

Supplementary Table 1 Complete demographic and disease characteristics of difficult-to-treat-Crohn's disease and non difficult-to-treat-Crohn's disease patients, *n* (%)/mean $\pm$ SD

Characteristics	Difficult-to-treat-Crohn's disease (<i>n</i> = 90)	Non difficult-to-treat-Crohn's disease (<i>n</i> = 85)	<i>P</i> value
Age (years)	32.00 (25.00-42.00)	34.00 (23.75-46.00)	
Gender			
Male	68 (75.6)	55 (64.7)	
Female	22 (24.4)	30 (35.3)	
Marital status			
Married	54 (60.0)	52 (61.2)	
Unmarried	36 (40.0)	32 (37.6)	
Disease duration (years)	4.92 (2.25-11.29)	3.59 (1.23-8.25)	0.057
Disease activity			
Active	22 (24.4)	35 (41.2)	
Remission	68 (75.6)	50 (58.8)	
Anal fistula			
(+)	85 (94.4)	53 (62.4)	
(-)	5 (5.6)	32 (37.6)	
Surgical history			
(+)	54 (60.0)	32 (37.6)	
(-)	36 (40.0)	53 (62.4)	
Age at diagnosis			
< 17y	5 (5.6)	5 (5.9)	
17-40y	72 (80.0)	60 (70.9)	
> 40y	13 (14.4)	20 (23.5)	
Behavior			
B1	34 (37.8)	27 (31.8)	

B2	39 (43.3)	43 (50.6)	
B3	11 (12.2)	6 (7.1)	
B2+B3	6 (6.7)	9 (10.6)	
Location			
L1	20 (22.2)	29 (34.1)	
L1+L4	7 (7.8)	3 (3.6)	
L2	3 (3.3)	5 (5.9)	
L2+L4	1 (1.1)	3 (3.5)	
L3	49 (54.4)	37 (43.5)	
L3+L4	9 (10.0)	6 (7.1)	
L4	0	2 (2.4)	
Enteral nutrition			
NEN	37 (41.1)	37 (43.5)	
PEN	37 (41.1)	30 (35.3)	
TEN	16 (17.8)	4 (4.7)	
Type of biologics			
0	10 (11.1)	27 (31.8)	
1	37 (41.1)	58 (68.2)	
2	39 (43.3)	NA	
3	4 (4.4)	NA	
Interleukin (pg/mL)			
1	1.01 (0.58-1.38)	0.66 (0.41-1.35)	
2	1.46 (0.77-2.61)	1.58 (0.96-2.47)	
4	1.28 (0.88-1.97)	1.36 (0.89-2.03)	
5	1.13 ± 0.71	0.86 ± 0.54	0.005
6	7.06 (4.22-11.29)	6.17 (3.29-10.61)	
8	8.57 (5.69-15.48)	7.88 (3.93-14.19)	
10	3.35 (2.64-4.77)	3.32 ± 1.47	0.099
12	0.86 (0.50-1.33)	1.19 ± 1.54	
17	1.49 (0.81-2.08)	1.56 ± 0.90	

Ca (mmol/mL)	2.21 ± 0.15	2.20 ± 0.19	
P (mmol/mL)	1.12 ± 0.24	1.17 ± 0.21	
Mg (mmol/mL)	0.92 (0.88-0.97)	0.93 (0.88-0.99)	
Fe (mmol/mL)	12.10 (7.18-18.43)	11.60 (5.68-16.40)	
Ferritin (mmol/mL)	48.70 (19.33-109.80)	47.15 (18.50-105.18)	
Vitamin B12 (pg/mL)	236.50 (182.75-383.25)	296.00 (176.75-437.50)	
Folate (µg/L)	10.40 (5.60-18.53)	10.05 (7.38-17.58)	
CRP (mg/L)	2.16 (0.50-8.48)	1.34 (0.50-10.89)	
Hemoglobin (g/L)	142.00 (126.00-150.00)	132.00 (115.75-147.00)	0.011
MFI	52.56 ± 13.57	50.71 ± 12.96	
General fatigue	11.16 ± 3.49	10.90 ± 3.66	
Physical fatigue	11.62 ± 3.78	12.00 (9.00-15.00)	
Mental fatigue	10.00 (7.00-12.00)	9.00 (6.00-11.00)	0.032
Reduced activity	11.32 ± 3.14	11.00 (9.00-12.25)	
Reduced motivation	8.00 (6.00-11.00)	8.00 (7.00-10.00)	

Normally distributed data are expressed as mean ± SD, with *P* values derived from Student's *t*-test or analysis of variance; non-normally distributed data are expressed as median with interquartile range, with *P* values derived from the Mann-Whitney *U* test or the Kruskal-Wallis test, respectively. Anal fistula: (+) previous simple or complex anal fistula (-) without any anal fistula or perianal disease. Surgical history: (+): CD-related surgery; (-): Without any CD-related surgery. Number of biologics or small molecule with different mechanism: (1) Anti-tumor necrosis factor (Infliximab,

Adalimumab); (2) Integrin receptor antagonist (Vedolizumab); (3) Interleukin antagonist (Ustekinumab); and (4) Janus kinase inhibitor (Tofacitinib)[18].