Guck, Jonathan

From: adaptsepsistrial, Resource
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To: adaptsepsistrial, Resource
Subject: ADAPT-Sepsis July Newsletter

ADAPT-Sepsis July Newsletter

Biomarker-guided antibiotic duration for sepsis

@AdaptSepsis Trial Website Trial Email

Welcome to the new email format of the ADAPT-Sepsis 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.

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Trial Update

Hello all, thank you for your hard work in helping us pass the **500** mark for patient recruitment! Congratulations to Southmead for recruiting number 500.

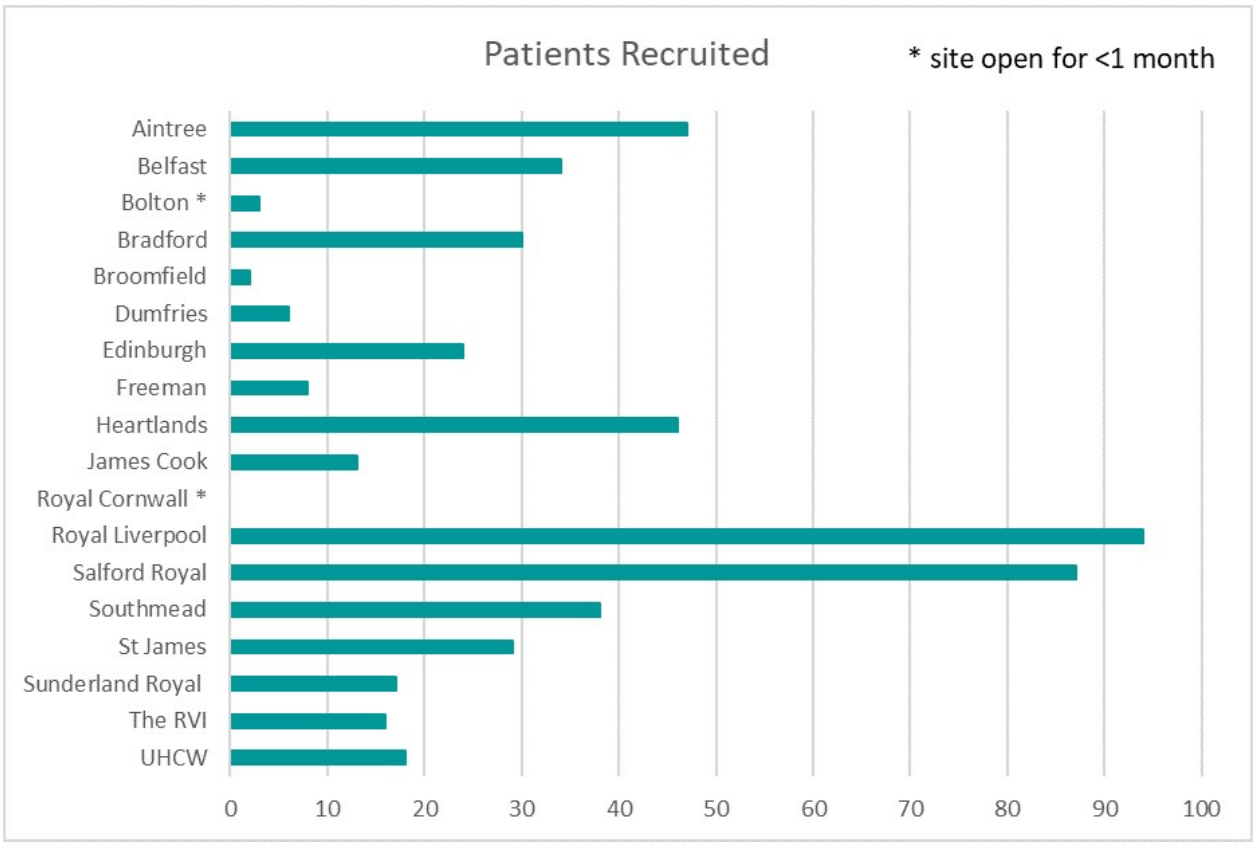
Since our last update we have welcomed Bolton, Broomfield and Royal Cornwall to the study - congratulations in particular to Broomfield for recruiting within their first 2 hours! It was also great to meet with the teams at Cwm Taf, Wythenshawe and Lancaster recently who are all keen to get started. We have a number of further SIVs planned for the coming weeks so look forward to progressing set up at further sites.

Trial Milestones

512 patients recruited so far

18 sites open to recruitment

22 sites initiated to date



ACB Focus Conference 2019

Nicola and Johnny attended the Association for Clinical Biochemistry Focus conference in Glasgow last month to give a presentation on the trial and staff a research stand. We were aided in this venture by our lab lead from St James' University Hospital, Helena Baker, who shared her experiences of the study so far. Thanks for your help, Helena!

This was a great opportunity for us to engage with the biochemistry community and to convey the importance of our study. We look forward to progressing site set up discussions with a number of the attendees.

UKCCRG

Prof Dark and Maddy attended the UKCCRF in Leeds and held a brief trial update meeting with the A-STOP trial team. Thanks for all who attended.

New Site FAQs

Can I still be involved in the trial if our site does not provide local laboratory PCT analysis?

Yes – we can work with you and your team to facilitate NHS adoption of a laboratory PCT assay for your Clinical Biochemistry Department. This includes financial support.

Can CRP continue to be used as per standard care in trial participants?

Yes. You can continue to measure CRP daily if this an agreed unit level standard at your hospital. We use an extra trial blood sample in order to test either CRP or PCT levels, and you would be blinded to the result.

We already use PCT though do not have a protocol for discontinuation of antibiotics. Should we be selected as a site would "standard care" be our current practice, or would be have to stop measuring PCT routinely for patients in the "standard care" group?

You will not be able to continue routinely measuring PCT for trial patients and must be able to ensure a position of equipoise for an individual trial patient. This is because the guidance for stopping antibiotics utilising PCT is better defined than the guidance for CRP.

For patients **not** enrolled in the study, PCT can proceed as normal.

Learning Points

Antibiotic Data

Please remember to add in any stop dates for antibiotics once these become known.

Immunosuppressants

One of our exclusion criteria pertains to patients who are severely immunocompromised. Patients who have lower levels of immunodeficiency should still be considered for the trial and it is only those patients who are showing evidence of severe immunosuppression, e.g. severe neutropenia, that should be excluded. Please don't hesitate to discuss with the coordinating team if you have any queries.

Non-trial PCT

Please remember that routine or non-trial PCT should not be performed in ADAPT-Sepsis participants from the time of randomisation until Day 28. If a PCT test is performed, please complete a protocol deviation form to document the occurrence.

Telephone Consent

Just to emphasise a change in our last protocol amendment (V2.0) - it is now permitted to gain verbal telephone consent from personal consultees, friends or relatives prior to obtaining written informed consent. We hope this will assist with gaining consent within our tight inclusion window.

Eligibility Clarifications

The 24 hour clock for antibiotic treatment starts when a patient is administered antibiotics specifically for sepsis, regardless of if they have received antibiotic treatment for an infection leading up to the sepsis episode. We have included a couple of examples to help illustrate this:

Scenario 1:

64y male patient arrives at A&E with signs and symptoms of a lower respiratory tract infection (pneumonia) of low severity, with no clear signs of sepsis. It is not thought safe to discharge the patient home due to complex social circumstances and the fact he has not been drinking very well and has a persistent fever. He is treated in the Emergency Assessment Unit (EAU) overnight with a single first line iv community

acquired antibiotic based on local hospital guidance and iv fluids. The following day, 36 hours after admission, his condition is worsening with a low blood pressure - not improving with iv fluids - his oxygen saturation is falling despite mask supplementary oxygen, his urine output is falling and he has become confused. He is reviewed urgently by the EAU team, his iv antibiotics are escalated to dual therapy appropriate for severe community acquired pneumonia and sepsis, and he is referred to critical care.

Overall, he has received 36 hours of iv antibiotics since admission but has only just received iv antibiotics for a severe infection/sepsis – he is therefore eligible for consideration for recruitment into the ADAPT-Sepsis study assuming the senior treating clinician agrees.

Scenario 2:
A 64y female patient is day 3 after large bowel resection surgery for a tumour. She is making good progress and starting to take oral fluids. An old iv cannula site is looking red, feels hot to touch and she has a mild fever. Her treating surgical team decide that she may have a cellulitis and treat her with iv flucloxacillin through another iv canula having already removed the old canula. The following day, 36 hours after commencing iv flucloxacillin, she becomes very unwell with clear signs of septic shock. Her iv antibiotics are escalated to broad spectrum – including two agents – and she is referred to critical care.

Although she has received at least 36 hours of iv antibiotics, the iv antibiotics for septic shock have only just been commenced and she is eligible for consideration for recruitment to ADAPT-Sepsis assuming the senior treating clinician agrees.

Co-enrolment

Below is our current list of approved co-enrolling trials with more in progress.

- A2B
- A-STOP
- BIT (Immune biomarkers and clinical outcome in trauma patients)
- BLING III
- FLO-ELA
- GenOMICC
- ILoNIS
- INNATE-LIKE T CELLS IN SEPSIS (ILTIS): IMPLICATIONS FOR EARLY DIAGNOSIS AND RESCUE OF IMMUNE SUPPRESSION – A FEASIBILITY STUDY
- INTACT
- PQIP
- RADAR-2
- REALIST
- RESORP
- REST
- STARRT-AKI
- SNAP-IT
- STRESS-L
- The 65 Trial
- Understanding stroke-induced B cell changes and their relationships with stroke-associated infection

Co-enrolment with observational studies is a fast tracked process. Where co-enrolment with observational studies will take place, please forward the relevant trial protocols for our records and approval.

For interventional studies, we will conduct a thorough review process with the respective coordinating teams. Please inform us of any current or upcoming interventional studies to prioritise.