Online Supplementary Table 1: Definitions of pre-specified protocol deviations

Deviation Code	Description	Exclusion code	Time of visit	Identification method	Details
IC001	Lack of written informed consent	SAFETY	Baseline/V1	P	Informed consent date in CRF is missing
IC002	<50 years of age	-	Baseline/V1	P	
IC003	None of the following conditions was fulfilled: eye(s) eligible for ranibizumab treatment, with a BCVA below 2/10 due to nAMD or - second eye eligible for ranibizumab treatment, with first eye treated (currently or previously) with ranibizumab, regardless of BCVA. In bilateral nAMD patients, the second eye can be included only if the first eye has been treated at least 14 days before with ranibizumab. Patients developing fellow eye nAMD affection (newly diagnosed) while the study is running satisfy the present criterion and are consecutively eligible for enrollment.	-	Baseline/V1	M	
EC001	Active intraocular inflammation (grade trace or above) in either eye	-	Baseline/V1	M	Signs of intraocular inflammation are: cell infiltration or floaters in anterior or posterior chamber. Types of inflammation are: anterior uveitis (iritis, iridocyclitis), intermediate uveitis (vitritis), posterior uveitis (retinitis, coroiditis, vasculitis), chorioretinitis, endophthalmitis
EC002	Any ocular or periocular active infection (current or suspected) in either eye	-	Baseline/V1	M	Including conjunctivitis, keratitis, endophthalmitis, blepharitis, vitritis, chorioretinitis, neuroretinitis, scleritis, uveitis

EC003	Retinal pigment epithelial tear (evidence at time of enrollment)	-	Baseline/V1	M	
EC004	Ocular disorders that may confound interpretation of results compromise visual acuity or require medical or surgical intervention during the study period including mature cataract (instrumental evidence at enrollment), retinal vascular occlusion, preretinal membrane, retinal detachment or macular hole	-	Baseline/V1	M	Including clinically relevant cataract, retinal vascular occlusion, retinal detachment or macular hole
EC005	Uncontrolled glaucoma in either eye (IOP ≥ 30 mmHg on medication or according to investigator's judgment)	-	Baseline/V1	M/P	
EC006	History of vitrectomy in the study eye	-	Baseline/V1	M	
EC007	History of stroke (brain ischemia) or TIA or myocardial ischemia in the 3 months prior to study enrollment	-	Baseline/V1	M	
EC008	Systemic treatment with any VEGF inhibitor (including bevacizumab, ziv-aflibercept) the 90 days prior to study enrollment	-	Baseline/V1	M	Bevacizumab (Avastin®) ziv-aflibercept (Zaltrap®)
EC009	Ocular treatment of the study eye with any anti-angiogenic drugs including any anti-VEGF drug, i.e. bevacizumab, aflibercept, pegaptanib, vPDT) within 1 month prior to study enrollment	-	Baseline/V1	M	Including bevacizumab (Avastin®, unlicensed for intravitreal use), pegaptanib Macugen®), aflibercept (Eylea®) vPDT
Ec010	Any intraocular surgery in the study eye within 28 days prior to enrollment	-	Baseline/V1	M	Including refractive surgery, cataract surgery, glaucoma surgery, vitrectomy, post-traumatic surgery
EC011	Women of childbearing potential unless using effective methods of contraception during treatment	-	Baseline/V1	M	Urine pregnancy stick test will be performed locally at enrollment to women of child-bearing potential
EC012	Pregnant or lactating women	-	Baseline/V1	M	
EC013	Simultaneous participation in a study that includes	-	Baseline/V1	M	

	administration of any investigational drug				
EC014	Known hypersensitivity to ranibizumab, any component of the ranibizumab formulation, or known hypersensitivity to drugs of similar chemical class, to fluorescein or any other component of fluorescein formulation, or to indocyanine green or any other component of indocyanine green formulation	-	Baseline/V1	M	
EC015	Inability to comply with study procedures	-	Baseline/V1	M	
CMED1	Chronic concomitant therapy with topical ocular corticosteroids, administered for more than 30 days consecutively (i.e. loteprednol etabonate, prednisolone acetate, dexamethasone, fluorometholone)	-	Any	M	Including loteprednol etabonate (Lotemax®), prednisolone acetate (Idrocortisone acetato), dexamethasone (Cloradex®, Visumetazone®), fluorometholone (Fluaton®, Fluorometol®, Flarex® Gentacort®) (principal use: keratoconjunctivitis sicca – dry eye, allergic seasonal conjunctivitis, post-surgery)
CMED2	Other intravitreal medications in the study eye (including intravitreal corticosteroids, i.e. dexamethasone, triamcinolone acetonide)	-	Any	M	Including Dexamethasone (Ozurdex®), triamcinolone acetonide (Taioftal®)
CMED3	Systemic medications known to be toxic to the lens, retina or optic nerve including deferoxamine, chloroquine/ hydroxychloroquine (Plaquenil®), tamoxifen, phenothiazines and ethambutol	-	Any	M	
CMED4	Treatment with glitazones when newly started during the study	-	Any	M	Pioglitazone
CMED5	Systemic treatment with any VEGF inhibitor in the 90 days prior to study enrollment (including bevacizumab, ziv-aflibercept)	-	Any	M	Including bevacizumab [Avastin®], ziv-aflibercept [Zaltrap®]

CMED6	Ocular treatment of the study eye with any anti-angiogenic drugs within 1 month prior to study enrollment (including any anti-VEGF drugs, i.e. bevacizumab , aflibercept, pegaptanib and vPDT [verteporfin photodynamic therapy])	-	Baseline/V1	M	Bevacizumab (Avastin®, unlicensed for intravitreal use), pegaptanib Macugen®), aflibercept (Eylea®)
CMED7	Any other investigational drug at any time during the study	-	Any	M	
WITH1	Subject did not interrupt the study drug administration despite decrease in BCVA of ≥30 letters compared with the last assessment of visual acuity	-	Any	M	
WITH2	Subject did not interrupt the study drug administration despite retinal break	-	Any	M	
WITH3	Subject did not interrupt the study drug administration despite subretinal hemorrhage involving the center of the fovea, or, if the size of the hemorrhage is ≥50% of the total lesion area	-	Any	M	
WITH4	Subject did not interrupt the study drug administration despite intraocular pressure of ≥30 mmHg	-	Any	M	
WITH5	Subject did not interrupt the study drug administration despite he/she performed planned intraocular surgery within the previous or next 28 days	-	Any	M	
WITH6	Subject did not discontinue the study drug administration despite rhegmatogenous retinal detachment or stage 3 or 4 macular holes (according to approved label)	-	Any	M	
WITH7	Subject did not discontinue the study drug administration despite he/she experienced TIA or stroke during the study	-	Any	M	
WITH8	Subject did not discontinue the study drug administration despite pregnancy	-	Any	M	

WITH9	Subject did not discontinue the study drug administration despite he/she withdrew the informed consent	-	Any	M	
WITH10	Any other protocol deviation that resulted in a significant risk to the patient's safety	-	Any	M	
WITH11	Subject did not discontinue the study drug administration despite a cataract evidence occurs in the study eye, and surgical intervention is required, but the patient is injected during the monthly visit and treatment is not interrupted	-	Any	M	
PROC1	The duration of the study was greater than 12 months + 7 days per eye.	-	Baseline/V3	P	
PROC2	Patient was not contacted by telephone 2 (±1) days following each visit when program drug was administered	-	Any	M	
PROC3	IOP did not performed prior to ranibizumab dosing and 1 hour post-dose in the study eye(s)	-	Any	M/P	
PROC4	Subject who had no post-baseline safety assessments	SAFETY	Any	M	Safety assessments consisted in monitoring and recording: AEs (including SAEs), ophthalmic examination, IOP or vital signs
PROC5	VA assessment was not performed according to protocol at the scheduled visits	-	Any	M/P	
PROC6	IOP was not measured according to protocol at the scheduled visits	-	Any	M/P	
PROC7	Ocular examination was not performed according to protocol at the scheduled visits	-	Any	M/P	
DRUG1	For patients who treated both eyes, time between injection was lower than 14 days	-	Any	P	
DRUG2	Procedures for the administration of the drug had not been met	-	Any	M	

DRUG3	Patient was not monitored monthly for VA and treatment	-	Any	M	
DRUG4	Expired investigational treatment	-	Any	M	
DRUG5	Investigational treatment did not handled and stored properly (including temperature control)	-	Any	M	
DRUG6	Subject who did not received at least one dose of study drug	SAFETY	Any	P	
DRUG7	Patient who assumed commercial ranibizumab	-	Any	M	
DRUG8	Time from Visit 1 date and date of first administration greater than 7 days	-	Baseline/V1	P	
OTH01	Written informed consent after study specific assessment	-	Baseline/V1	P	Study informed consent date after a study assessment date
OTH02	Subject signed an obsolete version of informed consent	-	Any	M	
OTH03	Non-compliance with SAE reporting procedures	-	Any	M	
OTH04	AE did not followed until its resolution despite not judged to be permanent	-	Any	M	
OTH05	Re-screened subject	-	Patient info	M	

CMED, concomitant medication; DRUG, study drug; EC, exclusion criteria; IC, inclusion criteria; IOP, intraocular pressure; M, manual check; nAMD, neovascular age-related macular degeneration; OTH, other; P, programmed check; PROC, protocol procedure; SAE, serious adverse event; SAFETY, patient excluded from safety population; TIA, transient ischemic attack; V, visit; VA, visual acuity; VEGF, vascular endothelial growth factor; vPDT, verteporfin photodynamic therapy; WITH, treatment withdrawal/interruption.