

used in the management of retinopathy of prematurity, its use is controversial, because of the potential for serious adverse effects when used in young babies (see panel on page 46).

In practice, the major adverse effects of these drugs appear to be associated with the intraocular injection rather than the active drug.

Treatment regimes in adults

Regardless of the treatment indication, there are essentially two regimes for administering anti-VEGF drugs: **continuous** and **intermittent/as required** (or *pro re nata*, **PRN** for short).

Most of the initial trials were done as a **continuous** regime, with regular monthly injections over the course of 2 years, i.e. patients would have 24 injections in total. These trials showed that treatment delivered in this way was effective, but it is also expensive and inconvenient for both the patient and the health care provider.

A number of other trials have examined **PRN** regimes. These are all fairly similar and consist of three injections given over 3 months, followed by review. At this point the patient may:

- be much better, in which case no additional treatment is needed
- have no improvement at all, in which case further treatment is futile
- have some improvement, which would justify further injections.

Even among those patients who do very well, and do not require more than three injections initially, many will relapse and require further injections in the future.

This means they must be regularly reviewed in the clinic, i.e. every 1–2 months, which involves testing of visual acuity and/or retinal thickness. If patients' visual acuity is lower by one or more lines, or if they develop worsening macular oedema, they need a further injection of anti-VEGF.

Trials of this dosing regime for AMD and diabetic macular oedema have shown that an average of seven injections are required in the first year of treatment and that outcomes are as good as for regular monthly injections. The trials used as their indication for re-treatment with anti-VEGF either a reduction in visual acuity or an increase in retinal thickness (measured using optical coherence tomography [OCT]); both were assessed at each visit.

While visual acuity is easily measured, retinal thickness can only be measured accurately by OCT. These machines are costly and will only be available in major

Continues overleaf ►

FROM THE FIELD

Use of anti-VEGF drugs at the Instituto de la Visión de Montemorelos



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1 Which anti-VEGF agents do we use?

We use bevacuzimab (Avastin) – the dose used is 2.5 mg (0.1 ml). This anti-VEGF agent is used because of its:

- proven efficacy and effectiveness (CATT & IVAN studies)
- low cost, making it affordable for our patients.

2 What are the indications?

- Vitreous haemorrhage secondary to proliferative diabetic retinopathy – particularly when there has been no previous laser.
- Prior to vitrectomy for proliferative diabetic retinopathy.
- Clinically significant macular oedema due to diabetic retinopathy.
- Macular oedema secondary to branch or central retinal vein occlusion.
- Exudative age-related macular degeneration.
- Neovascular glaucoma.

3 Who gives the injections?

Intra-vitreous injections are always given by an ophthalmologist, for example:

- retina specialists
- retina subspecialty trainees
- ophthalmology residents in the retinal service.

4 Are anti-VEGF agents used without OCT?

Anti VEGF agents are used without OCT in selected cases:

- vitreous haemorrhage secondary to proliferative diabetic retinopathy – particularly when there has been no previous laser
- prior to vitrectomy for proliferative diabetic retinopathy
- clinically significant macular oedema due to diabetic retinopathy
- neovascular glaucoma.



Anti-VEGF injections are given in a clean room

5 What are the outcomes?

Clinical experience has been very positive and we believe this is a cost-effective treatment for our patients.

Vitreous haemorrhage secondary to proliferative diabetic retinopathy:

We have been pleased with our results. Anti-angiogenic therapy reduces the vitreous haemorrhage in many patients with diabetic retinopathy, allowing us to apply laser and avoid vitrectomy surgery.

Prior to vitrectomy for proliferative diabetic retinopathy:

Application 3–5 days before surgery reduces the risk of intra-operative and post-operative bleeding.

Neovascular glaucoma: In these patients, we are careful to avoid further increases in the IOP. When the rubeosis regresses we apply pan-retinal laser, giving us more control of the iris neovascularisation.

Clinically significant macular oedema:

In clinically significant macular oedema due to diabetic retinopathy, we normally apply three doses of Avastin with 1-month intervals between injections. After the last injection, a macular OCT is requested and, if the oedema has decreased, we apply focal laser.

Age-related macular degeneration (AMD):

In patients with exudative AMD, an injection is given every month for several months to improve visual acuity and to control the disease, following the 'treat and extend' protocol.

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