Supplementary Table 1. Image aqcuisitions at each center

No.	Center	FFA	FFA-serial	4 wide-field CFP	CFP-serial	Spectral domain OCT	OCT-serial
1	Shanghai General Hospital	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2-KT-00641)	Topcon Corporation 50DX	Serial #(947899)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(KT-01003)
2	He Eye Hospital	Topcon Corporation 50DX	Serial #(948122)	Topcon Corporation 50DX	Serial #(948122)	Topcon Corporation 3D-OCT 1000	Serial #(209079)
3	The Third Affiliated Hospital of Third Military Medical University	Heidelberg Engineering, Inc. HRA2	Serial #(KT-00285)	Carl Zeiss Meditec, Inc. Visucam	Serial #(1103225)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(TR-KT-00525)
4	Wuhan General Hospital of Guangzhou Military	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2-KT-01419)	Topcon Corporation NW7SF	Serial #(677290)	Topcon Corporation 3D-OCT 1000	Serial #(209032)
5	The First Affiliated Hospital of the Fourth Military Medical University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(04734-S1600)	Topcon Corporation 50DX	Serial #(948084)	Topcon Corporation 3D-OCT 2000	Serial #(688057)
6	The Eye Hospital of Wenzhou Medical University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2-00445)	Topcon Corporation 50DX	Serial #(947590)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(H2E-12052-010-005)

7	Wuxi No. 2 People's Hospital	Topcon Corporation 50IX	Serial #(175258)	Topcon Corporation 50IX	Serial #(175258)	Carl Zeiss Meditec, Inc. Cirrus	Serial #(4000-12023)
8	Southwest Hospital	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(H2E-11774-004-002)	Kowa Company, Ltd nonmyd a-DIII	Serial #(1579000605)	Topcon Corporation 3D-OCT 1000	Serial #(209032)
9	The Ophthalmological Research Institute of Henan	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(TSP-02572)	Carl Zeiss Meditec, Inc. FF450 Plus	Serial #(988819)	Carl Zeiss Meditec, Inc. Cirrus	Serial #(4000-6040)
10	Peking University Third Hospital	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2 00093)	Carl Zeiss Meditec, Inc. FF450 Plus	Serial #(2019990 88)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(TR-KT1248)
11	Beijing Tongren Hospital, Capital Medical University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(04768-S3600)	Topcon Corporation 50DX	Serial #(870707)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(04768-S3600)
12	TianJin University Medical Eye Hospital	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(H2E-15131-003-001)	Topcon Corporation 50EX	Serial #(274768)	Topcon Corporation 3D-OCT 2000	Serial #(608102)
13	Shanghai Renji Hospital	Carl Zeiss Meditec, Inc. Visucam 500	Serial #(1100811)	Carl Zeiss Meditec, Inc. Visucam 500	Serial #(1100811)	Carl Zeiss Meditec, Inc. Cirrus	Serial #(4000-8143)

14	West China Hospital, Sichuan University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2-00617)	Topcon Corporation 50DX	Serial #(948400)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(01596-S2000)
15	The First Affiliated Hospital of Chongqing Medical University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(01848-S1300)	Canon, Inc. CR-DGi	Serial #(DGI311808 - BX00271)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(03721-S2000)
16	Peking Union Medical College Hospital	Topcon Corporation 50DX	Serial #(8710039)	Topcon Corporation 50DX	Serial #(8710039)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(03986-S3600)
17	Zhongshan Ophthalmic Center, Sun Yat-Sen University	Heidelberg Engineering, Inc. Spectralis (cSLO)	Serial #(HRA2-KT-03251)	Topcon Corporation 50DX	Serial #(948133)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(2867-5-3600)
18	Peking University People's Hospital	Topcon Corporation 50DX	Serial #(945906)	Carl Zeiss Meditec, Inc. FF450 Plus	Serial #(1076503)	Heidelberg Engineering, Inc. Spectralis (OCT)	Serial #(01225-S3300)

CFP, Color fundus photography; FFA, fundus fluorescein angiography; OCT, optical coherence tomography.

Supplementary Table 2. Patient disposition in the extension study

	Conbercept	Laser	Total
Enrolled, n	76	81	157
Enrolled but not treated, n (%)	1 (1.3)	1 (1.2)	2 (1.3)
Completed the study, n (%)	67 (88.2)	75 (92.6)	142 (90.4)
Withdrew from the study, n (%)	9 (11.8)	6 (7.4)	15 (9.6)
Adverse event	4 (5.3)	1 (1.2)	5 (3.2)
Investigator judgement	3 (3.9)	3 (3.7)	6 (3.8)
Withdrawal of consent	1 (1.3)	1 (1.2)	2 (1.3)
Lost to follow up	1 (1.3)	0	1 (0.6)
Death	0	1 (1.2)	1 (0.6)

Supplementary Table 3. Treatment experience

	Sailing study (baseline to month 12)			Extension study (month 12 to month 24)		
	Conbercept (n=125)	Laser (n=123)	P	Conbercept (n=76)	Laser (n=81)	P
Number of intravitreal injections	9.5±2.8	9.7±3.1 [a]	0.538	8.5±3.5	8.6±3.4	
Number of laser photocoagulation treatments	2.6±1.3 [b]	2.7±1.3	0.604	NA	NA	NA
Rescue treatment	5 (4.0)	25 (20.3)	<0.001	NA	NA	NA

NA, not applicable.

a. In the laser group, the number of sham injections was counted and did not include all treatments after the first rescue treatment.

b. In the conbercept group, the number of sham laser treatment was counted and did not include all treatments after the first rescue treatment.

Supplementary Table 4. Visual distribution in the Sailing Study

	6 months			12 months		
Variables	Conbercept (n=121)	Laser (n=118)	P	Conbercept (n=112)	Laser (n=87)	P
Vision gain						
≥0 letter	110(90.9)	65(55.1)	<0.001	104(92.9)	62(71.3)	<0.001
≥5 letters	81(66.9)	40(33.9)	<0.001	81(72.3)	46(52.9)	0.005
≥10 letters	51(42.1)	20(16.9)	<0.001	56(50.0)	26(29.9)	0.004
≥15 letters	21 (17.4)	8 (6.8)	0.012	28 (25.0)	13 (14.9)	0.082
Vision loss						
≥0 letter	11(9.1)	53(44.9)	<0.001	8(7.1)	25(28.7)	<0.001
≥5 letters	7(5.8)	25(21.2)	0.001	4(3.6)	6(6.9)	0.287
≥10 letters	6(5.0)	15(12.7)	0.034	3(2.7)	3(3.4)	0.753
≥15 letters	2 (1.7)	4 (3.4)	0.391	0	1 (1.1)	0.255

Subjects

Subjects can be included in this study if they meet all of the following inclusion criteria and do not meet any of the exclusion criteria during the screening.

1.1 Inclusion criteria:

1) The subjects have provided the written informed consent, and are willing to receive the follow-up at the time points as specified in the trial;
2) The subjects are males or females at least 18 years of age;
3) The subjects have confirmed Type 1 or type 2 diabetes;
4) The glycated hemoglobin (HbA1c) is ≤ 10%;
5) The target eye shall meet the following requirements:
   - DME involving the fovea and leading to decreased vision is present;
   - BCVA measured ≥ 24 letters and ≤ 73 letters at the 4m/1m ETDRS eye chart (equivalent to 20/40 to 20/320 of the Snellen eye chart);
   - The OCT examination shows CRT ≥ 300 μm (using spectral domain OCT, the measured values of CRT shall be subject to confirmation by the imaging reading center);
   - There is absence of opaque opacity of the refractive medium and pupil contraction affecting fundus examination.
6) The BCVA of the subject's non-target eye ≥ 24 letters (equivalent to 20/320 of the Snellen vision).

Note: Only one target eye of a subject can be selected in the study. If both eyes of a subject meet the inclusion criteria, the investigators shall determine the target eye from the medical perspective.

1.2 Exclusion criteria

1.2.1 Patients with any of the following eye diseases:

1) Active eye infection occurs in either eye (e.g., blepharitis, keratitis, scleritis, and conjunctivitis, etc.);
2) Proliferative diabetic retinopathy (PDR) occurs in the target eye, with the exception of PDR resolving after full retina photocoagulation, and inactive, and fibrotic PDR;
3) The target eye has a history of vitreous bleeding within 2 months prior to screening;
4) The target eye has structural damage of the retina that involves the fovea (e.g., retinal pigment epithelium (RPE) atrophy, retinal fibrosis, laser scar, and dense hard exudation), or the investigators believe that there are other retinal damage in the target eye that may prevent vision improvement following resolution of macular edema.
5) The target eye, in addition to DR, has other ophthalmic conditions leading to macular edema or alterations in vision (e.g., retinal vein occlusion (RVO), CNV, retinal detachment, macular hole, traction of macular retina, and preretinal membrane, etc.);
6) The target eye contains iris neovascularization;

7) The target eye has uncontrolled glaucoma (which is defined as an intraocular pressure ≥ 25 mmHg) after the treatment with anti-glaucoma drugs, or a history of glaucoma filtering surgery.
8) The investigators believe that cataract of the target eye may affect the examination or judgment of the trial results, or surgical treatment is required within the next 6 months; or
9) The target eye has no crystal (inclusion is acceptable if there is artificial lens).

1.2.2 Patients having undergone any of the following eye treatment

10) Either eye has been intraocularly injected with corticosteroids (e.g., triamcinolone) within 3 months prior to screening, or particularly injected with corticosteroids within 1 month prior to screening;
11) The target eye has a history of vitrectomy;
12) The target eye has undergone panretinal photocoagulation within 6 months prior to screening, or there is a possibility of panretinal photocoagulation during the study;
13) The target eye has undergone ≥ 2 times of local/grid retinal photocoagulation, or local/grid retinal photocoagulation within 3 months prior to screening;
14) The target eye or the general system has been treated with anti-VEGF drugs (e.g., aflibercept, pegaptanib sodium, ranibizumab, and bevacizumab, etc.) within 6 months prior to screening, or the non-target eye has been treated with anti-VEGF drugs within the first 3 months prior to screening;

15) The target eye has received any type of intraocular surgery (e.g., cataract surgery, and YAG posterior capsulotomy, etc.) within 3 months prior to screening; or

16) The target eye has undergone eye surgery that involves the macular region (e.g., PDT, and macular transposition, etc.), except for local/grid retinal photocoagulation;

1.2.3 Patients with any of the following systemic diseases

17) The blood glucose is not well controlled within 3 months prior to screening (which is defined as the switch from the oral administration of hypoglycemic drugs to the insulin therapy, initiation of the insulin pump therapy, or an increase in the number of daily insulin injections);

18) Impaired renal function (Crea is 2-fold the upper limit of the normal value in the laboratory of this center) or abnormal hepatic function (ALT and AST are 2-fold the upper limit of the normal value in the laboratory of this center) are identified;

19) Poor control of blood pressure (which is defined as systolic blood pressure ≥ 150 mmHg or diastolic blood pressure ≥ 95 mmHg following treatment with antihypertensive medications) is noted;

20) Patients are now developing systemic infections requiring oral, intramuscular or intravenous administration;

21) Patients have stroke, transient ischemic attack, myocardial infarction or acute

congestive heart failure within 6 months prior to screening;

22) Patients have abnormal blood coagulation function (prothrombin time ≥ 3s above the upper limit of the normal value, activated partial thromboplastin time ≥ 10s above the upper limit of the normal value);

23) Patients are currently receiving drugs toxic to the lens, retina or optic nerve or may do so during the study (e.g., deferoxamine, chloroquine, hydroxychloroquine (chloroquinine), tamoxifen, phenothiazine or ethambutol, etc.);

24) Patients have confirmed systemic immune diseases (e.g., ankylosing spondylitis, and systemic lupus erythematosus, etc.) or any uncontrollable clinical conditions (e.g., AIDS, malignancies, active hepatitis, and severe mental, neurological, cardiovascular and respiratory diseases, etc.); or

25) Patients have allergic reactions or a history of allergy to sodium fluorescein, a history of allergy to therapeutic or diagnostic protein products, allergy to two or more drugs and/or non-drug factors, or allergic diseases currently;

1.2.4 Others

26) Subjects who have not undergone effective contraception;

Note: the following circumstances do not fall into the scope of exclusion.

i. Amenorrhea for 12 months under the natural conditions, or amenorrhea for 6 months with the level of serum follicle stimulating hormone > 40 mIU/ml;

ii. Bilateral ovariectomy with or without hysterectomy received 6 weeks ago;

iii. One or several acceptable contraception means as follows haven been used:
   - Sterilization (bilateral vasoligation or vasectomy in males)
   - Hormonal contraception (implanted, patch, and oral)
   - Intrauterine contraceptive devices, double blocking

iv. Use of reliable contraceptives throughout the study until 30 days after the discontinuation of the study drug (The unacceptable contraceptive methods include regular abstinence - by calendar, ovulation period, temperature measurement, post-ovulation, and coitus interruptus).

27) Pregnant (pregnancy is defined as a positive testing of the urine pregnancy in this trial) and lactating women;

28) Patients participating in any drug (not including vitamins and minerals) clinical trials within 3 months prior to screening (If the study drug has a long half-life and the duration of 5 half-life is > 3 months, then the 5 half-life is used); or

29) Patients whose exclusion investigators deem necessary.