

Electronic Supplementary Materials

Stratified Patient Profiling for Vedolizumab Effectiveness in Crohn's Disease: Identifying Optimal Subgroups for Enhanced Treatment Response in the EVOLVE Study

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Fig. S1 Prediction model of clinical remission. *LASSO* least absolute shrinkage and selection operator, *RPART* recursive partitioning and regression tree, *TNF α* tumor necrosis factor α

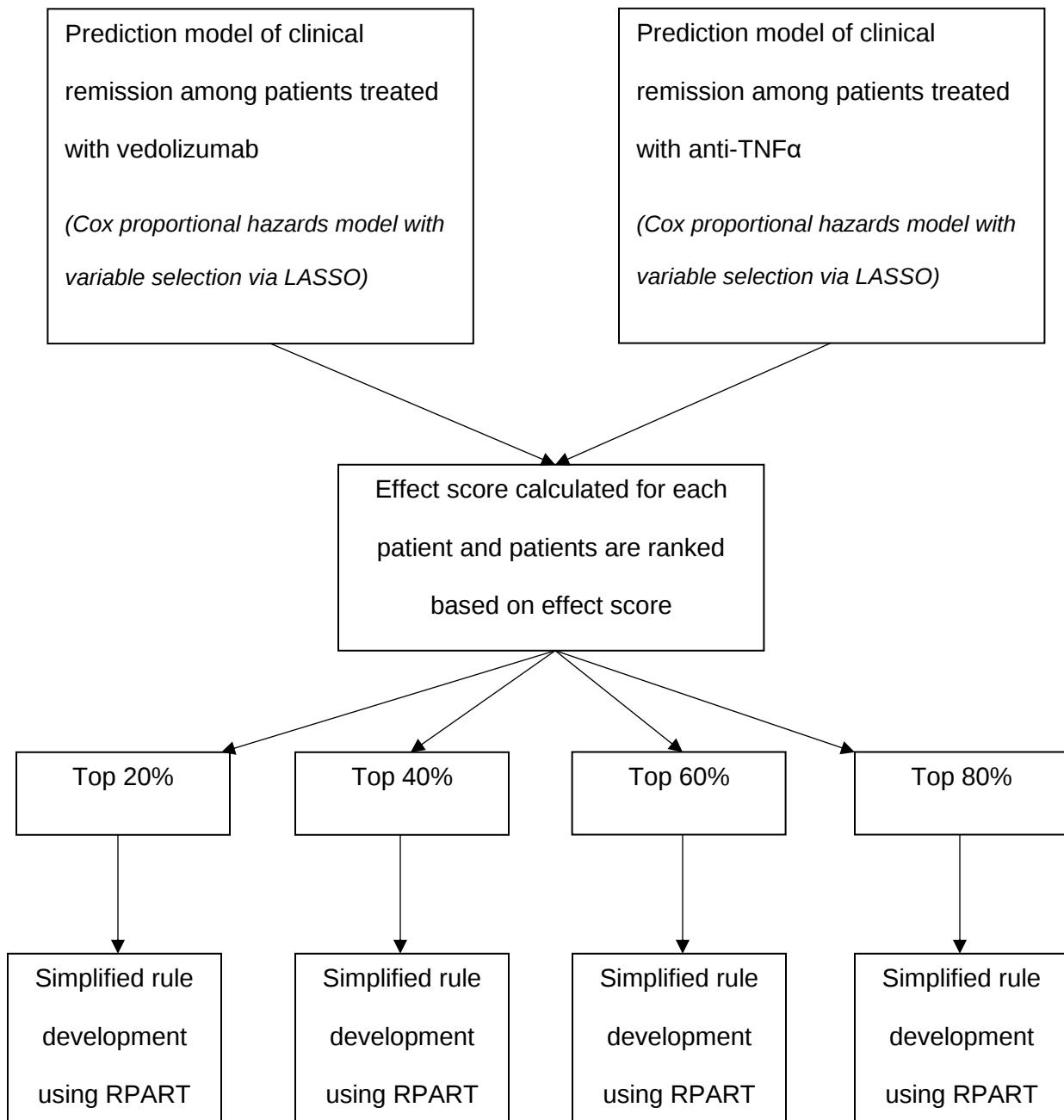


Table S1 Investigators, sites, and contact details for Ethics Committees/Institutional Review Boards

United States		
Investigating Physician	Site Type	Site Name/Address
Mazer Ally	Clinic/Outpatient Facility	United Medical Doctors 477 N. El Camino Real Suite A308 San Diego, California 92130
Brian Behm	University/Teaching Hospital	University of Virginia School of Medicine 1301 Jefferson Park Avenue Box 800708 Charlottesville, Virginia 22908
Charles Berkelhammer	Clinic/Outpatient Facility	Southwest Gastroenterology 9921 Southwest Highway Oak Lawn, Illinois 60453
Philip Ginsburg	Clinic/Outpatient Facility	Medical Research Center of Connecticut 2200 Whitney Avenue Suite 300 Hamden, Connecticut 06518
Emanuelle Bellaguarda	University/Teaching Hospital	Northwestern University 676 North Saint Clair Street Suite 1400 Chicago, Illinois 60611
William Holderman	Clinic/Outpatient Facility	Washington Gastroenterology 2202 South Cedar Suite 330 Tacoma, Washington 98405
Ilyas Ikramuddin	Clinic/Outpatient Facility	Dayton Gastroenterology Inc. 75 Sylvania Drive Dayton, Ohio 45440
Manreet Kaur	University/Teaching Hospital	Baylor College of Medicine Gastroenterology Department 7200 Cambridge Street Suite A10.184 Houston, Texas 77030
Udayakumar Navaneethan	Other Hospital	Florida Hospital 601 East Rolling Street Orlando, Florida 32803
Lilani Perera	University/Academic Hospital	Medical College of Wisconsin 9200 West Wisconsin Avenue Milwaukee, Wisconsin 53226
Timothy Ritter	Clinic/Outpatient Facility	Texas Digestive Disease Consultants and Research Center 505 South Nolen Drive Southlake, Texas 76092

David Rubin	University/Teaching Hospital	The University of Chicago Medical Center – Inflammatory Bowel Disease Center 5758 South Maryland Avenue DCAM 0301 MC 9028 Chicago, Illinois 60637
David Sales	Clinic/Outpatient Facility	Northwest Gastroenterology 1415 South Arlington Heights Road Arlington Heights, Illinois 60005
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Canada		
Mark Silverberg	General Hospital	Mount Sinai Hospital-Joseph & Wolf Lebovic Health Complex 600 University Avenue Toronto, ON, M5G 1X5
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Jean-Rene La Chance	University/Teaching Hospital	Hôpital Maisonneuve-Rosemont 5415, boulevard de l'Assomption Montreal, QC, H1T 2M4
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Ranjit Singh	Dedicated Research Facility	PerCuro Clinical Research Ltd. 1120 Yates Street, #305 Victoria, BC, V8V 3M9
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Christodoulou Dimitrios	Academic (University) Hospital	Ioannina University Hospital Leof. Stavrou Niarchou, Ioannina 455 00, Greece
George Papatheodoridis	General Hospital	Laiko Hospital Agiou Thoma 17, Athens 115 27, Greece

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Thomopoulos Kostantinos	Academic (University) Hospital	Patra Rio University Hospital Pfo 265 04, Greece
Soufleris Kostantinos	General Hospital	Theageneio Hospital Al. Papanastasiou 11, Thessaloniki 546 39, Greece
Xourgias Basilios	General Hospital	Tzaneio Leoforos Afentouli ke Zanni, Pireas 185 36, Greece
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Koutroubakis Ioannis	Academic (University) Hospital	University Hospital of Crete Crete 714 09, Greece
Tzouvala Maria	General Hospital	General Hospital of Nikaia Nikea 184 53, Greece

Table S2 List of variables included in the LASSO model

Variables included in the LASSO model	Variables excluded from the LASSO model^a
ASA at index	Race/ethnicity
Location of intestinal involvement at most recent assessment prior to index event	Smoking status
Sex	Height, m
Type of disease behavior at most recent assessment prior to index event	Weight, kg
Age, years	BMI, kg/m ²
Charlson comorbidity index (modified version)	Patients with pre-index biopsy
CS at index	Patients with pre-index non-endoscopic/imaging procedures
Patients with one or more EIMs in 12 months prior to index	Patients with one or more exacerbations within 6 months prior to index
IBD-related surgical procedures since diagnosis	Patients with active fistulae at diagnosis
IMM at index	Location of intestinal involvement at diagnosis
Fistulae at most recent assessment prior to index event	Time from diagnosis to index treatment, years
Patients with one or more pre-existing EIMs ongoing at index	Type of disease behavior at diagnosis
Patients who had an exacerbation ongoing at index	General well-being at baseline
Patients with pre-index endoscopic procedure	Abdominal pain at baseline
Pre-index antibiotic use	Abdominal mass at baseline
Patients with ED/ER visits prior to index	Physician global assessment at baseline
Patients with hospitalization prior to index	Disease activity at baseline
Pre-index IBD-related hospitalization (12 months prior)	Overall disease severity at baseline
Patients with surgical procedures prior to index	Primary reason for selecting index treatment (recoded)
HCP visits/referrals prior to index	CS use prior to index
Patients with prior non-biologic therapy	IMM use prior to index
Steroid dependency/refractory status	ASA use prior to index
	Azathioprine use prior to index
	Prednisone use prior to index
	Mesalazine use prior to index

Biochemical index

Albumin at baseline

CRP at baseline

ASA aminosalicylate, *BMI* body mass index, *CRP* C-reactive protein, *CS* corticosteroid, *ED/ER* emergency department/emergency room, *EIM* extraintestinal manifestation, *HCP* healthcare provider, *IBD* inflammatory bowel disease, *IMM* immune modulator, *LASSO* least absolute shrinkage and selection operator

^aVariables included in the EVOLVE study but excluded from this analysis owing to overlap or because of incomplete/missing data

Table S3 Weighted values of covariates for the top 20% subpopulation

	Anti-TNFα (n = 43)	Vedolizumab (n = 45)	Mean difference (vedolizumab – anti-TNFα)	Standardized mean difference	P value
Age, years, mean $\pm$ SD	47.90 $\pm$ 16.37	54.66 $\pm$ 16.52	6.75 $\pm$ 3.51	0.411	0.119
Sex, %				0.057	0.816
Female	52.62	49.79	–2.83		
Male	47.38	50.21	2.83		
Patients with pre-index endoscopic procedure, %	67.52	73.64	6.12	0.135	0.593
Patients who had an exacerbation ongoing at index, %	90.38	82.12	–8.26	0.242	0.29
Fistulae at most recent assessment prior to index event, %	4.50	0.00	–4.50	0.307	–
Location of intestinal involvement at most recent assessment prior to index event, %				0.223	0.842
Colonic with/without upper GI disease	51.33	41.62	–9.71		
Ileal with/without upper gastrointestinal	21.27	28.70	7.43		
Ileocolonic with/without upper GI disease	13.37	16.41	3.04		
Unspecified/unknown	14.02	13.26	–0.76		

Type of disease behavior at most recent assessment prior to index event, %				0.208	-
Non-stricturing, non-penetrating with/without perianal disease	59.39	65.08	5.68		
Penetrating with/without perianal disease	10.86	8.88	-1.98		
Stricturing with/without perianal disease	9.31	12.23	2.92		
Unspecified/unknown	20.43	13.81	-6.62		
ASA at index, %	66.07	69.89	3.82	0.082	0.741
CS at index, %	41.52	45.83	4.31	0.087	0.722
IMM at index, %	24.34	24.45	0.10	0.002	0.992
Pre-index antibiotic use, %	13.96	6.84	-7.13	0.235	-
Patients with prior non-biologic therapy, %	100.00	98.57	-1.43	0.170	-
Steroid dependency/refractory status, %				0.025	-
Dependent	21.21	20.21	-1.00		
Refractory	0.00	0.00	0.00		
Neither	78.79	79.79	1.00		
HCP visits/referrals prior to index, %	26.37	19.81	-6.56	0.156	0.477
Patients with hospitalization prior to index, %	46.19	32.11	-14.08	0.292	0.246
Patients with surgical procedures prior to index, %	6.94	5.12	-1.82	0.077	-

Pre-index IBD-related hospitalization (12 months prior), %	22.97	18.22	−4.75	0.118	0.608
IBD-related surgical procedures since diagnosis, %	0.00	1.43	1.43	0.170	—
Patients with one or more EIMs in 12 months prior to index, %	54.07	48.59	−5.48	0.110	0.653
Patients with one or more pre-existing EIMs ongoing at index, %	36.26	32.81	−3.45	0.073	0.756
Charlson comorbidity index (modified version), mean ± SD	0.13 ± 0.41	0.26 ± 0.66	0.13 ± 0.12	0.237	0.25

ASA aminosalicylate, CS corticosteroid, EIM extraintestinal manifestation, GI gastrointestinal, HCP healthcare provider, IBD inflammatory bowel disease, IMM immune modulator, SD standard deviation, TNF α tumor necrosis factor α

Table S4 Weighted values of covariates for the top 40% subpopulation

	Anti-TNFα (n = 87)	Vedolizumab (n = 89)	Mean difference (vedolizumab – anti-TNFα)	Standardized mean difference	P value
Age, years, mean $\pm$ SD	47.27 $\pm$ 16.64	50.79 $\pm$ 15.97	3.52 $\pm$ 2.46	0.216	0.206
Sex, %				0.019	0.913
Female	48.21	47.28	–0.92		
Male	51.79	52.72	0.92		
Patients with pre-index endoscopic procedure, %	63.44	66.34	2.89	0.061	0.724
Patients who had an exacerbation ongoing at index, %	78.16	73.35	–4.81	0.112	0.501
Fistulae at most recent assessment prior to index event, %	1.88	0.00	–1.88	0.196	–
Location of intestinal involvement at most recent assessment prior to index event, %				0.104	0.946
Colonic with/without upper GI disease	35.71	33.27	–2.44		
Ileal with/without upper gastrointestinal	22.82	26.13	3.32		
Ileocolonic with/without upper GI disease	24.90	26.41	1.50		
Unspecified/unknown	16.57	14.19	–2.38		

Type of disease behavior at most recent assessment prior to index event, %				0.114	0.926
Non-stricturing, non-penetrating with/without perianal disease	54.86	59.46	4.60		
Penetrating with/without perianal disease	7.09	7.69	0.60		
Stricturing with/without perianal disease	14.84	13.76	-1.08		
Unspecified/unknown	23.22	19.09	-4.12		
ASA at index, %	73.43	75.07	1.64	0.038	0.825
CS at index, %	39.61	37.05	-2.56	0.053	0.749
IMM at index, %	28.59	24.18	-4.41	0.100	0.560
Pre-index antibiotic use, %	11.30	6.99	-4.31	0.150	0.325
Patients with prior non-biologic therapy, %	94.24	93.73	-0.51	0.022	0.903
Steroid dependency/refractory status, %				0.127	—
Dependent	18.38	16.02	-2.36		
Refractory	0.00	0.63	0.63		
Neither	81.62	83.35	1.73		
HCP visits/referrals prior to index, %	35.35	34.06	-1.29	0.027	0.871
Patients with hospitalization prior to index, %	32.20	26.34	-5.86	0.129	0.453
Patients with surgical procedures prior to index, %	8.48	7.97	-0.51	0.018	0.910

Pre-index IBD-related hospitalization (12 months prior), %	18.26	14.99	−3.28	0.088	0.600
IBD-related surgical procedures since diagnosis, %	0.00	1.25	1.25	0.159	-
Patients with one or more EIMs in 12 months prior to index, %	45.88	41.47	−4.42	0.089	0.599
Patients with one or more pre-existing EIMs ongoing at index, %	25.95	25.35	−0.59	0.014	0.935
Charlson comorbidity index (modified version), mean ± SD	0.13 ± 0.41	0.19 ± 0.60	0.06 ± 0.08	0.110	0.499

ASA aminosalicylate, CS corticosteroid, *EIM* extraintestinal manifestation, *GI* gastrointestinal, *HCP* healthcare provider, *IBD* inflammatory bowel disease, *IMM* immune modulator, *SD* standard deviation, *TNFα* tumor necrosis factor α

Table S5 Weighted values of covariates for the top 60% subpopulation

	Anti-TNFα (n = 136)	Vedolizumab (n = 128)	Mean difference (vedolizumab – anti-TNFα)	Standardized mean difference	P value
Age, years, mean $\pm$ SD	44.93 $\pm$ 15.95	47.45 $\pm$ 17.14	2.52 $\pm$ 2.04	0.152	0.275
Sex, %				0.001	0.994
Female	46.98	47.04	0.05		
Male	53.02	52.96	–0.05		
Patients with pre-index endoscopic procedure, %	66.39	67.99	1.60	0.034	0.803
Patients who had an exacerbation ongoing at index, %	65.89	63.76	–2.13	0.045	0.739
Fistulae at most recent assessment prior to index event, %	3.35	1.70	–1.65	0.106	–
Location of intestinal involvement at most recent assessment prior to index event, %				0.098	0.916
Colonic with/without upper GI disease	30.65	29.19	–1.47		
Ileal with/without upper gastrointestinal	23.91	26.09	2.18		
Ileocolonic with/without upper GI disease	28.08	30.27	2.20		
Unspecified/unknown	17.37	14.45	–2.92		

Type of disease behavior at most recent assessment prior to index event, %				0.103	0.902
Non-stricturing, non-penetrating with/without perianal disease	52.15	54.02	1.86		
Penetrating with/without perianal disease	5.59	7.01	1.42		
Stricturing with/without perianal disease	21.25	21.56	0.31		
Unspecified/unknown	21.00	17.41	-3.59		
ASA at index, %	75.65	77.29	1.63	0.038	0.779
CS at index, %	34.14	32.67	-1.47	0.031	0.814
IMM at index, %	25.07	23.13	-1.94	0.045	0.743
Pre-index antibiotic use, %	10.70	7.57	-3.13	0.109	0.412
Patients with prior non-biologic therapy, %	91.84	91.87	0.03	0.001	0.994
Steroid dependency/refractory status, %				0.043	—
Dependent	14.77	14.33	-0.45		
Refractory	0.63	1.01	0.38		
Neither	84.60	84.67	0.07		
HCP visits/referrals prior to index, %	41.01	40.07	-0.94	0.019	0.888
Patients with hospitalization prior to index, %	23.75	20.98	-2.77	0.066	0.622
Patients with ED/ER visits prior to index, %	0.00	0.41	0.41	0.090	—

Patients with surgical procedures prior to index, %	7.82	7.52	−0.30	0.011	0.931
Pre-index IBD-related hospitalization (12 months prior), %	13.09	11.73	−1.36	0.041	0.756
IBD-related surgical procedures since diagnosis, %	0.66	1.41	0.74	0.073	–
Patients with one or more EIMs in 12 months prior to index, %	38.71	37.01	−1.70	0.035	0.798
Patients with one or more pre-existing EIMs ongoing at index, %	21.59	20.49	−1.10	0.027	0.842
Charlson comorbidity index (modified version), mean ± SD	0.17 ± 0.57	0.20 ± 0.60	0.03 ± 0.07	0.051	0.715

ASA aminosalicylate, CS corticosteroid, ED/ER emergency department/emergency room, EIM extraintestinal manifestation, GI gastrointestinal, HCP healthcare provider, IBD inflammatory bowel disease, IMM immune modulator, SD standard deviation, TNF α tumor necrosis factor α

Table S6 Weighted values of covariates for the top 80% subpopulation

	Anti-TNFα (n = 187)	Vedolizumab (n = 165)	Mean difference (vedolizumab – anti-TNFα)	Standardized mean difference	P value
Age, years, mean $\pm$ SD	43.99 $\pm$ 16.23	46.90 $\pm$ 16.83	2.91 $\pm$ 1.77	0.176	0.151
Sex, %				0.026	0.829
Female	49.82	48.55	–1.28		
Male	50.18	51.45	1.28		
Patients with pre-index endoscopic procedure, %	65.37	67.19	1.82	0.038	0.749
Patients who had an exacerbation ongoing at index, %	57.67	54.85	–2.82	0.057	0.632
Fistulae at most recent assessment prior to index event, %	6.22	2.72	–3.50	0.170	0.241
Location of intestinal involvement at most recent assessment prior to index event, %				0.091	0.903
Colonic with/without upper GI disease	26.35	24.89	–1.47		
Ileal with/without upper gastrointestinal	27.59	30.63	3.04		
Ileocolonic with/without upper GI disease	29.47	30.37	0.90		
Unspecified/unknown	16.59	14.11	–2.48		

Type of disease behavior at most recent assessment prior to index event, %				0.076	0.935
Non-stricturing, non-penetrating with/without perianal disease	47.19	49.42	2.23		
Penetrating with/without perianal disease	6.51	5.80	-0.71		
Stricturing with/without perianal disease	25.26	26.36	1.09		
Unspecified/unknown	21.04	18.43	-2.61		
ASA at index, %	78.56	80.26	1.69	0.042	0.726
CS at index, %	33.16	30.92	-2.24	0.048	0.683
IMM at index, %	24.81	22.21	-2.60	0.061	0.607
Pre-index antibiotic use, %	10.39	7.72	-2.67	0.093	0.417
Patients with prior non-biologic therapy, %	87.53	87.09	-0.45	0.013	0.911
Steroid dependency/refractory status, %				0.031	—
Dependent	12.53	12.86	0.33		
Refractory	1.36	1.71	0.35		
Neither	86.11	85.43	-0.68		
HCP visits/referrals prior to index, %	48.54	46.61	-1.93	0.039	0.745
Patients with hospitalization prior to index, %	21.26	19.10	-2.16	0.054	0.649
Patients with ED/ER visits prior to index, %	2.47	1.99	-0.48	0.032	—

Patients with surgical procedures prior to index, %	10.83	9.61	-1.22	0.040	0.729
Pre-index IBD-related hospitalization (12 months prior), %	12.29	10.82	-1.47	0.046	0.682
IBD-related surgical procedures since diagnosis, %	0.55	1.10	0.55	0.061	–
Patients with one or more EIMs in 12 months prior to index, %	36.39	34.15	-2.24	0.047	0.695
Patients with one or more pre-existing EIMs ongoing at index, %	20.51	19.11	-1.40	0.035	0.768
Charlson comorbidity index (modified version), mean $\pm$ SD	0.15 $\pm$ 0.57	0.18 $\pm$ 0.56	0.03 $\pm$ 0.06	0.045	0.722

ASA aminosalicylate, CS corticosteroid, ED/ER emergency department/emergency room, EIM extraintestinal manifestation, GI gastrointestinal, HCP healthcare provider, IBD inflammatory bowel disease, IMM immune modulator, SD standard deviation, TNF α tumor necrosis factor α

Table S7 Weighted values of covariates for all patients

	Anti-TNF α (<i>n</i> = 245)	Vedolizumab (<i>n</i> = 195)	Mean difference (vedolizumab – anti-TNF α)	Standardized mean difference	<i>P</i> value
Age, years, mean $\pm$ SD	43.43 $\pm$ 15.89	46.08 $\pm$ 17.05	2.65 $\pm$ 1.59	0.161	0.144
Sex, %				0.022	0.839
Female	48.51	47.43	–1.08		
Male	51.49	52.57	1.08		
Patients with pre-index endoscopic procedure, %	67.79	68.46	0.67	0.014	0.894
Patients who had an exacerbation ongoing at index, %	52.29	50.86	–1.44	0.029	0.787
Fistulae at most recent assessment prior to index event, %	10.66	6.57	–4.10	0.146	0.225
Location of intestinal involvement at most recent assessment prior to index event, %				0.086	0.889
Colonic with/without upper GI disease	24.29	23.46	–0.82		
Ileal with/without upper gastrointestinal	29.24	32.20	2.95		
Ileocolonic with/without upper GI disease	32.24	32.45	0.21		
Unspecified/unknown	14.23	11.89	–2.34		
Type of disease behavior at most recent assessment prior to index event, %				0.030	0.994

Non-stricturing, non-penetrating with/without perianal disease	43.95	44.95	1.00		
Penetrating with/without perianal disease	6.54	6.64	0.11		
Stricturing with/without perianal disease	30.89	30.86	−0.03		
Unspecified/unknown	18.63	17.55	−1.08		
ASA at index, %	79.89	80.09	0.20	0.005	0.963
CS at index, %	31.66	30.57	−1.09	0.023	0.825
IMM at index, %	25.88	21.90	−3.98	0.093	0.392
Pre-index antibiotic use, %	12.22	9.92	−2.30	0.073	0.491
Patients with prior non-biologic therapy, %	84.29	83.49	−0.80	0.022	0.834
Steroid dependency/refractory status, %				0.054	—
Dependent	13.05	14.41	1.36		
Refractory	1.30	1.73	0.43		
Neither	85.66	83.87	−1.79		
HCP visits/referrals prior to index, %	55.83	52.80	−3.03	0.061	0.568
Patients with hospitalization prior to index, %	19.65	18.07	−1.57	0.040	0.706
Patients with ED/ER visits prior to index, %	10.21	9.34	−0.87	0.029	0.787
Patients with surgical procedures prior to index, %	11.32	10.02	−1.30	0.042	0.690
Pre-index IBD-related hospitalization (12 months prior), %	10.82	9.74	−1.08	0.036	0.727

IBD-related surgical procedures since diagnosis, %	1.05	1.03	−0.01	0.001	—
Patients with one or more EIMs in 12 months prior to index, %	34.00	32.30	−1.69	0.036	0.739
Patients with one or more pre-existing EIMs ongoing at index, %	18.32	18.16	−0.16	0.004	0.969
Charlson comorbidity index (modified version), mean ± SD	0.14 ± 0.52	0.16 ± 0.51	0.02 ± 0.05	0.045	0.691

ASA aminosalicylate, *CS* corticosteroid, *ED/ER* emergency department/emergency room, *EIM* extraintestinal manifestation, *GI* gastrointestinal, *HCP* healthcare provider, *IBD* inflammatory bowel disease, *IMM* immune modulator, *SD* standard deviation, *TNFα* tumor necrosis factor α