FOLIA MEDICA CRACOVIENSIA
Vol. LVII, 3, 2017: 113–119
PL ISSN 0015-5616

Outcome of the first year of treatment for exudative age-related macular degeneration under a treatment programme using aflibercept — own experience

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Abstract: Study objective: Anatomic and functional (function improvement) outcome of the aflibercept treatment for exudative age-related macular degeneration was analysed after the first year of treatment.
Material and methods: 62 patients treated with intravitreal aflibercept injections according to the adapted regimen. The treatment efficacy was understood as a reduction in oedema (and the central retinal thickness), with an increase in or stabilisation of the best corrected visual acuity.
Results: In nearly all patients, a reduction in the central retinal thickness was observed, with stabilisation of or improvement in the best corrected visual acuity.
Conclusion: The aflibercept treatment for exudative age-related macular degeneration is a promising and efficient treatment method.

Key words: exudative age-related macular degeneration, aflibercept, anti-VEGFs.

Introduction

Exudative age-related macular degeneration (AMD) is a dangerous disease which, when left untreated, usually leads to a permanent loss in visual acuity due to oedema, injury and secondary scaring of the central retina [1]. With the gradually increasing

length of life its medical and social importance grows. Currently, a therapy for exudative AMD is based on inhibitors of vascular endothelial growth factor (VEGF), medicines of well-known efficacy [2–5]. Two medicines from this group, aflibercept and ranibizumab, are registered for ophthalmic therapy, with bevacizumab used off-label. From the molecular point of view, bevacizumab and ranibizumab are monoclonal antibodies, while aflibercept is a fusion protein of chemical affinity to VEGF exceeding that of the above components [5]. When compared to ranibizumab, aflibercept also has a longer half-life in the vitreous humour [5–7]. These pharmacokinetics may underlie better therapeutic outcomes reported for this formulation when used for AMD, versus other anti-VEGF [8–16]. The described treatment programme used in Poland in patients with exudative age-related macular degeneration came into force on May 1, 2015, and covers treatment with two medicines: aflibercept and aflibercept [7]. This treatment is initiated in patients meeting established criteria, and an appropriate treatment regimen is applied, approved by the Coordinating Team for Treatment of Neovascular Age-Related Macular Degeneration. The complete management programme is monitored on-line by the Central Medical System. The programme covers: patient inclusion and exclusion criteria, a dosing regimen, a medicine administration route, a list of diagnostic tests performed during patient qualification for treatment and required for their follow-up.

Inclusion criteria for the first year of treatment:

— Presence of an active (primary or secondary) classic, occult or mixed choroidal neovascularization (CNV) involving over 50% of the lesion in AMD, confirmed by OCT and a fluorescein angiography.
— Patients over the age of 45.
— The lesion of a size below 12 DA (12 disc area).
— Best corrected visual acuity (BCVA) in the treated eye of 0.1–0.8 as determined with the Snellen chart.
— Patient consent to intravitreal injections.
— No dominant geographic atrophy.
— No dominant haemorrhage.

All inclusion criteria must be met.

Material and methods

The study concerned 62 patients treated with intravitreal aflibercept (2 mg/0.05 ml) injections under the standard treatment regimen at the Voivodship Ophthalmic Hospital "Na Wzgórzach". Newly presenting (previously untreated) patients received 7 aflibercept injections according to the following regimen: 3 monthly injections followed by 4 injections every two months. Patients continuing the treatment

(previously treated with aflibercept or ranibizumab injections) received intravitreal aflibercept injections under the PRN (pro re nata) regimen. For more detailed evaluation of treatment outcomes, patients were classified into two age groups: 61–70 YOA and 71–99 YOA. In the group of the newly presenting patients, the first year of the treatment programme was completed by 8 patients from the 61–70 YOA group and 36 patients from the 71–99 YOA group. In the group of the patients continuing the treatment, the first year of the treatment programme was completed by 1 patient from the 61–70 YOA group and 17 patients from the 71–99 YOA group.

The evaluated parameters included the best corrected visual acuity (BVCA) expressed on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale and central retinal thickness (measured as micrometres), verified in each age group during the first visit (following treatment qualification for treatment), fourth visit (following the saturation dose) and eighth visit (after one year of treatment).

Results

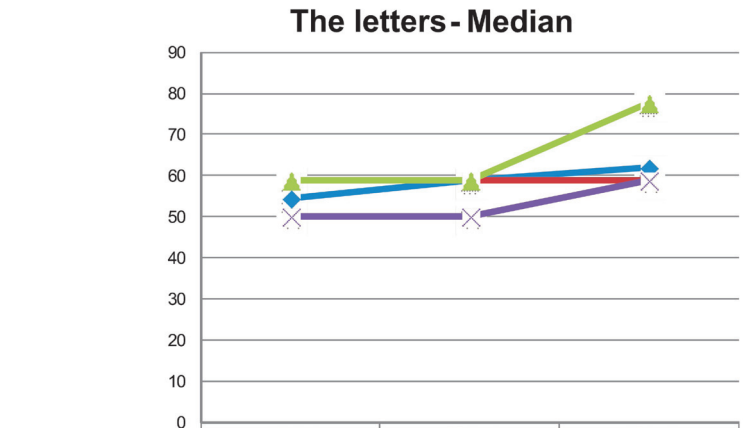
In the newly presenting patients, an improvement in the best corrected visual acuity (BCVA) by 7 letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) scale was found in the age group of 61–70 YOA, while the best corrected visual acuity (BCVA) was maintained on a stable level in the age group of 71–99 YOA.

In the patients continuing the treatment, an improvement in the best corrected visual acuity (BCVA) by 19 letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) scale was found in the age group of 61–70 YOA, while an improvement by 9 letters was noted in the age group of 71–99 YOA.

In all age groups of the newly presenting patients and patients counting the treatment, a reduction in the central retinal thickness was observed, for the newly presenting patients by 113 μm in the 61–70 YOA age group and by 92 μm in the 71–99 YOA age group, and for the group of patients continuing treatment, by 260 μm in the 61–70 YOA age group and by 141 μm in the 71–99 YOA age group.

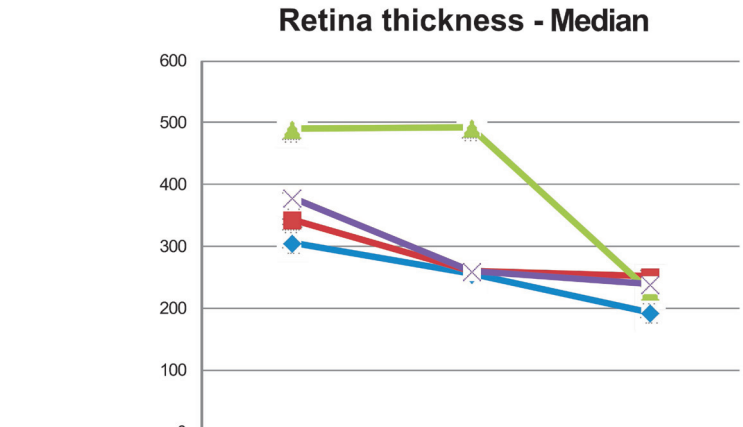
Discussion

The therapy described above has a significant advantage over other methods used for treatment of the exudative age-related macular degeneration in the past. The first effective therapy for exudative age-related macular degeneration was the laser photodynamic therapy (PDT) [17]. However, in the long-term follow-up this therapy did not bring the expected results. Observed effects included a reduction in the macular function, decreased choroid circulation, and even secondary lesions in the pigmented epithelium by hypoxia caused by closing of choriocapillars following



	Visit 1	Visit 4	Visit 8
New Patient - 61-70	55	59	62
New Patient - 71-99	59	59	59
After treatment - 61-70	59	59	78
After treatment - 71-99	50	50	59

Fig. 1. A relationship between the visual acuity and a number of injections.
In the patients continuing the treatment, an improvement in the best corrected visual acuity scale was found.



	Visit 1	Visit 4	Visit 8
New Patient - 61-70	307	256	194
New Patient - 71-99	344	262	252
After treatment - 61-70	490	492	230
After treatment - 71-99	380	261	239

Fig. 2. A relationship between the retinal thickness and a number of injections.
In all age groups of the newly presenting patients and patients counting the treatment, a reduction in the central retinal thickness was observed.

the applied photodynamic therapy (PDT) [18–19]. In consequence, patients lost over 10 letters in the Early Treatment Diabetic Retinopathy Study (EDTRS) scale after one year of treatment [20].

The aflibercept therapy also has a very significant advantage over previously used intravitreal injections of pegaptanib (also belonging to anti-VEGFs). During one-year follow-up of the pegaptanib therapy, where patients received intravitreal injections of 0.3 mg of the medicine every 6 weeks, only a 15% slower loss of the visual acuity was noted versus the placebo group [21].

The intensive and large-scale therapy for exudative age-related macular degeneration (AMD) using intravitreal anti-VEGF medicines currently conducted in Poland offers an opportunity to follow up and describe results of the new treatment programme. The results from our centre presented above confirm efficacy and usefulness of the therapeutic programme for exudative age-related macular degeneration (AMD) using intravitreal aflibercept injections, proving it is an effective therapeutic method providing an expected, advantageous treatment outcome under this regimen. Permanent availability of the medicine throughout the therapy definitely significantly facilitates disease management for a doctor in charge and is the best option for continuous and efficient treatment for a patient. This significantly improves relations between the doctor and the patient, and offers a chance for the effective therapy.

In the future, we expect similar systemic solutions increasing availability of anti-VEGF formulations to patients with other ophthalmic diseases, for which efficiency of those medicines was proved. Patients with macular oedema secondary to retinal vein occlusion or diabetes form a particularly large group here. Aflibercept efficacy was proven both for occlusive [22–25] and diabetic [26–28] macular oedema; and for the Polish patient, the main problem remains availability of this therapy.

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