Author Contributions: Dr Greenberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Intravitreal Bevacizumab in Advanced-Stage Neovascular Age-Related Macular Degeneration With Visual Acuity Lower Than 20/200**

Although intravitreal anti–vascular endothelial growth factor has greatly improved the management of subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration, little is known regarding the effects in more advanced stages associated with low visual acuity. We designed a randomized clinical trial to address this subject.

**Methods.** The randomized clinical trial compared the effects of the intravitreal bevacizumab injection (1.25 mg) vs observation for age-related macular degeneration–related naive subfoveal CNV with best-corrected visual acuity (BCVA) lower than 20/200, with follow-up for 6 months. After institutional review board approval, the study was registered at [http://www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT01327222). Inclusion criteria were the following: naive subfoveal CNV, BCVA lower than 20/200 on the Early Treatment Diabetic Retinopathy Study chart, and activity documented by fluorescein leakage and fluid on optical coherence tomography. We excluded patients with retinal or subretinal hemorrhage or subretinal fibrosis greater than 50% of the lesion, recent intraocular surgery, other ocular disease, or severe cardiovascular disorders. Sequentially numbered envelopes were used to randomize patients. Each patient contributed 1 study eye and underwent a complete ophthalmologic examination, including the National Eye Institute 25-item Visual Function Questionnaire and best-corrected visual acuity at baseline and at the final visit.

Fluorescein angiography and optical coherence tomography results were independently read and intravitreal bevacizumab injection was performed by 2 masked investigators (A.P. and D.S.K.). After the loading phase with 3 monthly consecutive injections, re-treatments were administered on a pro re nata basis if monthly examinations by a masked examiner revealed subretinal or intraretinal fluid, fluorescein leakage, or new hemorrhages.

Primary outcome measures were changes in the mean BCVA and proportion of eyes improving by more than 1 and more than 3 lines at the 6-month examination. Secondary outcome measures included changes in the mean central macular thickness and National Eye Institute 25-item Visual Function Questionnaire score. We used t test for statistical analyses. P < .05 was considered statistically significant.

The study was designed to detect a 10-letter difference (SD 1 line) on the Early Treatment Diabetic Retinopathy Study chart. About 6 eyes in each arm are required to detect this difference (90% power, 2-sided 5% significance level).

**Results.** Twenty-one of 28 patients were recruited, with 7 excluded owing to cataract. The mean (SD) age was 71.5 (4.2) years, and 13 of the recruited patients were female. The mean (SD) symptom duration was 23.3 (4.0) months. Among the 21 patients, 11 and 10 were randomized to the treated and control arms, respectively.

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domized to intravitreal bevacizumab injection and observation, respectively. The BCVA changed from 1.32 to 1.18 in the patients receiving intravitreal bevacizumab injection ($P = .28$) and from 1.34 to 1.30 in control patients ($P = .23$).

The logMAR values in the groups randomized to intravitreal bevacizumab injection and observation are shown in Figure 1. No eye improved by 1 or more lines after 6 months.

The mean central macular thickness decreased from 366 to 350 µm in the group that received intravitreal bevacizumab injection ($P = .34$). In the control group, the mean central macular thickness decreased from 363 to 355 µm ($P = .31$) (Figure 2).

The National Eye Institute 25-item Visual Function Questionnaire composite scores at baseline and 6 months were 78 and 78, respectively, in the group that received intravitreal bevacizumab injection and 77 and 78, respectively, in the control group.

Comment. Management of advanced age-related macular degeneration–related CNV is controversial, and subgroup analyses for eyes with BCVA lower than 20/200 have not been presented for the most important randomized clinical trials.1–4 The identification of signs of activity, including blood, fluorescein leakage, and fluid on optical coherence tomography, suggests that even old CNVs could still grow, causing further visual impairment.

Our randomized clinical trial has provided disappointing results. The commonly used treatment algorithm, a scheduled loading phase followed by pro re nata–based re-treatments, does not seem to offer benefit. This outcome may be due to an inadequate treatment regimen, the use of bevacizumab rather than ranibizumab, or, more likely, an advanced stage with irreversible photoreceptor–retinal pigment epithelial cell damage. It also appears improbable that a more prolonged treatment could offer advantages in longer-term follow-up.

Our investigation has many limitations, including a small number of patients, lack of sham treatment, and short follow-up. Further studies are warranted to determine whether a different therapeutic approach is useful for advanced CNV.

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Mortality From Cerebral Vasculitis Associated With Rapid Steroid Taper During Treatment of Acute Posterior Multifocal Placoid Pigment Epitheliopathy

The clinical course associated with acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is usually benign, with complete resolution of both ocular and systemic symptoms.1 Rarely, APMPPE has been associated with cerebral vasculitis.2 We report a case of APMPPE complicated by cerebral vasculitis and ultimately death.

Report of a Case. A 53-year-old woman had an intense, constant headache for 3 weeks without viral prodrome. She subsequently developed sudden bilateral dimming of central vision and photopsias. Findings on initial neurological evaluation and magnetic resonance imaging of the brain with and without contrast were normal. Her medical history was significant only for Crohn disease. Visual acuities were 20/400 OD and counting fingers at 3 ft OS. Neither eye had anterior chamber or vitreous inflammation. Both maculae had creamy, yellow, placoid lesions that blocked fluorescence early and stained late by fluorescein angiography (Figure 1 and Figure 2). Spectral-domain optical coherence tomography showed irregularly thickened and disrupted retinal pigment epithelium with overlying photoreceptor disorganization and mild subretinal fluid bilaterally. The diagnosis of APMPPE was made, and the patient began treatment with 80 mg of oral prednisone daily.

One week later, visual acuities improved to 20/40 OD and counting fingers at 4 ft OS, and the intensity of the headaches decreased. Oral prednisone was tapered from 80 mg/d to 20 mg/d over 5 days. On the sixth day, when the patient received 20 mg of prednisone, she developed a worsening headache and decreased responsiveness. She was admitted to a tertiary care academic hospital, where