Evaluation and treatment of Ulcerative Colitis in a patient with PSC

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Disclaimers

- Research support: BMS, Eli Lilly, AbbVie, Sanofi, Teva, Ipsen, Madrigal, Exact Sciences, Intercept, Janssen, Pfizer, Abivax, Cymabay, Takeda, Prometheus Biosciences, Chemomab, Inventiva, NST, Corcept, Astra Zeneca, Roche Genentech
- Advisory Board: Exact Sciences, Cymabay, AbbVie, BMS, Madrigal
- Speaker: Eli Lilly, AbbVie, BMS, Janssen, Takeda, Pfizer

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Objective

. Patient journey

. Association between PSC and IBD

. Special characteristics of IBD patients with PSC

. Overview of UC management

. Special considerations for patients with PSC

. Special consideration for advanced liver disease

. Cancer risk

Patient Journey

- Mark is a 26 year old male presented to PCP due to fatigue and lack of appetite. Did also describe intermittent pruritus
- On routine labs was noted to have alk phos of 240 and T. bili of 1.6
- Referred to hepatologist and was found to have classic changes of PSC on MRCP
- Originally did not volunteer GI sxs but when pressed him he did acknowledge that he has been experiencing intermittent bouts of diarrhea and abdominal cramping

Patient Journey

- CRP normal
- Fecal calprotectin 520
- Colonoscopy shows mild to moderate diffuse pancolitis with erythema, congestion, erosions, friability
- Inflammation slightly more severe in Rt colon and very mild to absent in the rectum

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PSC and IBD

- Up to 85% of patients with PSC have underlying IBD
- Of these about 80% have UC, 15% CD, and 5% indeterminate colitis
- PSC can be present before or after IBD
- IBD is often mild on initial presentation and can sometimes be only obvious on biopsies- meaning random biopsies are required
- Most typical phenotype is pancolitis with worse inflammation in Rt colon and relative rectal sparing

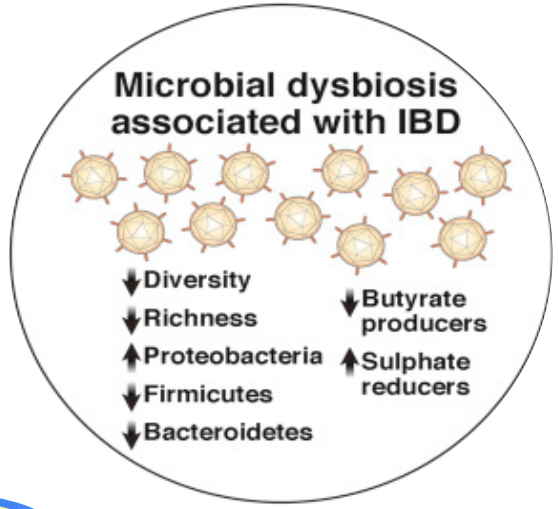
PSC and IBD

- PSC patients have increased risk of pouchitis after colectomy and IAPA
- IBD has even been described as developing AFTER liver transplantation in patients with PSC
- Increased risk of colon cancer (Odds ratio 4.79 in large metaanalysis)

Inflammatory Bowel Disease: Pathogenesis

Genetics
GWAS
> 240 Loci

Microbiome



Genetic susceptibility

IBD

Environmental triggers

Intestinal Barrier/Immune response

Environmental Factors
- Smoking
- Diet
- Medications

Somineni HK et al. CGH. 2019

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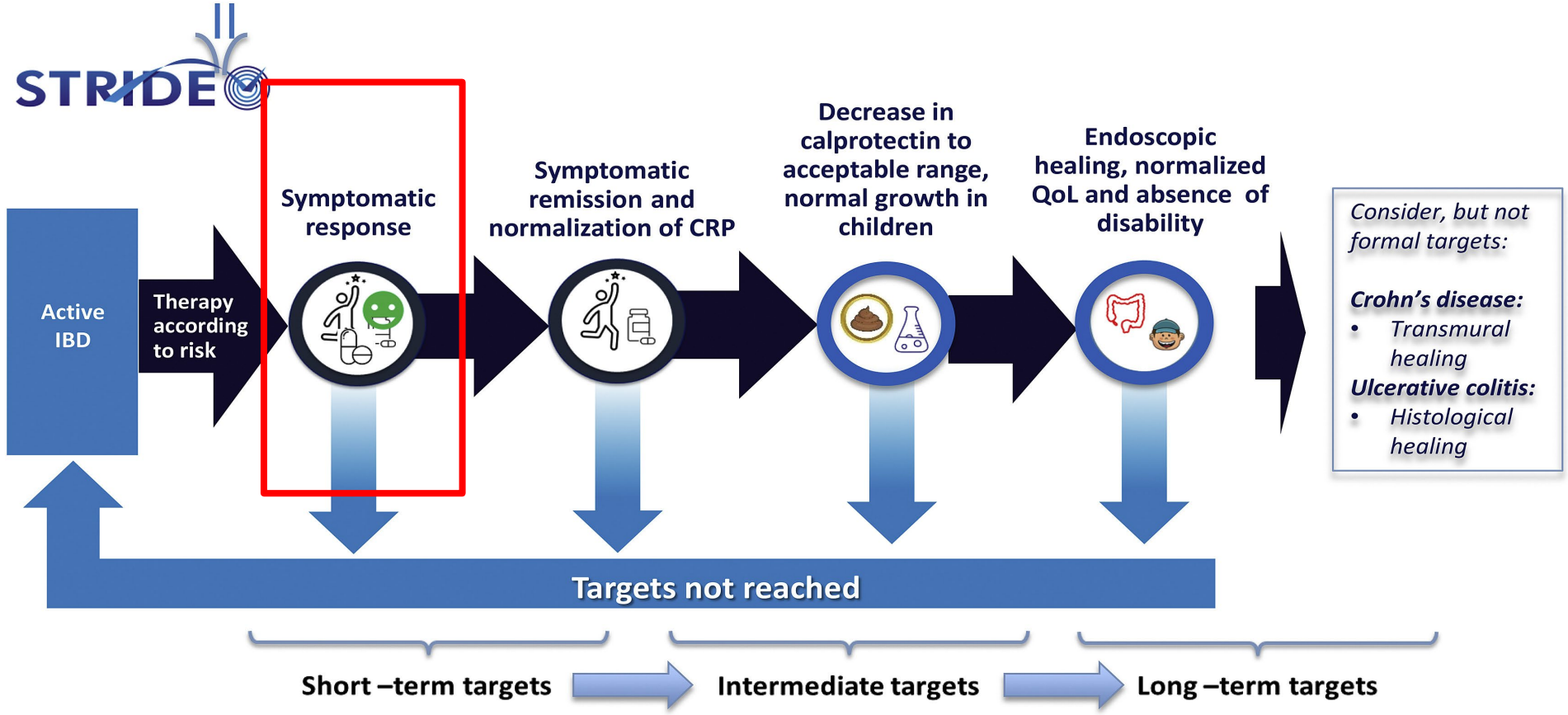
Defining Disease Activity – ACG Definition

	Remission	Mild	Moderate-Severe	Fulminant
Stools (#/day)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
Fecal calprotectin (µg/g)	<150-200	>150-200	>150-200	>150-200
Endoscopy (Mayo subscore)	0-1	1	2-3	3
UCEIS	0-1	2-4	5-8	7-8

Rubin DT, et al. Am J Gastroenterol. 2019 Mar;114(3):384-413.

STRIDE-II: An Update on Selecting Therapeutic Targets in IBD (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD)



Turner D, et al. Gastroenterology 2021;160:1570-1583

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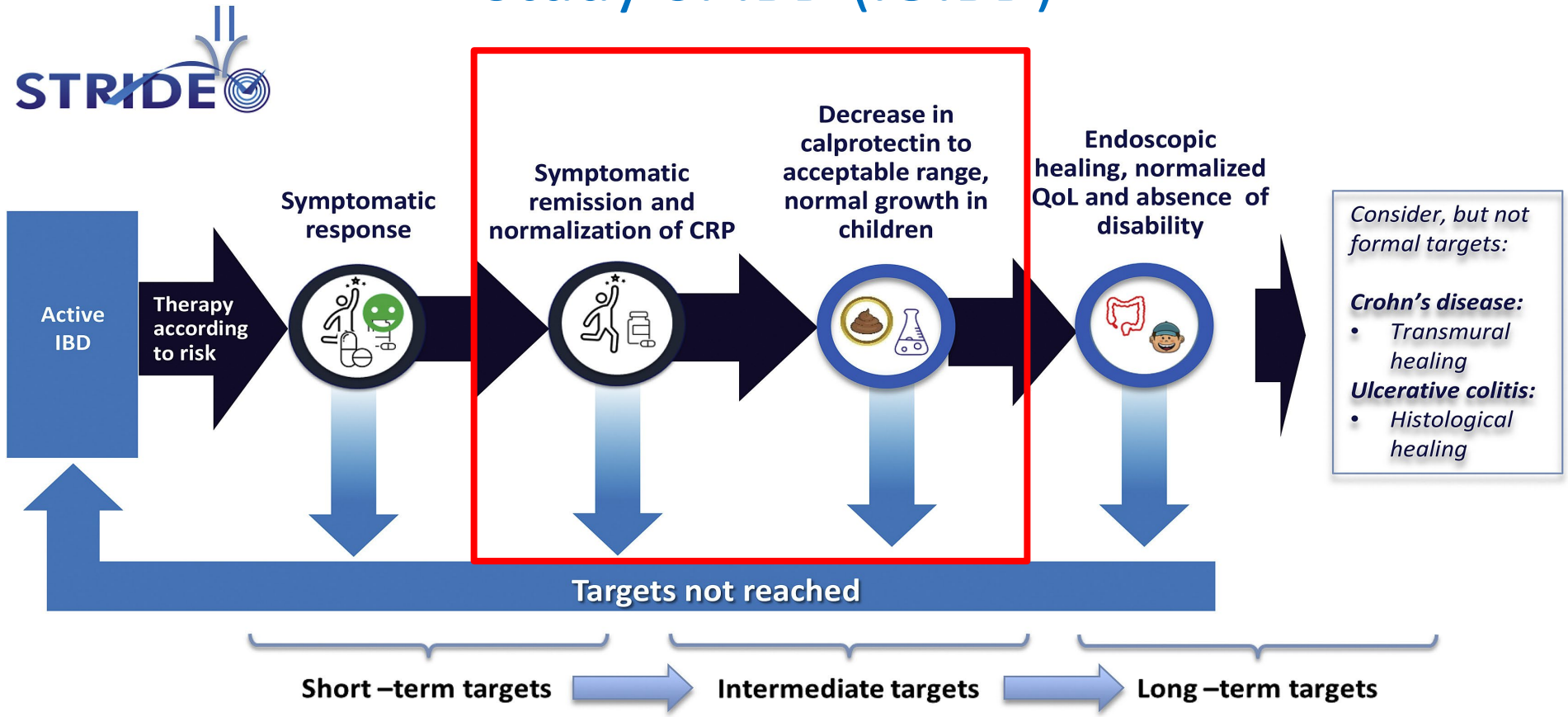

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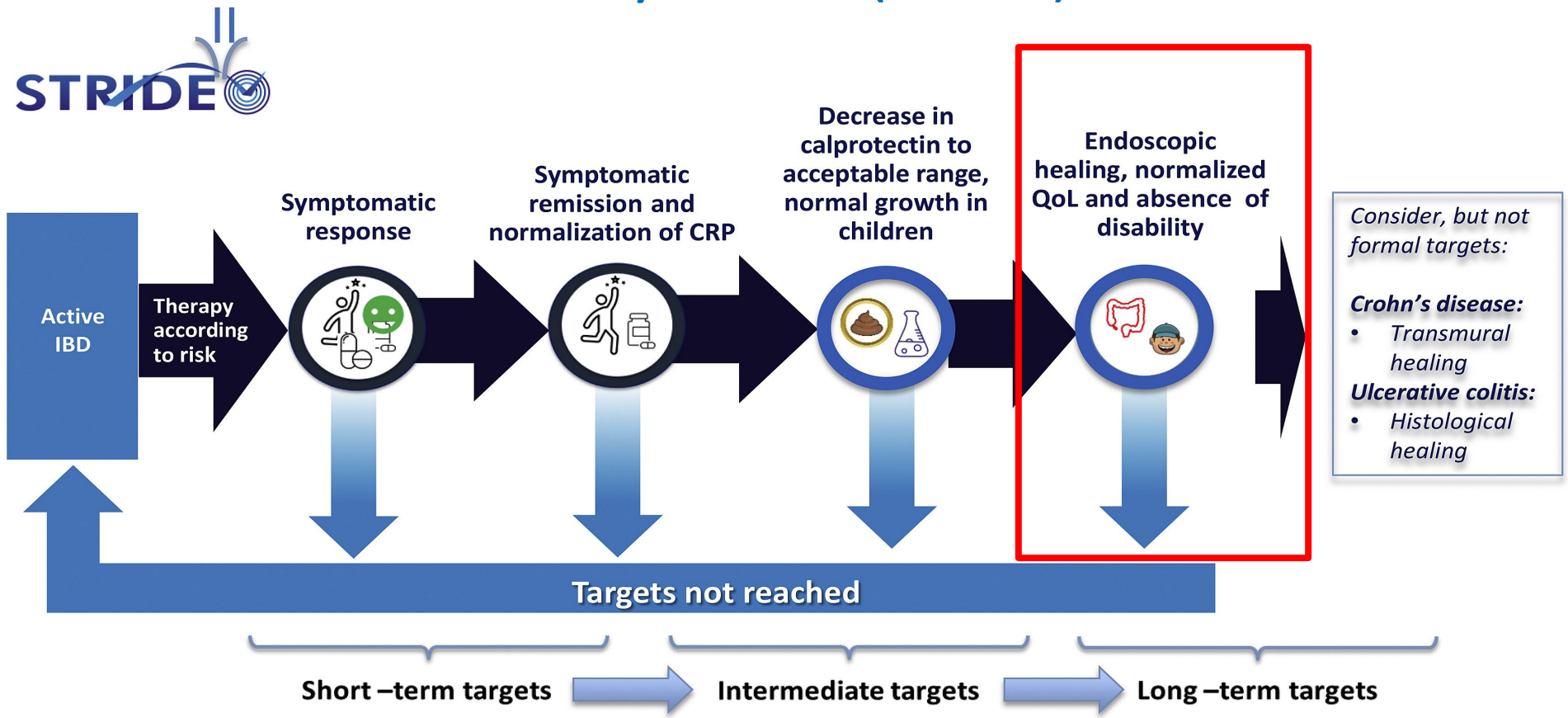

Turner D, et al. Gastroenterology 2021;160:1570-1583

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Mild-Moderate UC

Induction:

- Mild proctitis→ **rectal 5-ASA** recommended (1 g/day)[1,2,3,4,5]
- Left-sided mild UC→ **rectal 5-ASA** (≥1 g/day) in combination with **oral 5-ASA** (≥ 2.0 g/day)[1,2,3,4,5,6]
- Mild extensive UC→ **oral 5-ASA** (≥ 2.0 g daily)[1,5]
- UC failing to respond to 5-ASA therapy→ **oral systemic corticosteroids** including budesonide MMX, early use of **biologics**[6]

Maintenance:

- Mildly active proctitis→ **rectal 5-ASA** (1 g daily)[1,2,7]
- Mildly active left-sided or extensive UC→ **oral 5-ASA** therapy (≥ 2 g/day)[1,2,3,4]
- Recommend against systemic steroids[1,3,7]

[1]Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413.[2]Hardbord M, et al. *J Crohns Colitis*. 2017;11(7):769-784. [3]Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058.e3. [4]Coi CH, et al. *Intest Res*. 2017;15(1):7-37. [5]Ko CW, et al. *Gastroenterology*. 2019; 156(3):748-764. [6]Feuerstein, JD et al. *Gastroenterology*. 2020;158(5):1450-1461, [7]Wei CS, et al. *Intest Res.* 2017;15(3):266-284.

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Advanced therapies for UC

- Anti-TNF therapy using **infliximab, adamimumab, or golimumab**
- **Anti-Integrin: Vedolizumab**
- **IL12/IL23: Ustekinumab and Mirikizumab**
- **S1P inhibitors: Ozanimod and Etrasimod**
- **JAK inhibitors: Tofacinib and Updacitinib**
- Recommend against monotherapy with thiopurines *or* methotrexate[1,3,6]

[1]Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413, [2]Hardbord M, et al. *J Crohns Colitis* 2017;11(7):769-784, [3]Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058.e3., [4]Coi CH, et al. *Intest Res*. 2017;15(1):7-37, [5]Sands BE, et al. *N Engl J Med*. 2019;381:1215-26, [6]Feuerstein, JD et al. *Gastroenterology*. 2020;158(5):1450-1461, [7]Sandborn WJ et al. *N Engl J Med*. 2021;385:1280-91.

Initial therapy

- Therapy was appropriately initiated with 5-aminosalicilate
- Plan was to have patient comeback for fecal calprotectin at 3 month and repeat lower GI endoscopy at 6-12 months
- Patient symptoms resolved and he did not keep his GI follow-ups
- Over the next several years he kept having his 5-asa medication refilled by his PCP
- His liver disease did worsen some and he had to undergo ERCP with stricture dilatation and had bouts of bacterial cholangitis

Disease worsening

- Mark is now 30 years old
- Had rapid worsening in diarrhea and started experiencing rectal bleeding and abdominal pain leading to hospitalization
- Stool testing negative for enteric pathogens
- Sigmoidoscopy with moderate to severe UC
- Improved with IV steroids and discharged on oral prednisone
- Next steps?

Biologic therapy

- Time to step up advanced therapies
- Choices include anti-TNFs, JAK inhibitors, anti-Integrin, IL-12/23, S1P inhibitors
- Choice for first line and for second line therapy is through shared decision and adjusting for comorbidities
- For level of immune suppression most experts consider anti-TNF and JAK inhibitors as highest, IL12/23 mid, and anti-integrin and S1P inhibitors lowest
- JAK inhibitors only indicated for anti-TNF failures

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Network Meta-Analysis in UC

Outcome	Population	Findings
Efficacy	Biologic-naïve	**Infliximab** ranked highest for induction of remission and endoscopic improvement (OR vs placebo, 4.07; 95% CI, 2.67–6.21; SUCRA, 0.95)
	Prior anti-TNF exposure	**upadacitinib** ranked highest for induction of clinical remission (SUCRA, 0.87) Both **Ustekinumab, Mirakizumab** and **tofacitinib**, were superior to vedolizumab and adalimumab
Safety		**Vedolizumab** had the lowest risk of infections (SUCRA, 0.81), followed by **Ustekinumab/mirikizumab** (SUCRA, 0.63) in maintenance trials

OR: odds ratio; SUCRA: surface under the cumulative ranking

Singh S et al. Clin Gastroenterol Hepatol. 2020;18:2179-91

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Therapy of Moderate/Severe UC: Efficacy of Induction & Maintenance

Trial	Clinical Remission Week 8		Delta	Clinical Remission Week 48 or 52 or 54		Delta
	Placebo	**Therapy**		**Placebo**	**Therapy**	
ACT-1 (IFX)	15.0%	39.0%	24.0%	17.0%[1]	35.0%[1]	18%[1]
ACT-2 (IFX)	6.0%	34.6%	28.6%	-	-	
Ultra-1 (ADA)	9.2%	18.5%	9.3%	-	-	
Ultra-2 (ADA)	9.3%	16.5%	7.2%	8.5%[1]	17.3%[1]	8.8%[1]
Ultra-2 (TNF naïve)	11.0%	21.3%	10.3%	11.4%[1]	22.0%[1]	10.6%[1]
Pursuit (GOL)	6.3%*	18.7%*	12.4%	15.4%**[2]	28.6%**[2]	13.2%[2]
Gemini (VEDO)	5.4%*	16.9%*	11.5%	15.9%[2]	41.8%[2]	25.9%[2]
UNIFI (UST)	5.3%	15.5%	10.2%	24.0%[2]	43.8%[2]	19.8%
OCTAVE (TOFA)	3.6-8.2%	16.6-18.5%	10-13%	11.1%[2]	34.3-40.6%[2]	23-29%
U-ACHIEVE, U-ACCOMPLISH (UPA)	4-5%	26-34%	22-29%	12%	42-52%	30-40%

* Week 6

**Week 30 and 54

[1] straight through; [2] only responders of induction

Rutgeerts et al. 2005, Reinisch et al. 2011, Sandborn et al. 2012; Sandborn et al. 2014; Feagan et al. 2014, Sandborn et al. 2017, Sands et al. 2019, Danese et al. 2022

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EIMs and Infections

Other Organ System Involvement		Treatment
EIMs * More advanced inflammation	Joints Skin Eyes Hepatobiliary Others	(Moderate to Severe Treatment Options) Anti-cytokine therapies Consider vedolizumab if IBD-related
Infections	Fungal, Viral, recurrent bacterial infections	Consider vedolizumab as 1st choice Avoid AntiTNFs, JAK inhibitors?, Ustekinumab

Loss of Response

Non-Response Rates

- 10-30% of IBD patients are primary non-responders to anti-TNF medications
- Annual risk for loss of response to infliximab or adalimumab estimated to be 13 and 24%, respectively (secondary non-responders)
  - Immunogenicity
  - Suboptimal dosing
  - Mechanistic loss of response

Options for Treatment if Loss of Response Occurs

- Dose escalation (increase the dose or decrease the interval)
- Switch within class (anti-TNF 1 → anti-TNF2)
- Switch out of class (other mechanism of action)

Allez M, et al. J Crohns Colitis 2010;4:355–66; D'Haens G, et al. Am J Gastroenterol 2011;106:199–212; Gisbert J, et al. Am J Gastroenterol 2009;104(3):760-7; Billioud V, et al. Am J Gastroenterol 2011; 106(4):674-84

Medication safety in advanced liver disease

- Mark's liver disease has worsened. His bilirubin is now 3, his albumin 2.8 and he has mild ascites. He is being evaluated for liver transplant. He is concerned about the safety of his IBD treatment
- All advanced therapies have potential to increase liver enzymes and potentially cause liver damage- Ustekinumab only medications where liver toxicity is not listed in the PI
- JAK inhibitors and S1P inhibitors not recommended in Child C cirrhosis. Tofacinib dose need to be reduced to 5 mg in Child B cirrhosis. Ozanimod needs to be given every other day in patients with Child A or B cirrhosis
- Frequent monitoring is key

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Colorectal Cancer Prevention and Screening

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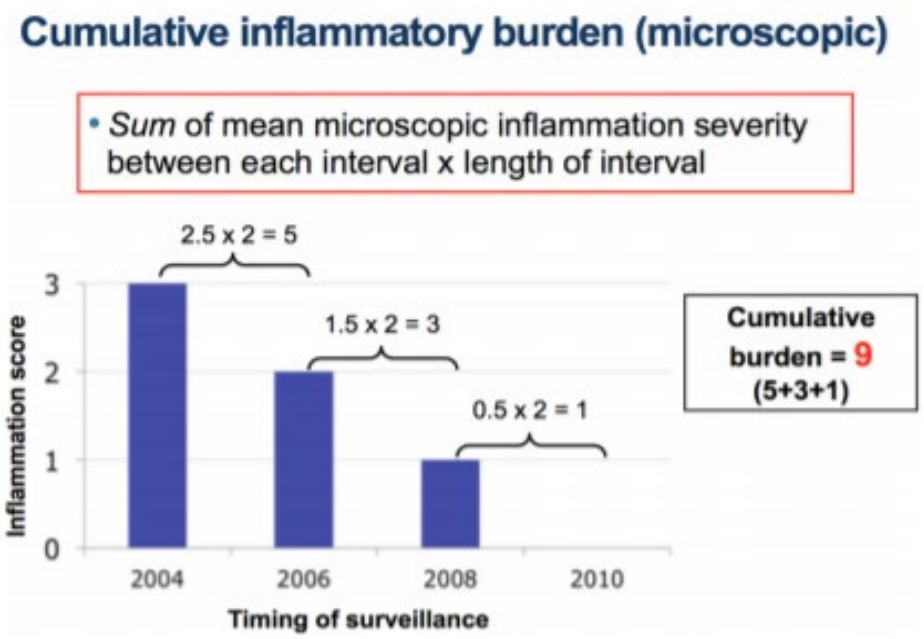
Risk Factors for Colorectal Dysplasia and Cancer in UC

- Increased inflammatory activity
- Pseudopolyps
- Prior dysplasia
- Male gender
- Longer duration of disease
- Greater extent of colonic disease
- Family history of CRC
- Primary sclerosing cholangitis
- Younger age of diagnosis

Askling J et al. *Gastroenterol.* 2001;120(6):1356–1362.
Lindberg BU et al. *Dis Colon Rectum*. 2001;44(1):77-85.
Lutgens M et al. *Inflamm Bowel Dis*. 2013;19(4):789-99.
Rutter M et al. *Gastroenterology.* 2004;126(2):451-9.
Rubin DT et al. *Clin Gastroenterol Hepatol.* 2013;11(12):1601-8.

Cumulative Inflammation Burden Predicts Colorectal Neoplasia in UC



- N = 987 at St. Marks' Hospital[1]
- Microscopic cumulative inflammation burden is strongly associated with risk of developing CRN in patients with UC

- N = 62 at University of Chicago using St. Marks' methodology[2]
- Cumulative histologic inflammation is significantly associated with CRN in patients with UC

	Cases (n=26)	Controls (n=36)	p-value
Mean HIA Scores			
Cumulative Burden	12.63	7.98	0.03919*
Mean Severity	1.82	1.58	0.1525
Maximum Severity	2.42	1.94	0.06182
Persistency of Inflammation	0.31	0.27	0.5815
Maximum HIA Scores			
Cumulative Burden	22.63	13.93	0.0206*
Mean Severity	3.36	2.80	0.0266*
Maximum Severity	4.15	3.64	0.0643
Persistency of Inflammation	0.93	0.76	0.009193*

[1]Choi CR, et al. *Gut*. 2019;68(3):414-22.
[2]Yvellez OV, et al. *Inflamm Bowel Dis*. 2020. [Epub ahead of print].

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Colorectal Cancer Prevention

- Inflammation is a significant risk[1,5]
- Start surveillance 8 years after SYMPTOM onset[1,2,4,5,6]
- Target is dysplasia detection (but no direct evidence of cancer or mortality prevention)
  - Standard def colonoscopes → dye spray chromo[1,2,3,6] with methylene blue or indigo carmine[2,3]
  - High def colonoscopes → white light endoscopy with NBI or dye spray chromoendoscopy with methylene blue or indigo carmine[2,3]
- Endoscopic resection, segmental resection, and active surveillance are possible[2,3]
- High def scopes + dye spray chromoendoscopy was **not** better at finding dysplasia than high def scopes + white light with non-targeted biopsies[7]

[1]Magro F, et al. *J Crohn's Colitis*. 2017;11(6):649-670.
[2]Rubin DT, et al. *Am J Gastroenterol*. 2019;114(3):384-413.
[3]Laine L, et al. *Gastrointest Endosc.* 2015;81(3):489-501.e26.
[4]Ross H, et al. *Dis Colon Rectum*. 2014;57(1):5-22.
[7]Yang, DH, et al. *Am J Gastroenterol*. 2019;114(10):1642-48.

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Skin Cancer Risk

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IBD is a Risk Factor For Skin Cancer

- IBD patients have an increased risk of non-melanoma skin cancer:
  - 912/100,000 vs 623/100,000
- IBD patients have an increased risk of melanoma skin cancer:
  - 57.1/100,000 vs 44.1/100,000
- CD has a slightly higher risk than UC for both

Long MD, et al. *Gastroenterology* 2012;143(2):390-399

Risk of Skin Cancers in IBD Patients and Therapy Exposure

- Retrospective cohort and nested case-control studies using administrative data from the LifeLink Health Plan Claims Database
- 1997-2009
- N=108,579 patients with IBD, matched to 4 individuals without IBD

Table 5. Multivariate Analyses of Medication Use and Skin Cancer Outcomes in Patients With IBD, Overall and by CD or UC

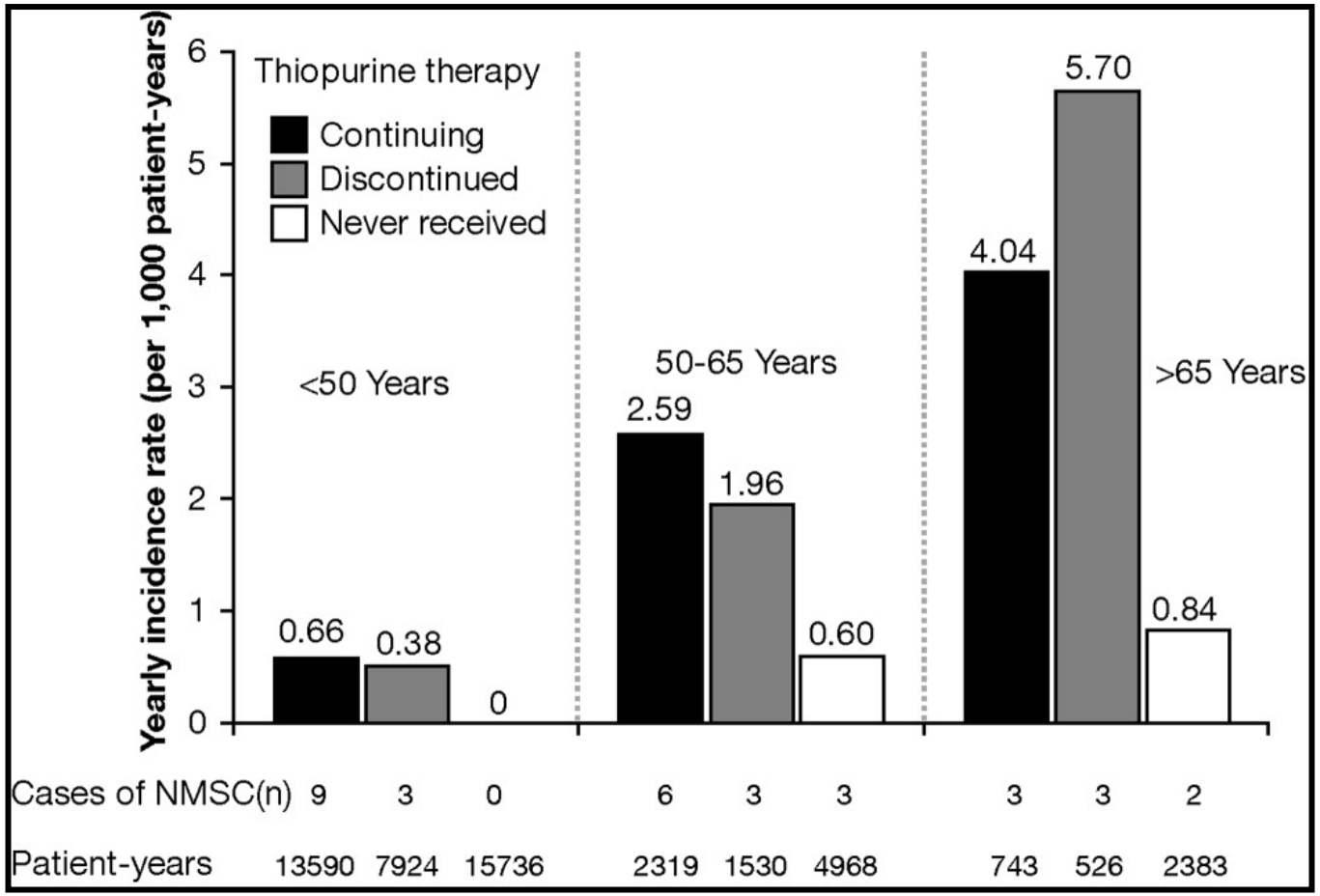
	IBD overall		CD		UC	
Medication[a]	Melanoma	NMSC	Melanoma	NMSC	Melanoma	NMSC
Any use						
5-ASA	1.06 (0.77–1.45)	0.99 (0.92–1.08)	0.98 (0.63–1.53)	1.01 (0.90–1.13)	1.22 (0.76–1.96)	0.99 (0.89–1.11)
Biologic	1.88 (1.08–3.29)	1.14 (0.95–1.36)	1.94 (1.03–3.68)	1.16 (0.95–1.41)	1.73 (0.53–5.63)	1.06 (0.69–1.64)
Thiopurine	1.10 (0.72–1.67)	1.85 (1.66–2.05)	0.92 (0.53–1.59)	1.99 (1.73–2.27)	1.31 (0.66–2.60)	1.63 (1.36–1.94)

Long MD, et al. *Gastroenterology* 2012;143:390-399

Skin Cancer Risk and Thiopurine Use

Non-melanoma skin cancer

- Ongoing treatment (HR 5.9)
- Prior treatment (HR 3.9)
- ***Current treatment and increased age associated with greatest risk***



Peyrin-Biroulet et al. Gastroenterology, 2011.
Long et al. Gastroenterology, 2012.

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Recommendations for Melanoma and NMSC

- Education of patients and physicians related to risk factors
  - Fair skin pigmentation
  - Overall UV exposure
  - Personal or family history of melanoma
  - Thiopurines (NMSC) predominantly
- Primary protection:
  - Sun avoidance
  - Sun protection via sunscreen or sun-protective clothing
- Secondary prevention:
  - Yearly dermatology screening of patients on immunosuppressives

Long MD, et al. *Gastroenterology* 2012;143:390-399
Skin Cancer screening. http://www.cancer.gov/cancertopics/pdq/screening/skin/HealthProfessional/page2)

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Lymphoma Risk in IBD Patients

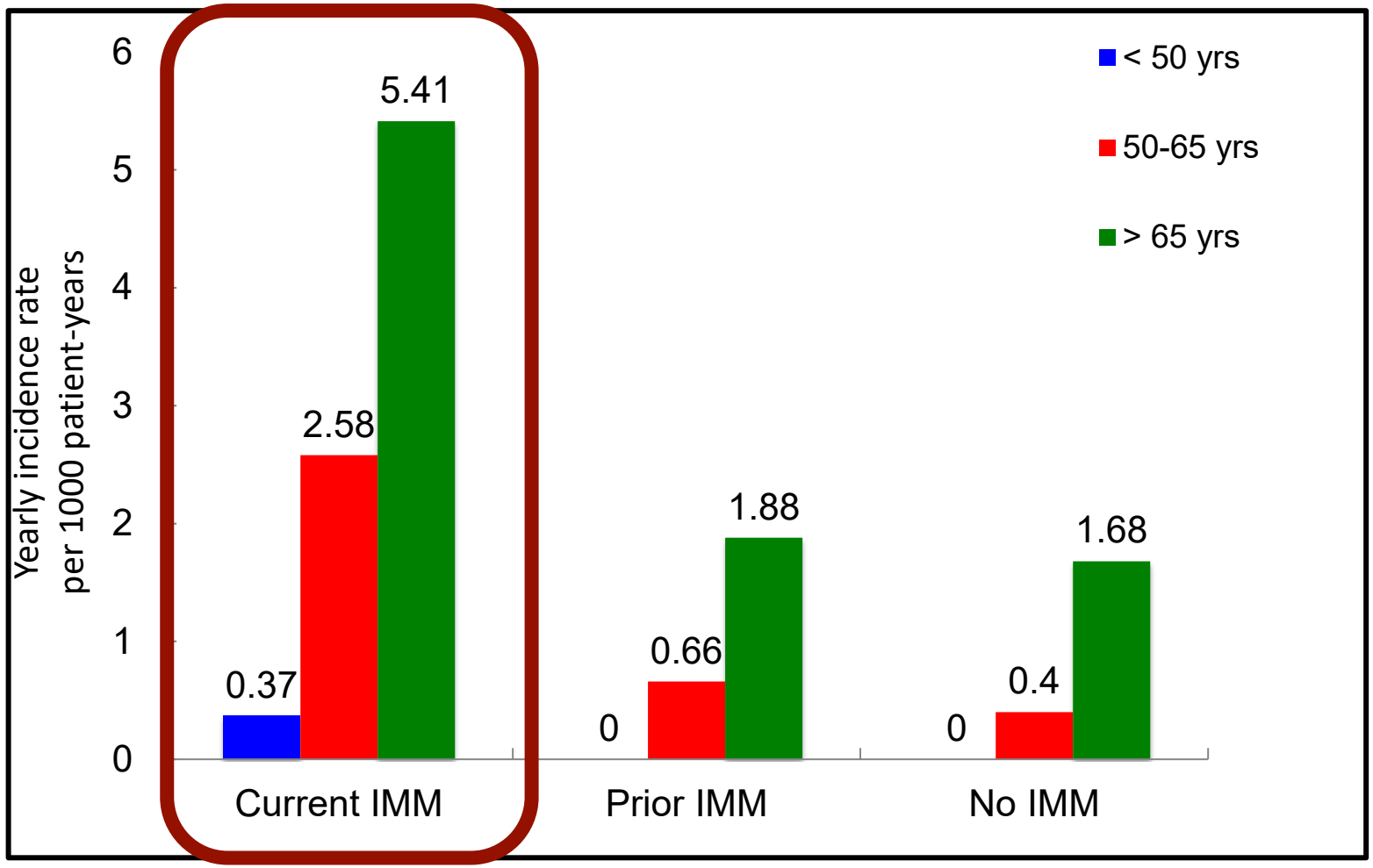
Lymphoma Risk in IBD

- Large population-based study from Denmark with long-term follow-up found an increased risk of lymphoma in CD patients, not UC patients[1]
  - SIR: 3.43; 95% CI 1.38 – 7.07, independent of thiopurine exposure
- A study using a Canadian administrative claims database found an increased risk of lymphoma in CD patients, especially males, compared to general population[2]
  - IRR: 3.63; 95% CI, 1.53–8.62, no prior exposure to thiopurines
- Hepatosplenic T-cell lymphoma (HSTCL)
  - Extremely rare, uniformly fatal, not EBV-related
- The risk of HSTCL in IBD patients on thiopurines[3]
  - < 1:20,000 person-years, almost exclusively men < 35 on thiopurine or dual therapy; no cases of HSTCL in IBD patients on anti-TNF monotherapy

1. Jess T, et al. *Am. J. Gastroenterol*. 2013:108(12):1869-76.
2. Bernstein CN, et al. *Cancer* 2001;91(4):854-62.
3. Kotlyar D, et al. *Clin. Gastroenterol. Hepatol.* 2014;13(5):847-58.

Thiopurines & Lymphoma

Overall incidence rates among current thiopurine users = 9 per 10,000
Hazard ratio thiopurine exposed vs naïve = 5.3 (2.0-13.9)



Adapted from Cosnes et al. Lancet. 2010.

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No Risk of Solid Tumors with Anti-TNF Therapy

Rheumatoid Arthritis

- 13,000 patients, ½ on biologics

Type of Cancer	Odds Ratio
All cancers	1.0 (0.8-1.2)
All solid tumors	1.0 (0.8-1.2)
Colon	0.8 (0.3-1.7)
Lung	1.1 (0.7-1.8)
Breast	0.9 (0.5-1.3)
Pancreas	0.5 (0.1-2.6)
Melanoma	2.3 (0.9-5.4)
Non-melanoma	1.5 (1.2-1.8)

Inflammatory Bowel Disease

- Limited data

Type of study	Associated risk
Population based 651 patients	SIR 0.7 (0.2-1.7)
Single center 734 patients	OR 0.97 (0.56-1.65)

No clear evidence that anti-TNF is associated with (non-skin) solid tumors

Wolfe F and Michaud K. *Arthritis and Rheumatism*. 2007;56(9):2886-95.
Mason M and Siegel CA. *Inflamm Bowel Dis*. 2013;19(6):1306-21.

Checklists for IBD Patients

CROHN'S & COLITIS FOUNDATION

Health Maintenance Summary

Vaccines and Infections

Influenza: All patients >6 months of age should receive annual inactivated influenza vaccine, irrespective of immunosuppression status.

MMR: IBD Patients not immune to MMR should receive a 2-dose series, at least 4 weeks apart. If immune status is uncertain, IgG antibody titer should be checked. MMR should not be given to patients currently on systemic immunosuppressive* therapy.

Pneumococcus: All patients >19 years age receiving systemic immunosuppression* should receive PCV13, followed by PPSV23 at least 8 weeks later, and a booster of PPSV23 5 years later.

Varicella: Seroprotection status should be checked with varicella zoster virus IgG antibodies in all patients without documented vaccination record or exposure. All patients who are not immune should receive a 2-dose series, 4–8 weeks apart, ≥4 weeks before immunosuppression, if therapy can be postponed.

Zoster: All patients receiving JAK inhibitor therapy should receive the recombinant adjuvanted zoster vaccine. Risk of zoster should be considered with combinations of other immunosuppressive* therapies.

TB: Screen for latent TB in all patients with IBD, at baseline. Perform clinical risk assessment for TB exposure annually in all patients with IBD.

Cancer Screening

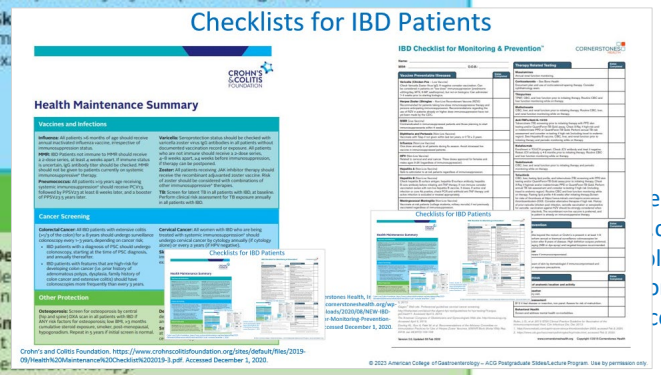
Colorectal Cancer: All IBD patients with extensive colitis (>1/3 of the colon) for ≥ 8 years should undergo surveillance colonoscopy every 1–3 years, depending on cancer risk;

- IBD patients with a diagnosis of PSC should undergo colonoscopy, starting at the time of PSC diagnosis, and annually thereafter.
- IBD patients with features that are high-risk for developing colon cancer (i.e. prior history of adenomatous polyps, dysplasia, family history of colon cancer and extensive colitis) should have colonoscopies more frequently than every 3 years.

Cervical Cancer: All women with IBD who are being treated with systemic immunosuppression* should undergo cervical cancer by cytology annually (if cytology alone) or every 2 years (if HPV negative).

Other Protection

Osteoporosis: Screen for osteoporosis by central (hip and spine) DXA scan in all patients with IBD if ANY risk factors for osteoporosis; low BMI, >3 months cumulative steroid exposure, smoker, post-menopausal, hypogonadism. Repeat in 5 years if initial screen is normal.



IBD Checklist for Monitoring & Prevention™

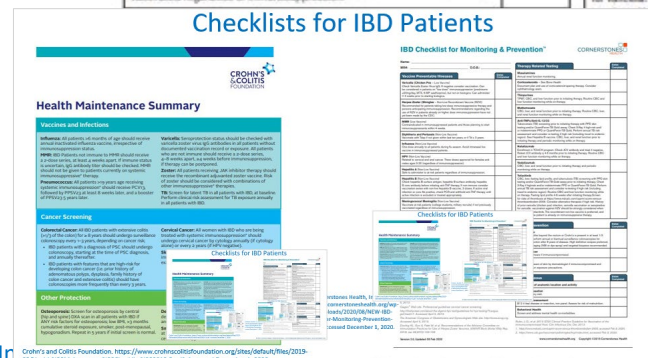
CORNERSTONES HEALTH

Name: _____

MR#: _____ D.O.B.: _____

Vaccine Preventable Illnesses	Dates Completed
Varicella (Chicken Pox – Live Vaccine) Check Varicella Zoster Virus IgG. If negative consider vaccination. Can be considered in patients on "low dose" immunosuppression (prednisone ≤20mg/day, MTX, 6 MP, azathioprine), but not on biologics. Can administer > 4 weeks prior to starting biologics.	
Herpes Zoster (Shingles – Non-Live Recombinant Vaccine (RZV)) Recommended for patients taking low-dose immunosuppressive therapy and persons anticipating immunosuppression. Recommendations regarding the use of RZV in patients already on higher dose immunosuppression have not yet been made by the CDC.	
MMR (Live Vaccine) Contraindicated in immunosuppressed patients and those planning to start immunosuppressants within 4 weeks.	
Diphtheria and Pertussis (Non-Live Vaccine) Vaccinate with Tdap if not given within last ten years, or if Td ≥ 2 years.	
Influenza (Non-Live Vaccine) One dose annually to all patients during flu season. Avoid intranasal live vaccine in immunosuppressed patients.	
HPV (Non-Live Vaccine) Related to cervical and anal cancer. Three doses approved for females and males ages 9-26 (regardless of immunosuppression).	
Hepatitis A (Non-Live Vaccine) Safe to administer to at-risk patients regardless of immunosuppression.	
Hepatitis B (Non-Live Vaccine) Check hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody before initiating anti-TNF therapy. If non-immune consider vaccination series with non-live hepatitis B vaccine, 3 doses. If active viral infection or core Ab positive, check PCR and withhold anti-TNF therapy until active infection is excluded or treated appropriately.	
Meningococcal Meningitis (Non-Live Vaccine) Vaccinate at-risk patients (college students, military recruits) if not previously vaccinated regardless of immunosuppression.	

Therapy Related Testing	Dates Completed
Mesalamines Annual renal function monitoring.	
Corticosteroids – See Bone Health Document plan and use of corticosteroid-sparing therapy. Consider ophthalmology exam.	
Thiopurines TPMT, CBC, and liver function prior to initiating therapy. Routine CBC and liver function monitoring while on therapy.	
Methotrexate CBC, liver, and renal function prior to initiating therapy. Routine CBC, liver, and renal function monitoring while on therapy.	
Anti-TNFα/Anti-IL-12/23 Tuberculosis (TB) screening prior to initiating therapy with PPD skin testing and/or QuantiFeron-TB Gold assay. Chest X-Ray if high-risk and/or indeterminate PPD or QuantiFeron-TB Gold. Perform annual TB risk assessment and consider re-testing if high risk (including travel to endemic region). See Hepatitis B vaccine. CBC, liver, and renal function prior to initiating therapy and periodic monitoring while on therapy.	
Natalizumab Enrollment in TOUCH program. Check JCV antibody and treat if negative. Retest JCV antibody q 4-6 months prior to initiating therapy. Routine CBC and liver function monitoring while on therapy.	
Vedolizumab CBC, liver, and renal function prior to initiating therapy and periodic monitoring while on therapy.	
Tofacitinib CBC, liver, fasting lipid profile, and tuberculosis (TB) screening with PPD skin testing and/or QuantiFeron-TB Gold assay prior to initiating therapy. Chest X-Ray if high-risk and/or indeterminate PPD or QuantiFeron-TB Gold. Perform annual TB risk assessment and consider re-testing if high risk (including travel to endemic region). Routine CBC and liver function monitoring while on therapy. Fasting lipid profile 4-8 weeks after initiating therapy. Screen for risks of thrombosis at https://www.mdcalc.com/caprini-score-venous-thromboembolism-2005. Consider alternative therapies if high risk. History of prior varicella (chicken pox) infection, varicella vaccination or seropositive for varicella: vaccination against HZV should be strongly considered when tofacitinib. The recombinant non-live vaccine is preferred, and the patient is already on immunosuppressive therapy.	



Crohn's and Colitis Foundation. https://www.crohnscolitisfoundation.org/sites/default/files/2019-09/Health%20Maintenance%20Checklist%202019-3.pdf. Accessed December 1, 2020.

Summary

- Patients with PSC and IBD have milder disease on presentation but carry increased colon cancer risk
- 5-ASA medications still mainstay of therapy for milder disease
- Achieving remission is critical to improve outcomes and lower cancer risks
- Immunomodulators are out of favor but fortunately we have many choices for advanced therapies
- Close monitoring in patients with advanced liver disease