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IBD Digest

2022 has been a very busy year for those of us on the IBD and Behavioral Health study team. We have welcomed many new participants to the study; conducted in-person, digital, and telephone-based surveys, and begun analysis on our first round of patient interviews. We hope that we can share more of our findings with you as we move into 2023!

There is other exciting news coming out of the IBD research world, including research on potential new treatments. This includes two new medications approved by the Food & Drug Administration (FDA) in 2022 for the treatment of Crohn's disease and ulcerative colitis.

- Risankizumab (brand name Skyrizi®) was approved for the treatment of moderate to severe Crohn's disease in adult patients in June. This medication is initially delivered via an IV infusion, but can eventually be self-administered by a patient via an injection pen every eight weeks. Clinical study results showed improvement in patients' symptoms and endocopy results within 12 weeks.[1]
- Upadacitinib (brand name Rinvoq®) was approved for adult patients with moderate to severe ulcerative colitis in March. This medication is taken as a daily pill, and it treats ulcerative colitis by blocking inflammatory pathways that can cause IBD. Evidence from clinical trials showed that patients experience reduced symptoms in as little as two weeks.[2]

For a medication to be approved, it must go through a rigorous process involving three "phases" of research, which start with a small group of people (generally fewer than 100) and work up to thousands of participants. Any new medication must have data to support that it is both safe and effective before it becomes publically available.

There are numerous ongoing trials to test other potential treatments, many of which focus on new medications for individuals who no longer respond to their current therapies, or which target gut-specific inflammation instead of the entire immune system. As researchers continue to learn more about what causes IBD and how it impacts the body, these medications will evolve to reflect this new information.

Medication management is an important part of caring for your IBD, and since every person is different, deciding on the treatment that's right for you should be an important and ongoing conversation between you, your gastroenterologist, and the rest of your care team. There are a number of approved therapies currently available, the most common of which are described in more detail on the next page.

1. D'Haens G, Panaccione R, Baert F, et al. Risankizumab as induction therapy for Crohn's disease: results from the phase 3 ADVANCE and MOTIVATE induction trials. *Lancet*. 2022 May 28;399(10340):2015-2030.

2. Danese S, Vermeire S, Zhou W, et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. *Lancet*. 2022 Jun 4;399(10341):2113-2128.

STUDY PROGRESS

As of **Oct. 4,** 2022, we have enrolled

510

participants across the three study locations!

We are **52%** of the way to our goal.

REMEMBER!

Participants are asked to complete questionnaires at three points:

- Upon enrolling in the study
- Six months after enrolling
- One year after enrolling

You will be paid $20 each for the initial and six-month questionnaires and $40 for the final questionnaire.

Understanding Treatment Options:

Learning your options for medical treatments for your IBD can feel overwhelming, whether you have been recently diagnosed or have been managing your condition for decades. Your gastroenterologist will work with you to recommend an appropriate treatment option for you based on factors such as the severity of your symptoms, the location of your inflammation, your preferred type of delivery (such as a pill or infusion), and your medical history. Below is a brief overview of the main types of medications used to treat IBD.

Aminosalicylates (5-ASA)

Examples: Balsalazide (Colazal®); Mesalamine (Apriso®); Olsalazine (Dipentum®); Sulfasalazine (Azulfidine®)

These medications decrease inflammation in your digestive tract and can either be taken as pills, enemas, or suppositories. They can be used to treat both Crohn's and ulcerative colitis, though evidence shows that they work best when inflammation is located in the colon.

Corticosteroids

Examples: Budesonide (Entocort®); Methylprednisolone (A-Methapred®); Prednisolone (Oraped®); Prednisone (Deltasone®)

Corticosteroids do not target the gut specifically; instead, they suppress a person's entire immune system to calm inflammation. These are usually used to treat more active disease or symptomatic flares, not as a long-term medication.

Immunomodulators

Examples: Azathioprine (Imuran®); Mercaptopurine (Purinethol®); Methotrexate (Rheumatrex®)

Like corticosteroids, immunomodualtors work by suppressing the immune system to combat inflammation. However, they are more appropriate for long-term use, and are often prescribed when 5-ASAs or steroids have not been enough to help a person receive remission.

Biologics/Biosimilars

Examples: Adalimumab (Humira®); Certolizumab (Cimzia®); Golimumab (Simponi®); Infliximab (Remicade®); Natalizumab (Tysabri®); Risankizumab (Skyrizi®); Ustekinumab (Stelara®); Vedolizumab (Entyvio®)

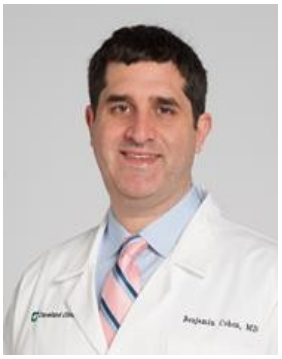
Biologics are different from the above classes of medications because they are lab-grown antibodies instead of chemical compounds. These antibodies can stop gut proteins from causing inflammation, and so they are more targeted than corticosteroids or immunomodulators. There is evidence that they help heal inflamed intestinal tissue. Biologics are often given as an injection or regular infusion.

Targeted Synthetic Small Molecules

Examples: Ozanimod (Zeposia®); Tofacitinib (Xeljanz®); Upadacitinib (Rinvoq®)

These medications work by targeting specific inflammation for individuals with diseases like ulcerative colitis and rheumatoid arthritis. As the name suggests, these pills contain small molecules which can influence the immune system by blocking inflammatory pathways or immune cell migration.

Meet a Study Co-Investigator



Benjamin Cohen, MD

Co-Section Head and Clinical Director for Inflammatory Bowel Disease at Cleveland Clinic; Study Co-Investigator

What made you decide to become a physician?

I was drawn to medicine because it is a unique career centered around helping others. As a physician, you get to accomplish this goal not only by direct patient care but by working in teams, applying science, and answering research questions. Members of my family had colon cancer and IBD, which is why I wanted to be a gastroenterologist.

What are some of your personal research interests?

My personal interest has been in the optimal use and safety of the medications we use for IBD in the perioperative period (from the beginning of considering surgery through recovery).

What interests you about this study the most?

Treatment of IBD is best done through a multidisciplinary team approach involving behavioral health and nutrition, but access is limited for many patients. Finding ways to reach more patients, including through tech-based interventions, is critical and what interests me the most.

What is the most rewarding part of your job?

I love being able to impact people's lives in a meaningful way and particularly to help patients navigate the complex decision-making around treatment choices in IBD.

What piece of information about IBD do you wish you could share with all of your patients?

We are in a period of rapid growth of available medical therapies for IBD. In order to best understand how to use these treatments it's important for patients to participate in research. With their help we can continue to improve the lives of all patients and hopefully find a cure for the diseases.

What's your favorite thing to do in your spare time?

I enjoy spending time with my young son and daughter, cheering for my favorite sports teams (Yankees, Giants, and Knicks), and going to concerts.

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TIPS

Understanding the Brain-Gut Connection

A common phrase that you might hear when learning about IBD is the "brain-gut" or "mind-gut" connection. But what exactly does this mean, without needing a neuroscientist to explain the details? Essentially, the brain-gut connection is the way your mind is able to communicate with your digestive system via the enteric nervous system (ENS). The ENS is generally hard at work without your knowledge, and helps your brain control and monitor processes related to digestion, like breaking down foods and absorbing nutrients. But what happens when something happens to disrupt that connection?

Does the brain control the gut … or does the gut control the brain?

This connection likely runs both ways. Some research suggests that anxiety and depression were major contributors to functional bowel problems that characterize conditions like irritable bowel syndrome (IBS), such as constipation, diarrhea, and having an upset stomach.[1] However, other researchers believe that it may be the other way around—that these physical issues with chronic abdominal pain may make people experiencing these symptoms more likely to feel depressed or anxious.[2]

What's the impact of this on someone with IBD?

Research suggests that there are a number of different ways in which stress, anxiety, and depression can negatively impact the digestive system. This includes increased production of hormones and proteins that contribute to inflammation.[3] Another study's findings suggest that inflammation in the digestive system can potentially "shut down" communication between the gut and the brain; closing down this connection may be the body's way of protecting the inflammation in the gut from spreading to the brain. It may be this disruption that contributes to IBD symptoms such as anxiety, depression, and brain fog.[4]

1. Bonaz BL, Bernstein CN. Brain-gut interactions in inflammatory bowel disease. *Gastroenterology*. 13 Jan;144(1):36-49.

2. Regueiro M, Greer JB, Szigethy E. Etiology and treatment of pain and psychosocial issues in patients with inflammatory bowel diesease. *Gastroenterology*. 2017 Feb;152(2):430-439.e4

3. Brzozowski B, Mazur-Bialy A, Pajdo R, et al. Mechanisms by which stress affects the experimental and clinical inflammatory bowel disease (IBD): role of brain-gut axis. *Curr Neuropharmacol*. 2016;14(8):892-900.

What can someone do to promote a better brain-gut connection?

There are a number of different treatments that have been shown to result in better outcomes for IBD patients experiencing this kind of disregulation.

- *Whole-person health care*, such as the Total Care IBD Clinic, which includes providers who are able to address both your physical and emotional health care.
- *Mindfulness techniques*, including meditation, which can help a person be more present in the moment and prevent negative thoughts from making them feel worse.
- *Cognitive behavioral therapy (CBT)*, which is focused on learning skills to better respond to upsetting thoughts and has been demonstrated to potentially help people become less focused on chronic pain.
- *Hypnosis* with a licensed clinician, such as a therapist, psychologist, or psychiatrist. This process can help some patients better be able to respond to therapy and distance themselves from feelings of pain.[2]

How can I learn more about this?

As always, talking to your medical providers is generally the best place to begin. By participating in this study, you have access to the therapists and psychiatrist on the Total Care team, who will work with you to find the best suitable treatment for you. Additionally, if you've been randomly selected to participate in the TECH arm of the study, the RxWell app includes instruction in many CBT and mindfulness techniques.

4. Carloni S, Bertocchi A, Mancinelli S, et al. Identification of a choroid plexus vascular barrier closing duing intestinal inflammation. *Science*. 2021 Oct;374(6566):439-448.

Contact

If you have any questions, please contact a member of the research team at **412-208-5235** or email us at **IBDStudy@upmc.edu**. We can help you:

- Address concerns about your Vincent Payment Card.
- Update your contact information.
- Resolve issues you may be having with the RxWell app.
- Schedule a time to complete your follow-up questionnaires.