

chronic debilitating diseases, such as glaucoma, diabetes, hypertension and ischaemic heart disease. To benefit from reimbursement, the patient must file an application with a certificate from a physician, who must document the presence of certain predefined criteria for each diagnosis. In cases of glaucoma, the criteria are intraocular pressure (IOP) > 30 mmHg or two of the following: IOP > 21 mmHg in repeated measurements; glaucomatous cupping of the optic disc, and glaucomatous visual field defect. If the certificate verifies the presence of these common criteria, reimbursement is granted and the patient is listed on the Institution's register.

We reviewed the records of 519 patients to whom free medication for chronic open-angle glaucoma had been granted between June 2004 and December 2005. The type of glaucoma was classified as either POAG or EG; 20 patients with primary angle-closure or secondary glaucoma were excluded. The diagnosis of exfoliation was based on recorded observations of typical greyish flakes at the papillary margin, the lens surface, or both. Typically, charts on POAG contained the specific statement: 'no exfoliation deposits'. Of the remaining 499 patients, those who reportedly had fundus changes compatible with non-exudative or exudative AMD and a best corrected visual acuity  $\leq 0.3$  in at least one eye were considered to have AMD for the purpose of this study.

The null hypothesis was that the frequency of AMD does not differ between POAG and EG. The alternative hypothesis was that EG is associated with a higher frequency of AMD. Type of glaucoma as a predic-

tor of AMD was analysed by binary logistic regression. Analysis was performed using Stata statistical software (Version 7; Stata Co., College Station, TX, USA).

Of 499 patients with open-angle glaucoma, 344 (69%) had POAG and 155 (31%) had EG. The groups were comparable in terms of gender (66% versus 70% females, POAG versus EG;  $P = 0.47$ , Fisher's exact test), but patients with POAG were younger than patients with EG (median age: 69 years versus 74 years, respectively;  $P = 0.0001$ , Mann-Whitney  $U$ -test); 98.8% of the patients were aged  $\geq 40$  years.

The frequency of AMD was 4.0% (95% confidence interval [CI] 2.5–6.1). Frequency rates in the POAG and EG groups were comparable, at 4.1% versus 3.9%, respectively (unadjusted odds ratio [OR] 1.04 for EG,  $P = 0.92$ , likelihood ratio test) (Fig. 1A). Presence of AMD was associated with increasing age (OR 3.33 for each decade,  $P < 0.0001$ ) and, after adjusting for age, with male gender (adjusted OR 3.53,  $P = 0.011$ ), but not with diabetes ( $P = 0.27$ ), hypertension ( $P = 0.50$ ) or ischaemic heart disease ( $P = 0.75$ ). Adjusting for age and gender decreased the OR (adjusted OR 0.70 [95% CI 0.25–1.93] for EG,  $P = 0.49$ ) (Fig. 1B), which remained not significant. The null hypothesis of no difference was accepted.

The overall prevalence of AMD among Finnish open-angle glaucoma patients receiving free medication was almost three times as high as in the US general population (Friedman et al. 2004). The present findings agree with previous reports in which exfoliation was assessed as a predictor of

AMD, and which found that ES and EG were not associated with a higher frequency of AMD, when controlling for age (Hirvelä et al. 1994; Allingham et al. 2001).

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## Intravitreal and intracameral bevacizumab to treat neovascular complications of retinopathy of prematurity

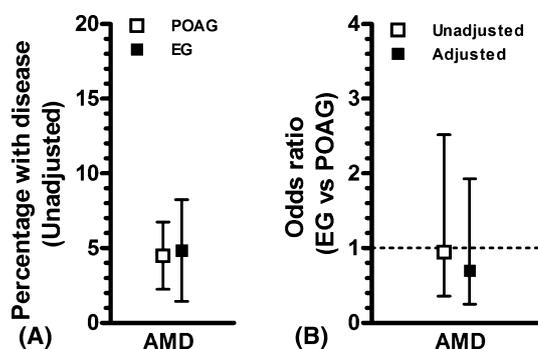
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doi: 10.1111/j.1600-0420.2007.01106.x

Editor,

A 26-year-old White woman was referred for management of



**Fig. 1.** (A) Percentage of subjects with age-related macular degeneration (AMD), and (B) unadjusted and adjusted odds ratios for presence of AMD among 499 patients who received free medication for primary open-angle (POAG) and exfoliation (EG) glaucoma. The crossbars indicate 95% confidence intervals.

neovascular glaucoma complicating retinopathy-of-prematurity-related retinal detachment. She had previously undergone cryotherapy and scleral buckling for mixed tractional and exudative retinal detachment in the right eye (RE) and had lost her left eye because of phtisis bulbi.

Visual acuity (VA) was hand movements (HM); intraocular pressure (IOP) was 31 mmHg. There was iris neovascularization in all quadrants, the drainage angle was open with

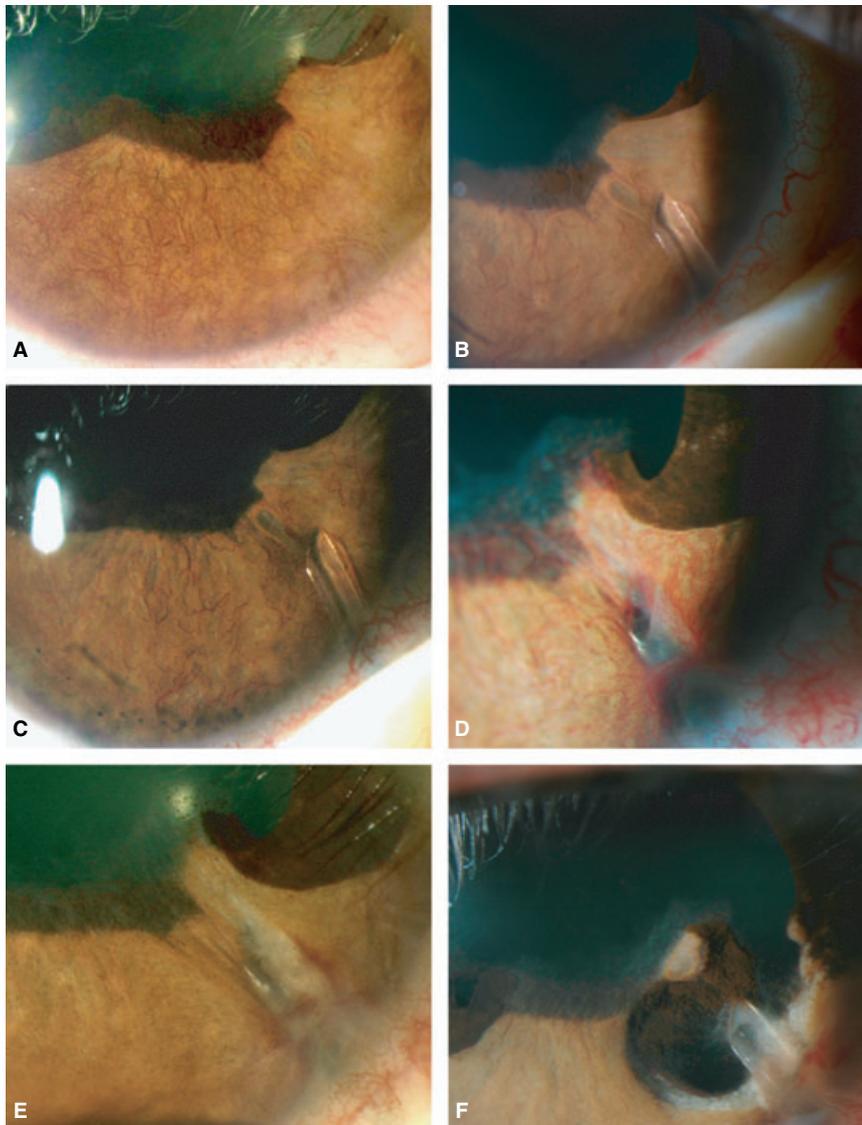
isolated areas of peripheral anterior synechiae (PAS) and there was a long-standing partial retinal detachment. Treatment was started with topical hypotensive therapy but within 2 months the pain became worse with corneal oedema, florid iris neovascularization, ectropion uveae (Fig. 1A), angle neovascularization and 330° PAS. VA remained HM but IOP was 68 mmHg and unresponsive to oral acetazolamide. Photocoagulation was not feasible because of the retinal

detachment. We treated the RE with an intravitreal injection of bevacizumab (1.25 mg in 0.05 ml) (Avastin®; Genentech Inc., San Francisco, California, USA). Two weeks after the injection, iris neovascularization had substantially regressed and we implanted a vicryl-ligated Baerveldt 350 mm<sup>2</sup> aqueous shunt (AMO Groningen B.V. Groingen, the Netherlands) (Fig. 1B). One month later, IOP was 9 mmHg without ocular hypotensive medication, although iris new vessels had become more prominent in appearance (Fig. 1C).

Three months after the operation, the eye became painful again. IOP was 48 mmHg and the intracameral lumen of the Baerveldt tube was obstructed by proliferating neovascular tissue (Fig. 1D). We applied Nd-YAG-laser to tube opening, re-establishing aqueous outflow: IOP fell to 18 mmHg. An hour later, we gave an intracameral injection of bevacizumab (0.625 mg in 0.025 ml). Three days later, iris neovascularization had regressed (Fig. 1E) and at surgery we created a large surgical iridectomy adjacent to the tube lumen to remove the scaffold for recurrent fibrovascular proliferation (Fig. 1F). Five weeks later, VA was still HM and the eye was comfortable with an IOP of 18 mmHg.

Bevacizumab is a recombinant, full length, anti-vascular endothelial growth factor (VEGF) monoclonal antibody able to bind all isoforms of VEGF-A. Previous case reports (Davidorf et al. 2006; Iliev et al. 2006; Silva Paula et al. 2006) have shown that bevacizumab can induce regression of anterior-segment neovascularization. We used anti-VEGF as a preoperative intravitreal injection before surgical treatment for neovascular glaucoma to reduce the risk of perioperative bleeding and gave a second injection 3 months later intracamerally to induce regression of a recurrent neovascular membrane occluding a glaucoma drainage device.

A recent report (Beer et al. 2007) has shown that in humans, a single dose of intravitreal bevacizumab is likely to provide complete intravitreal VEGF blockade for a minimum of 4 weeks. Our patient developed recurrent neovascularization 6 weeks after injection. When this occluded the drainage tube, we chose to give



**Fig. 1.** (A) Florid iris neovascularization and ectropion uveae at presentation. (B) Partial regression of iris new vessels following intravitreal bevacizumab injection and Baerveldt tube implant (10 days postoperatively). (C) More prominent iris new vessels at 6 weeks postoperatively. (D) Obstruction of the Baerveldt tube intracameral lumen by proliferating neovascular tissue (3 months postoperatively). (E) Partial resolution of the obstruction and regression of the iris new vessels 3 days after application of Nd-YAG laser and intracameral injection of bevacizumab. (F) Appearance of the anterior segment at the last follow-up, 5 weeks after intracamerally injected bevacizumab: note the large surgical iridectomy to prevent recurrent tube occlusion and the substantial regression of iris new vessels.

bevacizumab via intracameral rather than intravitreal injection because the need was to treat an anterior chamber neovascular membrane; furthermore, intracameral injection is simpler and more comfortable for the patient.

There is one previous report to our knowledge (Grisanti et al. 2006) of intracameral use of bevacizumab for treatment of neovascular glaucoma. Three patients were given 0.04 ml intracameral bevacizumab with a dramatic reduction of leakage demonstrated by iris fluorescein angiography, which was still evident 30 days after injection. In our case, a significantly lower intracameral dose of bevacizumab resulted in rapid iris neovascularization regression.

Intraocular bevacizumab, by either intravitreal or intracameral injection, can prove useful as an adjunct to glaucoma drainage surgery.

## Acknowledgements

The authors would like to thank the technicians Kanom Bibi, the photographer Matthew Richardson and the research officer Laura Gangadeen. This article has been supported by the National Health Service, Research and Development, UK.

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## Intravitreal pegaptanib sodium (Macugen®) for radiation retinopathy following episcleral plaque radiotherapy

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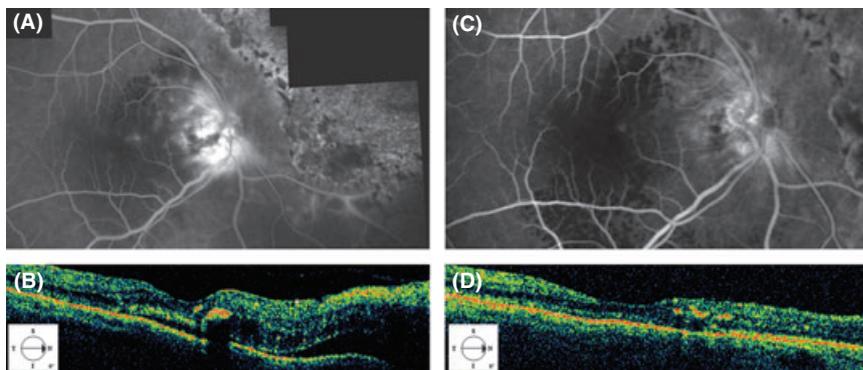
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doi: 10.1111/j.1600-0420.2007.01101.x

### Editor,

A 63-year-old woman was referred to our department with a best-corrected visual acuity (BCVA) of 20/25 in her right eye and 20/20 in her left eye. She presented with a posterior uveal mass of her right eye; this was diagnosed as choroidal melanoma, involving the superonasal quadrant. The tumour sizes were 12.54 mm (base) and 4 mm (height).

The patient underwent episcleral plaque radiotherapy with a notched Ruthenium 106 plaque. Fourteen months after plaque treatment, the patient developed early radiation retinopathy involving the fovea – consisting of capillary changes, retinal haemorrhages and retinal exudation (non-proliferative radiation retinopathy) – and was therefore offered sector laser photocoagulation to prevent progression of radiation retinopathy (Finger 1997). Three months later, the patient developed disc neovascularization (proliferative radiation retinopathy) and massive retinal exudation involving the fovea, as evaluated by fundus biomicroscopy, fluorescein angiography (FA) (Fig. 1A) and optical coherence tomography (OCT-3; Humphrey-Zeiss, San Leandro, California, USA) (Fig. 1B); BCVA dropped to 20/200. After discussing adjunctive treatment options and being presented with the option of intravitreal pegaptanib sodium [Macugen®; (OSI) Eyetech and Pfizer Inc., Melville, New York, USA], the patient requested that the treatment be given. Intravitreal pegaptanib sodium 0.3 mg was administered without complication. At the 1-month follow-up, BCVA improved to 20/40; fundus biomicroscopy, FA and OCT revealed almost total resolution of the retinal and macular exudation and partial regression of disc neovascularization. At the time of writing, 6 months after the injection, the patient's BCVA remained 20/40, with no recurrence of retinal and macular



**Fig. 1.** Fluorescein angiography frame (A) and OCT-3 scan (B) of the right eye showing disc neovascularization and massive retinal exudation involving the fovea 3 months after sector scatter laser photocoagulation. Fluorescein angiography frame (C) and OCT-3 scan (D) of the right eye showing partial regression of disc neovascularization and resolution of the retinal and macular exudation 6 months after intravitreal injection of pegaptanib sodium.