

Assessing the efficacy and safety of methotrexate vs ciclosporin in the treatment of severe atopic eczema in children: the TREATment of severe Atopic eczema in children Taskforce (TREAT) randomised controlled trial

We are proposing a study of the effectiveness and safety of two immunosuppressive medicines, methotrexate (MTX) and ciclosporin (CyA), in the treatment of severe, difficult to manage eczema in children.

Eczema affects 1 in 4 children in the UK. It causes inflamed, itchy skin and typically affects the folds of the body such as behind the knees, inside the elbows as well as the neck. Flare ups are common and the impact on health service costs and patients and families quality of life is similar to diabetes or asthma. Eczema treatment aims to reduce the skin inflammation, relieve itching and prevent flare-ups. Usually, this can be achieved with regular application of emollients and steroid creams and the majority of children grow out of their eczema over time. However, in a small group of patients the disease is so severe that immuno-suppressive medication is required. So far, there has been very limited research into this area in children, and clinical management is therefore primarily guided by studies performed in adults. A survey we conducted among dermatologists in 8 European countries showed that CyA is the by far commonest immuno-suppressive medication used in children. However, it can have a negative effect on kidney function, the eczema often flares after stopping the medication, and it is expensive. There is therefore a need to find alternative treatments, as highlighted by a recent priority setting exercise in the UK, which included medical experts, parents and patients with eczema. MTX, in addition to the more widely used CyA, was specifically mentioned, partly because there are now two small studies suggesting that it could be an effective alternative to CyA.

Studies in children with rheumatoid arthritis suggest that MTX's tolerability and long-term safety profile is good. In addition, it is cheaper than CyA. We propose to investigate the benefit (efficacy) of CyA vs. MTX in the treatment of severe eczema that has not responded to regular application of emollients and potent topical corticosteroids. In addition to the effect on disease severity, we will compare the impact on patients' quality of life after 12 and 36 weeks of treatment and for six months after stopping MTX and CyA. We will also study how well the two medications control flares and their safety and tolerability (adverse reactions). Although MTX has been extensively used in a number of diseases, such as rheumatoid arthritis, we do not know how it works, and this will also be examined in our trial. For this, blood tests will be required but not more frequently than during routine NHS clinical care. We will also use a special sticky tape to collect samples from the skin of participating children. This is not traumatic and will allow us to study the immune response in the skin. Patients will be recruited through the main Anglo-Irish paediatric dermatology departments.

The study team has vast experience in conducting clinical trials and consists of children's dermatologists, research methodologists and experts in dermatopharmacology (drug reactions) and immunobiology (inflammation and immune cell interactions). The study will be submitted to UK and Irish ethics committees and regulatory authorities, where all aspects of the study will be assessed. Independent monitoring throughout the study will ensure that it is conducted to the highest international standards.