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,1-4 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 (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 treatment and control arms, respectively. The randomization was stratified by sex and baseline BCVA (20/200 vs worse).

Figure 1. Mean best-corrected visual acuity (BCVA) values during the 6-month follow-up.

Figure 2. Mean central macular thickness (CMT) values during the 6-month follow-up.
domized to intravitreal bevacizumab injection and ob-
servation, 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 pa-
tients (P = .23).

The logMAR values in the groups randomized to in-
travitreal 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 be-
vacizumab 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, re-
spectively, in the control group.

Comment. Management of advanced age-related macu-
lar degeneration–related CNV is controversial, and sub-
group analyses for eyes with BCVA lower than 20/200
have not been presented for the most important random-
ized clinical trials.1-4 The identification of signs of activ-
ity, including blood, fluorescein leakage, and fluid on op-
tical 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 out-
come 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 im-
probable that a more prolonged treatment could offer ad-
vantages 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 deter-
mine 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 poste-
rior multifocal placoid pigment epitheliopathy
(APMPPE) is usually benign, with complete reso-
lution 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 vas-
culitis 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 neu-
rological 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 in-
flammation. 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 ep-
ithelium 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