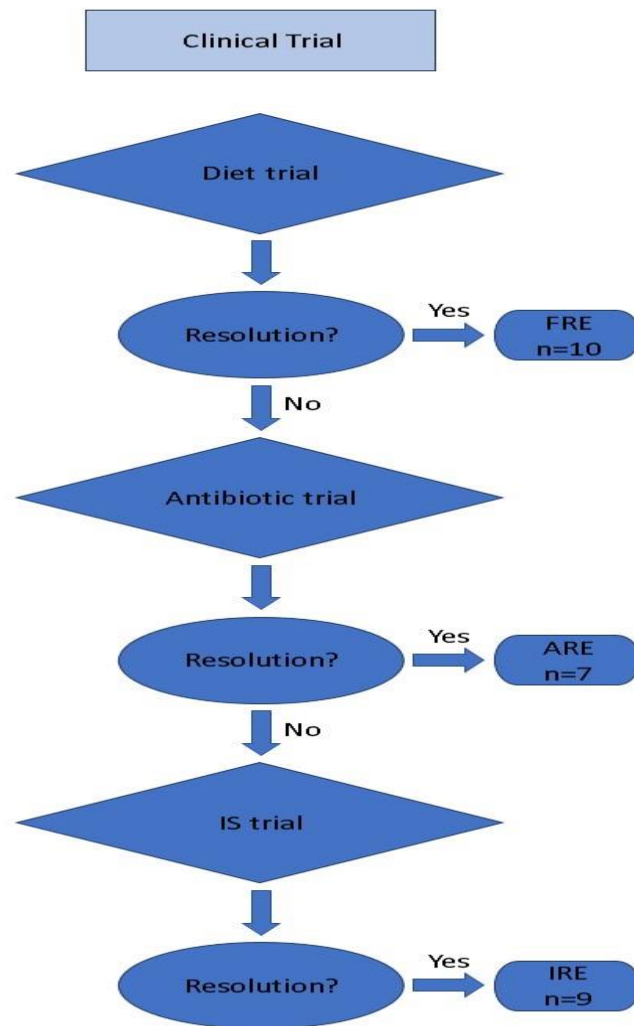


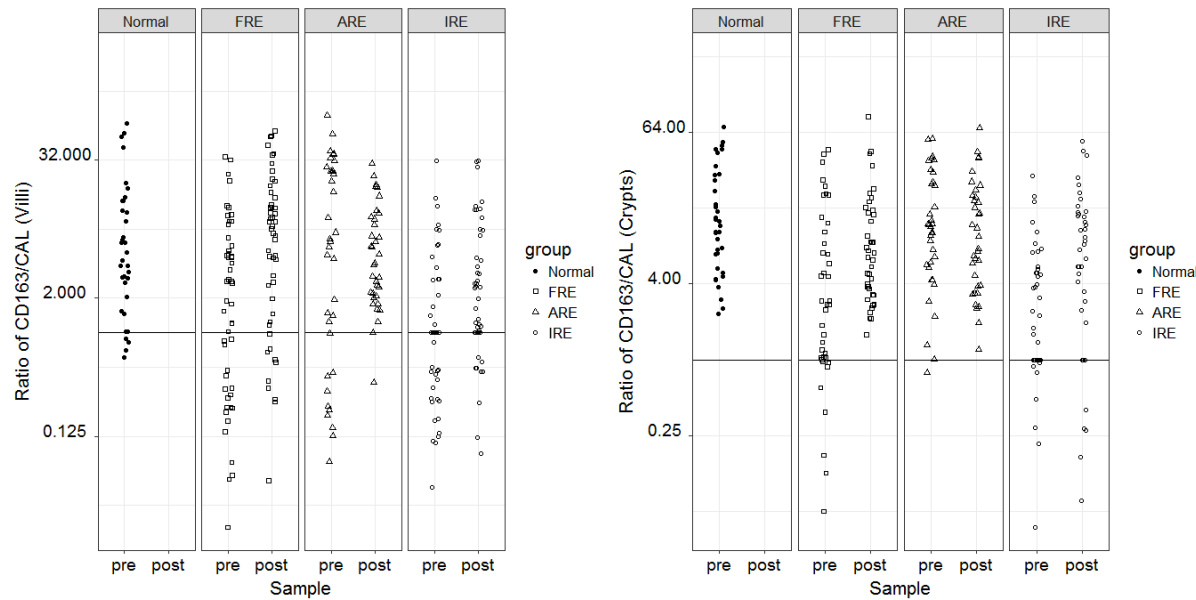
Supplemental Material

Supplementary Fig 1



Supplement 1: Summary of clinical trial. ARE: antibiotic-responsive enteropathy. FRE: Food-responsive enteropathy. IRE: immunosuppressant-responsive enteropathy. IS: immunosuppressant trial. n: number of dogs.

Supplement Fig 2. Dot plots of calprotectin and CD163 labelling index in duodenal villi and crypts. ARE: Antibiotic responsive enteropathy. FRE: Food responsive enteropathy. IRE: Immune-suppressive responsive enteropathy. Normal: healthy dogs. pre: pre-treatment. post: post-treatment. Dots have been randomly jittered on the x-axis for presentation.



Supplement fig 3. Dot plots of the ratio of CD163 and calprotectin labelling index in duodenal villi and crypts. The horizontal line represents a ratio of 1. Ratios are presented on logged scales. CAL: calprotectin. ARE: Antibiotic responsive enteropathy. FRE: Food responsive enteropathy. IRE: Immune-suppressive responsive enteropathy. Normal: healthy dogs. pre: pre-treatment. post: post-treatment. Dots have been randomly jittered on the x-axis for presentation.

Supplementary Table 1 : Dogs demographics.

Dog	Origin	Outcome	Age [mo]	Breed	Sex	CIBDAI-	CIBDAI-
						1	2
1	MU	ARE	26	Labrador Retriever	FS	4	0
2	MU	FRE	30	Great Dane	MC	4	0
3	MU	FRE	29	Staffordshire Bull Terrier	MC	11	0
4	MU	FRE	15	GSD	M	3	0
5	MU	FRE	30	Toy Poodle	MC	8	0
6	UoM	FRE	21	Weimaraner	MC	4	0
7	UoM	ARE	18	Japanese Spitz	FS	7	1
8	UoM	ARE	44	GSD	M	9	0
9	UoM	FRE	60	Maltese cross	FS	6	0
10	UoM	ARE	18	GSD	FS	9	0
11	UoM	ARE	35	Basset Hound	M	5	0
12	UoM	ARE	60	Border Collie	MC	5	1
13	UoM	FRE	60	Golden Retriever	MC	6	0
14	UoM	IRE	60	Spoodle	M	5	0
15	UoM	FRE	114	Labrador Retriever	FS	10	1
16	UoM	FRE	14	GSD	FS	6	0
17	UoM	IRE	120	Labrador Retriever	FS	6	0
18	UoM	ARE	24	Greyhound	FS	7	1
19	UoM	FRE	108	Chihuahua	MC	6	0
20	ISU	IRE	120	Pointer	M	8	0
21	ISU	IRE	18	Cocker Spaniel	FS	7	0
22	ISU	IRE	96	Newfoundland	MC	5	0
23	ISU	IRE	72	GSP	FS	6	0

24	ISU	IRE	48	Great Swiss Mountain Dog	MC	11	0
25	ISU	IRE	n/a	n/a	M	16	0
26	ISU	IRE	48	GSD	FS	5	0

Origin

ISU Iowa State University
 MU Murdoch University
 UoM University of Melbourne

Outcome

ARE Antibiotic-responsive enteropathy
 FRE Food-responsive enteropathy
 IRE Immunesuppressant-responsive
 enteropathy

Breed

GSD German Shepherd Dog
 German Shorthaired
 GSP Pointer

Sex

F Female S Speyed
 M Male C Castrated

CIBDAI-1 Clinical Inflammatory Bowel Disease Activity Index before
 treatment

CIBDAI-2 Clinical Inflammatory Bowel Disease Activity Index after
 treatment

n/a Not
 available

Supplement Table 2: Least square-means and confidence interval for CD163 and calprotectin labelling index in duodenal villi (A) and crypts (B).
 ARE: Antibiotic-responsive enteropathy. CI: Confidence interval. CTRL: Healthy dogs. FRE: Food responsive enteropathy. IRE: Immune-suppressive responsive enteropathy. Labelling index: the ratio number of positively stained cells / total number of cells × 100 per 10,000 square microns. n: number of dogs. PRE: Pre-treatment. POST: Post-treatment.

A. Villi

		CD163			CALPROTECTIN		
		n	Labelling index [%]	95% CI	n	Labelling index [%]	95% CI
CTRL		7	4.53	2.69, 7.48	7	0.74	0.30, 1.65
FRE	PRE	10	1.64	1.03, 2.57	10	1.02	0.50, 1.95
	POST	10	2.12	1.35, 3.31	10	0.34	0.14, 0.72
ARE	PRE	7	2.01	1.16, 3.41	7	0.43	0.15, 1.00
	POST	7	1.54	0.88, 2.65	7	0.27	0.07, 0.66
IRE	PRE	9	0.49	0.27, 0.83	9	0.49	0.21, 1.03
	POST	9	0.92	0.54, 1.51	9	0.36	0.14, 0.78

B. Crypts

		CD163			CALPROTECTIN		
		n	Labelling index [%]	95% CI	n	Labelling index [%]	95% CI
CTRL		7	4.63	2.75, 7.65	7	0.28	0.13, 0.53
FRE	PRE	8	1.57	0.93, 2.61	8	0.44	0.24, 0.75
	POST	8	2.54	1.53, 4.15	8	0.25	0.12, 0.46
ARE	PRE	7	2.57	1.50, 4.35	7	0.16	0.06, 0.33
	POST	7	2.36	1.37, 4.00	7	0.15	0.05, 0.31
IRE	PRE	9	0.37	0.20, 0.64	9	0.12	0.04, 0.25
	POST	8	0.76	0.43, 1.28	8	0.08	0.01, 0.18

Supplement Table 3. Least square-means and confidence interval for the ratio CD163/Calprotectin in duodenal villi and crypts. ARE: Antibiotic-responsive enteropathy. CAL: Calprotectin. CD163⁺/CAL⁺ ratio: ratio CD163/Calprotectin. CI: Confidence interval. n: number of dogs. CTRL: Healthy dogs. FRE: Food responsive enteropathy. PRE: Pre-treatment. POST: Post-treatment. IRE: Immune-suppressive responsive enteropathy.

		VILLI			CRYPTS		
		n	CD163 ⁺ /CAL ⁺ ratio	95% CI	n	CD163 ⁺ /CAL ⁺ ratio	95% CI
CTRL		7	5.51	2.32, 13.10	7	12.31	6.65, 22.81
FRE	PRE	10	1.56	0.76, 3.22	8	3.10	1.74, 5.52
	POST	10	5.02	2.43, 10.35	8	7.45	4.19, 13.27
ARE	PRE	7	4.00	1.68, 9.51	7	10.27	5.54, 19.02
	POST	7	4.49	1.89, 10.68	7	9.85	5.32, 18.25
IRE	PRE	9	0.99	0.46, 2.13	9	2.08	1.21, 3.59
	POST	9	2.21	1.03, 4.74	8	4.82	2.74, 8.48

Supplement Table 4. Kendall's tau correlation coefficients for the labelling index for CD163, calprotectin, and ratio CD163:CAL with the histology score. CAL: calprotectin labelling index. CD163: CD163 labelling index. CD163:CAL: ratio of the labelling index of CD163 and calprotectin. Score: histology score.

Villi	CD163	-0.15
	CAL	0.08
	CD163:CAL	-0.18
Crypts	CD163	-0.34

Correlation:

High	$P > 0.70 $
Moderate	$ 0.50 > P \leq 0.70 $
Low	$ 0.30 > P \leq 0.50 $

CAL	0.03
CD163:CAL	-0.23
Score	1
	Score

Weak $P \leq |0.30|$