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Reporting on IBD

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Complications and Prognostic factors related to IBD

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Clostridium difficile Infection in Ulcerative Colitis: Increased Risk of Colectomy and Postoperative Infectious Complications (55)

Negron M et al

ACG 2011

Methods

- Background
  - UC patients diagnosed with *C. difficile* in hospital have worse outcomes
  - The majority of studies have only evaluated the influence of in-hospital diagnosis of *C. difficile*
- Objectives
  - To determine whether UC patients diagnosed with *C. difficile* infections in-hospital and up to 90 days prior to admission were more likely to have an emergent colectomy; whether *C. difficile* increased the risk of postoperative complications following colectomy
- Methods
  - Retrospective analysis of a regional healthcare database

Results

- Patients diagnosed with *C. difficile* 90 days before or during hospitalization (n=18) were at 2.87-fold higher risk for colectomy vs *C. difficile* negative patients

- UC patients who underwent emergent colectomy and were diagnosed with *C. difficile* prior to surgery were not at a statistically higher risk of developing postoperative complications in general (OR=3.48)

- Preoperative *C. difficile* infection increased the risk of specified infectious complications (OR=4.56) in the postoperative period

Conclusions

- UC patients were significantly less likely to be medically responsive and hence, required a colectomy when they were diagnosed with a *C. difficile* infections in-hospital or within 90 days of admission

- UC patients who had concomitant *C. difficile*, preoperatively were at a higher risk of infectious complications following colectomy

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A Prospective Study of Aspirin, Non-Steroidal Anti-inflammatory Drug Use and Risk of Crohn's Disease and Ulcerative Colitis (6)

Ananthakrishnan A et al

ACG 2011

Methods

- Background
  - The effect of aspirin on risk for CD and UC is unclear
- Methods
  - Prospective cohort study of 76,814 women enrolled in the Nurses' Health Study (NHS)
  - Diagnoses of CD and UC were subsequently confirmed by medical record review by two gastroenterologists
  - Cox proportional hazards models were used to examine the RR for CD and UC after adjusting for potential confounders

Results

- 18 years and 1,295,317 person-years of follow-up
  - 123 incident cases of CD and 117 cases of UC
  - 44% of women reported regular use of aspirin
  - 37% reported regular use of NSAIDs
- Compared to non-users, women who used NSAIDs for >15 days/month had:
  - 1.59-fold greater risk for CD (95% CI 0.99 - 2.56)
  - 1.87-fold greater risk for UC (95% CI 1.16 - 2.99)
- Women who used >5 tablets of NSAIDs per week also had:
  - 1.71-fold increased risk for CD
  - 1.78-fold increased risk for UC
- Women with >6 years of NSAID use had a 2.83- and 2.00-fold increased risk for CD and UC, respectively

Conclusions

- Use of NSAIDs (but not aspirin), greater frequency of use, higher doses, and longer duration of use was associated with an increased risk of incident CD and UC

- Biological mechanisms associated with the action of NSAIDs that are not shared with aspirin may contribute to the pathogenesis of CD and UC

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Prognostic Factors for Post-surgical Complications in Inflammatory Bowel Diseases: A Novel Predictive Score (58)

Yarur A et al

ACG 2011

Methods

- Objectives
  - Create a predictive model for risk of post-operative morbidity in patients undergoing IBD-related surgeries
- Methods
  - Patients (N=91) undergoing non-emergent intra-abdominal IBD-related surgery between January 1998 and March 2011 were included
  - Demographics, IBD phenotype, nutritional status, comorbidities, laboratory parameters, histologic findings and medical treatment for IBD were considered for use in the predictive model.
  - Primary outcome: Development of postoperative medical or surgical complication

Risk Score Algorithm

- 10 predictive factors were identified to create a risk score algorithm

C-reactive protein x 0.72
Age x 0.14
(Absolute neutrophil count/Absolute lymphocyte count) x 0.09
(Blood urea nitrogen/Serum creatinine) x 0.14
Blood urea nitrogen x -0.17
Creatinine x 2.66
Serum Sodium x -0.47
Serum Potassium x -2.46
If patient is a smoker add 2.76
If patient has ulcerative colitis add 5

Calculating the Risk Score

$$\text{Predictive risk Of a post-surgical complication} = \frac{1}{(1+e^{-RS+58})}$$

Conclusions

- This model may be useful for identifying patients with IBD who are at risk for postoperative complications
  - Sensitivity: 86.4%
  - Specificity was 97.1%
  - Positive predictive value: 90.5%
  - Negative predictive value: 95.7%
- This preliminary data suggests that the major driver of postoperative complications may be severity of illness and not medications

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Complications Related to Therapy

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Low Risk of Pneumocytis jirovecii Pneumonia in Patients with IBD Receiving Chronic Corticosteroid Therapy Does Not Justify Prophylaxis: A Population Based Study (P706)

Gathaiya N et al

ACG 2011

Methods

- Objective
  - To assess the risk of PCP in a population-based cohort of IBD patients treated with corticosteroids and/or immunosuppressive medications
- Methods
  - Rochester Epidemiology Project database used to identify all cases of CD or UC from 1970 to 2004
  - Cohort cross-referenced with microbiology database

Results and Conclusions

- 678 patients identified
  - Corticosteroids used in 56%
  - Immunosuppressive medications and/or biologics were used in 26%
  - Combination therapy with corticosteroids and immunosuppressive medications used in 24%
  - Triple therapy used in 13%
  - None of these medications were used in 41%
- No cases of PCP observed in any group
- Trimethoprim-sulfamethoxazole used in only 10 patients
- Conclusions
  - In this population-based cohort treated with corticosteroids, immunosuppressive medications, and biologics, there were no cases of PCP, despite very infrequent use of PCP prophylaxis
  - In patients receiving singe therapy immunosuppression, PCP prophylaxis is probably not necessary

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Non-Melanoma Skin Cancer in Patients with Inflammatory Bowel Disease: A Consequence of Anti-Metabolite Therapy? (P315)

Blonski W et al

ACG 2011

Methods

- Objective
  - Assess the characteristics of patients with IBD who were diagnosed with NMSC
- Methods
  - Retrospective review of electronic medical records of all IBD outpatients seen at our institution from January 1997 to May 2011 and identified those who were diagnosed with NMSC
    - 15,919 patients with ICD-9 codes for IBD. 430 patients were identified with ICD-9 codes for both IBD and NMSC
    - Clinical information was available in 63 patients (36 patients with Crohn's disease and 27 patients with ulcerative colitis)
  - Variables assessed:
    - Age at the diagnosis of IBD
    - Age at the diagnosis of NMSC
    - Exposure to IBD medications (5-ASA, azathioprine/6-mercaptopurine, anti-TNF agents, and corticosteroids)

Results and Conclusions

- The majority of NMSC that occurs in patients with IBD occurs in patients exposed to immunosuppressive medications
  - 51% (32/63) of IBD patients who developed NMSC were treated with anti-metabolite therapy
    - 32% (20/63) of these patients had anti-metabolite therapy alone
    - 12/63 (19%) had antimetabolite therapy in combination with anti-TNF therapy

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Biologic Use Is Associated With a Major Reduction in Venous Thromboembolic Events Compared With Steroid Use in the Treatment of Inflammatory Bowel Disease (P301)

Higgins P et al

ACG 2011

Methods

- Background
  - IBD is associated with increased rates of VTE
  - Corticosteroids might have a prothrombotic effect, and thereby independently contribute to VTE risk
- Objective
  - To determine whether use of biologic therapies for treatment of active IBD would have a reduced risk of VTE compared to use of steroids
- Methods
  - Retrospective analysis of adults with diagnoses of CD or UC using large database
  - Patients were included if they had no VTE in the 6 months prior to the index date and insurance coverage in the 6 months prior to and 12 months following index date
- Outcomes
  - Incidence of VTE in the 12 month follow-up period

Results

- 15,100 patients included in the analysis
  - 325 events occurred in the study period
- Rate of VTE:
  - Steroid without biologic: 2.3%
  - Biologic without steroid: 0.4%
  - Biologic and steroid: 2.5%
- Compared to reference treatment (steroids without biologics), patients on biologics had an odds ratio of 0.21 (95% CI, 0.05–0.84) for VTE
- Subjects on both steroids and biologics had an OR of 0.99 for VTE
- Significant covariates included:
  - Age (OR, 1.02 per year of age)
  - Recent IBD surgery (OR, 3.62)
  - Recent IBD hospitalization (OR, 1.51)
  - Cancer (OR, 2.33)
  - Indeterminate colitis (OR, 1.61)

Conclusions

- Compared with corticosteroid therapy, biologic therapy was associated with nearly a 5-fold reduction in VTE risk
- Combination therapy with corticosteroids and biologics is associated with the same VTE risk as corticosteroids alone

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Malignancy in Patients with Crohn's Disease: Data from the TREAT™ Registry with More Than 5 Years of Follow-up (20)

Lichtenstein G et al

ACG 2011

Methods

- Background
  - The association between malignancy and anti-TNF therapy remains under investigation
- Methods
  - Prospective evaluation of the incidence of malignancy in TREAT registry
  - Data compared with expected number for general US population using SEER 2009 database

Malignancies in TREAT: Comparison vs SEER Database

Type of malignancy	Infliximab-treated (observed/expected; SIR[1] (95%CI)	Other-treatments-only (observed/expected; SIR[1] (95%CI)
No. of patients/median pt-yrs of follow-up	**3764/5.6**	**2509/5.5**
Bladder	2/2.97; 0.67 (0.08/2.43)	1/3.60;0.28 (0.01, 1.55)
Breast	11/19.98; 0.55 (0.27, 0.98)	6/17.5; 0.34 (0.13, 0.75)
Uterine	0/1.65; 0.00 (0.00, 1.81)	3/1.64; 1.83 (0.38, 5.36)
Cervical	1/0.94; 1.06 (0.03, 5.92)	0/0.74; 0.00 (0.00, 4.07)
Colon	13/7.32; 1.78 (0.95, 3.04)	3/7.99; 0.38 (0.08, 1.10)
Hematologic	1/1.12; 0.89 (0.02, 4.97)	3/1.12; 2.68 (0.55, 7.82)
Lung	10/8.44; 1.18 (0.57, 2.18)	15/9.81; 1.53 (0.86, 2.52)
Lymphoma	9/4.01; 2.25 (1.03, 4.27)	8/3.85; 2.08 (0.90, 4.09)
Melanoma	7/6.70; 1.04 (0.42, 2.15)	4/5.87; 0.68 (0.19, 1.74)
Oral	3/1.70; 1.76 (0.36, 5.15)	3/1.58; 1.89 (0.39, 5.54)
Prostate	8/10.94; 0.73 (0.32, 1.44)	4/12.91; 0.31 (0.08, 0.79)
Renal	2/2.54; 0.79 (0.10, 2.84)	4/2.59; 1.55 (0.42, 3.96)

[1]Based on comparison with SEER (2009) database. CI=confidence interval; SIR=standardized incidence ratio

Malignancies in TREAT: Effect of Risk Factors

Risk Factors	Adjusted[1,2] Hazard Ratio (95% CI)	*P*
Age at baseline (years)	1.05 (1.04, 1.06)	<0.001
Race: Caucasian vs. other/unknown	1.96 (0.87, 4.44)	0.12
Disease duration at enrollment	1.05 (1.01, 1.09)	0.013
Known smoker	1.38 (1.01, 1.88)	0.045
infliximab vs. no infliximab[3]	0.79 (0.56, 1.10)	0.17
Immunomodulator vs. no immunomodulator[3,4]	1.60 (1.11, 2.30)	0.011
Prednisone vs. no prednisone	0.84 (0.61, 1.16)	0.28
Narcotic analgesics vs. no narcotic analgesics[3]	1.14 (0.80, 1.63)	0.48

[1]Results are based on a Cox Proportional Hazard model of time to first malignancy based on exposure (historical and at any time during Registry participation)
[2]Adjusted for age, gender, and race
[3]Time-varying medication use is defined as any use between enrollment and the event or censoring
[4]Immunomodulators include azathioprine, methotrexate, and 6-mercaptopurine. CI=confidence interval

Conclusions

- Infliximab did not independently increase the risk of malignancies over other treatments
- Immunomodulator use, age, duration of disease and smoking independently predicted time to first malignancy
- Consistent with reports in the literature, CD patients, independent of infliximab treatment, appear to have a higher lymphoma risk than the general US population

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Evolving Concepts with Biologic Therapy

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Adalimumab Therapy Reduces Hospitalization and Colectomy Rates in Patients with Ulcerative Colitis: Data From Controlled Trials (57)

Feagan B et al

ACG 2011

Methods and Results

- Effect of adalimumab on risk reduction of all-cause and UC-related hospitalization and colectomy assessed in 2 clinical trials (data pooled for analysis)

	ADA		Placebo		Risk Ratio (Placebo/ ADA)	*P*
	n/TAR	IR (n/100-PYs)	n/TAR	IR (n/100-PYs)	RR [95% CI]	
Percentage of patients hospitalized						
All-cause	67/378	18	57/214	27	1.5 [1.1, 2.2]	0.022
UC-related	45/389	12	47/215	22	1.9 [1.3, 2.8]	0.002
Number of hospitalizations						
All-cause	82/401	20	70/224	31	1.5 [1.1, 2.1]	0.0095
UC-related	53/401	13	57/224	25	1.9 [1.3, 2.8]	0.0006
Colectomy	14/399	3.5	10/223	4.5	1.3 [0.6, 2.9]	0.554

Conclusions

- ADA-treated patients had a significantly lower risk for UC-related and all-cause hospitalization compared with placebo-treated patients
- Colectomy rates were lower than in the ACT trials, likely due to crossover, reducing power

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Inflammatory Markers in IBD

Inflammatory Markers in IBD

First Author	No.	Title
Colombel J-F	P731	*Baseline C-Reactive Protein is Associated With Disease Progression in Patients with Crohn's Disease*
Sandborn W	P281	*Association of Baseline C-Reactive Protein with Maintenance of Remission in Patients with Moderate to Severe Crohn's Disease Treated with Adalimumab*
Sandborn W	P280	*Baseline C-reactive Protein (CRP) and Plasma Anti-TNF Concentration in Patients with Active Crohn's Disease Treated with Certolizumab Pegol*
Sandborn W	P711	*Fecal Calprotectin Concentration and Clinical Response to Certolizumab Pegol in Patients with Active Crohn's Disease: Results from PRECiSE 2*
Sandborn W	P712	*Inflammatory Biomarkers and Clinical Remission in Patients With Active Crohn's Disease: Results from PRECiSE 2*

Data from the CHARM study

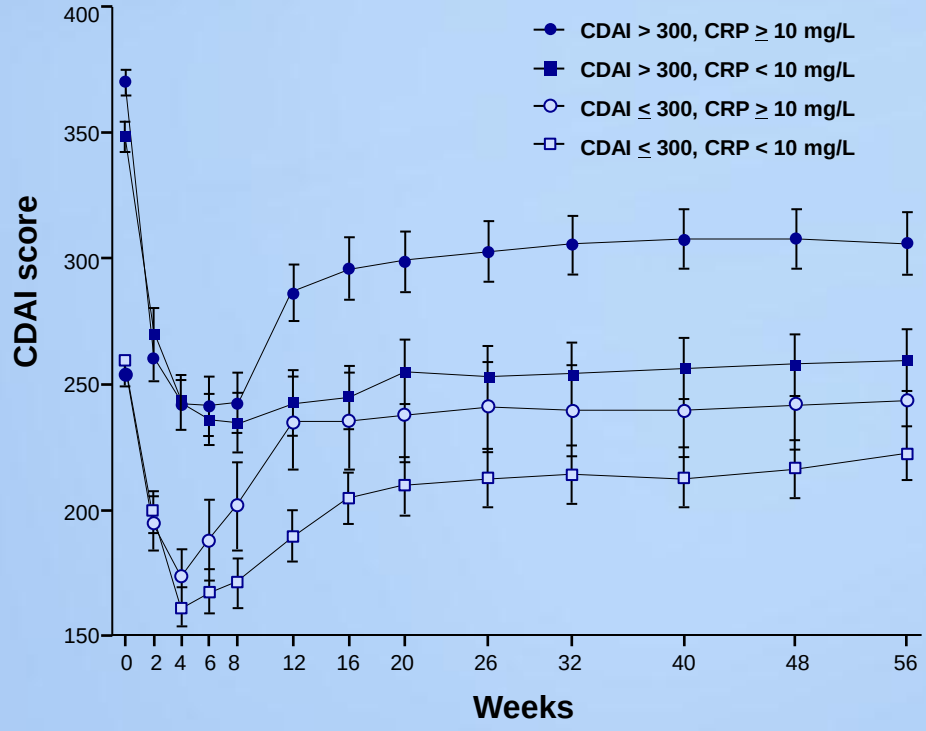
Data from the certolizumab studies

Effect of Baseline CRP Concentrations on Disease Progression and Maintenance of Remission—Data From CHARM

- Objectives
  - Evaluate the association of baseline CRP and change in CDAI over time in patients with moderate to severe CD (Colombel et al; abstract P731)
  - Examine the effect of baseline CRP concentrations on maintenance of remission with weekly vs eow weekly of adalimumab (ADA) (Sandborn et al; abstract P281)
- Methods
  - Post-hoc analyses of the CHARM study
    - All patients received 4-week induction with open-label ADA (80mg at week 0, 40 mg at week 2)
    - At week 4, all patients were randomized to receive double-blind maintenance ADA (40 mg weekly or eow) or placebo for 52 weeks
  - Change in CDAI assessed by baseline CDAI and CRP (high: ≥10mg/L, or low: <10mg/L)
  - Clinical remission at weeks 26 and 56 by baseline CRP was determined for patients who achieved remission at week 4 and were randomized to placebo, eow or weekly ADA treatment groups

Results: Mean CDAI by Baseline CDAI and CRP in the CHARM Study

- Mean CDAI decreased from baseline in all subgroups after adalimumab induction
- By week 56, mean CDAI in all subgroups increased compared with week 4 and was greater in patients who had higher CDAI and CRP at baseline



Results: Remission Rates by CRP in the CHARM Study

- Remission rates for high CRP patients randomized to weekly dosing were approximately 50% higher than for patients in the eow group (weeks 26 and 56, table)
- In contrast, adalimumab-treated patients with low baseline CRP had consistent rates of remission at both time points, regardless of dose group

	CRP ≥10mg/L			CRP <10mg/L		
	Placebo N=34	ADA 40 mg eow N=39	ADA 40 mg weekly N=28	Placebo N=39	ADA 40 mg eow N=42	ADA 40 mg weekly N=33
Baseline CRP, mg/L, median (range)	37 (10-287)	32 (12-162)	29 (10-350)	4.1 (0.2-9.9)	4.4 (0.4-9.8)	2.5 (0.4-9.7)
Remission at Wk 26, %	29.4	51.3	78.6	30.8	47.6	42.4
Remission at Wk 56, %	11.82	41.0	64.3	17.9	42.9	42.4

Impact of Inflammatory Biomarker Levels on Plasma Anti-TNF Concentrations, Clinical Response, and Clinical Remission: Data from Certolizumab Studies

- Background
  - Greater treatment effects with anti-TNFs have been reported in patients with higher baseline CRP concentrations
- Objectives
  - Explore the relationship between baseline inflammatory biomarkers, plasma concentration of certolizumab, and clinical response and remission to anti-TNF therapy
- Methods
  - Post-hoc analyses of the PRECiSE 2 and/or WELCOME studies of certolizumab in patients with CD

Results: Impact of Baseline CRP Concentration on Certolizumab Plasma Levels

- Week 6 certolizumab levels were lower in patients with CRP ≥10 mg/L than in those with CRP <10 mg/L

	Patients with BL CRP ≥10 mg/L		Patients with BL CRP <10 mg/L	
Subgroup at Wk 6	**BL gmCRP (mg/L) (CV)**	**Wk 6 gmCZP (µg/mL) (CV)**	**BL gmCRP (mg/L) (CV)**	**Wk 6 gmCZP (µg/mL) (CV)**
P2 Overall (n=567)	27.8 (93.7)	25.3 (48.9)	3.4 (56.5)	31.4 (47.6)
Remission at Wk 6 (n=276)	27.2 (96.7)	27.1 (48.1)	3.4 (58.5)	33.8 (43.9)
No remission at Wk 6 (n=290)	27.9 (83.6)	24.1 (48.8)	3.4 (54.3)	28.8 (51.9)
WEL Overall (n=484)	29.3 (79.7)	23.7 (67.0)	2.2 (82.5)	34.3 (60.8)
Remission at wk 6 (n=206)	27.5 (64.1)	30.5 (57.5)	2.0 (86.3)	38.0 (56.2)
No remission at wk 6 (n=278)	30.5 (84.7)	20.1 (72.6)	2.3 (79.7)	31.5 (64.5)

BL=baseline; P2=PRECiSE 2 study; WEL=Welcome Study

Results: Remission Deltas by Inflammatory Marker Status

- Highest remission deltas were achieved in certolizumab patients with high baseline CRP or FC levels

Week 26 remission by baseline CRP and FC cut-offs, % of pts (n/N)				Plasma CZP concentration geometric mean, µg/mL (coefficient of variation %)
	Placebo	CZP 400 mg q4w	Delta	CZP 400 mg q4w
Neither CRP nor FC elevated	39% (17/44)	51% (19/37)	12%	Overall: 25.5 (35.2) Remission: 24.9 (30.3) No remission: 27.1 (44.6)
Both CRP and FC elevated	19% (18/96)	41% (41/101)	22%	Overall: 15.9 (47.6) Remission: 18.0 (45.1) No remission: 13.0 (49.7)
Both CRP and FC very elevated	20% (13/64)	37% (28/75)	17%	Overall: 18.0 (45.2) Remission: 19.5 (45.2) No remission: 16.2 (44.0)
CRP low, FC high	25% (5/20)	63% (19/30)	38%	Overall: 27.2 (49.2) Remission: 26.4 (50.8) No remission: 33.3 (47.1)
CRP high, FC low	33% (10/30)	58% (14/24)	25%	Overall: 20.0 (43.2) Remission: 18.8 (40.6) No remission: 26.5 (51.2)

Changes in Fecal Calprotectin Over Time in Patients Treated With Certolizumab

- FC concentrations at baseline and week 6 were *lower* among week 6 responders vs nonresponders, but failed to reach significance

FC concentration (µg/g)	Nonresponders at Week 6 Baseline n=115	Responders at Week 6 Baseline n=368	*P*
Baseline	419.10	341.95	.1258
Week 6	394.78	299.66	.0576

FC Concentrations: Nonremitters vs Remitters

- FC levels at baseline and week 6 were significantly lower in patients in remission at weeks 6 and 26 vs FC concentrations at baseline and week 6 in week 6 nonremitters

gm FC concentration (µg/g)	Nonremitters at Wk 6	Remitters at Wks 6 and 26				
	Baseline n=133	Overall baseline n=107	*P* for Wk 6 nonremitters vs Wks 6 and 26 remitters	Placebo baseline n=41	CZP 400 mg baseline n=66	*P* for placebo vs CZP 400 mg
Baseline	398.60	244.00	.0130	180.65	294.08	.0842
Week 6	414.82	205.32	.0006	144.51	255.38	.0622

Conclusions

- These post-hoc analyses explored the relationship between inflammatory markers, anti-TNF plasma levels and short and long-term responses to mAb treatment in Crohn's disease
- Patients with high inflammatory burden based on CRP and FC had better short-term response to treatment than individuals with lower inflammatory burdens at baseline
- However, on a long-term basis elevated baseline CRP and/or FC were associated with reduced anti-TNF plasma levels, reduced remission rates, and higher disease scores after one year
- Higher dosages may be required during maintenance therapy for patients with elevated pretreatment inflammatory biomarkers

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Long-term Effectiveness and Tolerability of Allopurinol and Thiopurine Combination Therapy in Inflammatory Bowel Disease Patients (27)

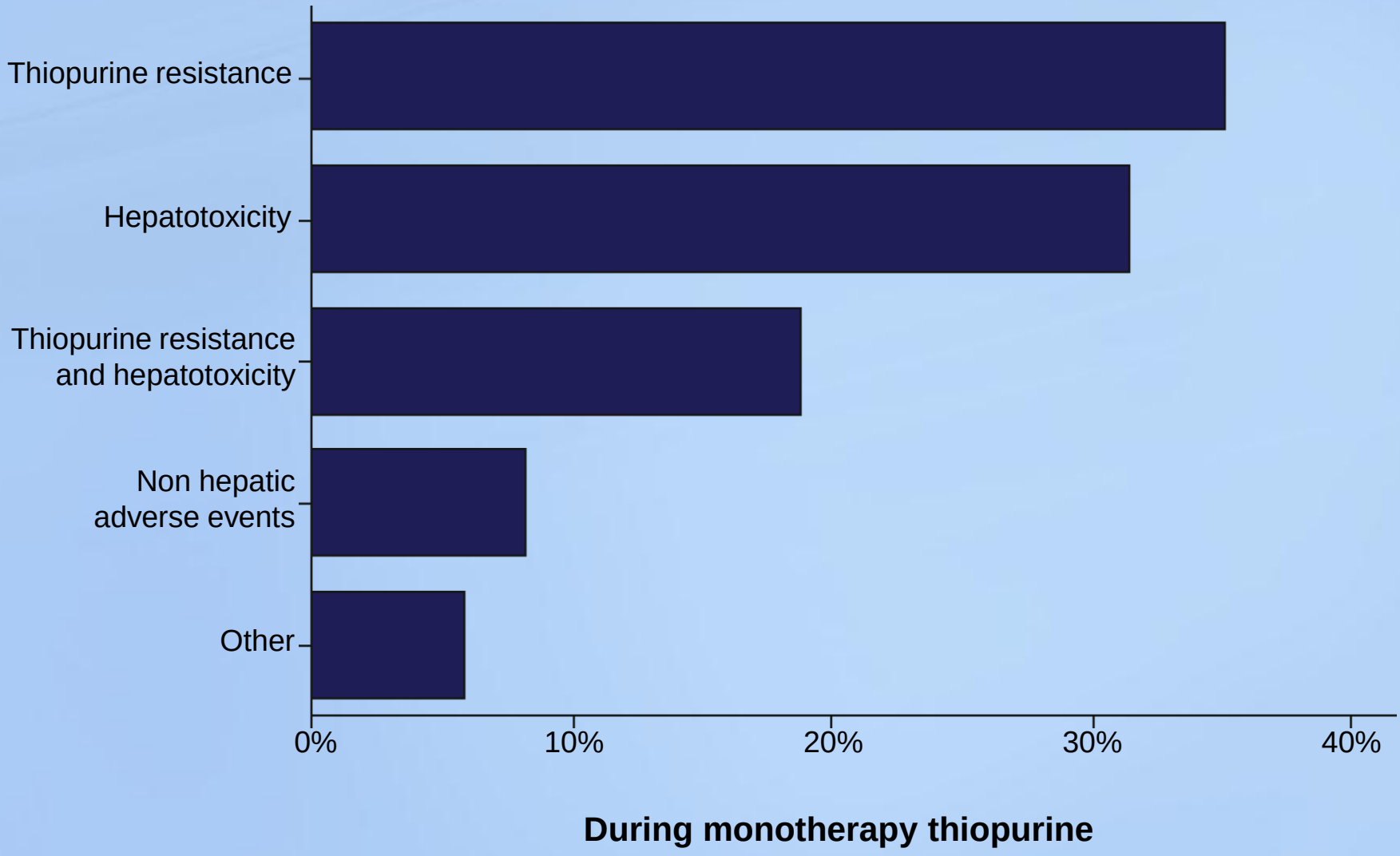
Hoentjen F et al

ACG 2011

Methods

- Objective
  - Assess maintenance effectiveness and tolerability of allopurinol-thiopurine therapy in a larger multicenter cohort of IBD patients
- Methods
  - Adult IBD patients failing monotherapy with thiopurines and subsequently treated with combination therapy of allopurinol and low-dose thiopurine were selected from two tertiary referral IBD centers
  - Therapeutic effectiveness was assessed by calculating the cumulative number of patients still using combination therapy at 6, 12, 24, and 60 months while being in clinical remission

Results: reasons for initiating combination therapy



Results

- Patients (N=85) followed for a mean of 20.4 months
  - Crohn's disease (n=54)
  - Ulcerative colitis (n=28)
  - Miscellaneous (n=3)
- Mean 6-TGN concentration increased from 268 at baseline to 484 pmol/8x10^8 RBC (*P*<.001)
- Mean 6-MMP concentrations decreased from 12,721 to 803 pmol/8x10^8 (*P*<.001)
- Leukopenia occurred in 11 patients
- Seventeen (20%) patients had to discontinue combination therapy, usually within 2 months, due to adverse reactions (n=6), lack of efficacy (n=7) or others (n=3)

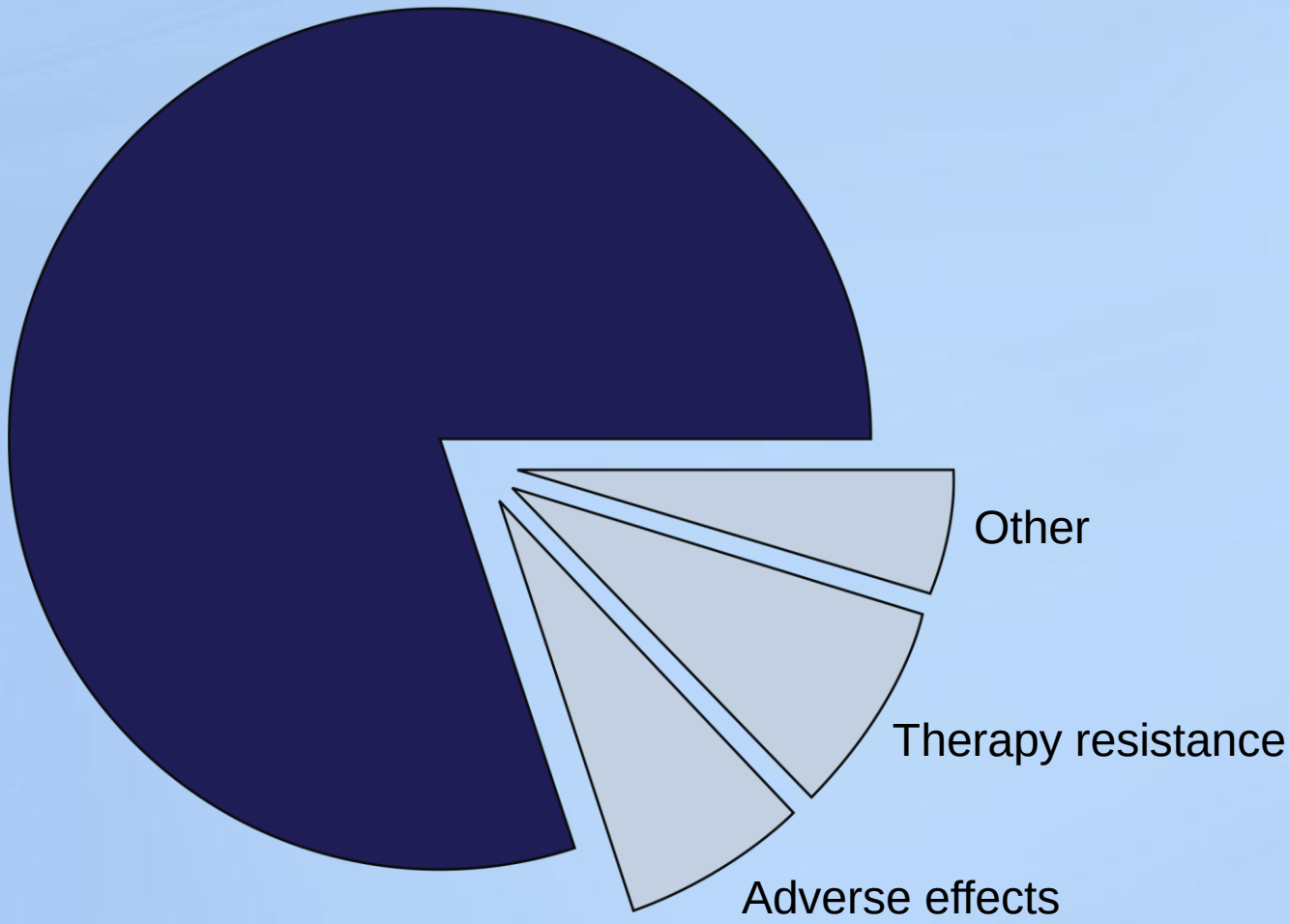
Results: laboratory results

	Monotherapy	Combination therapy	p-value
Leukocyte count 10^3/µl	6.8 (5.3-8.9)	5.4 (3.8-7.0)	<0.001
Platelet count 10^3/µl	310 (270-403)	275 (222-337)	<0.001

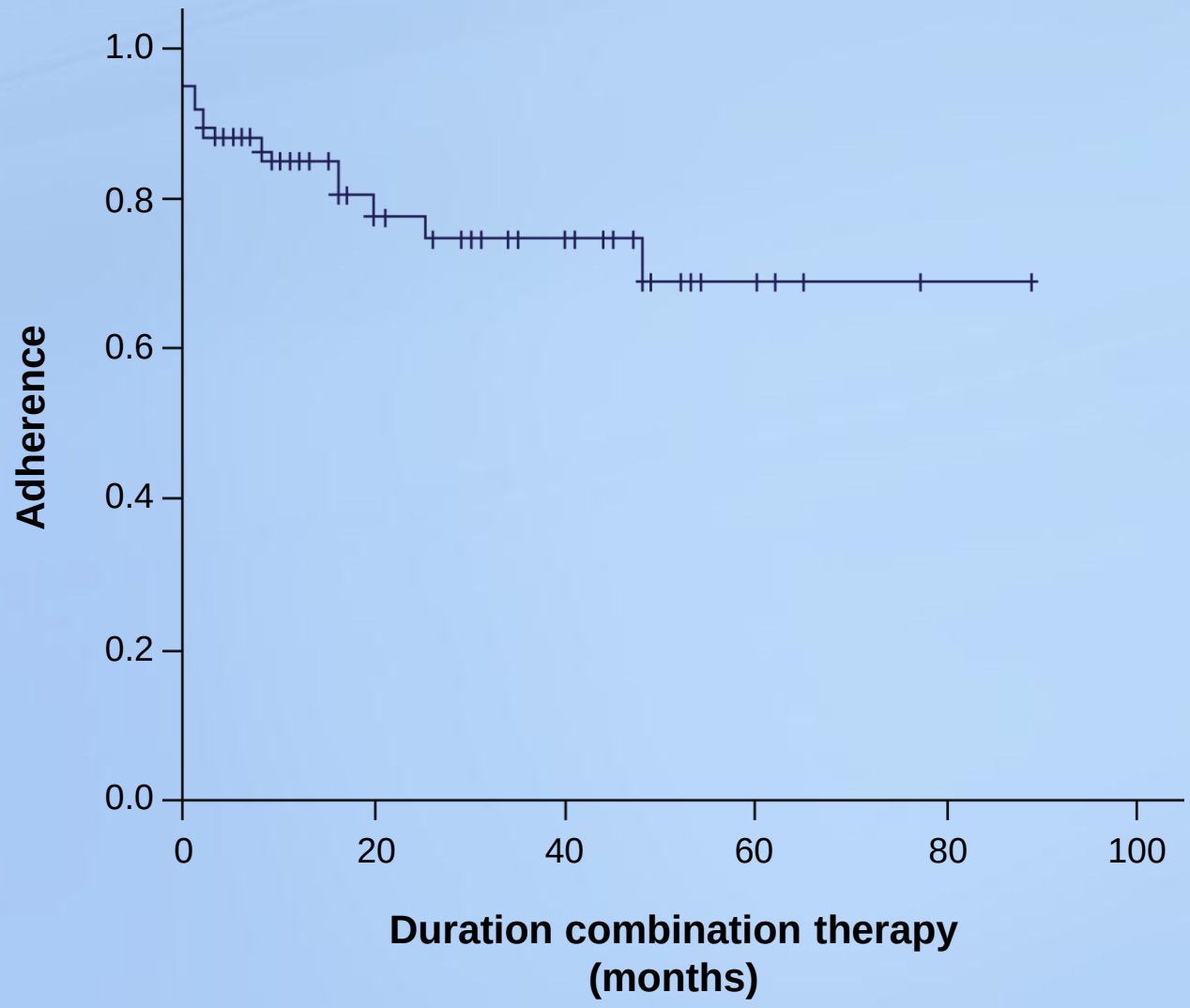
Effectiveness

- Allopurinol/thiopurine combination therapy
- 60% steroid-free remission
- 20% steroid-dependent or active disease
- 20% discontinuation

Results: 20% discontinuation combination therapy



Results: adherence



Conclusions

- Combination therapy with allopurinol and low dose thiopurines is an effective and well tolerated treatment
- This therapy is an alternative long-term maintenance strategy for IBD patients failing conventional thiopurine therapy with a preferential 6-MP metabolism to 6-MMP due to high, functional TPMT activity
- Reduced dose of thiopurine to 25% minimizes risk of leukopenia
- Patients continue to require monitoring for long term hepatic consequences of thiopurines such as nodular regenerative hyperplasia and veno-occlusive disease
- This study protocol is investigational

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Induction of Clinical and Endoscopic Remission of Mild to Moderately Active Ulcerative Colitis with Budesonide MMX® 9 mg: Analysis of Pooled Data from Two Phase 3 Studies (P1133)

Sandborn W et al

ACG 2011

Methods

- Objective
  - Evaluate the efficacy and safety of budesonide MMX® (B-MMX) 6 mg and 9 mg oral tablets vs placebo in patients with active mild to moderate UC when administered for 8 weeks
- Methods
  - Pooled data were analyzed from 2 Phase 3 studies evaluating patients achieving clinical and endoscopic remission with B-MMX 9 mg or 6 mg tablets once daily vs placebo
  - Primary endpoint: Induction of clinical and endoscopic remission
  - Clinical improvement, endoscopic improvement, and symptom resolution were also evaluated at week 8

Results

- 672 patients from the pooled mITT were treated with placebo, B-MMX 9 mg, or B-MMX 6 mg
- Clinical and endoscopic remission for B-MMX 9 mg vs. placebo was 17.7% vs. 6.2% (*P*=.0002)
- Symptom resolution was 26.3% vs. 14.3%, respectively (*P*=.0018)
- Clinical improvement and endoscopic improvement were both numerically greater for B-MMX 9 mg than placebo but not statistically different
- Treatment related adverse events, including potential glucocorticoid effects, occurred with similar frequencies across study groups

Outcomes

	Placebo (N=210) n (%)	B-MMX 9 mg (N=232) n (%)	B-MMX 6 mg (N=230) n (%)
Clinical and Endoscopic Remission, n (%)	13 (6.2)	41 (17.7)	25 (10.9)
Δ vs placebo, %		11.5	4.7
95% CI		12.8-22.6	6.8-14.9
P value*		0.0002**	0.0809
Clinical Improvement, n (%)	60 (28.6)	87 (37.5)	65 (28.3)
P value*		0.0466	0.9425
Endoscopic Improvement, n (%)	68 (32.4)	97 (41.8)	71 (30.9)
P value*		0.0407	0.7334
Symptom Resolution, n (%)	30 (14.3)	61 (26.3)	50 (21.7)
P value*		0.0018†	0.0429†

Conclusions

- Pooled data showed that B-MMX 9 mg given once daily is safe and effective for inducing clinical and endoscopic remission and symptom resolution in patients with mild to moderately active UC

XPERT PERSPECTIVES

...from ACG

Reporting on IBD

Novel Therapies Ustekinemab and Budesonide

XPERT PERSPECTIVES ...from ACG

Reporting on IBD

A Multicenter, Randomized, Double-blind, Placebo-controlled Phase 2b Study of Ustekinumab, a Human Monoclonal Antibody to Il-12/23p40, in Patients with Moderately to Severely Active Crohn's Disease: Results through Week 36 from the CERTIFI Trial (P1147)

Feagan B et al

ACG 2011

Methods

- Objective
  - To evaluate ustekinumab in patients with moderate to severe CD failing anti-TNFs
- Methods
  - Patients with CDAI score 220-450 were randomized to:
    - IV placebo
    - Ustekinumab 1, 3, or 6 mg/kg at week 0
  - At week 8,week 6 responders and nonresponders who received IV UST were separately re-randomized to subcutaneous 90 mg ustekinumab or placebo maintenance at weeks 8 and 16
  - During maintenance, steroid tapering was mandated and assessments were at week 22
  - Patients were followed until week 36
  - Primary endpoint was clinical response at week 6

Results

	Placebo	UST 1mg/kg	UST 3mg/kg	UST 6mg/kg	Combined UST
N	**132**	**131**	**132**	**131**	**394**
Clinical response[a]					
Week 6	23.5%	36.6%*	34.1%	39.7%*	36.8%*
Week 8	17.4%	32.1%*	31.8%*	43.5%*	35.8%*
Clinical remission[b]					
Week 6	10.6%	16.0%	15.9%	12.2%	14.7%
Week 8	10.6%	17.6%	18.2%	18.3%	18.0%*

[a]≥100 point reduction in CDAI; [b]CDAI<150;**P*<.05 vs.placebo by CMH

Results (Continued)

- At week 6, 39.7% in the 6 mg/kg group were in clinical response vs 23.5% of placebo patients (*P*=.005)
- All 3 doses were associated with significant changes vs placebo in CRP, IBDQ, mean CDAI, 70 point drop, and lactoferrin/calprotectin
- In maintenance therapy, among patients in clinical response to ustekinumab at week 6, 41.7% on ustekinumab were in remission at week 22 vs 27.4% of placebo patients (*P*=.029)
- 69.4% vs 42.5% remained in clinical response (p<.001) and 30.6% vs 17.8% were in steroid-free remission at week 22 (*P*=.048)
- Adverse events
  - Proportions of AEs and infections were similar in the ustekinumab and placebo groups during both induction and maintenance
  - No major adverse CV events, deaths, serious opportunistic infections, or TB

Conclusions

- In moderate to severe CD patients previously failing anti-TNFs, ustekinumab induced and maintained clinical response

XPERT PERSPECTIVES
...from ACG

Reporting on IBD

YouTube: Friend or Foe When You are Taking Care of IBD Patients (P290)

Mukewar S et al

ACG 2011

Methods

- Background
  - 55% of IBD patients are not satisfied with information provided at time of diagnosis
  - More than 50% of IBD patients use the internet as a source of information for IBD
  - Health caregivers have concerns about quality and validity of information from internet-based sources for patients
- Objective
  - Analyze IBD-related YouTube videos for content, popularity and as a source of patient education information
- Methods
  - Searched YouTube with key words “Inflammatory Bowel Disease,” “Ulcerative Colitis” and “Crohn’s Disease”
  - The 100 most viewed videos with relevant information on IBD were analyzed

Results and Conclusions

- Results
  - With regard to patient education, overall content was poor
  - Among videos discussing personal experience, the most common reason for positive attitude towards treatment was surgery (60%) and for negative attitude was failure of medical treatment (80%)
- Conclusions
  - Clinicians need to be aware of misleading information posted, particularly by the patients and pharmaceutical companies
  - Health care providers as well as professional societies need to provide more educational and efficient materials using this powerful internet tool to counteract misleading information

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Reporting on IBD

Meta-analysis of the Incidence of Hepatosplenic T-cell Lymphoma in Inflammatory Bowel Disease: An Update (P286)

Kotlyar D et al

ACG 2011

Methods

- Three population-based studies included in analysis:
  - Armstrong 2010 (*Am J Gastroenterol*)
  - CESAME 2009 (*Lancet*)
  - ENEIDA 2010 (*Gastroenterology*)
- Results
  - 2 cases of HSTCL identified
  - Overall incidence: 1.88 cases/100,000 person-years (NNH: 1:52,865)
  - Incidence in patients aged <36 years: 4.43/100,000 person-years (NNH 1:22,556)

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Reporting on IBD

Is Inflammatory Bowel Disease a Risk Factor for Fracture? An Analysis Using the Fracture Risk Assessment Tool (FRAX) (P260)

Targownik L et al

ACG 2011

Methods and Results

- Objective
  - Assess risk for fracture in patients with IBD
- Methods
  - Analysis of data from a large epidemiologic databases
  - Relationship between IBD, BMD, FRAX probability scores, and medication use
- Results
  - 752 patients with IBD underwent at least one DXA
  - FRAX score was strongly predictive of fracture in both IBD and non-IBD cohorts
  - IBD *was not* associated with an increased risk for major osteoporotic fracture after controlling for FRAX score
  - IBD *was* associated with an increased risk for hip fracture

Conclusions

- IBD alone is not an independent risk factor for osteoporotic fracture
- The FRAX score is useful in predicting osteoporotic fracture in patients with IBD

XPERT PERSPECTIVES
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Reporting on IBD

Factors Predicting Bleeding Cessation, Mucosal Healing and Clinical Remission in Patients Receiving Topical Mesalamine with Active Distal Ulcerative Colitis (P708)

Harris MS et al

ACG 2011

Methods

- Objective
  - Evaluate the influence of patient demographics, prior and concomitant medications, and disease severity on treatment outcomes with topical mesalamine therapy in active distal UC
- Methods
  - Reanalysis of data from placebo-controlled multicenter trial (N=153 subjects with active distal UC)
  - Trial compared 6 weeks of therapy with 4 g mesalamine rectal suspension to placebo
  - Analyses performed to examine effects of baseline demographics, prior/concomitant therapies, and disease severity

Results

- Topical mesalamine therapy had a positive effect on treatment outcome (6 week results)
  - Bleeding cessation: HR 3.69 ($P<.01$)
  - Bleeding resolution: OR 5.71 ($P<.03$)
  - Mucosal healing: OR 2.57 ($P<.03$)
- Prior and concomitant prednisone therapy resulted in a 3.85-fold less chance of achieving MH at Week 6
- Prior or concomitant sulfasalazine or AZA-6MP use did not impact outcome
- Disease extent had no consistent effect on treatment responsiveness
- Stool frequency negatively impacted early outcome:
  - Bleeding cessation: HR 0.78 ($P< .05$)
  - Bleeding resolution: OR 0.566 ($P< .005$)
  - Clinical remission: OR 0.634 ($P< .02$)
  - This effect did not persist through Week 6
- Male sex adversely affected likelihood of mucosal healing at Week 6 (0R 0.4, $P<.05$)
- No other demographic factors or factors of baseline severity significantly affected treatment responsiveness

Conclusions

- Prior and concomitant prednisone represents a significantly negative effect for successful treatment outcome using topical mesalamine in distal active UC
- Baseline disease severity and disease extent do not consistently influence the responsiveness of distal active UC to topical mesalamine treatment