Association Between Hospitalization for Crohn's Disease (CD) or Ulcerative Colitis (UC) and Biologic Drug Therapy Adherence

K. Bowen, MD, MBA[1], and P.P. Gleason, PharmD[1,2]. [1]Prime Therapeutics LLC, Eagan, MN, United States; [2]University of Minnesota College of Pharmacy, Minneapolis, MN, United States.

No external funding provided for this research

Background

- Biologic therapy (BT) Food and Drug Administration (FDA)-approved for Crohn's disease (CD) and ulcerative colitis (UC) includes:
  - Tumor necrosis factor-alpha (TNFa) antagonists (adalimumab and infliximab for both CD and UC, certolizumab pegol for CD, and golimumab for UC)
  - Anti-integrin monoclonal antibodies (natalizumab for CD and vendolizumab for both CD and UC)
  - Anti-interleukin (IL)-12/IL23 ustekinumab for CD
- Clinical trials have shown hospitalization risk reduction in moderate to severe CD or UC treated with BT.[1,2,3,4]
- Little is known of the real-world CD or UC hospitalization rate or difference in rate among BT adherent and non-adherent members.

Objectives

- In a 15 million member commercially insured population, to:
  1) assess the association between adherence to biologic therapy and hospitalization for UC and CD, and
  2) determine the incremental claims cost associated with hospitalization for UC or CD, excluding the cost of BT.

4085-E © Prime Therapeutics LLC 03/19
2900 Ames Crossing Road, Eagan, MN 55121

AMCP, March 2019, San Diego, CA, USA

Patrick Gleason, 800.858.0723, ext. 5190
pgleason@primetherapeutics.com

Methods

- CD and UC members were defined, respectively, as all continuously eligible July 2014 to June 2018 (four years) with five or more medical claims with a CD or UC diagnosis code and majority of ten most recent claims with a CD or UC diagnosis code for the respective diagnosis.[5]
- Hospitalization for CD (UC) was defined as an inpatient facility claim with CD (UC) as primary diagnosis code. Members were divided into those with any (Hosp) or no (NoHosp) hospitalization for CD (UC). Members in the Hosp group were assigned earliest hospitalization claim date as their index date.
- BT for CD was defined as pharmacy claims or medical outpatient claim lines for: adalimumab (Humira®), certolizumab (Cimzia®), infliximab (Remicade®, Inflectra®, Renflexis®), ustekinumab (Stelara®), vedolizumab (Entyvio), or natalizumab (Tysabri®). Natalizumab claims were only classified as CD treatment if from a medical claim with a diagnosis code for CD but not for multiple sclerosis.
- BT for UC was defined as pharmacy claims or medical outpatient claim lines for: adalimumab, golimumab (Simponi®), infliximab, or vedolizumab.
- To assess association between BT adherence and hospitalization for CD (UC), the Hosp group was limited to those with index date later than August 2015 to create a sample of members with at least 14 months continuous eligibility and analyzable claims prior to first hospitalization.
  - Members in the NoHosp group were each randomly assigned one of the Hosp index dates.
  - For all members in the Hosp and NoHosp groups who had any BT in the 12 months preceding index date:
    - BT proportion of days covered (PDC) during these 12 months was determined from claim dates and days supply on pharmacy BT claims or assumed as the lesser of the number of days to next claim or the recommended dosing interval for medical BT claims.
    - PDC calculation accounted for claims incurred up to two months prior to the 12-month measurement interval, since several of the agents have a recommended maintenance dosing interval of 56 days.
  - "Adherent" was defined as PDC greater than 80 percent.
  - Odds ratio (OR) with 95 percent confidence interval was calculated as Hosp divided by NoHosp odds of adherent.
  - Number need to treat (NNT) to avoid one hospitalization was estimated from absolute hospitalization risk reduction (ARR) associated with BT adherence.
- To determine the incremental total cost of care, excluding BT cost, integrated medical and pharmacy claims allowed cost associated with hospitalization for UC or CD; the Hosp group was further limited to members with index date prior to July 2017 to create a sample of members with at least 12 months continuous eligibility and analyzable claims before and after first observed hospitalization. Mean allowed claims cost, excluding BT cost, was calculated by 30-day intervals for the 360 days preceding and following index date.

Results

- In four years (July 2014 to June 2018), 1,386 of 8,652 (16.0 percent) CD members and 856 of 7,977 (10.7 percent) UC members had one or more hospitalization for CD or UC (Hosp group); the remaining 7,266 CD and 7,121 UC had no hospitalizations (NoHosp group).
- Association between BT adherence and hospitalization for CD or UC **(see Tables 1 and 2)**:
  - Of the Hosp group, 917 CD and 555 UC members had an index date later than August 2015; 431 of these 917 (47.0 percent) CD and 124 of 555 (22.3 percent) UC had a claim for a biologic agent in the 12 months before index date, of whom 209 of 431 (48.5 percent) and 56 or 124 (45.2 percent) were adherent.
  - Of the NoHosp group, 2,929 of 7,266 (40.3 percent) CD and 1314 of 7121 (18.5 percent) UC had a biologic in the 12 months before index date, of whom 1,969 of 2,929 (67.2 percent) and 858 of 1314 (65.3 percent) were adherent.
  - OR was 0.46 (95 percent confidence limits [CL] 0.37, 0.56, p<0.001) CD and 0.44 (95 percent CL 0.30, 0.64, p<0.001) UC.
  - ARR associated with adherence was 9.2 percent for CD and 6.9 percent for UC, for an NNT of 10.9 and 14.6, respectively.
- Incremental 12-month total cost care associated with hospitalization for CD or UC **(see Figures 1 and 2)**:
  - Of the Hosp group, 607 CD and 377 UC members had index date later than August 2015 and earlier than July 2017.
  - Excluding the cost of any BT claims, the mean increase in total cost of care for the 12 months following index date compared with the 12 months preceding was:
  - CD: $46,083 total; $1,895 medical outpatient, $43,216 inpatient, and $972 pharmacy
  - UC: $64,014 total; $6,158 medical outpatient, $56,915 inpatient, and $941 pharmacy
  - **Figures 1 and 2** show mean claims cost by 30-day intervals before and after index date.

Table 1. Crohn's Disease Association Between 12-Month Biologic Therapy (BT) Adherence and Hospitalization

Any biologic therapy in 12 months preceding index date	Any hospitalization for Crohn's disease		
	No	Yes	Total
Yes	2,929	431	**3,360**
No	4,337	486	**4,823**
Total	**7,266**	**917**	**8,183**

Biologic therapy PDC adherence in 12 months preceding index date	Any hospitalization for Crohn's disease		
	No	Yes	Total
>=80% Yes	1,969	209	**2,178**
<80% No	960	222	**1,182**
Total	**2,929**	**431**	**3,360**

Odds ratio = 0.46, 95% CL (0.37, 0.56)
Risk not adherent = 222/2,178 = 18.8%
Risk adherent = 209/2,178 = 9.6%
Absolute risk reduction (ARR) = 9.2%
Number needed to treat (NNT) = 1/ARR = 10.9
PDC = proportion days covered

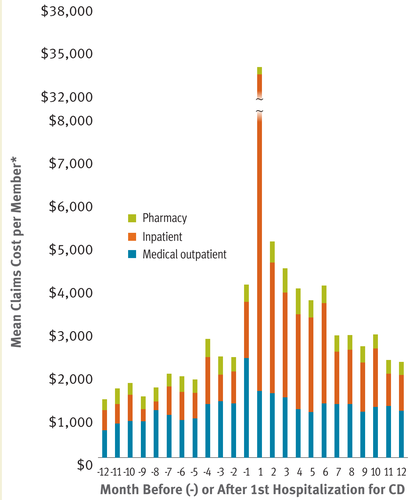
Table 2. Ulcerative Colitis Association Between 12-Month Biologic Therapy (BT) Adherence and Hospitalization

Any biologic therapy in 12 months preceding index date	Any hospitalization for ulcerative colitis		
	No	Yes	Total
Yes	1,314	124	**1,438**
No	5,807	431	**6,238**
Total	**7,121**	**555**	**7,676**

Biologic therapy PDC adherence in 12 months preceding index date	Any hospitalization for ulcerative colitis		
	No	Yes	Total
>=80% Yes	858	56	**914**
<80% No	456	68	**524**
Total	**1,314**	**124**	**1,438**

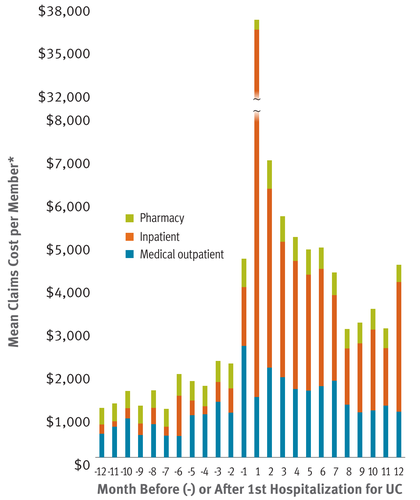
Odds ratio = 0.44, 95% CL (0.30, 0.63)
Risk not adherent = 68/524 = 13.0%
Risk adherent = 56/914 = 6.1%
Absolute risk reduction (ARR) = 6.9%
Number needed to treat (NNT) = 1/ARR = 14.6
PDC = proportion days covered

Figure 1. Crohn's Disease (CD) Total Claims Cost of Care* Associated with Hospitalization



*Costs include all medical and pharmacy allowed costs, **excluding biologic therapy cost.**
Month = 30-day interval. Month 1 = first hospitalization date of admission + 29 days.

Figure 2. Ulcerative Colitis (UC) Total Claims Cost of Care* Associated with Hospitalization



*Costs include all medical and pharmacy allowed costs, **excluding biologic therapy cost.**
Month = 30-day interval. Month 1 = first hospitalization date of admission + 29 days.

Limitations

- This study uses only information from administrative claims to determine which members have CD or UC. Some study members may be misclassified. The researchers did not have access to clinical information that may make it possible to stratify patients into meaningful phenotypes.[6]
- This is an observational study, not a randomized controlled comparison, and may be affected by confounding variables. The members with and without hospitalization for IBD were all selected for, and accepted, BT, but were otherwise unmatched.
- Adherence is assessed using claims data and may inaccurately identify a member as adherent or non-adherent. In addition, the adherence cut point of 80 percent or greater PDC is an arbitrary adherence determinate.
- Costs attributed to hospitalization were limited to direct, claim line expenses. However, hospitalization will also have significant indirect and intangible costs and an association, not well characterized, with long-term outcomes.
- These findings are limited to commercially insured members who were continuously enrolled for four years and may not be representative of the general population with CD or UC taking BT.

Conclusions

- Using real world integrated medical and pharmacy claims data for commercially insured members to assess biologic therapy (BT) adherence and the associated hospitalization risk among CD or UC members treated, we found those who were adherent to BT for 12 months had approximately two-fold associated lower odds of hospitalization.
- The number needed to treat (i.e., number needed to become BT adherent for one year from BT non-adherent) to avoid one hospitalization was estimated to be 11 for CD and 15 for UC.
- Among those hospitalized with CD or UC, the mean post hospitalization 12-month incremental additional total cost of care associated with hospitalization was $46,000 for CD and $64,000 for UC. This real world total cost of care post CD or UC hospitalization is an important direct medical cost burden, and does not account for patient or care giver burden.
- Although, CD and UC 12-month post hospitalization costs are considerable, the CD or UC BT wholesale acquisition cost (WAC) is over $50,000 per year and, from this analysis, 11 CD or 15 UC individuals would need to be moved from non-adherent to adherent to prevent one hospitalization, thus incurring substantial biologic drug cost investment to prevent a hospitalization.
- These findings can be used for managed care clinical program justification and value-based contracting.

References

1. Costa J, *et al.* Infliximab reduces hospitalizations and surgery interventions in patients with inflammatory bowel disease: A systematic review and meta-analysis. *Inflamm Bowel Dis* 2013; 19:2098–2110.
2. Feagan BG, *et al.* Adalimumab therapy is associated with reduced risk of hospitalization in patients with ulcerative colitis. *Gastroenterology* 2014; 146:110–118.
3. Feagan BG, *et al.* Effects of adalimumab therapy on incidence of hospitalization and surgery in Crohn's disease: Results from the CHARM study. *Gastroenterology* 2008; 135:1493–1499.
4. Sandborn WJ, *et al.* Reduced rates of Crohn's-related surgeries, hospitalizations and alternate biologic initiation with ustekinumab in the IM-UNITI study through 2 years. *Gastroenterology* 2018; 154:6:S377–378.
5. Benchimol ET, *et al.* Validation of international algorithms to identify adults with inflammatory bowel disease in health administrative data from Ontario, Canada. *J Clinical Epidemiol* 2014; 67:887–896.
6. Rao BB, *et al.* The cost of Crohn's disease: varied healthcare expenditure patterns across distinct disease trajectories. *Inflamm Bowel Dis* 2017; 23:107–115.

03003900