Appendix 1

Table. Patient Eligibility Criteria

Inclusion Criteria
Male or female, at least 18 years of age
Prior diagnosis of diabetes mellitus (type 1 or type 2)
Presence of macular edema associated with DR in the SE, defined as macular thickening by OCT assessed by the investigator, involving the center of the macula (fovea) and with visual acuity decrease attributable to the macular edema
BCVA score ≥34 and ≤70 letters (approximately 20/200 to 20/40 Snellen equivalent) using the ETDRS method in the SE at the screening visit and confirmed at the randomization visit
SE mean retinal thickness by spectral domain OCT in the 1-mm central macular subfield of ≥300 µm with Spectralis (Heidelberg), ≥275 µm with Cirrus (Zeiss), or ≥250 µm with Stratus III (Zeiss) as determined by the investigator at the screening visit and confirmed at randomization visit
Both eyes: media clarity, pupillary dilation, and patient cooperation sufficient for all study procedures
Written informed consent obtained in accordance with state and country privacy requirements
Exclusion Criteria
Uncontrolled systemic disease
History of disease, metabolic dysfunction, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of the investigational drug, might affect the interpretation of study results, or render the patient at high risk from treatment complications
Untreated diabetes mellitus, or initiation of additional oral antidiabetic medication or insulin within 4 months prior to baseline, or anticipated change (increase) of antidiabetic medications during the 1-year study participation
Renal failure requiring hemodialysis or peritoneal dialysis within 6 months prior to baseline, or anticipated need for hemodialysis or peritoneal dialysis at any time during the study, or calculated and adjusted glomerular filtration rate of <50 mL/min
Use of systemic (eg, oral, intravenous, intramuscular, epidural, rectal, or extensive dermal) corticosteroids within 1 month prior to screening, or anticipated use of systemic corticosteroids during the study
Any current or history of ocular disease in the SE other than DME that, in the opinion of the investigator, may confound assessment of the macula or affect central vision (eg, exudative age-related macular degeneration, geographic atrophy, macular edema due to retinal vein occlusion, uveitis, angioid streaks, histoplasmosis, active or inactive cytomegalovirus, pathological myopia, retinal detachment, macular traction, macular fibrosis or scarring, macular hole, or significant cataract)
Elevated IOP (≥22 mmHg) or a diagnosis of glaucoma at screening or Day 1
Any active ocular inflammation or ocular infection (ie, bacterial, viral, parasitic, or fungal) in either eye at the screening visit
Aphakia in the SE or break in the posterior capsule in the SE, unless it is a small break resulting from a YAG laser posterior capsulotomy in association with prior posterior intraocular lens implantation
Anticipated need for ocular surgery in the SE during the 1-year study participation

Exclusion Criteria (continued)
Active proliferative DR and/or rubeosis
BCVA score <34 letters in the fellow eye
Laser photocoagulation to the retina of the SE within 3 months prior to screening
Use of anti-VEGF treatment in the SE within 3 months prior to screening, or use of systemic anti-VEGF within 6 months prior to screening
Use of intravitreal triamcinolone within 6 months prior to screening
Use of topical intraocular, intravitreal (except triamcinolone, see above), or periocular corticosteroids within 3 months prior to screening in the SE, or ocular conditions in the SE that require chronic concomitant therapy with topical, local, ocular or systemically administered corticosteroids
History of use of DEX within 9 months prior to screening
History of cataract surgery within the 3 months prior to screening
History of vitrectomy
History of incisional glaucoma surgery
Known allergy, hypersensitivity, or contraindication to the study medications, its components, fluorescein, or povidone iodine
Female patients who are pregnant, nursing, or planning a pregnancy, or who are of childbearing potential and not using a reliable means of contraception NOTE: Female patients of childbearing potential must have a negative pregnancy test at screening and baseline
Current enrollment in any observational or investigational drug or device study, or participation in such a study within the 30 days prior to Day 1
A condition or a situation that, in the investigator's opinion, may put the patient at significant risk, may confound the study results, or may interfere significantly with the patient's participation in the study

BCVA, best-corrected visual acuity; DEX, dexamethasone intravitreal implant; DME, diabetic macular edema; DR, diabetic retinopathy; ETDRS, Early Treatment Diabetic Retinopathy Study; IOP, intraocular pressure; OCT, optical coherence tomography; SE, study eye; VEGF, vascular endothelial growth factor; YAG, yttrium aluminum garnet

Appendix 2

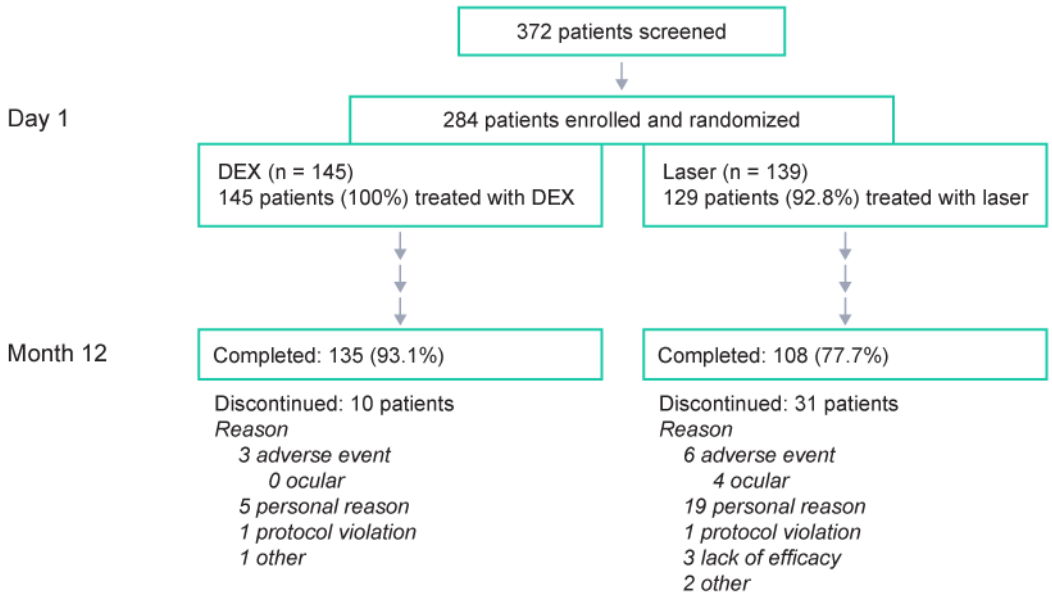

Figure. Patient flow through the study.

DEX, dexamethasone intravitreal implant 0.7 mg.

Appendix 3

Table. Baseline Patient and Study Eye Characteristics (Chinese Patient Subgroup of mITT Population)

Parameter	DEX (N=129)	Laser (N=113)
Age, mean (SD), years	59.1 (7.9)	59.3 (7.7)
Male gender, n (%)	72 (55.8)	53 (46.9)
Chinese ethnicity, n (%)	129 (100)	113 (100)
Lens status, n (%)		
Phakic	97 (75.2)	94 (83.2)
Pseudophakic	32 (24.8)	19 (16.8)
Duration of DME, median (25%, 75% percentile), months	6.7 (0.5, 21.5)	6.0 (0.5, 21.8)
BCVA, mean (SD), letters	55.4 (11.4)	54.4 (10.1)
34–49 letters, n (%)	39 (30.2)	31 (27.4)
50–70 letters, n (%)	90 (69.8)	82 (72.6)
CRT, mean (SD), µm	506.3 (156.8)	499.1 (147.2)
Total macular leakage area, mean (SD), mm^2	29.7 (10.6)	30.4 (9.5)
IOP, mean (SD), mmHg	15.4 (3.3)	15.3 (3.0)

BCVA, best-corrected visual acuity; CRT, central retinal thickness; DEX, dexamethasone intravitreal implant 0.7 mg; DME, diabetic macular edema; IOP, intraocular pressure; mITT, modified intent-to-treat; SD, standard deviation.

Appendix 4

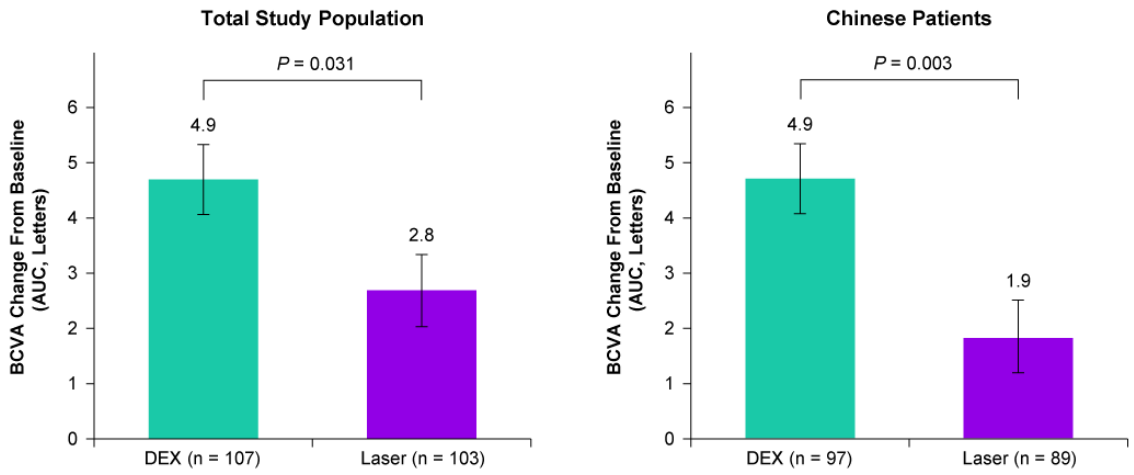

Figure. Analysis of the primary endpoint (mean average change in BCVA from baseline over 12 months) using the per-protocol population. The total per-protocol population included 107 patients in the DEX group (38 patients from the mITT population were excluded, 28 because they did not receive all 3 protocol-specified DEX injections and 10 because they had no evaluable BCVA assessment at Month 12) and 103 patients in the laser group (24 patients from the mITT population were excluded, all because they had no evaluable BCVA assessment at Month 12). Values shown are least squares means ± standard errors from analysis of covariance models using observed values with treatment group as the main effect and baseline BCVA as the covariate.

AUC, area under the curve; BCVA, best-corrected visual acuity; DEX, dexamethasone intravitreal implant 0.7 mg; mITT, modified intent-to-treat.

Appendix 5

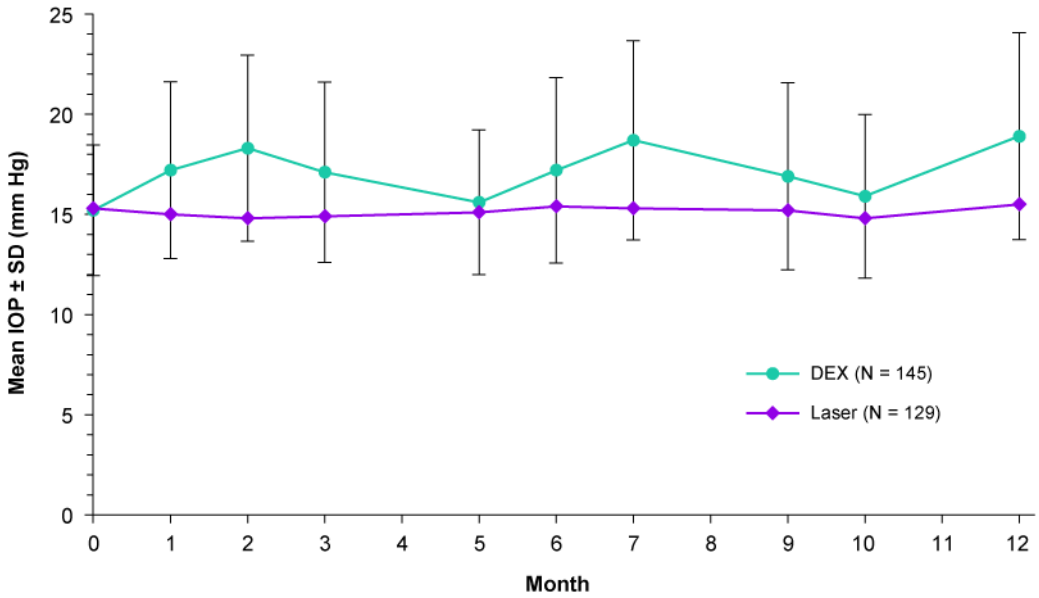

Figure. Mean IOP in the study eye at each visit (safety population).

DEX, dexamethasone intravitreal implant 0.7 mg; IOP, intraocular pressure; SD, standard deviation.