IBD RISK STRATIFICATION & SELECTING THE IDEAL INITIAL THERAPY

IBDH

ARS QUESTION 1

Which of the following is **NOT** a predictor of disabling Crohn's disease course?

A. Multiple steroid courses
B. Recurrent perianal disease
C. Prior intestinal resection
D. Cannabis exposure

ARS QUESTION 2

All are associated with higher risk of colectomy in UC EXCEPT:

A. History of Campylobacteria infection
B. Pancolitis
C. Need for steroids
D. Hospitalization

CLINICAL CASE 1

IBDH

45-year-old male with newly diagnosed Crohn’s disease, with mild abdominal pain and normal inflammatory markers. BMI is 32 kg/m2 and is actively smoking. Colonoscopy showed small perianal fistula and large ileal ulcerations with no stricture, colon otherwise normal mucosa.

IBD Risk Stratification & Selecting the Ideal Initial Therapy

Kindra Clark-Snustad, DNP

KINDRA CLARK-SNUSTAD

Kindra Clark-Snustad is a board certified nurse practitioner with a clinical focus on inflammatory bowel disease (IBD). She works as a nurse practitioner at the University of Washington, Digestive Health Center, Inflammatory Bowel Disease Clinic, caring for patients with Crohn's disease and ulcerative colitis.

Kindra is an investigator at the University of Washington, IBD Research Program, assisting with clinical trials and investigator initiated studies.

IBDHORIZONS

DISCLOSURE

Advisor

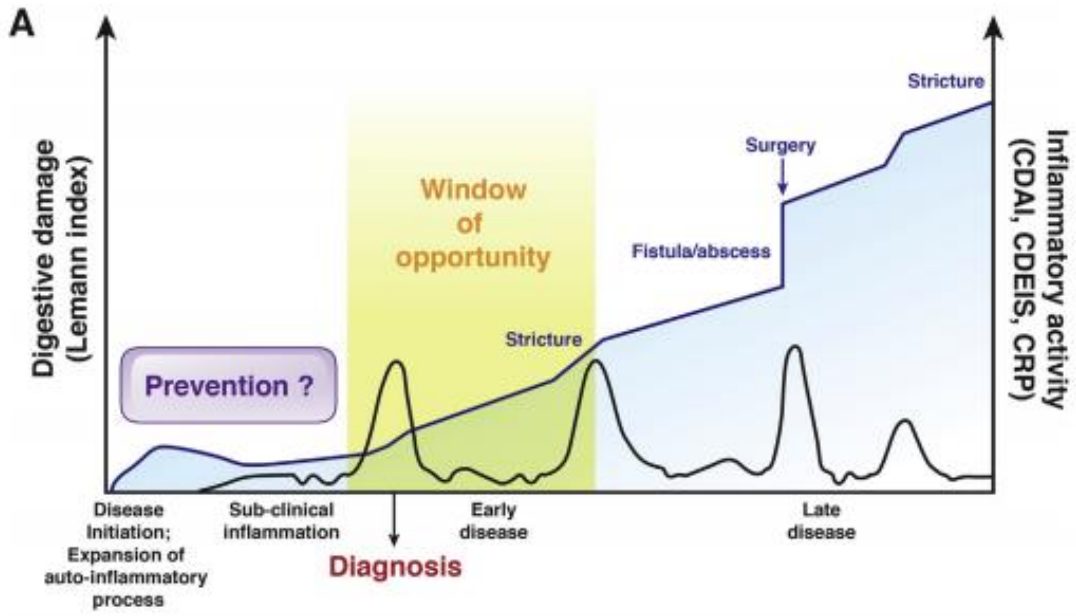
- BMS, AbbVie, Takeda, Pfizer

Objectives

- Prognostic factors for IBD course
- Tools for IBD risk stratification at diagnosis
- Predictors of therapeutic response
- Clinical impact of risk stratification on selecting initial IBD therapy or management approach

Natural disease course

CD



UC

- Risk of colectomy
  - 24% after 10 years, ~30% after 20 years
- Risk of colorectal cancer
- Long term structural & functional issues
  - Proximal extension
  - Stricturing
  - Pseudopolyps
  - Dysmotility
  - Anorectal dysfunction

(Langholz, Munkholm et al. 1994; Torres, Billioud et al. 2012; Colombel, Narula et al. 2017)

Disease activity vs severity

Activity

- *Short term* assessment of current disease
  - Symptoms - HBI, SCCAI
  - Labs - CRP, FC, albumin, hematocrit
  - Endoscopic - SESCD, Mayo score

Severity

- *Long term* assessment of disease characteristics that may predict future disease course
- Should direct therapy decisions to modify risk of disease complications

Symptoms don't always reflect endoscopic disease.

Current picture doesn't always predict risk of long-term complications.

Risk stratify – ulcerative colitis

Low risk

- Limited extent
- Mild endoscopic disease

High risk

- Age of diagnosis <40
- Pancolitis
- Deep ulcers
- Steroid dependent, IV steroids
- Hospitalization
- C. difficile, cytomegalovirus infection

(Sandborn 2014; Agrawal, Spencer et al. 2021; Torres, Mehandru et al. 2017; Rubin, Ananthakrishnan et al. 2019)

Risk stratify – Crohn's disease

Low risk

- Limited extent
- Mild endoscopic disease

High risk

- Age of diagnosis <30
- Extensive disease (extensive ileal, pancolitis)
- Deep ulcers
- Severe rectal disease
- Strictures or fistulas
- Steroid dependent, IV steroids
- Hospitalization
- Smoker

(Sandborn 2014; Agrawal, Spencer et al. 2021; Torres, Mehandru et al. 2017; Rubin, Ananthakrishnan et al. 2019)

Treatment approach

Low risk/mild disease

- Thorough assessment for disease complications/risk factors
- Asymptomatic
  - Consider close monitoring with periodic labs (CRP, FC, albumin, hematocrit) and colonoscopy every 1-2 years
- Mild symptoms
  - Consider steroid (prefer budesonide) for induction of remission
  - Mild ileal CD – taper off steroids and monitor
  - Mild colonic disease – consider 5 ASA maintenance
- Monitor! If not achieving remission, progressive disease, risk factors, or need >1 steroid course every 1-2 years, then advance therapy

High risk/moderate-severe disease

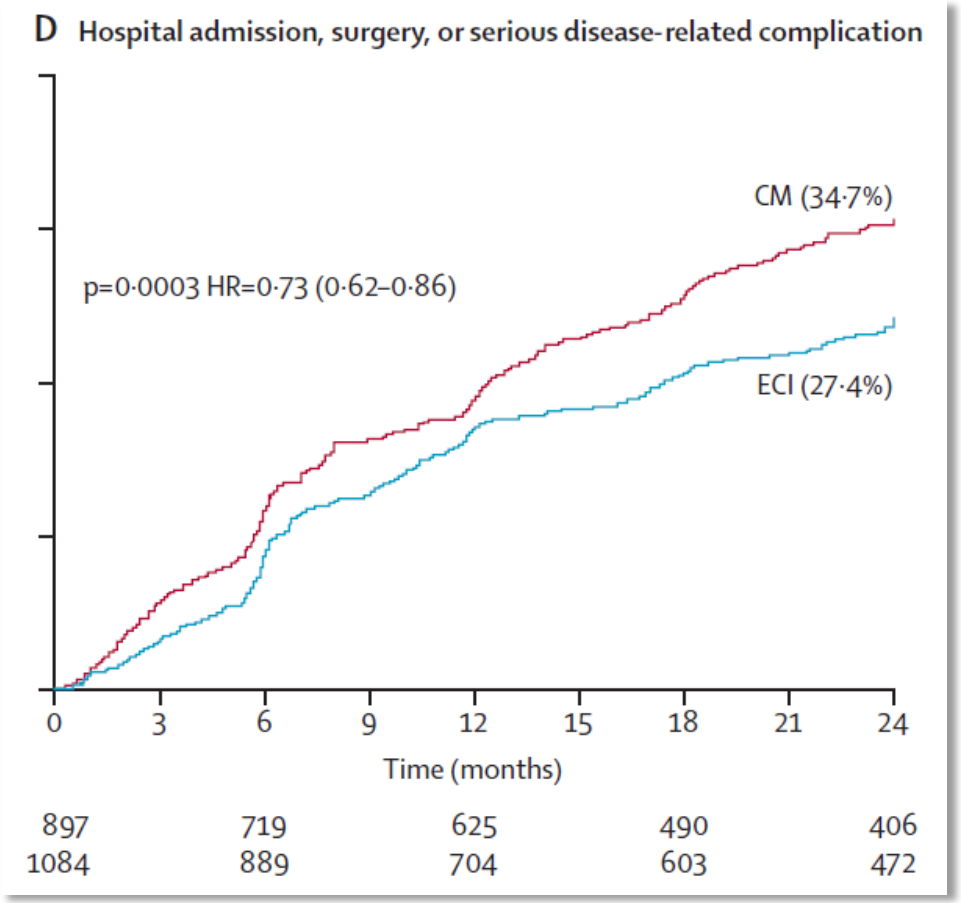
→ early appropriate therapy with biologics or small molecules

(Nguyen, Singh et al. 2020)

REACT trial

- Open-label, cluster randomized controlled trial of 1809 patients with Crohn's disease
- Early combined immunosuppression (ECI) vs. conventional management (CM)
- The 24-month rate of major adverse outcomes (surgery, hospital admissions, or serious disease related complications) was lower in ECI vs. CM
  - 27.4% vs. 34.7% (ARD = 7.3%, HR =0.73; 95% CI 0.62-0.86; P=0.0003)

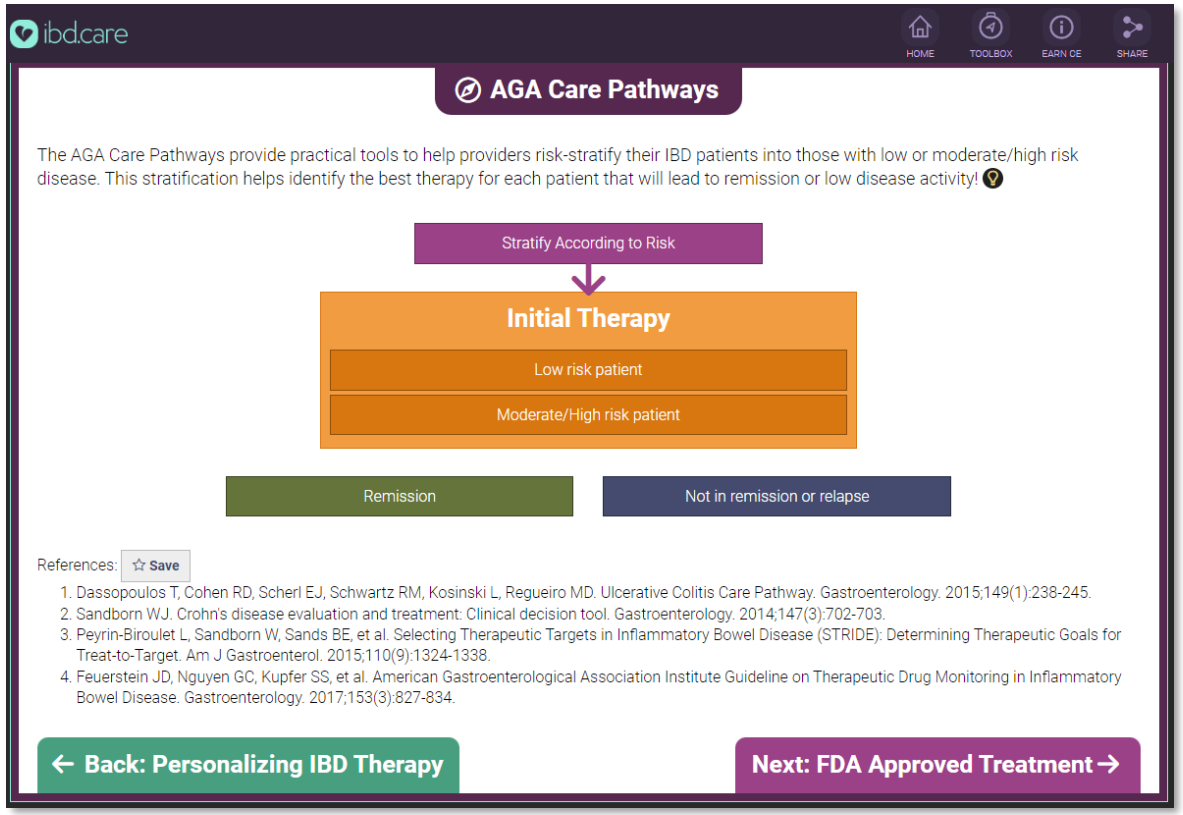
(Khanna, Bressler et al. 2015)



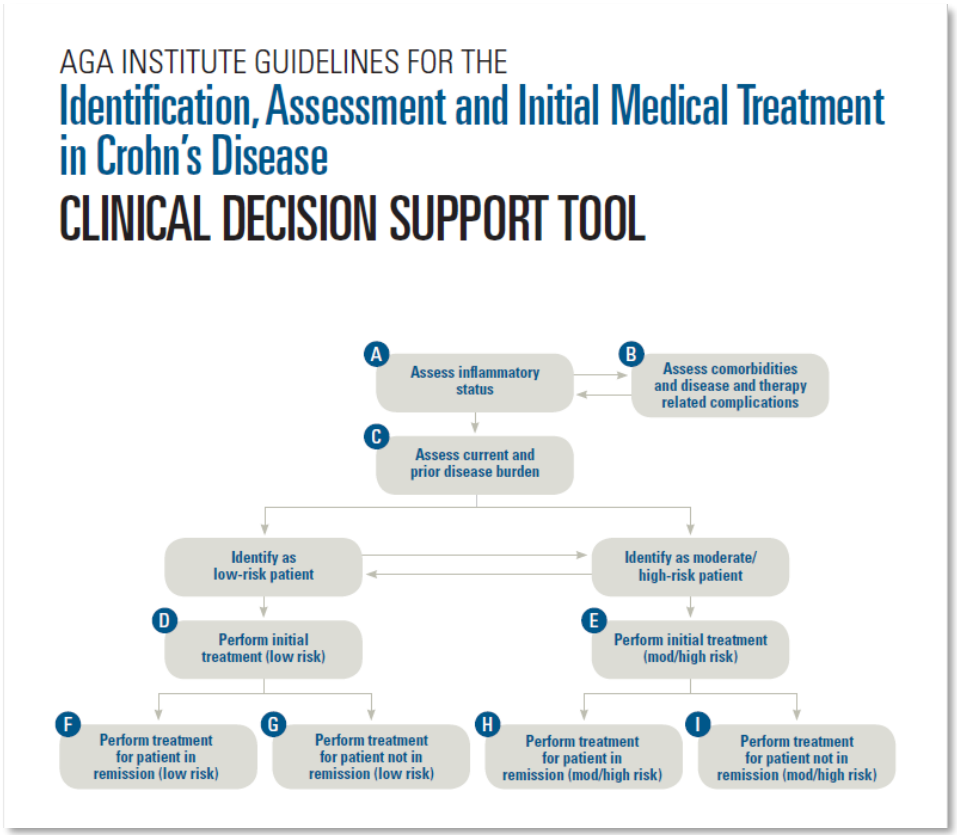
IBDHorizons

Tools for IBD risk stratification

AGA Care Pathways
https://www.ibd.care/care-navigator/aga-care-pathways



AGA Clinical Decision Support Tool for CD
(Sandborn 2014)



IBDHorizons

Predictors of response to therapy

- Characteristics associated with poor response are common across biologics. These may be more predictive of difficult to treat IBD.
    - More severe disease, higher inflammatory burden
    - Prior surgery, complications
    - Prior TNF exposure, low biologic trough levels
- High CRP and low albumin predict rapid biologic clearance
    - Consider small molecule or optimized biologic
- Comparative trials
    - No trials evaluate optimal sequence of all available therapy
    - Network metanalyses – indirect comparison
    - Head-to-head randomized controlled trials
- Insurance plays a significant role

(Singh, Murad et al. 2020; Singh, Fumery et al. 2018; Nguyen, Singh et al. 2020)

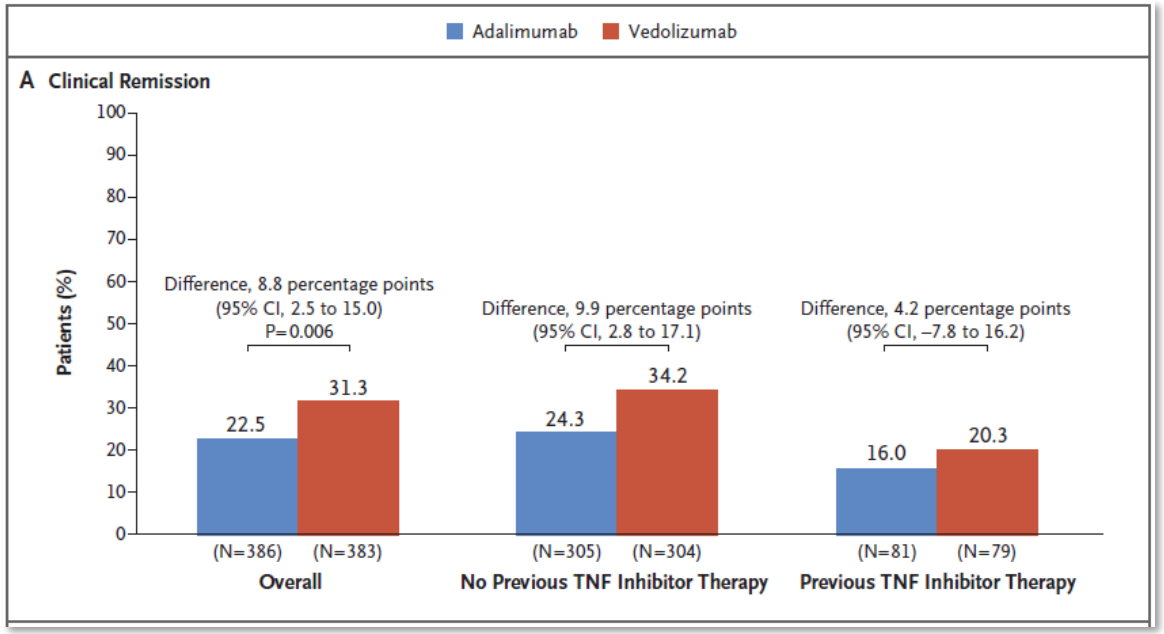
Head-to-head - VARSITY

Methods

- 3b double blind, randomized controlled trial comparing vedolizumab vs adalimumab
- 769 patients with mod-severe UC
- 25% of patients had prior TNF exposure
- Dose escalation was not permitted

Results

- At week 52, statistically more patients on vedolizumab achieved
  - clinical remission (31.3% vs. 22.5%; P = 0.006)
  - endoscopic improvement (39.7% vs 27.7%; p <.001)



(Sands, Peyrin-Biroulet et al. 2019)

IBDHorizons

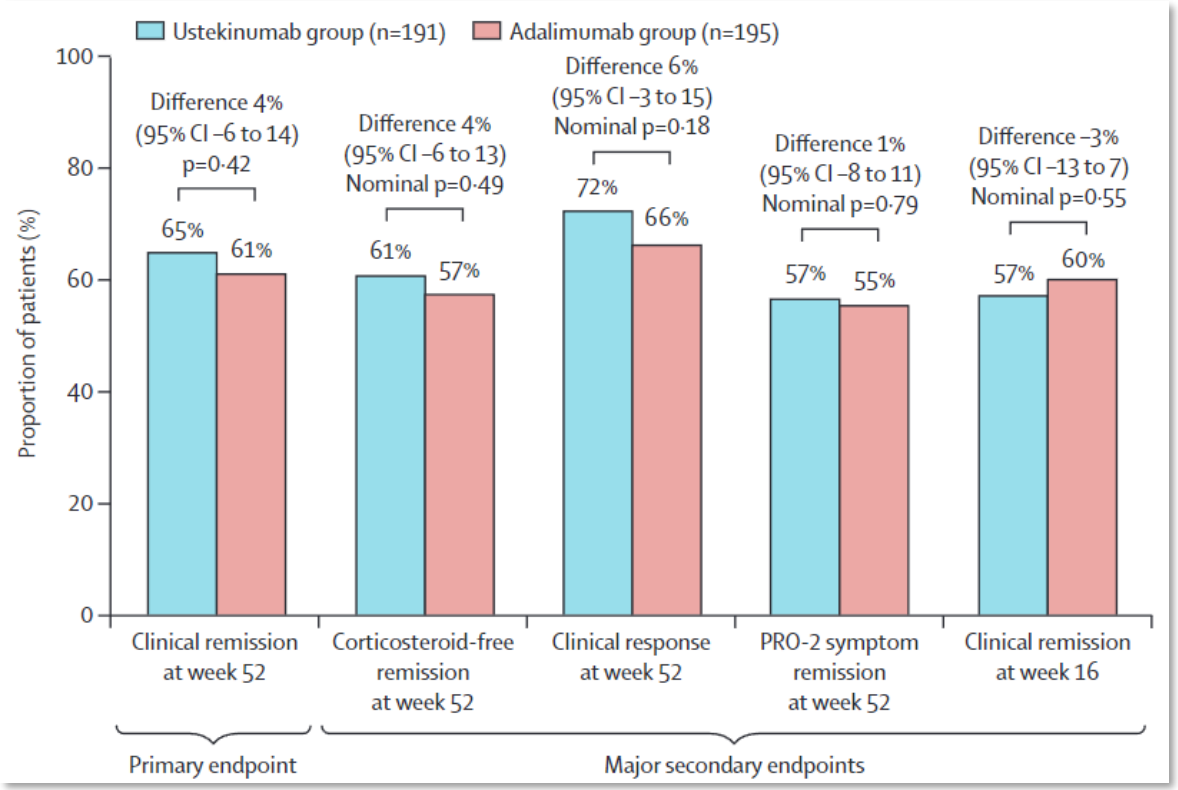
Head-to-head - SEAVUE

Methods

- 3b double blind, randomized controlled trial comparing ustekinumab and adalimumab
- 386 biologic naïve patients with CD
- Monotherapy, no dose optimization

Results

- At week 52 there were no significant differences in clinical remission
- ustekinumab may be safer



(Sands, Irving et al. 2022)

IBDHorizons

Therapy considerations for high-risk patients

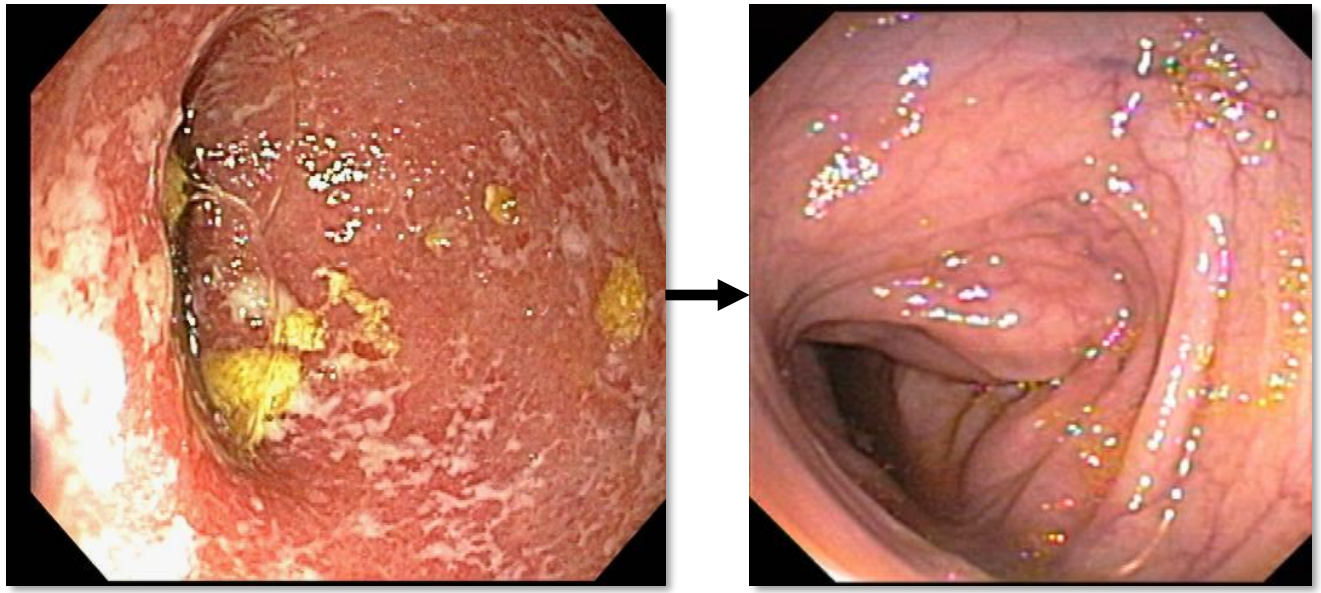
	Safety	Comorbid autoimmune disease	OK in pregnancy?	Efficacy	Route	Antibody risk
IL 12/23 ustekinumab **IL 23** risankizumab	Likely safer	Treats psoriasis and psoriatic arthritis	Yes	SEAVUE: ustekinumab = adalimumab in CD	IV, then SC	Low
A4β7 vedolizumab	Likely safer	Only treats IBD	Yes	VARSITY: vedolizumab > adalimumab in UC	IV	Low
S1P (UC) ozanimod	Appears safe, await long term data	Treats MS	No		PO	NA
TNF infliximab, adalimumab, certolizumab, golimumab	-Higher infection risk -Relative contraindication in CHF, MS, areas endemic for opportunistic infection	Treats RA, psoriasis, psoriatic arthritis, ankylosing spondylitis, etc.	Yes	Metanalysis suggests largest effect for infliximab	IV or SC	Higher
JAK (UC) tofacitinib upadacitinib	-Higher infection risk -Avoid in smokers, significant CV disease, malignancy	Treats RA, psoriatic arthritis, ankylosing spondylitis	No	Must try TNF first	PO	NA

(Sands, Peyrin-Biroulet et al. 2019; Sands, Irving et al. 2022)

IBDHorizons

Treat to target

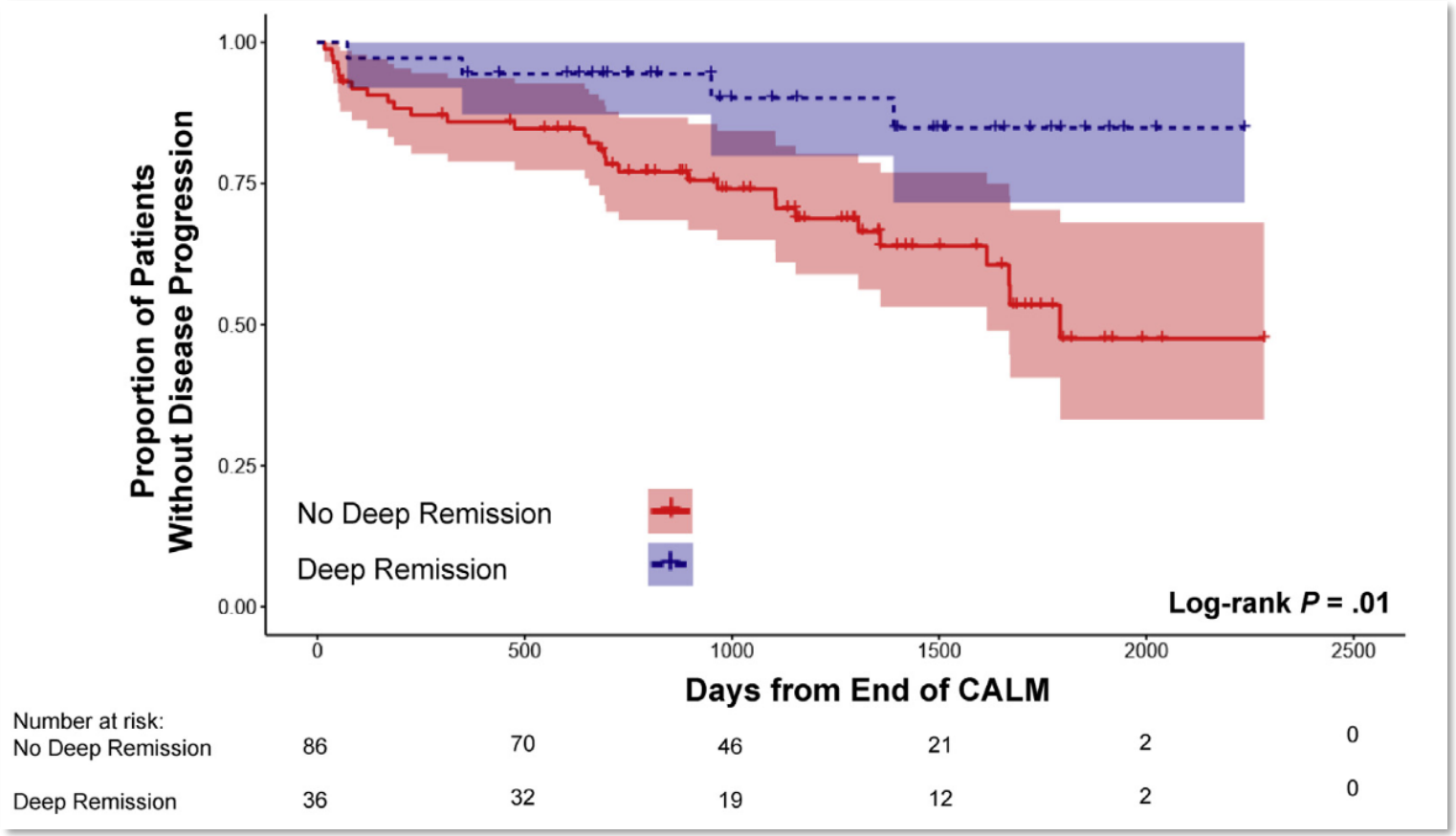
- Improve symptoms & quality of life
- Minimize side effects of medications
- **Steroid free endoscopic remission**
  - decreases risk of stricture, fistula, colorectal cancer/dysplasia, hospitalizations & surgery



(Turner, Ricciuto et al. 2021; Shah, Colombel et al. 2016; Gupta, Harpaz et al. 2007)

Follow up data from CALM

Patients with early CD who achieved deep remission had a **significantly lower risk** of new fistula, abscess, hospitalization or surgery (adjusted HR 0.19; 95% CI, 0.07-0.31)



(Ungaro, Yzet et al. 2020, Colombel, Panaccione et al. 2017)

IBDHorizons

Summary

- **Risk stratify & treat appropriately**
  - Low risk – budesonide, mesalamine or monitor
  - High risk – early appropriate therapy with biologics or small molecules
- **No trials on ideal sequence of all therapies**
  - Vedolizumab > adalimumab in UC
  - Consider safety, pregnancy, comorbidities
- **Treat to target**

Low risk

- Limited extent
- Mild endoscopic disease

High risk

- Age of diagnosis <30
- Extensive disease (extensive ileal, pancolitis)
- Deep ulcers
- Severe rectal disease
- Strictures or fistulas
- Steroid dependent, IV steroids
- Hospitalization
- Smoker
- C. diff or CMV (UC)

IBDHorizons

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Kindra is an investigator at the University of Washington, IBD Research Program, assisting with clinical trials and investigator initiated studies.

IBDHORIZONS

PANEL DISCUSSION

IBDH

Panel Discussion

Moderator: Ghassan Wahbeh, MD

Kindra Clark-Snustad, DNP

Erica Heagy, FNP

Scott D. Lee, MD

Jeff Jacobs, MD

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3rd IBDHORIZONS UPDATES FOR APP

IBDH

King Street Ballroom, October 29, 202