

IBD Alliance
Program

2014

Optimizing Therapies for Severe Ulcerative Colitis

October 19, 2014

Ellen J. Scherl, MD, FACP, FACG, AGAF, FASGE, NYSGEF

Director Jill Roberts Center for Inflammatory Bowel Disease
Jill Roberts IBD Research Institute

Professor of Medicine Weill Medical College Cornell University
New York Presbyterian Hospital/Weill Cornell Medical Center

Adjunct Professor of Medicine
at Columbia University College of Physicians and Surgeons



Weill Cornell Medical College

NewYork-Presbyterian Hospital
Weill Cornell Medical Center

Accredited by:

PURDUE
UNIVERSITY

This program is supported by educational grants from
AbbVie, Janssen Biotech, Inc., Takeda Pharmaceuticals
and Prometheus Laboratories.

Sponsored by:

Gii Gastrointestinal
Health Foundation

Severe Ulcerative Colitis

“The role of the physician is to keep the patient entertained while nature takes its course”

Voltaire

**Moderate to severe UC:
Optimization strategies, Role of AntiTNFs,
Anti-Integrins, IDA**

Exception: Acute Fulminant Colitis

Defining Severity of UC: When Does Severe Become Fulminant Colitis

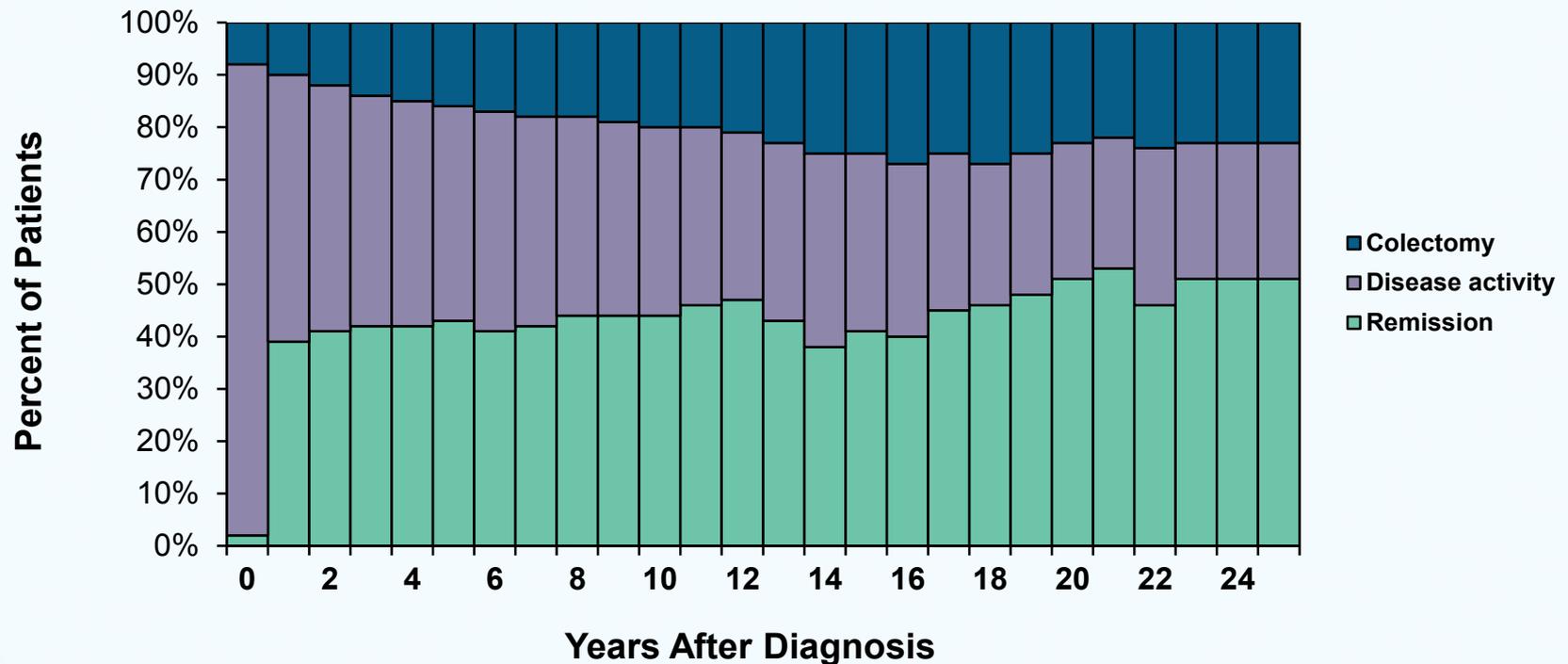
Mild	<4 stools/day ± blood normal ESR no signs of toxicity
Moderate	≥4 stools/day minimal signs of toxicity
Severe	>6 bloody stools/day + fever, tachycardia, anemia, elevated ESR
Fulminant	>10 stools/day, continuous bleeding, toxicity, abdominal tenderness/distension, transfusion requirement, colonic dilation on x-ray

Fulminant UC: Is Ulcerative Colitis a Surgical Disease?

- *When should gastroenterologists call a surgeon? When does Severe UC transition to Fulminant UC?*
- What % of UC patients require colectomy **WITHIN A YEAR** after a severe first attack?

UC: Natural History

- 10% Of Patients HAVE A SEVERE FIRST ATTACK REQUIRING COLECTOMY, and the majority NEVER achieve remission during the FIRST YEAR



Percent of patients with disease activity, in remission, or having colectomy performed each year after diagnosis

Clinical Insights in Ulcerative Colitis

- Approximately 1.2 million Americans are living with IBD with about half suffering from ulcerative colitis (UC).¹
- Current treatment approaches in UC have been moderately effective with ongoing disease activity present in approximately 50% of all patients with UC.^{2,3}
- Colectomy rates remain high and absence from social activities, unemployment, impaired quality-of-life, sick leave, and disability pensions, are higher in patients with UC than in the general population.³
- **Despite continuing advances in medical therapies for UC there is a reluctance to treat SELECT UC patients early with effective regimens.**

Personalized Medicine

- We will focus on the individual who presents with an initial severe attack. Never achieves remission and is at risk for colectomy within the first year.

Case

- 22 y/o man with newly diagnosed medically refractory severe UC presenting to your office to discuss concerns regarding initiating biologic therapy, which was recommended within the past month
- PMHx : Severe UC diagnosed 14 months prior to consultation with you.

IBD History

- Diagnosed with UC pancolitis over 1 year ago
 - Initially started on Asacol 4.8g and prednisone 60mg
- Over past 14 months has had 5 courses of steroids (between 60 and 20mg)
- 6MP started 6 months ago.
No steroid sparing
 - 6TG level therapeutic at 263

Current Presentation

- Presents to your clinic:
 - Currently on Prednisone 20mg and 6MP 100mg
 - ~10-12 stools daily (both bloody and non-bloody)
 - +nocturnal symptoms
 - No abdominal pain or tenesmus
 - 30lb weight loss over past year
 - New onset of lightheadedness and pleuritic L-sided chest pain x 2 days

Impression: Severe Medically Refractory UC

- Currently refractory to prednisone (14 months) and optimized 6MP (6 months)
- You admit him to ER noting that he is diaphoretic and experiences a pre-syncopal episode in clinic.

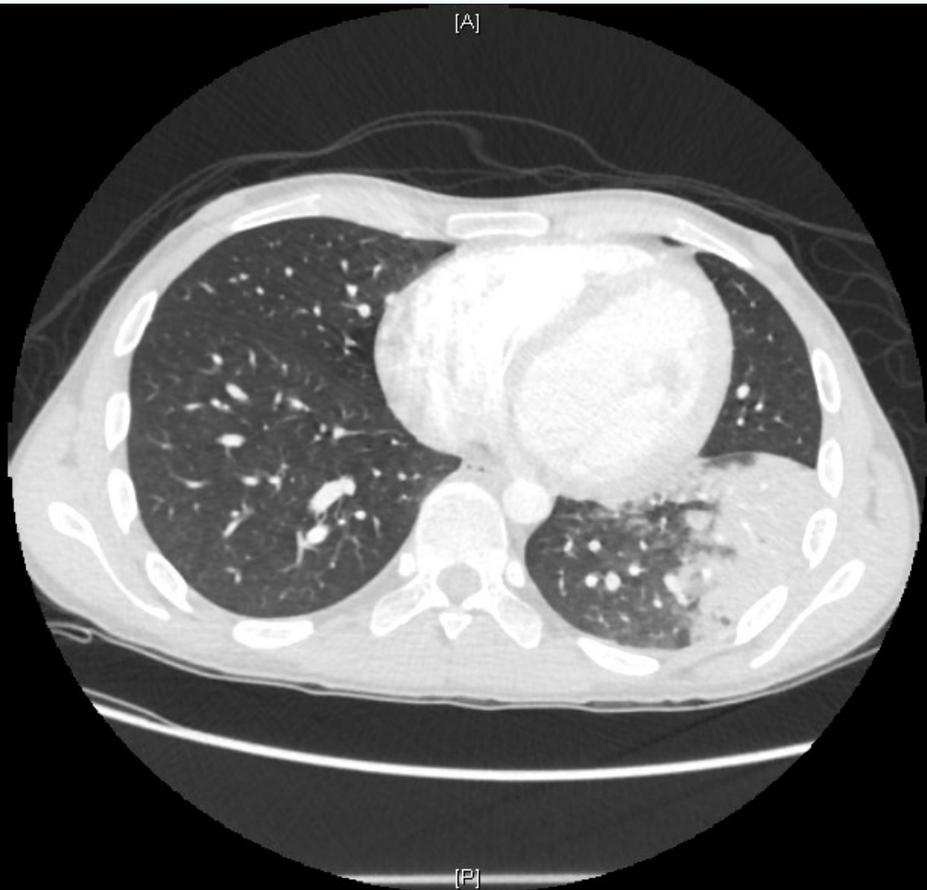
Admission Data

- PE:
 - Thin young man, abdomen soft, nontender, +BS
- Labs:
 - $5.1 > 11.7 / 34.6 < 202$
 - Albumin 2.8
 - ESR 115
- Imaging: CT scan with left lower lobe pneumonia
- Flex sig:
 - moderate to severe colitis
 - Path: chronic active colitis with erosion and ulcer; negative for CMV

Defining Severity of UC: Is This Severe or Fulminant Colitis?

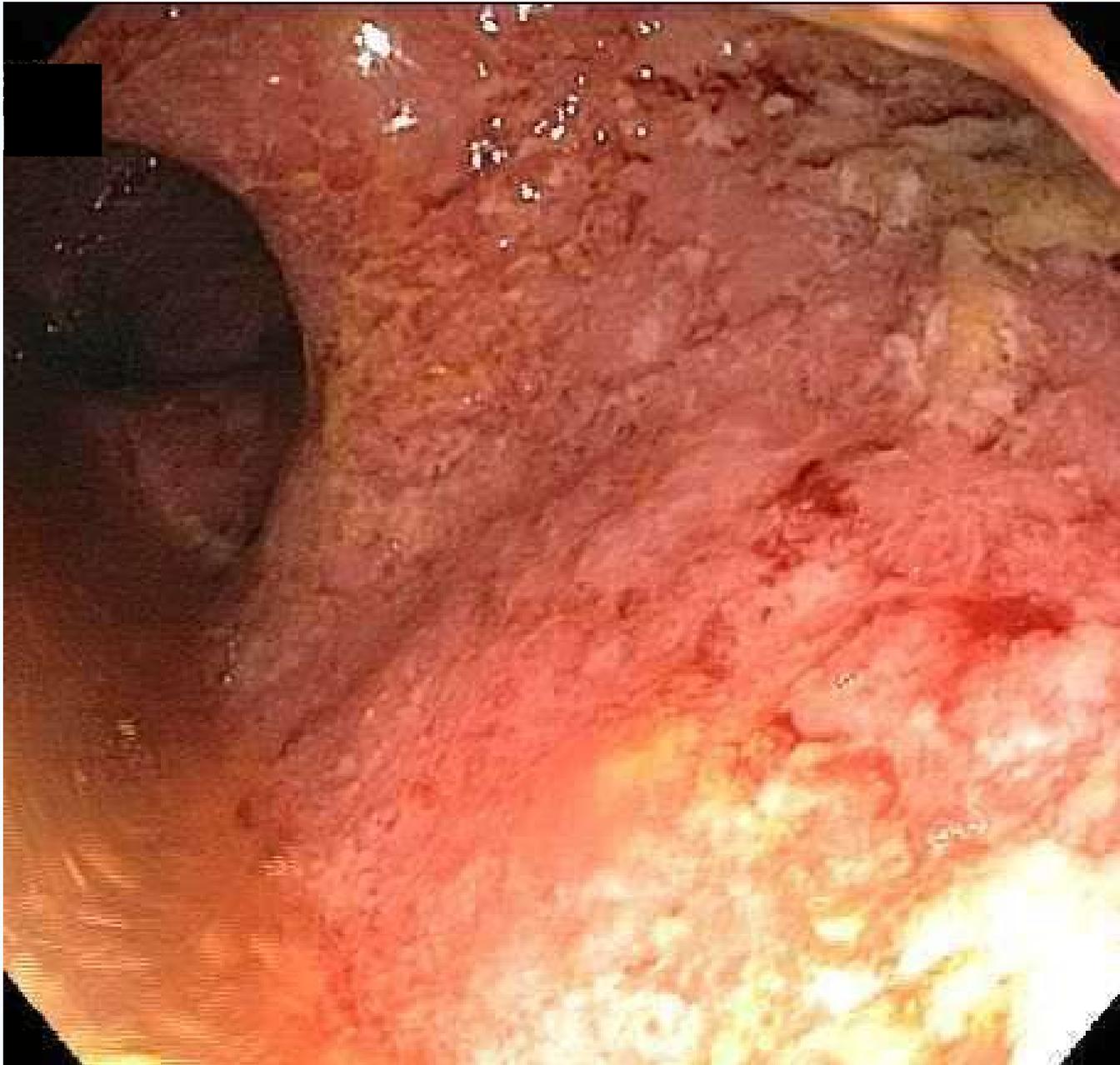
Mild	<4 stools/day ± blood normal ESR no signs of toxicity
Moderate	≥4 stools/day minimal signs of toxicity
Severe	>6 bloody stools/day + fever, tachycardia, anemia, elevated ESR
Fulminant	>10 stools/day, continuous bleeding, toxicity, abdominal tenderness/distension, transfusion requirement, colonic dilation on x-ray

Se:2
Im:162



1.25MM
OMNIPAQUE

C-498
W1465



What Are His Therapeutic Options, Now? What Are His Concerns? (Colectomy Avoidance)

Anti-TNF optimization:

Infliximab/Adalimumab/Golimumab

Anti-Integrin: Vedolizumab

Cyclosporine

TPC vs STC

What Were His Therapeutic Options After 1 Month of Steroid Therapy? What Were His Concerns?

Anti-TNF optimization:

Infliximab, Adalimumab, Golimumab

Anti-Integrin: Vedolizumab

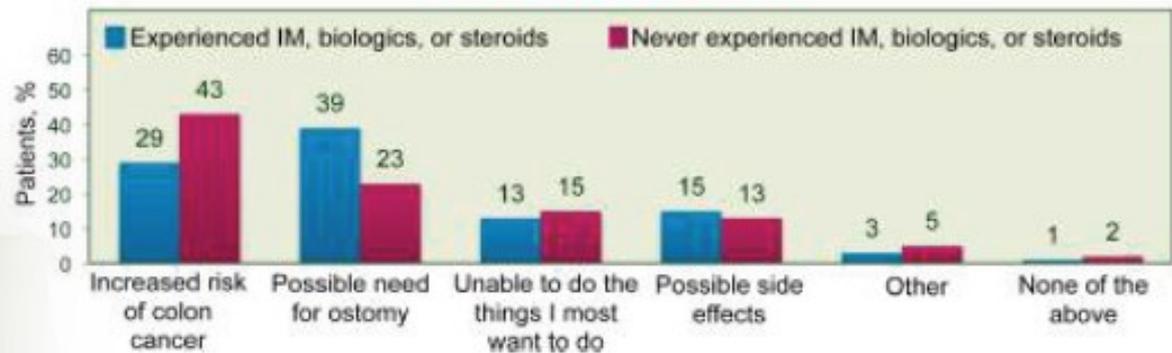
Cyclosporine

TPC vs STC

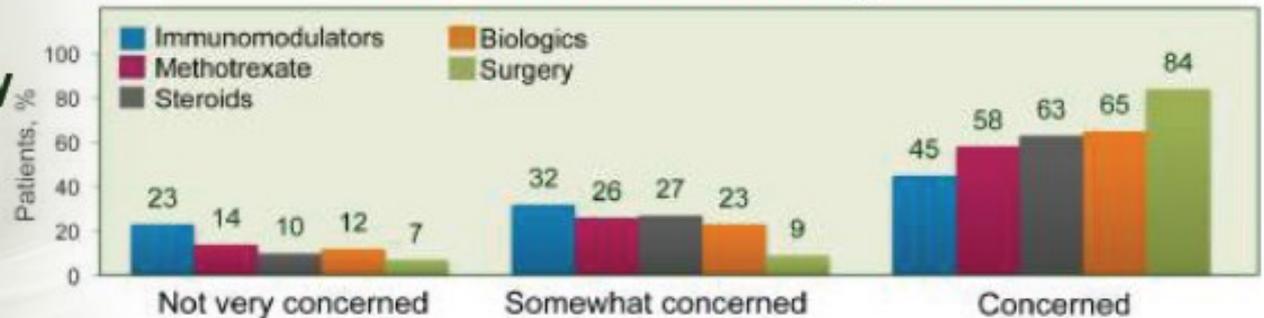
Patient Concerns in UC

- Survey of UC patients in US and Australia (N=460)
- Patients are most fearful of colon cancer and needing an ostomy
- Patients were equally fearful of steroids and biologics

Fears of UC Patients



Medication Concerns Among UC Patients



Patients with UC are more concerned about complications of their disease than medication side effects. It is important to discuss strategies for decreasing the risk of colectomy and CRC.



Now let's discuss patient concerns and toxicity BEFORE we review efficacy

Adverse Events with Steroids

Tolerability

- Psychosis/Cognitive disorders
- Steroid withdrawal symptoms
- Cushingoid/bruising/acne/edema

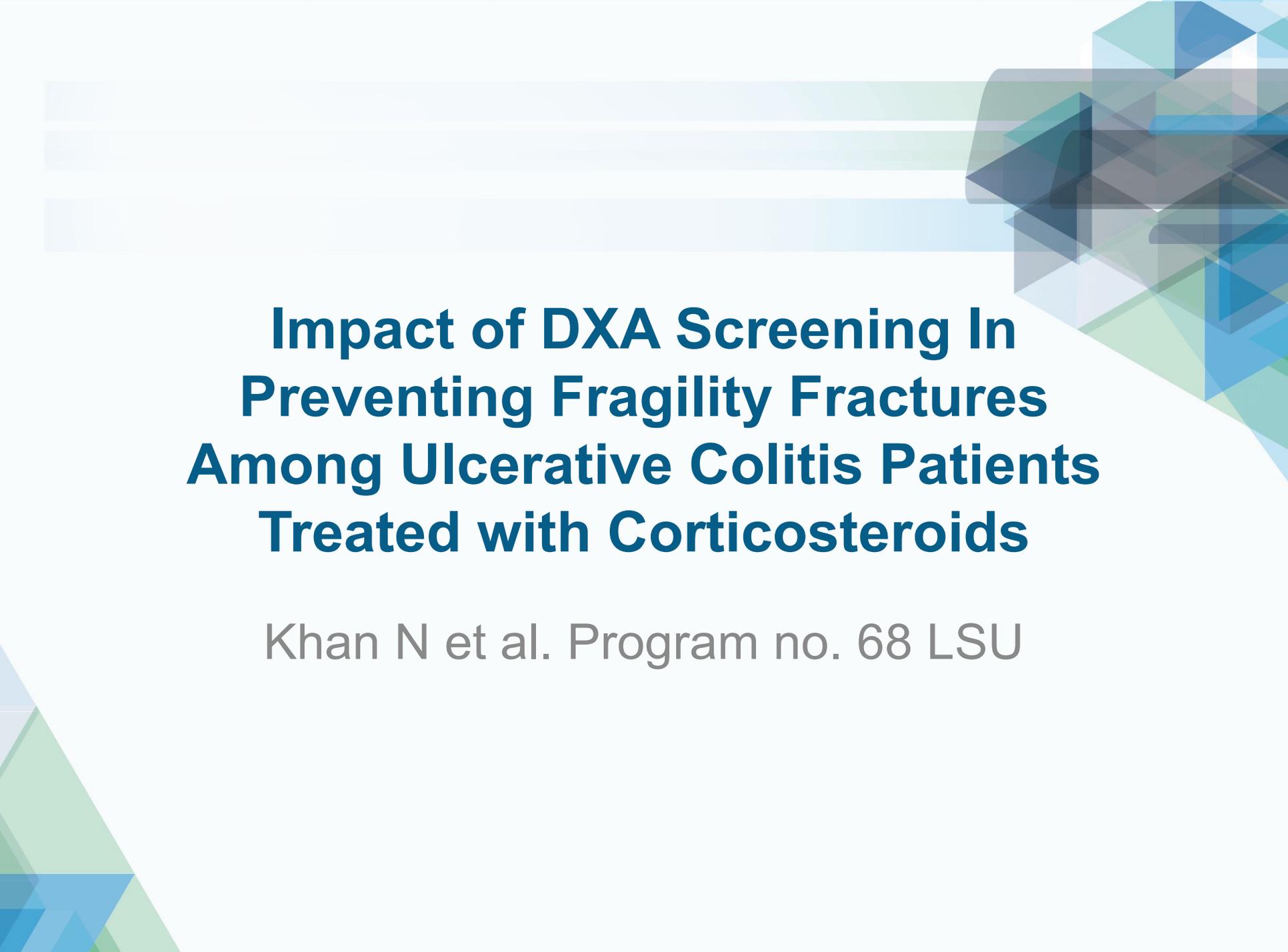
Development of adrenal suppression

Infection

Cataracts

Osteoporosis/AVN

Hypertension

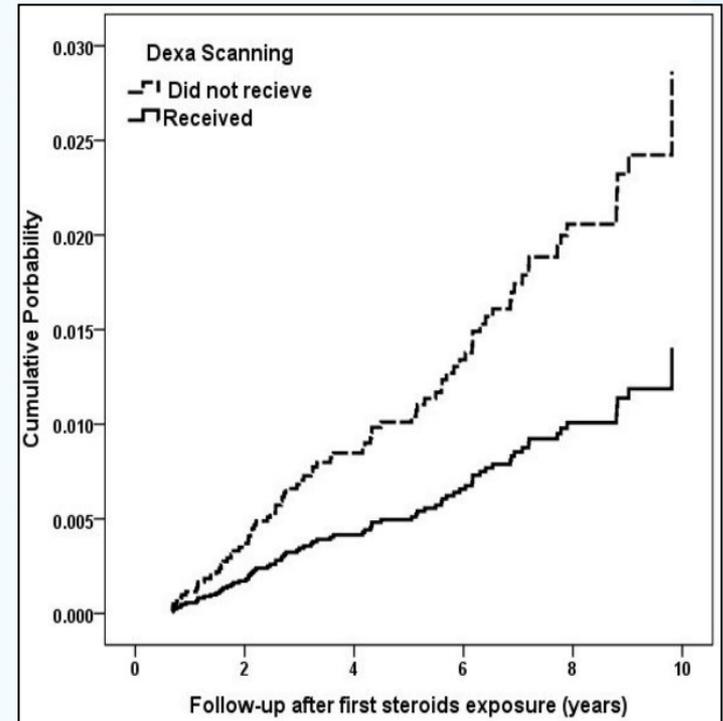


Impact of DXA Screening In Preventing Fragility Fractures Among Ulcerative Colitis Patients Treated with Corticosteroids

Khan N et al. Program no. 68 LSU

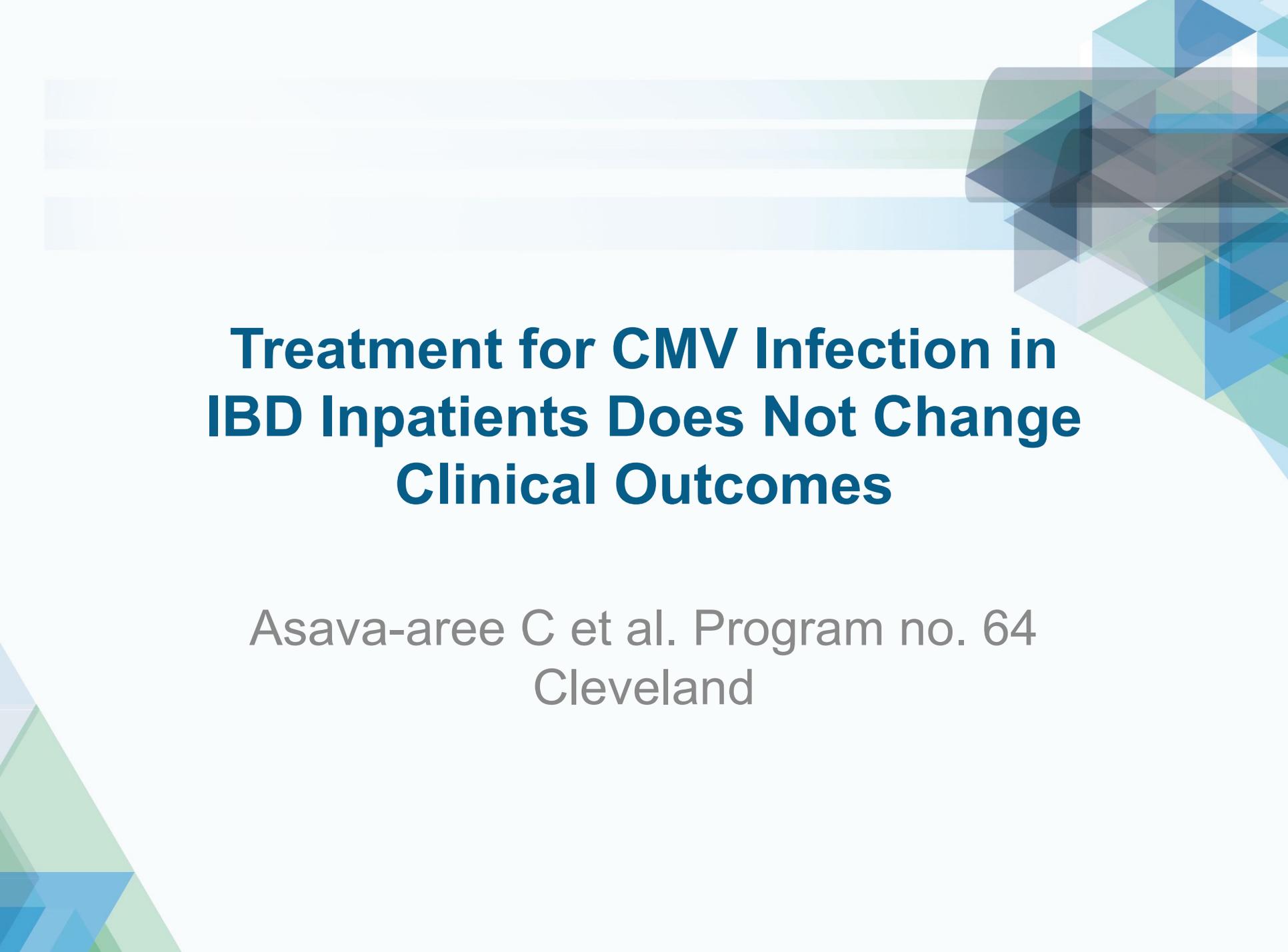
Impact of DXA Scanning on Fragility Fracture in Patients With Ulcerative Colitis Taking Corticosteroids

- Purpose
 - To assess the adherence to these guidelines and the benefits of dual energy X-ray absorptiometry (DXA) screening among corticosteroid-treated UC patients
- Patients and methods
 - Data derived from Veterans Affairs system
 - Occurrence of fragility fractures identified using ICD-9 codes
 - Exposure to corticosteroids assessed using pharmacy data
- Results
 - Only 20% to 48% of patients received a DEXA scan
 - Those who received DEXA scans were 50% less likely to have a fragility fracture (HR=0.5; 95% CI 0.3-0.9; $P=.03$)



Conclusion

- Rates of DXA screening were low among CS-treated UC patients.
- Those who received DXA screening had 50% reduction in the risk of fragility fractures.
- More efforts should be directed towards raising the adherence to AGA guidelines and the awareness of DXA benefits in preventing fragility fractures.



Treatment for CMV Infection in IBD Inpatients Does Not Change Clinical Outcomes

Asava-aree C et al. Program no. 64
Cleveland

Impact of CMV Treatment on Outcomes

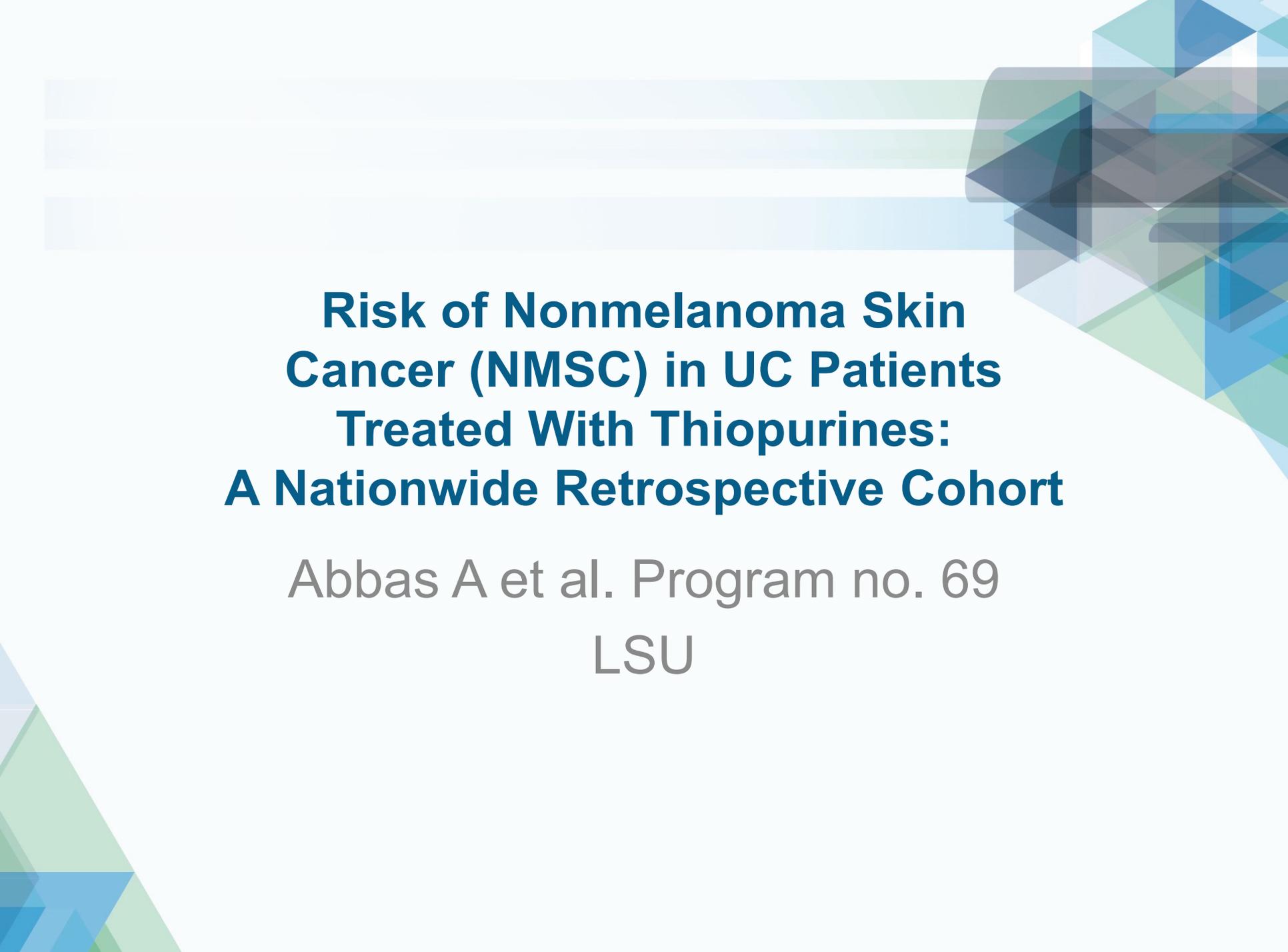
- Purpose
 - To compare the clinical outcomes between CMV negative and positive patients
- Patients and methods
 - Patients with IBD (N=140) admitted for active colitis with a colon biopsy for CMV
 - Six clinical outcomes assessed for CMV negative vs positive and CMV-positive patients with and without treatment:
 - Length of hospital stay
 - ICU transfer
 - Requirement for gastrointestinal surgeries within 30 days
 - Requirement for gastrointestinal surgeries within 12 months
 - Rehospitalization
 - Mortality

Impact of CMV Treatment on Outcomes: Results and Conclusions

Variables	All recruited patients (N=140)			All CMV positive patients (n=33)		
	CMV negative (n=107)	CMV positive (n=33)	<i>P</i>	With treatment (n=28)	Without treatment (n=5)	<i>P</i>
Length of hospital stay (days, mean+/-SD)	9.16 ± 6.89	12.39 ± 7.65	.0346	12.25 ± 7.89	13.2 ± 6.83	.7892
ICU transfer	6 (5.6%)	4 (12.1%)	.2457	4 (14.3%)	0 (0%)	1
Requirement for GI surgeries within 12 months	47 (43.9%)	20 (60.6%)	.1124	16 (57.1%)	4 (80%)	.6253
Requirement for GI surgery within 30 days	42 (39.3%)	15 (45.5%)	.5486	11 (39.3%)	4 (80%)	.1523
ER visit or rehospitalization (non-CMV-related)	42 (39.3%)	22 (66.7%)	.002	18 (64.3%)	4 (80%)	1
Mortality within 12 months	1 (0.01%)	0	NA	0 (0%)	0 (0%)	NA

Conclusion

- 23.6% of IBD inpatients had positive CMV colon infection
- Older age, preadmission use of mesalamine, and extra-intestinal manifestations were associated with increased risk for CMV infection
- Treatment in positive patients did not improve outcomes



**Risk of Nonmelanoma Skin
Cancer (NMSC) in UC Patients
Treated With Thiopurines:
A Nationwide Retrospective Cohort**

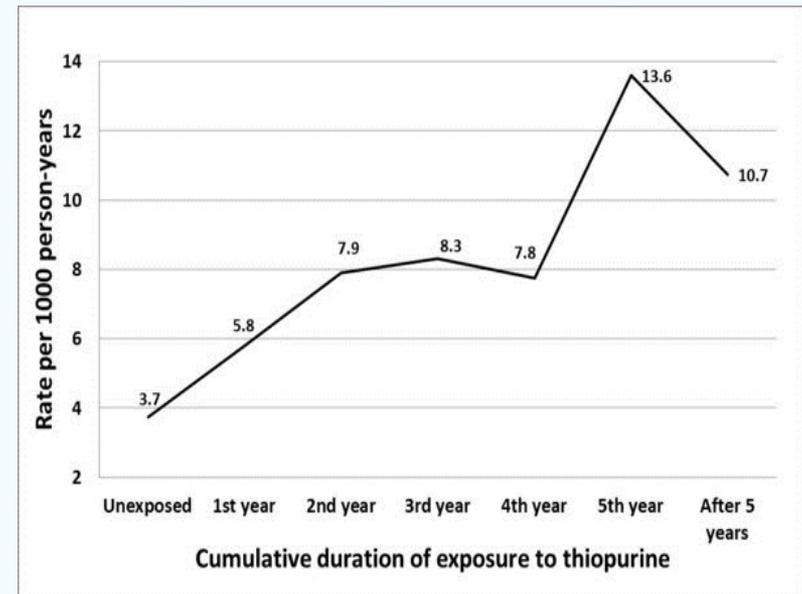
Abbas A et al. Program no. 69

LSU

Risk of Nonmelanoma Skin Cancer (NMSC) in UC Patients Treated With Thiopurines

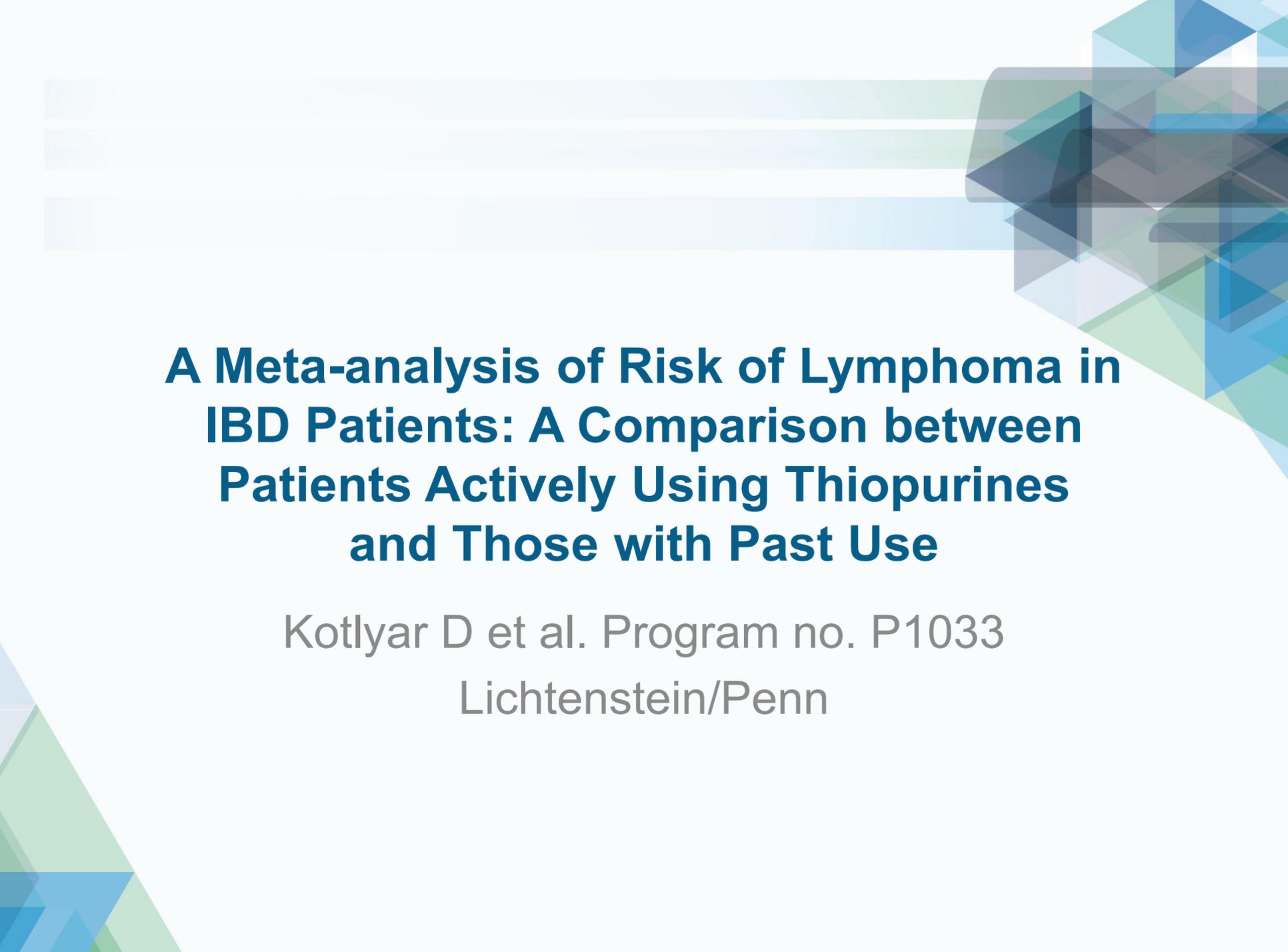
- Purpose
 - To assess the rate of NMSC by ongoing, residual, and cumulative exposure to thiopurines
- Patients and methods
 - Data derived from Veterans Affairs system
 - Cox regression used to determine association between thiopurine use and NMSC
- The adjusted hazard ratios of developing NMSC vs unexposed patients were:
 - 2.1 (95% CI 1.6-2.6; $P < .0001$) while on thiopurines
 - 0.7 (95% CI 0.5-1.0; $P = .07$) after stopping thiopurine

Rate of NMSC by Cumulative Duration of Exposure to Thiopurines



Conclusion

- In this nationwide cohort, patients had two-fold increase in the risk of NMSC while on thiopurine.
- The incidence rate of NMSC significantly increased after the second year of cumulative exposure to thiopurines
- Stopping thiopurine reduces the risk of NMSC to pre-exposure levels



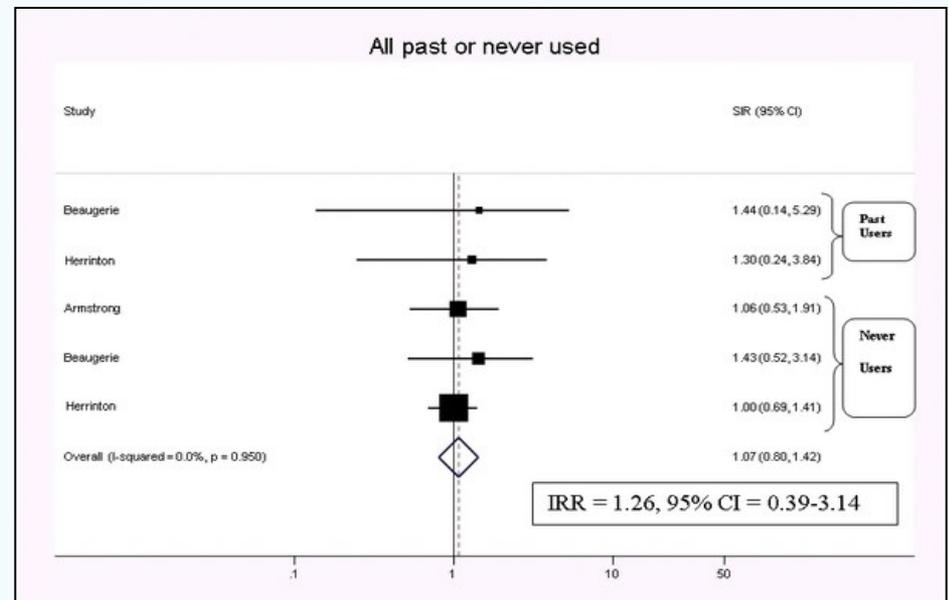
A Meta-analysis of Risk of Lymphoma in IBD Patients: A Comparison between Patients Actively Using Thiopurines and Those with Past Use

Kotlyar D et al. Program no. P1033

Lichtenstein/Penn

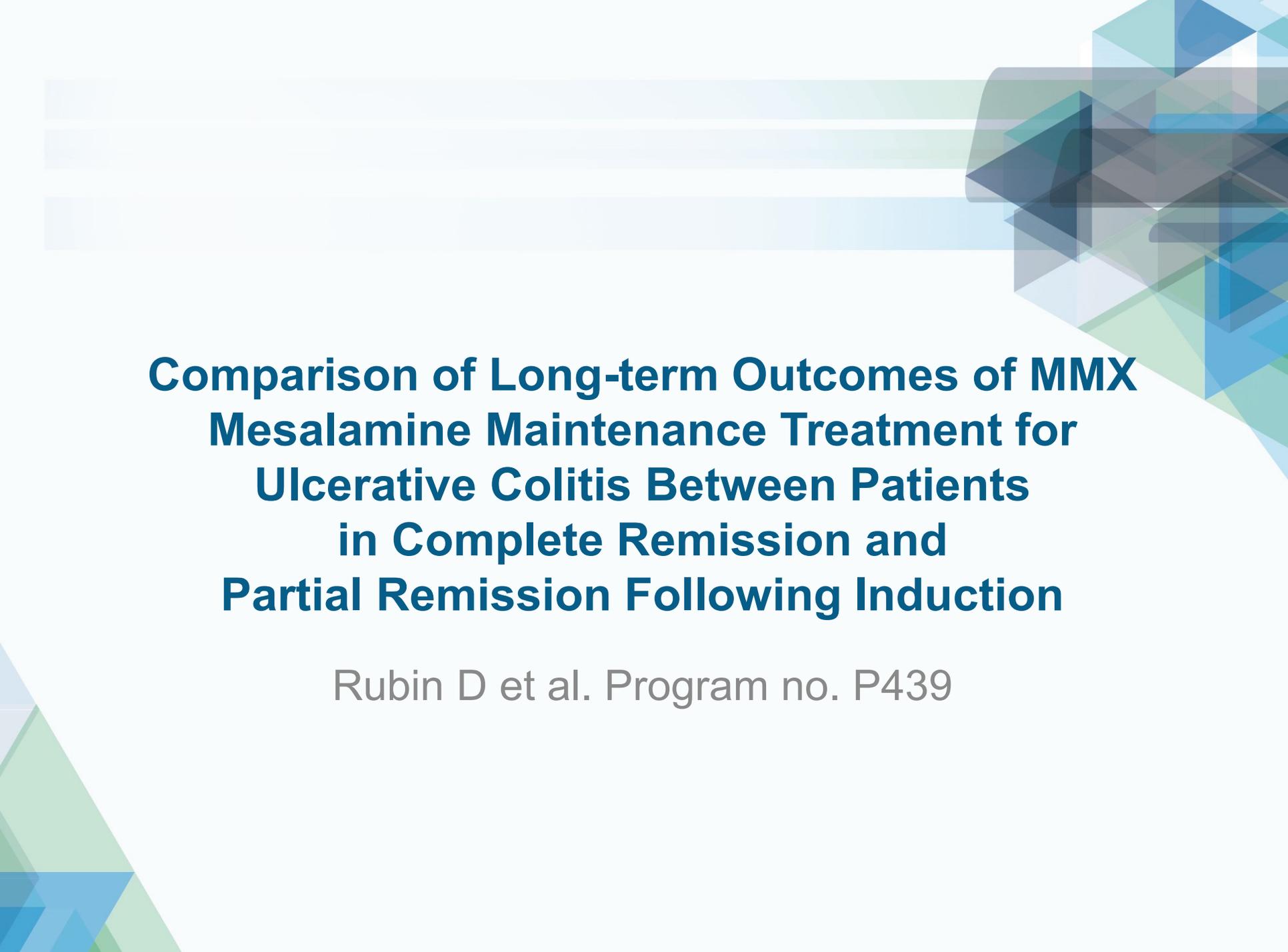
Risk of Lymphoma in Thiopurine Users

- Purpose
 - Compare the standardized incidence ratios for lymphoma between patients actively using thiopurines to patients with past use.
- Patients and methods
 - Literature search and meta-analysis
- Results
 - The incidence rate ratio (IRR) between active users and never-users was 3.73 (95% CI 2.15-6.27), $P < .0001$
 - For current vs past use, the IRR was significantly elevated at 2.96 (95% CI 1.09-10.0), $P = .0095$
 - Past use of thiopurines was not associated with an increased incidence of lymphoma vs never-users (IRR 1.26; 95% CI 0.39-3.14), $P = .30$



Conclusion

- Past users of thiopurines do not have elevated SIRs as compared to IBD pts who have never used thiopurines.
- Previous studies (Beaugerie 2010, Loftus 2000) discussed how IBD alone is not a risk factor for lymphoma; those never using thiopurines or have had past use are not at a higher risk for lymphoma.
- Anti-TNF use may also be associated with lymphoma, but is not studied here.
- Pts without anti-TNF exposure and who have had thiopurines in the past may be counseled that they do not have an elevated risk of lymphoma.
- These data imply that increased risk of lymphoma with current use of thiopurines does not appear to continue after stopping therapy.



**Comparison of Long-term Outcomes of MMX
Mesalamine Maintenance Treatment for
Ulcerative Colitis Between Patients
in Complete Remission and
Partial Remission Following Induction**

Rubin D et al. Program no. P439

Long-term Outcomes of MMX Mesalamine With Scheduled Dose Reduction for Treatment for UC

(Difficult to maintain remission if you have NOT INDUCED remission)

- Purpose
 - To determine whether patients with UC who achieved complete response (clinical and endoscopic remission) after induction therapy with MMX mesalamine had better long-term outcomes than those who demonstrated only PR after induction therapy with MMX mesalamine
- Patients and methods
 - Phase 3b/4 open-label, prospective study
 - Patients with active mild-to-moderate UC (N=772)
 - Patients received MMX mesalamine 4.8 g once daily for 8 weeks
 - Patients achieving either complete remission or partial remission by week 8 were eligible to enroll in 12 months of maintenance treatment with MMX mesalamine 2.4 g once daily
 - Primary efficacy end point: Proportion of patients in complete remission at month 12

Results

	Patients in complete response at Month 0 n=182	Patients in Partial Response at Month 0 n=277
Patients in complete remission at month 12, n (%)	87 (47.8%)	72 (26.0%)
Difference in proportions (complete: partial), %		21.8
Odds ratio (complete:partial)		2.61
95% confidence interval for odds ratio		(1.76, 3.87)
<i>P</i>		<.001

Conclusion

- Significantly more patients were in complete response at month 12 who began maintenance in complete response compared with those who began maintenance in partial response

Anti-TNF- α Risks

- Immunogenicity (all biologics)
- Infliximab specific
 - Infusion reactions
- Class effect
 - Drug-induced lupus
 - Injection site reactions (adalimumab, certolizumab pegol)
 - Non-Hodgkin's lymphoma (including hepatosplenic T-cell lymphoma in children on infliximab + azathioprine)
 - Serious infections (~3%)
 - Opportunistic infections (including tuberculosis, histoplasmosis, coccidiomycosis)
 - Demyelination

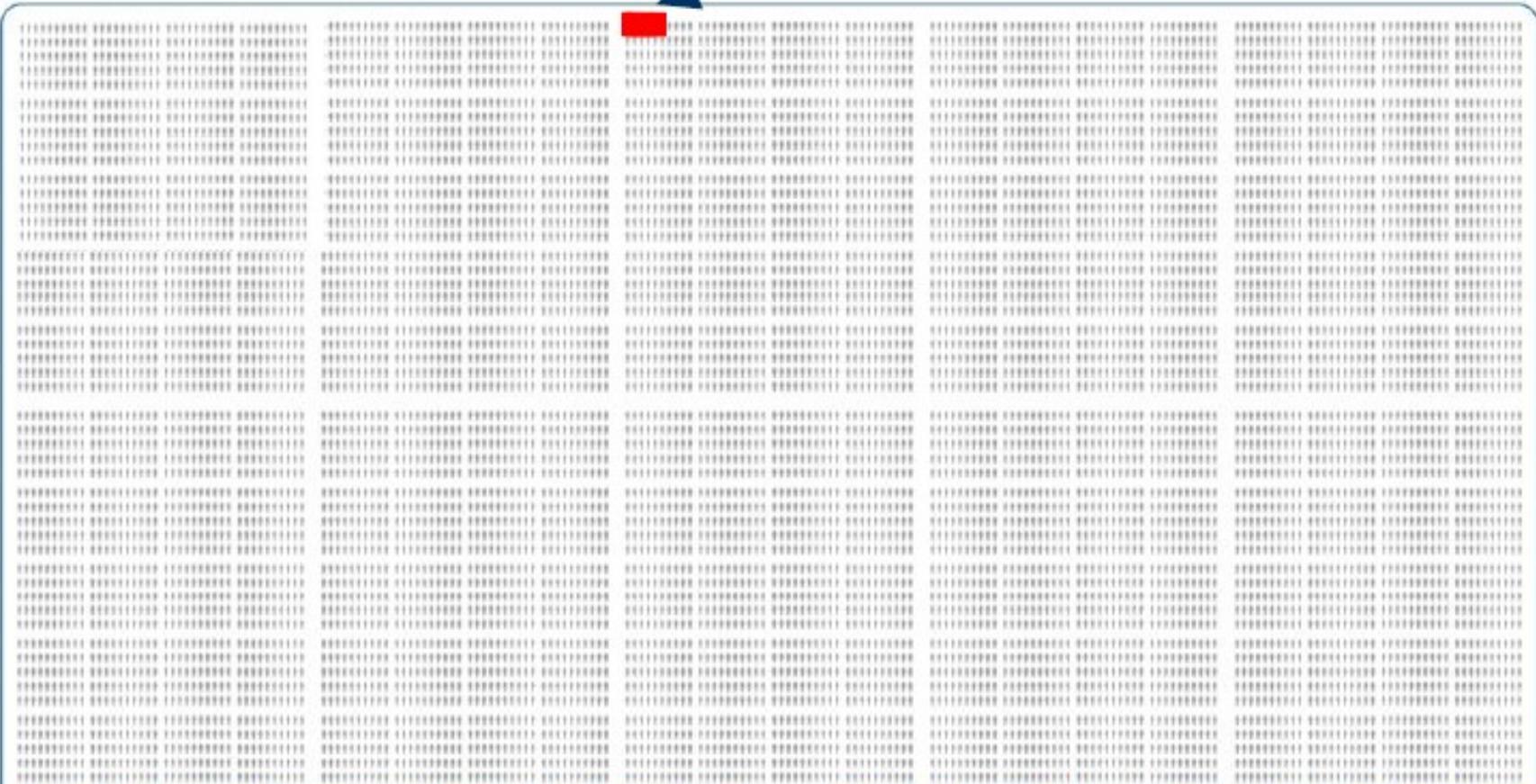
Risk of Developing NH Lymphoma

20 year old male receiving anti-TNF + Immunomodulator Therapy

Ten Thousand People

– pictures to help you see your odds

Risk with combination therapy

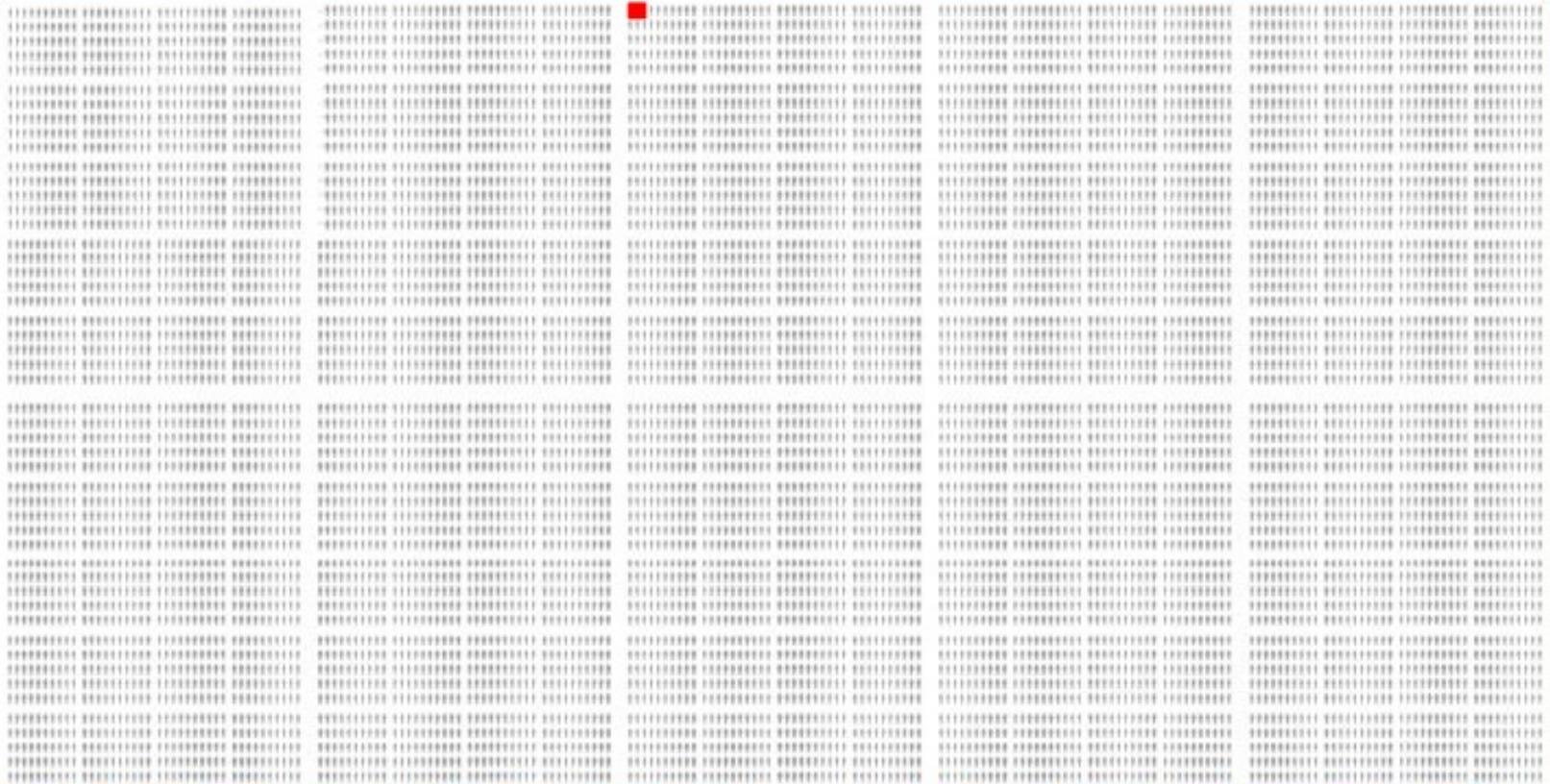


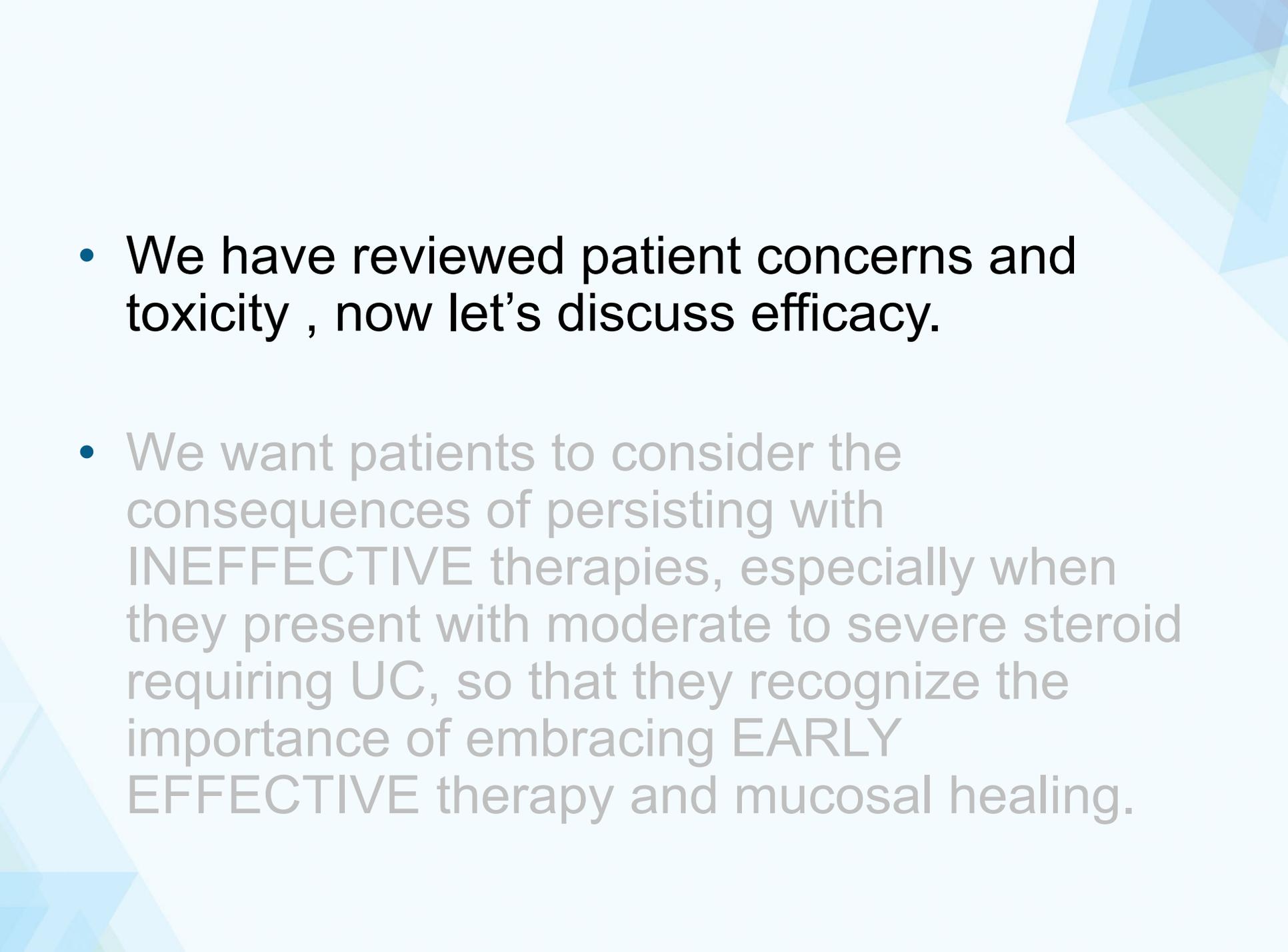
Risk of Developing PML

If 10,000 patients were treated with natalizumab for 1 year

Ten Thousand People
- pictures to help you see your odds

Estimated annual risk =
3 per 10,000 treated patients



- 
- We have reviewed patient concerns and toxicity , now let's discuss efficacy.
 - We want patients to consider the consequences of persisting with INEFFECTIVE therapies, especially when they present with moderate to severe steroid requiring UC, so that they recognize the importance of embracing EARLY EFFECTIVE therapy and mucosal healing.

ANTI-TNF

- **Infliximab: ACT 1 and 2 (remission week 8 ACT1:38%vs 15% PBO ACT2: 34% vs 6% at 5mg/kg)**
- **Adalimumab: Ultra 1 and 2 (U2 Remission w8 16.5% vs 9% PBO Week 52: 17% vs 8.5%)**
- **Golimumab: PURSUIT (Remission W 6: 19%vs 9.5%PBO Week 54:29% vs 15% PBO at 100mg BEST W6: 29% vs 9.5% based on highest serum GOL levels)**

ANTI-INTEGRIN

- **Vedolizumab: Gemini 1 (Remission W6:17%vs5%PBO BEST W52: 45% VDZ q4 vs 14% pbo Steroid free remission**
- **W6 INDUCTION Prior AntiTNF:10% vs 3% PBO NO AntiTNF 23% vs 6.6%PBO)**

Vedolizumab Induction Therapy for Ulcerative Colitis: Results of Gemini I, a Randomized, Placebo-Controlled, Double-Blind, Multicenter Phase 3 Trial

Systemically administered TOPICALLY active BIOLOGIC targeting a small percent (1%) of Gut specific T Lymphocytes

- **Objective:** Assess efficacy and safety of vedolizumab (anti- $\alpha 4\beta 7$ integrin) as induction therapy in patients with moderately to severely active UC in whom ≥ 1 previous therapy failed
- **Methods:** Treatments (3:2 randomization)
 - 300 mg vedolizumab IV or placebo on days 1 and 15
 - Primary outcome of induction phase: Clinical response

Results

Clinical Response, Clinical Remission, and Mucosal Healing at 6 Weeks (ITT Population; N=374)

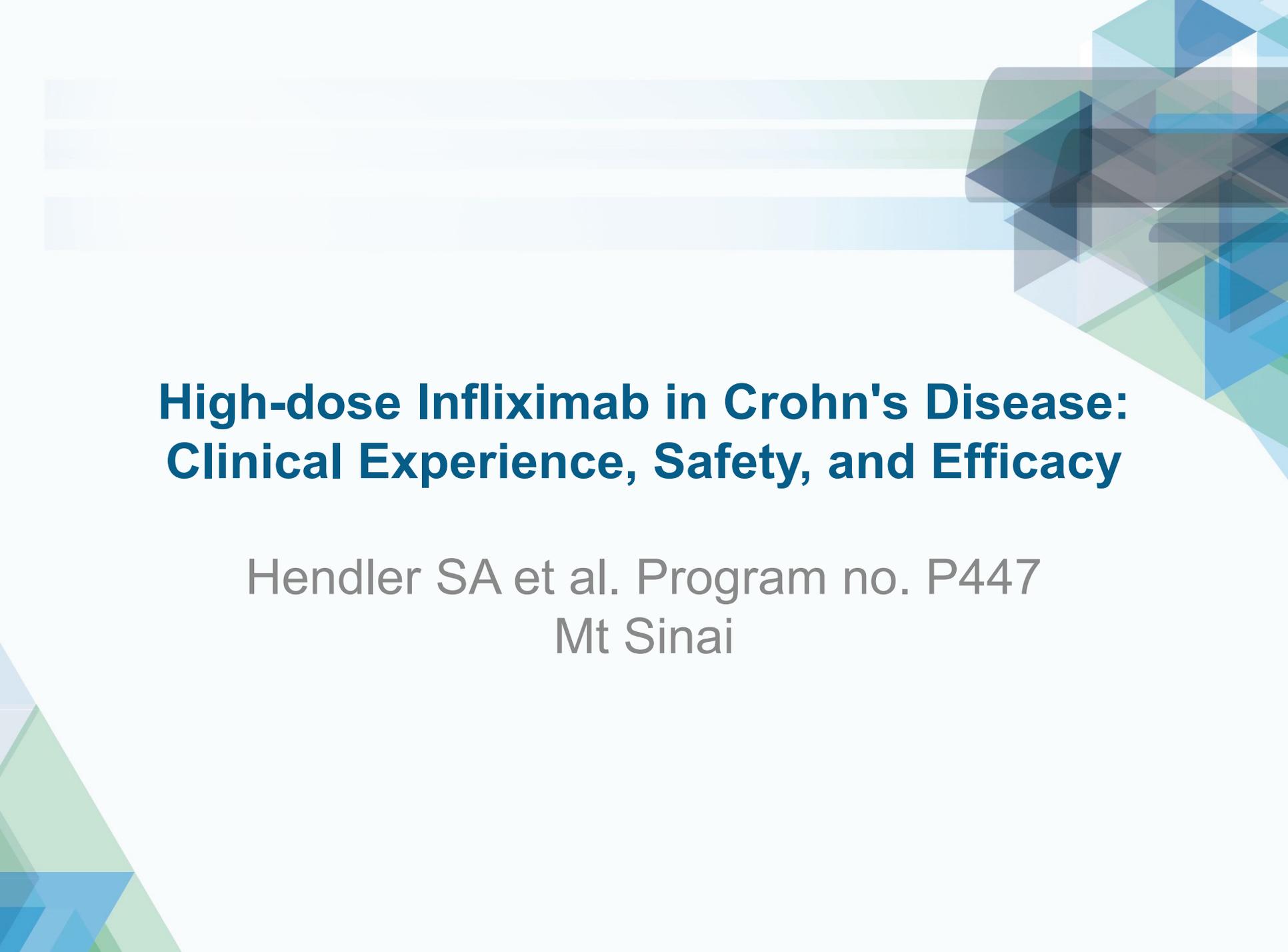
Endpoint	Placebo N = 149	Vedolizumab N = 225	Difference
Clinical response (%)	25.5	47.1	21.7
Clinical remission (%)	5.4	16.9	11.5
Mucosal healing (%)	24.8	40.9	16.1

Clinical Response and Remission at 6 Weeks in Patients With Prior Anti-TNF Failure and Without Anti-TNF Exposure (ITT Population)

Patients With Prior Anti-TNF Failure				
Endpoint	Placebo N=63	Vedolizumab N=82	Difference	95% CI +
Clinical Response (%)	20.6	39.0	18.4	3.9, 32.9
Clinical Remission (%)	3.2	9.8	6.6	-9.8, 22.8
Patients Without Anti-TNF Exposure				
Endpoint	Placebo N=76	Vedolizumab N=130	Difference	95% CI +
Clinical Response (%)	26.3	53.1	26.8	13.7, 39.9
Clinical Remission (%)	6.6	23.1	16.5	2.4, 30.2

Conclusions

- **Induction therapy with vedolizumab was significantly more effective than placebo in achieving clinical response, clinical remission, and mucosal healing in a population of UC patients with a high rate of prior anti-TNF failure**
- Similar rates of AEs were observed in the vedolizumab and placebo groups
- **Further Study: May be of interest to evaluate pANCA titers in UC vedolizumab responders and IFX nonresponders**



High-dose Infliximab in Crohn's Disease: Clinical Experience, Safety, and Efficacy

Hendler SA et al. Program no. P447
Mt Sinai

High-dose Infliximab in Crohn's Disease

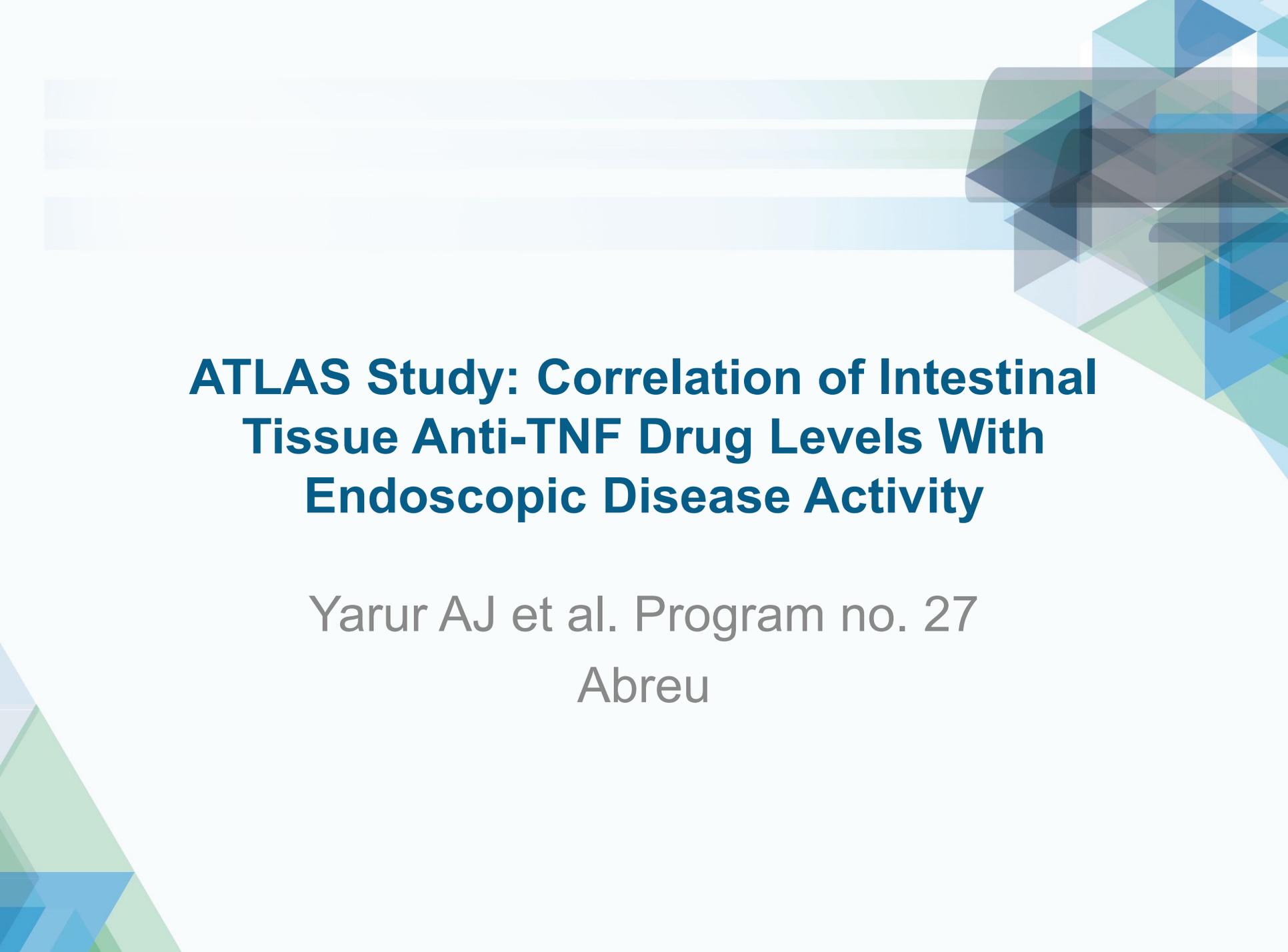
- Purpose
 - To evaluate safety and efficacy of high-dose infliximab (>10 mg/kg every (eight weeks or equivalent) in CD and characterize predictors of response to infliximab dose intensification
- Patients and methods
 - Electronic medical records were queried for CD patients who received high-dose infliximab (10 mg/kg every 7 weeks to 20 mg/kg every 4 weeks) during 2010-2012
 - EMRs fulfilling criteria were reviewed for history, medications, and laboratory data
 - Safety and efficacy of dose intensification was analyzed

Results

- A total of 319 patients with CD were identified; 87 received high-dose infliximab
- At 4, 24, and 52 weeks of therapy, 20%, 28%, and 18% of patients experienced a full response, and 46%, 30%, and 23% experienced a partial response, respectively
- Patients who responded fully or partially at 4 weeks had a higher median baseline CRP than those who did not respond (24.9 vs. 3.5 mg/L, $P=.04$)
- Safety of high-dose therapy was consistent with known side effect profile of anti-TNF therapy

Conclusion

- HD IFX therapy may offer a therapeutic benefit to CD patients who have failed to achieve a response with standard treatment doses, or to patients who have failed other therapies.
- Safety of HD IFX therapy appears to be consistent with the known side effect profile of anti-TNF therapy.
- Baseline CRP value may be a predictor for clinical response to IFX dose intensification.



ATLAS Study: Correlation of Intestinal Tissue Anti-TNF Drug Levels With Endoscopic Disease Activity

Yarur AJ et al. Program no. 27

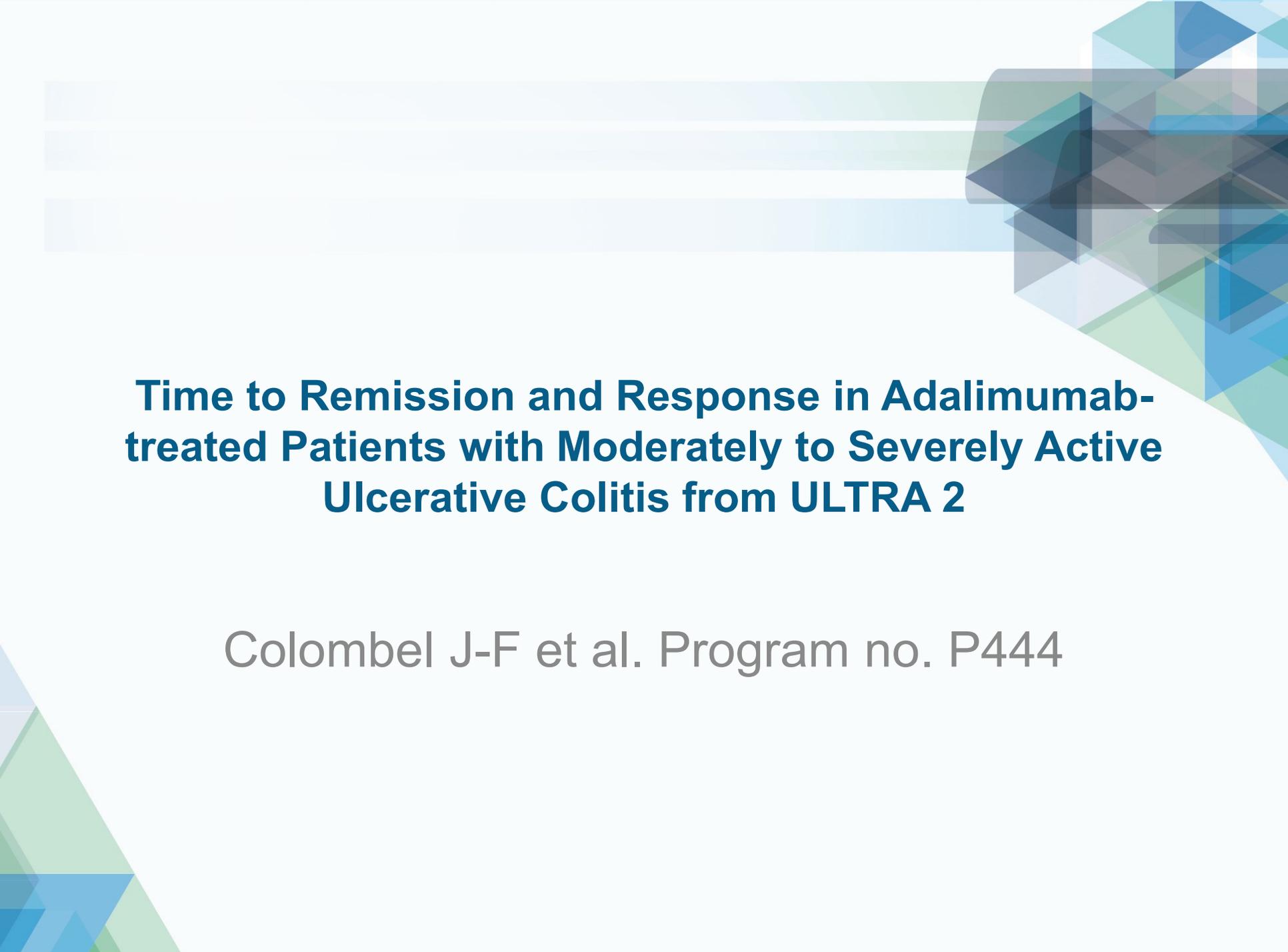
Abreu

Correlation of Intestinal Tissue Anti-TNF Drug Levels With Endoscopic Disease Activity

- Purpose
 - To assess whether tissue anti-TNF levels correlated with endoscopic mucosal inflammation, and whether the levels varied in inflamed, versus normal, tissue
- Patients and methods
 - Prospective cross-sectional study of patients (N=25) receiving treatment with infliximab or adalimumab for CD or UC
 - TNF and anti-TNF levels measured in biopsy samples and correlated with endoscopic disease activity
- Results
 - Patients with active mucosal inflammation had a significantly lower level of anti-TNF in both tissue and serum ($P < .04$ for all)
 - A higher numeric value of TNF was found in tissue and serum of patients with endoscopic mucosal inflammation ($P = \text{NS}$)
 - Anti-TNF levels in tissue and serum correlated ($P = .01$)
 - In patients on adalimumab, body weight was inversely correlated with tissue, but not serum drug levels but this was not found in patients on infliximab

Conclusion

- A lower anti-TNF level in the gastrointestinal tissue is associated with intestinal mucosal inflammation in CD and UC.
- Lower levels in the tissue also correlate with lower serum levels.
- In patients on ADA, tissue, but not serum levels, were inversely correlated with the patient's body mass.
- This finding was not seen on those receiving IFX, which may suggest that tissue drug monitoring may play a role in a selected group of patients.



Time to Remission and Response in Adalimumab-treated Patients with Moderately to Severely Active Ulcerative Colitis from ULTRA 2

Colombel J-F et al. Program no. P444

Time to Remission and Response in ULTRA 2

- Purpose
 - To determine the time to achieve remission and response per partial Mayo score in patients with moderately to severely active UC treated with adalimumab
- Patients and methods
 - ULTRA 2 was a 52-week trial
 - Patients received double-blind adalimumab 160/80 mg at weeks 0/2, followed by adalimumab 40 mg every other week or placebo
 - Patients with inadequate response could receive open-label adalimumab 40 mg every other week beginning at week 12, followed by 40 mg weekly

Results

- Median time to remission was significantly shorter for adalimumab vs placebo-treated patients
- Similar results observed for median time to response
- In subgroup analyses, treatment-naïve patients achieved remission and response significantly faster than placebo patients
- In anti-TNF experienced patients, median time to response was similar for both treatment groups

	All Patients		Anti-TNF-naive		Anti-TNF-experienced	
	Placebo N=246	Adalimumab N=248	PBO N=145	Adalimumab N=150	PBO N=101	Adalimumab N=98
Time to remission (weeks)	29	20*	20	12*	44	NR
Time to response (weeks)	10	4*	8	4*	12	8

*Statistically significant

Conclusion

- In ULTRA 2, pts with moderately to severely active UC randomized to ADA had shorter times to remission and response than pts randomized to PBO, even though the latter included pts who moved from PBO to OL ADA.
- Pts naïve to anti-TNF therapy derived the greatest treatment benefit



Long-term Safety of Vedolizumab for the Treatment of Ulcerative Colitis or Crohn's Disease

Colombel J-F et al. Program no. P466

Long-term Safety Profile of Vedolizumab

- Design
 - Ongoing open-label extension study to assess safety of vedolizumab (anti- α 4 β 7 integrin) for treating UC or CD
- Patients
 - Moderately to severely active UC or CD
 - Vedolizumab naïve or had participated in a phase 2 or 3 trial
- Treatments
 - 300 mg vedolizumab IV every 4 weeks

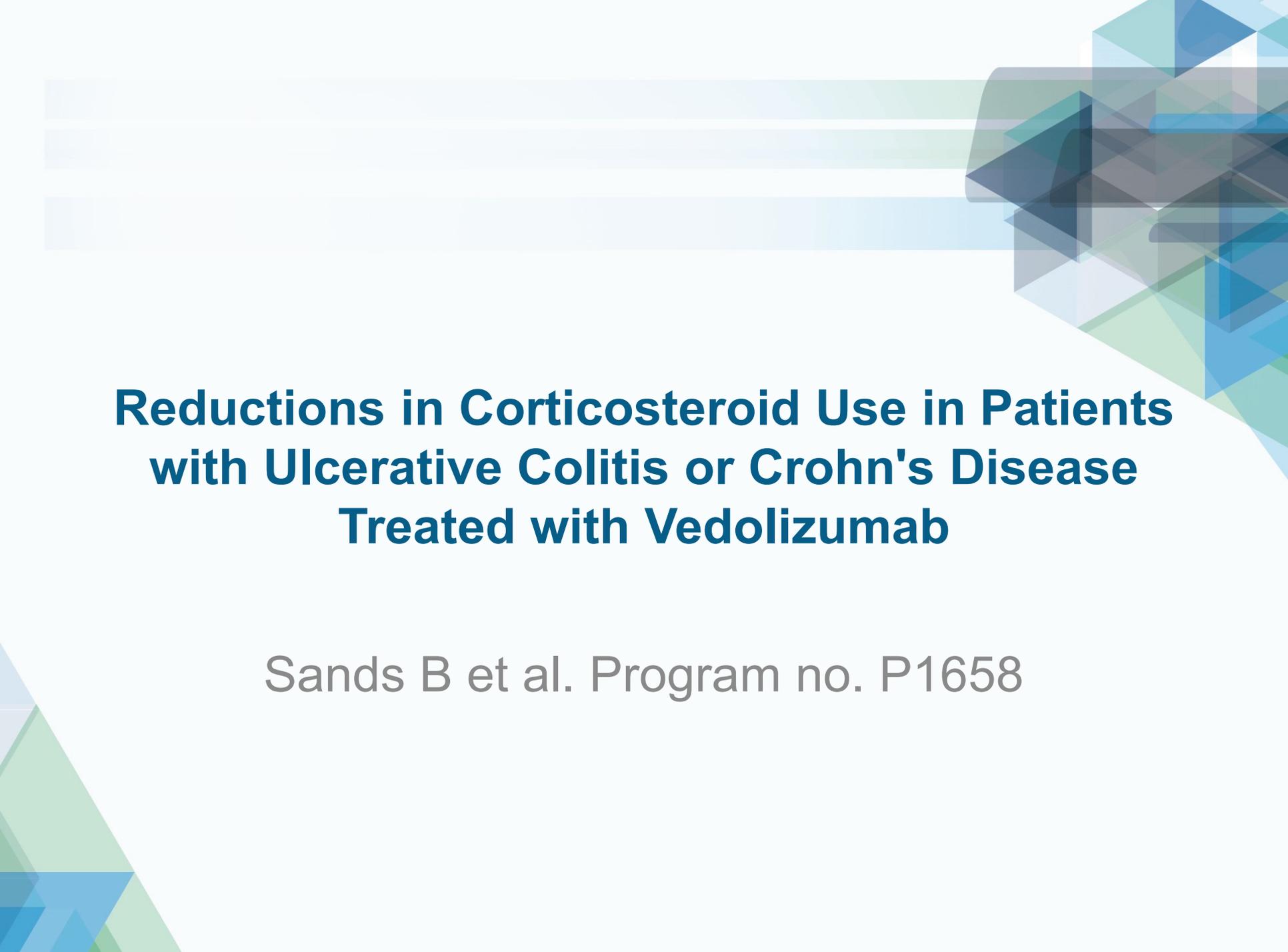
Adverse Events*

Adverse Event (AE) Category, n (%) 00	UC (n=704)	CD (n=1118)
Drug-related AE	258 (37)	447 (40)
AE leading to discontinuation	61 (9)	108 (10)
Serious AE	127 (18)	285 (25)
Serious infection	30 (4)	74 (7)
Drug related	15 (2)	51 (5)
Leading to discontinuation	23 (3)	65 (6)
Death	3 (<1) ^a	3 (<1) ^b

Across VDZ studies, VDZ exposure was ≥ 6 , ≥ 12 , and ≥ 24 months for 1534, 1149, and 502 patients, respectively

Conclusion

- Results support the long-term safety of VDZ treatment in UC and CD.
- The safety profile was consistent with that observed in previous 1-year, phase 3 randomized, placebo-controlled trials.



Reductions in Corticosteroid Use in Patients with Ulcerative Colitis or Crohn's Disease Treated with Vedolizumab

Sands B et al. Program no. P1658

Effect of Vedolizumab on Corticosteroid Use in Patients With UC or CD

- Purpose
 - Evaluate the effect of vedolizumab on corticosteroid use
- Design
 - Two phase 3 studies (GEMINI I and GEMINI II)
 - Patients randomized to placebo or vedolizumab 300 mg intravenously during induction (weeks 0 and 2) and maintenance (weeks 6-52, every 8 or 4 weeks)
 - Patients on corticosteroids began tapering at week 6
- End point
 - Week 52 corticosteroid-free remission rate

Results

	UC (GEMINI I)			CD (GEMINI II)		
	Vedolizumab		Placebo	Vedolizumab		Placebo
	Q8W	Q4W		Q8W	Q4W	
	n=70	n=73	n=72	n=82	n=80	n=82
Wk 52 CS-free remission, % p value	31.4 .0120	45.2 <.0001	13.9 -	31.7 .0154	28.8 .0450	15.9 -
Wk 52 remission and CS free for 90 d, % p value	30.0 .0192	45.2 <.0001	13.9 -	30.5 .0240	25.0 .1433	15.9 -
Wk 52 remission and CS free for 180 d, % p value	28.6 .0082	42.5 <.0001	11.1 -	30.5 .0139	23.8 .1353	14.6 -
Wk 6 mucosal healing and wk 52 CS-free remission, % p value	n=48 41.7 .0043	n=56 50.0 .0002	n=51 15.7 -	- - -	- - -	- - -
Wk 6 remission and wk 52 CS-free remission, % p value	n=23 39.1 .1230	n=29 58.6 .0030	n=23 17.4 -	n=29 48.3 .1449	n=29 37.9 .3418	n=35 28.6 -

Conclusion

- VDZ treatment led to corticosteroid-free remission in UC and CD patients.
- Future studies are needed to confirm whether 6-week clinical remissions and/or mucosal healing are predictive of 52-week steroid-free remissions.

Mucosal Healing: ACG Guidelines

- “Newer goals of therapy include the induction and maintenance of mucosal (and histological) healing that are beginning to translate into changing the ‘natural history’ of CD”¹
- [In UC] “long-term mucosal healing may reduce the risk of dysplasia and predicts a better long-term outcome”²

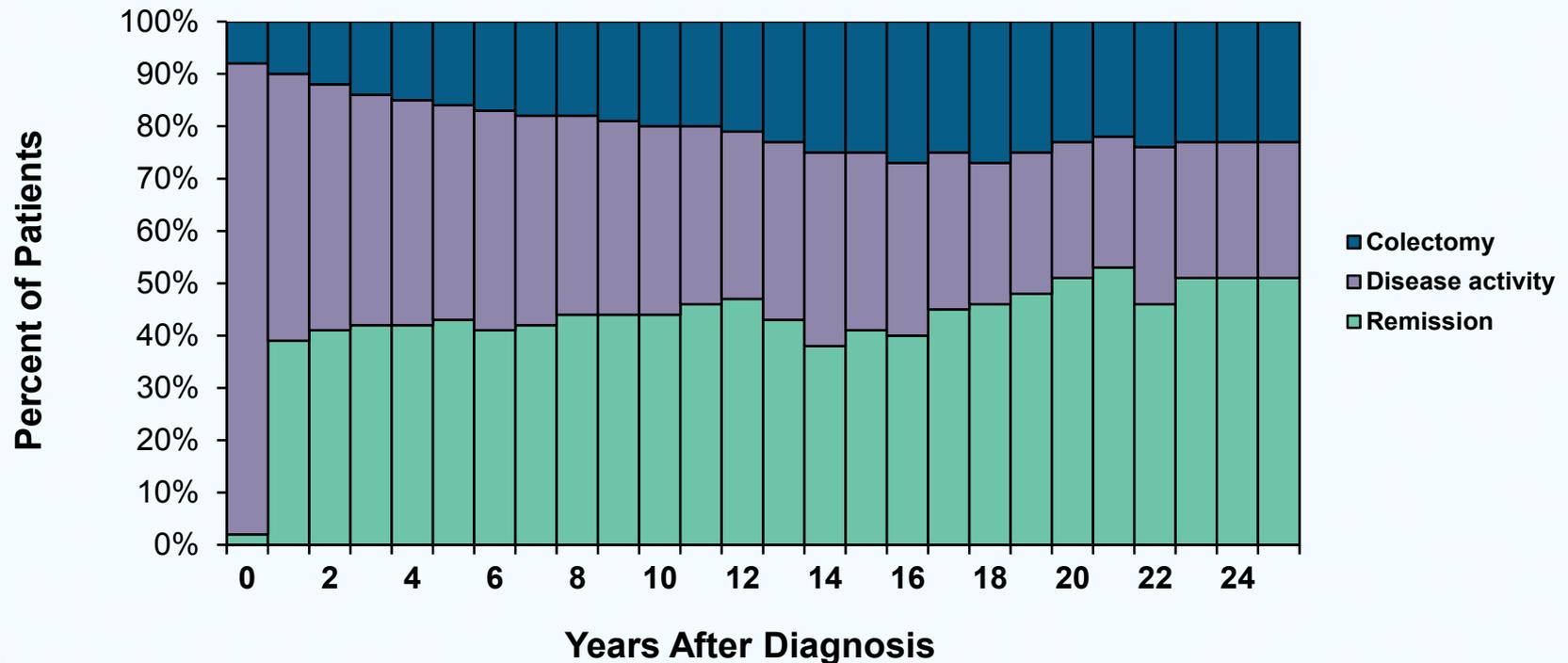


K25RGU121005

1. Lichtenstein GR, et al. Am J Gastroenterol. 2009;104:465-483.
2. Kornbluth A, et al. Am J Gastroenterol. 2010;105:510-523.

UC: Natural History

- 10% Of Patients HAVE A SEVERE FIRST ATTACK REQUIRING COLECTOMY, and the majority NEVER achieve remission during the FIRST YEAR



Percent of patients with disease activity, in remission, or having colectomy performed each year after diagnosis

Recognize and Reverse Natural History of Severe First Attack of UC

- Up to 10% of patients with a severe FIRST attack ultimately require colectomy and nearly **90% never achieve remission.**
- **Except for the first year** with higher initial colectomy rates for extensive UC, the **percent of patients in remission (50%)** did not differ between left sided and universal UC.

IBD Alliance
Program

2014

**The goal is to find an a therapy
that provides sound basis for
much hope.**

Philip Hench

1950.

Sounds like:

IBD Alliance
Program 2014

**A good idea. Treat SELECT UC patients
early with effective regimens
2014**

**Control inflammation and
mucosal healing**