When and How to Use Immunomodulators and Biologics in IBD

Gary R. Lichtenstein, MD
University of PA School of Medicine
Philadelphia, PA
DISCLOSURES

**Grants/Research Support:** Ferring, Janssen Biotech, Prometheus Laboratories, Inc., Salix Pharmaceuticals, Santarus, Shire Pharmaceuticals, UCB, Warner Chilcott

**Consultant:** Abbott Corporation/AbbVie, Actavis, Alaven, Ferring, Hospira, Janssen Biotech, Luitpold/American Regent, Pfizer Pharmaceuticals, Prometheus Laboratories, Inc., Salix Pharmaceuticals, Santarus, Shire Pharmaceuticals, Takeda, UCB, Warner Chilcott

**Honorarium Recipient:** Ironwood, Luitpold/American Regent (CME programs)

**Editorial Board Involvement:** Clinical Advances in Gastroenterology, Gastroenterology and Hepatology

**Other Financial Material Support:** SLACK, Inc. (book royalty)
Key Points

• Anti-TNF antibodies and Anti-Integrin therapies are the most effective therapies available to treat IBD

• Select patients who will benefit: those with active inflammatory disease, ideally before onset of complicated disease behavior

• Address identifiable safety risks in advance, and educate patient about signs/symptoms of adverse events that are not preventable

• Optimal and more durable response is obtained when combined with an immune modulator
  – Need to select the correct population
• **Indications and Drug Selection**
• Contraindications and safety
• **Immunomodulators**
• Optimization
• Prognostication
Indications:
Consider the Clinical Scenario

- Disease: Crohn’s disease or ulcerative colitis
- Age of patient
- Severity of flare
- Hospitalized or outpatient?
- Refractory to “conventional therapy”
  - which medication(s) were used previously?
- Fistulizing Crohn’s disease
- Extraintestinal manifestations
- Post-operative prophylaxis in Crohn’s disease?
- Newly diagnosed?
- Patient Prognosis
# Anti TNF: Drug Selection by Indication

<table>
<thead>
<tr>
<th>Condition</th>
<th>Infliximab</th>
<th>Adalimumab</th>
<th>Certolizumab Pegol</th>
<th>Golimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal CD</td>
<td>✔✔✔✔</td>
<td>✔✔✔</td>
<td>✔✔✔</td>
<td></td>
</tr>
<tr>
<td>Fistulizing CD</td>
<td>✔✔✔✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Mild to Moderate UC (Outpatient)</td>
<td>✔✔✔✔</td>
<td>✔✔✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate to Severe UC (Hospitalized)</td>
<td>✔✔</td>
<td>✔</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>✔✔</td>
<td>✔</td>
<td>✔✔✔</td>
<td>✔</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>✔✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
## Anti-Integrin: Drug Selection by Indication

<table>
<thead>
<tr>
<th>Condition</th>
<th>Natalizumab</th>
<th>Vedolizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal CD</td>
<td>✔✔✔</td>
<td>✔✔✔</td>
</tr>
<tr>
<td>Fistulizing CD</td>
<td>✔✔</td>
<td>✔✔</td>
</tr>
<tr>
<td>Mild to Moderate UC (Outpatient)</td>
<td></td>
<td>✔✔✔</td>
</tr>
<tr>
<td>Moderate to Severe UC (Hospitalized)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Pouch complications</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>✔✔</td>
<td>✔✔</td>
</tr>
</tbody>
</table>
Critical Component

Presence of Inflammation

The key patient selection factor for treatment with Anti-TNF therapy and Anti-Integrin therapy
Corticosteroid-Free Clinical Remission at Week 26 in Patients With Crohn’s Disease by Baseline Endoscopy Status

AZA, azathioprine; IFX, infliximab; UTD, unable to determine

Overview

- Indications and drug selection
- Contraindications and safety
- Immunomodulators
- Optimization
- Prognostication
Biologic Therapy: Contraindications and Safety

- Infection
  - TB
  - HBV
  - HIV
  - Serious Infections: Abscess, Sepsis,

- Congestive heart failure

- Multiple sclerosis/demyelinating disease

- Lymphoproliferative disorder

- Other Malignancies?

- Inability to give informed consent or does not desire biologic
Anti-TNF Therapy: Risk for Serious Opportunistic Infections

- Pneumocystosis
- Histoplasmosis
- Candidiasis
- Listeriosis
- CMV
- Atypical mycobacteria
- Aspergillosis
- Cocidiomycosis
- Cryptococcus
- Herpetic
- Salmonellosis
- Legionellosis
- Blastomycosis
- Other

Source:
3.) http://www.cimzia.com/assets/pdf/Prescribing_Information.pdf
Minimizing Toxicity for Anti-TNF and Anti-Integrin Therapy

- Exclude TB prior to initiation (Anti-TNF)
  - CXR, ppd, quantiferon TB gold
  - If immunocompromised, PPD and TB may be negative
- Exclude the presence of active infection prior to initiation
  - Abscess, C. difficile, CMV
- Check serology for Hepatitis B
- Vaccination for age-appropriate disease
  - Influenza, hepatitis A and B, pneumococcal pneumonia, herpes zoster

Vaccines in IBD Patients

### 2015 Recommended Immunizations for Adults: By Age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Flu Influenza</th>
<th>Td/Tdap Tetanus, diphtheria, pertussis</th>
<th>Shingles Zoster</th>
<th>Pneumococcal</th>
<th>Meningococcal</th>
<th>MMR Measles, mumps, rubella</th>
<th>HPV Human papillomavirus</th>
<th>Chickenpox Varicella</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hib Haemophilus influenzae type b</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-21 years</td>
<td>1 dose</td>
<td>1 dose or Td booster every 10 years</td>
<td>1 dose</td>
<td>1 or 2 doses</td>
<td>1 or more doses</td>
<td>3 doses</td>
<td>3 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>3 doses</td>
<td>1 or 3 doses</td>
</tr>
<tr>
<td>22-26 years</td>
<td>Flu vaccine every year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27-49 years</td>
<td>1 dose</td>
<td>1 dose or Td booster every 10 years</td>
<td>1 dose</td>
<td>1 or 2 doses</td>
<td>1 or more doses</td>
<td>3 doses</td>
<td>3 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>3 doses</td>
<td>1 or 3 doses</td>
</tr>
<tr>
<td>50-59 years</td>
<td>1 dose</td>
<td>1 dose or Td booster every 10 years</td>
<td>1 dose</td>
<td>1 or 2 doses</td>
<td>1 or more doses</td>
<td>3 doses</td>
<td>3 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>3 doses</td>
<td>1 or 3 doses</td>
</tr>
<tr>
<td>60-64 years</td>
<td>1 dose</td>
<td>1 dose or Td booster every 10 years</td>
<td>1 dose</td>
<td>1 or 2 doses</td>
<td>1 or more doses</td>
<td>3 doses</td>
<td>3 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>3 doses</td>
<td>1 or 3 doses</td>
</tr>
<tr>
<td>65+ years</td>
<td>1 dose</td>
<td>1 dose or Td booster every 10 years</td>
<td>1 dose</td>
<td>1 or 2 doses</td>
<td>1 or more doses</td>
<td>3 doses</td>
<td>3 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>3 doses</td>
<td>1 or 3 doses</td>
</tr>
</tbody>
</table>

### More Information:
- There are several flu vaccines available. Talk to your healthcare professional about which flu vaccine is right for you.
- *If you are pregnant, you should get a Tdap vaccine during the 3rd trimester of every pregnancy to help protect your babies from pertussis (whooping cough). You should get zoster vaccine even if you’ve had shingles before.*
- There are two different types of pneumococcal vaccines: PCV13 (conjugated) and PPSV23 (polysaccharide). Talk with your healthcare professional to find out if one or both pneumococcal vaccines are recommended for you.
- Your healthcare professional will let you know how many doses you need.
- **Recommended For You:** This vaccine is recommended for you unless your healthcare professional tells you that you cannot safely receive it or that you do not need it.
- **May Be Recommended For You:** This vaccine is recommended for you if you have certain risk factors due to your health, job, or lifestyle that are not listed here. Talk to your healthcare professional to see if you need this vaccine.

If you are traveling outside the United States, you may need additional vaccines. Ask your healthcare professional about which vaccines you may need at least 6 weeks prior to your travel.

## General Vaccination Considerations

### In the IBD Patient

**Titers to check at first office visit:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR</td>
<td>If vaccination history unknown</td>
</tr>
<tr>
<td>Varicella</td>
<td>If vaccination history or history of chicken pox/zoster unknown</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Except those with evidence of protective titer within 5 years of vaccine administration</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Except those with evidence of protective titer within 5 years of vaccine administration</td>
</tr>
</tbody>
</table>

**Vaccinations to administer in specific patient groups regardless of immunosuppressive drug use:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccine Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tdap</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td>HPV</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Influenza</td>
<td>Meningococcal</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccinations to consider if NO plans to start immunosuppressive therapy in 4-12 weeks:**

<table>
<thead>
<tr>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR</td>
</tr>
<tr>
<td>Varicella</td>
</tr>
<tr>
<td>Zoster</td>
</tr>
</tbody>
</table>

# Live Vaccine Recommendations

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Check titer before vaccination?</th>
<th>Before initiation of immunomodulator or biologic?</th>
<th>What to do if already on immunomodulator or biologic?</th>
<th>Can family members be vaccinated?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMR</strong> (measles, mumps, rubella)</td>
<td>Yes if vaccination history unknown</td>
<td>Contraindicated if plans to start therapy in 6 weeks</td>
<td>Contraindicated</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Zoster</strong> (for age &gt;60)</td>
<td>No</td>
<td>Contraindicated if plans to start therapy in 1-3 months</td>
<td>Contraindicated – could consider if on short-term corticosteroids (&lt; or = 20 mg prednisone for &lt; 14 days), or low doses of methotrexate (&lt;0.4 mg/kg/week), AZA (&lt;3.0 mg/kg/day), or 6-MP (1.5 mg/kg/day)</td>
<td>Yes. Vaccine recipients who have a vaccine-related rash should avoid contact with the immunosuppressed patient</td>
</tr>
<tr>
<td><strong>Varicella</strong></td>
<td>Yes if vaccination history unknown or no prior varicella infection</td>
<td>Contraindicated if plans to start therapy in 1-3 months</td>
<td>Contraindicated – no adequate data to suggest otherwise</td>
<td>Yes. Vaccine recipients who have a vaccine-related rash should avoid contact with the immunosuppressed patient</td>
</tr>
</tbody>
</table>

Overview

• Indications and drug selection
• Contraindications and safety
• Immunomodulators
• Optimization
• Prognostication
Immunomodulators

AZA and 6-MP
- Effective maintenance agents
- Response slow (8–16 weeks)
- Not tolerated by about 15% of patients
- Only about half of patients responsive to AZA/6-MP for steroid refractory or steroid-dependent disease
- About 5%–10% relapse despite treatment
- Safety/tolerance issues: nausea/malaise, lymphoma risk, opportunistic infections, pancreatitis, myelosuppression

Methotrexate
- An alternative for patients not responding to or intolerant of AZA/6-MP
  - Effective when given IM or SC
- Response over 8 to 16 weeks
- Effective maintenance agent
- Can be used to prevent immunogenicity: 12.5-15 mg po once weekly dosing
- Safety issues: hepatic fibrosis, interstitial pneumonitis, teratogenicity, nausea

Maintenance of Remission with Azathioprine in Crohn’s Disease

Early AZA Alone Is Ineffective in CD

**Rate of Trimesters in Remission per Patient During First 3 Y, %**
- Early AZA (n = 65): 67%
- Step-up Tx (n = 67): 56%

**P = NS**

Abbreviation: Tx, transplantation.

**Sustained Steroid-Free Clinical Remission to Wk 76, % of Patients**
- Early AZA (n = 68): 44%
- Placebo (n = 63): 37%

**P = NS**

Crohn’s Disease: Issues With AZA / 6-MP

- Take 6-12 weeks to work
- Side effects
  - Pancreatitis (4%), allergy (2%)
  - Bone marrow suppression (4%)
  - Liver toxicity (9%)
  - Infection (serious infection: 2%)
  - Increased risk of lymphoma (SIR-2.8 [95% CI, 3.10–7.78])
    - Under age 30: (SIR 6.99 [CI, 95% CI,2.99–16.4])
    - Over age 50: (The absolute risk was highest in patients > 50 years 1:354 cases per patient–year) RR=4.78
  - Nonmelanoma skin cancer
  - Abnormal Pap smears
- Require frequent labs
  - Complete blood count (CBC), liver function tests (LFTs)

18 studies (among 4383 citations) met inclusion criteria.

The SIR for lymphoma was
- Overall- 4.92 (95% CI, 3.10–7.78),
- 2.80 (95% CI, 3.10–7.78) in 8 population studies
- 9.24 (95% CI, 4.69–18.2) in 10 referral studies.

Population studies demonstrated an
- Increased risk among current users (SIR =5.71; 95% CI, 3.72–10.1) but
- No increased risk in former users (SIR =1.42; 95% CI, 0.86–2.34).

Risk of Lymphoma with AZA / 6-MP Use

- Risk Became Significant after One year of exposure

- **Sex**
  - Men have a greater risk than women (RR = 1.98; P < .05)
  - Both sexes were at increased risk for lymphoma
  - Men: SIR for men = 4.50 (95% CI 3.71–5.40)
  - Women: SIR for women = 2.29 (95% CI 1.69–3.05)

- **Age**
  - Age 30-59: 1 lymphoma per 2000 pt-yrs of follow-up
  - Patients < 30 years had the highest RR
    - SIR = 6.99 (CI, 95% CI, 2.99–16.4)
    - Younger men had the highest risk: Men < 30: SIR ~ 9
  - The absolute risk was highest in patients > 50 years 1:354 cases per patient–year RR = 4.78

*- subanalysis of 2 studies

Steroid Sparing and Toxicity of MTX in Active CD

Maintenance of Remission with Methotrexate in Crohn’s Disease


Week

Methotrexate

Placebo

Patients in remission (%)
Issues With MTX

- Often used intramuscularly in Crohn’s Disease\(^1\)
- Common side effects:\(^1\)
  - Nausea/vomiting
  - Bone marrow suppression
  - Scarring of the liver
- Liver biopsy is needed before and during MTX therapy in certain patients\(^1\)
- Requires continuous monitoring of CBC and LFTs\(^2\)
- Contraindicated if attempting pregnancy\(^2\)
  - Category X

Overview

• Indications and drug selection
• Contraindications and safety
• Immunomodulators
• Optimization
• Prognostication
Defining anti-TNF failure:
Secondary Non-response (Loss of Response)

- “Pseudo-failure” for symptoms unrelated to active inflammation
- Pharmacokinetic
  - Inadequate drug levels because of anti-drug antibody
  - Inadequate drug levels because of rapid drug clearance for other reasons
  - Inadequate dose
- Pharmacodynamic
  - Evolution of resistance to anti-TNF mechanism
- Dose-limiting adverse event
Optimal Therapy with Biologics: Maximizing Efficacy and Avoiding Loss of Response

- Give a loading dose
  - Infliximab 5 mg/kg IV at weeks 0, 2 and 6
  - Adalimumab 160 mg, 80 mg, then 40 mg SC EOW
  - Certolizumab pegol 400 mg SC EOW x3
  - Golimumab Load: 200 mg week 0, 100 mg week 2 then 100 mg q4w
  - Vedolizumab 300 mg iv mg/kg IV at weeks 0, 2 and 6
  - Natalizumab 300 mg iv every 4 weeks

- Give in combination with an immune modulator
  (6-mercaptopurine, azathioprine, or methotrexate)

- If not given in combination with immune modulator, give infliximab with hydrocortisone pretreatment

- Avoid episodic dosing

- Dose optimize early to avoid unintentional episodic dosing?
Is It Possible that the Future Management of IBD Patients on Monoclonal Antibody Medication will Include Proactive Levels?

Typical protocol for dose adjustment:

- **IFX undetectable**
  - No or low ATI -> Increase IFX by 2.5 mg/kg
  - High ATI -> Stop IFX

- **IFX < 5 (detectable)**
  - Increase IFX by 50-100 mg (if no/low ATI)

- **IFX 5 – 10**
  - No change

- **IFX > 10***
  - Decrease dose if > 5 mg/g or Increase interval if at 5 mg/kg

* On 2 occasions


IFX < 5 (detectable)
Is It Possible that the Future Management of IBD Patients on Monoclonal Antibody Medication will Include Proactive Levels?

TDM in Responder Patients

- Evaluate the efficacy and cost-effectiveness of a ‘treat-to-trough’ strategy in 263 inflammatory bowel disease
- Responders to maintenance infliximab therapy
- Optimal trough concentration range of 3 to 7 µg/mL
- Trough concentration Adapted infliXImab Treatment (TAXIT) randomized controlled trial (clinicaltrialsregister.eu 2011-002061-38)

TAXIT Trial Algorithm

TLI = trough level of infliximab, ATI = antibodies to infliximab.
Results - Optimization Phase
Dose Escalation (N=76)

CD: Harvey-Bradshaw ≤4/ UC: Partial Mayo ≤2

Dose escalation in CD patients with subtherapeutic levels results in better disease control

*Five patients (1 CD and 4 UC) were excluded from analysis because of withdrawal of consent during optimization phase. Vande Casteele N, et al. Gastroenterology 2015;148:1320–1329
Successful dose de-escalation of patients with supratherapeutic levels while retaining disease control

*One patient was excluded from analysis because of withdrawal of consent during optimization phase.
Results - Maintenance Phase
Primary End Point

*Harvey-Bradshaw Index score d4 (CD) or Partial MAYO score d2 (UC) and C-reactive protein level d5 mg/L. Primary end point could not be calculated for 3 patients (1 CD from CB and 1 UC and 1 CD from LB group); CB=clinically-based group; LB=level-based group.

Elevating Infliximab Concentration From Subtherapeutic Levels Is Effective in Regaining Response in HACA (-) Patients

Clinical Outcomes of Patients with Detectable Antibodies to Infliximab or Subtherapeutic Infliximab Concentrations

<table>
<thead>
<tr>
<th>Response to Test</th>
<th>Complete/Partial Response (%)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detectable HACA</td>
<td>Increase infliximab</td>
<td>1/6 (17)</td>
</tr>
<tr>
<td></td>
<td>Change anti-TNF</td>
<td>11/12 (92)</td>
</tr>
<tr>
<td>Subtherapeutic concentration</td>
<td>Increase infliximab</td>
<td>25/29 (86)</td>
</tr>
<tr>
<td></td>
<td>Change anti-TNF</td>
<td>2/6 (33)</td>
</tr>
</tbody>
</table>

HACA, human antichimeric antibody

Why give concomitant therapy?

- Lower rates of infusion reactions (infliximab)
- Lower rates of anti-drug antibody formation
- Higher drug levels (independent of effect on antibody formation)
- Independent effect of a 2nd active agent
- Lower rate of loss of response
- No signal for increased risk of infection (SONIC)
Concomitant Treatment with AZA and IFX is Associated with Higher Serum IFX Levels in SONIC

Median serum infliximab trough concentrations at Week 46

- IFX (n=73)
- IFX/AZA (n=76)

*infliximab- or infliximab/azathioprine-treated patients who had serum samples collected prior to infusion at Week 46 (N=149)

UC SUCCESS study


*P<.05 compared to IFX; #P<.05 compared to AZA
Overview

• Patient selection and indications
• Contraindications and safety
• Drug selection
• Optimization
• Prognostication
Personalized Medicine

Risk Stratification
- Clinical Factors
- Serology / Genetics
- Endoscopy

“High risk”
- Early anti-TNF/combination therapy

“Low risk”
- Budesonide or AZA

Principles of Crohn’s Disease Treatment

• Treatment algorithms
  - “Step up” for good prognosis or mild to moderate patients
  - “Early aggressive” for poor prognosis or moderate to severe patients
Clinical Predictors of Poor Disease Outcome

I. Clinical Relapse
   - Elevated CRP
   - Basal Plasmacytosis on Biopsy
   - Elevated Fecal Calprotectin
   - Complete Mucosal Healing - protective

II. Colectomy
   - Corticosteroid Use
   - Extensive Disease
   - Age > 50 years at diagnosis - protective against colectomy
   - Early (wk 8) Mucosal healing - protective (with infliximab)

5-Year Follow-Up of Patients With Nondisabling and Disabling Crohn’s Disease According to Characteristics at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Percent age of Patients</th>
<th>Independent Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nondisabling (n=166)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Disabling (n=957)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40.4</td>
<td>2.1 (P=0.0004)</td>
</tr>
<tr>
<td>Age &lt;40 yr</td>
<td>77.1</td>
<td>1.8 (P=0.01)</td>
</tr>
<tr>
<td>Disease location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small bowel only</td>
<td>44.6</td>
<td></td>
</tr>
<tr>
<td>Small bowel &amp; colon</td>
<td>25.9</td>
<td></td>
</tr>
<tr>
<td>Colon only</td>
<td>29.5</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>50.3</td>
<td>3.1 (P=0.0001)</td>
</tr>
<tr>
<td>Systemic findings</td>
<td>44.6</td>
<td></td>
</tr>
<tr>
<td>Perianal lesions</td>
<td>17.5</td>
<td></td>
</tr>
<tr>
<td>Steroids for first flare</td>
<td>37.3</td>
<td></td>
</tr>
</tbody>
</table>

Distribution of Patients by and Positive Predictive Value of Independent Factors for Disabling Crohn’s Disease

No factors (score = 0)
1 factor (score = 1)
2 factors (score = 2)
All 3 factors (score = 3)

A Prediction Tool to Help Children With Crohn’s Disease and Their Parents Understand Individualized Risks of Disease Complications and Response to Therapy

System Dynamics Modeling to Predict and Display Individual Crohn’s Disease Patient Outcomes

CA Siegel, LS Siegel, J Hyams, S Kugathasan, J Markowitz, J Rosh, N Leleiko, D Mack, W Crandall, J Evans, D Keljo, A Otley, M Oliva-Hemker, C Langton, IT Wrobel, G Wahbeh, A Quiros, G Silber, R Bahar, BE Sands, MC Dubinsky

What is system dynamics analysis?

• System dynamics analysis (SDA) is a methodology that addresses the inherent dynamic complexity of interactions between variables.

• Advantages of SDA over traditional statistical methods are:
  - Provides real-time individualized predictions of outcomes
  - Simple input “control panel”
  - Graphically conveys the outcomes over time

Complex clinical data → Patient-friendly results

Siegel CA et al. Inflamm Bowel Dis. 2011;17:30.
Control Panel and Output

16-year-old girl, small bowel and perianal disease, QSS group = 4

Risk of Complication

No treatment

Early IM treatment

Year From Present

0 1 2 3

Risk of Complication

No treatment

Early IM treatment

Siegel CA et al. Inflamm Bowel Dis. 2011;17:30.
Conclusions

• Document active inflammation before initiating anti-TNF and anti-Integrin therapy
• Always consider combination therapy
  - Assess Risk versus Benefit
  - Avoid AZA / 6-MP in males < 30 or >50- especially
• Avoid episodic dosing
• Load biologic therapy appropriately
• Treat active infection before starting Biologic Therapy
• Prevent preventable infections with vaccination