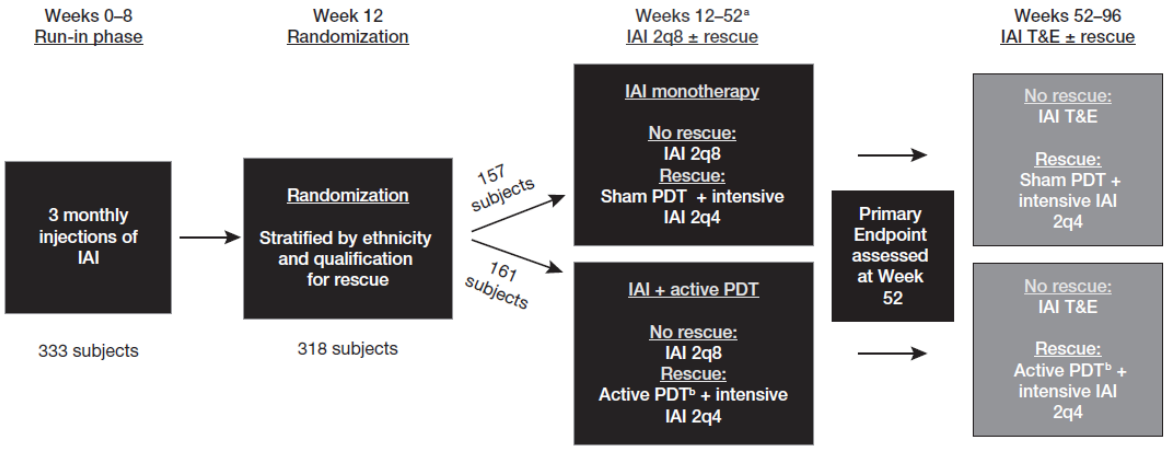
Supplementary Online Content

Lee WK, Iida T, Ogura Y, et al; PLANET Investigators. Efficacy and safety of intravitreal aflibercept for polypoidal choroidal vasculopathy in the PLANET study: a randomized clinical trial. *JAMA Opththalmol*. Published online May 2, 2018. doi:10.1001/jamaophthalmol.2018.1804

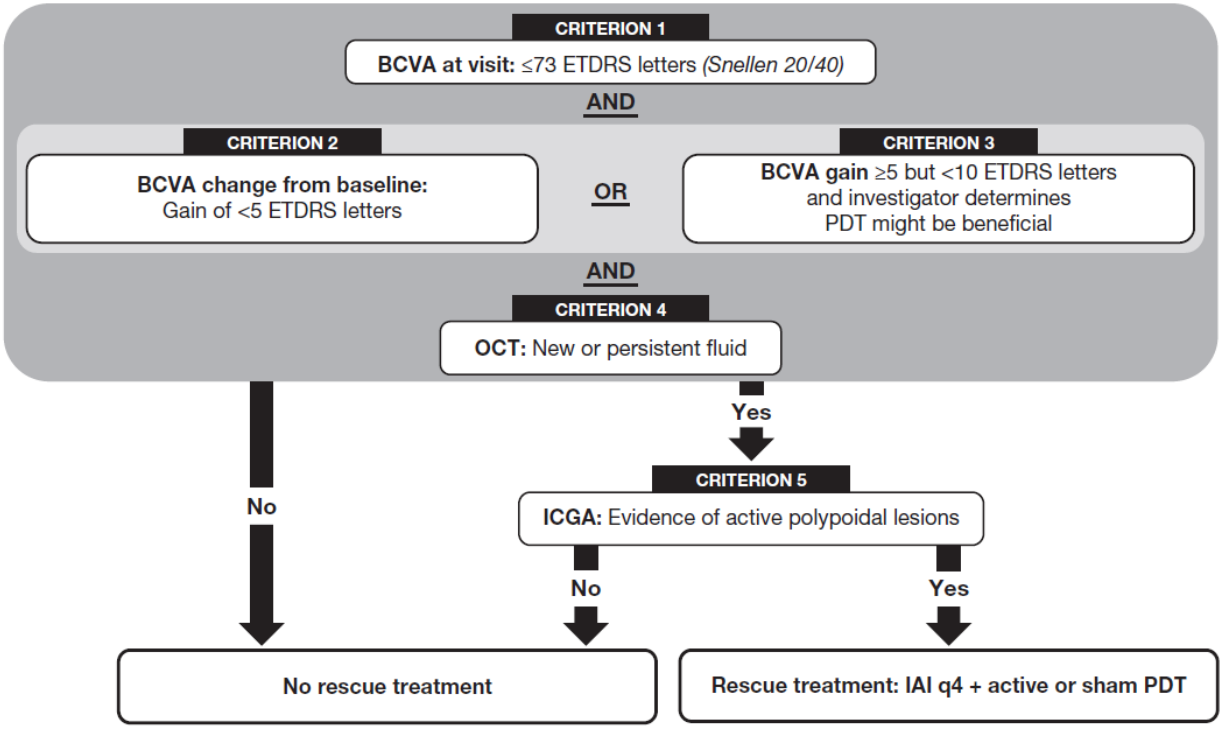
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Study Design.



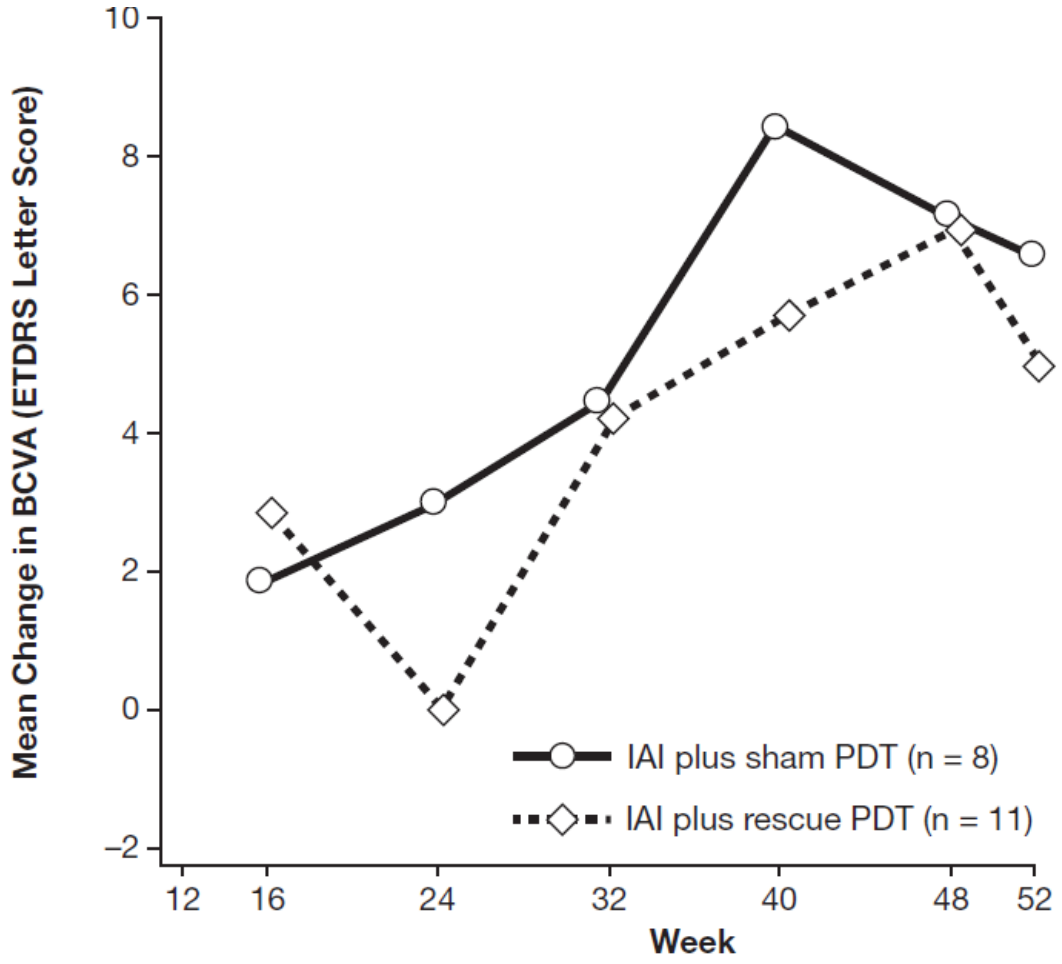
Only week 52 data are presented. [a]Assessment of rescue criteria; [b]PDT, intravenous verteporfin 6 mg/m^2; PDT (active or sham) was only administered if rescue criteria were met; administration was performed according to the locally approved label.
IAI, intravitreal aflibercept; PDT, photodynamic therapy; T&E, treat-and-extend.

eFigure 2. Criteria for Rescue Treatment



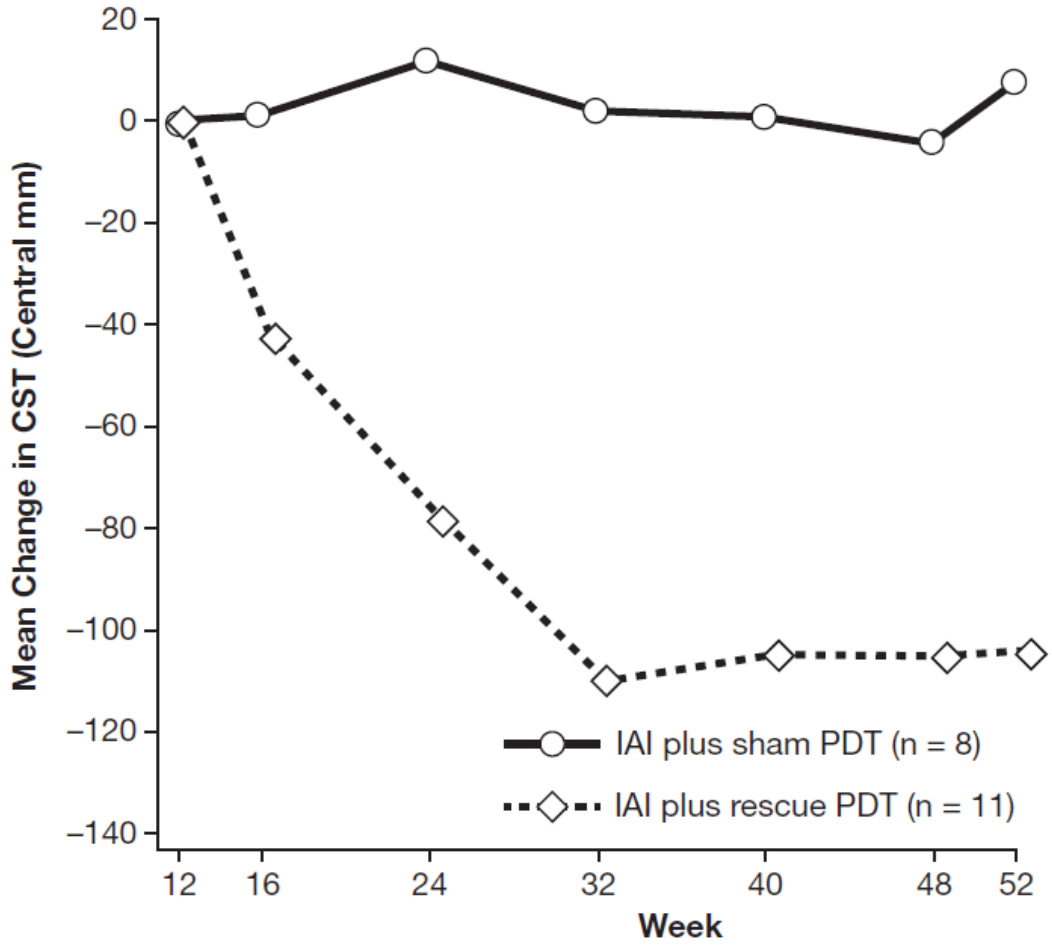
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ICGA, indocyanine green angiography; IAI, intravitreal aflibercept; OCT, optical coherence tomography; PDT, photodynamic therapy; q4, every 4 weeks.

eFigure 3A. Mean Change from Randomization (Week 12) to Week 52 in BCVA



BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IAI, intravitreal aflibercept; PDT, photodynamic therapy.

eFigure 3B. Mean Change from Randomization (Week 12) to Week 52 in CST



CST, central subfield thickness; IAI, intravitreal aflibercept; PDT, photodynamic therapy.

eTable 1. Inclusion/Exclusion Criteria

Inclusion Criteria	1. Able to read and understand the ICF (or, if unable to read due to visual impairment, to be read to verbatim by the person administering the informed consent or a family member) 2. Signed informed consent 3. Men and women aged ≥50 years 4. Diagnosis of symptomatic macular PCV in the study eye established by ICGA at the study center 5. Greatest linear dimension of the lesion of <5400 mm (approximately, 9 Macular Photocoagulation Study disc areas), assessed by ICGA 6. An ETDRS BCVA of 73 to 24 letters in the study eye 7. Women of childbearing potential and men, when sexually active, must agree to use adequate contraception from the time point of signing the informed consent form until 3 months after the last study drug administration. Acceptable methods of contraception include (1) condoms (male or female) with or without a spermicidal agent; (2) diaphragm or cervical cap with spermicide; (3) intra-uterine device; (4) hormone-based contraception 8. Willing, committed, and able to return for all clinic visits and complete all study-related procedures
Exclusion Criteria	1. Prior use of intravitreal or subtenon corticosteroids in the study eye within 3 months prior to study entry 2. Any prior use of intraocular anti-VEGF agents in the study eye, or systemic use of anti-VEGF products within 3 months prior to study entry 3. Prior macular laser treatment in the study eye including PDT 4. Only 1 functional eye (a functional eye is defined as one that is not legally blind) even if that eye is otherwise eligible for the study. Furthermore, subjects with only 1 eligible eye should not have other ocular conditions with poorer prognosis in the fellow eye 5. Any ocular disorders in the study eye that, in the opinion of the investigator, may confound interpretation of study results or interfere with subject safety, including, but not limited to: a. Significant media opacities, including cataract, which can interfere with visual acuity, or fundus photography b. Significant scarring or atrophy in the macula that indicates substantial irreversible vision loss, or other conditions limiting capacity for visual acuity improvement c. Decrease in BCVA due to causes other than wet AMD/PCV d. History or presence of diabetic macular edema or diabetic retinopathy e. Vitreomacular traction or epiretinal membrane in the study eye evident biomicroscopically or on OCT that is considered by the investigator to significantly affect central vision f. Ocular inflammation (including trace or above) or external ocular inflammation in the study eye. Evidence at examination of infectious blepharitis, keratitis, scleritis, or conjunctivitis in either eye or current treatment for serious systemic infection g. History of idiopathic or autoimmune uveitis in either eye h. Aphakia or absence of the posterior capsule; with the

	exception of pseudoaphakia or yttrium aluminum garnet (YAG) capsulotomy in the study eye 6. Concomitant systemic disease which may affect the patient´s regular visits or contraindicate use of PDT including, but not limited to: a. Uncontrolled hypertension defined as a single measurement of systolic >180 mm Hg, 2 consecutive measurements of systolic >160 mm Hg, or 1 measurement of diastolic >100 mmHg on optimal medical regimen b. Uncontrolled diabetes mellitus, in the opinion of the investigator c. History of cerebrovascular disease or myocardial infarction within 6 months prior to entry into the study d. Renal failure requiring dialysis or renal transplant e. Clinically relevant impairment of liver function, in particular porphyria 7. Participation in an investigational study within 30 days prior to the initial screening visit that involved treatment with any drug (excluding vitamins and minerals) or device 8. Pregnancy or lactation 9. History of allergy to fluorescein used in fluorescein angiography, iodine and/or indocyanine green 10. History of allergy to aflibercept, verteporfin, or their excipients

Abbreviations: AMD, age-related macular degeneration; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ICF, informed consent form; ICGA, indocyanine green angiography; OCT, optical coherence tomography; PCV, polypoidal choroidal vasculopathy; PDT, photodynamic therapy; VEGF, vascular endothelial growth factor.

eTable 2. Exploratory Endpoints for the PLANET Study

Exploratory endpoint examined in the PLANET study included, but were not limited to:	Change in central subfield thickness ([CST] thickness of the central 1 mm of retina) over time
	Percentage of subjects with active polypoidal lesions (investigator evaluated, using OCT and ICGA)
	Area involved by polypoidal lesions as measured on ICGA by reading center;
	Proportion of subjects with complete polypoidal lesion regression, evaluated by reading center as absence of polypoidal lesions on ICGA
	Proportion of subjects requiring rescue therapy during first year of study

eTable 3. Sensitivity Analyses for (A) Change in BCVA Letters from Baseline to Week 52 and (B) Proportion of Subjects Avoiding ≥15 ETDRS Letters Loss at Week 52

A. Change in BCVA in ETDRS letter score from baseline to week 52 (ANCOVA), multiple imputation, Full analysis set

	IAI Monotherapy n = 157	**IAI Plus Rescue PDT n = 161**
Least-square mean change (SE) in BCVA from baseline to week 52, ETDRS letters	6.3 (1.4)	7.1 (1.3)
Least-square mean difference (95% CI), P-value	-0.77 (-2.96, 1.43) P = 0.49	
Mean change (SD) in BCVA from baseline to week 52, ETDRS letters	11.3 (11.0)	11.6 (9.6)

B. Proportion of subjects who avoid ≥15 ETDRS letters loss at Week 52 (Worst case imputation), Full analysis set

	IAI Monotherapy n = 157	**IAI Plus Rescue PDT n = 161**
Subjects who avoid ≥15 ETDRS letters loss, n (%)	140 (89.2%)	150 (93.2%)
Difference, % (95% CI)*	-4.3 (-10.6, 2.1)	
P-value†	0.19	

* IAI plus rescue PDT minus IAI monotherapy; confidence internal using Mantel-Haenszel adjusted by ethnicity and qualification for rescue therapy at week 12.
†2-sided Cochran-Mantel-Haenszel test adjusted by ethnicity and qualification for rescue therapy at Week 12.

eTable 4. Change in Polypoidal Lesion Characteristics (as Assessed by ICGA) According to Rescue Treatment Criteria at Week 52, Full analysis set – last observation carried forward

	Participants Who Did Not Meet Rescue Criteria		Participants Who Met Rescue Criteria	
	IAI Monotherapy n = 138	IAI Plus Rescue PDT n = 138	IAI Monotherapy n = 19	IAI Plus Rescue PDT n = 23
Proportion of subjects with no active polypoidal lesions[a], n/N (%)	111/126 (88.1)	118/133 (88.7)	5/16 (31.3)	18/20 (90.0)
Proportion of subjects with complete polypoidal lesion regression, n/N (%)	48/111 (43.2)	52/116 (44.8)	1/15 (6.7)	8/18 (44.4)

[a]Defined as either: (1) absence of polypoidal lesions on ICGA or in case polypoidal lesions were identified, (2) absence of new or persistent fluid on OCT, or (3) absence of leakage on angiography. All parameters were determined by central reading center. Subjects with missing observations were excluded.
IAI, intravitreal aflibercept; ICGA, indocyanine green angiography; OCT, optical coherence tomography; PDT, photodynamic therapy.

eTable 5. Study Outcomes, Week 52: Japanese/Non-Japanese Stratification

	Japanese Subjects		Non-Japanese Subjects	
	IAI Monotherapy n = 75	**IAI Plus Rescue PDT n = 77**	**IAI Monotherapy n = 82**	**IAI Plus Rescue PDT n = 84**
Mean change in BCVA, ETDRS, ETDRS letters	9.1	10.6	12.2	11.0
No evidence of active polypoidal lesions, n/N (%)	54/67 (80.6)	64/72 (88.9)	62/75 (82.7)	72/81 (88.9)
Change in mean area of active polypoidal lesions, % reduction	62.7	57.0	68.5	64.3
Proportion of patients with complete polypoidal lesion regression, %	24/62 (38.7)	29/67 (43.3)	25/64 (39.1)	31/67 (46.3)

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; IAI, intravitreal aflibercept; PDT, photodynamic therapy.