



## Histological Inflammation Predicts Loss of Remission Among Crohn's Patients with Endoscopic Remission: A US Cohort Analysis

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### Introduction

- Patients with Crohn's Disease (CD) who have previously responded to advanced therapies may experience loss of remission (LOR), although reasons for LOR remain unclear.
- This study assessed the associations between clinical characteristics and LOR in a real-world US-based cohort of CD patients in endoscopic remission.

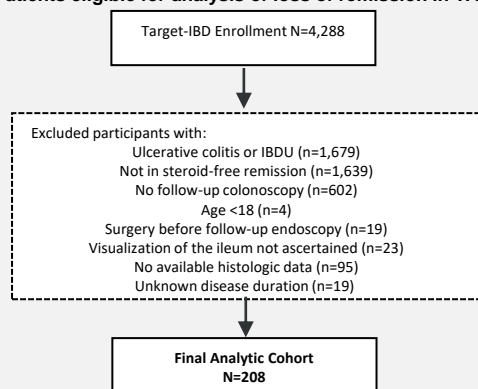
### Methods

- TARGET-IBD is a longitudinal cohort of patients receiving care in usual clinical practice in the US.
- Patients enrolled in TARGET-IBD from July 2017 to November 2020 were included.
- To be in remission a patient needed to be steroid-free and to have no evidence of endoscopic inflammation, erosion, ulceration or stricturing on index colonoscopy.
- LOR was defined as presence of endoscopic inflammation, erosion, ulceration, or stricturing on follow-up colonoscopy, or commencement of steroids.
- Patients who had surgery during follow-up were excluded.
- Patients with ileal disease were excluded if either index or follow-up colonoscopy did not visualize the ileum.
- Logistic regression was used to estimate association between index covariates and LOR.

### Results

- Of the 208 TARGET-IBD CD patients who were eligible for analysis, 112 patients (53.8%) experienced LOR during follow-up to second colonoscopy.
- In multivariable regression analysis, ileal disease at index was significantly associated with future LOR (odds ratio [OR] 3.19, 95% confidence interval [CI] 1.05-9.73) compared to isolated colonic disease (Figure 2).
- Evidence of histologic inflammation was associated with twice the odds of LOR (OR 2.0, 95% CI 1.08-3.68). Additional clinical variables assessed were not useful in predicting LOR, although a modest inverse association with age was noted (OR 0.97, 95% CI 0.94-0.99 per year).

Figure 1: Patients eligible for analysis of loss of remission in TARGET-IBD



Total N	208
Median age at index <sup>1</sup> (min – max)	40 (18 – 80)
Median age at diagnosis (min – max)	25 (3 – 70)
Duration of disease at index, median years (min – max)	10 (0 – 60)
Sex, n (%)	
Female	127 (61.1%)
Male	81 (38.9%)
Insurance type at index, n (%)	
Private	161 (77.4%)
Medicare	32 (15.4%)
Medicaid	11 (5.3%)
Supplemental/Other/Unknown	19 (9.1%)
Location of disease, n (%)	
Colon	49 (23.6%)
Ileocolon	97 (46.6%)
Ileum	24 (11.5%)
Not Reported	38 (18.3%)
Phenotype, n (%)	
Inflammatory (B1)	86 (41.3%)
Stricturing (B2)	14 (6.7%)
Fistulizing (B3)	63 (30.3%)
Prior CD surgery (non-B1 phenotype) <sup>2</sup>	45 (21.6%)
Number of unique biologics discontinued before index, n (%) <sup>3</sup>	
0	132 (63.5%)
1	50 (24.0%)
>1	26 (12.5%)
Biologic use ongoing at index, n (%)	
No	89 (42.8%)
Yes - combination therapy <sup>4</sup>	37 (17.8%)
Yes - monotherapy	82 (39.4%)
Inflammation on Biopsy, n (%)	
No	107 (51.4%)
Yes	101 (48.6%)

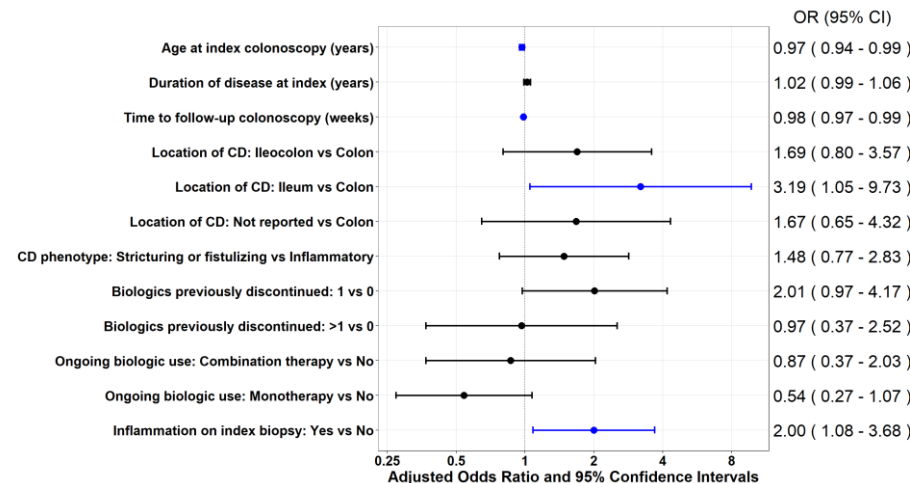
<sup>1</sup>Index is defined as the colonoscopy resulting in a diagnosis of remission

<sup>2</sup>Individuals who underwent prior CD surgery (i.e. intestinal resection) who therefore are non-B1 phenotype, but not known whether B2 or B3

<sup>3</sup>Biologics include: adalimumab, certolizumab, golimumab, infliximab, natalizumab, ustekinumab, vedolizumab

<sup>4</sup>Concurrent use of methotrexate, azathioprine, or mercaptopurine.

Figure 2: Association of Risk Factors with Loss of Remission in Crohn's Disease



### Conclusions

- Among steroid-free CD patients in remission as defined by endoscopy, histologic evidence of inflammation at that examination was a predictor of subsequent LOR.
- Histologic information in conjunction with endoscopic remission, therefore, is important in managing CD.
- Knowledge of disease distribution may also have a role in predicting subsequent LOR.
- Future research should focus on determining if treatment modification or intensification is effective at preventing LOR in patients with risk factors.

\* TARGET-IBD Investigators are the participating investigators who provided and cared for study patients; they are authors and non-author contributors. For the complete list, please see ClinicalTrials.gov (NCT03251178)

### Disclosures and Conflicts of Interest

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