

OC-035

**SUBCUTANEOUS RHIGF-1 SIGNIFICANTLY
INCREASES CIRCULATING IGF-1 CONCENTRATIONS
IN CHILDREN WITH CROHN'S DISEASE INDUCED
GROWTH FAILURE**

doi:10.1136/gut.2011.239301.35

A Rao,* S Naik, M O Savage, I R Sanderson *Centres for Digestive Diseases and
Endocrinology, Barts and the London School of Medicine and Dentistry, Queen Mary
University of London, London, UK*

Introduction Faltering growth is a complication of paediatric Crohn's disease, affecting up to a third of patients. There is no recognised treatment targeted at improving linear growth. These children have low circulating insulin-like growth factor-1 (IGF-1), a hormone essential for linear growth and the primary mediator of growth hormone (GH) action. Low IGF-1 concentrations occur despite normal GH response to stimulation testing – the children thus having a functional GH insensitivity. Injections with recombinant human IGF-1 (rhIGF-1) have been reported to improve growth in animal models of colitis and in children with genetic GH insensitivity syndrome using doses of 80–120 µg/kg bd. rhIGF-I therapy has never previously been used in children with Crohn's disease. We hypothesised that subcutaneous injections of rhIGF-1 would significantly increase circulating IGF-1 concentrations in children with Crohn's disease induced growth failure, and that twice daily injections would maintain these concentrations.

Methods Eight children with active Crohn's disease and growth failure were recruited for an open-label pharmacokinetics study of rhIGF-1 (Increlex). A subcutaneous injection of rhIGF-1 (dose 120 µg/kg) was given, and levels were measured over 24 h. Children were also studied over a second period (5 days) of repeated doses. Blood sugar levels were monitored as hypoglycaemia is a potential adverse effect. Protein losing enteropathy was measured by stool α 1-antitrypsin and related to IGF-1 levels attained.

Results The median age(range) of the children was 12 years(10–14). 4 were female, 4 male, mean (SD) Paediatric Crohn's Disease Activity Index (PCDAI) was 31.25(14.08). All the children had poor growth (mean growth velocity standard deviation score(SDS) –3.34 (SD 1.13)). All the subjects completed the study. The rhIGF-1 was well tolerated, with only one patient having an (asymptomatic) hypoglycaemic episode. All patients except for one had low baseline IGF-1 levels (mean SDS -1.78 (SD 1.37)) and all showed an increase in 3-h circulating IGF-1 levels following administration of rhIGF-1 (mean SDS 2.70 (SD 3.06)). This increase was significant($p = 0.007$). IGF-1 levels were maintained above 0.0 SDS by twice daily injections. This occurred without any change in PCDAI over the 5-day trial period ($p = 0.77$) Protein-losing enteropathy did not inhibit this response.

Conclusion Subcutaneous administration of rhIGF-1 significantly increased circulating concentrations of IGF-1 in children with Crohn's disease-related growth retardation. These results support the initiation of trials to assess the impact of long-term rhIGF replacement therapy on linear growth.

Competing interests A. Rao: None Declared, S. Naik: None Declared, M. Savage: None Declared, I. Sanderson Grant / Research Support from: Drug supplied by Ipsen Ltd UK. Research grant from Crohn's & Colitis Foundation of America

Keywords Crohn's disease, growth failure, insulin-like growth factor-1, paediatric.