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GENERIC DRUG NAME and COMPOUND NUMBER: Anrukinzumab / PF-05230917

PROTOCOL NO.: B2421003

PROTOCOL TITLE: A Phase 2a, Randomized, Double-Blind, Sponsor Unblinded, Placebo-Controlled, Multiple Dose Study to Evaluate the Pharmacodynamics, Pharmacokinetics and Safety of Anrukinzumab in Subjects With Active Ulcerative Colitis

Study Centers: A total of 38 centers participated and randomized subjects in this study; in Austria (1 center), Bulgaria (3 centers), Canada (2 centers), France (3 centers), Germany (4 centers), Hungary (2 centers), the Netherlands (3 centers), Poland (1 center), Spain (2 centers), and the United States (17 centers).

Study Initiation Date, Primary Completion, and Final Completion Dates:
Study Initiation Date: 11 March 2011
Primary Completion Date: 17 December 2012
Study Completion Date: 22 April 2013

Phase of Development: Phase 2a

Study Objectives:

Primary Objective:

- The primary objective was to characterize the change in the pharmacodynamics (PD) biomarker, fecal calprotectin, during treatment with anrukinzumab.

Secondary Objectives:

- Characterization of the pharmacokinetic (PK) profile and total interleukin 13 (IL-13) of 3 multiple escalating Intravenous (IV) doses of anrukinzumab versus placebo.

- Determination of safety, tolerability and immunogenicity of anrukinzumab in subjects with active ulcerative colitis (UC).

METHODS

Study Design: This was a Phase 2a, randomized, double-blind, sponsor-unblinded, placebo-controlled study evaluating the PD, PK, safety, and clinical activity of multiple IV infusions of 200, 400, or 600 mg anrukinzumab or placebo in subjects with active UC. Eligible subjects were stratified by previous exposure to treatment with immunosuppressives and/or tumor necrosis factor alpha inhibitor's (yes/no), and randomized (ratio 1:1:1:1) to

receive 200, 400, or 600 mg anrukinzumab, or placebo. Randomization occurred initially in a 1:1:1 fashion to the placebo, anrukinzumab 200 mg, and anrukinzumab 400 mg arms. After at least 3 subjects completed 2 doses plus 2 weeks follow-up in the anrukinzumab 400 mg arm, a safety review was conducted by the Sponsor. This review having identified no significant safety issues enrollment in the anrukinzumab 400 mg arm was allowed to proceed unrestricted and randomization to the anrukinzumab 600 mg arm was initiated. As a result of the staggered randomization, approximately 1/3 of subjects in the placebo, anrukinzumab 200 mg and anrukinzumab 400 mg group began treatment with study medication prior to randomization of the first subject to the anrukinzumab 600 mg group. Consequently, after the anrukinzumab 600 mg group was opened for randomization, randomization to the placebo, anrukinzumab 200 mg, anrukinzumab 400 mg and anrukinzumab 600 mg groups, proceeded, effectively, in a 2:2:2:3 fashion.

Subject participation for approximately 38 weeks included a ≤42-day Screening period, a 14-week treatment period including 5 IV administrations of study drug (anrukinzumab or placebo) at Weeks 0, 2, 4, 8, and 12, and an 18-week follow-up period (ie, approximately 5 half-lives from last dose of anrukinzumab). Total duration of this study was 110 weeks. The schedule of activities is summarized in Table 1.

Table 1. Schedule of Activities

Protocol Activity	Screening[a]	Baseline	Treatment Period								Follow-Up				
Study Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	EW Visit[b]	
Study Day/Week	Day -42 to -1	Week 0/ Day 1	Day 2	Day 4	Day 7	Week 2	Week 4	Week 8	Week 12	Week 14	Week 16	Weeks 18, 22, 26, 30	Weeks 20, 24, 28, 32	Initial EW visit	Post EW Visit(s)[b]
Visit Window	None	None	±1 Day based on Week 0/Day 1 visit			±7 Days based on Week 0/Day 1 visit									
Enrollment procedures															
Informed consent	X														
Biopsy informed consent	X														
Demography, medical & UC history, smoking history, and cardiovascular history	X														
Inclusion/exclusion criteria	X	X													
Medical procedures															
Complete physical examination[c]		X								X			X[d]	X	X[e]
Targeted physical examination[c]						X	X	X	X		X		X[f]		X[g]
ECG (12-lead)	X									X			X[d]	X	X[e]
Flexible sigmoidoscopy	X[h]									X				X	
Biopsy from normal and inflamed areas[i]	X									X				X	
Chest X-ray[j]	X														
Vital signs															
Blood pressure, pulse, and respiratory rate (after 5 minutes of rest)[k]	X	X				X[j]	X[k]	X[k]	X[k]	X	X		X	X	X
Temperature (oral or tympanic [°C or °F])	X	X				X	X	X	X	X	X		X	X	X
Weight (lbs or kg)	X	X				X	X	X	X	X	X		X	X	X
Height (in or cm)	X														
Laboratory assessments															
Blood chemistry (including HbA1c only at Screening), hematology, urinalysis	X	X				X	X	X	X	X	X		X	X	X

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Study Day/Week	Day -42 to -1	Week 0/ Day 1	Day 2	Day 4	Day 7	Week 2	Week 4	Week 8	Week 12	Week 14	Week 16	Weeks 18, 22, 26, 30	Weeks 20, 24, 28, 32	Initial EW visit	Post EW Visit(s)[b]
Visit Window	None	None	±1 Day based on Week 0/Day 1 visit			±7 Days based on Week 0/Day 1 visit									
Autoantibodies (includes: antinuclear, anti-double-stranded DNA, and anticardiolipin IgG and IgM antibodies)	X	X					X	X	X				X[l]	X	X
Urine pregnancy test (conducted site)[m]		X				X	X	X	X	X	X		X	X	X
Serum pregnancy test[m]	X														
Serum FSH (menopausal females)	X														
HBsAg and total HBcAb	X														
HCVAb (confirmed by HCV RNA)	X														
HIV screen (performed at local lab)[n]	X														
Stool culture/microscopy for enteric infections and parasitic infections[o]	X														
Tuberculosis test (PPD or IGRA per local guidelines [performed at local laboratories])[p]	X														
Pharmacokinetics															
Predose PK sample (within 2 hours before infusion)		X				X	X	X	X						
Post-Dose PK sampling (within 1 hour after the end of the infusion)		X				X	X	X	X						
PK sampling			X	X	X					X	X	X	X	X	X
Anti-anrukinzumab Abs (ADA) and neutralizing anti-anrukinzumab Abs (NAb)[q]		X					X	X	X	X	X		X	X	X
Pharmacodynamics															
hs-CRP (collected with blood chemistry)	X	X				X	X	X	X	X				X	
Total IL-13 sampling		X	X	X	X	X	X	X	X	X	X		X	X	X
Serum YKL-40 specimen		X				X	X	X	X	X				X	
Total IgE sampling		X					X			X					

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Study Day/Week	Day -42 to -1	Week 0/ Day 1	Day 2	Day 4	Day 7	Week 2	Week 4	Week 8	Week 12	Week 14	Week 16	Weeks 18, 22, 26, 30	Weeks 20, 24, 28, 32	Initial EW visit	Post EW Visit(s)[b]
Visit Window	None	None	±1 Day based on Week 0/Day 1 visit			±7 Days based on Week 0/Day 1 visit									
P-STAT6 sampling	X	X	X							X					
Stool specimen collection for fecal calprotectin, lactoferrin and YKL-40[r]	X[s]	X				X	X	X	X	X				X	
Treatment procedures															
Randomization (after all screening procedures are completed and results reviewed)		X													
Administration of IV anrukinzumab or Placebo		X				X	X	X	X						
30 minute post-infusion observation		X				X	X	X	X						
Assess for infusion site reactions		X	X	X	X	X	X	X	X	X	X		X	X	X
Adverse event monitoring	X----------														----X
Prior/concomitant medication/treatments	X----------														----X
Patient stool diary[t]	X[t]	X[t]							X[t]	X[t]					
Mayo score calculation		X[t]								X[t]					

ADA=Anti-anrukinzumab antibodies; DNA=Deoxyribonucleic acid; ECG=Electrocardiogram; EW=Early Withdrawal; FSH=Follicle stimulating hormone; HbA1c=Glycosylated hemoglobin; HBsAg=Hepatitis B surface antigen; HBcAb=Hepatitis B core antibody; HCV=Hepatitis C virus; HCVAb=hEpatitis C antibody; HCV RNA=Hepatitis C virus ribonucleic acid; HEENT=Head, eyes, ears, nose, and throat; HIV=Human immunodeficiency virus; hs-CRP=High sensitivity C-reactive protein; IgE= Immunoglobulin E; IgG=Immunoglobulin G; IgM=Immunoglobulin M; IGRA=Interferon gamma release assay; IL-13=INTERLEUKIN 13; IV=Intravenous; NAb=Neutralizing antibody against anrukinzumab; PD=Pharmacodynamic; PK=Pharmacokinetic; PPD=Purified protein derivative; P-STAT6=phosporylated signal transducer and activator of transcription 6; UC=Ulcerative colitis; YKL-40=Chitinase 3-like 1 (cartilage glycoprotein-39).

a. The Screening period lasted up to 6 weeks (±7 days). All screening procedures, laboratory results and repeat laboratory results were completed and reviewed prior to randomization.
b. Any subject who withdrew prematurely from the study had to return for a final evaluation (initial EW visit). Post EW visits occurred every 4 weeks (±7 Days) following the initial EW visit until 16 weeks after the final dose administered during the study. The same procedures were performed at all Post EW visits, except as noted in the protocol.
c. Complete physical examination included the review of the following body systems: general appearance, skin, HEENT, heart, lungs, abdomen, lower extremities, neurological, back, and lymph nodes. A targeted physical examination only included review of the following body systems: general appearance, heart, lungs, abdomen, lower extremities, and lymph nodes.
d. Performed during the Week 32 visit only.
e. Performed during the final EW visit only.

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Protocol Activity	Screening[a]	Baseline	Treatment Period								Follow-Up				
Study Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	EW Visit[b]	
Study Day/Week	Day -42 to -1	Week 0/ Day 1	Day 2	Day 4	Day 7	Week 2	Week 4	Week 8	Week 12	Week 14	Week 16	Weeks 18, 22, 26, 30	Weeks 20, 24, 28, 32	Initial EW visit	Post EW Visit(s)[b]
Visit Window	None	None	±1 Day based on Week 0/Day 1 visit			±7 Days based on Week 0/Day 1 visit									

f. Performed during the Week 20, 24 and 28 visits only.
g. Performed at all post EW visits except the final EW visit.
h. Flexible sigmoidoscopy was performed and results reviewed before the Baseline visit. This procedure was performed after all other eligibility criteria (including fecal calprotectin levels) were met.
i. Biopsies, from consented subjects only, were taken from normal appearing mucosa as well as abnormally inflamed colonic mucosa. Frankly ulcerated areas were avoided.
j. Chest radiograph were performed during the Screening period, unless a chest radiograph was performed within 12 weeks prior to screening. Official reading/report had to be located in the source documentation.
k. On dosing days, vital signs performed included measuring blood pressure, pulse and respiratory rate within 2 hours before infusion, approximately 15 minutes after initiating the infusion and again at the end of the 30 minute watching period after infusion.
l. Blood samples for autoantibodies were collected only on Weeks 24 and 32. For subjects that withdrawal from the study early, these samples were collected 24 weeks after Week 0 dosing and at the last visit.
m. For women of childbearing potential only, ie, who were not surgically sterile or did not meet the definition of menopause as per the inclusion/exclusion criteria.
n. Documentation of a negative HIV test result within 12 months of Screening was accepted and had to be available in source documentation.
o. Stool culture and sensitivity for ova and parasites and stool culture for C difficile toxin could be done by either the local or central laboratory.
p. A documented negative PPD test result 12 weeks prior to study entry were accepted and had to be available in the source documentation. IGRA official reading and method or test had to be available in source documentation.
q. ADA and NAb samples were to be collected prior to dosing.
r. A sample collected on the day of visit was preferred, but if this was not possible, a stool sample container was distributed at each visit except Visit Days 2, 4 and 7, the subject's follow-up visits, and the last visit. Subjects were asked to use the container to provide a stool sample at the subsequent visit.
s. At the Screening visit, a stool sample was collected for fecal calprotectin analysis only. At all other indicated times a stool sample was collected for fecal calprotectin, fecal lactoferrin and fecal YKL-40. Stool sample collection containers were distributed at the first Screening visit and subjects were asked to bring in a stool sample at their next Screening visit. The stool sample for the Screening visit was received prior to the Baseline visit and was not taken during the bowel preparation period preceding the flexible sigmoidoscopy.
t. Patient Stool diary was recorded by the subject on the 3 days immediately preceding the flexible sigmoidoscopy visit prior to the Week 0/Baseline visit and the Week 14 visit. Should any subject be required to perform bowel preparation prior to the flexible sigmoidoscopy at Week 0 and 14, the subject was instructed to complete the diary 1 day prior to initiating bowel preparation. A new Patient Stool diary was distributed during the first Screening visit and Week 12 visit. The Patient Stool diaries were collected and reviewed by site personnel at the flexible sigmoidoscopy visit during the Screening period and the Week 14 visit in order to calculate the Mayo score.

Number of Subjects (Planned and Analyzed): Approximately 80 subjects (20 subjects per arm) were planned to be enrolled. 84 subjects (21 subjects each in the placebo, anrukinzumab 200 mg, anrukinzumab 400 mg, and anrukinzumab 600 mg groups) were assigned to treatment; 6 in Austria, 8 in Bulgaria, 3 in Canada, 4 in France, 7 in Germany, 6 in Hungary, 6 in the Netherlands, 2 in Poland, 3 in Spain, and 39 in the United States.

Diagnosis and Main Criteria for Inclusion: Male and/or female subjects between the ages of ≥18 and ≤65 years, with positive histological and active UC determined within the screening period as defined by a Mayo score ≥4 and <10 points and with an endoscopic sub score (based upon flexible sigmoidoscopy) of ≥2 points, and with fecal calprotectin level of ≥100 mg/kg.

Study Treatment: Anrukinzumab or placebo was administered as an IV infusion, prepared by an unblinded dispenser and provided as a blinded test article to the blinded administrator. The infusion was approximately 1 hour in duration administered on Day 1, Weeks 2, 4, 8, and 12. Study drug details are provided in Table 2.

Table 2. Study Drug Details

Study Drug	Potency	Formulation
PF-05230917 (IMA-638) for injection, (5 mL vial)	100 mg/mL	Stoppered vial
Placebo for PF-05230917 (IMA-638) for injection (5 mL vial)	0 mg	Stoppered vial
PF-05230917 (IMA-638) for injection, (5 mL vial)	100 mg/mL	Stoppered vial
Placebo for PF-05230917 (IMA-638) for injection (5 mL vial)	0 mg	Stoppered vial

PF-05230917=Anrukinzumab.

Pharmacokinetic, Pharmacodynamic and Safety Endpoints:

Pharmacodynamic Endpoints:

Primary endpoint: Fold change from Baseline in fecal calprotectin at Week 14.

Secondary endpoints:

- Fold change from Baseline in fecal calprotectin at Weeks 2, 4, 8, 12, and 14.
- Total IL-13 (free IL-13 and IL-13 complexed with anrukinzumab) measured at pre-specified time points up to 32 weeks.

Pharmacokinetic endpoint: The PK of anrukinzumab were characterized from data obtained at pre specified time points up to 32 weeks. The PK parameters area under the concentration-time curve (AUC), and half-life were estimated using non-compartmental analysis and additional parameters may have been estimated using a population PK analysis.

Safety endpoints:

- The frequency of on treatment adverse events (AEs), serious adverse events (SAEs) and withdrawals due to AEs were summarized.

- Frequency of anti-anrukinzumab antibodies (ADAs) and neutralizing anti-anrukinzumab antibodies (Nabs), if observed, at pre-specified time points up to 32 weeks.

Safety Evaluations: Safety evaluations included AEs, clinical laboratory tests (hematology, chemistry, urinalysis and others), physical examination, vital signs, 12-lead ECGs and chest X-ray.

Statistical Methods:

Analysis of PK Parameters: Plasma concentrations of anrukinzumab were listed and plotted. Descriptive summary statistics were presented for all PK parameters.

Analysis of PD Parameters: The primary objective of this study was to characterize changes in the levels of the PD biomarker, fecal calprotectin, during treatment with anrukinzumab. To achieve the primary objective, a superiority analysis (treatment versus placebo) of changes from baseline in natural log-transformed fecal calprotectin at Week 14 was based on an analysis of covariance (ANCOVA) model. Unless specified otherwise, all the tests were conducted at 2-sided 0.2 alpha level and 80% confidence intervals (CIs) were provided. To evaluate the robustness of the PD analysis findings, a longitudinal data analysis (LDA) model was used for the primary biomarker analyses. The secondary PD endpoints including changes from baseline in natural log transformed fecal calprotectin at Weeks 2, 4, 8, and 12 were analyzed using ANCOVA and/or LDA model. All other secondary and exploratory PD biomarker endpoints such as high sensitivity C-reactive protein (hs-CRP), fecal lactoferrin and chitinase 3-like 1 (cartilage glycoprotein-39) (YKL-40) and serum YKL-40 and phosphorylated signal transducer and activator of transcription 6 (P-STAT6), and total Immunoglobulin E (IgE), etc, at each measured time points were analyzed using LDA model with appropriate data transformation as necessary. Descriptive statistics for IL-13 was summarized and plotted by treatment group.

Immunogenicity Assessments: Presence of ADA was listed and summarized by time post-dose.

Analysis of Safety Parameters: Safety data was summarized using descriptive statistics. Safety laboratory parameters were summarized with absolute value and change from baseline.

RESULTS

Subject Disposition and Demography: Approximately 80 subjects (20 subjects per arm) were planned to be enrolled in approximately 70 centers. A summary of the subject disposition is provided in Table 3. A total of 152 subjects were screened and 84 subjects (21 subjects each in the Placebo, anrukinzumab 200 mg, anrukinzumab 400 mg, and anrukinzumab 600 mg groups) were assigned to treatment. Because of the designed delayed initiation of randomization to the anrukinzumab 600 mg group, approximately 1/3 of subjects in the placebo, anrukinzumab 200 mg and anrukinzumab 400 mg group began treatment with study medication prior to randomization of the first subject to the anrukinzumab 600 mg group. All randomized subjects received at least 1 dose of assigned study medication. Of the 84 randomized subjects, 45 completed the assigned treatments, 39 subjects discontinued from

the study, including 1 subject (anrukinzumab 400 mg group) marked as "ongoing at date of cut-off" (Table 3), who was discontinued due to premature closing of 1 center for financial reasons, and data entry was incomplete for this subject. Subject ages ranged from 18-65 years; the mean age in the 400 mg group was 46.3 years compared to 36.6 in the placebo group, 37.5 in the 200 mg group and 37.0 in the 600 mg group. Overall 93% (78/84) of the subjects were white.

Table 3. Subject Study Disposition

Number of Subjects		Placebo	Anrukinzumab 200 mg	Anrukinzumab 400 mg	Anrukinzumab 600 mg
Screened	152				
Assigned to study treatment	84	21	21	21	21
Treated		21	21	21	21
Completed study		10	13	15	7
Discontinued from study		11	8	5	14
Relation to study drug not defined		3	1	2	5
No longer willing to participate		3	1	2	5
Related to study drug		3	3	3	3
Adverse event		0	1	0	2
Insufficient clinical response		3	2	2	1
Medication error without associated adverse event		0	0	1	0
Not related to study drug		5	4	0	6
Adverse event		4	4	0	3
Other		0	0	0	1
Protocol violation		1	0	0	2
Ongoing at date of cut-off		0	0	1	0
Analyzed for Pharmacodynamics					
mITT		21	21	21	21
PP		19	19	17	18
Analyzed for Pharmacokinetics					
PKP		0	20	20	21
PKC		0	21	20	21
Analyzed for Safety					
Adverse events		21	21	20	21
Laboratory data		21	21	21	21

Discontinuations had been attributed to the last study treatment received.
Completed Study - completed all phases of study, including treatment phase and follow-up phase.
Discontinued from Study - discontinued from study (including withdrawals after completion of treatment phase).
Treated - Received at least 1 dose of study medication.
Ongoing at date of cut-off - one subject discontinued, due to premature closing of one study center in USA for financial reasons, and data entry was incomplete for this subject.
mITT=modified intent-to-treat; PKC=pharmacokinetic concentration; PKP=pharmacokinetic parameters; PP=per-protocol.

Pharmacokinetic and Pharmacodynamic Results:

Pharmacokinetics Results:

Serum PK parameters derived from Day 1/Week 0 and Week 12 concentration-time profile are summarized in Table 4.

The PK profile of anrukinzumab was assessed following the first dose administration on Day 1/Week 0 and following the last dose administration on Week 12. Only trough and peak PK samples were collected for the doses administered in between. Peak serum anrukinzumab concentrations (C_{max}) generally occurred at 1 to 2 hours post-dose on both Day 1/Week 0 and Week 12 for all treatment groups. Serum anrukinzumab exposure (C_{max} and area under the concentration-time profile from time 0 to time tau, the dosing interval, where tau=672 hours [4 weeks] [AUC_{tau}]) increased with increasing dose from 200 to 600 mg and the increases appeared to be approximately dose proportional for both Day 1/Week 0 and Week 12. Dose-normalized C_{max} and AUC_{tau} values were generally similar for these 3 treatment groups although there was a trend toward lower values for dose-normalized AUC_{tau} with increasing dose on Week 12. These 3 treatment groups had essentially no accumulation for C_{max} (based on values for observed accumulation ratio for C_{max} ($R_{ac,}$ C_{max}) of 1.1, 1.1 and 0.98 for 200 mg, 400 mg and 600 mg group, respectively). The mean terminal half-life ($t_{½}$) on Week 12 was 392 hours, 471 hours and 362 hours, for the 200 mg, 400 mg and 600 mg group, respectively. The mean terminal $t_{½}$ on Week 12 was 392 hours, 471 hours and 362 hours, for the 200 mg, 400 mg and 600 mg group, respectively. Trough values generally increased from the first dose on Day 1/Week 0 through Week 4 (nominal time 672 hours post-dose) for all the treatment groups, then decreased slightly afterwards when dosing interval changed from 2 weeks to 4 weeks. Inter-subject variability for anrukinzumab exposure, based on percent coefficient of variation (%CV), ranged from 36%-61% for AUC_{tau} and 29%-75% for C_{max} on Day 1/Week 0 and Week 12 across all treatment groups.

Table 4. Summary of Serum Anrukinzumab Pharmacokinetic Parameter Values Following Single Doses on Day 1/Week 0 and Multiple Doses on Week 12

	Parameter Summary Statistics by Treatment[a]		
Parameter, Units	**Anrukinzumab 200 mg**	**Anrukinzumab 400 mg**	**Anrukinzumab 600 mg**
Day 1/Week 0 Single dose			
N	19	20	20
AUC_{tau}, ng•hr/mL	7670000 (44)	13500000 (44)	23160000 (36)
$AUC_{tau\ (dn)}$, ng•hr /mL/mg	38350 (44)	33710 (44)	38590 (36)
C_{max} , ng/mL	52530 (29)	94880 (39)	171000 (39)
$C_{max(dn)}$, ng/mL/mg	262.8 (28)	237.4 (39)	285.1 (39)
C_{max}, ng/mL	0.0001000 (0)	0.0004424 (3712000)	0.0008424 (86824444)
T_{max}, hr	1.27 (0.667-2.02)	1.58 (0.950-97.9)	1.60 (0.800-47.1)
Week 12 Multiple dose			
N, n	15, 14	16, 16	13, 7
AUC_{tau}, ng•hr /mL	19370000 (59)	33900000 (44)	44330000 (61)
$AUC_{tau\ (dn)}$, ng•hr/mL/mg	96860 (59)	84690 (44)	73880 (61)
C_{max} , ng/mL	57890 (75)	114100 (38)	175800 (62)
$C_{max(dn)}$, ng/mL/mg	289.6 (75)	285.3 (38)	293.0 (62)
T_{max}, hr	1.08 (0.000-336)	1.41 (0.967-504)	1.17 (0.883-2.00)
C_{min}, ng/mL	11010 (74)	18130 (81)	25600 (87)
$t_{½}$, hr	392.4±99.1	470.5±361	362.4±111
CL, L/day	0.2475 (59)	0.2833 (44)	0.3250 (61)
V_z, L	5.301 (41)	6.992 (75)	5.835 (36)
R_{ac},C_{max}	1.139 (72)	1.101 (27)	0.9841 (65)

For the parameters analyzed on the log scale, "0" values had been substituted with "0.0001" prior to log transformation.
The dosing interval (τ) was 336 hours for Day 1/Week 0 and 672 hours for Week 12.
AUC_{tau} = area under the concentration-time profile from time 0 to time tau, the dosing interval, where tau=672 hours (4 weeks); CL=clearance; CV=coefficient of variation; C_{max}= maximum observed plasma concentration; C_{min}=lowest plasma concentration observed during the dosing interval; dn=dose normalized; N=Number of subjects in the treatment group and contributing to the summaries; n=Number of subjects with reportable Vz and $t_{½}$ values; R_{ac}, C_{max}=observed accumulation ratio for C_{max}; SD=Standard deviation; T_{max}=time for C_{max}; $t_{½}$=terminal half-life; Vz=volume of distribution.

a. Geometric mean (geometric %CV) for all except: median (range) for T_{max} and arithmetic mean (±SD) for $t_{½}$.

Pharmacodynamic Results:

Primary PD endpoint:

Fold change from baseline in fecal calprotectin at Week 14: Observed data (DAO) for the mean fold change from Baseline in fecal calprotectin at Week 14 were available for 7/21 subjects in the placebo group, 14/21 subjects in the anrukinzumab 200 mg group, 15/21 subjects in the anrukinzumab 400 mg and 13/21 subjects in the anrukinzumab 600 mg group.

The DAO mean fold change from Baseline in fecal calprotectin at Week 14 was 0.41 in the placebo group, 0.29 in the anrukinzumab 200 mg group, 0.79 in the anrukinzumab 400 mg group and 1.24 in the anrukinzumab 600 mg group; none of these mean fold changes in the anrukinzumab treatment groups were, individually, statistically significantly (p-value <0.2)

different from the mean fold change in the placebo group (Table 5). However, at 600 mg anrukinzumab a p-value of 0.0666 was observed, but with an increase of fecal calprotectin levels instead of expected decrease.

Table 5. Summary of Statistical Analysis (ANCOVA) of Fold Change From Baseline in Fecal Calprotectin at Week 14 (mITT DAO)

Treatment	N	LS Mean	80% CI	Ratio to Placebo		
				Ratio	80% CI	P-Value
Placebo	7	0.41	(0.225, 0.766)			
Anrukinzumab 200 mg	14	0.29	(0.187, 0.446)	0.70	(0.329, 1.472)	0.532
Anrukinzumab 400 mg	15	0.79	(0.517, 1.203)	1.90	(0.900, 4.013)	0.27
Anrukinzumab 600 mg	13	1.24	(0.794, 1.949)	3.00	(1.403, 6.409)	0.0666

P-value from ANCOVA model with terms for treatment group, Baseline (in log scale).
LS mean, ratio and CI were based on back log-transformation of those from the ANCOVA model.
ANCOVA=Analysis of covariance; CI=Confidence interval; DAO=Data as observed; LS mean=Least square mean; mITT=Modified intent-to-treat; N=Total number of subjects.

Secondary PD Endpoints:

Fold change from baseline in fecal calprotectin at Weeks 2, 4, 8, 12, and 14: A summary of statistical analysis (ANCOVA) of fold change from Baseline in fecal calprotectin at Weeks 2, 4, 8, 12, and 14 is provided in Table 6. A graphical depiction of estimated fold changes from Baseline (LDA) in fecal calprotectin by treatment group and study week (mITT DAO; Weeks 2 through 14) are presented in Figure 1.

The fold change from Baseline in fecal calprotectin was <1 in all treatment groups at all time-points except at Week 8 in the anrukinzumab 400 mg group (1.14) and at Week 14 in the anrukinzumab 600 mg group (1.24); at all time-points, except Week 2, the greatest decrease from Baseline occurred in the anrukinzumab 200 mg group. The fold change decrease was statistically significantly (p-value <0.2) different from that observed in the placebo group at Week 4 (0.47 versus 0.92; p-value = 0.0885), Week 8 (0.36 versus 0.78; p-value = 0.1553) and Week 12 (0.19 versus 0.64; p-value = 0.0283) in the anrukinzumab 200 mg group and in the 600 mg group at Week 4 (0.55 versus 0.92; p-value = 0.1996).

At Week 14, there was a fold change increase in the anrukinzumab 600 mg group which was statistically significantly (p-value <0.2) different than the fold change decrease seen in the placebo group (1.24 versus 0.41; p-value = 0.0666). At this time-point, both the result in the placebo group (0.41) and the result in the anrukinzumab 600 mg group (1.24) were numerically disparate to those seen on assessments at other time-points, including the Week 12 time-point (placebo = 0.64; anrukinzumab 600 mg = 0.67). The results were relatively stable in both groups from Week 4 to Week 12. As with other fecal parameters the

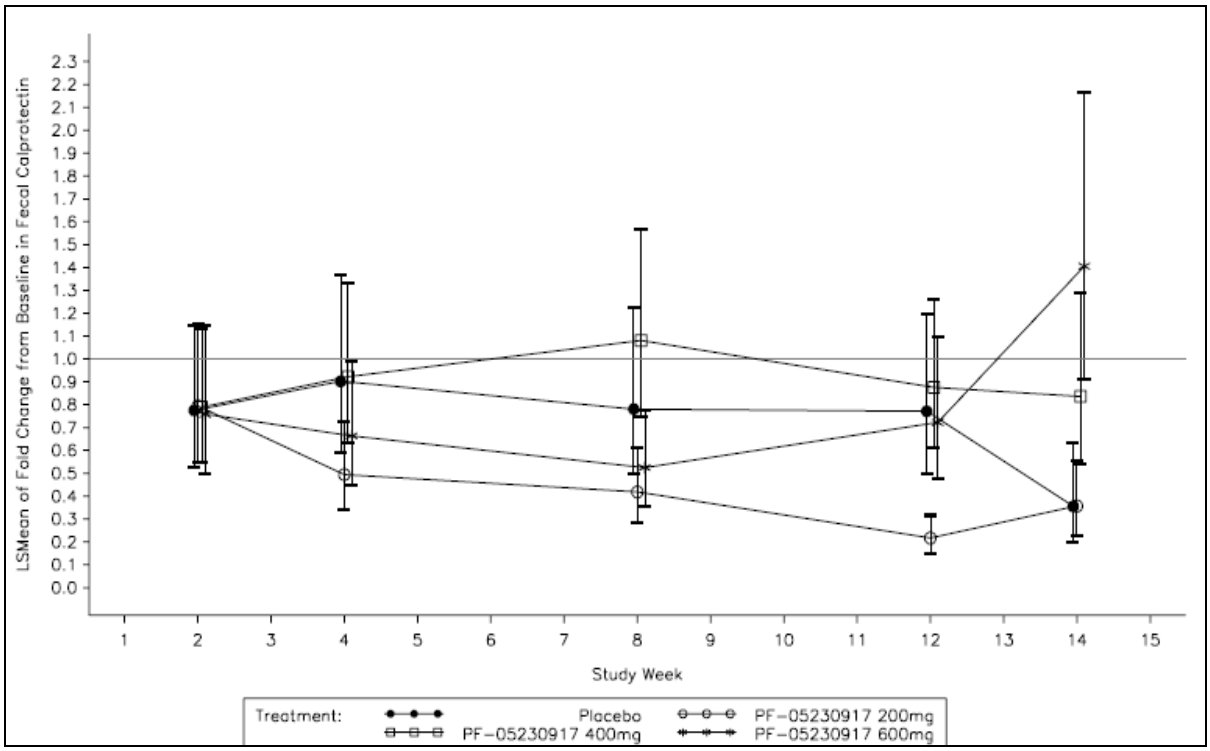
number of samples available for assessment decreased over time in all treatment groups such that Week 14 fecal calprotectin data was available for only 7/21 subjects in the placebo group, 14/21 subjects, in the anrukinzumab 200 mg group, 15/21 subjects in the anrukinzumab 400 mg group and 13/21 subjects in the anrukinzumab 600 mg group.

Table 6. Summary of Statistical Analysis (ANCOVA) of Fold Change From Baseline in Fecal Calprotectin at Week 2, 4, 8, 12 and 14 (mITT DAO)

Study Week	Treatment	N	LS Mean	80% CI	Ratio to Placebo		
					Ratio	80% CI	P-Value
Week 2	Placebo	15	0.7	(0.466, 1.048)			
	Anrukinzumab 200 mg	17	0.81	(0.552, 1.185)	1.16	(0.663, 2.021)	0.7352
	Anrukinzumab 400 mg	18	0.71	(0.488, 1.027)	1.01	(0.586, 1.753)	0.9754
	Anrukinzumab 600 mg	13	0.77	(0.500, 1.195)	1.11	(0.609, 2.008)	0.8277
Week 4	Placebo	14	0.92	(0.631, 1.328)			
	Anrukinzumab 200 mg	18	0.47	(0.339, 0.655)	0.51	(0.313, 0.846)	0.0885
	Anrukinzumab 400 mg	19	0.92	(0.669, 1.269)	1.01	(0.617, 1.644)	0.9856
	Anrukinzumab 600 mg	16	0.55	(0.388, 0.779)	0.6	(0.361, 1.000)	0.1996
Week 8	Placebo	10	0.78	(0.454, 1.331)			
	Anrukinzumab 200 mg	16	0.36	(0.236, 0.553)	0.46	(0.233, 0.926)	0.1553
	Anrukinzumab 400 mg	17	1.14	(0.757, 1.722)	1.47	(0.748, 2.882)	0.4633
	Anrukinzumab 600 mg	16	0.52	(0.338, 0.788)	0.66	(0.335, 1.316)	0.4409
Week 12	Placebo	9	0.64	(0.374, 1.084)			
	Anrukinzumab 200 mg	13	0.19	(0.122, 0.297)	0.3	(0.150, 0.598)	0.0283
	Anrukinzumab 400 mg	14	0.96	(0.623, 1.465)	1.5	(0.758, 2.970)	0.4434
	Anrukinzumab 600 mg	11	0.67	(0.411, 1.076)	1.04	(0.510, 2.141)	0.9372
Week 14	Placebo	7	0.41	(0.225, 0.766)			
	Anrukinzumab 200 mg	14	0.29	(0.187, 0.446)	0.70	(0.329, 1.472)	0.5320
	Anrukinzumab 400 mg	15	0.79	(0.517, 1.203)	1.90	(0.900, 4.013)	0.2700
	Anrukinzumab 600 mg	13	1.24	(0.794, 1.949)	3.00	(1.403, 6.409)	0.0666

P-value from ANCOVA model with terms for treatment group, Baseline (in log scale).
LS mean, ratio and CI were based on back log-transformation of those from the ANCOVA model.
ANCOVA=Analysis of covariance; CI=Confidence interval; DAO=Data as observed; LS mean=Least square mean; mITT=Modified intent-to-treat; N=Total number of subjects.

Figure 1. Estimated Fold Change From Baseline (LDA) in Fecal Calprotectin Versus Study Week (mITT DAO)



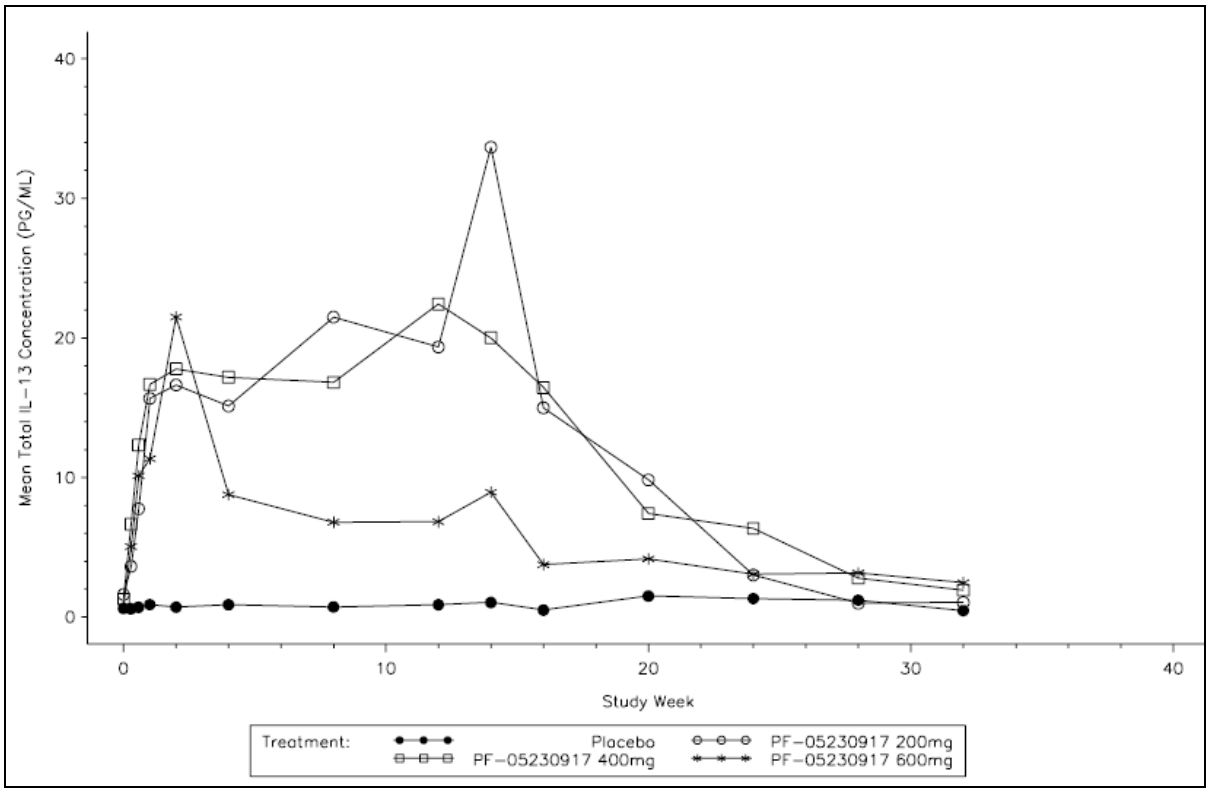
LS mean and CI were based on back log transformation of those from the longitudinal data analysis model with terms for treatment group, time (as categorical variable), time by treatment, Baseline (in log scale). Dot/circle/square/star represents the LS mean value, and whiskers represent the 80% CI.
CI=Confidence interval; DAO=Data as observed; LDA=Longitudinal data analysis; LS=Least square; mITT=Modified intent-to-treat.

Total IL-13: Total IL-13 assay measured both free IL-13 and IL-13 in complex with anrukinzumab in human serum. Mean total IL-13 versus time plot (mITT DAO) for each group is presented in Figure 2 and Table 7. Increases of total IL-13 post-treatment from Baseline were observed for all the dose groups. Maximal increase was observed at 2 weeks after treatment started. While in the anrukinzumab 200 mg and anrukinzumab 400 mg dose groups, the IL-13 levels appeared to maintain a fairly constant level through Week 14; in the anrukinzumab 600 mg, after reaching a peak similar to that seen in the other 2 dose groups at Week 2, IL-13 levels then appeared to decrease after Week 2. After the treatment was finished, total IL-13 then gradually declined towards the Baseline level as the drug concentration dropped for all 3 treatment groups. For some individual subjects, total IL-13 declined during the treatment period while the drug concentration was still high.

In many subjects in all 3 anrukinzumab dose groups IL-13 levels rose only moderately following initiation of treatment and those levels were maintained through the treatment period. In a smaller number of subjects IL-13 levels increased quite considerably following initiation of treatment and those levels were maintained through the treatment period. In other subjects a hybrid pattern was seen, where, after increasing considerably in the first 2 weeks following initiation of treatment. The anrukinzumab 600 mg group has the largest

number of subjects with early drop of total IL-13 levels which contributed to the early drop of mean IL-13 level for the anrukinzumab 600 mg group. One subject in the 200 mg group had a much higher total IL-13 increase after treatment compared with the rest of the group (Table 8).

Figure 2. Mean Total IL-13 Versus Time Plot (mITT DAO)



The lower limit of quantification was 0.3 pg/mL.
DAO=Data as observed; IL-13=Interleukin 13; mITT=Modified intent-to-treat.

Table 7. Descriptive Summary of Absolute Values in Total IL-13 (pg/mL) (mITT DAO)

Study Visit	Parameters	Treatment			
		Placebo N=21	Anrukinzumab 200 mg N=21	Anrukinzumab 400 mg N=21	Anrukinzumab 600 mg N=21
Baseline	N	15	21	20	19
	Mean	0.6247	1.6231	1.29	0.7525
	SD	0.97041	2.9519	2.07219	1.59494
	Median	0.27	0.303	0.354	0.27
	Min	0.27	0.19	0.27	0.27
	Max	4.07	12.3	7.59	7.27
Week 0/Day 2	N	21	19	17	18
	Mean	0.598	3.6373	6.6673	5.0474
	SD	0.81335	4.695	7.29515	4.97368
	Median	0.27	2.01	3.89	2.885
	Min	0.27	0.688	0.704	0.27
	Max	3.89	20.9	22	17.7
Week 0/Day 4	N	16	16	20	15
	Mean	0.7056	7.7698	12.341	10.1349
	SD	1.29166	9.02951	11.84611	10.24068
	Median	0.27	3.995	7.225	4.66
	Min	0.27	0.766	1.4	0.27
	Max	5.45	30.3	44.1	28.5
Week 0/Day 7	N	7	12	9	13
	Mean	0.8991	15.6742	16.67	11.36
	SD	1.15883	34.90836	16.73533	16.79136
	Median	0.27	5.445	7.34	5.61
	Min	0.27	1.5	3.23	1.58
	Max	3.3	126	49.3	58.7
Week 2	N	20	21	19	19
	Mean	0.7177	16.6373	17.7895	21.5021
	SD	0.98373	54.71391	18.53571	27.03784
	Median	0.27	3.92	8.82	8.41
	Min	0.27	0.414	1.41	0.38
	Max	3.86	255	61.7	78.4
Week 4	N	18	21	19	17
	Mean	0.8949	15.1244	17.1853	8.7807
	SD	1.47538	43.76893	15.00105	5.39145
	Median	0.3285	3.97	9.61	8.11
	Min	0.27	0.27	1.88	0.652
	Max	6.14	205	48.3	21.5
Week 8	N	16	18	18	15
	Mean	0.731	21.4964	16.82	6.8027
	SD	1.09524	72.31269	15.4702	3.4481
	Median	0.27	4.265	11.25	6.2
	Min	0.27	0.836	1.51	1.99
	Max	4.63	311	52.1	14.4
Week 12	N	12	14	17	11
	Mean	0.8925	19.3543	22.4335	6.8461
	SD	1.38386	52.0088	27.04635	4.19321
	Median	0.3315	4.015	8.83	6.92
	Min	0.27	0.88	1.33	0.657
	Max	5.06	199	77.2	13.3

Table 7. Descriptive Summary of Absolute Values in Total IL-13 (pg/mL) (mITT DAO)

Study Visit	Parameters	Treatment			
		Placebo N=21	Anrukinzumab 200 mg N=21	Anrukinzumab 400 mg N=21	Anrukinzumab 600 mg N=21
Week 14	N	12	14	16	13
	Mean	1.0545	33.6697	20.0044	8.9492
	SD	1.15526	110.9546	37.36283	6.33317
	Median	0.4845	3.79	6.06	8.19
	Min	0.27	0.356	0.27	1.18
	Max	3.55	419	151	26.8
Week 16	N	10	12	12	7
	Mean	0.5054	15.0002	16.4423	3.757
	SD	0.29982	40.41488	24.5491	2.91709
	Median	0.312	2.48	4.805	3.22
	Min	0.27	0.422	0.448	0.415
	Max	0.981	143	76	8.34
Week 20	N	8	15	15	8
	Mean	1.514	9.8396	7.4261	4.1745
	SD	1.8237	25.99516	8.00205	2.8422
	Median	1.171	2.34	4.33	4.33
	Min	0.27	0.37	0.439	0.986
	Max	5.79	103	25.1	9.59
Week 24	N	10	12	12	8
	Mean	1.33	3.014	6.3665	3.0913
	SD	1.41349	3.23912	7.85116	1.99098
	Median	0.695	1.82	3.325	2.38
	Min	0.27	0.328	0.328	1.27
	Max	4.1	11.2	25.1	7.17
Week 28	N	10	12	13	8
	Mean	1.2151	0.9936	2.8005	3.1724
	SD	2.23797	0.75719	2.67967	2.15647
	Median	0.4085	0.5705	1.95	3.04
	Min	0.27	0.27	0.27	0.849
	Max	7.51	2.2	8.3	5.7
Week 32	N	9	12	13	8
	Mean	0.4727	1.0548	1.9379	2.4725
	SD	0.37875	0.80675	1.99196	2.54141
	Median	0.27	0.7995	1.42	1.88
	Min	0.27	0.27	0.365	0.448
	Max	1.3	2.51	8.06	8.21

The lower limit of quantification is 0.3 pg/mL.
DAO=Data as observed; IL-13=Interleukin 13; max=maximum; min=minimum; mITT=Modified intent-to-treat; N=Total number of subjects in the treatment group in the indicated population; SD=Standard deviation.

Table 8. Descriptive Summary of Change from Baseline in Total IL-13 (pg/mL) (mITT DAO)

Study Visit	Parameters	Treatment			
		Placebo N=21	Anrukinzumab 200 mg N=21	Anrukinzumab 400 mg N=21	Anrukinzumab 600 mg N=21
Baseline	N	15	21	20	19
	Mean	0.6247	1.6231	1.29	0.7525
	SD	0.97041	2.9519	2.07219	1.59494
	Median	0.27	0.303	0.354	0.27
	Min	0.27	0.19	0.27	0.27
	Max	4.07	12.3	7.59	7.27
Week 0/Day 2	N	15	19	17	17
	Mean	-0.0348	2.0556	5.2881	4.4504
	SD	0.09187	3.05075	7.86449	4.64924
	Median	0	1.33	1.59	2.63
	Min	-0.289	-5.164	-5.92	0
	Max	0.048	8.6	21.442	16.828
Week 0/Day 4	N	13	16	20	15
	Mean	0.0665	5.7781	11.051	9.2738
	SD	0.40903	7.97269	11.82413	10.59675
	Median	0	3.082	6.15	3.73
	Min	-0.39	-3.32	0.85	-2.61
	Max	1.38	29.778	42.41	27.628
Week 0/Day 7	N	5	12	9	12
	Mean	-0.232	14.7089	16.181	11.0896
	SD	0.34492	35.02921	16.32622	17.44318
	Median	0	3.867	7.07	5.135
	Min	-0.77	1.23	2.96	-1.48
	Max	0	125.48	47.61	57.753
Week 2	N	15	21	19	18
	Mean	-0.011	15.0141	16.4458	21.6968
	SD	0.1767	55.07442	18.05638	27.57022
	Median	0	3.57	7.48	7.475
	Min	-0.39	-11.89	1.14	0.11
	Max	0.414	254.48	60.01	77.453
Week 4	N	13	21	19	16
	Mean	0.1702	13.5012	15.9163	8.2291
	SD	0.5887	44.16184	14.53151	6.0036
	Median	0	3.66	9.3	8.1425
	Min	-0.39	-12.03	1.61	-2.97
	Max	2.07	204.48	45.057	21.23
Week 8	N	12	18	18	14
	Mean	0.0136	20.375	15.4956	6.0095
	SD	0.2096	72.48033	15.51215	3.89597
	Median	0	3.195	9.885	5.3615
	Min	-0.39	-3.51	1.24	0.21
	Max	0.56	310.48	51.74	14.13
Week 12	N	9	14	17	10
	Mean	0.2283	18.0033	21.2129	6.8817
	SD	0.43591	52.19061	27.59936	4.03196
	Median	0	3.01	7.91	6.867
	Min	-0.028	-3.07	-6.18	0.387
	Max	1	198.48	76.84	13.03

Table 8. Descriptive Summary of Change from Baseline in Total IL-13 (pg/mL) (mITT DAO)

Study Visit	Parameters	Treatment			
		Placebo N=21	Anrukinzumab 200 mg N=21	Anrukinzumab 400 mg N=21	Anrukinzumab 600 mg N=21
Week 14	N	8	14	16	12
	Mean	0.3269	32.5659	18.5538	8.3694
	SD	0.99915	111.149	37.74352	6.75667
	Median	0	3.32	5.57	7.559
	Min	-0.52	-3.16	-2.95	0.91
	Max	2.645	418.48	150.26	26.53
Week 16	N	6	12	12	7
	Mean	-0.57	14.2457	15.3368	2.2993
	SD	1.54435	40.45675	24.88208	2.94095
	Median	0	2.25	3.456	2.605
	Min	-3.716	-0.507	0.178	-0.81
	Max	0.253	142.48	75.652	7.483
Week 20	N	4	15	15	8
	Mean	0.9175	8.5607	6.5727	2.9185
	SD	3.34362	26.16052	7.91298	3.22794
	Median	0.485	1.33	3.74	2.567
	Min	-2.67	-2.06	0.169	-1.75
	Max	5.37	102.48	24.357	8.733
Week 24	N	6	12	12	8
	Mean	0.0828	1.4762	5.4678	1.76
	SD	2.25162	4.06717	7.92073	2.94775
	Median	-0.056	1.125	2.575	1.637
	Min	-3.581	-3.33	-1.21	-4.09
	Max	3.2	10.678	24.204	6.313
Week 28	N	8	12	13	8
	Mean	0.4139	-0.2094	1.9397	1.8411
	SD	3.02626	1.94214	2.95887	3.70576
	Median	0	0.1415	0.95	2.4745
	Min	-3.8	-4.053	-3.29	-5.74
	Max	7.125	1.894	7.557	5.07
Week 32	N	7	12	13	8
	Mean	-0.558	-0.1509	0.8706	1.1413
	SD	1.43012	2.11017	2.78344	3.9053
	Median	0	0.1945	0.79	1.61
	Min	-3.8	-4.45	-4.57	-6.822
	Max	0.034	2.24	7.79	7.338

The lower limit of quantification is 0.3 pg/mL.
DAO=Data as observed; IL-13=Interleukin 13; max=maximum; min=minimum; mITT=Modified intent-to-treat; N=Total number of subjects in the treatment group in the indicated population; SD=Standard deviation.

Safety Results:

Treatment Emergent Adverse Events:

Treatment emergent adverse events (TEAEs) reported during the study are summarized in Table 9. At least 1 TEAE was reported in 15 subjects in the placebo group, 19 subjects in the anrukinzumab 200 mg group, 17 subjects in the anrukinzumab 400 group and 17 subjects in

the anrukinzumab 600 mg group; corresponding numbers for TEAEs considered causally related to treatment with study medication by the reporting investigator were 7, 7, 7, and 9, respectively.

Table 9. Summary of Treatment-Emergent Adverse Events (AE) - All Causality (AC) and Treatment-Related (TR)

Number of Subjects	Placebo		Anrukinzumab 200 mg		Anrukinzumab 400 mg		Anrukinzumab 600 mg	
	AC	TR	AC	TR	AC	TR	AC	TR
Subjects evaluable for AEs	21	21	21	21	21	21	21	21
Number of AEs	84	23	84	15	79	11	54	17
Subjects with AE	15	7	19	7	17	7	17	9
Subjects with SAE	4	0	4	1	2	0	4	2
Subjects with severe AEs	3	0	6	1	2	0	4	2
Subjects discontinued from study due to AE	4	0	5	1	1	0	5	2
Subjects with dose reduced or temporary discontinuation due to AE	0	0	1	0	0	0	1	0

Included all data collected since the first dose of study drug.
With the except for row entitled "Number of AEs", all numbers reflect number of subjects not number of events.
Treatment Related - according to the investigator's assessment that there was a reasonable possibility that event was related to study medication.
MedDRA (Version 16.0) coding dictionary applied.
AC=All causality; AE=Adverse event, MedDRA=Medical Dictionary for Regulatory Activities, SAE=Serious adverse event; TR=Treatment-related.

Non-Serious Adverse Events:

Treatment emergent non-serious AEs occurred in ≥5% of subjects is presented in Table 10. The most frequently reported events were UC, headache, abdominal pain, nausea and anemia.

Table 10. Treatment-Emergent Non-Serious Adverse Events occurred in ≥5 % Subjects in Any Treatment Group (All Causality)

Number (%) of Subjects	Placebo (N=21)	PF-05230917 200 mg (N=21)	PF-05230917 400 mg (N=21)	PF-05230917 600 mg (N=21)
Subjects With Adverse Events, n (%)	**12 (57.1)**	**18 (85.7)**	**13 (61.9)**	**15 (71.4)**
Blood and lymphatic system disorders	4 (19.0)	2 (9.5)	4 (19.0)	3 (14.3)
Anaemia	3 (14.3)	1 (4.8)	4 (19.0)	1 (4.8)
Eosinophilia	1 (4.8)	1 (4.8)	0	2 (9.5)
Eye disorders	0	2 (9.5)	0	0
Vision blurred	0	2 (9.5)	0	0
Gastrointestinal disorders	6 (28.6)	11 (52.4)	11 (52.4)	12 (57.1)
Abdominal pain	3 (14.3)	2 (9.5)	2 (9.5)	3 (14.3)
Colitis ulcerative	3 (14.3)	7 (33.3)	5 (23.8)	8 (38.1)
Diarrhoea	2 (9.5)	2 (9.5)	2 (9.5)	0
Flatulence	1 (4.8)	0	2 (9.5)	0
Nausea	2 (9.5)	2 (9.5)	2 (9.5)	3 (14.3)
Vomiting	3 (14.3)	1 (4.8)	2 (9.5)	0
General disorders and administration site conditions	5 (23.8)	3 (14.3)	2 (9.5)	1 (4.8)
Chest pain	2 (9.5)	0	0	0
Fatigue	0	1 (4.8)	2 (9.5)	1 (4.8)
Oedema peripheral	3 (14.3)	0	0	0
Pyrexia	2 (9.5)	2 (9.5)	1 (4.8)	0
Infections and infestations	4 (19.0)	8 (38.1)	6 (28.6)	5 (23.8)
Influenza	2 (9.5)	1 (4.8)	1 (4.8)	0
Nasopharyngitis	1 (4.8)	4 (19.0)	1 (4.8)	2 (9.5)
Upper respiratory tract infection	1 (4.8)	2 (9.5)	3 (14.3)	2 (9.5)
Urinary tract infection	1 (4.8)	2 (9.5)	3 (14.3)	1 (4.8)
Investigations	0	1 (4.8)	0	2 (9.5)
Blood creatine phosphokinase increased	0	1 (4.8)	0	2 (9.5)
Metabolism and nutrition disorders	2 (9.5)	0	0	0
Hypokalaemia	2 (9.5)	0	0	0
Musculoskeletal and connective tissue disorders	5 (23.8)	2 (9.5)	1 (4.8)	1 (4.8)
Arthralgia	2 (9.5)	2 (9.5)	0	1 (4.8)
Joint swelling	3 (14.3)	0	1 (4.8)	0
Nervous system disorders	4 (19.0)	4 (19.0)	0	3 (14.3)
Headache	4 (19.0)	4 (19.0)	0	3 (14.3)
Skin and subcutaneous tissue disorders	1 (4.8)	2 (9.5)	2 (9.5)	0
Acne	0	2 (9.5)	0	0
Pruritus	1 (4.8)	1 (4.8)	2 (9.5)	0

Subjects were only counted once per treatment for each row.
Included all data collected since the first dose of study drug.
MedDRA (Version 16.0) coding dictionary applied.
AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities; n=Number of subjects with AEs; N=Number of subjects evaluable for AEs.

Treatment-related TEAE occurred in ≥5% of subjects is presented in Table 11.

Table 11. Treatment-Emergent Adverse Events Reported in >1 Subject in Any Treatment Group by MedDRA Preferred Term - Treatment-Related

Number (%) of Subjects	Placebo (N=21)	PF-05230917 200 mg (N=21)	PF-05230917 400 mg (N=21)	PF-05230917 600 mg (N=21)
Gastrointestinal disorders	4	2	2	5
Abdominal pain	2	1	0	1
Colitis ulcerative	0	0	0	4
Vomiting	2	0	1	0
General disorders and administration site conditions	3	2	1	1
Chest pain	2	0	0	0
Pyrexia	0	2	0	0
Nervous system disorders	2	3	0	1
Headache	2	3	0	0

AEs and SAEs are not separated out.
AE=Adverse event; n=Number of subjects with AEs; N=Number of subjects evaluable for AEs.

Serious Adverse Events:

All serious TEAE is presented in Table 12. A total of 16 SAEs were reported in 14 subjects: 4 subjects in the placebo group, 4 subjects in the anrukinzumab 200 mg group, 2 subjects in the anrukinzumab 400 mg group and 4 subjects in the anrukinzumab 600 mg group. Among these 14 subjects, 9 subjects reported an SAE of UC: 3 subjects in the placebo group, 2 subjects in the anrukinzumab 200 mg group, 1 subject in the anrukinzumab 400 mg group and 3 subjects in the anrukinzumab 600 mg group.

Five (5) subjects had a total of 6 non-UC SAEs, 1 (anemia) in the placebo group, 2 (cellulitis and arthralgia; abdominal pain), 1 (sclerosing cholangitis) in the anrukinzumab 400 mg group and 1 (*Clostridum difficile* infection) in the anrukinzumab 600 mg group.

Three (3) SAEs, 1 (abdominal pain) in the anrukinzumab 200 mg group and 2 (both UC) in the anrukinzumab 600 mg group, were considered causally related to study treatment by the reporting investigator (Table 13).

Table 12. Treatment-Emergent Serious Adverse Events (All Causalities)

Number (%) of Subjects	Placebo (N=21)	PF-05230917 200 mg (N=21)	PF-05230917 400 mg (N=21)	PF-05230917 600 mg (N=21)
SOC **Preferred Term**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Subjects Evaluable for Adverse Events	**21**	**21**	**21**	**21**
Subjects With Adverse Events	**4 (19.0)**	**4 (19.0)**	**2 (9.5)**	**4 (19.0)**
Blood and lymphatic system disorders	1 (4.8)	0	0	0
Anaemia	1 (4.8)	0	0	0
Gastrointestinal disorders	3 (14.3)	3 (14.3)	1 (4.8)	3 (14.3)
Abdominal pain	0	1 (4.8)	0	0
Colitis ulcerative	3 (14.3)	2 (9.5)	1 (4.8)	3 (14.3)
Hepatobiliary disorders	0	0	1 (4.8)	0
Cholangitis sclerosing	0	0	1 (4.8)	0
Infections and infestations	0	1 (4.8)	0	1 (4.8)
Cellulitis	0	1 (4.8)	0	0
Clostridium difficile infection	0	0	0	1 (4.8)
Musculoskeletal and connective tissue disorders	0	1 (4.8)	0	0
Arthralgia	0	1 (4.8)	0	0

AE=Adverse event; n=Number of subjects with AEs; N=Number of subjects evaluable for AEs; SOC=System organ class.

Table 13. Treatment-Related Serious Adverse Events

Preferred Term[a]	Causality[b]	Clinical Outcome	Seriousness
Anrukinzumab 200 mg			
Abdominal pain	Related	Resolved	Hospitalization
Anrukinzumab 600 mg			
Colitis ulcerative	Related	Resolved with sequelae	Hospitalization
Colitis ulcerative	Related	Resolved	Hospitalization

AE=Adverse event; MedDRA=Medical Dictionary for Regulatory Activities.
a. AEs were coded using the MedDRA (Version 16.0).
b. Causality (relationship to the study treatment) as assessed by the investigator.

Deaths: There were no deaths reported during the study.

Dose Reductions or Temporary Discontinuations Due to Adverse Events:

A total of 2 subjects temporarily discontinued the study medication or had dose reduction of study medication due to a TEAE: 1 subject in the anrukinzumab 200 mg group and 1 subject in the anrukinzumab 600 mg group. Both the events (infusion site pain and upper respiratory tract infection) resolved and were considered by the investigator as unrelated to the study treatment.

Table 14. Temporary Discontinuation or Dose Reduction Due to Adverse Events

MedDRA[a] PT (Severity)	Start Day[b]	Stop Day[b]	Causality	Outcome
Anrukinzumab 200 mg				
Infusion site pain (mild)	15	15	Treatment-unrelated	Resolved
Anrukinzumab 600 mg				
Upper respiratory tract infection (moderate)	86	95	Treatment-unrelated	Resolved

AE=Adverse event; MedDRA=Medical Dictionary for Regulatory Activities; PT=Preferred term.
a. AEs were coded using the MedDRA (Version 16.0).
b. Start day and stop day are the start and stop of the AE relative to the start of the study treatment (Day 1).

Permanent Discontinuations Due to Adverse Events:

A total of 14 subjects permanently discontinued participation in the study due to AEs: 4 subjects in the placebo group, 5 subjects in the anrukinzumab 200 mg, 0 subjects in the anrukinzumab 400 mg group and 5 subjects in the anrukinzumab 600 mg group (Table 15).

Table 15. Permanent Discontinuation Due to Adverse Events

Number of Subject	MedDRA[a] PT (Severity)	Start Day[b]	Stop Day[b]	Causality	Outcome
Placebo					
1	Colitis ulcerative (Moderate)	22	43	Treatment-unrelated	Resolved
2	Oedema peripheral (Severe)	27	>29	Treatment-unrelated	Still present
3	Alcohol use (Mild)	1	123	Treatment-unrelated	Resolved
4	Colitis ulcerative (Severe)	160	197	Treatment-unrelated	Resolved with sequelae
Anrukinzumab 200 mg					
5	Colitis ulcerative (Severe)	147	>170	Treatment-unrelated	Still present
6	Gastroenteritis viral (Severe)	24	28	Treatment-unrelated	Resolved
7	Colitis ulcerative (Moderate)	66	>69	Treatment-unrelated	Unknown
8	Colitis ulcerative (Severe)	47	57	Treatment-unrelated	Resolved
9	Abdominal pain (Moderate)	24	74	Treatment-related	Resolved
Anrukinzumab 600 mg					
10	Clostridium difficile infection (Severe)	3	77	Treatment-unrelated	Resolved
11	Colitis ulcerative (Moderate)	22	102	Treatment-unrelated	Resolved
12	Bronchopneumonia (Moderate)	51	58	Treatment-related	Resolved
13	Colitis ulcerative (Severe)	9	30	Treatment-related	Resolved
14	Colitis ulcerative (Moderate)	102	124	Treatment-unrelated	Resolved

AE=Adverse event; MedDRA=Medical Dictionary for Regulatory Activities; PT=Preferred term
a. AEs were coded using the MedDRA (Version 16.0).
b. Start day and stop day are the start and stop of the AE relative to the start of the study treatment (Day 1).

Immunogenicity Results:

None of the ADA samples was tested positive for this study. Therefore, no sample was tested in the NAb assay.

CONCLUSIONS:

- In this study, treatment with each of the 3 doses of anrukinzumab (200 mg, 400 mg, 600 mg) did not have a statistically significant effect in subjects with active UC, as measured by changes in disease related PD parameters and clinical parameters. Numerical trends were observed in the clinical parameters for the 200 and 400 mg doses over placebo.

- Over the dose range of 200 to 600 mg, serum anrukinzumab exposure (C_{max} and AUC_{tau}) appeared to be approximately dose proportional following the first dose and the last dose (Week 12) administered. Trough serum anrukinzumab concentrations increased from Week 0 to Week 4 for all treatment groups, then decreased slightly when dosing interval changed from 2 weeks to 4 weeks, while there was essentially no accumulation for C_{max} from the first dose to the last dose.

- Total, peripheral, IL-13 levels increased with treatment for all 3 dose levels and reached maximal change by 2 weeks, and gradually declined towards Baseline level after treatment period ended.

- Treatment with anrukinzumab appeared to be well tolerated; no increased risk of infection was identified and no other safety concerns were revealed by the analyses of AE and laboratory parameter data.