OPENING THE WINDOW OF OPPORTUNITY

Strategies for Successful Treatment and Management of Patients with Crohn's Disease

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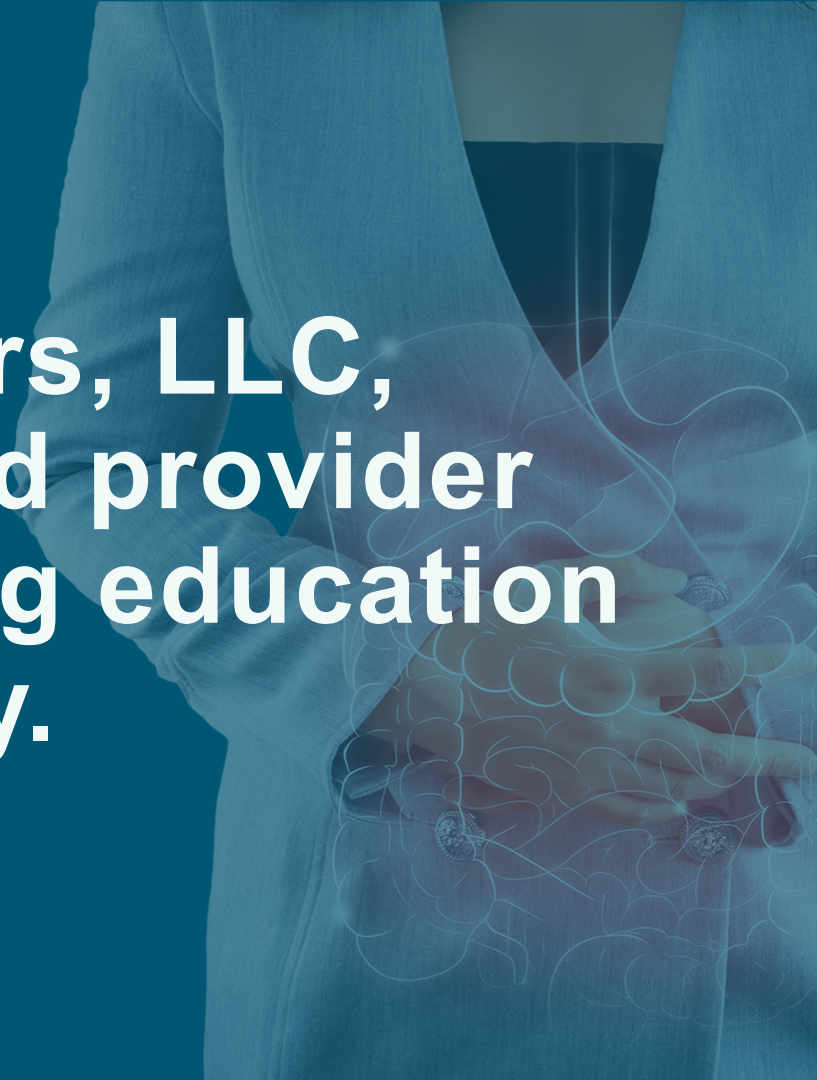

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What's New in Biologic Therapies in Crohn's Disease

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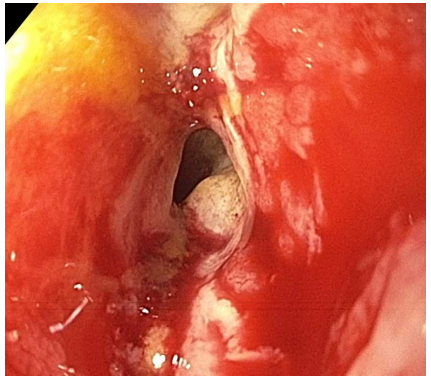
Differentiate biologic therapies in Crohn's disease (CD) based on their mechanisms of action (MOAs), efficacy, safety, and ability to induce rapid and durable treatment response.

LEARNING OBJECTIVE 1

Patient Case: Caitlin

- 24-year-old woman with intermittent, severe right-sided abdominal pain for the past year; increased frequency of bowel movements (BMs) (up to 5x daily); no blood visualized
- She has lost approximately 20 lbs
- She has had increasing abdominal distension and pain after eating in the past several weeks
- Significant iron deficiency anemia, albumin is 3.3
- Computed tomography (CT) done through a local urgent care center showed short segment stricture in the distal terminal ileum with pre-stenotic dilation

Case: Caitlin



- You perform colonoscopy:
  - Colon is normal
  - Severe stricture in the terminal ileum, not traversed
  - Path: severe chronic active ileitis
- She tells you that she is very interested in pregnancy
- She travels with work and infusions will be difficult

Audience Response

At this point, what would would recommend for Caitlin?

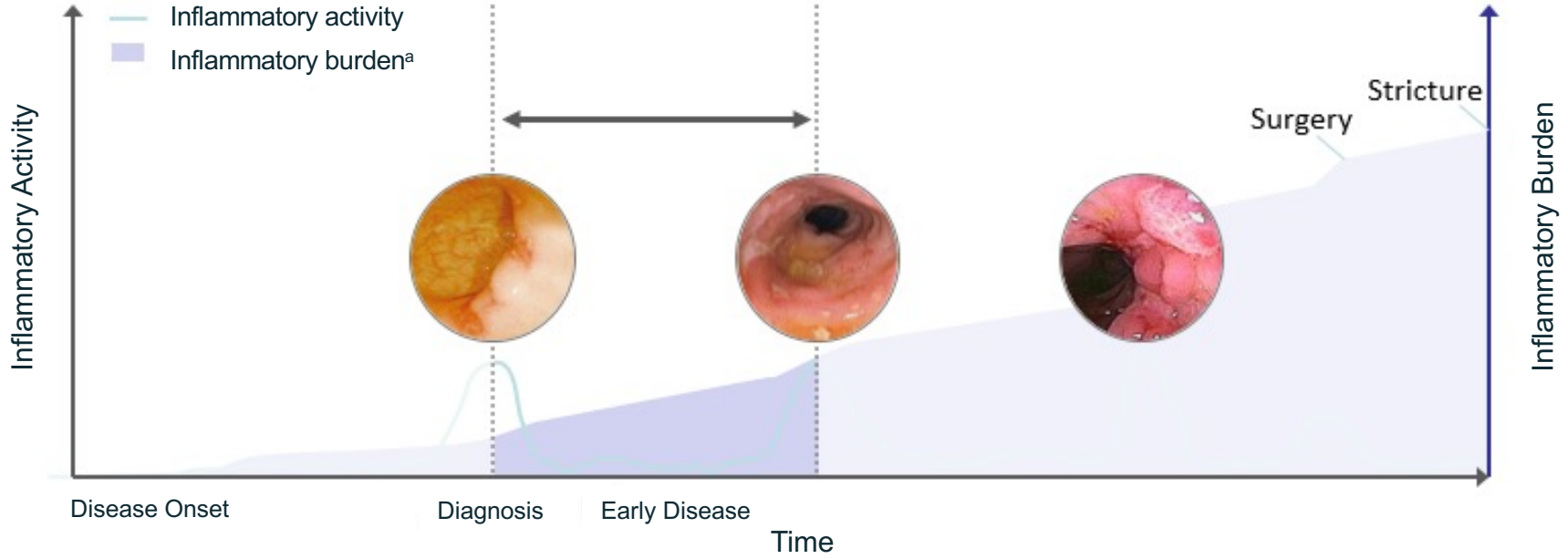
A. Surgical resection
B. Infliximab monotherapy
C. Adalimumab + azathioprine
D. Ustekinumab
E. Vedolizumab
F. I’m not sure

Outline: What's New in Biologic Therapy in CD

- Treatment targets in CD, beyond symptoms
  - A window of opportunity
- Therapies for moderate to severe CD
- Guideline recommendations
- Positioning of therapies
  - Extrapolation of data
- Safety
  - Pregnancy data
- Unmet needs for CD

Window of Opportunity in CD?

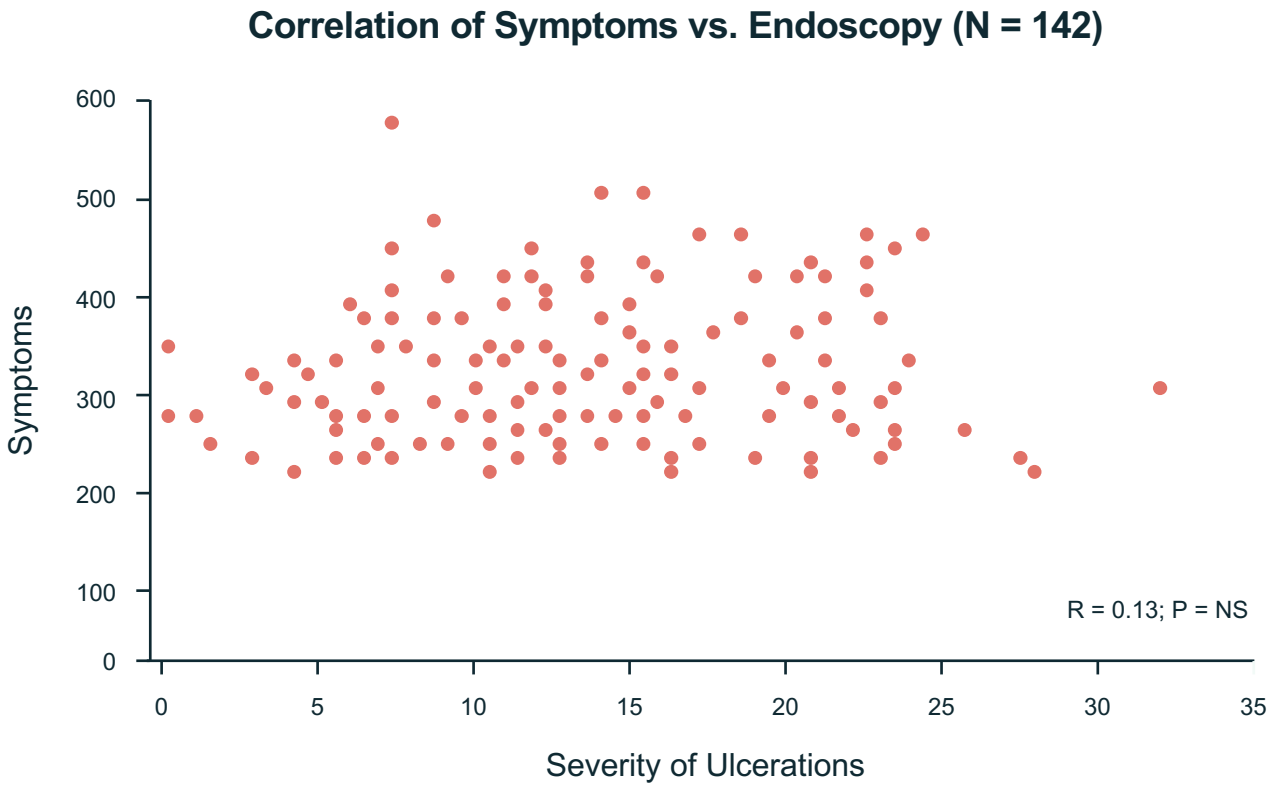
There may be a window of opportunity to minimize risk of permanent bowel damage



[a]Disease activity is a cross-sectional snapshot at one moment in time.
Inflammatory burden includes longitudinal and historical factors of disease severity, providing a more complete picture of disease course.[5]

1. Colombel JF, et al. *Gastroenterology.* 2017;152(2):351-361. 2. Modified graph from Pariente B, et al. *Inflamm Bowel Dis.* 2011;17(6):1415-1422. 3. Torres J, et al. *J Crohns Colitis.* 2016;10(12):1385-1394. 4. Torres J, et al. *Lancet.* 2017;389(10080):1741-1755. 5. Siegel CA, et al. *Gut*. 2018;67(2):244-254.

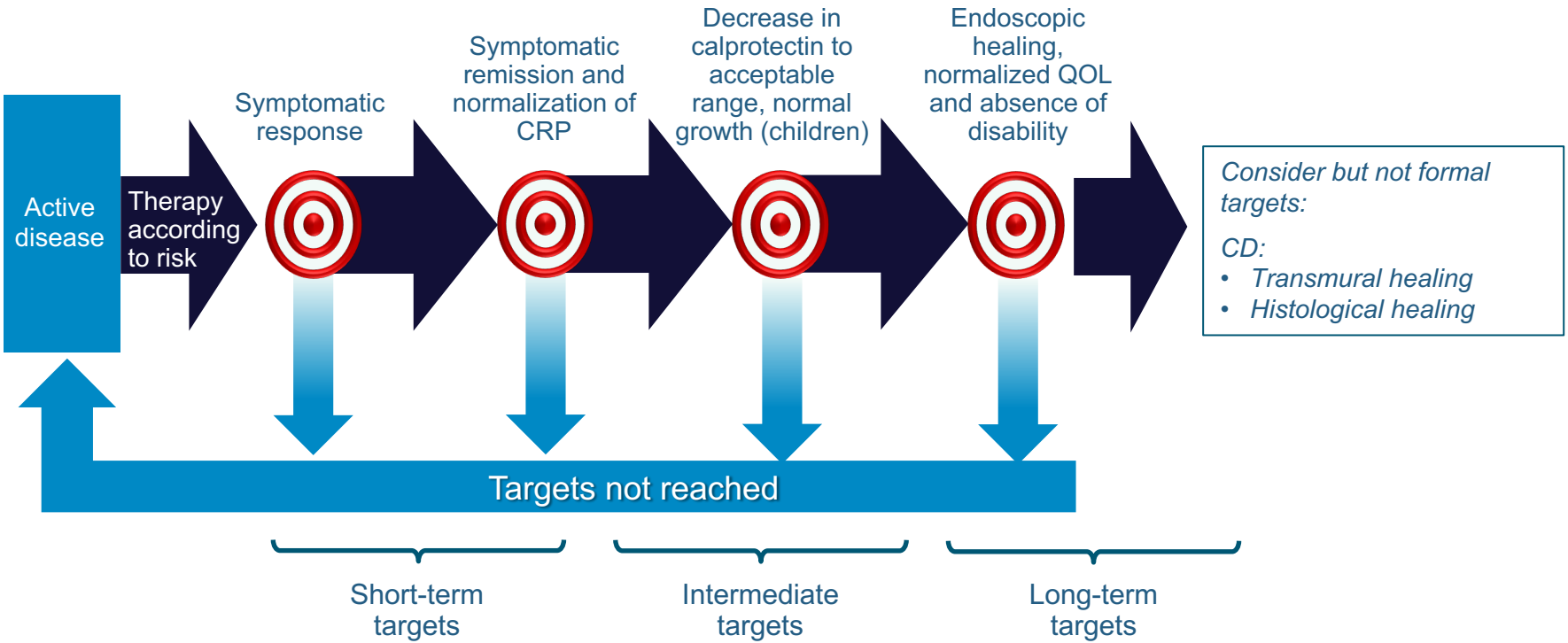
Symptoms Often Do Not Correlate with Inflammation



NS = not significant

Modigliani R, et al. *Gastroenterology*. 1990;98(4):811-818.

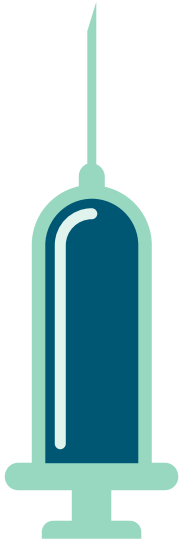
STRIDE-2: Treatment Targets in CD



CRP = C-reactive protein

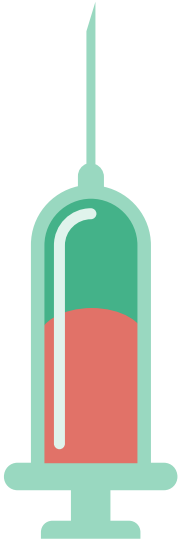
Turner D, et al. *Gastroenterology*. 2021;160(5):1570-1583.

Currently Available Biologics in CD



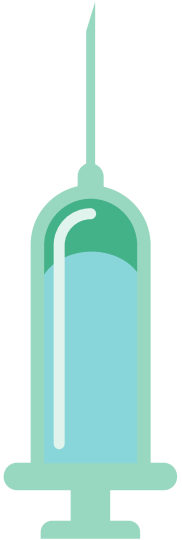
Anti-TNFs

Infliximab
Adalimumab
Certolizumab pegol



Anti-alpha4beta7 integrin antibody

Vedolizumab



Anti-p40 (IL-12/23) antibody

Ustekinumab

IL = interleukin; TNF = tumor necrosis factor

Options for INDUCTION Therapy: Moderate to Severe Disease

- **Oral steroids** → only for short-term induction agents for inflammatory CD
- **Anti-TNF agents** → steroid-resistant or thiopurine or methotrexate-refractory disease
- **Combination therapy with infliximab** → more effective than monotherapy with thiopurines or infliximab for ***NAÏVE*** patients
- **Anti-integrin** therapy → vedolizumab with or without immunomodulator
- **Ustekinumab** → for patients who failed steroids, thiopurines, methotrexate, anti-TNFs, or anti-TNF naïve

Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113:481-517.

Options for MAINTENANCE Therapy: Moderate to Severe Disease

- **Thiopurines/methotrexate** → steroid-induced remission
  - **STEROID-DEPENDENT → consider thiopurines/methotrexate with anti-TNFs**
- **Anti-TNFs** → maintain anti-TNF-induced remission
  - **COMBINATION therapy** recommended with thiopurines or methotrexate due to **IMMUNOGENICITY** and **LOSS OF RESPONSE**
- **Vedolizumab** → maintain vedolizumab-induced remission
- **Ustekinumab** → maintain ustekinumab-induced response

Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113:481-517.

What Do We Know About Sequencing or Positioning?

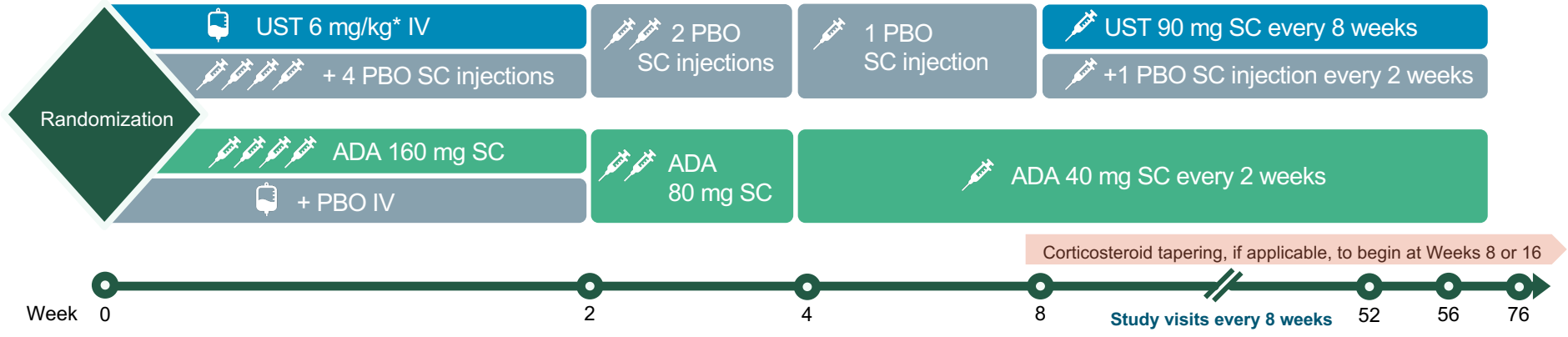
- Until now (SEAVUE), no head-to-head RCTs to demonstrate comparative efficacy in CD
- What data do we have now for positioning?
  - Reliance on subgroup analyses (SGA) in RCTs, real world evidence (RWE), and network meta-analysis (NMA)
- After failure of first TNFi, second-line biologics less effective, including second-line TNFis (SGA)
  - Ustekinumab still effective after failing ≥ 1 TNFi in CD[1] (SGA)
  - Ustekinumab also effective after failing vedolizumab[2] (SGA)
  - TNFi seems effective after failing vedolizumab[3] (RWE)
  - Vedolizumab is less effective after failing TNFi in CD[4] (RWE) and may have longer onset of effect in CD after TNFi failure[5] (RCT)

RCT = randomized, controlled trial; TNFi = TNF inhibitor

1. Feagan BG, et al. *N Engl J Med*. 2016;375:1946-1960. 2. Kassouri L, et al. *Dig Live Dis.* 2020;52(10):1148-1155. 3. Bressler B, et al. Presented at: American College of Gastroenterology Annual Meeting; Oct. 25-30, 2019; San Antonio, TX. Abstract 40. 4. Dulai P, et al. *Am J Gastroenterol*. 2016;111:1147-1155. 5. Sands BE, et al. *Gastroenterology.* 2014;147:618-627.

SEAVUE Study Design

Multicenter, randomized, blinded, active-controlled study

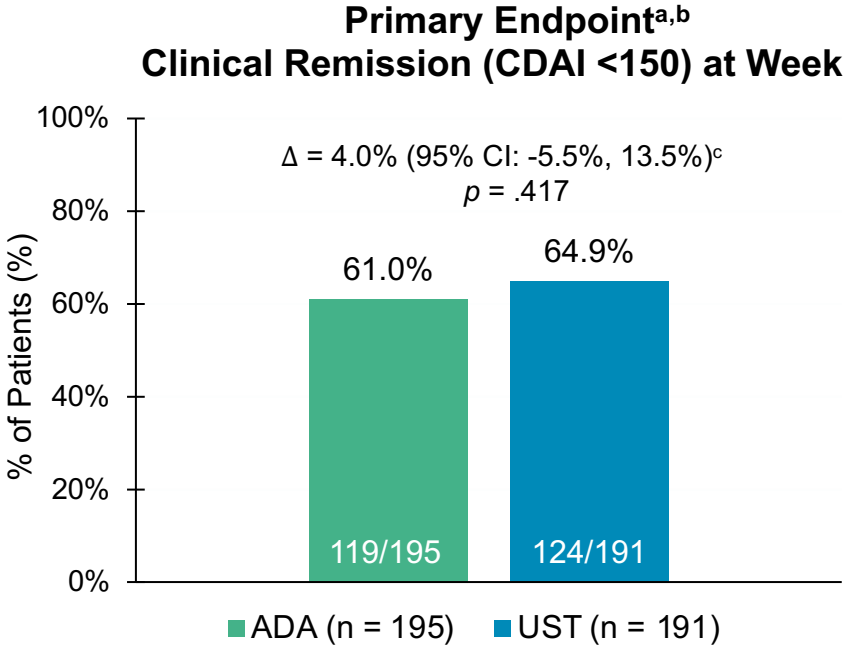


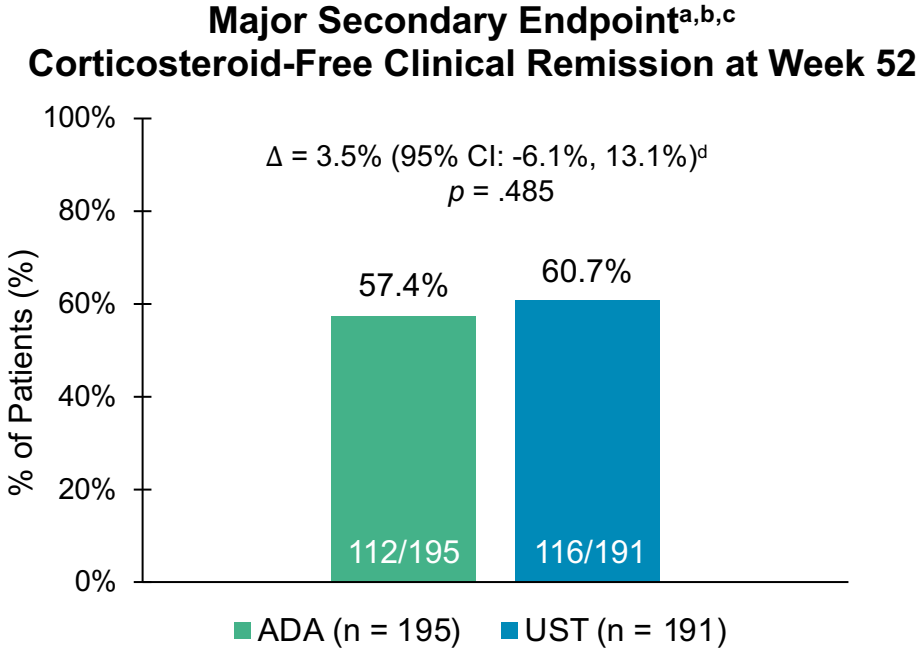
Adalimumab (ADA), n = 195
Ustekinumab (UST), n = 191
*UST 260 mg (weight ≤ 55 kg); UST 390 mg (weight > 55 kg and ≤ 85 kg); UST 520 mg (weight > 85 kg)

IV = intravenous; PBO = placebo; SC = subcutaneous

Sands B, et al. Ustekinumab versus adalimumab for induction and maintenance therapy in moderate-to-severe Crohn's disease: the SEAVUE study. Presented at Digestive Disease Week 2021; May 23, 2021.

SEAVUE Results





[a]Patients who had a prohibited CD-related surgery had prohibited concomitant medication changes, or discontinued study agent due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in clinical remission; [b]Patients who had insufficient data to calculate the Crohn's disease activity index (CDAI) score at the designated analysis timepoint are considered not to be in clinical remission; [c]Patients who had a missing data value in corticosteroid use at designated analysis timepoint had their last value carried forward; [d]The confidence intervals (Cis) were based on the Wald statistic with Mantel-Haenszel weight; NOTE: not receiving corticosteroids at Week 52 is defined as corticosteroid free for ≥ 30 days prior to Week 52.

Sands B, et al. Ustekinumab versus adalimumab for induction and maintenance therapy in moderate-to-severe Crohn's disease: the SEAVUE study. Presented at Digestive Disease Week 2021; May 23, 2021.

How Do We Put Together the Puzzle of Therapy Selection?

DRUG

Efficacy

Indication
Rapidity of onset
Durability
Pharmacokinetics/TDM
Combination vs. monotherapy
Positioning and sequence

Safety

Infection
Cancer
Specific concerns by agent or mechanism

PATIENT

Individual Characteristics

Ages, stages, comorbidities, and preferences

Disease Characteristics

CD vs. UC
Disease behavior/complication
Disease severity
Early vs. late
EIMs
Prior treatment success or failure

EIMs = extraintestinal manifestations; TDM = therapeutic drug monitoring

TNF Inhibitors

Considerations

PROS

- Rapid onset of effect
- Proven efficacy in fistulizing CD
- Proven efficacy in hospitalized acute IBD
- Effective for a variety of EIMs
- Relative abundance of safety data in pregnancy
- TDM well accepted (reactive)
- Robust data in post-operative setting for CD

CONS

- Infection risk
- Contraindicated for those with prior lymphoma, active cancer
- Psoriasiform and other skin eruptions
- Contraindicated in congestive heart failure, demyelinated disorders
- Requires careful screening for tuberculosis, hepatitis B
- Combination therapy preferred at least in 1st year

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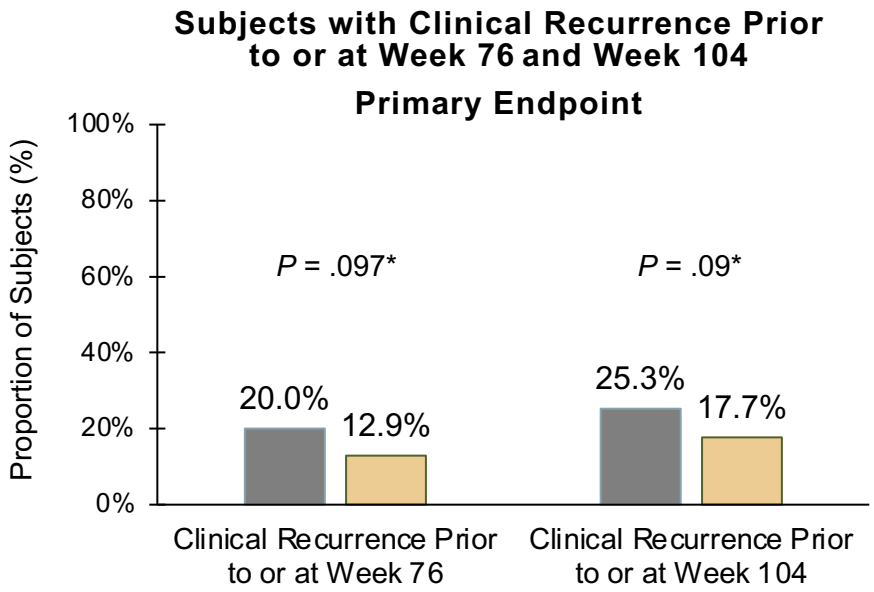
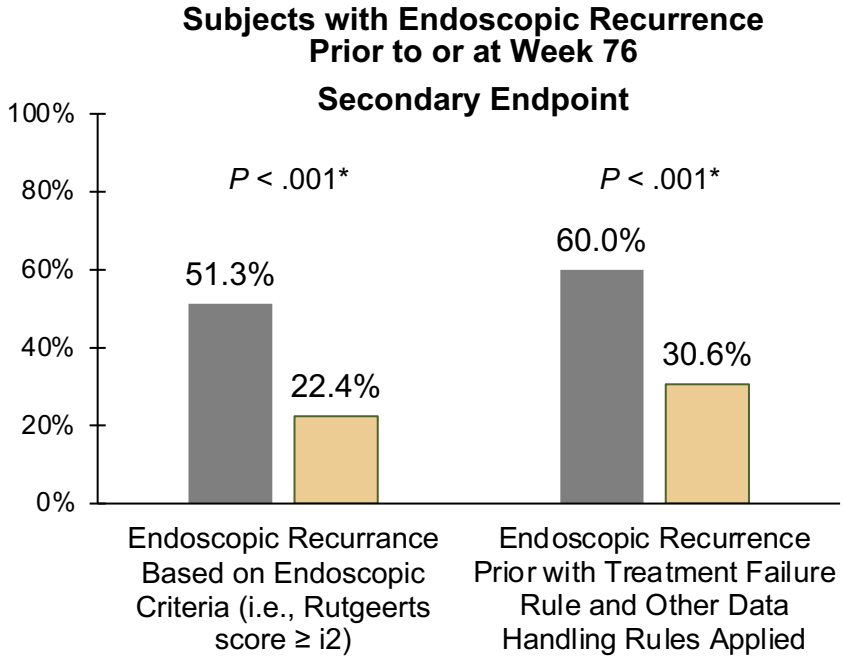
CME OUTFITTERS

PREVENT: Impact of Infliximab on Clinical and Endoscopic Recurrence





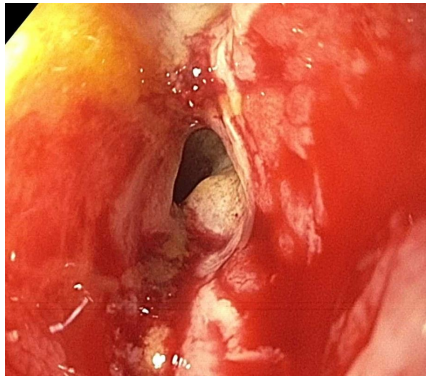
P values based on the Cochran-Mantel-Haenszel chi-square test stratified by the number of risk factors for recurrence of active CD (1 or > 1) and baseline use (yes/no) of an immunosuppressive (i.e., azathioprine, 6-mercaptopurine, or methotrexate)

*Nominal *p* value

Regueiro M, et al. *Gastroenterology*. 2016;150(7):1568-1578.

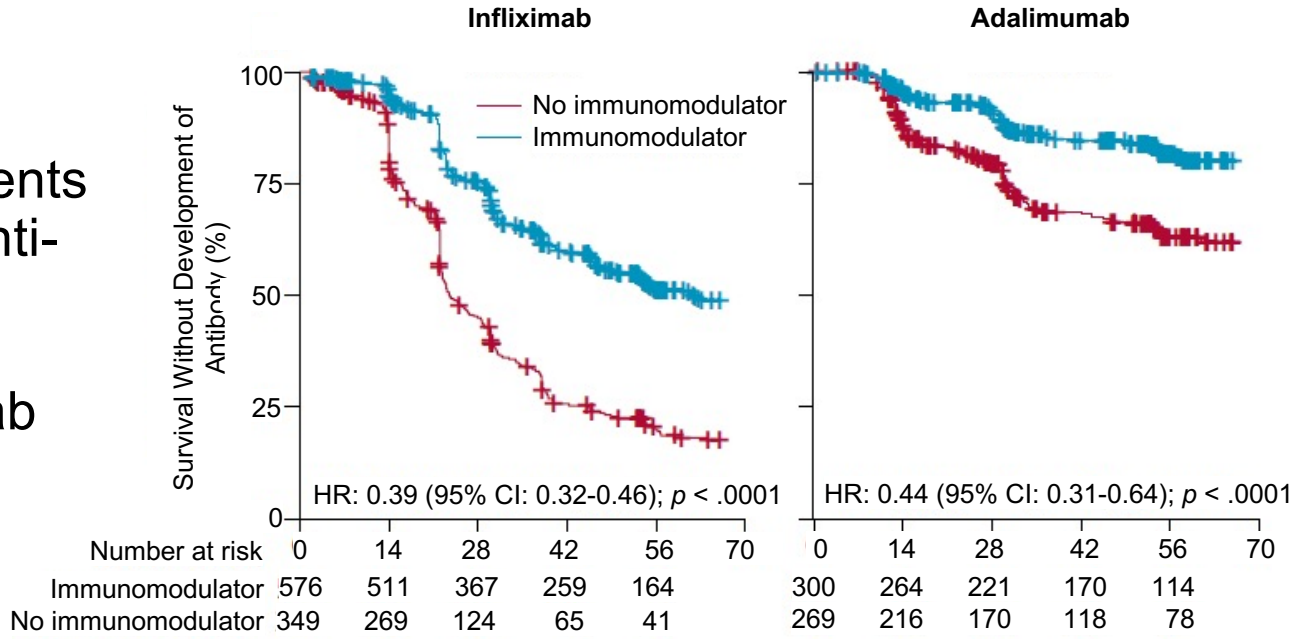
Case: Caitlin

- You perform colonoscopy:
  - Colon is normal
  - Severe stricture in the terminal ileum, not traversed
  - Path: severe chronic active ileitis



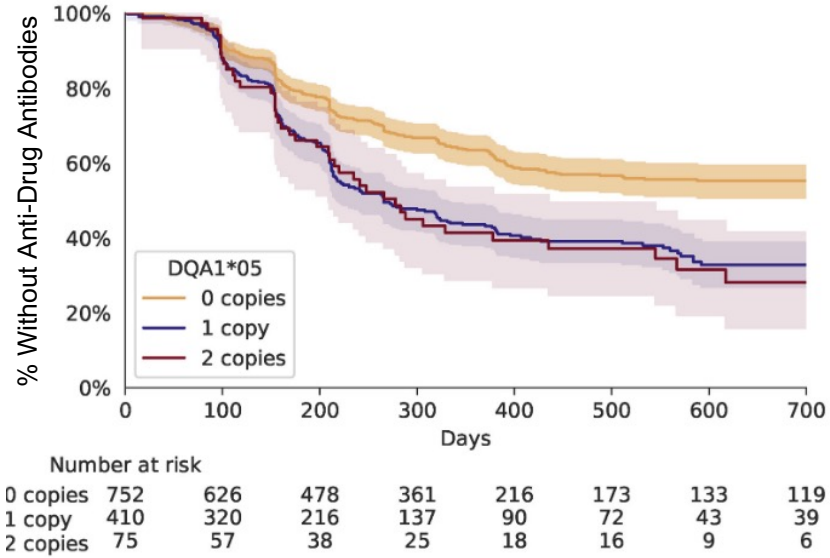
PANTS: Personalized Anti-TNF Therapy in CD

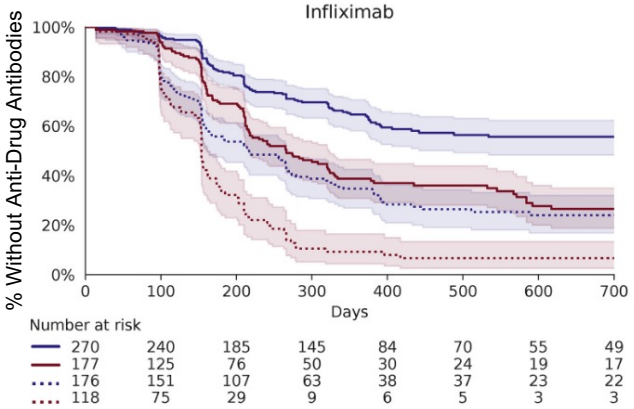
- High rates of immunogenicity: Proportion of patients who developed anti-drug antibodies: 62.8% infliximab, 28.5% adalimumab

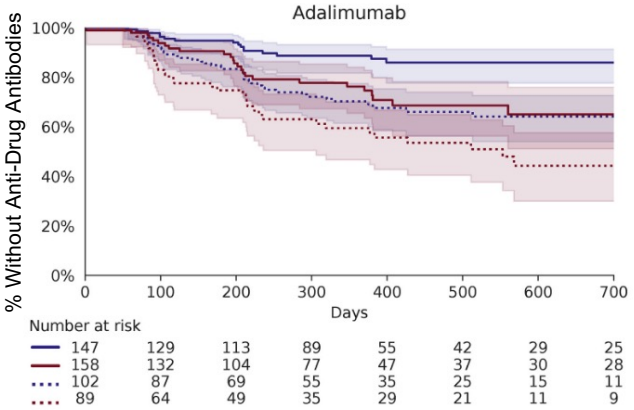


Kennedy NA, et al. *Lancet Gastroenterol Hepatol.* 2019;4(5):341-353.

PANTS: HLA-DQA1*05 and Immunogenicity







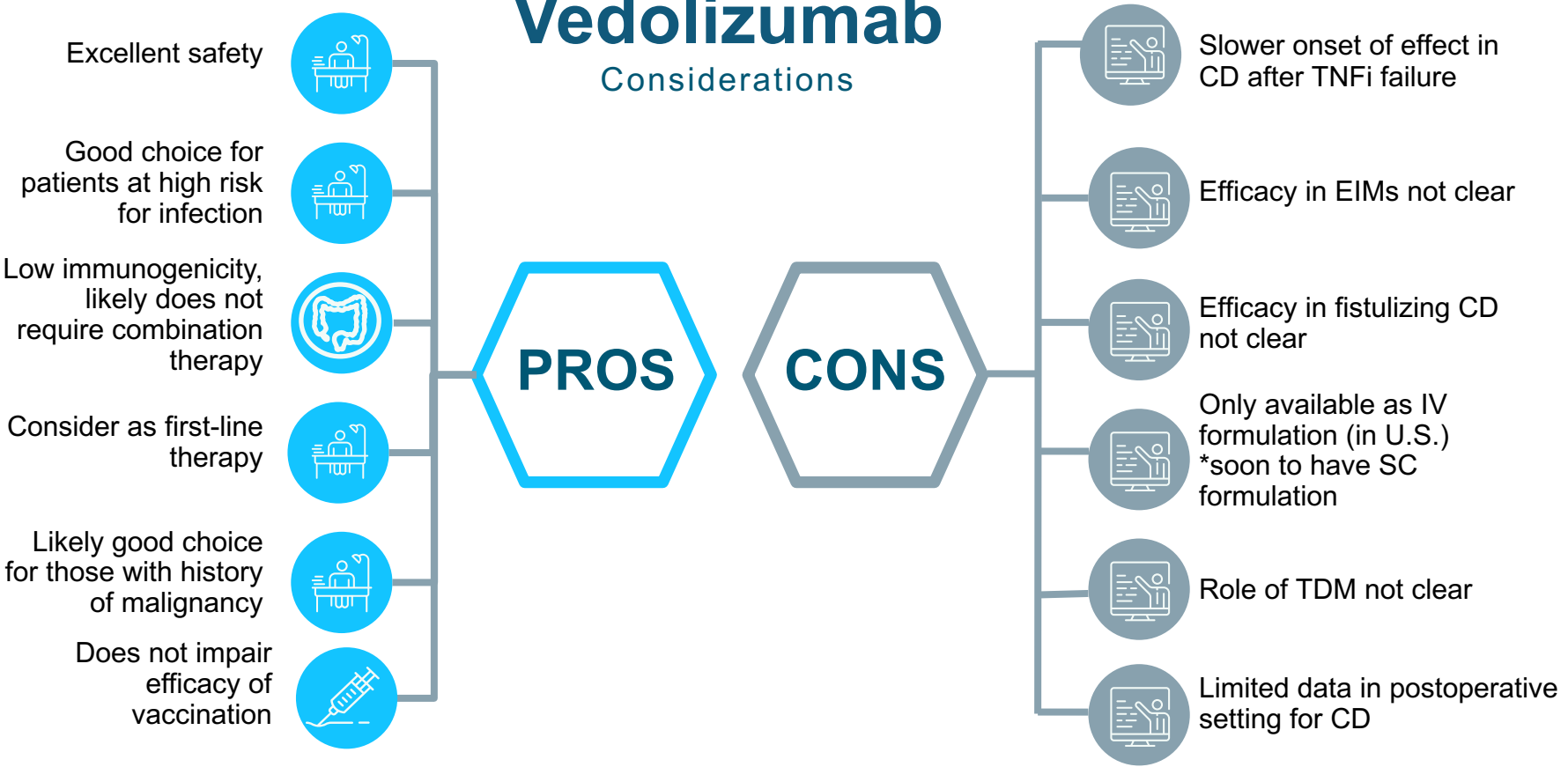
Blue = non-carriers
Red = carriers
Dotted = monotherapy
Solid = combination therapy

Sazanovs A, et al. *Gastroenterology*. 2020;158(1):189-199.

CME OUTFITTERS

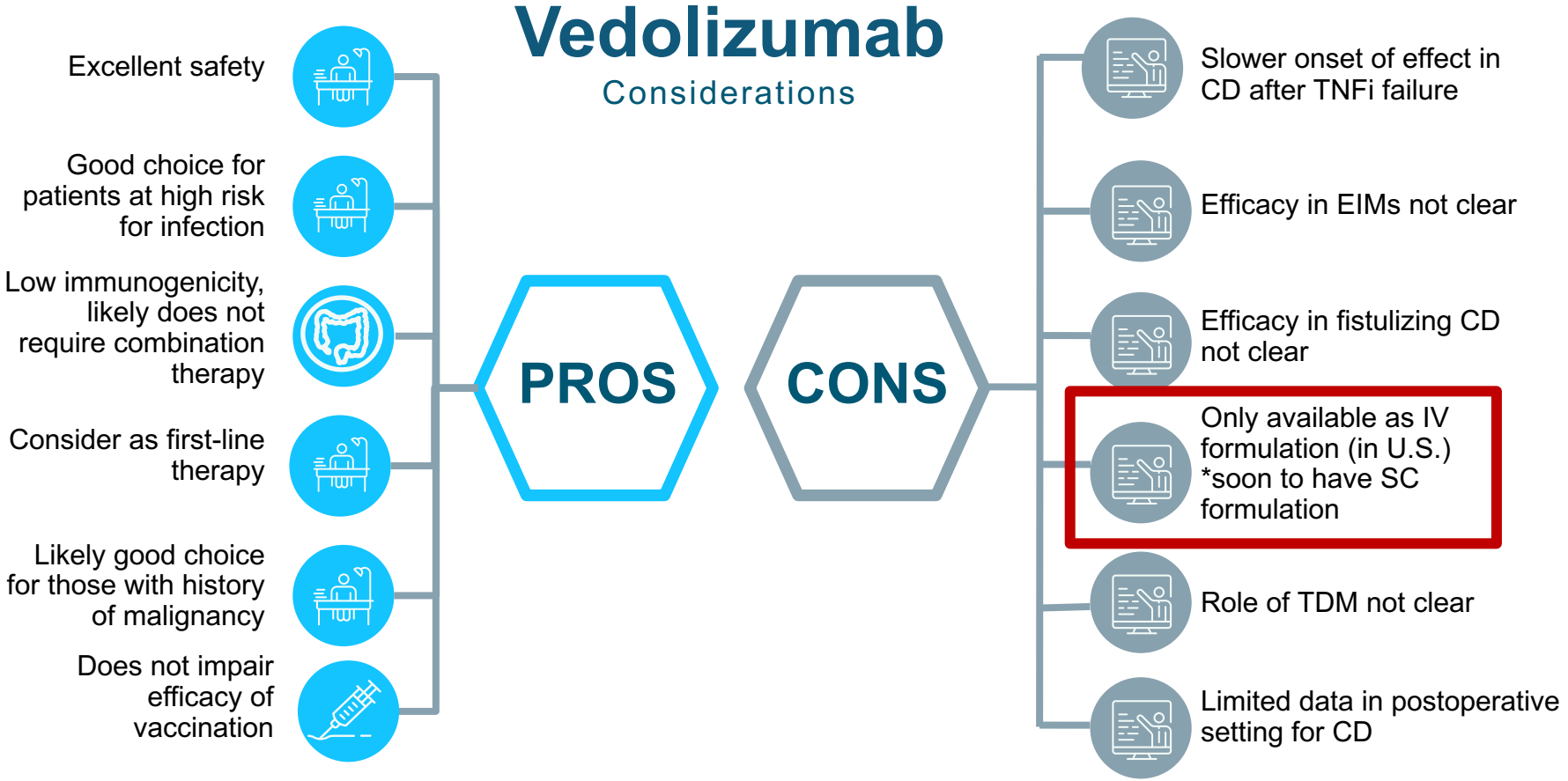
Vedolizumab

Considerations



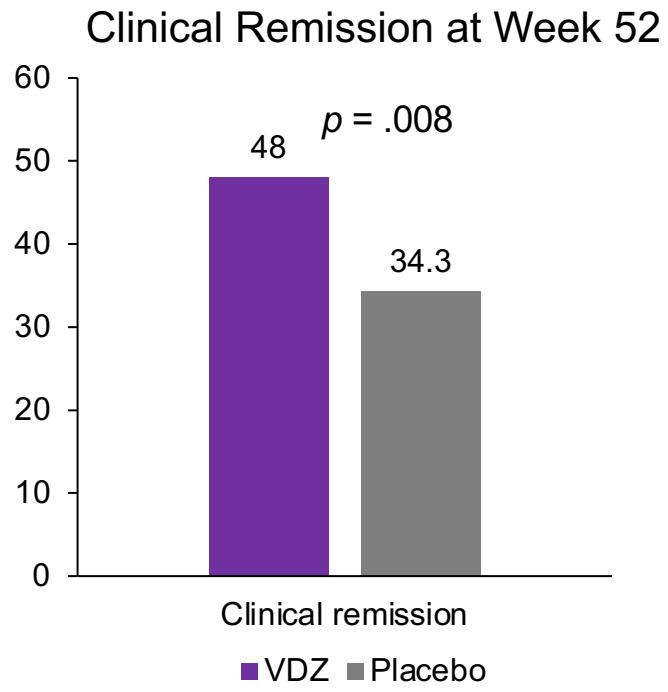
Vedolizumab

Considerations



VISIBLE 2: Vedolizumab Formulation in CD

- Phase III DB-RCT, 644 participants
- Patients with moderate to severe CD achieving response at week 6 (after two-dose, open-label IV induction), randomized to vedolizumab vs. placebo for 52 weeks
- Clinical remission: vedolizumab 48%, placebo 34.3% (p = .008)

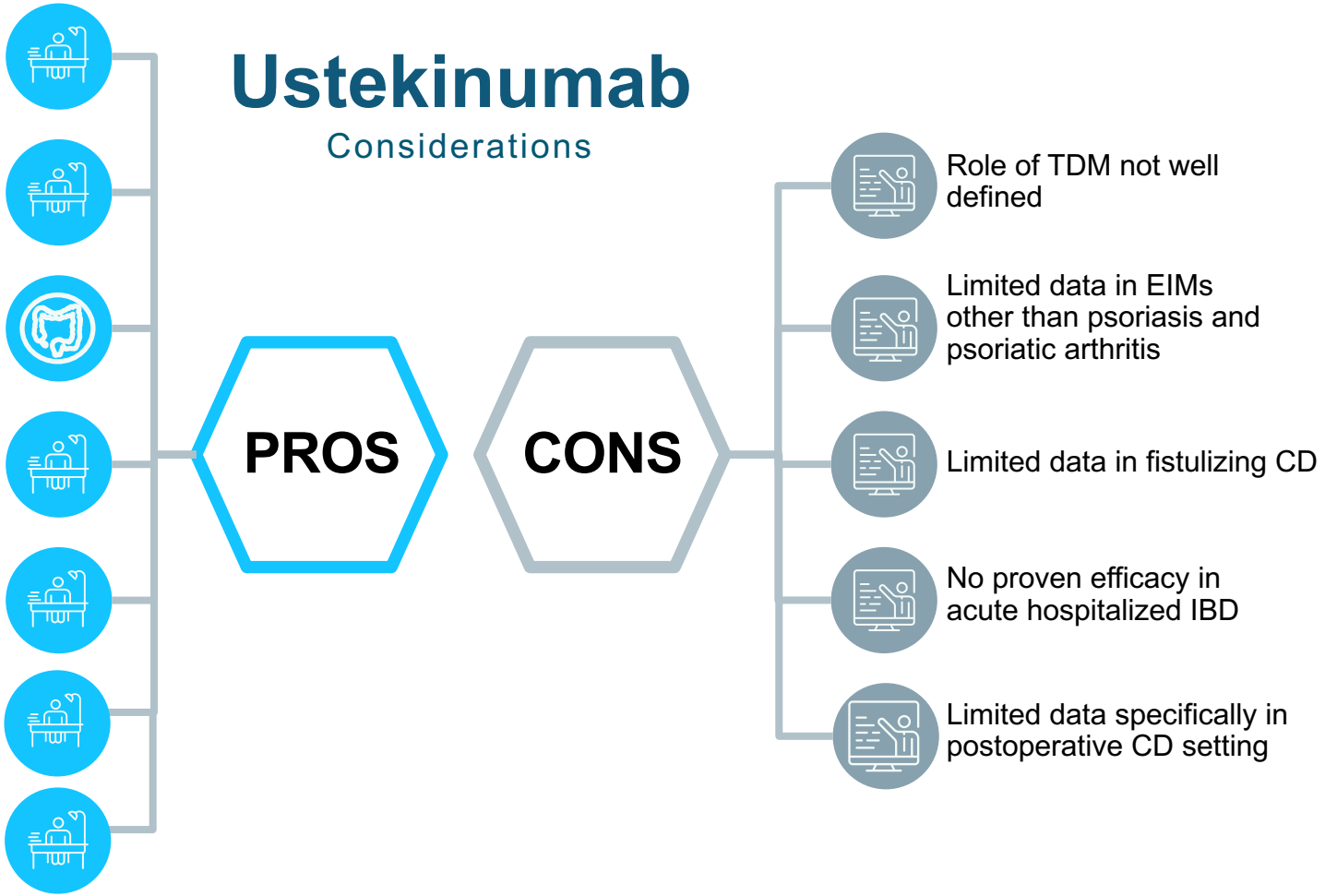


VDZ = vedolizumab

Vermeire S, et al. *J Crohns Colitis.* 2020;14(Suppl 1):S020-S021.

Ustekinumab

Considerations



Ustekinumab

Considerations

PROS

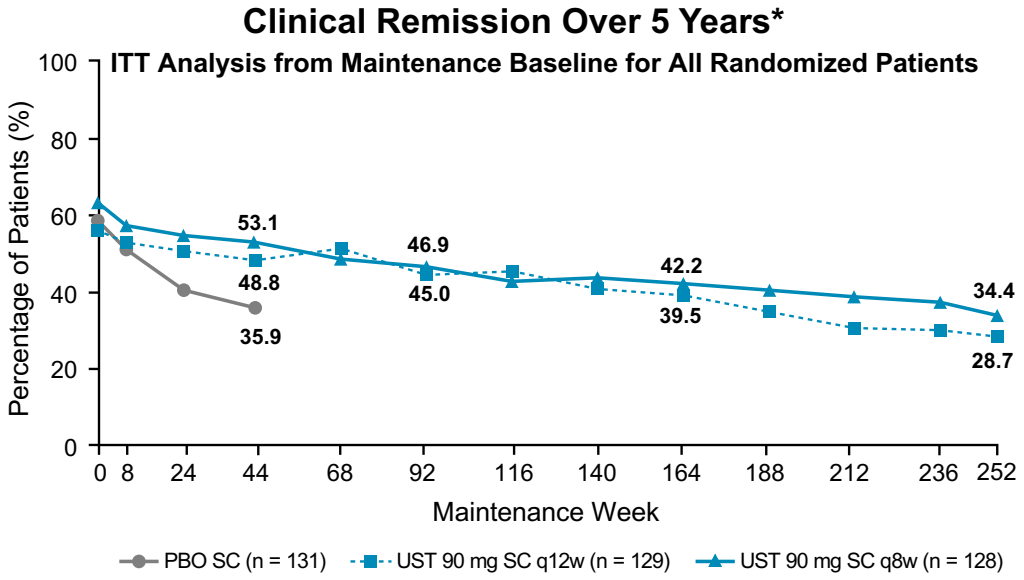
- Excellent safety
- Good choice for patients at high risk for infection
- Low immunogenicity, likely does not require combination therapy
- Consider as first-line therapy or second-line biologic
- Robust durability data
- SC dosing after IV load
- Good choice for those with psoriasis

CONS

- Role of TDM not well defined
- Limited data in EIMs other than psoriasis and psoriatic arthritis
- Limited data in fistulizing CD
- No proven efficacy in acute hospitalized IBD
- Limited data specifically in postoperative CD setting

IM-UNITI: Durability of Ustekinumab for CD Through 5 Years

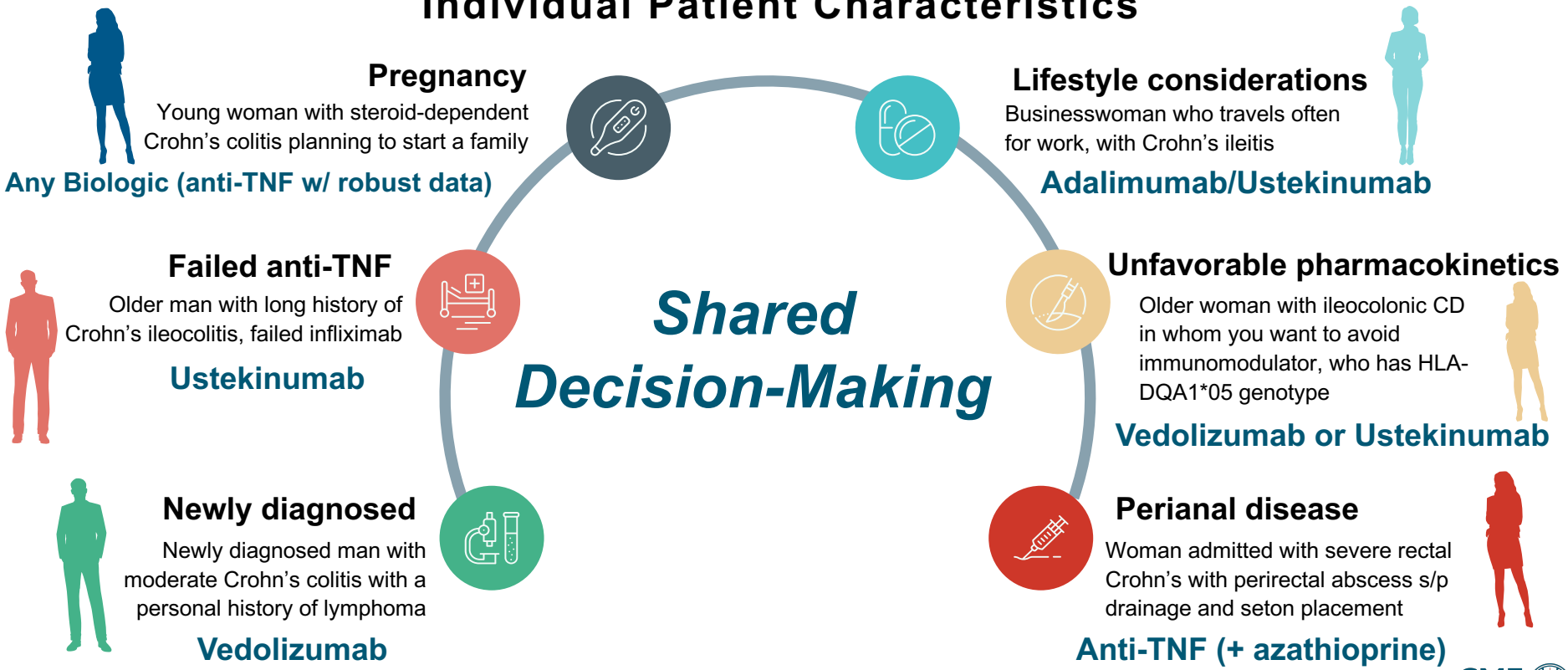
- 567 UST-treated patients (237 of whom had been randomized from the maintenance trial) continued UST in LTE at prior dose
- 151 PBO-treated patients terminated study at week 44
- Overall, 51% of patients entering LTE completed their last dosing visit at week 252



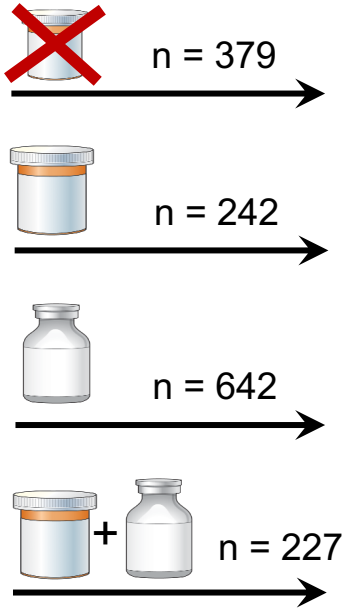
Long-term follow-up of UST in CD shows no new safety signals; of > 50% of CD patients in clinical remission 5 years after entering LTE, the majority (~ 90%) are steroid free

*Defined as CDAI score < 150
ITT = intention to treat; LTE = long-term extension; q8w = every 8 weeks; q12w = every 12 weeks
Sandborn W, et al. *Clin Gastroenterol Hepatol*. 2021:S1542-3565(22)00203-2. [Epub ahead of print]. PMID: 33618023.

Biologic Choice in CD in the Absence of Head-to-Head Data



Safety: Focus on Pregnancy (PIANO)

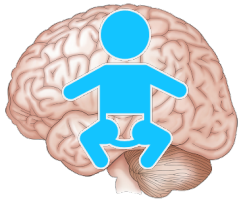


n = 1,431

No increase in:

- Congenital malformations
- Spontaneous abortions
- Preterm birth
- Low birth weight
- Infections in year
  - But ↑ with preterm birth

↑ Spontaneous abortion



No negative impact of drug exposure

Mahadevan U, et al. *Gastroenterology.* 2021;160(4):1131-1139.

Unmet Needs in CD

- Direct head-to-head comparative effectiveness studies for positioning
- Personalized therapy
  - Biomarkers that will predict response to certain classes
  - Disease location or other characteristics as a predictor of response
- Biomarkers that are more strongly correlated with endoscopic healing
- Data (beyond cases series) on combination biologic therapy in CD
- Postoperative recurrence prevention beyond TNF inhibitors
- Further long-term safety therapy on our newer agents to inform shared decision-making

Conclusions

- Window of opportunity exists prior to structural damage
- Targets for therapies include symptoms and endoscopy
- Guidelines support use of anti-TNF, anti-integrin, and anti–IL-12/23 agents in the management of CD
- Data on positioning are extrapolated from subgroup analyses, real world data, and network meta-analysis
- Individual patient characteristics should be considered in selection of a biologic agent
- All biologics have reassuring data for use during pregnancy in IBD

Assessing Your Patients with CD: Prognostic Tools and Control Strategies

David T. Rubin, MD, FACG, AGAF, FACP, FASGE

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Gastroenterology, Hepatology and Nutrition
Co-Director, Digestive Diseases Center
University of Chicago Medicine
Chicago, IL
@IBDMD

Incorporate elements of prognosis into treatment decisions in CD based on clinical research data and guideline recommendations.

LEARNING OBJECTIVE 2

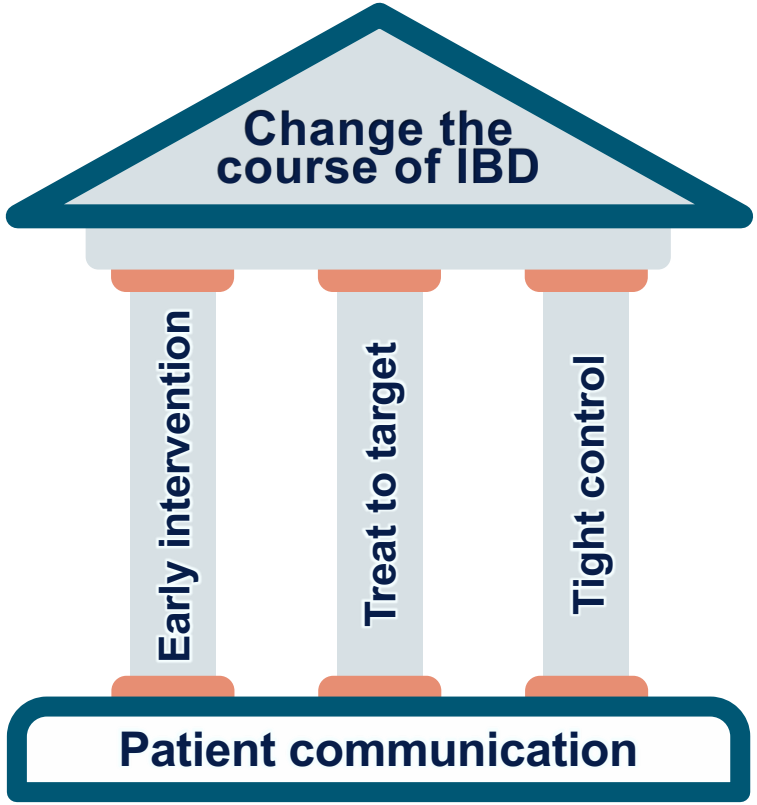
Patient Case: Madeline

- 50-year-old woman with ileocolonic CD
- She was stable on 6-mercaptopurine 50 mg daily but then stopped due to recurrent sinusitis symptoms
- Presented with worsening abdominal pain, diarrhea, and rectal bleeding
- Colonoscopy showed active ileocolonic CD
- Failed to respond to adalimumab and vedolizumab

What would you recommend for Madeline?

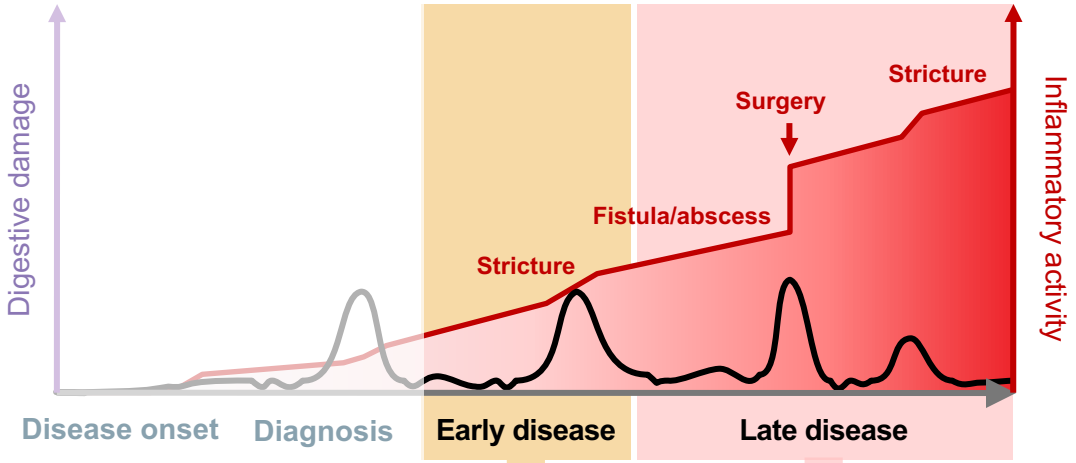
A. Infliximab monotherapy
B. Infliximab + azathioprine
C. Ustekinumab
D. Surgery
E. Something else
F. I’m not sure

The Three Pillars of IBD Care



Colombel JF, et al. *Gastroenterology*. 2017;152(2):351-361. Danese S, et al. *Curr Drug Targets*. 2014;15(11):1056-1063.

Consider the Patient: Treatment Goals May Differ in Early vs. Late Disease



Treatment goals

No symptoms	Noninflammatory symptoms stabilized
No disease progression, complications, or disability	No progression of damage or disability
Normal quality of life (QoL)	Improved QoL

- Symptomatic remission may not be achievable in late-stage disease[1]
- Mucosal healing as treatment goal may be difficult to achieve in patients[1,2]:
  - Diagnosed late in disease course
  - Who have already experienced a disease complication
- Earliest disease is postoperative prevention

1. Panaccione R, et al. *Inflamm Bowel Dis*. 2013;19:1645-1653. 2. Peyrin-Biroulet L, et al. *Am J Gastroenterology*. 2015;110:1324-1338.

Differentiating Disease Activity vs. Disease Severity

Disease activity (how the patient is doing now!)
- Good to assess response to therapy
- Used in clinical trials
- Lacks longitudinal assessment of disease course

Disease severity (what is the future like?)
- Guides early aggressive therapy in **severe** or **poor prognostic patients** in UC and CD

Therapy for IBD should take into account both disease activity and disease severity

Proposed Criteria to Classify Disease Severity in IBD

- Impact of the disease on the patient
  - Clinical symptoms
  - Quality of life
  - Fatigue
  - Disability
- Inflammatory burden
  - CRP
  - Mucosal lesions
  - Upper gastrointestinal involvement*
  - Disease extent
- Disease course
  - Structural damage
  - History/extension of intestinal resection
  - Perianal disease*
  - Number of flares
  - Extraintestinal manifestations

*CD only

Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol.* 2016;14:348-354.

Assessment of Disease Risk in CD

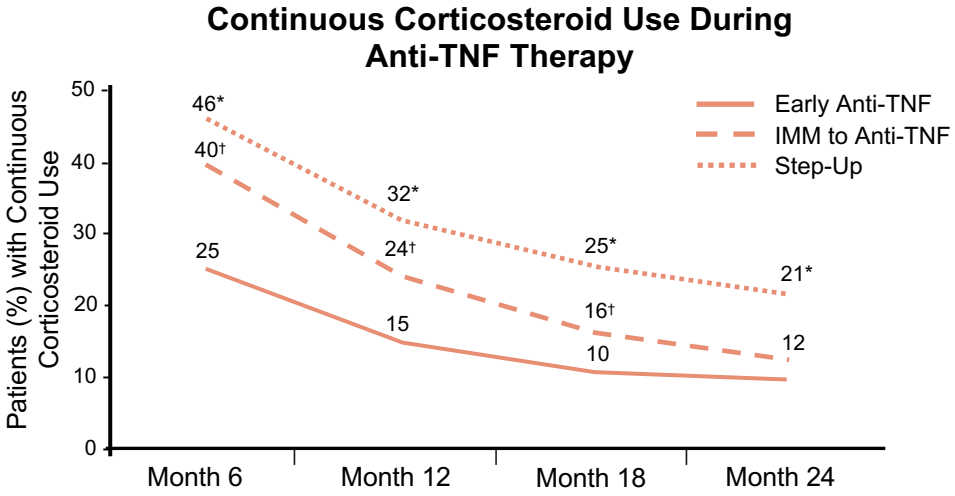
- Assess current and prior disease burden

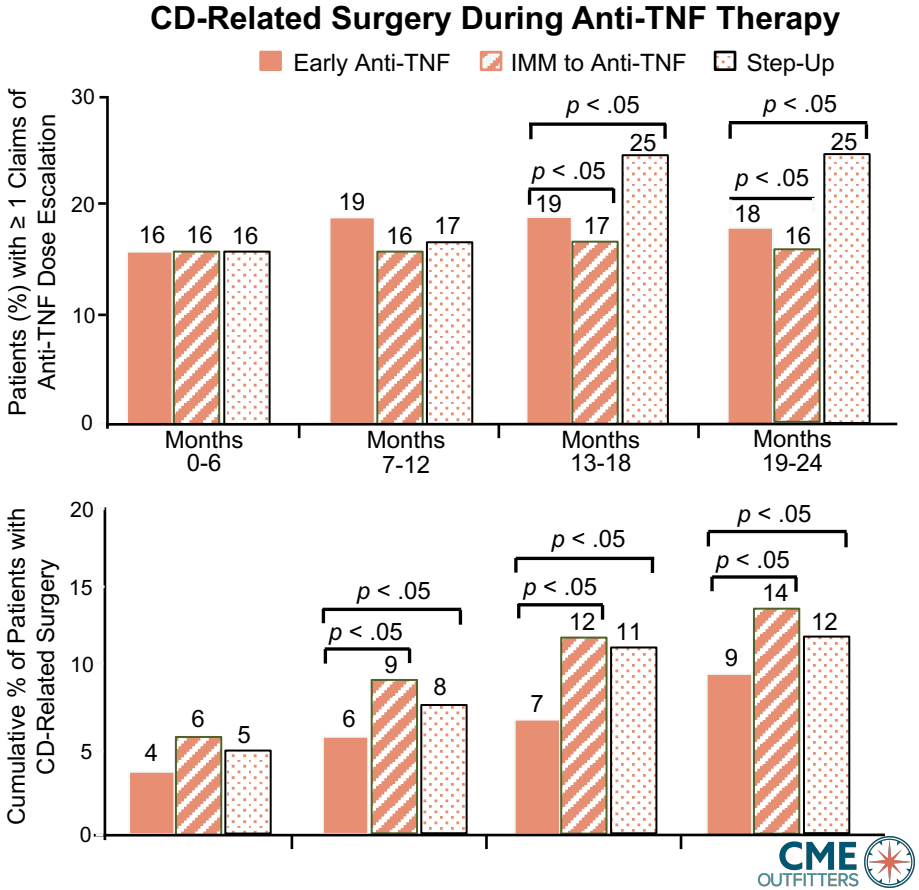
Low Risk	Moderate/High Risk
• Age at initial diagnosis > 30 years • Limited anatomic involvement • No perianal and/or severe rectal disease • Superficial ulcers • No prior surgical resection • No stricturing and/or penetrating behavior	• Age at initial diagnosis < 30 years • Extensive anatomic involvement • Perianal and/or severe rectal disease • Deep ulcers • Prior surgical resection • Stricturing and/or penetrating behavior • Smoking cigarettes

Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol*. 2016;14:348-354.

Earlier Use of Anti-TNF Biologic Therapy in CD Has Better Outcomes

- Claims data assessment
- > 3,700 patients; all received anti-TNF at some point

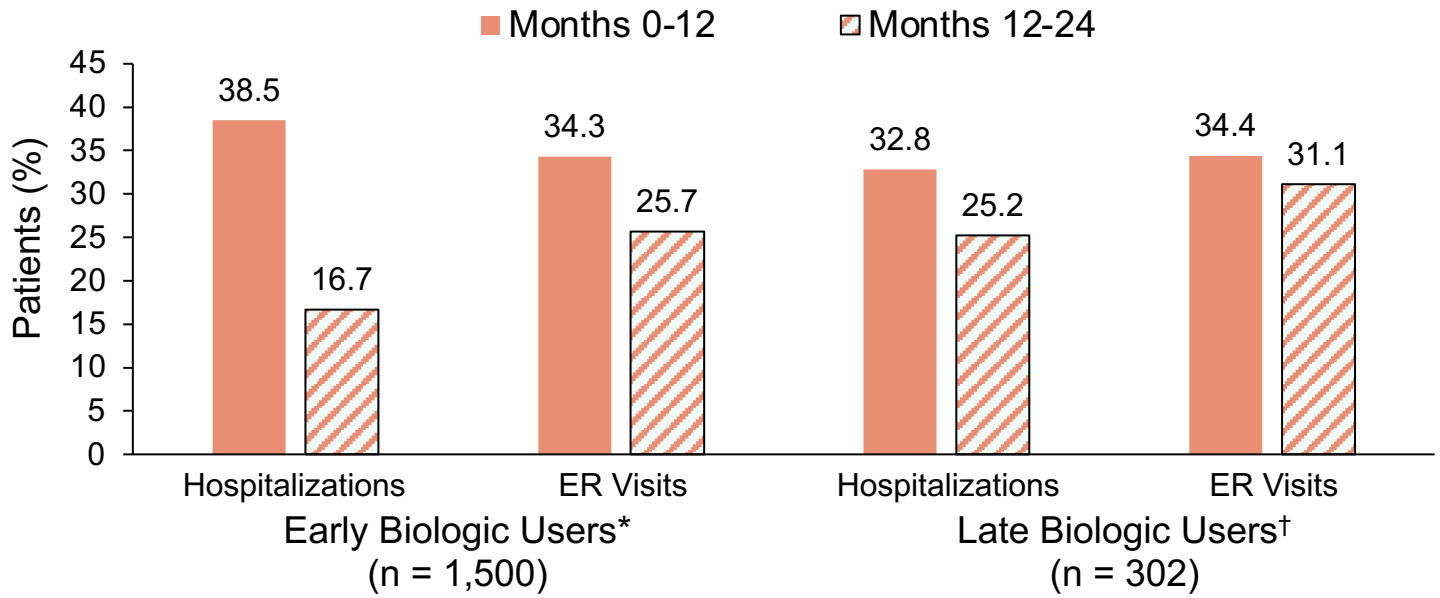




IMM = immunomodulator
*$p < .05$ for early anti-TNF groups vs. other groups
†$p < .05$ for IS to anti-TNF group vs. other groups
Rubin DT, et al. *Inflamm Bowel Dis*. 2012;18(12):2225-2231.

Effects of Early Biologic Initiation on ER Visits and Hospitalizations

Retrospective Observational Cohort Study of Medical and Pharmacy Claims in Patients with Moderate-Severe CD

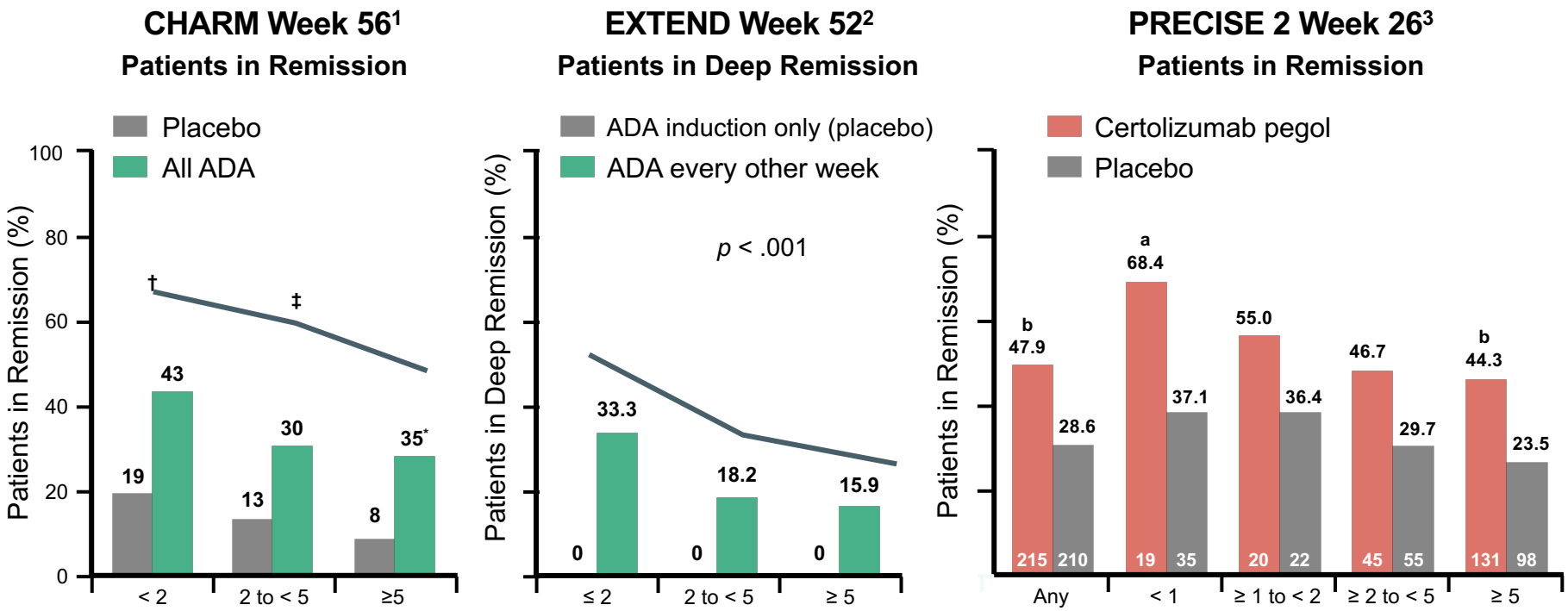


ER = emergency department

*≥ 1 biologic claim ≤ 12 months post CD diagnosis; †≥ 1 biologic claim 12-24 months post CD diagnosis

Ungaro RC, et al. *Gastroenterology.* 2020;158(6):S-725.

Post-Hoc Sub-Analyses of Disease Duration on Rates of Remission in CD

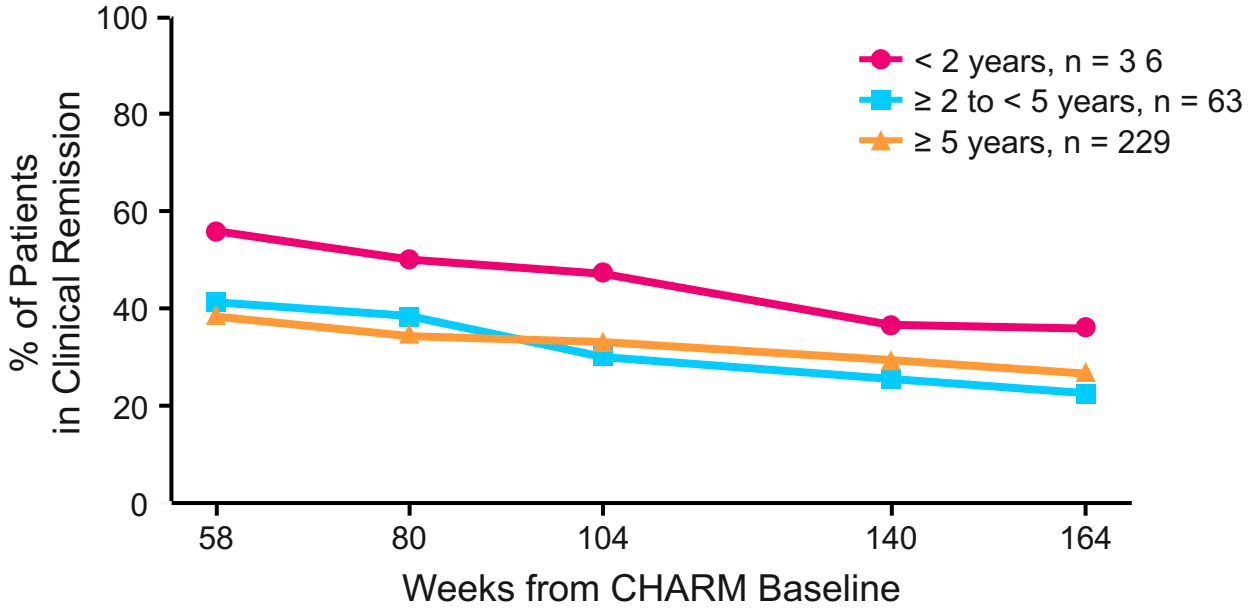


*p < .001; †p = .024; ‡p = .028 vs. placebo
[a]p < .05; [b]p < .001 vs. placebo
ADA = adalimumab

1. Schreiber S, et al. *J Crohns Colitis* 2013;7:213-221. 2. Colombel JF, et al. *Gut* 2010;59(Suppl 3):A80. Abstract OP371. 3. Schreiber S, et al. *Aliment Pharmacol Ther*. 2011;33:185-193.

Loss of Response Over Time Is Also Less Common with Shorter Duration of Disease

Clinical Remission Over Time in ADHERE (NRI):
All Patients Randomized to ADA Treatment in CHARM Who Enrolled in ADHERE



NRI = non-responder imputation

Schreiber S, et al. *J Crohns Colitis.* 2013;7(3):213-221.

Who Should Receive Early Intensive Therapy? Risk Stratification Is Necessary

Prognostic Factors for Disease Progression in CD

Ileal disease location, upper gastrointestinal involvement, and EIMs → complicated behavior
Younger age and perianal disease at diagnosis → disabling disease course
Smoking → therapy escalation, complicated disease, need for surgery, and postoperative recurrence
Endoscopic severity → penetrating complications
(Serologic reactivity to microbial antigens → complicated behavior)
(Mutations in some genes [e.g., NOD2] → complicated behavior)

AGA Crohn's Disease Clinical Care Pathway available at https://gastro.org/guidelines/ibd-and-bowel-disorders/.
Torres J, et al. *J Crohn's Colitis*. 2016;10(12):1385-1394.

AGA Care Pathway

AGA SECTION

Crohn's Disease Evaluation and Treatment: Clinical Decision Tool

William J. Sandborn

Division of Gastroenterology, University of California, La Jolla, California

Clinical Decision Support Tool available at:
https://via.juxlyapps.com/pathway/archemedx/ibd-cdst/index.html#/disease-selection

ACG Guidelines

CME

ACG Clinical Guideline: Management of Crohn's Disease in Adults

Gary R. Lichtenstein, MD, FACG[1], Edward V. Loftus Jr, MD, FACG[2], Kim L. Isaacs, MD, PhD, FACG[3], Miguel D. Regueiro, MD, FACG[4], Lauren B. Gerson, MD, MSc, MACG (GRADE Methodologist)[5,†] and Bruce E. Sands, MD, MS, FACG[6]

Sandborn WJ, et al. *Gastroenterology.* 2014;147:702-705. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113:481-517.

Predictors of Treatment Response: CD Decision Support Tools

Ustekinumab (UNITI)

Variable	Points Awarded	Probability of Response
No prior exposure to TNF antagonists	+2	0-1 points (total): **Low**
No prior bowel surgery	+2	
No current or prior smoking	+1	
No active fistulizing disease at baseline	+1	2-4 points: **Intermediate**
Baseline albumin:		
≤ 25 g/L	−3	
> 25-32 g/L	−1	≥ 5 points: **High**
> 32-39 g/L	0	
> 39-43 g/L	+1	
> 43 g/L	+3	

Vedolizumab (GEMINI, GETAID, VICTORY)

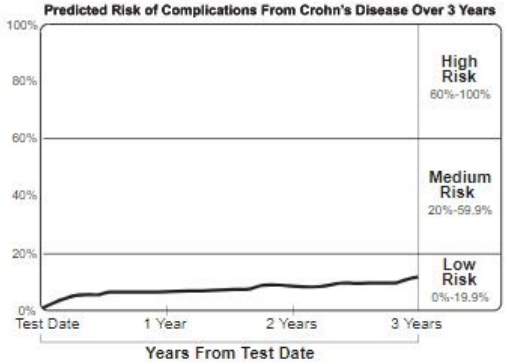
Variable	Points Awarded	Probability of Response
No prior exposure to TNF antagonists	+3	< 13 points: **Low**
No prior bowel surgery	+2	
No prior fistulizing disease	+2	13-19 points: **Intermediate**
Baseline albumin	+0.4 per g/L	
Baseline C-reactive protein		
3-10 mg/L	−0.5	
> 10 mg/L	−3	> 19 points: **High**

Dulai PS, et al. *Am J Gastroenterol*. 2018;155(3):687-695. Dulai PS, et al. *Am J Gastroenterol*. 2019;114:S373. Dulai PS, et al. *Aliment Pharmacol Ther.* 2020;51(5):553-564.

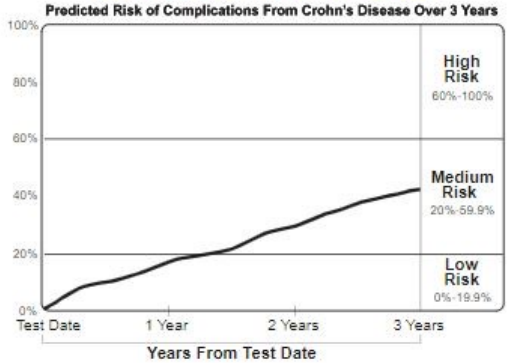
Risk of Disease Progression

The graphs below are examples of patient reports with low-, medium-, and high-risk profiles, respectively[1]:

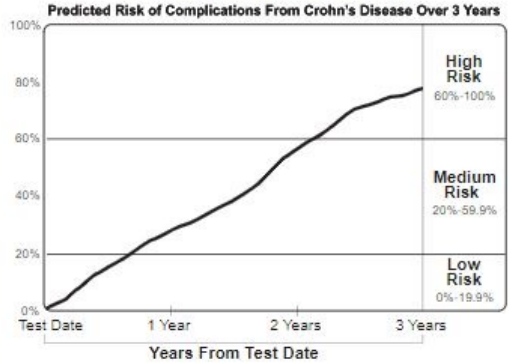
Example of LOW RISK result



Example of MEDIUM RISK result



Example of HIGH RISK result

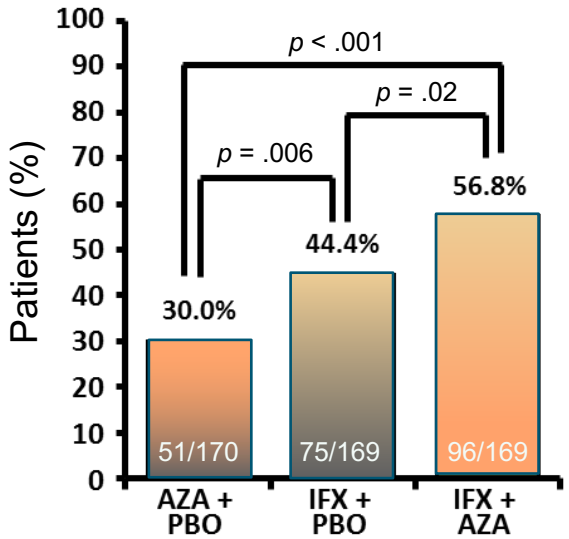


CDPATH Website. 2021. https://www.cdpath.com/patient/how-it-works. Accessed May 15, 2021.

Optimizing Treatment

- Combine therapies:
  - Anti-TNF with IMMs
  - Anti-TNF with antibiotics in perianal disease
- Judicious use of proactive therapeutic drug monitoring:
  - Post- or even intra-loading drug levels in high-risk patients (infliximab week 6, adalimumab week 4)
  - Pediatrics: proactive monitoring of adalimumab beneficial (PAILOT)[1]
  - 6-thioguanine metabolites to assess thiopurines

SONIC Trial (CD)[2]
Steroid-Free
Remission Week 26



1. Assa A, et al. *Gastroenterology*. 2019;157(4):985-996. 2. Colombel JF, et al. *N Engl J Med*. 2010;362(15):1383-1395.

Standard Versus High-Dose Adalimumab (SERENE UC and SERENE CD)

- Double-blind, randomized, multicenter study of higher versus standard adalimumab dosing for induction and maintenance therapy
- SERENE UC[1]
  - N = 952
  - Primary outcome: Week 8 clinical remission (Mayo); Week 8 responders achieving clinical remission at Week 52 (Mayo)
- SERENE CD[2]
  - N = 514
  - Primary outcome: Week 4 clinical remission (CDAI); Week 12 endoscopic response (SES-CD)

SES-CD = Simple Endoscopic Score for Crohn's Disease; UC = ulcerative colitis

1. US National Library of Medicine. Accessed October 12, 2020. https://clinicaltrials.gov/ct2/show/NCT02065622. 2. US National Library of Medicine. Accessed October 12, 2020. https://clinicaltrials.gov/ct2/show/NCT02065570.

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- SERENE UC[1]
  - N = 952
  - Primary
    Week 8
- SERENE C
  - N = 514
  - Primary outcome: Week 4 clinical remission (CDAI); Week 12 endoscopic response (SES-CD)

52 (Mayo)

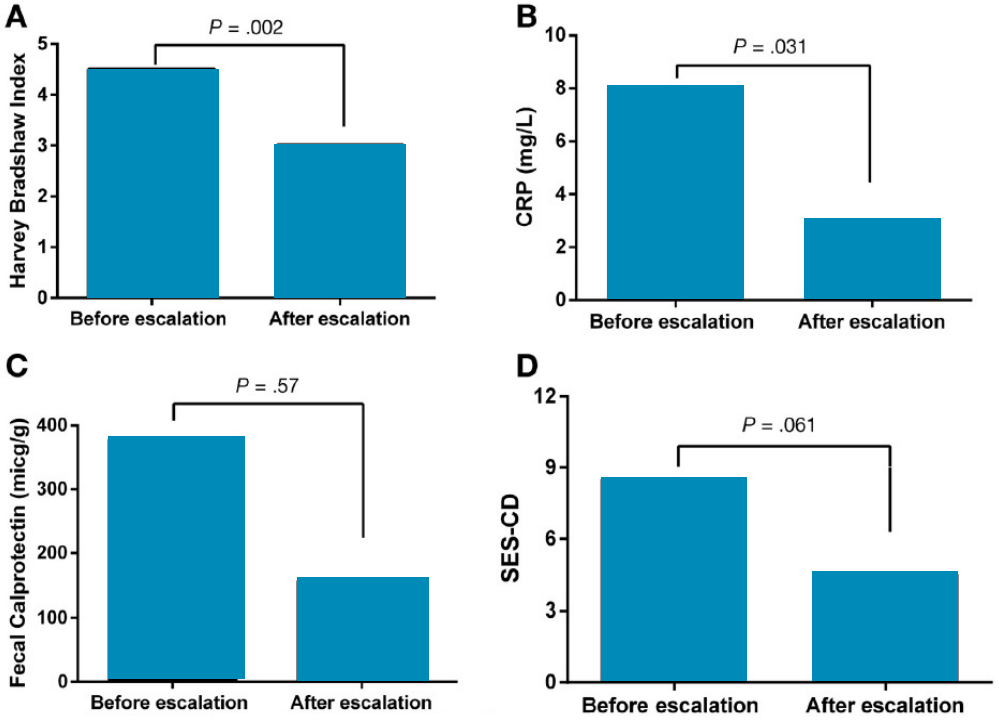
No benefit to higher-dose loading for induction of remission

1. US National Library of Medicine. Accessed October 12, 2020. https://clinicaltrials.gov/ct2/show/NCT02065622. 2. US National Library of Medicine. Accessed October 12, 2020. https://clinicaltrials.gov/ct2/show/NCT02065570.

Effectiveness of Ustekinumab Dose Escalation in CD

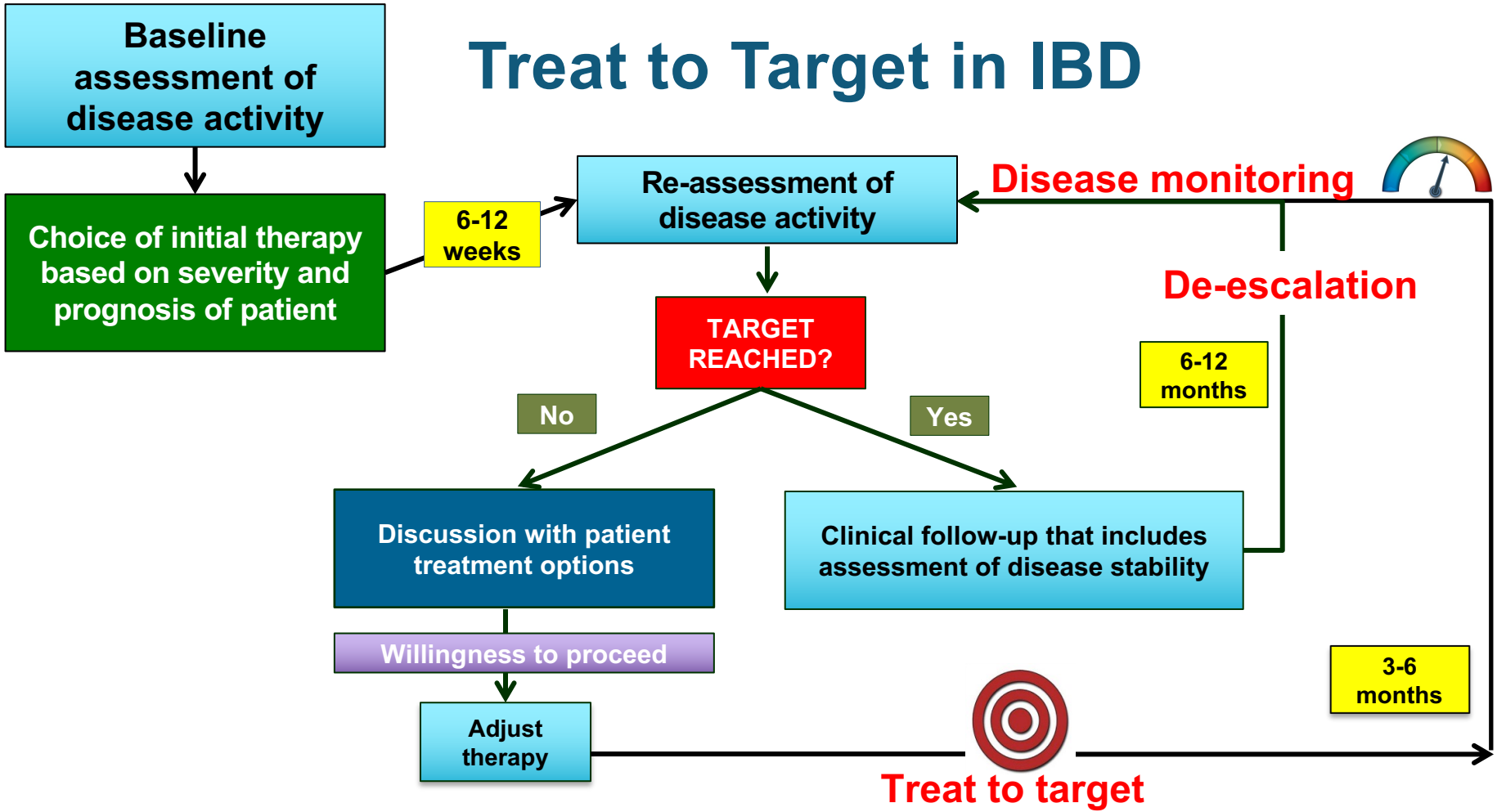
- N = 506
- 110 patients were dose escalated
- 90 mg every 8 weeks → 90 mg every 4 weeks
- Shortening the ustekinumab dose interval improved clinical and biological indices of disease activity
- Dose interval shortening was effective and safe

UChicago Experience



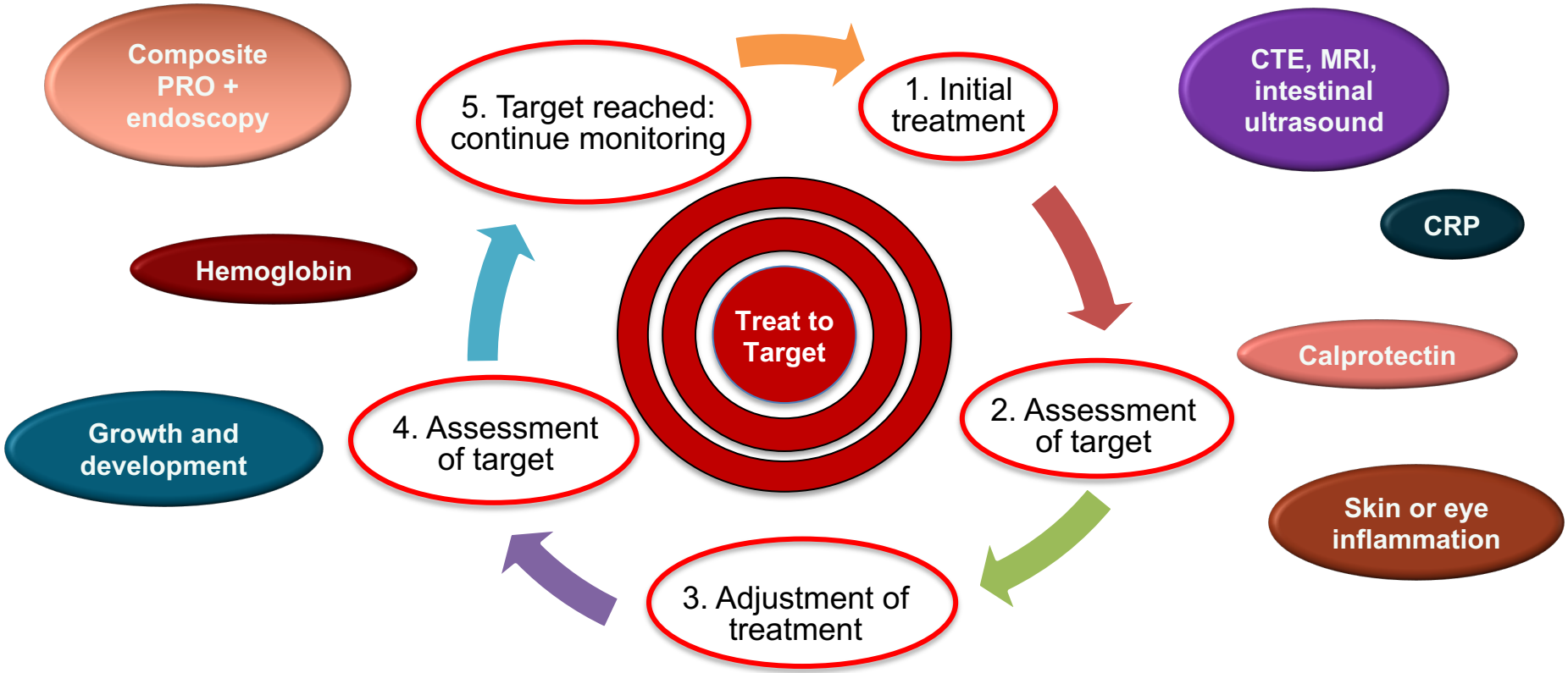
Ollech JE, et al. *Clin Gastroenterol Hepatol*. 2021;19(1):104-110.

Treat to Target in IBD



Christensen B, Rubin DT. In: Baumgart DC, ed. *Crohn's Disease and Ulcerative Colitis*. 2nd ed. Cham, Switzerland: Springer Nature; 2017:267-278.

Targets Can Be Individualized



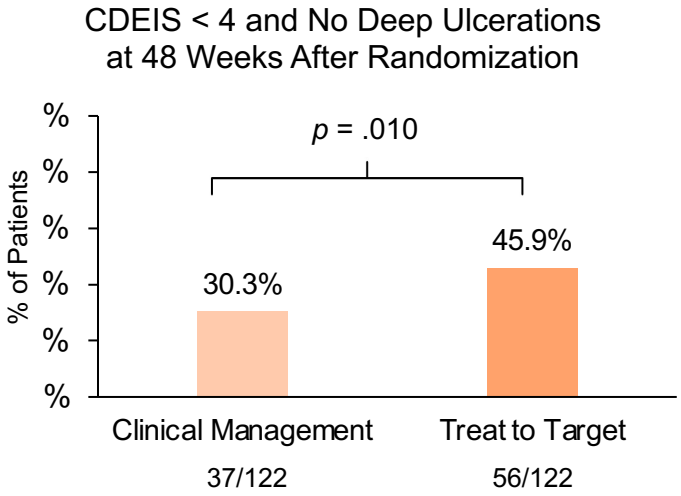
CTE = computed tomography enterography; MRI = magnetic resonance imaging

Peyrin-Biroulet L, et al. *Am J Gastroenterol*. 2015;110:1324-1338. Turner D, et al. *Gastroenterology*. 2021;160(6):1570-1583.

Treat-to-Target Studies in IBD (Dose Escalation)

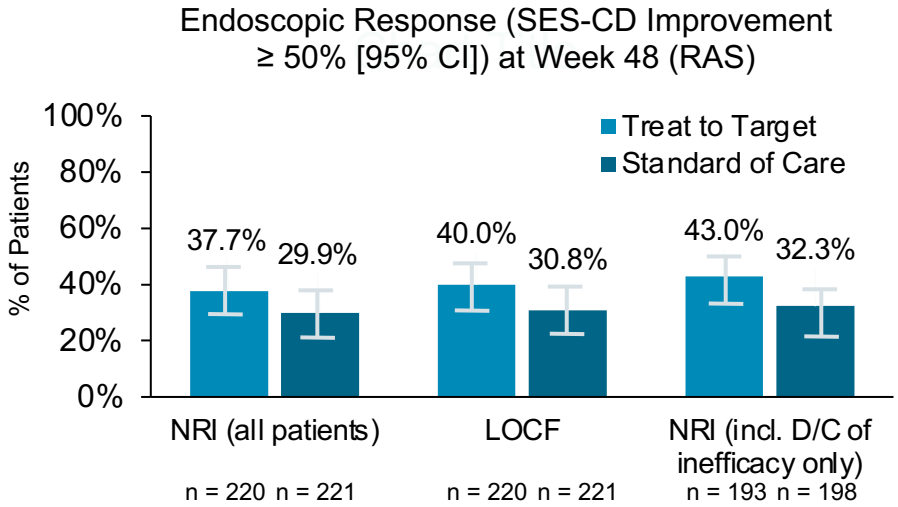
CALM

- Adalimumab +/- azathioprine
- CDAI, prednisone
- CRP, fecal calprotectin



STARDUST

- Ustekinumab
- Endoscopic response

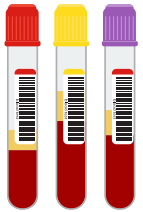


LOCF = last observation carried forward; NRI = non-responder imputation

Colombel JF, et al. *Lancet*. 2018;390(10114):2779-2789. Danese S, et al. UEGW Virtual 2020. Abstract LB11.

Monitoring Is Key

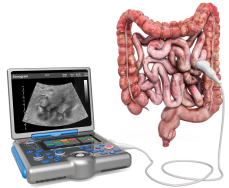
- Serum markers
  - CRP
  - Hemoglobin
  - Endoscopic Healing Index (EHI)



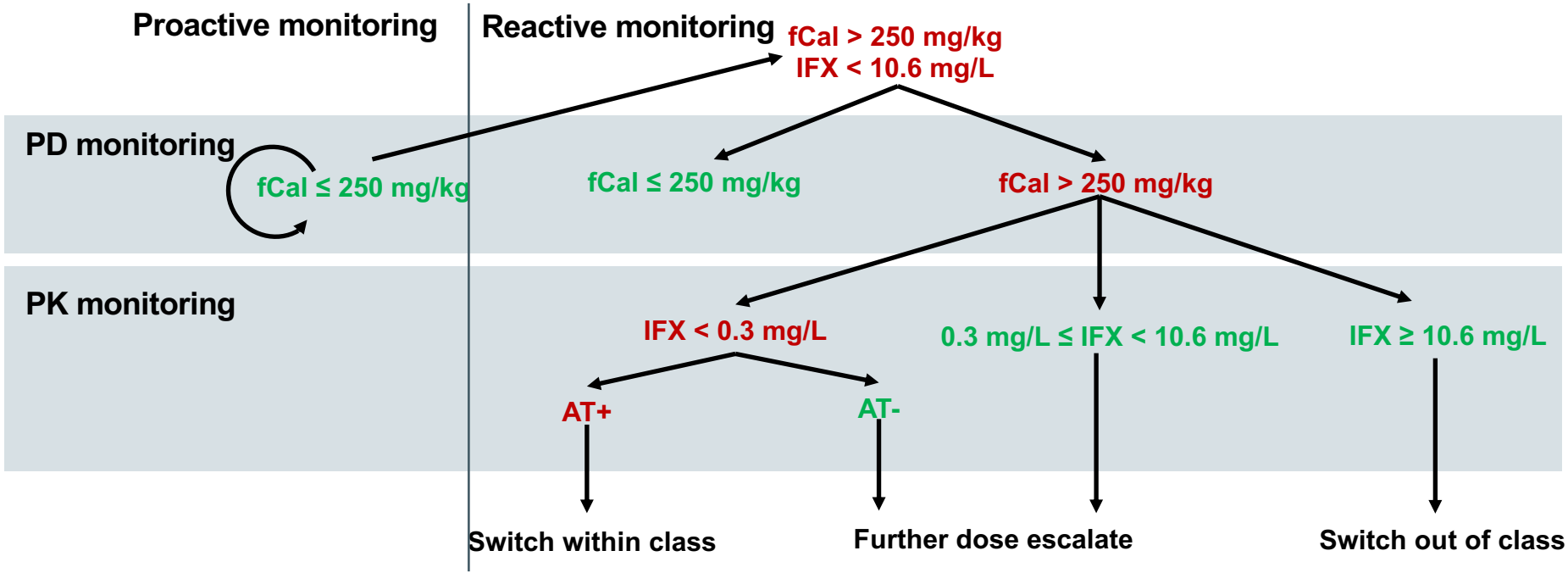
- Stool markers
  - Calprotectin
  - Lactoferrin

- Endoscopy

- Radiology
  - CTE
  - MRE
  - Intestinal ultrasound



Implementing a Tiered Approach for Monitoring During Infliximab Maintenance Therapy



ATI = antibodies to infliximab; fCal = fecal calprotectin; IFX = infliximab; PD = pharmacodynamic; PK = pharmacokinetic

Dreesen E, et al. *Clin Gastroenterol Hepatol*. 2020;18(3):637-646.e11.

Summary: Prognostic Tools and Control Strategies in CD

- Include prognosis in treatment decisions
- Treat early with effective therapy
- Employ treat-to-target strategies
- Every patient should have a disease monitoring plan

How Do Social Determinants of Health Impact CD Care?

Anita Afzali, MD, MPH, FACG, AGAF

Associate Professor of Medicine
Abercrombie & Fitch Endowed Chair in IBD
Medical Director, OSU IBD Center
Program Director, OSU Advanced IBD Fellowship
Division of Gastroenterology, Hepatology and Nutrition
The Ohio State University Wexner Medical Center
Columbus, OH
@IBD_Afzali

Implement strategies to engage all patients with CD in shared decision-making with the goal of increasing patient satisfaction and improving adherence.

LEARNING OBJECTIVE 3

Patient Case: Patricia

- 32-year-old African American female with new diagnosis of ileocolonic CD; she also has perianal disease with actively draining fistula; she has had symptoms for nearly 2 years and was recently diagnosed with CD
- Labs: CRP 32.2 mg/L, thiopurine methyltransferase (TPMT) normal, hepatitis B surface antigen negative, TB QuantiFERON negative
- Biologic naïve
- Mother with history of breast cancer
- *She is very hesitant to proceed with biologic therapy for her CD*

Audience Response

What would be your next step for Patricia?

A. Start prednisone and mesalamine to avoid malignancy risks

B. Discuss absolute risks vs. benefits with shared decision-making

C. Start vedolizumab monotherapy to avoid malignancy risks

D. Advise her that biologics do not cause cancer and initiate anti-TNF monotherapy

Survey Participants

2,100 Patients with UC

1,254 Physicians

Patient-Physician Communication

Patients

85% were satisfied with the communication they have with their MD...

...yet **46%** worry if they ask questions they will be seen as a difficult patient

81% were satisfied with discussions on treatment options

85% set UC management goals with their physician

72% wished they knew where to find information and support when first diagnosed

Physicians

74% wished for more time to discuss treatment options earlier

79% wished for longer appointment times

72% wanted more discussion of treatment goals

Conclusions

Patients were generally happy with what they talk about at appointments with their physician. However, many patients would still like more information and support.

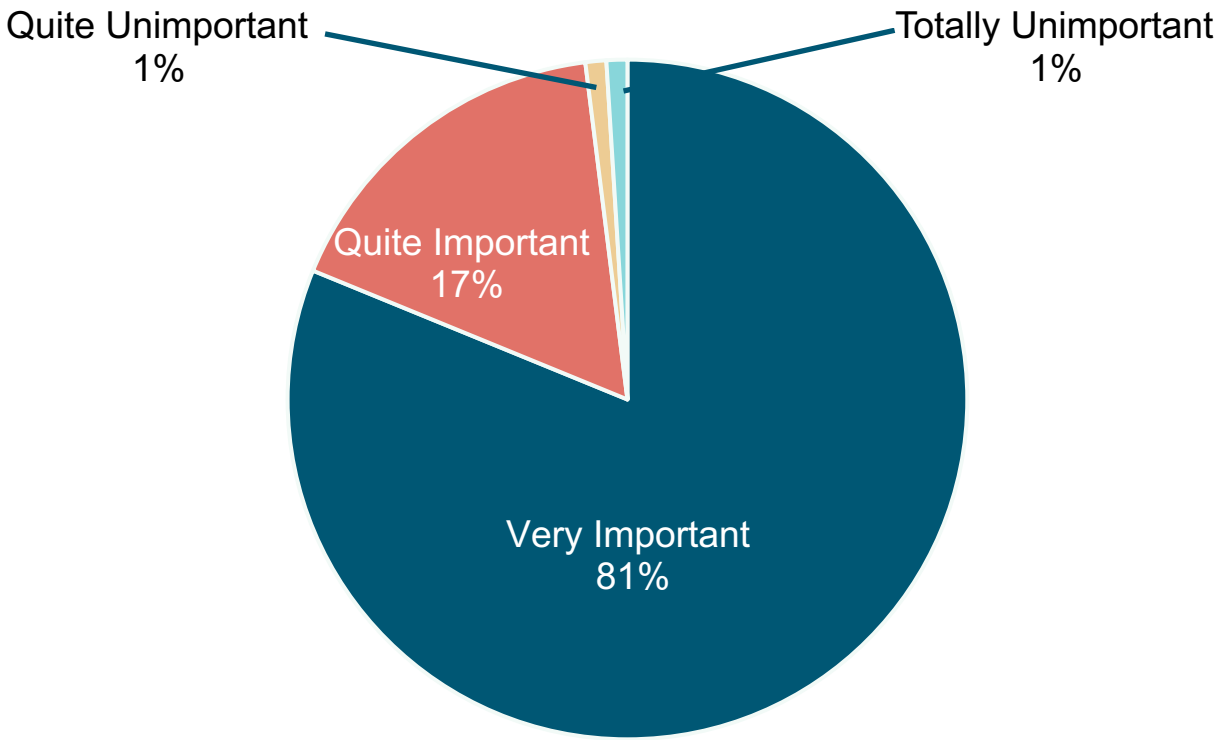
Adapted from Rubin DT, et al. *Inflamm Bowel Dis*. 2020 Oct 15;izaa257. doi: 10.1093/ibd/izaa257. [Epub ahead of print].

What Do Patients Prioritize in Therapy Decisions?

- Conjoint analysis including > 1,000 patients with IBD was conducted in many countries
- More efficacious drugs were preferred over those that were less efficacious, particularly in the U.S.
- Drugs with fewer adverse effects were preferred over those with more adverse effects
- Relationships were roughly linear (e.g., an increase from 35% to 45% efficacy was equally important as an increase from 45% to 55%)

Patel DB, et al. *Inflamm Bowel Dis*. 2020 Dec 10; izaa311. doi: 10.1093/ibd/izaa311. [Epub ahead of print].

How Important Do IBD Patients Feel It Is to Be Involved in Medical Decisions?



Siegel CA. *Gut*. 2012;61(3):459-465.

Decision-Making in IBD

	Paternalistic	Shared	Informed
Information exchanges	One way (largely) Physician → Patient Medical Minimum legally required	Two way Physician ⇄ Patient Medical and personal All relevant for decision-making	One way (largely) Physician → Patient Medical All relevant for decision-making
Deliberation	Health care professional(s)	Health care professional(s) and Patient	Patient
Deciding on treatment to implement	Health care professional(s)	Physician and Patient	Patient

Friesen-Storms JHHM. *Int J Nurs Stud*. 2015;52(1):393-402.

Decision-Making in IBD

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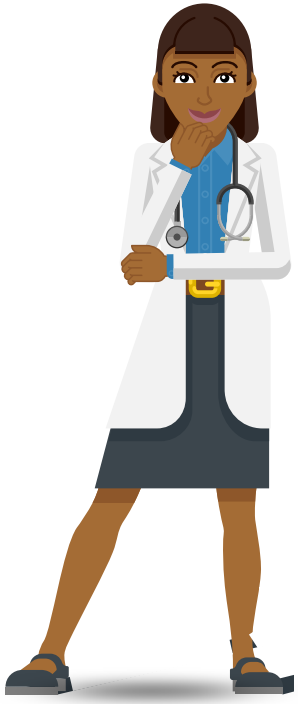
Friesen-Storms JHHM. *Int J Nurs Stud*. 2015;52(1):393-402.

Clinician

Patient



MATERNALISTIC/PATERNALISTIC:
Information and recommendations

INFORMED MEDICAL DECISION-MAKING:
Information

SHARED DECISION-MAKING:
Information and recommendations

Values and preferences

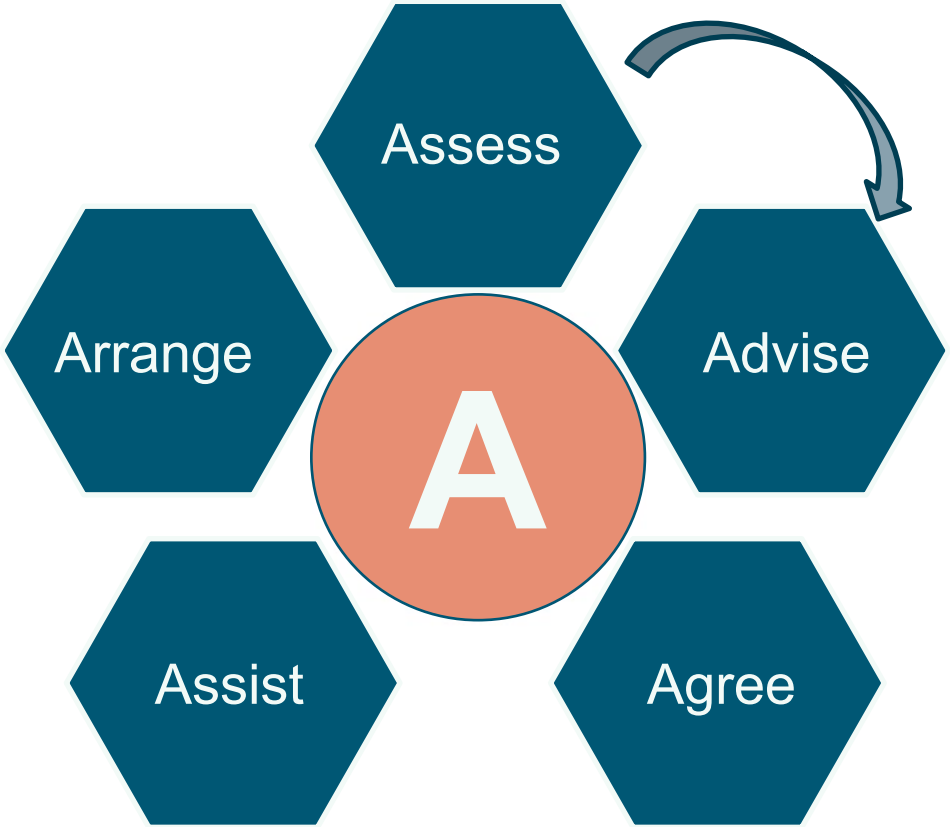
Adapted from Schrager SB, et al. *Fam Pract Manag.* 2017;24(3):5-10.

Shared Decision-Making

- Not appropriate in clinical scenarios where medical treatment clear (i.e., anticoagulation for an emboli)
- Beneficial in situations where more than one treatment decision is valid
- For IBD and CD management:
  - ✓ Many options for effective therapies
  - ✓ Early appropriate treatment improves outcomes
  - ✓ Risks and safety considerations related to therapies
  - ✓ Risks associated with natural progression of disease

Patients should understand all information and consider personal needs and values in order to make best management decisions for their CD

The Five A's Model



Schrager SB, et al. *Fam Pract Manag.* 2017;24(3):5-10.

How to Talk with Patients About Risk: Risk Communication

Absolute risk of a disease is your risk of developing the disease over a time period; expressed in different ways

- 1 in 10 risk
- 10% risk
- 0.1 risk

Relative risk is used to compare the risk in two different groups of people – need to know the absolute risk to frame this risk

- RR of 10
- 10-fold increased risk

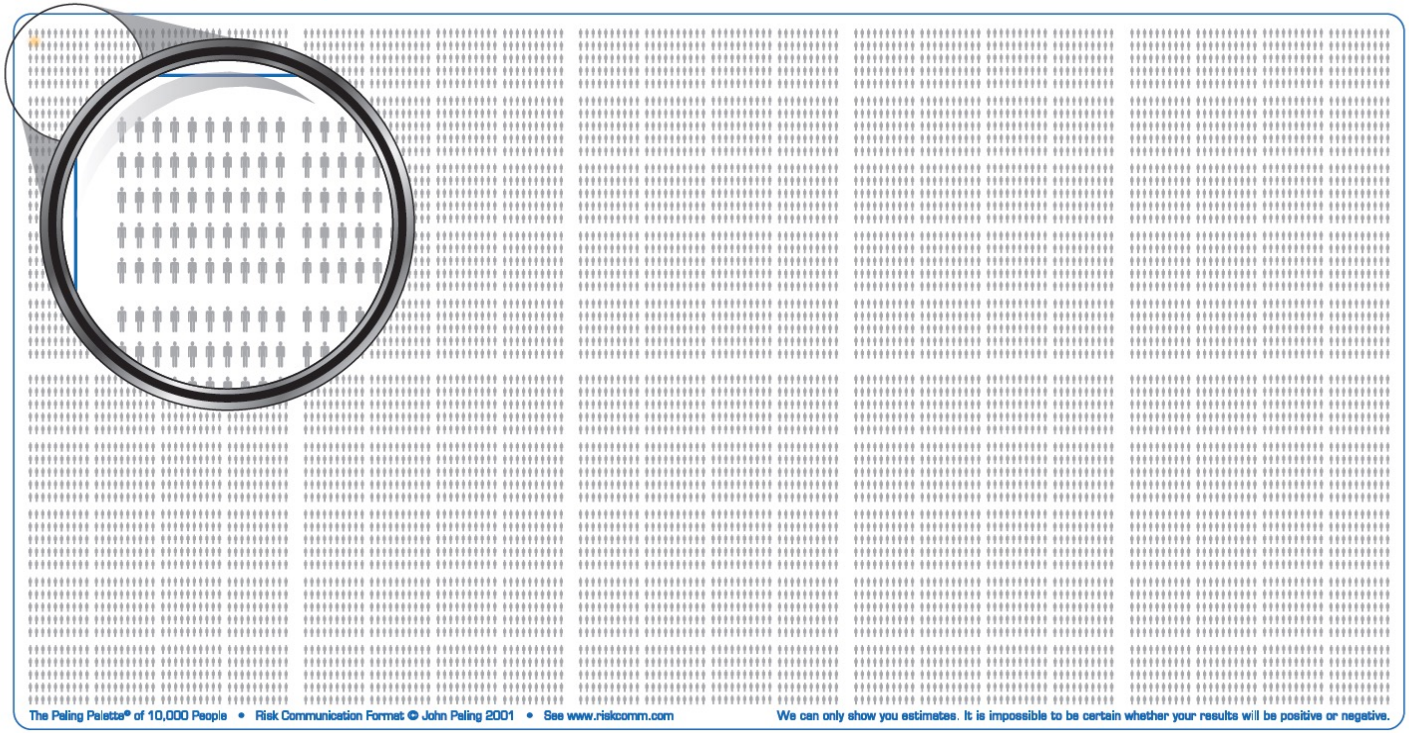
Clear Communication of Risk

- Risk presentation:
  - Avoid vague labels such as “low,” “very low,” “often,” or “very common,” which lead to inconsistent interpretations
- Absolute risks better than relative risk
- Avoid decimals (0.06%)
- Keep common denominators (x/10,000)
- Visual aids help (turn numbers into pictures)
- Give perspective to other disease and life risks

Fagerlin A, et al. *Am J Health Behav*. 2007;31(Suppl 1):S47-S54. Peters E, et al. *Health Affairs*. 2007;26:741-748.

Risk Communication: Absolute Risk – Visual Aids

Highlight the absolute risk and demonstrate how it changes with relative risk of a medication



Courtesy of Corey Siegel, MD.

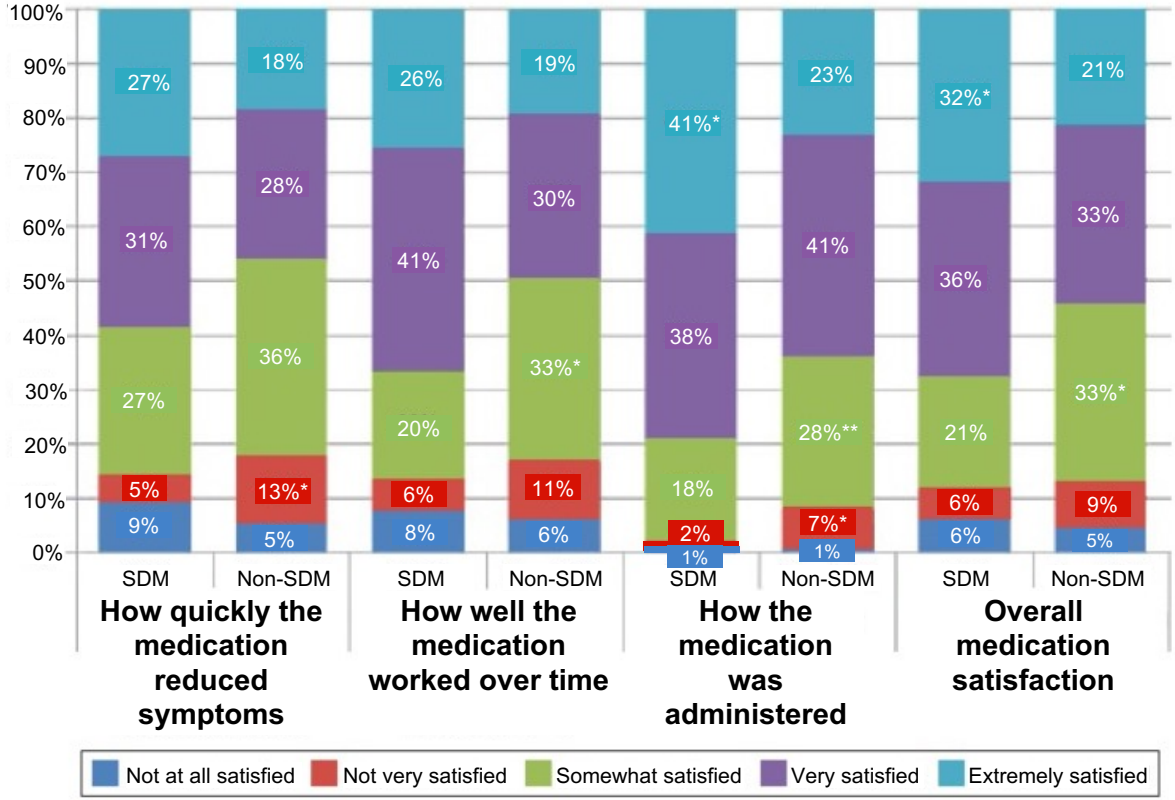
Risk Communication: Absolute Risk – Visual Aids

Highlight the absolute risk and demonstrate how it changes with relative risk of a medication

Courtesy of Corey Siegel, MD.

Why Shared Decision-Making?

- Improved rates of patient satisfaction and adherence, with reduced health care costs
- Autoimmune population
- 306 patients
- Linked to claims for outcomes



*$p < .05$; **$p < .075$ (comparing shared decision-making and non–shared decision-making patients answering each response identified by color)

Lofland JH, et al. *Patient Prefer Adherence*. 2017;11:947-958.

Shared Decision-Making: Patient-Centered Approach

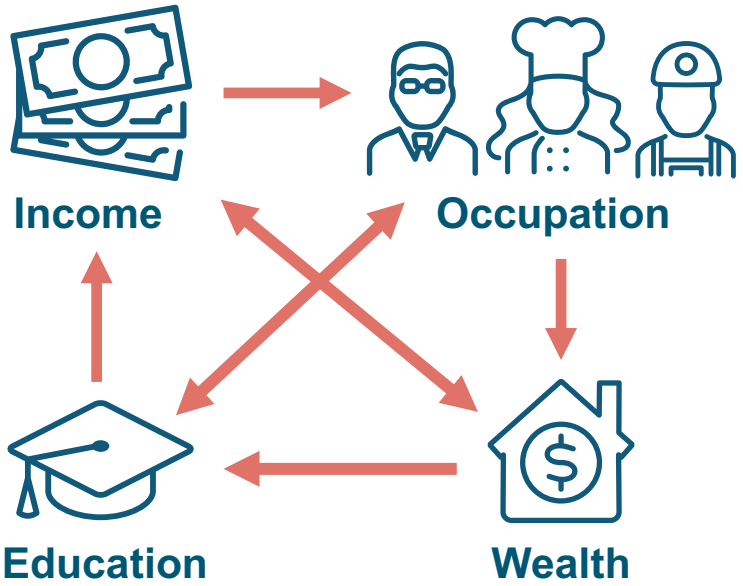
- Improves patients' knowledge and satisfaction
- Improves medical care and disease outcomes
- Positive effect on clinician-patient communication
- Decreased decisional conflict
- Improves patient adherence to treatment plan
- May reduce medical malpractice claims
- Reduces health inequities among underserved populations

Social Determinants of Health

- Socioeconomic status (SES)
- Common SES measures
  - Income
  - Occupation
  - Wealth
  - Education

How are these related?
Which one comes first?

SES Measures



Assess SDH to Tailor Health Care Delivery

Patients with IBD have higher financial toxicity

- National Health Interview Survey
  - 1 in 8 patients with IBD have food insecurity and lack of social support

- Manitoba Health Administrative Database:
  - Lower socioeconomic status (LSS) associated with more physician visits, hospitalizations, ICU admissions, steroid use, and death
  - Increased use of narcotics and psychotropic medications
  - Higher health care utilization for CD more than UC
  - Universal health care (Canada) did not ensure optimal health across socioeconomic spectrum

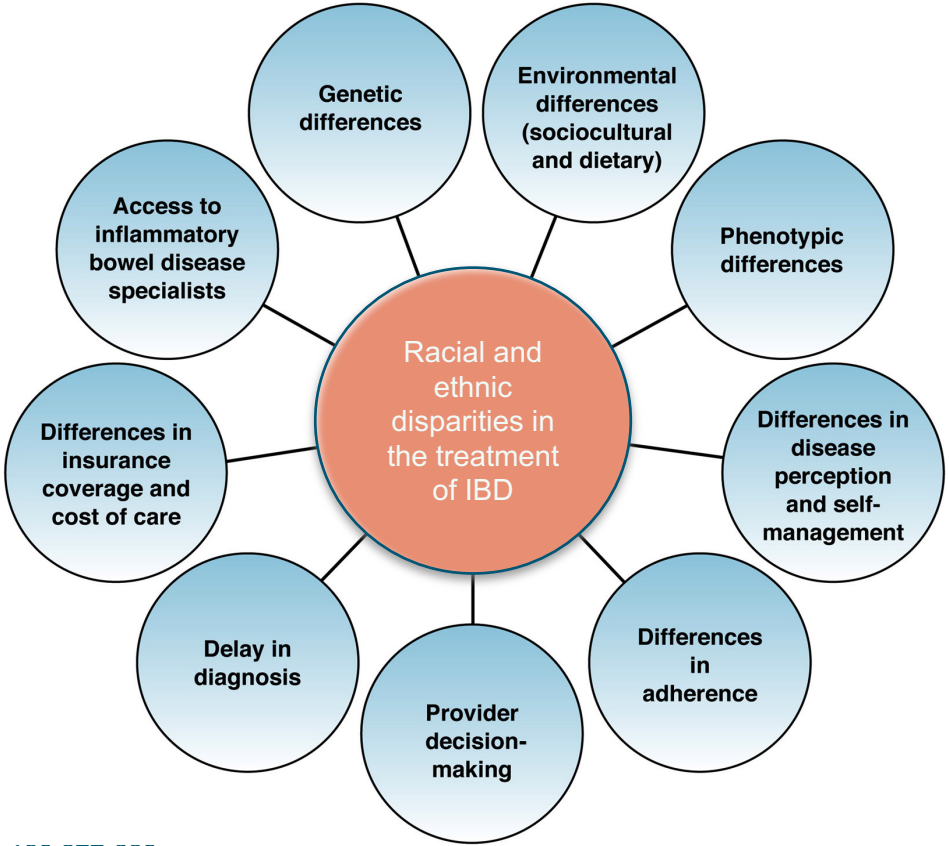
Nguyen NH, et al. *Clin Gastroenterol Hep.* 2020;18:1939-1948. Bernstein CN, et al. *Am J Gastroenterol*. 2020;115:2036-2046.

Effect of Race/Ethnicity on CD

- Most published studies of epidemiology and progression of IBD in the U.S. performed in predominantly White populations
- African Americans more likely to have penetrating disease, including perianal disease compared with White patients
- Differences in treatment: medical and surgical between racial/ethnic groups
  - Delay in time to diagnosis?
  - Due to gaps in health equity?
  - Differences in disease pathogenesis or progression?

Afzali A, Cross RK. *Inflamm Bowel Dis*. 2016;22:2023-2040. Shi HY, et al. *Clin Gastroenterol Hepatol*. 2018;16:190-197.

Racial/Ethnic Disparities in IBD Is Multifactorial



Barnes EL, et al. *Gastroenterology*. 2021;160:677-689.

Conclusions

- Patients desire more support/information at diagnosis
- Shared decision-making improves adherence, satisfaction, and costs
- Patients with IBD prioritize efficacy of therapy in decisions
- Risk communication best practices include:
  - Use of absolute numbers and visual aids, providing perspective to other disease/life risks
- SES is a predominant driver of poorer outcomes in IBD
- Higher financial toxicity in IBD
- Racial/ethnic disparities are multifactorial but imperative to understand and address

Revisit Our Patient Cases

Patient Case: Caitlin

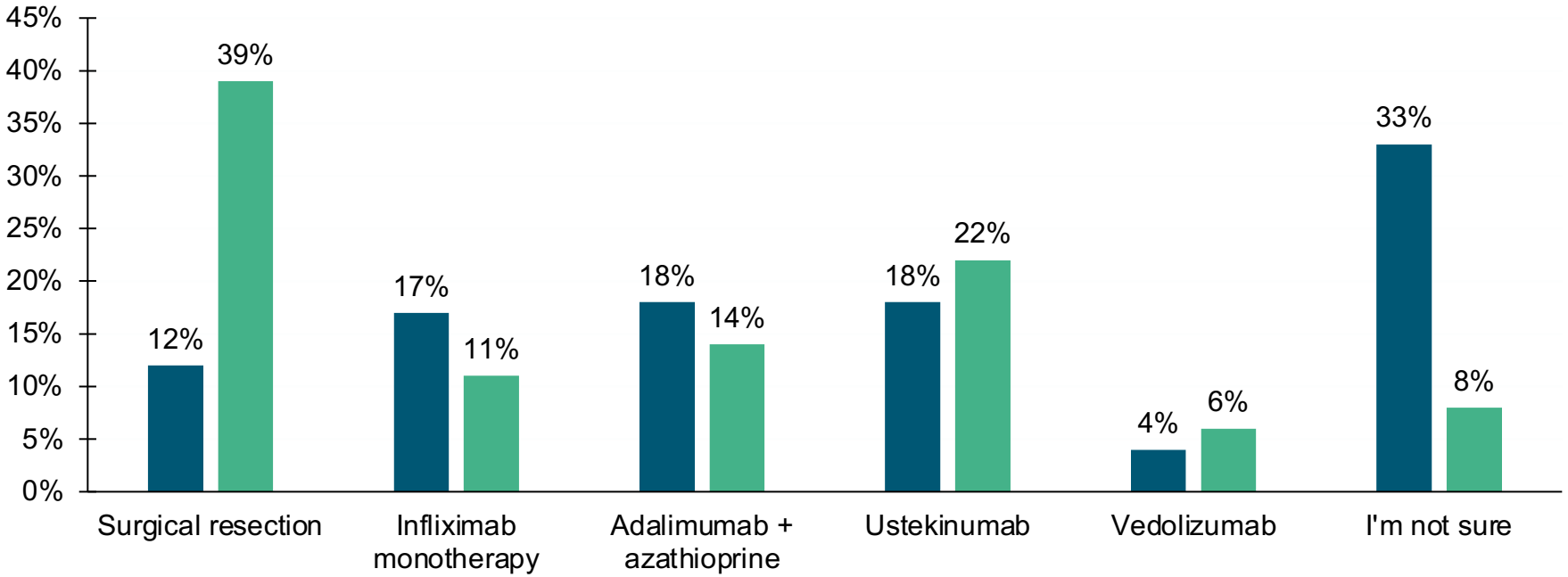
- 24-year-old woman with intermittent, severe right-sided abdominal pain for the past year; increased frequency of BMs (up to 5x daily); no blood visualized
- She has lost approximately 20 lbs
- She has had increasing abdominal distension and pain after eating in the past several weeks
- Significant iron deficiency anemia, albumin is 3.3
- Colonoscopy revealed severe stricture in the terminal ileum not traversed
- She is interested in pregnancy
- She travels with work and infusions would be difficult

Audience Response

What would would recommend for Caitlin?

A. Surgical resection
B. Infliximab monotherapy
C. Adalimumab + azathioprine
D. Ustekinumab
E. Vedolizumab
F. I’m not sure

Audience Response: Results



Results recorded on May 23, 2021.

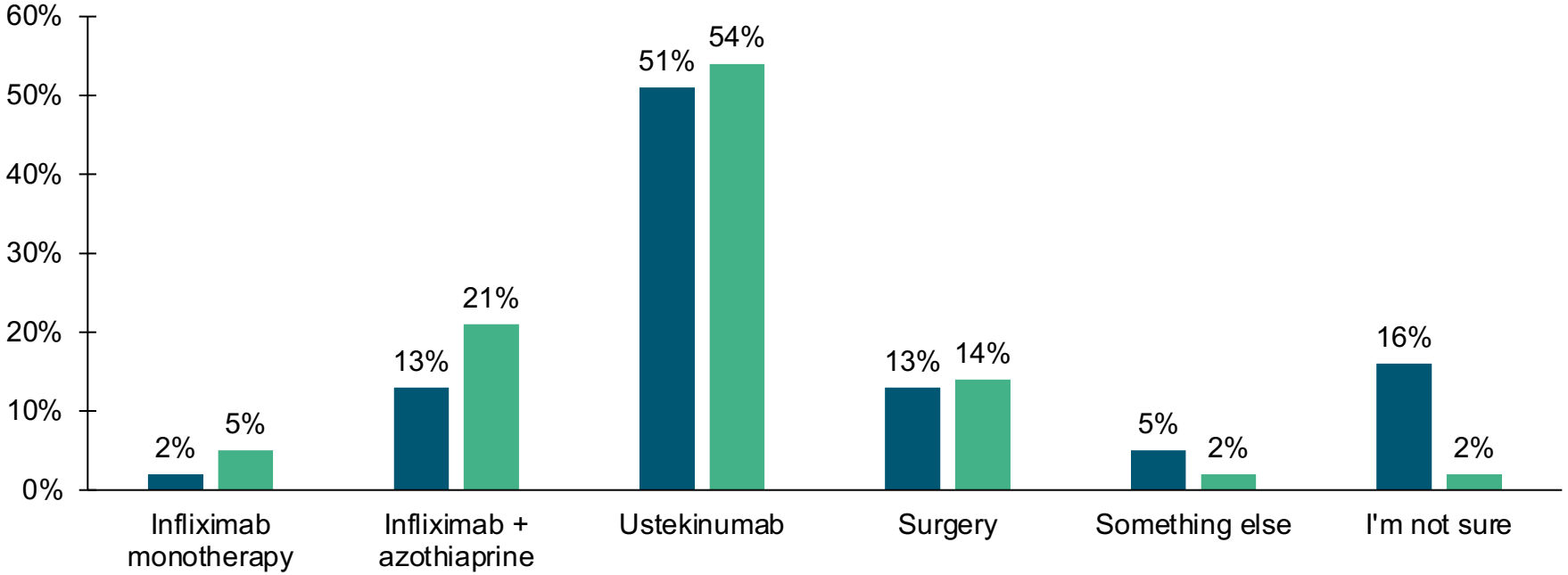
Patient Case: Madeline

- 50-year-old woman with ileocolonic CD
- She was stable on 6-mercaptopurine 50 mg daily but then stopped due to recurrent sinusitis symptoms
- Presented with worsening abdominal pain, diarrhea, and rectal bleeding
- Colonoscopy showed active ileocolonic CD
- Failed to respond to adalimumab and vedolizumab
- Ustekinumab started and symptoms improved

What would you recommend for Madeline?

A. Infliximab monotherapy
B. Infliximab + azathioprine
C. Ustekinumab
D. Surgery
E. Something else
F. I’m not sure

Audience Response: Results



Results recorded on May 23, 2021.

Patient Case: Patricia

- 32-year-old African American female with new diagnosis of ileocolonic CD; she also has perianal disease with actively draining fistula; she has had symptoms for nearly 2 years and was recently diagnosed with CD
- Labs: CRP 32.2 mg/L, TPMT normal, hepatitis B surface antigen negative, TB QuantiFERON negative
- Biologic naïve
- Mother with history of breast cancer
- *She is very hesitant to proceed with biologic therapy for her CD*

Audience Response

What would be your next step for Patricia?

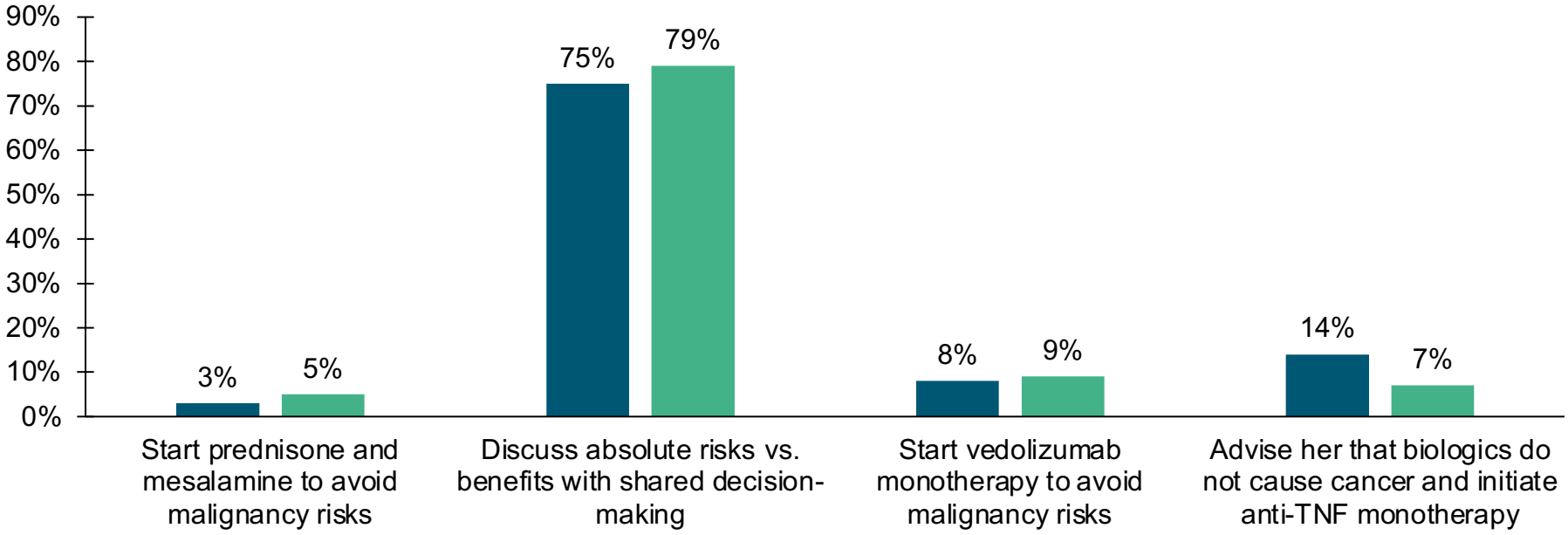
A. Start prednisone and mesalamine to avoid malignancy risks

B. Discuss absolute risks vs. benefits with shared decision-making

C. Start vedolizumab monotherapy to avoid malignancy risks

D. Advise her that biologics do not cause cancer and initiate anti-TNF monotherapy

Audience Response: Results



Results recorded on May 23, 2021.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

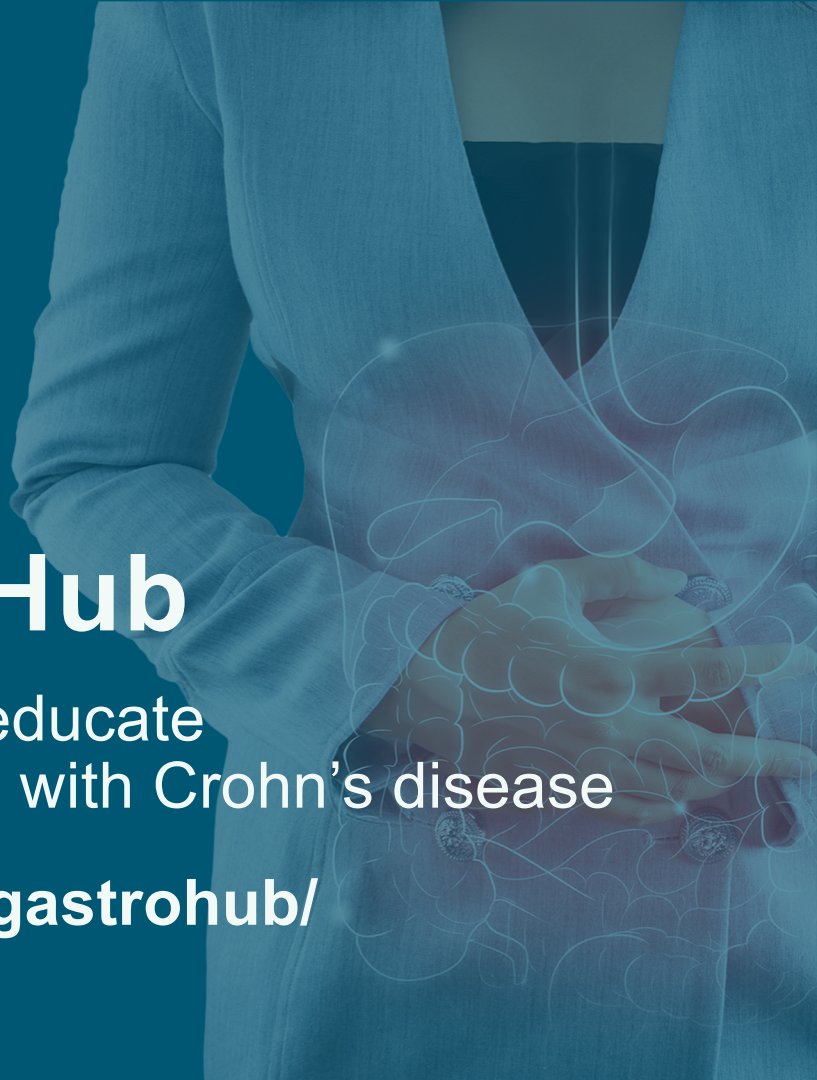
- Personalized, targeted therapy best sets patients up for success
- Integrate risk stratification and disease prognosis into your treatment decision-making
- Racial and ethnic disparities and inequities are multifactorial and we must pay attention to social determinants of health that impact patient outcomes

QUESTIONS & ANSWERS

Thank you for joining us. Don’t forget to collect your credit.

Questions recorded on May 23, 2021

CME OUTFITTERS



Visit the

Gastroenterology Hub

Free resources and education to educate health care providers and patients with Crohn's disease

https://www.cmeoutfitters.com/gastrohub/