IBD treatment: Goals of therapy

- Improved growth and nutrition
- Symptom improvement
- Normalization of labs
- Mucosal healing
IBD treatment: Goals of therapy

• 2 “step” process:
  • **Induction** of remission
  • **Maintenance** of remission
IBD treatment: Current Strategies

- **Dietary Therapy:** EEN and SCD

- **Step-up approach:**
  - 5-ASA or sulfasalazine
  - Prednisone or budesonide
  - Immunomodulators (AZA or 6-MP or MTX)
  - Biologic agents
  - Surgery

- **Top-down approach:**

- **Nutritional support**

- **Anti TNF-α (Remicade, Humira)**
IBD treatment: Targets of therapy

- Environmental Trigger
- Genes
- Gut Bacteria
- Immune Response
IBD treatment: New Targets for Therapy

Biologic Medications:
- Vedolizumab
- Ustekinumab
- Tofacitinib
- Mongersen
- Biosimilars

Dietary Therapy: EEN, SCD

Fecal microbiota Transplant (FMT)
Vedolizumab (Entyvio)

• “Anti-integrin”
• Approved for adults with IBD
• Studies suggest it is efficacious and safe in kids
• Currently used “off-label” for pediatric IBD
IBD treatment: What’s New?

**Ustekinumab** (Stelara)
- Neutralizes IL-12 and IL-23, prevents development of activated T cells
- Approved for adults with Crohn’s disease
- Approved for kids with psoriasis
Tofacitinib: (Xeljanz)

- **Oral** inhibitor of JAK 1, 2 and 3
- Blocks signaling of pro-inflammatory molecules
- Off-label use for ulcerative colitis
Mongersen:

- **Oral** SMAD7 Antisense Oligonucleotide
- Anti-inflammatory agent
- Clinical trials for adults with Crohn’s Disease

*Image Source: Monteleone et al. NEJM 2015*
Biosimilars:

- Biological product approved based on showing it is highly similar to an FDA-approved biological product
- Potentially less expensive product
IBD treatment: Special Considerations for Pediatric Patients

- Therapies approved for adults frequently used in pediatrics without sufficient data
- 2012: FDA implemented Pediatric Research Equity Act
- Pediatric Trials Network designed to boost pediatric clinical trials and product development
IBD treatment: New Targets for Therapy

**Biologic Medications:**
- Vedolizumab
- Ustekinumab
- Tofacitinib
- Ozanomunid
- Biosimilars

**Dietary Therapy:** EEN, SCD

**Fecal microbiota Transplant (FMT)**
IBD treatment: What’s New?

• **Dietary therapy:**
  • Exclusive Enteral Nutrition (EEN)
    • Formula only diet
    • Works for both induction and maintenance of remission
  • Specific Carbohydrate Diet (SCD)
    • Clinical remission demonstrated in study pediatric patients

Stay tuned! More to come on this…
IBD treatment: New Targets for Therapy

Biologic Medications:
- Vedolizumab
- Ustekinumab
- Tofacitinib
- Ozanomod
- Biosimilars

Dietary Therapy: EEN, SCD

Fecal microbiota Transplant (FMT)
IBD treatment: What’s New?

• **Fecal Microbiota Transplantation (FMT)**
  • Aim to restore “normal” intestinal bacteria by application of fecal microorganisms from a healthy subject into the GI tract of a patient
  • FMT is most effective treatment for recurrent Clostridium difficile infections
  • So far, FMT can only be recommended for treatment of C diff infection in IBD
  • FMT in the management of IBD remains uncertain
Table 1
New therapies for Crohn disease and their respective immunologic targets

<table>
<thead>
<tr>
<th>Target</th>
<th>Therapeutic Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Extracellular</strong></td>
<td></td>
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<tr>
<td>(1) Leukocyte migration</td>
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<tr>
<td>(\alpha_4\beta_7) Integrin</td>
<td>Vedolizumab, Abrilumab (AMG 181)</td>
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<tr>
<td>(\beta_7) Integrin</td>
<td>Etrolizumab</td>
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<tr>
<td>MAdCAM-1</td>
<td>PF-00547659</td>
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<tr>
<td>CCR9</td>
<td>Vercimon</td>
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<tr>
<td>S1P receptor</td>
<td>Ozanimod</td>
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<tr>
<td>(2) Cytokine inhibitors</td>
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<tr>
<td>TNF-(\alpha)</td>
<td>Infliximab</td>
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<tr>
<td>IL-12/IL-23 (p40 subunit)</td>
<td>Adalimumab</td>
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<td>IL-23 (p19 subunit)</td>
<td>Certolizumab pegol</td>
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<td>IL-12/IL-23 (p40 subunit)</td>
<td>Ustekinumab</td>
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<td>IL-23 (p19 subunit)</td>
<td>Briakinumab</td>
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<td>Tildrakizumab (MK-3222)</td>
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<td>(MEDI2070), Risankizumab (BI 655066)</td>
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<td>(3) Antiinflammatory agents</td>
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<td>F8-IL-10</td>
<td>Dekavil</td>
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<td>SMAD7</td>
<td>Mongersen</td>
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<tr>
<td><strong>Intracellular and Intranuclear</strong></td>
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<tr>
<td>(1) JAK inhibitors</td>
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<td>JAK1, JAK2, JAK3</td>
<td>Tofacitinib</td>
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<tr>
<td>JAK1</td>
<td>Filgotinib, Upadacinib (ABT-494)</td>
</tr>
<tr>
<td>JAK1, JAK2</td>
<td>Baricitinib</td>
</tr>
</tbody>
</table>
Thank You

Questions?