Survey shows encouraging results for Avastin in the treatment of AMD

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in Frankfurt

INTRAVITREAL bevacizumab (Avastin, Genentech) shows such promising results for improving vision in patients with macular edema from AMD, DME, RVO, that retinal specialists are calling the preliminary experience remarkable.

“We are experiencing a particularly unique phenomenon which may never again be duplicated in our careers. The effect of Avastin on some patients is remarkable,” said retinal specialist, George W Williams MD, speaking at the Frankfurt Retina Meeting.

Although intravitreal Avastin is an off-label application, a recent retinal physician survey revealed that 19% of retinal specialists who treat wet AMD are currently using off-label Avastin with selected patients.

Furthermore, an ASRS survey from March 20, 2006 that was sent to 1,479 members, showed that out of 292 respondents from 12 countries, 92% had used Avastin for indications including AMD, DME, and RVO.

Of these, 16% used Avastin as salvage therapy, after approved therapies failed, while 12% used it for primary therapy, and 72% for either primary or salvage therapy. For treating AMD, 92% of the respondents felt that Avastin was ‘somewhat better’ or ‘much better’ than approved therapies, while 96% felt that Avastin was at least as safe as approved therapies.

Dr W Williams said that retinal specialists can either continue using approved therapies while telling their patients to be patient for the arrival of a more promising treatment, or they can try to provide something better today. On April 21 of this year, the AAO sent a letter supporting coverage of Avastin in select patients with AMD, he reported.

Avastin is used as salvage therapy in patients with CNV-AMD who have increasing lesion size, dramatic visual decline, treatment with an established agent (PDT, IV triamcinolone, Macugen) with persistent leakage, CME or SRF. Patients need to sign a detailed informed consent.

Dearth of data a concern

Specialists are concerned about the lack of long-term data about dosing, efficacy, and safety of intravitreal Avastin.

Dr W Williams stated that preliminary clinical experience suggests Avastin is effective and furthermore does not correlate with Genentech scientists’ theories that Avastin will not be effective. Sometimes theories are wrong, he said.

He predicted that ranibizumab (Lucentis, Genentech) could supplant Avastin in the management of wet AMD due to its proven efficacy and medicolegal considerations. But Avastin will continue to be used for wet AMD due to accrued experience and the price advantage, he said.

To meet patient needs, retinal specialists are looking for a treatment that improves vision, requires few retreatments, and is safe and cost-effective. Current therapies (PDT + triamcinolone and Macugen) are inconvenient, expensive, and improve vision in less than 10% of cases, while most patients actually lose vision, Dr W Williams said.

Clinical and price considerations have stratified the market and sparked much interest for the initiation of a head-to-head clinical trial of Lucentis vs. Avastin. The US National Eye Institute is considering such a trial.

While some believe Lucentis to be the upcoming ‘monotherapy gold-standard’, it may not be available until later this year. Although it is safe and effective, with a high number of ‘gainers and maintainers’, the cost of therapy is higher than Avastin therapy, Dr W Williams said.

Richard Spaide MD shared Dr W Williams’ enthusiasm for Avastin, relaying the encouraging short-term results of his own trials.

“Although these are the short term results of only one centre in NY, they seem to be similar to the Lucentis results and are very encouraging,” he observed.

In one investigation, Dr Spaide injected a 1.25mg dose ($16/dose) of intravitreal Avastin in 266 patients with choroidal neovascularisation and exudative AMD. He followed 240 patients for one month, 249 for one or more months, and had telephone contact with almost all the other 17 patients. The mean follow-up time was 98 days.

The great majority of patients, 70%, had previous treatments that failed. The rest were primary cases. Dr Spaide set no specific exclusion criteria for patient acceptance. The baseline visual acuity was 20/184 and the mean baseline central macular thickness was 340µm. One month after Avastin injection, Dr Spaide noted a statistically significant increase in visual acuity. He defined visual improvement by halving of the visual angle. This was seen in 74 patients (30.3%) by one month. The mean central macular thickness decreased to 247µm by the month one follow-up. Visual acuity was 20/122 and 20/109 (representing an almost 40% improvement in visual acuity) at two and three months, respectively. The mean central macular thickness was 213µm at month three.

Dr Spaide said that previous Macugen and PDT treatments had little influence on the results and that the improvements in vision and OCT were statistically significant among patients who had either previous Macugen or photodynamic therapy at all time points. Furthermore, the anterior chamber showed no sign of inflammatory cells and the cells found in the vitreous of two patients, one of which had a previous history of recurrent uveitis.
In 631 injections, Dr Spaide noted two cases of uveitis, and no other ocular complications. Specifically there were no cases of intraocular haemorrhage, retinal tear or detachment, and no cases of endophthalmitis. Systemically, transient ischemic attacks were noted in two patients, both of whom had no permanent deficits. All in all, the death rate of patients in Dr Spaide’s investigation was similar to rates seen in this age group.

In a parallel investigation on the effects of intravitreal Avastin in 16 eyes with CRVO, Dr Spaide reported impressive short-term anatomical and visual results and are very encouraging.

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Murat Karacorlu MD directly compared the one and three month results of combined PDT + Avastin (1.25mg injection) to PDT + triamcinolone acetone (4mg) in patients with minimally classic/occult only CNVs secondary to AMD, who received no prior therapy. Direct comparison revealed a better overall visual improvement rate in patients who received Avastin, but in particular of improvements of ≥3 lines (almost 40%) over triamcinolone (0%), and less retreatments at three months,” Dr Karacorlu observed.

Each treatment group included 26 patients and had a baseline visual acuity range of 20/40 to 20/200. Patients in Group A received PDT/Avastin while those in Group B received PDT/triamcinolone. The surgeon gave the intravitreal injection the same day following standard PDT.

At one month, visual acuity improved from 20/80 to 20/50 in Group A and to 20/63 in Group B. At three months, vision remained unchanged in both groups.

At three months, Group A showed visual acuity improvements of at least three lines in 10 patients (38.5%), while no member of the triamcinolone group showed visual improvements of three or more lines improvement.

Nine patients in Group A (34.6%) and eight in Group B (30.8%) had visual improvements of 1-2 lines. Dr Karacorlu observed no change in visual acuity in six Group A and eight Group B patients. He noted decreased vision in one Group A patient and in three Group B patients.

Retinal thickness measurements by OCT revealed a reduction in Group A from 277µm (baseline) to 249µm (one month) to 224µm (three months). Group B went from 281µm (baseline) to 255µm (two months) and 234µm (three months).

Retreatments had to be performed in three Group A patients (11.5%), and in five from group B (19.2%), at three months. Dr Karacorlu noted that a longer follow-up time would better show the retreatment rate, systemic effects, and visual stability, among other factors.

Hugo Quiroz-Mercado MD reported results of intravitreal Avastin (0.1ml = 2.5mg dose) six months (9/05-3/06) following injection in 711 eyes. He performed clinical examinations, fluorescein angiography, OCT, and measured the systemic blood pressure.

He reported a re-injection rate of 28%, with overall visual and retinal thickness results that matched all other reports so far. Of his patient collective, 321 had diabetic retinopathy, 298 had AMD, 37 had vascular occlusion, 16 had myopic CNV, and 13 had idiopathic CNV.

Eighty-four of AMD eyes required more than one injection. The mean baseline BCVA was 20/300. This improved to 20/200 at one week, 20/100 at four weeks, and to 20/80 at 12 weeks. The median foveal thickness in these patients was 388µm (157-1237µm) at baseline and 247µm (108-1263µm) at 12 weeks.

Diabetic retinopathy patients with severe non-proliferative, proliferative and active disease improved from the mean baseline visual acuity of 20/80 to 20/50 at the one-week evaluation and to 20/40 at 12 weeks.

The mean initial visual acuity in diabetic macular oedema patients improved from 20/100 to 20/80 at one week and to 20/40 at 12 weeks.

In patients with vascular occlusion, 24% had CVO, one was bilateral, and 76% had branch occlusions. The mean baseline visual acuity improved from 20/800 to 20/400 at one week, and on to 20/60 at 12 weeks.

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