Current Treatments for Inflammatory Bowel Disease

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Disclosures
None
Pathogenesis of Inflammatory Bowel Disease

Environmental triggers (infection, bacterial products)

Failure to down-regulate

Chronic uncontrolled inflammation = IBD

Normal gut controlled inflammation

Moderately inflamed

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Pre-treatment Evaluation

History and Exam

Endoscopy/Histology

Laboratory Tests

Radiology

IBD
IBD: Systemic Manifestations
Endoscopic Spectrum of Severity

**UC - Spectrum of Disease**

- **Normal**
- **Mild**
- **Moderate**
- **Severe**
Crohn’s Disease
Capsule Endoscopy
Radiology

- X-ray, CT, MRI
- CTE and MRE
Serologies

Test Result

- **IBD Predicted**
- **Ulcerative Colitis Predicted**
- **Crohn's Disease Predicted**

### Assay Information

<table>
<thead>
<tr>
<th>Assay</th>
<th>ASCA IgA ELISA</th>
<th>ASCA IgG ELISA</th>
<th>Anti-OmpC IgA ELISA</th>
<th>Anti-CBl1 ELISA</th>
<th>Neutrophil-Specific Nuclear AutoAntibodies (NSNA) (IBD specific pANCA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay Value</td>
<td>109.4 EU/ml</td>
<td>113.8 EU/ml</td>
<td>26.0 EU/ml</td>
<td>50.2 EU/ml</td>
<td>AutoAntibody ELISA: &lt; 12.1 EU/ml, IFA Perinuclear Pattern: Not Detected, DNAse Sensitivity: Not Detected</td>
</tr>
</tbody>
</table>

*Note: Test result determined by the PROMETHEUS Predictive Algorithm without direct consideration of assay values relative to reference values. However, interpretation of prognostic information should be made based on relative differences between assay values and reference values.*
Can therapy safely alter the natural history of IBD?

- Induce and maintain gastrointestinal healing
- Prevent need for steroids
- Prevent strictures and penetrating complications
- Prevent extra-intestinal complications
- Decrease hospitalization/surgery
- Decrease long-term cost of care

Slide courtesy of Stephen B. Hanauer, MD.
Crohn’s and Colitis Foundation of America 2008 Advances in Inflammatory Bowel Disease.
IBD Therapy in 2015

Antibiotics
- Ciprofloxacin
- Metronidazole

Mesalamine
- Apriso
- Pentasa
- Asacol
- Sulfasalazine
- Lialda
- Colazal
- Rowasa
- Canasa

Steroids
- Entocort/Uceris
- Prednisone
- Hydrocortisone
- enemas
- Cortifoam

Immunomodulator
- 6 MP
- Azathioprine
- Methotrexate
- Tacrolimus
- Thalidomide

Anti-TNF
- Infliximab
- Adalimumab
- Certolizumab
- Golimumab

Anti-integrin
- Natalizumab
- Vedolizumab

Surgery

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Risk Versus Benefit of Therapy

**Benefits**
- Maintenance of remission
- Improved function and QOL
- Early promotion of mucosal healing to prevent complications
- Decrease rate of hospitalizations, surgery, less steroid exposure

**Disadvantages**
- Side effects
- Cost
- Majority of patients may not require more potent treatments initially
- Risk of untreated disease

## Corticosteroids

<table>
<thead>
<tr>
<th>Event</th>
<th>Estimated Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any side effect leading to the d/c of prednisone</td>
<td>55%</td>
</tr>
<tr>
<td>Ankle swelling</td>
<td>11%</td>
</tr>
<tr>
<td>Facial swelling</td>
<td>35%</td>
</tr>
<tr>
<td>Easy bruising</td>
<td>7%</td>
</tr>
<tr>
<td>Acne</td>
<td>50%</td>
</tr>
<tr>
<td>Memory problems</td>
<td>7%</td>
</tr>
<tr>
<td>Psychosis</td>
<td>1%</td>
</tr>
<tr>
<td>Infections</td>
<td>13%</td>
</tr>
<tr>
<td>Cataracts</td>
<td>9%</td>
</tr>
<tr>
<td>Increased intraocular pressure</td>
<td>22%</td>
</tr>
<tr>
<td>HTN</td>
<td>13%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>33%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 X increased risk</td>
</tr>
</tbody>
</table>
## Adverse Effects Associated With Oral 5-ASAs

<table>
<thead>
<tr>
<th>Sulfasalazine</th>
<th>Olsalazine, Balsalazide, Mesalamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Headache</td>
<td>• Headache</td>
</tr>
<tr>
<td>• Nausea/vomiting</td>
<td>• Nausea</td>
</tr>
<tr>
<td>• Dyspepsia</td>
<td>• Rash</td>
</tr>
<tr>
<td>• Anorexia</td>
<td>• Hair loss</td>
</tr>
<tr>
<td>• Rash</td>
<td>• Interstitial nephritis</td>
</tr>
<tr>
<td>• Bone marrow suppression</td>
<td>• Pericarditis</td>
</tr>
<tr>
<td>• Interstitial nephritis</td>
<td>• Hepatitis</td>
</tr>
<tr>
<td>• Megaloblastic anemia</td>
<td>• Pneumonitis</td>
</tr>
<tr>
<td>• Apparently reversible oligospermia</td>
<td>• Hepatitis</td>
</tr>
<tr>
<td>• Folate malabsorption</td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>• Connective tissue disease</td>
<td>• Paradoxical exacerbation of colitis</td>
</tr>
</tbody>
</table>

- Pancreatitis
- Pericarditis
- Paradoxical exacerbation of colitis
- Secretory diarrhea (olsalazine)

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Sands B. *Gastroenterology.* 2000;118:S68.
AZA/6MP: Adverse Effects

Direct toxicities:

• Pancreatitis (3.3%)
• BM suppression (2%)
• Hypersensitivity reaction (2%)
• Hepatitis (0.3%)
• Nausea (1.3-6%)
Monoclonal Antibodies, Fusion Proteins and Fc-Free Fab’ Fragments Against TNFα

Chimeric monoclonal antibody

Human monoclonal antibody

Human recombinant receptor/Fc fusion protein

Humanized Fc-Free Fab’ fragment

Infliximab (Remicade®)

Adalimumab (Humira®)

Etanercept (Enbrel®)

Certolizumab pegol (Cimzia®)
<table>
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<tr>
<th>Risk of serious infections such as sepsis</th>
<th>Neurologic reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis (TB), invasive fungal infections, and other opportunistic infections</td>
<td>Hematologic reactions</td>
</tr>
<tr>
<td>Malignancies</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Autoimmunity</td>
</tr>
<tr>
<td>Hepatitis B reactivation</td>
<td>Drug interactions</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Lupus-like reaction</td>
</tr>
<tr>
<td></td>
<td>Psoriasis-like reaction</td>
</tr>
</tbody>
</table>
## Meta-analysis of lymphoma rate associated with anti-TNF agents

<table>
<thead>
<tr>
<th>Event</th>
<th>Estimated Frequency (annual, pt-years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hodgkin Lymphoma (baseline)</td>
<td>2/10,000</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma (on IM)</td>
<td>6/10,000</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma (on anti-TNF)</td>
<td>6/10,000</td>
</tr>
<tr>
<td>Hepatosplenic T-cell Lymphoma</td>
<td>Unknown</td>
</tr>
<tr>
<td>Death from sepsis</td>
<td>4/1000</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>5/10,000</td>
</tr>
</tbody>
</table>


Risk factors for Opportunistic Infections in IBD: a Case-Control Study (100 cases, 1983-2003)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Odds Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids alone</td>
<td>2.2 (1.1–4.8)</td>
<td>0.037</td>
</tr>
<tr>
<td>6MP/AZA alone</td>
<td>2.5 (1.2–5.1)</td>
<td>0.015</td>
</tr>
<tr>
<td>IFX alone</td>
<td>11.2 (0.8–153.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>6MP/AZA – steroids</td>
<td>15.7 (4.1–59.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6MP/AZA – IFX</td>
<td>1.6 (0.1–18.7)</td>
<td>0.71</td>
</tr>
<tr>
<td>6MP/AZA – IFX – steroids</td>
<td>Infinite</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

1 medication                   | 2.7 (1.5–4.8)       | 0.0014  |
2 medications                  | 9.7 (3.3–28.2)      | <0.0001 |
3 medications                  | Infinite            |         |

Overall p<0.0001

Follow-Up

Assessing Response
- Clinical
- Biochemical
- Radiographic
- Endoscopic

Assessing Side Effects

**Ultimate Goal:** Get our patients well and keep them well