Outcomes of early vs. delayed advanced therapy among patients with moderate ulcerative colitis in the United States: TARGET-IBD

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Introduction

- Ulcerative colitis (UC) is an idiopathic, chronic inflammatory disease of the colon and rectum characterized by intermittent periods of disease relapse and remission with no single treatment pathway
- An often-overlooked population is patients with UC and moderate disease severity, as this group is frequently combined with severe UC patients, but can have different needs
- Patients who achieve endoscopic remission have been shown to have a significantly lower risk of clinical relapse (than patients achieving clinical remission)[1]

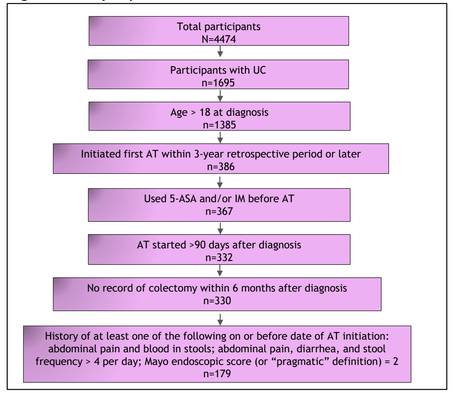
Objective

- The purpose of this study was to compare endoscopic remission between patients with early vs. delayed advanced therapy (AT) initiation among adult patients with moderate UC

Methods

- TARGET-IBD is a non-interventional, longitudinal cohort study of patients receiving care for inflammatory bowel disease at 34 US academic or community gastroenterology sites
- Adult moderate severity patients with UC were included if they:
  - Initiated a conventional therapy (5-aminosalicyclic acid (5-ASA) or immunomodulator(IM)) before AT
  - Had no AT (Biologics/Janus Kinase Inhibitors (JAKi)) use for at least 90 days after first clinical diagnosis
  - No colectomy for at least 6 months after diagnosis
  - Presence of at least one of the following before AT initiation
    - Abdominal pain and blood in stools
    - Abdominal pain, diarrhea, and stool frequency $\geq$ 4 per day
    - Mayo endoscopic score (or "pragmatic" definition) = 2
- AT initiators were divided into two groups:
  1) early initiators received treatment 0 to 2 years after diagnosis,
  2) delayed initiators received treatment >2 years after diagnosis
- Kruskal-Wallis test was used to assess the association between continuous variables and timing of AT initiation, and the Cochran-Mantel-Haenszel (CMH) test and Fisher's exact test were used for categorical variables
- Multivariable Cox regression models were fit to assess the association between early vs. delayed initiation of AT and endoscopic remission after AT initiation

Figure 1. Study Population



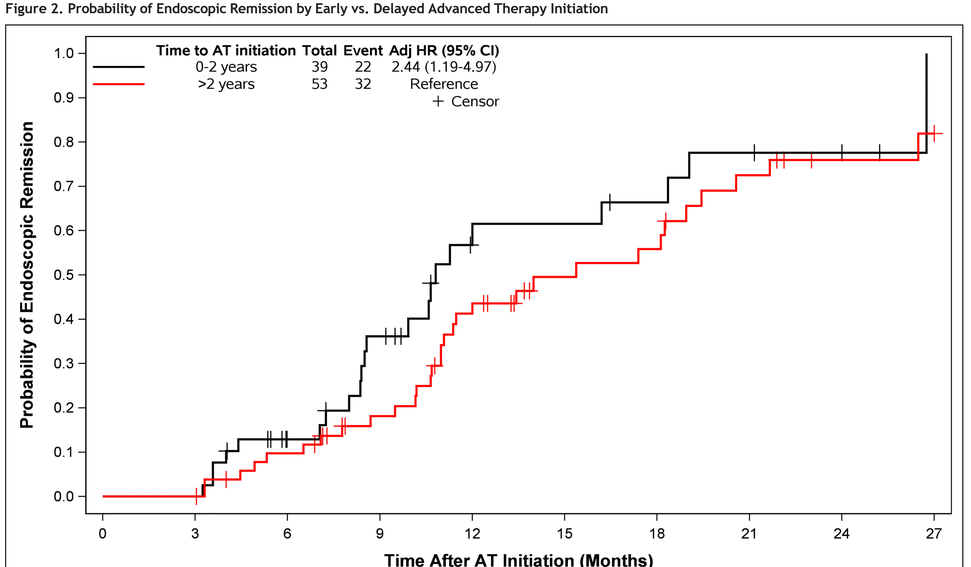
5-ASA, 5-aminosalicylic acid; AT, Advanced Therapy; IM, immunomodulator; "pragmatic" Mayo Endoscopic Score based on presence/severity of inflammation and ulcerations/erosions

Results

- Of 4,474 patients in TARGET-IBD, 179 patients met criteria for moderate UC (Figure 1)
- Compared to delayed initiators, early initiators were younger at diagnosis (median 30 vs. 33 years) and had more females (51% vs. 48%). Most early initiators had private insurance (80%) and were predominantly treated at academic sites (75%) (**Table 1**)
- Median time from initiation of an AT to endoscopic remission for early initiators (0-2 years) was 10.8 months (IQR 8.4-19.0) while delayed initiators (>2 years) had a median of 15.4 months (IQR: 10.6-21.7)
- In the multivariable Cox model, early initiators of AT (0-2 years after diagnosis) had an increased likelihood of endoscopic remission compared to delayed initiators (HR=2.44, 95% CI 1.19-4.97) (**Figure 2**)
- Patients who initiated an AT after <1 year had about 3.5 times the likelihood of endoscopic remission compared to those who initiated an AT >2 years after diagnosis (HR=3.44, 95% CI 1.45-8.15)

Among patients with moderate UC, early initiators (0-2 years after diagnosis) of an advanced therapy were more than 2 times as likely to experience endoscopic remission compared to delayed initiators (>2 years after diagnosis) of an advanced therapy

Figure 2. Probability of Endoscopic Remission by Early vs. Delayed Advanced Therapy Initiation



Note: Hazard ratio is adjusted for age at AT initiation, sex, BMI at AT initiation, private insurance, history of conventional therapy use, and UC location at AT initiation

Table 1. Patient Characteristics by Early vs. Delayed Advanced Therapy Initiation

	Time from diagnosis to AT initiation			
	Early Initiators 0-2 years (N=71)	Delayed Initiators >2 years (N=104)	All Participants (N=175)	P-value
Age at diagnosis (years), median (IQR)	30 (23 - 49)	33 (27 - 45)	33 (25 - 46)	0.49
Age at AT initiation (years), median (IQR)	31 (24 - 51)	47 (36 - 59)	40 (30 - 57)	<.001
Sex, n (%)				
Female	36 (50.7)	50 (48.1)	86 (49.1)	0.73
Male	35 (49.3)	54 (51.9)	89 (50.9)	
BMI (kg/m^2) at AT initiation, median (IQR)	24.1 (21.8 - 28.6)	29.6 (23.0 - 35.2)	27.1 (22.3 - 34.0)	0.002
Insurance at enrollment, n (%)				
Private	57 (80.3)	71 (68.3)	128 (73.1)	0.38
Medicare	8 (11.3)	14 (13.5)	22 (12.6)	
Medicaid	5 (7)	13 (12.5)	18 (10.3)	
Other	1 (1.4)	5 (4.8)	6 (3.4)	
Uninsured	0 (0)	1 (1.0)	1 (0.6)	
Location of UC at AT initiation, n (%)				
Proctitis	6 (8.5)	2 (1.9)	8 (4.6)	0.22
Left-Sided	18 (25.4)	32 (30.8)	50 (28.6)	
Extensive	44 (62.0)	66 (63.5)	110 (62.9)	
Not Reported	3 (4.2)	4 (3.8)	7 (4.0)	
Site type, n (%)				
Academic	53 (74.6)	70 (67.3)	123 (70.3)	0.30
Community	18 (25.4)	34 (32.7)	52 (29.7)	

Limitations

- Due to the strict treatment and disease severity requirements, the sample size is limited
- Examining endoscopic remission in a larger cohort over a longer period would provide additional understanding of this understudied population
- Moderate disease severity definition needs further validation

Conclusions

- Among patients with moderate UC, early initiators (<2 years after diagnosis) of an AT were more than 2 times as likely to experience endoscopic remission compared to delayed initiators of an AT (> 2 years after diagnosis)
- Findings suggest that by prioritizing early AT, health care providers may be able to optimize clinical outcomes in this group of patients

References

1. Yoon H, et al. Incremental benefit of achieving endoscopic and histologic remission in patients with ulcerative colitis: A systematic review and meta-analysis. *Gastroenterology* 2020, 159(4), 1262-1275.

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Declaration of interests

ELB served as a consultant for Target RWE. SS and HAA are employees and/or shareholders of Bristol Myers Squibb. DG, HLM, and JMC are employees of Target RWE. DTR has received grant support from Takeda, and has served as a consultant for AbbVie, Altrubio, Bellatrix Pharmaceuticals, Boehringer Ingelheim Ltd., Bristol Myers Squibb, Syneos, Dizal Pharmaceuticals, Galapagos, Ichnos Sciences S.A., InDex Pharmaceuticals, Iterative Health, Janssen Pharmaceuticals, Lilly, Pfizer, Prometheus Biosciences, Reistone, and Takeda.

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