Pegaptanib sodium clinical experience replicates pivotal trial outcomes

Daniel Roth

EXPERIENCE with pegaptanib sodium (Macugen, Pfizer/OSI-Eyetech) in daily practice supports the results seen in clinical trials, according to reports at the annual meeting of ARVO.

Daniel Roth, MD, a vitreoretinal specialist in New Jersey, presented data on behalf of his subspecialty-oriented, community-based practice showing that pegaptanib sodium was extremely safe and also effective in providing stabilisation or improvement in vision in a cohort of patients consisting mostly of individuals who had failed previous therapy.

“Our experience validates the use of intravitreous pegaptanib sodium in the treatment of exudative AMD and also confirms that, with adherence to the same treatment protocol, results of large, multicentre, randomised clinical trials can be replicated and have relevance in daily practice,” said Dr Roth, professor of ophthalmology, Robert Wood Johnson Medical School, New Brunswick, New Jersey.

He described the experience of eight vitreoretinal specialists who collectively treated 50 eyes of 50 patients according to the same injection protocol used in VISION (VEGF Inhibition Study in Ocular Neovascularisation), the pegaptanib sodium pivotal trial. A small minority (four per cent) of the 50 eyes had predominantly or 100 per cent classic lesions, while the rest were minimally classic or occult. The lesions measured 4 MPS disc areas or larger in 58 per cent of eyes. There was a significant amount of haemorrhage present in about one-fourth of cases. Over two-thirds of the eyes were refractory to previous treatments, which included verteporfin (Visudyne/Novartis) photodynamic therapy and/or intravitreal triamcinolone acetonide. Pre-injection acuity ranged from 20/25 to 20/400, but was 20/100 or worse in 68 per cent of eyes.

“This population is representative of that which would be treated with a brand new therapeutic modality, but the fact that most patients in the group had failed previous therapy placed pegaptanib sodium at a disadvantage for demonstrating efficacy,” noted Dr Roth.

All of the eyes included in the review had received two pegaptanib sodium injections at an interval of six weeks and had a minimum follow-up of 12 weeks. The proportion of eyes with VA of 20/100 or worse at week six, prior to the second injection, had decreased to only 18 per cent, and it remained stable at about 20 per cent at week 12. At that last follow-up 80 per cent of eyes had stable vision (loss of less than three lines) compared with baseline, eight per cent had gained visual acuity, and 12 per cent had a three line or greater loss.

“Some clinicians wonder about the activity of pegaptanib sodium because the lesions still appear active on fluorescein angiography and there is no marked improvement in OCT. Furthermore, in contrast to vision improvement, the vision stabilisation it provides is not appreciated by patients or emotionally satisfying for treating physicians. However, considering the challenges presented by this study population and the likelihood that they may have experienced deteriorating vision over the same follow-up period, it is reassuring to see such a high proportion had stable visual acuity and that we even had some with significant vision gains, especially among patients with more moderate sized lesions and after longer follow-up,” Dr Roth said.

There were no complications in the series, and post-injection ocular inflammation was only minimal.

“Commenting on the current role of pegaptanib sodium Dr Roth noted that its use has been greatly reduced after the recent approval of ranibizumab (Lucentis/Genentech). However, a greater role in the future cannot be ruled out.

“Throughout our experience the use of intravitreous pegaptanib sodium in the treatment of exudative AMD and also confirms that, with adherence to the same treatment protocol, results of large, multicentre, randomised clinical trials can be replicated and have relevance in daily practice”

“In theory, pegaptanib sodium, which selectively targets VEGF-165, may have a safety advantage compared with ranibizumab that binds all forms of VEGF. On that basis, there may be a place for using pegaptanib sodium as maintenance treatment after initial injection with ranibizumab. However, until there are data from clinical trials investigating that approach and given the lack of evidence that local pan-VEGF suppression is problematic, I expect that most retinal specialists will be favouring ongoing treatment with ranibizumab either with scheduled or as-needed repeat injections,” Dr Roth said.

Ophthalmologists from the department of ophthalmology and visual science, John A Moran Eye Center, University of Utah Health Science Center, Salt Lake City, similarly reported findings in their retrospective chart review that pegaptanib sodium treatment was associated with outcomes paralleling those reported in the VISION trial.

The Utah study included 82 eyes of 77 patients. About half of the eyes had pre-treatment acuity of 20/200 or worse, and each eye on average received five injections.

Based on last follow-up, both visual acuity and mean central macular thickness measured by OCT showed improvement from baseline. However, neither change was statistically significant. LogMAR VA (Snellen chart) was 1.08 pre-treatment and 1.18 at last follow-up, while mean baseline central macular thickness was 263.2 microns and decreased to 248.5 microns post-treatment.

Slightly more than one-fourth of eyes had improvement in vision, about one-third maintained stable acuity with a loss of three lines or less, 18 per cent experienced a loss in vision of up to three lines, and vision declined by more than three lines in 22 per cent of eyes. A subgroup analysis considering the eyes that had 20/200 or better visual acuity at entry revealed a greater tendency for vision loss. Among those 40 eyes, mean pre-treatment acuity was 0.694 and improved, not significantly, to 0.963. Twenty per cent of eyes gained acuity and acuity was stable in 15 per cent, while 35 per cent demonstrated a loss of up to three lines and 30 per cent lost more than three lines.

Other subgroup analyses categorising the eyes based on angiographic lesion subtype or size found responses were similar whether the presentation was minimally classic, predominantly classic, or occult and across the range of greatest linear dimensions.

“In all respects, our study findings mirrored the prospective data presented to the FDA to gain approval of pegaptanib sodium. However, the advent of data indicating that more favourable outcomes can be achieved with intravitreal ranibizumab as well as with off-label bevacizumab has now limited the role of pegaptanib sodium in the management of patients with exudative AMD,” said William Barlow, MD, an ophthalmology resident at John A Moran Eye Center.

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