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COMPOUND NUMBER: PF-04523655

PROTOCOL NO.: B0451001 (MONET)

PROTOCOL TITLE: Phase II, Open Label, Multicenter, Prospective, Randomized, Age Related, Macular Degeneration, Comparator Controlled, Study Evaluating PF-04523655 Versus Ranibizumab in the Treatment of Subjects With Choroidal Neovascularization (Monet Study)

Study Centers: Twenty six (26) centers took part in the study and randomized subjects: 5 in United States (US), 5 in Israel, 4 in India, 3 in Korea Republic of, 2 in Philippines, 2 in Spain and 1 each in Austria, Denmark, Hong Kong, Taiwan and Turkey.

Study Initiation and Final Completion Dates: 11 November 2009 to 07 July 2011

Phase of Development: Phase 2

Study Objectives:

Primary Objective:

- To evaluate the efficacy of different dosing paradigms of PF-04523655 versus ranibizumab (comparator) in subjects with neovascular age-related macular degeneration (AMD).

Secondary Objectives:

- To evaluate the safety and tolerability of repeat intravitreal (IVT) injections of PF-04523655 in subjects with choroidal neovascularization (CNV) associated with AMD;
- To evaluate changes in retinal central subfield thickness and retinal lesion thickness by optical coherence tomography (OCT);
- To evaluate changes in lesion morphology following IVT administration of PF-04523655 by fundus fluorescein angiography (FFA).

METHODS

Study Design:

This was a Phase 2, prospective, randomized, open-label, parallel, comparator controlled exploratory study of PF-04523655 versus ranibizumab in subjects with neovascular AMD.

The study was designed to explore different dosing paradigms to determine potential bioactivity of PF-04523655 alone and in combination with ranibizumab. Subjects were screened up to 14 days prior to the Baseline visit. OCT test results were evaluated by the Duke Reading center to determine study eligibility. OCT eligibility was determined by the Investigator at the site if there was a delay in receiving results from the central reading center.

Subjects were randomized at Baseline to 1 of 5 possible treatment cohorts in a 1:1:1:1:1 ratio:

- PF 1 mg: Ranibizumab (0.5 mg) given at Baseline followed by PF-04523655 (1 mg) given every 4 weeks (Q4W) from Week 4 to Week 12;
- PF 3 mg: Ranibizumab (0.5 mg) given at Baseline followed by PF-04523655 (3 mg) given Q4W from Week 4 to Week 12;
- PF 3 mg Every 2 Weeks (Q2W): Ranibizumab (0.5 mg) given at Baseline followed by PF-04523655 (3 mg) given Q2W from Week 4 to Week 12;
- PF 1 mg/Ranib Combo: Ranibizumab (0.5 mg) administered first followed by PF-04523655 (1 mg) 30 minutes later Q4W from Baseline to Week 12;
- Ranib-Only: Ranibizumab (0.5 mg; comparator arm) given Q4W from Baseline to Week 12.

Note: Since all treatment groups (except PF 3 mg Q2W) administered study medication Q4W, only treatment group PF 3 mg Q2W uses the "Q2W" acronym within this public disclosure synopsis (PDS) as a group identifier.

All subjects enrolled in the study were treated at Baseline with ranibizumab 0.5 mg via IVT injection (as induction) and 1 group received ranibizumab in combination with PF 1 mg. This permitted initial treatment with the current standard-of-care to maximize potential improvement in visual acuity and/or retinal structure prior to dosing with PF-04523655. Subjects received study treatment from Baseline to Week 12 inclusively. Independent of dosing frequency, all subjects were to have maintained the same visit schedule. Subjects had ophthalmic assessments at Weeks 4, 6, 8, 10, 12, 16, 24 and 48. During the study, personnel were unmasked to study treatments except those that measured best corrected visual acuity (BCVA) and conducted fundus photography (FP)/FFA/OCT tests.

Ocular and systemic adverse event (AE) evaluations occurred throughout the course of the study. FP and OCT were performed at monthly visits from Baseline to Week 16. FA was

performed at Baseline and at Week 16. Laboratory tests, electrocardiograms, and pregnancy tests were conducted at Baseline and at Week 16. Blood samples were optionally taken at Baseline for exploratory molecular profiling.

After Week 12 (Month 3), subjects were followed until the End of Study (Month 12). At Week 16 (Month 4) primary efficacy was assessed. All subjects were followed for safety until the End of the Study (Month 12).

To ensure subjects received optimal therapy, subjects were evaluated for rescue therapy (ie, ranibizumab, the current standard-of-care) beginning at Week 10. Subjects were eligible for rescue if <7 letters of BCVA were gained from Baseline. Rescued subjects were to remain in the study for Follow-up until the End of Study. During the Follow-up period (ie, beginning on Week 16 until Week 48), all subjects received ranibizumab as needed.

Three (3) interim analyses were conducted during the study (after approximately):
50 subjects completed Week 10 visit (or discontinued by Week 10); 75 subjects completed Week 10 visit (or discontinued by Week 10); and 75 subjects completed Week 16 visit (or discontinued by Week 16).

Enrollment continued during the interim analyses. Following the second interim analysis, the PF 3 mg Q2W and PF 1 mg dose groups were terminated based on predetermined futility criteria. At the time when those 2 dose groups were terminated, the study had already been fully enrolled. Subjects in those 2 dose groups who had not completed the Week 10 visit were mandatorily discontinued from treatment and optionally rescued with ranibizumab at the discretion of the Investigators. All subjects in those 2 dose groups were followed until the End of the Study.

Table 1 presents the schedule of activities for this study.

Table 1. Schedule of Activities

Study Activity	Screening Day -14 to Day 0	Treatment Phase (Visit ±7 Days)						Follow-Up Phase (Visit ±7 Days)		
		Baseline Day 0	Week 4	Week 6	Week 8	Week 10	Week 12	Week 16	Week 24/Month 6	Week 48/Month 12[a]
Informed consent	X									
Medical history and physical examination	X									
Vital signs (BP/pulse)	X	X						X		
Hematology		X						X		
Blood chemistry		X						X		
Urinalysis		X						X		
Coagulation		X						X		
Pregnancy test[b]		X						X		
FSH		X						X		
ECG		X						X		
Review eligibility criteria		X								
Randomization		X								
PF 1 mg, Q4W		Ranib 0.5 mg	X		X		X			
PF 3 mg, Q4W		Ranib 0.5 mg	X		X		X			
PF 3 mg, Q2W		Ranib 0.5 mg	X	X	X	X	X			
PF 1 mg/ranib combo, Q4W		Ranib + PF	X		X		X			
Ranib - only 0.5 mg, Q4W		X	X		X		X			
Assess rescue criteria						X				
Adverse events	X	X	X	X	X	X	X	X	X	X
Concomitant medication	X	X	X	X	X	X	X	X	X	X
BCVA	X	X	X	X	X	X	X	X	X	X
Slit lamp exam	X	X	X	X	X	X	X	X	X	X
IOP	X	X	X	X	X	X	X	X	X	X
Fundus photography	X	X	X		X		X	X		
FFA	X	X						X		
OCT	X	X	X		X		X	X		
Pharmacogenomics' sample[c]		X								

Table 1. Schedule of Activities

BCVA = best corrected visual acuity; BP = blood pressure; ECG = electrocardiogram; FFA = fundus fluorescein angiography; FSH = follicle stimulating hormone; IEC = Independent Ethics Committee; IOP = intraocular pressure; IRB = Institutional Review Board; OCT = optical coherence; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab.

a. End of Study.
b. Pregnancy tests may have been repeated at the requests of IRBs/IECs, or if it was required by local regulations.
c. Sample was de-identified, details can be found in the molecular profiling.

Number of Subjects (Planned and Analyzed): Approximately 150 subjects were to be enrolled into the study.

A total of 152 subjects were randomized in the study (25 in US, 51 in Israel, 18 in India, 23 in Korea Republic of, 6 in Philippines, 8 in Spain, 1 in Austria, 10 in Denmark, 6 in Hong Kong, 1 in Taiwan and 3 in Turkey). Of these, 151 subjects received study treatment.

Diagnosis and Main Criteria for Inclusion and Exclusion: Males and females aged ≥50 years with active primary or recurrent subfoveal CNV secondary to AMD, with active CNV defined as any leakage detected on FFA or OCT; female subjects aged 50-60 years of age who were amenorrheic for at least 2 years, with a serum follicle stimulating hormone level within the laboratory reference range for postmenopausal women; total area of CNV (including both classic and occult components) encompassed within the lesion ≥50% of the total lesion area; total lesion size ≤12 disc areas; BCVA using Early Treatment Diabetic Retinopathy Study (ETDRS) protocol of 20/40 to 20/320 (letter score ≤73) in the study eye at the Screening visit; BCVA in the fellow eye of 20/400 or better (letter score of ≥19) at the Screening visit and subjects with retinal central subfield thickness ≥250 μm measured using Stratus OCT were included in the study.

Exclusion Criteria: Subjects with prior treatment with verteporfin photodynamic therapy, external-beam radiation therapy, or transpupillary thermotherapy in the study eye; previous subfoveal focal laser photocoagulation in the study eye; laser photocoagulation (juxtafoveal or extrafoveal) in the study eye within 1 month preceding Baseline, history of vitrectomy, submacular surgery or other surgical intervention for AMD in the study eye; previous participation in any studies with investigational drugs or treatments administered 1 month preceding Baseline visit such as systemic glucocorticoids, ocular or periocular steroids (eg, triamcinolone, anecortave acetate), anti-angiogenic drugs such as pegaptanib (Macugen), ranibizumab (Lucentis), bevacizumab (Avastin) in the study eye; subretinal hemorrhage in the study eye that involves the fovea, if the size of the hemorrhage either ≥50% of the total lesion area or 1 or more disc areas in size; CNV in either eye of other etiology, eg, ocular histoplasmosis, trauma, or pathologic myopia; presence of subfoveal scarring; and with retinal pigment epithelial tear involving the macula in the study eye were excluded from the study.

Study Treatment: PF-04523655 investigational drug product was formulated and supplied by the Sponsor as a sterile solution for IVT injection. PF-04523655 drug product was formulated to deliver the specified dose levels when diluted as directed.

Two (2) strengths of PF-04523655 study medication were provided: 10 mg/mL in 0.4 mL vials and 30 mg/mL in 0.4 mL vials. The 1 mg dose of PF-04523655 monotherapy was prepared using the 10 mg/mL strength. For the 1 mg PF-04523655 dose to be administered in combination with ranibizumab, the 30 mg/mL vial was diluted. The 3 mg dose of PF-04523655 was prepared using the 30 mg/mL strength. Study medication was provided as single use vials with a tamper-evident seal on each vial.

Following physical and ophthalmic examinations, dose cohort treatments were administered to the respectively randomized cohort subjects. Both ranibizumab and PF-04523655 were administered through IVT injections under sterile conditions.

Subjects randomized to the PF 1 mg/Ranib Combo cohort were to receive ranibizumab (0.5 mg) first followed by PF-04523655 approximately 30 minutes later for all treatments during the study (including at Baseline).

Following study drug injections, the ophthalmic examinations were performed as described in Table 1.

Efficacy and Safety Endpoints:

Primary Endpoint:

Mean change from Baseline in the BCVA score measured using the ETDRS protocol by Week 16.

Secondary Endpoints:

- Mean change from Baseline over time (16 weeks) in the BCVA score, as measured using the ETDRS protocol;
- Percent of subjects gaining ≥15 letters in the BCVA score at 16 weeks compared to Baseline, as measured using the ETDRS protocol;
- Incidence and severity of ocular AEs identified by ophthalmic examination and or spontaneously reported;
- Incidence and severity of systemic AEs identified by physical examination, changes in vital signs, clinical laboratory abnormalities and or spontaneously reported;
- Change from Baseline to Weeks 4, 8, 12, and 16 in retinal central subfield thickness and retinal lesion thickness assessed by OCT;
- Change from Baseline in lesion size on FFA at Week 16.

Safety Evaluations: Safety was one of the secondary endpoints as described above. Ophthalmic examinations included slit lamp biomicroscopy of the anterior segment performed without fluorescein staining and pupil dilatation; intraocular pressure measured using the Goldmann applanation tonometry; ophthalmoscopy of the posterior segment (ie, vitreous body, optic nerve head, macular and peripheral retina); BCVA using the ETDRS chart; FP, FFA and OCT imaging.

Statistical Methods:

Intent-to-Treat (ITT) Population: All analyses were performed using the ITT population, which included all enrolled subjects who received at least 1 dose of study medication.

Per-Protocol (PP) Population: The PP population included enrolled subjects who met inclusion criteria based on central OCT reading, received at least 1 dose of study medication, had at least 1 post-Baseline visual acuity score, and had no major protocol violations. The primary efficacy endpoint was analyzed in both ITT and PP populations if there were large discrepancies between the number of subjects included in ITT and PP populations (ie, if there were large numbers of subjects who were excluded from the PP population). Secondary endpoints were only analyzed in ITT population and not in PP population.

Primary Endpoint: The primary efficacy endpoint was the change in BCVA from Baseline to Week 16. The difference in mean BCVA change from Baseline to Week 16 between any of the PF-04523655 treatment groups (including the combination treatment group) and the Ranib-Only group was analyzed using a 1-way analysis of variance (ANOVA) model with treatment group as the factor. p-Values were not adjusted for multiple comparisons or for the interim evaluations.

Residual plots were examined to evaluate whether the normality and homogeneity of variance assumptions for the ANOVA model were met.

Secondary Endpoints: For endpoints based on dichotomous outcome (eg, % subjects eligible for rescue at Week 10, % subjects gaining ≥15 or ≥10 letters in BCVA), treatment-group comparison between any of the PF-04523655 treatment groups (including the combination treatment group) and the Ranib-Only group were performed using a Chi-square test.

For endpoints based on continuous outcome (eg, change from Baseline in BCVA, retinal central subfield thickness, lesion thickness, and CNV area), treatment-group comparison between any of the PF-04523655 treatment groups (including the combination treatment group) and the Ranib-Only group were performed using a 1-way ANOVA model with treatment group as the factor.

Interim Analysis: For the first 2 interim analyses, the eligible-for-rescue rate in each of the PF-04523655 dosing groups was compared against the eligible-for-rescue rate in the Ranib-Only comparator group. For the third interim analysis, the mean BCVA change from Baseline in each of the PF-04523655 dosing groups was compared against the mean BCVA change from Baseline in the Ranib-Only comparator group.

At each interim analysis, a data monitoring committee evaluated safety results. In addition, the eligible-for-rescue rates were compared at the first and second interim analyses and efficacy was evaluated at the third interim analysis. Futile PF-04523655 dosing groups were terminated based on prespecified criteria. Any treatment group may have been terminated at any time point if there were overt safety signals observed within that particular treatment group.

RESULTS

Subject Disposition and Demography:

A total of 152 subjects were randomized and 151 subjects were treated. One hundred thirty-five (135) subjects (89.4%) completed the 12 month study period (ie, a 3-month active treatment period and a 9-month Follow-up safety period). The disposition of subject discontinuations is displayed in Table 2.

The discontinuation rate was higher in the PF 3 mg Q2W and PF 1 mg dose groups (5 subjects each; 17.2% and 16.7%, respectively) compared with other treatment groups. Across all treatment groups, AEs unrelated to study drugs was the most frequent cause of study discontinuation (6 subjects; 4.0%).

Due to the rescue criteria, a large proportion of subjects did not complete the 12-week study treatment phase, ie, 34 subjects did not complete the treatment phase and 25 of them were due to insufficient clinical response. The proportions of subjects who did not complete treatment phase were higher in the PF 3 mg Q2W and PF 1 mg dose groups than in other groups (Table 2).

Table 2. Subject Disposition

Number (%) of Subjects	Treatment Groups				
	PF-04523655 1 mg Q4W	PF-04523655 3 mg Q4W	PF-04523655 3 mg Q2W	PF-04523655 1 mg/Ranib Combo Q4W	Ranib - Only Q4W
Screened N=245					
Assigned to study treatment	30	31	30	30	31
Treated	29	31	30	30	31
Completed	24	28	25	28	30
Discontinued from study	5	3	5	2	1
Subject died	3	0	0	0	0
Related to study drug	1	1	0	0	0
Insufficient clinical response	1	1	0	0	0
Not related to study drug	1	2	5	2	1
AE	0	1	3	1	1
Lost to follow-up	0	0	0	1	0
No longer willing to participate	1	0	2	0	0
Protocol violation	0	1	0	0	0
Total discontinued from study	5	3	5	2	1
Discontinued from treatment phase					
Related to study drug	9	6	8	1	1
Insufficient clinical response	9	6	8	1	1
Not related to study drug	2	1	3	2	1
AE	0	1	1	1	1
Lost to follow-up	0	0	0	1	0
No longer willing to participate	0	0	1	0	0
Other	2	0	1	0	0
Total discontinued from treatment phase	11	7	11	3	2

AE = adverse event; N = number of subjects; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab.

The primary efficacy endpoint was analyzed in both ITT and the PP populations. Secondary endpoints were only analyzed in ITT population. There were 8 subjects from the

ITT population who did not meet the PP population criteria: 4 subjects had major protocol violations, and 4 other subjects did not have central retinal thickness >250 μm at Screening (Table 3).

Table 3. Data Sets Analyzed

Number (%) of Subjects	Treatment Groups				
	PF-04523655 1 mg Q4W N=29	PF-04523655 3 mg Q4W N=31	PF-04523655 3 mg Q2W N=30	PF-04523655 1 mg/Ranib Combo Q4W N=30	Ranib – Only Q4W N=31
Assigned to study treatment	30	31	30	30	31
Treated	29	31	30	30	31
Analyzed for efficacy					
ITT	29	31	30	30	31
PP	29	27	27	29	31
Analyzed for safety					
AEs	29	31	30	30	31
Laboratory data	28	30	28	28	30

AE = adverse event; ITT = intent-to-treat; N = number of subjects; PP = per protocol; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab.

Baseline characteristics and demographics are summarized in Table 4. Subjects were 50 to 93 years old with a mean age of 74.6 years. There were slightly more female (56.3%) than male (43.7%) subjects, and 64.2% of subjects were White and 35.8% were Asian. Age, race, gender, and BCVA distributions at Baseline were similar across all treatment groups.

Table 4. Demographic and Baseline Characteristics (ITT Population)

Parameters	Treatment Groups					
	PF-04523655 1 mg Q4W N=29	PF-04523655 3 mg Q4W N=31	PF-04523655 3 mg Q2W N=30	PF-04523655 1 mg/Ranib Combo Q4W N=30	Ranib – Only Q4W N=31	Total N=151
Number of subjects,						
Male	10	16	15	12	13	66
Female	19	15	15	18	18	85
Age, (years)						
50-<65	6 (20.7)	4 (12.9)	5 (16.7)	5 (16.7)	5 (16.1)	25 (16.6)
65-<80	10 (34.5)	17 (54.8)	19 (63.3)	16 (53.3)	14 (45.2)	76 (50.3)
≥80	13 (44.8)	10 (32.3)	6 (20.0)	9 (30.0)	12 (38.7)	50 (33.1)
Mean (SD)	74.7 (9.6)	76.0 (9.6)	72.5 (8.4)	74.0 (10.0)	75.5 (8.7)	74.6 (9.3)
Range	50-88	55-93	51-89	52-91	59-89	50-93
Race, n (%)						
White	22 (75.9)	19 (61.3)	18 (60.0)	20 (66.7)	18 (58.1)	97 (64.2)
Asian	7 (24.1)	12 (38.7)	12 (40.0)	10 (33.3)	13 (41.9)	54 (35.8)
Primary diagnosis, n (%)						
Age-related macular degeneration	29 (100%)	31 (100%)	30 (100%)	30 (100%)	31 (100%)	151 (100%)
Duration since diagnosis, months						
Mean (SD)	1.0 (1.6)	2.1 (4.7)	2.1 (6.8)	1.1 (1.2)	0.9 (0.9)	NC
Range	0.2-8.7	0.2-21.4	0.2-37.7	0.1-6.0	0.2-4.4	NC
Study eye, n (%)						
Left eye	19 (65.5)	16 (51.6)	14 (46.7)	13 (43.3)	18 (58.1)	80 (53.0)
Right eye	10 (34.5)	15 (48.4)	16 (53.3)	17 (56.7)	13 (41.9)	71 (47.0)
Baseline BCVA, letters						
Mean	52.0	53.0	48.2	49.5	53.3	NC
(SD)	(13.5)	(15.7)	(16.1)	(13.7)	(11.7)	
Range	25-70	13-72	18-71	27-73	26-73	NC

BCVA = best corrected visual acuity; ITT = intent-to treat; n = number of subjects in the pre-specified criteria; N = number of subjects; NC = not calculated; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab; SD = standard deviation.

Efficacy Results:

Primary Endpoint:

Week 16 Data With Missing Values Imputed Using Last Observation Carried Forward (LOCF) Method in ITT Population:

The mean BCVA letter changes from Baseline to Week 16 (LOCF) in all 3 PF-04523655 monotherapy dose groups were less than the Ranib-Only group. The mean BCVA letter change from Baseline to Week 16 in the PF 1 mg/Ranib Combo treatment group (9.5 letters) was greater than the Ranib-Only group (6.8 letters) by 2.7 letters, but the difference was not statistically significant (Table 5). Trends observed in the PP population were similar to the ITT population.

Table 5. Summary of BCVA Letters and its Change From Baseline in the Study Eye by Study Visit - Excluding Observations Collected After Receiving Ranibizumab Treatment Other Than at Baseline (LOCF; ITT Population)

	Treatment Groups				
	PF 1 mg Q4W N=29	PF 3 mg Q4W N=31	PF 3 mg Q2W N=30	PF 1 mg/Ranib Combo Q4W N=30	Ranib-Only Q4W N=31
ITT Population					
Baseline: mean (SD)	52.0 (13.5)	53.0 (15.7)	48.2 (16.1)	49.5 (13.7)	53.3 (11.7)
Week 16: change in mean (SD)	2.5 (10.7)	3.4 (11.8)	2.5 (10.2)	9.5 (10.8)	6.8 (10.9)
Treatment vs Ranib-Only					
Mean difference	-4.4	-3.4	-4.3	2.73	NA
(80% CI)	(-8.0, -0.7)	(-7.0, 0.2)	(-7.9, -0.7)	(-0.9, 6.3)	
p-Value[a]	0.12	0.22	0.13	0.33	NA

In all treatment groups except the Ranib-Only monotherapy cohort, observations collected after ranibizumab rescue or post-Week 16 ranibizumab concomitant treatments were excluded from the summary.
BCVA = best corrected visual acuity; CI = confidence interval; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; NA = not applicable; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab; SD = standard deviation.
a. p-Value from 1-way analysis of variance model with treatment group as the factor.

Secondary Endpoints:

Mean Change in BCVA From Baseline Over Time (16 Weeks): All dose groups using PF-04523655 had larger changes from Baseline in the mean BCVA compared with Ranib-Only through Week 8 (Table 6). However, it is important to note that the mean changes in BCVA letters from Baseline to Week 4 in PF monotherapy groups were attributed to the initial ranibizumab treatment administered at Baseline.

The PF 1 mg/Ranib Combo dose group consistently had the largest mean changes in BCVA letters from Baseline to all study visits compared to other treatment groups (ie, Week 4 through Week 16, Table 6).

Table 6. Summary of BCVA Letters and its Change From Baseline in the Study Eye by Study Visit (LOCF; ITT Population)

	Treatment Groups				
	PF 1 mg Q4W N=29	PF 3 mg Q4W N=31	PF 3 mg Q2W N=30	PF 1 mg/Ranib Combo Q4W N=30	Ranib-Only Q4W N=31
Baseline: mean (SD)	52.0 (13.5)	53.0 (15.7)	48.2 (16.1)	49.5 (13.7)	53.3 (11.7)
Week 4: change in mean (SD)	3.0 (6.7)	3.2 (6.8)	4.2 (9.3)	5.9 (9.3)	0.3 (7.0)
Treatment vs Ranib-Only	2.8	2.9	3.9	5.6	NA
Mean difference (80% CI)	(0.1,5.4)	(0.4,5.5)	(1.3,6.6)	(3.0,8.3)	
p-Value[a]	0.1766	0.1464	0.0538	0.0061	NA
Week 6: change in mean (SD)	4.1 (7.8)	4.2 (8.7)	5.6 (7.8)	6.6 (9.4)	3.1 (6.5)
Treatment vs Ranib-Only	1.0	1.1	2.6	3.6	NA
Mean difference (80% CI)	(-1.6,3.7)	(-1.5,3.8)	(-0.1,5.2)	(0.9,6.2)	
p-Value[a]	0.6188	0.5824	0.2156	0.0862	NA
Week 8: change in mean (SD)	4.1 (9.4)	4.8 (8.8)	6.1 (9.6)	7.2 (9.5)	3.1 (8.4)
Treatment vs Ranib-Only	1.1	1.8	3.0	4.1	NA
Mean difference (80% CI)	(-2.0,4.1)	(-1.2,4.8)	(0.03,6.1)	(1.1,7.1)	
p-Value[a]	0.6497	0.4455	0.1963	0.0815	NA
Week 10: change in mean (SD)	4.1 (9.6)	5.5 (9.8)	3.5 (9.0)	8.7 (12.1)	3.7 (13.6)
Treatment vs Ranib-Only	0.4	1.7	-0.3	4.9	NA
Mean difference (80% CI)	(-3.3,4.0)	(-1.9,5.3)	(-3.9,3.3)	(1.3,8.5)	
p-Value[a]	0.8988	0.5332	0.9222	0.0820	NA
Week 12: change in mean (SD)	2.7 (11.6)	5.2 (10.2)	4.0 (10.3)	9.4 (11.0)	5.6 (13.4)
Treatment vs Ranib-Only	-2.9	-0.3	-1.6	3.9	NA
Mean difference (80% CI)	(-6.6,0.9)	(-4.0,3.4)	(-5.3,2.2)	(0.14,7.6)	
p-Value[a]	0.3315	0.9111	0.5953	0.1838	NA
Week 16: change in mean (SD)	2.5 (10.7)	3.4 (11.8)	2.5 (10.2)	9.5 (10.8)	6.8 (10.9)
Treatment vs Ranib-Only	-4.4	-3.4	-4.3	2.7	NA
Mean difference (80% CI)	(-8.0,-0.7)	(-7.0,0.2)	(-7.9,-0.7)	(-0.9,6.3)	
p-Value[a]	0.1242	0.2235	0.1254	0.3307	NA

In all treatment groups except the Ranib-only group, observations collected after ranibizumab rescue or post-Week 16 ranibizumab concomitant treatments were excluded from the summary.
BCVA = best corrected visual acuity; CI = confidence interval; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; NA = not applicable; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab; SD = standard deviation, vs = versus.
a. p-Value from 1-way analysis of variance model with treatment group as the factor.

Proportion of Subjects With BCVA Improvement or Deterioration: A larger percentage of subjects in the PF-04523655 dose groups gained BCVA ≥15 letters from Baseline through Week 8 compared with subjects in the Ranib-Only group (Table 7). However, it is important to note that the gained letters from Baseline to Week 4 were all attributed to initial ranibizumab treatment administered at Baseline for treatment groups PF 1 mg, PF 3 mg, PF 3 mg Q2W, and Ranib-Only.

Following Week 10, a larger percentage of subjects in the PF 1 mg/Ranib Combo and the Ranib-Only treatment groups gained BCVA ≥15 letters compared with the 3 PF-04523655 monotherapy dose groups.

At Week 16 (LOCF), the proportion of subjects who lost ≥15 BCVA letters from Baseline across all treatment groups were as follows: PF 1 mg (3 subjects, 10.3%), PF 3 mg (1 subject,

3.2%), PF 3 mg Q2W (1 subject, 3.3%), PF 1 mg/Ranib Combo (0%), and Ranib-Only (1 subject, 3.2%).

Table 7. Percent Subjects With Improvement or Deterioration in BCVA Letters by Study Visit - Excluding Observations Collected After Receiving Ranibizumab Treatment Other Than at Baseline (Study Eye; LOCF; ITT Population)

	Treatment Groups				
	PF 1 mg Q4W N=29	PF 3 mg Q4W N=31	PF 3 mg Q2W N=30	PF 1 mg/Ranib Combo Q4W N=30	Ranib-Only Q4W N=31
Week 4					
Gain ≥15 letters n (%)	2 (6.9%)	2 (6.5%)	5 (16.7%)	5 (16.7%)	1 (3.2%)
Gain ≥10 letters n (%)	5 (17.2%)	4 (12.9%)	7 (23.3%)	7 (23.3%)	2 (6.5%)
Week 6					
Gain ≥15 letters n (%)	2 (6.9%)	3 (9.7%)	5 (16.7%)	6 (20.0%)	1 (3.2%)
Gain ≥10 letters n (%)	7 (24.1%)	8 (25.8%)	7 (23.3%)	8 (26.7%)	6 (19.4%)
Week 8					
Gain ≥15 letters n (%)	6 (20.7%)	5 (16.1%)	5 (16.7%)	7 (23.3%)	1 (3.2%)
Gain ≥10 letters n (%)	7 (24.1%)	9 (29.0%)	9 (30.0%)	10 (33.3%)	7 (22.6%)
Week 10					
Gain ≥15 letters n (%)	5 (17.2%)	6 (19.4%)	2 (6.7%)	9 (30.0%)	5 (16.1%)
Gain ≥10 letters n (%)	8 (27.6%)	10 (32.3%)	8 (26.7%)	14 (46.7%)	10 (32.3%)
Week 12					
Gain ≥15 letters n (%)	6 (20.7%)	5 (16.1%)	4 (13.3%)	9 (30.0%)	7 (22.6%)
Gain ≥10 letters n (%)	9 (31.0%)	8 (25.8%)	8 (26.7%)	13 (43.3%)	10 (32.3%)
Week 16					
Gain ≥15 letters n (%)	4 (13.8%)	5 (16.1%)	3 (10.0%)	10 (33.3%)	8 (25.8%)
Gain ≥10 letters n (%)	8 (27.6%)	6 (19.4%)	7 (23.3%)	12 (40.0%)	10 (32.3%)

BCVA = best corrected visual acuity; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; n = number of subjects meeting prespecified criteria; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab.

Change in Retinal Central Subfield Thickness From Baseline: At Week 16 (LOCF), the PF 1 mg/Ranib Combo and Ranib-Only dose groups had similar magnitudes of reduction in central subfield retinal thickness while all 3 PF-04523655 monotherapy treatment groups exhibited smaller reductions in retinal thickness (Table 8).

Change in Retinal Lesion Thickness From Baseline: There were no statistical differences in the reduction of retinal lesion thickness from Baseline to Week 4 and through Week 16 between any of the treatment groups (Table 9).

Table 8. Summary of Retinal Central Subfield Thickness (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
Baseline raw values					
N	29	31	30	29	31
Mean (SD)	489.8 (160.1)	509.8 (191.3)	550.3 (236.8)	458.7 (152.9)	447.5 (162.5)
Median	457.0	419.0	449.5	410.0	398.0
Range	(235.0, 864.0)	(212.0, 958.0)	(320.0, 1180)	(274.0, 795.0)	(239.0, 869.0)
Week 4 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	300.6 (121.7)	326.9 (132.7)	414.9 (200.3)	278.1 (83.99)	293.2 (132.1)
Median	268.0	298.0	322.5	262.0	269.0
Range	(185.0,723.0)	(156.0,659.0)	(192.0,964.0)	(164.0,536.0)	(149.0,796.0)
Change					
N	29	31	30	29	31
Mean (SD)	-189 (146.7)	-183 (157.8)	-135 (171.4)	-181 (172.1)	-154 (165.8)
Median	-148	-133	-121	-133	-122
Range	(-560,18.00)	(-548,160.0)	(-509,329.0)	(-593,149.0)	(-584,230.0)
Treatment vs Ranibizumab					
Mean diff	-35.02	-28.71	18.89	-26.39	
80% mean diff CI	(-89.25,19.22)	(-82.03,24.61)	(-34.87,72.65)	(-80.63,27.84)	
p-Value[a]	0.4072	0.4893	0.6517	0.5319	
Week 6 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	300.2 (121.9)	321.8 (135.7)	414.9 (200.3)	278.1 (83.99)	291.6 (132.0)
Median	268.0	277.0	322.5	262.0	269.0
Range	(185.0,723.0)	(156.0,659.0)	(192.0,964.0)	(164.0,536.0)	(149.0,796.0)
Change					
N	29	31	30	29	31
Mean (SD)	-190 (146.6)	-188 (154.2)	-135 (171.4)	-181 (172.1)	-156 (165.5)
Median	-159	-136	-121	-133	-146
Range	(-560,18.00)	(-548,160.0)	(-509,329.0)	(-593,149.0)	(-584,230.0)
Treatment vs Ranibizumab					
Mean diff	-33.78	-32.13	20.54	-24.75	

Table 8. Summary of Retinal Central Subfield Thickness (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
80% mean diff CI	(-87.75,20.18)	(-85.19,20.93)	(-32.96,74.03)	(-78.71,29.21)	
p-Value[a]	0.4216	0.4369	0.6219	0.5558	
Week 8 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	327.1 (138.2)	364.7 (179.1)	458.8 (211.6)	275.6 (108.5)	264.2 (117.3)
Median	276.0	310.0	419.5	236.0	248.0
Range	(183.0,735.0)	(145.0,817.0)	(201.0, 1065)	(168.0,541.0)	(109.0,713.0)
Change					
N	29	31	30	29	31
Mean (SD)	-163 (144.3)	-145 (144.2)	-91.4 (175.1)	-183 (196.7)	-183 (165.0)
Median	-146	-125	-81.5	-147	-144
Range	(-459,75.00)	(-428,156.0)	(-474,278.0)	(-615,255.0)	(-652,27.00)
Treatment vs Ranibizumab					
Mean diff	20.50	38.10	91.82	0.12	
80% mean diff CI	(-34.71,75.71)	(-16.18,92.38)	(37.09,146.56)	(-55.09,55.33)	
p-Value[a]	0.6333	0.3677	0.0324	0.9978	
Week 10 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	323.8 (141.3)	366.5 (178.4)	451.1 (213.0)	274.3 (107.1)	264.2 (117.3)
Median	294.0	310.0	395.0	240.0	248.0
Range	(167.0,735.0)	(145.0,817.0)	(220.0, 1065)	(168.0,541.0)	(109.0,713.0)
Change					
N	29	31	30	29	31
Mean (SD)	-166 (143.8)	-143 (144.2)	-99.2 (176.8)	-184 (195.6)	-183 (165.0)
Median	-146	-125	-107	-151	-144
Range	(-459,75.00)	(-428,156.0)	(-474,278.0)	(-615,255.0)	(-652,27.00)
Treatment vs Ranibizumab					
Mean diff	17.26	39.87	84.09	-1.16	
80% mean diff CI	(-37.97,72.48)	(-14.43,94.17)	(29.34,138.84)	(-56.38,54.07)	
p-Value[a]	0.6880	0.3460	0.0499	0.9785	
Week 12 raw values (LOCF)					

Table 8. Summary of Retinal Central Subfield Thickness (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
N	29	31	30	29	31
Mean (SD)	352.5 (164.2)	407.3 (180.4)	461.8 (189.5)	272.1 (92.86)	262.2 (92.12)
Median	303.0	341.0	419.5	257.0	244.0
Range	(144.0,865.0)	(215.0,842.0)	(188.0,875.0)	(138.0,536.0)	(125.0,443.0)
Change					
N	29	31	30	29	31
Mean (SD)	-137 (160.0)	-103 (150.0)	-88.5 (235.9)	-187 (184.4)	-185 (189.9)
Median	-111	-80.0	-30.5	-148	-147
Range	(-528,75.00)	(-417,277.0)	(-600,327.0)	(-596,144.0)	(-666,58.00)
Treatment vs Ranibizumab					
Mean diff	47.91	82.74	96.76	-1.40	
80% mean diff CI	(-14.09,109.92)	(21.78,143.70)	(35.29,158.23)	(-63.40,60.61)	
p-Value[a]	0.3215	0.0827	0.0445	0.9769	
Week 16 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	376.0 (164.8)	428.3 (169.0)	478.0 (176.6)	258.0 (86.50)	248.3 (101.5)
Median	331.0	370.0	468.0	237.0	220.0
Range	(159.0,866.0)	(226.0,842.0)	(192.0,828.0)	(110.0,435.0)	(136.0,563.0)
Change					
N	29	31	30	29	31
Mean (SD)	-114 (157.9)	-81.6 (134.2)	-72.2 (225.3)	-201 (190.2)	-199 (194.1)
Median	-63.0	-76.0	-26.5	-180	-169
Range	(-448,134.0)	(-380,256.0)	(-533,382.0)	(-614,149.0)	(-692,111.0)
Treatment vs Ranibizumab					
Mean diff	85.37	117.61	126.96	-1.50	
80% mean diff CI	(24.51,146.22)	(57.78,177.44)	(66.64,187.28)	(-62.35,59.35)	
p-Value[a]	0.0730	0.0124	0.0076	0.9748	

In all treatment groups except the ranibizumab monotherapy arm, observations collected after ranibizumab rescue or post-Week 16 ranibizumab concomitant treatments were excluded from the summary.
ANOVA = analysis of variance; CI = confidence interval; diff = difference; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab, SD = standard deviation; vs = versus.

Table 8. Summary of Retinal Central Subfield Thickness (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	PF 3 mg Q4W N=31	PF 3 mg Q2W N=30	PF 1 mg/Ranib Combo Q4W N=30	Ranib-Only Q4W N=31

a. p-Value from 1-way ANOVA model with treatment group as the factor.

Table 9. Summary of Lesion Thickness at Fovea (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
Baseline raw values					
N	29	31	30	29	31
Mean (SD)	201.0 (122.5)	225.9 (182.1)	279.3 (249.9)	153.7 (103.2)	165.5 (87.60)
Median	167.0	179.0	180.0	136.0	159.0
Range	(48.00,464.0)	(25.00,761.0)	(32.00,984.0)	(22.00,516.0)	(43.00,382.0)
Week 4 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	131.7 (103.8)	149.1 (113.2)	208.5 (198.1)	106.3 (79.34)	114.6 (73.55)
Median	102.0	118.0	117.5	79.00	91.00
Range	(41.00,430.0)	(34.00,532.0)	(39.00,753.0)	(34.00,430.0)	(43.00,330.0)
Change					
N	29	31	30	29	31
Mean (SD)	-69.3 (84.50)	-76.7 (149.1)	-70.7 (128.2)	-47.3 (97.03)	-51.0 (80.75)
Median	-52.0	-45.0	-57.0	-25.0	-47.0
Range	(-328,32.00)	(-707,126.0)	(-397,269.0)	(-310,153.0)	(-313,165.0)
Treatment vs Ranibizumab					
Mean diff	-18.38	-25.77	-19.77	3.66	
80% mean diff CI	(-55.46,18.71)	(-62.24,10.69)	(-56.53,17.00)	(-33.43,40.74)	
p-Value[a]	0.5245	0.3643	0.4900	0.8991	
Week 6 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	131.8 (103.7)	147.4 (114.1)	208.5 (198.1)	106.3 (79.34)	114.4 (73.62)
Median	102.0	109.0	117.5	79.00	90.00
Range	(43.00,430.0)	(34.00,532.0)	(39.00,753.0)	(34.00,430.0)	(43.00,330.0)
Change					
N	29	31	30	29	31
Mean (SD)	-69.2 (84.50)	-78.5 (148.5)	-70.7 (128.2)	-47.3 (97.03)	-51.2 (80.88)
Median	-52.0	-46.0	-57.0	-25.0	-47.0
Range	(-328,32.00)	(-707,126.0)	(-397,269.0)	(-310,153.0)	(-313,165.0)
Treatment vs Ranibizumab					
Mean diff	-18.01	-27.32	-19.54	3.88	

Table 9. Summary of Lesion Thickness at Fovea (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
80% mean diff CI	(-55.05,19.02)	(-63.74,9.09)	(-56.26,17.18)	(-33.15,40.92)	
p-Value[a]	0.5322	0.3356	0.4943	0.8928	
Week 8 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	138.4 (106.5)	171.4 (149.9)	216.7 (178.6)	111.8 (96.74)	103.2 (69.12)
Median	122.0	133.0	151.0	66.00	79.00
Range	(43.00,452.0)	(32.00,681.0)	(32.00,742.0)	(34.00,430.0)	(44.00,315.0)
Change					
N	29	31	30	29	31
Mean (SD)	-62.6 (92.88)	-54.5 (143.1)	-62.6 (182.8)	-41.9 (111.0)	-62.4 (77.85)
Median	-40.0	-38.0	-18.5	-26.0	-54.0
Range	(-315,75.00)	(-707,151.0)	(-796,224.0)	(-310,223.0)	(-317,100.0)
Treatment vs Ranibizumab					
Mean diff	-0.20	7.90	-0.21	20.49	
80% mean diff CI	(-42.56,42.16)	(-33.74,49.55)	(-42.20,41.78)	(-21.87,62.85)	
p-Value[a]	0.9952	0.8073	0.9948	0.5344	
Week 10 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	136.4 (107.6)	173.9 (149.4)	216.3 (178.6)	110.1 (97.11)	103.2 (69.12)
Median	122.0	133.0	151.0	66.00	79.00
Range	(27.00,452.0)	(32.00,681.0)	(32.00,742.0)	(34.00,430.0)	(44.00,315.0)
Change					
N	29	31	30	29	31
Mean (SD)	-64.6 (92.88)	-52.0 (142.4)	-62.9 (182.8)	-43.6 (108.5)	-62.4 (77.85)
Median	-45.0	-38.0	-23.5	-26.0	-54.0
Range	(-315,75.00)	(-707,165.0)	(-796,224.0)	(-317,223.0)	(-317,100.0)
Treatment vs Ranibizumab					
Mean diff	-2.16	10.39	-0.55	18.80	
80% mean diff CI	(-44.33,40.00)	(-31.07,51.84)	(-42.34,41.25)	(-23.36,60.96)	
p-Value[a]	0.9474	0.7475	0.9866	0.5668	
Week 12 raw values (LOCF)					

Table 9. Summary of Lesion Thickness at Fovea (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
N	29	31	30	29	31
Mean (SD)	143.2 (120.4)	200.7 (162.5)	207.7 (140.5)	112.0 (87.96)	105.5 (67.06)
Median	122.0	143.0	156.5	82.00	88.00
Range	(39.00,480.0)	(29.00,641.0)	(34.00,611.0)	(41.00,430.0)	(48.00,328.0)
Change					
N	29	31	30	29	31
Mean (SD)	-57.8 (103.6)	-25.1 (152.9)	-71.6 (215.7)	-41.6 (101.7)	-60.1 (84.77)
Median	-41.0	-7.00	-30.0	-26.0	-51.0
Range	(-315,143.0)	(-707,214.0)	(-764,300.0)	(-312,146.0)	(-317,122.0)
Treatment vs Ranibizumab					
Mean diff	2.24	34.94	-11.54	18.44	
80% mean diff CI	(-44.44,48.92)	(-10.96,80.83)	(-57.81,34.74)	(-28.24,65.12)	
p-Value[a]	0.9509	0.3287	0.7487	0.6118	
Week 16 raw values (LOCF)					
N	29	31	30	29	31
Mean (SD)	132.3 (102.3)	204.1 (156.3)	227.4 (142.7)	92.90 (69.57)	89.13 (49.08)
Median	122.0	154.0	171.0	65.00	79.00
Range	(36.00,452.0)	(34.00,641.0)	(63.00,555.0)	(36.00,327.0)	(38.00,283.0)
Change					
N	29	31	30	29	31
Mean (SD)	-68.7 (115.0)	-21.8 (156.1)	-51.9 (222.0)	-60.8 (106.8)	-76.4 (96.01)
Median	-41.0	-19.0	-8.00	-36.0	-85.0
Range	(-405,143.0)	(-707,236.0)	(-764,300.0)	(-407,154.0)	(-332,118.0)
Treatment vs Ranibizumab					
Mean diff	7.76	54.65	24.52	15.66	
80% mean diff CI	(-41.07,56.60)	(6.63,102.66)	(-23.90,72.93)	(-33.18,64.50)	
p-Value[a]	0.8381	0.1450	0.5154	0.6803	

In all treatment groups except the ranibizumab monotherapy arm, observations collected after ranibizumab rescue or post-Week 16 ranibizumab concomitant treatments were excluded from the summary.
ANOVA = analysis of variance; CI = confidence interval; diff = difference; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab, SD = standard deviation, vs = versus.

Table 9. Summary of Lesion Thickness at Fovea (mm) and its Change From Baseline (LOCF) by Study Visit - Study Eye, ITT Population Excluding Observations Collected After Receiving Ranibizumab Treatment

	Treatment Groups				
	PF 1 mg Q4W N=29	PF 3 mg Q4W N=31	PF 3 mg Q2W N=30	PF 1 mg/Ranib Combo Q4W N=30	Ranib-Only Q4W N=31

a. p-Value from 1-way ANOVA model with treatment group as the factor.

Change in Total Area of CNV From Baseline: At Week 16, the PF 1 mg/Ranib Combo and Ranib-Only dose groups had similar magnitudes of reduction in the total CNV (mm^2) area while all 3 PF-04523655 monotherapy treatment groups exhibited smaller reductions in the total CNV (mm^2) area (Table 10).

Table 10. Summary of Total Area of CNV (mm^2) and its Change From Baseline by Study Visit - Excluding Observations Collected After Receiving Ranibizumab Treatment Other Than at Baseline (Study Eye; LOCF; ITT Population)

	Treatment Groups				
	PF 1 mg Q4W N=29	**PF 3 mg Q4W N=31**	**PF 3 mg Q2W N=30**	**PF 1 mg/Ranib Combo Q4W N=30**	**Ranib-Only Q4W N=31**
Baseline: mean (SD)	6.7 (5.3)	7.6 (6.7)	6.7 (5.8)	8.1 (7.2)	6.4 (5.4)
Week 16: change in mean (SD)	-1.8 (4.8)	-2.2 (4.8)	-1.1 (3.0)	-5.5 (6.2)	-5.1 (5.0)
Treatment vs Ranib-Only					
Mean difference	3.3	2.8	4.0	-0.4	NA
(80% CI)	(1.6,4.9)	(1.2,4.5)	(2.4,5.6)	(-2.1,1.2)	
p-Value[a]	0.0110	0.0246	0.0019	0.7275	NA

CI = confidence interval; CNV = choroidal neovascularization; ITT = intent-to-treat; LOCF = last observation carried forward; N = number of subjects; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab; SD = standard deviation.
a. p-Value from 1-way analysis of variance model with treatment group as the factor.

Safety Results:

Adverse Events: All-causality, non serious, treatment-emergent adverse events are presented in Table 11 and treatment-related AEs are presented in Table 12.

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Number (%) of subjects:					
Evaluable for adverse events	29	31	30	30	31
With adverse events	25 (86.2)	20 (64.5)	26 (86.7)	19 (63.3)	20 (64.5)
Blood and lymphatic system disorders	3 (10.3)	0	1 (3.3)	0	1 (3.2)
Anaemia	3 (10.3)	0	1 (3.3)	0	1 (3.2)
Cardiac disorders	1 (3.4)	0	1 (3.3)	1 (3.3)	1 (3.2)
Arrhythmia	0	0	0	0	1 (3.2)
Cardiac failure congestive	0	0	1 (3.3)	0	0
Myocardial infarction	1 (3.4)	0	0	0	0
Palpitations	0	0	0	1 (3.3)	0
Ear and labyrinth disorders	1 (3.4)	0	1 (3.3)	1 (3.3)	1 (3.2)
Ear disorder	1 (3.4)	0	0	0	0
Vertigo	0	0	1 (3.3)	1 (3.3)	1 (3.2)
Endocrine disorders	0	0	1 (3.3)	0	0
Goitre	0	0	1 (3.3)	0	0
Eye disorders	17 (58.6)	16 (51.6)	20 (66.7)	17 (56.7)	16 (51.6)
Age-related macular degeneration, both eyes	0	0	0	0	1 (3.2)
Age-related macular degeneration, fellow eye	0	0	0	2 (6.7)	0
Age-related macular degeneration, study eye	0	0	1 (3.3)	2 (6.7)	0
Anterior chamber flare, both eyes	0	0	0	1 (3.3)	0
Blepharitis, both eyes	0	0	1 (3.3)	2 (6.7)	1 (3.2)
Blepharitis, fellow eye	0	0	0	0	1 (3.2)
Blepharitis, study eye	0	0	0	0	1 (3.2)
Cataract cortical, both eyes	0	0	0	0	1 (3.2)
Cataract cortical, fellow eye	0	0	1 (3.3)	0	0
Cataract cortical, study eye	0	0	0	1 (3.3)	0
Cataract nuclear, both eyes	0	0	1 (3.3)	0	0
Cataract nuclear, fellow eye	1 (3.4)	1 (3.2)	0	0	0
Cataract nuclear, study eye	0	0	0	1 (3.3)	0
Cataract subcapsular, fellow eye	0	0	1 (3.3)	0	0
Cataract subcapsular, study eye	0	1 (3.2)	1 (3.3)	1 (3.3)	0
Cataract, fellow eye	0	0	0	0	1 (3.2)
Chalazion, study eye	0	0	1 (3.3)	0	0

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Choroidal neovascularisation, fellow eye	0	1 (3.2)	2 (6.7)	0	0
Choroidal neovascularisation, study eye	1 (3.4)	2 (6.5)	1 (3.3)	1 (3.3)	0
Conjunctival bleb, study eye	0	1 (3.2)	0	0	0
Conjunctival haemorrhage, fellow eye	0	1 (3.2)	0	0	1 (3.2)
Conjunctival haemorrhage, study eye	1 (3.4)	2 (6.5)	6 (20.0)	3 (10.0)	2 (6.5)
Conjunctival hyperaemia, study eye	0	0	1 (3.3)	1 (3.3)	0
Conjunctival irritation, both eyes	1 (3.4)	0	1 (3.3)	0	0
Conjunctival irritation, study eye	0	0	1 (3.3)	1 (3.3)	0
Conjunctival oedema, study eye	0	0	1 (3.3)	0	0
Conjunctivitis, both eyes	0	0	1 (3.3)	0	0
Conjunctivitis, fellow eye	0	1 (3.2)	2 (6.7)	0	0
Conjunctivitis, study eye	1 (3.4)	0	0	0	0
Corneal disorder, study eye	0	0	2 (6.7)	0	0
Corneal epithelium defect, study eye	0	0	2 (6.7)	0	0
Corneal erosion, study eye	0	1 (3.2)	1 (3.3)	0	0
Corneal oedema, study eye	0	0	1 (3.3)	0	0
Cystoid macular oedema, fellow eye	0	0	0	2 (6.7)	0
Cystoid macular oedema, study eye	0	0	1 (3.3)	0	0
Dacryostenosis acquired, fellow eye	0	0	0	1 (3.3)	0
Dacryostenosis acquired, study eye	0	0	0	1 (3.3)	0
Detachment of retinal pigment epithelium, fellow eye	0	1 (3.2)	1 (3.3)	0	0
Detachment of retinal pigment epithelium, study eye	2 (6.9)	0	1 (3.3)	0	0
Dry eye, both eyes	1 (3.4)	0	1 (3.3)	1 (3.3)	1 (3.2)
Eye disorder, study eye	0	0	0	0	1 (3.2)
Eye haemorrhage, fellow eye	0	0	0	2 (6.7)	0
Eye haemorrhage, study eye	0	0	1 (3.3)	0	1 (3.2)
Eye pain, fellow eye	1 (3.4)	0	0	0	0
Eye pain, study eye	4 (13.8)	1 (3.2)	2 (6.7)	1 (3.3)	0
Eye pruritus, both eyes	0	0	1 (3.3)	0	0
Eye pruritus, study eye	2 (6.9)	0	0	0	0
Eyelid oedema, both eyes	0	1 (3.2)	0	0	0

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Eyelid ptosis, fellow eye	1 (3.4)	0	0	0	0
Eyelids pruritus, both eyes	0	0	1 (3.3)	0	0
Foreign body sensation in eyes, both eyes	0	0	0	0	1 (3.2)
Keratoconjunctivitis sicca, both eyes	0	0	0	0	1 (3.2)
Lacrimation increased, study eye	0	1 (3.2)	1 (3.3)	0	0
Macular cyst, fellow eye	0	0	0	1 (3.3)	0
Macular degeneration, fellow eye	0	0	0	1 (3.3)	0
Macular oedema, fellow eye	1 (3.4)	0	0	0	2 (6.5)
Macular oedema, study eye	1 (3.4)	0	1 (3.3)	0	0
Macular scar, fellow eye	0	0	1 (3.3)	0	0
Macular scar, study eye	0	0	1 (3.3)	0	0
Maculopathy, fellow eye	0	0	0	0	1 (3.2)
Metamorphopsia, fellow eye	0	0	0	0	1 (3.2)
Metamorphopsia, study eye	0	1 (3.2)	0	0	0
Ocular discomfort, study eye	0	0	0	1 (3.3)	0
Ocular hyperaemia, both eyes	0	0	0	1 (3.3)	0
Ocular hypertension, both eyes	0	0	0	1 (3.3)	0
Ocular hypertension, study eye	1 (3.4)	0	0	0	0
Posterior capsule opacification, fellow eye	0	0	0	0	1 (3.2)
Punctate keratitis, both eyes	0	0	3 (10.0)	1 (3.3)	0
Punctate keratitis, fellow eye	0	0	1 (3.3)	0	0
Punctate keratitis, study eye	0	0	0	2 (6.7)	0
Retinal cyst, fellow eye	0	0	0	1 (3.3)	0
Retinal degeneration, study eye	1 (3.4)	0	0	0	0
Retinal disorder, study eye	1 (3.4)	0	0	0	0
Retinal haemorrhage, both eyes	0	0	0	1 (3.3)	0
Retinal haemorrhage, fellow eye	1 (3.4)	2 (6.5)	1 (3.3)	2 (6.7)	1 (3.2)
Retinal haemorrhage, study eye	5 (17.2)	1 (3.2)	6 (20.0)	1 (3.3)	0
Retinal oedema, fellow eye	0	0	1 (3.3)	0	1 (3.2)
Retinal oedema, study eye	2 (6.9)	2 (6.5)	6 (20.0)	5 (16.7)	1 (3.2)
Retinal vascular disorder, both eyes	0	0	0	1 (3.3)	0
Subretinal fibrosis, study eye	0	0	1 (3.3)	0	0
Trichiasis, study eye	0	0	0	0	1 (3.2)

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Visual acuity reduced, fellow eye	0	0	1 (3.3)	0	0
Visual acuity reduced, study eye	5 (17.2)	2 (6.5)	5 (16.7)	1 (3.3)	1 (3.2)
Visual impairment, study eye	0	1 (3.2)	0	0	0
Vitreous detachment, fellow eye	0	1 (3.2)	0	0	0
Vitreous detachment, study eye	1 (3.4)	0	1 (3.3)	0	1 (3.2)
Vitreous disorder, study eye	0	0	2 (6.7)	0	0
Vitreous floaters, fellow eye	0	0	1 (3.3)	0	0
Vitreous floaters, study eye	1 (3.4)	0	1 (3.3)	1 (3.3)	0
Vitreous haemorrhage, fellow eye	0	0	0	0	1 (3.2)
Vitreous haemorrhage, study eye	0	0	0	0	1 (3.2)
Vitreous opacities, study eye	1 (3.4)	0	0	0	0
Gastrointestinal disorders	5 (17.2)	2 (6.5)	4 (13.3)	1 (3.3)	3 (9.7)
Abdominal discomfort	0	0	1 (3.3)	0	0
Abdominal pain upper	0	0	0	0	1 (3.2)
Constipation	0	1 (3.2)	0	0	0
Diarrhoea	3 (10.3)	0	2 (6.7)	0	0
Dyspepsia	0	1 (3.2)	1 (3.3)	0	0
Gastritis	1 (3.4)	0	0	0	0
Nausea	0	0	1 (3.3)	0	0
Periodontitis	0	0	0	1 (3.3)	0
Tooth impacted	0	0	0	0	1 (3.2)
Toothache	1 (3.4)	0	0	1 (3.3)	1 (3.2)
General disorders and administration site conditions	2 (6.9)	1 (3.2)	3 (10.0)	1 (3.3)	4 (12.9)
Asthenia	0	1 (3.2)	0	0	1 (3.2)
Chest pain	0	0	0	0	1 (3.2)
Fatigue	0	0	2 (6.7)	0	0
Oedema peripheral	1 (3.4)	0	1 (3.3)	1 (3.3)	2 (6.5)
Pyrexia	1 (3.4)	0	0	0	0
Immune system disorders	0	0	0	1 (3.3)	0
Hypersensitivity	0	0	0	1 (3.3)	0
Infections and infestations	7 (24.1)	6 (19.4)	4 (13.3)	5 (16.7)	7 (22.6)
Abscess limb	1 (3.4)	0	0	0	0
Adenoviral conjunctivitis, both eyes	0	0	1 (3.3)	0	0

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Bronchitis	0	2 (6.5)	0	0	0
Bronchopulmonary aspergillosis allergic	0	1 (3.2)	0	0	0
Cystitis	1 (3.4)	0	0	0	1 (3.2)
Gastroenteritis	0	0	0	0	1 (3.2)
Herpes simplex ophthalmic, study eye	0	0	0	1 (3.3)	0
Infection	1 (3.4)	0	0	0	0
Localised infection	0	0	0	1 (3.3)	0
Nasopharyngitis	1 (3.4)	1 (3.2)	1 (3.3)	2 (6.7)	0
Otitis externa	0	0	0	0	1 (3.2)
Pneumonia	0	0	0	0	1 (3.2)
Upper respiratory tract infection	1 (3.4)	1 (3.2)	1 (3.3)	1 (3.3)	3 (9.7)
Urinary tract infection	4 (13.8)	1 (3.2)	1 (3.3)	0	0
Injury, poisoning and procedural complications	1 (3.4)	1 (3.2)	2 (6.7)	2 (6.7)	4 (12.9)
Animal bite	0	0	0	1 (3.3)	0
Bone fissure	0	0	0	0	1 (3.2)
Corneal abrasion, study eye	0	0	1 (3.3)	0	0
Excoriation	0	0	0	0	1 (3.2)
Fall	0	1 (3.2)	1 (3.3)	0	2 (6.5)
Laceration	0	0	0	0	1 (3.2)
Muscle strain	0	1 (3.2)	0	0	0
Suture related complication, fellow eye	0	0	0	1 (3.3)	0
Tooth fracture	0	0	0	0	1 (3.2)
Wound	1 (3.4)	0	0	0	0
Investigations	1 (3.4)	2 (6.5)	6 (20.0)	2 (6.7)	2 (6.5)
Blood creatinine increased	0	0	0	0	1 (3.2)
Blood glucose increased	0	0	1 (3.3)	0	0
Blood potassium increased	0	0	0	0	1 (3.2)
Blood urea abnormal	0	0	0	0	1 (3.2)
Electrocardiogram QT prolonged	0	0	0	1 (3.3)	0
Electrocardiogram abnormal	0	1 (3.2)	0	0	0
International normalised ratio increased	0	0	0	0	1 (3.2)
Intraocular pressure increased, study eye	1 (3.4)	0	4 (13.3)	1 (3.3)	0
Intraocular pressure test normal, study eye	0	0	1 (3.3)	0	0

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Platelet count decreased	0	0	0	0	1 (3.2)
Platelet count increased	0	0	1 (3.3)	0	0
Prothrombin time prolonged	0	1 (3.2)	0	0	1 (3.2)
Weight decreased	0	0	0	0	1 (3.2)
Metabolism and nutrition disorders	1 (3.4)	1 (3.2)	2 (6.7)	0	0
Diabetes mellitus	0	0	1 (3.3)	0	0
Hypercalcaemia	1 (3.4)	0	0	0	0
Hypercholesterolaemia	0	0	1 (3.3)	0	0
Hyperlipidaemia	0	1 (3.2)	0	0	0
Musculoskeletal and connective tissue disorders	1 (3.4)	1 (3.2)	1 (3.3)	3 (10.0)	4 (12.9)
Arthralgia	0	0	0	0	1 (3.2)
Arthritis	0	0	0	0	1 (3.2)
Back pain	1 (3.4)	0	1 (3.3)	1 (3.3)	0
Myalgia	0	0	0	1 (3.3)	0
Osteoporosis	0	0	0	0	1 (3.2)
Pain in extremity	0	1 (3.2)	0	1 (3.3)	1 (3.2)
Rheumatoid arthritis	0	0	0	0	1 (3.2)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (3.4)	0	1 (3.3)	0	1 (3.2)
Hepatobiliary neoplasm	1 (3.4)	0	0	0	0
Nasal cavity cancer	0	0	1 (3.3)	0	0
Neurofibroma	0	0	0	0	1 (3.2)
Nervous system disorders	1 (3.4)	2 (6.5)	1 (3.3)	1 (3.3)	2 (6.5)
Dizziness	0	1 (3.2)	0	1 (3.3)	1 (3.2)
Headache	0	1 (3.2)	1 (3.3)	0	0
Transient ischaemic attack	0	0	0	0	1 (3.2)
Tremor	1 (3.4)	0	0	0	0
Psychiatric disorders	1 (3.4)	0	0	1 (3.3)	0
Anxiety	1 (3.4)	0	0	0	0
Insomnia	0	0	0	1 (3.3)	0
Renal and urinary disorders	1 (3.4)	0	0	0	0
Renal colic	1 (3.4)	0	0	0	0
Reproductive system and breast disorders	1 (3.4)	0	0	1 (3.3)	1 (3.2)

Table 11. Treatment-Emergent Non Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Prostatitis	1 (3.4)	0	0	1 (3.3)	0
Vulvovaginal discomfort	0	0	0	0	1 (3.2)
Respiratory, thoracic and mediastinal disorders	0	3 (9.7)	4 (13.3)	1 (3.3)	6 (19.4)
Bronchiectasis	0	0	0	0	1 (3.2)
Bronchitis chronic	0	0	0	0	1 (3.2)
Cough	0	1 (3.2)	1 (3.3)	1 (3.3)	3 (9.7)
Dyspnoea	0	1 (3.2)	0	0	1 (3.2)
Interstitial lung disease	0	0	1 (3.3)	0	0
Nasal congestion	0	0	1 (3.3)	0	0
Rhinitis allergic	0	0	0	0	1 (3.2)
Upper respiratory tract congestion	0	1 (3.2)	1 (3.3)	0	0
Skin and subcutaneous tissue disorders	2 (6.9)	0	2 (6.7)	2 (6.7)	5 (16.1)
Alopecia	1 (3.4)	0	1 (3.3)	0	0
Eczema	0	0	0	0	1 (3.2)
Eczema, study eye	0	0	0	1 (3.3)	0
Ingrowing nail	0	0	0	0	1 (3.2)
Night sweats	0	0	0	0	1 (3.2)
Pruritus	0	0	0	1 (3.3)	1 (3.2)
Rash	0	0	1 (3.3)	1 (3.3)	1 (3.2)
Urticaria	1 (3.4)	0	0	0	0
Surgical and medical procedures	1 (3.4)	0	1 (3.3)	0	0
Intraocular lens implant, fellow eye	1 (3.4)	0	1 (3.3)	0	0
Intraocular lens implant, study eye	1 (3.4)	0	0	0	0
Vascular disorders	0	1 (3.2)	1 (3.3)	0	2 (6.5)
Hypertension	0	1 (3.2)	1 (3.3)	0	2 (6.5)

Subjects were only counted once per treatment for each row.
Includes data up to 999 days after last dose of study drug.
MedDRA (version 14.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects meeting prespecified criteria; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks.

Table 12. Treatment-Emergent Adverse Events (Treatment-Related) by System Organ Class and Preferred Term During Entire Study Period

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W	PF 3 mg Q4W	PF 3 mg Q2W	Ranibizumab + PF Q4W	Ranibizumab
	n	n	n	n	n
Number of subjects:					
Evaluable for adverse events	29	31	30	30	31
Blood and lymphatic system disorders	0	0	1	0	0
Anaemia	0	0	1	0	0
Eye disorders	3	1	2	2	2
Conjunctival hyperaemia, study eye	0	0	0	1	0
Eye disorder, study eye	0	0	0	0	1
Eye haemorrhage, fellow eye	0	0	0	1	0
Macular oedema, fellow eye	0	0	0	0	1
Retinal degeneration, study eye	1	0	0	0	0
Retinal haemorrhage, study eye	1	0	0	0	0
Retinal oedema, study eye	0	1	1	0	0
Subretinal fibrosis, study eye	0	0	1	0	0
Vitreous opacities, study eye	1	0	0	0	0
Gastrointestinal disorders	0	0	2	0	0
Diarrhoea	0	0	1	0	0
Nausea	0	0	1	0	0
Investigations	0	0	3	0	0
Intraocular pressure increased, study eye	0	0	1	0	0
Intraocular pressure test normal, study eye	0	0	1	0	0
Platelet count increased	0	0	1	0	0
Nervous system disorders	0	0	0	0	2
Ischaemic stroke	0	0	0	0	1
Transient ischaemic attack	0	0	0	0	1
Skin and subcutaneous tissue disorders	0	0	1	0	0
Alopecia	0	0	1	0	0
Total preferred term events	3	1	9	2	4

Includes data up to 999 days after last dose of study drug.
MedDRA (version 14.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects meeting prespecified criteria; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks.

Serious Adverse Events (SAEs): Fourteen (14) subjects (9.3%) had SAEs during the study (ie, within 28 days before the last study dose; Table 13). All SAEs except 2 were unrelated to study treatment. One (1) subject experienced a transient ischemic attack and other experienced an ischemic stroke, both were considered related to Ranib-Only treatment.

Table 13. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Number (%) of subjects:					
Evaluable for adverse events	29	31	30	30	31
With adverse events	3 (10.3)	5 (16.1)	3 (10.0)	5 (16.7)	5 (16.1)
Blood and lymphatic system disorders	0	0	1 (3.3)	0	0
Pancytopenia	0	0	1 (3.3)	0	0
Cardiac disorders	0	1 (3.2)	0	0	0
Atrial fibrillation	0	1 (3.2)	0	0	0
Cardiac failure congestive	0	1 (3.2)	0	0	0
Ear and labyrinth disorders	0	1 (3.2)	0	0	0
Vertigo	0	1 (3.2)	0	0	0
Eye disorders	0	1 (3.2)	1 (3.3)	0	0
Retinal haemorrhage, study eye	0	0	1 (3.3)	0	0
Retinal pigment epithelial tear, study eye	0	1 (3.2)	0	0	0
Visual acuity reduced, study eye	0	0	1 (3.3)	0	0
Gastrointestinal disorders	0	2 (6.5)	0	0	0
Abdominal pain	0	1 (3.2)	0	0	0
Abdominal pain upper	0	1 (3.2)	0	0	0
Vomiting	0	1 (3.2)	0	0	0
General disorders and administration site conditions	0	1 (3.2)	0	1 (3.3)	0
Chest pain	0	1 (3.2)	0	1 (3.3)	0
Infections and infestations	1 (3.4)	1 (3.2)	0	2 (6.7)	1 (3.2)
Eczema infected	0	0	0	0	1 (3.2)
Gastroenteritis	0	1 (3.2)	0	0	0
Malaria	0	0	0	1 (3.3)	0
Sepsis	1 (3.4)	0	0	0	0
Tinea pedis	0	0	0	1 (3.3)	0
Injury, poisoning and procedural complications	0	0	0	0	1 (3.2)
Facial bones fracture	0	0	0	0	1 (3.2)
Fall	0	0	0	0	1 (3.2)
Humerus fracture	0	0	0	0	1 (3.2)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	2 (6.9)	0	0	0	0
Bladder cancer	1 (3.4)	0	0	0	0

Table 13. Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (All-Causalities)

Adverse Events by System Organ Class Preferred Term	PF 1 mg Q4W n (%)	PF 3 mg Q4W n (%)	PF 3 mg Q2W n (%)	Ranibizumab + PF Q4W n (%)	Ranibizumab n (%)
Gastric cancer stage 0	1 (3.4)	0	0	0	0
Metastases to liver	1 (3.4)	0	0	0	0
Transitional cell carcinoma	1 (3.4)	0	0	0	0
Nervous system disorders	1 (3.4)	1 (3.2)	0	1 (3.3)	2 (6.5)
Headache	0	1 (3.2)	0	0	0
Ischaemic stroke	0	0	0	0	1 (3.2)
Transient ischaemic attack	1 (3.4)	0	0	1 (3.3)	1 (3.2)
Renal and urinary disorders	1 (3.4)	0	0	0	0
Renal failure acute	1 (3.4)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	0	0	1 (3.3)	1 (3.3)	1 (3.2)
Chronic obstructive pulmonary disease	0	0	0	1 (3.3)	0
Pleural effusion	0	0	0	0	1 (3.2)
Tracheal stenosis	0	0	1 (3.3)	0	0
Surgical and medical procedures	0	0	0	1 (3.3)	1 (3.2)
Hip arthroplasty	0	0	0	1 (3.3)	0
Knee arthroplasty	0	0	0	0	1 (3.2)

Subjects were only counted once per treatment for each row.
Includes data up to 999 days after last dose of study drug.
MedDRA (version 14.0) coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects meeting prespecified criteria; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks.

Permanent Discontinuations due to Adverse Events: Subjects who permanently discontinued study treatment due to AEs are listed in Table 14. The following numbers of subjects discontinued treatment from the respective dose groups: PF 1 mg (5 subjects, 17.2%), PF 3 mg (1 subject, 3.2%), PF 3 mg Q2W (4 subjects, 13.3%), PF 1 mg/Ranib Combo (1 subject, 3.3%), Ranib-Only (2 subjects, 6.5%).

Disease under study was a common causality that led subjects to permanently discontinue due to AEs from the 3 PF-04523655 monotherapy treatment groups (ie, PF 1 mg, PF 3 mg, and PF 3 mg Q2W).

A single subject discontinued due to an AE with study drug causality. This subject experienced a mild, ischemic stroke, attributed to Ranib-Only treatment.

Table 14. Discontinuations due to Adverse Events

Subject Serial Number	AE Leading to Discontinuation	Discontinued From Study or Treatment	Severity/ Outcome	Related to Study Drug	Causality	SAE
PF 1 mg Q4W						
1	Reduced visual acuity, study eye	Treatment	Severe/ unknown	No	Submacular hemorrhage on OS	No
2	Retinal edema, study eye	Treatment	Mild/ resolved	No	Disease under study	No
3	Reduced visual acuity, study eye	Treatment	Mild/ resolved	No	Disease under study	No
4	Myocardial infarction	Treatment	Severe/ resolved	No	Age	No
5	Reduced visual acuity, study eye	Treatment	Mild/ resolved	No	Disease under study	No
PF 3 mg Q4W						
6	Retinal pigment epithelial tear, study eye	Study	Severe/ still present	No	Disease under study	Yes
PF 3 mg Q2W						
7	Retinal hemorrhage, study eye	Study	Severe/ resolved	No	Disease under study	Yes
	Reduced visual acuity, study eye	Study	Severe/ still present	No	Worsening of sub macular hemorrhage	Yes
8	Nasal cavity cancer	Study	Moderate/ still present	No	Idiopathic illness	No
9	Reduced visual acuity, study eye		Moderate/ Resolved	No	Disease under study	No
10	Retinal hemorrhage, study eye	Study	Moderate/ still present	No	Disease under study	No
PF 1 mg/Ranib Combo Q4W						
11	TIA	Study	Severe/ resolved	No	Previous history of TIA and stroke	Yes
Ranib-Only Q4W						
12	TIA	Study	Severe/ still present	No	Cardiac embolism (due to coronary artery heart disease)	No
13	Ischemic stroke	Rx	Mild/ resolved	Yes	Study drug	Yes

MedDRA version 14.0 coding dictionary applied.
AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities; OS = left eye; PF = PF-04523655; Q2W = every 2 weeks; Q4W = every 4 weeks; Ranib = ranibizumab; SAE = serious adverse event; TIA = transient ischemic attack.

Deaths: Two (2) subjects died in the PF 1 mg treatment group within 28 days after the last study dose. Both deaths were unrelated to study treatment (Table 15). There was 1 additional death (myocardial infarction) in the PF 1 mg treatment group that was unrelated to study treatment, which occurred more than 28 days after the last study dose.

Table 15. Summary of Deaths Within 28 Days After the Last Study Dose

Subject Serial Number	Event With Fatal Outcome	Cause of Death
1	Gastric cancer Stage 0; metastases to liver; sepsis; acute renal failure	Sepsis
2	Bladder cancer	Bladder cancer

MedDRA version 14.0 coding dictionary applied.
MedDRA = Medical Dictionary for Regulatory Activities.

CONCLUSIONS:

Treatment with IVT PF-04523655 was generally safe and well-tolerated, with few AEs considered treatment-related and the majority of AEs were mild or moderate in severity.

At Week 16 (LOCF), all 3 PF-04523655 monotherapy regimens resulted in less mean BCVA change from Baseline than the Ranib-Only group. The PF 1 mg/Ranib Combo group had a greater BCVA improvement than the Ranib-Only group, although the difference was not statistically significant. In addition, the PF 1 mg/Ranib Combo group consistently had a numerically greater mean change in BCVA, and larger proportions of subjects who gained at least 10 or 15 letters compared with the Ranib-Only group (from Week 4 through Week 16). The mean reduction in central subfield retinal thickness at Week 16 (LOCF) was similar for the PF 1 mg/Ranib Combo and Ranib-Only dose groups, while all PF-04523655 monotherapy dose groups exhibited smaller reductions.