

SUPPLEMENTAL TABLES

	First-line IFX n=35	Conventional n=39	P-value
6-MMP levels	1400 (800-2700)	1500 (597-2875)*	0.818
6-TGN levels	567 (438-660)	490 (224-650)	0.258
6-MMP/6-TGN ratio	3.21 (1.57-5.38)	2.91 (1.25-6.35)*	0.881

Supplemental Table 1. Azathioprine metabolites measured according to clinical practice. *Three out of 29 6MMP levels were missing. IFX=infliximab; 6 MMP=6-methylmercaptopurine; 6 TGN=6-thioguanine nucleotide.

		Exclusive enteral nutrition (n=27)	Oral prednisolone (n=20)	P value
Age at diagnosis, years		14.5 (12.4-16.5)	13.8 (11.6-15.6)	0.282
Male sex		16 (59%)	10 (50%)	0.528
Height, cm		164.3 (149.2-175.0)	157.4 (143.5-16.6)	0.169
Weight, kg		48.5 (33.8- 56.3)	41.8 (31.1-53.9)	0.240
wPCDAI		60.0 (48.8-67.8)	53.8 (45.6-81.3)	0.909
CRP, mg/L		34.5 (24.7-65.9)	39.5 (20.5-69.0)	0.921
ESR, mm/hour		27.0 (17.0-47.5)	34.0 (22.5-71.0)	0.091
SES-CD		15 (6-22)	19 (6-28)	0.275
Leukocytes, 10⁹/L		8.9 (6.8-11.7)	9.1 (6.2-11.8)	0.982
Faecal calprotectin, µg/g		1197 (1033-1661)	592 (555-1133)	0.014
Perianal disease†		5 (19%)	4 (20%)	0.898
Paris classification				
Age at diagnosis	<10 years	4 (15%)	3 (15%)	0.757
	10-17 years	20 (74%)	16 (80%)	
	17-40 years	3 (11%)	1 (5%)	
Disease location	L1	6 (22%)	5 (25%)	0.755
	L2	6 (22%)	6 (35%)	
	L3	15 (56%)	9 (45%)	
	Isolated L4	-	-	
Upper disease location	No upper GI	14 (52%)	11 (55%)	0.942
	L4a	12 (44%)	8 (45%)	
	L4b	1 (4%)	1 (5%)	
Disease behavior	B1	25 (93%)	16 (80%)	0.201
	B2	2 (7%)	4 (20%)	
	B3	-	-	
	B2B3	-	-	
Growth delay		1 (4%)	1 (5%)	0.828
Time between diagnostic endoscopy and start of treatment, days		7 (1-13)	8 (3-17)	0.266

Supplemental Table 2A: Baseline characteristics of patients treated with exclusive enteral nutrition versus oral prednisolone. Data are presented as n (%) or median (IQR). wPCDAI, weighted paediatric Crohn's disease activity index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SES-CD, Simple Endoscopic Score for Crohn's Disease; †perianal disease comprised inactive fistula, skin tags, or anal fissures.

	FL-IFX (n=27)	Conventional (n=30)	P value	
Age at diagnosis, years	15.1 (11.9-16.6)	14.1 (11.3-16.1)	0.181	
Male sex	15 (49%)	18 (54%)	0.734	
Height, cm	168 (151-177)	161 (143-174)	0.136	
Weight, kg	52.0 (34.0-63.0)	43.2 (28.8-55.0)	0.248	
wPCDAI	57.5 (47.5-65)	50 (45-75.6)	0.937	
CRP, mg/L	29.0 (12.0-46.0)	39.5 (22.0-65.9)	0.091	
ESR, mm/hour	35.0 (27.0-55.0)	28.0 (18.0-60.0)*	0.795	
SES-CD	19 (9-24)	17 (6-19)	0.869	
Leukocytes, 10⁹/L	8.6 (7.4-10.4)	9.3 (7.4-12.1)	0.895	
Faecal calprotectin, µg/g	1045 (684-1228.0)	1078 (617-1661)	0.765	
Perianal disease†	2 (7%)	7 (23%)	0.100	
Paris classification				
Age at diagnosis	<10 years	2 (7.5%)	5 (17%)	0.568
	10-17 years	23 (75%)	23 (76%)	
	17-40 years	2 (7.5%)	2 (7%)	
Disease location	L1	8 (30%)	5 (17%)	0.392
	L2	5 (18%)	9 (30%)	
	L3	13 (48%)	16 (53%)	
	Isolated L4	1 (4%)	-	
Upper disease location	No upper GI	12 (44%)	16 (53%)	0.252
	L4a	15 (56%)	12 (40%)	
	L4b	-	2 (7%)	
Disease behavior	B1	25 (92%)	26 (87%)	0.467
	B2	2 (8%)	4 (13%)	
	B3	-	-	
	B2B3	-	-	
Growth delay	0 (0%)	2 (7%)	0.172	
Treated with exclusive enteral nutrition		16 (53%)		
Time between diagnostic endoscopy and start of treatment, days	9 (6-13)	8.5 (2-14.5)	0.860	

Supplemental Table 2B: Baseline characteristics of patients that underwent an endoscopic evaluation at week 10. Data are presented as n (%) or median (IQR). FL-IFX, first-line IFX; wPCDAI, weighted paediatric Crohn's disease activity index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SES-CD, Simple Endoscopic Score for Crohn's Disease; EEN, exclusive enteral nutrition. *1 missing data point. †perianal disease comprised inactive fistula, skin tags, or anal fissures.

	FL-IFX (n=18)	Conventional (n=14)	P value	
Age at diagnosis, years	15.5 (11.1-16.6)	12.0 (9.4-14.6)	0.168	
Male sex	10 (55.6%)	8 (57.1%)	0.928	
Height, cm	160.9 (146.4-174.3)	147.9 (135.0-167.6)	0.193	
Weight, kg	45.6 (31.3-55.5)	36.3 (24.9-43.0)	0.338	
wPCDAI	56.3 (49.4-73.1)	52.5 (45.0-61.9)	0.338	
CRP, mg/L	28.5 (7.8-40.3)	27.0 (17.8-46.0)	0.168	
ESR, mm/hour	39.0 (30.0-40.0)	29.5 (19.8-62.5)	0.694	
SES-CD	16 (10-23)	15 (8-15)	0.346	
Leukocytes, 10⁹/L	8.6 (7.4-10.4)	7.5 (5.4-11.7)		
Faecal calprotectin, µg/g	1076 (652-1445)	1033 (555-1087)	0.337	
Perianal disease†	2 (6%)	7 (23%)	0.109	
Paris classification				
Age at diagnosis	<10 years	3 (17%)	5 (36%)	0.250
	10-17 years	13 (72%)	9 (64%)	
	17-40 years	2 (11%)	-	
Disease location	L1	4 (22%)	4 (28.5%)	0.773
	L2	4 (22%)	4 (28.5%)	
	L3	9 (50%)	6 (49%)	
	Isolated L4	1 (6%)	-	
Upper disease location	No upper GI	9 (50%)	11 (78%)	0.073
	L4a	9 (50%)	2 (14%)	
	L4b	-	1 (7%)	
Disease behavior	B1	17 (94%)	10 (71%)	0.075
	B2	1 (6%)	4 (29%)	
	B3	-	-	
	B2B3	-	-	
Growth delay	0 (0%)	1 (7%)	0.249	
Treated with exclusive enteral nutrition		7 (50%)		
Time between diagnostic endoscopy and start of treatment, days	10 (4-13.3)	9 (4-18)	0.837	

Supplemental Table 2C: Baseline characteristics of patients that underwent an endoscopic evaluation at week 52. Data are presented as n (%) or median (IQR). FL-IFX, first-line IFX; wPCDAI, weighted paediatric Crohn's disease activity index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SES-CD, Simple Endoscopic Score for Crohn's Disease; EEN, exclusive enteral nutrition. †perianal disease comprised inactive fistula, skin tags, or anal fissures.

Received treatment escalation	First-line IFX		p-value	Conventional		P-value
	Yes	No		Yes	No	
wPCDAI, median (IQR)	17.5 (0.0-35.0)	0.0 (0.0-22.5)	0.109	21.3 (8.1-31.9)	10 (0.0-20.0)	0.020
Fcal, µg/g, median (IQR)	312 (193-896)	89 (34-496)	0.027	572 (403-219)	139 (93-806)	0.023
CRP, mg/L, median (IQR)	2.0 (1.1-4.6)	0.7 (0.0-2.6)	0.003	10.0 (0.9-26.5)	4.8 (0.9-8.7)	0.277
ESR, mm/hour, median (IQR)	12.0 (5.5-24.5)	3.0 (1.0-6.3)	0.023	17.0 (2.8-33.8)	10.0 (3.0-17.0)	0.176

Supplemental Table 3: Levels of inflammatory markers after induction treatment in patients that received and did not receive treatment escalation. Levels are depicted per treatment group. wPCDAI scores, CRP levels and ESR levels are obtained 14 weeks after start of induction treatment. Fcal levels were obtained 10 weeks after start of induction treatment. IFX=infliximab; wPCDAI= weighted paediatric Crohn's disease activity index; Fcal=faecal calprotectin level; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate.

	First-line IFX (n=47)	Conventional (n=42)	P-value
Baseline QOL score, median (IQR)	59.6 (49.5-72.0) [n=36]	61.1 (49.5-70.9) [n=28]	0.660
Week 14 QOL score, median (IQR)	81.8 (70.7-86.8)* [n=36]	77.1 (68.6-85.7)* [n=27]	0.297
Week 52 QOL score, median (IQR)	80.0 (71.4-88.6)* [n=31]	77.5 (66.6-85.5)* [n=28]	0.261

Supplemental Table 4: Quality of life assessment based on the IMPACT III questionnaire. The total IMPACT III score ranges from 0 to 100 with a higher score indicating a better quality of life. IFX=infliximab; QOL=quality of life.

*significantly higher compared to the score at baseline (p<0.001)