JPPT | Single Center Retrospective Study

A Review of Therapeutic Escalation for Pediatric Patients Admitted for Inflammatory Bowel Disease Flares

Danielle N. Koubek, PharmD; Rebecca A. Pulk, PharmD, MS; and Joseph V. Rosano, PharmD

OBJECTIVES The objective was to complete a single hospital quality assessment to characterize the use, safety, and outcomes of the 5 specialty medications (infliximab, adalimumab, tofacitinib, ustekinumab, and vedolizumab) used for the treatment of pediatric inflammatory bowel disease following admission due to a disease flare.

METHODS This was a single-center, retrospective, quality assessment of the current clinical practice. The electronic medical record was queried to identify patients ages 0 to 18 years admitted to our institution during a 2-year period from September 1, 2019, to September 30, 2021, who received infliximab, adalimumab, tofacitinib, ustekinumab, and/or vedolizumab for the treatment of Crohn's disease or ulcerative colitis followed by manual data collection and cohort analysis.

RESULTS The total population comprised 20 patients during 23 encounters. The biologic-naive group included 12 patients during 12 encounters, 2 of which are also included in the biologic-experienced group, which captured a total of 10 patients during 11 encounters. In the biologic-naive group, infliximab monotherapy comprised the largest percentage of therapy plans across encounters (91.6%), with a statistically significant greater number of readmissions within 6 months of discharge ($p = 0.00031$). The biologic-experienced cohort had a statistically significant longer duration of intravenous corticosteroid administration ($p = 0.016$) and a large variety of therapy plans.

CONCLUSIONS The diversity of practice observed within our institution supports the need for guidelines to define standard of therapy or guide selection of second-line therapies based on patient-specific factors.

ABBREVIATIONS CD, Crohn's disease; ECCO-ESPGHAN, European Crohn's and Colitis Organization and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition; EMR, electronic medical record; IBD, inflammatory bowel disease; IV, intravenous; IVCS; intravenous corticosteroids; LFT, liver function test; PUCAI, pediatric ulcerative colitis activity index; TNF, tumor necrosis factor; UC, ulcerative colitis

KEYWORDS children; Crohn's disease; gastroenterology; infliximab; tofacitinib; ulcerative colitis

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Introduction

Inflammatory bowel disease (IBD) includes ulcerative colitis (UC) and Crohn's disease (CD). Ulcerative colitis and CD are both chronic, progressive, and incurable inflammatory disorders of the gastrointestinal tract, with up to 25% of patients presenting before 18 years of age.[1] Despite many shared characteristics, UC and CD can be distinguished by differences in genetic predisposition and risk factors as well as diagnostic clinical, endoscopic, and histologic features.

Compared with adults, children with IBD are more likely to have dynamic and extensive intestinal involvement as well as an aggressive disease course.[2–4] The treatment of childhood-onset IBD presents unique challenges given limited therapeutic options approved by the US Food and Drug Administration for this special population and limited evidence-based recommendations for escalation of care in pediatric CD patients or medication selection for those who fail initial biologic therapy.[1]

The Pediatric Ulcerative Colitis Activity Index (PUCAI; see Supplementary Table) was developed to stratify the severity of UC in pediatric patients by combining essential subjective information, clinical findings, and laboratory values into a single score. The European Crohn's and Colitis Organization and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ECCO-ESPGHAN) consensus guideline recommends collecting daily PUCAI scores for patients admitted with acute severe colitis in order to assess response to pharmacologic intervention(s).[5] Both the ECCO-ESPGHAN and the American Gastroenterological

Association recommend initiation of intravenous corticosteroids (IVCS) for all pediatric patients presenting to the hospital with an acute exacerbation of UC or CD.[5–7]

Patients with IBD, however, often fail to respond to IVCS alone and require escalation of therapy. The ECCO-ESPGHAN guideline recommends initiation of second-line pharmacologic interventions in patients where disease activity remains high despite 5 days of IVCS, defined as a PUCAI score greater than 65 for UC patients.[5]

Many of the second-line pharmacologic interventions are high-cost, direct-acting agents that are only available through limited supply channels. Within this paper, the term *specialty medications* refers to agents that fit this definition, whether they are biologic or small molecule agents. Use of specialty medications in the inpatient setting remains limited. Unlike use in the outpatient setting, specialty medications administered in the hospital setting cannot be directly billed to payers and are reimbursed only through diagnosis resource group billing. To ensure specialty medications are applied where they will confer the largest patient benefit, our institutional policy requires a pharmacist consult and review to ensure eligibility and permit order entry. When multiple therapeutic options exist, agents found to offer the best cost-benefit and safety profiles are designated as preferred, formulary agents and alternatives as non-preferred, non-formulary agents.

The goal of this retrospective review is to characterize the use, safety, and outcomes of the 5 specialty medications (infliximab, adalimumab, tofacitinib, ustekinumab, and vedolizumab) used within our institution for the escalation of treatment of pediatric IBD following admission due to a disease flare. Results are presented for both the entire patient cohort as well as biologic-naive and biologic-experienced subgroups. Biologic-experienced patients were defined as patients who have received at least 1 dose of 1 biologic. Outcomes assessed included IVCS administration, therapy plans, adherence to biologic screening guidelines, incidence of adverse effects, and incidence of colectomy procedures.

Methods

Data Collection. This was a single-center, retrospective, cohort, manual chart review of the current clinical practice used at our institution. The electronic medical record (EMR) was queried to identify patients ages 0 to 18 years admitted to our institution during a 2-year period from September 1, 2019, to September 30, 2021, who received infliximab, adalimumab, tofacitinib, ustekinumab, and/or vedolizumab for the treatment of CD or UC. Patients were identified by searching the Epic Clarify database using study inclusion criteria. Data were collected by the Joint Data Analytics Team at Yale New Haven Health System and by investigator review of medical records in the Epic.

Statistical Analysis. Because our quality work was primarily focused on providing a descriptive analysis of our single-center experience, measures of central tendency as median bounded by IQR were used. The data collected on all cases were primarily continuous in nature and assumed to have 2-sided equal variance. When comparing outcomes of the biologic-naive and biologic-experienced groups, *t* tests were performed on log-transformed continuous, and the *a priori* level of significance was defined as an α of 0.5.

Results

Demographics. The total population included in the final analysis comprised 20 patients, numbered 1 to 20, across 23 encounters. There was an even distribution by sex but slight majority with a primary diagnosis of CD (55%) in the total population (Table 1). Typical of disease onset, patients were a median of 15 years old. The biologic-naive group included 12 patients during 12 encounters, 2 of which are also included in the biologic-experienced group, which captured a total of 10 patients during 11 encounters. There were no significant differences in age between the groups.

Hospital Course. All but 2 of the reviewed encounters had a documented administration(s) of intravenous (IV) methylprednisolone. The biologic-experienced cohort had a statistically significant longer duration of IV methylprednisolone administration at a median of 7.75 days (IQR, 5–12.6) compared with a median of 4 days (IQR, 2.25–5.5) for the biologic-naive group ($p = 0.016$; Table 2). The biologic-experienced group also had a shorter time from admission to administration of a specialty medication at a median of 2 days (IQR, 1–8).

In the biologic-naive group, infliximab monotherapy comprised the largest percentage of therapy plans across encounters (91.6%; Table 3). For biologic-experienced patients, a large variety of therapy plans were used. Within the biologic-experienced cohort, 4 patients (40%) were initiated on a new therapy during their admission and 3 patients (30%) received an acceleration of their outpatient maintenance therapy (Table 2). Treatment acceleration was defined as the practice of administering a medication from the current treatment regimen at a more frequent time scale.

Prescriber Screening Adherence. Of the total population, 13 patients (65%) had a hepatitis B panel, and 18 patients (90%) had a QuantiFERON-TB collected within a standard of 1 year prior to inpatient biologic administration (Table 4). Sixteen patients (80%) had a hepatitis B panel, and 19 patients (95%) had a QuantiFERON-TB collected within 2 years prior to inpatient biologic administration. No patient had a positive result for hepatitis B or tuberculosis.

The PUCAI scores were calculated and documented in the EMR progress note for patients with acute severe UC. Review of PUCAI score documentation in the

Table 1. Patient Characteristics

	Total Population (N = 20)	Subgroups	
		Biologic-Naive Patients (n = 12)	Biologic-Experienced Patients* (n = 10)
Age, median (IQR), yr	15 (14–16)	14 (11–16)	16 (15–16)
Sex, n (%)			
Male	10 (50)	7 (58.3)	4 (40)
Female	10 (50)	5 (41.6)	6 (60)
Race, n (%)			
White	12 (60)	5 (41.6)	9 (90)
African American	3 (15)	3 (25)	0
American Indian/Alaska Native	1 (5)	1 (8.3)	0
Other	4 (20)	3 (25)	1 (10)
Hispanic ethnicity, n (%)	2 (10)	1 (8.3)	1 (10)
Diagnosis, n (%)			
Ulcerative colitis	9 (45)	4 (33.3)	6 (60)
Crohn's disease	11 (55)	8 (66.6)	4 (40)
New diagnosis on admission, n (%)	6 (30)	6 (50)	—

* Includes 2 patients from biologic-naive group (repeat admission).

Table 2. Comparison of Outcomes Across Patients

	Total Population (N = 20)	Biologic-Naive (n = 12)	Biologic-Experienced* (n = 10)	P value†	P value‡
Duration of hospitalization, median (IQR), days	6 (4–12)	5 (3–7.5)	8 (6–14)	0.3037	0.07
Duration MP administration, median (IQR), days	5 (3–8.5)	4 (2.25–5.5)	7.75 (5–12.6)	0.059	0.016
Time to biologic administration, median (IQR), days	3 (1–8)	3 (1–9)	2 (1–8)	—	—
Biologic administration to discharge, median (IQR), days	6 (2–9)	3 (2–28.5)	7 (4–9.25)	—	—
Readmission within 6 mo, n (%)	6 (30)	4 (33.3)	2 (20)	0.00031	
Colectomy, n (%)	5 (25)	3 (25)	2 (20)§	0.258	
Patients with new therapy, n (%)	15 (75)	12 (100)	4 (40)¶	—	—
Biologic acceleration >7 days, n (%)	3 (15)	—	3 (30)	—	—
Infusion reaction, n (%)	0 (0)	0 (0)	0 (0)	—	—

MP, methylprednisolone

* Includes 2 patients from the biologic-naive group (repeat admission).
† Includes colectomy procedures.
‡ Excludes colectomy procedures.
§ One patient colectomy prior to admission.
¶ Includes 1 patient from the biologic-naive group.

EMR was evaluated to assess escalation of therapy throughout admission according to guideline recommendations. There were a total of 11 encounters with a patient diagnosis of UC. Of those 11 encounters, 9% of encounters had PUCAI scores documented on days 1, 3, and 5 of hospitalization.

Adverse Effects. No patient in the total population experienced an infusion-related reaction, defined as

Table 3. Comparison of Therapy Plans Across Encounters

	Subgroups	
	Biologic-Naive Encounters (n = 12)	Biologic-Experienced Encounters (n = 11)
Individual biologic administrations, n (%)		
Infliximab	11 (91.6)	4 (36.4)
Infliximab + tofacitinib	0	1 (9.1)
Adalimumab	0	1 (9.1)
Adalimumab + tofacitinib	1 (8.3)	2 (18.2)
Tofacitinib	0	1 (9.1)
Vedolizumab	0	1 (9.1)
Ustekinumab	0	1 (9.1)
Biologic dose, median		
Infliximab, mg/kg	10	10
Adalimumab, mg/dose	160	80
Tofacitinib, mg/dose	10	10
Vedolizumab, mg/dose	—	300
Ustekinumab, mg/dose	—	260

documented administration of epinephrine and/or diphenhydramine following biologic administration (Table 2). Additionally, of the 14 patients that received infliximab, 12 patients (85.7%) had a liver function test (LFT) panel collected at our institution within 1 year following infliximab administration to monitor for drug-induced transaminitis (Table 4). Of the 12 infliximab patients who underwent liver function monitoring, 2 patients had clinically significant transaminitis, defined as any value greater than or equal to 3 times the upper limit of normal. Both cases of transaminitis are noted to have been transient and were successfully managed to complete resolution in the outpatient setting. Of note, LFT elevations were not investigated to determine alternative causes, such as coadministration of hepatoxic medications and/or viral infection(s).

Clinical Outcomes. The p values were calculated for incidence of colectomy procedures and readmission within 6 months. Within the 20-patient total population, 4 patients progressed to colectomy, 3 from the biologic-naive subgroup and 1 from the biologic-experienced subgroup (p = 0.258; Table 2). The biologic-naive group experienced a statistically significant greater number of readmissions within 6 months of discharge (p = 0.00031).

Discussion

Comparison of Current Practice to Guideline Recommendations. Prompt and effective management of flares in pediatric patients with IBD increases the likelihood of disease remission and mucosal healing, allowing for normal growth and development, and positive patient outcomes. The accepted treatment algorithms for pediatric patients presenting with moderate to severe disease activity stress the appropriateness of hospitalization to allow for IVCS administration yet offer limited guidance on specialty medication selection.

The ECCO-ESPGHAN guideline for acute severe UC is based on published evidence detailed in Table 5. The guideline recommends the use of daily PUCAI scores in the management of a UC flare as a validated tool that can be used to assess the efficacy of IVCS and prompt treatment escalation. The current pediatric guideline mirrors the accepted time frame to full corticosteroid activity seen in adults—focusing on evaluation of response, measured by PUCAI scores from days 3 to 5 of IVCSs, as key guideposts for treatment decisions. Clinical teams are advised to begin planning for alternative treatment in pediatric UC patients when PUCAI scores remain above 45 on day 3 of IVCS, and to initiate

Table 4. Adherence to Screening and Monitoring Recommendations Across Patients

	Total Population (N = 20)	Biologic-Naive (n = 12)	Biologic-Experienced* (n = 10)
Hepatitis B panel within 1 yr prior to biologic, n (%)	13 (65)	9 (75)	4 (40)
QuantiFERON-TB within 1 yr prior to biologic, n (%)	18 (90)	12 (100)	6 (60)
LFT panel within 1 yr for infliximab recipients, n (%)	12 (85.7)†	9 (81.8)‡	5 (100)§

Hepatitis panel, includes hepatitis surface antigen and antibody, hepatitis core antibody and total relex Igm; LFT, liver function test; LFT panel, includes aspartate aminotransferase, alanine transferase, alkaline phosphatase, total and direct bilirubin, total protein, albumin, globulin

* Includes 2 patients from the biologic-naive group (repeat admission).
† Of 14 patients.
‡ Of 11 patients.
§ Of 5 patients.

Table 5. Literature Review of Ulcerative Colitis (UC) Guideline Recommendations

Citation	Study Design	Patient Population	Intervention	Objective	Results
Truelove[10]	Single-center, prospective, longitudinal cohort	49 patients (11–79 yr) with severe UC	60 mg/day IV prednisolone-21-phosphate x 5 days		75% entirely symptom-free after 5 days (33 of the 36 patients who were symptom-free remained so during the next 6 wk).
Turner[11]	Single-center, retrospective, longitudinal cohort	99 patients (2–17 yr) with acute severe UC		Evaluate predictors of response to guide timing of second-line therapy	PUCAI >45 points on day 3 predicted non-response to IVCS with a specificity of 50%, PPV of 58%, sensitivity 93%, NPV 88%. PUCAI >70 points on day 5 predicted non-response to IVCS with a specificity of 93%, PPV of 87%, sensitivity 44%, NPV 63%.
Turner[12]	Multi-center, prospective, cohort	128 patients (2–18 yr) with acute severe UC		Assess outcomes and identify predictors of non-response to IVCS	PUCAI >45 points on day 3 predicted non-response to IVCS with a specificity of 50%, PPV 43%, sensitivity 92%, and NPV 94%. PUCAI >65 points on day 5 was associated with IVCS failure with a specificity of 96%, PPV 82%, sensitivity 49%, and NPV 82%. PUCAI >70 points on day 5 was associated with IVCS failure with a specificity of 100%, PPV 100%, sensitivity 35%, and NPV 79%.

IVCS; intravenous corticosteroids; NPV, negative predictive value; PPV, positive predictive value; PUCAI, pediatric ulcerative colitis activity index

alternative treatment in patients whose symptoms warrant a PUCAI score above 65 after 5 days of IVCSs. The ECCO-ESPGHAN guideline also indicates that ineffective steroid therapy should not be prolonged unnecessarily and that therapeutic alternatives be considered early. Consequently, corticosteroids should only be continued for 2 to 5 additional days for patients with a PUCAI score below 65 points on the fifth day of IVCS and discontinued for patients with a PUCAI score above 65 receiving second-line medical therapy.[5]

Tumor necrosis factor (TNF) α inhibitors tend to be the most common second-line pharmacologic therapy option for children with IBD. Use of infliximab in pediatric practice is supported by greater familiarity with this agent, the ability to continue as maintenance therapy, and the overall positive risk-benefit profile. Thus, infliximab is designated as the preferred formulary agent at our institution and within guideline-directed management of biologic-naive children failing IVCS for UC and is accepted as the first-choice biologic for CD despite the lack of specific guideline recommendations. Adalimumab is classified as a non-formulary agent at our institution but may be used for specific patients following review of such factors as anticipated outpatient non-adherence to infusion center appointments and patient satisfaction, which may prompt the care team to favor at-home adalimumab injections versus infliximab.

Unfortunately, one third of patients with pediatric-onset IBD are expected to lose response to a TNF-α inhibitor with prolonged use and require further escalation of therapy. Although guidelines present calcineurin inhibitors as an alternative second-line therapy in UC, their use has fallen out of favor because of their side effect profile and the availability of newer specialty agents.

Additional biologic agents with short onset to action and favorable safety profiles may also be considered in this patient population, but there is a lack of evidence to guide their application and therefore no consensus among the guidelines regarding their exact place in therapy. Two additional antibody-based therapies were used within the treatment regimens reviewed for this study: vedolizumab, an integrin receptor antagonist, and ustekinumab, an interleukin 12 and interleukin 23 receptor antagonist. Both of these agents are designated as non-preferred, non-formulary in our institution and are reserved for use in more severe, biologic-experienced patients.

Recently, Janus kinase inhibitors have also emerged as a promising alternative and are approved for moderate to severe UC in adults. Tofacitinib has been used off label for pediatric refractory UC but there is a noted absence of

compelling evidence of efficacy or safety in this population.[8] As such, tofacitinib remains non-formulary at our institution but was used within the care of pediatric patients hospitalized with IBD flares.

In our institution, the care provided by our pediatric gastroenterology team is highly individualized and the escalation of care to second-line medical therapy is guided by individual provider assessment. Time to escalation to a second-line therapy did not differ between the subgroups and occurred at a median of 3 days after hospitalization (IQR, 1–8), earlier than the guideline recommendation for administration on the fifth day of IVCS (day 5 of hospitalization). Although the duration of methylprednisolone use in the biologic-naive group was consistent with the guideline recommendations at a median of 4 days (IQR, 2.25–5.5) of therapy, use in the biologic-experienced group was 7.75 days (IQR, 5–12.6), perhaps a response to their more complicated history of failed treatment response. Given the small sample size and descriptive, retrospective nature, we are unable to evaluate if these noted differences influenced hospital course or patient outcomes.

Characterization of Therapy Plans. ***Biologic-Naive Therapy Plans*****.** During the 2-year period covered by this study, 12 biologic-naive pediatric patients, numbered 1 to 12, were admitted for IBD disease flares. Eleven of these patients (91.6%), denoted patients 1 to 11, received infliximab monotherapy at a median dose of 10 mg/kg per dose (Table 3), aligning with the ECCO-ESPGHAN guideline recommendations. One outlying patient, patient 12, in this cohort received adalimumab and tofacitinib combination therapy following a new diagnosis of UC. Adalimumab was initiated on day 4 of hospitalization and administered at a dose of 160 mg on day zero, followed by 80 mg on day 7 and 160 mg on day 10. After failing a 14-day course of tofacitinib and 3 doses of adalimumab administered at an accelerated induction schedule, the patient ultimately underwent a colectomy on day 33 of hospitalization.

Biologic-Experienced Therapy Plans**.** The 10 biologic-experienced patients admitted for IBD disease flares within this same 2-year capture window possessed a greater variety of therapy plans across encounters. Of note, 2 of the 10 biologic-experienced patients were also included from the biologic-naive cohort as readmissions. This cohort comprised patients numbered 13 to 20 as well as patients 3 and 8, who experienced subsequent readmissions. Biologic monotherapy was the most frequent approach observed in this patient cohort (7 of 10 patients; 70% of cases).

Infliximab monotherapy remained the most frequently observed specialty medication regimen within the biologic-experienced cohort. Four patients (36.4%; patients 8 and 13–15) received this treatment, all for a primary diagnosis of UC. Three of these four (patients 8, 13, and 14) had previously been treated with infliximab, with 2 cases undergoing treatment acceleration receiving their next dose a median of 16 days early (patients 8 and 14). The remaining case had been previously treated using vedolizumab (patient 15). It should be noted that this patient was readmitted within 6 months of discharge for a subsequent disease flare while being treated with infliximab.

Three biologic-experienced patients were treated in line with their outpatient monotherapy specialty medication regimen while admitted for a disease flare. Adalimumab monotherapy was administered on schedule for 1 member of this cohort with UC (patient 17). Vedolizumab monotherapy was administered on schedule for a patient with a CD flare (patient 18) who had a history of infliximab therapy failure. Ustekinumab monotherapy was administered to 1 patient with CD who had been managed with this specialty medication in the outpatient setting (patient 19). In this case, the care team chose a reinduction strategy, accelerating administration of ustekinumab so that it was 41 days early. Notably, this patient had also previously failed infliximab therapy.

Adalimumab and tofacitinib combination therapy was observed in 2 encounters for 1 patient with UC (patient 16). This patient had 2 disease flares, approximately 3 months apart, and ultimately underwent a colectomy 2 months after their last admission.

Infliximab and tofacitinib combination therapy was used for patient 3, and the clinical details of this patient will be discussed in "Characterization of Tofacitinib Use" below.

Tofacitinib monotherapy was initiated for the final member of this cohort (patient 20), whose flare occurred in spite of outpatient infliximab therapy.

Characterization of Tofacitinib Use. Although tofacitinib has emerged as an adjunctive treatment in patients with refractory UC, the data in pediatric patients are limited, particularly regarding the effect of this agent in combination with TNF-α inhibitors (Table 6). In pediatrics, use of the lowest effective dose is advised given a boxed warning noting an increased risk of pulmonary embolism observed in adult rheumatoid arthritis patients with additional risk factors. Further safety considerations include dose-dependent herpes zoster infection rates and lipid abnormalities as well as CYP3A4 drug interactions that may require empiric dose adjustment.[9]

Tofacitinib has been used in refractory UC as monotherapy or as adjunct when combined with biologic therapy but has been most frequently described in combination with vedolizumab. Within our institution, tofacitinib is leveraged primarily as an add-on therapy, specifically applied to prevent or delay a colectomy procedure. In this study, a total of 4 patients (patients 3, 12, 16, and 20) were administered tofacitinib monotherapy or in combination with a TNF-α inhibitor.

Table 6. Literature Review of Tofacitinib in Combination with Biologic Therapies in Pediatric Inflammatory Bowel Disease (IBD)

Citation	Study Design	Patient Population	Intervention	Results	Safety
Dolinger[13]	Ongoing, single-center, longitudinal, observational, cohort	12 pediatric patients with UC, CD, or unclassified IBD who failed previous biologic (all failed infliximab)	Tofacitinib 10 mg twice daily induction × 10 wk	Vedolizumab + tofacitinib in 4 patients (3 with UC and 1 with CD). Steroid-free remission achieved in 2 patients (1 with UC and 1 with CD).	No serious AEs (infections, hospitalizations, or VTE). Serum lipid panel obtained in 5 patients at approximately 1 mo (all were normal).
Dolinger[14]	Single-center, observational, cohort	16 pediatric patients with UC, CD, or unclassified IBD who failed previous biologic (all failed infliximab)	Ustekinumab + vedolizumab *OR* Ustekinumab + tofacitinib 10 mg twice daily *OR* Vedolizumab + tofacitinib 10 mg twice daily x 6 mo	12 patients (75%) achieved steroid-free remission. 9 of 12 patients received tofacitinib combination therapy. 2 patients (1 with UC and 1 with CD) who received tofacitinib combination therapy discontinued therapy at 5 and 2 mo, respectively, because of persistent symptoms.	1 patient (vedolizumab + tofacitinib + prednisone) developed septic arthritis and DVT but achieved steroid-free remission and complete mucosal healing and was transitioned to vedolizumab monotherapy.
Moore[15]	Single-center, retrospective cohort	21 patients, <21 yr, biologic therapy non-responder, with UC or indeterminate IBD	Tofacitinib 5-10 mg twice daily or 11 mg once daily with dose adjustments	Clinical response achieved at week 12 in 9 of 21 patients (42.9%) and at week 52 in 7 of 17 patients (41.2%). 6 patients (28.6%) required a colectomy.	11 serious AEs were reported that required hospitalization. Most because of a disease flare with no clotting events reported.

AE, adverse event; DVT, deep vein thrombosis; VTE, venous thromboembolic

Patient 3 was administered a combination of tofacitinib and infliximab after failing infliximab and prednisone outpatient. Patient 3 had been discharged following a 6-day hospitalization for a new diagnosis of CD then readmitted 2 days later. Tofacitinib was initiated on day 13 of hospitalization during the second admission at a dose of 10 mg twice daily then discontinued after 7 days because of insufficient response.

Patient 20, with a diagnosis of CD, was administered tofacitinib monotherapy inpatient after failing infliximab and prednisone outpatient. On day 5 of hospitalization, tofacitinib was initiated at 5 mg twice daily for 3 days then increased to 10 mg twice daily for the remainder of the hospitalization because of inadequate response. Long-term outcomes and disease course for this patient were not evaluated after discharge.

A total of 2 UC patients underwent a colectomy procedure after receiving a combination of adalimumab and tofacitinib. Patient 12 in the biologic-naive cohort was initiated on tofacitinib 10 mg twice daily on day 19 of hospitalization following a new diagnosis of UC. Fourteen days later, the patient underwent a colectomy.

Patient 16 was started on tofacitinib for outpatient management approximately 8 months prior to their colectomy procedure. The patient was continued on their home dose of tofacitinib 10 mg twice daily during the first admission and 5 mg twice daily during the second admission. Approximately 2 months after discharge from the second admission, the patient underwent a colectomy procedure.

Of note, the incidence of clot formation, lipid abnormalities, and herpes zoster infection were not evaluated in this study. As such, the safety of combination therapy cannot be evaluated at this time.

Comparison of Outcomes. Outcomes observed included duration of hospitalization, readmission within 6 months of discharge, and incidence of colectomy procedures. The biologic-experienced subgroup experienced a statistically insignificant longer median duration of hospitalization (8 days; IQR, 6–14) compared with the biologic-naive group (5 days; IQR, 3–7.5; Table 2). There was an even distribution of colectomy procedures between subgroups. Of note, in the biologic-experienced subgroup, 1 of the 2 patients received surgical intervention prior to admission. These data were limited to documented colectomy procedures in the EMR for the study population. Lastly, the biologic-naive group experienced a statistically significant greater number of readmissions within 6 months of discharge ($p = 0.00031$). Of note, readmissions were also limited to encounters at our institution only.

Limitations. This study retrospectively describes the inpatient management of IBD flares for 20 pediatric patients during a 2-year period in a single institution. The goal was to understand our internal practice to allow for quality improvement activities. Findings presented were descriptive in nature; however, there are future opportunities for statistical analyses with a larger cohort. Additionally, this study did not assess long-term outcomes and was therefore unable to define a causal relationship between specialty therapy and long-term management of symptoms. The time period captured does coincide with the peak of the COVID-19 pandemic, which may have limited the number of pediatric IBD admissions and readmissions observed. Finally, this study did not evaluate the use of biosimilar agents because of a hospital-wide practice implementation that occurred halfway through the study period.

Conclusions

All pediatric patients admitted to our health system for an IBD disease flare within the 2-year period received 1 or more specialty therapeutics during their admission. The preferred use of infliximab in biologic-naive patients, as well as the high rates of use for biologic-experienced patients, aligns with the availability of data supporting the safety and efficacy of this agent in this population. The heterogeneity of treatment plans leveraged for biologic-experienced patients is reflective of the lack of guidance available. Decisions regarding pharmacotherapy in UC and CD patients who are experiencing a flare despite biologic treatment should be determined on a case-by-case basis. Our work indicates that the standard inclusion of hepatitis B panel, QuantiFERON-TB, and LFT panels to the admission order sets of patients presenting with an IBD flare would improve patient safety and minimize delay of treatment escalation. Additionally, there is an opportunity to standardize care and the pharmacist approval process for IBD admissions by creating EMR care pathways that incorporate daily PUCAI scoring for UC patients to guide therapy escalation and selection in accordance with guideline recommendations. Based on our observations, patients may benefit from earlier inpatient administration of second-line specialty therapies. More data, however, are needed to specifically evaluate the role of Janus kinase inhibitors in management of pediatric IBD. Overall, there is a need for a consensus approach to management of pediatric IBD flares within the inpatient setting. Moreover, providers should continue to describe efficacy and safety data regarding the use of tofacitinib in pediatric IBD.

Article Information

Affiliations. Department of Pharmacy Services (DNK, JVR), Yale New Haven Hospital, New Haven, CT; Corporate Pharmacy Services (RAP), Yale New Haven Health, New Haven, CT.

Correspondence. Danielle Koubek, PharmD, BCPPS; dnkoubek@gmail.com

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