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FACTORS ASSOCIATED WITH BIOLOGIC TREATMENT DE-ESCALATION IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION

- Crohn's disease (CD) is a chronic and relapsing inflammatory disease involving the gastrointestinal tract affecting around 1 million people in the United States.[1]
- Biologic treatment has been demonstrated to reduce bowel damage and disease progression[2] in patients with CD. However, long-term biologic treatment can pose important economic and safety concerns.[3]
- Biologic de-escalation has been recently proposed as a treatment strategy for patients with CD. De-escalation involves withdrawal of biologic treatment when remission is achieved and restarting treatment when the disease flares up again.[4,5]

OBJECTIVE

- To characterize biologic de-escalation among CD patients in remission on biologic treatment in a real-world dataset.
- To examine patient-specific factors associated with biologic de-escalation.

METHOD

- Retrospective cohort study using the Merative MarketScan Research Databases from 2009-2021.
- We identified our study cohort as adult CD patients in remission on biologic treatment by applying the following criteria: 1) patients initiated a biologic for CD between 01/01/2010 and 12/31/2020; 2) patients had at least 1 year of biologic treatment; and 3) patients had ≥ 6-month steroid-free period during their biologic treatment. The earliest date when both 1-year biologic treatment and 6-month steroid-free were met on continuous biologic treatment was defined as the index date. Patients with any indications of treatment failure, including intravenous (IV) steroid use, CD-related ED visit or hospitalization during 3-month period prior to index date were excluded **(FIGURE 1).**
- Biologic de-escalation, defined by a biologic discontinuation not due to treatment failure, was identified starting from the index date. Biologic discontinuation was defined by a treatment gap greater than 90 days after days supply was considered. If patients exhibited any indications of treatment failure within the month leading up to discontinuation of the biologic, that discontinuation would be attributed to treatment failure. Otherwise, it would be classified as biologic de-escalation.
- Patients were followed from index date until the first of the following: 1) de-escalation; 2) biologic discontinuation due to treatment failure; 3) switched to a different biologic; 4) disenrollment; or 5) end of the dataset (12/31/2021).
- We compared those with de-escalation to individuals that continued treatment and identified factors associated with de-escalation using cause-specific hazard models.
- Post biologic de-escalation, time to re-treatment or switch to a different biologic was assessed as a proxy of time to relapse.

RESULTS

FIGURE 1: COHORT IDENTIFICATION DIAGRAM

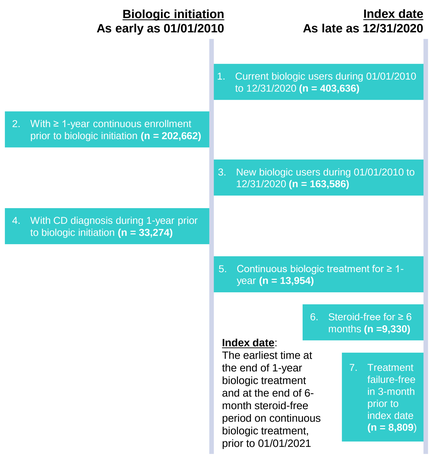


TABLE 1: BASELINE CHARACTERISTICS

Baseline Characteristics	N = 8,809[1]
Age	40 (25, 53)
Gender, female	4,324 (49%)
Cohort entry since 2016	4,737 (54%)
Annual biologic out-of-pocket cost	600 (233, 1,405)
Employment status	
Active employment	5,854 (66%)
Other/Unknown	2,044 (23%)
Retired/COBRA/ Disability	911 (10%)
Health plan with capitation	1,019 (12%)
CCI > 1	1,678 (19%)
Renal disease	192 (2.2%)
Anemia	1,515 (17%)
Weight loss	303 (3.4%)
IV steroid use	1,992 (23%)
Prior CD-related ED visit	958 (11%)
Prior CD-related hospitalization	763 (8.7%)
Prior surgeries	510 (5.8%)
Fistula of intestine	169 (1.9%)
Intestinal stricture	644 (7.3%)
Disease location	
Colon	1,212 (14%)
Ileum	1,522 (17%)
Ileum/colon	3,720 (42%)
Not specified	2,355 (27%)

[1]Median (IQR); n (%)

- A total of 8,809 patients were identified as the study cohort **(TABLE 1).** Over a median (IQR) follow-up period of 14.0 (5.6, 26.4) months, 1844 (21%) patients were identified as having a biologic de-escalation. At 24 months post index date, the cumulative incidence of biologic de-escalation was 22% **(FIGURE 2)**, while the cumulative incidence of treatment failure (composite of biologic discontinuation due to treatment failure and switch) was 14%.

FIGURE 2:
CUMULATIVE INCIDENCE FOR BIOLOGIC DE-ESCALATION

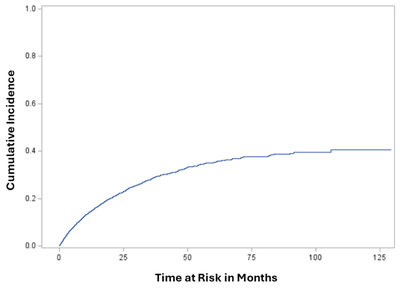
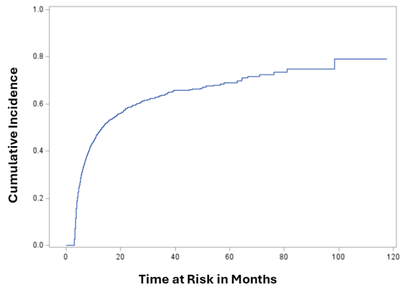


FIGURE 3:
RE-TREATMENT/SWITCH POST DE-ESCALATION



- In univariate regression, biologic with IV administration (HR: 1.40; 95% CI: 1.28-1.55), anemia (HR: 1.14; 95% CI: 1.01-1.28), and disease location not specified (HR:1.47; 95% CI: 1.32-1.64) were associated with biologic de-escalation. On the other hand, cohort entry since 2016 (HR: 0.67; 95% CI: 0.61-0.73), IV steroid use (HR: 0.83; 95% CI: 0.75-0.93), higher annual biologic out-of-pocket costs (HR: 0.85; 95% CI: 0.76-0.94), and male gender (HR: 0.87; 95% CI: 0.79-0.95) were associated with continuous biologic treatment **(TABLE 2).**

RESULTS

- Among 1844 individuals who were identified as biologic de-escalators, 849 (46%) of them experienced re-treatment (n=748, 41%) or switch (n=247, 13%). The cumulative incidence of re-treatment/switch was 54.6% and 58.9% at 1 year and 2 years after biologic de-escalation, respectively **(FIGURE 3).**

TABLE 2: UNIVARIATE ANALYSIS FOR FACTORS ASSOCIATED WITH BIOLOGIC DE-ESCALATION

Parameter	Hazard Ratio	95% Hazard Ratio Confidence Limits
Age	1.00	0.99 – 1.00
Male gender	0.87	0.79 - 0.95
Cohort entry since 2016	0.67	0.61 - 0.73
Higher (> Q3) annual biologic out-of-pocket costs (excluding deductible)	0.85	0.76 - 0.94
Employment status		
Other/Unknown vs. Active employment	1.09	0.97 - 1.22
Retired/COBRA/disability vs. Active employment	1.04	0.89 - 1.21
Health plan with capitation	0.90	0.78 - 1.04
Biologic with subcute administration	1.40	1.28 - 1.55
CCI > 1	1.06	0.94 - 1.19
Renal disease	1.09	0.80 - 1.47
Anemia	1.14	1.01 - 1.28
Weight loss	0.99	0.77 - 1.28
IV steroid use	0.83	0.75 - 0.93
Prior CD-related ED visit	0.98	0.84 - 1.13
Prior CD-related hospitalization	1.04	0.89 - 1.22
Prior surgeries	0.81	0.66 – 1.00
Fistula of intestine	1.10	0.79 - 1.54
Intestinal stricture	0.85	0.71 - 1.02
Disease location		
Colon vs. Ileum/colon	1.12	0.97 - 1.30
Ileum vs. Ileum/colon	1.12	0.98 - 1.28
Not specified vs. Ileum/colon	1.47	1.32 - 1.64

DISCUSSION

- In this analysis of real-world data, around 22% of patients were found to meet the definition of de-escalation of their biologic treatment. At one year post biologic de-escalation, 54.6% of patients had re-treatment or switched to a different biologic which may be indicative of a disease relapse.
- Despite the efforts made to identify biologic discontinuation not due to treatment failure as biologic de-escalation, there remains a risk of misclassifying treatment failure or nonadherence as de-escalation.
- Unexpectedly, higher biologic out-of-pocket costs and later cohort entrance were found to be associated with less biologic de-escalation. Among factors associated with increased disease severity, anemia was positively associated with de-escalation, while IV steroid use was negatively associated with de-escalation.
- Factors beyond patients' out-of-pocket costs and disease severity, for example provider level factors might be associated with biologic de-escalation. Continued examination of biologic de-escalation in real-world data is important to understand the degree to which this treatment strategy is being adopted and the implications of this strategy.

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