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Jointly provided by the Annenberg Center for Health Sciences at Eisenhower and Gastroenterology and Hepatology Advanced Practice Providers.
Updates in Crohn’s Disease

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Disclosures

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Disclosures

Bridget Howard, NP

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Objectives

• Discuss current treatment for Crohn’s disease
• Discuss treatment for complications of Crohn’s disease
• Discuss future therapies for Crohn’s disease

Q and A
Goals of Treatment

• Individualize therapy
• Change progression of disease
• Increase quality of life
• Decrease hospitalization and morbidity
• Avoid Steroids
AVOID Side Effects Of Steroids

- Emotional disturbance
- Enlarged sella turcica
- Moon facies
- Osteoporosis
- Cardiac hypertrophy (hypertension)
- Buffalo hump
- Obesity
- Adrenal tumor or hyperplasia
- Thin, wrinkled skin
- Abdominal striae
- Amenorrhea
- Muscle weakness
- Purpura
- Skin ulcers (poor wound healing)
Treat to Target – Individualize Therapy

Figure 1. Evolution of treatment goals in IBD.

Change course of disease
Deep remission
Mucosal healing
Steroid-free remission
Clinical remission
Improved symptoms

Treatment strategies must evolve as treatment goals evolve

Adapted from IOIBD
Low RISK Crohn’s – Treatment
Medical Therapy for Low Risk Crohn’s Disease

- Mesalamine?
- Steroids, budesonide, prednisone
- Reevaluate after above with inflammatory markers, or ileocolonoscopy after 3-6 months
Medical Therapy for Moderate to Severe Active Luminal Crohn’s Disease (High Risk)

- Oral and IV corticosteroids are effective for short-term induction of remission (flares) but do not consistently achieve mucosal healing.
- Biologic therapy is effective for induction and maintenance of remission and early use is recommended in patients with severe or complicated disease.
- Individualize old/current therapies with new therapies.
- Combo therapy with immunomodulatory medications and duo biologics.
Biologic Therapy for Crohn’s Disease

**Anti-TNF Therapy**
- Infliximab
- Adalimumab
- Certolizumab

**Anti-Adhesion Therapy**
- Natalizumab
- Vedolizumab

**Anti-IL12/23**
- Ustekinumab
Combination Therapy

**Duotherapy**
- Biologic combos
- Antibiotics and immune suppressants
- Diet plus medications

**With immunomodulator**
- AZA or MTX, or 6-MP
Pre-biologic Evaluation

- Tuberculosis screening prior to therapy
  - PPD vs Quantiferon – TB Gold assay
  - Chest X-Ray (especially if high risk)
  - Consider annual TB screening
- Hepatitis B screening
- Hepatitis C screening
- Arizona: baseline cocci serology
Risks of Anti-TNF’s

- Infection
  - Reactivation TB, HBV
  - Sepsis
  - OIs
- Lymphoma
- Demyelinating d/o (rare)
- Hepatotoxicity (rare)
- Drug-induced lupus (<1%)
Risks of Ustekinumab

- Increased risk of infections
- Lung inflammation
- Skin cancer
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) rare
- Allergic reactions
Risks of Vedolizumab

- Hepatotoxicity
- Headache
- Joint pain
- Fatigue
- Increased infections, primarily in gut
- Not PML
Which Drug to Choose? Shared Decision Making
Individualize Therapy With “Old Drugs”

- Route: IV vs injection
- Safety: Consider vedolizumab or ustekinumab
- Extraintestinal manifestations: Anti-TNF therapy
- Lymphoma: Avoid thiopurines
- Arthritis: Use methotrexate
- High Risk: Strongly consider combination therapy
Benefits
• Enhance effectiveness
• Outcomes better
• Save therapies
• Dose escalation/De-escalation
• Lower costs in proactive groups

Proactive/Reactive
• Both camps have points
SARS 2 Corona Virus and IBD

- COVIDIBD.ORG
- Interactive Map for cases
- US 837 (6 deaths) as of Sept 1, 2020
COVID Discussion

- Risk increases – Strong number of comorbidities
- Older age
- Use of systemic corticosteroids
- 43% exposed to Anti-TNFs (525 pts)
- Those on 5-ASA fared worse?
Crohn’s and + SARS 2

- Stop anti TNF, biologics, immunosuppression, until 14-20 days post initial symptoms
- Taper high-dose steroids
- Discussion on updates
Steps When Medication Not Working
Switch Therapy

• Loss of response?
• Confirm adherence
• Rule out infection
• Confirm inflammation
• Assess drug and antibody levels
## Can You Use the Same Medication Again?

**YES**
- Was disease too advanced when started and that was reason for lack of response?
- If inflammatory pathway reactivated

**NO**
- Due to anti-drug antibodies
- If disease progressed right through prior therapy
Remission, Now What?

my IBD journey
De-Escalate Plan

- Confirm deep remission for greater than 1 year
- Why is it reasonable?
- Deescalate dosing or one drug first
- Have a monitoring plan
- Have a plan for flare, rescue-prior therapy or new therapy
Fistulas

- Affect 40% of patients with Crohn’s
- Predictive or poor long-term outcomes
- Difficult to treat
- Surgery is option
- Stem cells potential better approach
- Dr. Faubion Study 10/12 Success-ongoing
Treatment of Fistulas

- Important to differentiate simple vs complex
- Simple perianal fistulas should be treated with Seton placement in combination with medical therapy
- Complex fistulas usually require surgery in combination with medical therapy
- High-output fistulas – Surgery usually
Medical Therapy for Simple Perianal Fistulizing Crohn’s Disease

• Perianal fistulas
  – Anti-TNF therapy (IFX best studied)
  – ? Certolizumab/vedolizumab/ustekinumab
  – Azathioprine and 6-MP
  – Tacrolimus
  – Ciprofloxacin and/or metronidazole

• Antibiotics and anti-TNF therapy increases efficacy

• Always exclude pyogenic complications prior to biologic therapy
Stem Cell for Fistula Disease

A

B

- Van Aasche Scale: P < 0.001
- Tract Length: P = 0.014
- Maximum Fistula Diameter: P = 0.307
Refractory disease may require
Strictures and Crohn’s
<table>
<thead>
<tr>
<th>Strictures in Crohn’s</th>
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<tbody>
<tr>
<td><strong>Small Bowel</strong></td>
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<tr>
<td>• % of patients</td>
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<tr>
<td>• Fixed strictures</td>
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<tr>
<td>• Medical therapy</td>
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<tr>
<td>• Bowel resection or stricturoplasty</td>
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<tr>
<td><strong>Colon</strong></td>
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<tr>
<td>• 10% of patients</td>
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Treat Strictures in Crohn’s Disease

- Balloon assisted enteroscopy 94.9% success
- Standard ileocolonoscopy 82.3% success
- Short Clinical success with balloon dilations and re-dilation in 38.8%
- Surgical Intervention may be necessary
- (Meta Analysis published in APT)
Indications for Surgery in CD

• Stricture and obstruction: most common indication
  – Common site: ileum
• Intraabdominal abscess and fistulæ—penetrating disease
• Perforation
• Failure of medical therapy
• GI bleeding
• Neoplasia or dysplasia
Post-Operative Prophylaxis of Crohn’s Disease

- Risks – cigarettes, multiple resections, penetrating disease, short duration prior to surgery
- All patients should stop smoking
- Azathioprine and 6-MP are more effective than mesalamine or placebo
- Anti-TNF therapy for high-risk patients
Post-Operative Prophylaxis of Crohn’s Disease

- Risks – cigarettes, multiple resections, penetrating disease, short duration prior to surgery
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Future Therapies

- **Anti-Adhesion**
  - AJM300 oral, interleukin

- **Anti-Chemotaxis Therapies**
  - RPC1063
  - Oral-ozanmod (MS)

- **JAK Inhibitors**
  - Filgotinib oral

- **Immune Cell Modulation**

- **Microbiome-Targeted and Antimicrobial Therapies**
Microbiota Manipulation

- Dietary therapies (exclusion diets)
- Antibiotics
- Probiotics/Prebiotics
- Microbiota transfers
- Bacterial-derived proteins
Is Diet Effective in Treatment?

Low FODMAP
- 4 studies 2016-2019
- Relief of functional symptoms
- No effect on fecal cal
- Improved quality of life

Data
- No foods shown to increase inflammation
- Exacerbate GI symptoms
- Gut Microbiome and intestinal barrier – IBD Risk
- Efficacy scarce – ET for Peds
Health Maintenance

- Inactivated Vaccines: Influenza, Pneumococcal
- Special Considerations, HPV, Zoster
- Cervical Dysplasia Screening
- Dermatology Exams
- Screen for nutritional deficiency
- Bone Dexa Scans
- Check list: Cornerstonehealth.org
Future of Individualized Management

- Smart apps and devices
- Ongoing monitoring
- Immune panels and ongoing search for inflammatory markers
- New dominant pathways identified to treat
- REMISSION!
Final Take-Aways

- Crohn’s disease is usually associated with progressive disease
- Classify patients into high- vs low-risk
- Combination therapy is more efficacious for induction of remission in high-risk patients
- The goal is mucosal healing and altering the natural history of the disease
- Therapeutic drug monitoring is important
- Decisions are complicated and must be individualized
- THANK YOU!!!
Q&A