has been entered correctly and generate a note to file to explain this.

Stopping Landiolol Infusion

Please refer to our new landiolol dosing laminates (V3.0 07 May 2019) which features our new Landiolol and Noradrenaline Interaction Flowchart.

Data Management

Urgent Landiolol Data Queries

Please be aware following findings from recent routine monitoring protocol compliance checks, an automatic report will be generated and sent to site if a Landiolol Dose has been entered on to the e-CRF which exceeds max dose of 40 mcg/kg/min or if it is not an integer. This helps us to monitor correct dosing of Landiolol. If the dose has been entered in decimal points due to local conversion system from ml/hr to mcg/kg/min this is acceptable but will still be queried to document the reason why.

Critical Eligibility Data queries

The Critical Eligibility Data queries report has recently been amended to include Heart Rate and Noradrenaline Dose

at randomisation to confirm the patient was eligible for the trial. Please ensure this data alongside, start date and time of vasopressors/noradrenaline is entered in the e-CRF within 24 hours following randomisation.

Adverse event reporting

Please remember to document any adverse events on the adverse events form.

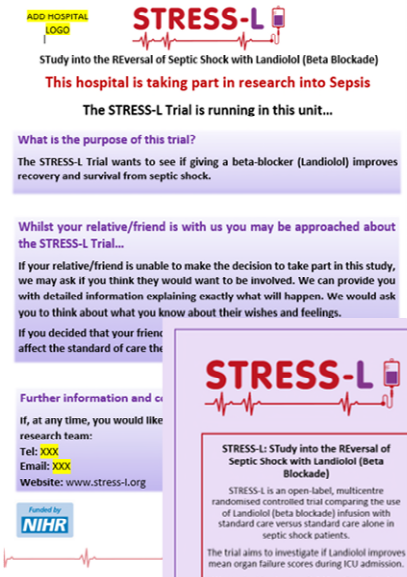
The following events are exempt from adverse event reporting AND serious adverse events as well as SUSAR's and SAR's UNLESS the investigator deems the event to be related to the administration of the study drug:

- Death Related to sepsis
- Cardiovascular failure, including the need for vasopressors / inotropes
- Respiratory failure, including mechanical ventilation and acute lung injury
- Hepatic impairment as measured by Transaminases <1000 IU/L
- Renal failure, including the need for renal replacement therapy
- Haematological / Coagulation failure, including thrombocytopaenia and disseminated intravascular coagulopathy
- Delirium / confusion

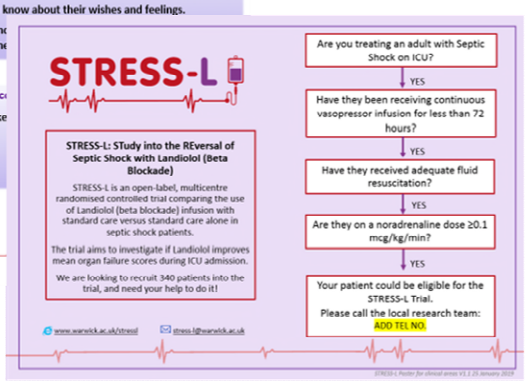
If an event occurs which is **not** included in one of the above outcomes, this must be reported as per safety reporting definitions. For example, if a patient has pyrexia and this is not related to the drug and not serious, this must be reported as an adverse event. Even though Pyrexia is expected in some cases to occur due to Sepsis, it should still be reported.

Trial Materials

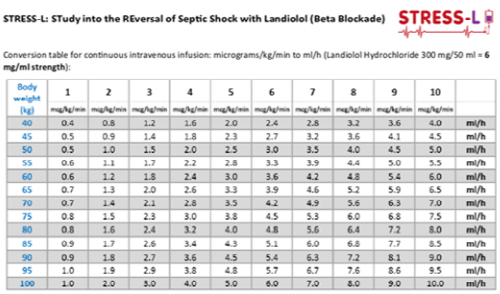
Please let us know if you would like to receive any of our trial materials below!



ICU Staff and Relative posters



Landiolol dosage chart laminates

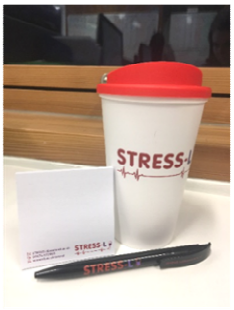


STRESS-L: STudy into the REversal of Septic Shock with Landiolol (Beta Blockade) STRESS-L

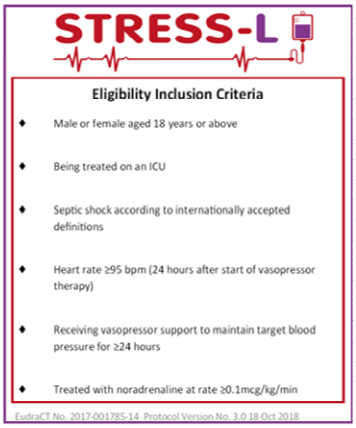
Conversion table for continuous intravenous infusion: micrograms/kg/min to ml/h (Landiolol Hydrochloride 300 mg/50 ml = 6 mg/ml strength):

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
- TAME
- VACIRiSS