ECUSTEC – RANDOMISATION NOTEPAD

A. Participant Details

Investigator:		Centre:	
Date of Birth:	D D / M M M / Y Y Y Y	Gender: Female ☐ Male ☐	

Patient's height: ☐☐☐.☐ cm	Patient's weight: ☐☐☐.☐ kg
Patient platelet count ☐☐☐ x10^9/l	
Volume of 0.9% saline received in the 48h prior to randomisation: ☐☐ ml/kg	

pRIFLE criteria category (please select 'Injury' or 'Failure')	
'Injury' ☐	'Failure' ☐
If Yes:	If Yes:
eGFR (Schwartz) value ☐☐	eGFR (Schwartz) value ☐☐
OR	**OR**
Urine output <0.5 ml/kg/hr for 16 hours? No ☐ Yes ☐	Urine output <0.3 ml/kg/hr for 24 hours? No ☐ Yes ☐
If yes, urine output ☐.☐☐ ml/kg/hr	If yes, urine output ☐.☐☐ ml/kg/hr
	OR
	Anuria for 12 hours? No ☐ Yes ☐

B. Eligibility Checklist (To be eligible, no shaded boxes must be ticked).

Inclusion	No	Yes
Is the patient aged 6 months or over and less than 19 years?		
Does the patient weigh 5kg or more?		
Has the patient been diagnosed with Haemolytic Uraemic Syndrome (HUS)?		
If yes, does the patient have micro-angiopathic haemolytic anaemia (indicated by fragmented red cells on blood film **OR** plasma lactate dehydrogenase above local centre reference range)?		
If yes, does the patient have thrombocytopenia (platelets <150x10^9/l)?		
If yes, does the patient have Acute Kidney Injury (AKI): 'injury' or 'failure' category of pRIFLE criteria despite correction of hypovolaemia? (See Protocol Figure 1.)		
Reported diarrhoea within 14 days prior to diagnosis of HUS (defined according to World Health Organisation as "the passage of three or more loose or liquid stools per day - or more frequent passage than is normal for the individual") **OR** Passage of blood per rectum within 14 days prior to diagnosis of HUS **OR** received a stool culture or shiga toxin polymerase chain reaction or STEC serology result indicating STEC in the patient **OR** Stool culture or shiga toxin polymerase chain reaction (PCR) or STEC serology result indicating STEC in a close contact (household or institutional) setting.		
Is the patient intended to be able to receive trial drug within 48 hours of the on-call paediatric nephrologist formally taking over the 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?		
Is the patient sexually active?		
If yes, does the patient agree to be practicing an effective, reliable and medically approved contraceptive regimen for 6 months after enrolment and, if female, has consented to and has provided a negative pregnancy test ≤48 hours prior to randomisation?		
Has the patient/parent/guardian given consent for antibiotic prophylaxis?		
Has the patient started antibiotic prophylaxis?		
Will prophylactic antibiotics be continued for a period of 8 weeks?		
Has the patient/parent/guardian reported that vaccinations are up to date according to the routine UK (or equivalent) immunisation schedule?		

Exclusion	No	Yes
Does the patient have a family history of atypical HUS?		
Has the patient had a previous episode of HUS?		
Does the patient have known pre-existing eGFR <90ml/min/1.73m^2?		
Does the patient have known or suspected pneumococcal infection?		
Does the patient have known or suspected meningococcal infection?		
Prior to diagnosis, was the patient taking a drug known to be associated with HUS, e.g. calcineurin inhibitors, chemotherapy, quinine, oral contraceptive pill?		
Does the patient have hypersensitivity to eculizumab, murine proteins or any of the excipients listed in the Summary of Product Characteristics?		
If female, is the patient pregnant or lactating?		
Does the patient have a malignancy?		
Does the patient have known Disseminated Intravascular Coagulopathy?		
Is the patient currently participating in another trial of an investigational medicinal product?		

Vaccination	**No**	**Yes**
Has the patient/parent/guardian given consent for meningococcal vaccination?	☐	☐
Has the patient received conjugate meningococcal ACWY vaccine (Nimenrix or Menveo)?	☐	☐
If no, will the patient receive conjugate meningococcal ACWY vaccine once platelet count is ≥50x10^9/l, if currently <50x10^9/l, or once systemic anticoagulation has been stopped for 24 hours if patient is currently receiving systemic anticoagulation, and before discharge from the trial site?	☐	☐
Has the patient received Meningococcal B vaccine (Bexsero™) as part of the UK immunisation programme?	☐	☐
If yes, has confirmation (e.g. red book documentation or written confirmation by GP practice team) been received?	☐	☐
Has the patient received Meningococcal B vaccine (Bexsero™) as part of the ECUSTEC trial?	☐	☐
If no, will the patient receive Meningococcal B vaccine (Bexsero™) once platelet count is ≥50x10^9/l if currently <50x10^9/l, or once systemic anticoagulation has been stopped for 24 hours if patient is currently receiving systemic anticoagulation, and before discharge from the trial site?	☐	☐
Consent	**No**	**Yes**
Has written informed consent been given by parent or guardian, or patient if aged 16-18yrs?	☐	☐
If yes, Consent Form Version no.:		
Has written assent been obtained from patient (if age appropriate)?	☐	☐
If yes, Assent Form Version no.:		
Samples	**No**	**Yes**
Has it been agreed that optional research blood and urine samples can be taken from the patient, stored and used for research to look for further evidence of what causes STEC HUS?	☐	☐
Has it been agreed that the DNA sample used to test the genes associated with HUS can undergo further optional detailed analysis of all potentially relevant genes?	☐	☐
Has it been agreed that the blood and urine samples that have been taken, together with extracted DNA, can be stored and used for research both within this study and in future related studies?	☐	☐
Has it been agreed that an additional, optional, one-off 10ml blood sample may be taken from the patient to see how their white blood cells interact with kidney cells in the laboratory?	☐	☐

C. Investigator Signature

I confirm that I have checked the eligibility criteria for the ECUSTEC trial and that the patient meets all of the inclusion criteria and none of the exclusion criteria as detailed above. I have documented this information in the patient medical records.

_____

Investigator Name (please print)

_____

Investigator Name (signature)

_____

Date

D. Randomisation:

Online randomisation: https://www.trials.bham.ac.uk/ECUSTEC (24hrs)
Telephone randomisation: 0800 953 0274 (toll free in the UK) available 9am to 5pm GMT

E. Randomisation Allocation (to be obtained from BCTU at randomisation)

ECUSTEC Trial Number:	☐☐☐☐☐	Randomisation Date:	D D / M M M / Y Y Y Y

Please forward copies of the ECUSTEC Prescription Forms to the local trial site pharmacy to order the appropriate trial medication.

Please forward a copy of the Day 1 Certificate of Vaccination to the local trial site pharmacy in order for the trial site pharmacist to dispense the first dose of Ecu/placebo.

Please forward a copy of the Day 1 Certificate of Vaccination to Alexion and to the ECUSTEC Trials Office no later than 48 hours after the 1st dose of Ecu/placebo

Original Randomisation Notepad to be kept in the ECUSTEC site file, one copy kept with patient's notes and one copy sent to BCTU (ECUSTEC Trials Office: Fax No.: 0121 415 9135 or email (ECUSTEC@Trials.bham.ac.uk).