

Retrospective Cohort Study Comparing Infliximab-dyyb and Infliximab in Biologic-Naive Patients With Inflammatory Bowel Disease in the United States

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Background: Real-world assessments of biosimilars are needed to understand their effectiveness and safety in practice settings that may differ from those seen in clinical trials or healthcare systems in different countries. To assess the effectiveness and safety of a biosimilar (infliximab-dyyb) and its reference product (infliximab) in patients with inflammatory bowel disease (IBD) in the United States.

Methods: We conducted a retrospective cohort study of biologic-naive patients with IBD who started treatment with infliximab-dyyb or infliximab. The study included 3206 patients identified through electronic health records in a US integrated healthcare delivery system. The effectiveness outcome was a composite of IBD-related surgery, IBD-related emergency room visit, and IBD-related hospitalization within 12 months of initiation. Safety outcomes included incidence of any or serious infection, cancer, acute liver dysfunction, and tuberculosis. We used a non-inferiority test with an upper-limit margin of 10% to analyze effectiveness. Doubly robust methods incorporating Cox proportional hazard regression with standardized inverse probability of treatment weighting were used to analyze both effectiveness and safety outcomes.

Results: The composite effectiveness outcome occurred in 107 of 870 patients (12.3%) in the infliximab-dyyb and 379 of 2336 patients (16.2%) in the infliximab groups. Infliximab-dyyb was non-inferior ($P < .01$) and was not different (hazard ratio [HR] 0.81; confidence interval [CI] 0.65–1.01; $P = .06$) to infliximab. Safety outcomes were not different between infliximab-dyyb and infliximab for any infections (HR 1.01; CI 0.86–1.17; $P = .95$), serious infections (HR 0.83; CI 0.54–1.26; $P = .38$), cancers (HR 0.83; CI 0.44–1.54; $P = .55$), and tuberculosis (HR 0.59; CI 0.10–3.55; $P = .57$).

Conclusions: Initiation of infliximab-dyyb was non-inferior to infliximab among biologic-naive patients with IBD in an US integrated healthcare delivery system.

Lay Summary

In this US-based, retrospective, multicenter, cohort study of 3206 biologic-naive patients with inflammatory bowel disease (IBD), treatment with the biosimilar infliximab-dyyb was non-inferior to reference product infliximab for the effectiveness composite of IBD-related surgery, IBD-related emergency room visit, and IBD-related hospitalization.

Key Words: biosimilar, infliximab-dyyb, inflammatory bowel disease

Introduction

Biosimilars have the promise of substantially reducing costs of and improving access to biologic therapy. They are biological products that have no clinically meaningful differences in terms of safety, purity, and potency to their reference product.¹ The United States' (US) Food and Drug Administration (FDA) approved Inflectra (infliximab-dyyb), a biosimilar for

reference product Remicade (infliximab), in April 2016.^{2–4} Infliximab-dyyb received approval for ulcerative colitis (UC) and Crohn's disease (CD), collectively known as inflammatory bowel disease (IBD), through a process called extrapolation. Extrapolation allows a biosimilar to be approved for its reference product's indications without having clinical trials for every indication, provided it is equivalent to at least one of the

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reference product's indications.¹ In the case of infliximab-dyyb, approval for IBD was extrapolated based on data from clinical trials in ankylosing spondylitis and rheumatoid arthritis.^{5,6}

Despite the FDA's oversight of biosimilar introduction, there has been slow uptake of them in the United States. Key concerns for clinicians and patients regarding the use of biosimilars include safety, effectiveness, and persistence, particularly for the indications where extrapolated data have been used to gain FDA approval.^{7,8} Real-world evidence (ie, data collected during routine clinical practice) of biosimilar use may address these concerns by filling data gaps for extrapolated indications, such as IBD.

The United States has a sizeable population of patients with IBD, but little data on biosimilar use have been published. Kaiser Permanente (KP), a large integrated healthcare delivery system in the United States, has treated patients with IBD with infliximab-dyyb since its approval in 2016; thus, it has extensive data on IBD treatment with infliximab-dyyb and infliximab. The aim of this study is to compare the effectiveness and safety with infliximab-dyyb and infliximab in biologic-naïve patients with IBD to provide real-world evidence for patients and clinicians.

Materials and Methods

Study Design and Setting

We conducted a retrospective, multicenter cohort study. Data were obtained from 3 KP regions: Colorado, Northern California, and Southern California. KP owns 39 hospitals and serves over 12.2 million members across 8 states and the District of Columbia.⁹ All sites use the same electronic health record (EHR) (HealthConnect, Epic Systems Corporation) that provides e-prescribing capabilities and interfaces with the internal pharmacy and laboratory systems. KP operates outpatient infusion centers where patients receive intravenous infusions, where detailed information about each infusion is captured electronically in the EHR. Coded and free-text medical, pharmacy, laboratory, emergency department, hospitalization, and membership information from the EHR, as well as from other contracted and affiliated facilities, are captured in KP's harmonized administrative and claims databases. The study was approved by the Institutional Review Boards at all participating sites (KP Colorado: CO-17-2472, KP Northern California: CN-17-3003, and KP Southern California: 11385) with a waiver for informed consent due to the retrospective nature of the study.

Study Population

Patients aged ≥ 18 years with IBD (ie, UC or CD) who were biologic-naïve and initiated biologic treatment with either infliximab-dyyb or infliximab between January 1, 2013 and September 30, 2018 were eligible for the study. The first infusion date of either infliximab-dyyb or infliximab was termed as the index date. IBD was defined as an inpatient or outpatient encounter with an International Classification of Disease Clinical Modification (ICD) ninth edition code of 555.x and 556.x or tenth edition code of K50.x and K51.x within 12 months prior to the index date. If a patient had both a CD and UC diagnosis, the patient was categorized based on the first occurring diagnosis. Biologic-naïve was defined as no record of adalimumab, certolizumab, golimumab, infliximab, natalizumab, ustekinumab, or vedolizumab administration

within 12 months prior to the index date. In addition, patients were required to have had ≥ 12 months of continuous health plan enrollment prior to the index date. Patients were followed for 12 months, until the termination of health plan membership, or death, whichever occurred first. Patients who switched from infliximab to infliximab-dyyb during follow-up were excluded due to non-medical switching, which was happening across the health system when infliximab-dyyb was available. These switches may not have been due to an intolerance or failure to infliximab.

Study Outcomes

The primary effectiveness outcome was a composite of IBD-related surgery, emergency room (ER) visit, or hospitalization.¹⁰ IBD-related surgeries included colectomy, colostomy, hemicolectomy, ileostomy, ileocectomy, and proctocolectomy. IBD-related ER visits and hospitalizations were identified by a primary diagnosis of UC or CD for the encounter. The safety outcomes included: ≥ 1 clinical encounter for any infection, ≥ 1 clinical encounter for serious infection that required hospitalization, new cancer diagnosis, ≥ 1 acute liver dysfunction diagnosis, and new tuberculosis diagnosis within the 60 days after the last infusion of index drug (diagnosis codes found in [Supplementary Table S1](#)).¹¹⁻¹⁴

The secondary outcome was switching, which was defined as starting of tofacitinib, a different biologic (adalimumab, certolizumab, golimumab, natalizumab, ustekinumab, or vedolizumab), or infliximab for patients whose index therapy was infliximab-dyyb.

Data Collection

Integrated electronic medical, pharmacy, and membership administrative records were used to identify patients, treatments, and outcomes for this study. Baseline characteristics of patients were collected using the data prior to the index date, including age at the index date, gender, race, Charlson comorbidity index (CCI), IBD medication history, IBD disease duration, IBD-related surgical history, IBD-related ER visit history, and hospitalization history. The history of IBD medication including aminosalicylates (mesalamine and sulfasalazine), oral budesonides, immunomodulators (azathioprine, mercaptopurine, and methotrexate), and systemic corticosteroids was obtained from pharmacy dispensing records during the 180 days prior to the index date. IBD disease duration was calculated from the date of first IBD diagnose recorded in the KP system to the index date. IBD-related surgical history was ascertained during the 24 months prior to the index date. IBD-related ER visit history and hospitalization history were extracted during the 180 days prior to the index date. The Quan adaptation of CCI¹⁵ was applied in the study. Each specific comorbidity used in the calculation of CCI was identified from the diagnosis records during the 1 year prior to the index date. Outcomes were identified from inpatient, emergency, and outpatient administrative and claims databases during the follow-up period.

Data Analysis

Based on our prior study,¹⁰ assuming an outcome rate of 10% for the infliximab-dyyb group and 17% for the infliximab group, with an absolute upper-limit non-inferiority margin of 10%, 50 patients would be needed in each group to reach 80% power at a 1-sided alpha level of 0.05. This more strin-

gent non-inferiority margin was selected as a 10% margin is closer to a clinically acceptable difference, as compared to the 15%–20% used in most prospective trials.^{16–18}

Baseline characteristics were reported as means with SD, medians with interquartile range, or frequencies with percentage, and were compared between the 2 groups using chi-squared or Fisher's exact tests for categorical values and Student's *t*-tests or Wilcoxon rank-sum tests for continuous values. Non-inferiority test with an upper-limit margin of 10% was used for the analysis of the effectiveness outcome only, as the FDA did not recommend or provide guidance on safety outcomes using non-inferiority analyses.¹⁸

Cox proportional hazards regression with a doubly robust approach were used to analyze all outcomes. To adjust for differences in baseline patient characteristics (Table 1), a propensity score of receiving infliximab-dyyb was calculated for each patient using multivariate logistic regression.¹⁹ Stabilized inverse probability of treatment weighting (sIPTW) were generated using propensity scores.²⁰ To evaluate the balance among all baseline covariates between groups after applying sIPTW, standardized differences were calculated and differences less than 10% were considered balanced. Adjusted hazard ratios (HRs) were reported using Cox proportional hazards regression with the sIPTW cohort. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute) and the alpha was set at 0.05.

Results

Patient Characteristics

Among 8615 patients who received infliximab-dyyb or reference product infliximab, 3206 biologic-naive patients with IBD met inclusion and exclusion criteria: 870 (27.1%) patients and 2336 (72.9%) patients began treatment with infliximab-dyyb and infliximab between January 2013 and September 2018, respectively. The mean age of the cohort was 44.3 years (SD 16.9 years) and women comprised of half of the cohort. Approximately half (54.7%) of the patients had a diagnosis of UC. The infliximab-dyyb group had a shorter median IBD disease duration ($P < .01$) and higher burden of chronic disease ($P < .01$), and was more likely to have had a history of IBD-related surgeries ($P < .01$), and an IBD-related medication including oral budesonide ($P < .01$), immunomodulators ($P < .01$), and corticosteroids ($P < .01$) (Table 1). After sIPTW weighting, all the standardized mean differences were below 0.1, so the baseline characteristics were considered balanced between the groups (Table 2).

Outcomes

The mean follow-up time for the cohort was 329 days (SD 82 days) and 78.8% of the patients were followed for 12 months. The composite effectiveness rate of IBD-related surgery, ER visit, and hospitalization was non-inferior in the 2 groups; occurring in 107 (12.3%) and 379 (16.2%) patients in the infliximab-dyyb and infliximab groups, respectively ($P < .01$ for non-inferiority) (Figure 1). There was no statistically significant difference in the risk of the composite outcome between the groups (HR 0.81; 95% confidence interval [CI] 0.65–1.01; $P = .06$). There were 906 (28.3%) patients who had an encounter for any infection; of which 126 (3.9%) were serious infections (Table 3). In addition, there were 60 (1.9%) cases of cancer, 3 (0.1%) acute liver dysfunctions, and 8 (0.2%) cases of tuberculosis. There were no statistic-

ally significant differences in the risks for any infections (HR 1.01; 95% CI 0.86–1.17; $P = .95$), serious infections (HR 0.83; 95% CI 0.54–1.26; $P = .38$), cancers (HR 0.83; 95% CI 0.44–1.54; $P = .55$), or tuberculosis (HR 0.59; 95% CI 0.10–3.55; $P = .57$). As there were no cases of acute liver dysfunction in the infliximab-dyyb group, adjusted analysis was not performed. There was a higher rate of switching from infliximab therapy to another biologic among patients in the infliximab-dyyb than infliximab group (21.0% vs 15.2%; HR 1.55; CI 1.30–1.85; $P < .01$).

Discussion

This retrospective, longitudinal, multicenter, cohort study of over 3200 patients with IBD who were naive to biologic treatment identified that the biosimilar infliximab-dyyb was non-inferior to the reference product infliximab in the composite effectiveness outcome. In addition, we identified no differences between the groups in safety outcomes using doubly robust statistical analyses. We also report that patients who received infliximab-dyyb had a higher likelihood of switching to another biologic. These findings are important as they provide real-world evidence of infliximab-dyyb's effectiveness and safety in the United States, a country with slow biosimilar uptake in contrast to more widespread use in Asia and Europe. This further supports the extrapolation review process that the FDA uses to approve biosimilars, and that biosimilars can be effective, safe, and cost-saving biologic therapies in the United States.

While studies have compared biosimilar infliximab to reference product infliximab, these studies are limited and their study populations and assessed outcomes differ from ours.^{16,21–23} Ye et al conducted a small ($N = 214$), international RCT comparing the infliximab-dyyb, also known as Remsima (CT-P13) to reference product infliximab in biologic-naive patients with CD.¹⁶ They reported infliximab-dyyb's non-inferior efficacy and safety to infliximab based on results from the Crohn's Disease Activity Index, Short Inflammatory Bowel Disease Questionnaire, and adverse events. Their study did not include patients with UC or report healthcare encounter effectiveness outcomes and their rigid inclusion/exclusion criteria precluded patients with various comorbidities from the study; thus, limiting the real-world applicability of their results. The PROSIT-BIO observational study of a mix of biologic-naive and non-naive patients with IBD from Italy reported that infliximab-dyyb was effective (based on clinical remission/response) and safe when compared to rates for infliximab previously reported.²¹ This study did not have a comparison group, had short follow-up (24 weeks), and did not assess healthcare encounter effectiveness outcomes.

Meyer et al assessed infliximab-dyyb and reference product infliximab in infliximab-naive patients with CD in a large, retrospective cohort study conducted in France.²² Based on a composite outcome of death, CD-related surgery, or all-cause hospitalization, infliximab-dyyb was reported to be equivalent for effectiveness; in addition, it reached statistical significance for a lower risk (HR 0.92; 95% CI 0.85–0.98). Safety outcomes were equivalent between the groups. Meyer et al also assessed infliximab-dyyb and reference product infliximab in infliximab-naive patients with UC.²³ They reported similar equivalency results; however, the infliximab-dyyb group did not reach statistical significance for the composite outcome

Table 1. Baseline characteristics of patients by biosimilar use status and overall

Characteristic	Infliximab-dyyb (n = 870)	Infliximab (n = 2336)	Overall (n = 3206)	P
Age, mean (SD), y	44.7 (16.6)	44.1 (17.0)	44.3 (16.9)	.28
Female, No. (%)	417 (47.9)	1199 (51.3)	1616 (50.4)	.09
Race, No. (%)				.40
White	559 (64.3)	1514 (64.8)	2073 (64.7)	
Black	73 (8.4)	240 (10.3)	313 (9.8)	
Hispanic	123 (14.1)	290 (12.4)	413 (12.9)	
Asian	69 (7.9)	174 (7.4)	243 (7.6)	
Other	46 (5.3)	118 (5.1)	164 (5.1)	
CCI score, No. (%)				<.01
0	578 (66.4)	1344 (57.5)	1922 (60.0)	
1	184 (21.1)	625 (26.8)	809 (25.2)	
2 or higher	108 (12.4)	367 (15.7)	475 (14.8)	
IBD type, No. (%)				.59
Crohn's disease	387 (44.5)	1064 (45.5)	1451 (45.3)	
Ulcerative colitis	483 (55.5)	1272 (54.5)	1755 (54.7)	
IBD disease duration, median (IQR), y	2.1 (0.4–7.3)	3.1 (0.7–8.6)	2.8 (0.6–8.3)	<.01
IBD-related surgeries within past 2 years, No. (%)	156 (17.9)	264 (11.3)	420 (13.1)	<.01
IBD-related ER visits within past 6 months, No. (%)	85 (9.8)	191 (8.2)	276 (8.6)	.15
IBD-related hospitalizations within past 6 months, No. (%)	152 (17.5)	444 (19.0)	596 (18.6)	.32
IBD medication history, No. (%)				
Aminosalicylates	486 (55.9)	1215 (52.0)	1701 (53.1)	.05
Budesonide	143 (16.4)	287 (12.3)	430 (13.4)	<.01
Immunomodulators	618 (71.0)	1533 (65.6)	2151 (67.1)	<.01
Corticosteroids	499 (57.4)	1113 (47.6)	1612 (50.3)	<.01
Dose of infliximab at index date, mean (SD), mg	428 (138)	421 (143)	423 (141)	.01

Abbreviations: CCI, Charlson comorbidity index; ER, emergency room; IBD, inflammatory bowel disease; IQR, interquartile range; y, year.

Table 2. Patient demographics in original and stabilized inverse probability of treatment weighting cohorts

Demographic	Before sIPTW			After sIPTW		
	IFX-dyyb (n = 870)	IFX-RP (n = 2336)	Standardized difference, %	IFX-dyyb (n = 860)	IFX-RP (n = 2341)	Standardized difference, %
Age, mean (SD), y			0.06			0.04
≤34	287 (33)	832 (35.6)		825 (35.2)	287 (33.4)	
35–55	301 (34.6)	808 (34.6)		812 (34.7)	300 (34.8)	
≥56	282 (32.4)	696 (29.8)		704 (30.1)	273 (31.8)	
Female, n (%)	417 (47.9)	1199 (51.3)	-0.06	429 (49.9)	1181 (50.4)	-0.04
Race, n (%)			0.08			0.03
White	559 (64.3)	1514 (64.8)		556 (64.7)	1513 (64.6)	
Black	73 (8.4)	240 (10.3)		82 (9.5)	228 (9.7)	
Hispanic	123 (14.1)	290 (12.4)		116 (13.5)	304 (13.0)	
Asian	69 (7.9)	174 (7.4)		66 (7.7)	177 (7.6)	
Other	46 (5.3)	118 (5.1)		40 (4.6)	118 (5.0)	
Region, n (%)			0.22			0.04
Colorado	127 (14.6)	190 (8.1)		88 (10.3)	233 (10.0)	
Northern California	409 (47.0)	1085 (46.4)		418 (48.6)	1096 (46.8)	
Southern California	334 (38.4)	1061 (45.4)		354 (41.1)	1011 (43.2)	
CCI score ≥1, n (%)	292 (33.6)	992 (42.5)	-0.18	340 (39.6)	935 (39.9)	-0.01
IBD disease duration, n (%)			-0.18			-0.01
<2 years	431 (49.5)	953 (40.8)		379 (44.1)	1015 (43.4)	
≥2 years	439 (50.5)	1383 (59.2)		481 (55.9)	1326 (56.6)	
IBD type, n (%)			0.01			0.04
Crohn's disease	387 (44.5)	1064 (45.5)		391 (45.5)	1061 (45.3)	
Ulcerative colitis	483 (55.5)	1272 (54.5)		469 (54.5)	1280 (54.7)	
IBD-related surgeries within past 2 years, n (%)	156 (17.9)	264 (11.3)	0.19	116 (13.4)	310 (13.2)	0.01
IBD-related ER visits within past 6 months, n (%)	85 (9.8)	191 (8.2)	0.06	76 (8.8)	203 (8.7)	0.01
IBD-related hospitalizations within past 6 months, n (%)	152 (17.5)	444 (19.0)	-0.04	163 (18.9)	434 (18.5)	0.01
Medication history, n (%)						
Budesonide	143 (16.4)	287 (12.3)	0.12	123 (14.3)	317 (13.6)	0.02
Corticosteroids	499 (57.4)	1113 (47.6)	0.20	442 (51.3)	1182 (50.5)	0.02

Abbreviations: CCI, Charlson comorbidity index; ER, emergency room; IBD, inflammatory bowel disease; IFX-dyyb, infliximab-dyyb; IFX-RP, infliximab reference product; sIPTW, stabilized inverse probability of treatment weighting; y, year.

(HR 1.04; 95% CI 0.94–1.15) but did for a serious infections safety outcome (HR 0.65; 95% CI 0.48–0.88). These study populations were drawn from patients who received their infusions from hospitals in France and did not use doubly robust statistical methods to balance their groups, leaving safety and efficacy assessed with vigorous methods in a purely US community-based settings unanswered.^{22,23} Our study narrows the evidence gap of a real-world assessment within the United States to provide data on the effectiveness and safety of infliximab-dyyb in a community practice setting with biologic-naive patients with IBD that differ from those reported in clinical trials or health systems within other countries.

Our rates of any infection and serious infection ranged from 25.2% to 29.4% and 3.1% to 4.2%, respectively. The rates of any infection for patients taking infliximab-dyyb among biologic-naive patients with IBD have not been evaluated in any real-world studies; however, our observations were consistent with the clinical trials for the infliximab in IBD which have shown the any infection rate ranged from 18.5% to 48.3%.²⁴ Similar rates of serious infections were reported in real-world studies of non-biologic-naive patients with IBD ranging from 2.1% to 6.5%.^{22,23}

The rates of biosimilar and reference product infliximab switching to another biologic were higher numerically in our study than those reported in the Meyers' studies.^{22,23} However, other studies have reported that approximately 9%–20% of patients initiating infliximab switched to another biologic in the first year, which was broadly similar to our results.^{25,26} We hypothesize that this may be due, in part, to how switches were defined and other trends in management during the study period. First, we might have inflated the switch rate for the infliximab-dyyb group by including switching from infliximab-dyyb to infliximab, as we cannot distinguish the reasons as treatment failure or nocebo effect, the latter defined as a switch mediated by of a negative belief

about a therapy (eg, biosimilar).^{27,28} A nocebo effect is unlikely to fully explain the observed difference as only 7% of the infliximab-dyyb patients who switched therapy received infliximab as the subsequent therapy. Second, higher switch rates may be related to the growing number of treatment options throughout the study period, thus patients started on infliximab-dyyb (all from after 2016) had other treatment options besides dose optimization or switch to a different TNF-inhibitor.^{3,29–34} Regardless, our real-world data highlight that higher rates of switches in biologic-naive patients who initiate biosimilar therapy may be observed. Future studies are warranted to understand specific reasoning for switching.

Our study exhibits several strengths. It had a large patient sample and was conducted in an integrated healthcare delivery system, which allowed for the opportunity to reliably ascertain all healthcare services (ie, clinic-administered medications, outpatient medication dispenses, hospitalizations, and surgeries for patients across 3 different geographic regions within the United States). All data were captured using uniform approaches from electronic databases. We limited the study cohort to biologic-naive patients to limit confounding arising from treatment with prior biologics. Lastly, we identified multiple safety outcomes including any and serious infections, cancers, acute liver dysfunction, and tuberculosis to strengthen our findings.

Our study also has limitations. Since the 2 cohorts were drawn from different time periods, residual confounding owing to practice changes may have influenced which patients received infliximab at the outset. To address this, we utilized propensity scores with sITPW to adjust for any imbalances between groups. Second, we identified IBD-related ER visits, hospitalizations, or surgeries as a proxy for disease worsening, which may have variability in the quality and reliability of associated coding. However, both groups were subject to same type of identification and this limitation should not bias 1 group over the other. Since we were unable to conduct chart reviews, we were not able to assess more nuanced markers of disease worsening such as disease activity, radiologic imaging, endoscopic data, nor biomarkers. Third, patients were followed for only 12 months, limiting our ability to identify and compare longer-term outcomes. Additional work is needed to carefully understand longer-term outcomes. Fourth, our results may not be generalizable outside of an insured population within the United States. Finally, we chose to analyze the primary effectiveness outcome on an intent-to-treat basis, not censoring patients at date of infliximab therapy discontinuation; thus, our findings likely represent a conservative estimate of the outcomes.

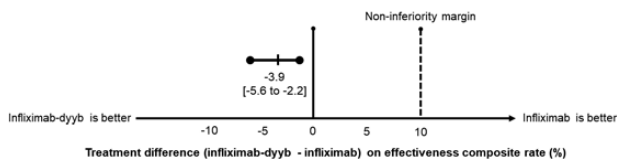


Figure 1. Effectiveness composite outcome (composite of inflammatory bowel disease-related surgery, emergency room visit, and hospitalization). The dashed vertical line represents the upper-limit non-inferiority margin of 10%.

Table 3. Safety outcomes by biosimilar status

Outcome, n (%)	Infiximab-dyyb (n = 870)	Infiximab (n = 2336)	Adjusted HR (95% CI) ^a	P
Any infection	219 (25.2)	687 (29.4)	1.01 (0.86–1.17)	.95
Serious infection ^b	27 (3.1)	99 (4.2)	0.83 (0.54–1.26)	.38
Cancer	11 (1.3)	49 (2.1)	0.83 (0.44–1.54)	.55
Acute liver dysfunction	0 (0)	3 (0.1)	— ^c	— ^c
Tuberculosis	1 (0.1)	7 (0.3)	0.59 (0.10–3.55)	.57

Abbreviations: CCI, Charlson comorbidity index; CI, confidence interval; ER, emergency room; HR, hazard ratio; IBD, inflammatory bowel disease.

^aModels are adjusted for age, gender, race, CCI, IBD disease duration, IBD type, Kaiser Permanente region, IBD-related surgical history, IBD-related ER visit history, IBD-related hospitalization history, budesonide exposure, and corticosteroid exposure.

^bSerious infection was defined as an infection requiring hospitalization.

^cAnalysis was not performed due to lack of events in infliximab-dyyb group.

Conclusions

Our findings suggest that the real-world effectiveness of infliximab-dyyb is non-inferior to infliximab in biologic-naive patients with IBD within 12 months of initiation. Our findings support the extrapolation review process to approve biosimilars and that biosimilars can be effective and safe cost-saving biologic therapies in the United States.

Supplementary Data

Supplementary data is available at *Crohn's and Colitis 360* online.

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Authors' Contributions

J.T.S., F.S.V., V.L., and R.L.H. contributed to the study concept and design. All authors contributed to the acquisition, analysis, or interpretation of data. J.T.S., F.S.V., T.D., F.N., and R.L.H. contributed to the drafting of the manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. J.T.S., F.N., and R.L.H. contributed to the statistical analysis. V.L. and K.L. contributed to administrative, technical, or material support. R.L.H. supervised the study. F.N. and R.L.H. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethical Approval

This study was reviewed and approved by the Institutional Review Boards of Kaiser Permanente Colorado, Northern California, and Southern California.

Informed Consent

Informed consent was waived for the study.

Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Conflicts of Interest

None declared.

Data Availability

Data not publicly available.

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