Pediatr Gastroenterol Hepatol Nutr. 2022 Nov;25(6):461-472
https://doi.org/10.5223/pghn.2022.25.6.461
pISSN 2234-8646·eISSN 2234-8840

Pediatric Gastroenterology, Hepatology & Nutrition
pghn

Original Article

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Long-Term Efficacy and Safety of Golimumab for Ulcerative Colitis in a Pediatric Inflammatory Bowel Disease Center in Japan

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OPEN ACCESS

Received: Feb 14, 2022
Revised: Jul 19, 2022
Accepted: Aug 9, 2022
Published online: Nov 2, 2022

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ABSTRACT

Purpose: Golimumab (GLM) is an anti-tumor necrosis factor (TNF)-α antibody preparation known to be less immunogenic than infliximab (IFX) or adalimumab. Few reports on GLM in pediatric patients with ulcerative colitis (UC) are available. This study aimed to review the long-term durability and safety of GLM in a pediatric center.
Methods: The medical records of 17 pediatric patients (eight boys and nine girls) who received GLM at the National Center for Child Health and Development were retrospectively reviewed.
Results: The median age at GLM initiation was 13.9 (interquartile range 12.0–16.3) years. Fourteen patients had pancolitis, and 11 had severe disease (pediatric ulcerative colitis activity index ≥65). Ten patients were biologic-naïve, and 50% achieved corticosteroid-free remission at week 54. Two patients discontinued prior anti-TNF-α agents because of adverse events during remission. Both showed responses to GLM without unfavorable events through week 54. However, the efficacy of GLM in patients who showed primary nonresponse or loss of response to IFX was limited. Four of the five patients showed non-response at week 54. Patients with severe disease had significantly lower corticosteroid-free remission rate at week 54 than those without severe disease. No severe adverse events were observed during the study period.
Conclusion: GLM appears to be safe and useful for pediatric patients with UC. Patients with mild to moderate disease who responded to but had some adverse events with prior biologics may be good candidates for GLM. Its safety and low immunogenicity profile serve as favorable options for selected children with UC.

Keywords: Treatment outcome; Safety; Golimumab; Ulcerative Colitis; Children

Funding

This work was supported by a Grant-in-Aid for the National Center for Child Health and Development (2019A-3) and Research Grants for Research on Intractable Disease (20FC1042) from the Ministry of Health, Labour and Welfare, Japan.

Conflict of Interest

The authors have no financial conflicts of interest.

INTRODUCTION

The number of children diagnosed with inflammatory bowel disease (IBD) is increasing worldwide [1-3]. Ulcerative colitis (UC) is a chronic bowel disorder characterized by recurrent episodes of inflammation, ulceration, and bleeding in the large intestine [4]. The emergence of infliximab (IFX) has markedly altered treatment algorithms for Crohn's disease (CD) and UC [5]. IFX and adalimumab (ADA) have been used to treat UC in children. Their efficacy has been reported in several clinical trials [6-9]. However, the secondary loss of response (sLOR) to IFX has become a problem that needs to be solved. This was partly due to the production of antibodies against IFX. Moreover, adverse events leading to the discontinuation of IFX was reported [10].

Golimumab (GLM) is an anti-tumor necrosis factor (TNF)-α monoclonal antibody produced by a murine hybridoma cell line with recombinant DNA technology using a transgenic mouse platform [11]. It is less immunogenic than IFX and ADA. In an adult trial of GLM, biologic-naïve patients with moderately to severely active UC, even with conventional treatments including 5-aminosalicylic acid (5-ASA), oral corticosteroids, and immunosuppressive drugs, were included, and >50% of these patients achieved clinical remission and mucosal healing [12-14]. For pediatric patients, an open-label pharmacokinetic (PK) study was conducted in patients with moderate-to-severe UC, wherein the PKs of GLM in pediatric and adult patients were comparable, suggesting that GLM has clinical benefits and a safe profile in pediatric patients with UC [15]. The PK and exposure–response relationships of the pediatric and adult populations were comparable, suggesting that the efficacy of GLM can be extrapolated from adults to pediatric patients with UC [16]. However, at present, only a few reports are available on the use of GLM in pediatric UC [15,16].

Therefore, this study aimed to investigate the long-term efficacy and safety of GLM at a pediatric IBD center in Japan to provide the first real-world data about pediatric patients with UC who were followed up for more than 1 year.

MATERIALS AND METHODS

Patient population

We retrospectively reviewed the medical records of patients with UC who were newly introduced to GLM, aged <18 years between June 2017 and August 2020, and followed up for at least 54 weeks at the National Center for Child Health and Development (NCCHD), a tertiary care Children's Hospital in Japan.

The diagnosis of UC was based on the diagnostic criteria developed by the Pediatric IBD Porto Group of the ESPGHAN [17]. Patients whose pediatric ulcerative colitis activity index (PUCAI) [18] could not be assessed because of severe intellectual disabilities were excluded from this study. This study was approved by the Institutional Ethics Review Board of NCCHD (2020-055). The need for written informed consent was waived owing to the retrospective study design.

Patient demographics

The following characteristics were analyzed: sex, age at diagnosis, age at GLM initiation, disease extent, GLM dosage, endoscopic findings, PUCAI at weeks 0, 2, 6, 10, 14, 30, 42,

and 54, previous and concomitant medications, and adverse events. According to the Paris classification [19], severe disease behavior (S1) was defined as a PUCAI ≥65 at any time during the clinical course.

For efficacy assessment, clinical remission was defined as a PUCAI of <10 without an increase in corticosteroid use. A reduction in PUCAI by at least 20 points or successful corticosteroid withdrawal without increasing PUCAI was regarded as a clinical response. Primary nonresponse (PNR) was defined as PUCAI remaining at ≥10 and failed to improve by ≥20 within 30 weeks. sLOR was defined as the worsening of disease activity after the initial response.

Endoscopic activity was evaluated using the modified score (MS; 0–15), which is the sum of the Mayo endoscopic scores from the five segments of the large intestine (ascending, transverse, descending, sigmoid colon, and rectum) [20-22].

Statistical analysis

Pearson's chi-square test or Fisher's exact test was used to compare patient characteristics whenever appropriate. Statistical significance was set at $p<0.05$. All statistical analyses were performed using GraphPad Prism V.8.4.2 (GraphPad Software Inc., San Diego, CA, USA).

RESULTS

Patient demographics

A total of 17 patients (eight boys and nine girls) with moderate-to-severe UC were included in this study. Patient background information is summarized in **Table 1**. The median age at GLM initiation was 13.9 (interquartile range 12.0–16.3) years. At week 0, eight patients were in the active phase (PUCAI ≥10) and nine were in remission (PUCAI <10). GLM was introduced during remission for the following reasons: steroid dependence in four (cases 1, 2, 4, and 10),

Table 1. Background of children with ulcerative colitis

No.	Sex	Age (yr)		Weight (kg)	Paris classification		Concomitant medications			Prior use of other biologics before GLM		
		At diagnosis	At introduction		Extent*	Severity†	AZA	Tac	CS	IFX	ADA	Reason for the cessation
1	F	10	12	30	E4	S1	-	-	+	-	-	-
2	F	5	9	48	E4	S0	+	-	+	-	-	-
3	M	10	16	62	E1	S0	+	-	+	-	-	-
4	M	7	8	31	E4	S0	+	-	+	-	-	-
5	F	13	13	44	E4	S1	+	-	-	-	-	-
6	F	9	15	46	E4	S1	+	-	-	-	-	-
7	M	14	16	60	E4	S1	+	-	+	-	-	-
8	M	12	13	32	E4	S1	-	+	+	-	-	-
9	M	8	14	46	E2	S1	-	-	+	-	-	-
10	F	13	13	63	E4	S1	+	-	+	-	-	-
11	M	11	17	72	E4	S1	-	-	-	+	-	Suspected AE
12	M	15	17	55	E3	S0	-	-	-	-	+	AE
13	F	8	11	25	E4	S1	-	-	-	+	-	PNR
14	F	12	13	44	E4	S0	+	-	-	+	-	sLOR
15	F	7	7	17	E4	S1	+	-	-	+	-	sLOR
16	M	12	16	52	E4	S1	+	-	-	+	-	sLOR
17	F	8	16	59	E4	S0	+	-	-	+	-	sLOR, AE

F: female, M: male, GLM: golimumab, AZA: azathioprine, Tac: tacrolimus, CS: corticosteroid, IFX: infliximab, ADA: adalimumab, AE: adverse events, PNR: primary non-response, sLOR: secondary loss of response.
*E1: ulcerative proctitis, E2: left-sided ulcerative colitis (distal to splenic flexure), E3: extensive (hepatic flexure distally), E4: pancolitis (proximal to hepatic flexure).
†S0: never severe, S1: severe at least once.
Severe was defined as a Pediatric Ulcerative Colitis Activity Index ≥65.

https://doi.org/10.5223/pghn.2022.25.6.461

intolerance to prior biologics in two (cases 11 and 12), sLOR to prior biologics (cases 16 and 17), and significant inflammatory findings on colonoscopy despite clinical remission with azathioprine in one case (case 6).

Overall clinical efficacy assessment

Fig. 1 shows the change in PUCAI after GLM initiation. Regarding the continuation rate of GLM, all patients remained on GLM at week 14. However, by week 30, 3 of the 17 (17.6%) patients discontinued GLM because of the difficulty in maintaining remission. Among them, two patients had sLOR to GLM. At week 54, 10 (58.8%) patients remained on GLM, and 5 of the 10 patients initiated GLM as the first biologic, whereas 2 were introduced as the second biologic because of intolerance to prior biologics. Additionally, one and two patients had PNR and sLOR, respectively, prior to biologics. The Kaplan–Meier curve of the GLM continuation rate in our patients is shown in **Fig. 2**. In patients who continued GLM, steroid-free remission rates were 29.4% (5/17) at GLM initiation, 29.4% (5/17) at week 10, 71.4% (10/14) at week 30, and 80.0% (8/10) at week 54 (**Fig. 3**).

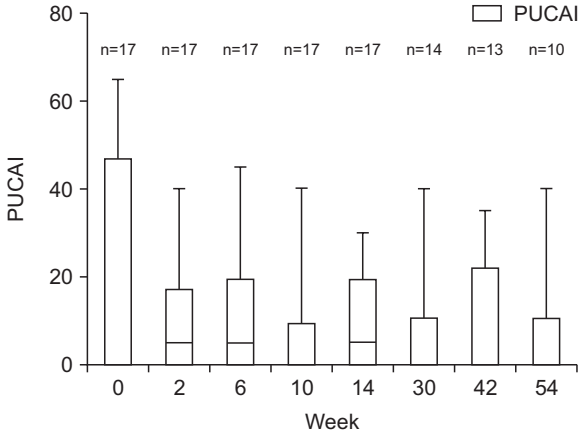

Fig. 1. Change in the PUCAI after GLM initiation. Each box shows the lower and upper quartiles and median PUCAI among patients who continued treatment with GLM. Notably, corticosteroids or tacrolimus was used in combination with GLM in some patients. The details of these concomitant medications are presented in Tables 1 and 2.
PUCAI: pediatric ulcerative colitis activity index, GLM: golimumab.

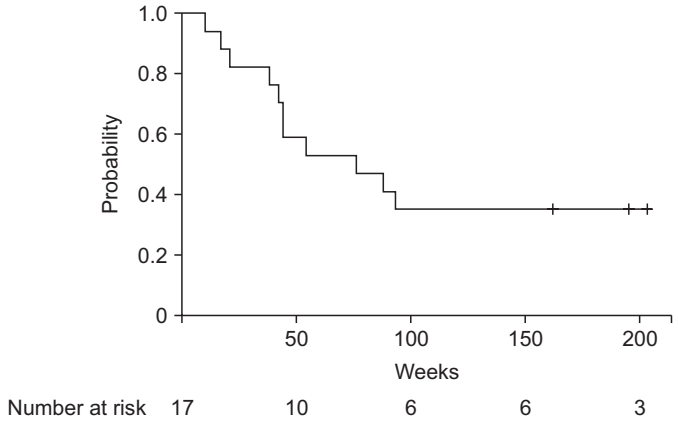

Fig. 2. Kaplan–Meier curve of the GLM continuation rate. All patients were included in this chart. Most patients who discontinued GLM were on treatment for less than 100 weeks, whereas responders continued with the treatment for a longer time.
GLM: golimumab.

https://doi.org/10.5223/pghn.2022.25.6.461

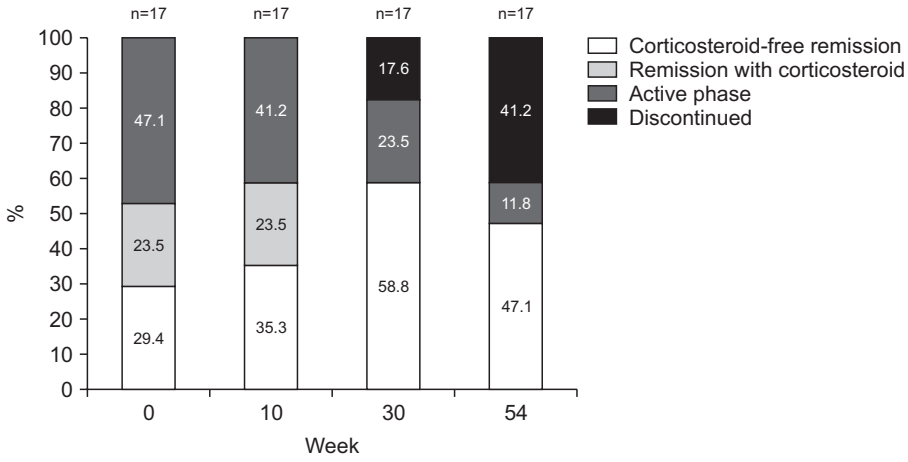

Fig. 3. Changes in the clinical remission rates after GLM initiation. All patients were included in this chart. Nearly half of the patients achieved corticosteroid-free remission at week 54, whereas others discontinued treatment with GLM or were in the active phase.
GLM: golimumab.

Assessment of the clinical efficacy stratified by the indication of golimumab

As shown in **Table 2**, patients were classified based on their previous biologic exposure as follows: i) GLM as the first biologic agent (cases 1–10), ii) intolerance to IFX or ADA (cases 11 and 12), iii) PNR to IFX (case 13), and iv) sLOR to IFX (cases 14–17).

GLM was introduced as the first biologic agent in 10 patients. At the time of GLM initiation, all patients failed to maintain remission with at least one of the following conventional therapies: oral 5-ASA, corticosteroids, and azathioprine. At week 0, 4 of the 10 patients were corticosteroid-dependent. However, 8 of the 10 patients achieved clinical remission (including those in the steroid withdrawal process) at week 8, and 5 (cases 1–4 and 6; 50%) achieved steroid-free remission at week 54. Follow-up colonoscopy revealed improved MS in three patients. The other five patients (cases 5 and 7–10; 50%) initially responded to GLM but lost response by week 54 and switched to IFX. None of the patients showed endoscopic remission. The diagnosis in case 10 was changed to CD after a small bowel lesion was noted at week 21.

Before GLM initiation, 11 and 12 patients were in clinical remission with IFX and ADA, respectively. However, they experienced adverse events and switched to GLM. In case 11, the patient was in clinical remission with IFX, but acne appeared and worsened. In case 12, the patient was in remission with ADA but developed a psoriasis-like skin rash. Both patients remained in clinical remission and continued GLM without any adverse events for 54 weeks. Moreover, endoscopic improvement and remission were confirmed in cases 11 and 12, respectively (**Table 2**).

In case 13, the patient showed PNR to IFX and GLM was initiated. Although the endoscopic findings improved with GLM therapy, the patient was unable to maintain clinical remission. The patient was diagnosed with CD after the identification of a duodenal lesion. Ustekinumab (UST) therapy was initiated at week 56.

Cases 14–17 initially responded to IFX, but gradually lost their responses. The GLM was then initiated. However, owing to insufficient response, two patients (cases 15 and 16) were

https://doi.org/10.5223/pghn.2022.25.6.461

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Table 2. Change in the clinical parameters before and after GLM introduction

No	Prior biologics	GLM dosage*	PUCAI			CRP (mg/dL)			ESR (mm/h)			Modified score†		PGA at week 54	Duration of GLM (wk)	Final outcome
			Week 0	Week 6	Week 54	Week 0	Week 6	Week 54	Week 0	Week 6	Week 54	Before	After			
1	First biologics	A	0§	0§	5	<0.01§	<0.01§	0.04	16§	8§	22	12§ (−5)	2 (63)	Remission	210	GLM ongoing
2	First biologics	Adult dose	0§	0§	0	0.06§	0.02	0.10	3§	1§	5	10§ (−3)	NA	Remission	203	GLM ongoing
3	First biologics	Adult dose	20§	0§	0	0.01§	-	0.01	1§	-§	3	NA	1 (48)	Remission	88	Switched to ADA (loss of response)
4	First biologics	A	0§	0§	0	<0.01§	0.01	0.21	8§	5§	20	9§ (−3)	1 (46)	Remission	162	GLM ongoing
5	First biologics	Adult dose	55	35§	35‡	0.23	0.02§	0.01‡	11	6§	5‡	7 (0)	7 (48)	Non-response‡	44	Switched to IFX (non-response)
6	First biologics	Adult dose	0	0	0	0.03	0.02	0.01	11	8	7	8 (−6)	6 (23)	Remission	195	GLM ongoing
7	First biologics	Adult dose	45§	5§	40‡	0.01§	0.03	0.01‡	5§	10§	7‡	10§ (−2)	10 (40)	Non-response‡	38	Switched to IFX (non-response)
8	First biologics	A→B (wk 36)	10‖	5‖	15‡,§	0.02‖	0.03	0.06‡,§	5‖	5‖	11‡,§	3§,‖ (−7)	9 (50)	Non-response‡	44	Switched to IFX (non-response)
9	First biologics	Adult dose	50§	15§	30‡,§	0.34§	0.04	0.14‡,§	42§	25§	11‡,§	8§ (−10)	4‡,§ (43)	Non-response‡	42	Switched to IFX (non-response)
10	First biologics	Adult dose	0§	0§	5‡	0.03§	0.01	0.08‡	10§	9§	17‡	15§ (−3)	15 (21)	Non-response‡	21	Switched to IFX (non-response)
11	IFX (suspected AE)	Adult dose	0	0	0	0.14	0.22	2.18	4	7	25	3 (−51)	2 (58)	Remission	228	Switched to ADA (loss of response)
12	ADA (AE)	Adult dose	0	0	0	0.33	-	0.01	10	-	4	0 (−58)	0 (42)	Remission	162	GLM ongoing
13	IFX (PNR)	B	25	25	30	0.32	0.1	1.78	15	25	31	13 (−2)	5 (51)	Non-response	54	Switched to UST (non-response)
14	IFX (sLOR)	Adult dose	55	25	40	0.07	0.02	0.08	26	9	21	5 (−38)	0 (90)	Non-response	93	Switched to VDZ (psoriasis)
15	IFX (sLOR)	B	65	45	10‡,§	1.04	1.04	0.02‡,§	70	76	3‡,§	7 (−2)	2‡,§ (19)	Non-response‡	17	Switched to UST (non-response)
16	IFX (sLOR)	Adult dose	0	10	25‡	0.39	0.09	0.06‡	8	6	9‡	5 (0)	5 (13)	Non-response‡	10	Switched to IFX (non-response)
17	IFX (sLOR/AE)	Adult dose	0	15	0	0.17	0.15	0.54	47	32	40	NA	4 (79)	Remission	76	Switched to VDZ (psoriasis)

PUCAI: pediatric ulcerative colitis activity index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, PGA: physician's global assessment, GLM: golimumab, IFX: infliximab, AE: adverse events, ADA: adalimumab, PNR: primary non-response, sLOR: secondary loss of response, UST: ustekinumab, VDZ: vedolizumab.

*Dosage: adult dose, 200 mg at week 0, followed by 100 mg at week 2, and then 50 mg every 4 weeks. (A) 90 mg/m^2 at week 0, followed by 45 mg/m^2 at week 2, and then 45 mg/m^2 every 4 weeks. (B) 115 mg/m^2 at week 0, 60 mg/m^2 at week 2, and then 60 mg/m^2 every 4 weeks.

†The modified score is the sum of the Mayo endoscopic score from the five segments of the large intestine (ascending, transverse, descending, sigmoid colon, and rectum; range, 0–15). The digits in brackets indicate the week of endoscopy before and after the first GLM infusion.

‡Data were assessed at the time of the last GLM infusion.

§Concomitant use of corticosteroids.

‖Concomitant use of tacrolimus.

https://doi.org/10.5223/pghn.2022.25.6.461

switched to UST or IFX by week 54. The other two patients (cases 14 and 17) remained on GLM at week 54 but eventually switched to vedolizumab. Patient 14 achieved corticosteroid-free endoscopic remission at week 90. However, the patient suffered from fecal incontinence, probably due to irritable bowel syndrome, and her PUCAI did not improve. Then, she developed psoriasiform dermatitis and was switched to vedolizumab at week 61. In case 17, the patient successfully maintained clinical remission with GLM until week 54. However, she had psoriasis on IFX, which temporarily improved on GLM, but flared up again. Therefore, the patient was switched to vedolizumab at week 81. In case 15, the patient did not respond sufficiently to GLM and eventually required corticosteroids. Endoscopic reevaluation revealed small-bowel involvement. The patient was diagnosed with CD, and UST was initiated at week 19. In case 16, the patient failed to respond to 10 mg/kg IFX every 6 weeks, and GLM was administered. The patient achieved remission during the induction phase, but the disease relapsed at week 10. The patient eventually started receiving vedolizumab at week 76.

Comparison of the effectiveness of golimumab by prior biologic exposure

No significant difference was found in week 54 steroid-free remission rates between biologic-naïve patients and those who had received prior anti-TNF-α antagonists (p>0.99) (**Fig. 4**).

Clinical efficacy assessment stratified by disease severity

Among the 11 patients with S1, only three (27.3%) continued GLM through week 54. By contrast, all six patients with S0 remained on GLM at week 54 (p<0.05). Patients with S1 had significantly lower steroid-free remission rates at week 54 than those with S0 (S1, 18.2% vs. S0, 83.3%; p<0.05).

Clinical efficacy assessment stratified by golimumab dosage

The GLM dosages used are presented in **Table 2**. GLM was administered to 12 patients (aged 9–17 years; body weight range, 44–72 kg) at an adult dose (200 mg at week 0, followed by 100 mg at week 2, and then 50 mg every 4 weeks). We defined the dosage in the GLM phase I study for pediatric UC (90 mg/m^2 at induction and 45 mg/m^2 at maintenance) [15] as dose A, and the dosage recommended in the ECCO/ESPGHAN guidelines (115 mg/m^2 for induction and 60 mg/m^2 for maintenance) [16] as dose B.

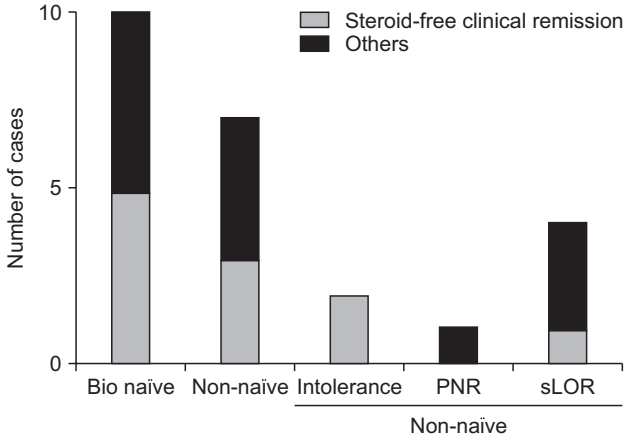

Fig. 4. Steroid-free remission rate at week 54 due to GLM initiation. No significant difference was found in the corticosteroid-free remission rates between biologic-naïve (i.e., GLM was introduced as the first biologic) and non-naïve (i.e., GLM was introduced as the second biologic) patients. Among non-naïve patients, those who responded to but had some adverse events with prior biologics (i.e., intolerance) had a higher possibility of achieving corticosteroid-free remission. intolerance, intolerance to prior biologics.
GLM: golimumab, PNR: primary non-response to prior biologics, sLOR: secondary loss of response to prior biologics.

https://doi.org/10.5223/pghn.2022.25.6.461

Two biologic-naïve patients started GLM at dose A, and they achieved remission by week 54 and continued on GLM thereafter. Dose B was adopted in two patients with IFX failure (one with PNR and one with sLOR). However, remission was not achieved even with dose B. One patient (case 8) showed an increase in dosage from dose A to dose B at week 36 due to non-response, but it did not improve responsiveness.

Adverse events

During the observation period, 16 patients experienced no significant adverse reactions requiring GLM discontinuation, including severe infections, systemic infusion reactions, or neoplasms. In two cases, psoriasis occurred and GLM administration had to be discontinued. No local reactions were observed at the injection sites. Although viral infections, such as influenza and upper respiratory tract infections, were observed in some patients, they were not severe. Two patients developed psoriasis with previous biologics. In both patients, psoriasis resolved after switching to GLM but relapsed and resulted in GLM discontinuation in one patient. Another patient developed new-onset psoriasis after GLM initiation, which was discontinued.

DISCUSSION

This study examined the long-term efficacy and safety of GLM, and our real-world experience suggests the effectiveness of GLM in children with UC, particularly in those who were biologic-naïve and never had severe disease (PUCAI >65). In addition, most patients continued on GLM without severe adverse events, except for two patients with psoriasis who required GLM discontinuation.

A phase III trial (PURSUIT-SC) evaluated the efficacy of GLM induction therapy in anti-TNF-α antagonist-naïve, moderate-to-severely active patients with UC, despite the use of conventional treatments such as 6-mercaptopurine, azathioprine, corticosteroids, and/or 5-ASA. The clinical response rate at week 6 was 51% [12]. However, the baseline corticosteroid dosage was continued at the same dosage in PURSUIT-SC. In addition, patients who used more than 40 mg prednisolone and/or tacrolimus within 8 weeks of study entry were excluded. Thus, this study included patients who received >40 mg prednisolone and/or tacrolimus. The corticosteroid dose was then reduced according to the disease activity.

Despite these demographic differences, our biologic-naïve patients showed a clinical remission rate (including patients in the steroid withdrawal process) of 80.0% (8/10) at week 6. Patients in the active phase at GLM initiation had a 60.0% (3/5) clinical remission rate and a 100.0% (5/5) clinical response rate, comparable to the outcomes in PURSUIT-SC. For long-term outcomes, our biologic-naïve patients who achieved remission by week 6 showed a 62.5% remission rate by week 54 (5/8), which was also comparable to the GLM maintenance trial (PURSUIT-M; 49.7%) [13].

No significant difference was found in the week 6 efficacy of GLM between patients in whom GLM was introduced as a first biologic and in whom GLM was introduced as a second biologic. In this regard, our results are consistent with those reported by Taxonera et al. [23].

However, the second biologic group included two patients who switched to GLM owing to adverse events (i.e., psoriasis) during the successful treatment of intestinal inflammation

https://doi.org/10.5223/pghn.2022.25.6.461

with IFX or ADA. In these patients, their diseases tended to be well controlled with GLM. Conversely, patients with PNR to IFX failed to maintain remission with drugs that have similar mechanisms of action. These tendencies were also reported in an adult study [24]. For pediatric UC, the latest ECCO/ESPGHAN consensus guidelines for pediatric UC stipulated that GLM has no role in patients with PNR to IFX [25]. In case 13, the patient showed PNR to IFX and could not sustain remission with GLM. Drugs with different mechanisms of action should be considered for such patients.

In this study, severe disease behavior (S1) was associated with GLM durability. Only 4 of the 11 patients with S1 remained on GLM at week 54. Compared with S0 patients, S1 patients were more likely to fail to maintain remission. Singh et al. [26] reported that GLM had a slower and weaker onset of effect than IFX.

In the PURSUIT-SC, the median serum GLM concentrations (SGC) at week 6 were 3.14 and 2.13 μg/mL in patients who achieved and did not achieve clinical remission, respectively [27]. The target week 6 SGC to achieve optimal clinical outcomes was calculated as 2.5 μg/mL. The pediatric dose was determined in the GLM phase I trial based on PK models derived from adult UC and juvenile idiopathic arthritis data [15]. In this trial, the dosage for children weighing <45 kg was 90 mg/m^2 for induction and 45 mg/m^2 for maintenance (dose A). However, week 6 SGC (1.1 μg/mL) was lower than the historical adult data (3.4 μg/mL) [15]. In the PURSUIT-PEDS-PK, an increased dosage (120 mg/m^2 for induction and 60 mg/m^2 for maintenance) was suggested [16]. Based on these results, the ECCO/ESPGHAN guidelines recommend a dose of 115 mg/m^2 for induction and 60 mg/m^2 for maintenance (dose B) [28].

However, in our study, dose B was not associated with a better response than dose A. As an explanation, our patients who were administered dose A were given GLM as the first biologics. By contrast, patients at dose B showed PNR or sLOR to prior anti-TNF-α antagonists. Patients who fail to respond to prior anti-TNF-α antagonists may have an inadequate response to GLM. These differences in patient background should be considered.

In this study, we could not assess the SGC and determine whether the dose was appropriate. The treat-to-target strategy utilizing SGC might improve the treatment outcome of these refractory patients, although it is not covered by the Japanese insurance.

In pediatric IBD, the diagnosis can change from UC to CD. In Norway, 14% of patients with UC are diagnosed with CD within 5 years [29]. Ten percent of children initially diagnosed with UC were subsequently diagnosed with CD [30]. In the present study, the diagnoses in three cases were changed from UC to CD. Therefore, regular monitoring of symptoms, laboratory findings, and treatment response in each patient is mandatory, and endoscopic re-evaluation should be considered if CD is suspected.

The rate of severe adverse events was 14.3% in the PURSUIT-M group, comparable to other TNF-α antagonists [12,13]. GLM was reported to have a low immunogenicity profile, and patients who developed infusion reactions or other adverse events due to IFX or ADA could tolerate GLM [7]. In our study, three patients discontinued IFX or ADA owing to adverse events. They were switched to GLM and remained in clinical remission without any adverse events until week 54. The Kaplan–Meier curve of the GLM continuation rate indicated that patients who could continue GLM for more than 100 weeks tended to continue GLM thereafter. This result shows a low immunogenicity profile for the GLM. Two of the 17

https://doi.org/10.5223/pghn.2022.25.6.461

patients in the GLM group developed psoriasis. Several studies have reported psoriasis caused by GLM, and care physicians should be aware of this adverse effect [31,32].

This study has several limitations. First, selection bias could have occurred because this was a retrospective study of a relatively small number of patients, conducted at a single tertiary care children's hospital. Second, various concomitant medications, including corticosteroids, might have affected the efficacy assessment, and the improvement in patient status might not be solely due to GLM. Third, the timing of endoscopy differed for each patient. Finally, the follow-up period from the start of GLM use was only 1 year.

In conclusion, GLM can be used effectively and safely in pediatric patients with mild-to-moderate UC. Specifically, patients whose intestinal inflammation was effectively treated with other anti-TNF-α antibodies but had to discontinue it because of adverse events, such as infusion reactions, could be preferable candidates for GLM. Data on the long-term efficacy, safety, and optimal dosage for pediatric patients with UC are mandatory. Its low immunogenicity profile and low risk of adverse events serve as favorable options for selected children with UC.

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