ECUSTEC Newsletter

Issue 6	June 2018

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 sixth issue of the ECUSTEC Newsletter!

Since ECUSTEC opened on the 10th July 2017, we are extremely pleased to inform you that **13 patients** have now been recruited to the trial! **10 centres** are open to recruitment with Birmingham Children's Hospital expecting to open imminently, and **66 secondary care** centres are now participating as **PICs**!
We would like to thank **Dr Ben Reynolds, Dr David Hughes and the team** at **Royal Hospital for Sick Children Glasgow**, **Dr Rachel Lennon and the team** at **Royal Manchester Children's Hospital**, **Dr Manish Sinha and the team** at **Evelina London Children's Hospital**, **Dr Aoife Waters and the team** at **Great Ormond Street Hospital** and **Dr Farida Hussain and the team** at **Nottingham Children's Hospital** for recruiting the latest 7 patients during March and June 2018.
We would also like to thank **Macclesfield District General Hospital** and the **Royal Free Hospital** for their involvement in facilitating recruitment into the trial.

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.

The pilot recruitment phase is well underway and we are now into the final few months. In order for the substantive trial to continue we need at least 26 patients by the **end of STEC season 2018**. Please continue to notify the Trials Team of any potential patients you become aware of.

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

Participating in ECUSTEC	We are pleased to announce we now have **10** 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 **2** 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

Notices to Investigators!

Screening Information

The Trials Team would like to take this opportunity to **thank ECUSTEC recruiting centres** for forwarding screening information promptly when requested by the Trials Team, and for continuing to inform us of any potential patients. This helps us to monitor the number of patients being screened for the trial, identify any barriers to recruitment and cross-reference against public health screening data.

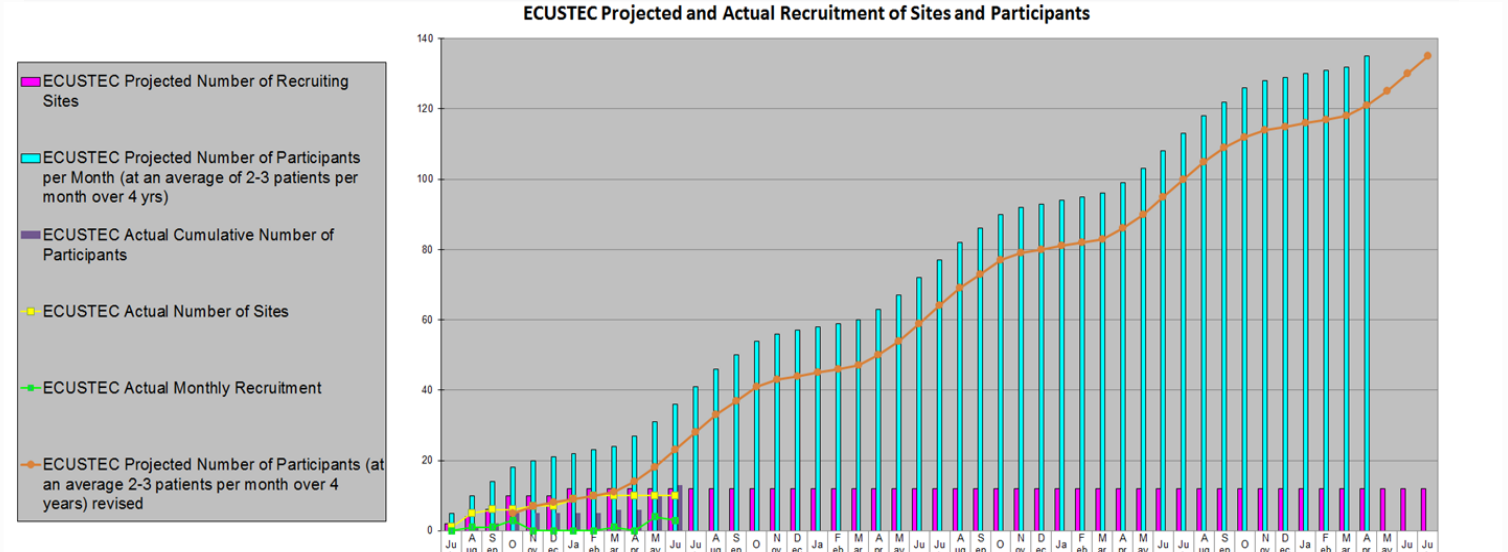
Patient Identification Centres

Thank you to all of the teams at **ECUSTEC PICs** for supporting and facilitating recruitment into ECUSTEC. We are continuing to **recruit secondary care centres** throughout the UK. If you are aware of any colleagues at secondary care centres who are interested in participating as an ECUSTEC PIC please forward their contact details to the Trials Team (**ECUSTEC@trials.bham.ac.uk**).

NHS.net Email Account

The sponsor have provided an nhs.net account (**ecustec.trial@nhs.net**) for consent forms and any other CRFs to be sent to **if** needed, dependent upon individual Trust policies. Please remember the ECUSTEC Trials Team do not continually monitor this account and recommend forms are sent to ECUSTEC@trials.bham.ac.uk when possible. If an **SAE** is **sent to the ECUSTEC.trial@nhs.net** account please **inform** the **Trials Team immediately** to ensure reporting time frames are met.

The graph below shows recruitment by month against current targets:



	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	Mar-21	Apr-21	May-21	Jun-21	Jul-21
ECUSTEC Projected Number of Recruiting Sites	2	4	6	10	10	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
ECUSTEC Projected Number of Participants per Month (at an average of 2-3 patients per month over 4 yrs)	5	10	14	18	20	21	22	23	24	27	31	36	41	46	50	54	56	57	58	59	60	63	67	72	77	82	86	90	92	93	94	95	96	99	103	108	113	118	122	126	128	129	130	131	132	135	
ECUSTEC Actual Cumulative Number of Participants	0	1	2	5	5	5	5	5	6	6	10	13																																			
ECUSTEC Actual Number of Sites	1	5	6	6	7	7	9	10	10	10	10	10																																			
ECUSTEC Actual Monthly Recruitment	0	1	1	3	0	0	0	0	1	0	4	3																																			
ECUSTEC Projected Number of Participants (at an average 2-3 patients per month over 4 years) revised				5	7	8	9	10	11	14	18	23	28	33	37	41	43	44	45	46	47	50	54	59	64	69	73	77	79	80	81	82	83	86	90	95	100	105	109	112	114	115	116	117	118	121	125	130	135

CRF and Data Management Notices

Case Report Form (CRF) Returns

Please can all sites ensure the Certificates of Vaccinations, CRFs and questionnaires are **completed** and **signed by the PI** as close to the **trial assessment point** as possible and then emailed to BCTU, the Trials Team will then check the forms and send data queries via Data Clarification Form for clarification.

Data Clarification Forms (DCFs)

Data queries will be forwarded via a DCF, please ensure these are carefully completed and **signed** off by the **PI** in order for all outstanding queries to be **resolved** in a timely manner.

CRF Completion Tips

- Please note **red blood cell** transfusions are **collected** on the Initial Admission for Trial Treatment Form and Day 30/60 forms. Red blood cell transfusions are **not** on the Day 1 and 8 Treatment Forms.
- If the patient is on renal replacement therapy (RRT) at discharge or day 30, please remember to add the **'end date'** of the **RRT** on the next assessment CRF if it has finished.
- If you are unable to answer one of the questions on the CRFs please remember to **advise** a reason. This will significantly **reduce** the amount of DCFs your site will receive.

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**.

Research Nurse and Pharmacy Teleconferences

The Trials Team will be arranging further teleconference meetings for August/September 2018.

Ordering IMP and Maintaining the Double Blind!!

We would like to **thank site pharmacies** for promptly forwarding your local processes for **ordering** ECUSTEC trial stock to the Trials Team and NIHR lead pharmacist (Mandy Wan) for review. If your site pharmacy have **not yet** forwarded your IMP ordering process to the team, please arrange for this to be sent to Emma Barsoum as soon as possible (**barsoume@bham.ac.uk**).

Please could we also **remind clinicians** at recruiting sites to be aware of any other areas where **potential unblinding** may occur i.e. financial monthly reports.

Investigator Launch Meeting

Thank you to all those who attended the ECUSTEC Launch Investigator Meeting on the 10th May 2018, we hope you found it useful. The meeting was a success and we look forward to holding further meetings in the future. You can view the slides for talks at the following link **ECUSTEC meeting slides**.

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 Summer ECUSTEC Newsletter!!!