Cancer Risk with IBD Therapies—How to Discuss with your Patients?

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Learning Objectives

1. Identify strategies to begin conversation with patients about IBD and IBD therapy
2. Understand risk profile of IBD therapy with regards to risk for cancer
3. Identify strategies to better communicate risk for cancer with various IBD therapies
## Faculty Disclosure

<table>
<thead>
<tr>
<th>Commercial Interest</th>
<th>Nature of Relevant Financial Relationship (Include all those that apply)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>What was received</td>
</tr>
<tr>
<td>• AbbVie</td>
<td>• Honoraria</td>
</tr>
<tr>
<td>• Gilead</td>
<td>• Honoraria</td>
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</tbody>
</table>
Where to Begin the Conversation?

Defining Disease Extent and Severity

Establishing that IBD is Chronic Illness

Setting Short Term and Long-Term Goals

Establishing remission as treatment goal
Where Do Patients Get Information?

- Negative feelings with biologics (54.6%)
- Decision making about biologics use (36.4%)
- Positive experiences with biologics (37.2%)
- Information seeking from peers (27.7%)
- Cost (8.4%)

Martinez et al. Inflamm Bowel Dis, 2017 (7): 1057-1064
Acknowledging Patient’s Concerns

PATIENT CONCERNS
- Employment, cost of care
- Incontinence and embarrassment
- Risks of treatment
- Being a burden
- Feeling helpless
- Social and sexual performance

PATIENT NEEDS
- Rapid to access to care
- Understand the importance of adherence
- Support for counseling/education
- Continuity of care/coordination of services
- Collaborative relationships

Hussain Ainflamm Bowel Dis 2004 10 (4): 444-450
Norton BA Patient Prefer Adherence 2012; 6: 509-520
Mitchell R et al J Crohn’s Colitis 2009; 3 (1) 1-3
Motivational Interviewing in IBD

OVERALL SATISFACTION WITH CARE

PERCEIVED EMPATHY

% of patients

BEFORE

AFTER

Mocciaro F Dig Liver Dis 2014
A Balanced Discussion

RISKS
- Side effects of therapy (i.e., injection/infusion reactions)
- Association of therapy with some cancers
- Inconvenience of long-term therapies on lifestyles

BENEFITS
- Improvement of quality of life
- Reduction of risk for surgery/hospitalizations
- Reduction in risk for inflammation-related cancers
- Avoid long-term use of steroids
Communicating Techniques

- Use Figures & Tables to Illustrate Risk
- Use absolute risk opposed to relative risk
- Avoid small percentages (0.06%), use 6 per 10,000 instead
- Describe both gains and loses to diminish framing
- Avoid vague descriptive words (ie, rare)

Siegel CA, Inflamm Bowel Dis 2010; 16 (12): 2168-2172
Natural History of IBD

**CROHN’S DISEASE**

- At 10-year, 53% develop stricturing/penetrating disease¹
- Factors predictive of severe disease course—age <40, perianal disease, small bowel disease, initial use of corticosteroids¹, ²
- Post-operative Rutgeert’s i2, i3, i4 correlate with 3-year clinical recurrence rates of 15, 40, 90% respectively³
- In remission for 1 year have 80% chance of staying in remission in subsequent years⁴

**ULCERATIVE COLITIS**

- Approximate 20-30% with UC will require colectomy for acute complications or medically refractory disease ⁵
- Early mucosal healing (ACT-1 and ACT-2)→ lower risk of colectomy⁶
- Extension of disease seen in 20% within 5 years⁷
- Mortality highest in first year of diagnosis (HR 2.4 95% Ci 2.3-2.6)⁸

References:
2. Cosnes J. Gut 2012; 61 (8): 1140
4. Lichtenstein GR, Am J Gastrol 2009; 102 (2); 456
5. Hoie O Am J Gastrol 2007; 102 (8) 1692
6. Colombel JF Gastroenterology 2011; 141 (3):1194
# Cancer Risk of Chronic Inflammation

<table>
<thead>
<tr>
<th>CANCER TYPE</th>
<th>STANDARDIZED INCIDENCE RATIO</th>
</tr>
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<tbody>
<tr>
<td>Colorectal Cancer</td>
<td>5.7 (95% CI 4.6-7.0)</td>
</tr>
<tr>
<td>Small bowel adenocarcinoma</td>
<td>27.1 (95% CI 14.9-49.2)</td>
</tr>
<tr>
<td>Intestinal Lymphoma</td>
<td>17.51 (95% CI 6.43-38.11)</td>
</tr>
</tbody>
</table>

1. Eaden JA Gut 200148: 526-535  
Cancer Related to Immunosuppression

- Direct alterations of DNA
- Activation of oncoproteins
- Reduction in physiologic immunosurveillance of malignant cells
- Impaired immune control of oncologic viruses
- TNF-alpha has antitumor effect by initiating cellular apoptosis of malignant cells

Zitvogel Nat Rev Immunol 2006; 6: 715-727
# Solid Tumor Risk Related to Thiopurines Therapy in IBD

<table>
<thead>
<tr>
<th>STUDY</th>
<th>TYPE OF CANCER</th>
<th>NO. OF PATIENTS</th>
<th>STATISTICALLY SIGNIFICANT?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armstrong 2010 (Am J Gastroenterol)</td>
<td>Breast, lung, biliary, pancreatic, lung, gastric</td>
<td>15471</td>
<td>NO</td>
</tr>
<tr>
<td>Fraser 2002 (Alimen Pharm Ther)</td>
<td>Breast, bronchial, renal</td>
<td>2204</td>
<td>NO</td>
</tr>
<tr>
<td>Connell 1994 (Lancet)</td>
<td>Gastric, lung, breast, cervical</td>
<td>755</td>
<td>NO</td>
</tr>
<tr>
<td>Bourrier 2016 (Alimen Pharm Ther)</td>
<td>Urinary tract cancer</td>
<td>19486</td>
<td>YES</td>
</tr>
</tbody>
</table>

**On Thiopurine: SIR 3.40**

H/O Thiopurine: 0.64

Non-exposed: 1.17
Skin Cancer Risk Related to Thiopurines in IBD

Year Incidence Rate per 1,000 patient-years

- < 50 YEARS
  - CONTINUING: 0.66
  - DISCONTINUED: 0.38
  - NEVER RECEIVED: 0

- 50-65 YEARS
  - CONTINUING: 2.59
  - DISCONTINUED: 1.96
  - NEVER RECEIVED: 0.60

- >65 YEARS
  - CONTINUING: 4.04
  - DISCONTINUED: 5.70
  - NEVER RECEIVED: 0.84

GET ANNUAL SKIN EXAMS!

Peyrin-Biroulet L Gastroenterology 2011; 141: 1621-1628
Lymphoproliferative Disorders Related to Thiopurines in IBD

OVERALL, ESTIMATED RATE TO BE 9 CASES in 10,000 PATIENT YEARS

Peyrin-Biroulet L Gastroenterology 2011; 141: 1621-1628
Solid Tumor Risk Related to Anti-TNF (Biologics) Therapy

Nyboe Andersen N JAMA 2014; 311: 2406-2413
Melanoma Skin Cancer Risk in Crohn’s Patients on Anti-TNF

Annual Melanoma Incidence per 100,000

CD
IRR 1.45 (95% 1.13-1.85)

UC
IRR 1.13 (95% 0.89-1.42)

IBD
IRR 1.29 (95% 1.09-1.53)

Non-IBD

CD or UC

Long MD, Gastroenterology, 2012; 143: 390-399
## Hematologic Malignancy Related to Anti-TNF in IBD

<table>
<thead>
<tr>
<th></th>
<th>NHL Rate per 10,000</th>
<th>SIR</th>
<th>95% CI</th>
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<tr>
<td>SEER all ages</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM Alone</td>
<td>3.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-TNF + IM</td>
<td>6.1</td>
<td>3.23</td>
<td>1.5-6.9</td>
</tr>
<tr>
<td>Anti-TNF + IM vs IM</td>
<td>6.1</td>
<td>1.7</td>
<td>0.5-7.1</td>
</tr>
</tbody>
</table>

Siegel C Clin Gastroenterol Hepatol 2009; 7(8): 874-881
What About Patients with History of Cancer?
No Risk for Recurrent Cancer with Thiopurines and Anti-TNF

Retrospective from New York Crohn’s and Collitis Organization
Comprised of 8 academic medical centers
Analysis of 333 IBD Patients
Follow-up: 5 years

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<tr>
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<th>HAZARD RATIO</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Anti-TNF alone</td>
<td>0.32</td>
<td>0.09-1.09</td>
</tr>
<tr>
<td>Anti-TNF +IM</td>
<td>0.64</td>
<td>0.26-1.59</td>
</tr>
<tr>
<td>IM Alone</td>
<td>1.08</td>
<td>0.54-2.15</td>
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Axelrad J Clin Gastroenterol Hepatol 2016; 14: 58-64
## Summary of Cancer Risks of Therapy

<table>
<thead>
<tr>
<th>IM</th>
<th>Anti-TNF</th>
<th>Anti-TNF with IM</th>
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| • Non-Hodgkin’s Lymphoma  
• Non-melanoma skin cancer  
• Urinary tract cancers | • Melanoma | • Non-Hodgkin’s lymphoma  
• Hepatosplenic T-cell lymphoma |
Conclusion

- Establish remission as treatment goal

- Discuss the risk and benefits of IBD therapy in setting of natural history of untreated/under treated disease

- IBD is a chronic illness and requires ongoing monitoring of disease activity and side effects of therapy (including cancer risks)
Thank You!