NON-BIOLOGIC MEDICATION USE PRE- AND POST-USTEKINUMAB INITIATION AMONG PATIENTS WITH ULCERATIVE COLITIS

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BACKGROUND

- The standard of care for patients with ulcerative colitis (UC) includes anti-inflammatory agents, such as corticosteroids, conventional systemic therapies (i.e., 5-aminosalicylate [5-ASA] agents, immunomodulators), and biologics/advanced therapy[1-3]
- Moreover, to control symptoms (e.g., pain and diarrhea), opioids, gastrointestinal (GI) antispasmodics, and anti-diarrheal medications are commonly used[4,5]
- Polypharmacy is common and combinations with immunomodulators, 5-ASA, and corticosteroids while receiving biologics occur frequently[6,7]
- The treatment landscape for UC has changed recently, notably with the approval by the US Food and Drug Administration (FDA) of ustekinumab, an anti-interleukin 12 (IL-12) and anti-interleukin 23 (IL-23) agent, in October 2019[8]
- There is limited real-world information on non-biologic medication use among patients with UC initiated on ustekinumab
- This study aimed to generate real-world evidence by evaluating non-biologic medication use among patients with UC initiated on ustekinumab

OBJECTIVE

To compare non-biologic medication use among patients with UC pre- and post-ustekinumab initiation

METHODS

Data Source

- The Symphony Health, an ICON plc Company, PatientSource® (04/01/2017 – 10/31/2020) database (SHS) was used
- The SHS database is a longitudinal patient data source, which captures prescription claims and medical utilization and costs across the US
- This database complies with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act

Study design

- A retrospective design was used
- Patients with UC initiated on ustekinumab were selected
- The index date corresponded to the date of ustekinumab initiation (first claim [paid pharmacy or medical] for ustekinumab, if the first claim was on or after 10/18/2019 [ustekinumab approved for UC on 10/18/2019])
- Patients were required to have ≥12 months of clinical activity prior to the index date (to ensure the first claim for ustekinumab corresponded to the initiation)
  - Given the open nature of the SHS database, clinical activity was created by selecting the first and last diagnosis, procedure, or pharmacy claim as the start and end dates of the continuous clinical activity
- The baseline period covered ≥6 months of clinical activity prior to the index date
- The follow-up period started at and included the index date and lasted for 6 months of clinical activity
- Patients were required to have ≥2 claims for ustekinumab within 90 days of the index date
- Use of non-biologic medication was reported in the 6 months before and the 6 months on and after the index date

Study sample

- Patients meeting the following criteria were included in the study sample:
  - ≥1 diagnosis for UC (International Classification of Diseases, Ninth Revision [ICD-9]: 556.x; International Classification of Diseases, Tenth Revision [ICD-10]: K51.x) in the baseline period before or on the index date
  - ≥2 pharmacy or medical claims for ustekinumab within 90 days of the index date, one of which was the index administration (on or after 10/18/2019)
  - ≥12 months of continuous clinical activity before the index date
  - ≥6 months of continuous clinical activity after the index date
  - ≥18 years of age as of index date
- Patients meeting the following criteria were excluded from the study sample:
  - ≥1 diagnosis for Crohn's disease (ICD-9: 550.x; ICD-10: K50.x) at any time
  - ≥1 claim for ankylosing spondylitis, atopic dermatitis, hidradenitis suppurativa, juvenile idiopathic arthritis, plaque psoriasis, psoriatic arthritis, relapsing polychondritis, rheumatoid arthritis, Sjogren's disease, systemic lupus erythematosus, and uveitis prior to the index date
  - Patients whose only method of payment is Medicaid during the continuous clinical activity

Outcome measures

- Non-biologic medication use in the 6-month period pre- and post-ustekinumab initiation included: immunomodulators, 5-ASA, corticosteroids, opioids, antidiarrheals, and GI antispasmodics
  - For corticosteroids, episodes of continuous use of ≥60 days and 90 days (a therapy exposure gap of 14 days of supply was used to define continuous use) and cumulative use of ≥60 and 90 non-overlapping corticosteroid days were also reported

Statistical analysis

- Descriptive statistics were reported as mean with standard deviation (SD) for continuous variables and as frequencies with proportion for categorical variables
- The use of non-biologic medication in the pre- and post-ustekinumab initiation period was compared with a logistic model estimated by generalized estimating equation adjusting for repeated measure per patient; results were reported as odds ratios (OR) with the 95% confidence interval (CI) and p-value

CONCLUSIONS

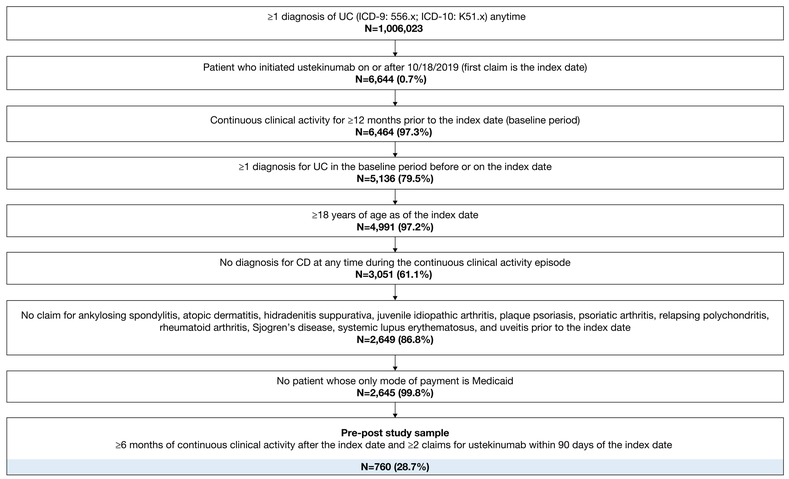
- **In this real-world study of patients with UC, being initiated on ustekinumab was associated with a significant decrease in the use of immunomodulators, 5-ASA and corticosteroids**
- **Longer-term data are necessary to better understand non-biologic medication use after biologic initiation and inform treatment choice for patients with UC**

RESULTS

Study population and baseline characteristics

- A total of 760 patients with UC were initiated on ustekinumab and selected for the pre-post study (**Figure 1**)

Figure 1. Sample selection flowchart



- The mean (SD) age was 44.6 [15.5] years and 48.9% were female, while the mean Charlson Comorbidity Index was 0.62
- Patients came from all regions of the US and most patients (77.5%) initiated ustekinumab in 2020
- Most patients (52.1%) used biologic and advanced therapy in the 6-month period before initiating ustekinumab; the most common biologics were in the tumor necrosis factor class (28.2%; **Table 1**)
  - These proportions are likely an underestimate due to the open nature of the database

Table 1. Selected baseline characteristics during the 6-month period before initiation of ustekinumab among patients with UC

Mean ± SD or n (%)	N=760
Age	44.6 ± 15.5
Female	372 (48.9%)
Charlson Comorbidity Index[1]	0.62 ± 1.5
Region of residence, N (%)	
Northeast	168 (22.1%)
Midwest	176 (23.2%)
South	261 (34.3%)
West	118 (15.5%)
Unknown	37 (4.9%)
Year of index date	
2019	171 (22.5%)
2020	589 (77.5%)
Symptoms and comorbidities (5 most frequent)	
Inflammatory arthritis or enteropathic arthropathies	146 (19.2%)
Diarrhea	126 (16.6%)
Pain	115 (15.1%)
Anemia	115 (15.1%)
Cardiovascular disease	104 (13.7%)
Use of biologics and advanced therapy	396 (52.1%)
Tumor Necrosis Factor inhibitors	214 (28.2%)
Adalimumab	131 (17.2%)
Infliximab	70 (9.2%)
Golimumab	19 (2.5%)
Anti-integrin agent (vedolizumab)	116 (15.3%)
Januse kinase inhibitors (tofacitinib)	97 (12.8%)

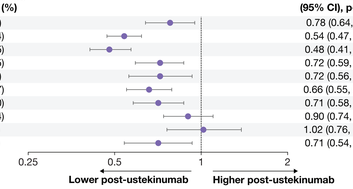
SD: standard deviation; UC: ulcerative colitis; 5-ASA: 5-aminosalicylic acid
Note:
[1]Quan H, Sundararajan V, Halfon P, et al.Medical Care. 2005;43(11):1130-1139.

Non-biologic medication use pre- and post-ustekinumab initiation

- Relative to before ustekinumab initiation, the likelihood of using immunomodulators and 5-ASAs decreased by 22% (p-value=0.014) and 46% (p-value<0.001), respectively, following the initiation of ustekinumab
- Similarly, relative to pre-index, patients were 52% less likely (p-value<0.001) to use any corticosteroids and 34% less likely (p-value<0.001) to use corticosteroids for ≥60 cumulative days, post-index
- There were no significant changes observed for the use of opioids (18.9% vs. 17.4%) or the use of anti-diarrheals (5.9% vs. 6.1%); however, patients were 29% less likely to use GI antispasmodics after ustekinumab initiation (p-value=0.013) relative to before (**Figure 2**)

Figure 2. Non-biologic medication use in the 6-month period before vs after the initiation of ustekinumab among patients with UC (N = 760 patients)

	Pre-ustekinumab initiation, N (%)	Post-ustekinumab initiation, N (%)	Odds ratio[1] (95% CI), p-value	
Use of immunomodulators	120 (15.8)	97 (12.8)	0.78 (0.64, 0.95)	0.014*
Use of 5-ASA	312 (41.1)	208 (27.4)	0.54 (0.47, 0.62)	<0.001*
Use of corticosteroids	481 (63.3)	346 (45.5)	0.48 (0.41, 0.57)	<0.001*
Cumulative use[2] ≥60 days	201 (26.4)	156 (20.5)	0.72 (0.59, 0.87)	<0.001*
Cumulative use[2] ≥90 days	118 (15.5)	89 (11.7)	0.72 (0.56, 0.93)	0.013*
≥1 episode[3] ≥60 days	243 (32.0)	180 (23.7)	0.66 (0.55, 0.79)	<0.001*
≥1 episode[3] ≥90 days	151 (19.9)	114 (15.0)	0.71 (0.58, 0.87)	0.001*
Use of opioids	144 (18.9)	132 (17.4)	0.90 (0.74, 1.10)	0.296
Use of antidiarrheals	45 (5.9)	46 (6.1)	1.02 (0.76, 1.38)	0.879
Use of GI antispasmodics	86 (11.3)	63 (8.3)	0.71 (0.54, 0.93)	0.013*

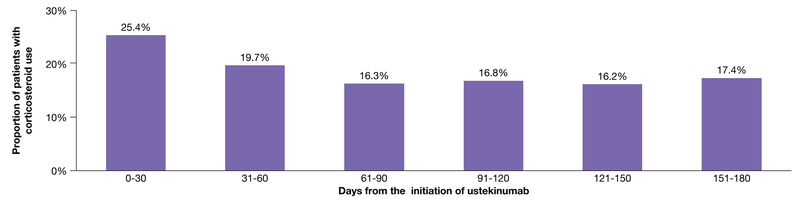


**: p-value ≤ 0.05*
CI: Confidence interval; GI: Gastrointestinal; UC: ulcerative colitis; 5-ASA: 5-aminosalicylic acid
Notes:
[1]Odds ratio obtained from a logistic model estimated with generalized estimating equation adjusted for repeated measure per patient.
[2]Non-overlapping days of supply of corticosteroids were included.
[3]A therapy exposure gap of 14 days of supply was used to define continuous use.

Use of corticosteroids after ustekinumab initiation

- Corticosteroids use numerically decreased at each month post-ustekinumab from 25.4% during the first 30 days following the initiation of ustekinumab compared to 17.4% within 150-180 days post-ustekinumab initiation (**Figure 3**)

Figure 3. Corticosteroid use during the 6 months post-ustekinumab initiation (N=760 patients)



Limitations

- Analyses of administrative claims depend on correct diagnosis, procedure, and drug codes
- As with all claims databases, prescription fills do not account for whether the medication dispensed was taken as prescribed
- Results may not be generalizable to patients without health insurance or with insurance other than commercial
- Given the open nature of the database (no included eligibility records) all claims for a given individual are not necessarily captured

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Acknowledgments

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