ENTHUSIASM for the potential therapeutic benefits of anti-VEGF agents in the management of exudative age-related macular degeneration should be tempered with caution, following reports of treatment-associated retinal pigment epithelial (RPE) tears, say researchers.

Several research groups reported cases of RPE tears in patients treated with intravitreal bevacizumab (Avastin) or ranibizumab (Lucentis) at the annual meeting of the Association for Research in Vision and Ophthalmology.

Sunir J Garg MD and colleagues presented findings from a retrospective review of eyes treated with intravitreal bevacizumab for exudative AMD. They found 16 cases of retinal tears, of which 15 occurred in eyes previously naïve to any treatment for exudative AMD. One eye had received seven injections of pegaptanib sodium (Macugen, Pfizer) prior to bevacizumab injection. Half of the RPE tears occurred after the first bevacizumab injection, six developed after the second treatment, and the remaining two occurred after the third injection.

Only four eyes (25 per cent) in the series had a serous pigment epithelial detachment (PED). Fifteen eyes had occult neovascularisation and the other had a minimally classic membrane.

The high rate of occult CNV was an interesting observation, but its significance is unclear considering this is a retrospective study and that occult neovascularisation accounts for about 90 per cent of all exudative AMD, said Dr Garg assistant professor of ophthalmology, Wills Eye Hospital, Philadelphia, Pennsylvania.

The incidence of RPE tears in eyes treated with intravitreal bevacizumab was estimated to be 1.6 per cent based on data from three retinal specialists who had 15 cases among 920 eyes treated with a total of 3339 injections.

If the tear spared the fovea, the vision was generally good and some of those patients even continued to have further visual improvement from ongoing treatment, presumably because the anti-VEGF treatment was controlling the underlying exudative AMD.

While the report focused on RPE tears after bevacizumab treatment, Dr Garg noted that these events have also occurred in patients treated with ranibizumab, pegaptanib sodium, photodynamic therapy, thermal laser, as well as part of the natural history of the disease. His impression was that the RPE tears have been most frequent with bevacizumab.

Any cause and effect relationship with intravitreal anti-VEGF treatment remains to be established, and it is hard to say whether the difference between agents is real. If the tears occur because the treatment induces rapid contraction of the neovascular membrane, it makes sense that they might be least common after pegaptanib sodium treatment, as it has a slower onset of action. It is less clear why there might be a difference between bevacizumab and ranibizumab. However, we look forward to prospectively collected data from the recently announced head-to-head comparison trial of bevacizumab and ranibizumab to see if evidence emerges to show any difference between the two compounds in the rate of RPE tears, Dr Garg said.

A report from Arif Samad MD revealed an even higher incidence of RPE tears in eyes treated with intravitreal bevacizumab. A review of 172 consecutive eyes of 164 patients identified RPE tears in seven (four per cent) eyes. All of the affected eyes had pre-existing PED and occult CNV. Only one eye experienced a decrease in vision after the event, while vision remained stable in two eyes and improved in four eyes.

"RPE tears are usually associated with a dramatic decrease in vision, but with the one exception, these patients were able to maintain or improve their vision with continued treatment," said Dr Samad, assistant professor of ophthalmology and visual sciences, Dalhousie University, Halifax, Canada.

He noted that recovering of the tear-exposed area of Bruch's membrane by a layer of hypopigmented RPE cells may allow for preservation of the photoreceptors.

Anna E Rosenfeld MD, and colleagues reviewed data from 60 eyes treated with intravitreal ranibizumab and reported RPE tears developed in four patients (6.7 per cent). Time to diagnosis post-injection ranged from 16 to 126 days. Two patients had received pegaptanib sodium or bevacizumab previously. Pre-treatment visual acuity ranged from 20/40 to 20/200, at the time of RPE tear diagnosis.

Visual acuity was either improved (in two eyes) or unchanged relative to that baseline level. All eyes with RPE tears had PED prior to initiating ranibizumab.

"One postulated mechanism for anti-VEGF therapy-induced RPE tears suggests that the resultant contraction of the CNV places shearing forces on the RPE, leading to contraction and a rip. PED may facilitate that process because it further weakens the RPE. However, we are still reviewing our data for all of the treated eyes to see how many had PED in order to better determine if it is a possible risk factor for RPE tears after ranibizumab," Dr Rosenfeld, Doheny Eye Institute, University of Southern California, Los Angeles.

Ophthalmologists from the Kellogg Eye Center, University of Michigan, Ann Arbor, reported on four patients who developed RPE tears between one and six weeks after intravitreal bevacizumab treatment and extracted data from their charts to see if they could identify possible predictors for this complication. AMD lesions with a serous PED component were present in all affected eyes and may represent a risk factor for developing RPE tears after intravitreal bevacizumab injection. In contrast to the other reports at the meeting, the vision worsened in most of their patients.