



Utilisation of advanced treatments in inflammatory bowel disease in Slovenia – national report from UR-CARE Registry for the year 2023

Uporaba naprednih zdravil pri bolnikih s kronično vnetno črevesno boleznijo v Sloveniji – nacionalni podatki iz UR-CARE registra za leto 2023

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ABSTRACT

Background. Due to the increasing incidence of inflammatory bowel disease (IBD) many patients are being treated with biologicals and small molecules. Data on advanced treatments in Slovenian IBD patients was lacking until recently. In 2020 Slovenia joined the European UR-CARE Registry. This article covers our second national epidemiological report from the UR-CARE Registry for 2023.

Aim. To characterise the use of advanced treatments in Slovenian IBD centres from inception of the registry until October 2023.

Material and Methods. Total UR-CARE Registry data were analysed with data lock on 1st October 2023.

Results. Out of 3759 IBD patients treated in Slovenian IBD centres in the year 2023, 1289 of Crohn's disease (CD) and 811 of ulcerative colitis (UC) patients received biological therapy. Overall, TNF-alpha inhibitors were preferred as first-line therapy in CD (adalimumab (39.6%), infliximab (34.9%)), and in UC (infliximab (35.5%), adalimumab (11.1%), golimumab (9.2%)). Ustekinumab dominated second and third-line biological therapy in CD (30.3%, 40.0%, respectively) and vedolizumab in UC (35.2%, 33.8%, respectively). Over half of patients persisted with their first-line treatment (CD 57.5%, UC 59.7%) at the end of follow-up. Persistence rates were higher for first-line ustekinumab (CD 77.7%, UC 81.8%) and vedolizumab (CD 75.6%, UC 66.7%), than for TNF-alpha inhibitors (infliximab: CD 47.1%, UC 45.5%, adalimumab: CD 49.1%, UC 40.0%). Prescription trends changed in 2023 in UC as vedolizumab was the most common first-line biological (57.7%). In CD, also in 2023 TNF-alpha inhibitors remained the most common first-line treatment chosen in slightly more than half of the patients. Janus kinase inhibitors use was low (104 patients).

Conclusions. Biological treatment patterns in Slovenia are comparable with those in the European Union. In 2023 inhibitors of TNF-alpha remain the

IZVLEČEK

Izhodišča. Incidenca kronične vnetne črevesne bolezni (KVČB) narašča in vse več bolnikov je zdravljenih z biološkimi zdravili in malimi molekulami. Podatki o naprednem zdravljenju slovenskih bolnikov s KVČB so bili do nedavnega pomanjkljivi. Leta 2020 se je Slovenija pridružila evropskemu registru UR-CARE. V članku je zajeto naše drugo epidemiološko poročilo registra UR-CARE za leto 2023.

Namen. Opredeliti uporabo naprednih zdravil v slovenskih centrih za KVČB od pričetka registra do oktobra 2023.

Metode. Analizirali smo podatke o naprednem zdravljenju bolnikov s KVČB, zbrane v UR-CARE registru do oktobra 2023.

Rezultati. V letu 2023 smo v Sloveniji zdravili 3759 KVČB bolnikov, od tega je biološko terapijo prejelo 1289 bolnikov s Crohnovo boleznijo (CB) in 811 bolnikov z ulceroznim kolitisom (UK). Zaviralci TNF-alfa so bili najpogosteje predpisano zdravilo prvega reda pri CB (adalimumab (39,6 %) in infliximab (34,9 %)) in pri UK (infliximab (35,5 %), adalimumab (11,1 %) in golimumab (9,2 %)). V drugi in tretji liniji biološke terapije pri CB je bil najpogosteje predpisan ustekinumab (30,3 % in 40,0 %), pri UK pa vedolizumab (35,2 % in 33,8 %). Ob izvozu podatkov iz registra je več kot polovica vseh bolnikov vztrajala z zdravilom prvega reda (CB 57,5 %, UK 59,7 %), pri čemer je bil delež vztrajajočih višji na ustekinumabu (CB 77,7 %, UK 81,8 %) in vedolizumabu (CB 75,6 %, UK 66,7 %) kot na zaviralcih TNF-alfa (infliximab: CB 47,1 %, UK 45,5 %, adalimumab: CB 49,1 %, UK 40,0 %). Trend predpisovanja biološke terapije v letu 2023 se je pri UK spremenil, najpogosteje predpisana prva linija terapije je bil vedolizumab (57,7 %). Pri CB so zaviralci TNF-alfa tudi v letu 2023 ostali najpogosteje predpisana prva linija terapije. Uporaba zaviralcev janus kinaz (JAK) je bila nizka (104 bolniki).

Zaključki. Vzorci predpisovanja bioloških zdravil v Sloveniji so podobni kot v drugih državah Evropske

most common first-line treatment in CD, but not in UC with vedolizumab being the most common first line choice. Prescription of JAK inhibitors was low.

unije. Zaviralci TNF-alfa tudi v letu 2023 ostajajo najbolj pogosto predpisana biološka zdravila prvega reda pri bolnikih s CB. Bolniki z UK so imeli najbolj pogosto predpisano kot prvo napredno zdravilo vedolizumab. Uporaba JAK zaviralcev je bila nizka.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic condition that continues to increase in incidence worldwide (1, 2). Several new treatments have become available recently, including monoclonal antibodies against tumour necrosis factor alpha, integrins, interleukins, and Janus kinase inhibitors (3), have become available in recent years.

Data on biological treatment in Slovenian IBD patients was lacking until recently. In 2020, Slovenia joined the European UR-CARE Registry. The UR-CARE platform is an established register for patients with IBD in Europe. We started entering data at the end of 2020 and our first national epidemiological report from the register, which included 6 centres, was published in 2022 (4). This report suggested that using biologicals in Slovenia was similar to that in Western Europe. Still, TNF-alpha inhibitors were the most prescribed biologicals in Slovenia in 2022. Another report (5) of Slovenian data suggested that treatment patterns were similar in Slovenian IBD centres, irrespective of whether being academic or non-academic centres.

As UR-CARE Registry is a continuous project we aim to analyse data every year. Two additional General Hospitals (GH) were included in the UR-CARE Registry-GH Slovenj Gradec and GH Nova Gorica, adding to the granularity of the epidemiological data in Slovenia since 2022.

This report updated Slovenian national UR-CARE Registry data that focuses on disease patterns and treatment patterns with advanced drugs until October 2023.

MATERIALS AND METHODS

We analysed the biological treatment and Janus kinase treatment (JAK) (together referred to as advanced treatments) of inflammatory bowel disease (IBD) patients in Slovenia. Patient data was prospectively collected from the UR-CARE Registry with data lock on 1st October 2023. The registry included data from the following medical centres: University Medical Centre Ljubljana (UMC Ljubljana), University Medical Centre Maribor (UMC Maribor), General Hospital Celje (GH Celje), General Hospital Izola (GH Izola), General Hospital Jesenice (GH Jesenice), General Hospital Slovenj Gradec (GH Slovenj Gradec), Diagnostic centre Bled (DC Bled) and General Hospital Nova Gorica (GH Nova Gorica). After exporting the data from the UR-CARE registry, data collection and analysis were performed using Microsoft Excel software (version 2301, build 16.0.16026.20196) and SPSS 21.0 (IBM Inc., Chicago, USA). Descriptive statistics are presented as the means \pm standard deviations for parametric variables and percentages for categorical variables. This study was approved by the National Medical Ethics Committee of Slovenia (ID 0120-576/2019/7).

RESULTS

Patient characteristics

At this data lock the UR-CARE Registry included 3759 patients with IBD. The majority of patients were diagnosed with Crohn's disease (CD; 48.2%), followed by ulcerative colitis (UC; 46.8%) and only a small number of patients were diagnosed with IBD unclassified (3.1%). A minority of data regarding the diagnosis (2.0%) were missing from the registry and were classified as missing. The genders were equally

distributed (male 50.7%, female 48.6%, missing data 0.7%). The age at diagnosis was 35.4 (standard deviation (SD) 15.3) and it was similar in most centres with except for GH Izola (40.4; SD 15.0), GH Jesenice (41.1; SD 17.3) and GH Slovenj Gradec (49.5; SD 16.0).

The majority of patients (45.0%) have never smoked and have no family history of IBD (71.5%). Only a minority of patients (9.0%) had a positive family history of IBD. Family history data were missing in 735 patients (19.5%). Patient demographics are shown in Table 1.

Table 1. Patient characteristics

	All centres (N=3759)	Ljubljana (n=2354)	Maribor (n=519)	Celje (n=278)	Izola (n=273)	Jesenice (n=109)	Slovenj Gradec (n=103)	Bled (n=85)	Nova Gorica (n=38)
Current age [years]	48,5 ±15,8	48,4 ±16,0	46,4 ±15,0	47,4 ±15,5	53,3 ±15,0	50,5 ±17,3	49,4 ±15,4	46,2 ±12,8	48,6 ±14,8
Age at diagnosis [years]	35,4 ±15,3	34,8 ±15,5	33,0 ±14,1	35,9 ±14,8	40,4 ±15,0	41,1 ±17,3	49,5 ±16,0	35,8 ±12,6	36,4 ±13,6
Gender									
Male	1905 (50,7%)	1123 (47,7%)	253 (48,7%)	144 (51,8%)	134 (49,1%)	58 (53,2%)	48 (46,6%)	44 (51,8%)	21 (55,3%)
Female	1825 (48,6%)	1231 (52,3%)	266 (51,3%)	125 (45,0%)	138 (50,5%)	40 (36,7%)	49 (47,6%)	40 (47,0%)	16 (42,1%)
Missing info	29 (0,8%)	0	0	9 (1,2%)	1 (0,4%)	11 (10,1%)	6 (5,8%)	1 (1,2%)	1 (2,6%)
Status of follow-up (database)*									
Ongoing	3671 (97,7%)	2308 (98,0%)	518 (99,8%)	255 (98,8%)	272 (99,6%)	108 (99,1%)	96 (93,2%)	84 (98,8%)	30 (78,9%)
End of follow-up	47 (1,3%)	45 (1,9%)	1 (0,2%)	1	0	0	0	0	0
Missing info	41 (1,1%)	1 (0,1%)	0	22 (3,2%)	1 (0,4%)	1 (0,9%)	7 (6,8%)	1 (1,2%)	8 (21,1%)
Diagnosis									
Crohn's disease	1810 (48,2%)	1134 (48,2%)	277 (53,4%)	136 (48,9%)	142 (52,0%)	35 (32,1%)	38 (36,9%)	37 (43,5%)	11 (28,9%)
Ulcerative colitis	1758 (46,8%)	1138 (48,3%)	178 (34,3%)	125 (45,0%)	122 (44,7%)	66 (60,6%)	59 (57,3%)	45 (52,9%)	25 (65,8%)
IBD unclassified	117 (3,1%)	82 (3,5%)	14 (2,7%)	7 (2,5%)	6 (2,2%)	5 (4,6%)	2 (1,9%)	1 (1,2%)	0
Missing data	74 (2,0%)	0	50 (9,6%)	10 (3,6%)	3 (1,1%)	3 (2,8%)	4 (3,9%)	2 (2,4%)	2 (5,3%)
Smoking									
Yes	486 (12,9%)	379 (16,1%)	21 (4,0%)	28 (10,0%)	7 (2,6%)	20 (18,3%)	21 (20,4%)	10 (11,8%)	0
Previous smoker	767 (20,4%)	661 (28,1%)	31 (6,0%)	31 (11,2%)	6 (2,2%)	16 (14,7%)	16 (15,5%)	6 (7,1%)	0
No	1691 (45,0%)	1279 (54,3%)	79 (15,2%)	120 (43,2%)	25 (9,2%)	65 (59,6%)	58 (56,3%)	62 (72,9%)	3 (7,9%)
Info not available	396 (10,5%)	26 (1,1%)	20 (3,9%)	86 (30,9%)	232 (85,0%)	5 (4,6%)	2 (1,9%)	5 (5,9%)	20 (52,6%)
Missing info	419 (11,1%)	9 (0,4%)	368 (70,9%)	13 (4,7%)	3 (1,1%)	3 (2,8%)	6 (5,8%)	2 (2,4%)	15 (39,5%)

Table 1. Continued

	All centres (N=3759)	Ljubljana (n=2354)	Maribor (n=519)	Celje (n=278)	Izola (n=273)	Jesenice (n=109)	Slovenj Gradec (n=103)	Bled (n=85)	Nova Gorica (n=38)
Family history									
Yes	338 (9,0%)	283 (12,0%)	13 (2,5%)	11 (4,0%)	6 (2,2%)	8 (7,3%)	10 (9,7%)	7 (8,2%)	0
No	2686 (71,5%)	2035 (86,4%)	113 (21,8%)	153 (55,0%)	128 (46,9%)	97 (89,0%)	82 (79,6%)	73 (85,9%)	5 (13,2%)
Info not available	305 (8,1%)	24 (1,0%)	19 (3,7%)	100 (36,0%)	136 (49,8%)	0	4 (3,9%)	3 (3,5%)	19 (50,0%)
Missing info	430 (11,4%)	12 (0,5%)	374 (72,1%)	14 (5,0%)	3 (1,1%)	4 (3,7%)	7 (6,8%)	2 (2,4%)	14 (36,8%)

Disease phenotype

In three medical centres (UMC Maribor, GH Celje and GH Izola), the majority of patients had CD. In UMC Ljubljana, the proportion of patients with CD and UC was comparable (CD 48.2%, UC 48.3%). In the other four medical centres (GH Jesenice, GH Slovenj Gradec, GH Nova Gorica and DC Bled), more patients had UC.

Figure 1 shows disease extension for all Slovenian IBD centres for CD, and Figure 2 for UC patients. Seventy-two percent of patients with CD had ileal involvement and approximately half had colonic disease. Approximately 40% of UC patients had disease extension beyond the splenic flexure. Most, but not all, patients with UC had an affected rectum (96.4%).

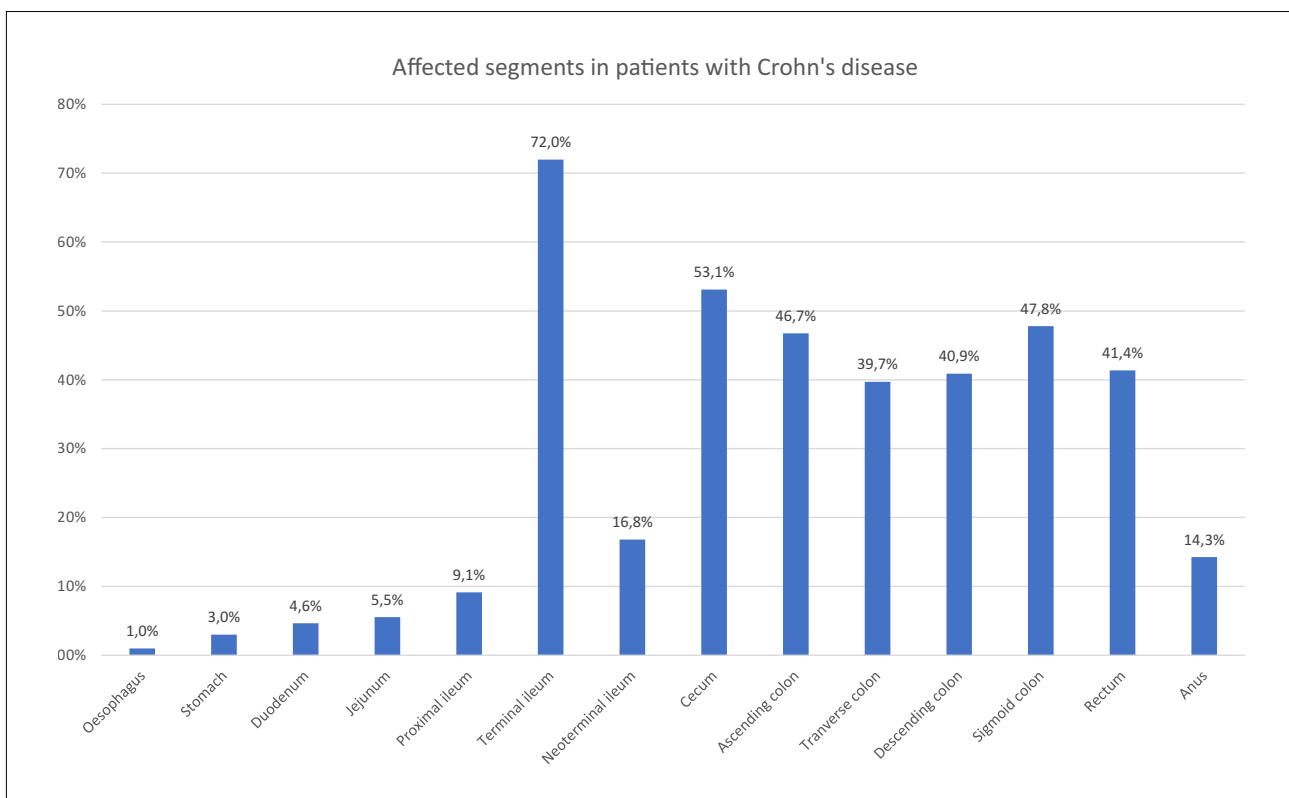


Figure 1. Disease extension in patients with Crohn's disease in all Slovenian Inflammatory bowel disease centres

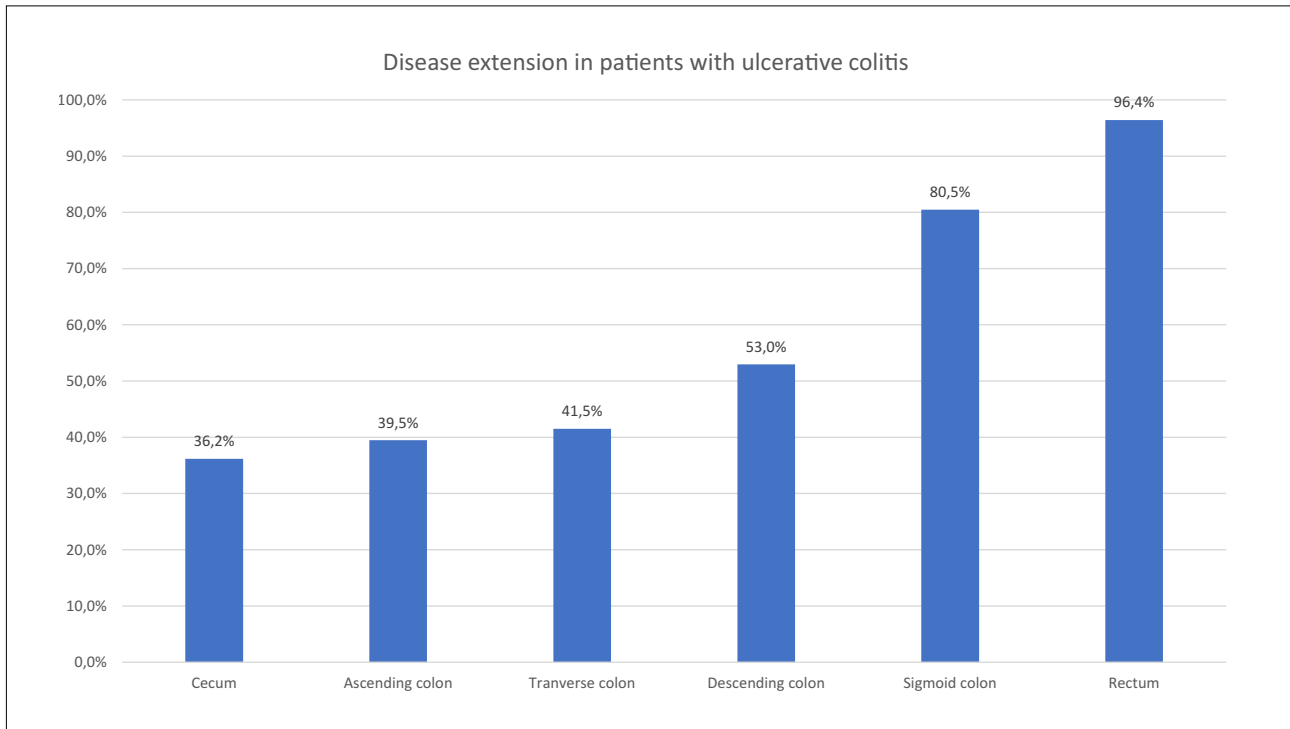


Figure 2. Disease extension patients with ulcerative colitis in all Slovenian Inflammatory bowel disease centres

The proportions of CD patients with risk factors for disease complications (ileal disease, perianal disease) were similar in most centres, except for GH Izola and DC Bled, where more patients had the ileal disease, and GH Izola, GH Slovenj Gradec, GH Nova Gorica and DC Bled, where less patients had perianal disease. In total, the perianal disease was detected in 354 (19.6%) out of 1810 patients with CD.

Patients with CD were on average younger than patients with UC at diagnosis. The median age at diagnosis for CD was 33.7 years (SD 15.1) and for UC 37.0 years (SD 15.3). Extraintestinal manifestations (EIM) were present in 18.7%. Overall characteristics of patients were similar between all medical centres. Phenotype data for every IBD centre are shown in Table 2.

Advanced treatments used in patients with Crohn's disease

In total, 1289 patients with CD received 2199 treatment episodes with biological drugs. The most commonly prescribed first-line treatments (overall, from the inception of the registry) were TNF-alpha inhibitors

(adalimumab 39.6% and infliximab 34.9%), followed by vedolizumab (13.0%) and ustekinumab (12.2%). As a second, third and fourth line of treatment, the most frequently prescribed biological was

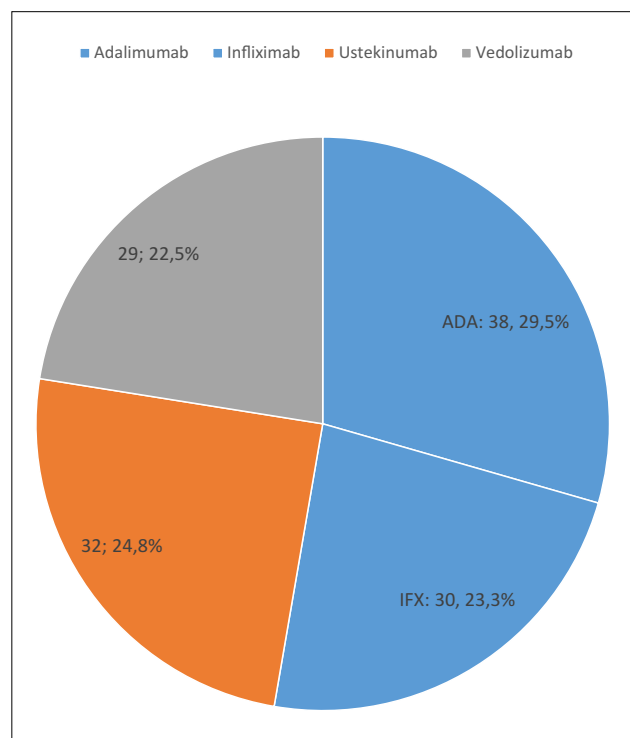


Figure 3. Choice of first-line biological in Crohn's disease in 2023 in Slovenia

Table 2. Disease phenotype in inflammatory bowel disease centres in Slovenia

	All centres	UMC Ljubljana	UMC Maribor	GH Celje	GH Izola	GH Jesenice	GH Slovenj Gradec	GH Nova Gorica	DC Bled
Total number of patients with IBD***	3759	2354	519	278	273	109	103	38	85
Crohn's disease*- N (%)	1810 (48,2%)	1134 (48,2%)	277 (53,4%)	136 (48,9%)	142 (52,0%)	35 (32,1%)	38 (36,9%)	11 (28,9%)	37 (43,5%)
Ulcerative colitis**- N (%)	1758 (46,8%)	1138 (48,3%)	178 (34,3%)	125 (45,0%)	122 (44,7%)	66 (60,6%)	59 (57,3%)	25 (65,8%)	45 (52,9%)
IBDU - N (%)	117 (3,1%)	82 (3,5%)	14 (2,7%)	7 (2,5%)	6 (2,2%)	5 (4,6%)	2 (1,9%)	0	1 (1,2%)
Crohn's with isolated ileum disease - N (% of all CD)	394 (21,8%)	260 (22,9%)	46 (16,6%)	29 (21,3%)	24 (16,9%)	14 (40,0%)	4 (10,5%)	2 (18,2%)	15 (40,5%)
Crohn's with ileocolonic disease - N (% of all CD)	67 (3,7%)	43 (3,8%)	8 (2,9%)	6 (4,4%)	3 (2,1%)	3 (8,6%)	4 (10,5%)	0	0
Crohn's perianal - N (% of all CD)	354 (19,6%)	235 (20,7%)	63 (22,7%)	26 (19,1%)	15 (10,6%)	6 (17,1%)	4 (10,5%)	1 (9,1%)	4 (10,8%)
Age at diagnosis CD [years]	33,7 ±15,1	33,0 ±15,4	32,5 ±13,7	34,2 ±14,7	39,2 ±14,5	40,1 ±17,2	37,1 ±17,4	36,3 ±12,4	33,5 ±10,1
Age at diagnosis UC [years]	37,0 ±15,3	36,4 ±15,2	33,7 ±14,6	37,9 ±14,8	41,7 ±15,4	41,9 ±17,6	40,2 ±17,8	36,5 ±14,3	37,7 ±14,3
Disease duration until biologic initiation [years]	10,2 ±9,3	10,7 ±9,3	10,1 ±8,9	7,9 ±8,3	9,6 ±9,3	8,7 ±7,4	8,7 ±9,6	7,9 ±8,6	9,4 ±8,1
Extraintestinal manifestations - N (% of all IBD patients)	703 (18,7%)	520 (22,1%)	62 (11,9%)	43 (15,5%)	29 (10,6%)	29 (26,6%)	10 (9,7%)	0	10 (11,8%)

*UMC – University Medical centre, GH – General hospital, DC – Diagnostic centre, IBDU – inflammatory bowel disease unclassified, CD – Crohn's disease, UC – ulcerative colitis

ustekinumab (30.3%, 40.0%, 38.0%, respectively), followed by vedolizumab (14.2%, 20.8%, 23.9%, respectively).

Patients with CD discontinued first-line biologicals in 42.5% (548/1289), second-line biologicals in 18.2% (235/1289) and third-line biologicals in 7.1% (92/1289). Detailed prescription sequence of biologicals in CD is shown in Table 3.

Drug utilisation in the year 2023

In 2023, the most common biologicals started as first-line treatment were TNF-alpha inhibitors (adalimumab 29.4% and infliximab 23.3%), followed

by ustekinumab (24.8%) and vedolizumab (22.5%) (Figure 3). Patients with CD started first-line biological in 2023 after a median of 2.53 months from the diagnosis.

Out of 1289 patients with CD, 713 (55.3%) were still treated with a first-line biological at the time of data export, 267 (20.7%) with a second line and 116 (9.0%) with a third-line biological. The proportion of patients that persisted with the first-line biological was the highest for ustekinumab (122/157, 77.7%), followed by vedolizumab (127/168, 75.6%), infliximab (212/450, 47.1%) and adalimumab (251/511, 49.1%). Several patients with CD who persisted on specific biological are shown in Table 4.

Table 3. Number of prescriptions (treatment episodes) in respective lines of therapy for Crohn's disease (from the inception of UR-CARE Registry)

Line	All	Adalimumab / biosimilars	Adalimumab / Humira	Certolizumab	Golimumab	Guselkumab	Infliximab/ biosimilars	Infliximab/ Remicade	Natalizumab	Risankizumab	Ustekinumab	Vedolizumab
First line	1289	200 (15,5%)	311 (24,1%)	2 (0,2%)	0	0	259 (20,1%)	191 (14,8%)	1 (0,1%)	0	157 (12,2%)	168 (13,0%)
Second line	548	35 (6,4%)	116 (21,2%)	1 (0,2%)	0	0	101 (18,4%)	49 (8,9%)	1 (0,2%)	1 (0,2%)	166 (30,3%)	78 (14,2%)
Third line	235	10 (4,3%)	32 (13,6%)	2 (0,9%)	0	0	34 (14,5%)	14 (6,0%)	0	0	94 (40,0%)	49 (20,9%)
Fourth line	92	6 (6,5%)	5 (5,4%)	0	0	0	15 (16,3%)	9 (9,8%)	0	0	35 (38,0%)	22 (23,9%)
Fifth line	28	1 (3,6%)	2 (7,1%)	1 (3,6%)	2 (7,1%)	3	5 (17,9%)	2 (7,1%)	0	0	4 (14,3%)	8 (28,6%)
Sixth line	6	1 (16,7%)	3 (50,0%)	0	0	1 (16,7%)	0	0	0	0	0	1 (16,7%)
Seventh line	1	0	0	0	0	0	0	0	0	0	0	1 (100%)
Total*	2199	253 (11,5%)	469 (21,3%)	6 (0,3%)	2 (0,1%)	4 (0,2%)	414 (18,8%)	265 (12,0%)	2 (0,1%)	1 (0,05%)	456 (20,7%)	327 (14,9%)

Table 4. Number of patients, who remained on biologic in respective line of treatment for Crohn's disease (from inception of UR-CARE Registry)

Line	All	Adalimumab / biosimilars	Adalimumab / Humira	Certolizumab	Golimumab	Guselkumab	Infliximab/ biosimilars	Infliximab/ Remicade	Natalizumab	Risankizumab	Ustekinumab	Vedolizumab
First line	713	119 (16,7%)	132 (18,5%)	0	0	0	149 (20,9%)	63 (8,8%)	1 (0,1%)	0	122 (17,1%)	127 (17,8%)
Second line	267	17 (6,4%)	28 (10,5%)	0	0	0	57 (21,3%)	7 (2,6%)	1 (0,4%)	0	130 (48,7%)	27 (10,1%)
Third line	116	2 (1,7%)	3 (2,6%)	0	0	0	18 (15,5%)	2 (1,7%)	0	0	68 (58,6%)	23 (19,8%)
Fourth line	50	3 (6,0%)	4 (8,0%)	0	0	0	7 (14,0%)	1 (2,0%)	0	0	24 (48,0%)	11 (22,0%)
Fifth line	14	1 (7,1%)	0	0	0	3 (21,4%)	3 (21,4%)	0	0	0	4 (28,6%)	3 (21,4%)
Sixth line	2	1 (50,0%)	0	0	0	0	0	0	0	0	0	1 (50,0%)
Seventh line	1	0	0	0	0	0	0	0	0	0	0	1 (100%)
Total*	1163	143 (12,3%)	167 (14,4%)	0	0	3 (0,3%)	234 (20,1%)	73 (6,3%)	2 (0,2%)	0	348 (29,9%)	193 (16,6%)

Table 5. Number of prescriptions (treatment episodes) in respective lines of therapy for ulcerative colitis (from the inception of UR-CARE Registry)

Line	All	Adalimumab / biosimilars	Adalimumab / Humira	Certolizumab	Golimumab	Guselkumab	Infliximab/ biosimilars	Infliximab/ Remicade	Natalizumab	Risankizumab	Ustekinumab	Vedolizumab
First line	811	31 (3,8%)	59 (7,3%)	0	75 (9,2%)	0	191 (23,6%)	97 (12,0%)	0	0	55 (6,8%)	303 (37,4%)
Second line	327	13 (4,0%)	43 (13,1%)	0	13 (4,0%)	0	78 (23,9%)	25 (7,6%)	0	1 (0,3%)	39 (11,9%)	115 (35,2%)
Third line	151	4 (2,6%)	0	0	4 (2,6%)	0	30 (19,9%)	4 (2,6%)	0	3 (2,0%)	47 (31,1%)	51 (33,8%)
Fourth line	40	1 (2,5%)	8 (20,0%)	0	1 (2,5%)	0	7 (17,5%)	3 (7,5%)	0	0	19 (47,5%)	7 (17,5%)
Fifth line	11	0	0	0	2 (18,2%)	0	1 (9,1%)	4 (36,4%)	0	0	3 (27,3%)	1 (9,1%)
Sixth line	2	0	1 (50,0%)	0	0	0	0	0	0	0	1 (50,0%)	0
Seventh line	0	0	0	0	0	0	0	0	0	0	0	0
Total*	1342	49 (3,7%)	111 (8,3%)	0	95 (7,1%)	0	307 (22,9%)	134 (10,0%)	0	4 (0,3%)	164 (12,2%)	478 (35,6%)

Advanced treatments used in patients with ulcerative colitis

In UC, 811 patients received 1342 treatment episodes with biologicals in total. The most commonly prescribed first-line treatments (overall, from the inception of the registry) were TNF-alpha inhibitors (all TNF-alpha inhibitors together 55.8%: infliximab 35.5%, adalimumab 11.1% and golimumab 9.2%), followed by vedolizumab (37.4%) and ustekinumab (6.8%). As a second and third-line drug vedolizumab was the most frequently prescribed among all biologicals (35.2% and 33.8%, respectively) and ustekinumab as a fourth-line of treatment (47.5%).

Patients with UC discontinued first-line biologicals in 40.3% (327/811), second-line biologicals in 18.6% (151/811) and third-line biologicals in 4.9% (40/811). The detailed prescription sequence of biologicals in UC is shown in Table 5. The median time to the initiation of first-line biological in 2023 was 3.63 months after the diagnosis.

Drug utilization in year 2023

In 2023 the most common first-line treatment was vedolizumab (57.7%), followed by TNF-alpha inhibitors (all TNF-alpha inhibitors together 34.7%: infliximab 19.3%, adalimumab 6.7% and golimumab 8.7%) and ustekinumab (7.7%) (Figure 4).

Prescriptions of JAK inhibitors among Slovenian IBD centres are presented in Table 6. Tofacitinib was prescribed in 83 patients, filgotinib in 12 and upadacitinib in 9 patients with UC. The proportion of patients that persisted with JAK inhibitors was 45.8% (38/83) for tofacitinib, 83.3% (10/12) for filgotinib and 77.8% (7/9) for upadacitinib at the time of data lock.

Out of 811 patients with UC, 437 (53.9%) were still being treated with a first-line biological, 130 (16.0%) with a second-line and 76 (9.4%) with a third-line biological. The proportion of patients that persisted with the first-line biological was the highest for ustekinumab (45/55, 81.8%), followed by vedolizumab

Table 6. Prescriptions of janus kinase inhibitors among Slovenian Inflammatory Bowel Disease centres (from inception of UR-CARE Registry)

	All centres	UMC Ljubljana	UMC Maribor	GH Celje	GH Izola	GH Jesenice	GH Slovenj Gradec	GH Nova Gorica	DC Bled
tofacitinib									
Ever treated	83	52 (62,7%)	17 (20,5%)	3 (3,6%)	3 (3,6%)	3 (3,6%)	0	0	5 (6,0%)
Ongoing	38	17 (44,7%)	11 (28,9%)	1 (2,6%)	2 (5,3%)	3 (7,9%)	0	0	4 (10,5%)
filgotinib									
Ever treated	12	11 (91,7%)	1 (8,3%)	0	0	0	0	0	0
Ongoing	10	9 (90,0%)	1 (10,0%)	0	0	0	0	0	0
upadacitinib									
Ever treated	9	9 (100%)	0	0	0	0	0	0	0
Ongoing	7	7 (100%)	0	0	0	0	0	0	0

*UMC – University Medical centre, GH – General hospital, DC – Diagnostic centre

Table 7. Number of patients, who remained on biologic in the respective line of treatment for ulcerative colitis (from the inception of UR-CARE Registry)

Line	All	Adalimumab / biosimilars	Adalimumab / Humira	Certolizumab	Golimumab	Guselkumab	Infliximab/ biosimilars	Infliximab/ Remicade	Natalizumab	Risankizumab	Ustekinumab	Vedolizumab
First line	437	14 (3,2%)	22 (5,0%)	0	23 (5,3%)	0	98 (22,4%)	33 (7,6%)	0	0	45 (10,3%)	202 (46,2%)
Second line	130	6 (4,6%)	7 (5,4%)	0	4 (3,1%)	0	23 (17,7%)	3 (2,3%)	0	1 (0,8%)	23 (17,7%)	63 (48,5%)
Third line	76	1 (1,3%)	1 (1,3%)	0	1 (1,3%)	0	15 (19,7%)	0	0	1 (1,3%)	32 (42,1%)	25 (32,9%)
Fourth line	22	0	0	0	0	0	5 (22,7%)	1 (4,5%)	0	0	13 (59,1%)	3 (13,6%)
Fifth line	6	0	0	0	2 (33,3%)	0	1 (16,7%)	0	0	0	3 (50,0%)	1 (16,7%)
Sixth line	1	0	0	0	0	0	0	0	0	0	1 (100%)	0
Seventh line	0	0	0	0	0	0	0	0	0	0	0	0
Total*	673	21 (3,1%)	30 (4,5%)	0	30 (4,5%)	0	142 (21,1%)	37 (5,5%)	0	2 (0,3%)	117 (17,4%)	294 (43,7%)

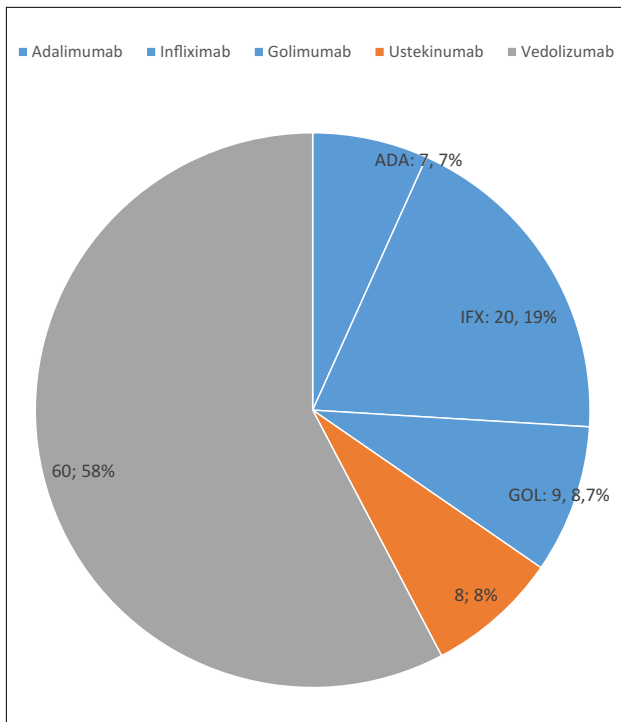


Figure 4. First-line biological in ulcerative colitis in 2023

(202/303, 66.7%), infliximab (131/288, 45.5%), adalimumab (36/90, 40.0%) and golimumab (23/75, 30.7%). The number of patients with UC that persisted with biological treatment is shown in Table 7.

Clinical disease activity

Patient-reported outcomes for CD are summarised in Figure 5–7.

The majority of patients had no abdominal pain (75.8%), bowel movements were normal (56.1%) and were generally feeling good (78.7%).

Patient-reported outcomes for UC are summarised in Figure 8–10.

The majority of patients had normal bowel movements (60.7%), no rectal bleeding (80.3%) and normal PGA (81.2%).

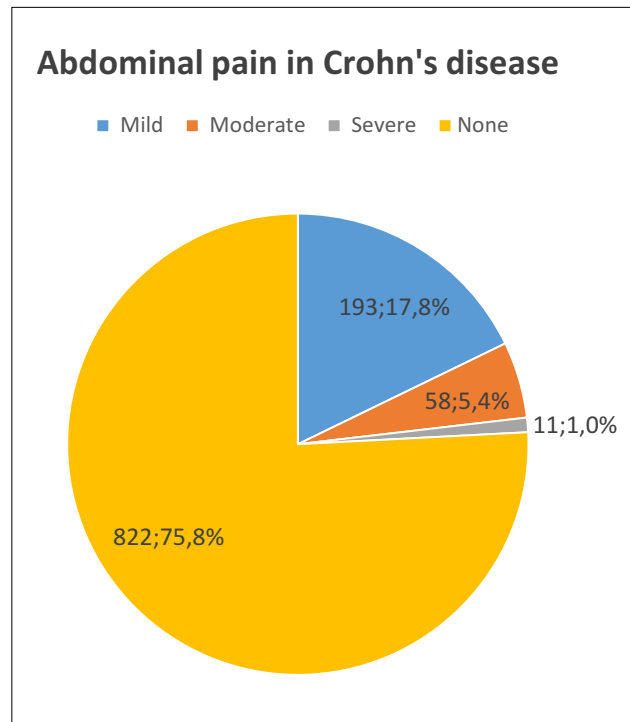


Figure 5. Abdominal pain score in Crohn's disease

DISCUSSION

This article covers our second national epidemiological report from UR-CARE Registry for 2023. Our analysis demonstrated that the usage of advanced treatments in Slovenia is in line with other countries in

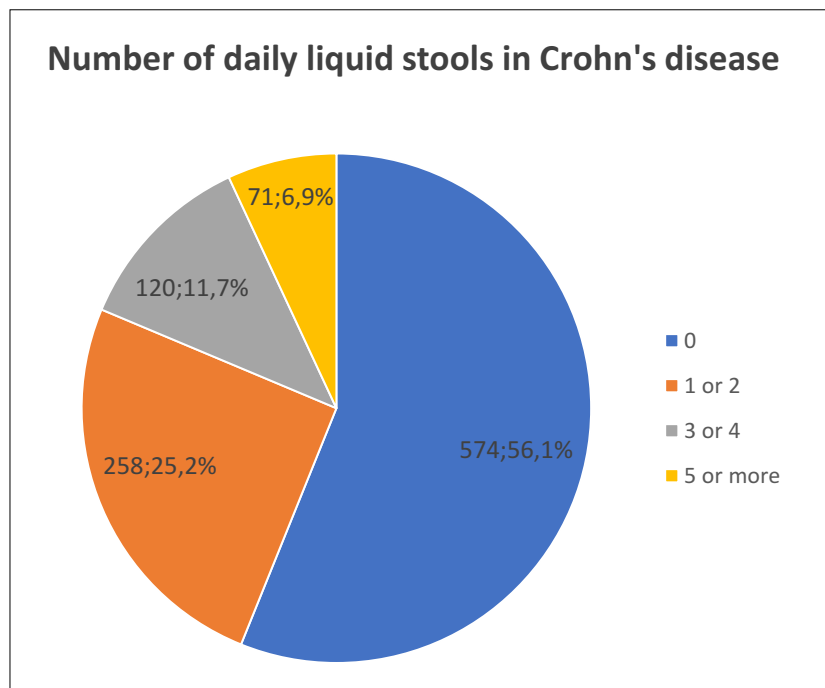


Figure 6. Daily liquid stools in Crohn's disease

Western Europe. The strength of this study is that we reported data on therapy used across 8 Slovenian IBD centres, 2 academic and 6 non-academic centres. Inhibitors of TNF-alpha remain the most common first-line drug in Crohn's disease also in 2023 as this was the drug of choice in approximately half of the pa-

tients. In ulcerative colitis, vedolizumab was the most common first-line treatment in 2023 as this was prescribed as first-line biological in more than half of the cases. JAK inhibitors are not a common choice in Slovenia in 2023.

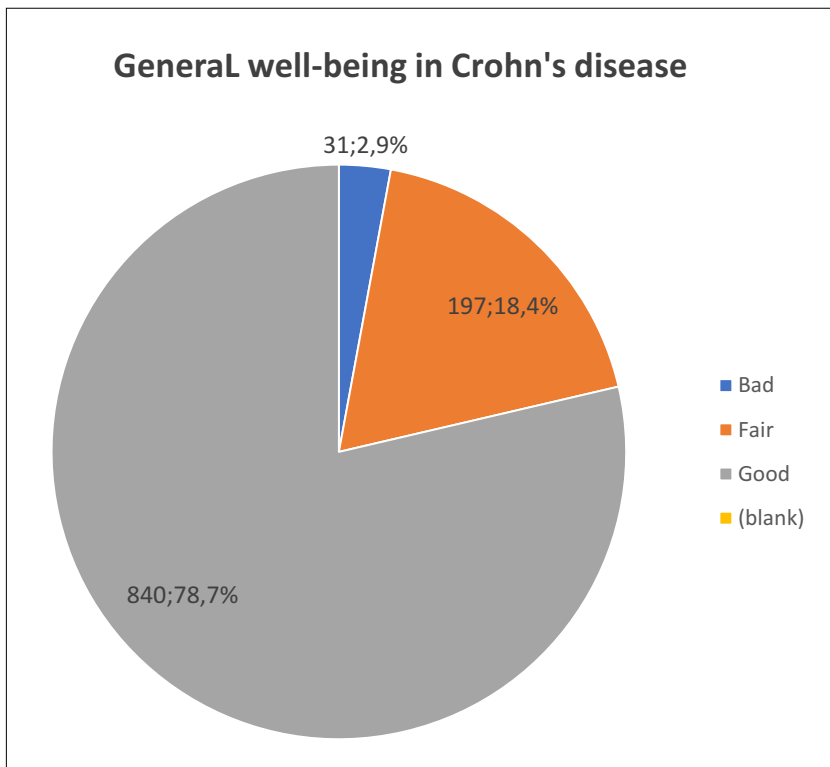


Figure 7. General well-being in Crohn's disease

The disease phenotype and disease location of our IBD patients were roughly similar in all Slovenian IBD centres and comparable with those reported by others (6). The proportion of extraintestinal manifestations was comparable with the literature (7–9), but we might have underestimated its true incidence as data capture was insufficient across all centres. The observed proportion of perianal fistulizing disease in patients with CD (19.6%) was similar to the reported literature (10–14). Generally, IBD phenotypes and treatment choices were comparable between all IBD centres (5). This can be explained of good access and support from the multidisciplinary meetings in academic centres.

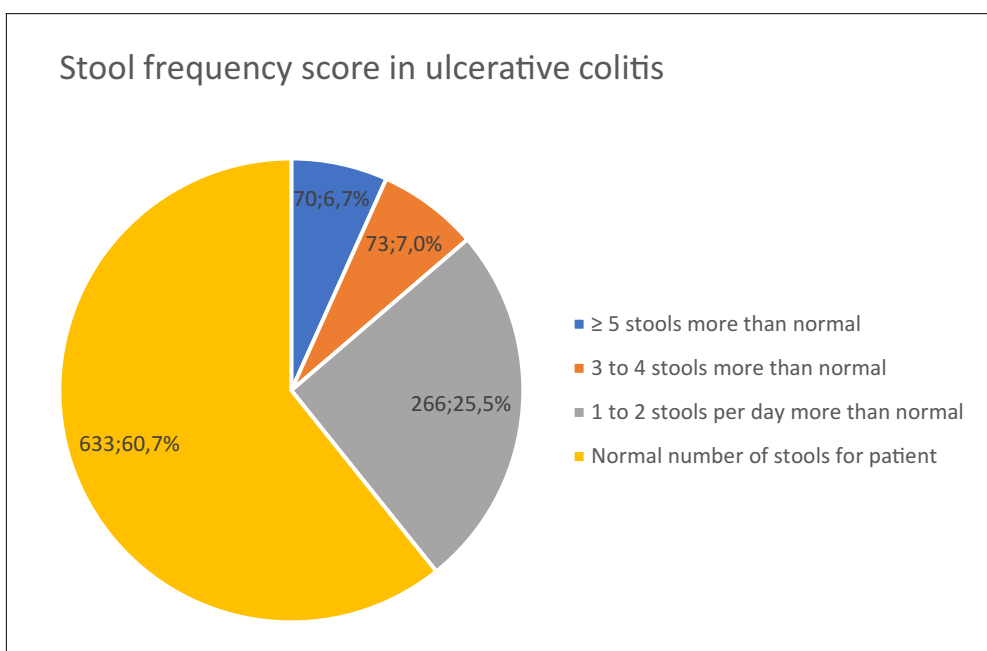


Figure 8. Stool frequency score in ulcerative colitis

Treatment patterns with biological therapy were generally in line with those reported elsewhere (6). More than half of patients received TNF-alpha inhibitors as a first-line treatment, especially before 2019 when constraints on the choice of first-line biological were present in Slovenia and vedolizumab and ustekinumab were reserved

for second-line treatment. This will likely change in the following years. In CD, adalimumab and infliximab were prescribed with similar frequencies. However, in UC infliximab was prescribed three times more frequently than adalimumab or golimumab. Unfortunately, our report does not include any analysis

for changing trends for first-line therapy over time. However, this would shed some light on prescription patterns after the release of constraints limiting the choice of first-line therapy. We analysed the data for 2023 and noticed a significant increase in the proportion of UC patients treated with vedolizumab.

Consequently, vedolizumab was the most frequently prescribed first-line treatment in UC patients, this is different from the observations in previous years (15–17).

We acknowledge some important limitations of our report. The most important limitation of this report is that data entry was not complete in all IBD centres in Slovenia, particularly in those which only recently joined the UR-CARE registry. Also,

some centres did not update biological use from the last report (4). In addition, not all centres treating IBD patients are included in UR-CARE so far. Most centres only entered patients treated with biologicals, thus, we cannot compare the proportion of patients treated with biologicals vs. conventional drugs in different centres. As reporting from the UR-CARE registry is a continuous project, we hope that in time we will be able to report also on conventional therapy, combined immunosuppression and drug optimisation of biologicals as this data would be important for a more accurate presentation of IBD therapy in use in Slovenia. Although

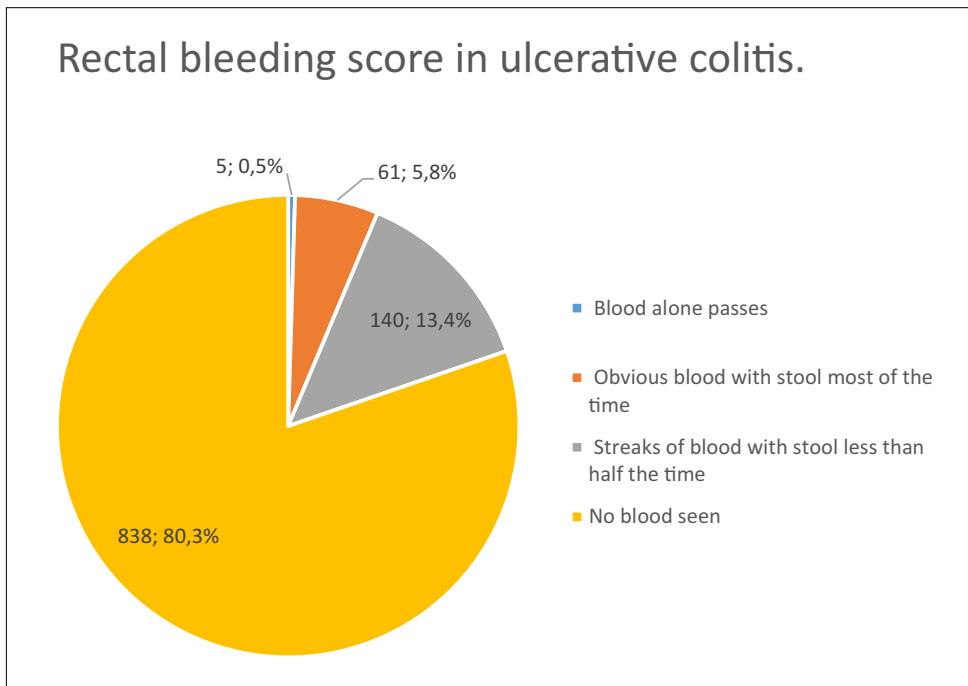


Figure 9. Rectal bleeding score in ulcerative colitis

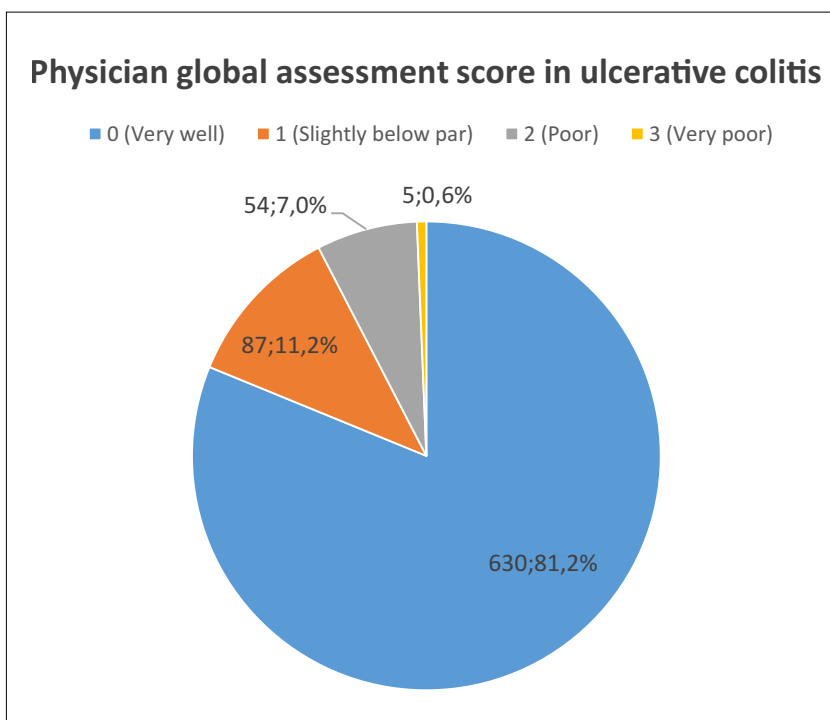


Figure 10. Physician global assessment score in ulcerative colitis

we report on the use of JAK inhibitors for the first time, these data should be interpreted carefully as many IBD centres underreported its use. Also, the follow-up time was short, therefore persistence to treatment with JAK inhibitors cannot be assessed at this stage.

In summary, the utilisation of biologicals in IBD in Slovenia was similar to that in other countries of the European Union in 2023. Inhibitors of TNF-alpha remain the most common first-line choice in Crohn's disease in 2023. However, in ulcerative colitis novel biologicals (vedolizumab 58%, ustekinumab 8%) outnumbered TNF-alpha inhibitors as a first-line treatment choice in 2023. Janus kinase inhibitors use was still low in 2023 in Slovenia.

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