U.S. News & World Report and Cleveland Clinic. Signs that your child might have Crohn's Disease. https://health.clevelandclinic.org/signs-child-might-crohns-disease/ Date created: February 1, 2016.

Developing personalised therapy for children with Crohn's disease

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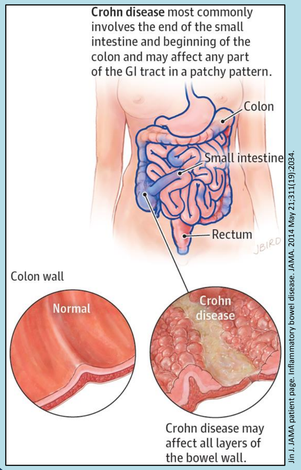
1. What is Crohn's disease?



- Lifelong inflammatory condition of the gut
- Negatively impacts quality of life
- Symptoms are disabling and often hidden, and include:

abdominal pain
tiredness
weight loss
diarrhoea
bloody stool

2. Why do the study?

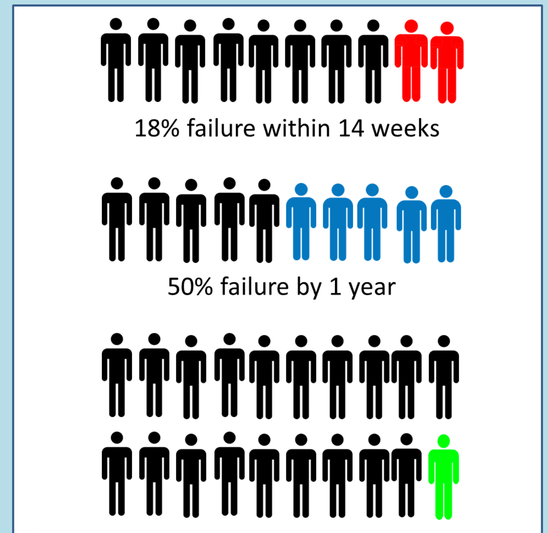
- To date, therapy used to treat Crohn's disease include anti-TNF drugs, infliximab and adalimumab.
- However, patients lose response to the medicine because their immune system recognises the drug as a threat rather than a medicine.
- This leads to formation of antibodies to the drug; immunogenicity.
- As well as reducing the effectiveness of treatment, antibodies may cause adverse drug reactions such as skin rash, difficulty breathing, and low blood pressure.
- Alternative medication with an immunomodulator (immune system suppressing drug) may reduce development of antibodies.

3. What did we do?

- Personalised Anti-TNF Therapy in Crohn's disease (PANTS) is a three-year prospective, observational UK-wide study.
- We performed a subgroup analysis on 219 paediatric patients reporting treatment failure, safety, and immunogenicity data.

4. What did we find?

1. Treatment failure is common:



2. Many children experience treatment failure as a result of antibody formation to drug. This can be prevented by:

- Ensuring anti-TNF drug dose at week 14 is optimal (Hazard Ratio (HR) 0.88 (95% CI 0.82 – 0.95))
- Using an immumodulator and anti-TNF drug together (HR 0.34 (95% CI 0.21 – 0.57)) (see figure below)

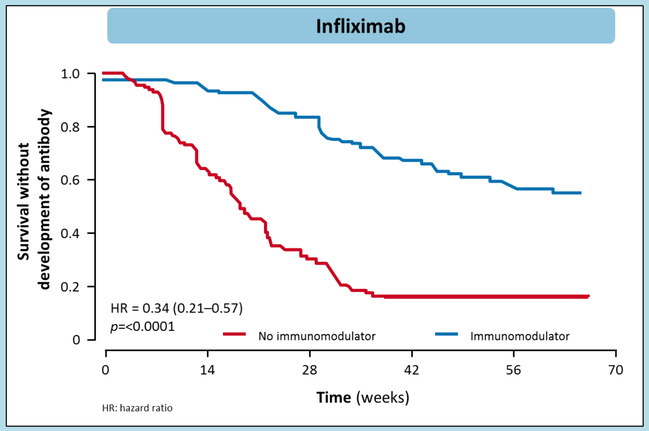


Figure: Kaplan-Meier curve demonstrating survival without development of antibody to infliximab anti-TNF therapy (defined as 10 arbitrary units per mL or more) according to use of immunomoduloator prior to starting infliximab anti-TNF treatment

Study Highlights

1. Anti-TNF treatment for Crohn's disease has high failure rates at week 14 and one-year. Predicting who is likely to fail is imperative to personalising treatment.
2. Immunogenicity majorly contributes to treatment failure; co-prescription with an immunomodulator is protective against development of antibodies.
3. These findings will help us deliver the most effective, safest, and longest-lasting treatment for children with Crohn's disease first-time.