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

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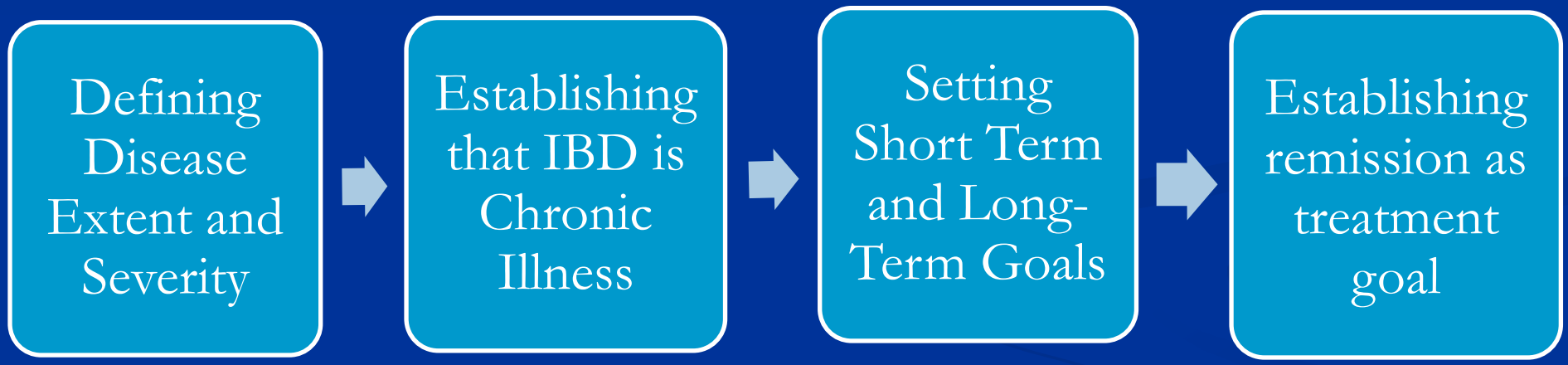
Learning Objectives

- Identify strategies to begin conversation with patients about IBD and IBD therapy
- Understand risk profile of IBD therapy with regards to risk for cancer
- Identify strategies to better communicate risk for cancer with various IBD therapies

Faculty Disclosure

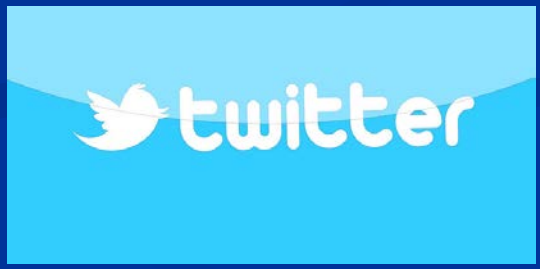
Commercial Interest	Nature of Relevant Financial Relationship (Include all those that apply)	
	What was received	**For what role**
• AbbVie	• Honoraria	• Speaking, Advisory Board
• Gilead	• Honoraria	• Speaking, Advisory Board

Where to Begin the Conversation?



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

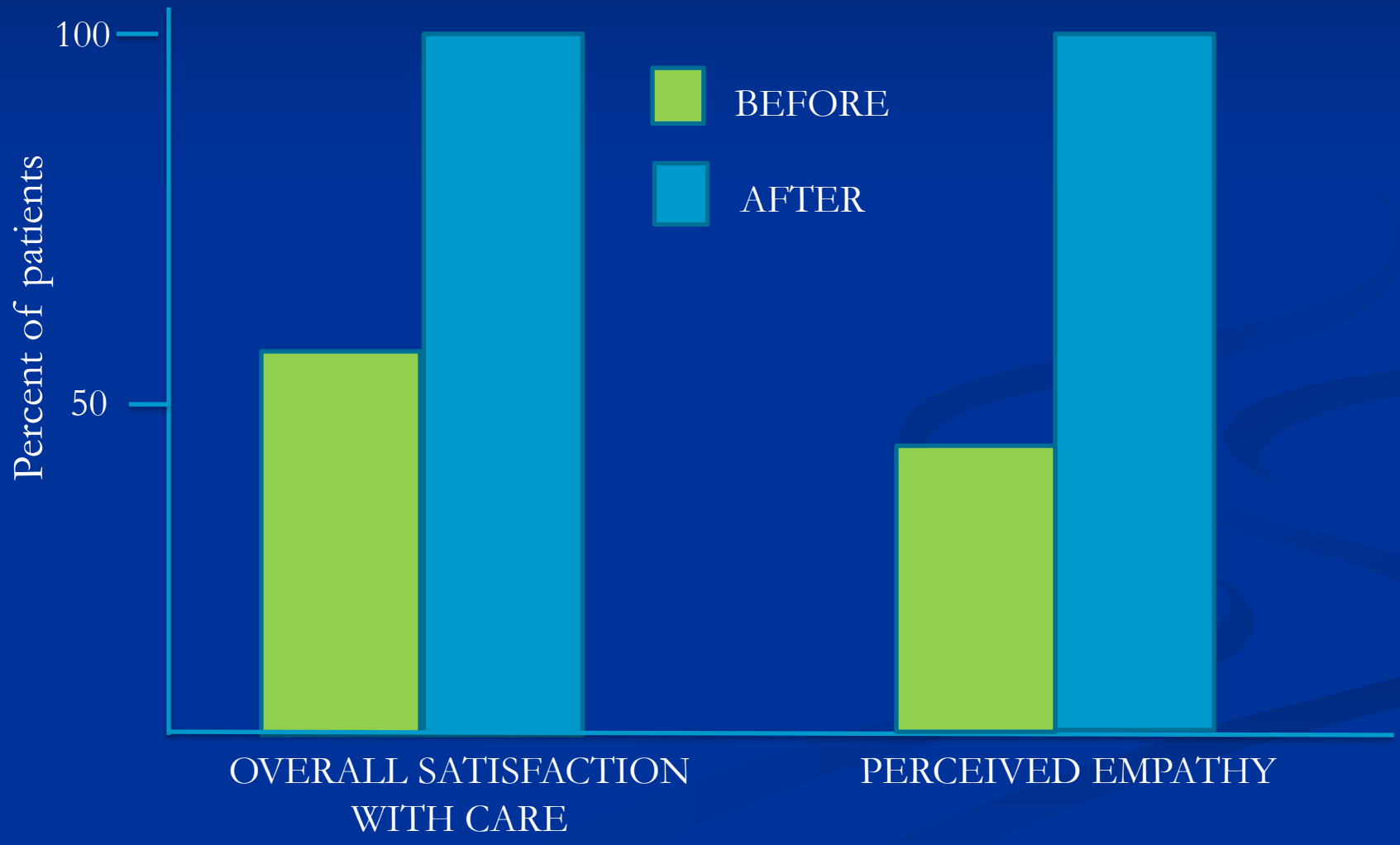
- Employment, cost of care
- Incontinence and embarrassment
- Risks of treatment
- Being a burden
- Feeling helpless
- Social and sexual performance

PATIENT NEEDS

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

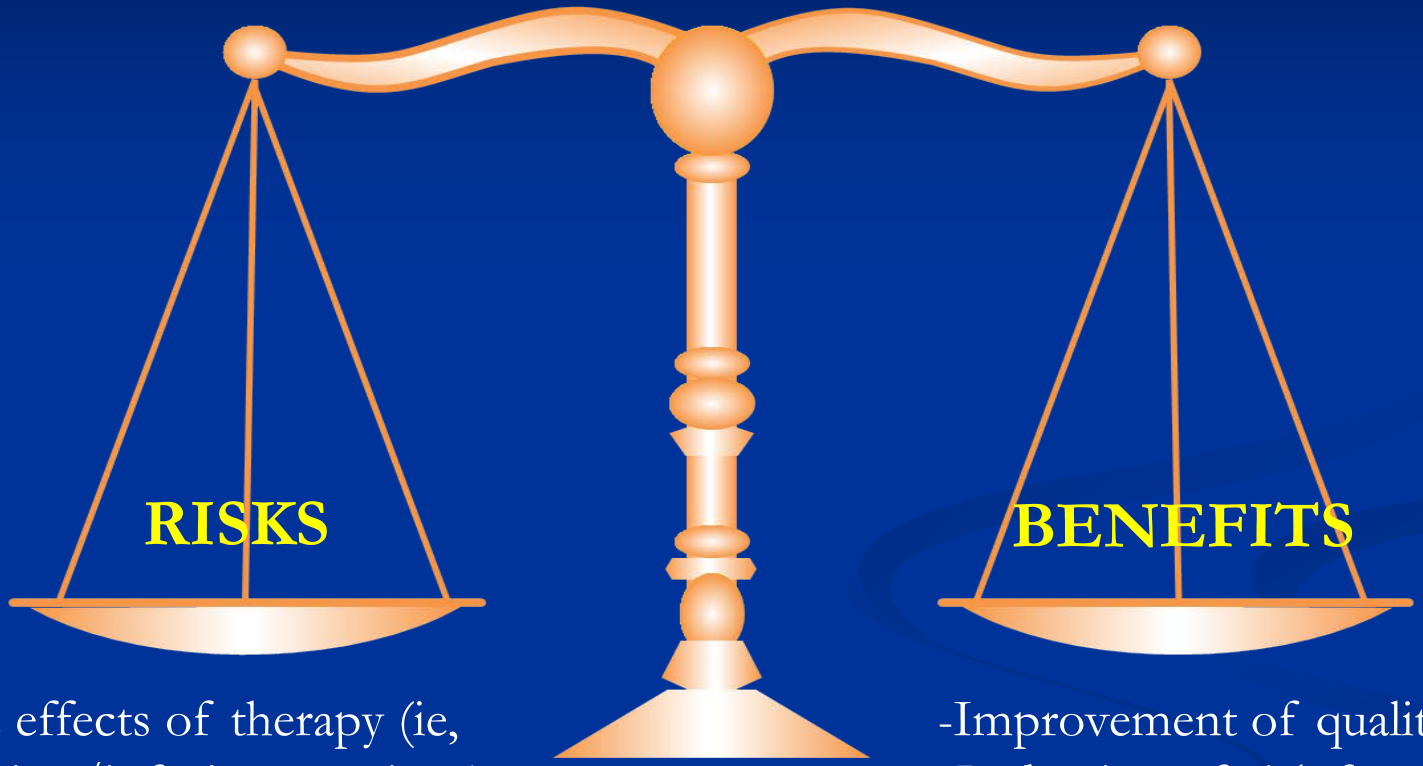
Hussain Ainflamm Bowel Dis 2004 10 (4): 444-450
Norton BA Patient Prefer Adherence 2012; 6: 509-520
Mitchell R et al J Crohn's Colitis 2009; 3 (1) 1-3

Motivational Interviewing in IBD



Mocciaro F Dig Liver Dis 2014

A Balanced Discussion



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

-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 10,0000 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 disease[1]
- Factors predictive of severe disease course—age <40, perianal disease, small bowel disease, initial use of corticosteroids[1, 2]
- Post-operative Rutgeert's i2, i3, i4 correlate with 3-year clinical recurrence rates of 15, 40, 90% respectively[3]
- In remission for 1 year have 80% chance of staying in remission in subsequent years[4]

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 colectomy[6]
- Extension of disease seen in 20% within 5 years[7]
- Mortality highest in first year of diagnosis (HR 2.4 95% Ci 2.3-2.6) [8]

1. Solberg IC Clin Gastro Hepatol 2007; 5 (12):1430
2. Cosnes J. Gut 2012; 61 (8): 1140
3. Rutgeert's Gastro 1990; 99; 956.
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
7. Gower-Rousseau. Am J Gastrol 2009; 104(8): 2080
8. Jess T. Clin Gastroenterol Hepatol 2013; 11(1):43

Cancer Risk of Chronic Inflammation

CANCER TYPE	STANDARDIZED INCIDENCE RATIO
Colorectal Cancer[1]	**5.7** (95% CI 4.6-7.0)
Small bowel adenocarcinoma[2]	**27.1** (95% CI 14.9-49.2)
Intestinal Lymphoma[3]	**17.51** (95% CI 6.43-38.11)

1. Eaden JA Gut 200148: 526-535
2. Jess T Am J Gastroenterol 2005; 100: 2724-2729
3. Sokol H. Inflamm Bowel Dis 2012; 18: 2063-2071

DIRECT ALTERATIONS OF DNA

ACTIVATION OF ONCOGENES

REDUCTION IN PHYSIOLOGIC IMMUNOSURVEILLANCE OF MALGNANT CELLS

Cancer Related to Immunosupression

IMPAIRED IMMUNE CONTROL OF ONCOLOGIC VIRUSES

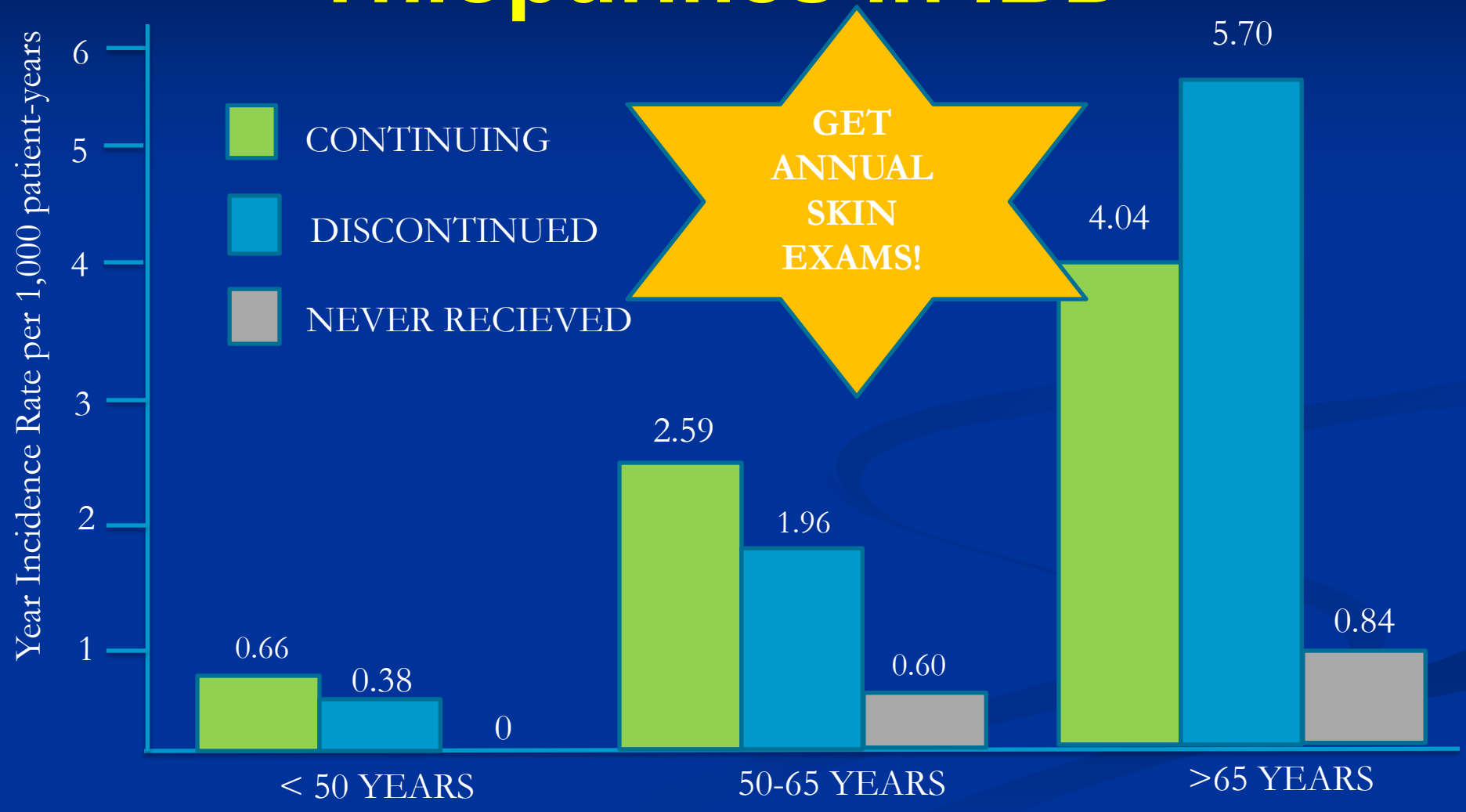
TNF-alpha HAS ANTITUMOR EFFECT BY INITIATING CELLULAR APOPTOSIS OF MALIGNANT CELLS

Zitvogel Nat Rev Immunol 2006; 6: 715-727
Balkwill F. Nat Rev Cancer 2009; 9: 361-371

Solid Tumor Risk Related to Thiopurines Therapy in IBD

STUDY	TYPE OF CANCER	NO. OF PATIENTS	STATISTICALLY SIGNIFICANT?
Armstrong 2010 (Am J Gastroenterol)	Breast, lung, biliary, pancreatic, lung, gastric	15471	NO
Fraser 2002 (Alimen Pharm Ther)	Breast, bronchial, renal	2204	NO
Connell 1994 (Lancet)	Gastric, lung, breast, cervical	755	NO
Bourrier 2016 (Alimen Pharm Ther)	Urinary tract cancer	19486	**YES** **On Thiopurine: SIR 3.40**** H/O Thiopurine: 0.64 Non-exposed: 1.17

Skin Cancer Risk Related to Thiopurines in IBD



Peyrin-Biroulet L Gastroenterology 2011; 141: 1621-1628

Lymphoproliferative Disorders Related to Thiopurines in IBD

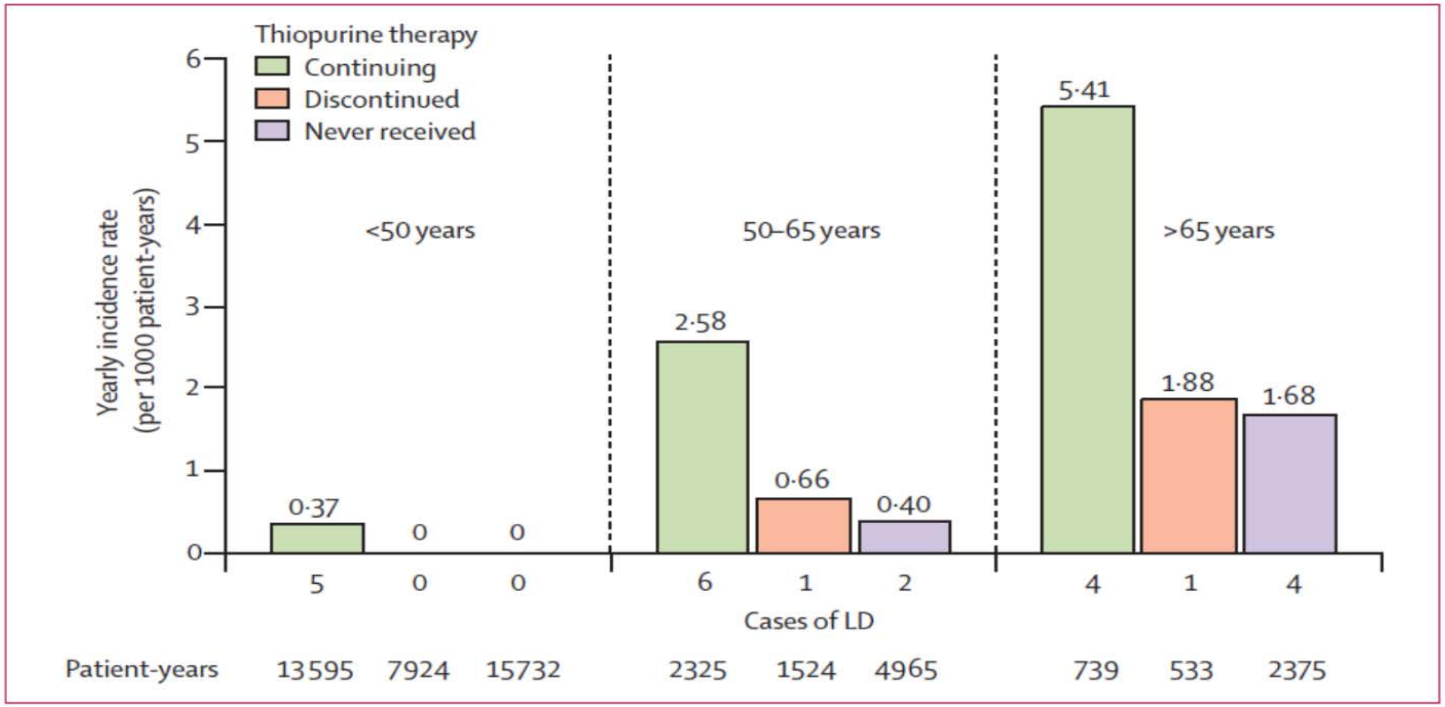
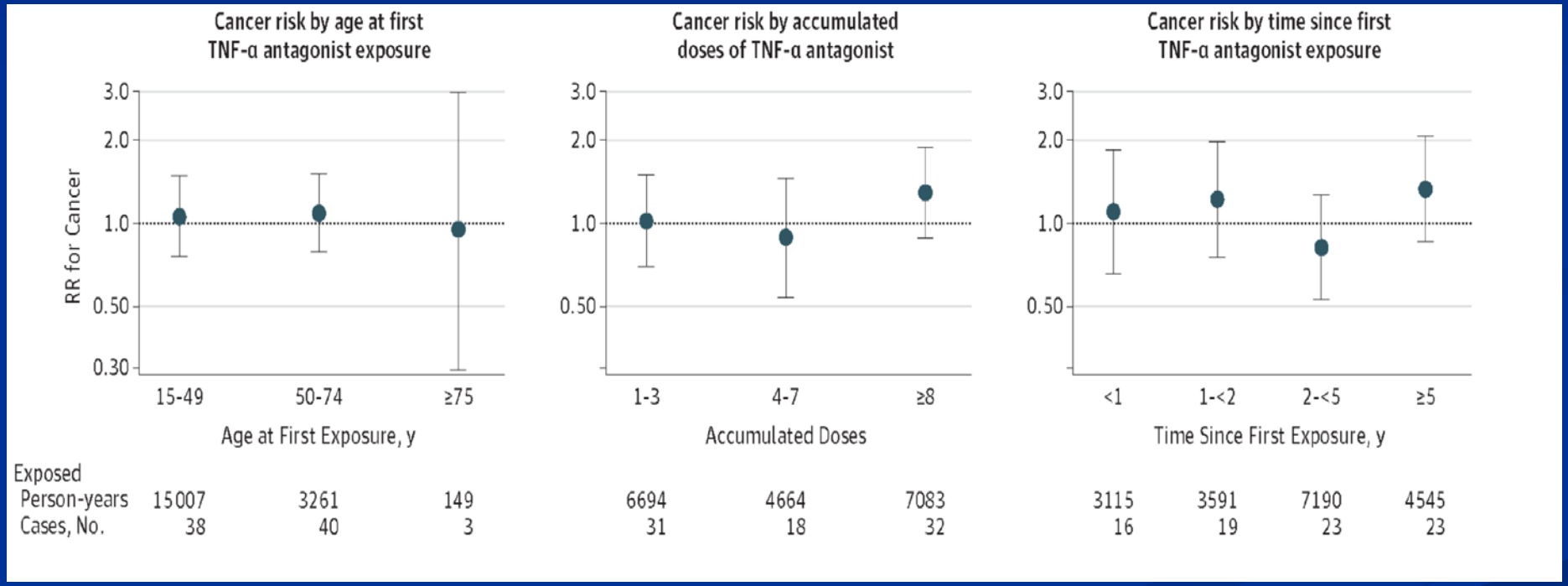


Figure: Incidence rates of lymphoproliferative disorders according to thiopurine exposure grouped by age at entry in the cohort
LD=lymphoproliferative disorder.

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

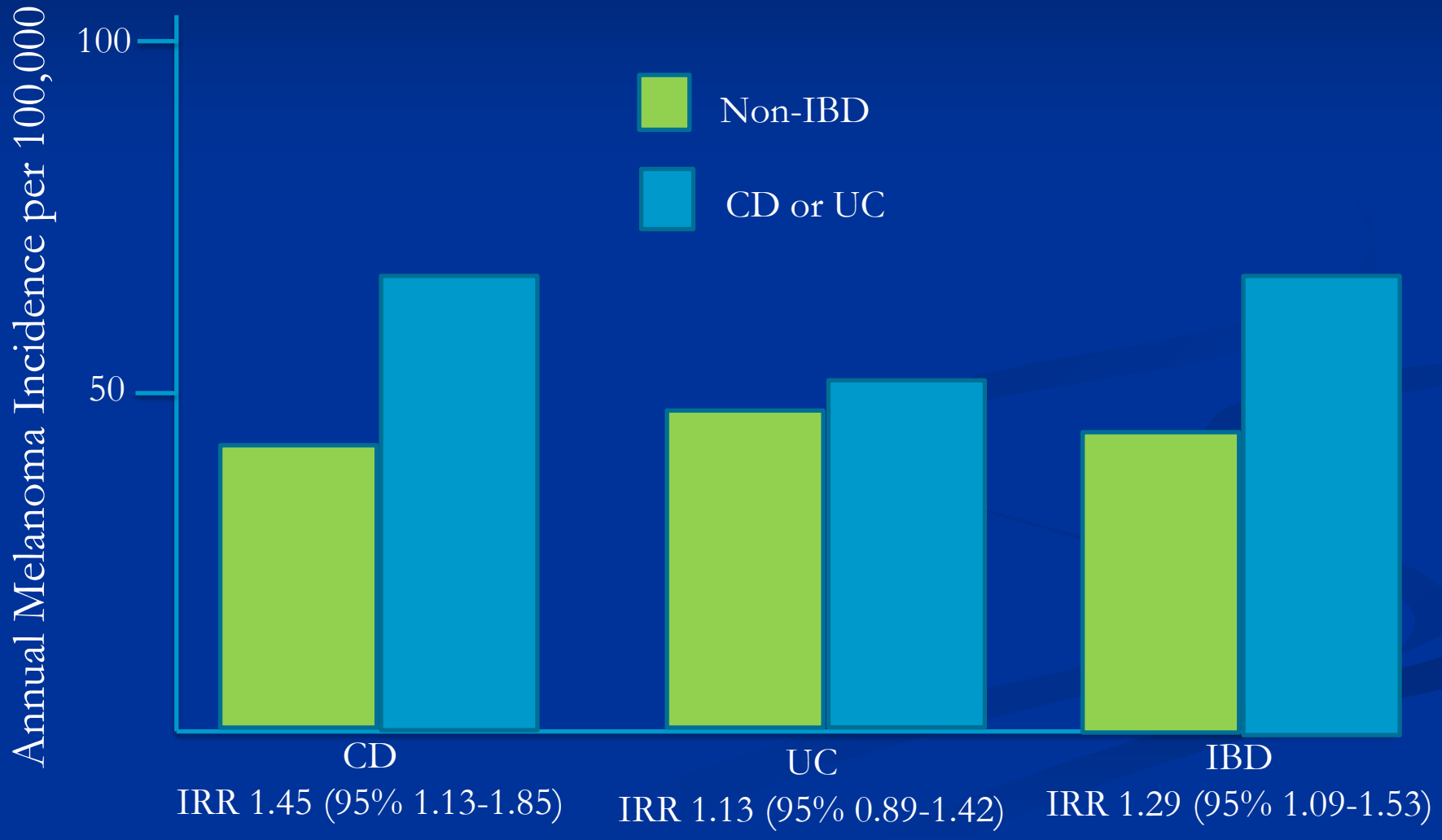
Peyrin-Biroulet L Gastroenterology 2011; 141: 1621-1628

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



Long MD, Gastroenterology, 2012; 143: 390-399

Hematologic Malignancy Related to Anti-TNF in IBD

	NHL Rate per 10,000	SIR	95% CI
SEER all ages	1.9		
IM Alone	3.6		
Anti-TNF +IM	6.1	3.23	1.5-6.9
Anti-TNF + IM vs IM	6.1	1.7	0.5-7.1

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

	HAZARD RATIO	95% CI
Anti-TNF alone	0.32	0.09-1.09
Anti-TNF +IM	0.64	0.26-1.59
IM Alone	1.08	0.54-2.15

Axelrad J Clin Gastroenterol Hepatol 2016; 14: 58-64

Summary of Cancer Risks of Therapy

IM	Anti-TNF	Anti-TNF with IM
• 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!