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Long-Term Visual and Anatomic Outcomes Following Anti-VEGF Monotherapy for Retinal Angiomatous Proliferation

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Abstract

Purpose—To study the long-term visual and anatomic outcomes of anti-vascular endothelial growth factor (VEGF) monotherapy for the treatment of patients with retinal angiomatous proliferation (RAP).

Methods—Retrospective review of patients who were diagnosed with AMD and RAP lesions, and who received anti-VEGF injections as the only mode of therapy.

Results—20 eyes (15 patients; 9 women, 6 men) with RAP lesions treated by anti- VEGF were encountered. Mean patient age was 85.8 years (SD $\pm$ 4.54). Nine eyes were treated with intravitreal ranibizumab alone, 8 eyes with bevacizumab alone, and 3 eyes received both drugs. At the 1, 3 and 6 month follow-up the median VA had improved from baseline (20/72) to 20/52, (range: 20/25 to 20/400), 20/45 (range: 20/20 to 20/400), and 20/56 (range: 20/20 to 20/400), respectively, ($P > 0.001$, $P = 0.001$, and $P = 0.05$, respectively). At 24 month follow-up, the improvement of VA, defined as halving of the visual angle, occurred in 37.5% of the cases.

Conclusions—Anti-VEGF monotherapy represents a useful treatment option for RAP, with stable or improved visual acuity in 62.5% of patients at 2 years. 25% of eyes only required a single injection, however, in most cases (75%) repeated treatments were required, highlighting the need for long term follow up. Although in this small study, the results for visual improvement were not statistically significant beyond 3 months; our findings warrant further large-scale investigation.

Keywords

age-related macular degeneration; bevacizumab; long term follow-up; ranibizumab; retinal angiomatous proliferation

Yannuzzi and associates¹ coined the term retinal angiomatous proliferation (RAP) to describe a variant of neovascular age-related macular degeneration (AMD) characterized by

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neovascularization with a presumed retinal origin. They hypothesized that RAP begins as intraretinal neovascularization (stage I), progresses to subretinal neovascularization with or without serous pigment epithelial detachment (PED) (stage II), and ultimately results in choroidal neovascularization (CNV) (stage III).¹ A recent histopathologic study has confirmed the intraretinal origin of the neovascular process in RAP lesions.²

RAP is estimated to occur in 10%–15% of newly diagnosed cases of neovascular AMD, RAP lesions are frequently bilateral, and within a three-year period, all patients with unilateral RAP lesions developed bilateral disease.³ The natural history and response to therapy in RAP appears distinct from other neovascular AMD subtypes.^{4,5} Indeed, a number of treatments for neovascular AMD including photodynamic therapy (PDT) have not proven effective in the treatment of RAP.^{4,6}

More recently, anti-vascular endothelial growth factor (VEGF) agents have shown improved functional and anatomic outcome in phase III clinical trials for patients with neovascular AMD.^{7–11}

Preliminary evidence from small, short term, single-center case series suggests that the use of intravitreal anti-VEGF in the treatment of RAP leads to improved outcomes.^{12–14}

The purpose of the current study was to determine longer-term visual and anatomic outcomes of anti-VEGF monotherapy in patients with RAP.

Methods

We performed a retrospective review of medical records of all patients who underwent anti-VEGF treatment for AMD at the Doheny Eye Institute between August 1, 2005, and March 31, 2009. Patients were excluded if they had CNV secondary to conditions other than AMD if they received treatment other than anti-VEGF agents or had less than 6 months of follow-up.

Patients were included if they had AMD with typical manifestations of RAP, including preretinal, intraretinal, and/or subretinal hemorrhages, intraretinal edema, and the presence of neovascularization in one of the three stages of the disorder as confirmed by fluorescein or indocyanine green angiography and optical coherence tomography (OCT). At baseline, and at each monthly follow-up visit, best-corrected Snellen visual acuity (VA), and OCT were evaluated. Fluorescein angiography was performed at baseline and at physician's discretion at subsequent visits. Intravitreal injection of either bevacizumab (1.25 mg) or ranibizumab (0.5 mg) was also performed at the discretion of the treating physician. No initial loading doses were used.

The decision for retreatment was made at each monthly follow-up visit as determined by OCT-based criteria. Specifically, patients were re-treated for persistence or recurrence of intraretinal, subretinal or sub-RPE fluid, or for any increase in retinal thickness.

Evaluation of Anatomic Outcomes using OCT

Before 2007, all OCT images were obtained using Stratus OCT (Carl Zeiss Meditec Inc., Dublin, CA). With the availability of Fourier domain OCT (FDOCT), all OCT images were obtained using 3D-OCT 1000 (Topcon, Tokyo, Japan). The OCT images were qualitatively analyzed by two of the authors (TSH, PAK). The assessed parameters were subretinal fluid (SRF), intraretinal fluid (IRF), intraretinal cystoid spaces (ICS), and pigment epithelial detachment (PED). Intraretinal fluid included diffuse thickening of the retina as well as

intraretinal microcystic edema. Intraretinal cystoids spaces were defined as distinct, round areas with well-demarcated borders and central hyporeflectivity.

Statistical Methods

Statistical analysis was performed using SAS V9 programming language (SAS Inst. Cary, NC). Snellen VA was converted to logMAR for the purposes of statistical analysis. Because VA was not obtained by protocol refraction, a high threshold was used to identify a change in vision. Accordingly, a decrease in VA was defined as doubling of the visual angle (≥ 0.3 change on logMAR). An increase in VA was defined as halving of the visual angle (≤ -0.3 on logMAR). If the VA changed by a smaller amount, it was classified as being stable. Paired *t*-tests were used to evaluate the mean changes in VAL from baseline. Decline in VA was further analysed using a Kaplan- Meier graph.

Results

Baseline Characteristics

Twenty eyes of 15 patients were included in this study. Each eye had a diagnosis of AMD with a RAP lesion, treated with anti-VEGF monotherapy, with a documented follow- up of at least 6 months. Of the 15 patients, 9 were female and 6 were male, with a mean age of 85.8 years ($SD \pm 4.54$). Five eyes had stage II & 15 eyes had stage III lesions. The mean baseline VA was 20/72 (range 20/30 to 30/2000).

Baseline OCT

Subretinal fluid was present in 13 eyes (65%), IRF in 18 eyes (90%), ICS in 15 eyes (75%) and PED in 17 eyes (85%). The PED was classified as a fibrovascular in 14 eyes (70%) and as a serous in 3 eyes (15%). In the fellow eyes, RAP was present in 11 eyes, occult CNV without RAP in 1 eye, dry AMD with atrophy in 4 eyes, and advanced dry AMD with geographic atrophy in 3 eyes.

Treatment

Mean patient follow-up was 19.8 months (range 9–42 months). Nine eyes were treated exclusively with intravitreal ranibizumab; 8 eyes exclusively with bevacizumab; and 3 eyes received both ranibizumab and bevacizumab during the course of their follow-up. Fifteen of the 20 eyes (75%) required repeated injections throughout the follow-up period. For those 15 patients, the average frequency of reinjection was 3.45 months (range: 2 injections to 35 injections; median 3). 5/20 eyes (25%) required a single intravitreal injection. In the eyes that required reinjections, the range was 2–35 injections, with a mean and median of 6 and 4 injections respectively. At the last follow up visit, eleven of the 20 eyes (55%) required reinjection.

There were no documented systemic or local adverse events during the follow- up period.

Follow-up Visual Results (Figure 1)

At the 1-, 3- and 6-month follow-up, the median VA had improved from baseline (20/72) to 20/52, (range: 20/25 to 20/400), 20/45 (range: 20/20 to 20/400), and 20/56 (range: 20/20 to 20/400), respectively. The degree of improvement was statistically significant for 1 and 3 months, but not for 6 months ($P > 0.001$, $P = 0.001$, and $P = 0.05$, respectively, paired *t*-test).

At the 12-, 18- and 24-month follow-up, available for 15, 9 and 8 eyes, respectively, the median acuity was 20/85 (range: 20/40 to 20/400), 20/94 (range: 20/40 to 20/400), and 20/109 (range:

20/60 to 20/400). Compared to baseline, these VA were not statistically significant ($P=0.7$, $P=0.81$, $P=0.91$; paired t -test).

At 12 and 24 months, improvement of VA was seen in 40% and 37.5%, stable VA in 33.3% and 25% & decrease in VA in 26.7%, 37.5% of eyes, respectively.

At the 30-, 36- and 42-month follow-up, available for 4, 2 and 1 eyes, respectively, the median acuity was 20/100 (range: 20/40 to 20/200) and 20/265 (range: 20/200 to 20/400). The change in vision was not statistically significant ($P=0.26$ and $P=0.09$, respectively, paired t -test). At 30-month follow-up, 1 eye (25%) showed improvement of vision, , and 3 eyes (75%) showed decreased vision. 2 eyes that completed 36 months follow-up showed decrease in vision. At the 42-month follow-up, available for only a single eye, VA was stable from baseline (20/100).

Decrease in visual acuity

Kaplan-Meier cumulative survival curve (Figure 2) was used to display the change in vision over time. Five patients experienced a 3-line decrease in vision (deemed to be a “treatment failure”) during the follow-up period.. The cumulative survival at 6, 9, 12, and 30 months was 90%, 85%, 78% and 38%, respectively.

At the last follow up, decreased VA was attributable to disciform scar in 1, geographic atrophy in 3 and persistent SRF and IRF in 1 eye (receiving treatment).

Qualitative changes in OCT

Table 1 shows changes in OCT features between baseline and the last follow-up visit. At the last visit SRF was present in 4 eyes (20%), IRF in 12 eyes (60%), ICS in 11 eyes (55%) and PED in 15 eyes (75%).

Sample Cases

Case 1

An 81-year-old female presented with RAP in her left eye. She had a history of wet AMD with PED in the other eye. She received a single intra-vitreous bevacizumab injection. Her VA improved from 20/200 to 20/70, and she maintained that improvement for the entire follow-up period of 27 months. Preinjection fundus photographs, fluorescein angiogram, and OCT show a type III RAP with a serous PED, SRF, and cystoid macular edema (Figure 3, A–C). One month after injection, the PED and cystoids changes resolved, which was maintained throughout the follow-up period. (Figure 3,D)

Case 2

An 89-year-old man presented with RAP lesion in his right eye. He had a history of RAP lesion in the left eye treated with both PDT and intravitreal ranibizumab. He received 6 intravitreal ranibizumab injections over 42 months of follow-up. His VA was 20/60 at baseline and 20/100 at his last follow-up visit His preinjection fundus photograph, fluorescein angiogram, and OCT showed IRF with PED (Figure 4, A–B). At his last visit, OCT showed resolution of IRF with retinal thinning and RPE atrophy, consistent with progression to geographic atrophy, which explains the decreased vision. (Figure 4,C).

Discussion

In this retrospective review, eyes treated with intravitreal anti- VEGF for RAP had anatomic and visual improvement, which was maintained up to 2 years of follow up. All eyes (100%) had improved or stable VA at months 1 and 3; this figure declined to 62.5% at 2 years of follow-

up. Similar to the results reported by others,^{12–16} we found that eyes treated with either intravitreal bevacizumab^{12–15} or ranibizumab¹⁶ for RAP had significant short term functional benefit. Meyerle et al¹² showed that only 5.9% of eyes experienced decreased vision during the first 3 months of follow-up. Contrary to their results, our patients did not manifest any decrease in VA during the first 3 months.

We sought to compare our results to the analysis performed by the American Academy of Ophthalmology¹⁷ of different anti-VEGF treatment trials for AMD, none of which, to our knowledge, excluded RAP lesions. Table 2 summarizes the comparison, which shows similar visual results in our series. This comparison has to be taken in light of the differences in study design between our retrospective review where treatment decisions based on OCT, compared to MARINA and PIER, prospective studies, where monthly injections were performed regardless of OCT or VA. With these limitations in mind, our outcomes suggest that treatment based on OCT criteria (without initial loading dose), as performed in this study, can achieve acceptable visual and anatomic outcomes in RAP.

An interesting finding in our study was that 25% of eyes required a single treatment (see case 1). We were able to demonstrate this finding because our approach did not necessitate 3 initial loading injections, and as shown in that case, the patient developed geographic atrophy without recurrence over the course of subsequent 42 months. With the exception of the initial loading dose, our approach is similar to PrONTO.¹⁸ Over 24 months, median frequency of injections in our RAP cohort was 3 months, compared to 2 months in PrONTO patients with RAP (n=10). Reassuringly, the decreased frequency did not correlate with a decrease in outcome, with similar VAL outcome in the total AMD population in PrONTO at 24 months to our population (3 lines or more VA improvement in 43% compared to 37.5 % in our population).

Our functional results are similar to those of Rouvas et al,¹⁹ who compared intravitreal ranibizumab, intravitreal ranibizumab with PDT, and intravitreal triamcinolone with PDT for the treatment of RAP. Anti-VEGF monotherapy was associated with decrease in VA in 38.46% of their patients (26.7% in our group) at 12 months of follow-up

Since our study included patients who underwent FDOCT and time-domain OCT during their follow-up, we decided to study qualitative OCT parameters at baseline and last visit. Forooghian et al,²⁰ showed a significant difference between FDOCT and time-domain OCT in calculating macular thickness and volume. At baseline, 90% of our cohort had IRF, 75% ICS; and 65% had SRF. At the last visit, 60% of eyes had IRF, 55% ICS and only 20% SRF. Minimal improvement of PED was noted, with a decrease from 85% at baseline to 75% at the last visit. These results suggest that the fluid did not completely resolve, with the least effect on the PED. Our findings were generally biased toward detection of more fluid at the final visit since the last visit OCT was FDOCT with higher resolution and sensitivity. Keane et al²¹ performed a quantitative sub-analysis of OCT after treatment with ranibizumab for neovascular AMD using software for manual segmentation and grading (OCTOR, available at www.diesel.la). They similarly showed that, although neurosensory retinal edema and SRF showed an early reduction to nadir after the initiation of ranibizumab therapy, the effect was attenuated over time.

RAP lesions are considered “high-flow,”²² with histopathologic evidence of multiple growth factors, suggesting an ischemic and inflammatory component to the development and progression of RAP.²³ Anti-VEGF monotherapy targets only one component of RAP lesions with early improvement of vision. Long term results suggest that anti-VEGF alone may not be sufficient to maintain anatomic and functional improvement.

This review has several limitations related to the retrospective nature, small sample size, non standard protocol of VA measurements, use of both FD and time-domain OCT, and qualitative

OCT assessment. Our OCT results were biased toward better detection of fluid at the final visit, with residual SRF in 20%, IRF in 60% and PED in 75% of eyes. The presence of fluid on follow up is an expected corollary of our treatment approach as compared to other approaches, where patients are continued on treatment while OCT is dry (treat and extend).²⁴

Another limitation is the lack of eyes with stage 1 RAP lesions, which may be more responsive to anti-VEGF therapy. This may have biased our results towards a worse outcome, and may explain the long term decreased vision in 37.5% of patients followed to 2 years. In contrast, the long term functional outcome of untreated eyes with RAP appears dismal. Viola et al reported that most patients presenting with Stage I (6 of 9) and all of Stage II rapidly progressed to visual loss within 6 months. In 13 eyes (81%), VA deteriorated by 2 or more lines at 6 months.²⁵

To our knowledge, this is the longest follow-up study for RAP lesions treated with anti-VEGF monotherapy. Overall, our findings suggest that OCT-based anti-VEGF monotherapy for RAP represents an acceptable treatment approach and questions the need for 3 loading doses of anti-VEGF. Prospective studies with larger sample size, exploring various combination therapies and perhaps more aggressive anti-VEGF treatment approaches may help resolve the controversies surrounding RAP.

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References

1. Yannuzzi LA, Negrão S, Iida T, et al. Retinal angiomatous proliferation in age-related macular degeneration. *Retina* 2001;21:416–434. [PubMed: 11642370]
2. Monson DM, Smith JR, Klein ML, Wilson DJ. Clinicopathologic correlation of retinal angiomatous proliferation. *Arch Ophthalmol* 2008;126:1664–1668. [PubMed: 19064845]
3. Gross NE, Aizman A, Brucker A, et al. Nature and risk of neovascularization in the fellow eye of patients with unilateral retinal angiomatous proliferation. *Retina* 2005;25:713–718. [PubMed: 16141858]
4. Bottoni F, Massacesi A, Cigada M, et al. Treatment of retinal angiomatous proliferation in age-related macular degeneration: a series of 104 cases of retinal angiomatous proliferation. *Arch Ophthalmol* 2005;123:1644–1650. [PubMed: 16344434]
5. Bressler NM. Retinal anastomosis to choroidal neovascularization: a bum rap for a difficult disease. *Arch Ophthalmol* 2005;123:1741–1743. [PubMed: 16344449]
6. Boscia F, Parodi MB, Furino C, Reibaldi M, Sborgia C. Photodynamic therapy with verteporfin for retinal angiomatous proliferation. *Graefes Arch Clin Exp Ophthalmol* 2006;244:1224–1232. [PubMed: 16525824]
7. Gragoudas ES, Adamis AP, Cunningham ET Jr, et al. Pegaptanib for neovascular age-related macular degeneration. *N Engl J Med* 2004;351:2805–2816. [PubMed: 15625332]
8. Spaide RF, Laud K, Fine HF, et al. Intravitreal bevacizumab treatment of choroidal neovascularization secondary to age-related macular degeneration. *Retina* 2006;26:383–390. [PubMed: 16603955]
9. Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006;355:1419–1431. [PubMed: 17021318]
10. Kaiser PK, Blodi BA, Shapiro H, Acharya NR. MARINA Study Group. Angiographic and optical coherence tomographic results of the MARINA study of ranibizumab in neovascular age-related macular degeneration. *Ophthalmology* 2007;114:1868–1875. [PubMed: 17628683]

11. Bashshur ZF, Haddad ZA, Schakal A, et al. Intravitreal bevacizumab for treatment of neovascular age-related macular degeneration: a one-year prospective study. *Am J Ophthalmol* 2008;145:249–256. [PubMed: 18067876]
12. Meyerle CB, Freund KB, Iturralde D, et al. Intravitreal bevacizumab (Avastin) for retinal angiomatous proliferation. *Retina* 2007;27:451–457. [PubMed: 17420697]
13. Joeres S, Heussen FM, Treziak T, Bopp S, Joussen AM. Bevacizumab (Avastin) treatment in patients with retinal angiomatous proliferation. *Graefes Arch Clin Exp Ophthalmol* 2007;245:1597–1602. [PubMed: 17437123]
14. Costagliola C, Romano MR, dell'Omo R, Cipollone U, Polisena P. Intravitreal bevacizumab for the treatment of retinal angiomatous proliferation. *Am J Ophthalmol* 2007;144:449–451. [PubMed: 17765426]
15. Ghazi N, Knape R, Kirk T, Tiedeman J, Conway B. Intravitreal bevacizumab (avastin) treatment of retinal angiomatous proliferation. *Retina* 2008;28:689–695. [PubMed: 18463511]
16. Lai TY, Chan WM, Liu DT, Lam DS. Ranibizumab for retinal angiomatous proliferation in neovascular age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol* 2007;245:1877–1880. [PubMed: 17901972]
17. Ip MS, Scott IU, Brown GC, et al. Anti-vascular endothelial growth factor pharmacotherapy for age-related macular degeneration. a report by the American Academy of Ophthalmology. *Ophthalmology* 2008;115:1837–1846. [PubMed: 18929163]
18. Lalwani G, Rosenfeld P, Fung A, et al. A variable-dosing regimen with intravitreal ranibizumab for neovascular age-related macular degeneration: year 2 of the PrONTOn study. *Am J Ophthalmol* 2009;148:43–58. [PubMed: 19376495]
19. Rouvas A, Papakostas T, Vavvas D, et al. Intravitreal ranibizumab, intravitreal ranibizumab with PDT, and intravitreal triamcinolone with PDT for the treatment of retinal angiomatous proliferation. *Retina*. in Press.
20. Forooghian F, Cukras C, Meyerle C, Chew EY, Wong WT. Evaluation of time domain and spectral domain optical coherence tomography in the measurement of diabetic macular edema. *Invest Ophthalmol Vis Sci* 2008;49:4290–4296. [PubMed: 18515567]
21. Keane PA, Liakopoulos S, Ongchin SC, et al. Quantitative subanalysis of optical coherence tomography after treatment with ranibizumab for neovascular age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2008;49:3115–3120. [PubMed: 18408176]
22. Bearely S, Espinosa-Heidmann DG, Cousins SW. The role of dynamic indocyanine green angiography in the diagnosis and treatment of retinal angiomatous proliferation. *Br J Ophthalmol* 2008;92:191–196. [PubMed: 17962393]
23. Shimada H, Kawamura A, Mori R, Yuzawa M. Clinicopathological findings of retinal angiomatous proliferation. *Graefes Arch Clin Exp Ophthalmol* 2007;245:295–300. [PubMed: 16738855]
24. Spaide R. The as-needed treatment strategy for choroidal neovascularization: A feedback-based treatment system. *Am J Ophthalmol* 2007;143:679–680. [PubMed: 17386275]
25. Viola F, Massacesi A, Orzalesi N, et al. Retinal angiomatous proliferation natural history and progression of visual loss. *Retina* 2009;29:732–739. [PubMed: 19516115]

Figure 1.

Chart showing visual outcome of retinal angiomatous proliferation patients treated with anti-VEGF.

Figure 2.
Kaplan-Meier cumulative survival curve showing the visual decrease over time of follow-up.

Figure 3.

Red-free photograph, fluorescein angiogram (FA) and optical coherence tomography (OCT) of case 1 A, red-free photograph of retinal angiomatous proliferation (RAP) lesion with intraretinal hemorrhage, retinal angiomatous vessel (arrowhead) and hard exudates at the macular area. B. late frame FA showing dye leakage from the RAP lesion (arrowhead) and pooling within pigment epithelium detachment (PED) (white arrows). C. OCT vertical section through the lesion showing intraretinal fluid (IRF), intraretinal cystoid spaces (ICS) (white arrows), subretinal fluid (SRF) (blocked arrow) and fibrovascular PED (stars). D. OCT 27 months after treatment with absence of IRF, ICS, SRF and PED.

Figure 4.

A. Fluorescein angiography of retinal angiomatous proliferation (RAP) lesion of case 2, showing focal leakage at the site of RAP lesion (arrowhead). B. optical coherence tomography (OCT) of the lesion showing intraretinal fluid (IRF) and pigment epithelium detachment (PED) (white arrows). C. OCT at final visit, after six intravitreal ranibizumab injections over 42 months with disappearance of the IRF, retinal thinning and RPE atrophy, consistent with progression to geographic atrophy (white arrows).

Table 1
Changes in optical coherence tomography features between baseline and last visit follow up.

No	Eye Tested	Baseline				Last Visit			
		SRF	IRF	ICS	PED	SRF	IRF	ICS	PED
1	OS	NO	YES	YES	YES	NO	YES	YES	YES
2	OS	YES	YES	YES	YES	NO	NO	NO	NO
3	OD	YES	YES	YES	YES	YES	YES	YES	YES
4	OS	YES	YES	YES	YES	NO	YES	YES	YES
5	OS	YES	YES	YES	YES	NO	YES	YES	YES
6	OS	YES	NO	NO	NO	NO	NO	NO	NO
7	OD	YES	YES	YES	YES	NO	NO	NO	YES
8	OD	YES	YES	YES	YES	NO	NO	NO	YES
9	OS	NO	YES	YES	YES	NO	YES	YES	YES
10	OS	YES	YES	YES	YES	NO	NO	NO	NO
11	OS	NO	YES	YES	NO	NO	YES	NO	NO
12	OD	NO	YES	NO	YES	NO	NO	NO	YES
13	OD	YES	YES	YES	YES	NO	YES	YES	YES
14	OD	YES	YES	YES	YES	YES	YES	YES	YES
15	OD	YES	YES	YES	YES	YES	YES	YES	YES
16	OS	NO	YES	YES	YES	NO	YES	YES	YES
17	OD	YES	YES	YES	YES	YES	YES	YES	YES
18	OS	NO	YES	NO	YES	NO	YES	YES	YES
19	OD	YES	NO	NO	YES	NO	NO	NO	YES
20	OS	NO	YES	NO	NO	NO	NO	NO	NO

SRF: Subretinal Fluid, IRF: intraretinal fluid, ICS: intraretinal cystoid spaces, PED: pigment epithelium detachment.

Table 2

Comparison of visual outcome results in current study to previous reports.

Study	medication	Type of CNV	Treatment Design	Follow-up	Improvement of Vision *
MARINA	ranibizumab	Minimally Classic or Occult CNV	Monthly injections	1 year	34% of cases treated with 0.5 mg/0.1 ml
					25% of cases treated with 0.3 mg/0.1 ml
				2 years	33% of cases treated with 0.5 mg/0.1 ml
PIER	ranibizumab	Minimally Classic or Occult CNV	Monthly injections	1 year	26% of cases treated with 0.3 mg/0.1 ml
					13% of cases treated with 0.5 mg/0.1 ml
PRONTO	ranibizumab	Subfoveal CNV	3 initial loading injections then retreatment based on OCT criteria	2 years	12% of cases treated with 0.3 mg/0.1 ml
					43% of cases treated with 0.5 mg/0.1 ml
Current Study	ranibizumab or bevacizumab	RAP	Retreatment based on OCT criteria (without initial loading doses)	1 year	40% of cases
				2 years	37.5% of cases

* Improvement of vision defined as halving of the visual angle or gain of 15 letters or more