Table 2: Treatment pattern of pediatric UC and CD patients specified time points/intervals

Medication	Initial visit	1-year from initial visit	3-year from initial visit
Crohn's Disease			
	N=4720	N=4720	N=1920
5-ASA[1]	154 (3.3%)	120 (2.5%)	37 (1.9%)
Corticosteroid[2]	1898 (40.2%)	297 (6.3%)	71 (3.7%)
6-MP/AZA	873 (18.5%)	973 (20.6%)	321 (16.7%)
Methotrexate	584 (12.4%)	957 (20.3%)	403 (21.0%)
TNFi[3]	1375 (29.1%)	2846 (60.3%)	1285 (66.9%)
Ustekinumab	0	27 (0.6%)	42 (2.2%)
Vedolizumab	0	25 (0.5%)	30 (1.6%)
Other[4]	0	0	0
Ulcerative Colitis			
	N=1784	N=1784	N=599
5-ASA[1]	354 (19.8%)	258 (14.5%)	62 (10.4%)
Corticosteroid[2]	828 (46.4%)	229 (12.8%)	42 (7.0%)
6-MP/AZA	185 (10.4%)	364 (20.4%)	122 (20.4%)
Methotrexate	53 (3.0%)	144 (8.1%)	56 (9.3%)
TNFi[3]	225 (12.6%)	565 (31.7%)	232 (38.7%)
Ustekinumab			1 (0.2%)
Vedolizumab	6 (0.3%)	58 (3.3%)	39 (6.5%)
Other[4]		1 (0.1%)	3 (0.5%)

N=Number of patients at the start time point of the interval

[1]5-ASA: balsalazine, mesalamine

[2]Corticosteroid: prednisone, budesonide, methylprednisolone

[3]Tumor necrosis factor inhibitor (TNFi): infliximab, adalimumab, certolizumab, golimumab, and their biosimilars

[4]Other: natalizumab, tofacitinib

UNDERSTANDING REAL-WORLD BIOLOGIC MAINTENANCE DOSING PATTERNS AMONG PEDIATRIC ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS

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Objectives: To assess the initial and long-term maintenance dosing of biologic medications in pediatric UC and CD patients, using data in the ICN registry.

Methods: Pediatric patients (2–17 years) in the US who were diagnosed with UC or CD between June 1, 2013 and December 31, 2019, who, after enrollment in the ICN registry, initiated a biologic (adalimumab, infliximab, certolizumab, golimumab, ustekinumab, vedolizumab, and natalizumab) and were actively followed for at least 12 months after first maintenance dose were included in this study. Descriptive statistics of baseline patient demographics were summarized for the overall Inflammatory Bowel Disease (IBD) patient population and separately for UC and CD. Biologic maintenance dosage was calculated for UC and CD patients who had data for both dose and weight for each biologic at the baseline visit (first maintenance dose), 1-year and 3-year time points.

Results: A total of 1,887 pediatric IBD patients (UC=350; CD=1,537) were included in this study. Patients had a mean age at diagnosis of 12.9 years (UC=13.1; CD=12.9), 57.1% were male (UC=48.9%; CD=59.0%), and 80.6% were White (UC=79.8%; CD=80.8%) (Table 1). Infliximab (77.0%) was the most commonly prescribed biologic for UC, followed by adalimumab (12.4%), vedolizumab (10.1%), certolizumab (0.3%), and ustekinumab (0.3%). Similarly, infliximab (80.6%) was the most commonly prescribed biologic for CD, followed by adalimumab (16.5%), vedolizumab (1.6%), ustekinumab (1.2%), and certolizumab (0.1%) (Table 2).

At first maintenance dose, UC patients on infliximab were receiving a mean dose of 10.5mg/kg/8wk, patients on adalimumab (weight <40kg) were receiving a mean dose of 1.3mg/kg/2wk, patients on adalimumab (weight≥40kg) were receiving a mean dose of 0.8mg/kg/2wk, and patients on vedolizumab were receiving a mean dose of 6.9mg/kg/8wks. Mean dose of infliximab among UC patients increased from 10.5mg/kg/8wk at first maintenance dose to 11.8mg/kg/8wk at 1-year from first maintenance dose.

At the first maintenance dose, CD patients on infliximab were receiving a mean dose of 8.1mg/kg/8wk, patients on adalimumab (weight <40kg) were receiving a mean dose of 1.1mg/kg/2wk, patients on adalimumab (weight ≥40kg) were receiving a mean dose of 0.8mg/kg/2wk, patients receiving vedolizumab were receiving a mean dose of 10.5mg/kg/8wks. Mean dose of infliximab among CD patients increased from 8.1mg/kg/8wk at first maintenance dose to 9.6mg/kg/8wk at 1-year from first maintenance dose.

Conclusion: These results highlight the biologic maintenance dose changes among pediatric UC and CD patients. TNF inhibitors remain the most commonly used class of biologic, but the doses being used are double the standard dosing guidelines. There is little evidence of dose reduction over time among pediatric UC and CD patients in the ICN registry.

Table 1: Demographic and baseline characteristics

	CD (N=1,537)	UC (N=350)	Overall (N=1887)
Age at diagnosis in years			
Min-Max	2.1-17.9	3.2-17.9	2.1-17.9
Mean (SD)	12.9 (3.00)	13.1 (3.42)	12.9 (3.08)
Median (Q1, Q3)	13.2 (10.9, 15.3)	13.8 (11.3, 15.6)	13.3 (11.0, 15.3)
Age group at diagnosis			
2 – 5	21 (1.4%)	11 (3.1%)	32 (1.7%)
6 – 11	385 (25.0%)	69 (19.7%)	454 (24.1%)
12 – 17	1131 (73.6%)	270 (77.1%)	1401 (74.2%)
Gender			
Male	907 (59.0%)	171 (48.9%)	1078 (57.1%)
Female	630 (41.0%)	179 (51.1%)	809 (42.9%)
Race			
Black	157 (13.4%)	24 (9.5%)	181 (12.7%)
White	950 (80.8%)	201 (79.8%)	1151 (80.6%)
Other	69 (5.9%)	27 (10.7%)	96 (6.7%)
Missing	361	98	459
Ethnicity			
Hispanic	63 (4.7%)	33 (11.3%)	96 (5.8%)
Non-Hispanic	1287 (95.3%)	260 (88.7%)	1547 (94.2%)
Missing	187	57	244
Baseline* weight (kg)			
N	1513	346	1859
Min-Max	13.4-148.2	12.2-119.4	12.2-148.2
Mean (SD)	49.7 (17.96)	55.3 (18.96)	50.7 (18.28)
Median (Q1, Q3)	48.2 (36.3, 60.8)	55.2 (44.0, 67.2)	49.4 (37.3, 61.8)
Baseline* height (cm)			
N	1501	342	1843
Min-Max	97.5-190.8	95.3-188.7	95.3-190.8
Mean (SD)	154.7 (16.87)	158.0 (17.79)	155.3 (17.08)
Median (Q1, Q3)	157.0 (143.5, 167.0)	161.0 (150.6, 169.5)	157.8 (144.6, 167.6)

* Baseline is at biologic initiation

Table 2: Dosing interval of standardized biologic maintenance dose at the specified time points/intervals

Biologic agent	First Maintenance dose	1-year from first Maintenance dose	3-year from first Maintenance dose	Last recorded Maintenance dose for patients who did not discontinue
Crohn's Disease				
Infliximab (mg/kg/8 weeks)				
N[1]	1302	1049	313	982
N-miss[2]	31	71	19	7
Min-Max	0.2-31.5	1.8-41.5	2.5-31.4	0.4-41.5
Mean (SD)	8.1 (4.17)	9.6 (4.63)	10.0 (4.93)	10.4 (5.04)
Median (Q1, Q3)	6.6 (5.1, 9.8)	8.7 (5.9, 11.7)	9.3 (6.0, 12.6)	9.7 (6.7, 12.7)
Adalimumab (mg/kg/2 weeks) (weight < 40kg)				
N	66	33	3	21
N-miss	1	1	1	0
Min-Max	0.3-5.4	0.5-3.6	0.6-2.7	0.5-2.7
Mean (SD)	1.1 (0.68)	1.2 (0.59)	1.5 (1.12)	1.2 (0.64)
Median (Q1, Q3)	1.0 (0.7, 1.3)	1.1 (0.8, 1.3)	1.1 (0.6, 2.7)	1.1 (0.7, 1.4)
Adalimumab (mg/kg/2 weeks) (weight >= 40kg)				
N	201	180	26	174
N-miss	4	9	2	0
Min-Max	0.3-3.3	0.2-2.7	0.4-2.0	0.3-3.1
Mean (SD)	0.8 (0.32)	0.8 (0.38)	0.9 (0.38)	0.8 (0.36)
Median (Q1, Q3)	0.8 (0.6, 0.9)	0.7 (0.6, 0.9)	0.7 (0.6, 1.2)	0.7 (0.6, 0.9)
Certolizumab (mg/kg/4 weeks)				
N	2	2		1
N-miss	0	0		0
Min-Max	10.9-11.1	6.1-10.6		5.8-5.8
Mean (SD)	11.0 (0.12)	8.3 (3.22)		5.8 (.)
Median (Q1, Q3)	11.0 (10.9, 11.1)	8.3 (6.1, 10.6)		5.8 (5.8, 5.8)
Ustekinumab (mg/kg/8 weeks)				
N	19	15		13
N-miss	0	2		0
Min-Max	0.4-4.9	1.0-3.8		0.4-3.7
Mean (SD)	2.3 (1.21)	2.4 (1.00)		2.2 (1.18)
Median (Q1, Q3)	1.9 (1.4, 3.3)	2.4 (1.4, 3.4)		2.1 (1.3, 3.4)
Vedolizumab (mg/kg/8 weeks)				
N	26	19	3	18
N-miss	0	1	0	1
Min-Max	3.7-24.0	4.7-22.3	4.4-12.1	4.2-31.6
Mean (SD)	10.5 (6.17)	9.8 (5.13)	7.1 (4.33)	11.1 (6.72)
Median (Q1, Q3)	7.8 (5.8, 15.3)	7.3 (5.3, 13.0)	4.8 (4.4, 12.1)	10.6 (6.5, 13.5)
Ulcerative Colitis				
Infliximab (mg/kg/8 weeks)				
N[1]	291	212	43	192
N-miss[2]	6	15	4	3
Min-Max	2.2-44.0	4.2-37.9	4.7-21.2	4.2-25.8
Mean (SD)	10.5 (5.55)	11.8 (5.53)	11.0 (4.53)	11.2 (4.77)
Median (Q1, Q3)	9.4 (6.0, 13.0)	10.2 (8.3, 14.0)	9.8 (7.6, 14.3)	10.1 (7.9, 13.4)
Adalimumab (mg/kg/2 weeks) (weight < 40kg)				
N	5	1		
N-miss	0	0		
Min-Max	1.0-2.0	1.1-1.1		
Mean (SD)	1.3 (0.41)	1.1 (.)		
Median (Q1, Q3)	1.1 (1.1, 1.3)	1.1 (1.1, 1.1)		
Adalimumab (mg/kg/2 weeks) (weight >= 40kg)				
N	42	28	5	30
N-miss	0	2	0	0
Min-Max	0.5-1.7	0.4-1.9	0.5-1.1	0.4-1.8
Mean (SD)	0.8 (0.27)	0.9 (0.38)	0.8 (0.28)	0.9 (0.35)
Median (Q1, Q3)	0.7 (0.5, 0.9)	0.8 (0.6, 1.1)	0.6 (0.6, 1.0)	0.8 (0.6, 1.0)
Certolizumab (mg/kg/4 weeks)				
N	1	1	1	
N-miss	0	0	0	
Min-Max	4.4-4.4	3.8-3.8	3.2-3.2	
Mean (SD)	4.4 (.)	3.8 (.)	3.2 (.)	
Median (Q1, Q3)	4.4 (4.4, 4.4)	3.8 (3.8, 3.8)	3.2 (3.2, 3.2)	
Ustekinumab (mg/kg/8 weeks)				
N	1	1		1
N-miss	0	0		0
Min-Max	2.8-2.8	2.9-2.9		2.9-2.9
Mean (SD)	2.8 (.)	2.9 (.)		2.9 (.)
Median (Q1, Q3)	2.8 (2.8, 2.8)	2.9 (2.9, 2.9)		2.9 (2.9, 2.9)
Vedolizumab (mg/kg/8 weeks)				
N	38	30	1	29
N-miss	0	1	0	0
Min-Max	2.0-15.7	2.5-21.7	9.9-9.9	2.8-16.3
Mean (SD)	6.9 (2.88)	7.2 (4.33)	9.9 (.)	6.6 (3.66)
Median (Q1, Q3)	6.2 (4.8, 8.7)	5.8 (4.2, 10.6)	9.9 (9.9, 9.9)	5.7 (4.1, 6.8)

[1]N is the number of patients on the specific biologic who had maintenance dose data at the specified time points.
[2]N-miss is the number of patients on the specific biologic at the specified time points but had missing data in maintenance dose.
No patient was on Golimumab or Natalizumab.

Epithelial Cell Biology/Function in Inflammation

ADENOSINE A3 RECEPTOR INTERACTS WITH GASDERMIN D TO MODULATE INTESTINAL EPITHELIAL CELL PYROPTOSIS IN ULCERATIVE COLITIS

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Background: Adenosine A3 receptor (A3AR) plays a role in intestinal inflammation, but little is known about its mechnisms in intestinal inflammation such as ulcerative colitis (UC). Pyroptosis, characterized by Gasdermin D (GSDMD) activation, is implicated in the pathogenesis of UC. We investigated the role of A3AR in GSDMD-mediated pyroptosis in UC and its underlying molecular mechanisms.

Methods: The expression of A3AR in colonic mucosa of patients with UC were examined. A3AR agonist was used to study the role of A3AR in ex vivo colonic explants of UC patients. In addition, human intestinal epithelial cells Caco-2 were used to further verify the effect of A3AR on pyroptosis induced by LPS+ATP. RT-qPCR and western blotting were used to detect the expression levels of pyroptosis-associated factors including NLRP3, caspase-1, gasdermin-D N-terminal domain (GSDMD-NT), IL-1β and IL-18 in colonic tissues and Caco-2 cells. Immunofluorescence was used to detect the protein expression in tissues and cells. Enzyme-linked immunosorbent assay was used to determine the levels of IL-1β and IL-18 in tissue and cell culture