ECUSTEC Newsletter

Issue 5 | March 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 fifth issue of the ECUSTEC Newsletter!

Since ECUSTEC opened on the 10th July 2017, **6 patients** have been recruited to the trial and we are pleased to announce that **10 centres** are now open to recruit patients. We would like to congratulate and thank **Dr Ben Reynolds and the team** at the **Royal Hospital for Sick Children**, **Glasgow** for randomising the **6th patient** into the trial.

We are also extremely pleased to have **3 new centres** open to recruitment; **Prof Nicholas Webb and the team** at **Royal Manchester Children's Hospital**, **Dr Shivaram Hegde and the team** at **University Hospital of Wales** and **Dr Manish Sinha and the team** at **Evelina London Children's Hospital** which we would like to welcome to 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.
We would like to remind sites that we are currently in the pilot phase of the trial and require at least **26 patients** by **August 2018** for the substantive trial to continue. Please continue to notify the Trials Team of any potential patients you become aware of.

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.

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

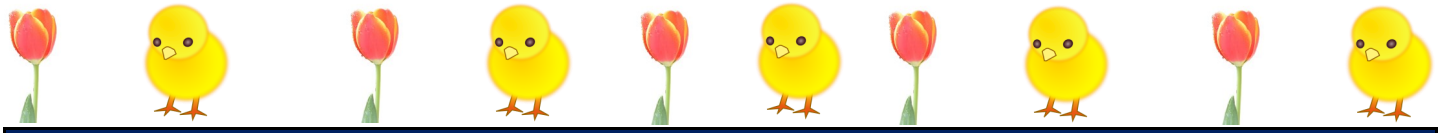
Easter Arrangements 2018

Please note that the ECUSTEC trial office will be closed from:
5pm Thursday 29th March 2018 until 9.00am Thursday 5th April 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 **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 for Investigators

Substantial Amendment 2

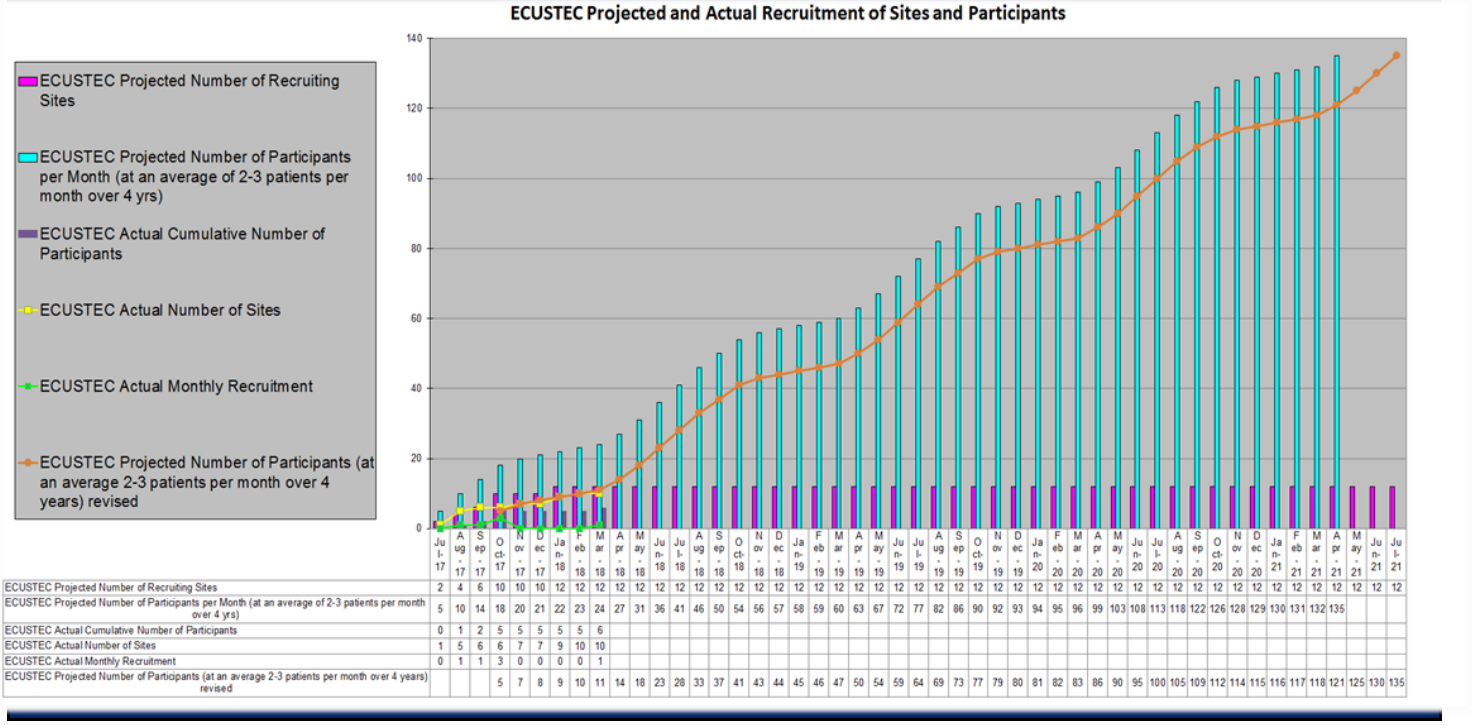
ECUSTEC Substantial Amendment 2 has been submitted to MHRA, REC and HRA and is currently **awaiting to be released to sites**. The substantial amendment involves an amendment to the protocol (ECUSTEC Protocol Version 4.0) including to the inclusion criteria window for IMP administration. The inclusion criteria will be amended to 'patient intended to be able to receive trial drug within **48 hours** of the **on-call paediatric nephrologist** formally taking over care of the patient at the trial site providing **inclusion criteria 3 is met**, or within 48 hours of meeting inclusion criteria 3 if not met at the time the on-call paediatric nephrologist takes over the care of the patient'. The amendment also includes an amendment to the Patient Information Sheets (PIS).

Details about the amendment and new document versions were circulated on the **20th February 2018**, please **do not** implement the amendment until the Trials Team have **formally released** the amendment. **The Trials Team will contact each PIC and recruiting centre once the amendment is ready to be released**.

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 informing 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.

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																																						
ECUSTEC Actual Number of Sites	1	5	6	6	7	7	9	10	10																																						
ECUSTEC Actual Monthly Recruitment	0	1	1	3	0	0	0	0	1																																						
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

Notices to ECUSTEC Investigators!!!

Case Report Form Data Queries

All sites that have recruited patients will be contacted by the trials team in the coming weeks regarding outstanding data queries. Data queries will be forwarded via a **Data Clarification Form (DCF)**, please ensure these are carefully completed. Once complete, the DCF will need **sign off** by the **PI**.

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

A research nurse and pharmacy teleconference took place on **27th February 2018**, the trials team would like to thank all those that attended. The trials team will arrange further 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 and Happy Easter!!!