

# Management of Inflammatory Bowel Disease in 2022

## “The Story of Laura”

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# Financial Disclosures

- Scientific Advisory Boards
  - Iterative Scopes
  - Menten AI

# Learning Objectives

- To understand the diagnostic and therapeutic algorithm for IBD
- To discuss the efficacy and safety of treatments for the management of IBD

# “Laura”

- 19 year old female college student
- 3 months history of bloody diarrhea, 5-8 times per day, 2 times at night.
- Intermittent crampy abdominal pain associated with a BM
- Non-smoker
- No family history of IBD
- Abdominal exam reveals **mild Lt LQ tenderness.**
- Physical exam is unremarkable
- Laboratory findings include **mild anemia (Hb 11, MCV 79).**  
Albumin is 3.4 g/dL

# “Laura”

- \_ You recommend a colonoscopy but Laura is reluctant to have an invasive procedure.
- \_ “Are there other tests that can help establish a diagnosis?”

# Non-invasive tests for IBD

## Fecal calprotectin and Lactoferrin

- Non-specific markers of gastrointestinal inflammation
- Does not differentiate from other inflammatory GI diseases
- Can also be used to monitor inflammation in those with established IBD

Fecal Calprotectin Cut-off	Sensitivity	Specificity
50 µg/g	0.92 (0.90-0.94)	0.60 (0.52-0.67)
100 µg/g	0.84 (0.80-0.88)	0.66 (0.59-0.73)
250 µg/g	0.80 (0.76-0.84)	0.82 (0.77-0.86)

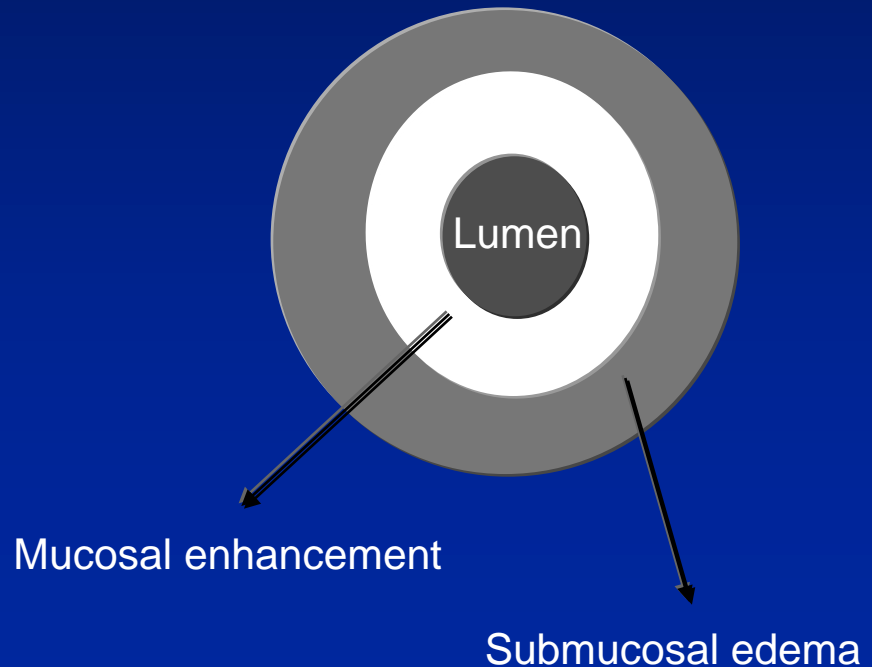
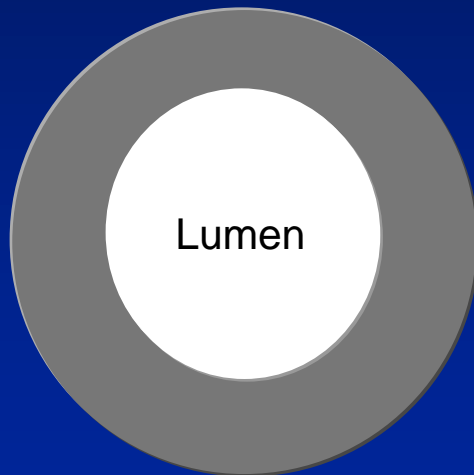
# “Laura”

- You suspect underlying inflammatory bowel disease and recommend a colonoscopy.
- Colonoscopy:
  - Confluent inflammation from anus to splenic flexure with erythema and granularity
  - Normal terminal ileum
- You decide to image her small bowel to rule out more proximal involvement given her abdominal pain

# Imaging in IBD

## CT enterography

- CT scan with IV contrast and large volumes of neutral oral contrast to achieve luminal distention
- Allows for better mucosal resolution (active inflammation), obstructive lesions (by distending lumen)
- Less useful for extra-luminal complications

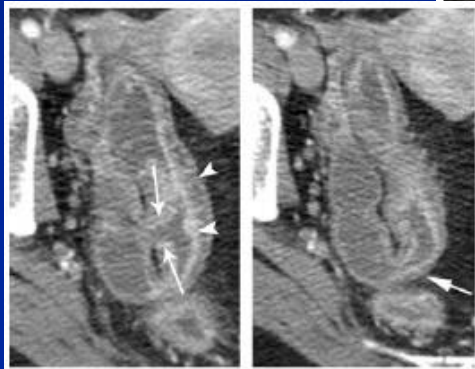
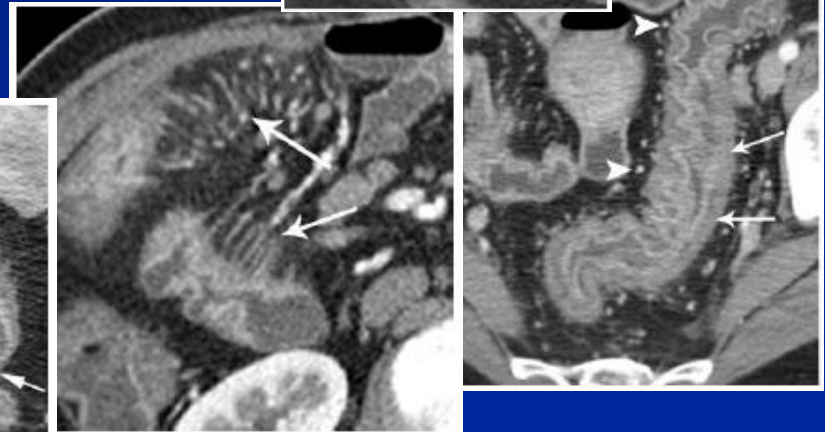
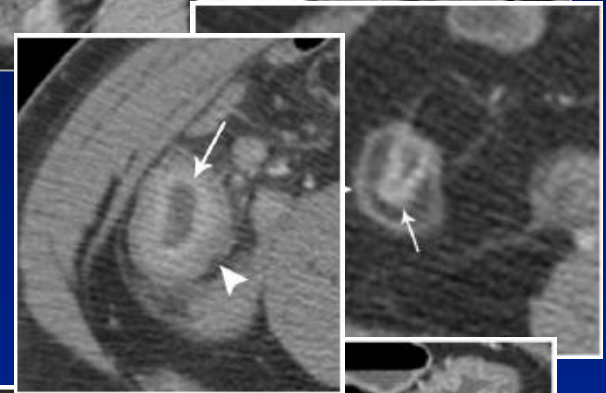
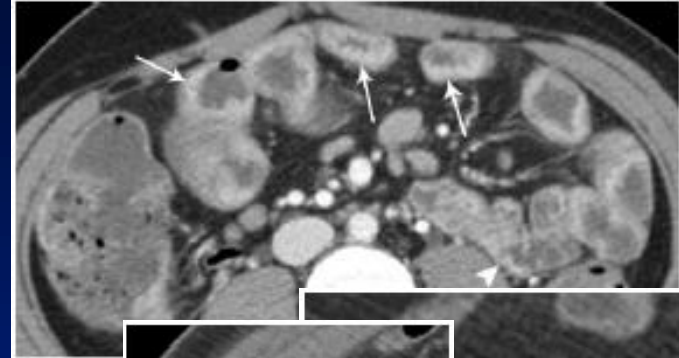




# Imaging in IBD

## CT enterography

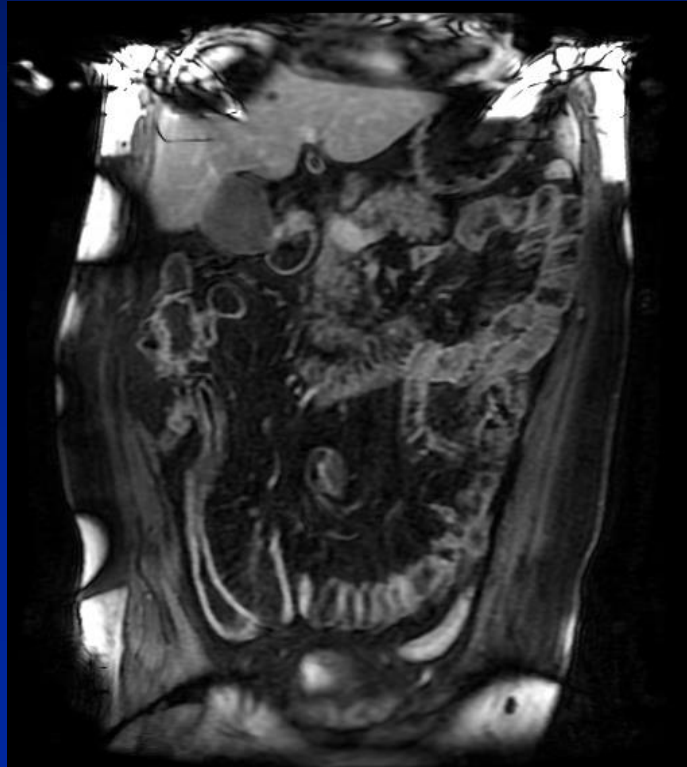
- Active inflammation
  - Mural hyperenhancement
  - Mural stratification
    - Acute (water), chronic (fat)
  - Engorged vasa recta
  - Fat stranding
- Fistulas



# Imaging in IBD

## MR enterography

- No radiation exposure
- Similar (or slightly superior) performance as CTE for assessment of active inflammation



## Management of IBD

# Therapeutic Goals in IBD

- Normal bowel function and improved quality of life (QOL)
- Induce remission rapidly
- Maintain steroid-free remission over time (deep remission)
- Modify long-term outcomes of the disease
  - Avoid hospitalization and surgery
  - Eliminate disability
  - Minimize exposure to steroids

# Management of IBD

## Probiotics and Antibiotics

### Probiotics

- No evidence of efficacy in Crohn's disease
- VSL#3 is effective in inducing and maintaining remission in mild-to-moderate ulcerative colitis

### Antibiotics

- Effective for treating abscesses and preventing post-operative recurrence in Crohn's disease (metronidazole)
- Single RCT demonstrated benefit for rifaximin in ileal Crohn's disease

## Management of IBD

# Fecal transplantation

- Four randomized controlled trials in ulcerative colitis
  - Three demonstrated benefit
    - Daily enema therapy x 6 weeks
    - Colonoscopic FMT once a week for 6 weeks
  - No benefit in a third trial with FMT via NG tube administration
- There likely is a donor effect
- No evidence of efficacy in Crohn's disease (except for case series)

## Management of IBD

# 5-Aminosalicylates

Mechanism: Local anti-inflammatory effect on the small intestine and colon

### Pros

- Asacol HD® (mesalamine), Lialda ®, Apriso®, sulfasalazine, balsalazide (colazal ®)
- \_ Available in oral and topical formulations (enemas, suppositories) for local therapy
- \_ No systemic immunosuppression
- \_ Effective in mild-to-moderate ulcerative colitis
- \_ Limited (No) efficacy in Crohn's disease

# Management of IBD

## Steroids, Immunomodulators

### Steroids

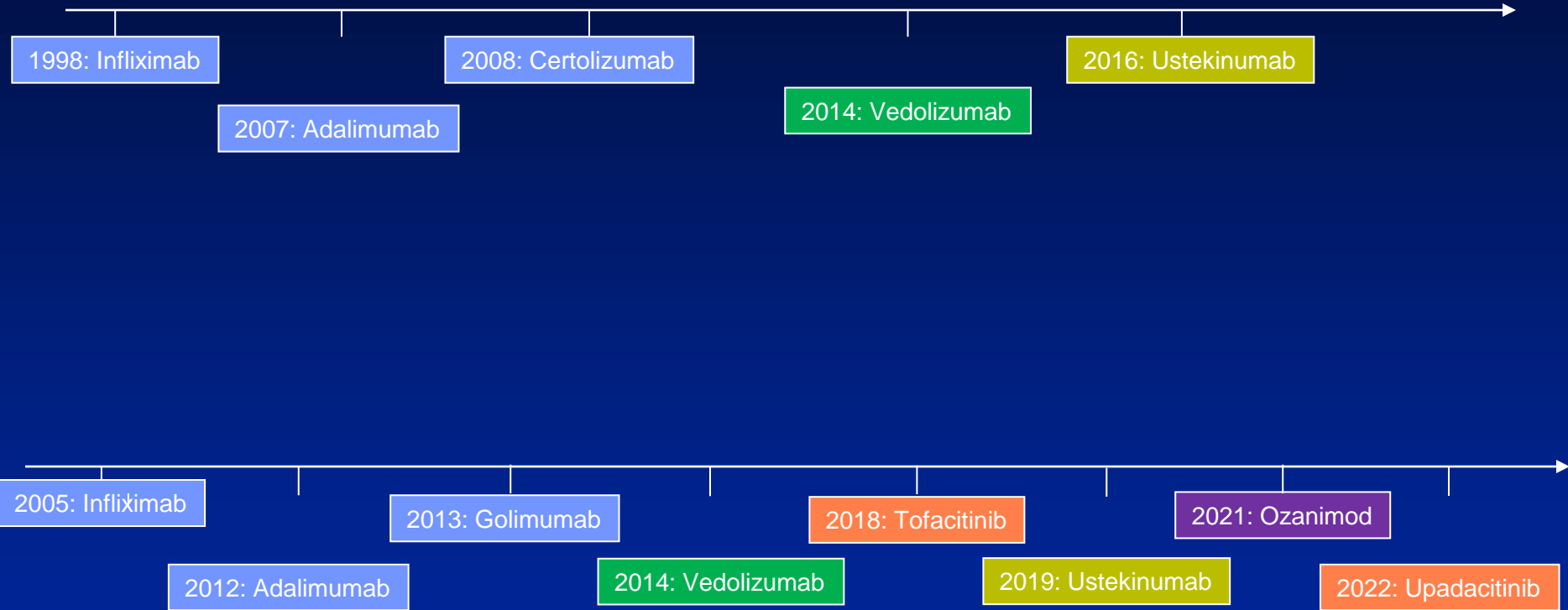
- Very effective for induction of remission
- Also available as controlled-release formulations - budesonide (Entocort®)
- No role in maintenance of remission
- Associated with significant long-term consequences

### Immunomodulators

- Azathioprine, 6-MP, methotrexate
- Effective for moderate severity disease
- Not effective for induction of remission (lag of 6-8 weeks of onset of action)

# Management of IBD

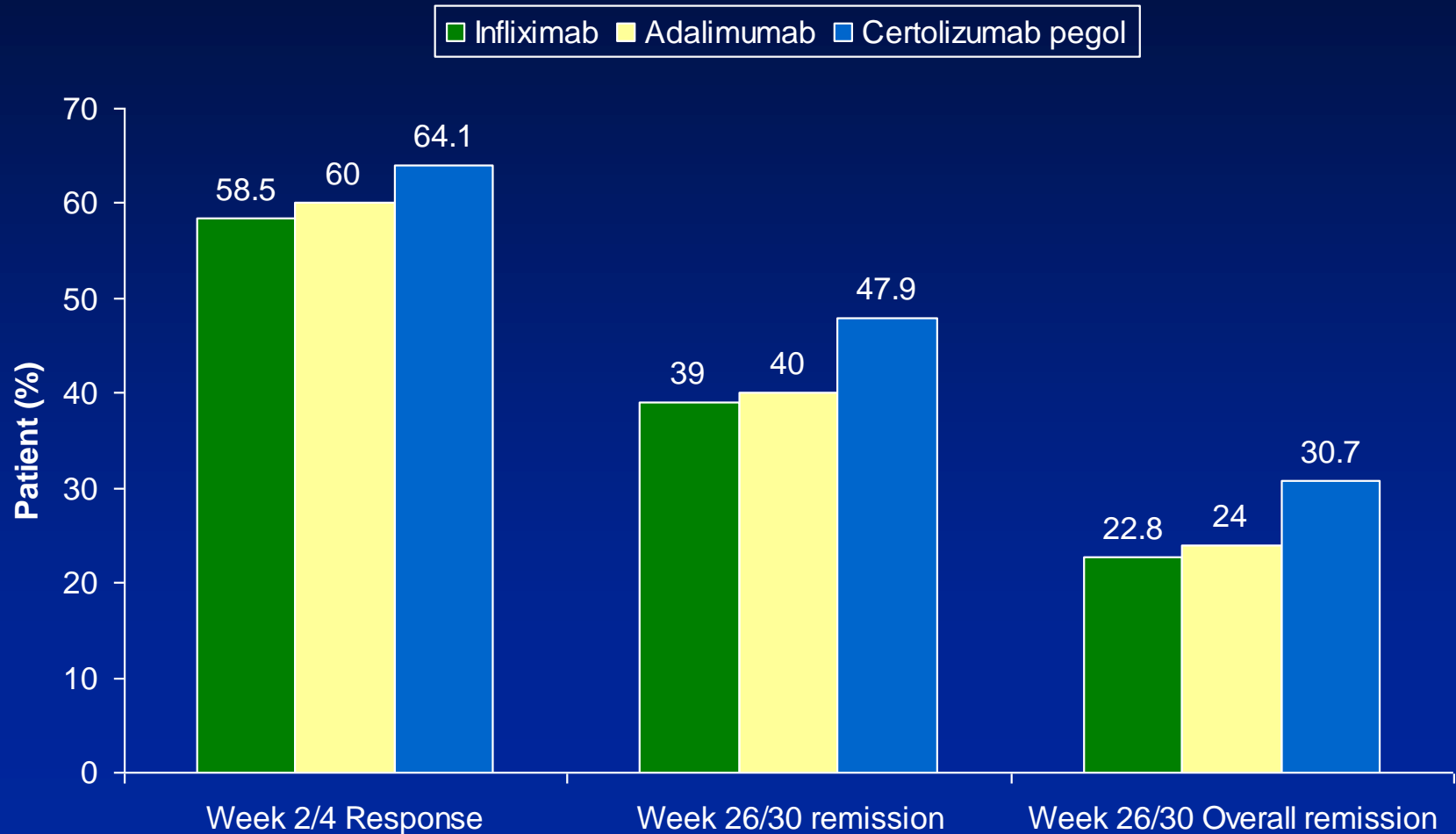
## Biologics and Small Molecules





# Management of IBD

## Anti-TNF biologics



# Management of IBD

## Other Biologics

### Vedolizumab:

- Monoclonal antibody against  $\alpha 4\beta 7$  integrin.
- Approved for use in both Crohn's disease and ulcerative colitis
- Gut-selective in its target  $\rightarrow$  no increase in risk of infections or malignancy

### Ustekinumab

- Anti-cytokine targeting IL12/IL23
- Relatively targeted in its action
- No increase in risk of infection or malignancy compared to placebo (in RCTs)

# Management of IBD

## Small molecules

### JAK inhibitors:

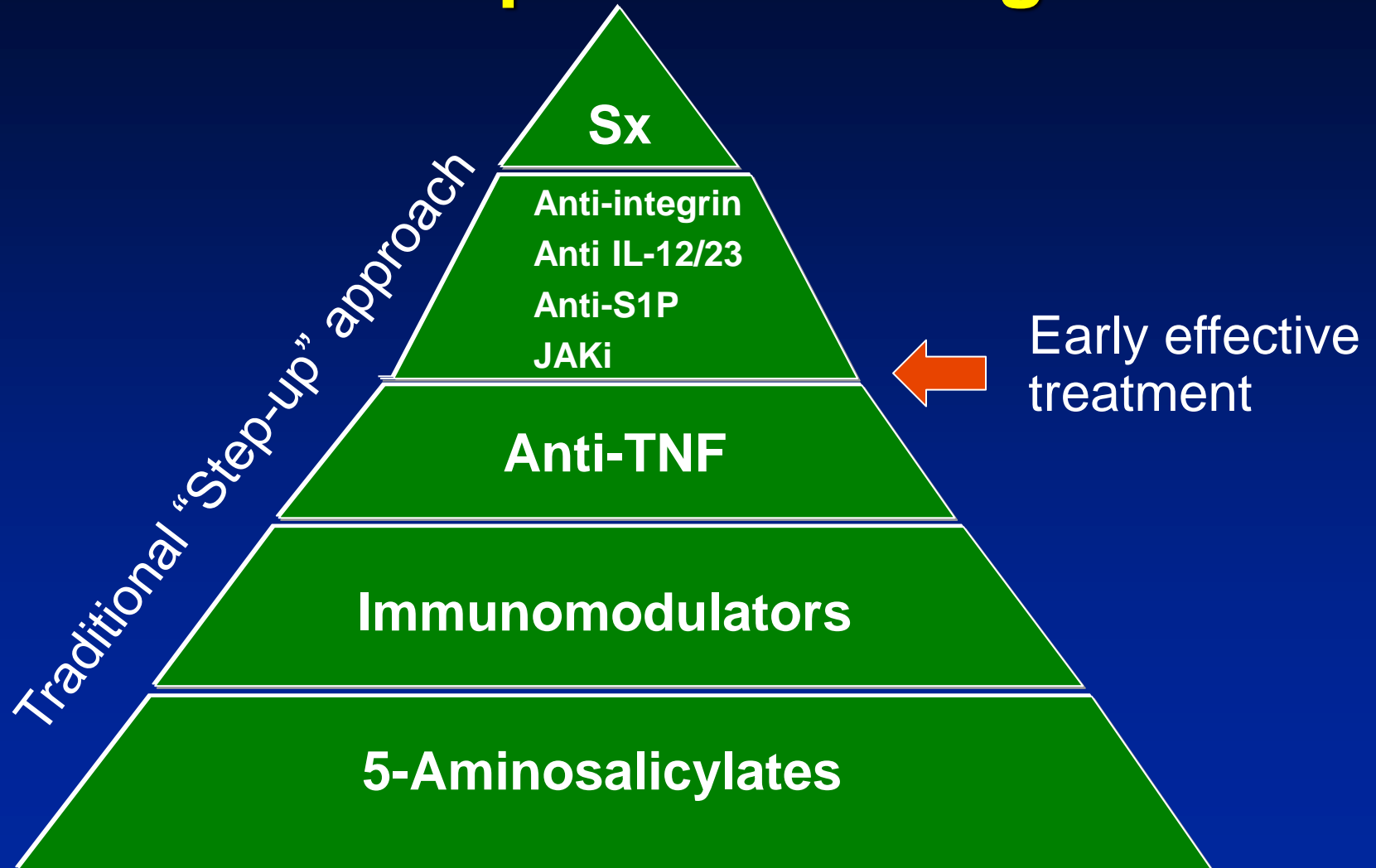
- Small molecule that inhibits Janus-kinase enzymes (Tofacitinib: JAK 1-3, TYK2; Filgotinib, upadacitinib: JAK1 selective inhibitors)
- Relative quick onset of action
- Increases risk of shingles, VTE and malignancy (when compared to anti-TNF)

### Ozanimod:

- S1P modulator; results in sequestration of lymphocytes in the lymph nodes
- Slight increase in risk of cardiac arrhythmias
- Interactions with SSRI and MAOI.

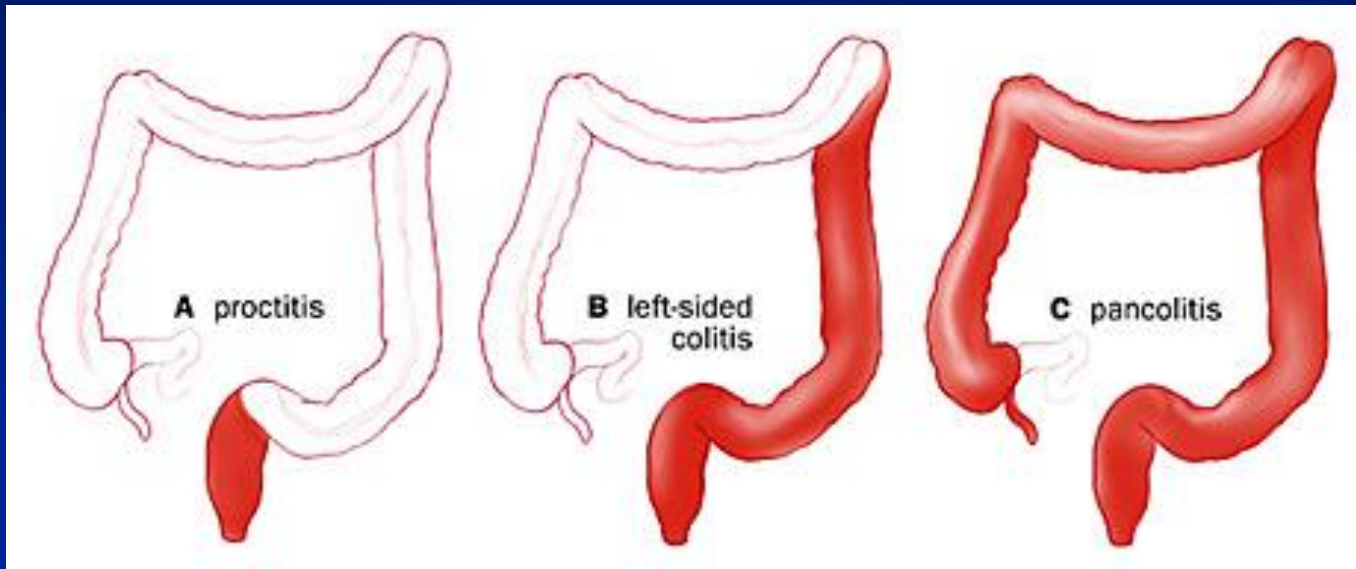
# Management of IBD

## New Therapeutic Paradigms

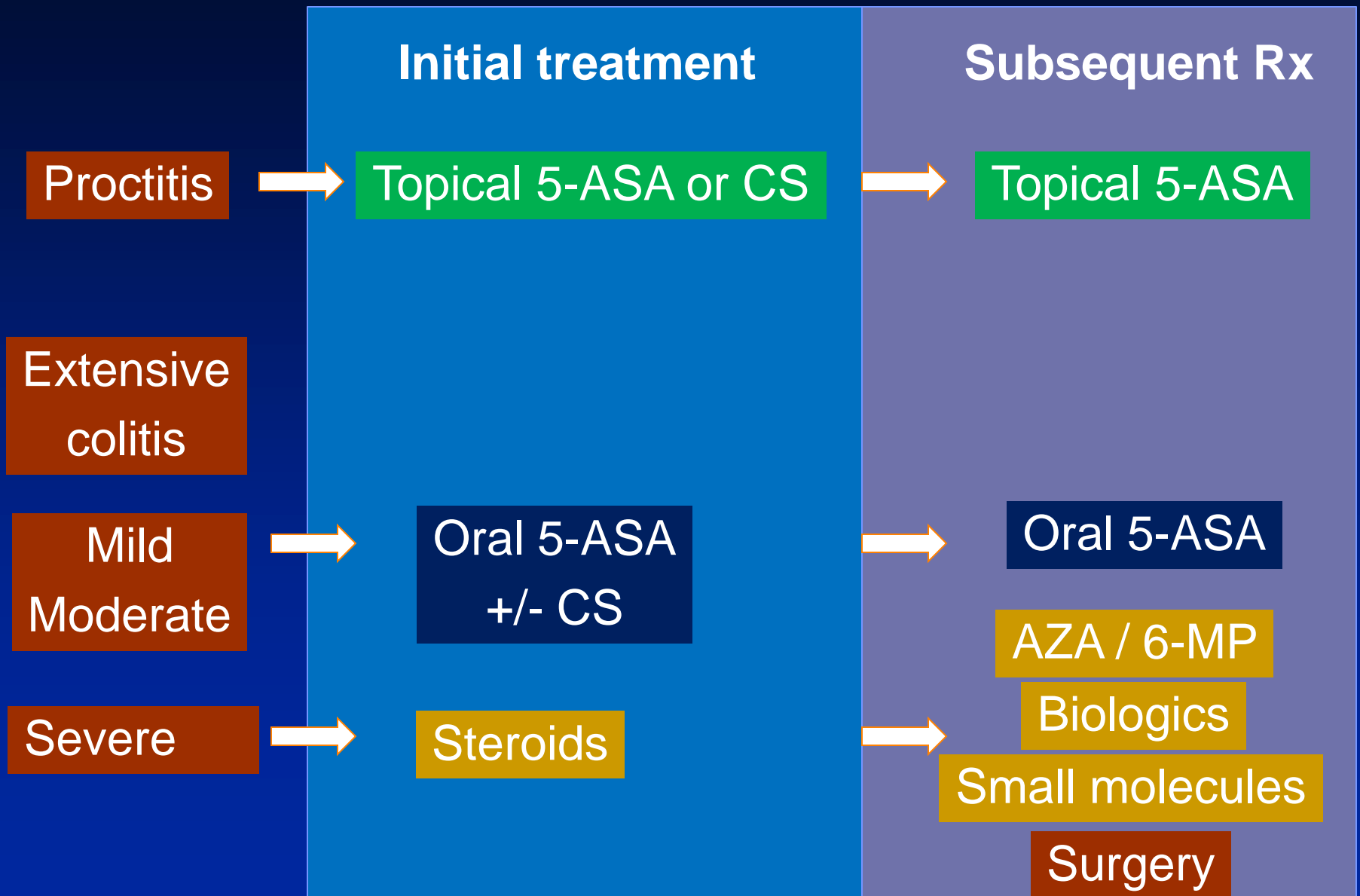


# Management of ulcerative colitis

Management of UC depends on (1) extent and (2) severity of disease



# Management of ulcerative colitis



# Management of IBD

## Complications of therapy

- \_ Unpredictable side-effects
  - \_ Drug hypersensitivity
  - \_ Pancreatitis (Azathioprine / 6-MP)
  - \_ Paradoxical flare (5-ASA)
  
- \_ “More” predictable side-effects
  - \_ Infections
  - \_ Cancer
    - Lymphoma: Approximately 5 in 10,000
    - Skin cancers (melanoma – anti-TNF; NMSC – thiopurines), Cervical cancer

# Pregnancy and IBD

- Crohn's disease and ulcerative colitis are not associated with reduced fertility (except with J-pouch)
- Disease activity at conception is an important determinant of patient outcome during pregnancy
- Most medications are safe during pregnancy (except methotrexate; steroids may cause cleft lip / palate)
- Slight increase in LBW and SGA but otherwise comparable fetal outcomes



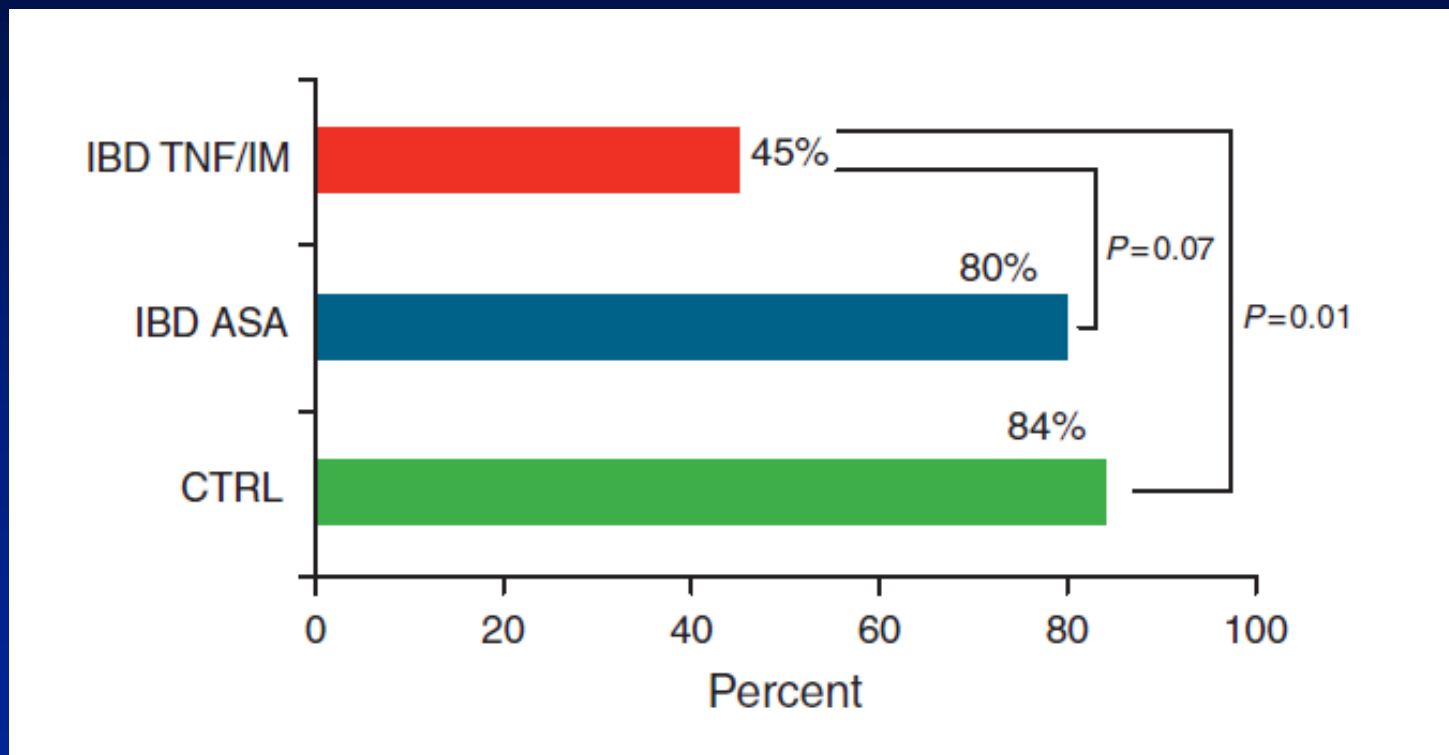
## Health maintenance in IBD

# Colon cancer surveillance

- Ulcerative colitis (not proctitis) and colonic Crohn's disease are at increased risk for colon cancer.
  - Estimated risk at 20 years: 10%
- Recommended surveillance:
  - Begin at 8 years after diagnosis
  - Every 1 – 3 years with a colonoscopy
  - Newer techniques include chromoendoscopy
  - Fecal DNA is under study
  - No clear guidance on when to stop → depending on age and comorbidity

# Health maintenance in IBD

## Vaccination



Melmed GY. Am J Gastroenterol 2006 Aug;101(8):1834-40.

Melmed GY. Am J Gastroenterol. 2010 Jan;105(1):148-54.

# Summary

## \_ Advances in diagnosis

- Non-invasive markers of inflammation
- Markers of prognosis
- Newer imaging modalities

## \_ Changing therapeutic paradigms

- Recognition of new goals of treatment
- New paradigms of treatment (“Early” / “Top-down”)
- Treat to target approach

## \_ “Comprehensive” IBD care



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