

Two-year VISION results support maintenance treatment with pegaptanib sodium

Cheryl Guttman
in Fort Lauderdale

AMD patients continue to benefit from ongoing treatment with pegaptanib sodium (Macugen®, Eyetech), suggests a long-term follow-up from the VEGF Inhibition Study In Ocular Neovascularisation (VISION).

The two-year results from the VISION trial showed that the treatment benefit observed after one year was sustained throughout the follow-up period, Donald J. D'Amico MD, Harvard Medical School, Boston, told the annual meeting of the Association for Research in Vision and Ophthalmology.

The data revealed better results in patients who continued pegaptanib treatment for two years versus the never-treated controls and patients who received pegaptanib for one year only or who stopped after one year and were later restarted on therapy.

The study also showed an association between compliance with the routine treatment schedule and better outcomes. The analyses also suggested particularly favourable results using this treatment in eyes with early lesions, said Dr D'Amico who served as the co-chairman of the safety committee for the VISION trial.

"A complex scheme for treatment re-randomisation after the first year in the VISION trial limits statistical power for between-group comparisons, but the data collected still allow us to make some important observations about the sustained efficacy of ongoing pegaptanib treatment," he added.

The VISION study enrolled patients with CNV lesions ≤ 12 disc areas and visual acuity between 20/40 and 20/320. The study randomised 1,190 patients to treatment with intravitreal pegaptanib sodium 0.3, 1.0 or 3.0 mg or sham injection (subconjunctival anaesthetic) every six weeks.

At the end of 54 weeks, 1,053 (88%) participants were re-randomised such that patients originally on any dose of pegaptanib were assigned 1:1 to discontinue treatment or continue on their same dose for the next 48 weeks.

Patients receiving sham injections for the first year could be randomised to any of the three pegaptanib dose groups, continued sham treatment, or

discontinuation. The protocol also included criteria for restarting therapy for patients whose treatment was discontinued but who experienced deterioration during follow-up.

Different doses yield similar effect

Results collected during the first year showed that treatment with all three doses of pegaptanib was similarly effective for providing rapid, statistically significant, and clinically meaningful vision benefit in a broad spectrum of patients with exudative AMD.

The 0.3 mg dose was associated with a 27% relative treatment effect at 54 weeks. Some 70% of eyes treated with pegaptanib 0.3 mg lost less than three lines of vision compared with 55% of eyes in the sham group. The controls were also twice as likely to lose at least six lines compared with those treated with pegaptanib 0.3 mg, while one-third of treated eyes maintained or gained vision compared with less than one-quarter of the controls.

After two years, patients who had received the 0.3 mg dose for the entire study period benefited with a statistically significant 45% relative treatment effect compared with controls receiving only usual care. Those patients showed a mean loss of 9.4 letters versus 17.0 letters for the other groups. Fifty-nine percent of patients treated for two years lost less than three lines of vision compared with only 45% of controls.

In addition, those patients treated for two years had a greater likelihood of maintaining or gaining vision compared with their counterparts who received only usual care. Patients treated with pegaptanib had a 33% chance of having vision at or better than baseline compared with 23% of controls.

Good compliance

Data on compliance showed excellent adherence to the treatment schedule of routine injection every six weeks. With 17 being the maximum number of possible injections administered for the entire two years of the study, the average number of injections received was 15.7.

Results from a retrospective analysis showed that patients who received a full course of

therapy had better outcomes than those who missed injections, Dr D'Amico added.

"Admittedly this high compliance was achieved in the context of a clinical trial and findings from a retrospective analysis need to be considered with caution. However, they show that continued pegaptanib sodium injections have essentially become a lifestyle choice for these patients and that better compliance appears to enhance results," he said.

Another analysis showed that patients who stayed on pegaptanib throughout the study fared better than those who discontinued it and then restarted treatment because of deterioration. Despite rescue pegaptanib treatment, the latter individuals experienced only limited visual recovery and never returned to the level of vision achieved by patients who continued treatment throughout the trial. The rate of re-leakage was also lower in patients who continued pegaptanib versus those who discontinued treatment.

"Certainly this comparison is not completely fair considering patients who restarted therapy did so because of a biologically active event. Nevertheless, there are warning signs in the available data suggesting that continued suppression with this anti-VEGF therapy is superior to rescue treatment," Dr D'Amico said.

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Early lesion results positive

The researchers also compared treatment effect in terms of two lesion sizes. The first group included small size (<2 disc areas) lesions, relatively good visual acuity (54 letters or better), no history of prior



Donald J. D'Amico

photodynamic therapy or thermal laser treatment, and absence of any scarring or atrophy. The second group included occult lesions with no lipid present and representing the first affected eye.

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"Certainly we could argue about the definition of what is an early lesion, but these are offered as two reasonable scenarios," Dr D'Amico said.

Within the VISION dataset there were 62 eyes fulfilling the Group 1 criteria. Based on one-year data, there were significant differences favouring the pegaptanib group versus the usual care controls for the proportions of eyes avoiding a three line or greater vision loss (77% vs. 54%), avoiding severe vision loss (3% vs. 29%), and improving three or more lines (35% vs. 12%).

Within Group 2, there was also a significant difference favouring pegaptanib treatment as 20% of eyes receiving pegaptanib achieved a three line or more increase in vision at one year compared with baseline versus none of those receiving usual care, Dr D'Amico reported.

Discussing some of the issues pertaining to the clinical use of pegaptanib, Dr D'Amico said that a key question is how to monitor for efficacy and safety. Various

methods have been used or suggested, but there are unknowns for each. For example, if visual acuity is followed, should patients be managed to achieve a specific level or stabilisation within a certain range, and whose expectations should targets be based on – the patients or physicians?

OCT has value for following anatomic changes, but how the information it provides may be helpful in guiding management is not clear, he noted.

"We don't know if repeated development of thickening, thinning, thickening, thinning, etc. is in and of itself detrimental to the retina and perhaps if it might be better to never experience recurrent thickening at all," he said.

Eyes can also be examined with ophthalmoscopy, but there is no good data on what changes are important to watch for, he

pointed out. While fluorescein angiography was performed in the VISION trial, there are many examples of patients with improved vision accompanied by fluorescein angiography outcomes that are equivocal or even show worsening, he added.

"Taken together, this information shows us how little our paradigm for usual monitoring can be translated into this new world of pharmacotherapy," Dr D'Amico said.

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