

Supplementary Online Content

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

eMethods

Patient inclusion and exclusion criteria

Inclusion criteria for patients

- Patients must provide written informed consent before any assessment is performed
- Male or female aged ≥ 18 years

Inclusion criteria for the study eye

- Confirmed diagnosis of symptomatic macular PCV defined by
 - Active macular polypoidal lesions shown by ICGA and
 - Presence of serosanguinous maculopathy (i.e. exudative or hemorrhagic features involving the macula on CF photography and FA)
- BCVA letter score between 78-24 (approximately 20/32 to 20/320 Snellen equivalent) using ETDRS VA chart measured at 4 m
- GLD of the total lesion area (BVN + polyps) $< 5400 \mu\text{m}$ (approximately 9 Macular Photocoagulation Study disc areas) as delineated by ICGA

Exclusion criteria for patients

- Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of study treatment.

Exclusion criteria for systemic medical history or conditions

- Any type of systemic disease or its treatment, including any medical condition (controlled or uncontrolled) that over the duration of the study could be expected to progress, recur, or change to such an extent that it may bias the assessment of the clinical status of the patient to a significant degree or put the patient at special risk
- History of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
- Stroke or myocardial infarction within the past 3 months prior to screening
- History of porphyria
- Uncontrolled blood pressure defined as systolic value of >160 mm Hg or diastolic value of >100 mm Hg while sitting at screening or baseline
- Known hypersensitivity to any of the study drugs (ranibizumab or verteporfin) or any component of their formulations or to drugs of similar chemical classes and to fluorescein or indocyanine green

Exclusion criteria for prior or current systemic medication

- Use of other investigational drugs within 30 days or 5 half-lives prior to screening, whichever is longer

- Previous treatment with systemic anti-VEGF drugs within 6 months prior to screening (e.g., sorafenib , sunitinib, bevacizumab)
- Use of systemic corticosteroids for more than 30 consecutive days during the past 3 months prior to screening
- Current or planned use of systemic medications known to be toxic to the lens, retina or optic nerve including deferoxamine, chloroquine/hydroxychloroquin, tamoxifen, phenothiazines, and ethambutol

Exclusion criteria for ocular medical history and conditions

- Presence of angioid streaks, macular fibrosis, presumed ocular histoplasmosis syndrome, or pathologic myopia (evidence of posterior segment abnormalities consistent with pathologic myopia)
- Tear (rip) of the retinal pigment epithelium involving the fovea at the time of screening or baseline
- Fibrosis or geographic atrophy involving the fovea
- Active ocular inflammation or infection (ocular or periocular) at the time of screening or baseline
- Uncontrolled intraocular hypertension or glaucoma (IOP \geq 30 mmHg) despite treatment with anti-glaucoma medication at the time of screening or baseline
- History of rhegmatogenous retinal detachment or macular hole (stage 3 or 4)
- Ocular disorders in the study eye (e.g. cataract, retinal vascular occlusion, diabetic retinopathy) that in the opinion of the investigator, may confound the interpretation of study results or compromise VA or require medical or surgical intervention during the study period
- Inability to obtain photographs, FAs, ICGAs, or OCTs to document the lesion (e.g. due to media opacity, insufficient pupillary dilation, or lack of venous access)

Exclusion criteria for prior or current ocular treatment

- Prior treatment with verteporfin PDT, external-beam radiation, subfoveal or extrafoveal focal laser photocoagulation, submacular surgery, or transpupillary thermotherapy
- Prior treatment with any anti-VEGF compound or any investigational treatment
- History of intraocular surgery in the study eye including pars plana vitrectomy and intraocular hemorrhage displacement (e.g. injection of gas with or without tissue plasminogen activator)
- Cataract surgery within 60 days prior to screening or prior complicated cataract surgery
- History of YAG laser posterior capsulotomy in the study eye within 30 days prior to screening
- Treatment with intravitreal or subtenon corticosteroid injection or device implantation within 90 days prior to screening

- Prior treatment with any anti-VEGF compound or any investigational treatment if administered <90 days before screening in the fellow eye

Randomization procedure

The randomization list was generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Randomization was balanced across all study sites. Patients, evaluating physician investigators, vision examiners, and CRC graders were masked to the identity of treatment. Due to the differences in the appearance and route of administration of the study drugs, the treating physician was unmasked to perform the administration of vPDT, sham PDT and ranibizumab treatments. To avoid any bias, the treating physician was not involved in any other aspect of the study.

Retreatment criteria

The protocol-specific re-treatment criteria were evaluated by the investigator and were driven by presence of disease activity (e**Figure 1**). BCVA loss and/or presence of OCT anomaly (unless reported as an adverse event) would trigger re-treatment with ranibizumab. Further ICGA or FA assessments were performed wherein the presence of active PCV (polyps or leakage) would trigger retreatment with PDT, as long as the previous PDT had not been administered within the last 3 months.

At month 3 after initiation of therapy, repeat FA and ICGA were performed. If there was disease activity with persistent or new polyps, repeat verteporfin or sham PDT with ranibizumab was administered. Repeated PDT was applied only to the active polyp lesions to limit the size of the treatment zone, thereby reducing the risk of retinal atrophy. If disease activity was present without polyps on ICGA, only ranibizumab was administered and continued on a PRN basis.

Statistical Superiority Testing

The overall alpha (family-wise error rate) was maintained at the one-sided α -level of 0.025¹ by using the following testing strategy: Step 1 was to demonstrate (at an overall one-sided 0.025 level) that combination therapy is non-inferior (according to a pre-defined non-inferiority margin of 5 letters) to ranibizumab monotherapy in patients with symptomatic macular PCV as

assessed by the BCVA change from baseline to month 12, and superior with respect to complete polyp regression assessed by ICGA at month 12.

If Step 1 was established, Step 2 was performed to show (at a one-sided α -level of 0.025) that combination therapy is superior to ranibizumab monotherapy as assessed by the BCVA change from baseline at month 12.

Efficacy Assessments

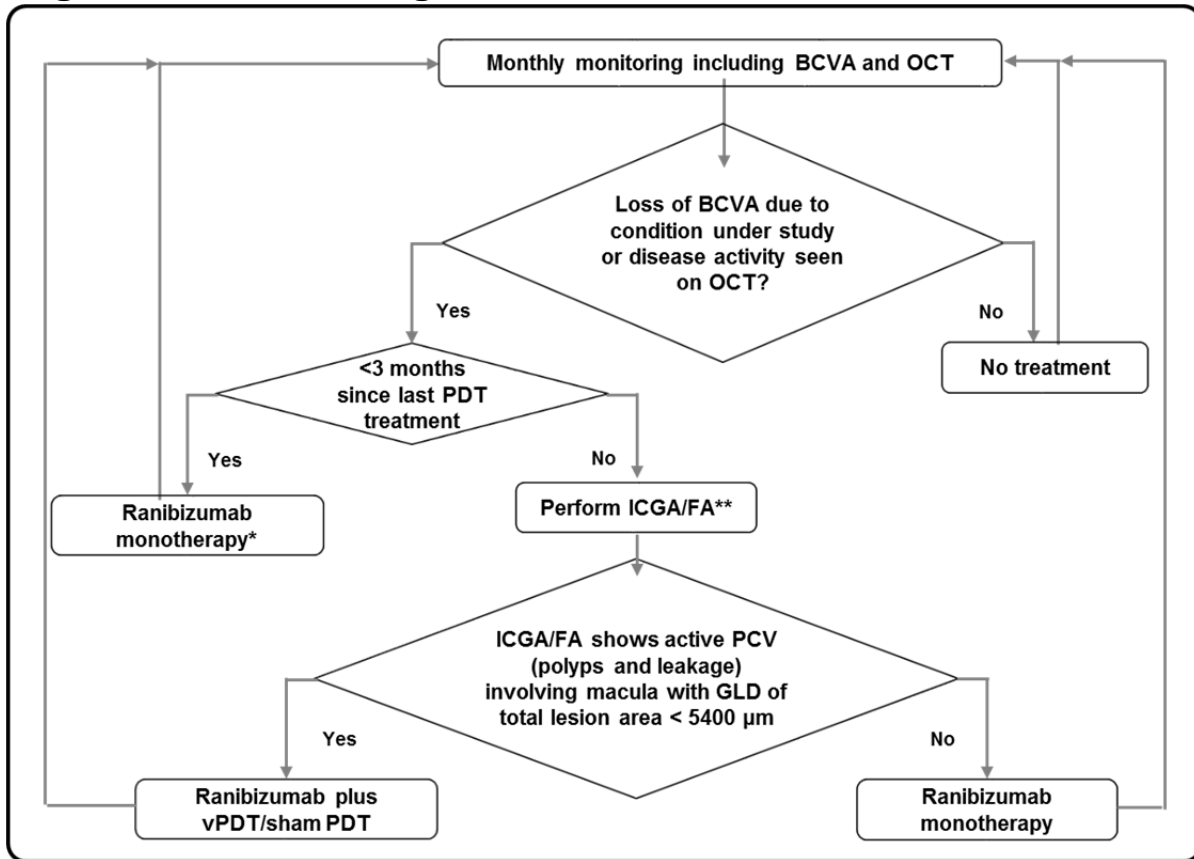
Best-corrected visual acuity: At each study visit, BCVA was assessed in a sitting position using ETDRS VA testing charts at an initial testing distance of 4 m after performing full refraction. If refraction or VA testing at 4 m was not possible because VA was too poor for the patient to read ≥ 4 letters on the refraction/VA chart, the refraction or VA testing was attempted at 1 m.

Indocyanine green angiography, fluorescein angiography and color fundus photography: ICGA was performed at screening visit or within 14 days prior to randomization during normal routine clinical practice, as well as at months 3, 6, and 12 using the Heidelberg HRA/Spectralis (Heidelberg Engineering, Heidelberg, Germany); and thereafter at other visits if required per the re-treatment algorithm at the investigator's discretion. ICGA was performed to evaluate the presence or absence of active polyp(s) and BVN. FA was performed after CF photography during screening and at months 3, 6 and 12 using Heidelberg HRA/Spectralis (Heidelberg Engineering, Heidelberg, Germany). CF was used to evaluate the presence of macular edema or subretinal fluid, massive submacular hemorrhage (hemorrhage ≥ 4 disc areas), serosanguineous hemorrhage (hemorrhage with the presence of blood and fluid), and presence of orange nodules. FA was performed to evaluate the presence of leakage, neovascularization and type of CNV.

Optical coherence tomography: OCT was performed at all visits (monthly) by the investigators using spectral domain OCT. OCT was performed to evaluate parameters such as retinal thickness and volumes, and to assess the status of disease activity.

The eligibility of the study eye was confirmed by expert graders from the CRC after assessment of ICGA, CF, FA and OCT images prior to randomization.

eFigure 1: Retreatment algorithm

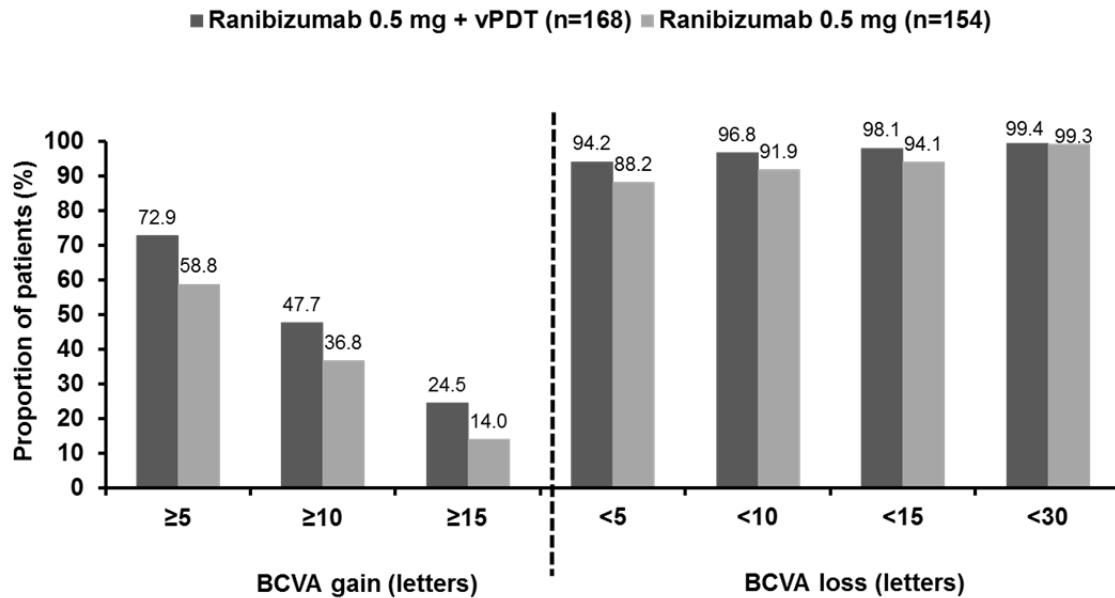


* Resume monthly monitoring

**Additional FA/ICGA images have to be obtained per the assessment schedule for Central Reading Center analysis.

BCVA, best-corrected visual acuity; FA, fluorescein angiography; GLD, greatest linear dimension; ICGA, indocyanine green angiography; OCT, optical coherence tomography; PCV, polypoidal choroidal vasculopathy; PDT, photodynamic therapy; vPDT, verteporfin photodynamic therapy

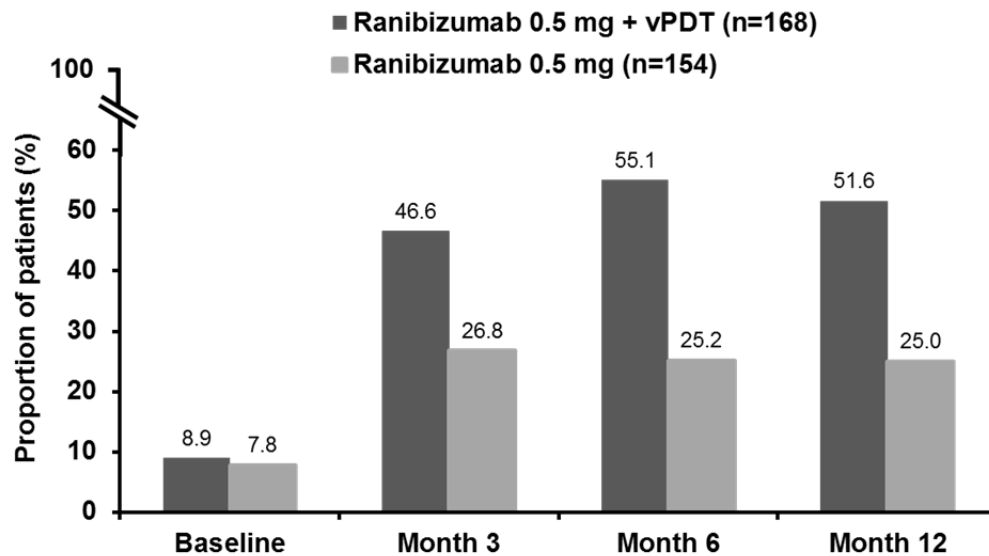
eFigure 2: Categorized change in BCVA at month 12 (FAS)



The total counts presented are the counts of patients with a BCVA value for both baseline and Month 12. These total counts are used as the denominator for the percentages.

BCVA, best-corrected visual acuity; FAS, full analysis set; vPDT, verteporfin photodynamic study

eFigure 3: Proportion of patients with no leakage in the study eye, by visit from months 3 to 12 (FAS)



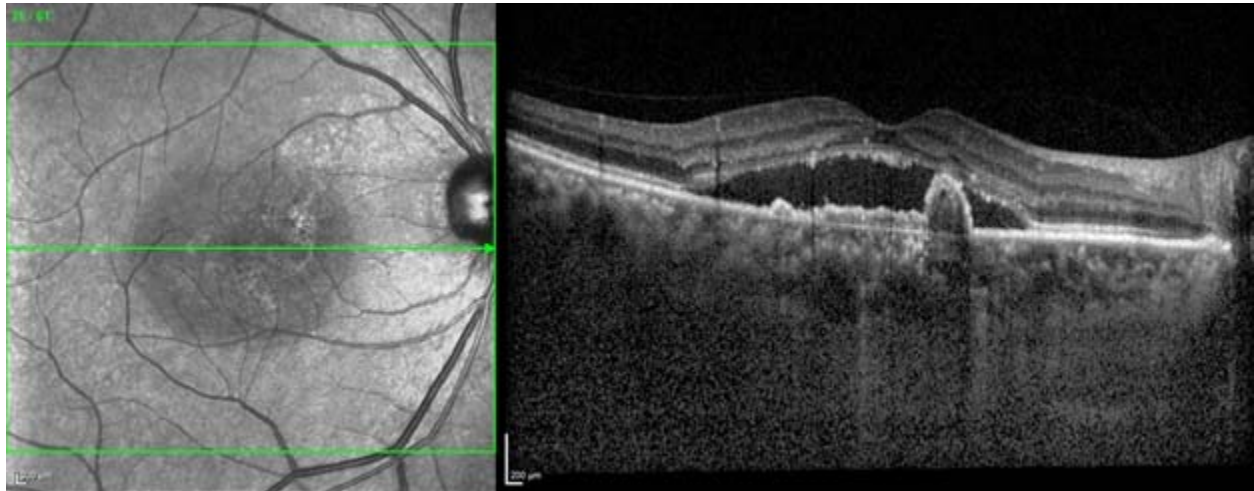
Assessed by fluorescein angiography as **total area of leakage (mm²) (study eye)**

n is the total number of patients in the FAS in the respective treatment group. Percentages are computed by considering the total number of patients in the respective treatment group who attended the specific visit as a denominator

FAS, full analysis set; vPDT, verteporfin photodynamic therapy

Case Study

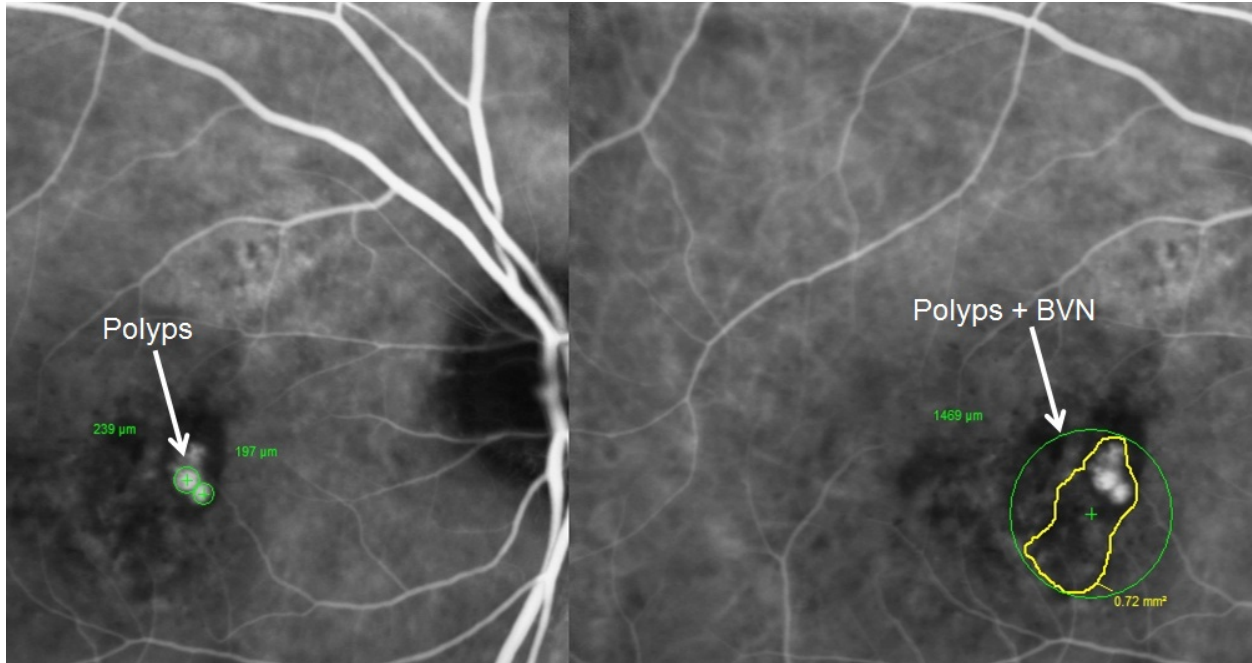
eFigure 4: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy – baseline OCT



66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) was 59 (20/63) and CSFT was 463 μm . The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses.

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

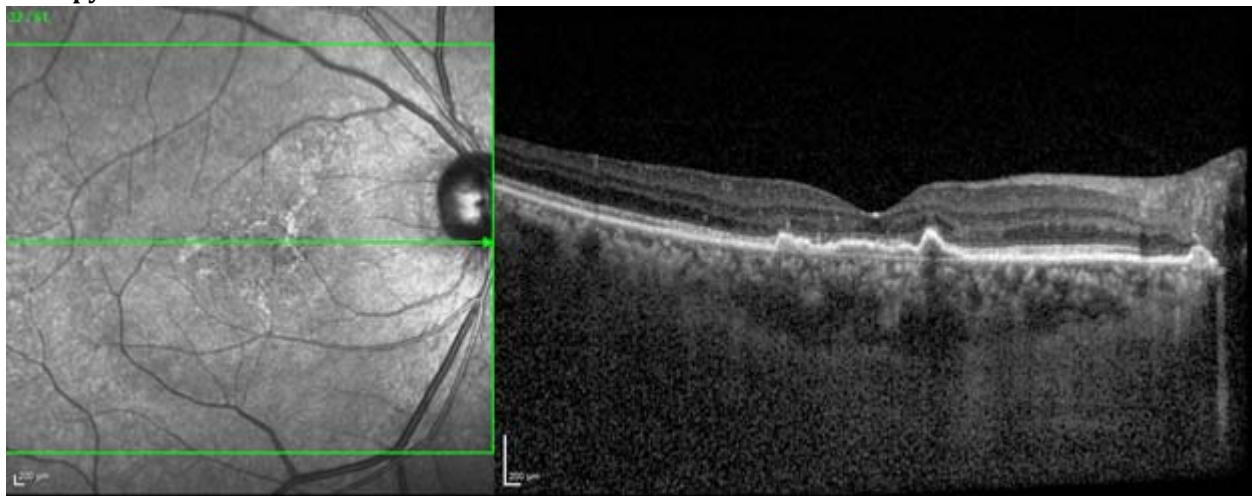
eFigure 4b: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy – baseline ICGA



66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) 59 (20/63) and CSFT was 463 μm. The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses.

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

eFigure 4c: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy – Month 3 OCT



66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) 59 (20/63) and CSFT was 463 μm. The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses. At Month 3, the BCVA letter score (approximate Snellen equivalent) 63 (20/50) and the CSFT was 222 μm

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

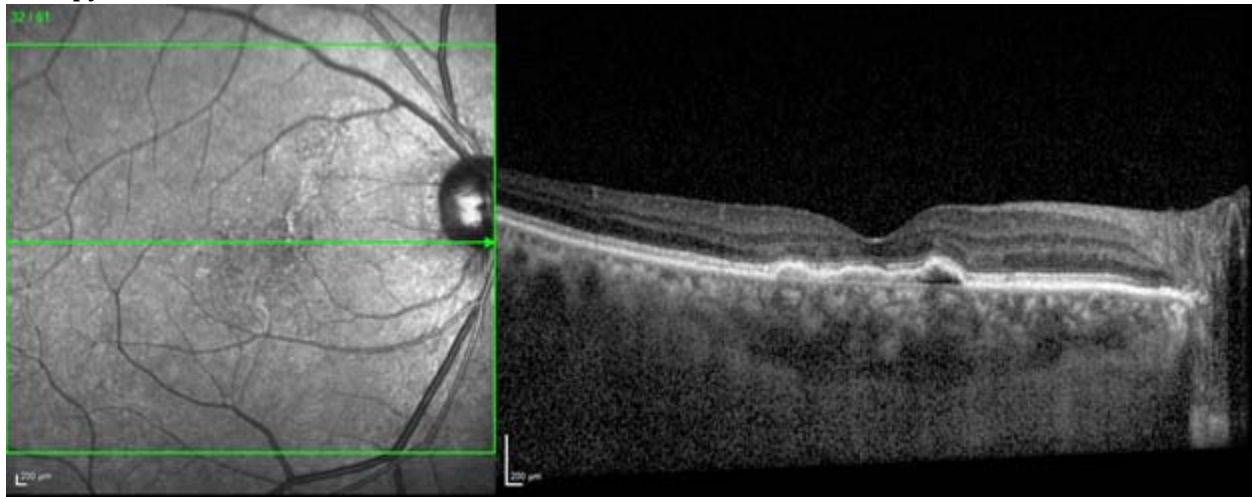
eFigure 4d: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy – Month 3 ICGA



66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) 59 (20/63) and CSFT was 463 μm . The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses. At Month 3, the BCVA letter score (approximate Snellen equivalent) 63 (20/50) and the CSFT was 222 μm

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

eFigure 4e: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy – Month 12 OCT



66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) 59 (20/63) and CSFT was 463 μm . The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses. At Month 12, the BCVA letter score (approximate Snellen equivalent) 74 (20/32) and CSFT was 235 μm

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

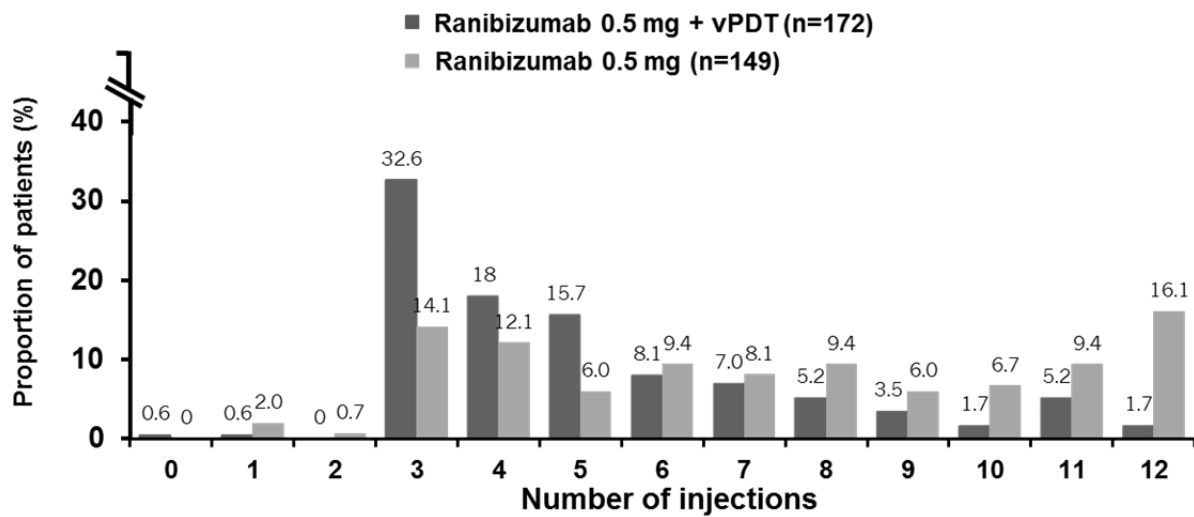
eFigure 4f: Example case of PCV patient treated with ranibizumab 0.5 mg + vPDT combination therapy - Month 12 ICGA



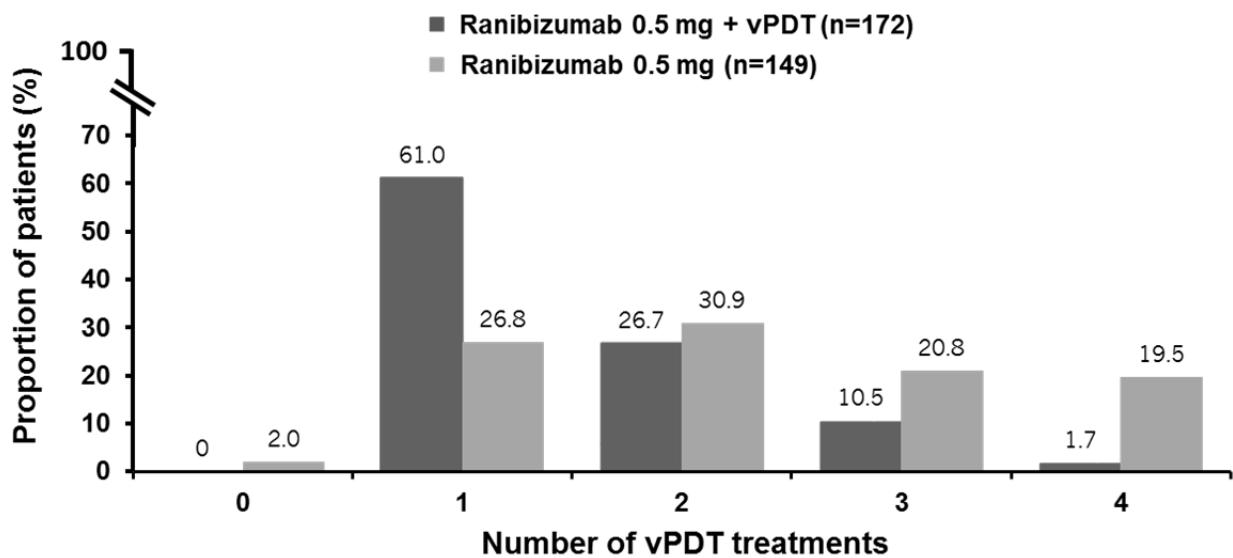
66 year-old male presented with PCV in the right eye. Baseline screening BCVA letter score (approximate Snellen equivalent) 59 (20/63) and CSFT was 463 μm . The patient was treated with vPDT + 3 ranibizumab (0.5 mg IVT) loading doses. At Month 12, the BCVA letter score (approximate Snellen equivalent) 74 20/32 and CSFT was 235 μm

BCVA, Best corrected visual acuity; CSFT, Central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

eFigure 5a: Frequency of ranibizumab injections administered over 12 months (safety set)*



eFigure 5b: Frequency of vPDT/sham PDT administered over 12 months (safety set)*

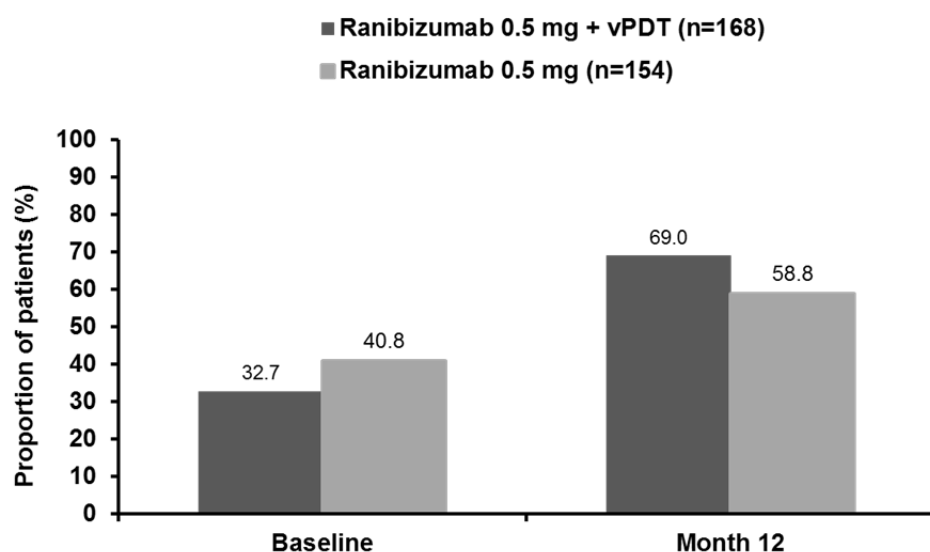


Safety set consisted of all patients who received at least one application of study treatment and had at least one post-baseline safety assessment.

*Three patients randomized in the ranibizumab + vPDT group did not receive any vPDT treatments (from which, one received a sham PDT), seven patients randomized in the ranibizumab monotherapy group received at least one vPDT treatments, and one patient randomized to ranibizumab monotherapy did not receive any treatment and hence was not included in the safety set.

PDT, photodynamic therapy; vPDT, verteporfin photodynamic therapy

eFigure 6: Proportion of patients with BCVA letter score (approximate Snellen equivalent) ≥ 69 (20/40 or better) at baseline and month 12 (FAS)



BCVA, best-corrected visual acuity; FAS- full analysis set vPDT, verteporfin photodynamic therapy.

The total counts presented are the counts of patients in the specific treatment group who attended the specific visit. These total counts are used as the denominator for the percentages.

BCVA, best-corrected visual acuity; FAS, full analysis set; vPDT, verteporfin photodynamic therapy

Primary Analysis

eTable 1: Treatment comparison for change in the best-corrected visual acuity from baseline at month 12 (FAS, LOCF)

Parameter	Ranibizumab 0.5 mg + vPDT (n=168)	Ranibizumab 0.5 mg (n=154)
n	167	151
LS Mean (SE)	8.3 (1.0)	5.1 (1.1)
95% CI for LS mean	(6.4, 10.3)	(3.0, 7.2)
Difference in LS means		
Ranibizumab 0.5 mg + vPDT minus Ranibizumab 0.5 mg	3.2	
95% CI for difference	(0.4, 6.1)	
One-sided <i>P</i> -value for non-inferiority*	<0.001	
One-sided <i>P</i> -value for superiority	0.013	
Analyzed using ANCOVA model including treatment group as fixed effect factor and centered baseline BCVA as covariate. n is the number of patients with data used in the model.		

*p-value for testing non-inferiority of ranibizumab 0.5 mg + vPDT with respect to ranibizumab 0.5 mg is calculated for pre-defined non-inferiority margin of 5 letters
 ANCOVA, analysis of covariance; CI, confidence interval; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; SE, standard error; vPDT, verteporfin photodynamic therapy

Sensitivity Analyses

eTable 2: Treatment comparison for change in the best-corrected visual acuity from baseline at month 12 (per protocol set, LOCF)

Parameter	Ranibizumab 0.5 mg + vPDT (n=161)	Ranibizumab 0.5 mg (n=148)
n	161	144
LS Mean (SE)	8.8 (1.0)	5.0 (1.0)
95% CI for LS mean	(6.9, 10.8)	(2.9, 7.0)
Difference in LS means		
Ranibizumab 0.5 mg + vPDT minus Ranibizumab 0.5 mg	3.9	
95% CI for difference	(1.1, 6.7)	
One-sided <i>P</i> -value for non-inferiority*	<0.001	
One-sided <i>P</i> -value for superiority	0.007	

n is the number of patients with data used in the model.
 Per protocol set is defined as participants who fulfill the protocol in terms of the eligibility, interventions, and outcome assessment.
 The baseline value is the last available, non-missing, value collected prior to first study treatment in the study eye
 Analyzed using ANCOVA model including treatment group as fixed effect factor and centered baseline BCVA as covariate.
 *p-value for testing non-inferiority of ranibizumab 0.5 mg + vPDT with respect to ranibizumab 0.5 mg is calculated for pre-defined non-inferiority margin of 5 letters.
 ANCOVA, analysis of covariance; CI, confidence interval; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; SE, standard error; vPDT, verteporfin photodynamic therapy

eTable 3: Treatment comparison for change in the best-corrected visual acuity from baseline at month 12 (FAS)

Parameter	Ranibizumab 0.5 mg + vPDT (n=168)	Ranibizumab 0.5 mg (n=154)
n	155	136
LS Mean (SE)	9.5 (0.9)	5.7 (0.9)
95% CI for LS mean	(7.9, 11.2)	(3.9, 7.5)
Difference in LS means		
Ranibizumab 0.5 mg + vPDT minus Ranibizumab 0.5 mg	3.8	
95% CI for difference	(1.4, 6.3)	
One-sided <i>P</i> -value for non-inferiority*	<0.001	
One-sided <i>P</i> -value for superiority	0.002	

n is the number of patients with data used in the model.

The baseline value is the last available, non-missing, value collected prior to first study treatment in the study eye

Analyzed using ANCOVA model including treatment group as fixed effect factor and centered baseline BCVA as covariate.

*p-value for testing non-inferiority of ranibizumab 0.5 mg + vPDT with respect to ranibizumab 0.5 mg is calculated for pre-defined non-inferiority margin of 5 letters

ANCOVA, analysis of covariance; CI, confidence interval; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; SE, standard error; vPDT, verteporfin photodynamic therapy

eTable 4: Treatment comparison for change in the best-corrected visual acuity from baseline at month 12 (FAS)

Parameter	Ranibizumab 0.5 mg + vPDT (n=168)	Ranibizumab 0.5 mg (n=154)
n	167	151
LS Mean (SE)	8.7 (0.91)	5.1 (1.07)
95% CI for LS mean	(6.92, 10.52)	(-2.96, 7.19)
Difference in LS means		
Ranibizumab 0.5 mg + vPDT minus Ranibizumab 0.5 mg	3.6	
95% CI for difference	(0.88, 6.2)	
One-sided <i>P</i> -value for non-inferiority*	<0.001	
One-sided <i>P</i> -value for superiority	0.005	

n is the number of patients with data used in the model.

The baseline value is the last available, non-missing, value collected prior to first study treatment in the study eye

Analyzed using MMRM model including treatment group, scheduled visit, centered baseline BCVA value, lesion type, treatment group by visit interaction, and visit by centered baseline BCVA interaction as fixed effect factors.

*p-value for testing non-inferiority of ranibizumab 0.5 mg + vPDT with respect to ranibizumab 0.5 mg is calculated for pre-defined non-inferiority margin of 5 letters.

ANCOVA, analysis of covariance; CI, confidence interval; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; MMRM, mixed-effect model repeated measure; SE, standard error; vPDT, verteporfin photodynamic therapy

eTable 5: Number of ranibizumab injections and PDT treatments administered over 12 months (safety set)

Parameter	Ranibizumab 0.5 mg + vPDT (n=172)*	Ranibizumab 0.5 mg (n=149)*
Number of ranibizumab injections		
n** (%)	171 (99.4)	149 (100.0)
Mean (SD)	5.2 (2.49)	7.3 (3.32)
Median	4.0	7.0
Number of vPDT/sham PDT treatments		
n** (%)	172 (100.0)	146 (98.0)
Mean (SD)	1.5 (0.8)	2.3 (1.1)
Median	1.0	2.0

Safety set consisted of all patients who received at least one application of study treatment and had at least one post-baseline safety assessment.

*Three patients randomized in the ranibizumab + vPDT group did not receive any vPDT treatments (from which, one received a sham PDT), seven patients randomized in the ranibizumab monotherapy group received at least one vPDT

treatments, and one patient randomized to ranibizumab monotherapy did not receive any treatment and hence was not included in the safety set.**n is the total number of subjects with at least one treatment.
SD, standard deviation; PDT, photodynamic therapy; vPDT, verteporfin photodynamic therapy.

eTable 6: Ocular and non-ocular serious adverse events regardless of study drug relationship up to month 12 (safety set)

Preferred term, n (%)	Ranibizumab 0.5 mg + vPDT (n=172)*	Ranibizumab 0.5 mg (n=149)*
Deaths	1 (0.6)	0 (0.0)
Ocular SAEs, total	1 (0.6)	3 (2.0)
Vitreous hemorrhage	1 (0.6)	3 (2.0)
Non-ocular SAEs, total	13 (7.6)	11 (7.4)
Asthma	1 (0.6)	0 (0.7)
Acute myocardial infarction	1 (0.6)	0 (0.0)
Aortic dissection	1 (0.6)	0 (0.0)
Anemia of chronic disease	0 (0.0)	1 (0.7)
Chronic obstructive pulmonary disease	1 (0.6)	0 (0.0)
Colitis	0 (0.0)	1 (0.7)
Embolic stroke	0 (0.0)	1 (0.7)
Fall	0 (0.0)	1 (0.7)
Femur fracture	0 (0.0)	1 (0.7)
Hemorrhagic stroke	1 (0.6)	0 (0.0)
Heat exhaustion	1 (0.6)	0 (0.0)
Herpes zoster	1 (0.6)	0 (0.0)
Hemoptysis	0 (0.0)	1 (0.7)
Inguinal hernia	2 (1.2)	0 (0.0)
Lower limb fracture	1 (0.6)	0 (0.0)
Lower respiratory tract infection	0 (0.0)	1 (0.7)
Lung adenocarcinoma	0 (0.0)	1 (0.7)

Metastases to bone	0 (0.0)	1 (0.7)
Metastases to central nervous system	0 (0.0)	1 (0.7)
Metastases to liver	0 (0.0)	1 (0.7)
Metastases to lymph nodes	0 (0.0)	1 (0.7)
Myocardial ischemia	0 (0.0)	1 (0.7)
Osteoarthritis	0 (0.0)	1 (0.7)
Pneumonia	0 (0.0)	2 (1.3)
Presyncope	1 (0.6)	0 (0.0)
Prostate cancer	1 (0.6)	0 (0.0)
Spinal column stenosis	1 (0.6)	0 (0.0)
Syncope	0 (0.0)	1 (0.7)
Thermal burn	1 (0.6)	0 (0.0)
Wound infection	0 (0.0)	1 (0.7)
<p>The safety set consisted of all patients who received at least one application of study treatment and had at least one post-baseline safety assessment</p> <p>*Three patients randomized in the ranibizumab + vPDT group did not receive any vPDT treatments (from which, one received a sham PDT), seven patients randomized in the ranibizumab monotherapy group received at least one vPDT treatments, and one patient randomized to ranibizumab monotherapy did not receive any treatment and hence was not included in the safety set.</p> <p>SAEs, serious adverse events; vPDT, verteporfin photodynamic therapy.</p>		

eTable 7: Ocular and non-ocular adverse events regardless of study drug relationship up to Month 12 by preferred term (>1.5% in any group; safety set)

Preferred term, n (%)	Ranibizumab 0.5 mg + vPDT (n=172)*	Ranibizumab 0.5 mg (n=149)*
Ocular AEs, total	46 (26.7)	38 (25.5)
Asthenopia	3 (1.7)	0 (0.0)
Conjunctivitis	3 (1.7)	5 (3.4)
Conjunctivitis allergic	1 (0.6)	3 (2.0)

Conjunctival hemorrhage	4 (2.3)	2 (1.3)
Dry eye	4 (2.3)	2 (1.3)
IOP increased	9 (5.2)	7 (4.7)
Macular fibrosis	3 (1.7)	0 (0.0)
Punctate keratitis	1 (0.6)	3 (2.0)
Retinal hemorrhage	6 (3.5)	1 (0.7)
Vitreous hemorrhage	1 (0.6)	4 (2.7)
Non-ocular AEs, total	73 (42.4)	56 (37.6)
Arrhythmia	3 (1.7)	0 (0.0)
Benign prostatic hyperplasia	3 (1.7)	0 (0.0)
Cough	3 (1.7)	3 (2.0)
Diarrhea	3 (1.7)	1 (0.7)
Dizziness	2 (1.2)	3 (2.0)
Nasopharyngitis	17 (9.9)	7 (4.7)
Eczema	4 (2.3)	0 (0.0)
Gastroenteritis	4 (2.3)	0 (0.0)
Hypertension	2 (1.2)	6 (4.0)
Influenza	2 (1.2)	4 (2.7)
Insomnia	3 (1.7)	0 (0.0)
Osteoarthritis	0 (0.0)	4 (2.7)
Pharyngitis	3 (1.7)	0 (0.0)
Spinal osteoarthritis	0 (0.0)	3 (2.0)
Upper respiratory tract infection	10 (5.8)	0 (0.0)
<p>The safety set consisted of all patients who received at least one application of study treatment and had at least one post-baseline safety assessment</p> <p>*Three patients randomized in the ranibizumab + vPDT group did not receive any vPDT treatments (from which, one received a sham PDT), seven patients randomized in the ranibizumab monotherapy group received at least one vPDT treatments, and one patient randomized to ranibizumab monotherapy did not receive any treatment and hence was not included in the safety set.</p> <p>AEs, adverse events; IOP, intraocular pressure; vPDT, verteporfin photodynamic therapy.</p>		

References

1. Maurer W HL, Lehmacher W. Multiple comparisons in drug clinical trials and preclinical assays: A-priori ordered hypotheses, in: Testing Principles in Clinical and Preclinical Trials. In: Vollmar J, ed. *Biometrie in der chemisch-pharmazeutischen Industrie*. Fischer Verlag Stuttgart 1995;6:3-18.