# ECUSTEC Newsletter


## Issue 1 | December 2016

**Full Title**: Eculizumab in Shiga-toxin producing E.Coli Haemolytic Uraemic Syndrome (ECUSTEC): A Randomised, Double-Blind, Placebo-Controlled Trial

**Short Title**: The ECUSTEC trial

**Welcome to the first issue of the ECUSTEC Newsletter!**
**We look forward to working with you in the New Year and we hope that ECUSTEC will start recruiting in early February 2017!**

**Design:**
Phase II randomised, parallel-group, double blind, placebo-controlled trial.

**Aim:**
To assess whether Eculizumab (Ecu) reduces the severity of Shiga-toxin producing Escherichia coli Haemolytic Uraemic Syndrome (STEC HUS) in children and young people.

### Birmingham Clinical Trials Unit (BCTU) Christmas Closure

Please note that the ECUSTEC trial office at BCTU will be closed from:
**2pm Thursday 22nd December 2016 until 9am Wednesday 4th January 2017**.

The ECUSTEC trial is supported by the Efficacy and Mechanism Evaluation (EME) Programme, an MRC and NIHR Partnership

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| **Participating in ECUSTEC** | The trial will take place in **12** centres across the UK with the assistance of the Clinical Research Network (CRN). Applications are currently in progress from **12** ECUSTEC sites to gain all the necessary NHS permissions to allow the trial to begin at each site. The table below shows the ECUSTEC sites that were included in the initial IRAS applications. |

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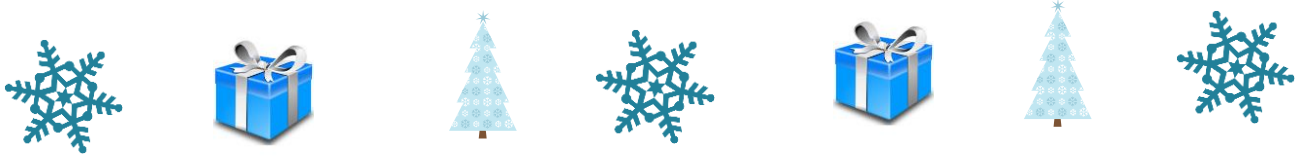
| **Alder Hey Children's Hospital** | **Leeds General Infirmary** |
| **Birmingham Children's Hospital** | **Nottingham Children's Hospital** |
| **Bristol Royal Hospital for Children** | **Royal Hospital for Children, Glasgow** |
| **Evelina London Children's Hospital** | **Royal Manchester Children's Hospital** |
| **Great North Children's Hospital** | **Southampton Children's Hospital** |
| **Great Ormond Street Hospital** | **University Hospital of Wales** |



**ECUSTEC Trial Details**

ECUSTEC is a randomised, parallel-group, double blind, placebo-controlled trial of eculizumab in 134 children aged 6 months to <19 years, inclusive, with STEC HUS. The trial contains an internal pilot phase of 18 months (12 months recruitment, 6 months follow up) to determine whether the substantive trial will continue.

**Background**

- STEC HUS is the most common single cause of paediatric acute kidney injury, affecting approximately 100 UK children each year.
- It has a 2-3% mortality rate and considerable morbidity, with 50-60% of children requiring dialysis.
- 20-25% develop severe disease with other organ involvement, including colonic necrosis and perforation, central nervous system disturbance, pancreatitis and myocardial dysfunction.
- Long term complications such as chronic kidney disease (CKD) or more rarely permanent brain injury occur in up to 1/3 of survivors.
- Previous trials have failed to demonstrate improved short term or long term outcomes with numerous interventions including anticoagulation, plasma infusion, corticosteroids or oral therapy with a Shiga toxin binding agent. There is limited evidence suggesting that early volume expansion with 0.9% saline may reduce the incidence of oligoanuria.
- There is evidence in the closely related condition of atypical HUS that Ecu (a monoclonal antibody that inhibits complement) is effective, and complement is believed to also play a role in the pathogenesis of STEC HUS. Whilst there has been some research into the administration of Ecu in patients with STEC HUS, it has been of low methodological quality and findings have been variable. Furthermore, within the descriptions published, Ecu has been administered later in the disease process after other therapeutic strategies, but data suggests complement activation occurs early in the disease.

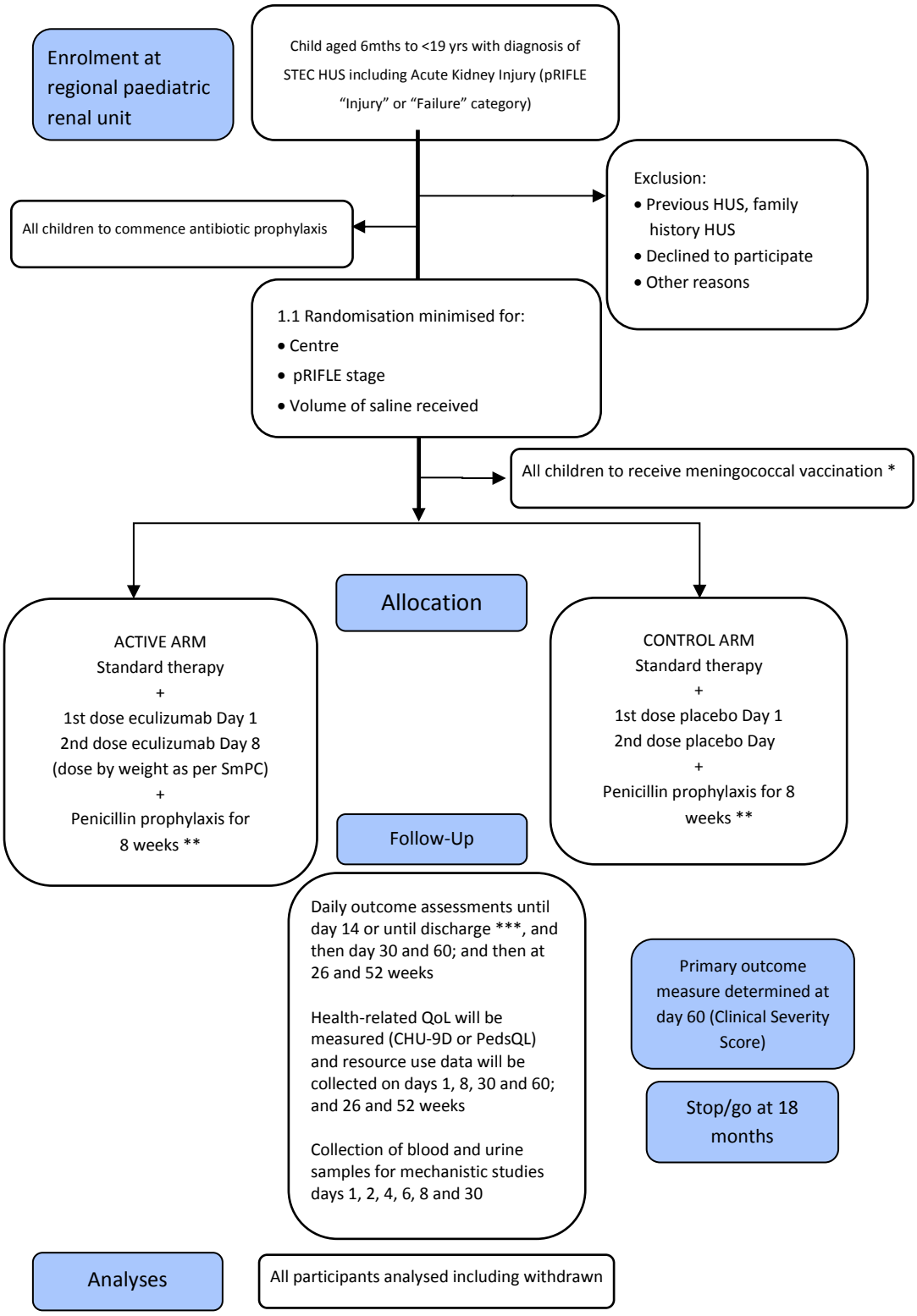
**Need for the ECUSTEC trial**

The use of eculizumab for the treatment of severe STEC HUS is increasing internationally, with no objective evidence of efficacy or safety in children, and at huge cost to the NHS and other health services. If the efficacy of eculizumab in STEC HUS is not properly evaluated in a prospective trial, unregulated use will increase until a controlled trial becomes unfeasible. The ECUSTEC trial provides the opportunity to evaluate eculizumab in STEC HUS objectively. If efficacious, this treatment may alter the natural history of STEC HUS, reducing acute mortality, morbidity and long term sequelae. If eculizumab is found to be ineffective, the trial will help to ensure that NHS resources are not wasted.

**Follow-up**

All participants will be followed-up for 52 weeks. **Daily until discharge** (reducing to weekly after Day 14 if still admitted), then at **30 and 60 days** and then **6 and 12 months** post randomisation.

## ECUSTEC Trial Schema




*Meningococcal B vaccine (Bexsero™) and conjugate meningococcal ACYW vaccine (Nimenrix or Menveo) will be given to all ECUSTEC trial participants (unless Bexsero™ already received as part of UK immunisation programme). Child <12 months Menveo; ≥12 months Menveo or Nimentrix. If platelet count $<50x10^9$/l defer vaccination until platelet $>50x10^9$/l
** erythromycin if penicillin allergic
*** assessment at day 21 and 30 if in-patient

| **ECUSTEC Details:** | | |
|---|---|---|
| **Trial Sponsor:** The Newcastle Upon Tyne Hospitals NHS Foundation Trust<br>**IRAS Project Code:** 199217 | | **Funding:** National Institute for Health Research Health, Efficacy and Mechanism Evaluation Programme (NIHR EME).<br>**Ref: 14/48/43** |
| **EUDRACT No:**<br>2016-000997-39<br>**CTA**:<br>Approval: TBC | **REC Ref No.:** 16/NE/0325 North East - Newcastle & North Tyneside 1 Research Ethics Committee<br>Approval: TBC | **The ECUSTEC trial has been adopted by the NIHR Clinical Research Network (CRN)** |

## The EUCSTEC trial team are always here to help. For further information about the ECUSTEC trial please contact us:

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**Thank you for taking the time to read the first ECUSTEC Newsletter. We look forward to the first participant being randomised!**

## We would like to take this opportunity to wish you a very Happy Christmas!