Efficacy and safety of eculizumab in children with Shiga-toxin-producing *Escherichia coli* haemolytic uraemic syndrome: the ECUSTEC RCT

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Plain language summary

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Why did we do this study?

Annually, approximately 100 United Kingdom children develop Shiga-toxin-producing *Escherichia coli* haemolytic uraemic syndrome after infection with a diarrhoea-causing bug. The bug makes a toxin (Shiga toxin) that damages blood vessels, especially in the kidneys. Half need dialysis (artificial kidney support), about a quarter suffer fits or a stroke and about 3% die. Most children fully recover, but about a quarter suffer permanent kidney or brain damage. There are no known effective treatments. Eculizumab, a medicine which blocks part of the immune system called complement, may work.

What was the question?

Does eculizumab reduce the severity of Shiga-toxin-producing *Escherichia coli* haemolytic uraemic syndrome?

What did we do?

We planned to recruit 134 children, but difficulties with recruitment and the COVID-19 pandemic meant the study was stopped early after 36 children had been recruited; 17 received eculizumab, 19 received a dummy medicine (placebo). We compared children in each group using a score that measured how their kidneys and other organs were affected. We studied samples of their blood and urine, and also how Shiga toxin damages kidney cells in the laboratory.

What did we find?

The severity of illness was similar in both groups; however, because we only studied a small number of children, we cannot be sure this means that eculizumab does not work. Eculizumab appeared to be safe in this condition. In the blood and urine samples, we saw evidence that complement is involved in the illness. We also discovered a new way that Shiga toxin damages kidney cells.

What does this mean?

We have been unable to show whether eculizumab is a worthwhile treatment for children with this condition. However, we have learnt lots about how the illness is caused and hope these results can be combined with other studies to give us a clearer answer.

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