

IBD Clinical Trials: What's Available to Me

Ronen Stein, MD

Assistant Professor of Clinical Pediatrics

Division of Gastroenterology, Hepatology, and Nutrition



Objectives

- Discuss why clinical trials are important in pediatric IBD
- Identify barriers to performing clinical trials in children with IBD
- Discuss how the CHOP IBD Center selects our participation in a clinical trial
- Review current and upcoming IBD clinical trials being performed at CHOP

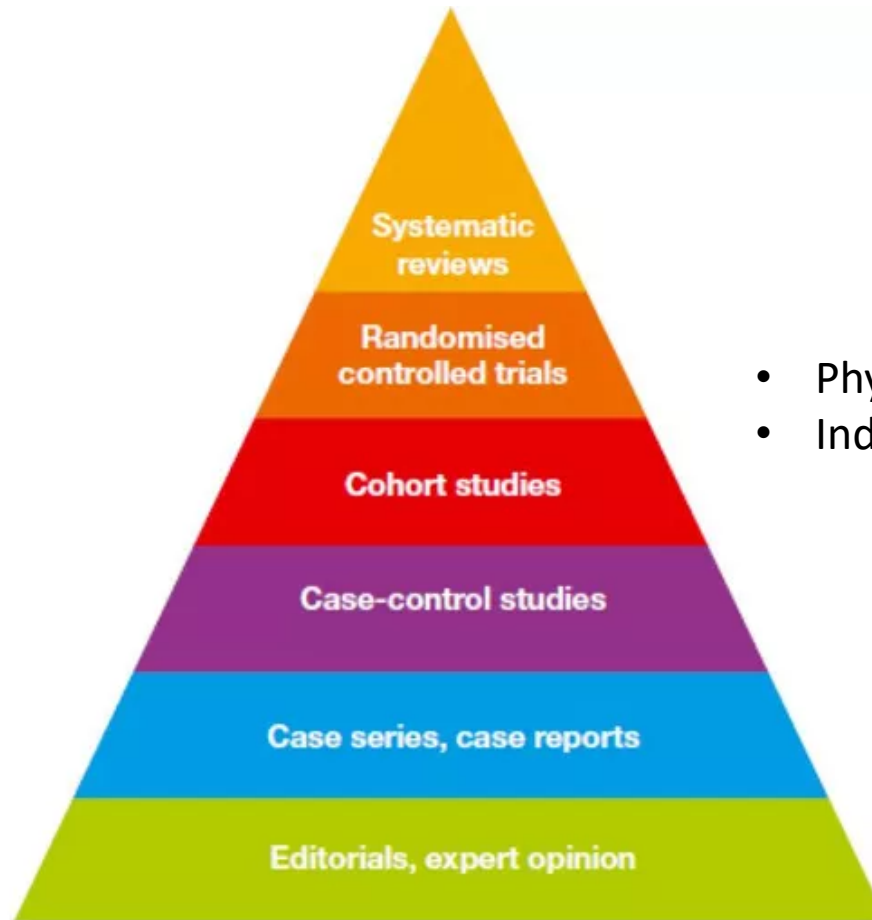
Why are new therapies needed for pediatric IBD?

- Not all medicines work for all patients
 - Inflammation occurs through a number of pathways
- The most potent medicines are given via injection or IV infusion
 - Oral medicines are easier to take and might be cost-effective
- Although medicines can be effective at treating IBD they do not cure IBD

Why do we need pediatric studies?

- Children are not just “little adults”
- Metabolism of drugs may be different in kids vs adults
- Pediatric IBD tends to be more aggressive
- There are unique considerations in kids
 - Growth
 - Puberty

Hierarchy of Scientific Evidence



- Physician-initiated trials
- Industry-sponsored trials

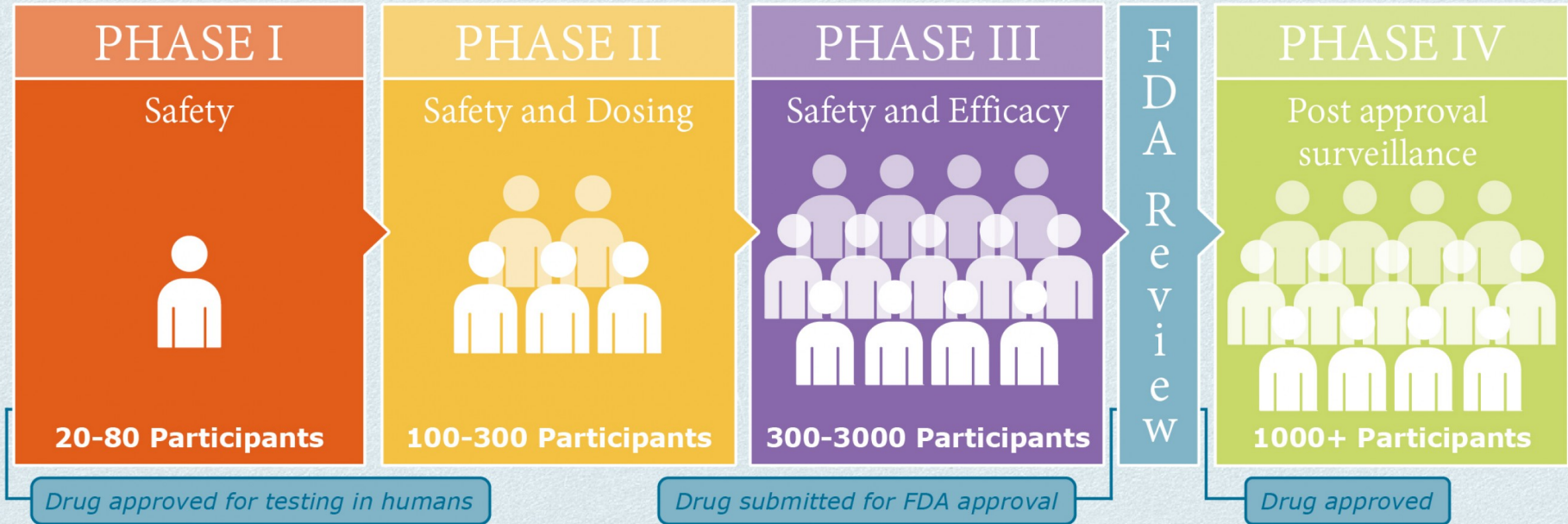
How many IBD medicines that we use in children are supported by pediatric randomized placebo-controlled trials?

0

Why are RCTs difficult in pediatrics?

- RCTs take a long time
- Adults are often studied first
 - We want to make sure that the drug is safe and works before exposing children
- Drugs come to market after efficacy is shown in adults
- By the time studies are considered in children the drug is already available “off-label”
- At that point a randomly controlled placebo trial may be unethical in kids

Clinical Trial Phases



How does the CHOP IBD Center choose to participate in clinical trials?

- How can this study help our patients?
 - Is this a medicine that is difficult/not possible to obtain off-label?
 - Does this medicine require closer safety monitoring?
 - Is this a well-designed study?
 - What is the dose/frequency of the medication?
 - If there are 2 doses tested what happens to kids on the lower dose who flare?
 - Do current medicines need to be changed/held and for how long?

A New Diet Study !



Investigators

Jessica Breton, MD
Lindsey Albenberg, DO
Robert Baldassano, MD

Research Coordinators

Melissa Crisci
Naomi Pressman

TREATING IBD WITH INULIN (TII)

Who can be part of this study?

Inflammatory bowel disease (IBD) patients ages 8-21 who

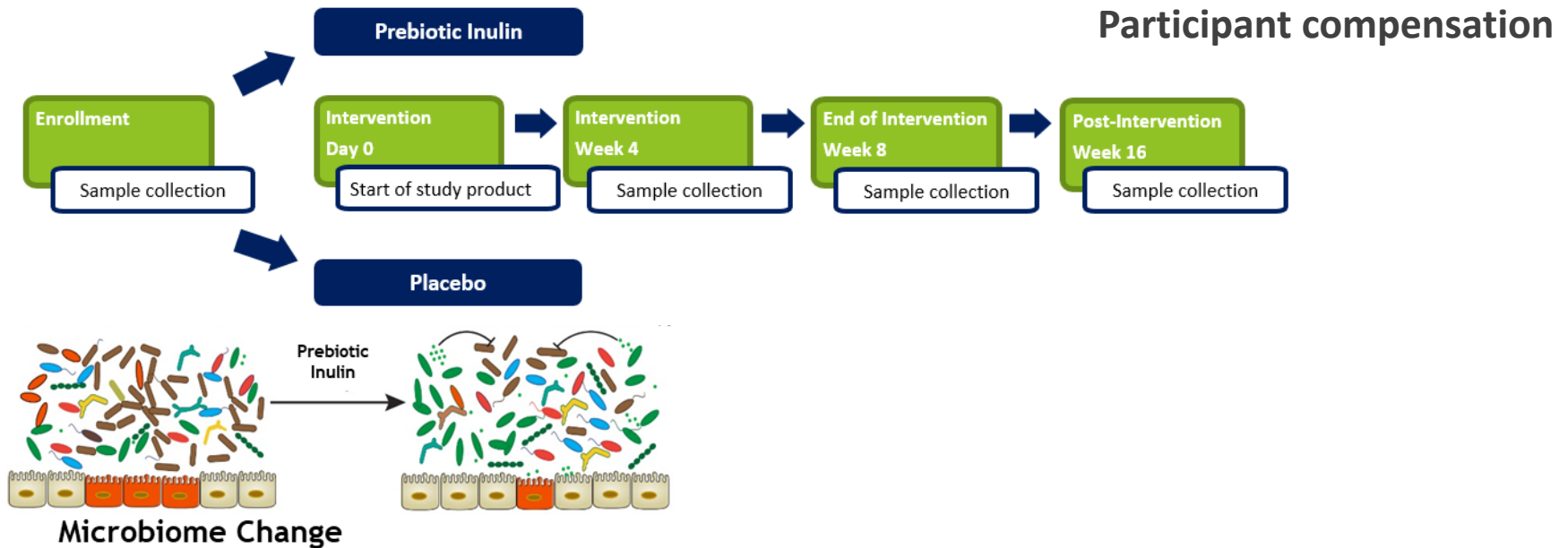
- Are in clinical remission (inactive IBD)
- Have no history of bowel resection
- Have not used oral steroids or antibiotics within past month

What will participants be asked to do?

- Take prebiotic fiber or a placebo (sugar) every day for 8 weeks
- Collect samples (stool, rectal swabs, and urine) at 4 time points
- Complete survey questions online

No in-person visit or change in treatment required

Randomized double-blind placebo-controlled trial

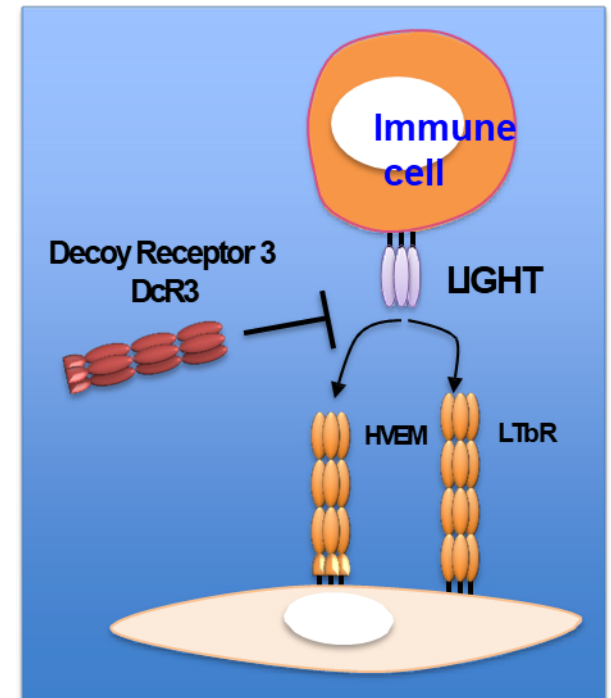




Evaluation of the Safety, Tolerability, and Efficacy of CERC-002 in Adults With Moderate to Severe Active Crohn's Disease

Rationale for anti-LIGHT approach

- LIGHT overexpressed in IBD
- DcR3 loss-of-function increases LIGHT
- DcR3 loss-of-function is linked to some cases of severe pediatric onset IBD

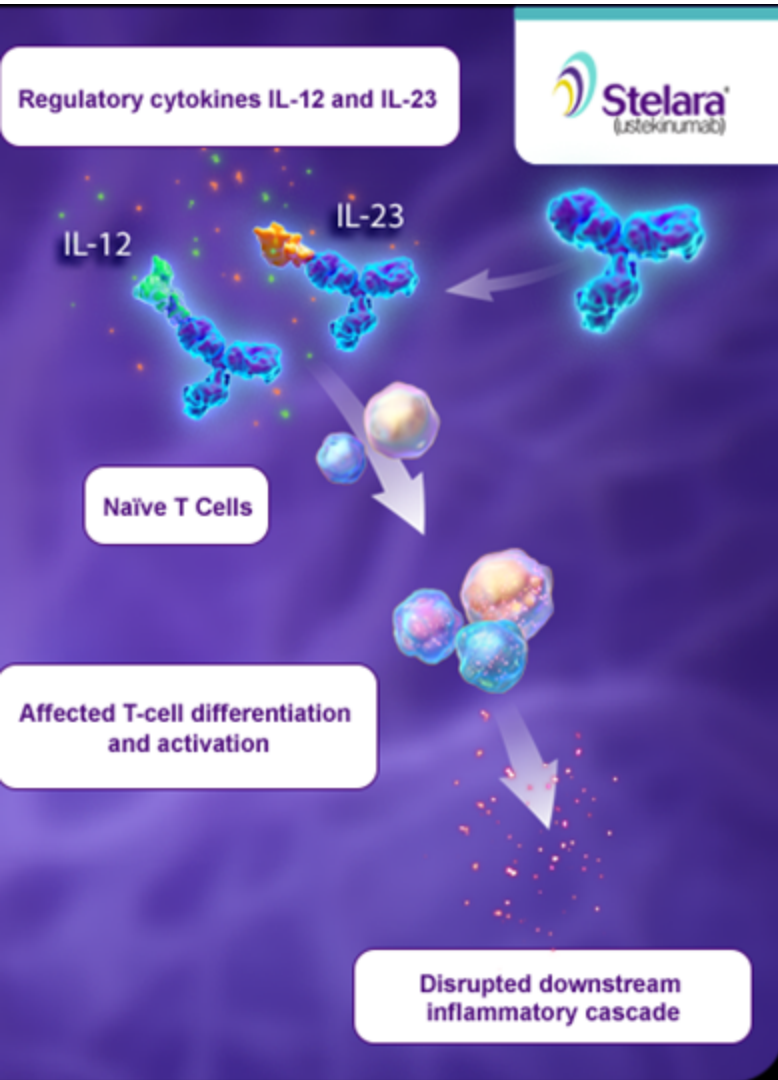


CERC-002 Phase 1b Trial

- Multicenter trial
- 18 years or older with moderate-to-severe Crohn disease
- Failed anti-TNF therapy
- 8 week trial
- Injections every 2 weeks
- Colonoscopy at baseline and at 8 weeks
- If response at 8 weeks then sponsor would need to ask permission from the FDA to continue treatment

A Study of Mirikizumab in Children and Teenagers With Ulcerative Colitis (SHINE 1) - COMING SOON

Rationale for targeting IL-23



- Ustekinumab (Stelara) blocks IL-12/23
- There is some evidence in psoriasis that specific targeting of IL-23 might work better
- Mirikizumab specifically targets IL-23

Figure from www.stelarainfo.com

Mirikizumab Phase 2 Trial – Eli Lilly

- Multicenter trial
- Ages 2-17 with moderate-to-severe active ulcerative colitis
- Failed at least 1 of the following therapies
 - Anti-TNF
 - Steroids
 - Immunomodulator
 - Tofacitinib
- Prior exposure to ustekinumab (Stelara) is not allowed

Mirikizumab Phase 2 Trial – Eli Lilly, Cont

- Medication is given via IV for induction (2 different doses are being studied) and then for maintenance it is given as a subcutaneous injection
- 3 endoscopies
 - Baseline = clinical endoscopy
 - Week 12, 52 = research endoscopy

**Evaluation of Oral Tofacitinib in Children Aged
2 to 17 Years Old with Moderate to Severe
Ulcerative Colitis-
COMING SOON**

Rationale for using small molecules

- Xeljanz (tofacitinib) blocks JAK/STAT pathway
- Small molecules are oral medications that may work faster. The body does not make antibodies against them.
- Xeljanz is approved for treatment of moderate-to-severe ulcerative colitis in adults, but is approved for children with juvenile idiopathic arthritis



Tofacitinib Phase 3 Trial – Pfizer

- Multicenter trial
- Ages 2-17 with moderate-to-severe active ulcerative colitis
- Failed Anti-TNF therapy
- 3 endoscopies
 - Baseline = clinical colonoscopy
 - Week 8/16, 52/60 = research endoscopy
- Study extension

Conclusions

- Children are not just small adults. Clinical trials involving children can provide strong evidence whether or not a new IBD treatment is safe and effective in pediatrics
- The FDA is now prioritizing inclusion of children earlier in the clinical trial process so that we can have good pediatric data prior to drug approval

Conclusions

- The CHOP IBD Center participates in a number of physician-initiated and industry-sponsored clinical trials that offer patients new treatments that may otherwise not be available to patients clinically
- Please email IBDRESEARCH@chop.edu with any further questions

Thank you