Efficacy of Brolucizumab in Polyp Regression of Treatment-Naïve Polypoidal Choroidal Vasculopathy and Its Effect on One-Year Treatment Outcome

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Running title: Brolucizumab in Polypoidal choroidal vasculopathy
ABSTRACT

Purpose: To evaluate the efficacy of intravitreal brolucizumab in polyp regression of treatment-naïve polypoidal choroidal vasculopathy (PCV) patients and its effect on one-year treatment outcome.

Methods: Medical records of 31 treatment-naïve PCV patients, who received three monthly intravitreal brolucizumab injections followed by as-needed injections for at least a year, were retrospectively reviewed. Visual and anatomical outcomes were evaluated at 3-month, 6-month, and 12-month. Complete polyp regression rate and percentage change of vascular lesion and polyp area were evaluated after three monthly injections of brolucizumab. The effect of complete polyp regression and the impact of vascular lesion and polyp reduction rate on one-year treatment outcome were also evaluated. Additionally, the incidence of brolucizumab-related intraocular inflammation (IOI) and its clinical course were examined.

Results: In terms of visual outcome, best-corrected visual acuity (BCVA) significantly improved after 12 month follow-up \( (p<0.001) \). In terms of anatomical outcome, central macular thickness (CMT) and central choroidal thickness (CCT) significantly decreased after 12 month follow-up \( (p<0.001) \). Complete polyp regression was observed in 74.2% \( (23/31) \) after three monthly injections. Group with complete polyp regression had a higher rate of achieving dry macula at 3-month \( (p=0.026) \) and fewer number of injections \( (p<0.001) \) compared to the group without complete polyp regression. Higher polyp reduction rate was significantly associated with higher CMT change from baseline at 3-month \( (p=0.048) \) while higher vascular lesion reduction rate was significantly associated with higher CMT change from baseline at 12-month \( (p=0.031) \) and fewer number of injections \( (p=0.012) \). Brolucizumab related IOI occurred in one eye \( (1/31, 3.2\%) \).

Conclusion: Intravitreal brolucizumab injection effectively improved visual and anatomical outcomes and achieved significant polyp regression in treatment-naïve PCV patients. Complete polyp regression and the reduction rate of vascular lesion size and polyp size after loading injection significantly influence the treatment outcome of PCV patients. However, careful monitoring and preoperative warning is warranted due to occurrence of brolucizumab-related IOI.

Keywords: Polypoidal choroidal vasculopathy, Brolucizumab, Polyp regression, Intraocular inflammation
INTRODUCTION

Polypoidal choroidal vasculopathy (PCV), a subtype of neovascular age-related macular degeneration (nAMD), is characterized by polypoidal lesions arising from branching neovascular network (BNN) beneath retinal pigment epithelium (RPE) which are typically seen on indocyanine green angiography (ICGA).[1, 2] PCV has been reported to account for approximately 27-41.3% of patients with nAMD in Asian population[3, 4], with a prevalence of 24.6% to 36.3% in Korean nAMD patients.[5-7] Although PCV has a relatively favorable natural course and prognosis compared to typical nAMD, it can sometimes lead to massive subretinal hemorrhage, breakthrough vitreous hemorrhage and geographic retinal pigment epithelium atrophy, resulting in permanent and severe visual impairment.[1, 8]

Anti-VEGF (vascular endothelial growth factor) monotherapy or combination therapy with photodynamic therapy (PDT) has been a standard treatment of PCV. Various anti-VEGF agents are currently used in Korea, and these include Bevacizumab (Avastin®, Genetech, South San Francisco, CA, USA), Ranibizumab (Lucentis®, Genetech, South San Francisco, CA, USA), Aflibercept (Eylea®, Regeneron, Tarrytown, NY, USA), and Brolucizumab (Beovu®, Novartis, Basel, Switzerland). Brolucizumab, which was approved by the Food and Drug Administration (FDA) in October 2019, is a high-affinity monoclonal antibody that inhibits vascular endothelial growth factor-A (VEGF-A).[9] It has a relatively low molecular weight (26 kDa) compared to other anti-VEGF agents which allows higher molar concentration per injection and offers increased duration of action and effective tissue penetration.[10] HAWK and HARRIER, worldwide phase 3 clinical studies, have demonstrated the non-inferiority of brolucizumab to aflibercept in terms of improving visual outcomes and the superiority in terms of improving anatomical outcomes by reducing intraretinal fluid (IRF), subretinal fluid (SRF), and subretinal pigment epithelial fluid.[11, 12] However, brolucizumab injections can sometimes lead to intraocular inflammation (IOI) presenting in various forms including vitritis, retinal artery occlusion or occlusive retinal vasculitis, resulting in severe visual impairment.[13]

Various prognostic factors influencing treatment outcome in PCV patients have been reported. Among them are factors such as size and number of polyps, size of vascular lesion including BNN and complete polyp regression rate after loading injection of anti-VEGF.[14, 15] As far as we know, only one study analyzed the effect of polyp size reduction on treatment outcome in cases where there was incomplete regression of polyp after loading injections.[15] Also, most of the previous studies mainly focused on the efficacy of ranibizumab, aflibercept and PDT combined with anti-VEGF in polyp regression and its effect on treatment outcome, but not brolucizumab.[15-17]
In the present study, we aimed to evaluate one-year treatment outcome of brolucizumab in Korean treatment-naïve PCV patients and analyze complete polyp regression rate after loading phase. Also, we aimed to analyze the effect of complete polyp regression and the impact of vascular lesion size and polyp area reduction in one-year treatment outcome. Furthermore, we sought to report the incidence and clinical course of brolucizumab-related intraocular inflammation during one year follow-up.

MATERIALS AND METHODS

The study protocol adhered to the tenets of the Declaration of Helsinki. The study was approved by the Institutional Review Board of Soonchunhyang University Hospital (No. SCHBC 2023-04-018-001). We conducted a retrospective analysis of medical records from August 2021 to December 2023 for 31 consecutive treatment-naïve patients with PCV who received three monthly intravitreal brolucizumab injections followed by as-needed injections at Soonchunhyang University Hospital of Bucheon. Diagnosis of PCV was made in the confirmation of polypoidal lesion(s) with or without branching vascular network on ICGA using a confocal scanning laser ophthalmoscope. (Heidelberg Spectralis® [Spectralis], Heidelberg Engineering, Heidelberg, Germany). Exclusion criteria was as follows: (1) a history of intravitreal injections of anti-VEGF, (2) a history of intraocular surgery such as vitrectomy, and (3) the coexistence of any other ocular disease that can affect visual acuity or alter anatomical structure, such as epiretinal membrane or retinal vein occlusion (4) follow-up period less than one year.

All patients were initially treated with three monthly brolucizumab injection and additional injection was made in a pro-re-nata (PRN; as-needed) basis. After the loading injection, follow-up visits were scheduled every 1 or 2 months, according to physician’s decision. Additional injection was performed when persistent or new exudative changes, including SRF, IRF or subretinal hemorrhage was observed in OCT (optical coherence tomography). After each consecutive injection, all patients were followed up one week later to check for the occurrence of brolucizumab-related intraocular inflammation (IOI). If no IOI was confirmed, the next scheduled follow-up was performed. All patients were prescribed prophylactic steroid eye drop (1% prednisolone acetate [Predbell®, Chong Kun Dang, Seoul, Korea]) for one week to prevent brolucizumab-related IOI and was discontinued if IOI was not confirmed after one-week follow-up.

The best corrected visual acuity (BCVA) of the participants was measured at baseline and at 3-months, 6-months, 12-months visit after the first injection using the Snellen chart and then was converted to logarithm of the minimum
angle of resolution (logMAR) for the statistical analysis. By using swept-source optical coherence tomography (OCT) (DRI-OCT; Topcon Medical Systems, Inc., Oakland, NJ, USA), central macular thickness (CMT) and central choroidal thickness (CCT) were measured at at 3-month, 6-month, 12-month visit. CMT was defined as the vertical distance between the internal limiting membrane and the surface of the RPE at the fovea, while CCT was defined as the vertical distance between the Bruch’s membrane and the choroido-scleral junction at the fovea. CMT and CCT were measured automatically using the built-in software of DRI-OCT machine. Also, percentage of patients of dry-macula status (macula without any exudative changes including IRF and SRF) was measured at 3-month, 6-month and 12-month. In addition, we evaluated the incidence of intraocular inflammation (IOI) during one-year follow-up and analyzed its clinical course and treatment outcome.

ICGA was taken at baseline and at 3-month visit. Area of vascular lesion including BNN and total polyp area were measured before and after loading injection. Area was measured with built-in software of Heidelberg Spectralis®[Spectralis] machine. ‘Complete polyp regression’ was defined as the complete disappearance of hyperfluorescence associated with polypoidal lesions. Complete polyp regression rate was calculated at 3-month visit. In cases of incomplete polyp regression, with residual polyp remaining, we calculated the reduction ratio of polyp area. Additionally, the reduction ratio of vascular lesions, including BNN, was calculated for each patient. Then, we analyzed the effect of complete polyp regression and the impact of reduction in size of vascular lesion and polyp area on treatment outcome. Two graders (L.S.H and H.J.W) independently evaluated ICGA images before and after treatment and calculated complete polyp regression rate and reduction rate. Average of the two measurements by two graders was used in the statistical analysis.

For statistical analysis, Wilcoxon signed-rank test was used to compare BCVA, CMT, and CCT at baseline and other time points. Student’s t-test and Fisher’s exact test were used to compare treatment outcome between the group with complete polyp regression and the group without. Spearman correlation test was used to analyze the correlation between percentage change of polyp area and vascular lesion and treatment outcome. All statistical analyses were performed using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA). A $p$-value of $<0.05$ was considered statistically significant.

RESULTS

A total of 31 eyes of 31 patients were included in this study. Baseline demographics and characteristics are summarized in Table 1. In terms of visual outcome, BCVA (logMAR) significantly improved from baseline 0.62
1. In terms of anatomical outcome, mean CMT (µm) significantly decreased from baseline 336.92 ± 103.06 to 198.12 ± 30.88 (3-month, p<0.001), 208.85 ± 56.20 (6-month, p<0.001), 205.54 ± 56.80 (12-month, p<0.001). (Fig. 1)

2. Also, mean CCT (µm) significantly decreased from baseline 210.96 ± 63.21 to 143.50 ± 62.43 (3-month, p<0.001), 152.08 ± 66.99 (6-month, p<0.001), 148.96 ± 65.55 (12-month, p<0.001). (Fig. 2) Dry macula status was achieved in 80.6% (25/31) of the eyes at 3-month, 77.4% (24/31) at 6-month, and 74.2% (23/31) at 12-month.

Complete regression of polyp after three monthly injections of brolucizumab was observed in 74.2% (23/31).

Baseline characteristics and one-year treatment outcome of groups with complete polyp regression and without are listed in Table 2. No significant difference in age (p=0.595), baseline BCVA (p=0.496), lesion area (p=0.530), polyp area (p=0.196), CMT (p=0.846) and CCT (p=0.713) were found between two groups. However, eyes with complete polyp regression had higher rate of achieving dry macula at 3-month (p=0.026), and fewer numbers of injections during one-year follow-up (p<0.001).

In terms of correlation between reduction rate of polyp area and vascular lesion area with one-year treatment outcome, polyp reduction rate was significantly associated with CMT change from baseline at 3-month (p=0.048). Also, vascular lesion reduction rate was associated with CMT change from baseline at 12-month (p=0.031) and total number of injections at 12-month (p=0.012). (Table 3)

Brolucizumab-associated IOI was observed in one of the 31 eyes (3.2%). This 67-year old woman had a scheduled visit to our clinic presenting with visual disturbance in her left eye one week after the second injection. A trace amount of cells at anterior chamber and mild vitreous cells (Grade 2+) were noted. Fundus examination revealed vascular sheathing with ischemic retina at the inferotemporal region. Suspecting brolucizumab-related IOI, a subtenon betamethasone injection (4mg/1ml) was administered, along with oral methylprednisolone(30mg/d for 1 week, 15mg/d for 1 week and 5mg/d for 1 week). Subsequently, after three weeks of steroid administration, the vitritis with vasculitis subsided without any other complications, and one additional brolucizumab injection was given one month after the second injection. However, her BCVA did not improve from baseline after one-year follow-up.

DISCUSSION

In this study, we analyzed one-year visual and anatomical outcomes following three monthly injections of brolucizumab followed by as-needed (PRN) injections in treatment-naïve PCV patients. We also assessed how...
complete polyp regression after the initial loading injection of brolucizumab affected one-year treatment outcome, along with analyzing the impact of percentage change of polyp area and vascular lesion on treatment outcome of a year.

Regarding visual outcome, BCVA showed significant improvement at every time point during one-year follow-up. Previous studies reporting long-term effect of brolucizumab in PCV patients showed similar results. Ito et al.[18] reported BCVA (logMAR) improvement from 0.28 ± 0.05 at baseline to 0.13 ± 0.06 after one year, and similarly, Cho et al.[19] reported BCVA improvement from 0.46 ± 0.40 to 0.35 ± 0.28 after one-year. Although the mean BCVA of our study subjects was lower (0.62 ± 0.42 at baseline) than that of the aforementioned studies, a significant BCVA improvement (0.44 ± 0.38 at 12-month) was also achieved. In terms of anatomical outcome, both CMT and CCT significantly decreased at every time point, after one-year follow-up. Previous studies have demonstrated similar results in improving anatomical outcomes.[18-20] In the study by Ito et al.[18], the decrease in CMT (μm) at one-year compared to baseline was reported as 51.0%, from baseline 421 to 206. Additionally, Cho et al.[19] reported a CMT decrease of 41.3%, from 418 to 246. In our current study, the baseline CMT was 336.92, which was lower compared to the subjects in the study by Ito et al. and Cho et al. Nevertheless, a similar degree of CMT decrease (38.9%) at one-year was observed in our study.

PCV is thought to be a part of pachychoroid spectrum diseases which is characterized by thickened choroidal vessels and thin choriocapillaries. However, several studies have reported that PCV patients have varying degrees of choroid thickness, including thin choroid.[21, 22] These studies demonstrated that thicker choroid was associated with a less favorable anatomical outcome. In this present study, mean baseline choroidal thickness was 210.96 ± 63.21 μm which are similar to two studies that reported one-year outcome of brolucizumab in PCV patients (Mean baseline choroidal thickness (μm) of Ito et al.[18]; 226 ± 35, Cho et al.[19]; 227 ± 93). These studies including ours achieved excellent anatomical outcome following one-year treatment of brolucizumab injection. Meanwhile, in a study of Matsumoto et al.[23], participants with a relatively thicker choroid vessels (264 ± 89 μm) also showed excellent anatomical outcome, with 94.4 % of 42 eyes achieving dry macula status after three monthly injections of brolucizumab.

When treating PCV patients, one of the main goal is achieving complete regression of polypoidal lesions, since polypoidal lesions are associated with poor visual outcome and necessity of more anti-VEGF injections.[14, 24] Several studies have reported various polyp regression rate of other anti-VEGF following three monthly loading injections. Polyp regression rate was noted to be around 30% with ranibizumab and approximately 50% with aflibercept after loading injection.[24-26] Also, PDT combined with anti-VEGF injection has been reported to
achieve complete regression of polypoidal lesions in 70–90% of patients after loading injection.[27, 28] In terms of brolucizumab, several studies have reported higher polyp regression rate than other anti-VEGF agents after loading phase and one-year after initial injection; polyp regression was observed in 78.6–82.0% of patients after loading injection of brolucizumab.[29, 30] Additionally, regression rate ranged from 73.9% to 93.1% one year after the initial administration of brolucizumab.[18, 31] In this present study, complete regression rate after loading phase with intravitreal brolucizumab was 74.2%, notably surpassing the outcomes of ranibizumab or aflibercept monotherapy, yet aligning closely with the regression rate observed after combining PDT with anti-VEGF injection. The complete polyp regression rate (74.2%) reported in this study is slightly lower, but similar to that of other studies which reported complete polyp regression rate after loading injection of brolucizumab in PCV patients. Matsumoto et al.[23] reported polyp regression rate of 78.9%, while Fukuda et al.[30] and Tanaka et al.[29] reported 78.6% and 82% respectively. It is speculated that the higher polyp regression rate of brolucizumab compared to other anti-VEGF agents may be attributed to its smaller molecular size, allowing for greater drug penetration into the sub-RPE space at higher concentration.[10]

Complete polyp regression has been reported to be associated with fewer number of anti-VEGF injections and lower recurrence rate.[31, 32] In a study of Morizane-Hosokawa et al., which analyzed the treatment outcome of PCV patients receiving T&E (treat-and-extend) regimen of aflibercept, it was found that patients with complete polyp regression after the loading injection required fewer injections and recurred less frequently during 2-year period.[32] Meanwhile in a study of Matsumoto et al. which analyzed the efficacy of brolucizumab, groups with complete polyp regression had fewer number of injections and longer treatment interval following one-year T&E injection of brolucizumab.[31] In our study, groups with complete polyp regression had higher rate of achieving dry macula at 3-month and fewer number of injections, thereby reducing the treatment burden of PCV patients.

In our study, we analyzed the impact of percentage change of vascular lesion including BNN and polyp area after loading injection in one-year treatment outcome. By far, only one study by Sayanagi et al. reported the effect of the percentage change of polyp reduction, in cases where incomplete polyp regression was found after loading injection in treatment outcome.[15] Sayanagi et al. reported that the degree of polyp reduction was associated with BCVA at 3-month but not with BCVA at 12-month, CMT at 3 and 12-month, total number of injections and dry macula status at 3 and 12-month. In our study, polyp reduction rate was associated with CMT change from baseline at 3-month but not with BCVA change at 3 and 12-month, dry macula status at 3 and 12-month and total number of injections. Based on the previous report by Sayanagi et al. and our study, it can be inferred that the degree of polyp reduction does not seem to have a significant impact on the long-term visual and anatomical outcome. In
terms of vascular lesion size, studies have been published regarding the impact of baseline vascular lesion size on treatment outcome. According to study reported by Tsujikawa et al.[33], PCV with smaller vascular lesion at baseline exhibit minimal progression and fewer vision-threatening complications, thereby maintaining good visual acuity for a longer duration compared to cases with larger vascular lesion. However, there have been no studies published on the impact of the percentage change in vascular lesion size after loading injection on treatment outcome. In our study, the degree of vascular lesion size reduction was associated with CMT change from baseline at 12-month and fewer number of treatment. Since our study is a single-center, retrospective study with a limited number of subjects, further research involving a larger number of patients is needed to determine whether the vascular lesion reduction rate can become a useful biomarker predicting treatment prognosis of PCV patients.

Despite the excellent efficacy of brolucizumab, caution is warranted during its injection due to the occurrence of IOI in a considerable number of patients. According to Bahram et al.[13], the incidence of IOI-related adverse events has been reported up to 10.5% (of 505 anti-VEGF naive and pretreated patients with nAMD), with 3.4% presenting IOI with retinal involvement. In our study, IOI occurred in 3.2% of patients (1 of 32 eyes) and the patient presented with vitritis and retinal vasculitis. This incidence rate of 3.2% is comparable to the previously reported incidence rate of IOI with retinal involvement by Bahram et al.[13], which was 3.4%. In our study, we scheduled close follow-up visits and administered prophylactic topical steroids to promptly detect and prevent brolucizumab-associated IOI. Despite these measures, IOI still occurred, and there was no improvement in BCVA although inflammation fully resolved after steroid treatment.

Our study has several limitations, including its retrospective nature, single-center design, and a small number of study participants. Additionally, our study focused solely on the single anti-VEGF agent, brolucizumab, in the treatment outcome of PCV patients. Further studies comparing brolucizumab with other anti-VEGF agents may need to be conducted.

In conclusion, intravitreal brolucizumab effectively improved visual and anatomical outcomes and achieved significant polyp regression in treatment-naïve PCV patients. Complete polyp regression and the reduction rate of vascular lesion size and polyp size after loading injection significantly influence the treatment outcome of PCV patients. However, careful monitoring and preoperative warning is warranted due to occurrence of brolucizumab-related IOI.

The authors have no financial or proprietary interests in any material discussed in this article.
REFERENCES


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Fig. 1. Best corrected visual acuity (BCVA) changes following 12 months of as-needed injection of brolucizumab injection in treatment-naïve PCV (polypoidal choroidal vasculopathy) patients (n=31). Significant improvement of BCVA compared to baseline was achieved at all time points. * Statistically significant improvement from baseline (*p<0.05)

Fig. 2. Changes of central macular thickness (CMT) and central choroidal thickness (CCT) following 12 months of as-needed injection of brolucizumab injection in treatment-naïve PCV (polypoidal choroidal vasculopathy) patients (n=31). (A) Central macular thickness (CMT) change (B) Central choroidal thickness (CCT) change. At all time points, significant decrease from baseline was found. (*p<0.05)
Table 1. Baseline demographics and characteristics of patients (n=31)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>70.50 ± 6.22</td>
</tr>
<tr>
<td>Sex (Male : Female)</td>
<td>19 : 12</td>
</tr>
<tr>
<td>BCVA (logMAR)</td>
<td>0.62 ± 0.42</td>
</tr>
<tr>
<td>CMT (μm)</td>
<td>336.92 ± 103.06</td>
</tr>
<tr>
<td>CCT (μm)</td>
<td>210.96 ± 63.21</td>
</tr>
<tr>
<td>Vascular lesion size (mm²)</td>
<td>3.18 ± 1.98</td>
</tr>
<tr>
<td>Polyp size (mm²)</td>
<td>0.32 ± 0.14</td>
</tr>
</tbody>
</table>

Values represented as mean ± standard deviation

BCVA = best-corrected visual acuity, logMAR = logarithm of minimal angle of resolution, CMT = central macular thickness, CCT = central choroidal thickness
Table 2. Baseline characteristics and one-year treatment outcome of groups with complete polyp regression (n=23) and without (n=8)

<table>
<thead>
<tr>
<th></th>
<th>Complete polyp regression (+) (N= 23)</th>
<th>Complete polyp regression (-) (N = 8)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>70.06</td>
<td>71.50</td>
<td>0.595*</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>14/9</td>
<td>5/3</td>
<td>1.000†</td>
</tr>
<tr>
<td>Baseline BCVA (logMAR)</td>
<td>0.58 ± 0.40</td>
<td>0.70 ± 0.46</td>
<td>0.496*</td>
</tr>
<tr>
<td>BCVA at 3-month (logMAR)</td>
<td>0.44 ± 0.40</td>
<td>0.49 ± 0.31</td>
<td>0.760*</td>
</tr>
<tr>
<td>BCVA at 12-month (logMAR)</td>
<td>0.40 ± 0.39</td>
<td>0.53 ± 0.37</td>
<td>0.426*</td>
</tr>
<tr>
<td>Baseline lesion area (mm²)</td>
<td>3.01 ± 1.98</td>
<td>3.55 ± 2.05</td>
<td>0.530*</td>
</tr>
<tr>
<td>Lesion area at 3-month (mm²)</td>
<td>1.97 ± 1.49</td>
<td>2.64 ± 1.90</td>
<td>0.341*</td>
</tr>
<tr>
<td>Baseline polyp area (mm²)</td>
<td>0.29 ± 0.09</td>
<td>0.39 ± 0.19</td>
<td>0.196*</td>
</tr>
<tr>
<td>Polyp area at 3-month (mm²)</td>
<td>0.16 ± 0.09</td>
<td>0.00</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Baseline CMT (μm)</td>
<td>334 ± 105</td>
<td>343 ± 106</td>
<td>0.846*</td>
</tr>
<tr>
<td>CMT at 3-month (μm)</td>
<td>192 ± 26</td>
<td>212 ± 37</td>
<td>0.115*</td>
</tr>
<tr>
<td>CMT at 12-month (μm)</td>
<td>197 ± 30</td>
<td>224 ± 93</td>
<td>0.278*</td>
</tr>
<tr>
<td>Baseline CCT (μm)</td>
<td>208 ± 68</td>
<td>218 ± 53</td>
<td>0.713*</td>
</tr>
<tr>
<td>CCT at 3-month (μm)</td>
<td>136 ± 60</td>
<td>160 ± 68</td>
<td>0.383*</td>
</tr>
<tr>
<td>CCT at 12-month (μm)</td>
<td>146 ± 69</td>
<td>156 ± 61</td>
<td>0.704*</td>
</tr>
<tr>
<td>Dry macula status at 3-month (n, %)</td>
<td>21/23 (86.9%)</td>
<td>4/8 (50%)</td>
<td>0.026†</td>
</tr>
<tr>
<td>Dry macula status at 12-month (n, %)</td>
<td>20/23 (82.6%)</td>
<td>3/8 (37.5%)</td>
<td>0.161†</td>
</tr>
<tr>
<td>Total number of injections (n)</td>
<td>3.50 ± 0.70</td>
<td>5.25 ± 1.16</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

Values are represented as mean ± standard deviation or numbers (percentage)

*Student's t-test, †Fisher’s exact test

BCVA = best-corrected visual acuity, logMAR = logarithm of minimal angle of resolution, CMT = central macular thickness, CCT = central choroidal thickness
Table 3. Correlation between percentage change of polyp area and vascular lesion with one-year treatment outcome

<table>
<thead>
<tr>
<th></th>
<th>Polyp reduction (%)</th>
<th>Vascular lesion reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation coefficient</td>
<td>p-value$^*$</td>
</tr>
<tr>
<td>BCVA change from baseline at 3-month</td>
<td>-0.120</td>
<td>0.778</td>
</tr>
<tr>
<td>BCVA change from baseline at 12-month</td>
<td>0.275</td>
<td>0.509</td>
</tr>
<tr>
<td>CMT change from baseline at 3-month</td>
<td>-0.690</td>
<td>0.048†</td>
</tr>
<tr>
<td>CMT change from baseline at 12-month</td>
<td>-0.167</td>
<td>0.693</td>
</tr>
<tr>
<td>CCT change from baseline at 3-month</td>
<td>0.078</td>
<td>0.704</td>
</tr>
<tr>
<td>CCT change from baseline at 12-month</td>
<td>-0.065</td>
<td>0.752</td>
</tr>
<tr>
<td>Dry macula status at 3-month</td>
<td>0.655</td>
<td>0.078</td>
</tr>
<tr>
<td>Dry macula status at 12-month</td>
<td>0.169</td>
<td>0.689</td>
</tr>
<tr>
<td>Total number of injections (n)</td>
<td>-0.082</td>
<td>0.847</td>
</tr>
</tbody>
</table>

$^*$Statistical analysis with Spearman correlation, †$p<0.05$

BCVA = best-corrected visual acuity, logMAR = logarithm of minimal angle of resolution, CMT = central macular thickness, CCT = central choroidal thickness