
Bugra KARASU1, Ozgur ARTUNAY2

ABSTRACT

Purpose: To compare visual and anatomical results of anti-vascular endothelial growth factor (VEGF) combined with photodynamic therapy (PDT) versus only performing anti-VEGF therapy in eyes with polypoidal choroidal vasculopathy (PCV).

Materials and Methods: Retrospective review of 60 PCV patients who underwent anti-VEGF combined with PDT (Group 1) or solely performing anti-VEGF therapy (Group 2) were enrolled. The best corrected visual acuity (BCVA), central macular thickness (CMT), presence of subretinal fluid (SF) were compared among the groups during the follow-up periods at baseline, 1st month, 3rd month, 6th month, 9th month, 12th month, 18th month, 24th month and final visit, respectively.

Results: The mean age of the patients was 71.96 ± 8.50 years (range, 52-88 years), and the mean follow-up period was 53.83 ± 14.86 (range, 20-85 months). The mean number of injections was observed as 10.56 ± 1.88 (range, 7 -15) in the first group and 11.83 ± 2.61 (range, 7 -17) in the second group, respectively (p = 0.039). In group 1, BCVA decreased from the logarithm of the minimum angle resolution (logMAR) of 0.59 ± 0.39 to 0.70 ± 0.41 logMAR in the final examination (p = 0.016), CMT initial 355.56 ± 95.54 μm decreased from to 296.76 ± 105.03 μm at the last examination (p <0.001), the presence of SRF showed a statistically significant decrease in follow-up periods compared to the initial period (p <0.001). In group 2, BCVA decreased from initial 0.65 ± 0.61 logMAR to 0.82 ± 0.56 logMAR in the final examination (p <0.001), CMT decreased from baseline 372.60 ± 114.21 μm to 287.06 ± 64.32 μm at the last examination (p = 0.001), the presence of SF showed a statistically significant decrease in follow-up periods compared to the initial period (p <0.001). In the last examination, there was no statistically significant difference between the groups in terms of presence of SF (p = 0.305).

Conclusion: Both full-dose PDT combined with anti-VEGF and only anti-VEGF applications are effective in the treatment of PCV. There was no significant difference in visual or anatomical results among the two groups. However, we observed that full dose PDT administration combined with anti-VEGF reduces the need for anti-VEGF usage.

Keywords: Polypoidal choroidal vasculopathy, photodynamic therapy, ranibizumab, aflibercept.

IINTRODUCTION

Polypoidal choroidal vasculopathy (PCV) is a chorioretinal disorder common in Asians. It was first described by Yannuzzi in 1990 as a clinical entity different from age-related macular degeneration (AMD) which is characterized by serous and hemorrhagic pigment epithelium detachment (PED)1, 2. In addition to macular involvement, it is characterized by two distinct vascular network: multiple lesions classified by complex and branching vascular network with ill-defined margins and polypoidal lesions classified by reddish-orange perimacular or peripapillary lesions with well-defined margins2.

The diagnosis of PCV is made by indocyanine green angiography (IGA) which clearly shows abnormal
vascular network. Visual acuity is preserved and macular involvement is lacking in approximately one-half of patients with PCV; however, loss of vision is observed in majority of remaining patients due to frequent, recurrent hemorrhages and exudate involving macula.

In PCV, treatment options include photodynamic treatment with verteporfin (PDT), intravitreal anti-vascular endothelial growth factor (VEGF) agents and thermal laser photocoagulation (TLP). In many studies, contradictory outcomes have been reported, particularly at long-term, by these treatment modalities.

Some authors reported promising short-term results with intravitreal bevacizumab (IVB) plus PDT combination in the treatment of PCV. In their study, Ruamviboonsuk et al. reported results of 12 eyes with PCV treated by combination therapy (PDT plus intravitreal ranibizumab (IVR)). The study showed encouraging results in visual recovery, reduction in subretinal hemorrhage incidence and polyp recurrence when compared to previous studies. However, there is no sufficient data for efficacy and safety of the combination therapy. In clinical practice, clinicians dealt with eyes with recurrent PCV following first PDT or eyes with chronic PCV refractory to anti-VEGF agents; nevertheless, there is limited data regarding efficacy of the combination therapy.

Photodynamic therapy is a non-invasive photochemical induction that leads localized oxidative injury in tissues following non-thermal photo-stress. In PDT, vaso-occlusion occurs via damage on vascular endothelial membrane resulting from platelet adhesion and degranulation. Intra-luminal vaso-occlusion occurs via removal of pathological neovascularization by intravenous photo-sensitizing substance (verteporfin) administration and use of lipophilic compounds that readily fuse with lipid cell membrane of endothelial vascular wall. It is known that PDT-induced occlusion have no effect on intact photoreceptors at choriocapillaris beneath normal retina and inhibits and treats choroidal neovascularization (CNV) by minimally damage in retina pigment epithelium (RPE) and photoreceptors at upper layers as a result of use of benzoporphyrin-derivative.

In this study, it was aimed to investigate efficacy and safety of anti-VEGF treatment alone compared to anti-VEGF plus PDT combination in symptomatic patients with PCV.

MATERIALS AND METHODS

In this study, we retrospectively reviewed medical records of 60 patients with PCV including 30 patients treated with anti-VEGF agent plus full-dose PDT (group 1) and 30 patients treated with anti-VEGF therapy alone (group 2) between June, 2010 and March, 2020. The study was approved by Ethics Committee on Clinical Research (approval#2019-07-08/08.04/2019). All patients gave written informed consent. The study was conducted in accordance to tenets of Helsinki Declaration.

The inclusion criteria were as follow:

1) Presence of symptomatic subfoveal PCV
2) Presence of exudative or hemorrhagic features with macular involvement
3) At least 24 months of follow-up.

The diagnosis of PCV was made based on presence of branching vascular network that terminated as polypoidal swelling on IGA.

The PCV was classified into 2 types according to IGA characteristics:

Type 1 PCV: Polyp or polyps having vascular network with marked branching (vascular network from both supplying and draining vessels).

Type 2 PCV: Polyp or polyps having no vascular network with branching (no supplying vessel)

In this study, there was subfoveal polypoidal lesions, a branching vascular network or type 1 and/or type 2 CNV. Eyes with additional macular disorders (AMD, pathological myopia, idiopathic CNV, angioid streaks or other secondary) CNV were excluded. In addition, eyes with history of intraocular surgery (vitrectomy) other than cataract were also excluded.

At baseline, best-corrected visual acuity (BCVA) assessment using Snellen charts, intraocular pressure (IOP) measurement by Goldmann applanation tonometry, indirect ophthalmoscopy, split-lamp biomicroscopy with contact lens, spectral domain-optical coherence tomography (SD-OCT) were performed while OCT-angiography, fundus fluorescein angiography (FFA) and IGA were also performed as needed.

In both groups, 3 monthly anti-VEGF injections were administered initially as loading dose; followed by pro-re-nata (PRN) regimen. In patients with impaired vision secondary to PCV, PDT in combination with either IVR (0.5 mg) injection or intravitreal aflibercept (2 mg/0.05 mL) injection (IVA) as intravitreal anti-VEGF agents or intravitreal anti-VEGF agent alone was administered. Intra-vitreal injections were administered under sterile conditions and prophylactic topical antibiotic were prescribed for one week after injection.
In group 1, regular-flow, full-dose PDT was applied using 689 nm diode laser unit one week after intravitreal anti-VEGF injection. Largest linear size of interest was selected based on previous FFA and IGA images. All polypoidal lesions (type 1 and 2) detected with IGA, all branching vascular network lesions, and all type 1 and 2 CNVs detected with FFA were included. No PDT was applied if no CNV was detected within serous PED lesion.

Modified PDT (attenuated total light energy 25 J/cm² and laser intensity 300 mW/cm²) using standard verteporfin dose (6 mg/m²) and standard duration of laser emission (83 sec) was applied as full-dose PDT.

In both groups, central macular thickness (CMT), subretinal fluid (SF) presence and BCVA were assessed at baseline (the day before anti-VEGF injection and on months 1, 3, 6, 9, 12, 18 and 24 and in final visit by SD-OCT. Mean number of injections were also recorded. If recurrent or residual polypoidal lesions were observed on IGA and exudative changes were recognized on SD-OCT, additional anti-VEGF injection plus PDT was applied in the group 1 whereas additional anti-VEGF injection alone was administered in the group 2. When residual polypoidal lesions were detected on IGA but not exudative change on SD-OCT, no additional therapy was given and the patient was re-assessed in the next visit. When only recurrent or residual exudative changes secondary to PCV were observed on SD-OCT, one additional anti-VEGF injection was administered even in the absence of polypoidal lesions or type 1 or type 2 CNV was observed on FFA or IGA. A comprehensive ophthalmological examination was performed one month after additional anti-VEGF injection.

Statistical analysis

Best corrected visual acuity was measured using Snellen charts and transformed into Log MAR units for statistical purposes. BCVA and anatomical changes during follow-up period were compared using MANOVA test. Normal data distribution was assessed using Kolmogorov-Smirnov test. Mean number of injections was compared between groups using Student’s t test. Pearson’s correlation rank test was used to analyze correlations among parametric data. Data were analyzed using IBM SPSS version 22.0 (SPSS, IBM, Chicago, IL). A p value <0.05 was considered as statistically significant.

FINDINGS

The mean age was 71.96±8.50 years (range: 52-88 years) in the study population. There were 47 men (78%) and 13 women (22%). Of the eyes included, 30 (50%) were right eye while 30 (50%) were left eye. Mean follow-up was 53.83±14.86 months (range: 20-85 months).

There were no significant differences in age (p=0.529), mean follow-up (p=0.251), PCV type (p=0.545), side (p=0.306), initial BCVA (p=0.302), CMT (p=0.589) and SF (p=0.351) between groups (Student’s t test).

No significant change was observed in IOP values during follow-up (p>0.05, MANOVA test).

Table 1 summarizes clinical data.

In group 1 (anti-VEGF plus PDT); mean number of injections was 10.56±1.88 (7-15); mean BVCA was 0.59 ± 0.39 log MAR, 0.49 ± 0.42 log MAR, 0.56 ± 0.37 log MAR, 0.52 ± 0.34 log MAR, 0.57 ± 0.38 log MAR, 0.61 ± 0.48 log MAR, 0.67 ± 0.45 log MAR and 0.71 ± 0.49 at baseline, on months 1, 3, 6, 9, 12, 18, 24 and in final visit, respectively (p=0.016; MANOVA test); mean CMT was 355.56 ± 95.54 μm, 302.10 ± 61.49 μm, 329.23 ± 95.45 μm, 312.76 ± 71.95 μm, 348.36 ± 100.26 μm, 308.36 ± 92.95 μm, 307.60 ± 102.88 μm, 317.33 ± 104.55 μm and

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Gender (female (f) / male (m))</td>
<td>8/22&lt;sup&gt;f&lt;/sup&gt;</td>
<td>5/25&lt;sup&gt;m&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Age (mean ±SD)</td>
<td>71.26±7.26</td>
<td>72.66±9.66</td>
<td>0.529</td>
</tr>
<tr>
<td>Duration of follow-up (mean ±SD)</td>
<td>51.56±14.56</td>
<td>55.80±14.54</td>
<td>0.251</td>
</tr>
<tr>
<td>Side (right (r) / left (l))</td>
<td>13/17&lt;sup&gt;r&lt;/sup&gt;</td>
<td>17/13&lt;sup&gt;l&lt;/sup&gt;</td>
<td>0.306</td>
</tr>
<tr>
<td>Number of injections (mean ±SD)</td>
<td>10.56±1.88</td>
<td>11.83±2.61</td>
<td>0.039&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>Number of injections (range)</td>
<td>7 to 15</td>
<td>7 to 17</td>
<td></td>
</tr>
<tr>
<td>PCV tipi (type 1/ type2)</td>
<td>24/6</td>
<td>22/8</td>
<td>0.545</td>
</tr>
</tbody>
</table>

PDT: photodynamic therapy; SD: standard deviation; VEGF: vascular endothelial growth factor
<sup>f</sup> female, <sup>m</sup> male; <sup>r</sup> right, <sup>l</sup> left; PCV, polypoidal choroidal vasculopathy
<sup>*</sup>Student’s t test
296.76 ± 105.03 μm at baseline, on months 1, 3, 6, 9, 12, 18, 24 and in final visit, respectively (p<0.001; MANOVA test).

In group 2 (anti-VGEF alone); mean number of injections was 10.56±1.88 (7-15); mean BVCA was 0.65 ± 0.61 log MAR, 0.57 ± 0.42 log MAR, 0.61 ± 0.46 log MAR, 0.63 ± 0.47 log MAR, 0.60 ± 0.51 log MAR, 0.63 ± 0.45 log MAR, 0.61 ± 0.45 log MAR, 0.67 ± 0.45 log MAR and 0.82 ± 0.56 log MAR at baseline, on months 1, 3, 6, 9, 12, 18, 24 and in final visit, respectively (p<0.001; MANOVA test); mean CMT was 372.60 ± 114.21 μm, 353.83 ± 119.33 μm, 343.83 ± 100.53 μm, 343.96 ± 96.29 μm, 357.66 ± 118.82 μm, 319.30 ± 88.04 μm, 315.16 ± 101.96 μm, 308.16 ± 112.26 μm and 287.06 ± 64.32 μm at baseline, on months 1, 3, 6, 9, 12, 18, 24 and in final visit, respectively (p<0.001; MANOVA test).

When groups were compared at assessment time points, there was significant improvement in SF in group 1 on month 6 (p=0.030; Student’s t test). A positive correlation was detected between BCV As obtained at baseline and in final visit (r=0.383; p=0.003; Pearson’s correlation rank test). It was found that final BCVA was decreased by increasing baseline CMT (r= -0.336; p=0.009; Pearson’s correlation rank test). A positive correlation was detected between CMTs obtained at baseline and in final visit (r=0.256; p=0.048; Pearson’s correlation rank test). In the study, PDT plus anti-VGEF combination decreased need for anti-VEGF (r=-0.272; p=0.036; Pearson’s correlation rank test).

Figure 2 presents BCVA, CMT and SF count. Table 2 presents BCVA, CMT and SF values at baseline and during follow-up.

No serious ocular adverse effect such as endophthalmitis or retinal detachment was observed. Despite loading dose and PRN regimen, SF presence was found to be higher in both groups. There was SF in 25 eyes (83%) in group 1 whereas 27 eyes (90%) in group 2. In group 1, 17 eyes (56%) were treated with IVA whereas 13 eyes (44%) by IVR. In 2 eyes, anti-VEGF treatment was switched to IVA from IVR. In group 1, 15 eyes (50%) were treated with IVRA whereas 15 eyes (50%) by IVR. In 3 eyes, anti-VEGF treatment was switched to IVA from IVR. There was no significant difference in injection types and switch rate (p>0.05; Student’s t test).

**DISCUSSION**

In this study, mean number of injections was 10.56±1.88 (range: 7-15) in anti-VEGF plus PDT group and 11.83±2.61 (range: 7-17) in anti-VEGF alone group, indicating decreased anti-VEGF need by PDT. Baseline BCVA, CMT and SF values were comparable between groups. In the anti-VEGF plus PDT group, worsening in final BCVA was delayed or prevented. We attributed this finding to decrease in SF presence and resultant reduction in the number of activation. In anti-VEGF plus PDT group, SF tended to decrease in all time points. In anti-VEGF alone group, no improvement was observed in SF until month 9; thus, there was no improvement in final BCVA gain. Although similar results were observed regarding anatomical and visual success in both groups, less anti-VEGF injection was required to achieve same effect in combined treatment group. In the literature, several studies reported efficacy of anti-VEGF agents in the treatment of exudative PCV 21-29. In a recent study, Cheng et al. reported results of IVB
injections at year 1 in PCV treatment. Authors reported that mean BCVA (Log MAR was improved to 0.67±0.51 from 0.79±0.42 by mean injection number of 3.3 over 12 months; however, complete regression in polypoidal lesions was confirmed in only 16.1% of eyes 29.

Kokame et al. showed that monthly ranibizumab injections successfully decreased exudative changes in PCV. However, regression was achieved in only 33% polypoidal lesions even with month injections and branching vascular network persisted in all eyes 27. Although anti-VEGF agents can lead BCVA gain with reduction in exudative changes secondary anti-VEGF agents, their effect on regression of vascular lesion seemed to be limited in PCV 26-30. On contrary, in a series of studies, promising results were shown in vascular lesions of PCV and a few PDT could generally achieve complete regression of polypoidal lesions 31-35.

In a study by Chan et al., it was shown that complete regression was achieved in 95% of PCV eyes underwent PDT 27. Although all polypoidal lesions regressed following PDT, effects on branching vascular network were limited and polypoidal lesions can recur ≥1 years after PDT 12-14, 33, 34, 36.

It is anticipated that anti-VEGF agents which lead rapid recovery of exudative changes in combination therapy (anti-VEGF plus PDT) would contribute permanent recovery in visual improvement together with regression polypoidal lesions due to PDT 21-29, 31-35. In addition, it was reported that visual improvement was more favorable in eyes with PCV than those with AMD after PDT; Gomi et al. showed that median change in BCVA was 7.0 letters in AMD and 8.0 letters in PCV 34.

Moreover, it seems reasonable to administer anti-VEGF agent before PDT since VEGF expression is increased.

In a study by Hikichi et al. it was reported that, in PCV treatment, 3 monthly IVR injections and extended injection program was effective in preserving BCVA but polypoidal lesions regression was lower when compared to PDT (40%) 41.

In the VIEW studies, it was shown that aflibercept is effective in all subgroups of neovascular AMD including PCV. Although many studies showed that aflibercept treatment in PCV resulted in favorable visual gain and polyp regression, these studies are limited with retrospective design42, 43.

The PLANET study is a randomized, clinical trial conducted to assess efficacy and safety of IVA in PCV. In the PLANET study, improvement was achieved in visual and/or functional outcomes >85% and no finding of leakage was observed in polypoidal lesions in >80% of patients treated with IVA monotherapy. Since less than 15% of patient fulfilled minimal response criteria for PDT, no conclusion was drawn on effects of adding PDT 44. There is limited data about combination therapy in PCV refractory to anti-VEGF therapy. This study showed that when PDT was combined either ranibizumab or aflibercept as anti-VEGF agents, somewhat visual improvement was achieved in PCV eyes even in those previously treated with anti-VEGF agents. Since anti-VEGF agents have limited

Immediately after PDT6-8, 11, 28, 37. In a study using bevacizumab plus PDT for PCV, Sato et al. reported that mean BCVA gain was 2.69 lines and that there was ≥3 lines improvement in 51.7% of patients. In addition, in a study using ranibizumab plus PDT combination in 12 eyes with PCV, Ruamviboonsuk et al. reported ≥15 letters improvement in 58.3% of eyes on month 12 7, 11.

The EVEREST study is randomized, controlled trial designed to compare PDT alone, IVR alone and PDT plus IVR combination in 3 groups of PCV eyes. PDT alone or PDT plus ranibizumab (0.5 mg) was found to be superior to ranibizumab monotherapy in regression of polyps in patients with symptomatic macular PCV on month 6 38.

Fujisan study is a prospective, randomized study designed to assess PDT timing by comparing IVR plus PDT at baseline and delayed PDT. When PDT alone and PDT plus IVR were compared with IVR alone, it was seen that regression rate for polypoidal lesions was higher but did not reach statistical significance and there was no significant difference in BCVA improvement among 3 groups. Although there was no significant difference in BCVA improvement and polyp regression rate among groups, number of ranibizumab injections was significantly lower in PDT group compared to IVR group at year 1 40. We also found similar results together with favorable effect of PDT on long-term follow-up.

In a study by Hikichi et al. it was reported that, in PCV treatment, 3 monthly IVR injections and extended injection program was effective in preserving BCVA but polypoidal lesions regression was lower when compared to PDT (40%) 41.

In the VIEW studies, it was shown that aflibercept is effective in all subgroups of neovascular AMD including PCV. Although many studies showed that aflibercept treatment in PCV resulted in favorable visual gain and polyp regression, these studies are limited with retrospective design42, 43.

The PLANET study is a randomized, clinical trial conducted to assess efficacy and safety of IVA in PCV. In the PLANET study, improvement was achieved in visual and/or functional outcomes >85% and no finding of leakage was observed in polypoidal lesions in >80% of patients treated with IVA monotherapy. Since less than 15% of patient fulfilled minimal response criteria for PDT, no conclusion was drawn on effects of adding PDT 44. There is limited data about combination therapy in PCV refractory to anti-VEGF therapy. This study showed that when PDT was combined either ranibizumab or aflibercept as anti-VEGF agents, somewhat visual improvement was achieved in PCV eyes even in those previously treated with anti-VEGF agents. Since anti-VEGF agents have limited

Figure 3: Central macular thickness values during follow-up.
effect on polypoidal lesions, combination therapy can be
treatment option when recurrent or persistent exudative
changes are seen after anti-VEGF therapies 1-29.

In a study on eyes with neovascular AMD, Astam et al.
assessed outcomes of PDT alone and combination therapy
in cases diagnosed as retinal angiomatous proliferation
(RAP) and PCV. In that study, PDT alone or PDT plus
IVB therapy was used in 8 eyes of 7 cases with RAP and
3 eyes of 3 cases with PCV. When all eyes with RAP was
assessed, visual acuity was improved in 4 of 8 eyes (50%);
remained stable in one eye (12.5%) and decreased in 3
eyes (37.5%). Anatomical success was achieved in 75%
of eyes with foveal contour formation in 6 eyes on SD-
OCT. PDT or combination treatment was given to 3 eyes
of 3 cases with PCV. Visual acuity was improved in 2 eyes
(66%) while remained stable in one eye (33%). Anatomical
success was achieved in 66% of eyes with foveal contour
formation in 2 eyes on SD-OCT. In most studies, effects of
PDT on anatomical and visual success as well as need for
anti-VEGF need were observed 30.

Rates of RPE tear, subretinal hemorrhage, fibrosis or
atrophy were higher in patients treated with verteporfin 36.
In our study, no intraocular complication or adverse effect
secondary to PDT was observed in two groups. Significant
reduction was observed in CMT and SF in both groups
in all time points other than month 9 while significant
improvement was observed in BCVA in both groups.
However, to achieve similar effect, number of injections
was lower in anti-VEGF plus PDT group when compared
to anti-VEGF group.

The advantages of our study included long-term follow-up
and being one of the rare studies in this field in our country;
thus, it can provide important data regarding treatment
response in PCV in Turkey. And also has some limitations
including small sample size, lack of pre- and post-
treatment measurements of polyp size and retrospective
design. There is a need for larger, prospective studies in
the management of PCV. In conclusion, no significant
difference was detected between groups regarding anatomical
and visual outcomes in our study. Significant
differences were detected in anti-VEGF plus PDT when
compared to anti-VEGF alone. Based on these results, anti-
VEGF plus PDT combination decreases need for injections
and aids achievement of visual and anatomical success.

REFERENCES

1. Spaide RF, Yannuzzi LA, Slakter JS, et al. Indocyanine
green videoangiography of idiopathic poloidal choroidal

2. Yannuzzi LA, Sorenson J, Spaide RF, et al. Idiopathic poloidal

3. Yannuzzi LA, Ciardella A, Spaide RF, et al. The expanding clinical
spectrum of idiopathic poloidal choroidal vasculopathy. Arch

2002.

choroidal vasculopathy: Evidence-based guidelines for clinical

photodynamic therapy and intravitreal bevacizumab for
idiopathic poloidal choroidal vasculopathy: oneyear follow-

therapy with verteporfin and intravitreal bevacizumab
for poloidal choroidal vasculopathy. Am J Ophthalmol

bevacizumab combined with photodynamic therapy for
poloidal choroidal vasculopathy. Am J Ophthalmol
2010;150(1):48-54.

following combined intravitreal bevacizumab and photodynamic
therapy for poloidal choroidal vasculopathy. Doc Ophthalmol

combined with intravitreal injection of vascular endothelial
growth factor antibody for poloidal choroidal vasculopathy.
Ophthalmologica 2011;225(3):169-175.

Photodynamic therapy combined with ranibizumab for poloidal
choroidal vasculopathy: results of a 1-year preliminary study. Br

photodynamic therapy for poloidal choroidal vasculopathy.

outcomes after photodynamic therapy in age-related macular
degeneration patients with or without poloidal choroidal

therapy of poloidal choroidal vasculopathy. Retina

mechanisms of photodynamic therapy of tumors. Pho-


of experimental choroidal neovascularization. Arch Ophthalmol

targeting in photodynamic occlusion of subretinal vessels.


