Clinical Trials in IBD: Why would anyone want to take part?

Shirley Cohen-Mekelburg M.D., M.S.
Division of Gastroenterology & Hepatology
University of Michigan
Clinical Trials in IBD

- Background
- Emerging therapies
- Clinical trials
Background

Wilks introduces ulcerative colitis into the medical vernacular

1875

Over 300 patients with ulcerative colitis hospitalized in London

1909

Paper on regional ileitis published in JAMA by Crohn

1932

IBD recognized throughout North America and Europe

1950

Ulcerative colitis is more common than Crohn’s disease

1960

IBD is a disease of Westernized nations with rising incidence

1970

Incidence of ulcerative colitis stabilizes, Crohn’s disease still rising

1980

The incidence of IBD rises in newly industrialized countries

1990

IBD is a global disease with increasing prevalence

2000
Current Treatment

- 5-ASA or sulfasalazine
- Prednisone or budesonide
- Immunomodulators (AZA or 6-MP or MTX)
- Biologic agents
- Surgery
- Nutritional support

- Step-up approach
- Top-down approach
Emerging Therapies
While we have seen tremendous improvements in the treatment of IBD...

- Some patients do not respond to initial treatment (primary non-responders), and some those who initially respond will lose response at some point in the disease course (secondary non-responders).
- There is a need for additional safe and effective therapeutic options to address unmet treatment needs.
Anti-adhesion Agents

- Prevent lymphocyte infiltration of the intestines by selectively targeting the adhesion molecules involved in this homing process.
  - **Natalizumab** (IV) - α4β7 and α4β1 inhibitor
  - **Vedolizumab** (IV) - α4β7 inhibitor
  - **Ertolizumab** (SC) - α4β7 and αEβ7 inhibitor
  - **AJM 300** (PO) - α4β7 and α4β1 inhibitor
  - **PF-00547659** (SC) - MAdCAM-1 inhibitor
IL-12 and IL-23 induce differentiation of naïve CD4+ T cells into T-helper 1 and T-helper 17 cells, which are important in the pathogenesis of IBD.

- **Ustekinumab** (IV, SC) - IL12/23 inhibitor
- **Risankizumab** (IV) - IL12 inhibitor
Cytokines mediate intracellular signaling by inducing the JAK/STAT signaling pathway. JAKs are a family of intracellular tyrosine protein kinases (JAK1, JAK2, JAK3, TYK2). Cytokines bind to receptors on JAK proteins, which works on STAT factors leading to inflammation.

- **Tofacitinib** (PO) - JAK1/3 inhibitor
- **Filgotinib** (PO) - JAK1 inhibitor
The S1P1 receptor is found on the cell surface of lymphocytes and is crucial in their migration from secondary lymphoid organs to the blood and tissues.

- **Ozanimod** (PO) - S1P1/5 inhibitor
Stem Cell Therapy

• Up to 1/3 of patients with Crohn’s disease will develop fistulas in their lifetime.
• However, surgical and medical options are limited.
• Mesenchymal stem cell injections may help due to the immunomodulatory and growth-promoting effects, leading to a reduction in inflammation and healing.
The Future of IBD Therapeutics is Promising…

Clinical trials are essential to these advancements!
Why Clinical Trials?

1. Wanting to find a therapy that works better than current options
2. To get more monitoring of my condition
3. Wanting to contribute to progress in IBD research
1. Worried they won't get the best therapy available?

Federal regulations require you to have the best therapy available PLUS any new therapy. You will not be denied effective therapy.
Concerns Addressed?

2. Worried about getting placebo?

• To truly test if a drug works, it must be compared to a placebo. Some patients in a randomized study will receive a placebo, in addition to their usual medicines.

• Most studies allow patients to cross-over to the experimental drug if they don't get better. Other studies allow patients access to the experimental drug after the study ends.
3. Worried about committing to a study and not being able to get out?

You can change your mind and get out of a study at any time. This is required by federal regulations on research.
Trials at Michigan Medicine

To learn more about clinical trials…

- Tel: (734) 615-4843
  E-mail: higginsSCteam@umich.edu
  [http://www.med.umich.edu/ibd/studies/index.html](http://www.med.umich.edu/ibd/studies/index.html)

- Clinicaltrials.gov
- www.ccf.org
Questions?