CMEO
BriefCase

Managing Your Patients with Psoriasis and IBD: A Conversation with the Experts

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CME OUTFITTERS

Anita Afzali, MD, MPH, MHCM, FACG, AGAF
Professor of Clinical Medicine
Interim Chief, Division of Digestive Diseases
Executive Vice Chair, Department of Internal Medicine
University of Cincinnati College of Medicine
Associate Chief Medical Officer
UC Health System
Cincinnati, OH

Learning Objective

Assess the genetic, pathophysiologic, and other links between PsO and IBD

Audience Response

Which of the following is true regarding the incidence of psoriasis and inflammatory bowel disease (IBD)?

A. No connection between the risk of IBD and psoriasis has been identified
B. There is an increased risk of developing IBD in patients with psoriasis
C. Psoriasis is associated with an increased risk of Crohn's with perianal fistulas
D. There is an increased risk of developing IBD in patients with psoriasis if environmental risk factors are present
E. I don't know

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Physician-Patient Interaction

Patient Case: Tasha

Patient Characteristics

- 27-year-old female, 3-month GI follow up for CD with via virtual visit
- Medical history
  - Crohn's disease: diagnosed 6 months ago, started on infliximab 5mg/kg every 8 weeks
  - Moderate disease activity at the time of diagnosis
- Review of systems
  - Skin: reports patches of scaly, itchy skin on elbows and knees
  - Extremities: pain in the small joints, left hand and bilateral feet
  - GI: occasional abdominal pain (maybe 1-2x per week), does not disrupt daily activities

Labs and Test Results

- Last results from 3 months ago:
  - CRP: 90 mg/L
  - FCP: 225 µ/mg
  - Albumin 3.7 g/dL
  - Hgb: 12.5 g/dL

Diagnostics

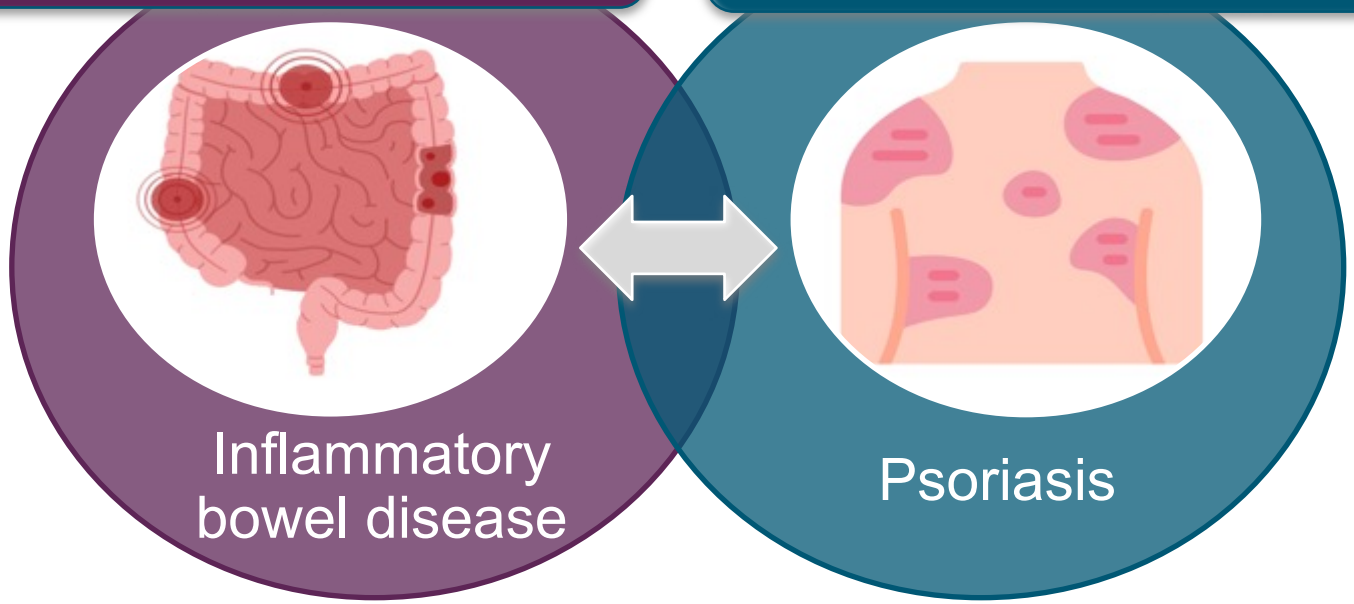
- Last colonoscopy 3 months ago:
  - Mild inflammation with erosions in terminal ileum
  - CDEIS: 3

CD = Crohn's disease; CDEIS = Crohn's disease endoscopic index of severity; CRP = C-reactive protein; FCP = fecal calprotectin; GI = gastrointestinal; Hgb = hemoglobin

Intersection of Psoriasis and IBD

IBD → **1.5x** increased risk of developing psoriasis

Psoriasis → **1.7x** increased risk of developing IBD



Prevalence of IBD in patients with psoriasis: **1-2%**

Prevalence of IBD in patients *without* psoriasis: **0.4%**

Fu Y, et al. *JAMA Dermatol.* 2018;1:154(12):1417-1423. Bernstein C, et al. *Gastroenterology.* 2005;129(3):827-36. Alinaghi F, et al. *J Crohns Colitis.* 2020;14(3):351-360.

Links between Psoriasis and IBD

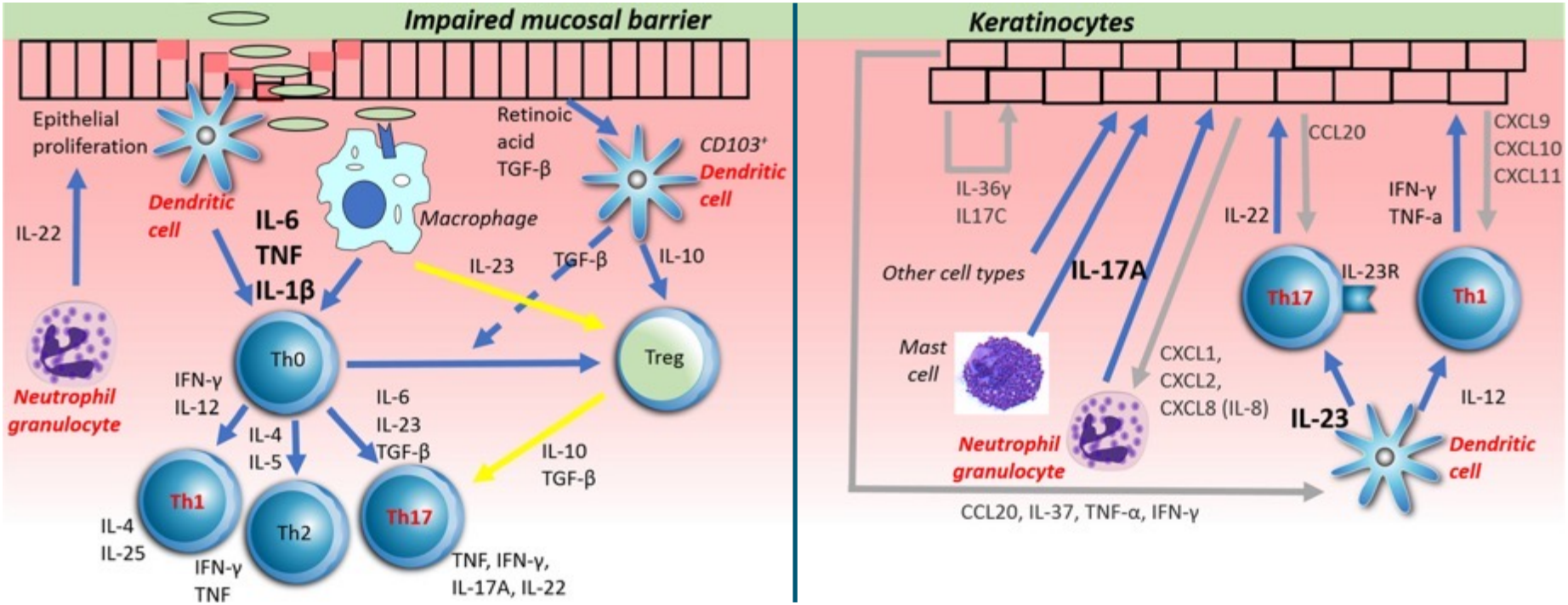
- Disease characteristics
  - Chronic
  - Inflammatory
  - Organotropic (tissue selective)
- Dysregulation of both innate and adaptive immune systems
- Genetic predisposition
  - Higher incidence 1st degree relatives
  - Shared genetic markers of disease seen between psoriasis and IBD
- Gut dysbiosis: similar alterations in gut microbiota seen in both conditions
- Environmental triggers: stress and smoking are shared triggers for both conditions

Vlachos C, et al. *Psoriasis (Auckl)*. 2016;6:73-92. Chia AYT, et al. *Front Med (Lausanne)*. 2021;8:737256.

Shared Pathophysiology of Psoriasis and IBD

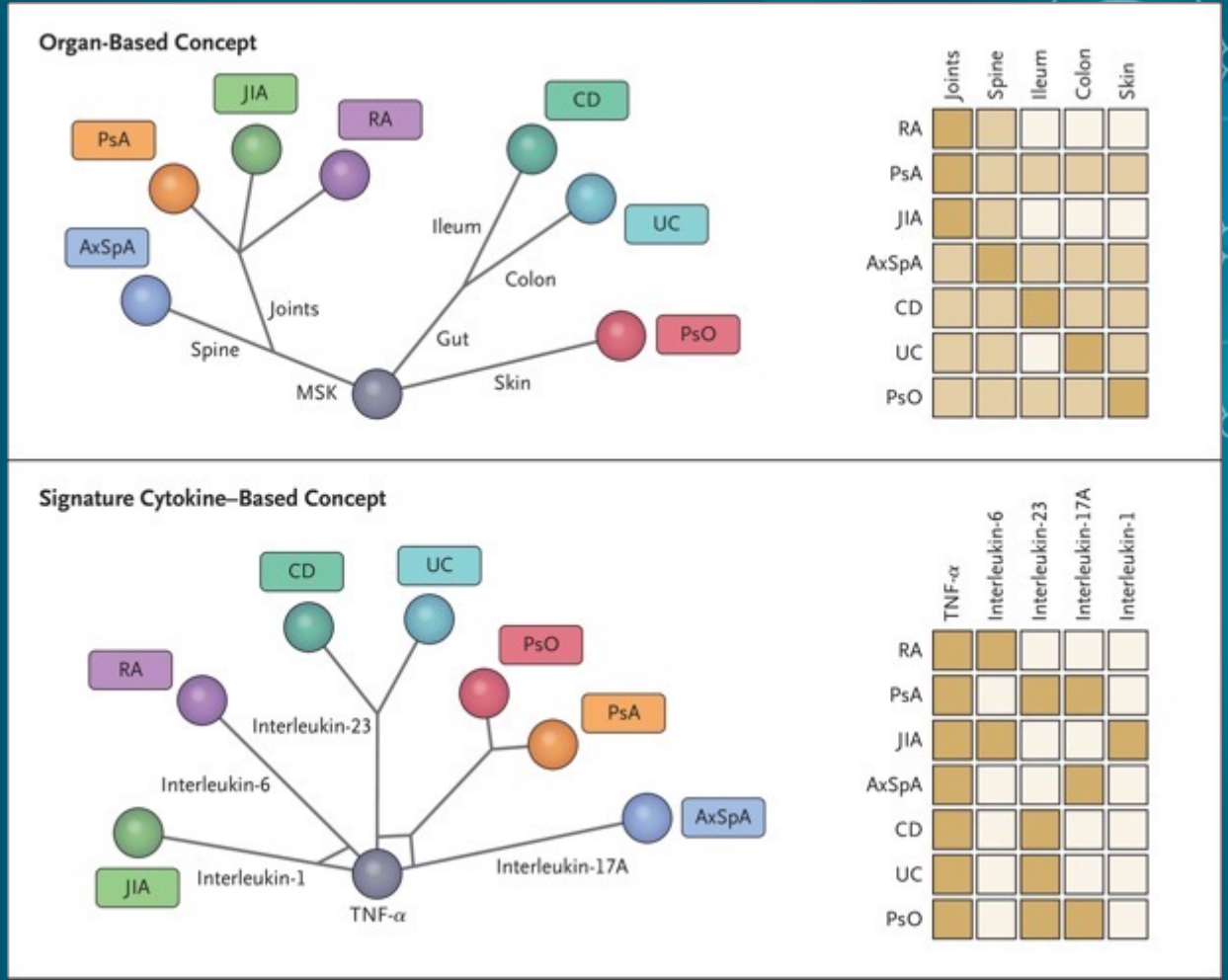
IBD

Psoriasis



Hedin CRH et al. *J Intern Med*. 2021;290(2):257-278

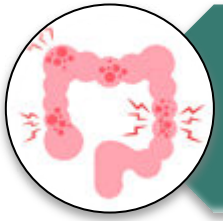
Cytokine Connections in Immune-Mediated Inflammatory Diseases



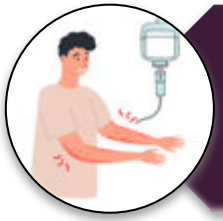
G Schett, et al. *N Engl J Med.* 2021;385:628-639

Psoriasis and Dermatologic Conditions in IBD

Independent immune-mediated disease



Secondary to underlying inflammation in IBD



Paradoxical adverse event from anti-TNF treatment

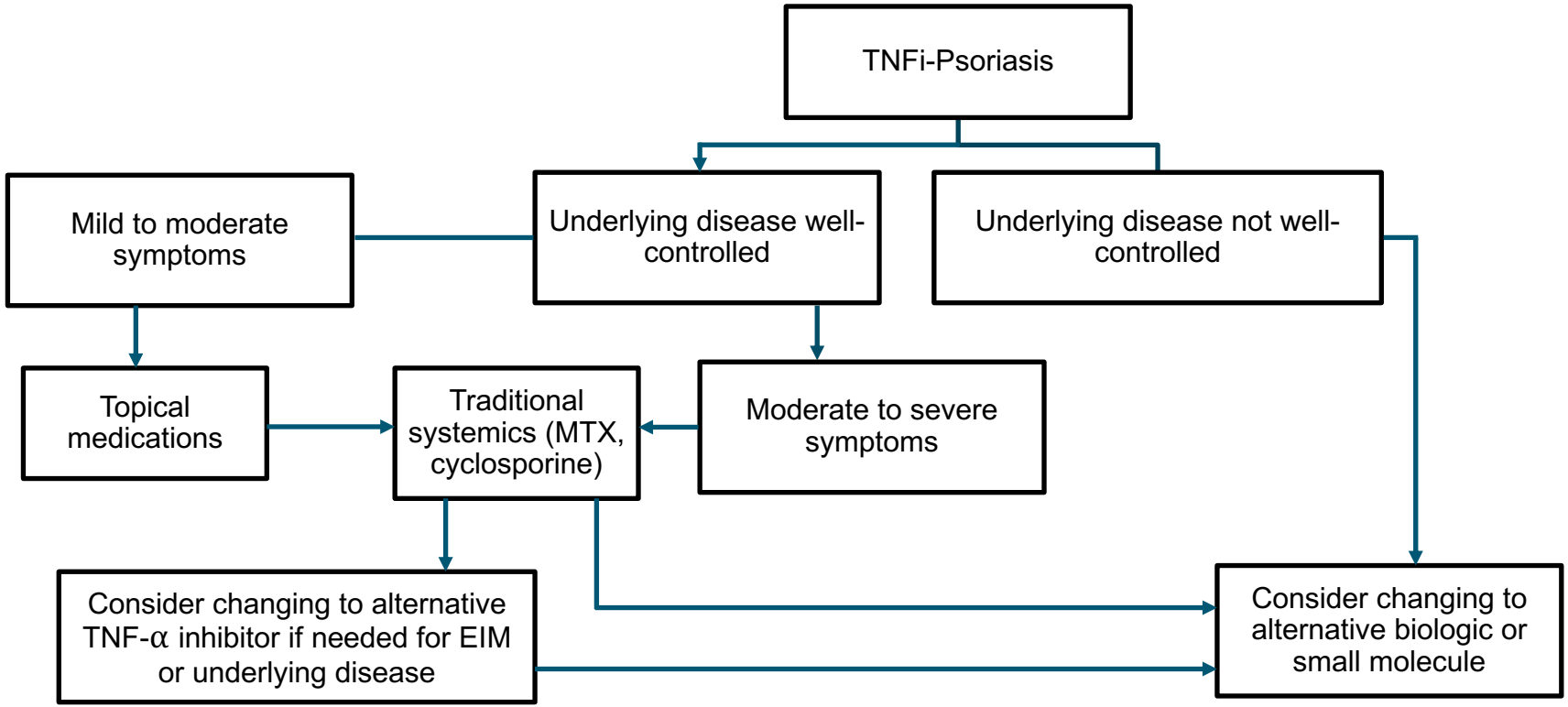
Fiorino G, et al. *J Crohns Colitis*. 2015;9(9):697-8

Extraintestinal Manifestations (EIM)

EIM	Parallel Activity	Separate Activity	May or May not Parallel
Psoriasis	✓		
Oral aphthous ulcers	✓		
Episcleritis	✓		
Erythema nodosum	✓		
Axial arthropathy		✓	
Peripheral arthropathy	✓ (Type 1)	✓ (Type 2)	
Pyoderma gangrenosum			✓
Uveitis			✓
PSC			✓

Vavricka S, et al. *Inflammatory Bowel Diseases*. 2015;21:8:1982-1992

Approach to Management of Anti-TNF Induced Psoriasiform Rash



MTX = methotrexate; TNFi = tumor necrosis factor-α inhibitor

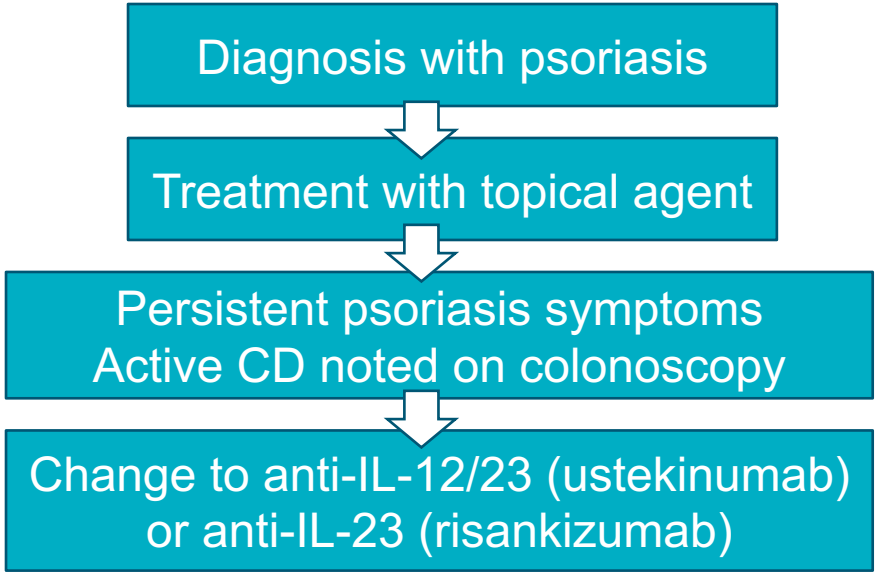
Mazloom SE, et al. *J Am Acad Dermatol*. 2020;83(6):1590-1598

Patient Care Plan: Tasha

- Patient case summary: infliximab every 8 weeks for treatment of CD diagnosed 6 months ago. New report of scaly, itchy rash.

Next steps:

- Evaluation by a dermatologist
- Evaluation of CD activity
- Determine if symptoms are due to an EIM, anti-TNF adverse reaction (psoriasiform rash) or new onset psoriasis?



Learning Objective

Select appropriate pharmacotherapeutic treatment for patients with co-existing PsO and IBD

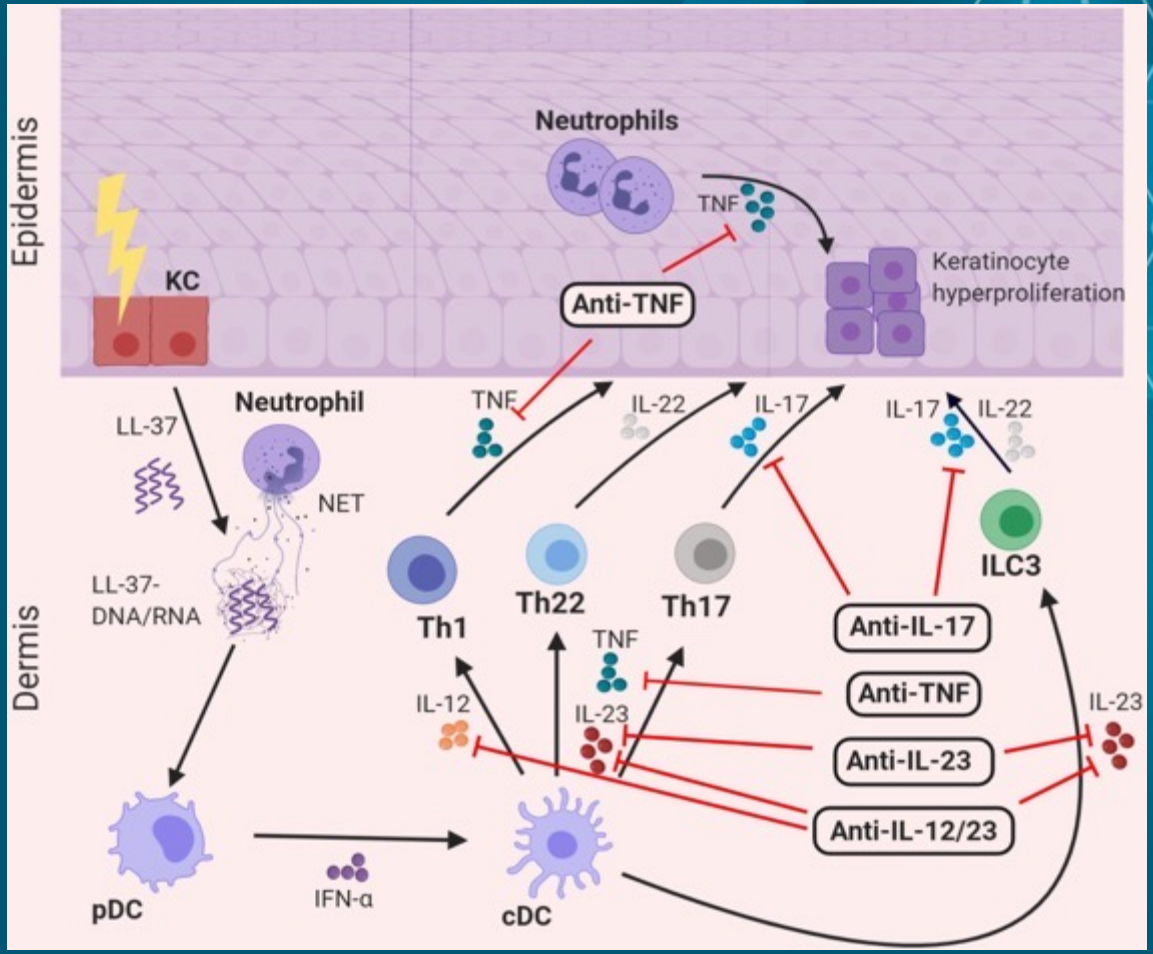
Physician-Patient Interaction

Patient Case: Yolanda

Patient Characteristics
• 33-year-old female establishing care with gastroenterologist after developing persistent diarrhea, abdominal pain, and blood in stools

Medical History	Symptoms
• Plaque psoriasis • Current treatment: secukinumab, started 6 months ago • IBS-D, occasional stomach cramping and diarrhea that would resolve after a few days	• Multiple episodes of diarrhea per day (3-6), pain not relieved with bowel movements, has noticed blood in stools • Symptoms have been going on for at least 3 weeks

IL-17 Psoriasis Pathogenesis



Ten Bergen LL, et al. *Scand J Immunol.* 2020;92(4):e12946

Audience Response

Which of the following treatments is FDA-approved to treat both Crohn's disease and psoriasis?

A. Brodalumab
B. Etanercept
C. Ustekinumab
D. Tofacitinib
E. I don't know

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Theory and Reality of IL-17 Blockade in IBD

Theory

Blocking IL-17 was thought to alleviate inflammation when chemically induced colitis was improved in IL-17A knock out mice

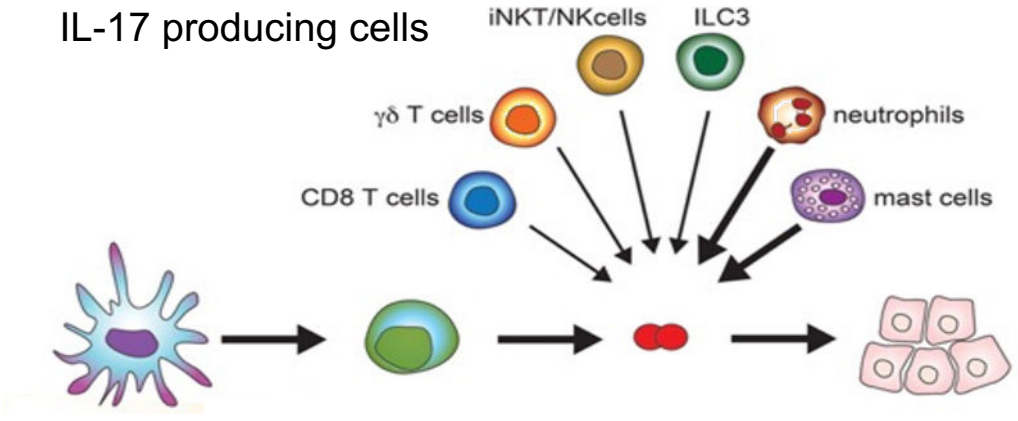
Reality

IL-17 neutralizing monoclonal antibody led to increased severity of chemically-induced colitis in treated mice

Clinical trials of anti-IL-17A or IL-17A receptor antagonists in patients with IBD resulted in worse outcomes compared to placebo

Hohenberger M, et al. *J Dermatolog Treat.* 2018;29(1):13-18

IL-17 in Inflammatory Bowel Disease



α-TNF

α-IL-12/IL-23 (p40)
α-IL-23(p19)

Mechanisms do not cause *complete* blockade of IL-17A activity

α-IL-17A
α-IL-17RA

Skin
Beneficial effects of IL-17 blockade

- Decreased keratinocyte proliferation/hyperplasia
- Decreased immune cell activation

Intestine
Deleterious effects of IL-17 blockade

- Worsening intestinal inflammation
- Increased gut permeability
- Increased susceptibility to infection (especially fungal)

Adapted from: Brembilla NC, et al. F*ront Immunol*. 2018;9:1682

IL-17 Targeting Therapies in Psoriasis

	Secukinumab (anti-IL-17)	Ixekizumab (anti-IL-17)	Brodalumab (IL-17-receptor antagonist)
Indications	• PsO: age 6 years and older • PsA: age 2 years and older • Ankylosing spondylitis • Non-radiographic axial spondyloarthritis • Enthesitis-related arthritis	• PsO: age 6 years and older • PsA: adult • Ankylosing spondylitis • Non-radiographic axial spondyloarthritis	• PsO: adult

Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals; 2021. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. Siliq [package insert]. Bridgewater, NJ: Baush Health US LLC; 2020.

Investigations of Anti-IL-17 Agents in IBD

Treatment	Study type	Patients (N)	Disease	Results
Brodalumab (IL-17 receptor antagonist)	Phase 2	130	CD	• Worsening CD more often with brodalumab (25.0% vs 6.3% placebo) • No statistically significant difference between brodalumab and placebo in CDAI scores
Secukinumab (anti-IL-17)	Phase 2	59	CD	• 14 serious adverse events • 31% early discontinuation • Higher reduction in CDAI scores in placebo group

CDAI = Crohn's disease activity index

Hueber W, et al. *Gut*. 2012;61(12):1693-1700; Targan SR et al. Am J Gastroenterol. 2016 Nov;111(11):1599-1607.

IBD Events in Anti-IL-17 Clinical Trials

Treatment and Data Source	Patients (N)	IBD Adverse Events
Ixekizumab Phase III psoriasis data	4209	8 new IBD cases (3= CD, 5=UC) 14 exacerbations in known IBD
Secukinumab Clinical trial and post-marketing data for psoriasis and psoriatic arthritis (up to 5 years)	6561	21 new IBD cases (6= CD, 12 = UC, 3= IBDU) 11 exacerbations out of 40 known IBD patients
Brodalumab Phase II and phase III psoriasis trial data	4,464	2 new cases of CD (1 case in placebo group) *patients with CD specifically excluded from phase 3 trials

Schreiber S, et al. *Ann Rheum Dis*. 2019;78(4):473-479.; Reich K et al. *J Am Acad Dermatol.* 2017 Mar;76(3):441-448.e2.; Reich K, et al. *Acta Derm Venereol*. 2022;102:adv00683.

Pharmacovigilance and Epidemiologic Studies

Reference	Study Group	Data Source	Results	Notes
Orrell et al. 2018	>5 million UC or CD patients	Patient data from adverse event reporting systems reviewed for SEC-related UC or CD	IBD cases identified from reviewed databases	Safety signal for SEC found in AE databases with a PRR of 4.65 (CI: 3.66–5.89)
Mohy-ud-din et al. 2019	62 million electronic health records	Patient data from Explorys (IBM, New York) from electronic medical records	2870 received SEC; IBD cases identified	Rates of de-novo IBD after SEC higher than the prevalence of IBD in general population (3.2 *versus* 0.74%; RR – 4.2; 95% CI: 3.45–5.18)

AE = adverse event; PRR = proportional reporting ratio; SEC = secukinumab

Fieldhouse KA, et al. *Drugs Context*. 2020;9:2020-2-1

Screening for IBD Risk when Considering Anti-IL-17 Treatment

- Ask the patient about a family history of IBD
- Search for gastrointestinal symptoms
- Counsel patients about the possible risk of gastrointestinal side effects
- Consider baseline fecal calprotectin level (usefulness in screening asymptomatic patients for potential IBD has not been established)
- Monitor for IBD symptoms during and after treatment (1 week to 4 years post-therapy)

Fauny M, et al. *Ann Rheum Dis*. 2020;79(9):1132-1138. Fieldhouse KA, et al. *Drugs Context*. 2020;9:2020-2-1.

GI Symptom Screening Checklist

- ☐ Abdominal pain
- ☐ Diarrhea
- ☐ Waking from sleep because of abdominal pain or diarrhea
- ☐ Blood or mucus in stool
- ☐ Unwanted/unintentional weight loss
- ☐ Fever
- ☐ Fatigue
- ☐ Prior GI diagnosis: IBS, food intolerance
- ☐ Use of antidiarrheals or GI antispasmodics

Patients may not volunteer GI history or GI symptoms during a dermatology visit. Make sure to ask specifically about GI symptoms!

Chmiel C, et al. *J Eval Clin Pract*. 2019;25(1):155-162

Reviewing Options for IBD and PsO

Mechanism of Action	Therapeutic Agent	Crohn's	Ulcerative Colitis	Psoriasis	Psoriatic Arthritis
Anti-TNF alpha	Infliximab	X	X	X	X
	Adalimumab	X	X	X	X
	Certolizumab	X	X	X	X
	Etanercept			X	X
IL-12/23 inhibitor	Ustekinumab	X	X	X	X
IL-23 inhibitor	Risankizumab	X		X	X
	Guselkumab	Phase 3		X	X
JAK-inhibitor	Tofacitinib*		X		X
	Upadacitinib*		X		X
Anti-IL-17	Secukinumab			X	X
	Ixekizumab			X	X
IL-17 receptor antagonist	Brodalumab			X	

*recommended for use after failure/intolerance to anti-TNF agent. Petit RG, et al. *Int J Mol Sci*. 2021;22(9):4983.

Overall Recommendations for IL-17 Targeting Agents

History of IBD

- Avoid IL-17 targeting agents
- Utilize agents with established efficacy in IBD and psoriasis

Symptoms or family history concerning for IBD

- Investigate any indicators of IBD risk before use of IL-17 targeting agents
- Consider alternative to IL-17 targeting agent if potential risk is unclear

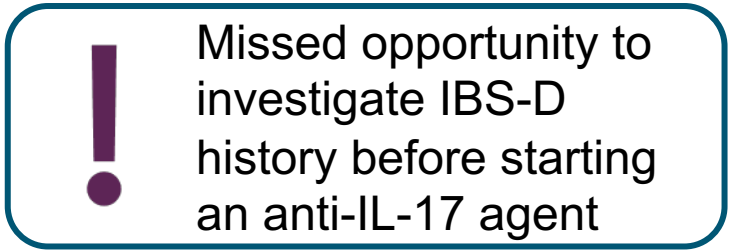
No history of IBD, no IBD symptoms, and no concerning family history

- Counsel patient regarding risks and the need to monitor for GI symptoms
- Monitor during and after treatment for development of IBD symptoms (range of onset varies from 1 week to several years)

Conforti C. et al. *J Dermatolog Treat*. 2022;33(3):1279-1286

Patient Case follow-up: Yolanda

- Case summary: 33 y/o female with persistent diarrhea, abdominal pain and blood in stools. History of psoriasis and IBS-D. Recently started secukinumab.
- Lab and diagnostic findings:
  - Inflammation consistent with IBD on endoscopic evaluation
  - Fecal calprotectin elevated
- Medication treatment plan:
  - Discontinue secukinumab
  - Transition to agent effective for psoriasis and IBD (anti-TNF, anti-IL-12/23 or anti-IL-23)



SMART Goals

- Incorporate consideration for the increased risk of developing IBD in patients with psoriasis
- Screen patients considered for treatment with an IL-17 inhibitor for symptoms or a family history of IBD
- Utilize alternatives to IL-17 targeting agents in patients with co-occurring psoriasis and IBD
- Consider the potential for new-onset IBD in patients who develop IBD symptoms after treatment with an IL-17 targeting agent

SMART = Specific, Measurable, Attainable, Relevant, Timely

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