Program Goals

- Review use of biologic therapy in Crohn’s disease and ulcerative colitis
- Help you understand risks and benefits of therapy
- Discuss importance of adherence to treatment
- Share resources to help you monitor your disease
Poll Question #1

Which best describes you?

A. I am a patient with Crohn’s disease
B. I am a patient with ulcerative colitis
C. I am a friend/family member of a patient with Crohn’s disease
D. I am a friend/family member of a patient with ulcerative colitis
E. Other

IBD Medicine Cabinet

- Over-the-Counter Medications
- Aminosalicylates
- Corticosteroids
- Immunomodulators
- Antibiotics
- Biologic therapies
Poll Question #2

Test your knowledge on Biologics

Which of the following statements is False?

A. Biologics are grown in living cells
B. Biologics target particular proteins, chemicals, or cells
C. Biologics are chemically made

What are Biologics?

• Many include proteins or antibodies which are part of the immune defense
• They are medicines made from living organisms
• Similar or identical to the actual biologic chemicals that our body makes
• Historically reserved for patients not responding to standard therapies, but increasingly used earlier in the course of treatment
Mechanism of Biologics

- How do they work?
  - Antibodies bind and help eliminate infections
  - Molecules bind to components of inflammatory process
- Block protein called tumor necrosis factor (TNF), made by white blood cells that can promote inflammation
- Block interaction between receptors on white blood cells with receptors on surface of intestinal lining

Overview of Biologics

- How are they different than other therapies?
  - Biologics are more complex
  - 1,000 times larger than conventional medicines
  - Mechanism of action is targeted to particular proteins, chemicals, or cells
  - Unlike corticosteroids, biologic agents act selectively
## Types of Biologics: Anti-TNF Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Indication</th>
<th>Most Effective For</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab (Humira®)</td>
<td>Taken as subcutaneous (under skin) injection&lt;br&gt;<strong>Indication:</strong> Crohn’s disease (adult and pediatric) and ulcerative colitis (adults)&lt;br&gt;<em>Most effective for</em> patients for whom conventional therapies fail</td>
<td></td>
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<tr>
<td>Certolizumab Pegol (Cimzia®)</td>
<td>Taken as subcutaneous injection&lt;br&gt;<strong>Indication:</strong> Crohn’s disease only (adults)&lt;br&gt;<em>Most effective for</em> maintaining clinical response; patients with inadequate response to other therapies</td>
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</tr>
<tr>
<td>Golimumab (Simponi®)</td>
<td>Taken as subcutaneous injection&lt;br&gt;<strong>Indication:</strong> Ulcerative colitis only (adults)&lt;br&gt;<em>Most effective for</em> patients whom conventional therapies fail; to induce and maintain clinical response, remission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infliximab (Remicade®)</td>
<td>Taken as intravenous (IV) infusion&lt;br&gt;<strong>Indication:</strong> Crohn’s disease and ulcerative colitis (adult and pediatric)&lt;br&gt;<em>Most effective for</em> maintaining remission; treating fistulizing Crohn’s</td>
<td></td>
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</tr>
</tbody>
</table>

### Common side effects include injection/infusion site reactions, risk of infections, psoriasis-like reaction
### Risks Associated with Anti-TNF Treatment

<table>
<thead>
<tr>
<th>Event</th>
<th>Estimated Frequency (annual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop therapy</td>
<td>10% (10/100)</td>
</tr>
<tr>
<td>Infusion or injection-site reactions</td>
<td>3%-21%</td>
</tr>
<tr>
<td>Drug-related lupus-like reaction</td>
<td>1% (1/100)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>3% (3/100)</td>
</tr>
<tr>
<td>Non Hodgkin’s Lymphoma (combination)</td>
<td>0.06% (6/10,000)</td>
</tr>
<tr>
<td>Multiple sclerosis, heart failure, serious liver injury</td>
<td>Case reports only</td>
</tr>
</tbody>
</table>

Siegel CA. Inflamm Bowel Dis. 2010;16(12):2168-2172.
Risk of Developing Non-Hodgkin’s Lymphoma

Patient with Crohn’s disease

Estimated annual risk = 2 per 10,000 treated patients

Risk of Developing Non-Hodgkin’s Lymphoma

Patient with Crohn’s disease receiving 6MP or Azathioprine

Estimated annual risk = 4 per 10,000 treated patients
Risk of Developing Non-Hodgkin’s Lymphoma

Patient with Crohn’s disease receiving combination anti-TNF + Immunomodulator Therapy

Estimated annual risk = 6 per 10,000 treated patients

Types of Biologics: Integrin Receptor Antagonists

| Natalizumab (Tysabri®) | - Taken: Intravenous (IV) infusion  
- Indication: Moderate-severe Crohn’s disease only (adults)  
- Most effective to Induce and maintain clinical response and remission |
|------------------------|-----------------------------------------------------------|
| Vedolizumab (Entyvio®) | - Taken: Intravenous (IV) medication  
- Indication: Moderate-severe Crohn’s disease and ulcerative colitis (adults)  
- Most effective for achieving corticosteroid free remission and  
  - UC: inducing and maintaining clinical response and remission;  
  - CD: achieving clinical response and remission |
Integrin Receptor Antagonists: Risks

<table>
<thead>
<tr>
<th>Biologic Medication</th>
<th>Pregnancy Recommendations</th>
<th>Breast-feeding Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natalizumab (Tysabri®)</td>
<td>Rare brain infection PML (blood test required prior to treatment) — screen for John Cunningham Virus</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Vedolizumab (Entyvio®)</td>
<td>Slightly increased risk of colds (nasopharyngitis)</td>
<td></td>
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</tbody>
</table>

Special Considerations

- **Pregnancy**
  - Studies show better prognosis if disease is inactive at time of conception
  - Biologic drug safety categories; biologics:

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<td>Low risk</td>
<td>Limited human data</td>
</tr>
<tr>
<td>Vedolizumab (Entyvio™)</td>
<td>No fetal harm observed; use only if benefits outweigh risk</td>
<td>Limited human data</td>
</tr>
<tr>
<td>Adalimumab (Humira®)</td>
<td>Low risk</td>
<td>Limited human data</td>
</tr>
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<td>Infliximab (Remicade®)</td>
<td>Low risk</td>
<td>Limited human data</td>
</tr>
<tr>
<td>Golimumab (Symponi®)</td>
<td>Low risk</td>
<td>No human data</td>
</tr>
<tr>
<td>Natalizumab (Tysabri®)</td>
<td>May cause fetal harm</td>
<td>Detected in human milk; effects unknown</td>
</tr>
</tbody>
</table>
Difficulty with Pediatric Treatments

- Limited data in pediatric IBD therapy
  - Treatment extrapolated from adult studies
  - Not “one size fits all”
- Concerns of drug toxicity
  - Infections
  - Cancer
  - Impact of lifetime therapy duration
- Outcomes for clinical trials needs to consider pediatric-specific outcomes

Therapeutic Monitoring

- Measure drug concentrations and antibody levels (currently infliximab and adalimumab, others to come)
- Helps to understand
  - If dosage is sufficient
  - If patient has developed antibodies to the drug
- Results can guide decisions for how to optimize medications that are working, or tell us when to move on
- Your doctor can “personalize” treatment by monitoring biologic therapy
### Option Grids

**http://www.optiongrid.co.uk**

<table>
<thead>
<tr>
<th>CD Decision Aid Sample Clips Benefits</th>
<th>CD Decision Aid Sample Clips Risks</th>
<th>CD Decision Aid Sample Clips Early Therapy</th>
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### CD Decision Aid Sample Clips

**Benefits**

- **Benefits**

**Risks**

- **Risks**

**Early Therapy**

- **Early Therapy**
Judging Response to Treatment

• How do I know if my treatment is working?

• If I am in remission, should I stop my treatment?
Judging Response to Treatment

- How do I know if my treatment is working?
- If I am in remission, should I stop my treatment?
- How much time should I allow before trying a new medication?

Adherence is Important!

Diagram showing factors affecting adherence:
- Missed appointments
- Barriers to care or medications
- Complexity of treatment
- Cost of medication, co-payment, or both
- Poor provider-patient relationship
- Patient’s lack of education about the disease
- Patient’s lack of belief in benefit of treatment
- Medication side effects
- Inadequate follow-up or discharge planning
- Treatment of asymptomatic disease
- Cognitive impairment
- Psychological problems, especially depression

Adherence
Biosimilars

Poll Question #3

Which of the following is True?

A. Generic biologic medications are currently available
B. Biosimilars are identical to biologics
C. Biosimilars are not generic biologics
**What are Biosimilars**

- Products that are “highly similar” to—but not exact copies of–biologic medicines
- As part of the Affordable Care Act (ACA), Food and Drug Administration (FDA) will review and approve biosimilar versions of FDA approved biologic medicines
- FDA issued guidance’s, but has not initiated formal rulemaking
- No US FDA approved biosimilars to date; expected approvals in the near future

Source: Patients for Biologics Safety and Access

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**More on Biosimilars**

- Are an effort to develop something like a generic for biologics
- Biosimilars are similar to a particular biologic, but they are not the same
- All biosimilars differ from biologics and from each other
- Biologics medications can not have generic versions
  - Active ingredients can only resemble at best
  - Ex. different fingerprints in identical twins

Source: Patients for Biologics Safety and Access
Things to Consider about Biosimilars

• Interchangeability
• Rigorous testing
• Naming
• Substitution/notification
• FDA Transparency

Poll Question #4

Which of these is your biggest concern about biologic therapy?

A. Risks and side effects of biologics
B. Insurance benefits and cost
C. Effectiveness of the treatment
D. Deciding which treatment to choose
E. Other
Talk to Your Healthcare Team

• Which treatment options may be right for me?
• What are the benefits and risks/side effects of these options?
• How long might it take before I see an improvement in my symptoms?
• What can I do to ensure I’m getting the most from my medication?
• What else can I do, in addition to taking my medication, to effectively manage my IBD?


Key Points on Biologic Therapy

• Biologic drugs made from living organisms and resemble chemicals in the body; different from conventional therapy
• Important to consider risks and benefits
• Response to biologics may differ for each person; adhering to treatment can improve outcomes and maintain remission
• Biosimilars would resemble biologics, but are not generic versions
• Communicate with your healthcare team

References

• CCFA website
  – http://www.ccfa.org/resources/biologic-therapies.html
• Rubin, DT. Treatment Options in IBD webcast: www.ccfa.org/resources/IBD-treatments-webcast.html
• Siegel CA. Lost in translation: helping patients understand the risks of inflammatory bowel disease therapy. Inflamm Bowel Dis. 2010;16(12):2168-2172.
• Food and Drug Administration website:
  http://www.ccfa.org/resources/biologic-therapies.html
• Irwin M. and Suzanne R. Rosenthal IBD Resource Center (IBD Help Center): 888.694.8872 or info@ccfa.org

QUESTIONS?
AGA Resources

- Patient guide to GI procedures: http://www.gastro.org/patient-center/procedures
- Patient guide to diets and medications: http://www.gastro.org/patient-center/diet-medications

CCFA Resources

- Irwin M. and Suzanne R. Rosenthal IBD Help Center
  M-F, 9:00 AM-5:00 PM ET
  - Phone: 1-888-694-8872
  - Email: info@ccfa.org
- Educational webcasts: www.ccfa.org/resources/webcasts.html
- Connect with other patients
  - CCFA Community website: www.ccfacommunity.org
  - Support groups and Power of Two (peer mentors): www.ccfa.org/chapters
- GI Buddy: online tracking tool and mobile app www.ccfa.org/gibuddy
- Local educational events, visit: www.ccfa.org
CCFA Partners

- Registry of patient-reported outcomes
- Available for pediatric and adult patients

www.ccfapartners.org

Get Involved!

Team Challenge

www.ccteamchallenge.org

Take Steps

www.cctakesteps.org