Diabetes Research Group, Denmark Hill Campus

KING'S College LONDON

10th April, 2019

Helen Critchley
Quality Manager
King's Health Partners Clinical Trials Office

Dear Helen,

Re: The effect of prednisolone versus hydrocortisone as glucocorticoid replacement therapy on hypoglycaemia frequency in people with Type 1 diabetes and adrenal insufficiency: a pilot study.
REC reference nos: 07/H0810/47; 11/LO/0658
EudraCT no: 2008-002336-15
KCH R and D No: 07DE08

I am writing to confirm and explain the failure of completion of the above study. We opened the study in Nov 2012, in order to examine the hypothesis that steroid replacement therapy in adults with type 1 diabetes as well as Addison's disease with a long acting steroid (prednisolone) would provide less risk of nocturnal hypoglycaemia than the then preferred hydrocortisone therapy – the latter being used clinically because levels could be measured to monitor efficacy of replacement and expected, on the basis of known pharmacokinetics, to provide little or no circulating hydrocortisone overnight. Both regimens were in use clinically so we did not anticipate any barriers to the trial, but late in preparing the regulatory applications we were informed that because prednisolone had no licence for Addison's disease, the study needed to be a CTIMP.

The study received ethical clearance in 2011, and we completed Pharmacy set up and were ready to recruit by the end of 2012. We approached other colleagues at KCH as well as colleagues at GSTT to make them aware of the project.

The study had been planned with a trainee doctor as an MSc project and had no other external funding. We were testing two generic treatments in common clinical use with no financial implications to our investigation. The protocol had been peer reviewed within King's, adjusted and approved. But by the time we completed regulatory issues, the junior doctor had moved to another post and project.

We kept the project open because we believe it addresses an important question. We hoped that we would find capacity to complete it within our research team and a series of junior researchers employed to do other studies tried to take it on. We were aware that patients with both Addison's and type 1 diabetes were not particularly common. We did recruit and complete the protocol with three patients but this was far too small a sample to make a meaningful analysis. In July 2017 we decided to close the study, in part because we felt the regulatory paperwork had been created under a different system from the current one and was old. We felt that to take this question forward we should review current management of Addison's disease and updated methods of continuous glucose monitoring and start the study afresh.

The three participants who completed the protocol did so without any SAE or AE.

Please let me know if you require further information

Yours sincerely,

Stephanie A Amiel, BSc, MD, FRCP
Professor of Diabetes Research, King's College London

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