Inflammation on Index Biopsy Predicts Loss of Remission Among Ulcerative Colitis Patients with Endoscopic Remission: A U.S. Cohort Analysis

Click, Benjamin H.[1]; Mao, Eric[2]; Ahmad, Harris[3]; Canavan, James[3]; Qiu, Ying[3]; Theigs, Cindy[4]; Crawford, Julie Mallory[5]; Long, Millie D.[6] on behalf of the TARGET-IBD Investigators[7]

1. University of Colorado, Aurora, CO, United States. 2. University of California Davis Health System, Sacramento, CA, United States. 3. Bristol Myers Squibb, Princeton, NJ, United States. 4. AbbVie Inc, North Chicago, IL, United States. 5. Target RWE, Durham, NC, United States. 6. University of North Carolina System, Chapel Hill, NC, United States. 7. TARGET-IBD Investigators are the participating investigators who provided and cared for study patients; they are author and non-author contributors. For the complete list, please see ClinicalTrials.gov (NCT03251118)

Introduction

- Patients with ulcerative colitis (UC) who have previously responded to advanced therapies may experience loss of remission (LOR), although reasons for LOR remain unclear.
- We assessed the associations between clinical characteristics and subsequent LOR in a real-world US-based cohort of UC patients in corticosteroid-free endoscopic remission at baseline.

Methods

- Corticosteroid-free adult UC patients in endoscopic remission on index colonoscopy (no evidence of endoscopic inflammation, erosions or ulceration), with an index histology assessment and known duration of disease, enrolled in TARGET-IBD from July 2017 to June 2021, were included.
- LOR definition: presence of endoscopic inflammation, erosion or ulceration on follow-up colonoscopy, or commencement of steroids.
- Multivariable Cox proportional hazards regression was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) of LOR in relation to several variables.
- Follow-up time: days from index colonoscopy to earliest of: LOR, death, discontinuation from the study, IBD surgery, or end of available data.

Table 1. Demographics, BMI, Disease Characteristics, and Treatment History Among Adult TARGET-IBD Participants – Ulcerative Colitis

Characteristics	All Participants (N=513)
Demographics	
Age at Baseline (years)[1]	
Median (n)	46 (513)
IQR	34-59
Age at Baseline by Category, n (%)[1]	
18-39	202 (39.4%)
40-64	223 (43.5%)
>= 65	88 (17.2%)
Age at Diagnosis (years)	
Median (n)	31 (513)
IQR	23-46
Duration of Disease at Baseline (years)[2]	
Median (n)	10 (513)
IQR	4-18
Sex, n (%)	
Female	272 (53.0%)
Race, n (%)	
White	447 (87.1%)
Black or African American	26 (5.1%)
Asian	12 (2.3%)
Other	8 (1.6%)
Not Reported	20 (3.9%)
Ethnicity, n (%)	
Hispanic or Latino	12 (2.3%)
Not Hispanic or Latino	475 (92.6%)
Other	1 (0.2%)
Not Reported	25 (4.9%)
BMI (kg/m^2) at Baseline[3]	
Median (n)	27 (390)
Disease Characteristics	
Location of Ulcerative Colitis, n (%)[4]	
Proctitis	35 (6.8%)
Left-Sided	127 (24.8%)
Extensive	248 (48.3%)
Not Reported	103 (20.1%)
Treatment History	
Number of Unique Biologics Discontinued Prior to Baseline, n (%)[5]	
0	433 (84.4%)
1	56 (10.9%)
>1	24 (4.7%)
Biologic Use Ongoing at Baseline, n (%)	
Yes - combination therapy[6]	71 (13.8%)
Yes - monotherapy	123 (24.0%)
5-ASA Derivative Use Ongoing at Baseline, n (%)	277 (54.0%)
Steroid Use Within 6 Months Before Baseline, n (%)	49 (9.6%)
Inflammation on Baseline Biopsy, n (%)	196 (38.2%)

Note: Colonoscopies with an unknown date or which occurred before a participant's IBD diagnosis have been excluded from analysis.
IQR stands for Interquartile Range.
[1]Age at Baseline calculated as year of baseline colonoscopy minus year of birth.
[2]Duration of Disease at Baseline calculated as year of baseline colonoscopy minus year of diagnosis.
[3]Based on most recent Body Mass Index at or before the baseline colonoscopy.
[4]Based on most recent IBD Status assessment at or before the baseline colonoscopy.
[5]Biologics include: adalimumab, certolizumab, golimumab, infliximab, natalizumab, ustekinumab, and vedolizumab.
[6]Combination therapy includes concurrent use of methotrexate, azathioprine, or mercaptopurine.

Table 2. Unadjusted and Multivariable-Adjusted Cox Models of Loss of Remission

	LOR n	Person-years	Unadjusted HR (95% CI)	Multivariable-adjusted[1] HR (95% CI)
Age at index colonoscopy (years)	188	967.3	0.989 (0.981, 0.999)	0.988 (0.978, 0.998)
Duration of disease at index (years)[2]	188	967.3	0.990 (0.976, 1.004)	1.00 (0.98, 1.01)
Location of ulcerative colitis				
Proctitis or left-sided	67	314.2	Ref	Ref
Extensive	86	465.6	0.88 (0.64, 1.22)	0.97 (0.70, 1.34)
Not reported	35	187.5	0.93 (0.62, 1.40)	1.08 (0.71, 1.64)
Number of unique biologics discontinued prior to index colonoscopy[3]				
0	159	847.1	Ref	Ref
>=1	29	120.2	1.18 (0.79, 1.76)	1.22 (0.81, 1.86)
Biologic use ongoing at index colonoscopy				
No	120	648.4	Ref	Ref
Yes – combination therapy[4]	23	127.0	0.92 (0.59, 1.44)	0.78 (0.49, 1.25)
Yes – monotherapy	45	192.0	1.14 (0.81, 1.60)	1.06 (0.74, 1.52)
Inflammation on index biopsy				
No	94	634.1	Ref	Ref
Yes	94	333.2	1.92 (1.44, 2.55)	2.01 (1.50, 2.69)

Abbreviations: LOR, loss of remission; HR, hazard ratios; CI, confidence interval. [1]Mutually adjusted for all other variables, [2]Calculated as year of index colonoscopy minus year of diagnosis, [3]Includes adalimumab, certolizumab, golimumab, infliximab, natalizumab, ustekinumab, and vedolizumab, [4]Includes concurrent use of methotrexate, azathioprine, or mercaptopurine
Note: Unadjusted and adjusted models included n=513 participants with available data for index disease duration and histology.

Conclusions

- Among corticosteroid-free UC patients in endoscopic remission, histologic inflammation was associated with a two-fold increased risk of subsequent LOR, often within a year.
- This real-world analysis is limited by collection criteria (endoscopy and histology results within collected medical records), and thus may not be fully representative.
- Future research should focus on determining if treatment modification or intensification may be effective at preventing LOR in patients with risk factors.

Results

- 513 UC patients were eligible for analysis (53.0% female; median age at diagnosis 31 years; median disease duration 10 years). (Table 1)
- Among these, 188 patients (36.6%) experienced LOR during follow-up.
- Median follow-up time was 21.3 months; among patients who experienced LOR, median time to LOR was 11.8 months (IQR 5.3 – 20.1 months).
- In the multivariable model, presence of histological inflammation on index biopsy was associated with greater risk of LOR (HR 2.01, 95% CI 1.50-2.69) compared to those with histologically quiescent disease. (Table 2)
- Results relating to inflammation on index biopsy were not modified by disease location, current biologic use, or number of previous biologics.
- Older age was associated with lower risk of LOR (HR 0.988, 95% CI 0.978-0.998). (Table 2)

Disclosures

B.H.C. : Speaker's bureau and consulting for Takeda, TARGET consulting. E.M. : Advisory Committee member at Prometheus Biosciences, Advisory Committee member at Pfizer. H.A. : Employed at Bristol Myers Squibb. J.C. : Employed at BMS. Y.Q. : Employed at BMS, Stockholder at BMS. C.T. : Employed at AbbVie and permitted to own stock in the company. J.M.C. : Employed at Target RWE. M.L. : Consulting fees from AbbVie, Pfizer, Janssen, Takeda, Prometheus, Salix, UCB, Target RWE, Research support from Takeda and Pfizer.

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Email: Benjamin.click@cuanschutz.edu