ECUSTEC Newsletter

Issue 4 | December 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

Welcome to the fourth issue of the ECUSTEC Newsletter!

Since ECUSTEC opened on the 10th July 2017, **5 patients** have been recruited to the trial and **7 centres** are now open to recruit patients. We would like to congratulate and thank **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** and **Dr Aoife Waters and the team** at **Great Ormond Street Hospital** who have recruited patients into the trial so far. We would also like to thank all of our investigators for their continued support and efforts in approaching potential patients/families to discuss the trial.

Please note **the internal pilot phase** of the ECUSTEC trial has commenced and the **recruitment phase** of the pilot is due **to end in July 2018**. We are now almost **half way** through the **recruitment pilot phase** of the trial with **7** out of the **12 participating tertiary centres** open to recruitment. The trials team urge sites that are not yet open to contact the trials team to finalise set-up and arrange a site initiation visit if one has not yet been arranged.

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

Christmas and New Year Arrangements 2017-2018

Please note that the ECUSTEC trial office will be closed from:
2.00pm Friday 22nd December 2017 until 9.00am Thursday 4th January 2018.
The online randomisation service will still be available during this time.

Please report any SAEs to Dr Sally Johnson by email during this period: Sally.johnson15@nhs.net

Participating in ECUSTEC	We are pleased to announce we now have **7** centres fully approved to randomise patients into the ECUSTEC trial. 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 **5** 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

Congratulations to Dr Rodney Gilbert and the team at Southampton Children's Hospital who opened to recruitment on the 30th November 2017!!! We would also like to thank Southampton's associated PICs who can now begin to refer patients for the trial once Confirmation of Capability and Capacity has been confirmed!

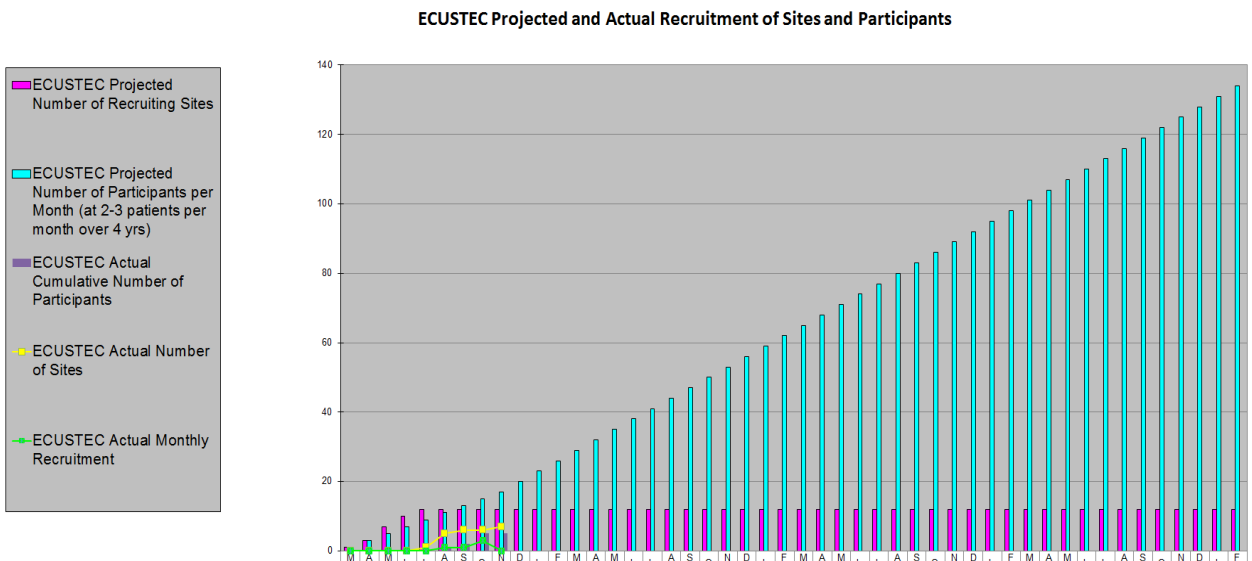
Message from the Chief Investigator

Dear ECUSTEC Investigators,

I am delighted that our long-awaited ECUSTEC study has finally opened in 2017! I would like to take this opportunity to thank you all for your support in bringing it to life. We are now open in **7 centres** with set-up in process in 5 further centres. **Five patients** have now been **recruited** which is excellent news. We have learned from both successful recruitment and from declined approaches and have put together a **"Top Tips"** document that you may find helpful when **approaching potential patients**. The tight time window for recruitment after arrival in the renal unit is proving challenging and we are submitting a substantial amendment to lengthen this window from 36h to 48h. Until this is through, the window remains at 36h. Our priorities now are to open the remaining centres and obtain approval for the amendment as soon as possible. Once again, may I thank you all for your participation.
With my very best wishes,

Sally Johnson
ECUSTEC Chief Investigator

The graph below shows recruitment by month against current targets:



	Mar-17	Apr-17	May-17	Jun-17	Jul-17	Aug-17	Sep-17	Oct-17	Nov-17	Dec-17	Jan-18	Feb-18	Mar-18	Apr-18	May-18	Jun-18	Jul-18	Aug-18	Sep-18	Oct-18	Nov-18	Dec-18	Jan-19	Feb-19	Mar-19	Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	Apr-20	May-20	Jun-20	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21	Feb-21
ECUSTEC Projected Number of Recruiting Sites	1	3	7	10	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
ECUSTEC Projected Number of Participants per Month (at 2-3 patients per month over 4 yrs)	1	3	5	7	9	11	13	15	17	20	23	26	29	32	35	38	41	44	47	50	53	56	59	62	65	68	71	74	77	80	83	86	89	92	95	98	101	104	107	110	113	116	119	122	125	128	131	134
ECUSTEC Actual Cumulative Number of Participants	0	0	0	0	0	1	2	5	5																																							
ECUSTEC Actual Number of Sites	0	0	0	0	1	5	6	6	7																																							
ECUSTEC Actual Monthly Recruitment	0	0	0	0	0	1	1	3	0																																							

Notices to ECUSTEC Investigators!!!

Randomisation Notepad

- If the **volume of saline** received in the **48 hours prior to randomisation** includes saline bolus received at the DGH, it **must** be documented in the **source data/medical notes**. If there is no record of saline received at the DGH please use the volume of saline received in the 48 hours prior to randomisation at the tertiary centre.
- Please ensure that the randomisation notepad forwarded to BCTU and kept in the medical notes is the version completed **at the time of randomisation**.

Certificates of Vaccination

- Alexion have reported missing Certificates of Vaccination for the ECUSTEC trial. Please may we remind sites to ensure that the **Day 1 and Pre-Discharge Certificate of Vaccinations** are forwarded to **both BCTU** and **Alexion**.

Screening Logs

- Please remember to **remove all** patient identifiable information from ECUSTEC Pre-Screening and Approach Logs **before** forwarding the documents to the trials team. This includes the hospital number, date of birth and patient initials.

Research Nurse and Pharmacy Teleconferences

The trials team will be contacting sites in the near future to arrange teleconferences for site staff. The aim of the teleconferences will be to share best practice and success stories to maximise recruitment opportunities and learn from the difficulties other centres have come across.

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)**

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.

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

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POSTAL ADDRESS: ECUSTEC Trial Office, Birmingham Clinical Trials Unit (BCTU), Institute of Applied Health Research, Public Health Building, University of Birmingham, Edgbaston, Birmingham B15 2TT

Thank you for taking the time to read the ECUSTEC Newsletter!!!