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MinTac: A prospective, multicentre, randomised controlled trial of tacrolimus vs prednisolone for adults with de novo minimal change disease.

Dr Nicholas Medjeral-Thomas[1], Dr Christopher Lawrence[2], Dr Marie Condon[3], Dr Paul Warwicker[2], Dr Heather Brown[4], Dr James Pattison[4], Professor Sunil Bhandari[5], Professor Jonathan Barratt[6], Professor Neil Turner[7], Professor Liz Lightstone[1], Professor Charles Pusey[1], Dr Jack Galliford[1], Dr Tom Cairns[1], Dr Megan Griffith[1]
[1]Imperial College Healthcare NHS Trust, London, United Kingdom, [2]The Lister Hospital, East and North Hertfordshire NHS Trust, , United Kingdom, [3]Epsom and St Helier University NHS Trust, UK, , United Kingdom, [4]Guy's and St Thomas' NHS Foundation Trust, , United Kingdom, [5]Hull and East Yorkshire NHS Trust, , , United Kingdom, [6]Department of Infection, Immunity and Inflammation, University of Leicester, , United Kingdom, [7]Centre for Inflammation Research, University of Edinburgh, , United Kingdom

Minimal change disease (MCD) is an important cause of nephrotic syndrome (NS) in adults. Corticosteroids are effective first-line therapy for MCD, but alternatives are needed to prevent morbidity from the significant side effects associated with steroids. Calcineurin inhibitors have been used as steroid sparing agents in relapsing disease, but there is little evidence for their use in de novo MCD. We hypothesised that tacrolimus is not inferior to prednisolone for the treatment of de novo MCD, and set up the MinTac study to compare the effectiveness of tacrolimus monotherapy vs prednisolone for the treatment of NS in adults with de novo MCD.

MinTac was a prospective, open-label, randomised control trial (EudraCT 2009-014292-52, UK NRES reference 09/H0711/68) across seven centres in the United Kingdom. Adult patients with first presentation of MCD and NS were randomised to oral tacrolimus (27 patients) at 0.05mg/kg twice daily, or prednisolone (25 patients) at 1mg/kg daily (up to 60mg daily). Twelve weeks after achieving remission, the tacrolimus dose was tapered over eight weeks and stopped. The prednisolone dose was tapered from one week post remission to provide at least 16 weeks of treatment. Two patients from the tacrolimus cohort were excluded from analysis because their treatment deviated from protocol before adequate follow-up data was acquired; one patient developed a rash after a single dose of tacrolimus, and one patient was admitted with pulmonary oedema and pneumonia after two doses of tacrolimus; both were switched to prednisolone. The primary outcome was the proportion of patients achieving complete remission (CR) of nephrotic syndrome at eight weeks. The secondary outcomes were the proportion of patients achieving CR at 16 and 24 weeks, the proportion and timings of relapses, change in estimated glomerular filtration rate (eGFR) from baseline and adverse events.

The two cohorts were similar in baseline characteristics. There were no significant differences between the tacrolimus and prednisolone treated cohorts in the proportion of patients achieving CR at eight weeks (19 of 25 (76%) for prednisolone and 15 of 25 (60%) for tacrolimus, p=0.36), 16 weeks (21 of 25 (84%) for prednisolone and 19 of 25 (76%) for tacrolimus, p=0.72), or 24 weeks (22 of 25 (88%) for prednisolone and 21 of 25 (84%) for tacrolimus, p>0.99). There were also no significant differences in relapse rates, times to relapse, and eGFR throughout follow-up. Eighteen adverse events were recorded in each cohort. There were three serious adverse events in the prednisolone cohort and one in the tacrolimus cohort.

This study shows that tacrolimus is as effective as prednisolone for the treatment of de novo MCD in adults. There was no significant difference in the proportion of patients achieving CR from nephrotic syndrome, the time to remission, or the frequency of relapse. This is the first study to show a comparable alternative to

steroids for the treatment of adults with de novo MCD, and is an exciting step forward in the development of steroid free regimens for the treatment of this disease.