

CATT PATIENT ELIGIBILITY CRITERIA

Inclusion Criteria

All patients must meet the following criteria for entry into the CATT: Lucentis-Avastin Trial:

- Signed informed consent form
- Age \geq 50 years of either gender
- Women must be postmenopausal for at least 12 months prior to trial entry, or surgically sterile. If of child bearing potential, a serum pregnancy test with a negative result must be obtained within 14 days prior to the first treatment. Women of child bearing potential must be practicing effective contraception implemented during the trial and for at least 60 days following the last dose of study medication.
- No condition that precludes follow-up for 2 years.
- No contraindication to intravitreal injection of Lucentis[®] or Avastin[®], as specified in the exclusion criteria below.

Eligibility criteria for study eyes

Study eyes must meet the following criteria for entry into the CATT: Lucentis-Avastin Trial:

- Newly diagnosed, angiographically documented, previously untreated, active CNV lesion (i.e., leakage on fluorescein angiography AND subretinal, intraretinal, or sub-RPE fluid on OCT) secondary to age-related macular degeneration.
- Best corrected visual acuity in the study eye, using e-ETDRS testing, between 20/25 and 20/320 (Snellen equivalent), inclusive.

Only one eye will be enrolled in the Study. If both eyes are eligible, the patient and study ophthalmologist will select the eye for entry.

- The CNV or sequela of the CNV (i.e., pigment epithelium detachment, subretinal or sub-RPE hemorrhage, blocked fluorescence, macular edema, or subretinal sub-RPE or intraretinal fluid) must involve the center of the fovea.
- The total area of fibrosis must comprise less than 50% of the total lesion.
- \geq 1 drusen ($>$ 63 microns) in either eye OR late AMD in fellow eye
- No previous treatment for CNV in the study eye
- Clear ocular media and adequate pupillary dilation to permit good quality fundus imaging.
- Disc and macula color stereoscopic photographs and fluorescein angiogram within 7 days of randomization.
- OCT of the macula within 7 days of randomization.

EXCLUSION CRITERIA

Subjects who meet any of the following criteria will be excluded from study entry:

Prior/Concomitant Treatment

- Previous treatment with verteporfin PDT, Macugen[®], Lucentis[®], intravitreal Avastin[®], thermal laser, external beam radiation or other AMD therapy in the study eye. Prophylactic treatment such as CAPT/CNVPT treatment does not exclude the patient.
- Previous treatment with intravenous Avastin[®]
- Concurrent treatment with an investigational drug or device in the non-study eye for any ocular condition
- History of submacular surgery or other surgical intervention for AMD in the study eye
- Previous participation in any studies of investigational drugs likely to have ocular effects within 30 days preceding the initial study treatment
- Concurrent use of systemic anti-VEGF agents.

Exclusionary Lesion Characteristics

- Fibrosis or geographic atrophy involving the center of the fovea in the study eye
- CNV in either eye due to other causes, such as ocular histoplasmosis, trauma, or pathologic myopia
- Retinal pigment epithelial tear involving the macula in the study eye

Exclusionary Concurrent Ocular Conditions

- Any concurrent intraocular condition in the study eye (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator, could either require medical or surgical intervention during the 2 year follow-up period to prevent or treat visual loss that might result from that condition, or, if allowed to progress untreated, could likely contribute to loss of at least 2 Snellen equivalent lines of best corrected visual acuity over the 2 year follow-up period.
- Active or recent (within 4 weeks) intraocular inflammation (grade trace or above) in the study eye
- Current vitreous hemorrhage in the study eye
- History of rhegmatogenous retinal detachment or macular hole in the study eye
- History of vitrectomy in the study eye
- Active infectious conjunctivitis, keratitis, scleritis, or endophthalmitis in either eye
- Spherical equivalent of the refractive error in the study eye demonstrating more than 8 diopters of myopia

- For subjects who have undergone prior refractive or cataract surgery in the study eye, the preoperative refractive error in the study eye cannot exceed 8 diopters of myopia.
- Intraocular surgery (including cataract surgery) in the study eye within 2 months preceding the first study treatment.
- Uncontrolled glaucoma in the study eye (defined as intraocular pressure ≥ 25 mmHg despite treatment with antiglaucoma medication)
- Patients who are unable to be photographed to document CNV due to known allergy to fluorescein dye, lack of venous access or cataract obscuring the CNV.
- Patients with other progressive retinal disease likely to affect visual acuity within the next 2 years. Patients with pattern dystrophy with CNV and drusen determined to be definitely AMD are eligible.
- Patients with other ocular diseases that can compromise the visual acuity of the study eye such as amblyopia and anterior ischemic optic neuropathy

Concurrent Systemic Conditions

- Premenopausal women not using adequate contraception (see Section 3.3)
- Pregnancy or lactation
- History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use an investigational drug or that might affect interpretation of the results of the study or render the subject at high risk for treatment complications
- Current treatment for active systemic infection
- Evidence of significant uncontrolled concomitant diseases such as cardiovascular disease, nervous system, pulmonary, renal, hepatic, endocrine, or gastrointestinal disorders
- History of recurrent significant infections or bacterial infections
- Inability to comply with study or follow-up procedures

DEFINITION OF TERMS PERTAINING TO ELIGIBILITY CRITERIA

Informed Consent: Written informed consent must be obtained from each patient prior to performing any study-specific procedures. The patient should be asked to sign the consent form only after the patient has been introduced to the study and had questions answered.

Age: Few patients below the age of 50 are anticipated to meet the criteria below. Patients below the age of 50 may have forms of macular degeneration other than age-related macular degeneration.

Images: Stereoscopic color photographs of the disc and macula of both eyes are required. In addition, a fluorescein angiogram with the early phase on the study eye is mandatory. An OCT of each eye is also required. All images must be taken within 7 days prior to randomization.

Effective Contraception: Acceptable methods of birth control are surgical sterilization, use of oral contraceptives, barrier contraception with either a condom or diaphragm in conjunction with spermicidal gel, an intrauterine device (IUD), or contraceptive hormone implant or patch.

Condition Precluding Follow-Up: Patients must have a high probability of completing 2 years of follow-up. The mere presence of serious health conditions in this population does not disqualify the patient from enrollment. However, if the severity of the condition is such that progression to a state where travel to the clinical center for regular follow-up visits would place undue burden on the patient or is such that death is almost certain to occur during the follow-up period, the patient should not be enrolled in the study. Patients with known plans to move to an area of the country without a nearby CATT clinical center should not be enrolled.

Contraindications to Lucentis[®] or Avastin[®] injections: No previous inflammatory reactions following intravitreal Lucentis[®] or Avastin[®] treatment in the non-study eye.

Active CNV includes **both** of the following: leakage on fluorescein angiography AND subretinal or intraretinal fluid on OCT.

CNV lesion: A contiguous area of abnormal tissue in the macula that encompasses angiographically documented CNV with possible additional components of subretinal hemorrhage, blocked fluorescence not from hemorrhage, serous detachment of the retinal pigment epithelium, and fibrosis.

AMD: Clinical and/or angiographic signs consistent with AMD (e.g., drusen, retinal pigment epithelial changes, choroidal neovascularization) with no other likely etiologic explanations for the degenerative changes.

Sequela of CNV: Sequela of the lesion includes pigment epithelial detachment, subretinal, sub-RPE hemorrhage, blocked fluorescence, macular edema, or subretinal, sub-RPE or intraretinal fluid contiguous with the CNV lesion.

Visual Acuity Score: The best corrected E-ETDRS visual acuity score for a study eye must be ≥ 23 letters (20/320 or better) and ≤ 82 letters (20/25 or worse).

Cataract Surgery: Eyes that have had lens extraction or lens implantation within the last 2 months are ineligible. Eyes that have had a capsulotomy within the past 2 months are ineligible.

Lens Opacities: Lens opacities may be present but must be such that at enrollment and for the next 2 years the view of the posterior pole for ophthalmoscopy and photography is unobstructed. Patients likely to undergo cataract extraction in the study eye within the next 2 years should not be enrolled in the Lucentis-Avastin Trial Study.

Myopia: Eyes with fundus changes consistent with high myopia, such as lacquer cracks, are ineligible. Eyes with a spherical equivalent more negative than -8.00 diopters are ineligible even if there are no myopic changes apparent in the fundus.

Progressive Ocular Disease: Any condition that is likely to decrease visual acuity over the course of 2 years excludes the patient from the study.