Supplementary file

VEDOLIZUMAB IS ASSOCIATED WITH LONGER DRUG SUSTAINABILITY COMPARED TO INFLIXIMAB IN MODERATE-TO-SEVERE ULCERATIVE COLITIS: LONG TERM REAL-WORLD COHORT DATA

Table S1. Baseline characteristics of those treated with subsequent second drug.

	IFX	VDZ	All	p-value
N (%)	8 (28.5)	20 (71.4)	28 (100)	
Male (%)	6 (75)	10 (50)	16 (57.1)	0.401
Extensive Colitis (%)	4 (50)	6 (30)	10 (35.7)	0.400
Left-sided UC (%)	2 (25)	14 (70)	16 (57.1)	0.044
Proctitis(%)	2 (25)	0 (0)	2 (7.1)	0.074
Combination therapy (%)	2 (25)	1 (5)	3 (10.7)	0.188
Age at diagnosis (years, median, IQR)	25.5 (18-37)	39 (21.5-49)	35.5 (20-46)	0.101
Age at treatment start (years, median, IQR)	32.5 (20-46)	48.5 (30-59.5)	42 (27.57.5)	0.108
Disease length (years, median, IQR)	4 (0.5-8.5)	5 (1.5-11)	5 (1-10.5)	0.794
Calprotectin (µg/g, median, IQR)	3850 (1100-5570)	4215 (24-9838)	4032 (1100-5570)	1
Hemoglobin (Hb) (g/dL, median, IQR)	12.8 (10.3-13.8)	13 (10.8-14)	12.9 (10.8-14)	0.710
Platelets (K/micl, median, IQR)	238.5 (193-409.5)	273 (234-398)	271 (217.5-409.5)	0.795
Hematocrit (Hct) (%, median, IQR)	40.5 (34-43.7)	39.7 (34.7-40.8)	39.8 (34.6-41.3)	0.645
Hb/Hct ratio (median, IQR)	0.3 (0.3-0.3)	0.3 (0.3-0.3)	0.3 (0.3-0.3)	0.014
Eosinophils (K/micl, median, IQR)	0.2 (0.1-0.5)	0.2 (0.1-.3)	0.2 (0.1-0.3)	0.353
Neutrophils (K/micl, median, IQR)	6.15 (5-6.9)	5.5 (3.9-7.7)	5.7 (4-7.3)	0.917

Lymphocytes (K/micl, median, IQR)	2.5 (2.3-4.1)	2 (1.6-2.4)	2.3 (1.6-2.5)	0.037
Neutrophil-to-lymphocyte ratio (median, IQR)	2.2 ((1.5-2.5)	2.8 (2.1-4.3)	2.4 (1.8-3.5)	0.088
Leukocytes (K/micl, median, IQR)	10 (8.1-12.6)	8.3 (7.1-10.2)	9 (7.2-11.1)	0.281
Albumin (g/dL, median, IQR)	4.1 (3.6-4.5)	4.1 (4-4.4)	4.1 (3.9-4.4)	0.912
Creatinine (mg/dL, median, IQR)	0.9 (0.8-1)	0.7 (0.6-0.8)	0.7 (0.6-0.9)	0.265
CRP (mg/dL, median, IQR)	0.3 (0.1-1.1)	0.5 (0.2-1.9)	0.5 (0.2-1.8)	0.263
CPK (U/L, median, IQR)	95 (75-115)	53 (41-69)	55 (42-75)	0.527
Phosphorus (mg/dL, median, IQR)	3.6 (3.1-4.1)	3.7 (3.3-3.9)	3.7 (3.3-3.9)	0.601
Total protein (g/dL, median, IQR)	7.3 (6.4-7.8)	7.3 (6.7-7.8)	7.3 (6.7-7.8)	0.502

UC – Ulcerative colitis, IQR – interquartile range, CRP – C-reactive protein, CPK – creatine phosphokinase.

Table S2. Parameters associated with DS of subsequent treatment.

Parameter		HR (95% CI)	p-value	Adjusted* HR (95% CI)	Adjusted* p-value
Drug - VDZ		0.3 (0.1-1.3)	0.145	0.0 (0.0-14.7)	0.316
Male		1.6 (0.4-5.4)	0.410	446.4 (5.3-36943)	0.006
Disease extent	Extensive colitis	1.4 (0.4-4.5)	0.533	--	--
	Left sided colitis	0.69 (0.2-2.1)	0.527	--	--
	Proctitis	1.6 (0.2-10.2)	0.579	--	--
Combination therapy		0.8 (0.1-5.1)	0.865	0.0 (0.0-0.0)	0.0053
Age at diagnosis		0.9 (0.9-0.9	0.032	--	--
Age at treatment start		0.9 (0.9-1)	0.064	0.8 (0.7-0.9)	0.026
Length of diagnosis		1 (0.9-1.1)	0.750	--	--
Calprotectin		1 (0.0-2.3E)	0.999	--	--
Hemoglobin(Hb)		0.7 (0.5-1)	0.072	0.26 (0.0-9.6)	0.465
Hematocrit (Hct)		0.9 (0.8-1)	0.261	0.9 (0.2-4)	0.944
Hb/Hct ratio		0.0 (0.0-0.9)	0.000	--	--
Platelets		1 (1-1)	0.059	--	--
Leukocytes		1.1 (1-1.3)	0.035	--	--
Eosinophils		1.4 (0.0-30)	0.792	0.0 (0.0-0.0)	0.001
Neutrophils		1.1 (0.9-1.3)	0.087	--	--
Lymphocytes		1.9 (0.9-3.7)	0.0502	--	--
Neutrophil-to-lymphocyte ratio		1.1 (0.7-1.6)	0.549	3.5 (0.6-19.8)	0.148
Albumin		0.4 (0.1-1.8)	0.265	0.0 (0.0-0.3)	0.025
Creatinine		0.6 (0.0-9.3)	0.778	--	--
CRP		0.9 (0.6-1.2)	0.618	0.1 (0.0-1.7)	0.138
CPK		1 90.9-1)	0.303	--	--
Phosphorus		4.5 (1.4-14.5)	0.011	--	--
Total protein		1.7 (0.5-5.5)	0.328	1207.9 (6.4-22E)	0.007

*Adjustment for factors affecting disease severity, including hemoglobin, hematocrit, neutrophil-to-lymphocyte ratio, albumin, CRP, total protein, age and combination therapy with an immunomodulator. UC – Ulcerative colitis, IQR – interquartile range, CRP – C-reactive protein, CPK – creatine phosphokinase.

Table S3. Baseline differences between patients with long-term follow-up.

Parameter		Infliximab	Vedolizumab	ALL	p-value
N (%)		49 (100)	33 (100)	82 (100)	
Male (%)		31 (63.2)	17 (51.5)	48 (58.5)	0.362
Combination therapy (%)		6 (12.2)	1 (3)	7 (8.5)	0.233
Disease extent					0.208
	Extensive colitis (%)	14 (28.5)	9 (27.2)	23 (28)	1
	Left-sided UC (%)	29 (59.1)	15 (45.4)	44 (53.6)	0.263
	Proctitis (%)	6 (12.2)	9 (27.2)	15 (18.2)	0.143
Age at diagnosis (years, median, IQR)		36 (22-49)	31 (20-54)	35.5 (21-51)	0.990
Age at treatment start (years, median, IQR)		43 (26-56)	45 (28-59)	44 (26-57)	0.543
Length of diagnosis at treatment start (years, median, IQR)		2 (1-5)	4 (1-11)	2 (1-10)	0.212
Calprotectin (median, IQR)		5714 (1114-7011)	575 (255-1197)	1114 (378-5714)	0.111
Hemoglobin (median, IQR)		11.3 (10.4-13.2)	12.9 (11.6-13.9)	12.4 (10.8-13.5)	0.001
Platelets (median, IQR)		309 (260-393)	269 (208-339)	301 (231-376)	0.05
Hematocrit (median, IQR)		35 (32-39.9)	39 (36.4-42.7)	37.8 (33.5-42.3)	<.001
Hb/Hct ratio (median, IQR)		0.3 (0.3-0.3)	0.3 (0.3-0.3)	0.3 (0.3-0.3)	0.701
Eosinophils (median, IQR)		0.1 (0.0-0.2)	0.3 (0.1-0.4)	0.2 (0.1-0.3)	0.001
Neutrophils (median)		6 (4.5-8.4)	4.8 (4-6.2)	5.6 (4.2-7.8)	0.434
Lymphocytes (median, IQR)		1.3 (1-2)	2 (1.3-2.4)	1.6 (1.1-4)	0.069
Neutrophil-to-lymphocyte ratio (median, IQR)		4.3 (2.7-5.7)	2.4 (2-3.1)	3.3 (2.2-5.5)	0.233
Leukocytes (median, IQR)		8.9 (7.1-10.8	7.9 (6.5-9.7)	8.4 (6.5-10.3)	0.629
Albumin (median, IQR)		4 (3.1-4.2)	4.4 (4-4.5)	4.1 (3.4-4.5)	<.001
Creatinine (median, IQR)		0.7 (0.6-0.9)	0.8 (0.6-0.9)	0.7 (0.6-0.9)	0.127
CRP (median, IQR)		1.6 (0.4-3.7)	0.4 (0.2-0.9)	0.7 (0.2-2.2)	0.013
CPK (median, IQR)		48 (30-94)	54 (38-69)	51 (34-85)	0.965
Phosphorus (median, IQR)		3.4 (3-3.8)	3.4 (2.9-3.8)	3.4 (3-3.8)	0.717
Total protein (median, IQR)		6.6 (5.6-8.1)	7.2 (6.9-7.7)	7 (6.4-7.5)	0.000

Table S4. Association between different parameters and long term (>156 weeks) sustainability.

parameter	Odds Ratio (CI 95%)	p-value (Chi-Sq)	Adjusted odds ratio (CI 95%)	Adjusted p-value
Vedolizumab vs Infliximab	18.1 (4.3-75.4)	<.000	67 (6-741.9)	0.000
Gender (male)	0.84 (0.3-2.0)	0.708	1.1 (0.2-5.4)	0.862
Left sided UC vs. Extensive colitis	1.2 (0.4-3.3)	0.700	--	--
Proctitis vs. Extensive colitis	1.9 (0.4-8.0)	0.334	--	--
Combination therapy	0.4 (0.0-2.1)	0.305	0.6 (0.0-4.7)	0.661
Age at diagnosis	0.9 (0.9-1)	0.785	--	--
Age at treatment start	0.9 (0.9-1)	0.916	0.9 (0.9-1)	0.627
Length of disease (years)	1 (0.9-1)	0.845	--	--
Calprotectin	1 (0.9-1)	1	--	--
Hemoglobin	1.1 (0.93-1.4)	0.167	1.5 (0.3-6.3)	0.568
Platelets	0.9 (0.9-1)	0.098	--	--
Hematocrit	1 (0.9-1.1)	0.168	0.7 (0.4-1.3)	0.367
Hb/Hc ratio	999.9 (0.0-999.9)	0.612	--	--
Eosinophils absolute number	6 (0.4-88.6)	0.191	0.3(0.0-43.7)	0.669
Neutrophils absolute number	0.9 (0.7-1)	0.211	--	--
Lymphocytes absolute number	0.9 (0.5-1.6)	0.935	--	--
Neutrophil-to-lymphocyte ratio	1 (0.9-1)	0.999	1 (0.9-1.2)	0.338
White blood count	0.9 (0.7-1)	0.190	--	--
Albumin	2.1 (1-4.2)	0.030	6.9 (0.4-116.9)	0.180
Creatinine	1.4 (0.3-5.3)	0.576	--	--
CRP	0.9 (0.8-1)	0.492	1 (0.8-1.2)	0.891
CPK	0.9 (0.9-1)	0.305	--	--
Phosphorus	0.4 (0.2-1)	0.055	--	--
Total protein	1.5 (0.9-2.4)	0.088	0.4 (0.0-1.9)	0.267