

# Intravitreal Bevacizumab for the Management of Age-Related Macular Degeneration

Damir Kovačević<sup>1</sup>, Tea Čaljkusić-Mance<sup>1</sup>, Tamara Mišljenović<sup>2</sup>,  
Maša Mikuličić<sup>2</sup> and Zvezdana Alpeza-Dunato<sup>1</sup>

<sup>1</sup> Department of Ophthalmology, University Hospital »Rijeka«, Rijeka, Croatia

<sup>2</sup> Eye Polyclinic »Dr L. Pavičević«, Rijeka, Croatia

## ABSTRACT

*The aim of this study is to report short-term effect of the treatment of »wet« ARMD (age-related macular degeneration) with intravitreal bevacizumab (Avastin). Prospective study included 36 patients (36 eyes) with »wet« form of ARMD. All patients were over 60 year old (22 female, 14 male). Changes of macula included minimally classic CNV (choroidal neovascularisation) (24), occult subfoveal CNV (10) and first stage of cicatrical CNV (2). Bevacizumab 1.25 mg was administered intravitreally through pars plana using a 27-gauge needle. Patients had no previous eye treatment. Ophthalmic exam before and after the treatment included: Snellen VA (visual acuity) and examination including measurement of IOP (intraocular pressure), FA (fluorescein angiography) and interview with patients. After 4–6 weeks 28 (78%) patients had significant improvement of VA. Median VA improved from 0.083 to 0.200 ( $p < 0.01$ ). Eight patients (22%) had no significant improvement in VA but three of them reported to see more light. FA showed complete resolution of macular edema in 6 patients (17%), partially resolved in 23 patients (64%) and no change in 7 patients (19%). No systemic side-effect was found. Short-term results suggest that intravitreally administered bevacizumab is well tolerated treatment for ARMD with very high number of patients showing improvement in VA.*

**Key words:** bevacizumab, choroidal neovascularization, age-related macular degeneration

## Introduction

ARMD affects patients in their retirement years (over 55)<sup>1,2</sup>. Degenerative changes of macular area results in damage of central vision. These changes lead to difficulty in driving and reading. There are two categories of ARMD: »dry« with drusen deposits and »wet« with CNV. In the »wet« type bleeding and scarring destroy overlying retina. For over three decades, standard laser therapy was the only viable treatment for patients with »wet« form. Only about 25% of patients with »wet« form were candidates for this treatment and of those treated about 50% would experience some form of recurrence of the disease. Almost none of patients who were treated with laser experienced improvement of their vision. In most of the cases slowing or stabilization of the disease was the best one could hope for. The newer treatment modalities were photodynamic therapy, surgical intervention and radiation therapy<sup>3</sup>. These treatments are in a class of drugs called »anti-VEGF« therapy. VEGF (Vascular Endothelial Growth Factor) is a protein that is important in forming new blood vessels. Abnormally high concentrations of

VEGF can lead to damage by the growth of new blood vessels where they would not be, such as under the macula in the »wet« form of ARMD. This new class of drugs acts by blocking VEGF and preventing it from stimulating the growth of these abnormal blood vessels. Pegaptanib (Macugen) represented the first use of anti-VEGF factor in the eye<sup>4-6</sup>. Ranibizumab (Lucentis) was approved by the US Food and Drug Administration (FDA) at the end of June 2006 for use in »wet« ARMD. It was developed for intraocular use and besides preventing of visual loss it was capable of significantly improving VA of ARMD patients<sup>6-11</sup>. Following the reported benefits of Lucentis therapy in the summer of 2005, retina specialists turned their attention towards bevacizumab, which is medicine currently FDA approved for the treatment of metastatic colon cancer. Bevacizumab is molecularly similar to ranibizumab and acts in the same way<sup>4,6,12</sup>.

The advantage of using bevacizumab is lower price and longer time intervals between administrations<sup>4,6,7</sup>.

The purpose of our study was testing safety and efficacy of bevacizumab in our ARMD patients with CNV.

## Patients and Methods

Thirty-six patients (36 eyes) aged >60 years were included in this prospective interventional case study. Inclusion criteria were ARMD with active leakage from CNV documented by FA, best corrected VA > 0.017 and no previous eye treatment. The off-label use of bevacizumab was discussed with each patient and written informed consent was obtained before enrollment. Ophthalmic evaluation before and after the treatment included: Snellen VA, complete ophthalmic examination including measurement of IOP, FA and interview with patients. The treatment of bevacizumab was performed in operating theatre after povidone iodine preparation of eyelids and conjunctiva. Patients underwent topical anesthesia with Lidocain gel. Bevacizumab (1.25 mg) was administered intravitreally through the pars plana using a 27-gauge needle. After intravitreal treatment retinal artery perfusion, IOP and light appreciations from all four directions were checked. Patients were followed up every 4–6 weeks after receiving the first injection and received additional injection treatment when necessary. The main outcome measures were changes between baseline and visit after 4–6 weeks in best corrected VA and resolving of macular edema documented by FA. Changes between baseline and visit after 4–6 weeks were analyzed using at-test.

## Results

Thirty-six eyes of patients (22 female and 14 male), median age 69.2 (range 62–83) years with CNV secondary to ARMD were included. There were 24 eyes with minimally classic, 10 eyes with occult and two eyes with

first stage of cicatricial CNV documented by FA. Median duration of follow up was 5.37 (range 4–6 weeks). After that period 27 (78%) of 36 patients had significant improvement of VA. Median vision improved from 0.083 to 0.200 ( $p < 0.01$ ). Eight patients (22%) had no significant improvement of VA but three patients reported to see more light. FA showed complete resolved macular edema in 6 patients (17%), partially resolved edema in 23 patients (64%) and seven without change (19%). There were several local side effects. Transitory rise of IOP was found in four eyes the next day, hyposphagma after the injection in nine eyes and mild opacities in eight eyes. No systemic side-effects were found.

## Discussion and Conclusion

Before the introduction of anti-VEGF medications there was no known therapy for ARMD that can actually improve VA. Several different drugs were recommended (peptaganib, ranizumab, bevacizumab). Although bevacizumab is currently available only as off-label drug, many published case series and their results encourage further use in ARMD<sup>11,12</sup>.

Economic aspect is also very important because this drug is not expensive compared to other recommended<sup>7</sup>. Our short-term results after first injection and 4–6 weeks of following-up suggest that intravitreally administered bevacizumab in the dose of 1.25 mg is well tolerated and associated with reduction in FA leakage and significantly improvement of VA in most patients. Seventy-eight percent of our patients had significantly improvement of VA. No systemic side-effects were noticed. Lower cost of bevacizumab in comparison with other anti-VEGF-agents were also the important factor. We need further evaluation of intravitreal bevacizumab, especially long term results and frequency of additional intravitreal therapy.

## REFERENCES

1. NJIRIĆ S, MIŠLJENOVIĆ T, MIKULIČIĆ M, PAVIČEVIĆ L, Coll Antropol, 31 (2007) 107. — 2. PLEŠTIŃA-BORJAN I, KLINGER-LASIĆ M, Coll Antropolo, 31 (2007) 33. — 3. ŠARIĆ B, ŠIKIĆ J, KATUŠIĆ D, VUKOJEVIĆ N, Coll Antropol, 25 (2001) 89. — 4. LAZIĆ R, GABRIĆ N, Graefe's Arch Clin Exp Ophthalmol, 245 (2007) 68. — 5. FERRARA N, Endocr Rev, 25 (2005) 581. — 6. ROSENFELD PJ, BROWN DM, HEIER JS, BOYER DS, KAISER PK, CHUNG CY, KIM RY, N Engl J Med, 355 (2006) 1419. — 7. LAZIĆ R, GABRIĆ N, DEKARIS I, ŠARIĆ B, GAVRIĆ

M, Coll Antropol, 31 (2007) 77. — 8. LAZIĆ R, GABRIĆ N, DEKARIS I, GAVRIĆ M, BOSNAR D, Coll Antropol, 31 (2007) 71. — 9. FRAUN-FELDER F, Drugs Today (Barc), 41 (2005) 3. — 10. SPAIDE R, Ophthalmol, 113 (2006) 22. — 11. POLITO A, ISOLA M, LANZETTA NP, GREGORI D, BANDELLO F, Ann Acad Med Singapore, 35 (2006) 145. — 12. SPAIDE RF, LAUD K, FINE HF, KLANCNIK JMJR, MEYERLE CB, YANUZZI LA, SORENSON J, SLAKTER J, FISHER YL, COONEY MY, Retina, 26 (2006) 383.

D. Kovačević

Department of Ophthalmology, University Hospital »Rijeka«, Krešimirova 42, 51000 Rijeka, Croatia  
e-mail: damir.kovacevic@ri.t-com.hr

## **INTRAVITREALNI BEVACIZUMAB U LIJEČENJU SENILNE MAKULARNE DEGENERACIJE**

### **S A Ž E T A K**

Naša je namjera bila prikazati kratkoročne efekte liječenja vlažne senilne makularne degeneracije intravitrealno injiciranim bevacizumabom (Avastinom). Pacijenti su primili injekcije od 1.25 mg bevacizumaba, a kontrolirani su nakon razdoblja od 4–6 tjedana. Prospektivna studija uključila je 36 pacijenata, odnosno 36 očiju sa vlažnim oblikom senilne makularne degeneracije. Pacijenti nisu prethodno dobivali nikakvu očnu terapiju. Uključeno je 24 pacijenta s minimalno klasičnom, 10 sa okultnom i dva sa prvim stadijem ožiljkavanja. Bevacizumab u dozi od 1.25 mg injiciran je intravitrealno kroz pars plana. Nakon 4–6 tjedana 27 pacijenata (78%) imalo je poboljšanje vidne oštrine. Od 8 pacijenata kod kojih nije došlo do poboljšanja tri su navela da vide više svjetla. Prije i nakon perioda od 4–6 tjedana učinjen je potpun oftalmološki pregled uključujući vidnu oštrinu, mjerenje očnog tlaka, fluoresceinsku angiografiju te razgovor s pacijentom. Potpuno povlačenje makularnog edema zabilježili smo kod 6 pacijenata (17%), djelomično kod 23 pacijenta (64%), a nepromijenjeno stanje edema kod 7 pacijenata (19%). Zabilježene su bezazlene lokalne nuspojave dok sustavnih nije bilo. Kratkoročni su rezultati ohrabrujući te pokazuju da pacijenti dobro podnose intravitrealni bevacizumab u dozi od 1.25 mg. Nakon ove terapije bitno se popravlja vidna oštrina i smanjuje edem makule kod većine pacijenata.