

Diabetic macular oedema without visual impairment

No benefit from immediate treatment with aflibercept

● According to the results of a trial in about 700 diabetic patients who had macular oedema without loss of visual acuity, after a follow-up of 2 years, treatment with *aflibercept* from the outset did not confer a demonstrated advantage in preventing deterioration of visual acuity compared to observation, with treatment only initiated if visual impairment occurred. This vascular endothelial growth factor inhibitor (anti-VEGF) a risk, in particular, of rare but serious systemic adverse effects.

Diabetic retinopathy is sometimes accompanied by macular oedema that causes severe decrease in visual acuity. Laser photocoagulation has some efficacy but is rarely sufficient for improving visual acuity. As an addition to laser therapy, intravitreal injections of vascular endothelial growth factor inhibitors (anti-VEGF) are an option. In this situation, *aflibercept* is a treatment of choice in patients with marked visual impairment (1).

What is the efficacy of *aflibercept* in patients with diabetic macular oedema without visual impairment

at the time of diagnosis? A trial published in 2019 provides some answers to this question (2).

This non-blinded multi-centre trial compared three management strategies in 702 diabetic patients with macular oedema, aged of 59 years on average: *aflibercept* by intravitreal injection, versus laser photocoagulation, versus observation. At baseline, the patients had no visual impairment and a visual acuity of at least 20/25 on the Snellen scale. In the laser photocoagulation and observation groups, provision was made for *aflibercept* injections to be carried out if visual acuity worsened (2).

After two years of follow-up, the proportion of patients who had a decrease of at least 1 line of visual acuity (the primary outcome measure), assessed using the ETDRS (Early Treatment of Diabetic Retinopathy Scale) was similar in each of the 3 groups: about 17% (a). Three-quarters of patients in the laser photocoagulation group and two-thirds of those in the observation group did not receive any *aflibercept* injections (2).

Intravitreal *aflibercept* injection mainly carries a risk of local adverse effects: conjunctival haemorrhage; eye pain and increased intraocular pressure; vitreous floaters; and punctate keratitis. Systemic adverse effects have also been reported, such as stroke, thromboembolic events and heart failure (1,3). In the trial described above, increased intraocular pressure was observed in 8% of patients in the *aflibercept* group versus 6% in the laser photocoagulation group and 3% in the observation group (2).

In practice For diabetic patients who have macular oedema with no loss of visual acuity, treatment from the outset with intravitreal injections of *aflibercept* does not seem to offer any tangible advantage compared to observation in preventing deterioration of visual acuity. There is no justification for early exposure of patients to the sometimes serious adverse effects of this anti-VEGF. It is better to reserve its use for patients with marked or worsening visual impairment.

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a- This scale consists of 14 lines of letters read at a distance of 2 metres and, for patients with impaired vision, 3 lines of letters read at 1 metre. Each line consists of 5 contrasting letters with a geometric progression of letter size from line to line (ref 4).

Selected references from Prescrire's literature search

- 1- Prescrire Editorial Staff "Aflibercept and diabetic macular oedema. A first-choice VEGF inhibitor in case of marked visual loss" *Prescrire Int* 2015; **24** (163): 207.
- 2- Baker CW et al. "Effect of initial management with aflibercept vs laser photocoagulation vs observation on vision loss among patients with diabetic macular edema involving the center of the macula and good visual acuity. A randomized clinical trial" *JAMA* 2019; **321** (19): 1880-1894.
- 3- Prescrire Rédaction "aflibercept intraveineux" *Interactions Médicamenteuses Prescrire* 2020.
- 4- Prescrire Rédaction "aflibercept (Eylea®) et néovascularisations liées à une myopie forte. Pas d'avantage démontré par rapport au ranibizumab intravitréen" *Rev Prescrire* 2016; **36** (397): 811-812.

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