INFLAMMATORY BOWEL DISEASE: RISK STRATIFICATION AND TREATMENT STRATEGIES

Faculty

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FACULTY DISCLOSURE

- Gerald W. Dryden, MD, MSPH, MSc, AGAF, FASGE
  - Speaker's Bureau – Abbvie, Takeda, EnteraHealth, Salix, Forest
  - Contracted Research – Abbvie, Johnson & Johnson/Centocor/Janssen, Merck, Takeda, Pfizer, Genetech

- Kimberly Carter, MS, PA-C
  - Nothing to disclose
LEARNING OBJECTIVES

• Identify the conditions referred to as inflammatory bowel disease (IBD), and recognize their clinical presentations and degree of severity

• Implement appropriate pharmacologic and non-pharmacologic therapeutic strategies for managing IBD in accordance with evidence-based guidelines

• Identify patients who are at high risk of complications from IBD and who may benefit from new mechanisms of action in IBD therapy

• Employ approaches for effectively communicating the risks and benefits of IBD treatment options and facilitating adherence

PRE-TEST QUESTIONS
PRE-TEST QUESTION 1

On a scale of 1 to 5, please rate how confident you would be in treating a patient with inflammatory bowel disease (IBD)?

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident

PRE-TEST QUESTION 2

Which of the following scenarios most likely represents a patient presenting with IBD?

1. 37 year old male stopped smoking 9 months ago. He presents with progressive rectal bleeding and diarrhea over past 3 months.
2. 22 year old female who develops intermittent rectal bleeding during third trimester. She also complains of constipation.
3. 58 year old female experiences worsening diarrhea with streaks of blood. She recently received antibiotics to treat a septic knee.
4. All of the above
5. None of the above
PRE-TEST QUESTION 3

Which testing method will most accurately identify the cause/severity of GI symptoms in a patient with a suspected IBD flare?

1. Stool culture, ova and parasite
2. Anoscopy
3. Capsule endoscopy
4. Sigmoidoscopy/colonoscopy
5. No need to evaluate further, history tells me enough to make an accurate call on etiology and severity
A 34 yo male recently diagnosed with moderate UC presents with continued diarrhea (8-10 BM/day), rectal bleeding (< 50% of BM) and left-sided abdominal cramps. He was initially started on oral mesalamine 4.8gm/day approximately 6 months ago. He was then hospitalized and started prednisone, infliximab + azathioprine 6 weeks later due to poor response. He is now asking you for help with his severe uncontrolled symptoms. Which of the following regimens would you recommend?

1. Initiate induction with adalimumab 160/80/40mg then 40mg every 2 wks
2. Increase oral prednisone from 40mg to 60mg daily
3. Discontinue infliximab and initiate induction dosing with vedolizumab 300mg at 0, 2, and 6 weeks followed by maintenance every 8 weeks
4. Maintain total dose of 5-ASA to 4.8gm/day and add rectally administered 5-ASA in the form of an enema or suppository
5. All of the above

An 18 year old male diagnosed with ulcerative colitis returns from college. He complains of increased symptoms since he left home. After you question him closely, you determine that he has only intermittently taken his medications. What important steps are most likely to enhance his compliance with medications?

1. You employ the OARS communication technique to motivate patient and refer him to CCFA website for disease specific info
2. You threaten to call his mother and report his non-compliance if he doesn’t turn around
3. You switch to a once daily 5-ASA and counsel him on its benefit in reducing number of flares
4. You use a one-time survey to document medical compliance
5. 1 and 3
6. 2 and 4
7. All of the above
8. None of the above
THE BEGINNINGS OF IBD: HOST AND ENVIRONMENT INTERACTIONS


COURSE OF IBD CAN BE DEBILITATING
SUCCESS OF MEDICAL THERAPY DEPENDENT ON DEGREE OF STRUCTURAL DAMAGE AND VELOCITY OF PROGRESSION

Cosnes et al. Inflamm Bowel Dis 2002;8:244-50

SX ASSOCIATED WITH IBD

- DIARRHEA: mucus or blood may be present in the stool; can occur at night; incontinence may occur
- ABDOMINAL PAIN: commonly present in RLQ in CD; peri-umbilically or LLQ in moderate to severe UC
- CONSTIPATION: may be primary symptom in ulcerative colitis and inflammation limited to rectum; obstipation may occur and may proceed to bowel obstruction
- ABNORMAL BMs: pain or rectal bleeding may be present, as well as severe urgency and tenesmus
- NAUSEA & VOMITING: occurs more often in CD than UC

WGO Global Guideline. Inflammatory bowel disease: a global perspective. Munich, Germany: World Gastroenterology Organization (WGO); 2009
DISTINGUISHING IBD FROM IBS

• Differentiate purulent exudate from mucus
  – Presence of blood suggests pus associated with IBD

• Presence of blood in stool favors IBD
  – Bleeding more likely in UC than CD

• Scrutinize ROS for systemic sx, extraintestinal sx

• Specifically ask about prior history of peri-anal abscess, fistula, or fissure
  – May predate onset of IBD by years

DISTINGUISHING IBD FROM IBS

• Alternating diarrhea and constipation more strongly suggestive of IBS than IBD

• Nocturnal diarrhea more common in IBD

• Functional symptoms remaining after bout of enteric infection may confuse the clinical diagnosis
  – Lingering abdominal pain, loose/urgent stools should prompt objective evaluation by endo/path
  – Post infectious IBS common but don’t want to miss IBD triggered by infection
HOW TO CONFIRM THE DIAGNOSIS OF IBD

• Clinical picture

• Endoscopic information/pathologic specimens

• Radiographic evidence

• Chronic course of symptoms

ENDOSCOPIC FEATURES OF IBD

ULCERATIVE COLITIS

• Continuous inflammation extending from rectum proximally
• Variable mucosal changes from mild to severe
• Presence of ulcerations suggestive of fulminant colitis
• Evaluate for other causes of symptoms (infection, ischemia)

Normal  Mild  Moderate  Severe
ENDOSCOPIC FEATURES OF IBD
*CROHN’S DISEASE*

- Patchy edema, erythema
  - Discontinuous
- Apthous ulcerations
- Coalescing ulcerations
- Cobblestoning

**CLINICAL SCENARIO # 1**

- A 34 year old female diagnosed with Crohn’s disease presents with recurrent abdominal pain, diarrhea and bloating
- She has a low grade fever on exam, with RLQ tenderness
- She has no gastroenterologist at this time, and has been in and out of the ER
- Review of her records reveals 3 abdominal CT scans in the past 6 months alone
CLINICAL SCENARIO # 1

You are not sure whether she has an abdominal abscess, active Crohn’s disease, or a small bowel stricture. Which of the following tests would be most appropriate to order?

1. Stool culture/ova and parasites
2. Clostridium difficile toxin by ELISA and reflex PCR
3. MR enteroscopy
4. Repeat CT scan of the abdomen with oral contrast

EVALUATING CROHN’S BEFORE THE PE-MACHINE
BURDEN OF IONIZING RADIATION IN IBD

- Retrospective studies of IBD patients determined elevated ionizing radiation exposure over time (CD > UC)
- Mean 5y dose 10-14.3mSv
- Exposure levels vary
  - 58.3% = >10mSv
  - 18.1% = >25mSv
  - 6.3-7% = >50mSv
- Cancer risk:
  - Acute exposure 50mSv
  - Chronic exposure 50-100mSv

Butcher. Scan J Gastro 2012.47:10;1192-99

MR ENTEROGRAPHY: ALTERNATIVE TO CT IN CD

- Good visualization requires bowel distension
- NJ tube to jejunum or oral gavage (6-7 bottles contrast)
- Detects mucosal ulcerations, fistulas and abscesses
- Differentiates acute inflammation from fibrosis

CURRENT THERAPIES FOR IBD

- 5-ASA (UC)
  - Oral delayed release/sustained release formulations
  - Pro-drugs: Sulfasalazine, Olsalazine, Balsalazide
  - Once daily formulations: Apriso, Lialda
- Immunomodulators (UC, CD)
  - 6-mercaptopurine, azathioprine
  - Methotrexate
- Biologics – Anti-TNF Ab
  - Infliximab/Remicade (CD, UC)
  - Adalimumab/Humira (CD, UC)
  - Certolimumab/Cimzia (CD)
  - Golimumab/Simponi (UC)
- Biologics – Anti-Integrin Ab
  - Natalizumab/Tysabri (CD)
  - Vedolizumab/Entyvio (CD, UC)
- Steroids (UC, CD)
  - Prednisone
  - Methylprednisolone
  - Budesonide
  - Uceris (UC)
  - EnteroCort (CD)

TRADITIONAL APPROACH TO CD THERAPY

Disease severity at presentation:
- Severe
- Moderate
- Mild

- Induction
  - Aminosalicylate
  - Systolic Corticosteroids

- Maintenance
  - Aminosalicylate

- Surgery
  - Thiopurine

- Anti-TNFa
  - Aminosalicylate / Thiopurine

- Anti-TNFa
DETERMINING ACTIVITY/SEVERITY
OF CD

• Difficult task
  – No correlation between clinical score and colonoscopy

CDAI = Crohn’s Disease Activity Index
CDEIS = Crohn’s Disease Endoscopic Index of Severity


BIOMARKERS VS COLONOSCOPY

<table>
<thead>
<tr>
<th>SENS %</th>
<th>SPEC %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>ACCU %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calprotectin &gt;70ug/g</td>
<td>89</td>
<td>72</td>
<td>88</td>
<td>76</td>
</tr>
<tr>
<td>CRP &gt; 5 mg/l</td>
<td>68</td>
<td>58</td>
<td>88</td>
<td>29</td>
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<tr>
<td>WBC &gt; 7.9 g/l</td>
<td>55</td>
<td>50</td>
<td>83</td>
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<tr>
<td>CDAI &gt; 150</td>
<td>33</td>
<td>68</td>
<td>80</td>
<td>20</td>
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<table>
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<tr>
<th>IL-6</th>
<th>Calprotectin</th>
<th>Lactoferrin</th>
<th>CDAI</th>
<th>SES-CD</th>
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<tr>
<td>hs-CRP</td>
<td>0.65</td>
<td>0.47</td>
<td>0.52</td>
<td>0.16</td>
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<tr>
<td>IL-6</td>
<td>0.45</td>
<td>0.55</td>
<td>0.15</td>
<td>0.43</td>
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<tr>
<td>Calprotectin</td>
<td>0.76</td>
<td>0.23</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>0.19</td>
<td>0.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDAI</td>
<td>0.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CLINICAL SCENARIO # 2

• A 43 year old female recently diagnosed with ileal Crohn’s disease was started by the endoscopist on mesalamine 800mg TID.

• She shows up in your office 4 weeks later stating that she is no better. She is requesting a medication that works. Her symptoms would be classified as mild-moderate in severity.

ANSWER # 2

Based on current treatment guidelines, which regimen would you recommend?

1. Tell her to hang in there, the medication should start working in the next few weeks.
2. Increase her total daily dose of 5-ASA to 4.8 gm
3. Switch her to budesonide 9 mg daily for 8 weeks
4. Prepare her for combination tx with anti-TNF and immunomodulator
5. All of the above
6. None of the above
5-ASA IN CROHN’S DISEASE

- No evidence for efficacy of 5-ASA for:
  - Inducing or maintaining ileal Crohn's disease
  - Maintaining prednisone induced remission
  - Maintaining surgically induced remission
- Possible evidence for inducing remission in mild colonic disease (4g sulfasalazine/day)
- Best to consider other form of therapy
  - Budesonide EC (mild)
  - Prednisone + immunomodulator (mod-severe)

AMERICAN COLLEGE OF GASTROENTEROLOGY:
ADULT CD TREATMENT GUIDELINES

- Mild to moderate Crohn’s disease:
  - Use of oral mesalamine or sulfasalazine is:
    • Minimally effective compared to placebo (A)
    • Less effective than budesonide or prednisone (A)
- Moderate to severe Crohn’s disease:
  - Use of oral prednisone 40-60mg daily is effective (A)
    • > 50% of treated patients become dependent/resistant
    • Elemental diets are less effective than prednisone, but can spare side effects (A)
    • AZA is effective at maintaining steroid induced remission (A)
    • MTX is effective at maintaining steroid induced remission (A)
    • Anti-TNF Ab are effective at inducing remission (A)

**BEWARE OF STEROID COMPLICATIONS!**

- INFECTIONS!
- Osteopenia / Osteoporosis
- Avascular necrosis
- Fluid / Electrolyte disturbances
- Cataracts
- Psychosis
- Endocrine dysfunction
- Diabetes Mellitus / Weight gain

1. Lichtenstein GR et al. ACG 2008;Abstract 14

**MANAGING STEROID RISK**

- Crohn’s patients – consider baseline DEXA
  – Ca++ absorption may impaired by inflammation\(^1,2\)
- Supplement with Ca/Vit D while taking steroids
  – Stable Crohn’s only needs standard therapy\(^2,3\)
- Check Vit D levels, replace as necessary
- Assess BMD q 1-2 years for steroid exposed
- Consider annual opthalmologic exams\(^4\)
- Implement exit strategy upon steroid initiation

4. Lichtenstein GR Gastro 2006;130(3):935-9
PREDICTORS OF RAPID PROGRESSION TO SURGERY

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds ratio (95% CI)</th>
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<tbody>
<tr>
<td>Current smoker</td>
<td>3.09 (1.47-6.51)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1.82 (1.05-3.18)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>2.07 (1.04-4.10)</td>
</tr>
<tr>
<td>Ileal localization only</td>
<td>2.22 (1.30-3.81)</td>
</tr>
<tr>
<td>Oral corticosteroid use</td>
<td>3.79 (1.90-7.55)</td>
</tr>
</tbody>
</table>


PROGNOSIS OF CD PATIENTS WITH SEVERE COLONIC ULCERATIONS

- Retrospective cohort
- 102 pts with active CD
- Severe endoscopic lesions (SEL) defined as deep ulcerations >10% of mucosal area with at least one colonic segment involved
- Risk of colectomy associated with SELs, high CDAI, absence of immunosuppression

RISK FACTORS THAT IDENTIFY HIGH-RISK PATIENTS FOR COMBINATION THERAPY

• Complex fistula
• Deep ulcerations on endoscopy
• Young age
• Steroid resistance/dependence
• High risk anatomic locations (foregut disease, extensive disease, perianal disease)
• Severe disease activity (evidenced by wt loss, low albumin, anemia)

CONSIDERATIONS PRIOR TO IMMUNOMODULATOR TX
AZA (AZATHIOPRINE), 6-MP (MERCAPTOPURINE), MTX (METHOTREXATE)

• Commonly used as steroid sparing agents for long-term management
• Many long-term risks
  – Bone marrow suppression / Infection
  – Lymphoma
• Need routine testing for safety
  – CBC, LFTs
• Pre-AZA testing: thiopurine methyl-transferase (TPMT)
  – Homozygous recessive: excess BM suppression
  – Interaction with allopurinol
CONSIDERATIONS PRIOR TO ANTI-TNF THERAPY

• Preparation for therapy
  – Quantiferon Gold +/- TB skin test (ppd)
  – Chest X-ray
  – Hepatitis B - HepBsAg, HepBsAb, HepBcoreAb

• Contraindications:
  – History of CHF, MS/optic neuritis, active infection

• Ongoing therapy requires monitoring
  – Regular CBC, CMP testing

SONIC: COMBINATION THERAPY FOR CD

• Subjects 21 years of older:
  – Moderate to severe CD (CDAI >220 and <450)
  – No prior exposure to biologics/immunomodulators
  – Normal TPMT

• Randomized to one of three arms:
  – Azathioprine 2.5mg/kg/day
  – Remicade 5mg/kg
  – Azathioprine + Remicade

• 1\textsuperscript{0} endpoint: steroid-free remission at week 26
Inflammatory Bowel Disease: Risk Stratification and Treatment Strategies

**Sonic**

**Steroid-Free Remission at Week 26**

*Primary Endpoint*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion (%)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>AZA + placebo</td>
<td>51/170</td>
<td></td>
</tr>
<tr>
<td>IFX + placebo</td>
<td>75/169</td>
<td>p=0.006</td>
</tr>
<tr>
<td>IFX + AZA</td>
<td>96/169</td>
<td>p&lt;0.001</td>
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</table>


**Mucosal Healing at Week 26**

*Secondary Endpoint*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion (%)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>AZA + placebo</td>
<td>18/109</td>
<td></td>
</tr>
<tr>
<td>IFX + placebo</td>
<td>28/93</td>
<td>p=0.023</td>
</tr>
<tr>
<td>IFX + AZA</td>
<td>47/107</td>
<td>p=0.055</td>
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MUCOSAL HEALING PREDICTS DISEASE COURSE IN CROHN’S

Top-level Recommendations for CD

- Objective evidence of the presence of inflammation should drive clinical decision making, not the presence of symptoms alone
- Combining antimetabolite therapy and a TNFα-inhibitor results in optimal efficacy and protects the latter against sensitization
- Step-care is obsolete in CD
- Earlier intervention with combination therapy in high-risk patients will likely lead to improved results
TRADITIONAL APPROACH TO UC THERAPY

Disease severity at presentation

Severe

Moderate

Mild

Surgery

Thiopurine

Anti-TNFα

Anti-TNFα

Systemic Corticosteroids

Aminosalicylate / Thiopurine

Induction

Maintenance

SITE OF DELIVERY

BASED ON 5-ASA FORMULATION

- Topical therapy’s ability to reduce inflammation directly linked to ability to reach site of inflammation

20% pancolitis

Oral

30-40% beyond sigmoid Enema

40-50% rectosigmoid Suppository
Inflammatory Bowel Disease: Risk Stratification and Treatment Strategies

**DETERMINING UC SEVERITY**

*Truelove and Witt’s Mayo Score*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild</th>
<th>Severe</th>
<th>Fulminant</th>
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</thead>
<tbody>
<tr>
<td>Stools</td>
<td>&lt;4</td>
<td>&gt;6</td>
<td>Continuous</td>
</tr>
<tr>
<td>Blood</td>
<td>Intermit</td>
<td>Freq</td>
<td>Continuous</td>
</tr>
<tr>
<td>Temp</td>
<td>Nl</td>
<td>&gt;37.5</td>
<td>&gt;37.5</td>
</tr>
<tr>
<td>Pulse</td>
<td>Nl</td>
<td>&gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Hgb</td>
<td>Nl</td>
<td>&lt;75%</td>
<td>Transfusion</td>
</tr>
<tr>
<td>ESR</td>
<td>&lt;30mm</td>
<td>&gt;30</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

All mild parameters = mild severity

Fewer than all six severe = moderate

All 6 severe = severe

Stool frequency
0 = Normal
1 = 1-2 stools/day more than normal
2 = 3-4 stools/day more than normal
3 = > 5 more stools/day more than normal

Rectal bleeding
0 = None
1 = Visible blood with less than 50% of stools
2 = Visible blood with more than 50% of stools
3 = Passing blood alone

Mucosal appearance on endoscopy
0 = Normal or inactive disease
1 = Mild disease
2 = Moderate disease
3 = Severe disease

Physician rating of disease severity
0 = Normal
1 = Mild
2 = Moderate
3 = Severe

< 2 = remission
3-6 = moderate
6-12 = moderate to severe

**ACG PRACTICE GUIDELINES: ADULT ULCERATIVE COLITIS**

- UC suspected on clinical grounds should be confirmed by endoscopic and histologic data

- Left-sided UC can be treated with oral or topical 5-ASA or topical steroids (A)
  - Topical 5-ASA is more effective than oral (A)
  - Combination of oral and topical 5-ASA more effective than either alone (A)
  - Pts refractory to oral may still respond to topical (A)
  - Pts refractory to above or systemically ill may respond to prednisone 40-60mg or anti-TNF (C)

ACG PRACTICE GUIDELINES: ADULT ULCERATIVE COLITIS

• Mild to moderate extensive UC can be treated with 4-6g sulfasalazine or 4.8g mesalamine (A)

• Oral prednisone 40-60mg reserved for 5-ASA failures or those needing speedy relief (B)
  – AZA/6-MP effective for sx not completely relieved by steroids (A)
  – Infliximab is an effective strategy for steroid dependent patients (A)

• Pts with severe colitis not responding to oral therapy should be admitted for IV tx (B)


CLINICAL SCENARIO # 3

• A 34 year old male was diagnosed with left-sided ulcerative colitis of mild severity. He initiated 5-ASA therapy dosed on a TID basis.

• He responds well initially, but has a flare 6 months later. His gastroenterologist placed him on a 5-ASA suppository. Despite that, his diarrhea stools have increased to more than 5 per day. Half contain blood.
ANSWER # 3

You work up his diarrhea to rule out other causes and evaluate endoscopic appearance. There is no evidence of C diff or other infectious cause. Endoscopy reveals mild colitis.

Which regimen would limit steroid side effects?
1. Azathioprine 2.5mg/kg/day after TPMT testing
2. Once daily MMX budesonide (Uceris) 9mg x 8 wks
3. Remicade 5mg/kg 0, 2, 6 weeks then q8 weeks + azathioprine 2.5mg/kg/day
4. None of the above
5. All of the above

MMX BUDESONIDE (UCERIS) FOR UC

- Budesonide: potent CS with high first-pass metabolism
- Widely used clinically
- Previously available in ileal release form for CD
- New formulation provides alternative to systemic steroid therapy for mild to moderate UC
Inflammatory Bowel Disease: Risk Stratification and Treatment Strategies

MMX BUDESONIDE FOR UC

<table>
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<tr>
<th></th>
<th>Uceris 6 mg</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Overall CS side effect</td>
<td>14.5</td>
<td>11.5</td>
</tr>
<tr>
<td>Mood changes</td>
<td>6.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Sleep changes</td>
<td>4.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Acne</td>
<td>4.8</td>
<td>0</td>
</tr>
<tr>
<td>Moon face</td>
<td>4.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Abnormal DEXA</td>
<td>14.3</td>
<td>12.8</td>
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Travis et al. Gastroenterology 2012;142(Suppl 1): S556

SUCCESS: COMBO THERAPY FOR UC

- Subjects 21 years or older:
  - Moderate to severe UC (Mayo score 6-12)
  - Naive to biologics or immunomodulators (or off for at least 3 months)
  - Normal TPMT
- Randomized to one of three arms:
  - Azathioprine 2.5 mg/kg/day
  - Remicade 5 mg/kg at 0, 2, 6 weeks then q8 weeks
  - Azathioprine + Remicade
- 1° endpoint: steroid-free remission at week 16
Inflammatory Bowel Disease: Risk Stratification and Treatment Strategies

SUCCESS

CLINICAL REMISSION WITHOUT CORTICOSTEROIDS AT WEEK 16

Primary Endpoint

A

\[ \Delta = 17.67; P = .017 \]
\[ \Delta = 16.06; P = .032 \]
\[ \Delta = -1.61; P = .813 \]

\[
\begin{array}{c}
\text{AZA (N = 76)} \\
23.88 \\
22.08 \\
30.74 \\
\text{(95% CI)} \\
\end{array}
\]


SUCCESS

MUCOSAL HEALING AT WEEK 16

Secondary Endpoint

B

\[ \Delta = 8.28; P = .295 \]
\[ \Delta = 25.90; P = .001 \]
\[ \Delta = 17.70; P = .028 \]

\[
\begin{array}{c}
\text{AZA (N = 76)} \\
38.84 \\
54.55 \\
62.82 \\
\text{(95% CI)} \\
\end{array}
\]

ANTI-INTEGRIN THERAPY FOR IBD

GEMINI I

VEDOLIZUMAB FOR UC

Major Endpoints

Inflammatory Bowel Disease: Risk Stratification and Treatment Strategies

GEMINI II

VEDOLIZUMAB FOR CD

Major Endpoints

![Graph showing clinical remission and CDAI-100 response](image)


IBD PATIENT ADHERENCE

- ~40-60% of IBD patients are nonadherent\(^1\)-\(^3\)
- Key determinants\(^1\)
  - Young age
  - Male gender
  - Work constraints
  - Enter disease remission
  - Lack of effective communication

2. Cerveny et al. Inflamm Bowel Dis 2007;13(10);1244-1249
IMPROVING PATIENT ADHERENCE

- Empower patients
- Evaluate adherence at every office visit
  - Use patient adherence surveys
- Promote pt education and support groups
- Employ memory aids, minimize number of doses per day
- Use communication techniques to enhance patient-provider relationship


ENHANCED RELATIONSHIP VIA OARS COMMUNICATION TOOL

Motivational Communication Technique

1. Open-Ended Questions
   - Elicits conversation, builds empathy
2. Affirm the Patient
   - Recognize pt’s successes, strengths, positive efforts
3. Reflective Listening
   - Emphasize positive aspects of behavior
4. Summarize the Learning
   - Sum up what you heard, confirm accuracy
**SUMMARY IBD**

- Pts with active IBD must be evaluated with laboratory markers, advanced imaging or colonoscopy to determine active inflammation

- Remission should be the primary goal, with an emphasis on complete mucosal healing

- Steroids: effective short-term but use should be minimized by steroid-sparing agents

- Biologic therapy for UC and CD (esp. active luminal and fistulizing disease)

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**SUMMARY IBD**

- 5-ASA therapy should be dosed and delivered to the area of disease

- 5-ASA has no role in the treatment of Crohn’s disease

- Pts with risk factors predicting poor outcome should be offered combination therapy

- Consider newer therapies such as vedolizumab for patients failing conventional therapy or anti-TNF/immunomodulators
POST-TEST QUESTION 1

Which of the following scenarios most likely represents a patient presenting with IBD?

1. 37 year old male stopped smoking 9 months ago. He presents with progressive rectal bleeding and diarrhea over past 3 months.
2. 22 year old female who develops intermittent rectal bleeding during third trimester. She also complains of constipation.
3. 58 year old female experiences worsening diarrhea with streaks of blood. She recently received antibiotics to treat a septic knee.
4. All of the above
5. None of the above

POST-TEST QUESTION 2

Which testing method will most accurately identify the cause/severity of GI symptoms in a patient with a suspected IBD flare?

1. Stool culture, ova and parasite
2. Anoscopy
3. Capsule endoscopy
4. Sigmoidoscopy/colonoscopy
5. No need to evaluate further, history tells me enough to make an accurate call on etiology and severity
POST-TEST QUESTION 3
A 19 yo female with recently diagnosed Crohn’s disease is following up from a hospital admission for RLQ pain, frequent diarrhea, low grade fevers and weight loss. Colonoscopy revealed deep ulcerations in the terminal ileum and cecum. IV steroids initially controlled her symptoms, but they recurred as she tapered below 30mg prednisone daily. You recognize that this patient has a high risk for progressive disease. Which of the following regimens would you recommend that gives her the best chance for remission?

1. Mesalamine 800mg TID
2. Azathioprine 2.5mg/kg po daily
3. Infliximab 5mg/kg at 0, 2, and 6 weeks
4. Infliximab 5mg/kg + azathioprine 2.5mg/kg
5. Increase her prednisone to 60mg daily, then taper more slowly

POST-TEST QUESTION 4
A 34 yo male recently diagnosed with moderate UC presents with continued diarrhea (8-10 BM/day), rectal bleeding (< 50% of BM) and left-sided abdominal cramps. He was initially started on oral mesalamine 4.8gm/day approximately 6 months ago. He was then hospitalized and started prednisone, infliximab + azathioprine 6 weeks later due to poor response. He is now asking you for help with his severe uncontrolled symptoms. Which of the following regimens would you recommend?

1. Initiate induction with adalimumab 160/80/40mg then 40mg every 2 wks
2. Increase oral prednisone from 40mg to 60mg daily
3. Discontinue infliximab and initiate induction dosing with vedolizumab 300mg at 0, 2, and 6 weeks followed by maintenance every 8 weeks
4. Maintain total dose of 5-ASA to 4.8gm/day and add rectally administered 5-ASA in the form of an enema or suppository
5. All of the above
An 18 year old male diagnosed with ulcerative colitis returns from college. He complains of increased symptoms since he left home. After you question him closely, you determine that he has only intermittently taken his medications. What important steps are most likely to enhance his compliance with medications?

1. You employ the OARS communication technique to motivate patient and refer him to CCFA website for disease specific info
2. You threaten to call his mother and report his non-compliance if he doesn’t turn around
3. You switch to a once daily 5-ASA and counsel him on its benefit in reducing number of flares
4. You use a one-time survey to document medical compliance
5. 1 and 3
6. 2 and 4
7. All of the above
8. None of the above

On a scale of 1 to 5, please rate how confident you would be in treating a patient with inflammatory bowel disease (IBD)?

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
POST-TEST QUESTION 7

Which of the statements below describes your treatment of patients with inflammatory bowel disease?

1. I do not treat inflammatory bowel disease, nor do I plan to this year.
2. I did not treat inflammatory bowel disease before this course, but as a result of attending this course I’m thinking of treating it now.
3. I do treat inflammatory bowel disease and this course helped me change my treatment methods.
4. I do treat inflammatory bowel disease and this course confirmed that I don’t need to change my treatment methods.