



**Barts Health NHS Trust**

# Royal Research!

## IBD Research at the Royal London Hospital

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### Meet the Team

Welcome to the first edition of Royal Research! In this newsletter we aim to keep you up to date with all the research taking place in the Inflammatory Bowel Disease team at the Royal London Hospital.

Our work relies on close collaboration between the IBD consultants, IBD nurses, pharmacists, dieticians, IBD research nurses and of course you the patient!

Without your help and support we are unable to continue our work to identify new treatments and improve patient care. This can be as simple as answering a questionnaire in clinic, donating extra sam-

ples of blood and tissue, or entering a clinical trial.

We hope this newsletter will inform you about the research opportunities available and empower you to take part if there is a study suited to you.

There will also be updates on the results of previous studies for all our patients who have participated.

Please get in touch if you have any questions about the studies covered or wish to learn more. Our contact details are at the back.





Crohn's disease occurs when the gut immune system becomes allergic to its bacterial content, which causes bowel inflammation. Patients who have disease that does not respond to therapy suffer debilitating symptoms and poor quality of life.

Initial reports suggested that the disease could be 'cured' with stem cell therapy (HSCT), where a patient's own stem cells are given back after their current immune system is destroyed by chemotherapy. Our original ASTIC trial showed that cure is rarely seen and that high dose chemotherapy led to significant side effects, including one fatality. However, half the patients experi-

enced complete disease regression. As the side effects were related to the high dose chemotherapy used, the ASTICLite trial will test our belief that HSCT with much lower doses of chemotherapy will still be effective but also much safer. When we asked them, patients with refractory disease were keen to try this type of treatment.

We propose to recruit 99 patients with active disease who are failing current treatment. We will randomize 2 patients to low intensity HSCT for every patient that continues on standard care. At 24 weeks we will check whether HSCT patients have recurrent disease and treat them if

required. At 48 weeks we will see if HSCT is more likely to lead to disease regression than normal care. We will follow-up all patients for a further 4 years. Scientific studies will be performed to assess the mechanism by which this treatment works.

The trial has been designed by gastroenterologists, haematologists, scientists and patients. We anticipate it will give a clear answer as to whether HSCT is an effective and safe and option in Crohn's disease. If you would like to learn more please get in touch with Dominic (see contact details on the back page).

### PROFILE Study

The course of Crohn's disease varies substantially between affected individuals, but no reliable prognostic markers exist. The most common treatment strategy in Crohn's disease is based on a stepwise escalation in therapy, but only in response to recurrent flares or persistently active disease. This strategy (termed "Step Up") should not over-treat patients but exposes some to avoidable complications of persistently active disease (while weaker and potentially ineffective therapies are trialed). In 2008 it was shown that early

use of anti-TNF $\alpha$  therapy ("Top Down") was superior to conventional ("Step Up") management. However, use of combination therapy in all patients is potentially (1) unaffordable and (2) risky – exposing patients with mild disease to the side effects of drugs that their disease did not require.

The PROFILE trial will test a new biomarker that appears to identify individuals with Crohn's disease at high risk of relapse vs. low risk of relapse. It is thought that those with high risk of relapse may benefit most from

"Top Down" therapy whilst those with low risk might benefit most from "Step Up" therapy.

The study aims to recruit 16-75 year old patients with active CD, diagnosed within the previous 3 months. The aim will be to see if the use of the biomarker tools can guide the treatment strategy and so improve mucosal healing, quality of life, number of hospital admissions and operations, and cost effectiveness over 48 weeks. If you would like to know more please get in touch with Dominic (see contact details on the back page).



### IBD BioResource

Aims to help research into the causes of Crohn's and colitis and understand determinants of IBD severity and treatment response.

By understanding which genes and environmental factors are involved, and their impact on the immune system, we can investigate why some people get Crohn's or colitis, why some of the existing treatments work in

some patients but not in others, how better treatments might be developed and whether it might be possible to prevent or cure IBD.

#### Whats involved?

All volunteers donate a blood sample and complete a questionnaire. Volunteers also consent to be contacted and invited to participate in future medical research. This is based on analysis of their samples and information they have supplied. For all BioRe-

source subjects, this contact may relate to both IBD-focused studies and other research not related to IBD. Participation in any future studies is entirely voluntary and you decide when invited.

#### Is it for me?

This study is suitable for all patients with IBD. If you wish to participate or learn more please get in touch with Mary (see contact details on the back page).



Regular exercise training might be important in people with Crohn's disease (CD), because of its potential beneficial effects on physical fitness, mental health, and disease-related factors such as fatigue, bone weakening, and inflammation. EXACT was set up to research this in more detail.

Two types of exercise training were studied: 'moderate-intensity continuous training' ('MICT') which is doing 20 minutes or more of endurance exercise (e.g., cycling, swimming or running) at a continuous level of effort without resting; and 'high-intensity interval training' ('HIIT').

The EXACT study, funded by Crohn's and Colitis UK, tested MICT and HIIT in people with inactive or mildly-active CD. This was a pilot study which will be used to inform the design of a much larger follow-up study. The main aims were to: (1) establish the feasibility of conducting

a large study of exercise training, (2) provide information on the acceptability, safety and benefits or harm of HIIT and MICT in people with CD. The EXACT study is the first study in the world to test the effects of HIIT in CD.

Our findings suggest that it is possible to conduct a large-scale clinical trial of exercise training in CD. Secondly, our findings suggest that MICT and HIIT are acceptable, safe and useful forms of exercise training for people with CD.

In the interview feedback about both exercise programmes various physical benefits were reported, including feeling fitter and more energized, having a thinner waist and more-defined thigh muscles. Some participants also reported disease-specific benefits such as reduced inflammation, less frequent bowel movements, and a "calmer gut". Mental benefits included generally feeling bet-

ter, and improvements in wellbeing and mood. Very few negative side-effects were reported.

We concluded that cycle-based HIIT and MICT are feasible and acceptable exercise strategies in people with inactive or mildly-active Crohn's disease. Larger-scale clinical trials will provide a clearer understanding of the benefits and harms of different exercise programmes based on EXACT.

We are very grateful to the patients for supporting this research project.



## PREdiCCt

We are still far away from knowing exactly what causes someone to develop IBD. The course of IBD varies and can't be predicted. It isn't always active, but when it 'flares' it frequently leads to permanent bowel damage.

Treatment does calm it down (put it in remission) but we don't have enough data to predict if a patient's IBD will be mild or severe. Also, we don't know what causes IBD to flare again. This study will hopefully give us more information.

In this study we are gathering data on the genetic, dietary, gut flora and lifestyle contributors to developing flares.

### Whats Involved?

Participants in this study provide a sample of saliva for DNA analysis, a stool sample, complete a food diary for 4 days and a monthly lifestyle questionnaire.

### Is it for me?

This study is suitable for all patients with IBD who are over 6 years in age, in stable remission with no changes in their treatment for the last 2 months.

If finding out how to predict flares interests you please get in touch with Dominic (see contact details on the back page).



## Upadacitinib

Upadacitinib is a new oral drug that acts on an inflammatory pathway known as the JAK-STAT signaling pathway. This pathway is known to play a key part in inflammation in conditions such as Ulcerative Colitis and Crohn's disease. The drug acts to block part of the pathway and thereby reduce inflammation. Clinical trials, being conducted by pharmaceutical company Abbvie, are already underway across 475 sites worldwide, treating patients with moderate to severe Inflammatory Bowel Disease. So far Upadacitinib has been shown to be well tolerated and effective in patients when compared to the effects of taking a

placebo or 'dummy' drug. This clinical trial is divided into different sections or substudies, and at The Royal London we are anticipating that we will open the next substudy for patients with moderate to severe ulcerative colitis within the coming weeks. The trial is open to all patients who have not got better after trying at least one other standard therapy such as steroids, azathioprine or a biologic drug. If you are interested in finding out more about this trial and whether or not it might be beneficial for you then please get in touch with Marina (see contact details on the back page).



**Find any of the studies in this newsletter interesting?**

**Want to learn more?**

**Please get in touch with the IBD research team!**

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