Inflammatory Bowel Diseases: Emerging Therapies

Manreet Kaur M.D.
mkaur@bcm.edu

Therapy of Inflammatory Bowel Diseases

Crohn's Disease
 IFX
 1998

Ulcerative Colitis
 IFX

CMZ & NAT
 2007

ADA
 2005

GOL
 2012

VEDO
 2013

IFX
 2014

ADA

GOL

VEDO
Therapy of Inflammatory Bowel Diseases

- Anti-TNF agents
- Anti-adhesion molecules
- Anti IL12/23
- Janus kinase inhibitors
- Chemokine Receptor Antagonists

- Fecal Microbiota Transplant
- Stem Cell therapy
- ‘Worm’ Therapy
- HMPL-004
- Anti-IL6
Anti-adhesion Molecules

Primary endpoints in the trial of induction of remission:

- Placebo (N=148)
- Vedolizumab (N=220)

Clinical Remission: 6.8 vs. 74.5, P=0.02
CDAI-100 Response: 25.7 vs. 31.4, P=0.23

Vedolizumab For CD

NEJM 2013; 369:711-721
Vedolizumab For CD

Primary endpoints in the trial of maintenance of remission:

- Placebo (N=153)
- Vedolizumab, every 8 wk (N=154)
- Vedolizumab, every 4 wk (N=154)

- Placebo (N=153)
- Vedolizumab, every 8 wk (N=154)
- Vedolizumab, every 4 wk (N=154)

Vedolizumab for UC

- Placebo (N=145)
- Vedolizumab (N=223)

- Placebo vs. vedolizumab at 6 wk, P<0.001

- Placebo vs. vedolizumab every 8 wk for 52 wk, P<0.02
- Placebo vs. vedolizumab every 4 wk for 52 wk, P<0.01
Etrolizumab for UC: Phase 2

Endpoints in the trial of induction of remission for UC:

![Graph A](image1.png)

Anti MAd-CAM Ab PF-00547659 for CD: Phase 1

Phase 1 study did not show any effect on CNS immune surveillance following an induction course of PF-00547659 in moderate to severe CD.

Phase 2 study underway (Feb 2016)
Anti Adhesion Molecules

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Therapy of Inflammatory Bowel Diseases

- Anti-TNF agents
- Anti-adhesion molecules
- Anti IL12/23
- Janus kinase inhibitors
- Chemokine Receptor Antagonists
- Fecal Microbiota Transplant
- ‘Worm’ Therapy
Ustekinumab (Anti IL 12/23) for CD

Induction of remission in CD:

Maintenance of Remission in CD:

* Indicates p < 0.05
Janus Kinase Inhibitors

Tofacitinib (JAK inhibitor) in UC

Primary and Secondary End Points at 8 weeks:

A Clinical Remission

B Clinical Remission

D Endoscopic Remission
CCX282-B (CCR9 antagonist) for CD

Clinical response at weeks 8 & 12

Therapy of Inflammatory Bowel Diseases

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What About ‘Worm’ Therapy?

Phase I trial to assess safety of TSO:

Phase II study terminated at 12 weeks
What about Fecal Transplant for UC?

Fecal transplants can save lives.

Fecal transplants can save lives.

Inflamm Bowel Dis 2013;19:2155–2165

Alteration of intestinal dysbiosis by FMT does not induce remission in patients with UC

Inflamm Bowel Dis 2013;19:2155–2165
FMT for Treatment of UC

Temporal bacterial communities vary among UC patients after FMT

Table 1: Demographic and clinical information of patients

<table>
<thead>
<tr>
<th>PM</th>
<th>Sex</th>
<th>Age</th>
<th>Disease duration (years)</th>
<th>Disease extent</th>
<th>Smoker</th>
<th>Prior therapy</th>
<th>Concomitant therapy</th>
<th>Post-FMT baseline Mayo score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>27</td>
<td>1.7</td>
<td>Left-sided</td>
<td>No</td>
<td>Aza, C, A</td>
<td>5-ASA</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>37</td>
<td>1.3</td>
<td>Extensive</td>
<td>No</td>
<td>Aza, C, C, I</td>
<td>Place</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>44</td>
<td>4.9</td>
<td>Extensive</td>
<td>Yes</td>
<td>Aza, C, A, F, A, A, MTX</td>
<td>6-ASA</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>27</td>
<td>0.7</td>
<td>Extensive</td>
<td>Yes</td>
<td>C, A, A, A, F, A, A, MTX</td>
<td>PRO</td>
<td>8</td>
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Table 2: Fecal calprotectin in patients

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<tr>
<th>Patient</th>
<th>Post-antibiotics baseline</th>
<th>Week 12</th>
<th>Early termination</th>
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<tr>
<td>1</td>
<td>3.030</td>
<td>8.034</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.019</td>
<td>2.019</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.030</td>
<td>2.030</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3.030</td>
<td>3.030</td>
<td></td>
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<tr>
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<td>2.030</td>
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Calprotectin concentration in gram in mg/g
The antibiotic treatment resulted in the first mucosal transmembrane. (FMT 1)

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Helminthic therapy with TSO has not shown any benefit in CD
Unlike CDI, few cases of FMT as treatment of IBD have been published
- Numerous trials are underway
- No evidence of sustained benefit based on available data
Thank You