ECUSTEC PIC Newsletter

Issue 1 | August 2017

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

Design:	**Aim:**
Phase II randomised, parallel-group, double blind, placebo-controlled trial.	To assess whether Eculizumab (Ecu) reduces the severity of Shiga-toxin producing Escherichia coli Haemolytic Uraemic Syndrome (STEC HUS) in children and young people.

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

Welcome to the first Patient Identification Centre (PIC) Newsletter!

The ECUSTEC trial opened to recruitment on the 10th July 2017 and the 1st patient was randomised on the 11th August 2017 at Great Ormond Street Hospital!!!

Firstly, we would like to thank all of the ECUSTEC collaborators for supporting the trial and agreeing to participate as a PIC. Your support is very much appreciated. We are also pleased to inform you that **Dr Sally Johnson and the team** at the **Great North Children's Hospital**, **Prof Moin Saleem and the team** at **Bristol Royal Hospital for Children**, **Dr Aoife Waters and the team** at **Great Ormond Street Hospital** and **Dr Andrew Lunn and the team** at **Nottingham Children's Hospital** are now **fully approved** to randomise patients into the trial.

If one of the centres open to recruitment is your referral tertiary centre, and your patient has been accepted for transfer to the centre with suspected STEC HUS, you can now provide **ECUSTEC Patient Letters for PICs** to **potential patients/families** prior to transfer.

Please could PICs who have not yet confirmed capacity and capability contact the trials team (**ecustec@trials.bham.ac.uk**) who can assist in finalising set-up.

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.

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.

Notices to ECUSTEC Investigators at PICs!!!!

Definition of HUS

We would like to remind PICs that the inclusion criteria states for the **diagnosis of HUS**:

a) Micro-angiopathic haemolytic anaemia (indicated by fragmented red cells on blood film OR plasma lactate dehydrogenase (LDH) above local centre reference range)
AND
b) Thrombocytopenia (platelets <150x109/l)
AND
c) Acute Kidney Injury (AKI): "injury" or "failure" category of pRIFLE criteria despite correction of hypovolaemia

Please note the patient must meet ALL of the eligibility criteria to participate in the trial. Please refer to Section 5 of the ECUSTEC protocol (www.birmingham.ac.uk/ecustec/trialdocuments).

Steps for PICs if STEC HUS is suspected:

PIC investigator should contact the regional paediatric nephrologist at the tertiary centre (recruiting centre)

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Potential patients and/or parents/guardians can be given the ECUSTEC Parent/Participant 16-18yrs or Older Child Letter for PICs

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Ensure hypovolaemia is corrected prior to transfer to the tertiary centre if possible

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Remind patients/parents/guardians to obtain the red book for the tertiary centre

Recruiting Centres Participating in ECUSTEC	We are pleased to announce we now have **4** centres fully approved to randomise patients into the ECUSTEC trial. Patients will be recruited from **12 tertiary** centres across the UK with the assistance of the Clinical Research Network (CRN) and PICs. Applications are currently in progress from **8** ECUSTEC sites to gain all the necessary 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.

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**

* Site opened to recruitment

ECUSTEC Details:

Trial Sponsor: The Newcastle Upon Tyne Hospitals NHS Foundation Trust **IRAS Project Code:** 199217		**Funding:** National Institute for Health Research Health, Efficacy and Mechanism Evaluation Programme (NIHR EME). **Ref: 14/48/43**
EUDRACT No: 2016-000997-39 **CTA**: 17136/0282/001-0001 Approval: 3rd January 2017	**REC Ref No.:** 16/NE/0325 North East - Newcastle & North Tyneside 1 Research Ethics Committee Approval: 23rd January 2017	**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 ECUSTEC PIC Newsletter!!!